CHAPTER II
EXPERIMENTAL

2.1 General

All reactions were performed in oven-dried glasswares. The weight of all chemical substances was determined on a Mettler Toledo AB204-S electrical balance. Evaporation of solvents was carried out on a Büchi Rotavapor R-114 equipped with a Büchi B-480 Waterbath. The progress of the reactions was followed by thin layer chromatography (TLC) performed on Merck D.C. silica gel 60 F_{254} 0.2 mm precoated aluminium plates and visualized using UV light (254 nm), $KMnO_4$ solution, iodine, or 2,4-DNP reagent. Column chromatography was performed on 230-400 mesh silica gel for flash column chromatography or activated neutral aluminium oxide 90 (Activity I).

Normal phase high performance liquid chromatography (HPLC) separations were performed on a Water 600™ equipped with a UV/VIS detector using hexanes:^{i}PrOH as eluent. Daicel Chiralcel OD®, a Chiralcel OJ-H®, and a Chiralpak AD-H® columns were used for the determination of enantiomeric compositions. Gas chromatographic (GC) experiments were performed on a Fisons MFC 800 equipped with a flame ionization detector (FID) (model FISONS EL 980) using a 25 m × 0.25 mm × 0.25 μm CP Chirasil-Dex CB capillary column (isothermal; injector temperature = 250 °C, detector temperature = 250 °C). Melting points were measured on an Electrothermal 9100 melting point apparatus and were uncorrected. The optical rotations were measured at the ambient temperature with a Jasco P-1010 Polarimeter or a Perkin Elmer 241 Polarimeter. Elemental analysis was performed on CHNS/O Analyzer (Perkin Elmer PE2400 Series II) at Scientific and Technological Research Equipment Centre Chulalongkorn University.

Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded on a Varian Mercury-400 plus operating at 400 MHz (^{1}H) and 100 MHz (^{13}C) respectively or Bruker Avance 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz). Unless otherwise stated, the spectra were taken in $CDCl_3$. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) or using the residual

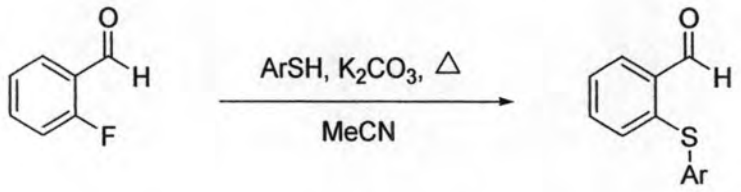
protonated solvent signal as a reference. Coupling constants (*J*) are proton-proton coupling unless otherwise noted and were reported in hertz (Hz). Multiplicities were designated as followed: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet.

2.2 Materials

All chemicals were purchased from Fluka, Merck, or Aldrich Chemicals Co., Ltd. and were used as received without further purification. Commercial grade solvents for column chromatography were distilled before use. Solvents for reactions were AR grade and dried with activated 4Å molecular sieves. HPLC grade hexanes and 2-propanol for chiral HPLC experiments were obtained from Merck and filtered through a membrane filter (0.5 μm Millipore®-FH) before use. Each sample was filtered through a Millex®-HV syringe filter unit prior to injection on to the chromatograph.

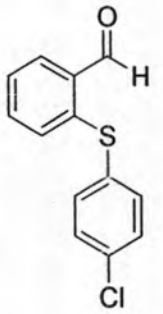
2.3 General procedure for the preparation of thiolated aldehydes

2.3.1 Synthesis of aromatic thiolated aldehydes



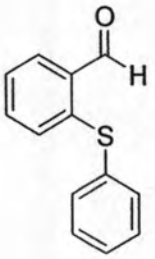
A mixture of acetonitrile, a 4-chlorothiophenol or thiophenol (1 equiv), 2-fluorobenzaldehyde (1 equiv), and anhydrous potassium carbonate (2.5 equiv) was refluxed for 2 h. The reaction mixture was allowed to cool at room temperature and diluted with water and extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was used for the next step without further purification.

2.3.1.1 2-[(4′-Chlorophenyl)sulfanyl]benzaldehyde (71a)



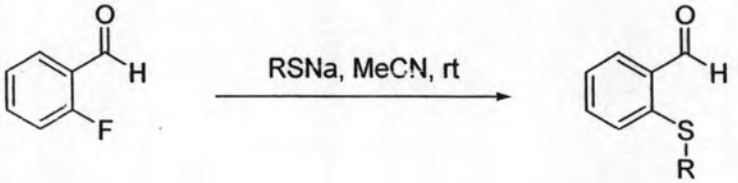
2-[(4′-Chlorophenyl)sulfanyl]benzaldehyde (**71a**) was prepared according to the general procedure from 2-fluorobenzaldehyde (2.48 g, 20 mmol) and 4-chlorothiophenol (2.89 g, 20 mmol). The product was obtained as a yellow crystalline solid (3.04 g, 61%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06 (1H, d, J = 8.0 Hz, Ar), 7.25-7.44 (6H, m, Ar), 7.87 and 7.89 (1H, 2×d, J = 1.6 Hz, Ar), 10.3 (1H, s, C*H*O).

2.3.1.2 2-(Phenylsulfanyl)benzaldehyde (71b)



2-(Phenylsulfanyl)benzaldehyde (**71b**) was prepared according to the general procedure from 2-fluorobenzaldehyde (1.24 g, 10 mmol) and thiophenol (1.10 g, 10 mmol). The product was obtained as light yellow oil in quantitative yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.10 (1H, d, J = 8.0 Hz, Ar), 7.30-7.46 (7H, m, Ar), 7.88 (1H, d, J = 7.6 Hz, Ar), 10.39 (1H, s, C*H*O).

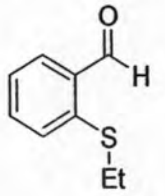
2.3.2 Synthesis of aliphatic thiolated aidehydes



A mixture of acetonitrile, a sodium ethanethiolate or sodium methanethiolate (1 equiv), and 2-fluorobenzaldehyde (1 equiv) was stirred at room temperature until

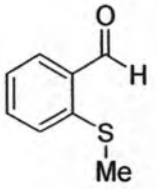
the aldehyde disappeared (TLC). The yellow slurry was diluted with water and extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was purified on siiica gel (5% ethyl acetate in hexanes).

2.3.2.1 2-(Ethylsulfanyl)benzaldehyde (71c)



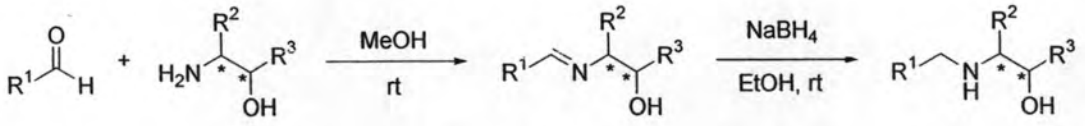
2-(Ethylsulfanyl)benzaldehyde (**71c**) was prepared according to the general procedure from 2-fluorobenzaldehyde (0.302 g, 2.4 mmol) and sodium ethanethiolate (0.205 g, 2.4 mmol). The product was obtained as light yellow oil (0.143 g, 35%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.37 (3H, t, J = 7.4 Hz, CH_2CH_3), 2.98 (2H, q, J = 7.4 Hz, CH_2CH_3), 7.27-7.33 (1H, m, Ar), 7.42 (1H, d, J = 8.0 Hz, Ar), 7.48-7.54 (1H, m, Ar), 7.83 (1H, d, J = 7.8 Hz, Ar), 10.38 (1H, s, C*H*O).

2.3.2.2 2-(Methylsulfanyl)benzaldehyde (71d)



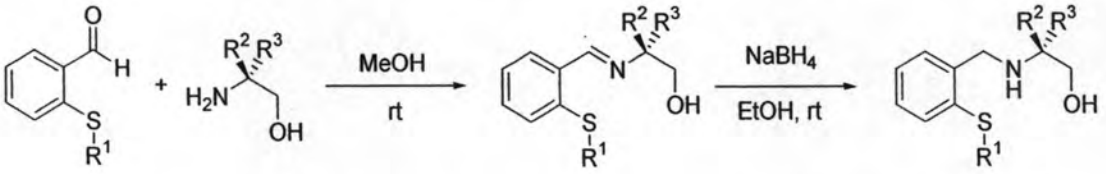
2-(Methylsulfanyl)benzaldehyde (**71d**) was prepared according to the general procedure from 2-fluorobenzaldehyde (0.302 g, 2.4 mmol) and sodium methanethiolate (0.169 g, 2.4 mmol). The product was obtained as light yellow oil (0.118 g, 32%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.50 (3H, s, SCH_3), 7.25-7.31 (1H, m, Ar), 7.34 (1H, d, J = 8.0, Ar), 7.50-7.56 (1H, m, Ar), 7.81 (1H, d, J = 7.8 Hz, Ar), 10.26 (1H, s, C*H*O).

2.4 General procedure for the preparation of chiral ligands

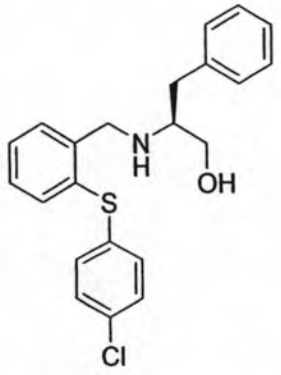


A mixture of an appropriate chiral amino alcohol or chiral amine (1.0 mmol), and an aldehyde (1.0 mmol) in methanol (2 mL) was stirred at room temperature until the starting materials were totally consumed. The solvent was removed *in vacuo* to afford the crude imine. The imine was dissolved in ethanol (2 mL) and cooled to 0 °C. Sodium borohydride (1.0 mmol) was then added. After the imine was consumed according to TLC analysis, the reaction was quenched with dil. HCl. After neutralization with saturated $NaHCO_3$, the reaction mixture was concentrated under reduced pressure and the residue was extracted with ethyl acetate and washed with water. The organic layer was dried over anhydrous Na_2SO_4 and the solvent removed. The crude products were purified by flash column chromatography (gradient of hexanes/ethyl acetate).

2.4.1 Synthesis of thiolated amino-alcohol ligands (69)



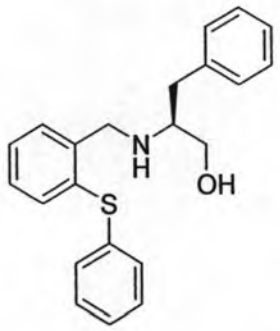
2.4.1.1 *N*-(2'-(4"-Chlorophenylsulfanyl))benzyl-(*S*)-2-amino-3-phenylpropan-1-ol [(*S*)-69a]



N-(2'-(4"-Chlorophenylsulfanyl))benzyl-(*S*)-2-amino-3-phenylpropan-1-ol [(*S*)-**69a**] was prepared according to the general procedure using the aldehyde **71a** (0.249 g, 1.0 mmol) and (*S*)-phenylalaninol (0.151 g, 1.0 mmol). The product was

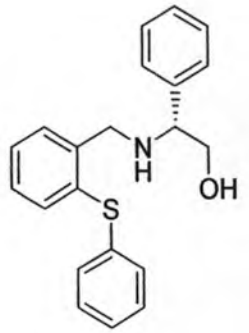
obtained as a white crystalline solid (0.276 g, 85%). m.p. 75-77 °C; $[\alpha]_D^{23}$ = -35.4 (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.78 and 2.79 (2H, 2×AB, *J* = 13.6 Hz, CHC*H*$_2$Ar), 2.95 (1H, AB*X*, J_{AX} = 3.8, J_{BX} = 5.4 Hz, C*H*NH), 3.36 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 5.4 Hz, CH_aH_bOH), 3.66 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 3.8 Hz, CH_aH_bOH), 3.89 (2H, s, C*H*$_2$NH), 7.09-7.33 (13H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 38.0, 49.6, 60.0, 62.6, 126.7, 128.5, 128.7, 128.8, 129.4, 129.6, 130.3, 130.8, 131.4, 133.0, 133.7, 134.1, 134.9, 138.4; Anal. Calcd for $C_{22}H_{22}ClNOS$: C, 68.82; H, 5.78; N, 3.65. Found: C, 68.63; H, 5.69; N, 3.63%.

2.4.1.2 *N*-2'-(Phenylsulfanyl)benzyl-(*S*)-2-amino-3-phenylpropan-1-ol [(*S*)-69b]



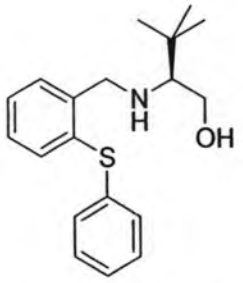
N-2'-(Phenylsulfanyl)benzyl-(*S*)-2-amino-3-phenylpropan-1-ol [(*S*)-**69b**] was prepared according to the general procedure using the aldehyde **71b** (0.214 g, 1.0 mmol) and (*S*)-phenylalaninol (0.151 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.307 g, 86%). m.p. 48-50 °C; $[\alpha]_D^{25}$ = -33.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.78 and 2.79 (2H, 2×AB, *J* = 13.6 Hz, CHC*H*$_2$Ar), 2.96 (1H, AB*X*, J_{AX} = 3.6, J_{BX} = 5.2 Hz, C*H*NH), 3.35 (1H, A*B*X, J_{AB} = 11.1, J_{BX} = 5.2 Hz, CH_aH_bOH), 3.66 (1H, *A*BX, J_{AB} = 11.1, J_{AX} = 3.6 Hz, CH_aH_bOH), 3.93 (2H, s, C*H*$_2$NH), 7.13-7.35 (14H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.3, 49.1, 59.9, 62.0, 126.5, 126.8, 128.1, 128.6, 128.8, 129.2, 129.3, 129.9, 130.3, 133.6, 134.3, 135.8, 137.9, 139.4; Anal. Calcd for $C_{22}H_{23}NOS$: C, 75.61; H, 6.63; N, 4.01. Found: C, 75.55; H, 6.64; N, 4.02%.

2.4.1.3 *N*-2'-(Phenylsulfanyl)benzyl-(*R*)-2-amino-2-phenylethanol [(*R*)-69c]



N-2'-(Phenylsulfanyl)benzyl-(*R*)-2-amino-2-phenylethanol [(*R*)-**69c**] was prepared according to the general procedure using the aldehyde **71b** (0.214 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.255 g, 73%). m.p. 80-82 °C; $[\alpha]_D^{23}$ = -54.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.56 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.4 Hz, CH_aH_bOH), 3.69 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.82 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.4 Hz, C*H*NH), 3.76 and 3.91 (2H, AB, *J* = 13.0 Hz, CH_2NH), 7.19-7.37 (14H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 49.7, 64.1, 66.3, 126.8, 127.4, 127.8, 127.9, 128.4, 128.7, 129.2, 130.1, 130.4, 133.5, 134.5, 136.0, 139.4, 140.0; Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18. Found: C, 75.13; H, 6.35; N, 4.18%.

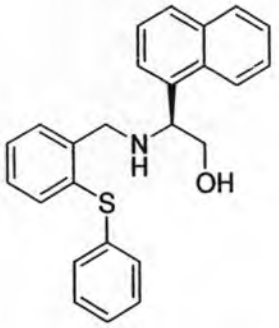
2.4.1.4 *N*-(2'-Phenylsulfanyl)benzyl-(*S*)-2-amino-3,3-dimethylbutan-1-ol [(*S*)-69d]



N-(2'-Phenylsulfanyl)benzyl-(*S*)-2-amino-3,3-dimethylbutan-1-ol [(*S*)-**69d**] was prepared according to the general procedure using the aldehyde **71b** (0.214 g, 1.0 mmol) and (*S*)-*tert*-leucinol (0.117 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.281 g, 80%). m.p. 38-40 °C; $[\alpha]_D^{23}$ = -20.4 (*c* 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (9H, s, 3×CH_3), 2.45 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 6.8

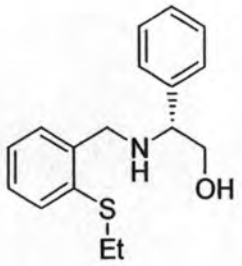
Hz, C*H*C(CH$_3$)$_3$), 3.53 (1H, A*B*X, J_{AB} = 11.2, J_{BX} = 6.8 Hz, CH$_a$*H*$_b$OH), 3.72 (1H, *A*BX, J_{AB} = 11.2, J_{AX} = 4.4 Hz, C*H*$_a$H$_b$OH), 4.04 and 4.19 (2H, AB, J = 12.8 Hz, C*H*$_2$NH), 7.20-7.35 (8H, m, Ar), 7.57 (1H, d, J = 7.6 Hz, Ar); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 27.1, 34.1, 52.2, 60.0, 67.5, 126.8, 128.3, 128.9, 129.3, 129.8, 131.1, 133.9, 134.3, 135.8, 139.4; Anal. Calcd for C$_{19}$H$_{25}$NOS: C, 72.34; H, 7.99; N, 4.44. Found: C, 72.26; H, 7.86; N, 4.53%.

