Electronic Supplementary Information

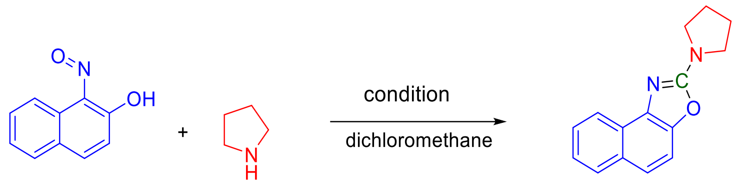
Proline Selective Labeling via On-Site Construction of Naphthoxazole (NapOx)

Subhra Kanti Roy,[a] Anisha Purkait,[a] Rajib Shome,[b] Saurav Das,[a] Debapratim Das,[a] Siddhartha Sankar Ghosh[b] and Chandan K. Jana*[a]

[a]Department of Chemistry, Indian Institute of Technology Guwahati, India-781039, E-mail: ckjana@iitg.ac.in

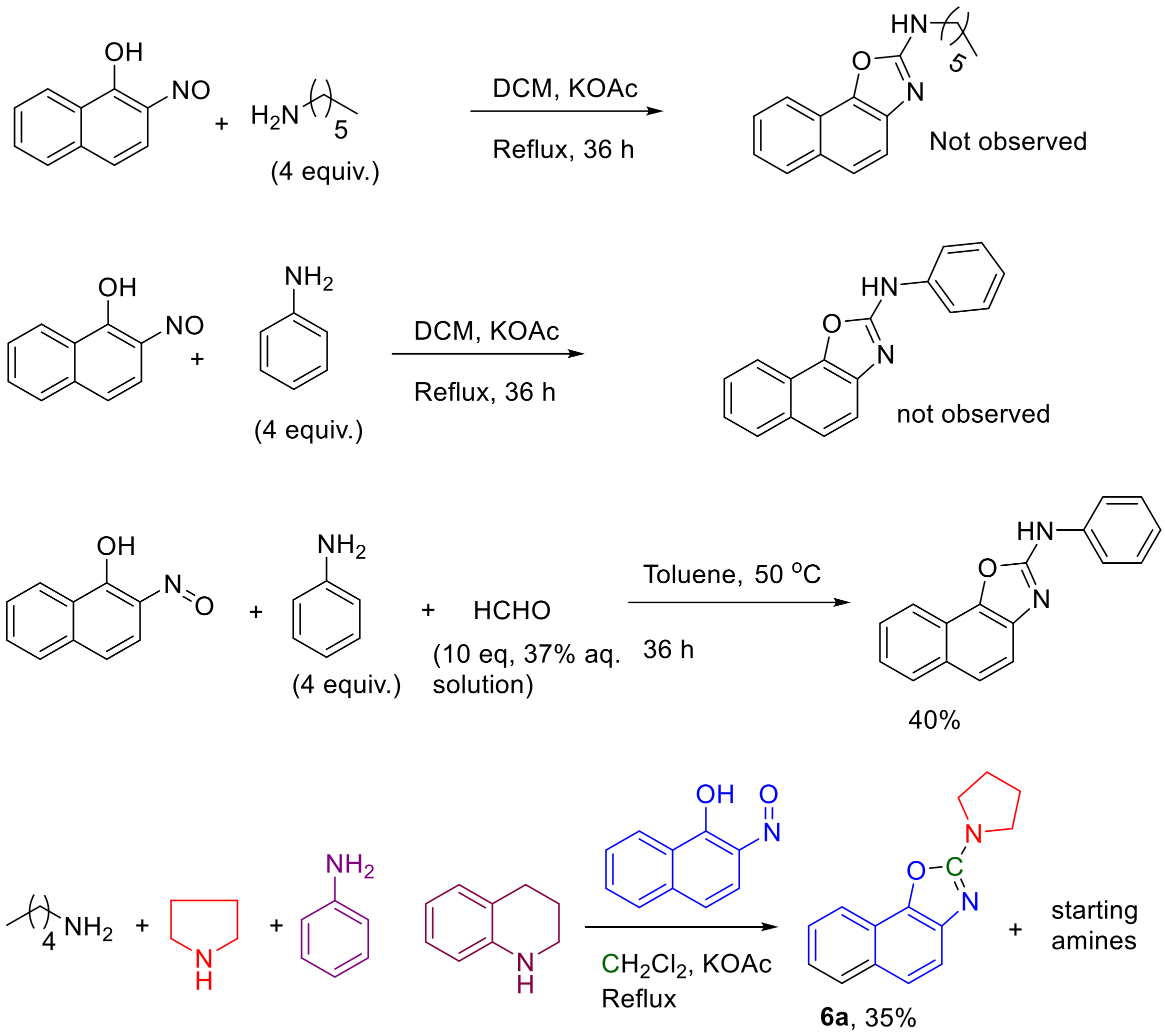
[b]Department of Biosciences and Engineering, Indian Institute of Technology Guwahati, 781039, India

Table S1: Variation of reagents and reaction conditions to obtain the best yields of **6a**.



Entry	conditions	Yield (%)
1	HCHO, Toluene, 40 °C, 48 h	43
2	CH_2Cl_2, reflux, 14 h	40
3	AcOH (20 mol%), CH_2Cl_2, reflux, 12 h	35
4	NEt_3 1 equiv., CH_2Cl_2, reflux, 14 h	41
5	KOAc 1 equiv., CH_2Cl_2, reflux, 14 h	42
6	KOAc 1 equiv., CH_2Cl_2, reflux, 24 h	54
7	KOAc 2 equiv., CH_2Cl_2, rt, 24 h	20
8	KOAc 2 equiv., CH_2Cl_2, reflux, 24 h	66
9	K_2CO_3 2 equiv., CH_2Cl_2, reflux, 24 h	43
10	Et_3N 2 equiv., CH_2Cl_2, reflux, 24 h	50
11	DBU 2 equiv., CH_2Cl_2, reflux, 24 h	60
12	KOAc 2 equiv., CH_2Cl_2, reflux, 36 h or 48 h	70
13	KOAc 1 equiv., CH_2Cl_2, reflux, 36 h	55
14	NaOH 2 equiv., CH_2Cl_2, reflux, 24 h	ND

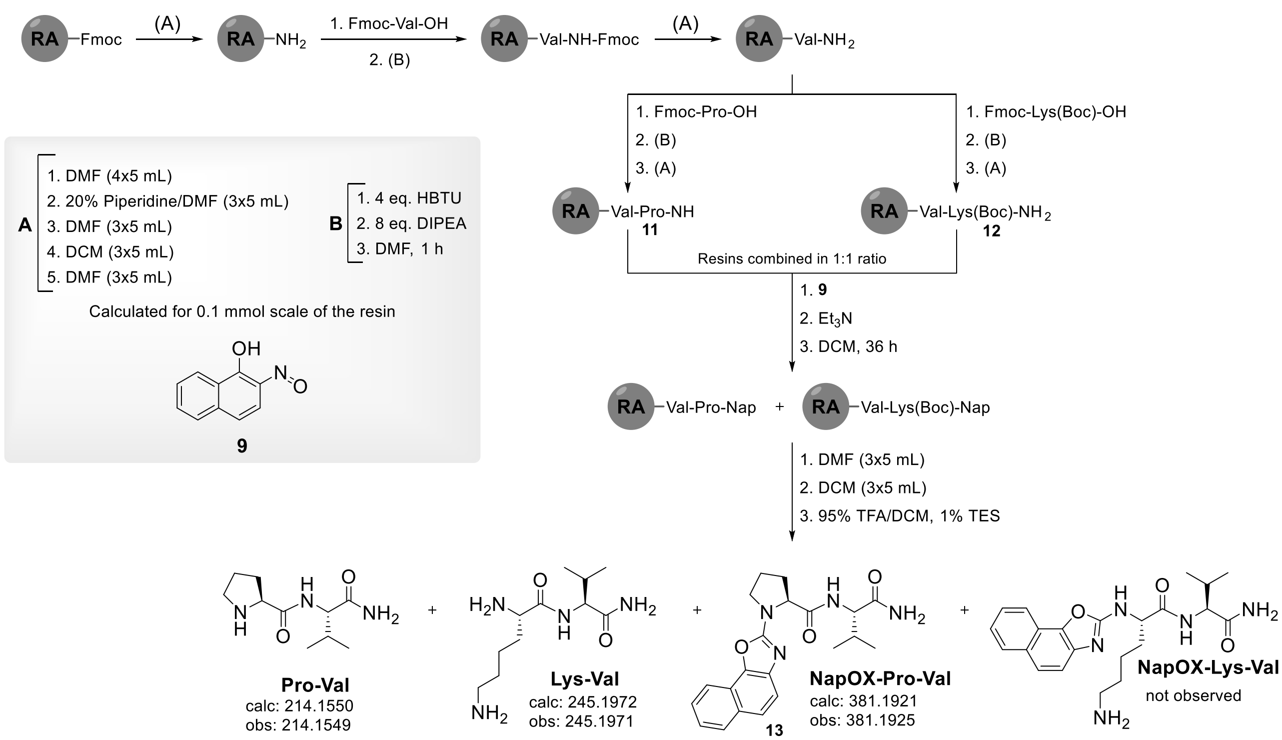
[a]All the reactions were carried out using 0.23 mmol of **4**, 0.94 mmol of pyrrolidine, 0.46 mmol of KOAc, and 4 mL dichloromethane.



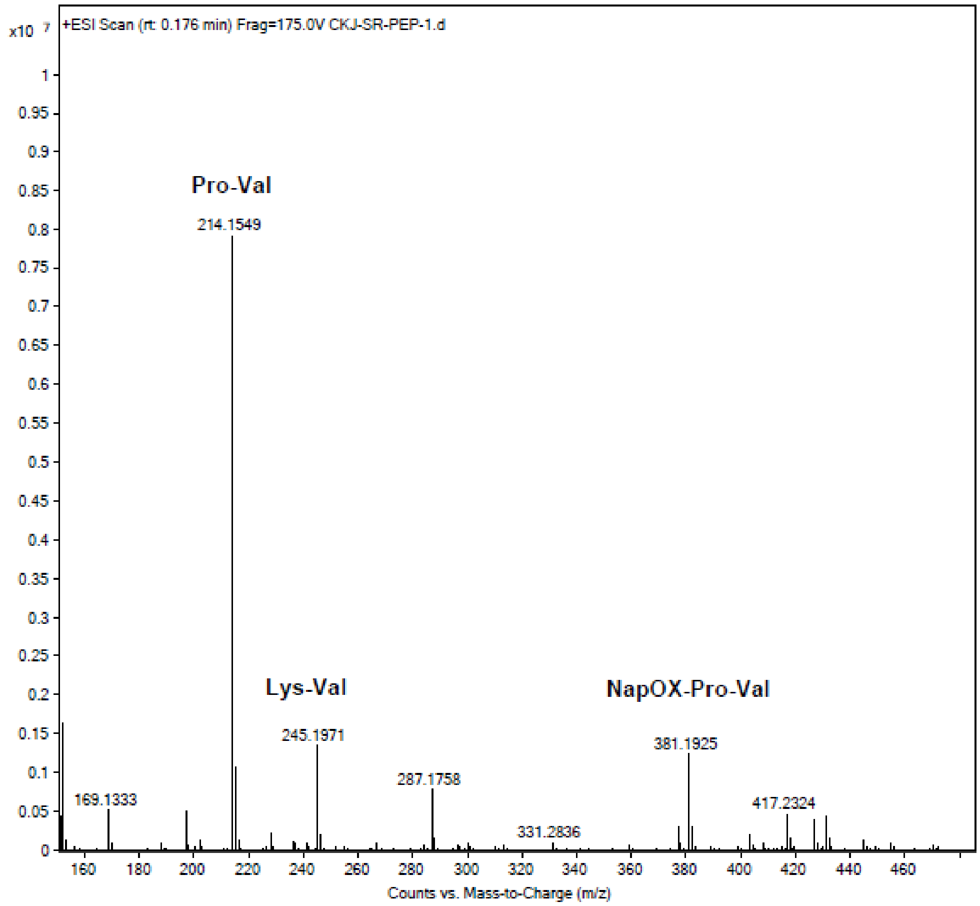
Scheme S1: Reactions with aliphatic and aromatic primary amines.

Preparation of Nap-PV-NH$_2$ in SPPS:

The peptides, PV and KV, were prepared separately using solid phase peptide synthesis (SPPS) technique employing Rink-amide MBHA resin as the solid support. Typically, 4 equiv. of Fmoc-protected amino acids were used for each coupling with respect to the loading capacity of the resin. For coupling, dimethyl formamide (DMF) was used as the solvent while, HBTU (4 equiv.) and DIPEA (8 equiv.) mixture was used for the coupling reaction. Fmoc deprotections were achieved by treating the resin bound peptides with 20% piperidine in DMF. After the final Fmoc deprotection, the peptide bound resins were washed several times with dichloromethane (DCM). The PV and KV peptide bound resins were combined together and suspended in DCM. To this, 2-nitrosonaphthalen-1-ol (2 equiv. with respect to the resin) and triethylamine (6 equiv.) were introduced and the resin was shaken at a constant speed for 36 h. The resin was then washed thoroughly with DCM and dried before the mixture of peptides were cleaved from it using 95% trifluoroacetic acid (TFA) in DCM containing 1% triethylsilane. The volatiles were removed under reduced pressure on a rotary evaporator. The residue was precipitated from cold ether to get a brown coloured solid which was dried and then lyophilized to get the crude peptide mixture. The peptide mixture was analysed using LCMS; 214.1480 (PV), 245.1976 (KV), 381.2231 (Nap-PV).



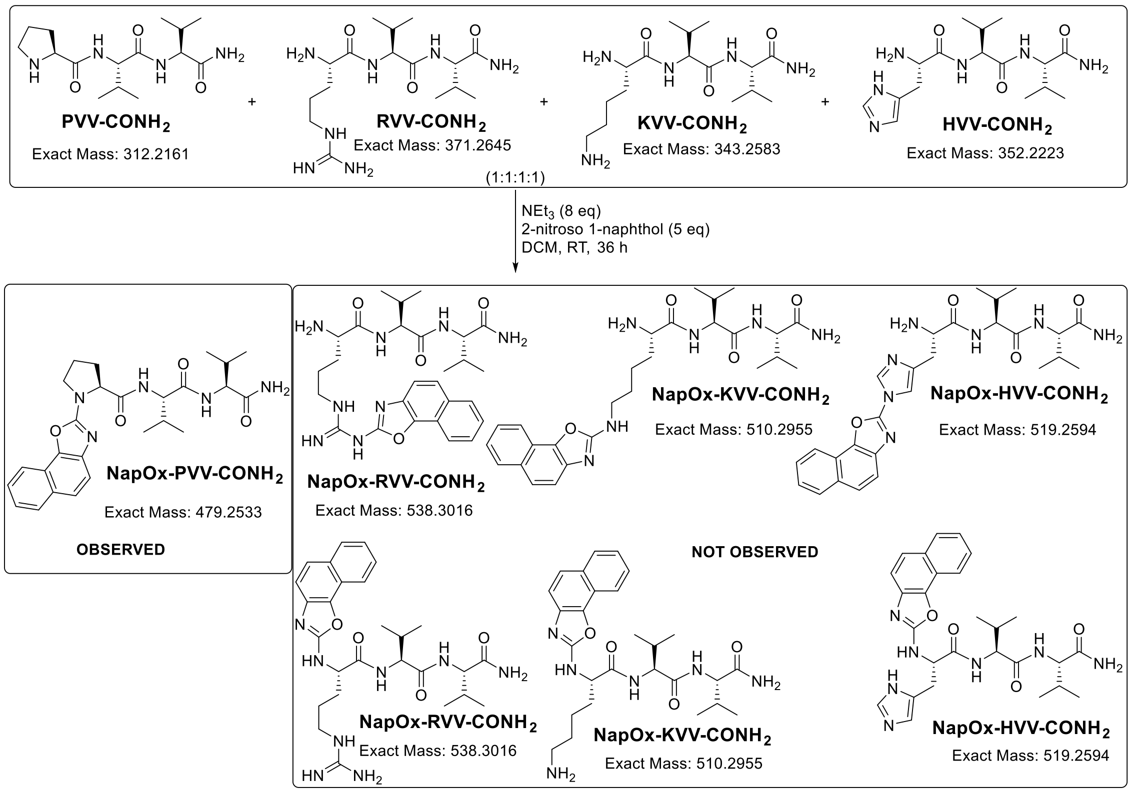
Scheme S2: Selective labeling at *N*-terminal proline in solid phase.



Selective labeling at N-terminal proline:

To check the Proline-selective labeling via the new methodology, four peptides (PVV-$CONH_2$, KVV-$CONH_2$, HVV-$CONH_2$, and RVV-$CONH_2$, Scheme s3) were synthesized using solid phase peptide synthesis protocol and purified via HPLC. An equimolar mixture of all four peptides was taken in dry dichloromethane and to this, 8 equiv. of triethylamine and 5 equiv. of 2-nitroso 1-naphthol were added. The reaction mixture was stirred under argon atmosphere at room temperature for 36 h. The solvent was removed under reduced pressure and the oily residue was washed with diethylether several times to leave a brown solid. A small portion of the solid was dissolved in Acetonitrile/H_2O (1:1) and mixed with 2,5-dihydroxybenzoic acid matrix solution (in Acetonitrile/H_2O (1:1) containing 0.1% trifluoroacetic acid) and the MALDI-MS was recorded. The MALDI-MS spectrum as shown in Fig. s1 clearly shows the peak corresponding to NapOx-PVV-$CONH_2$ while no trace of the NapOx-conjugates of the other peptides could be observed.

The results unequivocally prove the selectivity of the methodology toward *N*-terminal Proline containing peptides.



Scheme s3: Selective labeling at *N*-terminal proline

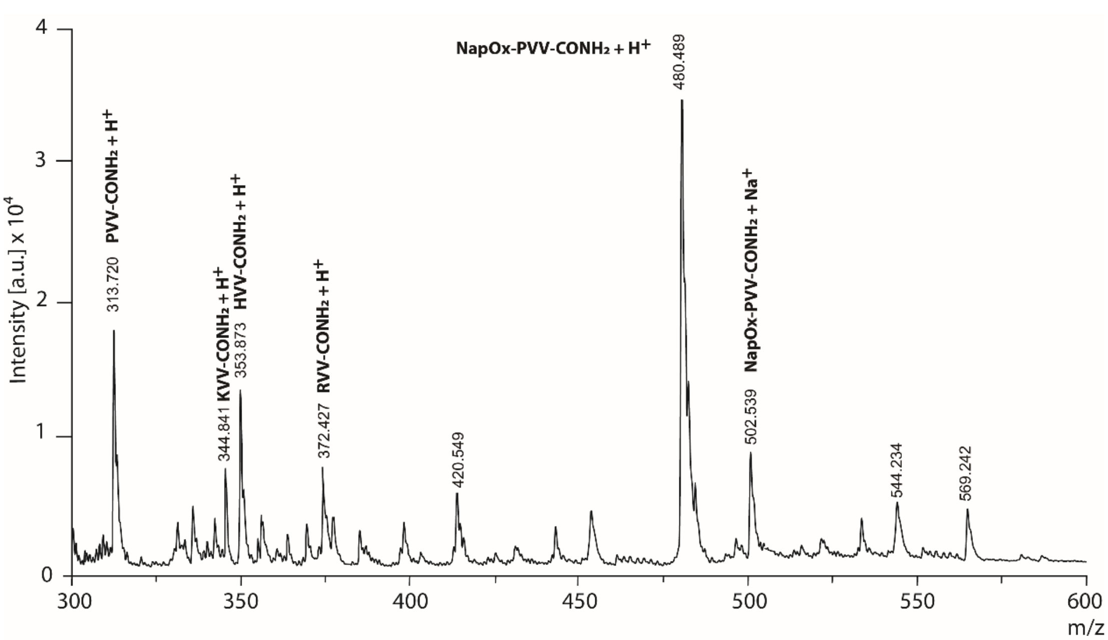


Figure s1: MALDI-MS spectrum of a mixture of PVV-CONH$_2$, KVV-CONH$_2$, HVV-CONH$_2$, and RVV-CONH$_2$ after treatment with 2-nitroso 1-naphthol in presence of trimethylamine.

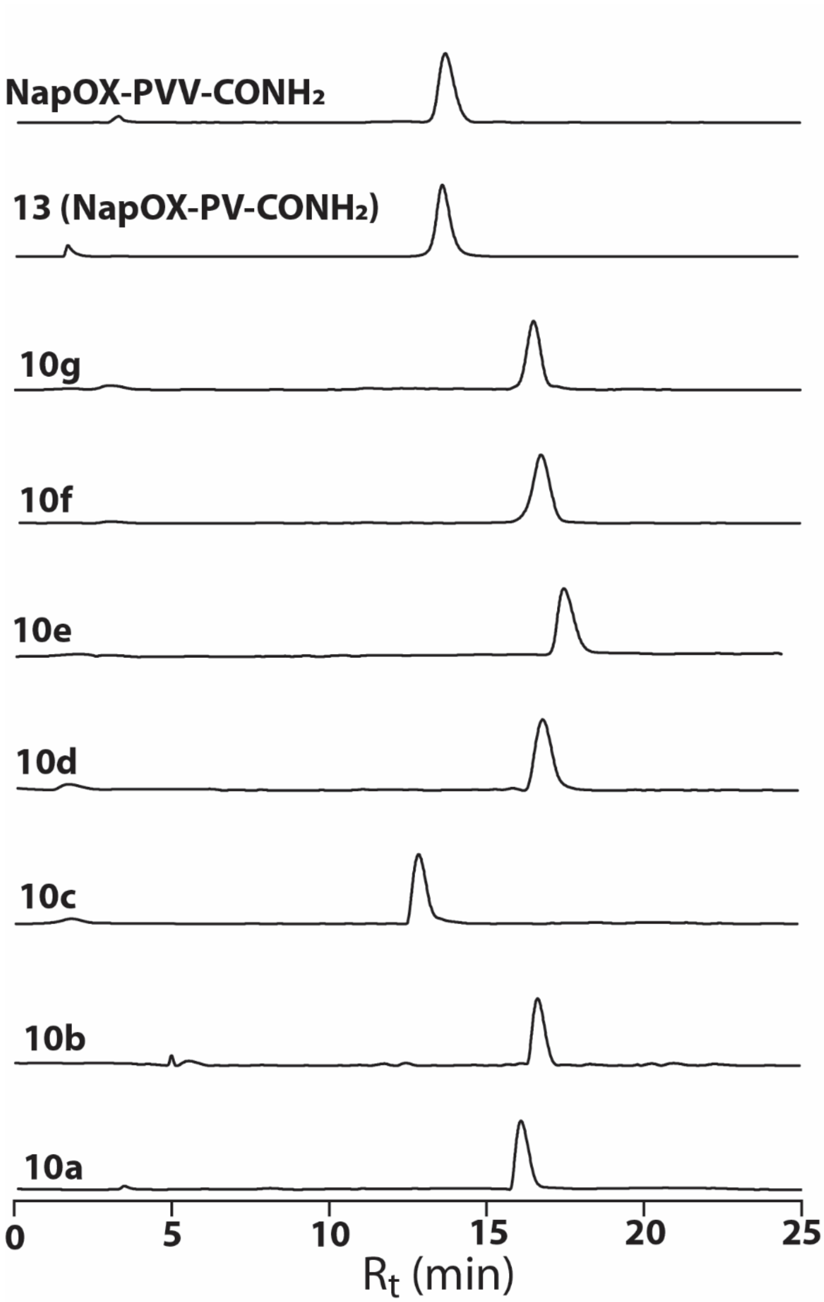


Figure s2: HPLC chromatogram of labeled peptides. The purity of the NapOx conjugated peptides were assessed through analytical HPLC using Dionex Ultimate 3000 HPLC system equipped with Luna 5 μm C18 column (Phenomenex) and using acetonitrile and water (containing 0.1% TFA each) as the mobile phase (HPLC Program= 5% to 100% Acetonitrile/Water in 20 minutes followed by 100% to 5% Acetonitrile/Water in 5 minutes).

Measurement of Relative fluorescence quantum yields and Fluorescence Lifetimes:

0.10 M H_2SO_4 solution of quinine sulfate was used as a standard reference dye to calculate the quantum yields of the modified peptides **10a-g** in DMSO solution. Quantum yield with respect to quinine sulphate (QS) in 0.1 M H_2SO_4, using the Parker-Rees equation.[i]

$\Phi_u = (A_sF_un_u^2/A_uF_sn_s^2)\ \Phi_s$

where, Φ_u = quantum yield of unknown fluorophore (sample); Φ_s = quantum yield of the standard fluorophore; A_s = absorbance of the standard fluorophore at the excitation wavelength; A_u= absorbance of the unknown fluorophore at the excitation wavelength; F_s = the area of integrated fluorescence intensity of the standard fluorophore when excited at the same excitation wavelength; F_u = the total area of integrated fluorescence intensity for the unknown fluorophore (sample) when excited at the same excitation wavelength; n_u= refractive index of the solvent of the unknown sample; n_s= refractive index of the solvent of the standard reference. To minimize the reabsorption of fluorescence light passing through the samples their absorption maximum was kept 0.1.
Quantum yield of quinine sulphate, Φ_s = 0.54;
Refractive Index: water = 1.33
Lifetime measurements were done using Eddinburg (FSP920) spectrophotometer.

	$A_sF_un_u^2$	$A_uF_sn_s^2$	$A_sF_un_u^2/A_uF_sn_s^2$	Φ_s	Φ_u	QY	Quantum yield in %	t_i (ns)
10g	1.37E+08	1.81E+08	7.58E-01	0.54	4.09E-01	**~0.41**	**40.9**	**23.577**
10d	1.57E+08	1.99E+08	7.88E-01	0.54	4.26E-01	**~0.43**	**42.6**	**23.681**
10b	1.33E+08	1.90E+08	7.02E-01	0.54	3.79E-01	**~0.38**	**37.9**	**23.665**
10c	1.28E+08	1.87E+08	6.85E-01	0.54	3.70E-01	**~0.37**	**37.0**	**23.364**
10a	1.22E+08	1.76E+08	6.91E-01	0.54	3.73E-01	**~0.37**	**37.3**	**23.226**
10f	1.50E+08	1.60E+08	9.35E-01	0.54	5.05E-01	**~0.5**	**50.5**	**23.674**
10e	1.34E+08	1.77E+08	7.55E-01	0.54	4.08E-01	**~0.41**	**40.8**	**23.549**

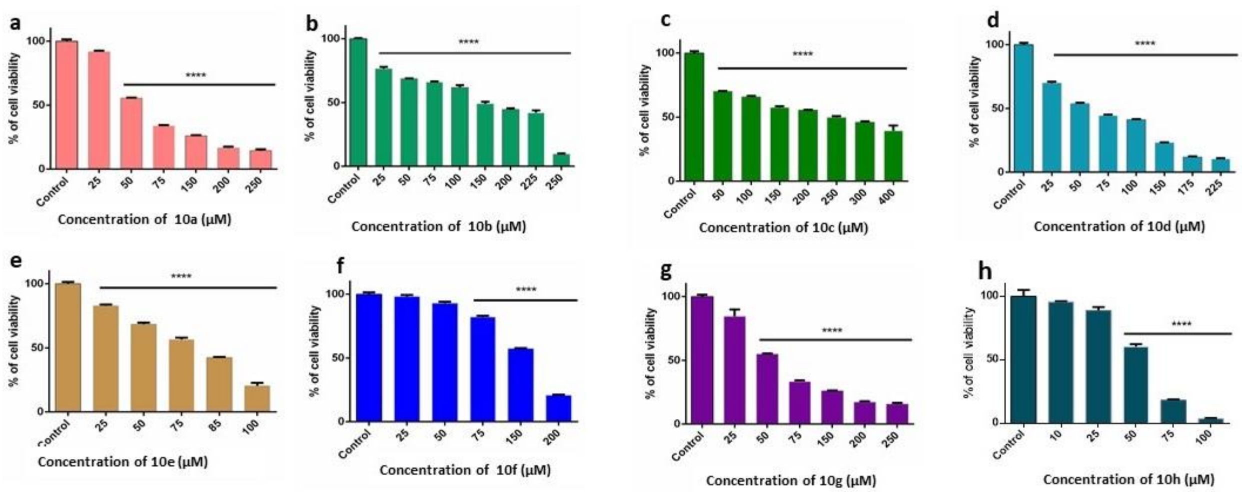


Figure S3: Determination of viability of HeLa cells upon treatment with synthesized compounds for 48 h. (a), (b), (c), (d), (e), (f), (g), (h), (i) and (j) refers to treatment with compound **10a**, **10b**, **10c**, **10d**, **10e**, **10f** and **10g** respectively. (h) refers to determined IC_{50} values of the respective compounds. Results expressed as the mean ± SEM are based on at least three independent experiments. The statistical significance was assessed versus that of the untreated cells. The significance level was set at $p \leq 0.05$ (*), $p \leq 0.01$ (**), $p \leq 0.001$ (***) or $p \leq 0.0001$ (****).

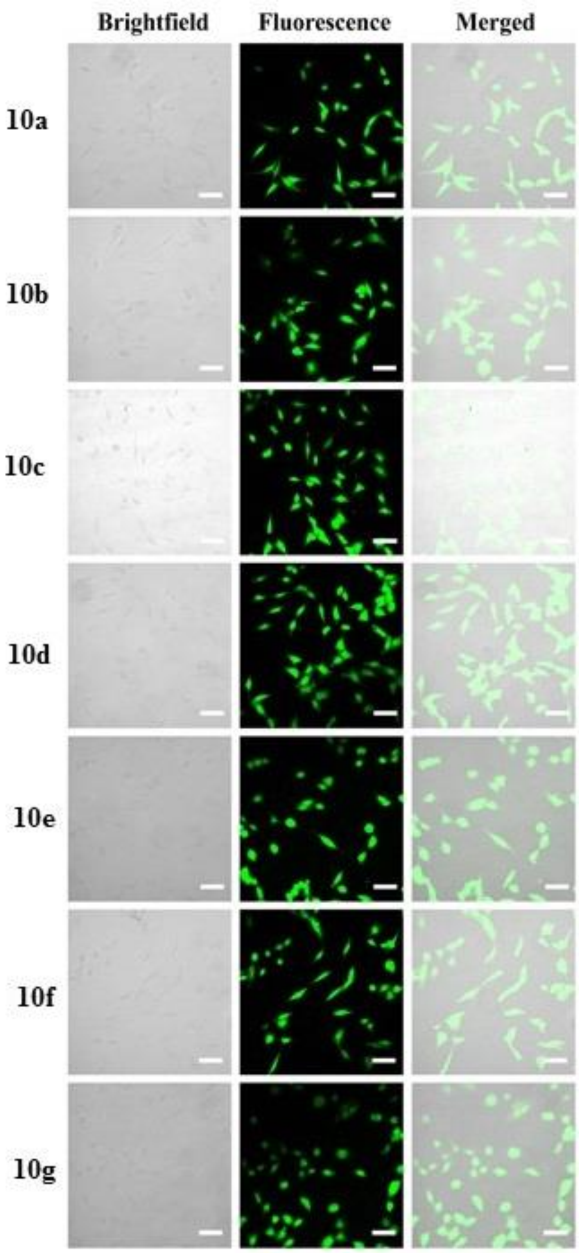


Figure S4: Confocal laser scanning microscopy images of HeLa cells stained with **10a-g** respectively. Cells were incubated with 40 µM of the compounds for 20 min. Excitation: 458 nm; Emission range: 480-605 nm; Scale bar: 50 µm.

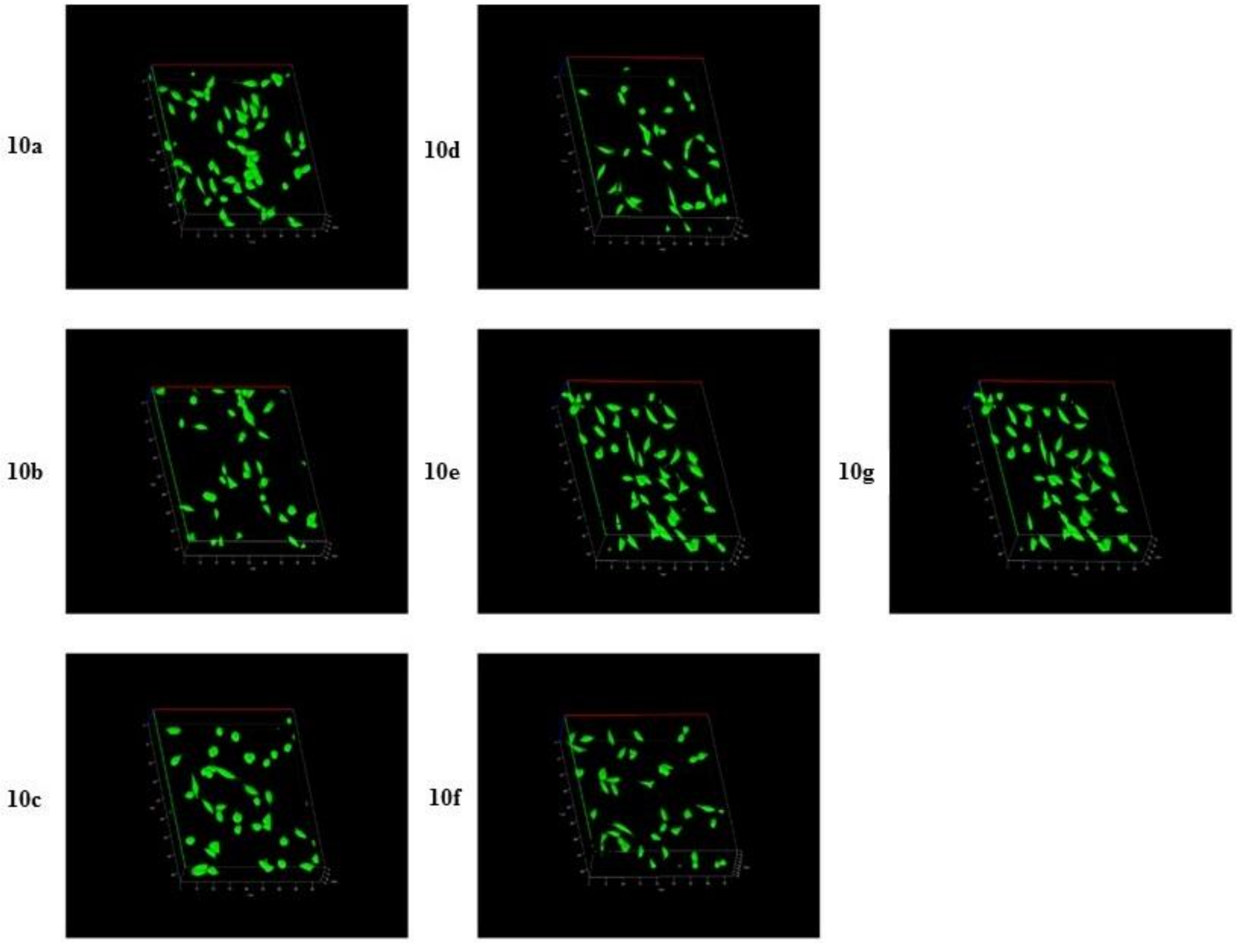


Figure S5: 3D Confocal laser scanning microscopy images of HeLa cells obtained by Z-stacking. Cells were treated with compounds **10a-g** respectively, at a concentration of 40 µM for 20 min. Excitation: 458 nm; Emission range: 480-605nm.

Materials and methods for biological evaluation:

Materials:

Dulbecco's modified eagle's medium (DMEM), phosphate-buffered saline (PBS), paraformaldehyde, and dimethyl sulfoxide (DMSO) were purchased from Sigma Aldrich (USA). Antibiotic-antimycotic, alamarBlue, trypsin-EDTA, and fetal bovine serum (FBS) were purchased from Thermo Fisher Scientific (USA). All the cell culture plastic wares were purchased from Eppendorf (Hamburg, Germany).

Cell Culture:

Human cervical cancer cell line HeLa was obtained from National Centre for Cell Sciences (NCCS), Pune. Cells were cultured in DMEM media supplemented with 10% FBS and 1% antibiotic-antimycotic solution. The culture was kept in a humidified atmosphere at 37 °C in a 5% carbon dioxide incubator. The media was changed at an interval of 3 days and subcultured upon reaching confluence.

Cell Viability Assay:

Cell viability was examined using the alamarBlue assay. Resazurin, the active ingredient of alamarBlue, is converted to its reduced form resorufin when entering into living cells. Hela cells were seeded in a 96 well plate at a density of 5000 cells/ well. After allowing the cells to attach to the plate surface for 12 h, they were treated with varying concentrations of synthesized compounds for 48 h. After the completion of the treatment, 10 µl alamarBlue was directly added to the wells and incubated for 2 h at 37 °C under 5% CO_2 humidified conditions. The absorbance was measured at 570 nm with a reference wavelength of 600 nm (normalized to the 600 nm value). The treatments were done in triplicate, and the experiments were repeated thrice. Cell viability was calculated using the following formula –

$$Cell\ viability\ (\%) = \frac{(abs570 - abs600)Sample}{(abs570 - abs600)Control} \times 100$$

The statistical tests were performed using GraphPad Prism software.

Fluorescence microscopy:

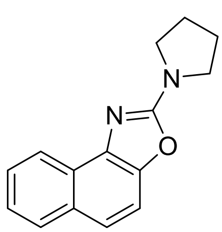
Sterilized glass coverslips were placed inside 6 well plates, and HeLa cells were seeded at a density of 0.5 X 10^6 cells per well. Following 12 h incubation, cells were treated with the compounds at a concentration of 300 µM for 15 minutes in complete media. After incubation, the media was removed, and cells were washed 3 times with PBS. To fix the cells, PBS was removed, and cells were incubated with 4% paraformaldehyde for 15 minutes. Following incubation, cells were washed 3 times with PBS. Next, glass coverslips were placed on a glass-slide by inverting, and the mounting medium was added in between for preservation. Untreated cells were used as control. Images were taken using Nikon Eclipse Ti S Fluorescence Microscope and processed using NIS

Elements Viewer and ImageJ software, respectively. Images were taken using the blue excitation laser and green emission filter.

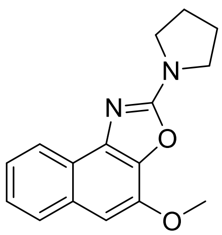
General: All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in oven-dried glassware under an argon atmosphere. Dichloromethane (CH_2Cl_2) was freshly distilled from phosphorus (V) oxide (P_2O_5). Commercial grade xylene, benzene and toluene were distilled over CaH_2 before use. All other solvents and reagents were purified according to standard procedures or were used as received from Aldrich, Acros, Merck and Spectrochem. ^{1}H, ^{13}C NMR spectroscopy: *Varian Mercury plus 400 MHz, Bruker 600 MHz* (at 298 K). Chemical shifts, δ (in ppm), are reported relative to TMS δ (^{1}H) 0.0 ppm, δ (^{13}C) 0.0 ppm) which was used as the inner reference. Otherwise the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (^{1}H) 7.26 ppm, δ (^{13}C) 77.2 ppm; CD_3OD, (^{1}H) 3.31 ppm, δ (^{13}C) 49.0 ppm) were used for calibration. Column chromatography: Merck or Spectrochem silica gel 60-120 under gravity. IR: spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520, and peaks are given in *m/z* (% of basis peak). Nitrosoarene derivatives were synthesized by literature procedures.[ii]

General procedure for the synthesis of 2-aminooxazole derivatives (GP-1):
Nitrosoarene (0.23 – 0.40 mmol) was added to a mixture of secondary amine (2 – 4 equiv.) and potassium acetate (2 equiv) in dry dichloromethane (4 – 6 mL) and the reaction mixture was refluxed for 36 – 72 h under argon atmosphere. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated under vacuum to obtain brown gummy residue which was purified by column chromatography to afford analytically pure 2-aminooxazole derivatives.

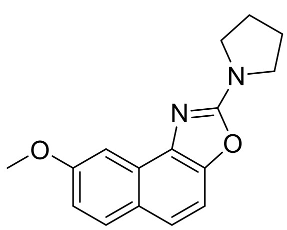
2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6a): According to GP-1: 1-nitroso-2-naphthol (40 mg, 0.23 mmol), pyrrolidine (76 µL, 0.92 mmol) and KOAc (46 mg, 0.46 mmol) were reacted for 36 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:5) of the crude gave **6a** as a brown solid (39 mg, 70%). FTIR (KBr): $\tilde{\nu}$ = 2964, 2927, 2874, 1649, 1618, 1571, 1481, 1345, 1261, 1086, 1025, 796, 726 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.39 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 15.2 Hz, 3H), 7.44 – 7.42 (m, 1H), 3.75 – 3.72 (m,



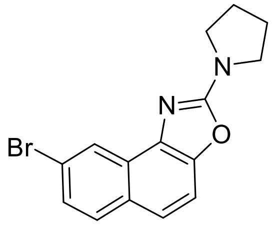
4H), 2.08 – 2.05 (m, 4H). ^{13}C NMR (151 MHz, CDCl3) δ = 161.0, 144.9, 138.3, 131.1, 128.3, 125.6, 124.8, 124.5, 122.4, 120.4, 109.7, 47.7, 25.7. HRMS (ESI) exact mass calculated for $C_{15}H_{15}N_2O^+$ ($[M + H]^+$): 239.1179; Found: 239.1184.



4-methoxy-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6b): According to GP-1: 3-methoxy-1-nitrosonaphthalen-2-ol (52 mg, 0.25 mmol), pyrrolidine (83 µL, 1.0 mmol) and KOAc (49 mg, 0.50 mmol) were reacted for 48 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6b** as a brown solid (56 mg, 83%). FTIR (KBr): $\tilde{\nu}$ = 2964, 2882, 2839, 1737, 1653, 1625, 1596, 1467, 1433, 1372, 1231, 1028, 825, 726 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.29 – 8.27 (m, 1H), 7.77 – 7.76 (m, 1H), 7.41 – 7.39 (m, 2H), 6.89 (s, 1H), 4.06 (s, 3H), 3.75 – 3.73 (m, 4H), 2.06 – 2.04 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 161.4, 144.5, 140.6, 136.1, 132.1, 127.3, 125.3, 123.5, 122.4, 121.1, 99.8, 56.0, 47.9, 25.8. HRMS (ESI) exact mass calculated for $C_{16}H_{16}N_2O_2^+$ ($[M + H]^+$): 269.1285; Found: 269.1284.



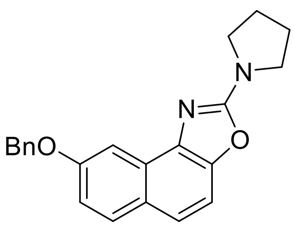
8-methoxy-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6c): According to GP-1: 7-methoxy-1-nitrosonaphthalen-2-ol (60 mg, 0.29 mmol), pyrrolidine (96 µL, 1.18 mmol) and KOAc (68 mg, 0.59 mmol) were reacted for 36 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6c** as a brown gum (53 mg, 67%). FTIR (KBr): $\tilde{\nu}$ = 2958, 2925, 2854, 1651, 1621, 1574, 1461, 1261, 1381, 1161, 1142, 805, 725 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 9.2 Hz, 1H), 7.63 (d, *J* = 2.4 Hz, 1H), 7.43 - 7.41 (m, 1H), 7.36 - 7.34 (m, 1H), 7.08 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.98 (s, 3H), 3.73 – 3.71 (m, 4H), 2.07 - 2.04 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 161.2, 158.0, 145.7, 138.0, 130.1, 126.7, 126.2, 120.5, 117.6, 107.4, 100.7, 55.8, 47.8, 25.9. HRMS (ESI) exact mass calculated for $C_{16}H_{17}N_2O_2^+$ ($[M + H]^+$): 269.1285; Found: 269.1292.



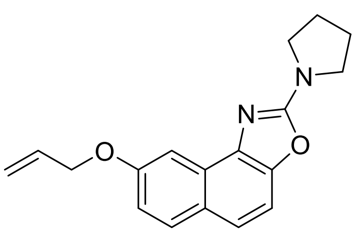
8-bromo-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6d): According to GP-1: 7-bromo-1-nitrosonaphthalen-2-ol (50 mg, 0.20 mmol), pyrrolidine (66 µL, 0.8 mmol) and KOAc (39 mg, 0.40 mmol) were reacted for 48 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **6d** as a colorless solid (38 mg, 60%). FTIR (KBr): $\tilde{\nu}$ = 2963, 2927, 2872, 1649, 1614, 1566, 1434, 1325, 1089, 881, 823, 771 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.45 (s, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.36 – 7.35 (m, 1H), 3.65 – 3.62 (m, 4H), 2.01 – 1.97 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 161.4, 145.7, 138.3, 130.2, 129.6, 128.0, 125.9, 124.8, 120.2, 120.0, 110.2, 47.8, 25.9. HRMS (ESI) exact mass calculated for $C_{15}H_{14}BrN_2O^+$ ($[M + H]^+$): 317.0284; Found: 317.0284.

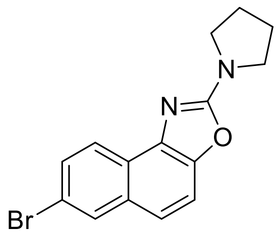
8-(benzyloxy)-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6e): According to GP-1: 7-(benzyloxy)-1-nitrosonaphthalen-2-ol (54 mg, 0.19 mmol), pyrrolidine (63 µL, 0.77 mmol) and KOAc (38 mg, 0.39 mmol) were reacted for 60 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6e** as a brown yellow gum (42 mg, 63%). FTIR (KBr): $\tilde{\nu}$ = 2962, 2923, 2853, 1647, 1624, 1596, 1579, 1457, 1261, 1022, 800, 729 cm^{-1}. ^{1}H NMR (400 MHz) δ = 7.79 (d, *J* = 8.8 Hz, 1H), 7.76 – 7.75 (m, 1H), 7.52 – 7.50 (m, 2H), 7.45 – 7.34 (m, 5H), 7.17 (dd, *J* = 9.2, 2.4 Hz, 1H), 5.24 (s, 2H), 3.75 – 3.72 (m, 4H), 2.09 – 2.05 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 161.2, 157.3, 145.8, 138.1, 137.3, 130.2, 128.8, 128.1, 128.0, 126.8, 126.2, 120.5, 118.0, 107.5, 101.9, 70.4, 47.8, 25.9. HRMS (ESI) exact mass calculated for $C_{22}H_{21}N_2O_2^+$ ($[M + H]^+$): 345.1598; Found: 345.1607.



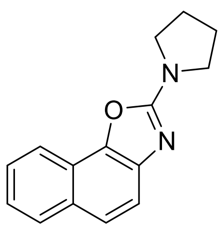
8-(allyloxy)-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6f): According to GP-1: 7-(allyloxy)-1-nitrosonaphthalen-2-ol (45 mg, 0.19 mmol), pyrrolidine (64 µL, 0.78 mmol) and KOAc (38 mg, 0.39 mmol) were reacted for 72 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:5) of the crude gave **6f** as a brown gum (45 mg, 78%). FTIR (KBr): $\tilde{\nu}$ = 2924, 2853, 1647, 1624, 1556, 1263, 1021, 822, 741 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 9.0 Hz, 1H), 7.65 – 6.64 (m, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 9.0 Hz, 1H), 7.12 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.18 – 6.13 (m, 1H), 5.51 – 5.48 (m, 1H), 5.33 – 5.31 (m, 1H), 4.74 – 4.73 (m, 2H), 3.74 – 3.72 (m, 4H), 2.08 – 2.06 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.6, 157.0, 145.4, 136.8, 133.4, 130.2, 126.7, 125.7, 120.9, 118.1, 117.9, 107.4, 101.8, 69.2, 48.0, 25.8. HRMS (ESI) exact mass calculated for $C_{18}H_{19}N_2O_2^+$ ($[M + H]^+$): 295.1441; Found: 295.1443.



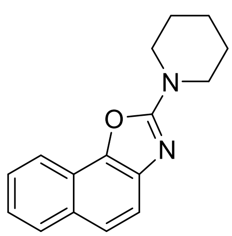
7-bromo-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (6g): According to GP-1: 6-bromo-1-nitrosonaphthalen-2-ol (0.10 g, 0.40 mmol), pyrrolidine (0.13 mL, 1.6 mmol) and KOAc (78 mg, 0.8 mmol) were reacted for 48 h in dry DCM (10 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6g** as a brown solid (76 mg, 60%). FTIR (KBr): $\tilde{\nu}$ = 2964, 2923, 2869, 1649, 1613, 1420, 1385, 1339, 1086, 904, 798 cm^{-1}. 1H NMR (600 MHz, $CDCl_3$) δ = 8.23 (d, *J* = 8.4 Hz, 1H), 8.02 (s, 1H), 7.58 – 7.56 (m, 1H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 3.72 – 3.70 (m, 4H), 2.07 – 2.05 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 161.5, 145.4, 139.2, 132.4 130.4, 128.8, 124.4, 123.4, 119.3, 118.5, 110.9, 47.8, 25.8. HRMS (ESI) exact mass calculated for $C_{15}H_{14}BrN_2O^+$ ($[M + H]^+$): 317.0284; Found: 317.0288.



2-(pyrrolidin-1-yl)naphtho[2,1-*d*]oxazole (6h): According to GP-1: 2-nitroso-1-naphthol (40 mg, 0.23 mmol), pyrrolidine (76 µL, 0.92 mmol) and KOAc (45 mg, 0.46 mmol) were reacted for 36 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:5) of the crude gave **6h** as a brown solid (44 mg, 80%). FTIR (KBr): $\tilde{\nu}$ = 2963, 2927, 2874, 1649, 1618, 1571, 1406, 1261, 1086, 1024, 797, 726 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.01 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.52 – 7.49 (m, 1H), 7.35 – 7.33 (m, 1H), 3.73 – 3.71 (m, 4H), 2.08 – 2.05 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 161.2, 143.2, 140.1, 129.4, 128.8, 126.4, 124.4, 123.4, 119.9, 118.9, 117.1, 47.7, 25.8. HRMS (ESI) exact mass calculated for $C_{15}H_{15}N_2O^+$ ($[M + H]^+$): 239.1179; Found: 239.1183.

