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Supporting Information

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‘Cassette’-ISES (In Situ Enzymatic Screening) Identifies Complementary Chiral Scaffolds for Hydrolytic Kinetic Resolution Across a Range of Epoxides

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I. General Experimental:

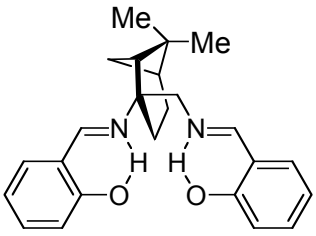
All reactions were conducted under nitrogen atmosphere using flame or oven-dried glassware, unless otherwise indicated. Methylene chloride was distilled from CaH_2. Toluene, THF and Et_2O were distilled from sodium benzophenone ketyl. Methanol was distilled from Mg, and ethanol from Na-diethyl phthalate. Alcohol dehydrogenase from equine liver (HLADH, EC 1.1.1.1), alcohol dehydrogenase from *Thermoanaerobium brockii* (TBADH, EC 1.1.1.2), alcohol dehydrogenase from *Lactibacillus kefir* (LKADH, EC 1.1.1.2), β-NAD^+ (sodium salt) and β-$NADP^+$ (sodium salt) were purchased from Sigma. 3,5-Di-*tert*-butylsalicylaldehyde (**a**) was purchased from Alfa-Aesar, 3,5-diiodosalicylaldehyde (**b**) from Lancaster, 1-hydroxy-2-naphthaldehyde (**d**) from TCI America salicylaldehyde (**c**), and cobalt(II)-acetate tetrahydrate from Aldrich. Flash chromatography was performed using Merck silica gel 60 (230-400 mesh). ^1H NMR spectra were recorded on Bruker-DRX-Avance-400 MHz, 500 MHz and 600 MHz instruments with chemical shifts reported relative to residual $CHCl_3$ (7.25 ppm) and CH_2Cl_2 (5.2 ppm). Proton-decoupled ^{13}C NMR spectra were acquired on Bruker-DRX-Avance-400 MHz, 500 MHz and 600 MHz instruments with chemical shifts reported relative to $CDCl_3$ (77.0 ppm). Optical rotations @589 nm were measured at 19 °C in an Autopol polarimeter. IR spectra were obtained using a Nicolet Avatar 360 FTIR spectrometer. Mass spectra were acquired at the Nebraska Center for Mass Spectrometry (University of Nebraska-Lincoln). Enzyme assays and ISES were performed on either a Shimadzu UV-2101PC spectrophotometer equipped with a CPS-260 six cell positioner and thermoelectric temperature control (set at 25 ºC for all experiments reported), or on a Shimadzu 2401 spectrophotometer, equipped with a 12-cell changer and water-jacketed cell holder for temperature control. A Chiralcel OD (0.46 mm x 25 cm) chiral stationary phase was used for enantiomeric excess determinations by HPLC.

II. Synthesis of Co^{III}-Salen Catalysts

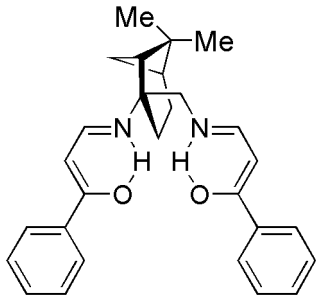
General Procedure A: Synthesis of Chiral 'Salen' Ligands (illustrated for 4a).

An oven-dried RB flask was charged with (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (300 mg, 1.5 mmol), 3,5-di-*tert*-butylsalicylaldehyde (703 mg, 3.0 mmol) and dry ethanol (5 mL). The reaction mixture was stirred at 70 °C for 12 h. Note: While the reaction temperature and time varied, from salen to salen (as indicated in the individual procedures) the salen product crystallized out of this solvent, in most cases. In the case of **2a**, the product could be obtained in pure form (890 mg, 94%) by simple trituration with cold ethanol. In other cases, if further purification was required, this was achieved by recrystallization or column chromatography.

***N,N'*-Bis(salicylidene)-[1*R*-(1α,2α,5α)]-2-amino-7,7-dimethyl-2-bicyclo[3.3.1]heptane-ethanamine (1c).** Diamine **1** was prepared from commercially available (1*S*)-(-)-β-pinene as described.[1] Following General Procedure A, from diamine **1** (500 mg, 2.97 mmol) and salicylaldehyde (600 mg, 5.35 mmol, 1.8 eq.), after heating at 60 °C for 24 h, filtration and trituration (cold EtOH), produced clean **1c** (776 mg, 81%): $[\alpha]^{19}_{D}$ +2.0 (*c* 1.11, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (d, *J* = 10.3 Hz, 1H), 1.22 (s, 3H), 1.35 (s, 3H), 1.94-2.06 (m, 3H), 2.19-2.28 (m, 3H), 2.41 (br t, 1H), 3.75 (d, *J* = 12.3 Hz, 1H), 3.88 (d, *J* = 12.3 Hz, 1H), 6.80 (m, 2H), 6.98 (d, *J* = 2 Hz, 1 H), 7.04 (d, *J* = 2 Hz, 1H), 7.32 (d, *J* = 2 Hz, 1H), 7.33 (d, *J* = 2 Hz, 1H), 8.15 (s, 1H), 8.19 (s, 1H), 13.3 (br s, 1H), 14.1 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 23.8, 25.6,25.7, 28.1, 28.4, 38.4, 39.9, 48.1, 67.5, 68.6, 116.9, 117.0, 118.3, 118.52, 118.55, 118.58, 131.4, 131.7, 132.1, 132.3, 161.0, 161.3, 161.6, 166.7; HRMS (FAB, 3-NOBA) calcd for $C_{24}H_{28}N_2O_2$ $(M+H)^+$ 377.2231, obsd. 377.2234.



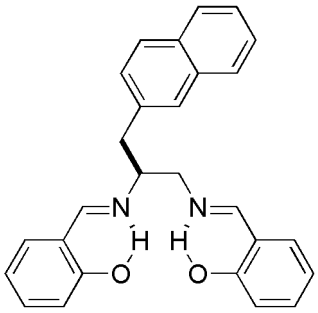
***N,N'*-Bis(3'-*Z*-hydroxy-3'-phenylpropenylidene)-[1*R*-(1α,2α,5α)]-2-amino-7,7-dimethyl-2-bicyclo[3.3.1]heptane-ethanamine (1e)**. The sodium salt of benzoylacetaldehyde was prepared from acetophenone and ethyl formate in presence of sodium ethoxide, as described[2]. The title baen was obtained, following General Procedure A, from diamine **1** (190 mg, 1.13 mmol) and benzoylacetaldehyde (301 mg, 2.03 mmol, 1.8 eq.). After heating at 40 °C for 12 h, silica gel column



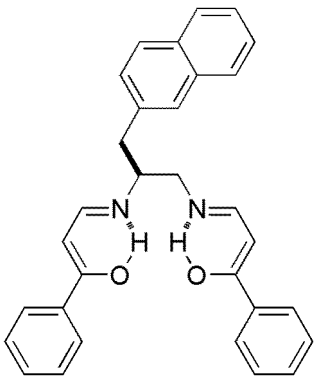
^{1}H NMR (400 MHz, $CDCl_3$)

chromatography (25→50% EtOAc in hexanes) provided pure **1e** (221 mg, 51%): $[\alpha]^{19}_D$ -24.8 (*c* 3.05, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10(s, 3H), 1.25 (m, 1H), 1.34 (s, 3H), 1.80-2.00 (m, 7H), 3.27 (dd, *J* = 13.9, 7.8 Hz, 1H), 3.44 (dd, *J* = 13.9, 6.0 Hz, 1H), 5.64 (dd, *J* = 7.5 Hz, 1H), 5.69 (dd, J = 7.5 Hz, 1H), 6.72 (dd, *J* = 12.4, 7.5 Hz, 1H), 6.83 (dd, *J* = 13.1, 7.6 Hz, 1H), 7.35 – 7.45 (m, 4 H), 7.49 – 7.65 (m, 4 H), 7.80 – 7.88 (m, 8 H), 10.47 (m, 1H), 10.66 (d, *J* = 13.1 Hz, 1H),: ^{13}C NMR (100 MHz, $CDCl_3$) δ23.6, 25.0, 27.7, 28.0, 28.4, 37.9, 40.1, 46.3, 59.2, 62.6, 90.5, 90.9, 126.99, 127.04, 128.14, 128.15, 128.2, 128.5, 128.6, 130.0, 130.8, 131.0, 133.2, 134.0, 136.3, 138.1, 139.4, 139.5, 150.7, 155.2, 189.5, 190.3, 194.8; HRMS (FAB, 3-NOBA) calcd for $C_{28}H_{33}N_2O_2$ $(M+H)^+$ 429.2542, obsd 429.2538.

***N,N'*-Bis(salicylidene)-(1*S*)-(β-naphthylmethyl)-1,2-ethylenediamine (2c).** (1S)-β-(Naphthylmethyl)-1,2-ethylenediamine **2**[3] was prepared from 3-(β-naphthyl)-L-alanine (Chem-Impex International). Following General Procedure A, stirring at 70 °C for 24 h, from (1*S*)-(β-naphthylmethyl)-1,2-ethylenediamine (305 mg, 1.525 mmol) and salicylaldehyde (325 mg, 2.9 mmol, 1.9 eq.), was obtained **2c**. Purification by trituration with ethanol yielded a bright yellow solid (520 mg, 92%): $[\alpha]^{19}_D$ -47.9 (*c* 1.95, CH_2Cl_2); ^{1}H NMR (400 MHz, CDCl3) δ 3.15 (dd, *J* = 13.6, 8.0 Hz, 1H), 3.28 (dd, *J* = 13.6, 5.1 Hz, 1H), 3.77 (dd, *J* = 12.0, 7.6 Hz, 1H), 3.85 (m, 1H), 4.01 (ddd, *J* = 12.0, 3.9, 1.2 Hz, 1H), 6.77 (dappt, J = 7.5, 1.0 Hz, 1H), 6.84(dappt, *J* = 7.5, 1.1 Hz, 1H), 6.92 (s, 1H), 6.94 (s, 1H), 7.03 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.19 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.23 – 7.33 (m, 3H), 7.43 (m, 2H) 7.64 (s, 1H), 7.74 – 7.79 (m, 3H), 8.04 (s, 1H), 8.31 (s, 1H), 13.22 (br s, 2H); ^{13}C NMR (100 MHz, CDCl3) δ 41.1, 64.1, 71.5, 116.8, 116.9, 118.4, 118.59, 118.63, 118.67, 125.5, 126.1, 127.5, 127.6, 127.8, 128.1, 131.5, 131.6, 132.2, 132.36, 132.42, 133.5, 135.2, 160.88, 160.96, 165.5, 166.8; HRMS (FAB, 3-NOBA) calcd for $C_{27}H_{25}N_2O_2$ $(M+H)^+$ 409.1918, obsd 409.1929.

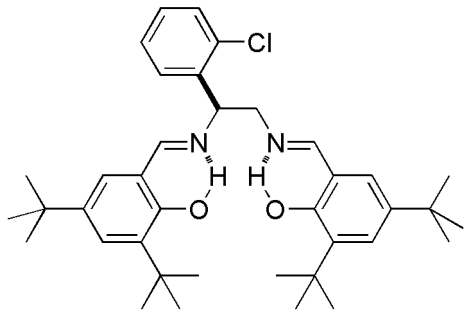


***N,N'*-Bis(3'-*Z*-hydroxy-3'-phenylpropenylidene)-(1*S*)-(β-naphthylmethyl)-1,2-ethylenediamine (2e).** The target baen was obtained following General Procedure A, starting from (1*S*)-(β-naphthylmethyl)-1,2-ethylenediamine (145 mg, 0.728 mmol) and benzoylacetaldehyde (252 mg, 1.45 mmol, 1.9 eq.) with stirring at 50 °C for overnight. Silica gel column chromatography (25→50% EtOAc in hexanes) provided

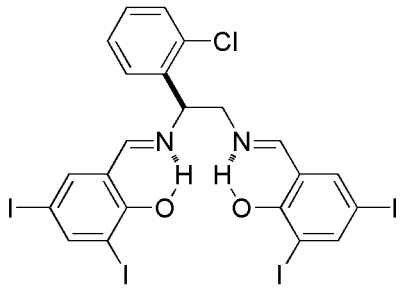


pure **2e** (252 mg, 72 %): $[\alpha]^{19}_D$ -13.3 (*c* 0.75, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04 (dd, *J* = 13.8 , 7.7 Hz, 1H), 3.12 (dd, *J* = 13.8, 5.6 Hz, 1H), 3.28 (m, 1H), 3.54 (m, 2H), 5.58 (d, *J* = 7.5 Hz, 1H), 5.71 (d, *J* = 7.5 Hz, 1H), 6.67 (dd, *J* = 12.3, 7.5 Hz, 1H), 6.85 (dd, *J* = 12.4, 7.5 Hz, 1H), 7.31 – 7.48 (m, 9H), 7.76 – 7.87 (m, 8H), 10.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40, 53.9, 63.0, 91.1, 91.3, 125.8, 126.3, 127.12, 127.13, 127.2, 127.61, 127.63, 128.1, 128.2, 128.5, 131.1, 132.4, 133.5, 134.0, 139.4, 153.4, 154.5, 190.4, 190.5; HRMS (FAB, 3-NOBA) calcd for $C_{31}H_{29}N_2O_2$ $(M+H)^+$ 461.2229, obsd 461.2228.

***N,N*'-Bis(3',5'-di-*tert*-butylsalicylidene)-(1S)-ortho-chlorophenyl-1,2-ethylenediamine (3a)**. (1S)-o-Chlorophenyl-1,2-ethylenediamine **3**[3] was prepared from *L*-(+)-2-chlorophenylglycine (Aldrich, 95%). Following General Procedure A, from (1*S*)-o-chlorophenyl-1,2-ethylenediamine (334 mg, 1.96 mmol) and 3,5-di-*tert*-butylsalicylaldehyde (826 mg, 3.53 mmol, 1.8 eq.), after stirring at 50 °C for 12 h, was obtained **3a**. Trituration with ethanol provided pure salen (941 mg, 89%): $[\alpha]^{19}_D$ +48.6 (*c* 1.13, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 9H), 1.26 (s, 9H), 1.41 (s, 9H), 1.44 (s, 9H), 3.87 (dd, *J* = 12.2, 8.9 Hz, 1H), 4.15 (dd, *J* = 12.2, 3.4 Hz, 1H), 5.18 (dd, *J* = 8.9, 3.4 Hz, 1H), 7.03 (d, *J* = 2.4 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 7.24 (dappt, *J* = 7.7, 1.7 Hz, 1H), 7.32 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.35 (dd, *J* = 5.5, 2.5 Hz, 1H), 7.41 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.65 (dd, *J* = 7.8, 1.6 Hz, 1H), 8.36 (s, 1H), 8.48 (s, 1H), 13.51 (br s, 1H), 13.54 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.40, 29.44, 31.40, 31.43, 34.1, 35.0, 64.8, 70.0, 117.75, 117.79, 126.1, 126.6, 127.1, 127.36, 127.39, 128.7, 128.8, 129.8, 132.6, 136.5, 136.6, 138.1, 140.0, 140.3, 157.9, 158.0, 167.96, 168.04; HRMS (FAB, 3-NOBA) calcd for $C_{38}H_{52}O_2N_2Cl$ $(M+H)^+$ 603.3719, obsd 603.3700.

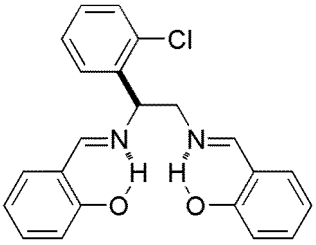


***N,N*'-Bis(3',5'-diiodosalicylidene)-(1*S*)-ortho-chlorophenyl-1,2-ethylenediamine (3b).** Following General Procedure A, from (1*S*)-o-chlorophenyl-1,2-ethylenediamine (350 mg, 2.05 mmol) and 3, 5-diiodosalicylaldehyde (1.38 g, 3.7 mmol, 1.8 eq.), after stirring at 70 °C for 20 h, was obtained **3b**. Trituration with ethanol provided pure salen (1.59 g, 98%): $[\alpha]^{19}_D$ +21.9 (*c* 1.08, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (dd, *J* = 12.5, 8.9 Hz, 1H), 4.22 (dd, *J* = 12.5, 3.4 Hz, 1H), 5.22 (dd, *J* = 8.9, 3.4 Hz, 1H), 7.27 -7.33 (m, 2H), 7.42 (dd, *J* = 7.8,



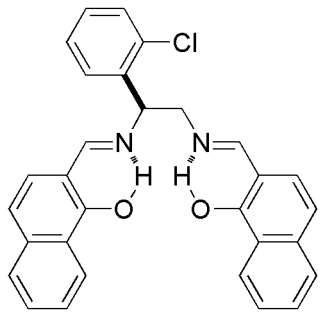
1.2 Hz, 1H), 7.45 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 1.9 Hz, 1H), 7.52 (dd, *J* = 7.6, 1.5 Hz, 1H), 8.00 (d, *J* = 2 Hz, 1H), 8.02 (d, *J* = 1.9 Hz, 1H), 8.10 (s, 1H), 8.24 (s, 1H), 14.22 (br s, 1H), 14.27 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.7, 69.5, 79.6, 80.1, 86.9, 87.4, 119.6, 119.7, 127.7, 128.2, 129.4, 130.1, 132.6, 136.2, 140.0, 140.4, 148.9, 149.0, 159.9, 160.4, 165.0, 165.1; HRMS (FAB, 3-NOBA) calcd for $C_{22}H_{16}O_2N_2I_4Cl$ $(M+H)^+$ 882.7081, obsd 882.7071.

***N,N'*-Bis(salicylidene)-(1*S*)-ortho-chlorophenyl-1,2-ethylenediamine (3c).** Following General Procedure A, from (1*S*)-o-chlorophenyl-1,2-ethylenediamine (360 mg, 2.11 mmol) and salicylaldehyde (464 mg, 3.8 mmol, 1.8 eq.), after stirring at 70 °C for 24 h, was obtained **4c**. Trituration with ethanol provided pure salen (534 mg, 74%): $[\alpha]^{19}_D$ +8.3 (*c* 1.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.95 (ddd, *J* = 12.3, 8.2, 0.6 Hz, 1H), 4.16 (ddd, *J* = 12.3, 3.8, 1.1 Hz, 1H), 5.19 (dd, *J* = 8.2, 3.8 Hz, 1H),

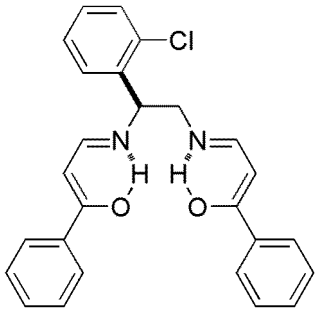


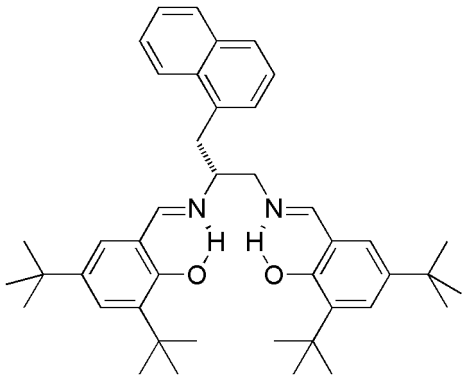
6.83 (d, *J* = 7.3, Hz, 1H), 6.87 (d, *J* = 8.3, Hz, 1H), 6.93 (d, *J* = 8.3, Hz, 1H), 6.96 (d, *J* = 8.3, Hz, 1H), 7.18 – 7.33 (m, 1H), 7.42 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.61 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.31 (s, 1H), 8.46 (s, 1H), 13.03 (s, 1H), 13.21 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 64.6, 69.9, 116.75, 116.80, 118.38, 118.41, 118.5, 118.8, 127.3, 128.5, 128.8, 129.7, 131.5, 131.9, 132.35, 132.44, 132.7, 137.5, 160.7, 160.8, 166.6, 166.8; HRMS (FAB, 3-NOBA) calcd for $C_{22}H_{20}O_2N_2Cl$ $(M+H)^+$ 379.1215, obsd 379.1209.

***N,N'*-Bis(1'-hydroxy-2'-naphthylidene)-(1*S*)-ortho-chlorophenyl-1,2-ethylenediamine (3d).** Following General Procedure A, from (1*S*)-o-chlorophenyl-1,2-ethylenediamine (350 mg, 2.05 mmol) and α-hydroxy-β-naphthaldehyde (365

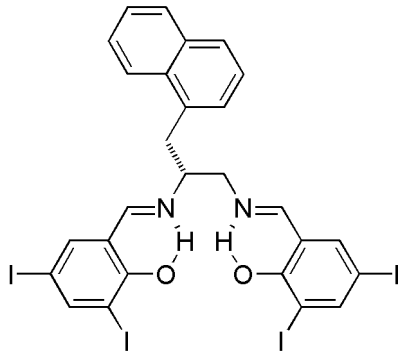


mg, 3.7 mmol, 1.8 eq.), after stirring at 50 °C for 14 h, was obtained **3d**. Trituration with ethanol provided pure 'salen' (624 mg, 71%): $[\alpha]^{19}_D$ +326 (*c* 1.12, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (dd, *J* = 13, 8.7 Hz, 1H), 4.14 (dd, *J* = 13, 3.3 Hz, 1H), 5.22 (dd, *J* = 8.7, 3.3 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 7.29 (d appt, *J* = 7.6, 1.6 Hz,1H), 7.36 (d appt, *J* = 7.6, 1.2 Hz,1H), 7.40–7.59 (m, 6H), 7.63 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.91 (s, 1H), 8.32 (s, 1H), 8.40 (d, *J* = 8.1 Hz, 1H), 8.43 (d, *J* = 8 Hz, 1H), 13.75 (br s, 1H) 14.46 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 59.1,68.0, 109.78, 110.8, 115.9, 117.5, 124.1, 124.9, 125.2, 125.4, 126.5, 127.2, 127.4, 127.5, 127.7, 128.3, 128.4, 129.3, 129.4, 129.9, 130.1, 132.6, 136.36, 136.39, 137.0, 163.5, 165.6, 165.9, 172.4; HRMS (FAB, 3-NOBA) calcd for $C_{30}H_{24}N_2O_2Cl$ $(M+H)^+$ 479.1528, obsd 479.1516.

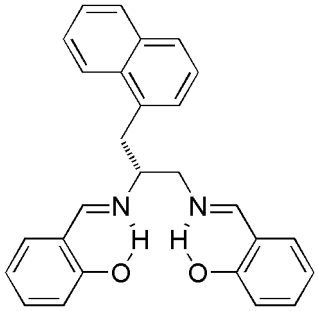
***N,N'*-Bis(3'-*Z*-hydroxy-3'-phenylpropenylidene)-(1*S*)-ortho-chlorophenyl-1,2-ethylenediamine (3e).**  Following General Procedure A, from (1*S*)-o-chlorophenyl-1,2-ethylenediamine (218 mg, 1.28 mmol) and benzoylacetaldehyde (379 mg, 2.56 mmol), after stirring at 50 °C for 14 h, was obtained **3e**. The product was purified by silica gel column chromatography (25→50% EtOAc in hexanes) (80 mg, 13%): $[\alpha]^{19}_{D}$ +57 (*c* 1.0, CH_2Cl_2); ^{1}H MR (400 MHz, $CDCl_3$) □ 3.43 (d app t, *J* = 14.2, 8.2 Hz, 1H), 3.75 (ddd, *J* = 14.1, 5.7, 3.9 Hz, 1H), 4.85 (app t d, J = 9.0, 3.8 Hz, 1H), 5.73 (d, J = 7.6 Hz, 1H), 5.78 (d, J = 7.6, 1H), 6.90 (dd, J = 12.4, 7.6 Hz, 1H), 6.95 (dd, J = 12.1, 7.6 Hz, 1H), 7.26 – 7.48 (m, 10 H), 7.83 – 7.89 (m, 4H), 10.4 (m, 1H), 10.98 (t, J = 10.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.2, 62.0, 91.6, 92.2, 127.16, 127.21, 127.53, 127.82, 128.2, 128.3, 129.6, 130.1, 131.1, 131.3, 132.5, 135.9, 139.3, 139.4, 153.4, 154.1, 190.5, 190.9; HRMS (FAB, 3-NOBA) calcd for $C_{26}H_{24}N_2O_2Cl$ $(M+H)^+$ 431.1526, obsd 431.1532.

***N,N'*-Bis(3',5'-di-*tert*-butylsalicylidene)-(1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (4a).**  The requisite diamine, (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine **2**[3], was prepared from 3-(α-naphthyl)-D-alanine (Chem-Impex International). Following General Procedure A, from (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (300 mg, 1.5 mmol), 3,5-di-*tert*-butylsalicylaldehyde (703 mg, 3.0 mmol) after heating at 70 °C for 12 h, was obtained **2a**. Filtration and trituration with ice-cold ethanol provided pure salen (890 mg, 94%): $[\alpha]^{19}_{D}$ +37.7 (*c* 1.06, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ1.23 (s, 9H), 1.29 (s, 9H), 1.44 (s, 9H), 1.47 (s, 9H), 3.37 (dd, *J* = 13.9, 7.7Hz, 1H), 3.68 (dd, *J* =13.9, 5.2 Hz, 1H), 3.84 (dd, *J* = 11.8, 7.2 Hz, 1H), 3.93 (m, 1H), 4.02 (dd, *J* =11.8, 3.8 Hz, 1H), 6.85 (d, *J* = 2.4 Hz, 1H), 7.06 (d, *J* = 2.4 Hz, 1H), 7.35 (m, 4H), 7.48 (dt, *J* = 6.8, 1.1 Hz, 1H), 7.54 (dt, *J* = 6.9, 1.4 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.98 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 8.38 (s, 1H), 13.66 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ29.4, 29.44, 31.4, 31.44, 34.03, 34.08, 34.99, 37.92, 64.25, 70.4, 117.6, 117.8, 123.7, 125.4, 125.6, 126.05, 126.14, 127.0, 127.08, 127.4, 128.2, 128.9, 131.9, 133.9, 134.1, 136.4, 136.6, 139.9, 140.0, 157.9, 158.1, 166.6, 167.8; HRMS (FAB, 3-NOBA) calcd for $C_{43}H_{57}N_2O_2$ $(M+H)^+$ 633.442, obsd 633.4402.

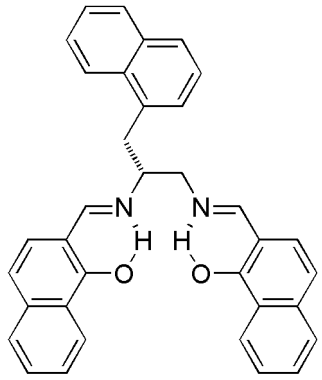
***N,N'*-Bis(3',5'-diiodosalicylidene)-(1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (4b).** Following General Procedure A, from (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (330 mg, 1.65 mmol), 3,5-diiodosalicylaldehyde (1.23 g, 3.3 mmol, 2 eq.), heating for 15 h at 70 °C, was obtained **4b**. Purification was achieved by trituration with cold ethanol to give the final product (1.21 g, 80%): $[\alpha]^{19}_{D}$ +48.2 (*c* 0.96, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ3.29 (dd, *J* = 14, 8.5 Hz, 1H), 3.62 (dd, *J* = 14, 5 Hz, 1H), 3.85 (dd, *J* = 12.3, 8.1 Hz, 1H), 3.98 (m, 1H), 4.1 (dd, *J* = 12.3, 3.1 Hz, 1H), 7.18 (d, *J* = 1.8 Hz, 1H), 7.21 (d, *J* = 6.9 Hz, 1H), 7.33 (t, *J* = 7.1 Hz, 1H), 7.45 -7.58 (m, 3H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 2 Hz, 1H), 8.01 (d, *J* = 2 Hz, 1H), 8.11 (s, 1H), 14.35 (br s, 1H), 14.43 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ37.8, 63.3, 69.7, 79.4, 79.5, 79.56, 87.2, 87.5, 119.4, 119.6, 123.1, 125.4, 125.9, 126.5, 128.0, 128.3, 129.1, 131.5, 132.6, 134, 139.9, 140.0, 148.7, 148.9, 160.3, 160.6, 163.8, 164.9; HRMS (FAB, 3-NOBA) calcd for $C_{27}H_{21}N_2O_2I_4$ $(M+H)^+$ 912.7782, obsd 912.7766.



