Enantioselective Henry Reaction Catalyzed by $C_2$-Symmetric Chiral Diamine-Copper (II) Complex

Sermadurai Selvakumar, Dhanasekaran Sivasankaran, and Vinod K. Singh*

Department of Chemistry, Indian Institute of Technology, Kanpur
India–208 016. Fax: +91-512-2597436

vinodks@iitk.ac.in

Electronic Supporting Information

General Methods 2

Procedures and characterization data for important compounds 2-25

1a, 2a-b, 3a-b, 4a-b, 5a-b, 6a-g, 7a-g, 8a-g, 9a-g, 10a-r, 11a-f, 12, 13

$^1$H and $^{13}$C NMR Spectra for 2a-b, 3a-b, 4a-b, 5a-b, 6a-g, 26-51

7a-g, 8a-g, 9a-g, 12, 13

$^1$H NMR Spectra for 11a-f and HPLC Spectra for 10-r, 11a-f, 13 52-88

References 88-89
Experimental Section

General Methods. $^1$H and $^{13}$C NMR spectra were recorded on JEOL JNM-LA 400 and Jeol ECX 500 spectrometer. Chemical shifts are expressed in ppm downfield from TMS as internal standard, and coupling constants are reported in Hz. Mass spectrometric analyses were done on Waters Q Tof Premier Micromass (ESI) spectrometer. Routine monitoring of reactions were performed by TLC, using 0.2 mm Kieselgel 60 F$^{254}$ precoated aluminium sheets, commercially available from Merck. Visualization was done by fluorescence quenching at 254 nm, exposure to iodine vapor, and/or 2,4-dinitrophenylhydrazine solution. All the column chromatographic separations were done by using silica gel (Acme’s, 60-120 mesh). HPLC was done on a Daicel chiral column having 0.46 cm internal diameter × 25 cm length. Petroleum ether used was of boiling range 60-80 °C. Reactions that needed anhydrous conditions were run under the atmosphere of nitrogen or argon using flame-dried glassware. The organic extracts were dried over anhydrous sodium sulfate. Evaporation of solvents was performed at reduced pressure. CH$_2$Cl$_2$, CHCl$_3$ and triethylamine (Et$_3$N) were distilled from CaH$_2$.

$(5aS,10aS)$-decahydodipyrrolo[1,2-a:1',2'-d]pyrazine (1a).$^1$

This compound was synthesized according to literature known procedure. Yield: 79%; White solid; mp 48 °C; $[\alpha]_D^{25} +7.8$ (c 2.6, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 2961; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.61-1.73 (m, 3H), 1.90 (m, 1H), 2.52 (m, 2H), 2.66 (m, 2H), 2.90 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.9, 26.8, 53.2, 54.5, 61.3; HRMS (ES+) calc. for C$_{10}$H$_{18}$N$_2$ 167.1548, [M+H]$^+$ found 167.1543.

General procedure for the coupling of N-Boc acid with amino esters.
A solution of (S)-N-Boc amino acid (10 mmol) and N-methylmorpholine (12 mmol) in CH₂Cl₂ (30 mL) was treated with ethyl chloroformate (12 mmol) at 0 °C for 10 min. Amino ester (12 mmol) was then added dropwise at the same temperature and the mixture was stirred for 16 h (0 °C to rt). After completion of the reaction (monitored by TLC), the reaction mixture was diluted with CH₂Cl₂ (20 mL) and washed with water and brine. The organic layer was dried, and the solvent was evaporated in vacuo. Purification by column chromatography over silica gel gave pure coupled product 2 or 6.

(S)-methyl 2-((S)-2-(tert-butoxycarbonylamino)-3-phenylpropanaamido)-3-phenylpropanate (2a).²

Yield: 87%; White solid; mp 114-116 °C; [α]D²⁵ +3.2 (c 0.5, DMSO); TLC Rf 0.80 (40%, EtOAc/Pet ether); IR νmax/cm⁻¹ (pellet) 3330, 3062, 1745, 1689, 1665; ¹H NMR (400 MHz, CDCl₃): δ 1.43 (s, 9H), 3.04 (m, 4H), 3.66 (s, 3H), 4.31 (m, 1H), 4.78 (d, J = 6.4 Hz, 1H), 6.25 (d, J = 6.8 Hz, 1H), 6.98 (m, 2H), 7.17-7.30 (m, 8H); ¹³C NMR (125 MHz, CDCl₃): δ 28.3, 38, 38.3, 52.4, 53.3, 55.7, 80.3, 127, 127.2, 128.6, 128.8, 129.3, 129.5, 135.7, 136.5, 155.3, 170.8, 171.7.

(R)-methyl 2-((S)-2-(tert-butoxycarbonylamino)-3-methylbutanamido)-2-phenylacetate (2b).

Yield: 70%; White solid; mp 104 °C; [α]D²⁵ –131.0 (c 1.0, CHCl₃); TLC Rf 0.80 (40%, EtOAc/Pet ether); IR νmax/cm⁻¹ (pellet) 3326, 2968, 1741, 1689, 1656; ¹H NMR (400 MHz, CDCl₃): δ 0.90 (dd, J = 6.8, 17.6 Hz, 6H), 1.45 (s, 9H), 2.17 (m, 1H), 3.72 (s, 3H), 4.0 (m, 1H), 5.64 (d, J = 6.6 Hz, 1H), 6.93 (d, J = 6.1 Hz, 1H), 7.31-7.35 (m, 5H); ¹³C NMR (125 MHz, CDCl₃): δ 17.5, 19.4, 28.4, 30.9, 52.9, 56.5, 59.8, 80.2, 127.2, 127.3,
128.7, 129.1, 136.3, 156.0, 171.0, 171.2; Anal. Calcd. for C_{19}H_{28}N_{2}O_{5}: C, 62.62; H, 7.74; N, 7.69. Found: C, 62.75; H, 7.72; N, 7.71.

(S)-methyl1-((S)-2-(tert-butoxycarbonylamino)-4-methylpentanoyl)pyrrolidine-2-carboxylate (6a).

Yield: 80%; Yellow liquid; [α]_{D}^{25} –7.8 (c 1.0, CHCl_{3}); TLC R_{f} 0.60 (40%, EtOAc/Pet ether); IR ν_{max}/cm^{-1} (film) 3313, 2956, 1748, 1709, 1650; ^{1}H NMR (500 MHz, CDCl_{3}): δ 0.96 (m, 6H), 1.27 (m, 1H), 1.45 (s, 9H), 1.96 (m, 1H), 2.04 (m, 3H), 2.22 (m, 1H), 3.6 (m, 1H), 3.72 (s, 3H), 3.77 (m, 1H), 4.52 (m, 2H), 5.12 (d, J = 9 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_{3}): δ 21.8, 23.4, 24.5, 24.9, 28.3, 28.9, 41.9, 46.7, 50.2, 52.2, 58.6, 79.5, 155.7, 171.9, 172.5; Anal. Calcd. for C_{17}H_{30}N_{2}O_{5}: C, 59.63; H, 8.83; N, 8.18. Found: C, 59.79; H, 8.85; N, 8.20.

(S)-methyl 1-((S)-2-(tert-butoxycarbonylamino)propanoyl)pyrrolidine-2-carboxylate (6b).

Yield: 69%; Colorless liquid; [α]_{D}^{25} –77.3 (c 1.0, CHCl_{3}); TLC R_{f} 0.50 (30%, EtOAc/Pet ether); IR ν_{max}/cm^{-1} (pellet) 3320, 2978, 1746, 1710, 1650; ^{1}H NMR (500 MHz, CDCl_{3}): δ 1.34 (d, J = 6.9 Hz, 3H), 1.42 (s, 9H), 1.98-2.05 (m, 3H), 2.22 (m, 1H), 3.61 (m, 1H), 3.7 (m, 1H), 3.72 (s, 3H), 4.47 (m, 1H), 4.53 (m, 1H), 5.34 (m, 1H); ^{13}C NMR (125 MHz, CDCl_{3}): δ 18.4, 25.0, 28.4, 29.0, 46.8, 47.8, 52.3, 58.8, 79.7, 155.3, 171.8, 172.5; Anal. Calcd. for C_{14}H_{24}N_{2}O_{5}: C, 55.98; H, 8.05; N, 9.33. Found: C, 55.78; H, 8.03; N, 9.30.

(S)-methyl1-((S)-2-(tert-butoxycarbonylamino)-3-methylbutanoyl)pyrrolidine-2-carboxylate (6c)^{3}

This compound was prepared as per our general procedure, isobutyl chloroformate was used in place of ethyl chloroformate. Yield: 34%; Yellow liquid; [α]_{D}^{25} –57.8 (c 1.0,
CHCl₃); TLC $R_f$ 0.60 (30%, EtOAc/Pet ether); IR $\nu_{\text{max}}$/cm⁻¹ (film) 3315, 2972, 1748, 1708, 1709, 1646; $^1$H NMR (500 MHz, CDCl₃): δ 0.91-1.06 (m, 6H), 1.26 (m, 1H), 1.45 (s, 9H), 1.98 (m, 3H), 2.22 (m, 1H), 3.67 (m, 1H), 3.72 (s, 3H), 3.78 (m, 1H), 4.28 (m, 1H), 4.53 (m, 1H), 5.25 (m, 1H); $^{13}$C NMR (125 MHz, CDCl₃): δ 17.4, 19.2, 25.0, 28.3, 29.0, 31.3, 47.1, 52.2, 56.8, 79.5, 155.9, 171.2, 172.5.

(S)-methyl-1-((2S,3S)-2-(tert-butoxycarbonylamino)-3-methylpentanoyl)pyrrolidine-2-carboxylate (6d).

This was prepared as per our general procedure, isobutyl chloroformate was used in place of ethyl chloroformate. Yield: 35%; Viscous liquid; $[\alpha]_{D}^{25}$ −50.5 (c 1.0, CHCl₃); TLC $R_f$ 0.80 (40%, EtOAc/Pet ether); IR $\nu_{\text{max}}$/cm⁻¹ (film) 3322, 2967, 1748, 1708, 1643; $^1$H NMR (500 MHz, CDCl₃): δ 0.89 (m, 3H), 1.12 (m, 3H), 1.14 (m, 1H), 1.59 (s, 9H), 1.6-1.98 (m, 2H), 2.01 (m, 3H), 2.24 (m, 1H), 3.66 (m, 1H), 3.72 (s, 3H), 3.83 (m, 1H), 4.29 (m, 1H), 4.53 (m, 1H), 5.19 (m, 1H); $^{13}$C NMR (125 MHz, CDCl₃): δ 11.2, 15.2, 24.1, 24.9, 28.3, 29.0, 37.8, 47.2, 52.1, 56.2, 58.8, 79.5, 155.8, 171.5, 172.4.

