Catalyst-Controlled Stereodivergent Synthesis of Atropisomeric Multi-Axis Systems

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General Information

All chemicals were reagent grade and used as supplied unless stated otherwise. 2-Iodoxybenzoic acid (IBX) was prepared according to a literature procedure.[1] (*Z*)-4-(2-bromophenyl)but-3-en-1-ol was prepared as previously reported.[2] *n*-Dibutylmagnesium solution in heptane was purchased from *Acros* (No. 37777-1000), *n*-butyllithium solution in hexane from *Acros* (No. 18127-1000), citrate buffer solution (pH 5) from *J.T. Baker* (No. 10646631), DMF (peptide synthesis grade) from *Acros* (No. 35483-0010) and chloroform (EtOH-free) from *Sigma Aldrich* (No. C2432). All reactions were carried out in oven dried glassware and under an argon atmosphere. All other solvents used were ACS grade. Extracts were dried over technical grade Na_2SO_4. Analytical and preparative thin layer chromatography (TLC) was performed on pre-coated *Merck* silica gel 60 F_{254} plates (0.25 mm) and visualized by UV (254 nm). Column chromatography was carried out on *Silicycle* SiliaFlash P60 (230 – 400 mesh). Concentration *in vacuo* was perfomed by rotary evaporation to ~10 mbar at 40 °C. Final products were dried at ~10^{-2} mbar and RT. ^{1}H NMR and ^{13}C NMR spectra were recorded on a *BrukerAdvance III* (500 MHz) and *BrukerAvance* (400 MHz) at 298 K in $CDCl_3$ or C_6D_6 supplied by *Cambridge Isotope Laboratories*. Chemical shifts (δ) are reported in ppm relative to $CDCl_3$ (7.26 ppm/77.16 ppm) or C_6D_6 (7.16 ppm/128.06 ppm). The multiplicities are reported in Hz as: s = singlet, d = doublet and m = multiplet. Melting points (m.p.) were measured on a *Büchi B-545* melting point apparatus and are uncorrected. Infrared (IR) spectra were measured on an ATR *Varian Scimitar 800* FT-IR spectrometer and are reported in cm^{-1}. Optical rotations were obtained at RT on a *JASCO P-2000* polarimeter using a 1.00 mL cell with a length of 100 mm; the concentrations are reported in g/100mL. High-resolution ESI mass spectrometry (HR-ESI) was performed by Dr. Heinz Nadig and Dr. Michael Pfeffer of the University of Basel on a *Bruker maXis 4G* QTOF ESI mass spectrometer. High-resolution MALDI mass spectrometry (MALDI-FTICR) was performed by Dr. B. Gerrits, L. Bertschi and O. L. Greter of the ETH Zurich on a *Bruker solariX* mass spectrometer.

General Procedures

Preparation of the diol precursors, general procedure A[2]

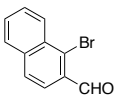
(*Z*)-4-(2-Bromophenyl)but-3-en-1-ol (**1**, 1.50 eq.) in dry THF was cooled to 0 °C and *n*-Bu_2Mg (in heptane, 0.78 eq.) was added over 5 min. The solution was stirred at 0 °C for 30 min before *n*-BuLi (in hexanes, 1.56 eq.) was added over 5 min. The mixture was stirred for 1 h at 0 °C, before it was added over 5 min to a solution of a naphthaldehyde (1.00 eq.) in THF (70 $mmolL^{-1}$ unless stated otherwise). The mixture was stirred for 25 min at RT and H_2O (10 mL/mmol) followed by aq. sat. NH_4Cl (50 mL/mmol) was added. The layers were separated and the aqueous layer was extracted with EtOAc (2x 30 mL/mmol). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude products were purified by column chromatography.

In situ double oxidation, general procedure B

IBX was added to a suspension of a diol-precursor (1.00 eq.) in MeCN (20 mM) and the suspension was vigorously stirred at 60 °C. The mixture was cooled to RT, filtered and concentrated *in vacuo*. $CHCl_3$ (20 $mmolL^{-1}$) was added to the residue and the mixture was filtered to yield a solution of the keto-aldehyde, which was directly used in the next step.

Catalyst-controlled Stereodivergent Synthesis, Bromine End-Group

1-Bromo-2-naphthaldehyde (2)



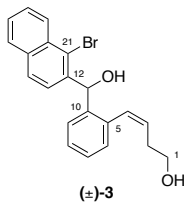
2

$Co(OAc)_2 \cdot 4\ H_2O$ (9.96 g, 40.0 mmol, 20.0 mol%) and 2-butanone (5.37 mL, 60.0 mmol, 30.0 mol%) were added to 1-bromo-2-methylnaphthalene (90%, 34.6 mL, 200 mmol, 1.00 eq.) in acetic acid (400 mL). The solution was heated to 95 °C for 21 h. The mixture was poured on ice (1.5 L), conc. HCl (400 mL) was added and the mixture was extracted with EtOAc (1x 800 mL, 2x 400 mL). The combined organic layers were extracted with aq. NaOH (2.0 $molL^{-1}$, 5x 400 mL). The aqueous extracts were cooled to 0 °C, carefully acidified with conc. HCl (450 mL) and extracted with EtOAc (3x 500 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield the crude product which was used without further purification.[3]

Crude 1-bromo-2-naphthoic acid (**3**) was dissolved in THF (400 mL), cooled to 0 °C and borane dimethylsulfide in THF (2.0 $molL^{-1}$, 117 mL, 234 mmol, 1.17 eq.) was added over 10 min. The mixture was heated to reflux for 2 h, cooled back to 0 °C and H_2O (150 mL) was carefully added (gas evolution!). Aq. HCl (1.0 $molL^{-1}$, 50 mL) was added and the mixture was extracted with EtOAc (2x 350 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was used without further purification.

The crude (1-bromonaphthalene-2-yl)methanol was dissolved in CH_2Cl_2 (1.5 L) and MnO_2 (174 g, 2.00 mol, 10.0 eq.) was added. The mixture was stirred for 19 h at RT and filtered over Celite®. The Celite® pad was rinsed with CH_2Cl_2 (2x 150 mL), the combined filtrates were concentrated *in vacuo* and the residue was recrystallized from MeOH (1.2 L, 64 °C to 0 °C) to yield product **2** as a yellowish solid (35.3 g, 150 mmol, 75% over three steps): m.p. 109.0–110.0 °C; R_f 0.32 (*n*-pentane:Et_2O 50:1); ν_{max} (neat): 3354w, 3059w, 2923w, 2866m, 2742w, 1666s, 1592m, 1554m, 1496w, 1453m, 1308m, 1252s, 1212s, 1209w, 969m, 886m, 808s, 751s, 665m; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.68 (1H, d, ^4J 4.4, C*H*O), 8.53–8.47 (1H, m), 7.94 (1H, d, ^3J 8.5), 7.90–7.83 (2H, m), 7.71–7.66 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.0 (*C*HO), 137.4, 132.3, 131.5, 131.3, 129.9, 128.6, 128.4, 128.4, 128.3, 124.2; in agreement with literature data.[4] No unexpected or unusually high safety hazards were encountered.

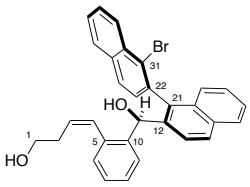
(*Z*)-4-(2-((1-bromonaphthalen-2-yl)(hydroxy)methyl)phenyl)but-3-en-1-ol (3, diol A)



(±)-3

Prepared according to the general procedure **A** using 1-bromo-2-naphthaldehyde (**2**, 14.1 g, 60.0 mmol, 1.00 eq.), (*Z*)-4-(2-bromophenyl)but-3-en-1-ol (**1**, 60 $mmolL^{-1}$, 20.4 g, 90.0 mmol, 1.50 eq.), *n*-Bu_2Mg (0.59 $molL^{-1}$, 80.0 mL, 46.8 mmol, 0.78 eq.) and *n*-BuLi (1.71 $molL^{-1}$, 54.7 mL, 93.6 mmol, 1.56 eq.) to yield a colorless solid (15.1 g, 39.4 mmol, 66%): m.p. 112.5–114.3 °C; R_f 0.19 (*n*-pentane:Et_2O 1:1); ν_{max} (neat): 3307m, 2922w, 1484w, 1420w, 1328w, 1257w, 1177w, 1035s, 1965m, 897w, 760s, 654m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.29 (1H, d, ^3J 8.6, C19*H*), 7.85 (1H, d, ^3J 8.6, C14*H*), 7.83 (1H, d, ^3J 8.1, C16*H*), 7.77 (1H, d, ^3J 8.6, C13*H*), 7.58 (1H, ddd, ^3J 8.3, 6.8, ^4J 1.4, C18*H*), 7.52 (1H, ddd, ^3J 8.1, 6.9, ^4J 1.3, C17*H*), 7.25 (1H, ddd, ^3J 7.5, 7.3, ^4J 1.4, C7*H*), 7.20–7.16 (2H, m, C8*H*, C6*H*), 7.10 (1H, dd, ^3J 8.5, ^4J 1.8, C9*H*), 6.93 (1H, d, ^3J 11.3, C4*H*), 6.52 (1H, s, C11*H*), 5.82 (1H, ddd, ^3J 11.3, 9.1, 5.9, C3*H*), 3.67–3.57 (2H, m, C1H_2), 2.51–2.41 (1H, m, C2*H*), 2.36 (2H, s, O*H*), 2.25–2.17 (1H, m, C2*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.9 (*C10*), 140.2 (*C12*), 136.8 (*C5*), 134.2 (*C15*), 132.4 (*C20*), 130.9 (*C4*), 130.8 (*C3*), 129.8 (*C9*), 128.3 (*C16*), 127.8 (*C14*), 127.6 (*C7*), 127.6 (*C8*), 127.6 (*C18*), 127.4 (*C19*), 127.0 (*C6*), 126.7 (*C17*), 125.7 (*C13*), 123.1 (*C21*), 72.9 (*C11*), 62.2 (*C1*), 31.5 (*C2*); ESI-MS: m/z calcd. for $C_{21}H_{19}OBrNaO_2^+$ 405.0461 found 405.0442 [M+Na^+]. No unexpected or unusually high safety hazards were encountered.

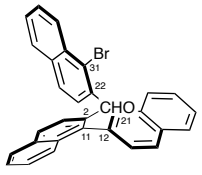
(*Z*,*R*,*S*$_a$)-4-(1'-Bromo-([1:2']-binaphthalen-2-yl(hydroxy)methyl)phenyl)but-3-en-1-ol (6, diol B)



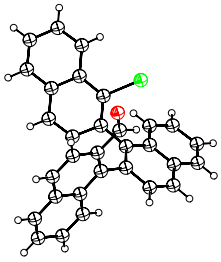
6

The in situ double-oxidation was performed according to the general procedure **B** using **3** (10.2 g, 26.6 mmol, 1.00 eq.) and IBX (22.3 g, 79.8 mmol, 3.00 eq.) with 4 h reaction time. To the keto-aldehyde solution (*S*)-(–)-5-(2-pyrrolidinyl)-1*H*-tetrazole (925 mg, 6.65 mmol, 25.0 mol%) in DMF (650 mL) and H_2O (650 mL) was added and the mixture was vigorously stirred at RT for 17 h. The layers were separated and the aq. layer was extracted with CH_2Cl_2. The combined organic layers were concentrated at 55 °C. To remove remaining DMF, toluene (1.0 L) was added and the solution was concentrated again. The crude aldol addition product was dissolved in $CHCl_3$ (1.3 L) and Amberlite® IRA-96 (50.0 g, washed with 2x MeOH and 2x CH_2Cl_2) was added. The mixture was stirred for 2 h at RT, filtered, dried over Na_2SO_4, filtered again and concentrated to give crude (S_a)-1'-bromo-[1:2']-binaphthalene-2-carbaldehyde, (S_a)-**5**. According to the general procedure **A** crude (S_a)-**5**, was treated with building block **1**, which was prepared from (*Z*)-4-(2-bromophenyl)but-3-en-1-ol (**1**, 60 mmolL^{-1}, 9.06 g, 39.9 mmol, 1.50 eq.), *n*-Bu_2Mg (0.54 M, 38.4 mL, 20.7 mmol, 0.78 eq.) and *n*-BuLi (1.61 M, 25.8 mL, 41.5 mmol, 1.56 eq.) to give after column chromatography (*n*-pentane:Et_2O 1:1) unreacted aldehyde (S_a)-**5** (1.54 g, 4.27 mmol, 16%) and the desired diol **6** as a colorless solid (7.49 g, 14.7 mmol, 55% over four steps): m.p. 83.1–84.9 °C; R_f 0.19 (*n*-pentane:Et_2O 1:1); $[\alpha]_D$ +34.6 (*c* 1.0 in $CHCl_3$); ν_{max} (neat): 3354m, 3058w, 2924w, 1496w, 1391w, 1321w, 1254w, 1213w, 1045s, 953m, 865w, 818s, 748s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.41 (1H, dd, ^3J 8.5, ^4J 1.1, C29*H*), 8.00 (1H, d, ^3J 8.7, C14*H*), 7.92 (1H, d, ^3J 7.9, C16*H*), 7.91–7.86 (2H, m, C13*H,* C26*H*), 7.68 (1H, ddd, ^3J 8.2, 7.0, ^4J 1.4, C28*H*), 7.67 (1H, d, ^3J 8.7, C24*H*), 7.61 (1H, ddd, ^3J 8.1, 6.9, ^4J 1.2, C27*H*), 7.47 (1H, ddd, ^3J 8.1, 6.9, ^4J 1.2, C17*H*), 7.33–7.28 (2H, m, C9*H,* C18*H*), 7.20–7.16 (2H, m, C7*H,* C8*H*), 7.14 (1H, dd, ^3J 8.6, ^4J 1.1, C19*H*), 6.95–6.92 (1H, m, C6*H*), 6.87 (1H, d, ^3J 8.3, C23*H*), 5.86 (1H, s, C11*H*), 5.79 (1H, d, ^3J 11.3, C4*H*), 5.41 (1H, ddd, ^3J 11.3, 8.8, 6.2, C3*H*) 3.43–3.34 (2H, m, C1*H*), 2.20–2.10 (1H, m, C2*H*), 2.02 (2H, s br, O*H*), 1.91–1.84 (1H, m, C2*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.4 (*C10*), 138.3 (*C12*), 137.5 (*C22*), 137.3 (*C21*), 136.3 (*C5*), 134.0 (*C25*), 133.1 (*C15*), 132.5 (*C30*), 132.0 (*C20*), 130.5 (*C4*), 130.0 (*C3*), 129.4 (*C6*), 129.3 (*C23*), 128.5 (*C14*), 128.4 (*C26*), 128.2 (*C16*), 127.9 (*C28*), 127.8 (*C29*), 127.7 (*C9*), 127.4 (*C24*), 127.3 (*C7/8*), 127.3 (*C7/8*), 127.1 (*C27*), 126.5 (*C18*), 126.1 (*C17*), 125.9 (*C19*), 124.7 (*C13*), 124.5 (*C31*), 70.8 (*C11*), 62.0 (*C1*), 31.3 (*C2*); ESI-MS: m/z calcd. for $C_{31}H_{25}BrNaO_2^+$ 531.0930 found 531.0930 [M+Na$^+$]; The e.r. (>99:1) of (S_a)-(1'-bromo-[1,2'-binaphthalen]-2-yl)methanol (obtained by reduction of (S_a)-**5** with $NaBH_4$, MeOH, RT, 30 min) was determined by HPLC using a *Chiralcel OD-H* column (1.0 mLmin^{-1}, *i*-PrOH:*n*-heptane 10:90): (S_a) t_R = 10.7 min and (R_a) t_R = 18.5 min; racemic reference material was obtained with *rac*-5-(2-pyrroidinyl)-1*H*-tetrazole as catalyst; This hydroxyl-derivative of (S_a)-**5** decomposed before racemization was observed upon heating in DMF or neat to 170 °C. No unexpected or unusually high safety hazards were encountered.

(*R*$_a$,*S*$_a$)-1''-Bromo-[1:2']-ternaphthalene-2-carbaldehyde, (*R*$_a$,*S*$_a$)-7



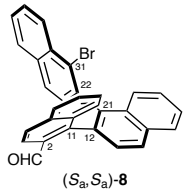
(*R*$_a$,*S*$_a$)-**7**



The in situ double-oxidation was performed according to the general procedure **B** using **6** (50.8 mg, 99.7 μmol, 1.00 eq.) and IBX (83.8 mg, 299 μmol, 3.00 eq.) with 4 h reaction time. To the keto-aldehyde solution at RT was added *N*-benzylcinchonidinium chloride (420 μg, 997 nmol, 1.00 mol%), followed by aq. KOH (1.0 molL^{-1}, 2.0 mL). The mixture was stirred for 16 h at RT, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) gave the aldol condensation product as colorless solid (33.5 mg, 68.8 μmol, 69% over two steps, d.r. = 94:6): m.p. 240.2 °C (decomp.); R_f 0.55 (toluene); $[\alpha]_D$ +498 (*c* 0.5 in $CDCl_3$); ν_{max} (neat): 3054w, 2851w, 2361w, 1676s, 1498m, 1385m, 1316m, 1223m, 1145w, 1025w,

950m, 870w, 816s, 754s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.26 (1H, d, ^4J 0.9, C1*H*), 8.25 (1H, dd, ^3J 8.7, ^4J 0.9, C29*H*), 8.12 (1H, d, ^3J 8.3, C14*H*), 8.08 (1H, d, ^3J 8.3, C16*H*), 7.86 (1H, d, ^3J 8.7, C3*H*), 7.79 (1H, d, ^3J 8.6, C6*H*), 7.70 (1H, d, ^3J 8.6, C4*H*), 7.65 (1H, d, ^3J 8.4, C9*H*), 7.63–7.55 (4H, m, C7*H*, C13*H*, C17*H*, C26*H*), 7.53 (1H, ddd, ^3J 8.3, 7.0, ^4J 1.3, C28*H*), 7.49–7.41 (3H, m, C8*H*, C18*H*, C27*H*), 7.38 (1H, dd, ^3J 8.5, ^4J 1.0, C19*H*), 7.29 (1H, d, ^3J 8.3, C24*H*), 7.02 (1H, d, ^3J 8.4, C23*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 192.7 (*C1*), 145.6 (*C11*), 140.0 (*C21*), 136.7 (*C22*), 135.9 (*C5*), 133.6 (*C25*), 133.3 (*C15*), 133.0 (*C10*), 132.5 (*C12*), 132.1 (*C30*), 132.0 (*C20*), 131.5 (*C2*), 128.7 (*C7, C13*), 128.5 (*C16*), 128.4 (*C4*), 128.4 (*C6*), 128.3 (*C23*), 128.2 (*C14*), 128.0 (*C9, C26*), 127.8 (*C29*), 127.7 (*C28*), 127.3 (*C18*), 126.9 (*C24*), 126.9 (*C27*), 126.8 (*C17*), 126.7 (*C19*), 126.7 (*C8*), 124.8 (*C31*), 122.1 (*C3*); ^{1}H–^{1}H NOESY (500 MHz, $CDCl_3$) = C9*H*–C23*H*, C19*H*–C23*H*; MALDI-FTICR: m/z calcd. for $C_{31}H_{19}BrO^{+\bullet}$ 486.0614 found 486.0614 [$M^{+\bullet}$]; Crystals suitable for X-ray crystallographic analysis were obtained by diffusion of *n*-pentane into a solution of (R_a,S_a)-**7** in toluene. Examination of catalysts and conditions can be found on page S16-S18. No unexpected or unusually high safety hazards were encountered.

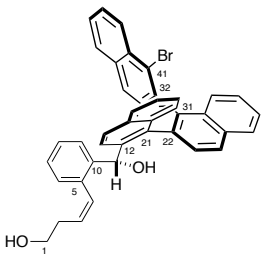
(S_a,S_a)-1''-Bromo-[1:2']-ternaphthalene-2-carbaldehyde, (S_a,S_a)-8



(S_a,S_a)-**8**

The in situ double-oxidation was performed according to the general procedure **B** using **6** (2.04 g, 4.00 mmol, 1.00 eq.) and IBX (3.36 g, 12.0 mmol, 3.00 eq.) with 4 h reaction time. To the keto-aldehyde solution at RT was added (*S*)-(–)-5-(2-pyrrolidinyl)-1*H*-tetrazole (223 mg, 1.6 mmol, 40.0 mol%) in DMF (133 mL) and citrate buffer (pH 5, 133 mL). The mixture was vigorously stirred at RT for 48 h. The layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 200 mL). The combined organic layers were concentrated *in vacuo* at 55 °C. The residue was dissolved in toluene (300 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to remove remaining DMF. The crude aldol condensation product was purified by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) to yield a colorless solid (1.41 g, 2.90 mmol, 72% over two steps, d.r. = 97:3): m.p. 206.8 °C (decomp.); R_f 0.61 (toluene); $[\alpha]_D$ +230 (*c* 0.5 in $CDCl_3$); ν_{max} (neat): 3056w, 3844w, 2733w, 2361w, 1675s, 1593w, 1499w, 1326m, 1233m, 1147w, 1027w, 950m, 869w, 815s, 749s, 660m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.09 (1H, d, ^4J 0.8, C*H*O), 8.11–8.05 (3H, m) 7.98 (1H, d, ^3J 8.5), 7.88 (1H, d, ^3J 8.5), 7.73–7.68 (3H, m), 7.64–7.59 (3H, m), 7.51–7.41 (4H, m), 7.40–7.34 (2H, m), 7.20 (1H, d, ^3J 8.4); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 192.5 (*C*HO), 145.7, 140.0, 136.7, 136.0, 133.5, 133.4, 132.5, 132.3, 132.1, 132.0, 131.4, 129.6, 129.0, 128.9, 128.8, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 127.6, 127.4, 127.3, 126.9, 126.8, 126.8, 126.3, 125.2, 121.7; MALDI-FTICR: m/z calcd. for $C_{31}H_{19}BrO^{+\bullet}$ 486.0614 found 486.0614 [$M^{+\bullet}$]. Examination of catalysts and conditions can be found on page S16-S18. No unexpected or unusually high safety hazards were encountered.

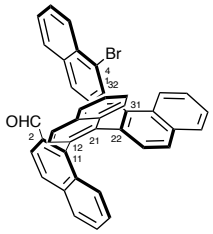
(*Z*,*R*,S_a,S_a)-4-(1''-Bromo-([1:2']-ternaphthalen-2-yl(hydroxy)methyl)phenyl)but-3-en-1-ol (diol C)



Prepared according to the general procedure **A** using (S_a,S_a)-**8** (1.40 g, 2.87 mmol, 1.00 eq.), (*Z*)-4-(2-bromophenyl)but-3-en-1-ol (**1**, 60 mmolL^{-1}, 978 mg, 4.31 mmol, 1.50 eq.), *n*-Bu_2Mg (0.55 molL^{-1}, 4.07 mL, 2.24 mmol, 0.78 eq.) and *n*-BuLi (1.49 molL^{-1}, 3.00 mL, 4.48 mmol, 1.56 eq.) to yield after purification by column chromatography (CH_2Cl_2:Et_2O 100:1 to 10:1) a colorless solid (1.37 g, 2.15 mmol, 75%): m.p. 188.8 °C (decomp.); R_f 0.13 (CH_2Cl_2:Et_2O 50:1); $[\alpha]_D$ +83.8 (*c* 1.0 in $CDCl_3$); ν_{max} (neat): 3281w, 3056w, 2900w, 1498w, 1391w, 1315w, 1214w, 1030m, 864w, 820m, 744s, 663w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (1H, d, ^3J 8.4), 7.98 (1H, d, ^3J 8.4), 7.93 (1H, d, ^3J 8.7), 7.77–7.71 (3H, m), 7.64 (1H, d, ^3J 7.8), 7.57–7.53 (2H, m), 7.50 (1H, d, ^3J 8.4), 7.40 (1H, ddd, ^3J 8.3, 7.0, ^4J 1.4), 7.31–7.25 (3H, m), 7.25–7.18 (4H, m), 7.14 (1H, ddd, ^3J 8.7, 7.1,

^4J 1.1), 7.06 (1H, dd, ^3J 7.7, ^4J 1.1), 7.01 (1H, d, ^3J 7.4), 6.74 (1H, d, ^3J 8.4), 6.18 (1H, s, C11*H*), 5.73 (1H, d, ^3J 11.6, C4*H*), 5.46–5.39 (1H, m, C3*H*), 3.57–3.50 (1H, m, C1*H*), 3.47 (2H, O*H*), 3.27–3.20 (1H, m, C1*H*), 2.34–2.22 (1H, m, C2*H*), 1.91–1.82 (1H, m, C2*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.8, 138.0, 137.8, 137.2, 137.0, 136.1, 135.2, 133.4, 132.9, 132.6, 132.2, 132.2, 132.1, 131.5, 130.5, 129.6, 129.2, 128.5, 128.4, 128.4, 128.2, 128.0, 127.8, 127.6, 127.6, 127.5 (3C, HMQC), 127.4, 127.2, 126.9, 126.8, 126.5, 126.2, 125.7, 125.4, 125.1, 124.3, 70.7, 61.3, 30.9; since diol **C** slowly decomposes in chloroform, additional NMR in C_6D_6 were recorded: ^{1}H NMR (500 MHz, C_6D_6): δ = 8.26 (1H, d, ^3J 8.9, C13*H*), 8.16 (1H, dd, ^3J 8.6, ^4J 0.7, C39*H*), 8.03 (1H, dd, ^3J 8.4, ^4J 0.6, C19*H*), 7.92 (1H, d, ^3J 8.5, C33*H*), 7.70 (1H, d, ^3J 8.2, C26*H*), 7.59 (1H, d, ^3J 8.6, C14*H*), 7.48–7.44 (2H, m, C24*H*, C34*H*), 7.42–7.36 (3H, m, C9*H*, C16*H*, C29*H*), 7.26 (1H, ddd, ^3J 8.0, 6.9, ^4J 0.9, C27*H*), 7.18 (1H, ddd, ^3J 8.4, 7.0, ^4J 1.4, C18*H*), 7.12–6.97 (6H, m, C6*H*, C7*H*, C8*H*, C17*H*, C28*H*, C38*H*), 6.85–6.80 (3H, m, C23*H*, C36*H*, C37*H*), 6.52 (1H, s, C11*H*), 5.83 (1H, d, ^3J 11.6, C4*H*), 5.22–5.16 (1H, m, C3*H*), 3.19–3.13 (1H, m, C1*H*), 2.92–2.85 (1H, m, C1*H*), 2.27–2.16 (1H, m, C2*H*), 1.53–1.45 (1H, m, C2*H*); ^{13}C NMR (126 MHz, C_6D_6): δ = 143.0 (*C*10), 138.8 (*C*12), 138.4 (*C*31), 137.8 (*C*5), 137.5 (*C*32), 136.7 (*C*21), 135.8 (*C*22), 133.8 (*C*35), 133.3 (*C*25), 133.0 (*C*10), 132.8 (*C*30), 132.7 (*C*20), 132.5 (*C*40), 132.2 (*C*3), 130.6 (*C*4), 129.9 (*C*6), 129.4 (*C*23), 129.0 (*C*9), 128.9 (*C*33), 128.7 (*C*19), 128.4 (*C*26), 127.8 (*C*8), 127.7 (*C*39), 127.5 (*C*7), 127.4 (*C*38), 127.3 (*C*29), 127.2 (*C*28), 126.6 (*C*37), 126.3 (*C*27), 126.0 (*C*17), 125.8 (*C*18), 125.5 (*C*41), 124.8 (*C*13), 71.0 (*C*11), 61.0 (*C*1), 61.1 (*C*2); ESI-MS: m/z calcd. for $C_{41}H_{31}OBrNaO_2^+$ 657.1400 found 657.1409 [M+Na^+]. No unexpected or unusually high safety hazards were encountered.

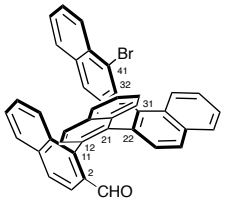
(*R*$_a$,*S*$_a$,*S*$_a$)-1'''-Bromo-[1:2']-quaternaphthalene-2-carbaldehyde, (*R*$_a$,*S*$_a$,*S*$_a$)-13



(*R*$_a$,*S*$_a$,*S*$_a$)–**13**

The in situ double-oxidation was performed according to the general procedure **B** using diol **C** (48.3 mg, 75.9 μmol, 1.00 eq.), IBX (106 mg, 380 μmol, 5.00 eq.) and 4.5 h reaction time. To the keto-aldehyde solution aq. KOH (1.0 molL^{-1}, 2.0 mL) was added. The mixture was stirred for 16 h at RT, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) yielded the aldol condensation product as colorless solid (25.7 mg, 41.9 μmol, 55% over two steps, d.r. = 87:13): m.p. 240.4 °C (decomp.); R_f 0.34 (*n*-pentane:CH_2Cl_2 1:1); $[\alpha]_D$ –264 (*c* 1.0 in $CDCl_3$); ν_{max} (neat): 3056w, 2855w, 1685m, 1500w, 1316w, 1228m, 1032w, 951w, 870w, 818s, 745s, 670m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.59 (1H, d, ^4J 0.9, C1*H*), 8.04 (1H, d, ^3J 8.3, C39*H*), 7.94 (1H, d, ^3J 8.6, C3*H*), 7.93–7.90 (2H, m, C16*H*, C19*H*), 7.85–7.82 (3H, m, C4*H*, C14*H*, C36*H*), 7.80–7.75 (3H, m, C23*H*, C24*H*, C26*H*), 7.73–7.70 (2H, m, C6*H*, C9*H*), 7.58–7.46 (4H, m, C17*H*, C34*H*, C37*H*, C38*H*), 7.46–7.40 (2H, m, C7*H*, C18*H*), 7.38 (1H, ddd, ^3J 8.1, 6.9, ^4J 1.1, C27*H*), 7.33 (1H, ddd, ^3J 8.2, 6.9, ^4J 1.4, C8*H*), 7.18–7.13 (2H, m, C13*H*, C28*H*), 6.83 (1H, d, ^3J 8.5, C29*H*), 6.01 (1H, d, ^3J 8.3, C33*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 192.2 (*C1*), 145.7 (*C11*), 139.1 (*C31*), 139.0 (*C21*), 137.1 (*C32*), 135.6 (*C5*), 134.9 (*C22*), 133.8 (*C35*), 133.7 (*C15*), 133.4 (*C20*), 133.2 (*C2*), 132.8 (*C25*), 132.8 (*C30*), 132.3 (*C23*), 131.9 (*C40*), 131.6 (*C12*), 131.2 (*C33*), 131.0 (*C10*), 130.8 (*C13*), 129.6 (*C19*), 128.9 (*C9*), 128.6 (*C4*), 128.5 (*C7*), 128.3 (*C36*), 128.2 (*C6*), 128.0 (*C14*, *C16*), 127.9 (*C26*), 127.8 (*C39*), 127.6 (*C38*), 127.2 (*C34*), 127.2 (*C37*), 126.8 (*C24*), 126.6 (*C17*), 126.5 (*C29*), 126.3 (*C28*), 126.2 (*C27*), 126.1 (*C8*), 126.0 (*C18*), 125.4 (*C41*), 122.6 (*C3*); MALDI-FTICR: m/z calcd. for $C_{41}H_{25}BrO^{+\bullet}$ 612.1083 found 612.1084 [$M^{+\bullet}$]. Examination of catalysts and conditions can be found on page S18-S21. No unexpected or unusually high safety hazards were encountered.