2.4.1.5 *N*-2'-(Phenylsulfanyl)benzyl-(*S*)-2-amino-2-naphthylethanol [(*S*)-69e]



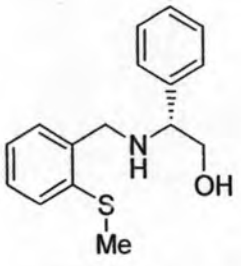
N-2'-(Phenylsulfanyl)benzyl-(*S*)-2-amino-2-naphthylethanol [(*S*)-**69e**] was prepared according to the general procedure using the aldehyde **71b** (0.043 g, 0.2 mmol) and (*S*)-naphth-1-ylglycinol [131] (0.037 g, 0.2 mmol). The product was obtained as a white crystalline solid (0.059 g, 89%). m.p. 110-111 °C; $[\alpha]_D^{25}$ = +23.6 (*c* 0.5, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz) δ 3.82-3.86 (2H, m, C*H*$_2$OH), 4.03 (2H, AB, J = 13.2 Hz, C*H*$_2$NH), 4.99 (1H, t, J = 5.8 Hz, C*H*NH), 7.04-7.28 (8H, m, Ar), 7.49-7.57 (4H, m, Ar), 7.84-7.96 (4H, m, Ar); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 48.7, 59.8, 64.9, 122.1, 125.0, 125.7, 125.9, 126.7, 126.8, 128.3, 128.9, 129.0, 129.1, 129.2, 129.3, 129.4, 129.8, 130.2, 131.3, 133.9, 134.9, 135.5; Anal. Calcd for C$_{25}$H$_{23}$NOS: C, 77.89; H, 6.01; N, 3.63. Found: C, 77.90; H, 6.05; N, 3.65%.

2.4.1.6 *N*-(2'-Ethylsulfanyl)benzyl-(*R*)-2-amino-2-phenylethanol [(*R*)-69f]



N-(2'-Ethylsulfanyl)benzyl-(*R*)-2-amino-2-phenylethanol [(*R*)-**69f**] was prepared according to the general procedure using the aldehyde **71c** (0.133 g, 0.8 mmol) and (*R*)-phenylglycinol (0.110 g, 0.8 mmol). The product was obtained as a white crystalline solid (0.216 g, 87%). m.p. 83-85 °C; $[\alpha]_D^{23}$ = -67.7 (*c* 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.29 (3H, t, J = 7.4 Hz, CH_2CH_3), 2.92 (2H, q, J = 7.4 Hz, CH_2CH_3), 3.60 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.6 Hz, CH_aH_bOH), 3.72 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.2 Hz, CH_aH_bOH), 3.75 and 3.89 (2H, AB, J = 13.2 Hz, CH_2NH), 3.84 (1H, AB*X*, J_{AX} = 4.2, J_{BX} = 8.6 Hz, C*H*NH), 7.13 (1H, t, J = 7.4 Hz, Ar), 7.21-7.26 (2H, m, Ar), 7.29-7.39 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.2, 27.6, 49.6, 64.0, 66.3, 125.7, 127.5, 127.9, 128.1, 128.7, 129.9, 136.4, 137.9, 139.3; Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04; H, 7.36; N, 4.87. Found: C, 71.06; H, 7.40; N, 4.85%.

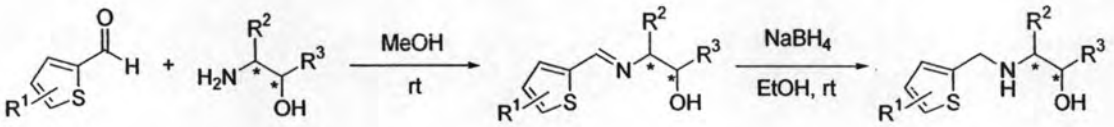
2.4.1.7 *N*-(2'-Methylsulfanyl)benzyl-(*R*)-2-amino-2-phenyl-ethanol [(*R*)-69g]



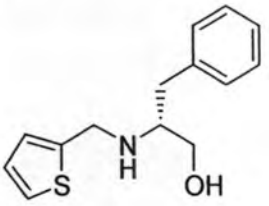
N-(2'-Methylsulfanyl)benzyl-(*R*)-2-amino-2-phenyl-ethanol [(*R*)-**69g**] was prepared according to the general procedure using the aldehyde **71d** (0.107 g, 0.7 mmol) and (*R*)-phenylglycinol (0.096 g, 0.7 mmol). The product was obtained as a white crystalline solid (0.174 g, 83%). m.p. 72-75 °C; $[\alpha]_D^{23}$ = -71.4 (*c* 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.46 (3H, s, CH_3), 3.63 (1H, AB*X*, J_{AX} = 4.0, J_{BX} = 8.4

Hz, C*H*NH), 3.72 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.4 Hz, CH_aH_bOH), 3.74 and 3.89 (2H, AB, J = 13.2 Hz, CH_2NH), 3.85 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.0 Hz, CH_aH_bOH), 7.09-7.13 (1H, m, Ar), 7.22-7.38 (8H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.0, 49.4, 64.1, 66.2, 125.0, 126.2, 127.5, 128.0, 128.3, 128.8, 129.8, 136.2, 138.1, 138.9; Anal. Calcd for $C_{16}H_{19}NOS$: C, 70.29; H, 7.00; N, 5.12. Found: C, 70.20; H, 7.09; N, 5.09%.

2.4.2 Synthesis of thiophene-substituted amino-alcohol ligands (70)

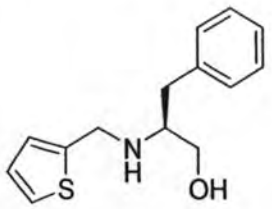


2.4.2.1 (*R*)-3-Phenyl-2-[(2′-thienylmethyl)amino]propan-1-ol [(*R*)-70a]



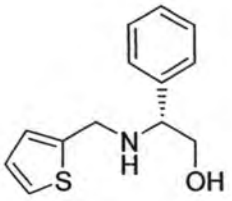
(*R*)-3-Phenyl-2-[(2′-thienylmethyl)amino]propan-1-ol [(*R*)-**70a**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*R*)-phenylalaninol (0.151 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.234 g, 92%). m.p. 85-87 °C; $[\alpha]_D^{23}$ = +11.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.79 (1H, AB, J = 13.6 Hz, CH_aH_bPh), 2.81 (1H, AB, J = 13.6 Hz, CH_aH_bPh), 3.01 (1H, AB*X*, J_{AX} = 4.0, J_{BX} = 5.6 Hz, C*H*NH), 3.36 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 5.6 Hz, CH_aH_bOH), 3.64 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.0 Hz, CH_aH_bOH), 4.00 (2H, AB, J = 14.0 Hz, CH_2NH), 6.86 (1H, d, J = 2.4 Hz, thienyl), 6.93 (1H, dd, J = 3.6 Hz, thienyl), 7.16-7.32 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.9, 45.6, 59.1, 62.5, 124.7, 125.1, 126.5, 126.7, 128.6, 129.2, 138.2, 143.3; Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66. Found: C, 67.99; H, 6.97; N, 5.73%.

2.4.2.2 (*S*)-3-Phenyl-2-[(2′-thienylmethyl)amino]propan-1-ol [(*S*)-70a]



(*S*)-3-Phenyl-2-[(2′-thienylmethyl)amino]propan-1-ol [(*S*)-**70a**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-phenylalaninol (0.151 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.207 g, 84%). m.p. 85-87 °C; $[\alpha]_D^{23}$ = -11.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.79 (1H, AB, *J* = 13.6 Hz, C*H*$_a$H$_b$Ph), 2.80 (1H, AB, *J* = 13.6 Hz, CH$_a$*H*$_b$Ph), 3.01 (1H, AB*X*, J_{AX} = 3.8, J_{BX} = 5.8 Hz, C*H*NH), 3.36 (1H, A*B*X, J_{AB} = 11.0, J_{BX} = 5.8 Hz, CH$_a$*H*$_b$OH), 3.64 (1H, *A*BX, J_{AB} = 11.0, J_{AX} = 3.8 Hz, C*H*$_a$H$_b$OH), 4.00 (2H, AB, *J* = 14.0 Hz, C*H*$_2$NH), 6.86 (1H, d, *J* = 2.8 Hz, thienyl), 6.93 (1H, dd, *J* = 3.6 Hz, thienyl), 7.16-7.32 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.8, 45.6, 59.1, 62.5, 124.7, 125.1, 126.5, 126.7, 128.6, 129.2, 138.2, 143.3; Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66. Found: C, 68.00; H, 6.94; N, 5.65%.

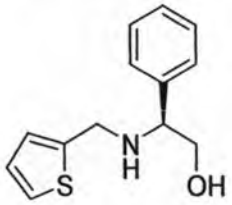
2.4.2.3 (*R*)-2-Phenyl-2-[(2′-thienylmethyl)amino]ethanol [(*R*)-70b]



(*R*)-2-Phenyl-2-[(2′-thienylmethyl)amino]ethanol [(*R*)-**70b**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.242 g, 93%). m.p. 58-60 °C; $[\alpha]_D^{23}$ = -97.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.59 (1H, A*B*X, J_{AB} = 11.0, J_{BX} = 8.8 Hz, CH$_a$*H*$_b$OH), 3.71 (1H, *A*BX, J_{AB} = 11.0, J_{AX} = 4.0 Hz, C*H*$_a$H$_b$OH), 3.87 (1H, AB*X*, J_{AX} = 4.0, J_{BX} = 8.8 Hz, C*H*NH), 3.81 and 3.96 (2H, AB, *J* = 14.0 Hz, C*H*$_2$NH), 6.86-6.90 (1H, m, thienyl), 6.94 (1H, dd, *J* = 3.6 Hz, thienyl), 7.21-7.40 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.6, 63.4, 66.6, 124.7, 125.2, 126.7, 127.4, 127.8, 128.8, 139.8, 143.3;

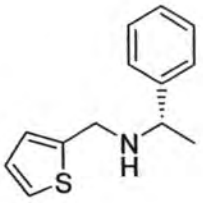
Anal. Calcd for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48; N, 6.00. Found: C, 66.99; H, 6.47; N, 6.02%.

2.4.2.4 (*S*)-2-Phenyl-2-[(2′-thienylmethyl)amino]ethanol [(*S*)-70b]



(*S*)-2-Phenyl-2-[(2′-thienylmethyl)amino]ethanol [(*S*)-**70b**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.161 g, 89%). m.p. 58-60 °C; $[\alpha]_D^{23}$ = +97.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.59 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.71 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.87 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 3.81 and 3.96 (2H, AB, *J* = 14.0 Hz, CH_2NH), 6.88 (1H, d, *J* = 2.8 Hz, thienyl), 6.94 (1H, dd, *J* = 3.6 Hz, thienyl), 7.22 (1H, d, *J* = 5.2 Hz, thienyl), 7.30-7.40 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.6, 63.4, 66.6, 124.6, 125.3, 126.7, 127.4, 127.8, 128.8, 139.7, 143.2; Anal. Calcd for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48; N, 6.00. Found: C, 66.93; H, 6.48; N, 6.01%.

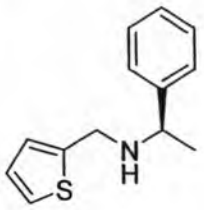
2.4.2.5 (*S*)-1-Phenyl-*N*-(2′-thienylmethyl)ethanamine [(*S*)-70c]



(*S*)-1-Phenyl-*N*-(2′-thienylmethyl)ethanamine [(*S*)-**70c**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-α-methylbenzylamine (0.121 g, 1.0 mmol). The product was obtained as colorless oil (0.207 g, 92%). $[\alpha]_D^{25}$ = -61.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (3H, d, *J* = 6.8 Hz, CH_3CH), 3.80-3.91 (3H, m, C*H*NH and CH_2NH), 6.85-6.91 (1H, m, thienyl), 6.95 (1H, dd, *J* = 3.4 Hz, thienyl), 7.21-7.38 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.3, 46.0, 57.0, 124.3, 124.9, 126.6, 126.8, 127.1,

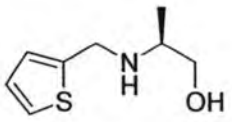
128.5, 144.1, 145.0; Anal. Calcd for $C_{13}H_{15}NS$: C, 71.84; H, 6.96; N, 6.44. Found: C, 71.82; H, 6.94; N, 6.48%.

2.4.2.6 (*R*)-1-Phenyl-*N*-(2′-thienylmethyl)ethanamine [(*R*)-70c]



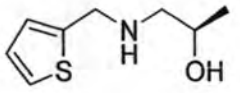
(*R*)-1-Phenyl-*N*-(2′-thienylmethyl)ethanamine [(*R*)-**70c**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*R*)-α-methylbenzylamine (0.121 g, 1.0 mmol). The product was obtained as colorless oil (0.223 g, 94%). $[\alpha]_D^{25}$ = +59.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (3H, d, *J* = 6.4 Hz, C*H*$_3$CH), 3.80-3.90 (3H, m, C*H*NH and C*H*$_2$NH), 6.88 (1H, d, *J* = 3.2 Hz, thienyl), 6.93-6.97 (1H, m, thienyl), 7.21-7.37 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.3, 46.0, 57.0, 124.3, 124.9, 126.6, 126.8, 127.1, 128.5, 144.1, 145.0; Anal. Calcd for $C_{13}H_{15}NS$: C, 71.84; H, 6.96; N, 6.44. Found: C, 71.83; H, 6.91; N, 6.44%.

2.4.2.7 (*S*)-2-Methyl-2-[(2′-thienylmethyl)amino]propan-1-ol [(*S*)-70d]



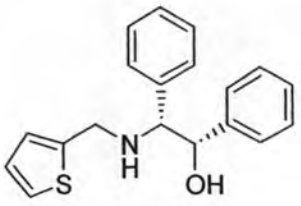
(*S*)-2-Methyl-2-[(2′-thienylmethyl)amino]propan-1-ol [(*S*)-**70d**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-alaninol (0.075 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.180 g, 90%). m.p. 53-55 °C; $[\alpha]_D^{25}$ = +52.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08 (3H. d, *J* = 6.4 Hz, C*H*$_3$CH), 2.87 (1H, m, *J* = 4.0 Hz, CH$_3$C*H*), 3.29 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 6.8 Hz, CH$_a$*H*$_b$OH), 3.59 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 2.8 Hz, C*H*$_a$H$_b$OH), 3.94 and 4.09 (2H, AB, *J* = 14.2 Hz, C*H*$_2$NH), 6.91-6.96 (2H, m, thienyl), 7.20 and 7.21 (1H, 2×d, *J* = 2.2 Hz, thienyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.9, 45.5, 53.5, 65.5, 124.6, 125.0, 126.7, 143.7; Anal. Calcd for $C_8H_{13}NOS$: C, 56.10; H, 7.65; N, 8.18. Found: C, 56.11; H, 7.64; N, 8.20%.

2.4.2.8 (*R*)-1-[(2′-Thienylmethyl)amino]propan-2-ol [(*R*)-70e]



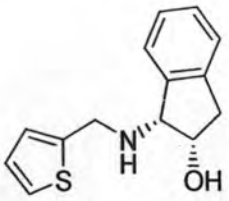
(*R*)-1-[(2′-Thienylmethyl)amino]propan-2-ol [(*R*)-**70e**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*R*)-1-amino-propan-2-ol (0.075 g, 1.0 mmol). The product was obtained as colorless oil (0.158 g, 85%). $[\alpha]_D^{25}$ = -39.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, d, *J* = 6.0 Hz, C*H*$_3$CH), 2.46 (1H, A*B*X, J_{AB} = 12.1, J_{BX} = 9.2 Hz, CH$_a$*H*$_b$OH), 2.75 (1H, *A*BX, J_{AB} = 12.1, J_{AX} = 3.2 Hz, C*H*$_a$H$_b$OH), 3.81 (1H, m, C*H*OH), 4.00 (2H, s, C*H*$_2$NH), 6.91-6.96 (2H, m, thienyl), 7.20 and 7.21 (1H, 2×d, *J* = 1.4 Hz, thienyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.5, 47.9, 55.9, 65.6, 124.7, 125.3, 126.7, 143.2; Anal. Calcd for $C_8H_{13}NOS$: C, 56.10; H, 7.65; N, 8.18. Found: C, 56.34; H, 7.85; N, 8.33%.