(S)-methyl-1-((S)-2-(tert-butoxycarbonylamino)-2-phenylacetyl)pyrrolidine-2-carboxylate (6e).

Yield: 92%; Colorless liquid; $[\alpha]_{D}^{25}$ +18.2 (c 0.32, CHCl₃); TLC $R_f$ 0.50 (40%, EtOAc/Pet ether); IR $\nu_{\text{max}}$/cm⁻¹ (film) 3331, 2924, 1746, 1708, 1652; $^1$H NMR (400 MHz, CDCl₃): δ 0.86 (m, 1H), 1.25 (m, 1H), 1.41 (m, 10H), 1.90 (m, 1H), 3.14 (m, 1H), 3.72 (m, 4H), 4.56 (m, 1H), 5.45 (d, $J = 8.3$ Hz, 1H), 5.81 (d, $J = 7.6$ Hz, 1H), 7.37 (m, 5H); $^{13}$C NMR (125 MHz, CDCl₃): δ 24.8, 28.3, 28.9, 46.6, 52.1, 56.4, 59.1, 79.8, 128.2, 128.3, 128.8, 136.9, 155.2, 168.8, 171.15; Anal. Calcd. for C₁₉H₂₆N₂O₅: C, 62.97; H, 7.23; N, 7.73. Found: C, 63.20; H, 7.25; N, 7.76.
(S)-methyl 1-((S)-2-(tert-butoxycarbonylamino)-3-phenylpropanoyl)pyrrolidine-2-carboxylate (6f).

Yield: 85%; Colorless liquid; $[\alpha]_D^{25} -20.5 \ (c \ 1.2, \ CHCl_3)$; TLC $R_f 0.50 \ (40\%, \ EtOAc/Pet ether)$; IR $\nu_{\text{max}}/\text{cm}^{-1} \ (\text{film}) \ 3313, 3028, 1746, 1711, 1647$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta 0.85 \ (m, 1H), 1.32-1.46 \ (m, 10H), 1.90-2.15 \ (m, 2H), 2.89 \ (m, 1H), 3.04-3.16 \ (m, 2H), 3.57 \ (m, 1H), 3.72 \ (m, 4H), 4.47 \ (m, 1H), 4.61 \ (m, 1H), 5.25 \ (d, J = 9 Hz, 1H), 7.20-7.29 \ (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta 24.8, 28.2, 29.0, 46.8, 52.2, 52.7, 58.9, 79.6, 126.7, 128.3, 128.5, 129.7, 136.3, 156.0, 170.6, 172.3$.

(S)-methyl 1-((R)-2-(tert-butoxycarbonylamino)-2-phenylacetyl)pyrrolidine-2-carboxylate (6g).

Yield: 72%; White solid; mp 112 °C; $[\alpha]_D^{25} -113.8 \ (c \ 1.0, \ CHCl_3)$; TLC $R_f 0.50 \ (40\%, \ EtOAc/Pet ether)$; IR $\nu_{\text{max}}/\text{cm}^{-1} \ (\text{pellet}) \ 3418, 2981, 1752, 1708, 1641$; $^1$H NMR (500 MHz, CDCl$_3$): $\delta 0.85 \ (m, 1H), 1.39 \ (m, 10H), 1.78 \ (m, 1H), 1.92 \ (m, 1H), 3.13 \ (m, 1H), 3.71 \ (m, 4H), 4.41 \ (m, 1H), 5.41 \ (d, J = 7.5 Hz, 1H), 6.09 \ (d, J = 7.5 Hz, 1H), 7.25-7.43 \ (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta 24.8, 28.3, 29.0, 46.7, 52.3, 52.7, 56.6, 59.1, 59.2, 79.6, 127.9, 128.2, 128.9, 137.6, 154.8, 168.8, 172.3$; Anal. Calcd. for C$_{19}$H$_{26}$N$_2$O$_5$: C, 62.97; H, 7.23; N, 7.73. Found: C, 63.17; H, 7.26; N, 7.70.

General procedure for the synthesis of diketopiperazide.

A solution of amide 2 or 6 (2.0 mmol) in dry CH$_2$Cl$_2$ (6 mL) was treated with TFA (800 µL) at rt for 3 h. Solvent was then evaporated and the reaction mixture was dissolved in 2-butanol:toluene (4:2 mL) followed by addition of triethylamine (2 mmol). The mixture was allowed to reflux for 16 h. After the evaporation of solvent, diketopiperazide 3 or 7...
precipitated as a white solid, which was filtered off, washed with MeOH, and used for next step without further purification.

(3S,6S)-3,6-dibenzylpiperazine-2,5-dione (3a).²

Yield: 82%; White solid; mp 292 ºC; IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3313, 3086, 1660; $^1$H NMR (500 MHz, DMSO-d$_6$): δ 2.18 (m, 2H), 2.53 (m, 2H), 3.92 (m, 2H), 6.98-7.26 (m, 10H), 7.9 (bs, 2H); HRMS (ES+) calc. for C$_{18}$H$_{18}$N$_2$O$_2$ 295.1447, [M+H]$^+$ found 295.1448.

(3S,6R)-3-isopropyl-6-phenylpiperazine-2,5-dione (3b).

Yield: 43%; White solid; $[\alpha]_D^{25}$ –56.4 (c 0.5, DMSO); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3188, 3047, 1667; $^1$H NMR (500 MHz, DMSO-d$_6$): δ 0.9 (d, $J$ = 7 Hz, 3H), 0.98 (d, $J$ = 7 Hz, 3H), 2.26 (m, 1H), 3.8 (m, 1H), 4.91 (s, 1H), 7.3-7.38 (m, 5H); HRMS (ES+) calc. for C$_{13}$H$_{16}$N$_2$O$_2$ 233.1291, [M+H]$^+$ found 233.1290.

(3S,8aS)-3-isobutylhexahydropyrrolo[1,2-a]pyrazine-1,4-dione (7a).

Yield: 75%; White solid; mp 164ºC; $[\alpha]_D^{25}$ –137.2 (c 0.5, DMSO); TLC $R_f$ 0.50 (5%, MeOH/Dichloromethane); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3429, 2993, 1670, 1634; $^1$H NMR (400 MHz, CDCl$_3$): δ 0.99 (m, 6H), 1.54 (m, 1H), 1.78-2.15 (m, 5H), 2.35 (m, 1H), 3.57 (m, 2H), 4.02 (m, 1H), 4.12 (m, 1H), 6.30 (bs, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 21.3, 22.8, 23.3, 24.7, 28.1, 38.6, 45.5, 53.4, 59, 166.3, 170.3; HRMS (ES+) calc. for C$_{11}$H$_{18}$N$_2$O$_2$ 211.1446, [M+H]$^+$ found 211.1445.

(3S,8aS)-3-methylhexahydropyrrolo[1,2-a]pyrazine-1,4-dione (7b).

Yield: 65%; White solid; mp 168 ºC; $[\alpha]_D^{25}$ –95.8 (c 0.5, DMSO); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3289, 2948, 1675; $^1$H NMR (500 MHz, DMSO-d$_6$): δ 1.20 (d, $J$ = 6.8 Hz, 3H), 1.81 (m, 3H), 2.1 (m, 1H), 3.34 (m, 2H), 4.08 (m, 1H), 4.17 (m, 1H), 8.14 (bs, 1H); $^{13}$C NMR (125
for C₈H₁₂N₂O₂ 169.0978, [M+H]⁺ found 169.0973.

(3S,8aS)-3-isopropylhexahydropyrrolo[1, 2-α]pyrazine-1, 4-dione (7c).
Yield: 86%; White solid; mp 180 °C; [α]D²⁵ –184.6 (c 0.5, DMSO); IR νmax/cm⁻¹ (pellet) 3211, 2962, 1675; ¹H NMR (500 MHz, DMSO-d₆): δ 0.83 (d, J = 6.9 Hz, 3H), 1.0 (d, J = 7.4 Hz, 3H), 1.76-1.86 (m, 3H), 2.12 (m, 1H), 2.32 (m, 1H), 3.3 (m, 2H), 3.9 (m, 1H), 4.1 (m, 1H), 7.96 (bs, 1H); ¹³C NMR (125 MHz, DMSO-d₆): δ 21.6, 23.6, 27.3, 32.9, 49.9, 60.2, 63.5, 64.7, 170.5, 175.6; HRMS (ES+) calc. for C₁₀H₁₆N₂O₂ 197.1291, [M+H]⁺ found 197.1290.

(3S, 8aS)-3-sec-butylhexahydropyrrolo[1, 2-a]pyrazine-1, 4-dione (7d).
Yield: 61%; White solid; mp 136 °C; [α]D²⁵ –107.2 (c 0.5, DMSO); IR νmax/cm⁻¹ (pellet) 3221, 2963, 1671; ¹H NMR (500 MHz, DMSO-d₆): δ 0.79 (t, J = 7.4 Hz, 3H), 0.93 (d, J = 7.2 Hz, 3H), 1.2-1.32 (m, 2H), 1.73-1.83 (m, 3H), 1.98-2.1 (m, 2H), 2.47 (m, 1H), 3.36 (m, 1H), 3.9 (m, 1H), 4.08 (m, 1H), 7.9 (bs, 1H); ¹³C NMR (125 MHz, DMSO-d₆): δ 12.9, 15.5, 22.5, 24.4, 28.5, 35.3, 42.5, 58.7, 59.8, 164.8, 170.6; HRMS (ES+) calc. for C₁₁H₁₈N₂O₂ 211.1447, [M+H]⁺ found 211.1446.

