Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Exploration of Chiral Diastereomeric Spiroketal (SPIROL)-based Phosphinite Ligands in Asymmetric Hydrogenation of Heterocycles.

Siyuan Sun and Pavel Nagorny*
Department of Chemistry, University of Michigan, Ann Arbor, MI 48109, USA
nagorny@umich.edu

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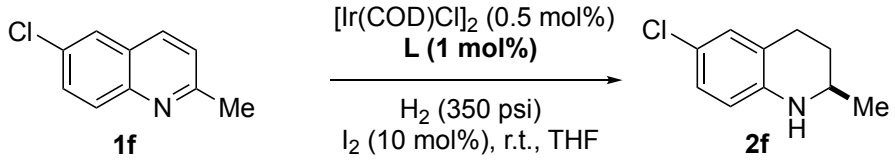
General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring, unless otherwise noted. Air-sensitive reagents and solutions were transferred via syringe or cannula and were introduced to the apparatus through rubber septa. Reactions were cooled via external cooling baths: ice water (0°C), dry ice-acetone (-78°C), or Neslab CB 80 immersion cooler (0 to -60°C). Heating was achieved using a silicone oil bath with regulated by an electronic contact thermometer. Deionized water was used in the preparation of all aqueous solutions and for all aqueous extractions. Solvents used for extraction and column chromatography were ACS or HPLC grade. Dry tetrahydrofuran (THF), dichloromethane (DCM), toluene (PhMe), and diethyl ether (Et_2O) was prepared by filtration through a column (Innovative Technologies) of activated alumina under nitrogen atmosphere. Reactions were monitored by nuclear magnetic resonance (NMR, see below) or thin layer chromatography (TLC) on silica gel precoated glass plates (0.25 mm, SiliCycle, SiliaPlate). TLC plate visualization was accomplished by irradiation with UV light at 254 nm or by staining with a potassium permanganate (KMnO4) or cerium ammonium molybdate (CAM) solution. Flash chromatography was performed using SiliCycle SiliaFlash P60 (230-400 mesh) silica gel. Powdered 4 Å molecular sieves were pre-activated by flame-drying under vacuum before use.

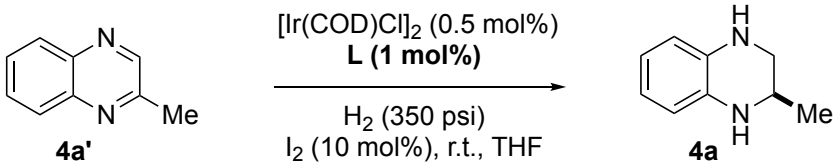
Proton (1H), deuterium (D), carbon (13C), and phosphorus (31P) NMR spectra were recorded on Varian VNMRS-700 (700 MHz), Varian VNMRS-500 (500 MHz), Varian INOVA 500 (500 MHz), or Varian MR400 (400 MHz). 1H, 13C, and 31P NMR spectra are referenced on a unified scale, where the single reference is the frequency of the residual solvent peak in the 1H NMR spectrum. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane for 1H and 13C NMR, 85% phosphoric acid for 31P. Data is reported as (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration). Slight shape deformation of the peaks in some cases due to weak coupling (e.g. aromatic protons) is not explicitly mentioned. High resolution mass spectra (HRMS) were recorded on Micromass AutoSpec Ultima or VG (Micromass) 70-250-S Magnetic sector mass. The enantiomeric excesses were determined by HPLC analysis employing a chiral stationary phase column and conditions specified in the individual experiment. HPLC experiments were performed using a Waters Alliance e2695 Separations Module instrument. Optical rotations were measured at room temperature in a solvent of choice on a JASCO P-2000 digital polarimeter at 589 nm (D-line). Fourier-transform infrared spectroscopy (FT-IR) were performed at room temperature on a Thermo-Nicolet IS-50 and converted into inverse domain (wavenumbers in cm^{-1}).

Table S1. Screening of the catalysts



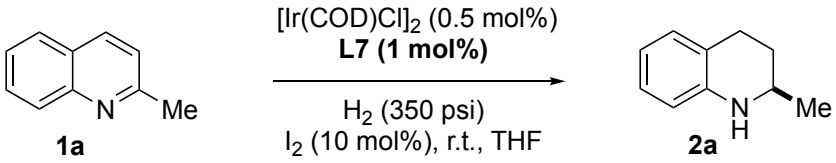
entry	ligand	H_2 (psi)	time (h)	conv. (%)	ee (%)
1	L1	350	10	99	80
2	L2	350	10	99	1
3	L3	350	10	99	89
4	L4	350	10	99	69
5	L7	350	10	99	90
6	L7	600 (0 ºC)	3	99	93

Table S2. Screening of the catalysts



entry	ligand	H_2 (psi)	time (h)	conv. (%)	ee (%)
1	L1	350	10	99	79
2	L2	350	10	99	23
3	L3	350	10	99	76
4	L4	350	10	99	74
5	L7	350	10	99	89

Table S3. Study of time vs. conv.



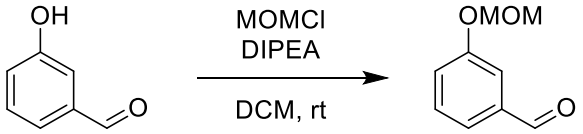
Time	1 hr	2 hr	4 hr	7 hr	10 hr
conv.	95%	96%	97%	98%	99%

[a] Unless noted otherwise, all reactions were carried out at room temperature with 0.1 mmol substrate using Ir complex generated in situ from $[Ir(COD)Cl]_2$ (0.5 mol%), ligand **L1** to **L7** (1.1 mol%), and I_2 (10 mol%) under pressurized H_2 in 1 ml of solvent. [b] The conversion was determined by 1H NMR and the enantioselectivity was determined by HPLC analysis with a Chiralpak OJ-H column. The product was in (*R*)-configuration.

Synthesis of diphosphinite (*R, S, S*)-SPIRAPO

Compounds SI-1a, SI-2a, were prepared following the published procedures.[1] Compound SI-1a is commercially available and could be purchased from TRC, TCI America or other commercial suppliers.

3-(methoxymethoxy)benzaldehyde (SI-1a)



SI-1a

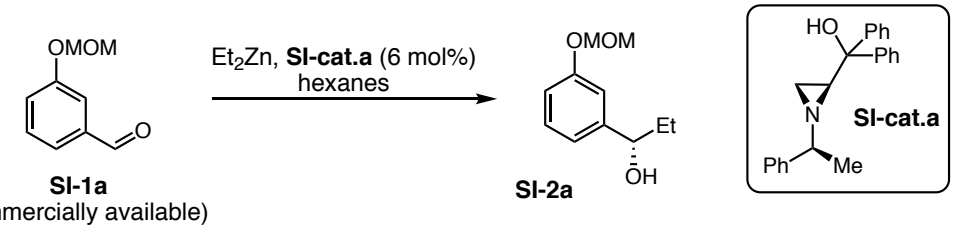
3-Hydroxybenzaldehyde (16.00 g, 131.0 mmol), DCM (150 mL), and *N,N*-diisopropylethylamine (67.0 mL, 393 mmol) were cooled to 0 °C before adding chloromethyl methyl ether (16.7 mL, 196 mmol) over 1 hour with a venting needle to handle the fumes. Reaction mixture was then warmed to room temperature. After 17 hours at room temperature, reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (170 mL). After separating the phases, the aqueous layer was extracted with DCM twice. Combined organic was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Crude was purified by FCC (SiO_2, 10-20% EtOAc in hexanes) to obtain the desired product **SI-1a** as pale yellow liquid (20.8 g, 96.2% yield).

^{1}H NMR (700 MHz, Chloroform-*d*): δ 9.98 (s, 1H), 7.57–7.51 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.32–7.28 (m, 1H), 5.24 (s, 2H), 3.49 (s, 3H).

^{13}C NMR (176 MHz, Chloroform-*d*): δ 192.0, 157.8, 137.8, 130.1, 123.8, 122.8, 115.9, 94.4, 56.2.

IR (film, cm^{-1}): 2956, 2923, 2849, 2730, 1699, 1585, 1463, 1454, 1389, 1248.

(*S*)-1-(3-(methoxymethoxy)phenyl)propan-1-ol (SI-2a).



SI-1a
(commercially available)

SI-2a

Hexanes (100 mL), and diphenyl((*R*)-1-((*S*)-1-phenylethyl)aziridin-2-yl)methanol (**SI-cat.a**)[2] (2.47 g, 7.50 mmol) were cooled to 0 °C before adding 1 M solution of diethylzinc in hexanes (275 mL, 275 mmol) dropwise. Reaction mixture was stirred at 0 °C before the addition of aldehyde **SI-1a** (20.78 g, 125.0 mmol) dropwise. After 20 hours at 0°C and 20 hours at room temperature, raction mixture was quenched with a saturated solution of NH_4Cl (200 mL). After separating the layers, the aqueous fraction was with EtOAc (3 x 100 mL). Combined organic was washed with brine,

dried over Na_2SO_4, and concentrated *in vacuo*. Crude was purified by FCC (SiO_2, 20% EtOAc in hexanes) to obtain **(*S*)-SI-2a** (23.3 g, 95.0 % yield, 99.8% ee) as pale yellow oil.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.29 – 7.24 (m, 1H), 7.03 (t, *J* = 2.0 Hz, 1H), 6.99 (dt, *J* = 7.4, 1.2 Hz, 1H), 6.96 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 5.19 (s, 2H), 4.60 – 4.55 (m, 1H), 3.49 (s, 3H), 1.85 – 1.71 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H).

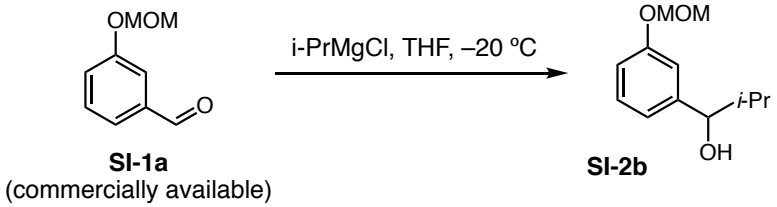
^{13}C NMR (176 MHz, Chloroform-*d*): δ 157.4, 146.4, 129.4, 119.5, 115.2, 113.9, 94.4, 75.8, 56.0, 31.8, 10.2.

IR (film, cm^{-1}): 3411 (br), 2961, 2932, 1586, 1486, 1451, 1242, 1149.

ESI-HRMS: Calcd. for $C_{11}H_{17}O_3^+$ 197.1171 $[M+H]^+$, found 197.1175.

HPLC: (Chiralpak IA column, 96:4 hexanes/isopropanol, 1.0 ml/min), t_r = 15.4 min (minor, *R*), 17.0 min (major, *S*)

(*rac*)-1-(3-(benzyloxy)phenyl)-2-methylpropan-1-ol (SI-2b)



SI-1a
(commercially available)

SI-2b

1.6 M solution isopropylmagnesium chloride in THF (5.30 mL, 8.48 mmol) and THF (5.0 mL) were cooled to -20 °C followed by slow addition of the aldehyde **SI-1a** (697 mg, 4.20 mmol) over 20 minutes. After 5 hours at -20 °C the reaction mixture was quenched with the saturated solution of NH_4Cl (20 mL). After separating the layers, the aqueous fraction was with EtOAc three times. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant crude oil was purified by FCC (SiO_2, 15% EtOAc in hexanes) to obtain **SI-2b** (841 mg, 95 % yield) as a pale yellow oil.

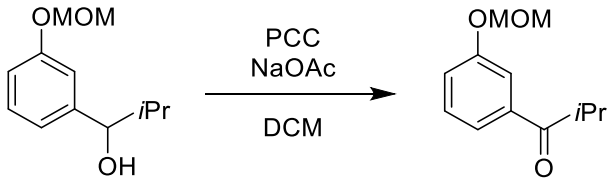
^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.21 (m, 1H), 6.98 (m, 1H), 6.96 – 6.86 (m, 2H), 5.16 (d, *J* = 0.7 Hz, 2H), 4.33 (dd, *J* = 6.8, 3.4 Hz, 1H), 3.47 (s, 3H), 1.93 (h, *J* = 6.8 Hz, 1H), 1.78 (br s, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*): δ 157.2, 145.4, 129.2, 120.1, 115.1, 114.5, 94.5, 79.8, 56.0, 35.2, 19.0, 18.1.

IR (film, cm^{-1}): 3431 (br), 2957, 2898, 2872, 2826, 1585, 1485, 1450, 1404, 1382, 1243, 1207, 1147, 1076, 834 cm^{-1}

ESI-HRMS: Calcd. for $C_{12}H_{19}O_3^+$ 211.1329 $[M+H]^+$, found 211.1328.

1-(3-(methoxymethoxy)phenyl)-2-methylpropan-1-one (SI-3)



SI-2b **SI-3**

Pyridinium chlorochromate (1.29 g, 6.00 mmol) and sodium acetate (393 mg, 4.80 mmol) were dissolved into dry DCM (25 mL) at the room temperature under the nitrogen. The mixture was stirred for 10 minutes before the addition of solution of 1-(3-(benzyloxy)phenyl)-2-methylpropan-1-ol (**SI-2b**) (840 mg, 4.00 mmol) in DCM (8.0 mL). After 5 hours at room temperature diethyl ether (10 mL) was added to the mixture and then filtered through a fritted funnel. Black insoluble solids were washed with Et_2O three times. Combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Crude was purified by FCC (SiO_2, 10% EtOAc in hexanes) to obtain **SI-3** (711 mg, 85.0 % yield) as colorless oil.

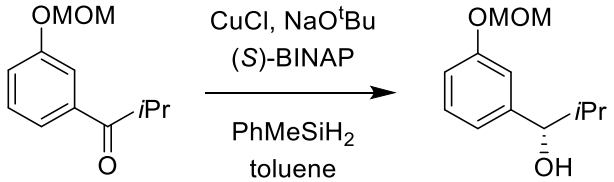
^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.67 – 7.53 (m, 2H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.21 (m, 1H), 5.20 (s, 2H), 3.56 – 3.48 (m, 1H), 3.47 (s, 3H), 1.20 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*): δ 204.1, 157.5, 137.7, 129.6, 121.8, 120.7, 115.8, 94.4, 56.1, 35.5, 19.2.

IR (film, cm^{-1}): 2970, 2933, 2904, 2826, 1682, 1581, 1485, 1467, 1435, 1247, 1149, 1078, 1017, 999, 979, 745.

ESI-HRMS: Calcd. for $C_{12}H_{17}O_3^+$ 209.1172 $[M+H]^+$, found 209.1176.

(*S*)-1-(3-(benzyloxy)phenyl)-2-methylpropan-1-ol (SI-2b)



SI-3 **SI-2b**

Following similar published procedure,[3] a dry flask was charged with CuCl (17.0 mg, 0.17 mmol), NaO^{t}Bu (16 mg, 0.17 mmol) and (*S*)-BINAP (106 mg, 0.17 mmol) in the glove box. Dry toluene (15 mL) was added under nitrogen and the bright yellow solution was stirred for 20 minutes at room temperature. After cooling this mixture to –78 °C, $PhMeSiH_2$ (0.93 mL, 6.80 mmol) was added dropwise over 5 minutes followed by the dropwise addition of 1-(3-(methoxymethoxy)phenyl)-2-methylpropan-1-one (**SI-3**) (710 mg, 3.40 mmol). After 15 hours at –78 °C, the saturated solution of K_2CO_3 in methanol was added (12 mL), and the resulting solution was stirred for 1 hour at room temperature. The organic phase was concentrated *in vacuo*, and the crude oil was purified by FCC (SiO_2, 15% EtOAc in hexanes) to obtain pure **(*S*)-SI-2b** (175 mg,

24% yield, 92% ee, 82% BRSM) as a pale yellow oil. This material was further enriched by recrystallization to 99% ee level following the procedure described in Ref. 11.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.21 (m, 1H), 6.98 (m, 1H), 6.96 – 6.86 (m, 2H), 5.16 (d, *J* = 0.7 Hz, 2H), 4.33 (dd, *J* = 6.8, 3.4 Hz, 1H), 3.47 (s, 3H), 1.93 (h, *J* = 6.8 Hz, 1H), 1.78 (br s, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*): δ 157.2, 145.4, 129.2, 120.1, 115.1, 114.5, 94.5, 79.8, 56.0, 35.2, 19.0, 18.1.

IR (film, cm^{-1}): 3431 (br), 2957, 2898, 2872, 2826, 1585, 1485, 1450, 1404, 1382, 1243, 1207, 1147, 1076, 834.

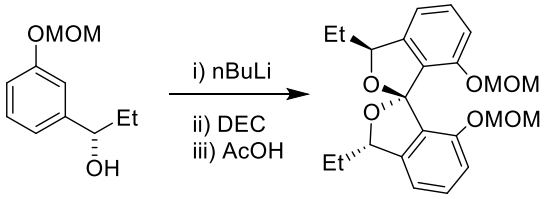
$[\alpha]_D$: –22.8 (c = 4.00 in CH_2Cl_2)

ESI-HRMS: Calcd. for $C_{12}H_{19}O_3^+$ 211.1329 $[M+H]^+$, found 211.1328.

HPLC: (Chiralpak IA column, 95:5 hexanes/isopropanol, 1.0 ml/min), t_r = 10.3 min (*R*), 11.3 min (*S*)

Compounds (*R,S,S*)-4a, was prepared following the published procedures described in Ref.1.[1]

(*1R,3S,3'S*)-3,3'-diethyl-7,7'-bis(methoxymethoxy)-3H,3'H-1,1'-spirobi[isobenzofuran] ((*R,S,S*)-4a).



SI-2a **(*R,S,S*)-4a**

The solution of alcohol **SI-2a** (23.30 g, 118.7 mmol) in PhMe (250 mL) was cooled to 0 °C prior to the addition of 2.5 M solution *n*-butyllithium in hexanes (45 mL over 15 minutes, then 51 mL over 1.2 hours, 239.8 mmol). The resultant mixture was then warmed to room temperature. After stirring this suspension for 3 hours, it was dissolved using 10.0 mL of THF and cooled again to 0 °C. Diethyl carbonate (7.85 mL, 64.8 mmol) was slowly added over the course of 2 hours at 0 °C. Reaction mixture was allowed to warm slowly to room temperature overnight (12 hours). Glacial acetic acid (100 mL) was then added slowly to this mixture at room temperature. After 4 hours at room temperature, the resultant solution was quenched with 80 mL of water, followed by the careful addition of 20 g of $NaHCO_3$. After separating the layers, the aqueous fraction was washed with DCM three times. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant crude oil was purified by FCC (SiO_2, 10-25% EtOAc in hexanes) to provide 19.33 g of the desired ***(R,S,S)*-4a** (81 % yield) as a pale yellow oil and 1.30 g (6 % yield) of the starting material **SI-2a** (87% yield, BRSM).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.29 (t, *J* = 7.8 Hz, 2H), 6.88 (dd, *J* = 7.9, 3.6 Hz, 4H), 5.40 (dd, *J* = 7.4, 3.9 Hz, 2H), 4.95 (d, *J* = 6.6 Hz, 2H), 4.82 (d, *J* = 6.6 Hz, 2H), 3.07 (s, 6H), 1.98 (dtd, *J* = 14.8, 7.3, 3.9 Hz, 2H), 1.86 (dq, *J* = 14.3, 7.3 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 6H).

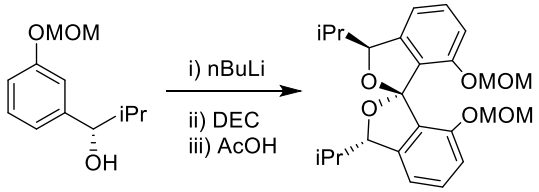
^{13}C NMR (126 MHz, Chloroform-*d*): δ 152.4, 145.6, 130.6, 127.8, 115.9, 114.0, 112.2, 93.3, 83.2, 55.6, 28.1, 9.74.

IR (film, cm^{-1}): 2962, 2934, 1614, 1599, 1479, 1256, 1152, 1002, 960.

$[\alpha]_D$: –67.8 (c = 0.083 in CH_2Cl_2).

ESI-HRMS: Calcd. for $C_{23}H_{29}O_6^+$ 401.1964 $[M+H]^+$, found 401.1958.

(*1R,3S,3'S*)-3,3'-diisopropyl-7,7'-bis(methoxymethoxy)-3H,3'H-1,1'-spirobi[isobenzofuran] ((*R,S,S*)-4b)



SI-2b **(*R,S,S*)-4b**

The solution of alcohol **SI-2b** (175 mg, 0.83 mmol) in PhMe (3.0 mL) was cooled to 0 °C followed by the addition of 2.5 M solution *n*-butyllithium in hexanes (0.67 mL, 1.67 mmol) over 35-minute period. The resultant reaction mixture was then warmed to room temperature and stirred for 4 hours, before being cooled to 0 °C again. Diethyl carbonate (55 μL, 0.45 mmol) was slowly added over 40 minutes. Subsequently, the resultant reaction mixture was allowed to warm slowly to room temperature overnight (11 hours). To this reaction mixture, glacial acetic acid (1.0 mL) was then added slowly, and the resultant solution was left stirring for 4 hours before being quenched with 3 mL of saturated $NaHCO_3$ solution. After separating the layers, the aqueous fraction was extracted with DCM three times. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The subsequent purification by FCC (SiO_2, 10-25% EtOAc in hexanes) resulted in 81 mg of the desired ***(R,S,S)*-4b** (43.4 % yield) as a pale yellow oil and 72 mg (41%) of the starting material **SI-2b** (83% yield, BRSM).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.30 (t, *J* = 7.8 Hz, 2H), 6.96 – 6.91 (m, 4H), 5.32 (d, *J* = 3.3 Hz, 2H), 4.95 (d, *J* = 6.6 Hz, 2H), 4.80 (d, *J* = 6.7 Hz, 2H), 3.14 (s, 6H), 2.23 (pd, *J* = 6.9, 3.4 Hz, 2H), 1.11 (d, *J* = 6.9 Hz, 6H), 0.92 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (176 MHz, Chloroform-*d*): δ 152.9, 145.2, 130.4, 128.4, 114.4, 112.0, 93.7, 85.9, 55.8, 32.1, 18.9, 16.7.

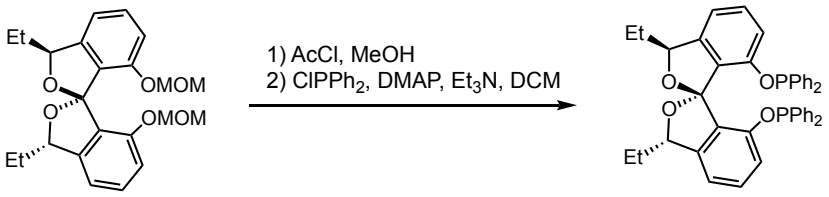
$[\alpha]_D$: –32.9 (c = 1.00 in CH_2Cl_2)

IR (film, cm^{-1}): 2962, 2930, 2849, 1653, 1465, 1209, 1151, 1079, 995, 969.

ESI-HRMS: Calcd. for $C_{25}H_{33}O_6^+$ 429.2272 $[M+H]^+$, found 429.2268.

A) One-pot synthesis for the diphosphinite ligand L7 (performed following the published procedures described in Ref.1):

(((*1R,3S,3'S*)-3,3'-diethyl-3H,3'H-1,1'-spirobi[isobenzofuran]-7,7'-diyl)bis(oxy))bis(diphenylphosphane) ((*R,S,S*)-SPIRAPO, L7)



(*R,S,S*)-4a (*R,S,S*)-SPIRAPO (L7)

The solution of spiroketal **(*R,S,S*)-4a** (40 mg, 0.10 mmol) in methanol (1.0 mL) was cooled to 0 °C and acetyl chloride (14 µL, 0.20 mmol) was added to this solution dropwise. The reaction mixture was then warmed to room temperature, stirred for 6 hours, and the volatiles were removed *in vacuo*. To the resultant crude oil of diol in the reaction vessel, 4-dimethylaminopyridine (1.2 mg, 0.01 mmol) and DCM (1.0 mL) were added, and to this solution triethylamine (0.13 mL, 1.0 mmol) and chlorodiphenylphosphine (46 µL, 0.25 mmol) were slowly added over 30 minutes. Thus obtained solution was left stirring for 12 hours, before being concenrated *in vacuo*, and purified by FCC (SiO_2 treated with 5% TEA, 4%→ 9% EtOAc in hexanes) to afford **(*R,S,S*)-SPIRAPO (L7)** (34 mg, 56% yield) as a white solid.

^{1}H NMR (399.54 MHz, Chloroform-*d*): δ 7.31-7.21 (m, 12H), 7.14 (t, J = 7.4 Hz, 2H), 7.06 (m, 6H), 6.97 – 6.90 (m, 4H), 6.86 – 6.81 (m, 2H), 5.26 (dd, J = 8.2, 4.2 Hz, 2H), 1.57 (m, 2H), 1.41 (m, 2H), 0.87 (t, J = 7.4 Hz, 6H).

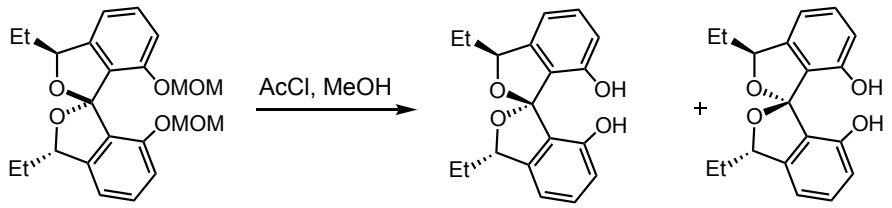
^{13}C NMR (100 MHz, Chloroform-*d*): δ 152.4, 152.3, 146.3, 140.1, 139.9, 139.9, 139.7, 130.7, 130.6, 130.5, 129.7, 129.6, 129.5, 128.9, 128.4, 128.3, 128.3, 128.2, 115.3, 115.2, 115.1, 114.7, 82.9, 28.0, 10.3.

^{31}P NMR: (161.75 MHz, $CDCl_3$) δ 105.3

ESI-HRMS: Calcd. for $C_{43}H_{39}O_4P_2^+$ 681.2317 $[M+H]^+$, found 681.2316.

B) Two-step synthesis of diphosphinite ligands L2–L10:

Formation of (*R,S,S*)- and (*S,S,S*)-SPIROLs from (*R,S,S*)-4a:



(*R,S,S*)-4a **(*R,S,S*)-SPIROL** **(*S,S,S*)-SPIROL**

The deprotection of the MOM group using AcCl in MeOH for 6 hours at room temperature provided less thermodynamically stable **(*R,S,S*)-SPIROL** is the major product. However, exposure of this compound to SiO_2 or other acidic conditions results in epimerization leading to **(*S,S,S*)-SPIROL**. These results agree with the calculated ΔG^o = 1.0 kcal/mol favoring **(*S,S,S*)-SPIROL**. Consequently, neutralizing HCl upon completion of MOM deprotection yields the material enriched in **(*R,S,S*)-SPIROL**, while performing chromatographic purification of the concentrated reaction mixture provides **(*S,S,S*)-SPIROL**-enriched material, as described below.

–Deprotection leading to (*R,S,S*)-SPIROL-enriched material:

Spiroketal **(*R,S,S*)-4a** (1.38 g, 3.44 mmol) was dissolved in MeOH (15 mL). This solution was cooled to 0 °C, and then acetyl chloride (480 μL, 6.90 mmol) was added slowly. The resultant reaction mixture was warmed to room temperature and stirred for 6 hours before being quenched with a saturated solution of $NaHCO_3$. The aqueous phase was extracted three times with DCM, and then combined organic phases were dried with Na_2SO_4, and concentrated *in vacuo* to afford an oil enriched in ***(R,S,S)*-SPIROL** (400.9 mg, 93% yield, dr = 1:7.1 of **(*S,S,S*)-SPIROL:(*R,S,S*)-SPIROL**. This mixture was used in the subsequent reactions without additional purification.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.34 (t, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 7.5, 2H), 6.77 (d, *J* = 8.0, 2H), 5.41 (dd, *J* = 6.7, 4.1 Hz, 2H), 4.73 (s, 2H), 2.07 (m, 2H), 1.83 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 151.9, 145.4, 132.3, 123.3, 115.5, 113.6, 83.1, 27.76, 9.18.

ESI-HRMS: Calcd. for $C_{19}H_{21}O_4^+$ 314.1440 $[M+H]^+$, found 314.1435.

–Deprotection leading to (*S,S,S*)-SPIROL-enriched material:

The solution of spiroketal **(*R,S,S*)-4a** (2.82 g, 7.04 mmol) in MeOH (35 mL) was cooled to 0 °C, and then acetyl chloride (1.0 mL, 14.1 mmol) was added slowly. The reaction mixture was warmed to room temperature. After 6 hours, this solution was concentrated *in vacuo*, and purified by FCC (SiO_2, 30%→40% EtOAc in hexanes) to obtain oil enriched in **(*S,S,S*)-SPIROL** (2.15 g, 98% yield 1:5.7:11.0 of **(*S,R,S*)-SPIROL:(*R,S,S*)-SPIROL:(*S,S,S*)-SPIROL**).

This material could be further enriched to generate pure **(*S,S,S*)-SPIROL** using the following recrystallization protocol. Thus, 2.0 g of the SPIROL mixture enriched in (*S,S,S*)-diastereomer and

obtained above was placed into a dry 50 mL Erlenmeyer flask and hot DCM was quickly added dropwise by a pipette to the flask while constant swaying movement was maintained. Once all solids were dissolved in hot DCM, the flask was then transferred and placed into a glass jar prefilled with hexanes. The jar was capped and hexanes were allowed to slowly diffuse into the flask. After 5 days, colorless hexagonal crystals were grown in the solution. The mother liquid was filter off and crystals were washed by ice-cold hexanes and dried *in vacuo* to afford pure **(*S*,*S*,*S*)-SPIROL.**

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.31 (t, *J* = 7.8 Hz, 2H), 6.86 (d, *J* = 7.5 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 2H), 5.27 (dd, *J* = 7.6, 4.4 Hz, 2H), 4.60 (s, 2H), 1.99 – 1.85 (m, 4H), 1.07 (t, *J* = 7.3 Hz, 6H).

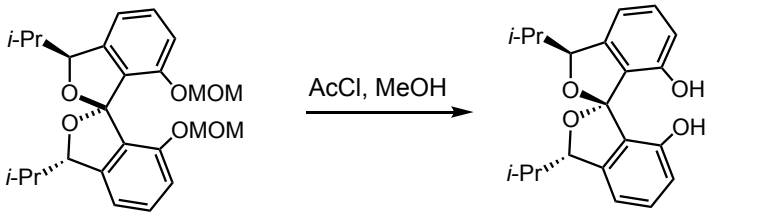
^{13}C NMR (126 MHz, Chloroform-*d*): δ 151.7, 145.2, 132.0, 123.4, 115.5, 113.8, 84.9, 30.6, 9.74.

IR (powder, cm^{-1}): 3299 (br), 2971, 2961, 2928, 1625, 1604, 1476, 1350, 1251, 1202, 1162, 1058, 1004, 959, 828.

$[\alpha]_D$: –42.2 (c = 0.20 in CH_2Cl_2).

ESI-HRMS: Calcd. for $C_{19}H_{21}O_4^+$ 314.1440 $[M+H]^+$, found 314.1435.

Formation of (*R*,*S*,*S*)-*i*-Pr-SPIROL (5b) from (*R*,*S*,*S*)-4b.



(*R*,*S*,*S*)-4a **(*R*,*S*,*S*)-*i*-Pr-SPIROL (5b)**

The solution of spiroketal **(*R*,*S*,*S*)-4b** (77.0 mg, 0.18 mmol) in MeOH (1.5 mL) was cooled to 0 °C, and then acetyl chloride (24 μL, 0.36 mmol) was added slowly. The resultant reaction mixture was warmed to room temperature, stirred for 14 hours and then was quenched with a saturated solution of $NaHCO_3$. The aqueous phase was extracted three times with DCM, and then the combined organic phases were dried with Na_2SO_4, and concentrated *in vacuo* to afford diol ***(R,S,S)-i*-Pr-SPIROL (5b)** as a white solid (51.1 mg, 83% yield).

^{1}H NMR (401 MHz, Methanol-d_4): δ 7.18 (t, *J* = 7.7 Hz, 2H), 6.73 (d, *J* = 7.5 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 2H), 5.17 (d, *J* = 3.3 Hz, 2H), 2.17 (pd, *J* = 6.8, 3.4 Hz, 2H), 1.07 (d, *J* = 6.9 Hz, 6H), 0.86 (d, *J* = 6.9 Hz, 6H).

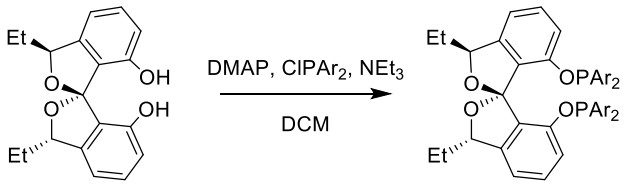
^{13}C NMR (100 MHz, Methanol-d_4): δ 153.41, 144.80, 130.04, 125.39, 113.81, 111.46, 85.92, 32.11, 18.31, 15.50.

$[\alpha]_D$: –32.4 (c = 0.50 in CH_2Cl_2).

IR (film, cm^{-1}): 3408 (br), 2961, 2930, 2873, 1743, 1715, 1601, 1457, 1343, 985, 836.

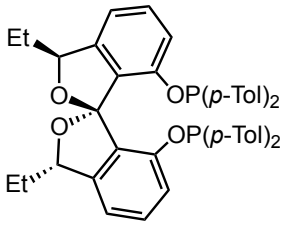
ESI-HRMS: Calcd. for $C_{21}H_{25}O_4^+$ 341.1747 $[M+H]^+$, found 341.1743.

General procedure for the formation of (*R,S,S*)- ligands L8 and L9 from (*R,S,S*)-SPIROL:



(*R,S,S*)-5a (*R,S,S*)-6

(*R,S,S*)-SPIROL-enriched material (7.1:1 = **(*R,S,S*)-SPIROL:(*S,S,S*)-SPIROL**) from above (100 mg, 0.32 mmol), 4-dimethylaminopyridine (6.4 mg, 0.050 mmol) were dissolved in dry DCM (6.0 mL) at room temperature, and to this solution triethylamine (0.51 mL, 3.9 mmol) and chlorodiarylphosphine (0.77 mmol) were added over 30 min. After 12 h, the reaction mixture was concentrated *in vacuo*, and the crude oil was purified by FCC (SiO_2 pretreated with 5% TEA, 4%→ 9% EtOAc in hexanes) to afford **(*R,S,S*)-** ligand **L8** or **L9**.



(*R,S,S*)-ligand (L8)

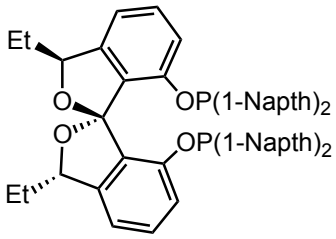
The procedure from above provided **L8** as a white foam, 180.0 mg, 76% yield.

^{1}H NMR (500 MHz, Benzene-d_6): δ 7.31 (t, *J* = 7.9 Hz, 6H), 7.09 (t, *J* = 7.6 Hz, 4H), 7.03 (t, *J* = 7.8 Hz, 2H), 6.80 (dd, *J* = 14.4, 7.7 Hz, 8H), 6.57 (d, *J* = 7.5 Hz, 2H), 5.32 (dd, *J* = 8.2, 4.5 Hz, 2H), 1.93 (d, *J* = 3.8 Hz, 12H), 1.57 – 1.45 (m, 4H), 0.92 (t, *J* = 7.3 Hz, 6H).

^{13}C NMR (126 MHz, Benzene-d_6): δ 146.9, 139.3, 138.6, 130.9, 130.7, 130.2, 130.1, 129.9, 129.2, 129.1, 129.0, 115.4, 115.2, 114.4, 82.8, 28.3, 20.8, 10.5.

^{31}P NMR (202 MHz, Benzene-d_6): δ 106.24.

ESI-HRMS: Calcd. for $C_{47}H_{47}O_4P_2^+$ 737.2944 $[M+H]^+$, found 737.2941.



(*R,S,S*)-ligand (L9)

The procedure from above provided **L9** as a white foam, 230.0 mg, 81% yield.

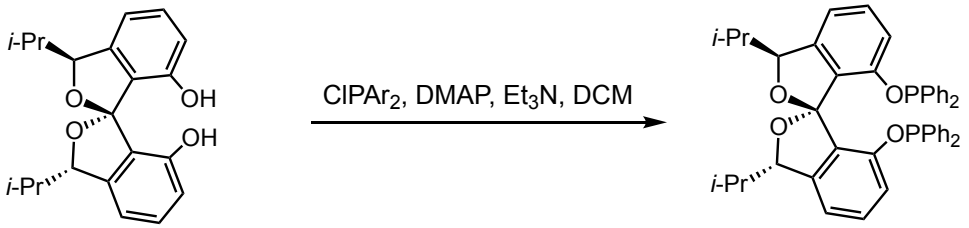
^{1}H NMR (400 MHz, Benzene-d_6): δ 8.43 (ddd, *J* = 17.8, 8.1, 3.4 Hz, 4H), 7.48 – 7.43 (m, 8H), 7.41 (d, *J* = 8.2 Hz, 4H), 7.25 – 7.15 (m, 4H), 7.07 – 6.94 (m, 8H), 6.90 (t, *J* = 7.6 Hz, 2H), 6.70 (t, *J* = 7.8 Hz, 2H), 6.22 (d, *J* = 7.5 Hz, 2H), 5.09 (dd, *J* = 9.6, 3.5 Hz, 2H), 1.21 – 1.04 (m, 4H), 0.65 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (100 MHz, Benzene-d_6): δ 152.5, 146.4, 145.5, 136.7, 135.3, 134.7, 133.5, 131.7, 130.5, 130.2, 128.6, 128.3, 126.5, 126.4, 125.8, 125.7, 125.4, 125.0, 121.1, 115.5, 114.3, 113.9, 83.1, 28.1, 10.5.

^{31}P NMR (202 MHz, Benzene-d_6) δ 92.46.

ESI-HRMS Calcd. for $C_{59}H_{47}O_4P_2^+$ 881.2944 $[M+H]^+$, found 881.2938.

Preparation of (R,S,S)-ligand (L10):



(*R,S,S*)-*i*-Pr-SPIROL (5b) **(*R,S,S*)-ligand (L10)**

(*R,S,S*)-*i*-Pr-SPIROL (5b) (49 mg, 0.14 mmol) and 4-dimethylaminopyridine (2.9 mg, 0.022 mmol) were dissolved in dry DCM (2.0 mL) at room temperature, and to this mixture triethylamine (0.23 mL, 1.8 mmol) and chlorodiphenylphosphine (66 μL, 0.36 mmol) were added over 30 minutes. This mixture was stirred for 12 hours, before being concentrated *in vacuo*, and purified by FCC (SiO_2 treated with 5% TEA, 1% TEA in hexanes) to afford **(*R,S,S*)-ligand L10** (84 mg, 84% yield) as a white solid.

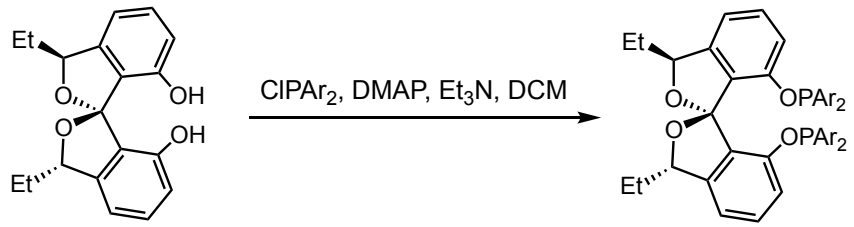
^{1}H NMR (500 MHz, Benzene-d_6): δ 7.47 – 7.40 (m, 4H), 7.20 (q, *J* = 10.9, 9.3 Hz, 6H), 7.02 – 6.95 (m, 8H), 6.91 (d, *J* = 5.5 Hz, 6H), 6.66 (d, *J* = 7.5 Hz, 2H), 5.32 (d, *J* = 4.4 Hz, 2H), 1.88 (dq, *J* = 11.1, 6.7 Hz, 2H), 0.96 (d, *J* = 6.8 Hz, 6H), 0.77 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (126 MHz, Benzene-d_6): δ 153.3, 146.7, 141.2, 141.1, 140.8, 130.9, 130.8, 130.7, 130.6, 129.8, 129.3, 128.8, 128.7, 128.6, 128.6, 116.3, 116.1, 115.6, 86.1, 32.5, 19.7, 17.6.

^{31}P NMR (202 MHz, Benzene-d_6): δ 107.75.

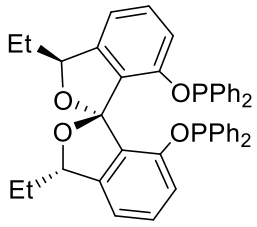
ESI-HRMS: Calcd. for $C_{45}H_{43}O_4P_2^+$ 709.2631 $[M+H]^+$, found 709.2636.

General procedure for the formation of (*S,S,S*)- ligands L4–L6 from (*S,S,S*)-SPIROL:



(*S,S,S*)-SPIROL **(*S,S,S*)-ligands (L4–L6)**

Recrystallized ***(S,S,S)*-SPIROL** (100 mg, 0.32 mmol) and 4-dimethylaminopyridine (6.4 mg, 0.05 mmol) were dissolved in dry DCM (6.0 mL) at room temperature, and to this solution triethylamine (0.51 mL, 3.9 mmol) and chlorodiarylphosphine (0.77 mmol) were added over 30 minutes. After stirring for 12 hours, this solution was concentrated *in vacuo*, and the resultant crude oil was purified by FCC (SiO_2 treated with 5% TEA, 4%→ 9% EtOAc in hexanes) to afford **(*S,S,S*)-ligands L4–L6.**



(*S,S,S*)-SPIRAPO ligand L4

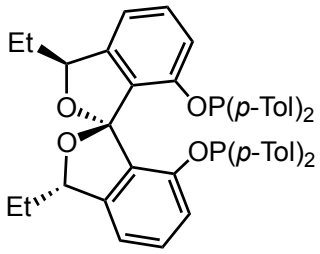
Following the general procedure outlined above, product **L4** was obtained as a white foam, 197 mg, 90% yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.34 – 7.19 (m, 12H), 7.15 (t, *J* = 7.7 Hz, 2H), 7.13 – 6.99 (m, 6H), 6.97 (t, *J* = 7.4 Hz, 4H), 6.71 (d, *J* = 7.5 Hz, 2H), 4.78 (dd, *J* = 7.2, 4.5 Hz, 2H), 1.89 – 1.72 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 145.8, 130.8, 130.6, 130.5, 130.5, 129.8, 129.6, 129.6, 129.0, 128.2, 128.3, 115.1, 114.7, 84.2, 30.2, 9.74.

^{31}P NMR (202 MHz, Chloroform-*d*): δ 104.21.

ESI-HRMS: Calcd. for $C_{43}H_{39}O_4P_2^+$ 681.2317 $[M+H]^+$, found 681.2318.



(*S,S,S*)-SPIRAPO ligand (L5)

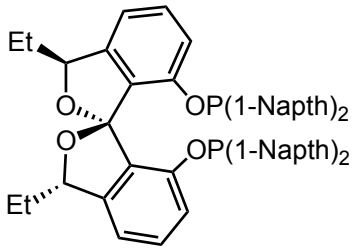
Following the general procedure outlined above, product **L5** was obtained as a white foam, 230 mg, 97% yield

^{1}H NMR (500 MHz, Benzene-d_6): δ 7.35 (dd, *J* = 8.1, 3.5 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 4H), 7.03 (t, *J* = 7.7 Hz, 6H), 6.84 (d, *J* = 7.7 Hz, 4H), 6.77 (d, *J* = 7.6 Hz, 4H), 6.55 (d, *J* = 7.5 Hz, 2H), 4.94 (t, *J* = 5.7 Hz, 2H), 1.95 (d, *J* = 6.8 Hz, 12H), 1.88 – 1.77 (m, 4H), 1.05 (t, *J* = 7.3 Hz, 6H),

^{13}C NMR (126 MHz, Benzene-d_6): δ 153.0, 152.9, 146.2, 139.4, 138.7, 137.8, 137.7, 137.5, 137.4, 131.1, 130.9, 130.2, 130.1, 130.0, 129.1, 129.0, 129.0, 115.0, 114.8, 114.4, 84.0, 30.0, 20.9, 20.9, 9.67.

^{31}P NMR (202 MHz, Benzene-d_6): δ 105.47.

ESI-HRMS: Calcd. for $C_{47}H_{47}O_4P_2^+$ 737.2944 $[M+H]^+$, found 737.2943.



(*S,S,S*)-SPIRAPO ligand (L6)

Following the general procedure outlined above, product **L6** was obtained as a white foam, 211 mg, 74% yield.

^{1}H NMR (500 MHz, Benzene-d_6): δ 8.54 (dd, *J* = 8.3, 3.4 Hz, 2H), 8.40 (dd, *J* = 8.4, 3.5 Hz, 2H), 7.53 – 7.45 (m, 10H), 7.28 (t, *J* = 6.2 Hz, 2H), 7.12 (m, 4H), 7.05 (td, *J* = 7.6, 3.9 Hz, 6H), 6.95 (td, *J* = 7.5, 4.7 Hz, 4H), 6.66 (t, *J* = 7.8 Hz, 2H), 6.08 (d, *J* = 7.5 Hz, 2H), 4.40 (dd, *J* = 6.6, 4.7 Hz, 2H), 1.58 (qd, *J* = 12.5, 11.3, 6.7 Hz, 4H), 0.84 (t, *J* = 7.3 Hz, 6H).

^{13}C NMR (126 MHz, Benzene-d_6): δ 152.9, 145.9, 136.3, 136.1, 135.9, 135.8, 135.2, 135.0, 133.9, 130.7, 130.6, 130.5, 130.4, 129.0, 127.0, 126.8, 126.3, 126.2, 126.1, 125.9, 125.9, 125.7, 125.5, 116.7, 114.8, 114.6, 114.4, 84.1, 30.0, 9.92.

^{31}P NMR (202 MHz, Benzene-d_6): δ 94.52.

ESI-HRMS: Calcd. for $C_{59}H_{47}O_4P_2^+$ 881.2944 $[M+H]^+$, found 881.2946.

General Procedure for Asymmetric Hydrogenation of Substrates 1 and 4:

A) Preparation of the catalyst solution:

$[Ir(cod)_2Cl]_2$ (3.4 mg, 0.005 mmol) and **(*R,S,S*)-SPIRAPO (L7)** (7.6 mg, 0.011 mmol) was added to a Schlenk tube with a stir bar under the atmosphere of nitrogen in the glovebox. After the Schlenk tube taken out of the glovebox, dry THF (1 mL) was added and the mixture was stirred at room temperature for 2 hours.

B) Hydrogenation of substrates 1 and 4:

An oven-dried 1-dram vial was charged with a stir bar, the corresponding substrate (0.1 mmol), I_2 (2.5 mg, 0.01 mmol) and dry THF (0.9 mL) under the nitrogen. To this solution was added 100 μL of the pre-mixed catalyst solution (see above). The vial equipped with a rubber septum containing 18G needle was then brought into the high-pressure reactor. The inner atmosphere of the reactor was purged by charging and carefully releasing 100 psi of hydrogen for 5 times before setting to 350 psi of hydrogen. The reaction was stirred at 350 psi of hydrogen for 10 hours before being removed from the reactor and concentrated *in vacuo*. The residual crude oil was purified by FCC (SiO_2, 10% EtOAc in hexanes) to obtain the desired product. The identity of the purified product was confirmed by NMR and ESI-HRMS and its purity and enantiomeric excess was analyzed by HPLC.

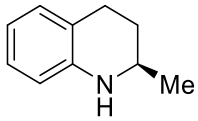
Note: benzoxazinone substrates **4e-4k** were reduced using (*S,R,R*)-enantiomer of SPIRAPO ligand **L7**.

Determination of Configuration:

1. The (*R*)-configuration of the 2-alkyal tetrahydroquinolines and (*S*)-configuration of 2-aryl tetrahydroquinolines is assigned based on the comparison of their optical rotation values with the corresponding parameters of the previously reported compounds. Ref. 5 provides optical rotation values for compounds **2d**, **2g** and **2i** and validates the absolute configuration of these derivatives by X-ray crystallographic analysis for the 2-(3-bromophenyl)-tetrahydroquinoline[5].

2. The (*R*)-configuration of tetrahydroquinoxalines is assigned based on the comparison of their optical rotation values with the corresponding parameters of the previously reported compounds. Ref. 6 provides the optical rotation values for compounds **4b**, **4c**, and **4d**, and the absolute configuration of these and other compounds described in Ref.6 is validated by the X-ray crystallographic analysis of *(R)*-7-Chloro-2-phenyl-1,2,3,4-tetrahydroquinoxaline.[6]

3. The absolute (*S*)-configuration of 3,4-dihydro-2*H*-1,4-benzoxazin-2-ones is assigned based on the comparison of their optical rotation values with the corresponding parameters of the previously reported compounds. Ref. 7 provides the optical rotation values for compound **(*R*)-4e,** which is validated by solving the X-ray crystal structure of (*S*)-3-(2-thienyl)-3,4-dihydro-2H-1,4-benzoxazin-2-one.[7]



(*R*)-2-methyl-1,2,3,4-tetrahydroquinoline (2a),

Known compound[8]; colorless oil, 14.5 mg, 99% yield, 95% ee

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.09 – 6.95 (m, 2H), 6.84 – 6.62 (m, 2H), 4.13 – 3.99 (br s, 1H), 3.50 (ddq, *J* = 9.8, 6.4, 3.5 Hz, 1H), 2.86 (ddd, *J* = 16.9, 11.2, 5.8 Hz, 1H), 2.77 (ddd, *J* = 16.5, 5.0, 3.6 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.70 (dddd, *J* = 13.2, 11.2, 9.9, 5.4 Hz, 1H), 1.32 (d, *J* = 6.3 Hz, 3H).

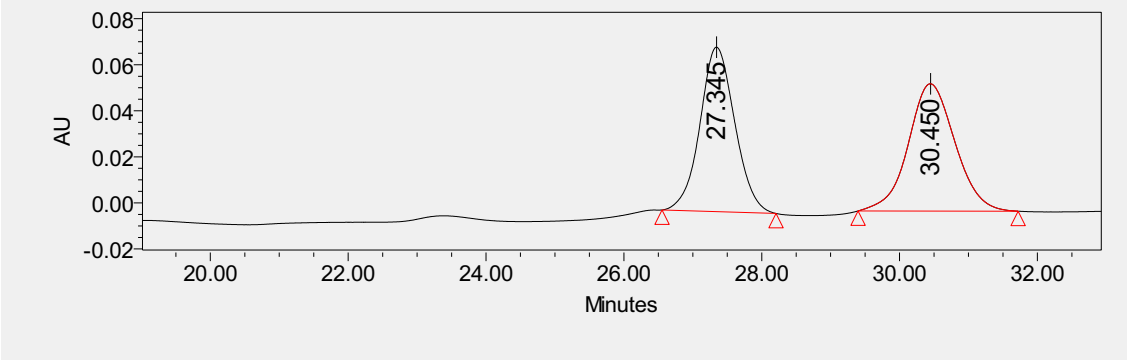
^{13}C NMR (176 MHz, Chloroform-*d*): δ 142.0, 129.4, 126.8, 122.8, 119.2, 115.8, 48.0, 29.5, 26.2, 21.7.

IR (powder, cm^{-1}): 3283, 3037, 2955, 2923, 2858, 1597, 1543, 1424, 1383, 1211, 1036, 958, 888 825.

$[\alpha]_D$: +79.8 (c = 1.00 in $CHCl_3$); **literature $[\alpha]_D$:** +84.3 (c = 0.20 in $CHCl_3$) for 99% ee.

ESI-HRMS: Calcd. for $C_{10}H_{14}N^+$ 148.1120 $[M+H]^+$, found 148.1118.

HPLC: (Chiralpak OJ-H column, 95:5 hexanes/isopropanol, 0.5 ml/min), tr = 26.3 min (minor, S), 28.9 min (major, R).



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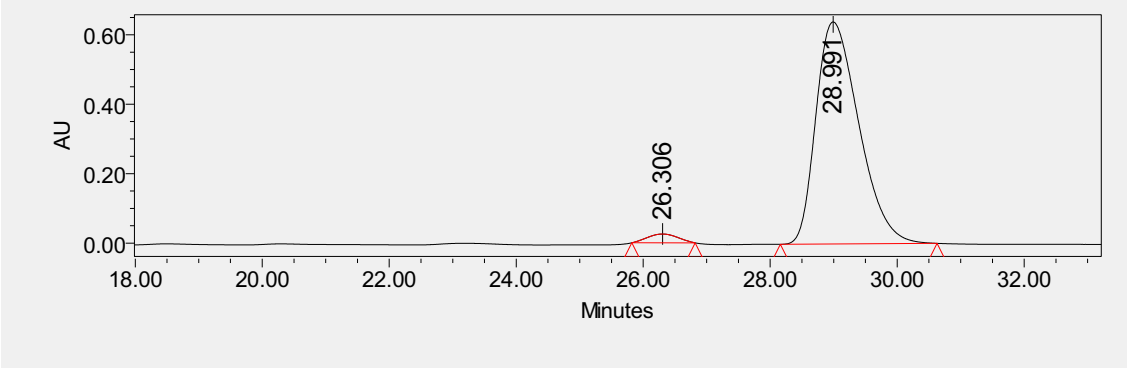
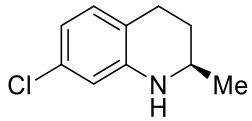
2	30.450	2601958	50.90	55287



	Retention Time	Area	% Area	Height
1	26.306	838726	2.72	25352
2	28.991	30024126	97.28	639683



(*R*)-7-chloro-2-methyl-1,2,3,4-tetrahydroquinoline (2b)

Known compound[4]; white solids, 17.1 mg, 94% yield, 93% ee.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.85 (dt, *J* = 8.0, 1.0 Hz, 1H), 6.54 (dd, *J* = 8.0, 2.1 Hz, 1H), 6.43 (d, *J* = 2.1 Hz, 1H), 3.75 (br s, 1H), 3.39 (dqd, *J* = 9.4, 6.3, 3.0 Hz, 1H), 2.85 – 2.62 (m, 2H), 1.96 – 1.87 (m, 1H), 1.62 – 1.49 (m, 1H), 1.20 (d, *J* = 6.3 Hz, 3H).

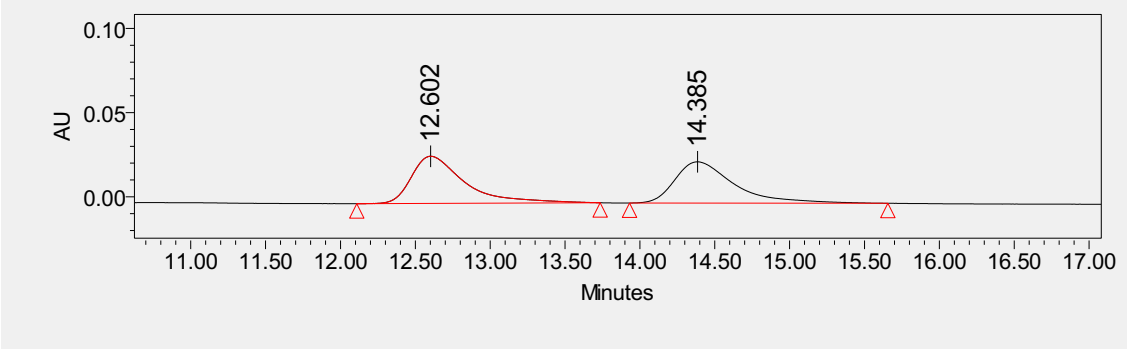
^{13}C NMR (100 MHz, Chloroform-*d*): δ 145.7, 131.9, 130.1, 119.3, 116.5, 113.2, 47.0, 29.7, 26.0, 22.5.

IR (powder, cm^{-1}): 3411, 3055, 2912, 1607, 1596, 1494, 1405, 1332, 1218, 1066, 1035, 970, 912, 901, 837.