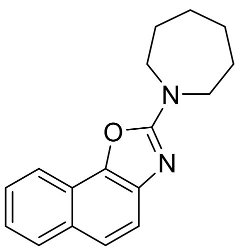


2-(piperidin-1-yl)naphtho[2,1-*d*]oxazole (6i): According to GP-1: 2-nitroso-1-naphthol (70 mg, 0.40 mmol), piperidine (0.16 mL, 1.62 mmol) and KOAc (79 mg, 0.81 mmol) were reacted for 36 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6i** as a colorless solid (75 mg, 73%). FTIR (KBr): $\tilde{\nu}$ = 3059, 2984, 2936, 2857, 1940, 1633, 1562, 1520, 1451, 1289, 1253, 1024, 859, 806, 748, 683, 422 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.51 – 7.49 (m, 1H), 7.36 – 7.33 (m, 1H), 3.73 – 3.72 (m, 4H), 1.74 – 1.69 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.6, 142.8, 139.7, 129.5, 128.8, 126.4, 124.4, 123.5, 119.8, 118.8, 117.0, 46.9,

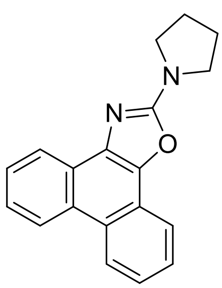


25.4, 24.2. HRMS (ESI) exact mass calculated for $C_{16}H_{17}N_2O^+$ ([M + H]$^+$): 253.1335; Found: 253.1334.

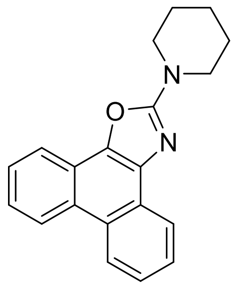
2-(azepan-1-yl)naphtho[2,1-*d*]oxazole (6j): According to GP-1: 2-nitroso-1-naphthol (70 mg, 0.40 mmol), azepane (0.18 mL, 1.62 mmol) and KOAc (79 mg, 0.81 mmol) were reacted for 36 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6j** as a colorless solid (71 mg, 66%). FTIR (KBr): $\tilde{\nu}$ = 2963, 2925, 2851, 1627, 1564, 1289, 1260, 1095, 1024, 804, 724 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.51 – 7.48 (m, 1H), 7.34 – 7.32 (m, 1H), 3.78 – 3.74 (m, 4H), 1.90 – 1.87 (m, 4H), 1.63 – 1.62 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.8, 143.0, 140.2, 129.3, 128.8, 126.4, 124.3, 123.3, 119.8, 118.8, 117.0, 48.3, 28.5, 27.7. HRMS (ESI) exact mass calculated for $C_{17}H_{19}N_2O^+$ ([M + H]$^+$): 267.1492; Found: 267.1492.



2-(pyrrolidin-1-yl)phenanthro[9,10-*d*]oxazole (6k): According to GP-1: 10-nitrosophenanthren-9-ol (60 mg, 0.27 mmol), pyrrolidine (89 µL, 1.08 mmol) and KOAc (53 mg, 0.54 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6k** as a colorless solid (54 mg, 69%). FTIR (KBr): $\tilde{\nu}$ = 3056, 2955, 2942, 1646, 1609, 1355, 1261, 1097, 1028, 963, 899, 803, 752, 725 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.72 – 8.70 (m, 2H), 8.46 (d, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.60 (m, 3H), 7.55 –7.51 (m, 1H), 3.78 – 3.75 (m, 4H), 2.08 – 2.06 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 161.3, 140.7, 136.2, 128.6, 127.0, 126.9, 125.9, 125.4, 124.1, 123.7, 123.4, 123.0, 121.2, 119.3, 47.8, 25.9. Total count of ^{13}C is less than expected due to the merging of signal in the aromatic region. HRMS (ESI) exact mass calculated for $C_{19}H_{17}N_2O^+$ ([M + H]$^+$): 289.1335; Found: 289.1338.

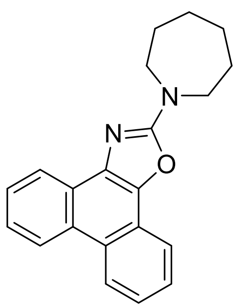


2-(piperidin-1-yl)phenanthro[9,10-*d*]oxazole (6l): According to GP-1: 10-nitrosophenanthren-9-ol (50 mg, 0.22 mmol), piperidine (88 µL, 0.9 mmol) and KOAc (44 mg, 0.45 mmol) were reacted for 72 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane, 1:40) of



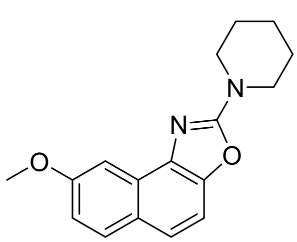
the crude gave **6l** as a yellow gum (38 mg, 56%). FTIR (KBr): $\tilde{\nu}$ = 2960, 2923, 2852, 1673, 1646, 1624, 1609, 1451, 1356, 1261, 1096, 753, 726 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 8.4 Hz, 2H), 8.42 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.69 – 7.66 (m, 1H), 7.65 – 6.61 (m, 2H), 7.55 – 7.52 (m, 1H), 3.80 – 3.79 (m, 4H), 1.79 – 1.77 (m, 4H), 1.76 – 1.72 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.8, 140.5, 136.1, 128.7, 127.1, 127.1, 126.9, 126.0, 125.5, 124.2, 123.8, 123.5, 123.0, 121.3, 119.4, 47.1, 25.5, 24.3. HRMS (ESI) exact mass calculated for $C_{20}H_{19}N_2O^+$ ($[M + H]^+$): 303.1492; Found: 303.1493.

2-(azepan-1-yl)phenanthro[9,10-*d*]oxazole (6m): According to GP-1: 10-nitrosophenanthren-9-



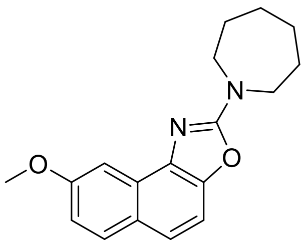
ol (60 mg, 0.27 mmol), azepane (0.12 mL, 1.08 mmol) and KOAc (53 mg, 0.54 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:20) of the crude gave **6m** as a colorless solid (59 mg, 69%). FTIR (KBr): $\tilde{\nu}$ = 2922, 2877, 2847, 1643, 1604, 1562, 1356, 1332, 876, 752, 724 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.72 –8.70 (m, 2H), 8.45 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.60 (m, 3H), 7.55 –7.51 (m, 1H), 3.86 – 3.83 (m, 4H), 1.95 – 1.90 (m, 4H), 1.68 – 1.64 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.9, 140.4, 136.4, 128.6, 127.0, 126.83, 126.77, 125.9, 125.4, 124.0, 123.8, 123.4, 123.0, 121.2, 119.2, 48.3, 28.6, 27.9. HRMS (ESI) exact mass calculated for $C_{22}H_{21}N_2O^+$ ($[M + H]^+$): 317.1648; Found: 317.1649.

8-methoxy-2-(piperidin-1-yl)naphtho[1,2-*d*]oxazole (6n): According to GP-1: 7-methoxy-1-

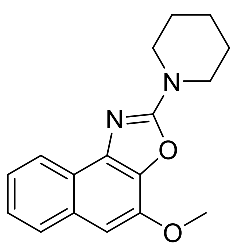


nitrosonaphthalen-2-ol (70 mg, 0.34 mmol), piperidine (0.15 mL, 1.37 mmol) and KOAc (67 mg, 0.69 mmol) were reacted for 48 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6n** as a brown gum (72 mg, 74%). FTIR (KBr): $\tilde{\nu}$ = 3061, 2962, 2921, 2849, 1641, 1610, 1496, 1450, 1414, 1351, 1264, 1084, 1005, 745 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 9.0 Hz, 1H), 7.61– 7.60 (m, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.09 – 7.07 (m, 1H), 3.99 (s, 3H), 3.73 – 3.72 (m, 4H), 1.74 – 1.70 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.5, 158.0, 145.4, 137.7, 130.2, 126.6, 126.2, 120.7, 117.6, 107.3, 100.5, 55.7, 46.9, 25.5, 24.3. HRMS (ESI) exact mass calculated for $C_{17}H_{19}N_2O_2^+$ ([M + H]$^+$): 283.1441; Found: 283.1447.

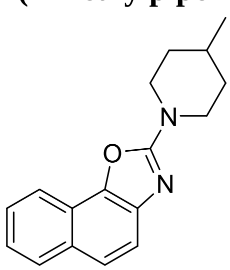
2-(azepan-1-yl)-8-methoxynaphtho[1,2-*d*]oxazole (6o): According to GP-1: 7-methoxy-1-nitrosonaphthalen-2-ol (70 mg, 0.34 mmol), azepane (0.16 mL, 1.37 mmol) and KOAc (67 mg, 0.69 mmol) were reacted for 36 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6o** as a brown solid (71 mg, 70%). FTIR (KBr): $\tilde{\nu}$ = 2920, 2580, 1644, 1620, 1581, 1472, 1374, 1279, 1027, 819, 875, 741, 725 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 9.0 Hz, 1H), 7.65 – 7.64 (m, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 9.0 Hz, 1H), 7.09 – 7.07 (m, 1H), 4.00 (s, 3H), 3.77 (t, *J* = 6.0, 4H), 1.89 – 1.86 (m, 4H), 1.64 – 1.62 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.6, 157.9, 145.4, 138.0, 130.1, 126.6, 126.0, 120.1, 117.5, 107.3, 100.6, 55.9, 48.2, 28.6, 27.8. HRMS (ESI) exact mass calculated for $C_{18}H_{21}N_2O_2^+$ ([M + H]$^+$): 297.1598; Found: 297.1598.



4-methoxy-2-(piperidin-1-yl)naphtho[1,2-*d*]oxazole (6p): According to GP-1: 3-methoxy-1-nitrosonaphthalen-2-ol (50 mg, 0.25 mmol), piperidine (0.10 mL, 0.98 mmol) and KOAc (48 mg, 0.49 mmol) were reacted for 48 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **6p** as a colorless solid (46 mg, 66%). FTIR (KBr): $\tilde{\nu}$ = 2960, 2924, 2854, 1647, 1614, 1572, 1387, 1261, 1097, 1020, 804, 726 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.25 – 8.24 (m, 1H), 7.77 – 7.76 (m, 1H), 7.41 – 7.39 (m, 2H), 6.90 (s, 1H), 4.06 (s, 3H), 3.74 – 3.74 (m, 4H), 1.72 – 1.71 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.8, 144.5, 140.3, 135.8, 132.1, 127.3, 125.3, 123.6, 122.4, 121.2, 100.0, 56.0, 47.0, 25.5, 24.5. HRMS (ESI) exact mass calculated for $C_{17}H_{19}N_2O_2^+$ ([M + H]$^+$): 283.1441; Found: 283.1443.

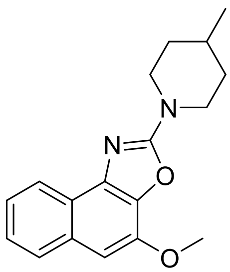


2-(4-methylpiperidin-1-yl)naphtho[2,1-*d*]oxazole (6q): According to GP-1: 2-nitroso-1-naphthol (70 mg, 0.40 mmol), 4-methylpiperidine (0.19 mL, 1.62 mmol) and KOAc (79 mg, 0.81 mmol) were reacted for 36 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6q** as a colorless solid (68 mg, 63%). FTIR (KBr): $\tilde{\nu}$ = 2955, 2923, 2850, 1625, 1563, 1455, 1369, 1290, 1260, 1086, 806 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz,

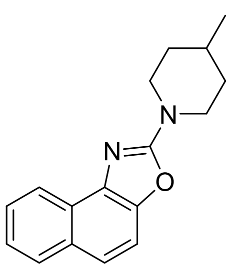


1H), 7.52 – 7.50 (m, 1H), 7.36 – 7.34 (m, 1H), 4.38 – 4.35 (m, 2H), 3.14 – 3.10 (m, 2H), 1.80 – 1.78 (m, 2H), 1.67 – 1.64 (m, 1H), 1.37 – 1.32 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.7, 142.9, 139.8, 129.5, 128.8, 126.5, 124.5, 123.5, 119.8, 118.9, 117.1, 46.4, 33.6, 30.8, 22.1. HRMS (ESI) exact mass calculated for $C_{17}H_{19}N_2O^+$ ($[M + H]^+$): 267.1492; Found: 267.1489.

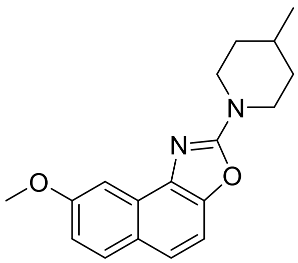
4-methoxy-2-(4-methylpiperidin-1-yl)naphtho[1,2-*d*]oxazole (6r): According to GP-1: 3-methoxy-1-nitrosonaphthalen-2-ol (50 mg, 0.25 mmol), 4-methylpiperidine (0.12 mL, 1.0 mmol) and KOAc (48 mg, 0.49 mmol) were reacted for 48 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **6r** as a colorless solid (51 mg, 70%). FTIR (KBr): $\tilde{\nu}$ = 3066, 3012, 2919, 2848, 1887, 1668, 1643, 1581, 1472, 1374, 1256, 1026, 819, 725 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.26 – 8.2 (m, 1H), 7.78 – 7.76 (m, 1H), 7.41 – 7.39 (m, 2H), 6.89 (s, 1H), 4.41 – 4.38 (m, 2H), 4.05 (s, 3H) 3.14 – 3.07 (m, 2H), 1.79 – 1.76 (m, 2H), 1.68 – 1.59 (m, 1H), 1.37 – 1.27 (m, 2H), 1.00 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.7, 144.4, 140.2, 135.8, 132.1, 127.3, 125.3, 123.6, 122.3, 121.1, 99.9, 56.0, 46.4, 33.7, 30.8, 22.1. HRMS (ESI) exact mass calculated for $C_{18}H_{21}N_2O_2^+$ ($[M + H]^+$): 297.1598; Found: 297.1597.



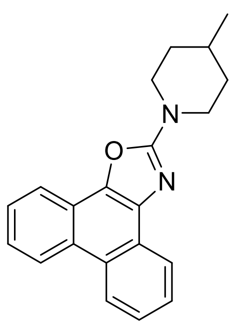
2-(4-methylpiperidin-1-yl)naphtho[1,2-*d*]oxazole (6s): According to GP-1: 1-nitroso-2-naphthol (70 mg, 0.40 mmol), 4-methylpiperidine (0.19 mL, 1.62 mmol) and KOAc (79 mg, 0.81 mmol) were reacted for 48 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:20) of the crude gave **6s** as a brown solid (88 mg, 81%). FTIR (KBr): $\tilde{\nu}$ = 2948, 2925, 2836, 2811, 1636, 1598, 1571, 1453, 1413, 1347, 1259, 878, 767, 731 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.54 – 7.52 (m, 1H), 7.50 – 7.48 (mz, 2H), 7.44 –7.42 (m, 1H), 4.39 – 4.37 (m, 2H), 3.13 – 3.09 (m, 2H), 1.80 – 1.78 (m, 2H), 1.67 – 1.62 (m, 1H), 1.37 – 1.29 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.8, 144.9, 138.6, 131.3, 128.5, 125.8, 125.1, 124.6, 122.4, 120.7, 109.9, 46.4, 33.7, 30.8, 22.1. HRMS (ESI) exact mass calculated for $C_{17}H_{19}N_2O^+$ ($[M + H]^+$): 267.1492; Found: 267.1497.



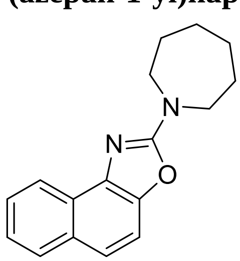
8-methoxy-2-(4-methylpiperidin-1-yl)naphtho[1,2-*d*]oxazole (6t):According to GP-1: 7-methoxy-1-nitrosonaphthalen-2-ol (70 mg, 0.34 mmol), 4-methylpiperidine (0.16 mL, 1.37 mmol) and KOAc (67 mg, 0.69 mmol) were reacted for 36 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6t** as a brown gum (73 mg, 72%). FTIR (KBr): $\tilde{\nu}$ = 3016, 2949, 2926, 2848, 1643, 1595, 1579, 1468, 1432, 1363, 1345, 1276, 1026, 876, 828 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 9.0 Hz, 1H), 7.60 – 7.59 (m, 1H), 7.44 – 7.42 (m, 1H), 7.34 – 7.33 (m, 1H), 7.08 (dd, *J* = 9.0, 2.4 Hz, 1H), 4.38 – 4.34 (m, 2H), 3.99 (s, 3H), 3.13 – 3.08 (m, 2H), 1.81 – 1.77 (m, 2H), 1.67 - 1.62 (m, 1H), 1.36 – 1.30 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H). 13C NMR (151 MHz, $CDCl_3$) δ = 162.5, 158.0, 145.4, 137.7, 130.1, 126.6, 126.2, 120.7, 117.6, 107.4, 100.5, 55.7, 46.3, 33.7, 30.8, 22.1. HRMS (ESI) exact mass calculated for $C_{18}H_{21}N_2O_2^+$ ($[M + H]^+$): 297.1598; Found: 297.1604.



2-(4-methylpiperidin-1-yl)phenanthro[9,10-*d*]oxazole (6u): According to GP-1: According to GP-1: 10-nitrosophenanthren-9-ol (50 mg, 0.21 mmol), 4-methylpiperidine (0.11 mL, 0.84 mmol) and KOAc (44 mg, 0.42 mmol) were reacted for 72 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:20) of the crude gave **6u** as a colorless solid (40 mg, 60%). FTIR (KBr): $\tilde{\nu}$ = 2924, 2853, 1630, 1565, 1455, 1290, 726 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 8.4 Hz, 2H), 8.42 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.69 – 6.66 (m, 1H), 7.65 – 7.62 (m, 2H), 7.55 – 7.53 (m, 1H), 4.45 – 4.43 (m, 2H), 3.19 – 3.14 (m, 2H), 1.84 – 1.82 (m, 2H), 1.69 – 1.67 (m, 1H), 1.42 – 1.35 (m, 2H), 1.03 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.8, 140.5, 136.0, 128.7, 127.0, 127.0, 126.9, 125.9, 125.4, 124.2, 123.7, 123.4, 122.9, 121.2, 119.3, 46.4, 33.7, 30.8, 22.0. HRMS (ESI) exact mass calculated for $C_{21}H_{20}N_2O_3^+$ ($[M + H]^+$): 317.1648; Found: 317.1652.

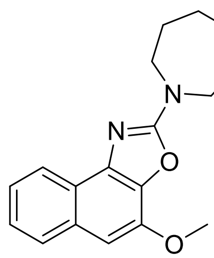


2-(azepan-1-yl)naphtho[1,2-*d*]oxazole (6v): According to GP-1: 1-nitroso-2-naphthol (70 mg, 0.40 mmol), azepane (0.18 mL, 1.62 mmol) and KOAc (79 mg, 0.81 mmol) were reacted for 36 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:20) of the crude gave **6v** as a brown solid (76 mg, 70%). FTIR (KBr): $\tilde{\nu}$ = 2922, 2849, 1644, 1611, 1568, 1443, 1407, 1365, 1273,

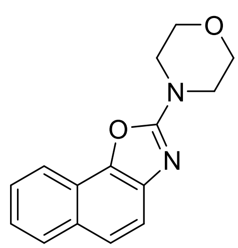


998, 802, 722 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.37 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.47 (m, 3H), 7.44 – 7.42 (m, 1H), 3.78 (t, *J* = 6.0 Hz, 4H), 1.90 – 1.86 (m, 4H), 1.64 – 1.63 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.9, 145.0, 139.0, 131.3, 128.5, 125.6, 125.0, 124.6, 122.6, 120.1, 109.8, 48.3, 28.6, 27.8. HRMS (ESI) exact mass calculated for $C_{17}H_{19}N_2O^+$ ($[M + H]^+$): 267.1492; Found: 267.1494.

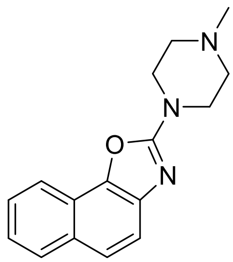
2-(azepan-1-yl)-4-methoxynaphtho[1,2-*d*]oxazole (6w): According to GP-1: 3-methoxy-1-nitrosonaphthalen-2-ol (50 mg, 0.24 mmol), azepane (0.11 mL, 0.98 mmol) and KOAc (48 mg, 0.49 mmol) were reacted for 36 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6w** as a brown gum (56 mg, 77%). FTIR (KBr): $\tilde{\nu}$ = 3045, 2961, 2932, 2879, 1651, 1621, 1573, 1480, 1381, 1163, 805, 728 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.27 – 8.25 (m, 1H), 7.77 – 7.76 (m, 1H), 7.40 – 7.38 (m, 2H), 6.88 (s, 1H), 4.06 (s, 3H), 3.81 – 3.80 (m, 4H), 1.90 – 1.87 (m, 4H), 1.65 –1.63 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.9, 144.4, 140.6, 135.8, 132.0, 127.3, 125.2, 123.5, 122.5, 121.0, 99.6, 56.0, 48.3, 28.5, 27.8. HRMS (ESI) exact mass calculated for $C_{18}H_{21}N_2O_2^+$ ($[M + H]^+$): 297.1598; Found: 297.1593.



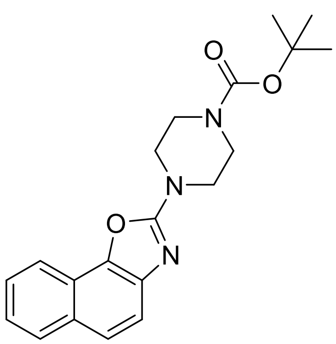
2-morpholinonaphtho[2,1-*d*]oxazole (6x): According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), morpholine (0.12 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:4) of the crude gave **6x** as a brown gum (37 mg, 42%). FTIR (KBr): $\tilde{\nu}$ = 2962, 2920, 2863, 1610, 1562, 1287, 1245, 1118, 894, 812, 736 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.69 – 7.68 (m, 1H), 7.60 – 7.58 (m, 1H), 7.54 – 7.52 (m, 1H), 7.40 – 7.37 (m, 1H), 3.88 – 3.87 (m, 4H), 3.78 – 3.76 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.3, 143.2, 139.2, 129.8, 128.9, 126.7, 124.8, 123.9, 119.9, 118.9, 117.22, 66.4, 46.1. HRMS (ESI) exact mass calculated for $C_{15}H_{15}N_2O_2^+$ ($[M + H]^+$): 255.1128; Found: 255.1124.



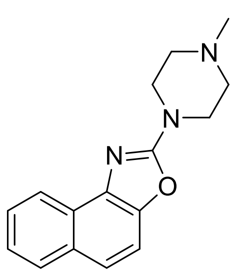
2-(4-methylpiperazin-1-yl)naphtho[2,1-d]oxazole (6y): According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), 1-methylpiperazine (0.15 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; MeOH : DCM, 1:20) of the crude gave **6y** as a brown gum (48 mg, 52%). FTIR (KBr): $\tilde{\nu}$ = 2960, 2922, 2849, 1644, 1619, 1471, 1366, 1262, 1026, 799, 741 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.39 – 7.35 (m, 1H), 3.82 – 3.79 (m, 4H), 2.59 – 2.57 (m, 4H), 2.38 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.4, 143.1, 139.5, 129.7, 128.9, 126.6, 124.7, 123.8, 119.9, 118.9, 117.2, 54.4, 46.5, 45.9. HRMS (ESI) exact mass calculated for $C_{16}H_{18}N_3O^+$ ($[M + H]^+$): 268.1444; Found: 268.1445.



***tert*-butyl 4-(naphtho[2,1-*d*]oxazol-2-yl)piperazine-1-carboxylate (6z)**: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), 1-Boc-piperazine (0.26 g, 0.94 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 72 h in dry DCM (4 mL). Column chromatography (neutral allumina; EtOAc : Hexane, 1:4) of the crude gave **6z** as a brown solid (49 mg, 40%). FTIR (KBr): $\tilde{\nu}$ = 3054, 2970, 2923, 2854, 1697, 1628, 1565, 1364, 1167, 747 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 9.0 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 9.0 Hz, 1H), 7.55 – 7.52 (t, *J* = 8.0 Hz, 1H), 7.40 – 7.37 (m, 1H), 3.76 – 3.74 (m, 4H), 3.63 – 3.61 (m, 4H), 1.50 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.2, 154.8, 143.2, 139.3, 129.8, 128.9, 126.7, 124.8, 123.9, 119.9, 118.9, 117.2, 80.7, 45.9, 43.3, 28.6. HRMS (ESI) exact mass calculated for $C_{20}H_{24}N_3O_3^+$ ($[M + H]^+$): 354.1812; Found: 354.1818.

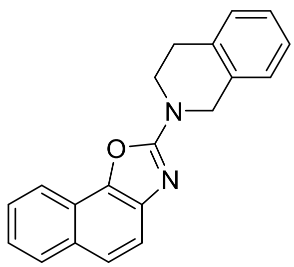


2-(4-methylpiperazin-1-yl)naphtho[1,2-*d*]oxazole (6aa): According to GP-1: 1-nitrosonaphthalen-2-ol (50 mg, 0.29 mmol), *N*-methyl-pipirazine (0.13 mL, 1.2 mmol) and KOAc (50 mg, 0.58 mmol) were reacted for 72 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : MeOH, 10:1) of the crude gave **6aa** as a brown gum (27 mg, 40%). FTIR (KBr): $\tilde{\nu}$ = 2962, 2925, 2853, 1643, 1452, 1406, 1366, 1262, 1022, 798, 746 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.49 (m,

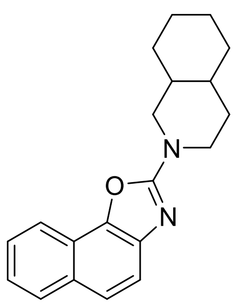


3H), 7.45 – 7.43 (m, 1H), 3.81 – 3.79 (m, 4H), 2.58 – 2.57 (m, 4H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.5, 145.1, 138.4, 131.3, 128.6, 125.9, 125.3, 124.8, 122.4, 121.1, 109.9, 54.5, 46.5, 45.9. HRMS (ESI) exact mass calculated for $C_{16}H_{18}N_3O^+$ ([M + H]$^+$): 268.1444; Found: 268.1444.

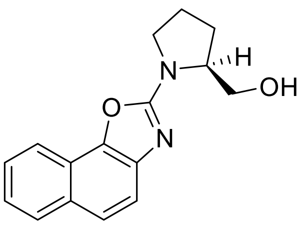
2-(3,4-dihydroisoquinolin-2(1H)-yl)naphtho[2,1-*d*]oxazole (6ab): According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), tetrahydroisoquinoline (0.17 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 60 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:10) of the crude gave **6ab** as a colorless solid (51 mg, 49%). FTIR (KBr): $\tilde{\nu}$ = 2958, 2922, 2852, 1627, 1564, 1457, 1261, 1087, 749 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.04 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.68 – 7.66 (m, 1H), 7.61 – 7.60 (m, 1H), 7.53 – 7.51 (m, 1H), 7.37 – 7.35 (m, 1H), 7.24 – 7.18 (m, 4H), 4.92 (s, 2H), 4.03 – 4.01 (m, 2H), 3.04 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.1, 143.1, 139.6, 134.2, 132.5, 129.6, 129.0, 128.8, 127.0, 126.7, 126.57, 126.56, 124.6, 123.6, 119.8, 118.9, 117.1, 47.4, 43.4, 28.7. HRMS (ESI) exact mass calculated for $C_{20}H_{17}N_2O^+$ ([M + H]$^+$): 301.1335; Found: 301.1336.



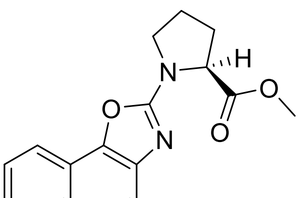
2-(octahydroisoquinolin-2(1*H*)-yl)naphtho[2,1-*d*]oxazole (6ac): According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), perhydroisoquinoline (0.20 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:20) of the crude gave **6ac** as a colorless solid (68 mg, 64%). FTIR (KBr): $\tilde{\nu}$ = 2924, 2851, 1646, 1565, 1297, 1248, 1210, 1153, 814, 746 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.66 –7.64 (m, 1H), 7.59 – 7.58 (m, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.35 – 7.33 (m, 1H), 4.42 – 4.39 (m, 1H), 4.25 – 4.23 (m, 1H), 3.10 –3.06 (m, 1H), 2.72 – 2.68 (m, 1H), 1.78 – 1.75 (m, 2H), 1.70 – 1.66 (m, 3H), 1.43 – 1.36 (m, 1H), 1.32 – 1.29 (m, 3H), 1.16 – 1.15 (m, 1H), 1.05 – 0.99 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.4, 142.8, 139.7, 129.4, 128.6, 126.2, 124.2, 123.2, 119.7, 118.7, 116.9, 52.0, 46.7, 41.5, 41.4, 32.9, 32.3, 29.9, 26.2, 25.8. HRMS (ESI) exact mass calculated for $C_{20}H_{23}N_2O^+$ ([M + H]$^+$): 307.1805; Found: 307.1803



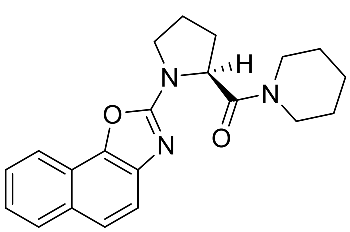
(*S*)-(1-(naphtho[2,1-*d*]oxazol-2-yl)pyrrolidin-2-yl)methanol (6ad): According to GP-1: 2-nitroso-1-naphthol (50 mg, 0.29 mmol), (*S*)-prolinol (0.11 mL, 1.2 mmol) and KOAc (57 mg, 0.58 mmol) were reacted for 72 h in dry DCM (5 mL). Column chromatography (silica; EtOAc : Hexane: DCM, 10:10:1) of the crude gave **6ad** as a colorless solid (34 mg, 44%). (KBr): $\tilde{\nu}$ = 3.63, 2952, 2924, 2854, 1628, 1566, 1457, 1288, 1258, 1050, 808, 728 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD) δ = 7.98 – 7.96 (m, 1H), 7.90 – 7.88 (m, 1H), 7.70 – 7.67 (m, 1H), 7.54 – 7.48 (m, 2H), 7.38 – 7.34 (m, 1H), 4.21 – 4.18 (m, 1H), 3.84 – 3.67 (m, 4H), 2.25 – 2.09 (m, 3H), 2.07 – 2.02 (m, 1H). ^{13}C NMR (101 MHz, CD_3OD) δ = 162.5, 143.8, 139.9, 130.9, 129.7, 127.7, 125.7, 124.7, 120.9, 119.5, 117.1, 63.6, 62.4, 49.8, 29.4, 24.9. HRMS (ESI) exact mass calculated for $C_{16}H_{17}N_2O_2^+$ ($[M + H]^+$): 269.1285; Found: 269.1287.



methyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolinate (6ae): 2-nitroso-1-naphthol (50 mg, 0.29 mmol), L-proline methyl ester hydrochloride (0.19 g, 1.16 mmol) and Et_3N (0.20 mL, 1.44 mmol) were reacted for 72 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:1) of the crude gave **6ae** as a colorless solid (43 mg, 50%). FTIR (KBr): $\tilde{\nu}$ = 2921, 2853, 1741, 1627, 1567, 1513, 1450, 1097, 810, 743 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.38 – 7.34 (m, 1H), 4.75 – 4.72 (m, 1H), 4.00 – 3.95 (m, 1H), 3.87 – 3.78 (m, 1H), 3.78 (s, 3H), 2.45 – 2.40 (m, 1H), 2.27 – 2.21 (m, 1H), 2.18 – 2.10 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.1, 160.5, 143.5, 139.8, 129.6, 128.8, 126.5, 124.6, 123.7, 119.9, 119.0, 117.4, 60.6, 52.7, 48.4, 31.1, 24.3. HRMS (ESI) exact mass calculated for $C_{17}H_{17}N_2O_3^+$ ($[M + H]^+$): 297.1234; Found: 297.1239.

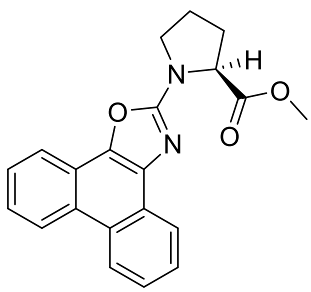


(1-(naphtho[2,1-*d*]oxazol-2-yl)pyrrolidin-2-yl)(piperidin-1-yl)methanone (6af): According to GP-1: 2-nitroso-1-naphthol (30 mg, 0.17 mmol), (*S*)-1-prolylpiperidine (63 mg, 0.35 mmol) and KOAc (34 mg, 0.35 mmol) were reacted for 72 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:1) of the crude gave **6af** as a brown solid (37 mg, 60%). FTIR (KBr): $\tilde{\nu}$ =2924, 2849, 1760, 1634, 1563, 1448, 1101, 1021, 806, 750 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.92 (d, *J* = 8.0 Hz,

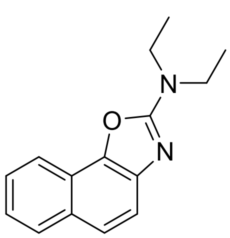


1H), 7.86 (d, J = 8.5 Hz, 1H), 7.63 (d, J = 8.5 Hz, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.50 – 7.47 (m, 1H), 7.35 – 7.31 (m, 1H), 5.02 (dd, J = 8.0, 3.0 Hz, 1H), 4.04 – 4.00 (m, 1H), 3.89 – 3.84 (m, 1H), 3.68 – 3.61 (m, 2H), 3.56 – 3.52 (m, 2H), 2.39 – 2.33 (m, 1H), 2.26 – 2.20 (m, 1H), 2.12 – 2.04 (m, 2H), 1.86 – 1.81 (m, 2H), 1.77 – 1.72 (m, 2H), 1.68 – 1.62 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.0, 160.7, 143.3, 140.1, 129.5, 128.8, 126.3, 124.3, 123.3, 119.9, 118.8, 117.4, 58.60, 58.57, 48.5, 46.8, 43.7, 30.8, 26.8, 25.8, 24.8, 24.1. HRMS (ESI) exact mass calculated for $C_{21}H_{24}N_3O_2^+$ ([M + H]$^+$): 350.1863; Found: 350.1864.

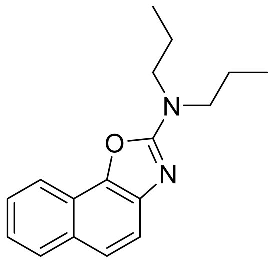
methyl phenanthro[9,10-*d*]oxazol-2-ylprolinate (6ag): 10-nitrosophenanthren-9-ol (30 mg, 0.13 mmol), L-proline methyl ester hydrochloride (84 mg, 0.50 mmol) and Et_3N (88 µL, 0.50 mmol) were reacted for 80 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:5) of the crude gave **6ag** as a colorless solid (19 mg, 43%). FTIR (KBr): $\tilde{\nu}$ = 3056, 2927, 1741, 1632, 1566, 1453, 1017, 821, 744 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.71 (d, J = 8.4 Hz, 2H), 8.43 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.68 – 7.66 (m, 1H), 7.65 – 7.61 (m, 2H), 7.56 – 7.53 (m, 1H), 4.80 – 4.78 (m, 1H), 4.05 – 4.01 (m, 1H), 3.92 – 3.89 (m, 1H), 3.80 (s, 3H), 2.48 – 2.42 (m, 1H), 2.28 – 2.24 (m, 1H), 2.22 – 2.16 (m, 1H), 2.15 – 2.11 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.4, 160.5, 141.1, 136.1, 128.7, 127.2, 127.1, 126.9, 126.0, 125.6, 124.4, 123.8, 123.5, 123.2, 121.2, 119.4, 60.8, 52.7, 48.5, 31.1, 24.4. HRMS (ESI) exact mass calculated for $C_{21}H_{19}N_2O_3^+$ ([M + H]$^+$): 347.1390; Found: 347.1386.



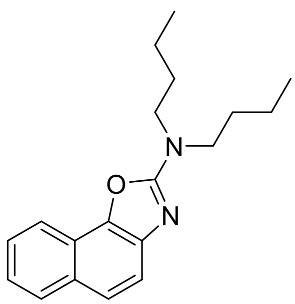
***N,N*-diethylnaphtho[2,1-*d*]oxazol-2-amine (7a)**: According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), diethylamine (0.14 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 60 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **7a** as a yellow gum (65 mg, 78%). FTIR (KBr): $\tilde{\nu}$ = 3063, 2958, 2927, 2858, 1629, 1566, 1522, 1408, 1373, 1290, 1259, 808, 748 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.01 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.66 – 7.65 (m, 1H), 7.60 – 7.59 (m, 1H), 7.52 – 7.49 (m, 1H), 7.35 – 7.33 (m, 1H), 3.67 (q, J = 7.2 Hz, 4H), 1.34 (t, J = 7.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.4, 143.0, 140.1, 129.3, 128.8, 126.4, 124.3, 123.3, 119.8, 118.8, 117.0, 43.2, 13.6. HRMS (ESI) exact mass calculated for $C_{15}H_{17}N_2O^+$ ([M + H]$^+$): 241.1335; Found: 241.1335.



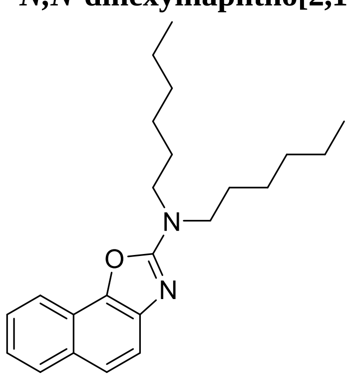
***N*,*N*-dipropylnaphtho[2,1-*d*]oxazol-2-amine (7b):** According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), dipropylamine (0.19 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 48 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:30) of the crude gave **7b** as a brown gum (71 mg, 76%). FTIR (KBr): $\tilde{\nu}$ = 3060, 2963, 2929, 2873, 1628, 1566, 1522, 1291, 1244, 1150, 809, 747 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.66 – 7.64 (m, 1H), 7.61 – 7.59 (m, 1H), 7.52 – 7.49 (m, 1H), 7.35 – 7.32 (m, 1H), 3.57 – 3.55 (m, 4H), 1.81 – 1.74 (m, 4H), 1.01 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.8, 142.8, 140.1, 129.3, 128.8, 126.4, 124.3, 123.3, 119.8, 118.8, 117.0, 50.7, 21.4, 11.5. HRMS (ESI) exact mass calculated for $C_{17}H_{21}N_2O^+$ ($[M + H]^+$): 269.1648; Found: 269.1641.



***N*,*N*-dibutylnaphtho[2,1-*d*]oxazol-2-amine (7c)**: According to GP-1: 2-nitroso-1-naphthol (70 mg, 0.40 mmol), di-butylamine (0.27 mL, 1.62 mmol) and KOAc (79 mg, 0.81 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **7c** as a colorless solid (92 mg, 77%). FTIR (KBr): $\tilde{\nu}$ = 3061, 2959, 2931, 2870, 1628, 1565, 1522, 1371, 1257, 1109, 809, 747, 728 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.60 – 7.59 (m, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.35 – 7.33 (m, 1H), 3.56 (t, *J* = 7.8 Hz, 4H), 1.75 –1.70 (m, 4H), 1.47 – 1.40 (m, 4H), 1.00 (t, *J* = 7.8 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.8, 142.8, 140.2, 129.3, 128.8, 126.4, 124.3, 123.3, 119.8, 118.8, 117.1, 48.6, 30.3, 20.3, 14.1. HRMS (ESI) exact mass calculated for $C_{19}H_{25}N_2O^+$ ($[M + H]^+$): 297.1961; Found: 297.1964.

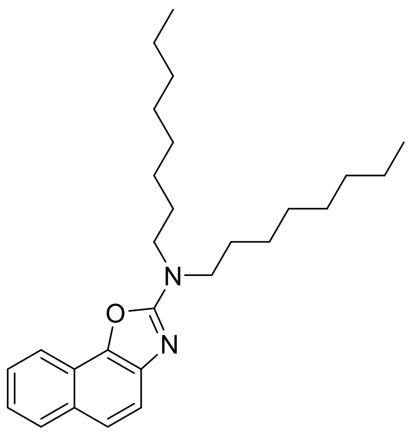


***N*,*N*-dihexylnaphtho[2,1-*d*]oxazol-2-amine (7d):** According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), dihexylamine (0.32 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 60 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **7d** as a yellow oil (67 mg, 55%). FTIR (KBr): $\tilde{\nu}$ = 2951, 2924, 2854, 1647, 1628, 1573, 1459, 1103, 877, 747 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.66 –

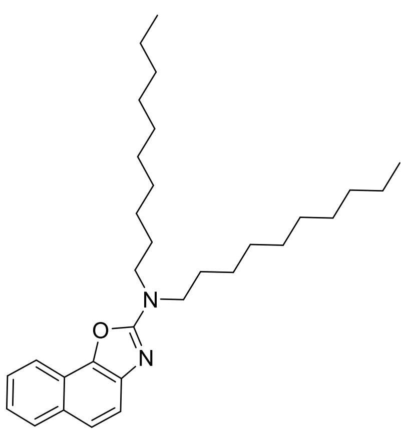


7.64 (m, 1H), 7.61 – 7.59 (m, 1H), 7.52 – 7.49 (m, 1H), 7.35 – 7.33 (t, *J* = 7.8 Hz, 1H), 3.60 – 3.57 (m, 4H), 1.76 – 1.71 (m, 4H), 1.41 – 1.34 (m, 12H), 0.93 – 0.90 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.8, 142.9, 140.2, 129.3, 128.8, 126.4, 124.3, 123.3, 119.8, 118.8, 117.1, 49.0, 31.8, 28.2, 26.7, 22.8, 14.2. HRMS (ESI) exact mass calculated for $C_{23}H_{33}N_2O^+$ ($[M + H]^+$): 353.2587; Found: 353.2581.

***N,N*-dioctylnaphtho[2,1-*d*]oxazol-2-amine (7e):** According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), dioctylamine (0.42 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:25) of the crude gave **7e** as a brown gum (93 mg, 66%). FTIR (KBr): $\tilde{\nu}$ = 3062, 2955, 2926, 2855, 1628, 1566, 1455, 1291, 1258, 1113, 808, 727 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.0 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.66 – 7.65(m, 1H), 7.62 – 7.60 (m, 1H), 7.52 – 7.49 (m, 1H), 7.35 – 7.33 (m, 1H), 3.60 – 3.57 (m, 4H), 1.75 – 1.71 (m, 4H), 1.40 – 1.36 (m, 8H), 1.31 – 1.29 (m, 12H), 0.89 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.8, 142.9, 140.2, 129.3, 128.8, 126.3, 124.2, 123.2, 119.8, 118.8, 117.1, 48.9, 32.0, 29.6, 29.4, 28.2, 27.0, 22.8, 14.2. HRMS (ESI) exact mass calculated for $C_{27}H_{41}N_2O^+$ ($[M + H]^+$): 409.3213; Found: 409.3213.

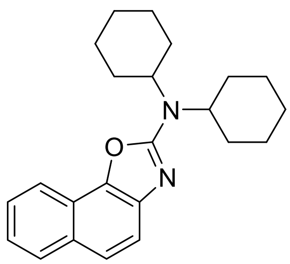


***N,N*-didecylnaphtho[2,1-*d*]oxazol-2-amine (7f):** According to GP-1: 2-nitroso-1-naphthol (50 mg, 0.29 mmol), didecylamine (0.43 mL, 1.2 mmol) and KOAc (57 mg, 0.58 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:40) of the crude gave **7f** as a yellow oil (90 mg, 67%). FTIR (KBr): $\tilde{\nu}$ = 3062, 2955, 2925, 2854, 1628, 1566, 1455, 1374, 1290, 1003, 808, 726 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.66 – 7.64 (m, 1H), 7.60 – 7.58 (m, 1H), 7.52 – 7.48 (m, 1H), 7.36 – 7.32 (m, 1H), 3.60 – 3.56 (m, 4H), 1.75 – 1.72 (m, 4H), 1.38 – 1.37 (m, 7H), 1.28 – 1.26 (m, 21H), 0.88 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.9, 142.9, 140.2, 129.3, 128.8, 126.4, 124.3, 123.3, 119.9, 118.8, 117.1, 49.0, 32.1, 29.81, 29.79, 29.6,

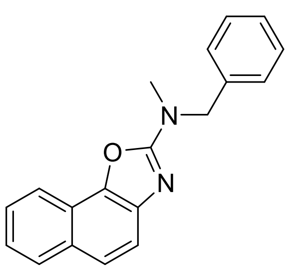


29.5, 28.2, 27.1, 22.9, 14.3. HRMS (ESI) exact mass calculated for $C_{31}H_{49}N_2O^+$ ($[M + H]^+$): 465.3839; Found: 465.3839.

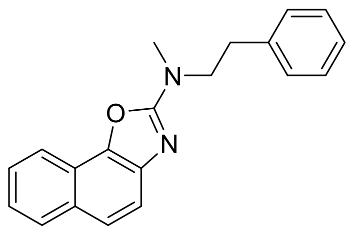
***N,N*-dicyclohexylnaphtho[2,1-*d*]oxazol-2-amine (7g):** According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), dicyclohexylamine (0.27 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 72 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:20) of the crude gave **7g** as a colorless solid (64 mg, 53%). FTIR (KBr): $\tilde{\nu}$ = 2962, 2924, 2852, 1649, 1582, 1566, 1434, 1262, 1090, 1018, 821, 771, 724 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.98 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.53 – 7.49 (m, 1H), 7.36 – 7.32 (m, 1H), 3.86 – 3.80 (m, 2H), 2.06 – 1.94 (m, 4H), 1.91 – 1.81 (m, 8H), 1.75 – 1.72 (m, 2H), 1.50 – 1.41 (m, 4H), 1.31 – 1.21 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.5, 142.6, 138.9, 129.3, 128.9, 126.5, 124.3, 123.4, 119.7, 118.8, 116.8, 57.3, 31.4, 26.4, 25.8. HRMS (ESI) exact mass calculated for $C_{23}H_{29}N_2O^+$ ($[M + H]^+$): 349.2274; Found: 349.2271.



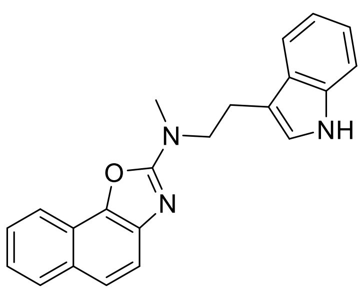
***N*-benzyl-*N*-methylnaphtho[2,1-*d*]oxazol-2-amine (7h):** According to GP-1: 2-nitroso-1-naphthol (60 mg, 0.35 mmol), *N*-benzylmethylamine (0.18 mL, 1.4 mmol) and KOAc (68 mg, 0.69 mmol) were reacted for 60 h in dry DCM (6 mL). Column chromatography (silica; EtOAc : Hexane, 1:15) of the crude gave **7h** as a violet solid (61 mg, 61%). FTIR (KBr): $\tilde{\nu}$ = 3026, 2961, 2924, 2853, 1631, 1565, 1453, 1409, 1261, 1094, 818, 723, 690 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.02 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.70 – 7.69 (m, 1H), 7.64 – 7.62 (m, 1H), 7.54 – 7.51 (m, 1H), 7.38 – 7.35 (m, 5H), 7.33 – 7.31 (m, 1H), 4.85 (s, 2H), 3.21 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 163.1, 143.2, 140.0, 136.7, 129.6, 129.0, 128.8, 128.0, 126.6, 124.6, 123.6, 119.9, 118.9, 117.2, 54.3, 35.5. Total count of ^{13}C is less than expected due to the merging of signal in the aromatic region. HRMS (ESI) exact mass calculated for $C_{19}H_{17}N_2O^+$ ($[M + H]^+$): 289.1335; Found: 289.1340.



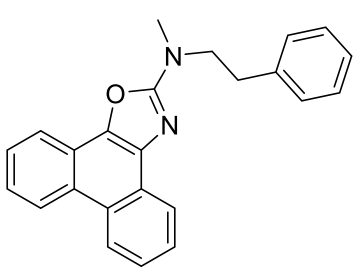
N-methyl-N-phenethylnaphtho[2,1-d]oxazol-2-amine (7i): According to GP-1: 2-nitroso-1-naphthol (45 mg, 0.26 mmol), *N*-methyl-phenylethylamine (0.14 g, 1.04 mmol) and KOAc (51 mg, 0.52 mmol) were reacted for 72 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:8) of the crude gave **7i** as a brown solid (30 mg, 38%). FTIR (KBr): $\tilde{\nu}$ = ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.54 – 7.51 (m, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.31 – 7.28 (m, 4H), 7.22 – 7.20 (m, 1H), 3.87 – 3.85 (m, 2H), 3.19 (s, 3H), 3.07 – 3.04 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.7, 143.2, 140.0, 138.9, 129.5, 129.1, 128.9, 128.8, 126.7, 126.5, 124.5, 123.5, 119.9, 118.9, 117.2, 52.7, 36.7, 34.4. HRMS (ESI) exact mass calculated for $C_{20}H_{19}N_2O^+$ ($[M + H]^+$): 303.1492; Found: 303.1491.



N-(2-(1H-indol-3-yl)ethyl)-N-methylnaphtho[2,1-d]oxazol-2-amine (7j): According to GP-1: 2-nitroso-1-naphthol (40 mg, 0.23 mmol), *N*-methyltryptamine (0.16 g, 1.62 mmol) and KOAc (79 mg, 0.92 mmol) were reacted for 96 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:3) of the crude gave **7j** as a colorless solid (36 mg, 46%). FTIR (KBr): $\tilde{\nu}$ = 3243, 2854, 2256, 1636, 1457, 1367, 1100, 1010, 746, 700 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.11 (s, 1H), 7.90 – 7.86 (m, 2H), 7.75 – 7.74 (m, 1H), 7.67 – 7.65 (m, 1H), 7.61 – 7.58 (m, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.37 – 7.33 (m, 2H), 7.23 – 7.17 (m, 2H), 7.05 (s, 1H), 3.97 – 3.93 (m, 2H), 3.23 (s, 3H), 3.22 – 3.19 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.7, 143.1, 139.8, 136.5, 129.4, 128.7, 127.5, 126.4, 124.4, 123.4, 122.3, 122.2, 119.8, 119.6, 118.8, 118.7, 117.0, 112.9, 111.4, 51.4, 36.5, 23.9. HRMS (ESI) exact mass calculated for $C_{22}H_{20}N_3O^+$ ($[M + H]^+$): 342.1601; Found: 342.1602.