(3S,8aS)-3-phenylhexahydropyrrolo[1, 2-a]pyrazine-1, 4-dione (7e).
Yield: 37%; White solid; mp 182 °C; [α]D²⁵ –71.0 (c 0.5, DMSO); IR νmax/cm⁻¹ (pellet) 3401, 3264, 2949, 1670; ¹H NMR (500 MHz, DMSO-d₆): δ 1.86 (m, 3H), 2.16 (m, 1H), 3.30 (m, 1H), 3.42 (m, 1H), 4.23 (t, J = 8 Hz, 1H), 5.14 (s, 1H), 7.21 (m, 2H), 7.31 (m, 3H), 8.37 (s, 1H); ¹³C NMR (125 MHz, DMSO-d₆): δ 22.6, 28.6, 45.5, 59.2, 60.3, 128.4, 128.6, 129.4, 137.4, 165.2, 169.9; HRMS (ES+) calc. for C₁₃H₁₄N₂O₂ 231.1134, [M+H]⁺ found 231.1134.
(3S,8aS)-3-benzylhexahydropyrrolo[1,2-a]pyrazine-1,4-dione (7f).\(^5\)

Yield: 65%; White solid; mp 126 °C; [α]$_D^{25}$ –121.2 (c 0.5, DMSO); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3266, 3034, 1691, 1660; $^1$H NMR (500 MHz, CDCl$_3$): δ 1.85-2.04 (m, 3H), 2.33 (m, 1H), 2.76 (dd, $J = 10.5$, 14 Hz, 1H), 3.53-3.66 (m, 3H), 4.06 (t, $J = 7.5$ Hz, 1H), 4.27 (dd, $J = 3.5$, 11 Hz, 1H), 5.63 (bs, 1H), 7.20-7.35 (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 22.5, 28.3, 36.7, 45.4, 56.1, 59.1, 127.5, 129.0, 129.2, 135.9, 165.0, 169.3; HRMS (ES+) calc. for C$_{14}$H$_{16}$N$_2$O$_2$ 245.1291, [M+H]$^+$ found 245.1291.

(3R,8aS)-3-phenylhexahydropyrrolo[1,2-a]pyrazine-1,4-dione (7g).

Yield: 71%; White solid; mp 164 °C; [α]$_D^{25}$ –62.0 (c 0.5, DMSO); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3263, 3029, 1657; $^1$H NMR (500 MHz, CDCl$_3$): δ 1.81 (m, 1H), 1.98 (m, 2H), 2.30 (m, 1H), 3.45 (m, 1H), 3.54 (m, 1H), 4 (m, 1H), 5.12 (d, $J = 4$ Hz, 1H), 7 (bs, 1H), 7.29-7.45 (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 22.4, 28.8, 45.9, 57.9, 60.9, 125.5, 128.6, 129.0, 129.2, 135.8, 164.5, 170.6; HRMS (ES+) calc. for C$_{14}$H$_{16}$N$_2$O$_2$ 231.1134, [M+H]$^+$ found 231.1134.

**General procedure for the synthesis of diketopiperazine**

To a solution of amide (2 mmol) 3 or 7 in dry THF (8 mL) was added LAH (10 mmol) in portions at 0 °C and stirred for 10 min. The reaction mixture was warmed slowly to room temperature and refluxed for 6-24 h. Reaction mixture was then cooled slowly to 0 °C and excess of LAH was destroyed by the addition of few drops of EtOAc. Water (200 µL) was added, followed by the same amount of 4N NaOH. After 5 min, 600 µL of water was again added and the mixture stirred for 15 min. The white precipitate formed was filtered off, the filtrate was dried, and solvent was evaporated. The crude product was purified by column chromatography using neutral alumina.
(2S,5S)-2,5-dibenzylpiperazine (4a).\textsuperscript{6}

Yield: 35%; Viscous liquid; [α]D\textsuperscript{25} +38.2 (c 1.0, CHCl\textsubscript{3}); IR \ ν\textsubscript{max}/cm\textsuperscript{-1} (pellet) 3226, 3024, 2923; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): δ 2.31 (bs, 1H), 2.80-2.95 (m, 4H), 3.05 (m, 1H), 7.21-7.33 (m, 5H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): δ 38.4, 47.6, 55.4, 126.4, 128.7, 129.3, 139.0; HRMS (ES+) calc. for C\textsubscript{18}H\textsubscript{22}N\textsubscript{2} 267.1861, [M+H]\textsuperscript{+} found 267.1861.

(2S,5R)-2-isopropyl-5-phenylpiperazine (4b).

Yield: 55%; Yellow solid; mp 126 °C; TLC R\textsubscript{f} 0.30 (Neat MeOH); [α]D\textsuperscript{25} –48.6 (c 0.5, DMSO); IR \ ν\textsubscript{max}/cm\textsuperscript{-1} (pellet) 3280, 3029, 2821; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 0.99 (m, 6H), 1.9 (m, 1H), 2.86 (m, 3H), 3.27 (m, 2H), 3.96 (m, 1H), 7.27-7.38 (m, 5H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): δ 18.7, 19.1, 30.2, 47.8, 51.2, 58.9, 60.4, 127.1, 128.4, 128.8, 139.3; HRMS (ES+) calc. for C\textsubscript{13}H\textsubscript{20}N\textsubscript{2} 205.1705, [M+H]\textsuperscript{+} found 205.1703.

(3S,8aS)-3-isobutyloctahydropyrrolo[1, 2-a]pyrazine (8a).

Yield: 74%; Colorless liquid; [α]D\textsuperscript{25} +12.8 (c 1.0, CHCl\textsubscript{3}); IR \ ν\textsubscript{max}/cm\textsuperscript{-1} (film) 3286, 2953; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 0.9 (m, 6H), 1.28 (m, 1H), 1.47 (m, 1H), 1.62-1.83 (m, 5H), 2.02 (m, 1H), 2.2-2.33 (m, 2H), 2.64-2.77 (m, 2H), 2.91-2.97 (m, 3H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): δ 20.7, 22.2, 23.1, 24.9, 26.7, 41.0, 45.6, 50.4, 54.6, 57.0, 63.2; HRMS (ES+) calc. for C\textsubscript{11}H\textsubscript{22}N\textsubscript{2} 183.1861, [M+H]\textsuperscript{+} found 183.1861.

(3S, 8aS)-3-methyloctahydropyrrolo[1, 2-a]pyrazine (8b).

Yield: 49%; Yellow liquid; [α]D\textsuperscript{25} +13.3 (c 1.0, CHCl\textsubscript{3}); IR \ ν\textsubscript{max}/cm\textsuperscript{-1} (film) 3390, 2924, 2852; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): δ 1.2 (d, J = 6.8 Hz, 3H), 1.47-1.51 (m, 1H), 1.61-1.72 (m, 2H), 1.78-1.80 (m, 1H), 1.85 (bs, 1H), 2.01-2.04 (m, 1H), 2.18-2.30 (m, 2H), 2.61 (m, 1H), 2.80 (m, 1H), 2.9-2.95 (m, 2H), 3.05 (m, 1H); \textsuperscript{13}C NMR (125 MHz,
CDCl₃): δ 19.0, 20.8, 26.7, 45.5, 54.7, 57.8, 63.0; HRMS (ES+) calc. for C₈H₁₆N₂ 141.1392, [M+H]⁺ found 141.1393.

**(3S, 8aS)-3-isopropyloctahydropyrrolo[1, 2-a] pyrazine (8c).**

Yield: 73%; Yellow liquid; [α]D₂⁵ +7.9 (c 1.0, CHCl₃); IR νmax/cm⁻¹ (film) 3315, 2956, 2787; ¹H NMR (500 MHz, CDCl₃): δ 0.90 (m, 6H), 1.44-1.50 (m, 1H), 1.61-1.7 (m, 2H), 1.78-1.83 (m, 1H), 1.94 (bs, 1H), 2.02-2.13 (m, 2H), 2.24-2.33 (m, 3H), 2.70 (m, 1H), 2.82 (m, 1H), 2.87-2.95 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 19.7, 20.4, 21.0, 46.0, 53.6, 54.7, 59.6, 62.7; HRMS (ES+) calc. for C₁₀H₂₀N₂ 169.1705, [M+H]⁺ found 169.1703.

**(3S,8aS)-3-sec-butyloctahydropyrrolo[1, 2-a]pyrazine (8d).**

Yield: 75%; Colorless liquid; [α]D₂⁵ +5.2 (c 1.0, CHCl₃); IR νmax/cm⁻¹ (film) 3257, 2965; ¹H NMR (500 MHz, CDCl₃): δ 0.83-0.89 (m, 6H), 1.07-1.11(m, 1H), 1.46-1.69 (m, 4H), 1.79 (m, 1H), 1.83 (bs, 1H), 2.14 (m, 1H), 2.26 (m, 2H), 2.43 (m, 1H), 2.71 (m, 1H), 2.79 (m, 1H), 2.86-2.96 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 11.0, 16.1, 21.0, 25.6, 26.5, 33.7, 46.1, 53.4, 54.7, 57.6, 62.7; HRMS (ES+) calc. for C₁₁H₂₂N₂ 183.1862, [M+H]⁺ found 183.1861.

**(3S,8aS)-3-phenyloctahydropyrrolo[1, 2-a]pyrazine (8e).**

Yield: 70%; Yellow liquid; [α]D₂⁵ +50.4 (c 0.5, CHCl₃); IR νmax/cm⁻¹ (film) 3271, 3059, 2789; ¹H NMR (500 MHz, CDCl₃): δ 1.68-1.89 (m, 4H), 2.46 (m, 2H), 2.60 (m, 1H), 2.91 (m, 3H), 3.13 (dd, J = 3.5, 12 Hz, 1H), 3.94 (m,1H), 7.15-7.45 (m, 5H); ¹³CNMR (125MHz, CDCl₃): δ 21.3, 25.8, 46.1, 54.6, 55.8, 57.1, 61.4, 126.8, 127.5, 128.1, 143.3; HRMS (ES+) calc. for C₁₃H₁₈N₂ 203.1549, [M+H]⁺ found 203.1548.

**(3S,8aS)-3-benzyloctahydropyrrolo[1,2-a]pyrazine (8f).**


Yield: 62%; Colorless liquid; $[\alpha]_D^{25} +10.7$ (c 1.0, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3293, 2932, 2792; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.51 (m, 1H), 1.66-1.86 (m, 4H), 2.05 (m, 1H), 2.17 (m, 1H), 2.35 (m, 1H), 2.81-3.11 (m, 6H), 7.29 (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.0, 27.3, 30.4, 38.2, 45.8, 54.5, 56.0, 63.4, 126.2, 128.6, 129.3, 140.2; HRMS (ES+) calc. for C$_{14}$H$_{20}$N$_2$ 217.1705, [M+H]$^+$ found 217.1703.