2.4.2.9 (1*S*,2*R*)-Diphenyl-2-[(2′-thienylmethyl)amino]ethanol [(1*S*,2*R*)-70f]



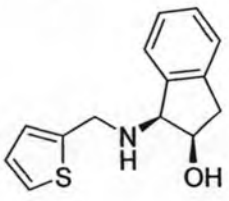
(1*S*,2*R*)-Diphenyl-2-[(2′-thienylmethyl)amino]ethanol [(1*S*,2*R*)-**70f**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (1*S*,2*R*)-2-amino-1,2-diphenylethanol (0.213 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.268 g, 91%). m.p. 150-152 °C; $[\alpha]_D^{25}$ = -44.6 (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.76 and 3.94 (2H, AB, *J* = 14.4 Hz, C*H*$_2$NH), 4.02 (1H, d, *J* = 5.6 Hz, C*H*OH), 4.90 (1H, d, *J* = 5.6 Hz, C*H*NH), 6.79 (1H, d, *J* = 2.8 Hz, thienyl), 6.92 (1H, dd, *J* = 3.4 Hz, thienyl), 7.10-7.30 (11H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.5, 67.5, 76.7, 125.1, 125.9, 126.9, 127.1, 128.0, 128.1, 128.3, 128.5, 128.8, 138.0, 140.4, 142.6; Anal. Calcd for $C_{19}H_{19}NOS$: C, 73.75; H, 6.19; N, 4.53. Found: C, 73.76; H, 6.26; N, 4.57%.

2.4.2.10 (1*R*)-[(Thiophen-2′-ylmethyl)-amino]-indan-(2*S*)-ol [(1*R*,2*S*)-70g]



(1*R*)-[(Thiophen-2′-ylmethyl)-amino]-indan-(2*S*)-ol [(1*R*,2*S*)-**70g**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (1*R*,2*S*)-(+)-*cis*-1-amino-2-indanol (0.149 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.213 g, 86%). m.p. 104-105 °C; $[\alpha]_D^{25}$ = -10.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.98 (1H, A*B*X, J_{AB} = 16.5, J_{BX} = 10.8 Hz, CH_aH_bCHOH), 3.07 (1H, *A*BX, J_{AB} = 16.5, J_{AX} = 3.2 Hz, CH_aH_bCHOH), 4.20 (3H, s, CH_2NHCH), 4.43 (1H, AB*X*, J_{AX} = 3.2, J_{BX} = 10.8 Hz, C*H*OH), 6.98 and 6.99 (1H, 2×d, *J* = 3.4 Hz, thienyl), 7.02-7.05 (1H, m, thienyl), 7.20-7.28 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.7, 46.9, 64.7, 70.8, 123.9, 124.9, 125.0, 125.5, 125.6, 126.8, 128.2, 141.1, 141.8, 143.1; Anal. Calcd for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.54; H, 6.20; N, 5.72%.

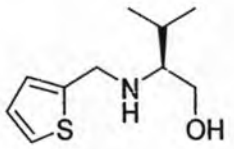
2.4.2.11 (1*S*)-[(Thiophen-2′-ylmethyl)-amino]-indan-(2*R*)-ol [(1*S*,2*R*)-70h]



(1*S*)-[(Thiophen-2′-ylmethyl)-amino]-indan-(2*R*)-ol [(1*S*,2*R*)-**70h**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (1*S*,2*R*)-(-)-*cis*-1-amino-2-indanol (0.149 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.164 g, 94%). m.p. 103-104 °C; $[\alpha]_D^{25}$ = +9.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.98 (1H, A*B*X, J_{AB} = 16.5, J_{BX} = 10.8 Hz, CH_aH_bCHOH), 3.07 (1H, *A*BX, J_{AB} = 16.5, J_{AX} = 3.2 Hz, CH_aH_bCHOH), 4.20 (3H, s, CH_2NHCH), 4.43 (1H, AB*X*, J_{AX} = 3.2, J_{BX} = 10.8 Hz, C*H*OH), 6.98 and 6.99 (1H, 2×d, *J* = 3.4 Hz, thienyl), 7.02-7.05 (1H, m, thienyl), 7.20-7.28 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.7, 46.9, 64.6, 70.8, 123.9, 125.0, 125.5, 125.6,

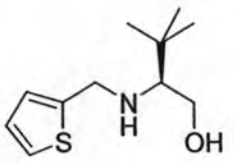
126.8, 126.9, 128.3, 141.1, 141.7, 142.9; Anal. Calcd for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.48; H, 6.07; N, 5.74%.

2.4.2.12 (*S*)-3-Methyl-2-[(2′-thienylmethyl)amino]butan-1-ol [(*S*)-70i]



(*S*)-3-Methyl-2-[(2′-thienylmethyl)amino]butan-1-ol [(*S*)-**70i**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-valinol (0.103 g, 1.0 mmol). The product was obtained as colorless oil (0.182 g, 95%). $[\alpha]_D^{25}$ = +9.5 (*c* 1.07, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91 and 0.96 (6H, 2×d, *J* = 6.8 Hz, $CH(CH_3)_2$), 1.85 (1H, m, *J* = 6.8 Hz, $CH(CH_3)_2$), 2.51 (1H, AB*X*, J_{AX} = 2.4, J_{BX} = 6.4 Hz, C*H*NH), 3.38 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 6.4 Hz, CH_aH_bOH), 3.63 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 2.4 Hz, CH_aH_bOH), 4.02 (2H, AB, *J* = 14.0 Hz, CH_2NH), 6.92-6.96 (2H, m, thienyl), 7.20 and 7.21 (1H, 2×d, *J* = 2.0 Hz, thienyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.4, 19.5, 28.8, 46.0, 60.5, 63.6, 124.6, 125.0, 126.7, 143.7; Anal. Calcd for $C_{10}H_{17}NOS$: C, 60.26; H, 8.60; N, 7.03. Found: C, 60.26; H, 8.57; N, 7.14%.

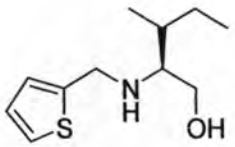
2.4.2.13 (*S*)-3,3-Dimethyl-2-[(2′-thienylmethyl)amino]butan-1-ol [(*S*)-70j]



(*S*)-3,3-Dimethyl-2-[(2′-thienylmethyl)amino]butan-1-ol [(*S*)-**70j**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-*tert*-leucinol (0.117 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.205 g, 94%). m.p. 40-42 °C; $[\alpha]_D^{25}$ = +2.4 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.95 (9H, s, 3×CH_3), 2.43 (1H, AB*X*, J_{AX} = 4.8, J_{BX} = 6.8 Hz, $CHC(CH_3)_3$), 3.41 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 6.8 Hz, CH_aH_bOH), 3.67 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.8 Hz, CH_aH_bOH), 4.03 and 4.18 (2H, AB, *J* = 14.0 Hz, CH_2NH), 6.93-6.97 (2H, m, thienyl), 7.21 and 7.22 (1H, 2×d, *J* = 1.6 Hz, thienyl); ^{13}C

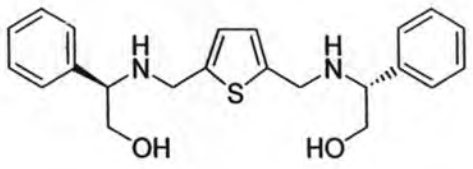
NMR ($CDCl_3$, 100 MHz) δ 27.3, 34.4, 48.8, 60.3, 67.0, 124.6, 125.0, 126.7, 144.0; Anal. Calcd for $C_{11}H_{19}NOS$: C, 61.93; H, 8.98; N, 6.57. Found: C, 61.95; H, 8.98; N, 6.62%.

2.4.2.14 (3*S*)-Methyl-(2*S*)-[(2′-thienylmethyl)amino]pentan-1-ol [(*S*,*S*)-70k]



(3*S*)-Methyl-(2*S*)-[(2′-thienylmethyl)amino]pentan-1-ol [(*S*,*S*)-**70k**] was prepared according to the general procedure using thiophene-2-carbaldehyde (0.112 g, 1.0 mmol) and (*S*)-isoleucinol (0.117 g, 1.0 mmol). The product was obtained as colorless oil (0.168 g, 91%). $[\alpha]_D^{25}$ = +22.8 (*c* 1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87 (3H, d, *J* = 6.8 Hz, C*H*$_3$CH), 0.91 (3H, t, *J* = 7.4 Hz, C*H*$_3$CH$_2$), 1.20 and 1.44 (2H, 2×m, CH$_3$C*H*$_2$), 1.65 (1H, m, CH$_3$C*H*), 2.64 (1H, m, C*H*NH), 3.36 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 6.8 Hz, CH$_a$*H*$_b$OH), 3.61 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.0 Hz, C*H*$_a$H$_b$OH), 3.94 and 4.09 (2H, AB, *J* = 13.8 Hz, C*H*$_2$NH), 6.92-6.97 (2H, m, thienyl), 7.21 and 7.22 (1H, 2×d, *J* = 2.4 Hz, thienyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.8, 14.4, 26.4, 35.1, 45.8, 60.3, 61.8, 124.6, 125.0, 126.7, 143.8; Anal. Calcd for $C_{11}H_{19}NOS$: C, 61.93; H, 8.98; N, 6.57. Found: C, 61.73; H, 9.06; N, 6.58%.

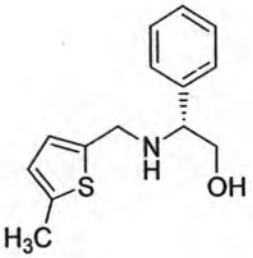
2.4.2.15 (*R*)-2-({5-[(2-Hydroxy-1-phenyl-ethylamino)-methyl]-thiophen-2-ylmethyl}-amino)-2-phenyl-ethanol [(*R*)-70l]



(*R*)-2-({5-[(2-Hydroxy-1-phenyl-ethylamino)-methyl]-thiophen-2-ylmethyl}-amino)-2-phenyl-ethanol [(*R*)-**70l**] was prepared according to the general procedure using thiophene-2,5-dicarbaldehyde (0.140 g, 1.0 mmol) and (*R*)-phenylglycinol (0.274 g, 2.0 mmol). The product was obtained as a white crystalline solid (0.325 g, 84%). m.p. 103-105 °C; $[\alpha]_D^{25}$ = -139.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.57 (2H, A*B*X, J_{AB} = 11.2, J_{BX} = 8.4 Hz, 2×CH$_a$*H*$_b$OH), 3.69 (2H, *A*BX, J_{AB} =

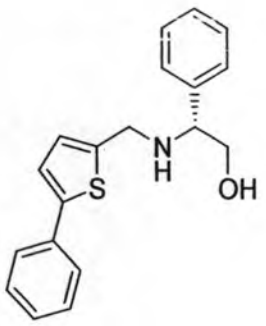
11.2, J_{AX} = 4.0 Hz, 2×CH_aH$_b$OH), 3.73 and 3.89 (4H, AB, J = 14.0 Hz, 2×CH_2NH), 3.86 (2H, ABX, J_{AX} = 4.0, J_{BX} = 8.4 Hz, 2×CHNH), 6.66 (2H, s, thienyl), 7.28-7.39 (10H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.9, 63.3, 66.7, 124.9, 127.4, 127.8, 128.7, 139.9, 142.8; Anal. Calcd for $C_{22}H_{26}N_2O_2S$: C, 69.08; H, 6.85; N, 7.32. Found: C, 69.16; H, 6.86; N, 7.38%.

2.4.2.16 (*R*)-2-{[(5′-Methyl-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-70m]



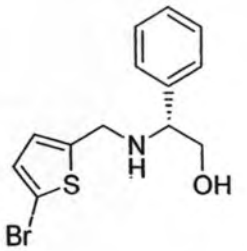
(*R*)-2-{[(5′-Methyl-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-**70m**] was prepared according to the general procedure using 5-methyl-2-thiophene carboxaldehyde (0.126 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.227 g, 91%). m.p. 83-85 °C; $[\alpha]_D^{23}$ = -103.3 (*c* 1.08, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.45 (3H, s, CH_3), 3.61 (1H, ABX, J_{AB} = 10.8, J_{BX} = 7.6 Hz, CH$_a$$H_b$OH), 3.71 (1H, ABX, J_{AB} = 10.8, J_{AX} = 4.4 Hz, CH_aH$_b$OH), 3.88 (1H, ABX, J_{AX} = 4.4, J_{BX} = 7.6 Hz, CHNH), 3.74 and 3.91 (2H, AB, J = 13.6 Hz, CH_2NH), 6.56-6.57 (1H, m, thienyl), 6.66 (1H, d, J = 3.2 Hz, thienyl), 7.32-7.40 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.4, 45.4, 63.1, 66.3, 124.7, 125.8, 127.5, 128.0, 128.8, 139.0, 139.5, 139.6; Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66. Found: C, 67.93; H, 6.94; N, 5.68%.

2.4.2.17 (*R*)-2-Phenyl-2-{[(5′-phenyl-2′-thienyl)methyl]amino}ethanol [(*R*)-70n]



(*R*)-2-Phenyl-2-{[(5′-phenyl-2′-thienyl)methyl]amino}ethanol [(*R*)-**70n**] was prepared according to the general procedure using 5-phenyl-2-thiophene carboxaldehyde (0.094 g, 0.5 mmol) and (*R*)-phenylglycinol (0.069 g, 0.5 mmol). The product was obtained as a white crystalline solid (0.148 g, 95%). m.p. 70-72 °C; $[\alpha]_D^{25}$ = -86.3 (*c* 0.54, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.63 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.74 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.81 and 3.97 (2H, AB, *J* = 14.2 Hz, CH_2NH), 3.92 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 6.84 (1H, d, *J* = 3.6 Hz, thienyl), 7.14 (1H, d, *J* = 3.6 Hz, thienyl), 7.25-7.41 (8H, m, Ar), 7.58 (2H, d, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.9, 63.3, 66.7, 122.6, 125.6, 126.2, 127.3, 127.4, 127.9, 128.7, 128.8, 134.5, 139.7, 143.0, 143.6; Anal. Calcd for $C_{19}H_{19}NOS$: C, 73.75; H, 6.19; N, 4.53. Found: C, 73.76; H, 6.15; N, 4.50%.

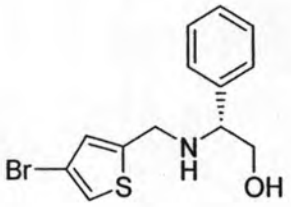
2.4.2.18 (*R*)-2-{[(5′-Bromo-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-70o]



(*R*)-2-{[(5′-Bromo-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-**70o**] was prepared according to the general procedure using 5-bromo-2-thiophene carboxaldehyde (0.191 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.122 g, 49%). m.p. 48-50 °C;

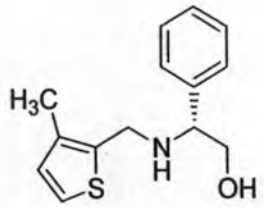
$[\alpha]_D^{23}$ = -82.5 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.59 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.4 Hz, CH_aH_bOH), 3.71 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.8 Hz, CH_aH_bOH), 3.74 and 3.87 (2H, AB, *J* = 13.6 Hz, CH_2NH), 3.85 (1H, AB*X*, J_{AX} = 4.8, J_{BX} = 8.4 Hz, C*H*NH), 6.61 (1H, d, *J* = 3.6 Hz, thienyl), 6.86 (1H, d, *J* = 3.6 Hz, thienyl), 7.30-7.42 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.9, 63.3, 66.7, 111.1, 125.4, 127.3, 127.9, 128.8, 129.4, 139.5, 145.4; Anal. Calcd for $C_{13}H_{14}BrNOS$: C, 50.01; H, 4.52; N, 4.49. Found: C, 50.00; H, 4.39; N, 4.59%.

2.4.2.19 (*R*)-2-{[(4′-Bromo-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-70p]



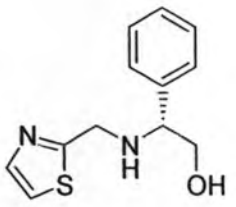
(*R*)-2-{[(4′-Bromo-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-**70p**] was prepared according to the general procedure using 4-bromo-2-thiophene carboxaldehyde (0.191 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as light yellow oil (0.289 g, 95%). $[\alpha]_D^{25}$ = -80.5 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.62 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.73 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.86 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 3.78 and 3.92 (2H, AB, *J* = 14.2 Hz, CH_2NH), 6.81 (1H, s, thienyl), 7.11 (1H, d, *J* = 1.6 Hz, thienyl), 7.30-7.40 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.3, 63.4, 66.6, 109.1, 122.0, 127.3, 127.8, 128.0, 128.9, 139.1, 144.5; Anal. Calcd for $C_{13}H_{14}BrNOS$: C, 50.01; H, 4.52; N, 4.49. Found: C, 49.83; H, 4.75; N, 4.22%.