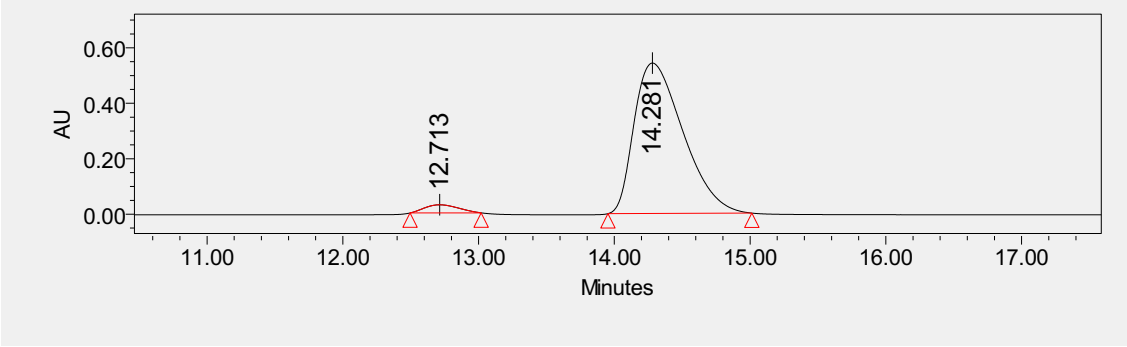
[α]$_D$: +61.1 (c = 0.25 in CH_2Cl_2); **literature [α]$_D$:** –68.5 (c = 0.5 in $CHCl_3$) for 90% ee.

ESI-HRMS: Calcd. for $C_{10}H_{13}ClN^+$ 182.0731 $[M+H]^+$, found 182.0733.

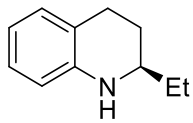
HPLC (Chiralpak OJ-H column, 92:8 hexanes/isopropanol, 1 ml/min), tr = 12.7 min (minor, S), 14.3 min (major, R).



	Retention Time	Area	% Area	Height
1	12.602	1888746	50.49	86618
2	14.385	1851983	49.51	75260



	Retention Time	Area	% Area	Height
1	12.713	505853	3.59	29294
2	14.281	13572112	96.41	542294



(*R*)-2-ethyl-1,2,3,4-tetrahydroquinoline (2c)

Known compound[8]; colorless oil, 15.9 mg, 99% yield, 93% ee

^{1}H NMR (700 MHz, Chloroform-*d*): δ 6.98 – 6.93 (m, 2H), 6.59 (td, *J* = 7.3, 1.2 Hz, 1H), 6.49 – 6.47 (m, 1H), 3.77 (br s, 1H), 3.17 (dtd, *J* = 9.5, 6.4, 2.9 Hz, 1H), 2.81 (ddd, *J* = 16.6, 11.2, 5.6 Hz, 1H), 2.73 (dt, *J* = 16.2, 4.6 Hz, 1H), 1.97 (dddd, *J* = 12.6, 5.6, 3.9, 2.9 Hz, 1H), 1.59 (dddd, *J* = 12.8, 11.2, 9.7, 5.2 Hz, 1H), 1.54 – 1.50 (m, 2H), 0.99 (t, *J* = 7.5 Hz, 3H).

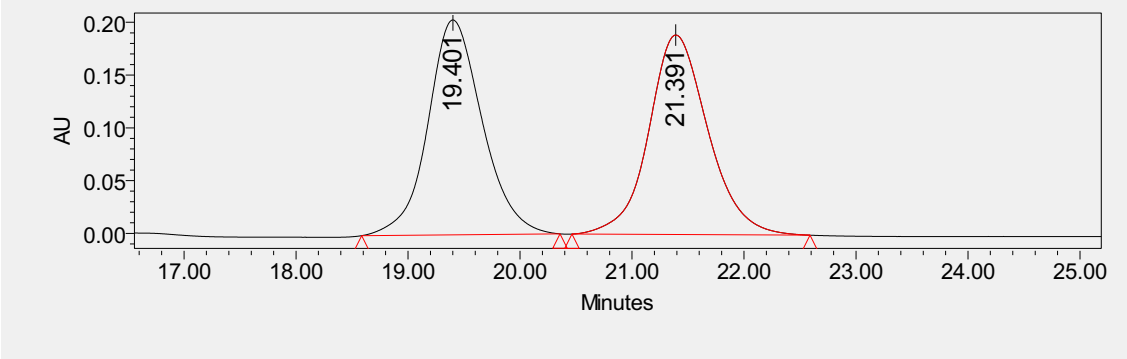
^{13}C NMR (176 MHz, Chloroform-*d*): δ 144.7, 129.2, 126.7, 121.4, 116.8, 114.0, 53.0, 29.4, 27.6, 26.4, 10.1.

IR (film, cm^{-1}): 3393, 2956, 2923, 2872, 2853, 1603, 1502, 1308, 1122, 745.

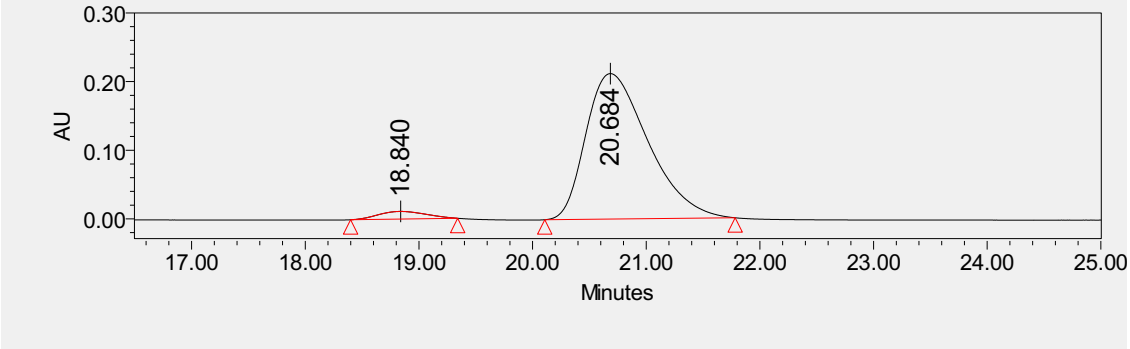
[α]$_D$: +72.4 (c = 1.02 in $CHCl_3$); **literature [α]$_D$:** +80.3 (c = 0.19 in $CHCl_3$) for 99% ee.

ESI-HRMS: Calcd. for $C_{11}H_{16}N^+$ 162.1277 $[M+H]^+$, found 162.1278.

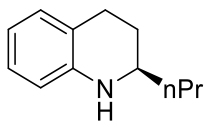
HPLC (Chiralpak OJ-H column, 90:10 hexanes/isopropanol, 0.5 ml/min), tr = 18.8 min (minor, S), 20.7 min (major, R).



	Retention Time	Area	% Area	Height
1	19.401	18166484	49.86	533752
2	21.391	18269512	50.14	494848



	Retention Time	Area	% Area	Height
1	18.840	324513	3.47	11151
2	20.684	9027447	96.53	211944



(*R*)-2-propyl-1,2,3,4-tetrahydroquinoline (2d)

Known compound[8]; colorless oil, 16.6 mg, 95% yield, 93% ee.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.06 – 6.89 (m, 2H), 6.58 (td, *J* = 7.4, 1.2 Hz, 1H), 6.46

(dd, *J* = 8.4, 1.3 Hz, 1H), 3.74 (br s, 1H), 3.24 (dtd, *J* = 9.4, 6.1, 2.9 Hz, 1H), 2.92 – 2.59 (m, 2H), 1.95 (dddd, *J* = 12.7, 5.6, 4.0, 2.9 Hz, 1H), 1.64 – 1.55 (m, 1H), 1.51 – 1.37 (m, 4H), 0.95 (t, *J* = 6.5 Hz, 3H).

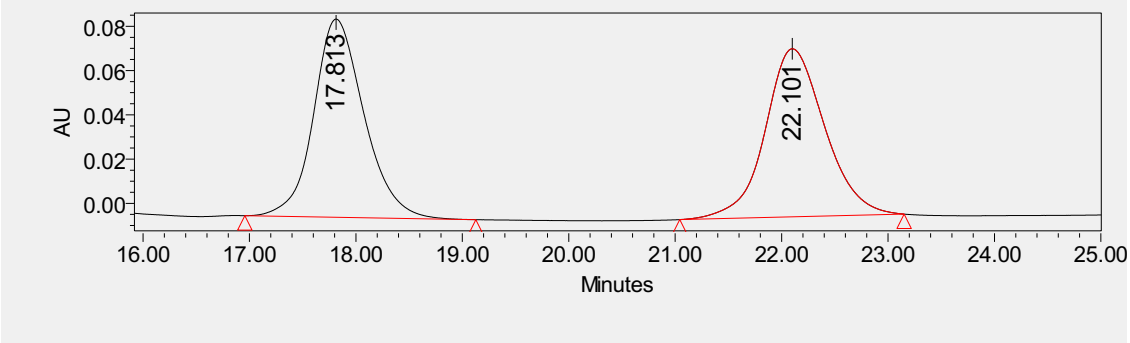
^{13}C NMR (100 MHz, Chloroform-*d*): δ 144.7, 129.2, 126.7, 121.4, 116.8, 114.0, 51.3, 38.9, 28.1, 26.4, 18.9, 14.2.

IR (film, cm^{-1}): 3395, 3331, 2956, 2927. 2870, 1601, 1502, 1457, 1309, 825, 781, 745.

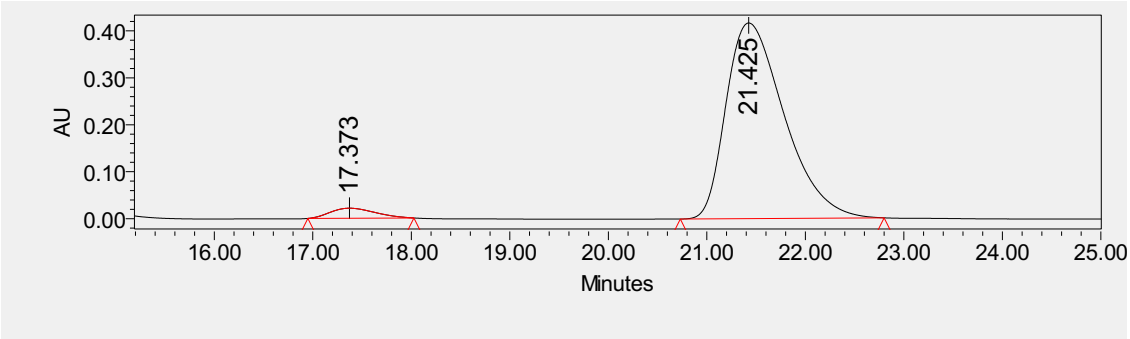
[α]$_D$: +74.3 (c = 1.21 in $CHCl_3$); **literature [α]$_D$:** +89.0 (c = 0.16 in $CHCl_3$) for 99% ee.

ESI-HRMS: Calcd. for $C_{12}H_{18}N^+$ 176.1433 $[M+H]^+$, found 176.1429.

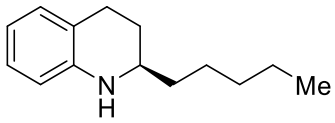
HPLC (Chiralpak OJ-H column, 90:10 hexanes/isopropanol, 0.5 ml/min), tr = 17.4 min (minor, S), 21.4 min (major, R).



	Retention Time	Area	% Area	Height
1	17.813	2945186	49.93	89523
2	22.101	2953952	50.07	75940



	Retention Time	Area	% Area	Height
1	17.373	675866	3.37	21407
2	21.425	19379505	96.63	416736



(*R*)-2-pentyl-1,2,3,4-tetrahydroquinoline (2e)

Known compound[5]; pale yellow clear oil, 19.7 mg, 97% yield, 94% ee

^{1}H NMR (500 MHz, Chloroform-d): δ 6.96 (t, J = 7.6 Hz, 2H), 6.60 (td, J = 7.3, 1.2 Hz, 1H), 6.51 – 6.44 (m, 1H), 3.77 (br s, 1H), 3.24 (dtd, J = 9.4, 6.3, 2.9 Hz, 1H), 2.88 – 2.69 (m, 2H), 2.03 – 1.91 (m, 1H), 1.60 (dddd, J = 13.0, 11.1, 9.5, 5.3 Hz, 1H), 1.50 (dt, J = 9.1, 5.8 Hz, 2H), 1.45 – 1.29 (m, 6H), 0.92 (t, J = 6.8 Hz, 3H).

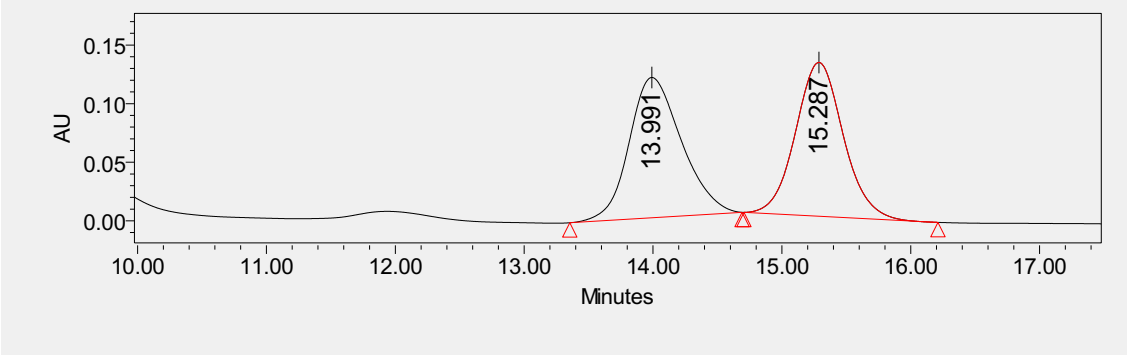
^{13}C NMR (126 MHz, Chloroform-d): δ 144.7, 129.2, 126.7, 121.4, 116.9, 114.0, 51.6, 36.7, 32.0, 28.1, 26.4, 25.4, 22.6, 14.1.

IR (film, cm^{-1}): 3369, 3059, 2956, 2926, 1463, 1340, 1113, 1076, 1018, 833.

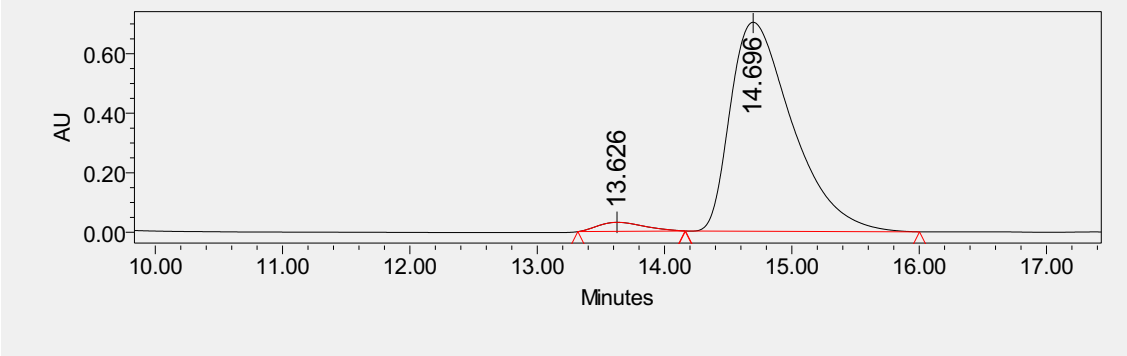
$[\alpha]_D$: +47.6 (c = 1.01 in CH_2Cl_2); **literature $[\alpha]_D$:** +51.4 (c = 1.0 in $CHCl_3$) for 90% ee.

ESI-HRMS: Calcd. for $C_{14}H_{22}N^+$ 204.1746 $[M+H]^+$, found 204.1747.

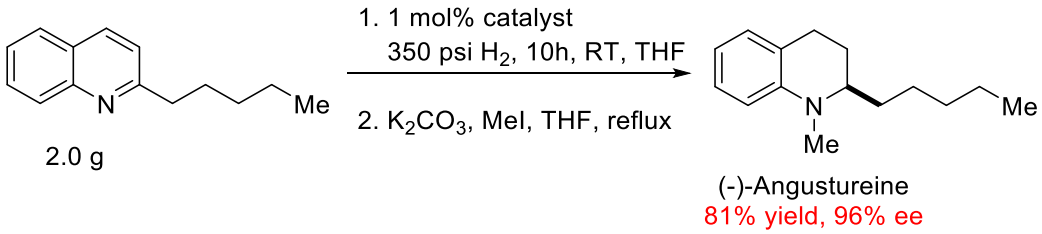
HPLC (Chiralpak OJ-H column, 90:10 hexanes/isopropanol, 0.5 ml/min), tr = 13.6 min (minor, S), 14.7 min (major, R).



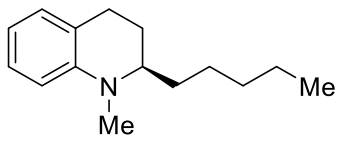
	Retention Time	Area	% Area	Height
1	13.991	2324435	49.95	83191
2	15.287	2328896	50.05	91094



	Retention Time	Area	% Area	Height
1	13.626	768900	3.13	30345
2	14.696	23758927	96.87	702236



Bis(1,5-cyclooctadiene)diiridium(I) dichloride (34 mg, 0.05 mmol) and (*R,S,S*)-SPIRAPO (76 mg, 0.11 mmol) were added to an oven-dried flask with a stir bar and sealed in the glovebox under the atmosphere of nitrogen. After the flask was taken out of the glovebox, dry THF (1 mL) was added and the mixture was stirred under the nitrogen atmosphere at room temperature for 2 hours. Dry solution of 2-pentylquinoline (2.0 g, 10.0 mmol) and I_2 (254.0 mg, 1.0 mmol) in THF (19 mL) was transferred to the flask with pre-mixed catalyst solution via a syringe. The flask was then brought into the high-pressure reactor and equipped with an 18G needle-penetrated vial septum. The inner atmosphere of the reactor was purged by charging and carefully releasing 100 psi of hydrogen for 5 times before setting to 350 psi of hydrogen. The reaction was stirred at 350 psi of hydrogen for 10 hours. After the reaction time the flask was taken out of the reactor. To this flask containing crude reaction mixture K_2CO_3 (4.10 g, 30.0 mmol) and MeI (1.25 mL, 20.0 mmol) were added, and the flask was fitted with a reflux condenser and refluxed for 17 hours before being cooled and quenched with DI water (50 mL). After separating the phases, the aqueous layer was extracted with DCM twice. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Crude was purified by FCC (SiO_2, 5-10% EtOAc in hexanes) to obtain the desired product as a pale yellow oil.



(*R*)-1-Methyl-2-pentyl-1,2,3,4-tetrahydroquinoline ((–)-(*R*)-angustureine).

Known compound[5]; pale yellow clear oil, 1.75 g, 81% yield (2 steps), 96% ee.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.12 – 7.04 (m, 1H), 6.96 (dd, *J* = 7.1, 1.7 Hz, 1H), 6.57 (td, *J* = 7.3, 1.1 Hz, 1H), 6.52 (d, *J* = 8.2 Hz, 1H), 3.23 (dq, *J* = 8.7, 4.2 Hz, 1H), 2.92 (s, 3H), 2.80

(ddd, *J* = 17.5, 11.4, 6.8 Hz, 1H), 2.65 (dt, *J* = 16.1, 4.3 Hz, 1H), 1.88 (ddt, *J* = 10.8, 7.4, 4.1 Hz, 2H), 1.64 – 1.55 (m, 1H), 1.46 – 1.23 (m, 7H), 0.89 (t, *J* = 6.9 Hz, 3H).

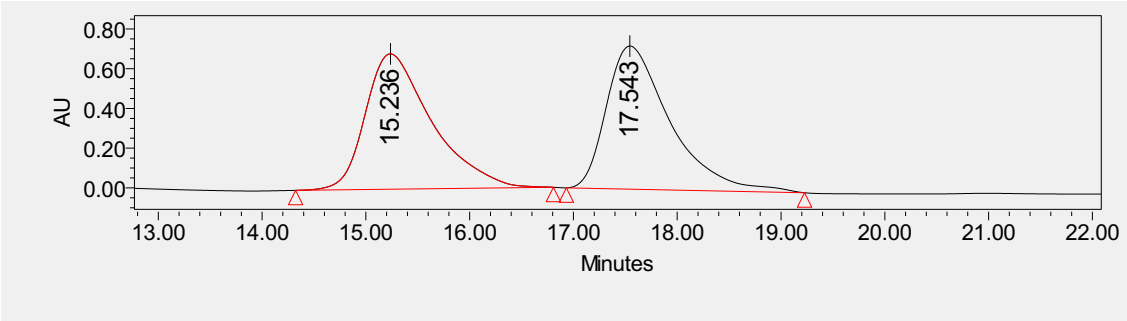
^{13}C NMR (126 MHz, Chloroform-*d*): δ 145.4, 128.6, 127.0, 121.8, 115.1, 110.4, 58.9, 37.9, 32.0, 31.2, 25.7, 24.4, 23.6, 22.7, 14.0.

IR (film, cm^{-1}): 2953, 2926, 2869, 2855, 2795, 1602, 1575, 1499, 1335, 1214, 742.

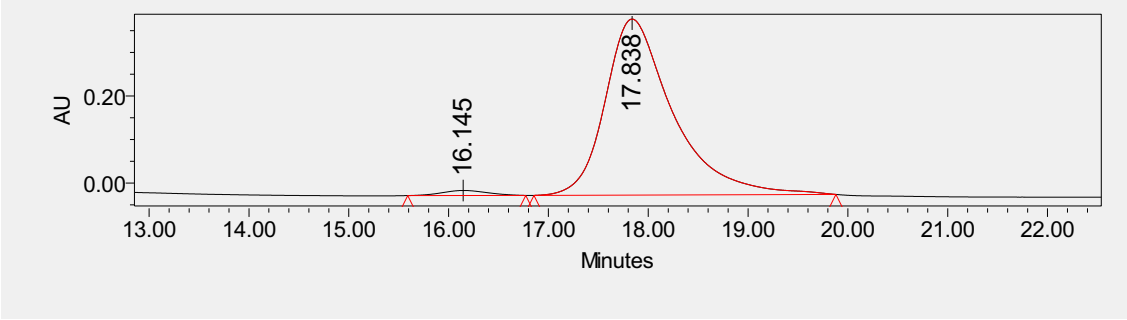
[α]$_D$: –9.6 (c = 1.32 in $CHCl_3$); **literature [α]$_D$:** –6.9 (c = 1.0 in $CHCl_3$) for 90% ee.

ESI-HRMS: Calcd. for $C_{15}H_{24}N^+$ 218.1902 $[M+H]^+$, found 218.1899.

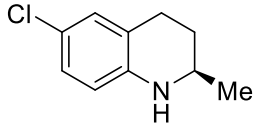
HPLC (Chiralpak OJ-H column, 99:1 hexanes/isopropanol, 0.4 ml/min), tr = 18.8 min (minor, S), 20.6 min (major, R).



	Retention Time	Area	% Area	Height
1	15.236	17439959	49.31	398804
2	17.543	17925412	50.69	422565



	Retention Time	Area	% Area	Height
1	16.145	364883	1.88	11521
2	17.838	19068464	98.12	403966



(*R*)-6-chloro-2-methyl-1,2,3,4-tetrahydroquinoline (2f)

Known compound[4]; colorless oil, 17.8 mg, 98% yield, 90% ee.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.94 – 6.84 (m, 2H), 6.36 (d, *J* = 8.4 Hz, 1H), 3.67 (br s, 1H), 3.36 (dqd, *J* = 9.3, 6.3, 2.9 Hz, 1H), 2.87 – 2.62 (m, 2H), 1.95 – 1.84 (m, 1H), 1.60 – 1.46 (m, 1H), 1.19 (d, *J* = 6.3 Hz, 3H).

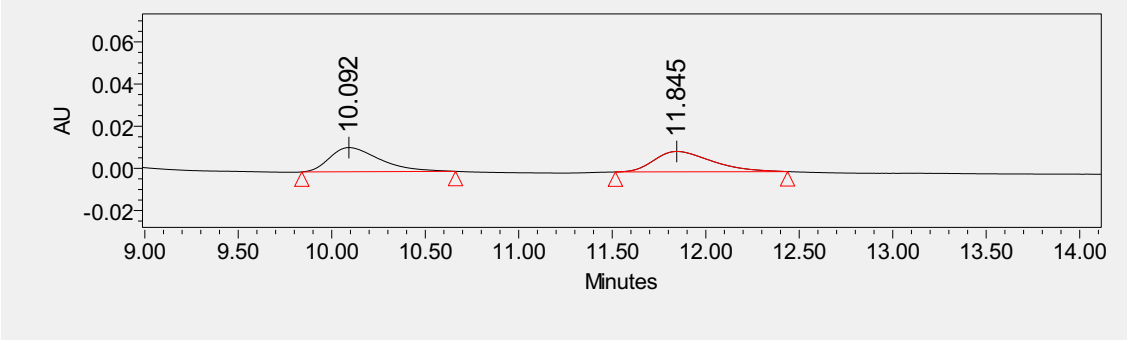
^{13}C NMR (100 MHz, Chloroform-*d*): δ 143.3, 128.8, 126.4, 122.6, 121.2, 114.9, 47.1, 29.7, 26.4, 22.5.

IR (film, cm^{-1}): 3404, 2964, 2926, 2849, 1604, 1492, 1298, 805.

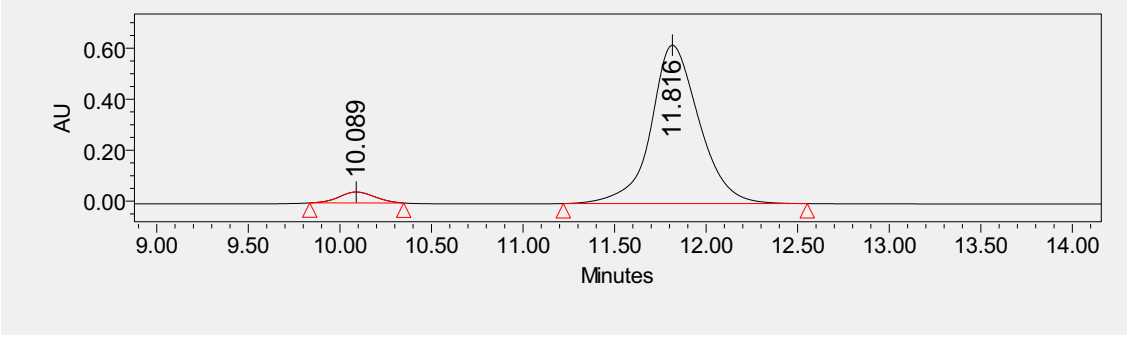
[α]$_D$: +77.6 (c = 0.50 in $CHCl_3$); **literature [α]$_D$:** –81.8 (c = 0.5 in $CHCl_3$) for 90% ee.

ESI-HRMS: Calcd. for $C_{10}H_{13}ClN^+$ 182.0731 $[M+H]^+$, found 182.0729.

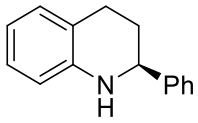
HPLC (Chiralpak OJ-H column, 92:8 hexanes/isopropanol, 1 ml/min), tr = 10.1 min (minor, S), 11.8 min (major, R).



	Retention Time	Area	% Area	Height
1	10.092	213628	50.77	11483
2	11.845	207115	49.23	9680



	Retention Time	Area	% Area	Height
1	10.089	577708	4.83	42946
2	11.816	11395334	95.17	621347



(*S*)-2-phenyl-1,2,3,4-tetrahydroquinoline (2g)

Known compound[5]; colorless oil, 19.2 mg, 92% yield, 89% ee.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.42 – 7.32 (m, 4H), 7.31 – 7.27 (m, 1H), 7.00 (dd, *J* = 7.4, 1.1 Hz, 2H), 6.65 (td, *J* = 7.4, 1.2 Hz, 1H), 6.56 – 6.50 (m, 1H), 4.43 (dd, *J* = 9.4, 3.3 Hz, 1H), 4.03 (br s, 1H), 2.92 (ddd, *J* = 16.2, 10.7, 5.5 Hz, 1H), 2.73 (dt, *J* = 16.3, 4.8 Hz, 1H), 2.12 (dq, *J* = 13.2, 4.5 Hz, 1H), 1.99 (dddd, *J* = 12.9, 10.6, 9.3, 5.1 Hz, 1H).

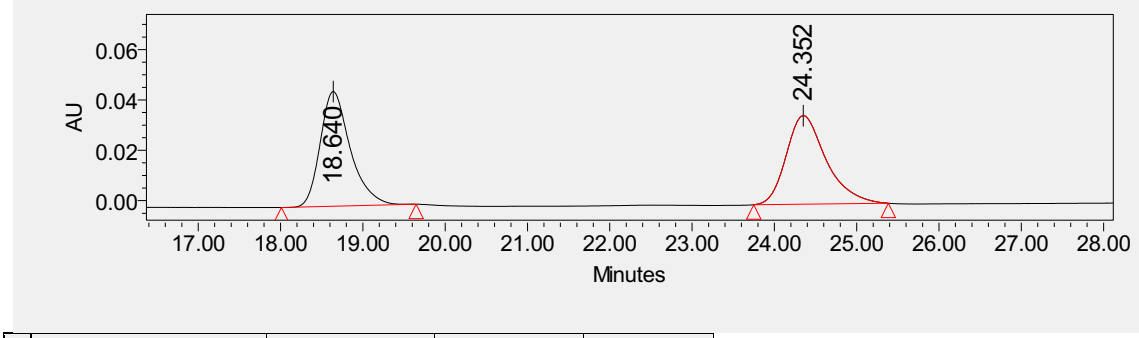
^{13}C NMR (100 MHz, Chloroform-*d*): δ 144.8, 144.7, 129.3, 128.6, 127.4, 126.9, 126.5, 120.9, 117.1, 114.0, 56.2, 31.0, 26.4.

IR (film, cm^{-1}): 3393, 3383, 3053, 2971, 2944, 2840, 1606, 1584, 1479, 1431, 1308, 1251, 1110, 1005, 924, 830, 815.

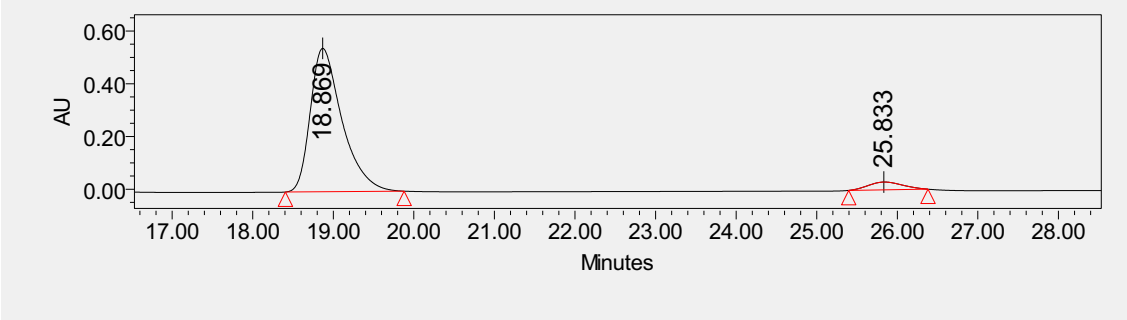
$[\alpha]_D$: –31.3 (c = 0.73 in $CHCl_3$); literature **$[\alpha]_D$:** –37.7 (c = 1.0 in $CHCl_3$) for 97% ee.

ESI-HRMS: Calcd. for $C_{15}H_{16}N^+$ 210.1277 $[M+H]^+$, found 210.1278.

HPLC (Chiralpak OD-H column, 95:5 hexanes/isopropanol, 0.6 ml/min), tr = 18.8 min (major, S), 25.8 min (minor, R).

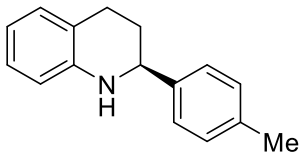


	Retention Time	Area	% Area	Height
1	18.640	1158602	49.43	45569
2	24.352	1185130	50.57	35183



	Retention Time	Area	% Area	Height

1	18.869	14861297	94.43	544071
2	25.833	875809	5.57	29625



(*S*)-2-(p-tolyl)-1,2,3,4-tetrahydroquinoline (2h)

Known compound[9]; colorless oil, 22.2 mg, 99% yield, 86% ee.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.29 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 7.7 Hz, 2H), 7.01 (t, *J* = 7.6 Hz, 2H), 6.65 (td, *J* = 7.4, 1.2 Hz, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 4.41 (dd, *J* = 9.5, 3.2 Hz, 1H), 4.00 (br s, 1H), 2.93 (ddd, *J* = 16.3, 10.9, 5.5 Hz, 1H), 2.75 (dt, *J* = 16.3, 4.7 Hz, 1H), 2.36 (s, 3H), 2.14 – 2.08 (m, 1H), 1.99 (dddd, *J* = 13.0, 10.9, 9.6, 5.0 Hz, 1H).

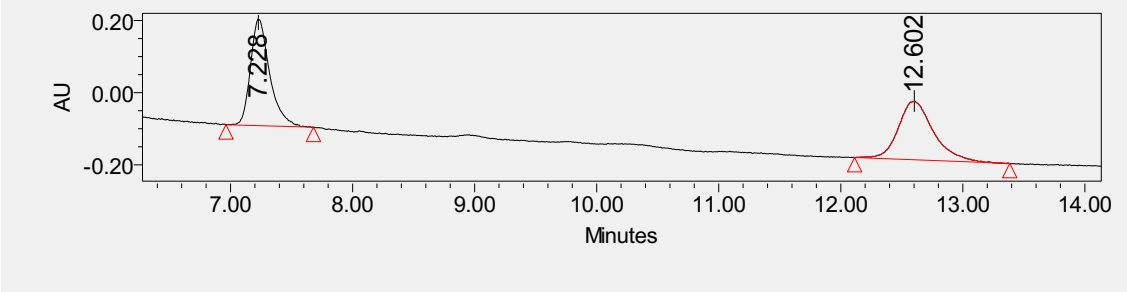
^{13}C NMR (176 MHz, Chloroform-*d*): δ 144.8, 141.8, 137.1, 129.3, 129.2, 126.9, 126. 5, 120.9, 117.1, 113.9, 56.0, 31.0, 26.5, 21.1.

IR (film, cm^{-1}): 3377, 3014, 2973, 2922, 2853, 1606, 1598, 1543, 1498, 1309, 1114, 1046, 971, 813.

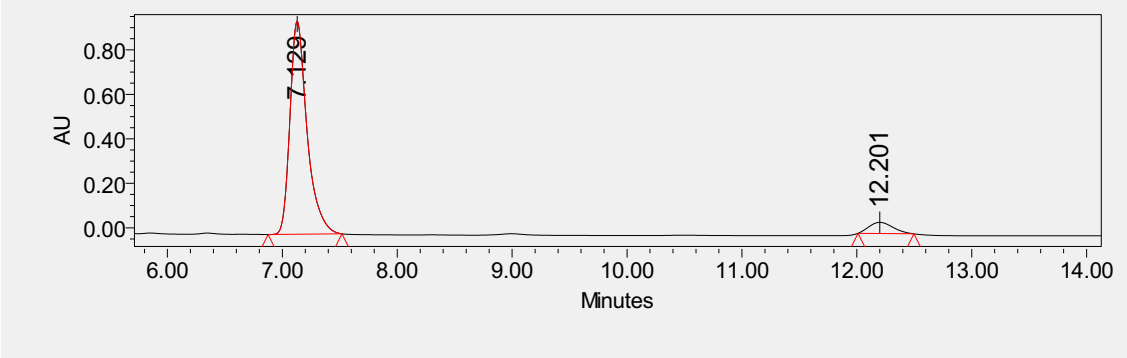
[α]$_D$: –15.7 (c = 0.68 in $CHCl_3$); literature **[α]$_D$:** –24.3 (c = 1.0 in $CHCl_3$) for 90% ee.

ESI-HRMS: Calcd. for $C_{16}H_{18}N^+$ 224.1434 $[M+H]^+$, found 224.1436.

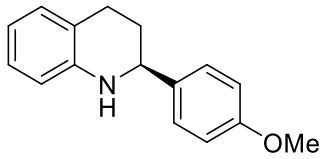
HPLC (Chiralpak OD-H column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 7.1 min (major, S), 12.2 min (minor, R).



	Retention Time	Area	% Area	Height
1	7.228	3232020	49.88	295451
2	12.602	3248172	50.12	162613



	Retention Time	Area	% Area	Height
1	7.129	9904243	93.17	957304
2	12.201	726272	6.83	50146



(*S*)-2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroquinoline (2i)

Known compound[5]; white solids, 23.4 mg, 98% yield, 91% ee.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.33 – 7.29 (m, 2H), 7.00 (t, *J* = 7.0 Hz, 2H), 6.91 – 6.86 (m, 2H), 6.64 (td, *J* = 7.4, 1.2 Hz, 1H), 6.54 – 6.50 (m, 1H), 4.40 – 4.36 (m, 1H), 3.98 (s, 1H), 3.81 (s, 3H), 2.92 (ddd, *J* = 16.4, 11.0, 5.5 Hz, 1H), 2.74 (dt, *J* = 16.3, 4.6 Hz, 1H), 2.08 (dd, *J* = 13.1, 4.3 Hz, 1H), 1.97 (dddd, *J* = 13.0, 11.0, 9.6, 5.0 Hz, 1H).

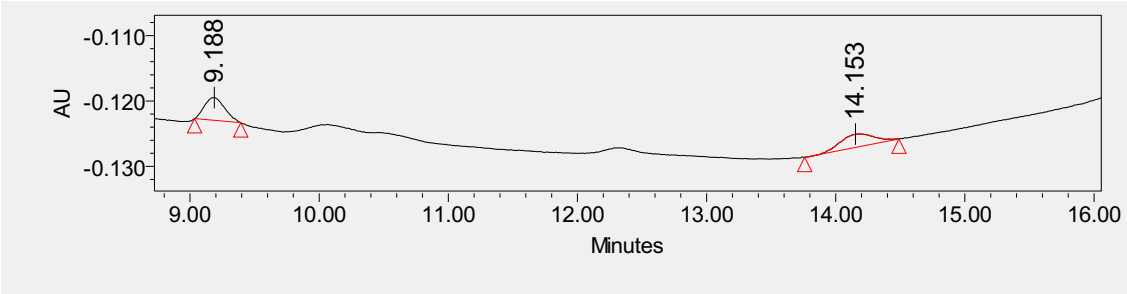
^{13}C NMR (176 MHz, Chloroform-*d*): δ 158.9, 144.8, 136.9, 129.3, 127.6, 126.8, 120.9, 117.1, 113.9, 113.9, 55.7, 55.3, 31.1, 26.5.

IR (film, cm^{-1}): 3381, 3012, 2959, 2839, 1604, 1551, 1248, 1175, 1028, 833.

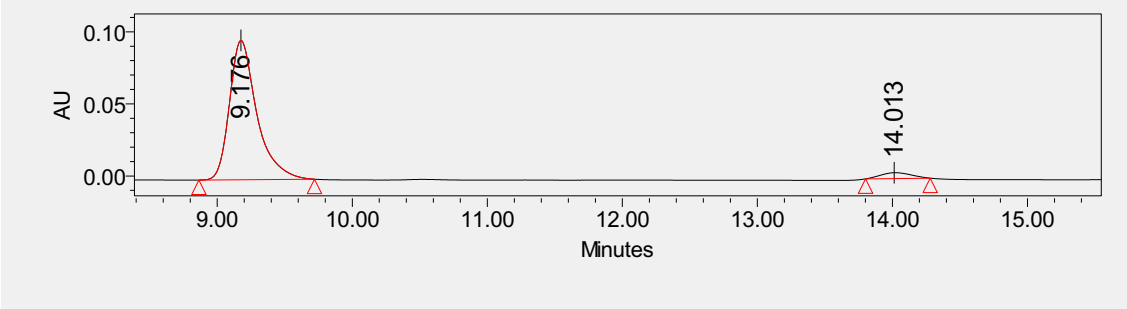
[α]$_D$: –24.7 (c = 0.22 in CH_2Cl_2); **literature [α]$_D$:** –18.6 (c = 1.0 in $CHCl_3$) for 98% ee.

ESI-HRMS: Calcd. for $C_{16}H_{18}NO^+$ 240.1383 $[M+H]^+$, found 240.1388.

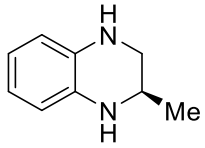
HPLC (Chiralpak OD-H column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 9.2 min (major, S), 14.0 min (minor, R).



	Retention Time	Area	% Area	Height
1	9.188	37815	50.96	3462
2	14.153	36388	49.04	2037



	Retention Time	Area	% Area	Height
1	9.176	1357374	95.54	96644
2	14.013	63407	4.46	4064



(*R*)-2-methyl-1,2,3,4-tetrahydroquinoxaline (4a)

Known compound[10]; yellow solids, 14.7 mg, 99% yield, 89% ee

^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.59 (ddt, *J* = 7.2, 3.9, 2.0 Hz, 2H), 6.55 – 6.46 (m, 2H), 3.60 (br s, 2H), 3.51 (dtd, *J* = 8.7, 6.3, 2.7 Hz, 1H), 3.32 (dd, *J* = 10.7, 2.8 Hz, 1H), 3.04 (dd, *J* = 10.7, 8.1 Hz, 1H), 1.19 (dd, *J* = 6.3, 0.9 Hz, 3H).

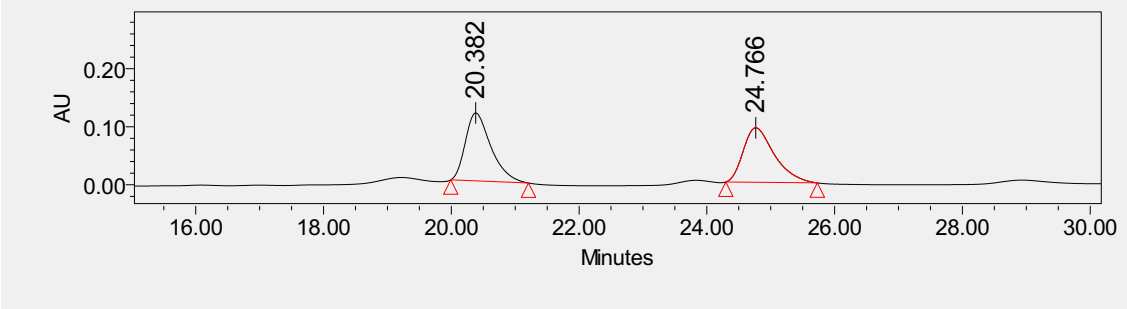
^{13}C NMR (126 MHz, Chloroform-*d*): δ 133.6, 133.2, 118.7, 118.7, 114.5, 114.4, 48.3, 45.7, 19.9.

IR (film, cm^{-1}): 3350, 3049, 2963, 2925, 2850, 1602, 1502, 1360, 1301, 910, 736.

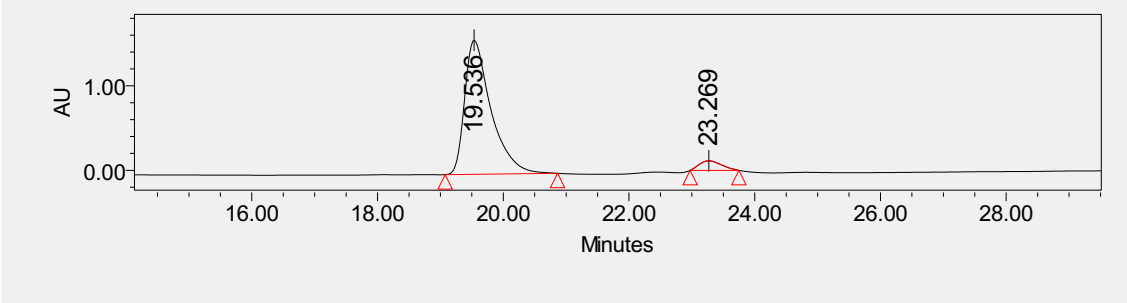
[α]$_D$: +18.2 (c = 0.80 in $CHCl_3$); **literature [α]$_D$:** +3.7 (c = 0.5 in CH_2Cl_2) for 98% ee.

ESI-HRMS: Calcd. for $C_9H_{13}N_2^+$ 149.1073 $[M+H]^+$, found 149.1070.

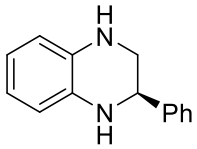
HPLC (Chiralpak OD-H column, 80:20 hexanes/isopropanol, 0.5 ml/min), tr = 19.5 min (major, R), 23.3 min (minor, S).



	Retention Time	Area	% Area	Height
1	20.382	10455967	50.64	368952
2	24.766	10191463	49.36	297423



	Retention Time	Area	% Area	Height
1	19.536	46222166	94.32	1587006
2	23.269	2783025	5.68	112915



(*R*)-2-Phenyl-1,2,3,4-tetrahydroquinoxaline (4b)

Known compound[6]; yellow solids, 20.8 mg, 99% yield, 83% ee.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.41 – 7.34 (m, 4H), 7.32 (ddt, *J* = 8.5, 6.3, 1.6 Hz, 1H), 6.67 – 6.61 (m, 2H), 6.61 – 6.55 (m, 2H), 4.48 (dd, *J* = 8.2, 3.1 Hz, 1H), 3.90 (br s, 1H), 3.81 (br s, 1H), 3.46 (dd, *J* = 11.1, 3.1 Hz, 1H), 3.33 (dd, *J* = 11.1, 8.2 Hz, 1H).

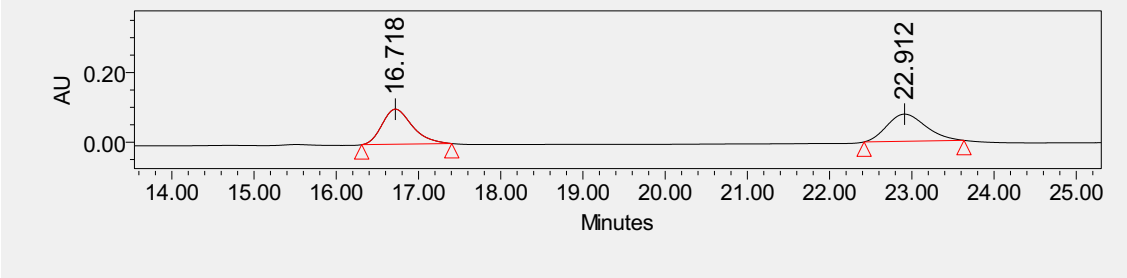
^{13}C NMR (176 MHz, Chloroform-*d*): δ 141.8, 134.1, 132.8, 128.6, 128.9, 127.0, 118.9, 118.8, 114.7, 114.4, 54.7, 49.1.

IR (film, cm^{-1}): 3362, 3025, 2849, 1594, 1502, 1451, 1342, 1299, 909, 737.

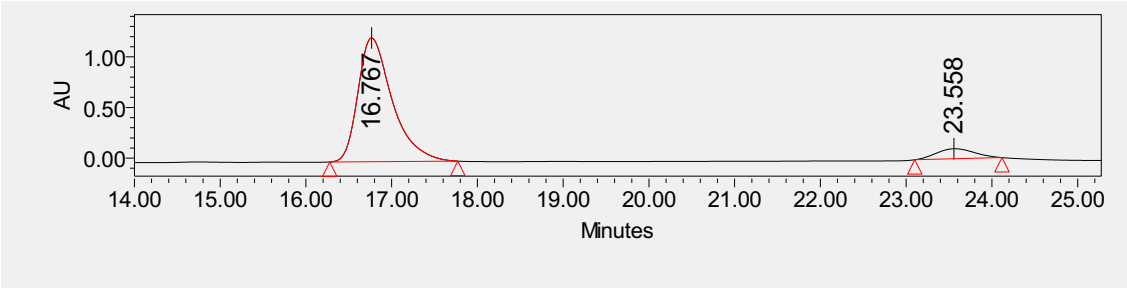
[α]$_D$: –97.5 (c = 0.63 in $CHCl_3$); **literature [α]$_D$:** –98.6 (c = 1.0 in $CHCl_3$) for 90% ee.

ESI-HRMS: Calcd. for $C_{14}H_{15}N_2^+$ 211.1229 $[M+H]^+$, found 211.1227.

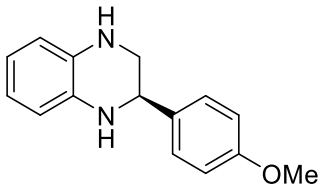
HPLC (Chiralpak OD-H column, 85:15 hexanes/isopropanol, 1.0 ml/min), tr = 16.7 min (major, R), 23.5 min (minor, S).



	Retention Time	Area	% Area	Height
1	16.718	2579944	50.21	100693
2	22.912	2558058	49.79	78000



	Retention Time	Area	% Area	Height
1	16.767	34013063	91.74	1221730
2	23.558	3060572	8.26	99559



(*R*)-1,2,3,4-tetrahydro-2-(4-methoxyphenyl)quinoxaline (4c)

Known compound[6]; yellow solids; 23.2mg, 96% yield, 92% ee.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.30 (d, *J* = 8.3 Hz, 2H), 6.92 – 6.88 (m, 2H), 6.63 (dt, *J* = 7.3, 3.7 Hz, 2H), 6.57 (td, *J* = 7.0, 5.9, 3.8 Hz, 2H), 4.43 (dd, *J* = 8.4, 3.0 Hz, 1H), 3.84 (br s, 2H), 3.81 (s, 3H), 3.42 (dd, *J* = 11.0, 3.1 Hz, 1H), 3.30 (dd, *J* = 11.0, 8.3 Hz, 1H).

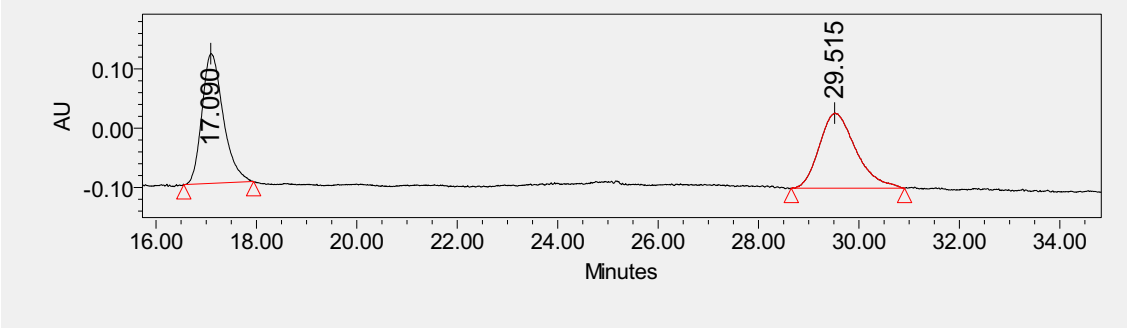
^{13}C NMR (176 MHz, Chloroform-*d*): δ 159.3, 134.2, 133.9, 132.8, 128.1, 118.8, 118.7, 114.6, 114.4, 114.0, 55.3, 54.1, 49.3.

IR (film, cm^{-1}): 3364, 3018, 2955, 2925, 2850, 1602, 1510, 1443, 1339, 1245, 1105, 908, 737.

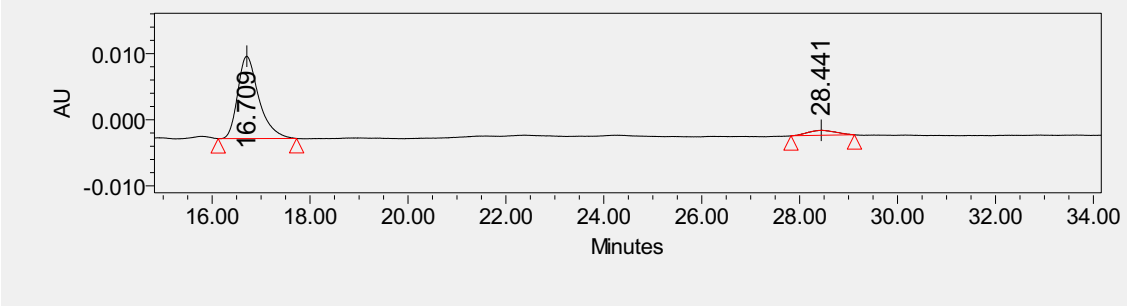
[α]$_D$: –51.9 (c = 0.78 in $CHCl_3$); **literature [α]$_D$:** –83.2 (c = 1.0 in $CHCl_3$) for 94% ee.

ESI-HRMS: Calcd. for $C_{15}H_{17}N_2O^+$ 241.1335 $[M+H]^+$, found 241.1331.

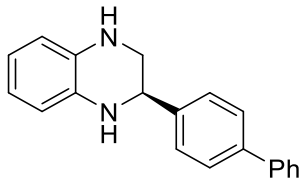
HPLC (Chiralpak OD-H column, 80:20 hexanes/isopropanol, 1.0 ml/min), tr = 16.7 min (major, R), 28.4 min (minor, S).



	Retention Time	Area	% Area	Height
1	17.090	6428801	50.17	219134
2	29.515	6385640	49.83	126889



	Retention Time	Area	% Area	Height
1	16.709	697477	95.89	12444
2	28.441	29895	4.11	768



(*R*)-2-([1,1'-Biphenyl]-4-yl)-1,2,3,4-tetrahydroquinoxaline (4d);

Pale yellow solids; 95% yield, 76% ee.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.63-7.55 (m, 4H), 7.50-7.41 (m, 4H), 7.40-7.32 (m, 1H), 6.69-6.63 (m, 2H), 6.63-6.57 (m, 2H), 4.55 (dd, J = 8.1, 3.0 Hz, 1H), 3.93 (br s, 2H), 3.51 (dd, J = 11.1, 3.1 Hz, 1H), 3.38 (dd, J = 11.0, 8.1 Hz, 1H).

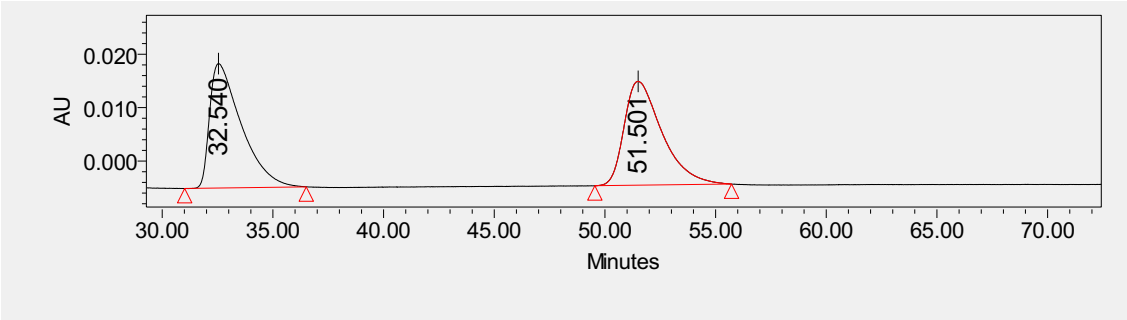
^{13}C NMR (176 MHz, Chloroform-*d*): δ 141.0, 140.9, 134.2, 132.8, 129.0, 127.6, 127.5, 127.5, 127.2, 119.2, 119.0, 115.0, 114.6, 54.6, 49.2.

IR (film, cm^{-1}): 3347, 3058, 3033, 2923, 2852, 1682, 1603, 1540, 1464, 956, 845, 764.

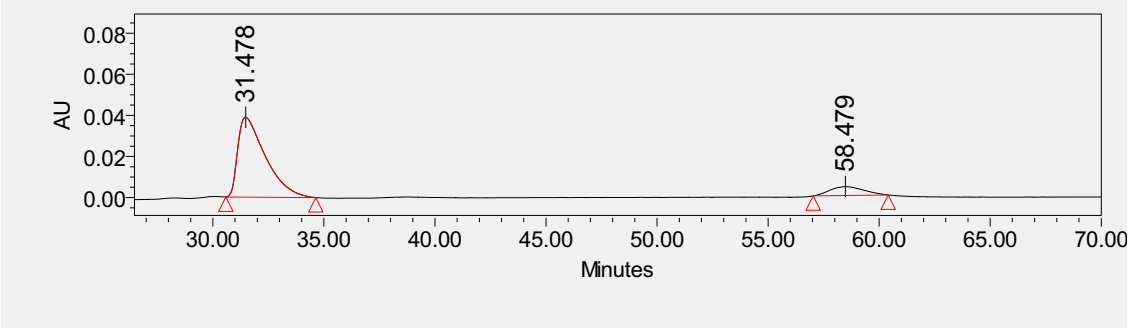
$[\alpha]_D$: –11.3 (c = 0.73 in CH_2Cl_2).