(3R,8aS)-3-phenyloctahydropyrrolo[1, 2-a]pyrazine (8g).

Yield: 40%; Yellow solid; mp 44 ºC; $[\alpha]_D^{25} -48.5$ (c 1.25, CHCl$_3$); TLC $R_f$ 0.50 (Neat MeOH); IR $\nu_{\text{max}}$/cm$^{-1}$ (pellet) 3257, 3060; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.42 (m, 1H), 1.72 (m, 1H), 1.79-1.86 (m, 3H), 2.05 (m, 1H), 2.12 (m, 2H), 2.68 (m, 1H), 2.82 (bs, 1H), 3.05 (m, 1H), 3.13 (dd, $J = 2.8$, 10.9 Hz, 1H), 3.3 (dd, $J = 2.8$, 10.9 Hz, 1H), 3.89 (m, 1H), 7.3 (m, 5H); $^{13}$C NMR (125MHz, CDCl$_3$); $\delta$ 21.2, 27.4, 51.2, 53.7, 60.0, 62.9, 127.2, 127.5, 128.5, 142.4; HRMS (ES+) calc. For C$_{13}$H$_{18}$N$_2$ 203.1549, [M+H]$^+$ found 203.1546.

**General procedure for the reductive amination of diketopiperazines.**

To a solution of amine 4 or 8 (2.5 mmol) in water (2.5 mL) was added formaldehyde (8.5 mmol, 39% in w/v) and formic acid (27.5 mmol) at room temperature. The reaction mixture was allowed to reflux for 16 h. It was cooled was then basified by the addition of saturated NaHCO$_3$ and 10$N$ NaOH solution. Aqueous layer was extracted with EtOAc and the organic layer was then washed with brine and dried over anhydrous Na$_2$SO$_4$. Solvent was removed in vacuum and the residue was purified by column chromatography using neutral alumina.

(2S,5S)-2,5-dibenzyl-1,4-dimethylpiperazine (5a).
Yield: 44%; White solid; mp 122 °C; [α]_D^{25} +12.8 (c 0.5, DMSO); TLC R_f 0.40 (5%, MeOH in CH₂Cl₂); IR ν_{max}/cm⁻¹ (pellet) 3028, 2891; ¹H NMR (400 MHz, CDCl₃): δ 2.23 (m, 1H), 2.34 (s, 3H), 2.47 (m, 1H), 2.57 (m, 1H), 2.75 (m, 1H), 2.99 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 29.8, 42.9, 55.6, 62.9, 125.9, 128.4, 129.5, 140.3; HRMS (ES+) calc. for C₂₀H₂₆N₂ 295.2175, [M+H]^+ found 295.2175.

(2S,5R)-2-isopropyl-1, 4-dimethyl-5-phenylpiperazine (5b).

Yield: 31%; Yellow solid; mp 48 °C; [α]_D^{25} –27.8 (c 0.5, DMSO); TLC R_f 0.60 (10%, MeOH in CH₂Cl₂); IR ν_{max}/cm⁻¹ (film) 3083, 2957; ¹H NMR (400 MHz, CDCl₃): δ 0.98 (m, 6H), 1.39 (m, 1H), 1.89-2.32 (m, 9H), 2.82 (m, 2H), 3.08 (m, 1H), 7.23-7.33 (m, 5H); ¹³C NMR (125 MHz, CDCl₃): δ 15.4, 19.9, 26.7, 41.7, 43.7, 54.9, 64.8, 67.4, 69.3, 126.6, 127.4, 128.3, 141.3; HRMS (ES+) calc. for C₁₅H₂₄N₂ 233.2018, [M+H]^+ found 233.2018.

(3S,8aS)-3-isobutyl-2-methyloctahydropyrrolo[1,2-a]pyrazine (9a).

Yield: 46%; Colorless liquid; [α]_D^{25} +26.3 (c 0.6, CHCl₃); TLC R_f 0.50 (100%, MeOH); IR ν_{max}/cm⁻¹ (film) 2954, 2794; ¹H NMR (400 MHz, CDCl₃): δ 0.89 (m, 6H), 1.25-1.84 (m, 7H), 2.1 (m, 2H), 2.27-2.38 (m, 5H), 2.61 (m, 2H), 2.81 (dd, J = 2.4, 10.8 Hz, 1H), 2.95 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 21.1, 22.0, 23.6, 26.3, 27.4, 32.9, 42.2, 53.9, 54.0, 54.9, 57.3, 62.2; HRMS (ES+) calc. for C₁₂H₂₄N₂ 197.2018, [M+H]^+ found 197.2018.

(3S, 8aS)-2,3-dimethyloctahydropyrrolo[1,2-a]pyrazine (9b).

Yield: 55%; Yellow liquid; [α]_D^{25} +13.8 (c 1.0, CHCl₃); IR ν_{max}/cm⁻¹ (film) 2962, 2795; ¹H NMR (500 MHz, CDCl₃): δ 1.06 (d, J = 6.6 Hz, 3H), 1.46 (m, 1H), 1.64-1.85 (m, 3H), 1.99 (m, 2H), 2.09-2.16 (m, 2H), 2.29 (s, 3H), 2.31-2.41 (m, 2H), 2.58 (m, 1H), 2.73 (m,
1H), 2.8 (m, 1H), 2.93 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 10.8, 21.4, 42.4, 53.6, 54.0, 54.2, 57.7, 62.9; HRMS (ES+) calc. for C$_9$H$_{18}$N$_2$ 155.1549, [M+H]$^+$ found 155.1548.

(3S,8aS)-3-isopropyl-2-methyloctahydropyrrolo[1,2-a]pyrazine (9c).

Yield: 56%; Colorless liquid; $[\alpha]_D^{25} +8.3$ (c 1.0, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 2956, 2785; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.87 (d, $J = 6.9$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H), 1.63-1.64 (m, 3H), 1.97-2.13 (m, 3H), 2.38 (s, 3H), 2.40 (m, 2H), 2.56-2.65 (m, 3H), 2.79-2.85 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 18.4, 20.7, 21.4, 26.4, 27.1, 42.9, 47.4, 54.7, 55.0, 57.9, 66.6; HRMS (ES+) calc. for C$_{11}$H$_{22}$N$_2$ 183.1862, [M+H]$^+$ found 183.1866.

(3S,8aS)-3-sec-butyl-2-methyloctahydropyrrolo[1, 2-a]pyrazine (9d).

Yield: 30%; Colorless liquid; $[\alpha]_D^{25} +67.8$ (c 1.0, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 2960, 2795; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.83 (d, $J = 6.8$ Hz, 3H), 0.87 (t, $J = 7.6$ Hz, 3H), 1.13 (m, 1H), 1.44 (m, 1H), 1.59-1.67 (m, 3H), 1.79-1.86 (m, 2H), 2.0-2.12 (m, 2H), 2.31 (s, 3H), 2.36 (dd, $J = 3.1$, 11 Hz, 1H), 2.46-2.62 (m, 3H), 2.81 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 12.0, 14.8, 21.5, 26.1, 27.1, 33.8, 42.7, 54.8, 55.4, 58.0, 65.1; HRMS (ES+) calc. for C$_{12}$H$_{24}$N$_2$ 197.2018, [M+H]$^+$ found 197.2018.

(3S,8aS)-2-methyl-3-phenyloctahydropyrrolo[1, 2-a]pyrazine (9e).

Yield: 92%; Colorless liquid; $[\alpha]_D^{25} +109.0$ (c 1.0, CHCl$_3$); TLC $R_f$ 0.50 (50%, MeOH in CH$_2$Cl$_2$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3024, 2789; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.72 (m, 2H), 1.98 (m, 2H), 2.05 (s, 3H), 2.55-2.87 (m, 7H), 3.23 (dd, $J = 3$, 8 Hz, 1H), 7.22-7.30 (m, 3H), 7.43 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.9, 25.4, 43.4, 54.3, 55.4, 56.0, 60.8, 67.0, 127.2, 128.0, 128.7, 141.1; HRMS (ES+) calc. for C$_{14}$H$_{20}$N$_2$ 217.1705, [M+H]$^+$ found 217.1705.
(3S,8aS)-3-benzyl-2-methyloctahydropyrrolo[1, 2-a]pyrazine (9f).

Yield: 66%; Colorless liquid; $[\alpha]_D^{25} +26.5$ (c 1.0, CHCl$_3$); TLC $R_f$ 0.70 (50%, MeOH in CH$_2$Cl$_2$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 2934, 2794; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.43 (m, 1H), 1.65-1.87 (m, 3H), 2.02-2.07 (m, 3H), 2.46 (m, 1H), 2.54 (s, 3H), 2.7 (dd, $J$ = 11.0, 3.0 Hz, 1H), 2.77-2.85 (m, 3H), 2.93-2.99 (m, 3H), 7.15-7.28 (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.5, 27.8, 29.2, 42.7, 53.1, 53.7, 54.2, 61.6, 62.8, 125.7, 128.4, 129.6, 141.4; HRMS (ES+) calc. for C$_{15}$H$_{22}$N$_2$ 231.1862, [M+H]$^+$ found 231.1862.

(3R,8aS)-2-methyl-3-phenyloctahydropyrrolo[1, 2-a]pyrazine (9g).

Yield: 78%; Colorless liquid; $[\alpha]_D^{25} –129.0$ (c 1.0, CHCl$_3$); TLC $R_f$ 0.30 (5%, MeOH in CH$_2$Cl$_2$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3083, 2940; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.44 (m, 1H), 1.68-1.86 (m, 3H), 2.07-2.13 (m, 2H), 2.18-2.22 (m, 2H), 3.01-3.14 (m, 4H), 7.24-7.33 (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.4, 27.8, 43.8, 53.3, 60.2, 60.8, 62.8, 68.9, 127.5, 128.0, 128.5, 141.7; HRMS (ES+) calc. for C$_{14}$H$_{20}$N$_2$ 217.1705, [M+H]$^+$ found 217.1706.

General Procedure for the enantioselective/diastereoselective Henry reaction.

