

# Supporting Information

## Co-Salen Complexes as Catalysts for the Asymmetric Henry Reaction – Reversed Enantioselectivity through Simple Ligand Modification

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## 1 General

All reagents were purchased from standard suppliers and used as received unless otherwise stated. Dichloromethane (HPLC grade) was dried by passing through columns of activated alumina (MBRAUN Solvent Purification System).

Nuclear magnetic resonance (NMR) spectra were recorded at room temperature on Bruker Avance-400/500/600 spectrometers.  $^{13}\text{C}$ -NMR spectra of small molecules were recorded in the attached proton test (APT) mode. Chemical shifts are reported in parts per million (ppm) relative to TMS. Multiplicities are denoted as singlet (s), doublet (d), doublet of doublets (dd), triplet (t), doublet of triplets (dt), and multiplet (m), and, where required, prefixed br (broad). Diaminocyclohexane is abbreviated DACH.

Mass spectrometry was performed on an Agilent LCMSD Trap XCT Mass Spectrometer (electrospray ionization, ESI). High resolution mass spectrometry (HRMS) was carried out on an Agilent 6224 TOF LC/MS (ESI) connected to a 1260 Infinity Quaternary LC System. A Bruker MALDI-TOF/TOF UltrafleXtreme MS Spectrometer was used for the analysis of the oligomers (dithranol was used as the matrix).

Gel-permeation chromatography (GPC) analyses were performed on a Shimadzu HPLC System with a LC-10AD pump, a SIL-10AF autoinjector, and a SPD-10A diode array detector, equipped with American Polymer Standards Corporation columns (linear mixed bed and 500 Å; 10  $\mu\text{m}$ ); THF was used as the mobile phase (flow rate at 1.0 mL).

UV-vis spectra were recorded on a Perkin Elmer Lambda 950 UV/VIS Spectrometer; analytes were dissolved in dichloromethane at concentrations of approximately 0.1  $\mu\text{mol/mL}$ .

IR-spectra were recorded on a Nicolet 6700 FT-IR spectrometer, equipped with a Smart iTR ATR accessory.

Gas chromatography/mass spectrometry (GCMS) was performed on a Thermo Finnigan TRACE GC/PolarisQ Ion Trap MS (electron ionization, EI), equipped with a Restek Rtx-5MS column (30m x 0.25mm x 0.25 $\mu\text{m}$ ).

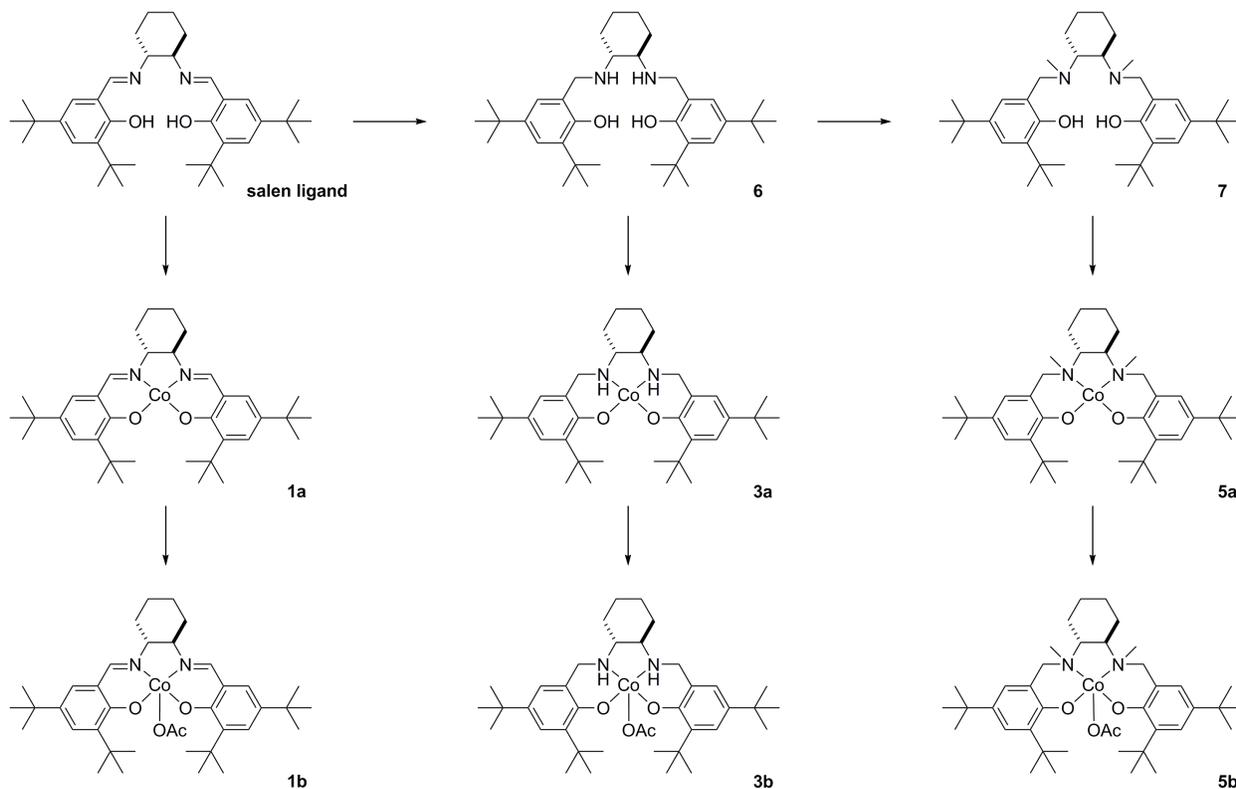
Elemental analysis (CHNX) and inductively coupled plasma mass spectrometry (ICP-MS) were conducted by Robertson Microlit Laboratories, Inc.

HPLC analysis to determine conversion and enantiomeric excess (ee) in the Henry reaction as well as the ee in the carbonyl-ene reaction was performed on an Agilent 1200 series with a diode array detector.

Gas chromatography (GC) for the analysis of the HKR experiments was performed on a Shimadzu GC 17-A, equipped with an FID detector and a Chiraldex  $\gamma$ -TA column (80 °C, isothermal).

## 2 Preparation

### 2.1 Small Molecule Catalysts



Scheme S1: Synthesis route to small molecule complexes **1**, **3**, and **5**.

**Co-salen (1)** [(1*R*,2*R*)-(-)-1,2-cyclohexanediamino-*N,N'*-bis(3,5-di-*t*-butylsalicylidene)cobalt(II)] was purchased from Strem Chemicals Inc. or prepared according to the literature.<sup>1,2</sup> The corresponding Co<sup>III</sup>-species was obtained via aerobic oxidation of Co<sup>II</sup>-salen in the presence of acetic acid.<sup>2,3</sup>

**Co-salan (3)** The Schiff-base (Jacobsen's salen ligand, Strem Chemicals Inc.) was reduced to the corresponding amine ligand (**6**) following a literature procedure.<sup>4</sup> The metalation was performed at room temperature in an atmosphere of nitrogen in the glove box. A solution of cobalt(II) acetate tetrahydrate (2 eq. against salen) in methanol (1.5 mL) was added to a solution of the salen ligand (**6**, 110 mg, 0.2 mmol) in dichloromethane (3 mL). After stirring overnight, the solvents were removed *in vacuo*. The residue was redissolved in dichloromethane (2.5 mL) and insoluble excess cobalt acetate was filtered off using a syringe filter. The filtrate was concentrated under reduced pressure and a light red solid was obtained (118 mg).

Aerobic oxidation, as described for the oxidation of the salen analogue, was used to obtain Co<sup>III</sup>-salan as a brown solid.

HRMS (ESI):  $m/z$  calculated for C<sub>36</sub>H<sub>56</sub>CoN<sub>2</sub>O<sub>2</sub> ([M]<sup>+</sup>) = 607.3668; found = 607.3690 (+3.6 ppm).

ICP-MS: calculated weight per cent of Co = 9.70 %; found = 8.30 %.

FT-IR (ATR, neat),  $\nu$  = 3282, 1478, 1662, 1361, 1299, 1236 cm<sup>-1</sup>.

UV-vis (CH<sub>2</sub>Cl<sub>2</sub>),  $\lambda$  = 277, 226 nm.

**Co-Me-salan (5)** The methylated salan ligand was obtained according to the literature.<sup>4</sup> Cobalt metalation was performed in the glove box as described for compound **3**. A solution of cobalt(II) acetate tetrahydrate (2 eq. against Me-salan) in methanol (1.5 mL) was added to a solution of the Me-salan ligand (**7**, 134 mg, 0.23 mmol) in dichloromethane (3 mL). After stirring overnight, the solvents were removed *in vacuo*. The residue was redissolved in dichloromethane (2.5 mL) and insoluble excess cobalt acetate was filtered off using a syringe filter. The filtrate was concentrated under reduced pressure and a light red solid was obtained (137 mg).

Aerobic oxidation, as described for the oxidation of the salen and salan analogues, was used to obtain Co<sup>III</sup>-Me-salan as a brown solid.