***N,N'*-Bis(salicylidene)-(1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (4c).** Following General Procedure A, from (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (450 mg, 2.25 mmol), salicylaldehyde (550 mg, 4.5 mmol, 2 eq.), heating at 70 °C for 24 h, was obtained **2c**. Purification was achieved by trituration with cold ethanol to give the final product (590 mg, 64%): $[\alpha]^{19}_{D}$ +129 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ3.34 (dd, *J* = 13.9, 8.2 Hz, 1H), 3.68 (dd, *J* = 13.9, 4.9 Hz, 1H), 3.86 (dd, *J* = 12, 7.1 Hz, 1H), 3.95 (m, 1H), 4.03 (dd, *J* = 11.9, 3.2 Hz, 1H), 6.78 (dt, *J* = 7.6, 0.9 Hz, 1H), 6.87 (dt, *J* = 7.6, 0.8 Hz, 1H), 6.94-7.02 (m, 3H), 7.2 – 7.4 (m, 4H), 7.52 (t, dt, *J* = 7.2 Hz, 1H), 7.58 (t, *J* =7 Hz, 1H), 7.75 (d, *J* = 8 Hz, 1H), 7.85 (s, 1H), 7.89 (d, *J* = 8 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.33 (s, 1H), 13.31 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.72, 64.25, 70.19, 116.69, 116.84, 118.22, 118.5, 118.6, 123.4, 125.3, 125.6, 126.1, 127.4, 128.2, 128.9, 131.4, 131.7, 132.2, 132.4, 133.6, 133.8, 160.8, 160.9, 165.4, 166.7 ; HRMS (FAB, 3-NOBA) calcd for $C_{27}H_{25}N_2O_2$ $(M+H)^+$ 409.1918, obsd 409.1913.

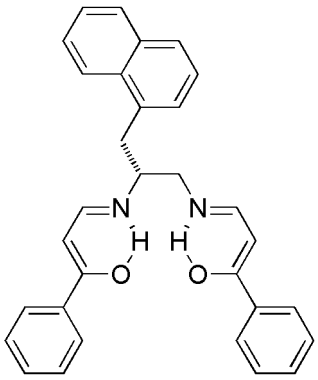


***N,N'*-Bis(1'-hydroxy-2'-naphthylidene)-(1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (4d).** Following General Procedure A, from (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (440 mg, 2.2 mmol), α-hydroxy-β-naphthaldehyde (758 mg, 4.4 mmol, 2 eq.), heating at 70 °C for 12 h, was obtained **4d**. Purification was achieved by trituration with cold ethanol to give the final product (710 mg, 64%): $[\alpha]^{19}_D$ -478.9 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41



(dd, *J* = 14, 8.1 Hz, 1H), 3.69 (dd, *J* = 14, 5.1 Hz, 3.83 (m, 1H), 3.95-4.08 (m, 2H), 6.77 (d, *J* = 8.7 Hz, 1H), 6.85 – 6.97 (m, 3H),7.33 – 7.36 (unresolved, 2H), 7.39 – 7.66 (m, 9H), 7.76 (dd, *J* = 7.2, 3.3 Hz, 1H), 7.87 (d, =8.2 Hz, 1H), 7.98 (br d, *J* = 3.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 8.2 Hz, 1H), 8.42 (d, *J* = 8.1 Hz, 1H), 13.91 (br s, 1H), 14.2 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.5, 58.5, 66.9, 109.7, 109.9, 115.9, 116.5, 123.1, 124.3, 124.7, 125.1, 125.2, 125.4, 125.8, 126.5, 127.2, 127.3, 127.5, 127.9, 128.2, 128.3, 129.1, 129.4, 129.8, 131.5, 132.6, 133.9, 136.5, 136.9, 163.7, 163.8, 168.4, 171.9; HRMS (FAB, 3-NOBA) calcd for $C_{25}H_{29}N_2O_2$ $(M+H)^+$ 509.2231, obsd 509.2238.

***N,N'*-Bis(3'-*Z*-hydroxy-3'-phenylpropenylidene)-(1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (4e).**



Following General Procedure A, from (1*R*)-(α-naphthylmethyl)-1,2-ethylenediamine (150 mg, 0.75 mmol), benzoylacetaldehyde (200 mg, 1.35 mmol, 1.8 eq.), after heating at 40 °C for 16 h and silica gel column chromatography (25→50% EtOAc in hexanes) provided pure **2e** (54 mg, 17%): $[\alpha]^{19}_D$ -18.9 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.26 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.34 (dd, *J* = 14, 6.8 Hz, 1H), 3.46 (dd, J = 14.1, 5.9 Hz, 1H), 3.54 (d appt, J = 13.8, 4.8 Hz, 1H), 3.63 (m, 1H), 5.53 (d, *J* = 7.5 Hz, 1H), 5.71 (d, *J* = 7.5 Hz, 1H), 6.53 (dd, *J* = 12.2, 7.5 Hz, 1H), 6.86 (dd, *J* = 12.3, 7.5 Hz, 1H), 7.36 – 7.56 (m, 9H), 7.75 – 7.97 (m, 8H), 10.5 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.0, 53.9, 62.1, 90.9, 91.3, 123, 125.5, 125.7, 126.5, 127.05, 127.07, 127.8, 128.1, 128.2, 129.0, 129.8, 131.0, 131.5, 132.6, 133.9, 139.4, 153.4, 154.5, 190.3, 190.4; HRMS (FAB, 3-NOBA) calcd for $C_{31}H_{29}N_2O_2$ $(M+H)^+$ 461.2229, obsd 461.2228.

General Procedure B: Synthesis of Cobalt(III)-Salen Complexes (illustrated for Co^{III}-2a-OAc): To a stirred solution of 'salen' ligand **(2a)** (107 mg, 0.169 mmol, 1 eq.) in CH_2Cl_2 (5 mL), was added a methanolic (3 mL) solution of cobalt(II) acetate tetrahydrate (42 mg, 0.169 mmol, 1.0 eq.), via cannula, under Ar. The Co^{II}-salen

complex precipitated out as a red solid. The Co^{II} complex was filtered and taken up in CH_2Cl_2 or toluene (5 mL) and stirred with acetic acid (>10 eq.) open to the air. The oxidation reactions were generally followed by TLC [Co^{III}-complex shows formation of a greenish-brown spot of lower R_f from the visibly red, higher R_f spot characteristic of the Co^{II}-salen]. When TLC indicated the completion of the reaction (2-12 h), the solvent was evaporated, and the Co^{III}-salen complex further dried *in vacuo*. The Co^{III} carboxylate complexes so prepared were generally used directly for HKR experiments, under ISES (biphasic) conditions or under neat conditions.[5]

Table S1: MS characterization of Co^{III}-acetate salen catalysts [generally (M – acetate)+ was observed].

Catalyst	Molecular Formula	Calcd (M – acetate)	obsd MS (FAB, 3-NOBA)
1c	$C_{26}H_{29}N_2O_4Co$	433.1326	433.1319
1e	$C_{30}H_{33}N_2O_4Co$	485.1639	485.1639
2c	$C_{29}H_{25}N_2O_4Co$	465.1013	465.1032
2e	$C_{33}H_{29}N_2O_4Co$	517.1326	517.1314
3a	$C_{39}H_{52}ClN_2O_4Co$	659.2815	659.2820
3c	$C_{24}H_{20}ClN_2O_4Co$	435.0311	435.0314
3d	$C_{32}H_{24}ClN_2O_4Co$	535.0624	535.0628
4a	$C_{45}H_{57}N_2O_4Co$	689.3517	689.3525
4c	$C_{29}H_{25}N_2O_4Co$	465.1013	465.1031
4e	$C_{33}H_{29}N_2O_4Co$	517.1326	517.1320

III. Reporting Enzyme Standardization

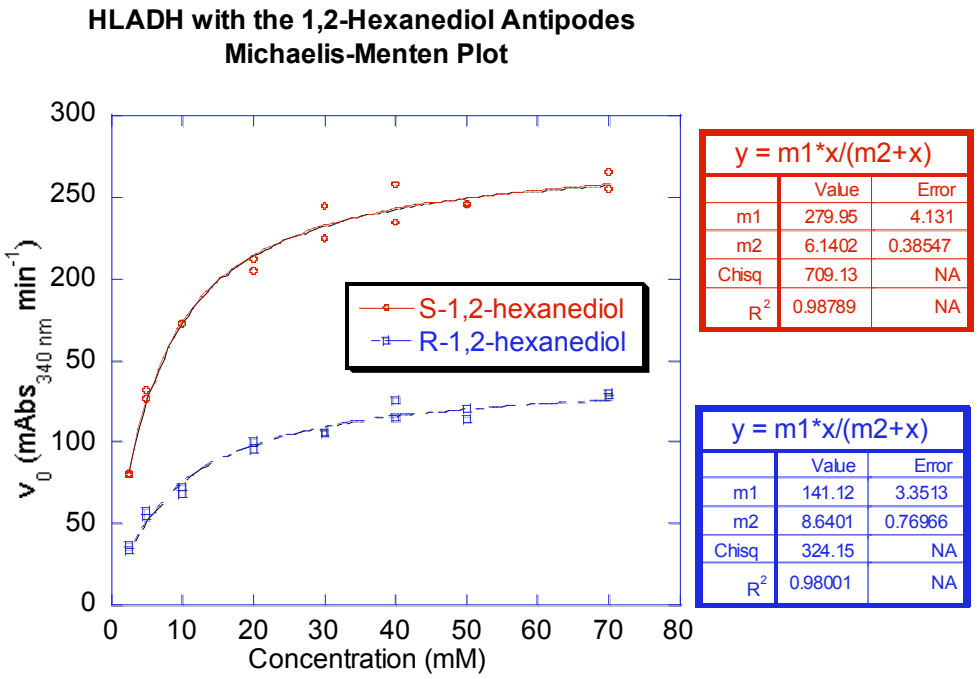
The following stock solutions were prepared for enzyme standardization: 220 mM -β-NAD^+, 220 mM β-$NADP^+$, alcohol dehydrogenases from horse liver (HLADH) (0.01-0.02 U/μL) and *Lactobacillus kefir* (LKADH) (0.05-0.07 U/μL) in 25 mM sodium phosphate buffer, pH 7.0, 150 mM magnesium chloride and 2M isopropanol in H_2O. Enzyme units were calculated by measuring the rate of formation of NAD(P)H at 340 nm for both dehydrogenases (*vide infra*). In each case, one S.I. unit is taken as the amount of enzyme catalyzing the formation of one μmol of NADH per minute. To screen the HKR of propylene oxide, both HLADH and TBADH were standardized with 200 mM (R)-1,2-propanediol.[4] In all cases, quartz cuvettes with 1 cm light paths and nominal 1 mL volumes were used.

Standardization of HLADH: The assay cuvette contained the following components: 7.2 mM (33 µL) of β-NAD^+, 2 µL (or 20 µL of a 1:10 dilution) of HLADH stock solution, 865 µL of 50 mM sodium pyrophosphate buffer, pH 8.8, and 200 mM (100 µL) of isopropanol. The reaction was initiated by the addition of 2-propanol, which typically gave a rate of 0.12 ± 0.01 Abs/min at 25 °C, 340 nm. This indicates an activity level of 0.010 unit of HLADH per µL of the stock solution. Comparison of HLADH activity between 2-propanol and *S*-1,2-hexanediol reveals that each 2-propanol unit (150 mM conc) contains four *S*-1,2-hexanediol units (200 mM conc.).

Standardization of LKADH: The assay cuvette contained the following components: 2.2 mM (10 µL) β-$NADP^+$, 1.5 mM (10 µL) $MgCl_2$, 2 µL (or 20 µL of 1:10 dilution) of LKADH stock solution, 878 µL of 50 mM sodium pyrophosphate buffer, pH 8.8, and 200 mM (100 µL) of 2-propanol. The reaction was initiated by the addition of 2-propanol, which typically gave a rate of 0.110 ± 0.001 Abs/min at 25 °C, 340 nm. This is indicative of 0.009 unit of LKADH per µL of the stock solution. For LKADH, 0.12 2-propanol (200 mM) units are equivalent to 0.20 S-1,2-hexanediol (150 mM) units.

IV. Reporting Enzyme Enantioselectivity

Previously, we reported (ref. 4) that HLADH is selective for (*S*)-1,2-propanediol over (*R*)-1,2-hexanediol and this ratio varies from 2.4 to 4.0 over the concentration range 4 to 100 mM concentration.

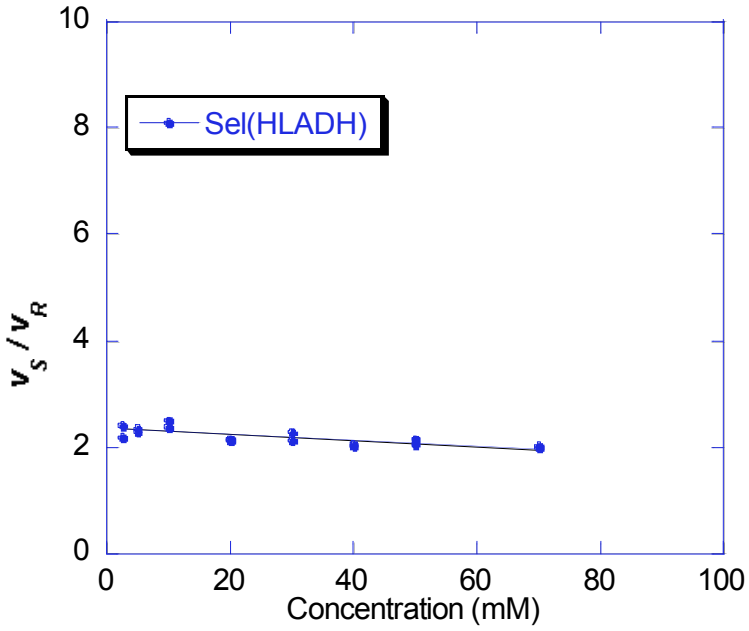


Similarly, TBADH is selective for (*R*)-1,2-propanediol over (*S*)-1,2-propanediol.

Hexanediol Reporting Enzymes:

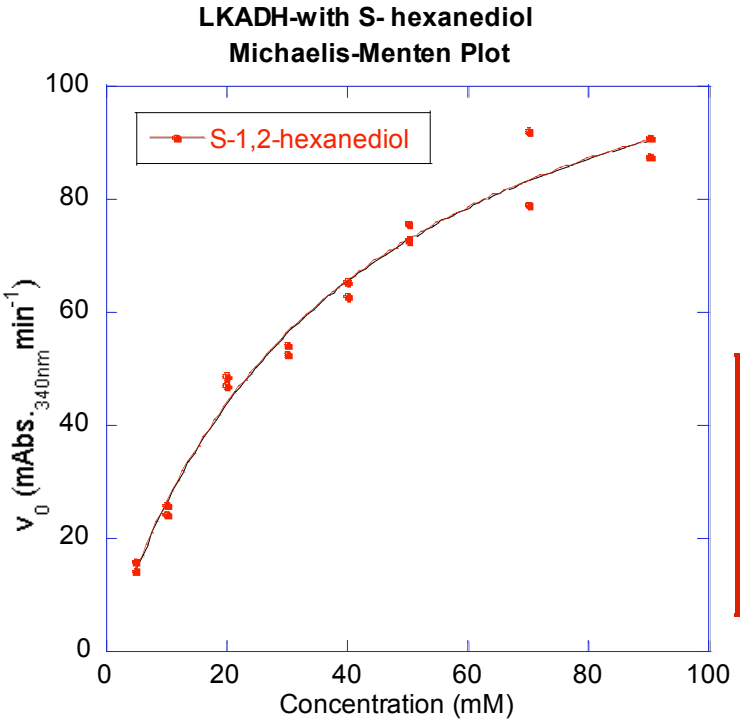
A. **HLADH:** The enantioselectivity of HLADH was estimated from the ratios of the initial velocities of (S)- and (R)-1,2-hexanediol at fixed concentration between 2.5 and 70 mM at 25 °C. Each data point is reported in duplicate. The composition of each assay cuvette was 7.2 mM NAD^+ (33 µL of 220 mM stock solution), 0.0118 2-propanol U of HLADH and various concentrations of either the (R)- or the (S)-enantiomer of 1,2-hexanediol. In all cases, the final volume was adjusted to 1 mL using 50 mM sodium pyrophosphate buffer at pH 8.8.

From the *Michaelis-Menten* plot, K_m values are in similar range, 6.1 and 8.6 mM for (*S)*- and (*R)*-1,2-hexanediol, respectively. But, $[(V_{max})_S \div (V_{max})_R] = 1.99$, which would be the selectivity parameter at large, saturating concentrations of 1,2-hexanediol. On the other hand, $[(V_{max}/K_m)_S \div (V_{max}/K_m)_R] = [45.59 \div 16.33] = 2.79$, which then corresponds to the selectivity parameter at very low concentrations of the diol. During HKR-ISES experiments, we estimate that the diol concentration is in the range of 2.5-70 mM, so the selectivity parameter falls in the rather narrow 2.0-2.5 range (2.2 was used for ISES-calculations).



[Diol] (mM)	2.5	5	10	20	30	40	50	70
Enantioselectivity (v_S/v_R)	2.30	2.32	2.46	2.13	2.22	2.05	2.10	2.01

B. **LKADH:** In a similar manner as for HLADH, we estimated the enantioselectivity of LKADH from the ratios of the initial velocities of (S)- and (R)-1,2-hexanediol at fixed concentrations between 2.5 and 70 mM at 25 °C. Each data point was obtained in duplicate. Each assay cuvette contained: 2.2 mM NAD^+ (10 µL of 220 mM stock solution), 1.5 mM $MgCl_2$ (10 µL of 150 mM stock solution), 0.0106 U of LKADH and various concentrations of either (R)- or (S)-1,2-hexanediol. In all cases, the final volume was adjusted to 1 mL using 50 mM sodium pyrophosphate buffer at pH 8.8. (S)-1,2-Hexanediol is oxidized at a much higher rate by LKADH than (R)-1,2-hexanediol (just above the noise). A selectivity factor of a ~20 in favor of S-hexanediol was used for cassette-ISES predictions. A Michaelis-Menten plot for the S-antipode is shown below:



y = m1*x/(m2+x)		
	Value	Error
m1	129.95	6.6431
m2	39.112	4.4573
Chisq	177.32	NA
R^2	0.98271	NA

V. 'Cassette'–ISES (In Situ Enzymatic Screening) Procedure

Previously, we reported[4] an HKR screening procedure for (±)-propylene oxide using 0.35 units (standardized with 200 mM R-1,2-propanediol) of HLADH (selective for the *S*-enantiomer) and TBADH (selective for the *R*-enantiomer). Note that for 1,2-hexanediol, we now have two reporting enzymes with apparently the same preferred antipode. However, the selectivity factors are sufficiently different that we felt they could be used to estimate product ee for HKR's of hexane oxide. As before, quartz cuvettes with 1 cm light paths and nominal 1 mL volumes were used. A general procedure for the hexene oxide side of 'cassette ISES' (see Figure 1 of the paper) is described below. For every catalyst, a four cuvette 'cassette screen' was

performed over the two different test substrates, propylene oxide and hexene oxide. For propylene oxide, cuvette A contains HLADH, and cuvette B, contains TBADH.[4] For hexene oxide, cuvette A contains HLADH, and cuvette B contains LKADH.

Organic Layer: Both cuvette A and B had the following composition: 140 µL of (±)-hexene oxide (116 mg, 1.16 mmols) 160 µL of CH_2Cl_2 and 2.0 mol% Co^{III}-salen-acetate catalyst. The total organic layer volume was maintained to 300 µL in all catalyst screens.

Aqueous Layer in Cuvette A: 5.0 µL (0.05 2-propanol Units) of HLADH stock solution, (0.01U/µL), 16.5 µL (7.2 mM) of β-NAD^+ stock and 478.5 µL of 50 mM sodium pyrophosphate buffer, pH 8.8.

Aqueous Layer in Cuvette B: 16.7 µL (0.15 2-propanol Units) of LKADH stock (0.009U/µL), 5 µL (2.2 mM) of β-$NADP^+$ stock, 5 µL (1.5 mM) of $MgCl_2$ and 473.5 µL of 50 mM sodium pyrophosphate buffer, pH 8.8.

Basically, for propylene oxide screens, similar numbers of R-1,2-propanediol U (~0.35) were loaded into the two (HLADH and TBADH) reporting cuvettes. And for hexene oxide screens, similar numbers of (S)-1,2-hexanediol U (~0.2) were used for both (HLADH and LKADH) reporting cuvettes. The total volume of the aqueous layer was maintained as 500 µL in both cuvettes in all ISES experiments.

Every catalyst screen was done across the two substrates, over four cuvettes. These four cuvettes therefore constitute the 'cassette' to which each catalyst is exposed. For the hexene oxide assay, for each cuvette, in two separate 1.5 mL micro-centrifuge tubes, 0.023 mmol of catalyst was dissolved in 160 µL of water-saturated CH_2Cl_2. For propylene oxide, 5.5 µmol catalyst was dissolved in 150 µL of $CHCl_3$ (amylene stabilized) in two separate 1.5 mL micro-centrifuge tubes. These solutions were stored in an ice bath. The organic layers were prepared (in the same micro-centrifuge tubes) by briefly mixing the catalyst solution with 140 µL (1.16 mmols) of (±)-hexene oxide, or 150 µL of (±)-propylene oxide. Immediately, all organic layers were loaded into the 1 mL quartz cuvettes, using 1 mL disposable syringes. The aqueous layer was then added carefully along the walls of the cuvette. Generally, the LKADH and TBADH cuvettes were loaded first, followed by the two HLADH cuvettes. Complete loading times of two layers for all four cuvettes were about 1.5 min, on average. Catalyst **1d** (very active) was tested at lower

loadings for both substrates: propylene oxide (0.05 mol%) and hexene oxide (1.5 mol%), respectively.

All four cuvettes were followed by the parallel observation of NAD(P)H formation at 340 nm using a UV/vis spectrophotometer with a multi-cell positioner, held at 25 °C. In this format, we were able to screen one catalyst for two different substrates, in parallel. Generally, duplicate data points were generated for each cassette screen. In principle, one could extend this concept to larger 'screening cassettes' to investigate selectivity over more than two test substrates.

VI. Estimation of HKR Catalyst Enantioselectivity

It remained to deconvolute the cassette reporting enzyme data thereby obtained into predictions of catalyst enantioselectivity for both propylene oxide and hexene oxide test substrates. To estimate the enantiomeric ratio for the HKR of propylene oxide, we followed our previously reported method[4] and %ee was typically predicted over a 15 to 35 min window, depending upon overall catalyst rate. For hexene oxide screens, we decided to use 2 mol% catalyst, and this had the practical consequence of permitting an estimate of catalyst enantioselectivity from the ΔAbs/time data over an initial 10 min window, for all catalysts. No prediction was attempted for slow catalysts, whose HLADH (probes for both R- and S-product!) reporting velocities were ≤ 15 mAbs/min over this 10 min time window.

For the hexene oxide screens, both cuvettes are loaded with similar numbers of S-1,2-hexanediol units. Given the earlier derivation (see ref. 4), if we assume Sel_E = (rate of S-diol/rate of R-diol)$_{\text{for enzyme E}}$, then we obtain:

$$\text{Catalyst Enantioselectivity} = \frac{[S]}{[R]} = \frac{\left[\left(\frac{Sel_{E2}}{Sel_{E1}}\right) \bullet v_{E2} - v_{E1}\right]}{Sel_{E2} \bullet (v_{E1} - v_{E2})}$$

- where the velocities in each of the reporting enzyme cuvettes, v_{E1} and v_{E2}, respectively, are taken as the ΔAbs_{340}/time values (typically the average of two runs) seen over the time window.
- The selectivity parameters Sel_{HLADH} = 2.2 and Sel_{LKADH} = 20 were used for all hexane oxide enantioselectivity estimations.

VII. Independent Measurement of Enantioselectivity

Next, we set to compare enantioselectivites predicted by the ISES-method under biphasic conditions with those observed under more typical synthetic HKR conditions. Specifically, viable Co^{III}-salen catalysts identified by 'cassette'-ISES

were evaluated in the HKR of both (±)-propylene oxide and (±)-hexene oxide, under neat conditions similar to those described by Jacobsen and co-workers.[5] Reactions were stopped after 3 h (propylene oxide; 0.25 mol% catalyst loading) and 0.5 h h (hexene oxide; 2 mol% catalyst loading), respectively, to obtain the 1,2-propanediol and 1,2-hexanediol products at relatively early reaction times, for comparison with ISES predictions.

The procedure used for (±)-propylene oxide HKR was as has been described before.[4] A typical procedure for (±)-hexene oxide HKR is as follows: To the Co(III)-salen catalyst derived from **2a** (18.7 mg, 25 μmol, 2.0 mol%) and (±)-hexene oxide (125 mg, 1.25 mmol) at 0 °C, was added water (12.4 μL, 0.688 mmol, 0.55 eq.). The reaction mixture was tightly capped, and allowed to warm to rt and stirred, most commonly for a total of 0.5 h. Percent conversion at 0.5 h was evaluated by ^{1}H NMR of an aliquot (cooled to 0 °C for the transfer), in $CDCl_3$. In most of these cases, the conversion was low enough after 0.5 h, that the unreacted epoxide (bp 32 ºC) was of relatively low ee, and was therefore removed by bulb to bulb distillation under vacuum (0.1 torr). When more than 50% conversion was observed, the reaction was done for 15 min and when the conversion was less than 5% by NMR after 0.5 h, reactions were continued for a longer time.

Upon removal of the starting epoxide by bulb to bulb distillation, the diol product was isolated by Kugelrohr distillation (~ 100 °C-oven temp; 0.1 torr). To determine ee, the isolated diol was derivatized using *p*-bromobenzoyl imidazole (2.2 eq.) in THF in the presence of NaH (4 eq.) at rt for 5 min. The bis(*p*-bromobenzoate) esters obtained following sequential washes with 1 N HCl and saturated sodium bicarbonate, were of sufficient purity to be used directly for chiral HPLC analysis (Chiralcel OD, 1-4% *i*-PrOH/hexane). A tabulation of observed ee's (chiral HPLC), percent conversions (NMR), isolated yields (Kugelrohr distallation) is presented in Table S2, below. Representative chiral HPLC traces are provided in Section XII.

