==========

ELECTRONIC SUPPORTING INFORMATION

==========

BELONGING TO THE PAPER

Hydrogen-bond mediated regio- and enantioselectivity in a C–H amination reaction catalysed by a supramolecular Rh(II) complex

Thorsten Höke, Eberhardt Herdtweck and Thorsten Bach*

1. Synthetic procedures and analytical data S2

2. NMR spectra of new compounds S38

3. HPLC traces of chiral products S66

4. Crystallographic data S76

5. References S85

1. Synthetic procedures and analytical data

General information

All reactions, sensitive to air or moisture, were carried out in flame-dried glassware under positive pressure of argon using standard techniques. Dry tetrahydrofuran (THF), dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were obtained from an MBraun MB-SPS 800 solvent purification system. Other dry solvents were obtained from Fluka and Acros in the highest purity available and used without further purification. All solvents for chromatography were distilled prior to use. TLC was performed on silica coated glass plates (silica gel 60 F254) with detection by UV (254 nm), $KMnO_4$ or ceric ammonium molybdate (CAM) with subsequent heating. Flash chromatography was performed on silica gel 60 (Merck, 230-400 mesh) with the indicated eluent. HPLC analyses were performed using a chiral stationary phase (ChiralPak AD-H, ChiralCell OD or ChiralPak AS-RH, UV detection; Daicel Chemical Industries) employing *n*-hexane/*i*-PrOH (AD-H, OD) or acetonitrile/water (AS-RH) as eluents. For the separation of enantiomers, semipreparative HPLC with a chiral stationary phase (Daicel ChiralPak AD, 250 × 20 mm) was used. IR-spectra were recorded on a JASCO IR-4100 (ATR), MS/HRMS-measurements were performed on a Finnigan MAT 8200 (EI), a Finnigan MAT 95S (HR-EI), a Finnigan LCQ classic (ESI), a Thermo Scientific LTQ Orbitrap XL (HRMS-ESI) or a Thermo Scientific LTQ_FT ultra (HRMS-ESI). ^{1}H-and ^{13}C-NMR-spectra were recorded in the stated solvent at 300 K on a Bruker AV-250, a Bruker AV-360 or a Bruker AV-500 spectrometer. Chemical shifts are reported in δ units relative to the residual non-deuterated solvent [$CHCl_3$: δ (^{1}H) = 7.26 ppm, δ (^{13}C) = 77.16 ppm, DMSO-d_6: δ (^{1}H) = 2.50 ppm, δ (^{13}C) = 39.52 ppm; THF-d_8: δ (^{1}H) = 1.73 ppm, 3.58 ppm; δ (^{13}C) = 25.30 ppm] or TMS [δ (^{1}H) = 0.00 ppm]. Apparent multiplets which occur as a result of coincidental equality of coupling constants to those of magnetically non-equivalent protons are marked as virtual (*virt.*). The multiplicity of the ^{13}C-NMR signals were determined by DEPT experiments and assignments are based on two-dimensional NMR spectroscopy (COSY, NOESY, HSQC, HMBC). Melting points were measured on a Büchi 510 and are not corrected. Specific rotations were measured using a Perkin-Elmer 241 MC (sodium vapor lamp or mercury lamp).

General procedures

General procedure 1 (GP1): Grignard addition to aldehydes

Magnesium turnings (2.5 eq) were suspended in a small amount of THF and approx. 1/3 of the corresponding neat aryl bromide (2.5 eq) was added. The mixture was stirred until the solution became turbid and heat evolution was observed (in case of no reaction one or two drops of 1,2-dibromoethane were added). A solution of remaining aryl bromide in THF (1.0 M, total Grignard concentration) was added over 10 minutes. The reaction mixture was heated at reflux for one hour, then was cooled to room temperature and added to a suspension of aldehyde **S1**[5] (1.0 eq) in THF (0.4 M) at 0 °C. After heating at reflux for two hours the reaction was quenched by addition of saturated NH_4Cl solution/water (3/1). The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 × ~16 mL/mmol aldehyde). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was redissolved in dichloromethane/methanol, loaded onto Celite and subjected to flash column chromatography.

General procedure 2 (GP2): Dehydroxylation of quinolones

To a suspension of the corresponding alcohol (1.0 eq) and triethylsilane (2.5 eq) in dichloromethane (0.2 M) was added trifluoroacetic acid (CH_2Cl_2/TFA = 2/1 or 5.0 eq TFA for substrate **S6a** respectively). The reaction mixture was stirred for 15-20 minutes at room temperature (40 minutes at 0 °C for substrate **S6a**) and then poured carefully into a saturated $NaHCO_3$ solution. The mixture was extracted with dichloromethane (3 × 20 mL/mmol quinolone) and the combined organic layers were dried over Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was dissolved in dichloro-methane/methanol, loaded onto Celite and subjected to flash column chromatography.

General procedure 3 (GP3): Synthesis of acid chlorides

The corresponding carboxylic acid (1.0 eq) was treated with thionyl chloride (2.5 eq) and heated at reflux for two hours. Excess thionyl chloride was removed at room temperature under high vacuum to afford the acid chloride, which was used without further purification.

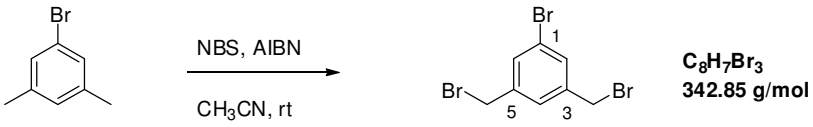
*General procedure 4 (GP4): Rh-catalyzed CH-amination reactions using **6** or Rh_2esp_2*[1]

A flask was charged with 2,2,2-trichloroethyl sulfamate (22.8 mg, 0.1 mmol, 1.0 eq), catalyst **6** or Rh_2esp_2 (2 µmol, 0.02 eq) and the corresponding quinolone (1.0 eq or 2.0 eq). The

mixture was dissolved in dry benzene (4 mM) and $PhI(OAc)_2$ was added (48.3 mg, 0.15 mmol, 1.5 eq) at room temperature in seven portions over the course of one hour (one portion every 10 minutes). The reaction was further stirred for 18 hours at room temperature. The solvent was removed under reduced pressure and the crude product subjected to flash column chromatography.

Synthesis of the Rhodium-catalyst 6 and the substrates

1-Bromo-3,5-bis(bromomethyl)benzene (2)[2]



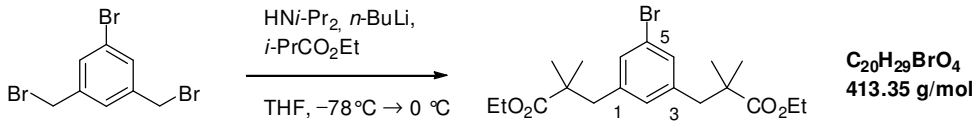
2

To a solution of 5-bromo-*m*-xylene (3.50 g, 18.9 mmol, 1.0 eq) and *N*-bromosuccinimide (7.07 g, 39.7 mmol, 2.1 eq) in acetonitrile (135 mL) was added azobisisobutyronitrile (62.1 mg, 0.378 mmol, 0.02 eq) and the reaction mixture heated at reflux for four hours. The solvent was then removed under reduced pressure. Carbon tetrachloride (60 mL) was added and the mixture was heated at reflux for 10 minutes. After cooling to room temperature, the solution was separated from insoluble succinimide by filtration. The solvent was removed under reduced pressure and the residue recrystallized twice from ethanol to afford the title compound as colorless needles (3.13 g, 48%).

^{1}H-NMR (250 MHz, $CDCl_3$): δ [ppm] = 4.41 (s, 4 H, CH_2Br), 7.32-7.36 (m, 1 H, 4-H), 7.47 (d, ^4J = 1.5 Hz, 2 H, 2-H, 6-H).
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 31.6 (t, CH_2Br), 122.8 (s, C-1), 128.4 (d, C-4), 132.1 (d, C-2, C-6), 140.4 (s, C-3, C-5).

The data obtained matched those reported in the literature.[2]

Diethyl 3,3'-(5-bromo-1,3-phenylene)bis(2,2-dimethylpropanoate) (3)



2 **3**

C$_{20}$H$_{29}$BrO$_4$
413.35 g/mol

To a solution of diisopropylamine (0.35 mL, 2.50 mmol, 2.5 eq) in THF (2 mL) was added *n*-butyllithium (1.0 mL, 2.50 mmol, 2.5 eq, 2.5 M in *n*-hexane) at 0 °C dropwise. The solution was stirred at this temperature for 30 minutes after which it was cooled to –78 °C and a solution of ethyl isobutyrate (290 mg, 2.50 mmol, 2.5 eq) in THF (2 mL) was added over 10 minutes. The reaction mixture was allowed to warm to 0 °C, stirred for 10 minutes and then was quenched by addition of saturated NH_4Cl solution (15 mL) and water (15 mL). The mixture was extracted with EtOAc (3 × 15 mL), the combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was subjected to flash column chromatography (SiO_2, 17 × 2 cm, pentane/EtOAc 95/5, CAM) to afford ester **3** as a colorless solid (378 mg, 92%).

m.p.: 66-67 °C

TLC: R_f = 0.60 (pentane/EtOAc = 6/1) [CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3015 (w, CH), 2927 (w, CH), 2870 (w, CH), 1721 (vs, C=O), 1567 (C=C), 1477 (w), 1386 (m), 1299 (m), 1188 (vs, C-O), 1131 (s), 1033 (m), 946 (w), 878 (m), 822 (m).

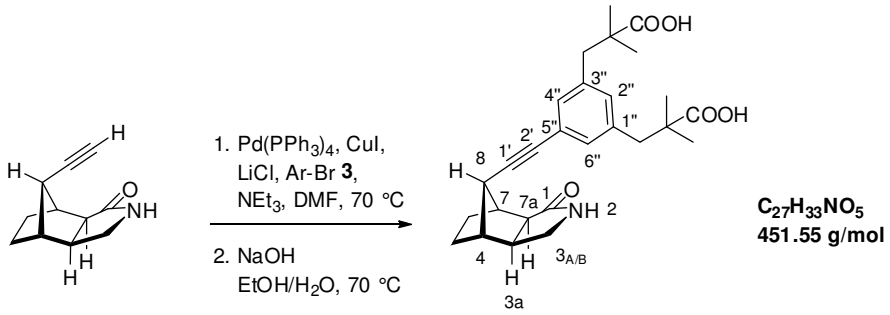
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.16 (s, 12 H, C(C$\underline{H}_3$)$_2$), 1.24 (t, ^3J = 7.1 Hz, 6 H, OCH$_2$C$\underline{H}_3$), 2.78 (s, 4 H, C$\underline{H}_2$Ar), 4.12 (q, ^3J = 7.1 Hz, 4 H, OC$\underline{H}_2$CH$_3$), 6.81 (s, 1 H, 2-H), 7.13 (s, 2 H, 4-H, 6-H).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 14.3 (q, OCH$_2$C$\underline{H}_3$), 25.1 (q, C(C$\underline{H}_3$)$_2$), 43.6 (s, C$\underline{(CH_3)_2}$), 45.8 (t, C$\underline{H}_2$Ar), 60.7 (t, OC$\underline{H}_2$CH$_3$), 121.7 (s, C-5), 131.1 (d, C-2), 131.2 (d, C-4, C-6), 139.9 (s, C-1), 177.2 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 414 (35) [M$^+$ (^{81}Br)], 412 (37) [M$^+$ (^{79}Br)], 366 (6), 340 (96), 338 (100), 294 (63), 265 (40), 225 (87), 185 (63), 128 (42).

HRMS (EI): $C_{20}H_{29}{}^{79}BrO_4$ [M$^+$]: calcd.: 412.1244; found: 412.1236.

3,3'-(5-(((3a*S*,4*R*,7*S*,7a*R*,8*R*)-1-oxooctahydro-1*H*-4,7-methanoisoindol-8-yl)ethynyl)-1,3-phenylene)bis(2,2-dimethylpropanoic acid) (5)



4 **5**

A mixture of alkyne **4**[3] (51.6 mg, 0.295 mmol, 1.0 eq), copper(I) iodide (5.6 mg, 29.4 µmol, 0.1 eq) and dry lithium chloride (74.9 mg, 1.77 mmol, 6 eq) in DMF (2.95 mL) and triethylamine (0.82 mL) was degassed by three *pump-freeze-thaw* cycles. Upon addition of $Pd(PPh_3)_4$ (34.0 mg, 29.4 µmol, 0.1 eq) the reaction was stirred at 70 °C for 20 hours. Water (15 mL) was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were successively washed with water (10 mL) and saturated NaCl solution (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO_2, 9 × 2.5 cm, pentane/EtOAc 3/7, CAM). The coupling product was obtained as a colorless solid (134 mg, max. 0.263 mmol), containing inseparable phosphine-impurities. The compound was dissolved in ethanol (1.3 mL) and sodium hydroxide (52.6 mg, 1.32 mmol, 5 eq) and water were successively added until the sodium hydroxide was dissolved (0.5 mL). The reaction mixture was stirred at 70 °C for 18 hours. Water (20 mL) was added and the aqueous layer was washed with Et_2O (2 × 6 mL), acidified (white precipitate) with HCl (3N) and extracted with Et_2O (3 × 15 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed under reduced pressure and the residue subjected to flash column chromatography (SiO_2, 11 × 2.5 cm, CH_2Cl_2/MeOH 99/1 + 1% AcOH, CAM) to afford the title compound as a colorless solid (97.7 mg, 73%).

m.p.: 177-179 °C

TLC: R_f = 0.47 (CH_2Cl_2/MeOH = 9/1) [CAM].

Specific Rotation: [98% *ee*, based on enantiomeric purity of compound **4**]

$[\alpha]_D^{20} = -27.6$ (c = 0.66, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3055 (w), 2964 (w, CH), 2922 (w, CH), 2877 (w, CH), 1697 (vs,

C=O), 1644 (s, C=O), 1596 (m, C=C), 1472 (m), 1450 (m), 1306 (m), 1202 (s), 1161 (m), 1129 (m), 929 (m), 884 (m), 852 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.06 (s, 6 H, $C(CH_3)_2$), 1.17-1.29 (m, 2 H, 5-H_{endo}, 6-H_{endo}), 1.25 (s, 6 H, $C(CH_3)_2$), 1.58-1.74 (m, 2 H, 5-H_{exo}, 6-H_{exo}), 2.44 (d, ^3J = 3.9 Hz, 1 H, 4-H), 2.48-2.55 (m, 2 H, 3a-H, 8-H), 2.57-2.63 (m, 3 H, CH_aH_bAr, 7a-H), 2.89 (d, ^3J = 3.9 Hz, 1 H, 7-H), 2.94 (d, ^2J = 13.0 Hz, 2 H, CH_aH_bAr), 3.47-3.56 (m, 2 H, 3-H), 6.82 (s, 1 H, 2''-H), 7.08 (s, 2 H, 4''-H, 6''-H), 7.55 (s, 1 H, NH), 9.75 (bs, 2 H, CO_2H).

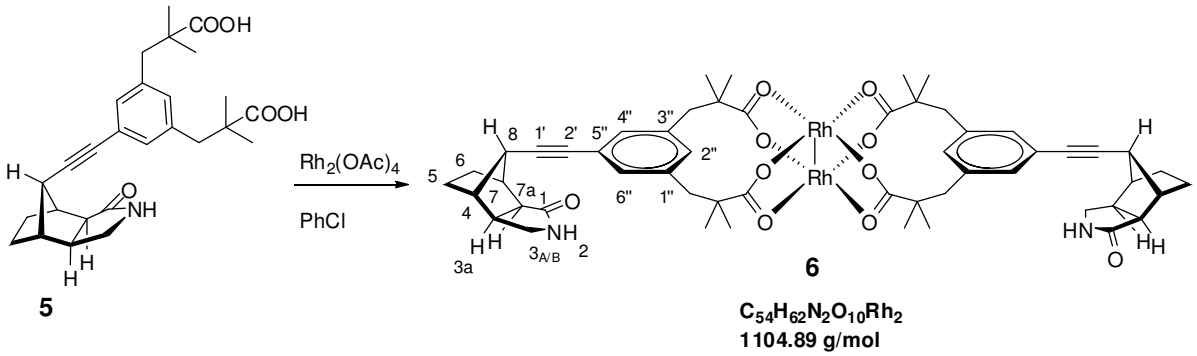
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 23.7 (q, $C(CH_3)_2$), 25.5 (q, $C(CH_3)_2$), 28.8, 28.8 (2 t, C-5, C-6), 39.0 (d, C-8), 41.8 (d, C-3a), 44.2 (s, $C(CH_3)_2$), 45.0 (d, C-7), 46.4 (d, C-4), 46.5 (t, CH_2Ar), 47.8 (t, C-3), 51.5 (d, C-7a), 83.0 (s, C-2'), 89.1 (s, C-1'), 123.0 (s, C-5''), 130.7 (d, C-4'', C-6''), 132.0 (d, C-2''), 137.7 (s, C-1'', C-3''), 181.1 (s, C-1), 182.4 (s, CO_2H).

HRMS (ESI): $C_{27}H_{34}NO_5$ $[(M+H)^+]$: calcd.: 452.2431; found: 452.2419

$C_{27}H_{33}NNaO_5$ $[(M+Na)^+]$: calcd.: 474.2250; found: 474.2235

$C_{54}H_{67}N_2O_{10}$ $[(2M+H)^+]$: calcd.: 903.4790; found: 903.4786.

Bis[rhodium(3,3'-(5-(((3a*S*,4*R*,7*S*,7a*R*,8*R*)-1-oxooctahydro-1*H*-4,7-methanoisoindol-8-yl)ethynyl)-1,3-phenylen)bis(2,2-dimethylpropanoate))] (6)



$Rh_2(OAc)_4$ (137 mg, 0.309 mmol, 1.0 eq) and **5** (293 mg, 0.649 mmol, 2.1 eq) were dissolved in chlorobenzene (35 mL) and the mixture was stirred at the boiling point (oilbath ~140-145 °C) while the solvent was slowly removed by distillation over the course of three hours. The crude product was dissolved in THF, loaded onto Celite and purified by flash column chromatography (SiO_2, 16 × 3.25 cm, CH_2Cl_2/MeOH 98/2 + 1% AcOH → 96/4 + 1% AcOH → 90/10 + 1% AcOH, UV/ CAM). The title complex **6** (318 mg, 93%) was obtained as a pale blue solid after repeated evaporation with toluene (removal of AcOH) under reduced pressure and drying over night *in vacuo* at 50 °C. If not sufficiently pure (^{1}H-NMR), complex **6** was further purified by repeated washing (2-3 times) with dichloromethane.

The structure of **6** was confirmed by X-ray diffraction analysis of a single crystal, obtained by slow diffusion of ethyl acetate vapor into a solution of **6** in DMSO.

m.p.: > 250 °C

TLC: R_f = 0.45 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

Specific Rotation: [98% *ee*, based on enantiomeric purity of compound **4**]

$[\alpha]_{365}^{20}$ = –43.2 (*c* = 0.25, THF).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] =2952 (w, CH), 2925 (w, CH), 2875 (w, CH), 1667 (s, C=O), 1580 (vs), 1407 (vs), 1257 (m), 1200 (w), 1137 (w), 1082 (w), 1049 (w) 1019 (w), 932 (w), 878 (m).

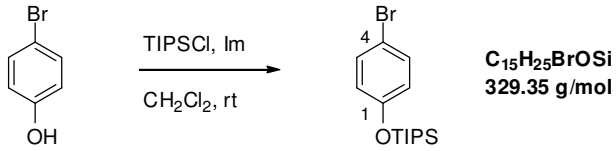
^{1}H-NMR (500 MHz, THF-d_8): δ [ppm] = 0.93 (s, 24 H, $C(CH_3)_2$), 1.15-1.25 (m, 4 H, 5-H_{endo}, 6-H_{endo}), 1.55-1.69 (m, 4 H, 5-H_{exo}, 6-H_{exo}), 2.28 (d, ^3J = 9.3 Hz, 2 H, 7a-H), 2.35 (d, ^3J = 3.4 Hz, 2 H, 4-H), 2.42-2.49 (m, 2 H, 3a-H), 2.52-2.57 (m, 10 H, 8-H, C$\underline{H}_2$Ar), 2.70 (d, ^3J = 3.4 Hz, 2 H, 7-H), 3.40-3.49 (m, 4 H, 3-H), 6.04 (s, 2 H, NH), 6.84 (d, ^4J = 1.4 Hz, 4 H, 4‘‘-H, 6‘‘-H), 6.88 (s, 2 H, 2‘‘-H).

^{13}C-NMR (125.8 MHz, THF-d_8): δ [ppm] = 26.1 (q, C($\underline{C}H_3)_2$), 29.4 (t, C-6), 29. 5 (t, C-5), 39.7 (d, C-8), 42.8 (d, C-3a), 45.3 (d, C-7), 46.2 (s, $\underline{C}(CH_3)_2$), 46.6 (t, C-3), 47.3 (t, $\underline{C}H_2$Ar), 47.6 (d, C-4), 51.0 (d, C-7a), 83.4 (s, C-2‘), 88.6 (s, C-1’), 123.3 (s, C-5’’), 131.3 (d, C-2’’), 131.5 (d, C-4’’, C-6’’), 139.1 (s, C-1’’, C-3’’), 177.5 (s, C-1), 195.9 (s, CO_2Rh).

HRMS (ESI): $C_{54}H_{63}N_2O_{10}Rh_2$ [$(M+H)^+$]: calcd.: 1105.2587; found: 1105.2553

$C_{54}H_{62}N_2NaO_{10}Rh_2$ [$(M+Na)^+$]: calcd.: 1127.2407; found: 1127.2361.

(4-Bromophenoxy)triisopropylsilane (S2)[4]



S2

To a solution of 4-bromophenol (1.73 g, 10.0 mmol, 1.0 eq) and imidazole (1.70 g, 25.0 mmol, 2.5 eq) in dichloromethane (63 mL) was added triisopropylsilyl chloride (2.56 mL, 12.0 mmol, 1.2 eq). The reaction was stirred over night at room temperature. The solvent was removed under reduced pressure and pentane (50 mL) and water (100 mL) were added. The layers were separated and the aqueous layer was extracted with pentane (2 × 50 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed

under reduced pressure. The residue was subjected to flash column chromatography (SiO_2, 14 × 3.25 cm, pentane, UV/CAM) to afford the title compound **S2** as colorless oil (3.26 g, 99%).

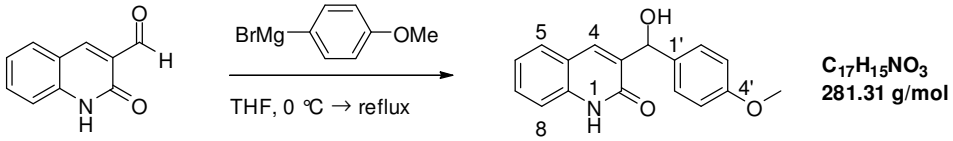
TLC: R_f = 0.57 (pentane) [UV, CAM].

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 1.10 (d, ^3J = 7.3 Hz, 18 H, Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.19-1.30 (m, 3 H, Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 6.73-6.79 (m, 2 H, 2-H), 7.29-7.34 (m, 2 H, 3-H).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 12.8 (d, Si(<u>C</u>H(CH$_3$)$_2$)$_3$), 18.0 (q, Si(CH(<u>C</u>H$_3$)$_2$)$_3$), 113.3 (s, C-4), 121.8 (d, C-Ar), 132.4 (d, C-Ar), 155.4 (s, C-1).

The data obtained matched those reported in the literature.[4]

3-(Hydroxy(4-methoxyphenyl)methyl)quinolin-2(1*H*)-one (S7a)



S1 **S7a**

$C_{17}H_{15}NO_3$
281.31 g/mol

According to *GP1*, aldehyde **S1**[5] (1.50 g, 8.66 mmol, 1.0 eq) in THF (22 mL) was reacted with the Grignard-reagent, prepared from magnesium turnings (528 mg, 21.7 mmol, 2.5 eq) and 4-bromoanisole (2.72 mL, 21.7 mmol, 2.5 eq) in THF (22 mL). After work-up, as described in *GP1*, the crude product was subjected to flash column chromatography (SiO_2, 15 × 3.25 cm, CH_2Cl_2/MeOH 98/2 → 97/3, UV/CAM) to afford the title compound as a colorless solid (1.93 g, 79%).

m.p.: 168-170 °C

TLC: R_f = 0.16 (CH_2Cl_2/MeOH = 97/3) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3009 (w, CH), 2935 (w, CH), 2889 (w), 2839 (w), 1651 (s, C=O), 1611 (m, C=C), 1566 (m, C=C), 1509 (m, C=C), 1430 (m), 1301 (m) 1240 (s, C-O), 1171 (m), 958 (m), 836 (m), 797 (m), 756 (vs).

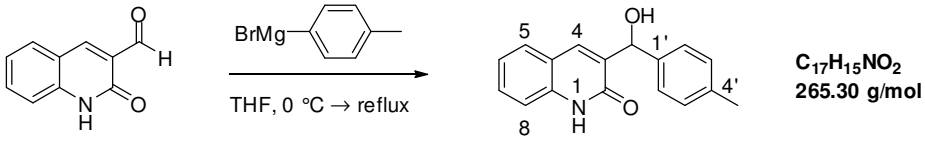
^{1}H-NMR (360 MHz, DMSO-d_6): δ [ppm] = 3.70 (s, 3 H, OCH_3), 5.71 (d, ^3J = 4.2 Hz, 1 H, CHO<u>H</u>), 5.75 (d, ^3J = 4.2 Hz, 1 H, C<u>H</u>OH), 6.81-6.86 (m, 2 H, 3'-H), 7.14-7.19 (*virt.* t, $^3J \approx$ 7.5 Hz, 1 H, 6-H), 7.26-7.33 (m, 3 H, 2'-H, 8-H), 7.42-7.47 (m, 1 H, 7-H), 7.71 (d, ^3J = 7.8 Hz, 1 H, 5-H), 8.02 (s, 1 H, 4-H), 11.71 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, DMSO-d_6): δ [ppm] = 55.0 (q, OCH_3), 68.5 (d, CHOH), 113.3 (d, C-

3‘), 114.7 (d, C-8), 119.2 (s, C-4a), 121.8 (d, C-6), 127.8 (d, C-5), 127.9 (d, C-2’), 129.6 (d, C-7), 133.8 (d, C-4), 136.0 (s, C-1’), 137.1 (s, C-3), 137.8 (s, C-8a), 158.2 (s, C-4’), 160.8 (s, C-2).

HRMS (ESI): $C_{17}H_{14}NO_2$ [$(M\text{-}OH)^+$]: calcd.: 264.1019; found: 264.1013
$C_{17}H_{16}NO_3$ [$(M+H)^+$]: calcd.: 282.1125; found: 282.1119
$C_{17}H_{15}NNaO_3$ [$(M+Na)^+$]: calcd.: 304.0944; found: 304.0937.

3-(Hydroxy(*p*-tolyl)methyl)quinolin-2(1*H*)-one (S4a)



S1 **S4a**

According to *GP1*, aldehyde **S1**[5] (500 mg, 2.89 mmol, 1.0 eq) in THF (7.2 mL) was reacted with the Grignard-reagent, prepared from magnesium turnings (175 mg, 7.22 mmol, 2.5 eq) and 1-bromo-4-methylbenzene (1.23 g, 7.22 mmol, 2.5 eq) in THF (7.2 mL). After work-up, as described in *GP1*, the crude product was subjected to flash column chromatography (SiO_2, 17 × 3.25 cm, CH_2Cl_2/EtOAc 4/1, UV/CAM) to afford the title compound as a colorless solid (721 mg, 94%).

m.p.: 157-158 °C

TLC: R_f = 0.52 (EtOAc) [UV, CAM].

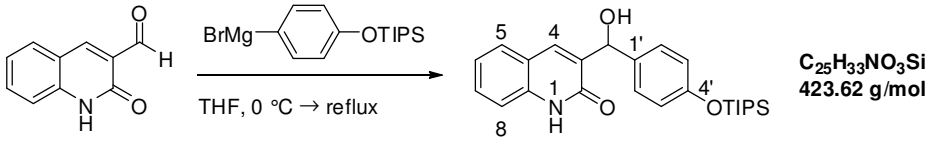
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3012 (w, CH), 2855 (w, CH), 1653 (vs, C=O), 1618 (m, C=C), 1571 (s, C=C), 1500 (m, C=C), 1431 (s), 1394 (m), 1256 (m), 1219 (s, C-O), 1009 (s), 950 (s), 902 (m), 749 (vs).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.36 (s, 3 H, CH_3), 4.75 (d, ^3J = 5.0 Hz, 1 H, CHOH), 5.95 (d, ^3J = 5.0 Hz, 1 H, CHOH), 7.20 (d, ^3J = 8.0 Hz, 2 H, 3’-H), 7.21 (*virt.* t, $^3J \approx$ 7.8 Hz, 1 H, 6-H), 7.29 (d, ^3J = 8.2 Hz, 1 H, 8-H), 7.41 (d, ^3J = 8.2 Hz, 2 H, 2’-H), 7.46-7.51 (m, 1 H, 7-H), 7.51 (d, ^3J = 8.1 Hz, 1 H, 5-H), 7.56 (s, 1 H, 4-H), 12.05 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 21.3 (CH_3), 73.4 (d, CHOH), 115.9 (d, C-8), 120.1 (s, C-4a), 123.2 (d, C-6), 126.9 (d, C-2’), 128.3 (d, C-5), 129.3 (d, C-3’), 130.6 (d, C-7), 134.4 (s, C-3), 137.2 (d, C-4), 137.5 (s, C-8a), 137.6 (s, C-4’), 138.6 (s, C-1’), 164.3 (s, C-2).

HRMS (ESI): $C_{17}H_{14}NO$ [$(M\text{-}OH)^+$]: calcd.: 248.1070; found: 248.1069
$C_{17}H_{16}NO_2$ [$(M+H)^+$]: calcd.: 266.1175; found: 266.1176
$C_{17}H_{15}NNaO_2$ [$(M+Na)^+$]: calcd.: 288.0995; found: 288.0997.

3-(Hydroxy(4-((triisopropylsilyl)oxy)phenyl)methyl)quinolin-2(1*H*)-one (S5a)



S1 **S5a**

$C_{25}H_{33}NO_3Si$
423.62 g/mol

According to *GP1*, aldehyde **S1**[5] (260 mg, 1.50 mmol, 1.0 eq) in THF (3.6 mL) was reacted with the Grignard-reagent, prepared from magnesium turnings (91.1 mg, 3.75 mmol, 2.5 eq) and arylbromide **S2** (1.24 g, 3.75 mmol, 2.5 eq) in THF (3.6 mL). After work-up, as described in *GP1*, the crude product was subjected to flash column chromatography (SiO_2, 17 × 3.25 cm, CH_2Cl_2/EtOAc 4/1, UV/CAM) to afford the title compound as a colorless solid (573 mg, 90%).

m.p.: 120-123 °C

TLC: R_f = 0.62 (EtOAc) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3164 (w), 3062 (w, CH), 2941 (m, CH), 2891 (w, CH), 2865 (m, CH), 1651 (vs, C=O), 1605 (m, C=C), 1571 (m, C=C), 1507 (s, C=C), 1462 (w), 1431 (w), 1261 (s, C-O), 910 (m), 882 (m), 753 (m) 682 (m).

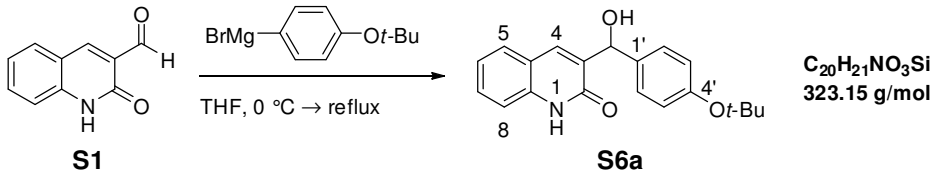
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.10 (d, ^3J = 7.6 Hz, 18 H, $Si(CH(C\underline{H}_3)_2)_3$), 1.21-1.31 (m, 3 H, $Si(C\underline{H}(CH_3)_2)_3$), 4.82 (d, ^3J = 4.5 Hz, 1 H, CHO<u>H</u>), 5.94 (d, ^3J = 4.5 Hz, 1 H, C<u>H</u>OH), 6.89-6.93 (m, 2 H, 3'-H), 7.21 (ddd, ^3J = 8.2 Hz, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1 H, 6-H), 7.31 (d, ^3J = 8.3 Hz, 1 H, 8-H), 7.35-7.39 (m, 2 H, 2'-H), 7.46 (s, 1 H, 4-H), 7.45-7.51 (m, 2 H, 5-H, 7-H), 12.26 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 12.8 (d, $Si(\underline{C}H(CH_3)_2)_3$), 18.1 (q, $Si(CH(\underline{C}H_3)_2)_3$), 73.1 (d, CHOH), 115.9 (d, C-8), 120.1 (d, C-3'), 120.1 (s, C-4a), 123.2 (d, C-6), 128.2, 128.3 (2 d, C-2', C-5), 130.6 (d, C-7), 133.8 (s, C-1'), 134.6 (s, C-3), 137.2 (d, C-4), 137.5 (s, C-8a), 155.9 (s, C-4'), 164.5 (s, C-2).

HRMS (ESI): $C_{25}H_{32}NO_2Si$ [$(M-OH)^+$]: calcd.: 406.2197; found: 406.2192

$C_{50}H_{67}N_2O_6Si_2$ [$(2M+H)^+$]: calcd.: 847.4532; found: 847.4533.

3-((4-(*tert*-Butoxy)phenyl)(hydroxy)methyl)quinolin-2(1*H*)-one (S6a)



According to *GP1*, aldehyde **S1**[5] (260 mg, 1.50 mmol, 1.0 eq) in THF (3.6 mL) was reacted with the Grignard-reagent, prepared from magnesium turnings (91.1 mg, 3.75 mmol, 2.5 eq) and 1-bromo-4-(*tert*-butoxy)benzene (859 mg, 3.75 mmol, 2.5 eq) in THF (3.6 mL). After work-up, as described in *GP1*, the crude product was subjected to flash column chromatography (SiO_2, 16 × 3.25 cm, CH_2Cl_2/EtOAc 4/1 → 1/1, UV/CAM) to afford the title compound as a colorless solid (396 mg, 82%).

m.p.: 183-184 °C

TLC: R_f = 0.60 (EtOAc) [UV, CAM].

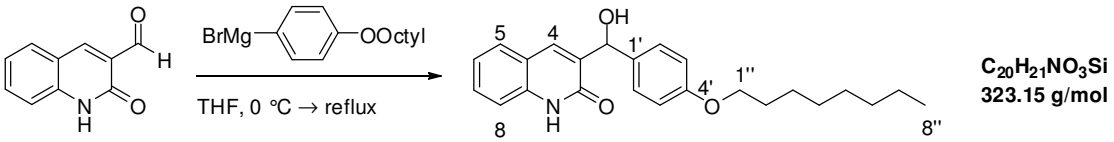
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2973 (w, CH), 1650 (vs, C=O), 1606 (m, C=C), 1570 (m, C=C), 1499 (m, C=C), 1364 (m), 1234 (m, C-O), 1160 (s), 898 (s), 858 (m), 757 (s).

^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] = 1.26 (s, 9 H, $C(CH_3)_3$), 5.76 (d, ^3J = 4.4 Hz, 1 H, CHOH), 5.77 (d, ^3J = 4.4 Hz, 1 H, CHOH), 6.86-6.90 (m, 2 H, 3'-H), 7.17 (ddd, ^3J = 8.3 Hz, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1 H, 6-H), 7.27-7.33 (m, 3 H, 8-H, 2'-H), 7.45 (ddd, ^3J = 8.3 Hz, ^3J = 7.1 Hz, ^4J = 1.5 Hz, 1 H, 7-H), 7.72 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, 5-H), 8.04 (s, 1 H, 4-H), 11.72 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, DMSO-d_6): δ [ppm] = 28.6 (q, $C(CH_3)_3$), 68.5 (d, CHOH), 77.7 (s, $C(CH_3)_3$), 114.8 (d, C-8), 119.2 (s, C-4a), 121.8 (d, C-6), 123.0 (d, C-3'), 127.4 (d, C-2'), 127.9 (d, C-5), 129.7 (d, C-7), 134.0 (d, C-4), 137.0 (s, C-3), 137.8 (s, C-8a), 138.6 (s, C-1'), 153.9 (s, C-4'), 160.9 (s, C-2).

HRMS (ESI): $C_{20}H_{20}NO_2$ [$(M-OH)^+$]: calcd.: 306.1489; found: 306.1489
$C_{20}H_{21}NNaO_3$ [$(M+Na)^+$]: calcd.: 346.1414; found: 346.1414
$C_{40}H_{42}N_2NaO_6$ [$(2M+Na)^+$]: calcd.: 669.2935; found: 669.2938.

3-(Hydroxy(4-(octyloxy)phenyl)methyl)quinolin-2(1*H*)-one (S3a)



S1 **S3a**

According to *GP1*, aldehyde **S1**[5] (173 mg, 1.00 mmol, 1.0 eq) in THF (2.5 mL) was reacted with the Grignard-reagent, prepared from magnesium turnings (60.8 mg, 2.50 mmol, 2.5 eq) and 1-bromo-4-(octyloxy)benzene (713 mg, 2.50 mmol, 2.5 eq) in THF (2.5 mL). After work-up, as described in *GP1*, the crude product was subjected to flash column chromatography (SiO_2, 17 × 2 cm, CH_2Cl_2/EtOAc 4/1 → 1/1, UV/CAM) to afford the title compound as a colorless solid (328 mg, 87%).

m.p.: 117-118 °C

TLC: R_f = 0.58 (EtOAc) [UV, CAM].

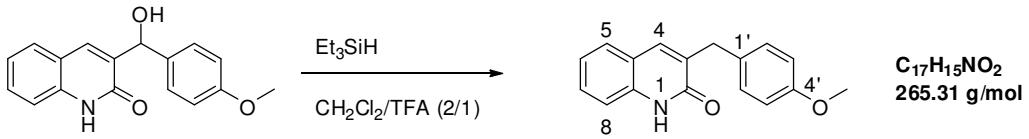
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2925 (w, CH), 2853 (w, CH), 1650 (vs, C=O), 1608 (m, C=C), 1568 (s, C=C), 1508 (s, C=C), 1394 (w), 1240 (vs, C-O), 1172 (m), 1021 (m), 832 (s), 756 (vs).

^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] = 0.84 (t, ^3J = 6.9 Hz, 3 H, 8''-H), 1.18-1.32 (m, 8 H, 4''-H, 5''-H, 6''-H, 7''-H), 1.33-1.40 (m, 2 H, 3''-H), 1.66 (*virt*. quint, $^3J \approx$ 6.8 Hz, 2 H, 2''-H), 3.89 (t, ^3J = 6.5 Hz, 2 H, 1''-H), 5.70 (d, ^3J = 4.2 Hz, 1 H, CHOH), 5.75 (d, ^3J = 4.2 Hz, 1 H, CHOH), 6.79-6.85 (m, 2 H, 3'-H), 7.16 (ddd, ^3J = 8.3 Hz, ^3J = 7.6 Hz, ^4J = 1.1 Hz, 1 H, 6-H), 7.26-7.32 (m, 3 H, 2'-H, 8-H), 7.44 (ddd, ^3J = 8.3 Hz, ^3J = 7.2 Hz, ^4J = 1.4 Hz, 1 H, 7-H), 7.71 (dd, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 1 H, 5-H), 8.02 (s, 1 H, 4-H), 11.71 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, DMSO-d_6): δ [ppm] = 13.9 (q, C-8''), 22.1 (t, CH_2), 25.5 (t, C-3''), 28.6, 28.7, 28.7 (3 t, C-2'', 2 CH_2), 31.2 (t, CH_2), 67.3 (t, C-1''), 68.5 (CHOH), 113.8 (d, C-3'), 114.7 (d, C-8), 119.2 (s, C-4a), 121.7 (d, C-6), 127.8 (d, C-5), 127.9 (d, C-2'), 129.6 (d, C-7), 133.8 (d, C-4), 135.8 (s, C-1'), 137.1 (s, C-3), 137.8 (s, C-8a), 157.6 (s, C-4'), 160.8 (s, C-2).

HRMS (ESI): $C_{24}H_{28}NO_2$ [$(M\text{-}OH)^+$]: calcd.: 362.2114; found: 362.2112
$C_{24}H_{29}NNaO_3$ [$(M+Na)^+$]: calcd.: 402.2040; found: 402.2042
$C_{48}H_{58}N_2NaO_6$ [$(2M+Na)^+$]: calcd.: 781.4187; found: 781.4198.

3-(4-Methoxybenzyl)quinolin-2(1*H*)-one (7)



S7a **7**

According to *GP2*, quinolone **S7a** (551 mg, 1.96 mmol, 1.0 eq) was reacted with triethylsilane (0.78 mL, 4.90 mmol, 2.5 eq) in dichloromethane/trifluoroacetic acid (9.4 mL/4.7 mL) at room temperature for 20 minutes. After work-up, as described in *GP2*, the crude product was subjected to flash column chromatography (SiO_2, 13 × 3.25 cm, CH_2Cl_2/MeOH 97/3, UV/CAM) to afford the title compound as colorless solid (515 mg, 99%).

m.p.: 185-186 °C

TLC: R_f = 0.65 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2837 (w, CH), 1651 (s, C=O), 1608 (w, C=C), 1572 (m, C=C), 1508 (m, C=C), 1239 (s, C-O), 1177 (m), 1029 (s), 909 (s), 760 (vs), 689 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.81 (s, 3 H, OCH_3), 3.96 (s, 2 H, $C\underline{H}_2Ar$), 6.87-6.91 (m, 2 H, 3'-H), 7.16 (ddd, ^3J = 8.0 Hz, ^3J = 7.2, ^4J = 1.1 Hz, 1 H, 6-H), 7.24–7.28 (m, 2 H, 2'-H), 7.29-7.32 (m, 1 H, 8-H), 7.41-7.46 (m, 3 H, 5-H, 4-H, 7- H), 11.57 (s, 1 H, NH).

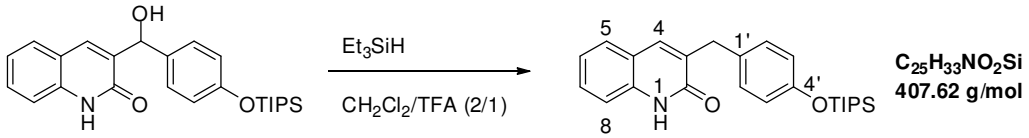
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 35.5 (t, $\underline{C}H_2Ar$), 55.4 (q, OCH_3), 114.1 (d, C-3'), 115.8 (d, C-8), 120.4 (s, C-4a), 122.5 (d, C-6), 127.4 (d, C-5), 129.7 (d, C-7), 130.5 (d, C-2'), 131.3 (s, C-1'), 134.0 (s, C-3), 137.4 (d, C-4), 137.6 (s, C-8a), 158.4 (s, C-4'), 164.2 (s, C-2).

HRMS (ESI): $C_{17}H_{16}NO_2$ [$(M+H)^+$]: calcd.: 266.1176; found: 266.1179

$C_{17}H_{15}NNaO_2$ [$(M+Na)^+$]: calcd.: 288.0995; found: 288.0999

$C_{34}H_{31}N_2O_4$ [$(2M+H)^+$]: calcd.: 531.2278; found: 531.2291.