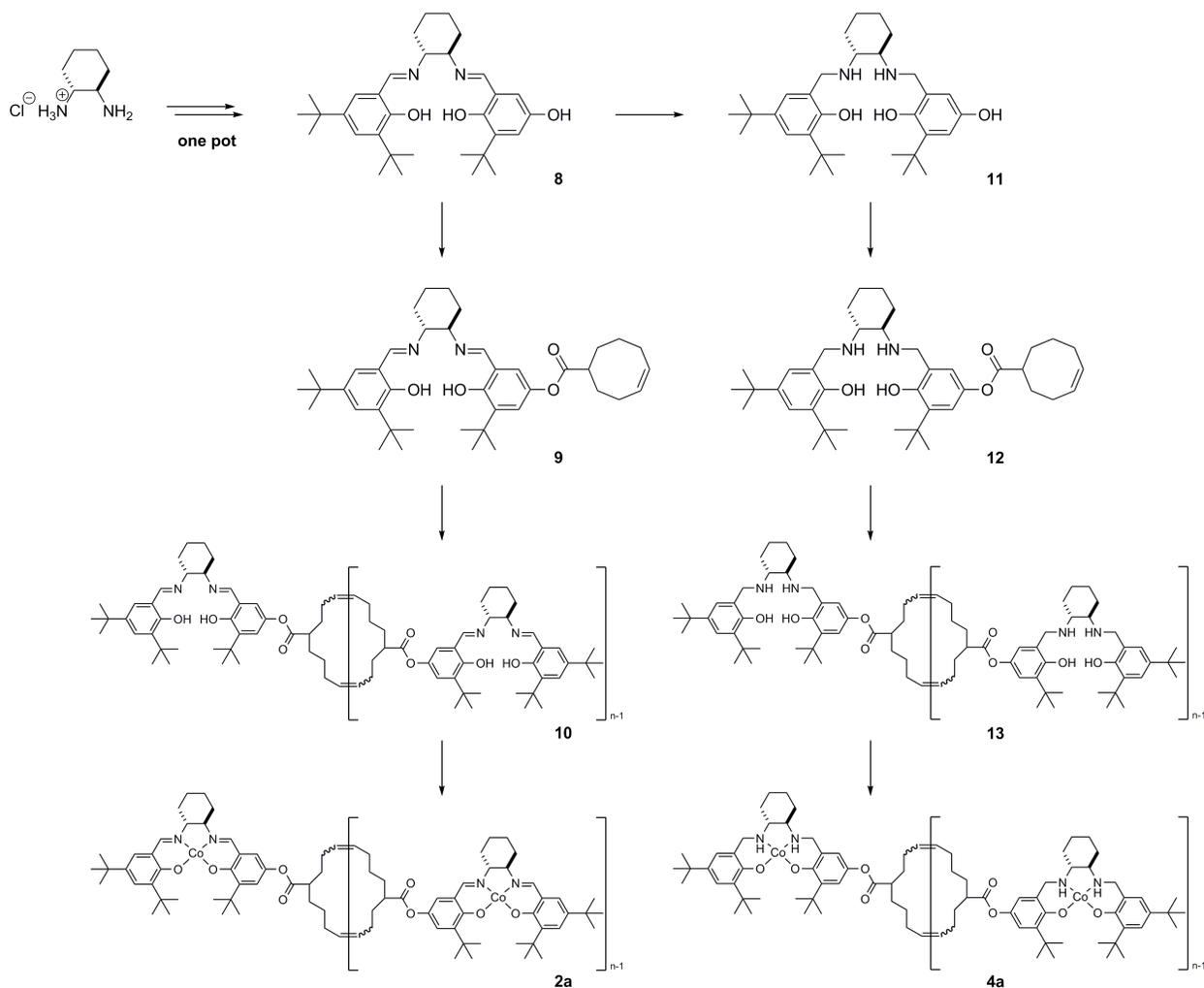
HRMS (ESI): m/z calculated for C<sub>38</sub>H<sub>60</sub>CoN<sub>2</sub>O<sub>2</sub> ([M]<sup>+</sup>) = 635.39863; found = 635.4006 (+3.1 ppm).

ICP-MS: calculated weight per cent of Co = 9.27 %; found = 3.32 %.

FT-IR (ATR, neat),  $\nu$  = 1684, 1480, 1360, 1234 cm<sup>-1</sup>.

UV-vis (CH<sub>2</sub>Cl<sub>2</sub>),  $\lambda$  = 287, 226 nm.

## 2.2 Oligomeric Catalysts



Scheme S2: Synthetic route to oligomeric complexes **2a** and **4a**.

Compounds **8**, **9**, **10**, and **2** were prepared following previously reported protocols.<sup>5,6</sup>

**Salan-OH (11)** Compound **8** (800 mg, 1.58 mmol) was dissolved in a mixture of methanol and dichloromethane (2:1, 60 mL). Sodium borohydride (477 mg, 12.6 mmol) was added in two portions over two hours, and the reaction mixture was stirred for 13 hours at room temperature. After removal of the solvents under reduced pressure, the residue was redissolved in dichloromethane; the solution was then washed with water and brine, and dried with magnesium sulfate. Recrystallization from hexane yielded the product as a light red solid in 43 % yield (350 mg).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  = 7.22 (d, 1H, <sup>4</sup>J = 2.37 Hz, CH), 6.87 (d, 1H, <sup>4</sup>J = 2.32 Hz, CH), 6.69 (d, 1H, <sup>4</sup>J = 2.99 Hz, CH), 6.38 (d, 1H, <sup>4</sup>J = 2.96 Hz, CH), 4.07-3.85 (m, 4H, CH<sub>2</sub>-N), 2.45-2.41 (m, 2H, CH-N), 2.21-2.12 (m, 2H, CH<sub>2</sub>), 1.70 (br s, 2H, CH<sub>2</sub>), 1.39 (s, 9H, CH<sub>3</sub>), 1.34 (s, 9H, CH<sub>3</sub>), 1.29 (s, 9H, CH<sub>3</sub>), 1.26-1.15 (m, 4H, CH<sub>2</sub>).

$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ ),  $\delta$  = 154.3 ( $\text{C}_{\text{Ar}}$ ), 150.6 ( $\text{C}_{\text{Ar}}$ ), 147.3 ( $\text{C}_{\text{Ar}}$ ), 140.7 ( $\text{C}_{\text{Ar}}$ ), 138.2 ( $\text{C}_{\text{Ar}}$ ), 136.0 ( $\text{C}_{\text{Ar}}$ ), 123.9 ( $\text{C}_{\text{Ar}}$ ), 123.1 ( $\text{C}_{\text{ArH}}$ ), 123.0 ( $\text{C}_{\text{ArH}}$ ), 122.3 ( $\text{C}_{\text{Ar}}$ ), 113.3 ( $\text{C}_{\text{ArH}}$ ), 112.9 ( $\text{C}_{\text{ArH}}$ ), 60.0 (CH-N), 59.9 (CH-N), 50.7 ( $\text{CH}_2\text{-N}$ ), 50.4 ( $\text{CH}_2\text{-N}$ ), 34.9 (2C,  $\text{C}_{\text{quart}}$ ), 34.7 ( $\text{CH}_2$ ), 34.1 ( $\text{C}_{\text{quart}}$ ), 31.7 (3C,  $\text{CH}_3$ ), 30.8 ( $\text{CH}_2$ ), 29.6 (3C,  $\text{CH}_3$ ), 29.4 (3C,  $\text{CH}_3$ ), 24.2 (2C,  $\text{CH}_2$ ). HRMS (ESI):  $m/z$  calculated for  $\text{C}_{32}\text{H}_{50}\text{N}_2\text{O}_3\text{Na}$  ( $[\text{M}+\text{Na}]^+$ ) = 533.371365; found 533.371015 (-0.65 ppm). CHNX: calculated for  $\text{C}_{32}\text{H}_{50}\text{N}_2\text{O}_3$  = C, 72.25; H, 9.87; N, 5.48; found = C, 75.28; H, 9.35; N, 5.45.

**Salan cyclooctene ester (12)** A 100 mL flask equipped with a reflux condenser was charged with compound **11** (300 mg, 0.58 mmol), dicyclohexyl carbodiimide (DCC, 120 mg, 0.58 mmol), and 4-dimethylaminopyridine (DMAP, 18 mg, 0.145 mmol) and purged with nitrogen. Dichloromethane (10 mL) was added, followed by the dropwise addition of a solution of cyclooct-4-enecarboxylic acid (90 mg, 0.58 mmol) in dichloromethane (10 mL). The reaction mixture was stirred and heated at reflux for 19 hours. Precipitates that had formed were separated by filtration and washed with dichloromethane. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (eluent: DCM/MeOH – 95/5) to yield the product as a pale purple solid (235 mg, 36%).

$^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta$  = 7.23 (d, 1H,  $^4J$  = 2.37 Hz, CH), 6.88 (d, 1H,  $^4J$  = 2.35 Hz, CH), 6.83 (d, 1H,  $^4J$  = 2.82 Hz, CH), 6.60 (d, 1H,  $^4J$  = 2.94 Hz, CH), 5.78-5.66 (m, 2H,  $\text{CH}=\text{CH}_{\text{cyclooct}}$ ), 4.08-3.89 (m, 4H,  $\text{CH}_2\text{-N}$ ), 2.71-2.66 (m, 1H,  $\text{H}_{\text{cyclooct}}$ ), 2.52-2.38 (br m, 3H,  $\text{CH-N}/\text{H}_{\text{cyclooct}}$ ), 2.23-2.18 (m, 6H,  $\text{H}_{\text{DACH}}/\text{H}_{\text{cyclooct}}$ ), 1.81-1.78 (m, 2H,  $\text{H}_{\text{cyclooct}}$ ), 1.71 (br s, 4H,  $\text{H}_{\text{DACH}}/\text{H}_{\text{cyclooct}}$ ), 1.39 (s, 9H,  $\text{CH}_3$ ), 1.35 (s, 9H,  $\text{CH}_3$ ), 1.29 (s, 9H,  $\text{CH}_3$ ), 1.27-1.15 (m, 5H,  $\text{H}_{\text{DACH}}/\text{H}_{\text{cyclooct}}$ ).

$^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ),  $\delta$  = 176.6 ( $\text{CO}_2\text{-C}$ ), 154.4 ( $\text{C}_{\text{Ar}}$ ), 154.2 ( $\text{C}_{\text{Ar}}$ ), 142.4 ( $\text{C}_{\text{Ar}}$ ), 140.7 ( $\text{C}_{\text{Ar}}$ ), 137.9 ( $\text{C}_{\text{Ar}}$ ), 136.0 ( $\text{C}_{\text{Ar}}$ ), 130.6 ( $\text{C}_{\text{cyclooctH}}$ ), 129.5 ( $\text{C}_{\text{cyclooctH}}$ ), 123.4 ( $\text{C}_{\text{Ar}}$ ), 123.2 ( $\text{C}_{\text{ArH}}$ ), 123.1 ( $\text{C}_{\text{ArH}}$ ), 122.2 ( $\text{C}_{\text{Ar}}$ ), 118.9 ( $\text{C}_{\text{ArH}}$ ), 118.8 ( $\text{C}_{\text{ArH}}$ ), 59.9 (CH-N), 59.7 (CH-N), 50.6 ( $\text{CH}_2\text{-N}$ ), 50.3 ( $\text{CH}_2\text{-N}$ ), 43.3 (CH- $\text{CO}_2$ ), 34.8 (2C,  $\text{C}_{\text{quart}}$ ), 34.7 ( $\text{CH}_2\text{,DACH}$ ), 34.1 ( $\text{C}_{\text{quart}}$ ), 31.7 (3C,  $\text{CH}_3$ ), 31.6 ( $\text{CH}_2\text{,cyclooct}$ ), 31.6 ( $\text{CH}_2\text{,cyclooct}$ ), 30.7 ( $\text{CH}_2\text{,DACH}$ ), 29.6 (3C,  $\text{CH}_3$ ), 29.5 ( $\text{CH}_2\text{,cyclooct}$ ), 29.5 ( $\text{CH}_2\text{,cyclooct}$ ), 29.3 (3C,  $\text{CH}_3$ ), 27.8 ( $\text{CH}_2\text{,cyclooct}$ ), 25.9 ( $\text{CH}_2\text{,cyclooct}$ ), 24.1 ( $\text{CH}_2\text{,DACH}$ ), 24.1 ( $\text{CH}_2\text{,DACH}$ ).