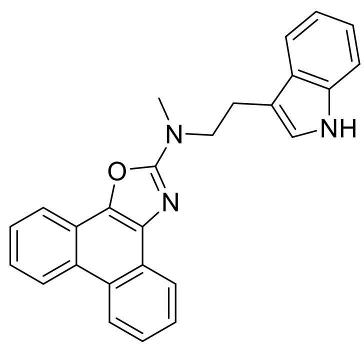


N-methyl-N-phenethylphenanthro[9,10-d]oxazol-2-amine (7k): According to GP-110-nitrosophenanthren-9-ol (40 mg, 0.17 mmol), *N*-methyl-phenylethylamine (90 mg, 0.67 mmol) and KOAc (33 mg, 0.52 mmol) were reacted for 90 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:3) of the crude gave **7k** as a yellow solid (17 mg, 28%). FTIR (KBr): $\tilde{\nu}$ = 2974, 2926,



2855, 1697, 1512, 1365, 1250, 1168, 699 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 8.4 Hz, 2H), 8.48 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.66 – 7.63 (m, 2H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.32 – 7.31 (m, 4H), 7.22 – 7.20 (m, 1H), 3.92 (t, *J* = 7.2 Hz, 2H), 3.28 (s, 3H), 3.10 (t, *J* = 7.2 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.5, 140.7, 138.9, 129.1, 128.85, 128.79, 128.7, 127.1, 127.0, 127.0, 126.7, 125.6, 124.3, 123.8, 123.5, 123.1, 121.1, 119.3, 52.8, 36.8, 34.3. Total count of ^{13}C is less than expected due to the merging of signal in the aromatic region. HRMS (ESI) exact mass calculated for $C_{24}H_{21}N_2O^+$ ($[M + H]^+$): 353.1648; Found: 353.1686.

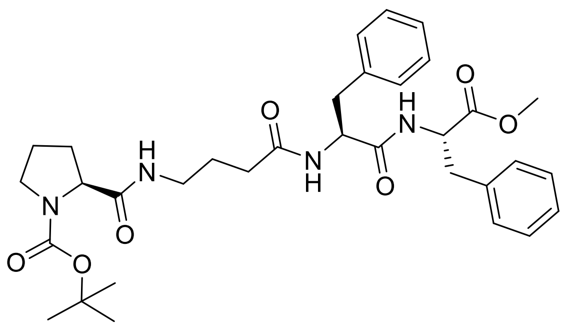
***N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-methylphenanthro[9,10-*d*]oxazol-2-amine (7l)**: According to



GP-1: According to GP-1: 10-nitrosophenanthren-9-ol (40 mg, 0.17 mmol), *N*-methyltryptamine (0.12 g, 0.67 mmol) and KOAc (33 mg, 0.34 mmol) were reacted for 96 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:5) of the crude gave **7l** as a red solid (24 mg, 36%). FTIR (KBr): $\tilde{\nu}$ = 2964, 2929, 2083, 1636, 1261, 1093, 1022, 800, 746 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.72 (dd, *J* = 8.5, 4.0 Hz, 2H), 8.47 – 8.45 (m, 1H), 8.00 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.82 (m, 1H), 7.70 – 7.67 (m, 1H), 7.65 – 7.60 (m, 2H), 7.56 – 7.52 (m, 1H), 7.36 – 7.34 (m, 1H), 7.23 – 7.21 (m, 2H), 7.08 (s, 1H), 4.00 (t, *J* = 7.5 Hz, 2H), 3.31 (s, 3H), 3.25 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.9, 140.7, 136.6, 136.3, 128.7, 127.7, 127.1, 126.9, 126.0, 125.5, 124.2, 123.8, 123.5, 123.1, 122.4, 122.3, 121.2, 119.7, 119.4, 119.0, 113.2, 111.5, 51.5, 36.6, 23.9. Total count of ^{13}C is less than expected due to the merging of signal in the aromatic region. HRMS (ESI) exact mass calculated for $C_{26}H_{22}N_3O^+$ ($[M + H]^+$): 392.1757; Found: 392.1758.

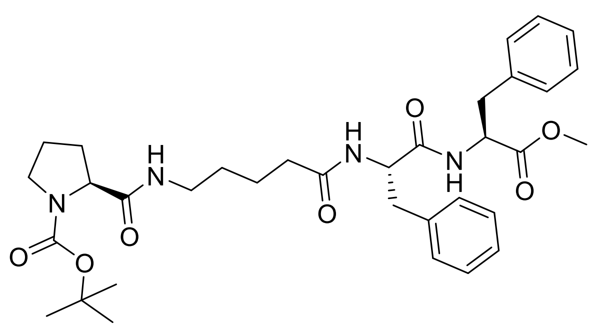
Synthesis of *N*-terminal proline peptides:

***tert-butyl* (*R*)-2-((4-(((*S*)-1-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobutyl)carbamoyl)pyrrolidine-1-carboxylate (10f'):**



(L)-Phe-(L)-Phe-methyl ester (0.14 g, 0.42 mmol), Boc-(L)-Pro-GABA (0.12 g, 0.42 mmol), *N*,*N*-diisopropylethylamine (0.28 mL, 1.67 mmol), EDC.HCl (79 mg, 0.42 mmol) and 1-hydroxybenzotriazole (56 mg, 0.42 mmol) were dissolved in a mixture of dichloromethane (4 mL) and DMF (1 mL)). After stirred for 5min at 0 ^{o}C then the reaction mixture was stirred for 72 h at room temperature. After completion of the reaction the solvent was evaporated in vacuo. The residue was neutralized with 0.1 N HCl solution and $NaHCO_3$ solution (15 mL) and extracted with ethylacetate (3x15 mL). Then the combined organic layers were dried over Na_2SO_4, concentrated under vacuum and the crude was purified by column chromatography via neutral alumina (EtOAc : hexane = 1:3) to afford Boc-(L)-Pro-GABA-(L)-Phe-(L)-Phe-OMe **10f'** (0.16 g, 62%). FTIR (KBr): $\tilde{\nu}$ = 3428, 3085, 2926, 2924, 2247, 1952, 1748, 1632, 1449, 1384, 1164, 913, 746 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.46 – 741 (m, 1H), 7.29 – 7.20 (m, 8H), 7.13 – 7.11 (m, 2H), 6.89 – 6.37 (m, 1H), 4.82 – 4.78 (m, 1H), 4.67 – 4.62 (m, 1H), 4.23 – 4.22 (m, 1H), 3.67 (s, 3H), 3.52 – 6.41 (m, 3H), 3.21 – 2.96 (m, 6H), 2.20 – 2.05 (m, 4H), 1.88 – 1.81 (m, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.6, 173.5, 171.8, 171.7, 155.5, 137.0, 136.1, 129.5, 129.4, 128.7, 128.7, 127.2, 127.0, 80.8, 60.4, 58.6, 55.1, 53.7, 52.4, 47.4, 38.04, 37.96, 32.3, 29.4, 28.6, 24.9. HRMS (ESI) exact mass calculated for $C_{33}H_{45}N_4O_7^+$ ([M + H]$^+$): 609.3283; Found: 609.3286.

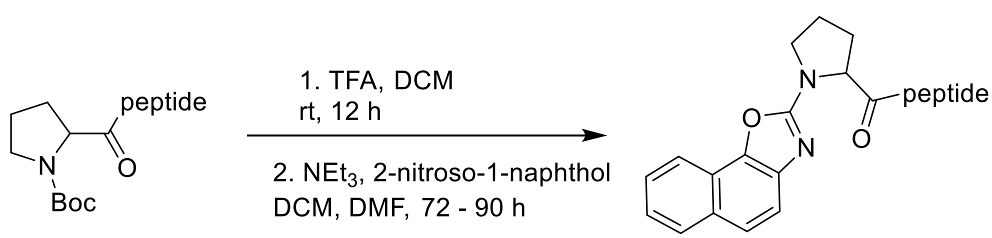
***tert-butyl* (*S*)-2-((5-(((*S*)-1-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-5-oxopentyl)carbamoyl)pyrrolidine-1-carboxylate (10g')**:



(L)-Phe-(L)-Phe-methyl ester (0.22 g, 0.67 mmol), Boc-(L)-Pro-DAVA (0.21 g, 0.67 mmol), *N*,*N*-diisopropylethylamine (0.45 mL, 2.67 mmol), EDC.HCl (127 mg, 0.67

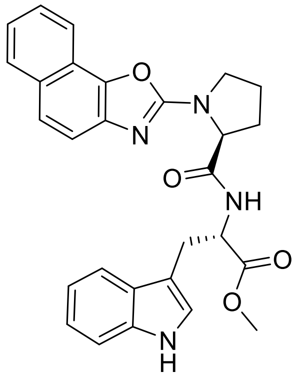
mmol) and 1-hydroxybenzotriazole (90 mg, 0.67 mmol) were dissolved in a mixture of dichloromethane (4 mL) and DMF (1 mL)). After stirred for 5 min at 0 °C then the reaction mixture was stirred for 72 h at room temperature. After completion of the reaction the solvent was evaporated in vacuo. The residue was neutralized with 0.1 N HCl solution and $NaHCO_3$ solution (15 mL) and extracted with ethylacetate (3x15 mL). Then the combined organic layers were dried over Na_2SO_4, concentrated under vacuum and the crude was purified by column chromatography via neutral alumina (EtOAc : hexane = 1:3) to afford Boc-(L)-Pro-DAVA-(L)-Phe-(L)-Phe-OMe **10g'** (0.21 g, 50%). FTIR (KBr): $\tilde{\nu}$ = 3437, 2972, 2930, 2861, 1742, 1647, 1548, 1445, 1384, 1259, 1163, 749 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.28 – 7.16 (m, 8H), 7.05 –7.04 (m, 2H), 6.85 – 6.84 (m, 1H), 6.61 – 6.54 (m, 1H), 4.74 – 4.67 (m, 2H), 4.24 – 4.18 (m, 1H), 3.64 (s, 3H), 3.46 – 3.18 (m, 4H), 3.08 – 3.03 (m, 2H), 3.00 – 2.94 (m, 2H), 2.60 – 2.57 (m, 2H), 2.17 – 2.12 (m, 3H), 1.96 –1.83 (m, 3H), 1.56 – 1.55 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 173.3, 173.0, 172.7, 171.6, 155.5, 136.8, 135.9, 129.4, 129.3, 128.6, 128.6, 127.1, 126.92, 61.5, 60.1, 54.4, 53.7, 52.3, 47.2, 38.8, 38.0, 37.9, 35.3, 31.3, 28.5, 24.6, 22.8. HRMS (ESI) exact mass calculated for $C_{34}H_{47}N_4O_7^+$ ($[M + H]^+$): 623.3439; Found: 623.3447.

Synthesis of *N*- terminal modified peptides: General Procedure 2 (GP-2):

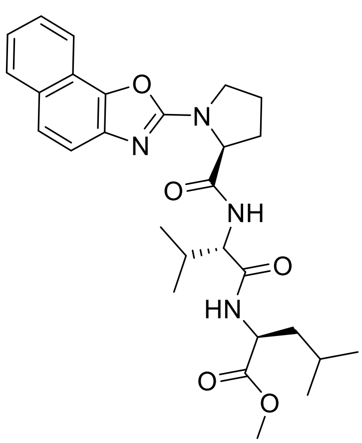


TFA (0.6 –1.5 mL) was added drop-wise to the solution of peptide in DCM. The reaction mixture was allowed to stir at room temperature for 12 h. The reaction mixture was diluted with methanol and the solvent was removed in vacuo. The residue was washed with diethylether and dried in vacuo to give the trifluroacetate salt of the peptide. Triethylamine (5 equiv.) was added to the solution of the residue either in mixture of DCM-DMF (4:1) or DCM-DMSO (4:1). After 5 min 2-nitroso-1-naphthol was added to the solution and the reaction mixture was heated at 50 °C for 72 h to 90 h. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated under vacuum to obtain gummy residue which was purified by column chromatography to afford analytically pure products.

methyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolyl-*L*-tryptophanate (10a): According to GP-2: 2-nitroso-1-naphthol (47 mg, 0.36 mmol), trifluroacetate salt of (L)-Pro-(L)-Trp-OMe[iii] (78 mg, 0.18 mmol) and NEt_3 (0.12 mL, 0.90 mmol) were reacted for 72 h in dry DCM (4 mL)/DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10a** as a brown solid (44 mg, 51%). FTIR (KBr): $\tilde{\nu}$ = 2958, 2925, 2851, 2078, 1637, 1654, 1347, 744, 684 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.96 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.67 – 7.66 (m, 2H), 7.53 – 7.50 (m, 3H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.05 – 7.00 (m, 3H), 6.83 – 6.82 (m, 1H), 4.97 – 4.94 (m, 1H), 4.57 – 4.56 (m, 1H), 3.65 (s, 3H), 3.61 – 3.57 (m, 2H), 3.36 – 3.33 (m, 1H), 3.26 – 3.22 (m, 1H), 2.41 – 2.37 (m, 1H), 2.10 – 2.04 (m, 1H), 1.97 – 1.94 (m, 1H), 1.90 – 1.86 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 172.1, 171.0, 161.0, 143.3, 138.9, 135.8, 129.5, 128.6, 127.5, 126.5, 124.5, 123.7, 122.6, 122.0, 119.7, 119.5, 118.9, 118.2, 116.9, 111.1, 109.9, 62.2, 53.1, 52.4, 48.6, 29.3, 27.3, 24.4. HRMS (ESI) exact mass calculated for $C_{28}H_{27}N_4O_4^+$ ($[M + H]^+$): 483.2027; Found: 483.2035.

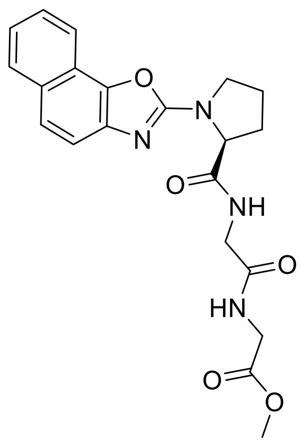


methyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolyl-*L*-valyl-*L*-leucinate (10b): According to GP-2: 2-nitroso-1-naphthol (38 mg, 0.22 mmol), trifluroacetate salt of (L)-Pro-(L)-Val-(L)-Leu-OMe[iv] (50 mg, 0.11 mmol) and NEt_3 (76 µL, 0.55 mmol) were reacted for 72 h in dry DCM (4 mL)/ DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10b** as a violet solid (32 mg, 57%). FTIR (KBr): $\tilde{\nu}$ = 3062, 2958, 2920, 2853, 1743, 1644, 1470, 1435, 1258, 1224, 1025, 818 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.65 (br.s, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.52 (m, 1H), 7.39 – 7.37 (m, 1H), 6.49 (d, *J* = 7.2 Hz, 1H), 4.66 – 4.65 (m, 1H), 4.59 – 4.55 (m, 1H), 4.30 – 4.28 (m, 1H), 3.95 – 3.92 (m, 1H), 3.81 – 3.77 (m, 1H), 3.71 (s, 3H), 2.49 – 2.45 (m, 1H), 2.25 – 2.17 (m, 3H), 2.14 – 2.11 (m, 1H), 1.63 – 1.58 (m, 2H), 1.51 – 1.48 (m, 1H), 0.89 – 0.86 (m, 6H), 0.85 – 0.84 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 173.3, 171.8, 171.0, 161.4, 143.6, 139.0, 129.8, 128.8, 126.7, 125.0, 124.0, 119.9, 119.0, 117.1, 62.8, 59.1, 52.5, 50.5, 49.1, 41.5, 30.7, 29.8, 25.03, 25.00,

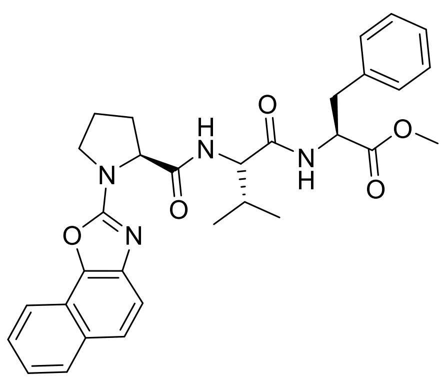


22.9, 22.0, 19.4, 17.9. HRMS (ESI) exact mass calculated for $C_{28}H_{37}N_4O_5^+$ ($[M + H]^+$): 509.2758; Found: 509.2755.

methyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolylglycylglycinate (10c): According to GP-2: 1-nitroso-2-naphthol (73 mg, 0.42 mmol), trifluroacetate salt of (L)-Pro-(L)-Gly-(L)-Gly-OMe (0.10 g, 0.28 mmol) and NEt_3 (0.19 mL, 1.4 mmol) were reacted for 90 h in dry DCM (4 mL)/DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10c** as a violet solid (53 mg, 46%). FTIR (KBr): $\tilde{\nu}$ = 3062, 2955, 2923, 1747, 1628, 1565, 1522, 1453, 1260, 1209, 811, 727 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.65 – 7.63 (m, 1H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.51 – 7.49 (m, 1H), 7.46 – 7.45 (m, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.35 (m, 1H), 4.56 – 4.54 (m, 1H), 4.11 (dd, *J* = 17.4, 6.6 Hz, 1H), 3.99 – 3.94 (m, 3H), 3.89 (dd, *J* = 18.0, 5.4 Hz, 1H), 3.83 – 3.78 (m, 1H), 3.52 (s, 3H), 2.35 – 2.31 (m, 2H), 2.21 – 2.16 (m, 1H), 2.10 – 2.06 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 172.5, 170.5, 169.8, 161.2, 143.5, 138.8, 129.8, 128.8, 126.9, 124.9, 124.1, 119.9, 119.0, 116.5, 63.0, 52.4, 49.1, 43.2, 41.1, 30.7, 24.9. HRMS (ESI) exact mass calculated for $C_{23}H_{27}N_4O_5^+$ ($[M + H]^+$): 411.1663; Found: 411.1664.

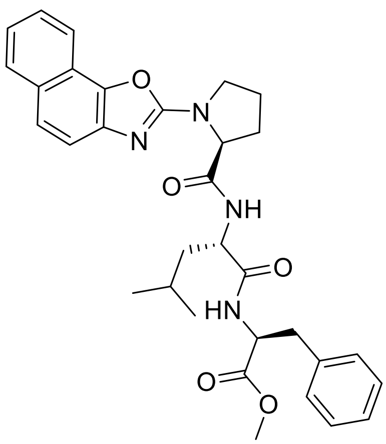


methyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolyl-*L*-valyl-*L*-phenylalaninate (10d): According to GP-2: 2-nitroso-1-naphthol (35 mg, 0.20 mmol), trifluroacetate salt of (L)-Pro-(L)-Val-(L)-Phe-OMe (50 mg, 0.10 mmol) and NEt_3 (69 µL mg, 0.50 mmol) were reacted for 72 h in dry DCM (4 mL)/DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10d** as a violet solid (27 mg, 50%). FTIR (KBr): $\tilde{\nu}$ = 3064, 2958, 2926, 2853, 1742, 1628, 1566, 1369, 1284, 1211, 1097, 1023, 811, 737 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 9.0 Hz, 1H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.52 – 7.49 (m, 1H), 7.39 – 7.36 (m, 1H), 7.27 – 7.20 (m, 3H), 7.21 – 7.20 (m, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 6.54 – 6.52 (m, 1H), 4.85 – 4.82 (m, 1H), 4.63 – 4.62 (m, 1H), 4.27 – 4.25 (m, 1H), 3.94 – 3.91 (m, 1H), 3.82 – 3.75 (m, 1H), 3.70 (s, 3H), 3.10 – 3.07 (m, 1H), 3.00 – 2.95 (m, 1H), 2.49 –

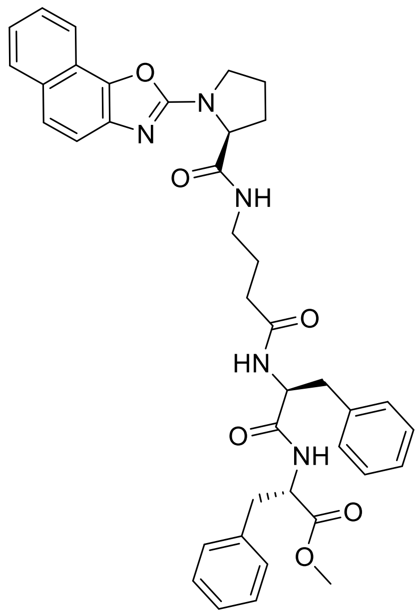


2.46 (m, 1H), 2.20 – 2.12 (m, 4H), 0.82 (d, J = 7.2 Hz, 3H), 0.77 (d, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.9, 171.7, 170.8, 161.5, 143.6, 139.0, 136.0, 129.8, 129.4, 128.9, 128.8, 127.3, 126.8, 125.0, 124.0, 119.9, 119.0, 117.1, 62.8, 59.0, 53.3, 52.5, 49.1, 38.1, 30.5, 29.6, 25.0, 19.4, 17.7. HRMS (ESI) exact mass calculated for $C_{31}H_{35}N_4O_5^+$ ([M + H]$^+$): 543.2602; Found: 543.2606.

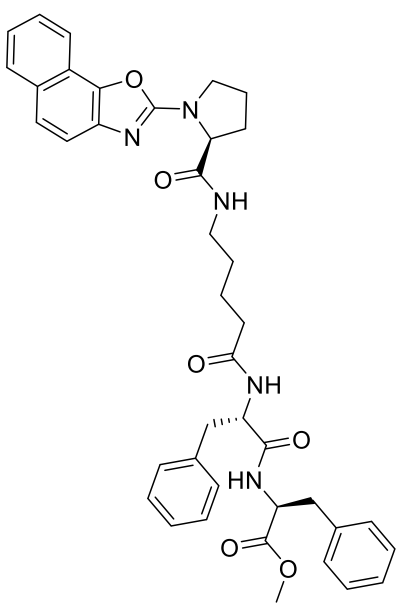
methyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolyl-*L*-leucyl-*L*-phenylalaninate (10e): According to GP-2: 1-nitroso-2-naphthol (40 mg, 0.23 mmol), trifluroacetate salt of (L)-Pro-(L)- Leu-(L)-Phe-OMe[v] (54 mg, 0.14 mmol) and NEt_3 (54 mg, 0.46 mmol) were reacted for 72 h in dry DCM (4 mL)/DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10e** as a violet solid (39 mg, 50%). FTIR (KBr): $\tilde{\nu}$ = 3299, 3062, 2951, 2871, 1752, 1650, 1627, 1565, 1593, 1280, 1208, 1105, 809, 700 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.54 – 7.49 (m, 3H), 7.39 – 7.37 (m, 1H), 7.27 – 7.24 (m, 2H), 7.21 – 7.19 (m, 1H), 7.08 (d, J = 7.2 Hz, 2H), 6.77 (d, J = 7.8 Hz, 1H), 4.83 – 4.79 (m, 1H), 4.59 (d, J = 8.4 Hz, 1H), 4.42 – 4.38 (m, 1H), 3.93 – 3.90 (m, 1H), 3.80 – 3.75 (m, 1H), 3.70 (s, 3H), 3.12 (dd, J = 14.4, 6.0 Hz, 1H), 3.01 (dd, J = 13.8, 6.6 Hz, 1H), 2.44 – 2.40 (m, 1H), 2.22 – 2.09 (m, 3H), 1.66 – 1.61 (m, 1H), 1.55 – 1.47 (m, 2H), 0.77 (d, J = 4.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.9, 171.6, 161.3, 143.5, 136.1, 129.8, 129.5, 128.8, 128.7, 127.2, 126.8, 125.0, 124.1, 119.9, 119.0, 117.0, 62.6, 53.4, 52.5, 52.3, 49.1, 40.6, 38.0, 29.7, 25.0, 23.0, 21.9. Total count of ^{13}C is less than expected due to the merging of signal in the aromatic region HRMS (ESI) exact mass calculated for $C_{32}H_{37}N_4O_5^+$ ([M + H]$^+$): 557.2758; Found: 557.2753.



methyl (4-((*R*)-1-(naphtho[2,1-*d*]oxazol-2-yl)pyrrolidine-2-carboxamido)butanoyl)-*L*-phenylalanyl-*L*-phenylalaninate (10f): According to GP-2: 2-nitroso-1-naphthol (33 mg, 0.19 mmol), trifluroacetate salt of (L)-Pro-GABA-(L)-Phe-(L)-Phe-OMe (60 mg, 0.10 mmol) and NEt_3 (67 µL, 0.48 mmol) were reacted for 72 h in dry DCM (4 mL)/DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10f** as a violet solid (40 mg, 61%). FTIR (KBr): $\tilde{\nu}$ = 3062, 2958, 2926, 2853, 1740, 1644, 1564, 1452, 1371, 1260, 1091, 802, 700 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.54 - 7.51 (m, 2H), 7.48 (br.d, *J* = 6.9 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.40 – 7.37 (m, 1H), 7.25 – 7.24 (m, 2H), 7.21 – 7.20 (m, 1H), 7.17 – 7.16 (m, 3H), 7.09 – 7.07 (m, 4H), 6.61 (d, *J* = 7.8 Hz, 1H), 4.77 – 4.74 (m, 1H), 4.60 – 4.56 (m, 2H), 4.00 – 3.97 (m, 1H), 3.85 – 3.79 (m, 1H), 3.64 (s, 3H), 3.26 – 3.22 (m, 1H), 3.14 – 3.08 (m, 2H), 3.02 – 2.95 (m, 2H), 2.92 – 2.89 (m, 1H), 2.39 – 2.232 (m, 3H), 2.23 – 2.17 (m, 1H), 2.13 – 2.10 (m, 2H), 1.84 – 1.80 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 173.7, 172.6, 171.7, 171.5, 161.0, 143.4, 139.1, 136.7, 136.0, 129.7, 129.5, 129.3, 128.9, 128.75, 128.74, 127.3, 127.1, 126.8, 124.9, 124.0, 119.9, 119.0, 116.7, 62.6, 55.0, 53.7, 52.5, 49.2, 38.4, 38.1, 37.8, 32.5, 30.8, 24.8, 24.6. HRMS (ESI) exact mass calculated for $C_{39}H_{42}N_5O_6^+$ ([M + H]$^+$): 676.3130; Found: 676.3110.

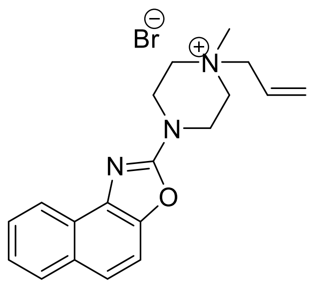


methyl (5-((R)-1-(naphtho[2,1-*d*]oxazol-2-yl)pyrrolidine-2-carboxamido)pentanoyl)-*L*-phenylalanyl-*L*-phenylalaninate (10g): According to GP-2: 1-nitroso-2-naphthol (40 mg, 0.23 mmol), trifluroacetate salt of (L)-Pro-DAVA-(L)-Phe-(L)-Phe-OMe (72 mg, 0.11 mmol) and NEt_3 (0.76 mL, 0.55 mmol) were reacted for 72 h in dry DCM (4 mL)/DMF (1 mL). Column chromatography (silica; EtOAc : Hexane, 2:1) of the crude gave **10g** as a brown solid (40 mg, 52%). FTIR (KBr): $\tilde{\nu}$ = 3290, 3062, 3030, 2927, 1742, 1665, 1639, 1542, 1286, 1257, 1108, 1029, 726, 699 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.52 – 7.50 (m, 1H), 7.46 (d, *J* = 5.4 Hz, 1H), 7.44 – 7.43 (m, 1H), 7.38 – 7.35 (m, 1H), 7.30 (bs, 1H), 7.24 – 7.19 (m, 3H), 7.09 – 7.08 (m, 3H), 7.05 – 7.04 (m, 2H), 6.98 – 6.97 (m, 2H), 6.68 – 6.67 (m, 1H), 4.74 – 4.71 (m, 1H), 4.64 – 4.58 (m, 2H), 3.99 – 3.95 (m, 1H), 3.80 – 3.75 (m,



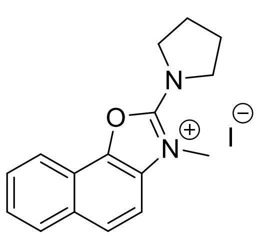
1H), 3.66 (s, 3H), 3.38 – 3.33 (m, 1H), 3.12 – 3.07 (m, 2H), 3.02 – 2.98 (m, 1H), 2.95 – 2.85 (m, 2H), 2.37 – 2.25 (m, 3H), 2.21 – 2.16 (m, 1H), 2.13 – 2.06 (m, 2H), 1.68 – 1.64 (m, 1H), 1.58 – 1.54 (m, 1H), 1.51 – 1.47 (m, 1H), 1.34 – 1.31 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 173.5, 172.2, 171.7, 171.5, 161.0, 143.4, 139.0, 136.6, 135.9, 129.6, 129.4, 129.2, 128.8, 128.7, 128.6, 127.2, 127.0, 126.7, 124.8, 123.9, 119.9, 119.0, 116.7, 62.4, 54.6, 53.8, 52.4, 49.1, 39.2, 38.0, 37.8, 34.8, 30.8, 27.6, 24.7, 22.9. HRMS (ESI) exact mass calculated for $C_{40}H_{44}N_5O_6^+$ ($[M + H]^+$): 690.3286; Found: 690.3285.

1-allyl-1-methyl-4-(naphtho[2,1-*d*]oxazol-2-yl)piperazin-1-ium bromide (16): Allybromide



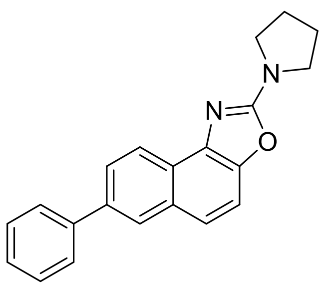
(0.170 mL, 2.0 mmol) was added to a solution of **6aa** (27 mg, 0.10 mmol) in DMF (1 mL) and the solution was stirred at room temperature for 24 h. The solvent was evaporated under reduced pressure and reaction mixture was diluted with ethylacetate. The precipitate was filtered and washed with ethyl acetate (5 mL). The ion **16** was obtained as brown solid (23 mg, 59%). FTIR (KBr): $\tilde{\nu}$ = 2783, 2433, 2094, 1643, 1616, 1468, 1571, 1427, 1368, 1283, 974 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD-d_4) δ = δ 8.17 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.46 – 7.44 (m, 1H), 7.38 – 7.35 (m, 1H), 6.14 – 6.04 (m, 1H), 5.77 – 5.71 (m, 2H), 4.17 (d, *J* = 7.4 Hz, 4H), 3.63 (s, 4H), 3.20 (s, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ = 161.1, 145.1, 136.8, 131.3, 129.0, 128.3, 125.9, 124.9, 124.6, 123.9, 122.1, 121.3, 109.6, 66.2, 58.3, 39.5, 34.1. HRMS (ESI) exact mass calculated for $C_{19}H_{22}N_3O^+$ ($[M + H]^+$): 308.1757; Found: 308.1768.

1-methyl-1-(naphtho[2,1-*d*]oxazol-2-yl)pyrrolidin-1-ium iodide (17): Methyl iodide (0.13 mL,

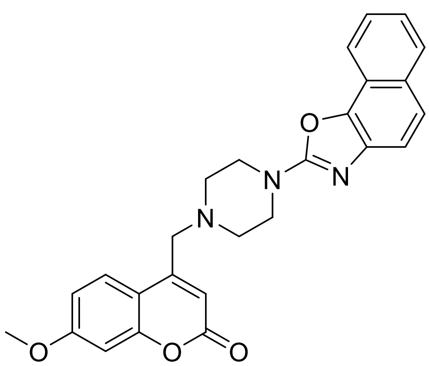


2.1 mmol) was added to a solution of **6h** (50 mg, 0.21 mmol) in toluene (2.0 mL) and the solution was stirred at 80 °C for 18 h. The precipitate was filtered and washed with ethyl acetate (10 mL). The ion **17** was obtained as white solid (40 mg, 51%). FTIR (KBr): $\tilde{\nu}$ = 2917, 2857, 2256, 2129, 1762, 1646, 1046, 1025, 826, 765 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.16 – 8.11 (m, 3H), 7.92 – 7.90 (m, 1H), 7.78 – 7.76 (m, 1H), 7.64 – 7.62 (m, 1H), 4.06 – 4.02 (m, 4H), 3.99 (s, 3H), 2.07 – 2.047 (d, *J* = 6.4 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 155.1, 138.2, 130.3, 128.9, 128.7, 128.6, 126.8, 126.1, 118.3, 118.1, 110.4, 49.9, 31.9, 24.9. HRMS (ESI) exact mass calculated for $C_{16}H_{17}N_2O^+$ ($[M + H]^+$): 253.1335; Found: 253.1332.

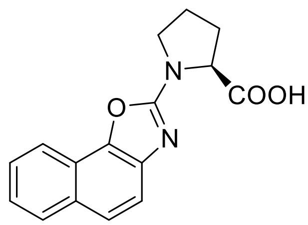
7-phenyl-2-(pyrrolidin-1-yl)naphtho[1,2-*d*]oxazole (18): Phenylboronic acid (23 mg, 0.19 mmol), $Ba(OH)_2$, $8H_2O$ (86 mg, 0.27 mmol), $Pd(PPh_3)_4$ (6 mg, 3.3 mol%), 1,4-dioxane (1.4 mL), H_2O (0.5 mL), and **6g** (46 mg, 0.15 mmol) were refluxed for 48 h under argon atmosphere. After completion of reaction 1,4-dioxane was removed under reduced pressure. The resulting mass was diluted with CH_2Cl_2 (30 mL), and the mixture was washed with 1 M HCl (3 × 20 mL) and then with brine solution (2 × 20 mL). Combined organic layers were dried over sodium sulfate and concentrated under vacuum to give crude product which was purified by column chromatography (SiO_2; EtOAc : Hexane, 1:1) to afford pure **18 (**42 mg, 92%). FTIR (KBr): $\tilde{\nu}$ = 3054, 2967, 2924, 2858, 1647, 1617, 1418, 1264, 1087, 994, 757, 695 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.44 (d, *J* = 8.4 Hz, 1H), 8.09 (s, 1H), 7.82 – 7.80 (m, 1H), 7.75 (d, *J* = 7.8 Hz, 2H), 7.56 – 7.52 (m, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 3.75 – 3.73 (m, 4H), 2.08 – 2.05 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 161.4, 145.4, 141.6, 138.9, 137.3, 131.5, 129.0, 127.6, 127.3, 126.5, 125.4, 124.1, 123.1, 120.7, 110.3, 47.8, 25.9. HRMS (ESI) exact mass calculated for $C_{21}H_{19}N_2O^+$ ($[M + H]^+$): 315.1492; Found: 315.1489.



7-methoxy-4-((4-(naphtho[2,1-*d*]oxazol-2-yl)piperazin-1-yl)methyl)-2H-chromen-2-one (20): According to GP-1: 2-nitroso-1-naphthol (40 mg, 0.23 mmol), **19**[vi] (0.13 g, 0.46 mmol) and NEt_3 (65 µL, 0.46 mmol) were reacted for 60 h in dry DCM (4 mL). Column chromatography (silica; EtOAc : Hexane, 1:3) of the crude gave **20** as a colorless solid (46 mg, 45%). FTIR (KBr): $\tilde{\nu}$ = 2953, 2924, 2854, 1719, 1616, 1454, 1287, 1144, 1066, 811, 743 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 9.0 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.38 – 7.36 (m, 1H), 6.86 – 6.83 (m, 2H), 6.41 (s, 1H), 3.87 (s, 3H), 3.82 – 3.80 (m, 4H), 3.66 (s, 2H), 2.71 – 2.69 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.9, 162.1, 161.5, 155.9, 151.7, 143.1, 139.4, 129.7, 128.8, 126.6, 125.9, 124.7, 123.8, 119.8, 118.9, 117.1, 112.5, 112.4, 112.2, 101.1, 59.3, 55.9, 52.8, 45.9. HRMS (ESI) exact mass calculated for $C_{22}H_{20}N_3O^+$ ($[M + H]^+$): 442.1761; Found: 442.1754.

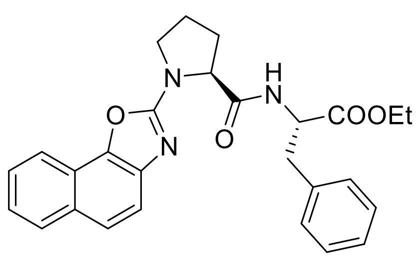


naphtho[2,1-*d*]oxazol-2-yl-*L*-proline (21): An aqueous solution of 2(N) NaOH (1 mL) was added



to a solution of Compound **6ae** (26 mg, 0.09) and the resulting solution was stirred at room temperature. After 4h the reaction mixture was concentrated in vacuum and poured in to a 1(N) HCl (1 mL) and the reaction mixture was extracted with dichloromethane (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vaccum to give the acid **21** (20 mg, 80%) as a pure compound. FTIR (KBr): $\tilde{\nu}$ = 2962, 2923, 2850, 1748, 1694, 1629, 1566, 1368, 1223, 1161, 1041, 750 cm^{-1}.^{1}H NMR (400 MHz, CD_3OD-d_4) δ = 8.02 – 8.00 (m, 2H), 7.88 – 7.76 (m, 1H), 7.59 – 7.54 (m, 2H), 7.46 – 7.42 (m, 1H), 4.79 – 4.58 (m, 1H), 3.96 – 3.82 (m, 2H), 2.60 – 2.50 (m, 1H), 2.34 – 2.18 (m, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ = 173.7, 159.9, 142.2, 137.2, 129.4, 128.0, 126.3, 124.4, 123.4, 119.2, 117.8, 115.1, 60.1, 30.2, 23.3. Total count of ^{13}C is less than the expected due to merged with the CD_3OD signals. HRMS (ESI) exact mass calculated for $C_{16}H_{15}N_2O_3^+$ ($[M + H]^+$): 283.1077; Found: 283.1077.

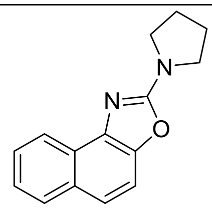
ethyl naphtho[2,1-*d*]oxazol-2-yl-*L*-prolyl-*L*-phenylalaninate (22): (L)-Phenylalanine ethyl



ester hydrochloride (0.22 g, 0.67 mmol), naphtho[2,1-d]oxazol-2-yl-*L*-proline **21** (20 mg, 0.070 mmol), *N,N*-diisopropylethylamine (0.49 µL, 0.28 mmol), EDC.HCl (20 mg, 0.11 mmol) and 1-hydroxybenzotriazole (10 mg, 0.070 mmol) were dissolved in a mixture of dichloromethane (1.5 mL) and DMF (0.3 mL)). The reaction mixture was stirred for 72 h at room temperature. After completion of the reaction the solvent was evaporated in vacuo. The residue was neutralized with 0.1 N HCl solution and $NaHCO_3$ solution (15 mL) and extracted with DCM (3x10 mL). Then the combined organic layers were dried over Na_2SO_4, concentrated under vacuum and the crude was purified by column chromatography (silica; EtOAc : hexane = 1:1.5) to afford **22** as a brown solid (30 mg, 94%). FTIR (KBr): $\tilde{\nu}$ = 2980, 2924, 2873, 1737, 1625, 1565, 1522, 1454, 1368, 1285, 1199, 1029, 809, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.0 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.43 – 7.39 (m, 1H), 7.02 (d, *J* = 4.4 Hz, 4H), 6.97 – 6.94 (m, 1H), 4.90 – 4.85 (m, 1H), 4.70 (d, *J* = 7.2 Hz, 1H), 4.15 – 4.09 (m, 2H), 3.80 – 3.78 (m, 1H), 3.74 – 3.68 (m, 1H), 3.20 (dd, *J* = 13.6, 5.6 Hz, 1H), 3.01 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.41 – 2.37 (m, 1H), 2.15 – 2.11 (dd, *J* = 18.8, 11.6 Hz, 1H), 2.07 – 2.03 (m, 2H), 1.17 (t, *J*

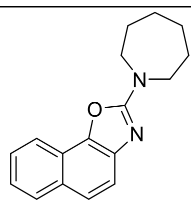
= 7.2 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 171.40, 170.8, 160.7, 143.3, 136.1, 129.9, 129.3, 128.8, 128.7, 128.4, 126.9, 126.9, 125.0, 124.1, 119.9, 119.0, 116.8, 62.3, 61.7, 53.5, 49.0, 38.0, 29.6, 24.6, 14.2. HRMS (ESI) exact mass calculated for $C_{27}H_{28}N_3O_4^+$ ([M + H]$^+$): 458.2074; Found: 458.2073.

Crystal of **6a:**

	 CCDC 2144927
Empirical formula	C_{15} H_{14} N_2 O
Formula weight	238.28
Crystal habit, colour	Block, colorless
Crystal size, mm^3	0.40X 0.38 X 0.35
Temperature, *T*	293(2)
Wavelength, λ(Å)	0.71073
Crystal system	monoclinic
Space group	*P 21/c*
Unit cell dimensions	a = 6.3429(12)Å b = 15.1467(18)Å c = 12.9960(16)Å α = 90°, β = 103.927(17)°, γ = 90°,
Volume, V(Å^3)	1211.9(3)
Z	4
Calculated density, Mg·m^{-3}	1.306
Absorption coefficient, μ(mm^{-1})	0.083

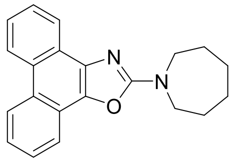
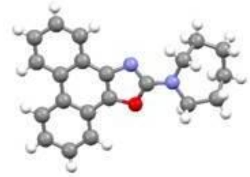
F(000)	504
θ range for data collection	3.230° to 24.997°
Limiting indices	$-7 \leq h \leq 4$, $-18 \leq k \leq 10$, $-15 \leq l \leq 15$
Reflection collected / unique	3001/ 1284 [*R*(int) = 0.0317]
Completeness to θ	84.5% (θ = 25.242°)
Refinement method	SHELXL-2013
Data / restraints / parameters	1284 / 0 / 163
Goodness–of–fit on F^2	1.096
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0746, *wR*2 = 0.1996
R indices (all data)	*R*1 = 0.0969, *wR*2 = 0.2267
Largest diff. peak and hole	0.240 and – 0.239 Å^{-3}

Crystal of **6j:**

	 CCDC 2144928
Empirical formula	$C_{17} H_{18} N_2 O$
Formula weight	266.33
Crystal habit, colour	Needle, colorless
Crystal size, mm^3	0.38 X 0.36X 0.32
Temperature, *T*	293(2)
Wavelength, λ(Å)	0.71073
Crystal system	monoclinic

Space group	*P 21/c*
Unit cell dimensions	a = 5.3217(4)Å b = 26.6790(17) Å c = 10.0784(6) Å α = 90°, β = 102.466(4) °, γ = 90°,
Volume, V(Å^3)	1397.17(16)
Z	4
Calculated density, Mg·m^{-3}	1.266
Absorption coefficient, μ(mm^{-1})	0.080
F(000)	568
θ range for data collection	1.53° to 25.00°
Limiting indices	$-6 \le h \le 6$, $-31 \le k \le 31$, $-11 \le l \le 11$
Reflection collected / unique	15150/ 1824 [R(int) = 0.0373]
Completeness to θ	99.9% (θ = 24.9 °)
Refinement method	SHELXL-2018/3 (Sheldrick, 2018)
Data / restraints / parameters	15150/ 0 / 182
Goodness–of–fit on F^2	1.593
Final R indices [I>2sigma(I)]	R1 = 0.0658, wR2 = 0.2117
R indices (all data)	R1 = 0.0837, wR2 = 0.2268
Largest diff. peak and hole	0.308 and – 0. 354 Å^{-3}

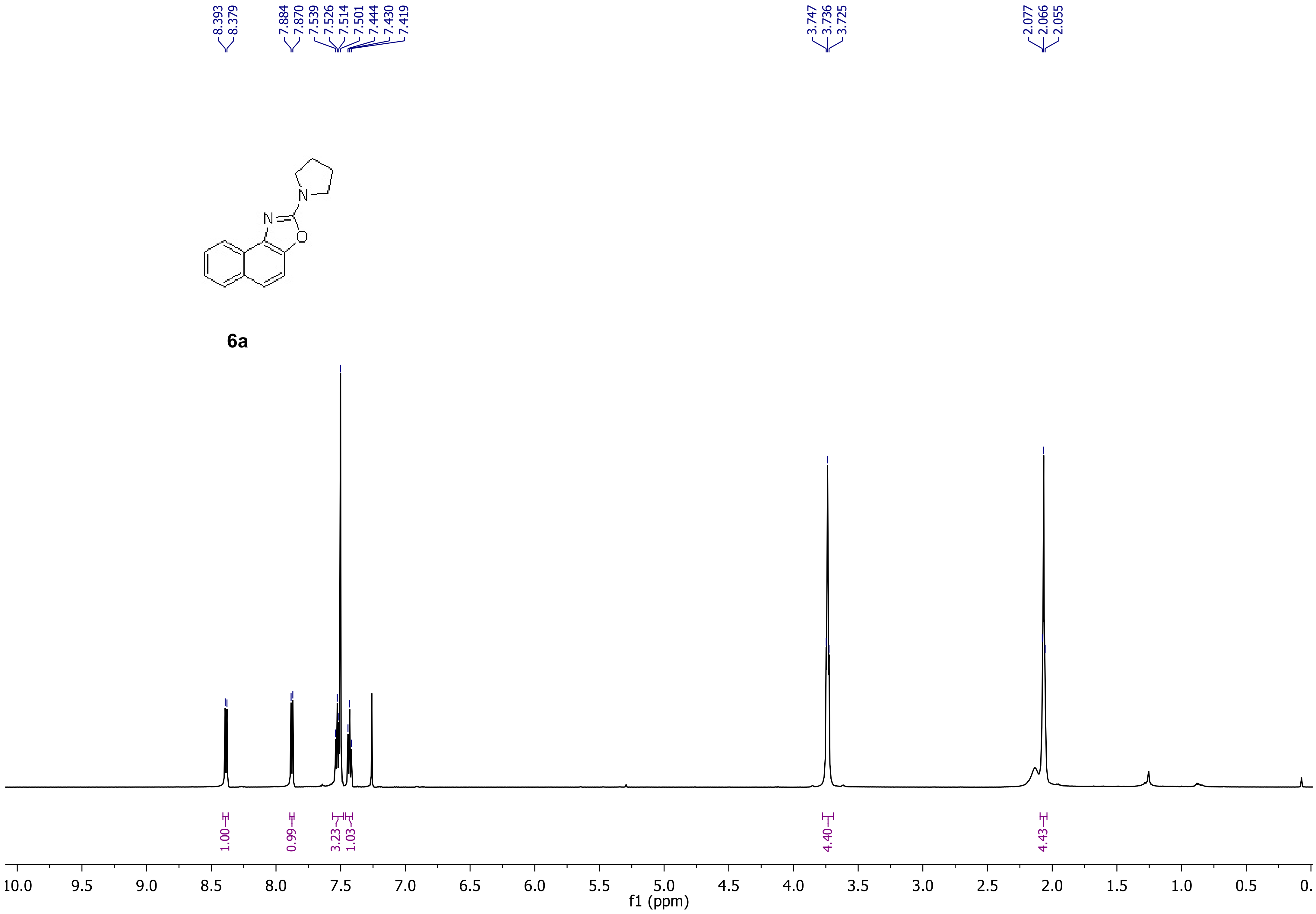
Crystal of **6m:**

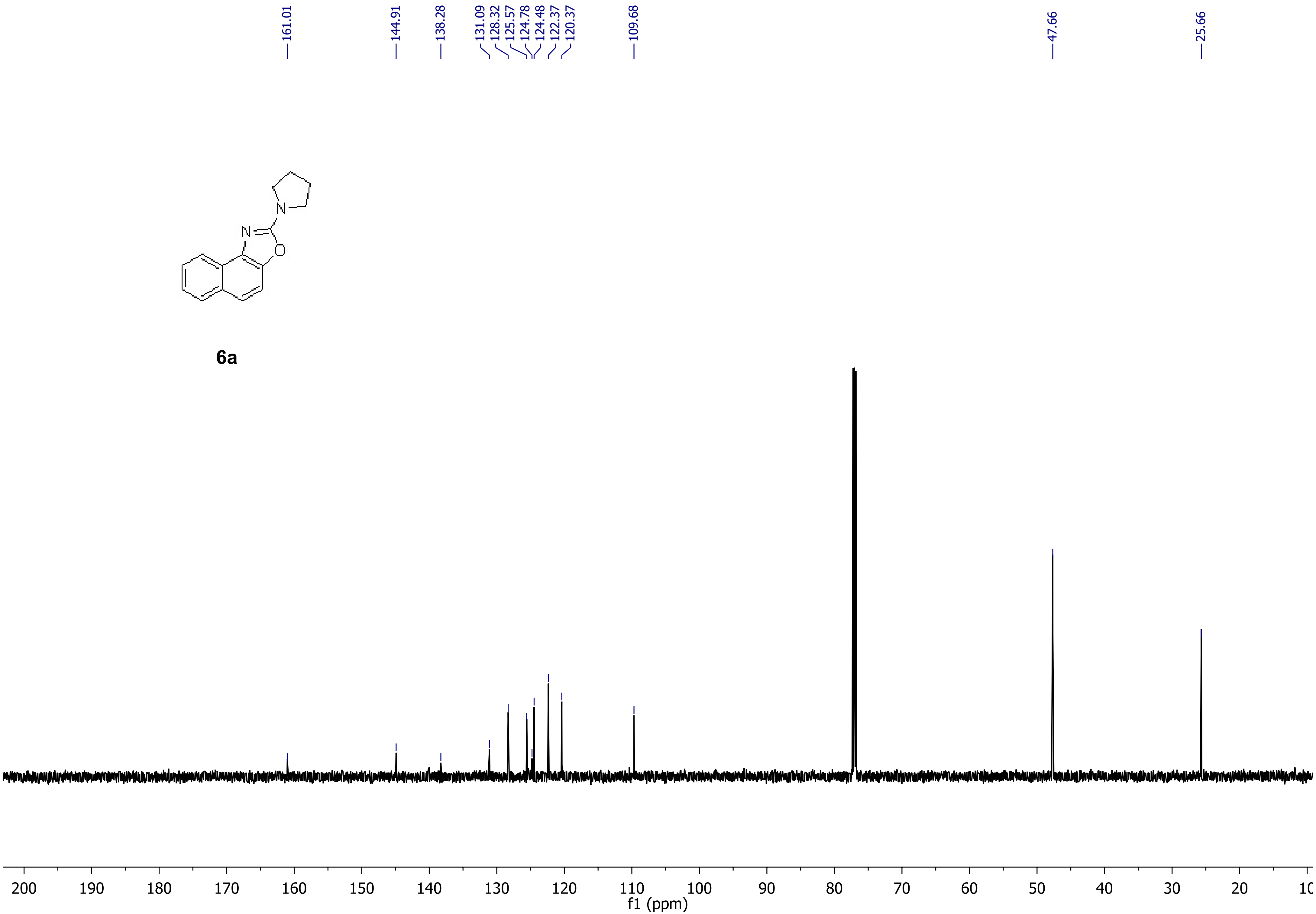
	 CCDC 2144943
Empirical formula	$C_{21} H_{20} N_2 O$
Formula weight	316.39
Crystal habit, colour	Needle, yellow
Crystal size, mm^3	0.35X 0.32X 0.30
Temperature, *T*	293(2)
Wavelength, λ(Å)	0.71073
Crystal system	monoclinic
Space group	*P 21*
Unit cell dimensions	*a* = 11.6978(6)Å *b* = 5.1772(2)Å *c* = 14.0219(7)Å α = 90°, β = 107.748(6)°, γ = 90°,
Volume, *V*(Å^3)	808.78(7)
Z	2
Calculated density, Mg·m^{-3}	1.299
Absorption coefficient, μ(mm^{-1})	0.081
F(000)	336
θ range for data collection	3.04° to 25.00°
Limiting indices	$-13 \le h \le 8$, $-6 \le k \le 5$, $-13 \le l \le 16$
Reflection collected / unique	2991/ 1986 [*R*(int) = 0.0115]

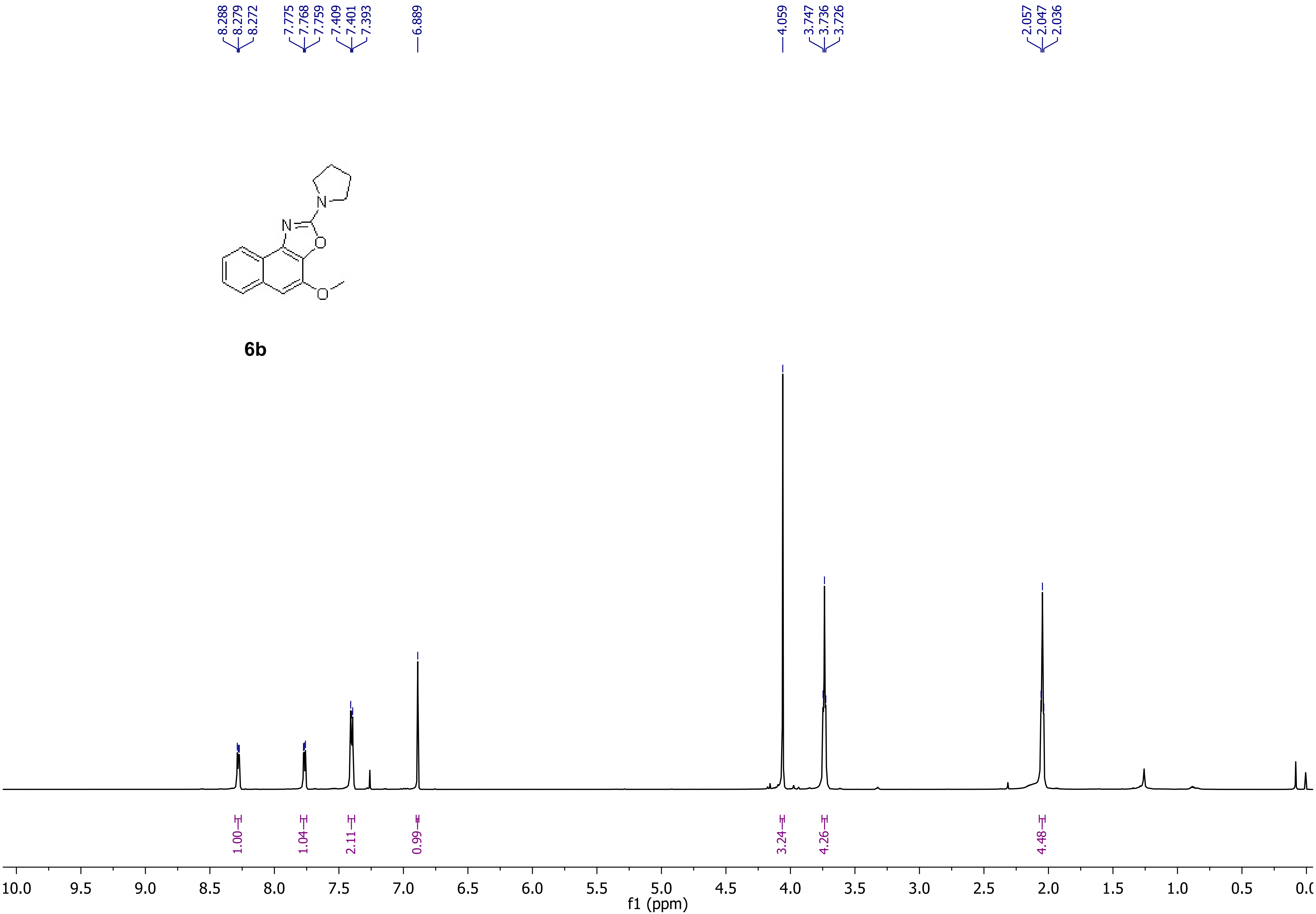
Completeness to θ	99.7% (θ = 25.00 °)
Refinement method	'SHELXL–97 (Sheldrick, 1997)
Data / restraints / parameters	1986 / 1 / 218
Goodness–of–fit on F^2	1.199
Final R indices [I>2sigma(I)]	R1 = 0.0428, wR2 = 0.1148
R indices (all data)	R1 = 0.0491, wR2 = 0.1205
Largest diff. peak and hole	0.206 and –0.141e·Å^{-3}

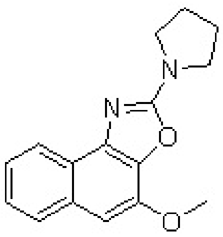
References:

[i] Md P. Sk and A. Chattopadhyay *RSC Adv.*, 2014, **4**, 31994.
[ii] A. Purkait, S. K. Roy, H. K. Srivastava and C. K. Jana, *Org. Lett.*, 2017, **19**, 2540.
[iii] E. Caballero, C. Avendaňo and J. C. Menéndez, *J. Org. Chem.*, 2003, **68**, 6944.
[iv] C. R. Shugrue, A. L. Featherston, R. M. Lackner, A. Lin and S. J. Miller, *J. Org. Chem.*, 2018, **83**, 4491.
[v] A. Mollica, M. P. Paradisi, K. Varani, S. Spisanic and G. Lucente, *Bioorg. Med. Chem.*, 2006, **14**, 2253.
[vi] S. H. Cho, J. Y. Kim, S. Y. Lee and S. Chang, *Angew. Chem., Int. Ed.* 2009, **48**, 9127.