3-(4-((Triisopropylsilyl)oxy)benzyl)quinolin-2(1*H*)-one (S5b)



S5a **S5b**

According to *GP2*, quinolone **S5a** (414 mg, 0.977 mmol, 1.0 eq) was reacted with triethylsilane (388 µL, 2.44 mmol, 2.5 eq) in dichloromethane/trifluoroacetic acid (4.9 mL/2.5 mL) at room temperature for 15 minutes. After work-up, as described in *GP2*, the

crude product was subjected to flash column chromatography (SiO_2, 18 × 2.5 cm, CH_2Cl_2/MeOH 99/1, UV/CAM) to afford the title compound as colorless solid (377 mg, 95%).

m.p.: 117-118 °C

TLC: R_f = 0.41 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2942 (w, CH), 2865 (w, CH), 1651 (s, C=O), 1606 (w, C=C), 1573 (m, C=C), 1504 (s, C=C),1258 (s, C-O), 908 (vs), 882 (vs), 811 (m), 750 (s), 672 (s).

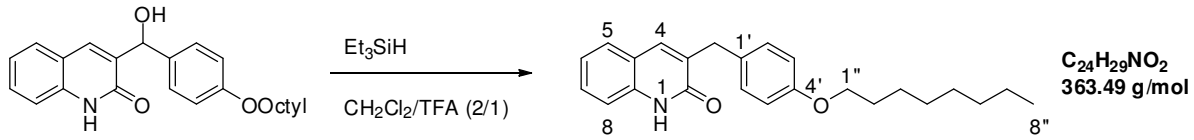
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.11 (d, ^3J = 7.4 Hz, 18 H, Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.21-1.32 (m, 3 H, Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 3.96 (s, 2 H, C<u>H</u>$_2$Ar), 6.84-6.89 (m, 2 H, 3'-H), 7.13-7.17 (m, 1 H, 6-H), 7.17-7.20 (m, 2 H, 2'-H), 7.35-7.38 (m, 2 H, 4-H, 8-H), 7.39-7.42 (m, 1 H, 5-H), 7.42-7.47 (m, 1 H, 7-H), 12.12 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 12.8 (d, Si(<u>C</u>H(CH$_3$)$_2$)$_3$), 18.1 (q, Si(CH(<u>C</u>H$_3$)$_2$)$_3$), 35.5 (t, <u>C</u>H$_2$Ar), 115.8 (d, C-8), 120.1 (d, C-3'), 120.4 (s, C-4a), 122.5 (d, C-6), 127.3 (d, C-5), 129.6 (d, C-7), 130.5 (d, C-2'), 131.5 (s, C-1'), 134.2 (s, C-3), 137.4 (d, C-4), 137.6 (s, C-8a), 154.7 (s, C-4'), 164.4 (s, C-2).

HRMS (ESI): $C_{25}H_{34}NO_2Si$ [$(M+H)^+$]: calcd.: 408.2353; found: 408.2356

$C_{50}H_{67}N_2O_4Si_2$ [$(2M+H)^+$]: calcd.: 815.4634; found: 815.4637.

3-(4-(Octyloxy)benzyl)quinolin-2(1*H*)-one (S3b)



S3a **S3b**

According to *GP2*, quinolone **S3a** (288 mg, 0.759 mmol, 1.0 eq) was reacted with triethylsilane (302 µL, 1.90 mmol, 2.5 eq) in dichloromethane/trifluoroacetic acid (3.6 mL/1.8 mL) at room temperature for 15 minutes. After work-up, as described in *GP2*, the crude product was subjected to flash column chromatography (SiO_2, 17 × 2 cm, CH_2Cl_2/MeOH 99/1 → 95/5, UV/CAM) to afford the title compound as colorless solid (261 mg, 95%).

m.p.: 116-117 °C

TLC: R_f = 0.62 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3054 (w, CH), 2954 (w, CH), 2920 (w, CH), 2848 (w, CH), 2767 (w),

1655 (s, C=O), 1610 (w, C=C), 1574 (m, C=C), 1508 (s, C=C), 1241 (vs, C-O), 1174 (m), 902 (s), 847 (m).

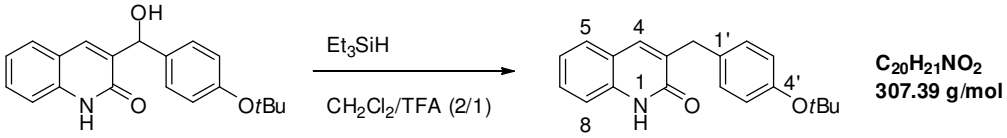
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 0.88 (t, ^3J = 6.7 Hz, 3 H, 8''-H), 1.22-1.38 (m, 8 H, 4''-H, 5''-H, 6''-H, 7''-H), 1.45 (*virt.* quint, $^3J \approx$ 7.0 Hz, 2 H, 3''-H), 1.77 (*virt.* quint, $^3J \approx$ 6.8 Hz, 2 H, 2''-H), 3.94 (t, ^3J = 6.6 Hz, 2 H, 1''-H), 3.96 (s, 2 H, C$\underline{H}_2$Ar), 6.85-6.89 (m, 2 H, 3'-H), 7.13-7.18 (m, 1 H, 6-H), 7.23-7.27 (m, 2 H, 2'-H), 7.34 (d, ^3J = 8.3 Hz, 1 H), 7.40-7.46 (m, 3 H, 4-H, 5-H, 7-H), 12.13 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 14.3 (q, C-8''), 22.8 (t, CH_2), 26.2 (t, C-3''), 29.4, 29.5, 29.5 (3 t, C-2'', 2 CH_2), 32.0 (t, CH_2), 35.5 (t, $\underline{C}H_2$Ar), 68.1 (t, C-1''), 114.7 (d, C-3'), 115.8 (d, C-8), 120.3 (s, C-4a), 122.5 (d, C-6), 127.4, 129.6 (2 d, C-5, C7), 130.5 (d, C-2'), 131.0 (s, C-1'), 134.0 (s, C-3), 137.4, 137.6 (d, C-4, s, C-8a), 157.9 (s, C-4'), 164.3 (s, C-2).

HRMS (ESI): $C_{24}H_{30}NO_2$ $[(M+H)^+]$: calcd.: 364.2271; found: 364.2267

$C_{48}H_{59}N_2O_4$ $[(2M+H)^+]$: calcd.: 727.4469; found: 727.4460.

3-(4-(*tert*-Butoxy)benzyl)quinolin-2(1*H*)-one (S6b)



S6a **S6b**

According to *GP2*, quinolone **S6a** (283 mg, 0.875 mmol, 1.0 eq) was reacted with triethylsilane (348 µL, 2.19 mmol, 2.5 eq) and trifluoroacetic acid (337 µL, 4.38 mmol, 5.0 eq) in dichloromethane (5.3 mL) at 0 °C for 40 minutes. After work-up, as described in *GP2*, the crude product was subjected to flash column chromatography (SiO_2, 17 × 2 cm, CH_2Cl_2/MeOH 98/2, UV/CAM) to afford the title compound as colorless solid (241 mg, 90%).

m.p.: 176-178 °C

TLC: R_f = 0.55 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3013 (w, CH), 2975 (w, CH), 2910 (w, CH), 2835 (w, CH), 1656 (vs, C=O), 1604 (w, C=C), 1572 (s, C=C), 1500 (s, C=C), 1435 (m), 1388 (w, $C(CH_3)_3$), 1362 (w, $C(CH_3)_3$), 1232 (s, C-O), 1160 (vs), 894 (vs).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.34 (s, 9 H, $C(CH_3)_3$), 3.97 (s, 2 H, C$\underline{H}_2$Ar), 6.94-6.98 (m, 1 H, 3'-H), 7.16 (ddd, ^3J = 8.0 Hz, ^3J = 7.1 Hz, ^4J = 1.0 Hz, 1 H, 6-H), 7.20-7.25 (m, 2 H, 2'-H), 7.31 (d, ^3J = 8.1 Hz, 1 H, 8-H), 7.40 (s, 1 H, 4-H), 7.41-7.47 (m, 2 H, 5-H, 7-H),

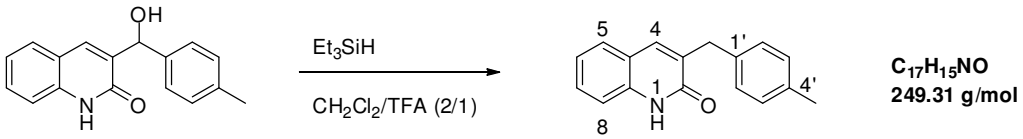
11.42 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 29.0 (q, C($\underline{C}H_3)_3$), 35.6 (t, $\underline{C}H_2Ar$), 78.4 (s, $\underline{C}(CH_3)_3$), 115.7 (d, C-3'), 120.3 (s, C-4a), 122.5 (d, C-6), 124.4 (d, C-3'), 127.4 (d, C-5), 129.7 (d, C-7), 130.0 (d, C-2'), 133.9 (s, C-3), 134.1 (s, C-1'), 137.6, 137.6 (d, C-4, s, C-8a), 154.0 (s, C-4'), 164.2 (s, C-2).

HRMS (ESI): $C_{20}H_{22}NO_2$ [$(M+H)^+$]: calcd.: 308.1645; found: 308.1643

$C_{20}H_{21}NNaO_2$ [$(M+Na)^+$]: calcd.: 330.1464; found: 330.1464.

3-(4-Methylbenzyl)quinolin-2(1*H*)-one (S4b)



S4a **S4b**

According to *GP2*, quinolone **S4a** (420 mg, 1.58 mmol, 1.0 eq) was reacted with triethylsilane (0.63 mL, 3.95 mmol, 2.5 eq) in dichloromethane/trifluoroacetic acid (7.9 mL/4.0 mL) at room temperature for 15 minutes. After work-up, as described in *GP2*, the crude product was subjected to flash column chromatography (SiO_2, 19 × 2.5 cm, CH_2Cl_2/MeOH 98/2, UV/CAM) to afford the title compound as colorless solid (368 mg, 93%).

m.p.: 177-178 °C

TLC: R_f = 0.35 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3148 (w), 3004 (w, CH), 2894 (w, CH), 2853 (w, CH), 2773 (w), 1650 (vs, C=O), 1620 (m, C=C), 1570 (s, C=C), 1511 (m, , C=C), 1434 (s), 1268 (w), 1229 (w), 1146 (w), 898 (s).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.34 (s, 3 H, CH_3), 3.99 (s, 2 H, $C\underline{H}_2Ar$), 7.13-7.17 (m, 3 H, 3'-H, 6-H), 7.24 (d, ^3J = 7.8 Hz, 2 H, 2'-H), 7.34 (d, ^3J = 8.3 Hz, 1 H, 8-H), 7.41-7.45 (m, 3 H, 4-H, 5-H, 7-H), 12.08 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 21.2 (q, CH_3), 35.9 ($\underline{C}H_2Ar$), 115.8 (d, C-8), 120.4 (s, C-4a), 122.5 (d, C-6), 127.3 (d, C-5), 129.4 (d, C-3'), 129.5 (d, C-2'), 129.6 (d, C-7), 133.9 (s, C-3), 136.0 (s, C-4'), 136.2 (s, C-1'), 137.5 (d, C-4), 137.7 (s, C-8a), 164.3 (s, C-2).

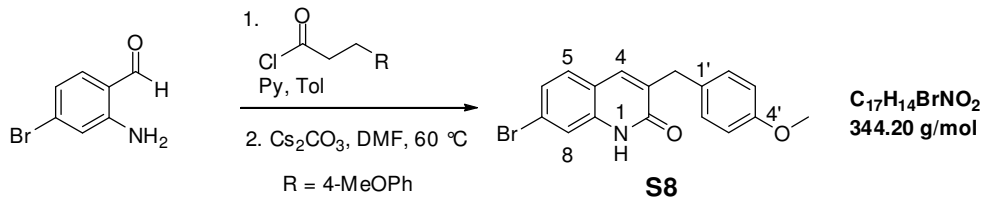
HRMS (ESI): $C_{17}H_{16}NO$ [$(M+H)^+$]: calcd.: 250.1226; found: 250.1226

$C_{17}H_{15}NNaO$ [$(M+Na)^+$]: calcd.: 272.1046; found: 272.1045

$C_{34}H_{31}N_2O_2$ [$(2M+H)^+$]: calcd.: 499.2380; found: 499.2384

$C_{34}H_{30}N_2NaO_2$ [$(2M+Na)^+$]: calcd.: 521.2199; found: 521.2202.

7-Bromo-3-(4-methoxybenzyl)quinolin-2(1*H*)-one (S8)[6]



$C_{17}H_{14}BrNO_2$
344.20 g/mol

According to *GP3*, 3-(4-methoxyphenyl)propanoic acid was converted to the corresponding acid chloride (1.52 g, 7.67 mmol, 1.3 eq), dissolved in toluene (8 mL) and added to a solution of 2-amino-4-bromobenzaldehyde[7] (1.18 g, 5.90 mmol, 1.0 eq) and pyridine (0.48 mL, 5.90 mmol, 1.0 eq) in toluene (18 mL) at 0 °C. The reaction mixture was stirred for two hours at room temperature, then was quenched with water (50 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were successively washed with HCl (25 mL, 0.25 M), saturated $NaHCO_3$ solution (25 mL) and saturated NaCl solution (25 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the residue was redissolved in DMF (61 mL). Cesium carbonate (9.61 g, 29.5 mmol, 5.0 eq) was added and the mixture stirred at 60 °C over night. The solvent was removed under reduced pressure and saturated NH_4Cl solution (100 mL) and water (100 mL) were added to the residue. The formed precipitate was collected by filtration, repeatedly washed with water and dried by evaporation with toluene under reduced pressure. The crude product was redissolved in dichloro-methane/methanol, loaded onto Celite and purified by flash column chromatography (SiO_2, 18 × 3.25 cm, CH_2Cl_2/EtOAc 9/1 → 4/1, UV/CAM) to afford the title compound as a colorless solid (1.37 g, 67%).

m.p.: 193-194 °C

TLC: R_f = 0.62 (EtOAc) [UV, CAM].

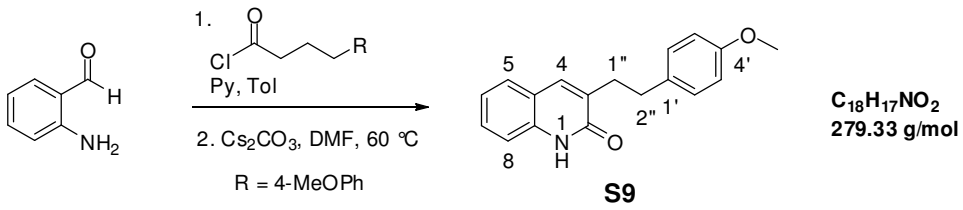
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3150 (w), 3001 (w, CH), 2932 (w, CH), 2834 (w, CH), 1659 (vs, C=O), 1605 (m, C=C), 1567 (s, C=C), 1509 (m, C=C), 1402 (w), 1241 (m, C-O), 1177 (w), 1034 (w), 805 (w).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.81 (s, 3, OCH_3), 3.93 (s, 2 H, $C\underline{H}_2Ar$), 6.88-6.92 (m, 2 H, 3'-H), 7.24-7.29 (m, 3 H, 2'-H, 6-H), 7.30 (d, ^3J = 8.4 Hz, 1 H, 5-H), 7.38 (s, 1 H, 4-H), 7.52 (s, 1 H, 8-H), 11.85 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 35.6 (t, $\underline{C}H_2Ar$), 55.4 (q, OCH_3), 114.2 (d, C-3'), 118.4 (d, C-8), 119.2 (s, C-4a), 123.7 (s, C-7), 126.0 (d, C-6), 128.7 (d, C-5), 130.6 (d, C-2'), 130.7 (s, C-1'), 134.5 (s, C-3) 136.8 (d, C-4), 138.4 (s, C-8a), 158.4 (s, C-4'), 164.1 (s, C-2).

HRMS (ESI): $C_{17}H_{15}BrNO_2$ [$(M+H)^+$]: calcd.: 344.0281; found: 344.0281
$C_{17}H_{14}BrNNaO_2$ [$(M+Na)^+$]: calcd.: 366.0100; found: 366.0099
$C_{34}H_{29}Br_2N_2O_4$ [$(2M+H)^+$]: calcd.: 687.0489; found: 687.0501
$C_{34}H_{28}Br_2N_2NaO_4$ [$(2M+Na)^+$]: calcd.: 709.0307; found: 709.0317.

3-(4-Methoxyphenethyl)quinolin-2(1*H*)-one (S9)[6]



According to *GP3*, 4-(4-methoxyphenyl)butanoic acid was converted to the corresponding acid chloride (1.52 g, 7.15 mmol, 1.3 eq), dissolved in toluene (8 mL) and added to a solution of 2-aminobenzaldehyde[8] (660 mg, 5.45 mmol, 1.0 eq) and pyridine (0.44 mL, 5.45 mmol, 1.0 eq) in toluene (24 mL) at 0 °C. The reaction mixture was stirred for one hour at 0 °C, then was quenched with water (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were successively washed with HCl (30 mL, 2 M), saturated $NaHCO_3$ solution (30 mL) and saturated NaCl solution (30 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the residue was redissolved in DMF (55 mL). Cesium carbonate (8.89 g, 27.3 mmol, 5.0 eq) was added and the mixture was stirred at 60 °C over night. After quenching the reaction with saturated NH_4Cl solution (40 mL) the mixture was extracted with dichloromethane (50 mL). The organic layer was washed with water (2 × 40 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was dissolved in dichloromethane/methanol, loaded onto Celite and subjected to flash column chromatography (SiO_2, 18 × 3 cm, pentane/EtOAc 2/1, UV/CAM) to afford the title compound as a colorless solid (350 mg, 23%).

m.p.: 174-176 °C

TLC: R_f = 0.57 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3011 (w, CH), 2909 (w, CH), 2835 (w, CH), 1655 (vs, C=O), 1611 (m, C=C), 1573 (s, C=C), 1509 (vs, C=C), 1243 (vs, C-O), 1175 (m), 1033 (s), 815 (s), 753 (vs).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.97-3.00 (m, 4 H, 1''-H, 2''-H), 3.79 (s, 3 H, OCH_3), 6.82-6.86 (m, 2 H, 3'-H), 7.16-7.21 (m, 4 H, 2'-H, 6-H), 7.40 (d, ^3J = 8.1 Hz, 1 H, 8-

H), 7.44-7.50 (m, 2 H, 5-H, 7-H), 7.53 (s, 1 H, 4-H), 11.86 (s, 1 H, NH).

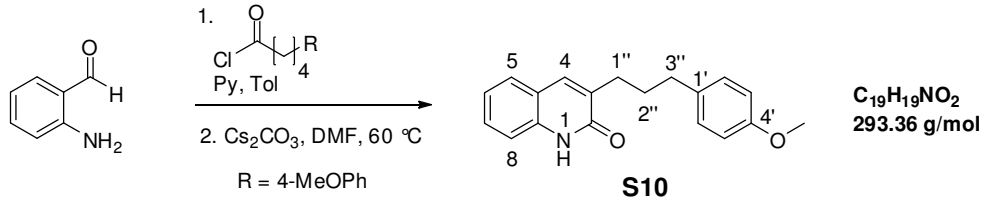
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 32.8 (t, C-1''), 33.9 (t, C-2''), 55.4 (q, OCH_3), 113.9 (d, C-3'), 115.7 (d, C-8), 120.4 (s, C-4a), 122.5 (d, C-6), 127.3 (d, C-5), 129.6 (d, C-7), 129.6 (d, C-2'), 133.4 (s, C-3), 133.9 (s, C-1'), 137.3 (d, C-4), 137.7 (s, C-8a), 158.0 (s, C-4'), 164.3 (s, C-2).

HRMS (ESI): $C_{18}H_{18}NO_2$ $[(M+H)^+]$: calcd.: 280.1332; found: 280.1334

$C_{18}H_{17}NNaO_2$ $[(M+Na)^+]$: calcd.: 302.1151; found: 302.1152

$C_{36}H_{35}N_2O_4$ $[(2M+H)^+]$: calcd.: 559.2591; found: 559.2577.

3-(3-(4-Methoxyphenyl)propyl)quinolin-2(1*H*)-one (S10)[6]



According to *GP3*, 5-(4-methoxyphenyl)pentanoic acid was converted to the corresponding acid chloride (1.33 g, 5.88 mmol, 1.3 eq), dissolved in toluene (8 mL) and added to a solution of 2-aminobenzaldehyde[8] (547 mg, 4.52 mmol, 1.0 eq) and pyridine (0.36 mL, 4.52 mmol, 1.0 eq) in toluene (16 mL) at 0 °C. The reaction mixture was stirred for one hour at 0 °C, then was quenched with water (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were successively washed with HCl (30 mL, 2 M), saturated $NaHCO_3$ solution (30 mL) and saturated NaCl solution (30 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure the residue was redissolved in DMF (20 mL). Cesium carbonate (7.36 g, 22.6 mmol, 5.0 eq) was added and the mixture stirred at 60 °C over night. After quenching the reaction with saturated NH_4Cl solution (40 mL) the mixture was extracted with dichloromethane (50 mL). The organic layer was washed with water (2 × 40 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was dissolved in dichloromethane/methanol, loaded onto Celite and subjected to flash column chromatography (SiO_2, 18 × 3, pentane/EtOAc 2/1, UV/CAM) to afford the title compound as a colorless solid (685 mg, 52%).

m.p.: 139-140 °C

TLC: R_f = 0.58 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3006 (w, CH), 2836 (w, CH), 1656 (s, C=O), 1608 (w, C=C), 1572 (s,

C=C), 1509 (s, C=C), 1240 (s, C-O), 1034 (s), 897 (s), 751 (vs), 695 (s).

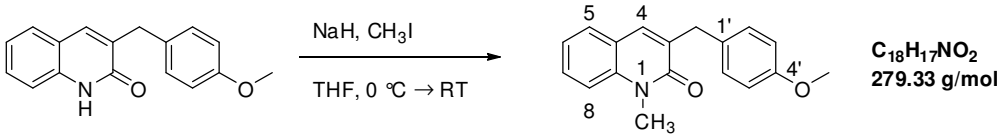
^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 1.97-2.10 (m, 2 H, 2''-H), 2.65-2.80 (m, 4 H, 1''-H, 3''-H), 3.79 (s, 3 H, OCH_3), 6.80-6.89 (m, 2 H, 3'-H), 7.13-7.23 (m, 3 H, 2'-H, 6-H), 7.35 (d, ^3J = 8.3 Hz, 1 H, 8-H), 7.45 (ddd, ^3J = 8.3 Hz, ^3J = 7.3 Hz, ^4J = 1.4 Hz, 1 H, 7-H), 7.48-7.52 (dd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1 H, 5-H), 7.59 (s, 1 H, 4-H), 11.63 (s, 1H).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 30.1 (t, C-1''), 30.4 (t, C-2''), 34.9 (t, C-3''), 55.4 (q, OCH_3), 113.9 (d, C-3'), 115.6 (d, C-8), 120.4 (s, C-4a), 122.5 (d, C-6), 127.2 (d, C-5), 129.5 (d, C-2'), 129.5 (d, C-7) 134.1 (s, C-3), 134.4 (s, C-1'), 136.8 (d, C-4), 137.6 (s, C-8a), 157.9 (s, C-4'), 164.2 (s, C-2).

HRMS (ESI): $C_{19}H_{20}NO_2$ $[(M+H)^+]$: calcd.: 294.1489; found: 294.1488

$C_{19}H_{19}NNaO_2$ $[(M+Na)^+]$: calcd.: 316.1308; found: 316.1307.

3-(4-Methoxybenzyl)-1-methylquinolin-2(1*H*)-one (S7b)



7 **S7b**

To a solution of quinolone **7** (60.0 mg, 0.226 mmol, 1.0 eq) was added sodium hydride (13.6 mg, 0.339 mmol, 1.5 eq, 60% dispersion in mineral oil) at 0 °C. After stirring at this temperature for one hour, the solution was treated with methyl iodide (28.3 µl, 0.452 mmol, 2.0 eq) and further stirred for 18 hours at room temperature. Saturated NH_4Cl solution (1 mL) was added, the mixture stirred for one hour and then diluted with water (5 mL). After extraction of the mixture with dichloromethane (3 × 10 mL), the combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product purified by flash column chromatography (SiO_2, 11 x 1.5 cm, pentane/EtOAc 4/1, UV/CAM) to afford quinolone **S7b** as colorless solid (56.0 mg, 89%).

m.p.: 82-84 °C

TLC: R_f = 0.48 (pentane/EtOAc = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3032 (w, CH), 2996 (w, CH), 2938 (w, CH), 2913 (w, CH), 2838 (w), 1645 (s, C=O), 1623 (m), 1593 (vs, C=C), 1573 (m, C=C), 1509 (s, C=C), 1461 (s), 1241, 1220 (vs, C-O, C-N), 1178 (s), 818 (s).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.75 (s, 3 H, NCH_3), 3.80 (s, 3 H, OCH_3), 3.92 (s, 2

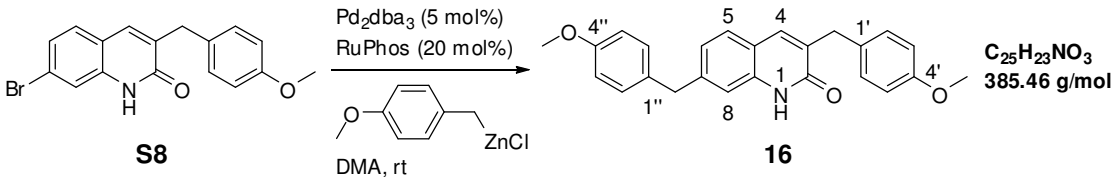
H, C<u>H</u>$_2$Ar), 6.86-6.89 (m, 2 H, 3'-H), 7.18 (*virt.* t, $^3J \approx 7.5$ Hz, 1 H, 6-H), 7.21-7.24 (m, 2 H, 2'-H), 7.31-7.34 (m, 2 H, 4-H, 8-H), 7.44 (dd, $^3J = 7.8$ Hz, $^4J = 1.5$ Hz, 5-H), 7.47-7.52 (m, 1 H, 7-H).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 29.9 (q, NCH_3), 36.3 (t, <u>C</u>H_2Ar), 55.4 (q, OCH_3), 114.0 (d, C-8), 114.1 (d, C-3'), 120.8 (s, C-4a), 122.1 (d, C-6), 128.4 (d, C-5), 129.7 (d, C-7), 130.5 (d, C-2'), 131.2 (s, C-1'), 133.9 (s, C-3), 135.7 (d, C-4), 139.1 (s, C-8a), 158.3 (s, C-4'), 162.5 (s, C-2).

HRMS (ESI): $C_{18}H_{18}NO_2$ [$(M+H)^+$]: calcd.: 280.1332; found: 280.1333

$C_{18}H_{17}NNaO_2$ [$(M+Na)^+$]: calcd.: 302.1151; found: 302.1151.

3,7-Bis(4-methoxybenzyl)quinolin-2(1*H*)-one (16)



Preparation of the organozinc stock solution (4-methoxybenzyl)zinc(II) chloride[9]

A flask was charged with dry lithium chloride (159 mg, 3.75 mmol, 1.25 eq) and dry zinc chloride (450 mg, 3.30 mmol, 1.1 eq). The mixture was heated twice under high vacuum until melting was observed. Magnesium turnings (182 mg, 7.5 mmol, 2.5 eq) and degassed THF (2.5 mL) were added and the magnesium was activated by treatment with diisobutyl-aluminium hydride (30 µL, 30.0 µmol, 0.01 eq, 1.0 M in THF). After stirring for 5 minutes at room temperature, 4-methoxybenzyl chloride (0.41 mL, 3.00 mmol, 1.0 eq) was added and the reaction mixture stirred for two hours at room temperature. The reaction solution was transferred into a syringe and filtrated through a preparative syringe filter into a new *Schlenk*-flask. The concentration of the organozinc solution was determined by iodometric titration (c = 0.82 M).

Negishi-coupling[10]

To a solution of quinolone **S8** (34.4 mg, 0.1 mmol, 1.0 eq), $Pd_2(dba)_3$ (4.58 mg, 5.0 µmol, 0.05 eq) and RuPhos-ligand (9.3 mg, 20.0 µmol, 0.2 eq) in degassed *N*,*N*-dimethylacetamide (0.5 mL) was added (4-methoxybenzyl)zinc(II) chloride (0.37 mL, 0.30 mmol, 3.0 eq, 0.82 M in THF). The reaction was stirred at room temperature until TLC control (pentane/EtOAC = 1/1) showed complete conversion (20 hours). Saturated NH_4Cl solution (5 mL) and water

(5 mL) were added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were successively washed with water (2 × 10 mL) and saturated NaCl solution (1 × 10 mL) and were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was subjected to flash column chromatography (SiO_2, 13 × 1.5 cm, CH_2Cl_2/EtOAc 9/1, UV/CAM) to afford the title compound as a colorless solid (23.5 mg, 61%).

m.p.: 163-165 °C

TLC: R_f = 0.36 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3136 (w), 3062 (w, CH), 3002 (w, CH), 2958 (w, CH), 2907 (w, CH), 2838 (w), 1648 (vs, C=O), 1609 (w, C=C), 1567 (m, C=C), 1509 (s, C=C), 1244 (s, C-O), 893 (m), 807 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.75 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.93 (s, 2 H, C^3-CH_2), 4.00 (s, 2 H, C^7-CH_2), 6.82-6.85 (m, 2 H, 3''-H), 6.85-6.89 (m, 2 H, 3'-H), 6.95-6.99 (m, 1 H, 6-H), 7.09-7.13 (m, 2 H, 2''-H), 7.16 (s, 1 H, 8-H), 7.22-7.27 (m, 2 H, 2'-H), 7.34 (d, ^3J = 8.1 Hz, 1 H, 5-H), 7.38 (s, 1 H, 4-H), 11.84 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 35.3 (t, C^3-$\underline{C}H_2$), 41.2 (t, C^7-$\underline{C}H_2$), 55.3 (q, OCH_3), 55.4 (q, OCH_3), 114.1 (d, C-3'), 114.1 (d, C-3''), 115.5 (d, C-8), 118.6 (s, C-4a), 123.7 (d, C-6), 127.5 (d, C-5), 130.1 (d, C-2''), 130.5 (d, C-2'), 131.3 (s, C-1'), 132.5 (s, C-1''), 133.1 (s, C-3), 137.2 (d, C-4), 137.8 (s, C-8a), 143.9 (s, C-7), 158.2 (s, C-4'), 158.2 (s, C-4''), 164.3 (s, C-2).

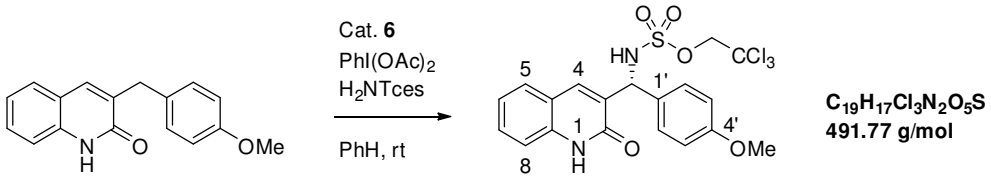
HRMS (ESI): $C_{25}H_{24}NO_3$ [$(M+H)^+$]: calcd.: 386.1751; found: 386.1752

$C_{25}H_{23}NNaO_3$ [$(M+Na)^+$]: calcd.: 408.1570; found: 408.1571

$C_{50}H_{47}N_2O_6$ [$(2M+H)^+$]: calcd.: 771.3429; found: 771.3447.

Rhodium-catalyzed C–H amination reactions

(*R*)-2,2,2-Trichloroethyl ((4-methoxyphenyl)(2-oxo-1,2-dihydroquinolin-3-yl)methyl)sulfamate (8)



Following *GP4*, quinolone **7** (53.1 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford the title compound as a colorless solid (25.8 mg, 52%, 71% *ee*) after purification by flash column chromatography (SiO_2, 15 × 1.5 cm, CH_2Cl_2/EtOAc 98/2 → 95/5 → 9/1 → 8/2, UV/CAM).

The enantiomers were separated by semipreparative HPLC chromatography on a chiral stationary phase (Daicel ChiralPak AD, 250×20 mm, *n*-hexane/*i*-PrOH = 1:1). The absolute configuration of the separated major enantiomer (>99% *ee*, (–)-(*R*)-**8**) was determined by X-ray diffraction analysis of a single crystal, obtained by slow evaporation of a methanolic solution.

m.p.: 171-174 °C (decomposition)

TLC: R_f = 0.47 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

Specific Rotation: [>99% *ee*, determined by chiral HPLC]

$[\alpha]_D^{20}$ = –8.5 (*c* = 0.33, $CHCl_3$).

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm): t_R [racemate] = 10.5 min ((–)-(*R*)-**8**), 12.3 min ((+)-(*S*)-**8**).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3007 (w, CH), 2947 (w, CH), 2839 (w), 2779 (w), 1651 (s, C=O), 1610 (m, C=C), 1570 (m, C=C), 1509 (m, C=C), 1421 (m), 1241 (m), 1174 (vs), 958 (s), 849 (vs), 824 (s).

^{1}H NMR (500 MHz, DMSO-d_6): δ [ppm] = 3.72 (s, 3 H, OCH_3), 4.59 (d, ^2J = 11.1 Hz, 1 H, $OCH_aH_bCCl_3$), 4.70 (d, ^2J = 11.1 Hz, 1 H, $OCH_aH_bCCl_3$), 5.82 (d, ^3J = 8.2 Hz, 1 H, CHNHTces), 6.89-6.93 (m, 2 H, 3'-H), 7.17-7.22 (m, 1 H, 6-H), 7.29-7.34 (m, 3 H, 2'-H, 8-H), 7.50 (ddd, ^3J = 8.4 Hz, ^3J = 7.2 Hz, ^3J = 1.3 Hz, 1 H, 7-H), 7.68 (d, ^3J = 7.3 Hz, 1 H, 5-H), 7.96 (s, 1 H, 4-H), 9.29 (d, ^3J = 8.2 Hz, 1 H, CHNHTces), 11.99 (s, 1 H, NH).

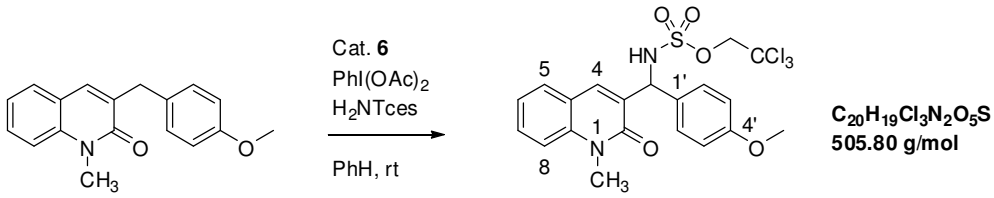
^{13}C-NMR (125.8 MHz, DMSO-d_6): δ [ppm] = 55.2 (q, OCH_3), 55.4 (d, CHNHTces), 77.3 (t,

O<u>C</u>H$_2$CCl$_3$), 93.8 (s, OCH$_2$<u>C</u>Cl$_3$), 113.8 (d, C-3'), 114.9 (d, C-8), 118.8 (s, C-4a), 122.1 (d, C-6), 128.1 (d, C-5), 128.7 (d, C-2'), 130.4 (d, C-7), 131.5 (s, C-1'), 132.9 (s, C-3), 136.1 (d, C-4), 138.0 (s, C-8a), 158.7 (s, C-4'), 160.6 (s, C-2).

HRMS (ESI): $C_{19}H_{18}Cl_3N_2O_5S$ [$(M+H)^+$]: calcd.: 490.9997; found: 490.9999

$C_{19}H_{17}Cl_3N_2NaO_5S$ [$(M+Na)^+$]: calcd.: 512.9816; found: 512.9819.

2,2,2-Trichloroethyl ((4-methoxyphenyl)(1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)methyl)sulfamate (13)



S7b **13**

Following *GP4*, quinolone **S7b** (55.9 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford the title compound as a colorless solid (14.6 mg, 29%, 10% *ee*). The compound **13** was obtained after purification by flash column chromatography (SiO_2, 15 × 1 cm, pentane/Et_2O 1/1, UV/CAM) yielding a mixture of starting material **S7b** and **13**, which were then separated by further flash column chromatography (SiO_2, 16 × 1 cm, CH_2Cl_2 → CH_2Cl_2/EtOAc 98/2, UV/CAM).

m.p.: 125-127 °C (decomposition)

TLC: R_f = 0.63 (CH_2Cl_2/MeOH 98/2) [UV, CAM].

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm): t_R [racemate] = 10.3 min, 12.8 min.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3355 (m), 3193 (br), 2957 (s, CH), 2920 (vs, CH), 2850 (s, CH), 1640 (vs, C=O), 1586 (vs), 1511 (s, C=C), 1460 (s), 1258 (s), 1175 (vs), 849 (m), 752 (s), 722 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.71 (s, 3 H, NCH_3), 3.77 (s, 3 H, OCH_3), 4.47 (d, ^2J = 10.7 Hz, 1 H, OC<u>H$_a$</u>H$_b$CCl$_3$), 4.51 (d, ^2J = 10.7 Hz, 1 H, OCH$_a$<u>H$_b$</u>CCl$_3$), 5.66 (d, ^3J = 9.4 Hz, 1 H C<u>H</u>NHTces), 6.82-6.88 (m, 2 H, 3'-H), 7.30 (*virt.* t, $^3J \approx$ 7.5 Hz, 1 H, 6-H), 7.36-7.41 (m, 3 H, 2'-H, 8-H), 7.53 (d, ^3J = 9.4 Hz, 1 H, CHN<u>H</u>Tces), 7.59-7.65 (m, 2 H, 5-H, 7-H), 7.83 (s, 1 H, 4-H).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 29.8 (q, NCH_3), 55.4 (q, OCH_3), 61.2 (d, <u>C</u>HNHTces), 78.1 (t, O<u>C</u>H$_2$CCl$_3$), 93.4 (s, OCH$_2$<u>C</u>Cl$_3$), 114.2 (d, C-3'), 114.4 (d, C-8), 120.2

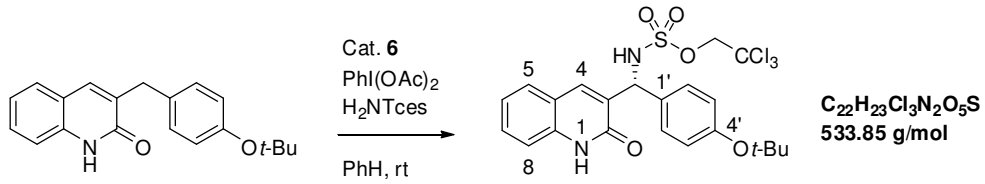
(s, C-4a), 123.1 (d, C-6), 127.8 (d, C-2'), 129.3 (d, C-5), 129.9 (s, C-3), 130.9 (s, C-1'), 131.2 (d, C-7), 137.7 (d, C-4), 139.5 (s, C-8a), 159.4 (s, C-4'), 161.5 (s, C-2).

HRMS (ESI): $C_{20}H_{20}Cl_3N_2O_5S$ $[(M+H)^+]$: calcd.: 505.0153; found: 505.0148

$C_{20}H_{19}Cl_3N_2NaO_5S$ $[(M+Na)^+]$: calcd.: 526.9972; found: 526.9966

$C_{40}H_{39}Cl_6N_4O_{10}S_2$ $[(2M+H)^+]$: calcd.: 1009.0233; found: 1009.0212.

(*R*)-2,2,2-Trichloroethyl ((4-(*tert*-butoxy)phenyl)(2-oxo-1,2-dihydroquinolin-3-yl)methyl)sulfamate (11)



S6b **11**

Following *GP4*, quinolone **S6b** (61.5 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford the title compound as a colorless solid (20.2 mg, 38%, 49% *ee*) after purification by flash column chromatography (SiO_2, 15 × 1.5 cm, CH_2Cl_2/EtOAc 98/2 → 95/5 → 9/1 → 4/1, UV/CAM).

m.p.: 168-170 °C (decomposition)

TLC: R_f = 0.42 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm): t_R [racemate] = 10.2 min ((*R*)-**11**), 12.3 min ((*S*)-**11**).

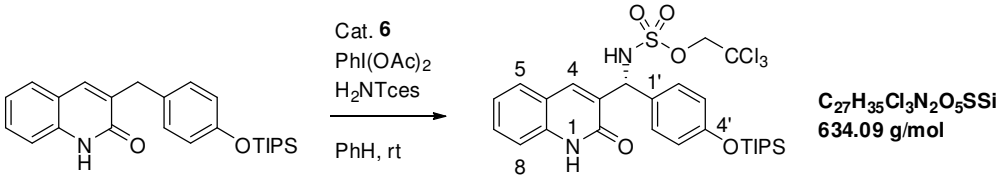
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2975 (w, CH), 2924 (w, CH), 2854 (w), 1656 (vs, C=O), 1608 (w, C=C), 1572 (m, C=C), 1505 (m, C=C), 1365 (m), 1242 (m), 1182 (s), 853 (s), 755 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.31 (s, 9 H, $C(CH_3)_3$), 4.46 (d, ^2J = 10.7 Hz, 1 H $OCH_aH_bCCl_3$), 4.49 (d, ^2J = 10.7 Hz, 1 H, $OCH_aH_bCl_3$), 5.69 (d, ^3J = 9.4 Hz, 1 H, CHNHTces), 6.92-6.96 (m, 2 H, 3'-H), 7.17 (d, ^3J = 8.2 Hz, 1 H, 8-H), 7.25-7.30 (m, 1 H, 6-H), 7.36-7.40 (m, 2 H, 2'-H), 7.51-7.55 (m, 1 H, 7-H), 7.59-7.62 (m, 1 H, 5-H), 7.67 (d, ^3J = 9.4 Hz, 1 H, CHNHTces), 7.89 (s, 1 H, 4-H), 10.52 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 29.0 (q, $C(CH_3)_3$), 60.9 (d, CHNHTces), 78.1 (t, OCH_2CCl_3), 78.9 (s, $C(CH_3)_3$), 93.4 (s, OCH_2CCl_3), 115.5 (d, C-8), 119.8 (s, C-4a), 123.7 (d, C-6), 124.2 (d, C-3'), 127.4 (d, C-2'), 128.4 (d, C-5), 130.0 (s, C-3), 131.4 (d, C-7), 133.4 (s, C-1'), 137.5 (s, C-8a), 139.4 (d, C-4), 155.5 (s, C-4'), 162.6 (s, C-2).

HRMS (ESI): $C_{22}H_{24}Cl_3N_2O_5S$ [$(M+H)^+$]: calcd.: 533.0466; found: 533.0469
$C_{22}H_{23}Cl_3N_2NaO_5S$ [$(M+Na)^+$]: calcd.: 555.0285; found: 555.0288
$C_{44}H_{47}Cl_6N_4O_{10}S_2$ [$(2M+H)^+$]: calcd.: 1065.0859; found: 1065.0868.

(*R*)-2,2,2-Trichloroethyl ((2-oxo-1,2-dihydroquinolin-3-yl)(4-((triisopropyl-silyl)oxy)phenyl)methyl)sulfamate (12)



Following *GP4*, quinolone **S5b** (81.5 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford a mixture of the title compound (24.9 mg*, 39%*, 72% *ee*) and H_2NTces (**12**/H_2NTces = 74/26) as a colorless solid after purification by flash column chromatography (SiO_2, 16 × 1 cm, CH_2Cl_2/EtOAc 99/1 → 98/2 → 95/5, UV/CAM). An analytically pure sample of **12** was obtained by repeated flash column chromatography and all analytical data refer to this sample.

* corrected yield based on NMR-integration

m.p.: 163-165 °C (decompsition)

TLC: R_f = 0.68 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

Specific Rotation: [72% *ee*, determined by chiral HPLC]

$[\alpha]_D^{20}$ = −10.3 (*c* = 0.68, $CHCl_3$).