A solution of ligand 1a (4.6 mg, 0.0275 mmol) and Cu(OAc)$_2$.H$_2$O (5 mg, 0.025 mmol) in dichloromethane (2 mL) was stirred overnight at room temperature. Solvent was removed under reduced pressure and the residue was dissolved in dry EtOH (2 mL). To the resulting blue solution, nitroalkane (5 mmol), Et$_3$N (7 µL, 0.050 mmol) and aldehyde (0.5 mmol) were added at –40 °C. The reaction mixture was stirred for appropriate time and the progress of the reaction monitored by TLC. After completion of the reaction, the volatile components were removed under reduced pressure and the residue was purified by column chromatography on silica gel (EtOAc/Petroleum ether) to afford the nitroaldol
product. The enantiomeric excess was determined by chiral HPLC and diastereoselectivity was determined by $^1$H NMR spectroscopy.

**Stereochemical Assignments:** The absolute configurations of nitroaldol products 10d, 10j, 10k and 10m were assigned by analogy. The absolute configurations of the remaining examples were assigned by comparison of their optical rotations with literature values.$^7,8$

**(S)-2-nitro-1-phenylethanol (10a).$^7**

This compound was obtained in 75% yield and 92% ee. The optical purity was determined by HPLC on chiralcel OD-H column [$n$-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; $\lambda = 254$ nm; $t_{R(\text{minor})} = 10.10$ min (R), $t_{R(\text{major})} = 11.85$ min (S); $[\alpha]_D^{25} +31.0$ (c 1.0, CHCl$_3$) [lit.$^1$ (S) ee = 86%; $[\alpha]_D^{25} +35.8$ (c 1.31, CH$_2$Cl$_2$)]; IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3542, 2922, 1554; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.8 (bs, 1H), 4.58 (m, 2H), 5.46 (dd, $J = 3.2$, 9.5 Hz, 1H), 7.34-7.43 (m, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 71.1, 81.3, 126.0, 129.1, 138.1.

**(S)-2-nitro-1-(2-nitrophenyl)ethanol (10b).$^7**

This compound was obtained in 91% yield and 87% ee. The optical purity was determined by HPLC on chiralcel OD-H column [$n$-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; $\lambda = 254$ nm; $t_{R(\text{minor})} = 10.92$ min (R), $t_{R(\text{major})} = 11.82$ min (S); $[\alpha]_D^{25} -182.4$ (c 1.0, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3528, 2923, 1555, 1526; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.34 (d, $J = 4.3$ Hz, 1H), 4.55 (m, 1H), 4.85 (dd, $J = 2.3$, 14.05 Hz, 1H), 6.05 (m, 1H), 7.53 (m, 1H), 7.72 (m, 1H), 7.96 (m, 1H), 8.08 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 66.8, 80.1, 125.1, 128.8, 129.8, 134.1, 134.5, 147.0.

**(S)-2-nitro-1-(4-nitrophenyl)ethanol (10c).$^7**
This compound was obtained in 69% yield and 78% ee. The optical purity was determined by HPLC on chiralcel OD-H column [n-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; \(\lambda = 254\) nm; \(t_{R\text{minor}} = 17.60\) min (\(R\)), \(t_{R\text{major}} = 21.34\) min (\(S\)); \([\alpha]_{D}^{25} +25.4\) (c 1.0, CHCl\(_3\)); IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (pellet) 3485, 3114, 1553; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.11 (d, \(J = 3.2\) Hz, 1H), 4.57 (m, 1H), 5.6 (m, 1H), 7.62 (d, \(J = 6.4\) Hz, 2H), 8.28 (d, \(J = 6.8\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 70.0, 80.6, 124.1, 126.9, 144.9, 148.1.

\((S)-2\text{-nitro-1-}(4\text{-}(\text{trifluoromethyl})\text{phenyl})\text{ethanol (10d).}\n
This compound was obtained in 60% yield and 90% ee. The optical purity was determined by HPLC on chiralcel OD-H column [n-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; \(\lambda = 254\) nm; \(t_{R\text{minor}} = 8.38\) min (\(R\)), \(t_{R\text{major}} = 9.94\) min (\(S\)); \([\alpha]_{D}^{25} +33.7\) (c 1.0, CHCl\(_3\)); IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (film) 3435, 2925, 1556; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.23 (bs, 1H), 4.51-4.61 (m, 2H), 5.53 (dd, \(J = 3.1, 6.0\) Hz, 1H), 7.53-7.67 (m, 4H), 7.33 (m, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 30.7, 70.4, 80.9, 125.0, 126.0, 131.4, 142.1.

\((S)-1\text{-}(4\text{-fluorophenyl})\text{-2\text{-nitroethanol (10e).}\n
This compound was obtained in 97% yield and 89% ee. The optical purity was determined by HPLC on chiralcel OD-H column [n-hexane/2-propanol 90:10]; flow rate 0.8 mL/min; \(\lambda = 254\) nm; \(t_{R\text{minor}} = 12.62\) min (\(R\)), \(t_{R\text{major}} = 14.6\) min (\(S\)); \([\alpha]_{D}^{25} +37.0\) (c 1.0, CHCl\(_3\)); IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (film) 3447, 3077, 1605, 1554; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 4.5 (m, 1H), 4.6 (m, 1H), 5.47 (m, 1H), 7.10 (m, 2H), 7.41 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 70.3, 81.1, 116.0, 127.8, 133.8, 161.9, 163.9.

\((S)-2\text{-nitro-1-}m\text{-tolylethanol (10f).}\n
This compound was obtained in 91% yield and 84% ee. The optical purity was determined by HPLC on chiralcel OD-H column [n-hexane/2-propanol 85:15]; flow rate
0.8 mL/min; \( \lambda = 254 \text{ nm} \); \( t_{R(\text{minor})} = 9.62 \text{ min (R)} \), \( t_{R(\text{major})} = 10.9 \text{ min (S)} \); \( [\alpha]_D^{25} +35.2 \text{ (c 1.0, CHCl}_3) \); IR \( \nu_{\text{max}/\text{cm}^{-1}} \) (film) 3429, 3027, 1553; \( ^1\text{H NMR (500 MHz, CDCl}_3) \): \( \delta 2.36 \text{ (s, 3H)} \), 2.80 (bs, 1H), 4.47-4.61 (m, 2H), 5.42 (m, 1H), 7.15-7.29 (m, 4H); \( ^{13}\text{C NMR (125 MHz, CDCl}_3) \): \( \delta 21.5, 71.1, 81.4, 123.0, 126.7, 129.0, 129.8, 138.2, 139.0 \).

(S)-1-(4-chlorophenyl)-2-nitroethanol (10g).\(^7\)

This compound was obtained in 93% yield and 85% ee. The optical purity was determined by HPLC on chiralcel OD-H column \([n\text{-hexane/2-propanol 85:15}]\); flow rate 0.8 mL/min; \( \lambda = 254 \text{ nm} \); \( t_{R(\text{minor})} = 10.67 \text{ min (R)} \), \( t_{R(\text{major})} = 12.9 \text{ min (S)} \); \( [\alpha]_D^{25} +32.4 \text{ (c 1.0, CHCl}_3) \); IR \( \nu_{\text{max}/\text{cm}^{-1}} \) (film) 3535, 3031, 1554; \( ^1\text{H NMR (500 MHz, CDCl}_3) \): \( \delta 2.9 \text{ (d, } J = 3.7 \text{ Hz, 1H)} \), 4.47 (dd, \( J = 3.2, 13.4 \text{ Hz, 1H)} \), 4.56 (m, 1H), 5.44 (m, 1H), 7.33-7.38 (m, 4H) (m, 1H); \( ^{13}\text{C NMR (125 MHz, CDCl}_3) \): \( \delta 70.2, 80.9, 127.3, 129.2, 134.8, 136.5 \).

(S)-2-nitro-1-\( p\)-tolylethanol (10h).\(^7\)

This compound was obtained in 94% yield and 87% ee. The optical purity was determined by HPLC on chiralcel OD-H column \([n\text{-hexane/2-propanol 85:15}]\); flow rate 0.8 mL/min; \( \lambda = 254 \text{ nm} \); \( t_{R(\text{minor})} = 11.05 \text{ min (R)} \), \( t_{R(\text{major})} = 13.34 \text{ min (S)} \); \( [\alpha]_D^{25} +16.4 \text{ (c 1.0, CHCl}_3) \); IR \( \nu_{\text{max}/\text{cm}^{-1}} \) (film) 3436, 3027, 1553; \( ^1\text{H NMR (500 MHz, CDCl}_3) \): \( \delta 2.36 \text{ (s, 3H)} \), 4.47-4.64 (m, 2H), 5.45 (m, 1H), 7.20-7.29 (m, 4H); \( ^{13}\text{C NMR (125 MHz, CDCl}_3) \): \( \delta 21.2, 70.8, 81.2, 125.8, 129.7, 135.1, 138.9 \).

(S)-1-(2-methoxyphenyl)-2-nitroethanol (10i).\(^7\)

This compound was obtained in 93% yield and 88% ee. The optical purity was determined by HPLC on chiralcel OD-H column \([n\text{-hexane/2-propanol 85:15}]\); flow rate 0.8 mL/min; \( \lambda = 254 \text{ nm} \); \( t_{R(\text{minor})} = 9.52 \text{ min (R)} \), \( t_{R(\text{major})} = 10.74 \text{ min (S)} \); \( [\alpha]_D^{25} +41.7 \text{ (c 1.0, CHCl}_3) \); IR \( \nu_{\text{max}/\text{cm}^{-1}} \) (film) 3421, 2923, 1555; \( ^1\text{H NMR (500 MHz, CDCl}_3) \): \( \delta 3.27 \text{ (s, 3H)} \), 4.47-4.61 (m, 2H), 5.42 (m, 1H), 7.15-7.29 (m, 4H); \( ^{13}\text{C NMR (125 MHz, CDCl}_3) \): \( \delta 21.5, 71.1, 81.4, 124.0, 126.7, 129.0, 129.8, 138.0, 139.0 \).
(m, 1H), 3.9 (s, 3H), 4.53-4.65 (m, 2H), 5.61 (m, 1H), 6.89-7.02 (m, 2H), 7.25-7.44 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 55.5, 67.9, 79.9, 110.6, 121.2, 126.1, 127.3, 129.9, 156.1.

$(S)$-1-(naphthalen-1-yl)-2-nitroethanol (10j).