2.4.2.20 (*R*)-2-{[(3′-Methyl-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-70q]



(*R*)-2-{[(3′-Methyl-2′-thienyl)methyl]amino}-2-phenylethanol [(*R*)-**70q**] was prepared according to the general procedure using 3-methyl-2-thiophene carboxaldehyde (0.126 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a light yellow crystalline solid (0.242 g, 90%). m.p. 84-85 °C; $[\alpha]_D^{25}$ = -101.2 (*c* 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.08 (3H, s, C*H*$_3$), 3.59 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.8 Hz, CH$_a$*H*$_b$OH), 3.72 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.4 Hz, C*H*$_a$H$_b$OH), 3.74 and 3.86 (2H, AB, *J* = 14.2 Hz, C*H*$_2$NH), 3.88 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 6.78 (1H, d, *J* = 5.2 Hz, thienyl), 7.12 (1H, d, *J* = 4.8 Hz, thienyl), 7.31-7.40 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.6, 43.5, 63.6, 66.6, 123.0, 127.3, 127.9, 128.8, 130.0, 134.2, 135.9, 139.7; Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66. Found: C, 67.61; H, 7.04; N, 5.47%.

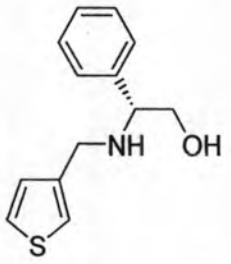
2.4.2.21 (*R*)-2-Phenyl-2-[(1′,3′-thiazol-2′-ylmethyl)amino]ethanol [(*R*)-70r]



(*R*)-2-Phenyl-2-[(1′,3′-thiazol-2′-ylmethyl)amino]ethanol [(*R*)-**70r**] was prepared according to the general procedure using thiazole-2-carboxaldehyde (0.339 g, 3.0 mmol) and (*R*)-phenylglycinol (0.412 g, 3.0 mmol). The product was obtained as light yellow oil (0.602 g, 88%). $[\alpha]_D^{25}$ = -70.4 (*c* 1.13, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.64 (1H, A*B*X, J_{AB} = 11.0, J_{BX} = 8.8 Hz, CH$_a$*H*$_b$OH), 3.74 (1H, *A*BX, J_{AB} = 11.0, J_{AX} = 4.4 Hz, C*H*$_a$H$_b$OH), 3.91 (1H, AB*X*, J_{AX} = 4.4 Hz, J_{BX} = 8.8 Hz, C*H*NH) 4.02 (2H, AB, *J* = 15.6 Hz, C*H*$_2$NH), 7.24-7.35 (6H, m, Ar), 7.68 (1H, d, *J* = 3.2 Hz, thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.2, 64.2, 66.8, 119.0, 127.4,

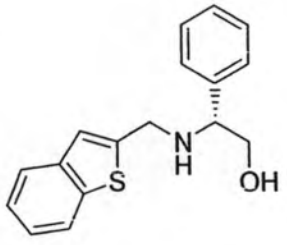
127.9, 128.8, 139.6, 142.4, 171.0; Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.51; H, 6.16; N, 11.94%.

2.4.2.22 (*R*)-2-Phenyl-2-[(3′-thienylmethyl)amino]ethanol [(*R*)-70s]



(*R*)-2-Phenyl-2-[(3′-thienylmethyl)amino]ethanol [(*R*)-**70s**] was prepared according to the general procedure using thiophene-3-carbaldehyde (0.112 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.160 g, 92%). m.p. 73-74 °C; $[\alpha]_D^{25}$ = -78.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.59 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 8.6 Hz, CH_aH_bOH), 3.71 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.2 Hz, CH_aH_bOH), 3.64 and 3.77 (2H, AB, *J* = 13.4 Hz, CH_2NH), 3.82 (1H, AB*X*, J_{AX} = 4.2, J_{BX} = 8.6 Hz, C*H*NH), 7.03 (1H, d, *J* = 4.8 Hz, thienyl), 7.08-7.12 (1H, m, thienyl), 7.26-7.39 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 46.1, 63.7, 66.6, 121.9, 125.9, 127.4, 127.6, 127.8, 128.7, 140.0, 140.7; Anal. Calcd for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48; N, 6.00. Found: C, 66.93; H, 6.48; N, 6.09%.

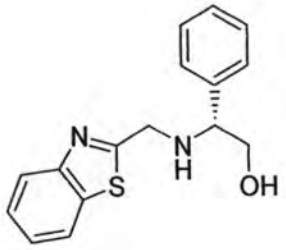
2.4.2.23 (*R*)-2-[(1′-Benzothien-2′-ylmethyl)amino]-2-phenylethanol [(*R*)-70t]



(*R*)-2-[(1′-Benzothien-2′-ylmethyl)amino]-2-phenylethanol [(*R*)-**70t**] was prepared according to the general procedure using 1-benzothiophene-2-carbaldehyde (0.162 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.181 g, 64%). m.p. 86-87 °C; $[\alpha]_D^{25}$ = -115.8 (*c*

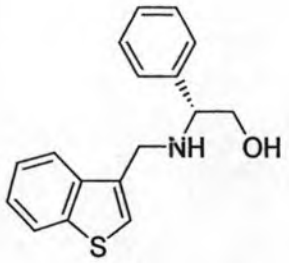
1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.71 (1H, A*B*X, J_{AB} = 11.2, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.75 (1H, *A*BX, J_{AB} = 11.2, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.91 and 4.12 (2H, AB, J = 14.4 Hz, CH_2NH), 3.95 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 7.13 (1H, s, thienyl), 7.26-7.41 (7H, m, Ar), 7.68 (1H, d, J = 8.4 Hz, Ar), 7.78 (1H, d, J = 7.2 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 46.1, 63.6, 66.5, 122.6, 122.8, 123.5, 124.4, 124.5, 127.8, 128.4, 129.1, 138.7, 139.8, 140.1, 143.0; Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; N, 4.94. Found: C, 72.05; H, 6.06; N, 4.95%.

2.4.2.24 (*R*)-2-[(1′,3′-Benzothiazol-2′-ylmethyl)amino]-2-phenylethanol [(*R*)-70u]



(*R*)-2-[(1′,3′-Benzothiazol-2′-ylmethyl)amino]-2-phenylethanol [(*R*)-**70u**] was prepared according to the general procedure using 1,3-benzothiazole-2-carbaldehyde (0.163 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a sticky yellow solid (0.160 g, 58%). $[\alpha]_D^{25}$ = -65.8 (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.74 (1H, A*B*X, J_{AB} = 11.0, J_{BX} = 8.6 Hz, CH_aH_bOH), 3.81 (1H, *A*BX, J_{AB} = 11.0, J_{AX} = 4.2 Hz, CH_aH_bOH), 4.00 (1H, AB*X*, J_{AX} = 4.2, J_{BX} = 8.6 Hz, C*H*NH), 4.16 (2H, AB, J = 16.0 Hz, CH_2NH), 7.29-7.38 (6H, m, Ar), 7.45 (1H, t, J = 7.8 Hz, Ar), 7.86 (1H, d, J = 7.8 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 49.0, 64.5, 66.9, 122.0, 123.0, 125.2, 126.3, 127.7, 128.3, 129.1, 135.2, 139.2, 153.3, 172.1; Anal. Calcd for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85. Found: C, 67.54; H, 5.65; N, 9.80%.

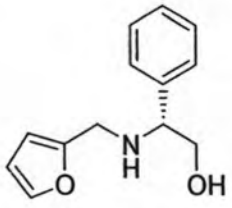
2.4.2.25 (*R*)-2-[(1′-Benzothien-3′-ylmethyl)amino]-2-phenylethanol [(*R*)-70v]



(*R*)-2-[(1′-Benzothien-3′-ylmethyl)amino]-2-phenylethanol [(*R*)-**70v**] was prepared according to the general procedure using 1-benzothiophene-3-carbaldehyde (0.162 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.258 g, 89%). m.p. 109-110 °C; $[\alpha]_D^{25}$ = -72.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.67 (1H, A*B*X, J_{AB} = 11.2, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.73 (1H, *A*BX, J_{AB} = 11.2, J_{AX} = 4.8 Hz, CH_aH_bOH), 3.92 and 4.05 (2H, AB, *J* = 13.6 Hz, CH_2NH), 3.95 (1H, AB*X*, J_{AX} = 4.8, J_{BX} = 8.8 Hz, C*H*NH), 7.31-7.40 (8H, m, Ar), 7.67-7.70 (1H, m, Ar), 7.82-7.86 (1H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.6, 64.4, 66.4, 122.0, 123.1, 124.4, 124.7, 124.8, 127.8, 128.4, 129.1, 133.3, 138.4, 138.9, 140.8; Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; N, 4.94. Found: C, 72.07; H, 6.09; N, 4.98%.

2.4.3 Synthesis of other heteroatom-substituted amino-alcohol ligands (72)

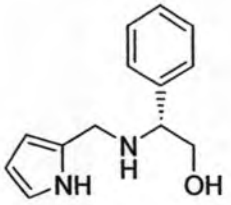
2.4.3.1 (*R*)-2-[(2′-Furylmethyl)amino]-2-phenylethanol [(*R*)-72a]



(*R*)-2-[(2′-Furylmethyl)amino]-2-phenylethanol [(*R*)-**72a**] was prepared according to the general procedure using furfural (0.096 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a light yellow crystalline solid (0.228 g, 94%). m.p. 55-56 °C; $[\alpha]_D^{25}$ = -98.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.64 and 3.81 (2H, AB, *J* = 14.6 Hz, CH_2NH), 3.66 (1H,

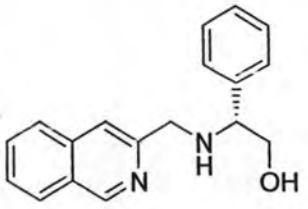
A*B*X, J_{AB} = 10.8, J_{BX} = 8.6 Hz, CH_aH_bOH), 3.74 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.6 Hz, CH_aH_bOH), 3.85 (1H, AB*X*, J_{AX} = 4.6, J_{BX} = 8.6 Hz, C*H*NH), 6.17 (1H, d, *J* = 2.8 Hz, furfuryl), 6.30 (1H, t, *J* = 1.6 Hz, furfuryl), 7.31-7.40 (6H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 43.2, 63.5, 66.2, 108.1, 110.3, 119.0, 127.6, 128.0, 128.8, 138.6, 142.2; Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.75; H, 6.93; N, 6.59%.

2.4.3.2 (*R*)-2-Phenyl-2-[(1*H*-pyrrol-2′-ylmethyl)amino]ethanol [(*R*)-72b]



(*R*)-2-Phenyl-2-[(1*H*-pyrrol-2′-ylmethyl)amino]ethanol [(*R*)-**72b**] was prepared according to the general procedure using 2-pyrrolecarbaldehyde (0.095 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a light brown crystalline solid (0.235 g, 85%). m.p. 89-90 °C; $[\alpha]_D^{25}$ = +5.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.58 and 3.73 (2H, AB, *J* = 13.6 Hz, CH_2NH), 3.61 (1H, A*B*X, J_{AB} = 11.4, J_{BX} = 8.4 Hz, CH_aH_bOH), 3.73 (1H, *A*BX, J_{AB} = 11.4, J_{AX} = 4.0 Hz, CH_aH_bOH), 3.80 (1H, AB*X*, J_{AX} = 4.0, J_{BX} = 8.4 Hz, C*H*NH), 5.97 (1H, s, pyrrole), 6.12 (1H, d, *J* = 2.4 Hz, pyrrole), 6.73 (1H, s, pyrrole), 7.30-7.41 (5H, m, Ar), 8.98 (1H, br, N*H*-pyrrole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 43.7, 63.5, 66.5, 107.1, 108.0, 117.8, 127.4, 127.9, 128.8, 129.3, 139.5; Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.17; H, 7.38; N, 12.95%.

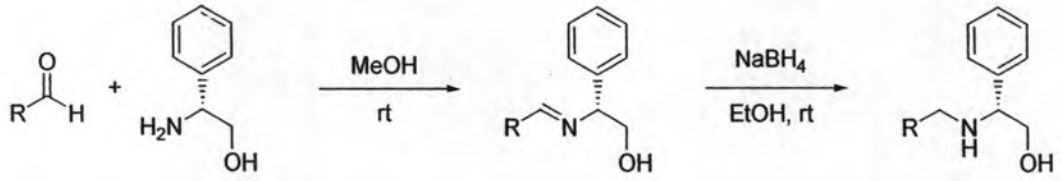
2.4.3.3 (*R*)-2-[(Isoquinolin-3′-ylmethyl)amino]-2-phenylethanol [(*R*)-72c]



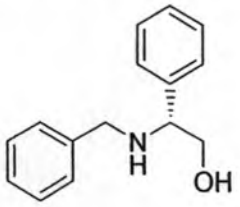
(*R*)-2-[(Isoquinolin-3′-ylmethyl)amino]-2-phenylethanol [(*R*)-**72c**] was prepared according to the general procedure using isoquinoline-3-carbaldehyde (0.159 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained

as viscous yellow oil (0.101 g, 36%). $[\alpha]_D^{25}$ = -43.2 (*c* 0.28, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.91 (1H, A*B*X, J_{AB} = 11.6, J_{BX} = 8.8 Hz, CH_aH_bOH), 4.10 (1H, *A*BX, J_{AB} = 11.6, J_{AX} = 3.6 Hz, CH_aH_bOH), 4.15 and 4.34 (2H, AB, *J* = 15.6 Hz, CH_2NH), 4.21 (1H, AB*X*, J_{AX} = 3.6, J_{BX} = 8.8 Hz, C*H*NH), 7.26-7.39 (4H, m, Ar), 7.48 (1H, s, Ar), 7.49 (1H, s, Ar), 7.54 (1H, t, *J* = 7.4 Hz, Ar), 7.70 (1H, t, *J* = 7.6 Hz, Ar), 7.79 (1H, d, *J* = 7.6 Hz, Ar), 8.09 (2H, t, *J* = 7.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 50.4, 65.0, 65.1, 119.9, 126.8, 127.5, 127.6, 128.1, 128.6, 128.7, 128.8, 128.9, 129.0, 130.1, 137.3, 147.1.

2.4.4 Synthesis of other bidentate amino-alcohol ligands (73)

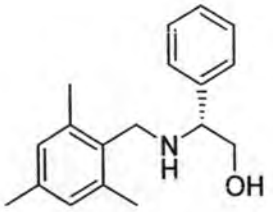


2.4.4.1 (*R*)-2-(Benzylamino)-2-phenylethanol [(*R*)-73a]



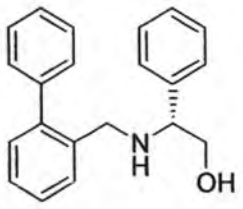
(*R*)-2-(Benzylamino)-2-phenylethanol [(*R*)-**73a**] was prepared according to the general procedure using benzaldehyde (0.106 g, 1.0 mmol) and (*R*)-phenylglycinol (0.137 g, 1.0 mmol). The product was obtained as a white crystalline solid (0.243 g, 94%). m.p. 89-90 °C; $[\alpha]_D^{25}$ = -83.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.61 and 3.79 (2H, AB, *J* = 12.8 Hz, CH_2NH), 3.61 (1H, A*B*X, J_{AB} = 11.0, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.72 (1H, *A*BX, J_{AB} = 11.0, J_{AX} = 4.0 Hz, CH_aH_bOH), 3.85 (1H, AB*X*, J_{AX} = 4.0, J_{BX} = 8.8 Hz, C*H*NH), 7.25-7.41 (10H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 50.9, 63.8, 66.4, 127.3, 127.4, 127.5, 127.9, 128.4, 128.5, 128.8, 128.9; Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.29; H, 7.56; N, 6.18%.