HPLC (AS-RH, 150 × 4.6 mm, CH_3CN/H_2O = 20/80 → 100/0, 1 mL/min, λ = 254 nm): t_R [racemate] = 23.5 min ((–)-(*R*)-**12**), 25.9 ((+)-(*S*)-**12**).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3301 (w, NH), 3158 (w), 3060 (CH), 2943 (m, CH), 2925 (m, CH), 2867 (m), 1651 (s, C=O), 1607 (m, C=C), 1570 (w, C=C), 1509 (m, C=C), 1267 (m), 1182 (m), 853 (w), 755 (w).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.06 (d, ^3J = 7.4 Hz, 18 H, Si(CH(C$\underline{H}_3$)$_2$)$_3$), 1.16-1.26 (m, 3 H, Si(C$\underline{H}$(CH$_3$)$_2$)$_3$), 4.45 (d, ^2J = 10.8 Hz, 1 H, OC$\underline{H}_a$H$_b$CCl$_3$), 4.50 (d, ^2J = 10.8 Hz, 1 H, OCH$_a$$\underline{H}_bCCl_3$), 5.67 (d, ^3J = 9.3 Hz, 1 H, C$\underline{H}$NHTces), 6.79-6.83 (m, 2 H, 3'-H), 7.14 (d, ^3J = 8.2 Hz, 1 H, 8-H), 7.24-7.29 (m, 1 H, 6-H), 7.30-7.34 (m, 2 H, 2'-H), 7.50-7.55 (m, 1 H, 7-H), 7.57-7.61 (m, 2 H, 5-H, CHN$\underline{H}$Tces), 7.87 (s, 1 H, 4-H), 10.74 (s, 1 H,

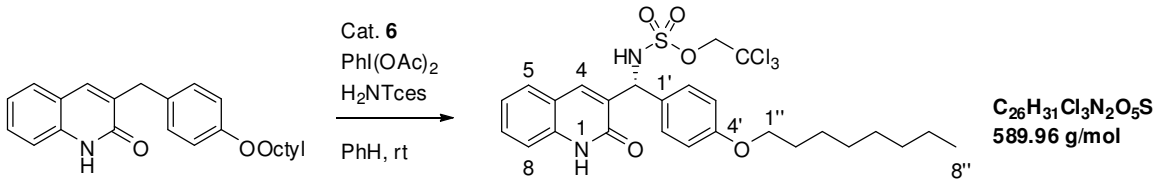
NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 12.8 (d, Si(<u>C</u>H$(CH_3)_2)_3$), 18.0 (q, Si(CH(<u>C</u>$H_3)_2)_3$), 60.8 (d, <u>C</u>HNHTces), 78.1 (t, O<u>C</u>H_2CCl_3), 93.4 (s, OCH_2<u>C</u>Cl_3), 115.5 (d, C-8), 119.8 (s, C-4a), 120.1 (d, C-3'), 123.6 (d, C-6), 127.9 (d, C-2'), 128.3 (d, C-5), 130.1 (s, C-3), 131.1 (s, C-1'), 131.3 (d, C-7), 137.5 (s, C-8a), 139.3 (d, C-4), 156.1 (s, C-4'), 162.7 (s, C-2).

HRMS (ESI): $C_{27}H_{36}Cl_3N_2O_5SSi$ [$(M+H)^+$]: calcd.: 633.1174; found: 633.1178

$C_{54}H_{71}Cl_6N_4O_{10}S_2Si_2$ [$(2M+H)^+$]: calcd.: 1265.2276; found: 1265.2288.

(*R*)-2,2,2-Trichloroethyl ((4-(octyloxy)phenyl)(2-oxo-1,2-dihydroquinolin-3-yl)methyl)sulfamate (10)



S3b **10**

Following *GP4*, quinolone **S3b** (72.7 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford the title compound as a colorless solid (9.0 mg, 15%, 75% *ee*) after purification by flash column chromatography (SiO_2, 15 × 1.5 cm, CH_2Cl_2/EtOAc 99/1 → 98/2 → 9/1 → 4/1, UV/CAM).

m.p.: 156-158 °C (decomposition)

TLC: R_f = 0.64 (CH_2Cl_2/MeOH = 95/5) [UV, CAM].

Specific Rotation: [75% *ee*, determined by chiral HPLC]

$[\alpha]_D^{20}$ = –3.5 (*c* = 0.31, $CHCl_3$).

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm): t_R [racemate] = 12.3 min ((–)-(*R*)-**10**), 17.6 min ((+)-(*S*)-**10**).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3283 (w, NH), 3021 (w, CH), 2923 (w, CH), 2855 (w), 1658 (s, C=O), 1611 (m, C=C), 1574 (m, C=C), 1510 (m, C=C), 1435 (m), 1248 (s), 1174 (vs), 958 (s), 851 (s).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 0.88 (t, ^3J = 6.8 Hz, 3 H, 8''-H), 1.22-1.36 (m, 8 H, 4''-H, 5''-H, 6''-H, 7''-H), 1.37-1.45 (m, 2 H, 3''-H), 1.70-1.77 (m, 2 H, 2''-H), 3.87-3.91 (m, 2 H, 1''-H), 4.46 (d, ^2J = 10.8 Hz, 1 H, OC<u>H$_a$H$_b$</u>CCl_3), 4.51 (d, ^2J = 10.8 Hz, 1 H, OCH_a<u>H$_b$</u>CCl_3), 5.70 (d, ^3J = 9.3 Hz, 1 H, C<u>H</u>NHTces), 6.81-6.85 (m, 2 H, 3'-H), 7.13 (d, ^3J =

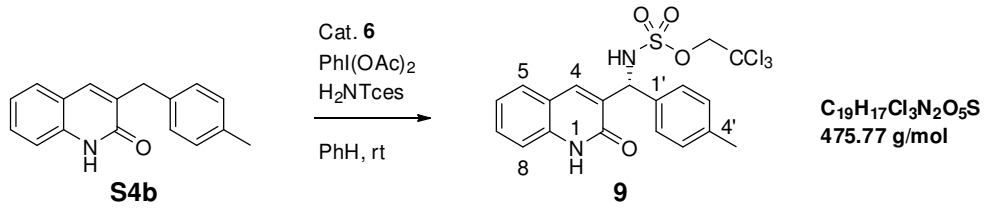
8.4 Hz, 1 H, 8-H), 7.24-7.29 (m, 1 H, 6-H), 7.36-7.41 (m, 2 H, 2'-H), 7.51 (ddd, ^3J = 8.4 Hz, ^3J = 7.2 Hz, ^4J = 1.3 Hz, 1 H, 7-H), 7.58-7.61 (m, 1 H, 5-H), 7.63 (d, ^3J = 9.3 Hz, 1 H, CHNHTces), 7.89 (s, 1 H, 4-H), 11.15 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 14.3 (q, C-8''), 22.8 (t, CH_2), 26.2 (t, C-3''), 29.3, 29.4, 29.5 (3 t, C-2'', 2 CH_2), 32.0 (t, CH_2), 60.7 (d, CHNHTces), 68.2 (t, C-1''), 78.1 (t, OCH_2CCl_3), 93.4 (s, OCH_2CCl_3), 114.7 (d, C-3'), 115.7 (d, C-8), 119.8 (s, C-4a), 123.6 (d, C-6), 127.9 (d, C-2'), 128.3 (d, C-5), 130.0 (s, C-3), 130.6 (s, C-1'), 131.3 (d, C-7), 137.6 (s, C-8a), 139.4 (d, C-4), 159.1 (s, C-4'), 163.0 (s, C-2).

HRMS (ESI): $C_{26}H_{32}Cl_3N_2O_5S$ [$(M+H)^+$]: calcd.: 589.1092; found: 589.1096

$C_{26}H_{31}Cl_3N_2NaO_5S$ [$(M+Na)^+$]: calcd.: 611.0911; found: 611.0916.

(*R*)-2,2,2-Trichloroethyl ((2-oxo-1,2-dihydroquinolin-3-yl)(*p*-tolyl)methyl)sulfamate (9)



S4b **9**

Following *GP4*, quinolone **S4b** (49.9 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford a mixture of the title compound (12.5 mg*, 26%*, 48% *ee*) and H_2NTces (**12**/H_2NTces = 79/21) as a colorless solid after purification by flash column chromatography (SiO_2, 15 × 1.5 cm, CH_2Cl_2/EtOAc 98/2 → 95/5 → 9/1 → 4/1, UV/CAM). An analytically pure sample of **9** was obtained by repeated flash column chromatography and all analytical data refer to this sample.

* corrected yield based on NMR integration

m.p.: 168-169 °C (decomposition)

TLC: R_f = 0.54 (CH_2Cl_2/MeOH 95/5) [UV, CAM].

Specific Rotation: [48% *ee*, determined by chiral HPLC]

$[\alpha]_D^{20}$ = –2.1 (*c* = 0.38, $CHCl_3$).

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm): t_R [racemate] = 15.5 min ((–)-(*R*)-**9**), 17.6 min ((+)-(*S*)-**9**).

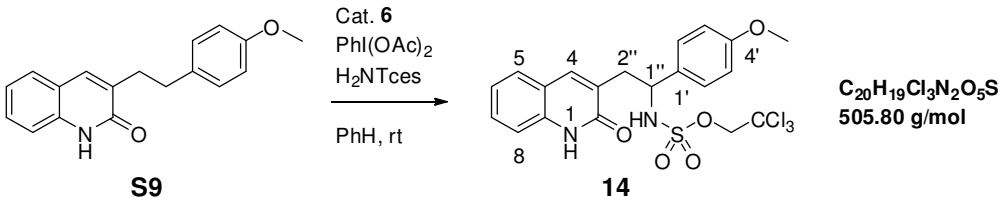
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3292 (w, NH), 3018 (w, CH), 2848 (w), 1652 (vs, C=O), 1619 (w, C=C), 1571 (m, C=C), 1434 (s), 1365 (s), 1178 (vs), 958 (s), 815 (s).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.30 (s, 3 H, CH_3), 4.46 (d, ^2J = 10.8 Hz, $OC\underline{H}_aH_bCCl_3$), 4.51 (d, ^2J = 10.8 Hz, 1 H, $OCH_a\underline{H}_bCCl_3$), 5.72 (d, ^3J = 9.3 Hz, 1 H, C<u>H</u>NHTces), 7.10-7.15 (m, 3 H, 3'-H, 8-H), 7.25-7.29 (m, 1 H, 6-H), 7.35-7.39 (m, 2 H, 2'-H), 7.48-7.53 (m, 1 H, 7-H), 7.59-7.62 (m, 1 H, 5-H), 7.70 (d, ^3J = 9.3 Hz, 1 H, CHN<u>H</u>Tces), 7.92 (s, 1 H, 4-H), 11.46 (s, 1 H, NH).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 21.2 (q, CH_3), 60.9 (d, <u>C</u>HNHTces), 78.1 (t, $O\underline{C}H_2CCl_3$), 93.4 (s, $OCH_2\underline{C}Cl_3$), 115.8 (d, C-8), 119.8 (s, C-4a), 123.6 (d, C-6), 126.6 (d, C-2'), 128.3 (d, C-5), 129.5 (d, C-3'), 129.9 (s, C-3), 131.3 (d, C-7), 135.8 (s, C-1'), 137.6 (s, C-8a), 138.0 (s, C-4'), 139.5 (d, C-4), 163.1 (s, C-2).

HRMS (ESI): $C_{19}H_{18}Cl_3N_2O_4S$ $[(M+H)^+]$: calcd.: 475.0047; found: 475.0044.

2,2,2-Trichloroethyl (1-(4-methoxyphenyl)-2-(2-oxo-1,2-dihydroquinolin-3-yl)ethyl)sulfamate (14)



Following *GP4*, quinolone **S9** (55.9 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford the title compound as a colorless solid (32.7 mg, 65%, 30% *ee*) after purification by flash column chromatography (SiO_2, 17 × 1 cm, CH_2Cl_2/EtOAc 9/1, UV/CAM).

m.p.: 184-186 °C (decomposition)

TLC: R_f = 0.70 (CH_2Cl_2/MeOH 9/1) [UV, CAM].

Specific Rotation: [30% *ee*, determined by chiral HPLC]

$[\alpha]_D^{20}$ = + 10.0 (*c* = 0.24, MeOH).

HPLC (OD, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 80/20, 1 mL/min, λ = 210 nm): t_R [enantioenriched] = 11.3 min ((–)-**14**), 14.5 min ((+)-**14**).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3319 (m, NH), 3154 (w), 3103 (w, CH), 3064 (w, CH), 3005 (w, CH), 2948 (w, CH), 2898 (m, CH), 1654 (s, C=O), 1612 (m, C=C), 1574 (m, C=C), 1512 (m, C=C), 1247 (m), 1174 (s), 851 (m), 754 (m).

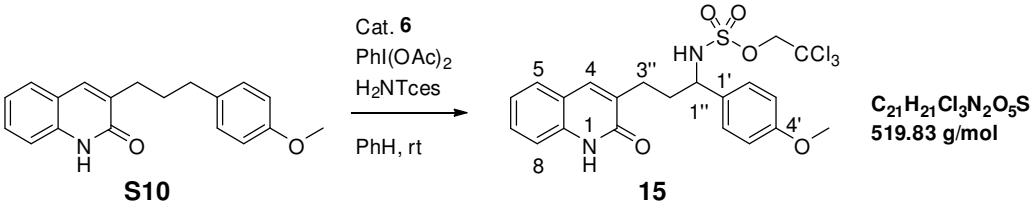
^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] = 2.87-2.98 (m, 2 H, 2''-H), 3.71 (s, 3 H, OCH_3),

4.15 (d, ^2J = 11.1 Hz, 1 H, OC<u>H</u>$_a$H$_b$CCl$_3$), 4.20 (d, ^2J = 11.1 Hz, 1 H, OCH$_a$<u>H</u>$_b$CCl$_3$), 4.79-4.86 (m, 1 H, 1''-H), 6.88-6.93 (m, 2 H, 3'-H), 7.14 (*virt.* t, $^3J \approx$ 7.5 Hz, 1 H, 6-H), 7.26-7.29 (m, 1 H, 8-H), 7.29-7.33 (m, 2 H, 2'-H), 7.44 (*virt.* t, $^3J \approx$ 7.7 Hz, 1 H, 7-H), 7.56 (d, ^3J = 7.8 Hz, 1 H, 5-H), 7.70 (s, 1 H, 4-H), 9.05 (d, ^3J = 8.5 Hz, 1 H, N<u>H</u>Tces), 11.86 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, DMSO-d$_6$): δ [ppm] = 38.6 (t, C-2''), 55.1 (q, OCH$_3$), 56.3 (d, C-1''), 77.0 (t, O<u>C</u>H$_2$CCl$_3$), 93.5 (s, OCH$_2$<u>C</u>Cl$_3$), 113.9 (d, C-3'), 114.9 (d, C-8), 119.2 (s, C-4a), 121.9 (d, C-6), 127.4 (d, C-5), 127.7 (d, C-2'), 129.3 (s, C-3), 129.7 (d, C-7), 134.0 (s, C-1'), 138.2 (s, C-8a), 138.6 (d, C-4), 158.6 (s, C-4'), 162.1 (s, C-2).

HRMS (ESI): $C_{20}H_{20}Cl_3N_2O_5S$ [$(M+H)^+$]: calcd.: 505.0153; found: 505.0152.

2,2,2-Trichloroethyl (1-(4-methoxyphenyl)-3-(2-oxo-1,2-dihydroquinolin-3-yl)propyl)sulfamate (15)



Following *GP4*, quinolone **S10** (58.7 mg, 0.2 mmol, 2.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford the title compound as a colorless solid (13.0 mg, 25%, 5% *ee*). The compound **15** was obtained after purification by flash column chromatography (SiO_2, 16 × 1 cm, CH_2Cl_2/EtOAc 98/2 → 9/1 → 4/1, UV/CAM) yielding a compound mixture which was purified by further flash column chromatography (SiO_2, 18 × 1 cm CH_2Cl_2/MeOH 99/1, UV/CAM).

m.p.: 153-155 °C (decomposition)

TLC: R_f = 0.58 (CH_2Cl_2/MeOH = 9/1) [UV, CAM].

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm): t_R [racemate] = 13.3 min, 15.2 min.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3305 (w, NH), 3277 (w), 3161 (w), 3108 (w), 3065 (w, CH), 2952 (w, CH), 2918 (w, CH), 2850 (w, CH), 1648 (vs, C=O), 1611 (m, C=C), 1574 (m, C=C), 1514 (m, C=C), 1426 (m), 1250 (m), 1174 (s), 753 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.24-2.40 (m, 2 H, 2''-H), 2.61-2.71 (m, 1 H, 3''-H_a), 2.71-2.80 (m, 1 H, 3''-H_b), 3.77 (s, 3 H, OCH_3), 4.21 (d, ^{2}J = 10.8 Hz, 1 H, $OC\underline{H}_aH_bCCl_3$), 4.33 (d, ^{3}J = 10.8 Hz, 1 H, $OCH_a\underline{H}_bCCl_3$), 4.55-4.62 (m, 1 H, 1''-H), 6.86-6.90 (m, 2 H, 3'-H), 7.19-7.23 (m, 1 H, 6-H), 7.29 (d, ^{3}J = 8.3 Hz, 1 H, 8-H), 7.38-7.42 (m, 2 H, 2'-H), 7.46 (ddd, ^{3}J = 8.3 Hz, ^{3}J = 7.3 Hz, ^{4}J = 1.2 Hz, 1 H, 7-H), 7.49-7.52 (m, 1 H, 5-H), 7.64 (s, 1 H, 4-H), 8.51 (d, ^{3}J = 6.1 Hz, 1 H, N$\underline{H}$Tces), 10.91 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 29.0 (t, C-3''), 35.8 (t, C-2''), 55.5 (q, OCH_3), 59.1 (d, C-1''), 78.0 (t, $O\underline{C}H_2CCl_3$), 93.6 (s, $OCH_2\underline{C}Cl_3$), 114.4 (d, C-3'), 115.7 (d, C-8), 120.4 (s, C-4a), 123.2 (d, C-6), 127.4 (d, C-5), 128.2 (d, C-2'), 130.1 (d, C-7), 132.7 (s, C-3), 133.3 (s, C-1'), 137.1 (s, C-8a), 138.4 (d, C-4), 159.4 (s, C-4'), 163.7 (s, C-2).

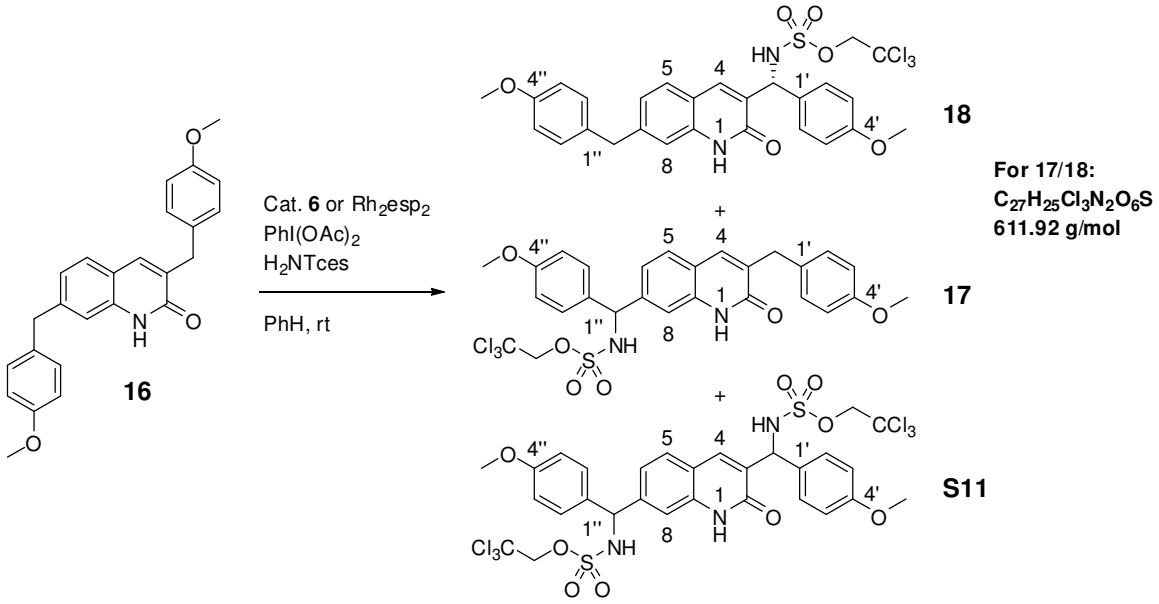
HRMS (ESI): $C_{21}H_{22}Cl_3N_2O_5S$ $[(M+H)^+]$: calcd.: 519.0310; found: 519.0312

$C_{21}H_{21}Cl_3N_2NaO_5S$ $[(M+Na)^+]$: calcd.: 541.0129; found: 541.0133

$C_{42}H_{43}Cl_6N_4O_{10}S_2$ $[(2M+H)^+]$: calcd.: 1037.0546; found: 1037.0546.

Competition experiment

(*R*)-2,2,2-Trichloroethyl ((7-(4-methoxybenzyl)-2-oxo-1,2-dihydroquinolin-3-yl)(4-methoxyphenyl)methyl)sulfamate (18) and 2,2,2-Trichloroethyl ((3-(4-methoxybenzyl)-2-oxo-1,2-dihydroquinolin-7-yl)(4-methoxyphenyl)methyl)sulfamate (17)



Racemic reaction with Rh_2esp_2[1] *as catalyst*

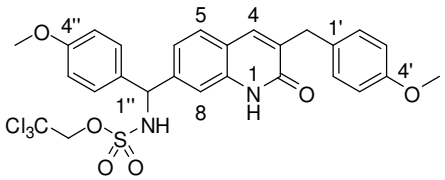
Following *GP4*, quinolone **16** (38.8 mg, 0.1 mmol, 1.0 eq) was reacted using Rh_2esp_2 (1.52 mg, 2.0 µmol, 0.02 eq) as catalyst. After the given reaction time, the solvent was removed under reduced pressure and the crude product directly subject to ^{1}H NMR analysis. The crude product was then purified by flash column chromatography (SiO_2, 18 × 1 cm, CH_2Cl_2/EtOAc 95/5 → 9/1 → 4/1, UV/CAM) to afford an analytically pure fraction of compound **18** as a colorless solid. Two further fractions were obtained consisting of a mixture of starting material **16** and minor amounts of **S11*** and a mixture of **16** and **17**. The latter was purified by further flash column chromatography (SiO_2, 14 × 1 cm CH_2Cl_2/MeOH 75/1, UV/CAM) to afford an analytically pure fraction of **17**. No improvement of purification was achieved by using preparative HPLC. The provided analytical data refer to the corresponding pure fractions obtained. The ratio of regioisomers **17** and **18** (**17/18** = 61/39) was calculated from the crude ^{1}H NMR by integration of the corresponding CH-signals (figure F1). For the determination of the right integral of **18**, the total integral of the CH-signal of **18** and one CH-signal of **S11** was determined (overlapping signals) and the integral of the second CH-proton of **S11** was subtracted.

* Structure **S11** was assigned to the byproduct (mixture of diastereoisomers). However, full analytical data were not available.

Enantio- and regioselective amination using catalyst **6**

Following *GP4* and the procedure for the racemic reaction (as described above), quinolone **16** (38.8 mg, 0.1 mmol, 1.0 eq) was reacted using catalyst **6** (2.21 mg, 2.0 µmol, 0.02 eq) to afford analytically pure fractions of **18** (69% *ee*) and **17** (6.7% *ee*). The ratio of the regioisomers (**17**/**18** = 37/63) was determined by ^{1}H NMR analysis of the crude product.

Analytical data for compound ***17***



m.p.: 158-160 °C (decomposition)

TLC: R_f = 0.26 (CH_2Cl_2/MeOH 95/5) [UV, CAM].

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm): t_R [racemate] = 23.4 min, 27.3 min.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3295 (br, NH), 3160 (br), 3068 (br), 2924 (m, CH), 2850 (m, CH), 1646 (vs, C=O), 1609 (s, C=C), 1568 (m, C=C), 1510 (vs, C=C), 1457 (m), 1246 (s), 1176 (s), 849 (m), 724 (m).

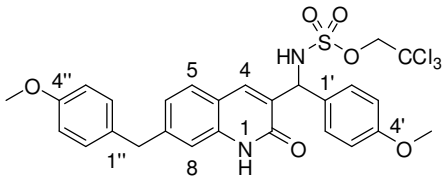
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.75 (s, 3 H, C$^{4''}$-OCH_3), 3.77 (s, 1 H, C$^{4'}$-OCH_3), 3.81 (d, ^2J = 15.5 Hz, 1 H, C^3-C$\underline{H}_a$H$_b$), 3.85(d, ^3J = 15.5 Hz, 1 H, C^3-CH$_a\underline{H}_b$), 4.42 (d, ^2J = 10.8 Hz, 1 H, OC$\underline{H}_a$H$_b$CCl$_3$), 4.48 (d, ^2J = 10.5 Hz, 1 H, OCH$_a\underline{H}_b$CCl$_3$), 5.85 (d, ^3J = 7.6 Hz, 1 H, C$\underline{H}$NHTces), 6.51-6.60 (m, 1 H, CHN$\underline{H}$Tces), 6.80-6.86 (m, 4 H, 3'-H, 3''-H), 7.11 (d, ^3J = 8.2 Hz, 1 H, 6-H), 7.16 (d, ^3J = 8.2 Hz, 2 H, 2'-H), 7.19 (d, ^3J = 8.3 Hz, 2 H, 2''-H), 7.30-7.32 (m, 2 H, 4-H, 8-H), 7.38 (d, ^3J = 8.2 Hz, 1 H, 5-H), 10.89 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 35.3 (t, C^3-$\underline{C}H_2$), 55.4 (q, C$^{4'}$-OCH3), 55.5 (q, C$^{4''}$-OCH_3), 61.5 (d, $\underline{C}$HNHTces), 78.1 (t, O$\underline{C}H_2CCl_3$), 93.4 (s, $OCH_2\underline{C}Cl_3$), 113.9 (d, C-8), 114.2 (d, C-3'), 114.5 (d, C-3''), 119.8 (s, C-4a), 122.5 (d, C-6), 128.0 (d, C-5), 129.0 (d, C-2''), 130.5 (d, C-2'), 130.5 (s, C-1'), 131.8 (s, C-1''), 134.3 (s, C-3), 137.2 (s, C-8a), 137.2 (d, C-4), 142.5 (s, C-7), 158.4 (s, C-4'), 159.7 (s, C-4''), 163.6 (s, C-2).

HRMS (ESI): $C_{27}H_{26}Cl_3N_2O_6S$ [(M+H)$^+$]: calcd.: 611.0572; found: 611.0577

$C_{27}H_{25}Cl_3N_2NaO_6S$ [(M+Na)$^+$]: calcd.: 633.0391; found: 633.0399.

Analytical data for compound ***18***



m.p.: 152-154 °C (decomposition)

TLC: R_f = 0.55 (CH_2Cl_2/MeOH 95/5) [UV, CAM].

Specific Rotation: [69% *ee*, determined by chiral HPLC]

$[\alpha]_D^{20} = -1.9$ (c = 0.69, $CHCl_3$).

HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 254 nm): t_R [racemate] = 15.9 min ((–)-(*R*)-**18**), 23.9 min ((+)-(*S*)-**18**).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3299 (br, NH), 3143 (br, NH), 3065 (w), 3002 (w, CH), 2954 (m, CH), 2923 (s, CH), 2850 (m, CH), 1648 (vs, C=O), 1610 (m, C=C), 1568 (w, C=C), 1509 (vs, C=C), 1439 (m), 1247 (s), 1175 (s), 847 (m), 753 (m).

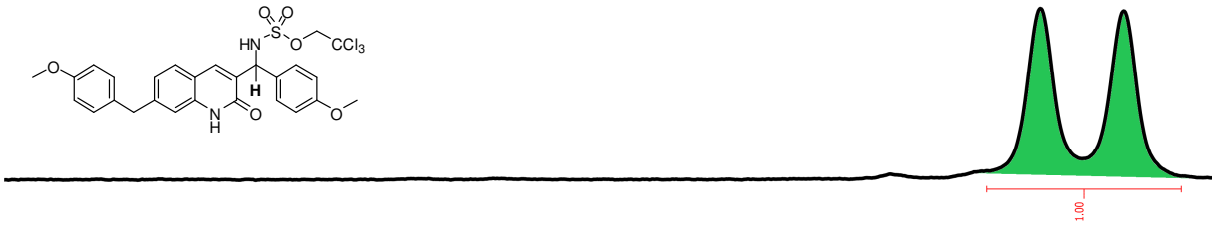
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.75 (s, 3 H, $C^{4'}$-OCH_3), 3.78 (s, 3 H, $C^{4''}$-OCH_3), 4.00 (s, 2 H, C^7-CH_2), 4.45 (d, ^2J = 10.8 Hz, 1 H, $OC\underline{H}_aH_bCCl_3$), 4.50 (d, ^2J = 10.8 Hz, 1 H, $OCH_a\underline{H}_bCCl_3$), 5.65 (d, ^3J = 9.2 Hz, 1 H, C<u>H</u>NHTces), 6.81-6.84 (m, 2 H, 3'-H), 6.84-6.87 (m, 2 H, 3''-H), 6.96 (s, 1 H, 8-H), 7.07-7.11 (m, 3 H, 2''-H, 6-H), 7.37 (d, ^3J = 8.4 Hz, 2 H, 2'-H), 7.50 (d, ^3J = 8.1 Hz, 2 H, 5-H), 7.63 (d, ^3J = 9.2 Hz, 1 H, CHN<u>H</u>Tces), 7.83 (s, 1 H, 4-H), 10.48 (s, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 41.2 (t, C^7-<u>C</u>H_2), 55.4, 55.4 (2 q, $C^{4'}$-OCH_3, $C^{4''}$-OCH_3), 60.8 (d, <u>C</u>HNHTces), 78.1 (t, O<u>C</u>$H_2$$C\underline{C}l_3$), 93.4 (s, $OCH_2\underline{C}Cl_3$), 114.2, 114.3 (2 d, C-3', C-3''), 115.2 (d, C-8), 118.0 (s, C-4a), 124.8 (d, C-6), 128.0 (d, C-2'), 128.4 (d, C-5), 129.2 (s, C-3), 130.1 (d, C-2''), 131.0 (s, C-1'), 131.8 (s, C-1''), 137.8 (s, C-8a), 139.1 (d, C-4), 146.0 (s, C-7), 158.4 (s, C-4''), 159.4 (s, C-4'), 162.7 (s, C-2).

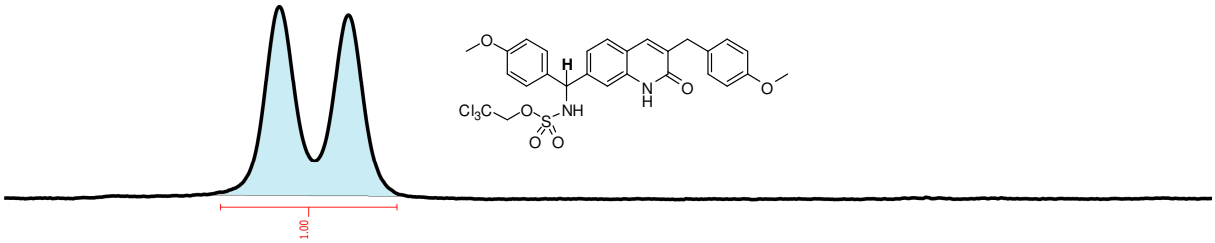
HRMS (ESI): $C_{27}H_{26}Cl_3N_2O_6S$ [$(M+H)^+$]: calcd.: 611.0572; found: 611.0575

$C_{27}H_{25}Cl_3N_2NaO_6S$ [$(M+Na)^+$]: calcd.: 633.0391; found: 633.0340.

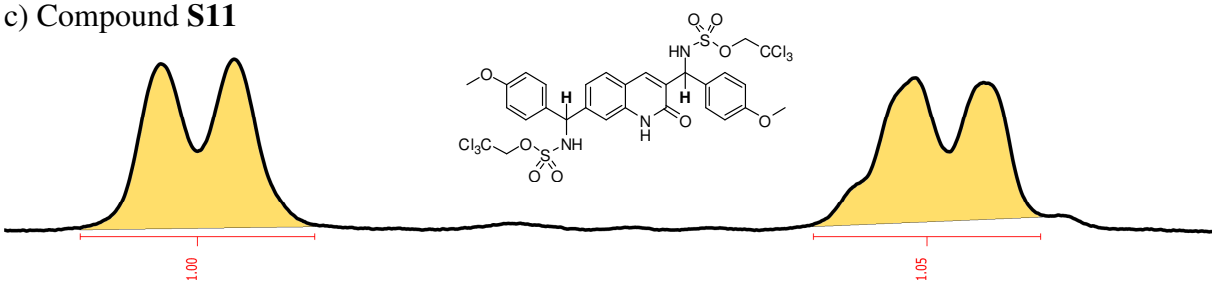
a) Compound **18**



b) Compound **17**



c) Compound **S11**



d) CH-amination using Rh_2esp_2 as catalyst

e) CH-amination using **6** as catalyst

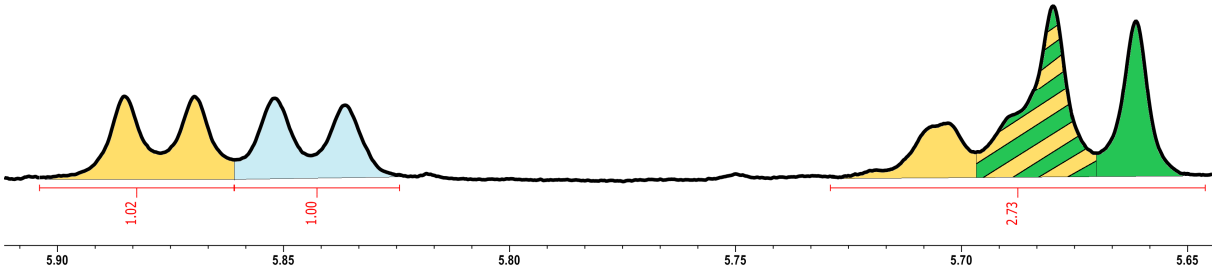
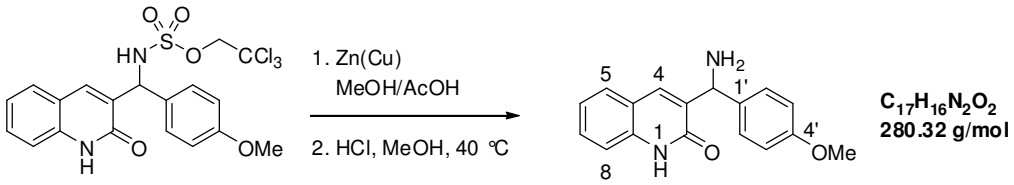


Figure F1: Determination of the ratio of regioisomers **18** and **17**. ^{1}H NMR spectra (500 MHz, $CDCl_3$): a) compound **18**; b) compound **17**; c) isolated compound **S11** for comparison; d) crude product using Rh_2esp_2 as amination-catalyst; d) crude product using **6** as amination-catalyst.

Deprotection of CH-amination product *rac*-8[11]

3-(Amino(4-methoxyphenyl)methyl)quinolin-2(1*H*)-one (*rac*-S12)



rac-**8** *rac*-**S12**

To a solution of **8** (24.6 mg, 0.05 mmol, 1.0 eq) in methanol (0.7 mL) was successively added zinc-copper couple (32.7 mg, 0.5 mmol, 10 eq) and acetic acid (0.7 mL). The reaction mixture was stirred for 20 hours at room temperature and then was filtered through a pad of Celite. The Celite was rinsed with methanol and the filtrate was concentrated under reduced pressure. The remaining acetic acid was removed by repeated evaporation with toluene under reduce pressure. The residue was dissolved in a solution of HCl in methanol (2 mL, prepared by adding 160 µL acetyl chloride to 2 mL of dry methanol) and the reaction mixture was stirred at 40 °C for 18 hours. The reaction was quenched by the addition of saturated K_2CO_3 solution followed by extraction with dichloromethane (3 × 8 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was subjected to flash column chromatography (SiO_2, 10 × 1 cm, CH_2Cl_2/MeOH 98/2 → 95/5 → 9/1, UV) to afford the amine *rac*-**S12** as a colorless solid (9.4 mg, 67%).

m.p.: 159-162 °C

TLC: R_f = 0.24 (CH_2Cl_2/MeOH = 4/1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3351 (w, NH), 3275 (w), 2994 (m, CH), 2923 (m, CH), 2849 (m, CH), 1649 (s, C=O), 1609 (m, C=C), 1567 (m, C=C), 1510 (m, C=C), 1432 (m), 1248 (s), 1179 (w), 917 (w), 754 (m).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.08 (bs, 2 H, NH_2), 3.79 (s, 3 H, OCH_3), 5.44 (s, 1 H, C<u>H</u>NH_2), 6.88 (d, ^3J = 8.2 Hz, 2 H, 3'-H), 7.15-7.23 (m, 2 H, 6-H, 8-H), 7.40-7.46 (m, 3 H, 7-H, 2'-H), 7.50 (d, ^3J = 7.8 Hz, 1 H, 5-H), 7.74 (s, 1 H, 4-H), 11.81 (bs, 1 H, NH).

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ [ppm] = 54.3 (d, C<u>H</u>NH_2), 55.4 (q, OCH_3), 114.0 (d, C-3'), 115.4 (d, C-8), 120.1 (s, C-4a), 122.7 (d, C-6), 128.1 (d, C-5), 128.6 (d, C-2'), 130.1 (d, C-7), 134.9 (s, C-1'), 136.3 (d, C-4), 137.4 (s, C-8a), 158.9 (s, C-4'), 163.0 (s, C-2).

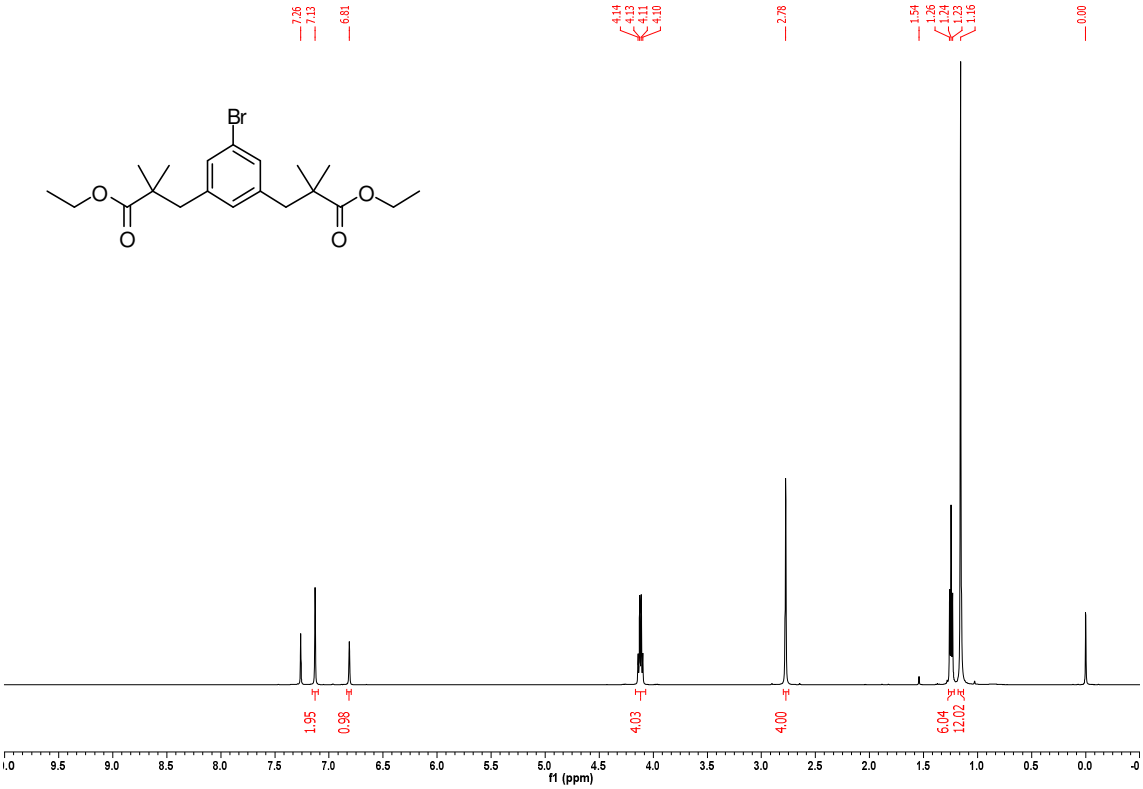
Due to signal overlap and broadening C-3 cannot be assigned.

HRMS (ESI): $C_{17}H_{14}NO_2$ [$(M\text{-}NH_2)^+$]: calcd.: 264.1019; found: 264.1022

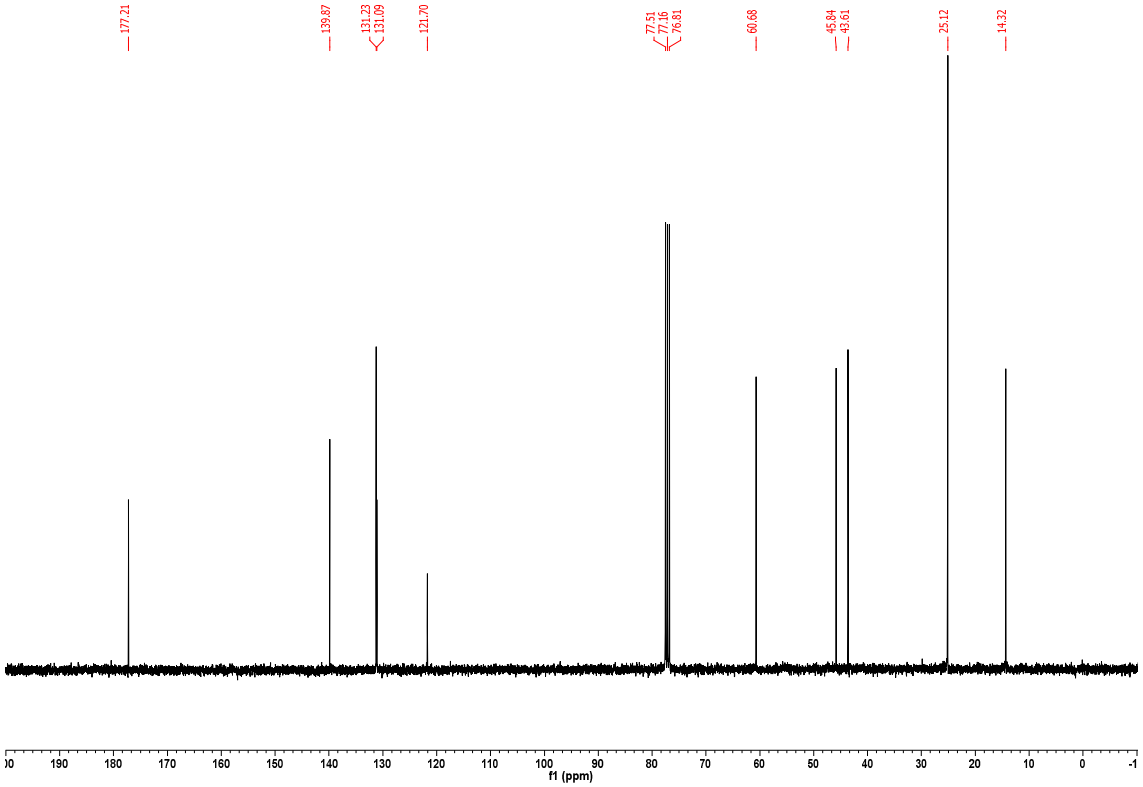
$C_{17}H_{17}N_2O_2$ [$(M+H)^+$]: calcd.: 281.1285; found: 281.1287.