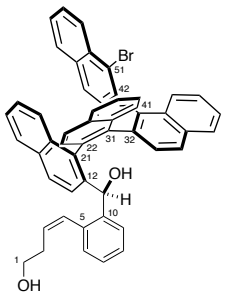
(S_a,S_a,S_a)-1'''-Bromo-[1:2']-quaternaphthalene-2-carbaldehyde, (S_a,S_a,S_a)-14



(S_a,S_a,S_a)-**14**

The in situ double-oxidation was performed according to the general procedure **B** using diol **C** (47.2 mg, 74.3 μmol, 1.00 eq.), IBX (104 mg, 372 μmol, 5.00 eq.) and 4.5 h reaction time. The keto-aldehyde solution was cooled to 0 °C and *N*-benzylcinchonium chloride (313 μg, 743 nmol, 1.00 mol%) was added, followed by cold aq. KOH (1.0 molL^{-1}, 2.0 mL). The mixture was stirred for 16 h at 0 °C, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) gave the aldol condensation product (S_a,S_a,S_a)-**14** as colorless solid (25.5 mg, 41.5 μmol, 56% over two steps, d.r. = 89:11). Diastereomerically pure material was obtained by reduction using $NaBH_4$, separation by preparative TLC (CH_2Cl_2) and reoxidation with Dess-Martin periodinane followed by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) to yield a colorless solid: m.p. 206.0 °C (decomp.); R_f 0.34 (*n*-pentane:CH_2Cl_2 1:1); $[\alpha]_D$ –546 (*c* 0.5 in $CDCl_3$); ν_{max} (neat): 3055w, 2853w, 2361w, 1694s, 1679s, 1596w, 1501w, 1425w, 1385w, 1313m, 1033w, 908m, 823s, 747s, 741s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.96 (1H, d, ^4J 0.8, C1*H*), 8.01–7.97 (2H, m, C24*H*, C39*H*), 7.94 (1H, d, ^3J 8.1, C23*H*), 7.91 (1H, d, ^3J 8.0, C26*H*), 7.89 (1H, d, ^3J 8.5, C19*H*), 7.87 (1H, d, ^3J 8.9, C14*H*), 7.84 (1H, d, ^3J 7.8, C6*H*), 7.82 (1H, d, ^3J 8.7, C4*H*), 7.76 (1H, d, ^3J 8.4, C3*H*), 7.60 (1H, d, ^3J 8.6, C23*H*), 7.57 (1H, ddd, ^3J 8.1, 7.0, ^4J 1.1, C17*H*), 7.45–7.38 (4H, m, C18*H*, C27*H*, C37*H*, C38*H*), 7.37–7.33 (2H, m, C7*H*, C36*H*), 7.28 (1H, d, ^3J 8.5, C13*H*), 7.15 (1H, ddd, ^3J 8.4, 7.1, ^4J 1.4, C28*H*), 6.75 (1H, dd, ^3J 8.5, 0.8, C29*H*), 6.63 (1H, d, ^3J 8.4, C9*H*), 6.33 (1H, ddd, ^3J 8.5, 7.2, ^4J 1.2, C8*H*), 6.28 (1H, d, ^3J 8.2, C34*H*), 5.33 (1H, d, ^3J 8.3, C33*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 192.5 (*C1*), 145.6 (*C11*), 140.4 (*C21*), 138.6 (*C31*), 136.5 (*C5*), 136.5 (*C32*), 134.2 (*C22*), 133.9 (*C10*, *C15*), 133.7 (*C20*), 133.5 (*C35*), 133.2 (*C25*), 133.1 (*C30*), 132.4 (*C23*), 131.7 (*C40*), 131.2 (*C12*), 130.3 (*C33*) 130.1 (*C2*), 130.0 (*C13*), 129.8 (*C19*), 128.4 (*C4*), 128.3 (*C7*), 128.2 (*C26*), 128.0 (*C16*), 128.0 (*C36*), 127.9 (*C6*), 127.7 (*C39*), 127.7 (*C9*), 127.6 (*C24*), 127.4 (*C14*), 126.9 (*C38*), 126.7 (*C17*), 126.6 (*C29*), 126.5 (*C8*), 126.4 (*C37*), 126.4 (*C27*, *C28*), 126.0 (*C18*), 125.3 (*C34*), 124.5 (*C41*), 122.2 (*C3*); ^{1}H–^{1}H NOESY (500 MHz, $CDCl_3$) = MALDI-FTICR: m/z calcd. for $C_{41}H_{25}BrO^{+\bullet}$ 612.1083 found 612.1084 [$M^{+\bullet}$]. Examination of catalysts and conditions can be found on page S18-S21. No unexpected or unusually high safety hazards were encountered.

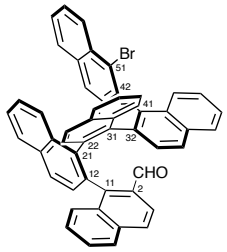
(*Z*,*R*,S_a,S_a,S_a)-4-(1'''-Bromo-([1:2']-quaternaphthalen-2-yl(hydroxy)methyl)phenyl)but-3-en-1-ol (diol D)



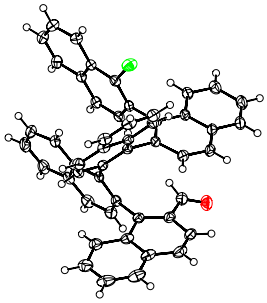
Prepared according to the general procedure **A** using (S_a,S_a,S_a)-**14** (884 mg, 1.44 mmol, 1.00 eq.), (*Z*)-4-(2-bromophenyl)but-3-en-1-ol (**1**, 60 mmolL^{-1}, 491 mg, 2.16 mmol, 1.50 eq.), *n*-Bu_2Mg (0.55 molL^{-1}, 2.04 mL, 1.12 mmol, 0.78 eq.) and *n*-BuLi (1.55 molL^{-1}, 1.45 mL, 2.25 mmol, 1.56 eq.) to yield after purification by column chromatography (CH_2Cl_2:Et_2O 100:1 to 10:1) a colorless solid (886 mg, 1.16 mmol, 81%): m.p. 209.3 °C (decomp.); R_f 0.14 (CH_2Cl_2:Et_2O 50:1); $[\alpha]_D$ –268 (*c* 1.0 in $CDCl_3$); ν_{max} (neat): 3568w, 3054w, 2954w, 1598w, 1503m, 1315m, 1169w, 1034m, 950m, 819s, 745s; ^{1}H NMR (500 MHz, C_6D_6): δ = 8.12 (1H, d, ^3J 8.5, C29*H*), 8.02 (1H, dd, ^3J 8.1, ^4J 1.4, C49*H*), 7.93 (1H, d, ^3J 8.5, C33*H*), 7.86 (1H, d, ^3J 8.5, C34*H*), 7.72 (1H, d, ^3J 8.5, C13*H*), 7.67–7.62, (3H, m, C9*H*, C26*H*, C36*H*), 7.54 (1H, d, ^3J 8.7, C14*H*), 7.48 (1H, d, ^3J 8.1, C16*H*), 7.38 (1H, d, ^3J 8.5, C24*H*), 7.32 (1H, ddd, ^3J 8.0, 6.9, ^4J 1.3, C27*H*), 7.27 (1H, ddd, ^3J 8.5, 6.9, ^4J 1.5, C28*H*), 7.18–7.01 (5H, m, C8*H*, C37*H*, C46*H*, C47*H*, C48*H*), 7.01–6.97 (2H, m, C6*H*, C7*H*), 6.96–6.88 (4H, m, C17*H*, C23*H*, C38*H*, C39*H*), 6.49 (1H, d, ^3J 8.7, C19*H*), 6.28 (1H, s, C11*H*), 6.21 (1H, d, ^3J 8.3, C44*H*), 6.07–6.00 (2H, m, C4*H*, C18*H*), 5.66 (1H, d, ^3J 8.4, C43*H*), 5.27 (1H, ddd, ^3J 11.3, 8.2, 6.7, C3*H*), 3.00–2.88 (2H, m, C1*H*), 2.00–1.91 (1H, m, C2*H*), 1.83 (1H, m, O*H*), 1.73–1.65 (1H, m, C2*H*), 0.56 (1H, s, O*H*);

^{13}C NMR (126 MHz, C_6D_6): δ =142.5 (*C10*), 140.0 (*C41*), 138.5 (*C12*), 138.3 (*C31*), 136.9 (*C42*), 136.6 (*C21*), 136.5 (*C5*), 135.6 (*C32*), 135.0 (*C22*), 134.7 (*C20*), 134.5 (*C30*), 134.0 (*C45*), 134.0 (*C25*), 133.7 (*C40*), 133.7 (*C15*), 133.3 (*C33*, *C35*), 132.2 (*C23*), 132.1 (*C50*), 131.3 (*C4*), 130.8 (*C43*), 130.1 (*C29*), 129.9 (*C3*), 129.6 (*C6*), 128.3 (*C14*, HMQC), 128.2 (*C36*, HMQC), 128.2 (*C26*, HMQC), 128.1 (*C46*, HMQC), 128.1 (*C49*, HMQC), 127.7 (*C34*), 127.6 (*C16*), 127.6 (*C9*), 127.5 (*C24*), 127.3 (*C8*), 127.2 (*C39*), 127.1 (*C19*), 127.0 (*C7*), 127.0 (*C38*), 126.9 (*C48*), 126.8 (*C37*), 126.3 (*C47*), 126.2 (*C27*), 126.0 (*C13*), 125.8 (*C44*), 125.8 (*C28*), 125.6 (*C18*), 125.4 (*C17*), 124.5 (*C51*), 70.3 (*C11*), 61.8 (*C1*), 31.7 (*C2*); ESI-MS: m/z calcd. for $C_{51}H_{37}OBrNaO_2^+$ 783.1869 found 783.1880 [M+Na$^+$]. Decomposes in chloroform and dichloromethane within hours at RT. No unexpected or unusually high safety hazards were encountered.

(*R*$_a$,*S*$_a$,*S*$_a$,*S*$_a$)-1''''-Bromo-[1:2']-quinquenaphthalene-2-carbaldehyde, (*R*$_a$,*S*$_a$,*S*$_a$,*S*$_a$)-15

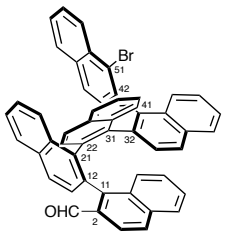


(*R*$_a$,*S*$_a$,*S*$_a$,*S*$_a$)-**15**



The in situ double-oxidation was performed according to the general procedure **B** using diol **D** (57.7 mg, 75.7 μmol, 1.00 eq.), IBX (212 mg, 75.7 μmol, 10.0 eq.) and 6 h reaction time. Aq. KOH (1.0 molL^{-1}, 2.0 mL) was added to the keto-aldehyde solution at RT. The mixture was stirred for 16 h at RT, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) gave the aldol condensation product (*R*$_a$,*S*$_a$,*S*$_a$,*S*$_a$)-**15** as colorless solid (21.6 mg, 29.2 μmol, 39% over two steps, d.r. = 97:3). Diastereomerically pure material was obtained by precipitation from CH_2Cl_2 with *n*-pentane: m.p. 213.1 °C (decomp.); R_f 0.33 (*n*-pentane:CH_2Cl_2 1:1); $[\alpha]_D$ –363 (*c* 1.0 in $CDCl_3$); ν_{max} (neat): 3051w, 2943w, 2852w, 2361w, 1691s, 1595w, 1503w, 1378w, 1231m, 1150w, 1034w, 951w, 865m, 819s, 745s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (1H, d, ^4J 0.6, C1*H*), 7.99–7.95 (1H, m, C49*H*), 7.92–7.88 (2H, m, C16*H*, C36*H*), 7.88–7.85 (2H, m, C3 *H*, C14*H*), 7.81 (1H, d, ^3J 8.7, C4*H*), 7.69–7.65 (2H, m, C26*H*, C46*H*), 7.61 (1H, d, ^3J 8.3, C34*H*), 7.57 (1H, d, ^3J 8.5, C24*H*) 7.48 (1H, ddd, ^3J 8.0, 6.8, ^4J 1.1, C37*H*), 7.45–7.40 (5H, C6*H*, C9*H*, C29*H*, C47*H*, C48*H*), 7.38 (1H, d, ^3J 8.6, C23*H*), 7.37–7.31 (2H, m, C7*H*, C27*H*), 7.24 (1H, ddd, ^3J 8.1, 7.0, ^4J 1.1, C17*H*), 7.19–7.12 (4H, m, C8*H*, C13*H*, C28*H*, C38*H*), 6.70 (1H, d, ^3J 8.6, C39*H*), 6.40–6.36 (2H, m, C19*H*, C44*H*), 6.08 (1H, ddd, ^3J 8.4, 6.9, ^4J 1.4, C18*H*), 6.03 (1H, d, ^3J 8.5, C33*H*), 5.70 (1H, d, ^3J 8.2, C43*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 190.9 (*C1*), 145.6 (*C11*), 139.5 (*C21*), 138.6 (*C41*), 138.4 (*C31*), 136.5 (*C42*), 135.5 (*C5*), 135.1 (*C20*), 134.7 (*C32*), 134.1 (*C22*), 133.8 (*C30*), 133.8 (*C45*), 133.5 (*C15*), 133.4 (*C33*), 133.3 (*C35*), 133.1 (*C25*), 133.0 (*C2*), 132.6 (*C40*), 132.5 (*C23*), 132.0 (*C12*), 131.7 (*C50*), 130.8 (*C13*), 130.8 (*C10*), 130.7 (*C43*), 129.5 (*C29*), 128.5 (*C9*), 128.4 (*C4*), 128.3 (*C7*), 128.1 (*C46*), 128.1 (*C6*), 128.0 (*C36*), 127.7 (*C49*), 127.7 (*C14*), 127.6 (*C16*), 127.6 (*C26*), 127.1 (*C19*), 126.9 (*C48*), 126.8 (*C34*), 126.5 (*C37*, *C18*), 126.5 (*C24*), 126.4 (*C39*), 126.3 (*C38*), 126.3 (*C47*), 126.1 (*C17*), 126.0 (*C8*), 125.9 (*C27*), 125.4 (*C44*), 125.0 (*C28*), 124.5 (*C51*), 123.0 (*C3*); MALDI-FTICR: m/z calcd. for $C_{51}H_{31}BrO^{+\bullet}$ 738.1558 found 738.1550 [M$^{+\bullet}$]; Crystals suitable for X-ray crystallographic analysis were obtained by slow evaporation of a chloroform solution. Examination of catalysts and conditions can be found on page S21–S22. No unexpected or unusually high safety hazards were encountered.

(S_a,S_a,S_a,S_a)-1''''-Bromo-[1:2']-quinquenaphthalene-2-carbaldehyde, (S_a,S_a,S_a,S_a)-16

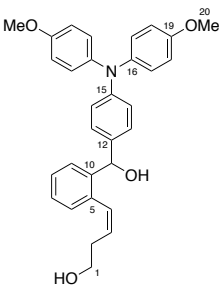


(S_a,S_a,S_a,S_a)-**16**

The in situ double-oxidation was performed according to the general procedure **B** using diol **D** (56.1 mg, 73.6 μmol, 1.00 eq.), IBX (206 mg, 736 μmol, 10.0 eq.) and 6 h reaction time. To the keto-aldehyde at RT was added *N*-(9-anthracenylmethyl)cinchonindinium chloride (3.84 mg, 7.36 μmol, 10.0 mol%) followed by NaH (60% in mineral oil, 17.7 mg, 443 μmol, 6.01 eq.). The mixture was stirred for 16 h at RT, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) yielded the aldol condensation product as colorless solid (22.2 mg, 30.0 μmol, 41% over two steps, d.r. = 77:23). Diastereomerically pure material was obtained by preparative TLC (*n*-pentane:CH_2Cl_2 1:2): m.p. 251.4 °C (decomp.); °C; R_f 0.26 (*n*-pentane:CH_2Cl_2 1:1); $[\alpha]_D$ –478 (*c* 1.0 in $CDCl_3$); ν_{max} (neat): 3052w, 2852w, 1725m, 1693m, 1678s, 1596w, 1503w, 1425w, 1309m, 1267m, 1235m, 1101m, 1033w, 822s, 742s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.69 (1H, d, ^4J 0.8, C1*H*), 7.98–7.94 (1H, m, C49*H*), 7.91–7.87 (2H, m, C14*H*, C16*H*), 7.84 (1H, d, ^3J 8.2, C6*H*), 7.83–7.79 (2H, m, C26*H*, C4*H*), 7.76 (1H, d, ^3J 8.3, C24*H*), 7.72 (1H, d, ^3J 8.6, C3*H*), 7.44–7.37 (6H, m, C27*H*, C29*H*, C36*H*, C46*H*, C47*H*, C48*H*), 7.34–7.28 (3H, m, C7*H*, C13*H*, C37*H*), 7.27–7.21 (2H, m, C17*H*, C23*H*), 7.16 (1H, ddd, ^3J 8.5, 6.8, ^4J 1.4, C28*H*), 7.08 (1H, ddd, ^3J 8.4, 6.7, ^4J 1.4, C38*H*), 6.92 (1H, d, ^3J 8.5, C9*H*), 6.69 (1H, dd, ^3J 8.5, ^4J 0.7, C39*H*), 6.44 (1H, d, ^3J 8.5, C34*H*), 6.40 (1H, dd, ^3J 8.4, ^4J 0.6, C44*H*), 6.33 (1H, d, ^3J 8.6, C19*H*), 6.26 (1H, ddd, ^3J 8.3, 6.8, ^4J 1.3, C8*H*), 6.09 (1H, ddd, ^3J 8.4, 6.9, ^4J 1.3, C18*H*), 5.93 (1H, d, ^3J 8.3, C43*H*), 5.60 (1H, d, ^3J 8.6, C33*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 192.3 (*C1*), 145.2 (*C11*), 141.1 (*C21*), 138.2 (*C31*), 137.6 (*C41*), 136.7 (*C5*), 136.7 (*C42*), 135.3 (*C20*), 134.1 (*C32*), 133.9 (*C30*), 133.7 (*C45*), 133.6 (*C15*), 133.5 (*C25*), 133.4 (*C10*), 133.3 (*C22*), 133.0 (*C35*), 132.4 (*C40*), 132.2 (*C23*), 131.8 (*C50*), 131.5 (*C33*), 131.3 (*C12*), 130.5 (*C43*), 130.0 (*C2*), 129.8 (*C13*), 129.6 (*C29*), 128.3 (*C4*), 128.1 (*C7*), 128.1 (*C46*), 128.0 (*C6*, *C26*), 127.8 (*C49*), 127.7 (*C36*), 127.5 (*C14*), 127.5 (*C19*), 127.2 (*C24*), 127.2 (*C16*), 126.9 (*C9*), 126.9 (*C48*), 126.5 (*C8*), 126.4 (*C18*), 126.3 (*C47*), 126.2 (*C17*, *C39*), 126.0 (*C27*), 125.7 (*C34*), 125.6 (*C37*), 125.6 (*C38*), 125.3 (*C44*), 125.1 (*C28*), 124.8 (*C51*), 122.2 (*C3*); MALDI-FTICR: m/z calcd. for $C_{51}H_{31}BrO^{+\bullet}$ 738.1558 found 738.1545 [$M^{+\bullet}$]. Examination of catalysts and conditions can be found on page S21-S22. No unexpected or unusually high safety hazards were encountered.

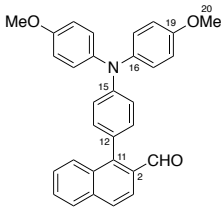
Catalyst-controlled Stereodivergent Synthesis, Triaryl Amine End-Group

(*Z*)-4-(2-((4-(Bis(4-methoxyphenyl)amino)phenyl)(hydroxy)methyl)phenyl)but-3-en-1-ol (diol E)



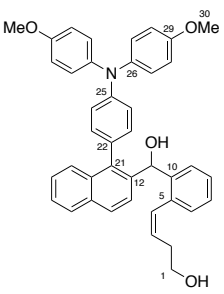
Prepared according to the general procedure **A** using 4-(bis(4-methoxyphenyl) amino)benzaldehyde (2.00 g, 6.00 mmol, 1.00 eq.), (*Z*)-4-(2-bromophenyl)but-3-en-1-ol (370 mmolL^{-1}, 2.04 g, 9.00 mmol, 1.50 eq.), *n*-Bu_2Mg (0.55 molL^{-1}, 8.51 mL, 4.68 mmol, 0.78 eq.) and *n*-BuLi (1.51 molL^{-1}, 6.20 mL, 9.36 mmol, 1.56 eq.), to yield after column chromatography (*n*-pentane:Et_2O 1:1 to 0:1) the desired diol as a pale yellow solid (2.23 g, 4.62 mmol, 77%): m.p. 51.3-55.0 °C; R_f 0.51 (*n*-pentane:Et_2O 1:3); ν_{max} (neat): 3352w, 3001w, 2356w, 2055w, 1605w, 1501s, 1236s, 1175w, 1106w, 1031m, 826m 762w; ^{1}H NMR (500 MHz, C_6D_6): δ = 7.66 (1H, d, ^3J 7.7, C9*H*), 7.24 (2H, d, ^3J 8.4, C13*H*), 7.13 (1H, d, ^3J 7.0, C6*H*), 7.11–7.05 (8H, m, C7*H*, C8*H*, C14*H*, C17*H*), 6.72 (4H, d, ^3J 8.6, C18*H*), 6.62 (1H, d, ^3J 11.5, C4*H*), 5.91 (1H, s, C11*H*), 5.52 (1H, ddd, ^3J 11.3, 7.5, 7.5, C3*H*), 3.30 (6H, s, C20*H*), 3.19 (2H, dd, ^3J 6.4, 6.2, C1*H*), 2.17–2.08 (6H, m, C2*H*), 2.05–1.96 (1H, m, C2*H*); ^{13}C NMR (126 MHz, C_6D_6): δ = 156.4 (*C19*), 148.5 (*C15*), 143.1 (*C10*), 141.7 (*C16*), 136.3 (*C12*), 136.0 (*C5*), 130.6 (*C4*), 130.4 (*C3*), 129.9 (*C6*), 128.3 (*C13*), 127.6 (*C7*/*C8*), 127.3 (*C9*), 127.1 (*C7*/*C8*), 126.9 (*C17*), 121.1 (*C14*), 115.2 (*C18*), 73.0 (*C11*), 62.0 (*C1*), 55.0 (*C20*), 32.0 (*C2*); ESI-MS: m/z calcd. for $C_{21}H_{21}NO_4Na^+$ 504.2145 found 504.2146 [M+Na^+]. No unexpected or unusually high safety hazards were encountered.

1-(4-(Bis(4-methoxyphenyl)amino)phenyl)-2-naphthaldehyde



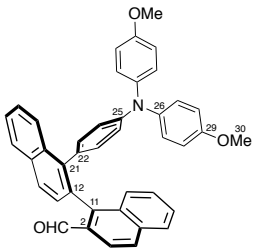
The in situ double-oxidation was performed according to the general procedure **B** using diol **E** (1.30 g, 2.70 mmol, 1.00 eq.) and IBX (2.27 g, 8.10 mmol, 3.00 eq.) with 3 h reaction time. To the keto-aldehyde solution *rac*-(±)-5-(2-pyrrolidinyl)-1*H*-tetrazole (150 mg, 1.08 mmol, 40 mol%) in DMF (43 mL) and H_2O (135 mL) was added and the mixture was vigorously stirred at RT for 17 h. The layers were separated and the aq. layer was extracted with CH_2Cl_2 (150 mL). The combined organic layers were concentrated *in vacuo*, the residue dissolved in Et_2O (150 mL). The resulting solution was washed with H_2O (4x 150 mL) to remove the remaining DMF. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude aldol addition product was dissolved in $CHCl_3$ (135 mL) and Amberlite® IRA-96 (6.30 g, washed with 2x MeOH and 2x CH_2Cl_2) was added. The mixture was stirred for 2 h at RT, filtered, and concentrated *in vacuo* to give the crude aldehyde. Purification by column chromatography (*n*-pentane:Et_2O 1:1) yielded 1-(4-(bis(4-methoxyphenyl)amino)phenyl)-2-naphthaldehyde as a yellow solid (890 mg, 1.94 mmol, 72% over two steps): m.p. 72.8 °C (decomp.); R_f 0.76 (*n*-pentane:Et_2O 2:1); ν_{max} (neat): 2835w, 1685m, 1602m, 1501s, 1461m, 1382w, 1284m, 1236s, 1179m, 1107w, 1032m, 908w, 821s, 749m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.01 (1H, d, ^3J 0.7, C1*H*), 8.04 (1H, d, ^3J 8.6, C3*H*), 7.92–7.88 (2H, m, C6*H*, C9*H*), 7.87 (1H, d, ^3J 8.4, C4*H*), 7.62 (1H, ddd, ^3J 8.2, 6.9, ^4J 1.3, C7*H*), 7.50 (1H, ddd, ^3J 8.3, 7.1, ^4J 1.4, C8*H*), 7.20–7.16 (6H, m, C13*H*, C17*H*), 7.06–7.02 (2H, m, C14*H*), 6.92–6.88 (4H, m, C18*H*), 3.82 (6H, s, C20*H*). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 193.4 (*C1*), 156.4 (*C19*), 149.1 (*C15*), 147.1 (*C11*), 140.6 (*C16*), 136.3 (*C5*), 132.9 (*C10*), 132.0 (*C13*), 131.6 (*C2*), 128.8 (*C7*), 128.4 (*C6*), 128.1 (*C4*), 128.0 (*C9*), 127.3 (*C17*), 126.8 (*C8*), 126.0 (*C12*), 122.4 (*C3*), 119.0 (*C14*), 115.0 (*C18*), 55.6 (*C20*); ESI-MS: m/z calcd. for $C_{31}H_{25}NO_3^{\bullet+}$ 459.1829 found 459.1827 [$M^{\bullet+}$]. No unexpected or unusually high safety hazards were encountered.

(*Z*)-4-(2-((1-(4-(Bis(4-methoxyphenyl)amino)phenyl)naphthalen-2-yl)(hydroxy)methyl)phenyl) but-3-en-1-ol (diol F)



Prepared according to the general procedure **A** using 1-(4-(bis(4-methoxyphenyl)amino) phenyl)-2-naphthaldehyde (846 mg, 1.84 mmol, 1.00 eq.), (*Z*)-4-(2-bromophenyl)but-3-en-1-ol (370 mmolL^{-1}, 627 mg, 2.76 mmol, 1.50 eq.), *n*-Bu_2Mg (0.55 molL^{-1}, 627 mg, 2.76 mmol, 0.78 eq.) and *n*-BuLi (1.51 molL^{-1}, 1.91 mL, 2.87 mmol, 1.56 eq.), to yield after column chromatography (*n*-pentane:Et_2O 1:1 to 0:1) the desired diol as a pale yellow solid (846 mg, 1.39 mmol, 76%): m.p. 87.4–90.7 °C; R_f 0.70 (*n*-pentane:Et_2O 1:3); ν_{max} (neat): 3349w, 2949w, 2358w, 1604w, 1501s, 1462w, 1385w, 1236s, 1177w, 1106w, 823m, 756w; ^{1}H NMR (500 MHz, C_6D_6): δ = 8.19 (1H, d, ^3J 8.6, C13*H*), 7.81–7.77 (2H, m, C14*H*, C19*H*), 7.71 (1H, dd, ^3J 8.0, ^4J 1.0, C16*H*), 7.48–7.44 (1H, m, C9*H*), 7.26 (1H, ddd, ^3J 8.1, 6.8, ^4J 1.3, C17*H*), 7.23–7.19 (5H, m, C18*H*, C27*H*), 7.16 (1H, dd, ^3J 8.3, ^4J 2.5, C24*H*/C24'*H*), 7.09 (1H, dd, ^3J 8.4, ^4J 2.1, C23*H*/C23'*H*), 7.06–7.01 (3H, m, C6*H*, C7*H*, C8*H*), 6.93 (1H, dd, ^3J 8.4, ^4J 2.4, C24*H*, C24'*H*), 6.81–6.77 (4H, m, C28*H*), 6.61 (1H, dd, ^3J 8.4, ^4J 2.0, C23*H*/C23'*H*), 6.30 (1H, d, ^3J 11.5, C4*H*), 6.28 (1H, s, C11*H*), 5.54–5.47 (1H, m, C3*H*), 3.98 (1H, s, O*H*), 3.33 (6H, s, C30*H*), 3.21–3.10 (2H, m, C1*H*), 2.29–2.19 (1H, m, C2*H*), 2.00 (1H, s, O*H*), 1.83–1.74 (1H, m, C2*H*); ^{13}C NMR (126 MHz, C_6D_6): δ = 156.6 (*C29*), 148.4 (*C25*), 143.6 (*C10*), 141.6 (*C26*), 139.4 (*C12*), 138.2 (*C21*), 137.0 (*C5*), 134.0 (*C20*), 133.6 (*C15*), 132.0 (*C23*), 131.2 (*C4*), 131.0 (*C23*'), 130.9 (*C3*), 129.6 (*C6*/*C7*/*C8*), 128.6 (*C22*), 128.4 (*C9*), 128.3 (*C16*), 127.8 (*C6*/*C7*/*C8*), 127.5 (*C14*), 127.2 (*C19*), 127.2 (*C6*/*C7*/*C8*), 127.0 (*C27*), 126.1 (*C18*), 125.8 (*C17*), 125.3 (*C13*), 121.0 (*C24*'), 120.7 (*C24*), 115.3 (*C28*), 70.7 (*C11*), 61.6 (*C1*), 55.1 (*C30*), 31.6 (*C2*); ESI-MS: m/z calcd. for $C_{41}H_{37}NO_4Na^+$ 630.2615 found 630.2614 [M+Na^+]. No unexpected or unusually high safety hazards were encountered.