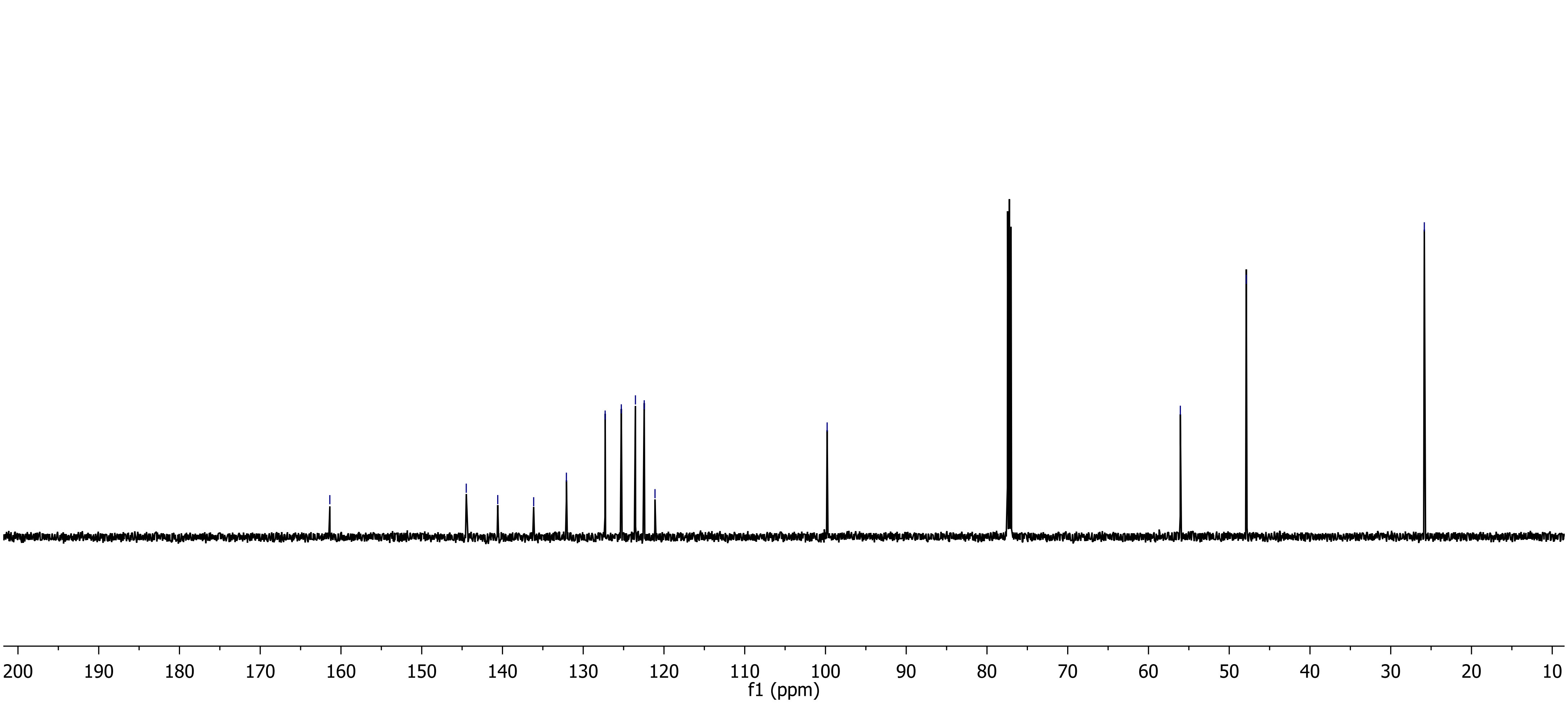

8.393
8.379
7.884
7.870
7.539
7.526
7.514
7.501
7.444
7.430
7.419
3.747
3.736
3.725
2.077
2.066
2.055
N
N
O
6a
1.00
0.99
3.23
1.03
4.40
4.43
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

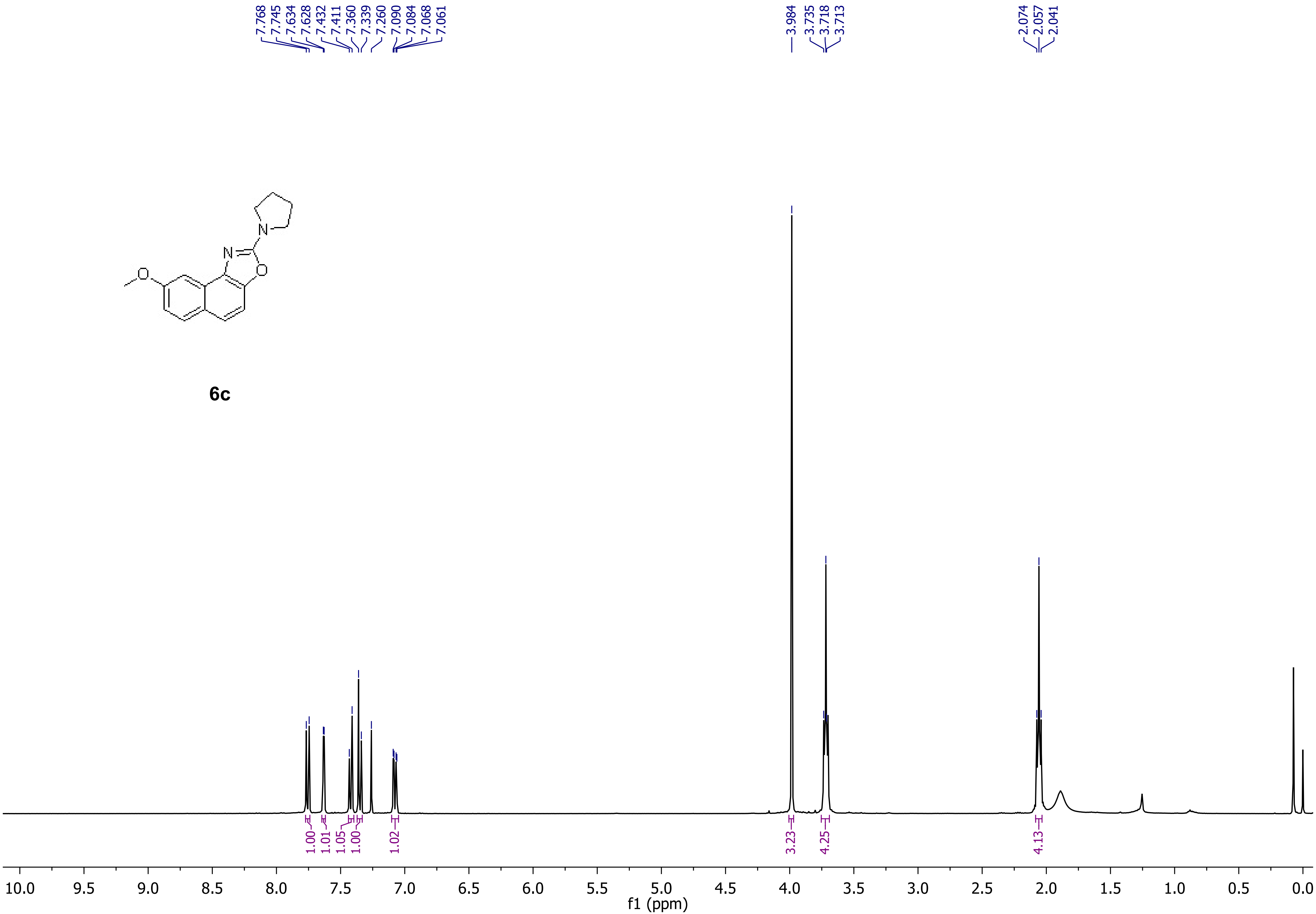

161.01
144.91
138.28
131.09
128.32
125.57
124.78
124.48
122.37
120.37
109.68
47.66
25.66
N
O
N
6a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.288
8.279
8.272
7.775
7.768
7.759
7.409
7.401
7.393
6.889
4.059
3.747
3.736
3.726
2.057
2.047
2.036
N
N
O
O
6b
1.00
1.04
2.11
0.99
3.24
4.26
4.48
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
f1 (ppm)

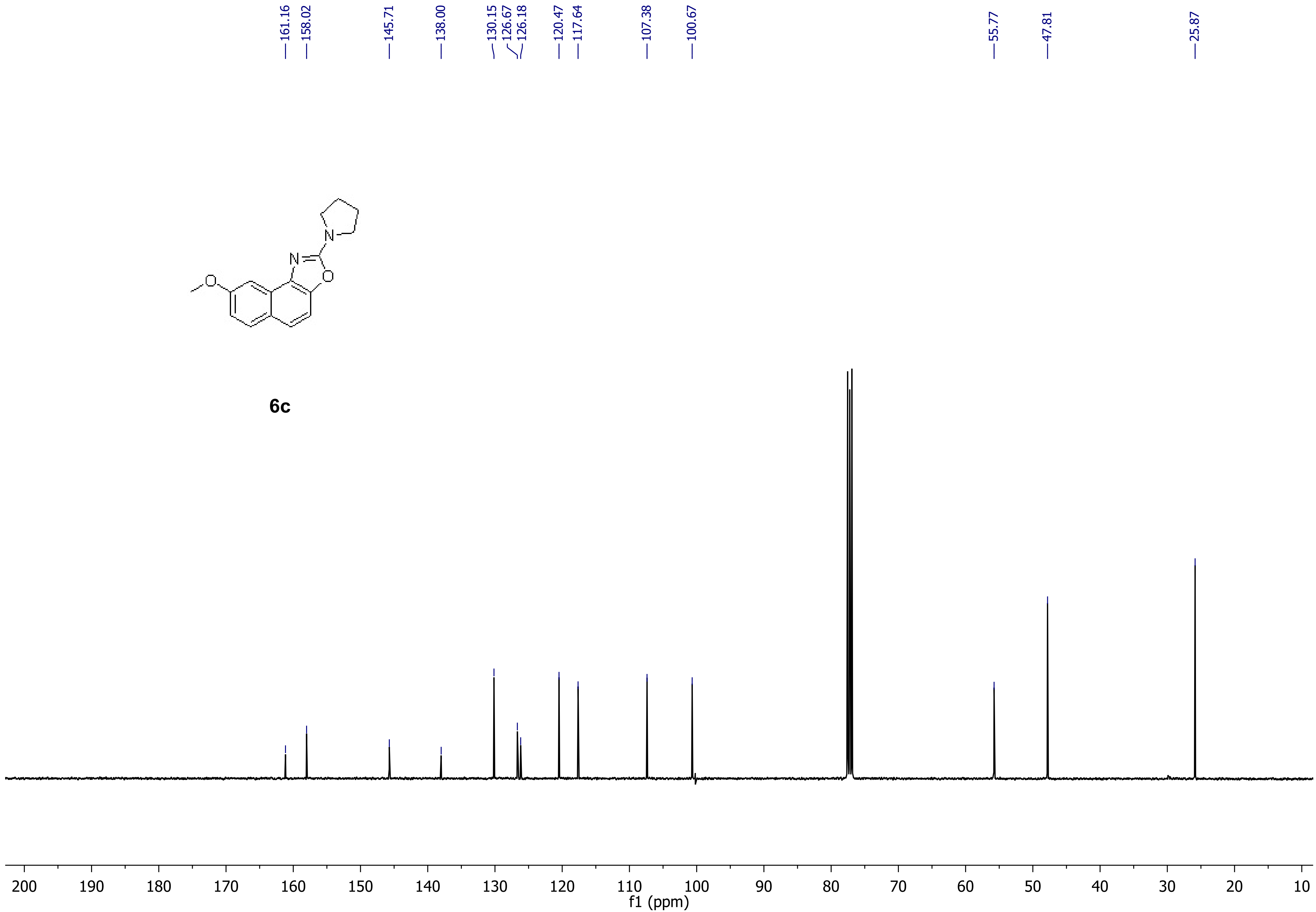

N
N
O
O

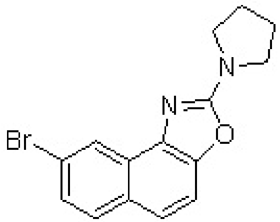
6b


161.38
144.48
140.58
136.14
132.08
127.28
125.28
123.53
122.45
121.11
99.79
56.05
47.89
25.84
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

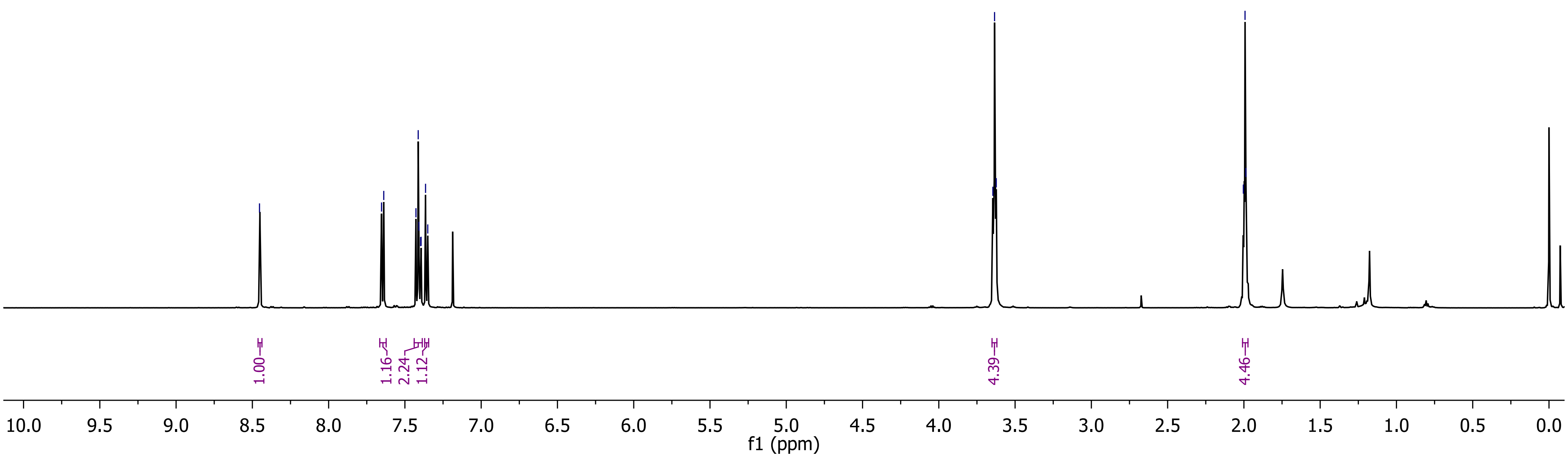

7.768
7.745
7.634
7.628
7.432
7.411
7.360
7.339
7.260
7.090
7.084
7.068
7.061
3.984
3.735
3.718
3.713
2.074
2.057
2.041
1.00
1.01
1.05
1.00
1.02
3.23
4.25
4.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

6c

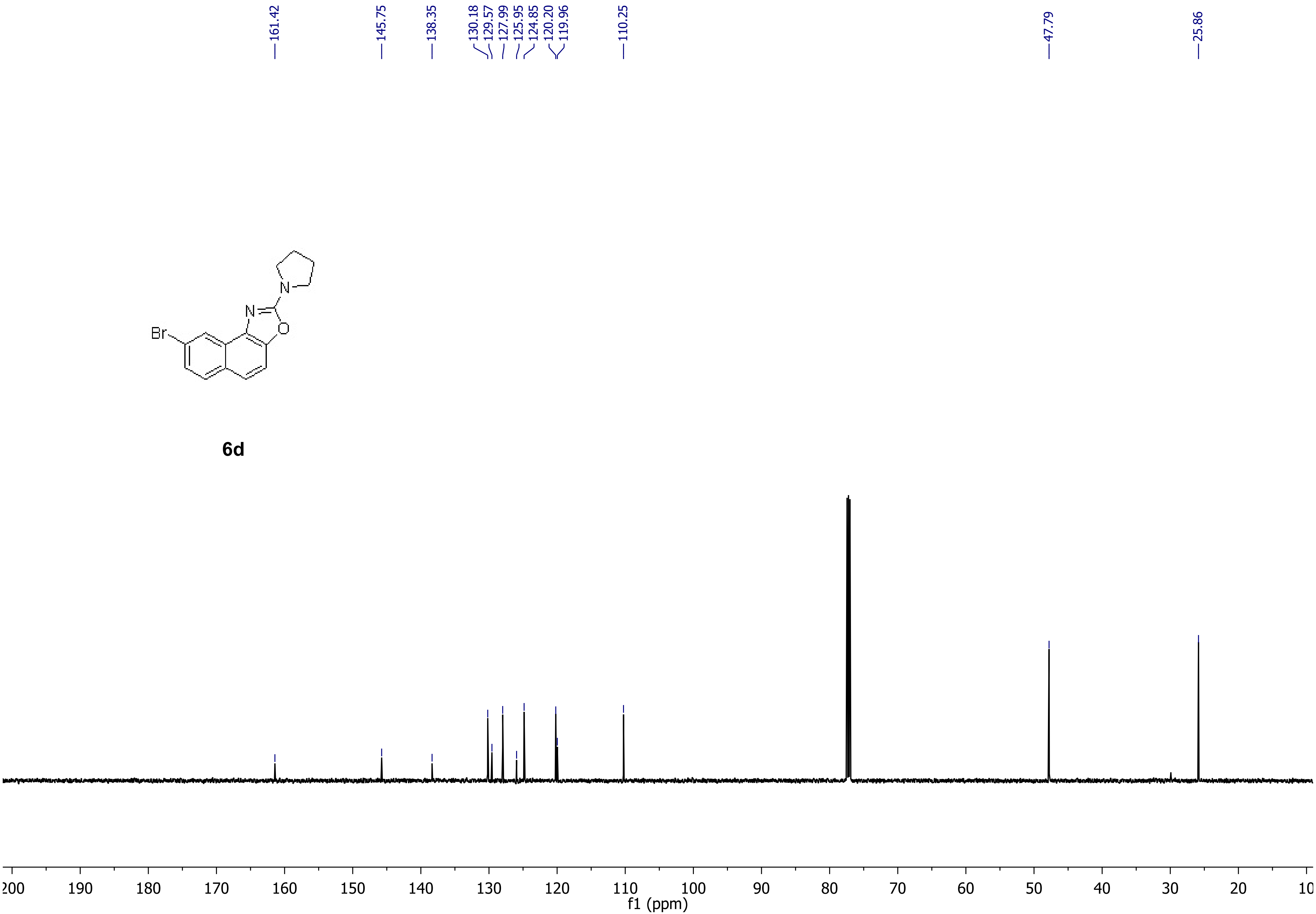

161.16
158.02
145.71
138.00
130.15
126.67
126.18
120.47
117.64
107.38
100.67
55.77
47.81
25.87
N
N
O
O
6c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



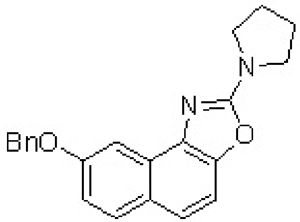
6d



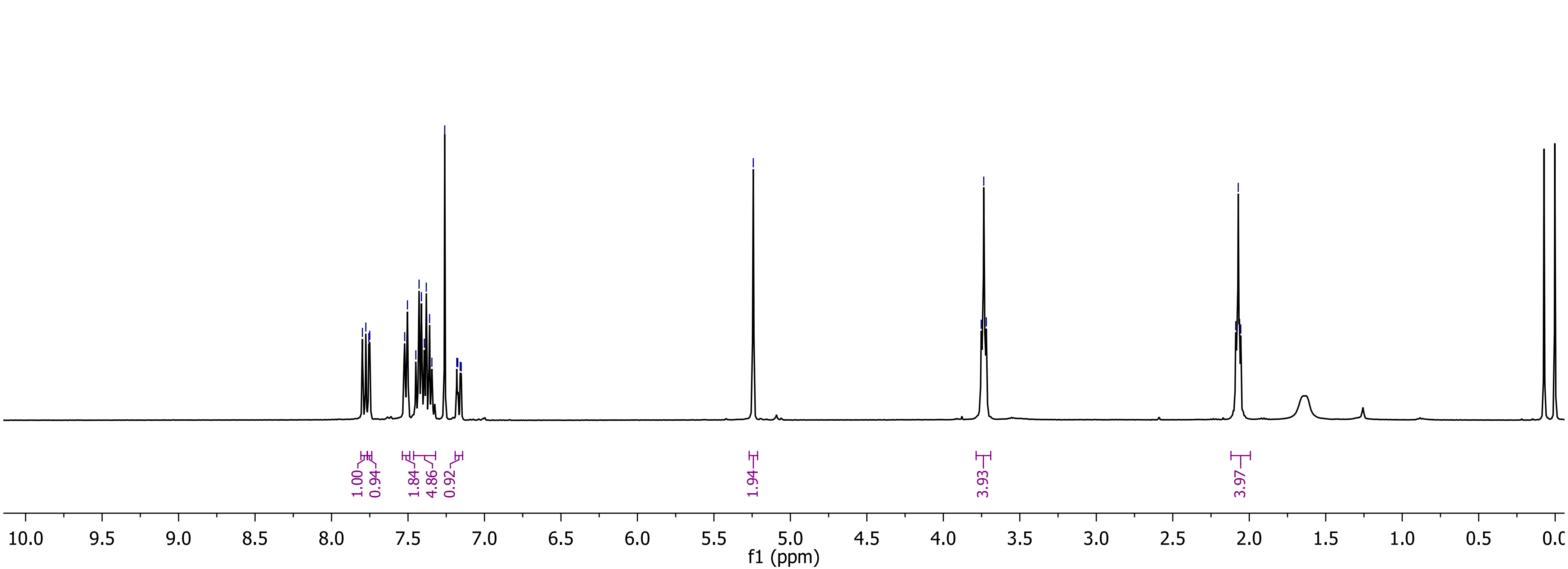
8.453
7.653
7.639
7.428
7.413
7.409
7.397
7.394
7.365
7.350
3.646
3.635
3.623
2.004
1.993
1.987
1.00
1.16
2.24
1.12
4.39
4.46
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

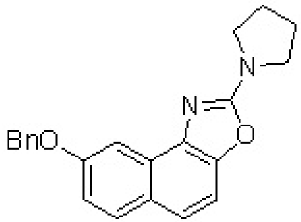

161.42
145.75
138.35
130.18
129.57
127.99
125.95
124.85
120.20
119.96
110.25
47.79
25.86
Br
N
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

6d

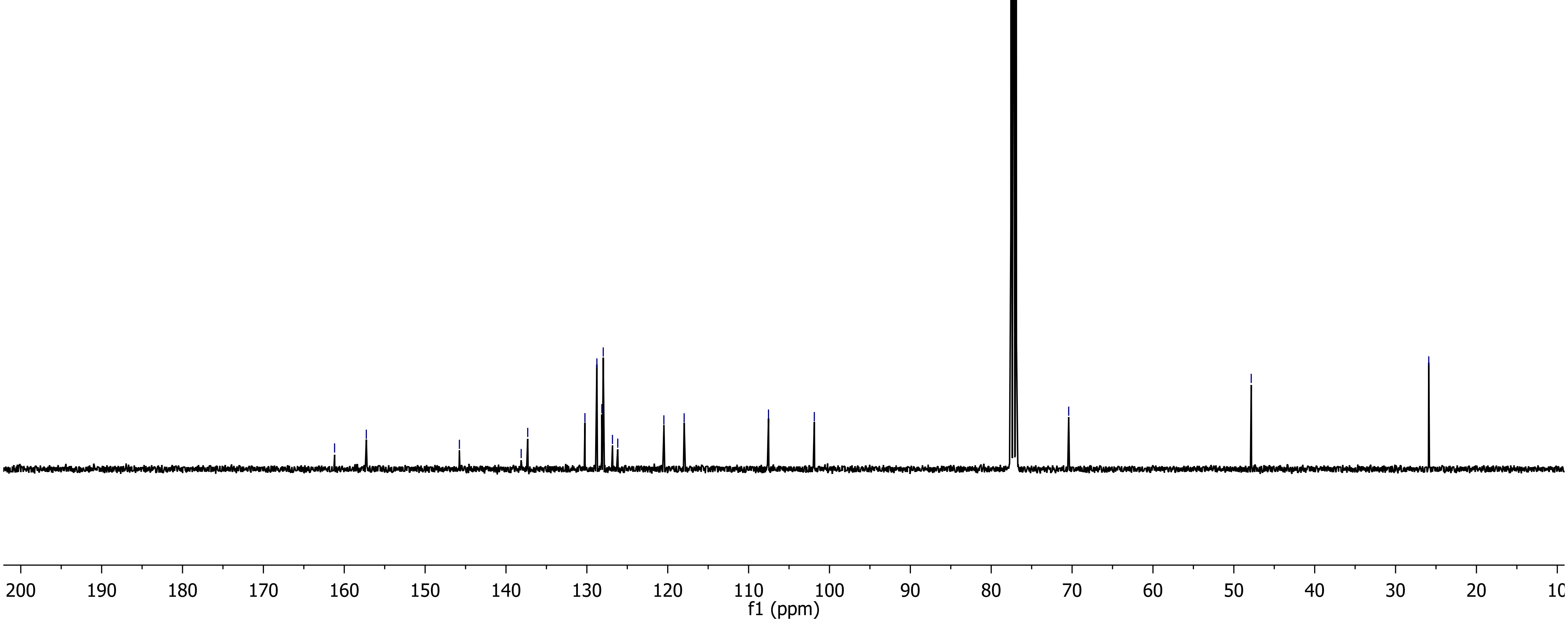

BnO
N
O
N

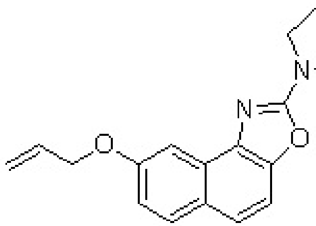
6e


7.798
7.776
7.756
7.750
7.522
7.504
7.449
7.428
7.412
7.393
7.381
7.359
7.344
7.260
7.181
7.175
7.158
7.152
5.243
3.752
3.736
3.719
2.089
2.072
2.055
1.00
0.94
1.84
4.86
0.92
1.94
3.93
3.97
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
f1 (ppm)

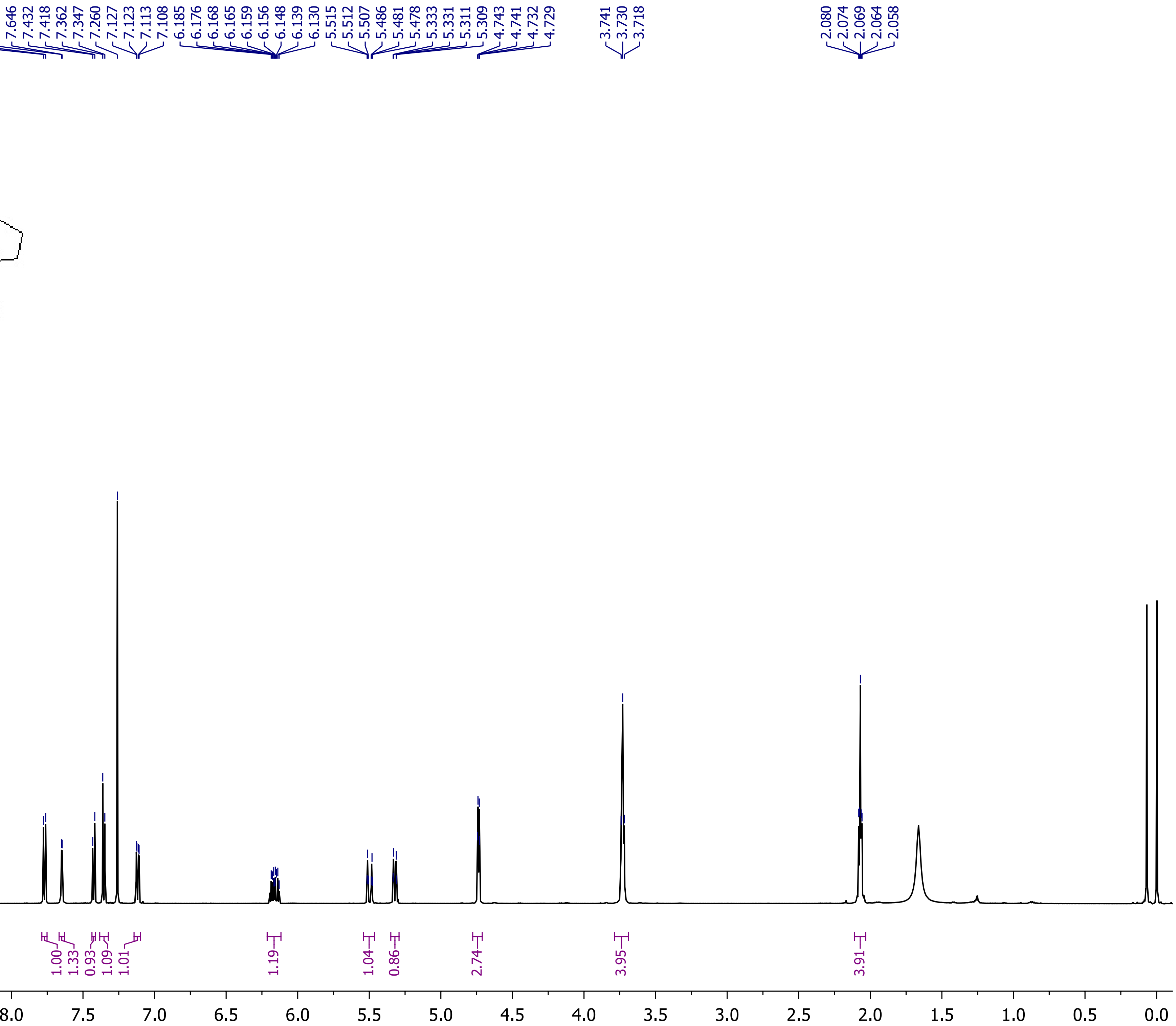

BnO
N
N
O

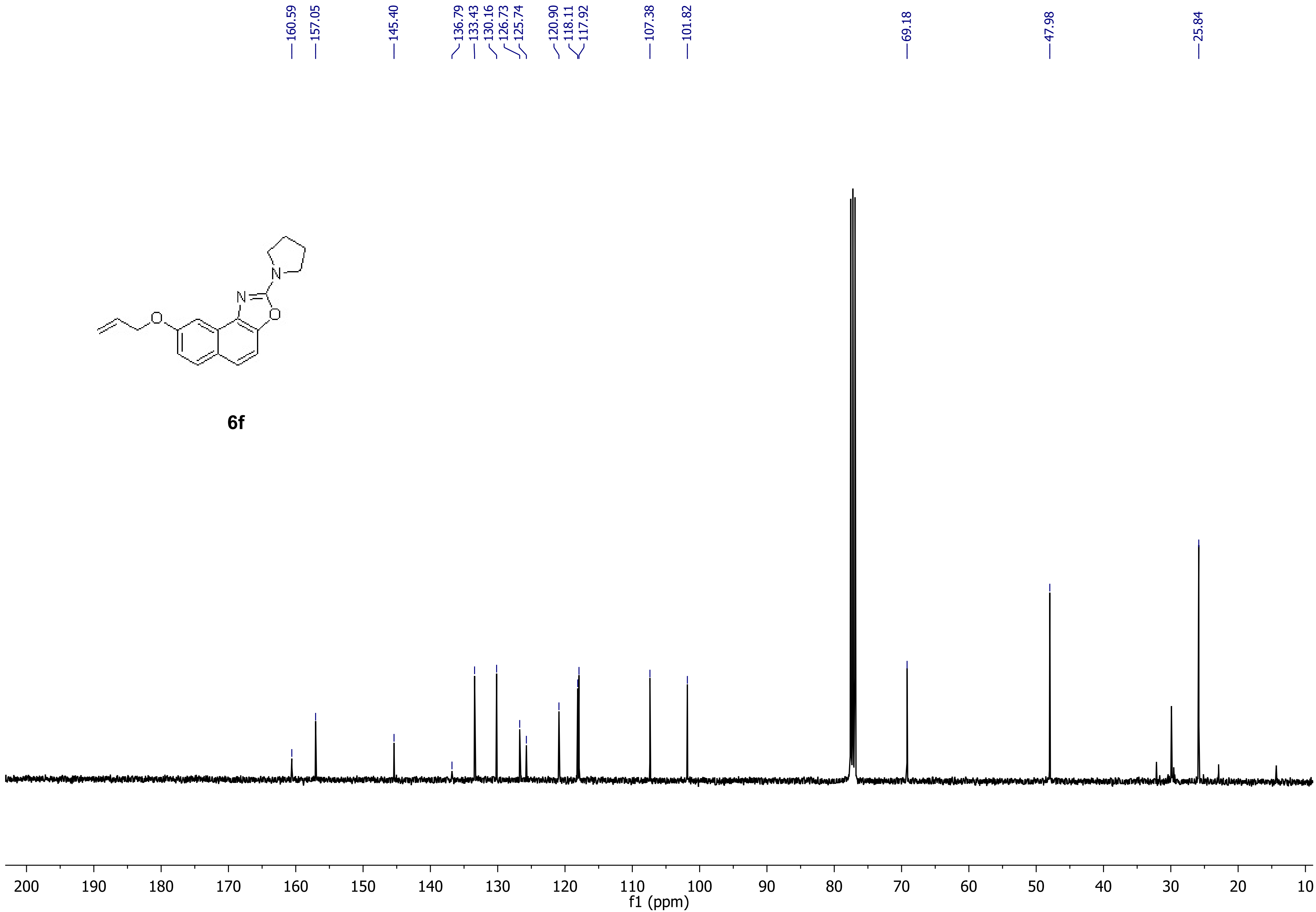
6e


161.20
157.27
145.76
138.12
137.31
130.24
128.76
128.15
127.98
126.83
126.18
120.48
117.97
107.54
101.87
70.42
47.85
25.90
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

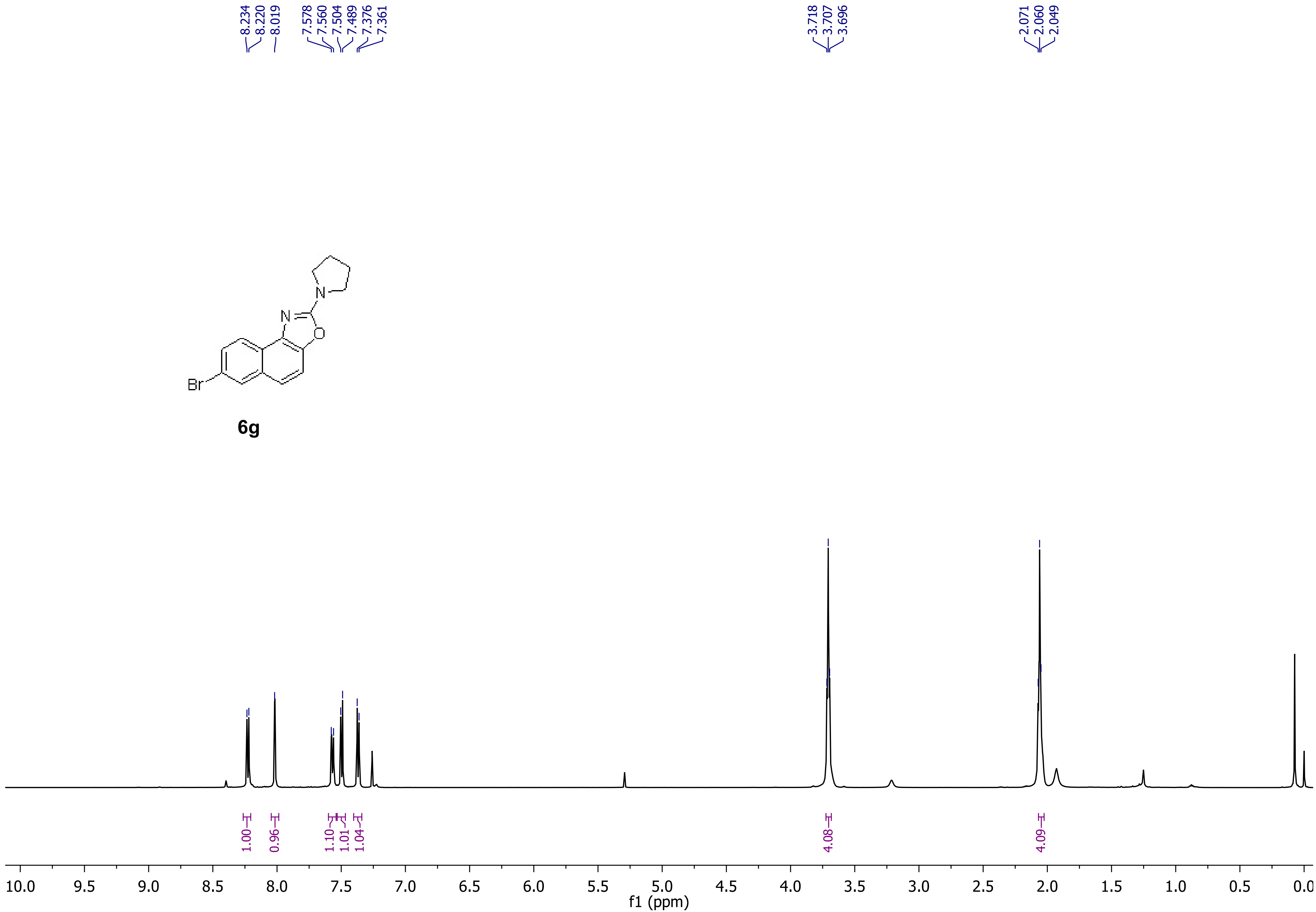


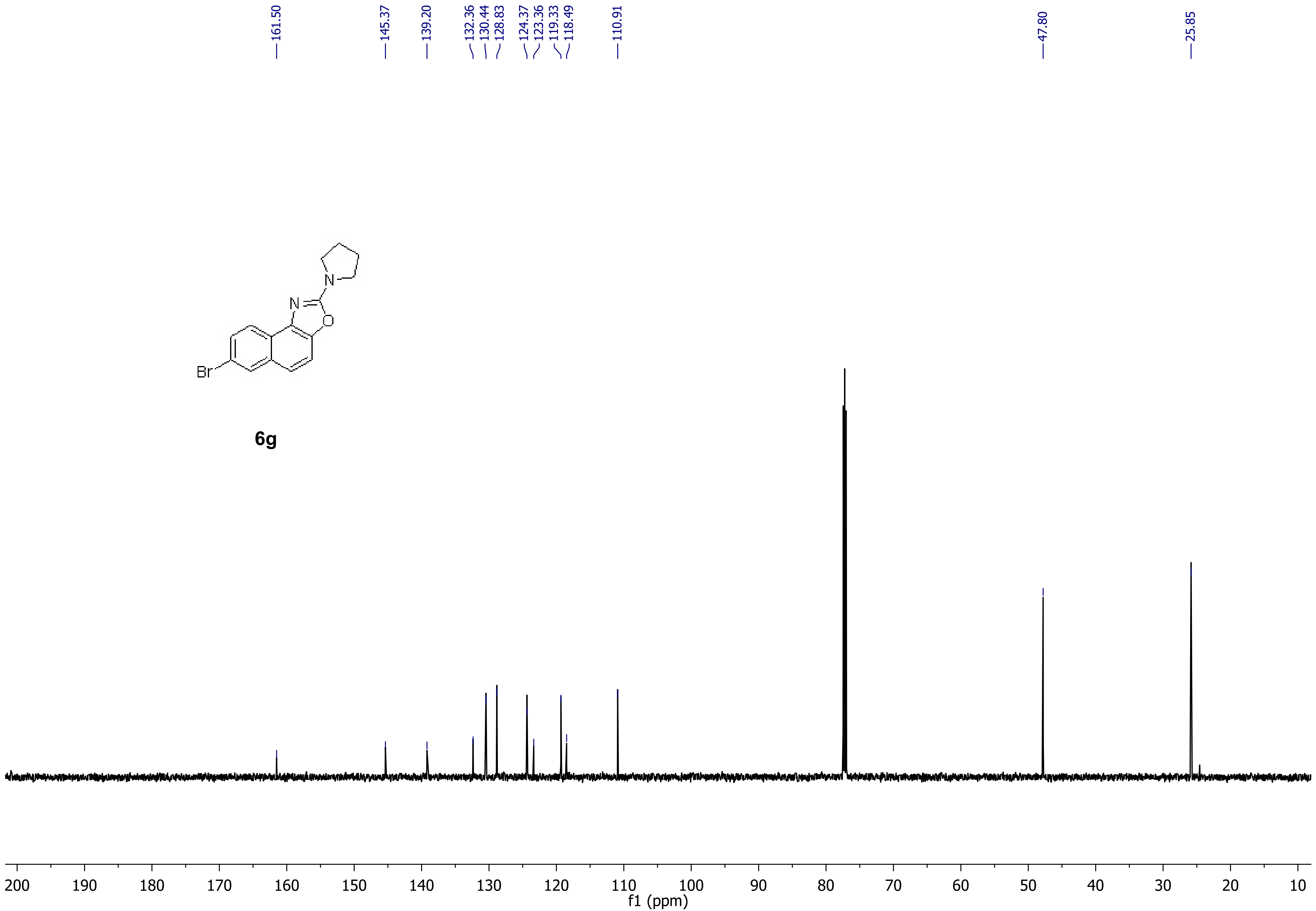
6f

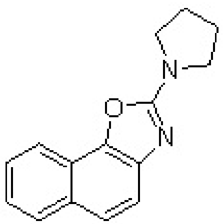

7.776
7.761
7.650
7.646
7.432
7.418
7.362
7.347
7.260
7.127
7.123
7.113
7.108
6.185
6.176
6.168
6.165
6.159
6.156
6.148
6.139
6.130
5.515
5.512
5.507
5.486
5.481
5.478
5.333
5.331
5.311
5.309
4.743
4.741
4.732
4.729
3.741
3.730
3.718
2.080
2.074
2.069
2.064
2.058
1.00
1.33
0.93
1.09
1.01
1.19
1.04
0.86
2.74
3.95
3.91
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



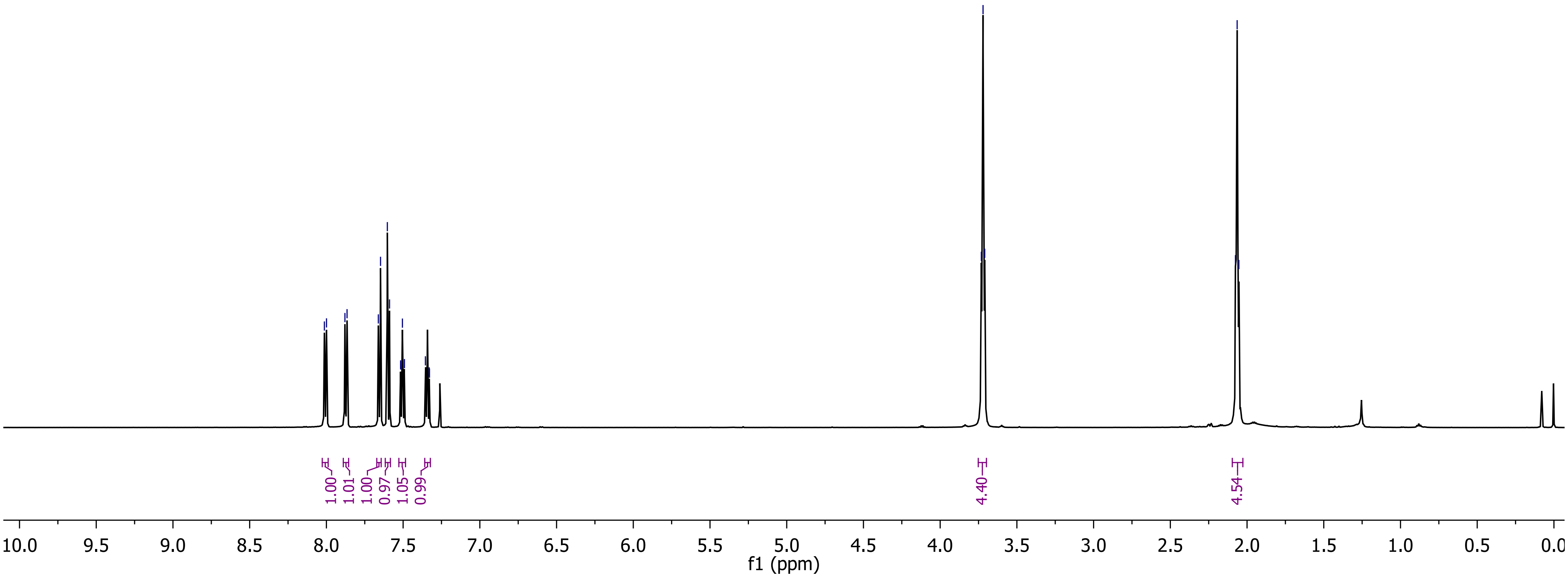
160.59
157.05
145.40
136.79
133.43
130.16
126.73
125.74
120.90
118.11
117.92
107.38
101.82
69.18
47.98
25.84
N
O
N
O
6f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.234
8.220
8.019
7.578
7.560
7.504
7.489
7.376
7.361
3.718
3.707
3.696
2.071
2.060
2.049
N
N
O
Br
6g
1.00
0.96
1.10
1.01
1.04
4.08
4.09
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
f1 (ppm)