2. NMR spectra of new compounds

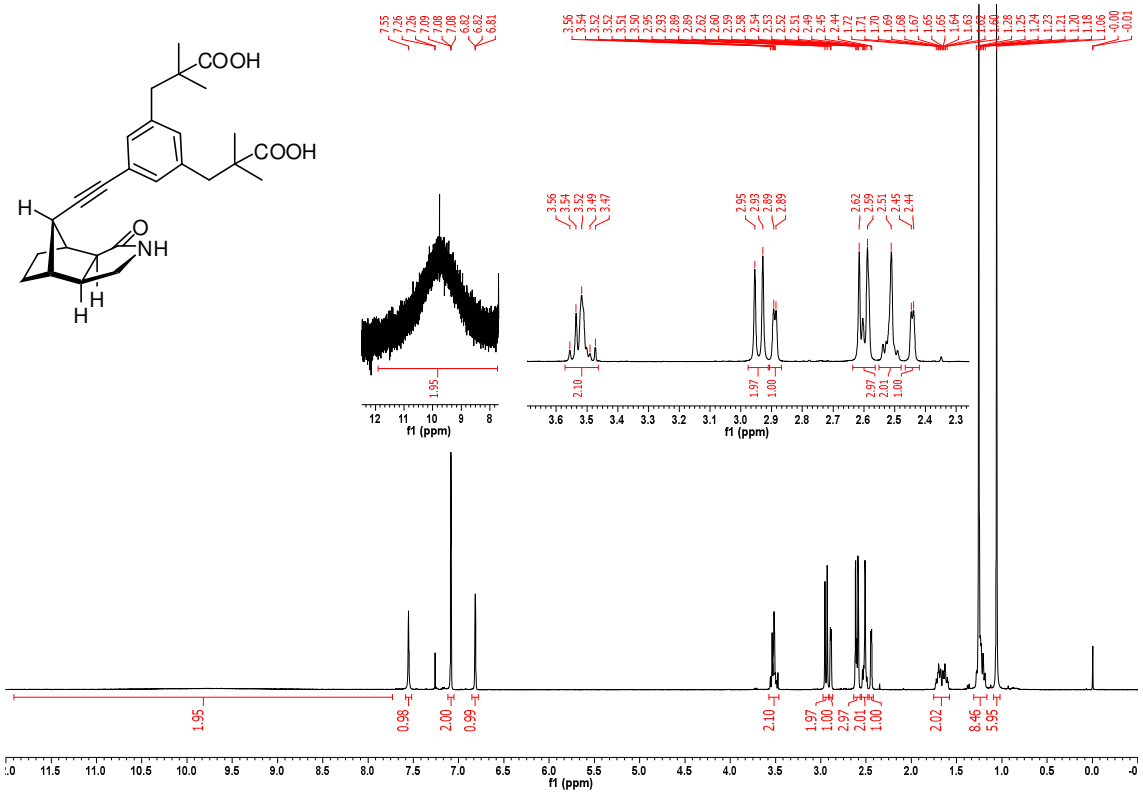
^{1}H NMR (300 K, $CDCl_3$)



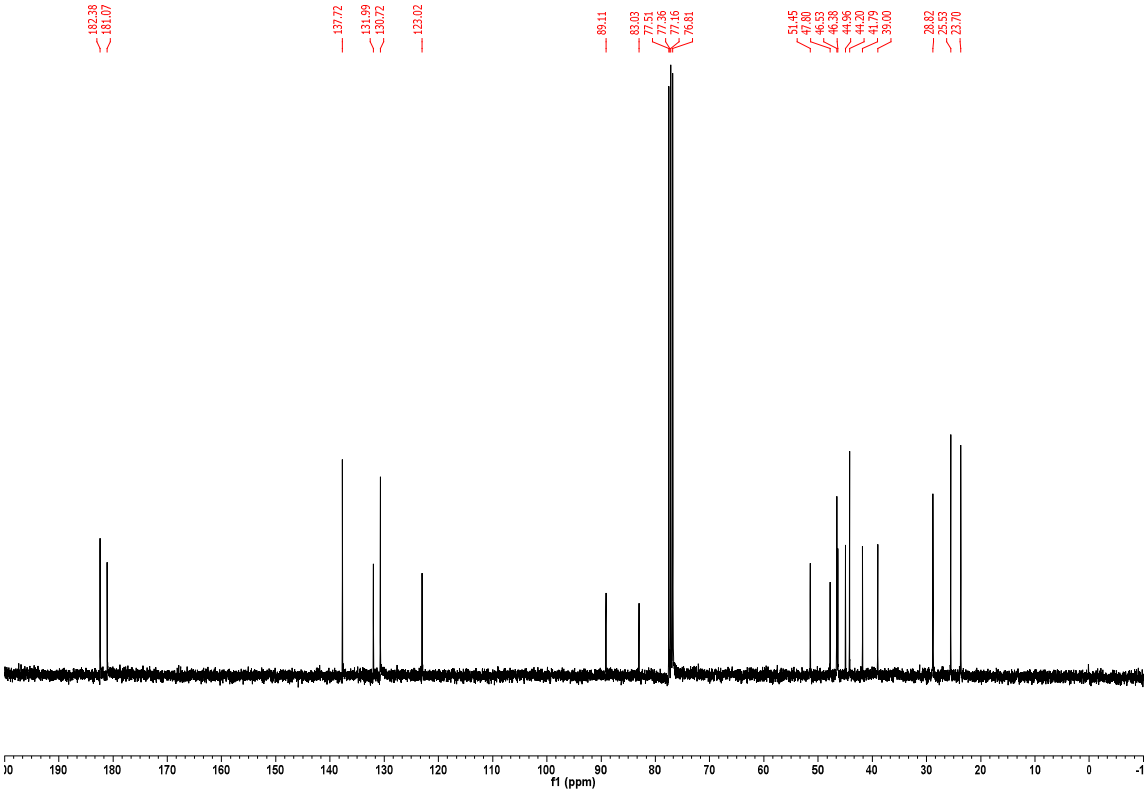
^{13}C NMR (300 K, $CDCl_3$)



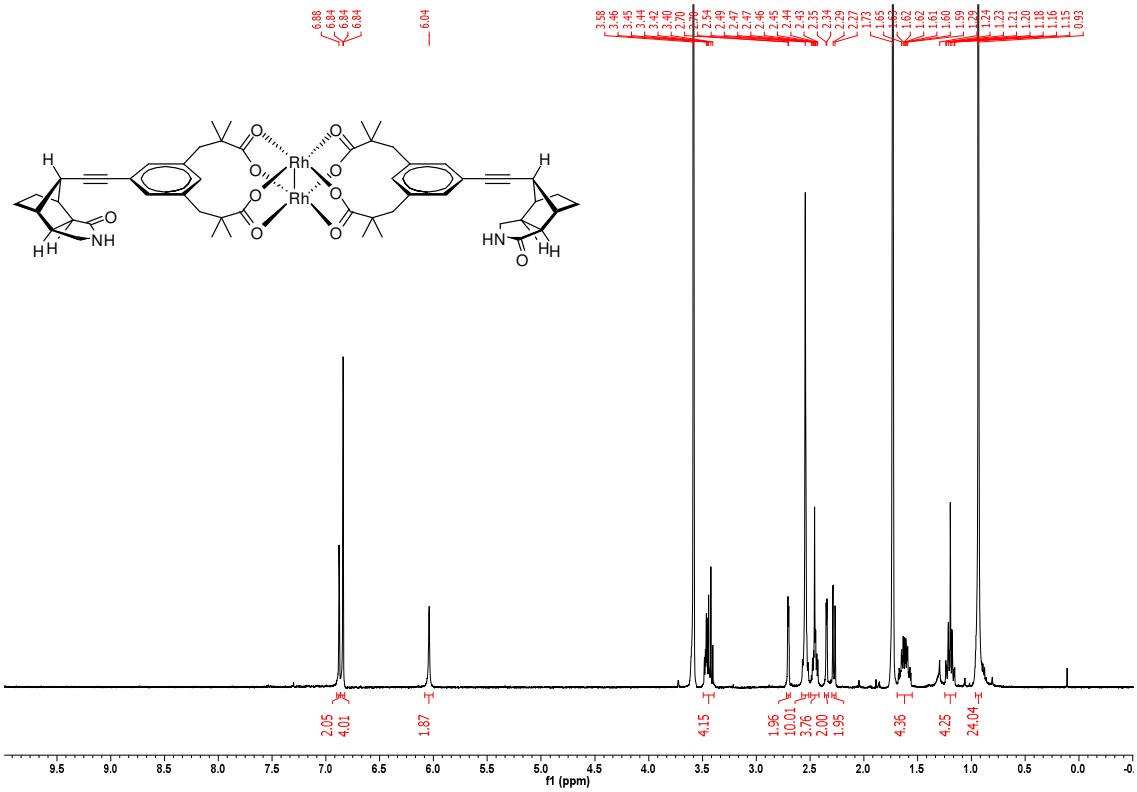
^{1}H NMR (300 K, $CDCl_3$)



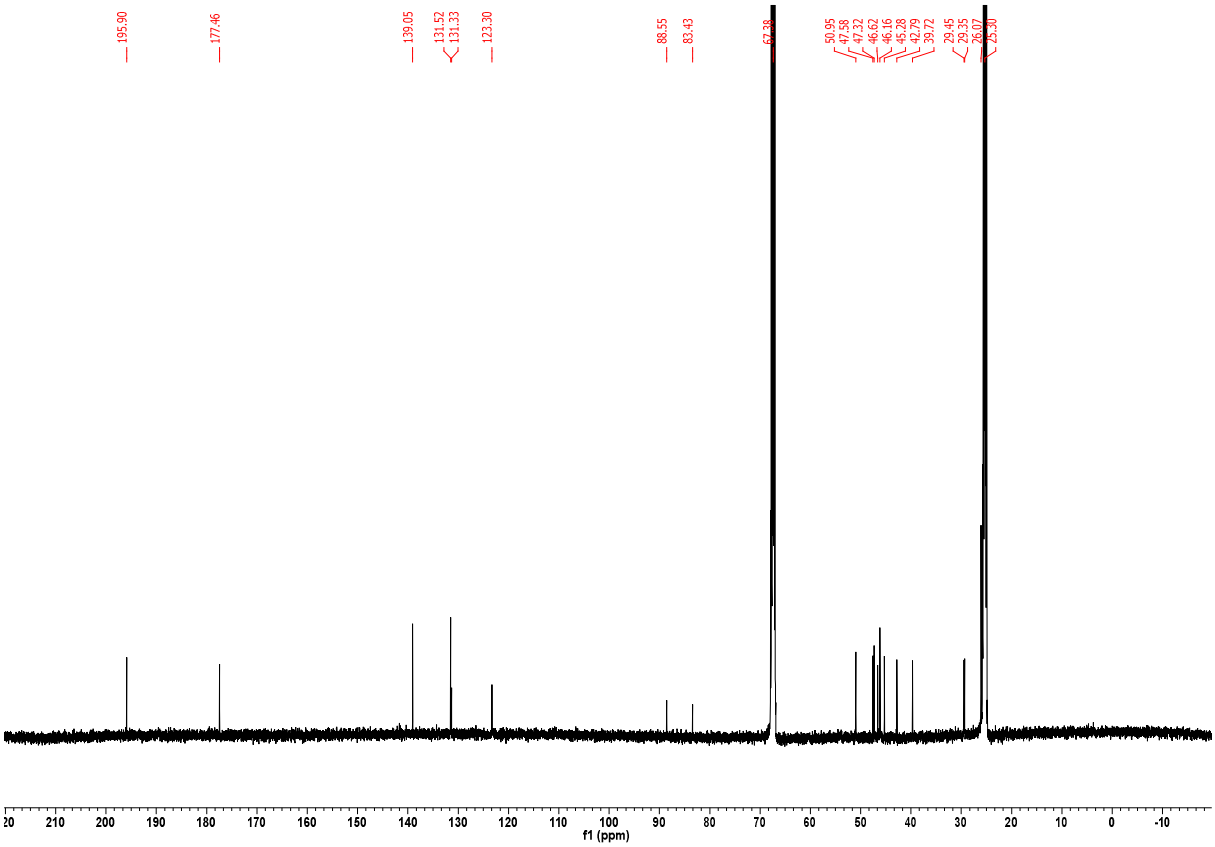
^{13}C NMR (300 K, $CDCl_3$)



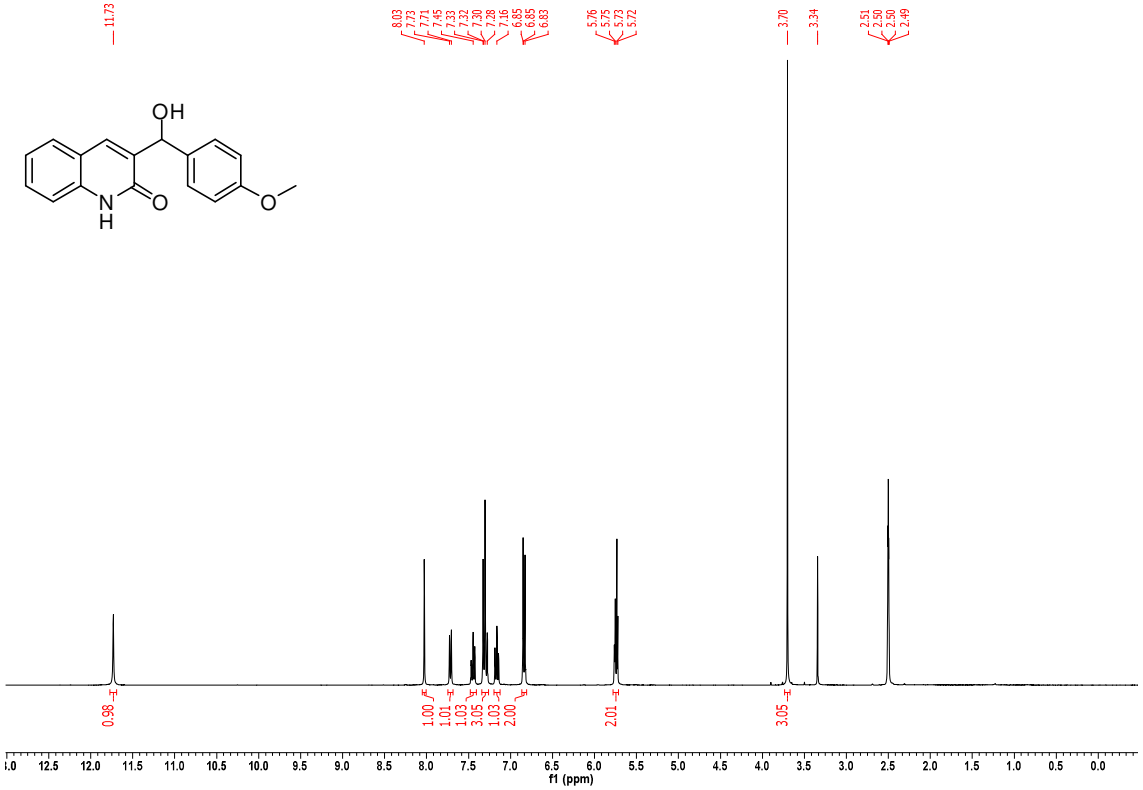
^{1}H NMR (300 K, THF-d_8)



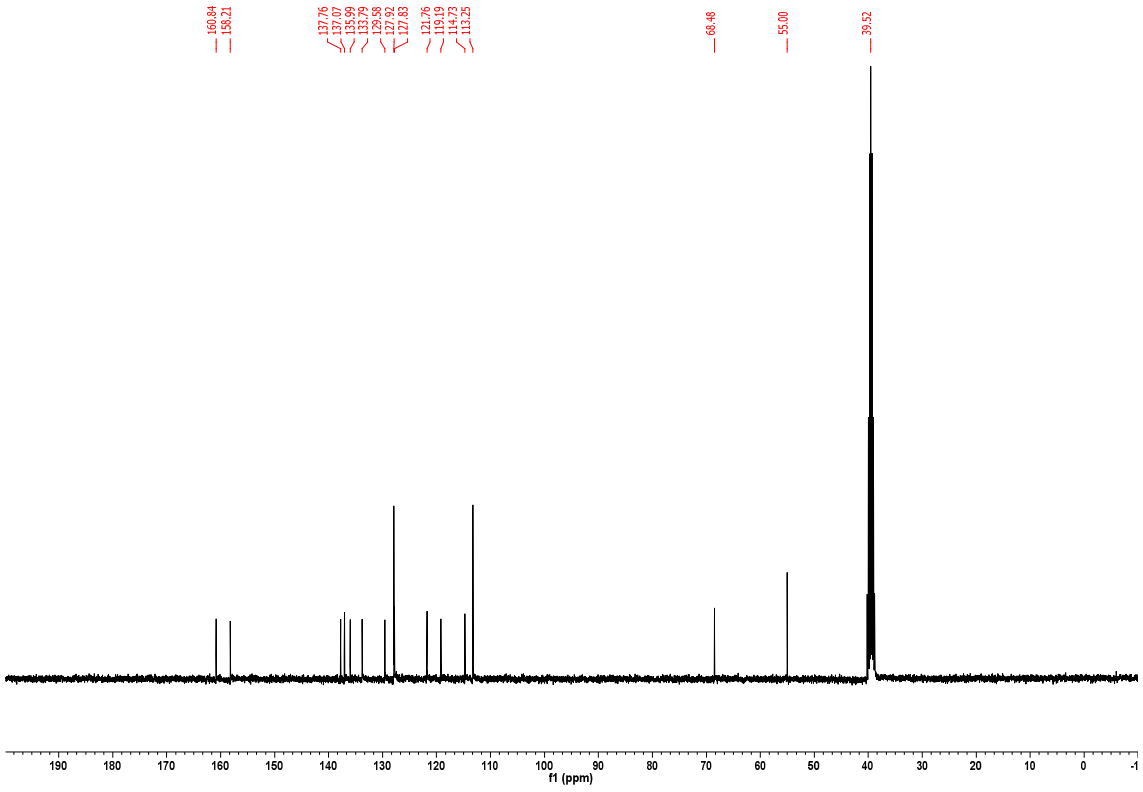
^{13}C NMR (300 K, THF-d_8)



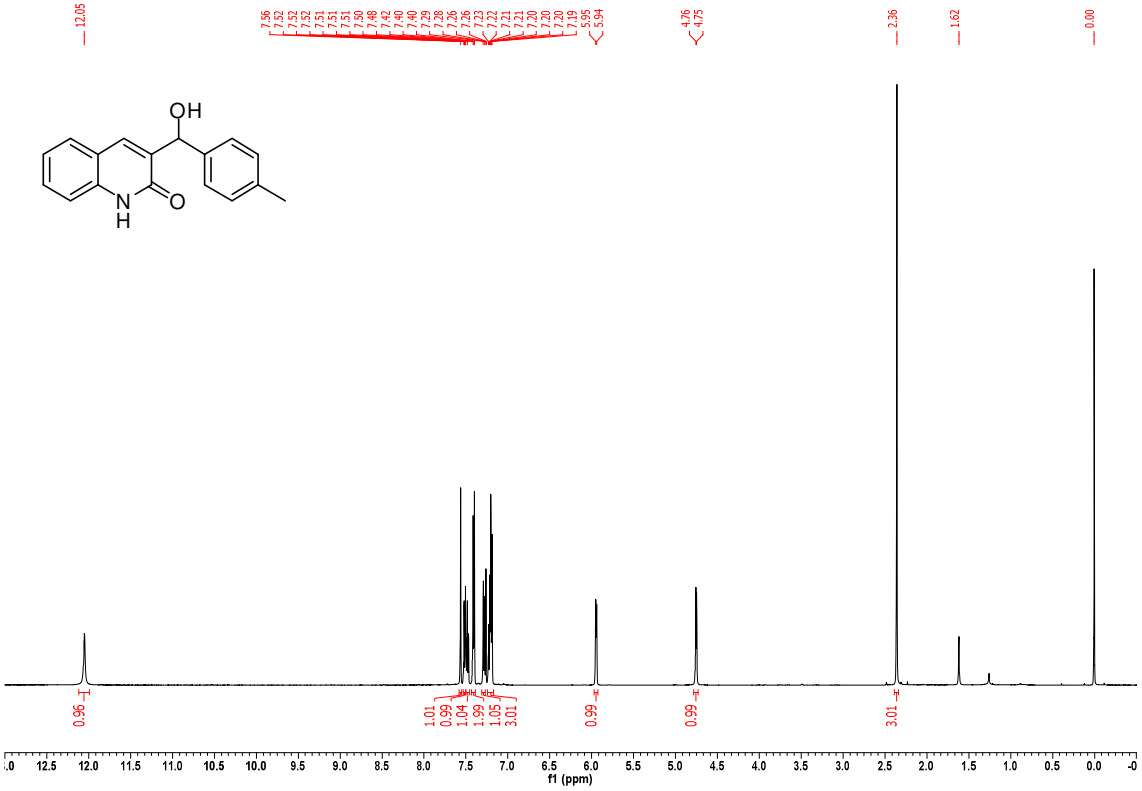
^{1}H NMR (300 K, DMSO-d_6)



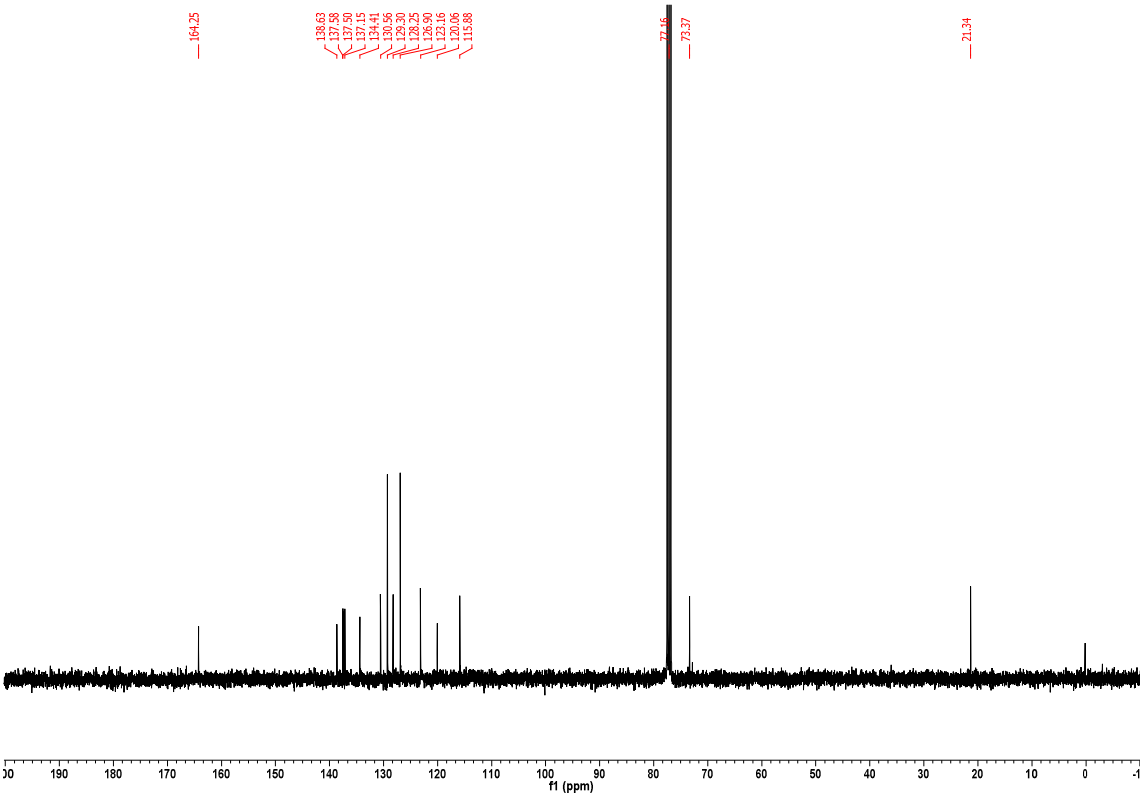
^{13}C NMR (300 K, DMSO-d_6)



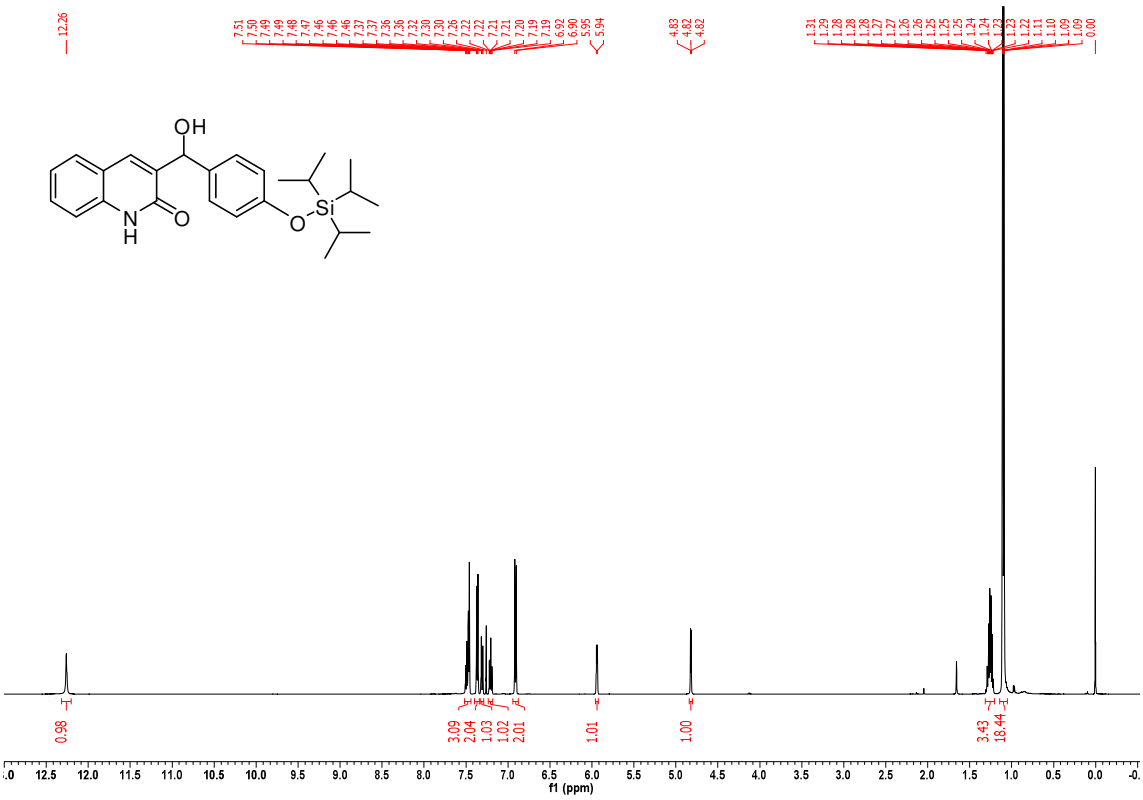
^{1}H NMR (300 K, $CDCl_3$)



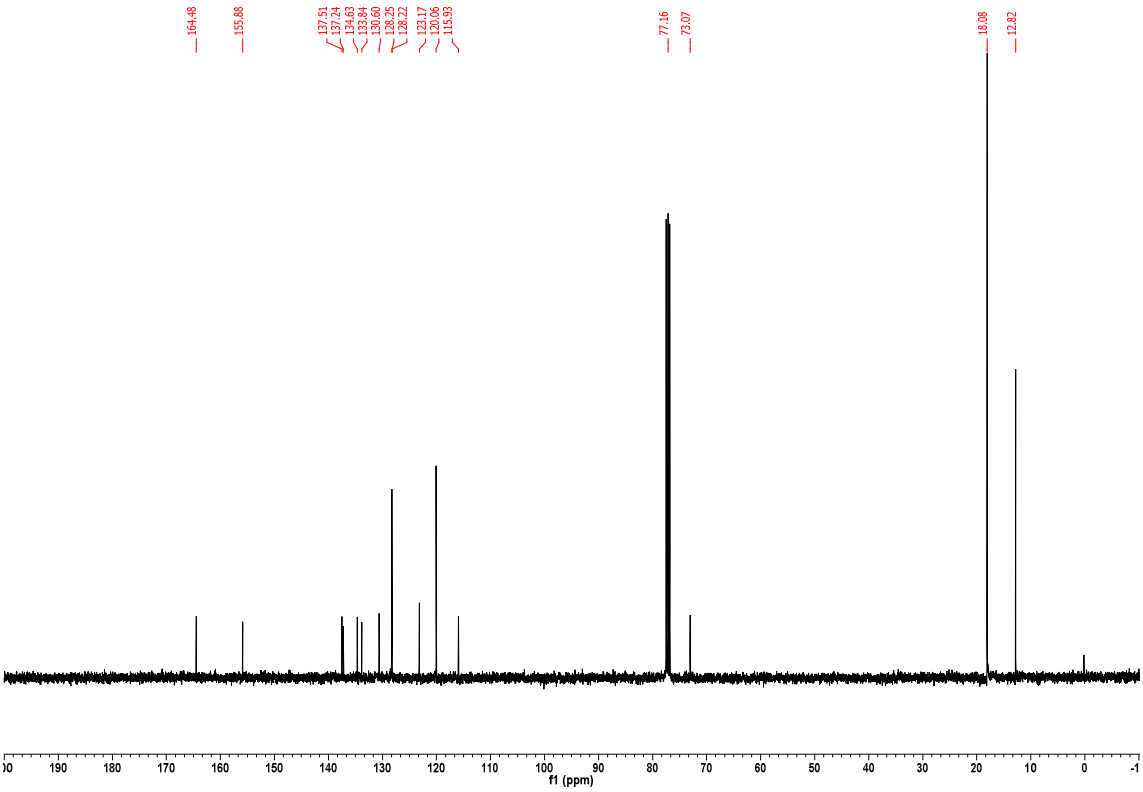
^{13}C NMR (300 K, $CDCl_3$)



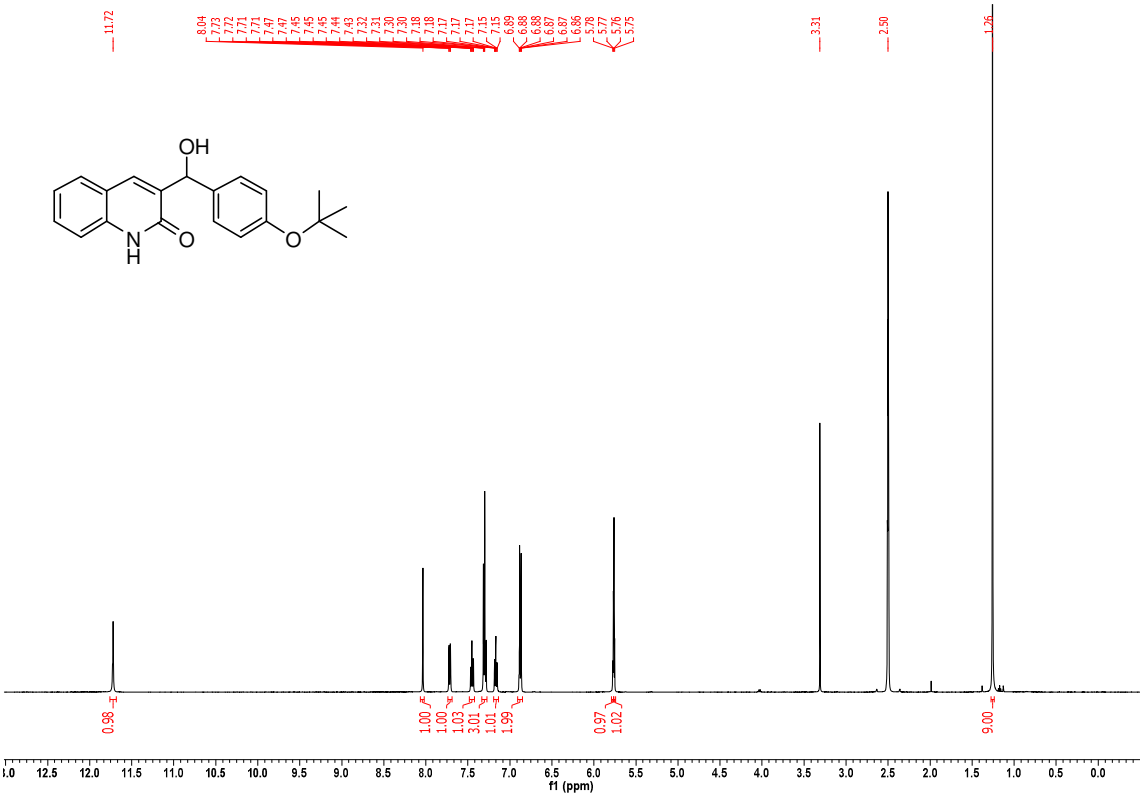
^{1}H NMR (300 K, $CDCl_3$)



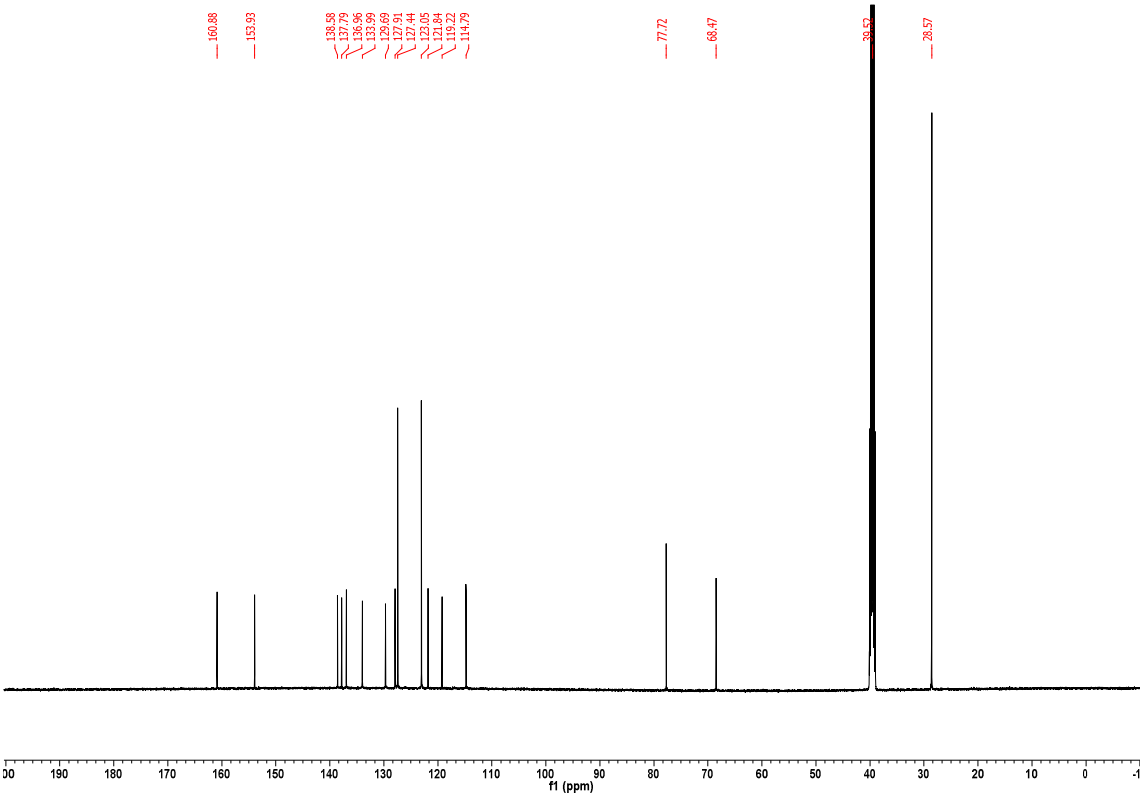
^{13}C NMR (300 K, $CDCl_3$)



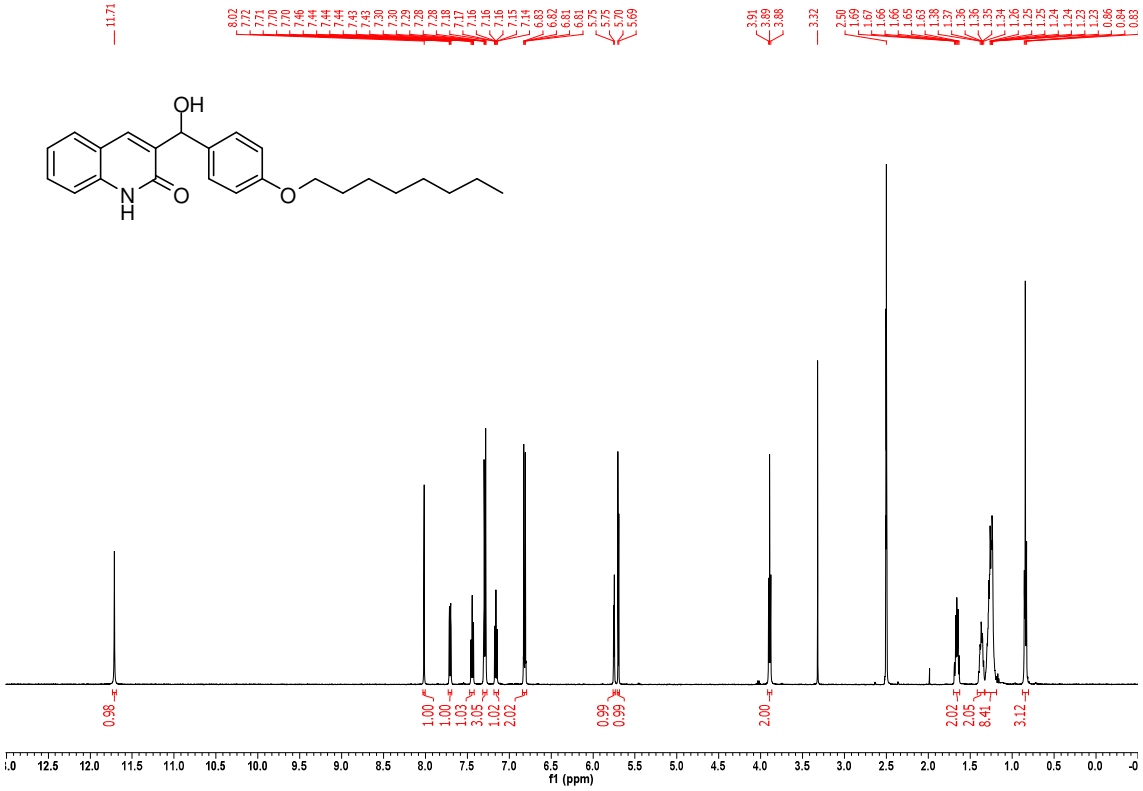
^{1}H NMR (300 K, DMSO-d_6)



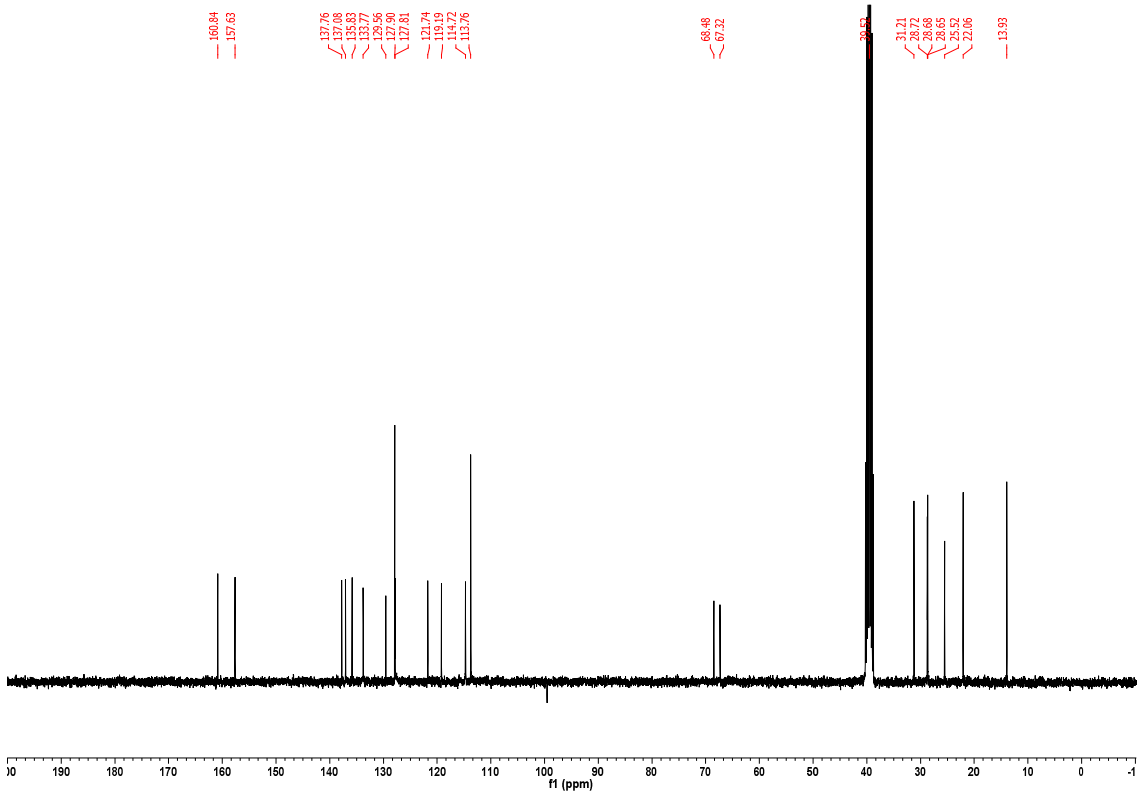
^{13}C NMR (300 K, DMSO-d_6)



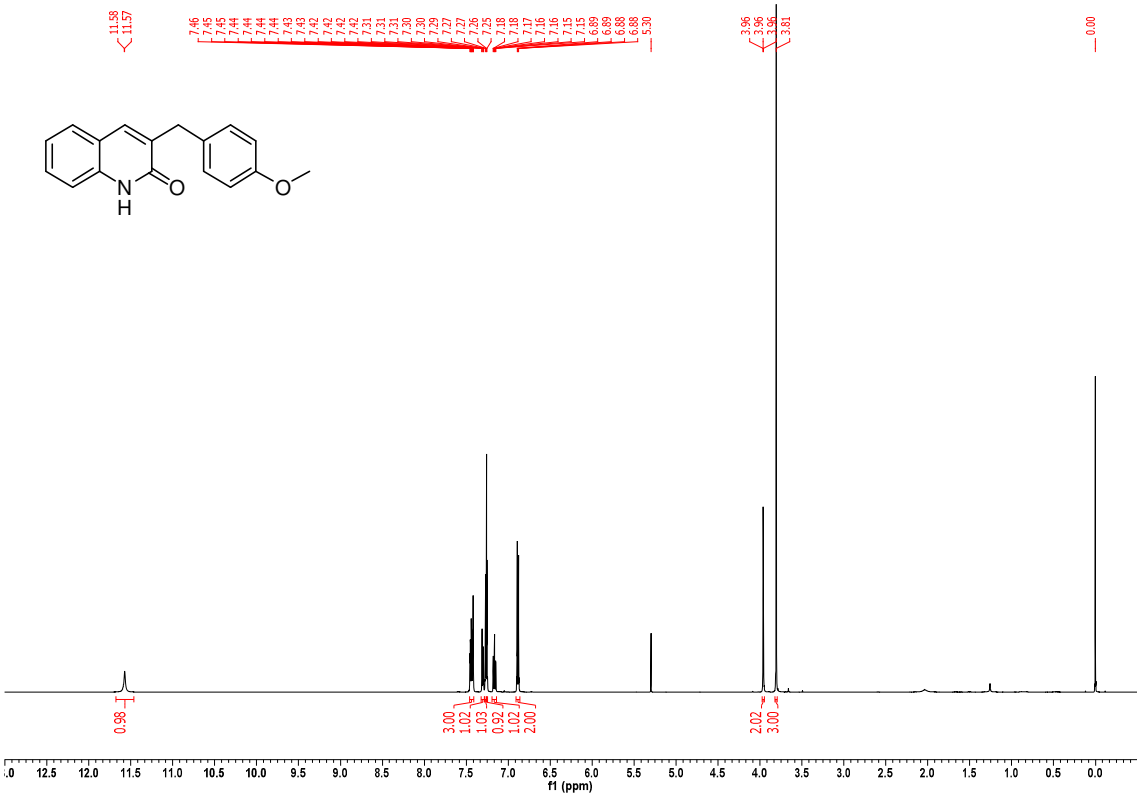
^{1}H NMR (300 K, DMSO-d_6)