(S_a)-1'-(4-(bis(4-methoxyphenyl)amino)phenyl)-[1,2'-binaphthalene]-2-carbaldehyde, (S_a)-18

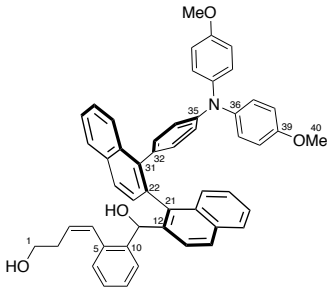


(S_a)-**18**

The in situ double-oxidation was performed according to the general procedure **B** using diol **F** (835 mg, 1.37 mmol, 1.00 eq.) and IBX (1.15 g, 4.11 mmol, 3.00 eq.) with 3 h reaction time. To the keto-aldehyde solution (*S*)-(–)-5-(2-pyrrolidinyl)-1*H*-tetrazole (76.3 mg, 548 µmol, 40 mol%) in DMF (22 mL) and citrate buffer (pH 5, 68 mL) was added and the mixture was vigorously stirred at RT for 60 h. The layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 150 mL). The combined organic layers were concentrated *in vacuo* and the residue was redissolved in Et_2O (150 mL). The resulting solution was washed with H_2O (4x 150 mL) to remove the remaining DMF. The organic phases were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The crude aldol addition product was dissolved in $CHCl_3$ (135 mL) and Amberlite® IRA-96 (8.35 g, washed with 2x MeOH and 2x CH_2Cl_2) was added. The mixture was stirred for 6 h at RT, filtered, and concentrated *in vacuo* to give the crude aldehyde. Purification by column chromatography (*n*-pentane:Et_2O 1:1) yielded (S_a)-**17** as a yellow solid (516 mg, 881 µmol, 64%): m.p. 102.8–105.8 °C; R_f 0.62 (*n*-pentane:Et_2O 2:1); $[\alpha]_D$ –279 (*c* 0.5 in $CHCl_3$); ν_{max} (neat): 2952w, 2836w, 1692m, 1606w, 1504s, 1241s, 1037w, 826m, 754m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.87 (1H, d, ^4J 0.8, C1*H*), 8.01 (1H, d, ^3J 8.2, C16*H*), 7.99 (1H, d, ^3J 8.3, C14*H*), 7.92 (1H, d, ^3J 8.5, C3*H*), 7.89–7.85 (2H, m, C6*H*, C19*H*), 7.83 (1H, d, ^3J 8.6, C4*H*), 7.64–7.58 (2H, m, C9*H*, C17*H*), 7.56 (1H ddd, ^3J 8.2, 6.9, ^4J 1.3, C7*H*), 7.54–7.50 (2H, m, C13*H*, C18*H*), 7.39 (1H, ddd, ^3J 8.3, 7.0, ^4J 1.4, C8*H*), 6.94 (1H, dd, ^3J 8.5, ^4J 2.1, C23*H*), 6.87–6.83 (4H, m, C27*H*), 6.78–6.72 (5H, m, C24*H*, C28*H*), 6.55 (1H, dd, ^3J 8.6, ^4J 2.3, C23'*H*), 6.42 (1H, dd, ^3J 8.4, ^4J 2.4, C24'*H*), 3.77 (6H, s, C30*H*); ^{13}C NMR (126 MHz, C_6D_6): δ = 192.5 (*C1*), 155.8 (*C29*), 147.6 (*C25*), 146.7 (*C11*), 140.9 (*C26*), 140.7 (*C21*), 136.0 (*C5*), 133.8 (*C15*), 133.1 (*C10*), 132.8 (*C20*), 132.0 (*C12*), 131.0 (*C23*), 130.9 (*C2*), 130.3 (*C23*'), 130.1 (*C22*), 128.7 (*C13*), 128.7 (*C7*), 128.3 (*C16*), 128.3 (*C6*), 128.2 (*C9*), 128.1 (*C4*), 127.2 (*C14*), 127.1 (*C19*), 126.9 (*C18*), 126.8 (*C8*), 126.6 (*C17*), 126.4 (*C27*), 121.9 (*C3*), 120.1 (*C24*'), 120.0 (*C24*), 114.7 (*C28*), 55.6 (*C30*); ESI-

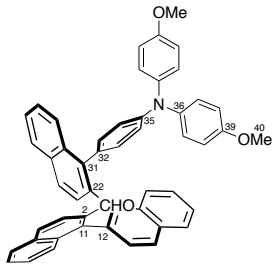
MS: m/z calcd. for $C_{41}H_{31}NO_3^{\bullet+}$ 585.2298 found 2301 [$M^{\bullet+}$]; The e.r. (>99:1) of (S_a)-**17** was determined by HPLC using a *Chiralcel AD-H* column (1.0 mLmin^{-1}, *i*-PrOH:*n*-heptane 10:90): (S_a) t_R = 10.1 min and (R_a) t_R = 11.5 min; racemic reference material was obtained with *rac*-5-(2-pyrroidinyl)-1*H*-tetrazole as catalyst. No unexpected or unusually high safety hazards were encountered.

(*Z*,*S*$_a$)-4-(2-((1'-(4-(Bis(4-methoxyphenyl)amino)phenyl)-[1,2'-binaphthalen]-2-yl)(hydroxy) methyl)phenyl)but-3-en-1-ol (diol G)



Prepared according to the general procedure **A** using (S_a)-**18** (464 mg, 792 µmol, 1.00 eq.), (Z)-4-(2-bromophenyl)but-3-en-1-ol (370 mmolL^{-1}, 270 mg, 1.19 mmol, 1.50 eq.), *n*-Bu_2Mg (0.55 molL^{-1}, 1.12 mL, 618 µmol, 0.78 eq.) and *n*-BuLi (1.51 molL^{-1} , 824 µL, 1.24 mmol, 1.56 eq.), to yield after column chromatography (*n*-pentane:Et_2O 1:1 to 0:1) the desired diol as a pale yellow solid (480 mg, 654 µmol, 83%): m.p. 111.1–112.9 °C; R_f 0.62 (*c-hexane*:EtOAc 1:1); $[\alpha]_D$ –165 (*c* 1.0 in $CHCl_3$); ν_{max} (neat): 3389br, 3054w, 2949w, 1604w, 1502s, 1462m, 1378w, 1318m, 1281m, 1237s, 1177m, 1107w, 1033s, 823s, 750m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.18 (1H, d, ^3J 8.1, C29*H*), 8.05 (1H, d, ^3J 8.6, C13*H*), 7.71 (1H, d, ^3J 7.9, C26*H*), 7.67 (1H, d, ^3J 8.6, C14*H*), 7.64–7.59 (2H, m, C9*H*, C16*H*), 7.54 (1H, dd, ^3J 8.4, ^4J 2.2, C33*H*), 7.50–7.45 (2H, m, C19*H*, C24*H*), 7.34–7.27 (2H, m, C27*H*, C28*H*), 7.22 (1H, ddd, ^3J 8.1, 6.9, ^4J 1.3, C17*H*), 7.13 (1H, ddd, ^3J 8.2, 6.9, ^4J 1.4, C18*H*), 7.10–7.03 (3H, m, C7*H*, C8*H*, C34*H*), 7.02–6.98 (2H, m, C6*H*, C23*H*), 6.94–6.85 (5H, m, C33'*H*, C37*H*), 6.66–6.62 (4H, m, C38*H*), 6.56 (1H, dd, ^3J 8.6, ^4J 2.5, C34'*H*), 6.20 (1H, s, C11*H*), 5.96 (1H, d, ^3J 11.5, C4*H*), 5.20 (1H, ddd, ^3J 11.3, 9.2, ^4J 5.8, C3*H*), 3.28 (6H, s, C40*H*), 2.99–2.86 (2H, m, C1*H*), 2.07–1.98 (1H, m, C2*H*), 1.63–1.54 (1H, m, C2*H*); ^{13}C NMR (126 MHz, C_6D_6): δ = 156.5 (*C39*), 148.4 (*C35*), 143.0 (*C10*), 141.2 (*C36*), 139.1 (*C31*), 139.0 (*C12*), 137.3 (*C21*), 137.0 (*C5*), 135.5 (*C22*) 134.0 (*C20*), 134.0 (*C25*), 133.6 (*C30*), 133.3 (*C15*), 131.6 (*C33*), 131.4 (*C33*'), 130.9 (*C4*), 130.5 (*C32*), 130.4 (*C3*), 130.1 (*C23*), 129.6 (*C6*), 128.5 (*C26*), 128.4 (*C16*), 128.3 (*C9*), 128.1 (*C14*), 127.5 (*C29*), 127.4 (*C19*), 127.4 (*C8*), 127.1 (*C7*), 127.1 (*C24*), 127.0 (*C37*), 126.5 (*C28*), 126.2 (*C18*), 126.2 (*C27*), 125.7 (*C17*), 125.6 (*C13*), 120.2 (*C34*'), 119.8 (*C34*), 115.1 (*C38*), 70.7 (*C11*), 61.7 (*C1*), 55.0 (*C40*), 31.5 (*C2*); ESI-MS: m/z calcd. for $C_{51}H_{43}NO_4Na^+$ 756.3084 found 756.3075. No unexpected or unusually high safety hazards were encountered.

(*Z*,*R*$_a$,*S*$_a$)-1''-(4-(Bis(4-methoxyphenyl)amino)phenyl)-[1:2']-ternaphthalene-2-carbaldehyde, (*R*$_a$,*S*$_a$)-19

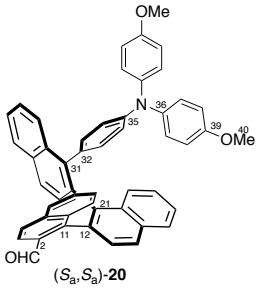


(R_a,S_a)-**19**

The in situ double-oxidation was performed according to the general procedure **B** using diol **G** (50.0 mg, 68.1 µmol, 1.00 eq.), IBX (57.2 mg, 204 µmol, 3.00 eq.) and 2 h reaction time. To the keto-aldehyde solution aq. KOH (1.0 molL^{-1}, 3.4 mL) was added. The mixture was stirred for 2 h at RT, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:Et_2O 5:1) yielded the aldol condensation product as a yellow solid (21.0 mg, 29.0 µmol, 43% over two steps, d.r. = 95:5): m.p. 160.2–162.5 °C; R_f 0.44 (*c*-hexane:EtOAc 4:1); $[\alpha]_D$ –84.7 (*c* 1.0 in $CHCl_3$); ν_{max} (neat): 3054w, 2952w, 2835w, 1688m, 1603m, 1503s, 1374w, 1286m, 1239s, 1179w, 1107w, 1035m, 909m, 823s, 731s, 647w; ^{1}H NMR (500 MHz, $CDCl_3$, line-broadening due to triaryl amine rotation): δ = 8.57 (1H, d, ^4J 0.7, C1*H*), 8.00 (1H, d, ^3J 8.3, C16*H*), 7.93 (1H, d, ^3J 8.5, C14*H*), 7.78 (1H, d, ^3J 8.6, C3*H*), 7.70–7.60 (5H, m, C4*H*, C6*H*, C9*H*, C26*H*, C29*H*), 7.58 (1H, ddd, ^3J 8.1, 6.8, ^4J 1.2, C17*H*), 7.55–7.52 (2H, m, C19*H*, C24*H*), 7.49 (1H, d, ^3J 8.5, C23*H*), 7.45 (1H, ddd, ^3J 8.3, 6.8, ^4J 1.4, C18*H*), 7.40 (1H, ddd, ^3J 8.1, 6.9, ^4J 1.2, C7*H*), 7.38–7.31 (2H, m, C8*H*, C27*H*), 7.29 (1H, d, ^3J 8.4, C13*H*), 7.28–7.24 (1H, m, C28*H*), 7.24–7.16 (4H, m br, C37*H*/C38*H*), 6.89–6.84 (4H, m br, C37*H*/C38*H*), 6.79–6.73 (1H, m br, C33*H*/C34*H*),

6.54–6.48 (1H, m br, C33*H*/C34*H*), 6.40–6.31 (1H, m br, C33*H*/C34*H*), 3.80 (6H, s, C40*H*); ^{13}C NMR (126 MHz, $CDCl_3$, line-broadening due to triaryl amine rotation): δ = 192.5 (*C1*), 156.3 (*C39*), 148.1 (*C35*), 145.1 (*C11*), 140.7 (*C36*), 139.6 (*C21*), 138.8 (*C31*), 135.4 (*C5*), 134.7 (*C20*), 134.0 (*C22*), 133.3 (*C15*, *C25*), 132.9 (*C2*, *C30*), 132.6 (*C32*/*C33*/*C33*'), 132.0 (*C12*), 131.3 (*C10*), 130.6 (*C23*), 130.5 (*C32*/*C33*/*C33*'), 130.0 (*C13*), 128.5 (*C9*), 128.4 (*C16*), 128.3 (*C4*), 128.2 (*C7*), 128.0 (*C6*), 127.9 (*C26*), 127.8 (*C32*/*C33*/*C33*'), 127.5 (*C14*), 127.4 (*C19*), 127.1 (*C18*), 126.9 (*C29*), 126.5 (*C17*), 126.0 (*C24*), 125.9 (*C8*), 125.8 (*C28*), 125.8 (*C37*), 125.7 (*C27*), 122.0 (*C3*), 118.2 (*C34*/*C34*'), 118.0 (*C34*/*C34*'), 114.8 (*C38*), 55.6 (*C40*); ESI-MS: m/z calcd. for $C_{51}H_{37}NO_3Na^+$ 734.2666 found 734.2669 [M+Na^+]. Test-reaction for the aldol condensation were performed with $KOH_{(S)}$ in the absence of water and showed the following selectivities: $CHCl_3$ 85:15, toluene 80:20, THF (>90:10). No unexpected or unusually high safety hazards were encountered.

(*Z*,R_a,S_a)-1''-(4-(Bis(4-methoxyphenyl)amino)phenyl)-[1:2']-ternaphthalene-2-carbaldehyde, (S_a,S_a)-20



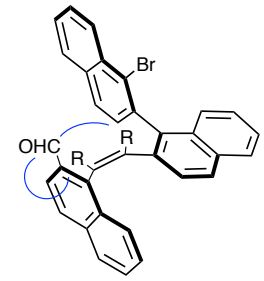
(S_a,S_a)-**20**

The in situ double-oxidation was performed according to the general procedure **B** using diol **G** (147 mg, 200 µmol, 1.00 eq.), IBX (168 mg, 600 µmol, 3.00 eq.) and 2 h reaction time. To the keto-aldehyde solution *N*-benzylcinchonium chloride (8.42 mg, 20.0 µmol, 10.0 mol%) and aq. KOH (1.0 $molL^{-1}$, 5.7 mL) were added. The mixture was stirred for 16 h at RT, H_2O (10 mL) was added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by preparative TLC (*n*-pentane:Et_2O 2:1) yielded a mixture of (R_a,S_a)-**19** and (S_a,S_a)-**18** (21.0 mg, 29.0 µmol, 43% over two steps, d.r. = 35:65). Diastereomerically pure material was obtained by preparative TLC (*c*-hexane:EtOAc 4:1): R_f 0.40 (*c*-hexane:EtOAc 4:1); $[\alpha]_D$ –272.1 (*c* 0.2 in $CHCl_3$); ν_{max} (neat): 3054w, 2928w, 2849w, 1678m, 1604m, 1503s, 1462w, 1379w, 1239s, 1180w, 1104w, 1034m, 909m, 824s, 731s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.93 (1H, d, ^4J 0.9, C1*H*), 8.01 (1H, dd, ^3J 8.5, ^4J 1.1, C16*H*), 7.97 (1H, d, ^3J 8.3, C14*H*), 7.81 (1H, d, ^3J 8.1, C26*H*), 7.79 (1H, d, ^3J 8.5, C24*H*), 7.71–7.67 (2H, m, C3*H*, C6*H*), 7.64 (1H, d, ^3J 8.8, C4*H*), 7.61–7.56 (2H, m, C17*H*, C19*H*), 7.48–7.43 (2H, m, C13*H*, C18*H*), 7.42–7.36 (4H, m, C7*H*, C23*H*, C27*H*, C29*H*), 7.25–7.21 (2H, m, C8*H*, C28*H*), 7.07–7.02 (4H, m, C37*H*), 6.92 (1H, d, ^3J 8.6, C9*H*), 6.86–6.81 (4H, m, C38*H*), 6.51 (dd, ^3J 8.4, ^4J 1.9, C33*H*), 6.41 (1H, dd, ^3J 8.4, ^4J 2.4, C34*H*) 5.80 (1H, dd, ^3J 8.4, ^4J 2.3, C34'*H*) 5.44 (1H, dd, ^3J 8.4, ^4J 1.9, C33'*H*), 3.80 (6H, s, C40*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 192.4 (*C1*), 156.2 (*C39*), 147.1 (*C35*), 145.7 (*C11*), 141.1 (*C21*), 140.6 (*C36*), 138.9 (*C31*), 136.1 (*C5*), 134.6 (*C20*), 133.9 (*C22*), 133.4 (*C25*), 133.4 (*C15*), 133.1 (*C30*), 132.9 (*C10*), 131.8 (*C33*'), 131.7 (*C12*), 130.5 (*C2*), 130.2 (*C23*), 129.9 (*C33*), 129.4 (*C13*), 128.6 (*C32*), 128.3 (*C16*), 128.2 (*C26*), 128.1 (*C4*), 128.1 (*C7*), 127.9 (*C6*, *C9*), 127.8 (*C19*), 127.3 (*C37*), 127.0 (*C14*), 126.9 (*C18*, *C24*, *C29*), 126.7 (*C8*), 126.6 (*C17*), 125.9 (*C28*), 125.8 (*C27*), 121.9 (*C3*), 117.5 (*C34*), 117.4 (*C34*'), 114.8 (*C38*), 55.6 (*C40*); ESI-MS: m/z calcd. for $C_{51}H_{37}NO_3Na^+$ 734.2666 found 734.2669 [M+Na^+]. No unexpected or unusually high safety hazards were encountered.

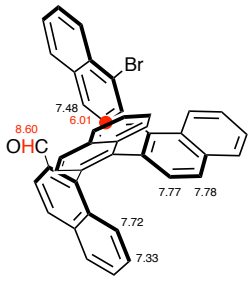
NMR Analysis of the Structures in Solution

strong nOe signal weak nOe signal

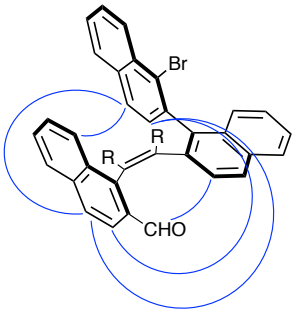
^{1}H signal (in ppm), ring current effect



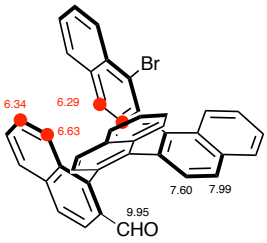
(R_a,S_a,S_a)–**13**



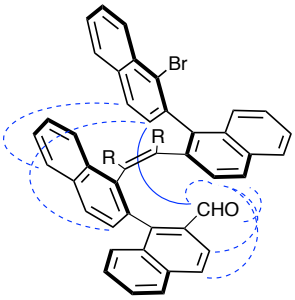
(R_a,S_a,S_a)–**13**



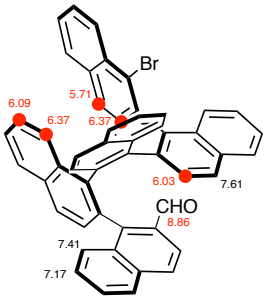
(S_a,S_a,S_a)-**14**



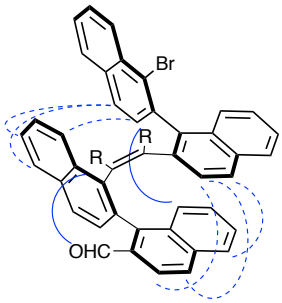
(S_a,S_a,S_a)-**14**



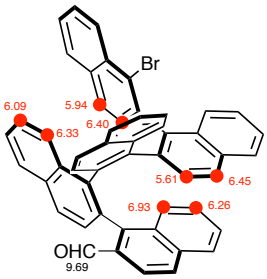
(R_a,S_a,S_a,S_a)-**15**



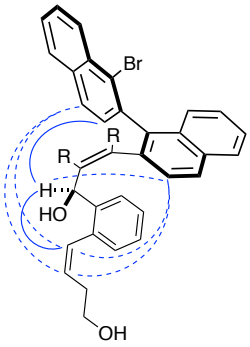
(R_a,S_a,S_a,S_a)-**15**



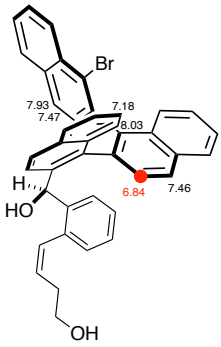
(S_a,S_a,S_a,S_a)-**16**



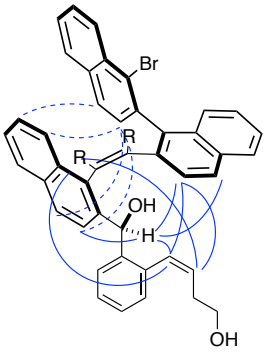
(S_a,S_a,S_a,S_a)-**16**



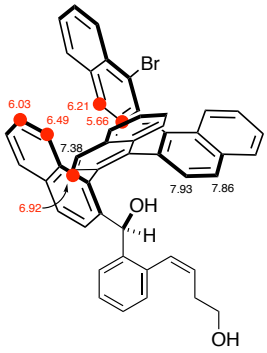
diol **C**



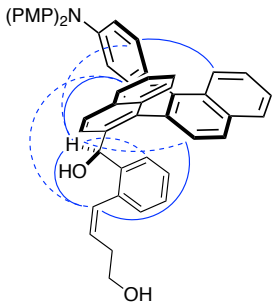
diol **C**



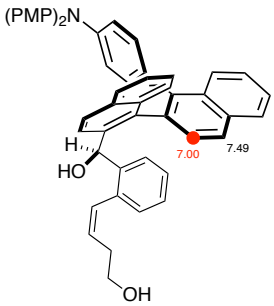
diol **D**



diol **D**



diol **G**



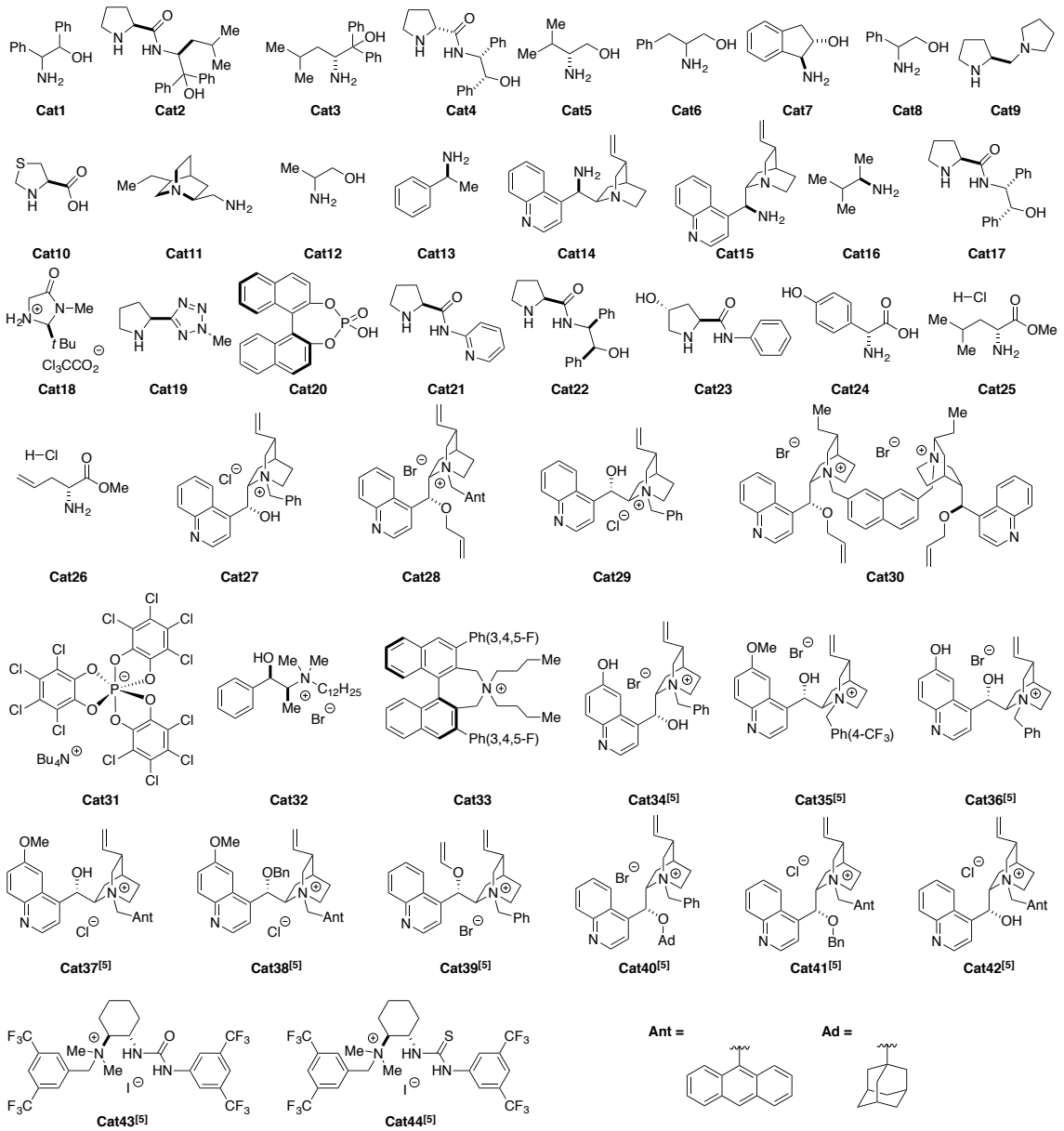
diol **G**

Evaluation of Catalysts and Conditions

General Procedure C for the examination of catalysts and conditions of the diastereoselective arene-forming aldol condensation:

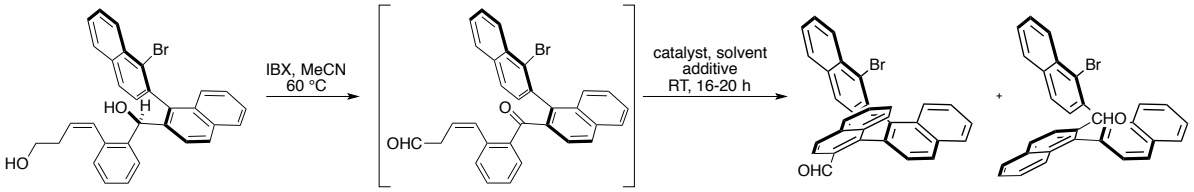
The in situ double-oxidations were performed in batches for several entries (3.0–4.0 mg of the diol per entry) using IBX (5.0–10 eq.) in MeCN (1.0 mL per entry) at 60 °C. After complete oxidation (monitored by ^{1}H NMR) the mixture was filtered, concentrated *in vacuo* and to the residue was added $CHCl_3$ (1.0 mL per entry). The mixture was filtered again and distributed into portions. For entries with $CHCl_3$ as solvent: co-solvents and catalysts were added directly. For entries with other solvents: solution was concentrated *in vacuo* and the residue dissolved in the solvent of choice. For entries with a temperature below RT: solution was cooled and catalyst (followed by base) was added. The mixtures were stirred for 14–20 h and poured on aq. sat. NH_4Cl (2.5 mL) and H_2O (2.5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (5.0 mL). The combined organic layers were concentrated *in vacuo* (co-evaporation with toluene for entries with DMF) and analyzed by ^{1}H NMR. The yields were estimated by integration of the product aldehyde peaks in comparison with aromatic signals.

Catalyst list[5]



Initial examination of catalysts and conditions for (R_a,S_a)-7 and (S_a,S_a)-8

The reactions were performed according to the general procedure **B**.



6 (S_a,S_a)-**8** (R_a,S_a)-**7**

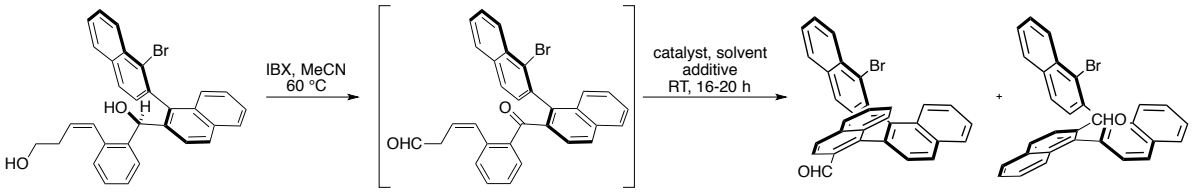
Entry	Catalyst[1]	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive	d.r. 8:7	Estimated Yield
1	(*S*)-Tet	$CDCl_3$	DMF	H_2O	3/1/1		92:8	46%[2]
2	(*R*)-Tet	$CDCl_3$	DMF	H_2O	3/1/1		2:98	<5%[2]
3	L-Met	$CDCl_3$	DMF	H_2O	3/1/1		92:8	<5%
4	(*S*,*S*)-Cat1	$CDCl_3$	DMF	H_2O	3/1/1		97:3	<5%
5	Cat2	$CDCl_3$	DMF	H_2O	3/1/1			<5%
6	Cat3	$CDCl_3$	DMF	H_2O	3/1/1			<5%
7	Cat4	$CDCl_3$	DMF	H_2O	3/1/1			<5%
8	Cat5	$CDCl_3$	DMF	H_2O	3/1/1			<5%
9	(*S*)-Cat6	$CDCl_3$	DMF	H_2O	3/1/1		97:3	~35%
10	Cat7	$CDCl_3$	DMF	H_2O	3/1/1		40:60	<5%
11	(*R*,*S*)-Cat1	$CDCl_3$	DMF	H_2O	3/1/1		95:5	~15%
12	(*S*,*R*)-Cat1	$CDCl_3$	DMF	H_2O	3/1/1		36:64	<5%
13	(*R*,*R*)-Cat1	$CDCl_3$	DMF	H_2O	3/1/1		8:92	~15%
14	(*R*)-Cat6	$CDCl_3$	DMF	H_2O	3/1/1		12:88	~20%
15	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1		10:90	~20%
16	Glycinol	$CDCl_3$	DMF	H_2O	3/1/1		36:64	<5%
17	*i*-Pr_2NH	$CDCl_3$	DMF	H_2O	3/1/1		7:93	~10%
18	Pyrrolidine	$CDCl_3$	DMF	H_2O	3/1/1			<5%
19	Piperidine	$CDCl_3$	DMF	H_2O	3/1/1		42:58	~5%
20	Me_2-piperidine	$CDCl_3$	DMF	H_2O	3/1/1		5:95	~5%
21	(H_4)-quinoline	$CDCl_3$	DMF	H_2O	3/1/1			<5%
22	Cy_2NH	$CDCl_3$	DMF	H_2O	3/1/1		<5:95	<5%
23	Bn_2NH	$CDCl_3$	DMF	H_2O	3/1/1			<5%
24	Morpholine	$CDCl_3$	DMF	H_2O	3/1/1			<5%
25	Me_4-piperidine	$CDCl_3$	DMF	H_2O	3/1/1		<5:95	~5%
26	Me_2N-Et-NH_2	$CDCl_3$	DMF	H_2O	3/1/1			~5%
27	Me_2N-Et-NMeH	$CDCl_3$	DMF	H_2O	3/1/1		50:50	<5%
28	Ph_2NH	$CDCl_3$	DMF	H_2O	3/1/1		13:87	<5%
29	Aniline	$CDCl_3$	DMF	H_2O	3/1/1			~5%
30	Me_2NH·HCl	$CDCl_3$	DMF	H_2O	3/1/1			<5%
31	(*R*)-Tet	$CDCl_3$		H_2O	3/0/1		2:98	<5%
32	(*R*)-Tet	$CDCl_3$	DMF	H_2O	30/1/10		2:98	<5%
33	(*R*)-Tet	$CDCl_3$	DMF	H_2O	6/1/1		2:98	<5%
34	(*R*)-Tet	$CDCl_3$	DMF	H_2O	30/1/30		2:98	<5%
35	(*R*)-Tet	$CDCl_3$	Toluene		1/1/0			<5%
36	(*R*)-Tet	$CDCl_3$	Br-benzene		1/1/0			<5%
37	(*R*)-Tet	$CDCl_3$	$MeNO_2$		1/1/0			<5%
38	(*R*)-Tet	$CDCl_3$	$Et(OMe)_2$		1/1/0			<5%
39	(*R*)-Tet	$CDCl_3$	EtOAc		1/1/0			<5%
40	(*R*)-Cat8	DMF			1/0/0			<5%
41	(*R*)-Cat8	DMF	H_2O		10/1/0			<5%
42	(*R*)-Cat8	THF			1/0/0			<5%
43	(*R*)-Cat8	THF	H_2O		10/0/0			<5%
44	(*R*)-Cat8	Toluene			1/0/0			<5%
45	(*R*)-Cat8	Toluene	H_2O		10/0/0			<5%
46	(*R*)-Cat8	$CDCl_3$	DMF		3/1/0			<5%
47	(*R*)-Cat8	DMSO			1/0/0			<5%
48	(*R*,*R*)-Cat1	DMF			1/0/0			<5%
49	(*R*,*R*)-Cat1	DMF	H_2O		10/1/0			<5%
50	(*R*,*R*)-Cat1	THF			1/0/0			<5%
51	(*R*,*R*)-Cat1	THF	H_2O		10/0/0			<5%
52	(*R*,*R*)-Cat1	Toluene			1/0/0			<5%
53	(*R*,*R*)-Cat1	Toluene	H_2O		10/0/0			<5%
54	(*R*,*R*)-Cat1	$CDCl_3$	DMF		3/1/0			<5%
55	(*R*,*R*)-Cat1	DMSO			1/0/0			<5%
56	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	Drop AcOH	19:81	~15%
57	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	Drop HCl (1.0 $molL^{-1}$)		
58	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	Drop conc. NH_4Cl	12:88	~15%
59	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	Drop NaOH (1.0 $molL^{-1}$)	22:78	<5%
60	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	Drop aq. H_2SO_4 (20%)		

Entry	Catalyst[1]	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive	d.r. 8:7	Estimated Yield
61	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	Drop aq. NH_4OH (25%)	10:90	~15%
62	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. Na_2CO_3	8:92	~20%
63	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 5	11:89	~20%
64	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Phosphate buffer pH 8	16:84	<5%
65	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Borate buffer pH 10		
66	(*R*)-Cat8	$CDCl_3$	DMF	H_2O	3/1/1	NH_4OAc (ca 0.2 mg)	16:84	~15%
67	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. Na_2CO_3	8:92	~20%
68	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. $NaHCO_3$	9:91	~5%
69	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. K_2CO_3	6:94	~40%
70	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. Na_2SO_4	11:89	~5%
71	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. Na_2SO_3	10:90	~10%
72	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. KNO_3	9:91	~15%
73	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. NaOAc	12:88	~5%
74	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. NaCl	8:92	~15%
75	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. $CaCl_2$	48:52	<5%
76	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. NaH_2PO_4	7:93	~5%
77	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. Na_2HPO_4	16:84	~5%
78	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6	12:88	~10%
79	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. K_2CO_3 (8.0 $molL^{-1}$)	7:93	~35%
80	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. K_2CO_3 (1.0 $molL^{-1}$)	6:94	~25%
81	(*R*)-Cat8	$CDCl_3$	DMF	Additive	3/1/1	Aq. K_2CO_3 (0.1 $molL^{-1}$)	10:90	~10%
82	(*S*)-Cat6	$CDCl_3$	DMF	H_2O	3/1/1		95:5	~40%
83	(*S*)-Cat6	$CDCl_3$	DMF	Additive	3/1/1	Aq. K_2CO_3 (4.0 $molL^{-1}$)	7:93	~35%
84		$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. K_2CO_3	8:92	48%[2]
85		$CDCl_3$		Additive	3/1/1	Aq. sat. K_2CO_3	18:82	64%[2]
86	Cat27	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	5:95	~60%
87	Cat28	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)		<5%
88	Cat29	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	10:90	~45%
89	Cat30	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	8:92	~35%
90	Cat31	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	21:79	~55%
91	Cat32	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	24:76	~50%
92	Cat33	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	22:78	~20%
93	Cat34	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	34:66	~45%
94	Cat35	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	11:89	~50%
95	Cat36	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	15:85	~35%
96	Cat37	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	31:69	~30%
97	Cat38	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)		<5%
98	Cat39	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	9:91	~35%
99	Cat40	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	5:95	~60%
100	Cat41	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)		<5%
101	Cat42	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	7:93	~45%
102	Cat43	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	26:74	~60%
103	Cat44	$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	53:47	~60%
104		$CDCl_3$		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	23:77	~55%

[1] 40 mol%; [2] isolated yield. (*S*)-Tet: (*S*)-5-(pyrrolidin-2-yl)-1H-tetrazole; (*R*)-Tet: (*R*)-5-(pyrrolidin-2-yl)-1H-tetrazole.