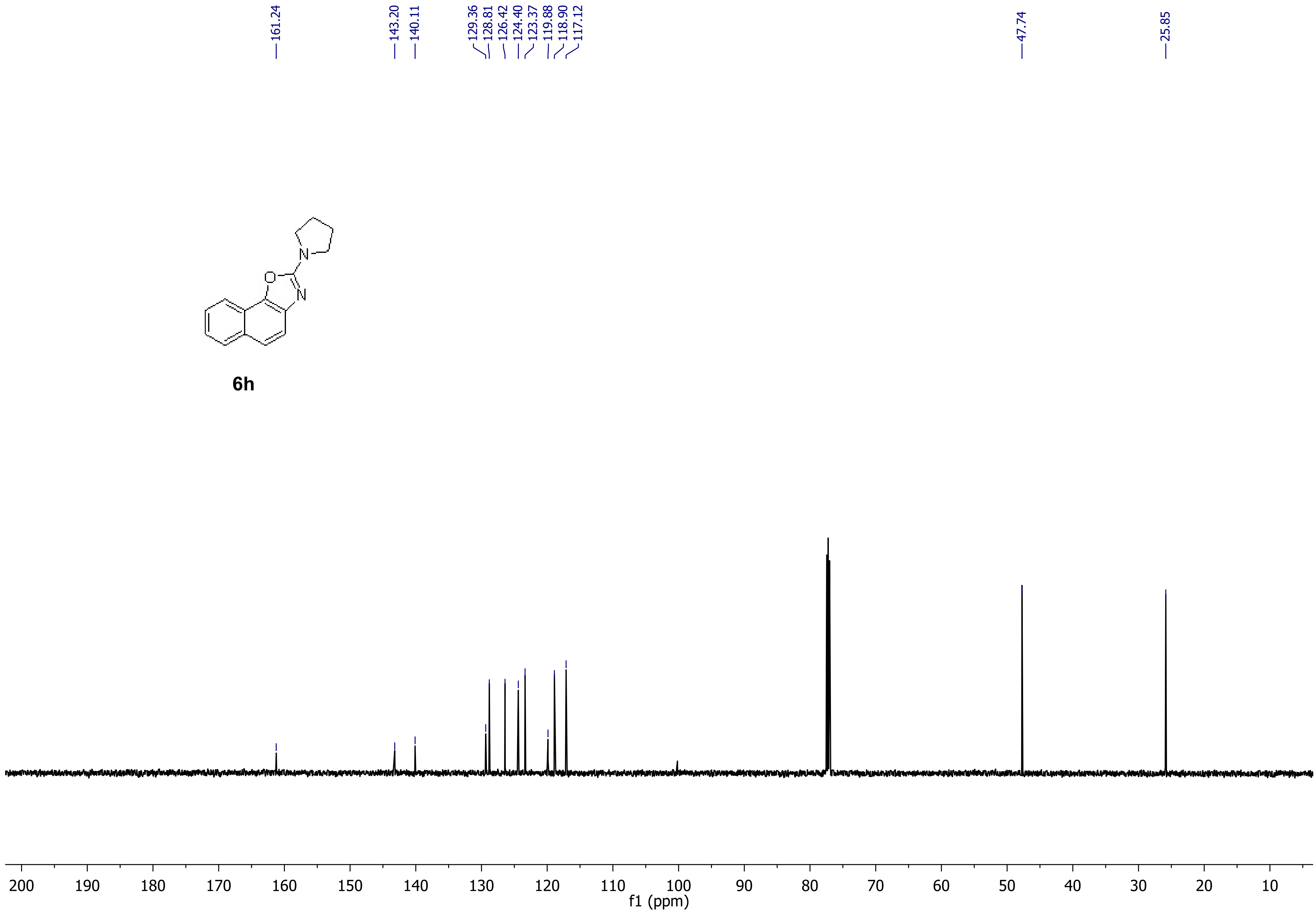

161.50
145.37
139.20
132.36
130.44
128.83
124.37
123.36
119.33
118.49
110.91
47.80
25.85
N
N
O
Br
6g
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

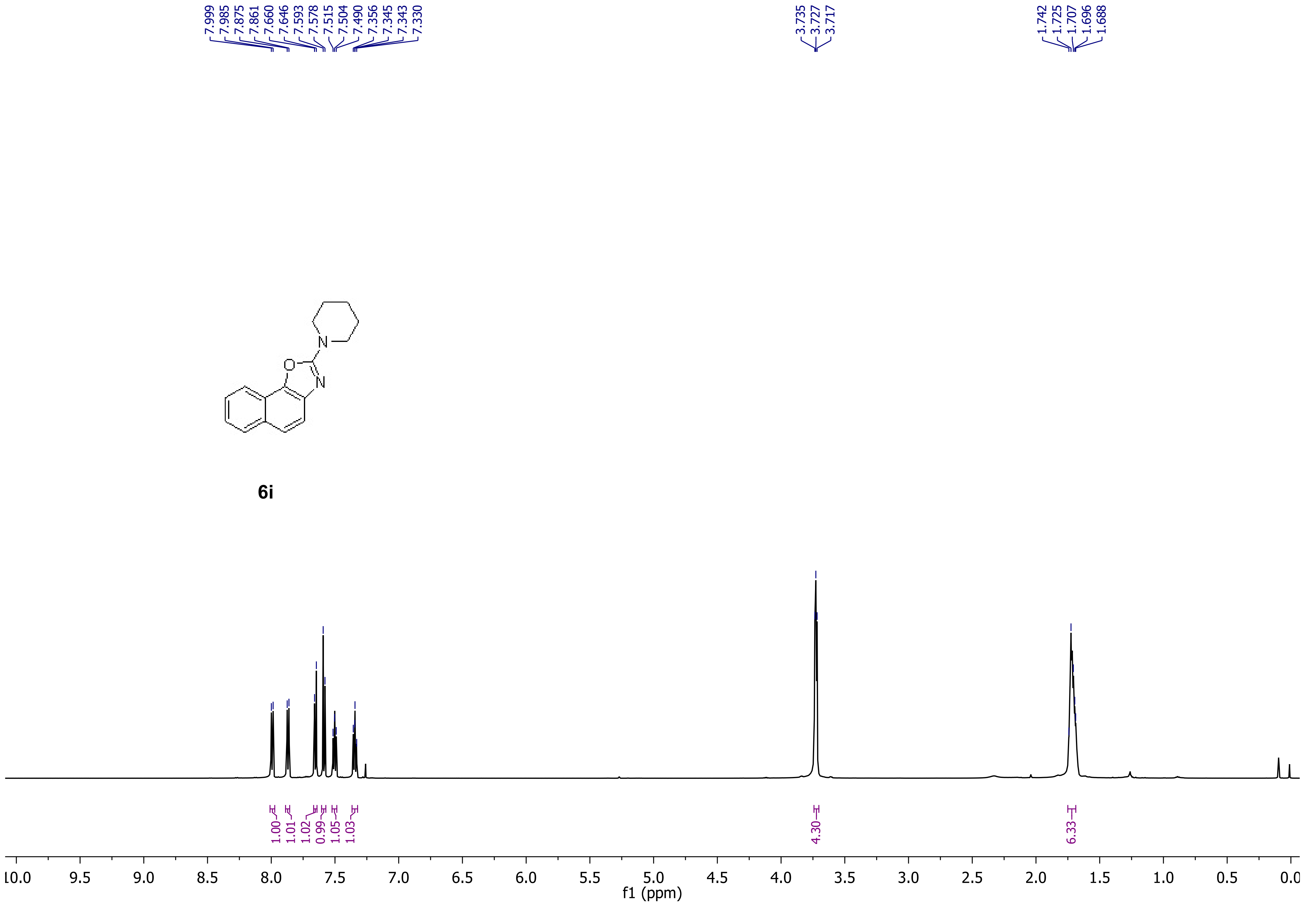


6h

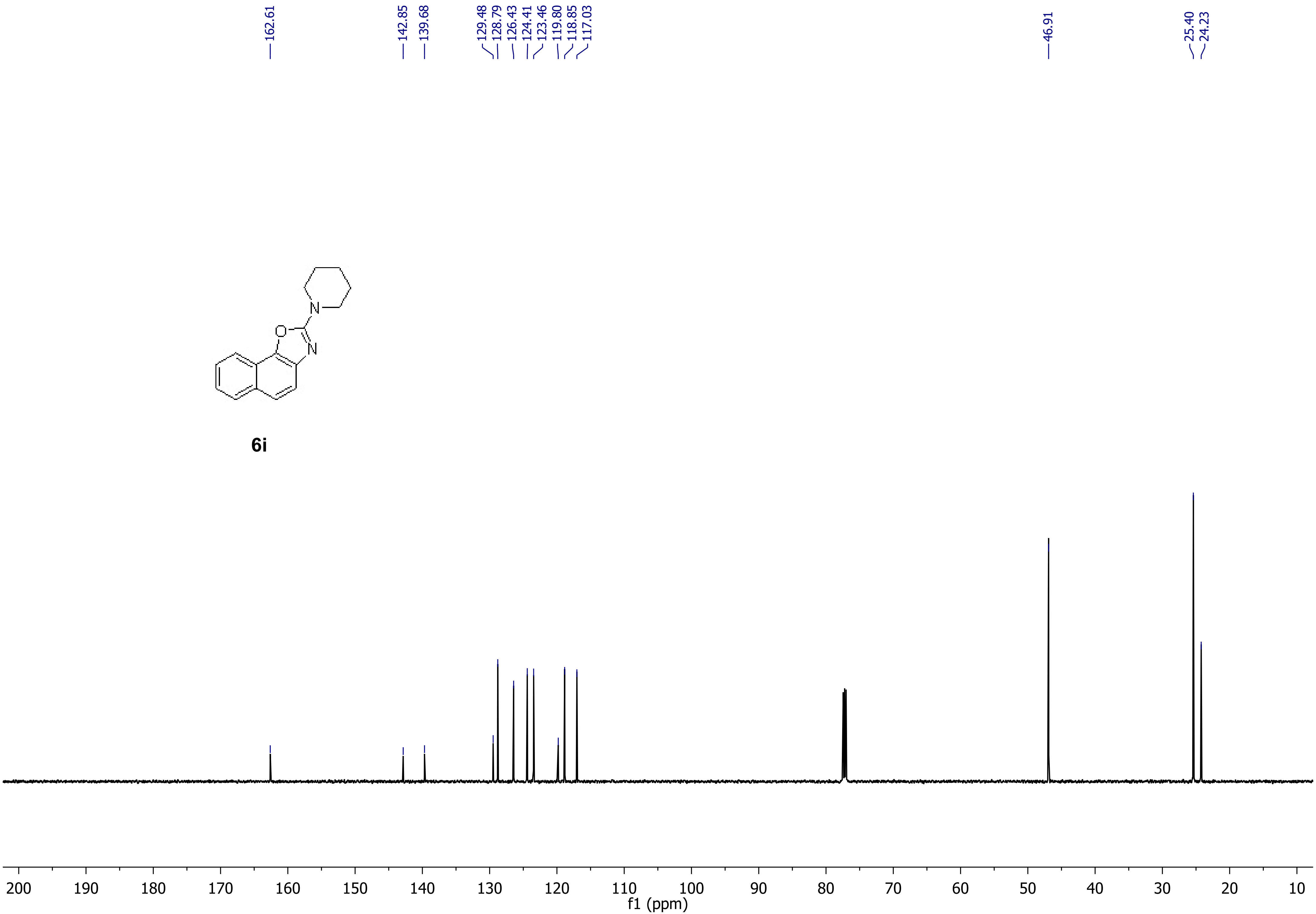


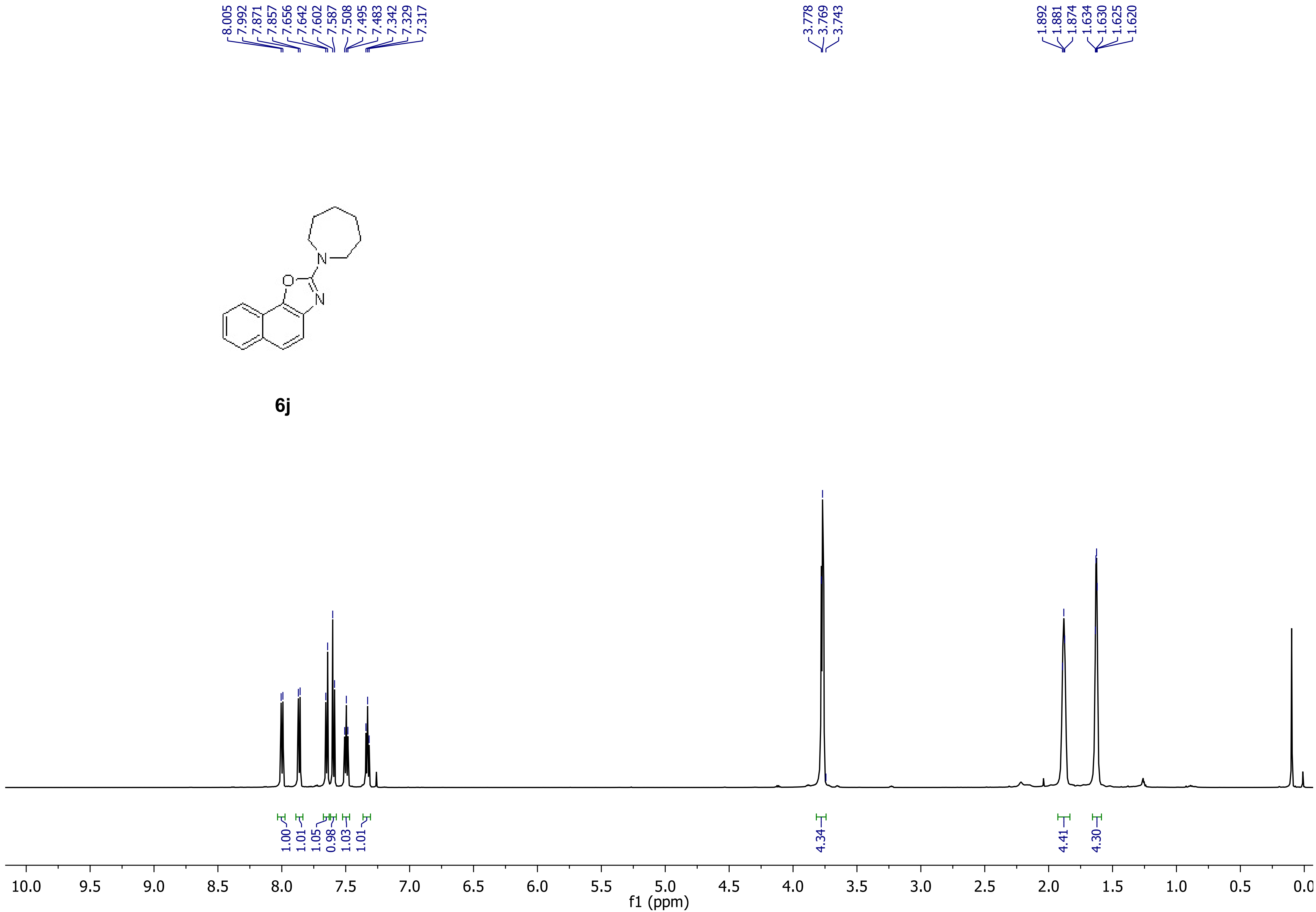
8.013
7.999
7.879
7.865
7.661
7.647
7.603
7.589
7.517
7.505
7.491
7.355
7.330
7.328
3.732
3.721
3.710
2.076
2.065
2.053
1.00
1.01
1.00
0.97
1.05
0.99
4.40
4.54
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


161.24
143.20
140.11
129.36
128.81
126.42
124.40
123.37
119.88
118.90
117.12
47.74
25.85
6h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



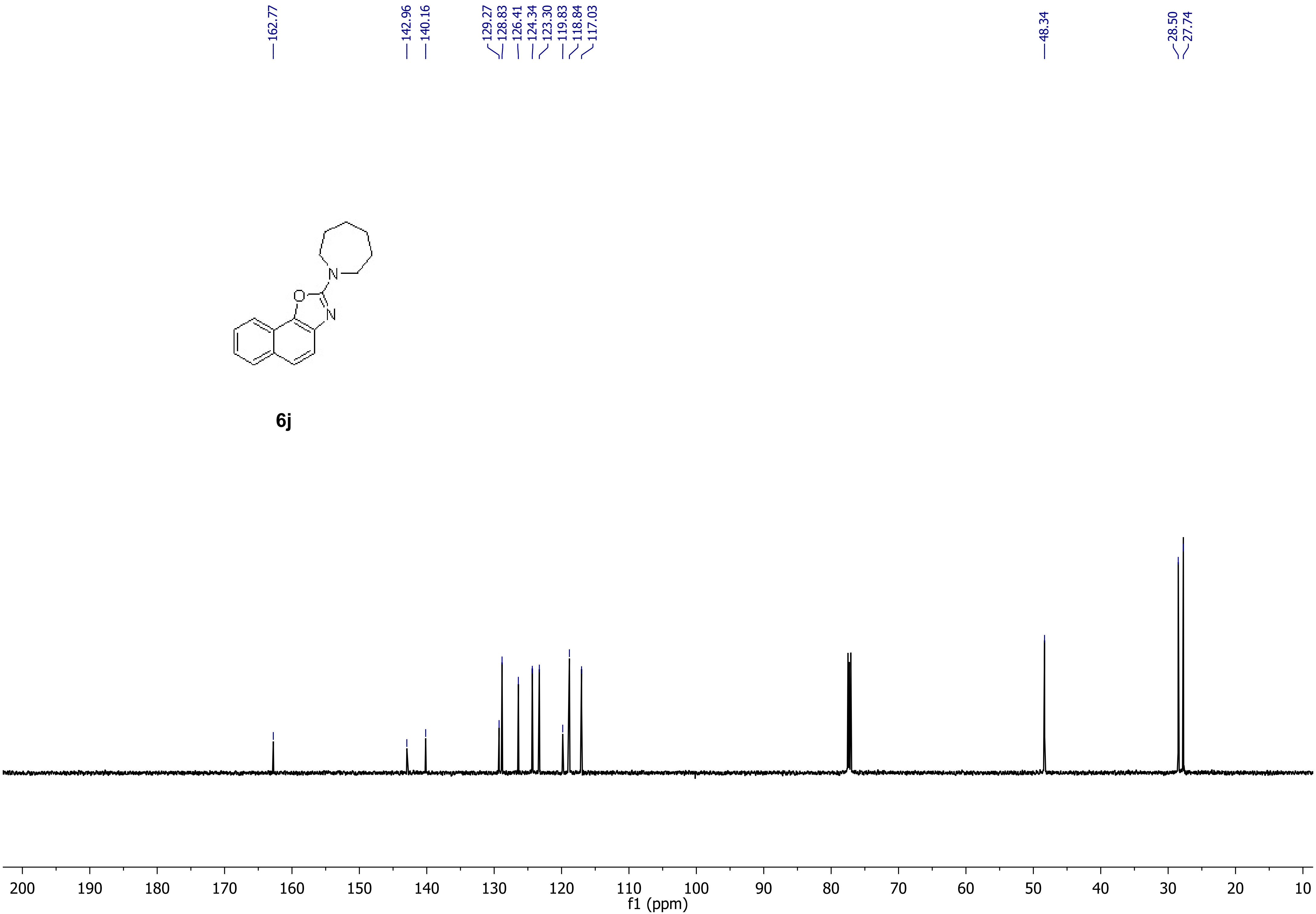
7.999
7.985
7.875
7.861
7.660
7.646
7.593
7.578
7.515
7.504
7.490
7.356
7.345
7.343
7.330
3.735
3.727
3.717
1.742
1.725
1.707
1.696
1.688
6i
1.00
1.01
1.02
0.99
1.05
1.03
4.30
6.33
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

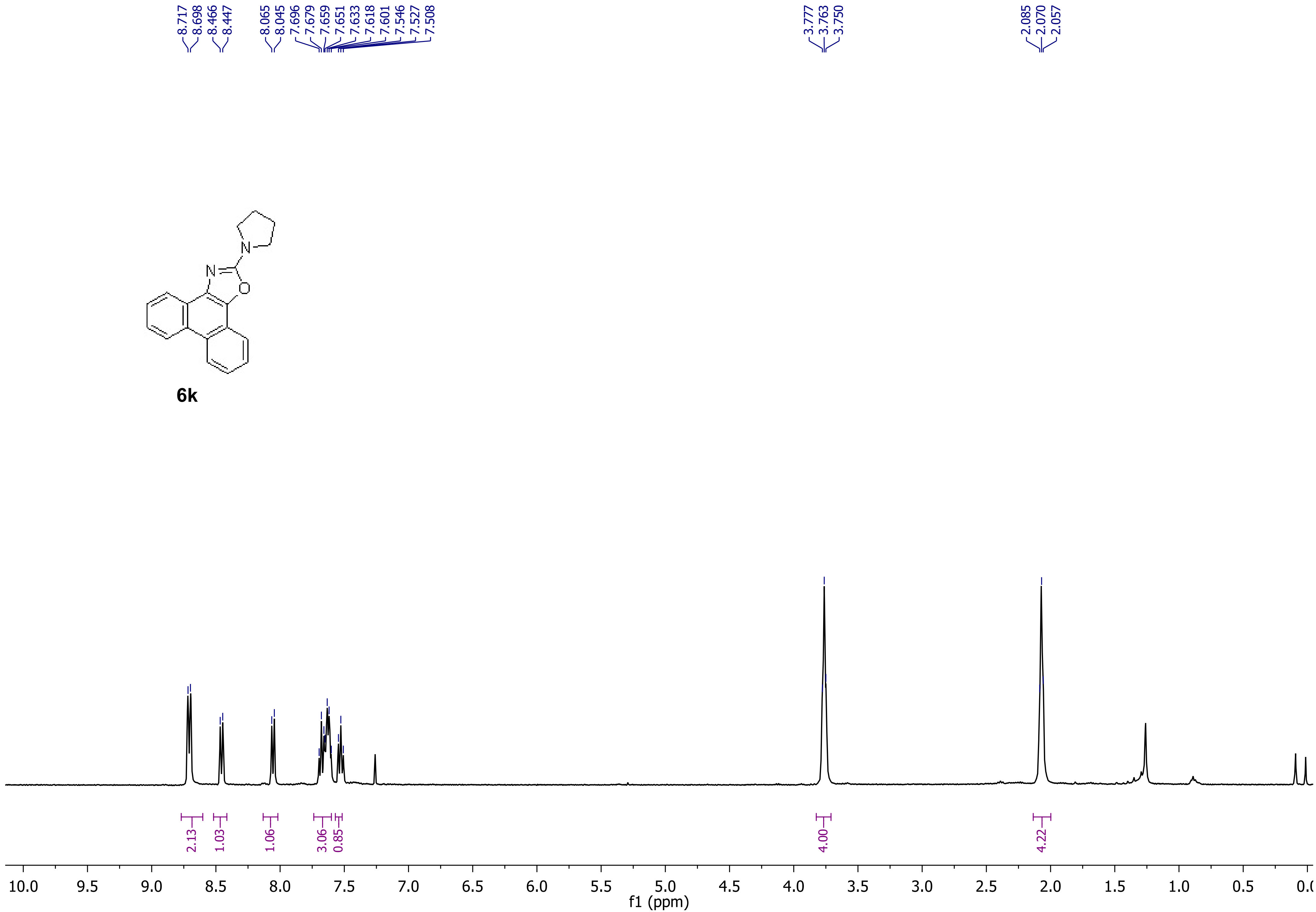

162.61
142.85
139.68
129.48
128.79
126.43
124.41
123.46
119.80
118.85
117.03
46.91
25.40
24.23
6i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



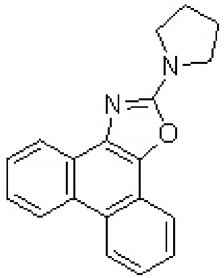
8.005
7.992
7.871
7.857
7.656
7.642
7.602
7.587
7.508
7.495
7.483
7.342
7.329
7.317
3.778
3.769
3.743
1.892
1.881
1.874
1.634
1.630
1.625
1.620
O
N
N
1.00
1.01
1.05
0.98
1.03
1.01
4.34
4.41
4.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

6j

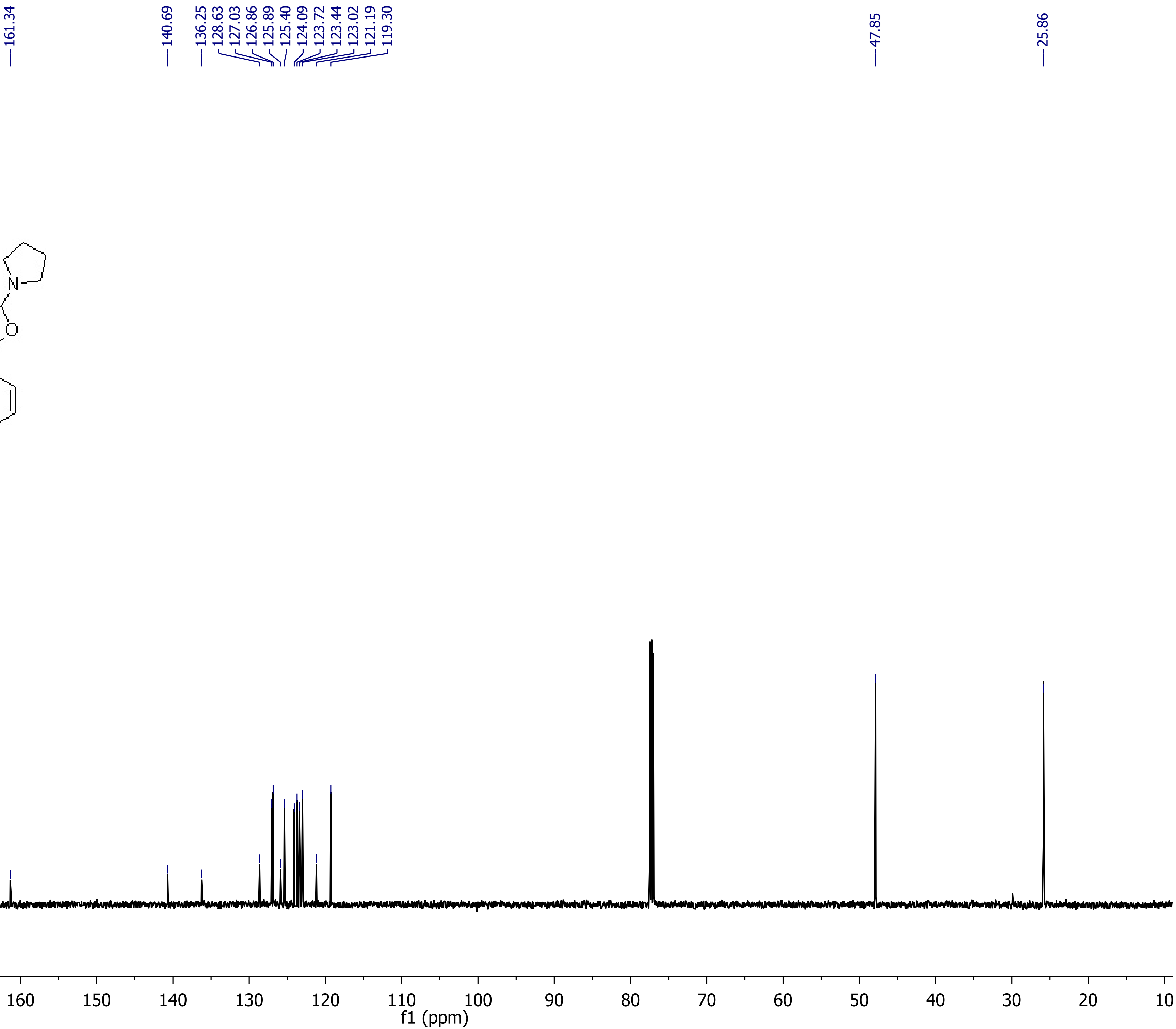

162.77
142.96
140.16
129.27
128.83
126.41
124.34
123.30
119.83
118.84
117.03
48.34
28.50
27.74
O
N
N
6j
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

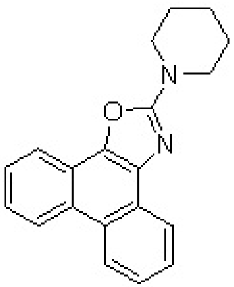


8.717
8.698
8.466
8.447
8.065
8.045
7.696
7.679
7.659
7.651
7.633
7.618
7.601
7.546
7.527
7.508
3.777
3.763
3.750
2.085
2.070
2.057
N
N
O
6k
2.13
1.03
1.06
3.06
0.85
4.00
4.22
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

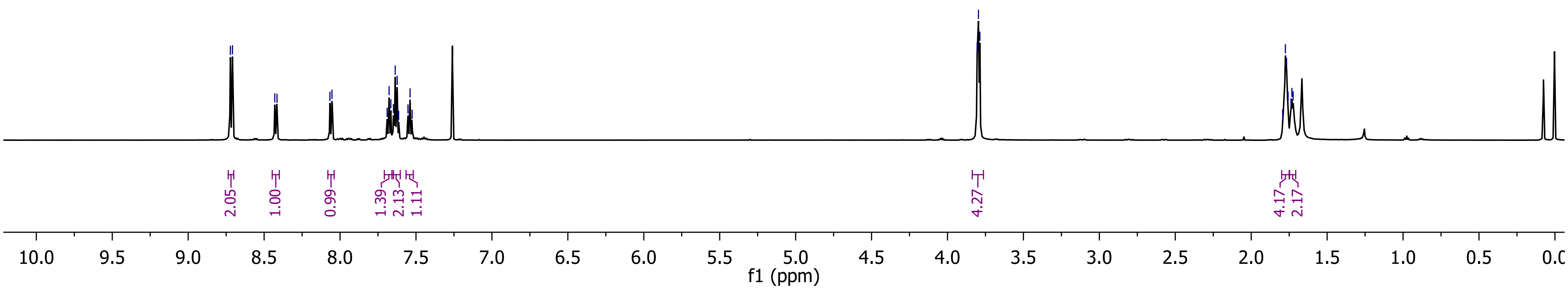


6k

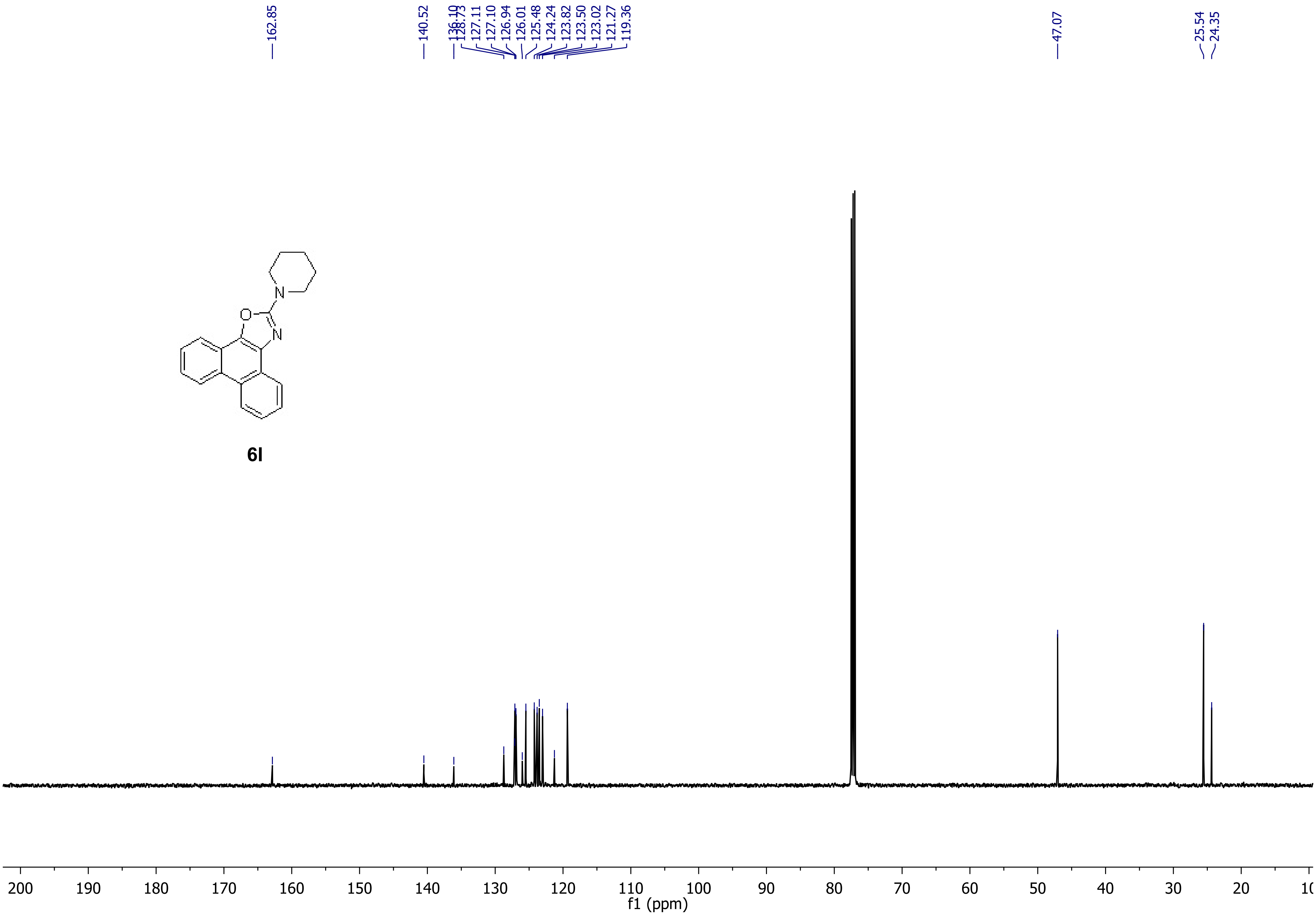

161.34
140.69
136.25
128.63
127.03
126.86
125.89
125.40
124.09
123.72
123.44
123.02
121.19
119.30
47.85
25.86
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

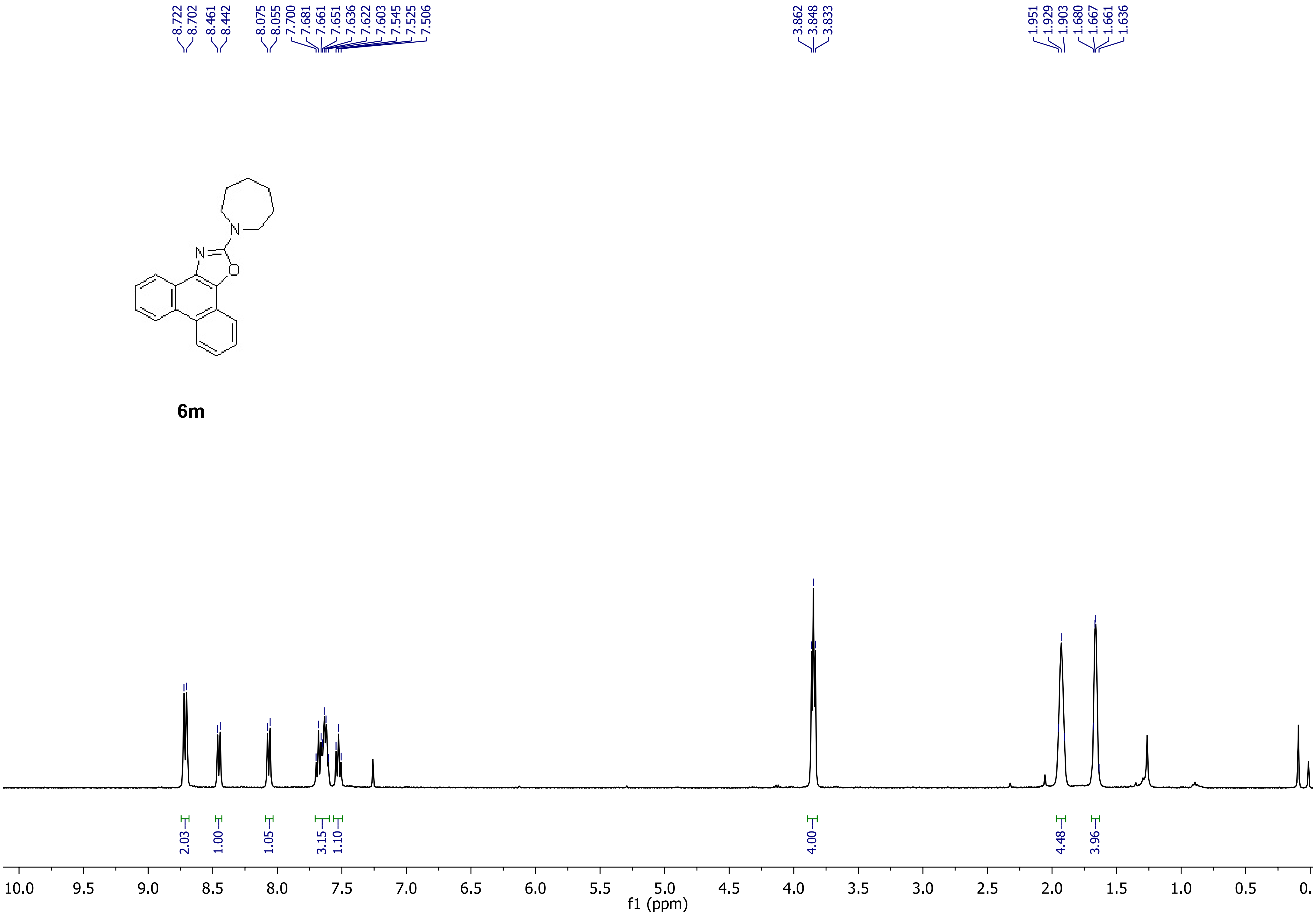


6l

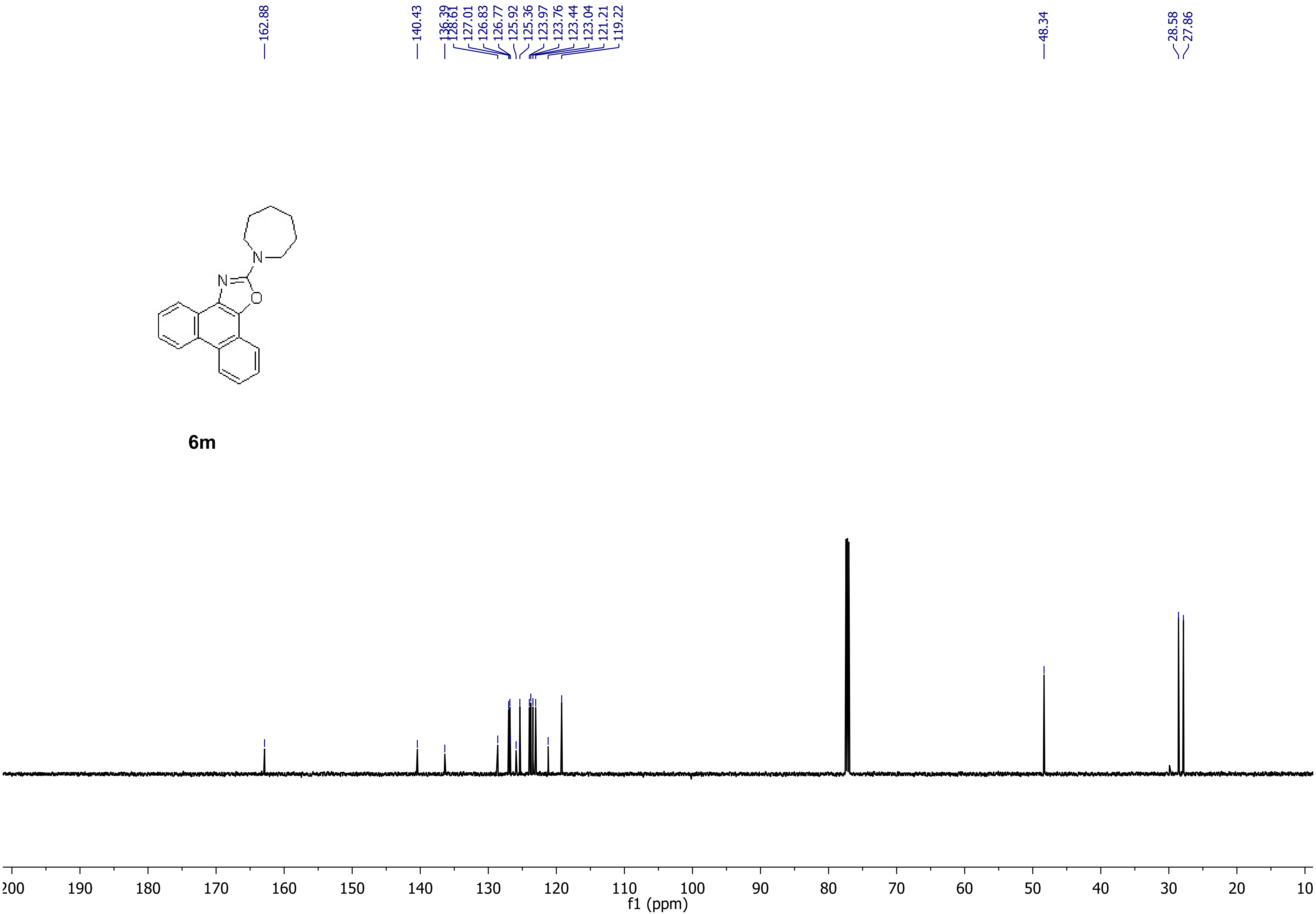


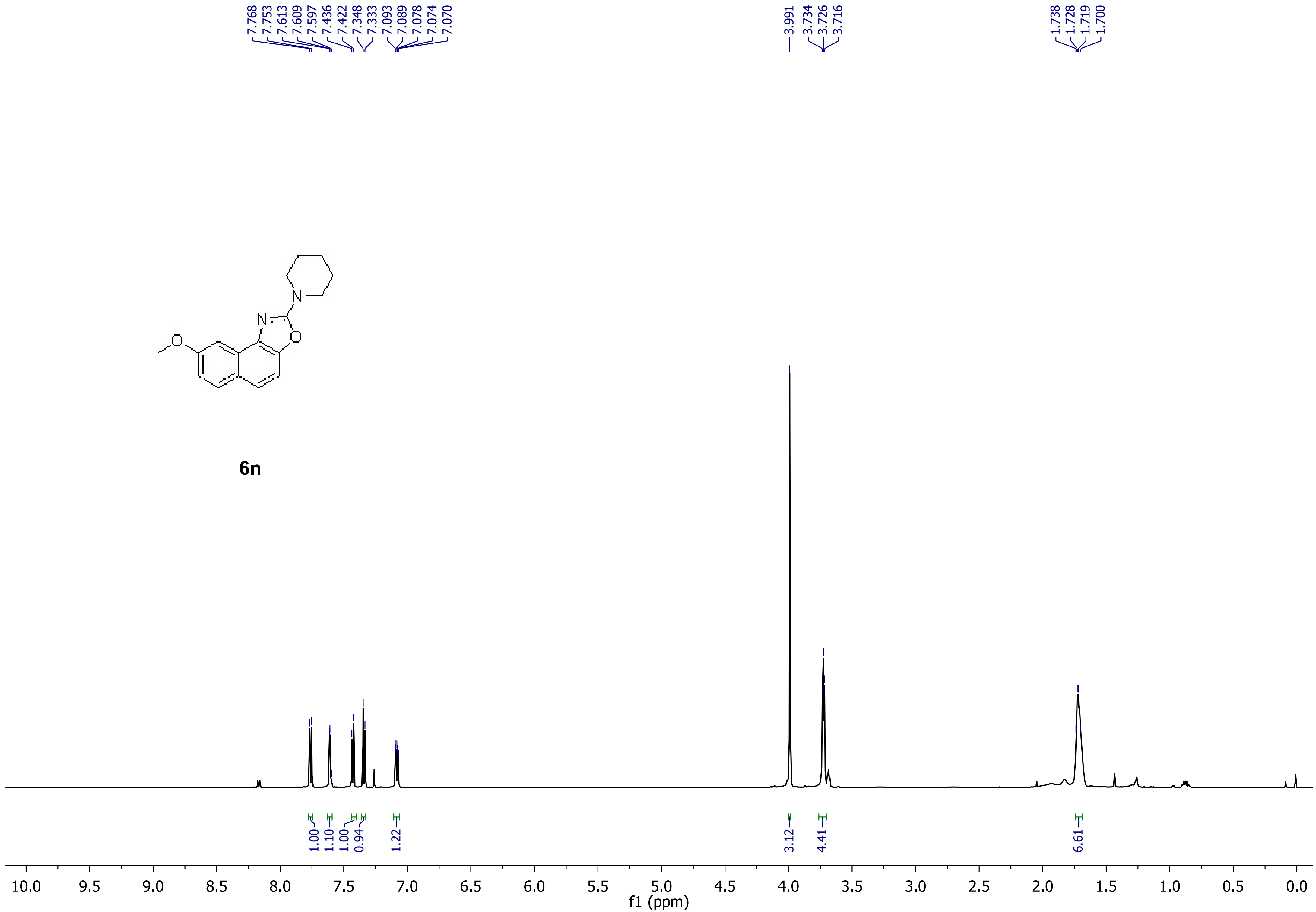
8.722
8.708
8.430
8.415
8.066
8.053
7.690
7.677
7.665
7.649
7.637
7.624
7.614
7.553
7.539
7.525
3.805
3.796
3.787
1.793
1.775
1.767
1.757
1.738
1.732
1.724
2.05
1.00
0.99
1.39
2.13
1.11
4.27
4.17
2.17
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

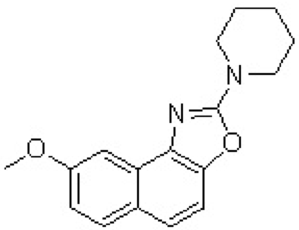

162.85
140.52
136.10
128.73
127.11
127.10
126.94
126.01
125.48
124.24
123.82
123.50
123.02
121.27
119.36
47.07
25.54
24.35
6l
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



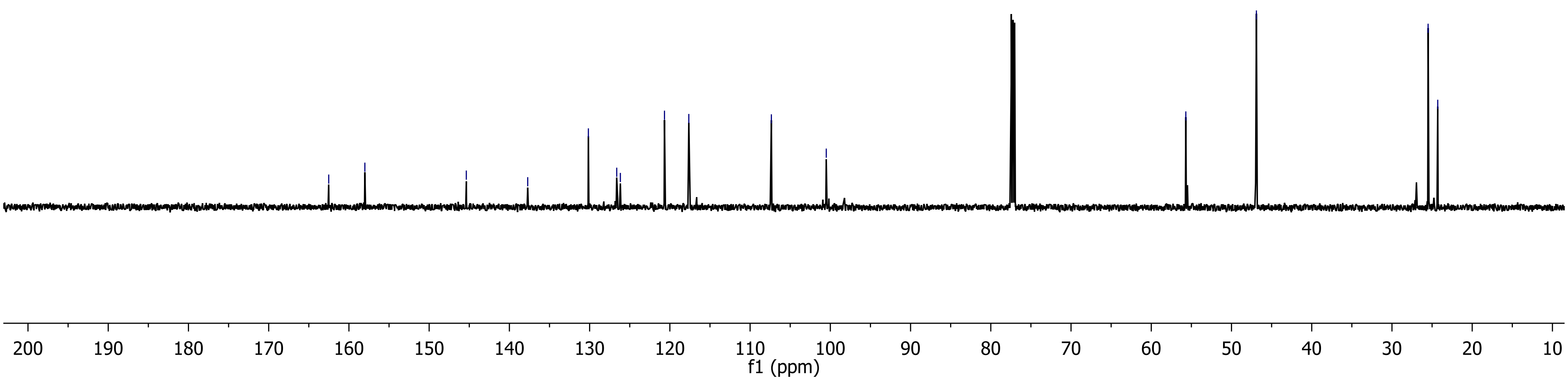
6m
8.722
8.702
8.461
8.442
8.075
8.055
7.700
7.681
7.661
7.651
7.636
7.622
7.603
7.545
7.525
7.506
3.862
3.848
3.833
1.951
1.929
1.903
1.680
1.667
1.661
1.636
2.03
1.00
1.05
3.15
1.10
4.00
4.48
3.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


162.88
140.43
136.39
128.61
127.01
126.83
126.77
125.92
125.36
123.97
123.76
123.44
123.04
121.21
119.22
48.34
28.58
27.86
N
N
O
6m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