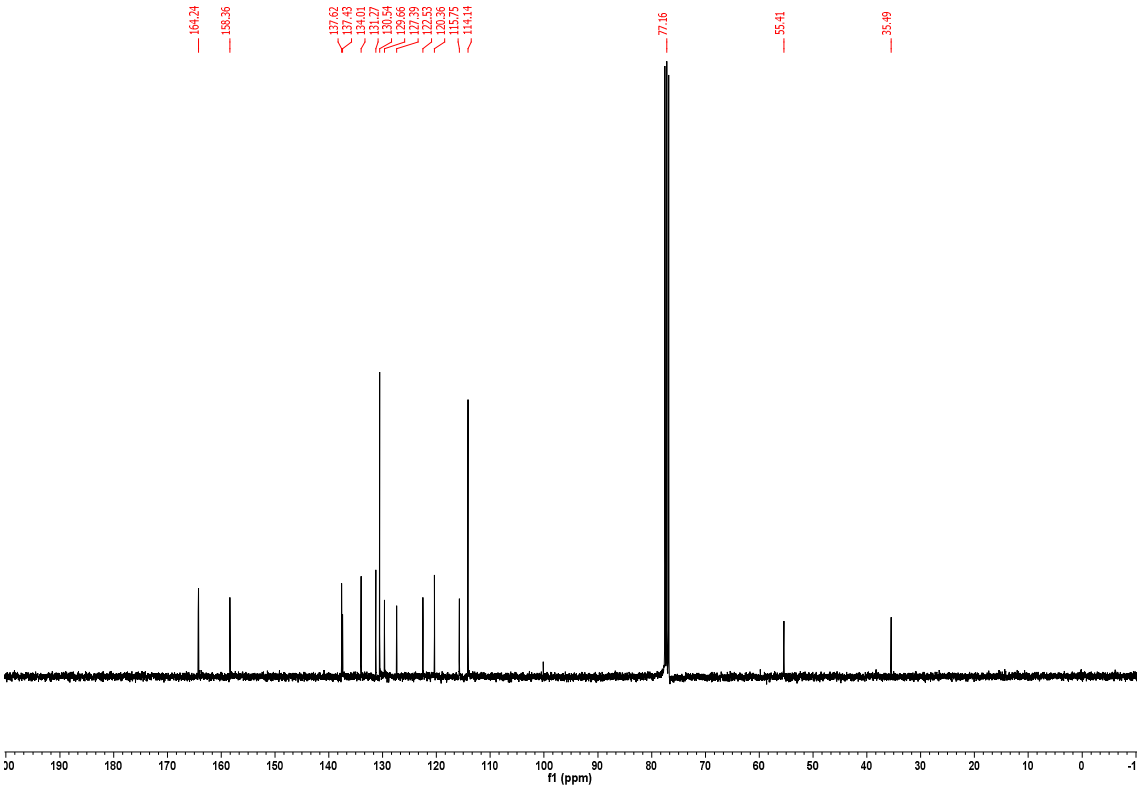
^{1}H NMR (300 K, DMSO-d_6)



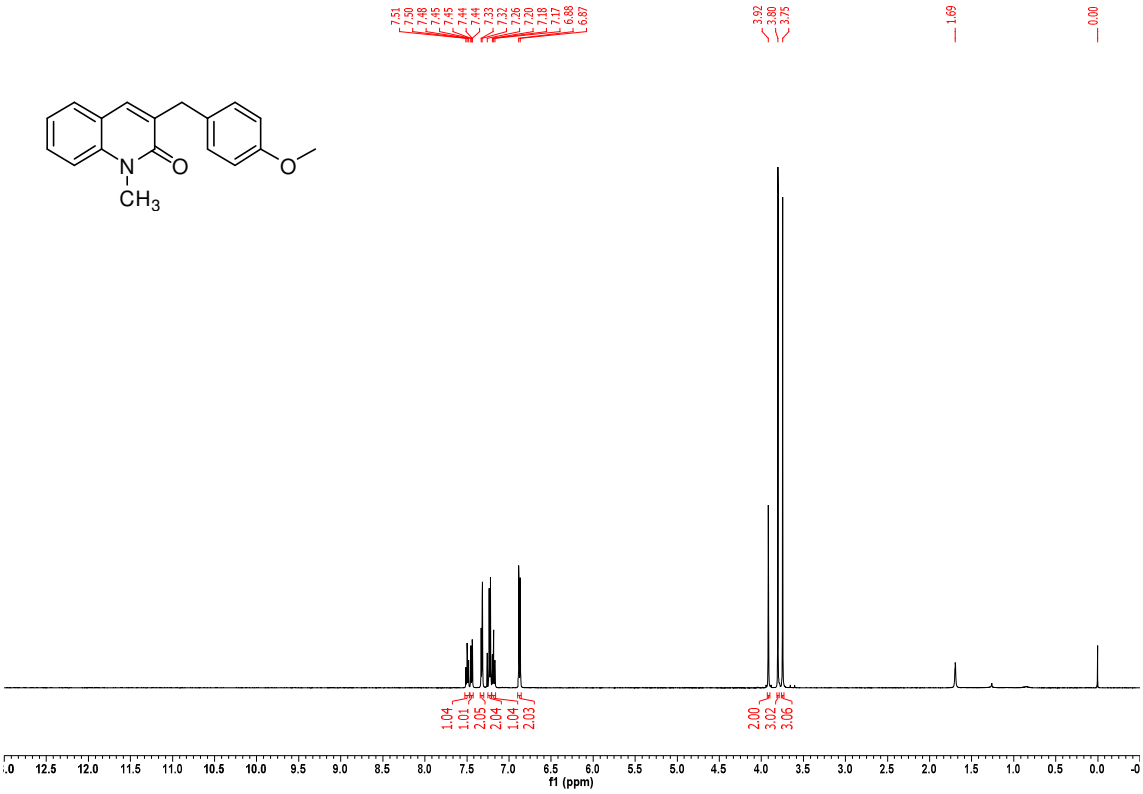
^{1}H NMR (300 K, $CDCl_3$)



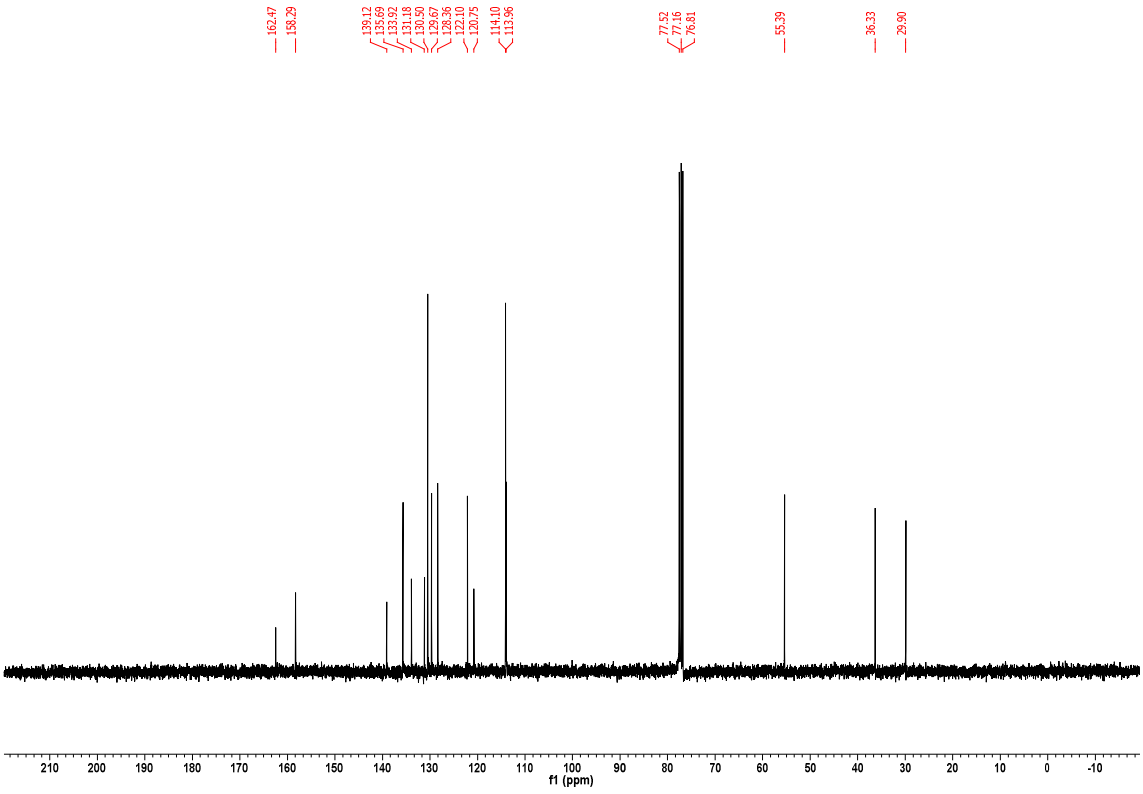
^{13}C NMR (300 K, $CDCl_3$)



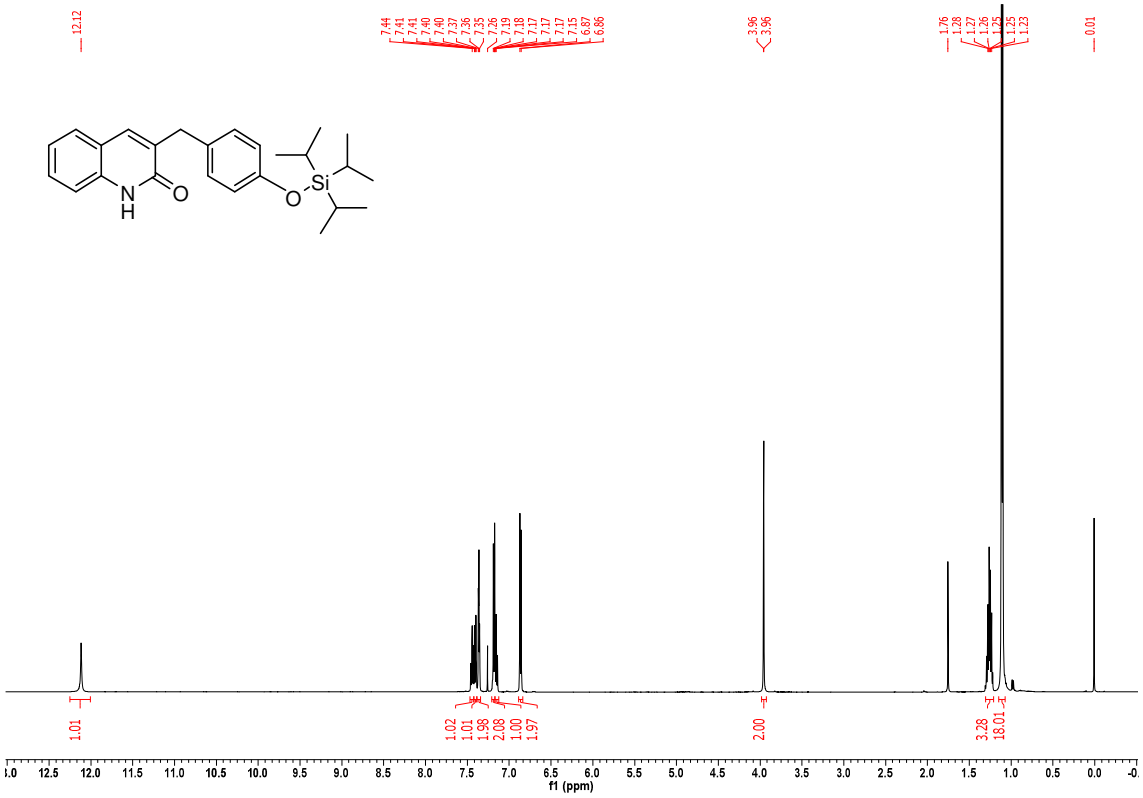
^{1}H NMR (300 K, $CDCl_3$)



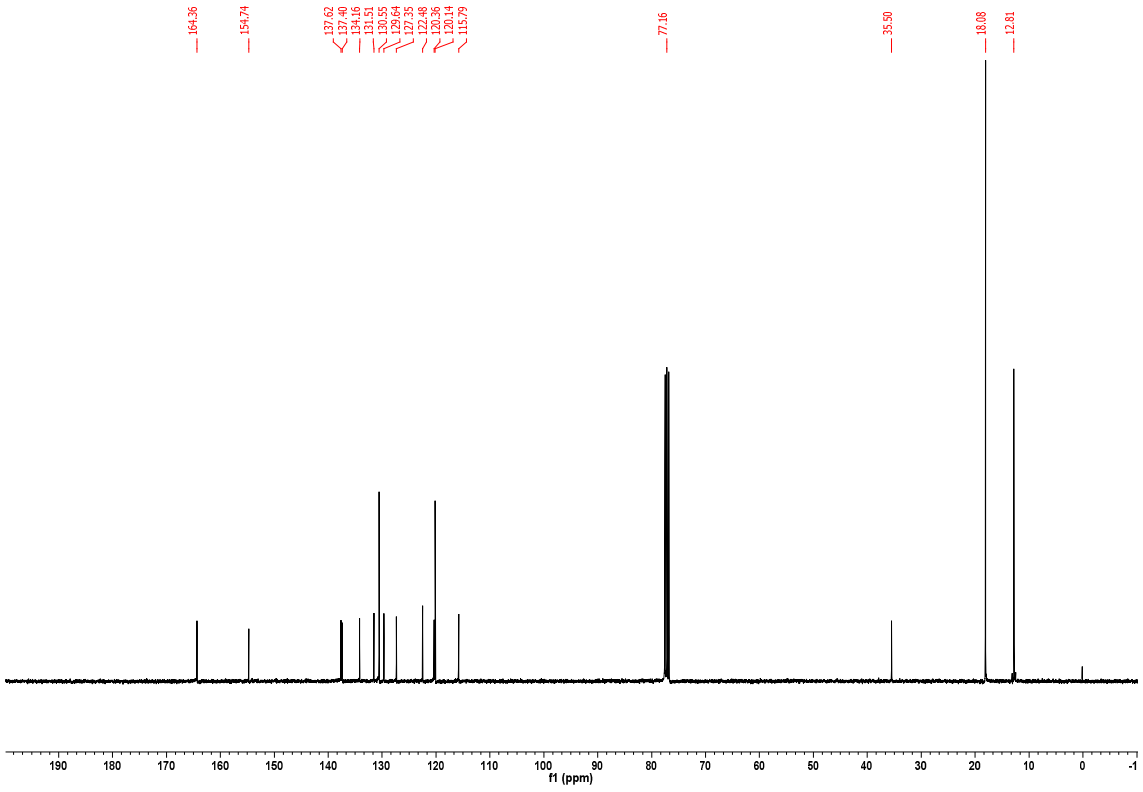
^{13}C NMR (300 K, $CDCl_3$)



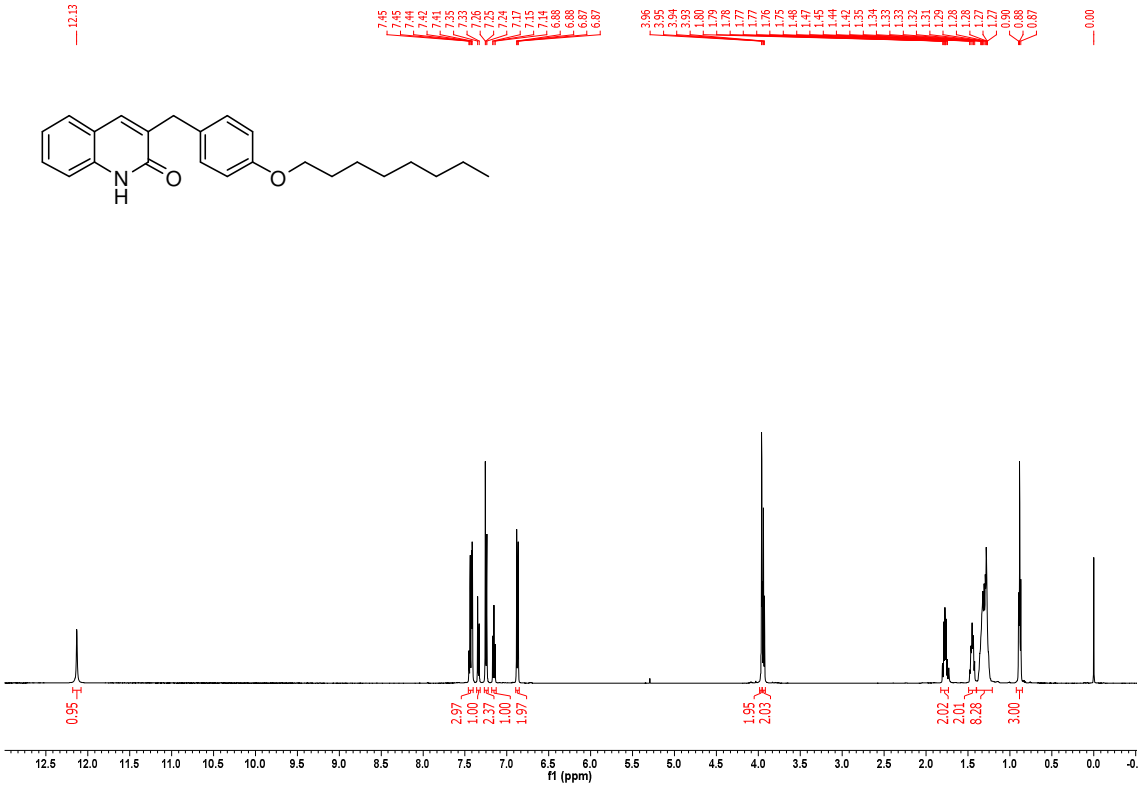
^{1}H NMR (300 K, $CDCl_3$)



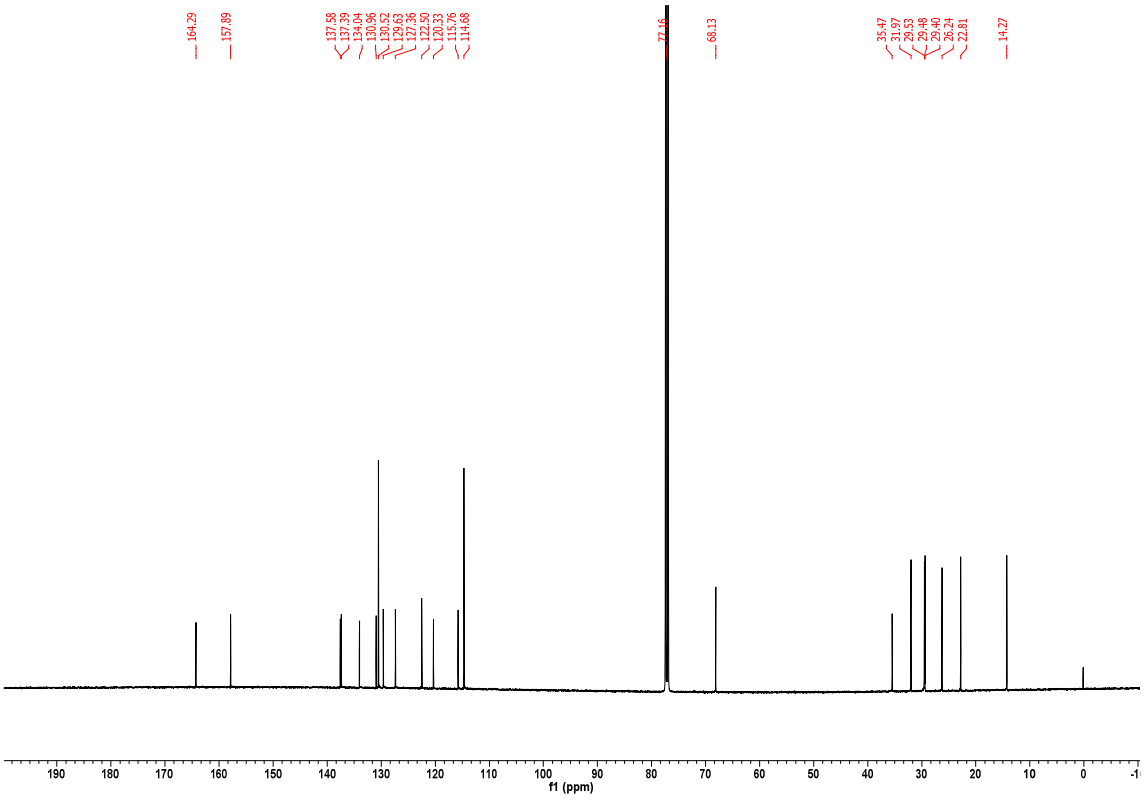
^{13}C NMR (300 K, $CDCl_3$)



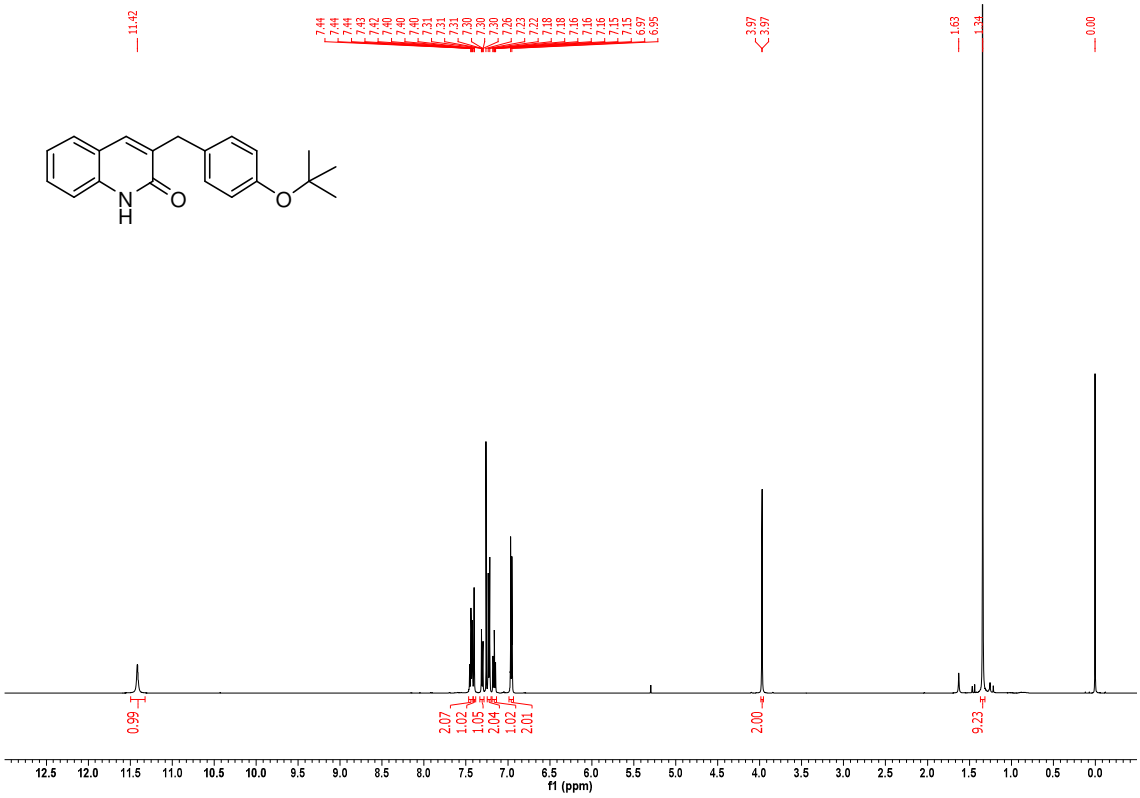
^{1}H NMR (300 K, $CDCl_3$)



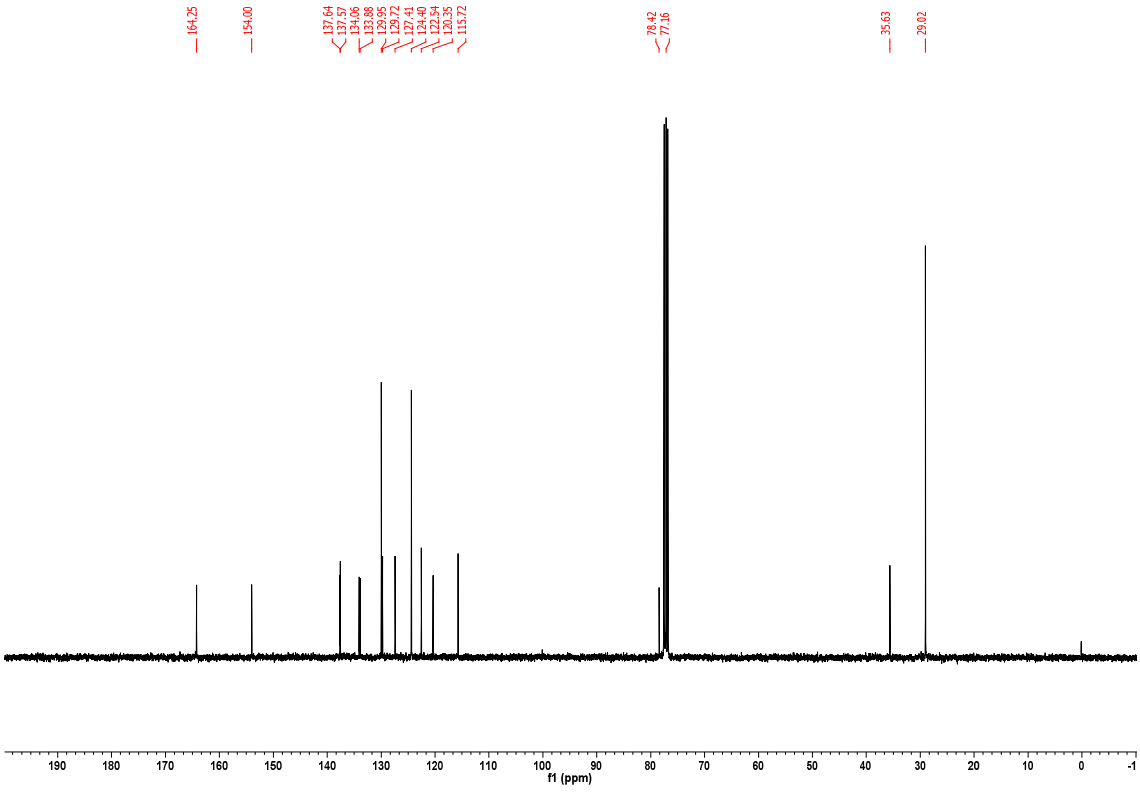
^{13}C NMR (300 K, $CDCl_3$)



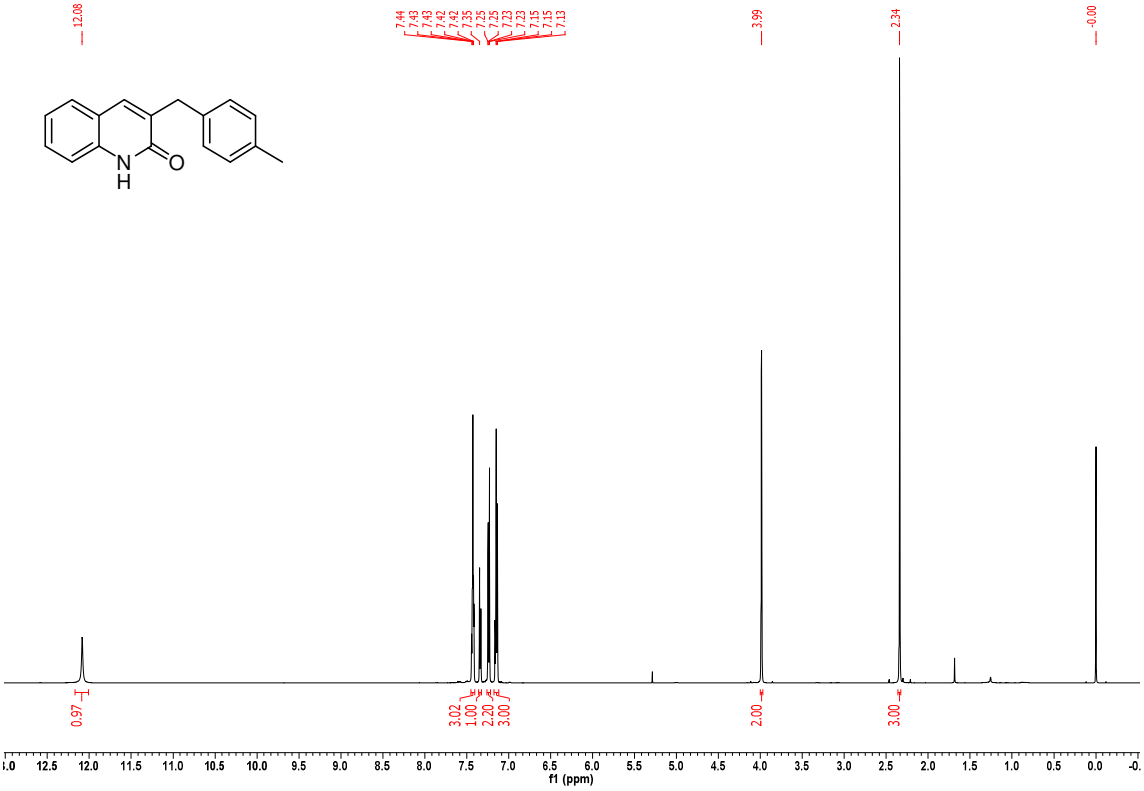
^{1}H NMR (300 K, $CDCl_3$)



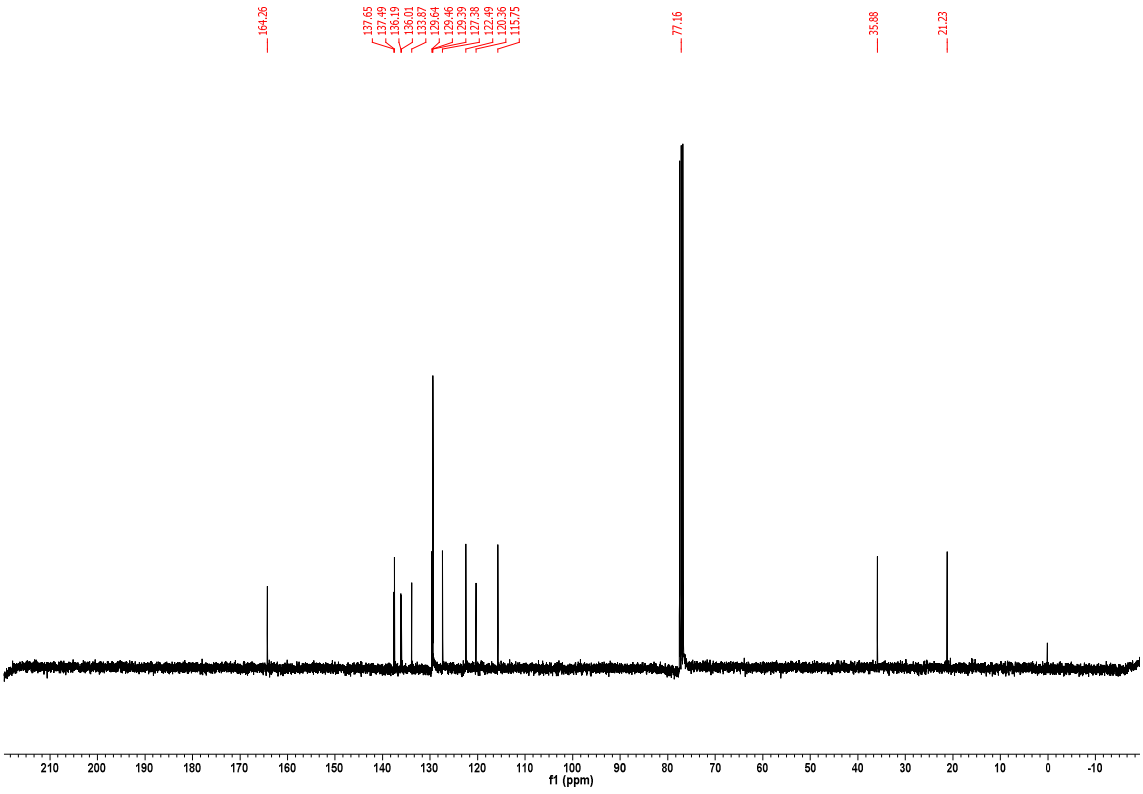
^{13}C NMR (300 K, $CDCl_3$)



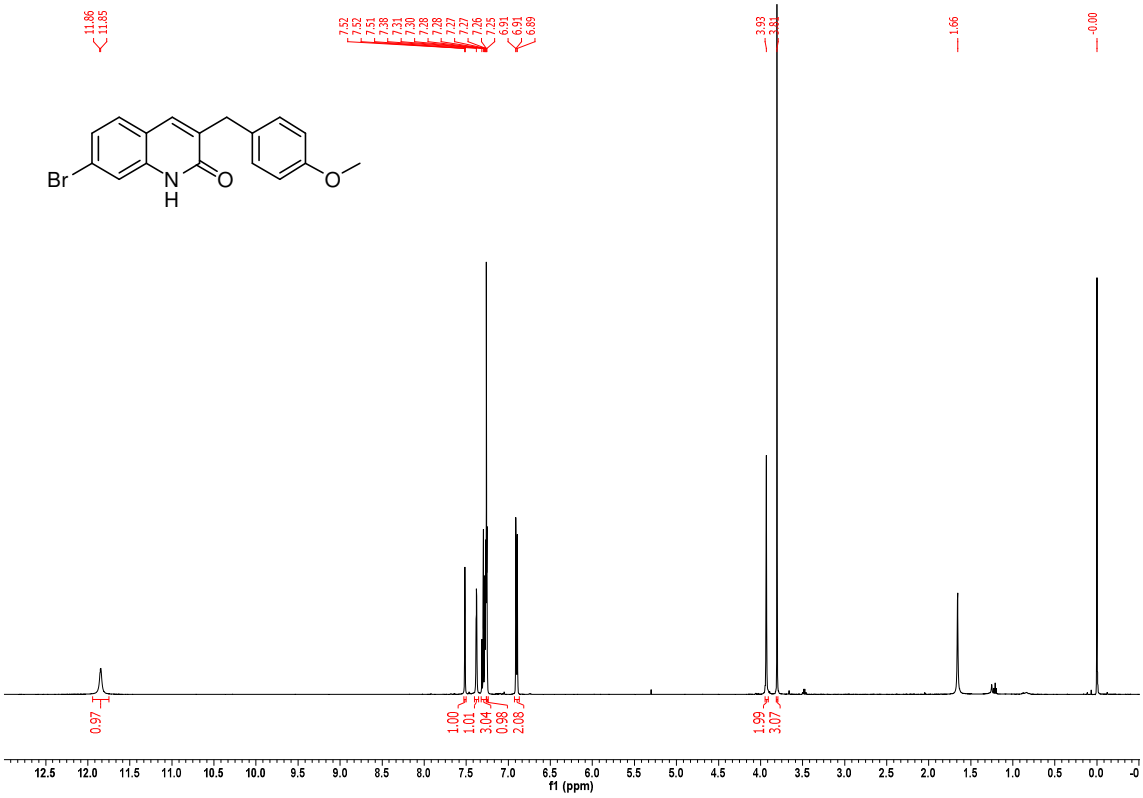
^{1}H NMR (300 K, $CDCl_3$)



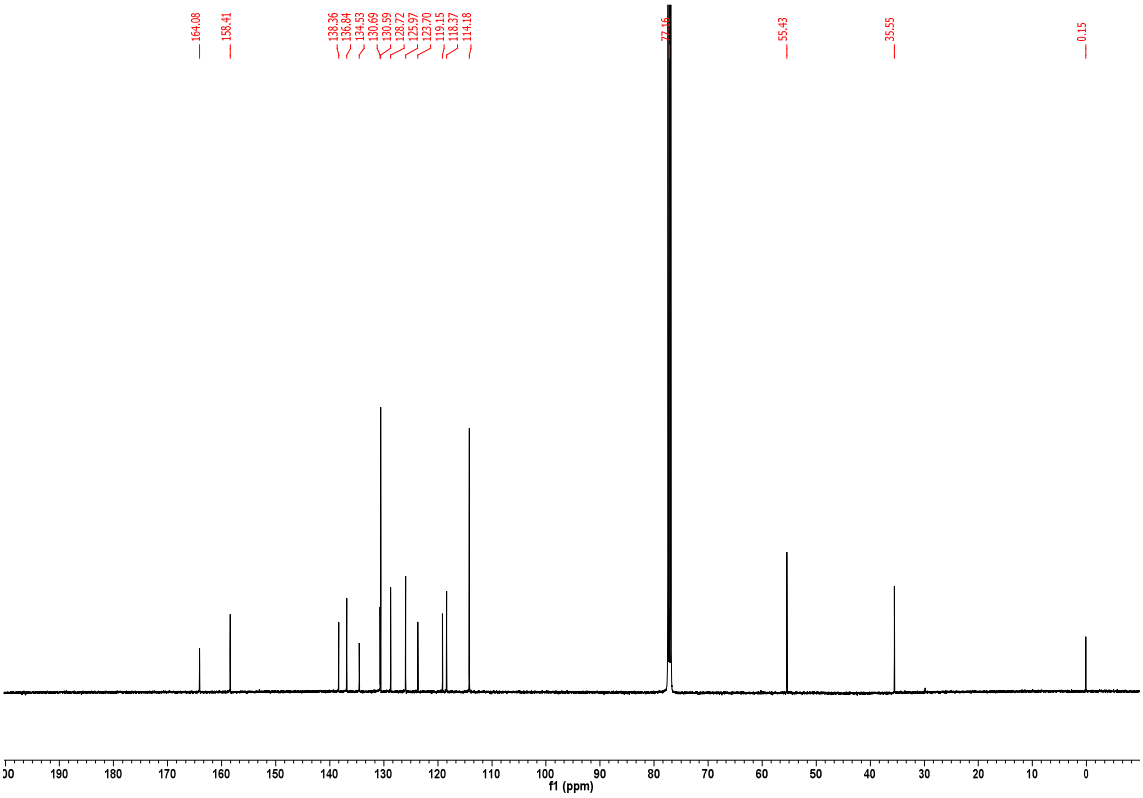
^{13}C NMR (300 K, $CDCl_3$)



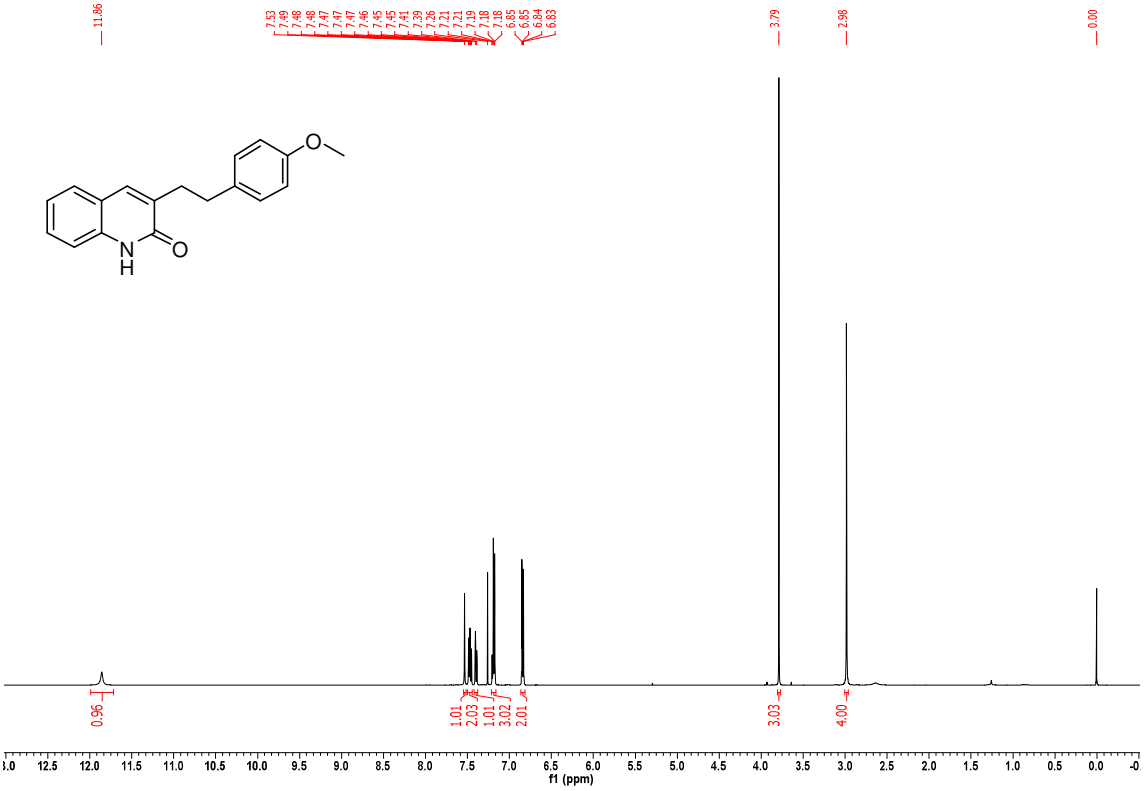
^{1}H NMR (300 K, $CDCl_3$)



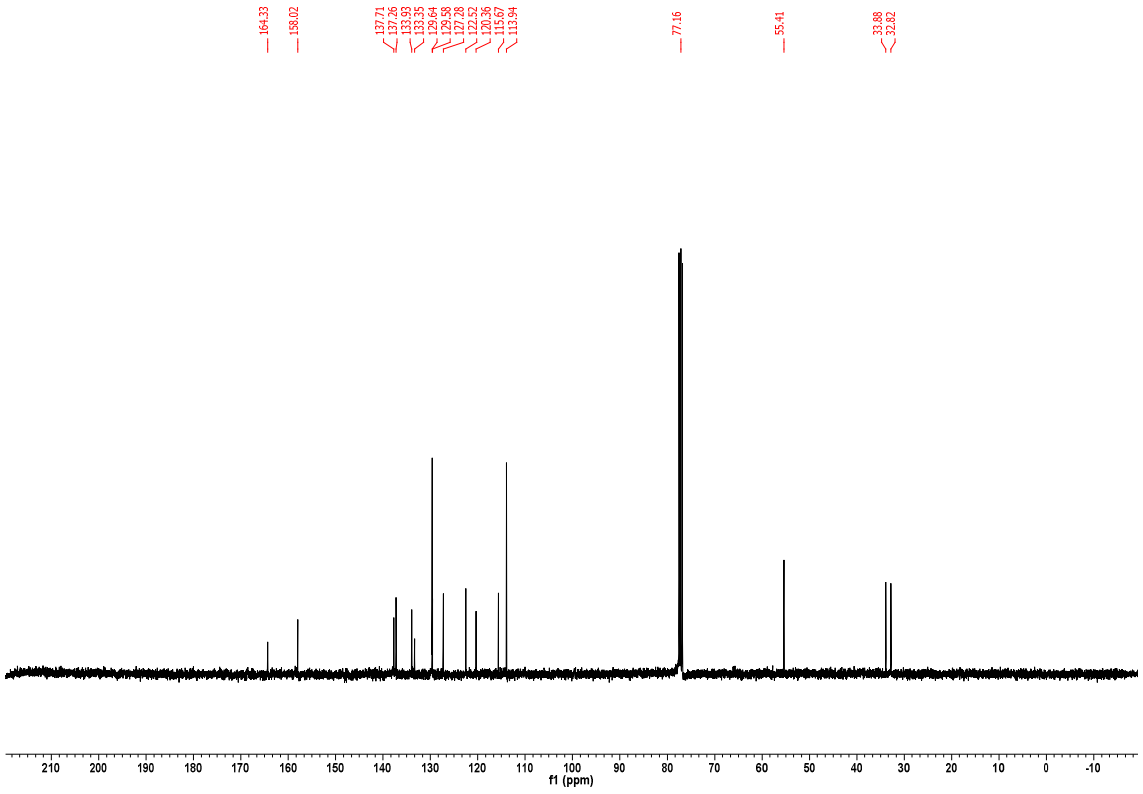
^{13}C NMR (300 K, $CDCl_3$)