2.4.4.2 (*R*)-2-[(2',4',6'-Trimethylbenzyl)amino]-2-phenylethanol [(*R*)-73b]



(*R*)-2-[(2',4',6'-Trimethylbenzyl)amino]-2-phenylethanol [(*R*)-**73b**] was prepared according to the general procedure using mesitaldehyde (0.089 g, 0.6 mmol) and (*R*)-phenylglycinol (0.082 g, 0.6 mmol). The product was obtained as a white crystalline solid (0.165 g, 88%). m.p. 97-99 °C; $[\alpha]_D^{25}$ = -35.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.24 (3H, s, C*H*$_3$), 2.26 (6H, s, 2×C*H*$_3$), 3.57 (1H, A*B*X, J_{AB} = 11.2, J_{BX} = 9.0 Hz, CH$_a$*H*$_b$OH), 3.60 and 3.69 (2H, AB, *J* = 12.4 Hz, C*H*$_2$NH), 3.69 (1H, *A*BX, J_{AB} = 11.2, J_{AX} = 4.2 Hz, C*H*$_a$H$_b$OH), 3.87 (1H, AB*X*, J_{AX} = 4.2, J_{BX} = 9.0 Hz, C*H*NH), 6.84 (2H, s, Ar), 7.30-7.42 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.5, 20.9, 45.3, 65.3, 66.2, 127.3, 128.0, 128.7, 129.1, 137.0, 137.2, 139.7, 139.8; Anal. Calcd for $C_{18}H_{23}NO$: C, 80.26; H, 8.61; N, 5.20. Found: C, 80.34; H, 8.75; N, 5.39%.

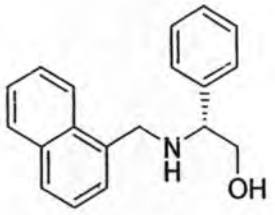
2.4.4.3 (*R*)-2-[(Biphenyl-2'-ylmethyl)amino]-2-phenylethanol [(*R*)-73c]



(*R*)-2-[(Biphenyl-2'-ylmethyl)amino]-2-phenylethanol [(*R*)-**73c**] was prepared according to the general procedure using 2-biphenylcarboxaldehyde (0.091 g, 0.5 mmol) and (*R*)-phenylglycinol (0.069 g, 0.5 mmol). The product was obtained as a white crystalline solid (0.136 g, 85%). m.p. 72-73 °C; $[\alpha]_D^{25}$ = -64.4 (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.42 (1H, A*B*X, J_{AB} = 10.4, J_{BX} = 8.4 Hz, CH$_a$*H*$_b$OH), 3.57 and 3.76 (2H, AB, *J* = 12.4 Hz, C*H*$_2$NH), 3.59 (1H, *A*BX, J_{AB} = 10.4, J_{AX} = 4.4 Hz, C*H*$_a$H$_b$OH), 3.65 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.4 Hz, C*H*NH), 7.10-7.20 (2H, m, Ar), 7.27-7.44 (12H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 49.1, 64.1, 66.5, 127.0,

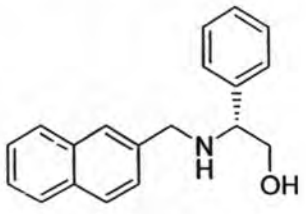
127.1, 127.3, 127.6, 128.2, 128.6, 129.0, 129.8, 130.3, 137.0, 140.0, 141.1, 142.1; Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.17; H, 7.00; N, 4.48%.

2.4.4.4 (*R*)-2-[(1′-Naphthylmethyl)amino]-2-phenylethanol [(*R*)-73d]



(*R*)-2-[(1′-Naphthylmethyl)amino]-2-phenylethanol [(*R*)-**73d**] was prepared according to the general procedure using 1-naphthaldehyde (0.094 g, 0.6 mmol) and (*R*)-phenylglycinol (0.082 g, 0.6 mmol). The product was obtained as a white crystalline solid (0.186 g, 97%). m.p. 99-100 °C; $[\alpha]_D^{25}$ = -61.3 (*c* 0.60, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.57 (1H, A*B*X, J_{AB} = 10.8, J_{BX} = 9.0 Hz, CH_aH_bOH), 3.70 (1H, *A*BX, J_{AB} = 10.8, J_{AX} = 4.2 Hz, CH_aH_bOH), 3.93 (1H, AB*X*, J_{AX} = 4.2, J_{BX} = 9.0 Hz, C*H*NH), 4.05 and 4.21 (2H, AB, *J* = 12.8 Hz, CH_2NH), 7.33-7.44 (7H, m, Ar), 7.46-7.52 (2H, m, Ar), 7.77 and 7.79 (1H, 2×d, *J* = 3.0 Hz, Ar), 7.85 and 7.86 (1H, 2×d, *J* = 2.8 Hz, Ar), 8.01 and 8.03 (1H, 2×d, *J* = 2.8 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.9, 64.5, 66.5, 123.7, 125.4, 125.7, 126.2, 126.6, 127.4, 127.9, 128.1, 128.7, 128.8, 131.8, 133.9, 135.0, 140.0; Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.30; H, 7.09; N, 5.09%.

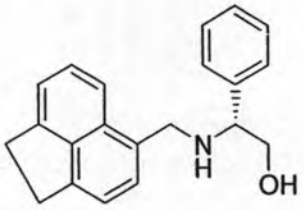
2.4.4.5 (*R*)-2-[(2′-Naphthylmethyl)amino]-2-phenylethanol [(*R*)-73e]



(*R*)-2-[(2′-Naphthylmethyl)amino]-2-phenylethanol [(*R*)-**73e**] was prepared according to the general proccdure using 2-naphthaldehyde (0.078 g, 0.5 mmol) and (*R*)-phenylglycinol (0.069 g, 0.5 mmol). The product was obtained as a white crystalline solid (0.141 g, 98%). m.p. 65-67 °C; $[\alpha]_D^{25}$ = -70.2 (*c* 0.5, $CHCl_3$); ^1H

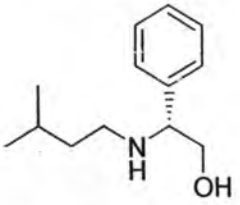
NMR ($CDCl_3$, 400 MHz) δ 3.69 (1H, A*B*X, J_{AB} = 11.2, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.74 (1H, *A*BX, J_{AB} = 11.2, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.77 and 3.99 (2H, AB, J = 13.2 Hz, CH_2NH). 3.90 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 7.32-7.47 (9H, m, Ar), 7.71 (1H, s, Ar), 7.78-7.81 (2H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.0, 63.8, 66.5, 125.8, 126.1, 126.6, 127.0, 127.5, 127.6, 127.7, 127.9, 128.2, 128.8, 132.7, 133.3, 136.5, 139.5; Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.23; H, 7.07; N, 4.92%.

2.4.4.6 (*R*)-2-[(1′,2′-Dihydroacenaphthylen-5′-ylmethyl)amino]-2-phenylethanol [(*R*)-73f]



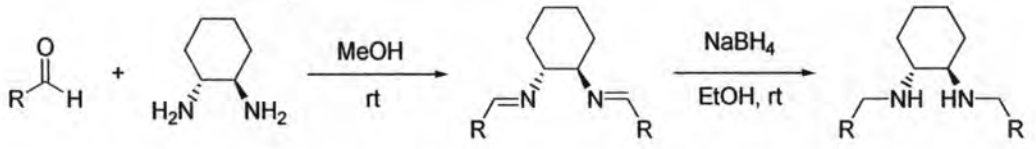
(*R*)-2-[(1′,2′-Dihydroacenaphthylen-5′-ylmethyl)amino]-2-phenylethanol [(*R*)-**73f**] was prepared according to the general procedure using 5-acenapthenecarboxaldehyde (0.091 g, 0.5 mmol) and (*R*)-phenylglycinol (0.069 g, 0.5 mmol). The product was obtained as a white crystalline solid (0.149 g, 95%). m.p. 142-144 °C; $[\alpha]_D^{25}$ = -60.6 (*c* 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.39 (4H, dd, J = 8.2 Hz, 2×CH_2), 3.56 (1H, A*B*X, J_{AB} = 10.6, J_{BX} = 8.8 Hz, CH_aH_bOH), 3.71 (1H, *A*BX, J_{AB} = 10.6, J_{AX} = 4.4 Hz, CH_aH_bOH), 3.91 (1H, AB*X*, J_{AX} = 4.4, J_{BX} = 8.8 Hz, C*H*NH), 4.00 and 4.17 (2H, AB, J = 12.8 Hz, CH_2NH), 7.22 (1H, d, J = 6.8 Hz, Ar), 7.30 (1H, d, J = 7.2 Hz, Ar) 7.35-7.48 (7H, m, Ar), 7.69 (1H, d, J = 8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.0, 30.6, 48.2, 64.2, 66.6, 118.8, 119.2, 119.3, 127.4, 127.8, 128.0, 128.1, 128.8, 130.3, 131.0, 139.6, 140.3, 145.8, 146.5; Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.18; H, 6.79; N, 4.75%.

2.4.4.7 (*R*)-2-[(3'-Methylbutyl)amino]-2-phenylethanol [(*R*)-73g]



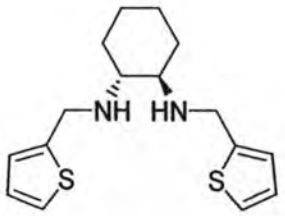
(*R*)-2-[(3'-Methylbutyl)amino]-2-phenylethanol [(*R*)-**73g**] was prepared according to the general procedure using isovaleraldehyde (0.052 g, 0.6 mmol) and (*R*)-phenylglycinol (0.082 g, 0.6 mmol). The product was obtained as colorless oil (0.097 g, 72%). $[\alpha]_D^{23}$ = -68.4 (*c* 0.53, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.84 (6H, 2×d, *J* = 6.8 Hz, 2×C*H*$_3$), 1.39 (2H, m, C*H*$_2$CH), 1.60 (1H, m, *J* = 6.7 Hz, C*H*$(CH_3)_2$), 2.45-2.63 (2H, m, C*H*$_2$OH), 3.55-3.64 (1H, m, C*H*NH), 3.70-3.83 (2H, m, C*H*$_2$NH), 7.26-7.35 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.5, 22.7, 26.0, 39.0, 45.5, 64.7, 66.4, 127.2, 127.6, 128.6, 140.4; Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.21; H, 10.49; N, 6.93%.

2.5 General procedure for the preparation of C_2-symmetrical bis-amino ligands (49)



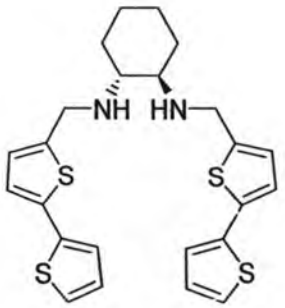
(1*R*,2*R*)-*trans*-Diaminocyclohexane (1 equiv) and the corresponding aldehyde (2 equiv) were dissolved in methanol (2 mL). The resulting mixture was stirred at room temperature until the starting materials were totally consumed. The solvent was evaporated in vacuum to obtain the crude imine. The imine was dissolved in ethanol (2 mL) and cooled to 0 °C. Sodium borohydride was then added. After the imine was consumed according to TLC analysis, the reaction was then quenched with dil. HCl. After neutralization with saturated $NaHCO_3$, the reaction mixture was concentrated under reduced pressure and the residue was extracted with ethyl acetate and washed with water. The organic layer was dried over anhydrous Na_2SO_4 and the solvent removed. The crude products were purified by flash column chromatography (gradient of petroleum ether/ethyl acetate).

2.5.1 (1*R*,2*R*)-*N*,*N*′-Bis(thien-2′-ylmethyl)cyclohexane-1,2-diamine (49a)



(1*R*,2*R*)-*N*,*N*′-Bis(thien-2′-ylmethyl)cyclohexane-1,2-diamine (**49a**) was prepared according to the general procedure using thiophene-2-carbaldehyde (0.282 g, 2.5 mmol) and (1*R*,2*R*)-*trans*-diaminocyclohexane (0.137 g, 1.2 mmol). The product was obtained as a white crystalline solid (0.253 g, 66%). m.p. 54-56 °C; $[\alpha]_D^{25}$ = -69.3 (*c* 0.61, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99-1.14 (2×1H, m, cyclohexyl), 1.18-1.29 (2×1H, m, cyclohexyl), 1.67-1.80 (2×1H, m, cyclohexyl), 2.10-2.18 (2×1H, m, cyclohexyl), 2.30-2.36 (2×1H, m, cyclohexyl) 3.90 and 4.13 (2×2H, AB, *J* = 14.0 Hz, C*H*$_2$NH), 6.91-6.97 (2×2H, m, thienyl), 7.17-7.22 (2×1H, m, thienyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 31.2, 45.2, 60.1, 124.3, 124.7, 126.6, 144.3.

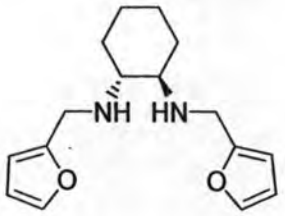
2.5.2 (1*R*,2*R*)-*N*,*N*′-Bis[5-(2,2′-bithienylmethyl)]cyclohexane-1,2-diamine (49b)



(1*R*,2*R*)-*N*,*N*′-Bis[5-(2,2′-bithienylmethyl)]cyclohexane-1,2-diamine (**49b**) was prepared according to the general procedure using 2,2′-bithiophene-5-carboxaldehyde (0.435 g, 2.2 mmol) and (1*R*,2*R*)-*trans*-diaminocyclohexane (0.128 g, 1.1 mmol). The product was obtained as a white crystalline solid (0.331 g, 63%). m.p. 98-99 °C; $[\alpha]_D^{25}$ = -5.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91-1.06 (2×1H, m, cyclohexyl), 1.10-1.30 (2×1H, m, cyclohexyl), 1.65-1.80 (2×1H, m, cyclohexyl), 1.85-2.20 (2×2H, m, cyclohexyl and CH_2NH), 2.25-2.36 (2×1H, m,

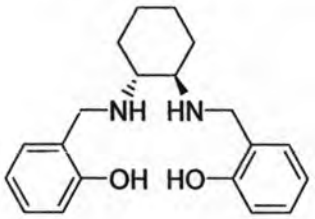
cyclohexyl) 3.85 and 4.10 (2×2H, AB, J = 14.0 Hz, CH_2NH), 6.80 (2×1H, d, J = 3.6 Hz, thienyl), 6.91-6.97 (2×2H, m, thienyl), 7.17-7.22 (2×2H, m ,thienyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.0, 31.6, 45.7, 60.5, 123.2, 123.3, 123.9, 125.0, 127.7, 136.1, 137.9, 144.6.

2.5.3 (1*R*,2*R*)-*N*,*N*'-Bis(2'-furylmethyl)cyclohexane-1,2-diamine (49c)



(1*R*,2*R*)-*N*,*N*'-Bis(2'-furylmethyl)cyclohexane-1,2-diamine (**49c**) was prepared according to the general procedure using 2-furaldehyde (0.229 g, 2.4 mmol) and (1*R*,2*R*)-*trans*-diaminocyclohexane (0.137 g, 1.2 mmol). The product was obtained as yellow oil (0.283 g, 87%). $[\alpha]_D^{25}$ = -75.0 (*c* 1.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.92-1.08 (2×1H, m, cyclohexyl), 1.12-1.30 (2×1H, m, cyclohexyl), 1.60-1.74 (2×1H, m, cyclohexyl), 1.90-2.10 (2×2H, m, cyclohexyl), 2.14-2.24 (2×1H, m, cyclohexyl) 3.68 and 3.83 (2×2H, AB, J = 14.4 Hz, CH_2NH), 6.10-6.19 (2×1H, m, furfuryl), 6.24-6.30 (2×1H, m, furfuryl), 7.30-7.35 (2×1H, m, furfuryl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.0, 31.4, 43.6, 60.7, 106.4, 110.1, 141.5, 154.6.

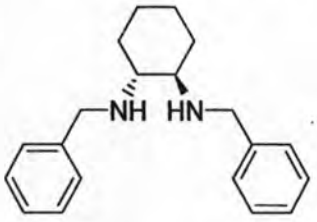
2.5.4 2,2'-[Cyclohexane-(1*R*,2*R*)-diylbis(iminomethylene)]diphenol (49d)



2,2'-[Cyclohexane-(1*R*,2*R*)-diylbis(iminomethylene)]diphenol (**49d**) was prepared according to the general procedure using salicylaldehyde (0.287 g, 2.3 mmol) and (1*R*,2*R*)-*trans*-diaminocyclohexane (0.128 g, 1.1 mmol). The product was obtained as a yellow solid (0.227 g, 59%). m.p. 98-100 °C; $[\alpha]_D^{25}$ = -37.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18-1.33 (2×2H, m, cyclohexyl), 1.65-1.80 (2×1H, m, cyclohexyl), 2.10-2.25 (2×1H, m, cyclohexyl), 2.44-2.56 (2×1H, m,

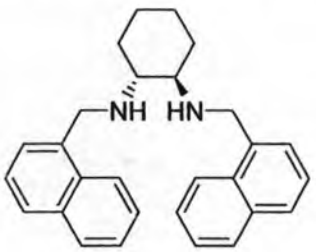
cyclohexyl), 3.88 and 4.04 (2×2H, AB, J = 13.6 Hz, CH_2NH), 6.74-6.90 (2×2H, m, Ar), 6.90-7.02 (2×1H, m, Ar), 7.11-7.19 (2×1H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.2, 30.4, 49.5, 59.7, 116.5, 119.3, 122.8, 128.4, 128.9, 157.9.