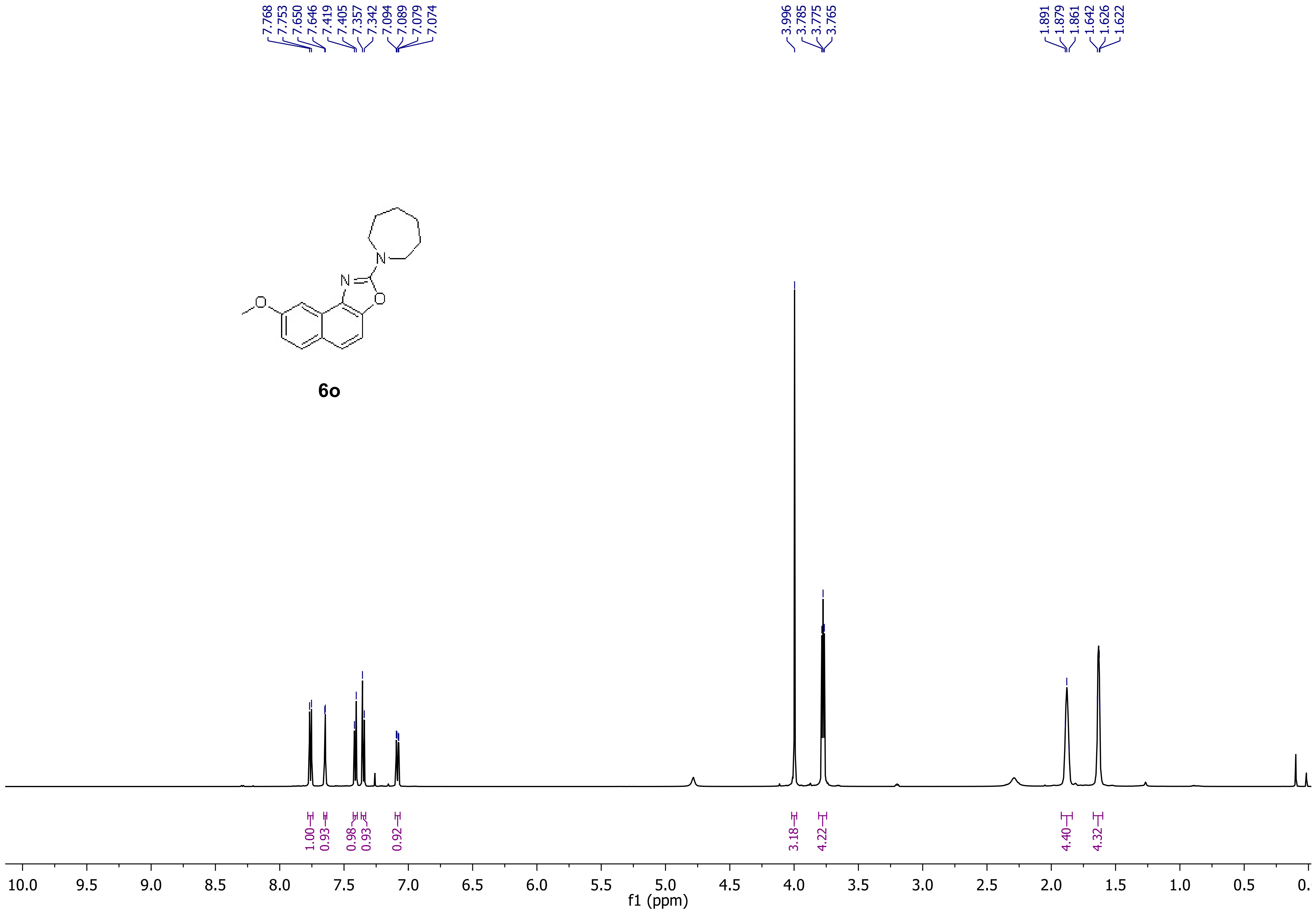

7.768
7.753
7.613
7.609
7.597
7.436
7.422
7.348
7.333
7.093
7.089
7.078
7.074
7.070
3.991
3.734
3.726
3.716
1.738
1.728
1.719
1.700
6n
1.00
1.10
1.00
0.94
1.22
3.12
4.41
6.61
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

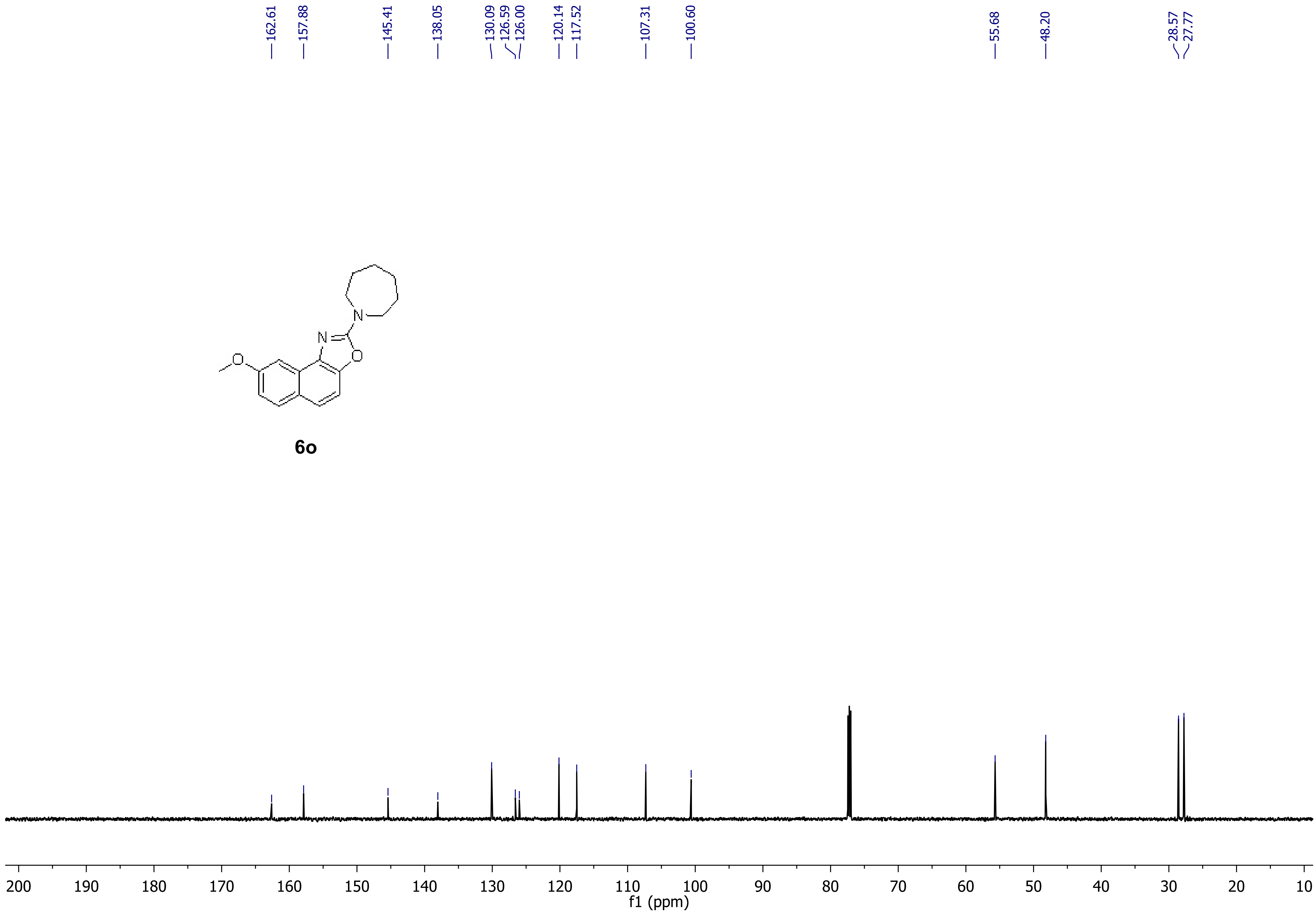


6n



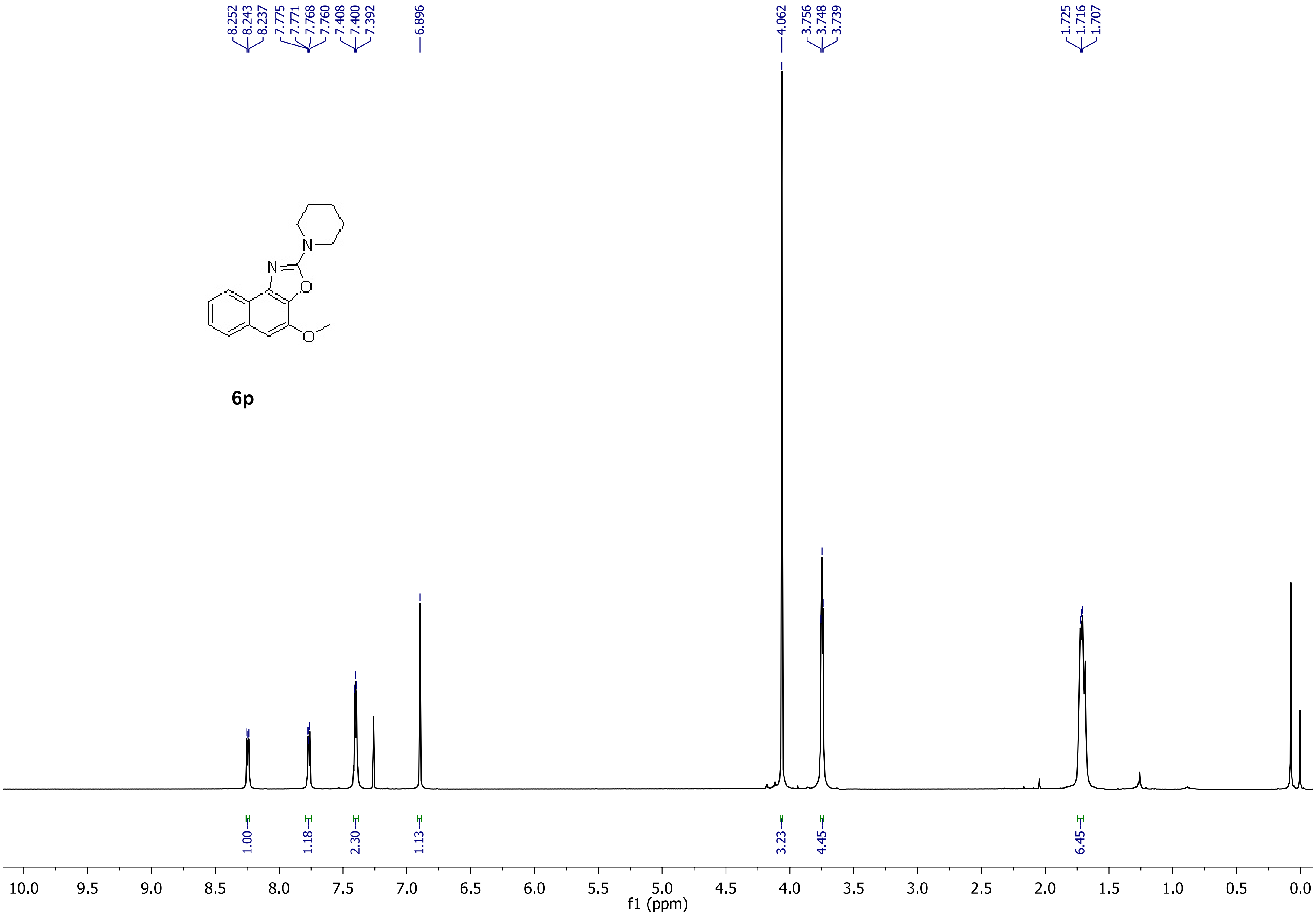
162.52
158.01
145.37
137.72
130.16
126.62
126.17
120.67
117.64
107.35
100.50
55.69
46.90
25.50
24.30
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.768
7.753
7.650
7.646
7.419
7.405
7.357
7.342
7.094
7.089
7.079
7.074
3.996
3.785
3.775
3.765
1.891
1.879
1.861
1.642
1.626
1.622
6o
1.00
0.93
0.98
0.93
0.92
3.18
4.22
4.40
4.32
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
f1 (ppm)

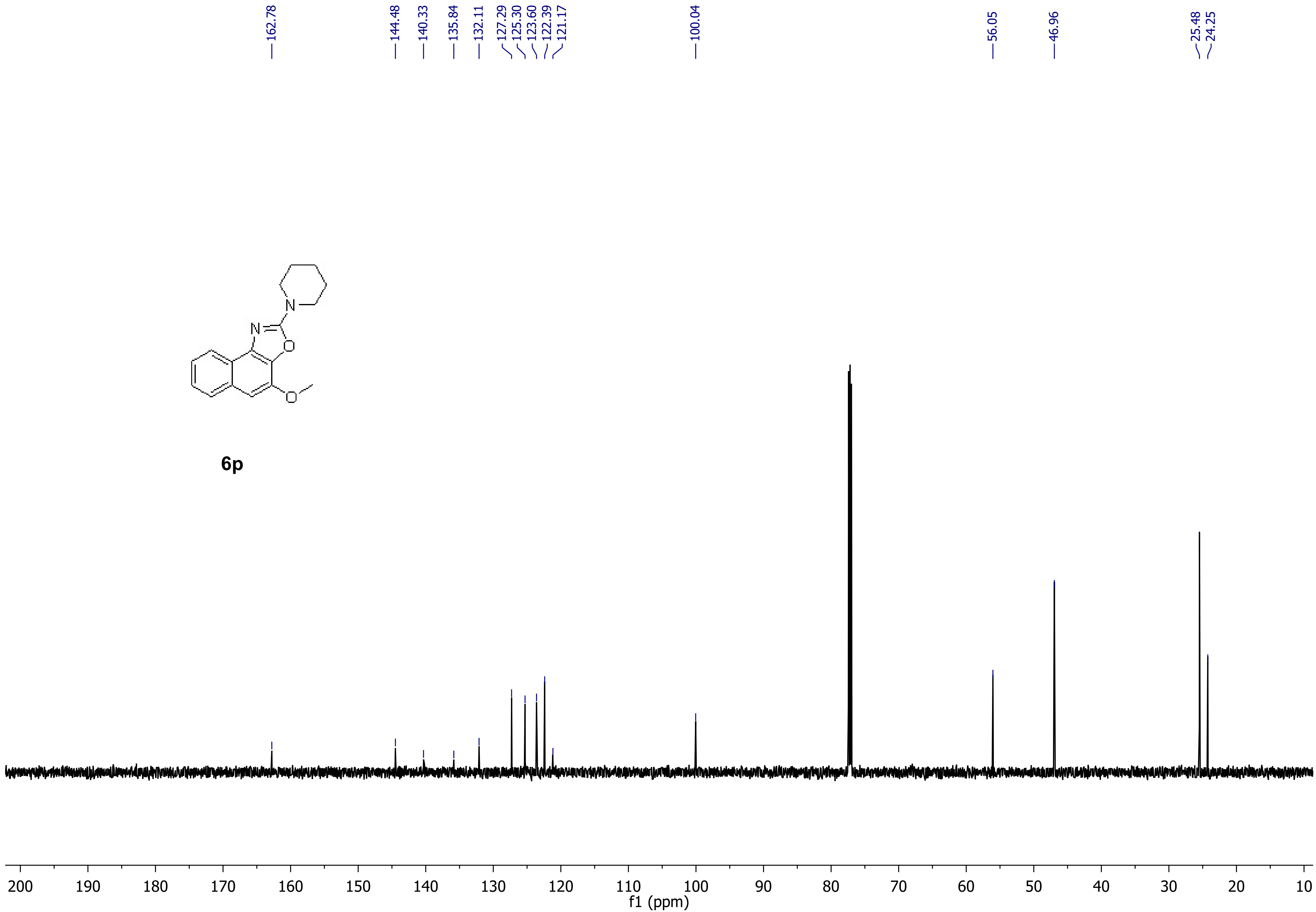


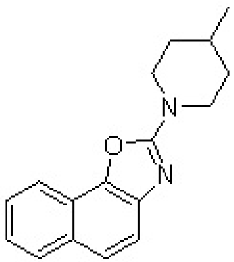
162.61
157.88
145.41
138.05
130.09
126.59
126.00
120.14
117.52
107.31
100.60
55.68
48.20
28.57
27.77
N
N
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

6o

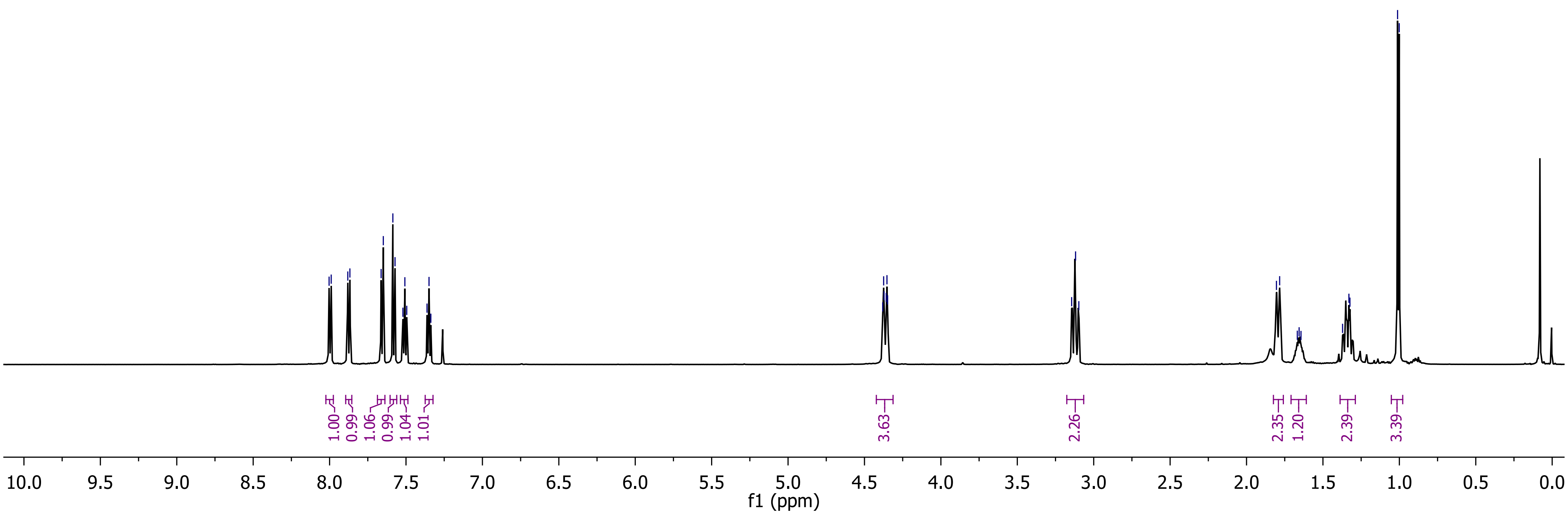

8.252
8.243
8.237
7.775
7.771
7.768
7.760
7.408
7.400
7.392
6.896
4.062
3.756
3.748
3.739
1.725
1.716
1.707
1.00
1.18
2.30
1.13
3.23
4.45
6.45
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

6p


162.78
144.48
140.33
135.84
132.11
127.29
125.30
123.60
122.39
121.17
100.04
56.05
46.96
25.48
24.25
N
O
N
O
6p
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

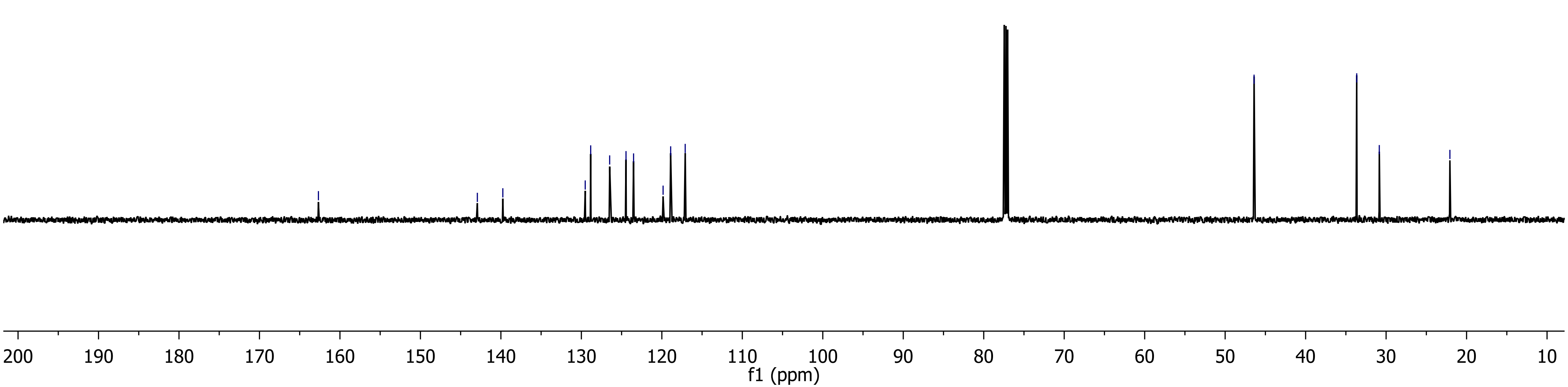


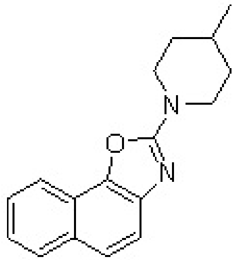
6q



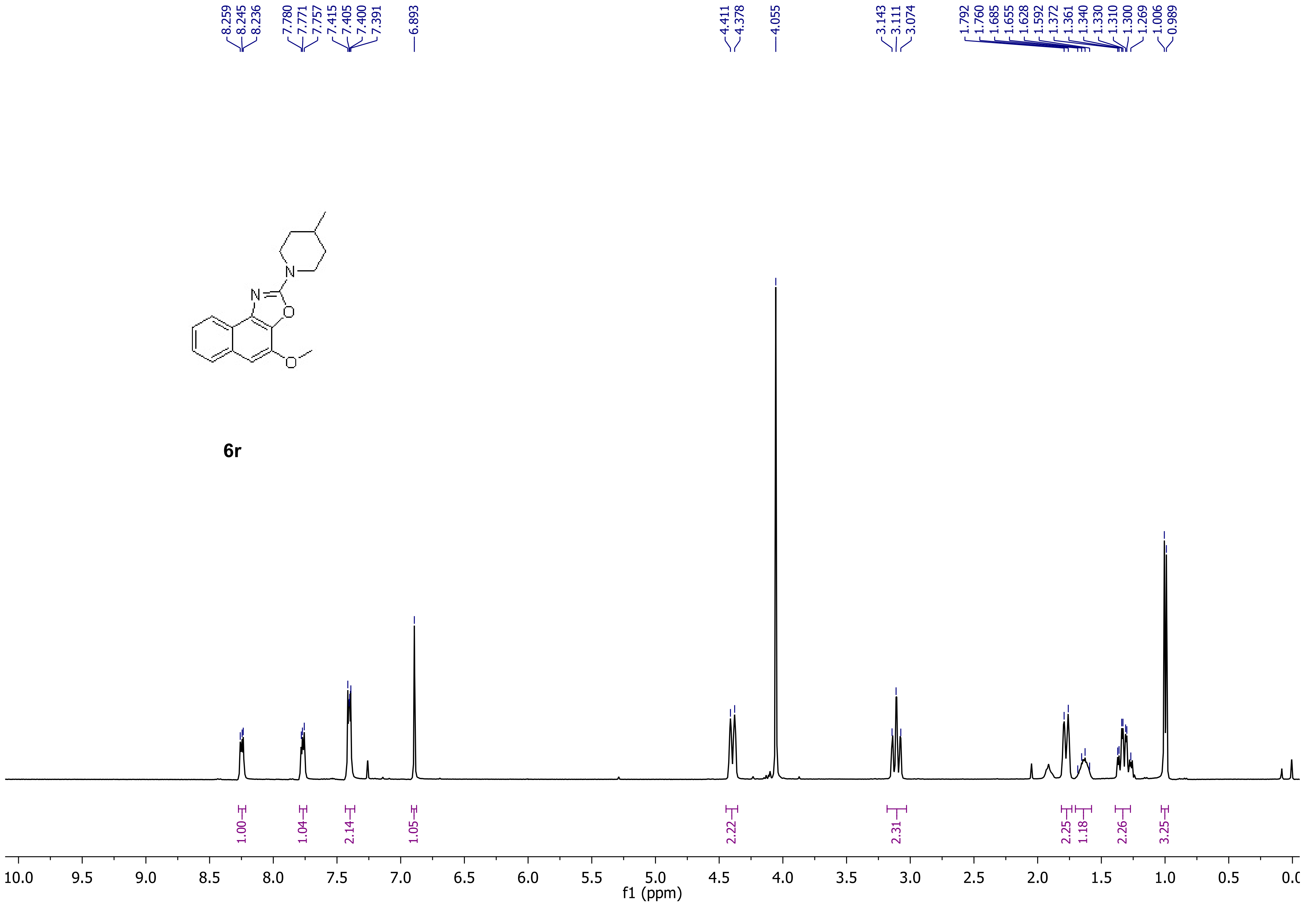
8.003
7.989
7.881
7.867
7.663
7.649
7.586
7.572
7.520
7.507
7.495
7.363
7.349
7.337
4.381
4.375
4.372
4.358
4.353
4.349
3.144
3.119
3.097
1.804
1.783
1.668
1.656
1.644
1.371
1.330
1.323
1.012
1.001
1.00
0.99
1.06
0.99
1.04
1.01
3.63
2.26
2.35
1.20
2.39
3.39
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

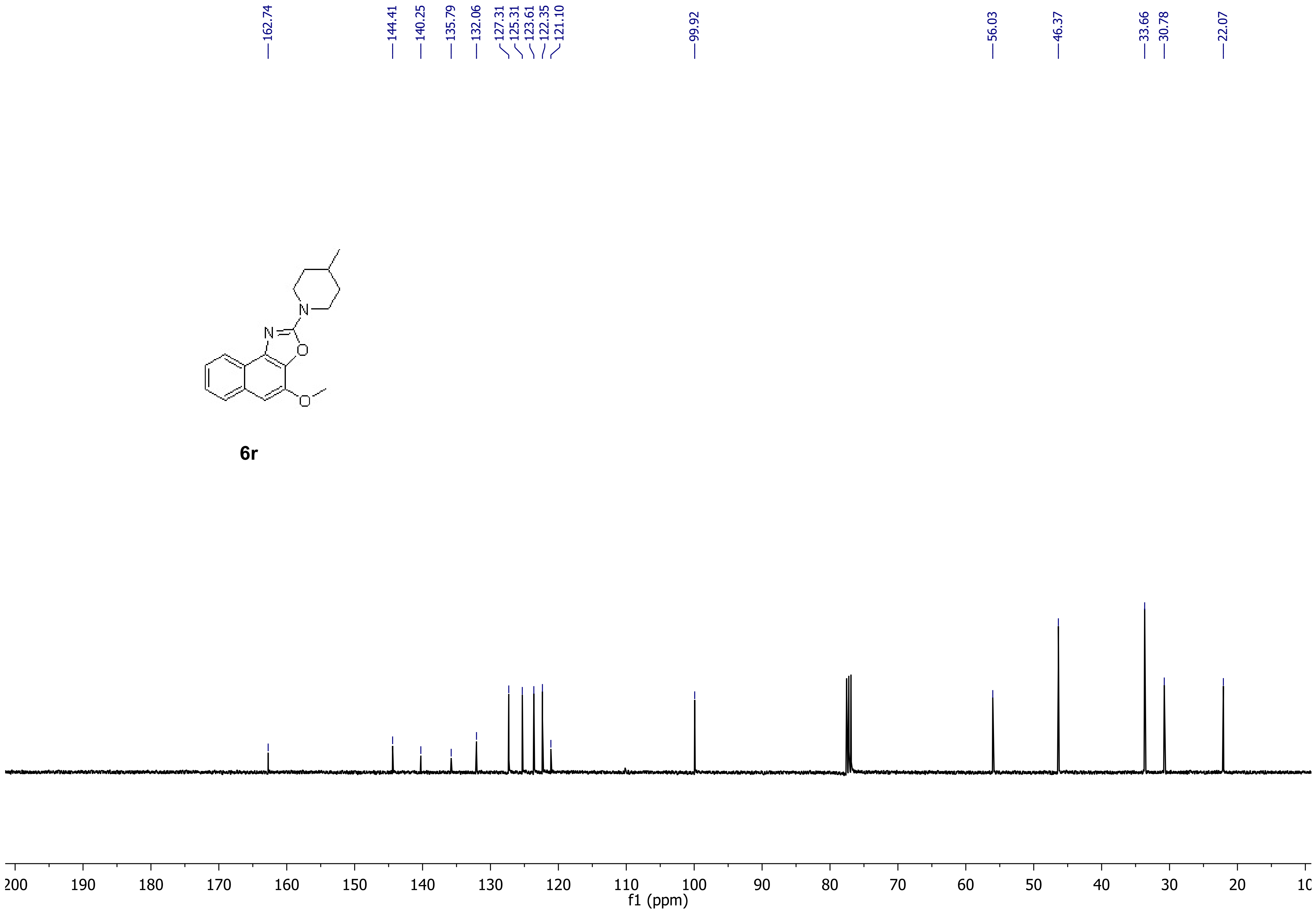
162.67
142.92
139.76
129.52
128.84
126.48
124.45
123.51
119.84
118.90
117.10
46.41
33.65
30.85
22.07



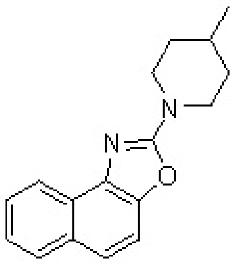


6q

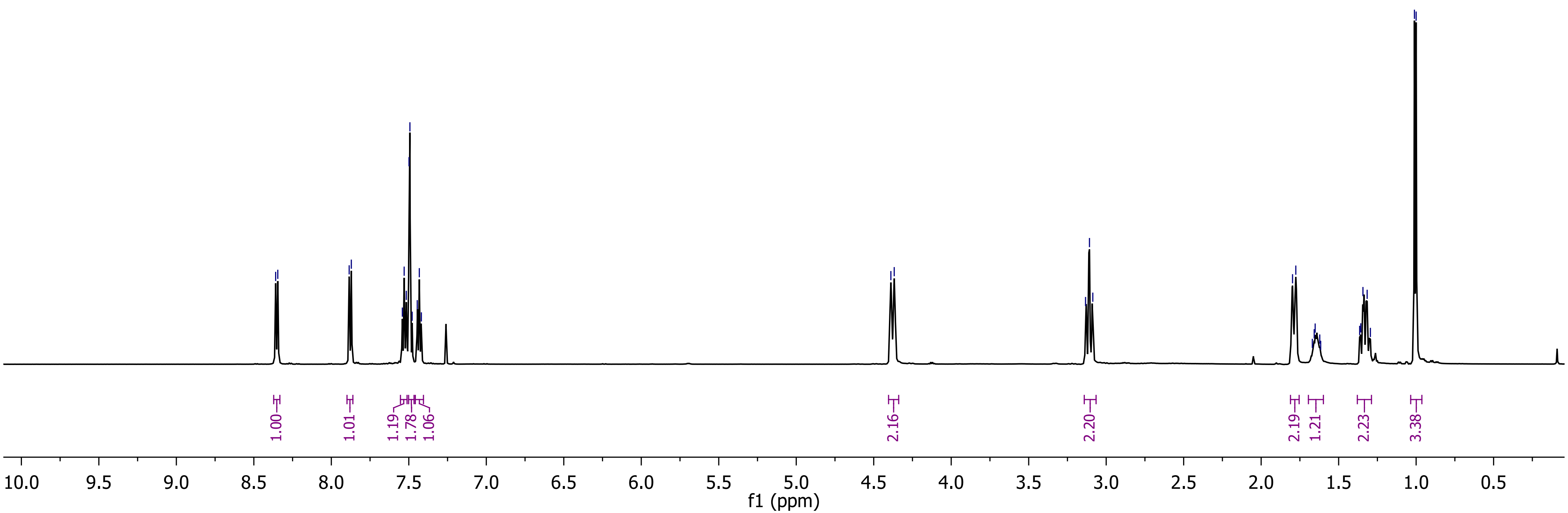

8.259
8.245
8.236
7.780
7.771
7.757
7.415
7.405
7.400
7.391
6.893
4.411
4.378
4.055
3.143
3.111
3.074
1.792
1.760
1.685
1.655
1.628
1.592
1.372
1.361
1.340
1.330
1.310
1.300
1.269
1.006
0.989
N
O
N
O
6r
1.00
1.04
2.14
1.05
2.22
2.31
2.25
1.18
2.26
3.25
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

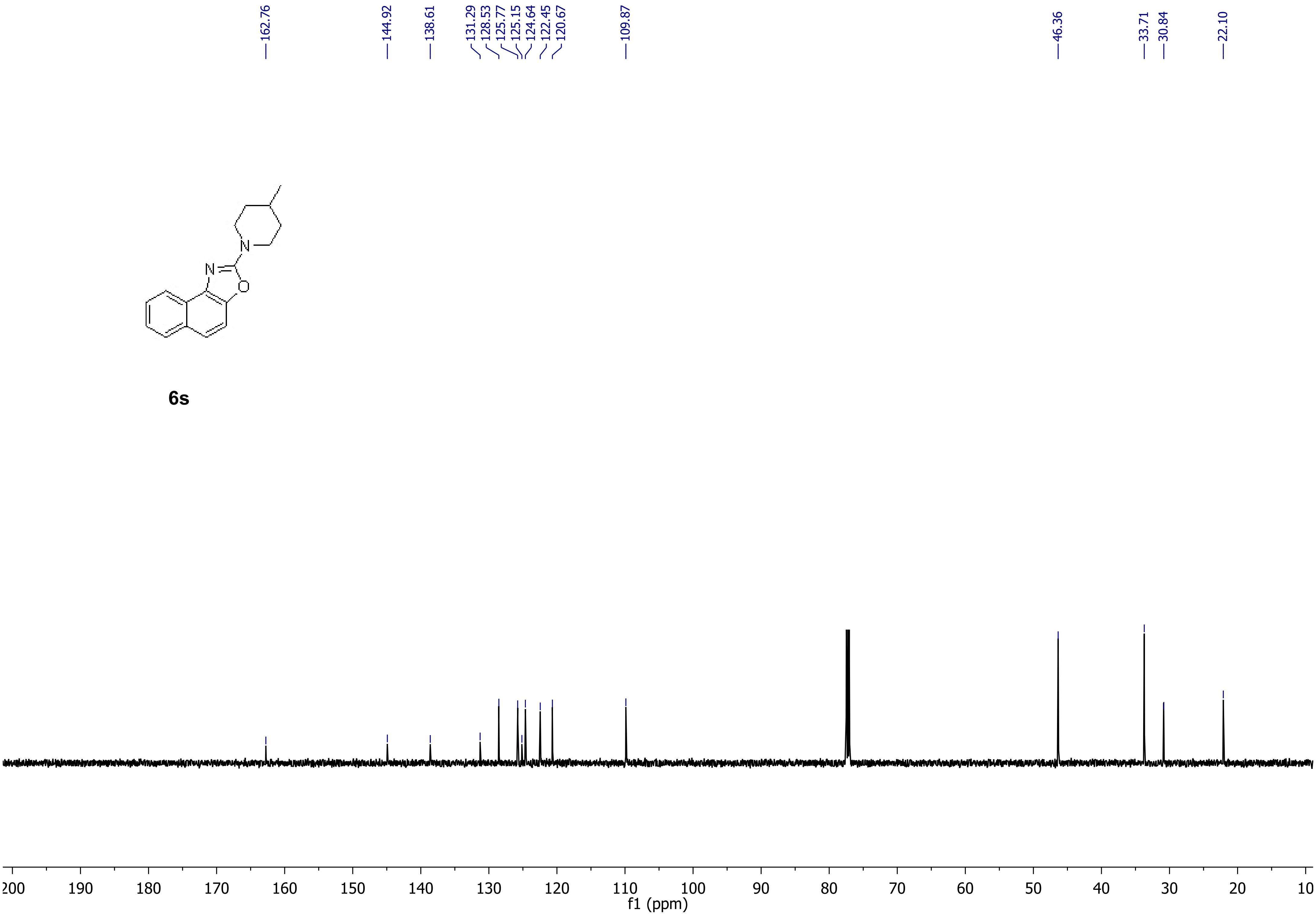


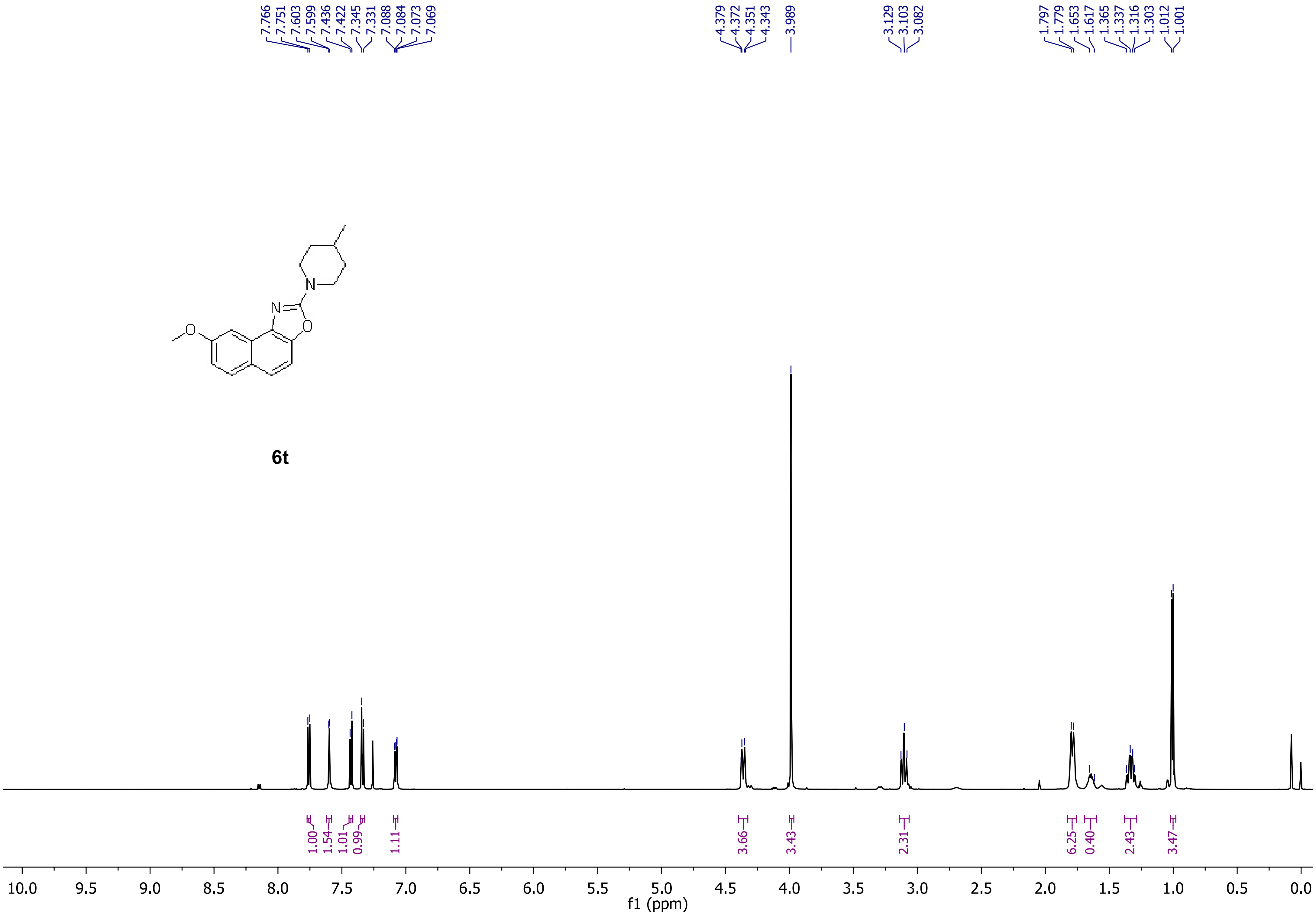
162.74
144.41
140.25
135.79
132.06
127.31
125.31
123.61
122.35
121.10
99.92
56.03
46.37
33.66
30.78
22.07
N
N
O
O
6r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



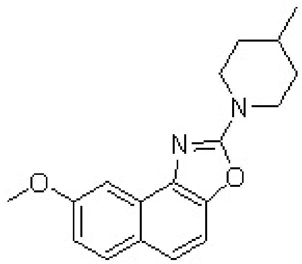
6s


8.359
8.345
7.885
7.871
7.542
7.530
7.516
7.499
7.493
7.478
7.445
7.432
7.419
4.389
4.368
3.133
3.108
3.086
1.797
1.776
1.670
1.658
1.651
1.622
1.616
1.364
1.357
1.343
1.316
1.295
1.011
1.000
1.00
1.01
1.19
1.78
1.06
2.16
2.20
2.19
1.21
2.23
3.38
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
f1 (ppm)

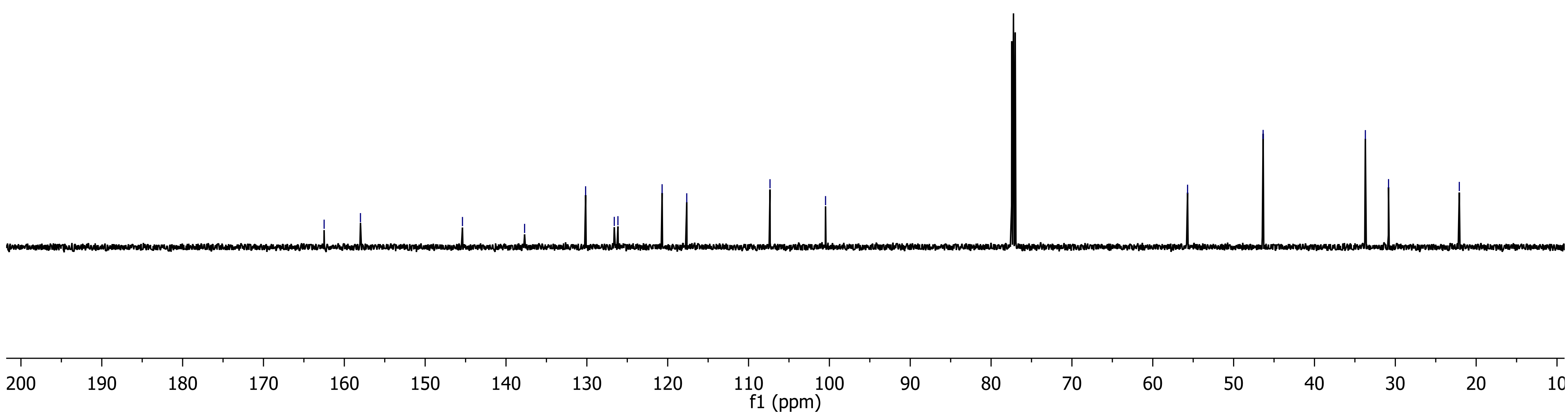

162.76
144.92
138.61
131.29
128.53
125.77
125.15
124.64
122.45
120.67
109.87
46.36
33.71
30.84
22.10
N
N
O
6s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



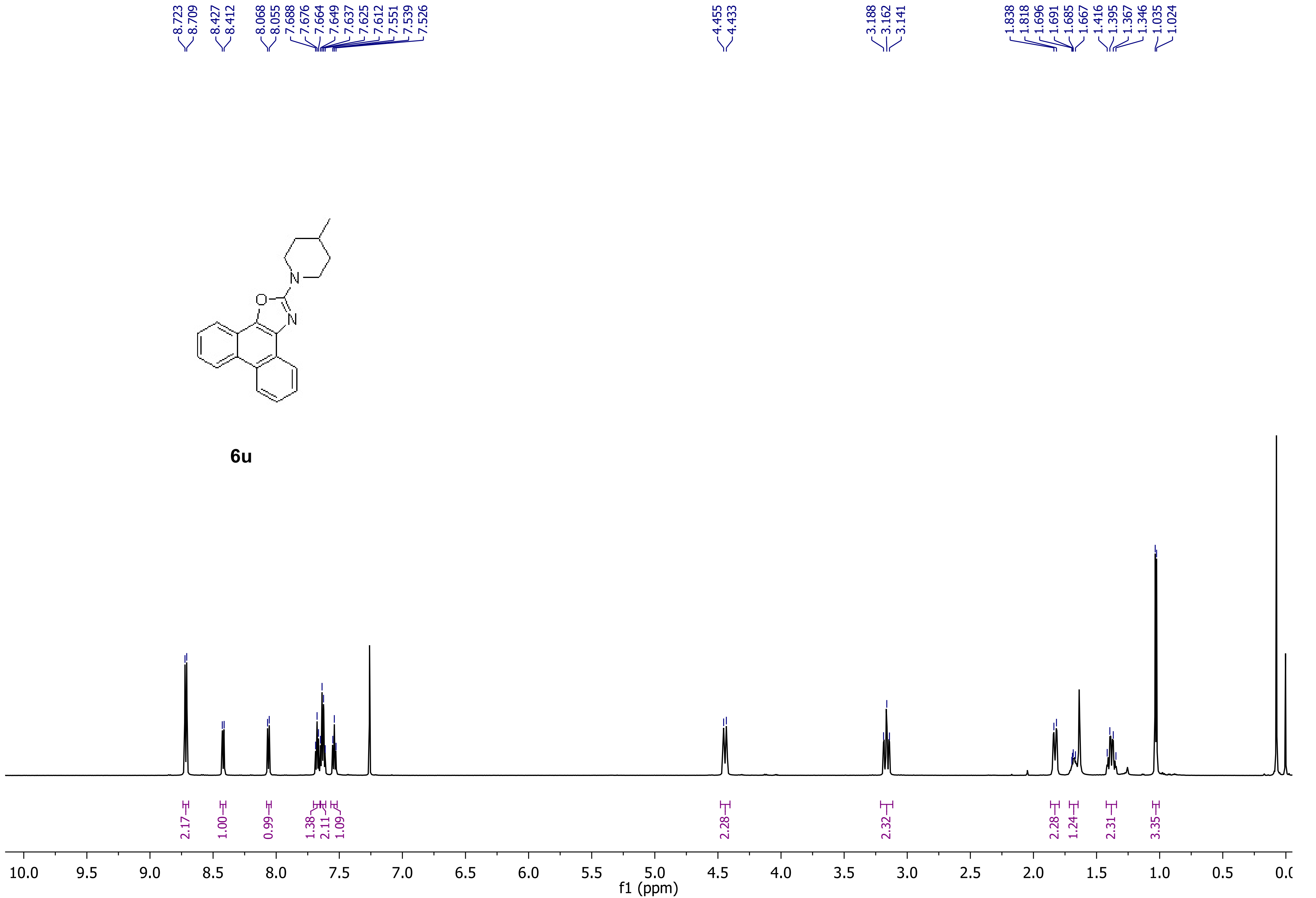
7.766
7.751
7.603
7.599
7.436
7.422
7.345
7.331
7.088
7.084
7.073
7.069
4.379
4.372
4.351
4.343
3.989
3.129
3.103
3.082
1.797
1.779
1.653
1.617
1.365
1.337
1.316
1.303
1.012
1.001
N
O
N
O
6t
1.00
1.54
1.01
0.99
1.11
3.66
3.43
2.31
6.25
0.40
2.43
3.47
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

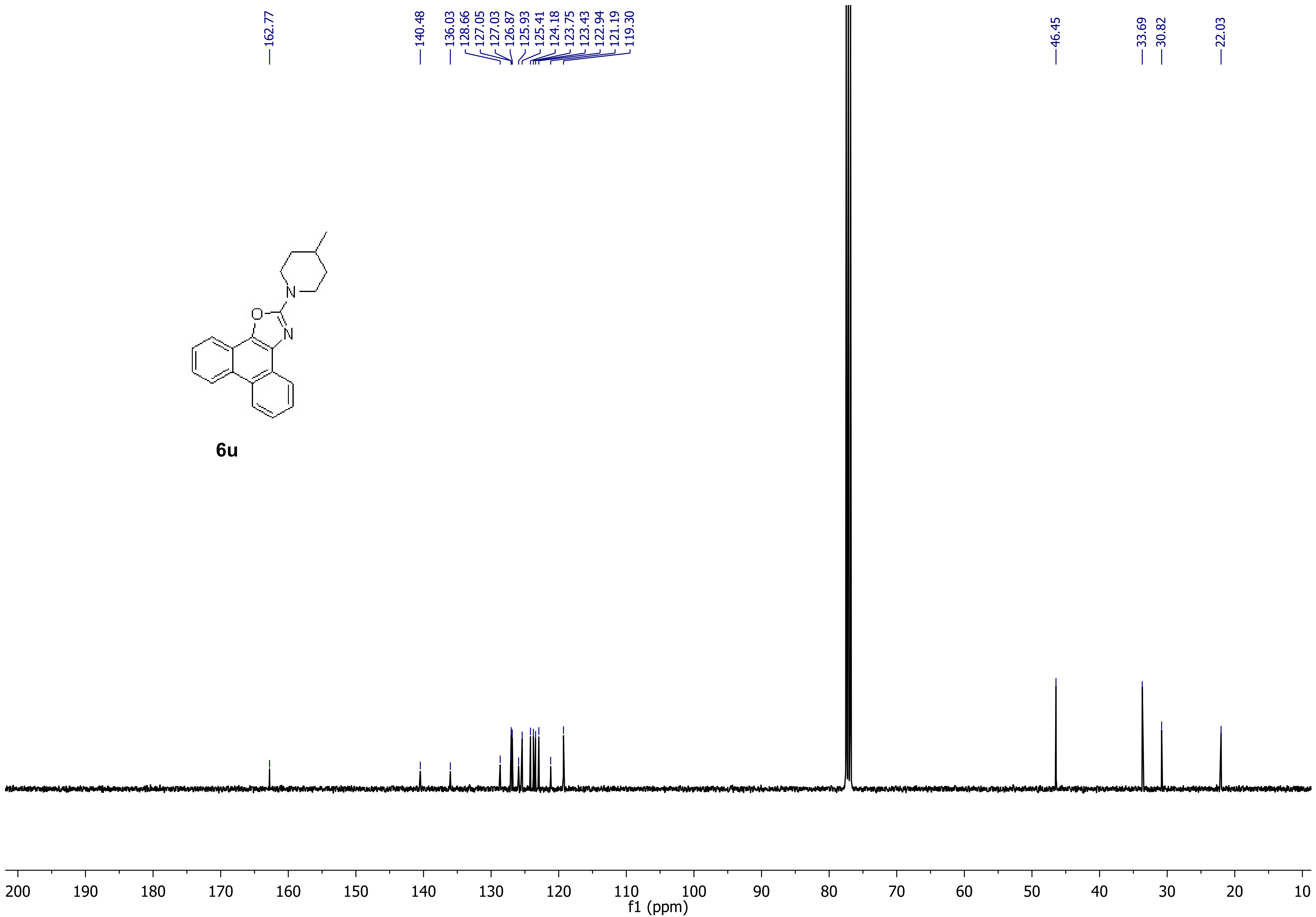


6t

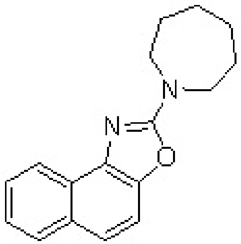


162.50
158.00
145.39
137.70
130.15
126.61
126.16
120.69
117.64
107.35
100.48
55.70
46.35
33.71
30.84
22.09
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