ESI-HRMS Calcd. for $C_{20}H_{19}N_2^+$ 287.1542 $[M+H]^+$, found 287.1534.

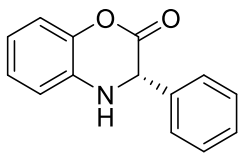
HPLC (Chiralpak OD-H column, 80:20 hexanes/isopropanol, 1.0 ml/min), tr = 31.5 min (major, R), 58.5 min (minor, S).



	Retention Time	Area	% Area	Height
1	32.540	2316704	50.05	23313
2	51.501	2312280	49.95	19445



	Retention Time	Area	% Area	Height
1	31.478	3353930	88.06	38871
2	58.479	454916	11.94	4319



(*S*)-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (4e)

Known compound[7]; white solids, 22.1 mg, 98% yield, 84% ee.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.45 – 7.34 (m, 5H), 7.08 – 7.00 (m, 2H), 6.87 (td, *J* = 7.8, 1.5 Hz, 1H), 6.82 (dd, *J* = 7.8, 1.5 Hz, 1H), 5.08 (d, *J* = 1.9 Hz, 1H), 4.22 (br s, 1H).

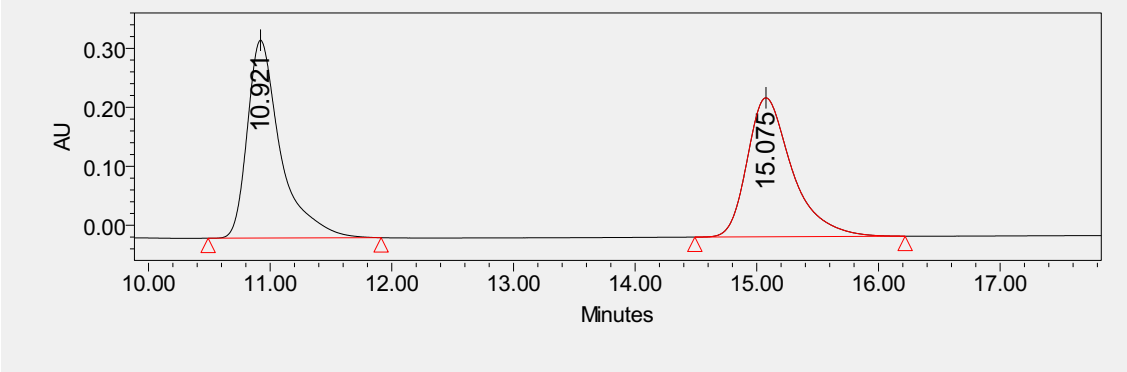
^{13}C NMR (126 MHz, Chloroform-*d*): δ 165.1, 140.9, 136.4, 132.3, 129.0, 129.0, 127.5, 125.2, 120.4, 117.0, 114.8, 59.3.

IR (powder, cm^{-1}): 3352, 3056, 2919, 2850, 1736, 1621, 1500, 1453, 1429, 1183, 1151, 917, 810, 738, 720, 698.

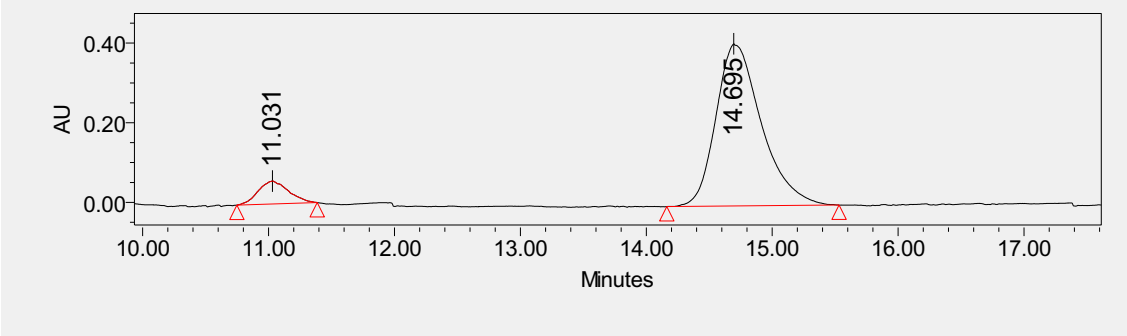
$[\alpha]_D$: +51.9 (c = 0.75 in CH_2Cl_2), **literature $[\alpha]_D$:** –46.3 (c = 1.0 in $CHCl_3$) for 99% ee (*S*).

ESI-HRMS: Calcd. for $C_{14}H_{12}NO_2^+$ 226.0863 $[M+H]^+$, found 226.0866.

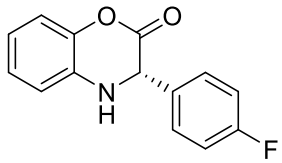
HPLC (Chiralpak OD-H column, 70:30 hexanes/isopropanol, 0.7 ml/min), tr = 11.0 min (minor, R), 14.6 min (major, S).



	Retention Time	Area	% Area	Height
1	10.921	1273154	50.57	66163
2	15.075	1244373	49.43	47488



	Retention Time	Area	% Area	Height
1	11.031	900474	8.11	57637
2	14.695	10202786	91.89	407359



(*S*)-3-(4-fluorophenyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (4f)

Known compound[9]; white solids, 24.1 mg, 99% yield, 83% ee.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.44 – 7.37 (m, 2H), 7.11 – 7.01 (m, 4H), 6.89 (td, *J* = 7.8, 1.5 Hz, 1H), 6.82 (dd, *J* = 7.8, 1.5 Hz, 1H), 5.04 (d, *J* = 2.0 Hz, 1H), 4.20 (s, 1H).

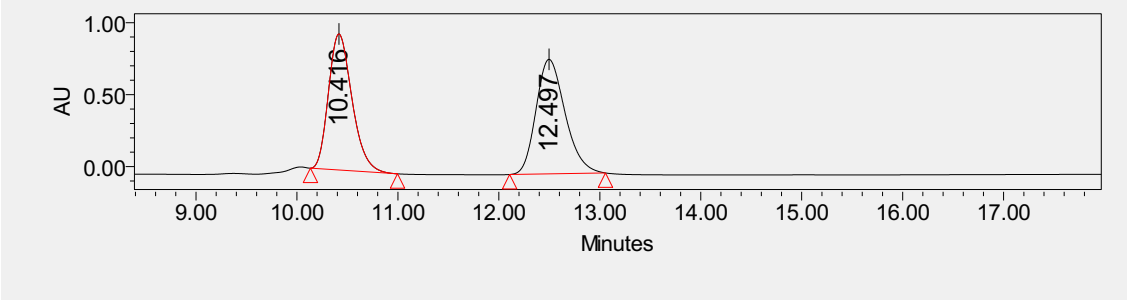
^{13}C NMR (126 MHz, Chloroform-*d*): δ 165.0, 163.1 (d, *J* = 248.17 Hz), 141.0, 132.2, 132.1 (d, *J* = 3.07 Hz), 129.4 (d, *J* = 8.44 Hz), 125.2, 120.7, 117.1, 116.0 (d, *J* = 21.04 Hz), 114.9, 58.7.

IR (film, cm^{-1}): 3354, 3068, 2954, 2924, 2853, 1758, 1650, 1617, 1499, 1411, 1292, 1193, 1156, 917, 802, 745.

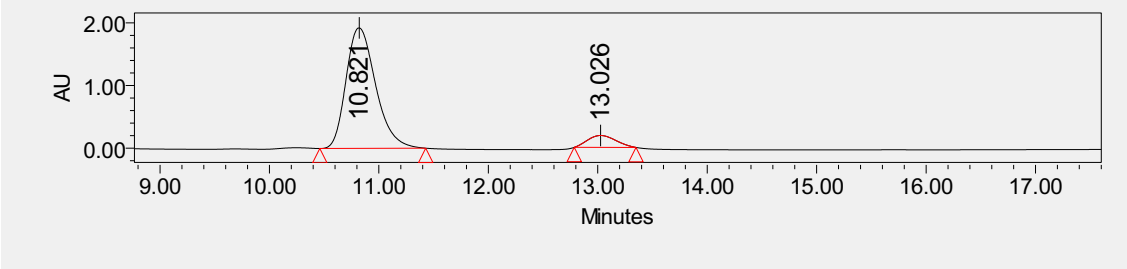
[α]$_D$: +81.9 (c = 0.63 in $CHCl_3$), **literature [α]$_D$:** –98.4 (c = 0.80 in $CHCl_3$) for 95% ee (*R*).

ESI-HRMS: Calcd. for $C_{14}H_{11}FNO_2^+$ 244.0768 $[M+H]^+$, found 244.0762.

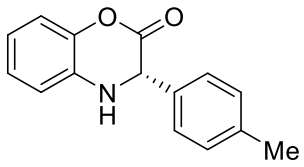
HPLC (Chiralpak IA column, 80:20 hexanes/isopropanol, 0.8 ml/min), tr = 10.8 min (major, S), 13.0 min (minor, R).



	Retention Time	Area	% Area	Height
1	10.416	15276584	48.99	944985
2	12.497	15908081	51.01	795297



	Retention Time	Area	% Area	Height
1	10.821	36172403	91.42	1920678
2	13.026	3396497	8.58	189871



(*S*)-3-(p-tolyl)-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (4g)

Known compound[9]; white solids, 23.4 mg, 98% yield, 73% ee.

^{1}H NMR (700 MHz, Chloroform-*d*): δ 7.31 – 7.27 (m, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.07 – 7.03 (m, 1H), 7.02 (td, *J* = 7.7, 1.4 Hz, 1H), 6.86 (td, *J* = 7.7, 1.4 Hz, 1H), 6.80 (dd, *J* = 7.8, 1.4 Hz, 1H), 5.03 (d, *J* = 1.9 Hz, 1H), 4.19 (s, 1H), 2.34 (s, 3H).

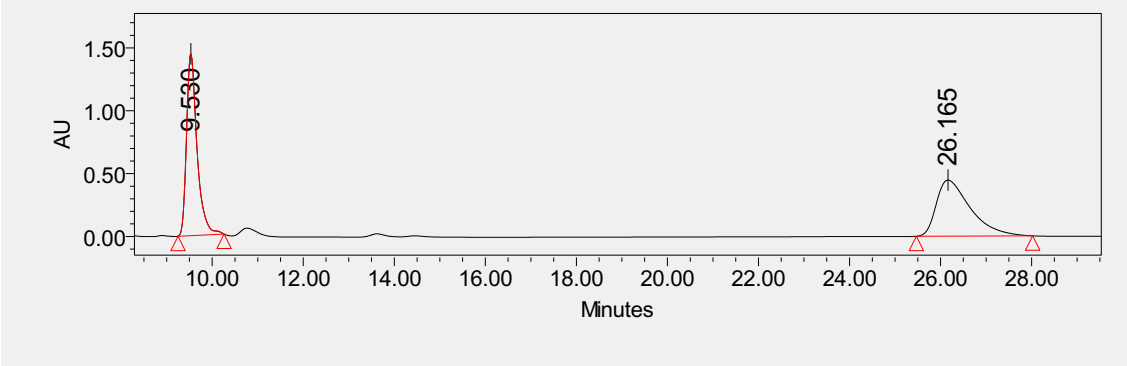
^{13}C NMR (176 MHz, Chloroform-*d*): δ 165.3, 141.0, 138.9, 133.4, 132.5, 129.7, 127.4, 125.1, 120.4, 117.0, 114.8, 77.2, 77.2, 77.0, 76.8, 59.1, 21.2.

IR (film, cm^{-1}): 3463, 3099, 2998, 2955, 2851, 1737, 1600, 1461, 1306, 1187, 1149, 970, 843, 760.

[α]$_D$: +67.2 (c = 0.78 in $CHCl_3$), **literature [α]$_D$:** –88.2 (c = 0.92 in $CHCl_3$) for 93% ee (*R*).

ESI-HRMS: Calcd. for $C_{15}H_{14}NO_2^+$ 240.1019 $[M+H]^+$, found 240.1014.

HPLC (Chiralpak OD-H column, 70:30 hexanes/isopropanol, 0.7 ml/min), tr = 10.1 min (minor, R), 24.9 min (major, S).



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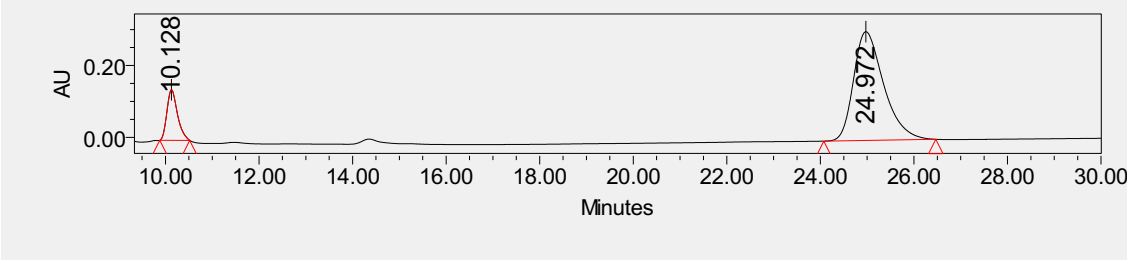
2	26.165	23087060	49.92	445562



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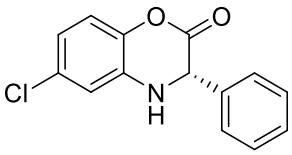
1	10.128	2201323	13.30	140444
2	24.972	14349978	86.70	302463



(*S*)-6-Chloro-3-phenyl-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (4h)

Known compound[9]; colorless solids, 25.1 mg, 97% yield, 88% ee.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.38 (s, 5H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.82 (dt, *J* = 11.0, 2.2 Hz, 2H), 5.09 (d, *J* = 1.5 Hz, 1H), 4.32 (s, 1H).

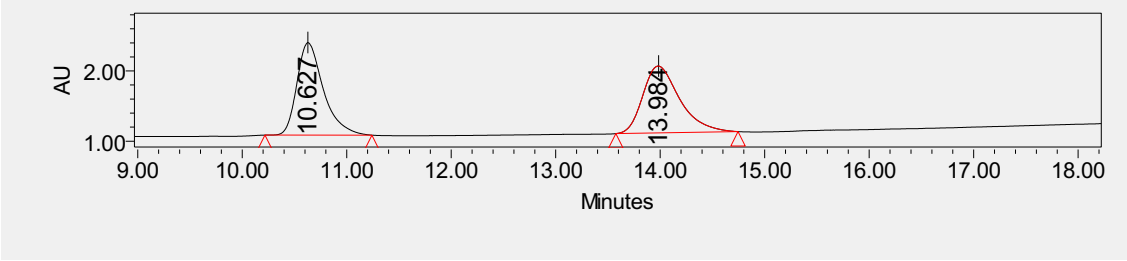
^{13}C NMR (126 MHz, Chloroform-*d*): δ 164.3, 139.4, 136.0, 133.1, 130.2, 129.2, 129.1, 127.3, 120.2, 118.0, 114.6, 58.8.

IR (powder, cm^{-1}): 3465, 3098, 3073, 2958, 2924, 1741, 1581, 1443, 1290, 1137, 1073, 972, 823.

$[\alpha]_D$: +89.4 (c = 0.80 in $CHCl_3$), **literature $[\alpha]_D$:** –109.9 (c = 0.90 in $CHCl_3$) for 89% ee (*R*).

ESI-HRMS: Calcd. for $C_{14}H_{11}ClNO_2^+$ 260.0473 $[M+H]^+$, found 260.0475.

HPLC (Chiralpak OD-H column, 70:30 hexanes/isopropanol, 0.7 ml/min), tr = 9.5 min (minor, R), 12.3 min (major, S).



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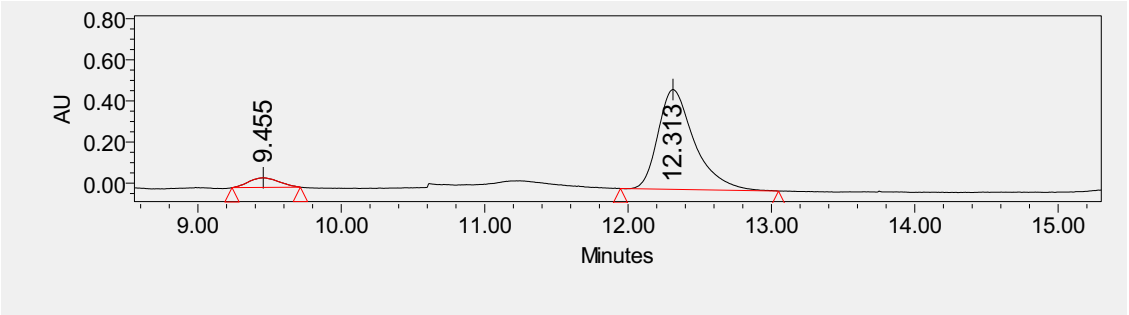

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1	9.455	1793922	5.92	46753
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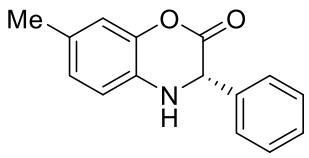


(*S*)-7-Methyl-3-phenyl-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (4i)

Known compound[9]; colorless oil, 23.6 mg, 99% yield, 80% ee.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.44 – 7.33 (m, 5H), 6.86 (d, *J* = 1.8 Hz, 1H), 6.83 (dd, *J* = 7.9, 1.9 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.03 (d, *J* = 2.1 Hz, 1H), 4.13 (s, 1H), 2.29 (s, 3H).

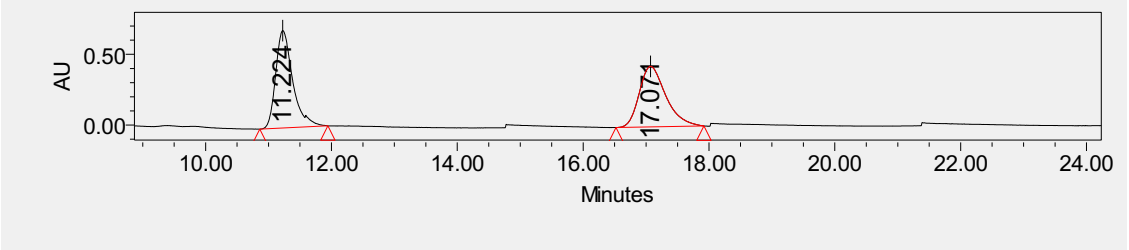
^{13}C NMR (126 MHz, Chloroform-*d*): δ 165.4, 140.9, 136.4, 130.4, 129.8, 129.0, 128.9, 127.5, 125.6, 117.4, 114.8, 59.5, 20.6.

IR (powder, cm^{-1}): 3455, 3062, 2957, 2923, 2851, 1734, 1445, 1242, 1074, 946, 815.

[α]$_D$: +66.7 (c = 0.84 in $CHCl_3$), **literature [α]$_D$:** –80.6 (c = 0.86 in $CHCl_3$) for 93% ee (*R*).

ESI-HRMS: Calcd. for $C_{15}H_{14}NO_2^+$ 240.1019 $[M+H]^+$, found 240.1018.

HPLC (Chiralpak OD-H column, 70:30 hexanes/isopropanol, 0.7 ml/min), tr = 11.2 min (minor, R), 17.0 min (major, S)



	Retention Time	Area	% Area	Height
1	11.224	12953816	50.83	689034
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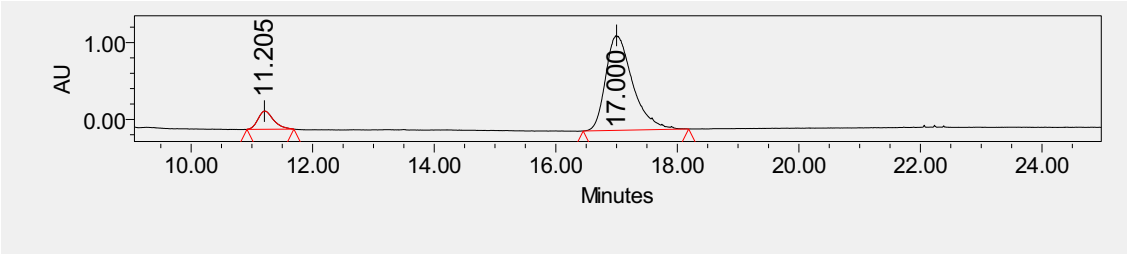
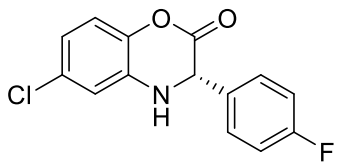


	Retention Time	Area	% Area	Height
1	11.205	4185537	9.92	236139
2	17.000	37993398	90.08	1234940



(*S*)-6-chloro-3-(4-fluorophenyl)-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (4j)

Colorless oil, 26.3 mg, 95% yield, 85% ee.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.41 – 7.35 (m, 2H), 7.12 – 7.05 (m, 2H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.90 – 6.80 (m, 2H), 5.06 (d, *J* = 2.0 Hz, 1H), 4.28 – 4.24 (m, 1H).

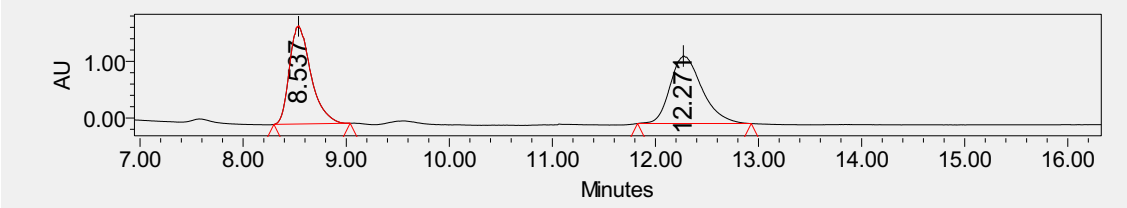
^{13}C NMR (176 MHz, Chloroform-*d*): δ 164.2, 163.8, 162.4, 139.4, 133.0, 131.7, 130.3, 129.3, 129.2, 120.4, 118.1, 116.1 (d, *J* = 21.90 Hz), 114.7, 58.2.

IR (film, cm^{-1}): 3400, 3383, 2976, 2875, 1741, 1598, 1506, 1224, 1155, 981, 837.

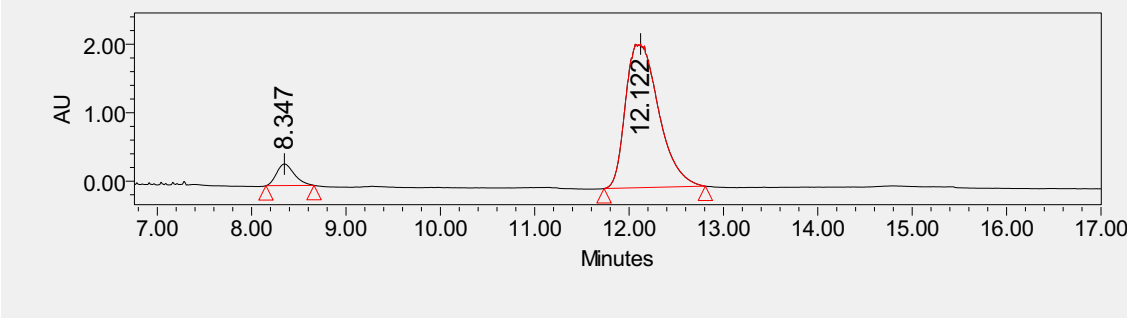
$[\alpha]_D$: +71.7 (c = 0.82 in $CHCl_3$).

ESI-HRMS Calcd. for $C_{14}H1_0ClFNO_2^+$ 278.0379 $[M+H]^+$, found 278.0374.

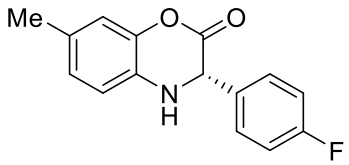
HPLC (Chiralpak OD-H column, 70:30 hexanes/isopropanol, 0.7 ml/min), tr = 8.3 min (minor, R), 12.1 min (major, S)



	Retention Time	Area	% Area	Height
1	8.537	25031120	49.44	1735241
2	12.271	25598370	50.56	1191790



	Retention Time	Area	% Area	Height
1	8.347	4085561	7.37	313660
2	12.122	51349001	92.63	2100018



(*S*)-7-methyl-3-(4-fluorophenyl)-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (4k)

White solid, 25.1 mg, 98% yield, 81% ee.

^{1}H NMR (401 MHz, Chloroform-*d*): δ 7.43 – 7.34 (m, 2H), 7.11 – 7.02 (m, 2H), 6.92 – 6.80 (m, 2H), 6.70 (d, *J* = 7.9 Hz, 1H), 4.99 (d, *J* = 2.2 Hz, 1H), 4.06 (s, 1H), 2.28 (s, 3H).

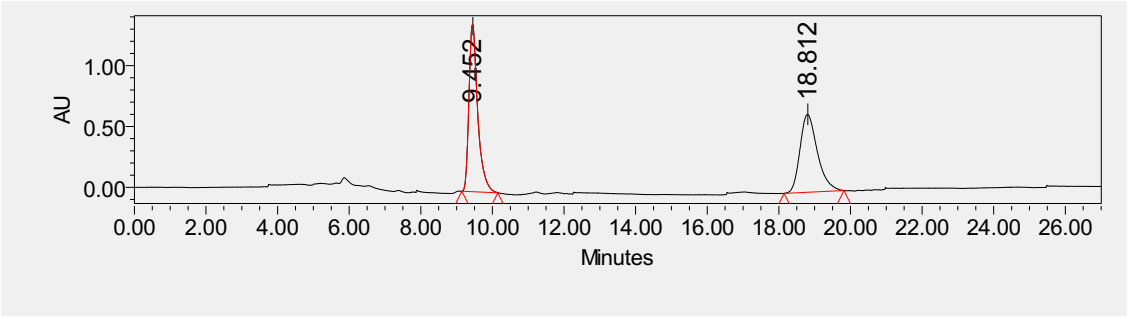
^{13}C NMR (126 MHz, Chloroform-*d*): δ 165.3, 163.0 (d, *J* = 250.66 Hz), 140.9, 132.1 (d, *J* = 3.21 Hz), 130.7, 129.7, 129.4 (d, *J* = 8.43 Hz), 125.7, 117.4, 115.9 (d, *J* = 21.07 Hz), 114.9, 58.9, 20.6.

IR (film, cm^{-1}): 3345, 2924, 1735, 1603, 1299, 1221, 1157, 1101, 834.

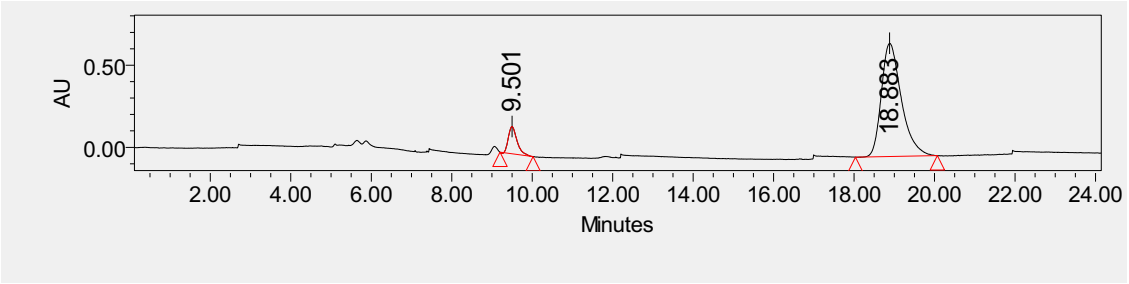
[α]$_D$: +58.8 (c = 0.84 in $CHCl_3$).

ESI-HRMS: Calcd. for $C_{15}H_{13}FNO_2^+$ 258.0925 $[M+H]^+$, found 258.0924.

HPLC (Chiralpak OD-H column, 80:20 hexanes/isopropanol, 1.0 ml/min), tr = 9.5 min (minor, R), 18.8 min (major, S).



	Retention Time	Area	% Area	Height
1	9.452	23385297	51.94	1375036
2	18.812	21635546	48.06	641190



	Retention Time	Area	% Area	Height
1	9.501	2503371	9.53	166123
2	18.883	23763113	90.47	689490

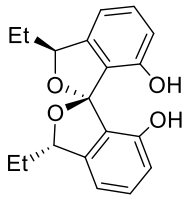
Characterization of (S,S,S)-SPIROL by X-ray crystallographic analysis.

Colorless hexagonal crystals of **ssspiro** were grown from a dichloromethane/hexanes solution of the compound at 22 deg. C. A crystal of dimensions 0.22 x 0.20 x 0.18 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (l = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in w. The exposure times were 1 sec. for the low angle images, 4 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 61312 reflections to a maximum 2q value of 138.33° of which 4949 were independent and 4874 were greater than 2s(I). The final cell constants (Table 1) were based on the xyz centroids of 33076 reflections above 10s(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2018/3) software package, using the space group P3(1)21 with Z = 9 for the formula $C_{19}H_{20}O_4$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in a combination of refined and idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0470 and wR2 = 0.1248 [based on I > 2sigma(I)], R1 = 0.0474 and wR2 = 0.1253 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).

CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).



(*S*,*S*,*S*)-SPIROL

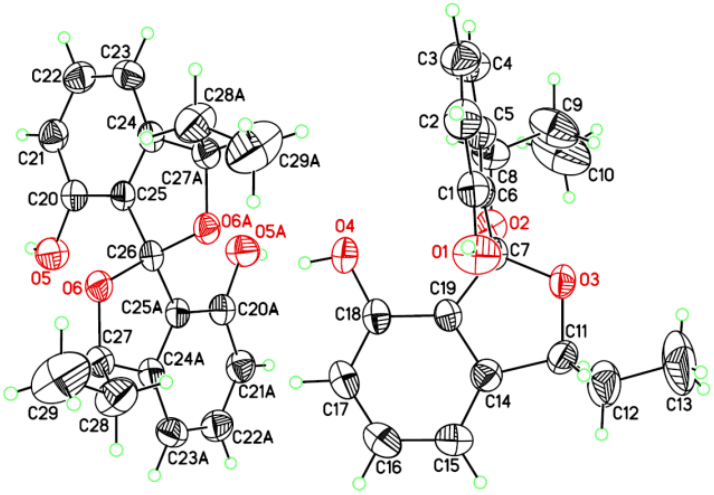


Table 1. Crystal data and structure refinement for ssspiro.

Identification code	ssspiro
Empirical formula	C19 H20 O4
Formula weight	312.35
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Trigonal, P3(1)21
Unit cell dimensions	a = 12.81980(10) A alpha = 90 deg. b = 12.81980(10) A beta = 90 deg. c = 27.9907(5) A gamma = 120 deg.
Volume	3983.88(9) A^3
Z, Calculated density	9, 1.172 Mg/m^3
Absorption coefficient	0.664 mm^-1
F(000)	1494
Crystal size	0.220 x 0.200 x 0.180 mm
Theta range for data collection	3.982 to 69.164 deg.
Limiting indices	-15<=h<=15, -15<=k<=15, -33<=l<=32
Reflections collected / unique	61312 / 4949 [R(int) = 0.0435]
Completeness to theta = 67.684	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.75742
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4949 / 0 / 328
Goodness-of-fit on F^2	1.062

Final R indices [I>2sigma(I)]	R1 = 0.0470, wR2 = 0.1248
R indices (all data)	R1 = 0.0474, wR2 = 0.1253
Absolute structure parameter	-0.11(6)
Extinction coefficient	0.0043(4)
Largest diff. peak and hole	0.372 and -0.258 e.A^-3

References

(1) Argüelles, A. J.; Sun, S.; Budaitis, B. G.; Nagorny, P. Design, Synthesis, and Application of Chiral C_2-Symmetric Spiroketal-Containing Ligands in Transition-Metal Catalysis. *Angew. Chem. Int. Ed.* **2018**, *57* (19), 5325–5329. https://doi.org/10.1002/anie.201713304.

(2) Wang, M.-C.; Wang, Y.-H.; Li, G.-W.; Sun, P.-P.; Tian, J.-X.; Lu, H.-J. Applications of Conformational Design: Rational Design of Chiral Ligands Derived from a Common Chiral Source for Highly Enantioselective Preparations of (R)- and (S)-Enantiomers of Secondary Alcohols. *Tetrahedron: Asymmetry* **2011**, *22* (7), 761–768. https://doi.org/10.1016/j.tetasy.2011.04.013.

(3) Issenhuth, J.-T.; Dagorne, S.; Bellemin-Laponnaz, S. Enantioselective Hydrosilylation of Prochiral Ketones Catalyzed by Chiral BINAP-Copper(I) Complexes. *Comptes Rendus Chimie* **2010**, *13* (3), 353–357. https://doi.org/10.1016/j.crci.2009.11.002.

(4) Gou, F.-R.; Li, W.; Zhang, X.; Liang, Y.-M. Iridium-Catalyzed Asymmetric Hydrogenation of Quinoline Derivatives with C3*-TunePhos. *Adv. Synth. Catal.* **2010**, *352* (14–15), 2441–2444. https://doi.org/10.1002/adsc.201000485.

(5) Rueping, M.; Antonchick, A. P.; Theissmann, T. A Highly Enantioselective Brønsted Acid Catalyzed Cascade Reaction: Organocatalytic Transfer Hydrogenation of Quinolines and Their Application in the Synthesis of Alkaloids. *Angew. Chem. Int. Ed.* **2006**, *45* (22), 3683–3686. https://doi.org/10.1002/anie.200600191.

(6) Rueping, M.; Tato, F.; Schoepke, Fenja. R. The First General, Efficient and Highly Enantioselective Reduction of Quinoxalines and Quinoxalinones. *Chem. Eur. J.* **2010**, *16* (9), 2688–2691. https://doi.org/10.1002/chem.200902907.

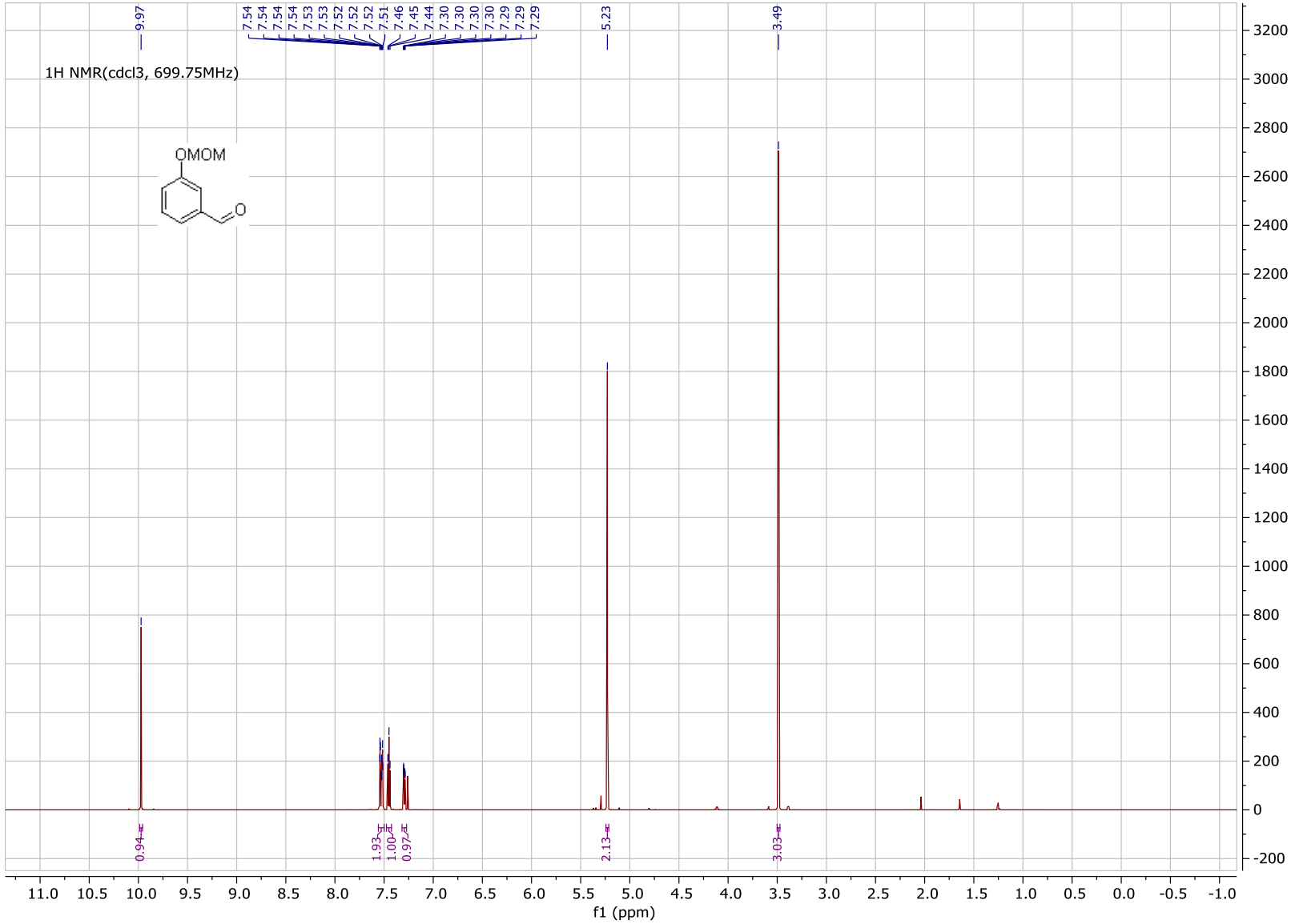
(7) Rueping, M.; Antonchick, A. P.; Theissmann, T. Geringste Katalysatormengen in der Brønsted-Säure-katalysierten Transferhydrierung: enantioselektive Reduktion von Benzoxazinen, Benzthiazinen und Benzoxazinonen. *Angew. Chem.* **2006**, *118* (40), 6903–6907. https://doi.org/10.1002/ange.200601832.

(8) Wang, T.; Zhuo, L.-G.; Li, Z.; Chen, F.; Ding, Z.; He, Y.; Fan, Q.-H.; Xiang, J.; Yu, Z.-X.; Chan, A. S. C. Highly Enantioselective Hydrogenation of Quinolines Using Phosphine-Free Chiral Cationic Ruthenium Catalysts: Scope, Mechanism, and Origin of Enantioselectivity. *J. Am. Chem. Soc.* **2011**, *133* (25), 9878–9891. https://doi.org/10.1021/ja2023042.

(9) Chen, Q.-A.; Gao, K.; Duan, Y.; Ye, Z.-S.; Shi, L.; Yang, Y.; Zhou, Y.-G. Dihydrophenanthridine: A New and Easily Regenerable NAD(P)H Model for Biomimetic Asymmetric Hydrogenation. *J. Am. Chem. Soc.* **2012**, *134* (4), 2442–2448. https://doi.org/10.1021/ja211684v.

(10) Qin, J.; Chen, F.; Ding, Z.; He, Y.-M.; Xu, L.; Fan, Q.-H. Asymmetric Hydrogenation of 2- and 2,3-Substituted Quinoxalines with Chiral Cationic Ruthenium Diamine Catalysts. *Org. Lett.* **2011**, *13* (24), 6568–6571. https://doi.org/10.1021/ol2029096.

(11) Kodama, K.; Kobayashi, Y.; Saigo, K. Two-Component Supramolecular Helical Architectures: Creation of Tunable Dissymmetric Cavities for the Inclusion and Chiral Recognition of the Third Components. *Chem.-Eur. J.* **2007**, *13*, 2144.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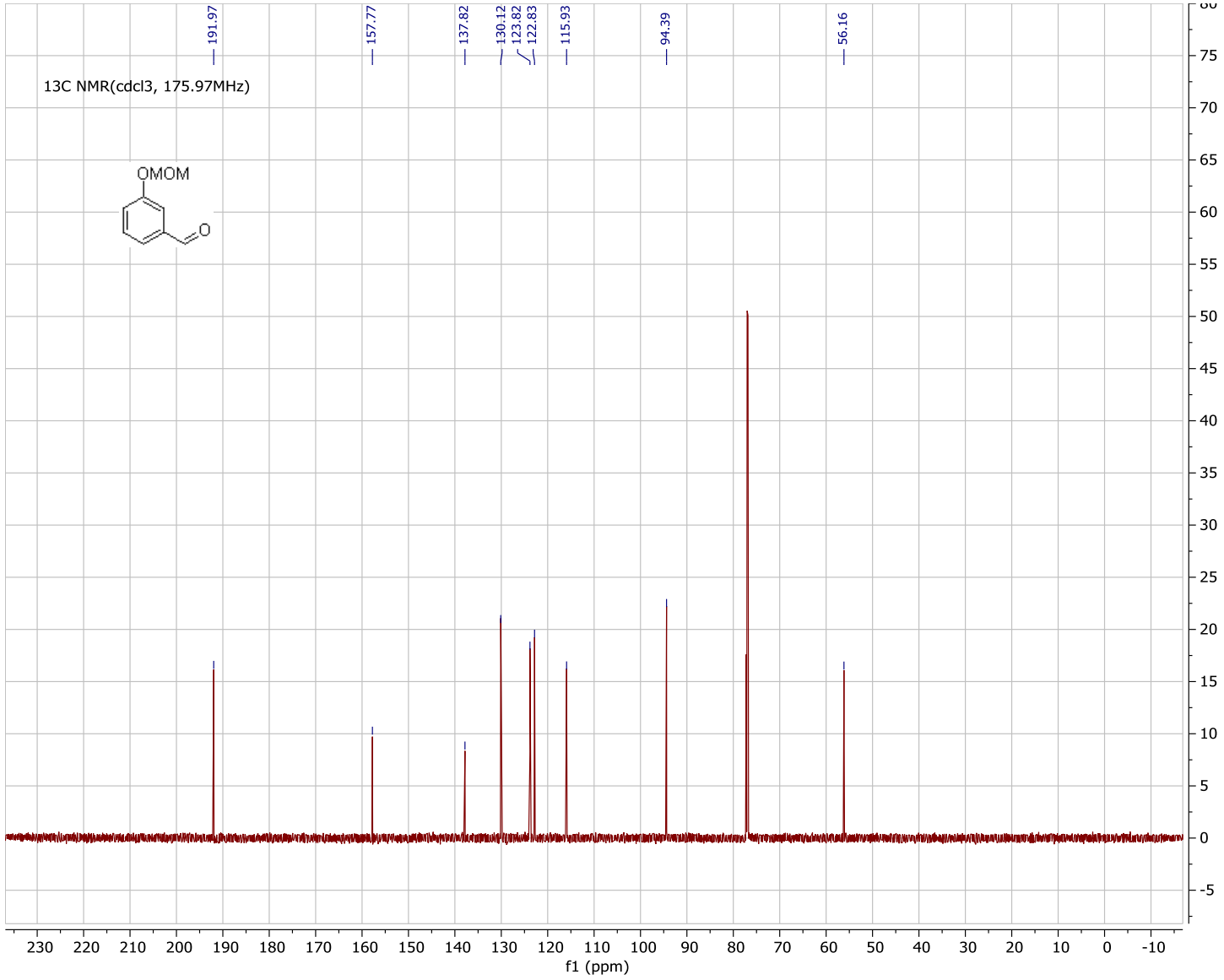
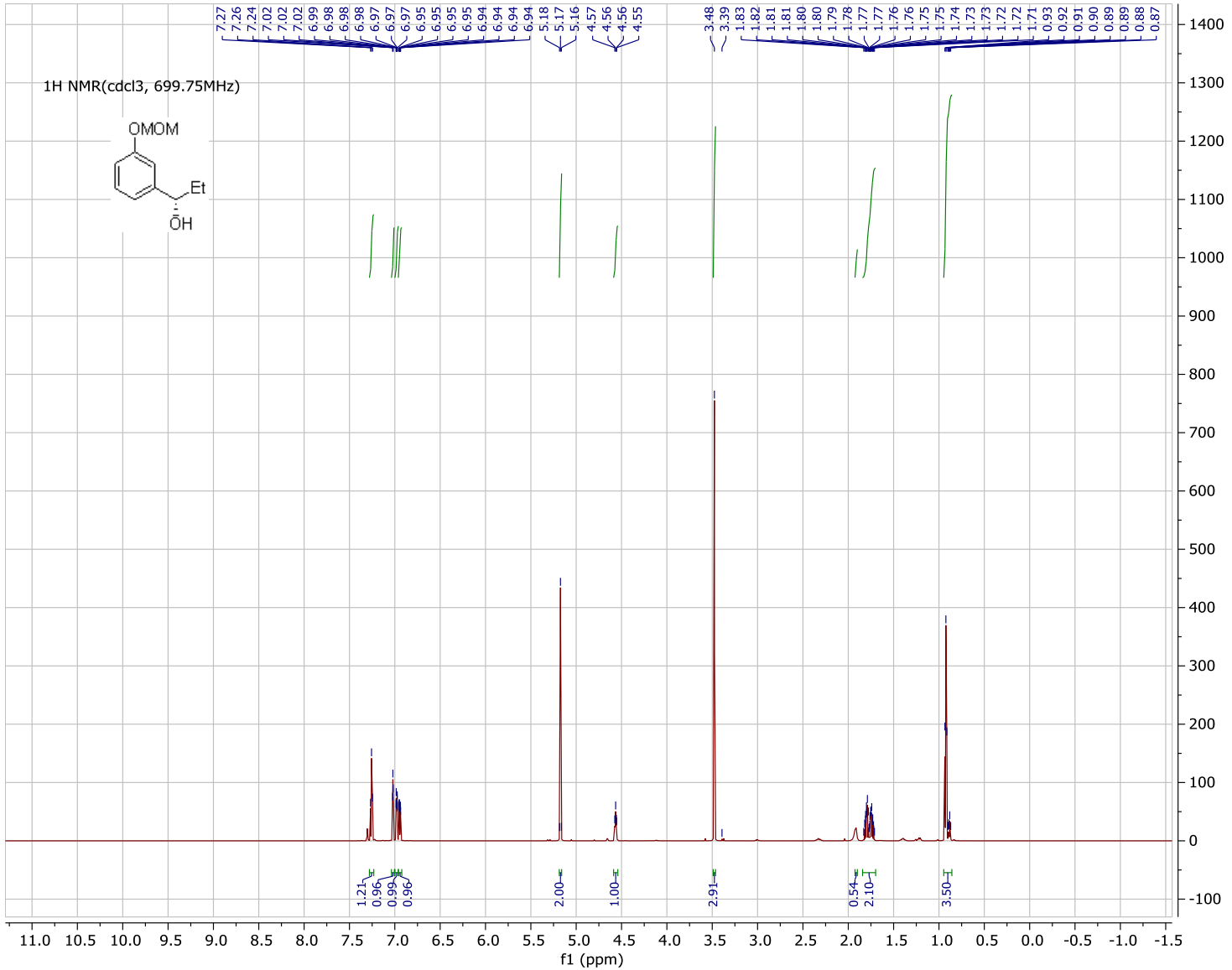
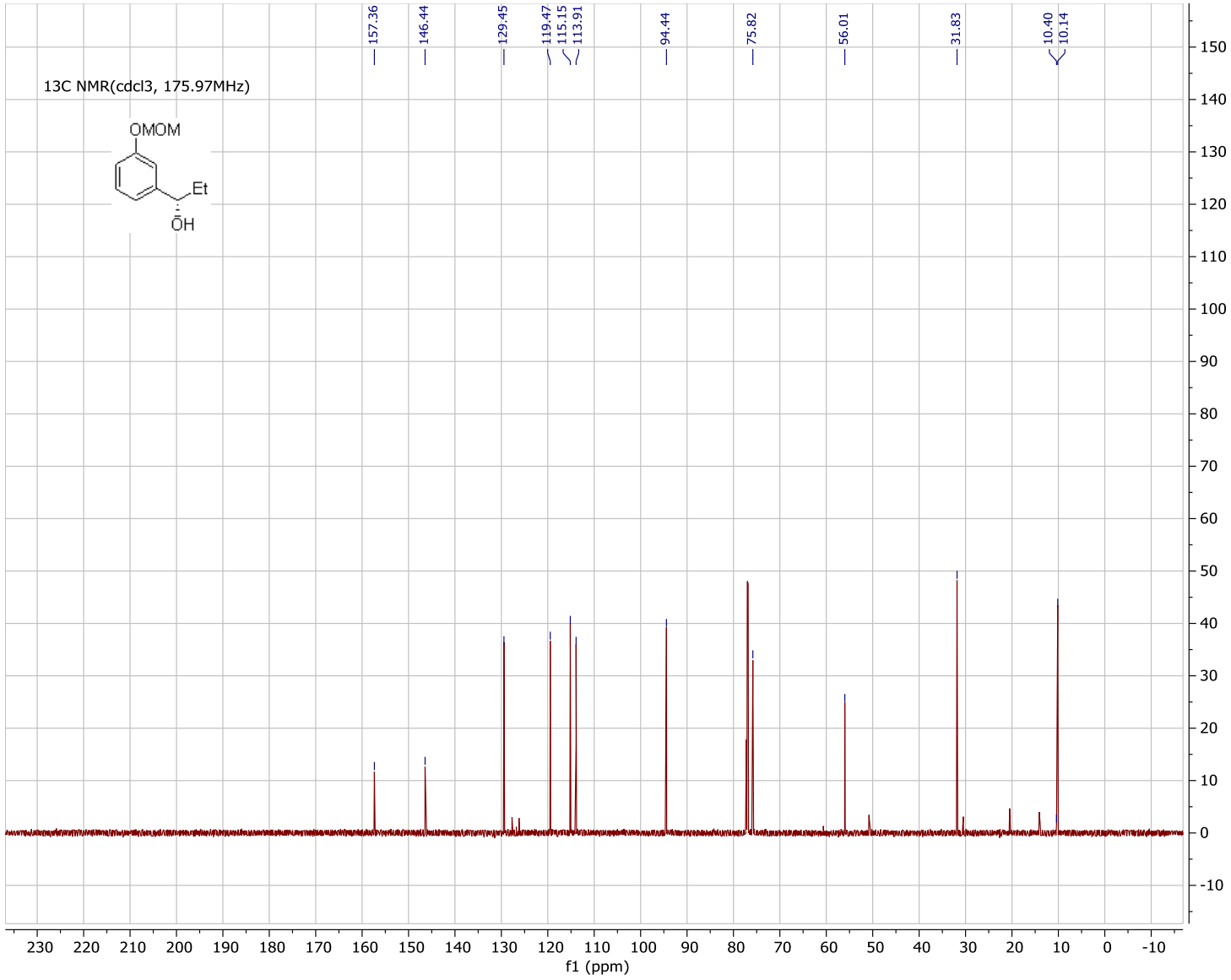
OMOM
O
9.97
7.54
7.54
7.54
7.54
7.53
7.53
7.52
7.52
7.52
7.51
7.46
7.45
7.44
7.30
7.30
7.30
7.29
7.29
7.29
5.23
3.49
0.94
1.93
1.00
0.97
2.13
3.03
f1 (ppm)


191.97
157.77
137.82
130.12
123.82
122.83
115.93
94.39
56.16
13C NMR(cdcl3, 175.97MHz)
OMOM
O
f1 (ppm)


1H NMR(cdcl3, 699.75MHz)
OMOM
Et
OH
f1 (ppm)