Final examination of catalysts and conditions for (R_a,S_a)-7 and (S_a,S_a)-8

The in situ double-oxidation was performed according to the general procedure **B** using **6** (50.8 mg, 99.7 μmol, 1.00 eq.) and IBX (83.8 mg, 299 μmol, 3.00 eq.) with 4 h reaction time. After the optional solvent switch, catalyst and the additive were added. The mixture was stirred for a given time at RT, aq. sat. NH_4Cl (5.0 mL) and H_2O (5.0 mL) were added, the layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography (*n*-pentane:CH_2Cl_2 4:1 to 1:4) gave the aldol condensation product.

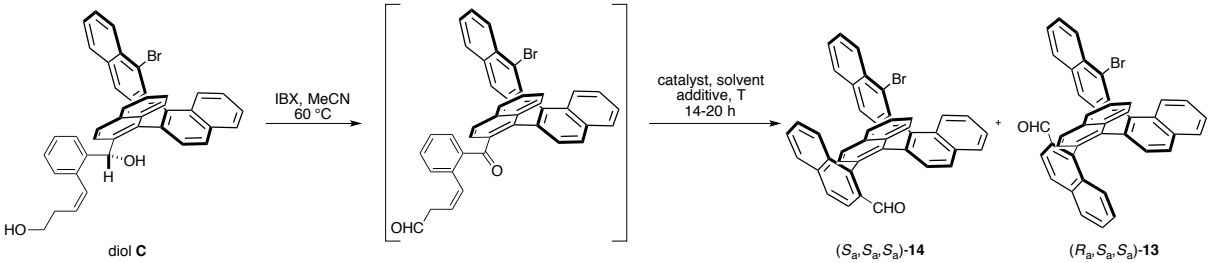


6 (S_a,S_a)-**8** (R_a,S_a)-**7**

Entry	Catalyst	Loading	Time	Solvent 1	Solvent 2	Solvent 3	Solvent ratio	Additive	d.r. 7:8	Isolated Yield
1			24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	80:20	65%
2	(*S*)-Tet	40	24	$CHCl_3$					8:92	13%
3	(*S*)-Tet	40	24	DMF	H_2O				3:97	55%
4	(*S*)-Tet	40	48	$CHCl_3$	DMF	H_2O			4:96	54%
5	(*S*)-Tet	40	48	$CHCl_3$	DMF	Additive		Citrate buffer pH 5	**3:97**	**75%**
6	(*R*)-Tet	40	48	$CHCl_3$	DMF			Citrate buffer pH 5	96:4	64%
7	Cat29	10	24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	89:11	54%
8	Cat33	10	24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	78:22	44%
9	Cat28	10	24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	78:22	18%
10	Cat27	10	24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	94:6	72%
11	Cat27	5	24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	94:6	70%
12	Cat27	1	24	$CHCl_3$	Additive			Aq. KOH (1.0 $molL^{-1}$)	94:6	**69%**

(*S*)-Tet: (*S*)-5-(pyrrolidin-2-yl)-1H-tetrazole; (*R*)-Tet: (*R*)-5-(pyrrolidin-2-yl)-1H-tetrazole.

Examination of catalysts and conditions for (R_a,S_a,S_a)-13 and (S_a,S_a,S_a)-14



diol **C** (S_a,S_a,S_a)-**14** (R_a,S_a,S_a)-**13**

Entry	Catalyst (mol%)	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive	d.r. 14:13	Estimated Yield
1	(*R*,*R*)-Cat1 (40)	$CDCl_3$	DMF	H_2O	3/1/1			<5%
2	(*S*,*S*)-Cat1 (40)	$CDCl_3$	DMF	H_2O	3/1/1			
3	(*R*,*S*)-Cat1 (40)	$CDCl_3$	DMF	H_2O	3/1/1			
4	(*S*,*R*)-Cat1 (40)	$CDCl_3$	DMF	H_2O	3/1/1			
5	(*S*)-Cat6 (40)	$CDCl_3$	DMF	H_2O	3/1/1			<5%
6	(*R*)-Cat6 (40)	$CDCl_3$	DMF	H_2O	3/1/1			<5%
7	(*S*)-Cat8 (40)	$CDCl_3$	DMF	H_2O	3/1/1			<5%
8	(*S*)-Tet (40)	$CDCl_3$	DMF	H_2O	3/1/1			
9	(*R*)-Tet (40)	$CDCl_3$	DMF	H_2O	3/1/1			
10	Cat9 (40)	$CDCl_3$	DMF	H_2O	3/1/1			<5%
11	Cat10 (40)	$CDCl_3$	DMF	H_2O	3/1/1			
12	Cat11 (40)	$CDCl_3$	DMF	H_2O	3/1/1			<5%
13	L-Ile (40)	$CDCl_3$	DMF	H_2O	3/1/1			
14	L-Pro (40)	$CDCl_3$	DMF	H_2O	3/1/1			
15	L-Met (40)	$CDCl_3$	DMF	H_2O	3/1/1			
16	L-Tyr (40)	$CDCl_3$	DMF	H_2O	3/1/1			
17	L-Ala (40)	$CDCl_3$	DMF	H_2O	3/1/1			
18	(*R*,*R*)-Cat1 (40)	$CDCl_3$						
19	(*R*)-Cat6 (40)	$CDCl_3$						<5%
20	(*S*)-Cat12 (40)	$CDCl_3$						<5%
21	(*R*)-Cat8 (40)	$CDCl_3$						
22	(*S*)-Cat11 (40)	$CDCl_3$						<5%
23	Cat13 (40)	$CDCl_3$						
24	Cat14 (40)	$CDCl_3$						
25	Cat15 (40)	$CDCl_3$						
26	Cat16 (40)	$CDCl_3$						
27	Cat17 (40)	$CDCl_3$						<5%
28	L-Lys (40)	$CDCl_3$						
29	(*R*)-Cat6 (40)	DCE					95:5	~10%
30	(*R*)-Cat6 (40)	Toluene					90:10	<5%
31	(*R*)-Cat6 (40)	THF						<5%
32	(*R*)-Cat6 (40)	EtOAc						<5%
33	(*R*)-Cat6 (40)	MeCN						<5%

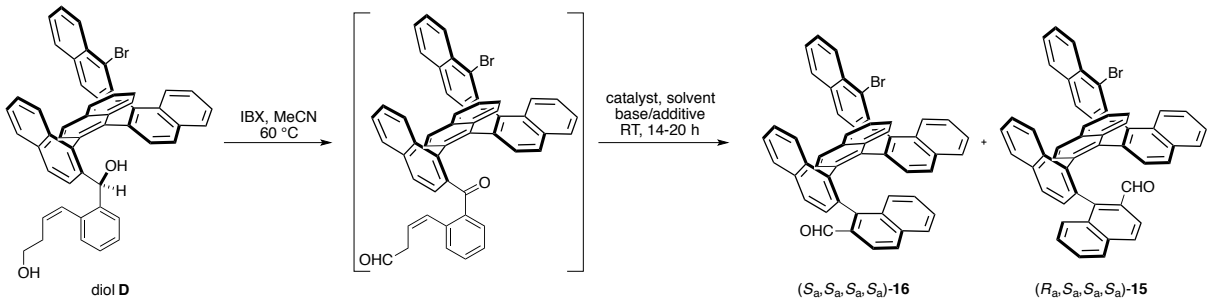
Entry	Catalyst (mol%)	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive	d.r. 14:13	Estimated Yield
34	(*R*)-Cat6 (40)	MTBE						<1%
35	(*R*)-Cat8 (40)	CH_2Cl_2						~5%
36	Cat11 (40)	CH_2Cl_2						<5%
37	(*S*)-Cat12 (40)	CH_2Cl_2						<5%
38	Cat13 (40)	CH_2Cl_2						
39	(*R*,*R*)-Cat1 (40)	CH_2Cl_2						
40	Cat9 (40)	CH_2Cl_2						
41	Cat17 (40)	CH_2Cl_2						
42	Cat18 (40)	CH_2Cl_2						
43	Cat19 (40)	CH_2Cl_2						
44	L -Phe (40)	CH_2Cl_2						<5%
45	L-Ala (40)	CH_2Cl_2						
46	L-Ser (40)	CH_2Cl_2						
47	L -Met (40)	CH_2Cl_2						
48	(*R*)-Tet (40)	CH_2Cl_2						
49	(*R*)-Cat6 (40)[1]	DCE						<1%
50	(*R*)-Cat8 (40)[1]	DCE						<1%
51	(*R*)-Cat6 (40)[2]	DCE						<1%
52	(*R*)-Cat8 (40)[2]	DCE						<1%
53	L-Phe (40)[2]	DCE						<1%
54	(*R*)-Cat12 (40)[2]	DCE						<1%
55	(*S*)-Cat20 (40)	Toluene						<1%
56	(*S*)-Cat20 (40)	CH_2Cl_2						<1%
57	(*S*)-Cat20 (40)	$CDCl_3$						
58	(*S*)-Cat20 (40)	DCE						
59	(*S*)-Cat20 (40)	THF						<1%
60	(*S*)-Cat20 (40)	MTBE						<1%
61	*n*-propylamine (~40)	$CDCl_3$					95:5	<5%
62	*n*-propylamine (~40)	$CDCl_3$	H_2O		7/1/0		95:5	<5%
63	*n*-propylamine (~40)	$CDCl_3$	DMF	H_2O	3/1/1		65:35	<5%
64	(*R*)-Tet (40)	$CDCl_3$						<1%
65	(*R*)-Tet (40)	$CDCl_3$				$KHCO_3$ (ca 10 mg)		<1%
66	(*R*)-Tet (40)	DMF	H_2O		7/1/0		80:20	~10%
67	(*S*)-Tet (40)	$CDCl_3$						<1%
68	(*S*)-Tet (40)	$CDCl_3$				$KHCO_3$ (ca 10 mg)	95:5	<5%
69	(*S*)-Tet (40)	DMF	H_2O		7/1/0		95:5	~5%
70	L-Phe (40)	DMF	H_2O		7/1/0			<1%
71	L-Ala (40)	DMF	H_2O		7/1/0			<1%
72	L-Ser (40)	DMF	H_2O		7/1/0		79:21	20%
73	L-Ile (40)	DMF	H_2O		7/1/0			<1%
74	D-Ile (40)	DMF	H_2O		7/1/0		80:20	20%
75	L-Met (40)	DMF	H_2O		7/1/0			<1%
76	Gly (40)	DMF	H_2O		7/1/0		73:27	10%
77	L-Thr (40)	DMF	H_2O		7/1/0		78:22	20%
78	L-Leu (40)	DMF	H_2O		7/1/0		56:44	<5%
79	L-Tyr (40)	DMF	H_2O		7/1/0			<1%
80	L-Pro (40)	DMF	H_2O		7/1/0			
81	D-Ala (40)	DMF	H_2O		7/1/0		70:30	~10%
82	Cat21 (40)	DMF	H_2O		7/1/0			<1%
83	D-Pro (40)	DMF	H_2O		7/1/0		95:5	<5%
84	D-Val (40)	DMF	H_2O		7/1/0		82:18	~15%
85	(*R*)-Cat8 (40)	DMF	H_2O		7/1/0		95:5	<5%
86	(*R*)-Cat6 (40)	DMF	H_2O		7/1/0		95:5	<5%
87	(*R*,*R*)-Cat1 (40)	DMF	H_2O		7/1/0		95:5	<5%
88	(*S*,*S*)-Cat1 (40)	DMF	H_2O		7/1		95:5	<5%
89	(*S*,*R*)-Cat1 (40)	DMF	H_2O		7/1		95:5	<5%
90	(*R*,*S*)-Cat1 (40)	DMF	H_2O		7/1		95:5	<5%
91	Cat22 (40)	DMF	H_2O		7/1		95:5	<5%
92	Cat23 (40)	DMF	H_2O		7/1		95:5	<5%
93	ethanolamine (40)	DMF	H_2O		7/1		30:70	<5%
94	D-Thr (40)	DMF	H_2O		7/1		85:15	~20%
95	Cat24 (40)	DMF	H_2O		7/1		72:28	<5%
96	Cat25 (40)	DMF	H_2O		7/1		95:5	<5%
97	Cat26 (40)	DMF	H_2O		7/1			<1%
98	D-Cys (40)	DMF	H_2O		7/1			<1%
99	(*R*)-Cat12 (40)	DMF	H_2O		7/1			<1%
100	Cat16 (40)	DMF	H_2O		7/1		24:76	<5%
101	Cy_2NH	$CDCl_3$	DMF	H_2O	3/1/1			
102	*i*-Pr_2NH	$CDCl_3$	DMF	H_2O	3/1/1			
103	Pyrrolidine	$CDCl_3$	DMF	H_2O	3/1/1			
104	*i*-Pr_2NH	$CDCl_3$						
105	Pyridine	$CDCl_3$						
106	AcOH	$CDCl_3$						
107		$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 5		< %
108		$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. K_2CO_3	21:79	35%

Entry	Catalyst (mol%)	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive	d.r. 14:13	Estimated Yield
109		$CDCl_3$		Additive	3/0/1	Aq. sat. K_2CO_3	33:66	65%
110		MeCN		Additive	3/0/1	Aq. sat. K_2CO_3		
111	$TiCl_4$ (100)	$CDCl_3$						
112		$CDCl_3$				KO*t*Bu (ca 10 eq)	35:65	65%
113		$CDCl_3$				NaH (ca 10 eq)	42:58	55%
114		$CDCl_3$		Additive	3/0/1	Citrate buffer pH 5		
115		$CDCl_3$		Additive	3/0/1	Citrate buffer pH 6		
116		$CDCl_3$		Additive	3/0/1	Aq. sat. NH_4Cl		
117		$CDCl_3$		Additive	3/0/1	Aq. NH_4OH (25%)	88:12	35%
118		$CDCl_3$		Additive	3/0/1	Aq. sat. Na_2CO_3		
119		$CDCl_3$		Additive	3/0/1	Aq. sat. Cs_2CO_3	35:65	5%
120		$CDCl_3$		Additive	3/0/1	Aq. sat. KNO_3		
121		$CDCl_3$		Additive	3/0/1	Aq. sat. NaCl		
122		$CDCl_3$		Additive	3/0/1	Aq. NaOH (1.0 $molL^{-1}$)	13:87	60%
123		$CDCl_3$		Additive	3/0/1	Aq. KOH (1.0 $molL^{-1}$)	14:86	65%
124		$CDCl_3$		Additive	3/0/1	Aq. sat. K_2CO_3	33:66	65%
125	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 5	92:8	<5%
126	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		<1%
127	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Phosphate buffer pH 7.4		<1%
128	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Phosphate buffer pH 8		<1%
129	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. NaCl	95:5	<5%
130	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat. KNO_3		<1%
131	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Aq. sat NH_4Cl	95:5	<5%
132	(*R*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Aq. AcOH (5%)	95:5	<5%
133	(*R*)-Cat6 (40)	$CDCl_3$		Additive	3/0/1	Citrate buffer pH 6	95:5	~10%
134	(*R*)-Cat6 (40)	$CDCl_3$		Additive	3/0/1	Aq. sat. NaCl	95:5	~10%
135	(*R*)-Cat6 (40)		DMF	Additive	0/7/1	Citrate buffer pH 6		<1%
136	(*R*)-Cat6 (40)	CH_2Cl_2					95:5	~10
137	(*S*)-Cat6 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		<1%
138	(*R*)-Cat8 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		<1%
139	Cat11 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		<1%
140	Cat12 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		<1%
141	Cat16 (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		15%
142	L-Lys (40)	$CDCl_3$	DMF	Additive	3/1/1	Citrate buffer pH 6		
143	L-Lys (40)	$CDCl_3$		Additive	3/0/1	Citrate buffer pH 6		
144	(*R*)-Cat6 (40)	Additiv				TPGS (2%)		<2%
145	(*R*)-Cat6 (40)	CH_2Cl_2		Additive	1/0/1	TPGS (2%)	92:8	
146	(*R*)-Cat6 (40)	Additiv				Nok (2%)		<10%
147	(*R*)-Cat6 (40)	CH_2Cl_2		Additive	1/0/1	Nok (2%)		<5%
148	(*R*)-Cat6 (40)	CH_2Cl_2	H_2O		5/1/0	Drop Triton B	40:60	~20%
149	D-Ile (40)	CH_2Cl_2	H_2O		5/1/0	Drop Triton B	30:70	~55%
150	(*R*)-Cat6 (40)	CH_2Cl_2	H_2O		5/1/0	Bu_4NBr (ca 1.0 mg)		~5%
151	D-Ile (40)	CH_2Cl_2	H_2O		5/1/0	Bu_4NBr (ca 1.0 mg		~30%
152	Cat27 (30)	CH_2Cl_2		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	85:15	~60%
153	Cat27 (30)	toluene		Additive	5/0/1	Aq. KOH (1.0 $molL^{-1}$)	57:43	~50%
154	Cat28 (20)	CH_2Cl_2		Additive	1/0/1	Aq. KOH (0.1 $molL^{-1}$)	12:88	~20%
155	Cat27 (20)	CH_2Cl_2		Additive	1/0/1	Aq. KOH (0.1 $molL^{-1}$)	78:22	~65%
156	Cat27 (20)	CH_2Cl_2		Additive	1/0/1	Aq. KOH (0.01 $molL^{-1}$)	77:23	~65%
157	(*S*)-Tet (40)	CH_2Cl_2		Additive	1/0/1	TPGS (2%)		
158	(*R*)-Tet (40)	CH_2Cl_2		Additive	1/0/1	TPGS (2%)		25%
159	D-Ile (40)	CH_2Cl_2		Additive	1/0/1	TPGS (2%)		25%
160	L-Ile (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	42:58	~40%
161	L-Ser (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	66:34	~10%
162	L-Thr (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	33:67	~40%
163	D-Thr (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	35:65	~45%
164	L-Phe (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	35:65	~45%
165	L-Val (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	35:65	~45%
166	D-Val (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	58:42	~20%
167	L-Pro (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	31:69	~50%
168	D-Pro (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	34:66	~50%
169	(*S*)-Tet (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	35:65	~45%
170	(*R*)-Tet (40)	CH_2Cl_2	H_2O		5/1	Drop Triton B	35:65	~35%
171	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. sat. K_2CO_3	78:22	~65%
172	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. sat. Na_2CO_3	78:22	~65%
173	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. sat. Cs_2CO_3	77:23	~65%
174	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. NaOH (2.0 $molL^{-1}$)	78:22	~70%
175	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. NaOH (0.5 $molL^{-1}$)	78:22	~65%
176	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. LiOH (2.0 $molL^{-1}$)	77:23	~65%
177	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. LiOH (0.5 $molL^{-1}$)	78:22	~65%
178	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. sat. NaOAc	77:23	~30%
179	Cat27 (20)	CH_2Cl_2		Additive	5/0/1	Aq. Na_2HPO_4 (1 $molL^{-1}$)		
180	Cat27 (20)	CH_2Cl_2				KOH (1 eq.)	78:22	~40%
181	Cat27 (20)	CH_2Cl_2				$CsOH*H_2O$ (1 eq.)	78:22	~40%
182	Cat27 (20)	CH_2Cl_2				Cs_2CO_3 (1 eq.)	78:22	~35%
183	Cat27 (20)	DCE		Additive	5/0/1	Aq. NaOH (2.0 $molL^{-1}$)	77:23	~65%

Entry	Catalyst (mol%)	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive	d.r. 14:13	Estimated Yield
184	Cat27 (20)	$CHCl_3$		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	81:19	~65%
185	Cat27 (20)	benzene		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	55:45	~60%
186	Cat27 (20)	DMF		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	35:65	~15%
187	Cat27 (20)	MeCN		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	28:72	~35%
188	Cat27 (20)	EtOAc		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	60:40	~55%
189	Cat27 (20)	MTBE		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	58:42	~60%
190	Cat27 (20)	THF		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	52:48	~50%
191	Cat27 (20)	Et_2O		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	54:46	~60%
192	Cat27 (20)	Dioxane		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	11:89	~35%
193	Cat27 (20)	CH_2Cl_2 (1/4)		Additive	1/0/1	Aq. NaOH (2.0 molL^{-1})	76:24	~60%
194	Cat27 (20)[3]	CH_2Cl_2		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	80:20	~60%
195	Cat29 (20)[4]	CH_2Cl_2		Additive	5/0/1	Aq. NaOH (2.0 molL^{-1})	64:36	~50%
196	Cat27 (20)[4]	CH_2Cl_2		Additive	20/0/1	Aq. CsOH (2.0 molL^{-1})	86:14	~40%
197	Cat27 (20)[4]	CH_2Cl_2		Additive	20/0/1	Aq. Sat. K_2CO_3	78:22	~20%
198	Cat27 (20)[4]	CH_2Cl_2				KOH (5-10 eq.)	86:14	~25%
199	Cat27 (20)[4]	CH_2Cl_2				*t*BuOK (5-10 eq.)	77:23	~55%
200	Cat27 (20)[4]	CH_2Cl_2				NaH (5-10 eq.)	80:20	~40%
201	Cat27 (20)	O_2N-methane		Additive	5/0/1	Aq. NaOH (1.0 molL^{-1})	35:65	~20%
202	Cat27 (20)	*p*-xylene		Additive	5/0/1	Aq. NaOH (1.0 molL^{-1})	54:46	~65%
203	Cat27 (20)	HFIP				KOH (ca 5 eq.)		
204	Cat27 (20)	$CHCl_3$	EtOH		5/1	KOH (ca 5 eq.)	56:44	~25%
205	Cat27 (20)	$CHCl_3$	*n*-BuOH		5/1	KOH (ca 5 eq.)	58:42	~40%
206	Cat27 (20)	$CHCl_3$		Additive	5/0/1	Aq. NH_4OH (25%)	82:18	~75%
207	Cat27 (20)[4]	CH_2Cl_2				CsOH•H_2O (2.0 mg)	79:21	~30%
208	Cat27 (40)[4]	CH_2Cl_2				CsOH•H_2O (2.0 mg)	86:14	~20%
209	Cat27 (40)[4]	CH_2Cl_2		Additive	100/0/1	Aq. CsOH (2.0 molL^{-1})	87:13	~25%
210	Cat27 (20)[4]	CH_2Cl_2				CsOH•H_2O (2.0 mg)	79:21	~20%
211	Cat27 (20)[4]	CH_2Cl_2				Drop Et_3N		<1%
212	Cat27 (20)[4]	CH_2Cl_2				Drop Pyridine		<1%
213	Cat27 (20)[4]	CH_2Cl_2				Drop DBU	85:15	~10%
214	Cat27 (20)[4]	CH_2Cl_2				Drop DABCO		<1%
215		THF				KOH (10 eq.)	30:70	
216		toluene				KOH (10 eq.)	27:73	

[1] –30 °C; [2] 60 °C; [3] 0 °C; [4] –78 °C.

Examination of catalysts and conditions for (R_a,S_a,S_a,S_a)-15 and (S_a,S_a,S_a,S_a)-16



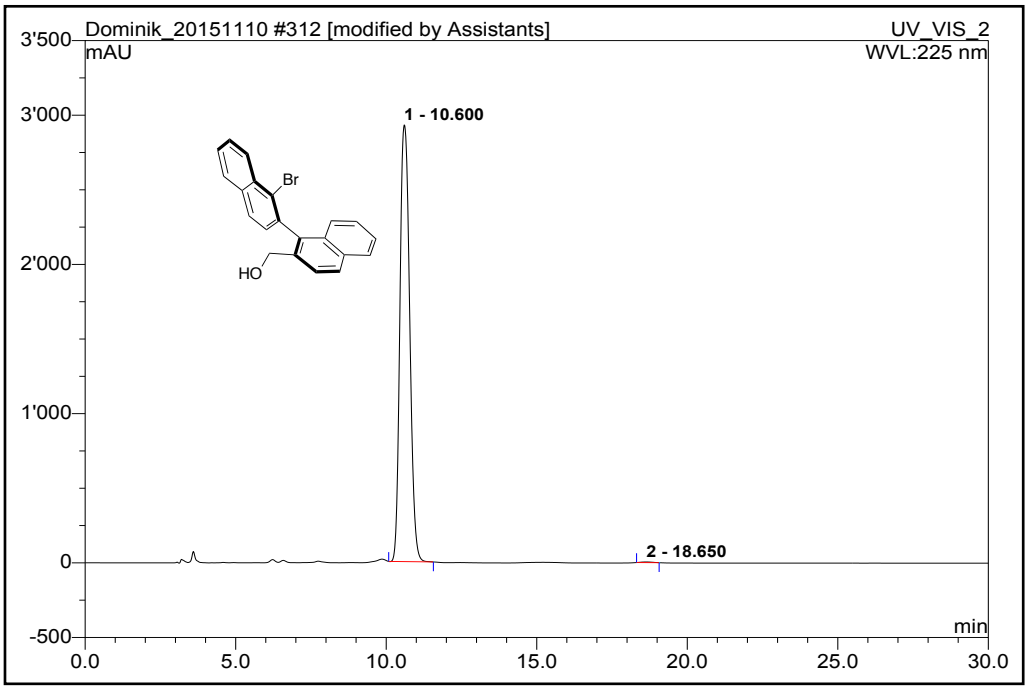
Entry	Catalyst (mol%)	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Base/Additive	d.r. 16:15	Estimated Yield
1	(*S*)-Tet (40)	$CHCl_3$	DMF	Citrate buffer pH5	3:1:1			
2	(*R*)-Tet (40)	$CHCl_3$	DMF	Citrate buffer pH5	3:1:1			<5%
3		CH_2Cl_2	H_2O		4:1	$BnNMe_3Cl$ (0.4 eq.)		
4	(*S*)-Tet (40)	CH_2Cl_2	H_2O		4:1	$BnNMe_3Cl$ (0.4 eq.)		
5	(*R*)-Tet (40)	CH_2Cl_2	H_2O		4:1	$BnNMe_3Cl$ (0.4 eq.)		
6	L-Ile (40)	CH_2Cl_2	H_2O		4:1	$BnNMe_3Cl$ (0.4 eq.)		
7	D-Ile (40)	CH_2Cl_2	H_2O		4:1	$BnNMe_3Cl$ (0.4 eq.)		
8		CH_2Cl_2				Triton B (0.4 eq.)	<5:95	~50%
9	(*S*)-Tet (40)	CH_2Cl_2				Triton B (0.4 eq.)	<5:95	~50%
10	(*R*)-Tet (40)	CH_2Cl_2				Triton B (0.4 eq.)	<5:95	~50%
11	L-Ile (40)	DMF	Citrate buffer pH5		2:1			
12	D-Ile (40)	DMF	Citrate buffer pH5		2:1			
13	L-Pro (40)	DMF	Citrate buffer pH5		2:1			
14	D-Pro (40)	DMF	Citrate buffer pH5		2:1			
15	(*S*)-Cat8 (40)	$CHCl_3$	DMF	Citrate buffer pH5	3:1:1			
16	(*R*)-Cat8 (40)	$CHCl_3$	DMF	Citrate buffer pH5	3:1:1			
17	(*S*)-Cat12 (40)	$CHCl_3$	DMF	Citrate buffer pH5	3:1:1			<5%
18	(*R*)-Cat12 (40)	$CHCl_3$	DMF	Citrate buffer pH5	3:1:1			
19		$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 molL^{-1})	1:99	~35%
20	Cat27 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 molL^{-1})	28:72	~35%
21		$CHCl_3$				Barton's base	26:74	~10%
22	Cat27 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 molL^{-1})	30:70	~35%

