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A Spiro-Pyrrolidine Organocatalyst and Its Application to Catalytic Asymmetric Michael Addition for the Construction of All-Carbon Quaternary Centers

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Contents:

1. General information --S2

2. Section 1: synthesis of catalyst 1, 2 and 3-------------------------------------S3-S5

3. Section 2: substrates preparation and scope -----------------------------------S6-S7

4. Section 3: products scope ---S8-S13

5. Section 4: the process of *in situ* NMR experiments ----------------------------S14-S16

6. Section 5: NMR, HPLC spectra Copies of new compounds ----------------------S17-S91

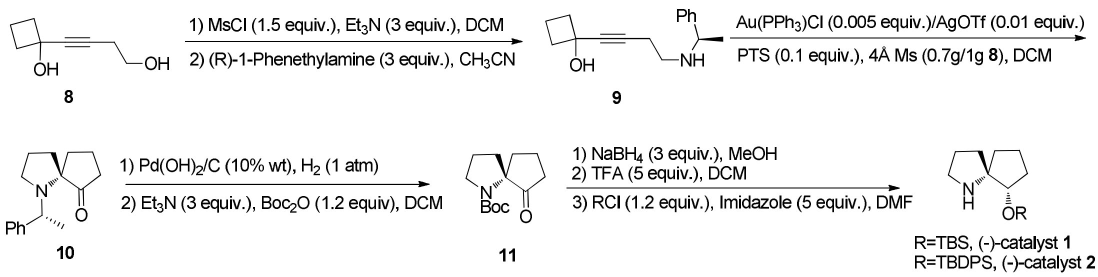
General information

All reactions requiring anhydrous conditions were carried out under argon atmosphere using oven-dried glassware (120 ^oC), which was cooled under argon. All solvents were purified and dried by standard techniques, and distilled prior to use. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on gel F254 plates. Silica gel (200~300 mesh) and petroleum ether (bp. 60~90 ^oC), ethyl acetate are used for product purification by flash column chromatography. ^1H and ^{13}C NMR spectra, which were recorded in $CDCl_3$ solution or Acetone-D6 solution, were acquired on a Bruker AM-400 MHz spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^1H NMR, 77.0 ppm for ^{13}C NMR; $(CD_3)_2CO$: 2.05 ppm for ^1H NMR, 29.9 ppm for ^{13}C NMR). The following abbreviations are used to indicate the multiplicity in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectral analysis (HRMS) data were determined on an APEXII 47e FT-ICR spectrometer by means of the ESI technique. IR spectra were recorded on a fourier transform infrared spectrometer. Melting points were measured on a melting point apparatus and were uncorrected. The enantiomeric excess (ee) of the products was determined by high performance liquid chromatography (HPLC) analysis employing Daicel Chiralpak AD, ID-3, IA-3 and Chiralcel OD-H column. Optical rotations were detected on RUDOLPH A21202-J APTV/GW.

Section 1: Synthesis of catalysts 1, 2 and 3

Catalysts **1** and **2** were prepared easily in gram-scale using tandem hydroamination/semipinacol rearrangement reaction as key reaction according to the procedure below. Instead of the asymmetric catalysis means in previous work, we took chiral induction strategy here to obtain optically pure catalyst. An 8-step synthesis route was performed to give catalysts **1** and **2** in about 30 % total yield from known compound 8.[1] More details are as follows:

1） Synthesis of catalysts **1** and **2**



Compound 9: To the solution of compound **8** (8.400 g, 60 mmol) in DCM (60 mL) were added Et_3N (25.2 mL, 180 mmol, 3 equiv.) and MsCl (6.9 mL, 90 mmol, 1.5 equiv.) at 0 ^{o}C. About 5 min later, 1 mL H_2O was added to quench the reaction. Then the system was extracted with DCM (3 x 100 mL), and the combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was used to the next step directly.

The crude product was dissolved in MeCN (80 mL), and R-phenethylamine (22.9 mL, 180 mmol, 3 equiv.) was added and the system was allowed to warm to 85 ^{o}C and stirred for 8 h. Then the system was concentrated in *vacuo,* and 30 mL 4 M HCl was added to neutralize most of the remaining R-phenethylamine. Next, the mixture was extracted with DCM (5 x 100 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 30) to give compound **9** (12.685 g, 87 % yield for two steps) as a white solid. **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.23-7.32 (m, 5 H), 3.79 (dd, *J* = 6.4 Hz, 13.2 Hz, 1 H), 2.53-2.64 (m, 2 H), 2.23-2.47 (m, 6 H), 1.72-1.81 (m, 2 H), 1.37 (m, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 144.7, 128.4, 126.9, 126.5, 85.9, 80.8, 67.1, 57.4, 45.5, 38.8, 23.9, 19.4, 12.8 ppm.

Compound 10: To the solution of compound **9** (6.342 g, 26 mmol) in DCM (50 mL) was added 4 Å MS (4.440 g), and it was stirred for 10 min at room temperature. Then PTS (221 mg, 1.3 mmol, 0.05 equiv.) was added to the system. About 5 min later, $Au(PPh_3)Cl$ (65 mg, 0.13 mmol, 0.005 equiv.) and AgOTf (67 mg, 0.26 mmol, 0.01 equiv.) mixed together were added to the system. Then PTS (221 mg, 1.3 mmol, 0.05 equiv.) was added to the system again, and the system was allowed to heat to reflux for 2 h. The system was filtered through celite and concentrated in *vacuo*. The crude residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 50) to give compound **10** (5.456 g for 2 pots, 43 % yield) as a colorless oil. **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.17-7.31 (m, 5 H), 3.87 (dd, *J* = 8.0 Hz, 1.6 Hz, 1 H), 3.15-3.19 (m, 1 H), 2.64-2.70 (m, 1 H), 2.18-2.25 (m, 1 H), 1.99 (m, 1 H), 1.69-1.80 (m, 6 H), 1.33-1.60 (m, 2 H), 1.25-1.39 (m, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 222.1, 144.9, 128.3, 127.9, 126.9, 60.0, 52.8, 38.9, 36.3, 32.5, 23.9, 22.6, 18.3 ppm;

Compound 11: To the solution of compound **10** (5.456 g, 22.5 mmol) in MeOH (30 mL) was added $Pd(OH)_2/C$

(272 mg, 5 % wt), and then the system was put into 1 atm H_2 and stirred for 10 h. The mixture was filtered through celite and concentrated in *vacuo*. Then the crude reside was dissolved in DCM (50 mL) at 0 °C, Et_3N (9.4 mL, 67.5 mmol, 3 equiv.) and Boc_2O (5.892 g, 27 mmol, 1.2 equiv.) were added to the system sequentially, and the solution was allowed to warm to room temperature and stirred for another 1 h. Then the system was extracted directly with DCM (3x60 mL), and the combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo.* The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 10) to give compound **11** (5.110 g, 95 % yield for two steps) as a colorless oil. **IR (neat)** cm^{-1} : 2971, 1745, 1676, 1402, 1161, 952; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 3.44-3.48 (m, 1 H), 3.37-3.41 (m, 1 H), 2.40-2.51 (m, 1 H), 2.16-2.29 (m, 2 H), 1.98-2.04 (m, 1 H), 1.72-1.89 (m, 5 H), 1.56-1.65 (m, 1 H), 1.34-1.36 (m, 9 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 218.4, 217.8, 153.3, 152.8, 80.3, 79.5, 69.9, 69.7, 47.8, 47.7, 37.3, 36.2, 36.1, 35.7, 34.3, 33.5, 28.3, 28.2, 23.8, 22.7, 18.7, 18.3 ppm; **HRMS ESI** Calcd for $C_{13}H_{21}N_1O_3Na_1$ $[M+Na]^+$: 262.1414, Found: 262.1404, Error: 3.8 ppm

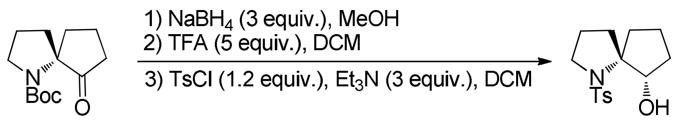
Catalyst 1 and **2:** Firstly, to the solution of compound **11** (1.700 g, 7.1 mmol) in MeOH (10 mL) was added $NaBH_4$ (810 mg, 21.3 mmol, 3 equiv.) at 0 °C. After 10 min later, 1 mL H_2O was added to quench the reaction, and the mixture was extracted with DCM (3 x 30 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo* to obtain crude residue.

Secondly, the crude residue was dissolved in DCM (10 mL), and TFA (2.7 mL, 35.5 mmol, 5 equiv.) was added at room temperature. About 3 h later, the system was concentrated in *vacuo* to remove most of TFA, and then 1 M NaOH was added to ensure that the PH of the mixture was 12-13. The mixture was extracted with DCM (3x30 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo* directly for the next step.

At last, the crude product was dissolved in DMF (10 mL), and imidazole (2.345 g, 35.5 mmol, 5 equiv.), TBSCl (1.284 g, 8.5 mmol, 1.2 equiv.) or TBDPSCl (2.2 mL, 8.5 mmol, 1.2 equiv.) were added sequentially at room temperature. About 30 min later, 10 mL H_2O was added to quench the reaction, and the system was extracted with DCM (3 x 30 mL). The combined organic phase was washed with saturated brine six times, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 1) to give catalyst **1** (1.450 g 80 % yield for three steps) as a colorless oil and catalyst **2** (2.235 g 83 % yield for three steps) as a colorless oil.

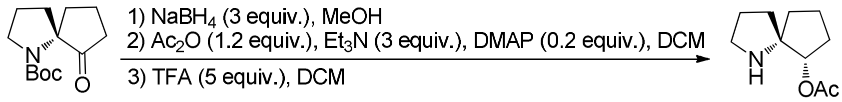
Catalyst **1**: **IR (neat)** cm^{-1} 3302, 2954, 2928, 1690, 1596, 1461, 1390, 1250, 1142, 836, 775; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 3.75 (t, *J* = 6.0 Hz, 1 H), 2.88-2.93 (m, 1 H), 2.79-2.86 (m, 1 H), 2.25 (s, 1 H), 1.43-1.89 (m, 10 H), 0.89 (s, 9 H), 0.12 (s, 6 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 77.1, 71.4, 45.9, 36.0, 35.0, 32.6, 25.9, 25.8, 19.5, 18.0, -4.4, -5.0 ppm; **HRMS ESI** Calcd for $C_{14}H_{30}N_1O_1Si_1$ $[M+H]^+$: 256.2091, Found: 256.2079, Error: 4.7 ppm. $[a]_D^{27}$ 12 (c 0.4, $CHCl_3$).

Catalyst **2**: **IR** (neat) cm^{-1} 3361, 2957, 2857, 1656, 1589, 1470, 1427, 1112, 739, 704, 507; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.67 (t, *J* = 7.2 Hz, 4 H),7.35-7.45 (m, 6 H), 3.85 (t, *J* = 5.6 Hz, 1 H), 2.80-2.84 (m, 2 H), 1.55-1.89 (m, 10 H), 1.34-1.47 (m, 4 H), 1.08 (s, 9 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 135.9, 134.3, 133.8, 129.7, 19.6, 127.6, 127.5, 78.3, 71.8, 45.8, 36.1, 34.8, 32.3, 27.1, 25.9, 19.4, 19.3 ppm; **HRMS ESI** Calcd for $C_{24}H_{34}$ $N_1O_1Si_1$ $[M+H]^+$: 380.2404, Found: 380.2387, Error: 4.5 ppm. $[a]_D^{27}$ -2 (c 0.6, $CHCl_3$).



11 **12**

Compound 12: After the reduction with $NaBH_4$ and removal of Boc group with TFA using the same procedure as the catalyst **1-2**, the crude product was taken to the next step directly. To the crude product (135 mg obtained from 1 mmol of (-)-**11**) in DCM (2 mL) were added Et_3N (400 uL, 2.9 mmol, 3 equiv.) and TsCl (218 mg, 1.2 mmol, 1.2 equiv.) at 0 ^oC. About 5 min later, 1 mL H_2O was added to quench the reaction, and the system was extracted with DCM (3 x 10 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 5) to give compound **12** (266 mg, 90 % for 3 steps). m.p. 125-127 ^oC, **IR** (neat) cm^{-1} 3500, 2958, 2925, 1598, 1451, 1332, 1153, 1091, 667, 592; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2 H),7.30 (d, *J* = 8.0 Hz, 2 H), 3.66-3.69 (m, 1 H), 3.58-3.65 (m, 1 H), 3.44-3.51 (m, 1 H), 2.63-2.71 (m, 1 H), 2.42 (s, 3 H), 1.71-1.96 (m, 6 H), 1.53-1.61 (m, 1 H), 1.29-1.43 (m, 2 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 143.2, 137.7, 129.5, 127.1, 77.4, 76.2, 50.6, 40.0, 32.4, 32.3, 22.1, 21.4, 20.4 ppm; **HRMS ESI** Calcd for $C_{15}H_{21}$ $N_1O_3S_1$ $[M+H]^+$: 296.1315, Found: 296.1312, Error: 4.4 ppm. $[a]_D^{27}$ -45 (c 0.6, $CHCl_3$).



11

(-)-catalyst **3**

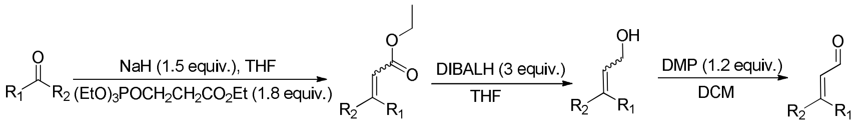
Catalyst 3: To the solution of compound **11** (478 mg, 2 mmol) in MeOH (3 mL) was added $NaBH_4$ (228 mg, 6 mmol, 3 equiv.) at 0 ^oC. About 10 min later, 0.2 mL H_2O was added to quench the reaction, and the mixture was extracted with DCM (3 x 10 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo* to obtain crude residue.

Next, the crude residue was dissolved in DCM (2 mL), and Et_3N (840 uL, 6 mmol, 3 equiv.), DMAP (49 mg, 0.4 mmol, 0.2 equiv.), Ac_2O (230 uL, 2.4 mmol, 1.2 equiv.) were added to the system sequentially at 0 ^oC. After the starting material was disappeared via TLC detection, TFA (740 uL, 10 mmol, 5 equiv.) was added. About 3 h later, the system was concentrated in *vacuo* to remove most of TFA, and then 1 M NaOH was added to ensure that the PH of the mixture was 12-13, and the mixture was extracted with DCM (3 x 30 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 1) to give catalyst **3** (311 g 85 % yield for three steps) as a colorless oil. **IR (neat)** cm^{-1} 3331, 2959, 1615, 1420, 1118; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 4.91 (d, *J* = 9.2 Hz, 1 H), 3.718 (dd, *J* = 4.8 Hz, 9.6 Hz, 1 H), 3.47-3.54 (m, 2 H), 2.65-2.71 (m, 1 H), 2.06 (s, 3 H), 1.79-1.96 (m, 6 H), 1.67-1.74 (m, 1 H), 1.35-1.47 (m, 2 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 172.4, 81.6, 74.1, 50.3, 41.1, 35.2, 34.1, 24.1, 23.0, 21.0 ppm; **HRMS ESI** Calcd for $C_{10}H_{18}N_1O_2$ $[M+H]^+$: 184.1332, Found: 184.1332, Error: 0.0 ppm. $[a]_D^{27}$ -59 (c 0.5, $CHCl_3$).

Section 2: Substrates preparation

All of the substrates in this article were prepared according to the literature or commercial available. **S1**, **S3, S8**, **S9** and **S12** were commercial available, **S2**, **S5**, **S10** and **S14** were known compounds according to the literature.[2] Synthesis of **S4**, **S6**, **S7**, **S11 and S13** was performed by use of Horner-Wadsworth-Emmons reaction, reduction and oxidation reaction procedure.

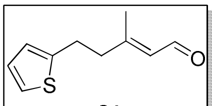
The general procedures are as follows:



Firstly, $(EtO)_3POCH_2CO_2Et$ (18 mmol, 1.8 equiv.) was added to the NaH (15 mmol, 1.5 equiv.) in THF (30 mL) at 0 °C. About 5 min later, the keto (10 mmol) was added to the system when the solution became clear. Then it was allowed to warm to 95 °C and stirred for 10 h. After it was cooled to room temperature, 10 mL H_2O was added to quench the reaction, the system was extracted with DCM (3 x 50 mL). Then the combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was used to the next step directly.

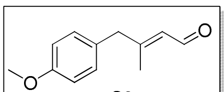
Next, to the conjugate olefinic ester in THF (30 mL) was added DIBALH (30 mmol, 3 equiv.) at 0 °C, and the reaction system was stirred for 30 min. Then 50 mL NH_4Cl saturated solution was added to quench the reaction, and the system was extracted with DCM (3 x 50 mL). The combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was used to the next step directly.

Last, to the crude allyl alcohol compound in DCM (30 mL) was added DMP (12 mmol, 1.2 equiv.) at 0 °C, and the reaction system was stirred for 30 min. Then 10 mL $NaHCO_3$ saturated solution was added to quench the reaction. About 5 min later, 10 mL NaS_2O_3 saturated solution was added to the system, and the mixture was extracted with DCM (3 x 50 mL). Then the combined organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 100 to 1 : 50) to give substrates.



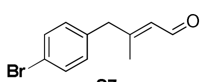
S4

(*E*)-Compound S4 was obtained in 52 % yield as a light yellow oil. **IR** (neat) cm^{-1} 2924, 2372, 1736, 1673, 1120; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 10.01 (d, *J* = 8.0 Hz, 1 H),7.24 (dd, *J* = 6.4 Hz, 1.2 Hz, 1 H), 6.88-6.94 (m, 2 H), 5.82 (dd, *J* = 8.0 Hz, 1.2 Hz, 1 H), 3.09 (t, *J* = 8.0 Hz, 2 H), 2.62 (t, *J* = 8.0 Hz, 2 H), 2.24 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 191.4, 162.6, 144.4, 128.6, 127.7, 125.7, 124.3, 42.9, 28.2, 17.5 ppm; **HRMS ESI** Clad for $C_{10}H_{13}$ O_1S_1 $[M+H]^+$: 181.0682, Found: 181.0683, Error: 0.6 ppm



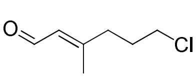
S6

(*E*)-Compound S6 was obtained in 64 % yield as a colourless oil. **IR** (neat) cm^{-1} 2932, 1671, 1512, 1179, 1035; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 9.98 (d, *J* = 8.0 Hz, 1 H),7.05-7.08 (m, 2 H), 6.83-6.87 (m, 2 H), 5.87 (dt, *J* = 1.2 Hz, 8.0 Hz, 1 H), 3.79 (s, 3 H), 3.43 (s, 2 H), 2.12 (d, *J* = 0.8 Hz, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 191.3, 162.8, 158.6, 130.1, 128.9, 128.1, 114.1, 55.2, 46.0, 17.2 ppm; **HRMS ESI** Calcd for $C_{12}H_{15}O_2$ $[M+H]^+$: 191.1067, Found: 191.1067, Error: 0 ppm



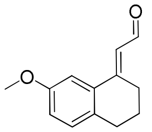
S7

(***E***)-**Compound S7** was obtained in 56 % yield as a colourless oil. **IR** (neat) cm^{-1} 2924, 1689, 1438, 1404, 1248, 1071, 1011; ^{1}**H NMR** (400 MH_Z, $CDCl_3$) δ 9.99 (d, *J* = 8.0 Hz, 1 H),7.43-7.46 (m, 2 H), 7.04 (d, *J* = 8.0 Hz, 2 H), 5.86 (dd, *J* = 1.2 Hz, 8.0 Hz, 1 H), 3.45 (s, 2 H), 2.11 (d, *J* = 0.8 Hz, 3 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 191.1, 161.2, 135.9, 131.8, 130.8, 128.6, 129.1, 46.2, 17.3 ppm; **HRMS ESI** Calcd for $C_{11}H_{12}Br_1O_1$ $[M+H]^+$: 239.0066, Found: 239.0066, Error: 0 ppm



S11

(***E***)-**Compound S11** was obtained in 48 % yield as a colourless oil. **IR** (neat) cm^{-1} 2926, 1737, 1596, 1450, 1243, 1148; ^{1}**H NMR** (400 MH_Z, $CDCl_3$) δ 10.06 (d, *J* = 8.0 Hz, 1 H),5.86 (dd, *J* = 8.0 Hz, 1.2 Hz, 1 H), 3.67-3.71 (m, 2 H), 2.43-2.47 (m, 2 H), 2.27 (s, 3 H), 2.01-2.11 (m, 4 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 191.5, 162.7, 128.5, 45.1, 38.1, 30.9, 17.5 ppm; **HRMS ESI** Calcd for C_7H_{12} Cl_1O_1 $[M+H]^+$: 147.0571, Found: 147.0570, Error: 0.7 ppm



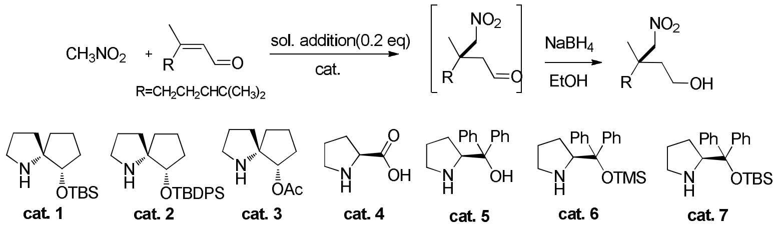
S13

(***E***)-**Compound S13** was obtained in 61 % yield as a light yellow solid. **IR** (neat) cm^{-1} 2934, 2838, 1731, 1658, 1495, 1429, 1278, 1242, 1144, 1036; ^{1}**H NMR** (400 MH_Z, $CDCl_3$) δ 10.20 (d, *J* = 8.0 Hz, 1 H), 7.26 (s, 1 H), 7.10 (d, *J* = 8.0 Hz, 1 H), 6.94 (dd, *J* = 8.0 Hz, 2.4 Hz, 1 H), 6.46 (d, *J* = 8.0 Hz, 1 H), 3.82 (s, 3 H), 3.09 (dt, *J* = 1.2 Hz, 6.4 Hz, 2 H), 2.78 (t, *J* = 6.4 Hz, 2 H), 1.64-1.92 (m, 2 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 191.5, 159.2, 157.3, 134.9, 133.4, 131.4, 123.3, 118.5, 109.8, 55.7, 27.4, 24.1 ppm; **HRMS ESI** Calcd for $C_{13}H_{15}O_2$ $[M+H]^+$: 203.1067, Found: 203.1069, Error: 1.0 ppm

Section 3: Reaction Condition Optimization and Substrate Scope

General procedure: To the substrate (0.125 mmol), catalyst (0.2 equiv.) in solvent (0.5 mL) were added additive (0.2 equiv.) and CH_3NO_2 (20 equiv.) and stirred until the substrate was disappeared. Then 0.5 ml EtOH and $NaBH_4$ (3 equiv.) were added at 0 ^oC sequentially. About 5 min later, 10 drops of H_2O was added to quench the reaction. The system was dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified through column chromatography (EtOAc : petroleum ether = 1 : 20 to 1 : 5) to give products.

Table 1: Michael addition of **S1** with CH_3NO_2[a]



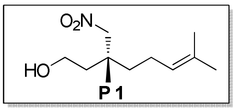
entry	Sol.	cat.	cat.amount	T(°C)	T(h)/con(%)	additive	Y(%)[b]	Ee(%)[c]
1	Tol.	**1**	0.2	RT	1d/100	BA	87	75
2	Tol.	**2**	0.2	RT	1d/100	BA	85	86
3	Tol.	**3**	0.2	RT	1d/100	BA	75	55
4	Tol.	**4**	0.2	RT	2d/24	BA	<5	1
5	Tol.	**5**	0.2	RT	2d/50	BA	<5	14
6	Tol.	**6**	0.2	RT	2d/75	BA	<5	70
7	Tol.	**7**	0.2	RT	2d/42	BA	8	60
8[d]	Tol.	**2**	0.2	RT	2d/50	---	40	85
9	Tol.	**2**	0.2	RT	1d/80	NaOAc	33	84
10	Tol.	**2**	0.2	RT	1d/50	Na_2CO_3	16	82
11	Tol.	**2**	0.2	RT	3d/---	PTS	---	---
12	Tol.	**2**	0.2	-5	2.5d/100	BA	85	90
13	Tol.	**2**	0.2	-10	7d/20	BA	16	89
14	Tol.	**2**	0.1	-5	7d/95	BA	65	88
15	Tol.	**2**	0.05	-5	7d/30	BA	19	88
16	Tol.	**2**	0.2	-5	2.5d/100	3-NO_2-BA	67	82
17	Tol.	**2**	0.2	-5	2.5d/100	4-NO_2-BA	64	84
18	Tol.	**2**	0.2	-5	2.5d/100	4-CF_3-BA	85	83
19	Tol.	**2**	0.2	-5	2.5d/90	2-F-BA	83	84
20	Tol.	**2**	0.2	-5	2.5d/100	2-MeO-BA	82	82
21	Tol.	**2**	0.2	-5	2.5d/100	4-MeO-BA	80	82
22	Tol.	**2**	0.2	-5	2.5d/100	HFIP	75	73
23	Tol.	**2**	0.2	-5	2.5d/80	H_2O	51	86
24	Tol.	**2**	0.2	-5	2.5d/100	Catechol	57	84
25	Tol.	**2**	0.2	-5	2.5d/90	hloroglucin	70	84

26	MeCN	**2**	0.2	-5	2.5d/75	BA	68	84
27	DCM	**2**	0.2	-5	2.5d/100	BA	86	86
28	MeOH	**2**	0.2	-5	2.5d/80	BA	43	87
29	Et_2O	**2**	0.2	-5	2.5d/80	BA	34	89

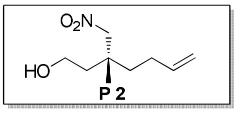
a): Unless other noted, all reactions were performed in the below condition: To the substrate (0.125 mmol), catalyst (0.2 equiv.) in solvent (0.5 mL) were added additive (0.2 equiv.) and CH_3NO_2 (20 equiv.). Then 0.5 mL EtOH, and 0.375 mmol $NaBH_4$ were added to the system at 0 ^oC after the appointed time and stirred for 5 min. Next 10 drops of H_2O was added to quench the reaction. And the system was dried with Na_2SO_4, concentrated in vacuo and purified by column chromatography. b): Isolated yield. c): The enantiomeric excess was determined by chiral HPLC analysis. d): without BA

Products P1-P14:

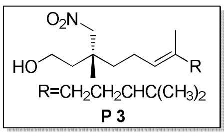
The products were obtained according to the optimized condition (entry 12, Table 1), the results are as bellows:



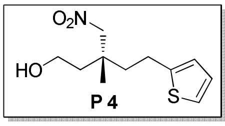
Compound P1 was obtained in 85% yield from (*E*)-**S1,** 82% yield from (*Z*)-**S1,** 83% yield from (*E and Z*)-**S1** as a colorless oil. **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 5.07 (t, *J* = 7.2 Hz, 1 H), 4.42 (dd, *J* = 10.8 Hz, 17.6 Hz, 2 H), 3.80 (dd, *J* = 7.6 Hz, 11.6 Hz, 2 H), 2.01 (dd, *J* = 6.4 Hz, 16.4 Hz, 2 H), 1.65-1.74 (m, 5 H), 1.61 (s, 3 H) 1.38-1.43 (m, 2 H), 1.10 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 132.3, 123.4, 83.7, 58.9, 39.3, 37.9, 37.3, 25.7, 23.1, 22.0, 17.6 ppm; $[a]_D^{27}$ 7 (c 0.5, $CHCl_3$). Enantiomeric excess is 90% determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 97/3, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 23.17 min; minor isomer: tr = 21.89 min.



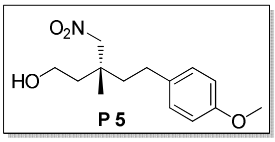
Compound P2 was obtained in 63% yield from (*E*)-**S2** as a colorless oil. **IR** (neat) cm^{-1} 3342, 2924, 2373, 1595, 1547, 1460, 1378, 1124; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 5.73-5.84 (m, 1 H), 4.96-5.08 (m, 2 H), 4.42 (dd, *J* = 10.8 Hz, 16.0Hz, 2 H), 3.79-3.81 (m, 2 H), 2.06-2.12 (m, 2 H), 1.65-1.74 (m, 2 H) 1.44-1.52 (m, 2 H), 1.11 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 137.8, 115.1, 83.7, 58.9, 39.3, 37.3, 37.1, 27.7, 23.1 ppm; **HRMS ESI** Calcd for $C_9H_{18}N_1O_3$ $[M+H]^+$: 188.1281, Found: 188.1283, Error: 1.1 ppm. $[a]_D^{27}$ 2 (c 0.5, $CHCl_3$). Enantiomeric excess is 86% determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 97/3, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 30.30 min; minor isomer: tr = 28.34 min.



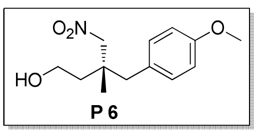
Compound P3 was obtained in 80% yield from (*E*)-**S3** as a colorless oil. **IR** (neat) cm^{-1} 3390, 2923, 1548, 1457, 1378, 1114; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 5.07 (t, *J* = 6.8 Hz, 2 H), 4.42 (dd, *J* = 10.8 Hz, 17.6 Hz, 2 H), 3.80 (t, *J* = 6.8 Hz, 2 H), 1.94-2.09 (m, 6 H), 1.67-1.72 (m, 5 H), 1.59-1.61 (m, 6 H) 1.38-1.43 (m, 2 H), 1.10 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 135.9, 131.5, 124.1, 123.2, 83.7, 58.9, 39.6, 39.3, 37.9, 37.3, 26.6, 25.7, 23.1, 21.9, 17.7, 16.0 ppm; **HRMS ESI** Calcd for $C_{16}H_{30}N_1O_3$ $[M+H]^+$: 284.2220, Found:284.2223, Error: 1.1 ppm. [a] $_D^{27}$ 5 (c 0.4, $CHCl_3$). Enantiomeric excess is 91% determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 97/3, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 17.22 min; minor isomer: tr = 16.58 min.



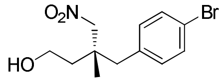
Compound P4 was obtained in 72% yield from (*E*)-**S4** as a colorless oil. **IR** (neat) cm^{-1} 3374, 2923, 2370, 1545, 1461, 1377, 1262, 1034, 699; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.13 (dd, *J* = 0.8 Hz, 4.8 Hz, 1 H), 6.92 (dd, *J* = 3.6 Hz, 4.8 Hz, 1 H), 6.80-6.82 (m, 1 H), 4.47 (dd, *J* = 10.8 Hz, 14.8 Hz, 2 H), 3.83 (dd, *J* = 6.4 Hz, 11.2 Hz, 2 H), 2.87-2.92 (m, 2 H), 1.69-1.86 (m, 4 H), 1.45-1.49 (m, 1 H), 1.17 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 144.1, 126.9, 124.3, 123.2, 83.5, 58.8, 40.1, 39.2, 37.5, 24.1, 23.1 ppm; **HRMS ESI** Calcd for $C_{11}H_{17}N_1O_3Na_1$ $[M+Na]^+$: 266.0821, Found: 266.0821, Error: 0.0 ppm. [a] $_D^{27}$ 2 (c 0.4, $CHCl_3$). Enantiomeric excess is 87% determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 97/3, flow rate = 1.0 mL/min, 220 nm): major isomer: tr = 68.05 min; minor isomer: tr = 63.64 min.



Compound P5 was obtained in 85% yield from (*E*)-**S5** as a colorless oil. **IR** (neat) cm^{-1} 3390, 2923, 1611, 1546, 1511, 1461, 1377, 1244, 1033, 821, 736; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.10 (d, *J* = 9.2 Hz, 2 H), 6.83 (dd, *J* = 1.6 Hz, 5.6 Hz, 2 H), 4.47 (dd, *J* = 10.4 Hz, 14.0 Hz, 2 H), 3.83 (t, *J* = 6.4 Hz, 2 H), 3.78 (s, 3 H), 2.56-2.62 (m, 2 H), 1.62-1.81 (m, 4 H), 1.16 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 157.9, 133.6, 129.2, 113.9, 83.5, 58.8, 55.3, 40.5, 39.3, 37.4, 28.9, 23.1 ppm; **HRMS ESI** Calcd for $C_{14}H_{21}N_1O_4Na_1$ $[M+Na]^+$: 290.1363, Found: 290.1362, Error: 0.3 ppm. [a] $_D^{27}$ 4 (c 0.4 mg/mL, $CHCl_3$). Enantiomeric excess is 86 % determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 220 nm): major isomer: tr = 23.06 min; minor isomer: tr = 20.35 min.

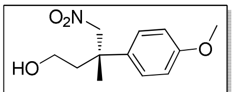


Compound P6 was obtained in 76% yield from (*E*)-**S6** as a colorless oil. **IR** (neat) cm^{-1} 3376, 2925, 2372, 1741, 1547, 1512, 1461, 1376, 1244, 1046; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.11 (d, *J* = 8.8 Hz, 2 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 4.37 (dd, *J* = 11.2 Hz, 34.3 Hz, 2 H), 3.86 (dt, *J* = 3.6 Hz, 6.4 Hz, 2 H), 3.80 (s, 3 H), 2.72 (dd, *J* = 13.6 Hz, 30.4 Hz, 2 H), 1.58-1.78 (m, 2 H), 1.05 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 158.5, 131.8, 128.2, 82.9, 59.0, 55.2, 43.3, 39.4, 38.3, 22.7 ppm; **HRMS ESI** Calcd for $C_{13}H_{19}N_1O_4Na_1$ $[M+H]^+$: 276.1206, Found: 276.1204, Error: 0.7 ppm. [a] $_D^{27}$ 6 (c 0.5, $CHCl_3$). Enantiomeric excess is 93 % determined by HPLC (Chiralpak AD, Hexane/Isopropanol 95/5, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 36.62 min; minor isomer: tr = 33.87 min.



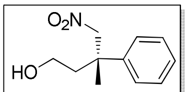
P 7

Compound P7 was obtained in 78% yield from (*E*)-**S7** as a colorless oil. **IR** (neat) cm^{-1} 3371, 2925, 1547, 1487, 1460, 1377, 1256, 1072, 1011; **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2 H), 7.10 (d, *J* = 8.4 Hz, 2 H), 4.37 (dd, *J* = 11.2 Hz, 27.6 Hz, 2 H), 3.83-3.87 (m, 2 H), 2.72 (dd, *J* = 13.6 Hz, 28.8 Hz, 2 H), 1.59-1.77 (m, 2 H), 1.05 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 135.2, 132.5, 131.4, 121.0, 82.6, 58.8, 43.6, 39.3, 38.2, 22.6 ppm; **HRMS ESI** Calcd for $C_{12}H_{16}Br_1N_1O_3Na_1$ $[M+Na]^+$: 324.0206/326.0185, Found:324.0203/326.0183, Error: 0.9 ppm. $[a]_D^{27}$ 3 (c 0.4, $CHCl_3$). Enantiomeric excess is 95 % determined by HPLC (Chiralpak AD, Hexane/Isopropanol 95/5, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 29.95 min; minor isomer: tr = 27.34 min.



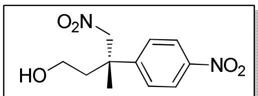
P 8

Compound P8 was obtained in 75% yield from (*E*)-**S8** as a colorless oil. **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.26 (d, *J* = 8.8 Hz, 2 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 4.64 (dd, *J* = 10.8 Hz, 14.8 Hz, 2 H), 3.80 (s, 3 H), 3.48-3.80 (m, 2 H), 2.15-2.22 (m, 1 H), 1.97-2.05 (m, 1 H), 1.58 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 158.6, 133.7, 127.1, 114.2, 86.2, 59.1, 55.2, 42.1, 40.9, 23.2 ppm. $[a]_D^{27}$ -32 (c 0.4, $CHCl_3$). Enantiomeric excess is 95 % determined by HPLC (Chiralpak OD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 25.46 min; minor isomer: tr = 21.73 min.



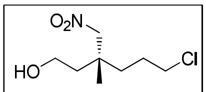
P 9

Compound P9 was obtained in 87% yield from (*E*)-**S9** as a colorless oil. **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.32-7.37 (m, 4 H), 7.26-7.31 (m, 1 H), 4.69 (dd, *J* = 11.2 Hz, 15.2 Hz, 2 H), 3.47-3.66 (m, 2 H), 2.17-2.25 (m, 1 H), 2.00-2.08 (m, 1 H), 1.60 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 141.9, 128.8, 127.3, 125.9, 85.9, 59.1, 42.1, 41.4, 23.0 ppm. $[a]_D^{27}$ -11 (c 0.5, $CHCl_3$). Enantiomeric excess is 96 % determined by HPLC (Chiralpak IA-3, Hexane/Isopropanol 95/5, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 31.82 min; minor isomer: tr = 30.63 min.



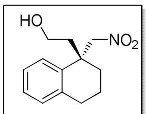
P 10

Compound P10 was obtained in 85% yield from (*E*)-**S10** as a colorless oil. **^{1}H NMR** (400 MH_Z, $CDCl_3$) δ 7.23 (d, *J* = 8.8 Hz, 2 H), 7.54 (d, *J* = 8.8 Hz, 2 H), 4.80 (dd, *J* = 12.0 Hz, 46.0 Hz, 2 H), 3.50-3.72 (m, 2 H), 2.03-2.19 (m, 2 H), 1.67 (s, 3 H) ppm; **^{13}C NMR** (100 MH_Z, $CDCl_3$) δ 149.9, 147.0, 127.1, 123.9, 85.0, 58.7, 42.3, 42.0, 23.1 ppm. $[a]_D^{27}$ -22 (c 0.1, $CHCl_3$). Enantiomeric excess is 98 % determined by HPLC (Chiralpak OD-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 220 nm): major isomer: tr = 54.47 min; minor isomer: tr = 52.39 min. The Specific rotation and the retention time was in complete agreement with the reference.[3]



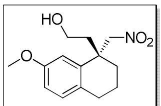
P 11

Compound P11 was obtained in 73% yield from (*E*)-**S11** as a colorless oil. **IR** (neat) cm^{-1} 3350, 2922, 2373, 1589, 1546, 1461, 1378, 1255; ^{1}**H NMR** (400 MH_Z, $CDCl_3$) δ 4.42 (m, 2 H), 3.81 (t, *J* = 6.4 Hz, 2 H), 3.54 (t, *J* = 6.4 Hz, 2 H), 1.79-1.87 (m, 2 H), 1.64-1.74 (m, 2 H) 1.51-1.60 (m, 2 H), 1.11 (s, 3 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 83.6, 58.8, 45.0, 39.2, 37.1, 35.2, 26.7, 23.1 ppm; **HRMS ESI** Calcd for C_8H_{16} $Cl_1N_1O_3Na_1$ $[M+Na]^+$: 232.0711, Found: 232.0711, Error: 0.0 ppm. [a] $_D$ ^{27} 3 (c 0.6, $CHCl_3$). Enantiomeric excess is 87 % determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 97/3, flow rate = 1.0 mL/min, 220 nm): major isomer: tr = 33.02 min; minor isomer: tr = 30.58 min.



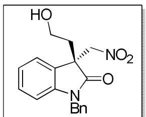
P12

Compound P12 was obtained in 78% yield from (*E*)-**S12** as a colorless oil. **IR** (neat) cm^{-1} 3335, 2923, 2373, 1592, 1546, 1460, 1377, 1251, 1121; ^{1}**H NMR** (400 MH_Z, $CDCl_3$) δ 7.11-7.29 (m, 4 H), 4.68 (dd, *J* = 10.8 Hz, 19.2 Hz, 2 H), 3.52-3.70 (m, 2 H), 2.78-2.82 (m, 2 H), 2.28-2.36 (m, 1 H) 1.99-2.12 (m, 2 H), 1.82-1.95 (m, 2 H) 1.23-1.26 (m, 1 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 137.9, 136.5, 130.1, 127.1, 126.7, 126.4, 84.7, 59.3, 41.1, 40.8, 31.0, 30.1, 19.0 ppm; **HRMS ESI** Calcd for $C_{13}H_{17}N_1O_3$ $[M+H]^+$: 258.1101, Found: 258.1100, Error: 0.4 ppm. [a] $_D$ ^{27} 5 (c 0.5, $CHCl_3$). Enantiomeric excess is 97 % determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 97/3, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 34.01 min; minor isomer: tr = 41.92 min.



P13

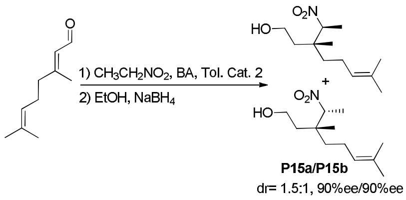
Compound P13 was obtained in 85% yield from (*E*)-**S13** as a light yellow solid. **IR** (neat) cm^{-1} 3349, 2923, 2372, 1591, 1259, 1120; ^{1}**H NMR** (400 MH_Z, $CDCl_3$) δ 7.02-7.05 (d, *J* = 8.4 Hz, 1 H), 6.73-6.80 (m, 2 H), 4.51 (dd, *J* = 10.8 Hz, 22.4 Hz, 2 H), 3.78 (s, 3 H), 3.54-3.70 (m, 2 H), 2.70-2.74 (m, 2 H), 2.25-2.32 (m, 1 H) 1.91-2.09 (m, 2 H), 1.79-1.90 (m, 3 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 157.9, 137.5, 130.9, 129.9, 112.8, 112.3, 84.7, 59.3, 55.3, 41.1, 40.1, 30.9, 29.2, 19.1 ppm; **HRMS ESI** Calcd for $C_{14}H_{20}$ N_1O_4 $[M+H]^+$: 266.1387, Found: 266.1389, Error: 2.6 ppm. [a] $_D$ ^{27} 12 (c 0.5, $CHCl_3$). Enantiomeric excess is 95 % determined by HPLC (Chiralpak ID-3, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 220 nm): major isomer: tr = 22.61 min; minor isomer: tr =29.96 min.