Table S2: HKR Under Standard Conditions with Co^{III}-Salen Catalyst 'Hits'

A) Propylene oxide:

Salen	Loading (mol%)	NMR conv. (time)	% Yield (time)	% ee (HPLC)	E-value
1a	0.25	12 (3 h)	14 (3 h)	+72 (*S*)	6.9
2a	0.25	36 (3 h)	30 (3 h)	+66 (*S*)	6.4
3a	0.25	30 (3 h)	31 (3 h)	-74 (*R*)	-9.2
4a	0.25	28 (3 h)	32 (3 h)	-82 (*R*)	-14.7
1b	0.25	n.d.	36 (3 h)	+28 (*S*)	2.1
2b	0.25	3 (3 h)	3 (3 h)	-5 (*R*)	-1.1
3b	0.25	6 (3 h)	8 (3 h)	-12 (*R*)	-1.3
4b	0.25	3 (3 h)	2 (3 h)	-15 (*R*)	-1.4
1d	0.25	n.d.	21 (1h), 33 (3h)	+81@1h,+67@3h(*S*)	11.7
2d	0.25	10 (3 h)	9 (3 h)	+11 (*S*)	1.3
3d	0.25	13 (3 h)	13 (3 h)	-20 (*R*)	-1.5
4d	0.25	8 (3 h)	11 (3 h)	-14 (*R*)	-1.3

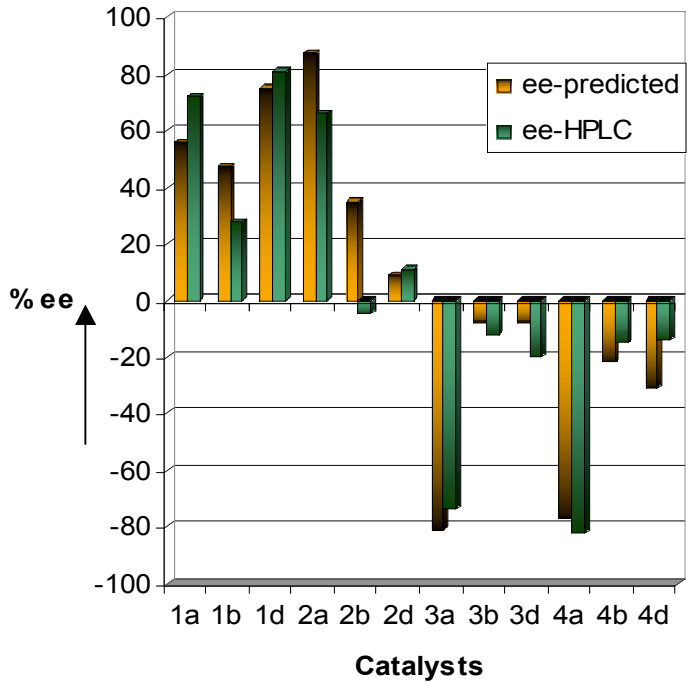
B) Hexene oxide:

Salen	Loading (mol%)	NMR conv. (time)	% Yield (time)	% ee (HPLC)	E-value
1a	2	21 (0.5 h)	26 (0.5)	+80 (*S*)	11.8
2a	2	6 (0.5 h)	17 (0.5 h)	+67 (*S*)	5.8
3a	2	24 (0.5 h)	16 (0.5 h)	-72 (*R*)	-7.0
4a	2	13 (0.5 h)	12 (0.5 h)	-86 (*R*)	-14.9
1b	2	48 (0.25 h)	41 (0.25 h)	+53 (S)	4.6
3b	2	n.d.	23 (0.5 h)	-5(*R*)	-1.1
1c	2	20 (7.5 h)	17 (h)	+71 (*S*)	6.8
1d	2	43 (1 h)	42 (1h)	+76 (S)	12.7
2d	2	7 (0.5 h)	8 (0.5 h)	0	1
3d	2	33 (0.5 h)	39 (0.5 h)	-21 (*R*)	-1.7
4d	2	9 (0.5 h)	5 (0.5 h)	-22 (*R*)	-1.6

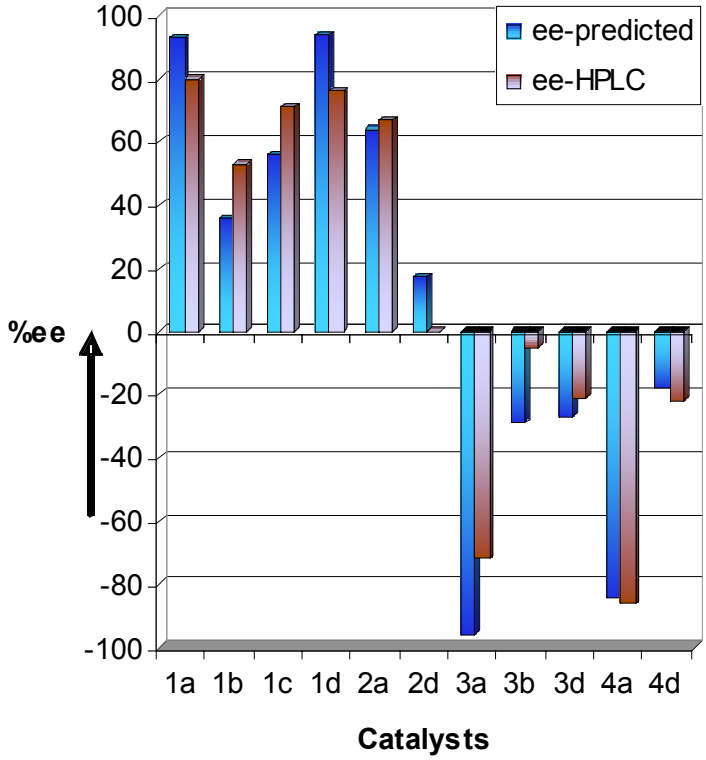
n.d. = not determined; A positive E-value means that the catalyst is S-selective and negative E-value means R-selective catalyst.

Predicted vs Observed Enantioselectivities for the HKR of (±)-Propylene Oxide and (±)-Hexene Oxide

A) Propylene oxide



B) Hexene oxide



Note: A positive deflection indicates (S)-selectivity, and a negative deflection represents (R)-selectivity.

VIII. HKR of the Expanded Epoxide Library

General procedure for HKR of epoxides: Two different general procedures were adapted based on the boiling points of the epoxides. In some cases, the epoxide was opened with phenyl selenide anion. This latter protocol may be of advantage (i) to decrease the volatility of leftover epoxides, (ii) to introduce a UV chromophore (for UV detection – HPLC) and/or (iii) to improve enantiomeric peak resolution in chiral-HPLC.

Procedure for epoxide opening by phenyl selenide: Phenyl selenide anion was prepared by slow addition of 3 eq. $NaBH_4$ into an ice-cold suspension of 1.5 eq. of diphenyl diselenide in ethanol (5-7 mL). The resulting mixture was heated at 40 °C for 20-40 min, until the solution became colorless. Then, either purified epoxide or the reaction mixture out of HKR was added to the ethanolic solution of phenyl selenide at 0 °C. The resulting reaction was slowly allowed to warm to rt and stirring was continued for 8 -10 h at rt. The reaction was quenched with ~1 mL of NH_4Cl. The mixture was diluted with dichloromethane and dried over anhyd Na_2SO_4. The crude product was obtained after filtration and the removal of the solvent. Silica gel column chromatography was used to isolate seleno-alcohol (and the diol, in cases, where the mixture of both epoxide and diol was added to phenyl selenide anion).

Mosher Ester Analysis: For some seleno-alcohols and 1,2-diols, enantiomeric excess was estimated via a classical Mosher esterification procedure [CH_2Cl_2, NEt_3 (10 eq.), DMAP (cat.), S-Mosher acid chloride] followed by ^1H NMR analysis (see Section XIII).

General Procedure C (Direct Treatment of the HKR Reaction Mixture with Phenyl Selenide): This procedure was adapted for butadiene monoxide and 1,2-epoxy-7-octene. Here, we describe the procedure for butadiene monoxide. In this case, catalyst **4a** (43 mg, 0.057 mmol, 1 mol% loading) was mixed with butadiene monoxide (400 mg, 5.71 mmol) and cooled to 0 °C. The reaction was initiated by addition of 51 µL (0.5 eq) of water, and stirring was continued for 12 h at 0 °C. For this substrate, the reaction mixture was added to the phenyl selenide solution at 0 °C. Workup and column chromatography provided selenoalcohol (907 mg, 70%, 0→50% ether in pentane) and 3-buten-1,2-diol (131 mg, 26%, 50→80% EtOAc in ether).

But-3-ene-1,2-diol: ^1H NMR (400 MHz, $CDCl_3$) δ 2.33(br s, 1H), 2.51 (br s, 1H), 3.50 (dd, *J* = 11.2, 7.3 Hz, 1H), 3.67 (dd, *J* = 11.2, 2.7 Hz, 1H), 4.25 (m, 1H), 5.22 (d app t, J = 10.6, 1.4 Hz, 1H), 5.35 (d app t, *J* = 17.3, 1.4 Hz, 1H), 5.84 (m, 1H).

4-(Phenylseleno)-1-buten-3-ol: ^1H NMR (400 MHz, $CDCl_3$) δ 2.42(m, 1H), 2.98 (dd, *J* = 12.6, 8.3 Hz, 1H), 3.14 (dd, *J* = 12.6, 4.2 Hz, 1H), 4.21 (m, 1H), 5.15 (d

appt, *J* = 10.5, 1.3 Hz, 1H), 5.29 (d appt, *J* = 17.2, 1.3 Hz, 1H), 5.86 (m, 1H), 7.24 – 7.29 (m, 3H), 7.52 – 7.55 (m, 2H).

The enantiomeric excess of the seleno-alcohol was estimated by converting it to the R-Mosher ester and using ^{19}F NMR -71.34 ppm (S), -71.51 ppm (R). On the other hand, the 3-buten-1,2-diol product was derivatized as the bis(p-bromobenzoate) and the enantiomeric excess determined via chiral HPLC [95:5 hexane:IPA, flow rate: 1 mL/min; t_R = 9.0 min (R), 10.1 min (S)].

General Procedure D (Chromatographic Separation of the Epoxide and Diol HKR Products):

(Illustrated for **6-[(t-butyldiphenylsilyl)oxy]-1,2-epoxyhexane**). This procedure was applicable to all remaining epoxides. Catalyst **4a** (21 mg, 0.028 mmol, 4 mol% loading) was mixed with 6-[(t-butyldiphenylsilyl)oxy]-1,2-epoxyhexane[7] (246 mg, 0.69 mmol) and 300 µL of THF. The mixture was cooled to 0 °C, and the reaction initiated by adding 6 µL (0.5 eq.) of water and stirring continued for 12 h at 0 °C. After the reaction, silica gel column chromatography (0→80% EtOAc in hexanes) provided the epoxide (146 mg, 59%) and 6-[(tert-butyldiphenylsilyl)oxy]-1,2-hexanediol (100 mg, 39%)[8].

The enantiomeric excess of the epoxide was determined by converting the epoxide to 6-[(tert-butyldiphenylsilyl)oxy]-1-(phenylseleno)-hexane-2-ol and using chiral HPLC (Chiralcel OD, 96:4 hexanes : IPA, flow rate 1mL/min, t_R 10 min (R), 11.5 min (S)). The enantiomeric excess of the diol was determined using chiral HPLC (96:4 hexanes : IPA, flow rate 1mL/min) t_R = 9.3 min (R), 11.8 min (S).

6-[(tert-Butyldiphenylsilyl)oxy]-1,2-epoxyhexane: ^1H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.50 – 1.65 (m, 6H), 2.43 (dd, *J* = 5.0, 2.7 Hz, 1H), 2.73 (app t, *J* = 4.5 Hz, 1H), 2.88 (m, 1H), 3.66 (t, *J* = 6.1 Hz, 2H), 7.34 – 7.44 (m, 6H), 7.64 – 7.68 (m, 4H).

6-[(tert-Butyldiphenylsilyl)oxy]-1-(phenylseleno)-hexane-2-ol: ^1H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 9H),1.40– 1.58 (m, 6H), 2.35 (br s,1H), 2.85 (dd, *J* = 12.5, 8.7 Hz, 1H), 3.11 (br d, *J* = 10.9 Hz, 1H), 3.63 (t, *J* = 6.1 Hz, 1H), 7.22 – 7.27 (m, 3H), 7.33 – 7.43 (m, 6H), 7.50 – 7.54 (m, 2H), 7.62 – 7.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ19.2, 22.0, 26.8, 32.3, 36.2, 37.1, 63.6, 69.8, 127.2, 127.6, 129.1, 129.5, 132.9, 134, 135.5. HRMS (FAB, 3-NOBA) calcd for $C_{28}H_{37}SeSiO_2$ $(M+H)^+$ 513.1728, obsd 513.1720.

1,2-Epoxy-7-octene: General Procedure C was followed, starting from 1,2-epoxy-7-octene (249 mg, 1.97 mmol), catalyst **4a** (15 mg, 0.02 mmol) and 18 µL (0.5 eq.) of water at 0 °C for 12 h. Direct ring-opening with phenyl selenide anion ensued. After

workup and column chromatography, were obtained both the seleno-alcohol (248 mg, 44%, 0→30% ether in pentane) and oct-7-ene-1,2-diol (160 mg, 56%, 50→80% EtOAc in ether).

8-(Phenylseleno)-1-octene-7-ol: $[\alpha]^{19}_{obsd}$ +34, $[\alpha]^{19}_{D}$ +37, calcd (*c* 1.3 , CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 – 1.58 (m, 6H), 2.04 (m, 2H), 2.37 (d, *J* = 3.4 Hz, 1H), 2.87 (dd, *J* = 12.8, 8.6 Hz, 1H), 3.13 (dd, *J* = 12.8, 3.5 Hz, 1H), 3.65 (m, 1H), 4.00 -5.00 (m, 2H), 5.77 (dddd, *J* = 16.9, 13.4, 10.2, 6.7 Hz, 1H), 7.24 – 7.27 (m, 3H), 7.51 – 7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.28, 28.80, 33.62, 36.39, 37.27, 69.72, 114.43, 127.28, 129.19, 129.27, 133.02, 138.77; HRMS (FAB, 3-NOBA) calcd for $C_{14}H_{20}SeO$ $(M)^+$ 284.0679, obsd 284.0688.

Oct-7-ene-1,2-diol: $[\alpha]^{19}_{obsd}$ +8.42 (for 71% ee of R), $[\alpha]^{19}_{D}$ +12.03 (calcd), lit.[9] $[\alpha]_D$ +12.1 (*c* 4.8 , CH_3OH).

The enantiomeric excess of the 8-(phenylseleno)-1-octene-7-ol was estimated using chiral HPLC (99:1 hexanes:IPA, flow rate 1mL/min) t_R 22.2 (R), 23.7 (S).

The enantiomeric excess of 7-octen-1,2-diol was determined by derivatization as its R-Mosher ester - ^{19}F NMR, -71.41 & -71.63 ppm (S) -71.60 & -71.63 ppm (R).

3-Phenoxy-1,2-epoxypropane: Following General Procedure D, catalyst **4a** (28 mg, 0.037 mmol, 2 mol% loading), 3-phenoxy-1,2-epoxypropane (278 mg, 1.85 mmol), THF (150 µL) and 16.7 µL of water at 0 °C for 12 h, provided the starting epoxide (125 mg, 45%, 5→50 % ether in pentane) and the product (171 mg, 55%, 100 % EtOAc→10 % EtOH in EtOAc) after silica gel column chromatography.

3-Phenoxy-1,2-epoxypropane: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.76 (dd, *J* = 4.9, 2.7 Hz, 1H), 2.90 (dd, *J* = 4.8, 4.2 Hz, 1H), 3.35 (m, 1H), 3.96 (dd, *J* = 11.0, 5.6 Hz, 1H), 4.21 (dd, *J* = 11.0, 3.2 Hz, 1H), 6.9 – 7.0 (m, 3H), 7.26 – 7.31 (m, 2H).

3-Phenoxy-1,2-propanediol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 1H), 3.26 (s, 1H), 3.73 (dd, *J* = 11.5, 5.8 Hz, 1H), 3.81 (dd, *J* = 11.5, 3.1 Hz, 1H), 4.00 (m, 2H), 4.10 (m, 1H), 6.90 (d, *J* = 7.8 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 7.27 (dt, *J* = 7.5, 1.1 Hz, 2H). For the diol isolated using catalyst **1d**, with 80% ee for R, $[\alpha]^{19}_{obsd}$ = -8.1, $[\alpha]^{19}_{D}$ = -10.1 (c = 2.5, EtOH) (calculated), lit.[5] $[\alpha]^{23}_{D}$ = -10.0 (*c* = 1.9, EtOH) .

The 3-phenoxy-1,2-epoxypropane antipodes separate on a Chiralcel OD column, (90:10 hexanes:IPA, flow rate 1mL/min) t_R = 8.6 min (R) and 14.4 min (S). Alternatively, the phenylseleno-alcohol was prepared from this epoxide and derivatized as its R-Mosher ester. ^{19}F NMR (-71.45 for S and -71.65 for R) was used to determine the enantiomeric excess of the ester. The diol is also resolvable on a Chiralcel OD column, (90:10 hexanes: IPA, flow rate 1 mL/min) showed t_R = 15

min (*R*) and 30 min (*S*). Alternatively, the R-Mosher ester of the diol could be used to determine enantiomeric excess from ^{19}F NMR, -71.58 & -71.62 ppm (*R*) and -71.63 & -71.71 ppm (*S*).

4-Benzyloxy-1,2-epoxybutane: Following General Procedure D, catalyst **1d** (26 mg, 0.044 mmol, 3 mol% loading), 4-benzyloxy-1,2-epoxybutane[7] (263 mg, 1.64 mmol), 100 µL of THF and 14.6 µL of water at 0 °C for 12 h provided the unreacted epoxide (126 mg, 48%, 0→50% ether in pentane) and the product diol (145 mg, 50%, 0→100% EtOAc in ether), after silica gel column chromatography.
The epoxide was treated with phenyl selenide anion to produce the phenylseleno-alcohol. The enantiomers of this seleno-alcohol are separable on Chiralcel OD (95:5 hexanes:IPA, flow rate 1mL/min) t_R = 22 min (R) and 42 min (S) at. The diol is also resolved on the same chiral column, and under the same conditions, t_R= 27 min (R) and 32 min (S).
4-Benzyloxy-1,2-butanediol: Using catalyst **1d**: $[\alpha]^{19}_{obsd}$ [91% (S)] = -18.45 (*c* = 2.0, EtOH), $[\alpha]^{19}_{D}$ = -20.3 (calcd), lit.[5] $[\alpha]^{23}_{D}$ = -22.5 (*c* = 1.1, EtOH)
4-Benzyloxy-1-phenylseleno-2-butanol: ^1H NMR (400 MHz, $CDCl_3$) δ 1.80 – 1.95 (m, 2H), 2.99 (dd, *J* = 12.6, 7.5 Hz, 1H), 3.07 (dd, *J* = 12.6, 5.1 Hz, 1H), 3.18 (d, *J* = 3.1, 1H), 3.65 (m, 2H), 3.95 (m, 1H), 4.49 (s, 2H), 7.22 – 7.25 (m, 3H), 7.27 – 7.35 (m, 5H), 750 – 7.54 (m, 2H);); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.8, 35.9, 68.2, 69.4, 73.2, 127, 127.6, 127.7, 128.4, 129.1, 129.7, 132.6, 137.8.

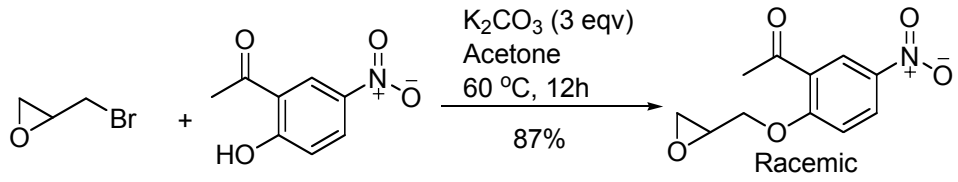
6-[(tert-Butoxycarbonyl)-amino]-1,2-epoxyhexane: Following General Procedure D, catalyst **1d** (10.6 mg, 0.0179 mmol , 2 mol% loading) with 6-[(tert-butoxycarbonyl)-amino]-1,2-epoxyhexane (193 mg, 0.896 mmol), 150 µL of THF and 8.1 µL of water at 0 °C for 12 h, provided the unreacted epoxide (134 mg, 70%, 10→30% EtOAc in hexane) and the diol (61 mg, 29%, 80% EtOAc/hexanes→10% ethanol in EtOAc) after silica gel column chromatography.
6-[(tert-Butoxycarbonyl)-amino]-1,2-epoxyhexane: : From catalyst **1d**: $[\alpha]^{19}_{obsd}$ [36% (R)] = +4.8, $[\alpha]^{19}_{D}$ = + 13.3 (*c* = 2.4, EtOH), ^1H NMR (400 MHz, $CDCl_3$) 1.46 (s, 9H), 1.49 – 1.62 (m, 6H), 2.49 (dd, *J* = 5, 2.7 Hz, 1H), 2.77 (dd, *J* = 4.9, 4.0 Hz, 1H), 2.93 (m, 1H), 3.1 – 3.2 (m, 2H), 4.55 (br s, 1H).
6-[(tert-Butoxycarbonyl)-amino]-1,2-hexanediol: ^1H NMR (400 MHz, $CDCl_3$) δ 1.2 – 1.9 (m, 15H), 3.07 (br d, *J* = 4.7 Hz, 1H), 3.2 – 4.2 (m, 5 H), 4.77 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 22.9, 28.4, 28.5, 29.9, 37.7, 40.2, 79.2, 156.3.
To determine the enantiomeric excess of the isolated epoxide, the epoxide was treated with phenyl selenide anion to give 6-[(tert-butoxycarbonyl)-amino]-1-

(phenylseleno)-hexan-2-ol. This is separable on a Chiralcel OD column (90:10/Hex:IPA, flow rate 1 mL/min) t_R = 11.4 min (R) and 12.8 min (S).

The diol was derivatized as its bis(p-bromobenzoate) ester, and the enantiomers were resolved on a Chiralcel OD column using 95:5 Hex:IPA, flow rate 1mL/min, t_R = 28 min (R) and 33 min (S).

6-[(tert-Butoxycarbonyl)-amino]-1-(phenylseleno)-hexan-2-ol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25- 1.55 (m, 15 H), 2.85 (dd, *J* = 12.7, 8.6 Hz, 1H), 3.05 – 3.14 (m, 3H), 3.64 (m, 1H), 4.51 (br s, 1H), 7.24 – 7.28 (m, 3H), 7.50 – 7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 28.1, 28.3, 29.8, 35.9, 36.8, 40.2, 69.6, 127.1, 129.1, 129.3, 132.8, 156.0.

2'-Acetyl-4'-nitro-*O*-phenylglycidol: This epoxide was prepared as illustrated:



Following General Procedure D, the epoxide (68 mg, 0.287 mmol), 300 µL of THF, catalyst **1d** (17 mg, 0.028 mmol, 10 mol% loading) and 3 µL of water at rt for 24 h provided unreacted epoxide (25 mg, 37%, 20→60% EtOAc in hexanes) and the product diol (46 mg, 63%, 20% EtOH in EtOAc) after silica gel column chromatography.

2'-Acetyl-4'-nitro-*O*-phenylglycidol: From catalyst **1d**: $[\alpha]^{19}_{obsd}$ [96% (S)] = +7.7, $[\alpha]^{19}_{D}$ = +8.0 (c = 0.7, EtOH), lit.[10] , $[\alpha]^{25}_{D}$ = -10.7 (c = 0.9, EtOH),

3-(2'-Acetyl-4'-nitrophenoxy)-1,2-propanediol: From catalyst **1d**: $[\alpha]^{19}_{obsd}$ [55% (R)] = +7.6, $[\alpha]^{19}_{D}$ = + 13.9 (c = 1.7, EtOH), lit.[10] , $[\alpha]^{25}_{D}$ = -5.31 (*S*-diol, c = 1.1, EtOH).

In this case, both epoxide and diol enantiomers are resolved on a Chiralcel OD column. For 2'-acetyl-4'-nitro-*O*-phenylglycidol, (96:4 Hex:IPA, flow rate 1 mL/min) t_R = 53 min (S) and 60 min (R); and for 3-(2'-acetyl-4'-nitrophenoxy)-1,2-propanediol, (85:15 Hex:IPA, flow rate 1 mL/min) t_R = 30 min (S) and 40 min (R).

***N*-(5',6'-Epoxyhexyl)-phthalimide:** Following General Procedure D, catalyst **1d** (25 mg, 0.024 mmol, 5 mol% loading), *N*-(5,6-epoxyhexyl)-phthalimide[7], THF (200 µL), and 7.7 µL (0.5 eq) of water at 0 °C for 12 h provided the unreacted epoxide (95 mg,

46%, 30→50% EtOAc in hexanes) and product diol (116 mg, 52%, 0→20% EtOH in EtOAc) by silica gel column chromatography.

***N*-(5',6'-Epoxyhexyl)-phthalimide:** For catalyst **1d**: $[\alpha]^{19}_{obsd}$ [70% (R)] = +5.0, $[\alpha]^{19}_{D}$ = +7.1 (*c* = 0.7, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 – 1.58 (m, 4H), 1.73 (m, 2H), 2.45 (dd, *J* = 5, 2.7 Hz, 1H), 2.72 (app t, *J* = 5 Hz, 1H), 2.88 (m, 1H), 3.69 (app t, *J* = 7.2 Hz, 2H), 7.70 (dd, *J* = 5.4, 3 Hz, 2H), 7.82 (dd, *J* = 5.5, 3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 28.3, 32, 37.7, 47, 52, 123.2, 132.1, 133.9, 168.4; HRMS (FAB, 3-NOBA) calcd for $C_{14}H_{16}NO_3$ $(M+H)^+$ 246.1130, obsd 246.1126.

***N*-Phthalimido-1-amino-5,6-hexanediol:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (m, 1H), 1.45 – 1.55 (m, 3H), 1.71 (m, 2H), 1.89 (t, *J* = 5.4 Hz, 1H), 2.10 (d, *J* = 4.1 Hz, 1H), 3.44 (m, 1H), 3.60 – 3.73 (m, 4H), 7.70 (dd, *J* = 5.5, 3 Hz, 2H), 7.83 (dd, *J* = 5.5, 3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 28.5, 32.5, 37.6, 66.7, 72, 123.22, 132.1, 133.9, 168.53; HRMS (FAB, 3-NOBA) calcd for $C_{14}H_{18}NO_4$ $(M+H)^+$ 264.1236, obsd 264.1241.

The enantiomeric excess of *N*-(5',6'-epoxyhexyl)-phthalimide was determined using chiral HPLC (Chiralcel OD - 97: 3 hex: IPA, flow rate 1 mL/min), t_R = 41.1 min (R) and 43 min (*S*). Derivativization of *N*-phthalimido-1-amino-5,6-hexanediol as the bis(p-bromobenzoate) ester produced enantiomeric resolution on HPLC with Chiralcel OD (90: 10 hex: IPA, flow rate 1 mL/min), t_R = 55 min (*S*) and 71 min (*R*).