HRMS (ESI):  $m/z$  calculated for  $\text{C}_{41}\text{H}_{63}\text{N}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ) = 647.47823; found 647.480337 (+3.2 ppm).

CHNX: calculated for  $\text{C}_{41}\text{H}_{62}\text{N}_2\text{O}_4$  = C, 76.12; H, 9.66; N, 4.33; found = C, 75.91; H, 9.91; N, 4.25.

**Oligomeric salan ligand (13)** Compound **12** (200 mg, 3.1 mmol) was dissolved in degassed dichloromethane (3 mL) under nitrogen. A solution of Grubbs' third generation catalyst (11 mg, 0.012 mmol) in dichloromethane (0.5 mL) was added. The mixture was stirred for 30 minutes at room temperature and then quenched by the addition of ethyl vinyl ether (200 mL). After concentration under reduced pressure, the residue was purified by flash column chromatography on silica gel (eluent: diethyl ether/hexanes – 5/5) to yield the product as a pale white solid, which was then redissolved in benzene and subjected to lyophilization (repeated twice). The product was obtained with residual traces of hexanes (148 mg, 74 %).

$^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta$  = 7.22 (s, 1H,  $\text{C}_{\text{ArH}}$ ), 6.88 (s, 1H,  $\text{C}_{\text{ArH}}$ ), 6.82 (s, 1H,  $\text{C}_{\text{ArH}}$ ), 6.61 (s, 1H,  $\text{C}_{\text{ArH}}$ ), 5.45 (br s, 2H,  $\text{CH}=\text{CH}_{\text{cyclooct}}$ ), 4.15-3.78 (br m, 4H,  $\text{CH}_2\text{-N}$ ), 2.57 (br s, 1H,  $\text{H}_{\text{cyclooct}}$ ), 2.46 (br s, 2H,  $\text{CH-N}$ ) 2.35-1.94 (br m, 6H,  $\text{H}_{\text{DACH}}/\text{H}_{\text{cyclooct}}$ ), 1.83 (br s, 1H,  $\text{H}_{\text{cyclooct}}$ ), 1.75-1.55 (br m, 6H,  $\text{H}_{\text{DACH}}/\text{H}_{\text{cyclooct}}$ ), 1.38 (s, 9H,  $\text{CH}_3$ ), 1.35 (s, 9H,  $\text{CH}_3$ ), 1.28 (s, 9H,  $\text{CH}_3$ ), 1.25-1.15 (m, 5H,  $\text{H}_{\text{DACH}}/\text{H}_{\text{cyclooct}}$ ).

$^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ),  $\delta$  = 175.2, 154.5, 154.2, 142.3, 140.9, 138.1, 136.2, 130.7-129.9 (m, overlapping signals), 123.4-123.3 (br, overlapping signals), 122.2, 118.9 (br, overlapping signals), 59.9, 59.7, 50.3 (br), 44.1 (br), 34.9, 34.7, 34.2, 31.7, 31.6, 30.6 (br), 29.7, 29.5, 29.3, 27.9-26.2 (overlapping signals), 24.1.

CHNX: calculated for  $\text{C}_{41}\text{H}_{62}\text{N}_2\text{O}_4$  = C, 76.12; H, 9.66; N, 4.33; found = C, 73.27; H, 9.67; N, 4.03.

FT-IR (ATR, neat),  $\nu$  = 3312, 1746, 1603, 1435, 1360, 1234, 1142, 968  $\text{cm}^{-1}$ .

UV-vis ( $\text{CH}_2\text{Cl}_2$ ),  $\lambda$  = 331, 267 nm.

**Oligomeric Co-salan (4)** In the glove box, a solution of cobalt(II) acetate tetrahydrate (1.5 eq. against salan) in methanol (1.5 mL) was added to a solution of the oligomeric salan ligand (**13**, 130 mg, 0.2 mmol) in dichloromethane. After stirring for 20 hours, the solvents were removed *in vacuo*. The residue was redissolved in dichloromethane (2.5 mL), and insoluble excess cobalt acetate was filtered off using a syringe filter. The filtrate was concentrated under reduced pressure and a light brownish solid was obtained (135 mg).

Aerobic oxidation, as described for the oxidation of the salen and (Me)-salan analogues, was used to obtain **oligomeric Co<sup>III</sup>-salan** as a brown solid.

MALDI-MS: m/z calculated for  $(C_{41}H_{61}CoN_2O_4)_n$  ( $[M_n+1]^+$ ); found 1408.3 ( $[M_2+1]^+$ ), 2112.8 ( $[M_3+1]^+$ ).

ICP-MS: calculated weight per cent of Co = 8.37 %; found = 4.56 %.

FT-IR (ATR, neat),  $\nu$  = 3321, 3280, 1748, 1659, 1625, 1440, 1361, 1232, 1141  $cm^{-1}$ .

UV-vis ( $CH_2Cl_2$ ),  $\lambda$  = 356, 275, 225 nm.

### 3 Spectra

#### 3.1 NMR

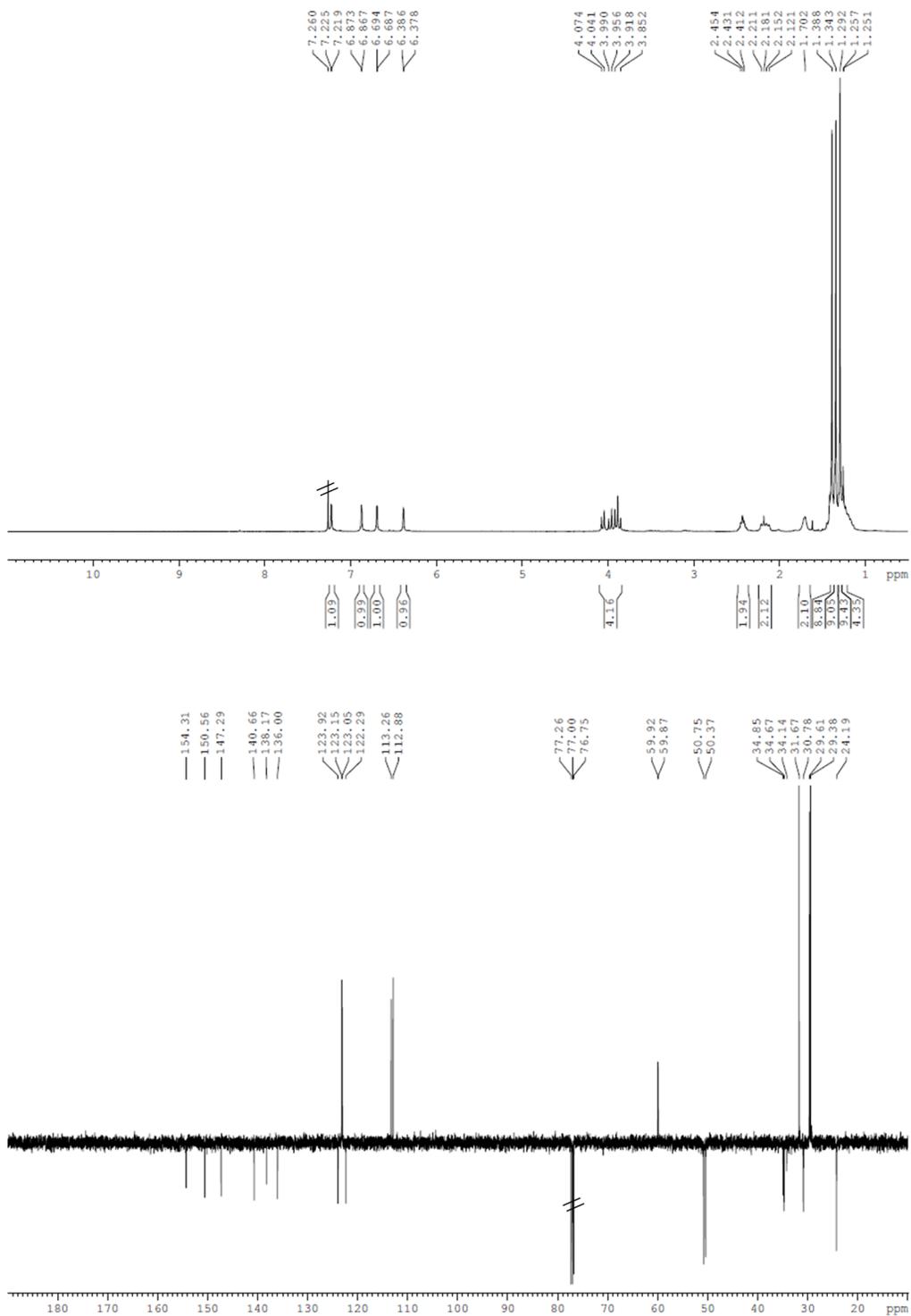


Figure S1:  $^1\text{H}$  and  $^{13}\text{C}$ -NMR (APT) spectra of salan-OH (11).