P14

Compound P14 was obtained in 85% yield from (*E/Z=3:1* to *4:1*)-**S14** as a colorless oil. **IR** (neat) cm^{-1} 3409, 2961, 2924, 1743, 1161, 1554, 1465, 1374, 1260, 1100, 1044, 800, 698; ^{1}**H NMR** (400 MHZ, $CDCl_3$) δ 7.19-7.32 (m, 7 H), 7.03-7.07 (m, 1 H), 6.75-6.78 (m, 1 H), 4.97-5.10 (m, 4 H), 3.61 (t, *J* = 5.6 Hz, 2 H), 2.03-2.19 (m, 2 H) ppm; ^{13}**C NMR** (100 MH_Z, $CDCl_3$) δ 177.2, 143.2, 135.4, 129.4, 128.9, 127.8, 127.4, 127.2, 123.0, 110.1, 78.7, 58.3, 50.0, 44.5, 38.1 ppm; **HRMS ESI** Calcd for $C_{18}H_{18}N_2O_4Na_1$ [M+Na]$^+$: 349.1159, Found: 349.1145, Error: 4.0 ppm. [a] $_D$ ^{27} 22 (c 0.3, $CHCl_3$). Enantiomeric excess is 83 % determined by HPLC (Chiralpak AD, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 28.05 min; minor isomer: tr = 31.17 min. The Specific rotation and the retention time was in complete agreement with the reference.[3]

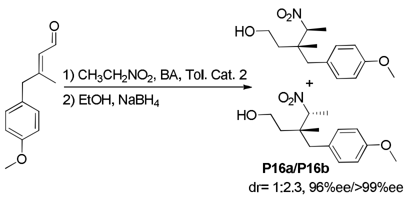
Michael addition of **S1** and **S6** with nitroethane



Compounds P15a and **P15b** were obtained separately as oils (dr = 1.5:1) in 70% total yield (25 mg, 0.125 mmol of **S1**).

Data for **P15a**: IR (neat) cm^{-1} 3373, 2925, 1592, 1547, 1455, 1385, 1041; **^{1}H NMR** (400 MH$_Z$, $CDCl_3$) δ 5.05 (t, *J* = 7.2 Hz, 1 H), 4.20 (dd, *J* = 7.2 Hz, 13.6 Hz, 1 H), 3.68-3.82 (m, 2 H), 1.83-2.07 (m, 2 H), 1.47-1.80 (m, 11 H), 1.36-1.38 (m, 2 H) 1.01 (s, 3H) ppm; **^{13}C NMR** (100 MH$_Z$, $CDCl_3$) δ 132.3, 123.5, 89.6, 58.9, 38.9, 38.2, 36.0, 25.7, 22.0, 20.6, 17.6, 13.8 ppm; **HRMS ESI** Calcd for $C_{12}H_{23}N_1O_3Na_1$[M+Na]$^+$: 252.1570, Found: 252.1573, Error: 1.2 ppm. [a] $_D$ ^{27} 17 (c 0.4, $CHCl_3$). Enantiomeric excess is 90 % determined by HPLC (Chiralpak AD, Hexane/Isopropanol 99/1, flow rate = 1.0 mL/min, 220 nm): major isomer: tr = 53.41 min; minor isomer: tr = 59.77 min.

Data for **P15b**: IR (neat) cm^{-1} 3373, 2925, 1592, 1547, 1455, 1385, 1041; **^{1}H NMR** (400 MH$_Z$, $CDCl_3$) δ 5.04 (t, *J* = 7.2 Hz, 1 H), 4.26 (dd, *J* = 6.4 Hz, 13.6 Hz, 1 H), 3.69-3.82 (m, 2 H), 1.84-2.07 (m, 2 H), 1.40-1.68 (m, 9 H), 1.33-1.40 (m, 4 H) 1.31 (s, 3H) ppm; **^{13}C NMR** (100 MH$_Z$, $CDCl_3$) δ 132.1, 123.5, 89.5, 58.8, 38.9, 37.8, 36.3, 25.7, 22.1, 20.7, 17.6, 14.0 ppm; ppm; **HRMS ESI** Calcd for $C_{12}H_{23}N_1O_3Na_1$[M+Na]$^+$: 252.1570, Found: 252.1569, Error: 0.4 ppm. [a] $_D$ ^{27} -13 (0.3 mg/mL, $CHCl_3$). Enantiomeric excess is 90 % determined by HPLC (Chiralpak OD-H, Hexane/Isopropanol 95/5, flow rate = 1.0 mL/min, 230 nm): major isomer: tr = 12.65 min; minor isomer: tr = 11.69 min.



Compounds P16a and **P16b** were obtained inseparablely (dr = 1:2.3) as oils in 75% total yield (25 mg, 0.125 mmol of **S6**).

Data for **P16a** and **P16b**: **IR** (neat) cm^{-1} 3399, 2929, 2370, 1610, 1546, 1512, 1250, 1180, 1038; **^{1}H NMR** (400 MH$_Z$, $CDCl_3$) δ 6.82-7.11 (m, 4 H), 4.70-4.76 (m, 1 H), 3.73-3.85 (m, 5 H), 2.57-2.75 (m, 2 H), 1.53-1.79 (m, 5 H), 0.97-0.99 (m, 3 H) 1.31 (s, 3H) ppm; **^{13}C NMR** (100 MH$_Z$, $CDCl_3$) δ 158.4, 131.8, 128.4, 113.6, 133.6, 89.3, 89.6, 58.8, 58.7, 55.2, 41.2, 40.7, 40.0, 38.1, 37.4, 21.0, 14.2 ppm; **HRMS ESI** Calcd for $C_{14}H_{22}N_1O_4$ [M+H]$^+$: 268.1543, Found: 268.1532, Error: 4.1 ppm. [a] $_D$ ^{27} 3 (c 0.6, $CHCl_3$). Enantiomeric excess is >99 % for **P16a** and 94 % for **P16b** determined by HPLC (Chiralpak OD-H, Hexane/Isopropanol 99/1, flow rate = 1.0 mL/min, 230 nm): **P16a:** major isomer: tr = 176.53 min; **P16b:** major isomer: tr = 150.05 min, minor isomer: tr = 157.28 min.

Section 5: ***In situ*** **NMR experiments**

To inspect the detail process of the asymmetric Michael addition, ***in situ*** NMR experiments were performed with **S8** and nitromethane under the catalysis of **2** in D-toluene on 600MHz spectrometer. According to the results, a possible process of this reaction was deduced to involve an initial dienamine formation, then fast Michael addition via imine intermediate, and final hydrolysis to release catalyst **2** and generate product **P8.** As for Jørgensen-Hayashi catalyst, only a mixture was observed in the corresponding experimentals.

1) Experiment 1 with **S8** and **2** in D-tuolene without BA and nitromethane

S8 (9.6 mg, 0.055 mmol) and catalyst **2** (21 mg, 0.055 mmol) were dissolved in 0.5 mL D-toluene in a NMR tube, and the system was shaken uninterruptedly. NMR monitoring experiments were taken sequentially. The selected results were recorded after 5 min, 30 min and 16 h from mix as follows (Figure 1):

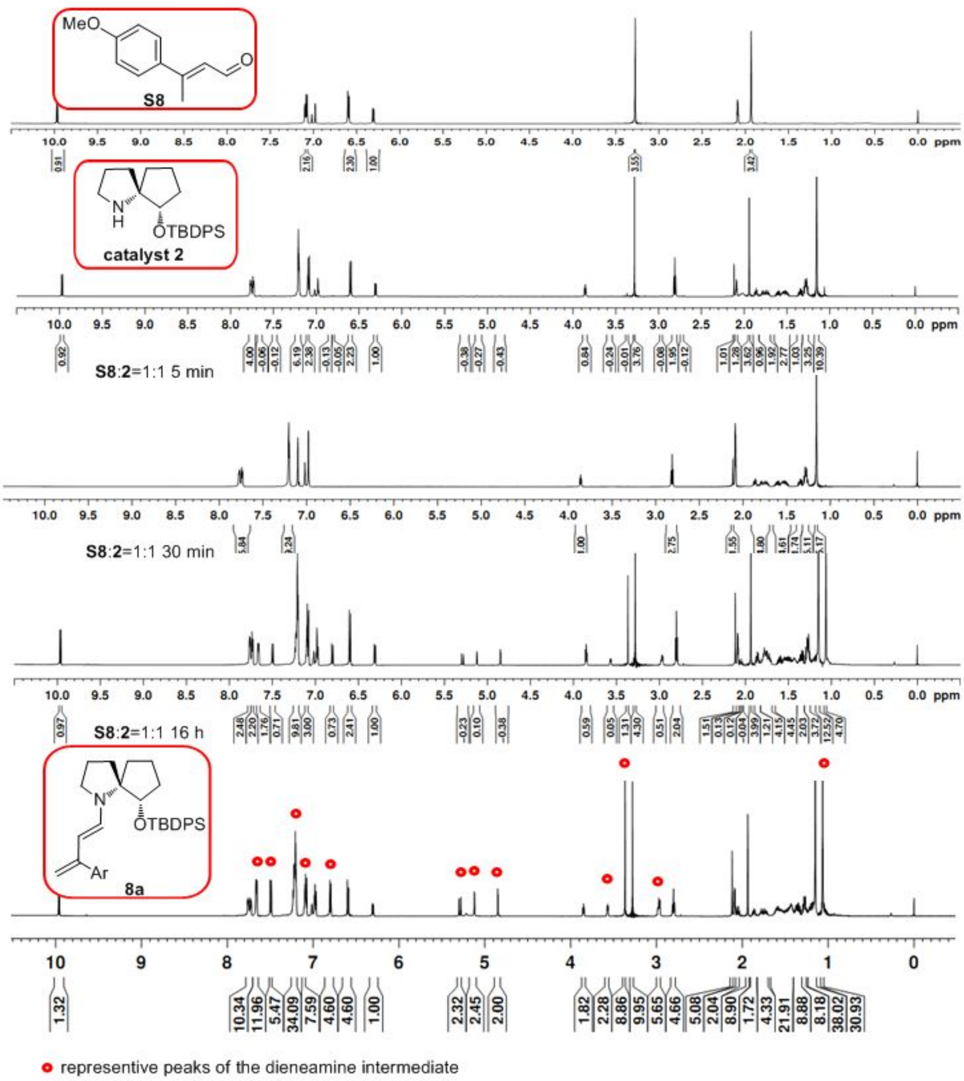


Figure 1: The Formation of The Dieneamine Intermidate with **S8** and **2.**

2) Experiment 2 inspecting the whole process of the Michael addition.

S8 (9.6 mg, 0.055 mmol) and catalyst **2** (21 mg, 0.055 mmol) were dissolved in 0.5 mL D-toluene in a NMR tube, About 5 min later, BA and CH_3NO_2 were added to the tube successively. And the system was shaked uninterruptedly, NMR monitoring experiments were taken sequentially. The selected results were recorded after 5 min, 30 min and 16 h from mix as follows (Figure 2). At last， 0.5 mL EtOH, and 3 equiv. $NaBH_4$ were added to the system. And **P8** was isolated in 70% yield and 92% ee.

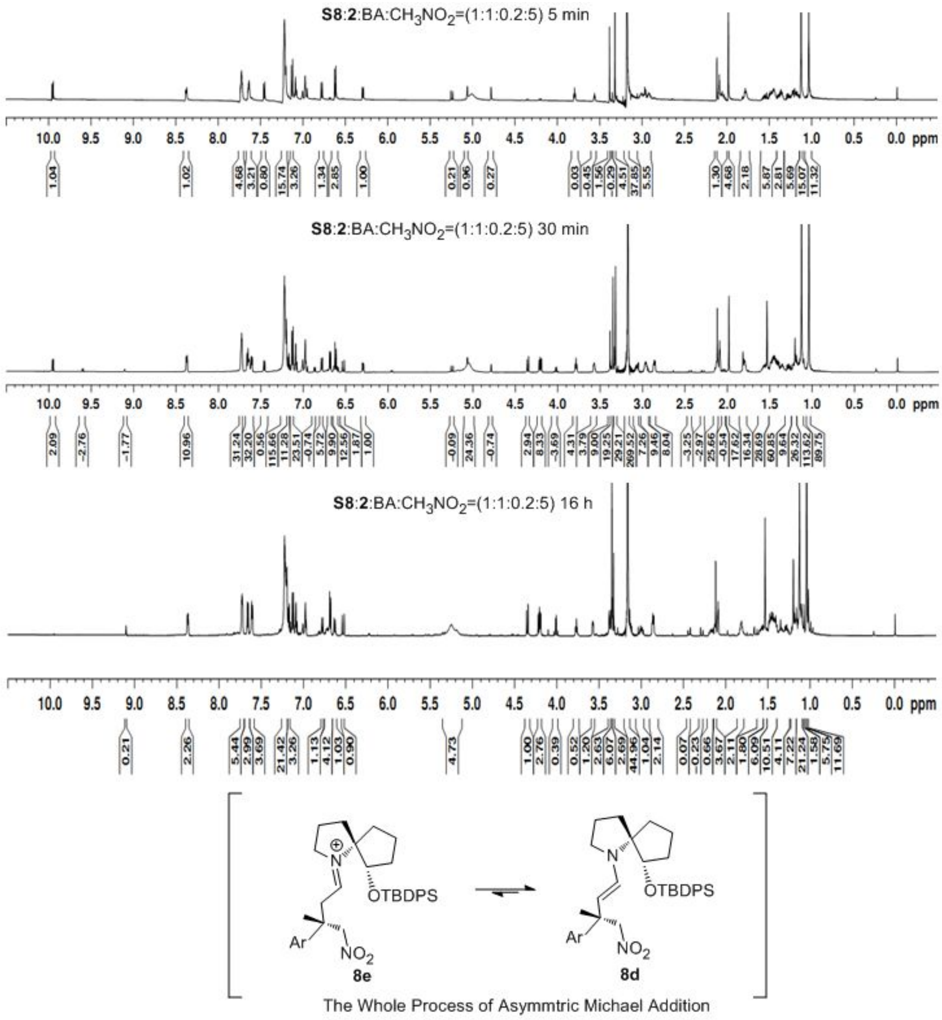


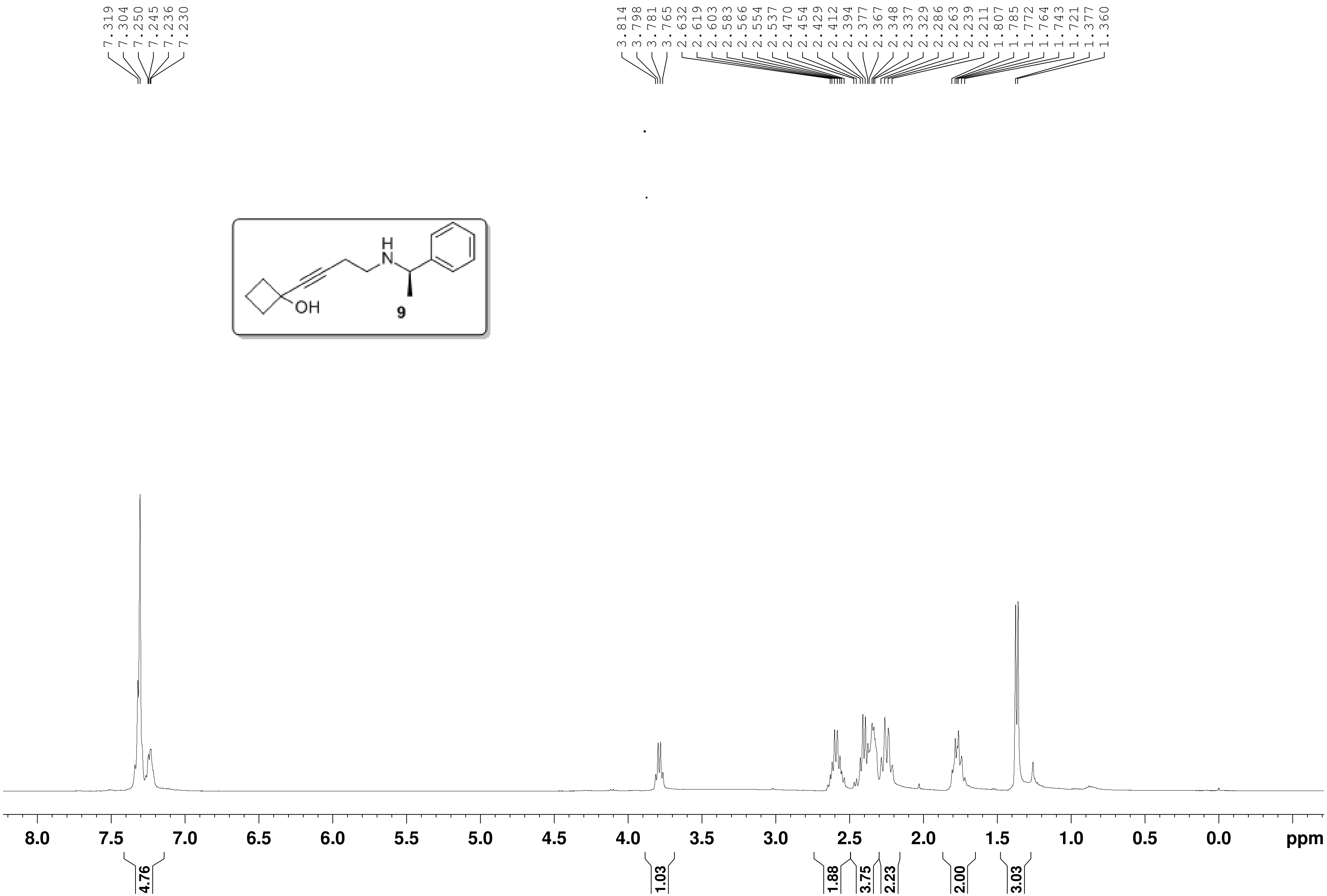
Figure 2: the whole process of the asymmetric Michael reaction with **S8,** 2, BA and nitromethane

References:

1 Q. -W. Zhang, K. Xiang, Y. -Q. Tu, S. -Y. Zhang, X. -M. Zhang, Y. -M. Zhao and T. -C. Zhang, *Chem. Asian. J.*, 2013, **7**, 8.

2 (a) G. A. Molander and C. D. P. Losada, *J. Org. Chem.*, 1997, **62**, 2935; (b) J. Takaya, K. Sasano and N. Iwasawa, *Org. Lett.*, 2011, **13**, 1698; (c) K. Akagawa and K. Kudo, *Angew. Chem. Int. Ed.* 2012, **51**, 12786; (d) M. benohoud, S. Tuokko and P. M. Pihko, *Chem. Eur. J.* 2011, **17**, 8404; (e) R. Liu and J. Zhang, *Org. Lett.*, 2013, **15**, 2266.

3 (a) Y. Hayashi, Y. Kawamoto, M. Honda, D, Okamura, S. Umemiya, Y. Noguchi, T. Mukaiyama and I. Sato, *Chem. Eur. J.*, 2014, **20**, 12072；(b) T. Mukaiyama, K. Ogata, I. Sato and Y. Hayashi, *Chem. Eur. J.*, 2014, **20**, 13583.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2.583
2.566
2.554
2.537
2.470
2.454
2.429
2.412
2.394
2.377
2.367
2.348
2.337
2.329
2.286
2.263
2.239
2.211
1.807
1.785
1.772
1.764
1.743
1.721
1.377
1.360
H
N
OH
9
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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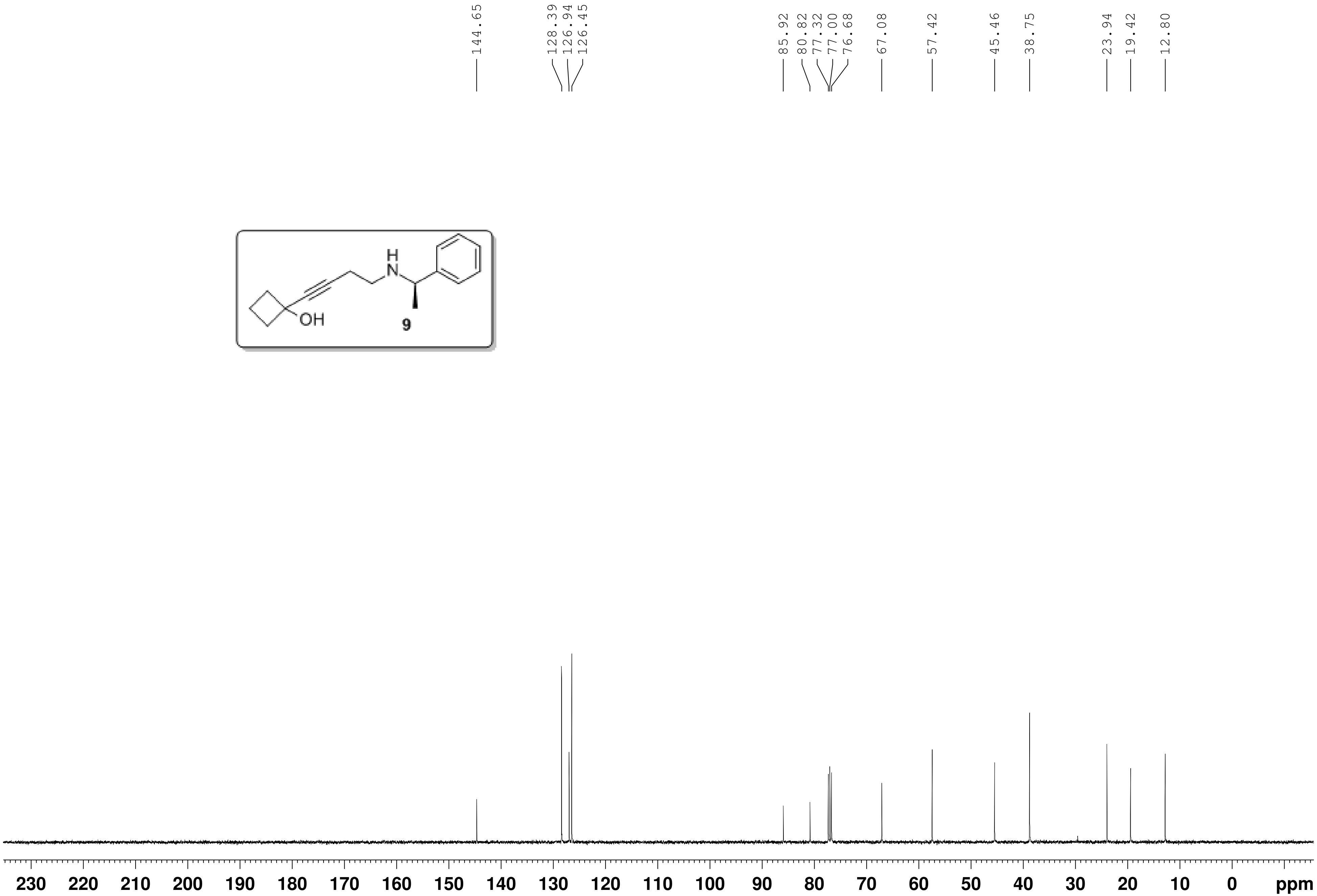
2.00
3.03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126.45
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80.82
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77.00
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67.08
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19.42
12.80
H
N
OH
9
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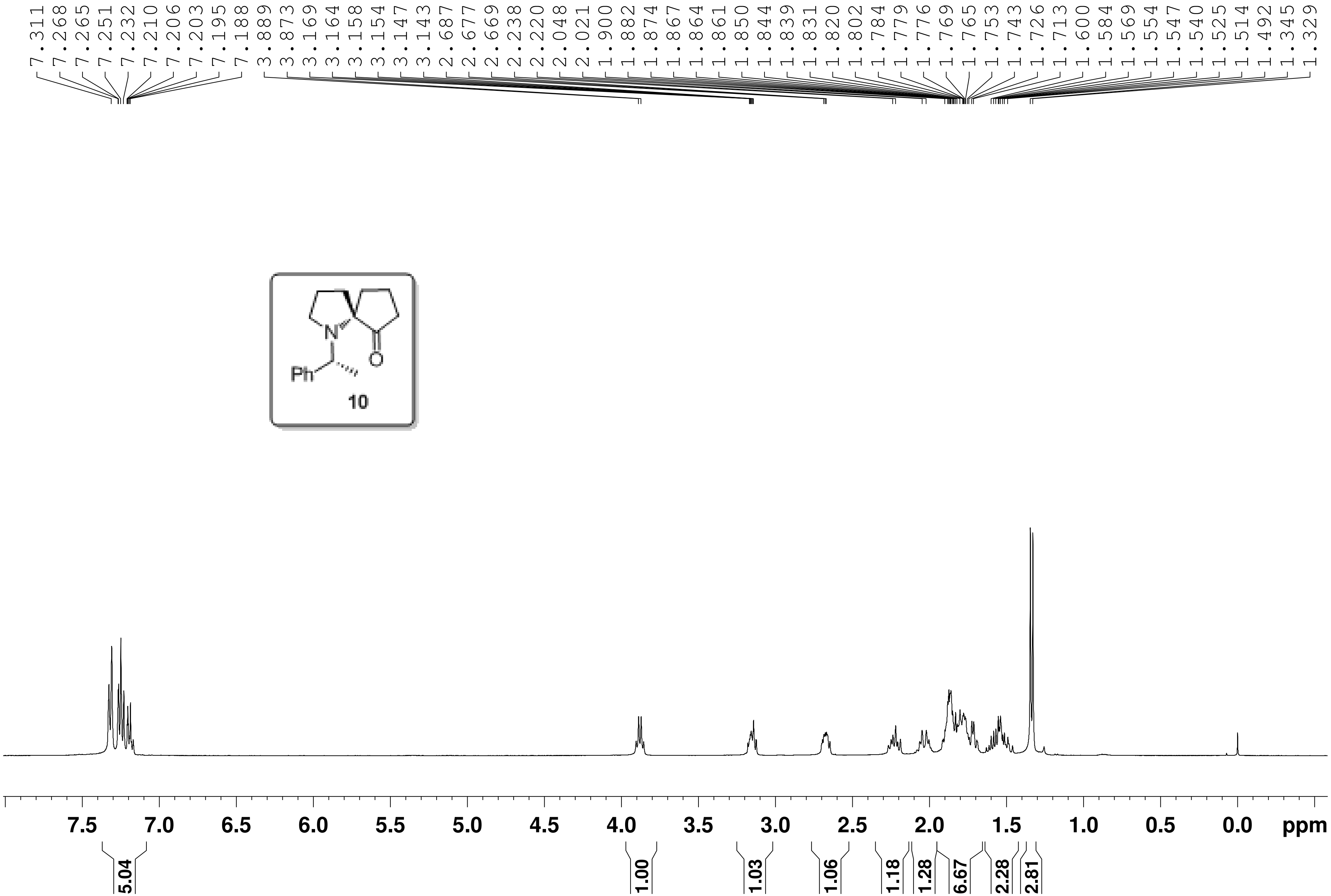
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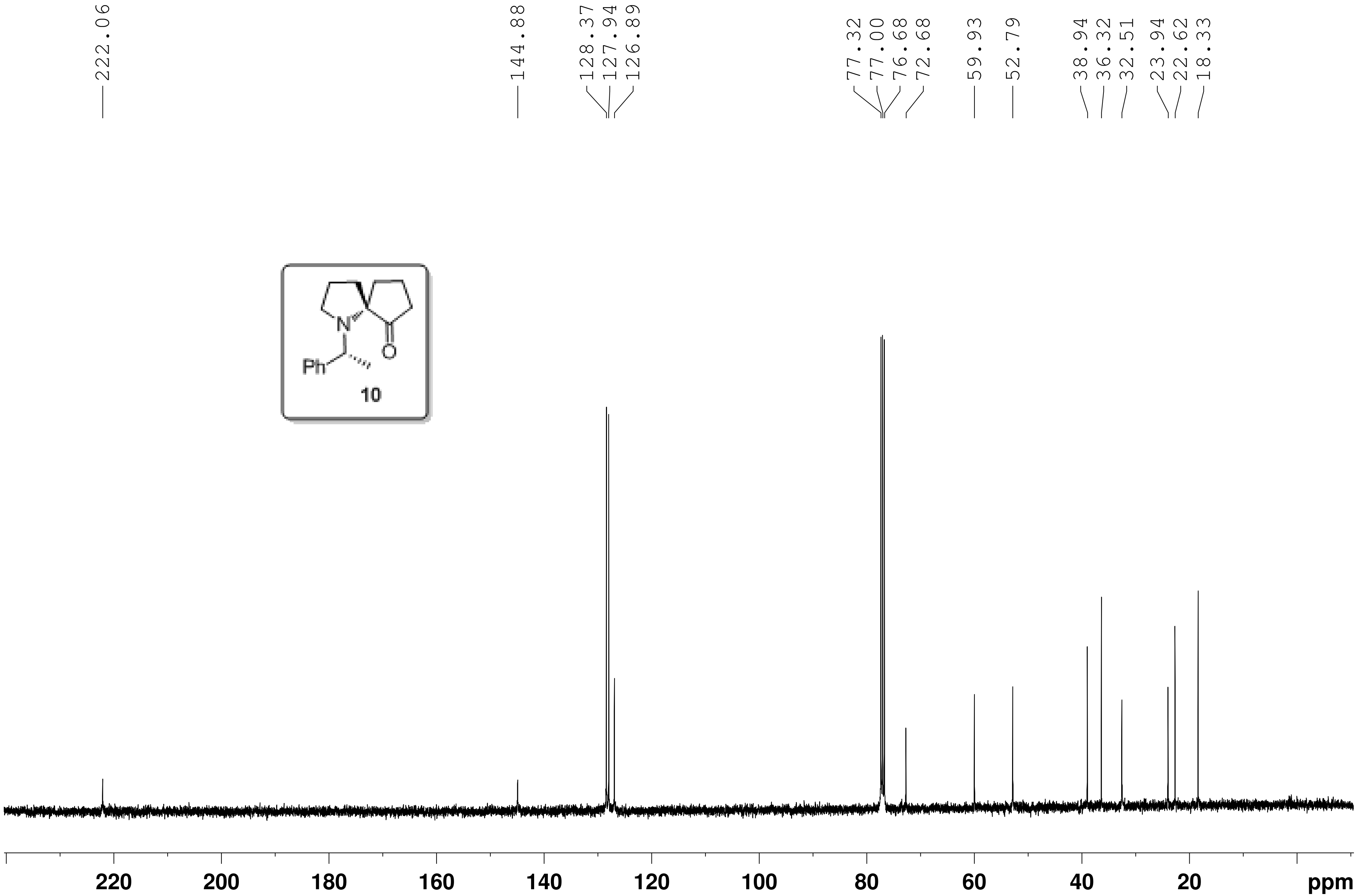
O
Ph