IX. References

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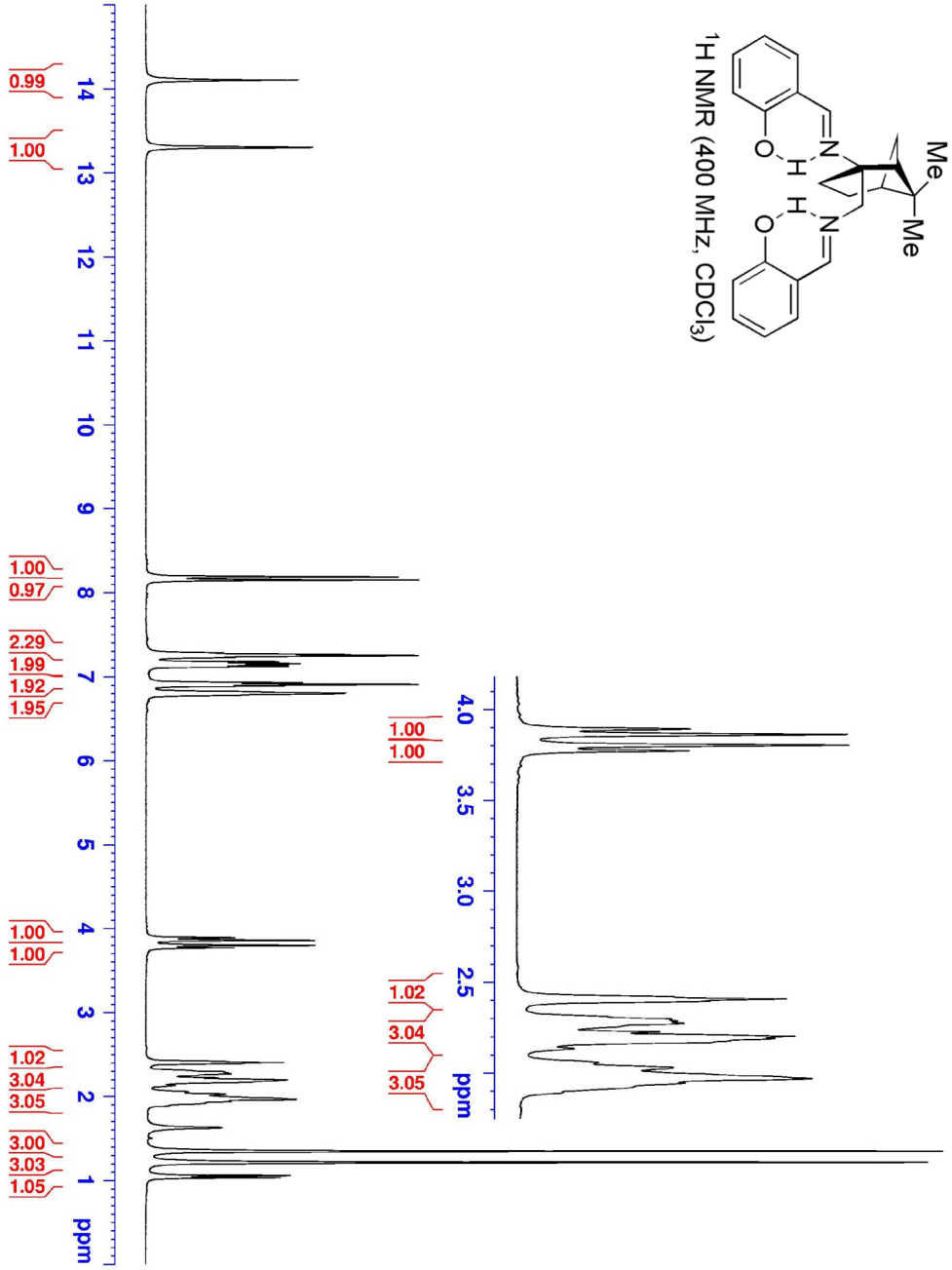
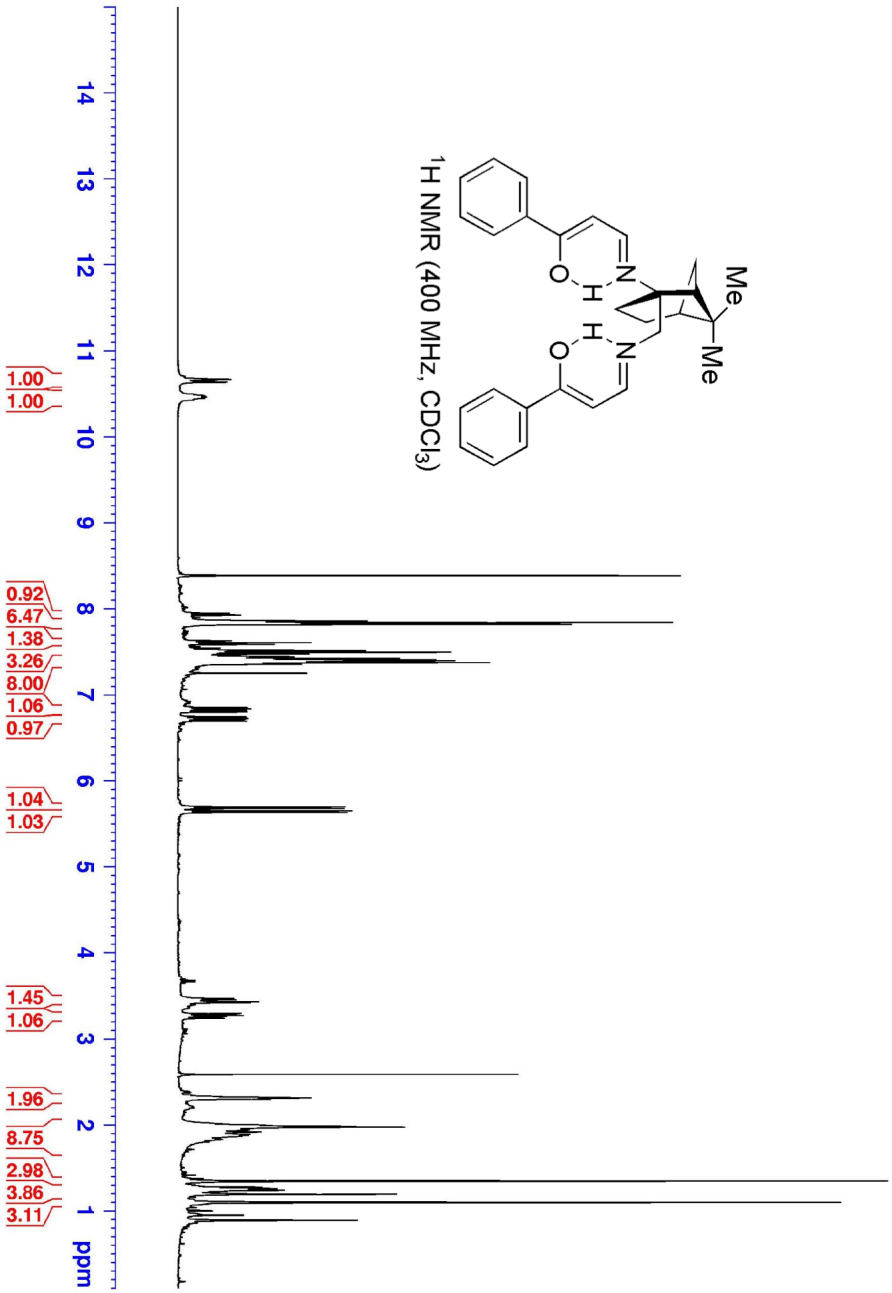
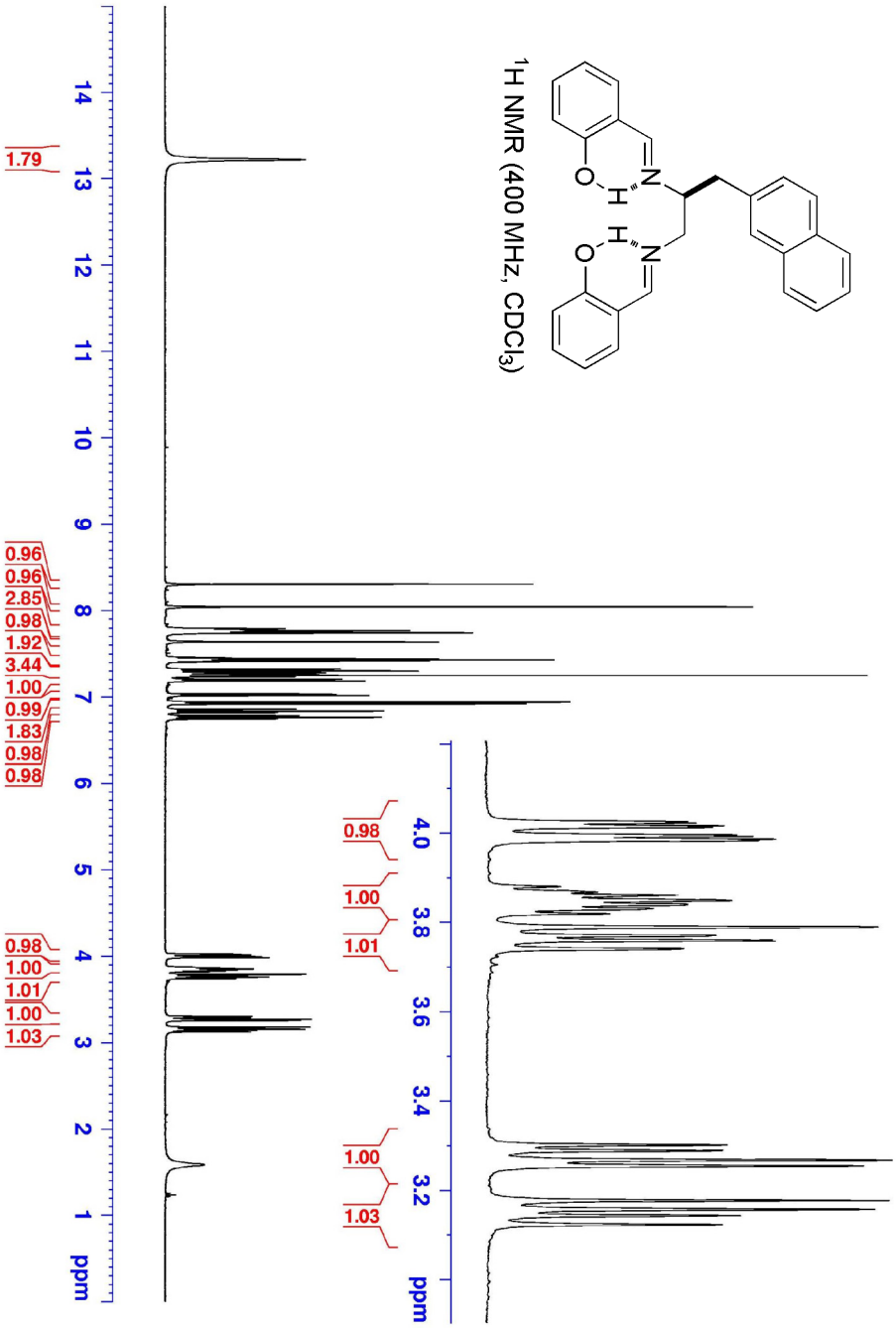
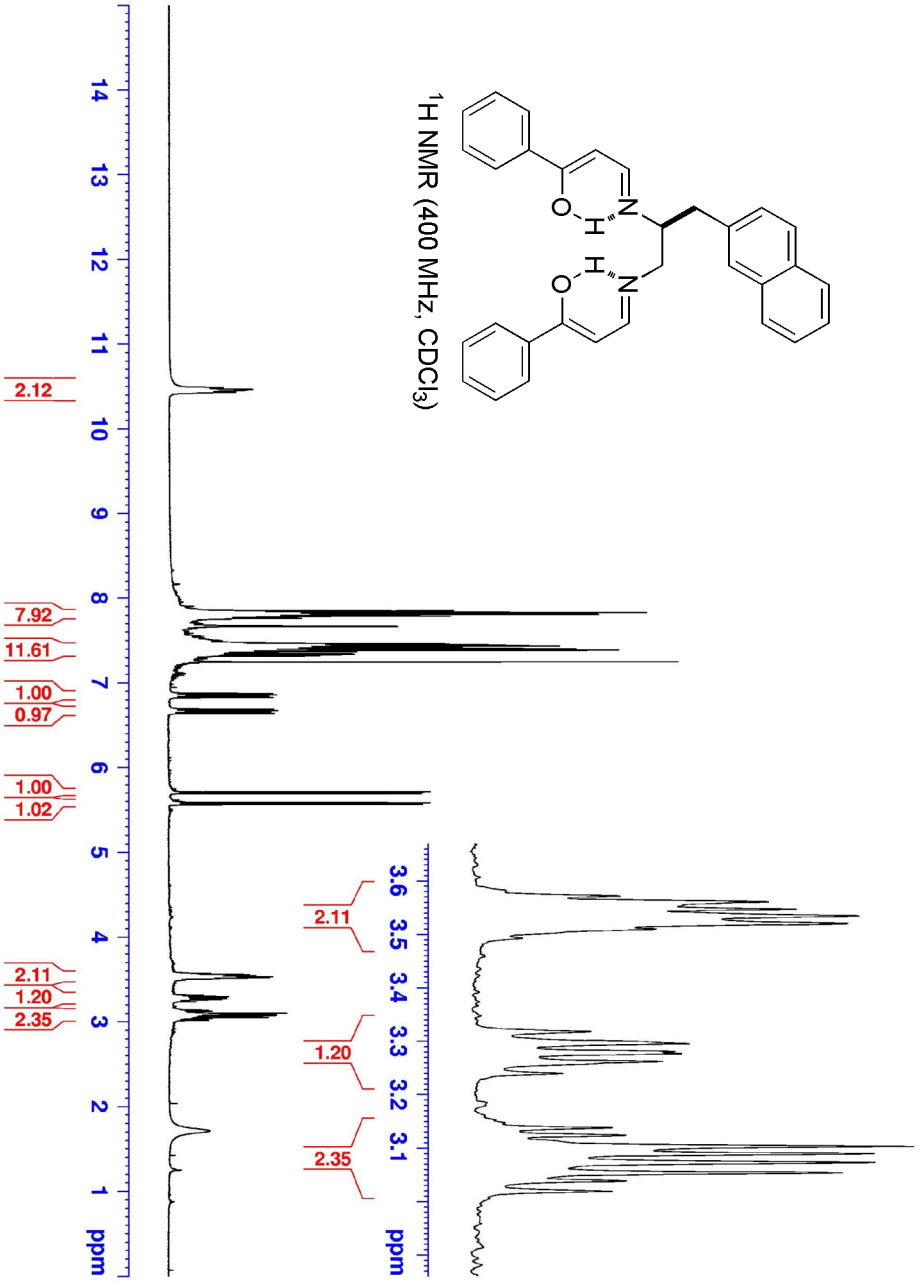
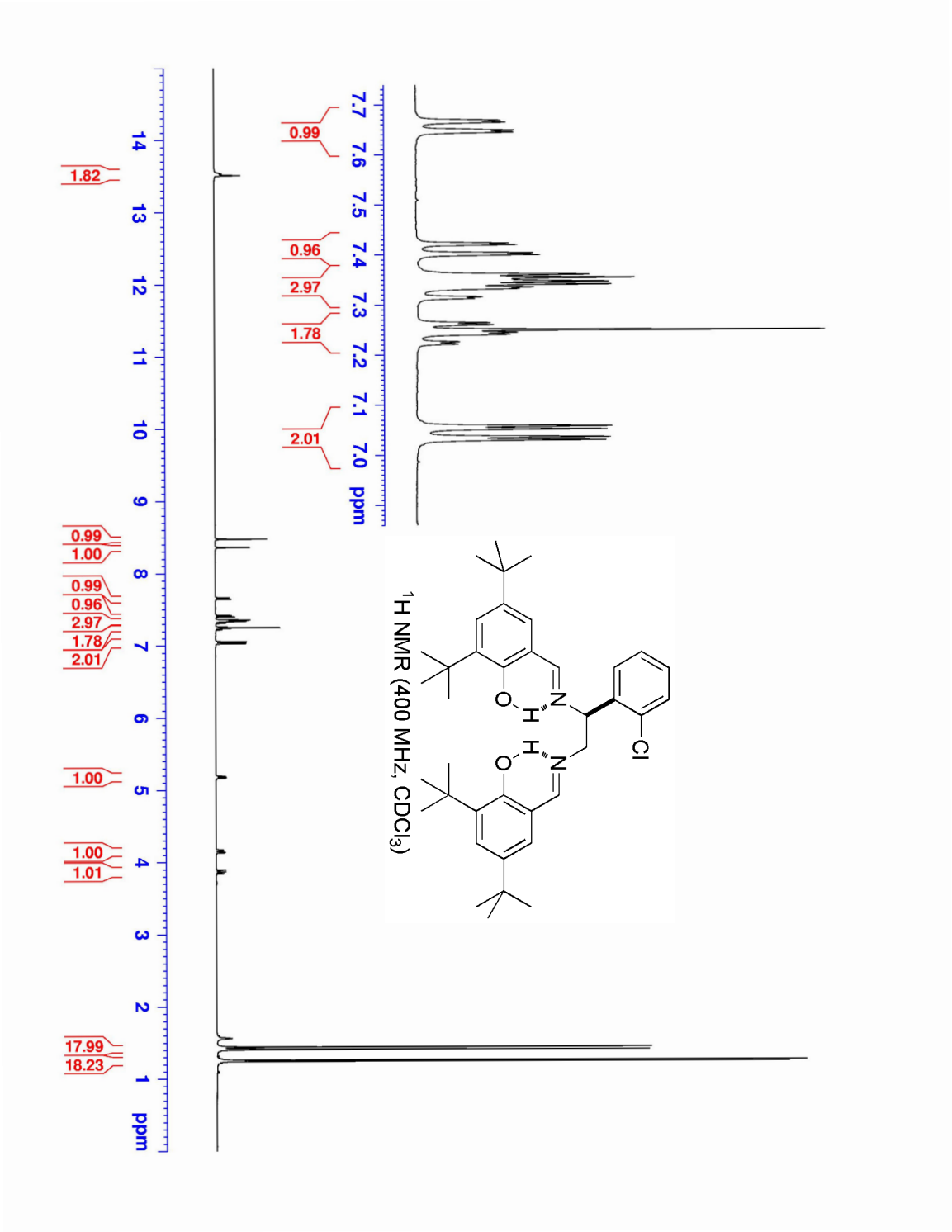
X. ^{1}H NMR Spectra for Salen Ligands

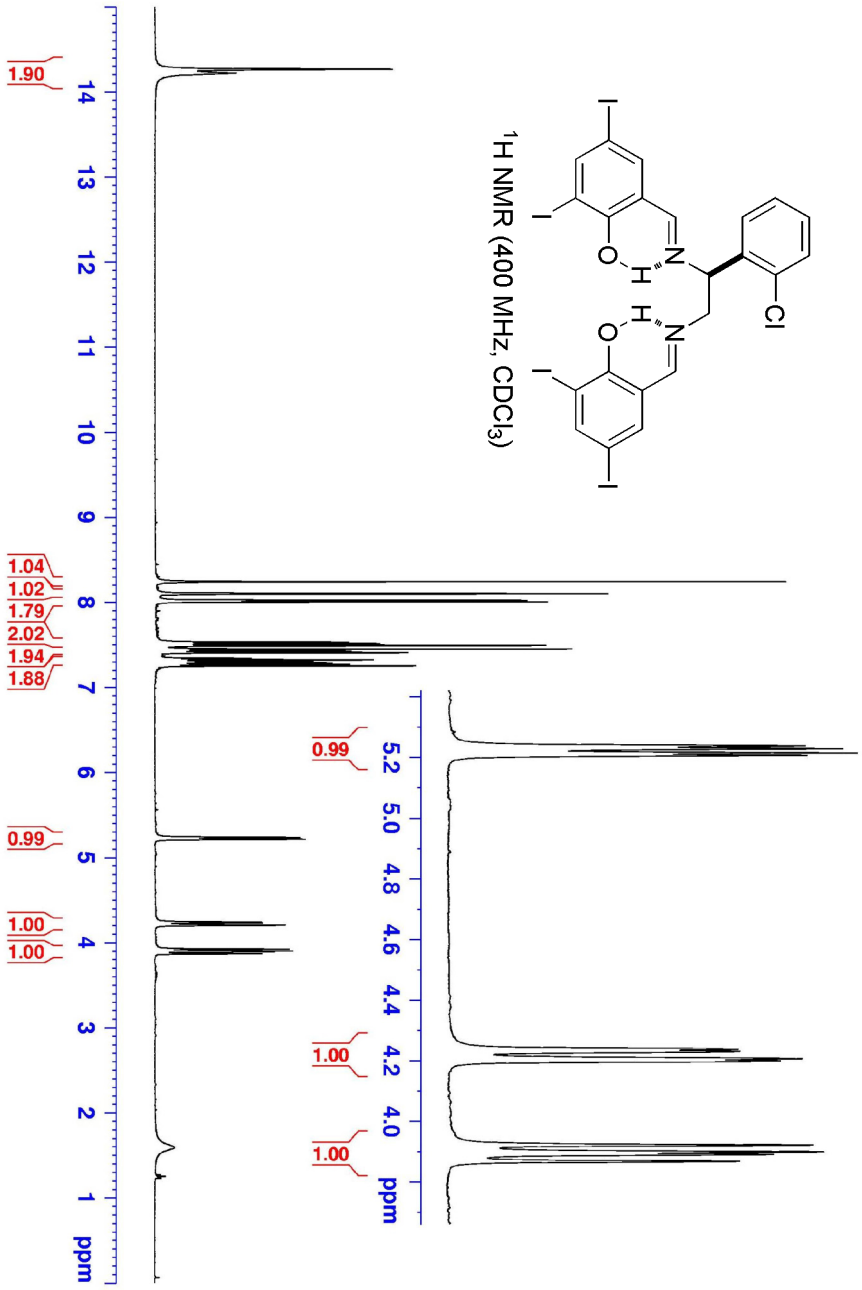


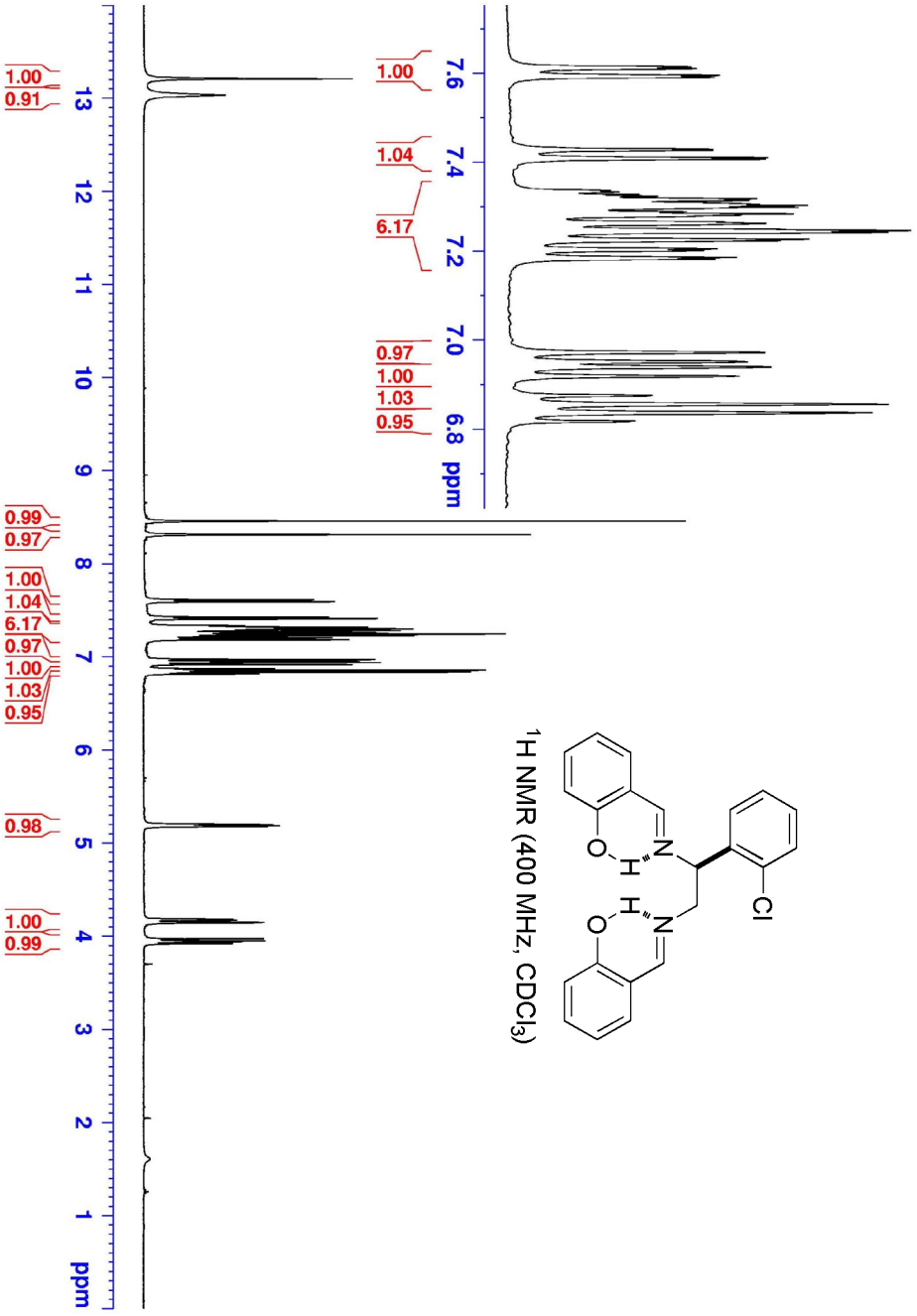

^{1}H NMR (400 MHz, CDCl$_3$)
Me
Me
N
O
H
1.00
1.00
0.92
6.47
1.38
3.26
8.00
1.06
0.97
1.04
1.03
1.45
1.06
1.96
8.75
2.98
3.86
3.11
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

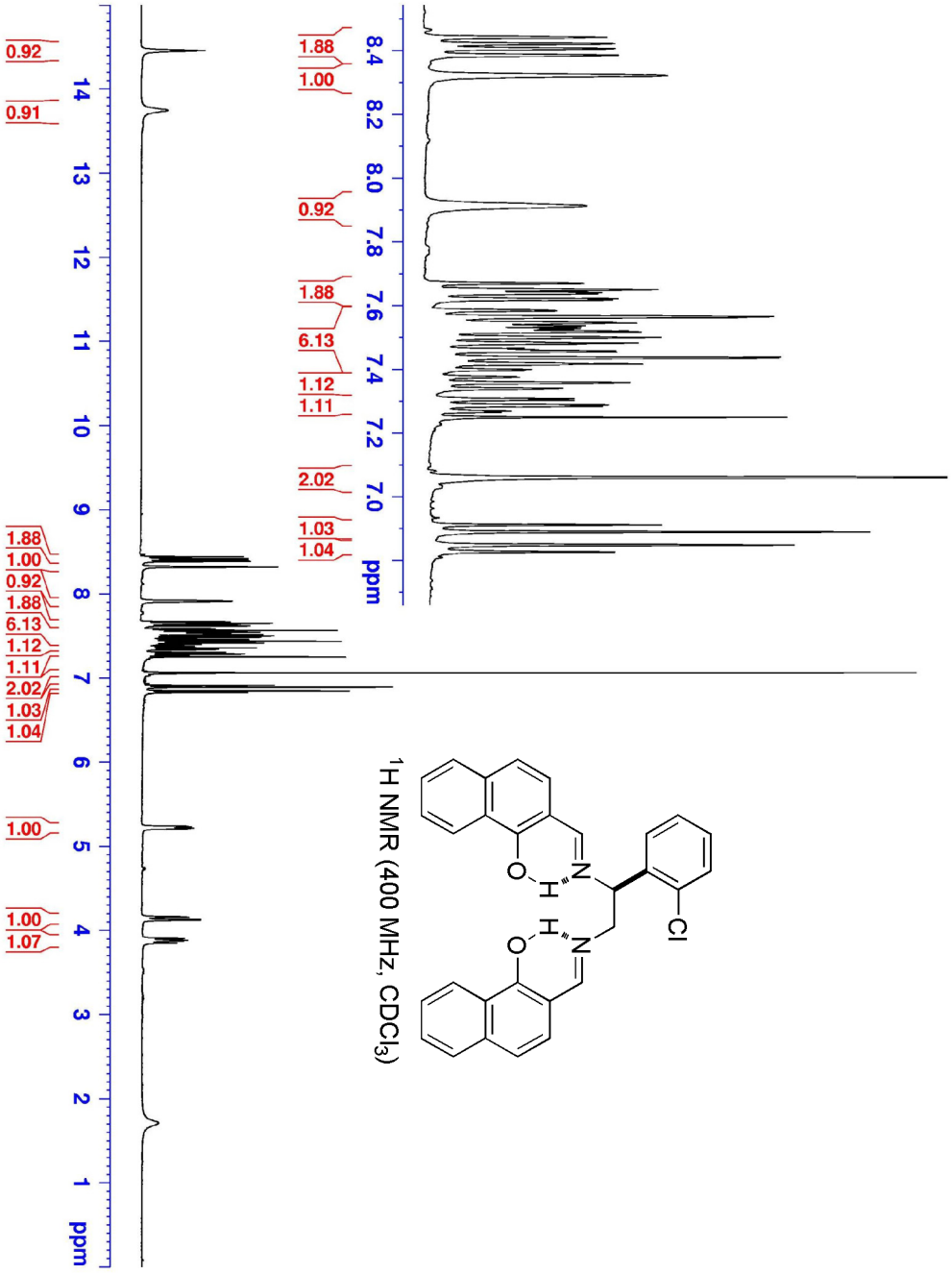

^{1}H NMR (400 MHz, CDCl$_3$)
1.79
0.96
0.96
2.85
0.98
1.92
3.44
1.00
0.99
1.83
0.98
0.98
0.98
1.00
1.01
1.00
1.03
0.98
1.00
1.01
1.00
1.03
ppm
ppm