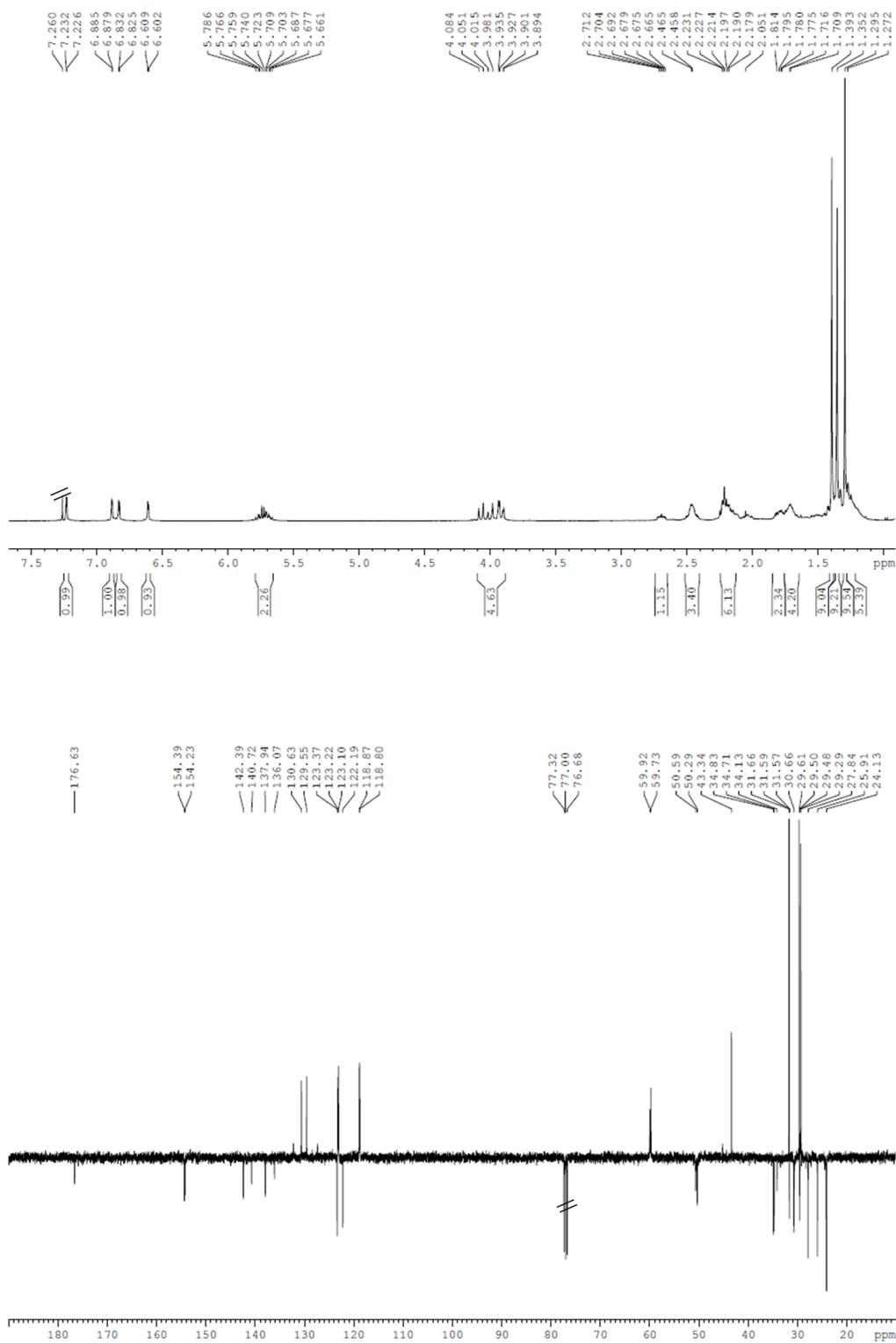


Figure S2: <sup>1</sup>H and <sup>13</sup>C-NMR (APT) spectra of salan cyclooctene ester (**12**).

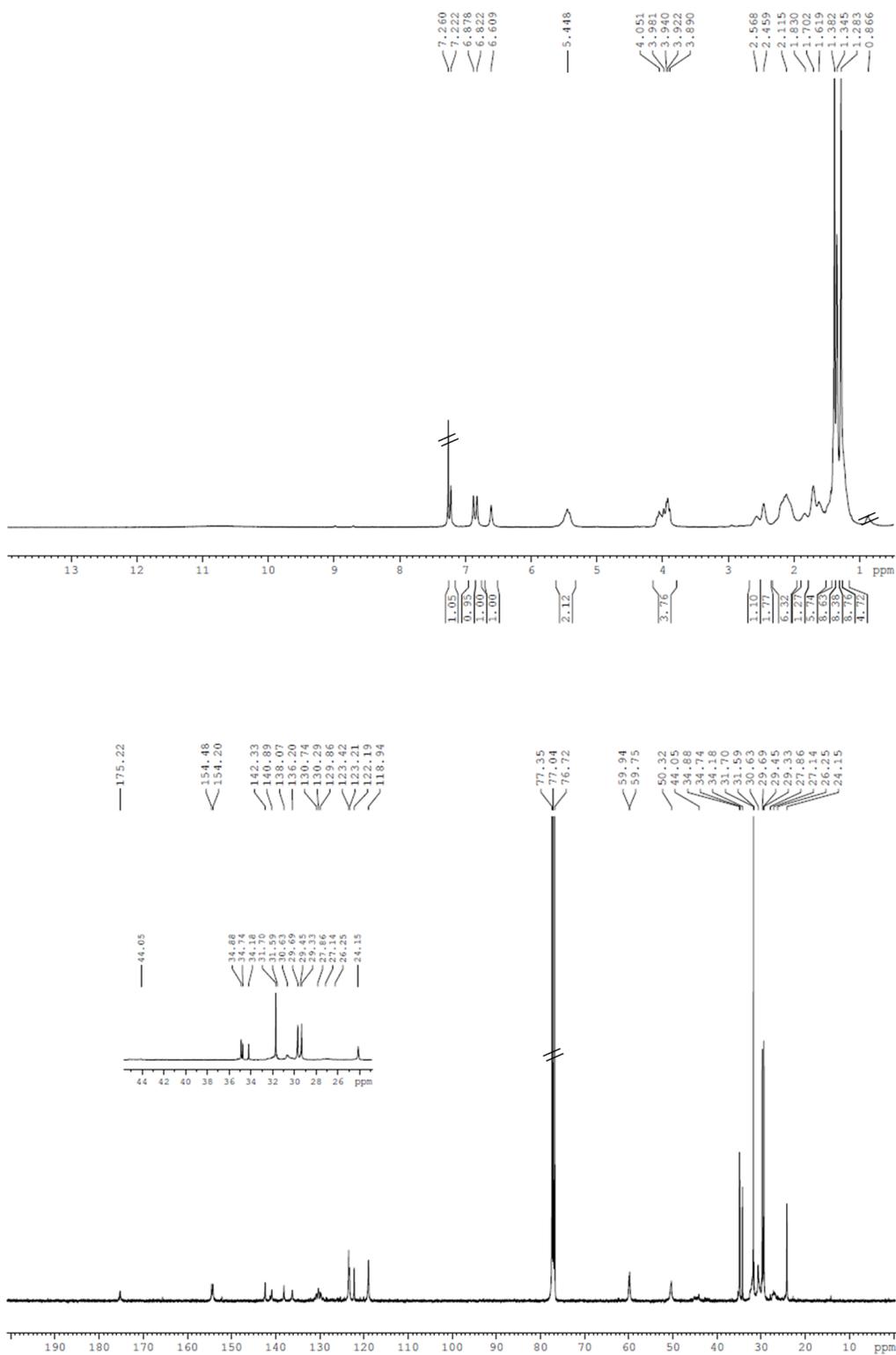


Figure S3:  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectra of oligomeric salan ligand (**13**).

## 3.2 MS

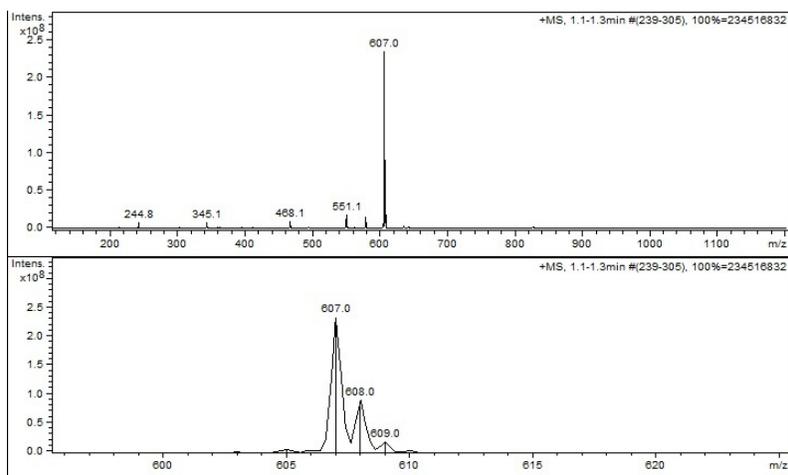


Figure S4: LCMS spectrum of Co-salan (**3**).

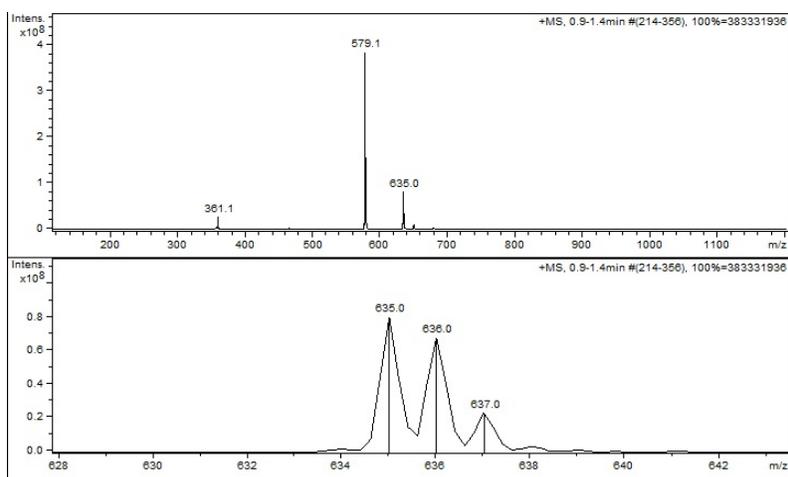


Figure S5: LCMS spectrum of Co-Me-salan (**5**).

Note: The signal at 579.1 corresponds to the Me-salan ligand (**8**,  $[M+1]^+$ ).