2.5.5 (1*R*,2*R*)-*N*,*N*'-Dibenzylcyclohexane-1,2-diamine (49e)



(1*R*,2*R*)-*N*,*N*'-Dibenzylcyclohexane-1,2-diamine (**49e**) was prepared according to the general procedure using benzaldehyde (0.236 g, 2.2 mmol) and (1*R*,2*R*)-*trans*-diaminocyclohexane (0.128 g, 1.1 mmol). The product was obtained as colorless oil (0.285 g, 87%). $[\alpha]_D^{25}$ = -78.4 (*c* 1.18, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.02-1.29 (2×2H, m, cyclohexyl), 1.66-1.80 (2×1H, m, cyclohexyl), 2.11-2.23 (2×1H, m, cyclohexyl), 2.27-2.38 (2×1H, m, cyclohexyl), 3.68 and 3.93 (2×2H, AB, J = 13.0 Hz, CH_2NH), 7.22-7.38 (2×5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 31.2, 50.6, 60.6, 127.0, 128.1, 128.4, 140.2.

2.5.6 (1*R*,2*R*)-*N*,*N*'-Bis(1'-naphthylmethyl)cyclohexane-1,2-diamine (49f)

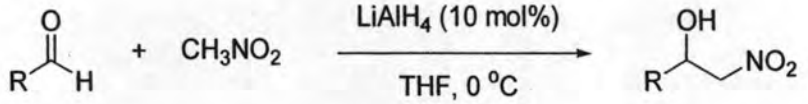


(1*R*,2*R*)-*N*,*N*'-Bis(1'-naphthylmethyl)cyclohexane-1,2-diamine (**49f**) was prepared according to the general procedure using 1-naphthaldehyde (0.352 g, 2.2 mmol) and (1*R*,2*R*)-*trans*-diaminocyclohexane (0.128 g, 1.1 mmol). The product was obtained as sticky oil (0.415 g, 93%). $[\alpha]_D^{25}$ = -16.2 (*c* 1.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.02-1.45 (2×2H, m, cyclohexyl), 1.65-2.15 (2×2H, m, cyclohexyl and CH_2NH), 2.30-2.50 (2×2H, m, cyclohexyl), 4.07 and 4.37 (2×2H, AB, J = 13.2 Hz, CH_2NH), 7.20-7.42 (2×4H, m, Ar), 7.74 (2×1H, d, J = 8.0 Hz, Ar), 7.81

(2×1H, d, J = 8.0 Hz, Ar), 7.91 (2×1H, d, J = 8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 31.7, 48.9, 61.5, 123.9, 125.3, 125.5, 125.9, 126.0, 127.6, 128.5, 131.8, 133.8, 136.4.

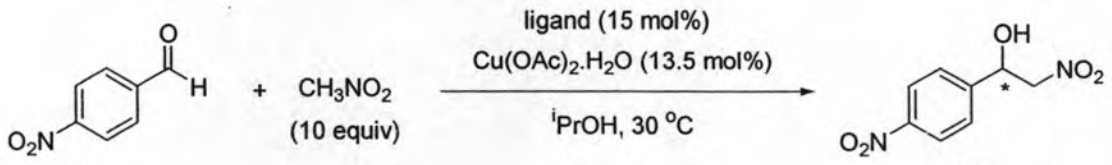
2.6 Asymmetric Cu-catalyzed nitro-aldol (Henry) reaction

2.6.1 General procedure for the preparation of racemic 2-nitroalkanols



Racemic 2-nitroalkanols was prepared according to the method by Kim *et al.*.[81] To a slurry of $LiAlH_4$ (0.050 mmol) in dry THF (2 mL), which had been stirred for 30 min at 0 °C, was added nitromethane (2.5 mmol). After 30 min, the aldehyde (0.50 mmol) was added in one portion. The mixture was stirred until the starting materials had disappeared (TLC), and then quenched with 1N HCl. The reaction mixture was allowed to warm to room temperature, poured into water, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the corresponding 2-nitroalkanol.

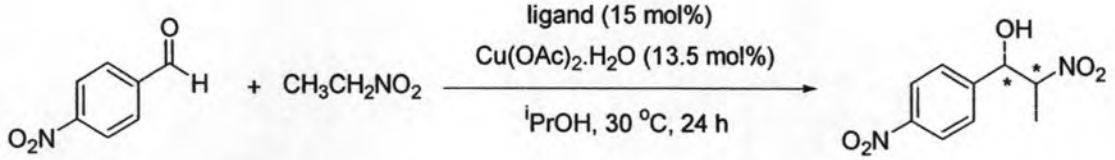
2.6.2 General procedure for screening of catalytic activities of ligands using nitromethane



74a

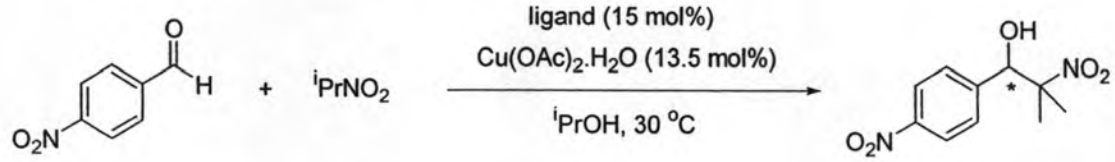
The chiral ligand (0.045 mmol) and $Cu(OAc)_2 \cdot H_2O$ (8.1 mg, 0.040 mmol) were placed in a 10-mL round-bottomed flask equipped with a stir bar. 2-Propanol (0.45 mL) was added and the mixture was stirred for 1 h at room temperature (30 °C). Subsequently, nitromethane (0.16 mL, 3.0 mmol) and 4-nitrobenzaldehyde (45 mg, 0.30 mmol) were added. After stirring for the amount of time indicated, the volatile components were removed *in vacuo* and the crude product purified by column chromatography on silica gel eluting with hexanes/ethyl acetate.

2.6.3 General procedure for screening of catalytic activities of ligands using nitroethane



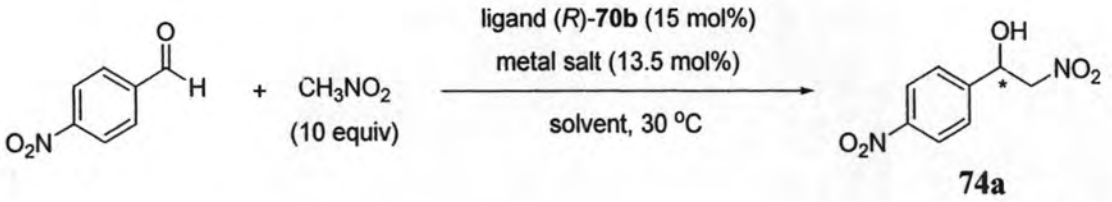
The chiral ligand (0.045 mmol) and $Cu(OAc)_2 \cdot H_2O$ (8.1 mg, 0.040 mmol) were placed in a 10-mL round-bottomed flask equipped with a stir bar. 2-Propanol (0.45 mL) was added and the mixture was stirred for 1 h at room temperature (30 °C). Subsequently, nitroethane (55 or 10 equiv) and 4-nitrobenzaldehyde (45 mg, 0.30 mmol) were added. After stirring for the amount of time indicated (24 h), the volatile components were removed *in vacuo* and the crude product purified by column chromatography on silica gel eluting with hexanes/ethyl acetate.

2.6.4 General procedure for screening of catalytic activities of ligands using 2-nitropropane



The chiral ligand (0.045 mmol) and $Cu(OAc)_2 \cdot H_2O$ (8.1 mg, 0.040 mmol) were placed in a 10-mL round-bottomed flask equipped with a stir bar. 2-Propanol (0.45 mL) was added and the mixture was stirred for 1 h at room temperature (30 °C). Subsequently, 2-nitropropane (55 equiv) and 4-nitrobenzaldehyde (45 mg, 0.30 mmol) were added. The reaction mixture was stirred until the starting materials had disappeared (TLC), the volatile components were removed *in vacuo* and the crude product purified by column chromatography on silica gel eluting with hexanes/ethyl acetate.

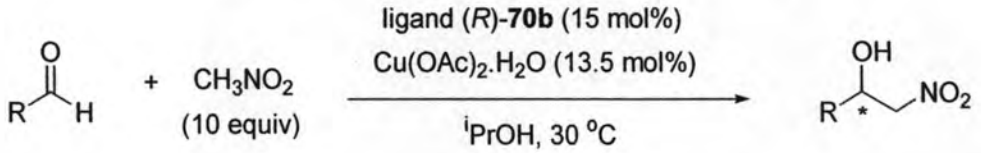
2.6.5 General procedure for optimization of conditions



74a

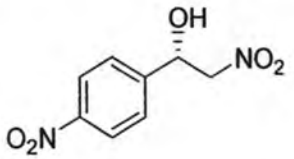
(*R*)-2-Phenyl-2-[(2′-thienylmethyl)amino]ethanol, (*R*)-**70b** (10.5 mg, 0.045 mmol) and metal salt (0.040 mmol) were placed in a 10-mL round-bottomed flask equipped with a stirrer bar. Solvent (0.45 mL) was added and the mixture was stirred for 1 h at room temperature (30 °C). Subsequently, nitromethane (0.16 mL, 3.0 mmol) and 4-nitrobenzaldehyde (45 mg, 0.30 mmol) were added. After stirring for the period of time indicated, the volatile components were removed *in vacuo* and the crude product purified by column chromatography on silica gel eluting with hexanes/ethyl acetate.

2.6.6 General procedure for Cu-catalyzed asymmetric nitro-aldol reactions between nitromethane and various aldehydes



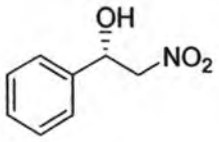
(*R*)-2-Phenyl-2-[(2′-thienylmethyl)amino]ethanol, (*R*)-**70b** (10.5 mg, 0.045 mmol) and $Cu(OAc)_2 \cdot H_2O$ (8.1 mg, 0.040 mmol) were placed in a 10-mL round-bottomed flask equipped with a stirrer bar and dissolved with 2-propanol (0.45 mL). The mixture was stirred for 1 h at ambient temperature to give a clear deep blue solution. Subsequently, nitromethane (0.16 mL, 3.0 mmol) and aldehyde (0.30 mmol) were added. After stirring for the amount of time indicated, the volatile components were removed *in vacuo* and the crude product purified by column chromatography on silica gel eluting with hexanes/ethyl acetate.

2.6.6.1 (*S*)-1-(4′-Nitrophenyl)-2-nitroethanol (74a)



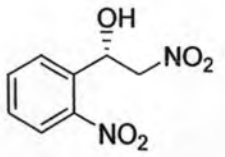
(*S*)-1-(4′-Nitrophenyl)-2-nitroethanol (**74a**) was prepared according to the general procedure using 4-nitrobenzaldehyde (45 mg, 0.30 mmol). The product was obtained as a off-white crystalline solid (61.8 mg, 97%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 80:20), flow 1.0 mL/min, 263 nm; minor enantomer t_R = 13.6 min; major enantiomer t_S = 16.4 min, 75% ee (lit.[106] (*R*-isomer), 78% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.53-4.65 (2H, m, C*H*$_2$NO$_2$), 5.61 (1H, dd, *J* = 12.4, 4.0 Hz, C*H*OH), 7.62 (2H, d, *J* = 8.8 Hz, Ar), 8.26 (2H, d, *J* = 8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 69.9, 80.6, 124.2, 126.9, 145.0, 148.1.

2.6.6.2 (*S*)-1-Phenyl-2-nitroethanol (74b)



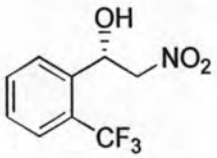
(*S*)-1-Phenyl-2-nitroethanol (**74b**) was prepared according to the general procedure using benzaldehyde (31 μL, 0.30 mmol). The product was obtained as colorless oil (38.8 mg, 77%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 90:10), flow 1.0 mL/min 215 nm; minor enantomer t_R = 15.9 min; major enantiomer t_S = 18.6 min, 69% ee (lit.[106] (*R*-isomer), 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.96 (1H, br, CHO*H*), 4.48 (1H, A*B*X, J_{AB} = 13.2, J_{BX} = 9.4 Hz, CH$_a$*H*$_b$NO$_2$), 4.57 (1H, *A*BX, J_{AB} = 13.2, J_{AX} = 2.0 Hz, C*H*$_a$H$_b$NO$_2$), 5.41 (1H, AB*X*, J_{AX} = 2.0, J_{BX} = 9.4 Hz, C*H*OH), 7.32-7.42 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 71.0, 81.2, 126.0, 128.9, 129.0, 138.2.

2.6.6.3 (*S*)-1-(2′-Nitrophenyl)-2-nitroethanol (74c)



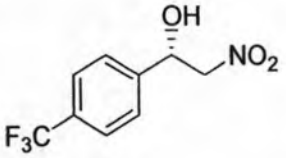
(*S*)-1-(2′-Nitrophenyl)-2-nitroethanol (**74c**) was prepared according to the general procedure using 2-nitrobenzaldehyde (45 mg, 0.30 mmol). The product was obtained as a green solid (62.5 mg, 98%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 90:10), flow 0.8 mL/min, 255 nm; minor enantiomer t_R = 21.2 min; major enantiomer t_S = 23.3 min, 85% ee (lit.[106] (*R*-isomer), 89% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.17 (1H, br, CHO*H*), 4.53 (1H, A*B*X, J_{AB} = 13.6, J_{BX} = 8.8 Hz, $CH_aH_bNO_2$), 4.83 (1H, *A*BX, J_{AB} = 13.6, J_{AX} = 2.2 Hz, $CH_aH_bNO_2$), 6.00 (1H, AB*X*, J_{AX} = 2.2, J_{BX} = 8.8 Hz, C*H*OH), 7.53 (1H, t, *J* = 7.8 Hz, Ar), 7.73 (1H, t, *J* = 7.6 Hz, Ar), 7.92 (1H, d, *J* = 7.8 Hz, Ar), 8.03 (1H, d, *J* = 8.2 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 66.8, 80.1, 125.0, 128.7, 129.7, 134,2, 134.4, 147.1.

2.6.6.4 (*S*)-1-(2′-Trifluoromethylphenyl)-2-nitroethanol (74d)



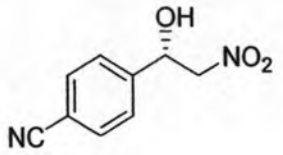
(*S*)-1-(2′-Trifluoromethylphenyl)-2-nitroethanol (**74d**) was prepared according to the general procedure using 2-(trifluoromethyl)benzaldehyde (40 μL, 0.30 mmol). The product was obtained as colorless oil (64.1 mg, 91%); HPLC analysis: Chiralcel OJ-H, isocratic (*n*-hexanes:2-propanol = 90:10), flow 0.8 mL/min, 206 nm; minor enantiomer t_R = 14.7 min; major enantiomer t_S = 17.5 min, 88% ee (lit.[117] (*R*-isomer), 79% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.87 (1H, br, CHO*H*), 4.47-4.55 (2H, m, CH_2NO_2), 5.85-5.92 (1H, m, C*H*OH), 7.48 (1H, t, *J* = 7.6 Hz, Ar), 7.61-7.71 (2H, m, Ar), 7.84 (1H, d, *J* = 7.6 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 66.6, 80.7, 122.7, 125.4, 126.0, 128.0, 129.0, 132.7, 136.8.