13C NMR(cdcl3, 175.97MHz)
OMOM
Et
OH
157.36
146.44
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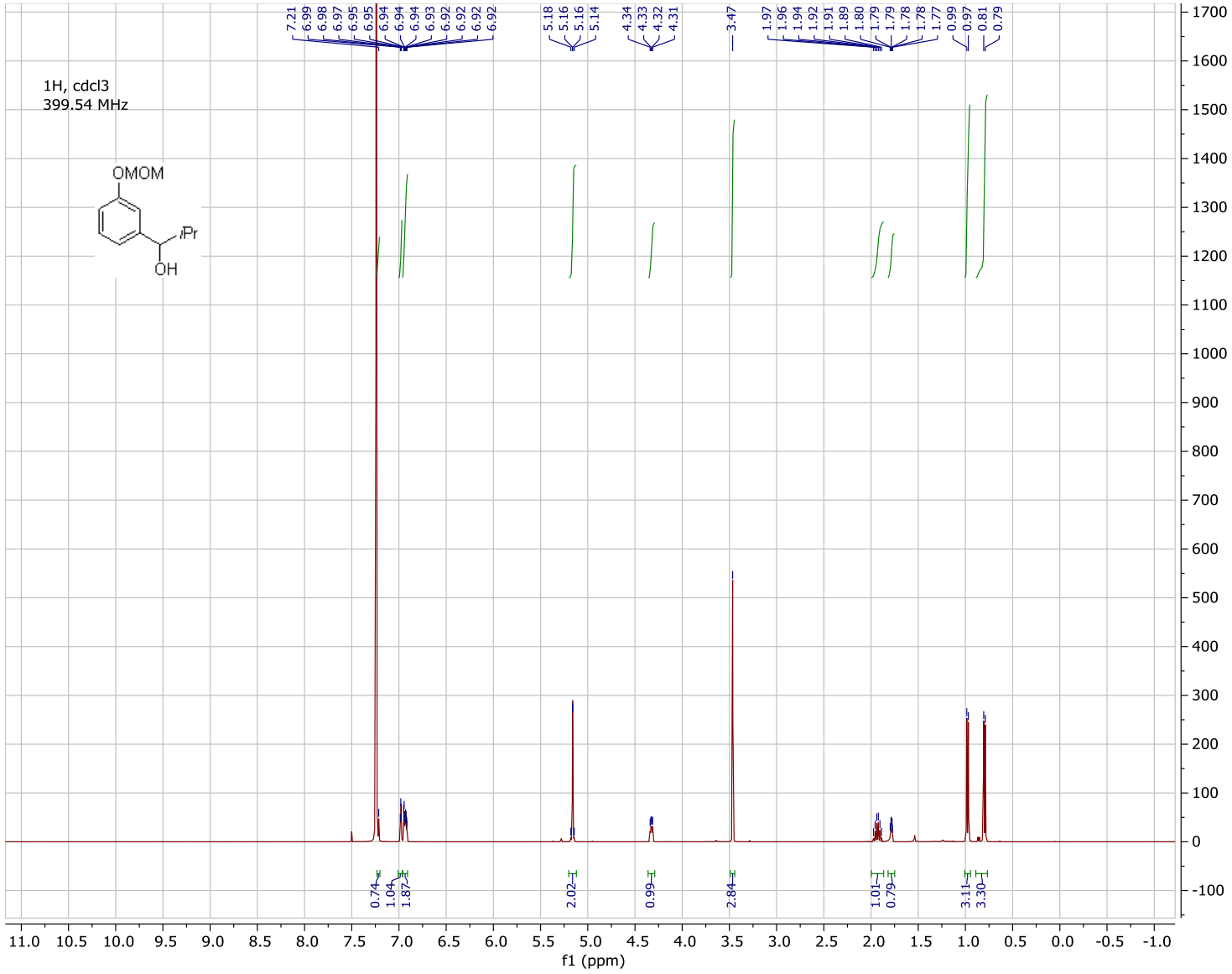
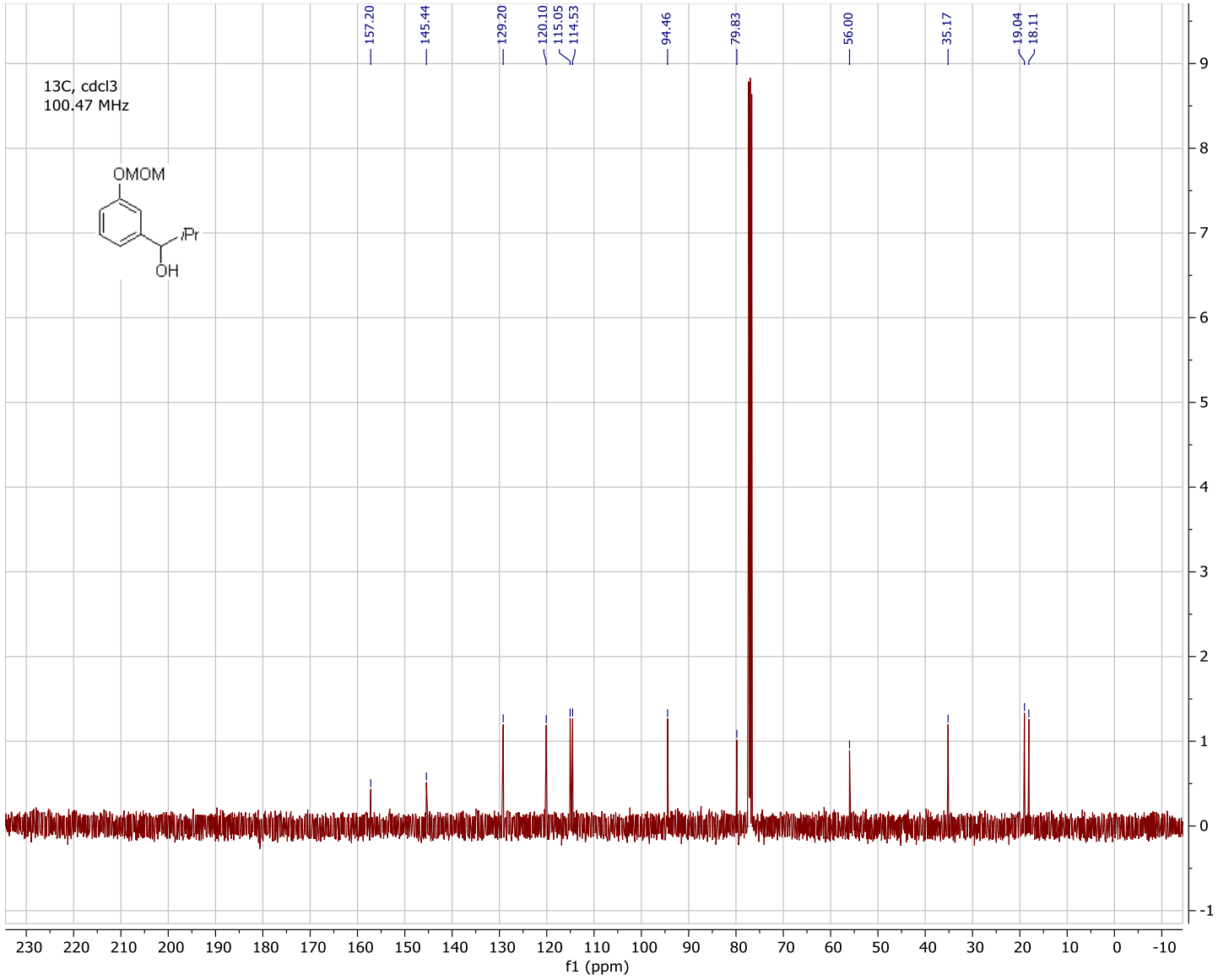
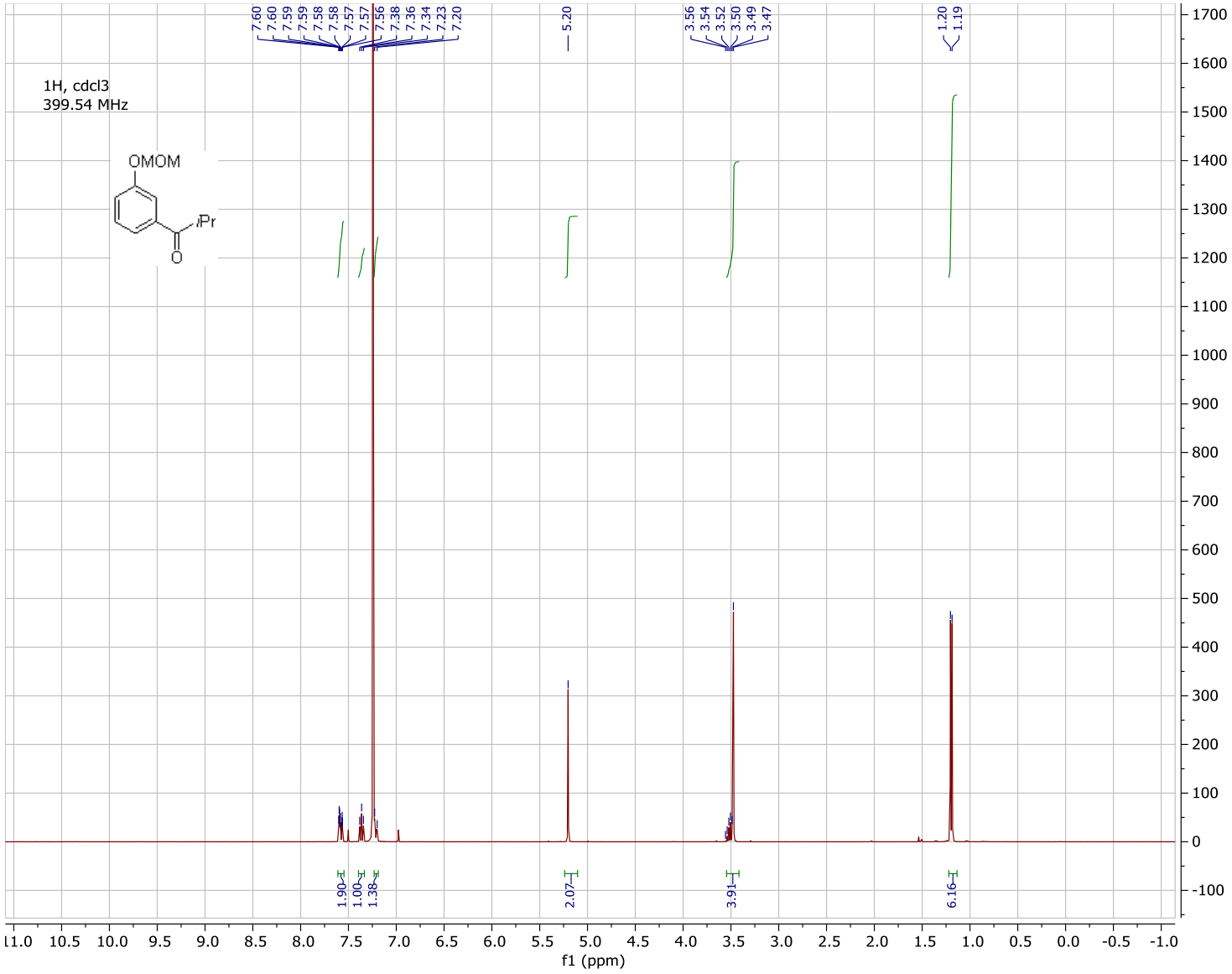
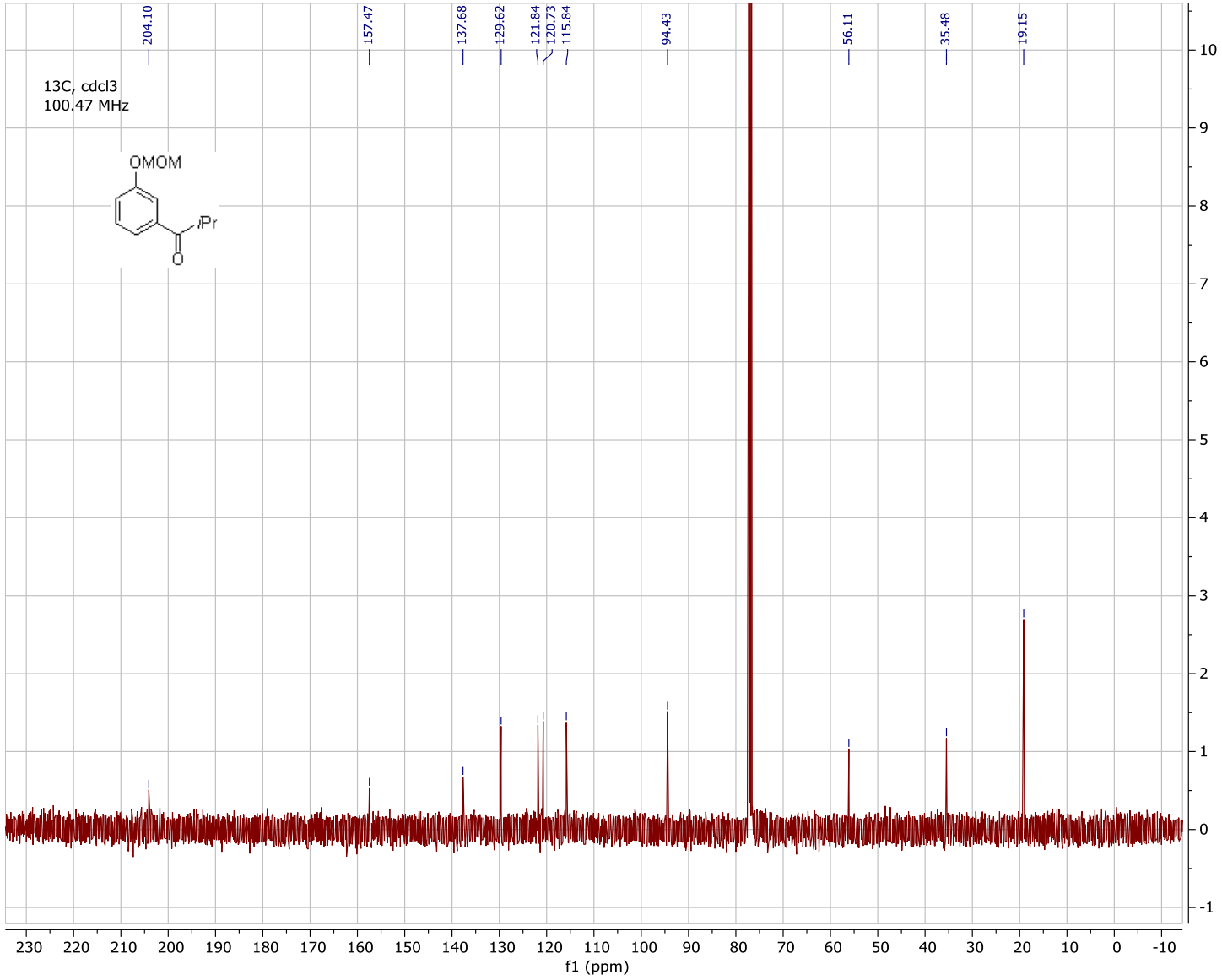
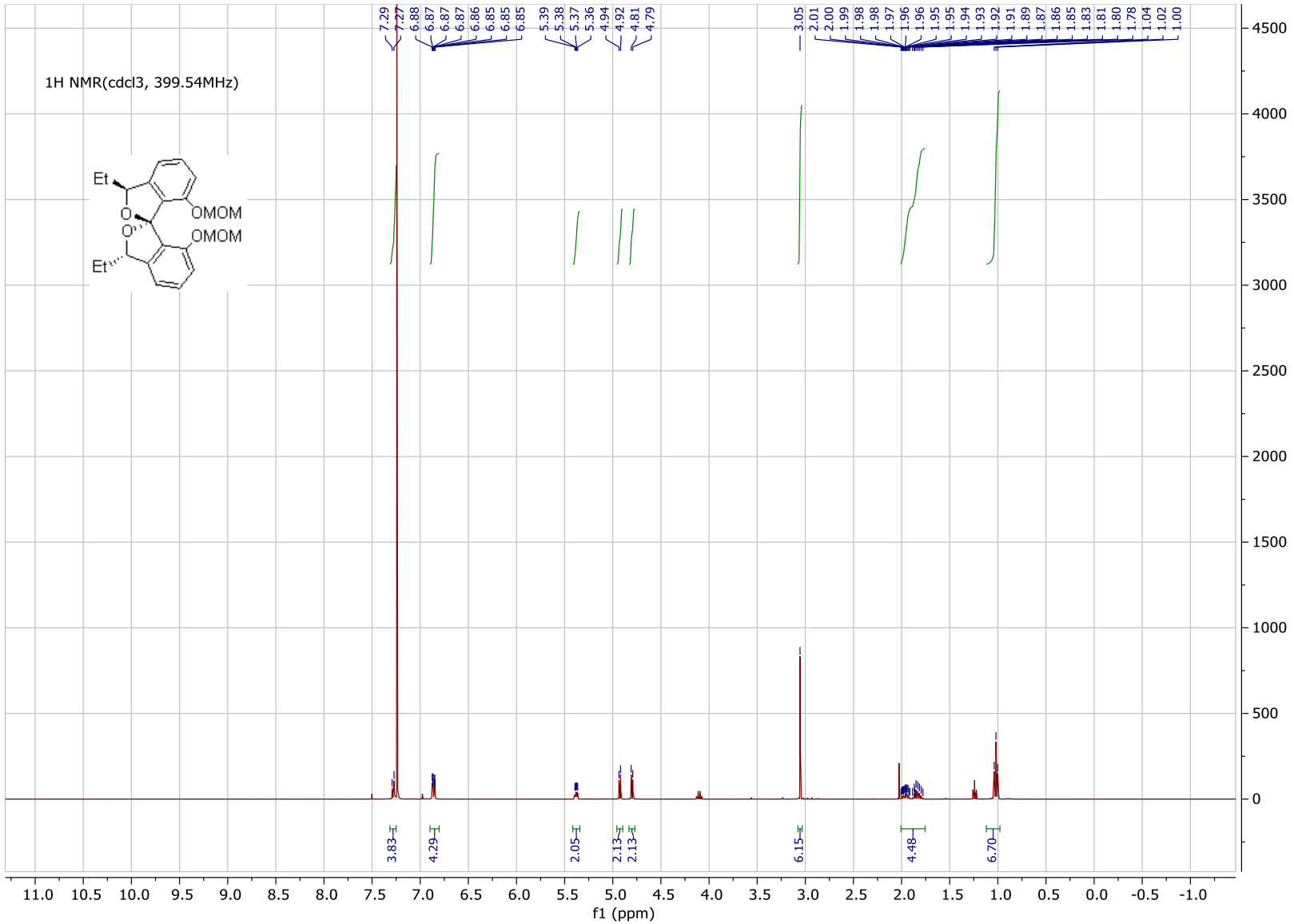
119.47
115.15
113.91
94.44
75.82
56.01
31.83
10.40
10.14
f1 (ppm)

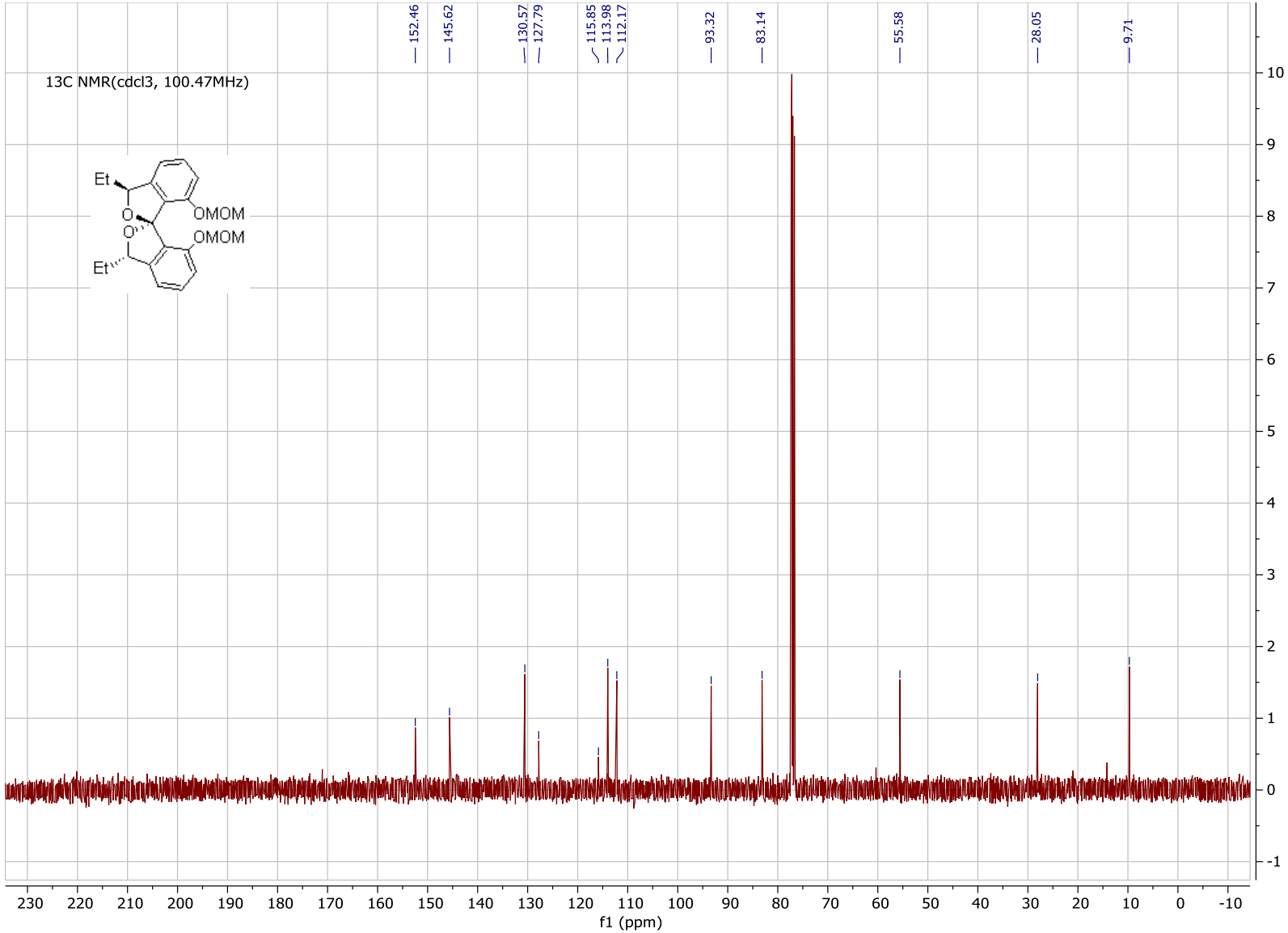

1H, cdcl3
399.54 MHz
OMOM
iPr
OH
7.21 6.99 6.98 6.97 6.95 6.95 6.94 6.94 6.94 6.93 6.92 6.92 6.92 6.92
5.18 5.16 5.16 5.14
4.34 4.33 4.32 4.31
3.47
1.97 1.96 1.94 1.92 1.91 1.89 1.80 1.79 1.79 1.78 1.78 1.77
0.99 0.97 0.81 0.79
0.74 1.04 1.87 2.02 0.99 2.84 1.01 0.79 3.11 3.30
f1 (ppm)

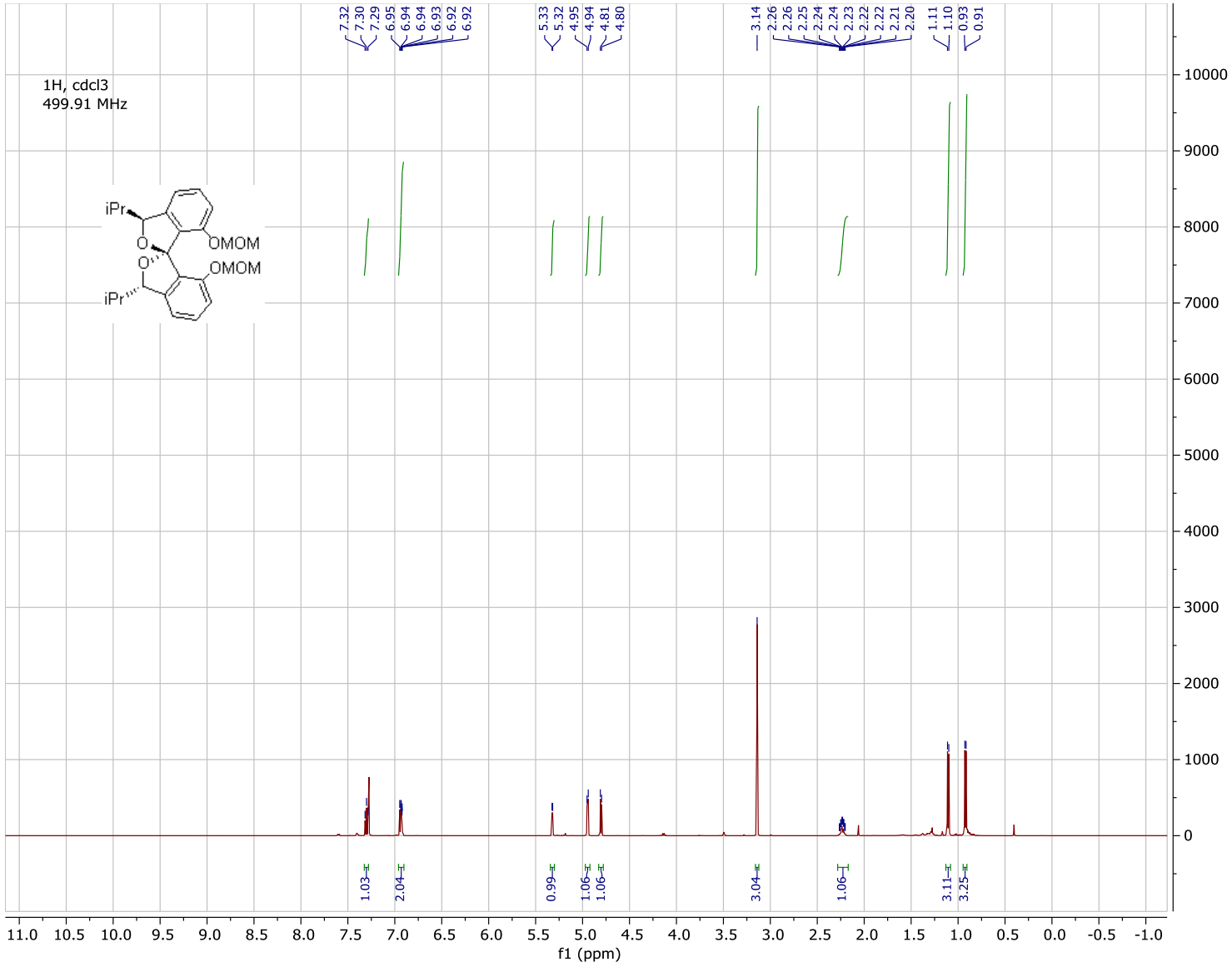

13C, cdcl3
100.47 MHz
OMOM
iPr
OH
157.20
145.44
129.20
120.10
115.05
114.53
94.46
79.83
56.00
35.17
19.04
18.11
f1 (ppm)

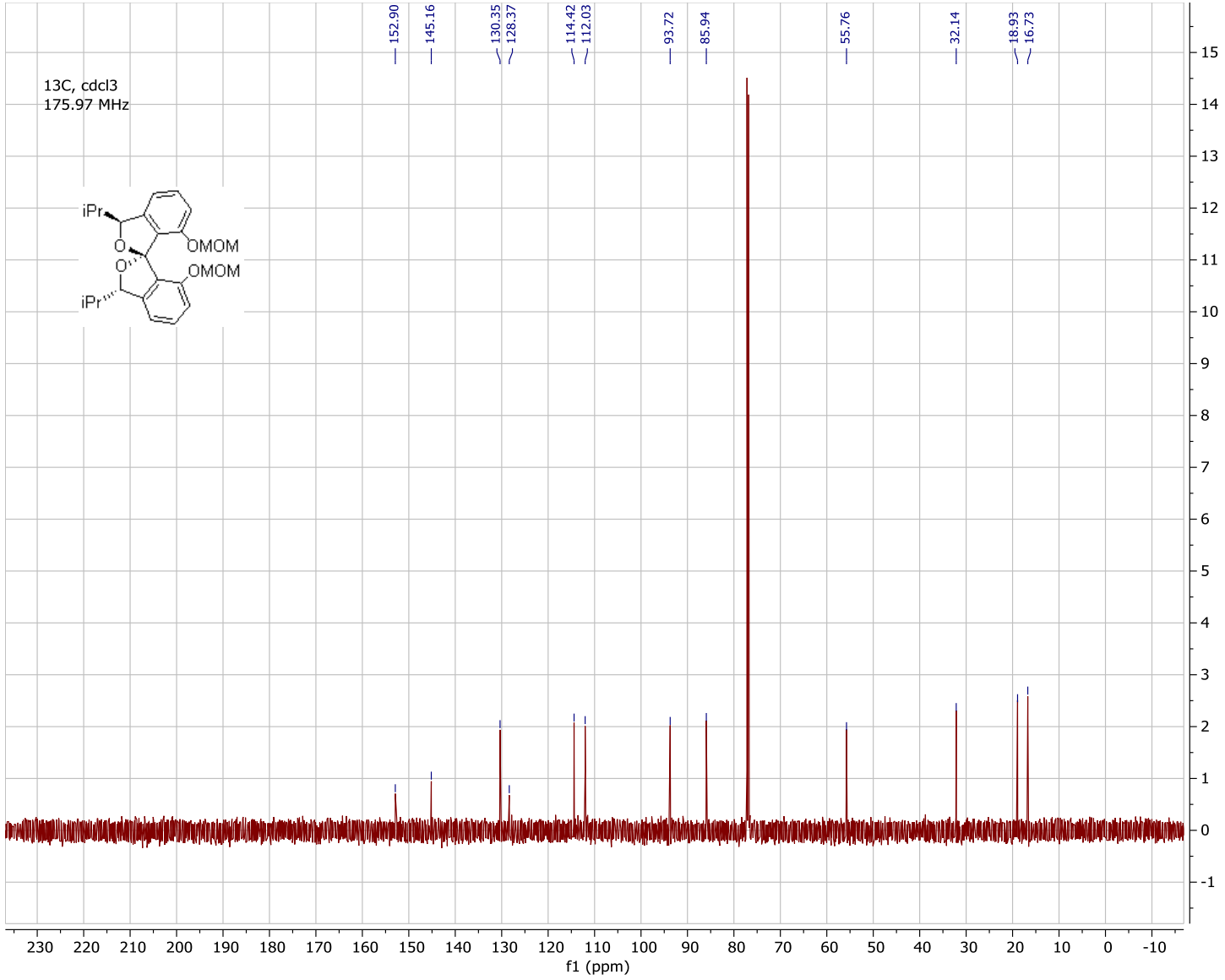

1H, cdcl3
399.54 MHz
OMOM
iPr
O
7.60
7.60
7.59
7.59
7.58
7.58
7.57
7.57
7.56
7.38
7.36
7.34
7.23
7.20
5.20
3.56
3.54
3.52
3.50
3.49
3.47
1.20
1.19
1.90
1.00
1.38
2.07
3.91
6.16
f1 (ppm)

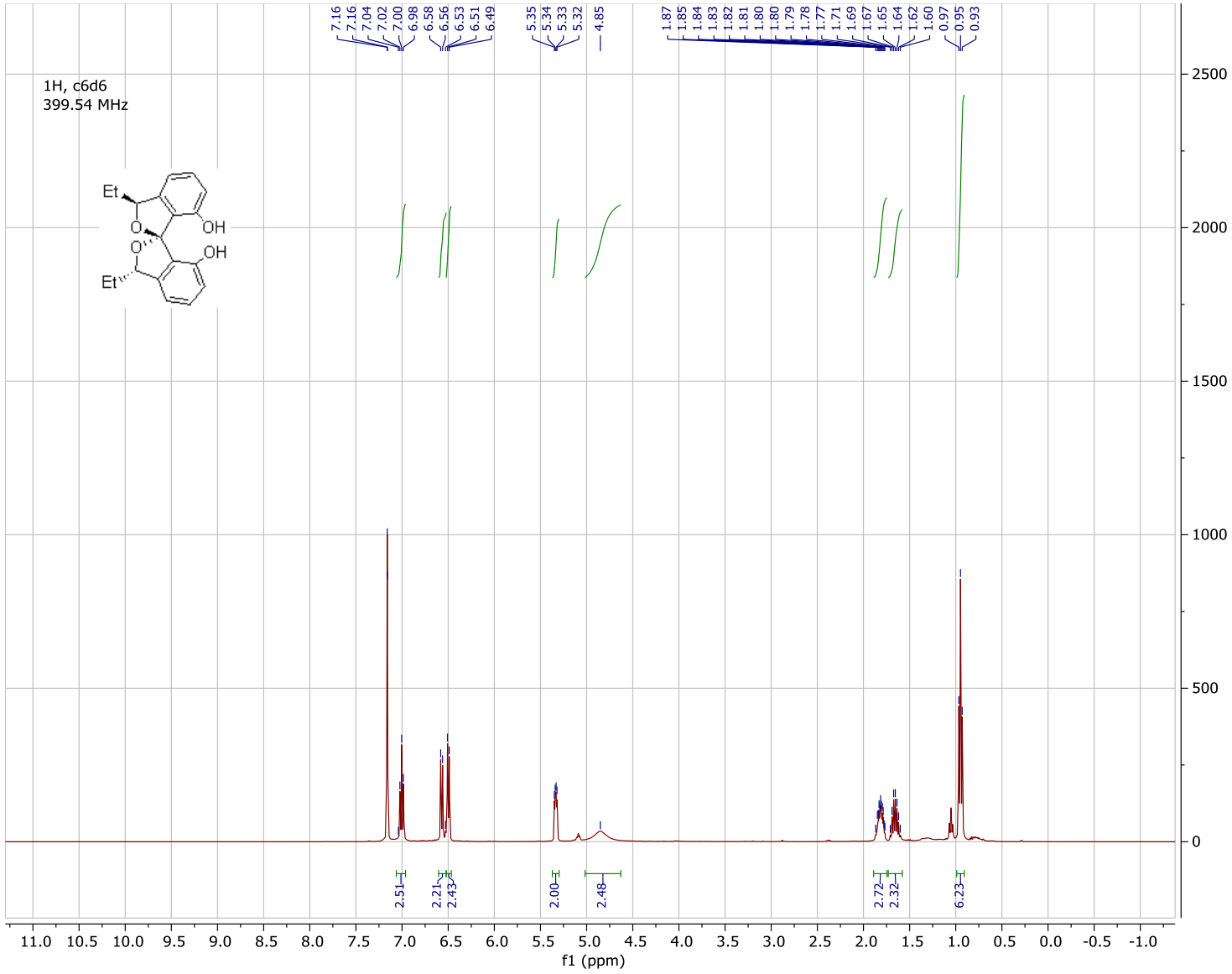

204.10
157.47
137.68
129.62
121.84
120.73
115.84
94.43
56.11
35.48
19.15
13C, cdcl3
100.47 MHz
OMOM
iPr
O
f1 (ppm)

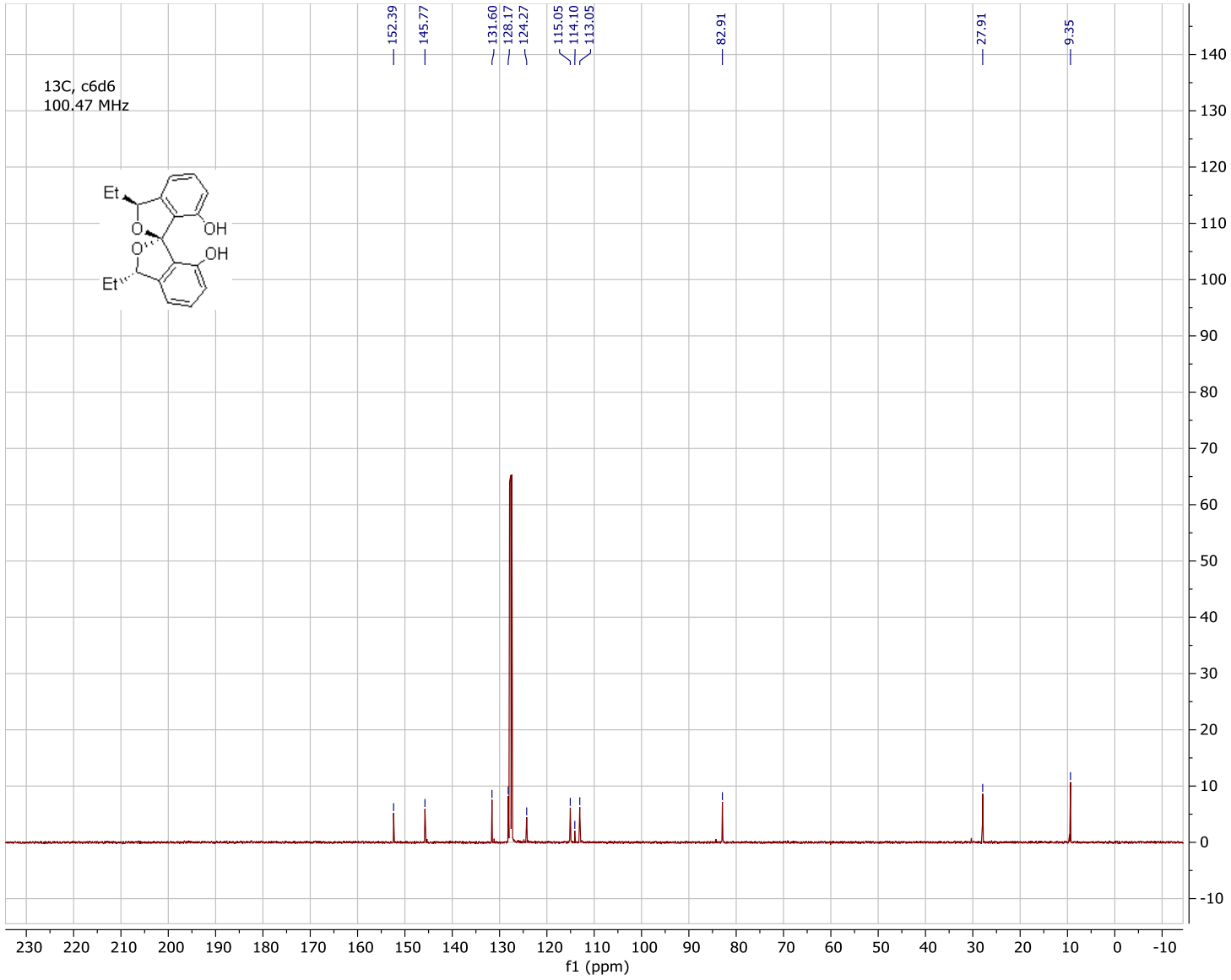

1H NMR(cdcl3, 399.54MHz)
Et
O
OMOM
O
OMOM
Et
7.29
7.27
6.88
6.87
6.87
6.87
6.86
6.85
6.85
6.85
5.39
5.38
5.37
5.36
4.94
4.92
4.81
4.79
3.05
2.01
2.00
1.99
1.98
1.98
1.97
1.96
1.96
1.95
1.95
1.94
1.93
1.92
1.91
1.89
1.87
1.86
1.85
1.83
1.81
1.80
1.78
1.04
1.02
1.00
3.83
4.29
2.05
2.13
2.13
6.15
4.48
6.70
f1 (ppm)

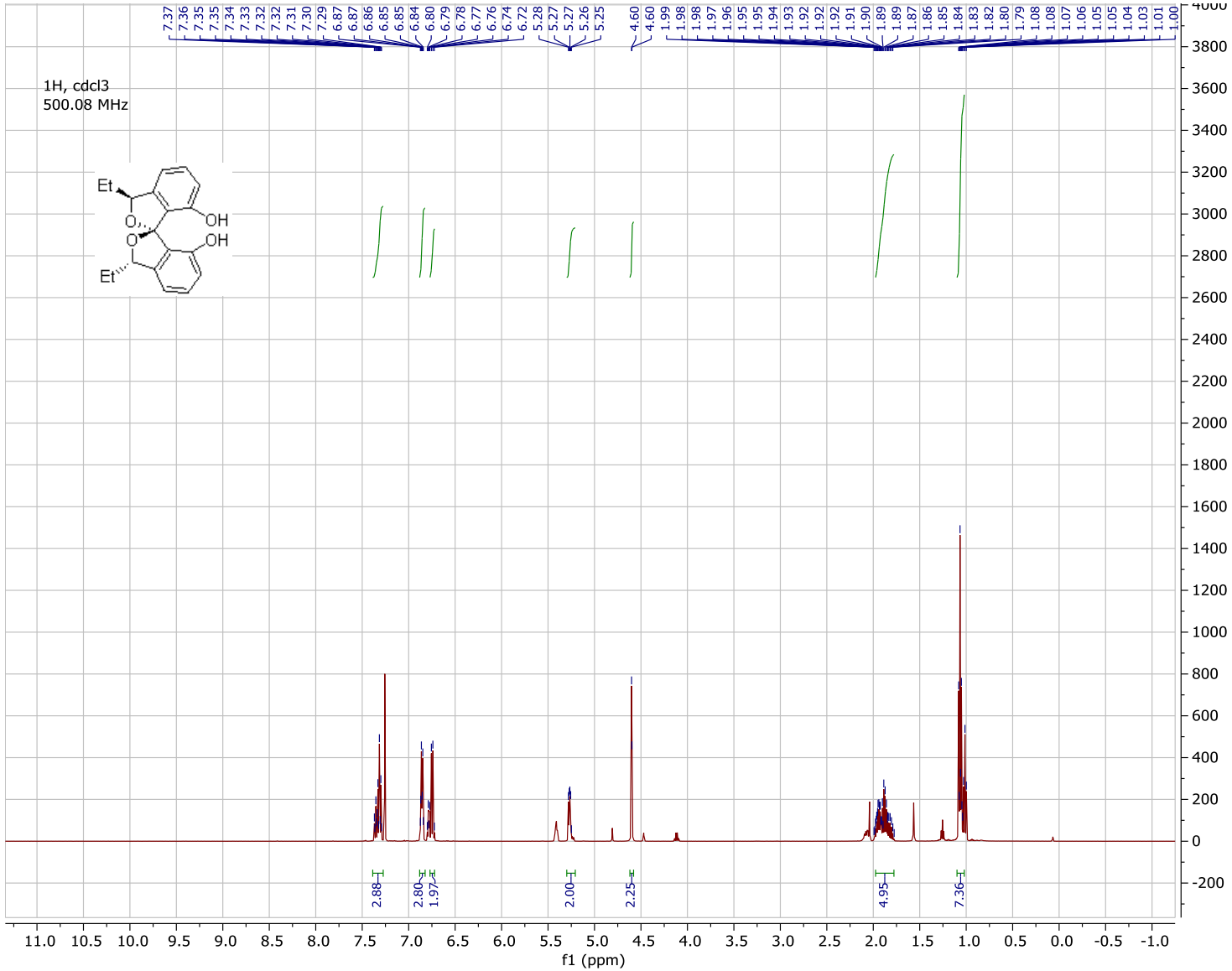

13C NMR(cdcl3, 100.47MHz)
152.46
145.62
130.57
127.79
115.85
113.98
112.17
93.32
83.14
55.58
28.05
9.71
Et
O
OMOM
O
OMOM
Et
f1 (ppm)

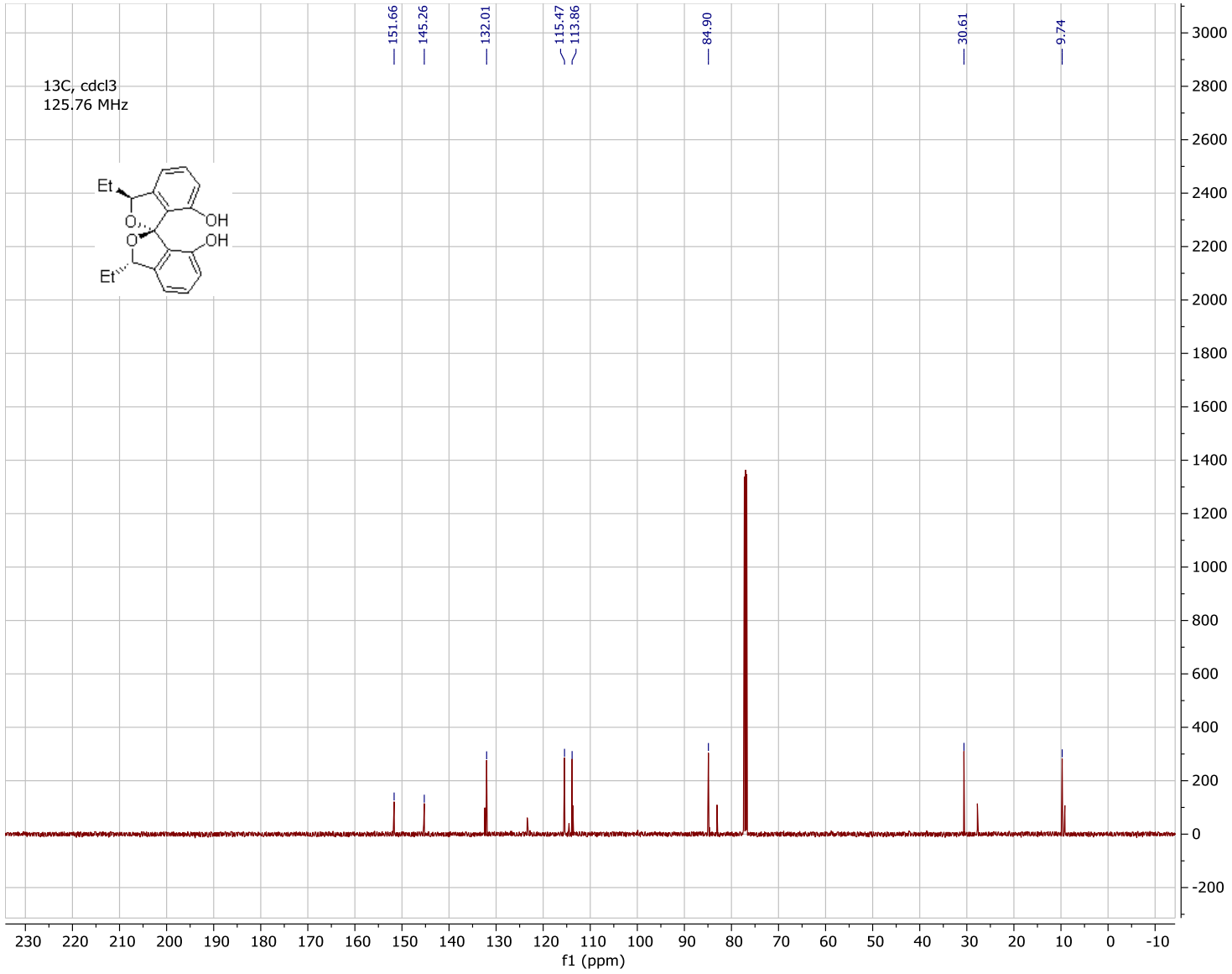

1H, cdcl3
499.91 MHz
iPr
O
OMOM
O
OMOM
iPr
7.32
7.30
7.29
6.95
6.94
6.94
6.93
6.92
6.92
5.33
5.32
4.95
4.94
4.81
4.80
3.14
2.26
2.26
2.25
2.24
2.24
2.23
2.22
2.22
2.21
2.20
1.11
1.10
0.93
0.91
1.03
2.04
0.99
1.06
1.06
3.04
1.06
3.11
3.25
f1 (ppm)

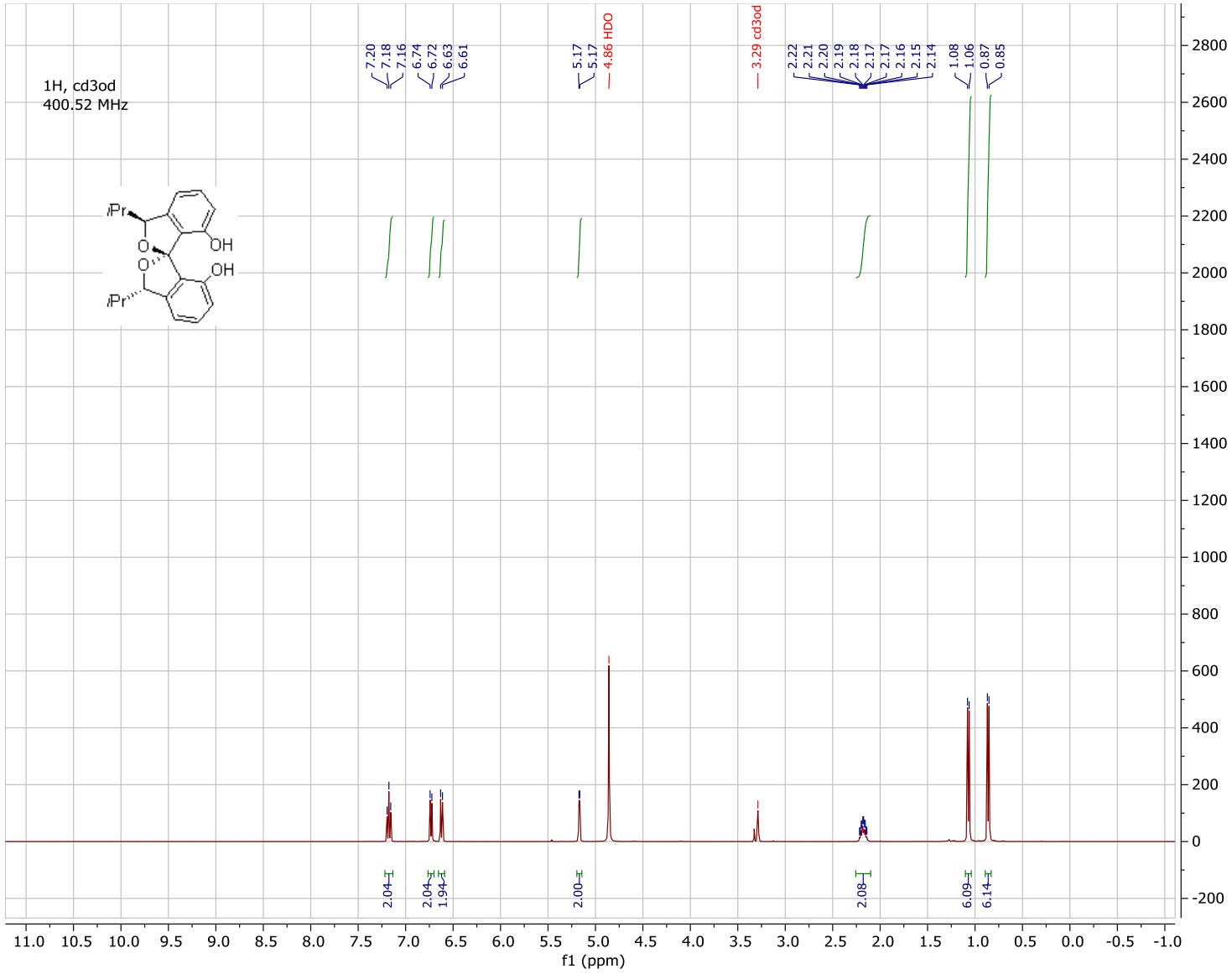

13C, cdcl3
175.97 MHz
iPr
O
OMOM
O
OMOM
iPr
152.90
145.16
130.35
128.37
114.42
112.03
93.72
85.94
55.76
32.14
18.93
16.73
f1 (ppm)

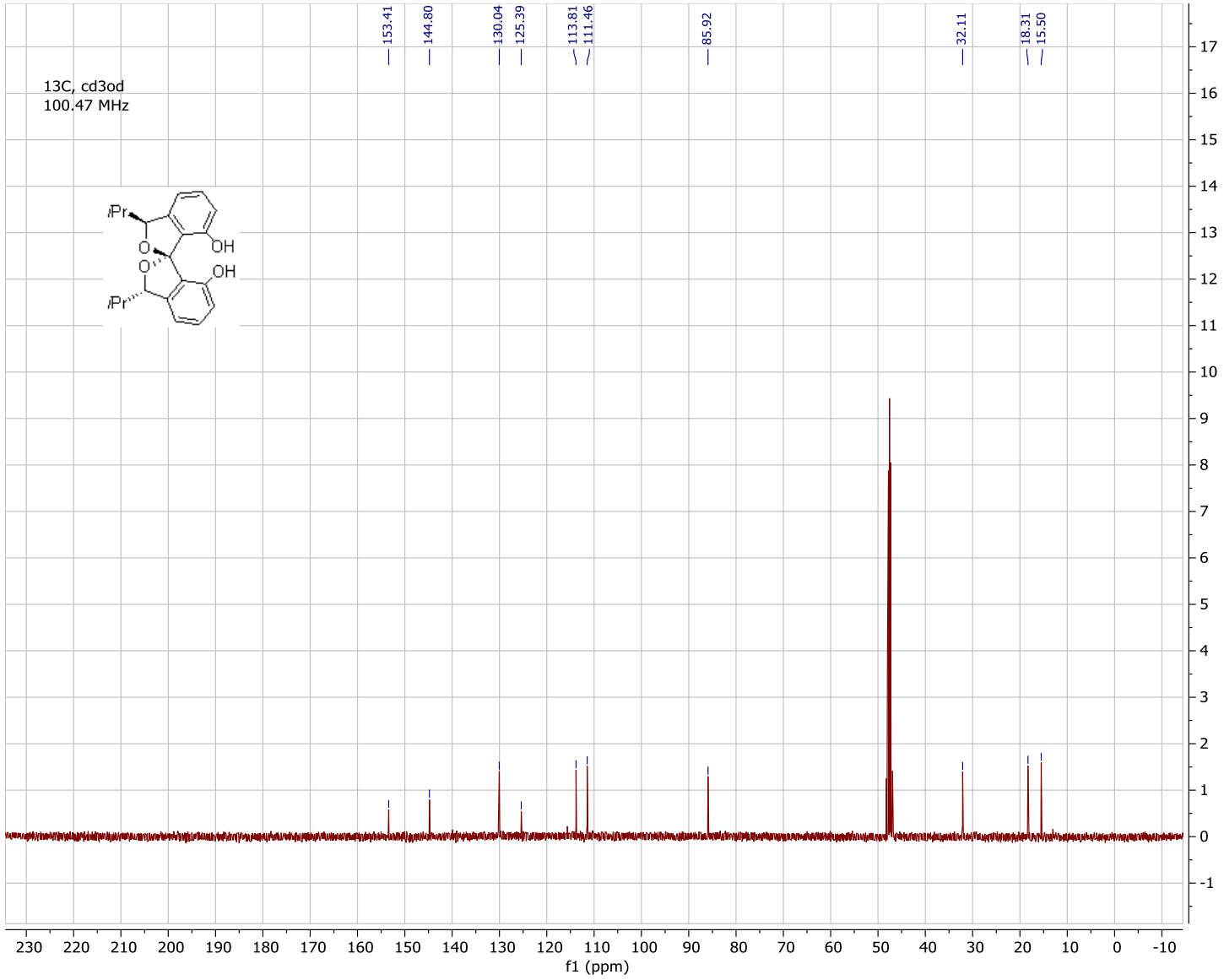

1H, c6d6
399.54 MHz
Et
O
O
Et
OH
OH
7.16
7.16
7.04
7.02
7.00
6.98
6.58
6.56
6.53
6.51
6.49
5.35
5.34
5.33
5.32
4.85
1.87
1.85
1.84
1.83
1.82
1.81
1.80
1.80
1.79
1.78
1.77
1.71
1.69
1.67
1.65
1.64
1.62
1.60
0.97
0.95
0.93
2.51
2.21
2.43
2.00
2.48
2.72
2.32
6.23
2500
2000
1500
1000
500
0
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

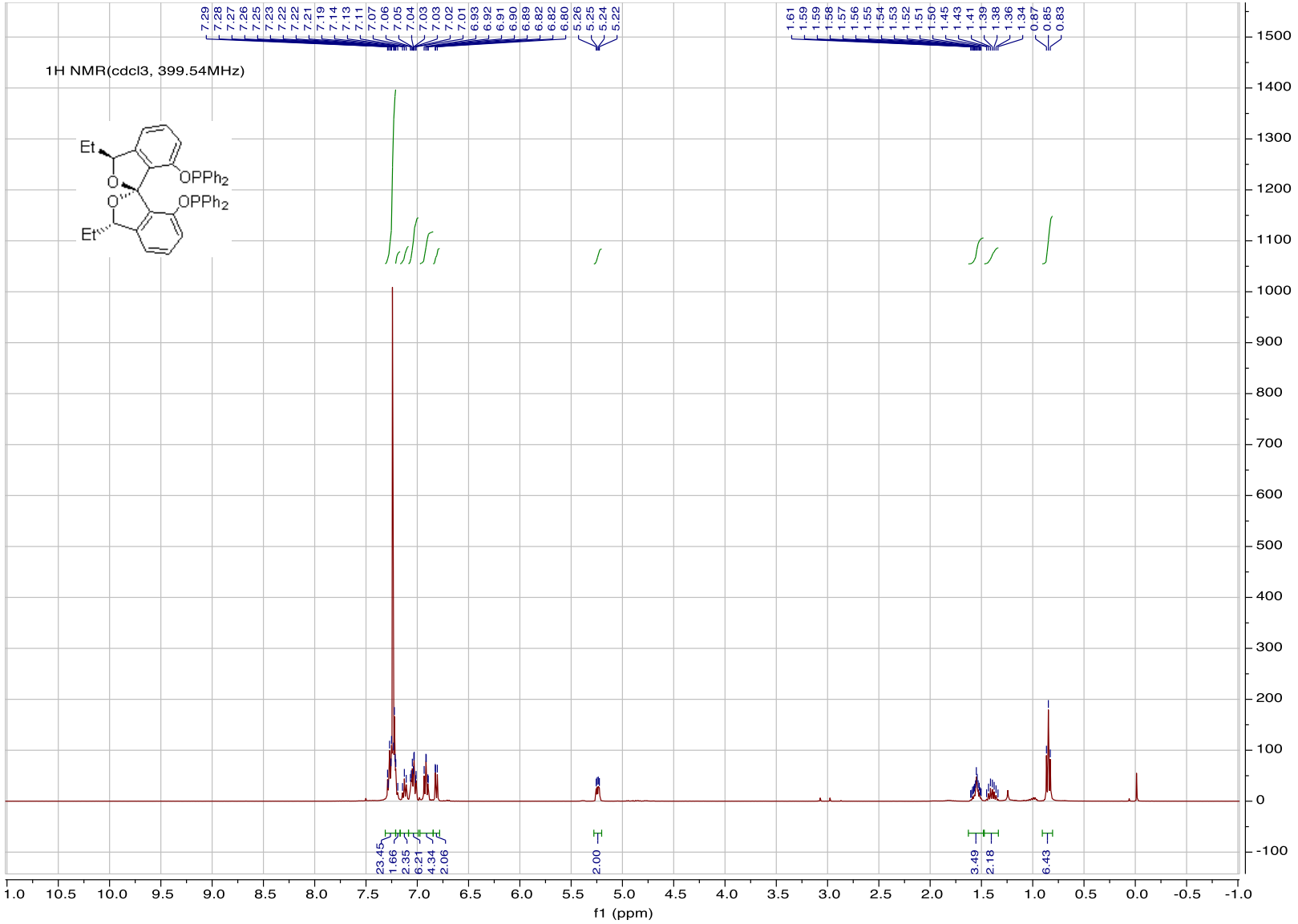

13C, c6d6
100.47 MHz
152.39
145.77
131.60
128.17
124.27
115.05
114.10
113.05
82.91
27.91
9.35
Et
O
O
OH
OH
Et
f1 (ppm)