Entry	Catalyst (mol%)	Solvent 1	Solvent 2	Solvent 3	Solvent Ratio	Additive/Base	d.r. 16:15	Estimated Yield
23	Cat36 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	54:46	<5%
24	Cat40 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	25:75	~35%
25	Cat42 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	45:55	~20%
26	Cat43 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	7:93	~35%
27	Cat44 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	5:95	~40%
28	Cat29 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	30:70	<10%
29	Cat31 (20)	$CHCl_3$	H_2O		4:1	Aq. KOH (1.0 $molL^{-1}$)	3:97	~45%
30	Cat27 (20)	$CHCl_3$				NaOH (ca 2.0 mg)	52:48	~30%
31	Cat27 (20)	$CHCl_3$	H_2O		4:1	Aq. Na_2CO_3 (0.1 $molL^{-1}$)	27:73	~30%
32	Cat27 (20)	$CHCl_3$	H_2O		4:1	NaOAc (sat.)		
33	Cat27 (20)	$CHCl_3$	H_2O		4:1	NH_4OH (25%)	17:83	~50%
34		$CHCl_3$	H_2O		4:1	NH_4OH (25%)		
35	Cat42 (20)[1]	$CHCl_3$				NaOH (ca 2.0 mg)		<5%
36	Cat27 (40)[1]	$CHCl_3$				NaOH (ca 2.0 mg)	38:62	~10%
37	Cat27 (20)[1]	$CHCl_3$				NaOH (ca 2.0 mg)	34:66	~5%
38	Cat27 (20)[1]	$CHCl_3$				K_2CO_3 (ca 2.0 mg)	13:87	~15%
39	Cat27 (20)[1]	toluene				NaOH (ca 2.0 mg)	20:80	~10%
40	Cat27 (20)[1]	MeCN				NaOH (ca 2.0 mg)	7:93	~10%
41	Cat27 (20)[1]	EtOAc				NaOH (ca 2.0 mg)	1:99	~5%
42	Cat27 (20)[1]	THF				NaOH (ca 2.0 mg)		<5%
43	Cat27 (20)[1]	THF	*t*BuOH		4:1	NaOH (ca 2.0 mg)	1:99	~10%
44	Cat27 (20)	CH_2Cl_2				Triton B (0.4 eq.)	<5:95	~35%
45	Cat27 (20)[2]	CH_2Cl_2				Triton B (0.1 eq.)		
46	Cat27 (20)[2]	CH_2Cl_2				Triton B (0.01 eq.)		
47	Cat27 (20)	CH_2Cl_2	H_2O		5:1	Triton B (0.1 eq.)	11:89	~20%
48	Cat28 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
49	Cat30 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
50	Cat32 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)	<5:95	~40%
51	Cat33 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
52	Cat34 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
53	Cat35 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)	20:80	~20%
54	Cat37 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
55	Cat38 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
56	Cat39 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
57	Cat41 (20)	CH_2Cl_2	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		<5%
58	Cat27 (20)	$CHCl_3$				$Ca(OH)_2$ (ca 2.0 mg)		<5%
59	Cat27 (20)	$CHCl_3$				$Mg(OH)_2$ (ca 2.0 mg)		<5%
60	Cat27 (20)	$CHCl_3$				$CaCO_3$ (ca 2.0 mg)		
61	Cat27 (20)	$CHCl_3$				KO*t*Bu (ca 2.0 mg)	55:45	~40%
62	Cat27 (20)	$CHCl_3$				NaH (ca 2.0 mg)	57:45	~40%
63	Cat27 (20)	$CHCl_3$				LiHMDS (ca 2.0 mg)		
64	Cat27 (20)	$CHCl_3$				Drop NEt_3		
65	Cat27 (20)	$CHCl_3$				Drop pyridine		
66	Cat27 (20)	$CHCl_3$				Drop Barton's base		
67	Cat27 (20)	$CHCl_3$				Drop DABCO		
68	Cat27 (20)	$CHCl_3$	MeOH		5:1	Aq. KOH (0.2 $molL^{-1}$)	<5:95	~15%
69	Cat27 (20)	$CHCl_3$	EtOH		5:1	Aq. KOH (0.2 $molL^{-1}$)	<5:95	~5%
70	Cat27 (20)	MTBE	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)	9:91	~50%
71	Cat27 (20)	$MeNO_2$	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)		
72	Cat27 (20)	DMF	H_2O		5:1	Aq. KOH (1.0 $molL^{-1}$)	12:88	~15%
73	Cat27 (20)	$CHCl_3$	Citrate buffer pH5		5:1	KOH (ca 2.0 mg)	28:72	~40-45%
74	Cat27 (20)[1]	$CHCl_3$				NaH (1 eq.)		<5%
75	Cat27 (20)[1]	$CHCl_3$				NaH (10 eq.)	28:72	~15%
76	[1]	$CHCl_3$				NaH (10 eq.)		<5%
77	Cat27 (20)[1]	$CHCl_3$				KOtBu (1 eq.)		<5%
78	Cat27 (20)[1]	$CHCl_3$				KOtBu (10 eq.)		<5%
79	[1]	$CHCl_3$				KOtBu (10 eq.)	<5:95	~5%
80	Cat42 (20)[1]	$CHCl_3$				NaH (10 eq.)	50:50	~10%
81	Cat42 (20)[1]	$CHCl_3$				KOtBu (10 eq.)		<5%
82	Cat27 (20)[1]	$CHCl_3$	H_2O		100:1	NaH (10 eq.)		<5%
83	Cat27 (20)[1]	$CHCl_3$	H_2O		100:1	KO*t*Bu (10 eq.)		
84	Cat27 (20)	$CHCl_3$				NaH (1 eq.)	60:40	~35%
85	Cat27 (20)	$CHCl_3$				NaH (10 eq.)	62:38	~35%
86		$CHCl_3$				NaH (10 eq.)	28:72	~35%
87	Cat27 (20)	$CHCl_3$				KO*t*Bu (1 eq.)	57:43	~30%
88	Cat27 (20)	$CHCl_3$				KO*t*Bu (10 eq.)	57:43	~30%
89		$CHCl_3$				KO*t*Bu (10 eq.)	23:77	~40%
90	Cat42 (20)	$CHCl_3$				NaH (10 eq.)	83:17	~25%
91	Cat42 (20)	$CHCl_3$				KO*t*Bu (10 eq.)	77:23	~20%
92	Cat27 (20)	$CHCl_3$	H_2O		100:1	NaH (10 eq.)	60:40	~35%
93	Cat27 (20)	$CHCl_3$	H_2O		100:1	KO*t*Bu (10 eq.)	55:45	~35%

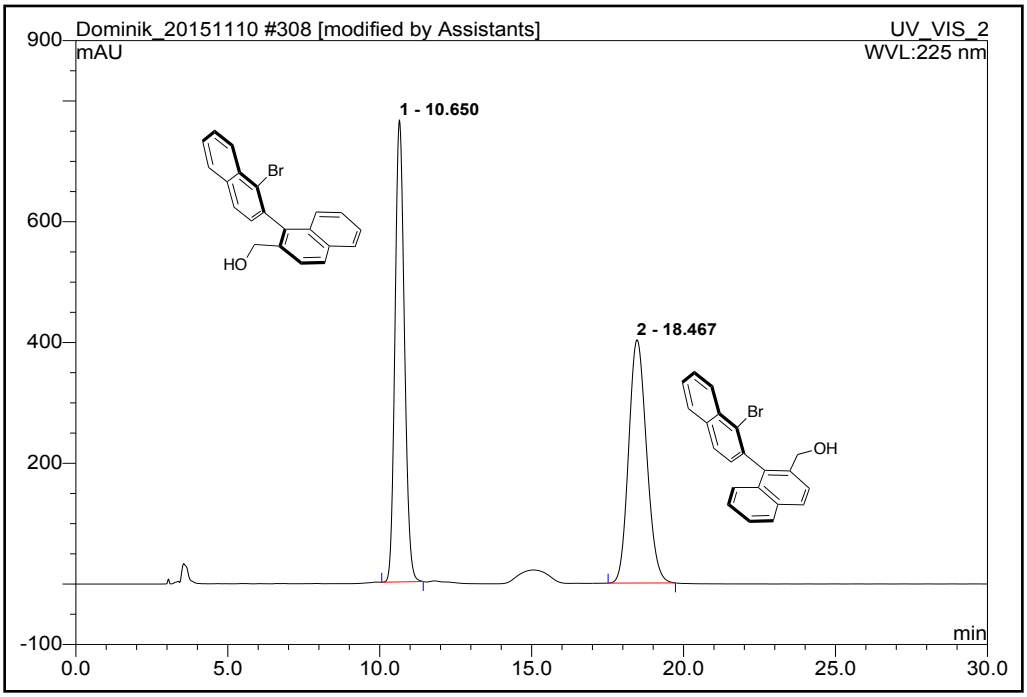
[1] –40 °C; [2] –78 °C.

HPLC Data

(S_a)-(1'-bromo-[1,2'-binaphthalen]-2-yl)methanol (*Chiralcel OD-H* column [1.0 $mLmin^{-1}$, *i*-PrOH/*n*-heptane 10:90])

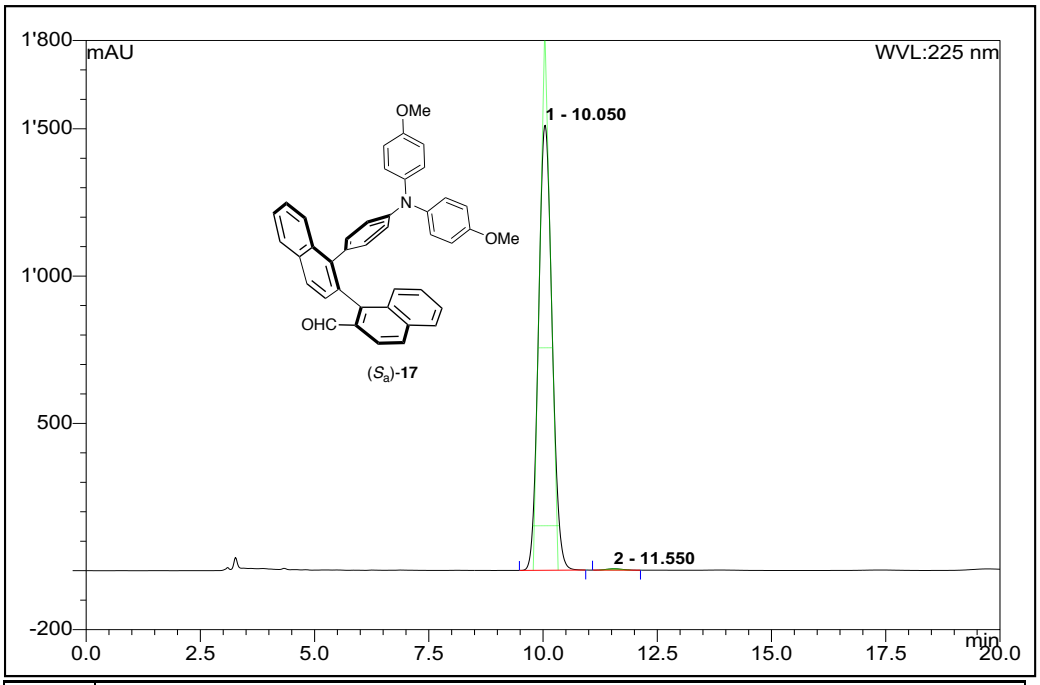


No.	Ret.Time (min)	Height (mAU)	Area (mAU*min)	Rel.Area (%)	Type
1	10.60	2926.863	1102.245	99.83	BMB*
2	18.65	4.217	1.883	0.17	BMB*
Total:		2931.079	1104.128	100.00	

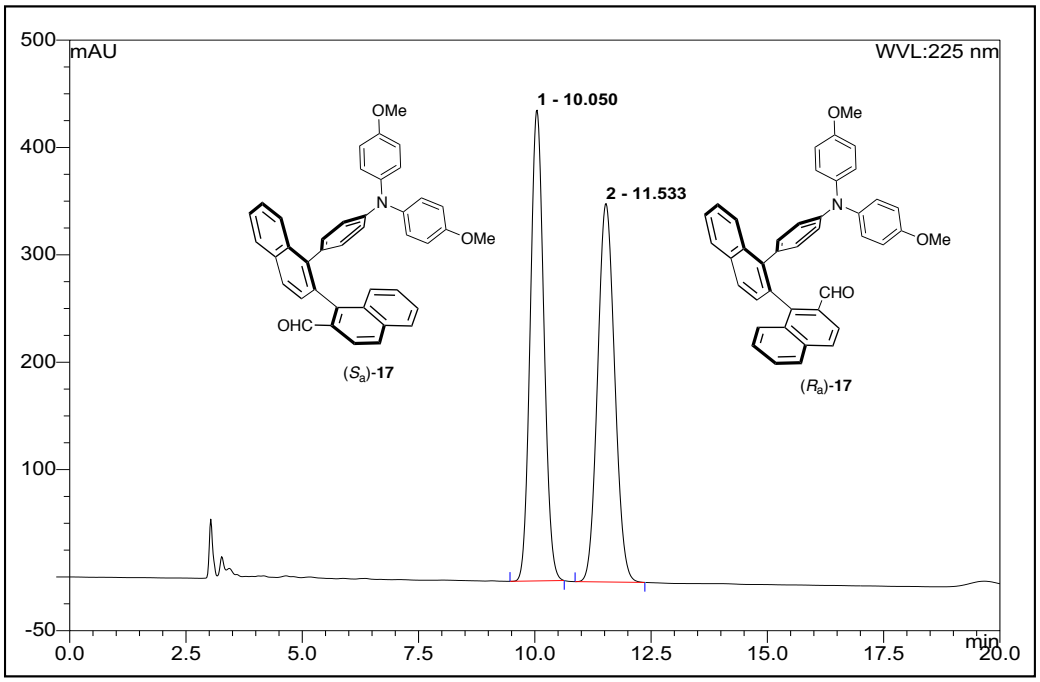


No.	Ret.Time (min)	Height (mAU)	Area (mAU*min)	Rel.Area (%)	Type
1	10.65	765.211	274.711	49.95	BMB*
2	18.47	402.948	275.238	50.05	BMB*
Total:		1168.159	549.949	100.00	

(S_a)-1'-(4-(bis(4-methoxyphenyl)amino)phenyl)-[1,2'-binaphthalene]-2-carbaldehyde (*Chiralcel AD-H* column [1.0 mLmin^{-1}, *i*-PrOH/*n*-heptane 10:90])



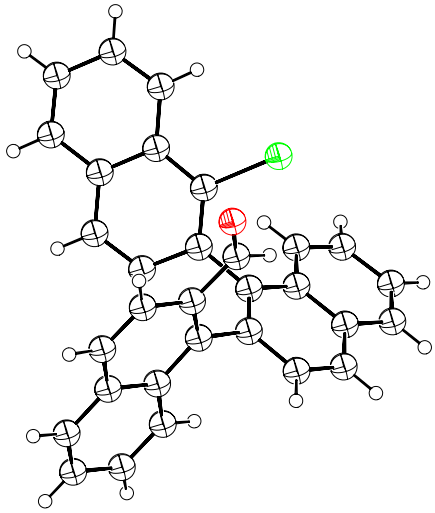
No.	Ret.Time (min)	Height (mAU)	Area (mAU*min)	Rel.Area (%)	Type
1	10.05	1510.616	520.966	99.65	BMB*
2	11.55	4.568	1.844	0.35	BMB*
Total:		1515.185	522.81	100.00	



No.	Ret.Time (min)	Height (mAU)	Area (mAU*min)	Rel.Area (%)	Type
1	10.05	438.531	148.692	49.80	BMB*
2	11.53	352.468	149.905	50.20	BMB*
Total:		790.999	298.597	100.00	

X-ray Crystallographic Analysis (Dr. Markus Neuburger)

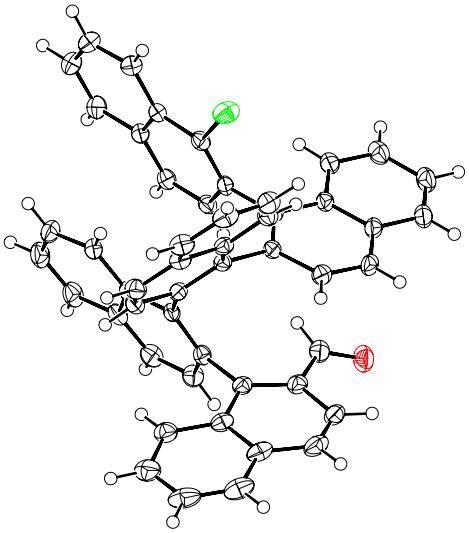
X-ray of (R_a,S_a)–7 (CCDC 1584599)



The crystal was measured on a *Bruker Kappa Apex2* diffractometer at 123K using graphite-monochromated Cu K_α-radiation with λ = 1.54178 Å, Θ_{max} = 68.976°. Minimal/maximal transmission 0.78/0.90, μ = 2.697 mm^{-1}. The Apex2 suite has been used for datacollection and integration. From a total of 28773 reflections, 4085 were independent (merging r = 0.030). From these, 4040 were considered as observed (I>2.0σ(I)) and were used to refine 299 parameters. The structure was solved by Other methods using the program Superflip. Least-squares refinement against F was carried out on all non-hydrogen atoms using the program CRYSTALS. R = 0.0167 (observed data), wR = 0.0186 (all data), GOF = 1.0888. Minimal/maximal residual electron density = –0.18/0.20 e $Å^{-3}$. Chebychev polynomial weights were used to complete the refinement.

Chemical formula	$C_{31}H_{19}BrO$
Formula weight	487.39
Z	4
$D_{calc.}$	1.465 Mg · m^{-3}
F(000)	992
Crystal description	colourless block
Crystal size	0.040 · 0.090 · 0.190 mm^3
Absorption coefficient	2.697 mm^{-1}
min/max transmission	0.78 / 0.90
Temperature	123K
Radiation (wavelength)	Cu K_α (λ = 1.54178 Å)
Crystal system	orthorhombic
Space group	P 2_1 2_1 2_1
Unit cell dimensions	a = 7.9226(9) Å b = 15.7270(18) Å c = 17.738(2) Å α = 90° β = 90° γ =90°
Volume	2210.1(4) $Å^3$
min/max Θ	3.756° / 68.976°
Number of collected reflections	28773
Number of independent refections	4085 (merging r = 0.030)
Number of observed reflections	4040 (I>2.0σ(I))
Number of refined parameters	299
R	0.0167
wR	0.0186
Goodness of fit	1.0888
Flack	0.004(8)

X-ray of (R_a,S_a,S_a,S_a)-15 (CCDC 1584600)

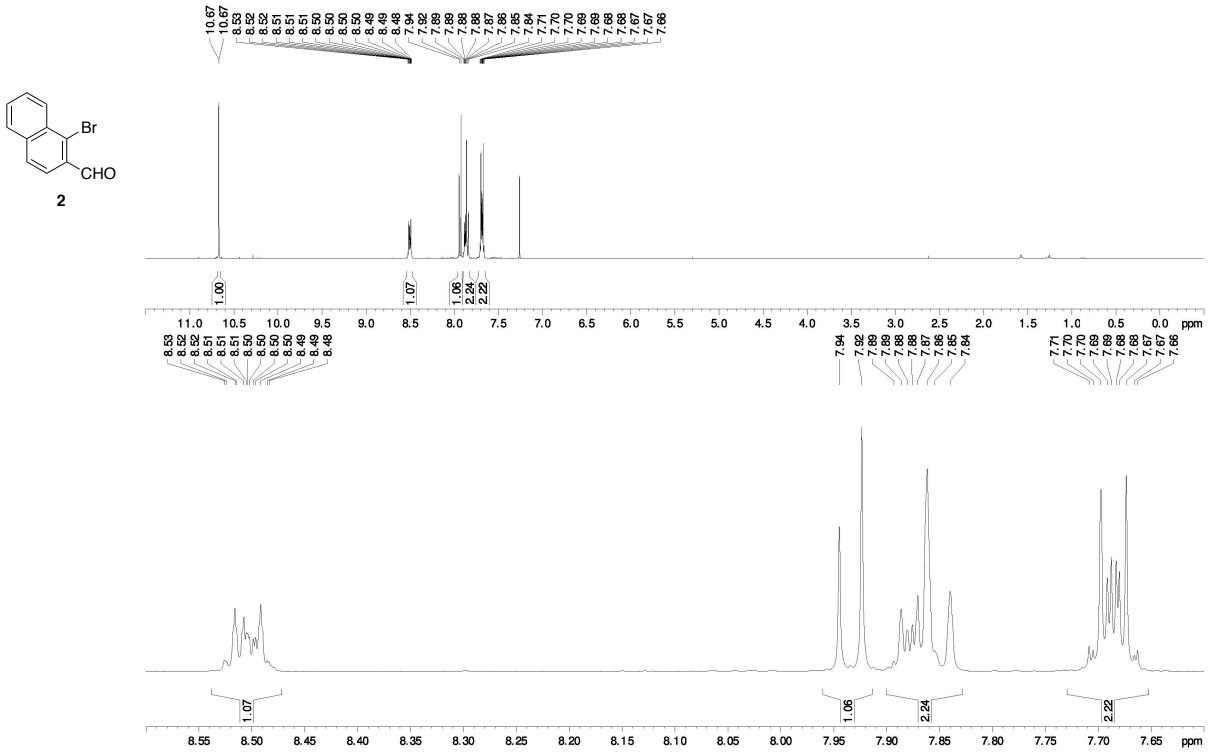


The crystal was measured on a *Stoe StadiVari* diffractometer at 123K using graded multilayer mirror-monochromated Ga K_α-radiation with λ = 1.34143 Å, Θ_{max} = 59.457°. Minimal/maximal transmission 0.79/0.82, μ = 3.330 mm^{-1}. The STOE X-AREA suite has been used for datacollection and integration. From a total of 55626 reflections, 9450 were independent (merging r = 0.030). From these, 8792 were considered as observed (I>2.0σ(I)) and were used to refine 551 parameters. The structure was solved by Other methods using the program Superflip. Least-squares refinement against F was carried out on all non-hydrogen atoms using the program CRYSTALS. R = 0.0360 (observed data), wR = 0.0425 (all data), GOF = 1.0558. Minimal/maximal residual electron density = –0.66/1.11 e $Å^{-3}$. Chebychev polynomial weights were used to complete the refinement.

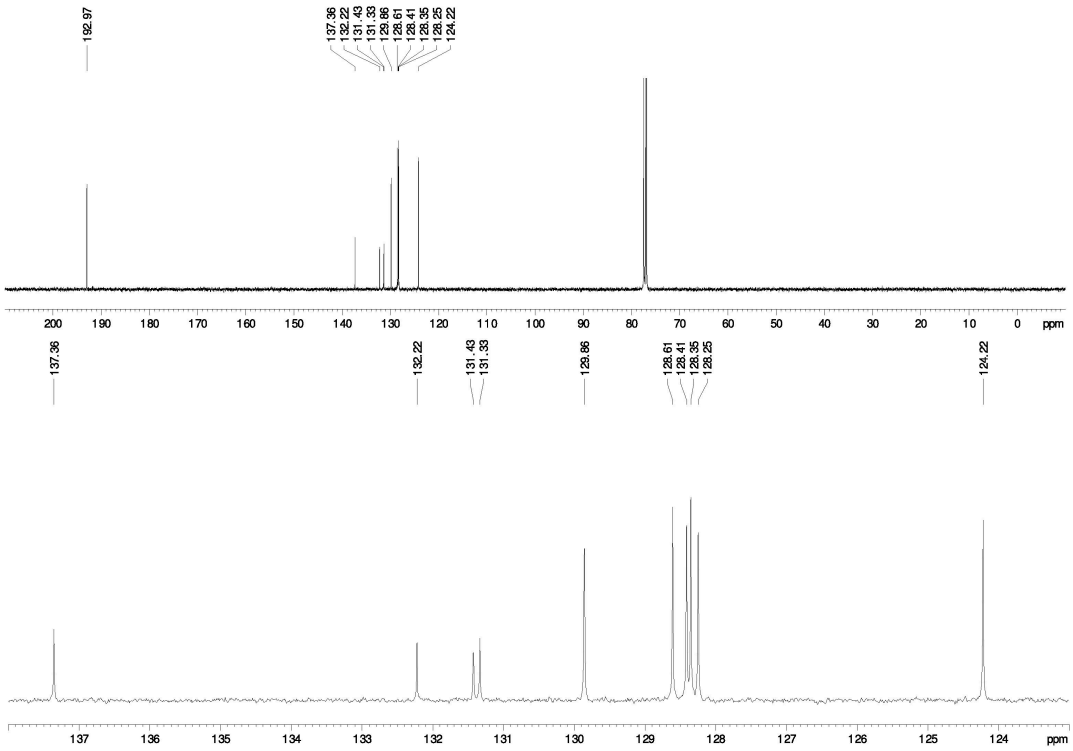
Chemical formula	$C_{51}H_{31}BrO \cdot 2\ CHCl_3$
Formula weight	978.47
Z	4
$D_{calc.}$	1.501 Mg · m^{-3}
F(000)	1984
Crystal description	colourless needle
Crystal size	0.060 · 0.070 · 0.180 mm^3
Absorption coefficient	3.330 mm^{-1}
min/max transmission	0.79 / 0.82
Temperature	123K
Radiation (wavelength)	Ga K_α (λ = 1.34143 Å)
Crystal system	orthorhombic
Space group	P 2_1 2_1 2
Unit cell dimensions	a = 21.3901(3) Å b = 20.8054(3) Å c = 9.73190(10) Å α = 90° β = 90° γ =90°
Volume	4330.98(10) $Å^3$
min/max Θ	2.578° / 59.457°
Number of collected reflections	55626
Number of independent refections	9450 (merging r = 0.030)
Number of observed reflections	8792 (I>2.0σ(I))
Number of refined parameters	551
R	0.0360
wR	0.0425
Goodness of fit	1.0558
Flack	–0.005(12)

NMR Data

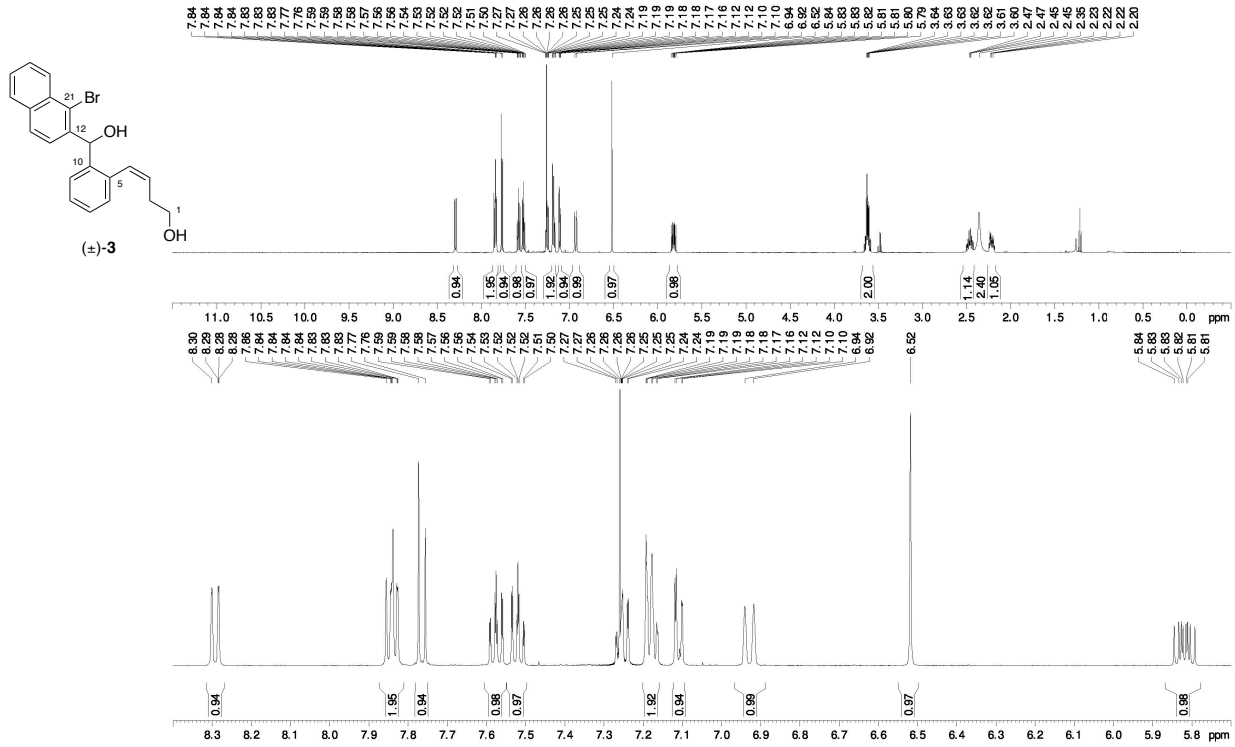
2, ^{1}H NMR (400 MHz, $CDCl_3$):



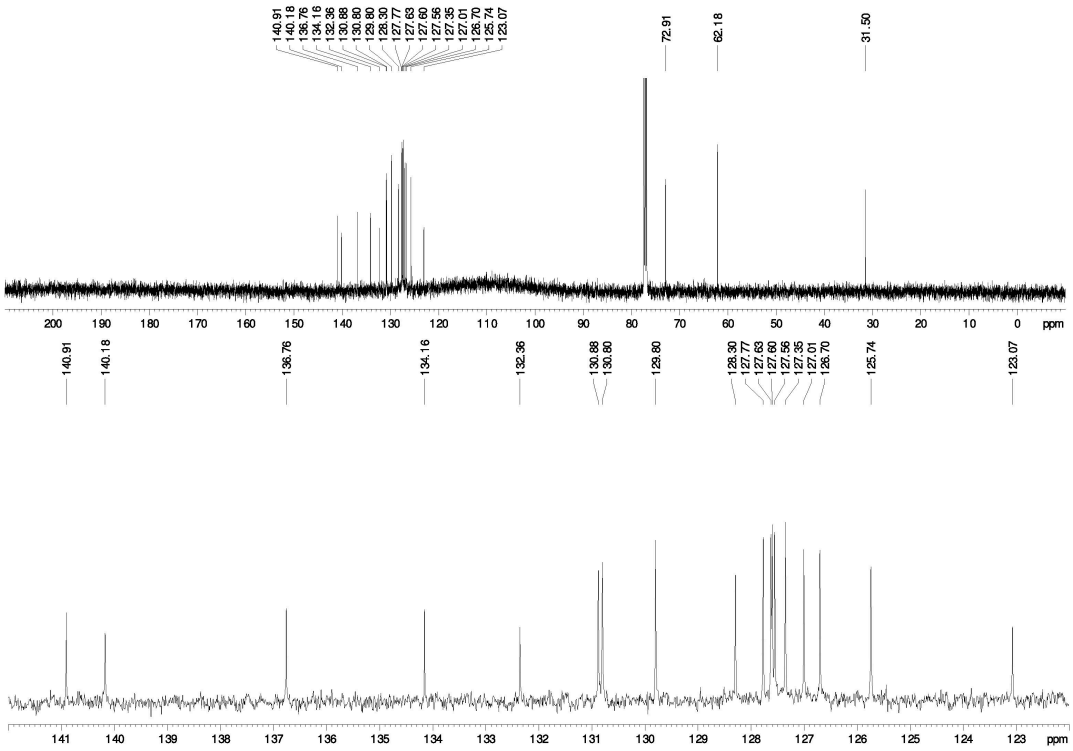
2, ^{13}C NMR (126 MHz, $CDCl_3$):