This compound was obtained in 70% yield and 80% ee. The optical purity was determined by HPLC on chiralcel OD-H column [$n$-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; $\lambda = 254$ nm; $t_{R(minor)} = 13.5$ min ($R$), $t_{R(major)} = 20.4$ min ($S$); $[\alpha]D^{25} +17.5$ (c 1.0, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3541, 3060, 1553; $^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.04 (bs, 1H), 4.61-4.69 (m, 2H), 6.25 (dd, $J = 3.45$, 8.95 Hz, 1H), 7.49-7.6 (m, 3H), 7.74-8.03 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 68.4, 80.9, 121.9, 123.9, 125.6, 126.2, 127.2, 129.4, 129.5, 129.6, 133.7, 133.8.

$(S)$-2-nitro-1-o-tolylethanol (10k).

This compound was obtained in 77% yield and 87% ee. The optical purity was determined by HPLC on chiralcel OD-H column [$n$-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; $\lambda = 254$ nm; $t_{R(minor)} = 9.32$ min ($R$), $t_{R(major)} = 13.42$ min ($S$); $[\alpha]D^{25} +47.1$ (c 1.0, CHCl$_3$); IR $\nu_{\text{max}}$/cm$^{-1}$ (film) 3436, 3027, 1554; $^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.38 (s, 3H), 2.81 (m, 1H), 4.41-4.56 (m, 2H), 5.67 (m, 1H), 7.17-7.27 (m, 3H), 7.51 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.4, 71.0, 81.2, 122.9, 126.6, 128.9, 129.7, 138.0, 138.6.

$(S)$-2-nitro-1-(thiophen-2-yl)ethanol (10l).

This compound was obtained in 66% yield and 84% ee. The optical purity was determined by HPLC on chiralcel OD-H column [$n$-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; $\lambda = 254$ nm; $t_{R(minor)} = 12.06$ min ($R$), $t_{R(major)} = 12.85$ min ($S$); $[\alpha]D^{25} +15.5$.
(c 1.84, CHCl₃); IR ν_max/cm⁻¹ (film) 3521, 3109, 2923, 1554; ¹H NMR (500 MHz, CDCl₃): δ 3.12 (bs, 1H), 4.58-4.78 (m, 2H), 5.71 (dd, J = 3.0, 9.2 Hz, 1H), 7.0-7.06 (m, 2H), 7.33 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 67.2, 80.9, 125.2, 126.3, 127.3, 141.3.

(S)-1-(2-chlorophenyl)-2-nitroethanol (10m).
This compound was obtained in 94% yield and 84% ee. The optical purity was determined by HPLC on chiralcel OJ-H column [n-hexane/2-propanol 99:1]; flow rate 0.9 mL/min; λ = 215 nm; t_R(minor) = 86.27 min (R), t_R(major) = 99.59 min (S); [α]_D²⁵ +50.7 (c 1.05, CHCl₃); IR ν_max/cm⁻¹ (film) 3521, 2922, 1555, 1382; ¹H NMR (500 MHz, CDCl₃): δ 3.22 (m, 1H), 4.44 (m, 1H), 4.65 (m, 1H), 5.84 (m, 1H), 7.26-7.39 (m, 3H), 7.64-7.67 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 67.8, 79.3, 127.4, 127.6, 129.7, 129.9, 131.4, 135.5.

(S)-1(3,5-dimethoxyphenyl)-2-nitroethanol (10n).⁷
This compound was obtained in 88% yield and 87% ee. The optical purity was determined by HPLC on chiralpak AD-H column [n-hexane/2-propanol 90:10]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 14.1 min (R), t_R(major) = 17.76 min (S); [α]_D²⁵ +21.8 (c 1.0, CHCl₃) IR ν_max/cm⁻¹ (film) 3458, 2924, 1600, 1552; ¹H NMR (500 MHz, CDCl₃): δ 2.9 (bs, 1H), 3.78 (s, 6H), 4.46-4.59 (m, 2H), 5.38 (m, 1H), 6.41 (m, 1H), 6.52 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 55.5, 71.1, 81.3, 100.7, 103.9, 140.7, 161.3.

(S)-2-nitro-1-(3,4,5-trimethoxyphenyl)ethanol (10o).⁷
This compound was obtained in 90% yield and 83% ee. The optical purity was determined by HPLC on chiralcel OD-H column [n-hexane/2-propanol 85:15]; flow rate 0.8 mL/min; λ = 254 nm; t_R(minor) = 24.09 min (R), t_R(major) = 29.33 min (S); [α]_D²⁵
+21.5 (c 1.12, CHCl3); IR νmax/cm−1 (film) 3482, 2946, 1598, 1554; 1H NMR (500 MHz, CDCl3): δ 3.3 (bs, 1H), 3.78 (s, 3H), 3.82 (s, 6H ), 4.46 (m, 1H), 4.57 (m, 1H), 5.36 (m, 1H), 6.6 (m, 2H); 13CNMR (125MHz, CDCl3): δ 56.2, 60.9, 71.2, 81.5, 102.8, 134.2, 137.9, 153.6.

(S)-1-nitro-4-phenylbutan-2-ol (10p).}

This compound was obtained in 91% yield and 87% ee. The optical purity was determined by HPLC on chiralpak AD-H column [n-hexane/2-propanol 90:10]; flow rate 1 mL/min; λ = 254 nm; τR(minor) = 9.94 min (R), τR(major) = 12.3 min (S); White solid; mp 102 °C; [α]D25 –14.4 (c 1.0, CHCl3); IR νmax/cm−1 (film) 3434, 3027, 1552; 1H NMR (500 MHz, CDCl3): δ 1.75-1.89 (m, 2H), 2.7-2.88 (m, 3H), 4.3 (bs, 1H), 4.41 (m, 2H), 7.19-7.37 (m, 5H); 13C NMR (125 MHz, CDCl3): δ 31.3, 35.0, 67.7, 80.5, 126.3, 128.4, 128.6, 140.6.

(S)-1-cyclohexyl-2-nitroethanol (10q).}

This compound was obtained in 42% yield and 93% ee. The optical purity was determined by HPLC on chiralpak AD-H column [n-hexane/2-propanol 97:03]; flow rate 0.8 mL/min; λ = 215 nm; τR(minor) = 20.9 min (R), τR(major) = 22.43 min (S); [α]D25 +7.4 (c 0.8, CHCl3); IR νmax/cm−1 (film) 3434, 2928, 1554; 1H NMR (500 MHz, CDCl3): δ 1.04-1.29 (m, 5H), 1.41-1.49 (m, 1H), 1.64-1.69 (m, 2H), 1.76-1.83 (m, 3H), 2.44 (bs, 1H), 4.09 (m, 1H), 4.39-4.49 (m, 2H); 13C NMR (125 MHz, CDCl3): δ 25.8, 26.0, 26.2, 28.0, 28.9, 41.5, 72.9, 79.4.

(S)-3-ethyl-1-nitropentan-ol (10r).}

This compound was obtained in 51% yield and 96% ee. The optical purity was determined by HPLC on chiralpak AD-H column [n-hexane/2-propanol 99:1]; flow rate
0.5 mL/min; \( \lambda = 215 \) nm; \( t_R(\text{minor}) = 50.95 \text{ min} (R), \ t_R(\text{major}) = 55.06 \text{ min} (S); \ [\alpha]_D^{25} +14.1 \ (c 1.9, \text{CHCl}_3); \ \text{IR} \ \nu_{\text{max/cm}^{-1}} \text{ (film)} \ 3448, \ 2965, \ 1555, \ 1382; \ ^1\text{H NMR} \ (500 \text{ MHz, CDCl}_3): \ \delta \ 0.92 \ (t, \ J = 7.4 \text{ Hz, 6H}), \ 1.24-1.50 \ (m, \ 5H), \ 2.5 \ (bs, \ 1H), \ 4.34 \ (m, \ 1H), \ 4.43 \ (m, \ 2H); \ ^{13}\text{C NMR} \ (125 \text{ MHz, CDCl}_3): \ \delta \ 11.4, \ 11.5, \ 21.4, \ 21.9, \ 44.8, \ 70.2, \ 79.6.

2-nitro-1-phenylpropan-1-ol (11a).\textsuperscript{8}

This compound was obtained in 78% yield and diastereomeric ratios (anti/syn, 62:38) were determined by \(^1\text{H NMR}.\) Enantiomeric excess were determined by chiral HPLC (Chiralpak AD-H), \( n\)-hexane/2-propanol 99:1, \( \lambda = 220 \text{ nm, flow rate 0.8 mL/min; \text{Antimajor} = 36.6 \text{ min, Antiminor} = 41.16 \text{ min, Synmajor} = 56.42 \text{ min, Synminor} = 63.22 \text{ min; } \ [\alpha]_D^{25} +11.7 \ (c 1.0, \text{CHCl}_3); \ \text{IR} \ \nu_{\text{max/cm}^{-1}} \text{ (film)} \ 3446, \ 2924, \ 1551; \ ^1\text{H NMR} \ (500 \text{ MHz, CDCl}_3, \text{mixture of diastereomers }): \ \delta \ 1.26-1.50 \ (m, \ 6H), \ 2.7 \ (bs, \ 1H), \ 4.7-4.79 \ (m, \ 2H), \ 5.03 \ (m, \ 1H), \ 5.4 \ (m, \ 1H), \ 7.31-7.42 \ (m, \ 10H); \ ^{13}\text{C NMR} \ (125MHz, \text{CDCl}_3): \ \delta \ 12.2, \ 16.6, \ 74.0, \ 76.4, \ 87.5, \ 88.5, \ 126.0, \ 127.0, \ 128.6, \ 128.8, \ 129.1, \ 129.3, \ 138.5.