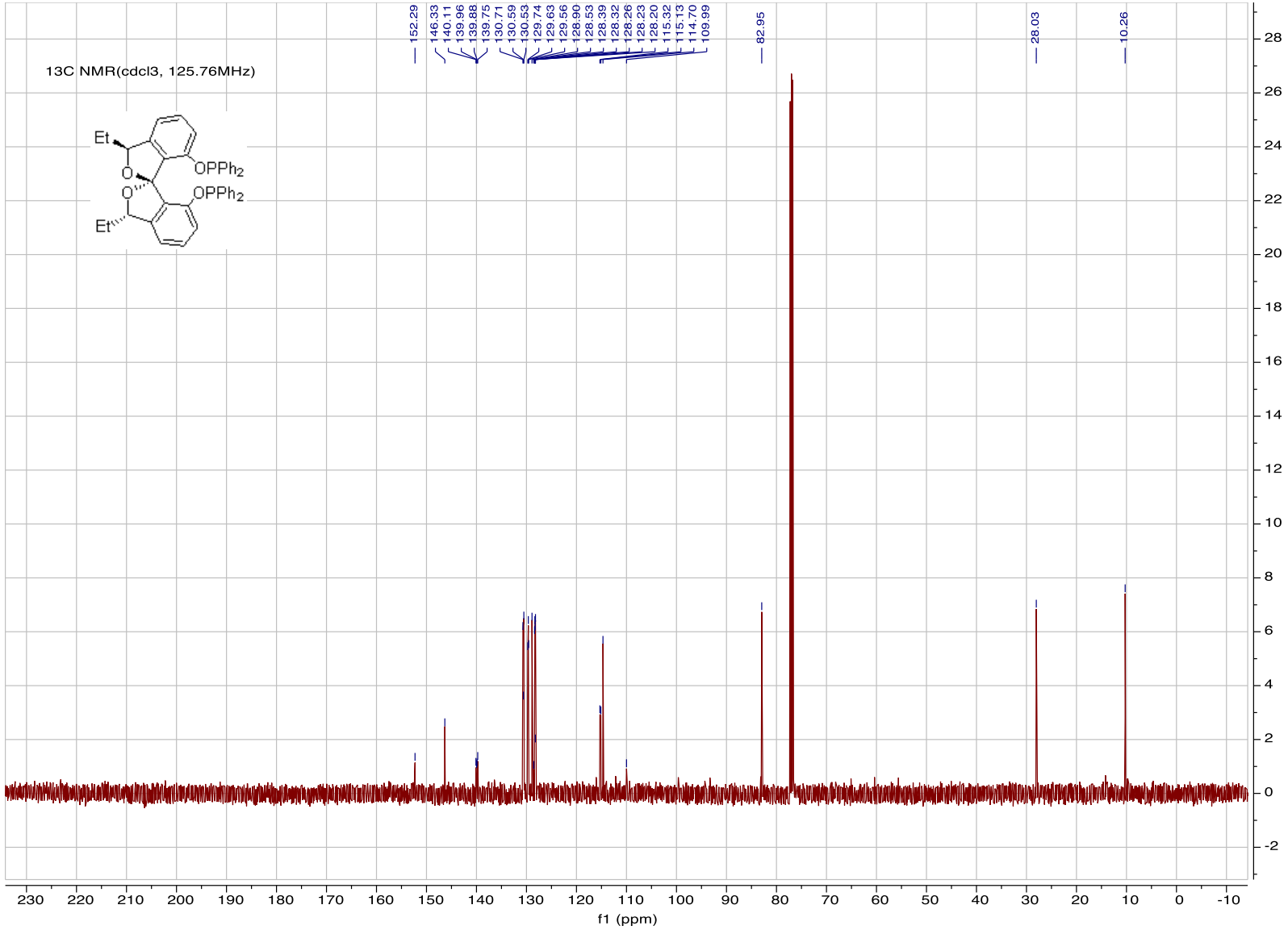

1H, cdcl3
500.08 MHz
Et
O
OH
OH
O
Et
f1 (ppm)

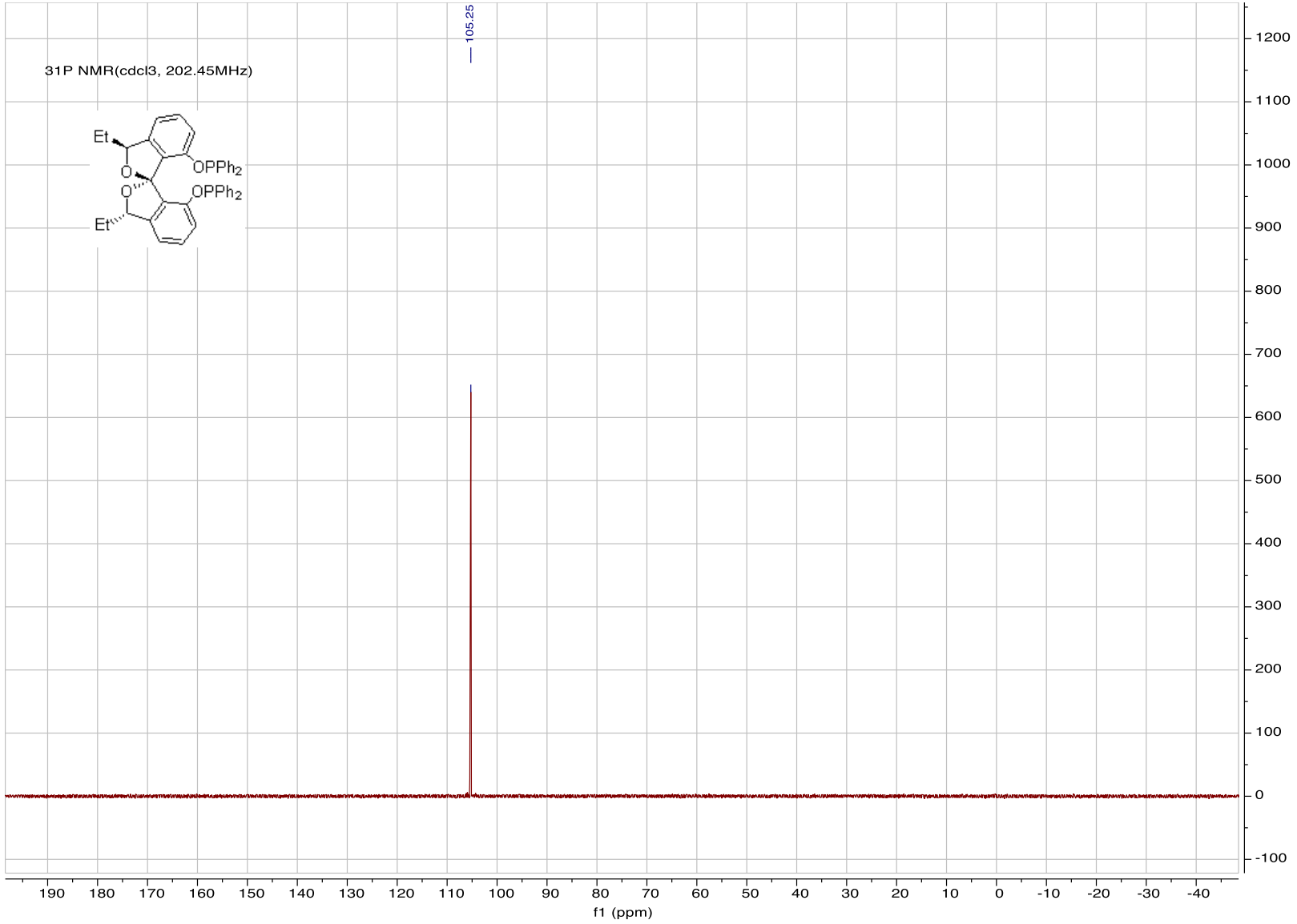

13C, cdcl3
125.76 MHz
Et
O
O
OH
OH
Et
151.66
145.26
132.01
115.47
113.86
84.90
30.61
9.74
f1 (ppm)

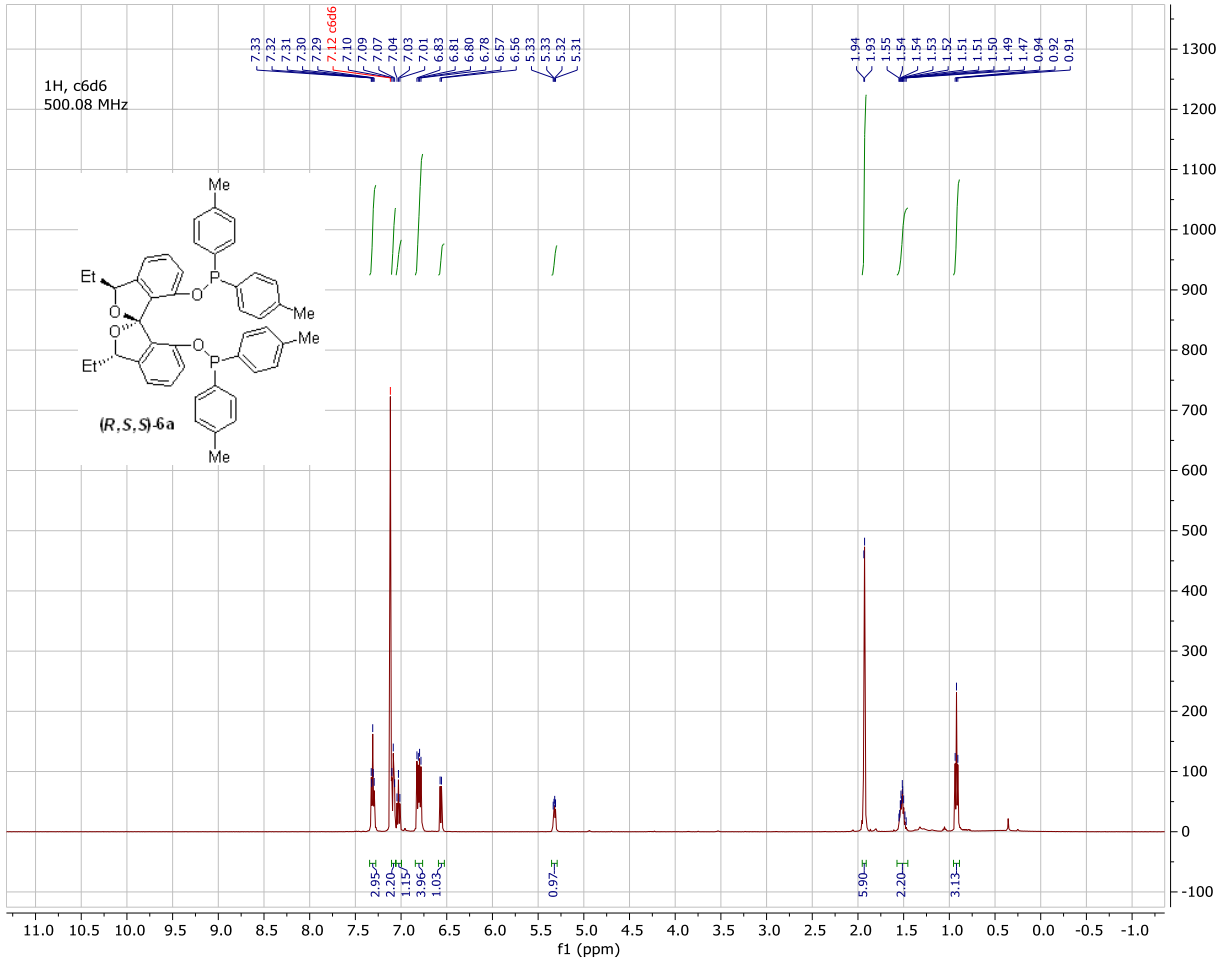

1H, cd3od
400.52 MHz
iPr
O
O
OH
OH
iPr
7.20
7.18
7.16
6.74
6.72
6.63
6.61
5.17
5.17
4.86 HDO
3.29 cd3od
2.22
2.21
2.20
2.19
2.18
2.17
2.17
2.16
2.15
2.14
1.08
1.06
0.87
0.85
2.04
2.04
1.94
2.00
2.08
6.09
6.14
f1 (ppm)

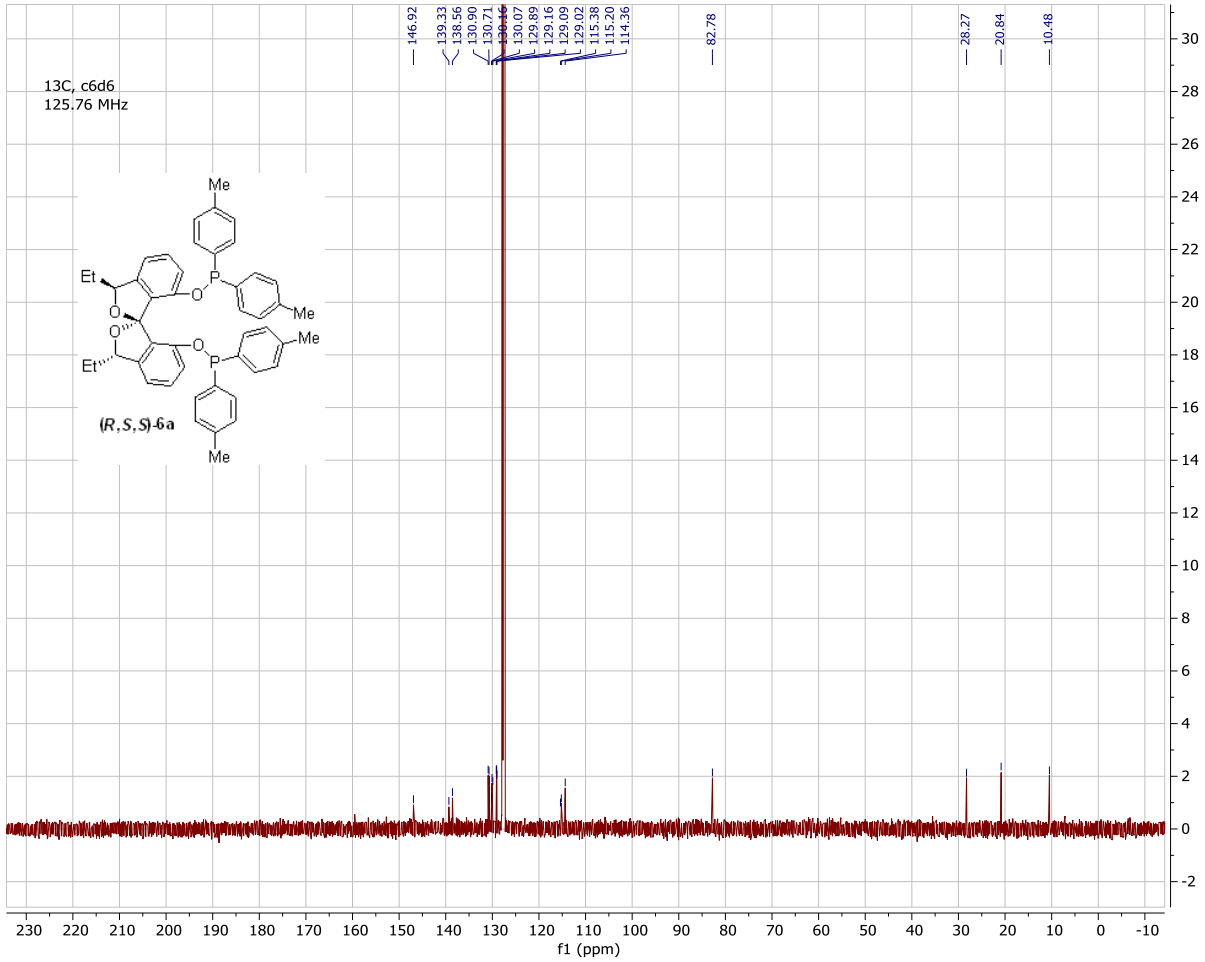

153.41
144.80
130.04
125.39
113.81
111.46
85.92
32.11
18.31
15.50
13C, cd3od
100.47 MHz
iPr
O
O
OH
OH
iPr
f1 (ppm)

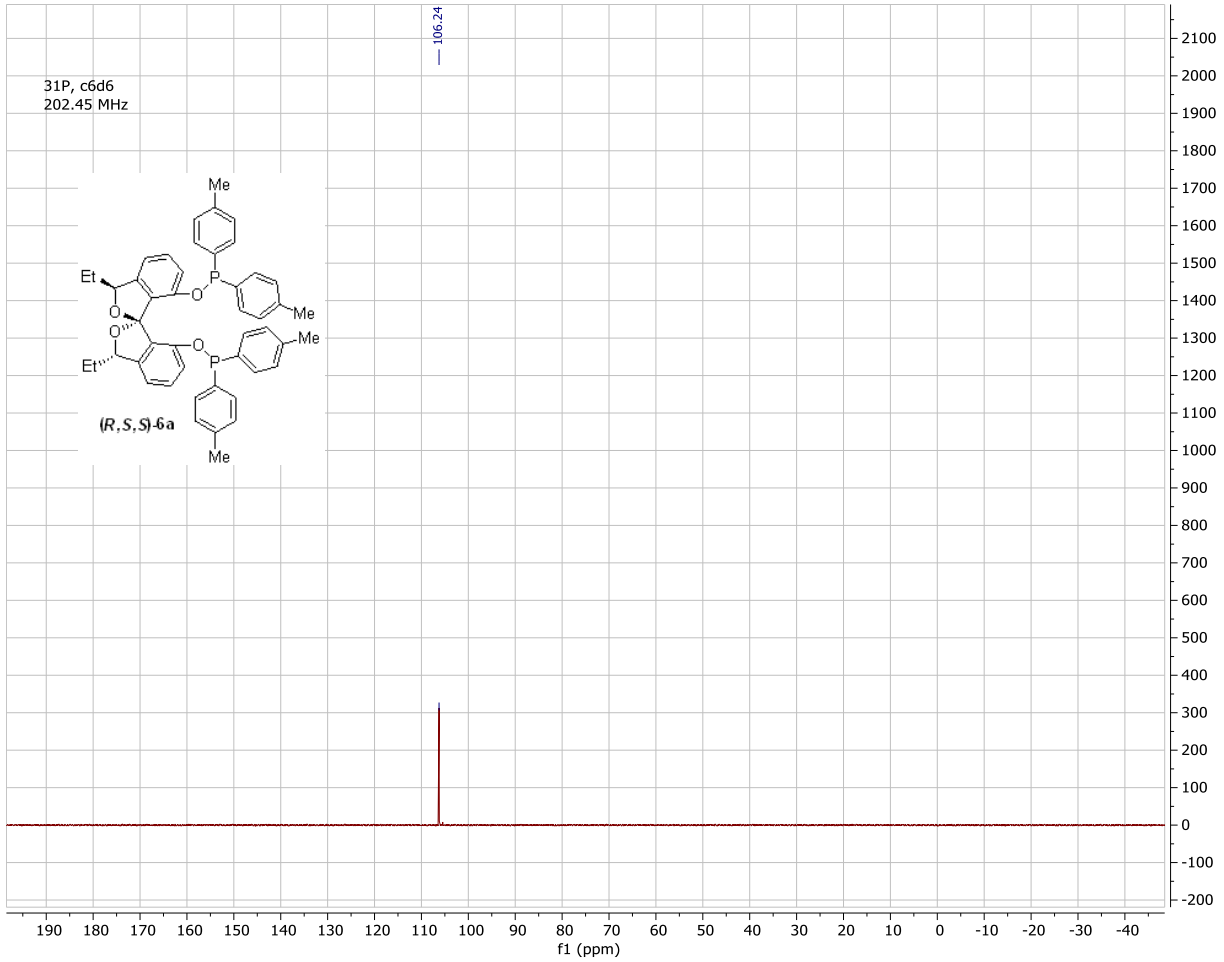

1H NMR(cdcl3, 399.54MHz)
Et
O
O
OPPh2
OPPh2
Et
7.29 7.28 7.27 7.26 7.25 7.23 7.22 7.22 7.21 7.19 7.14 7.13 7.11 7.07 7.06 7.05 7.04 7.03 7.03 7.02 7.01 6.93 6.92 6.91 6.90 6.89 6.82 6.82 6.80 5.26 5.25 5.24 5.22
1.61 1.59 1.59 1.58 1.57 1.56 1.55 1.54 1.53 1.52 1.51 1.50 1.45 1.43 1.41 1.39 1.38 1.36 1.34 0.87 0.85 0.83
23.45 1.66 2.35 6.21 4.34 2.06 2.00 3.49 2.18 6.43
f1 (ppm)

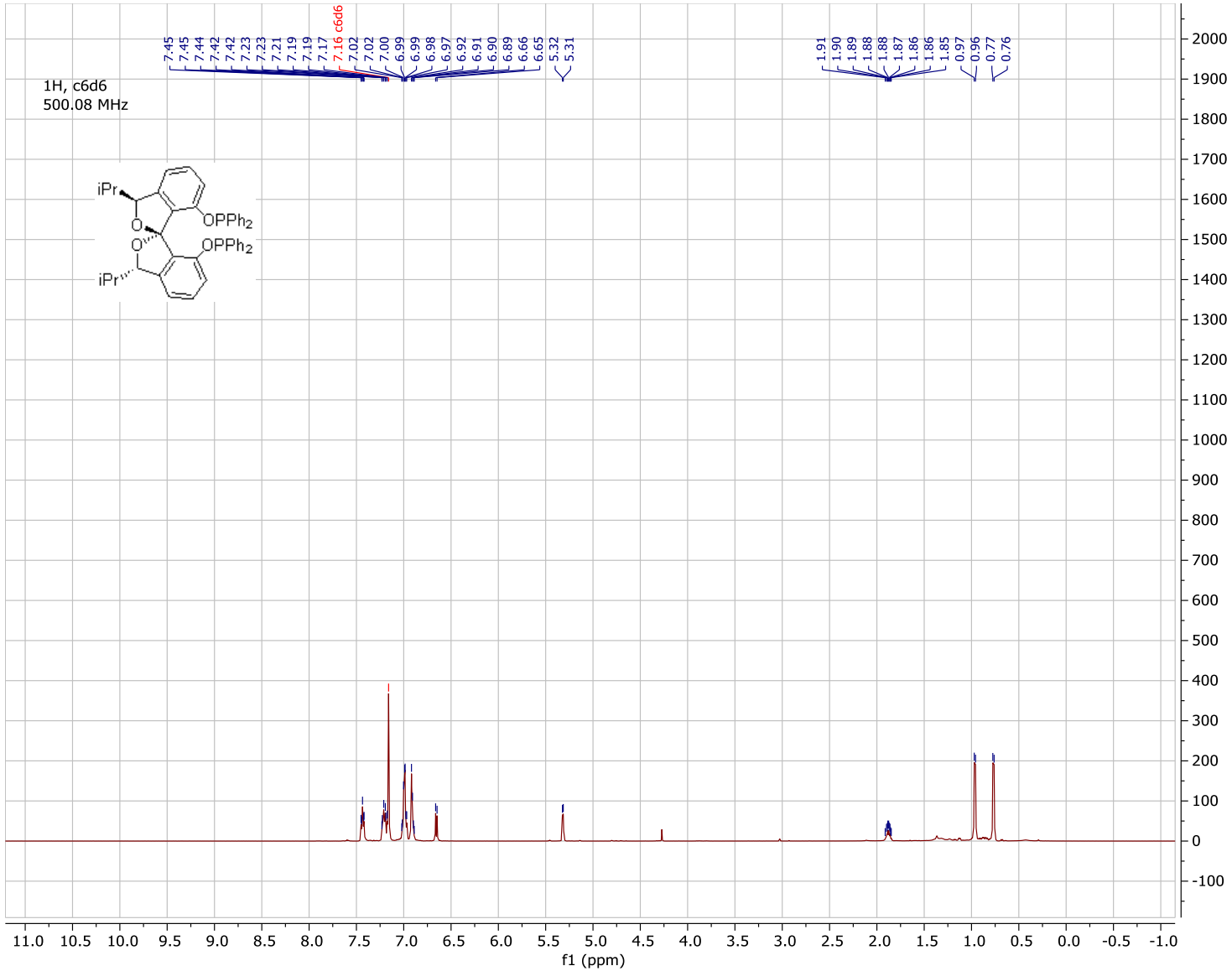

13C NMR(cdcl3, 125.76MHz)
Et
O
OPPh2
OPPh2
O
Et
152.29
146.33
140.11
139.96
139.88
139.75
130.71
130.59
130.53
129.74
129.63
129.56
128.90
128.53
128.39
128.32
128.26
128.23
128.20
115.32
115.13
114.70
109.99
82.95
28.03
10.26
f1 (ppm)

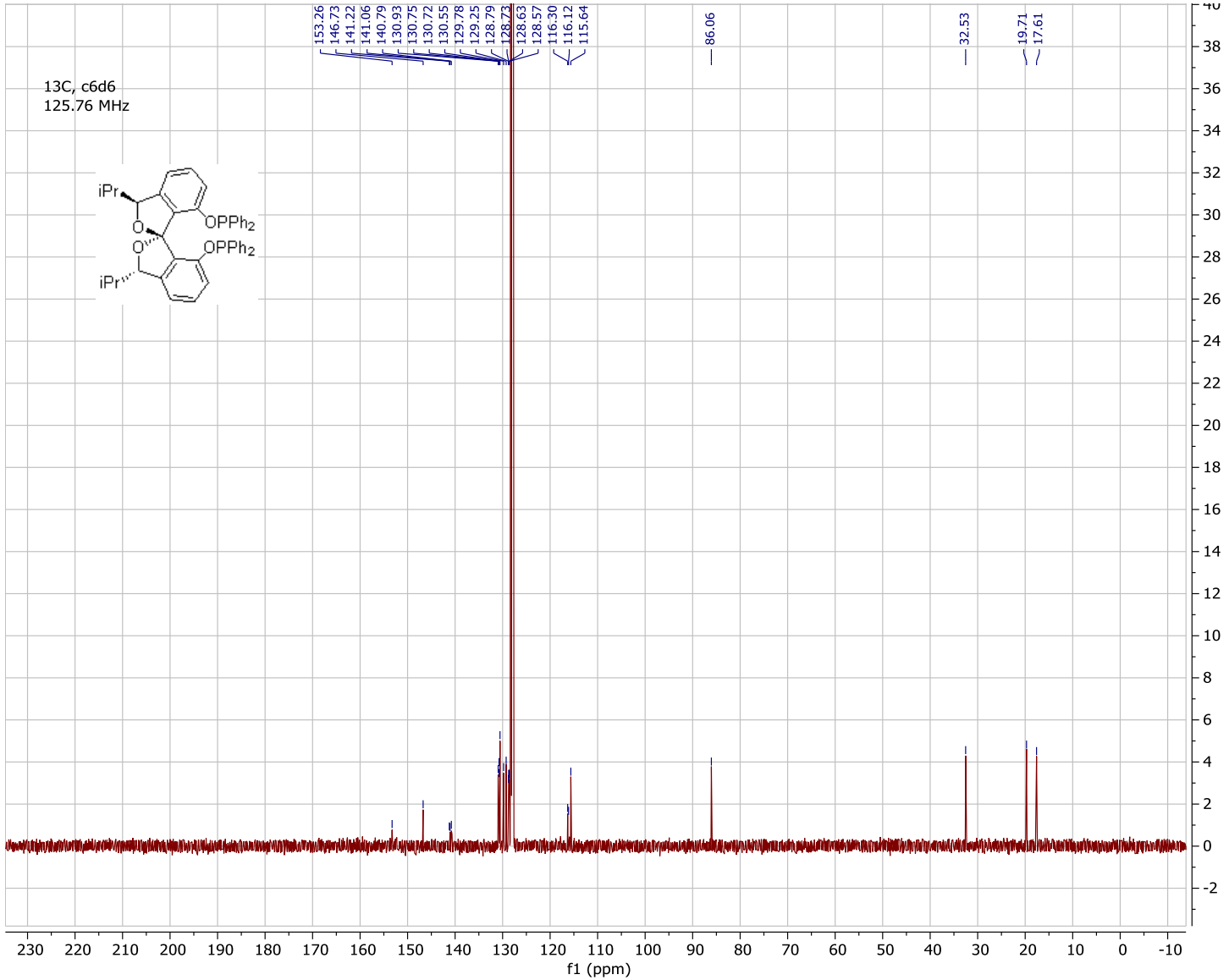

105.25
31P NMR(cdcl3, 202.45MHz)
Et
O
OPPh2
OPPh2
O
Et
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

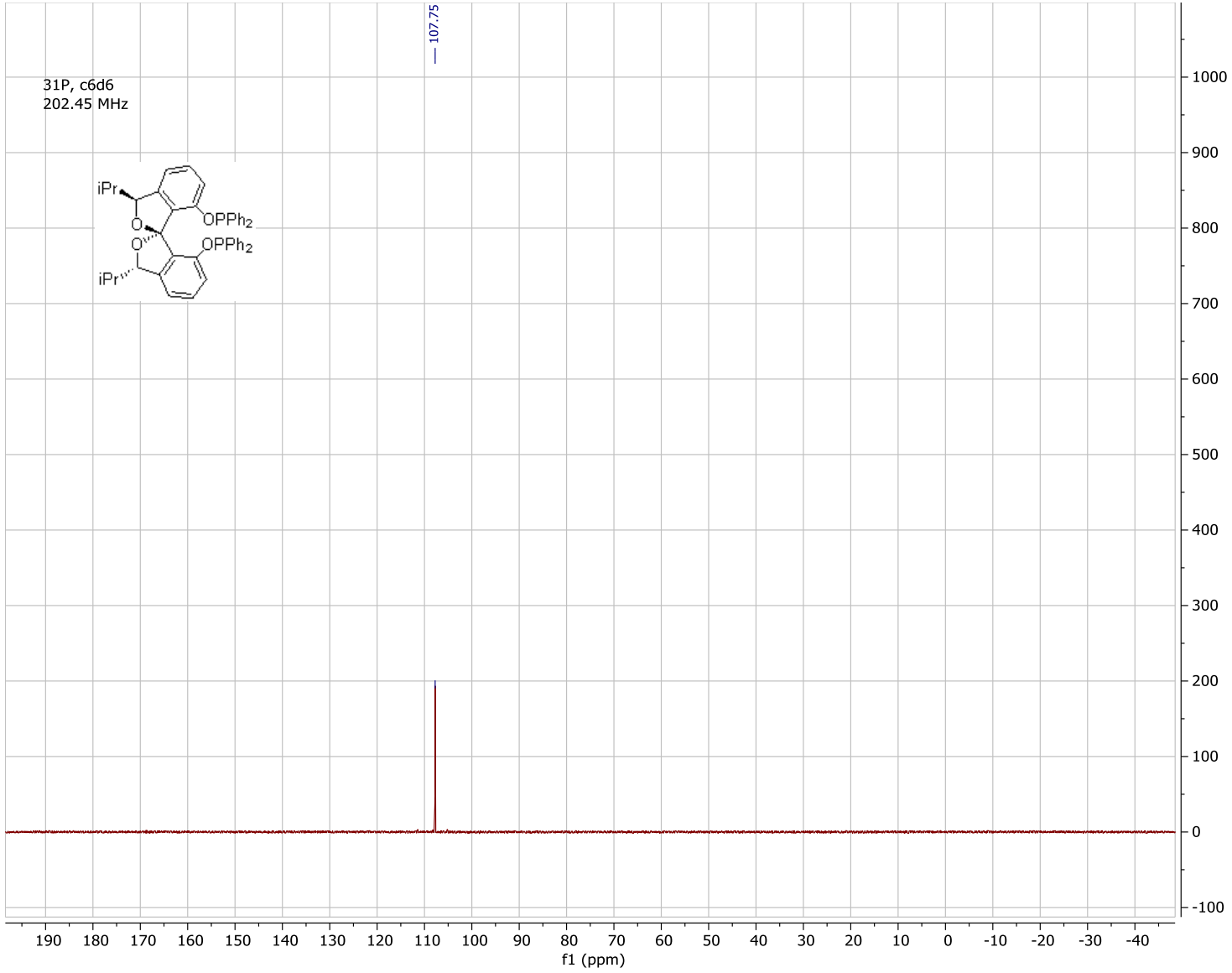

1H, c6d6
500.08 MHz
(R,S,S)-6a
f1 (ppm)

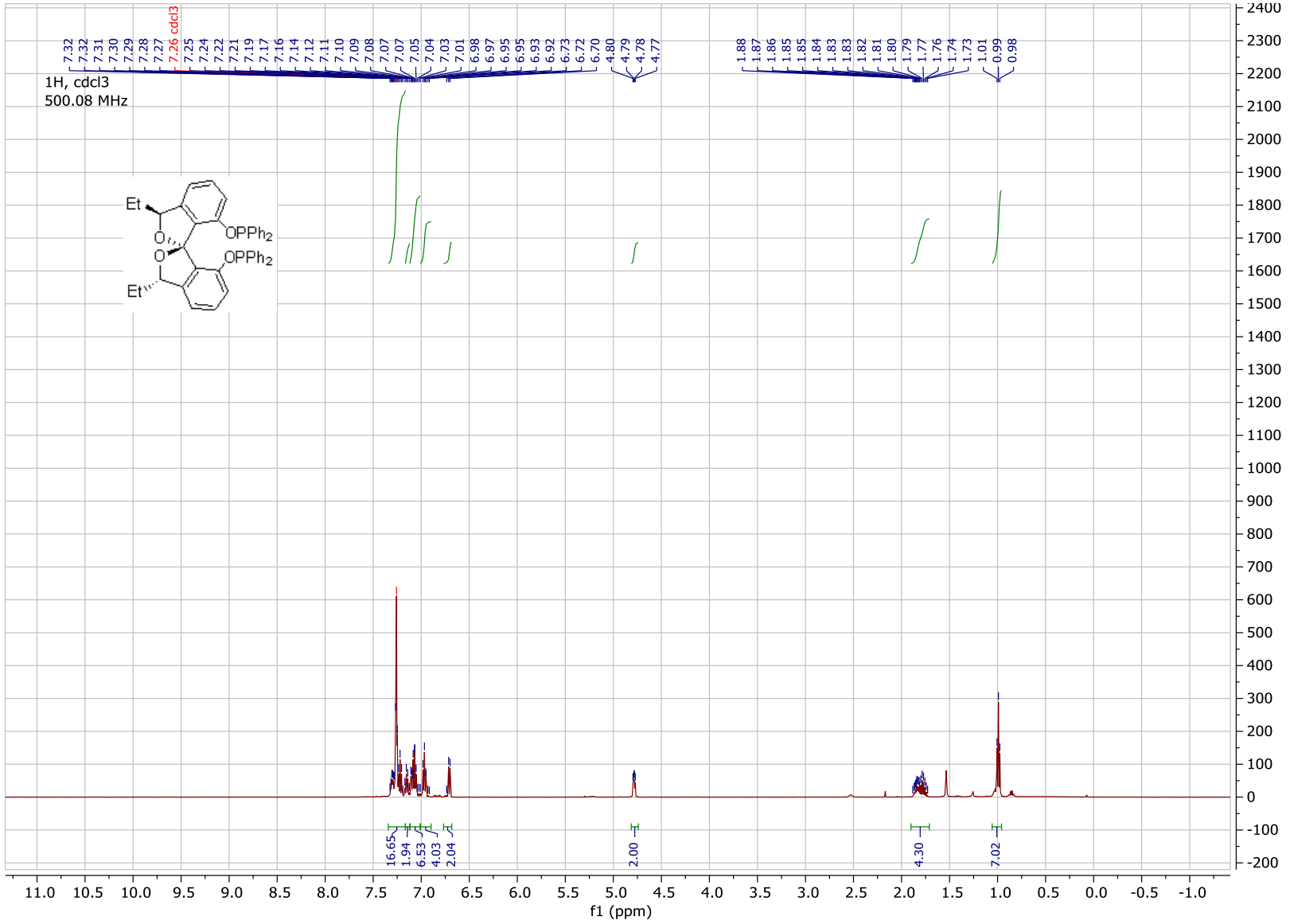

13C, c6d6
125.76 MHz
146.92
139.33
138.56
130.90
130.71
130.07
129.89
129.16
129.09
129.02
115.38
115.20
114.36
82.78
28.27
20.84
10.48
Me
Et
O
P
Me
Me
Et
(R,S,S)-6a
f1 (ppm)

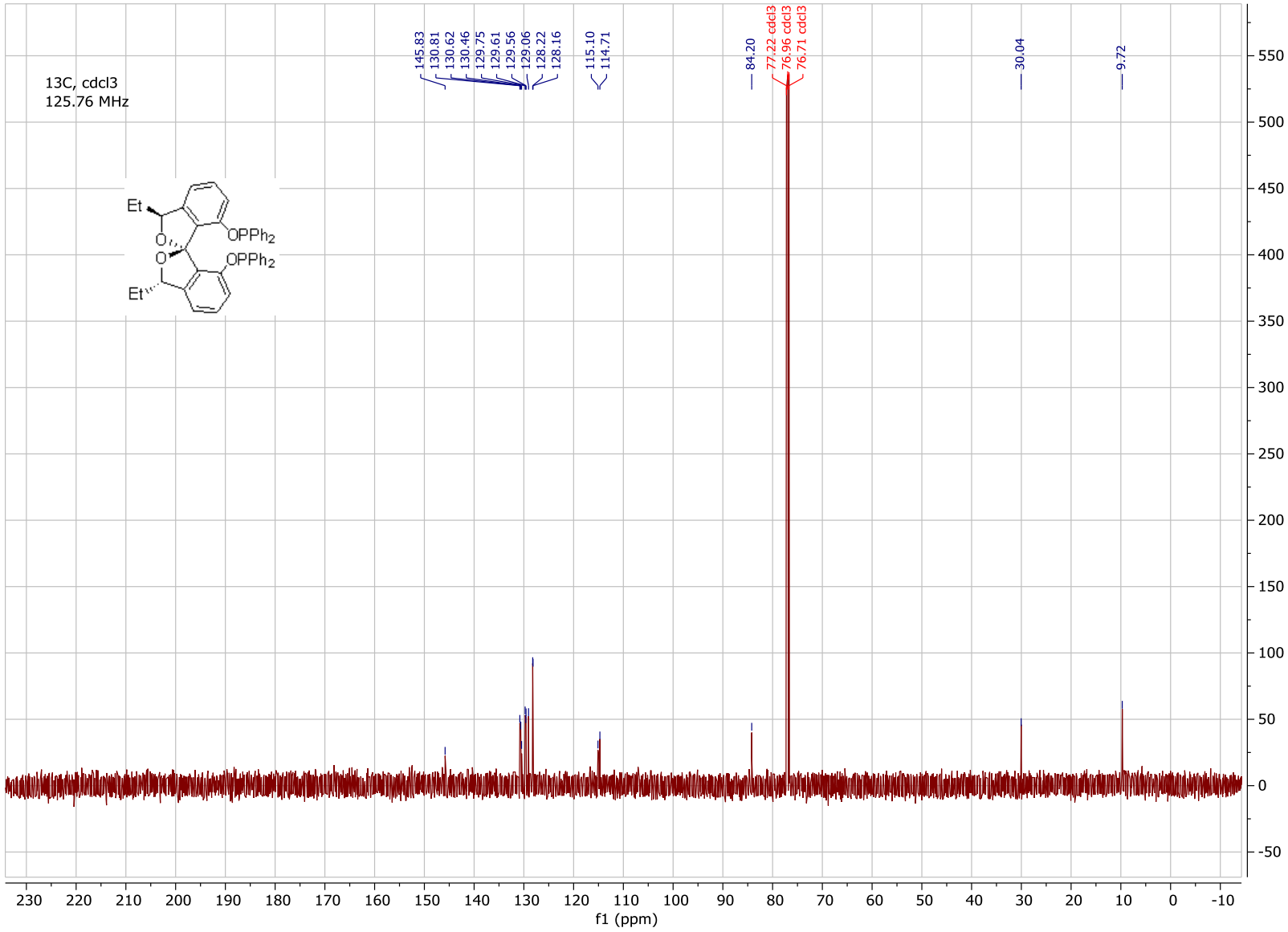

106.24
31P, c6d6
202.45 MHz
Me
Et
O
P
Me
Me
Et
(R,S,S)-6a
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

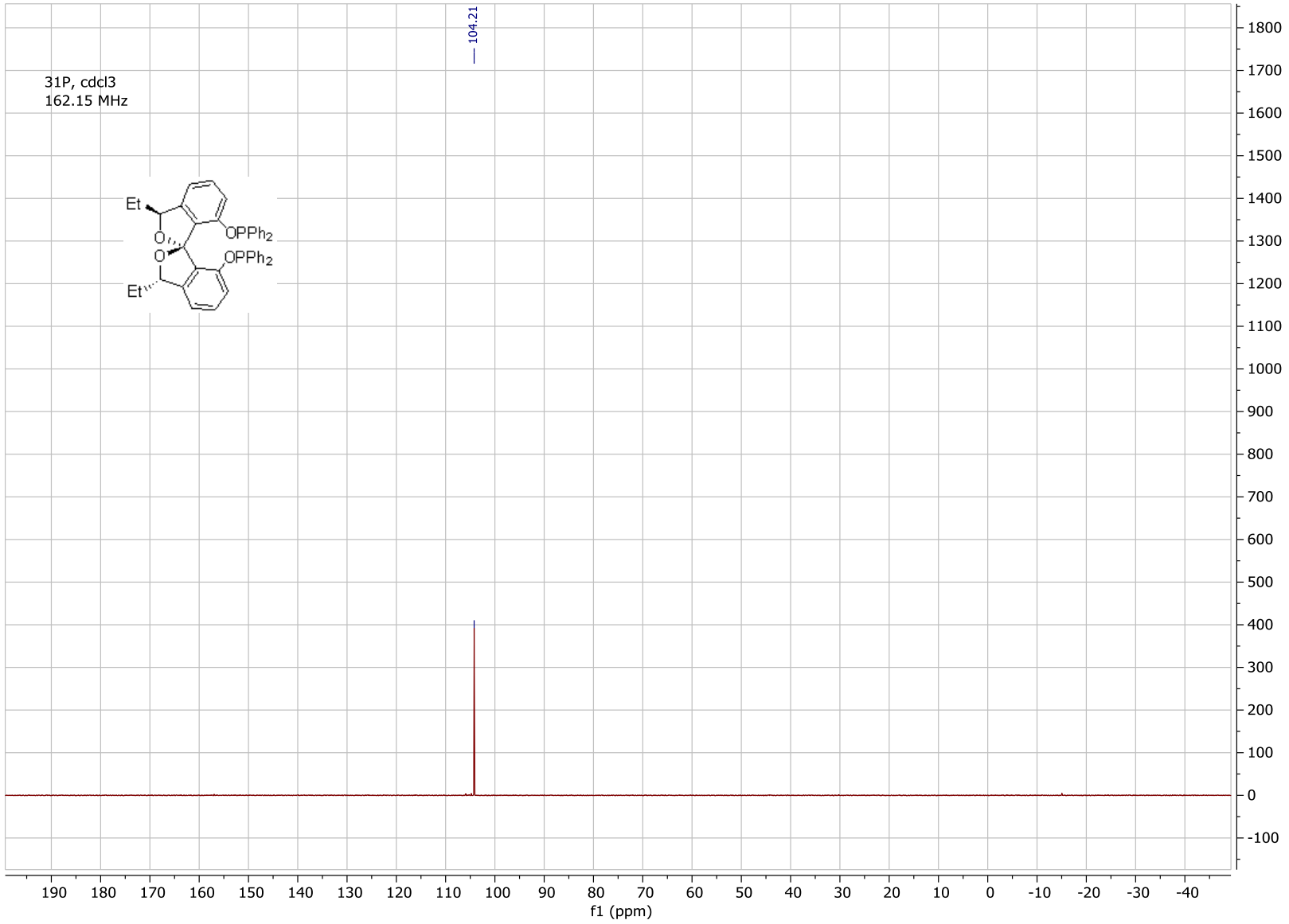

7.45
7.45
7.44
7.42
7.42
7.23
7.23
7.21
7.19
7.19
7.17
7.16 c6d6
7.02
7.02
7.00
6.99
6.99
6.98
6.97
6.92
6.91
6.90
6.89
6.66
6.65
5.32
5.31
1.91
1.90
1.89
1.88
1.88
1.87
1.86
1.86
1.85
0.97
0.96
0.77
0.76
1H, c6d6
500.08 MHz
iPr
OPPh2
OPPh2
iPr
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

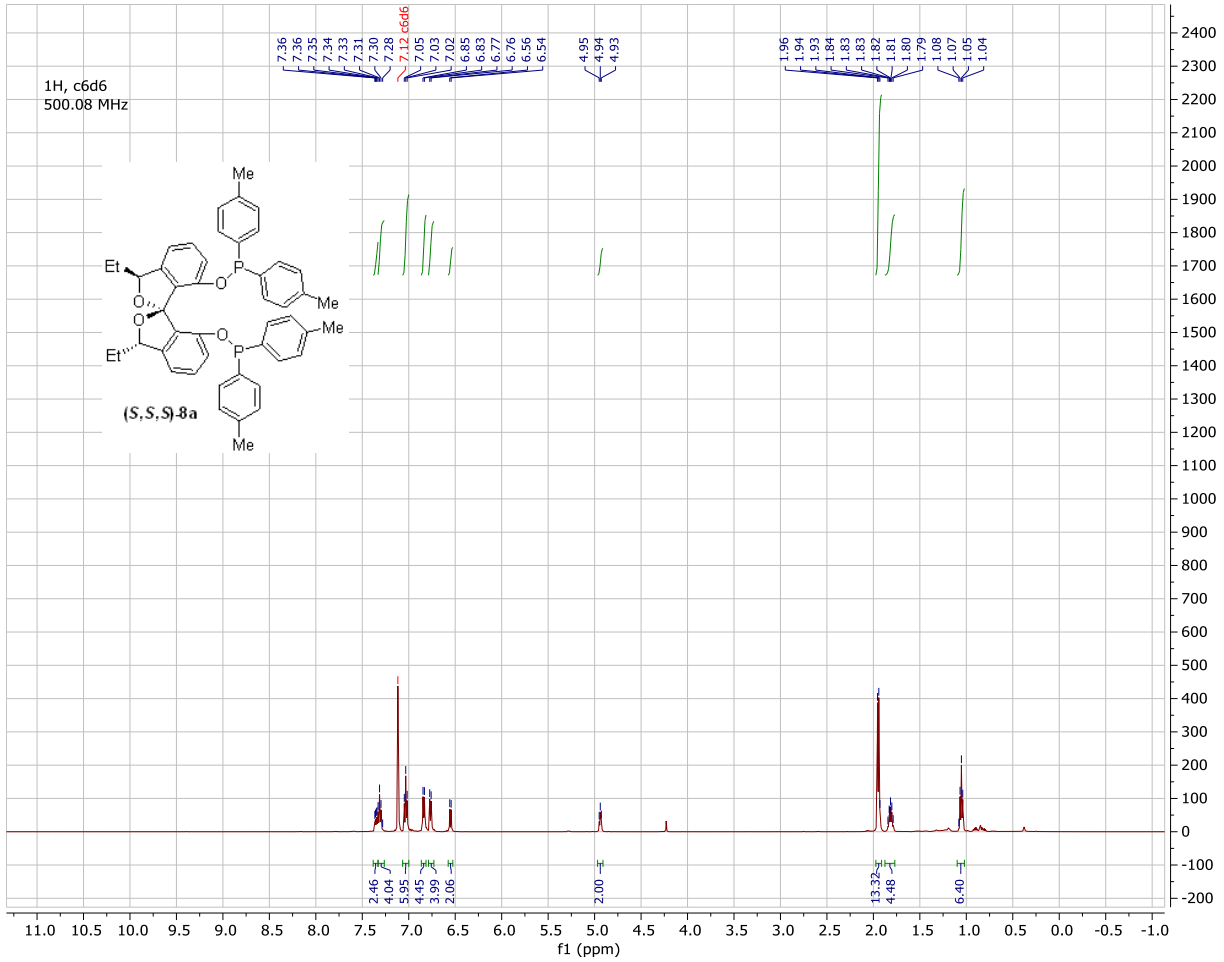

153.26
146.73
141.22
141.06
140.79
130.93
130.75
130.72
130.55
129.78
129.25
128.79
128.73
128.63
128.57
116.30
116.12
115.64
86.06
32.53
19.71
17.61
13C, c6d6
125.76 MHz
iPr
OPPh2
O
O
OPPh2
iPr
f1 (ppm)

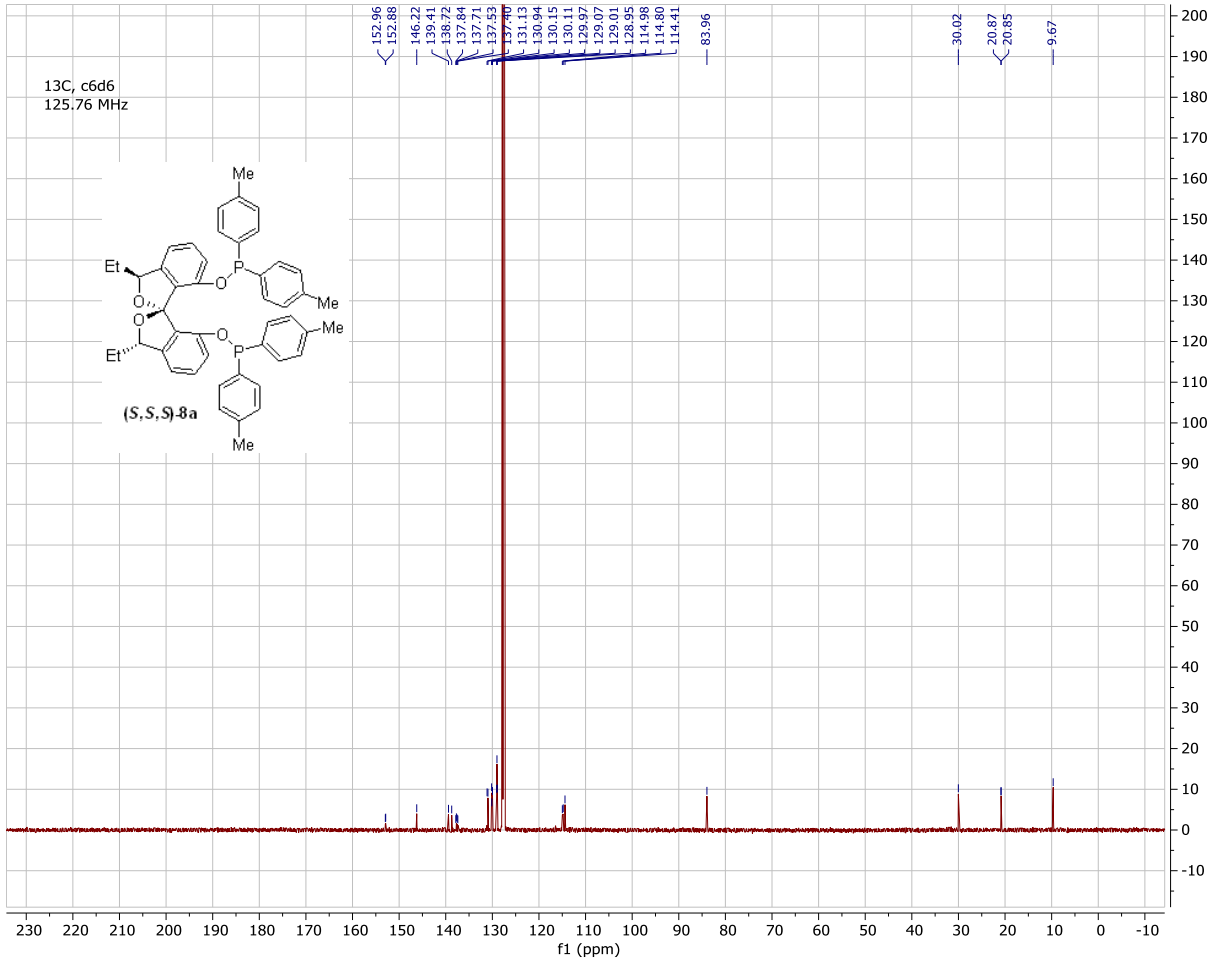

31P, c6d6
202.45 MHz
107.75
iPr
OPPh2
O
O
OPPh2
iPr
1000
900
800
700
600
500
400
300
200
100
0
-100
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

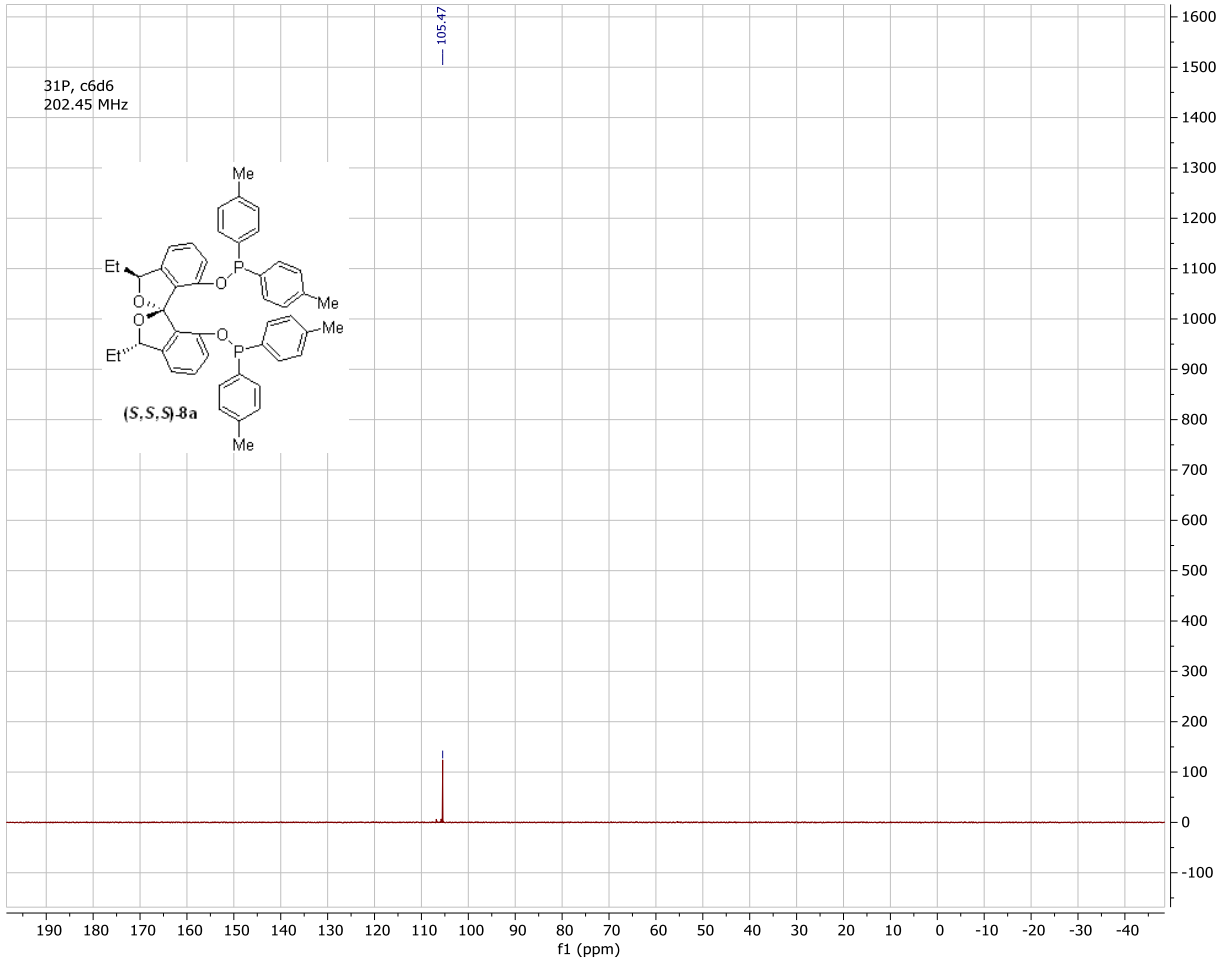

1H, cdcl3
500.08 MHz
Et
OPPh2
OPPh2
Et
f1 (ppm)

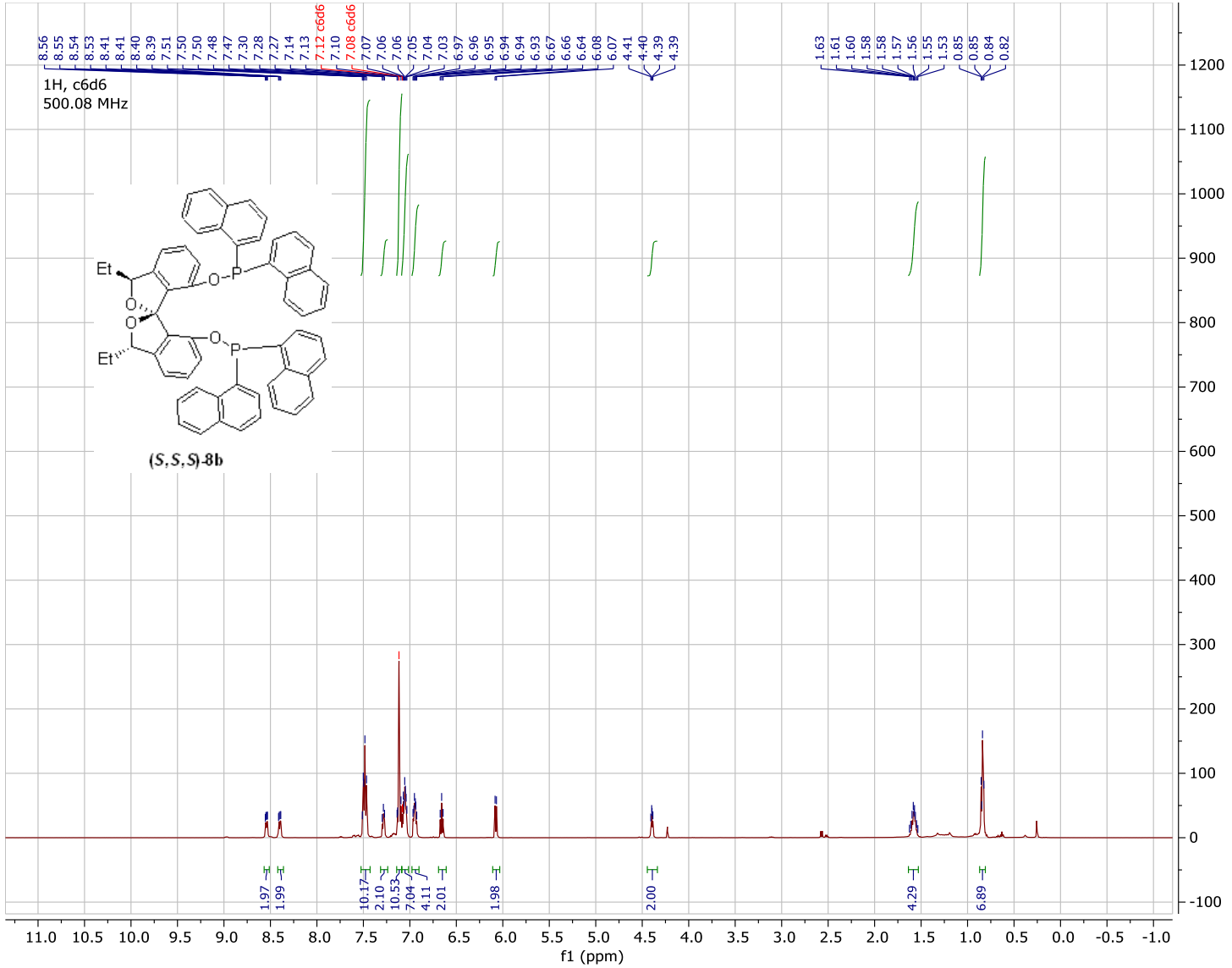

13C, cdcl3
125.76 MHz
145.83
130.81
130.62
130.46
129.75
129.61
129.56
129.06
128.22
128.16
115.10
114.71
84.20
77.22 cdcl3
76.96 cdcl3
76.71 cdcl3
30.04
9.72
Et
O
O
OPPh2
OPPh2
Et
f1 (ppm)