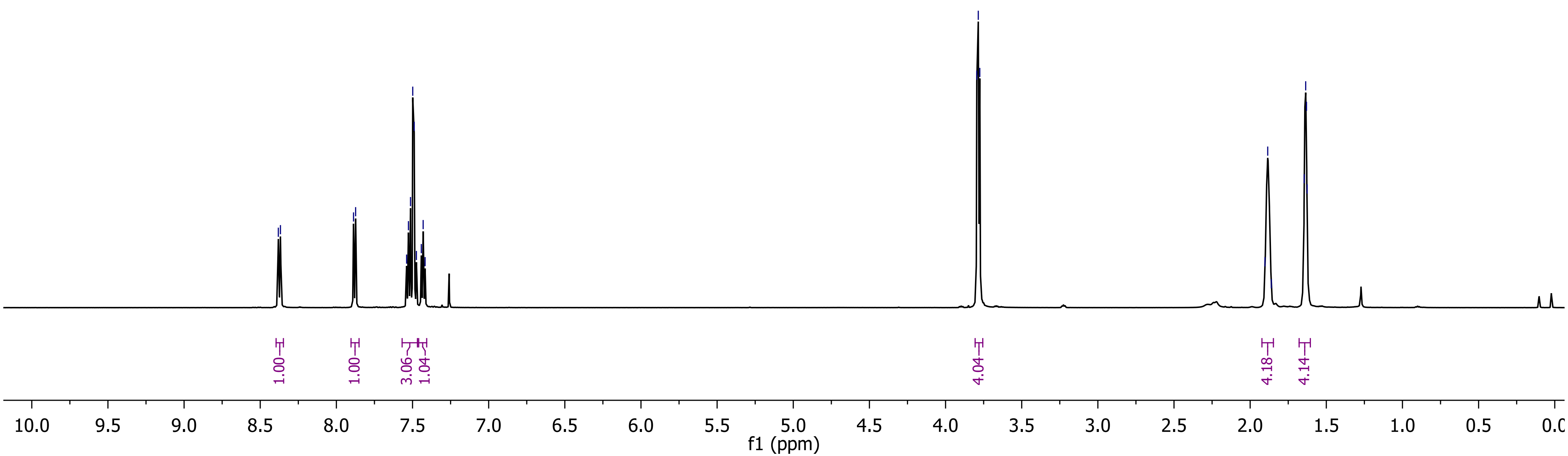

8.723
8.709
8.427
8.412
8.068
8.055
7.688
7.676
7.664
7.649
7.637
7.625
7.612
7.551
7.539
7.526
4.455
4.433
3.188
3.162
3.141
1.838
1.818
1.696
1.691
1.685
1.667
1.416
1.395
1.367
1.346
1.035
1.024
O
N
N
6u
2.17
1.00
0.99
1.38
2.11
1.09
2.28
2.32
2.28
1.24
2.31
3.35
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

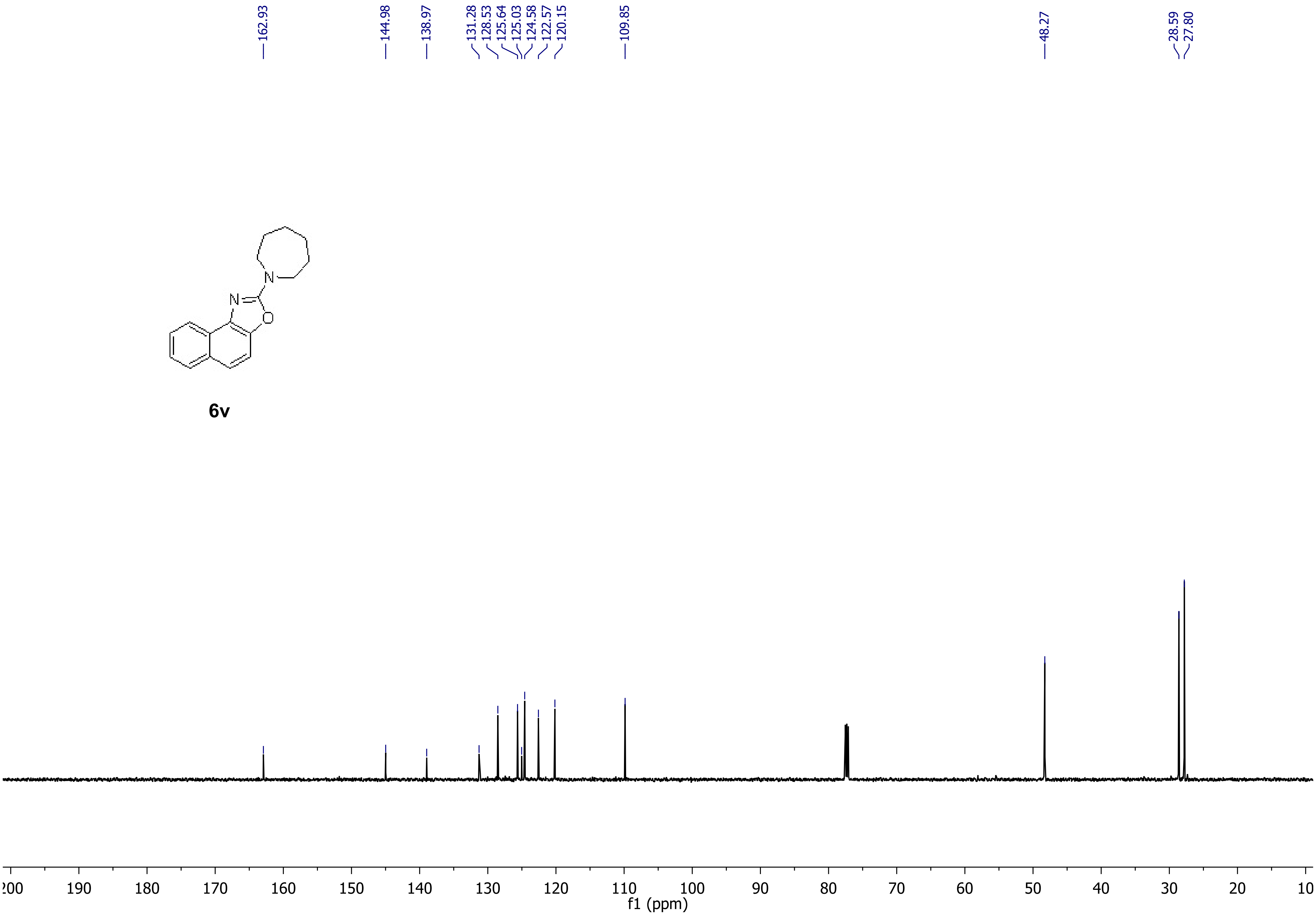

162.77
140.48
136.03
128.66
127.05
127.03
126.87
125.93
125.41
124.18
123.75
123.43
122.94
121.19
119.30
46.45
33.69
30.82
22.03
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

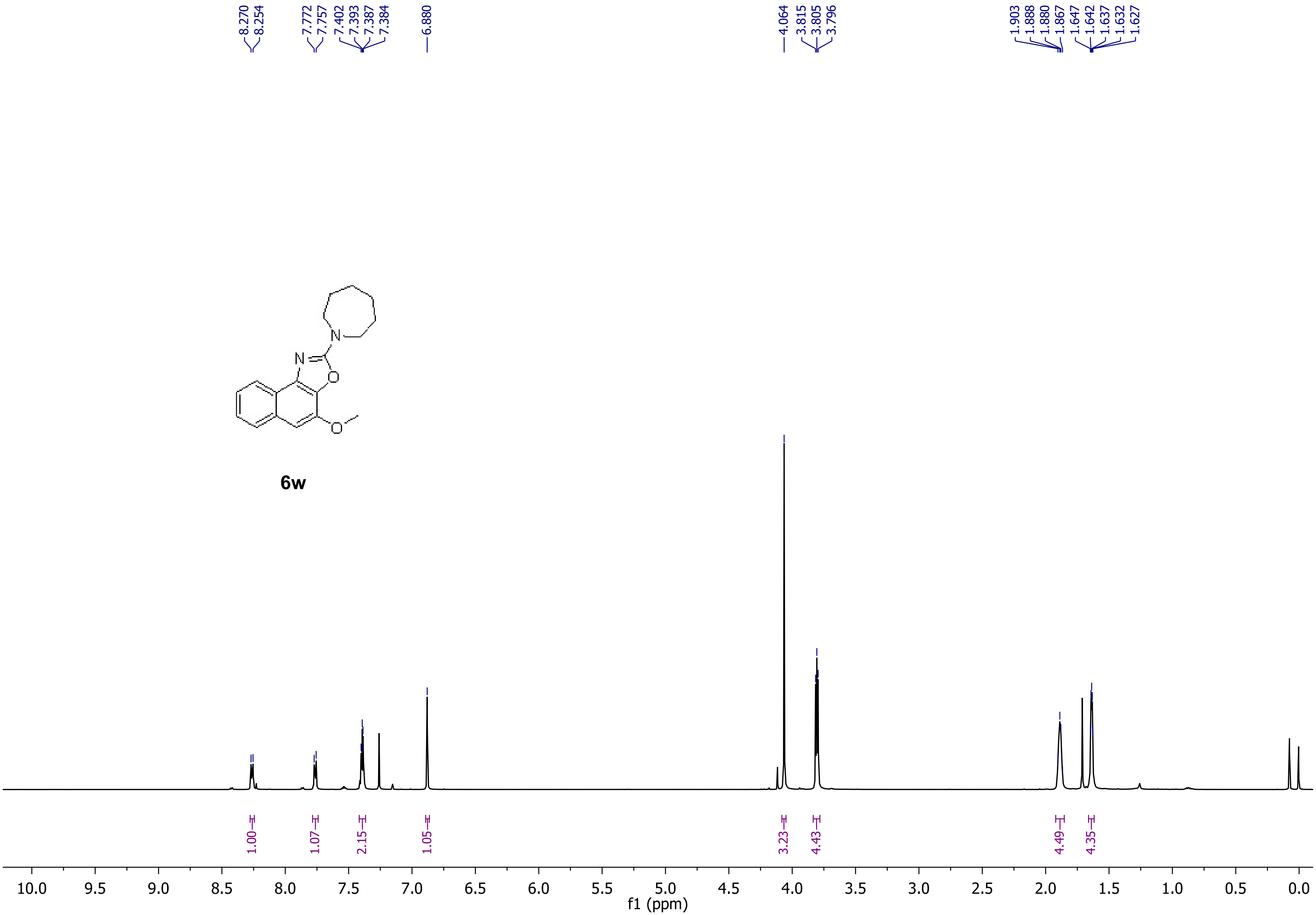
6u



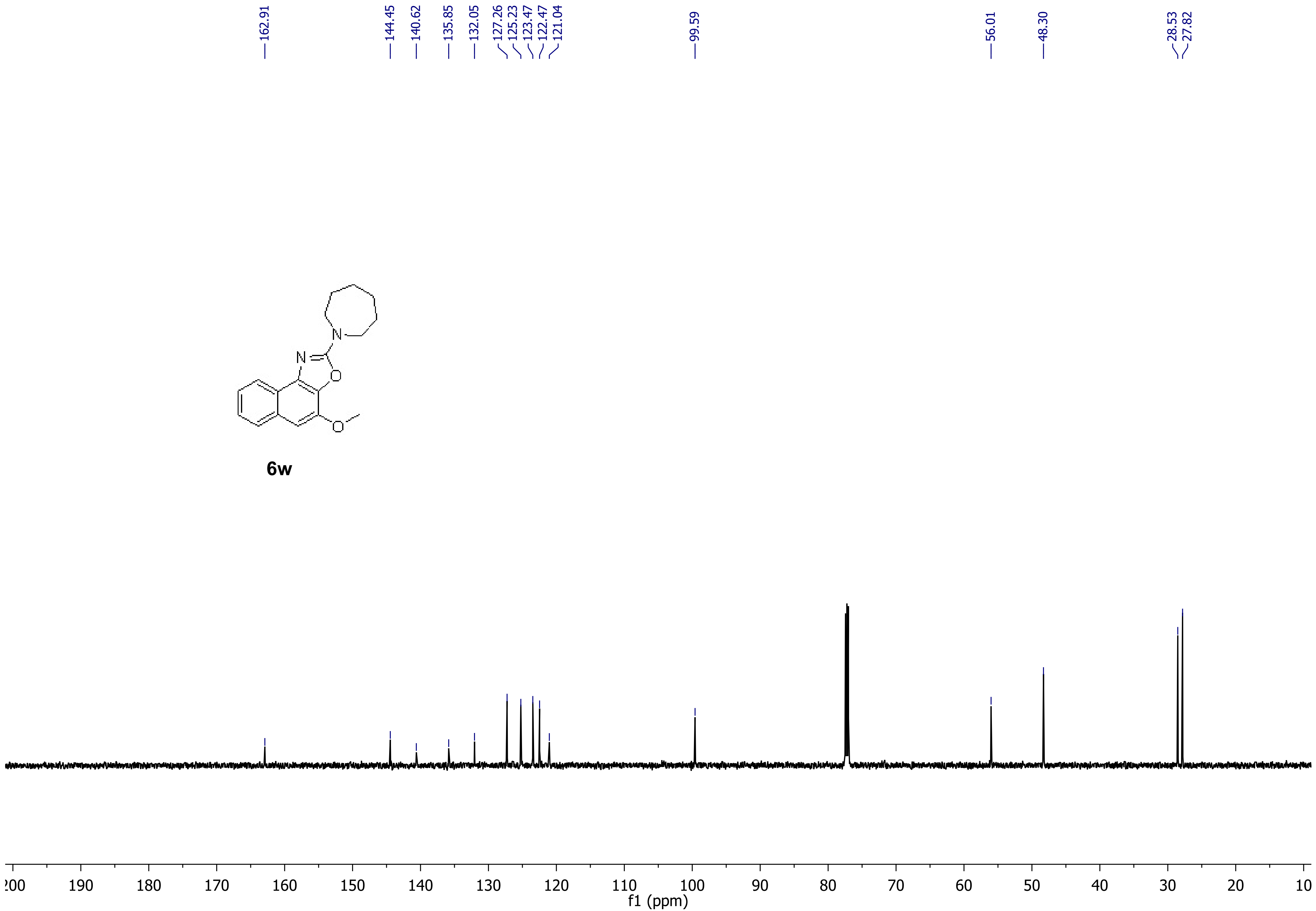
6v

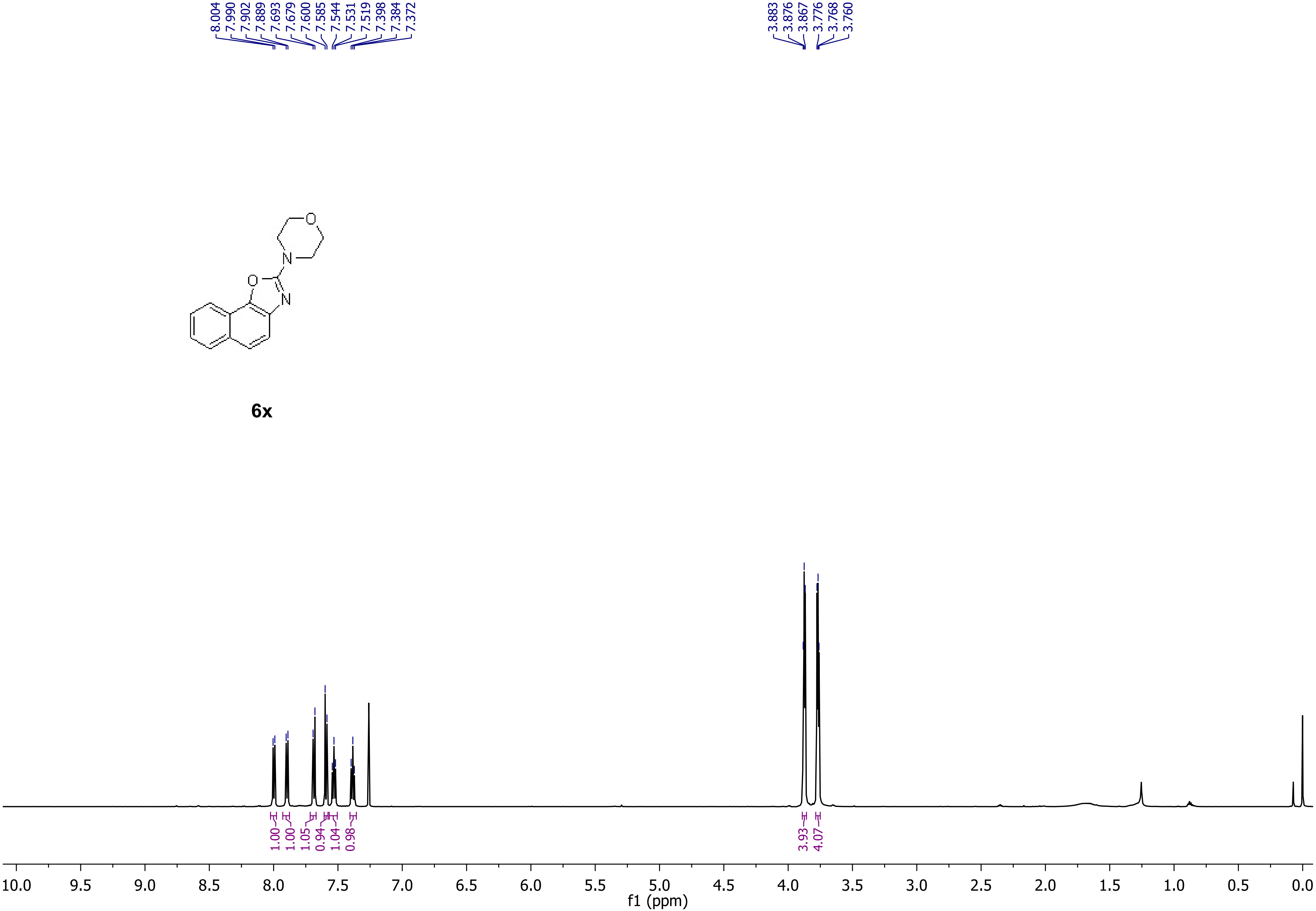

8.381
8.367
7.887
7.874
7.539
7.527
7.513
7.499
7.489
7.474
7.442
7.430
7.417
3.795
3.785
3.775
1.903
1.885
1.861
1.645
1.635
1.630
1.626
1.00
1.00
3.06
1.04
4.04
4.18
4.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.93
144.98
138.97
131.28
128.53
125.64
125.03
124.58
122.57
120.15
109.85
48.27
28.59
27.80
N
O
6v
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

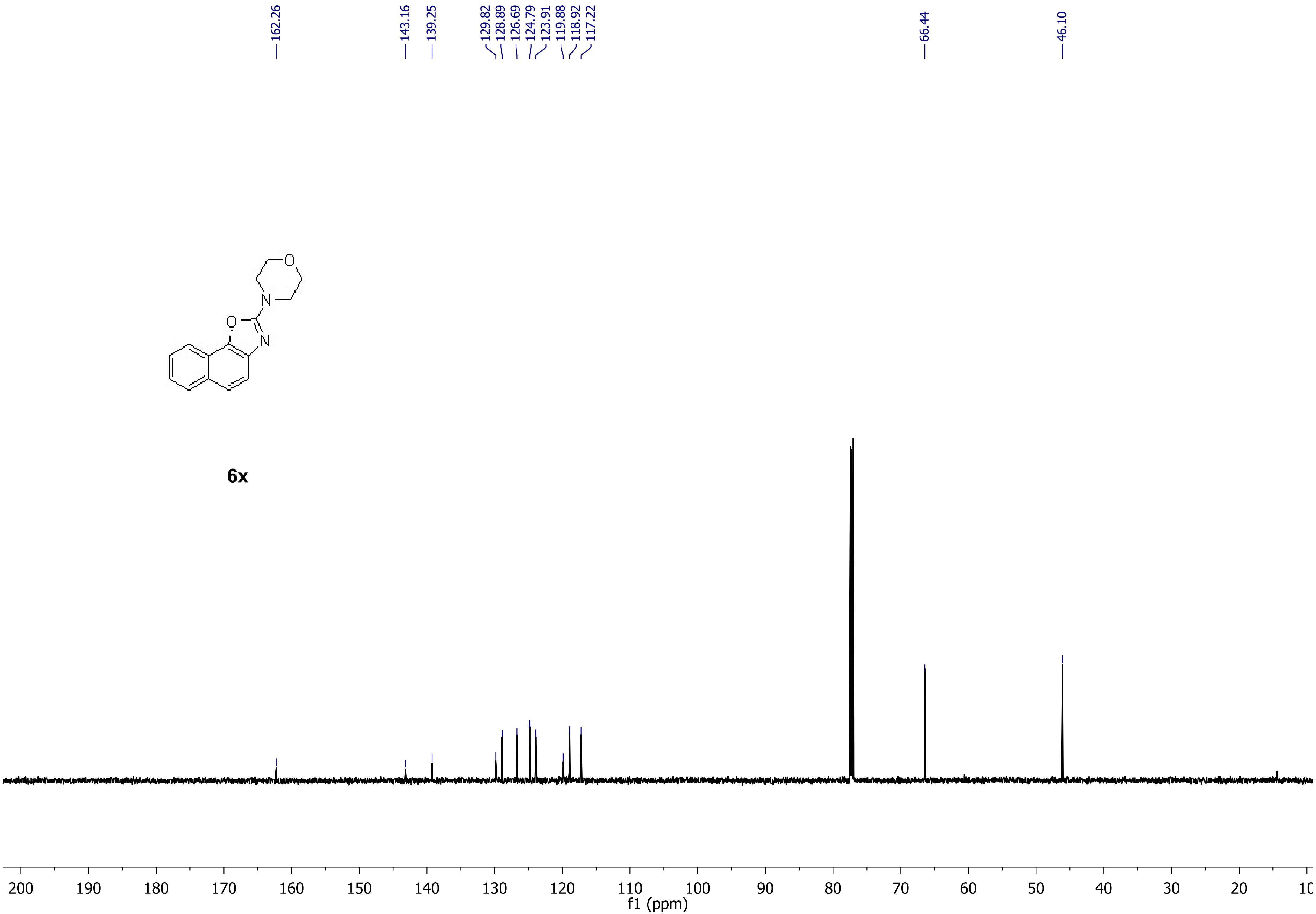


8.270
8.254
7.772
7.757
7.402
7.393
7.387
7.384
6.880
4.064
3.815
3.805
3.796
1.903
1.888
1.880
1.867
1.647
1.642
1.637
1.632
1.627
N
O
6w
1.00
1.07
2.15
1.05
3.23
4.43
4.49
4.35
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

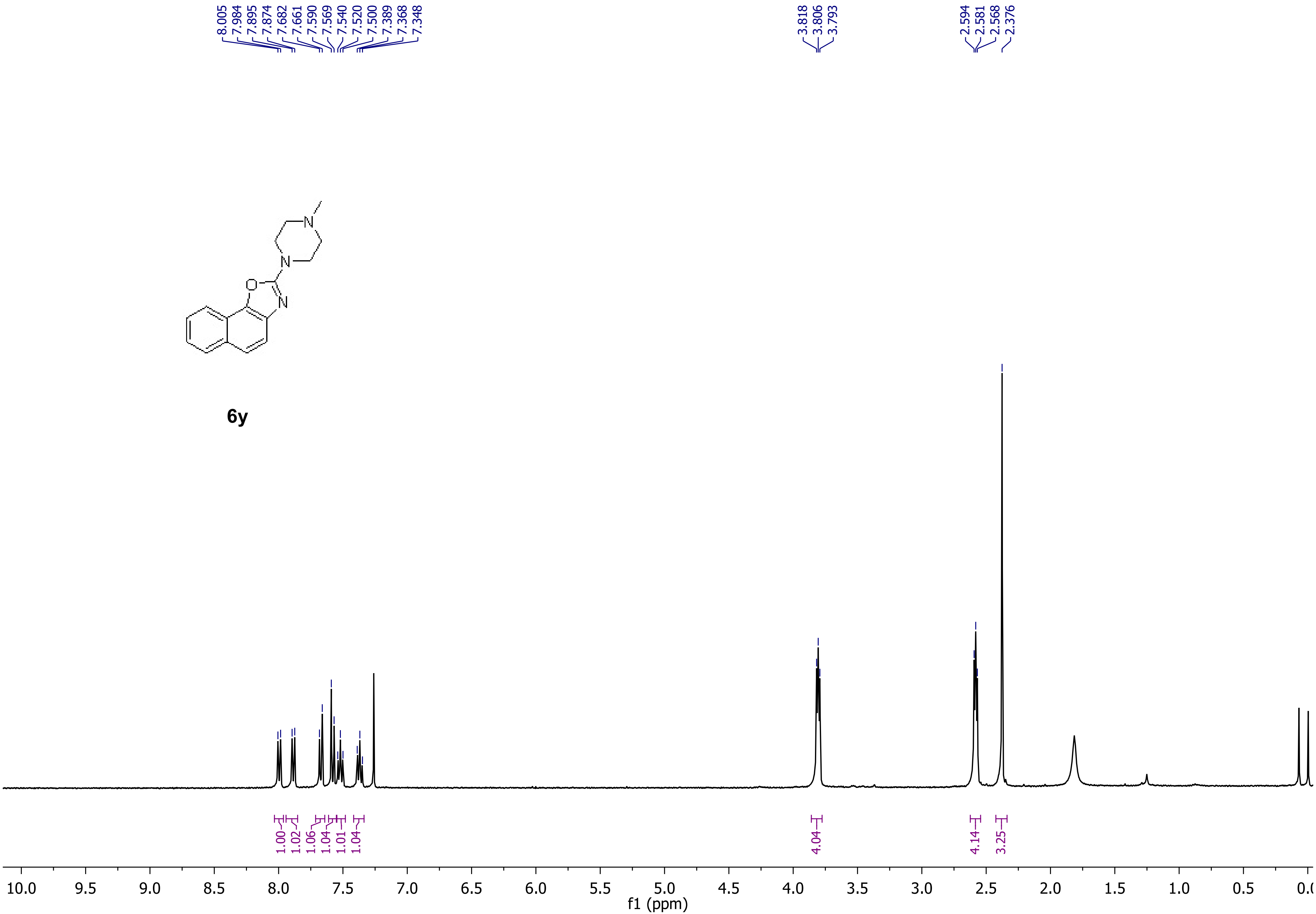

162.91
144.45
140.62
135.85
132.05
127.26
125.23
123.47
122.47
121.04
99.59
56.01
48.30
28.53
27.82
6w
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

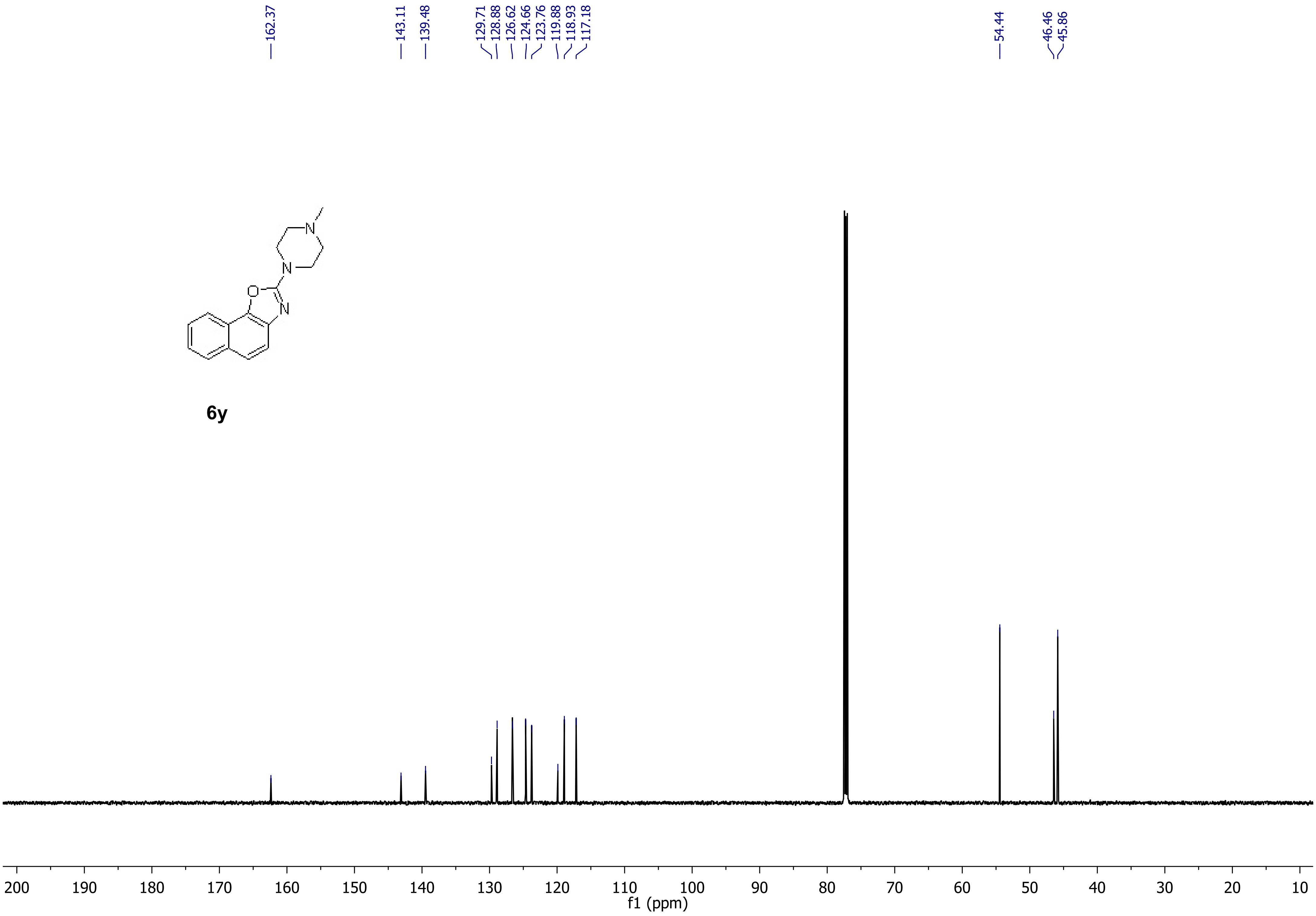

8.004
7.990
7.902
7.889
7.693
7.679
7.600
7.585
7.544
7.531
7.519
7.398
7.384
7.372
3.883
3.876
3.867
3.776
3.768
3.760
1.00
1.00
1.05
0.94
1.04
0.98
3.93
4.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

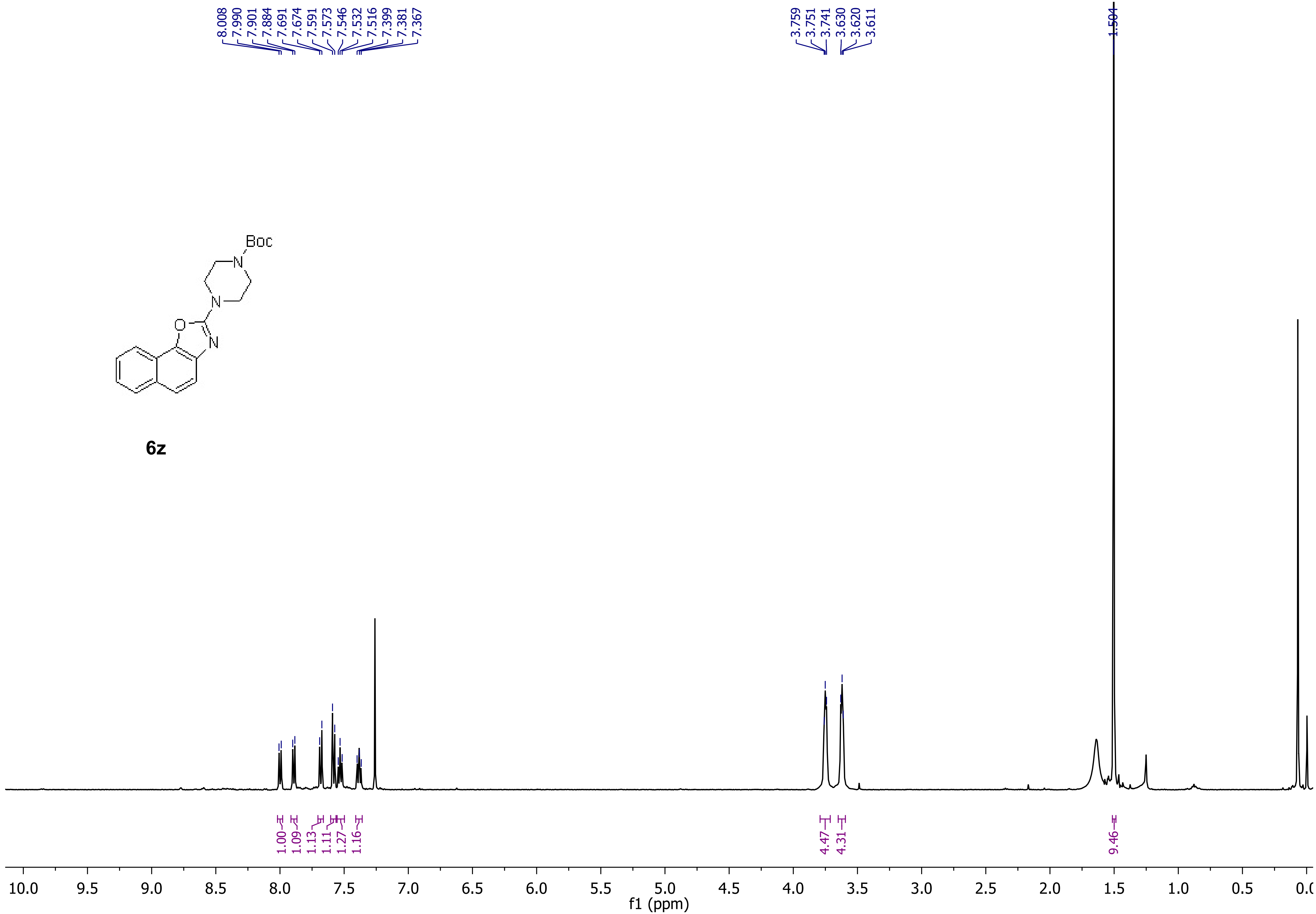
6x

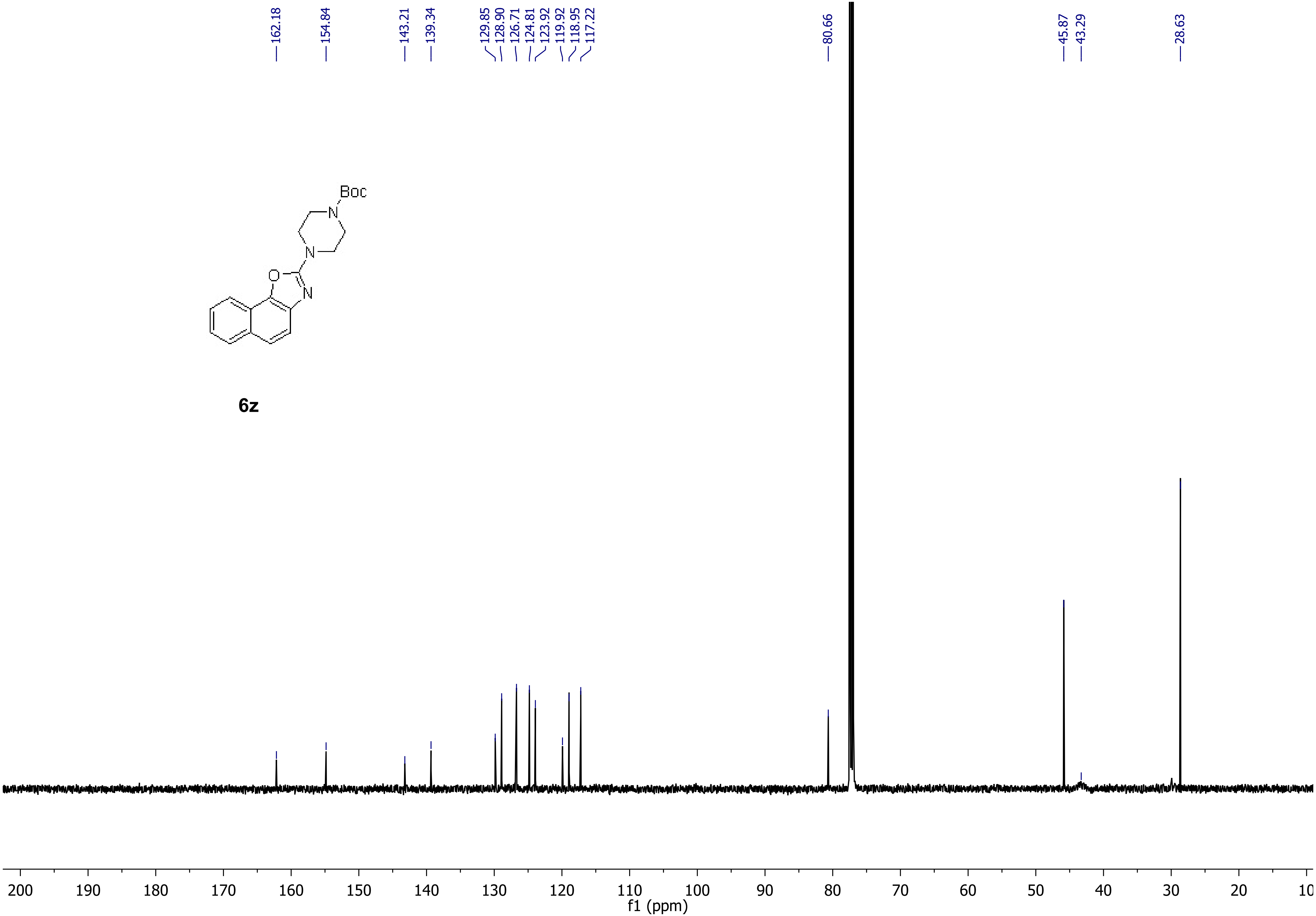


162.26
143.16
139.25
129.82
128.89
126.69
124.79
123.91
119.88
118.92
117.22
66.44
46.10
O
N
O
N
6x
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

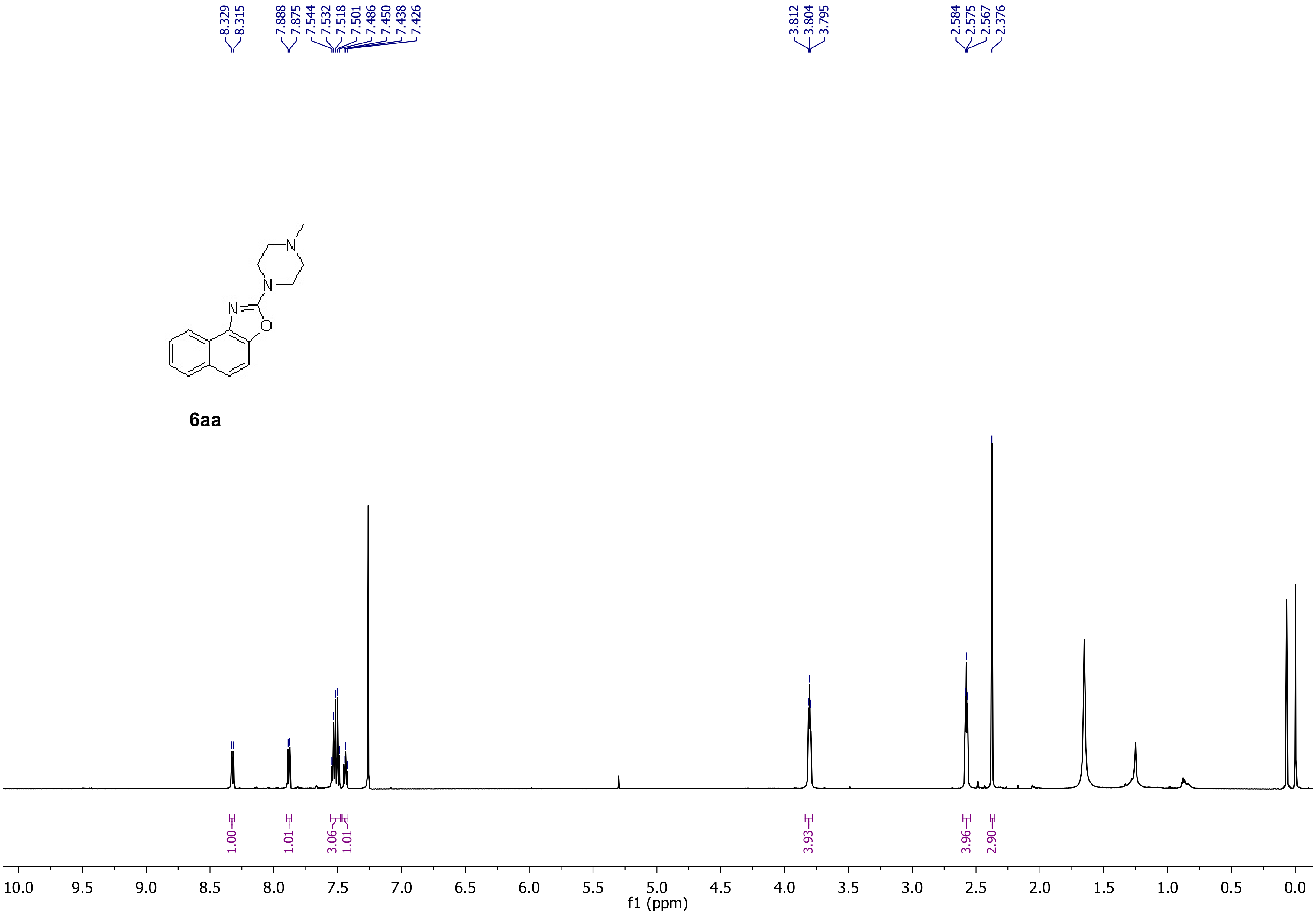

8.005
7.984
7.895
7.874
7.682
7.661
7.590
7.569
7.540
7.520
7.500
7.389
7.368
7.348
3.818
3.806
3.793
2.594
2.581
2.568
2.376
N
N
O
N
6y
1.00
1.02
1.06
1.04
1.01
1.04
4.04
4.14
3.25
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


162.37
143.11
139.48
129.71
128.88
126.62
124.66
123.76
119.88
118.93
117.18
54.44
46.46
45.86
O
N
N
N
6y
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

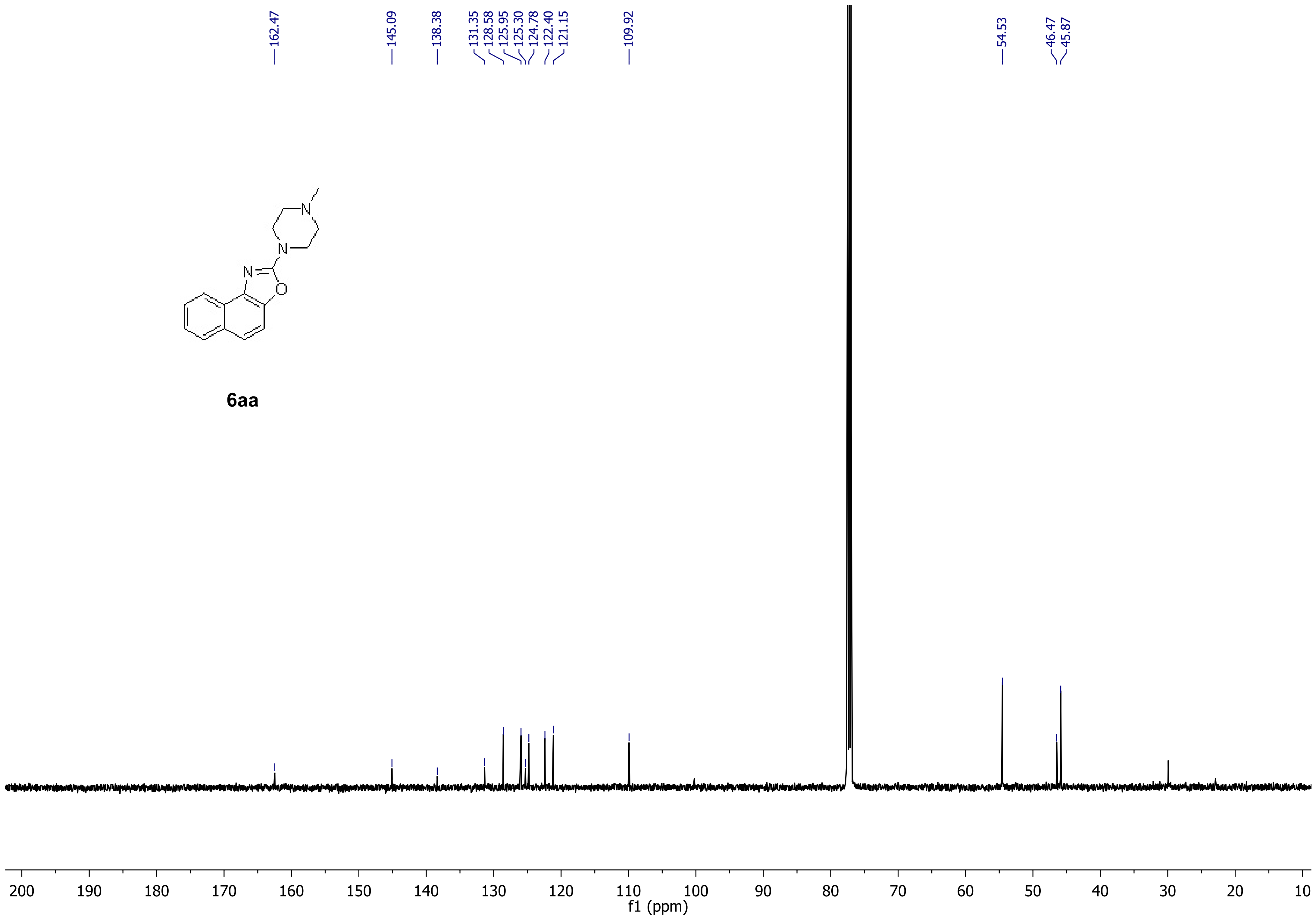

8.008
7.990
7.901
7.884
7.691
7.674
7.591
7.573
7.546
7.532
7.516
7.399
7.381
7.367
3.759
3.751
3.741
3.630
3.620
3.611
1.504
Boc
O
N
N
N
6z
1.00
1.09
1.13
1.11
1.27
1.16
4.47
4.31
9.46
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

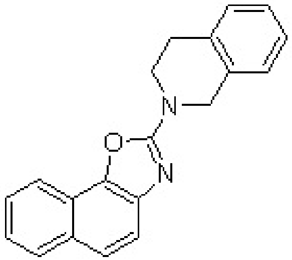

162.18
154.84
143.21
139.34
129.85
128.90
126.71
124.81
123.92
119.92
118.95
117.22
80.66
45.87
43.29
28.63
Boc
N
N
O
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

6z

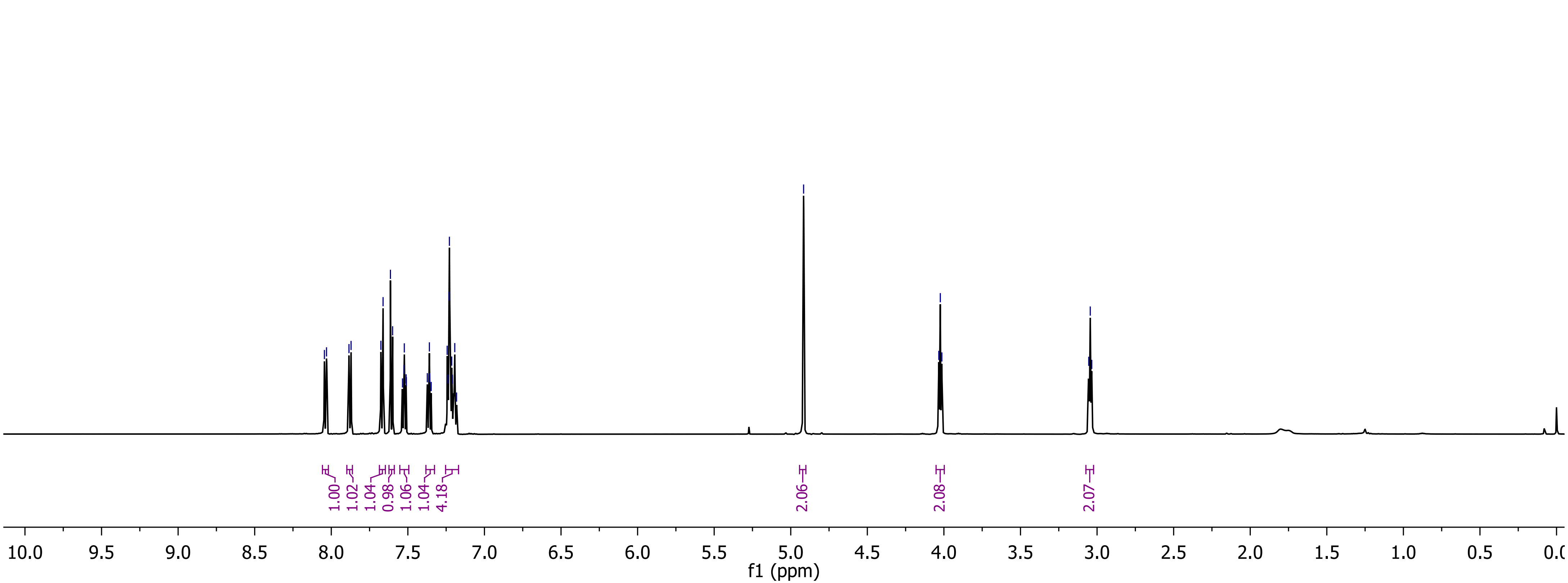


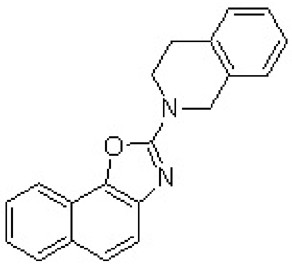
8.329
8.315
7.888
7.875
7.544
7.532
7.518
7.501
7.486
7.450
7.438
7.426
3.812
3.804
3.795
2.584
2.575
2.567
2.376
N
N
N
O
6aa
1.00
1.01
3.06
1.01
3.93
3.96
2.90
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.47
145.09
138.38
131.35
128.58
125.95
125.30
124.78
122.40
121.15
109.92
54.53
46.47
45.87
6aa
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