2.6.6.5 (*S*)-1-(4′-Trifluoromethylphenyl)-2-nitroethanol (74e)



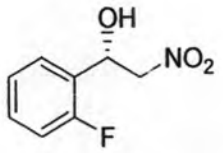
(*S*)-1-(4′-Trifluoromethylphenyl)-2-nitroethanol (**74e**) was prepared according to the general procedure using 4-(trifluoromethyl)benzaldehyde (40 μL, 0.30 mmol). The product was obtained as colorless oil (65.5 mg, 93%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 90:10), flow 1.0 mL/min, 207 nm; minor enantiomer t_R = 13.1 min; major enantiomer t_S = 16.8 min, 78% ee; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.13 (1H, br, CHO*H*), 4.48-4.63 (2H, m, CH_2NO_2), 5.51 (1H, dd, *J* = 11.6, 2.6 Hz, C*H*OH), 7.52 (2H, d, *J* = 8.0 Hz, Ar), 7.65 (2H, d, *J* = 8.0 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 70.3, 80.9, 125.9, 126.0, 126.3, 142.0.

2.6.6.6 (*S*)-1-(4′-Cyanophenyl)-2-nitroethanol (74f)



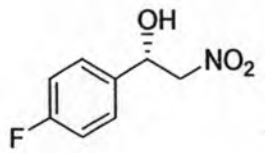
(*S*)-1-(4′-Cyanophenyl)-2-nitroethanol (**74f**) was prepared according to the general procedure using 4-cyanobenzaldehyde (39 mg, 0.30 mmol). The product was obtained as a white crystalline solid (56.5 mg, 98%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 80:20), flow 1.0 mL/min, 232 nm; minor enantiomer t_R = 14.5 min; major enantiomer t_S = 16.5 min, 76% ee (lit.[132] (*R*-isomer), 76% ee with Proton sponge® as additive, 64% ee with DBU as additive); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.50-4.61 (2H, m, CH_2NO_2), 5.54 (1H, dd, *J* = 12.4, 3.8 Hz, C*H*OH), 7.55 (2H, d, *J* = 8.4 Hz, Ar), 7.69 (2H, d, *J* = 8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 70.1, 80.7, 112.6, 118.3, 126.8, 132.8, 143.4.

2.6.6.7 (*S*)-1-(2′-Fluorophenyl)-2-nitroethanol (74g)



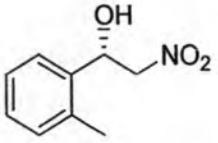
(*S*)-1-(2′-Fluorophenyl)-2-nitroethanol (**74g**) was prepared according to the general procedure using 2-fluorobenzaldehyde (31 μL, 0.30 mmol). The product was obtained as colorless oil (51.0 mg, 92%); HPLC analysis: Chiralcel OJ-H, isocratic (*n*-hexanes:2-propanol = 90:10), flow 0.5 mL/min, 262 nm; minor enantiomer t_R = 34.3 min; major enantiomer t_S = 37.2 min, 83% ee (lit.[117] (*R*-isomer), 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.78 (1H, br, CHO*H*), 4.54-4.65 (2H, m, CH_2NO$_2$), 5.73 (1H, dd, *J* = 12.0, 3.6 Hz, C*H*OH), 7.04-7.11 (1H, m, Ar), 7.18-7.24 (1H, m, Ar), 7.31-7.38 (1H, m, Ar), 7.52-7.58 (1H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 65.4, 80.0, 115.6, 124.8, 127.6, 130.4, 158.1, 160.5.

2.6.6.8 (*S*)-1-(4′-Fluorophenyl)-2-nitroethanol (74h)



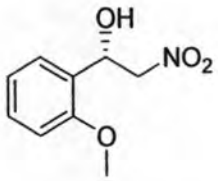
(*S*)-1-(4′-Fluorophenyl)-2-nitroethanol (**74h**) was prepared according to the general procedure using 4-fluorobenzaldehyde (32 μL, 0.30 mmol). The product was obtained as colorless oil (36.3 mg, 65%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 90:10), flow 1.0 mL/min, 265 nm; minor enantiomer t_R = 14.4 min; major enantiomer t_S = 17.1 min, 77% ee (lit.[106] (*R*-isomer), 92% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.78 (1H, br, CHO*H*), 4.48 (1H, A*B*X, J_{AB} = 13.6, J_{BX} = 9.4 Hz, $CH_aH_bNO_2$), 4.57 (1H, *A*BX, J_{AB} = 13.6, J_{AX} = 3.0 Hz, C$H_aH_bNO_2$), 5.43 (1H, AB*X*, J_{AX} = 3.0, J_{BX} = 9.4 Hz, C*H*OH), 7.08 (2H, t, *J* = 8.6 Hz, Ar), 7.34-7.40 (2H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 70.3, 81.1, 115.9, 116.1, 127.8, 134.0, 161.6, 164.1.

2.6.6.9 (*S*)-1-(2′-Methylphenyl)-2-nitroethanol (74i)



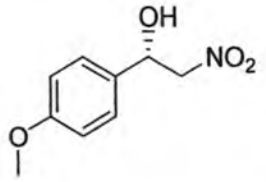
(*S*)-1-(2′-Methylphenyl)-2-nitroethanol (**74i**) was prepared according to the general procedure using 2-methylbenzaldehyde (35 μL, 0.30 mmol). The product was obtained as colorless oil (36.0 mg, 66%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 85:15), flow 1.0 mL/min, 206 nm; minor enantiomer t_R = 10.2 min; major enantiomer t_S = 15.1 min, 66% ee (lit.[106] (*R*-isomer), 93% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.38 (3H, s, OC*H*$_3$), 2.70 (1H, br, CHO*H*), 4.42 (1H, A*B*X, J_{AB} = 13.2, J_{BX} = 9.6 Hz, CH$_a$*H*$_b$NO$_2$), 4.53 (1H, *A*BX, J_{AB} = 13.2, J_{AX} = 2.8 Hz, C*H*$_a$H$_b$NO$_2$), 5.66 (1H, AB*X*, J_{AX} = 2.8, J_{BX} = 9.6 Hz, C*H*OH), 7.16-7.31 (3H, m, Ar), 7.47-7.54 (1H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.1, 68.2, 80.5, 125.9, 127.0, 128.9, 131.1, 134.7, 136.5.

2.6.6.10 (*S*)-1-(2′-Methoxyphenyl)-2-nitroethanol (74j)



(*S*)-1-(2′-Methoxyphenyl)-2-nitroethanol (**74j**) was prepared according to the general procedure using 2-methoxybenzaldehyde (41 mg, 0.30 mmol). The product was obtained as colorless oil (50.0 mg, 85%); HPLC analysis: Chiralcel OD, isocratic (*n*-hexanes:2-propanol = 90:10), flow 1.0 mL/min, 272 nm; minor enantiomer t_R = 13.8 min; major enantiomer t_S = 16.0 min, 75% ee (lit.[106] (*R*-isomer), 93% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.80 (1H, br, CHO*H*), 3.87 (3H, s, OC*H*$_3$), 4.56 (1H, A*B*X, J_{AB} = 13.0, J_{BX} = 9.2 Hz, CH$_a$*H*$_b$NO$_2$), 4.64 (1H, *A*BX, J_{AB} = 13.0, J_{AX} = 3.2 Hz, C*H*$_a$H$_b$NO$_2$), 5.62 (1H, AB*X*, J_{AX} = 3.2, J_{BX} = 9.2 Hz, C*H*OH), 6.91 (1H, d, *J* = 8.4 Hz, Ar), 7.00 (1H, t, *J* = 7.6 Hz, Ar), 7.32 (1H, t, *J* = 7.8 Hz, Ar), 7.43 (1H, d, *J* = 7.6 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.4, 67.8, 79.9, 110.5, 121.1, 126.0, 127.2, 129.8, 156.0.

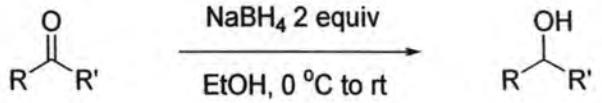
2.6.6.11 (*S*)-1-(4'-Methoxyphenyl)-2-nitroethanol (74k)



(*S*)-1-(4(-Methoxyphenyl)-2-nitroethanol (**74k**) was prepared according to the general procedure using 4-methoxybenzaldehyde (36 μL, 0.30 mmol). The product was obtained as colorless oil (23.2 mg, 39%); HPLC analysis: Chiralcel OD, isocratic (n-hexanes:2-propanol = 80:20), flow 1.0 mL/min, 223 nm; minor enantiomer t_R = 12.9 min; major enantiomer t_S = 16.2 min, 61% ee (lit.[109] (*R*-isomer), 80% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.30 (1H, br, CHO*H*), 3.81 (3H, s, OCH_3), 4.47 (1H, A*B*X, J_{AB} = 13.2, J_{BX} = 9.6 Hz, CHaH_bNO$_2$), 4.60 (1H, *A*BX, J_{AB} = 13.2, J_{AX} = 2.8 Hz, CH_aH$_b$NO$_2$), 5.41 (1H, AB*X*, J_{AX} = 2.8, J_{BX} = 9.6 Hz, C*H*OH), 6.91 (2H, d, *J* = 8.0 Hz, Ar), 7.32 (2H, d, *J* = 8.8 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.3, 70.7, 81.3, 114.4, 127.3, 130.6, 132.3.

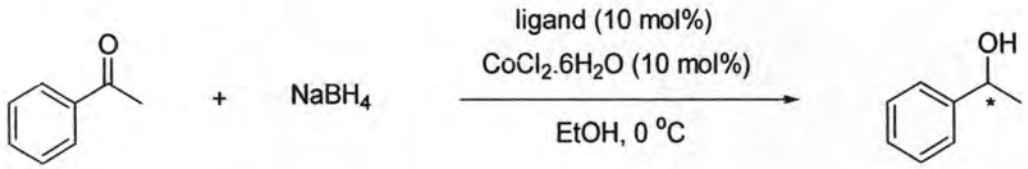
2.7 Asymmetric Co-catalyzed borohydride reduction of ketones

2.7.1 General procedure for the preparation of racemic secondary alcohols



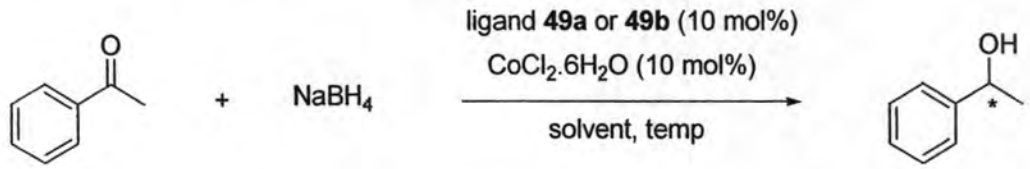
A solution of ketone (1 equiv) dissolved in absolute ethanol was cooled down to 0 °C, and then sodium borohydride (2 equiv) was added in portions. The reaction mixture was allowed to warm at room temperature. After the reaction was completed according to TLC analysis, water was added to destroy the excess sodium borohydride. The reaction mixture was extracted with dichloromethane. The combined extracts were dried over anhydrous $MgSO_4$ followed by filtration, and then concentrated to give crude products. The crude products were purified by flash column chromatography (petroleum ether/ethyl acetate).

2.7.2 General procedure for screening of the ligands



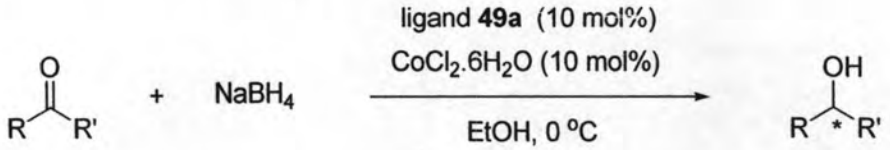
The chiral ligand (0.030 mmol) and $CoCl_2 \cdot 6H_2O$ (7.1 mg, 0.030 mmol) were placed in a 25-mL round-bottomed flask equipped with a stirrer bar. Absolute ethanol (1.0 mL) was added and the mixture was stirred for 1 h at room temperature to afford a blue-colored solution. Subsequently, acetophenone (35 μL, 0.30 mmol) was added, and then the reaction mixture was cooled down to 0 °C for 1 h. Sodium borohydride (22.7 mg, 0.60 mmol) was then added. After the ketone was consumed according to TLC analysis, water was added to destroy the excess sodium borohydride. The reaction mixture was extracted with dichloromethane. The combined extracts were dried over anhydrous $MgSO_4$, followed by filtration, and then concentrated to give crude products. The crude products were purified by flash column chromatography (petroleum ether/ethyl acetate).

2.7.3 General procedure for optimization of conditions



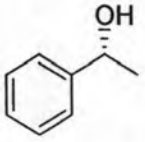
(1*R*,2*R*)-*N*,*N*′-Bis(thien-2′-ylmethyl)cyclohexane-1,2-diamine (**49a**) (9.2 mg, 0.030 mmol) or (1*R*,2*R*)-*N*,*N*′-bis[5-(2,2′-bithienylmethyl)]cyclohexane-1,2-diamine (**49b**) (14.1 mg, 0.030 mmol) and $CoCl_2 \cdot 6H_2O$ (7.1 mg, 0.030 mmol) were placed in a 25-mL round-bottomed flask equipped with a stirrer bar. Solvent (1.0 mL) was added and the mixture was stirred for 1 h at room temperature to afford blue color. Subsequently, acetophenone (35 μL, 0.30 mmol) was added, and then the reaction mixture was cooled down to suitable temperature for 1 h. Sodium borohydride (22.7 mg, 0.60 mmol) was then added. After usual work up procedure described above, the crude products were purified by flash column chromatography (petroleum ether/ethyl acetate).

2.7.4 General procedure for enantioselective reduction of ketones using sodium borohydride



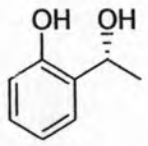
(1*R*,2*R*)-*N*,*N*'-Bis(thien-2'-ylmethyl)cyclohexane-1,2-diamine (**49a**) (9.2 mg, 0.030 mmol) and $CoCl_2 \cdot 6H_2O$ (7.1 mg, 0.030 mmol) were placed in a 25-mL round-bottomed flask equipped with a stirrer bar. Absolute ethanol (1.0 mL) was added and the mixture was stirred for 1 h at room temperature to afford blue color. Subsequently, a ketone (0.30 mmol) was added, and then the reaction mixture was cooled down to 0 °C for 1 h. Sodium borohydride (22.7 mg, 0.60 mmol) was then added. After the usual work up procedure described above, the crude products were purified by flash column chromatography (petroleum ether/ethyl acetate).

2.7.4.1 (*R*)-1-Phenylethanol



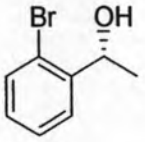
(*R*)-1-Phenylethanol was prepared according to the general procedure using acetophenone (35 μL, 0.30 mmol). The product was obtained as colorless oil (35.1 mg, 96%); GC analysis: column temperature = 90 °C; major enantiomer t_R = 16.9 min; minor enantiomer t_S = 19.5 min, 64% ee (lit.[133] (*S*-isomer), 32% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48 (3H, d, J = 6.4 Hz, CHC*H*$_3$), 2.05 (1H, br s, CHO*H*) 4.86 (1H, q, J = 6.4 Hz, C*H*CH$_3$), 7.20-7.45 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 70.4, 125.4, 127.5, 128.5, 145.9.

2.7.4.2 (*R*)-1-(2′-Hydroxyphenyl)ethanol



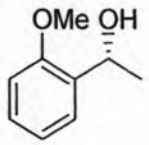
(*R*)-1-(2′-Hydroxyphenyl)ethanol was prepared according to the general procedure using 2′-hydroxyacetophenone (36 μL, 0.30 mmol). The product was obtained as colorless oil (11.1 mg, 27%); GC analysis + TMS imidazole: column temperature = 95 °C; minor enantiomer t_S = 21.5 min; major enantiomer t_R = 22.0 min, 31% ee; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60 (3H, d, J = 6.7 Hz, CHC*H*$_3$), 5.05 (1H, q, J = 6.4 Hz, C*H*CH$_3$), 6.80-6.89 (2H, m, Ar), 6.92-7.00 (1H, m, Ar), 7.12-7.20 (1H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.5, 71.7, 117.2, 119.9, 126.5, 128.4, 129.0, 155.5.