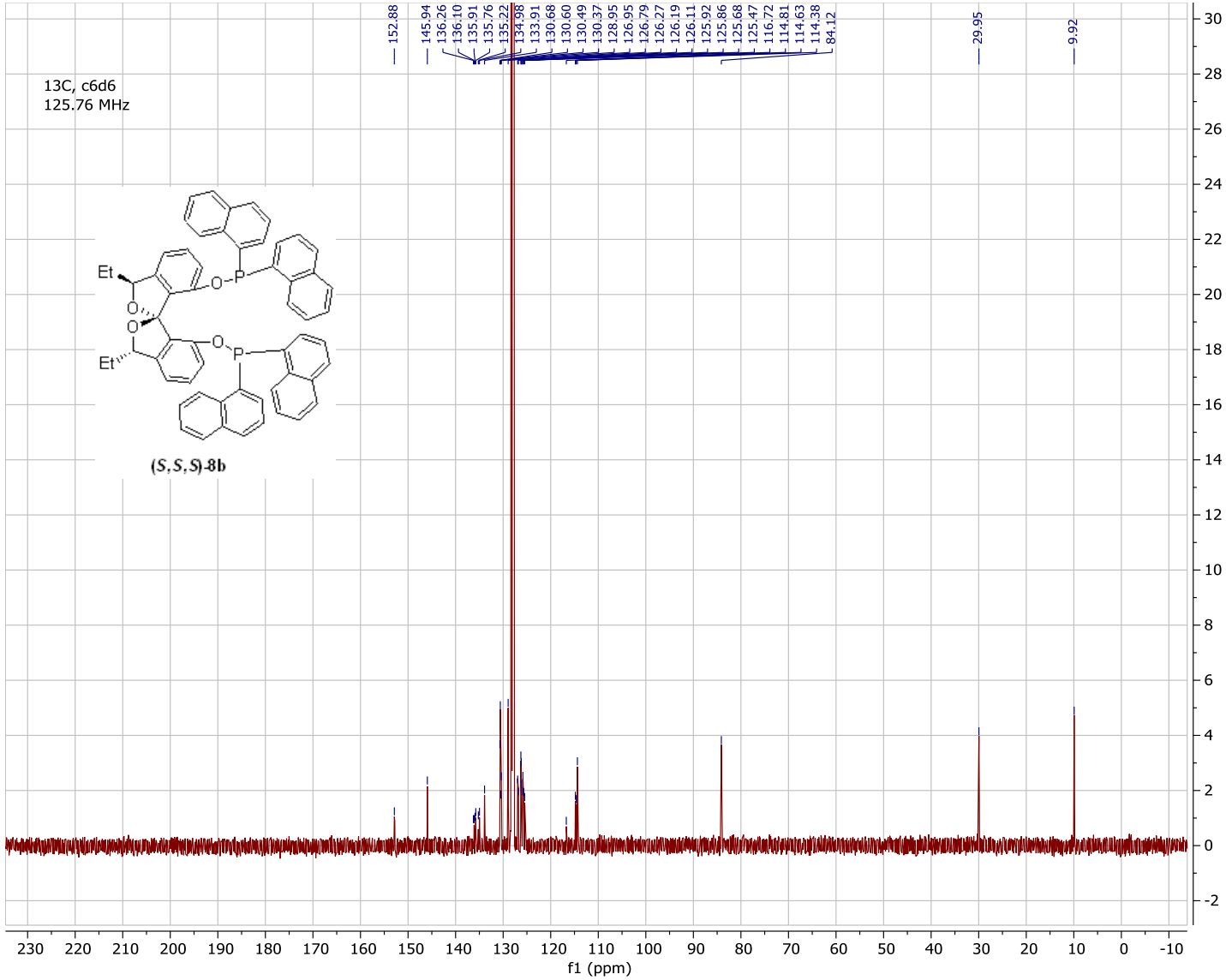

104.21
31P, cdcl3
162.15 MHz
Et
O
O
OPPh2
OPPh2
Et
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

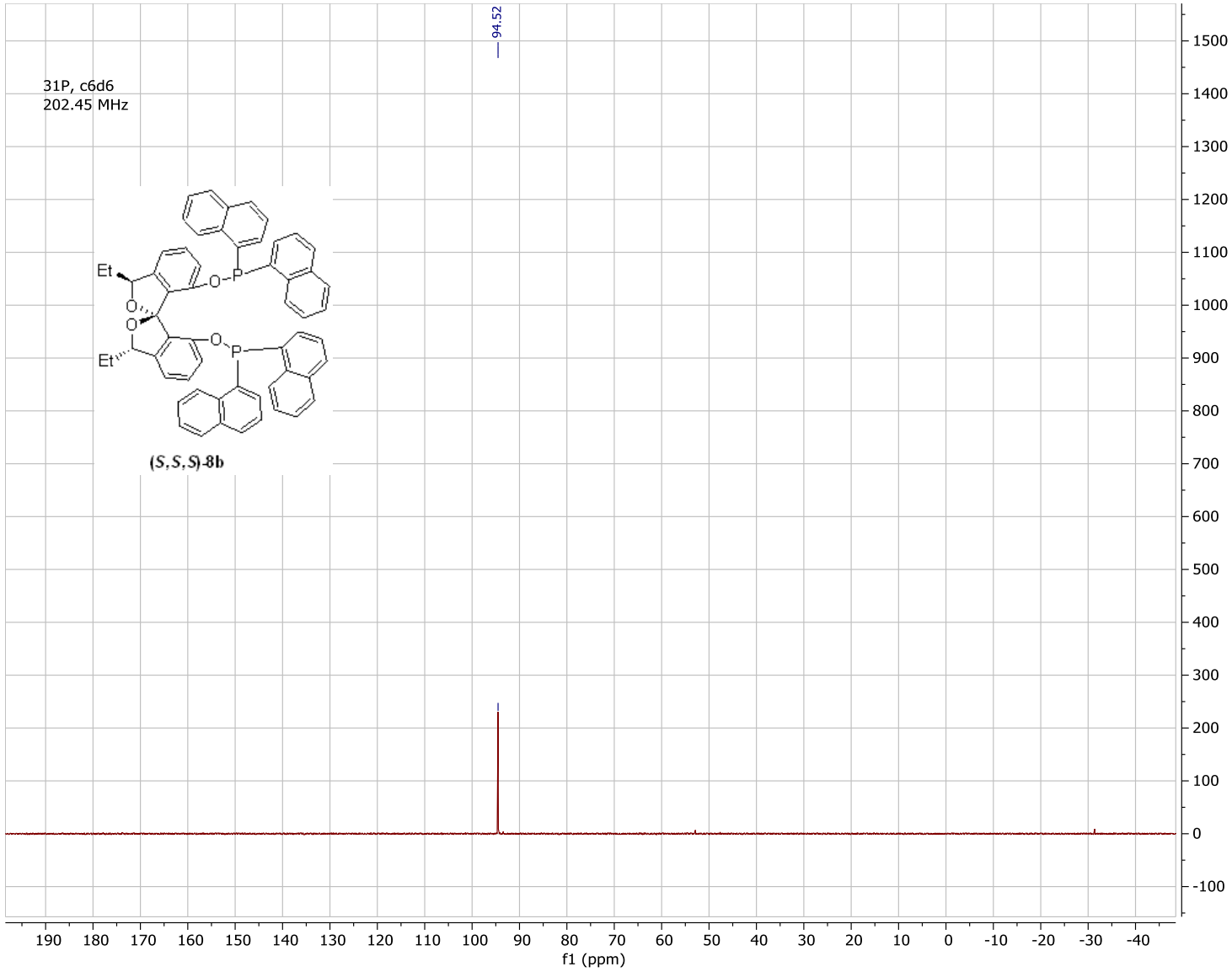

1H, c6d6
500.08 MHz
(S,S,S)-8a
f1 (ppm)

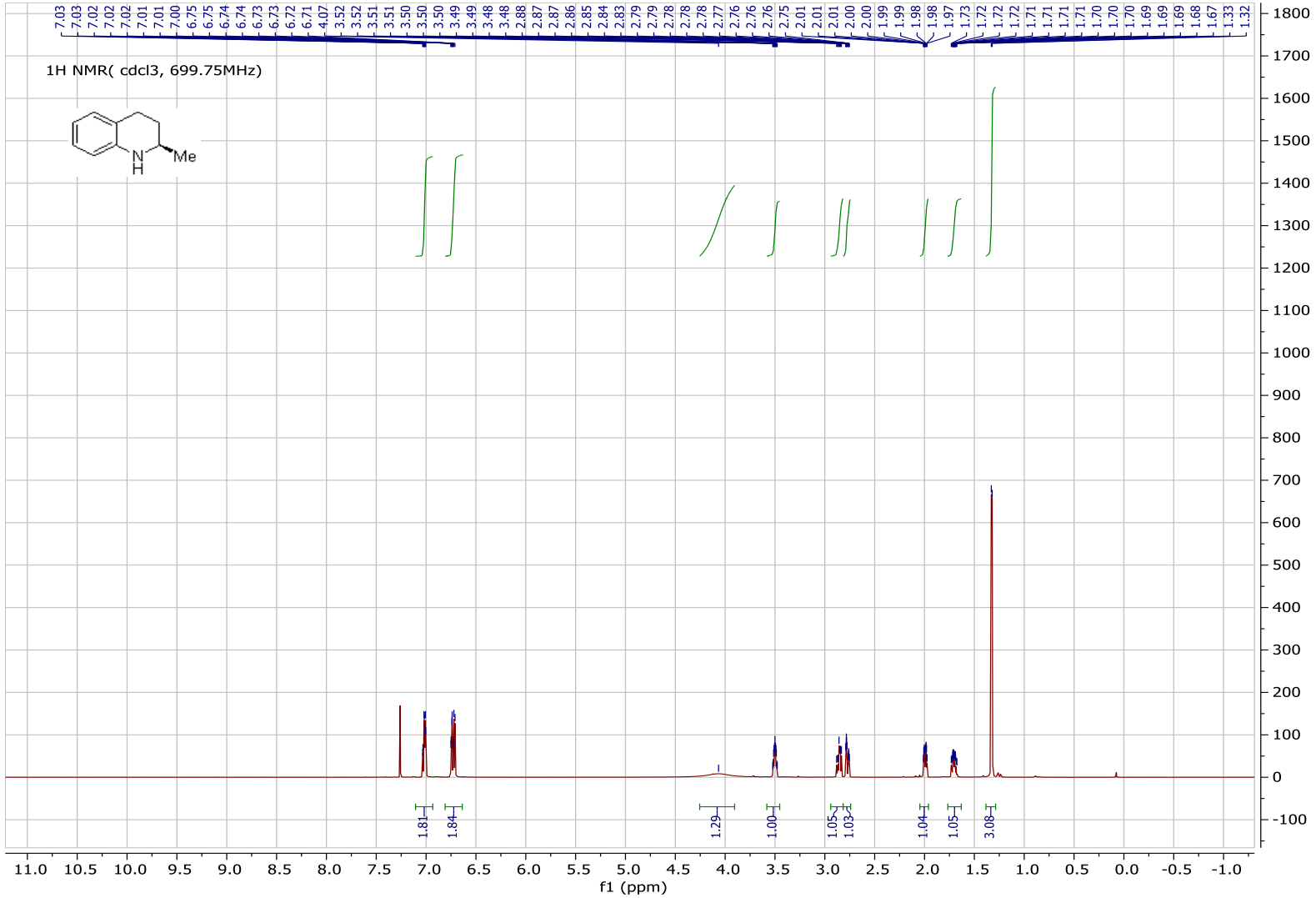

13C, c6d6
125.76 MHz
(S,S,S)-8a
152.96
152.88
146.22
139.41
138.72
137.84
137.71
137.53
137.40
131.13
130.94
130.15
130.11
129.97
129.07
129.01
128.95
114.98
114.80
114.41
83.96
30.02
20.87
20.85
9.67
f1 (ppm)

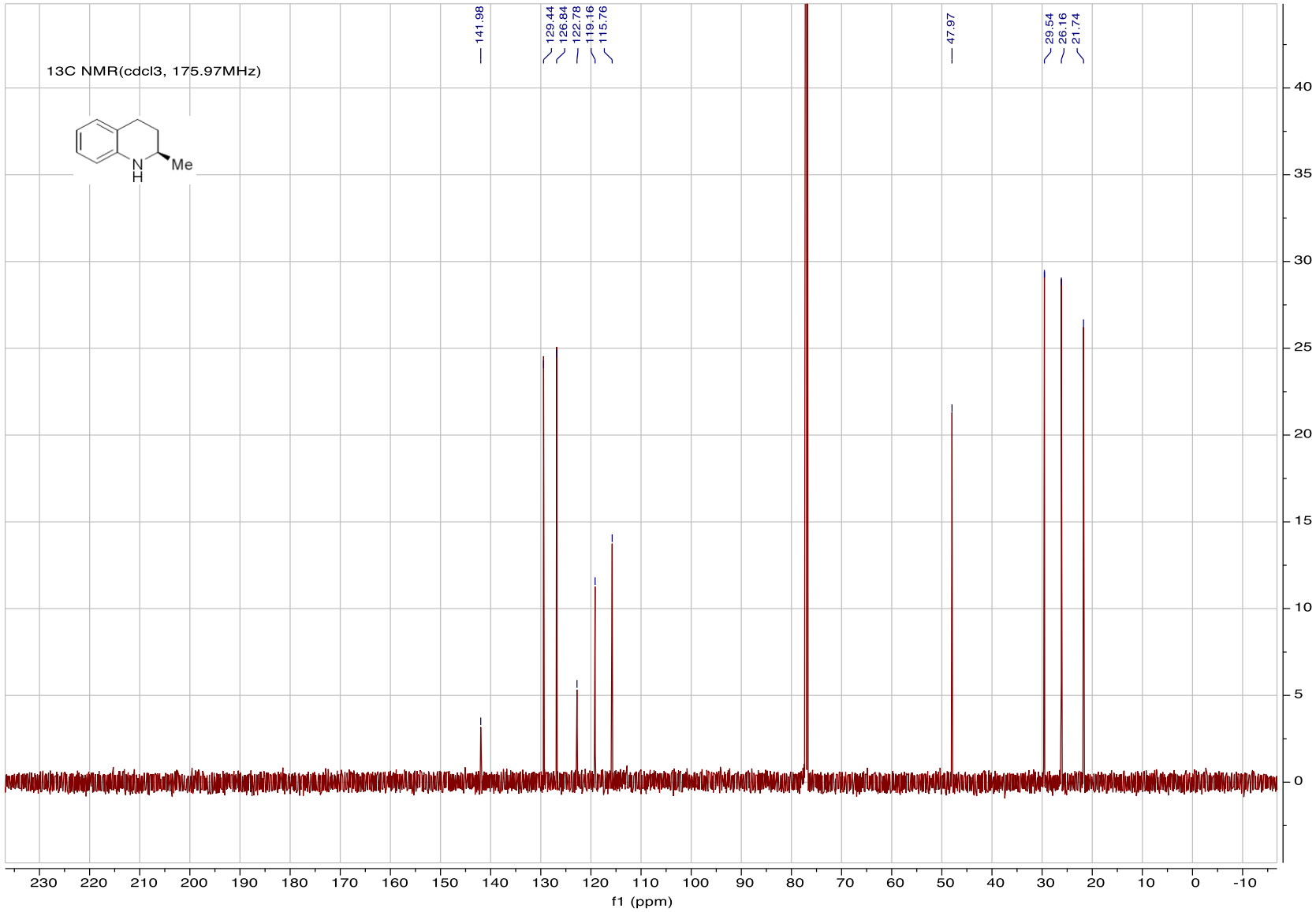

105.47
31P, c6d6
202.45 MHz
Me
Et
O
P
Me
Me
Et
(S,S,S)-8a
Me
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

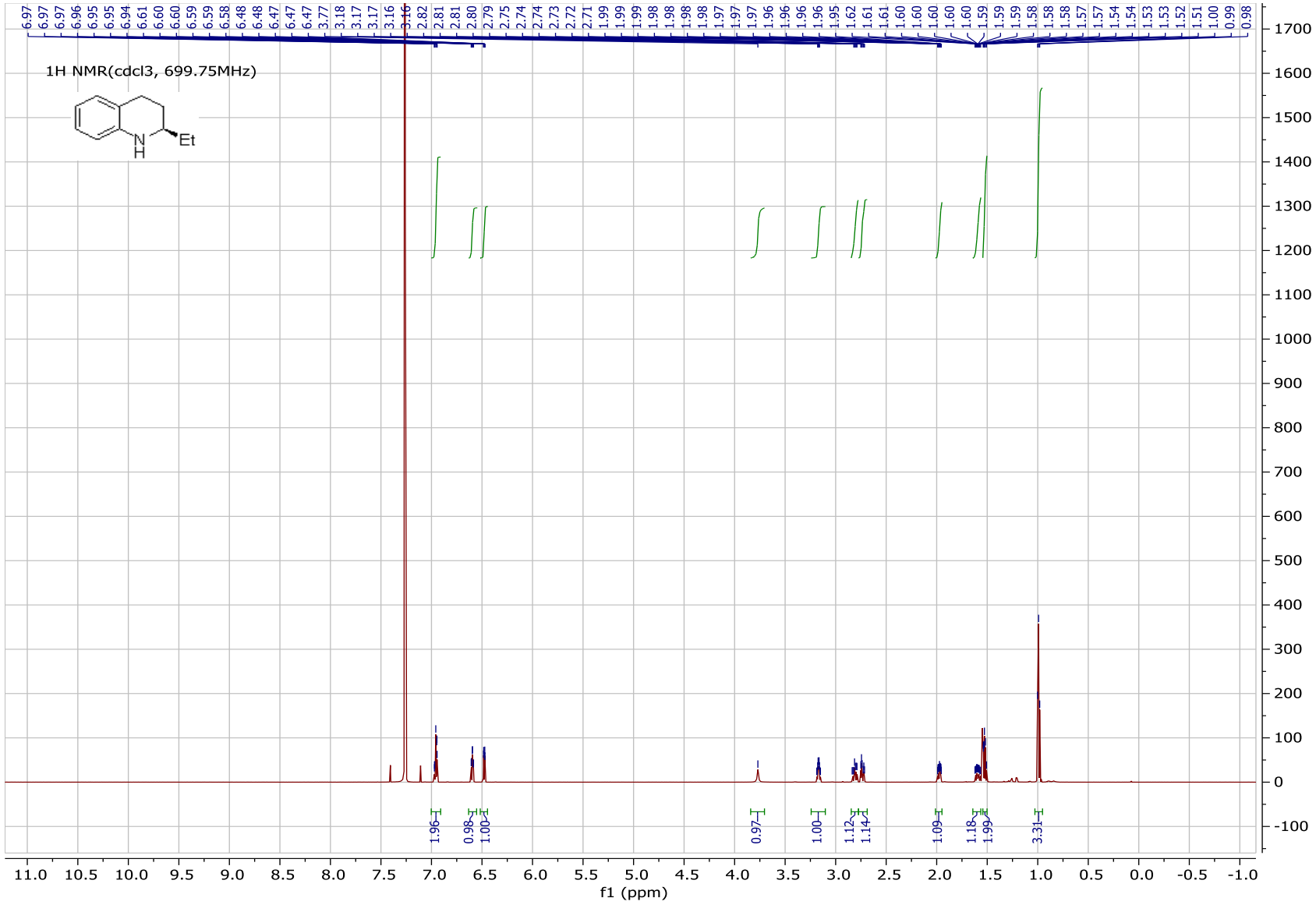

1H, c6d6
500.08 MHz
(S,S,S)-8b
f1 (ppm)

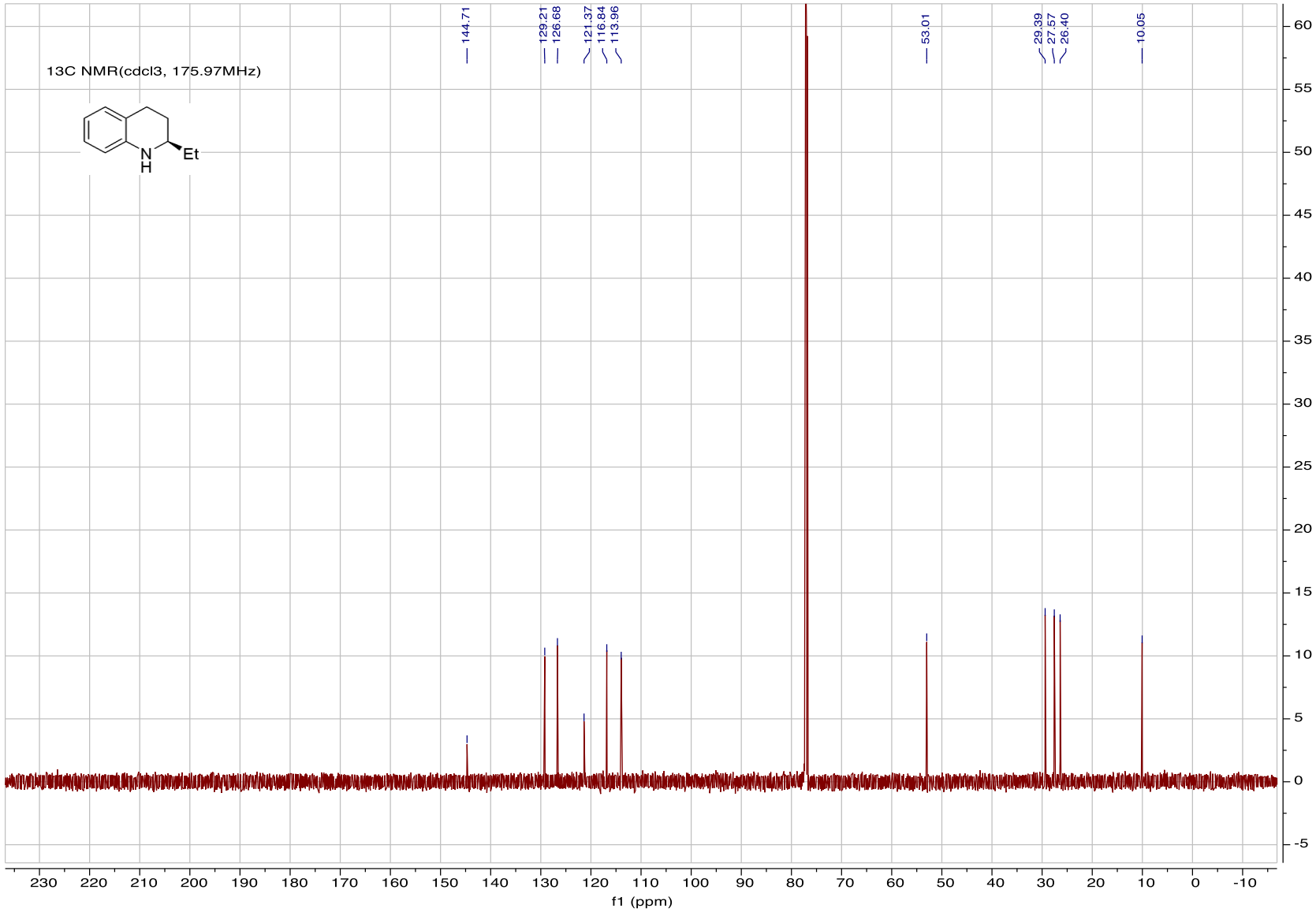

13C, c6d6
125.76 MHz
(S,S,S)-8b
152.88
145.94
136.26
136.10
135.91
135.76
135.22
134.98
133.91
130.68
130.60
130.49
130.37
128.95
126.95
126.79
126.27
126.19
126.11
125.92
125.86
125.68
125.47
116.72
114.81
114.63
114.38
84.12
29.95
9.92
f1 (ppm)


94.52
31P, c6d6
202.45 MHz
Et
O
O
O
P
O
P
Et
(S,S,S)-8b
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

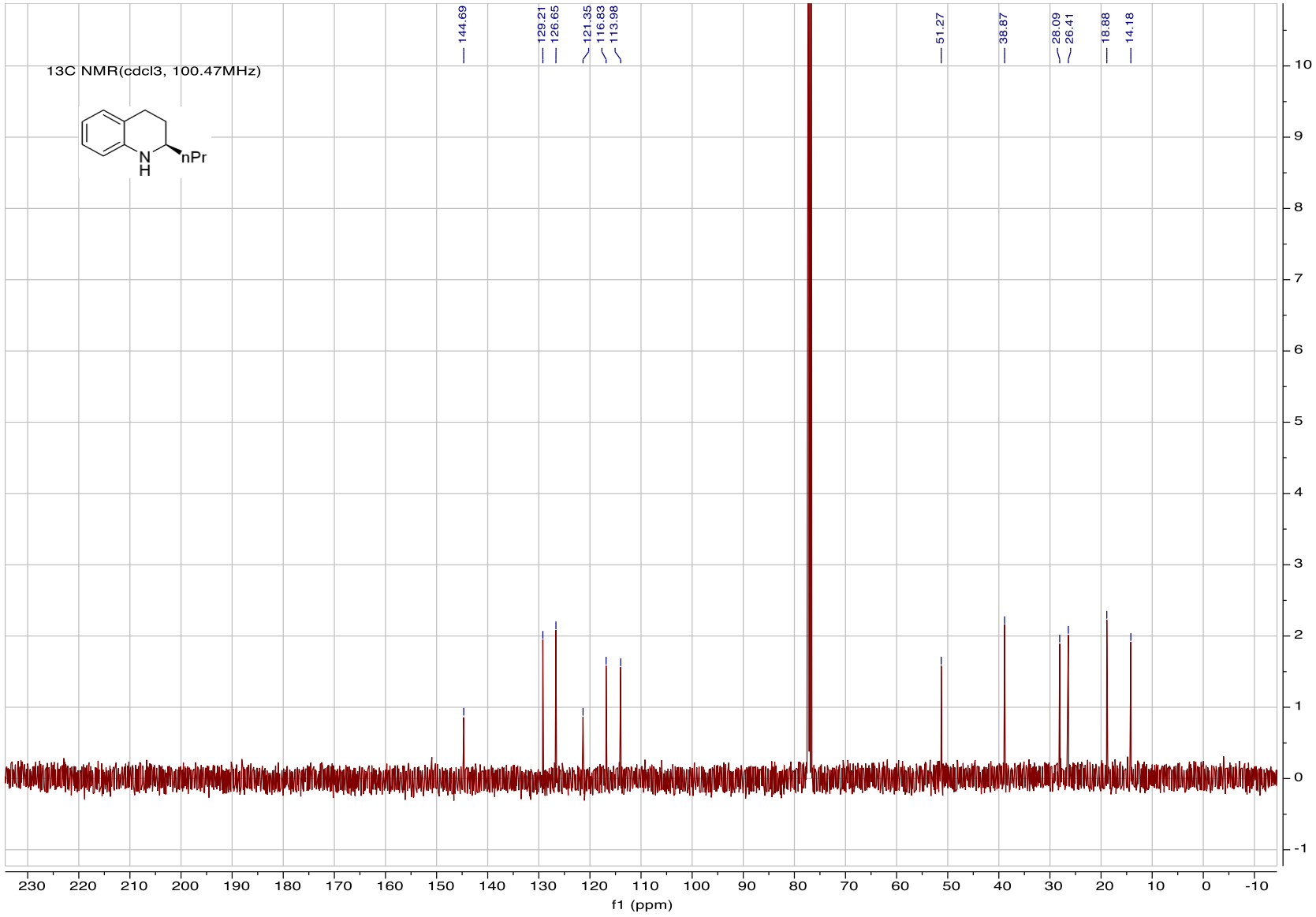

1H NMR(cdcl3, 699.75MHz)
Me
N
H
1.81
1.84
1.29
1.00
1.05
1.03
1.04
1.05
3.08
f1 (ppm)


13C NMR(cdcl3, 175.97MHz)
Me
N
H
141.98
129.44
126.84
122.78
119.16
115.76
47.97
29.54
26.16
21.74
f1 (ppm)

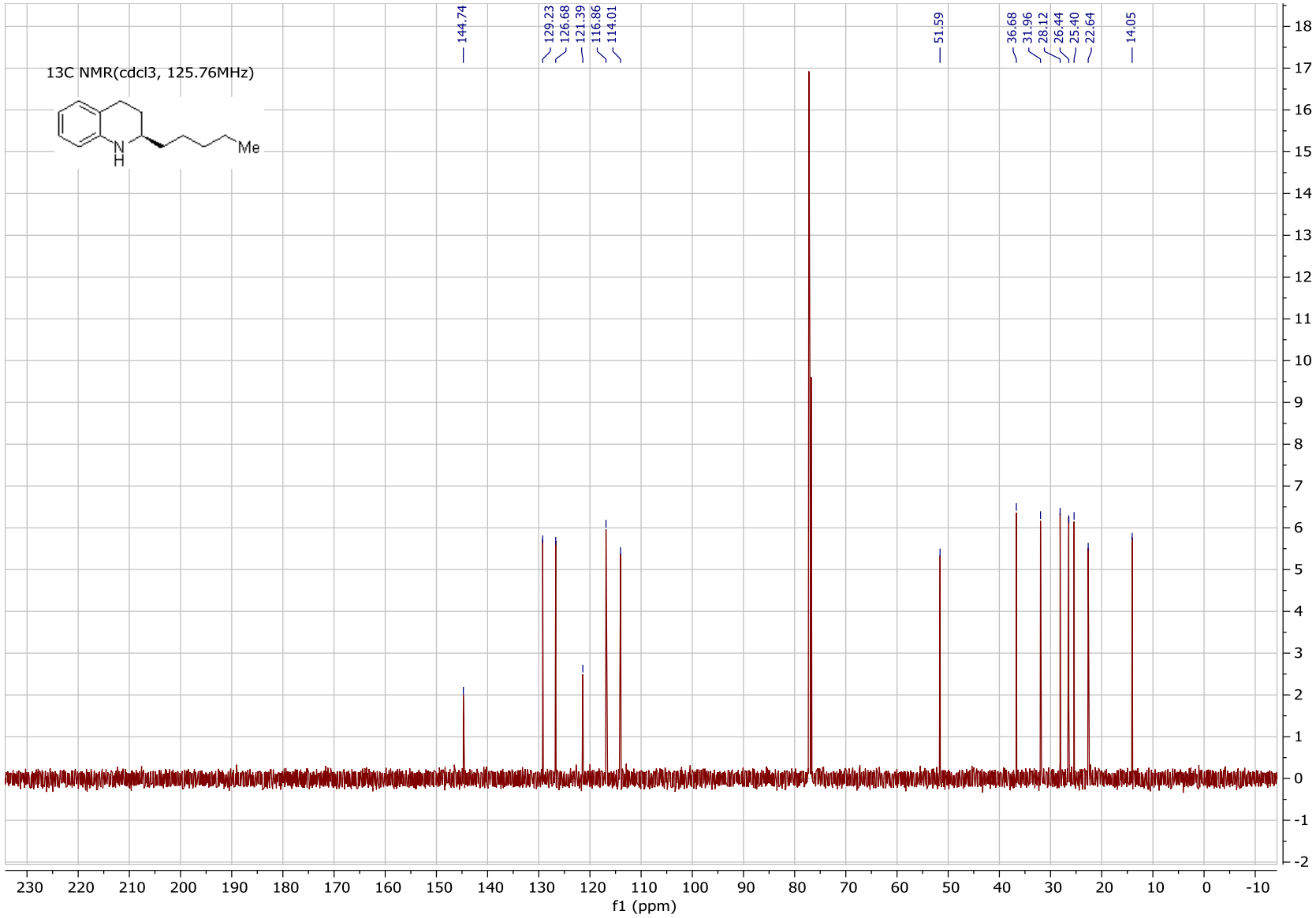

1H NMR(cdcl3, 699.75MHz)
Et
N
H
f1 (ppm)

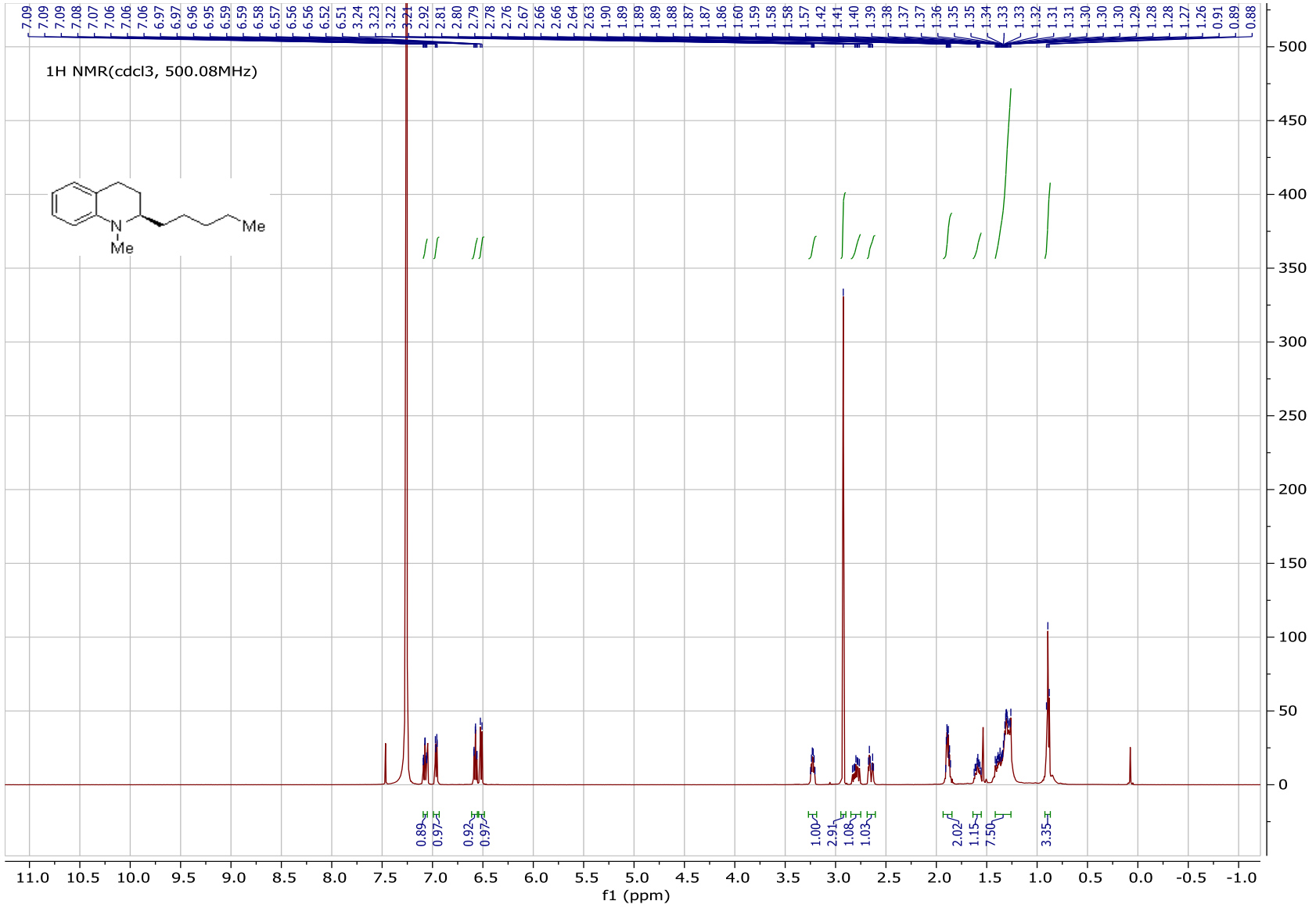

13C NMR(cdcl3, 175.97MHz)
N
H
Et
144.71
129.21
126.68
121.37
116.84
113.96
53.01
29.39
27.57
26.40
10.05
f1 (ppm)

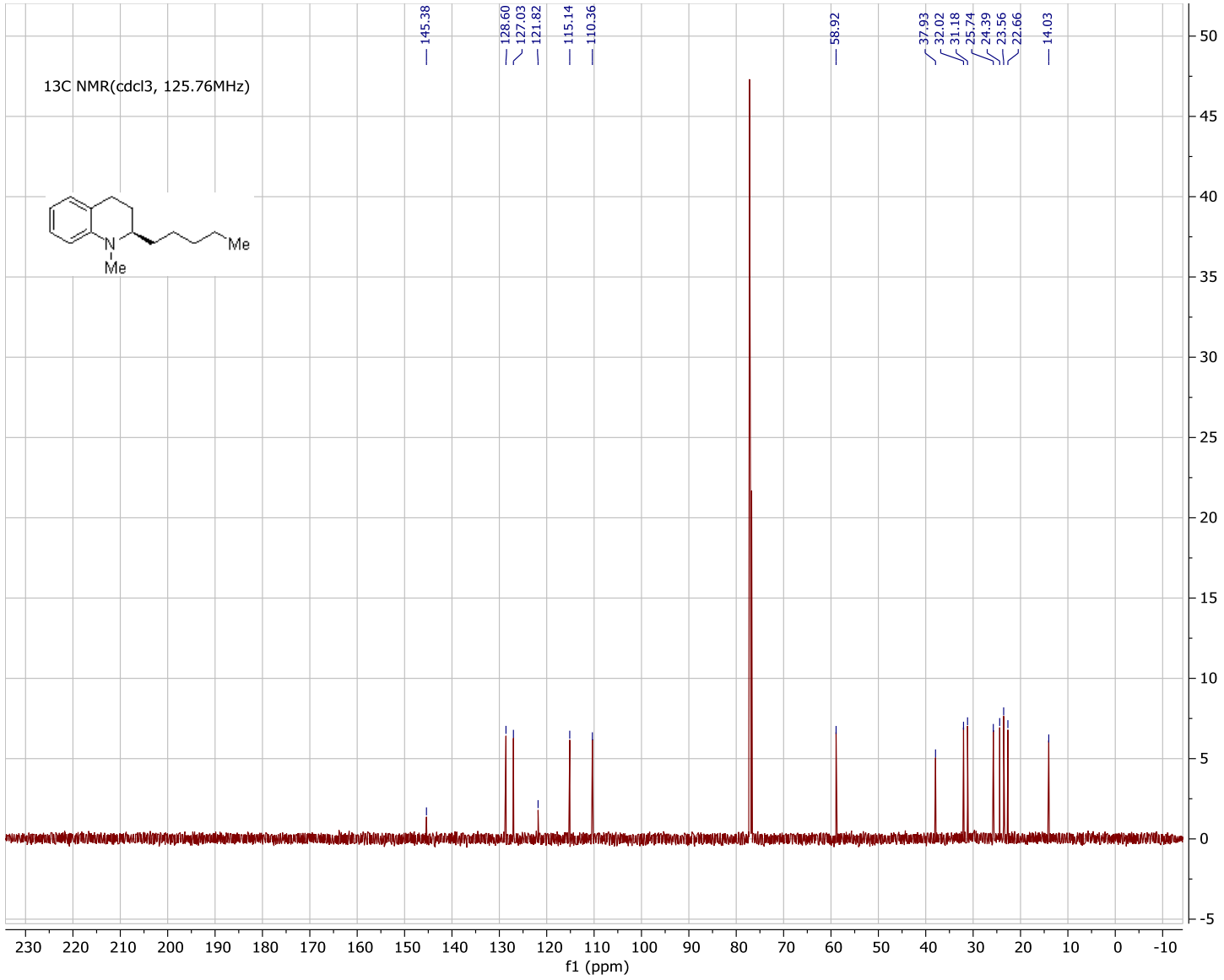

1H NMR(cdcl3, 399.54MHz)
N
H
nPr
f1 (ppm)

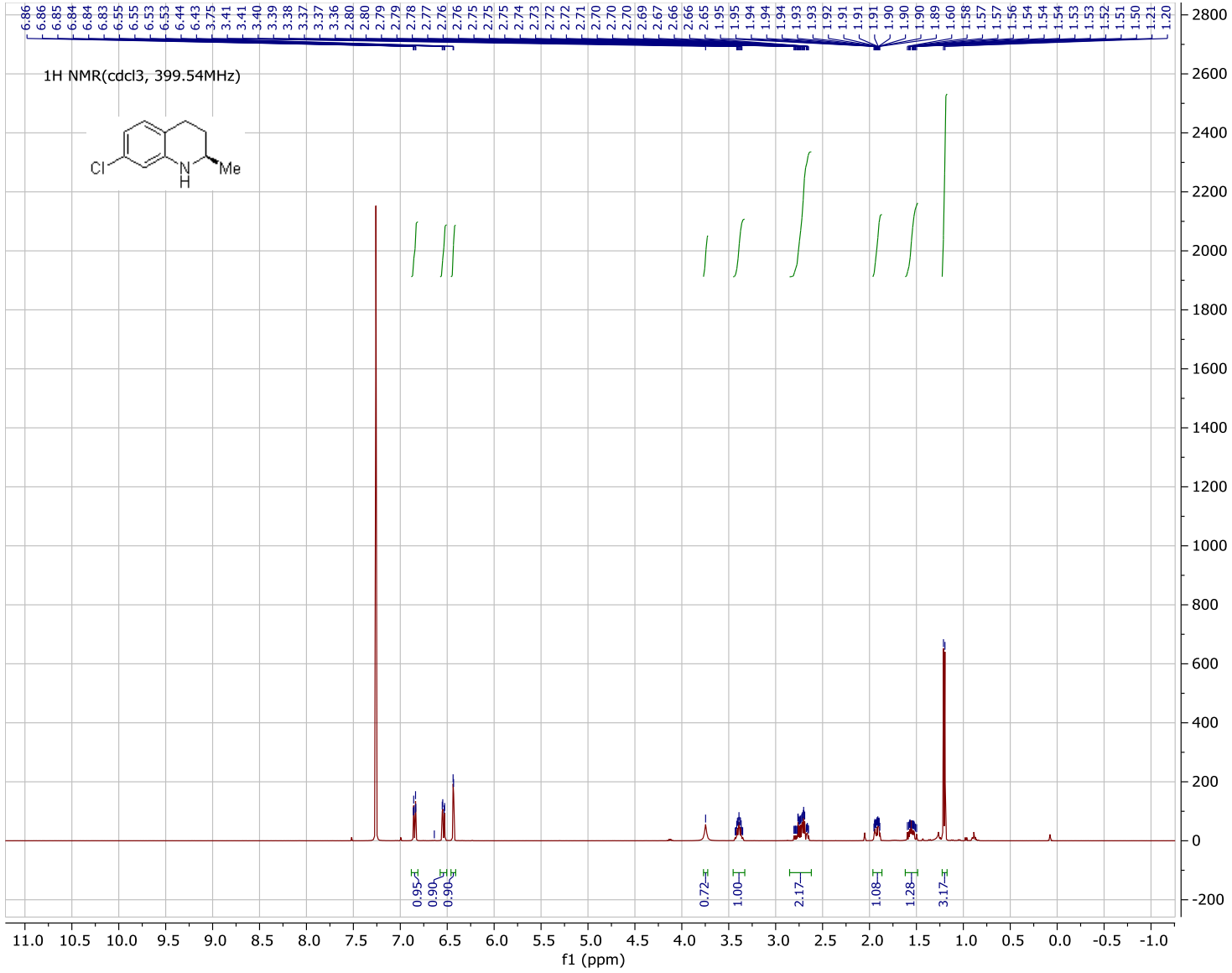

13C NMR(cdcl3, 100.47MHz)
144.69
129.21
126.65
121.35
116.83
113.98
51.27
38.87
28.09
26.41
18.88
14.18
nPr
N
H
f1 (ppm)

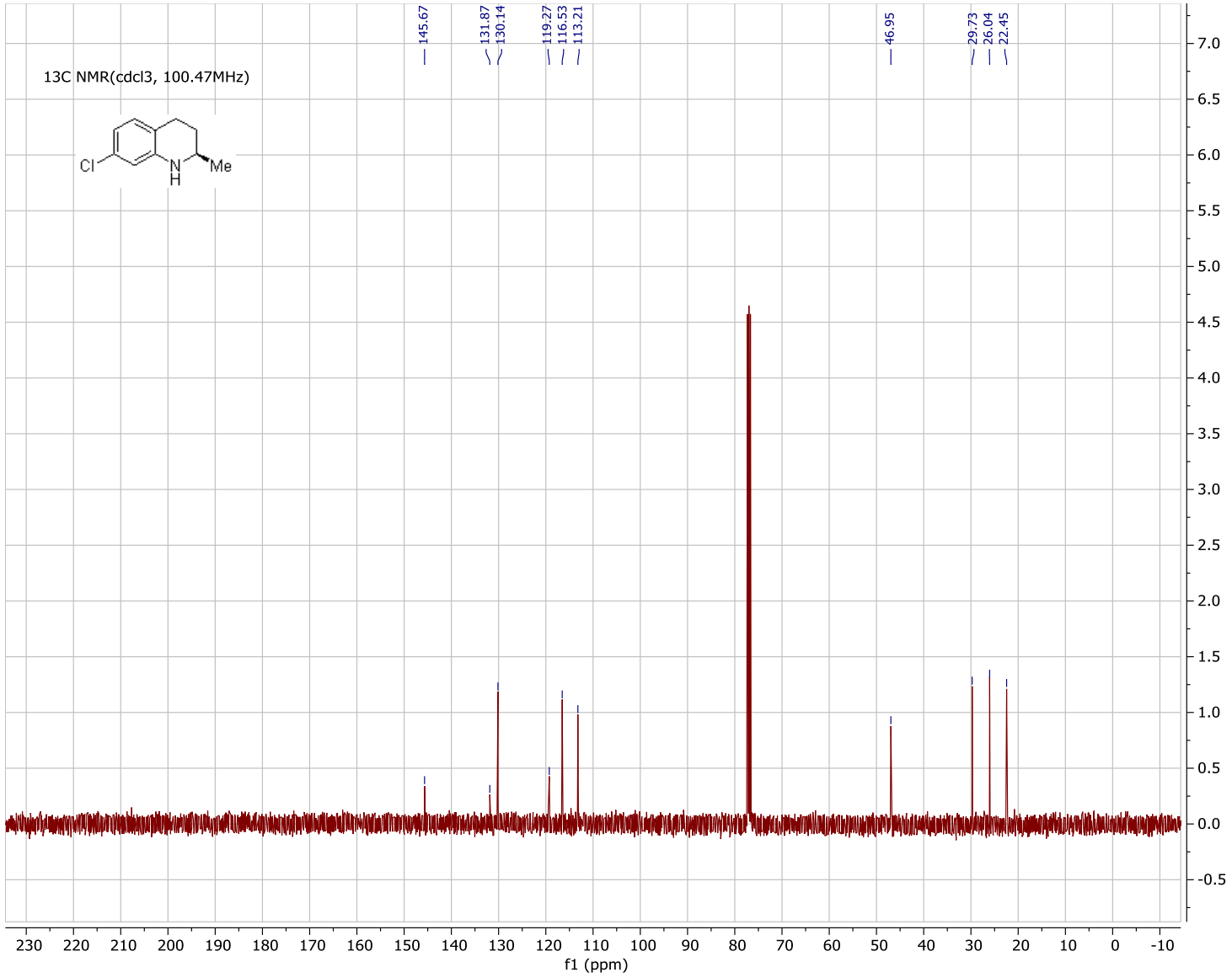

1H NMR(cdcl3, 500.08MHz)
Me
N
H
f1 (ppm)

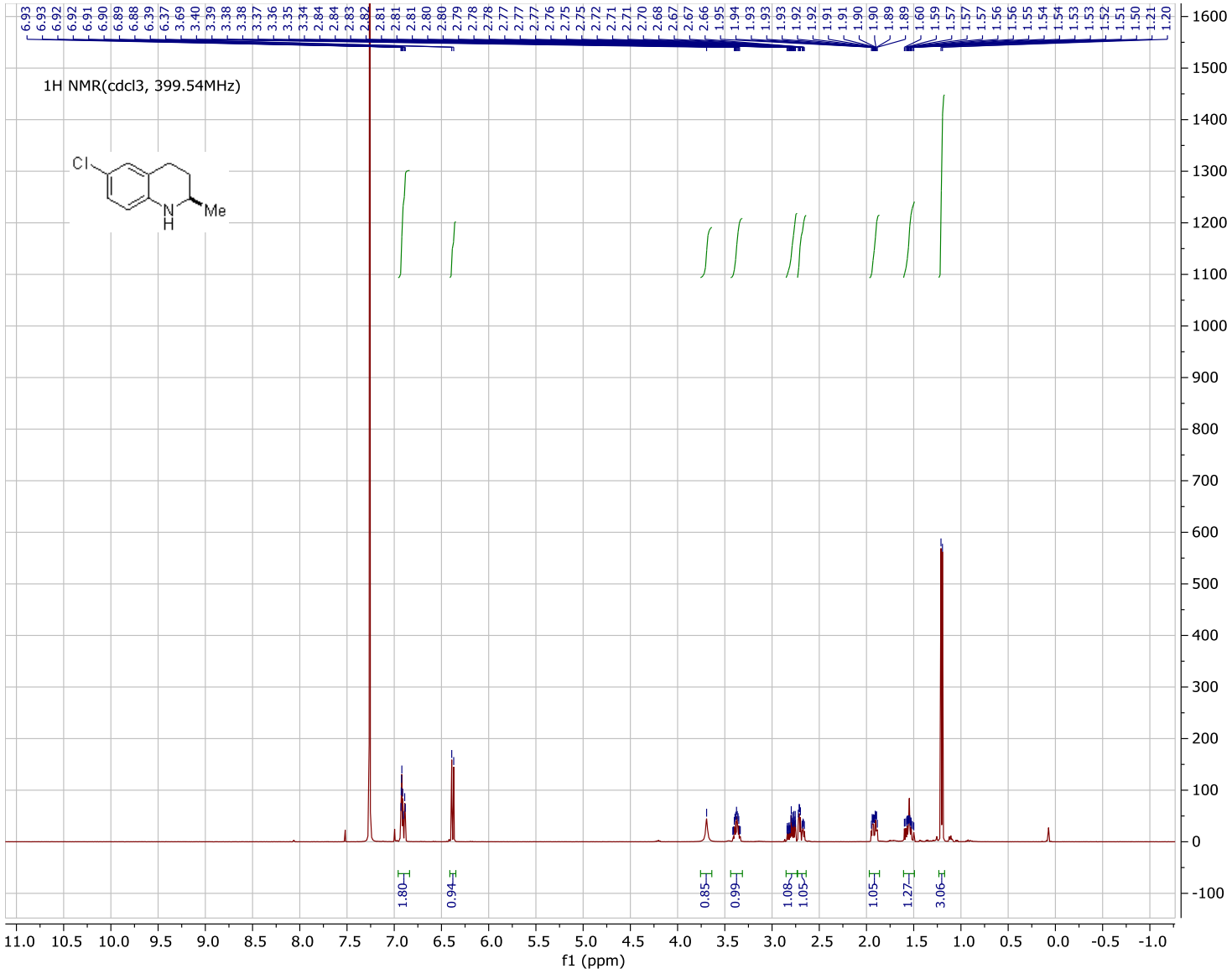

13C NMR(cdcl3, 125.76MHz)
Me
144.74
129.23
126.68
121.39
116.86
114.01
51.59
36.68
31.96
28.12
26.44
25.40
22.64
14.05
f1 (ppm)

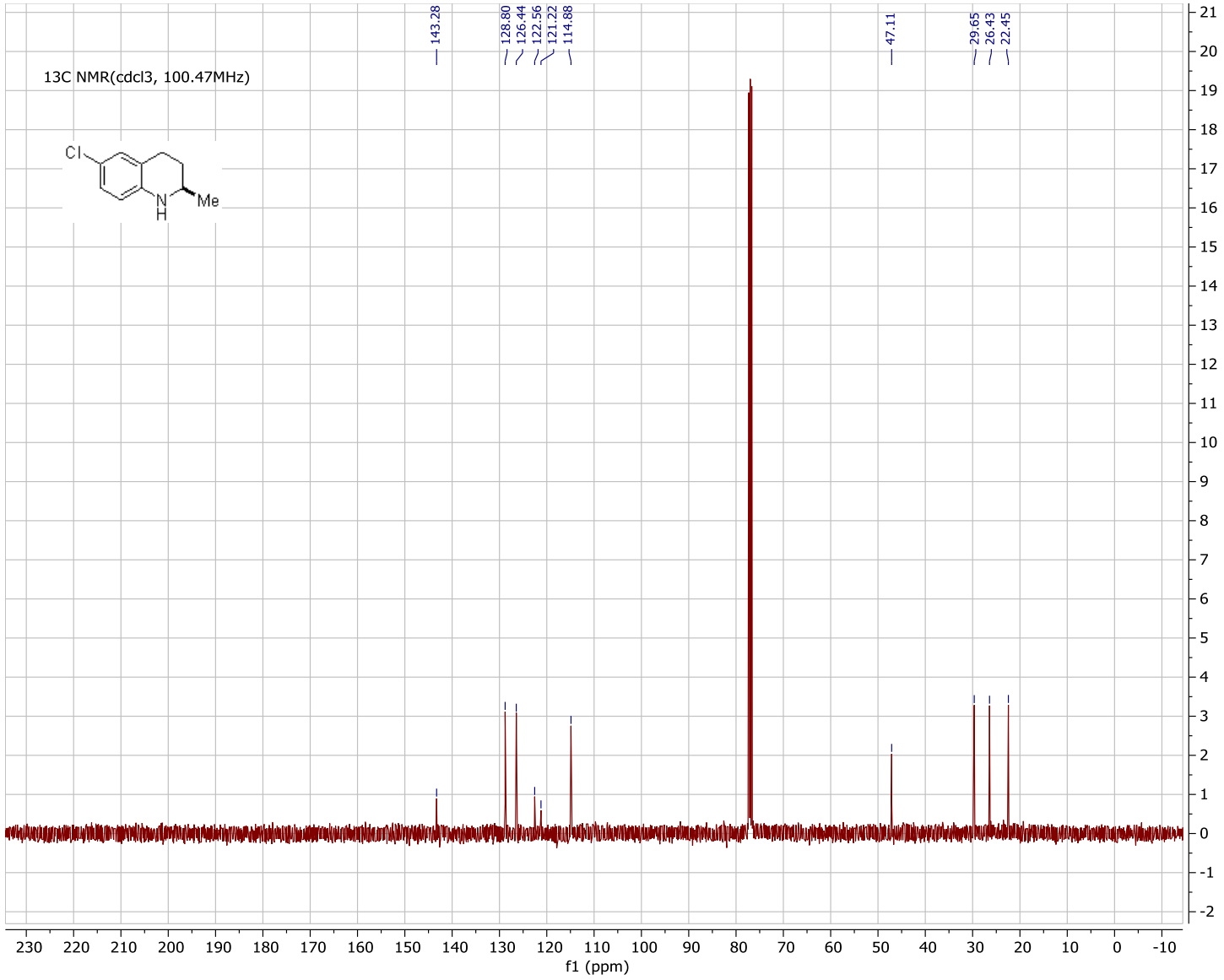

1H NMR(cdcl3, 500.08MHz)
N
Me
Me
f1 (ppm)