10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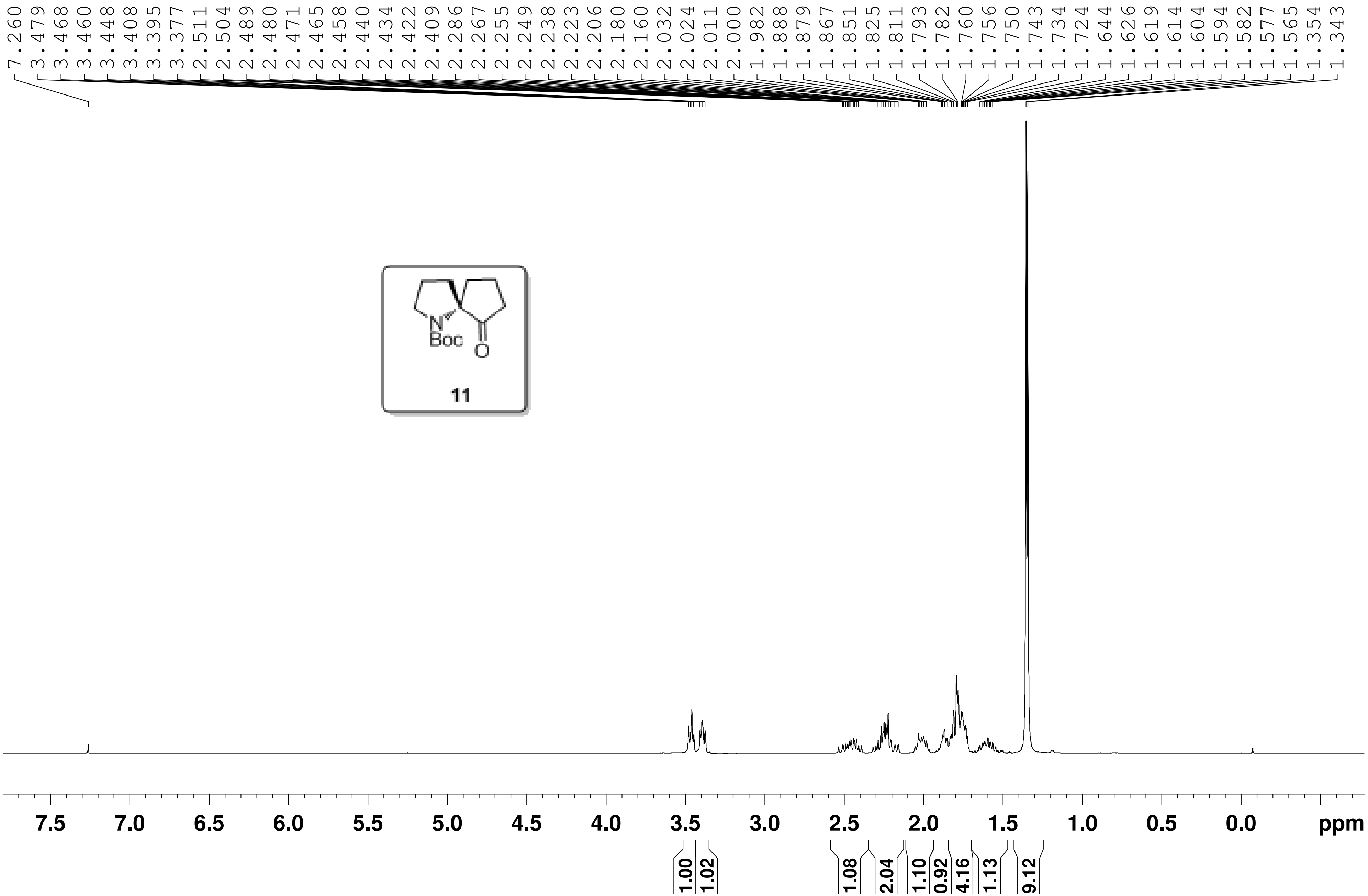
40
20
ppm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N
Boc
O
11
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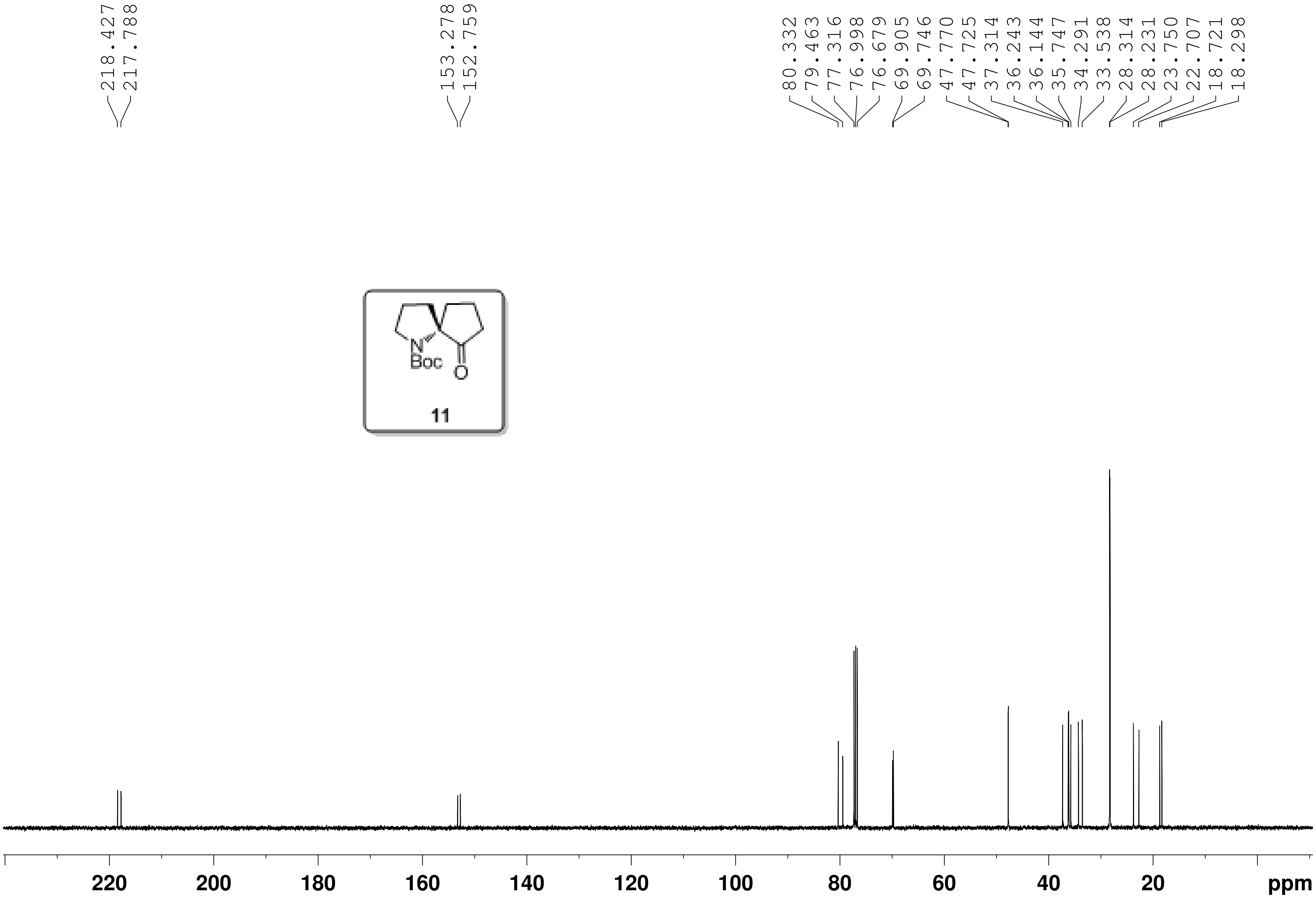
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47.725
37.314
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28.231
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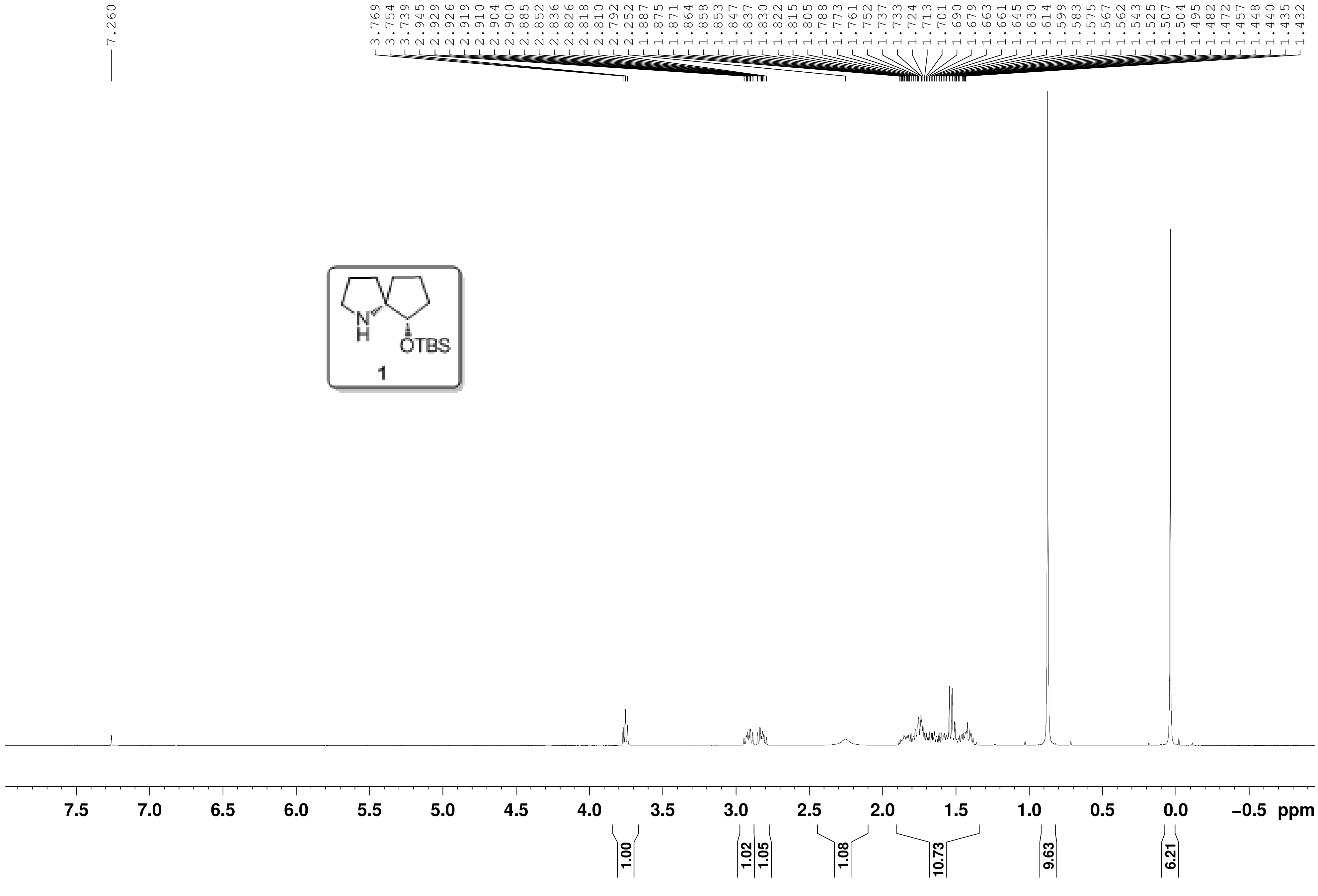
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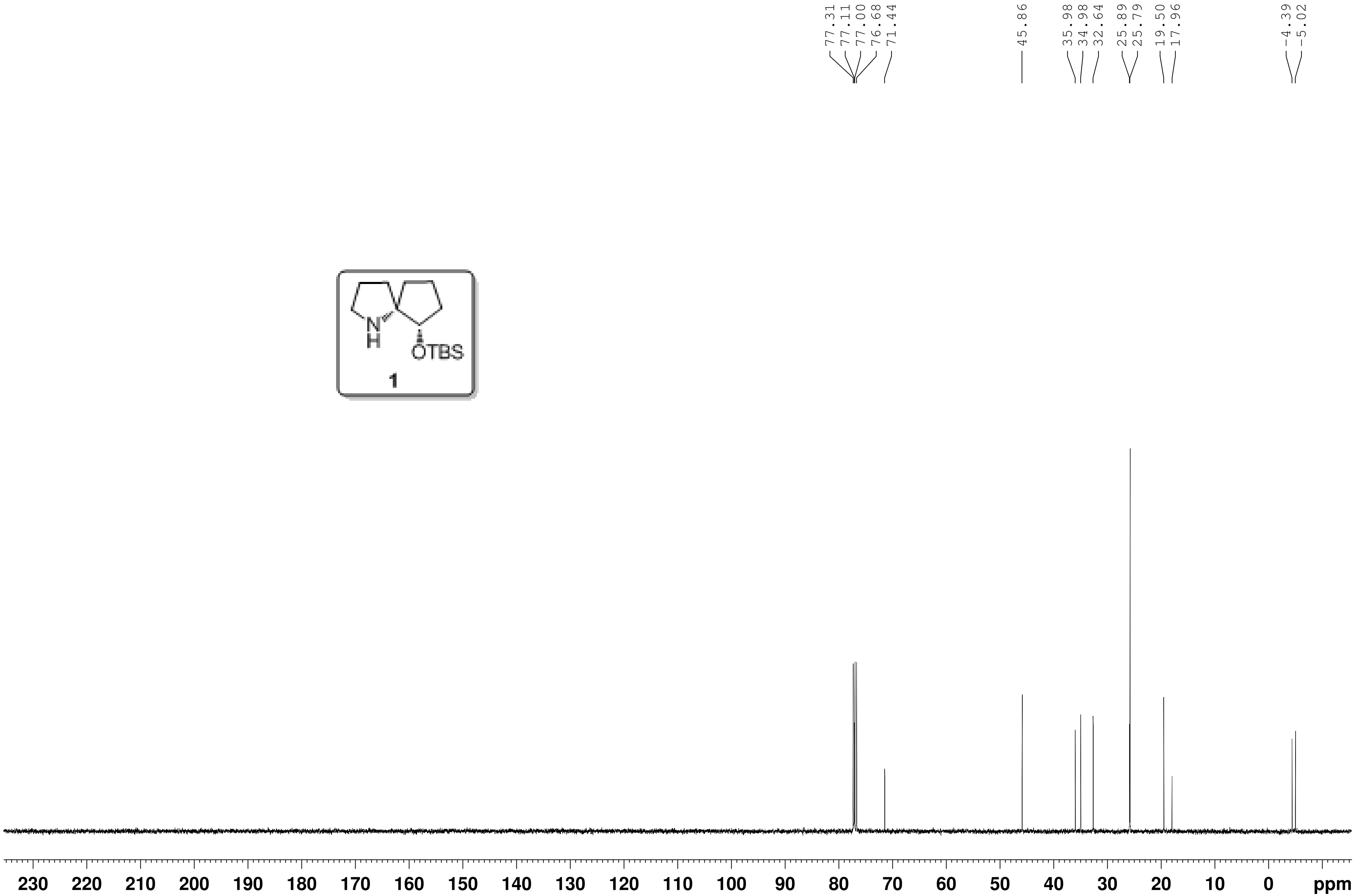
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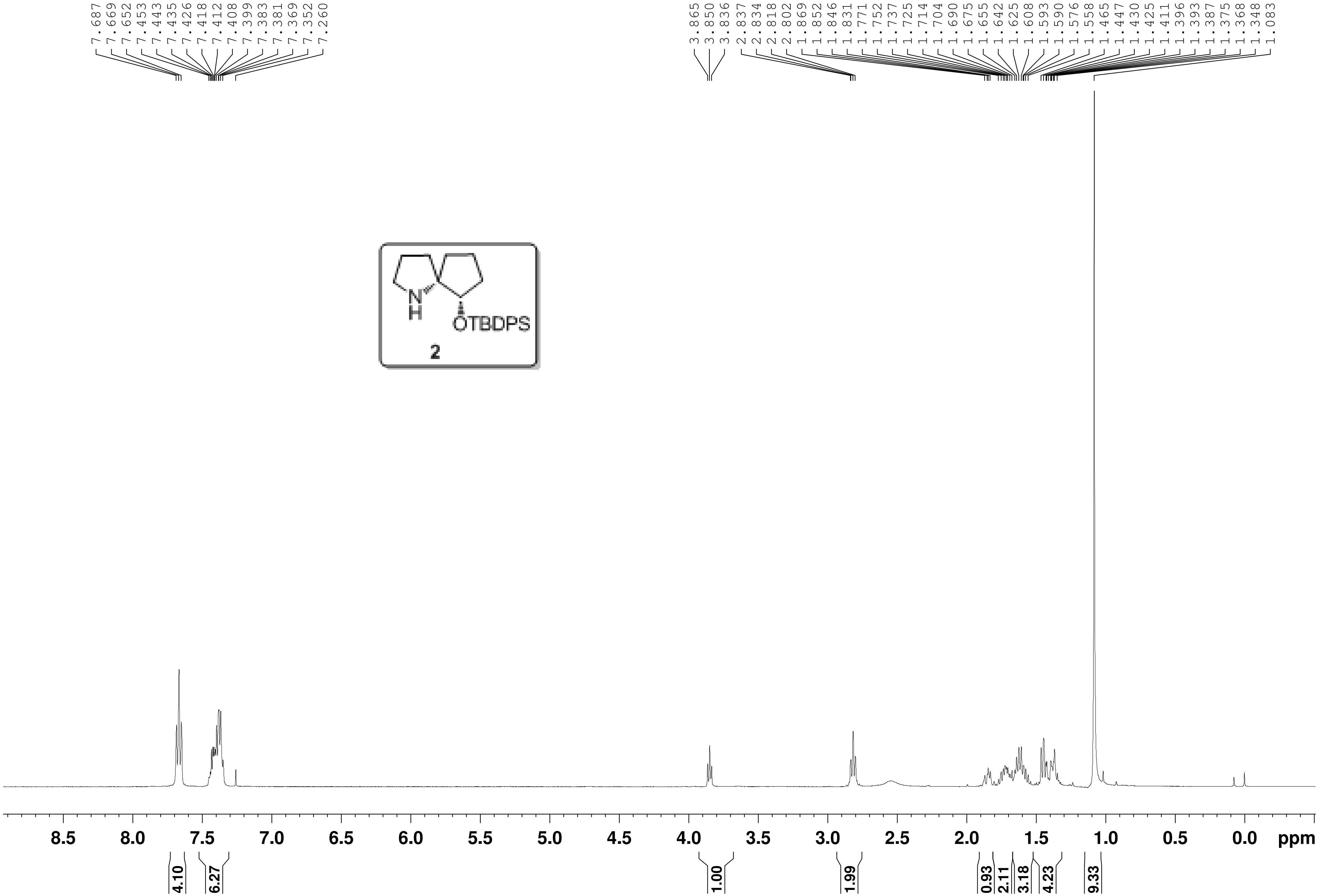
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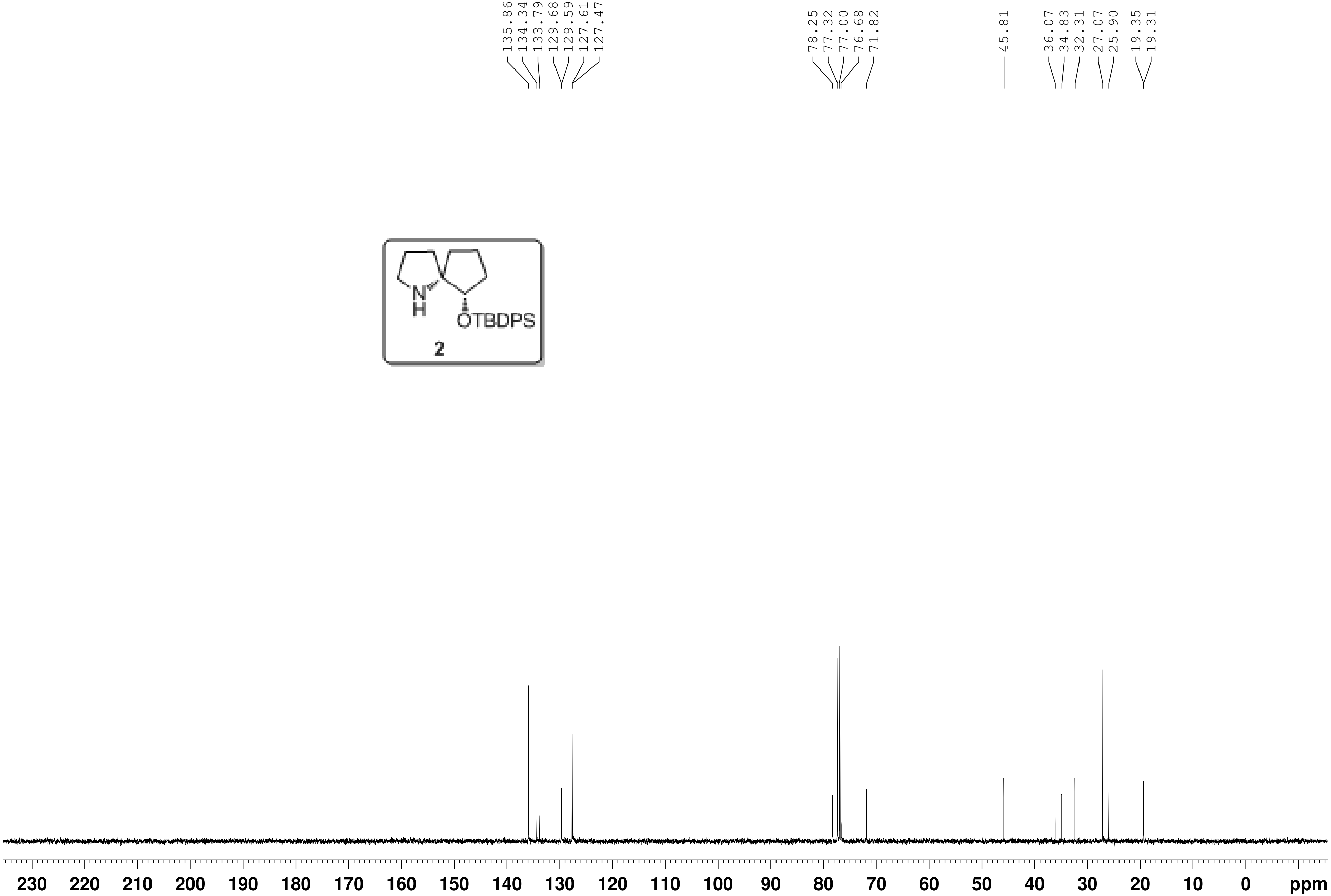
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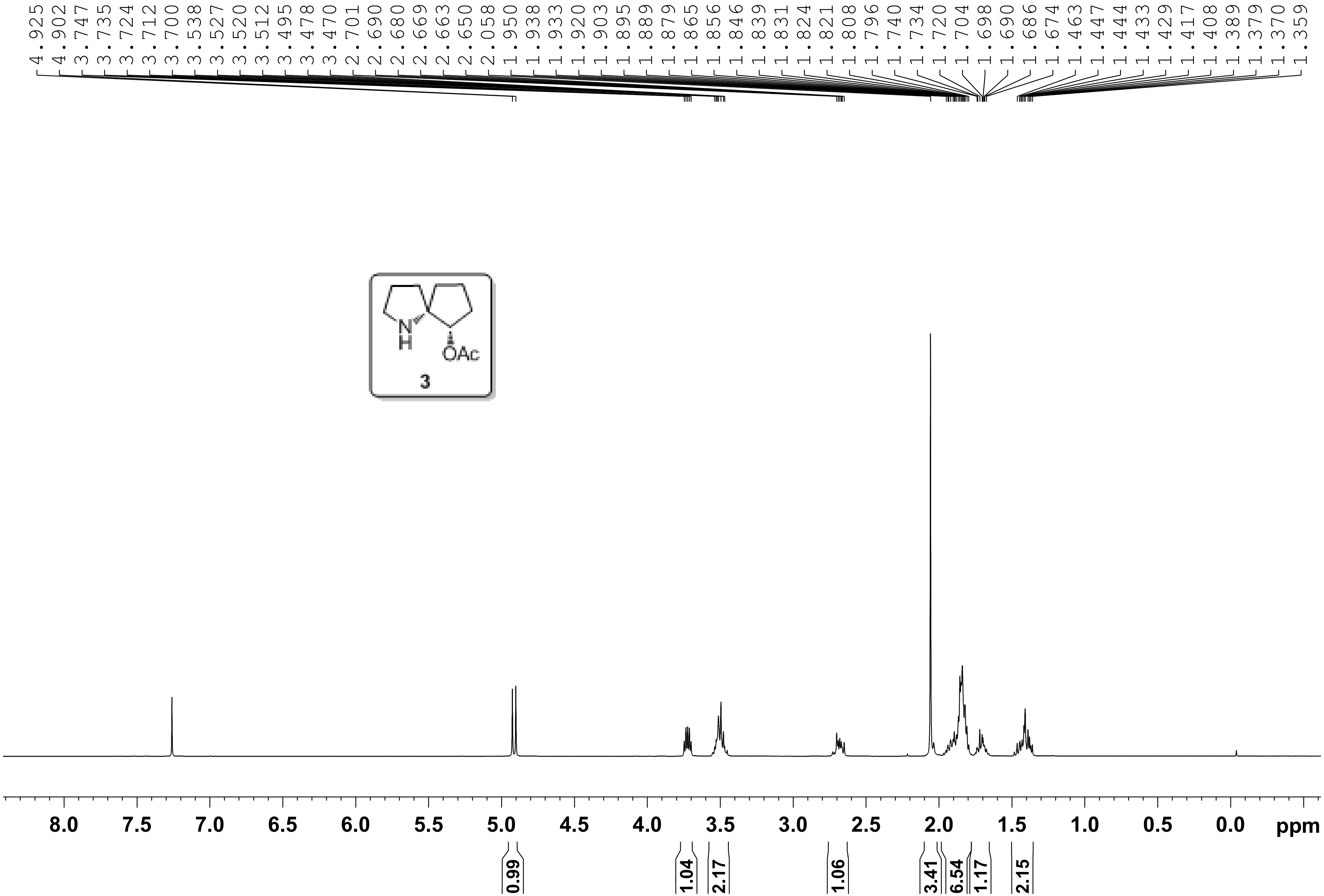
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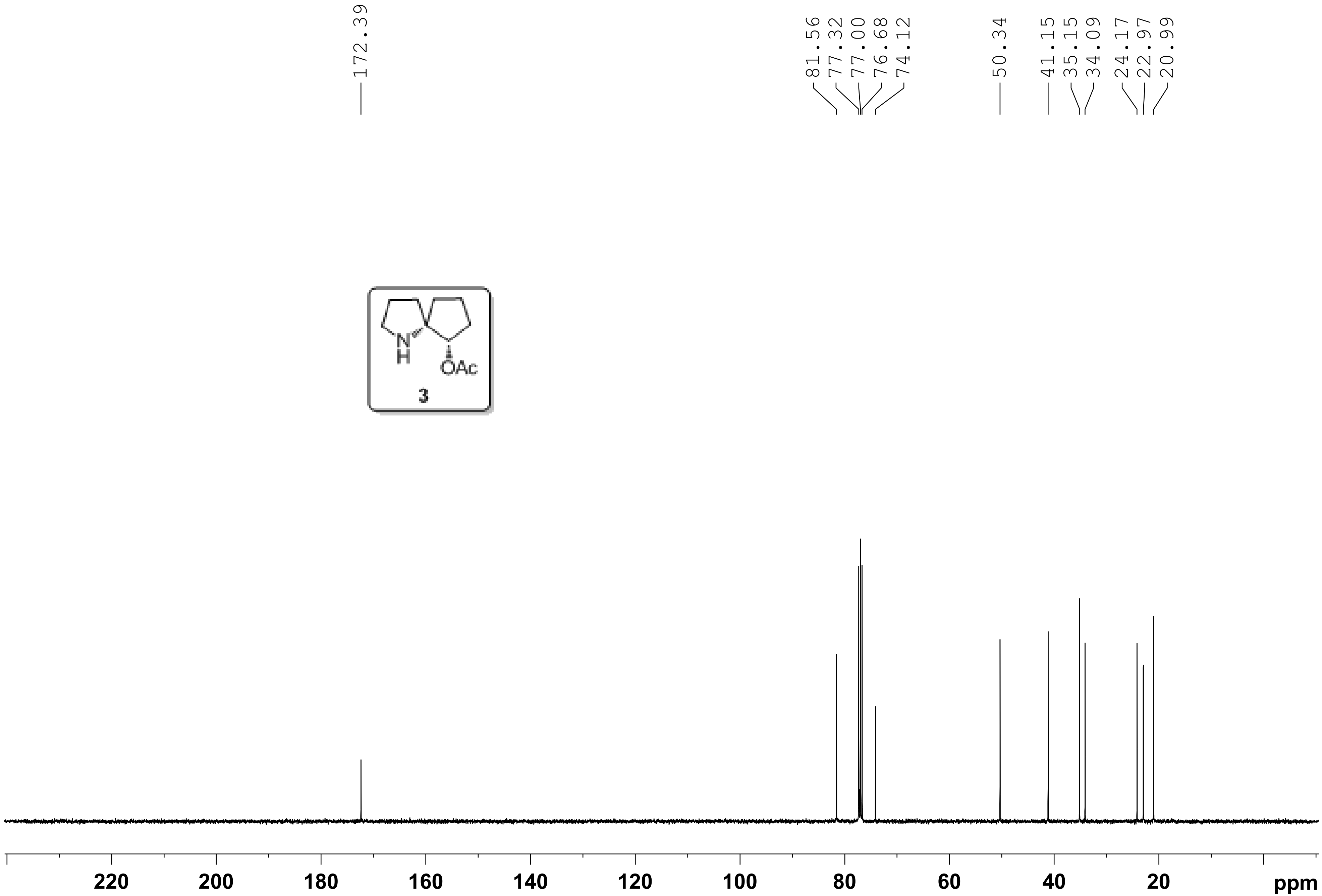
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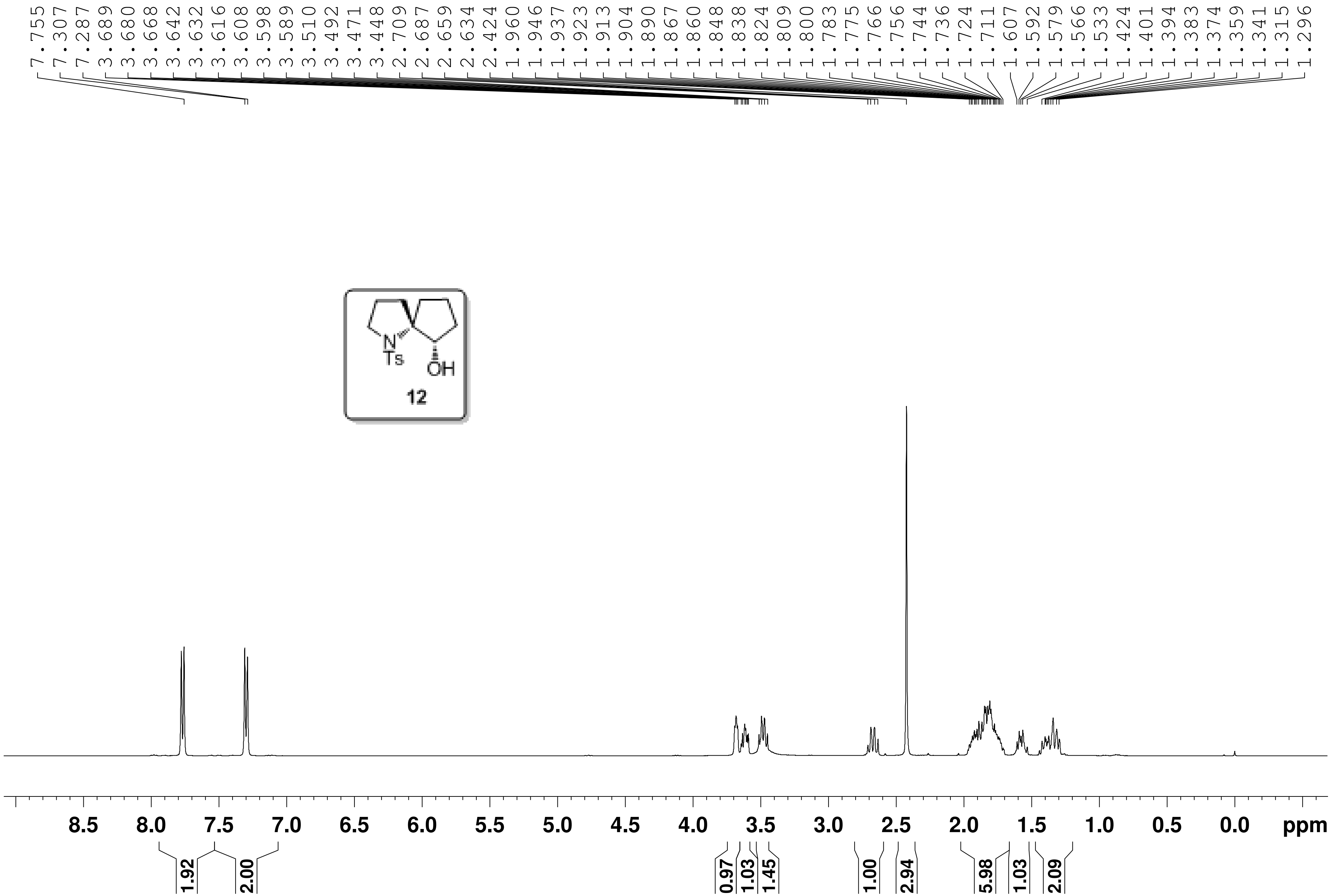
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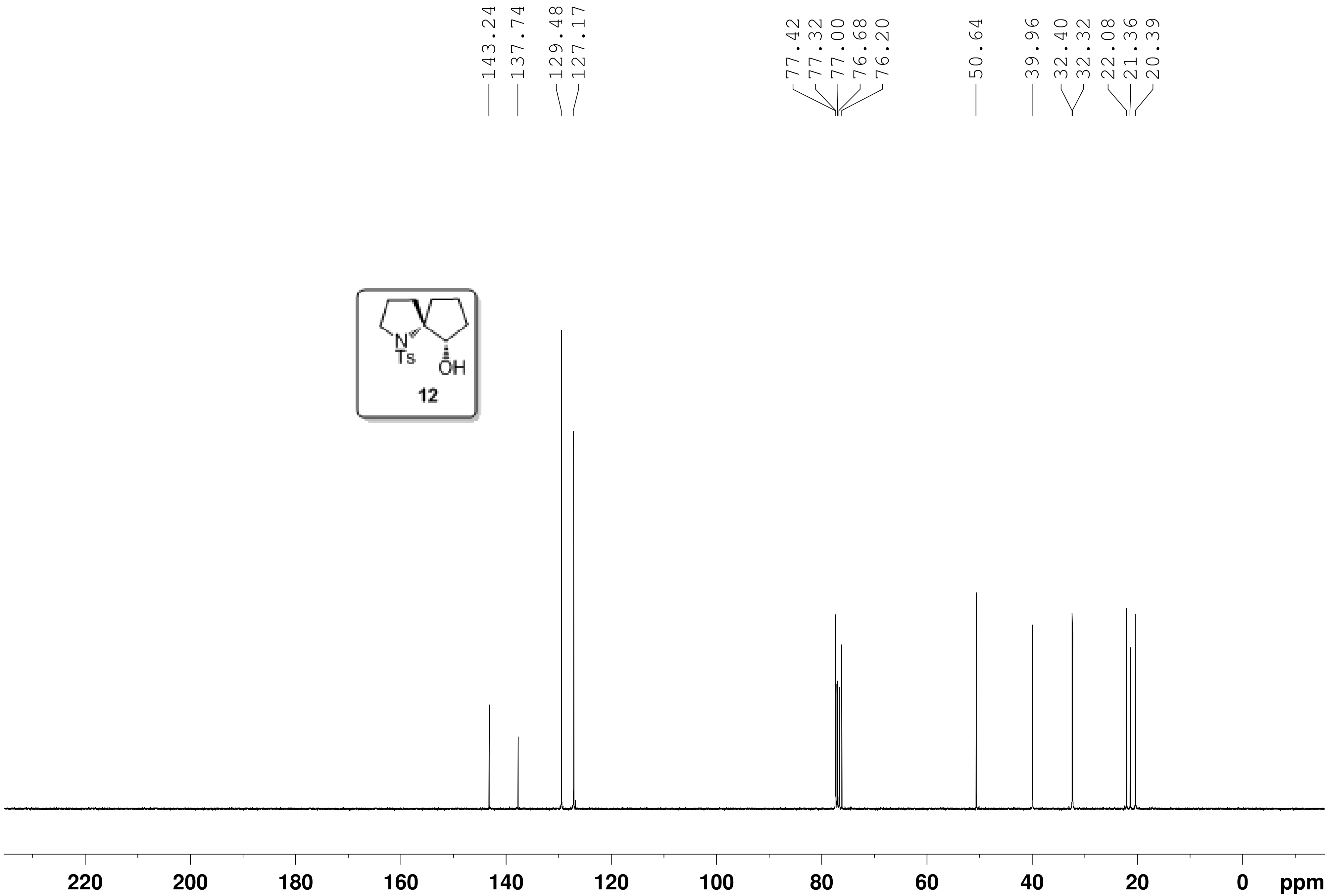
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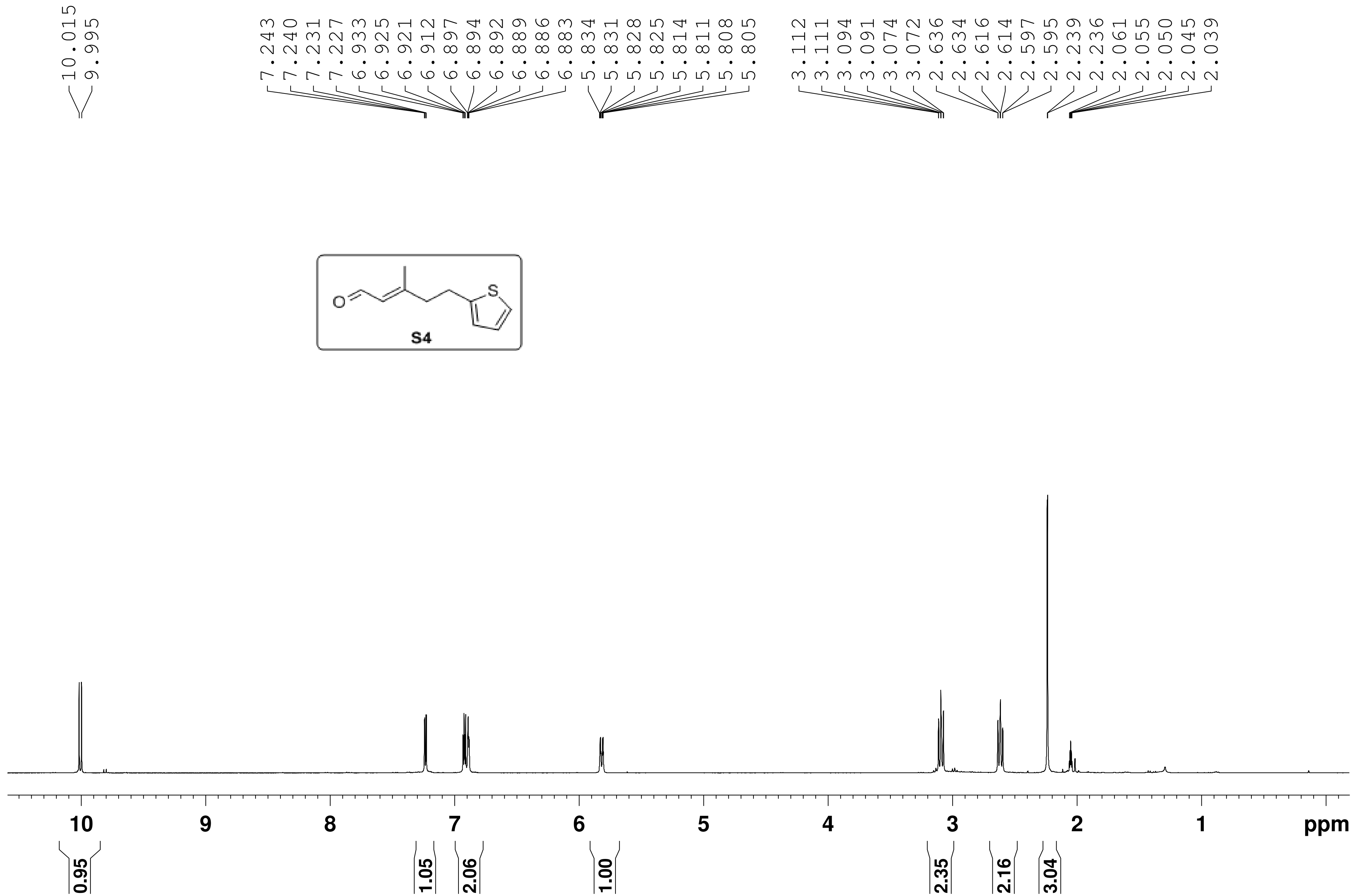
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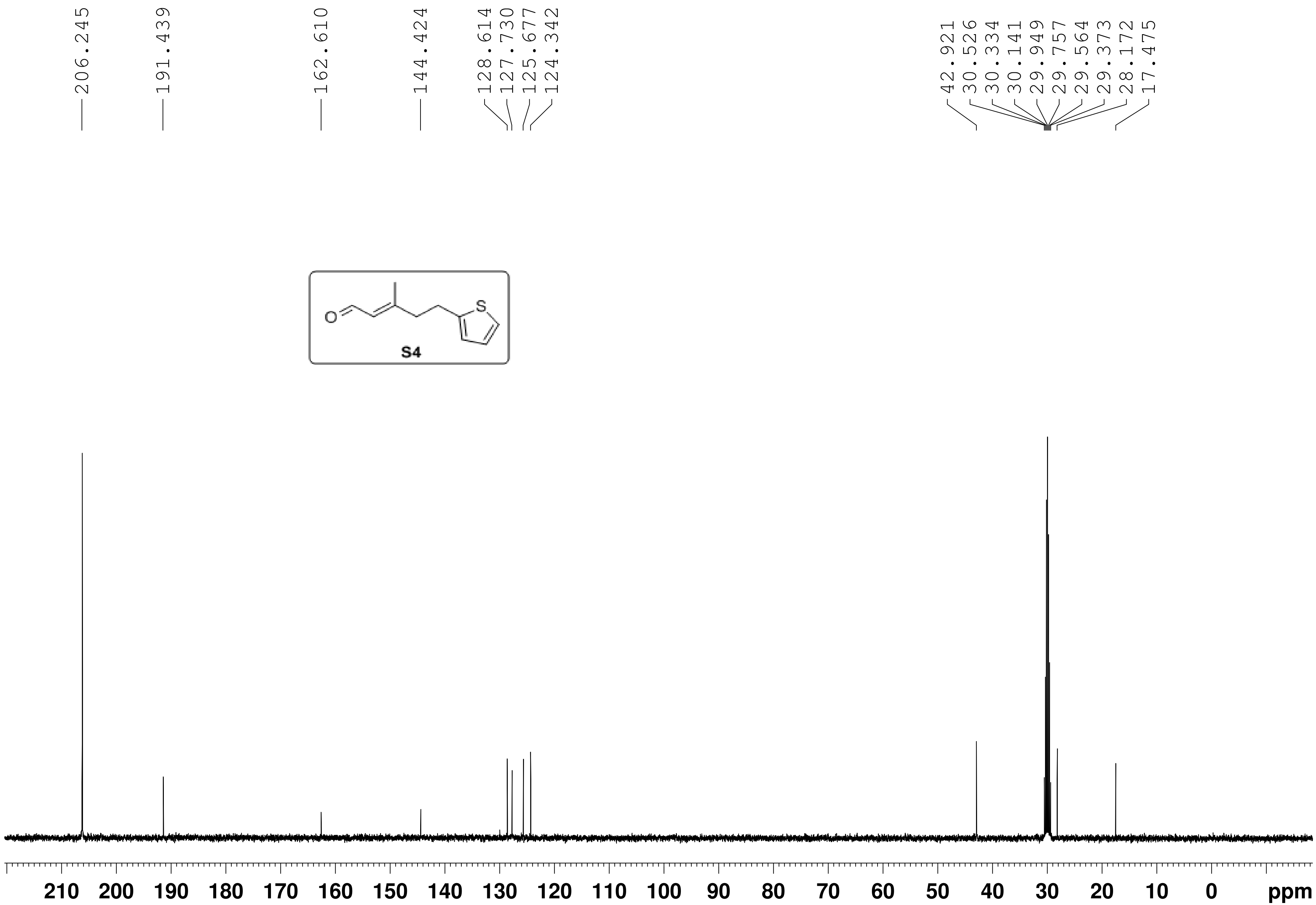