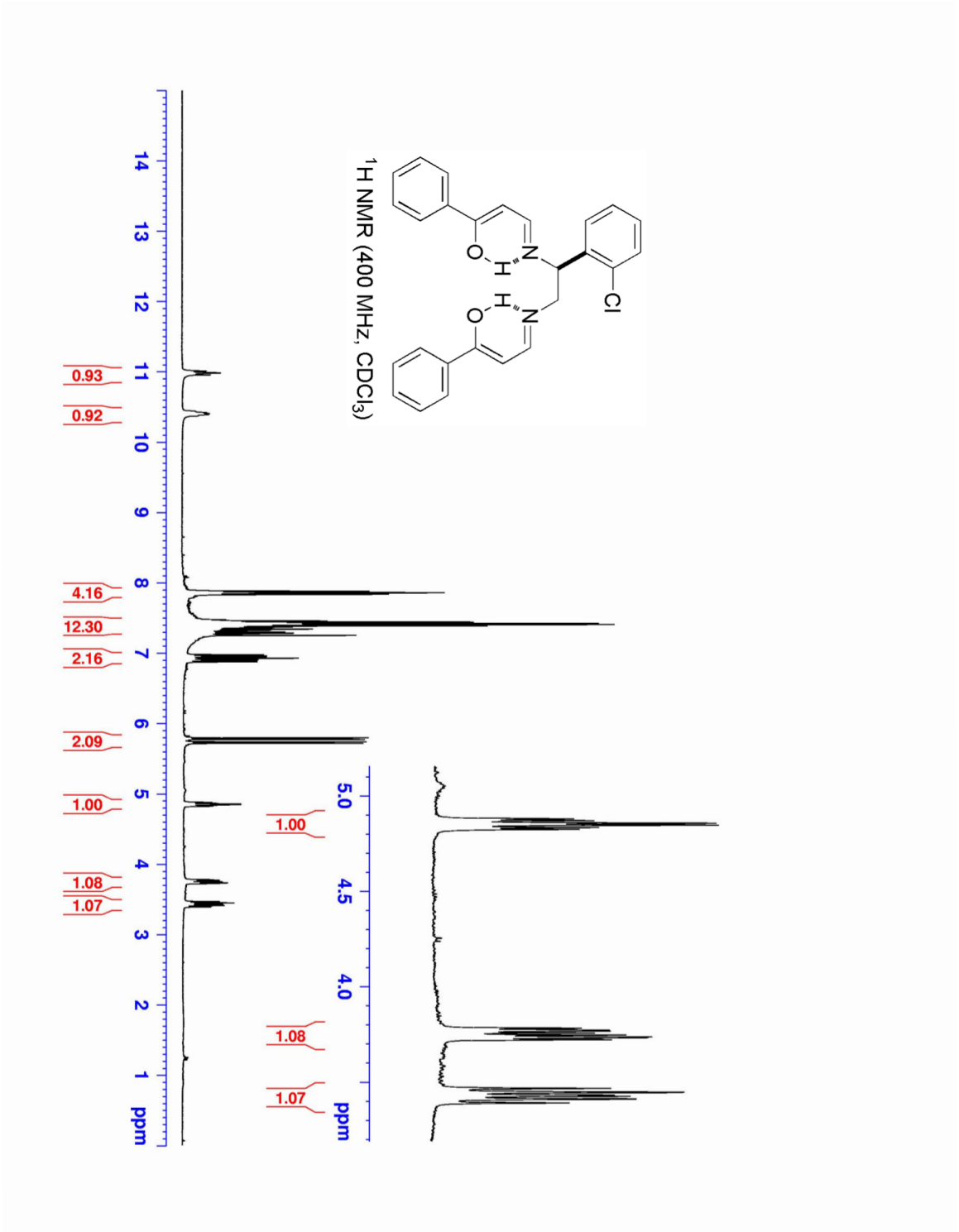

^{1}H NMR (400 MHz, CDCl$_3$)
2.12
7.92
11.61
1.00
0.97
1.00
1.02
2.11
1.20
2.35
2.11
1.20
2.35
ppm
ppm

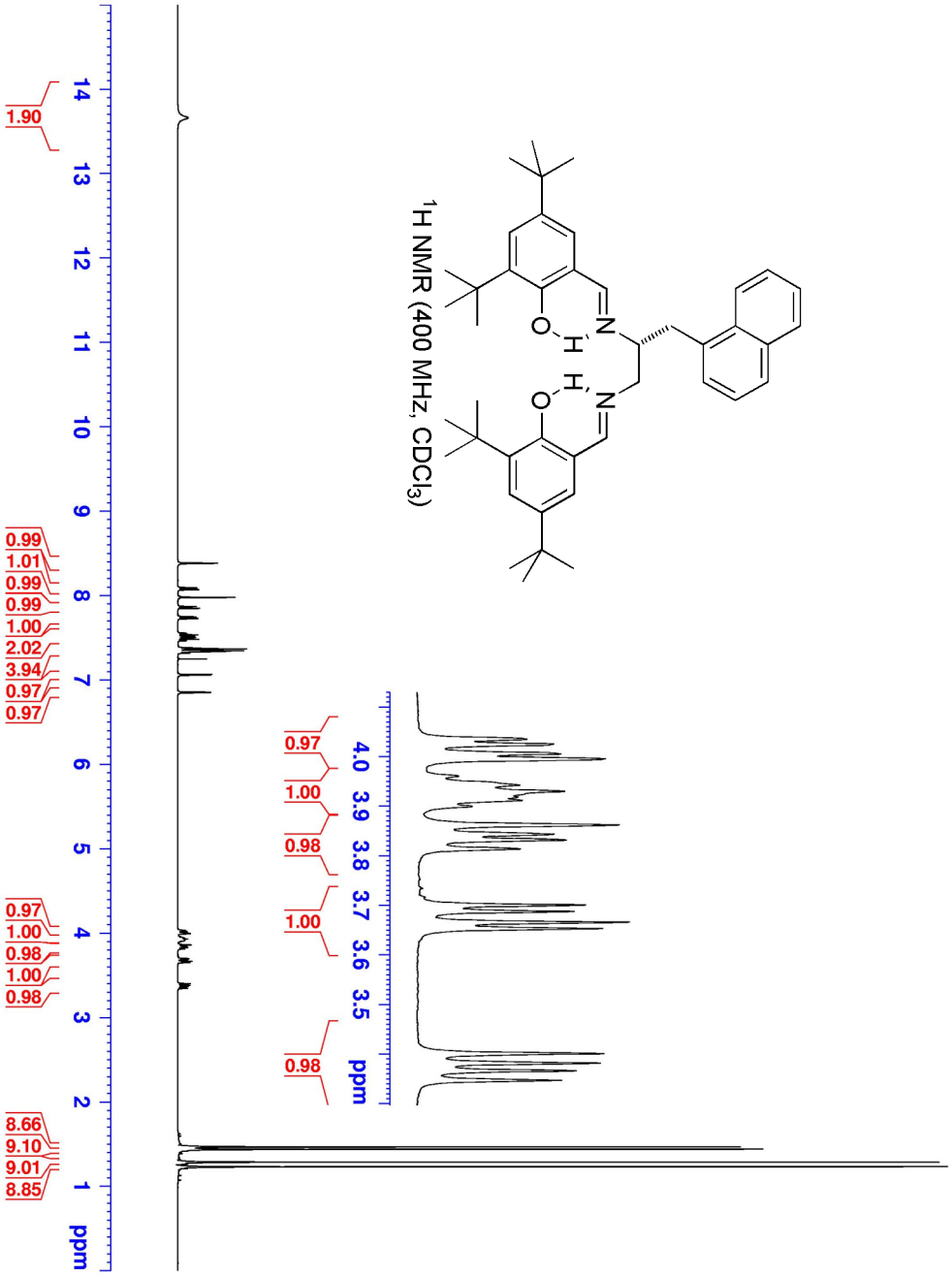

^{1}H NMR (400 MHz, CDCl$_3$)
Cl
N
H
O
0.99
0.96
2.97
1.78
2.01
1.82
1.00
1.01
17.99
18.23
ppm

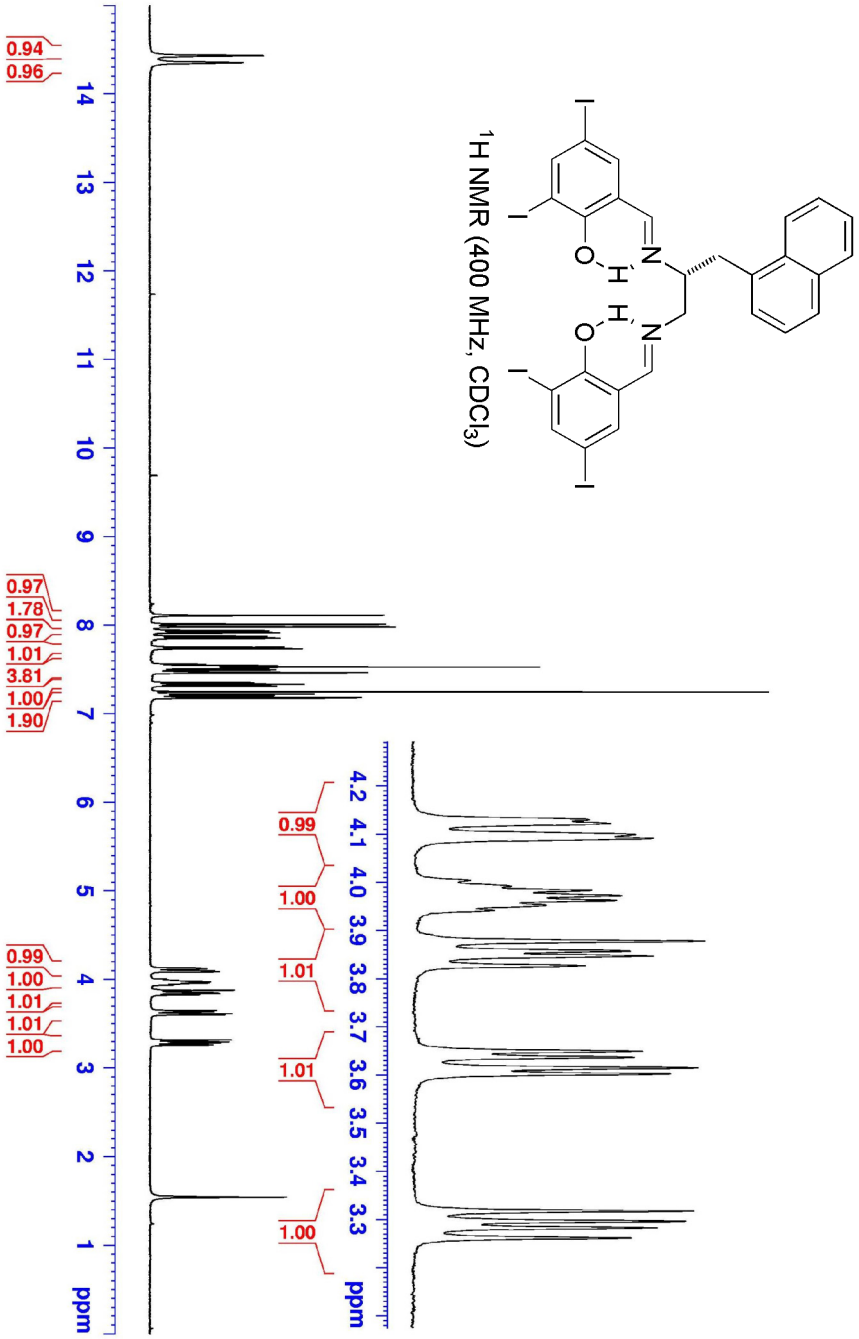

^{1}H NMR (400 MHz, CDCl$_3$)
1.90
1.04
1.02
1.79
2.02
1.94
1.88
0.99
1.00
1.00
0.99
1.00
1.00
ppm

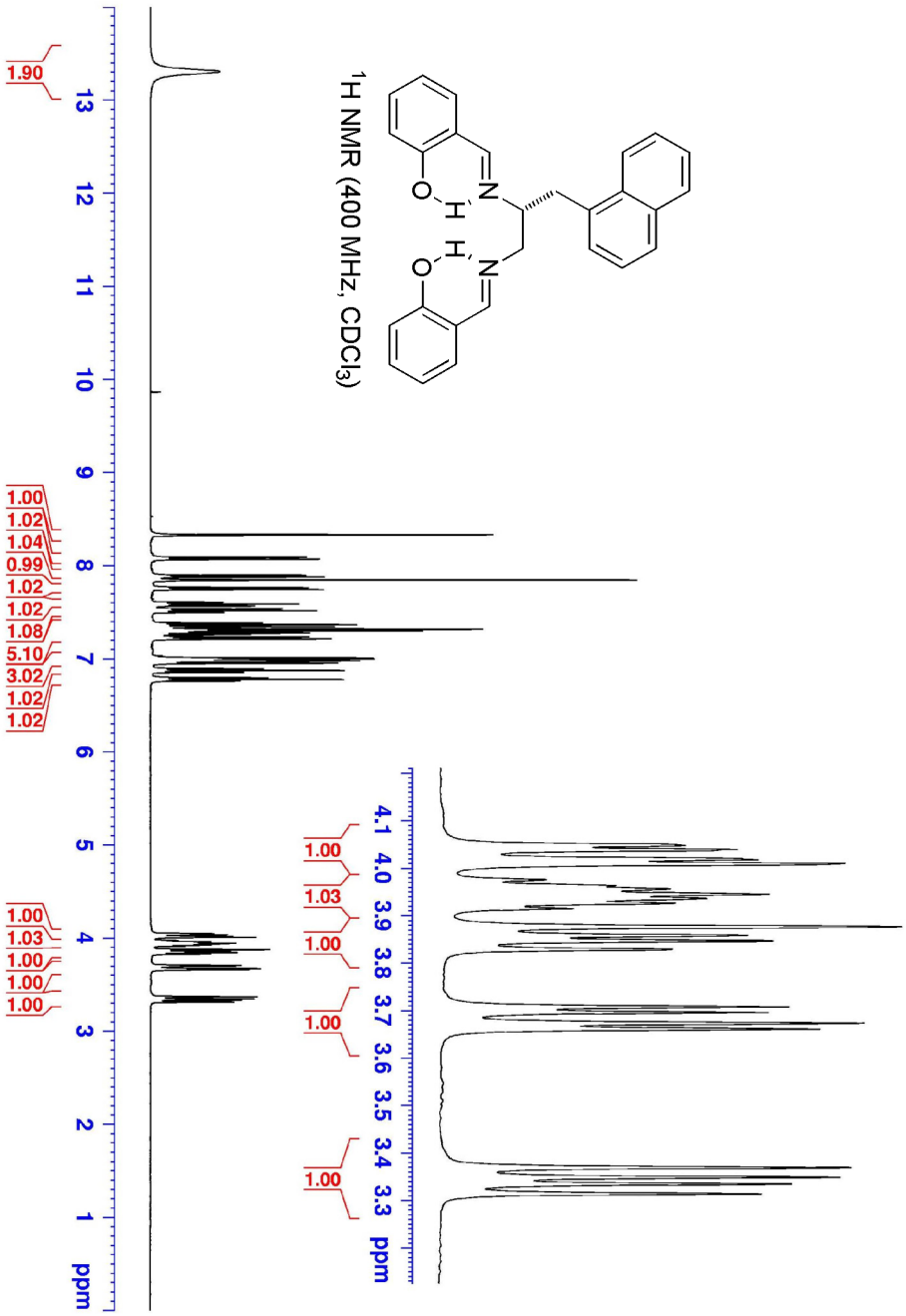

1.00
0.91
0.99
0.97
1.00
1.04
6.17
0.97
1.00
1.03
0.95
0.98
1.00
0.99
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.00
1.04
6.17
0.97
1.00
1.03
0.95
7.6 7.4 7.2 7.0 6.8 ppm
Cl
^{1}H NMR (400 MHz, CDCl$_3$)

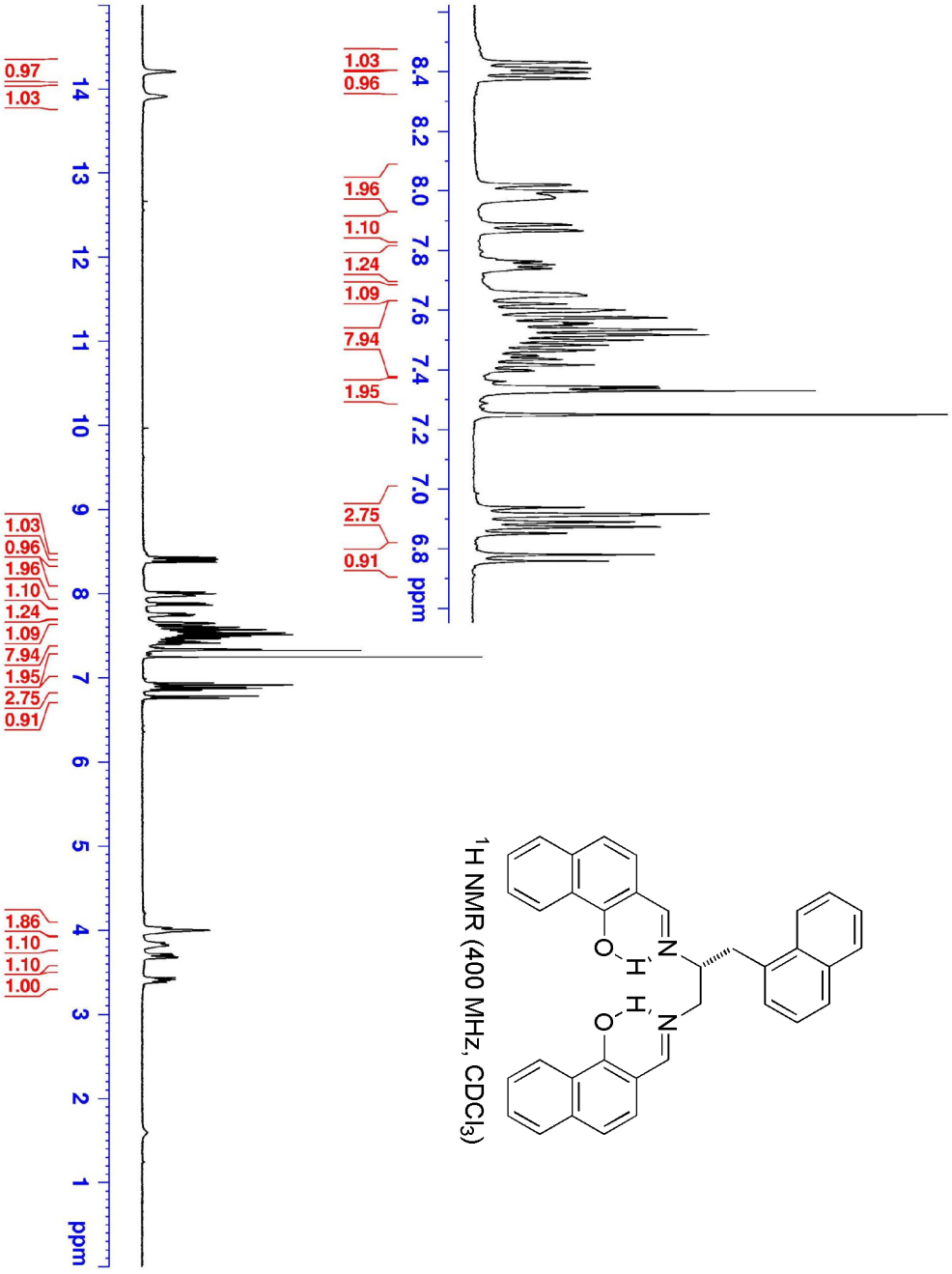

0.92
0.91
1.88
1.00
0.92
1.88
6.13
1.12
1.11
2.02
1.03
1.04
1.00
1.00
1.07
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 ppm
^{1}H NMR (400 MHz, CDCl$_3$)
N
O
H
Cl


^{1}H NMR (400 MHz, CDCl$_3$)
0.93
0.92
4.16
12.30
2.16
2.09
1.00
1.08
1.07
ppm
1.00
1.08
1.07
5.0
4.5
4.0
ppm
O
H
N
Cl

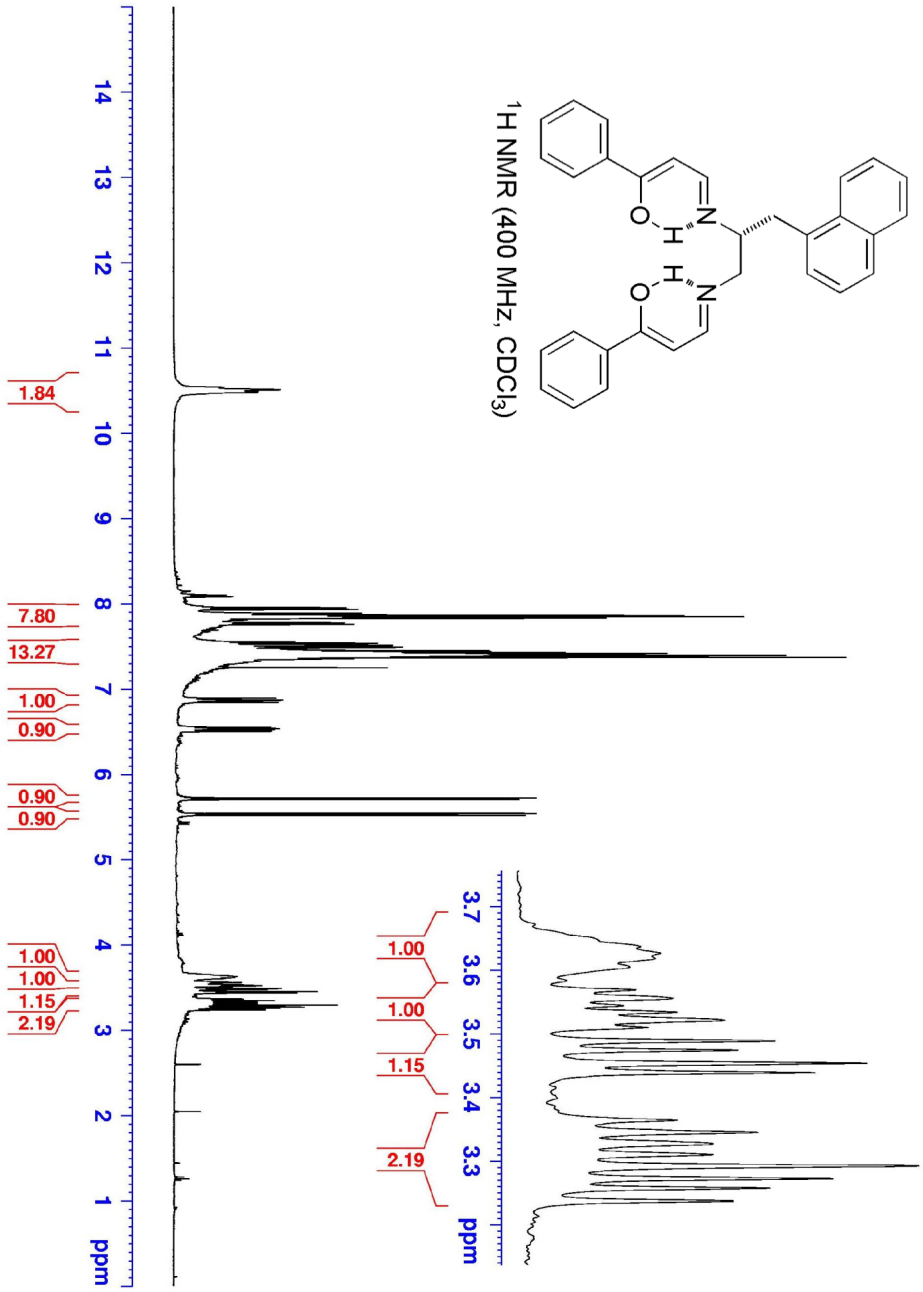

^{1}H NMR (400 MHz, CDCl$_3$)
1.90
0.99
1.01
0.99
0.99
1.00
2.02
3.94
0.97
0.97
0.97
1.00
0.98
1.00
0.98
8.66
9.10
9.01
8.85
ppm
0.97
1.00
0.98
1.00
0.98
4.0
3.9
3.8
3.7
3.6
3.5
ppm


^{1}H NMR (400 MHz, CDCl$_3$)
0.94
0.96
0.97
1.78
0.97
1.01
3.81
1.00
1.90
0.99
1.00
1.01
1.01
1.00
0.99
1.00
1.01
1.01
1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 ppm

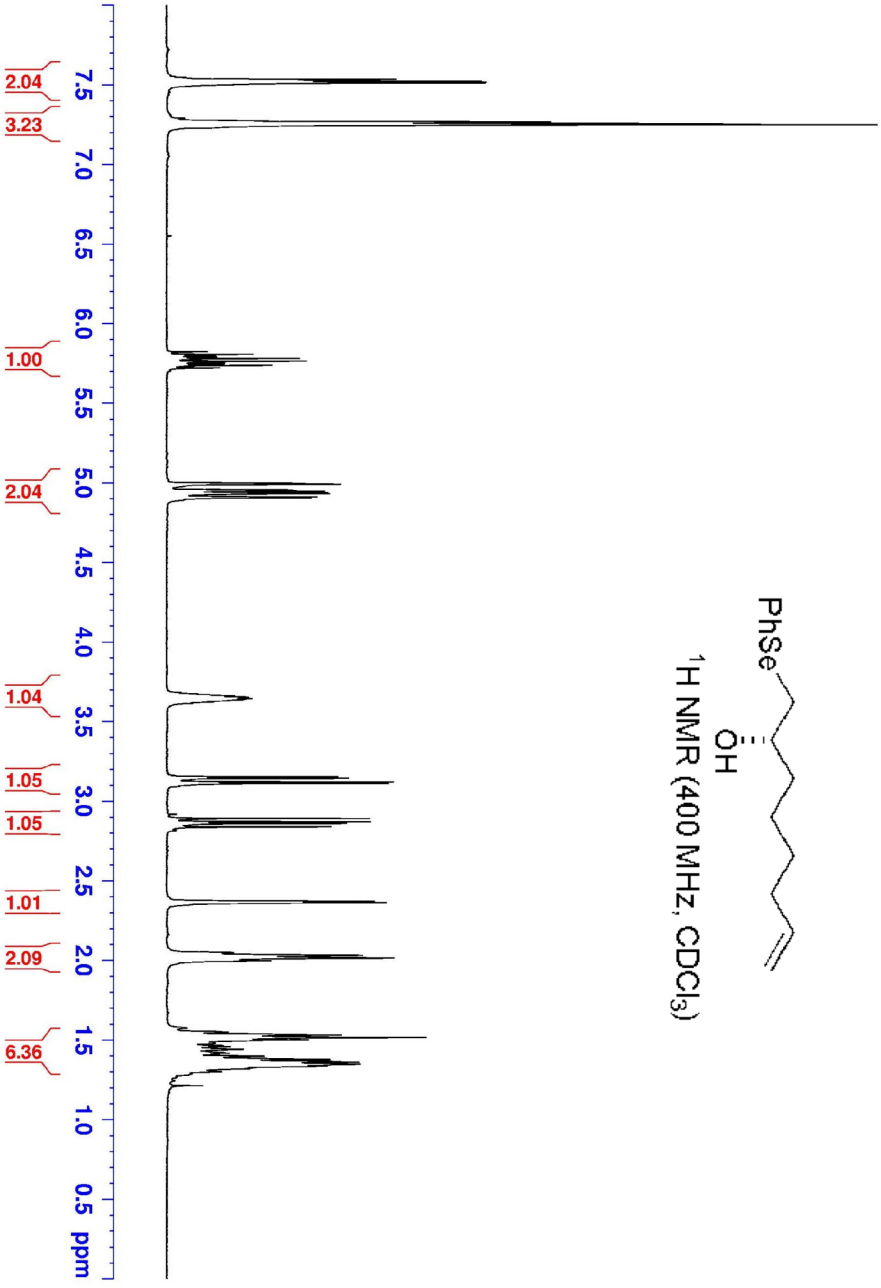

^{1}H NMR (400 MHz, CDCl$_3$)
1.90
1.00
1.02
1.04
0.99
1.02
1.02
1.08
5.10
3.02
1.02
1.02
1.00
1.03
1.00
1.00
1.00
1.00
1.03
1.00
1.00
1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 ppm