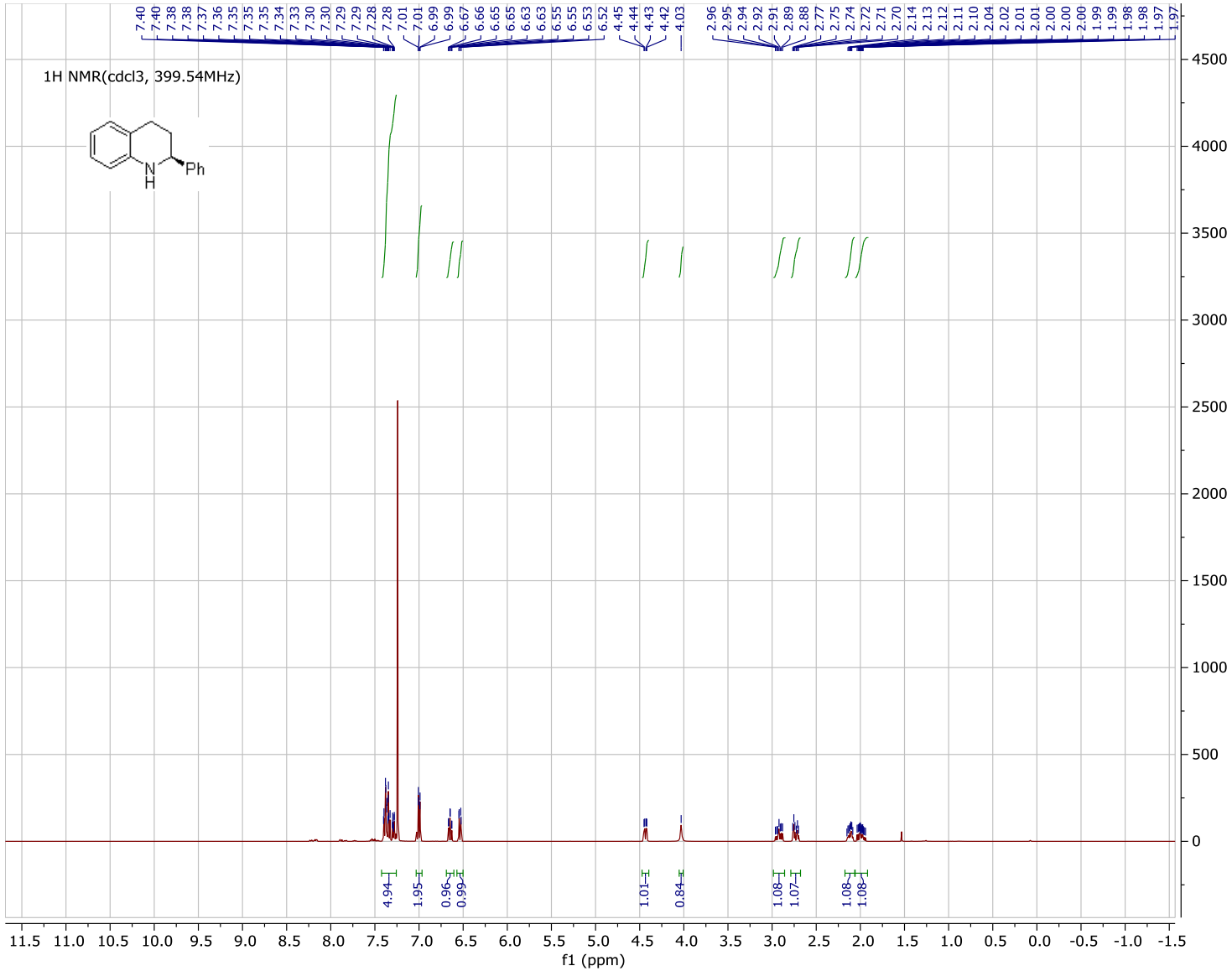

13C NMR(cdcl3, 125.76MHz)
145.38
128.60
127.03
121.82
115.14
110.36
58.92
37.93
32.02
31.18
25.74
24.39
23.56
22.66
14.03
N
Me
Me
f1 (ppm)

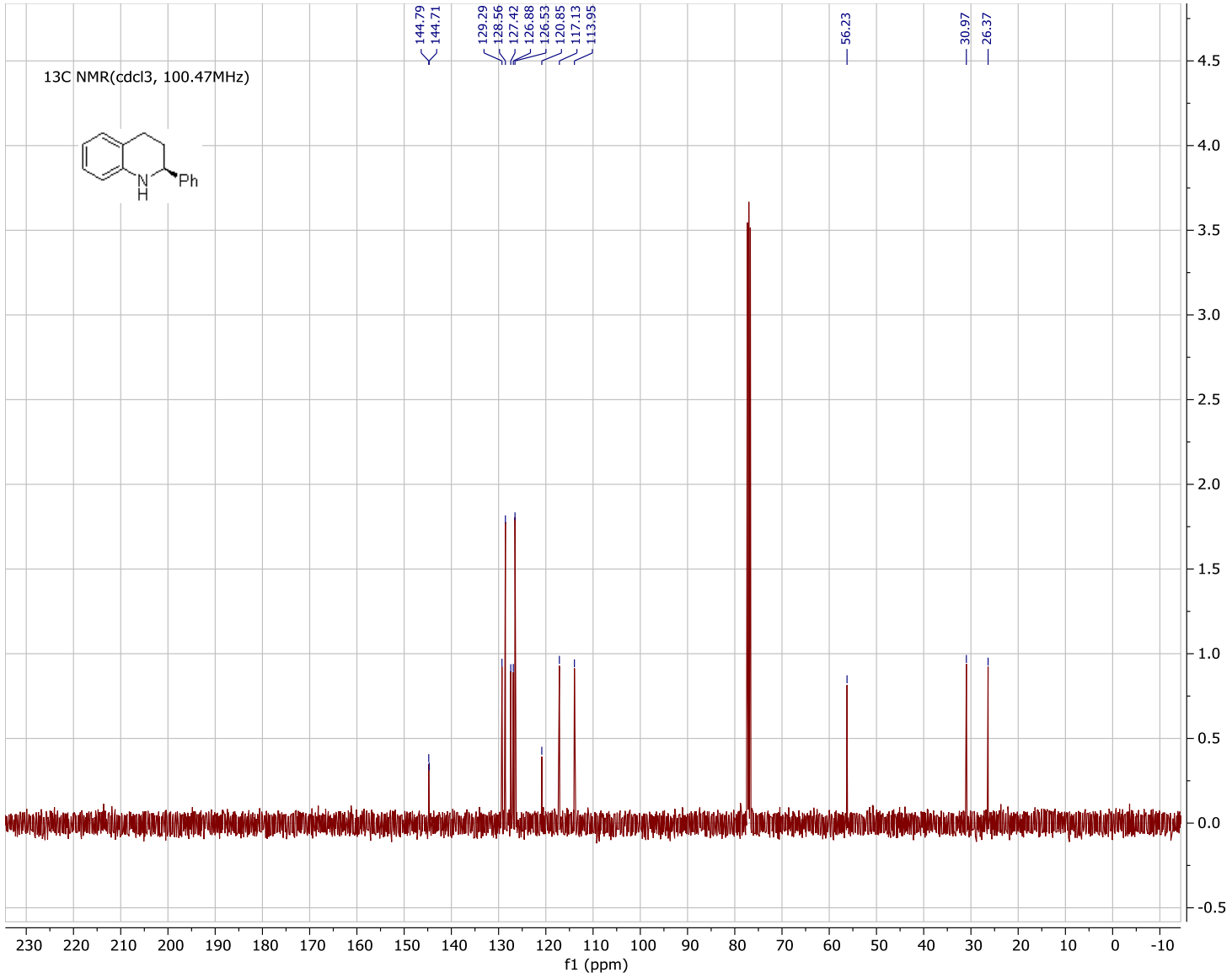

1H NMR(cdcl3, 399.54MHz)
Cl
N
H
Me
f1 (ppm)

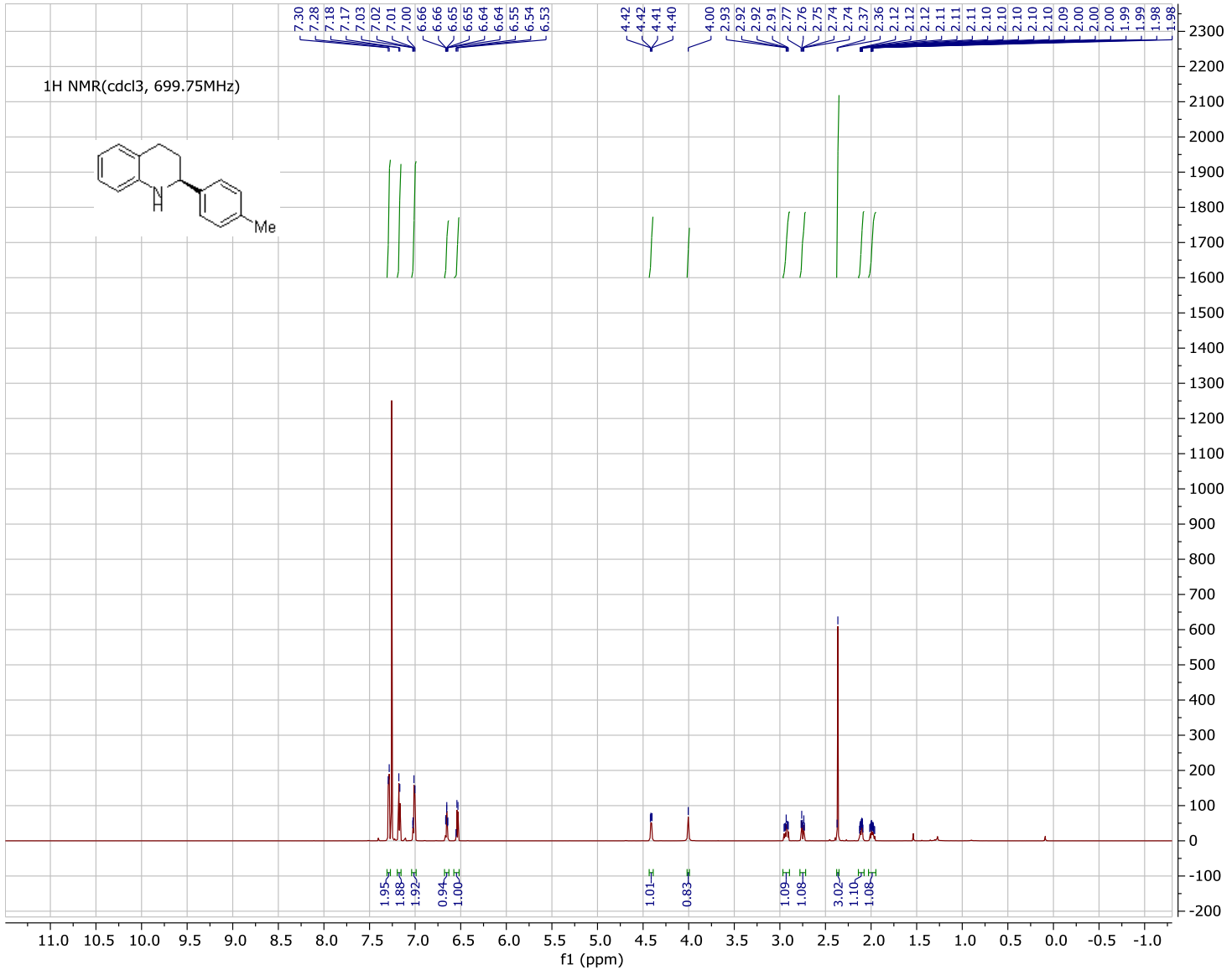

13C NMR(cdcl3, 100.47MHz)
Cl
N
H
Me
145.67
131.87
130.14
119.27
116.53
113.21
46.95
29.73
26.04
22.45
f1 (ppm)

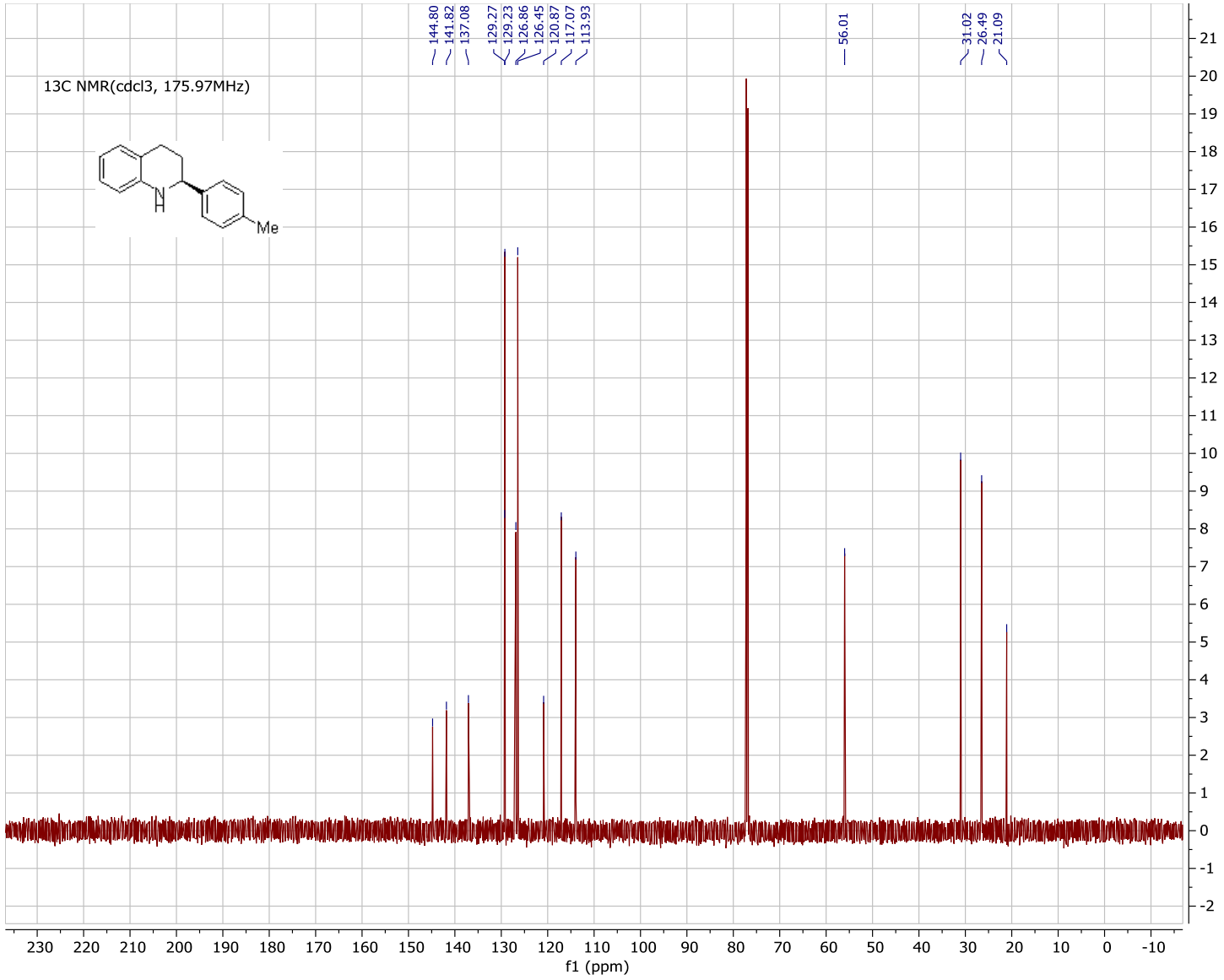

1H NMR(cdcl3, 399.54MHz)
Cl
N
H
Me
f1 (ppm)

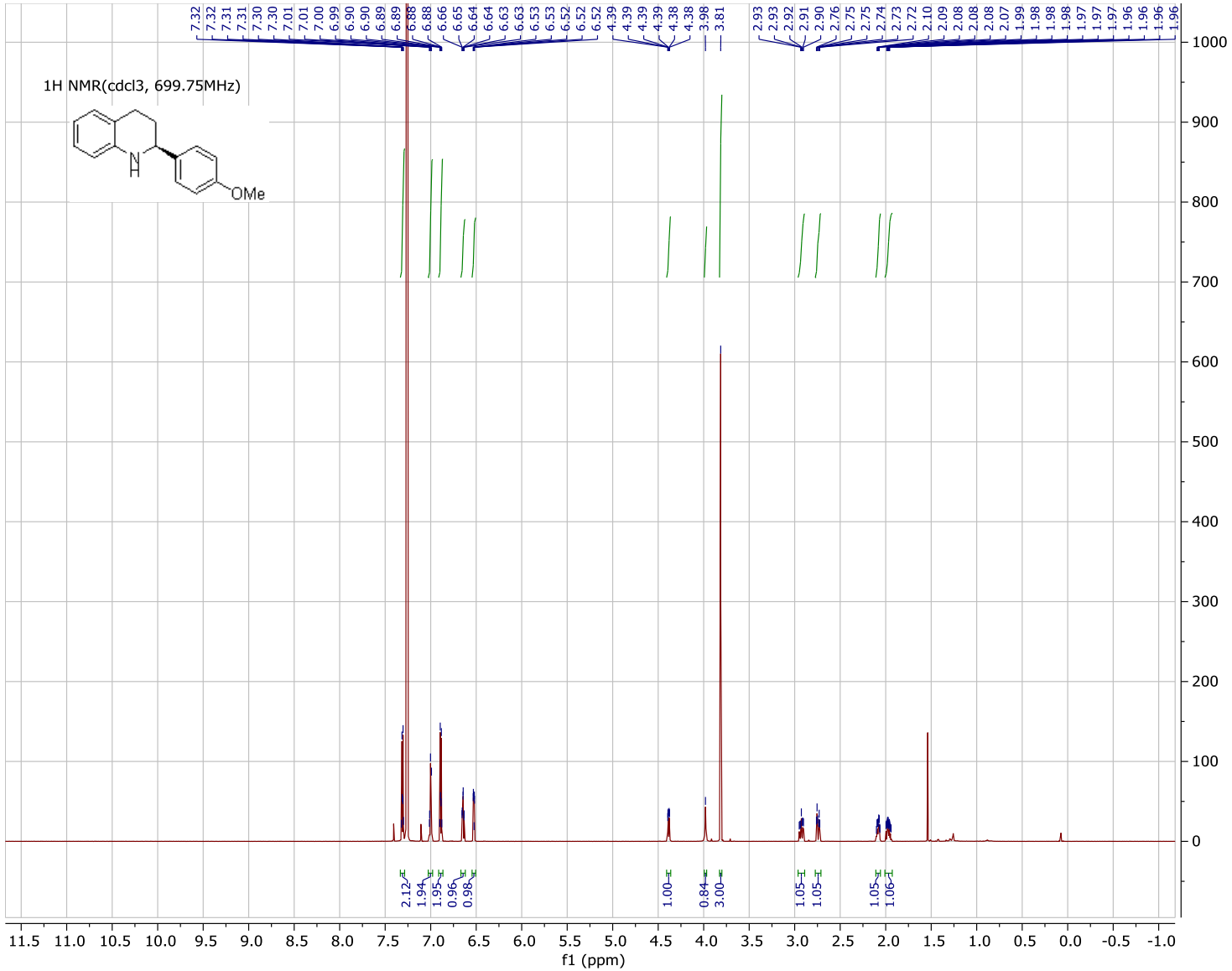

13C NMR(cdcl3, 100.47MHz)
Cl
N
H
Me
143.28
128.80
126.44
122.56
121.22
114.88
47.11
29.65
26.43
22.45
f1 (ppm)

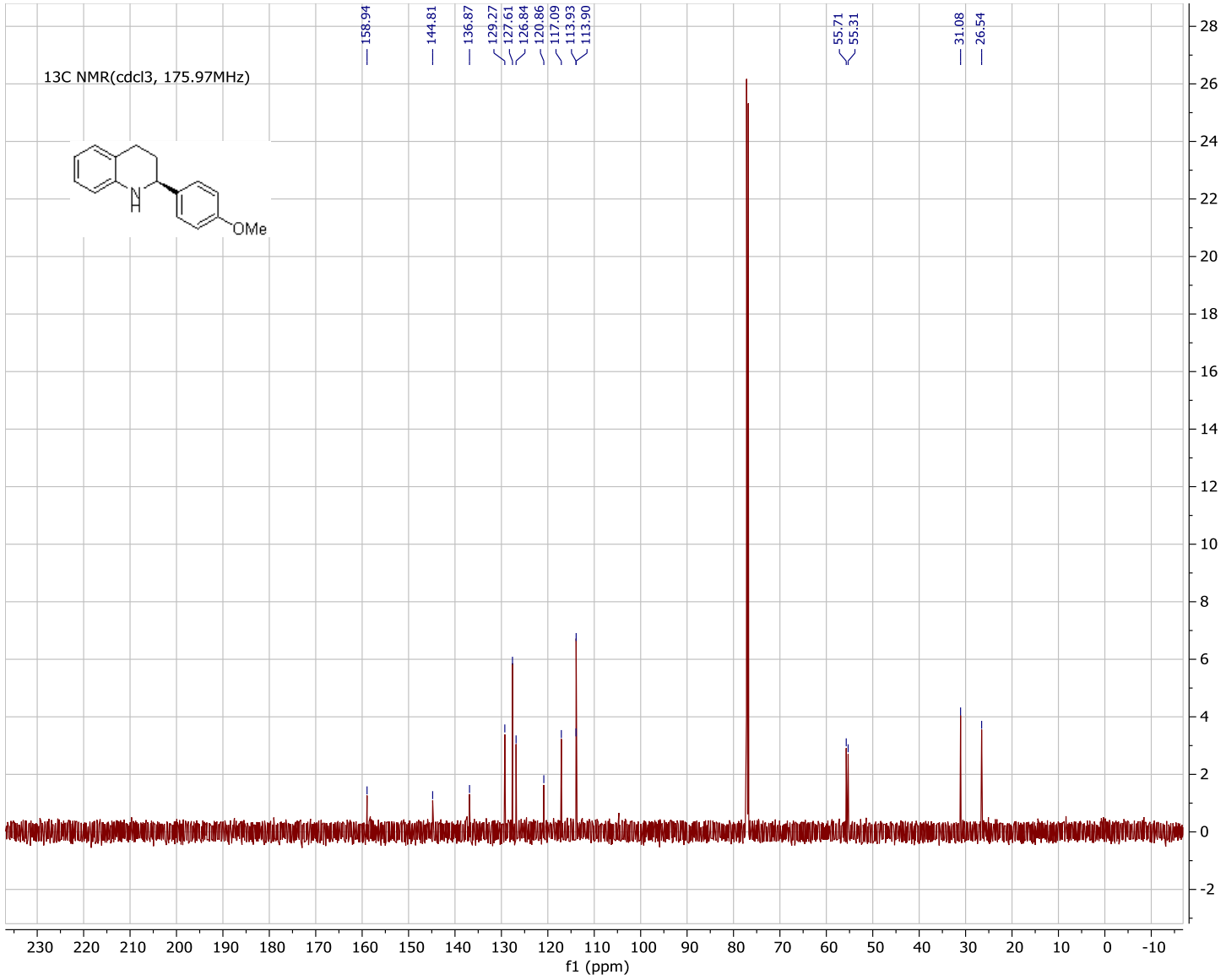

1H NMR(cdcl3, 399.54MHz)
Ph
N
H
f1 (ppm)

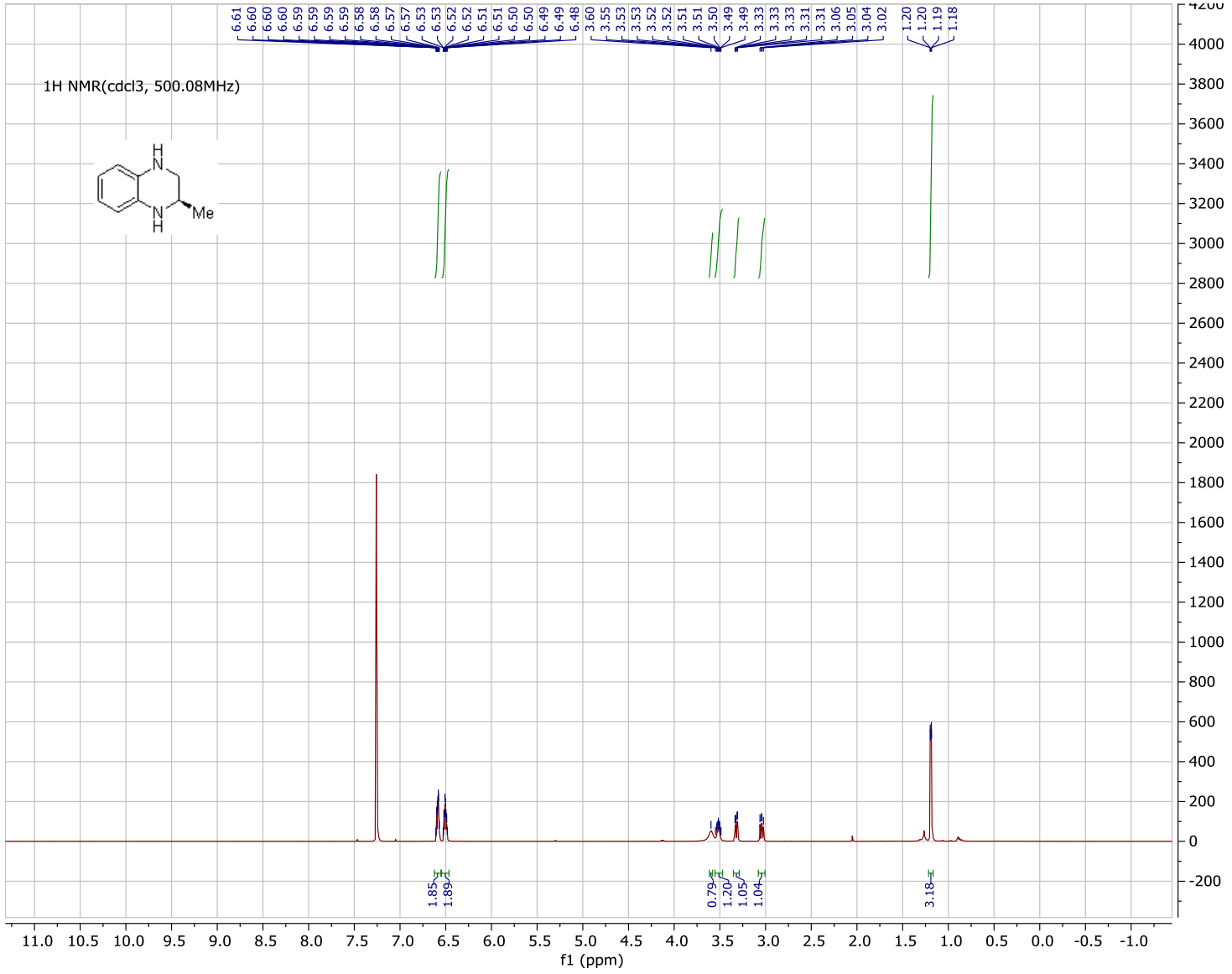

13C NMR(cdcl3, 100.47MHz)
144.79
144.71
129.29
128.56
127.42
126.88
126.53
120.85
117.13
113.95
56.23
30.97
26.37
Ph
N
H
f1 (ppm)

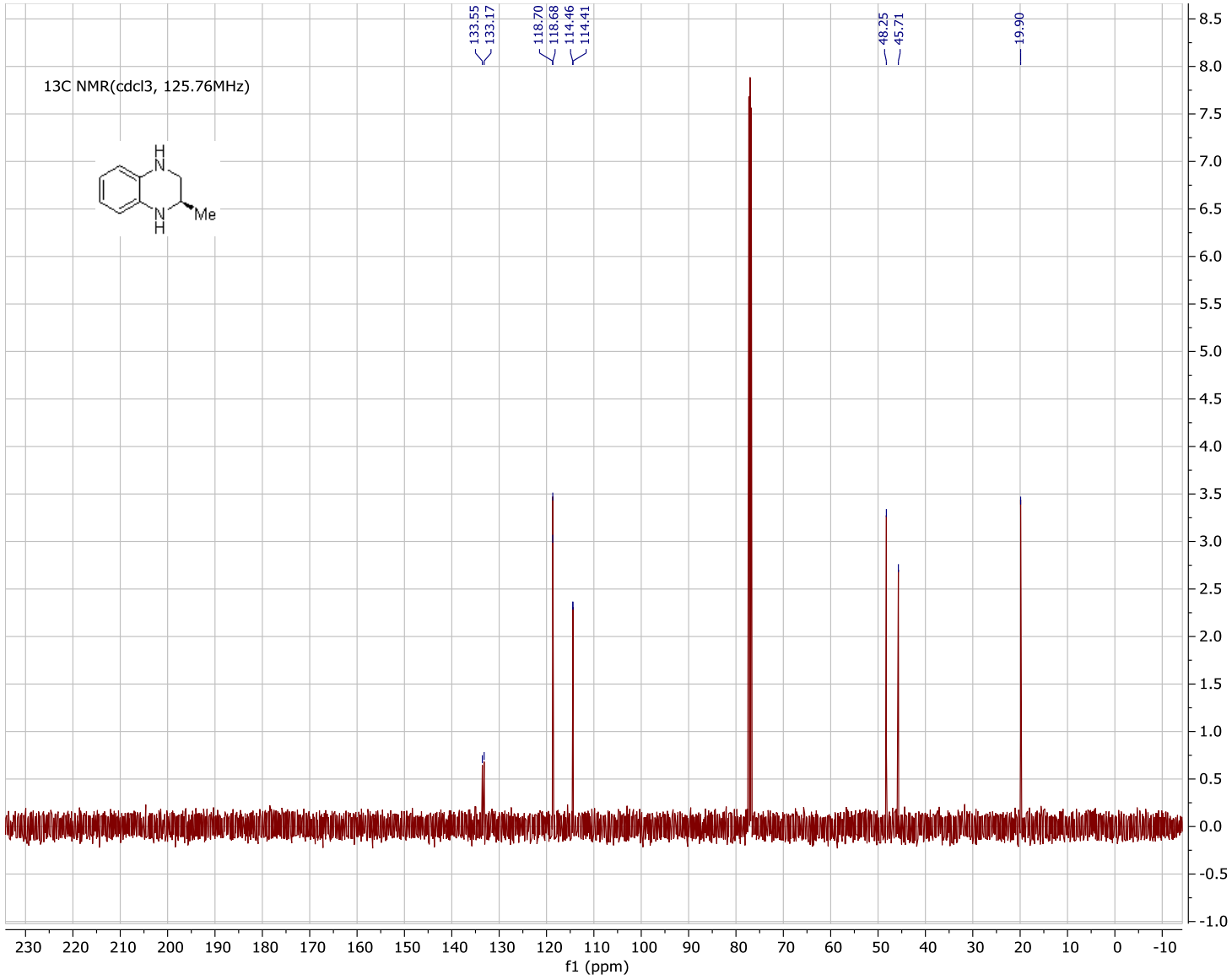

1H NMR(cdcl3, 699.75MHz)
Me
f1 (ppm)

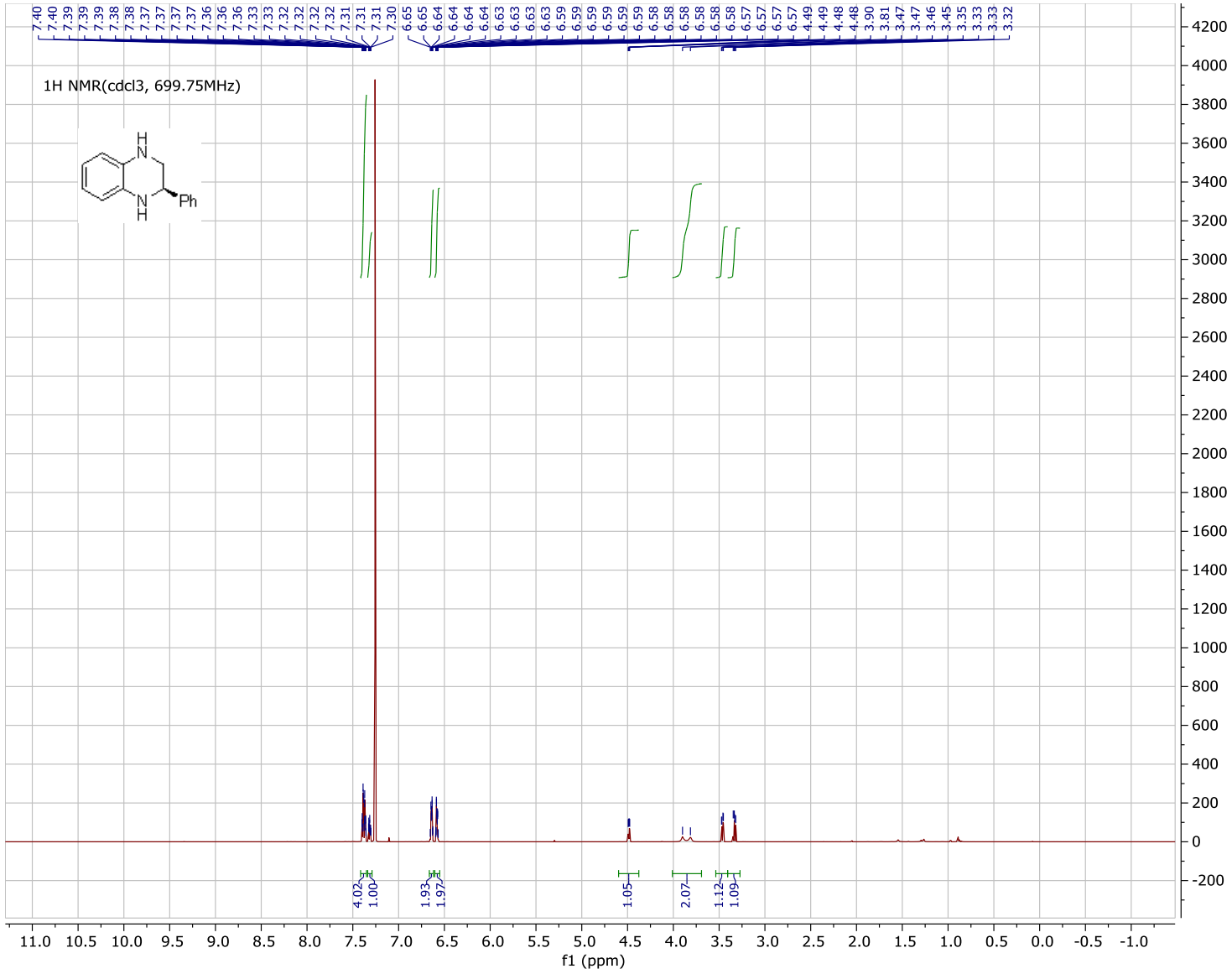

13C NMR(cdcl3, 175.97MHz)
Me
144.80
141.82
137.08
129.27
129.23
126.86
126.45
120.87
117.07
113.93
56.01
31.02
26.49
21.09
f1 (ppm)

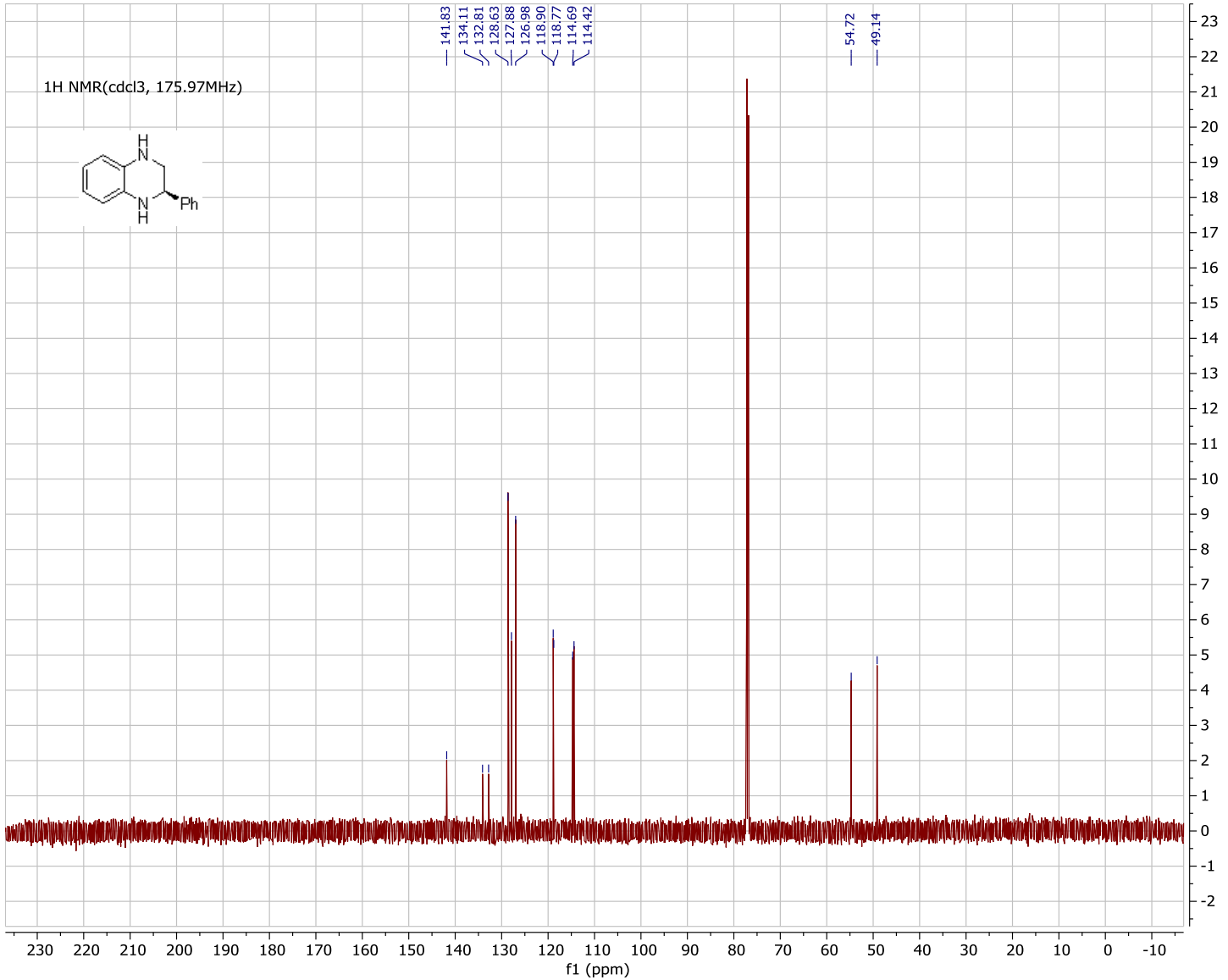

1H NMR(cdcl3, 699.75MHz)
OMe
f1 (ppm)

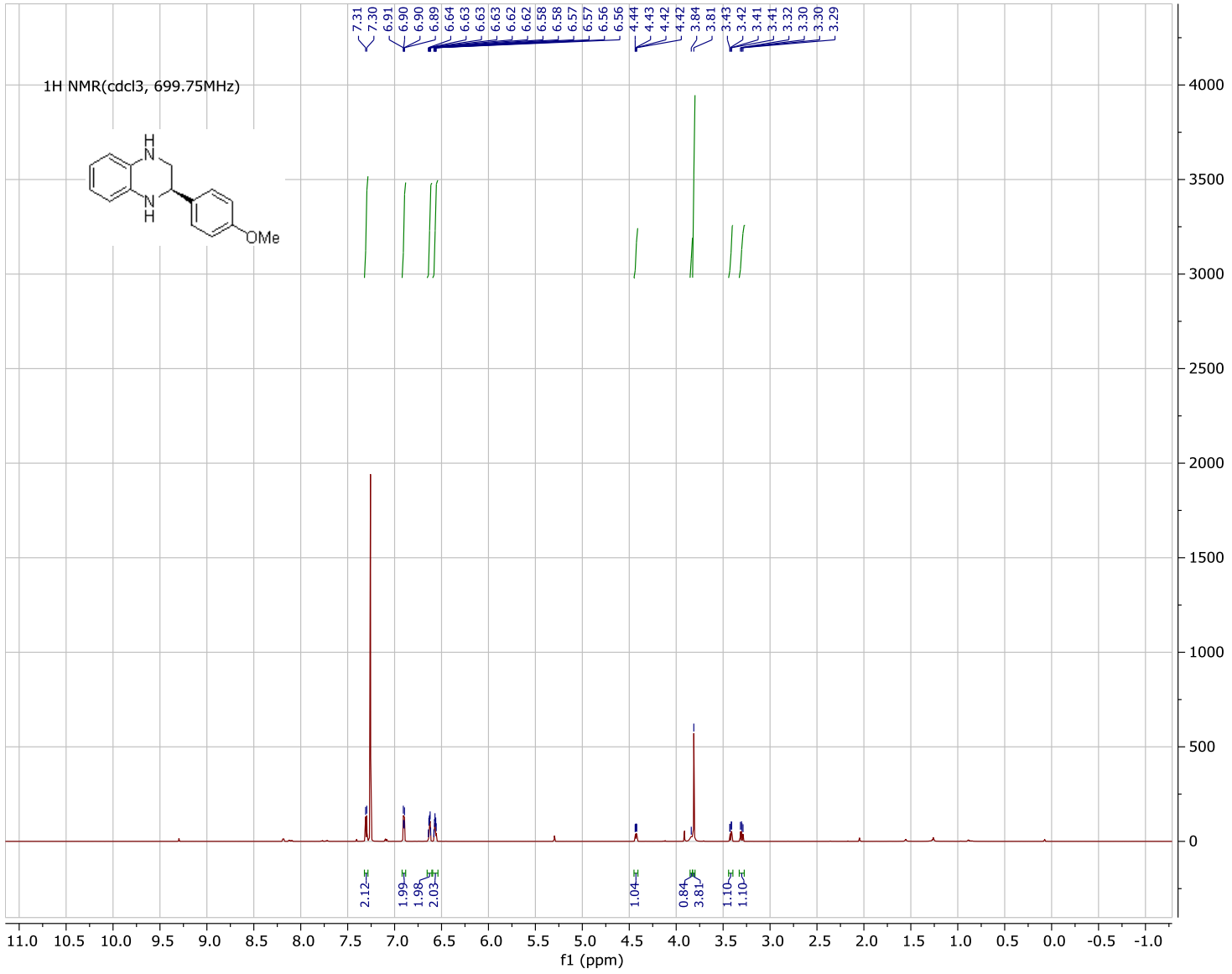

13C NMR(cdcl3, 175.97MHz)
OMe
158.94
144.81
136.87
129.27
127.61
126.84
120.86
117.09
113.93
113.90
55.71
55.31
31.08
26.54
f1 (ppm)

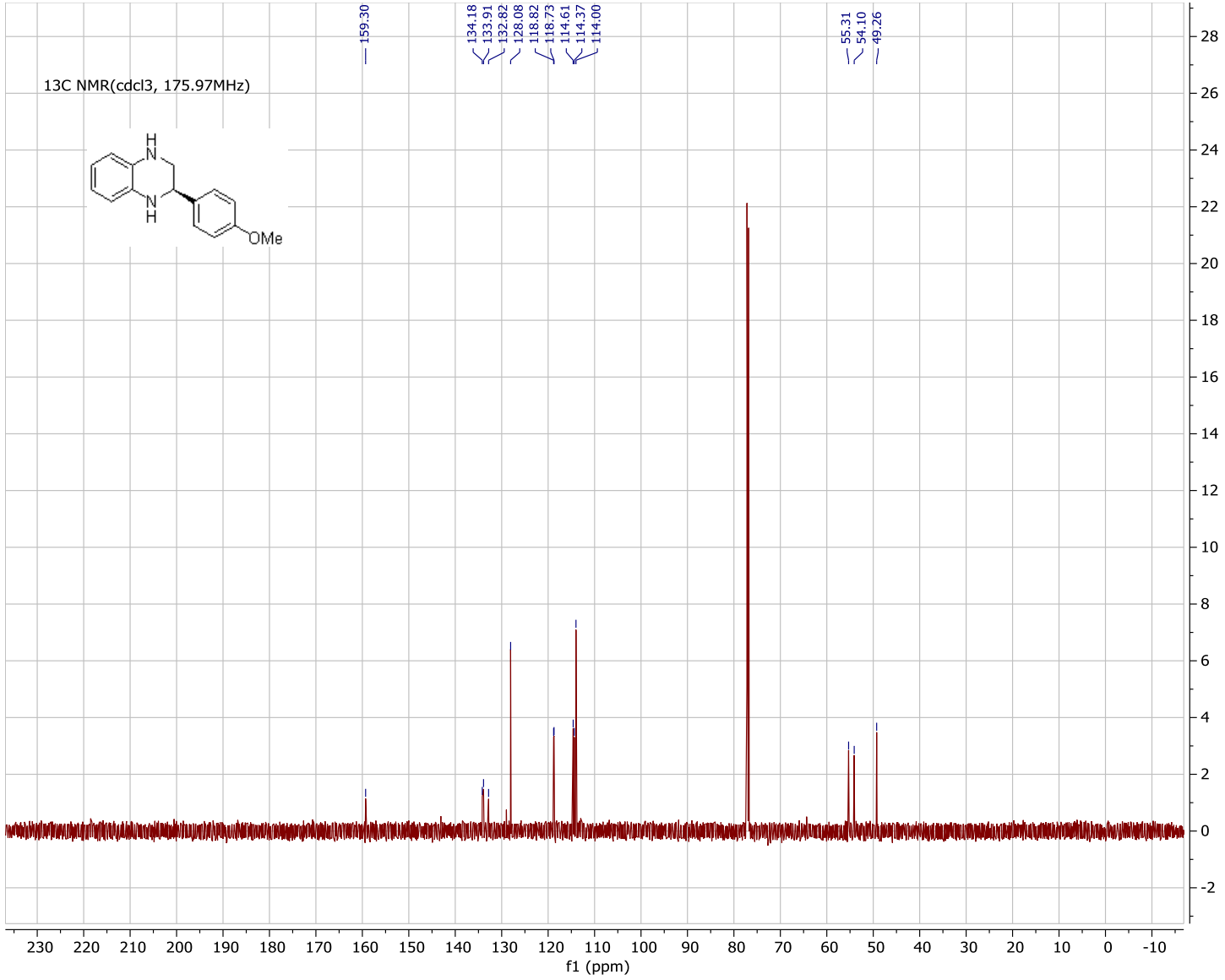

1H NMR(cdcl3, 500.08MHz)
Me
f1 (ppm)

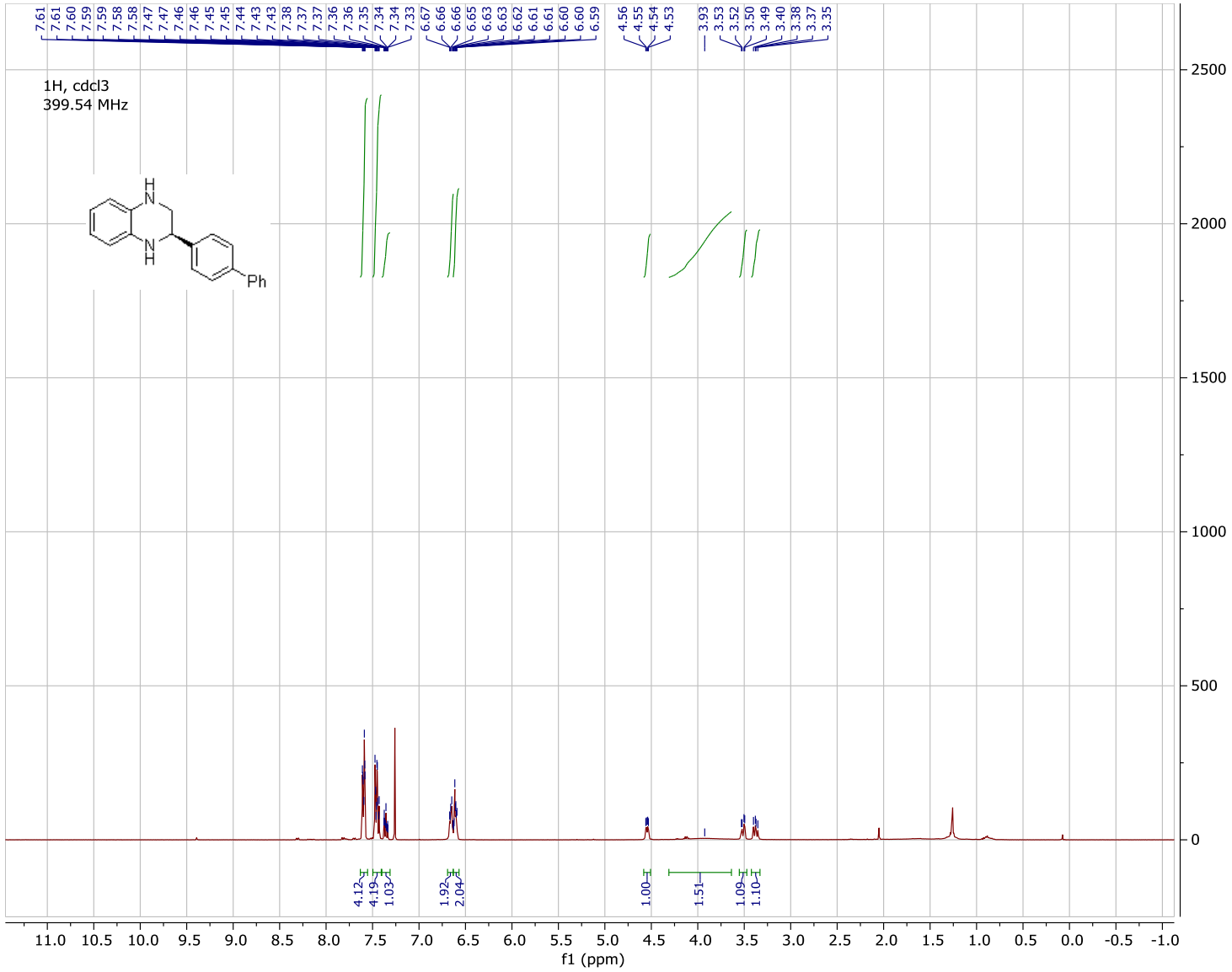

13C NMR(cdcl3, 125.76MHz)
133.55
133.17
118.70
118.68
114.46
114.41
48.25
45.71
19.90
Me
f1 (ppm)

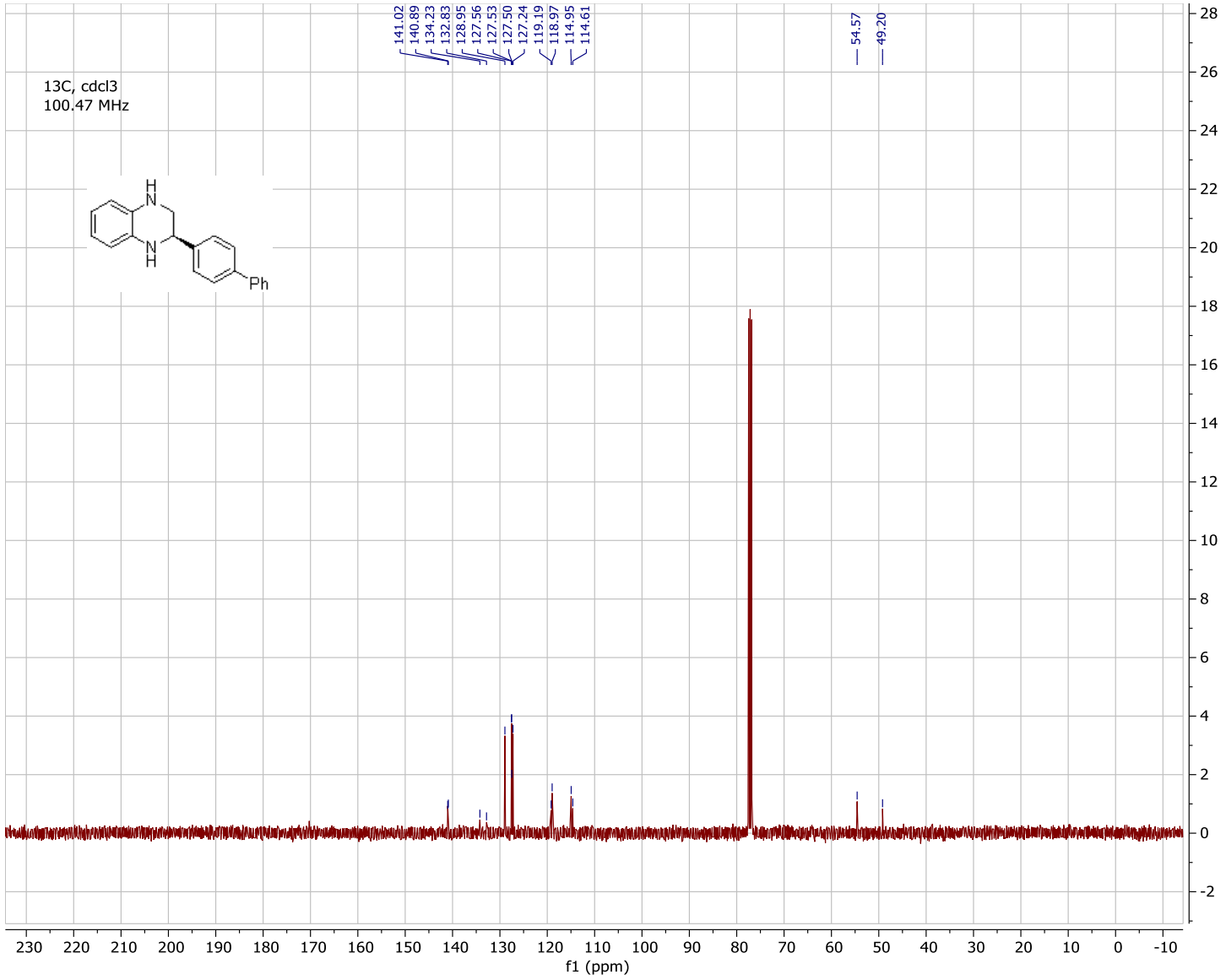

1H NMR(cdcl3, 699.75MHz)
Ph
f1 (ppm)

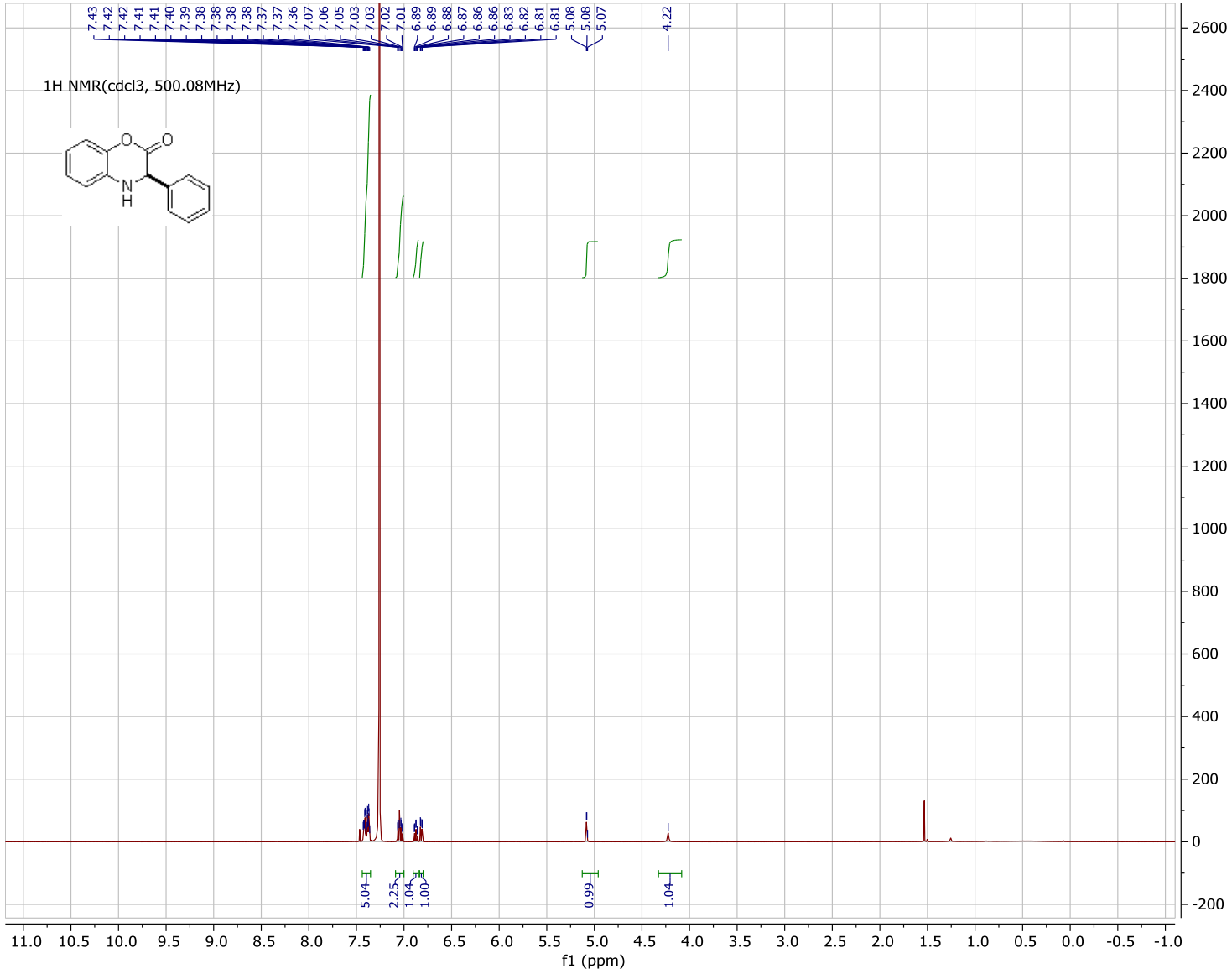

1H NMR(cdcl3, 175.97MHz)
141.83
134.11
132.81
128.63
127.88
126.98
118.90
118.77
114.69
114.42
54.72
49.14
Ph
f1 (ppm)