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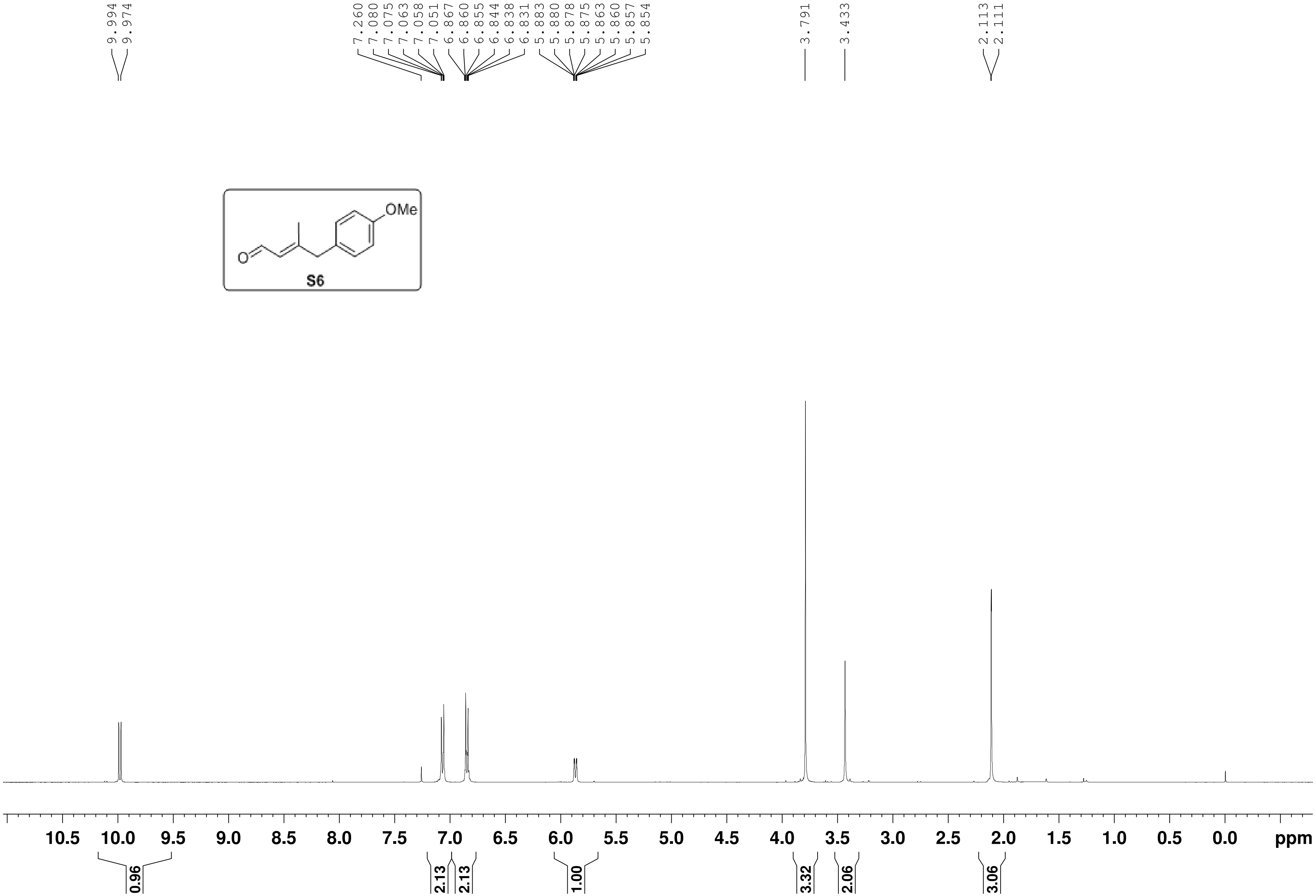
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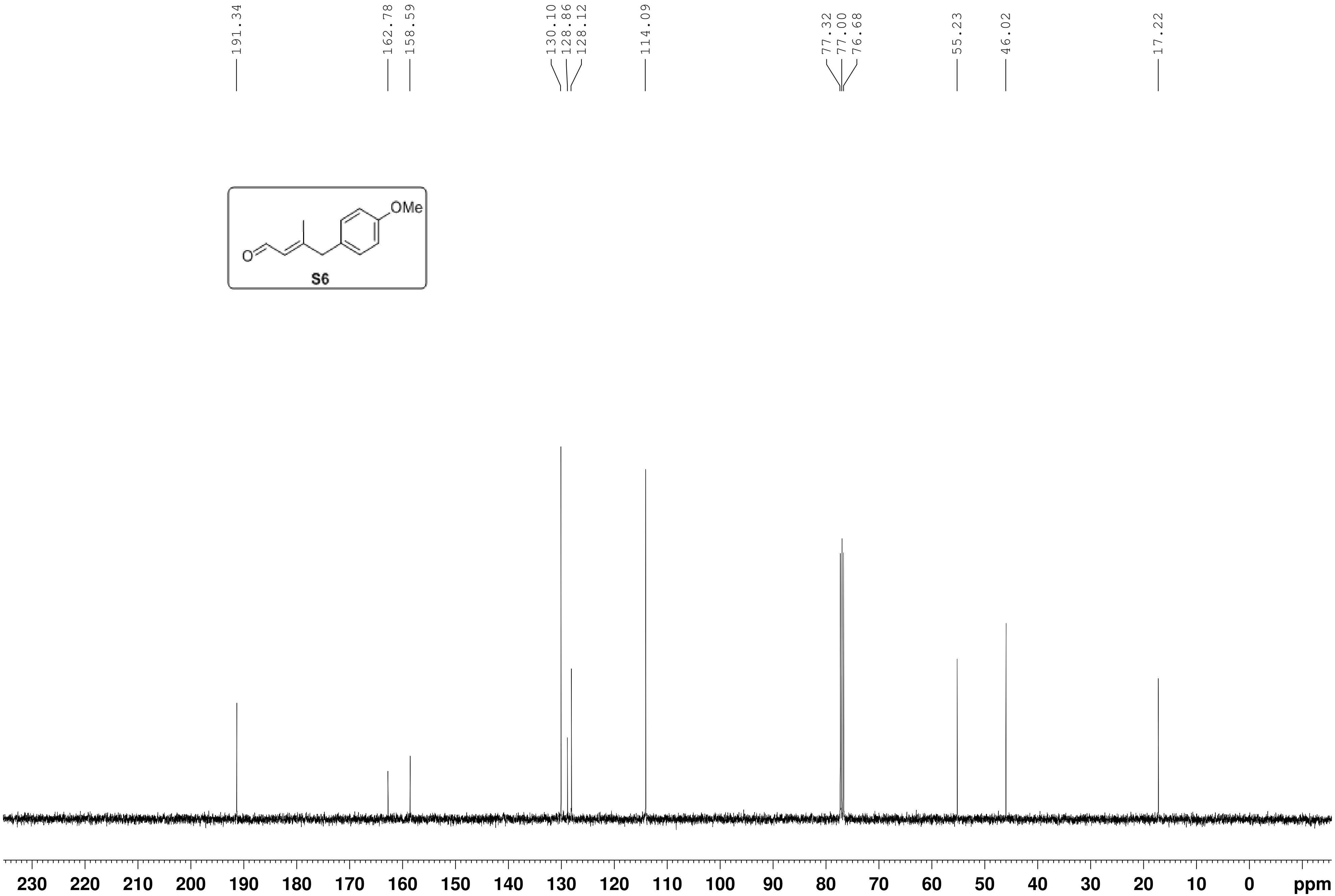
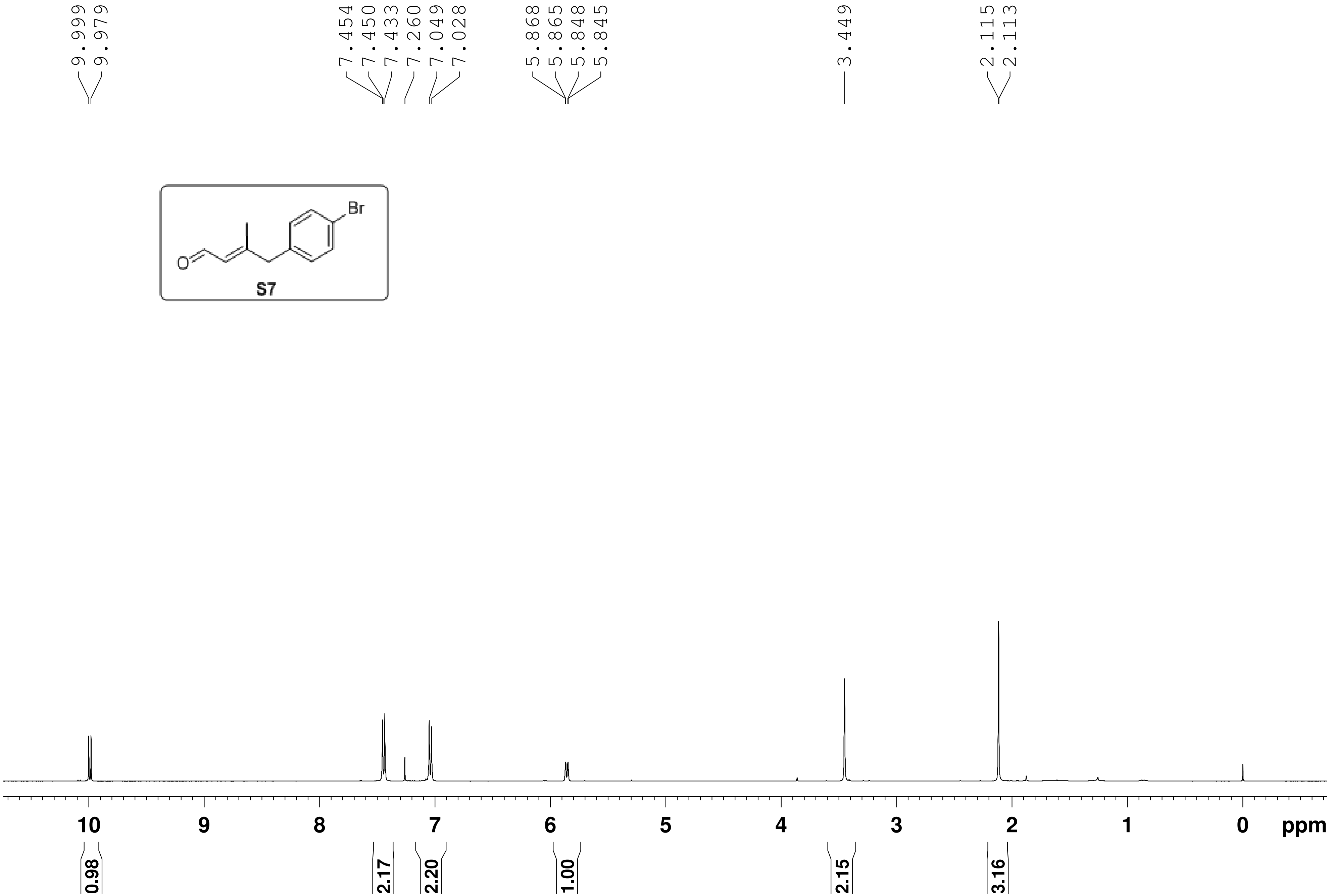
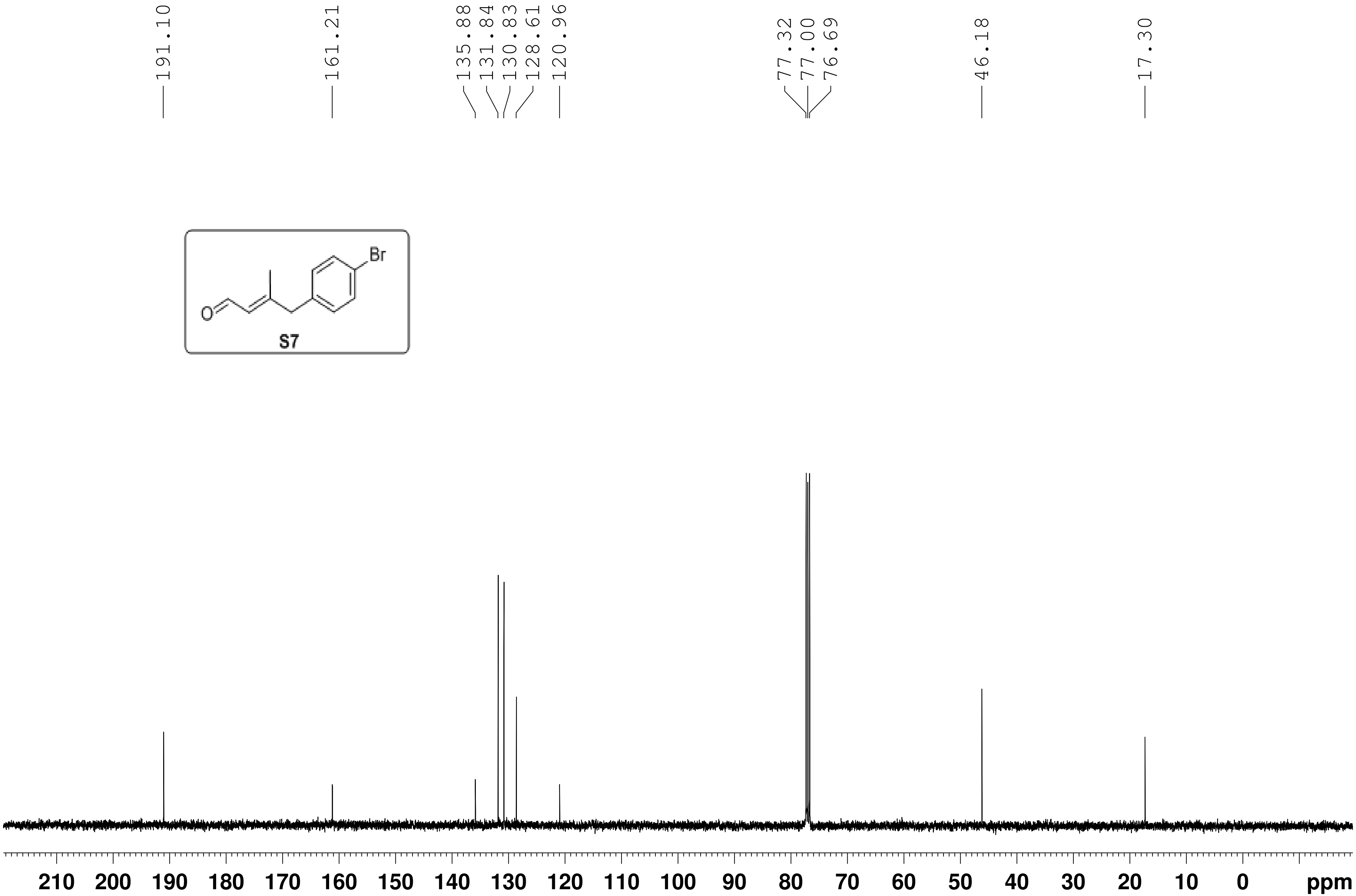
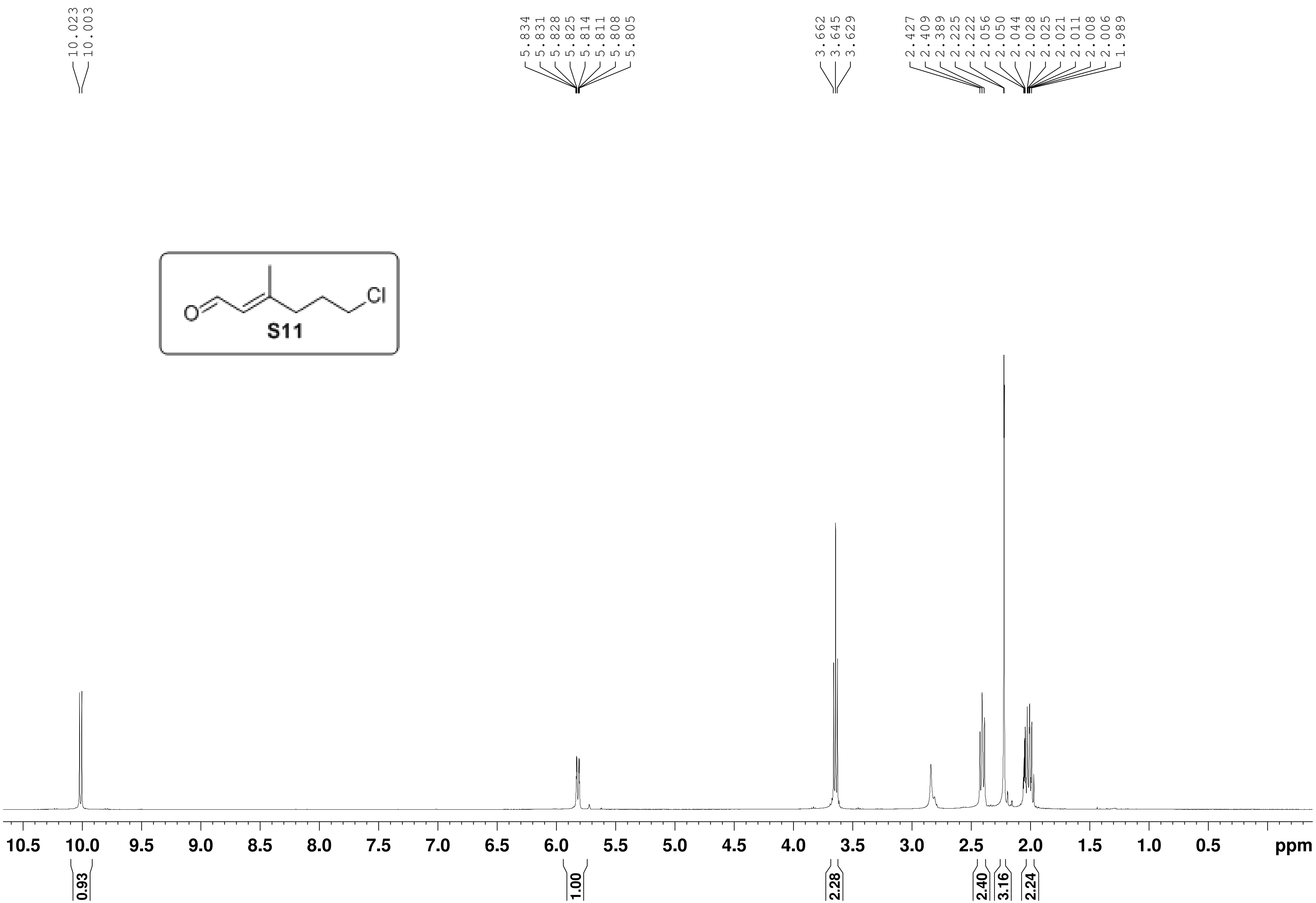
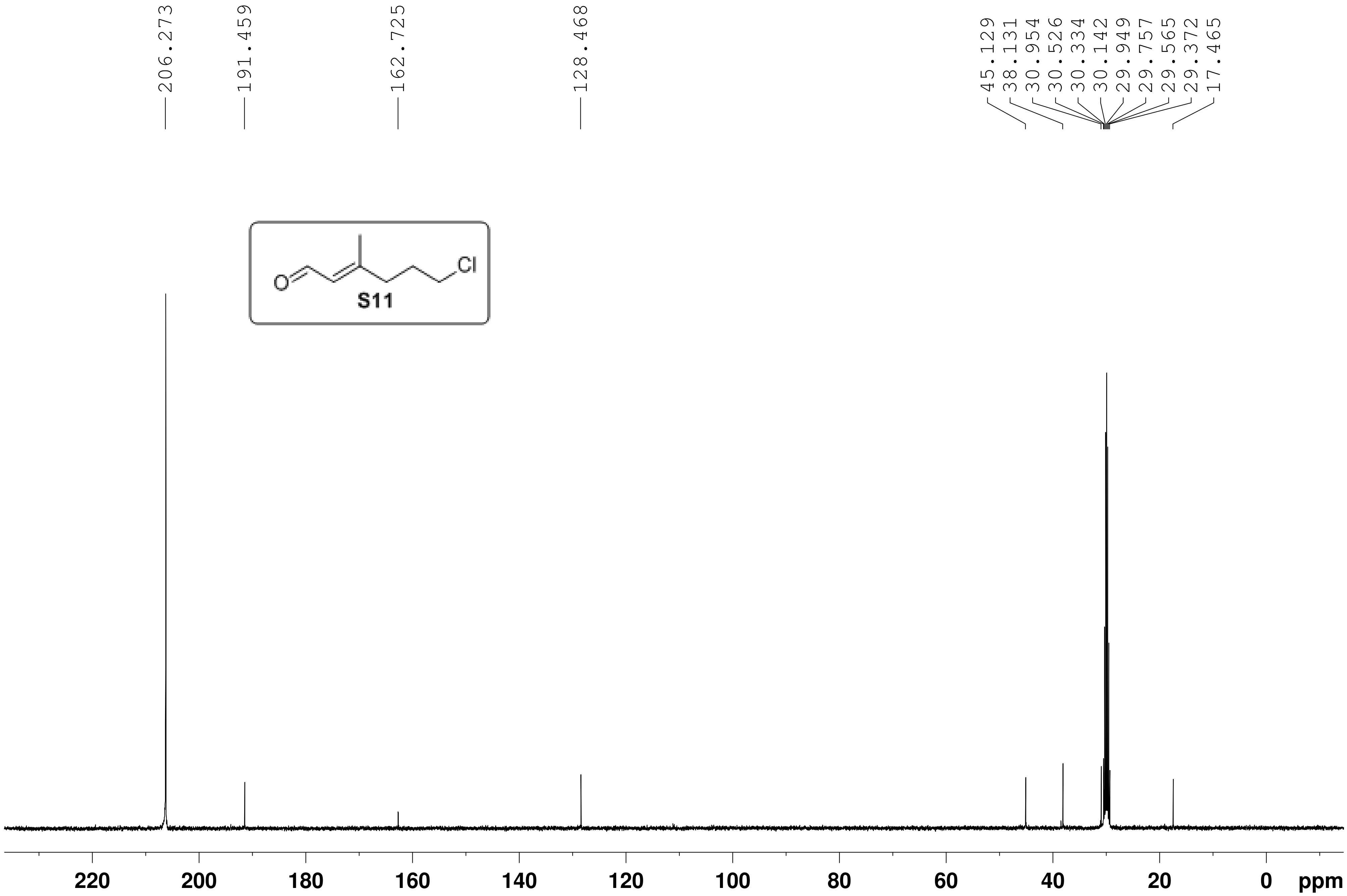
5.854
3.791
3.433
2.113
2.111
OMe
S6
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.96
2.13
2.13
1.00
3.32
2.06
3.06

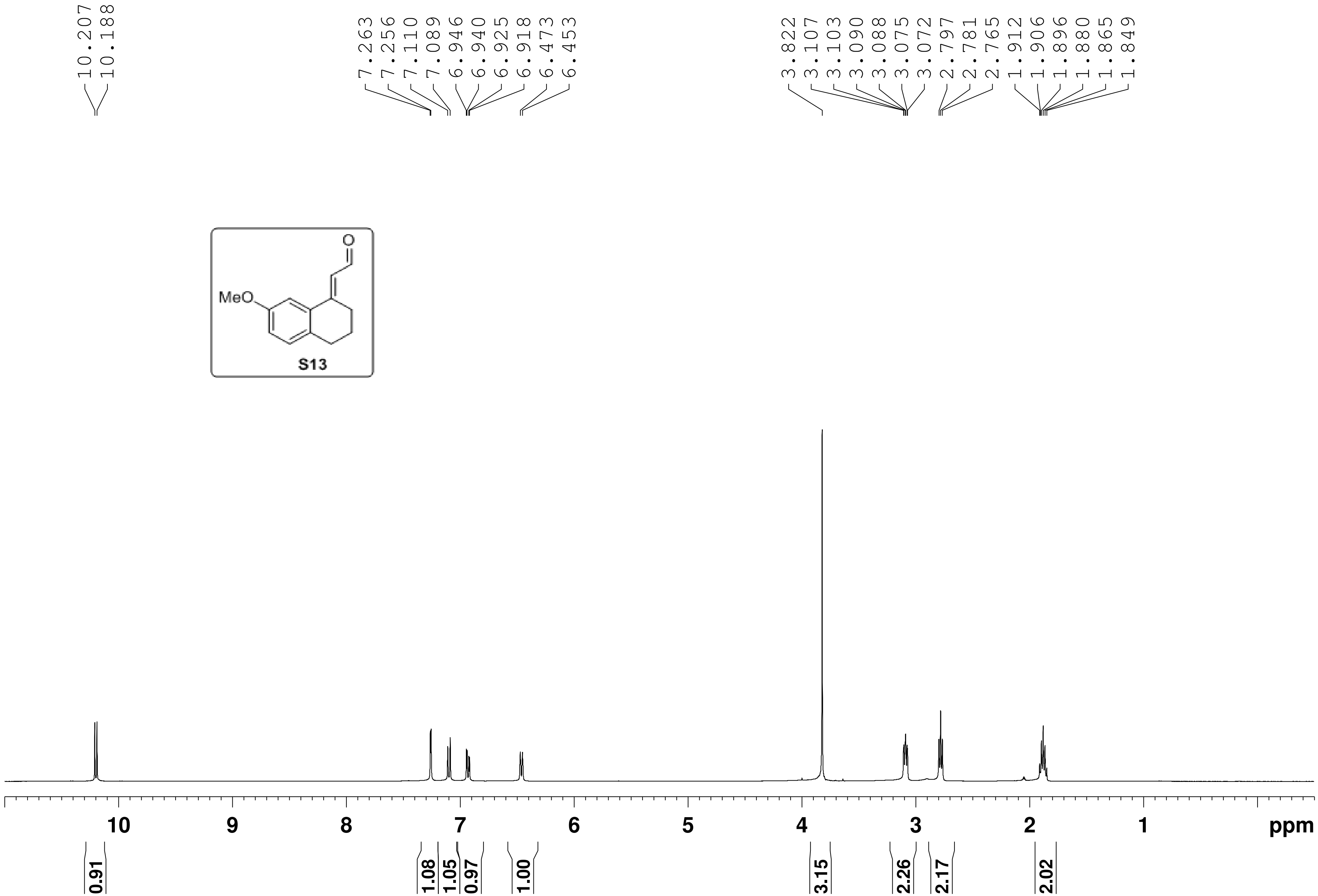

191.34
162.78
158.59
130.10
128.86
128.12
114.09
77.32
77.00
76.68
55.23
46.02
17.22
OMe
O
S6
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

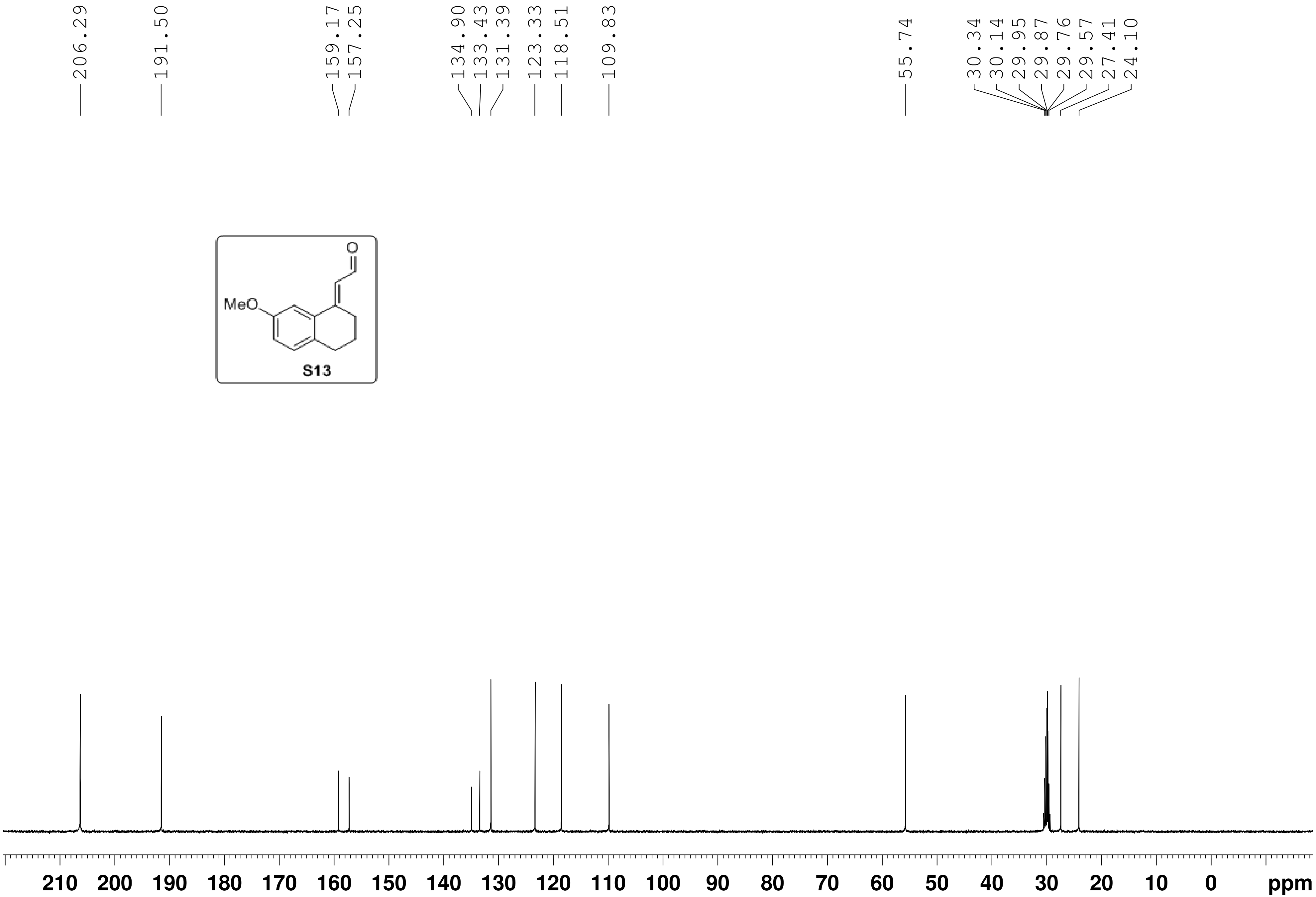

9.999
9.979
7.454
7.450
7.433
7.260
7.049
7.028
5.868
5.865
5.848
5.845
3.449
2.115
2.113
Br
O
S7
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
2.17
2.20
1.00
2.15
3.16


191.10
161.21
135.88
131.84
130.83
128.61
120.96
77.32
77.00
76.69
46.18
17.30
Br
O
S7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

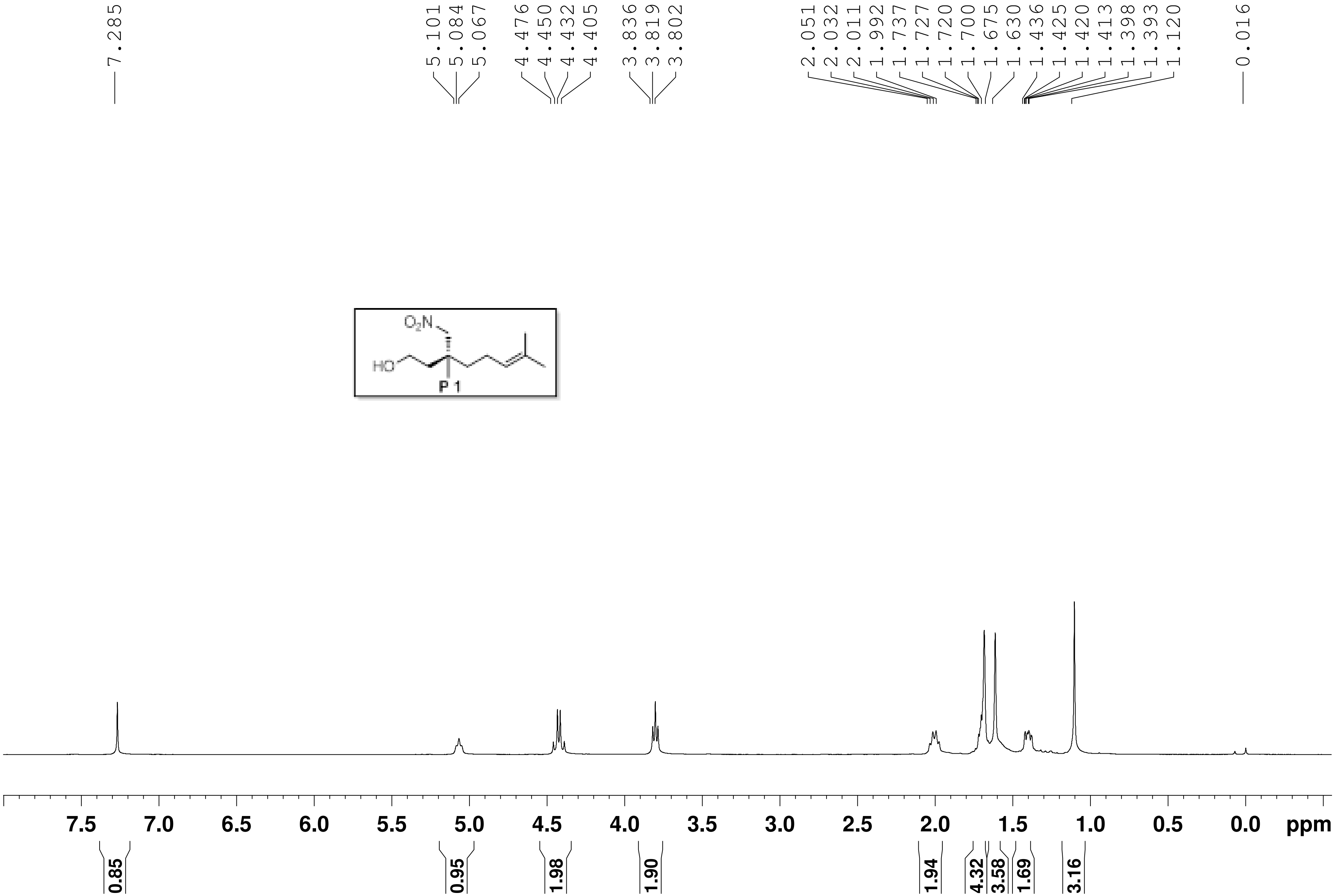

10.023
10.003
5.834
5.831
5.828
5.825
5.814
5.811
5.808
5.805
3.662
3.645
3.629
2.427
2.409
2.389
2.225
2.222
2.056
2.050
2.044
2.028
2.025
2.021
2.011
2.008
2.006
1.989
Cl
O
S11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.93
1.00
2.28
2.40
3.16
2.24

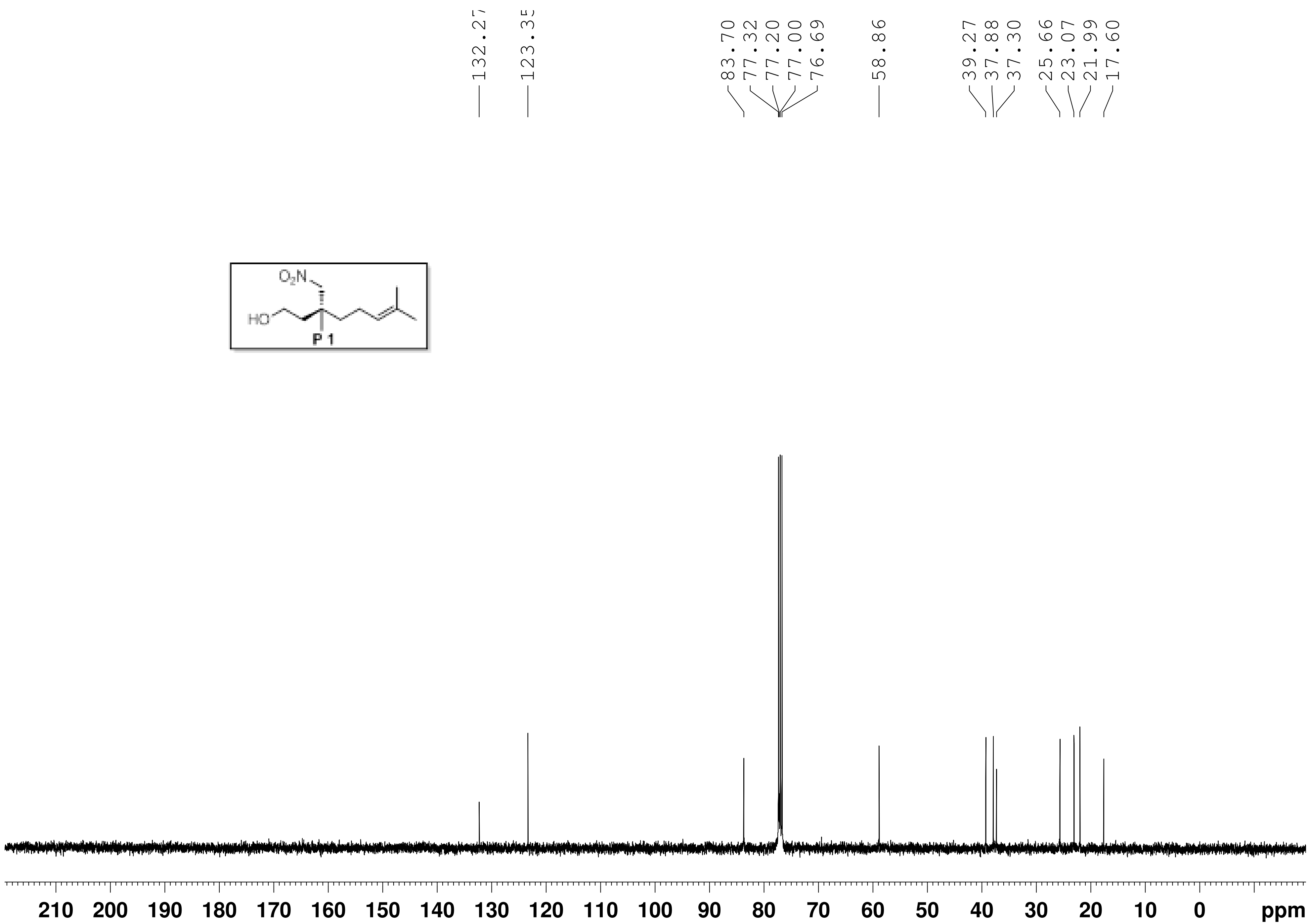

206.273
191.459
162.725
128.468
45.129
38.131
30.954
30.526
30.334
30.142
29.949
29.757
29.565
29.372
17.465
Cl
O
S11
220
200
180
160
140
120
100
80
60
40
20
0
ppm


10.207
10.188
7.263
7.256
7.110
7.089
6.946
6.940
6.925
6.918
6.473
6.453
3.822
3.107
3.103
3.090
3.088
3.075
3.072
2.797
2.781
2.765
1.912
1.906
1.896
1.880
1.865
1.849
MeO
O
S13
10
9
8
7
6
5
4
3
2
1
ppm
0.91
1.08
1.05
0.97
1.00
3.15
2.26
2.17
2.02

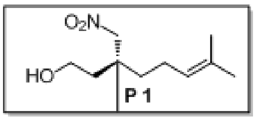

206.29
191.50
159.17
157.25
134.90
133.43
131.39
123.33
118.51
109.83
55.74
30.34
30.14
29.95
29.87
29.76
29.57
27.41
24.10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
MeO
O

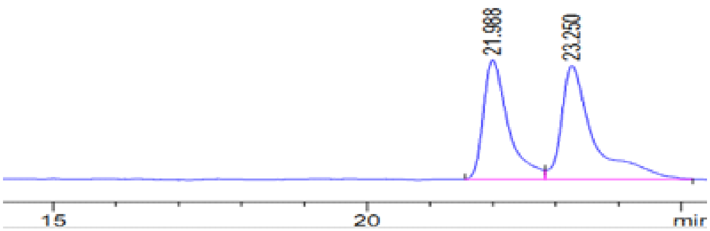
S13


7.285
5.101
5.084
5.067
4.476
4.450
4.432
4.405
3.836
3.819
3.802
2.051
2.032
2.011
1.992
1.737
1.727
1.720
1.700
1.675
1.630
1.436
1.425
1.420
1.413
1.398
1.393
1.120
0.016
O2N
HO
P 1
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 ppm
0.85
0.95
1.98
1.90
1.94
4.32
3.58
1.69
3.16


132.27
123.35
83.70
77.32
77.20
77.00
76.69
58.86
39.27
37.88
37.30
25.66
23.07
21.99
17.60
O2N
HO
P 1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

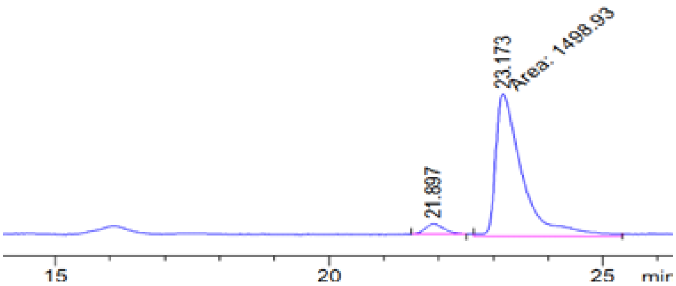
ID-3 hex:ipr=97:3 1.0 ml/min



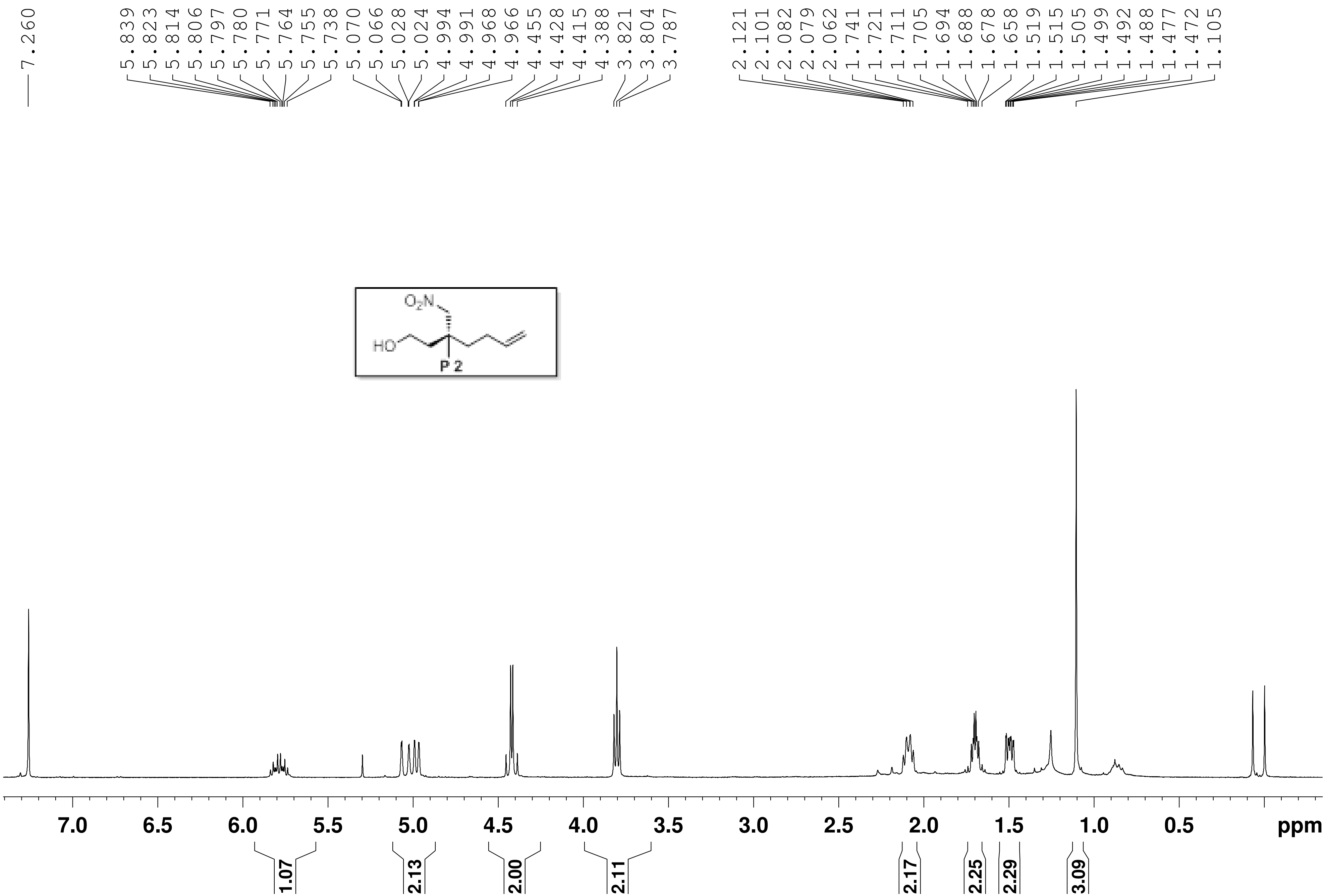


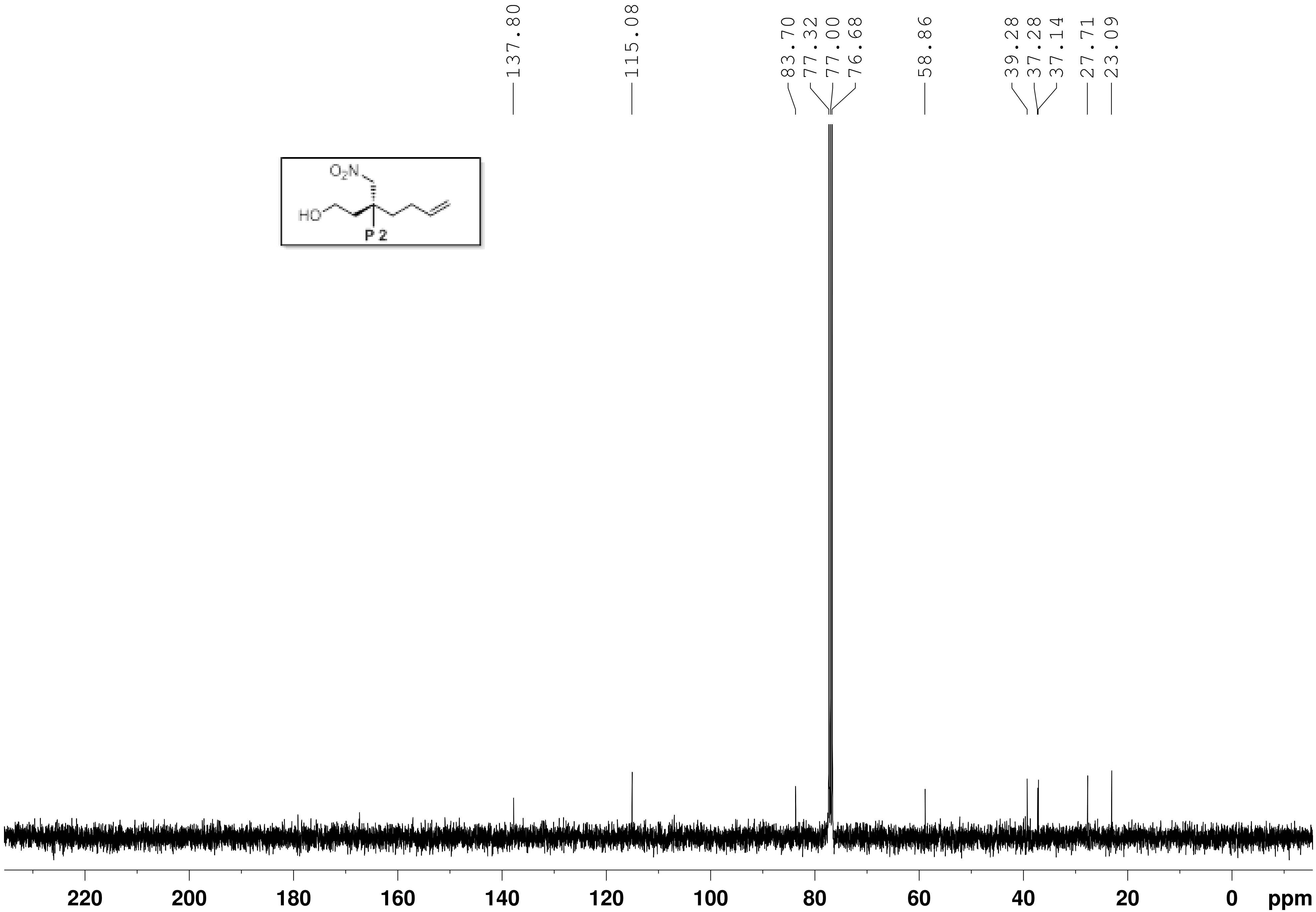
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.988	BV	0.4163	1901.72729	68.42447	45.0239
2	23.250	VB	0.5082	2322.08691	65.09370	54.9761

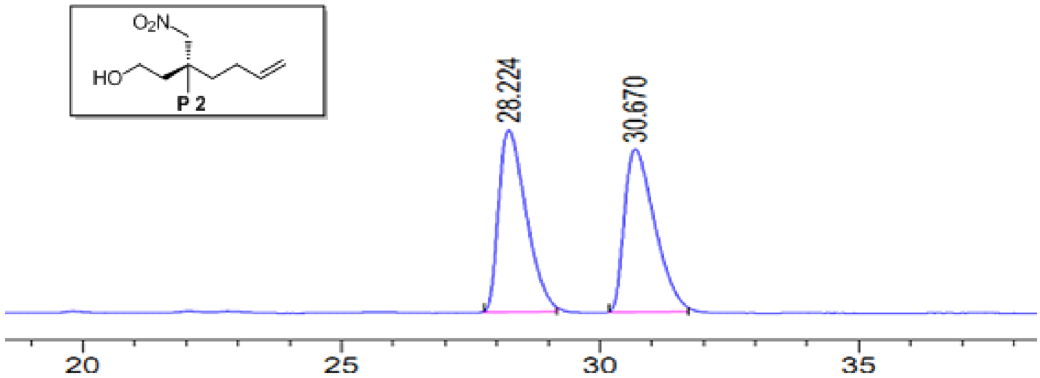


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.897	BB	0.3720	78.14959	3.21078	4.9553
2	23.173	MM	0.5636	1498.92664	44.32967	95.0447


7.260
5.839 5.823 5.814 5.806 5.797 5.780 5.771 5.764 5.755 5.738 5.070 5.066 5.028 5.024 4.994 4.991 4.968 4.966 4.455 4.428 4.415 4.388 3.821 3.804 3.787
2.121 2.101 2.082 2.079 2.062 1.741 1.721 1.711 1.705 1.694 1.688 1.678 1.658 1.519 1.515 1.505 1.499 1.492 1.488 1.477 1.472 1.105
O2N
HO
P 2
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.07 2.13 2.00 2.11 2.17 2.25 2.29 3.09