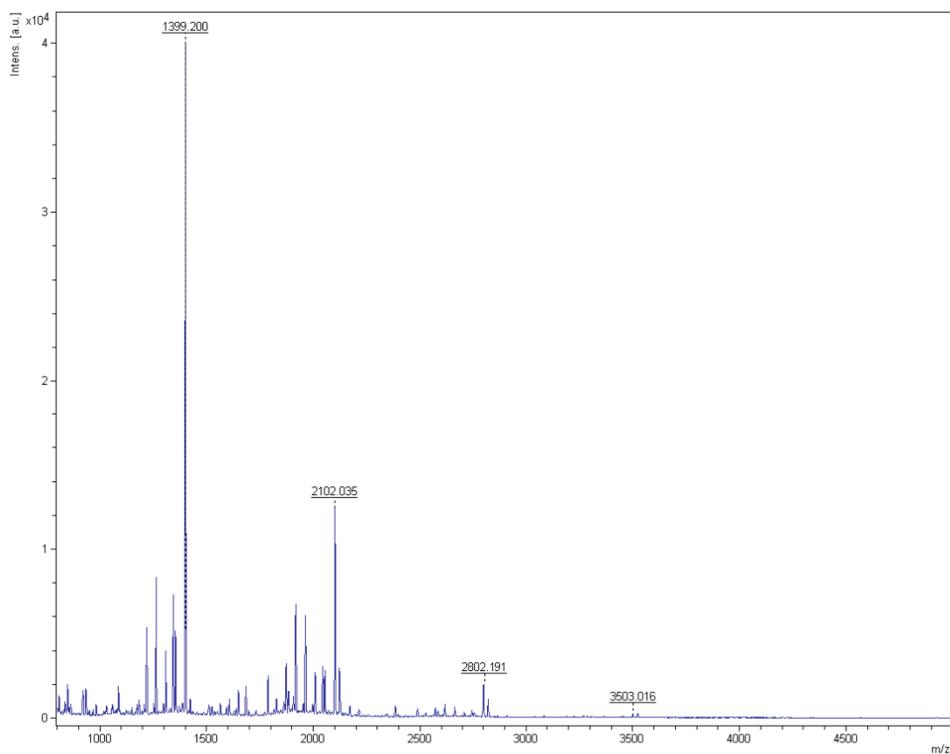


Figure S6: MALDI-TOF spectrum of macrocyclic oligomeric Co-salen complex (2).

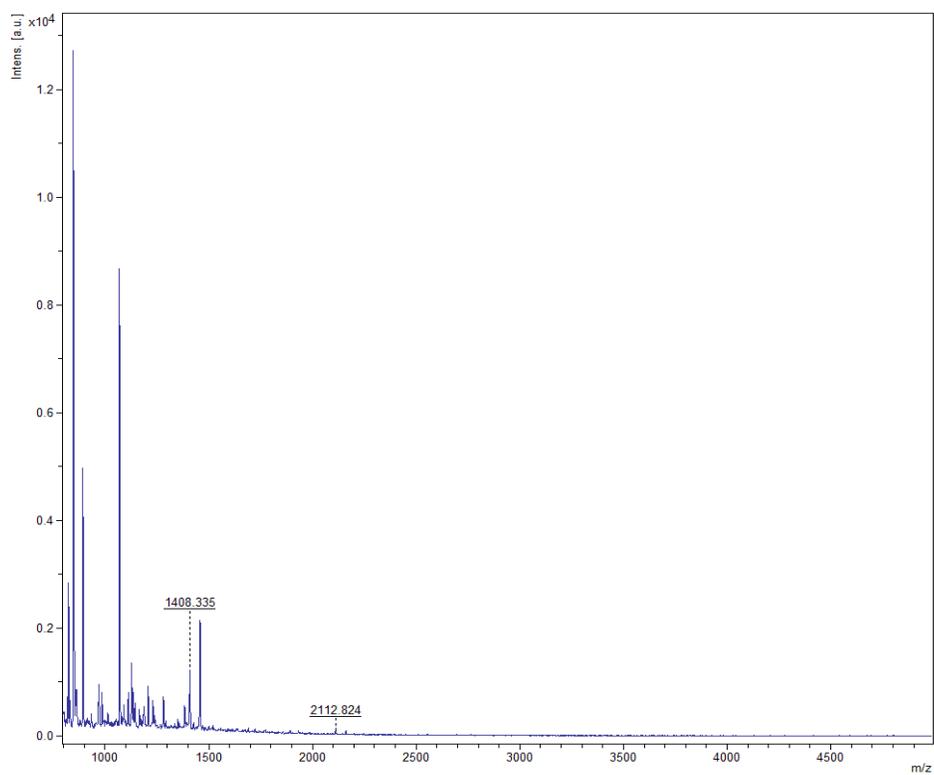


Figure S7: MALDI-TOF spectrum of macrocyclic oligomeric Co-salen complex (4).

### 3.3 GPC

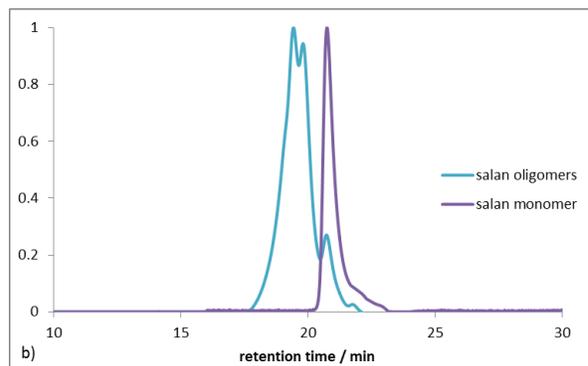
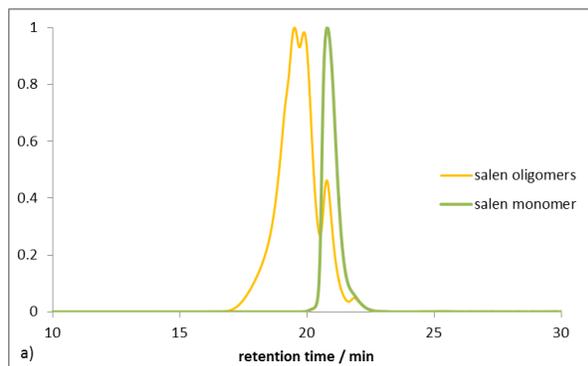


Figure S8: GPC traces of (a) salen oligomers (**10**) and (b) salan oligomers (**13**).

### 3.4 UV-vis

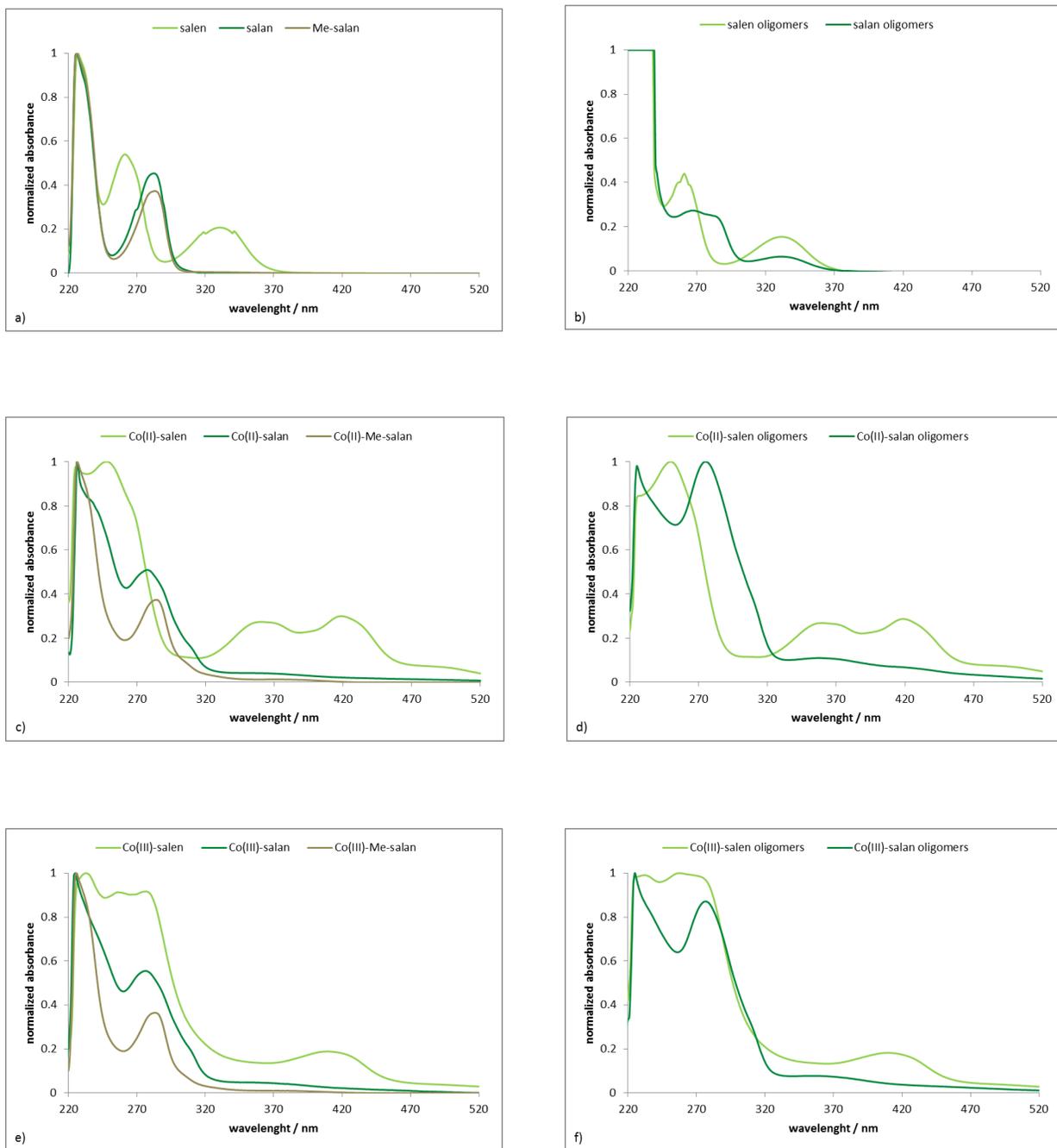


Figure S9: Normalized UV-vis spectra of salen and salan ligands and corresponding Co-complexes.