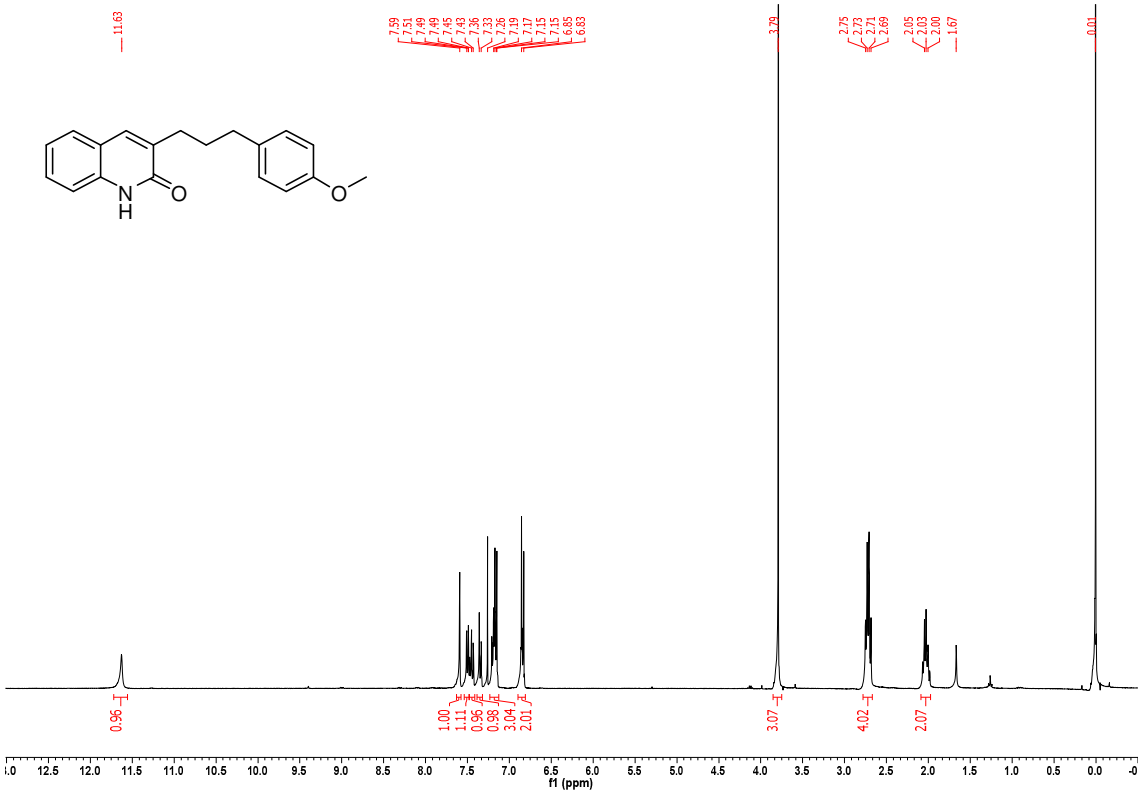
^{1}H NMR (300 K, $CDCl_3$)



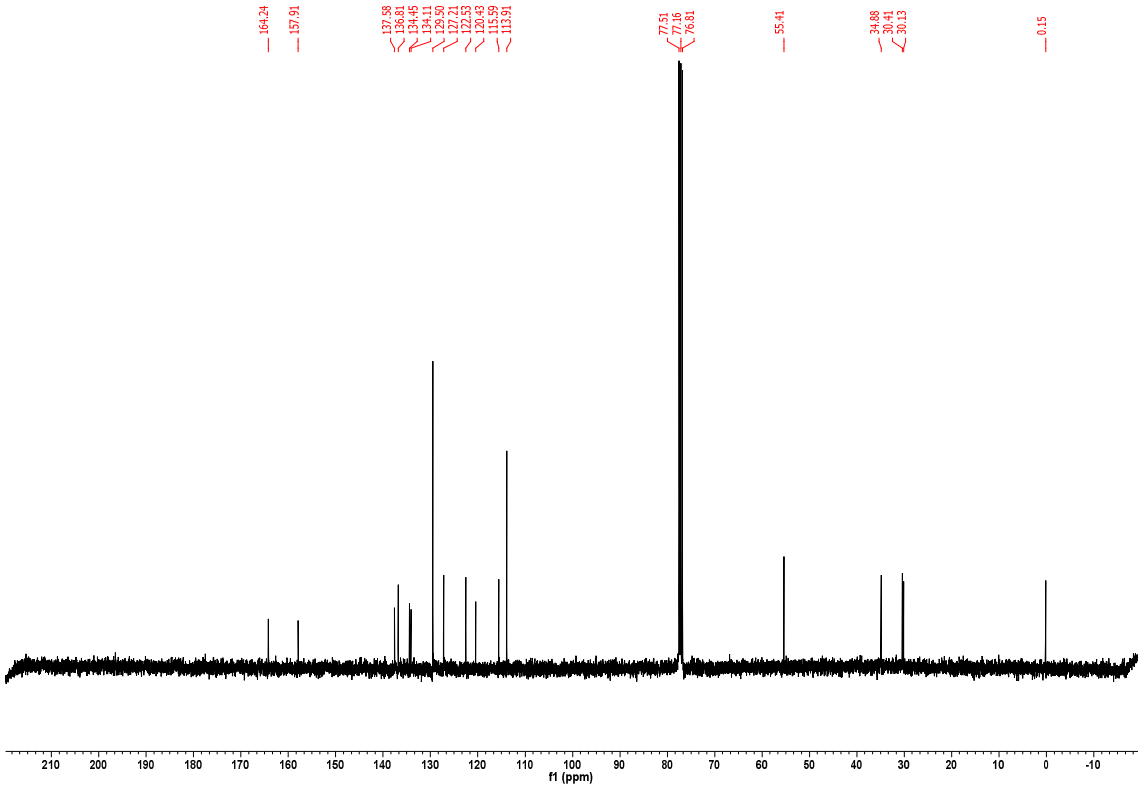
^{13}C NMR (300 K, $CDCl_3$)



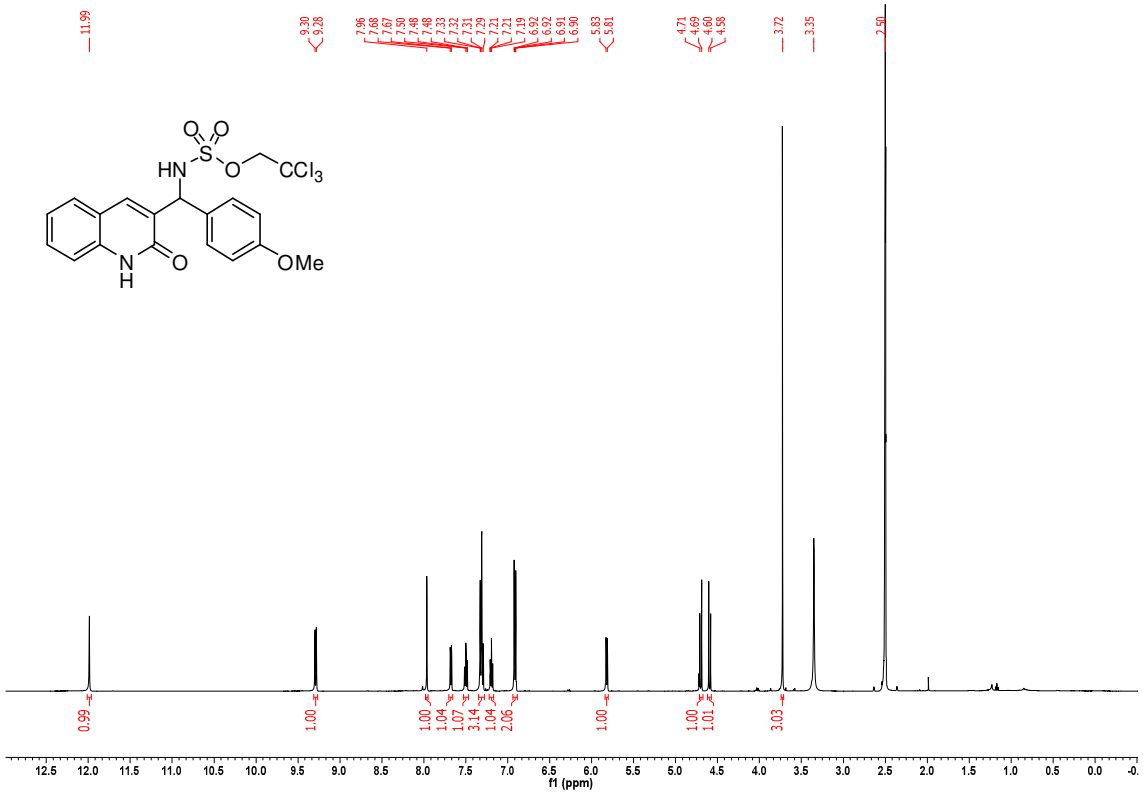
^{1}H NMR (300 K, $CDCl_3$)



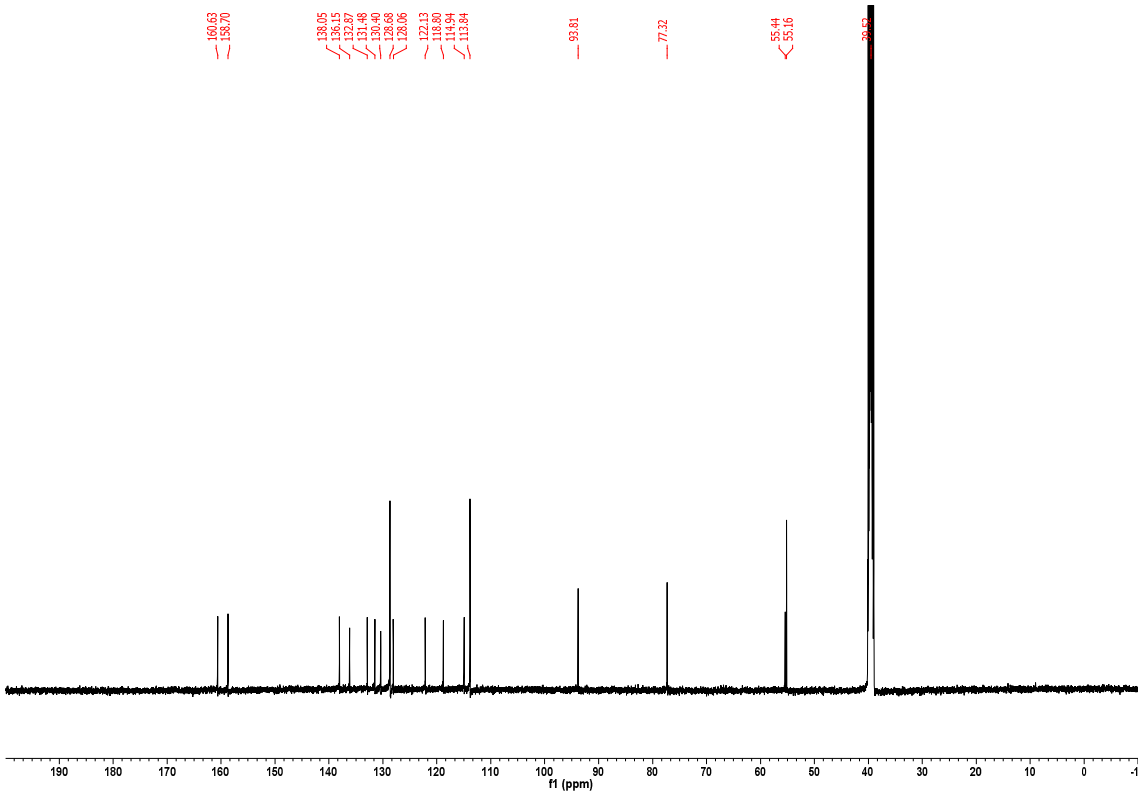
^{13}C NMR (300 K, $CDCl_3$)



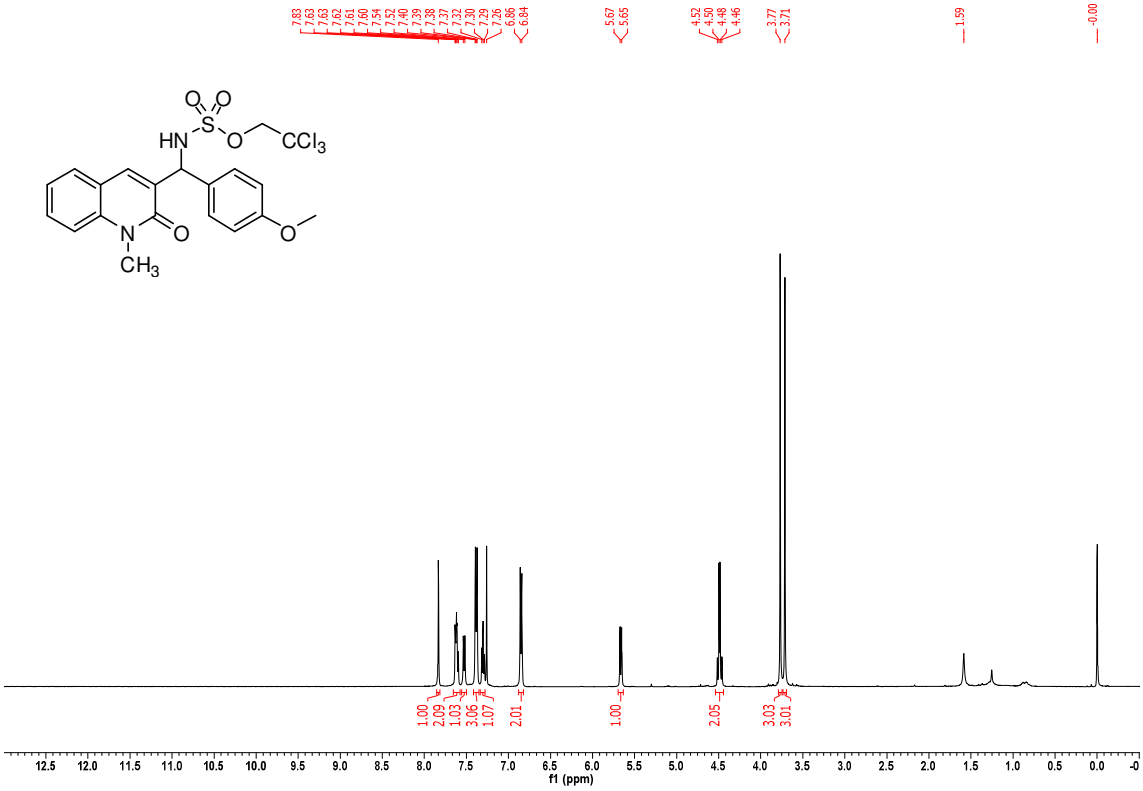
^{1}H NMR (300 K, DMSO-d_6)



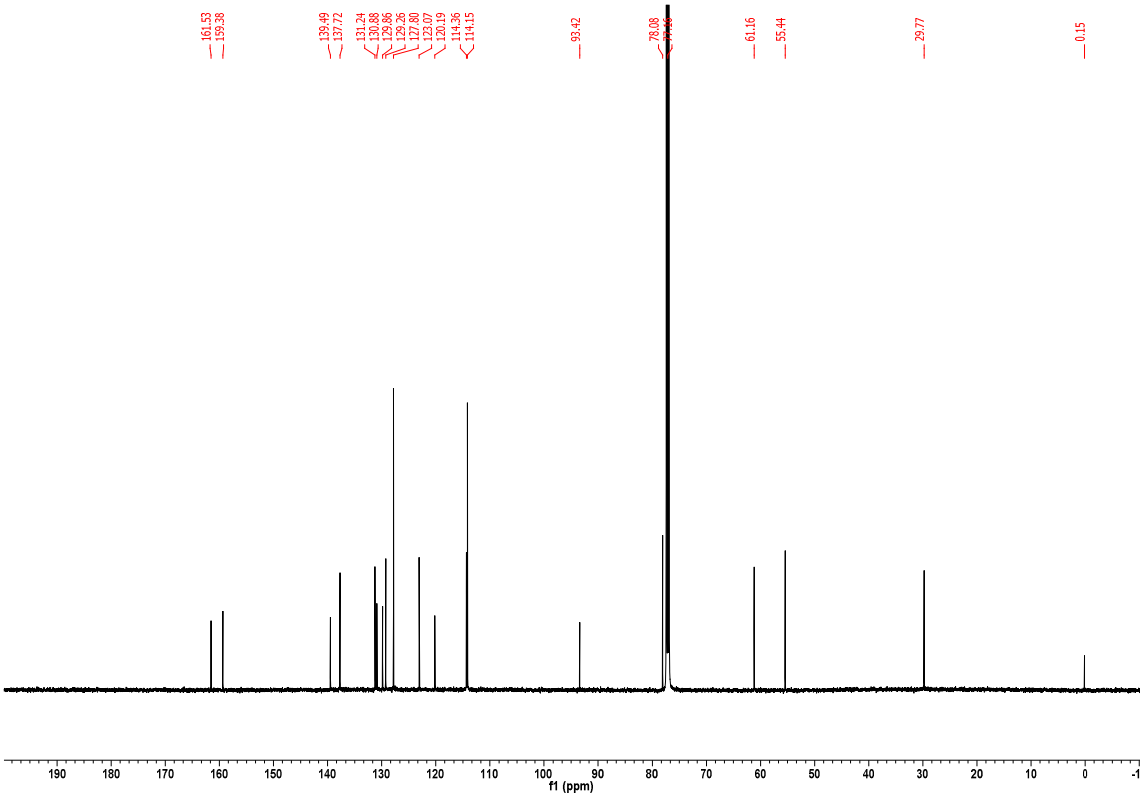
^{13}C NMR (300 K, DMSO-d_6)



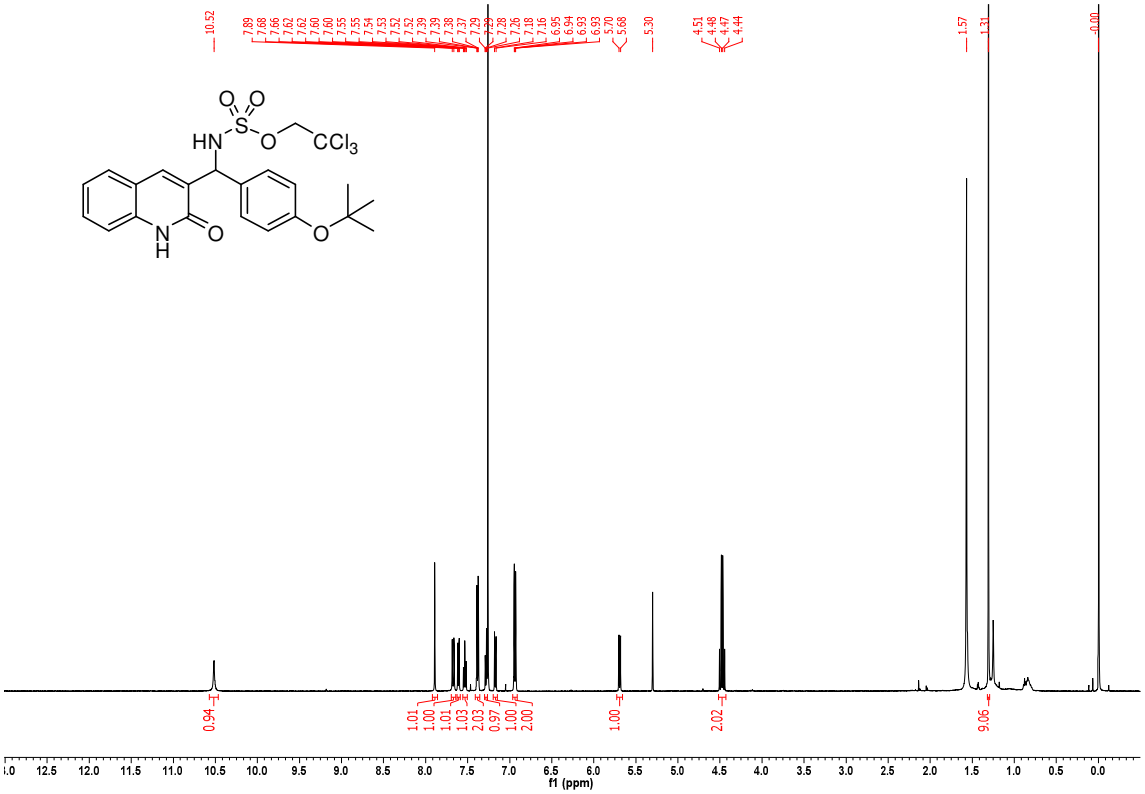
^{1}H NMR (300 K, $CDCl_3$)



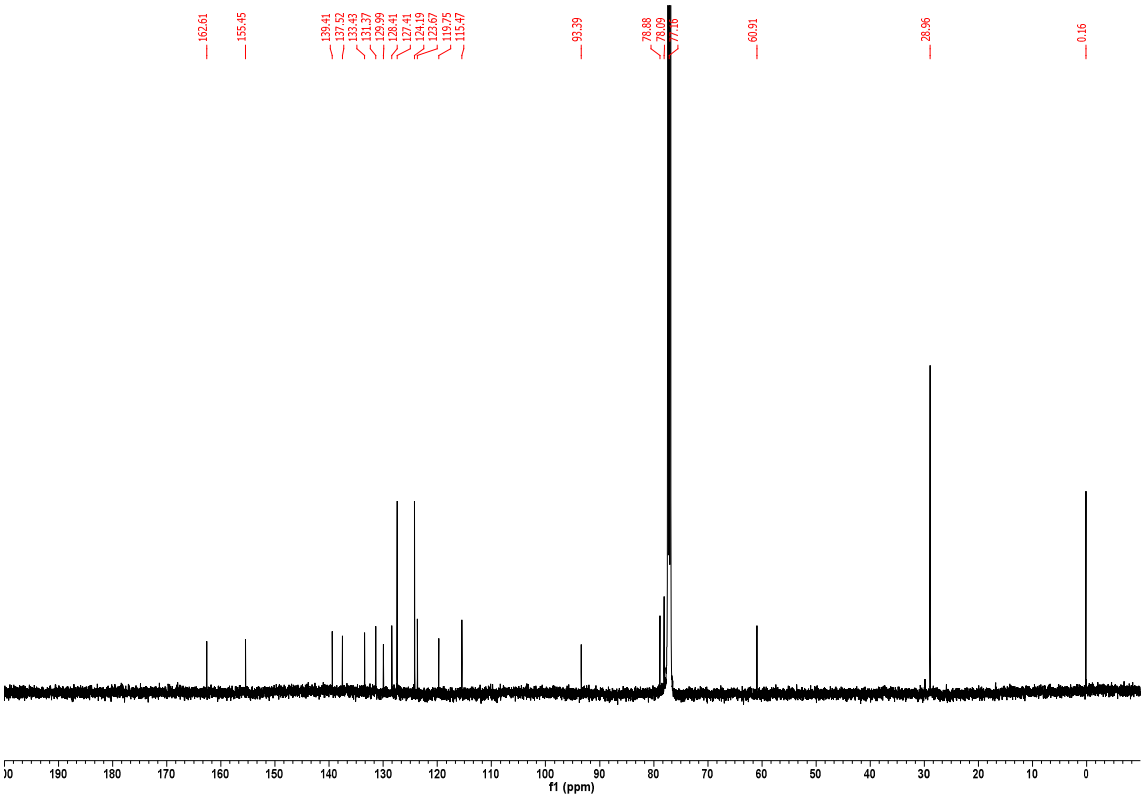
^{13}C NMR (300 K, $CDCl_3$)



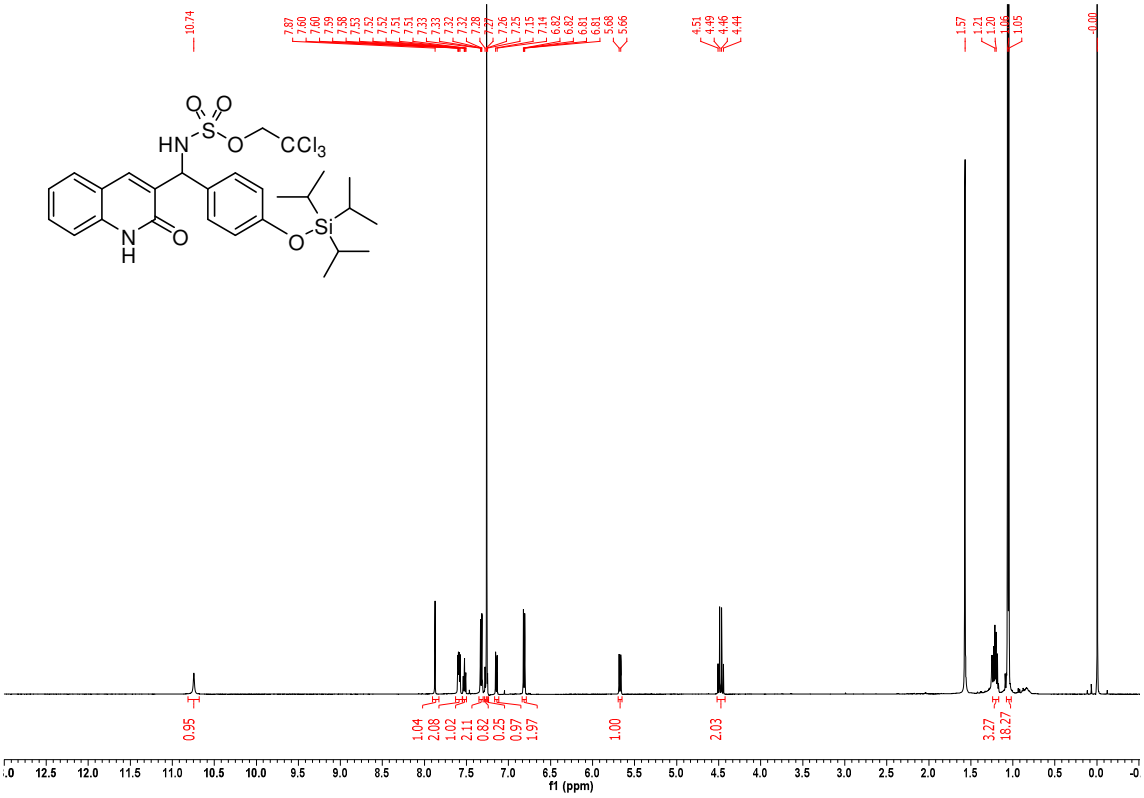
^{1}H NMR (300 K, $CDCl_3$)



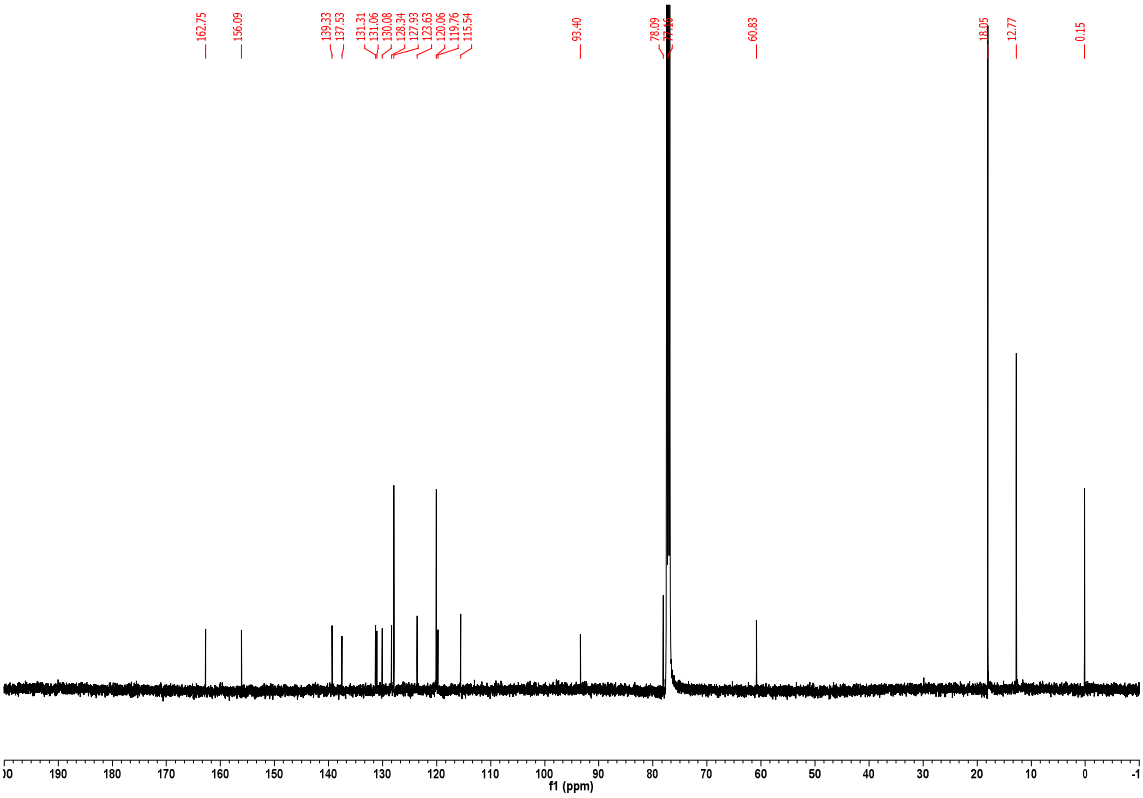
^{13}C NMR (300 K, $CDCl_3$)



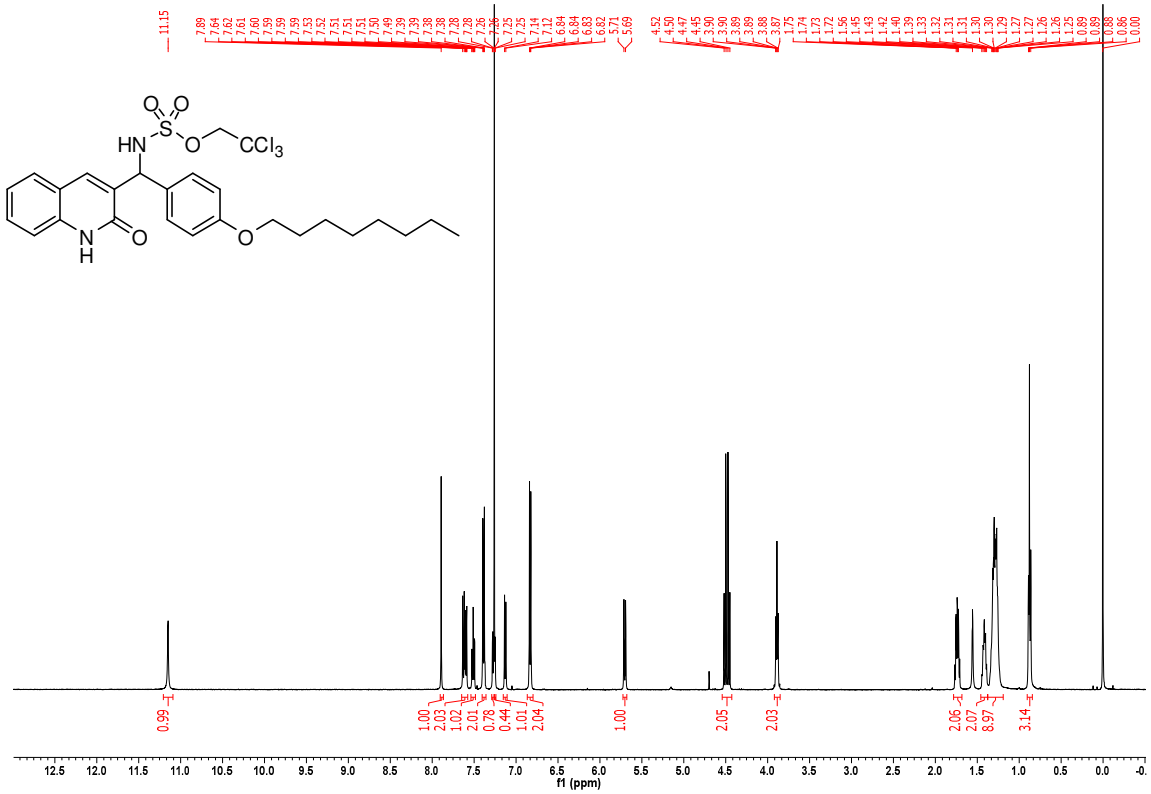
^{1}H NMR (300 K, $CDCl_3$)



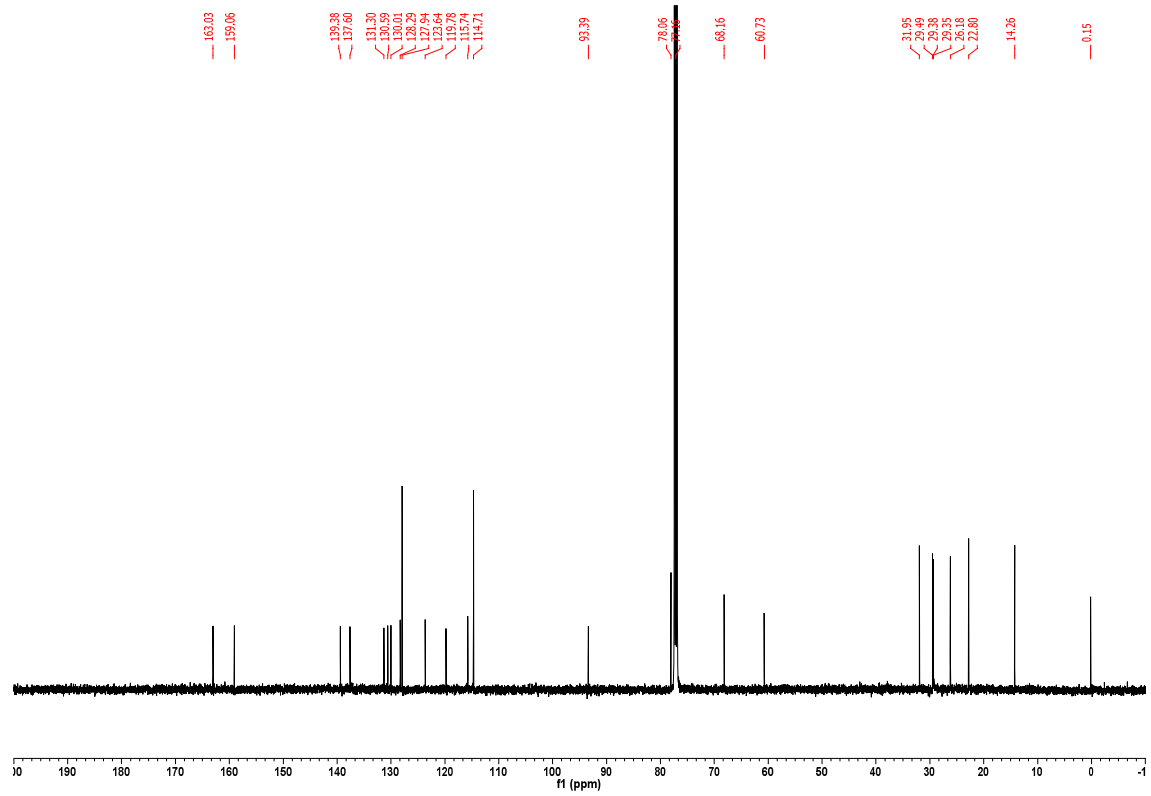
^{13}C NMR (300 K, $CDCl_3$)



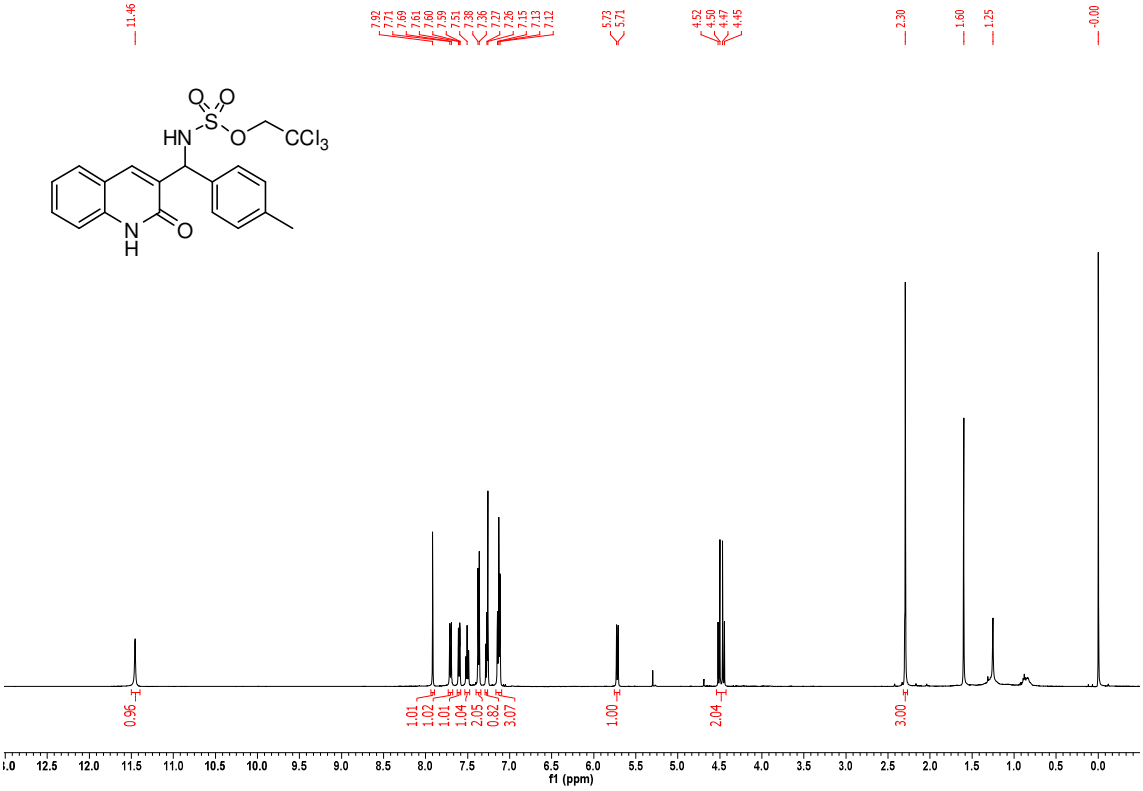
^{1}H NMR (300 K, $CDCl_3$)



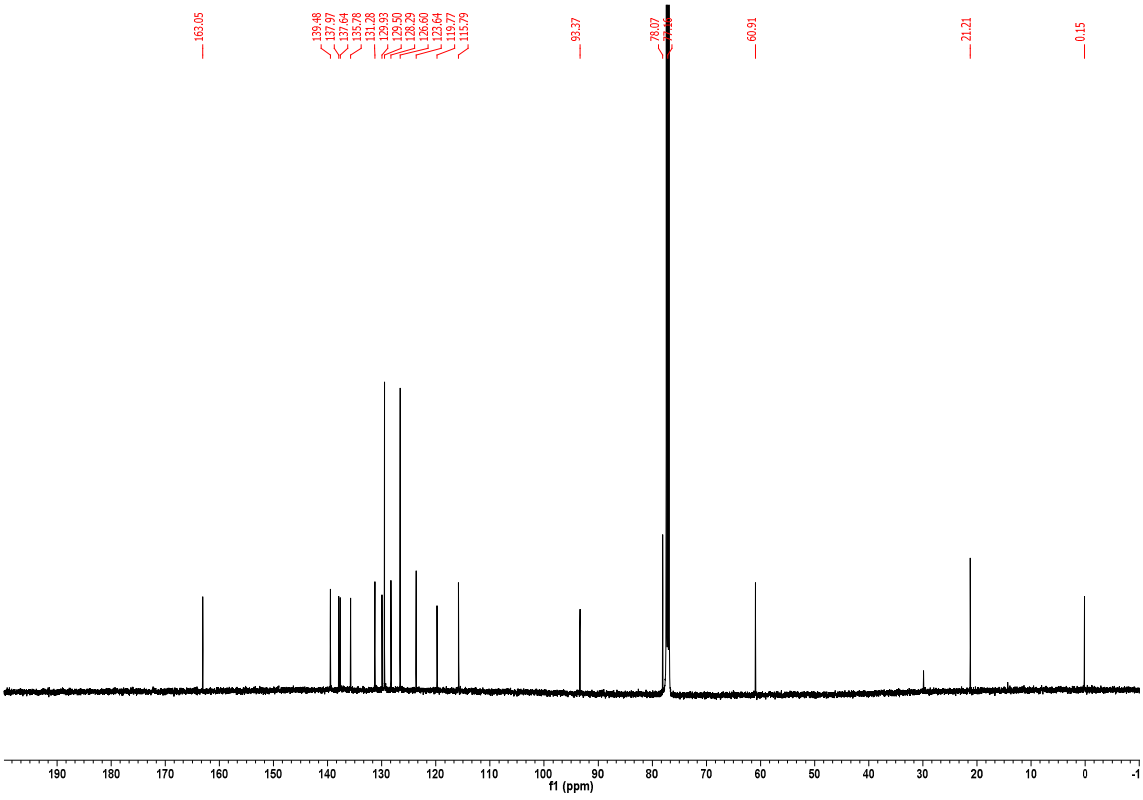
^{13}C NMR (300 K, $CDCl_3$)



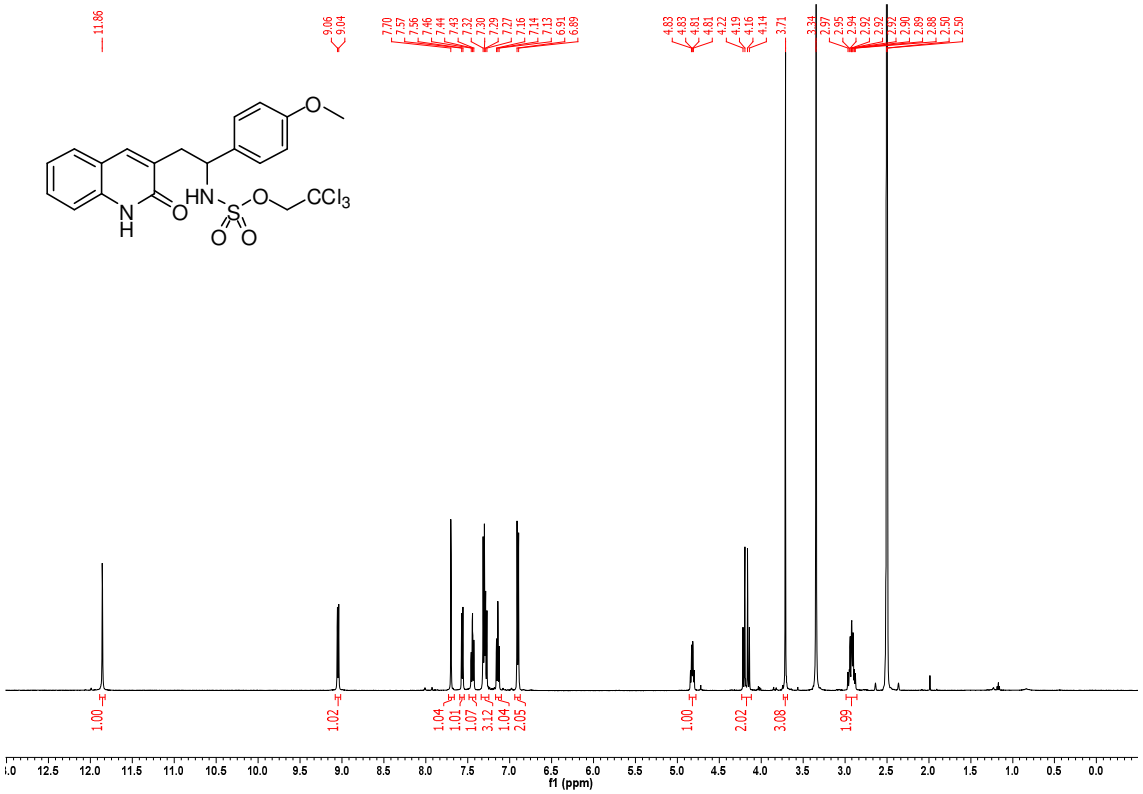
^{1}H NMR (300 K, $CDCl_3$)