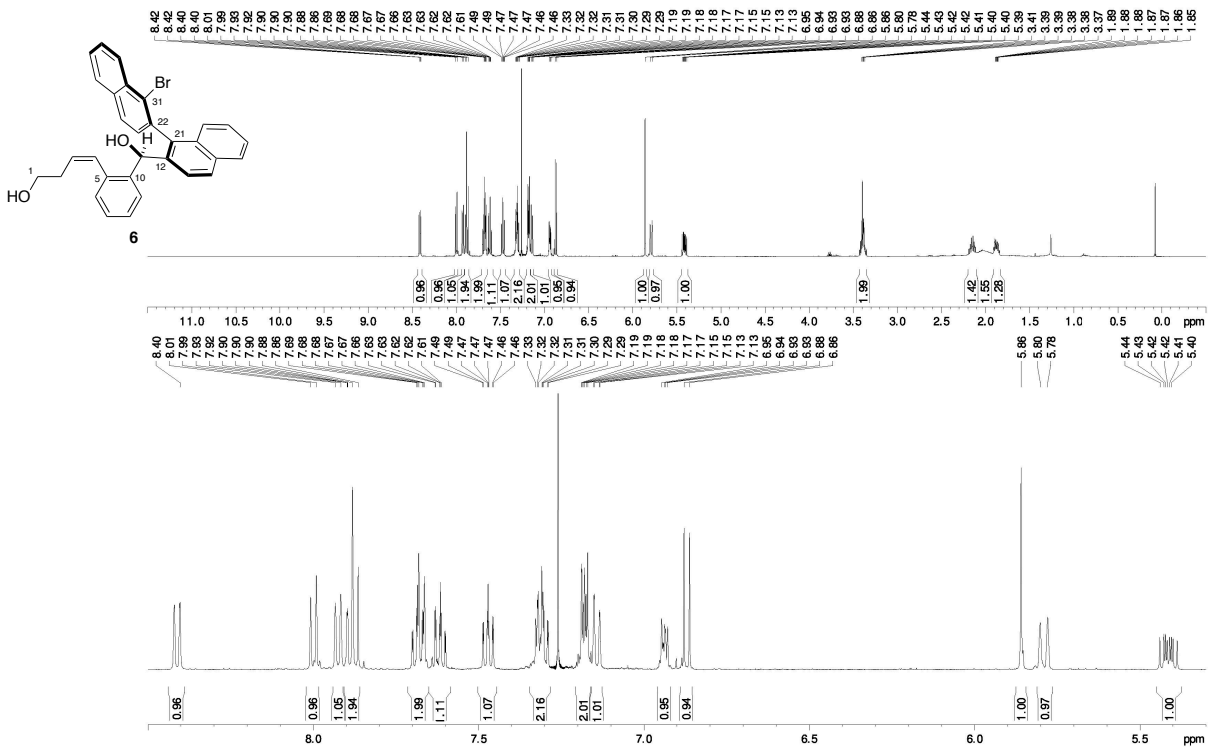
3, ^{1}H NMR (500 MHz, $CDCl_3$):



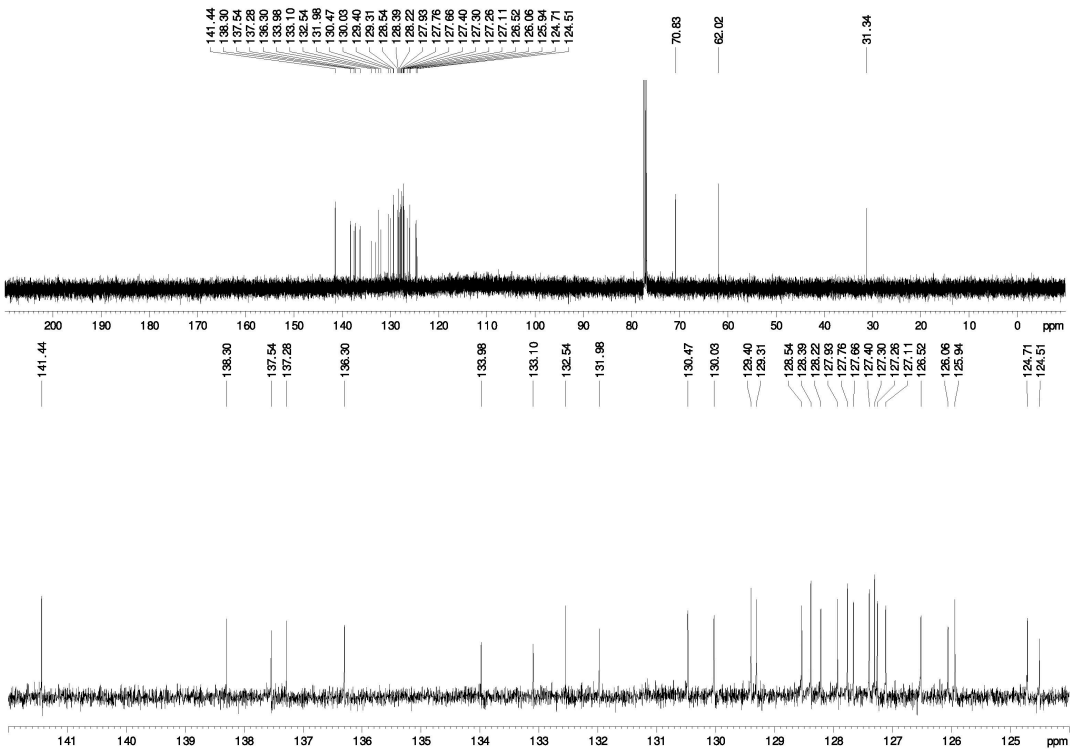
3, ^{13}C NMR (126 MHz, $CDCl_3$):



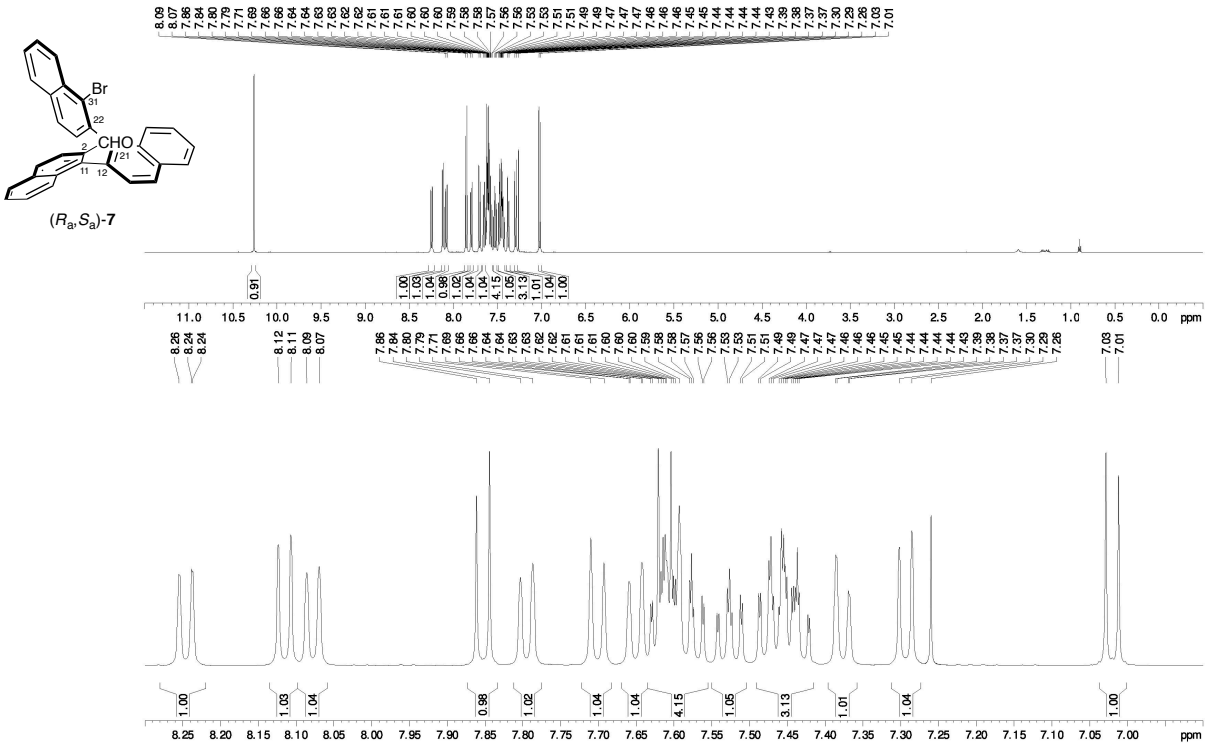
6, ^{1}H NMR (500 MHz, $CDCl_3$):



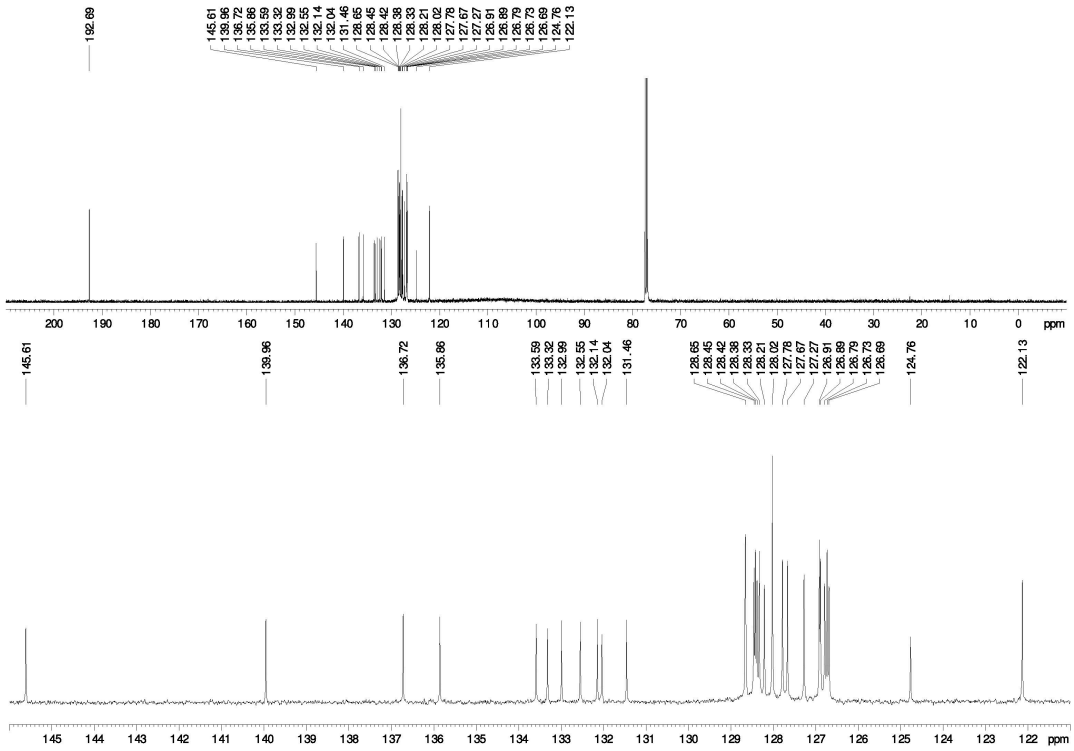
6, ^{13}C NMR (126 MHz, $CDCl_3$):



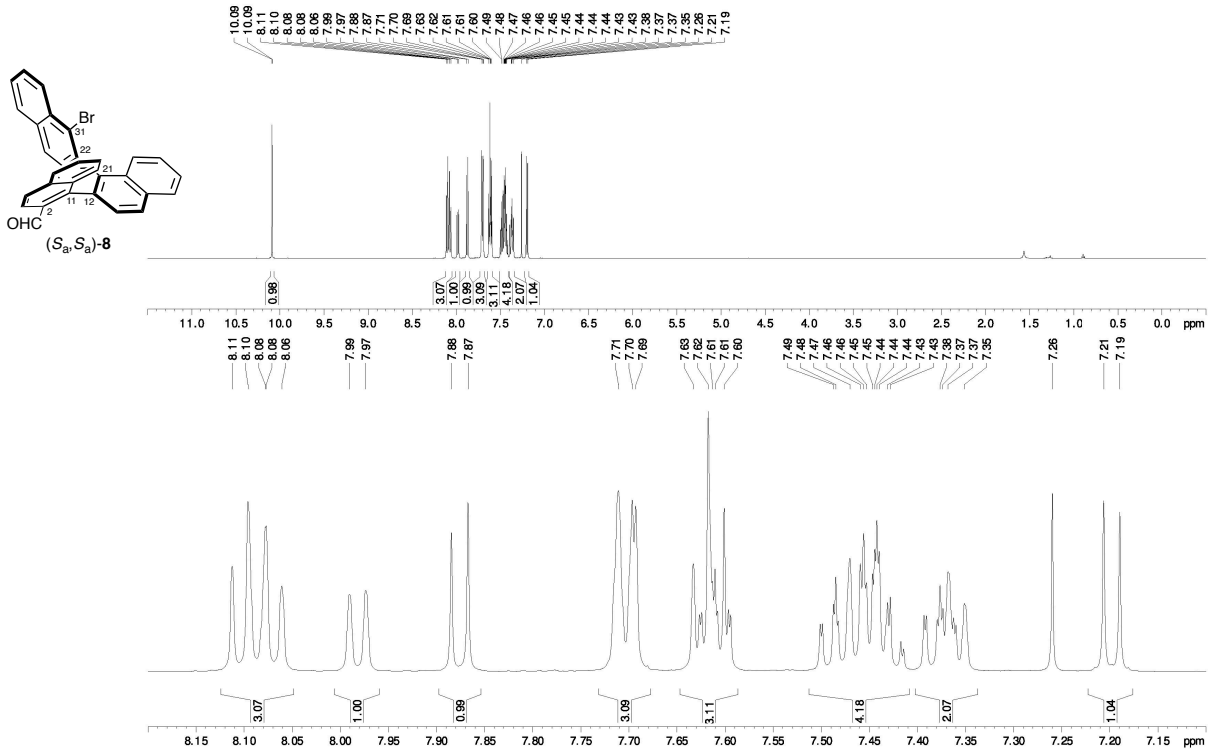
(R_a,S_a)-7, ^{1}H NMR (500 MHz, $CDCl_3$):



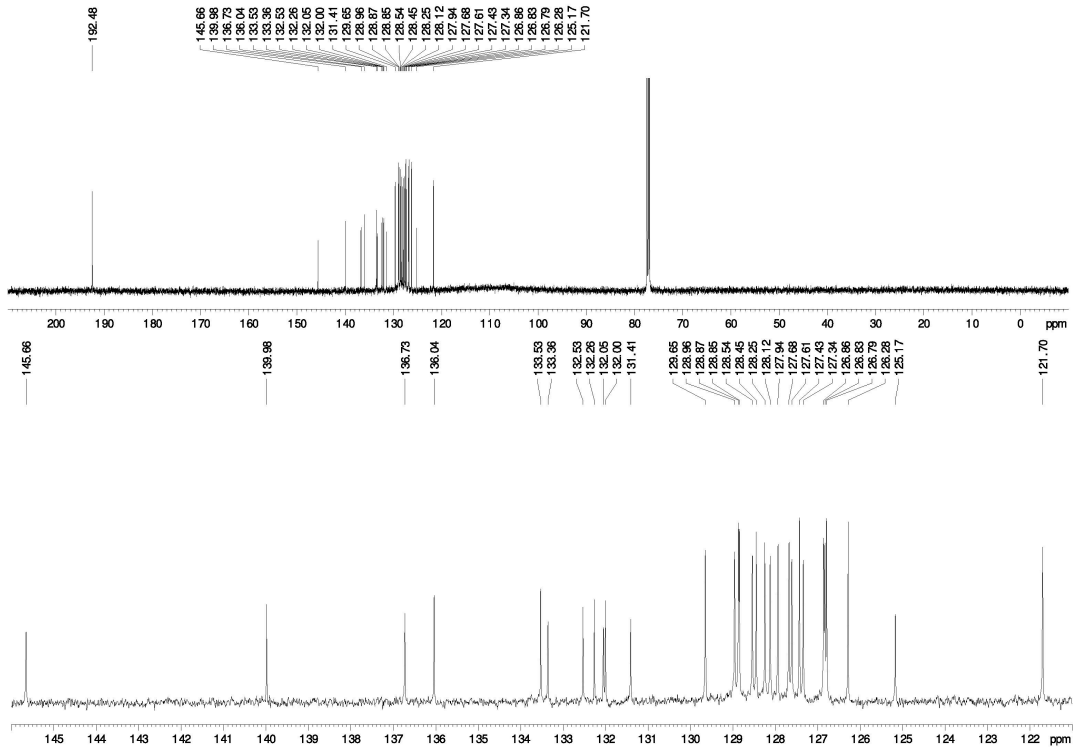
(R_a,S_a)-7, ^{13}C NMR (126 MHz, $CDCl_3$):



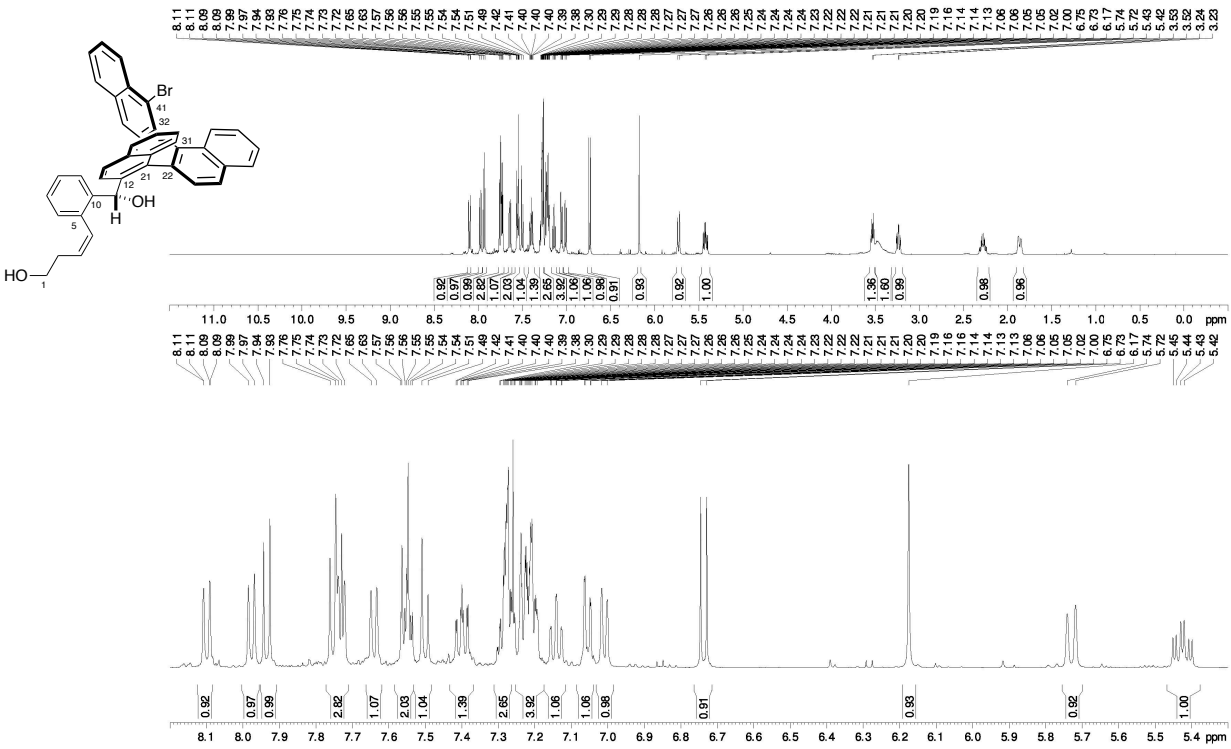
(S_a,S_a)-8, ^{1}H NMR (500 MHz, $CDCl_3$):



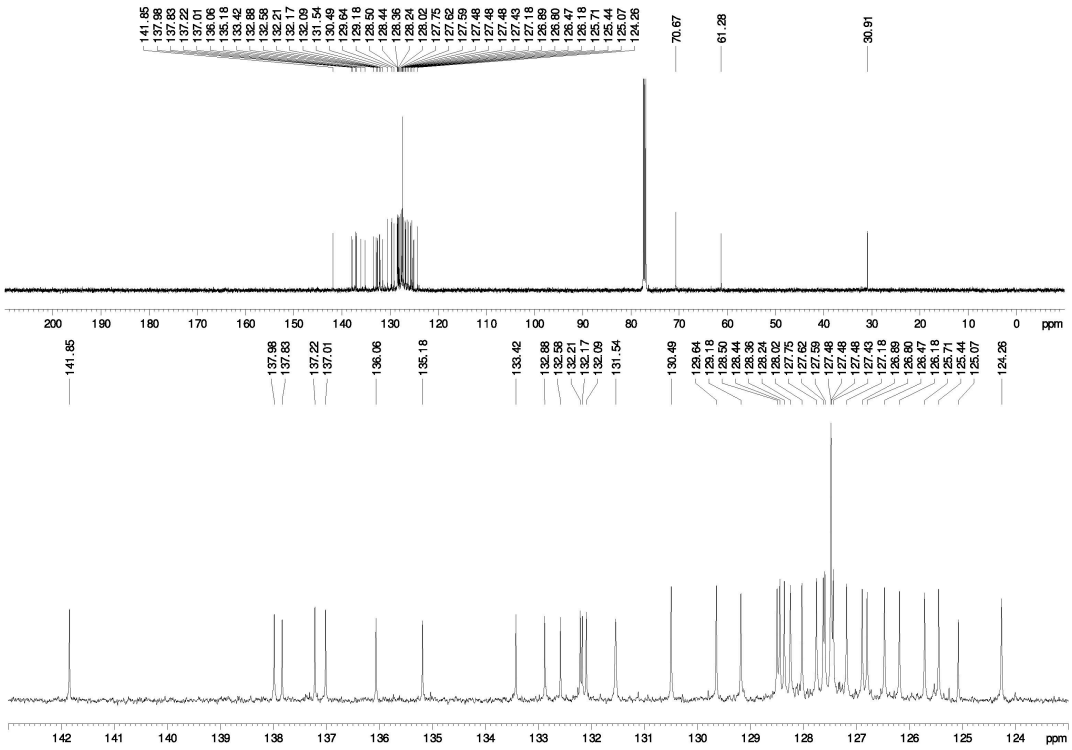
(S_a,S_a)-8, ^{13}C NMR (126 MHz, $CDCl_3$):



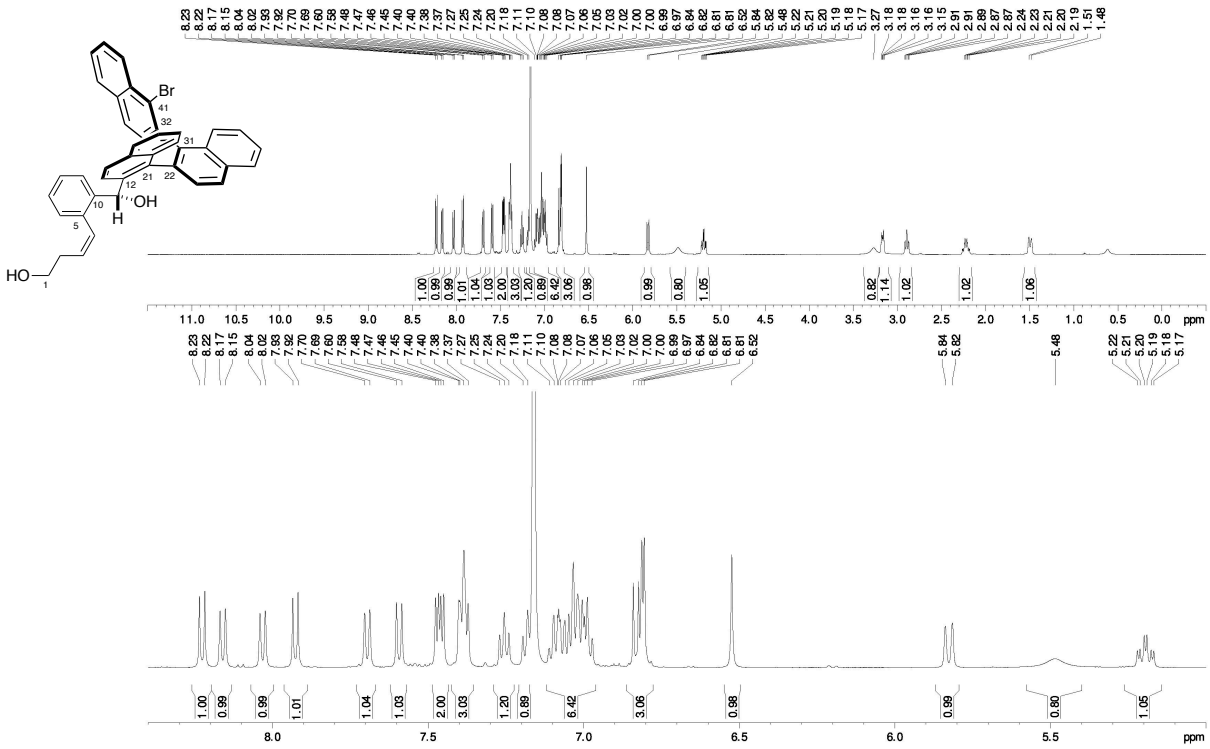
Diol C, ^{1}H NMR (500 MHz, $CDCl_3$):



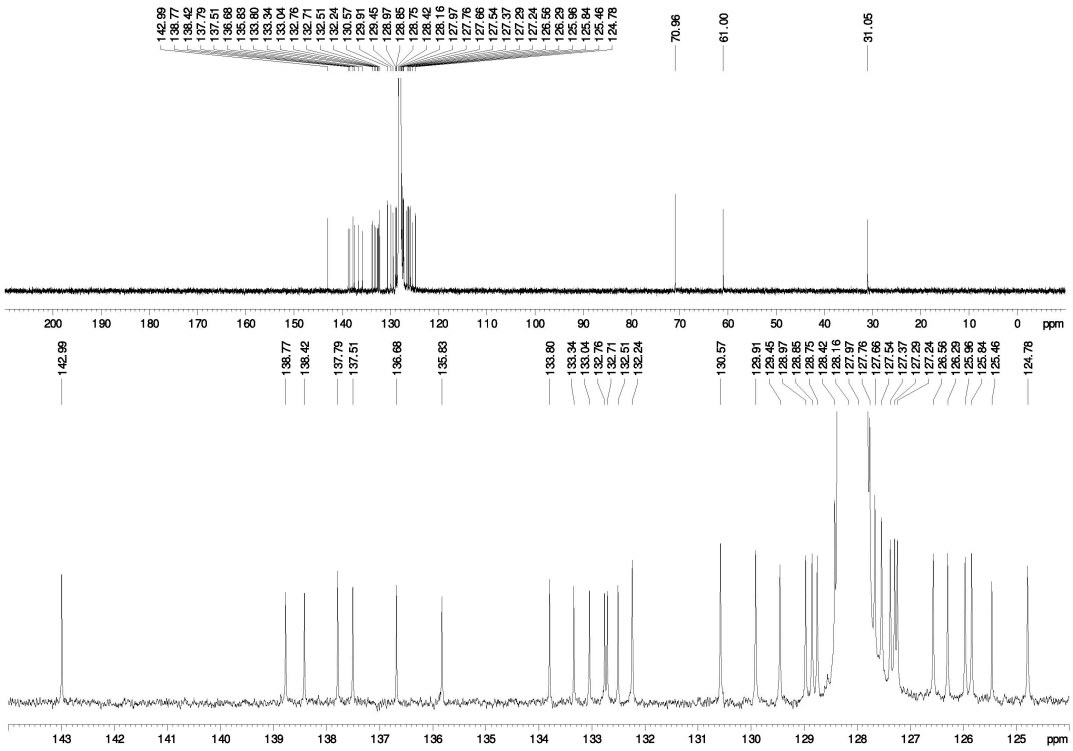
Diol C, ^{13}C NMR (126 MHz, $CDCl_3$):



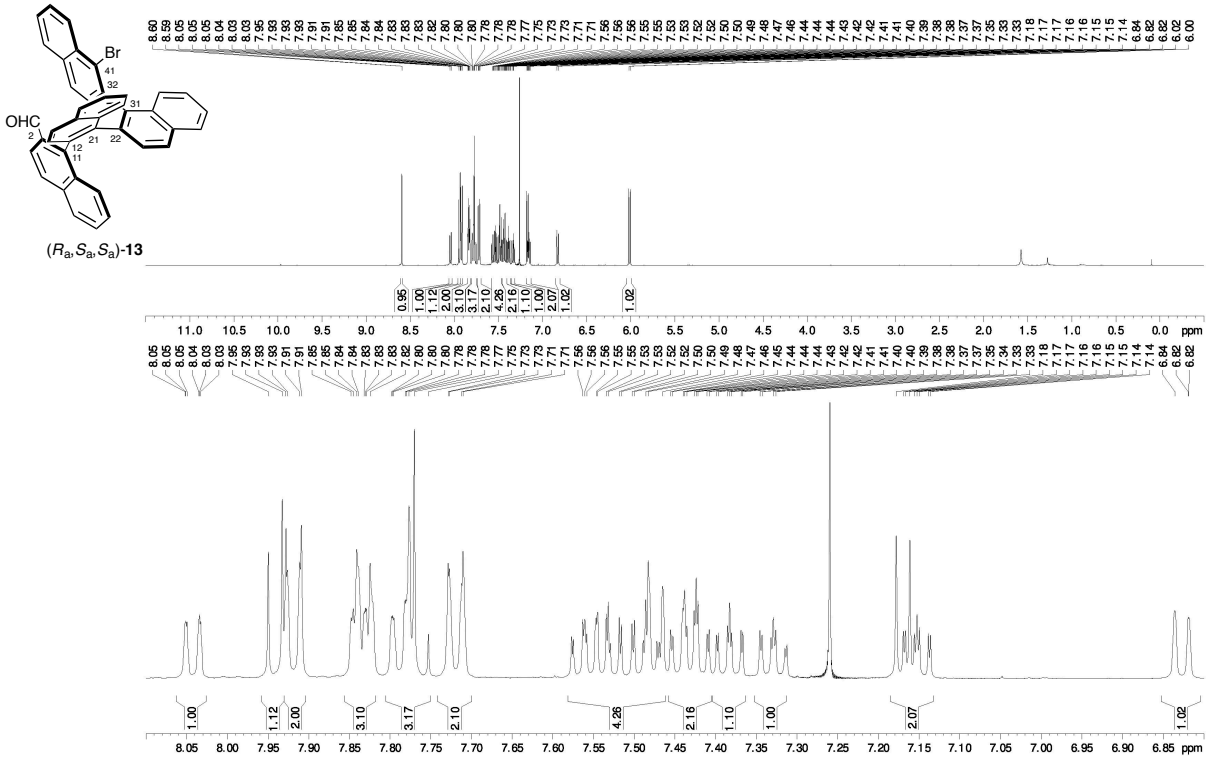
Diol C, ^{1}H NMR (500 MHz, C_6D_6):



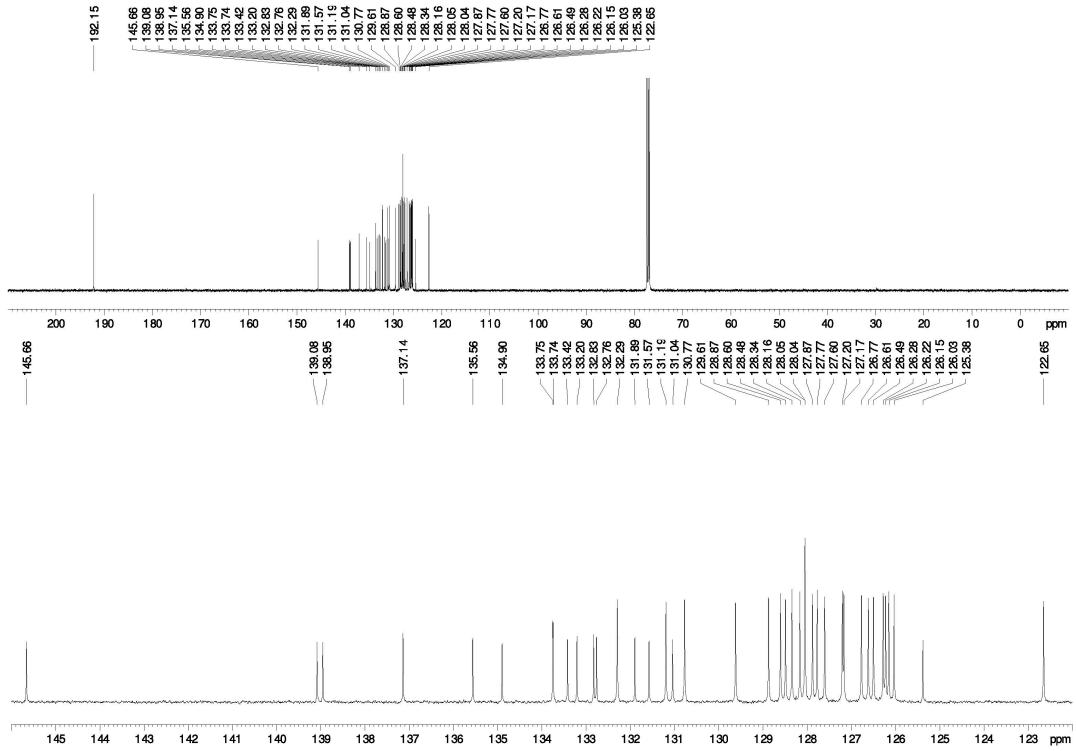
Diol C, ^{13}C NMR (126 MHz, C_6D_6):