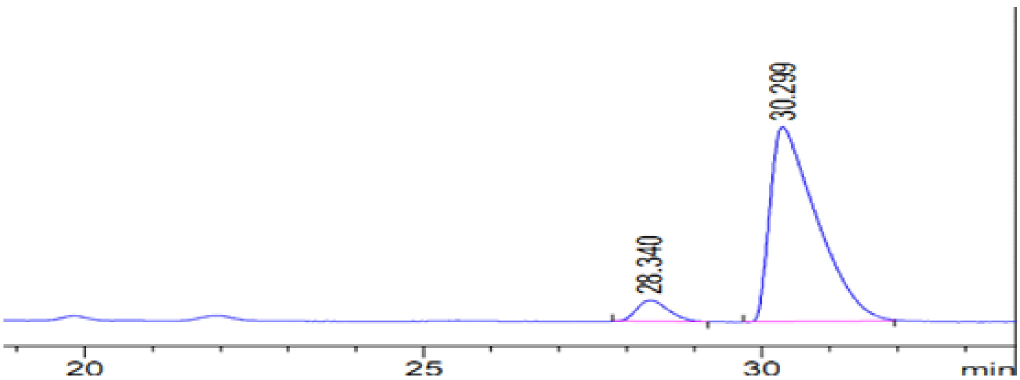

137.80
115.08
83.70
77.32
77.00
76.68
58.86
39.28
37.28
37.14
27.71
23.09
O2N
HO
P 2
220
200
180
160
140
120
100
80
60
40
20
0
ppm

ID-3 hex:ipr=97:3 1.0 ml/min

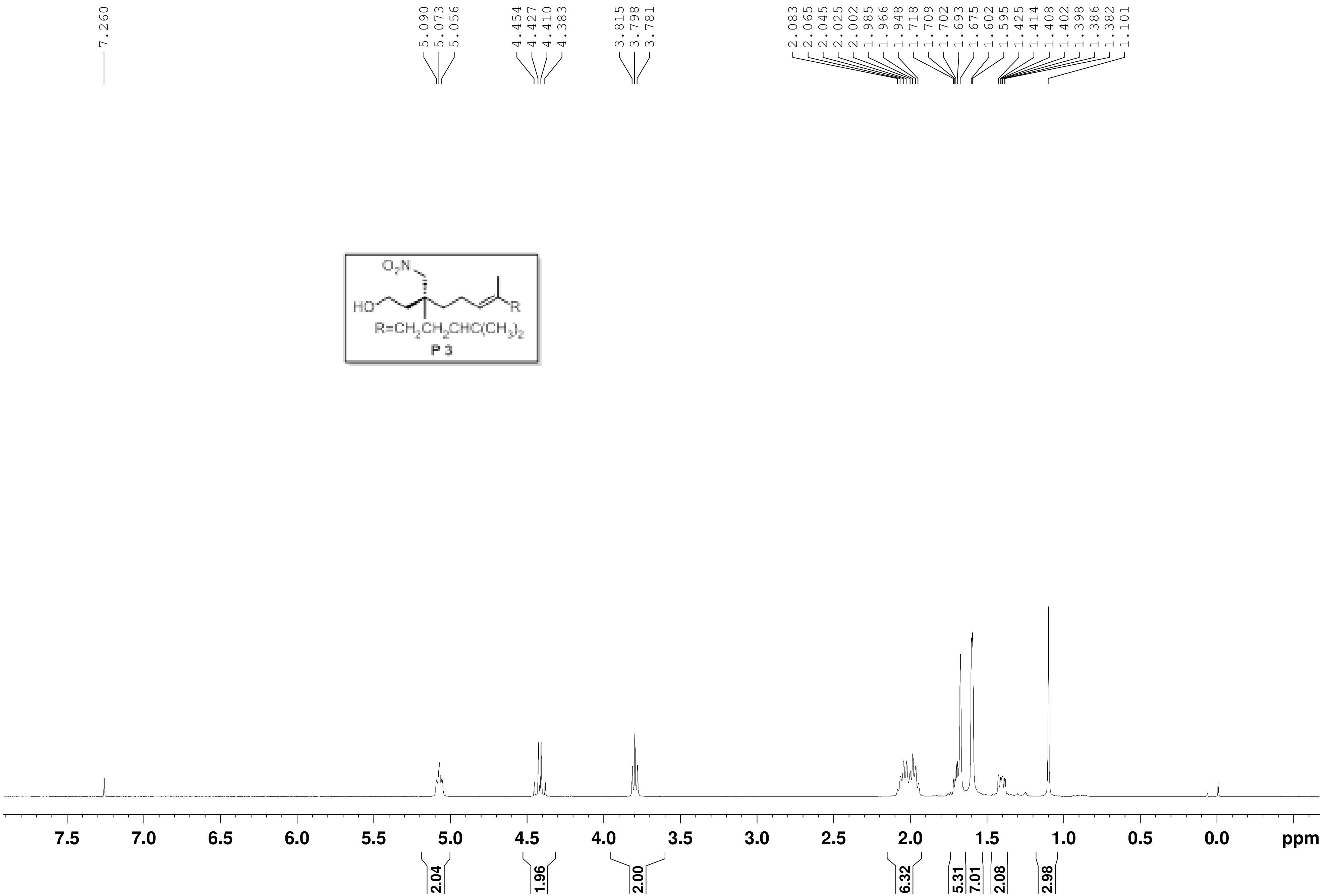


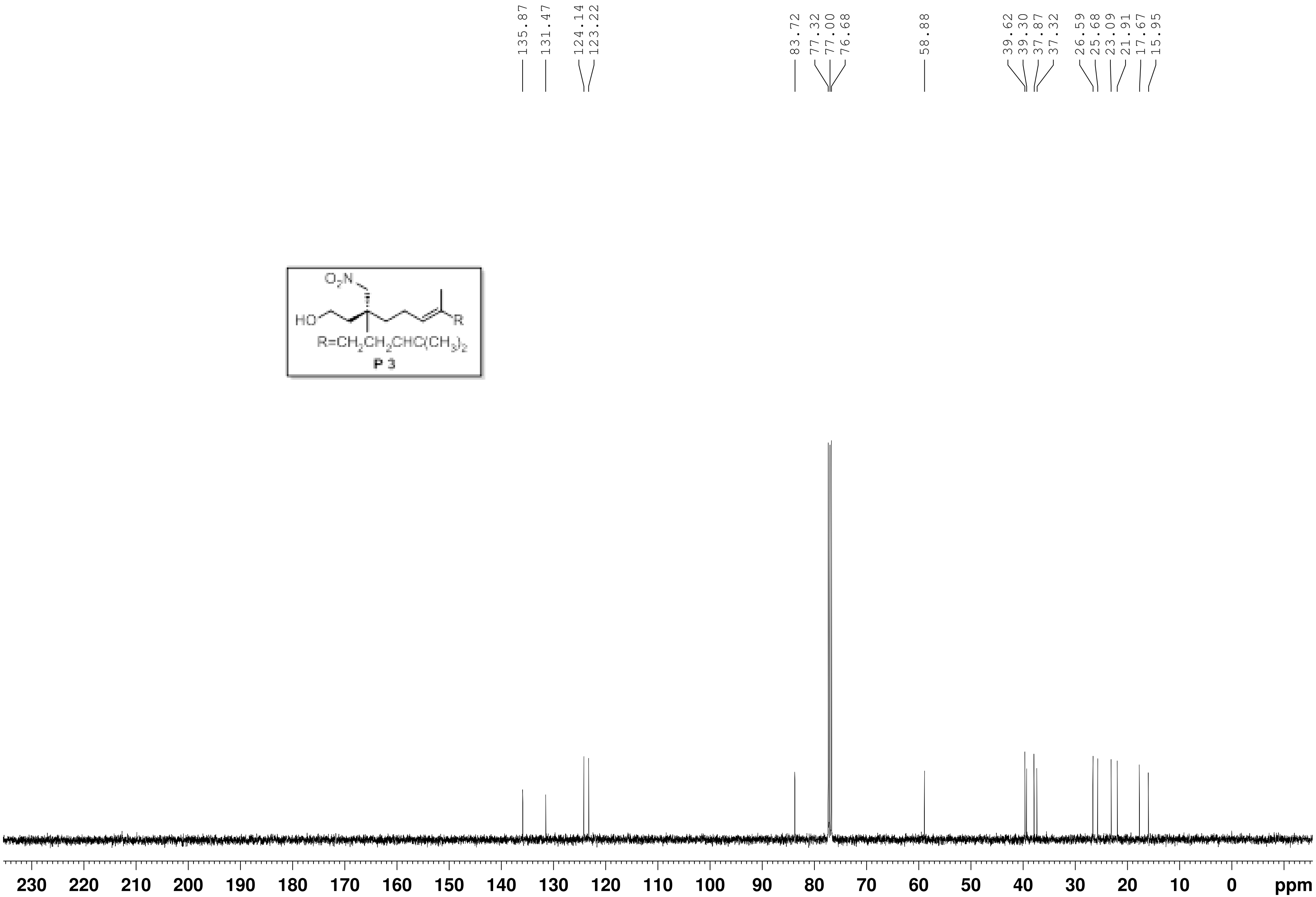
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.224	BB	0.5678	3984.33594	107.15290	50.3580
2	30.670	BB	0.6278	3927.67871	95.91160	49.6420

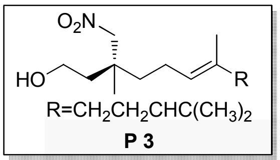


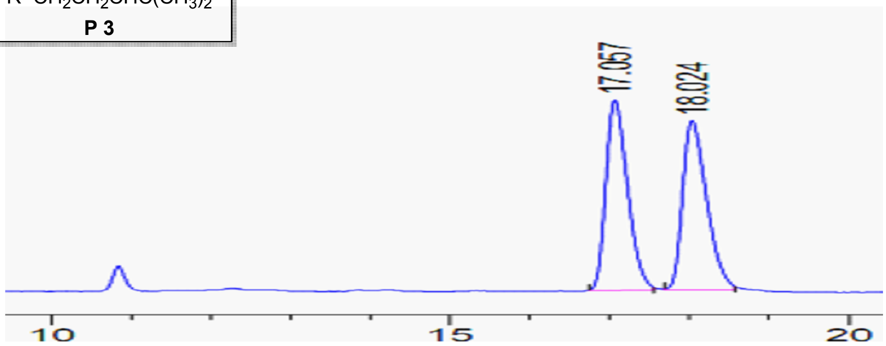
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.340	BB	0.5032	227.37657	6.85169	6.9869
2	30.299	PB	0.7243	3026.96240	62.58054	93.0131


7.260
5.090 5.073 5.056
4.454 4.427 4.410 4.383
3.815 3.798 3.781
2.083 2.065 2.045 2.025 2.002 1.985 1.966 1.948 1.718 1.709 1.702 1.693 1.675 1.602 1.595 1.425 1.414 1.408 1.402 1.398 1.386 1.382 1.101
O2N
HO
R
R=CH2CH2CHC(CH3)2
P 3
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 ppm
2.04 1.96 2.00 6.32 5.31 7.01 2.08 2.98


135.87
131.47
124.14
123.22
83.72
77.32
77.00
76.68
58.88
39.62
39.30
37.87
37.32
26.59
25.68
23.09
21.91
17.67
15.95
O_2N
HO
R
R=$CH_2CH_2CHC(CH_3)_2$
P 3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

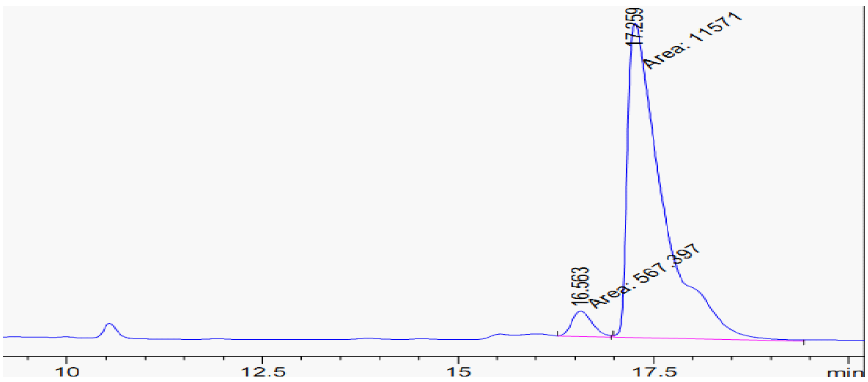
ID-3 hex:ipr=97:3 1.0 ml/min



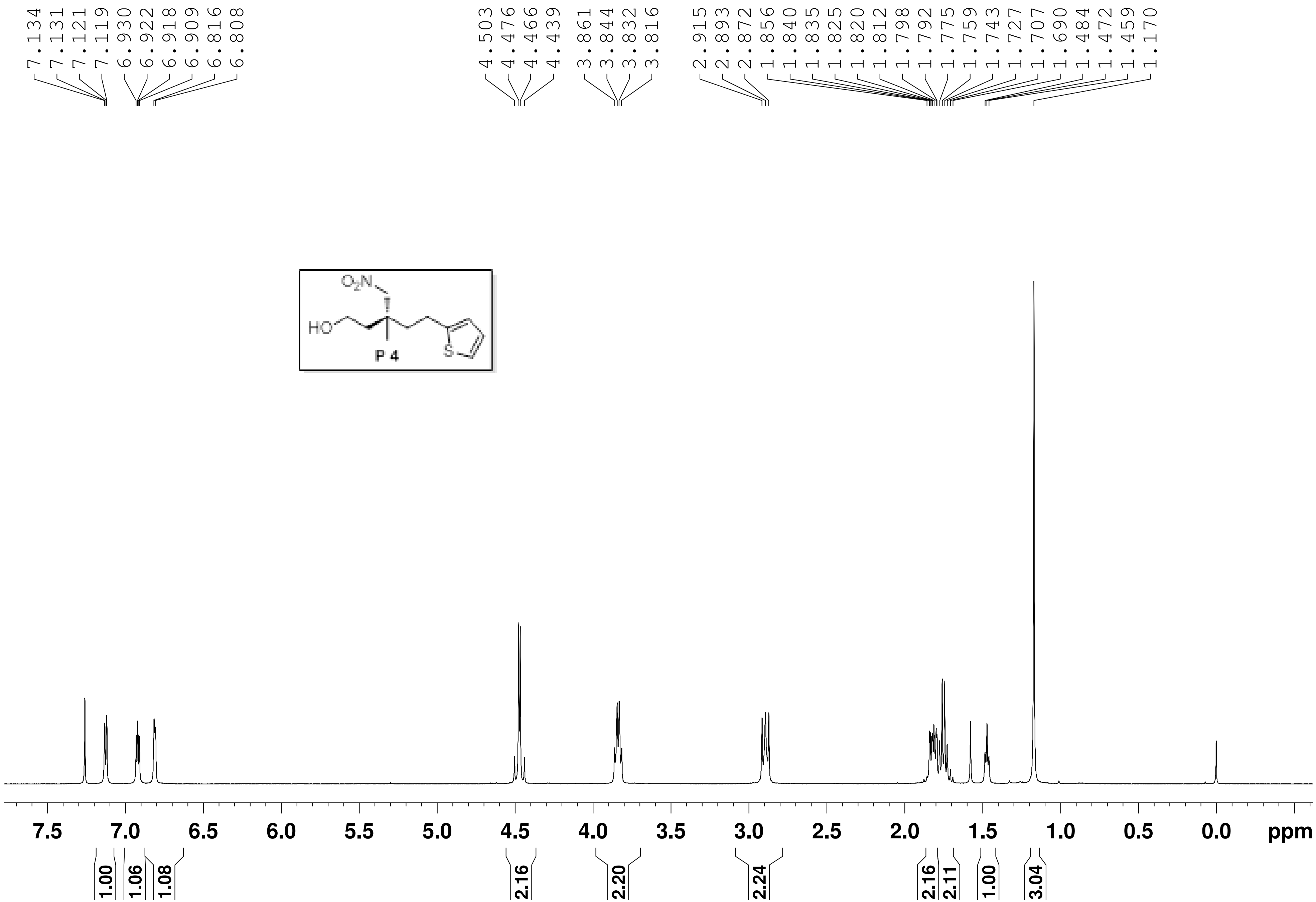


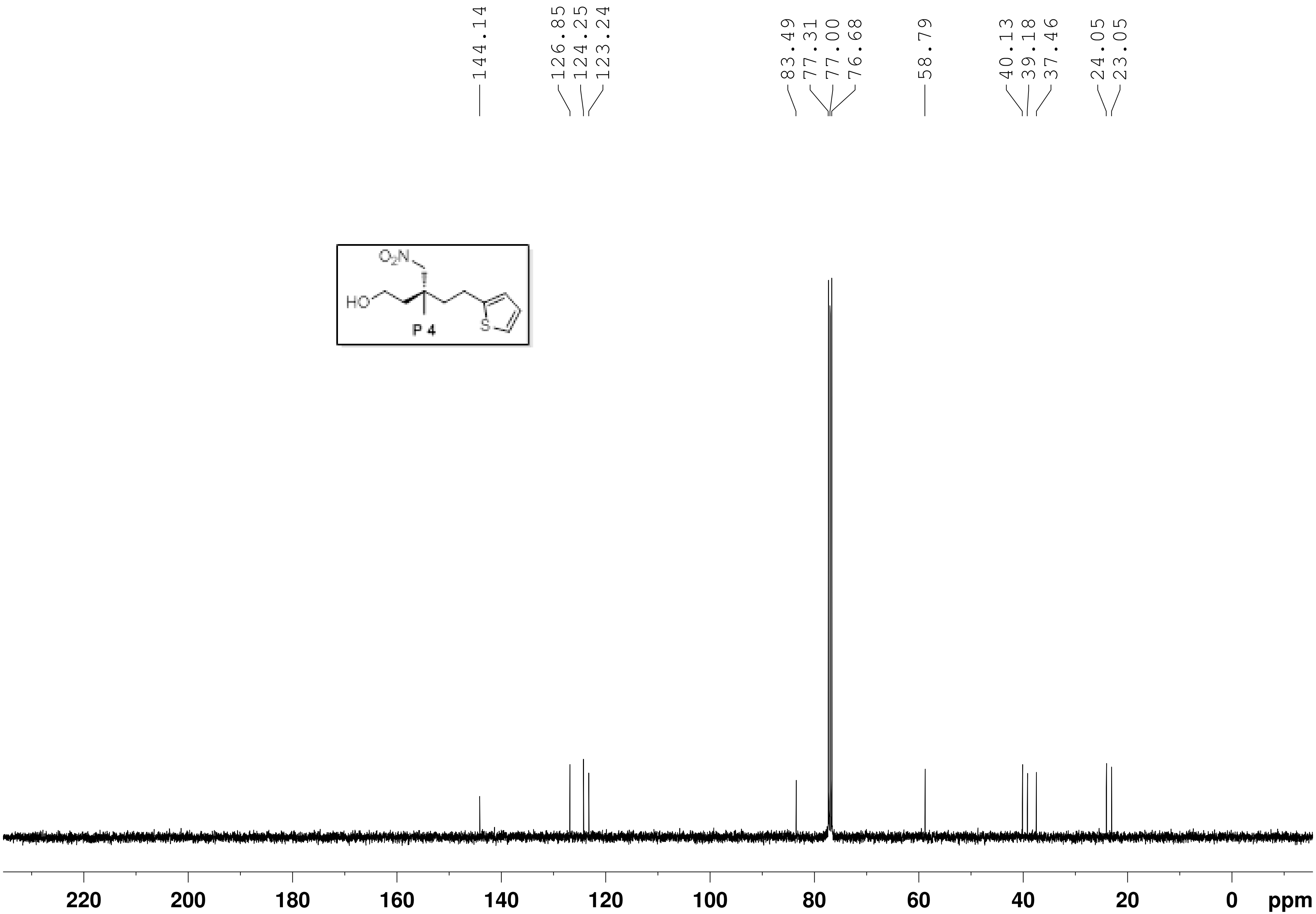
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.057	BB	0.2930	1721.53357	90.89281	50.2674
2	18.024	BB	0.3253	1703.21472	81.01857	49.7326

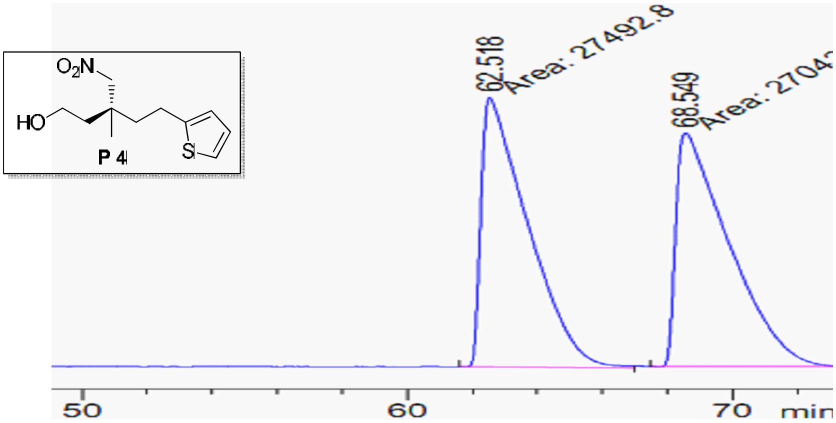


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.563	MM	0.3113	567.39661	30.37553	4.6744
2	17.259	MM	0.5190	1.15710e4	371.59860	95.3256


7.134
7.131
7.121
7.119
6.930
6.922
6.918
6.909
6.816
6.808
4.503
4.476
4.466
4.439
3.861
3.844
3.832
3.816
2.915
2.893
2.872
1.856
1.840
1.835
1.825
1.820
1.812
1.798
1.792
1.775
1.759
1.743
1.727
1.707
1.690
1.484
1.472
1.459
1.170
O_2N
HO
S
P 4
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
ppm
1.00
1.06
1.08
2.16
2.20
2.24
2.16
2.11
1.00
3.04

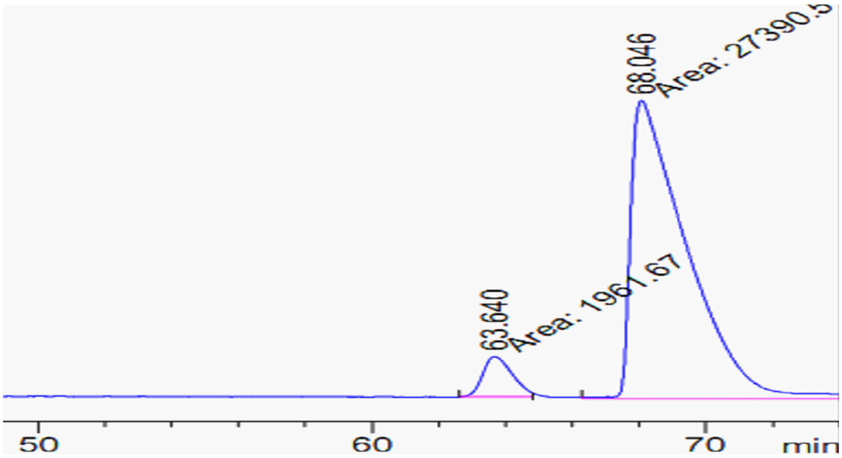

144.14
126.85
124.25
123.24
83.49
77.31
77.00
76.68
58.79
40.13
39.18
37.46
24.05
23.05
O2N
HO
S
P 4
220
200
180
160
140
120
100
80
60
40
20
0
ppm

ID-3 hex:ipr=97:3 1.0 ml/min

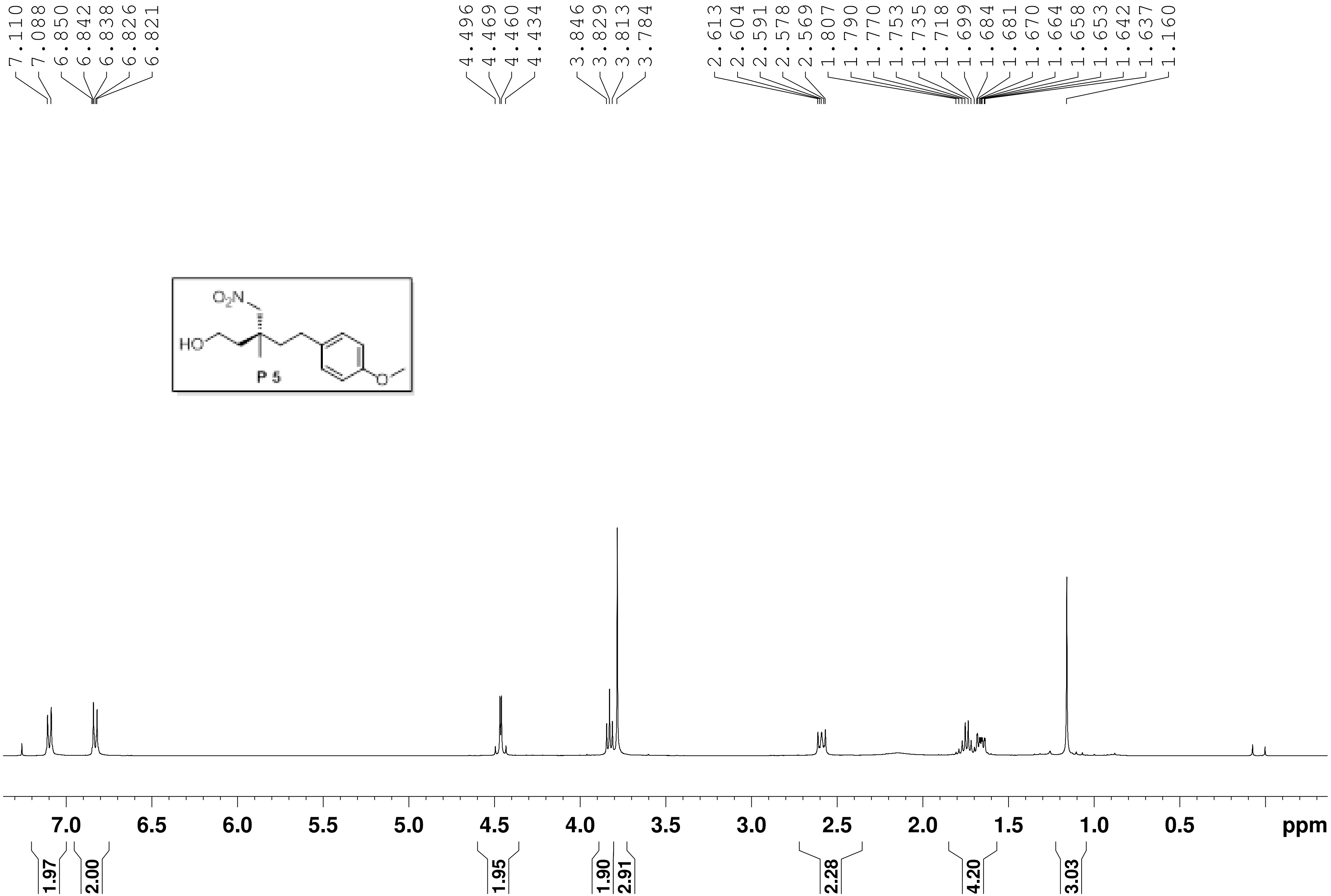


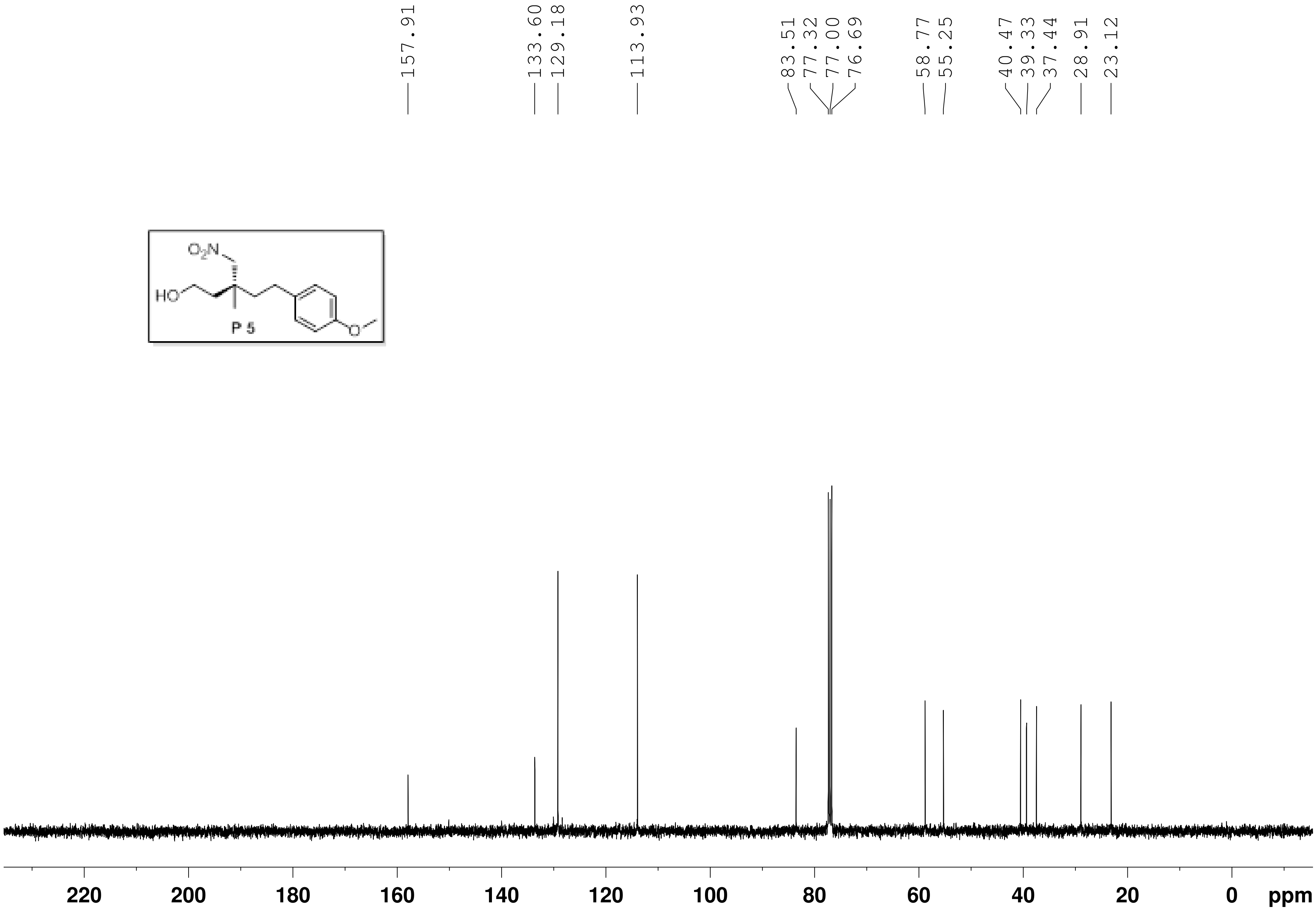
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	62.518	MM	1.6653	2.74928e4	275.14725	50.4133
2	68.549	MM	1.8885	2.70420e4	238.65352	49.5867



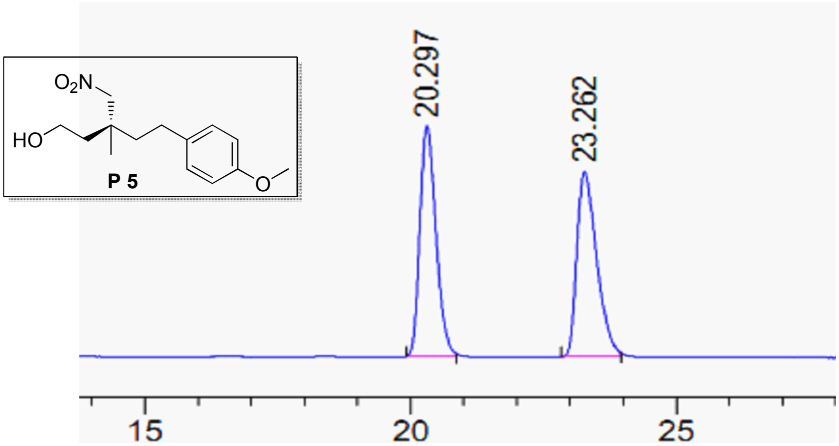
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	63.640	MM	1.0275	1961.67261	31.81915	6.6832
2	68.046	MM	1.9289	2.73905e4	236.66176	93.3168


7.110
7.088
6.850
6.842
6.838
6.826
6.821
4.496
4.469
4.460
4.434
3.846
3.829
3.813
3.784
2.613
2.604
2.591
2.578
2.569
1.807
1.790
1.770
1.753
1.735
1.718
1.699
1.684
1.681
1.670
1.664
1.658
1.653
1.642
1.637
1.160
O2N
HO
P 5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.97
2.00
1.95
1.90
2.91
2.28
4.20
3.03



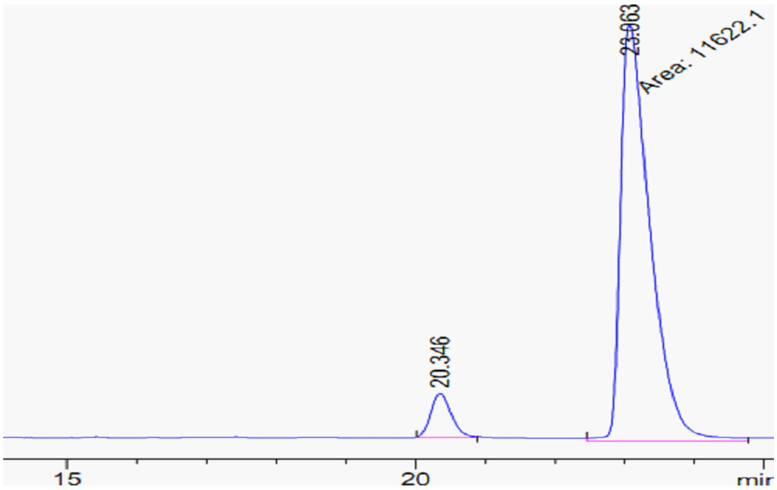
157.91
133.60
129.18
113.93
83.51
77.32
77.00
76.69
58.77
55.25
40.47
39.33
37.44
28.91
23.12
220
200
180
160
140
120
100
80
60
40
20
0
ppm
O2N
HO
O
P 5

ID-3 hex : ipr = 90 : 10 1.0 mL/min

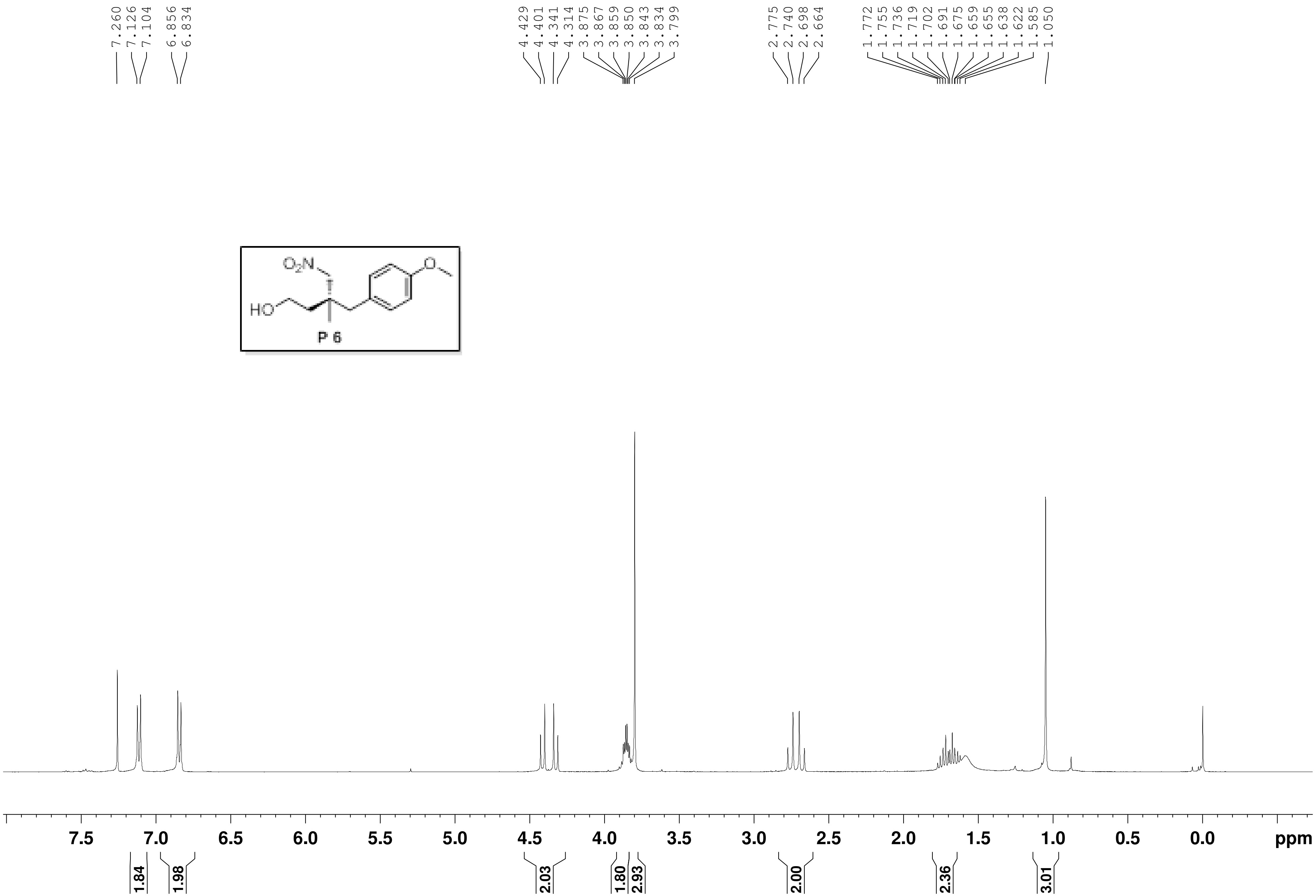


Signal 1: DAD1 A, Sig=220,16 Ref=360,100

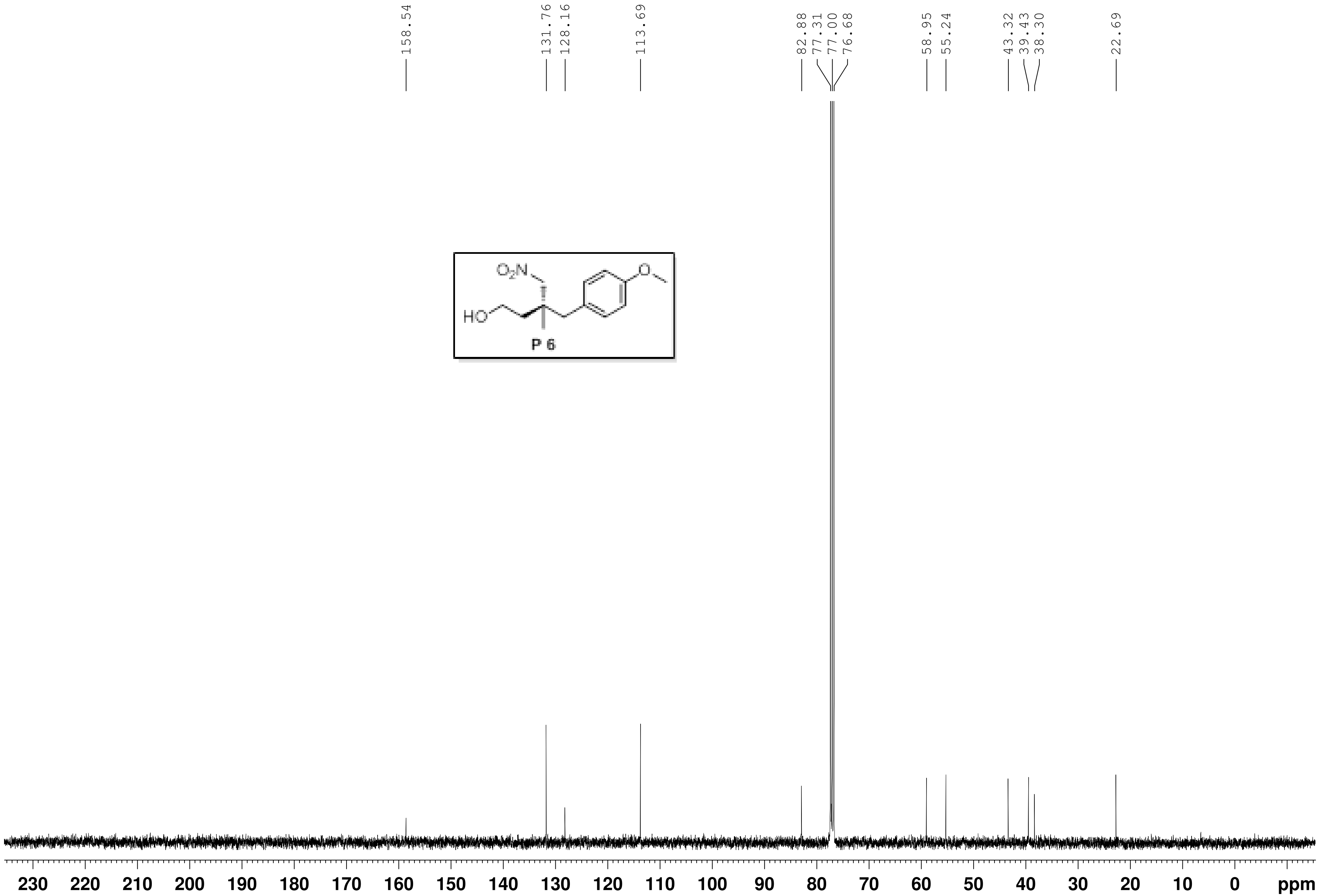
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.297	BB	0.3265	3436.25171	162.65038	50.2038
2	23.262	PB	0.4005	3408.34863	130.59279	49.7962