### 3.5 FT-IR

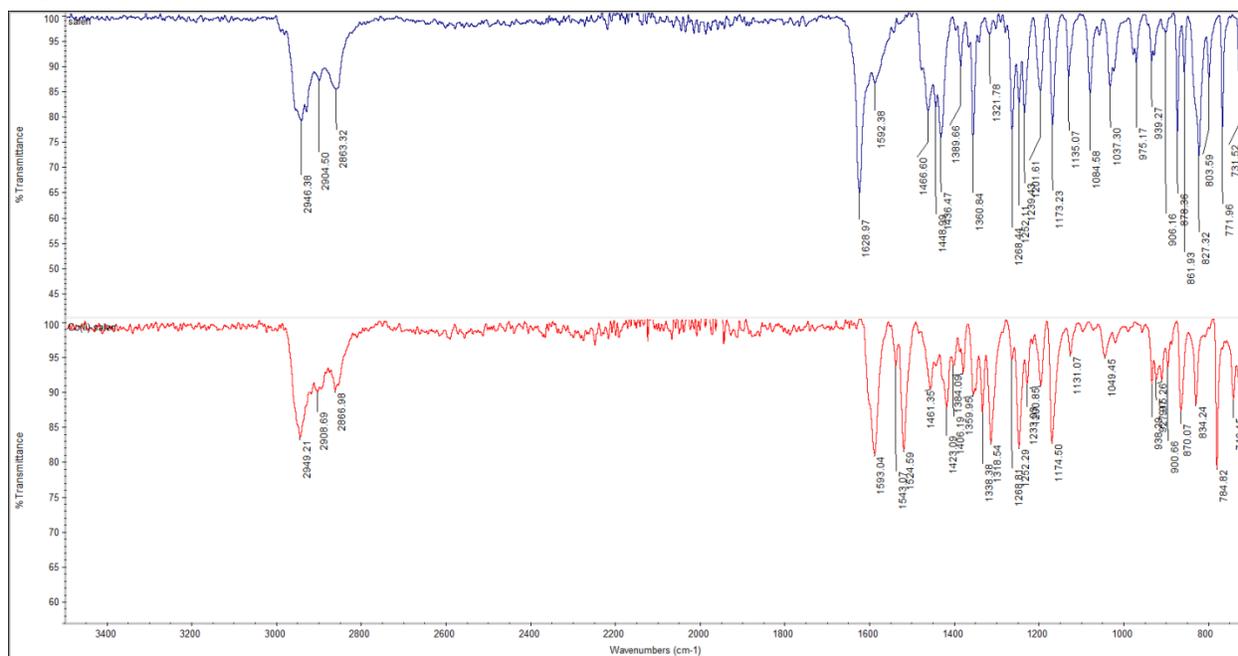


Figure S10: FT-IR spectra of salen ligand (top) vs. Co-salen complex (bottom).

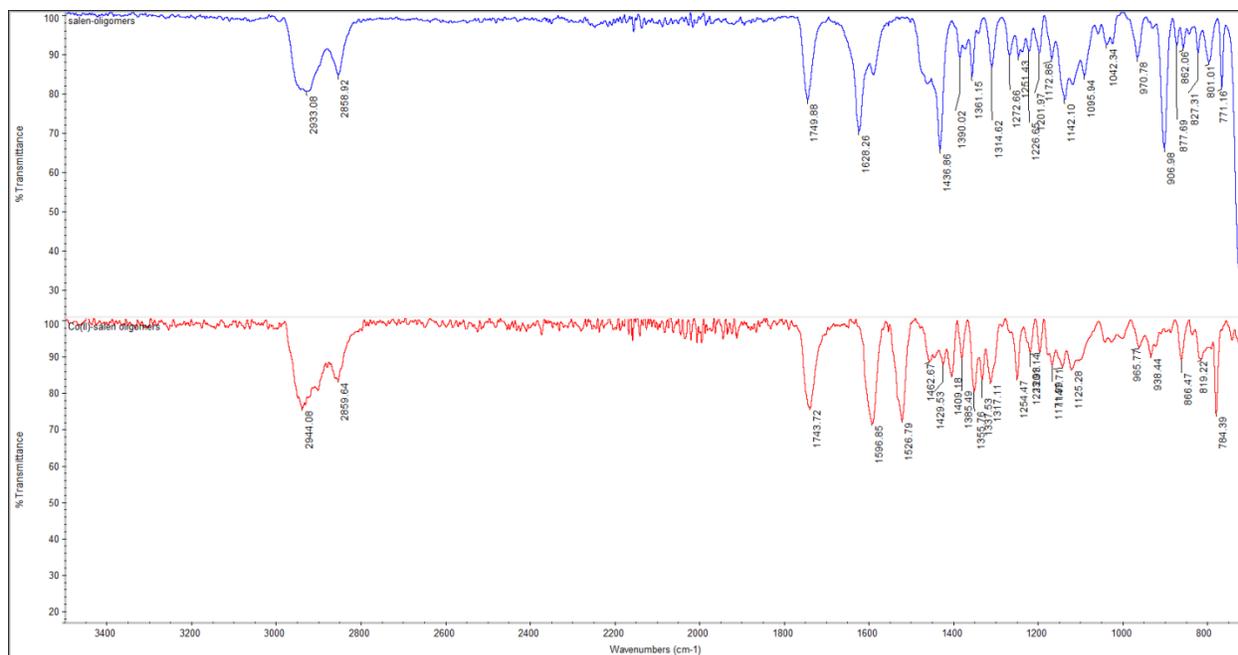


Figure S11: FT-IR spectra of oligomeric salen (top) vs. Co-salen oligomers (bottom).

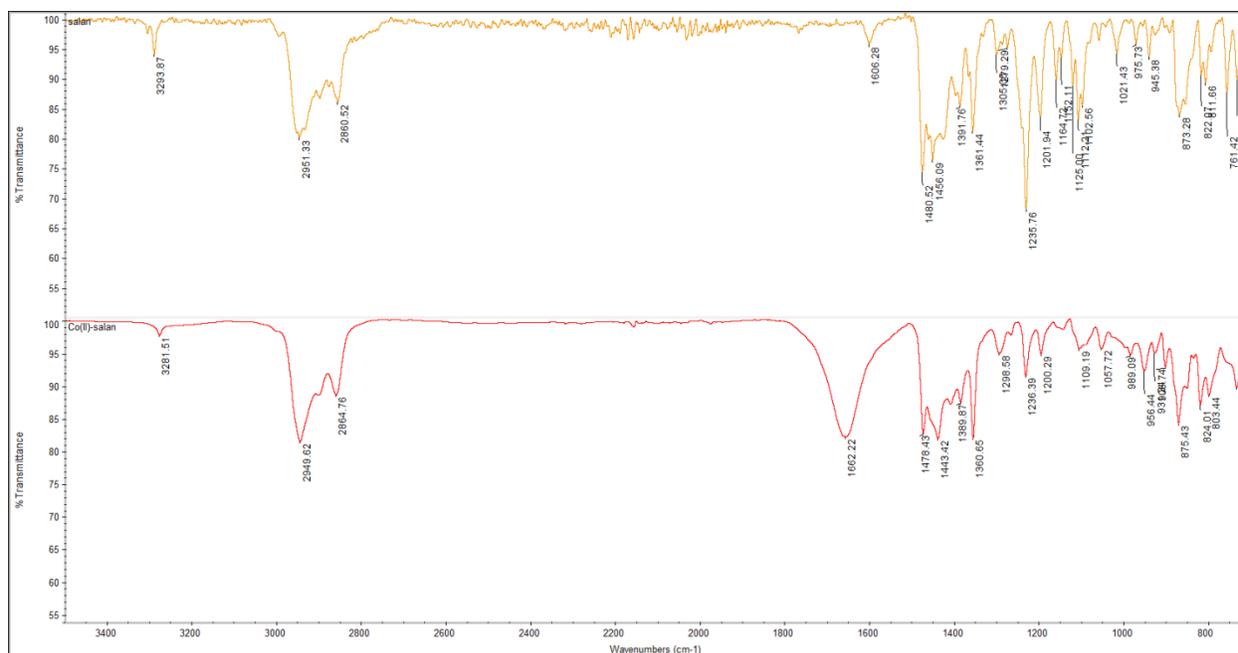


Figure S12: FT-IR spectra of salan ligand (top) vs. Co-salan complex (bottom).

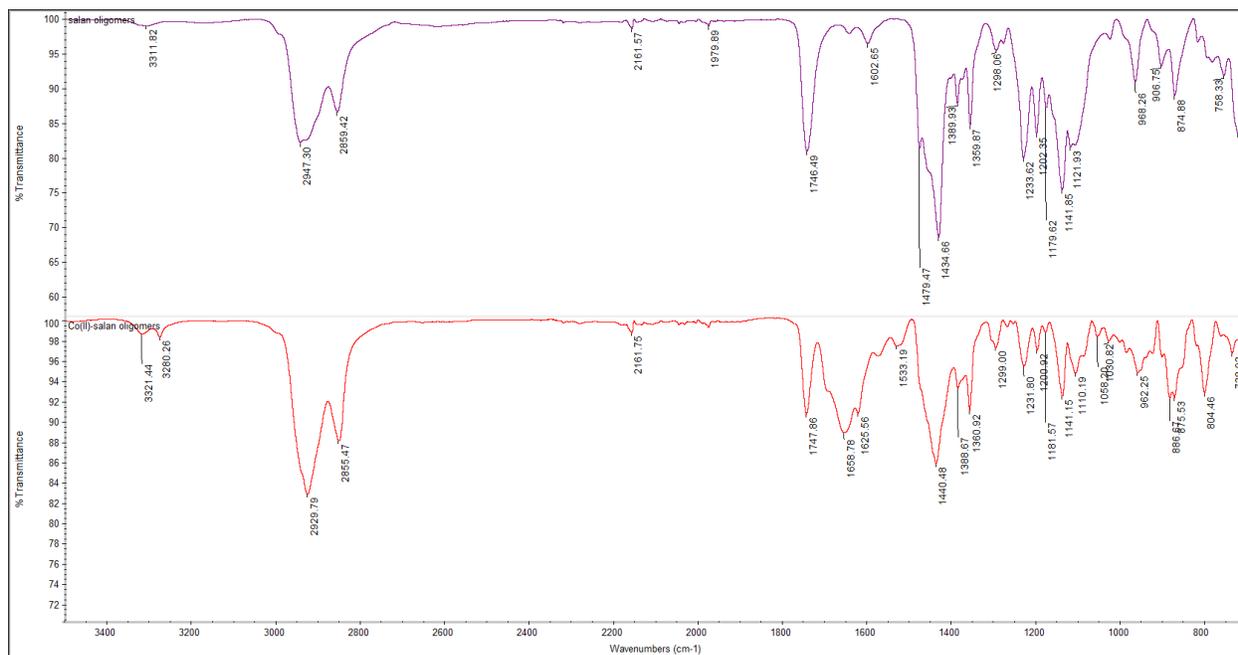


Figure S13: FT-IR spectra of oligomeric salan (top) vs. Co-salan oligomers (bottom).