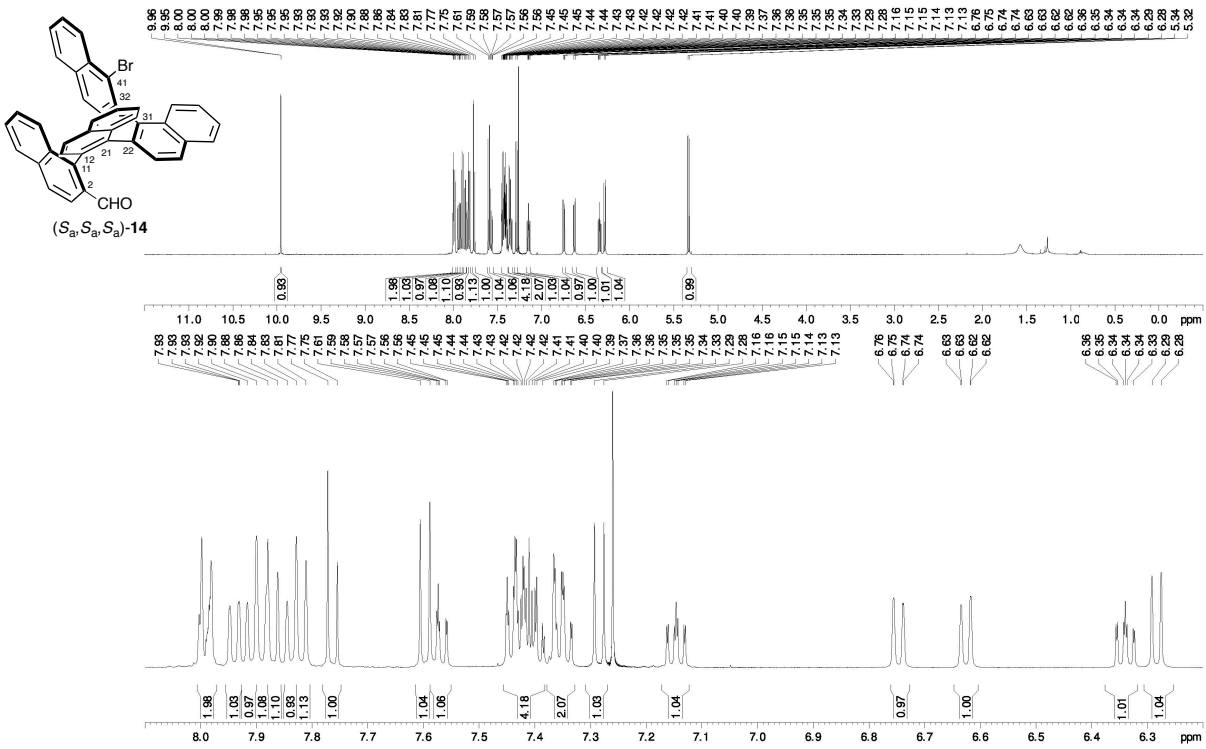
(R_a,S_a,S_a)-13, ^{1}H NMR (500 MHz, $CDCl_3$):



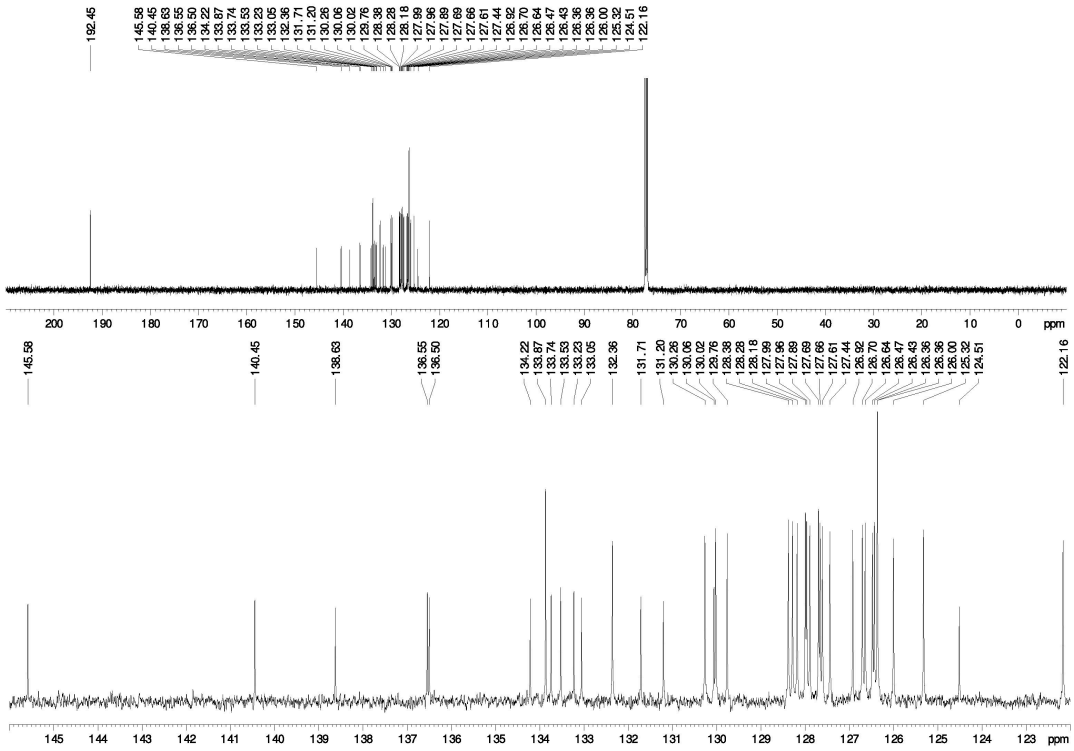
(R_a,S_a,S_a)-13, ^{13}C NMR (126 MHz, $CDCl_3$):



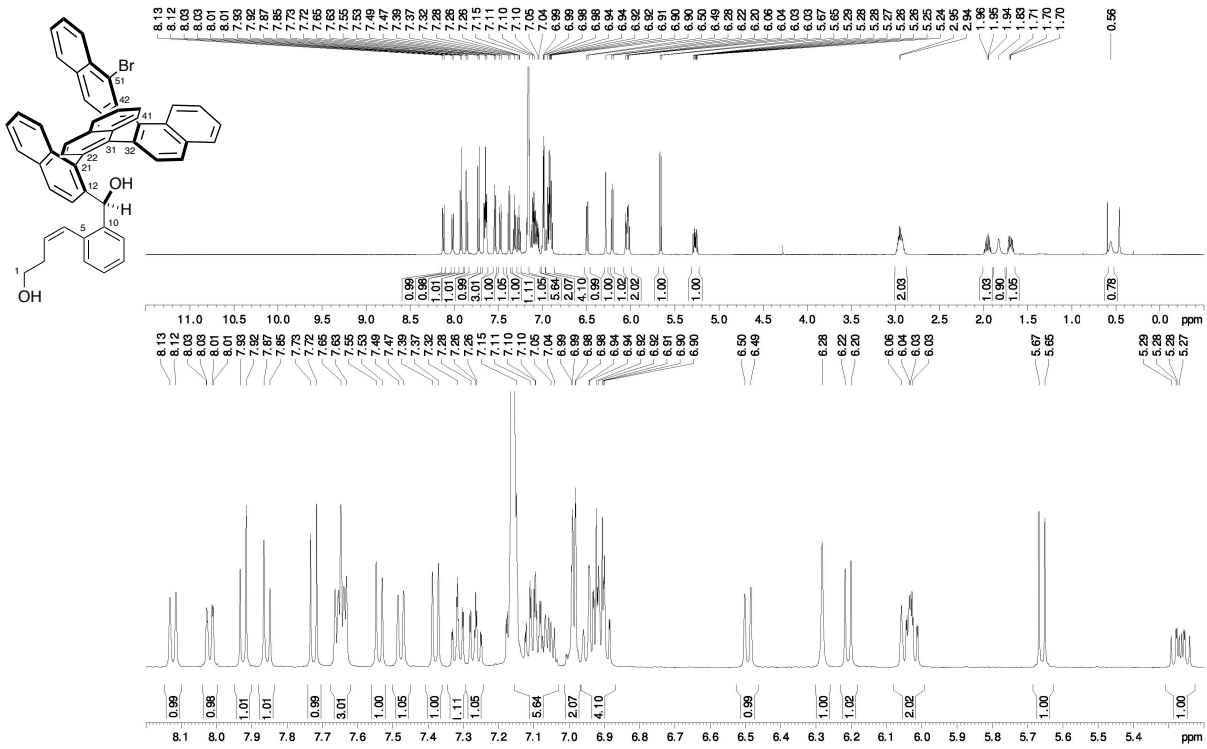
(*S*a,*S*a,*S*a)-14, ^{1}H NMR (500 MHz, $CDCl_3$):



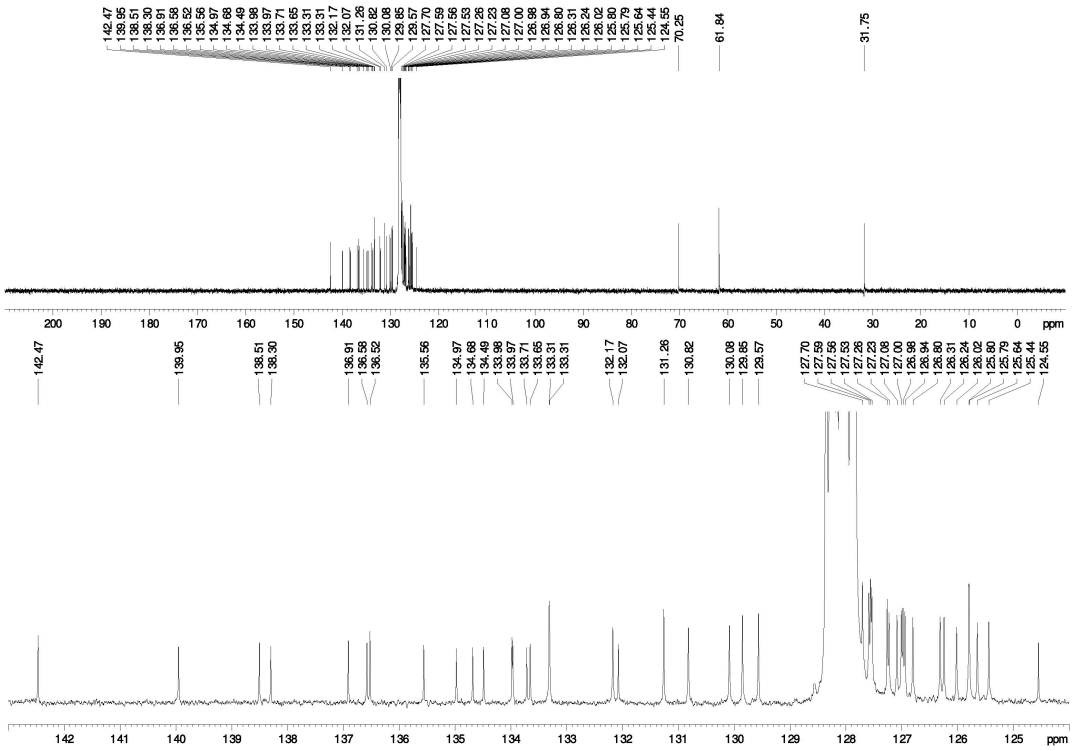
(*S*a,*S*a,*S*a)-14, ^{13}C NMR (126 MHz, $CDCl_3$):



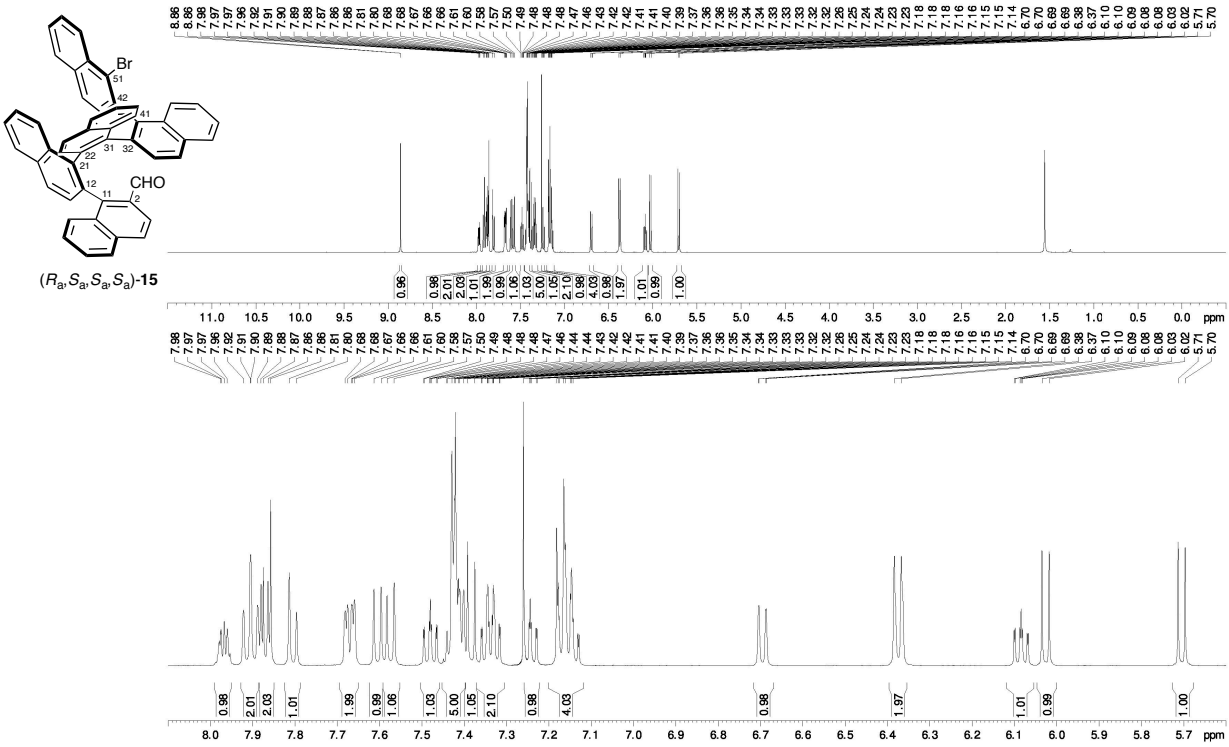
Diol D, ^{1}H NMR (500 MHz, C_6D_6):



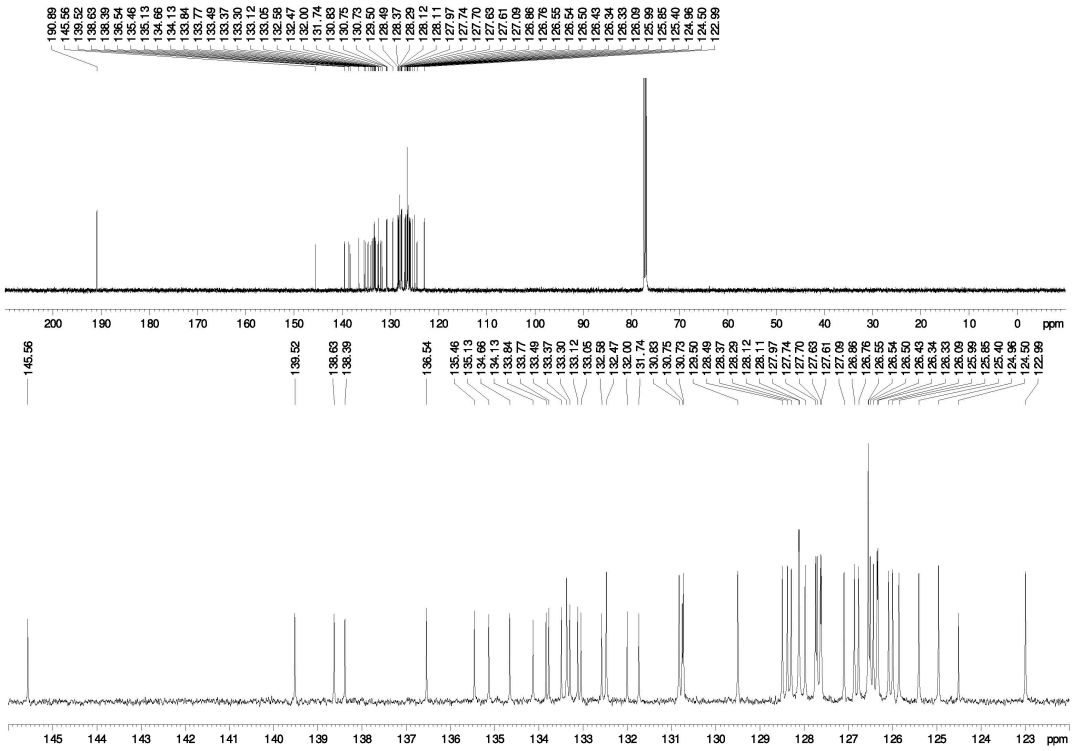
Diol D, ^{13}C NMR (126 MHz, C_6D_6):



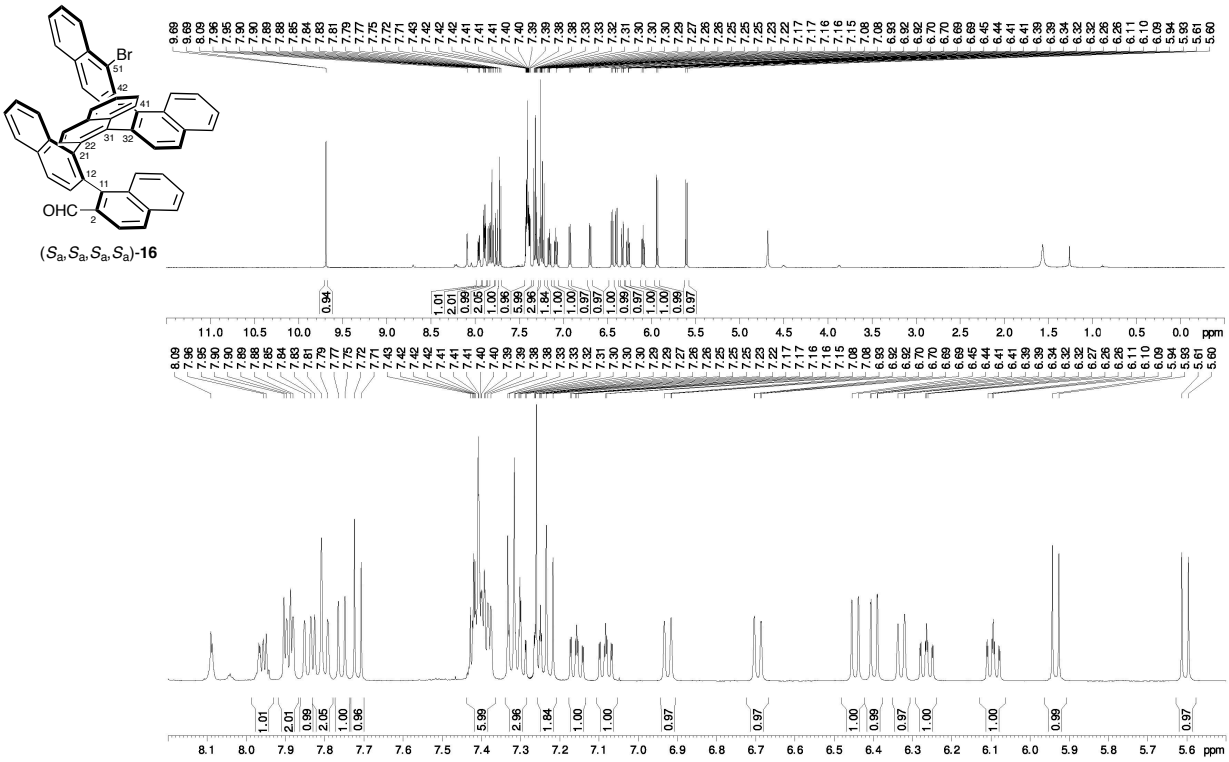
(R_a,S_a,S_a,S_a)-15, ^{1}H NMR (500 MHz, $CDCl_3$):



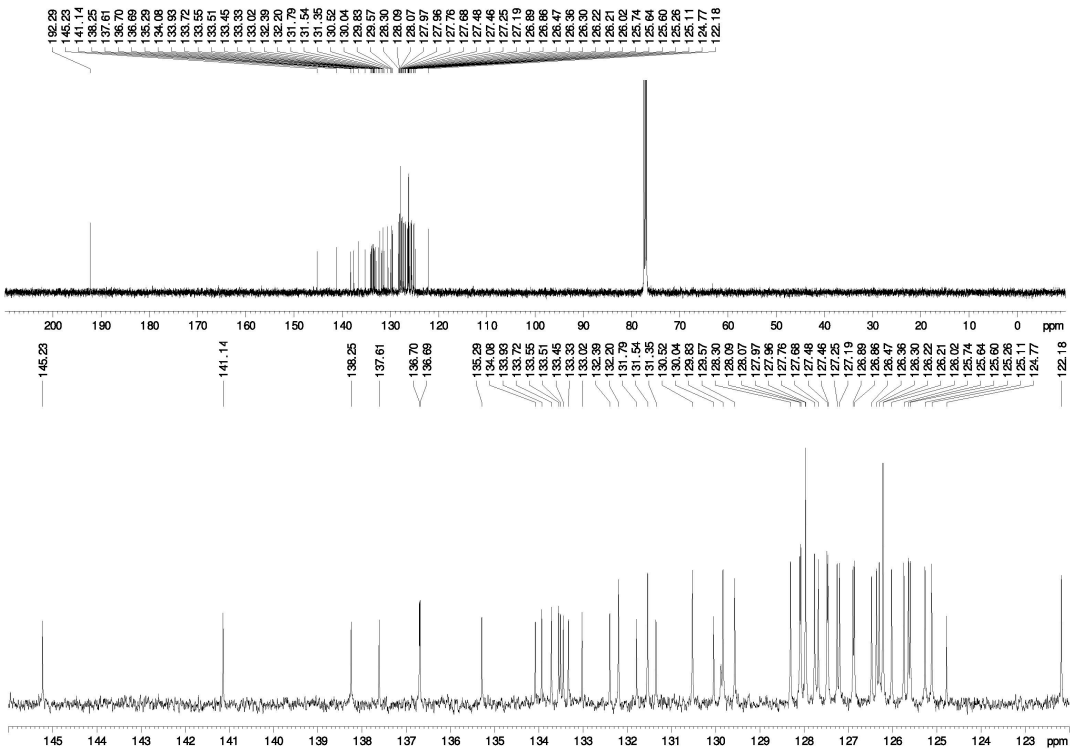
(R_a,S_a,S_a,S_a)-15, ^{13}C NMR (126 MHz, $CDCl_3$):



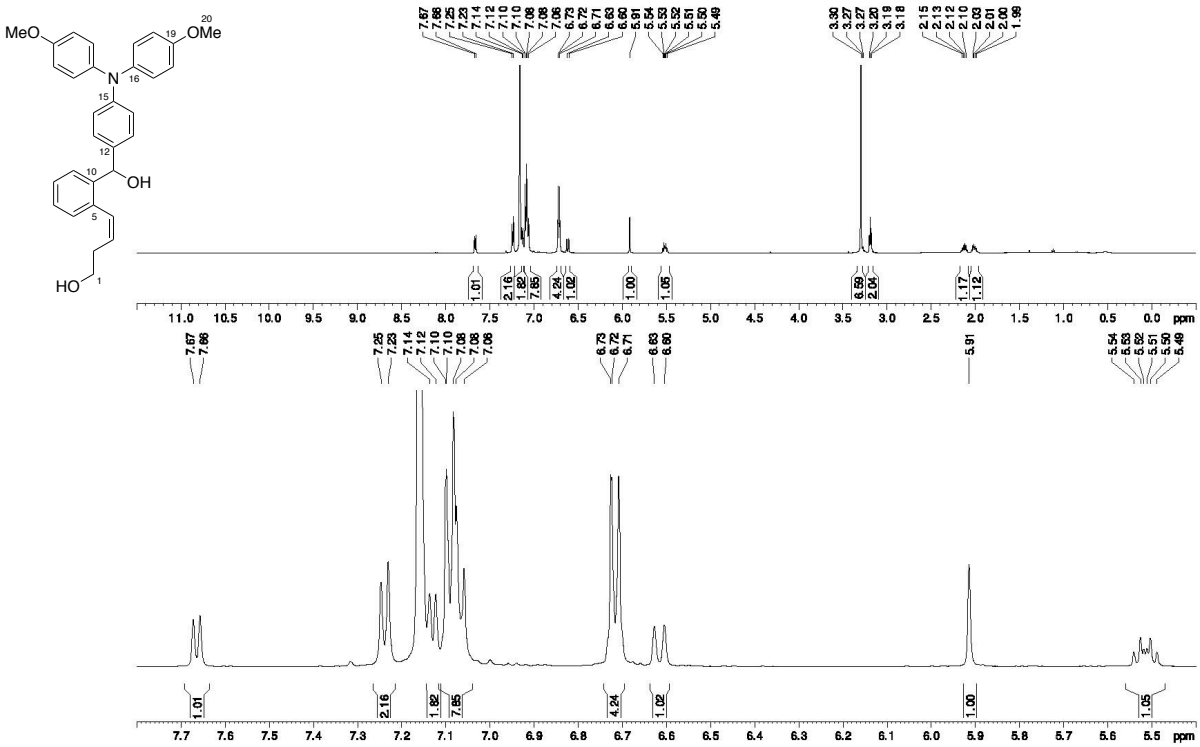
(S_a,S_a,S_a,S_a)-16, ^{1}H NMR (500 MHz, $CDCl_3$):



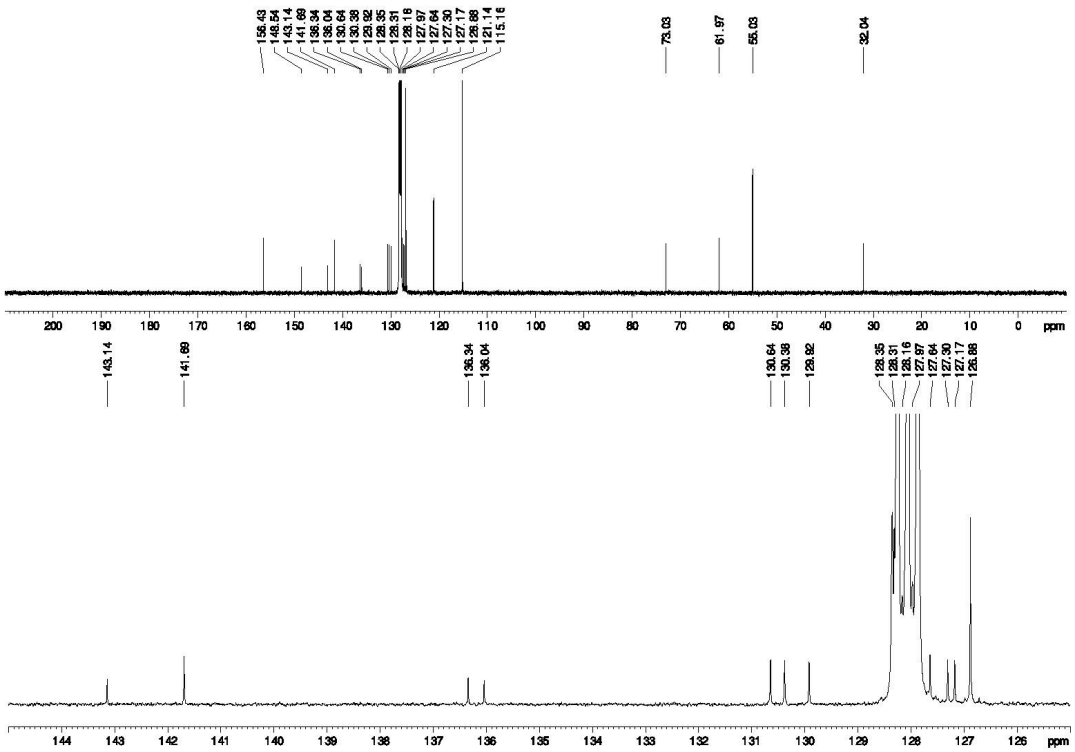
(S_a,S_a,S_a,S_a)-16, ^{13}C NMR (126 MHz, $CDCl_3$):



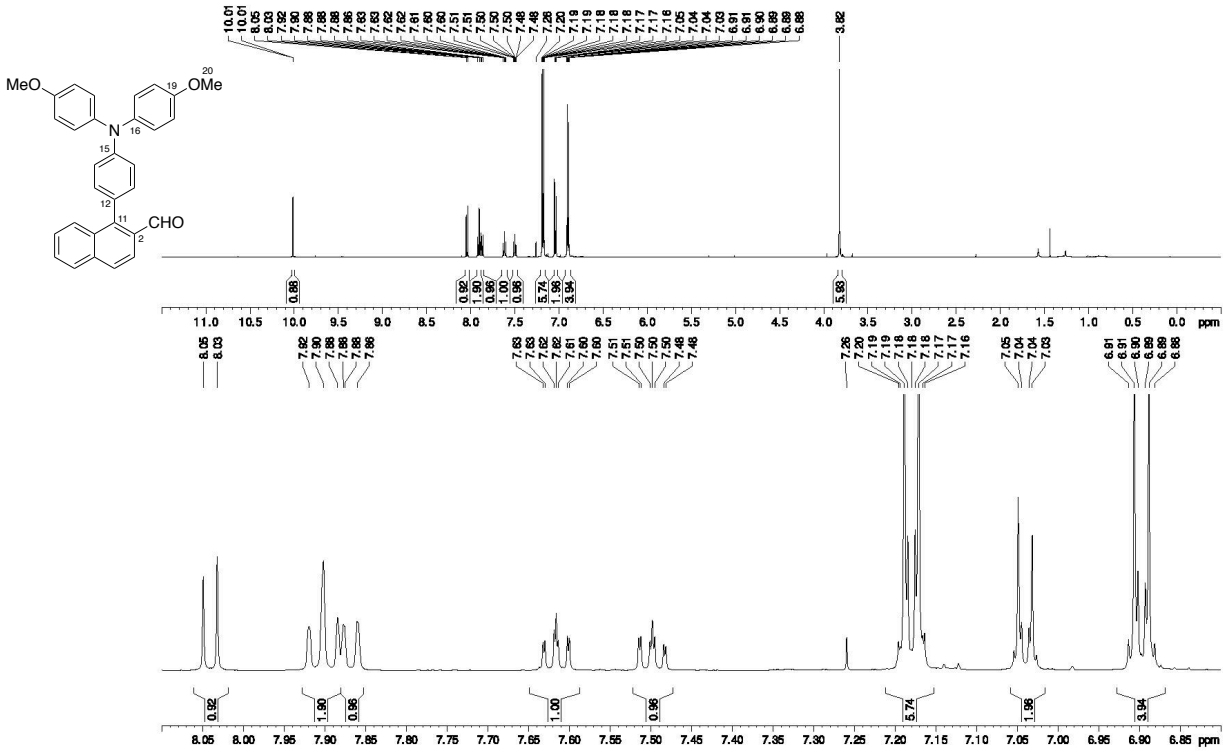
Diol E, ^{1}H NMR (500 MHz, C_6D_6):