2-nitro-1-o-tolylpropan-1-ol (11b).\textsuperscript{8}

This compound was obtained in 70% yield and diastereomeric ratios (anti/syn, 71:29) were determined by \(^1\text{H NMR}.\) Enantiomeric excess were determined by chiral HPLC (Chiralpak AD-H), \( n\)-hexane/2-propanol 99:1, \( \lambda = 220 \text{ nm, flow rate 0.8 mL/min; \text{Antimajor} = 29.71 \text{ min, Antiminor} = 33.93 \text{ min, Synmajor} = 45.95 \text{ min, Synminor} = 57.6 \text{ min; } \ [\alpha]_D^{25} +4.4 \ (c 1.0, \text{CHCl}_3); \ \text{IR} \ \nu_{\text{max/cm}^{-1}} \text{ (film)} \ 3522, \ 2925, \ 1549; \ ^1\text{H NMR} \ (500 \text{ MHz, CDCl}_3, \text{mixture of diastereomers }): \ \delta \ 1.32 \ (d, \ J = 6.8 \text{ Hz, 3H}), \ 1.52 \ (d, \ J = 6.9 \text{ Hz, 3H}), \ 2.37 \ (s, \ 3H), \ 2.43 \ (s, \ 3H), \ 2.57 \ (d, \ J = 3.4 \text{ Hz, 1H}), \ 4.63 \ (m, \ 1H), \ 4.86 \ (m, \ 1H), \ 5.37 \ (m, \ 1H), \ 5.63 \ (m, \ 1H), \ 7.16-7.54 \ (m, \ 8H); \ ^{13}\text{C NMR} \ (125 MHz, \text{CDCl}_3): \ \delta \ 11.6, \ 16.2,
18.9, 19.7, 71.0, 72.3, 85.4, 88.9, 126.0, 126.6, 126.8, 127.0, 128.5, 128.9, 130.9, 131.2, 134.4, 136.7.

1-(2-methoxyphenyl)-2-nitropropan-1-ol (11c).\(^8\)

This compound was obtained in 86% yield and diastereomeric ratios (anti/syn, 68:32) were determined by \(^1\)H NMR. Enantiomeric excess were determined by chiral HPLC (Chiralpak AD-H), \(n\)-hexane/2-propanol 99:1, \(\lambda = 220\) nm, flow rate 0.8 mL/min; \(\text{Anti}_{(\text{major})} = 39.05\) min, \(\text{Anti}_{(\text{minor})} = 50.44\) min; (Chiralpak AS-H), \(n\)-hexane/2-propanol 90:10, \(\lambda = 215\) nm, flow rate 1 mL/min; \(\text{Syn}_{(\text{major})} = 11.10\) min, \(\text{Syn}_{(\text{minor})} = 15.55\) min; \([\alpha]_D^{25} = 11.9\) (c 1.0, CHCl\(_3\)); IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (film) 3521, 2941, 1549; \(^1\)H NMR (500 MHz, CDCl\(_3\), mixture of diastereomers): \(\delta = 1.32\) (d, \(J = 6.55\) Hz, 3H), 1.48 (d, \(J = 6.85\) Hz, 3H), 3.04 (d, \(J = 5.5\) Hz, 1H), 3.27 (d, \(J = 8.6\) Hz, 1H), 3.86 (s, 3H), 3.89 (s, 3H), 4.88 (m, 1H), 5.01 (m, 1H), 5.14 (m, 1H), 5.53 (m, 1H), 6.87-7.42 (m, 8H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta = 12.7, 16.7, 55.5, 55.6, 70.8, 74.4, 85.1, 87.7, 110.4, 111.0, 121.0, 121.3, 126.2, 127.7, 129.2, 129.6, 130.2, 155.8.

1-(4-chlorophenyl)-2-nitropropan-1-ol (11d).\(^8\)

This compound was obtained in 73% yield and diastereomeric ratios (anti/syn, 52:48) were determined by \(^1\)H NMR. Enantiomeric excess were determined by chiral HPLC (Chiralpak AS-H), \(n\)-hexane/2-propanol 97:3, \(\lambda = 215\) nm, flow rate 0.5 mL/min; \(\text{Anti}_{(\text{major})} = 36.8\) min, \(\text{Anti}_{(\text{minor})} = 41.54\) min, \(\text{Syn}_{(\text{major})} = 50.4\) min, \(\text{Syn}_{(\text{minor})} = 65.94\) min; \([\alpha]_D^{25} = 1.0\) (c 1.4, CHCl\(_3\)); IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (film) 3499, 2923, 1551; \(^1\)H NMR (500 MHz, CDCl\(_3\), mixture of diastereomers): \(\delta = 1.29\) (m, 3H), 1.48 (m, 3H), 2.7 (bs, 1H), 2.8 (bs, 1H), 4.62-4.74 (m, 2H), 5 (m, 1H), 5.37 (m, 1H), 7.29-7.82 (m, 8H); \(^13\)C NMR (125
MHz, CDCl₃): δ 12.1, 16.5, 73.3, 75.6, 87.3, 88.2, 127.5, 128.4, 129.0, 129.3, 129.6, 131.0, 134.5, 135.2, 136.8, 136.9.

2-nitro-1-phenylbutan-1-ol (11e).  
This compound was obtained in 64% yield and diastereomeric ratios (anti/syn, 60:40) were determined by ¹H NMR. Enantiomeric excess were determined by chiral HPLC (Chiralpak AS-H), n-hexane/2-propanol 99:1, λ = 215 nm, flow rate 0.5 mL/min; Anti_{major} = 42.17 min, Anti_{minor} = 50.5 min, Syn_{major} = 61.94 min, Syn_{minor} = 89.1 min; [α]D ²⁵ +6.6 (c 1.0, CHCl₃); IR ν max/cm⁻¹ (film) 3439, 2925, 1550; ¹H NMR (500 MHz, CDCl₃, mixture of diastereomers): δ 0.94 (m, 3H), 1.27 (m, 3H), 1.89 (m, 2H), 2.15 (m, 2H), 2.5 (bs, 1H), 2.7 (bs, 1H), 4.55-4.61 (m, 2H), 5.03 (m, 1H), 5.17 (m, 1H), 7.31-7.4 (m, 10H); ¹³C NMR (125 MHz, CDCl₃): δ 10.2, 10.5, 21.1, 21.4, 74.3, 75.6, 94.8, 95.3, 126.3, 126.9, 128.8, 128.9, 129.1, 129.3, 138.6, 138.7.

4-nitro-1-phenylpentan-3-ol (11f).  
This compound was obtained in 45% yield and diastereomeric ratios (syn/anti, 54:46) were determined by ¹H NMR. Enantiomeric excess were determined by chiral HPLC (Chiralcel OJ-H), n-hexane/2-propanol 95:5, λ = 215 nm, flow rate 0.5 mL/min; Anti_{major} = 56.05 min, Anti_{minor} = 62.53 min, Syn_{major} = 67.96 min, Syn_{minor} = 75.3 min; [α]D ²⁵ −15.4 (c 2, CHCl₃); IR ν max/cm⁻¹ (film) 3434, 2923, 1549; ¹H NMR (500 MHz, CDCl₃, mixture of diastereomers): δ 1.54 (m, 6H), 1.7-1.84 (m, 4H), 2.7 (m, 2H), 2.88 (m, 2H), 3.89 (m, 1H), 4.12 (m, 1H), 4.48-4.55 (m, 2H), 7.18-7.31 (m, 10H); ¹³C NMR (125 MHz, CDCl₃): δ 12.6, 16.3, 31.5, 32.0, 34.7, 34.8, 71.2, 72.1, 86.4, 87.8, 126.4, 128.5, 128.7, 140.8, 140.9.

Synthesis of (S)-2-amino-1-phenylethanol (12)
β-Nitro alcohol 10a (0.4 mmol) in methanol (2 mL) was hydrogenated (H₂, 1 atm) in the presence of 10% Pd/C (20 mg) for 24 h. The solution was filtered over celite, and the methanol was removed under reduced pressure. The crude material was used without further purification. Yield 92%; White solid; m.p. 54-56 °C; [α]D25 +9.2 (c 1.68, EtOH); [lit.9 (S) ee = 100%; [α]D20 +47.9 (c 2.4, EtOH)]; IR νmax/cm⁻¹ (film) 3384, 2925, 2855; ¹H NMR (500 MHz, CDCl₃): δ 2.79 (m, 1H), 3 (m, 1H), 3.46 (bs, 1H), 4.63 (m, 1H), 7.25-7.36 (m, 5H); ¹³C NMR (125 MHz, CDCl₃): δ 49.3, 74.4, 125.9, 127.65, 128.5, 128.6, 142.6; HRMS (ES+) calc. for C₈H₁₁NO 138.0920, [M+H]+ found 138.0919.

Synthesis of (R)-2-phenyl-1-tosylaziridine (13)¹⁰

p-Toluene sulphonyl chloride (1.2 mmol) was added in portions to a solution of amino alcohol 12 (1 mmol) and diisopropylethylamine (2 mmol) in CH₂Cl₂ (4 mL) at 0 °C. The ice bath was then removed, and the reaction was allowed to warm to rt and further stirred for 6 h. The reaction mixture was then washed with water, brine and dried over anhydrous Na₂SO₄. The organic layer was then concentrated and the crude product was purified by column chromatography on silica gel to afford the sulfonylated amino alcohol. To this N-sulfonyl-substituted amino alcohol in dry THF (4 mL) was added triphenylphosphine (1.2 mmol) in one portion at rt. The reaction mixture was then cooled to 0 °C, and treated slowly with diisopropylazodicarboxylate (1.2 mmol). The ice bath was removed and the yellow solution was stirred at rt for 6 h. THF was evaporated, and the residue was purified by column chromatography to yield the chiral aziridine 13. Yield: 85%; White solid, mp 82-84 °C; TLC Rf 0.8 (40% EA in petroleum ether); [α]D25 – 86.4 (c 1.0, CHCl₃); IR νmax/cm⁻¹ (pellet) 3038, 1385; ¹H NMR (500 MHz, CDCl₃): δ 2.38 (m, 1H), 2.42 (s, 3H), 2.98 (m, 1H), 3.77 (m, 1H), 7.2-7.33 (m, 7H), 7.87 (m, 2H);
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.8, 36.1, 41.1, 126.7, 128.0, 128.4, 128.7, 129.9, 135.0, 135.1, 144.8; HRMS (ES+) calc. for C$_{15}$H$_{15}$NO$_2$S 274.0902, [M+H]$^+$ found 274.0903.; Enantiomeric excess was determined by HPLC with a chiralcel OJ-H column (n-hexane/2-propanol 90:10, $\lambda$ = 254 nm); flow rate 0.8 mL/min; $t_{R(\text{minor})} = 37.47$ min (S), $t_{R(\text{major})} = 44.43$ min (R).