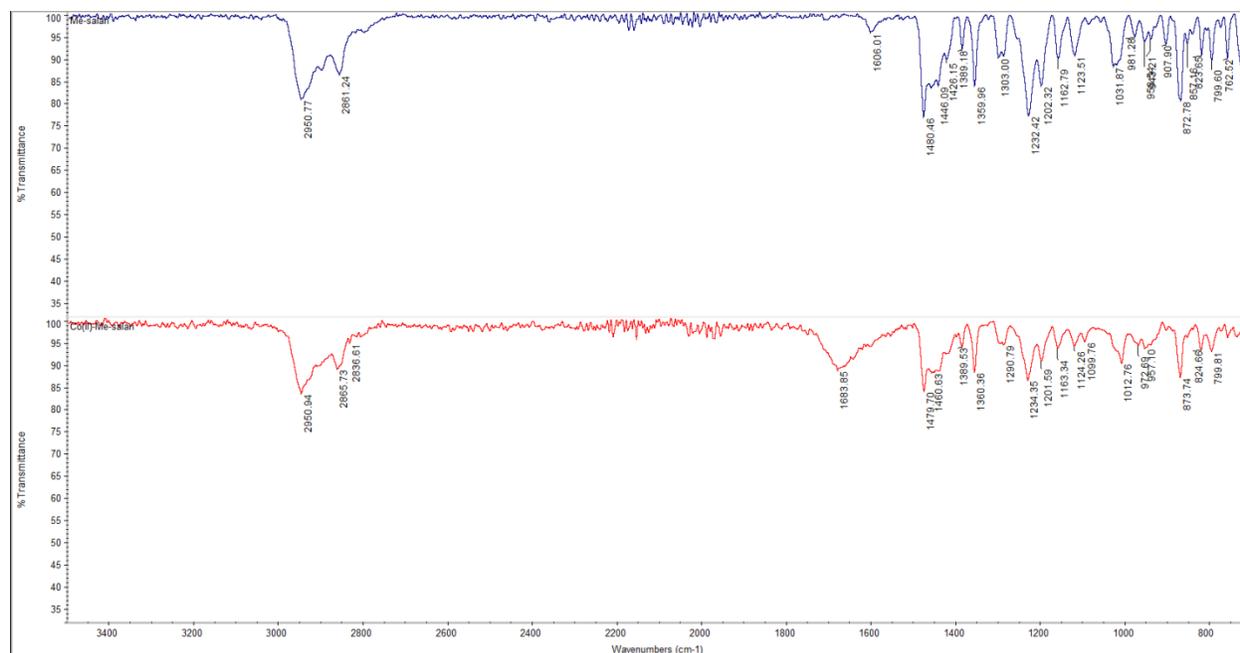
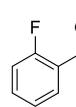


Figure S14: FT-IR spectra of Me-salan ligand (top) vs. Co-Me-salan complex (bottom).

## 4 Catalyst Testing

### 4.1 Standard Procedure for the Henry Reaction

Exemplary procedure for the synthesis of 1-(2-fluorophenyl)-2-nitroethanol. In an atmosphere of nitrogen, 2-fluorobenzaldehyde (105.3  $\mu\text{L}$ , 1 mmol), Co<sup>II</sup>-salen (3.0 mg, 0.5 mol% against aldehyde), nitromethane (537  $\mu\text{L}$ , 10 mmol, degassed), and mesitylene as an internal standard (139.1  $\mu\text{L}$ , 1 mmol) were dissolved in dichloromethane (3.0 mL, degassed). After stirring for 15 min at room temperature, an aliquot (20  $\mu\text{L}$ ) was taken for calibration and subjected to purification using a silica plug (eluent: hexane/2-propanol – 95/5). The reaction was started by the addition of DIPEA (85  $\mu\text{L}$ , 0.5 mmol) and the mixture was stirred for eight hours. Aliquots were taken hourly, and after running through a silica plug, the samples were stored over dry ice and protected from light prior to HPLC analysis from which the conversion and enantiomeric excess were calculated (HPLC analysis: Daicel Chiralpak OD-H column, 8 % isopropanol in hexane at 0.6 mL/min flow rate, detection at 230 nm). For the isolation of the product, the reaction mixture was concentrated under reduced pressure and subjected to column chromatography (eluent: hexane/ethyl acetate – 7/3) to yield the nitroaldol compound as a clear, brown oil (NMR analysis in agreement with findings by Yamada *et al.*<sup>7</sup>). The absolute configuration of the major isomer was determined to be (*S*) using *R,R*-Co-salen and (*R*) using *R,R*-Co-salan by comparison of the retention time with literature data.<sup>7-9</sup>

 <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  = 7.65-7.55 (m, C<sub>Ar</sub>H), 7.42-30 (m, C<sub>Ar</sub>H), 7.30-7.20 (m, C<sub>Ar</sub>H), 7.15-7.01 (m, C<sub>Ar</sub>H), 5.89-5.62 (m, 1H, CH-O), 4.75-4.49 (m, 2H, CH<sub>2</sub>), 3.18-2.95 (br s, OH).  
<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  = 159.4 (d,  $J_{CF}$  = 246.4 Hz, C<sub>Ar</sub>F), 130.5 (d,  $J_{CF}$  = 8.4 Hz, C<sub>Ar</sub>H), 127.6 (d,  $J_{CF}$  = 3.6 Hz, C<sub>Ar</sub>H), 125.2 (d,  $J_{CF}$  = 13.3 Hz, C<sub>Ar</sub>C), 124.8 (d,  $J_{CF}$  = 3.4 Hz, C<sub>Ar</sub>H), 115.6 (d,  $J_{CF}$  = 21.1 Hz, C<sub>Ar</sub>H), 79.7 (d,  $J_{CF}$  = 1.0 Hz, CH<sub>2</sub>), 65.5 (d,  $J_{CF}$  = 2.7 Hz, CH-OH).

GCMS (EI):  $m/z$  calculated for C<sub>8</sub>H<sub>8</sub>FNO<sub>3</sub> ([M]<sup>+</sup>) = 185.05; found 168.0 ([M-OH]<sup>+</sup>), 138.1 ([M-HNO<sub>2</sub>]<sup>+</sup>), 125.1 ([M-CH<sub>2</sub>NO<sub>2</sub>]<sup>+</sup>), 123.1 ([M-CH<sub>4</sub>NO<sub>2</sub>]<sup>+</sup>).

CHNX: calculated for C<sub>8</sub>H<sub>8</sub>FNO<sub>3</sub>, C 51.90, H 4.36, N 7.57, F 10.26; found C 51.97, H 4.42, N 7.57, F 10.48.

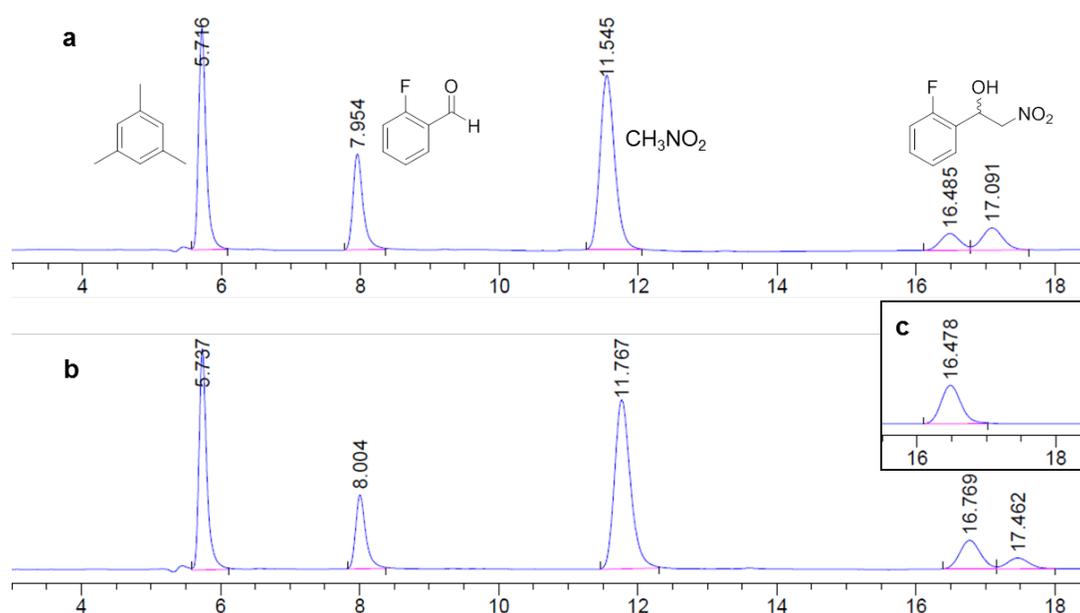
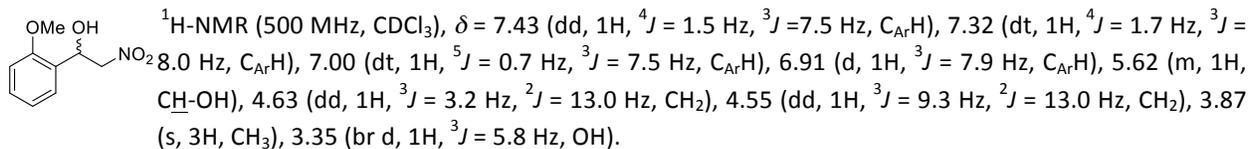


Figure S15: Exemplary chromatograms for the Co-salen catalyzed (a) and Co-salan catalyzed (b) Henry reaction of 2-fluorobenzaldehyde and nitromethane; (c) Co-salan catalyzed reaction under optimized conditions.

## 4.2 Substrate Screening for the Henry Reaction

### 1-(2-Methoxyphenyl)-2-nitroethanol (cf. reported data in the literature)<sup>7-9</sup>



<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>),  $\delta$  = 156.0, 129.8, 127.2, 126.1, 121.1, 110.6, 79.9, 67.8, 55.4.

The Enantiomeric excess was determined by HPLC using an OD-H column (92/8 – hexane/isopropanol, 0.6 mL/min), detection at 210 nm. The absolute configuration of the major isomer was determined to be (*S*) using *R,R*-Co-salen and (*R*) using *R,R*-Co-salan by comparison of the retention time with literature data.<sup>9</sup>

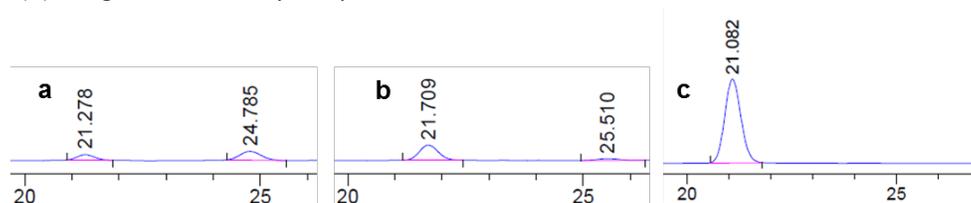
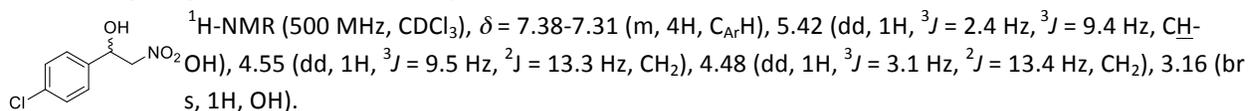


Figure S16: Exemplary chromatograms of 1-(2-methoxyphenyl)-2-nitroethanol formed in the Henry reaction; (a) Co-salen catalyzed, (b) Co-salan catalyzed, (c) Co-salan catalyzed under optimized conditions.