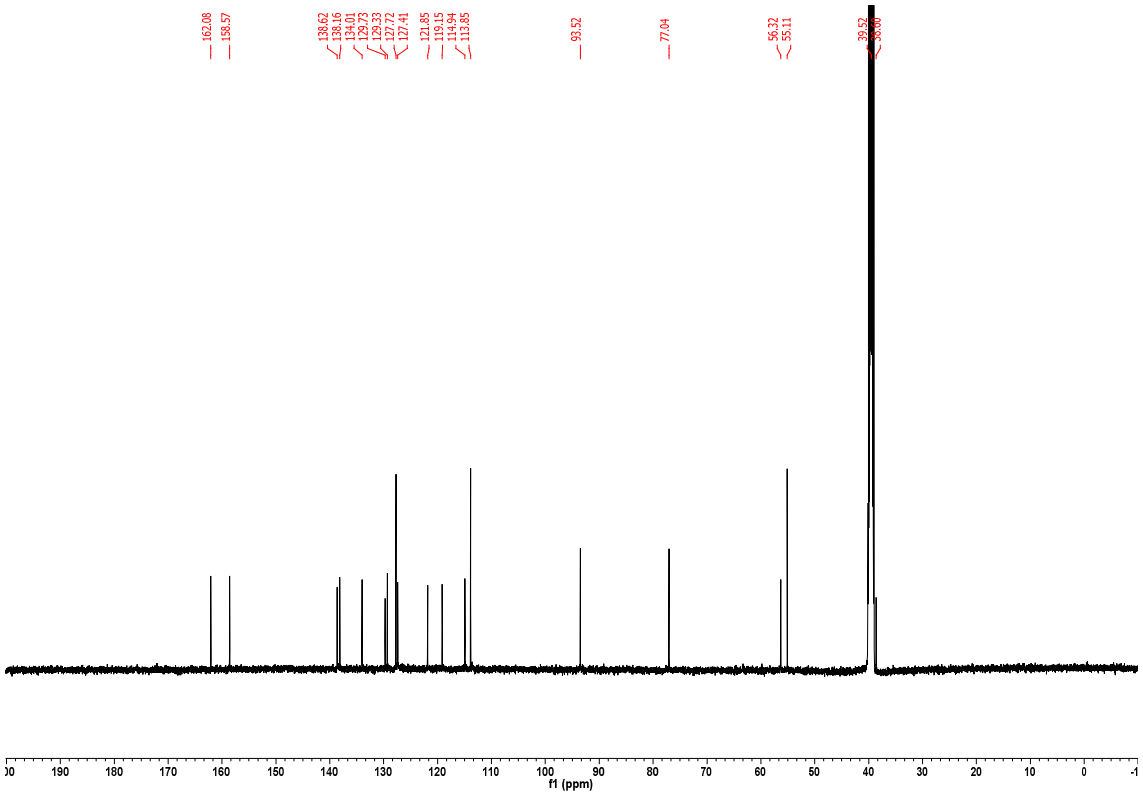
^{13}C NMR (300 K, $CDCl_3$)



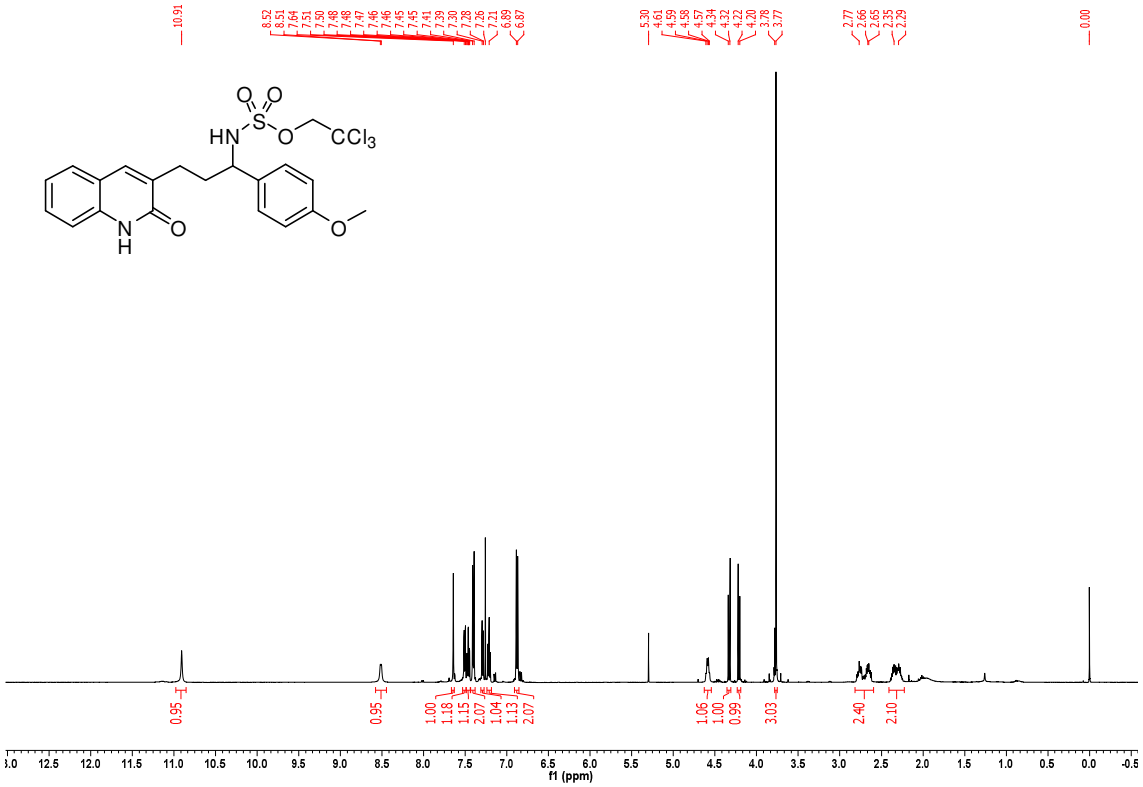
^{1}H NMR (300 K, DMSO-d$_6$)



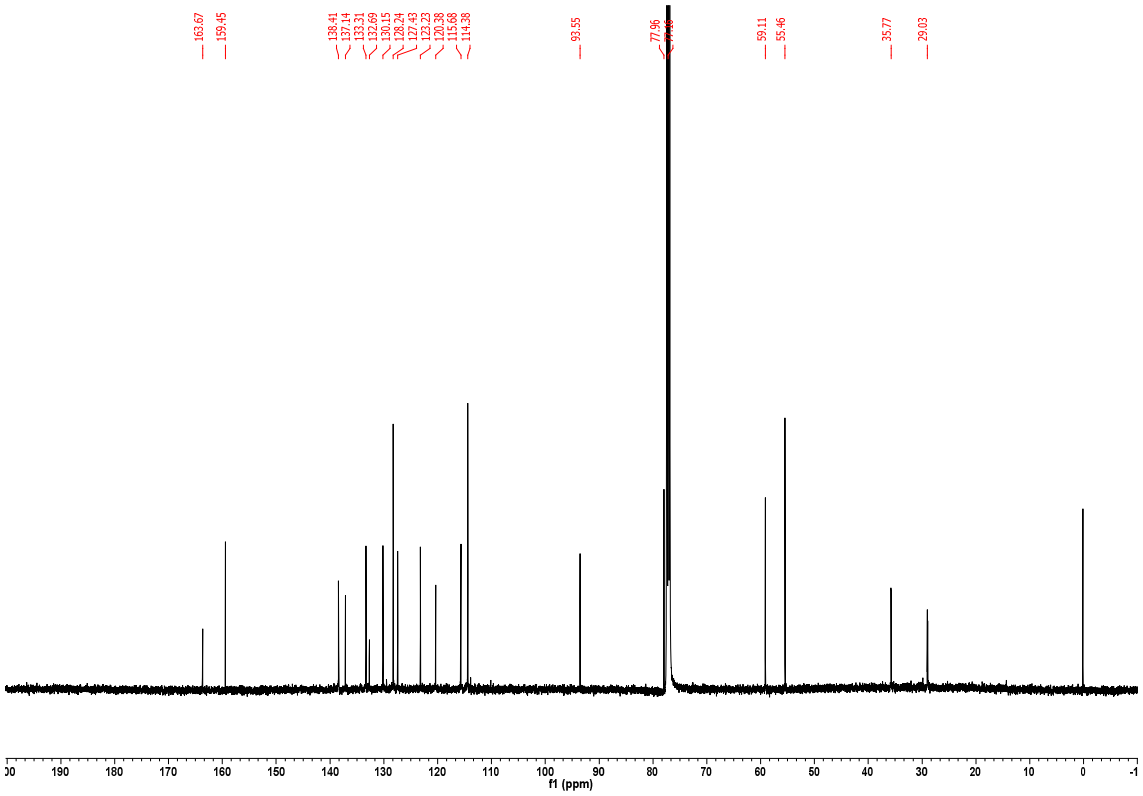
^{13}C NMR (300 K, DMSO-d$_6$)



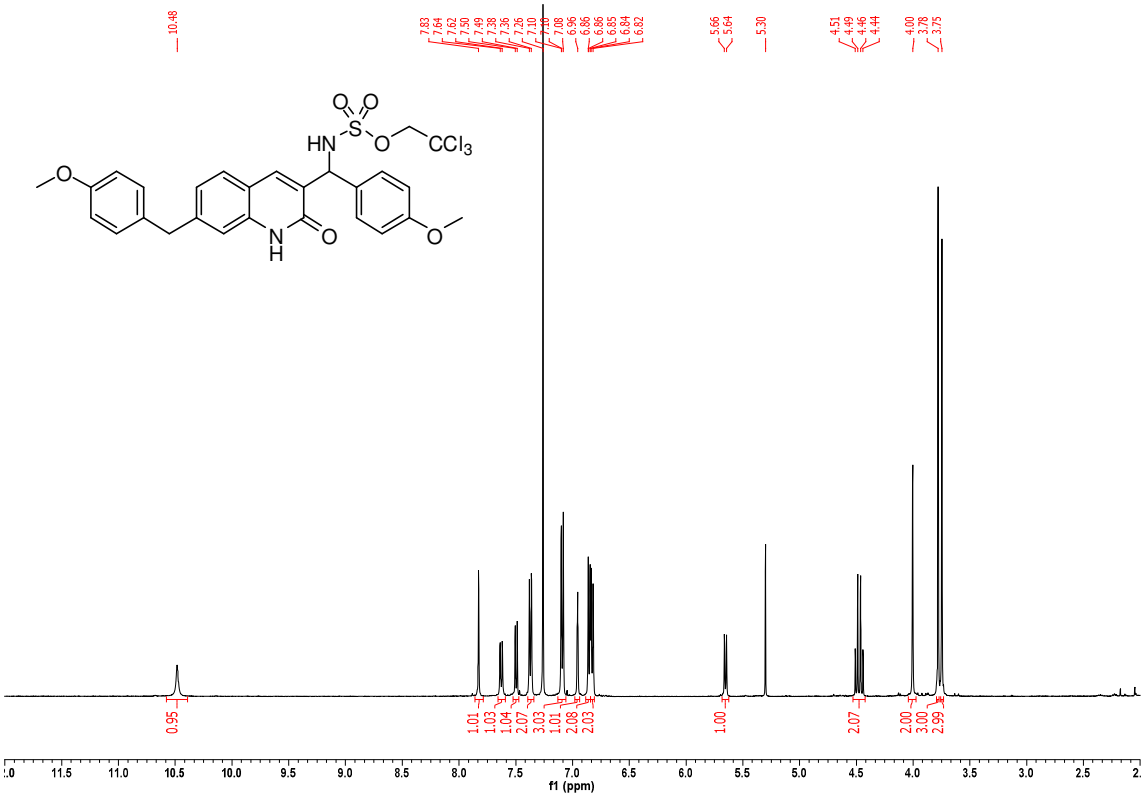
^{1}H NMR (300 K, $CDCl_3$)



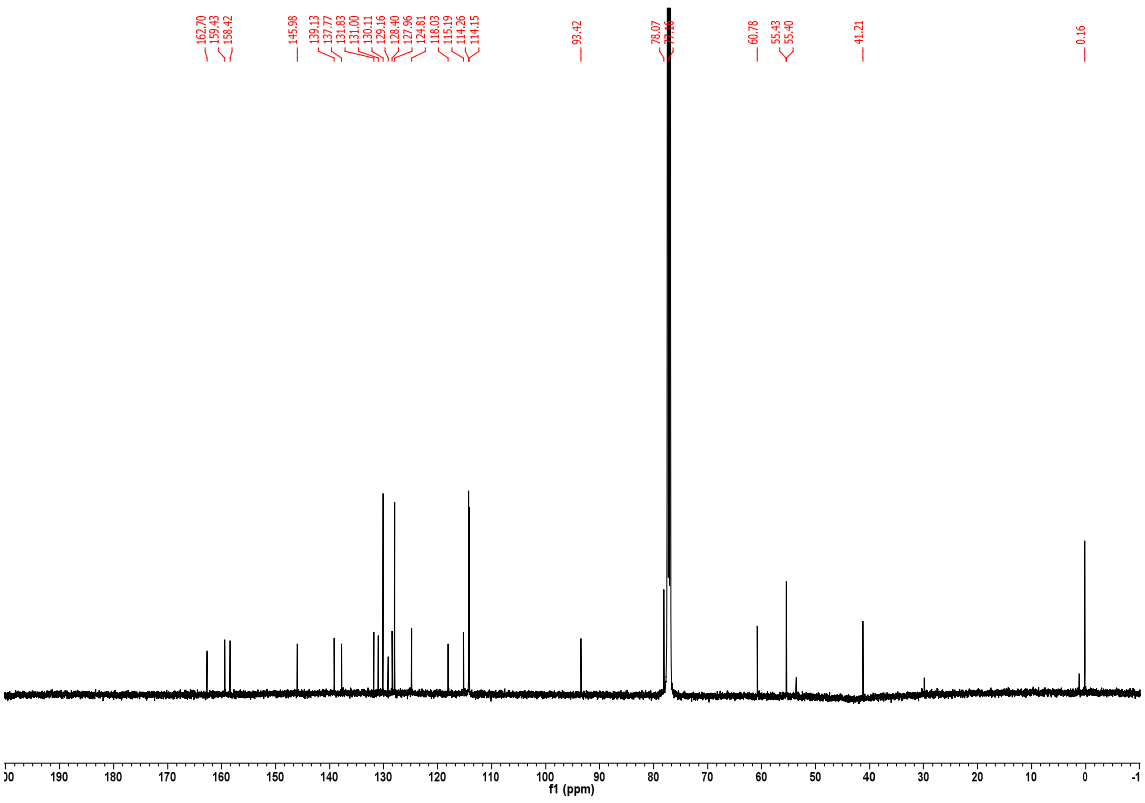
^{13}C NMR (300 K, $CDCl_3$)



^{1}H NMR (300 K, $CDCl_3$)

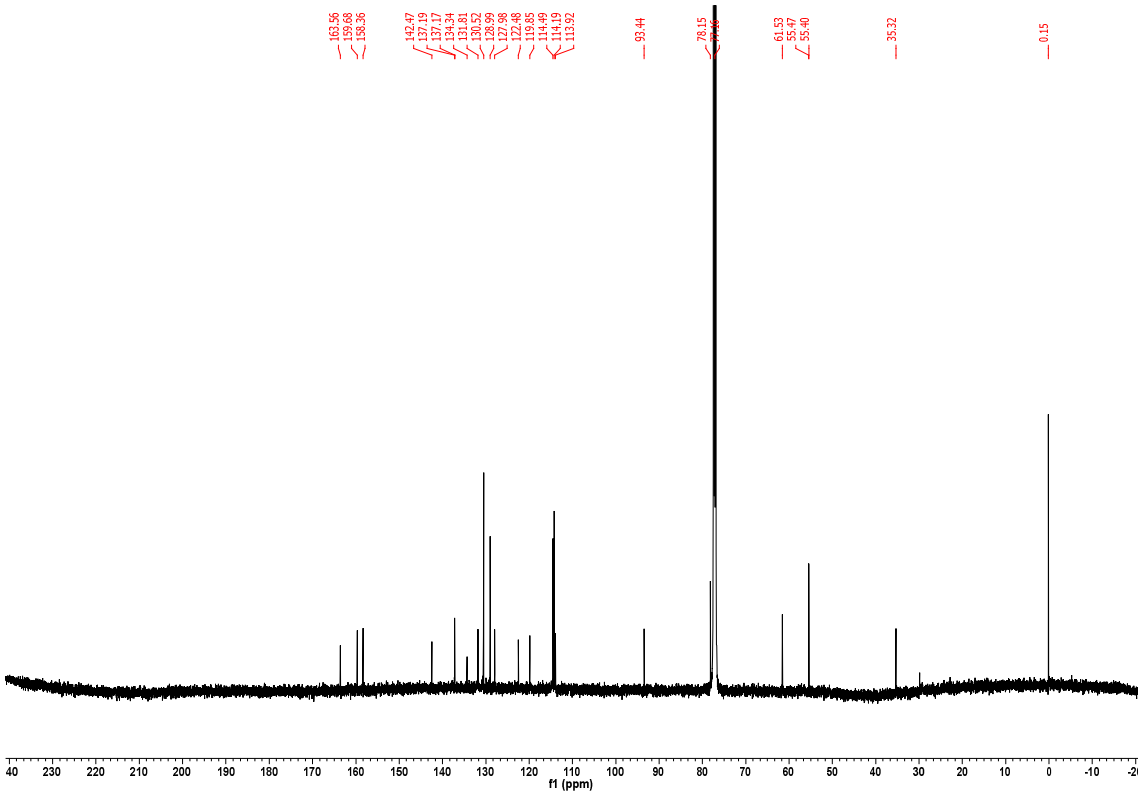


^{13}C NMR (300 K, $CDCl_3$)

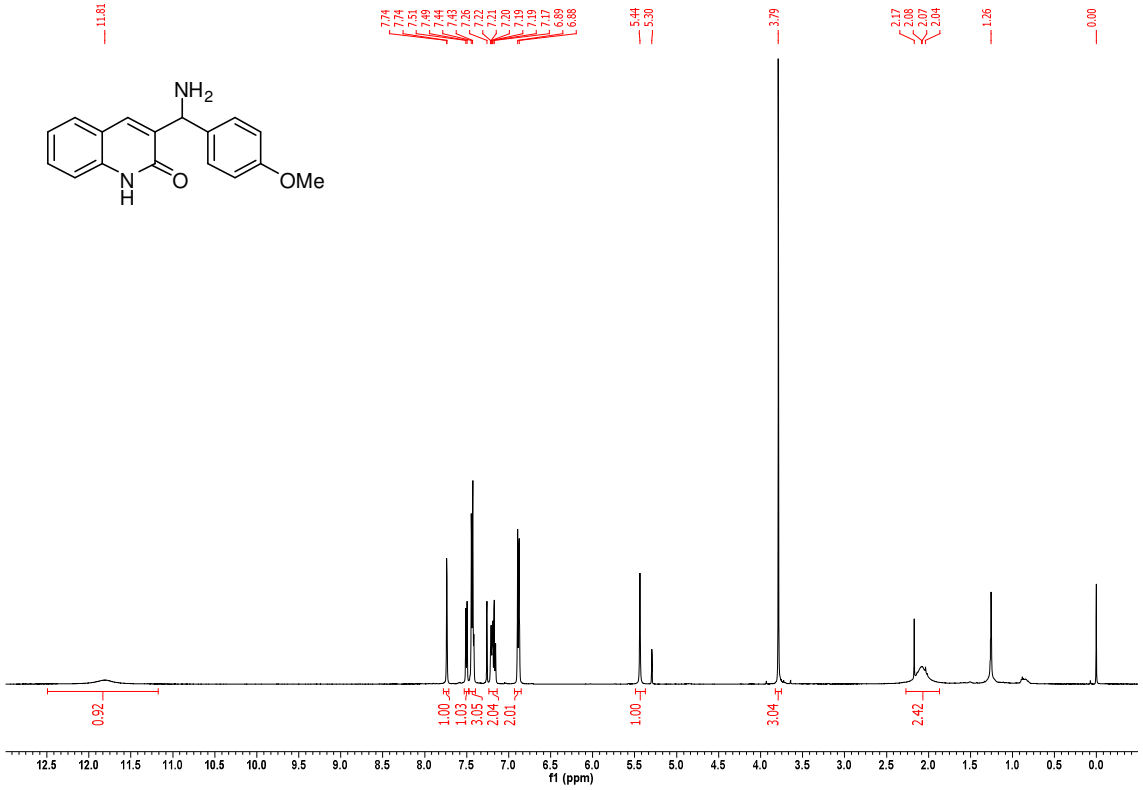


^{1}H NMR (300 K, $CDCl_3$)

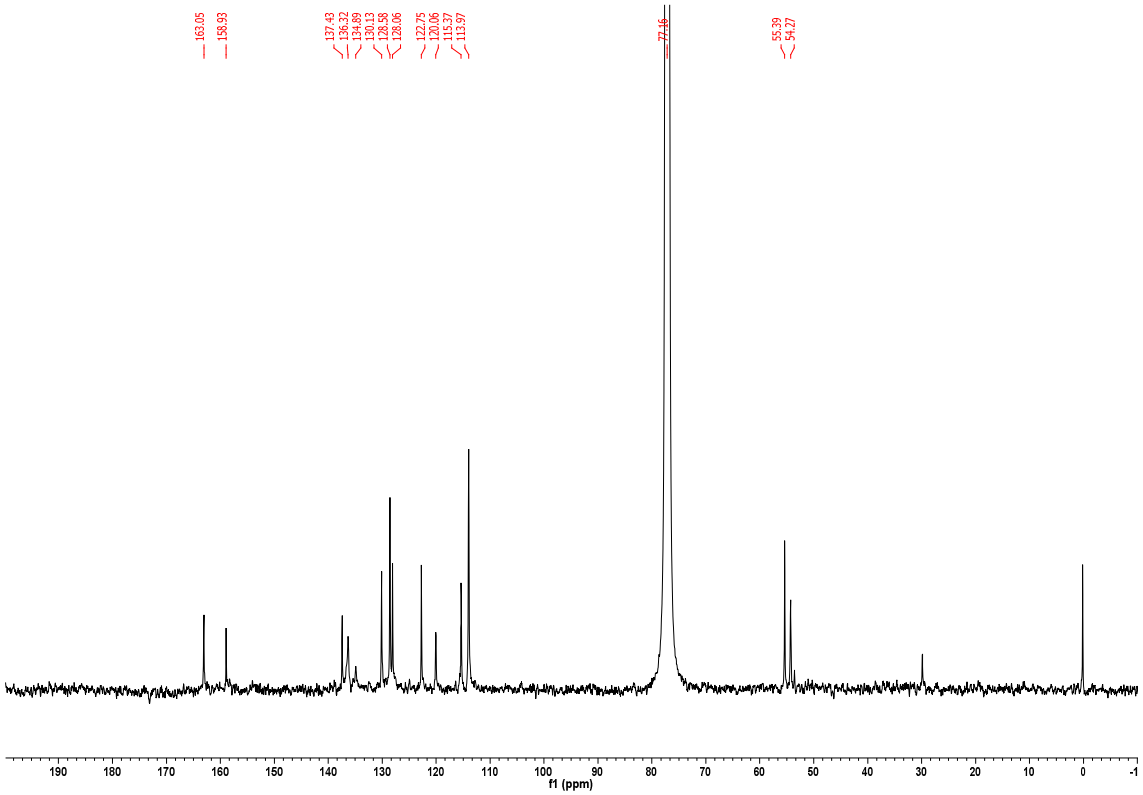
^{13}C NMR (300 K, $CDCl_3$)



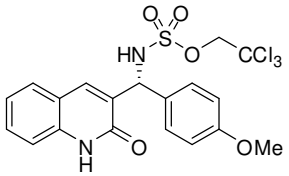
^{1}H NMR (300 K, $CDCl_3$)



^{13}C NMR (300 K, $CDCl_3$)



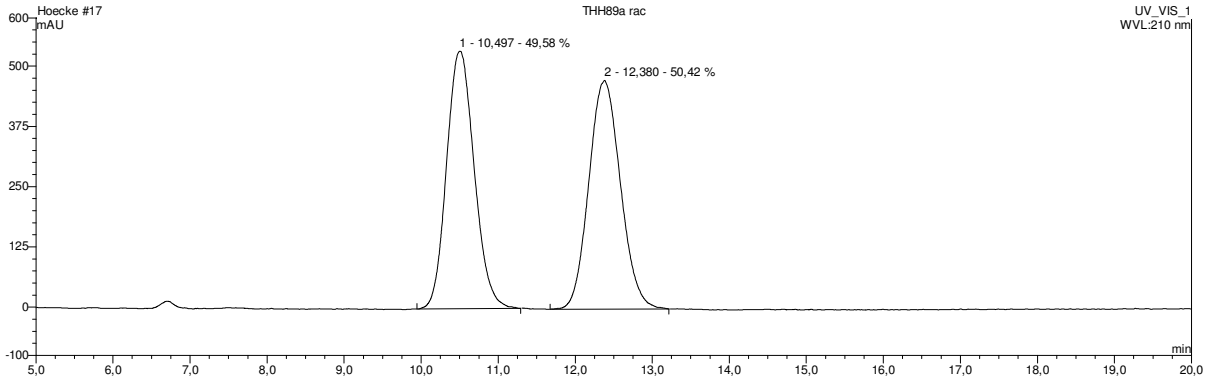
3. HPLC traces of chiral products



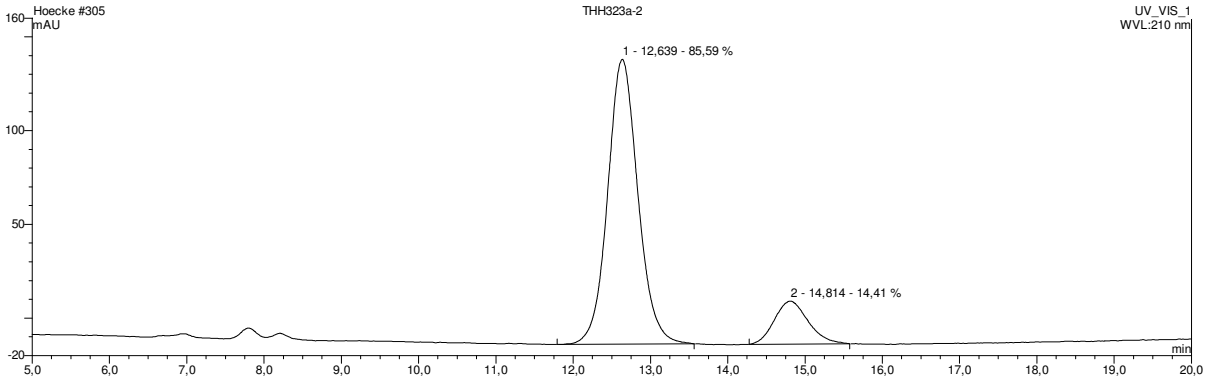
(-)-(*R*)-**8**

AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm

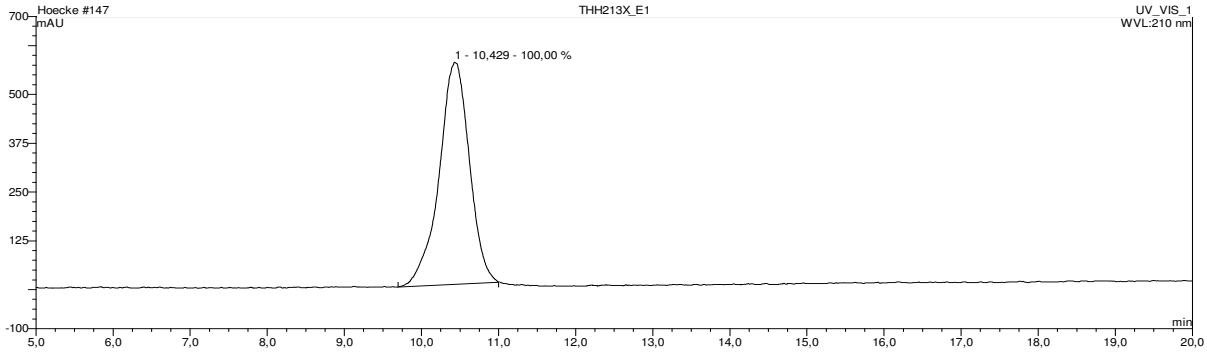
Racemic product

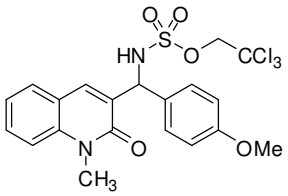


Enantioenriched product (71% *ee*)



Enantiomerically pure (–)-(*R*)-**8** (>99% *ee*; after separation of the enantiomers by semipreparative HPLC on a chiral stationary phase; s*ee* procedure)

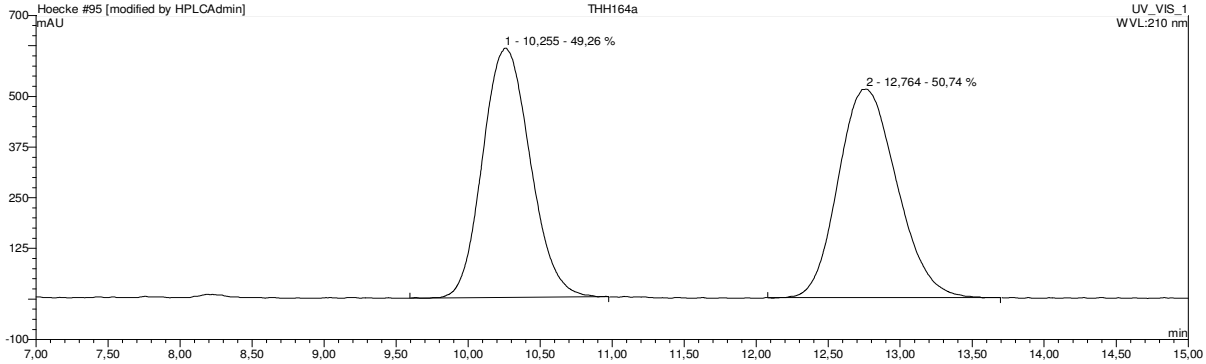




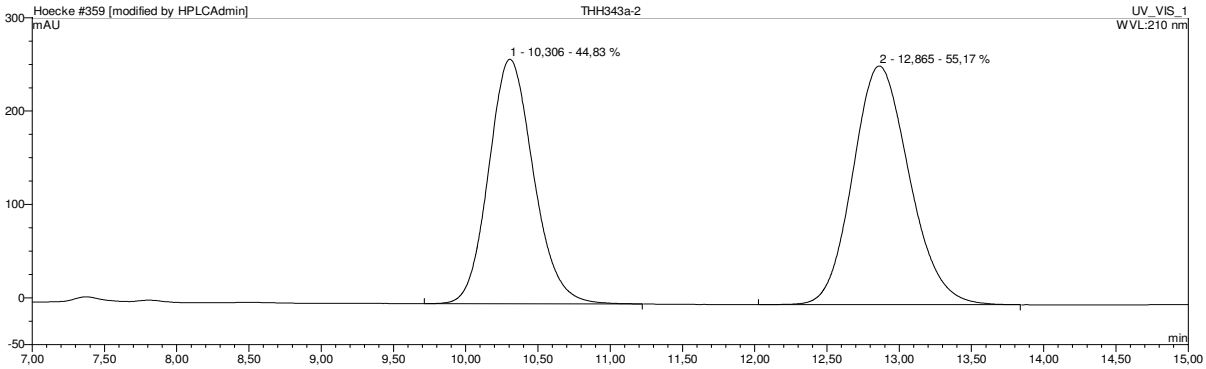
13

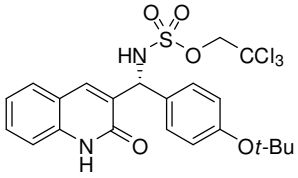
AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm

Racemic product



Enantioenriched product (10% *ee*)

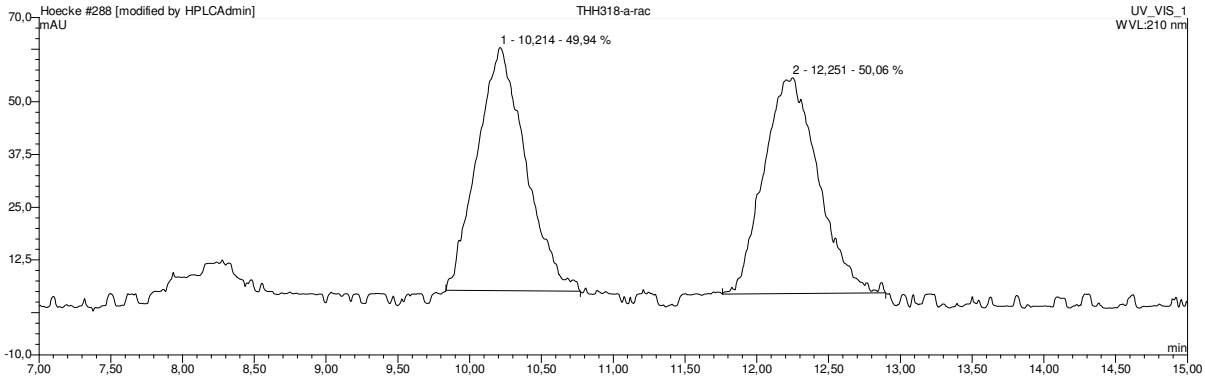




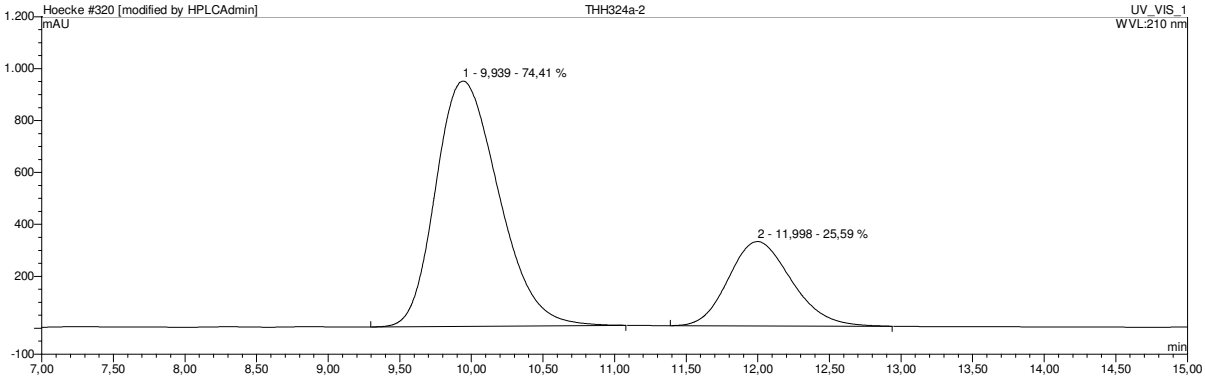
(*R*)-**11**

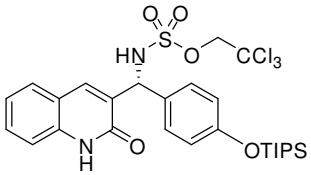
AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm

Racemic product



Enantioenriched product (49% *ee*)

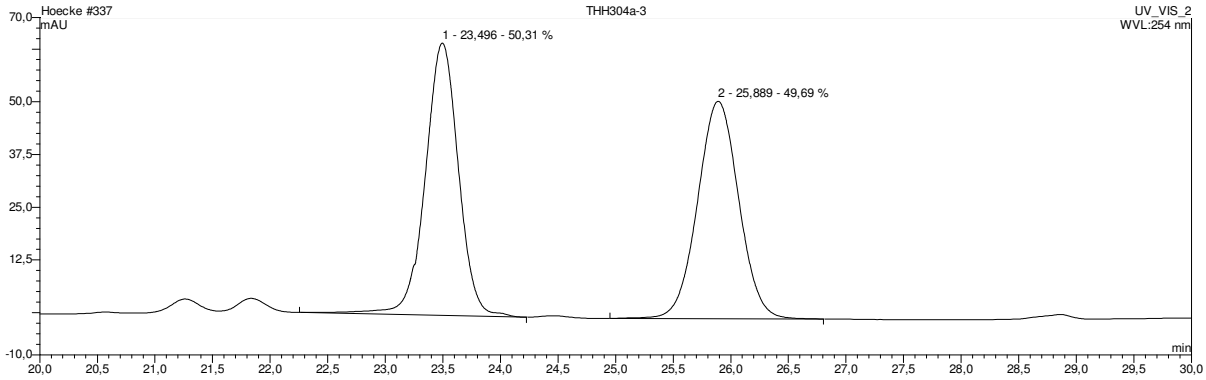




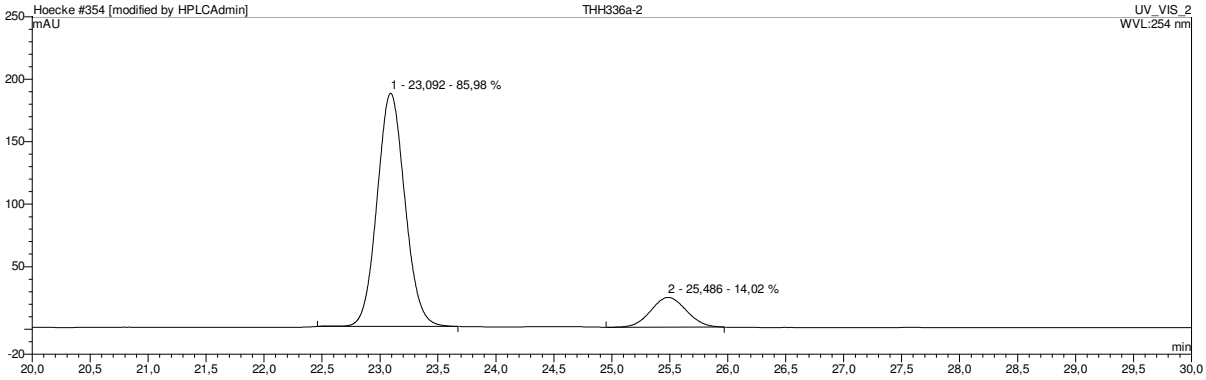
(-)-(*R*)-**12**

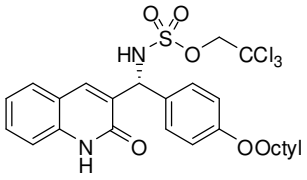
AS-RH, 150 × 4.6 mm, CH_3CN/H_2O = 20/80 → 100/0, 1 mL/min, λ = 254 nm

Racemic product



Enantioenriched product (72% *ee*)

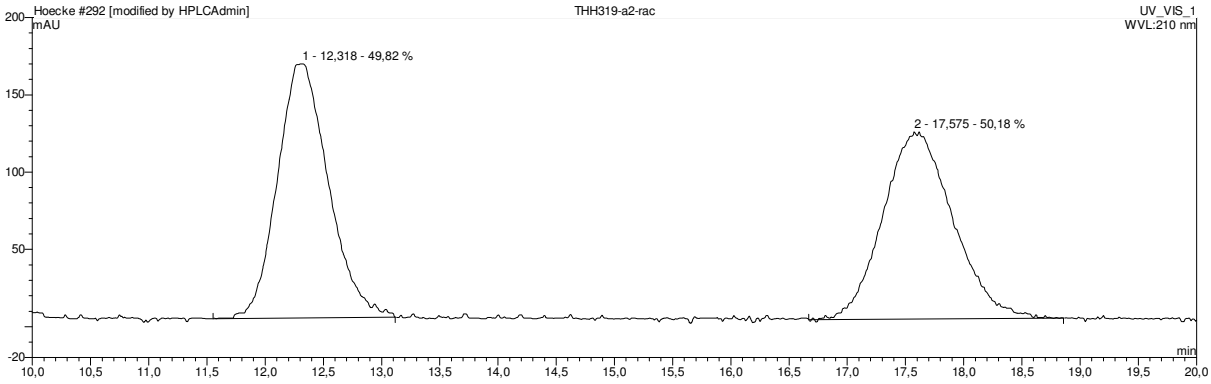




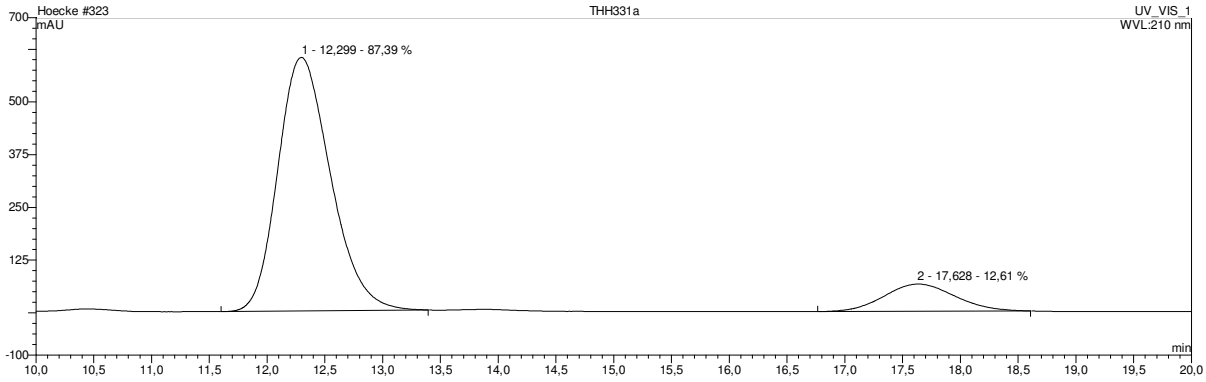
(-)-(*R*)-**10**

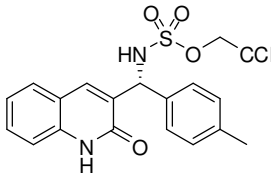
AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm

Racemic product



Enantioenriched product (75% *ee*)