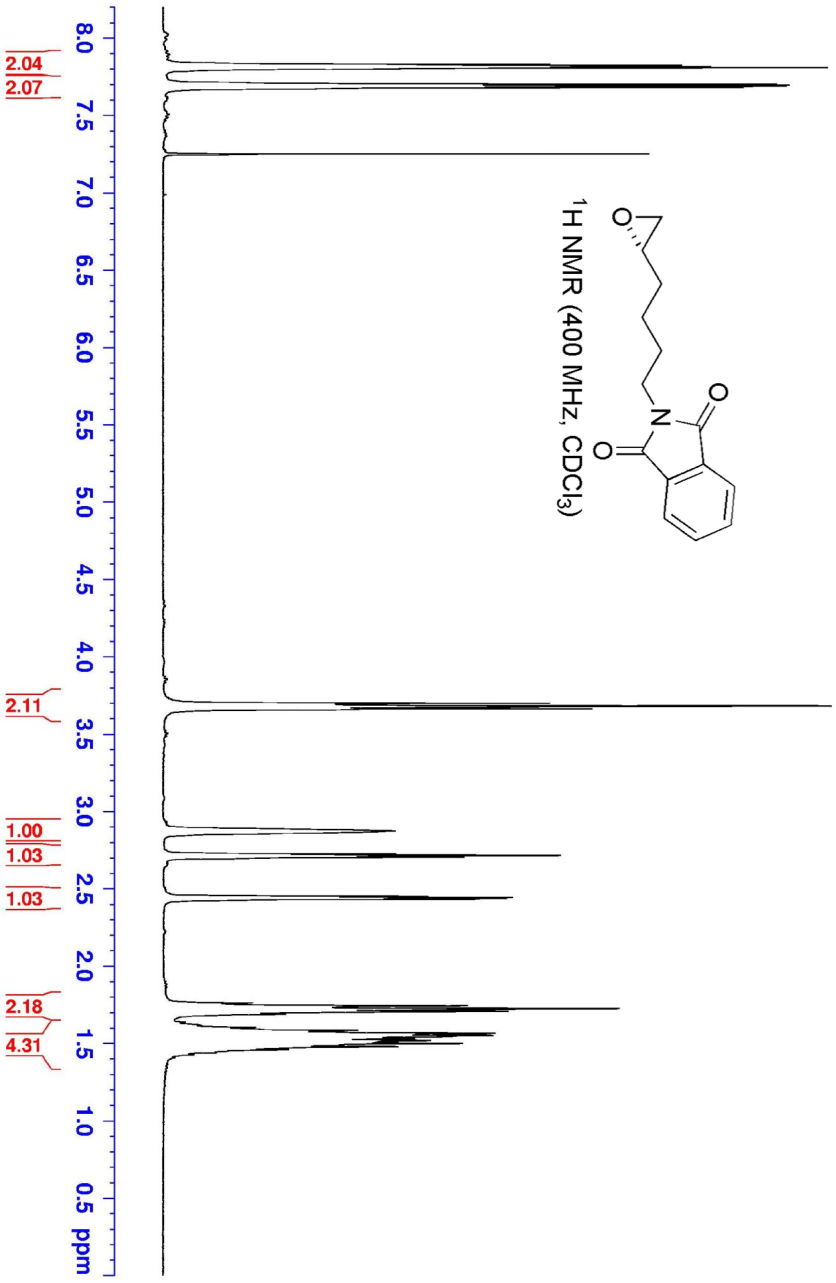


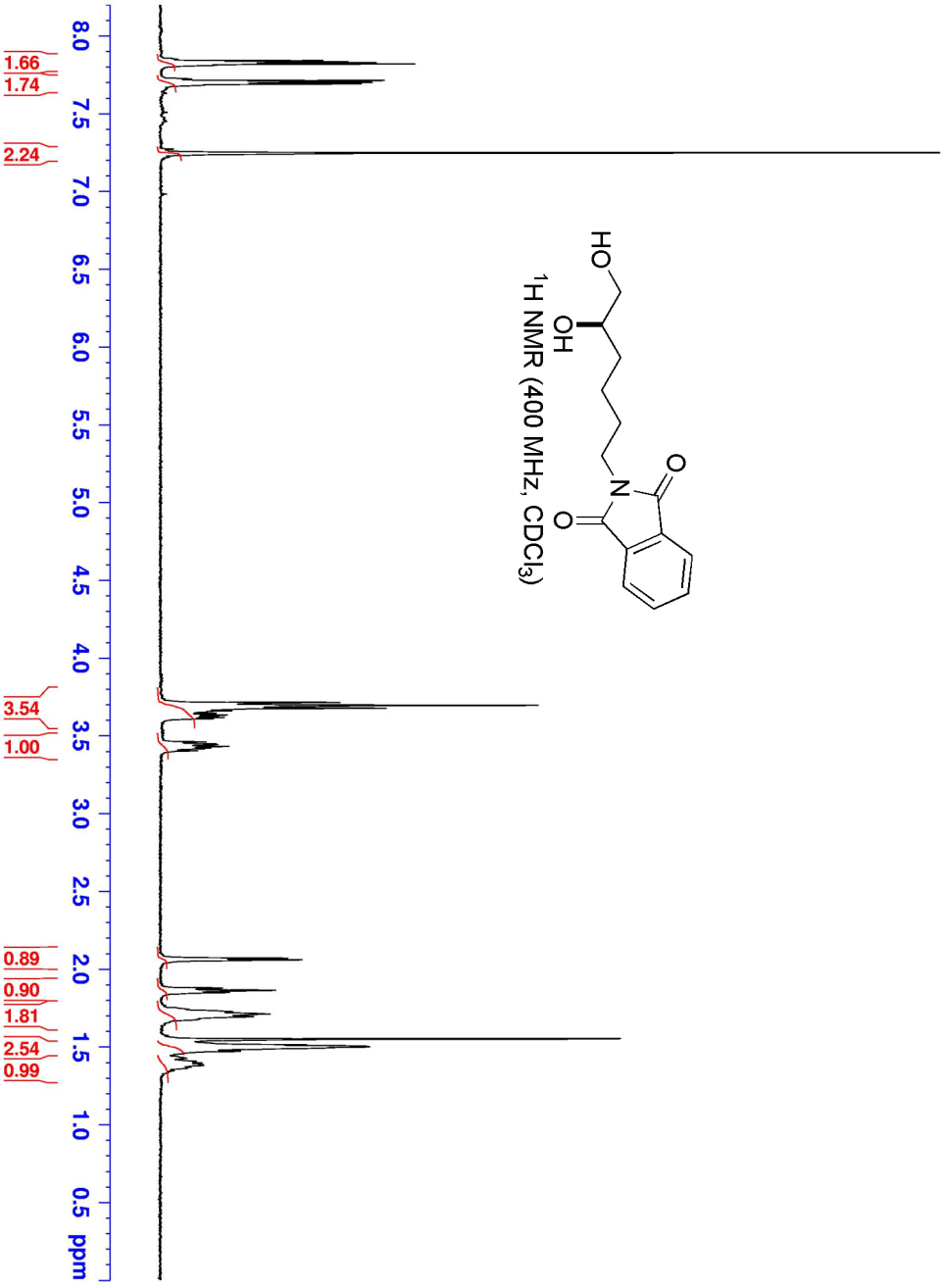
^{1}H NMR (400 MHz, $CDCl_3$)

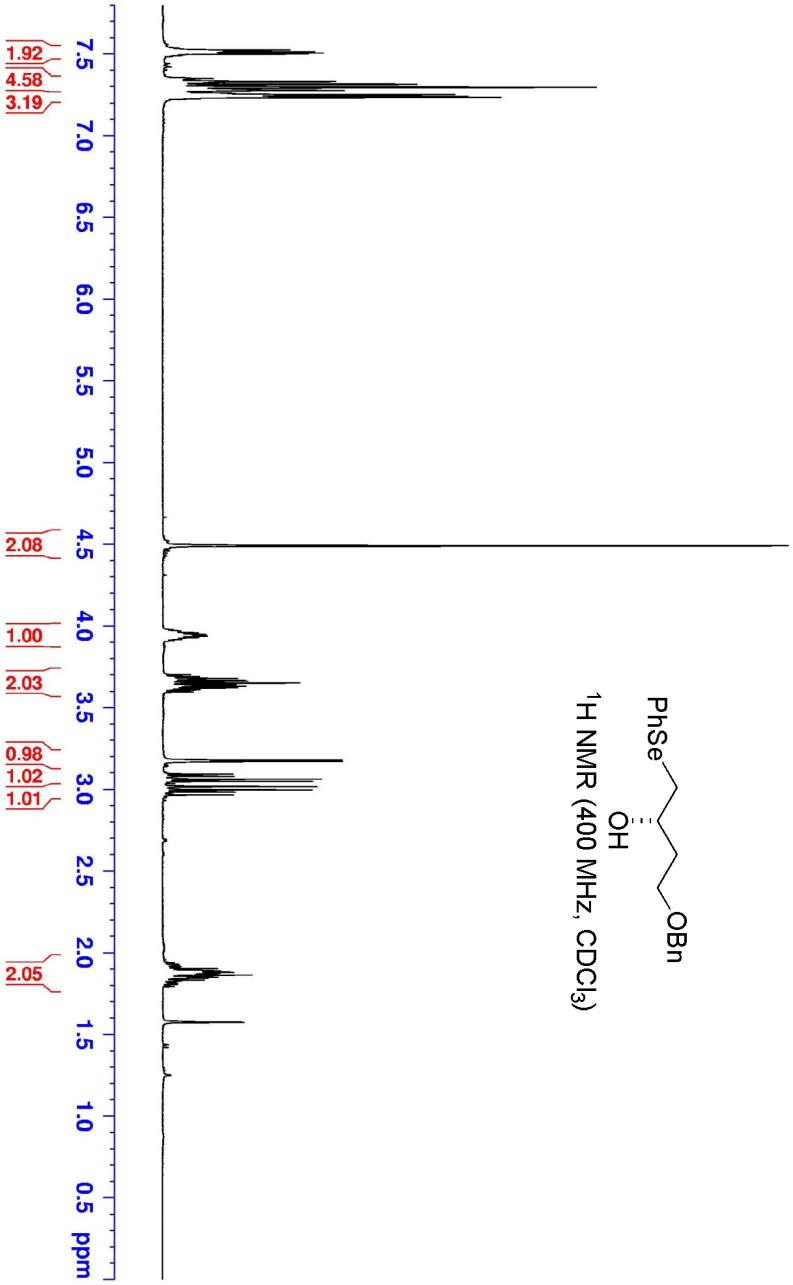

^{1}H NMR (400 MHz, CDCl$_3$)
1.84
7.80
13.27
1.00
0.90
0.90
0.90
1.00
1.00
1.15
2.19
1.00
1.00
1.15
2.19
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
3.7 3.6 3.5 3.4 3.3 ppm

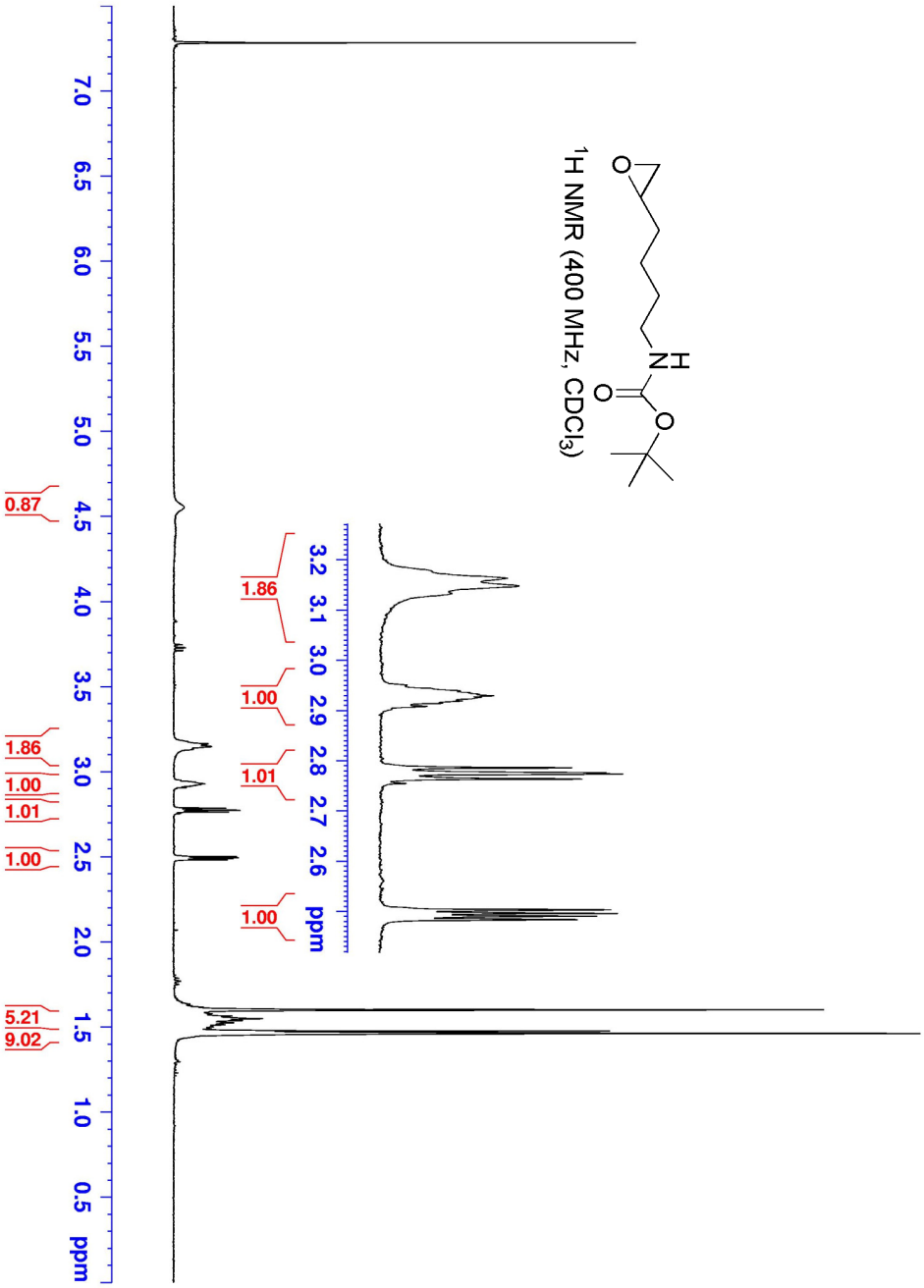
XI. Representative NMR Spectra for Kinetically Resolved Epoxides, Diols, and Seleno-Alcohols

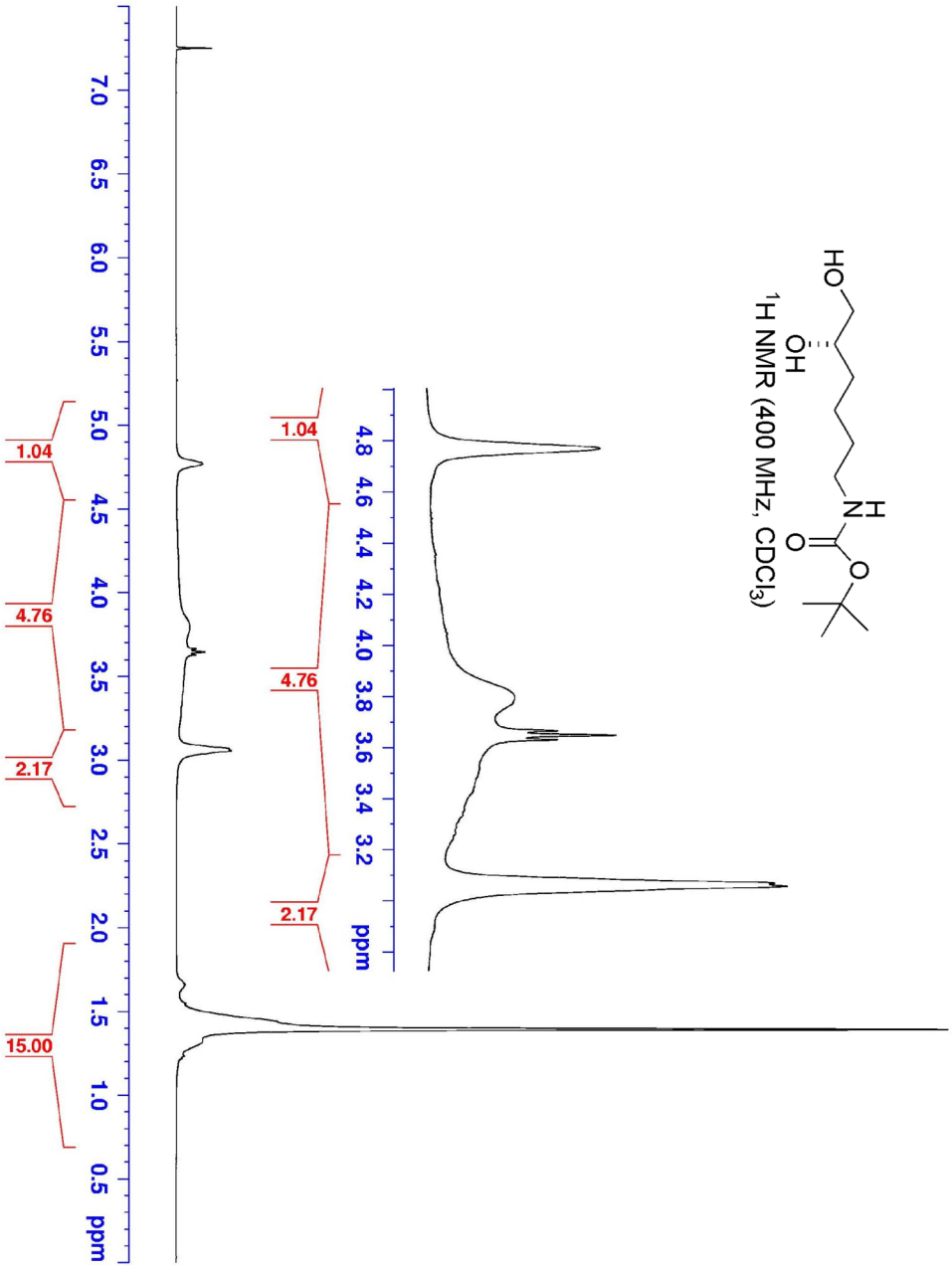


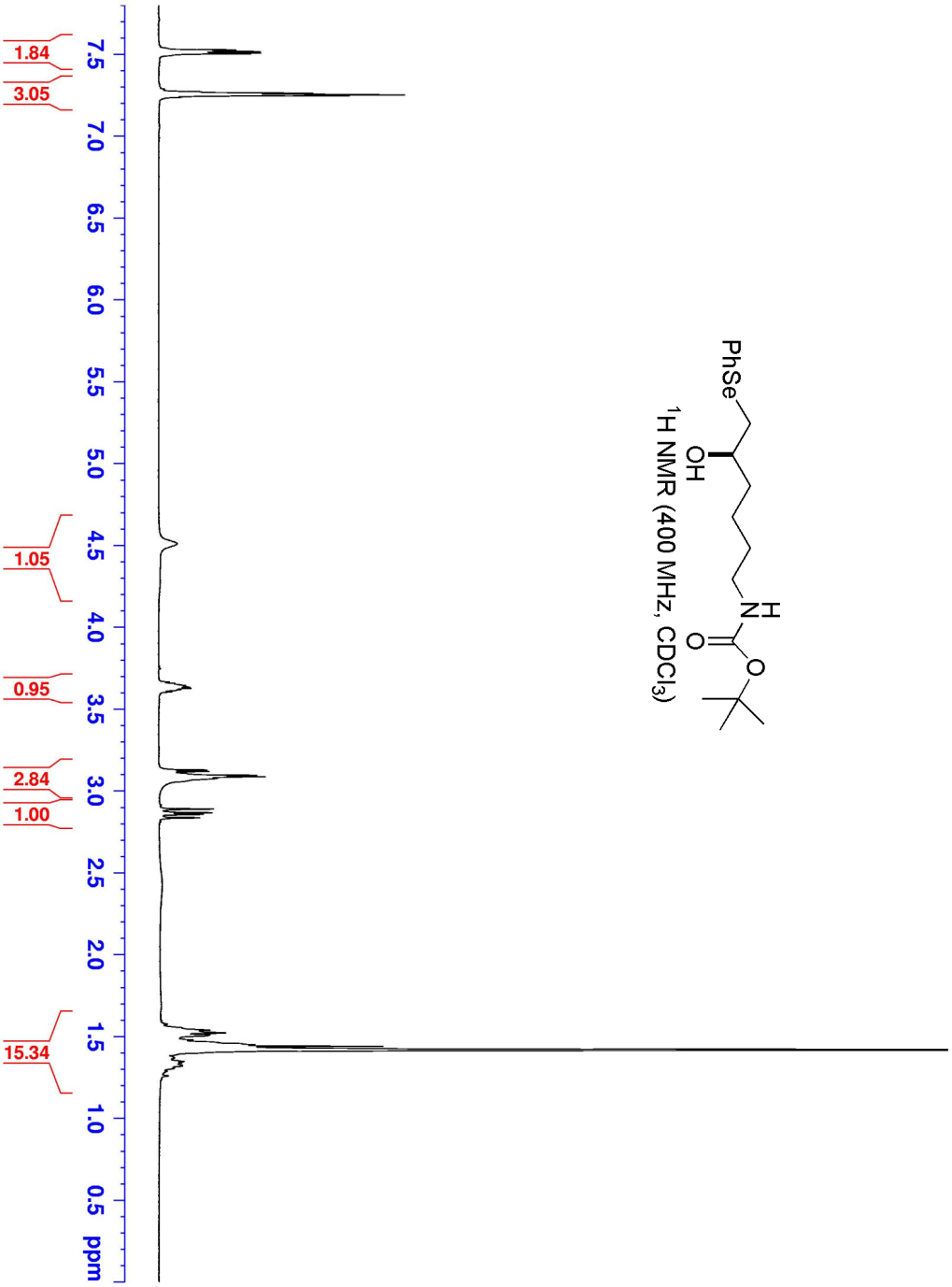

^{1}H NMR (400 MHz, CDCl$_3$)
2.04
2.07
2.11
1.00
1.03
1.03
2.18
4.31
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

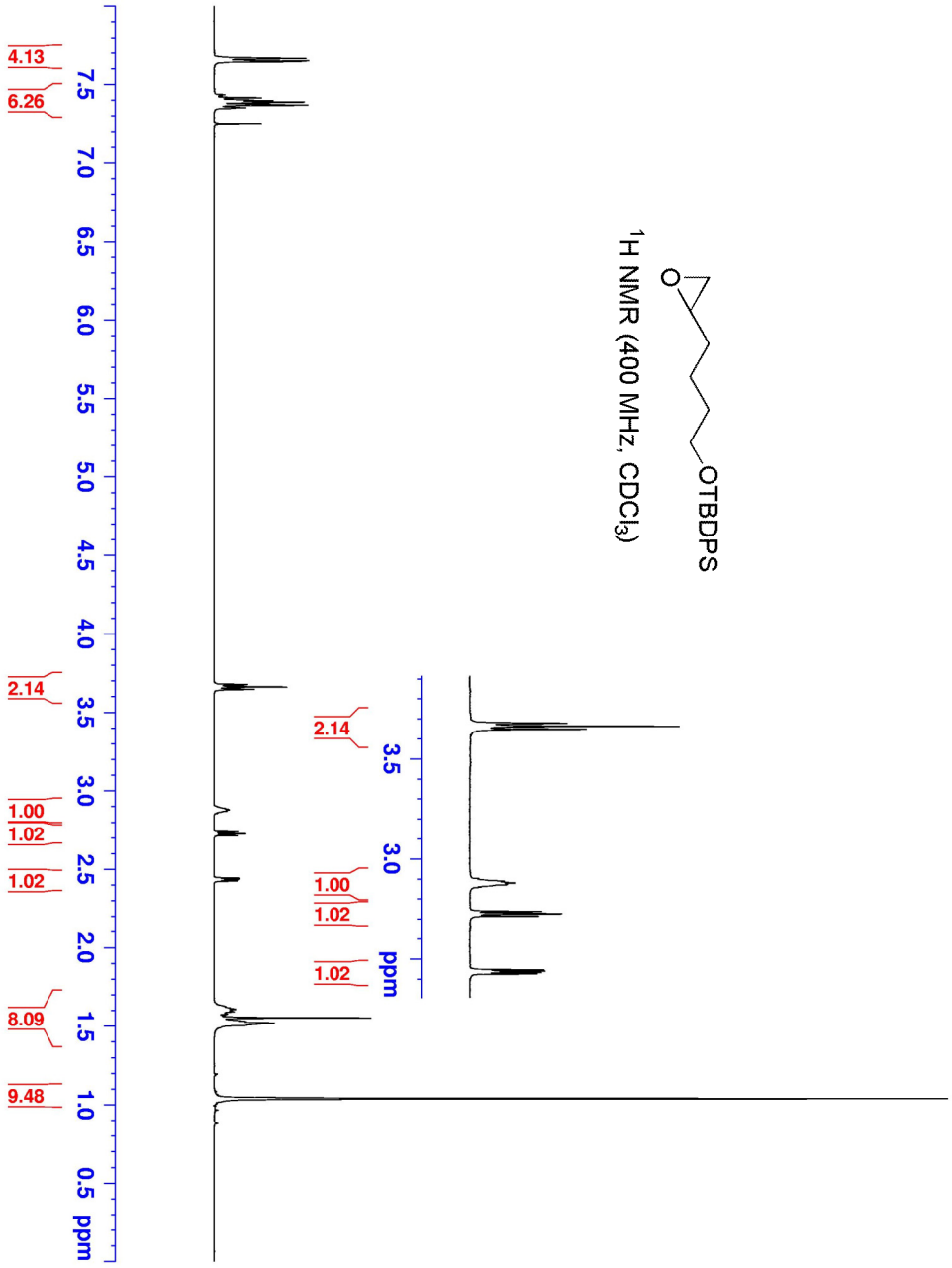

1.66
1.74
2.24
3.54
1.00
0.89
0.90
1.81
2.54
0.99
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
HO
OH
N
O
O
^{1}H NMR (400 MHz, CDCl$_3$)