2.7.4.3 (*R*)-1-(2′-Bromophenyl)ethanol



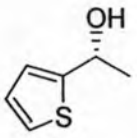
(*R*)-1-(2′-Bromophenyl)ethanol was prepared according to the general procedure using 2′-bromoacetophenone (41 μL, 0.30 mmol). The product was obtained as colorless oil in quantitative yield; GC analysis: column temperature = 140 °C; major enantiomer t_R = 7.96 min; minor enantiomer t_S = 10.1 min, 49% ee (lit.[134] (*S*-isomer), 99.2% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.46 (3H, d, J = 5.2 Hz, CHC*H*$_3$), 2.05 (1H, br s, CHO*H*), 5.22 (1H, q, J = 6.4 Hz, C*H*CH$_3$), 7.11 (1H, t, J = 7.6 Hz, Ar), 7.33 (1H, t, J = 7.6 Hz, Ar), 7.50 (1H, d, J = 7.8 Hz, Ar), 7.57 (1H, d, J = 7.6 Hz, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.6, 69.2, 121.7, 126.7, 127.9, 128.8, 132.7, 144.6.

2.7.4.4 (*R*)-1-(2′-Methoxyphenyl)ethanol



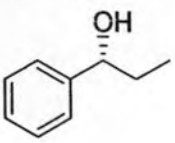
(*R*)-1-(2′-Methoxyphenyl)ethanol was prepared according to the general procedure using 2′-methoxyacetophenone (41 μL, 0.30 mmol). The product was obtained as colorless oil in quantitative yield; GC analysis: column temperature = 120 °C; minor enantiomer t_S = 12.1 min; major enantiomer t_R = 13.2 min, 69% ee; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.51 (3H, d, J = 6.4 Hz, CHCH_3), 2.65 (1H, br s, CHO*H*), 3.86 (3H, s, OCH_3), 5.10 (1H, q, J = 6.4 Hz, C*H*CH$_3$), 6.88 (1H, d, J = 8.4, Ar), 6.96 (1H, t, J = 7.6 Hz, Ar), 7.22-7.28 (1H, m, Ar), 7.34 (1H, d, J = 7.6 Hz, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.9, 55.3, 66.7, 110.4, 120.8, 126.1, 128.3, 133.4, 156.6.

2.7.4.5 (*R*)-1-(2′-Thienyl)ethanol



(*R*)-1-(2′-Thienyl)ethanol was prepared according to the general procedure using methyl-2-thienylketone (32 μL, 0.30 mmol). The product was obtained as colorless oil (26.1 mg, 68%); GC analysis: column temperature = 90 °C; major enantiomer t_R = 18.0 min; minor enantiomer t_S = 20.8 min, 47% ee (lit.[134] (*S*-isomer), 98% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.57 (3H, d, J = 6.2 Hz, CHCH_3), 2.00 (1H, br s, CHO*H*), 5.11 (1H, q, J = 6.2 Hz, C*H*CH$_3$), 6.93-7.00 (2H, m, thienyl), 7.20-7.25 (1H, m, thienyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.6, 66.1, 123.1, 124.3, 126.6, 150.0.

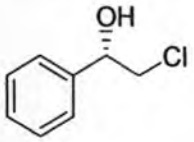
2.7.4.6 (*R*)-1-Phenylpropanol



(*R*)-1-Phenylpropanol was prepared according to the general procedure using ethyl phenyl ketone (40 μL, 0.30 mmol). The product was obtained as colorless oil

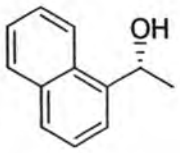
(39.8 mg, 97%); GC analysis: column temperature = 100 °C; major enantiomer t_R = 18.3 min; minor enantiomer t_S = 19.9 min, 70% ee (lit.[133] (*S*-isomer), 40% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (3H, t, J = 7.4 Hz, CH_2CH_3), 1.66-1.90 (3H, m, $OHCHCH_2$), 4.60 (1H, t, J = 6.6 Hz, $CHOH$), 7.20-7.45 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.2, 31.9, 76.1, 126.0, 127.5, 128.4, 144.6.

2.7.4.7 (*R*)-2-Chloro-1-phenylethanol



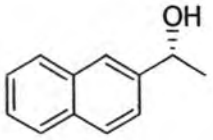
(*R*)-2-Chloro-1-phenylethanol was prepared according to the general procedure using 2-chloro-1-phenylethanone (46.4 mg, 0.30 mmol). The product was obtained as colorless oil (11.0 mg, 23%); GC analysis: column temperature = 120 °C; major enantiomer t_R = 15.6 min; minor enantiomer t_S = 17.2 min, 30% ee (lit.[129] (*S*-isomer), 86% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.63 (1H, s, CHO*H*), 3.65 (1H, A*B*X, J_{AB} = 11.2, J_{BX} = 8.8 Hz, CH_aH_bCl), 3.75 (1H, *A*BX, J_{AB} = 11.2, J_{AX} = 3.2 Hz, CH_aH_bCl), 4.91 (1H, AB*X*, J_{AX} = 3.2, J_{BX} = 8.8 Hz,, C*H*OH), 7.30-7.42 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.0, 74.1, 126.1, 128.5, 128.7, 139.9.

2.7.4.8 (*R*)-1-(1′-Naphthyl)ethanol



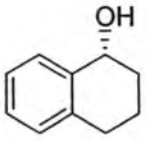
(*R*)-1-(1′-Naphthyl)ethanol was prepared according to the general procedure using 1-(1′-naphthyl)ethanone (46 μL, 0.30 mmol). The product was obtained as colorless oil (43.8 mg, 85%); GC analysis: column temperature = 145 °C; minor enantiomer t_S = 20.8 min; major enantiomer t_R = 22.5 min, 76% ee (lit.[133] (*S*-isomer), 63% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.68 (3H, d, J = 6.4 Hz, $CHCH_3$), 1.90 (1H, br s, CHO*H*), 5.68 (1H, q, J = 6.4 Hz, $CHCH_3$), 7.45-7.56 (3H, m, Ar), 7.69 (1H, d, J = 7.3 Hz, Ar), 7.79 (1H, d, J = 8.1 Hz, Ar), 7.84-7.91 (1H, m, Ar), 8.10-8.20 (1H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.4, 67.1, 122.0, 123.2, 125.5, 126.0, 127.9, 128.9, 130.2, 133.8, 141.4, 143.2.

2.7.4.9 (*R*)-1-(2′-Naphthyl)ethanol



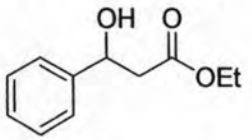
(*R*)-1-(2′-Naphthyl)ethanol was prepared according to the general procedure using 1-(2′-naphthyl)ethanone (51.1 mg, 0.30 mmol). The product was obtained as a white crystalline solid in quantitative yield; GC analysis: column temperature = 140 °C; major enantiomer t_R = 23.9 min; minor enantiomer t_S = 25.5 min, 75% ee (lit.[133] (*S*-isomer), 21% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.55 (3H, d, J = 6.7 Hz, CHC*H*$_3$), 1.95 (1H, br s, CHO*H*), 5.07 (1H, q, J = 6.4 Hz, C*H*CH$_3$), 7.42-7.53 (3H, m, Ar), 7.81-7.86 (4H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 70.6, 123.8, 125.8, 126.2, 127.7, 128.0, 128.3, 132.9, 133.3, 143.2.

2.7.4.10 (*R*)-1,2,3,4-Tetrahydro-1-naphthol



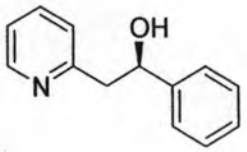
(*R*)-1,2,3,4-Tetrahydro-1-naphthol was prepared according to the general procedure using α-tetralone (40 μL, 0.30 mmol). The product was obtained as colorless oil (37.1 mg, 83%); HPLC analysis: Chiralcel OD, isocratic (*n*-heptane:2-propanol = 98:2), flow 0.8 mL/min, 254 nm; minor enantiomer t_S = 16.0 min; major enantiomer t_R = 17.6 min, 27% ee (lit.[133] (*R*-isomer), 12% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60-1.99 (5H, m, alkyl and OH), 2.69-2.87 (2H, m, alkyl), 4.79 (1H, br m, C*H*OH), 7.09-7.12 (1H, m, Ar), 7.17-7.23 (2H, m, Ar), 7.41-7.46 (1H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.8, 29.3, 32.3, 68.2, 126.2, 127.6, 128.7, 129.0, 137.1, 138.8.

2.7.4.11 Ethyl 3-hydroxy-3-phenylpropanoate



Ethyl 3-hydroxy-3-phenylpropanoate was prepared according to the general procedure using ethyl 3-oxo-3-phenylpropanoate (52 μL, 0.30 mmol). The product was obtained as colorless oil (13.3 mg, 23%); HPLC analysis: Chiralcel OD, isocratic (*n*-heptane:2-propanol = 95:5), flow 0.5 mL/min, 254 nm; t_R = 24.2 min; t_S = 34.3 min, 0% ee (lit.[129] (*R*-isomer), 99% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 2.70 (1H, dd, *J* = 16.4, 4.8 Hz, $CHCH_aH_b$), 2.77 (1H, dd, *J* 16.4, 8.4 Hz, $CHCH_aH_b$), 3.27 (1H, br s, CHO*H*), 4.18 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 5.13 (1H, dd, *J* = 8.4, 4.8 Hz, C*H*OH), 7.26-7.40 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 43.3, 60.9, 70.4, 125.7, 127.8, 128.6, 142.5, 172.5.

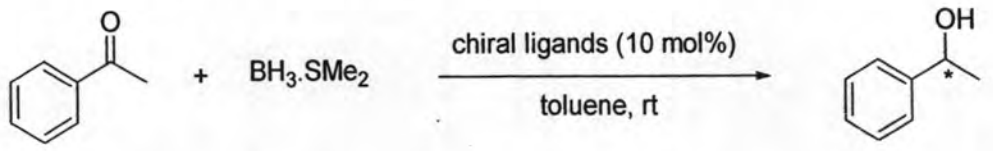
2.7.4.12 (*R*)-1-Phenyl-2-pyridin-2-ylethanol



(*R*)-1-Phenyl-2-pyridin-2-ylethanol was prepared according to the general procedure using 2-phenacylpyridine (59.2 mg, 0.30 mmol). The product was obtained as colorless oil (33.6 mg, 56%); HPLC analysis: Chiralcel OD, isocratic (*n*-heptane:2-propanol = 90:10), flow 0.5 mL/min, 254 nm; major enantiomer t_R = 22.2 min; minor enantiomer t_S = 36.7 min, 5% ee (lit.[135] (*R*-isomer), 85% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.10-3.22 (2H, m, CH_2CH), 5.15 (1H, t, *J* = 6.4 Hz, CH_2CH), 7.11-7.49 (7H, m, Ar), 7.59 (1H, t, *J* = 7.4 Hz, Ar), 8.53 (1H, d, *J* = 7.4 Hz, CH-pyridyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 45.5, 74.6, 121.0, 122.9, 127.2, 127.7, 129.0, 136.4, 140.7, 148.4, 159.9.

2.8 Asymmetric borane reduction

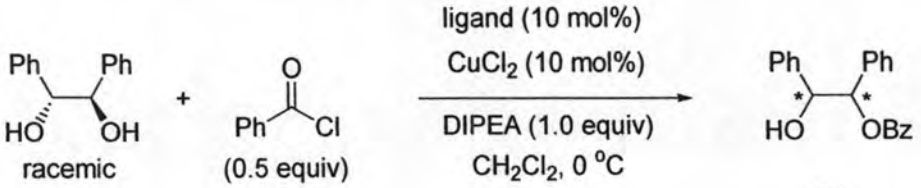
2.8.1 General procedure for screening of the ligands



To a solution of chiral ligand (0.030 mmol) in toluene was added $BH_3{\cdot}SMe_2$ (31 μL, 0.33 mmol) at room temperature over a period of 30 min and stirred for another 30 min. Acetophenone (35 μL, 0.30 mmol) in toluene was added slowly over a period of 120 min then stirred at room temperature until the starting material was disappeared (TLC). The reaction mixture was quenched with 2N NaOH and extracted twice with EtOAc. The combined organic layers were concentrated on reduced pressure and purified by column chromatography on silica gel eluting with petroleum ether/ethyl acetate.

2.9 Kinetic resolution of (±)-hydrobenzoin by asymmetric benzoylation

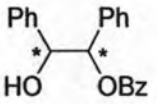
2.9.1 General procedure for screening of the ligands



75

Ligand (0.050 mmol) and $CuCl_2$ (6.7 mg, 0.050 mmol) were stirred in CH_2Cl_2 (2.5 mL) for 2 h to afford the green solution. Racemic *trans*-hydrobenzoin (0.107 g, 0.50 mmol) and diisopropylethylamine (DIPEA, 85 μL, 0.50 mmol) were dissolved in the catalyst solution and cooled to 0°C for 1 h. Benzoyl chloride (29 μL, 0.25 mmol) was added and the mixture was stirred at 0°C until the benzoyl chloride had disappeared (TLC). The reaction mixture was diluted with water and extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was purified on silica gel (petroleum ether/ethyl acetate = 3/1). Optical purities were determined by optical rotation.

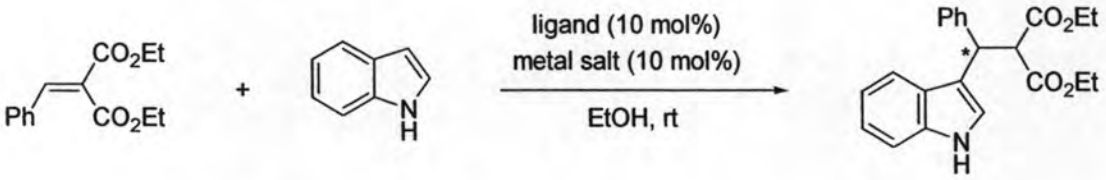
2.9.1.1 Benzoic acid 2-hydroxy-1,2-diphenyl-ethyl ester (75)



Benzoic acid 2-hydroxy-1,2-diphenyl-ethyl ester (**75**) was prepared according to the general procedure. The product was obtained as a white solid. m.p. 146-148 °C (lit.[136,137] m.p. 146-148 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.73-2.56 (1H, br, CHO*H*), 5.10 (1H, d, *J* = 7.4 Hz, C*H*OH), 6.11 (1H, d, *J* = 7.4 Hz, C*H*OBz), 7.30-7.16 (10H, m, Ar), 7.51-7.44 (2H, m, Ar), 7.62-7.55 (1H, m, Ar), 8.13-8.10 (2H, m, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz,) δ 77.3, 80.6, 127.2, 127.3, 128.1, 128.2, 128.3, 128.5, 129.8, 130.0, 133.3, 136.8, 139.0, 165.8.

2.10 Catalytic asymmetric Michael additions of indoles

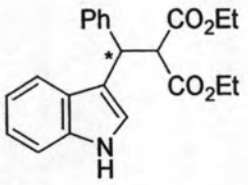
2.10.1 General procedure for optimization of conditions and screening of the ligands



76

To a 10 mL round bottom flask chiral ligand (0.030 mmol) and metal salt (0.030 mmol) were added under air atmosphere. Ethanol (0.6 mL) was added and the mixture was stirred for 1 h at room temperature (20-25°C). To the resulting solution benzylidene diethyl malonate (0.30 mmol, 1.0 equiv) in EtOH (0.6 mL) was added and stirring was continued for 20 min before the indole (0.36 mmol, 1.2 equiv) was added. After stirring for the amount of time indicated at room temperature, the red colored solution was concentrated under reduced pressure. The crude product purified by column chromatography (performed with petroleum ether/CH_2Cl_2 1:1, followed by CH_2Cl_2).

2.10.1.1 Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate (76)



Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate (**76**) was prepared according to the general procedure and purified by column chromatography (performed with hexanes/DCM 1:1, followed by DCM) to obtain the pure product as a white solid. m.p. 174-176 °C (lit.[138] m.p. 174-176 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.93-1.06 (6H, m, 2×CH_2CH_3), 3.93-4.06 (4H, m, 2×CH_2CH_3), 4.30 (1H, d, J = 11.8 Hz, $CH(CO_2Et)_2$, 5.09 (1H, d, J = 11.8 Hz, $CHPh$), 7.00-7.07 (1H, m, Ar), 7.09-7.31 (6H, m, Ar), 7.37 (2H, d, J = 7.4 Hz, Ar), 7.56 (1H, d, J = 8.0 Hz, Ar), 8.07 (1H, br, N*H*-indole); ^{13}C NMR ($CDCl_3$, 75 MHz,) δ 13.8, 42.9, 58.4, 61.4, 61.5, 111.0, 117.0, 119.4, 119.5, 120.9, 122.3, 126.7, 126.8, 128.2, 128.4, 136.2, 141.4, 167.9, 168.1; HPLC analysis: Chiralcel OD/OD-H, isocratic (*n*-heptane:2-propanol = 80:20), flow 0.5 mL/min, 254 nm; t_R = 14.7 min; t_S = 16.8 min.