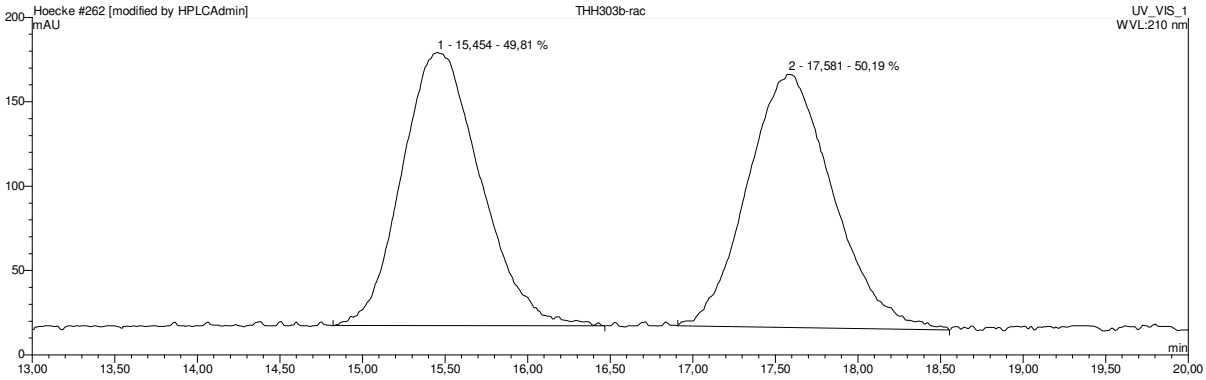




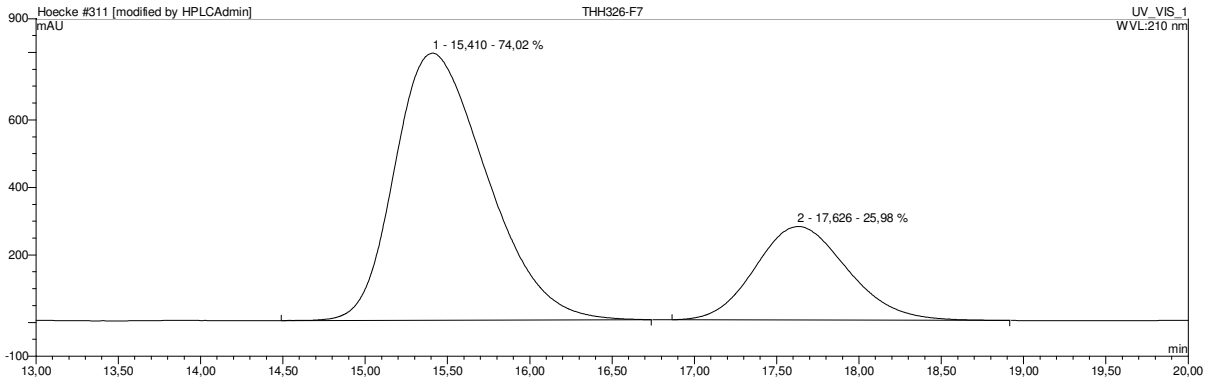
(-)-(*R*)-**9**

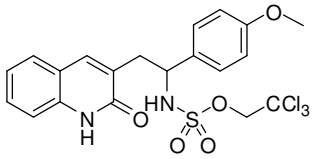
AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm

Racemic product



Enantioenriched product (48% *ee*)

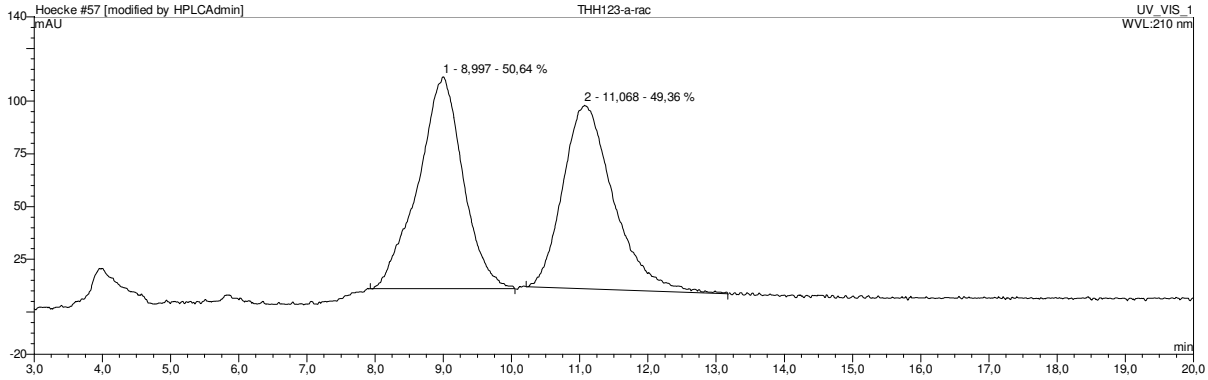




14

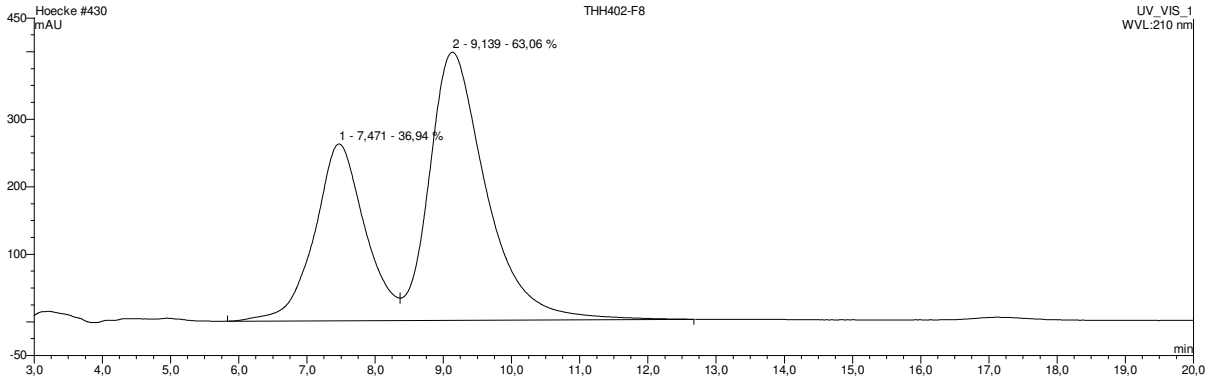
Racemic product

OD, 250 × 4.6 mm, hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm

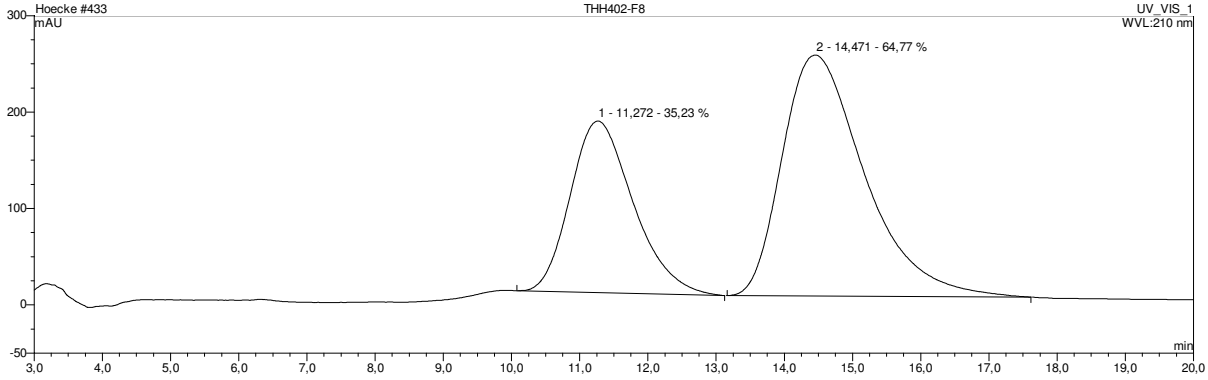


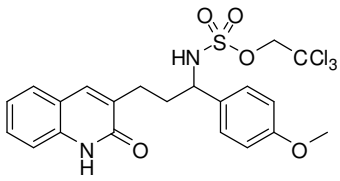
Enantioenriched product (30% *ee*, second figure)

OD, 250 × 4.6 mm, hexane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm



Due to changes in the separation performance of the column the conditions were slightly modified: OD, 250 × 4.6 mm, hexane/*i*-PrOH = 80/20, 1 mL/min, λ = 210 nm

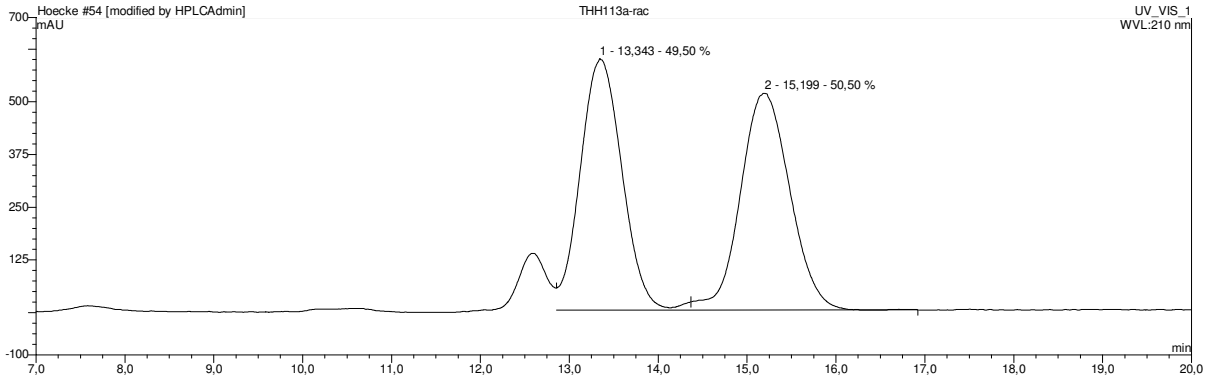




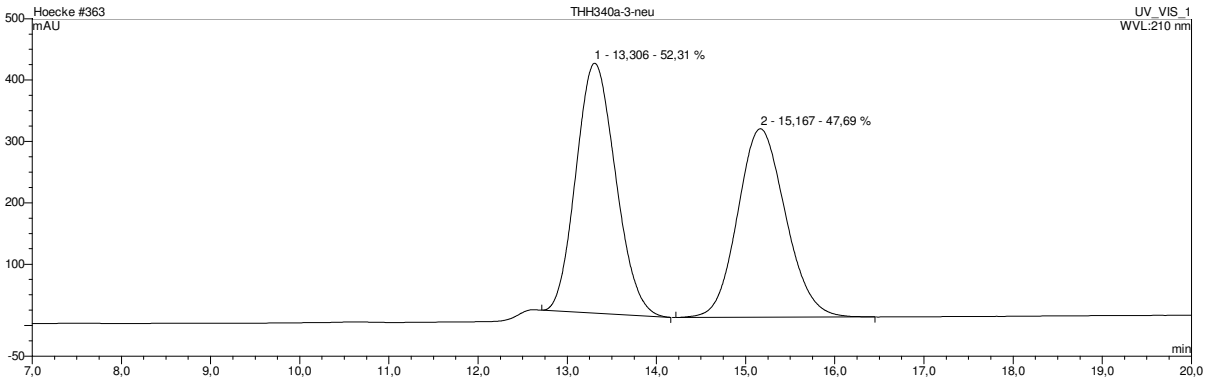
15

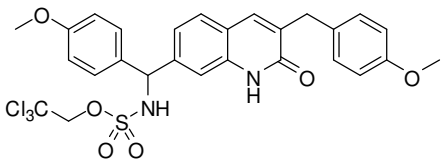
AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm

Racemic product



Enantioenriched product (5% *ee*)

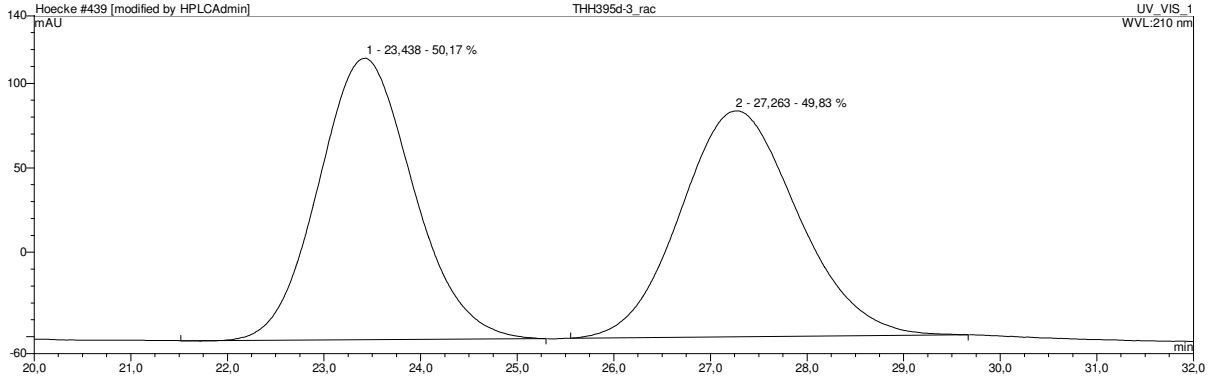




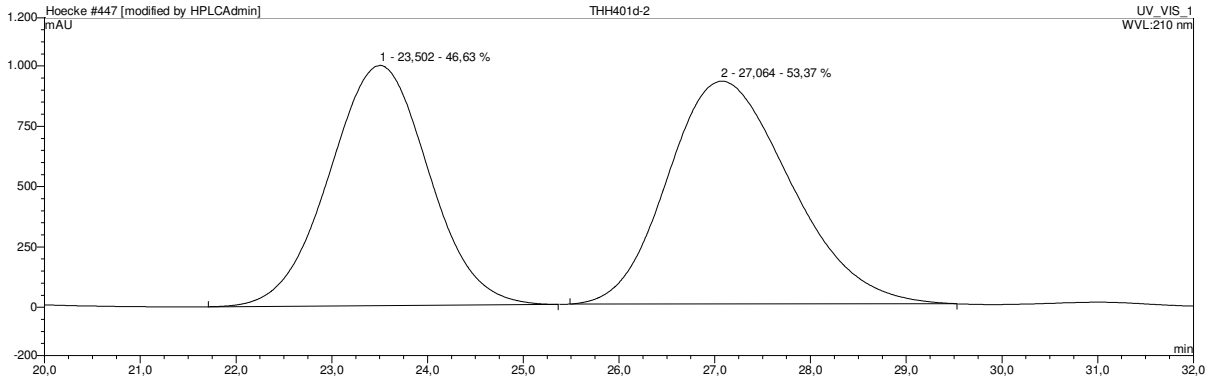
17

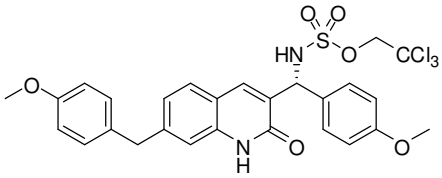
AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 210 nm

Racemic product



Enantioenriched product (6.7% *ee*)

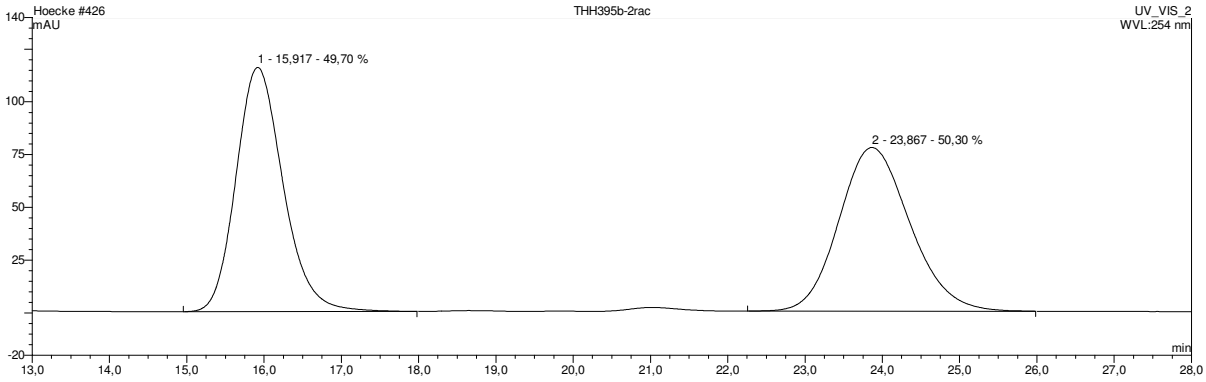




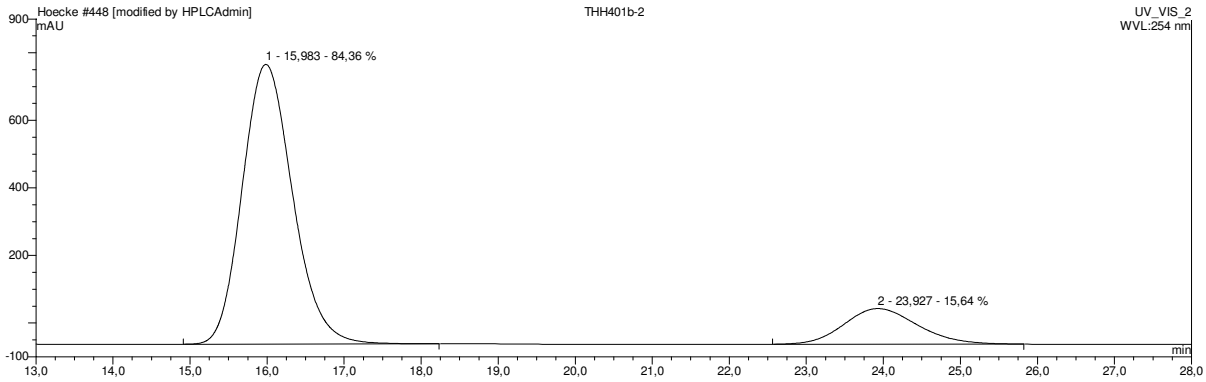
(-)-(*R*)-**18**

AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 50/50, 1 mL/min, λ = 254 nm

Racemic product



Enantioenriched product (69% *ee*)



4. Crystallographic data (Compound 4, Compound 6·2(DMSO)·(C_6H_{14}), Compound 8)

General information

Data were collected on an X-ray single crystal diffractometer equipped with a CCD detector (Bruker APEX II, κ–CCD), a rotating anode (Bruker AXS, FR591) with MoK_α radiation (λ = 0.71073 Å), and a graphite monochromator by using the SMART software package.[12] The measurements were performed on a single crystal coated with perfluorinated ether. The crystal was fixed on the top of a glass fiber and transferred to the diffractometer. The crystal was frozen under a stream of cold nitrogen. A matrix scan was used to determine the initial lattice parameters. Reflections were merged and corrected for Lorenz and polarization effects, scan speed, and background using SAINT.[13] Absorption corrections, including odd and even ordered spherical harmonics were performed using SADABS.[13] Space group assignments were based upon systematic absences, *E* statistics, and successful refinement of the structures. Structures were solved by direct methods with the aid of successive difference Fourier maps, and were refined against all data using WinGX[14] 7 based on SIR-92.[15] 3 If not mentioned otherwise, non-hydrogen atoms were refined with anisotropic displacement parameters. Methyl hydrogen atoms were refined as part of rigid rotating groups, with C–H = 0.98 Å and $U_{iso(H)}$ = 1.5$U_{eq(C)}$. Other H atoms were placed in calculated positions and refined using a riding model, with methyne, methylene and aromatic C–H distances of 1.00, 0.99 and 0.95 Å, respectively, and $U_{iso(H)}$ = 1.2·$U_{eq(C)}$. N–H distances were fixed at 0.88 Å with $U_{iso(H)}$ = 1.2·$U_{eq(N)}$. Full-matrix least-squares refinements were carried out by minimizing $\Sigma w(F_o^2-F_c^2)^2$ with SHELXL-97 [16] 5 weighting scheme. Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from *International Tables for Crystallography*.[17] Images of the crystal structures were generated by PLATON.[18] CCDC 932341 (**4**), CCDC 932342 (**6**·2(DMSO) (C_6H_{14})), and CCDC 932343 (**8**) contain the supplementary crystallographic data for this compound. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif or via https://www.ccdc.cam.ac.uk/services/structure_deposit/

Special:

4: The correct enantiomer is proved by analyses of Bijvoet-Pair Differences Parameter. Hydrogen atoms are refined freely.

6·2 DMSO·(C_6H_{14}): Unresolvable solvent molecules (104 electrons; a mixture of pentane/hexane) had to be removed with the SQUEEZE procedure.[18] The correct enantiomer is proved by Flack's Parameter. Therefore, the possible centrosymmetric space group $P2_1/c$ can be excluded.

8 The correct enantiomer is proved by Flack's Parameter.

Compound 4

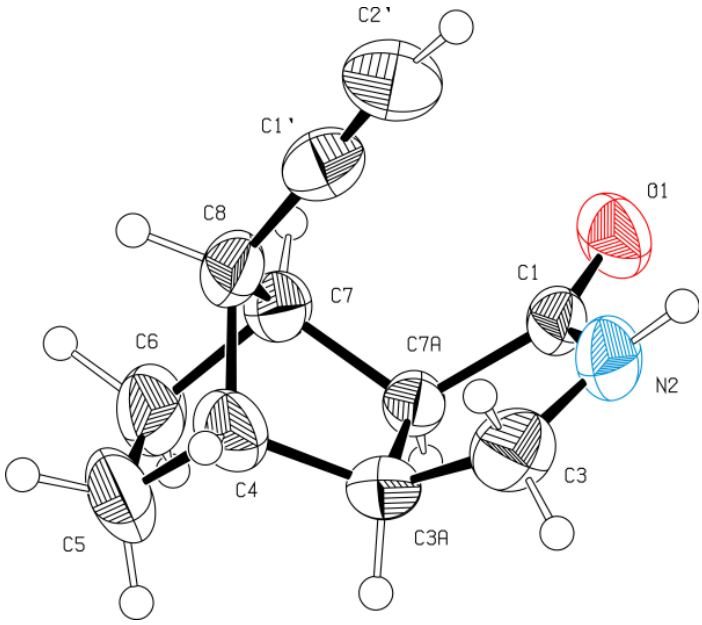


Figure F2: Ortep drawing of compound **4** with 50% ellipsoids.[18]

Operator:	*** Herdtweck ***
Molecular Formula:	C_{11} H_{13} N O
Crystal Color / Shape	Colorless fragment
Crystal Size	Approximate size of crystal fragment used for data collection: 0.30 × 0.38 × 0.64 mm
Molecular Weight:	175.22 a.m.u.
F_{000}:	752
Systematic Absences:	00l: l≠4n; h00: h≠2n
Space Group:	Tetragonal $P\,4_32_12$ (I.T.-No.: 96)
Cell Constants:	Least-squares refinement of 9918 reflections with the programs "APEX suite" and "SAINT"[12,13]; theta range 1.76° < θ < 25.38°;

	Mo($K\overline{\alpha}$); $\lambda = 0.71073$ Å
	$a =$ 6.4211(1) Å
	$b =$ a
	$c =$ 46.2039(9) Å
	$V = 1905.01(6)$ Å^3; $Z = 8$; $D_{calc} = 1.222$ g cm^{-3}; Mos. = 0.53
Diffractometer:	Kappa APEX II (Area Diffraction System; BRUKER AXS); rotating anode; graphite monochromator; 50 kV; 40 mA; $\lambda = 0.71073$ Å; Mo($K\overline{\alpha}$)
Temperature:	(20±1) °C; (293±1) K
Measurement Range:	$1.76° < \theta < 25.38°$; h: -7/7, k: -7/7, l: -55/55
Measurement Time:	2 × 10 s per film
Measurement Mode:	measured: 12 runs; 6627 films / scaled: 12 runs; 6627 films
	φ– and ω–movement; Increment: $\Delta\varphi/\Delta\omega = 0.50°$; dx = 100.0 mm
LP - Correction:	Yes[13]
Intensity Correction:	No/Yes; during scaling[13]
Absorption Correction:	Multi-scan; during scaling; $\mu = 0.078$ mm^{-1} [13]
	Correction Factors: T_{min} = 0.6860 T_{max} = 0.7452
Reflection Data:	29023 reflections were integrated and scaled
	111 reflections systematic absent and rejected
	28912 reflections to be merged
	1748 independent reflections
	0.033 R_{int}: (basis F_o^2)
	1748 independent reflections (all) were used in refinements
	1718 independent reflections with $I_o > 2\sigma(I_o)$
	99.8% completeness of the data set
	170 parameter full-matrix refinement
	10.3 reflections per parameter
Solution:	Direct Methods[15]; Difference Fourier syntheses
Refinement Parameters:	In the asymmetric unit:
	13 Non-hydrogen atoms with anisotropic displacement parameters
	13 Hydrogen atoms with isotropic displacement

parameters

Hydrogen Atoms:	All hydrogen atom positions were found in the difference map calculated from the model containing all non-hydrogen atoms. The hydrogen positions were refined with individual isotropic displacement parameters.
Atomic Form Factors:	For neutral atoms and anomalous dispersion[17]
Extinction Correction:	no
Weighting Scheme:	$w^{-1} = \sigma^2(F_o^2)+(a*P)^2+b*P$ with a: 0.0423; b: 0.5042; P: [Maximum(0 or F_o^2)+2$*F_c^2$]/3
Shift/Err:	Less than 0.001 in the last cycle of refinement:
Resid. Electron Density:	+0.12 $e_0^-/Å^3$; -0.12 $e_0^-/Å^3$
R1:	$\Sigma(\|\|F_o\|-\|F_c\|\|)/\Sigma\|F_o\|$
[$F_o > 4\sigma(F_o)$; N=1718]:	= 0.0363
[all reflctns; N=1748]:	= 0.0369
wR2:	$[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$
[$F_o > 4\sigma(F_o)$; N=1718]:	= 0.1050
[all reflctns; N=1748]:	= 0.1055
Goodness of fit:	$[\Sigma w(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$ = 1.155
Flack's Parameter :	x = -1(2)
Remarks:	Refinement expression $\Sigma w(F_o^2-F_c^2)^2$

The correct enantiomer is proved Analyses of Bijvoet-Pair Differences:

```
Bayesian Statistics
Type ....... Gaussian
Select Pairs      550
P2(true)....    0.999
P3(true)....    0.910
P3(rac-twin)    0.089
P3(false) ..    0.001
G ..........   1.6685
G (su) .....   0.7081
Hooft y ....     -0.3
Hooft (su) .      0.4
```

The correct enantiomer could **not** be proved by Flack's Parameter.

Compound 6·2(DMSO)·(C_6H_{14})

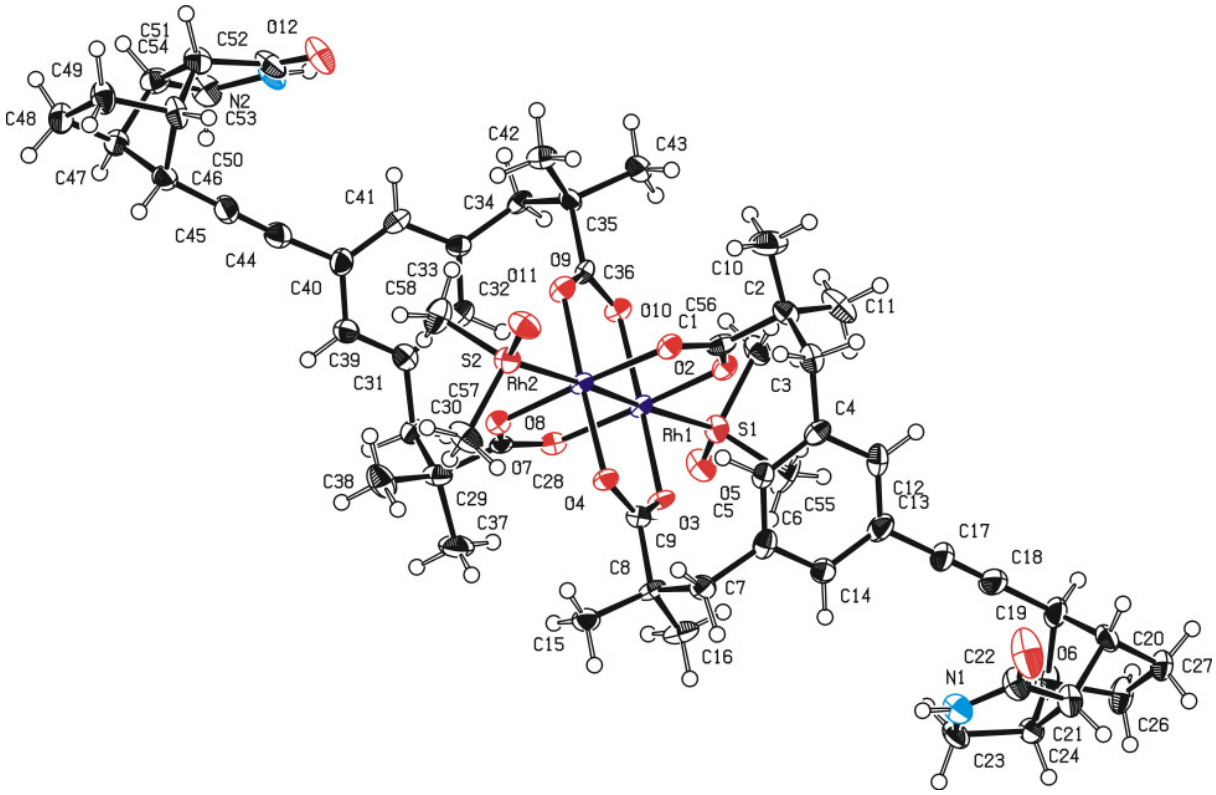


Figure F3: Ortep drawing drawing of compound **6**·2(DMSO)·(C_6H_{14}) with 50% ellipsoids.[18]

Operator:	*** Herdtweck ***
Molecular Formula:	$C_{64}\ H_{88}\ N_2\ O_{12}\ Rh_2\ S_2$
Crystal Color / Shape	Red plate
Crystal Size	Approximate size of crystal fragment used for data collection: $0.08 \times 0.20 \times 0.51$ mm
Molecular Weight:	1347.27 a.m.u.
F_{000}:	1408
Systematic Absences:	0k0: k≠2n
Space Group:	Monoclinic $P\ 2_1$ (I.T.-No.: 4)
Cell Constants:	Least-squares refinement of 9864 reflections with the programs "APEX suite" and "SAINT"[12,13]; theta range 0.74° < θ < 25.43°; Mo(K$\overline{\alpha}$); λ = 0.71073 Å
	a = 9.8534(2) Å
	b = 11.5276(3) Å β = 98.7291(9)°

	c = 27.9228(7) Å
	V = 3134.90(13)· Å^3; Z = 2; D_{calc} = 1.427 g cm^{-3}; Mos. = 0.61
Diffractometer:	Kappa APEX II (Area Diffraction System; BRUKER AXS); rotating anode; graphite monochromator; 50 kV; 40 mA; λ = 0.71073 Å; Mo($K\overline{\alpha}$)
Temperature:	(-150±1) °C; (123±1) K
Measurement Range:	0.74° < θ < 25.43°; h: -11/11, k: -13/13, l: -33/33
Measurement Time:	2 × 5 s per film
Measurement Mode:	measured: 14 runs; 5576 films / scaled: 14 runs; 5576 films
	φ– and ω–movement; Increment: $\Delta\varphi/\Delta\omega$ = 0.50°; dx = 55.0 mm
LP - Correction:	Yes[13]
Intensity Correction	No/Yes; during scaling[13]
Absorption Correction:	Multi-scan; during scaling; μ = 0.700 mm^{-1} [13]
	Correction Factors: T_{min} = 0.6785 T_{max} = 0.7452
Reflection Data:	83180 reflections were integrated and scaled
	75 reflections systematic absent and rejected
	83105 reflections to be merged
	11542 independent reflections
	0.025 R_{int}: (basis F_o^2)
	11542 independent reflections (all) were used in refinements
	11246 independent reflections with $I_o > 2\sigma(I_o)$
	99.6% completeness of the data set
	697 parameter full-matrix refinement
	16.6 reflections per parameter
Solution:	Direct Methods[15]; Difference Fourier syntheses
Refinement Parameters:	In the asymmetric unit:
	76 Non-hydrogen atoms with anisotropic displacement parameters
Hydrogen Atoms:	In the difference map(s) calculated from the model containing all non-hydrogen atoms, not all of the hydrogen positions could be determined from the highest peaks. For this reason, the hydrogen atoms were placed in calculated positions (d_{C-H} = 0.95, 0.98, 0.99,

1.00 Å; d_{N-H} = 0.88 Å). Isotropic displacement parameters were calculated from the parent carbon atom (U_H = 1.2/1.5 U_C; U_H = 1.2 U_N). The hydrogen atoms were included in the structure factor calculations but not refined.

Removing solvent molecules — Unresolvable solvent molecules (104 electrons; a mixture of pentane/hexane) had to be removed with the SQUEEZE procedure.[18]

Atomic Form Factors: For neutral atoms and anomalous dispersion[17]

Extinction Correction: no

Weighting Scheme: $w^{-1} = \sigma^2(F_o^2)+(a*P)^2+b*P$

with a: 0.0239; b: 1.2657; P: [Maximum(0 or F_o^2)+2$*F_c^2$]/3

Shift/Err: Less than 0.002 in the last cycle of refinement:

Resid. Electron Density: +0.39 e_0^-/Å^3; -0.32 e_0^-/Å^3

R1: $\Sigma(||F_o|-|F_c||)/\Sigma|F_o|$

[$F_o > 4\sigma(F_o)$; N=11246]: = 0.0186

[all reflctns; N=11542]: = 0.0192

wR2: $[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$

[$F_o > 4\sigma(F_o)$; N=11246]: = 0.0492

[all reflctns; N=11542]: = 0.0497

Goodness of fit: $[\Sigma w(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$ = 1.055

Flack's Parameter : x = 0.04(2)

Remarks: Refinement expression $\Sigma w(F_o^2-F_c^2)^2$

The correct enantiomer is proved by Flack's Parameter. Therefore the possible centrosymmetric space group $P2_1/c$ can be excluded.

Compound 8

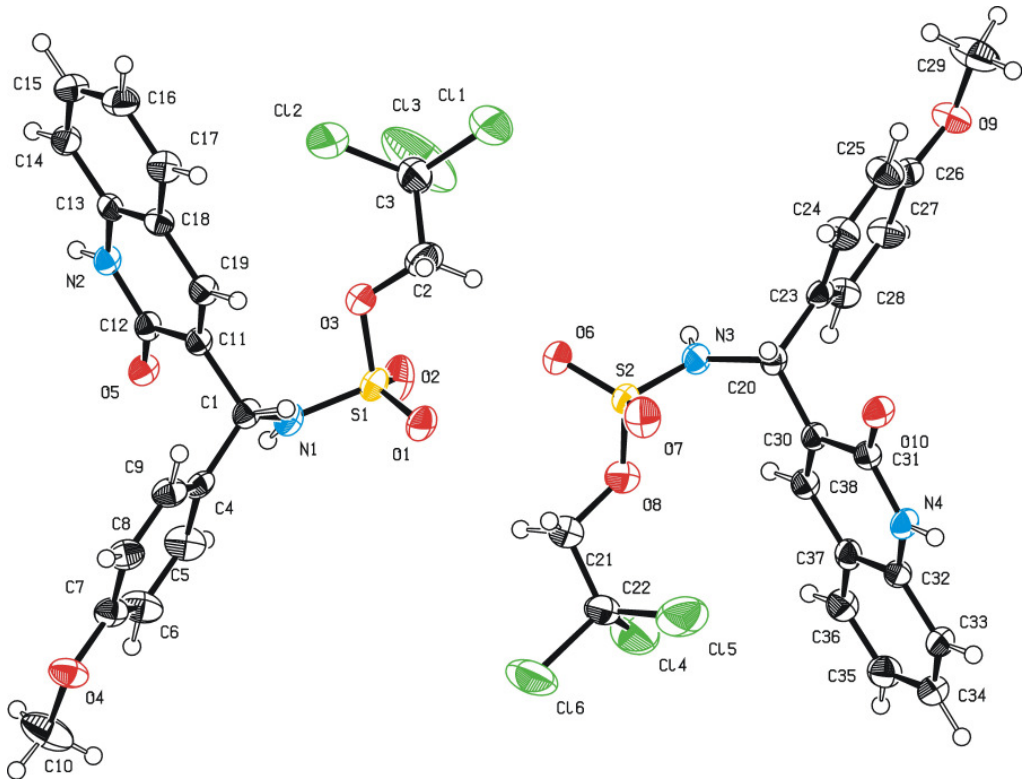


Figure F4: Ortep drawing drawing of compound **8** with 50% ellipsoids.[18]

Operator:	*** Herdtweck ***
Molecular Formula:	$C_{19}\ H_{17}\ Cl_3\ N_2\ O_5\ S$
Crystal Color / Shape	Colorless fragment
Crystal Size	Approximate size of crystal fragment used for data collection: $0.20 \times 0.36 \times 0.46$ mm
Molecular Weight:	491.77 a.m.u.
F_{000}:	504
Systematic Absences:	none
Space Group:	Triclinic $P\ 1$ (I.T.-No.: 1)
Cell Constants:	Least-squares refinement of 9756 reflections with the programs "APEX suite" and "SAINT"[12,13]; theta range 1.50° < θ < 25.45°; Mo($K\overline{\alpha}$); $\lambda = 0.71073$ Å

a =	6.4438(2) Å	α =	78.9069(15)°
b =	12.5194(4) Å	β =	86.3426(14)°
c =	13.8216(5) Å	γ =	75.5645(13)°

	V = 1059.50(6)· Å^3; Z = 2; D_{calc} = 1.541 g cm^{-3}; Mos. = 0.74
Diffractometer:	Kappa APEX II (Area Diffraction System; BRUKER AXS); rotating anode; graphite monochromator; 50 kV; 40 mA; λ = 0.71073 Å; Mo(K$\overline{\alpha}$)
Temperature:	(-100±1) °C; (173±1) K
Measurement Range:	1.50° < θ < 25.45°; h: -7/7, k: -15/15, l: -16/16
Measurement Time:	2 × 7.50 s per film
Measurement Mode:	measured: 8 runs; 4270 films / scaled: 8 runs; 4270 films
	φ– and ω–movement; Increment: $\Delta\varphi/\Delta\omega$ = 0.50°; dx = 45.0 mm
LP - Correction:	Yes[13]
Intensity Correction	No/Yes; during scaling[13]
Absorption Correction:	Multi-scan; during scaling; μ = 0.566 mm^{-1} [13]
	Correction Factors: T_{min} = 0.6772 T_{max} = 0.7452
Reflection Data:	29669 reflections were integrated and scaled
	29669 reflections to be merged
	7744 independent reflections
	0.029 R_{int}: (basis F_o^2)
	7744 independent reflections (all) were used in refinements
	7683 independent reflections with $I_o > 2\sigma(I_o)$
	98.5% completeness of the data set
	543 parameter full-matrix refinement
	14.3 reflections per parameter
Solution:	Direct Methods[15]; Difference Fourier syntheses
Refinement Parameters:	In the asymmetric unit:
	60 Non-hydrogen atoms with anisotropic displacement parameters
Hydrogen Atoms:	In the difference map(s) calculated from the model containing all non-hydrogen atoms, not all of the hydrogen positions could be determined from the highest peaks. For this reason, the hydrogen atoms were placed in calculated positions (d_{C-H} = 0.95, 0.98, 0.99, 1.00 Å, d_{N-H} = 0.88 Å). Isotropic displacement parameters were calculated from the parent carbon atom (U_H = 1.2/1.5 U_C, U_H = 1.2

	U_N). The hydrogen atoms were included in the structure factor calculations but not refined.	
Atomic Form Factors:	For neutral atoms and anomalous dispersion[17]	
Extinction Correction:	no	
Weighting Scheme:	$w^{-1} = \sigma^2(F_o^2)+(a*P)^2+b*P$	
	with a: 0.0680; b: 0.7404; P: [Maximum(0 or F_o^2)+2$*F_c^2$]/3	
Shift/Err:	Less than 0.001 in the last cycle of refinement:	
Resid. Electron Density:	+0.84 $e_0^-/Å^3$; -0.73 $e_0^-/Å^3$	
R1:	$\Sigma(\|\|F_o\|-\|F_c\|\|)/\Sigma\|F_o\|$	
[$F_o > 4\sigma(F_o)$; N=7683]:		= 0.0418
[all reflctns; N=7744]:		= 0.0420
wR2:	$[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$	
[$F_o > 4\sigma(F_o)$; N=7683]:		= 0.1121
[all reflctns; N=7744]:		= 0.1124
Goodness of fit:	$[\Sigma w(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$	= 1.050
Flack's Parameter :	x = 0.03(5)	
Remarks:	Refinement expression $\Sigma w(F_o^2-F_c^2)^2$	
	The correct enantiomer is proved by Flack's Parameter.	

5. References

[1] a) C. G. Espino, K. W. Fiori, M. Kim, J. Du Bois, *J. Am. Chem. Soc.* **2004**, *126*, 15378-15379; b) K. W. Fiori, J. Du Bois, *J. Am. Chem. Soc.* **2007**, *129*, 562-568.

[2] E. Díez-Barra, J. C. García-Martínez, S. Merino, R. del Rey, J. Rodríguez-López, P. Sánchez-Verdú, J. Tejeda, *J. Org. Chem.* **2001**, *66*, 5664-5670.

[3] P. Fackler, C. Berthold, F. Voss, T. Bach, *J. Am. Chem. Soc.* **2010**, *132*, 15911-15913.

[4] M. E. Hart, K. L. Suchland, M. Miyakawa, J. R. Bunzow, D. K. Grandy, T. S. Scanlan, *J. Med. Chem.* **2006**, *49*, 1101-1112.

[5] a) O. A. El-Sayed, H. Y. Aboul-Enein, *Arch. Pharm. Pharm. Med. Chem.* **2001**, *334*, 117–120; b) I. Devi, B. Baruah, P. J. Bhuyan, *Synlett* **2006**, 2593–2596; c) O. Meth-Cohn, B. Narine, B. Tarnowski, *J. Chem. Soc., Perkin Trans. I* **1981**, 1520-1530.

[6] K. K. Park, J. Y. Jung, *Heterocycles* **2005**, *65*, 2095-2105.

[7] a) P. Shanmugan, *Monat. Chem.* **1976**, *107*, 259-269; b) For the preparation of the precursor 4-bromo-2-nitrobenzaldehyde see: J. H. Seo, G. D. Artman III, S. M. Weinreb, *J. Org. Chem.* **2006**, *71*, 8891-8900.

[8] C. L. Diedrich, D. Haase, W. Saak, J. Christoffers, *Eur. J. Org. Chem.* **2008**, 1811-1816.

[9] F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chem. Eur.* J. **2009**, *15*, 7192-7202.

[10] D. Albrecht, F. Vogt, T. Bach, *Chem. Eur. J.* **2010**, *16*, 4284-4296.

[11] K. W. Fiori, J. Du Bois, *J. Am. Chem. Soc.* **2007**, *129*, 562-568.

[12] APEX suite of crystallographic software. APEX 2 Version 2008.4. Bruker AXS Inc., Madison, Wisconsin, USA, **2008**.

[13] SAINT, Version 7.56a and SADABS Version 2008/1. Bruker AXS Inc., Madison, Wisconsin, USA (2008).

[14] L. J. Farrugia, "**WinGX** (Version 1.70.01 January 2005) ", *J. Appl. Cryst.* **1999**, *32*, 837-838.

[15] A. Altomare, G.Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli "**SIR92**", *J. Appl. Cryst.* **1994**, *27*, 435-436.

[16] G. M. Sheldrick, "**SHELXL-97**", University of Göttingen, Göttingen, Germany, **1998**.

[17] International Tables for Crystallography, Vol. C, Tables 6.1.1.4 (pp. 500-502), 4.2.6.8 (pp. 219-222), and 4.2.4.2 (pp. 193-199), Wilson, A. J. C., Ed., Kluwer Academic Publishers, Dordrecht, The Netherlands, **1992**.

[18] Spek, A. L. "**PLATON**", A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, **2010**.