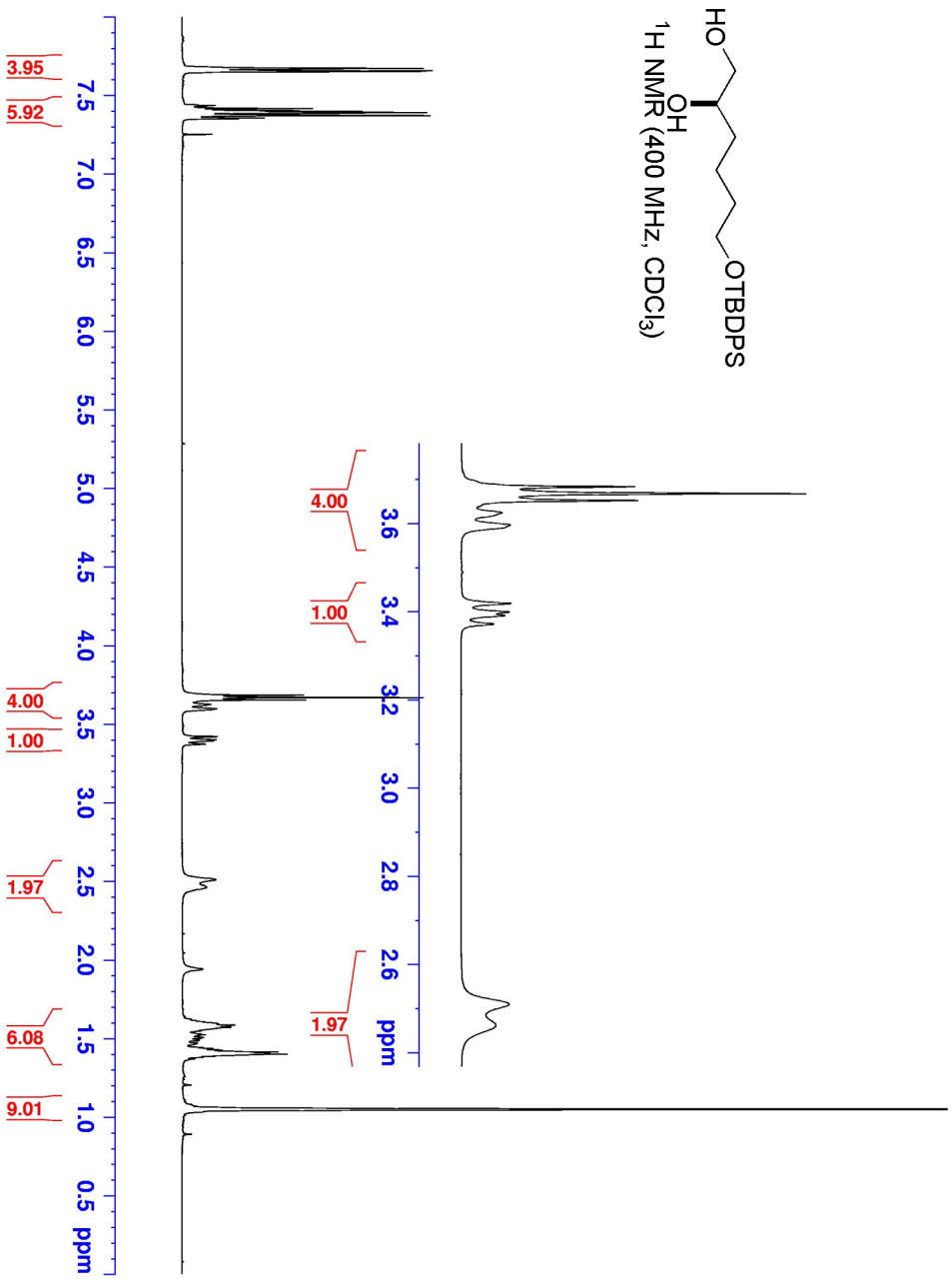

1.92
4.58
3.19
2.08
1.00
2.03
0.98
1.02
1.01
2.05
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
PhSe
OH
OBn
^{1}H NMR (400 MHz, $CDCl_3$)

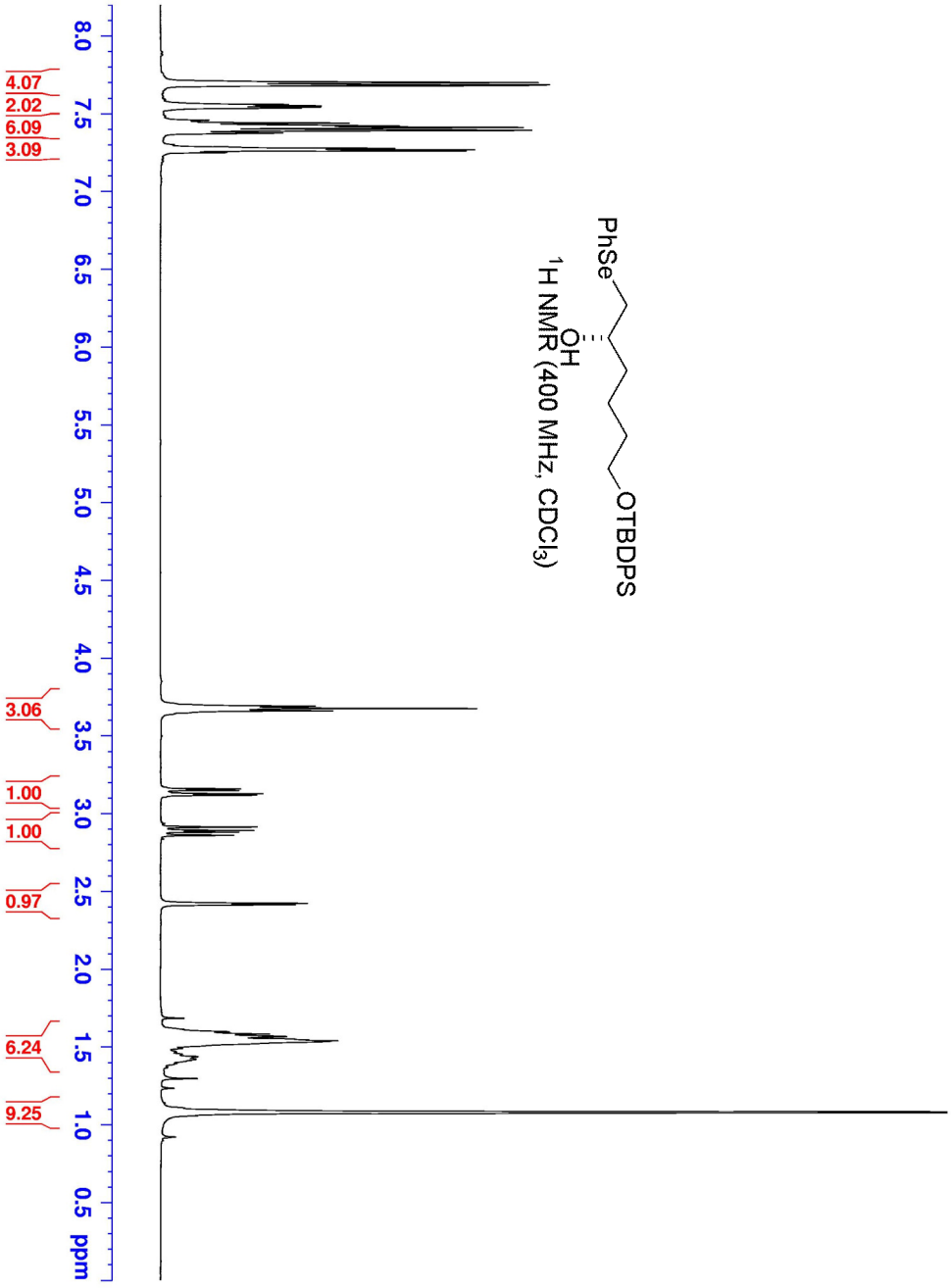

^{1}H NMR (400 MHz, CDCl$_3$)
0.87
1.86
1.00
1.01
1.00
5.21
9.02
1.86
1.00
1.01
1.00
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
3.2 3.1 3.0 2.9 2.8 2.7 2.6 ppm


HO
OH
H
N
O
O
^{1}H NMR (400 MHz, CDCl$_3$)
1.04
4.76
2.17
15.00
ppm

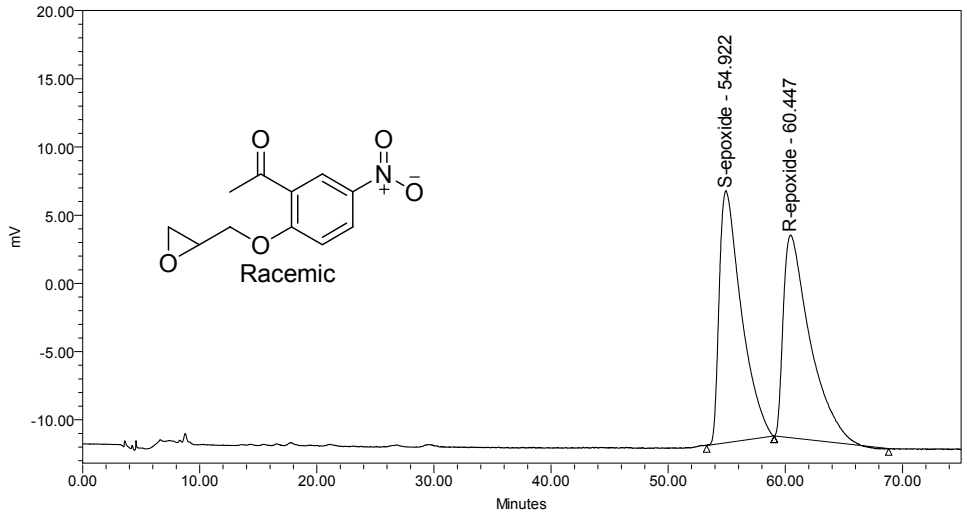

1.84
3.05
1.05
0.95
2.84
1.00
15.34
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
PhSe
OH
H
N
O
O
^{1}H NMR (400 MHz, CDCl$_3$)

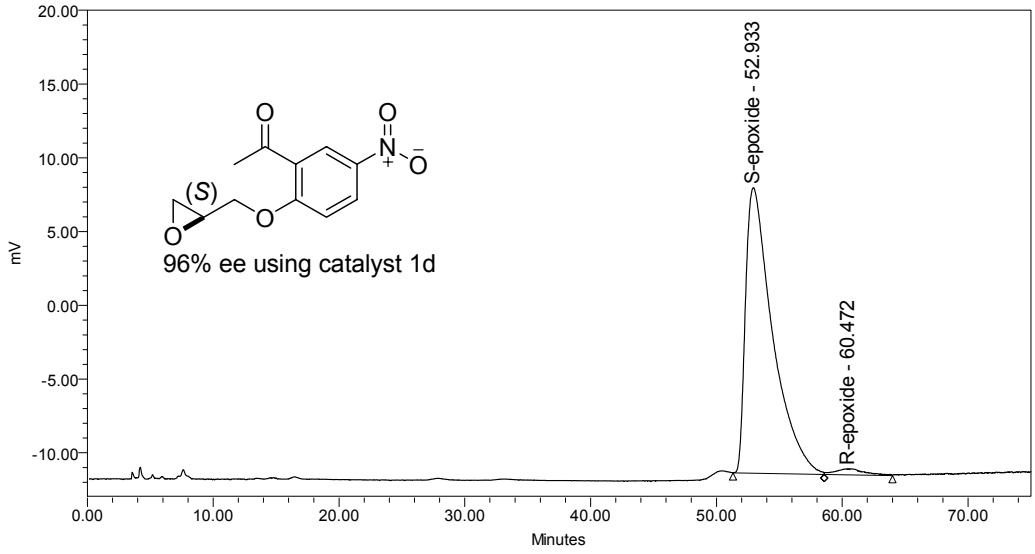

^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
4.13
6.26
2.14
1.00
1.02
1.02
8.09
9.48
2.14
1.00
1.02
1.02
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
3.5 3.0 ppm

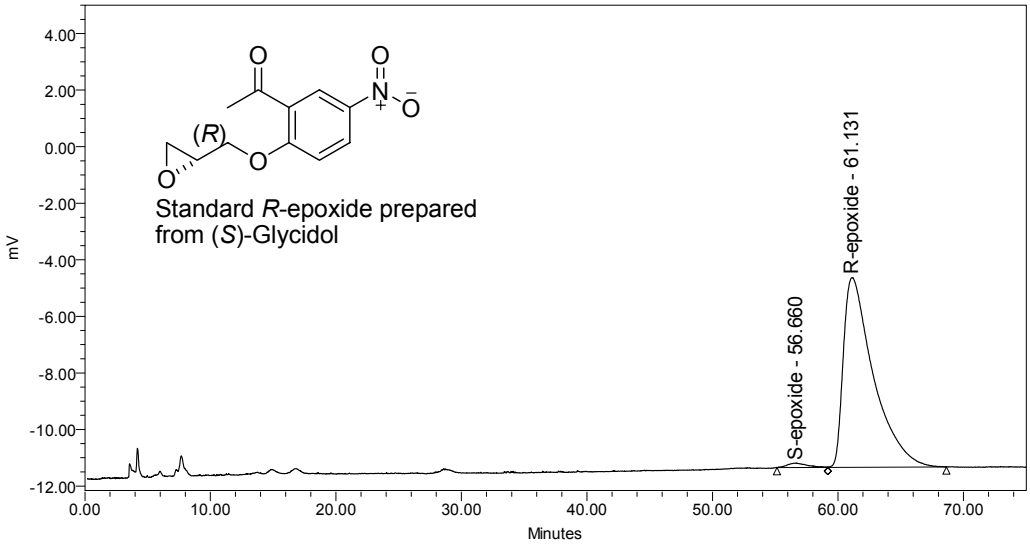

HO
OH
OTBDPS
^{1}H NMR (400 MHz, CDCl$_3$)
3.95
5.92
4.00
1.00
1.97
6.08
9.01
4.00
1.00
1.97
ppm

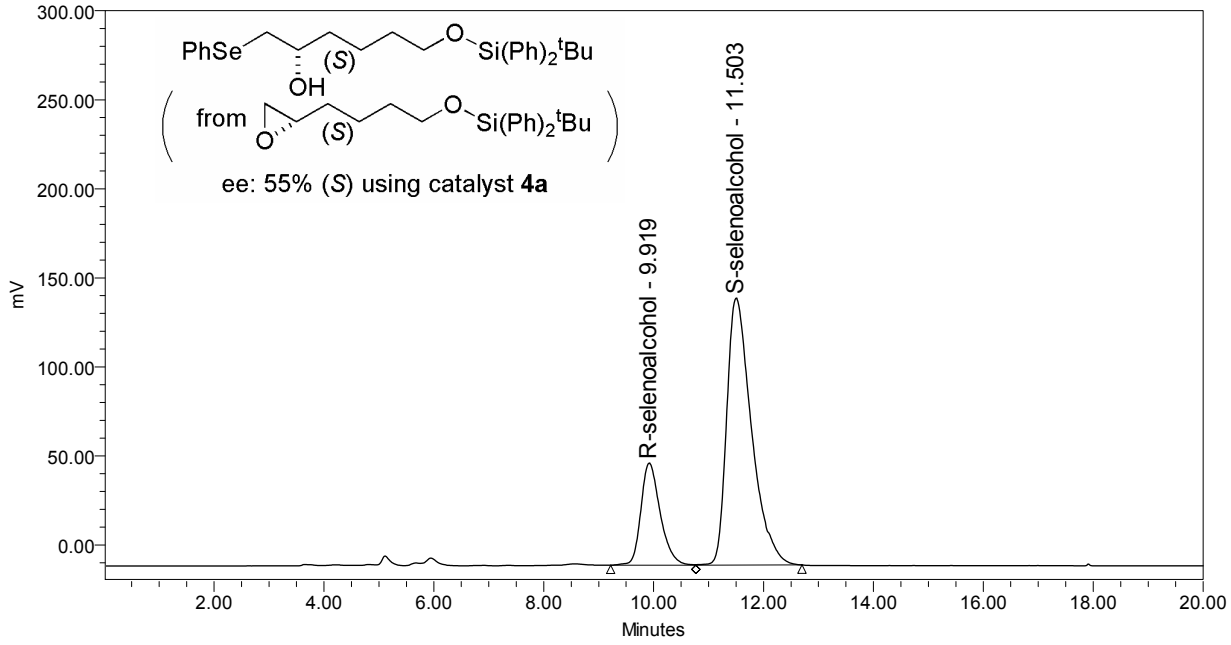

PhSe
OH
OTBDPS
^{1}H NMR (400 MHz, $CDCl_3$)
4.07
2.02
6.09
3.09
3.06
1.00
1.00
0.97
6.24
9.25
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

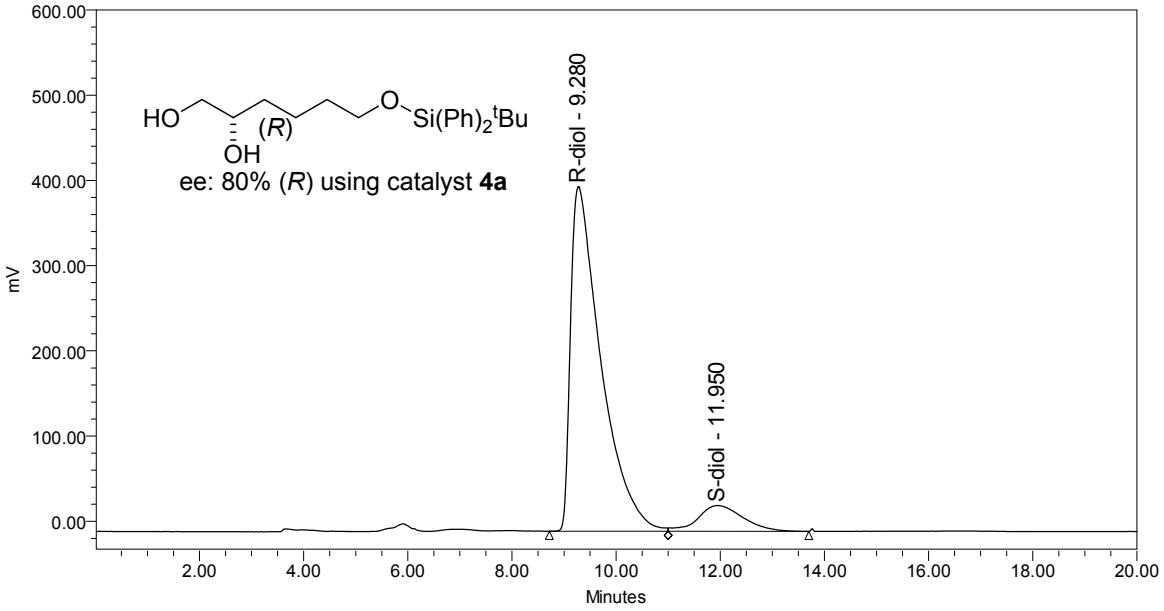
XII. Representativentative Chiral-HPLC Traces for Kinetically Resolved Epoxides, Diols, and Seleno-Alcohols

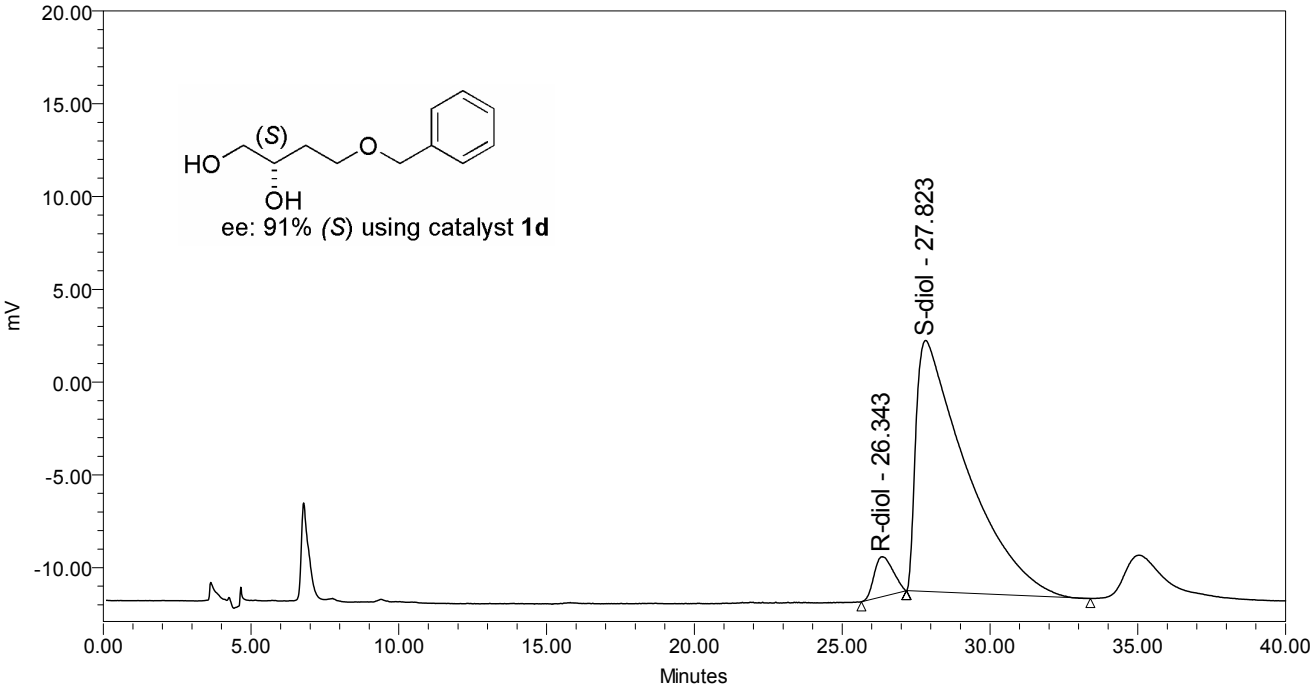


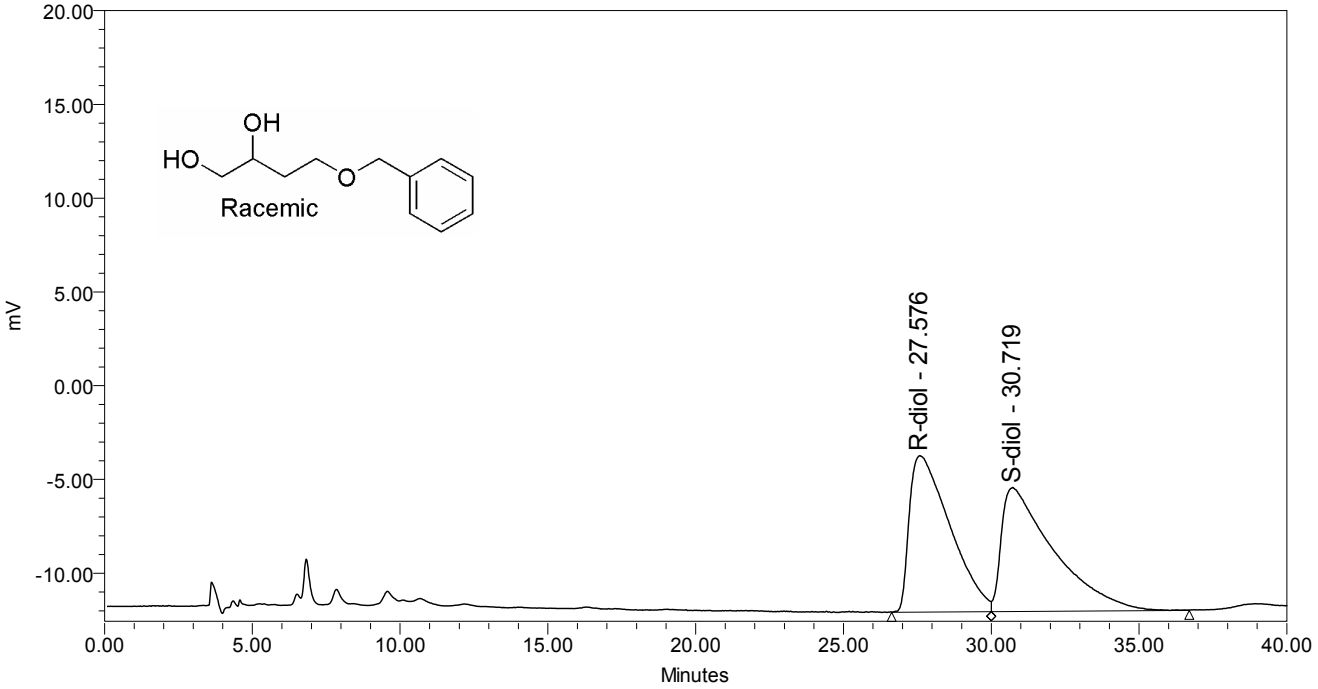


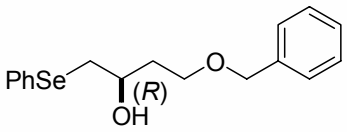



PhSe
(S)
OH
O
Si(Ph)2tBu
from
(S)
ee: 55% (S) using catalyst 4a
R-selenoalcohol - 9.919
S-selenoalcohol - 11.503
mV
Minutes

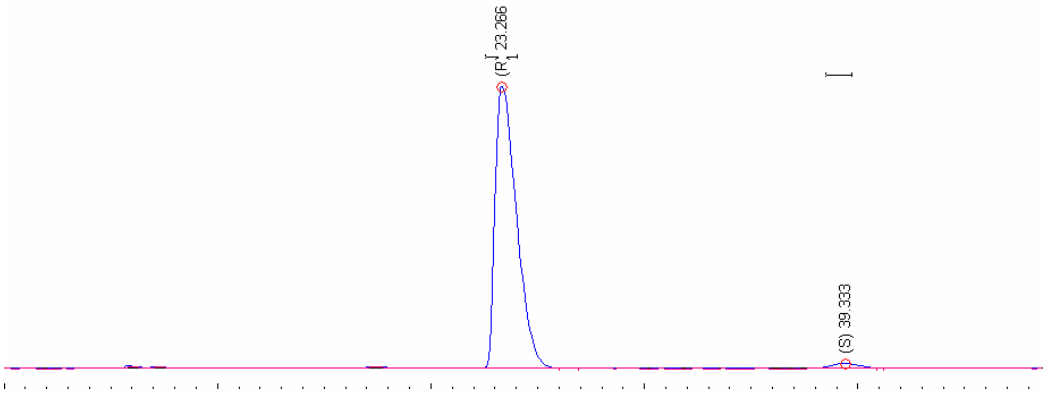

HO
(R)
OH
Si(Ph)2tBu
ee: 80% (R) using catalyst 4a
R-diol - 9.280
S-diol - 11.950
mV
Minutes

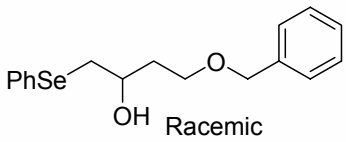

20.00
15.00
10.00
5.00
0.00
-5.00
-10.00
mV
(S)
HO
O
OH
ee: 91% (S) using catalyst 1d
R-diol - 26.343
S-diol - 27.823
0.00
5.00
10.00
15.00
20.00
25.00
30.00
35.00
40.00
Minutes


20.00
15.00
10.00
5.00
0.00
-5.00
-10.00
mV
OH
HO
O
Racemic
R-diol - 27.576
S-diol - 30.719
0.00
5.00
10.00
15.00
20.00
25.00
30.00
35.00
40.00
Minutes