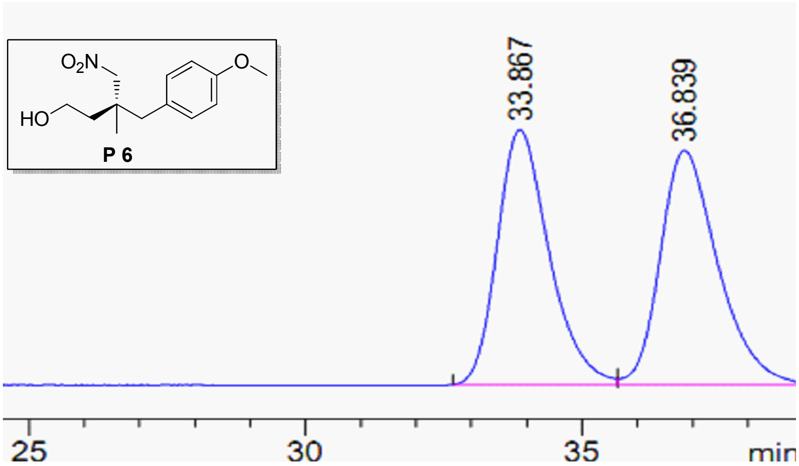
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.346	BB	0.3195	854.50879	41.62615	6.8489
2	23.063	MM	0.4929	1.16221e4	392.99231	93.1511



7.260
7.126
7.104
6.856
6.834
4.429
4.401
4.341
4.314
3.875
3.867
3.859
3.850
3.843
3.834
3.799
2.775
2.740
2.698
2.664
1.772
1.755
1.736
1.719
1.702
1.691
1.675
1.659
1.655
1.638
1.622
1.585
1.050
O_2N
HO
P 6
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 ppm
1.84 1.98 2.03 1.80 2.93 2.00 2.36 3.01

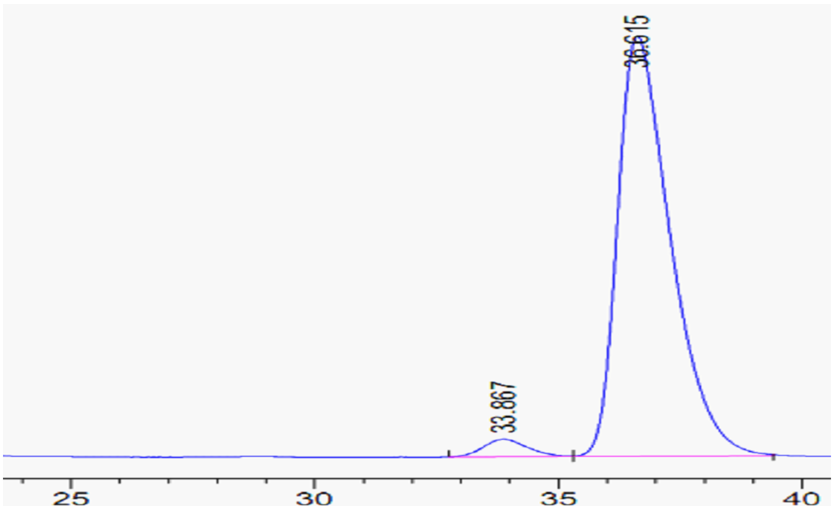

158.54
131.76
128.16
113.69
82.88
77.31
77.00
76.68
58.95
55.24
43.32
39.43
38.30
22.69
O2N
HO
P 6
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

AD hex:ipr=95:5 1.0 ml/min

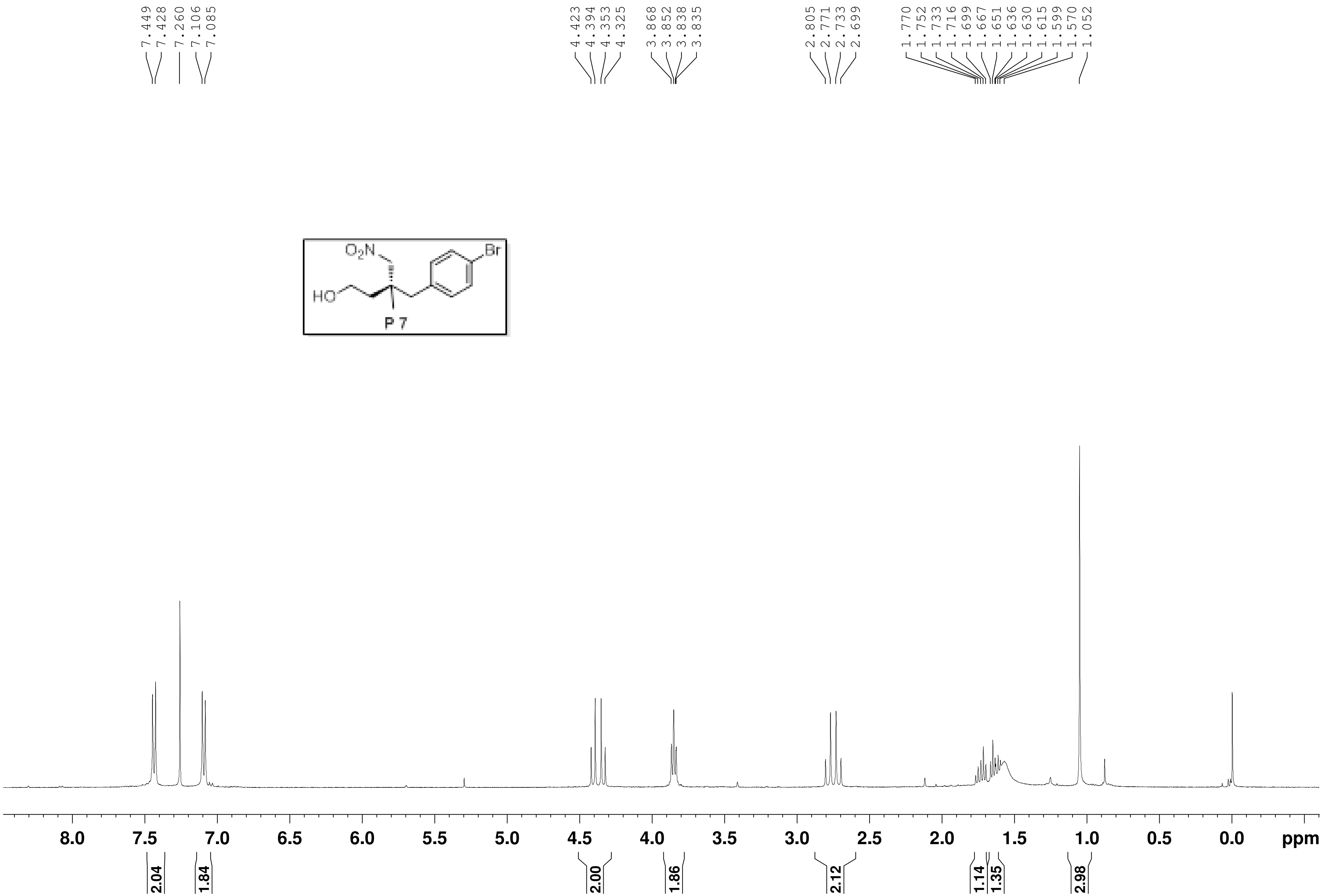


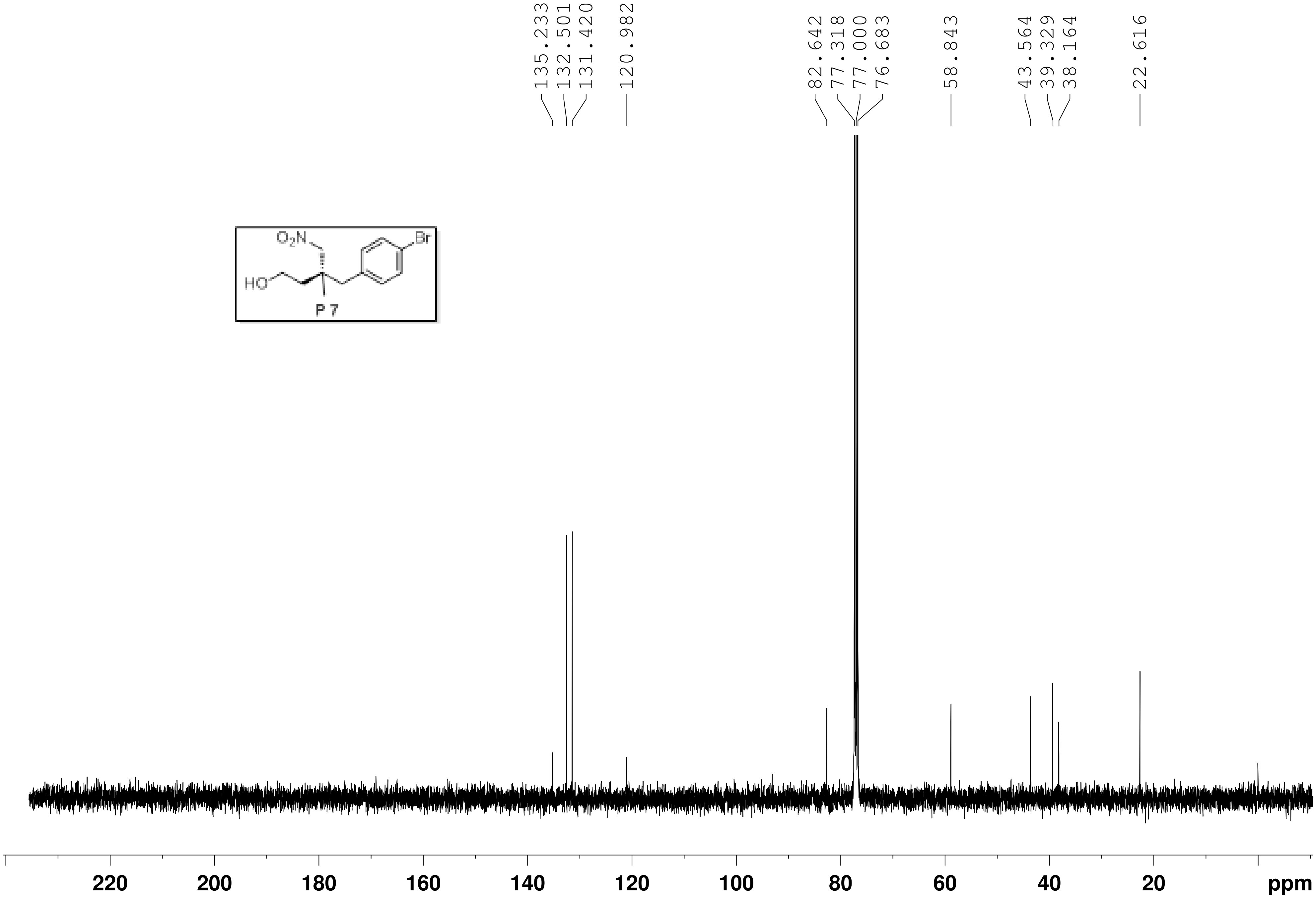
Signal 1: DAD1 B, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.867	BV	1.0002	8599.30957	131.27686	49.5032
2	36.839	VB	1.1051	8771.89258	120.53057	50.4968

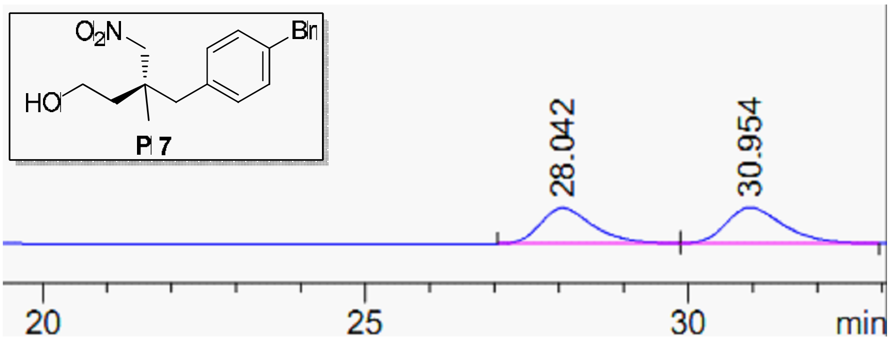


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.867	BV	0.9450	1206.83374	18.79728	3.4435
2	36.615	VB	1.1467	3.38403e4	447.27518	96.5565


7.449
7.428
7.260
7.106
7.085
4.423
4.394
4.353
4.325
3.868
3.852
3.838
3.835
2.805
2.771
2.733
2.699
1.770
1.752
1.733
1.716
1.699
1.667
1.651
1.636
1.630
1.615
1.599
1.570
1.052
O_2N
HO
Br
P 7
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 ppm
2.04
1.84
2.00
1.86
2.12
1.14
1.35
2.98

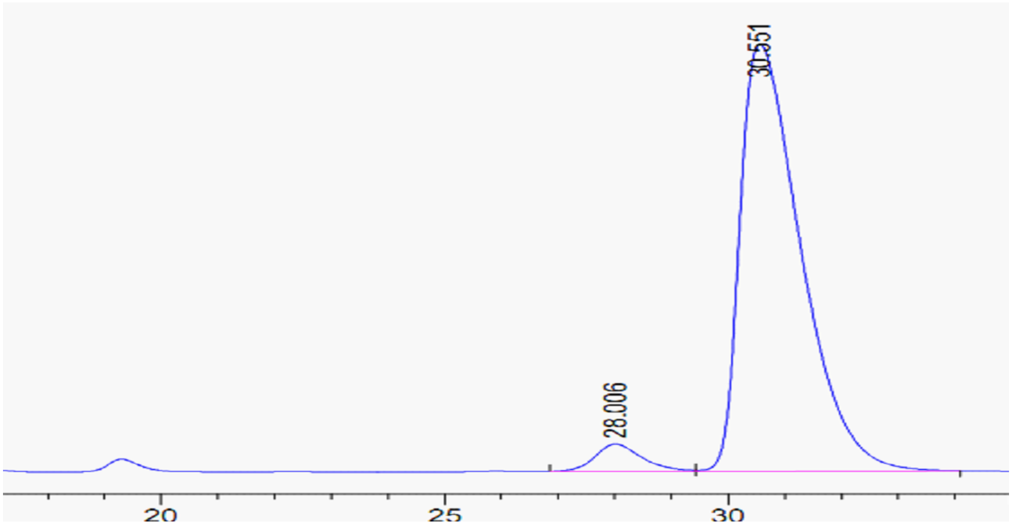

135.233
132.501
131.420
120.982
82.642
77.318
77.000
76.683
58.843
43.564
39.329
38.164
22.616
O2N
Br
HO
P 7
220
200
180
160
140
120
100
80
60
40
20
ppm

AD hex:ipr=95:5 1.0 ml/min

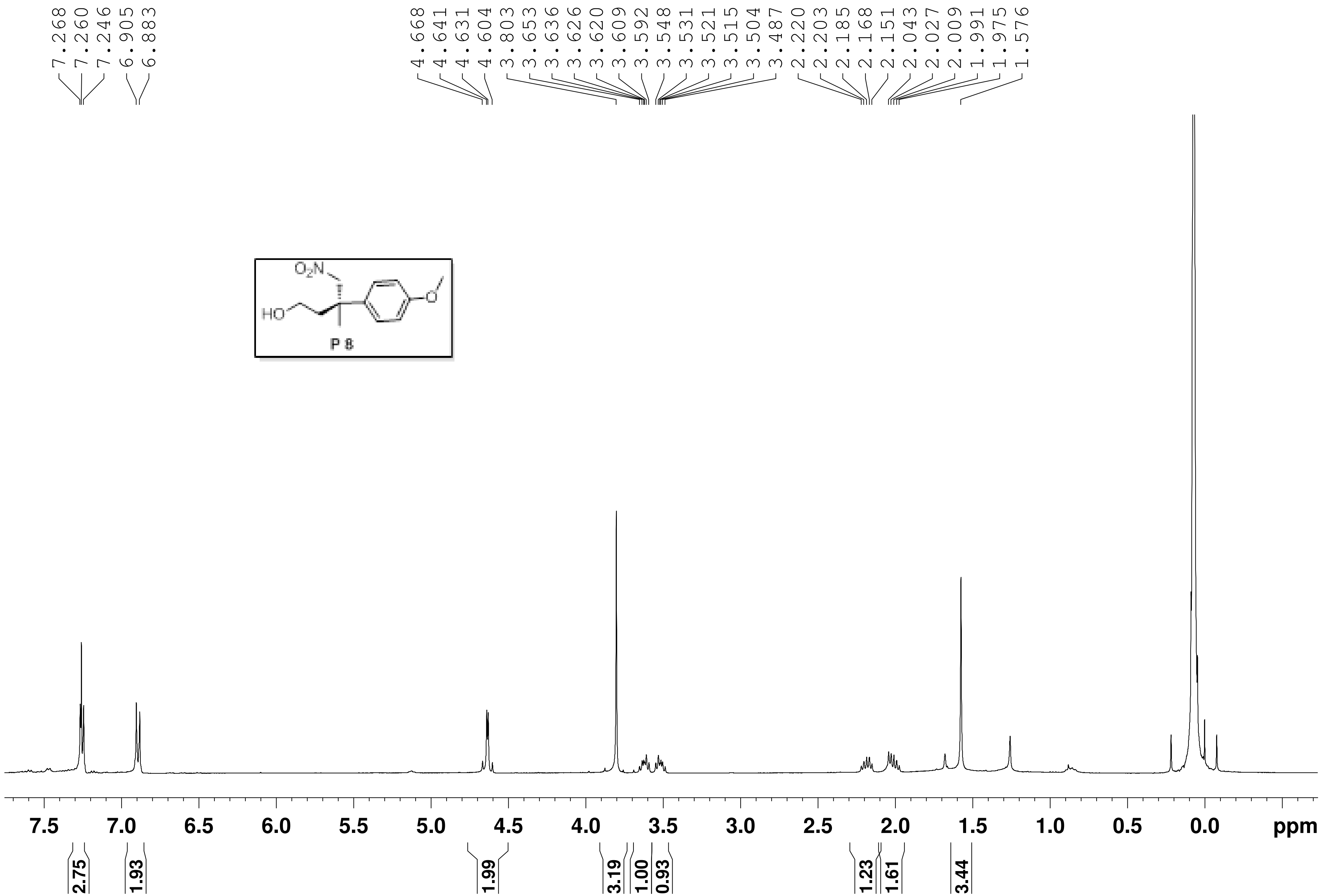


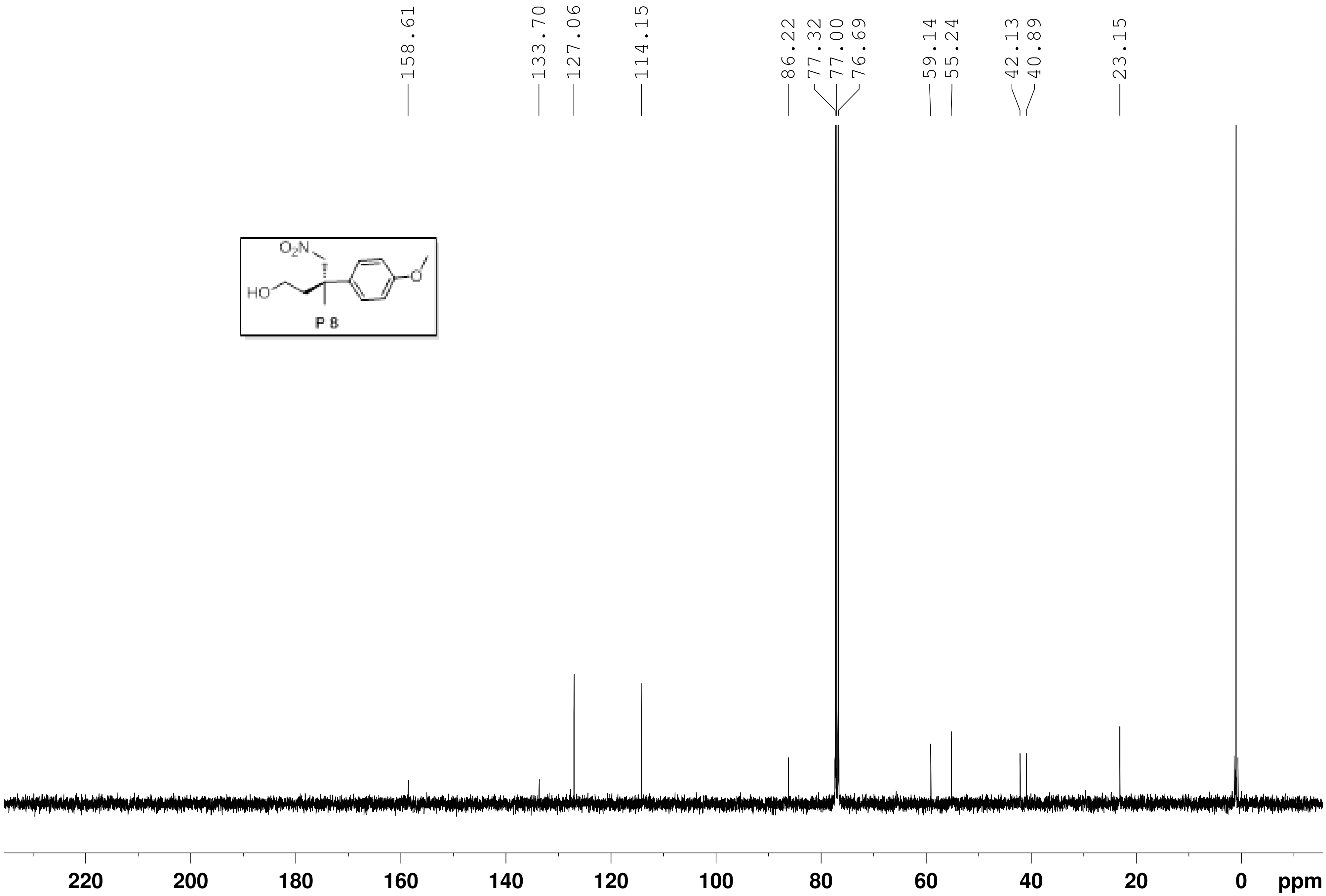
Signal 1: DAD1 B, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.042	BB	0.8762	4280.18799	74.29037	47.6748
2	30.954	BB	0.9516	4697.69922	74.91782	52.3252



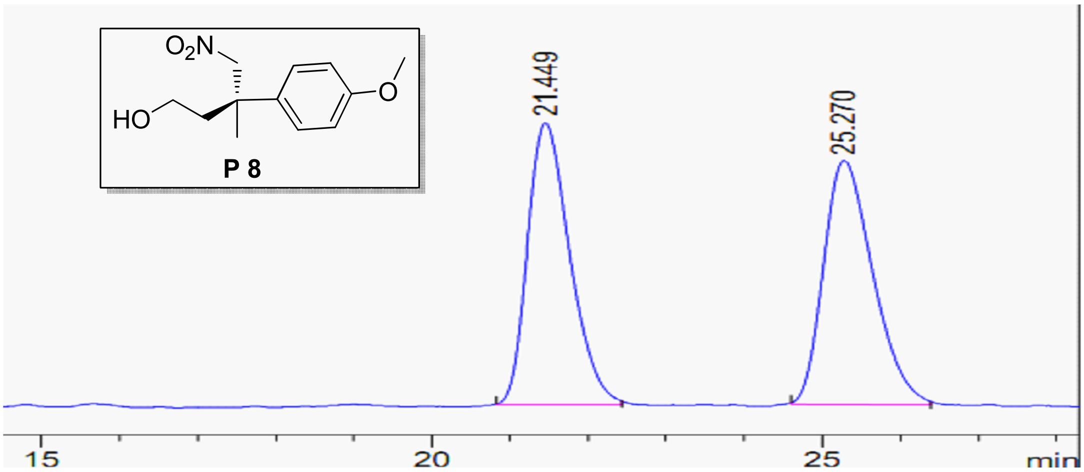
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.006	BV	0.8858	4478.40820	76.18421	4.8796
2	30.551	VB	1.1320	8.73004e4	1173.40027	95.1204


7.268
7.260
7.246
6.905
6.883
4.668
4.641
4.631
4.604
3.803
3.653
3.636
3.626
3.620
3.609
3.592
3.548
3.531
3.521
3.515
3.504
3.487
2.220
2.203
2.185
2.168
2.151
2.043
2.027
2.009
1.991
1.975
1.576
O2N
HO
P 8
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
ppm
2.75
1.93
1.99
3.19
1.00
0.93
1.23
1.61
3.44



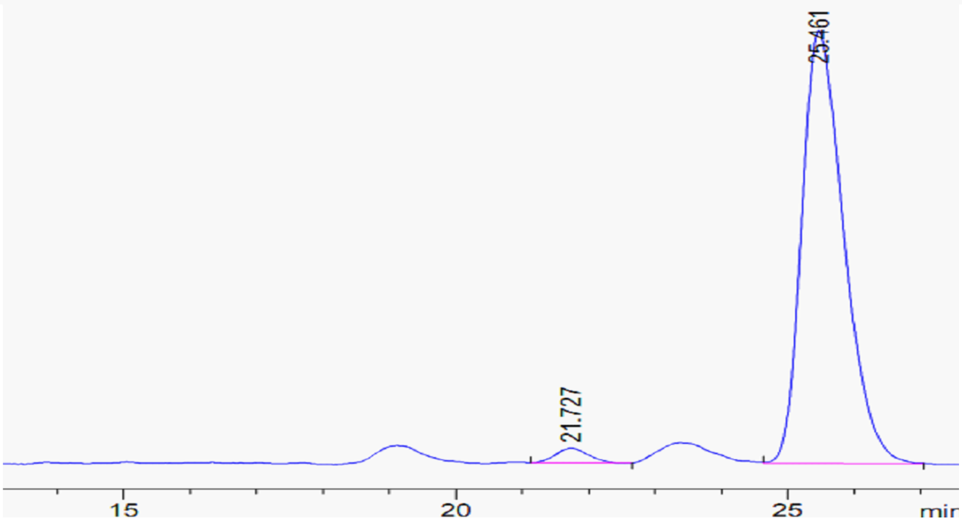
158.61
133.70
127.06
114.15
86.22
77.32
77.00
76.69
59.14
55.24
42.13
40.89
23.15
O_2N
HO
O
P 8
220
200
180
160
140
120
100
80
60
40
20
0
ppm

OD-H hex:ipr=80:20 0.8 ml/min

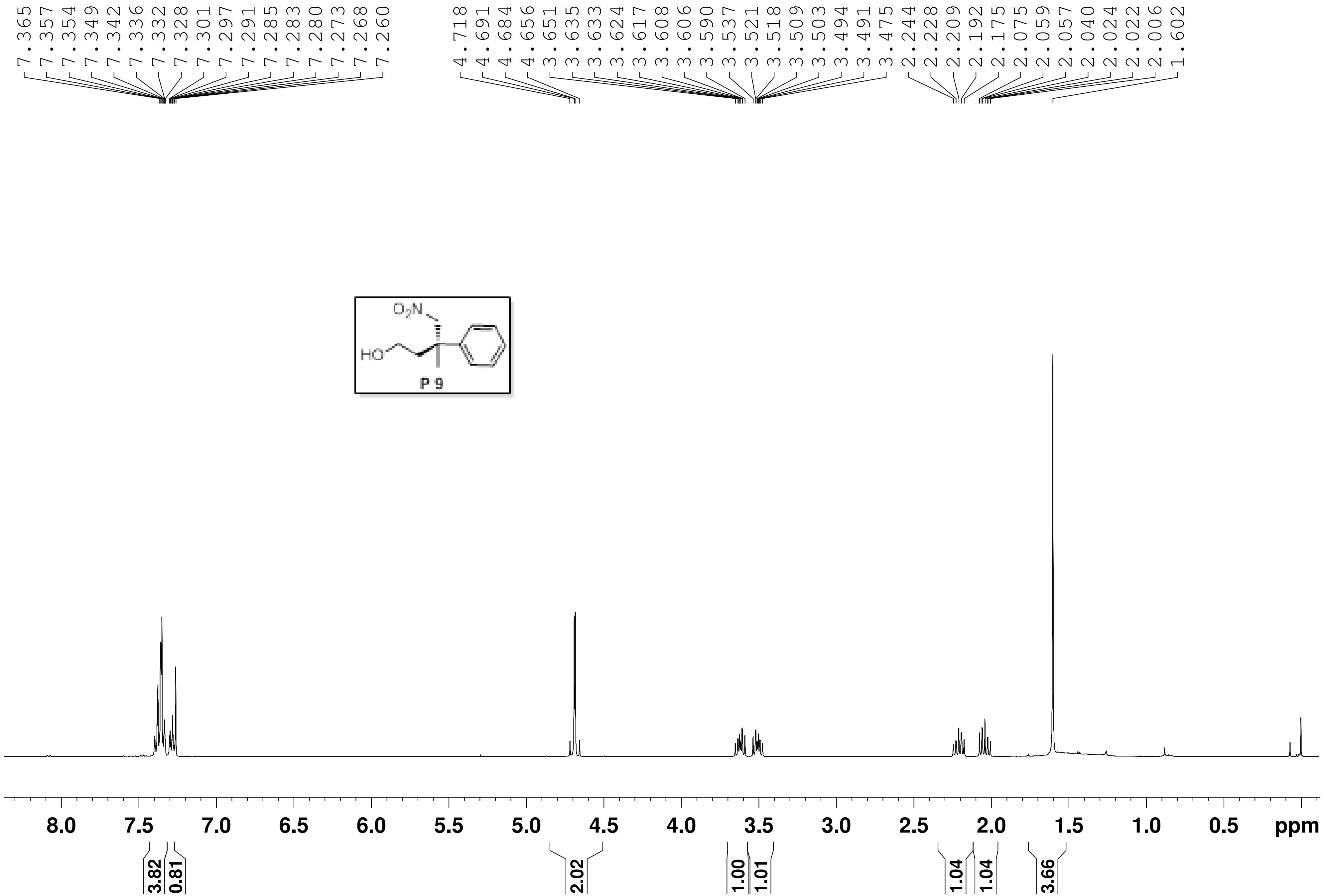


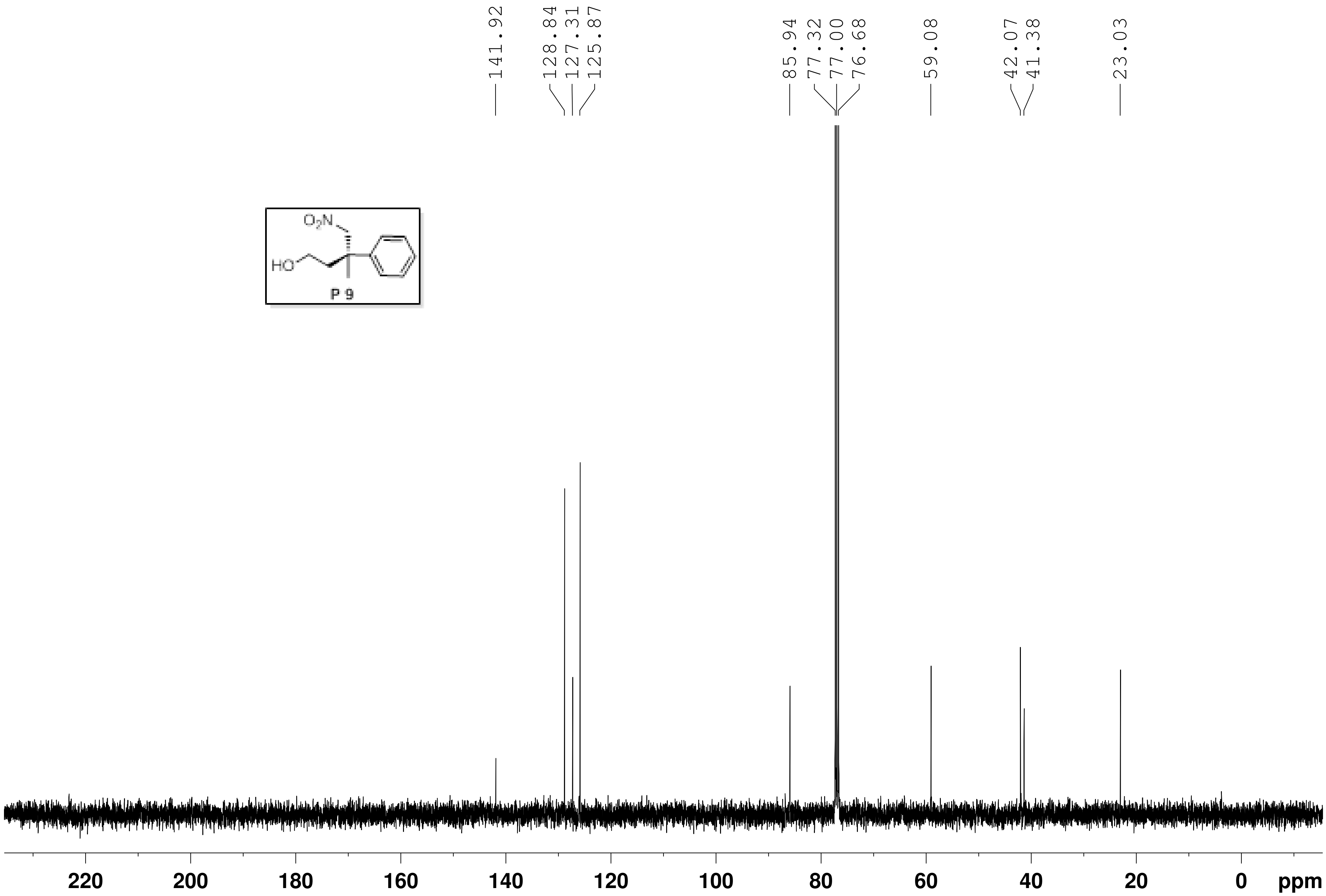
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.449	BB	0.5855	9533.71191	251.91045	49.9029
2	25.270	BB	0.6751	9570.79687	217.63286	50.0971

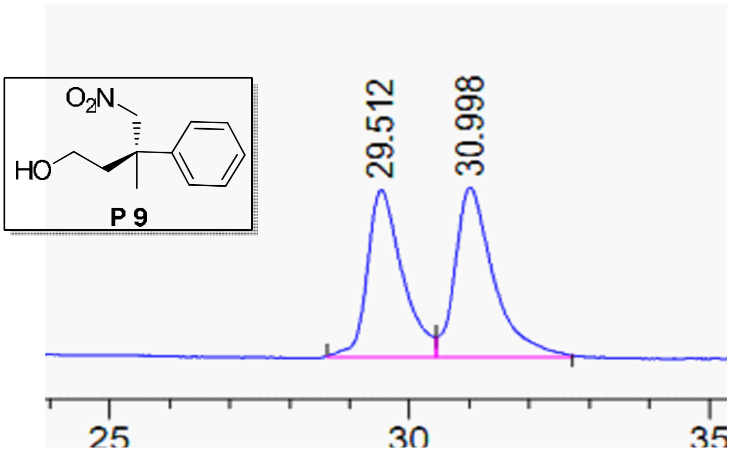


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.727	PB	0.4977	221.53888	6.49913	2.5887
2	25.461	VB	0.6898	8336.24609	189.28320	97.4113


7.365
7.357
7.354
7.349
7.342
7.336
7.332
7.328
7.301
7.297
7.291
7.285
7.283
7.280
7.273
7.268
7.260
4.718
4.691
4.684
4.656
3.651
3.635
3.633
3.624
3.617
3.608
3.606
3.590
3.537
3.521
3.518
3.509
3.503
3.494
3.491
3.475
2.244
2.228
2.209
2.192
2.175
2.075
2.059
2.057
2.040
2.024
2.022
2.006
1.602
O2N
HO
P 9
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.82
0.81
2.02
1.00
1.01
1.04
1.04
3.66

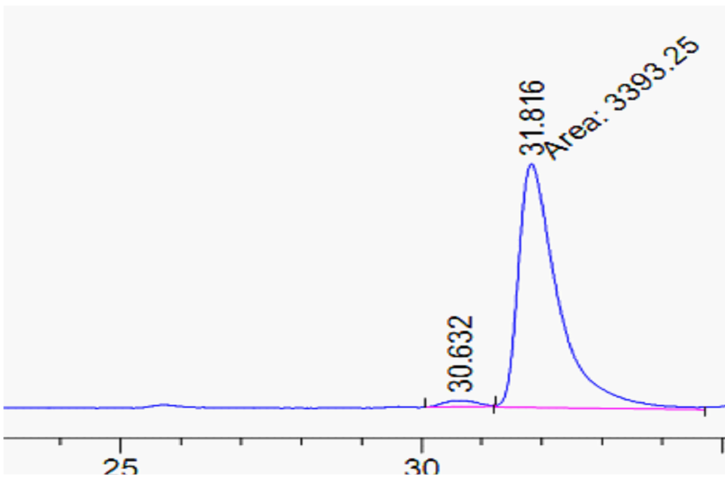

141.92
128.84
127.31
125.87
85.94
77.32
77.00
76.68
59.08
42.07
41.38
23.03
O2N
HO
P 9
220
200
180
160
140
120
100
80
60
40
20
0
ppm

IA-3 hex:ipr=95:5 1.0 ml/min

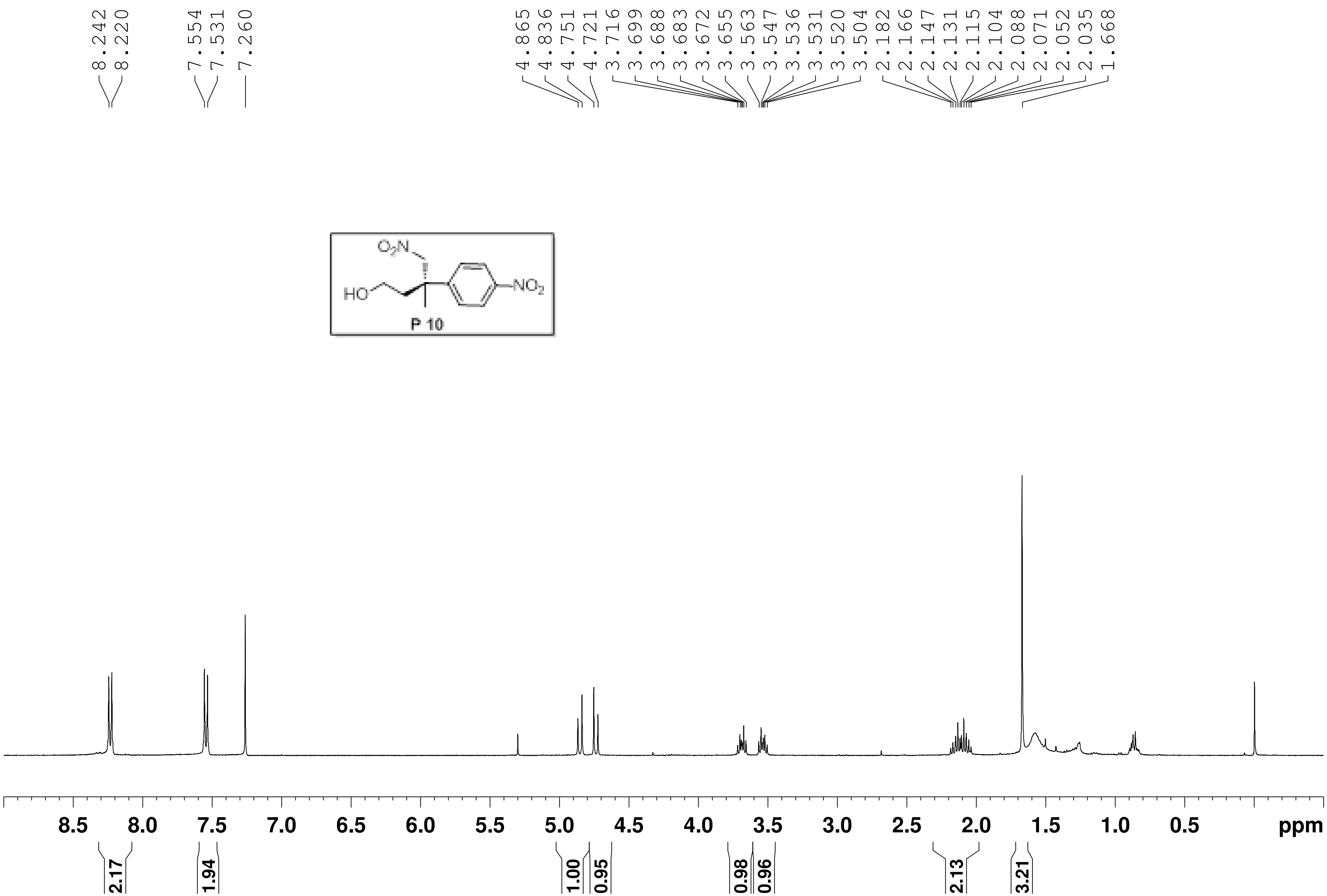


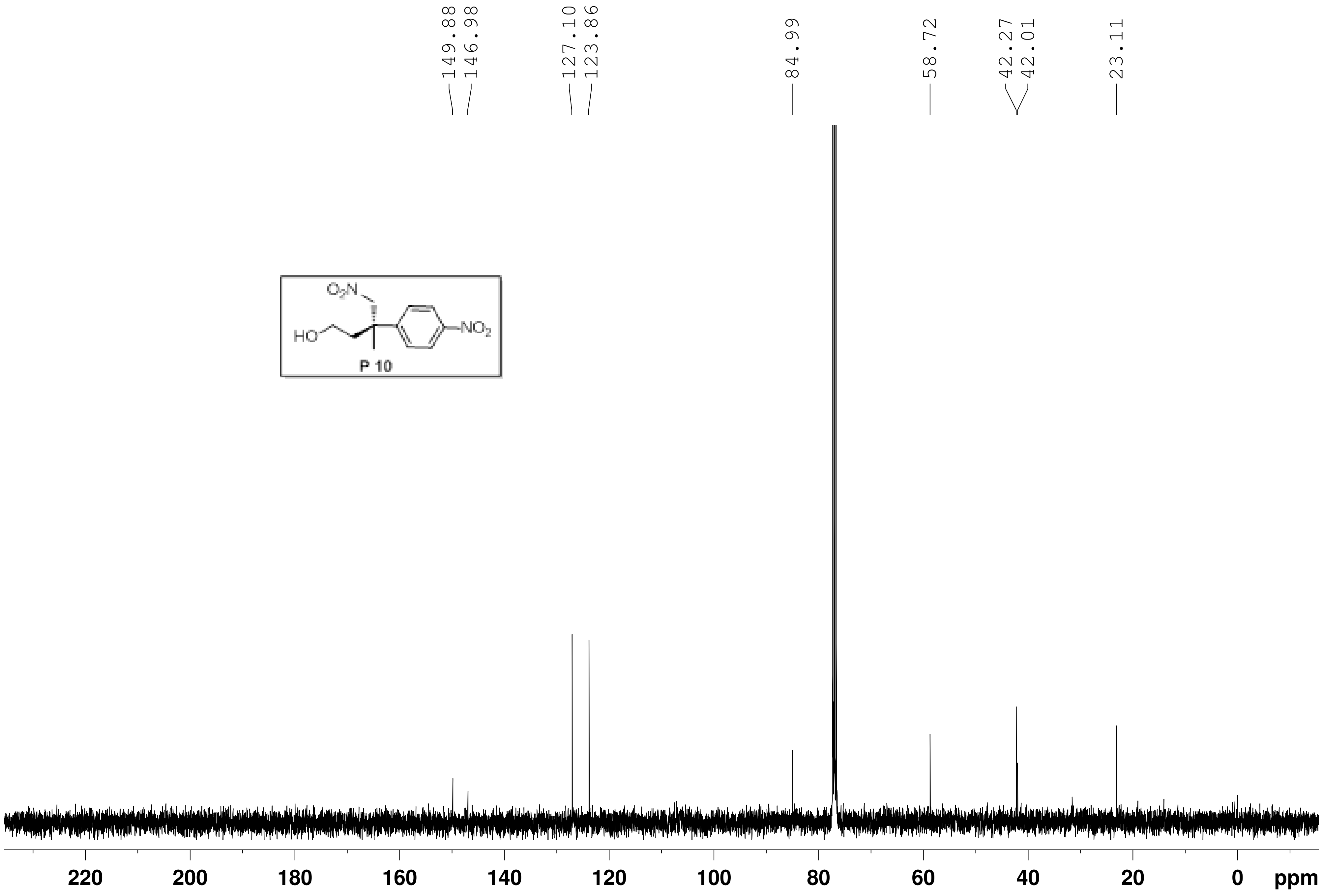
Signal 1: DAD1 B, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.512	BV	0.6172	967.35370	23.45455	47.4566
2	30.998	VB	0.6543	1071.04346	23.74224	52.5434