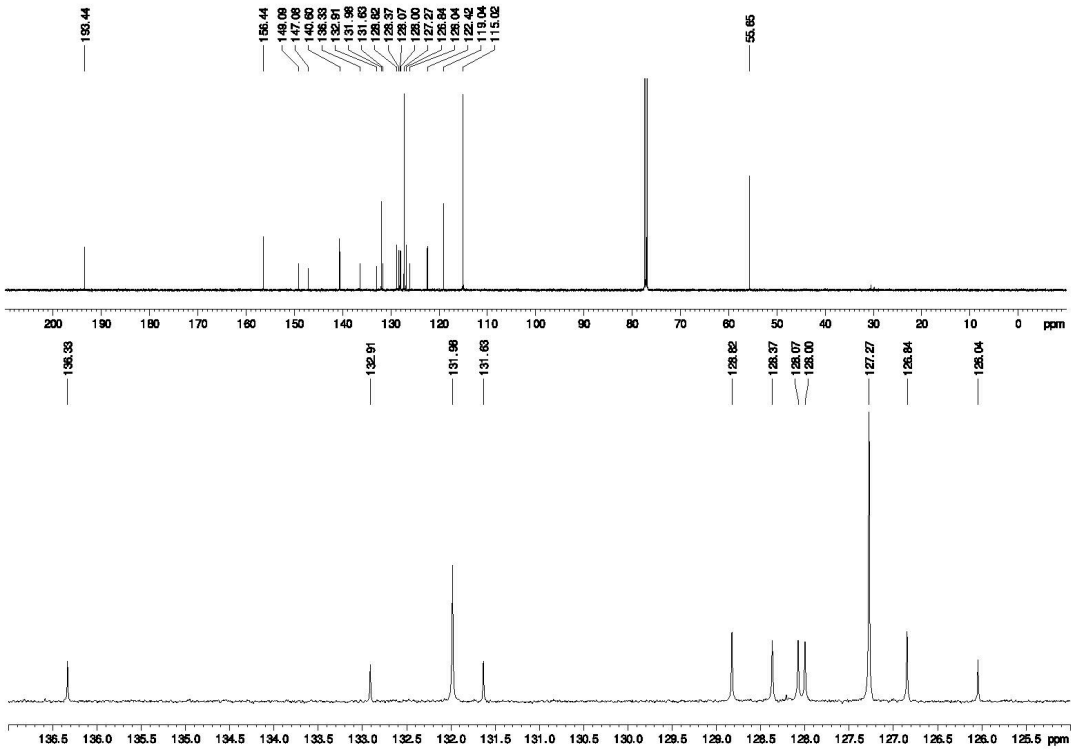
Diol E, ^{13}C NMR (126 MHz, C_6D_6):



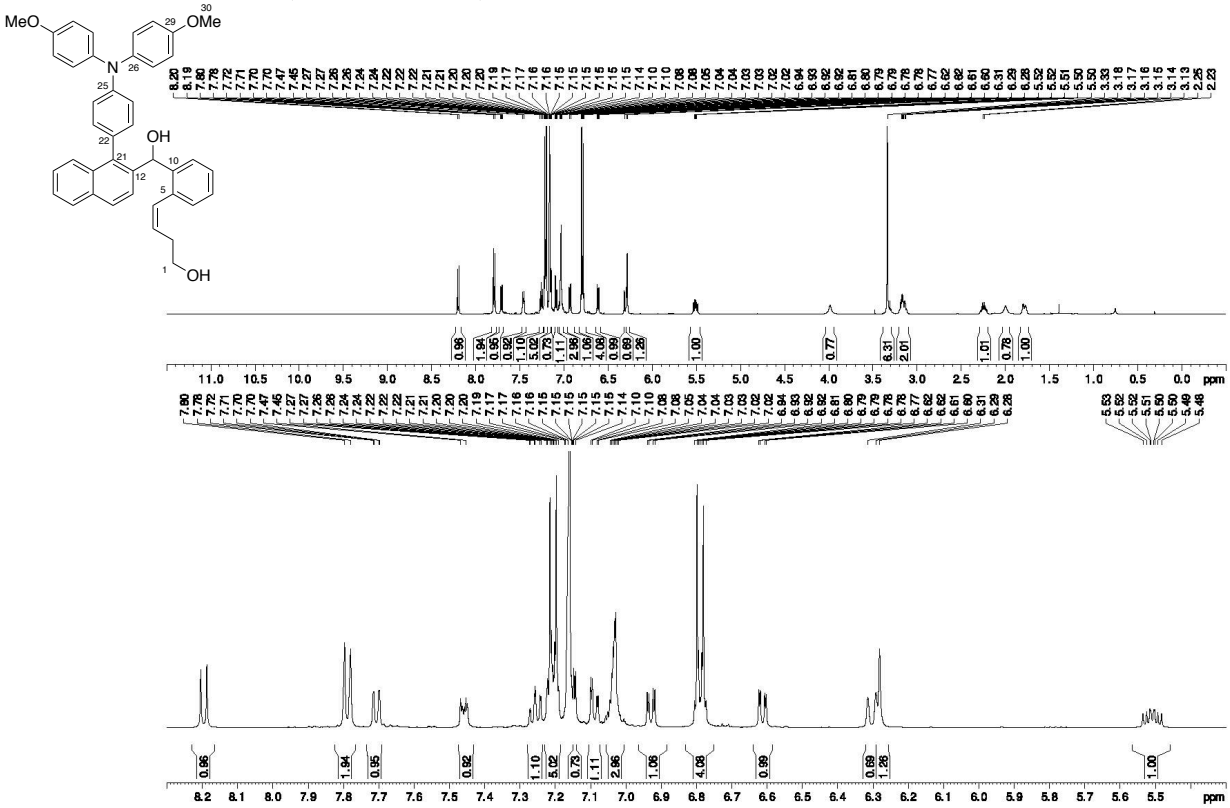
1-(4-(bis(4-methoxyphenyl)amino)phenyl)-2-naphthaldehyde, ^{1}H NMR (500 MHz, $CDCl_6$):



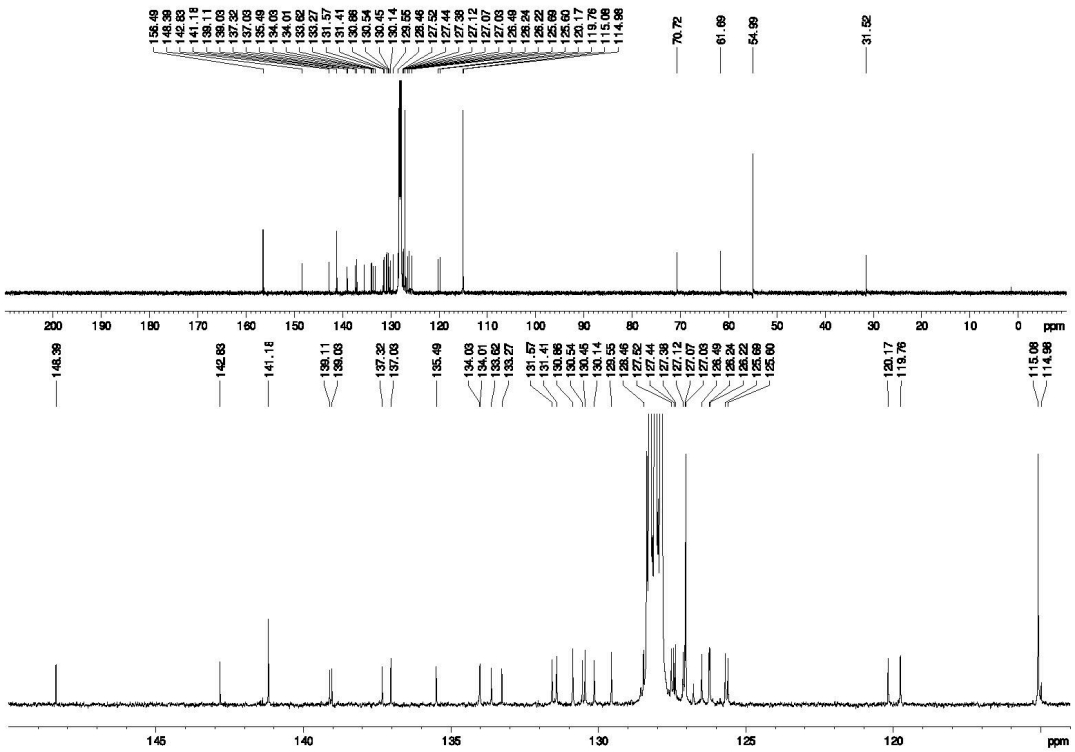
1-(4-(bis(4-methoxyphenyl)amino)phenyl)-2-naphthaldehyde, ^{13}C NMR (126 MHz, $CDCl_3$):



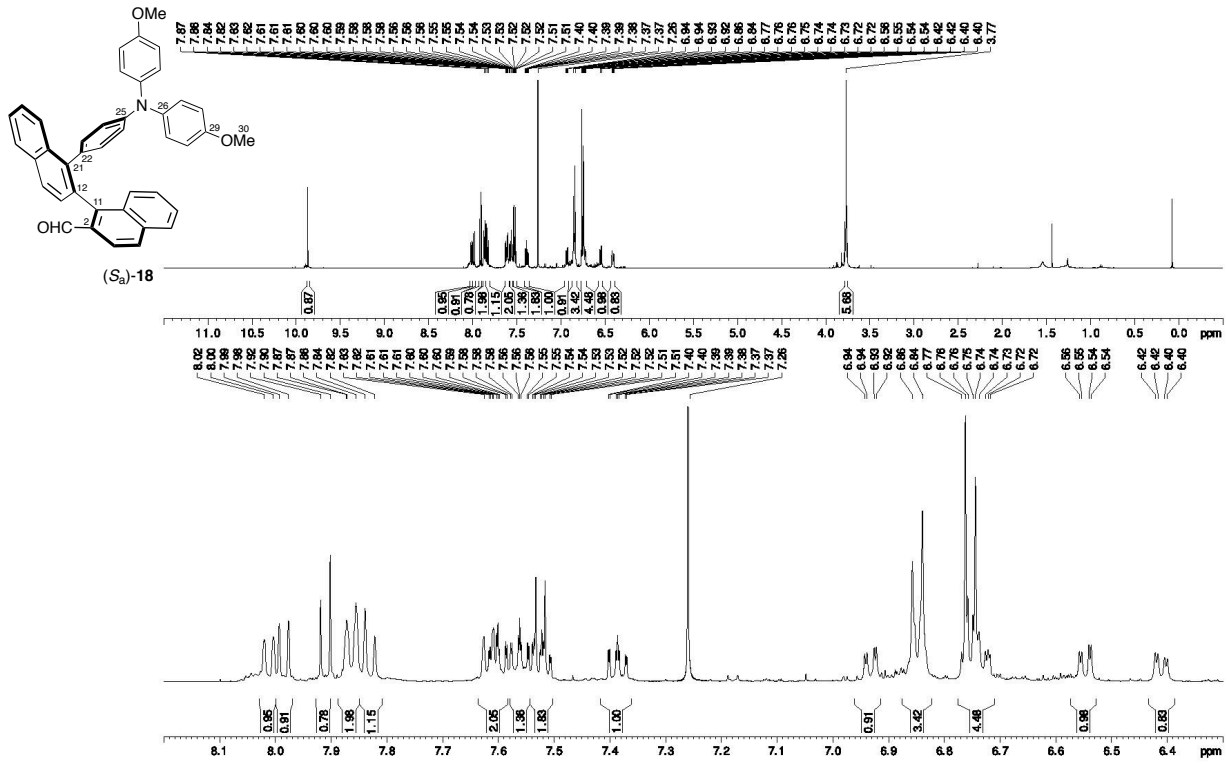
Diol F, ^{1}H NMR (500 MHz, C_6D_6):



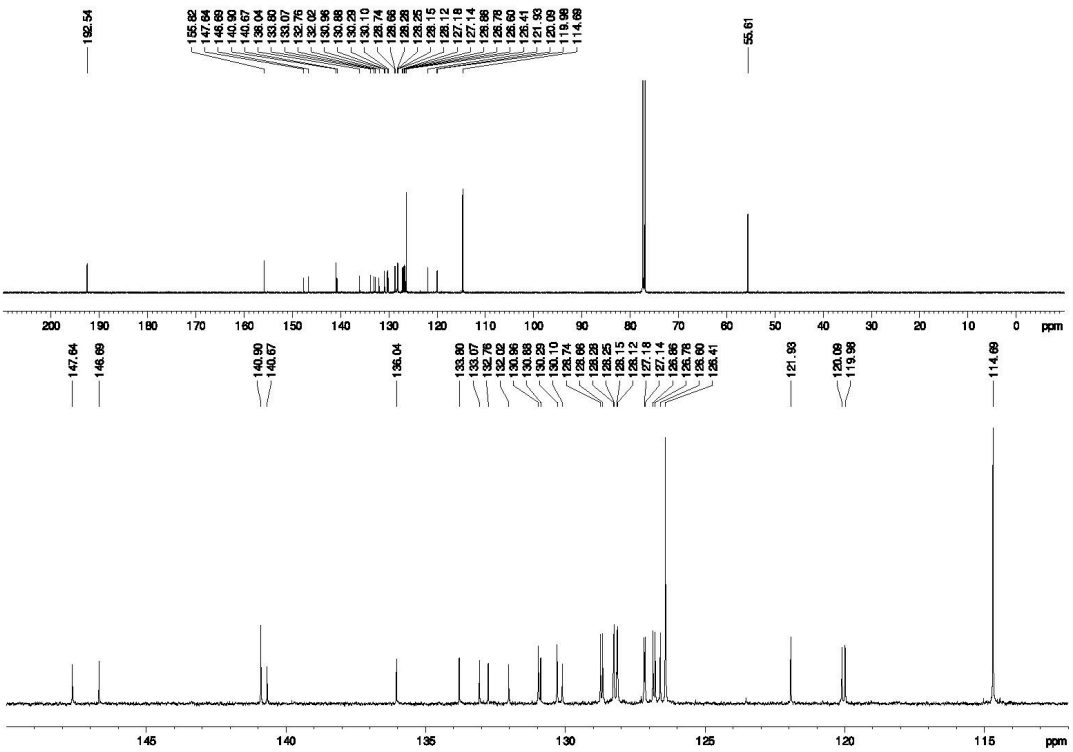
Diol F, ^{13}C NMR (126 MHz, C_6D_6):



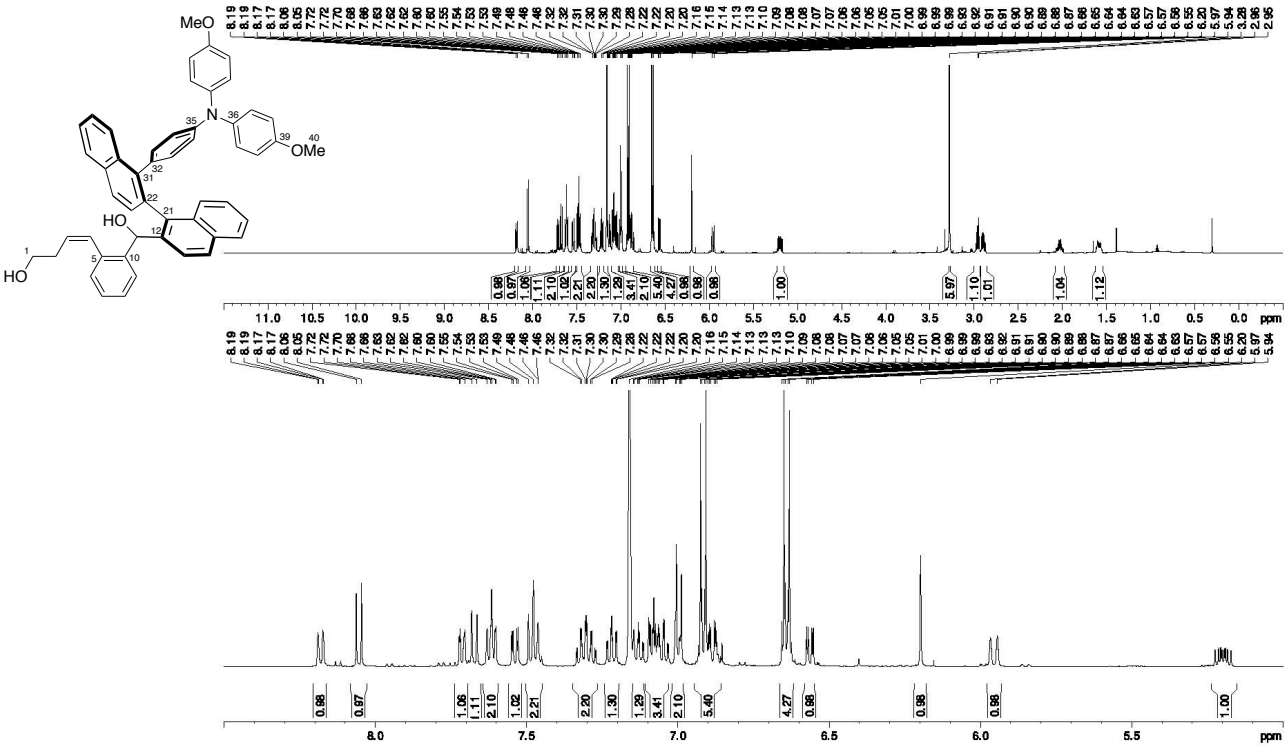
(S_a)-18, ^{1}H NMR (500 MHz, $CDCl_6$):



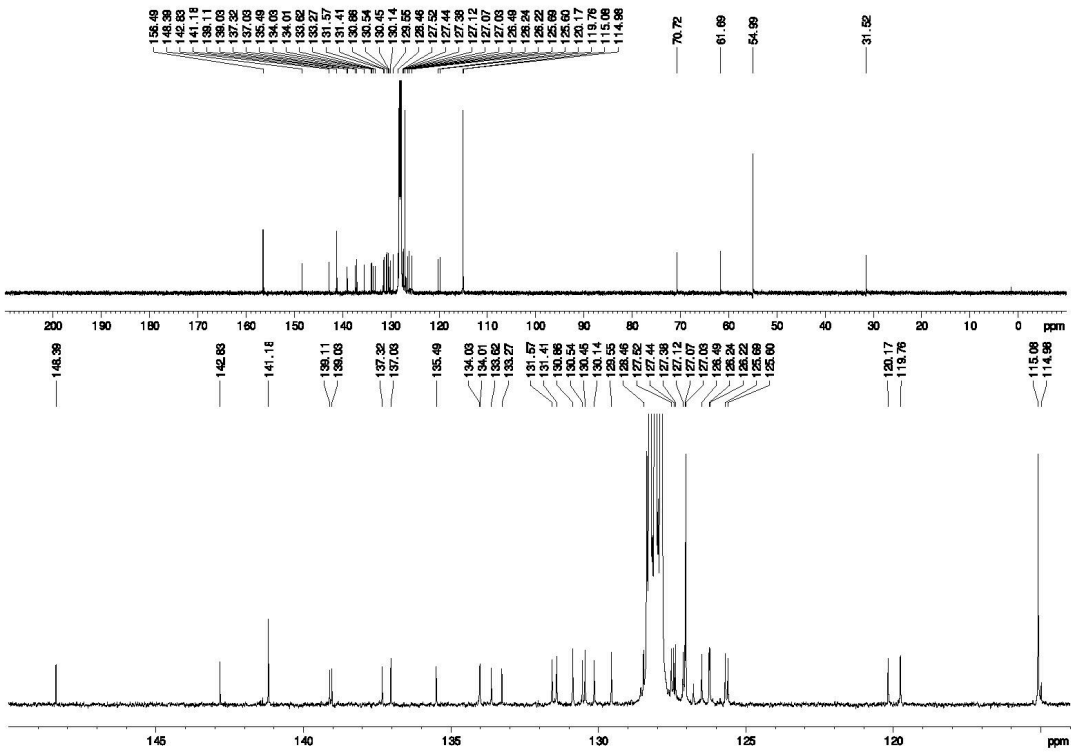
(S_a)-18, ^{13}C NMR (126 MHz, $CDCl_3$):



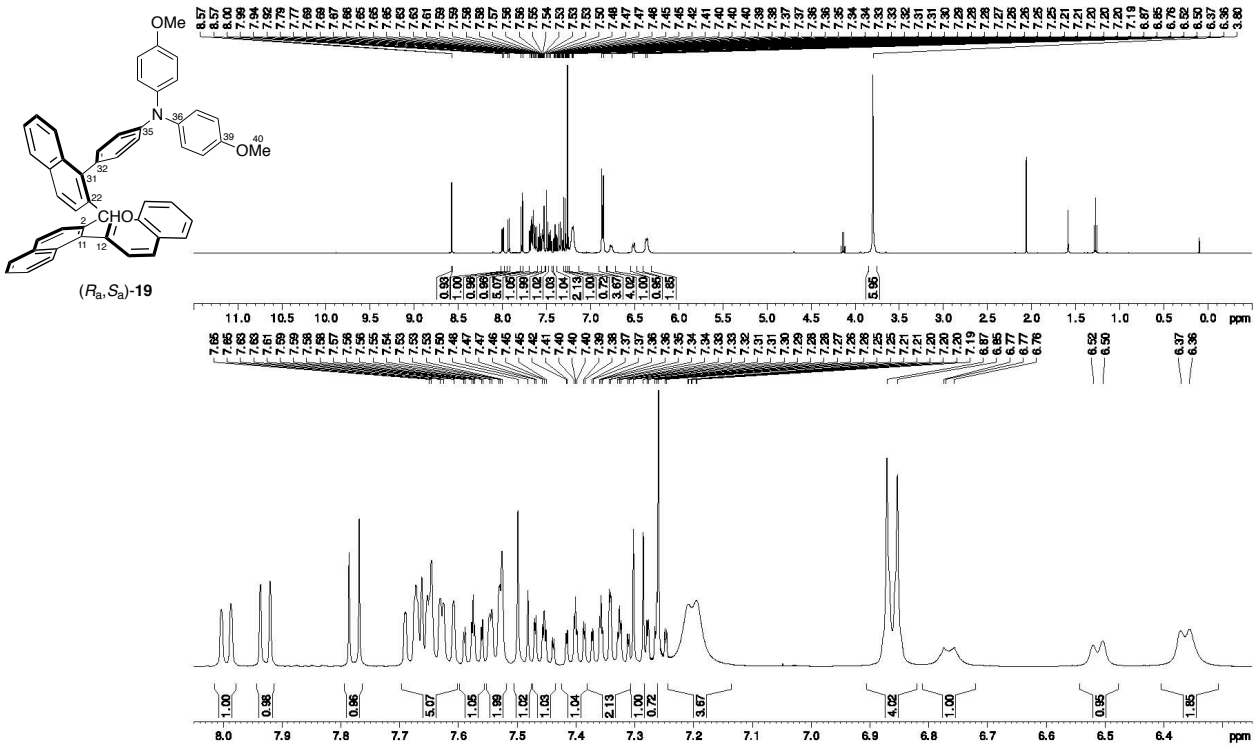
Diol G, ^{1}H NMR (500 MHz, C_6D_6):



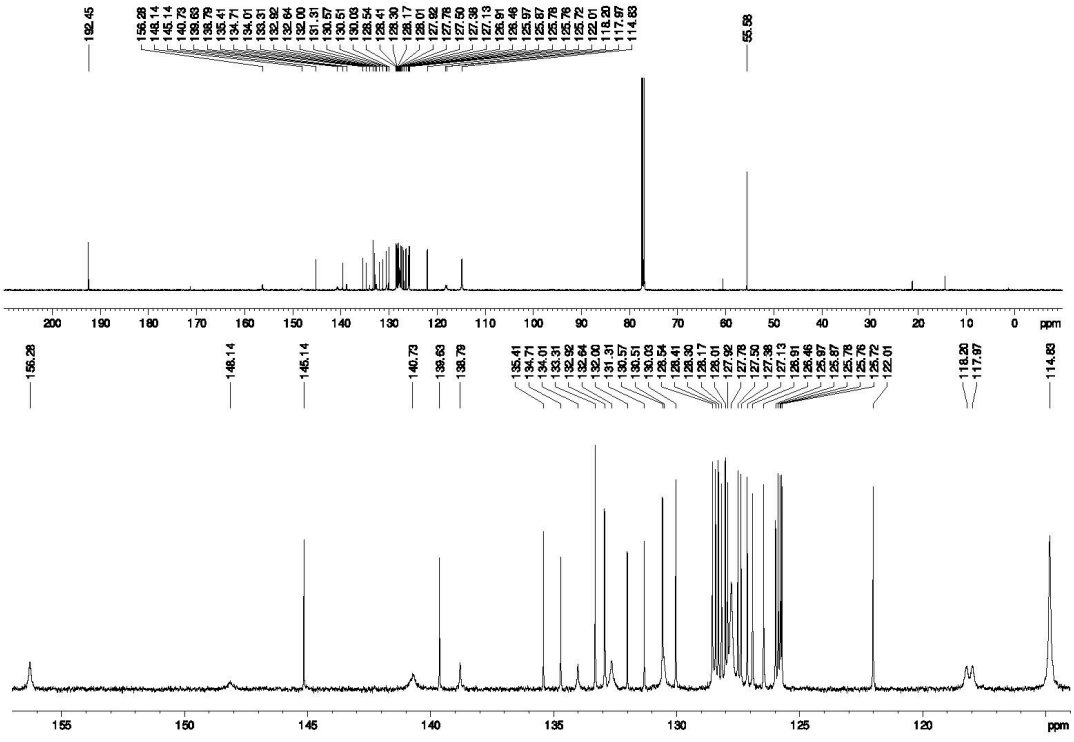
Diol G, ^{13}C NMR (126 MHz, C_6D_6):



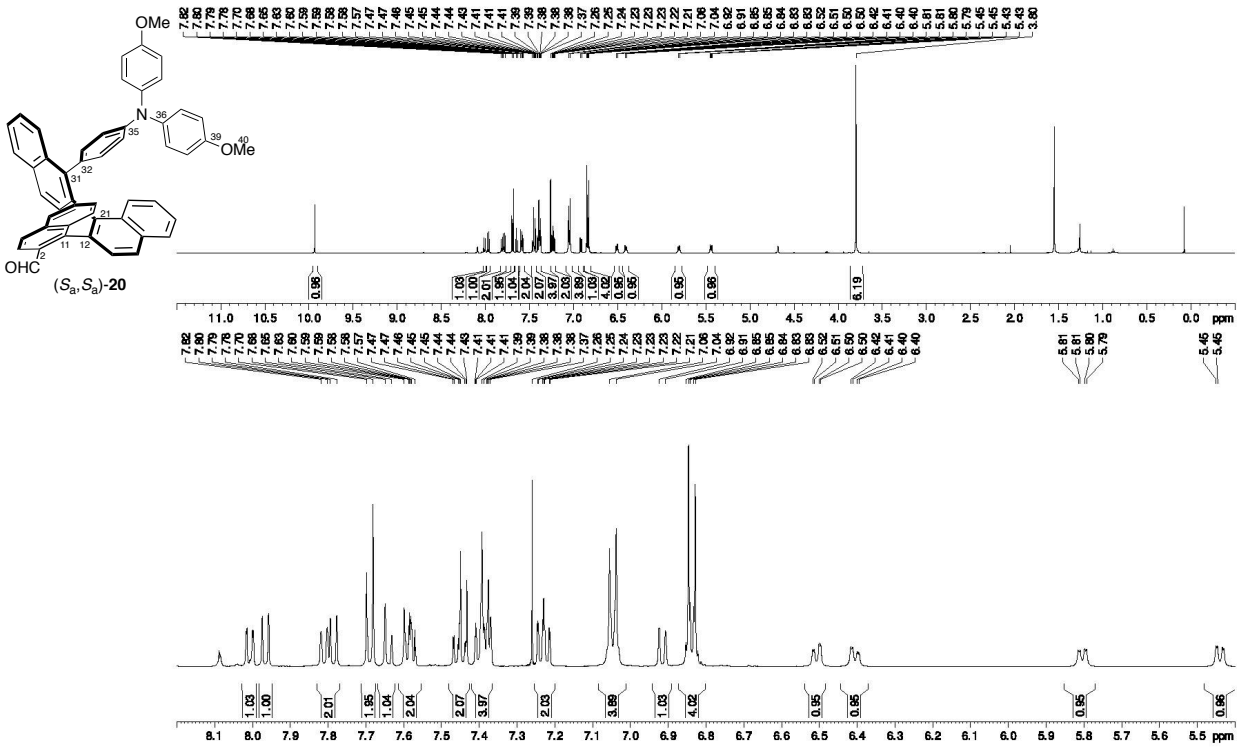
(R_a,S_a)-19, ^{1}H NMR (500 MHz, C_6D_6):



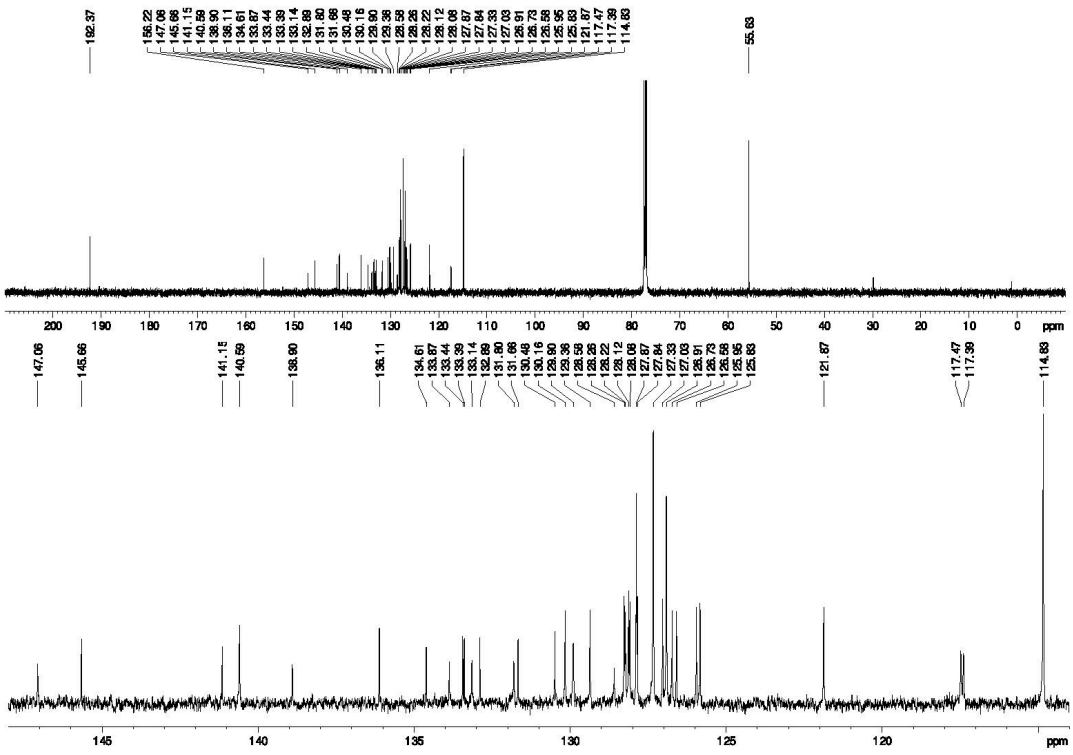
(R_a,S_a)-19, ^{13}C NMR (126 MHz, $CDCl_3$):



(S_a,S_a)-20, ^{1}H NMR (500 MHz, C_6D_6):



(S_a,S_a)-20, ^{13}C NMR (126 MHz, $CDCl_3$):



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[5] We thank Prof. M. Waser (JKU Linz) for generously providing catalyst **Cat34** – **Cat44** for our test reactions.