Spectras

$^{1}$H NMR Spectrum of 2c in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of 2c in CDCl$_3$

500 MHz $^1$H NMR Spectrum of 6a in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of $6a$ in CDCl$_3$

500 MHz $^1$H NMR Spectrum of $6b$ in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of 6b in CDCl$_3$

400 MHz $^1$H NMR Spectrum of 6e in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of 6e in CDCl$_3$

500 MHz $^1$H NMR Spectrum of 6g in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of 6g in CDCl$_3$

500 MHz $^1$H NMR Spectrum of 3b in DMSO-d$_6$
400 MHz $^1$H NMR Spectrum of 7a in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 7a in CDCl$_3$+DMSO-d$_6$
500 MHz $^1$H NMR Spectrum of $7b$ in DMSO-d$_6$.

125 MHz $^{13}$C NMR Spectrum of $7b$ in DMSO-d$_6$.
500 MHz $^1$H NMR Spectrum of 7c in DMSO-d$_6$  

125 MHz $^{13}$C NMR Spectrum of 7c in DMSO-d$_6$
500 MHz $^1$H NMR Spectrum of 7d in DMSO-d$_6$

125 MHz $^{13}$C NMR Spectrum of 7d in DMSO-d$_6$
500 MHz $^1$H NMR Spectrum of 7e in DMSO-d$_6$

125 MHz $^{13}$C NMR Spectrum of 7e in DMSO-d$_6$
500 MHz $^1$H NMR Spectrum of 7g in DMSO-d$_6$

125 MHz $^{13}$C NMR Spectrum of 7g in DMSO-d$_6$
400 MHz $^1$H NMR Spectrum of 4b in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 4b in CDCl$_3$
400 MHz $^1$H NMR Spectrum of 8a in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 8a in CDCl$_3$
400 MHz $^1$H NMR Spectrum of 8b in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 8b in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 8c in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 8c in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 8d in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 8d in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 8e in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 8e in CDCl$_3$
500 MHz $^1$H NMR Spectrum of $8g$ in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of $8g$ in CDCl$_3$
400 MHz $^1$H NMR Spectrum of 5b in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 5b in CDCl$_3$
400 MHz $^1$H NMR Spectrum of 9a in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 9a in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 9b in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 9b in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 9e in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 9e in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 9d in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 9d in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 9e in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 9e in CDCl$_3$
500 MHz $^1$H NMR Spectrum of 9f in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of 9f in CDCl$_3$
400 MHz $^1$H NMR Spectrum of \textit{9g} in CDCl$_3$

125 MHz $^{13}$C NMR Spectrum of \textit{9g} in CDCl$_3$
HPLC Graph for racemic 10a

HPLC Graph for Chiral 10a
HPLC Graph for racemic 10b

HPLC Graph for Chiral 10b

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [µV/µsec]</th>
<th>Area [%]</th>
<th>Height [µV]</th>
<th>Area [%]</th>
<th>Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>10.922</td>
<td>1555486.00</td>
<td>64523.49</td>
<td>6.35</td>
<td>6.35</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>11.828</td>
<td>2293694.74</td>
<td>583828.71</td>
<td>93.65</td>
<td>93.65</td>
<td></td>
</tr>
</tbody>
</table>

24492417.5 648352.20 100.00 100.00
HPLC Graph for racemic 10c

HPLC Graph for Chiral 10c
HPLC Graph for racemic 10d

HPLC Graph for Chiral 10d
HPLC Graph for racemic 10e

HPLC Graph for Chiral 10e
HPLC Graph for racemic 10f

HPLC Graph for Chiral 10f

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [µV·sec]</th>
<th>Height [µV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>9.620</td>
<td>375440.91</td>
<td>12676.43</td>
<td>7.91</td>
<td>7.91</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>10.870</td>
<td>4373300.31</td>
<td>109885.65</td>
<td>92.09</td>
<td>92.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4748741.22</td>
<td>122562.06</td>
<td>100.00</td>
<td>100.00</td>
</tr>
</tbody>
</table>
HPLC Graph for racemic 10g

HPLC Graph for Chiral 10g

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak #</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [µV sec]</th>
<th>Height [µV]</th>
<th>Area [%]</th>
<th>Nom. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>10.573</td>
<td>286502.14</td>
<td>8964.33</td>
<td>7.52</td>
<td>7.52</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>12.305</td>
<td>3524741.97</td>
<td>77912.03</td>
<td>92.48</td>
<td>92.48</td>
</tr>
</tbody>
</table>

3511344.11 86876.37 100.00 100.00
HPLC Graph for racemic 10h

HPLC Graph for Chiral 10h
HPLC Graph for racemic 10i

HPLC Graph for Chiral 10i

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak #</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [μV/sec]</th>
<th>Height [μV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>8.523</td>
<td>380508.99</td>
<td>16428.58</td>
<td>6.17</td>
<td>6.17</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>10.742</td>
<td>578605.47</td>
<td>172805.64</td>
<td>93.83</td>
<td>93.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>616563.68</td>
<td>189235.23</td>
<td>100.00</td>
<td>100.00</td>
<td>100.00</td>
</tr>
</tbody>
</table>
HPLC Graph for racemic 10j

HPLC Graph for Chiral 10j

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [µV/µsec]</th>
<th>Height [µV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>13.464</td>
<td>4529796.02</td>
<td>126037.46</td>
<td>9.60</td>
<td>9.60</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>20.394</td>
<td>4159000.44</td>
<td>623083.46</td>
<td>90.20</td>
<td>90.20</td>
</tr>
</tbody>
</table>

HPLC Graph for Chiral 10j
HPLC Graph for racemic 10k

HPLC Graph for Chiral 10k
HPLC Graph for racemic 10l

HPLC Graph for Chiral 10l
HPLC Graph for racemic 10m

HPLC Graph for Chiral 10m
HPLC Graph for racemic 10n

HPLC Graph for Chiral 10n
### DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [(\mu\text{V}\times\text{sec})]</th>
<th>Height [(\mu\text{V})]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>24.089</td>
<td>266880.35</td>
<td>2611.73</td>
<td>8.46</td>
<td>6.46</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>29.933</td>
<td>2996660.05</td>
<td>20003.13</td>
<td>91.54</td>
<td>91.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3153406.42</td>
<td>22615.90</td>
<td>100.00</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

HPLC Graph for Chiral 10o
HPLC Graph for racemic 10p

HPLC Graph for Chiral 10p
HPLC Graph for racemic 10q

HPLC Graph for Chiral 10q

**DEFAULT REPORT**

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [UV*sec]</th>
<th>Height [UV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>20.904</td>
<td>1706602.92</td>
<td>40347.57</td>
<td>3.55</td>
<td>3.56</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>22.434</td>
<td>46214722.45</td>
<td>490176.92</td>
<td>96.44</td>
<td>96.44</td>
</tr>
</tbody>
</table>

HPLC Graph for Chiral 10q
HPLC Graph for racemic 10r

HPLC Graph for Chiral 10r

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak #</th>
<th>Time [min]</th>
<th>Area [µV·s]</th>
<th>Height [µV]</th>
<th>Area [%]</th>
<th>Area/Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50.950</td>
<td>498058.00</td>
<td>4158.44</td>
<td>2.13</td>
<td>119.77</td>
</tr>
<tr>
<td>2</td>
<td>55.056</td>
<td>22872702.00</td>
<td>93026.75</td>
<td>97.87</td>
<td>245.87</td>
</tr>
<tr>
<td></td>
<td>23370760.00</td>
<td>97185.19</td>
<td>100.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HPLC Graph for Chiral 10r
500 MHz $^1$H NMR Spectrum of **11a** in CDCl$_3$

HPLC Graph for racemic anti-**11a**
Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is (c) The Royal Society of Chemistry 2009

**HPLC Graph for Chiral anti-11a**

**HPLC Graph for racemic syn-11a**
HPLC Graph for Chiral syn-11a

500 MHz $^1$H NMR Spectrum of 11b in CDCl$_3$
HPLC Graph for racemic anti-11b

HPLC Graph for Chiral anti-11b
HPLC Graph for racemic syn-11b

HPLC Graph for Chiral syn-11b
500 MHz $^1$H NMR Spectrum of 11c in CDCl$_3$

HPLC Graph for racemic anti-11c
HPLC Graph for Chiral anti-11c

HPLC Graph for racemic syn-11c
HPLC Graph for Chiral syn-11c

500 MHz $^1$H NMR Spectrum of 11d in CDCl$_3$
HPLC Graph for racemic anti-11d

HPLC Graph for Chiral anti-11d

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [µV/µsec]</th>
<th>Height [µV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>36.806</td>
<td>34216077.06</td>
<td>250767.52</td>
<td>82.04</td>
<td>82.04</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>41.540</td>
<td>7488499.80</td>
<td>71103.38</td>
<td>17.96</td>
<td>17.96</td>
</tr>
</tbody>
</table>

4170451.60   326691.29   100.00   100.00
HPLC Graph for racemic syn-11d

HPLC Graph for Chiral syn-11d

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak #</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [uV*sec]</th>
<th>Height [uV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>50.383</td>
<td>80432132.87</td>
<td>14626.56</td>
<td>62.12</td>
<td>62.12</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>65.940</td>
<td>10579565.93</td>
<td>54465.90</td>
<td>17.88</td>
<td>17.88</td>
</tr>
</tbody>
</table>

61412098.90 246993.46 100.00 100.00
500 MHz $^1$H NMR Spectrum of 11e in CDCl$_3$

HPLC Graph for racemic anti-11e
HPLC Graph for Chiral anti-11e

HPLC Graph for racemic syn-11e
HPLC Graph for Chiral syn-11e

500 MHz $^1$H NMR Spectrum of 11f in CDCl$_3$
HPLC Graph for racemic 11f

HPLC Graph for Chiral anti-11f

DEFAULT REPORT

<table>
<thead>
<tr>
<th>Peak</th>
<th>Component Name</th>
<th>Time [min]</th>
<th>Area [UV*sec]</th>
<th>Height [UV]</th>
<th>Area [%]</th>
<th>Norm. Area [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>55.050</td>
<td>27285960.07</td>
<td>129489.78</td>
<td>97.58</td>
<td>97.58</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>62.527</td>
<td>649369.11</td>
<td>5810.63</td>
<td>2.32</td>
<td>2.32</td>
</tr>
</tbody>
</table>
HPLC Graph for Chiral syn-11f

500 MHz $^1$H NMR Spectrum of 12 in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of 12 in CDCl$_3$

500 MHz $^1$H NMR Spectrum of 13 in CDCl$_3$
125 MHz $^{13}$C NMR Spectrum of 13 in CDCl$_3$

HPLC Graph for racemic 13
HPLC Graph for Chiral 13

References