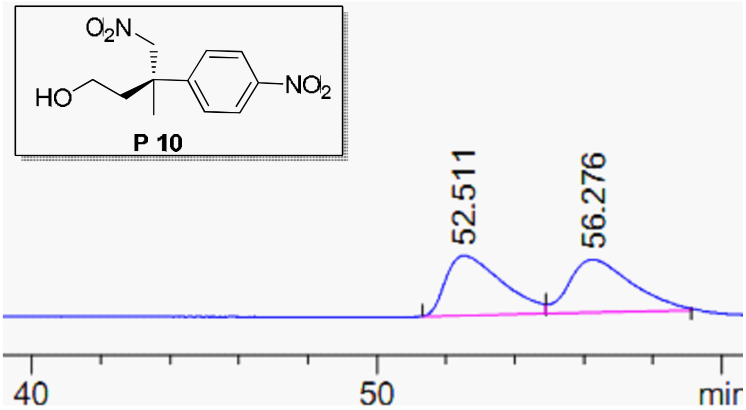


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.632	PV	0.4812	76.63940	1.91375	2.2087
2	31.816	MM	0.7726	3393.24976	73.20195	97.7913


8.242
8.220
7.554
7.531
7.260
4.865
4.836
4.751
4.721
3.716
3.699
3.688
3.683
3.672
3.655
3.563
3.547
3.536
3.531
3.520
3.504
2.182
2.166
2.147
2.131
2.115
2.104
2.088
2.071
2.052
2.035
1.668
O2N
HO
NO2
P 10
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 ppm
2.17
1.94
1.00
0.95
0.98
0.96
2.13
3.21

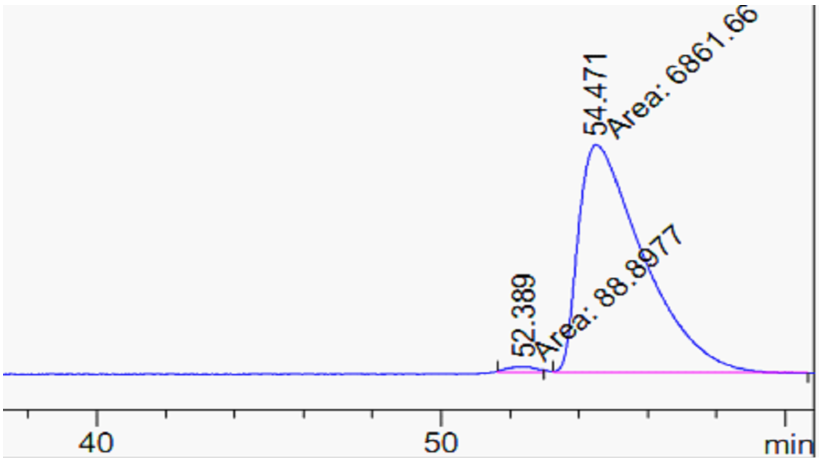

149.88
146.98
127.10
123.86
84.99
58.72
42.27
42.01
23.11
O_2N
HO
NO_2
P 10
220
200
180
160
140
120
100
80
60
40
20
0
ppm

OD-H hex:ipr=90:10 1.0 ml/min

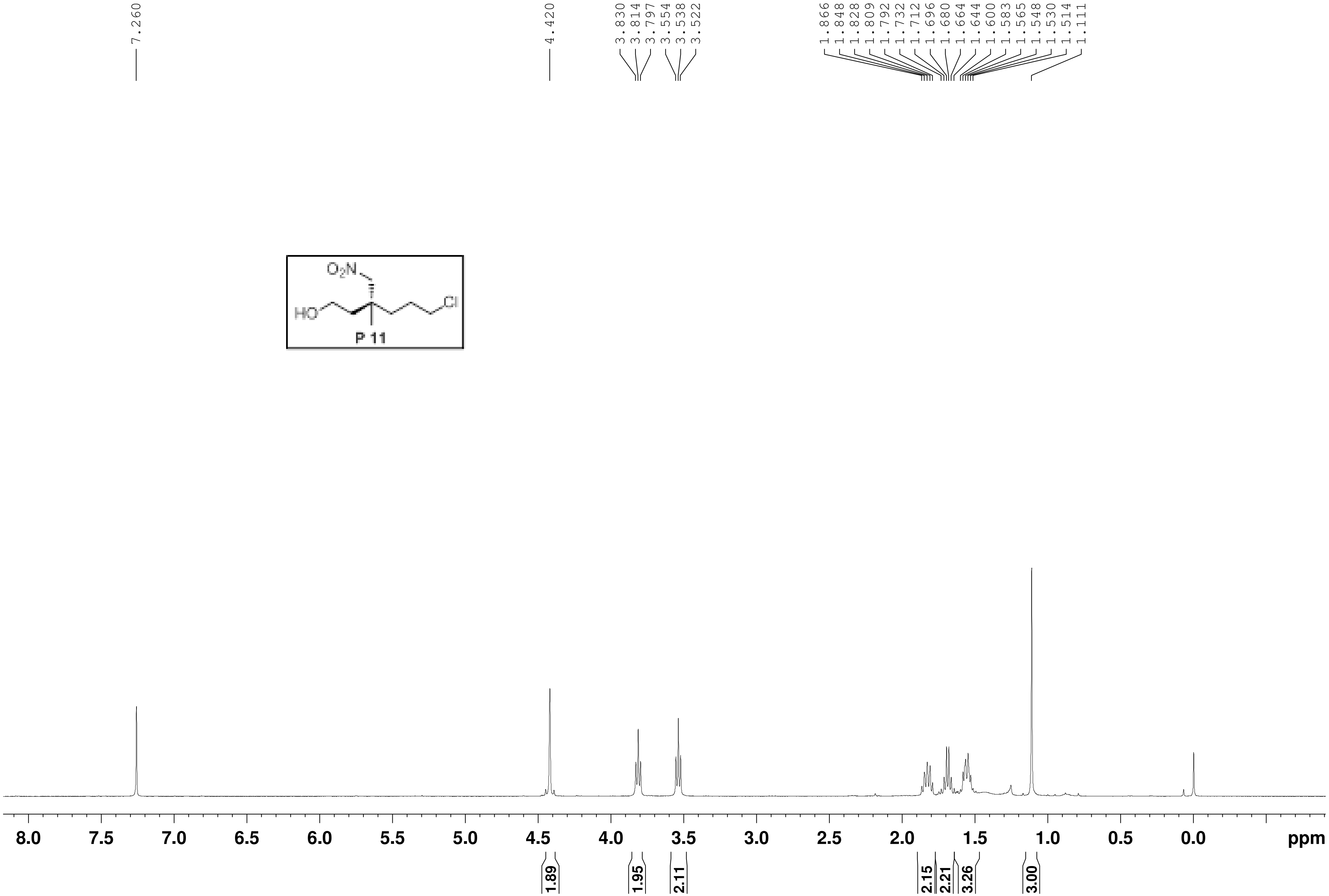


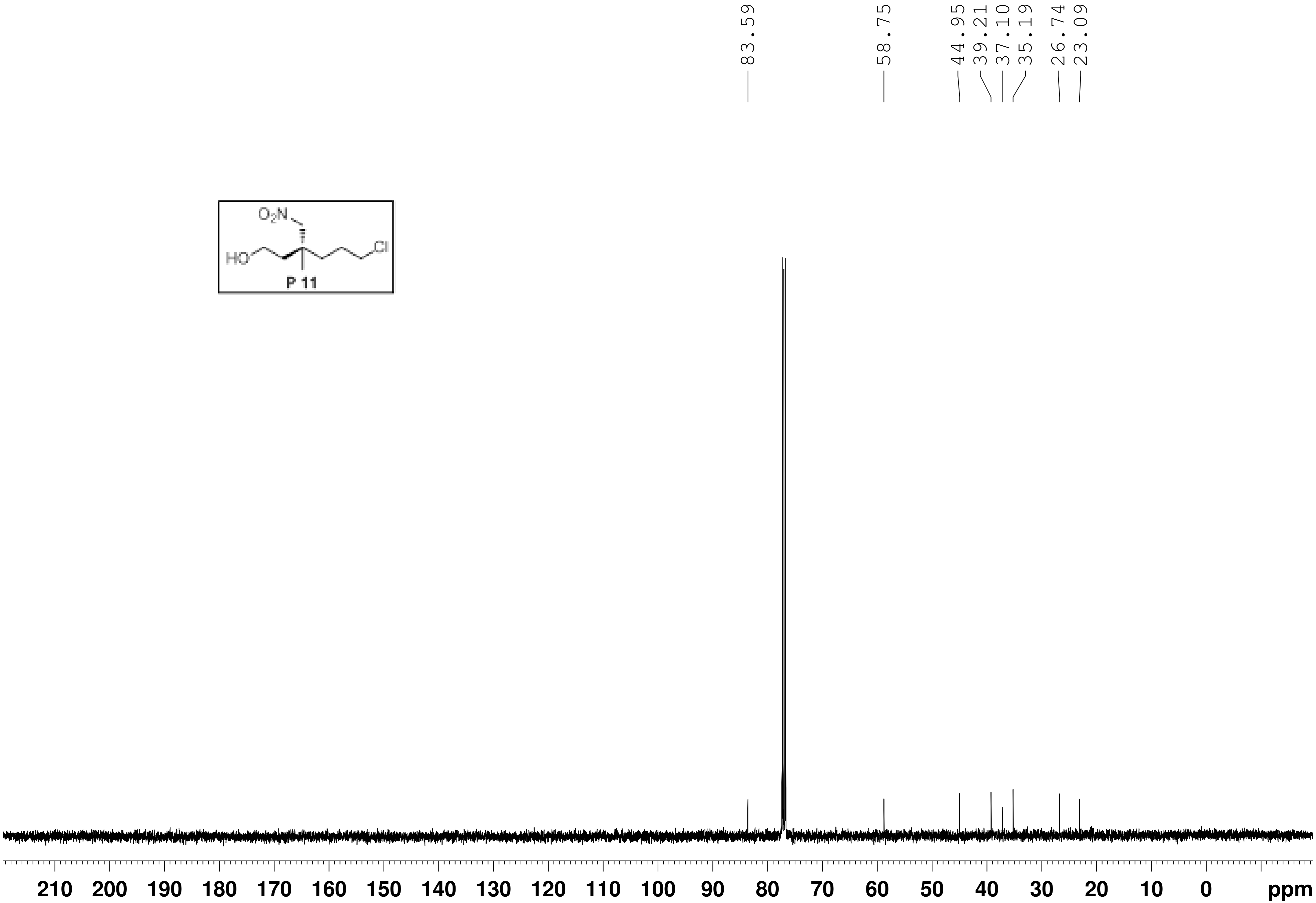
Signal 1: DAD1 B, Sig=215,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.511	BV	1.4028	5430.53564	47.82455	50.2148
2	56.276	VB	1.5215	5384.07031	42.28566	49.7852

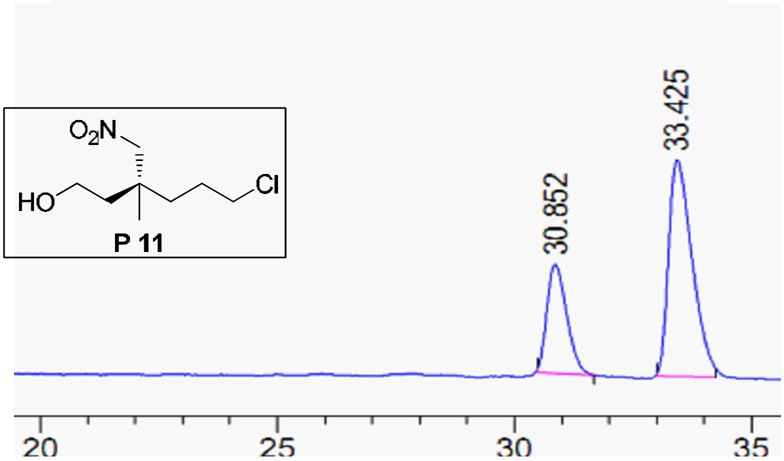


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.389	MM	1.0188	88.89774	1.45428	1.2790
2	54.471	MM	2.1933	6861.66064	52.14101	98.7210


7.260
4.420
3.830
3.814
3.797
3.554
3.538
3.522
1.866
1.848
1.828
1.809
1.792
1.732
1.712
1.696
1.680
1.664
1.644
1.600
1.583
1.565
1.548
1.530
1.514
1.111
O2N
HO
Cl
P 11
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 ppm
1.89
1.95
2.11
2.15
2.21
3.26
3.00

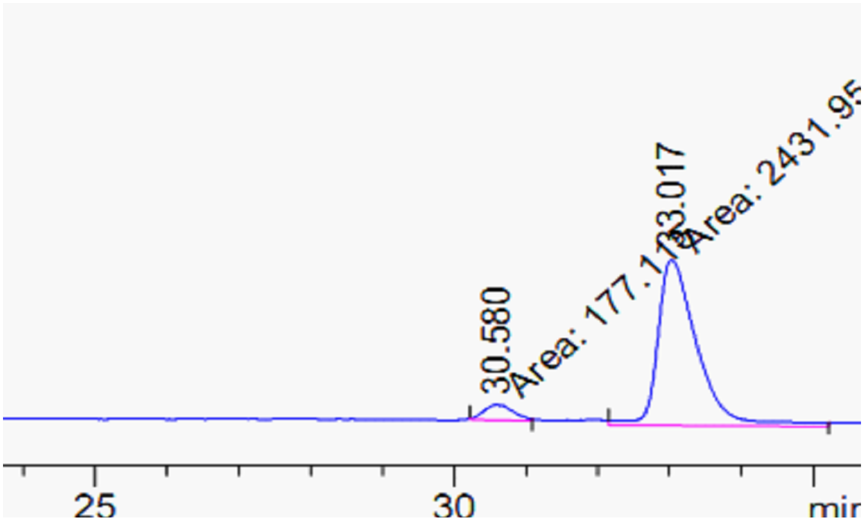

83.59
58.75
44.95
39.21
37.10
35.19
26.74
23.09
O2N
HO
Cl
P 11
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

ID-3 hex:ipr=97:3 1 ml/min

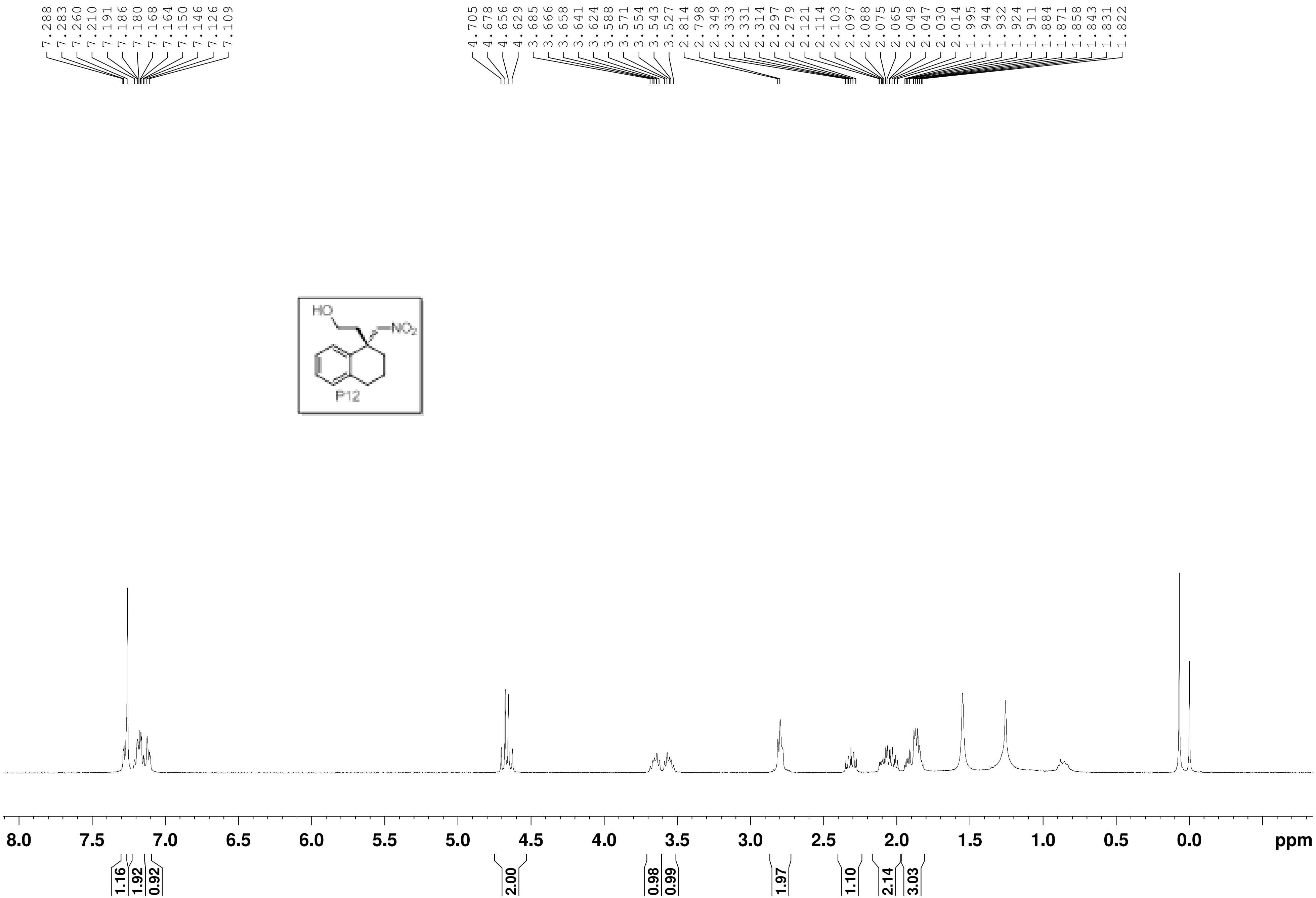


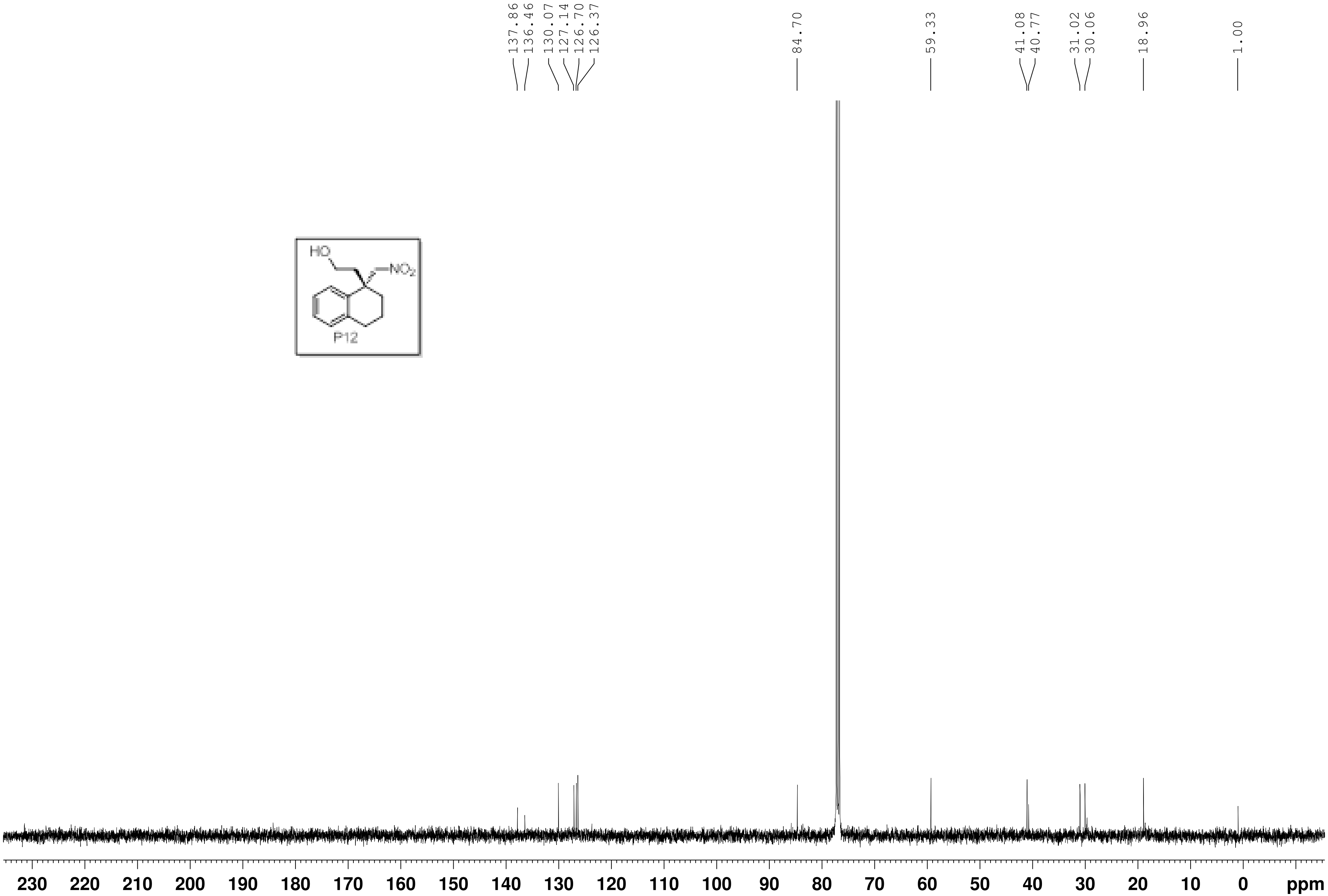
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.852	BB	0.4633	862.80481	29.49293	30.0349
2	33.425	BB	0.5160	2009.86633	58.33334	69.9651

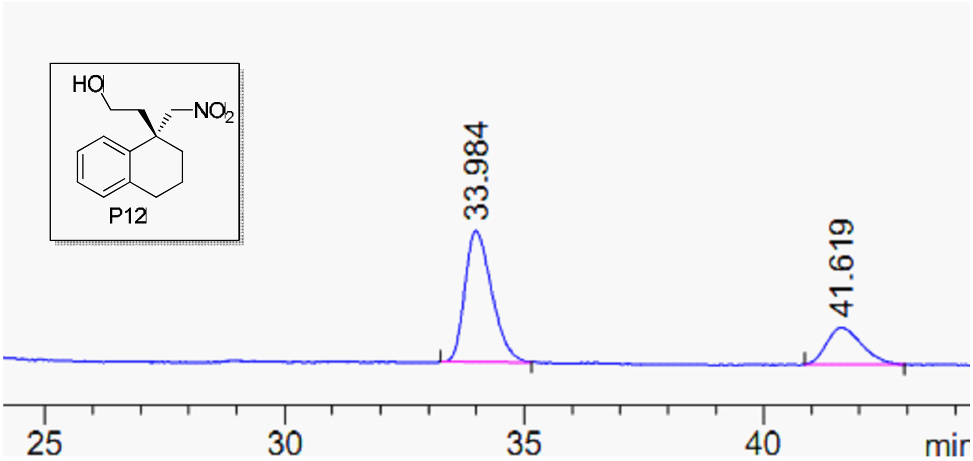


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.580	MM	0.4895	177.11530	6.03042	6.7884
2	33.017	MM	0.6464	2431.95459	62.70845	93.2116


7.288
7.283
7.260
7.210
7.191
7.186
7.180
7.168
7.164
7.150
7.146
7.126
7.109
4.705
4.678
4.656
4.629
3.685
3.666
3.658
3.641
3.624
3.588
3.571
3.554
3.543
3.527
2.814
2.798
2.349
2.333
2.331
2.314
2.297
2.279
2.121
2.114
2.103
2.097
2.088
2.075
2.065
2.049
2.047
2.030
2.014
1.995
1.944
1.932
1.924
1.911
1.884
1.871
1.858
1.843
1.831
1.822
HO
NO2
P12
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
ppm
1.16
1.92
0.92
2.00
0.98
0.99
1.97
1.10
2.14
3.03

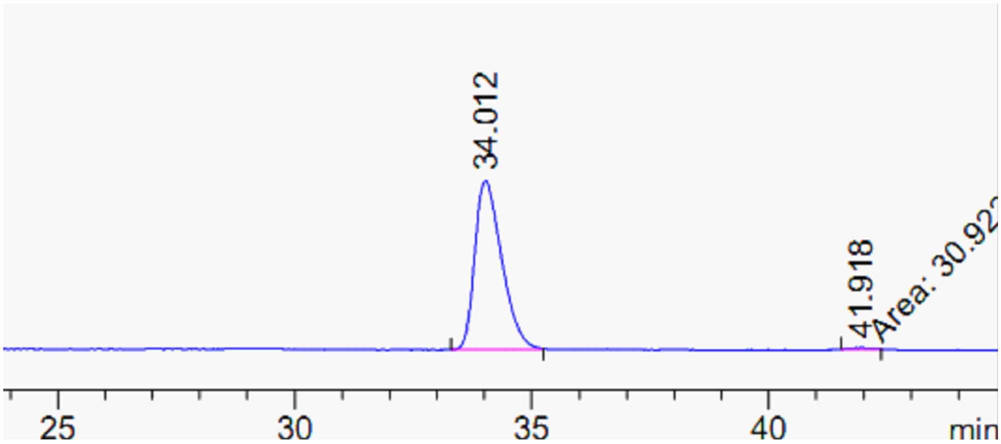

137.86
136.46
130.07
127.14
126.70
126.37
84.70
59.33
41.08
40.77
31.02
30.06
18.96
1.00
HO
NO2
P12
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

ID-3 hex:ipr=97:3 1 ml/min

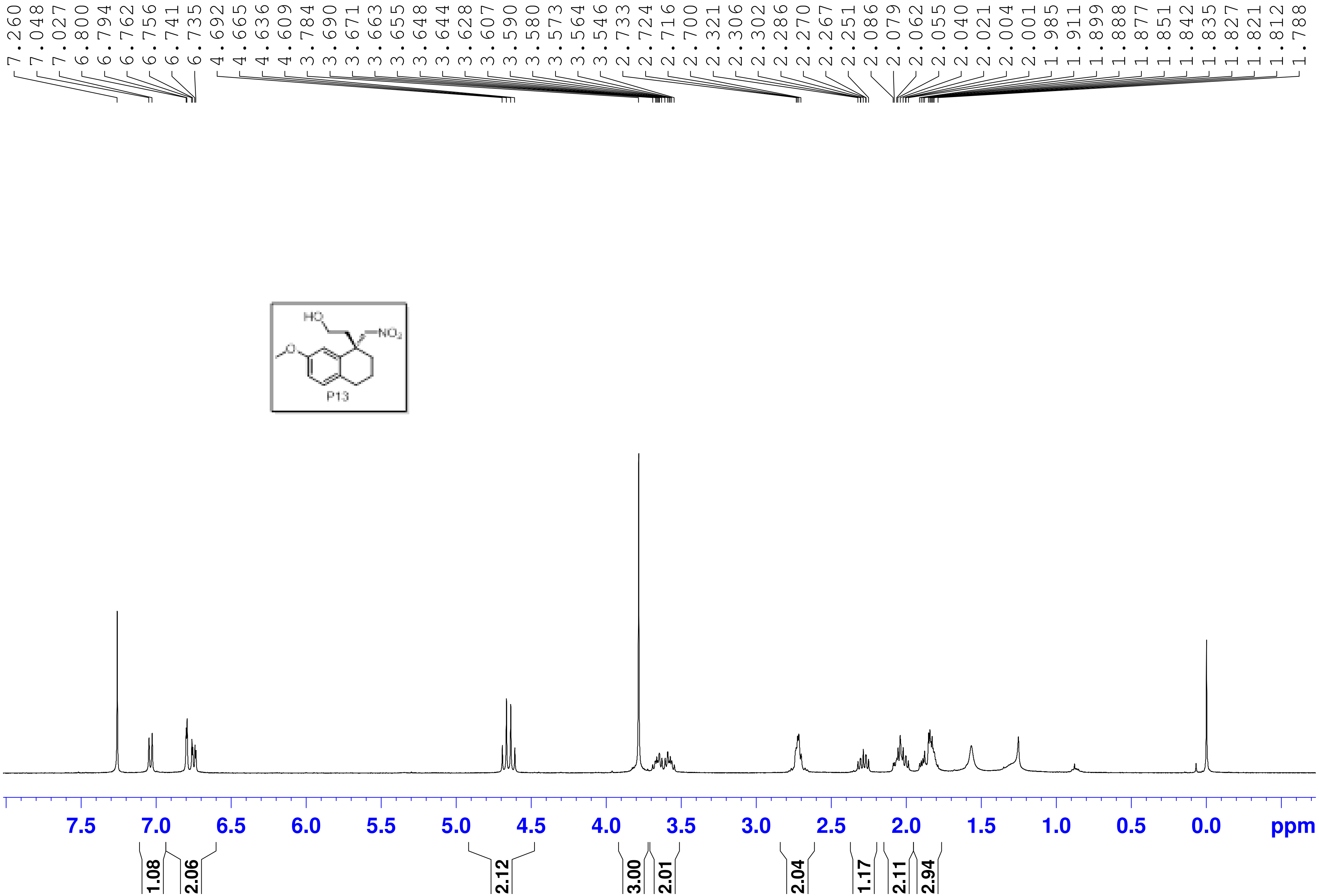


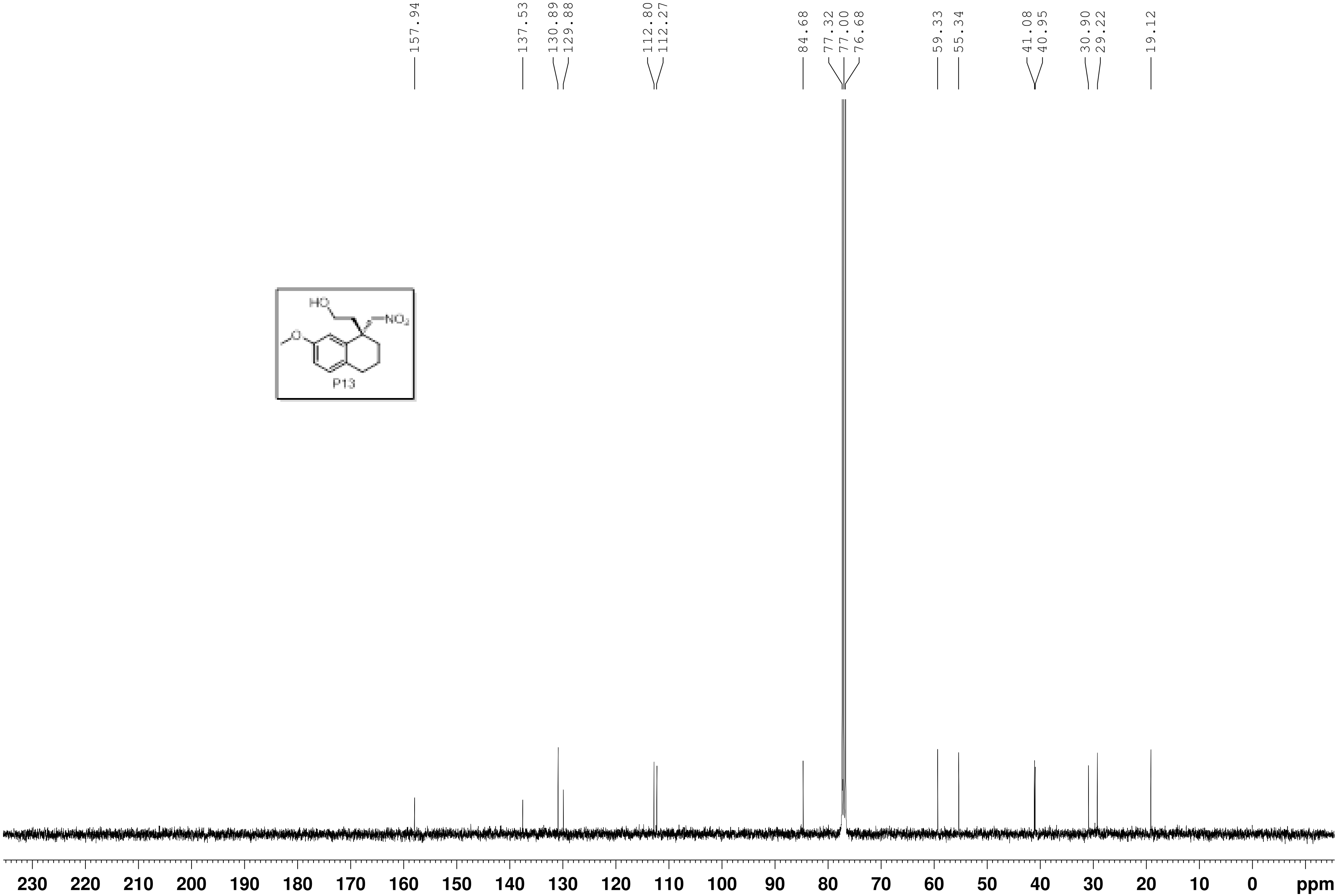
Signal 1: DAD1 B, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.984	BB	0.6019	1345.21216	34.27528	73.0147
2	41.619	BB	0.7893	497.17310	9.64558	26.9853

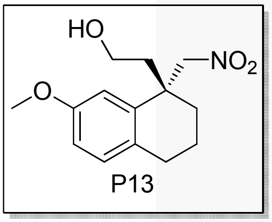


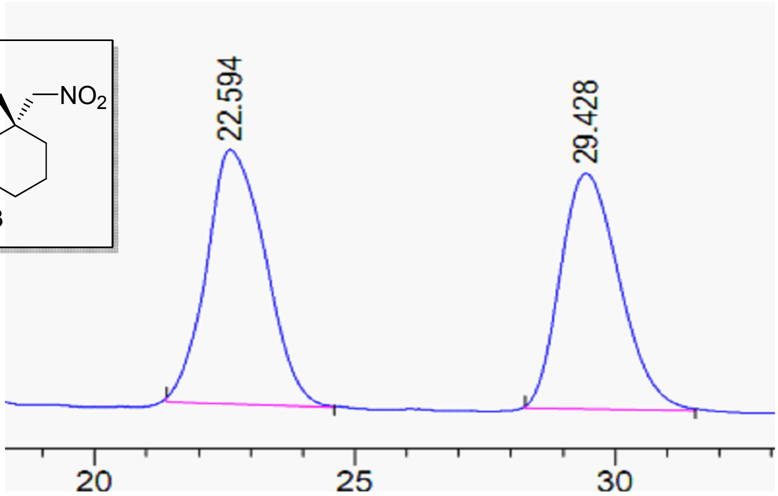
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.012	BB	0.6115	2266.38232	57.05105	98.6540
2	41.918	MM	0.6722	30.92251	7.66716e-1	1.3460


7.260
7.048
7.027
6.800
6.794
6.762
6.756
6.741
6.735
4.692
4.665
4.636
4.609
3.784
3.690
3.671
3.663
3.655
3.648
3.644
3.628
3.607
3.590
3.580
3.573
3.564
3.546
2.733
2.724
2.716
2.700
2.321
2.306
2.302
2.286
2.270
2.267
2.251
2.086
2.079
2.062
2.055
2.040
2.021
2.004
2.001
1.985
1.911
1.899
1.888
1.877
1.851
1.842
1.835
1.827
1.821
1.812
1.788
HO
NO2
O
P13
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
ppm
1.08
2.06
2.12
3.00
2.01
2.04
1.17
2.11
2.94


157.94
137.53
130.89
129.88
112.80
112.27
84.68
77.32
77.00
76.68
59.33
55.34
41.08
40.95
30.90
29.22
19.12
HO
NO2
P13
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