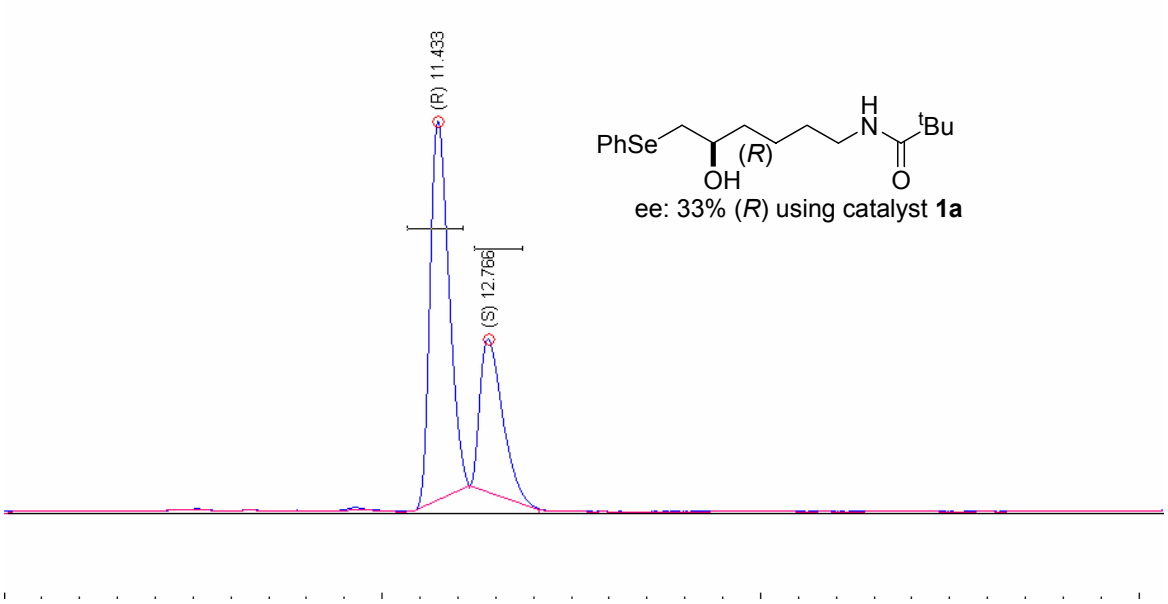


ee: 96% *(R)* using catalyst **1d**

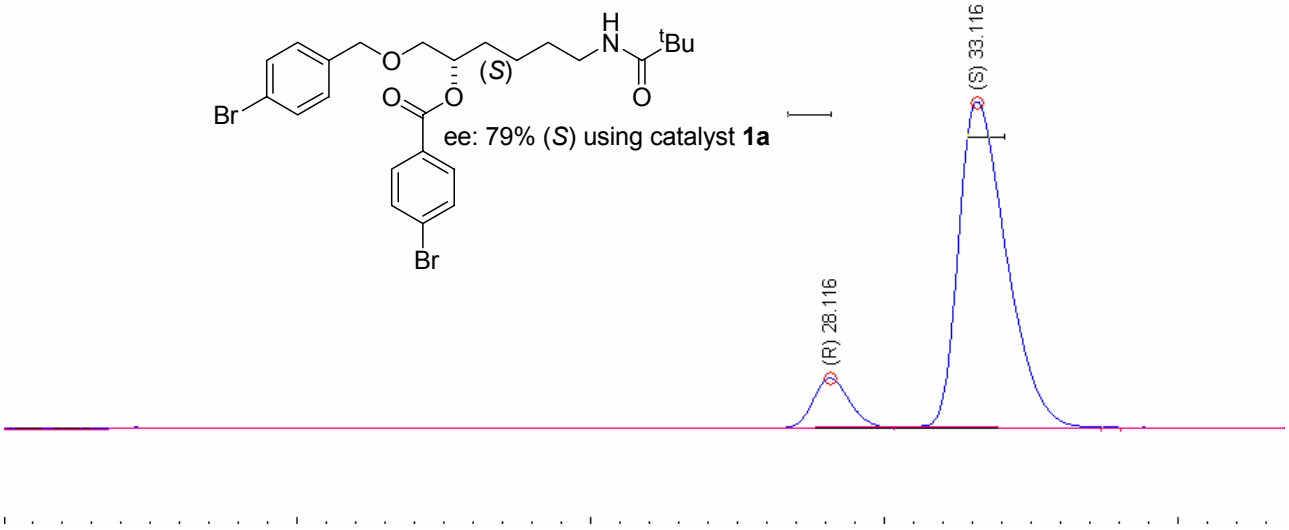




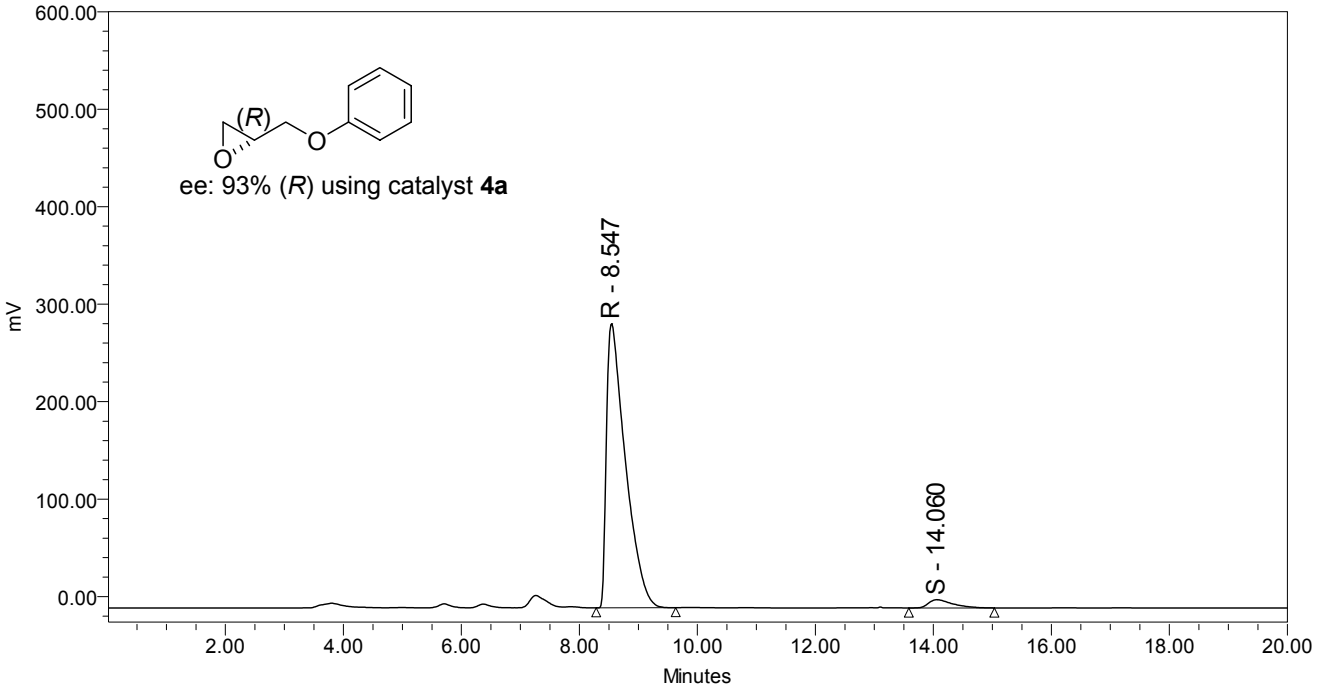
Racemic

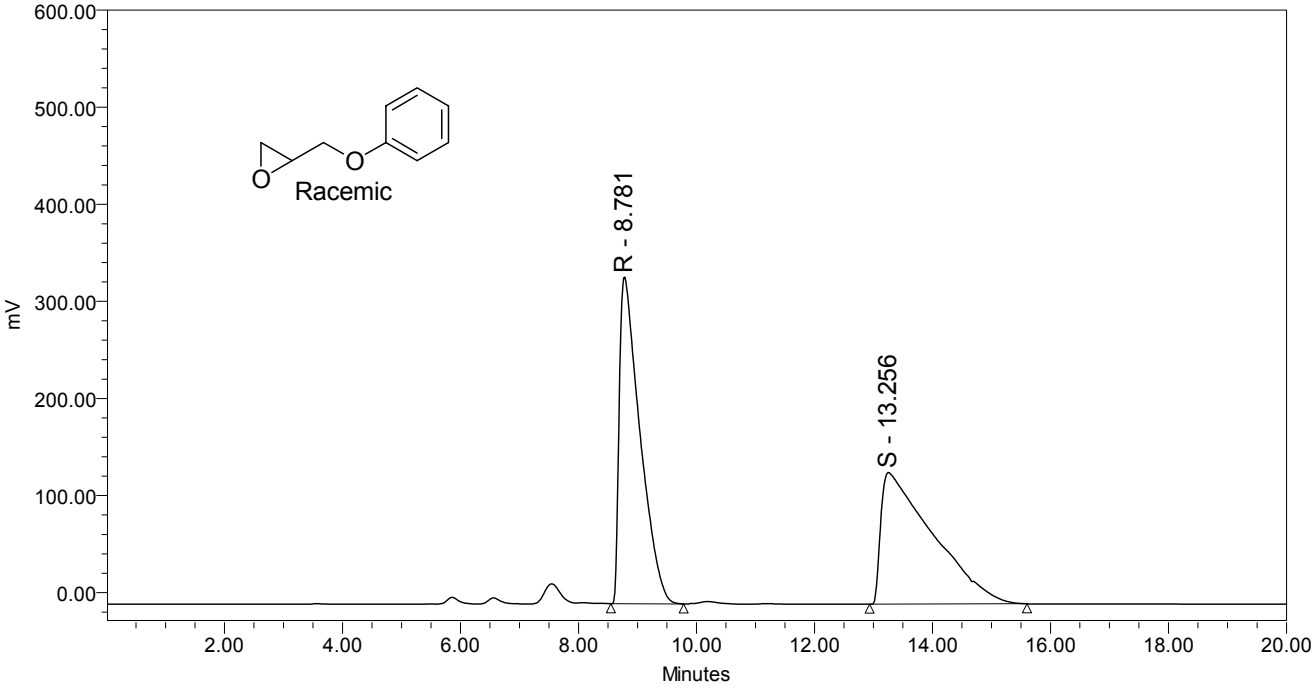


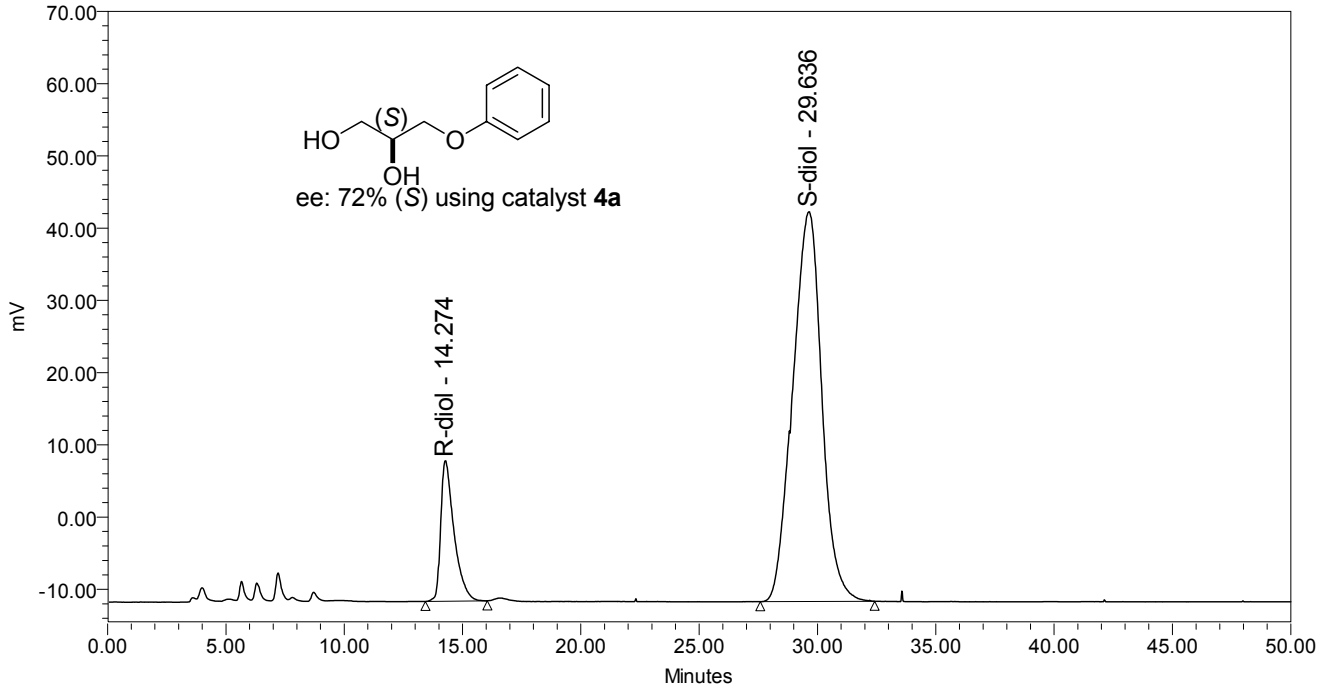
ee: 33% (*R*) using catalyst **1a**

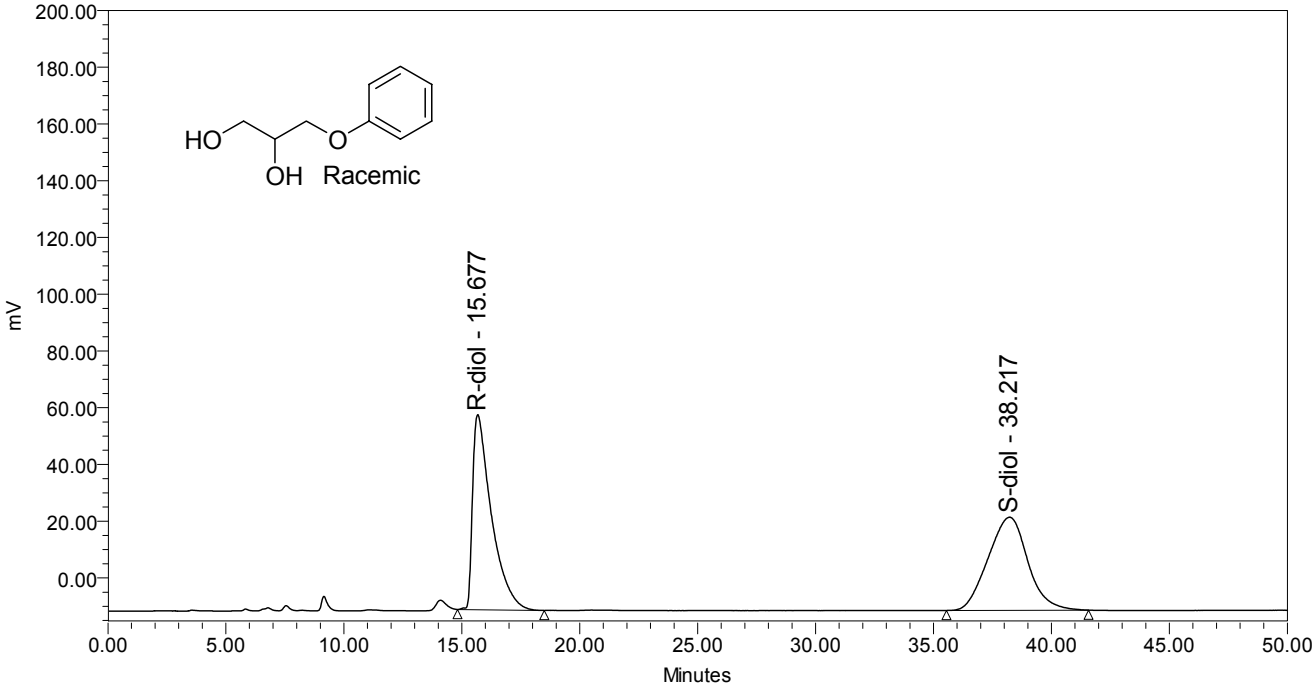


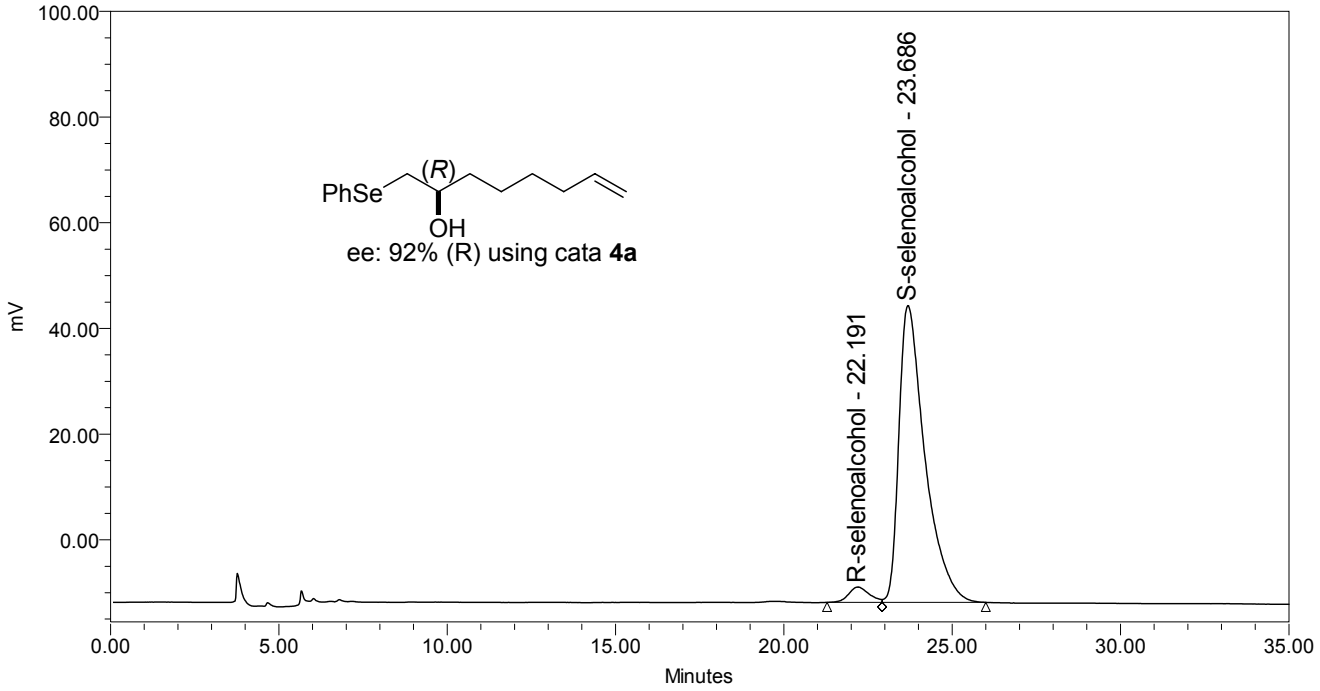
ee: 79% (*S*) using catalyst **1a**

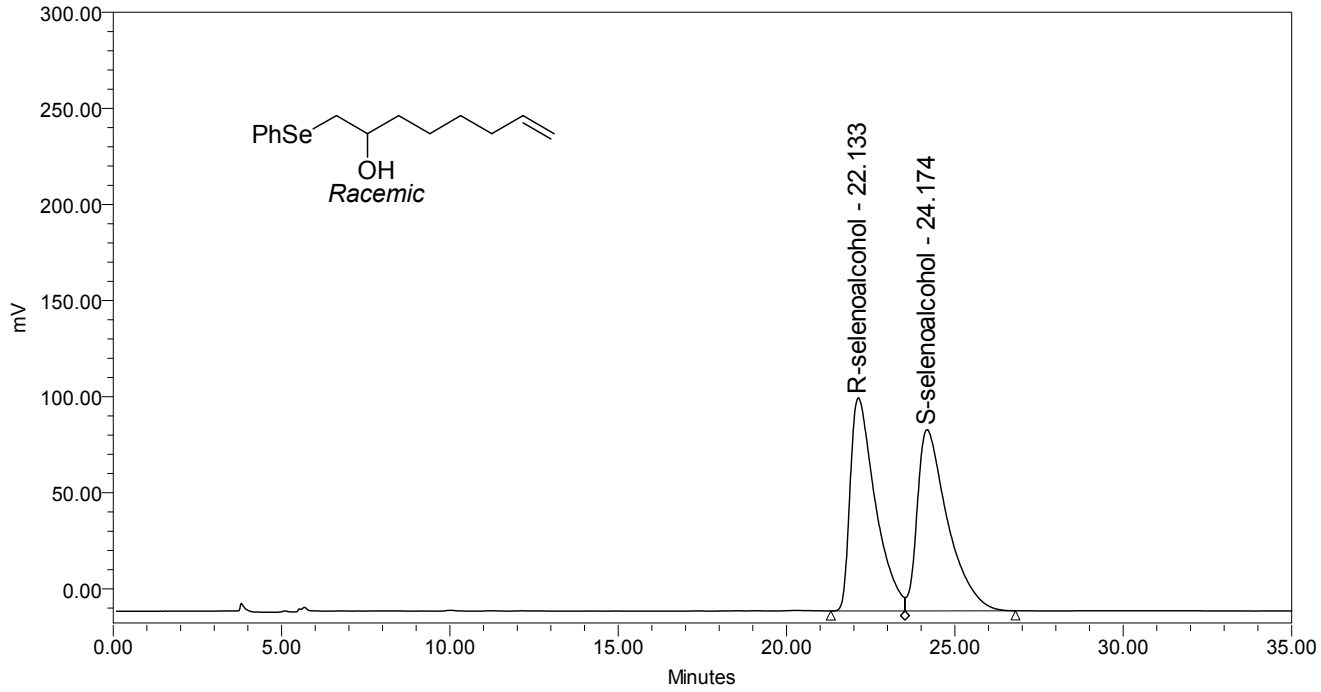

(R)
O
O
ee: 93% (R) using catalyst 4a
R - 8.547
S - 14.060
mV
600.00
500.00
400.00
300.00
200.00
100.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
Minutes


O
O
Racemic
R - 8.781
S - 13.256
mV
600.00
500.00
400.00
300.00
200.00
100.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
Minutes

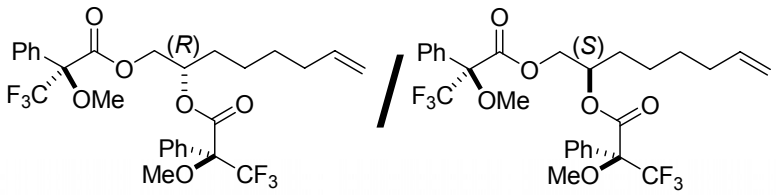

HO
(S)
O
OH
ee: 72% (S) using catalyst 4a
R-diol - 14.274
S-diol - 29.636
mV
Minutes


HO
O
OH Racemic
R-diol - 15.677
S-diol - 38.217
mV
Minutes

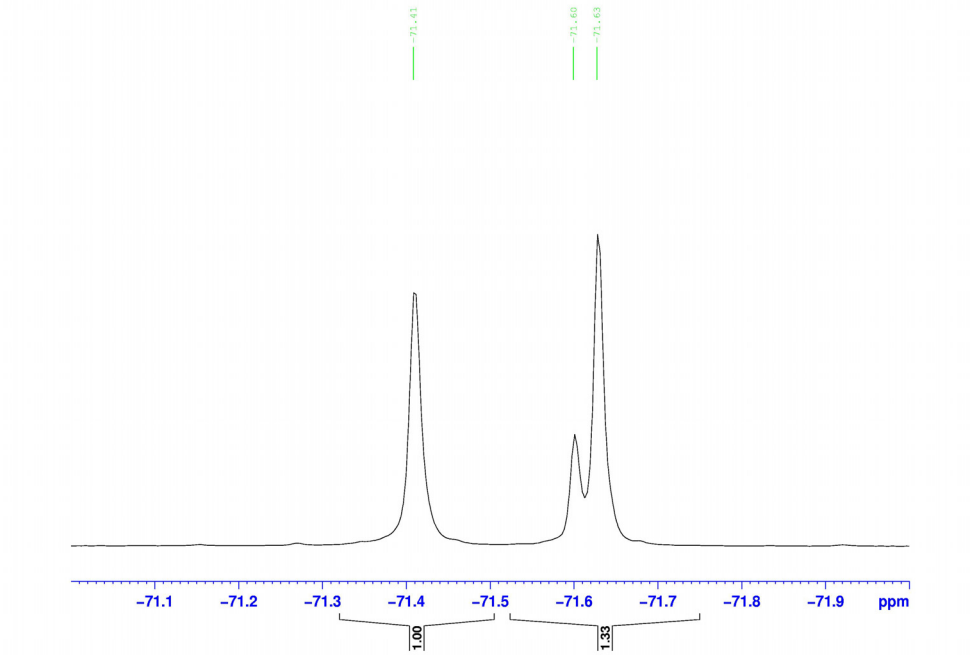

100.00
80.00
60.00
40.00
20.00
0.00
mV
PhSe
(R)
OH
ee: 92% (R) using cata 4a
R-selenoalcohol - 22.191
S-selenoalcohol - 23.686
0.00
5.00
10.00
15.00
20.00
25.00
30.00
35.00
Minutes


300.00
250.00
200.00
150.00
100.00
50.00
0.00
mV
PhSe
OH
Racemic
R-selenoalcohol - 22.133
S-selenoalcohol - 24.174
0.00
5.00
10.00
15.00
20.00
25.00
30.00
35.00
Minutes

XIII. Mosher Ester Data:



100/16.5



XIV. X-Ray Crystallography:

Crystallography for Co(II)-1d:

Crystals were grown using the slow diffusion method between CH_2Cl_2 and methanol, $C_{32}H_{30}CoN_2O_2$, M_r = 533.51; dimensions 0.43 X 0.05 X 0.04 mm, monoclinic, space group $P2_1$; *a* = 6.638(3), *b* = 22.112(8), *c* = 16.700(6) Å, α= 90, β= 91.203(8), γ= 90°, V 2450.7(17) Å^3, Z, Z'=4, 2; ρ_{calcd} = 1.446 Mg/m^3, 15567 reflections, 8514 independent reflections (R_{int} =0.0580); *R*1 = 0.0884, *wR*2 = 0.2401 for 667 parameters and 6561 reflections with [I > 2σ(I)]. Absorption coefficient 0.735 mm^{-1}, temperature 100(2) K; The intensity data were collected using a diffractometer with a Bruker APEX CCD area detector ((a) Data Collection: SMART Software Reference Manual (1998). Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA. (b) Data Reduction: SAINT Software Reference Manual (1998). Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA) and graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The structure was solved by direct methods and refined by full-matrix least-squares methods on F^2 ((a) G. M. Sheldrick (2000). SHELXTL Version 6.10 Reference Manual. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA. (b) *International Tables for Crystallography, Vol C*, Tables 6.1.1.4, 4.2.6.8, and 4.2.4.2, Kluwer: Boston (1995). Non-hydrogen atoms were refined with anisotropic displacement parameters.

This structure has been deposited at the *Cambridge Crystallographic Data Centre* and has been assigned the following entry number: **CCDC 641478**

Crystallography for Co(II)-4a:

Crystals (0.25 X 0.18 X 0.07 mm dimensions) suitable for single crystal X-ray diffraction were grown from a solution in CH_2Cl_2 diffused with ethanol. $C_{43}H_{54}CoN_2O_2$-CH_2Cl_2, M_r = 774.74; monoclinic, space group $P2_1$; *a* = 10.2438(7), *b* = 27.205(2), *c* = 15.8493(11) Å, α= 90, β = 108.2700(10), γ= 90°, V = 4194.3(5) Å^3; Z = 4, ρ_{calcd} = 1.227 g cm^{-3}; μ = 0.573 mm^{-1}; *T* = 120 K; flack parameter = 0.001(11). Refinement of 947 parameters based on 16493 independent (R_{int} =0.0518) out of totally 49499 reflections with $2\theta_{max}$ = 26.0° converged at *R1* = 0.0522, *wR*2 = 0.1298, and *GOF* = 1.059; the largest peak on the final difference map was 0.994 e Å^{-3}. Intensity data were collected with a Bruker Smart APEX CCD detector (Mo-Kα radiation, λ= 0.71073 Å, graphite monochromator) on a D8 goniometer. Temperature was controlled with an Oxford Cryosystems Series 700 instrument. Intensities were integrated with SAINT [Program for Reduction of Data Collected on Bruker CCD Area Detector Diffractometer, Bruker AXS Inc., Madison, WI, 2003] and corrected for absorption with SADABS. [G. M. Sheldrick, SADABS, Program for

Empirical Absorption Correction of Area Detector Data, University of Göttingen, Germany, 2003]. Structures were solved by direct methods and refined on F^2 with SHELXTL. [G. M. Sheldrick, SHELXTL, Program for solution and refinement of crystal structures, University of Göttingen, Germany, 2003].

This structure has been deposited at the *Cambridge Crystallographic Data Centre* and has been assigned the following entry number: **CCDC 641479**

Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge, CB21EZ, UK (fax: int. code + (1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk; web, www: http://www.ccdc.cam.ac.uk).