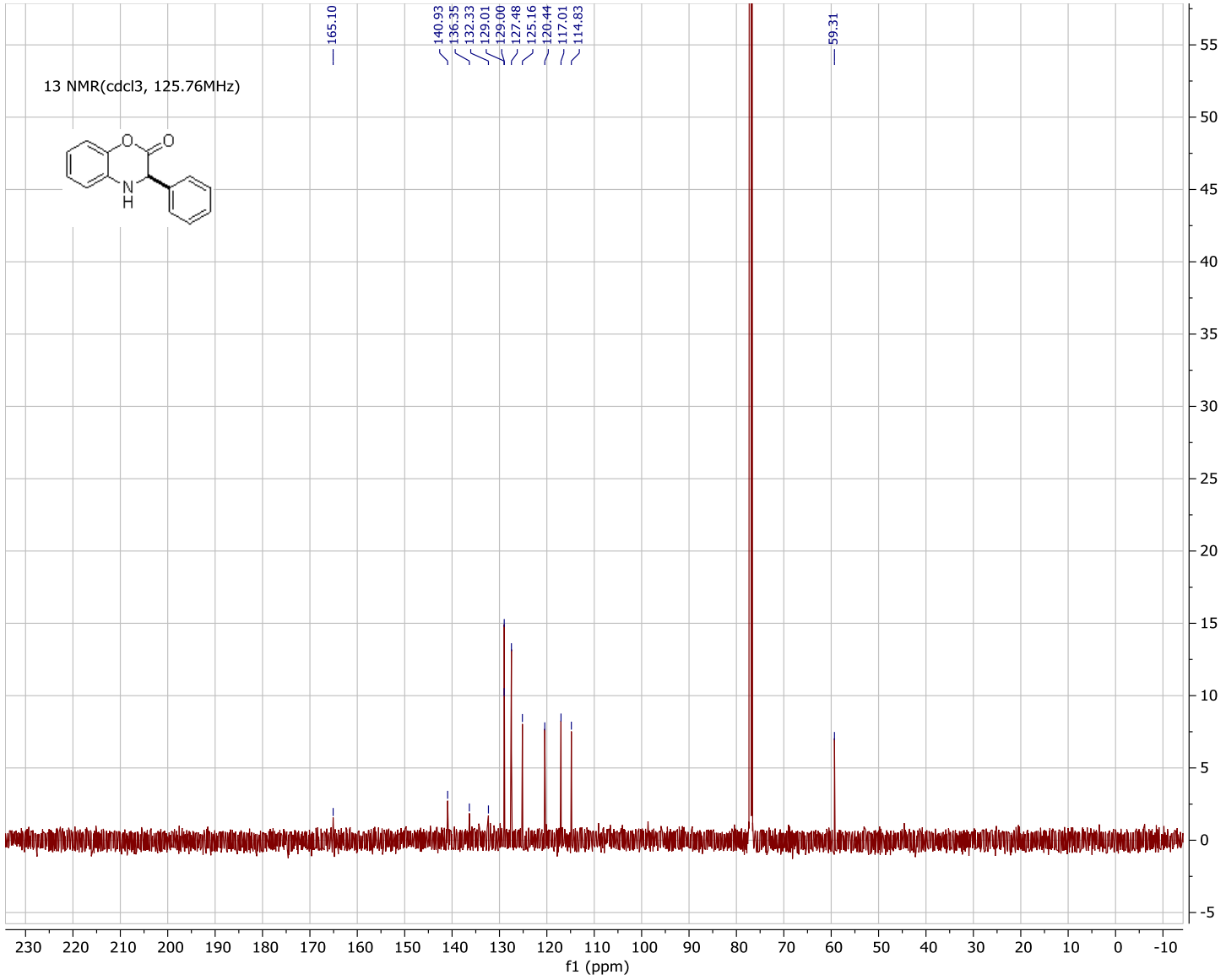

1H NMR(cdcl3, 699.75MHz)
OMe
7.31
7.30
6.91
6.90
6.90
6.89
6.64
6.63
6.63
6.63
6.62
6.62
6.58
6.58
6.57
6.57
6.56
6.56
4.44
4.43
4.42
4.42
3.84
3.81
3.43
3.42
3.41
3.41
3.32
3.30
3.30
3.29
2.12
1.99
1.98
2.03
1.04
0.84
3.81
1.10
1.10
f1 (ppm)

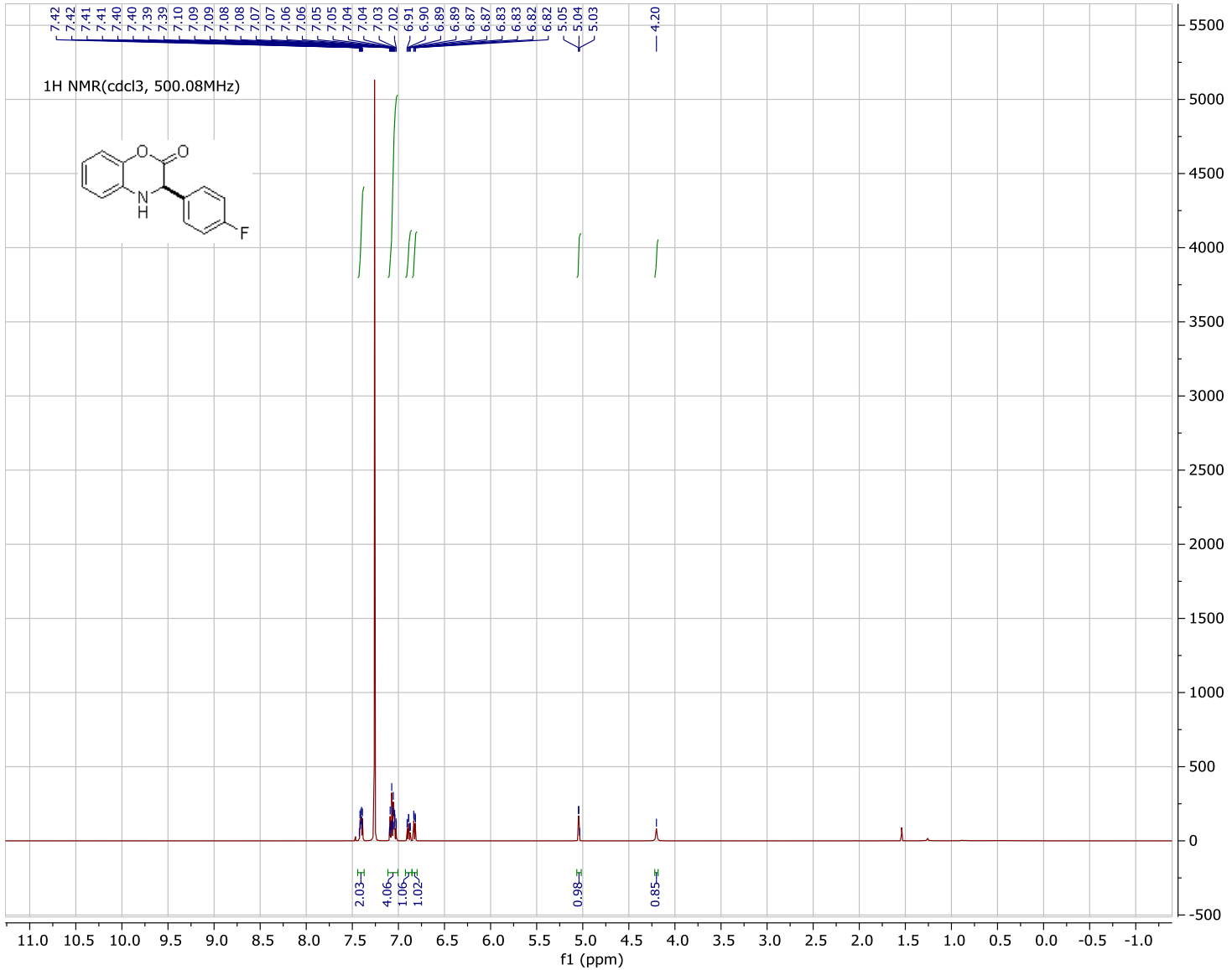

13C NMR(cdcl3, 175.97MHz)
159.30
134.18
133.91
132.82
128.08
118.82
118.73
114.61
114.37
114.00
55.31
54.10
49.26
OMe
f1 (ppm)

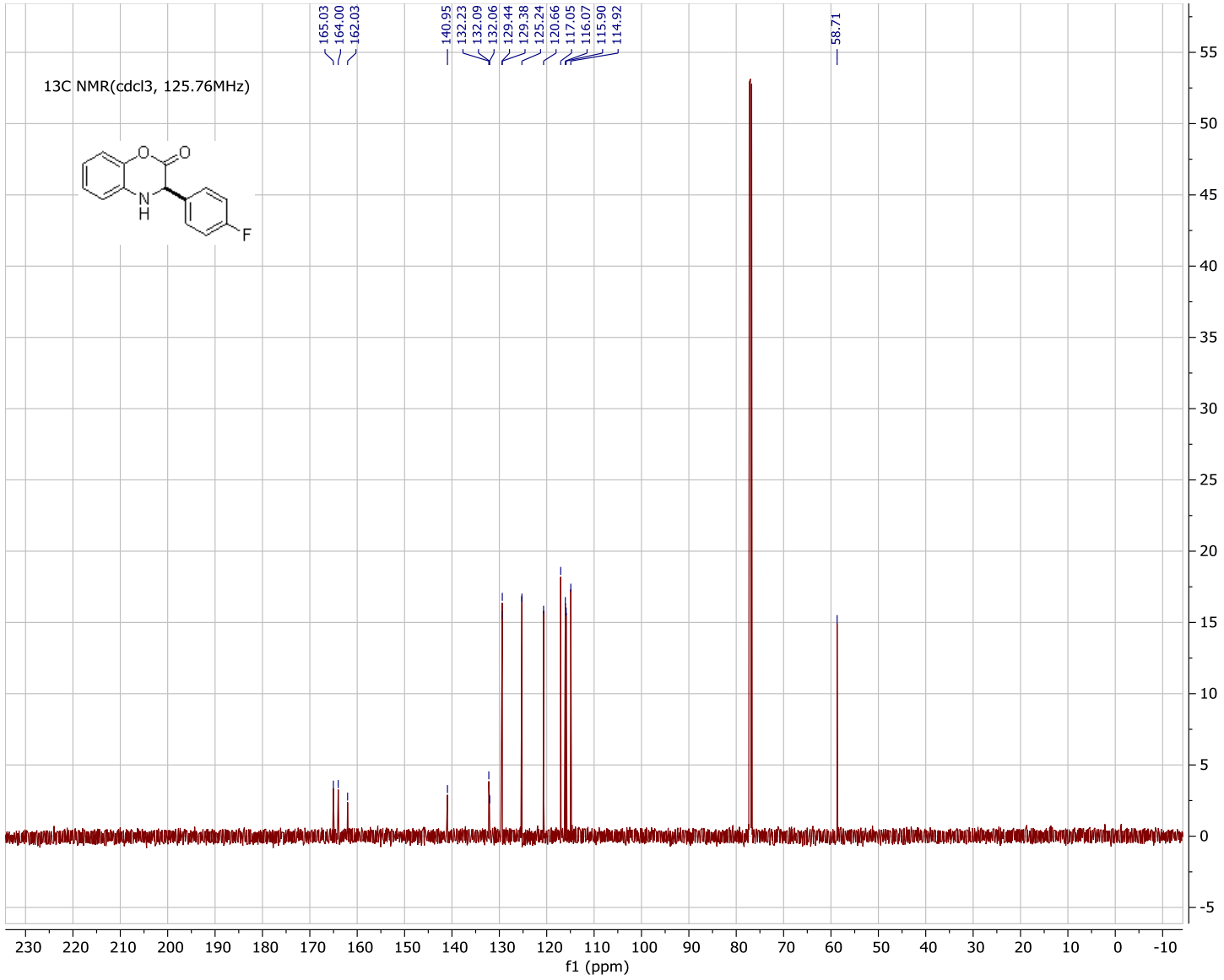

7.61 7.61 7.60 7.59 7.59 7.58 7.58 7.47 7.47 7.46 7.46 7.45 7.45 7.44 7.43 7.43 7.38 7.37 7.37 7.36 7.36 7.35 7.34 7.34 7.33
6.67 6.66 6.66 6.65 6.63 6.63 6.62 6.61 6.61 6.60 6.60 6.59
4.56 4.55 4.54 4.53
3.93 3.53 3.52 3.50 3.49 3.40 3.38 3.37 3.35
1H, cdcl3
399.54 MHz
Ph
2500
2000
1500
1000
500
0
4.12 4.19 1.03 1.92 2.04 1.00 1.51 1.09 1.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

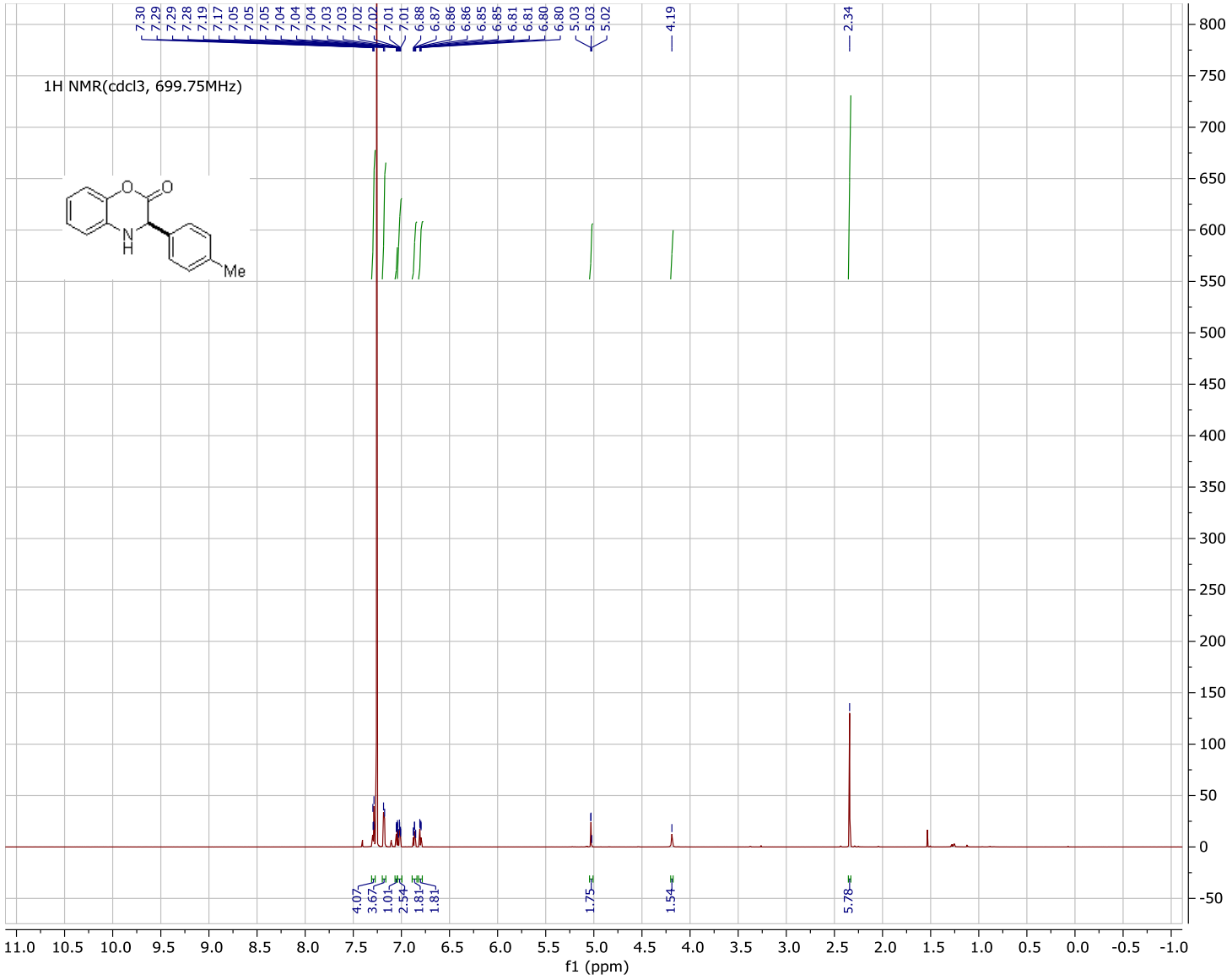

141.02
140.89
134.23
132.83
128.95
127.56
127.53
127.50
127.24
119.19
118.97
114.95
114.61
54.57
49.20
13C, cdcl3
100.47 MHz
H
N
N
H
Ph
f1 (ppm)

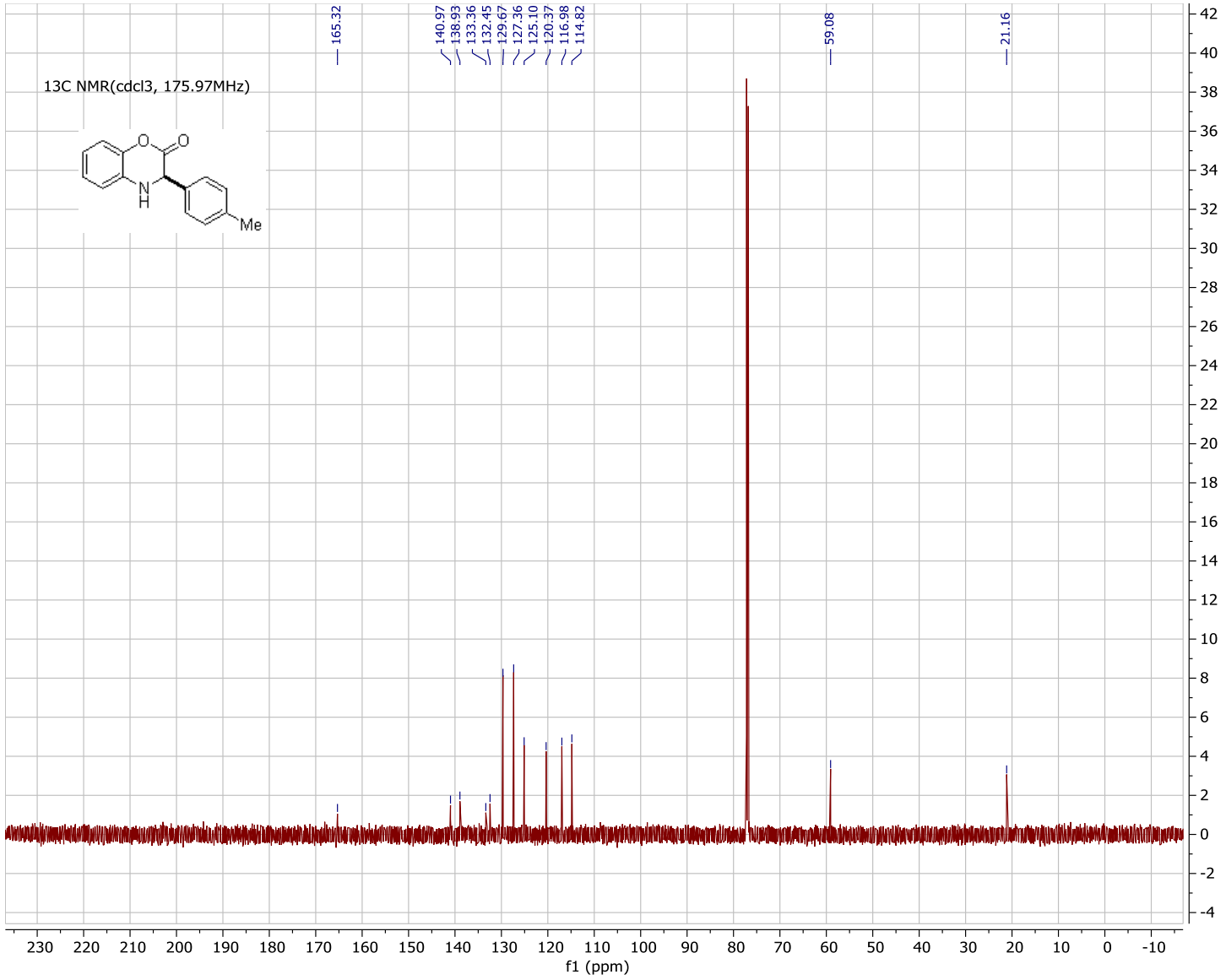

1H NMR(cdcl3, 500.08MHz)
7.43
7.42
7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.38
7.37
7.37
7.36
7.07
7.06
7.05
7.03
7.03
7.02
7.01
6.89
6.89
6.88
6.87
6.86
6.86
6.83
6.82
6.81
6.81
5.08
5.08
5.07
4.22
5.04
2.25
1.04
1.00
0.99
1.04
f1 (ppm)

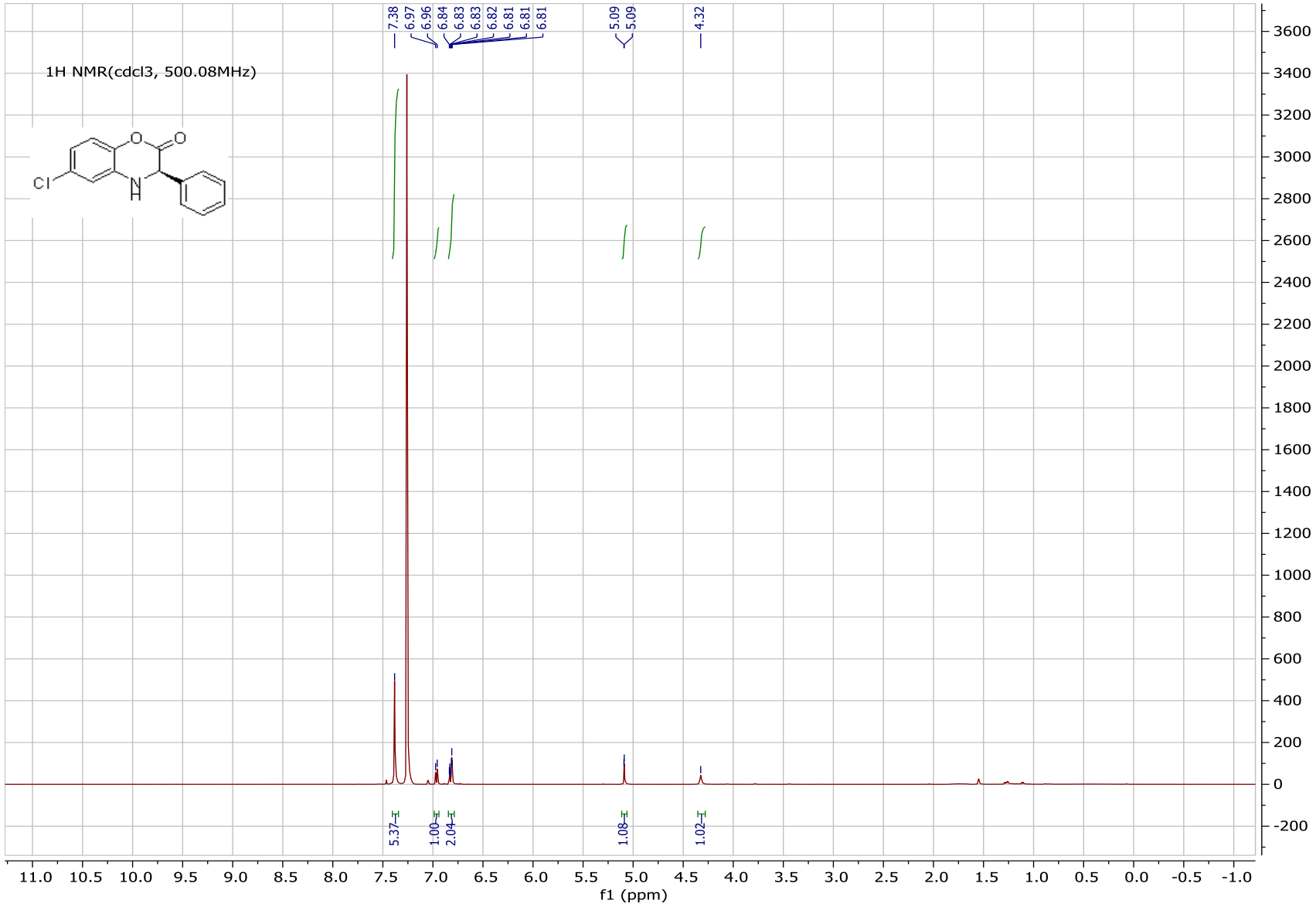

13 NMR(cdcl3, 125.76MHz)
165.10
140.93
136.35
132.33
129.01
129.00
127.48
125.16
120.44
117.01
114.83
59.31
f1 (ppm)

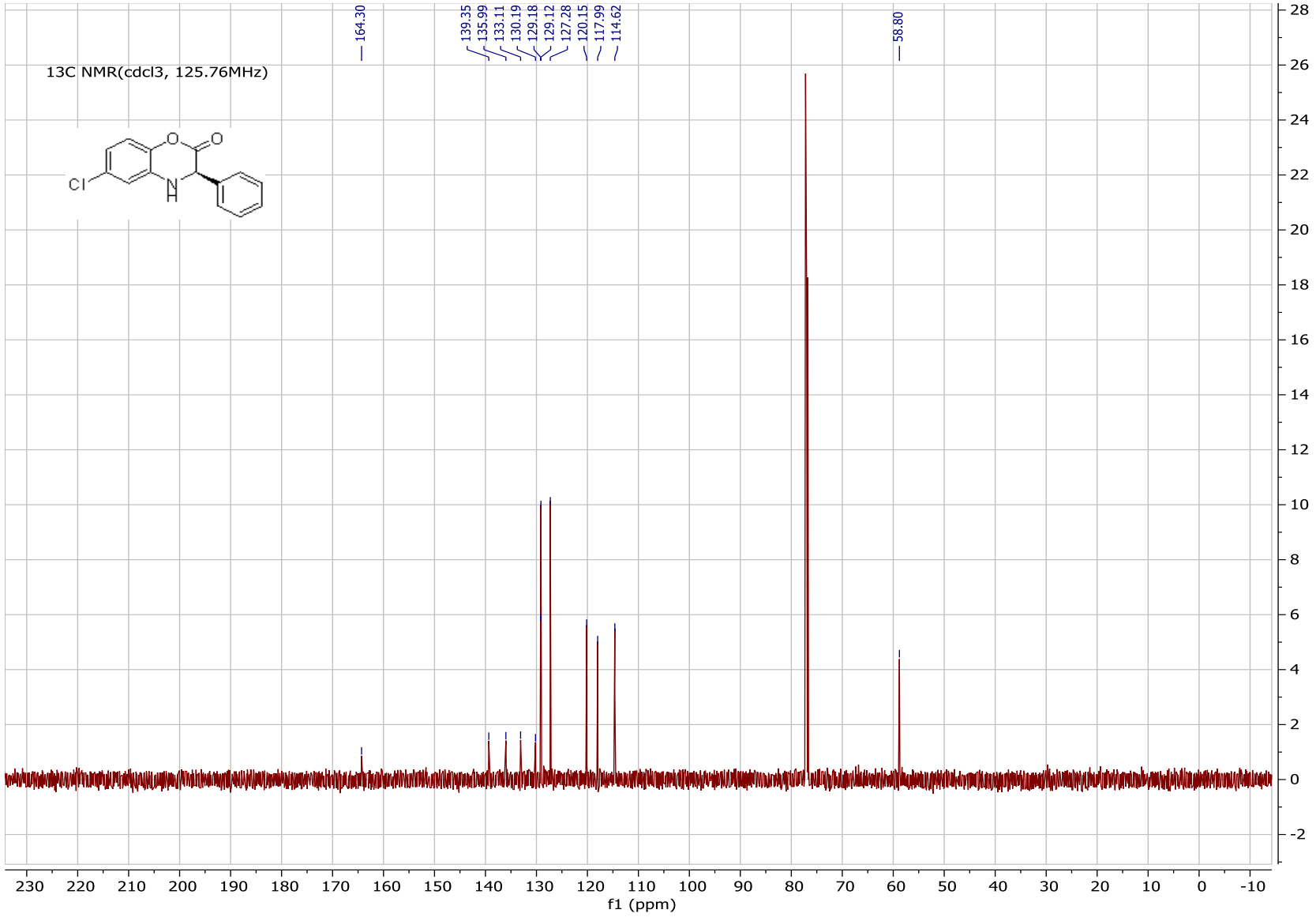

1H NMR(cdcl3, 500.08MHz)
7.42
7.42
7.41
7.41
7.40
7.40
7.39
7.39
7.10
7.09
7.09
7.08
7.08
7.07
7.07
7.06
7.06
7.05
7.05
7.04
7.04
7.03
7.02
6.91
6.90
6.89
6.89
6.87
6.87
6.83
6.83
6.82
6.82
5.05
5.04
5.03
4.20
O
O
N
H
F
2.03
4.06
1.06
1.02
0.98
0.85
f1 (ppm)

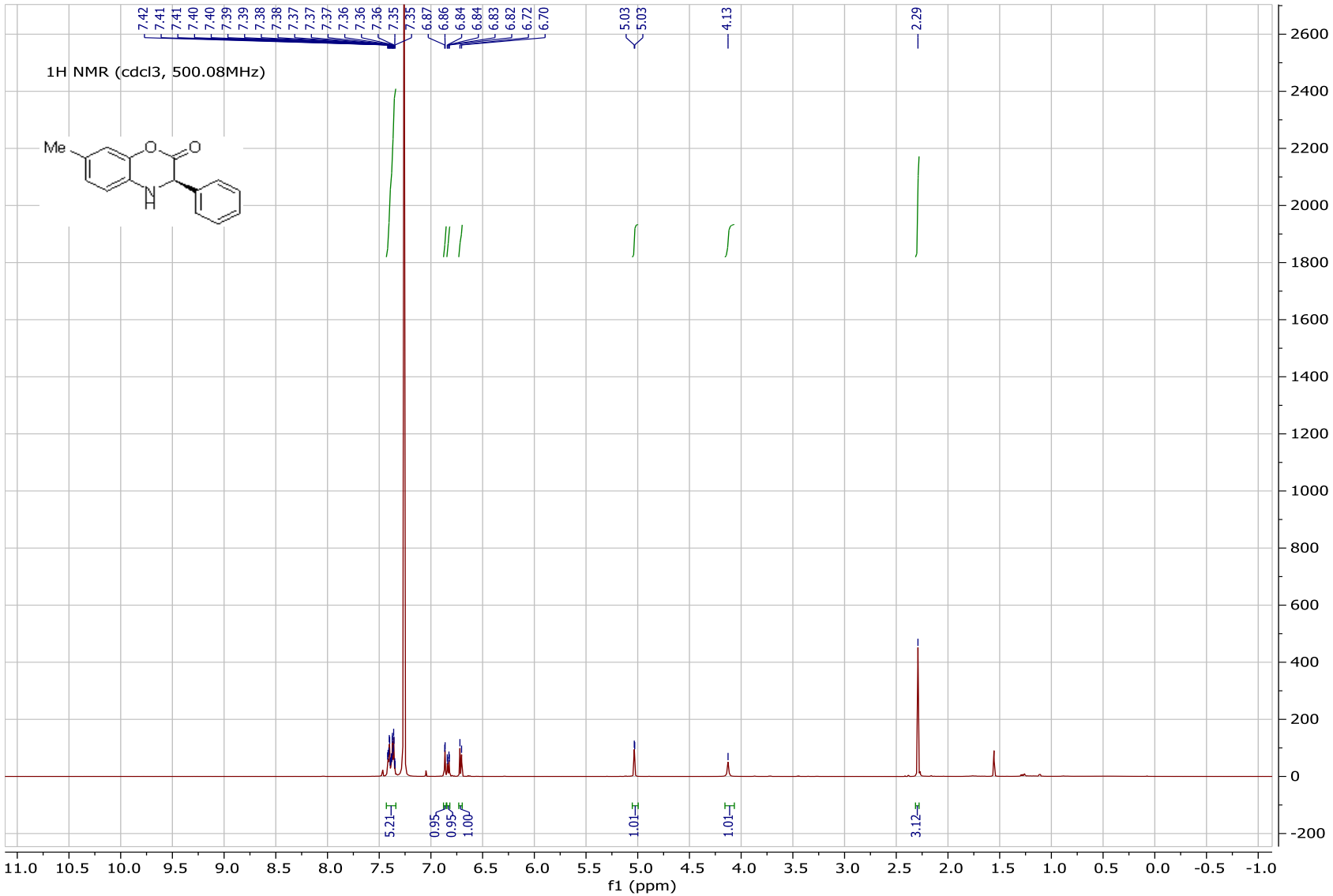

165.03
164.00
162.03
140.95
132.23
132.09
132.06
129.44
129.38
125.24
120.66
117.05
116.07
115.90
114.92
58.71
13C NMR(cdcl3, 125.76MHz)
O
O
N
H
F
55
50
45
40
35
30
25
20
15
10
5
0
-5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

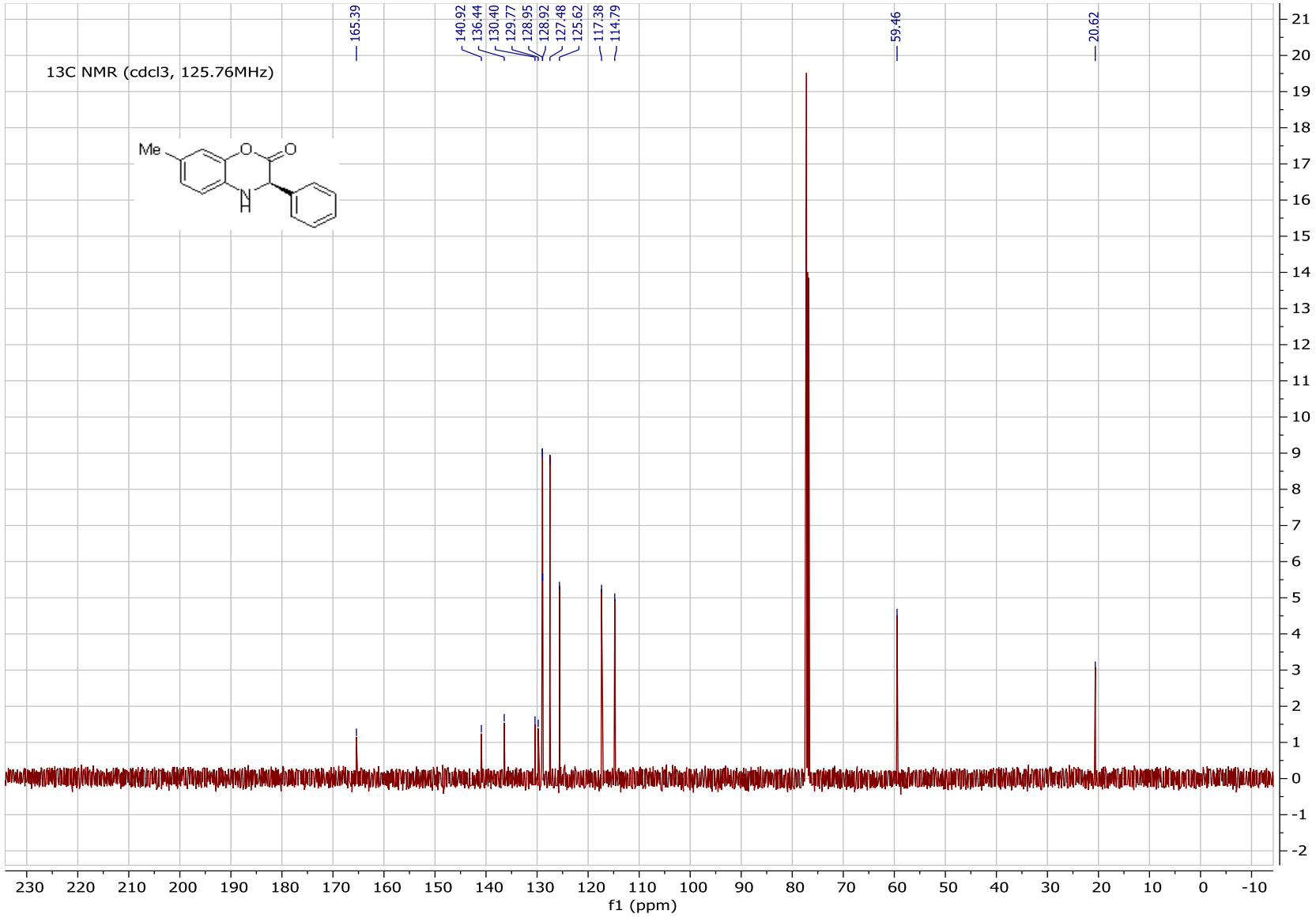

1H NMR(cdcl3, 699.75MHz)
7.30
7.29
7.29
7.28
7.19
7.17
7.05
7.05
7.05
7.04
7.04
7.04
7.03
7.03
7.02
7.02
7.01
7.01
6.88
6.87
6.86
6.86
6.85
6.85
6.81
6.81
6.80
6.80
5.03
5.03
5.02
4.19
2.34
O
O
N
H
Me
4.07
3.67
1.01
2.54
1.81
1.81
1.75
1.54
5.78
f1 (ppm)

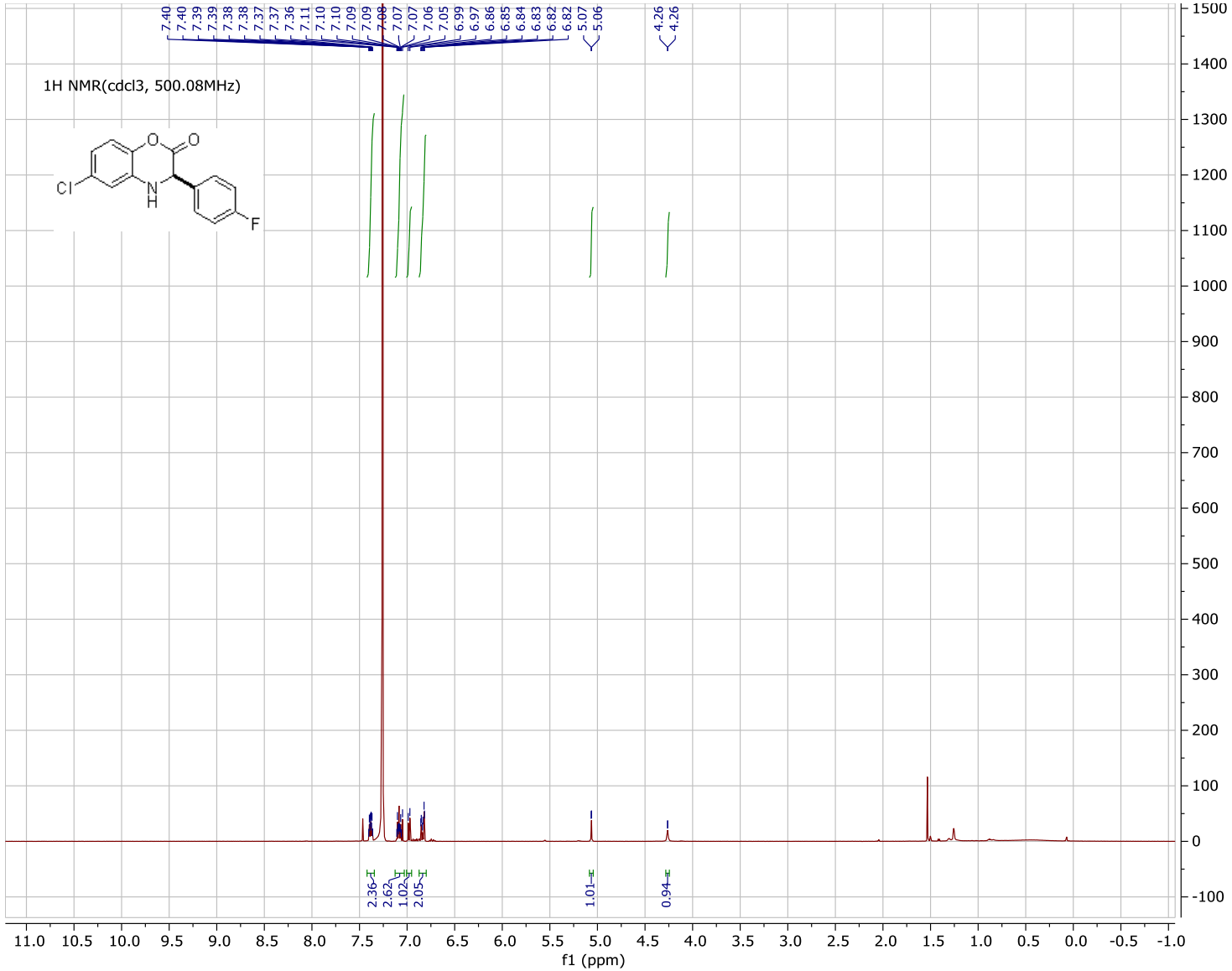

13C NMR(cdcl3, 175.97MHz)
O
O
N
H
Me
165.32
140.97
138.93
133.36
132.45
129.67
127.36
125.10
120.37
116.98
114.82
59.08
21.16
f1 (ppm)

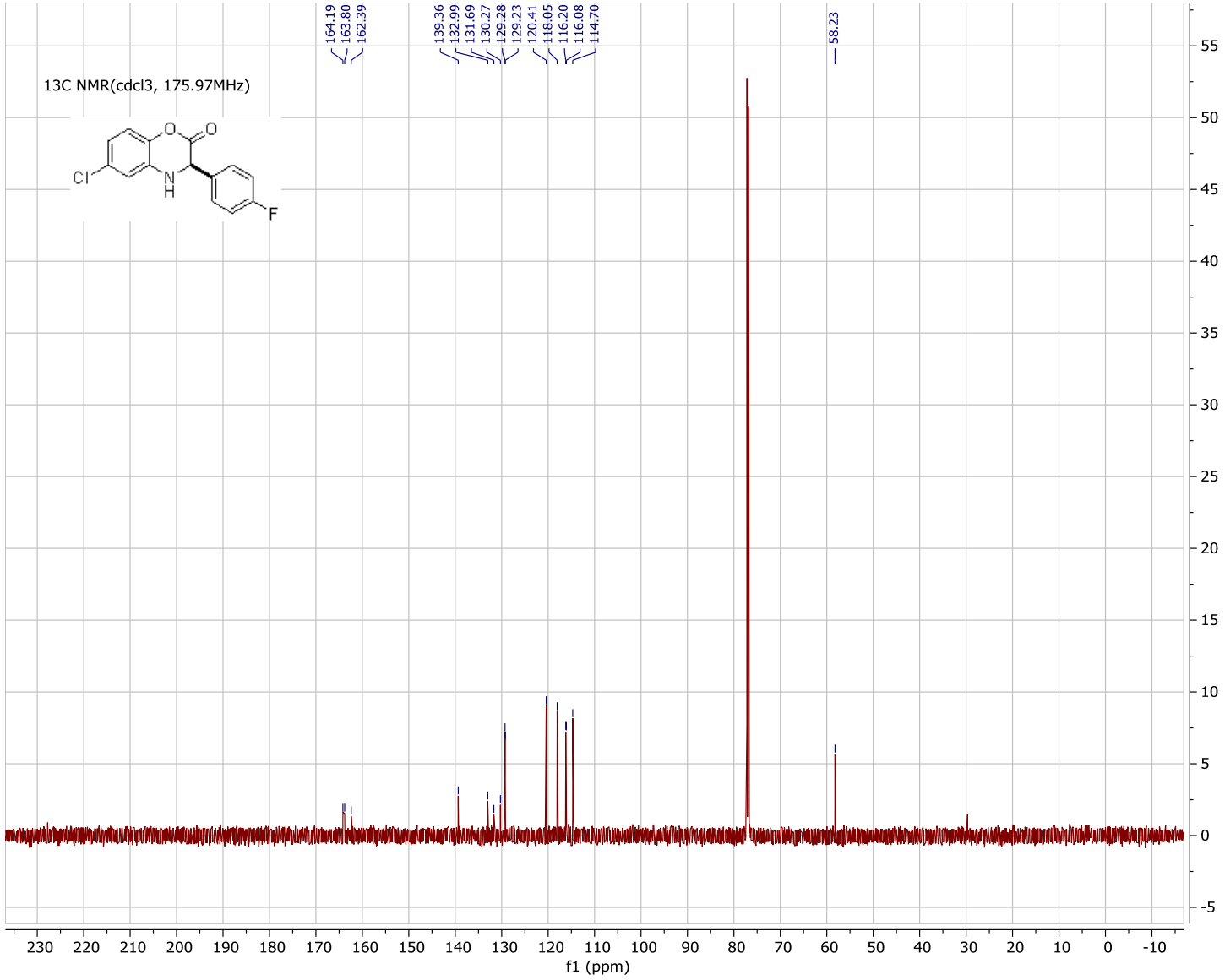

1H NMR(cdcl3, 500.08MHz)
7.38
6.97
6.96
6.84
6.83
6.83
6.82
6.81
6.81
6.81
5.09
5.09
4.32
5.37
1.00
2.04
1.08
1.02
f1 (ppm)

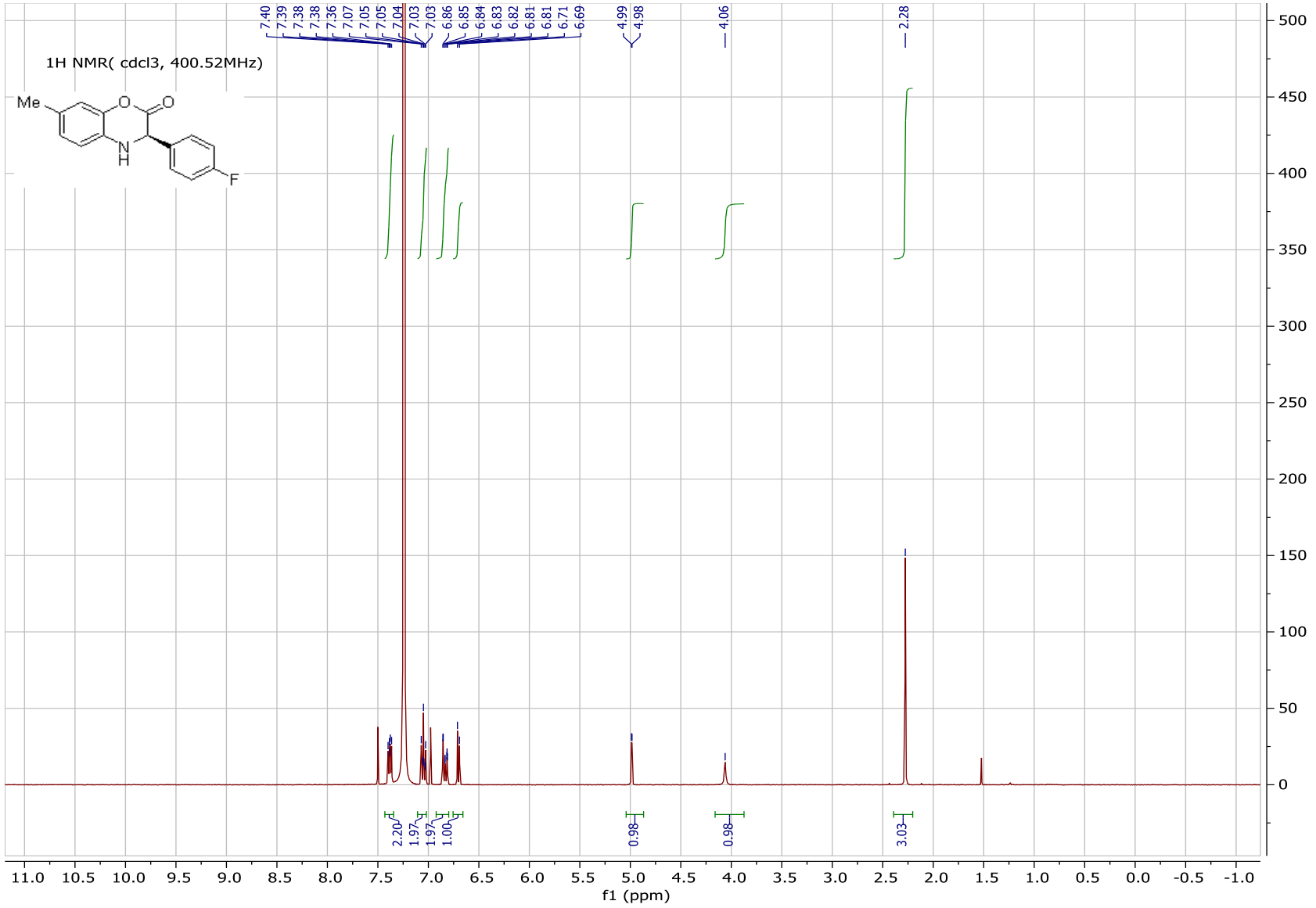

13C NMR(cdcl3, 125.76MHz)
164.30
139.35
135.99
133.11
130.19
129.18
129.12
127.28
120.15
117.99
114.62
58.80
f1 (ppm)

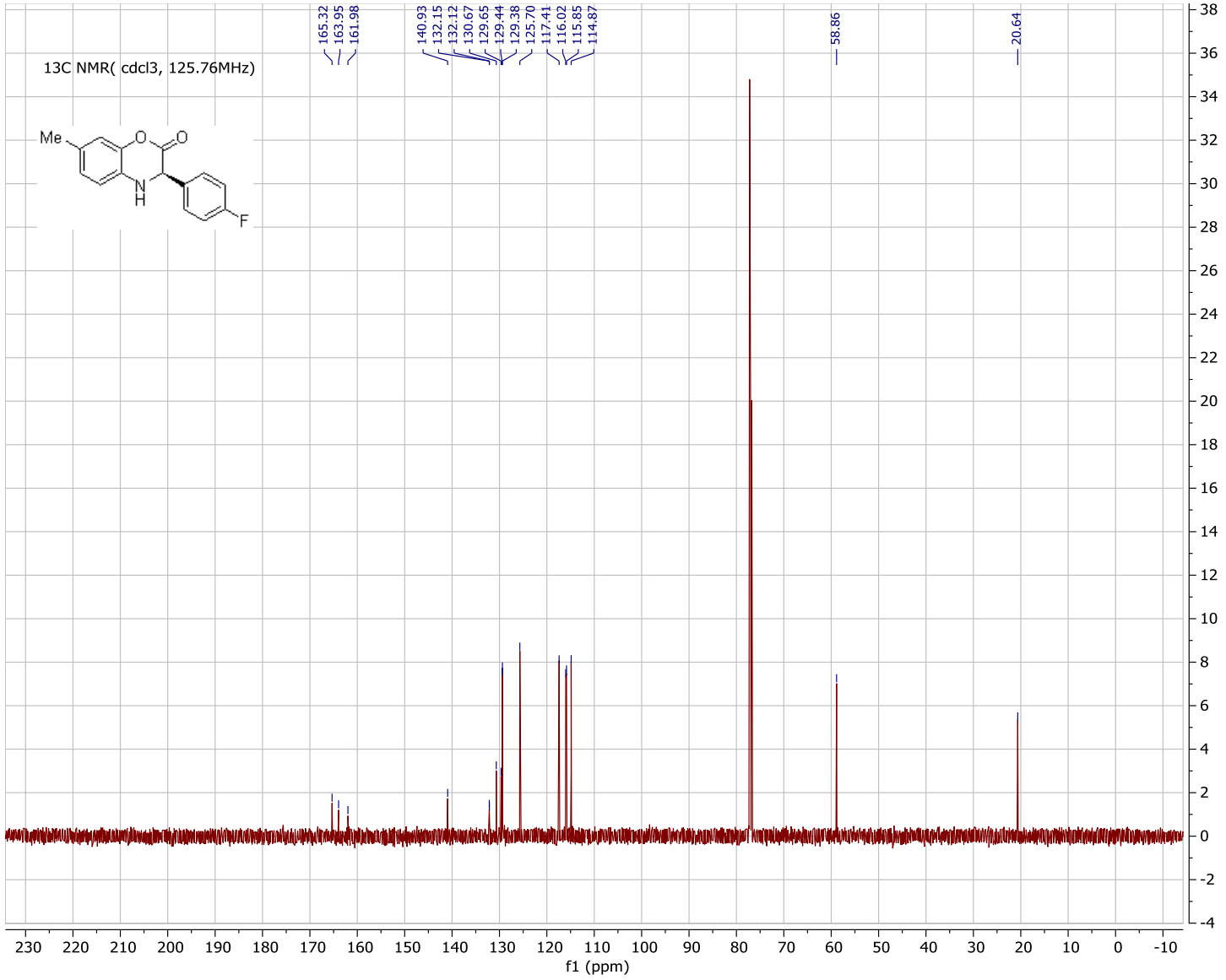

7.42
7.41
7.41
7.40
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.37
7.36
7.36
7.35
6.87
6.86
6.84
6.84
6.83
6.82
6.72
6.70
5.03
5.03
4.13
2.29
1H NMR (cdcl3, 500.08MHz)
Me
O
O
N
H
5.21
0.95
0.95
1.00
1.01
1.01
3.12
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


13C NMR (cdcl3, 125.76MHz)
Me
O
O
N
H
165.39
140.92
136.44
130.40
129.77
128.95
128.92
127.48
125.62
117.38
114.79
59.46
20.62
f1 (ppm)


1H NMR(cdcl3, 500.08MHz)
Cl
O
O
N
H
F
7.40
7.40
7.39
7.39
7.38
7.37
7.37
7.36
7.11
7.10
7.10
7.09
7.09
7.08
7.07
7.07
7.06
7.05
6.99
6.97
6.86
6.85
6.84
6.83
6.82
6.82
5.07
5.06
4.26
4.26
2.36
2.62
1.02
2.05
1.01
0.94
f1 (ppm)


13C NMR(cdcl3, 175.97MHz)
164.19
163.80
162.39
139.36
132.99
131.69
130.27
129.28
129.23
120.41
118.05
116.20
116.08
114.70
58.23
Cl
O
O
N
H
F
f1 (ppm)


1H NMR(cdcl3, 400.52MHz)
Me
O
O
N
H
F
7.40
7.39
7.38
7.38
7.36
7.07
7.05
7.05
7.04
7.03
7.03
6.86
6.85
6.84
6.83
6.82
6.81
6.81
6.71
6.69
4.99
4.98
4.06
2.28
2.20
1.97
1.97
1.00
0.98
0.98
3.03
f1 (ppm)


13C NMR(cdcl3, 125.76MHz)
Me
O
O
N
H
F
165.32
163.95
161.98
140.93
132.15
132.12
130.67
129.65
129.44
129.38
125.70
117.41
116.02
115.85
114.87
58.86
20.64
f1 (ppm)