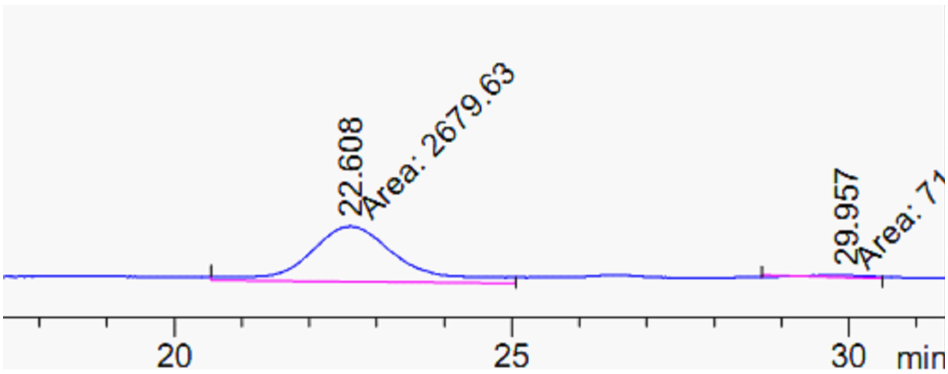
ID-3 hex:ipr=80:20 1 ml/min



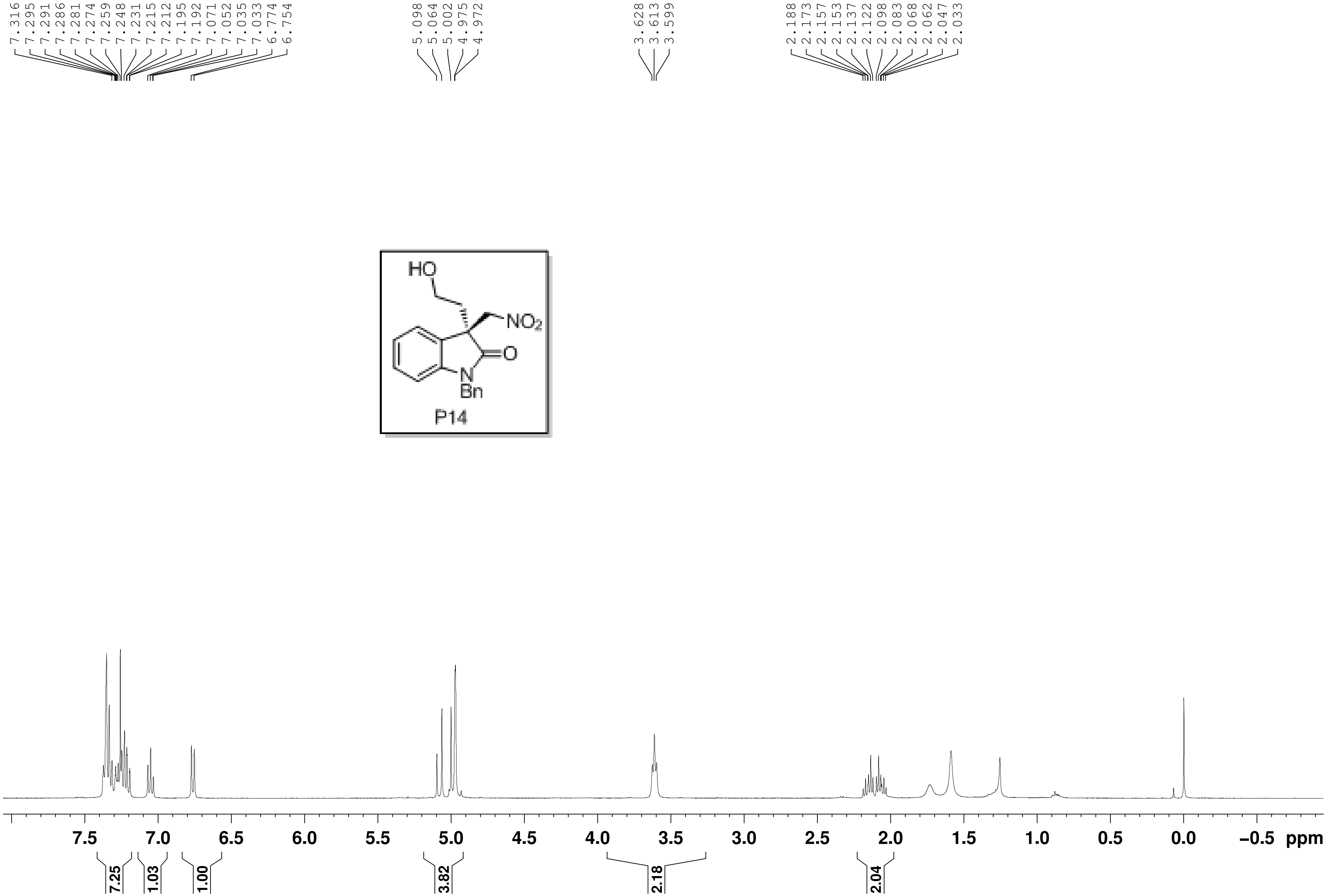


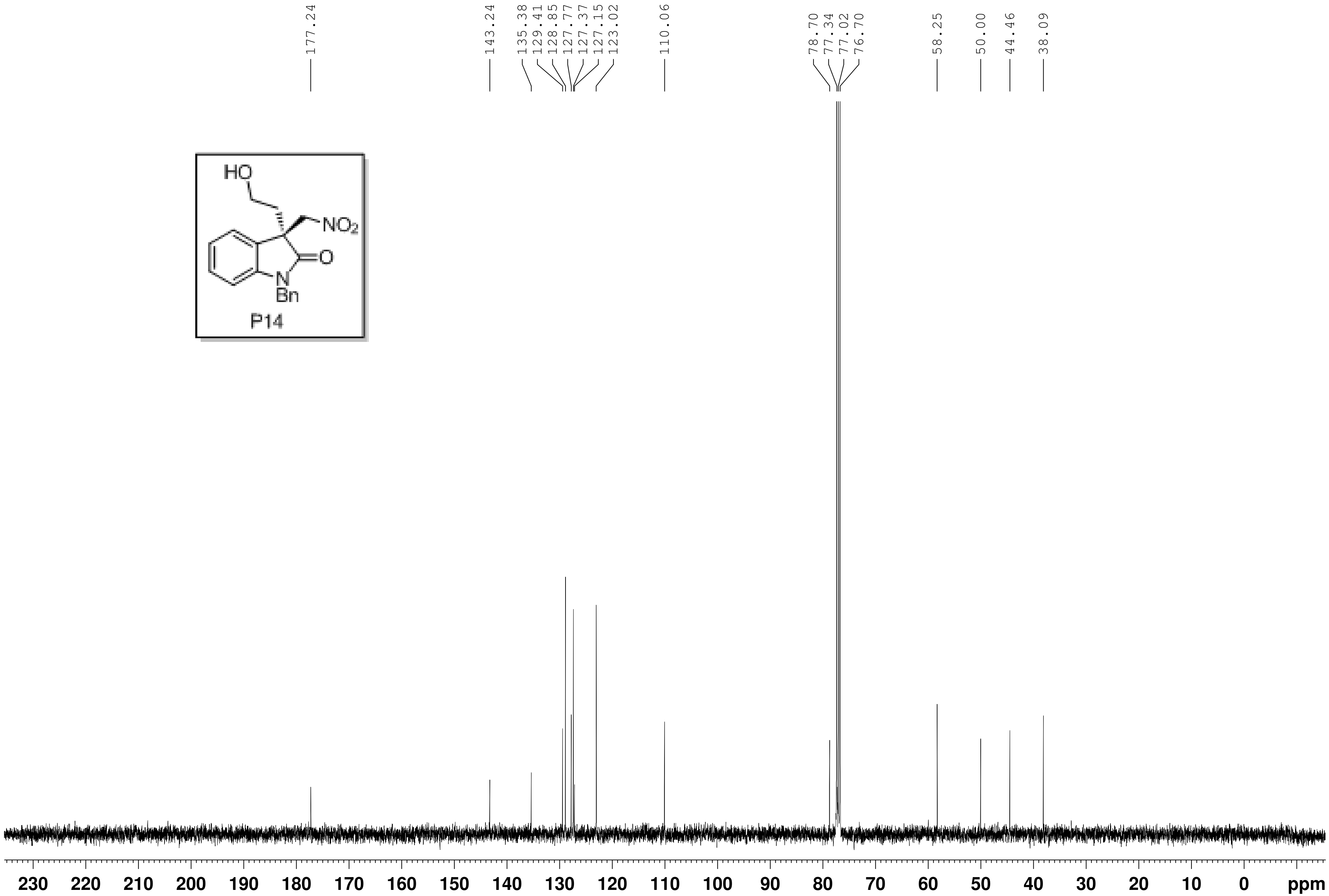
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.594	BB	1.2210	1.49366e4	189.21477	51.9077
2	29.428	BB	1.2381	1.38387e4	175.08640	48.0923

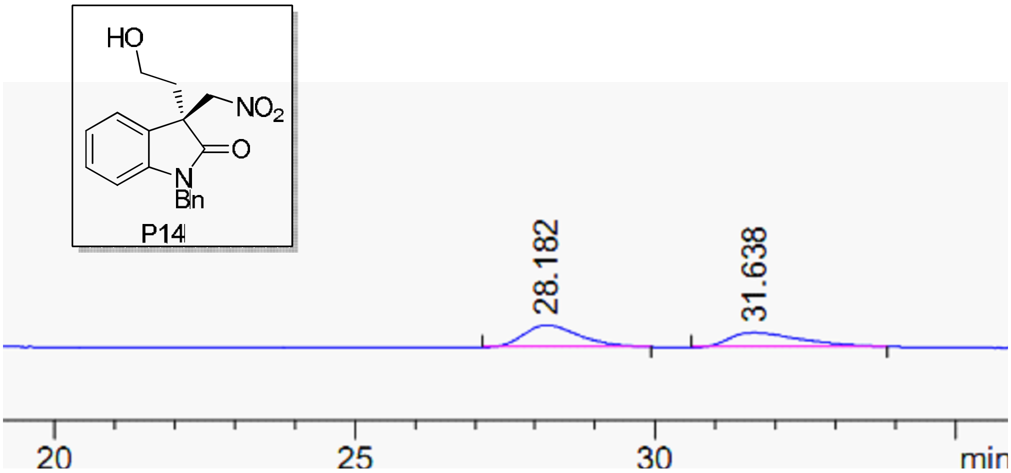


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.608	MM	1.5402	2679.63452	28.99701	97.4115
2	29.957	MM	0.9421	71.20647	1.25972	2.5885


7.316
7.295
7.291
7.286
7.281
7.274
7.259
7.248
7.231
7.215
7.212
7.195
7.192
7.071
7.052
7.035
7.033
6.774
6.754
5.098
5.064
5.002
4.975
4.972
3.628
3.613
3.599
2.188
2.173
2.157
2.153
2.137
2.122
2.098
2.083
2.068
2.062
2.047
2.033
HO
NO2
O
N
Bn
P14
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
ppm
7.25
1.03
1.00
3.82
2.18
2.04

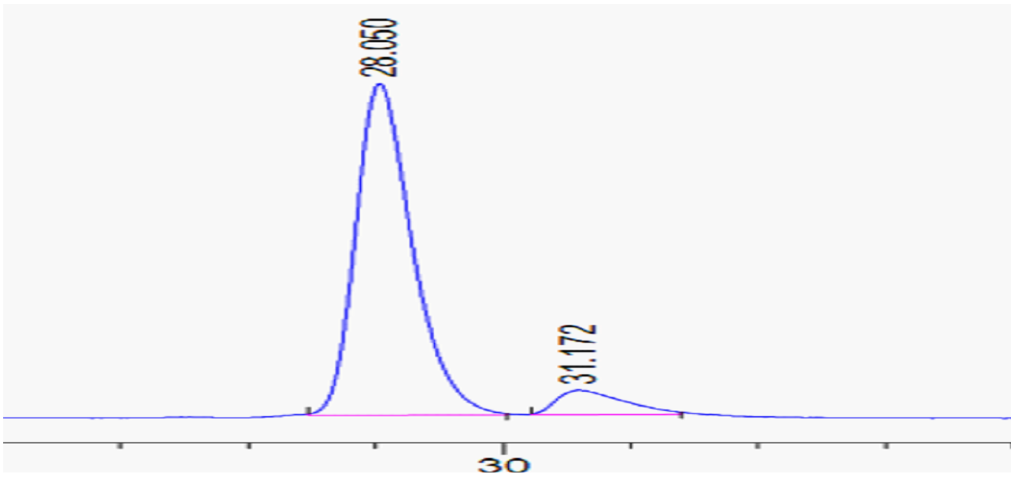

177.24
143.24
135.38
129.41
128.85
127.77
127.37
127.15
123.02
110.06
78.70
77.34
77.02
76.70
58.25
50.00
44.46
38.09
HO
NO2
O
N
Bn
P14
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

AD hex:ipr=90:10 1.0 ml/min

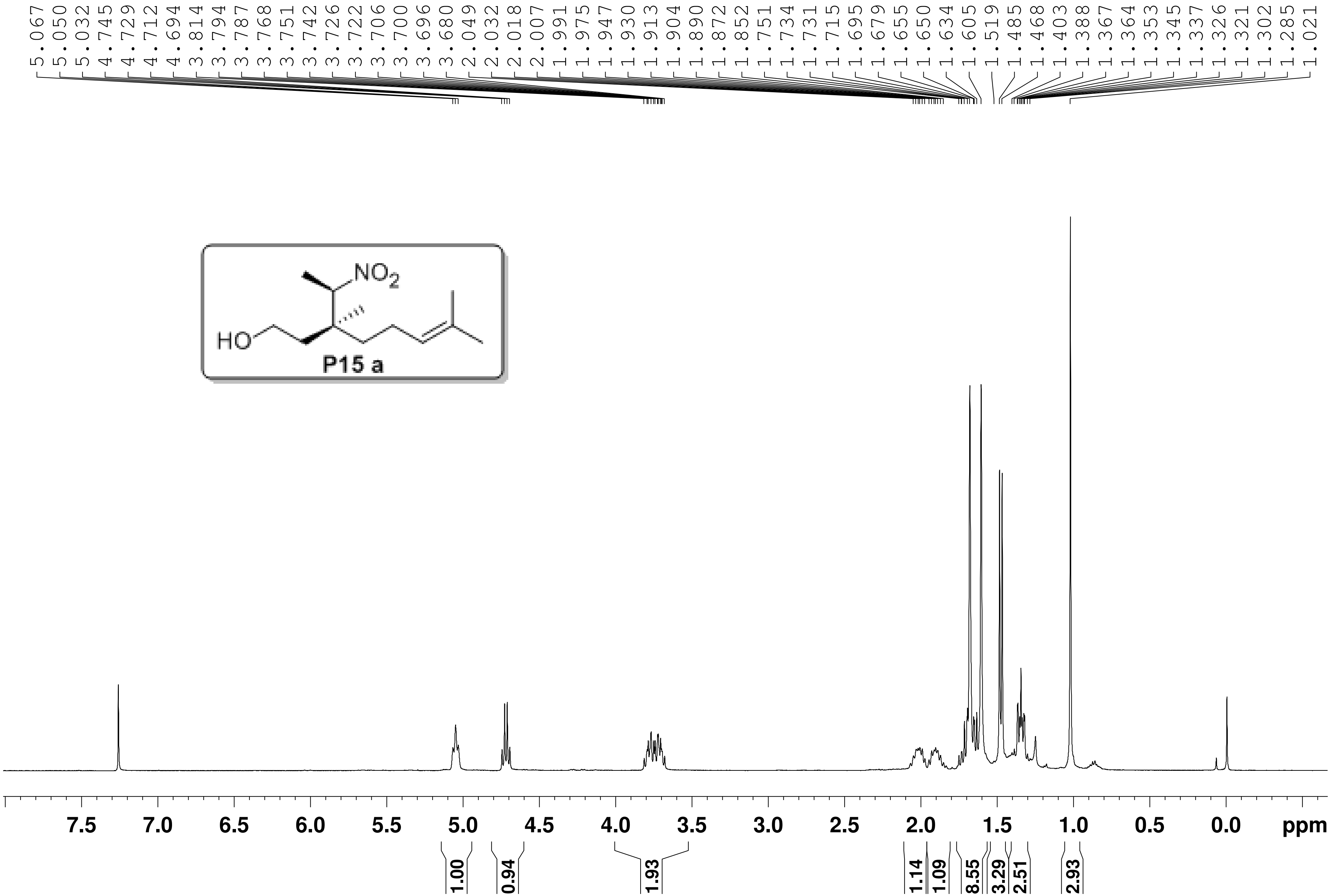


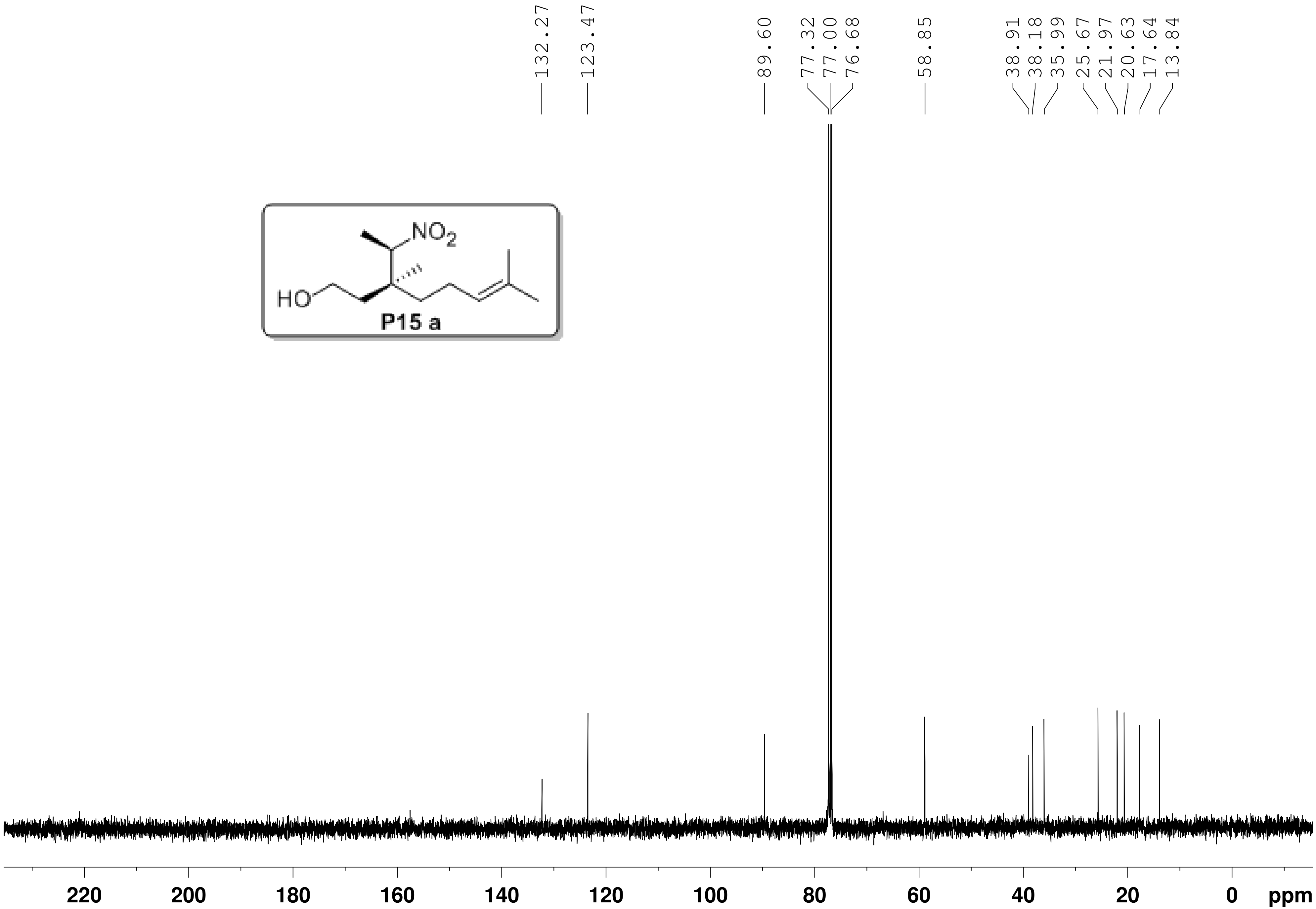
Signal 1: DAD1 B, Sig=215,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.182	BB	0.9761	2743.45557	41.24264	53.6686
2	31.638	PB	1.2011	2368.38940	26.84976	46.3314

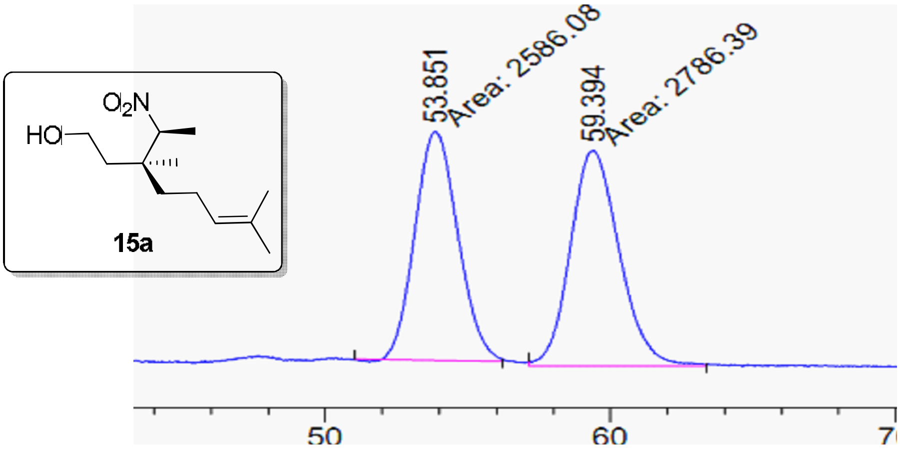


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.050	BB	0.9456	8488.09863	137.22565	91.6633
2	31.172	BB	1.0175	771.99005	10.26418	8.3367


5.067
5.050
5.032
4.745
4.729
4.712
4.694
3.814
3.794
3.787
3.768
3.751
3.742
3.726
3.722
3.706
3.700
3.696
3.680
2.049
2.032
2.018
2.007
1.991
1.975
1.947
1.930
1.913
1.904
1.890
1.872
1.852
1.751
1.734
1.731
1.715
1.695
1.679
1.655
1.650
1.634
1.605
1.519
1.485
1.468
1.403
1.388
1.367
1.364
1.353
1.345
1.337
1.326
1.321
1.302
1.285
1.021
NO2
HO
P15 a
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
ppm
1.00
0.94
1.93
1.14
1.09
8.55
3.29
2.51
2.93

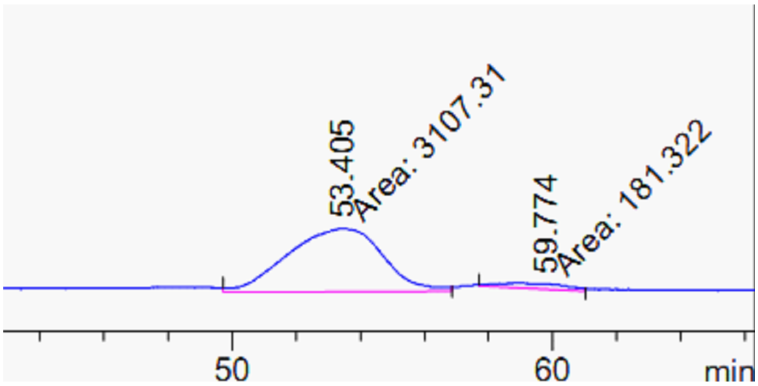

132.27
123.47
89.60
77.32
77.00
76.68
58.85
38.91
38.18
35.99
25.67
21.97
20.63
17.64
13.84
NO2
HO
P15 a
220
200
180
160
140
120
100
80
60
40
20
0
ppm

AD hex:ipr=99:1 1 ml/min

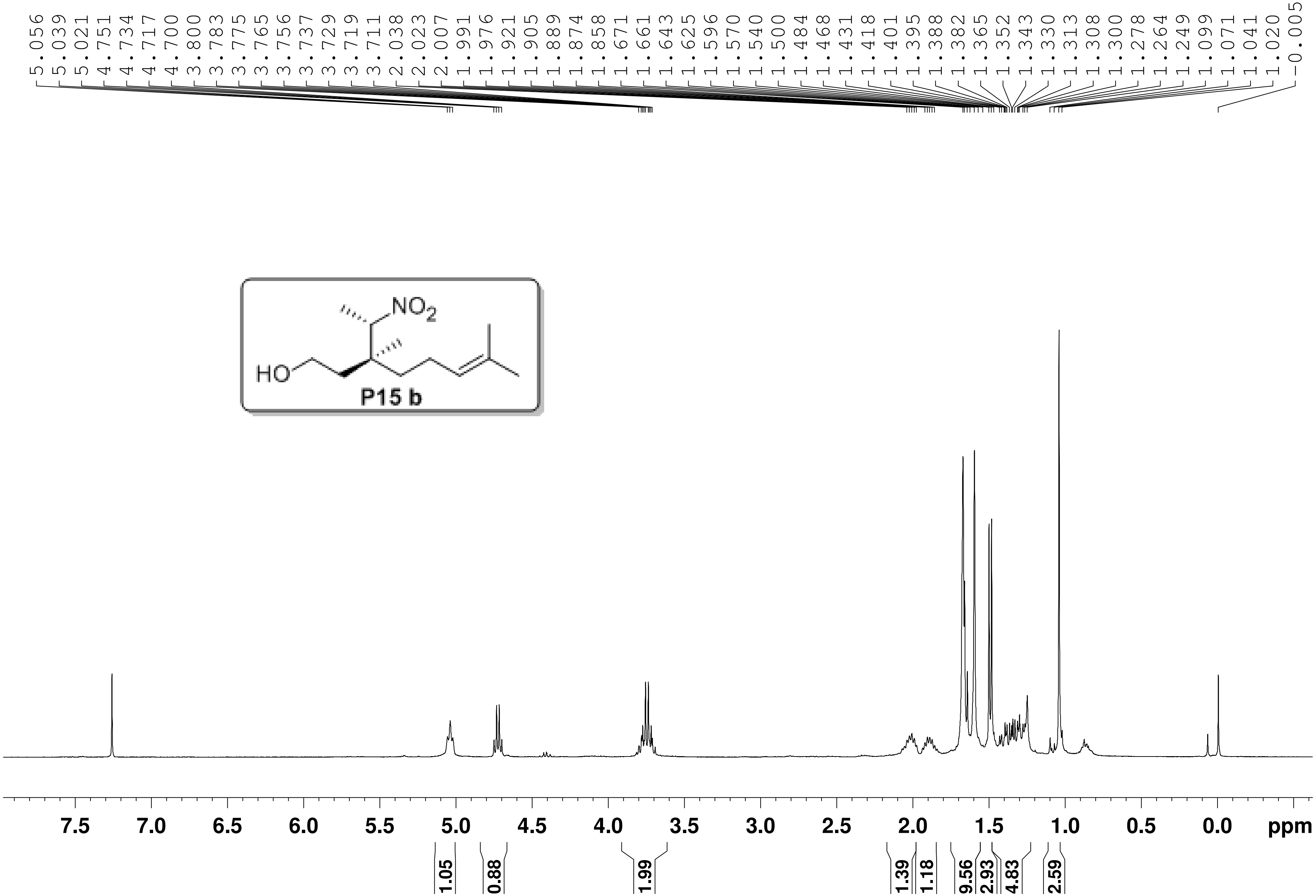


Signal 1: DAD1 A, Sig=220,16 Ref=360,100

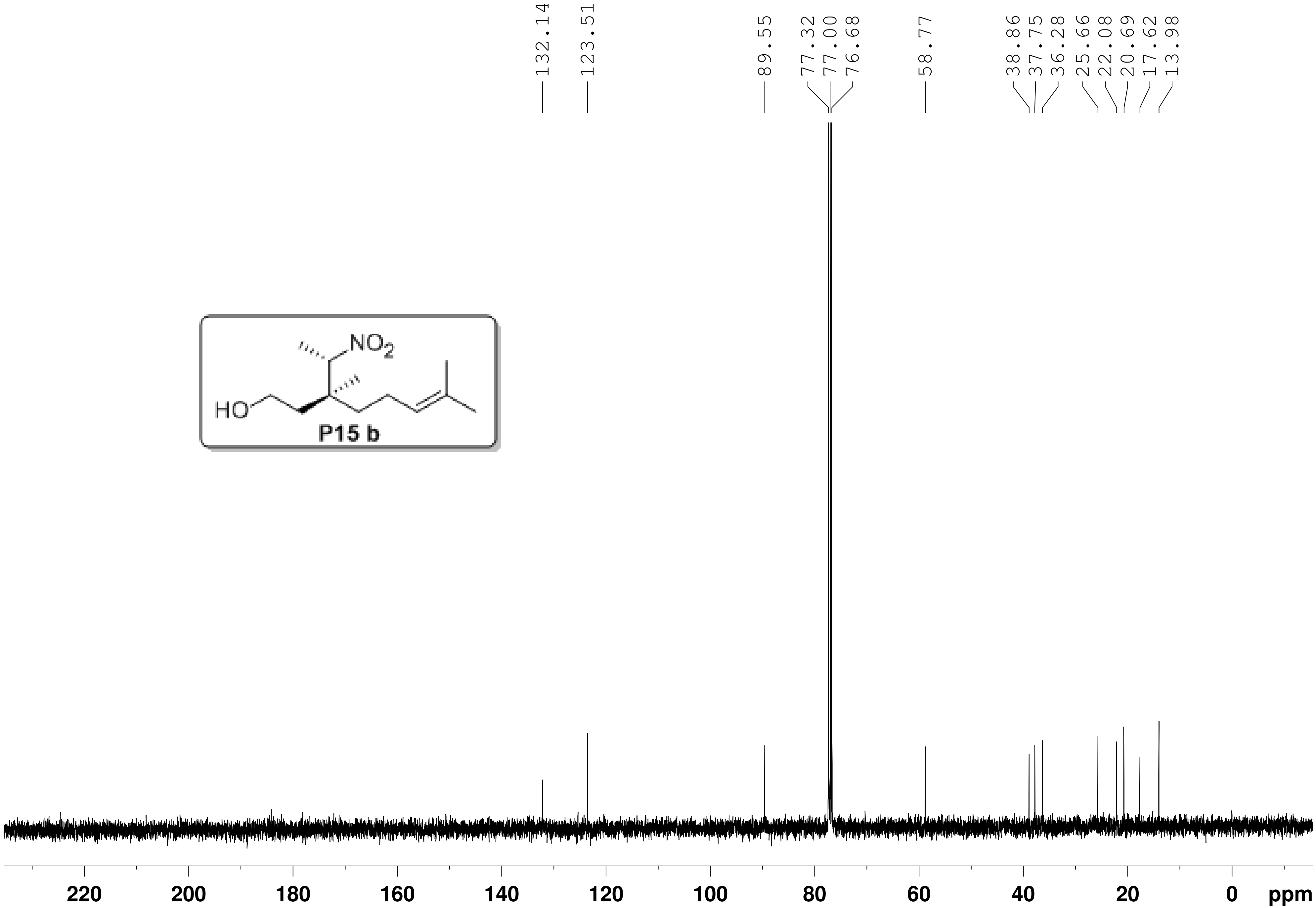
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	53.851	MM	1.7541	2586.07935	24.57149	48.1358
2	59.394	MM	2.0017	2786.38794	23.20014	51.8642



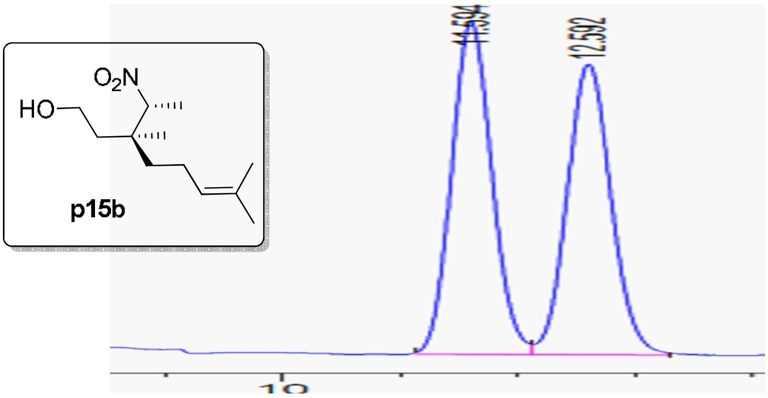
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	53.405	MM	3.4574	3107.31494	14.97918	94.4864
2	59.774	MM	2.4110	181.32164	1.25342	5.5136



5.056 5.039 5.021 4.751 4.734 4.717 4.700 3.800 3.783 3.775 3.765 3.756 3.737 3.729 3.719 3.711 2.038 2.023 2.007 1.991 1.976 1.921 1.905 1.889 1.874 1.858 1.671 1.661 1.643 1.625 1.596 1.570 1.540 1.500 1.484 1.468 1.431 1.418 1.401 1.395 1.388 1.382 1.365 1.352 1.343 1.330 1.313 1.308 1.300 1.278 1.264 1.249 1.099 1.071 1.041 1.020 -0.005
NO2
HO
P15 b
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 ppm
1.05 0.88 1.99 1.39 1.18 9.56 2.93 4.83 2.59

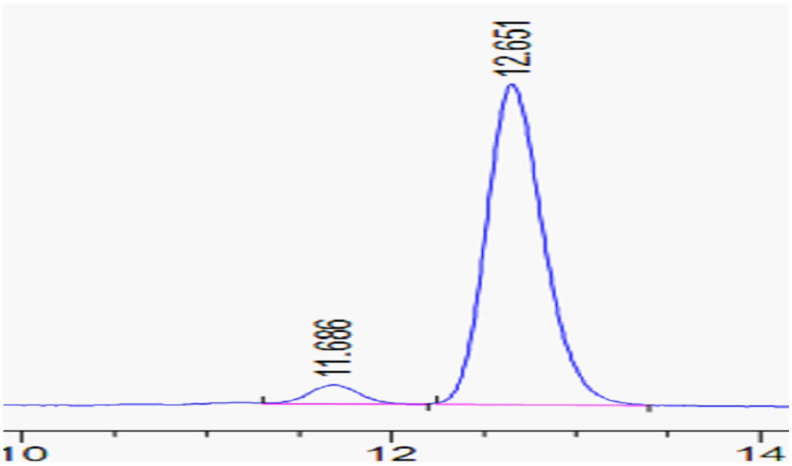

132.14
123.51
89.55
77.32
77.00
76.68
58.77
38.86
37.75
36.28
25.66
22.08
20.69
17.62
13.98
NO2
HO
P15 b
220
200
180
160
140
120
100
80
60
40
20
0
ppm

OD-H hex:ipr=95:5 1 ml/min

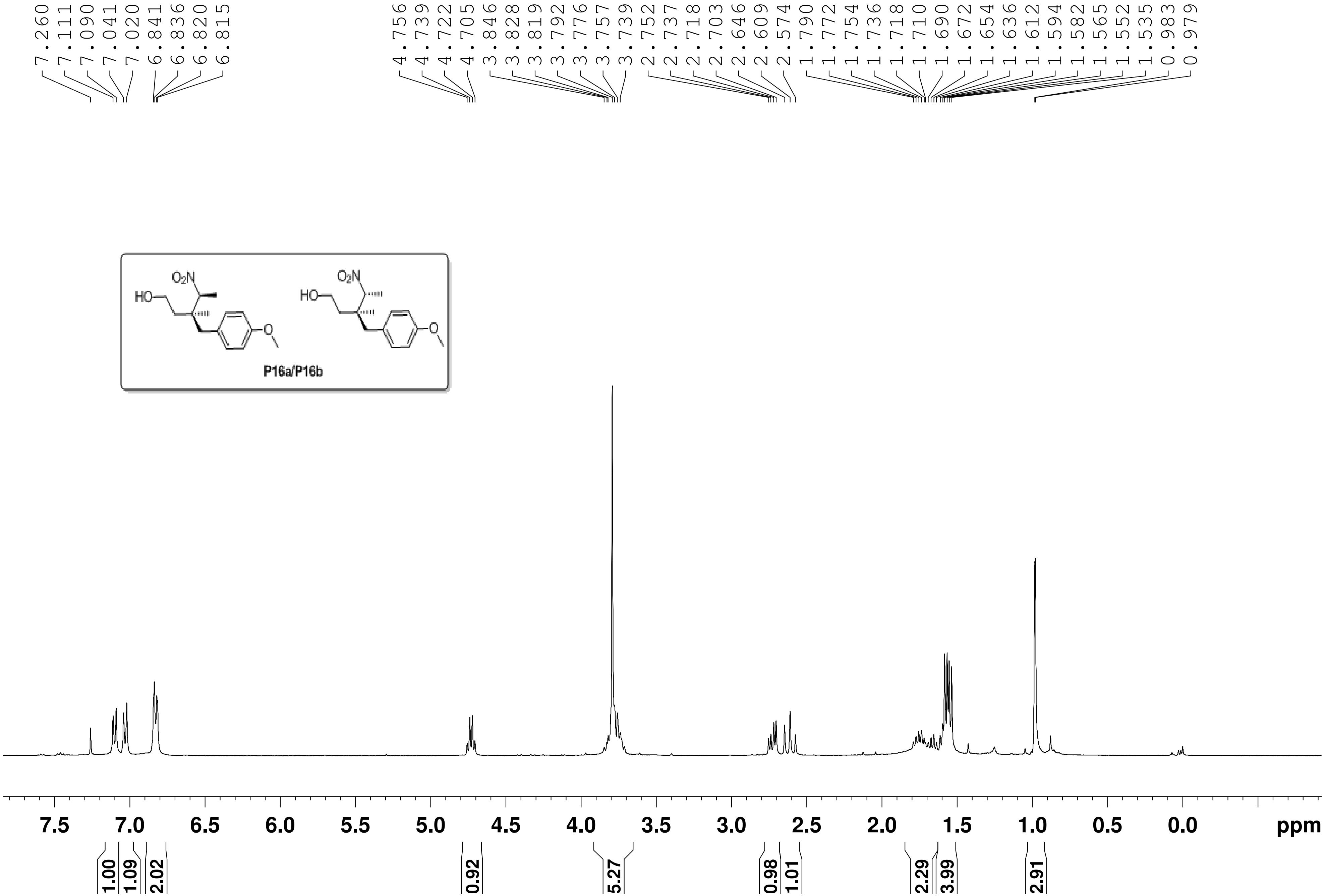


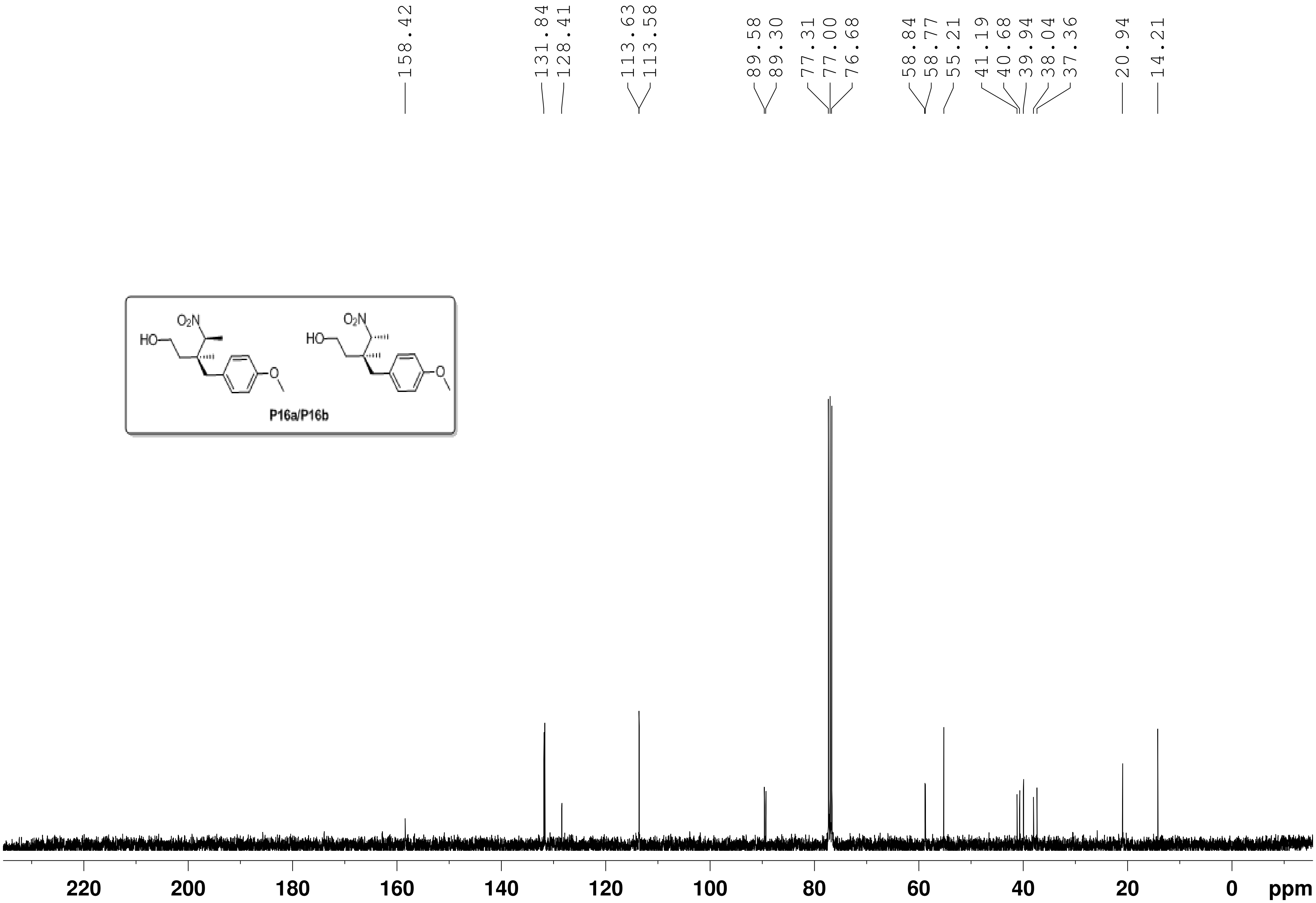
Signal 1: DAD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.594	BV	0.3722	5669.69189	237.74841	51.4323
2	12.592	VB	0.4055	5353.90771	207.19467	48.5677

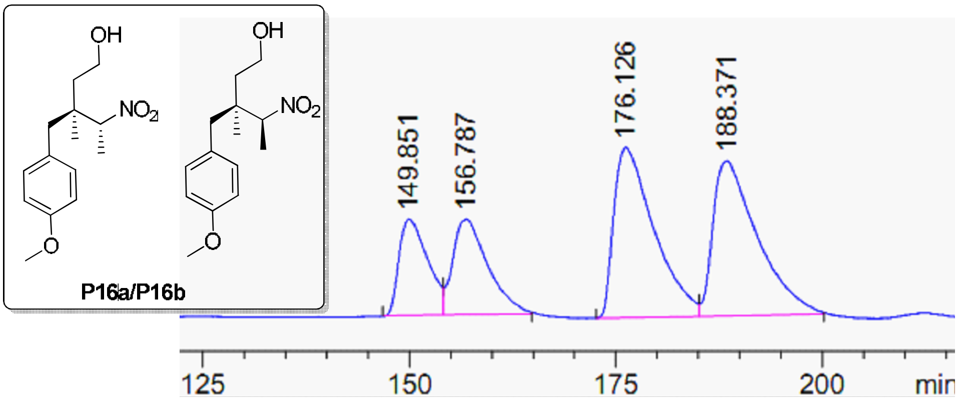


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.686	BB	0.3038	88.68507	4.54182	5.1814
2	12.651	BB	0.3356	1622.92761	75.26408	94.8186


7.260 7.111 7.090 7.041 7.020 6.841 6.836 6.820 6.815
4.756 4.739 4.722 4.705 3.846 3.828 3.819 3.792 3.776 3.757 3.739 2.752 2.737 2.718 2.703 2.646 2.609 2.574 1.790 1.772 1.754 1.736 1.718 1.710 1.690 1.672 1.654 1.636 1.612 1.594 1.582 1.565 1.552 1.535 0.983 0.979
HO
O2N
P16a/P16b
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 ppm
1.00 1.09 2.02 0.92 5.27 0.98 1.01 2.29 3.99 2.91

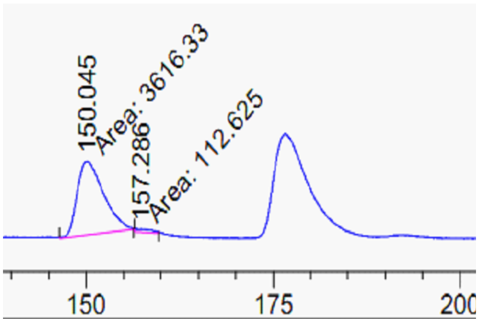

158.42
131.84
128.41
113.63
113.58
89.58
89.30
77.31
77.00
76.68
58.84
58.77
55.21
41.19
40.68
39.94
38.04
37.36
20.94
14.21
HO
O2N
O
P16a/P16b
220
200
180
160
140
120
100
80
60
40
20
0
ppm

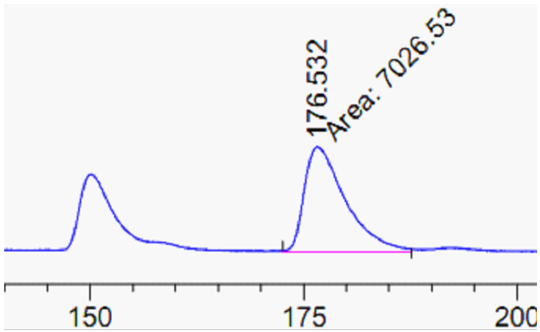
OD-H hex:ipr=99:1 1.0 ml/min



Signal 1: DAD1 B, Sig=230,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	149.851	PV	2.8962	7800.68945	31.95325	14.0210
2	156.787	VB	3.4665	9385.64453	31.80759	16.8699
3	176.126	BV	4.0347	1.91287e4	56.43111	34.3821
4	188.371	VB	4.4168	1.93206e4	51.40585	34.7270





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	150.045	MM	4.1282	3616.32739	14.60003	96.9797
2	157.286	MM	2.0417	112.62501	7.39666e-1	3.0203

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	176.532	MM	5.6333	7026.53174	20.78852	100.0000