### 1-(4-Chlorophenyl)-2-nitroethanol (cf. reported data in the literature)<sup>7,8,10</sup>



<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>),  $\delta$  = 136.6, 134.8, 129.8, 129.2, 128.3, 127.4, 81.0, 70.3.

The Enantiomeric excess was determined by HPLC using an OD-H column (92/8 – hexane/isopropanol, 0.6 mL/min), detection at 230 nm. The absolute configuration of the major isomer was determined to be (*S*) using *R,R*-Co-salen and (*R*) using *R,R*-Co-salan by comparison of the retention time with literature data.<sup>9</sup>

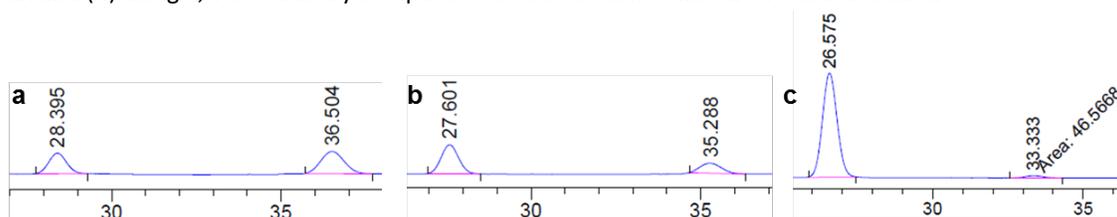
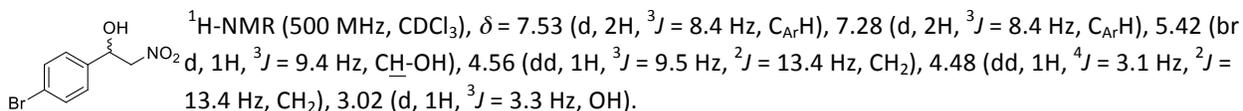


Figure S17: Exemplary chromatograms of 1-(4-chlorophenyl)-2-nitroethanol formed in the Henry reaction; (a) Co-salen catalyzed, (b) Co-salan catalyzed, (c) Co-salan catalyzed under optimized conditions.

### 1-(4-Bromophenyl)-2-nitroethanol (cf. reported data in the literature)<sup>9</sup>



<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>),  $\delta$  = 137.1, 132.2, 127.6, 122.9, 80.9, 70.4.

The Enantiomeric excess was determined by HPLC using an OD-H column (92/8 – hexane/isopropanol, 0.6 mL/min), detection at 230 nm. The absolute configuration of the major isomer was determined to be (*S*) using *R,R*-Co-salen and (*R*) using *R,R*-Co-salan by comparison of the retention time with literature data.<sup>9</sup>

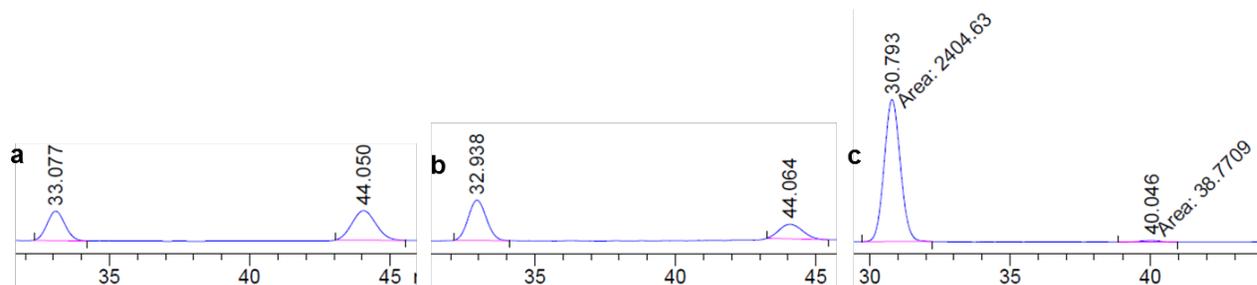


Figure S18: Exemplary chromatograms of 1-(4-bromophenyl)-2-nitroethanol formed in the Henry reaction; (a) Co-salen catalyzed, (b) Co-salan catalyzed, (c) Co-salan catalyzed under optimized conditions.

### 4.3 HKR

Exemplary procedure, following an adapted protocol previously established by our group.<sup>6</sup> The pre-oxidation of the Co<sup>II</sup>-species was conducted in an open 4 mL vial. Glacial acetic acid (5  $\mu$ L) was added to a solution of Co<sup>II</sup>-salen (**1a**, 1 mg, 0.0016 mmol, 0.5 mol% against epoxide) in dichloromethane (0.5 mL), and the mixture was stirred for 30 min. Solvent and excess acetic acid were then removed by rotary evaporation, followed by high vacuum treatment for 5 h. Co<sup>III</sup>-OAc-salen (**1b**) was obtained as a dark brown solid and dissolved in racemic epichlorohydrin (104.3  $\mu$ L, 0.33 mmol). Chlorobenzene was added as internal standard (0.5 eq.), and the reaction was started by addition of deionized water (67.6  $\mu$ L, 0.6 eq.). After the reaction was stirred at rt for 3 h, an aliquot (10  $\mu$ L) was taken, diluted in diethyl ether (1 mL), and passed through a plug of silica gel. After being thus prepared, the sample was subjected to GC analysis [ $t_{R,R-Co-salen}(S, \text{major}) = 6.9 \text{ min}$ ].

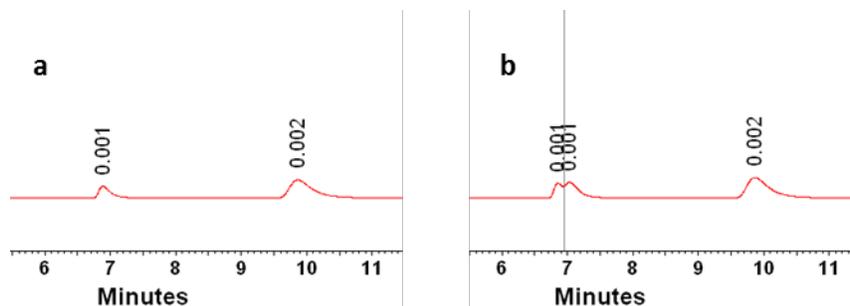


Figure S19: GC traces of epichlorohydrin after Co-salen catalyzed (a) and Co-salan catalyzed (b) HKR.

### 4.4 Carbonyl-ene Reaction

The synthesis of the Co<sup>III</sup>-salen hexafluoroantimonate complex followed the procedure by Rawal et al. and was used accordingly to prepare the Co-salan analogue.<sup>11</sup>

Exemplary procedure for carbonyl-ene reaction. A 4 mL screw-capped vial, equipped with a magnetic stir bar, was charged with the Co<sup>III</sup>-salen hexafluoroantimonate complex (0.01 mmol, 8.4 mg, 2 % loading). Ethyl glyoxylate (50

% in toluene, 1.5 mmol, 300  $\mu$ l) and  $\alpha$ -methyl styrene (0.5 mmol, 65  $\mu$ l) were added, and the reaction mixture was stirred at room temperature. After 20 hours of stirring, the mixture was directly loaded onto a silica column and eluted using a hexane/ethyl acetate (8:2) solution. The product was obtained as clear red/brown oil. The NMR spectroscopic analysis was in accordance with the data reported in the literature.<sup>11</sup>

CCOC(=O)[C@H](O)CC=Cc1ccccc1  
<sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>),  $\delta$  = 7.43-7.40 (m, 2H, C<sub>Ar</sub>H), 7.36-7.32 (m, 2H, C<sub>Ar</sub>H), 7.30-7.28 (m, 1H, C<sub>Ar</sub>H), 5.40 (d, 1H, <sup>4</sup>J = 1.1 Hz, C<sub>ene</sub>H<sub>2</sub>), 5.21 (d, 1H, <sup>4</sup>J = 1.0 Hz, C<sub>ene</sub>H<sub>2</sub>), 4.27 (dd, 1H, <sup>3</sup>J = 4.5 Hz, <sup>3</sup>J = 7.5 Hz, CH-OH), 4.14-4.00 (m, 2H, CH<sub>2</sub>-O), 3.06 (ddd, 1H, <sup>4</sup>J = 0.9 Hz, <sup>3</sup>J = 4.5 Hz, <sup>2</sup>J = 14.5 Hz, CH<sub>2</sub>-CHOH), 2.85 (ddd, 1H, <sup>4</sup>J = 0.6 Hz, <sup>3</sup>J = 7.6 Hz, <sup>2</sup>J = 15.1 Hz, CH<sub>2</sub>-CHOH), 1.23 (t, 3H, <sup>3</sup>J = 7.2 Hz, CH<sub>3</sub>).

<sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>),  $\delta$  = 174.5, 143.6, 140.3, 128.4, 127.7, 126.4, 116.3, 69.1, 61.4, 40.5, 14.1.

HPLC analysis (AD-H column): 1% isopropanol in hexane was used as the eluent at 0.7 mL/min flow rate, detection at 254 nm.

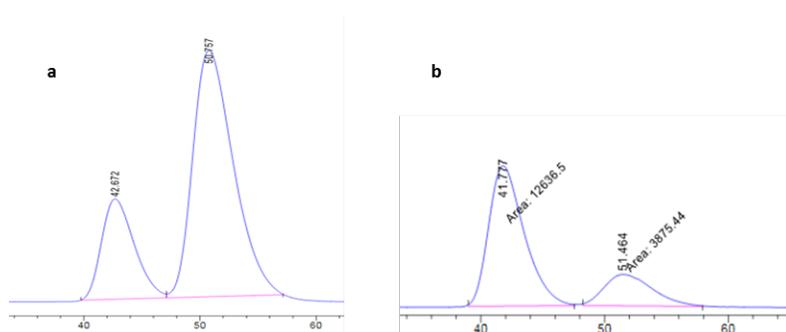


Figure S20: Chromatograms of ethyl 2-hydroxy-4-phenyl-4-pentenoate formed in the Co-salen catalyzed (a) and Co-salan catalyzed (b) carbonyl-ene reaction.

## 5 References

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