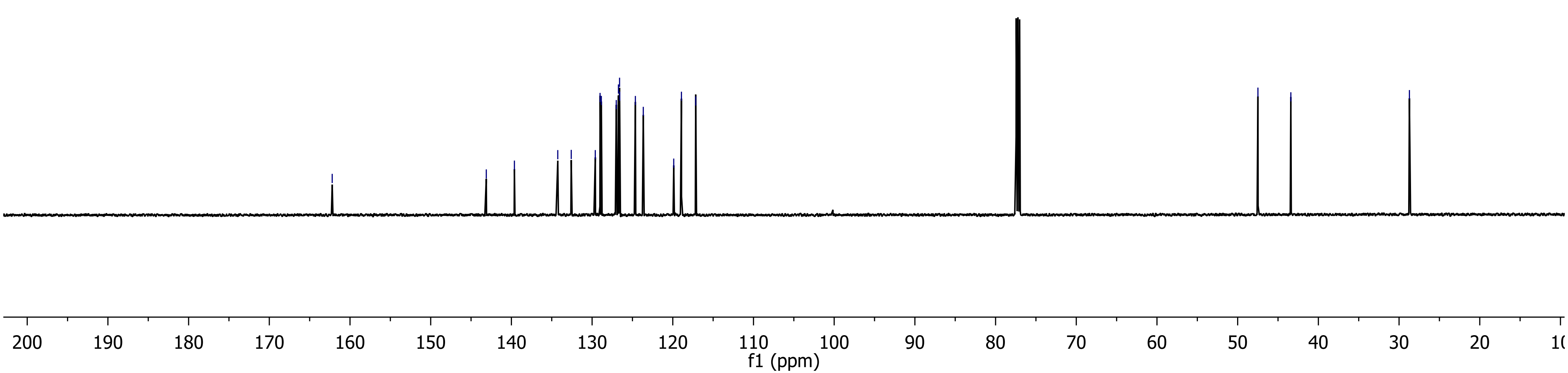


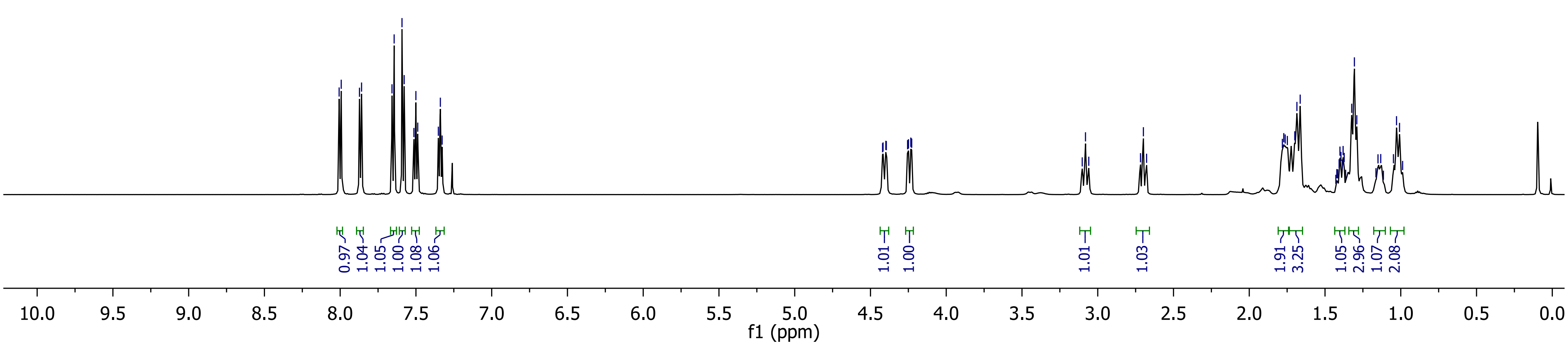
6ab


8.045
8.031
7.885
7.871
7.676
7.662
7.614
7.599
7.535
7.525
7.523
7.511
7.510
7.373
7.359
7.357
7.348
7.243
7.238
7.231
7.229
7.214
7.209
7.194
7.182
4.916
4.033
4.024
4.013
3.054
3.044
3.035
1.00
1.02
1.04
0.98
1.06
1.04
4.18
2.06
2.08
2.07
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
f1 (ppm)

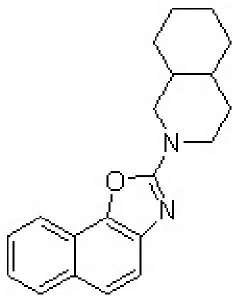


6ab


162.21
143.11
139.63
134.25
132.58
129.60
129.01
128.86
127.00
126.74
126.60
126.57
124.64
123.66
119.88
118.93
117.16
47.49
43.41
28.72
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

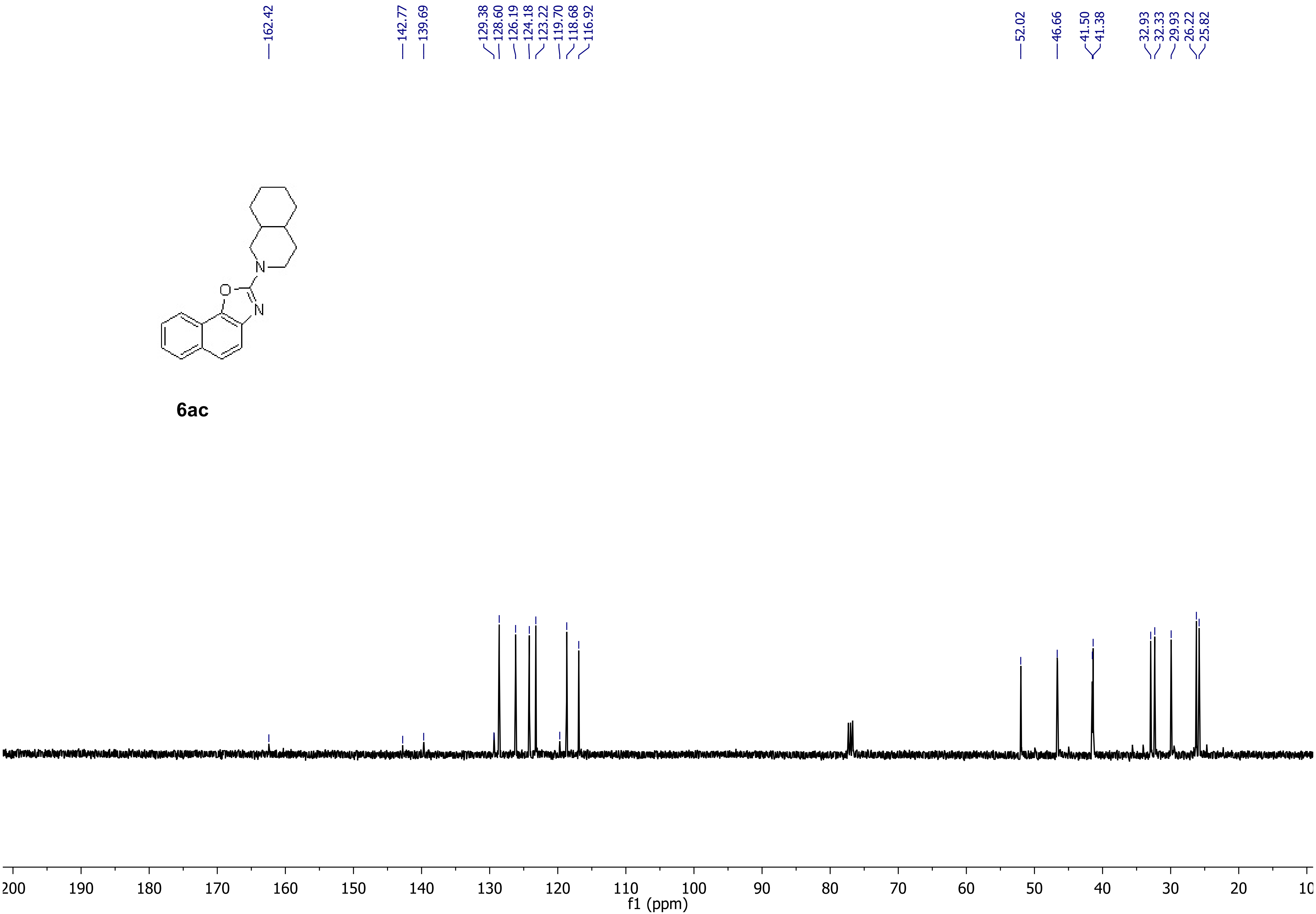


8.007
7.993
7.873
7.859
7.658
7.644
7.592
7.578
7.513
7.500
7.488
7.352
7.339
7.327
4.420
4.417
4.399
4.395
4.255
4.253
4.249
4.234
4.232
4.228
3.102
3.081
3.059
2.718
2.699
2.678
1.781
1.772
1.763
1.749
1.700
1.685
1.664
1.407
1.401
1.395
1.386
1.381
1.374
1.324
1.306
1.290
1.150
1.132
1.048
1.028
1.008
0.97
1.04
1.05
1.00
1.08
1.06
1.01
1.00
1.01
1.03
1.91
3.25
1.05
2.96
1.07
2.08
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
f1 (ppm)

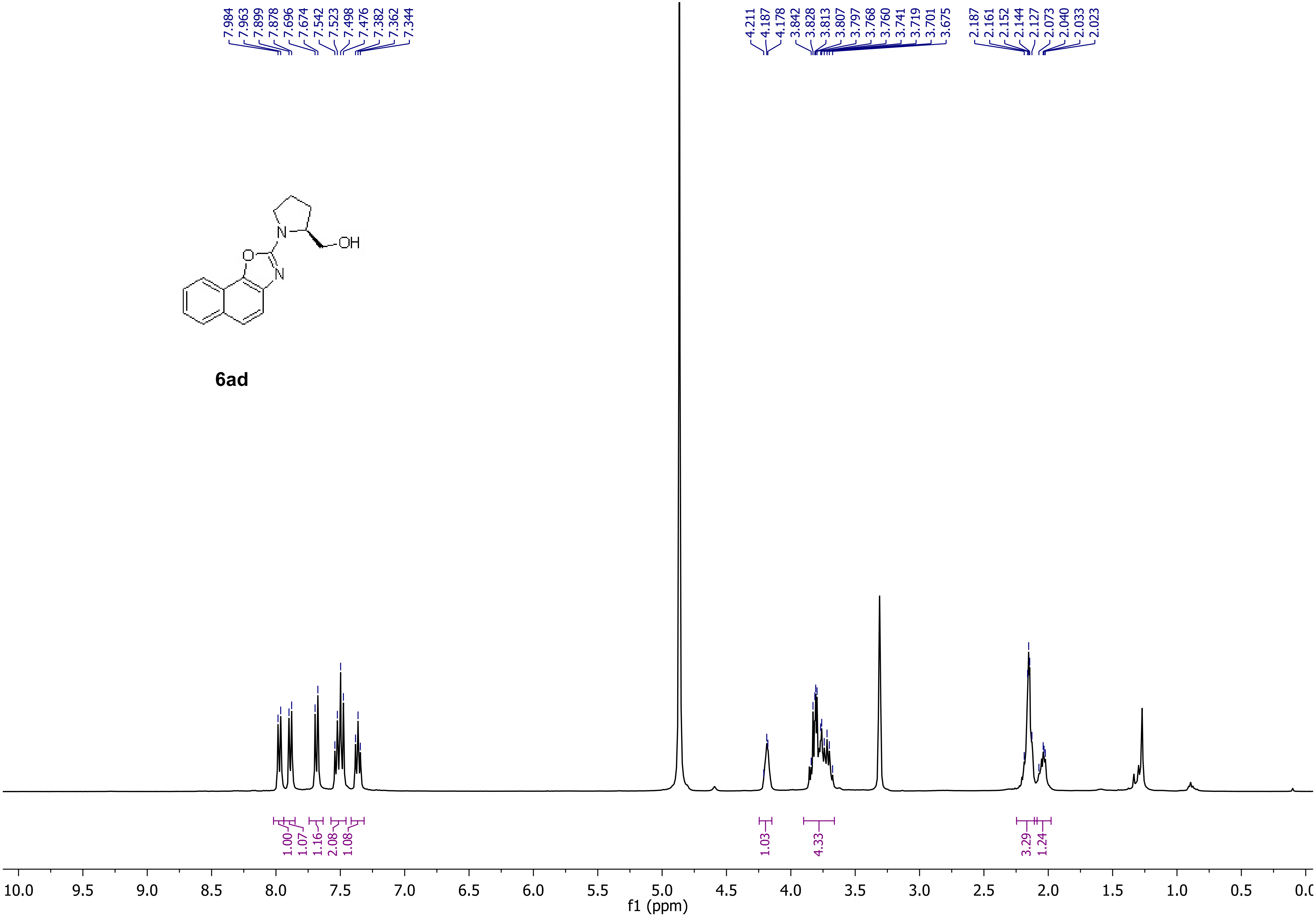


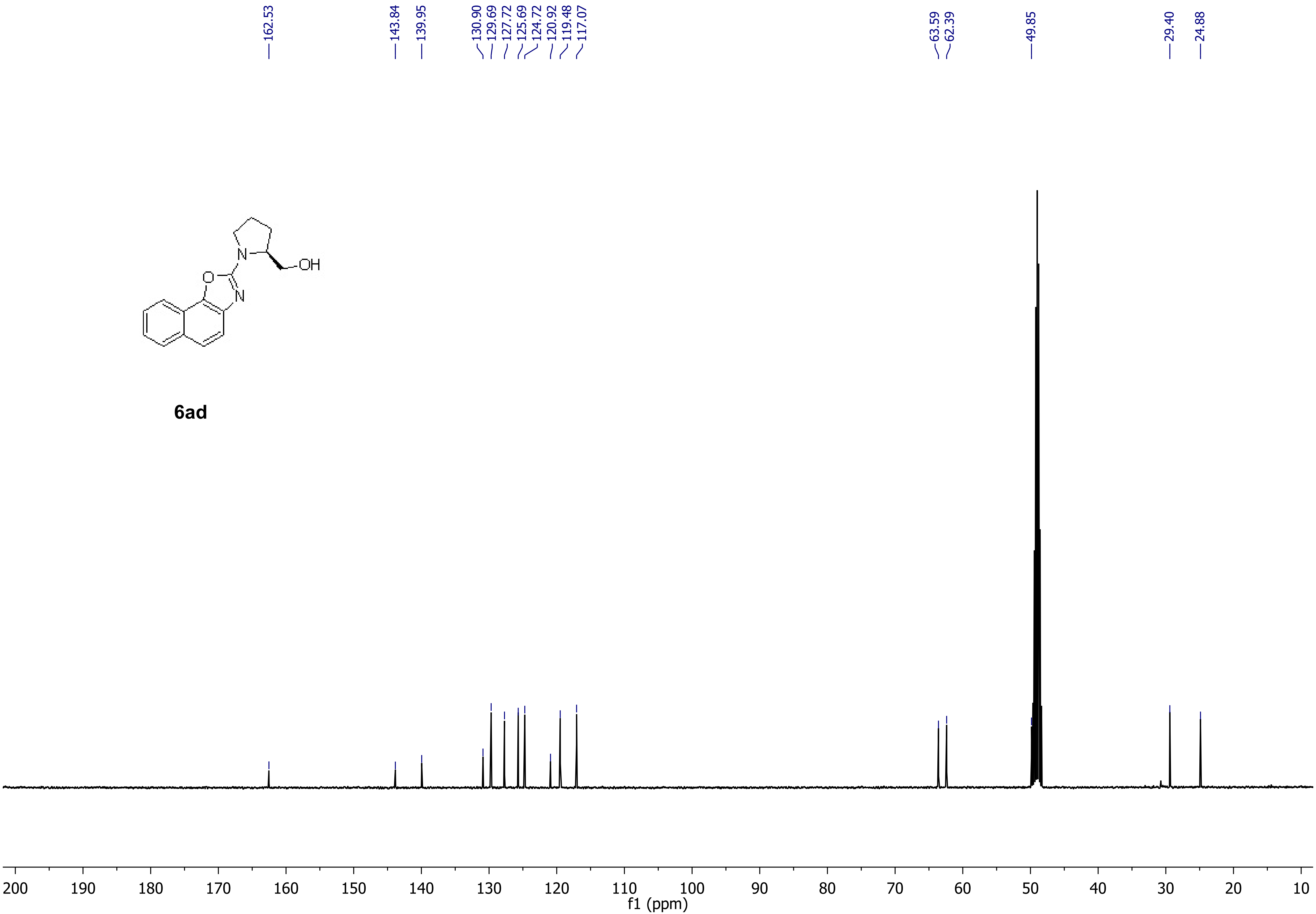
N
O
N

6ac

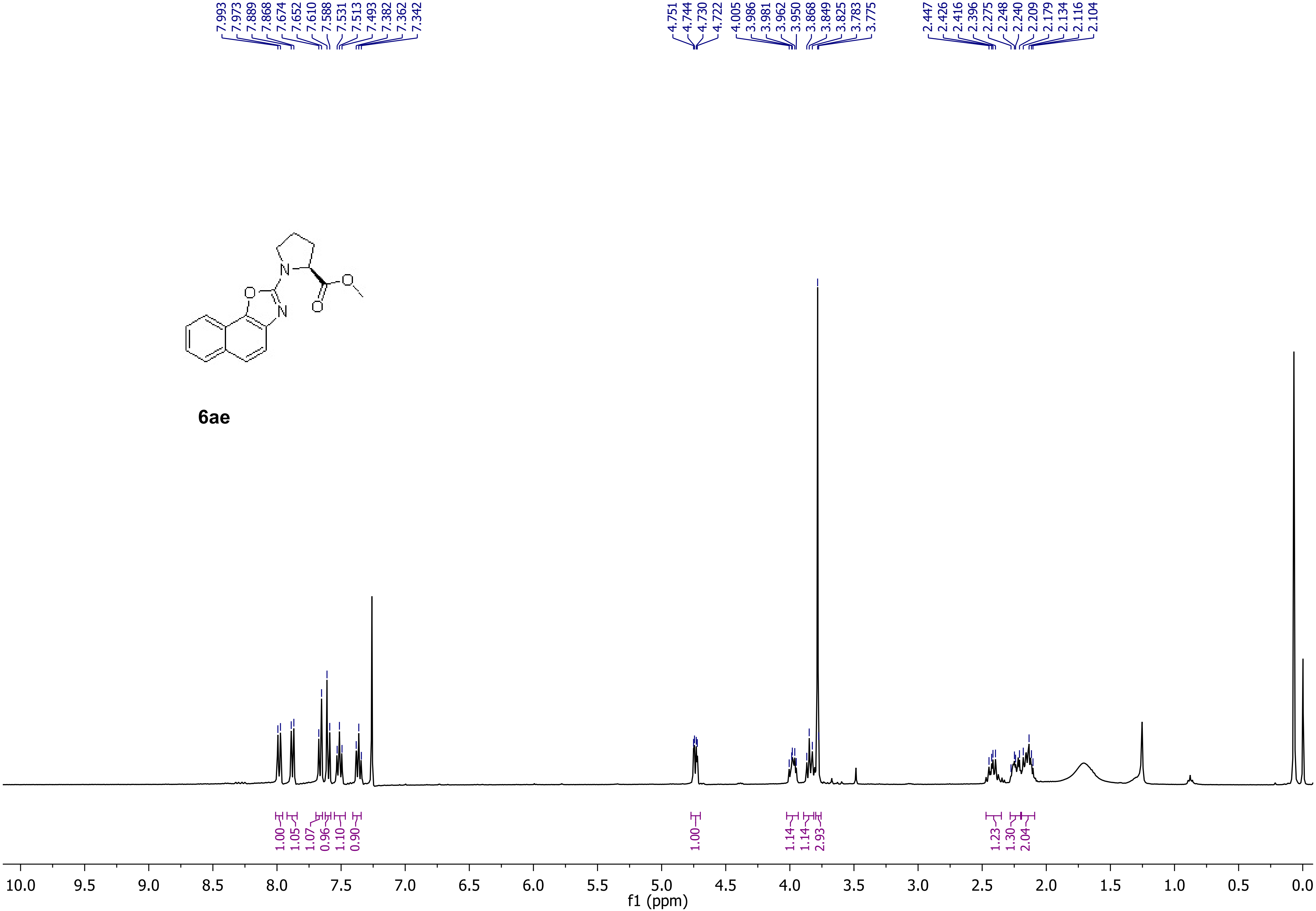

O
N
N
162.42
142.77
139.69
129.38
128.60
126.19
124.18
123.22
119.70
118.68
116.92
52.02
46.66
41.50
41.38
32.93
32.33
29.93
26.22
25.82
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

6ac

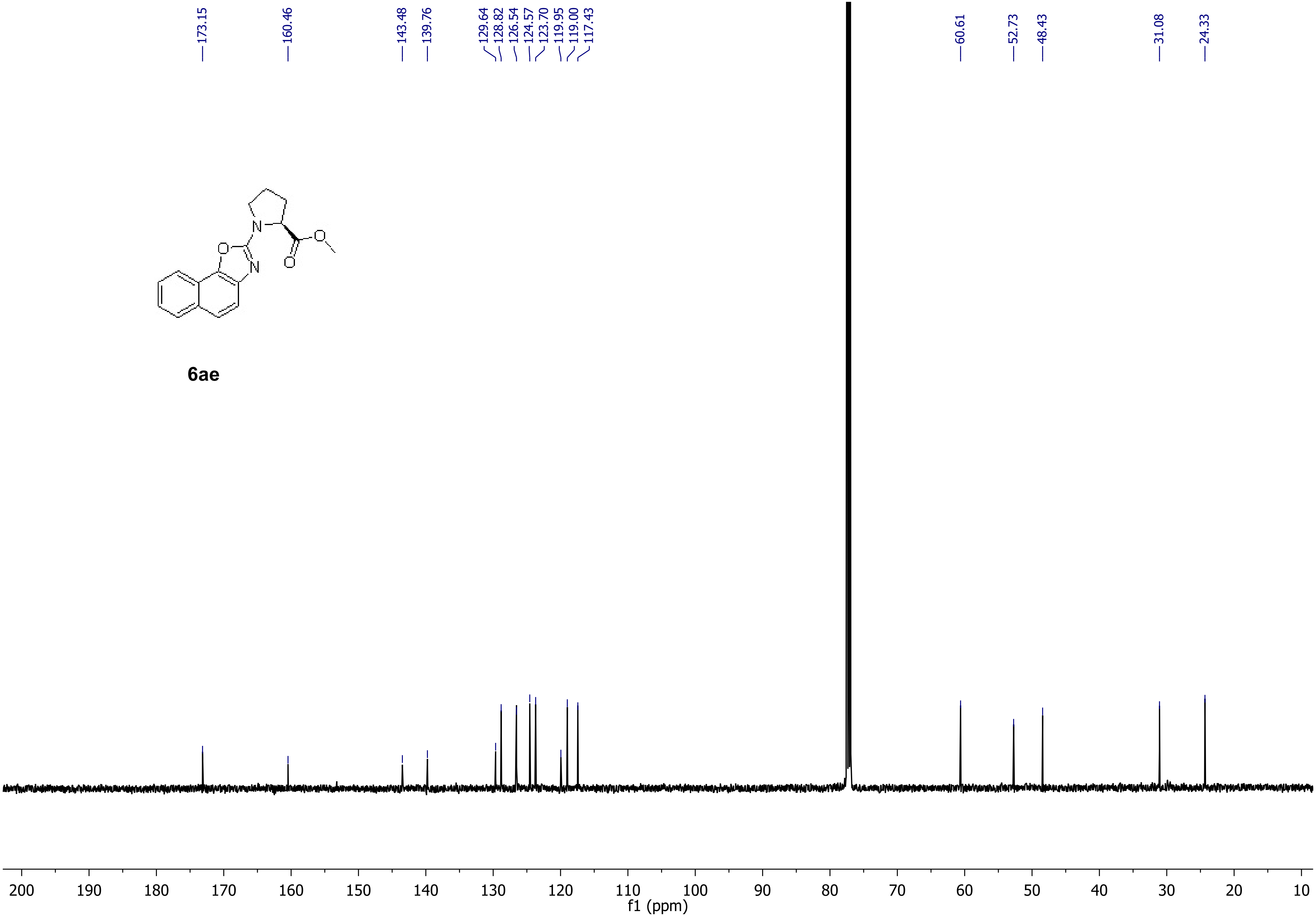

7.984
7.963
7.899
7.878
7.696
7.674
7.542
7.523
7.498
7.476
7.382
7.362
7.344
4.211
4.187
4.178
3.842
3.828
3.813
3.807
3.797
3.768
3.760
3.741
3.719
3.701
3.675
2.187
2.161
2.152
2.144
2.127
2.073
2.040
2.033
2.023
N
O
OH
6ad
1.00
1.07
1.16
2.08
1.08
1.03
4.33
3.29
1.24
10.0
9.5
9.0
8.5
8.0
7.5
7.0
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
f1 (ppm)



162.53
143.84
139.95
130.90
129.69
127.72
125.69
124.72
120.92
119.48
117.07
63.59
62.39
49.85
29.40
24.88
N
O
N
OH
6ad
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

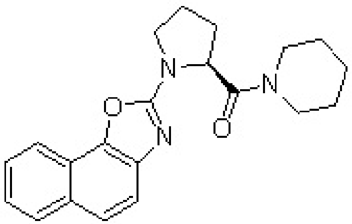

7.993
7.973
7.889
7.868
7.674
7.652
7.610
7.588
7.531
7.513
7.493
7.382
7.362
7.342
4.751
4.744
4.730
4.722
4.005
3.986
3.981
3.962
3.950
3.868
3.849
3.825
3.783
3.775
2.447
2.426
2.416
2.396
2.275
2.248
2.240
2.209
2.179
2.134
2.116
2.104
1.00
1.05
1.07
0.96
1.10
0.90
1.00
1.14
1.14
2.93
1.23
1.30
2.04
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
f1 (ppm)

6ae

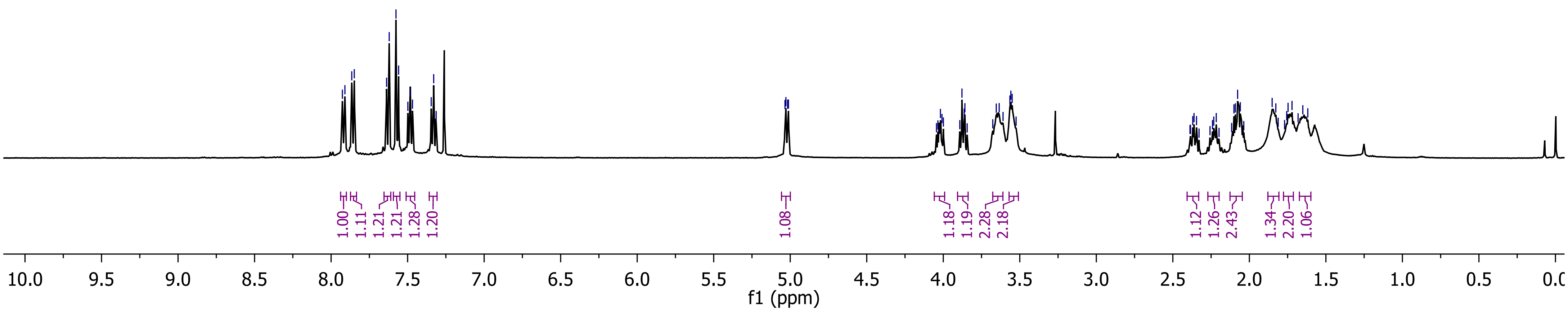


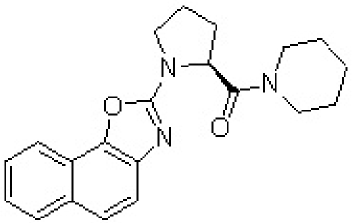
173.15
160.46
143.48
139.76
129.64
128.82
126.54
124.57
123.70
119.95
119.00
117.43
60.61
52.73
48.43
31.08
24.33
O
N
O
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

6ae

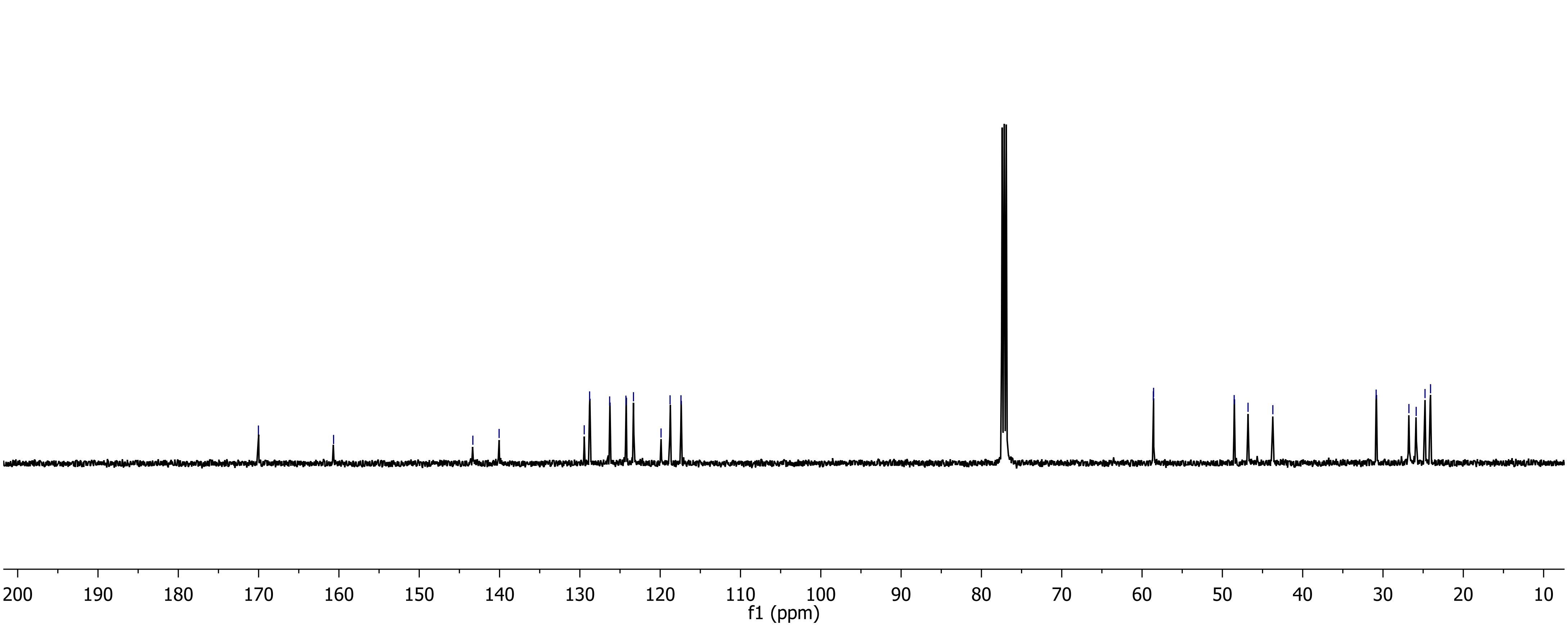

O
N
N
N
O

6af


7.926
7.910
7.865
7.848
7.637
7.620
7.576
7.559
7.498
7.484
7.468
7.346
7.330
7.314
5.034
5.028
5.017
5.012
4.044
4.035
4.018
4.009
3.999
3.892
3.878
3.863
3.859
3.844
3.677
3.654
3.635
3.609
3.565
3.558
3.550
3.524
2.388
2.385
2.370
2.362
2.345
2.257
2.241
2.233
2.216
2.198
2.116
2.101
2.092
2.077
2.059
2.036
1.851
1.827
1.812
1.770
1.756
1.747
1.721
1.682
1.651
1.00
1.11
1.21
1.21
1.28
1.20
1.08
1.18
1.19
2.28
2.18
1.12
1.26
2.43
1.34
2.20
1.06
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
f1 (ppm)

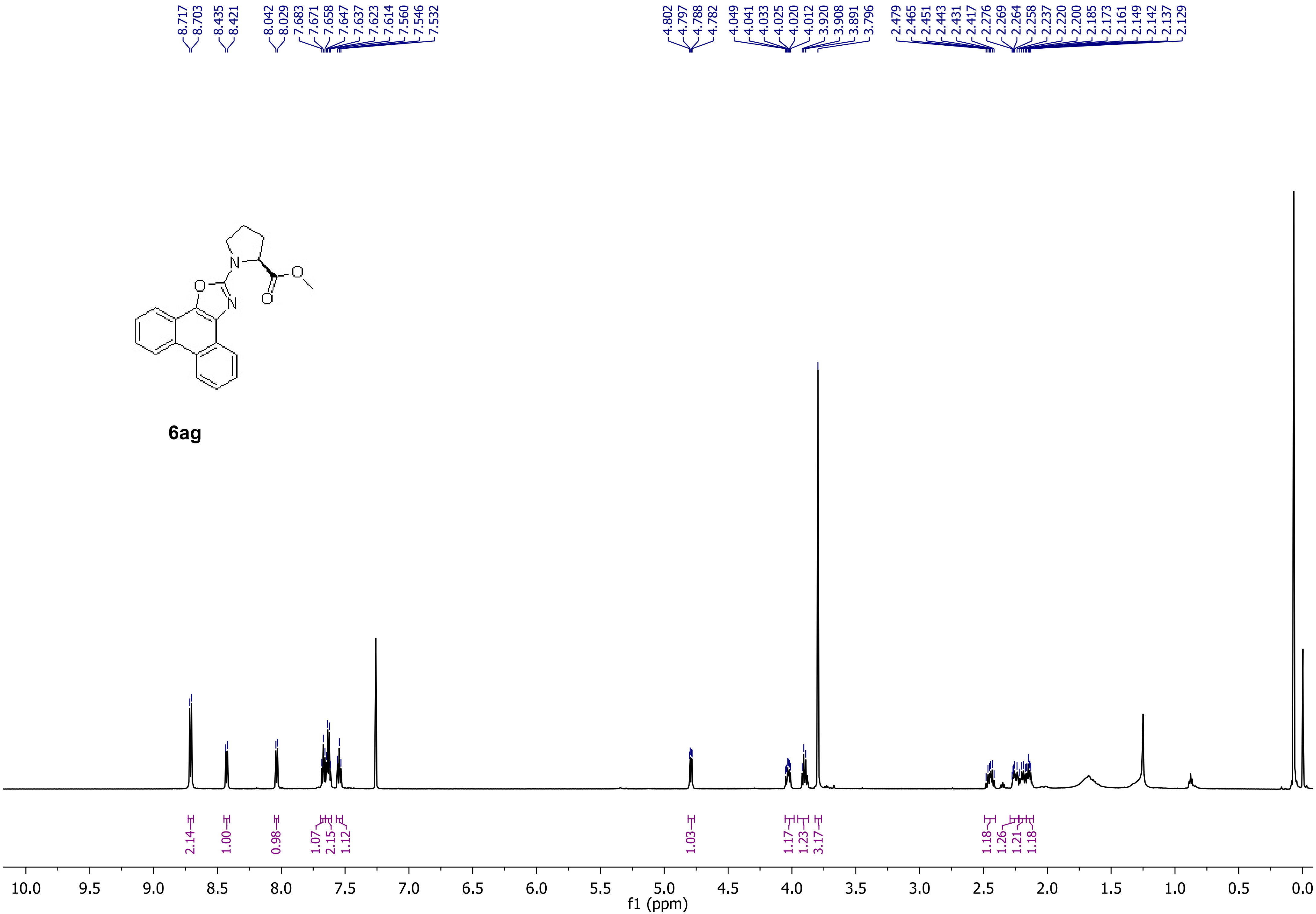


6af

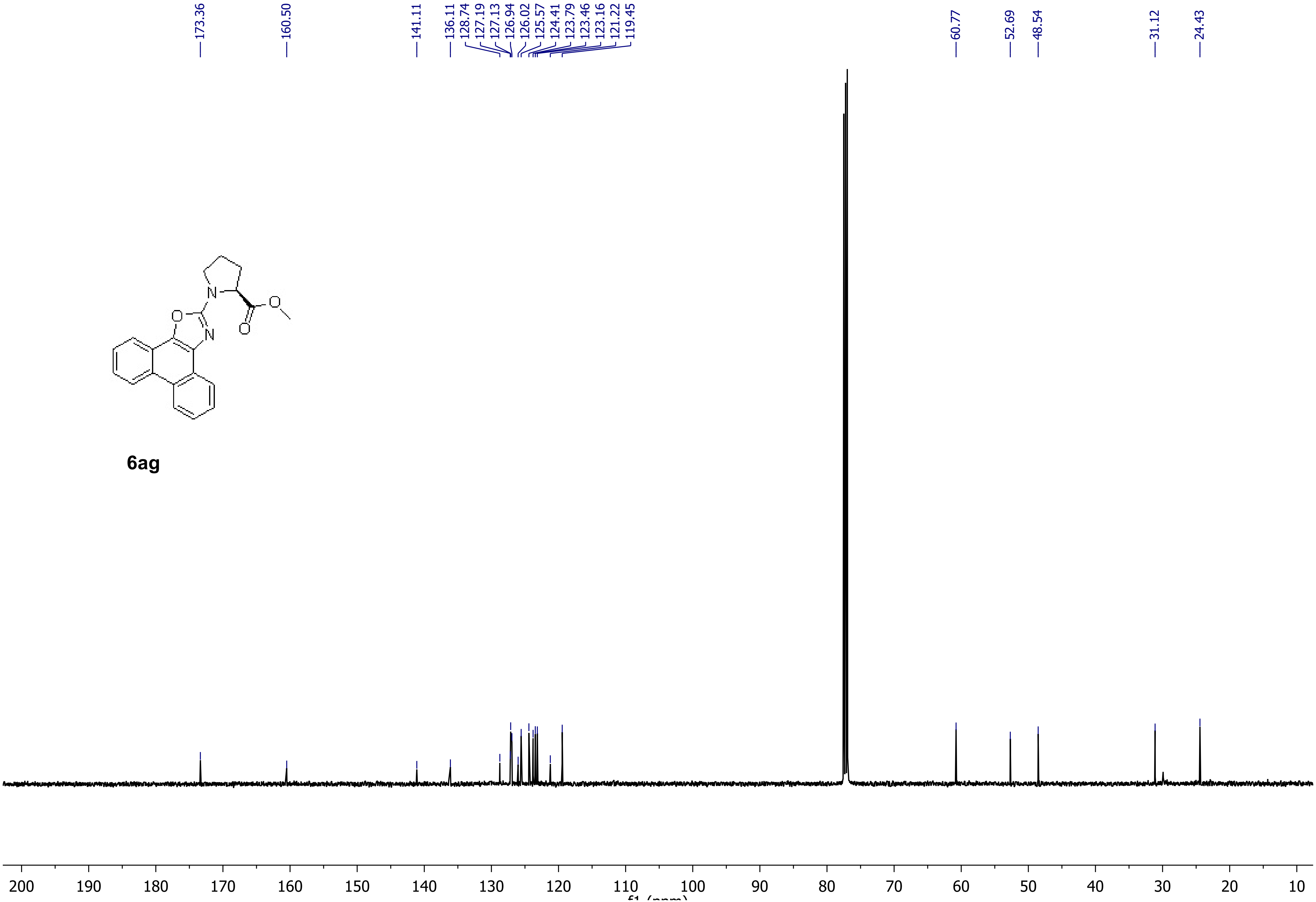


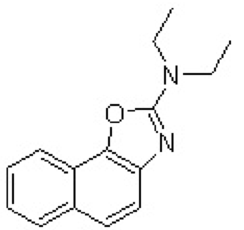
170.02
160.67
143.32
140.06
129.46
128.79
126.29
124.27
123.33
119.89
118.77
117.41
58.60
58.57
48.53
46.81
43.72
30.85
26.77
25.87
24.77
24.08
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

6ag

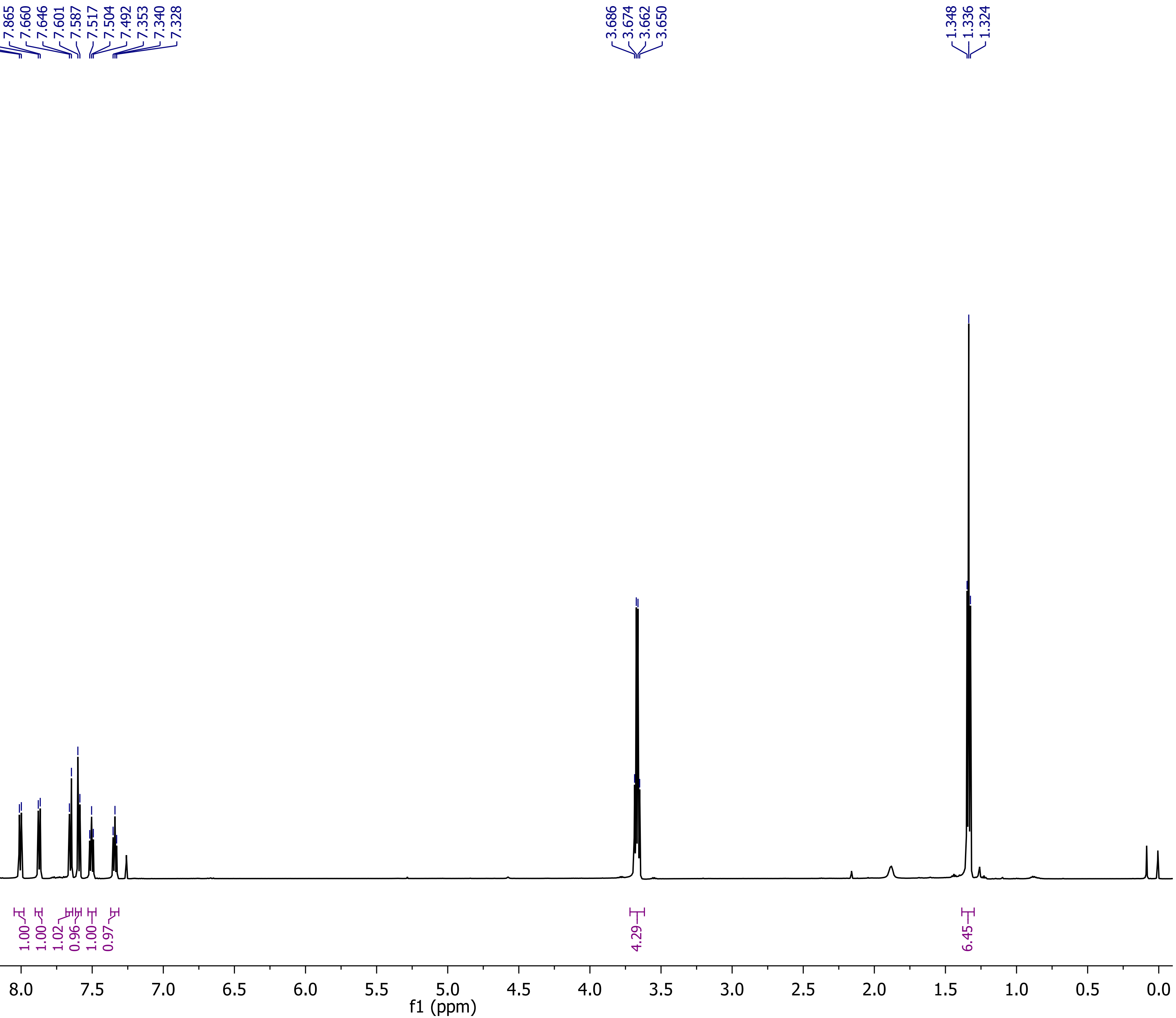


8.717
8.703
8.435
8.421
8.042
8.029
7.683
7.671
7.658
7.647
7.637
7.623
7.614
7.560
7.546
7.532
4.802
4.797
4.788
4.782
4.049
4.041
4.033
4.025
4.020
4.012
3.920
3.908
3.891
3.796
2.479
2.465
2.451
2.443
2.431
2.417
2.276
2.269
2.264
2.258
2.237
2.220
2.200
2.185
2.173
2.161
2.149
2.142
2.137
2.129
2.14
1.00
0.98
1.07
2.15
1.12
1.03
1.17
1.23
3.17
1.18
1.26
1.21
1.18
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
f1 (ppm)

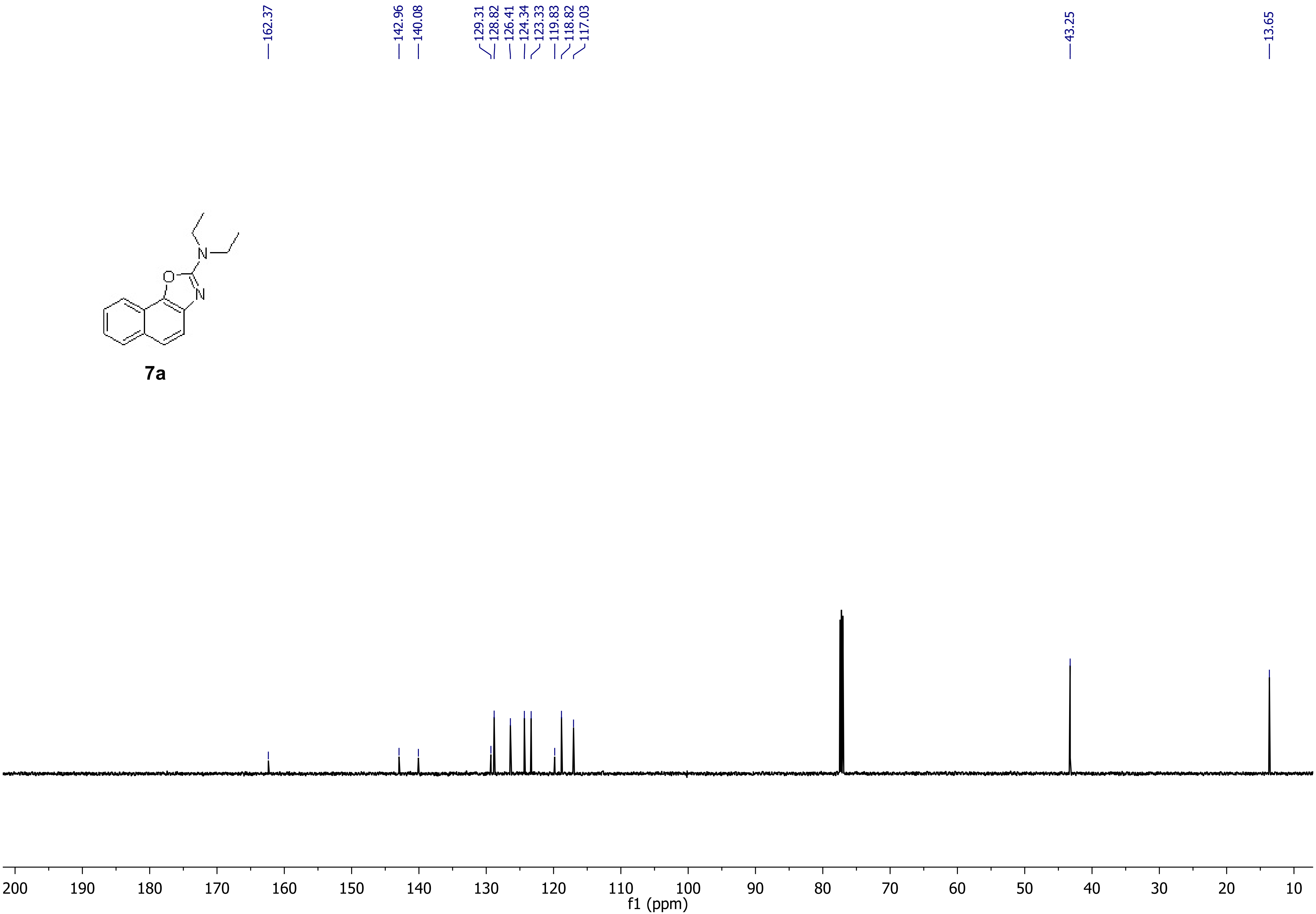

173.36
160.50
141.11
136.11
128.74
127.19
127.13
126.94
126.02
125.57
124.41
123.79
123.46
123.16
121.22
119.45
60.77
52.69
48.54
31.12
24.43
N
O
O
N
O
6ag
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

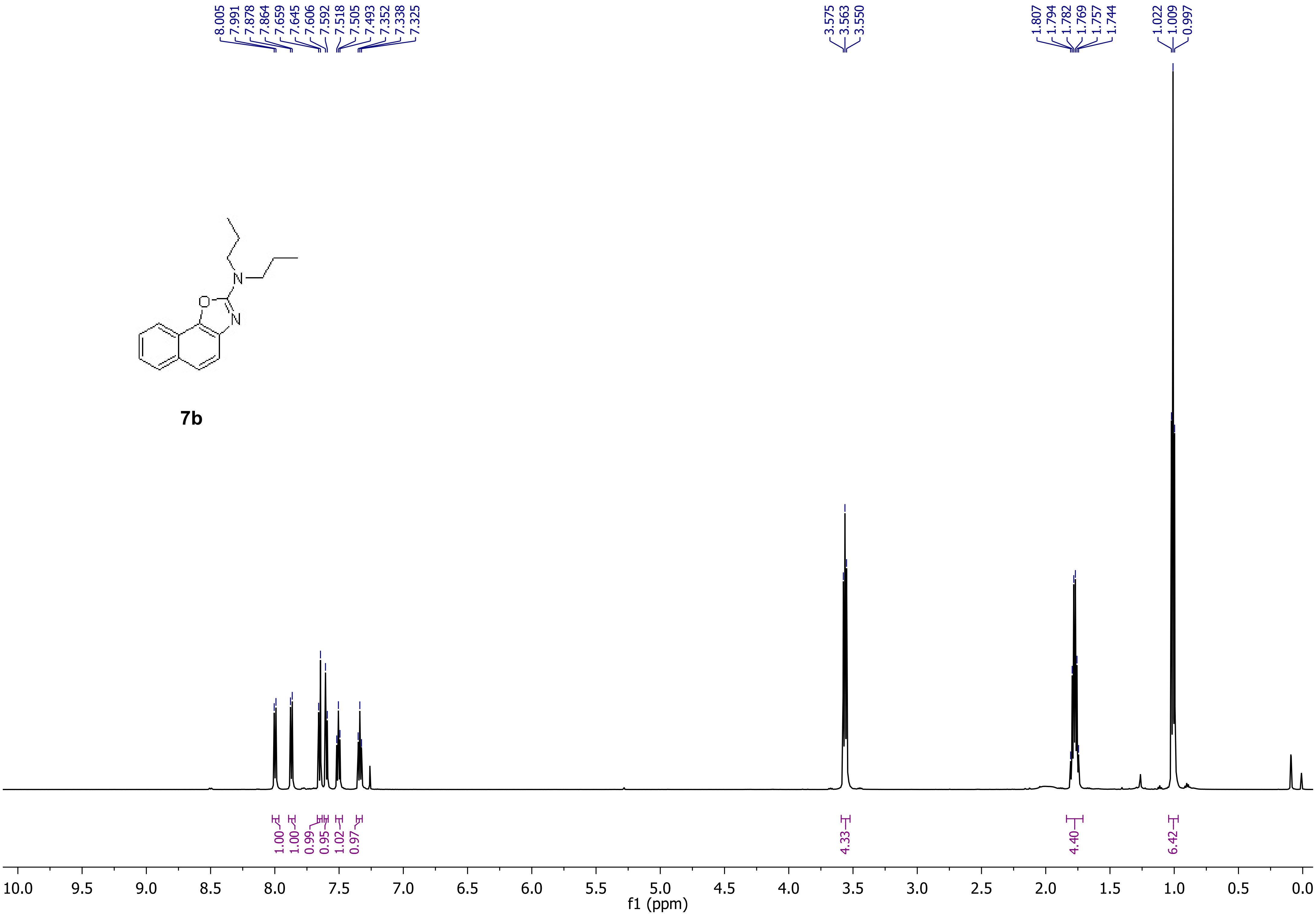


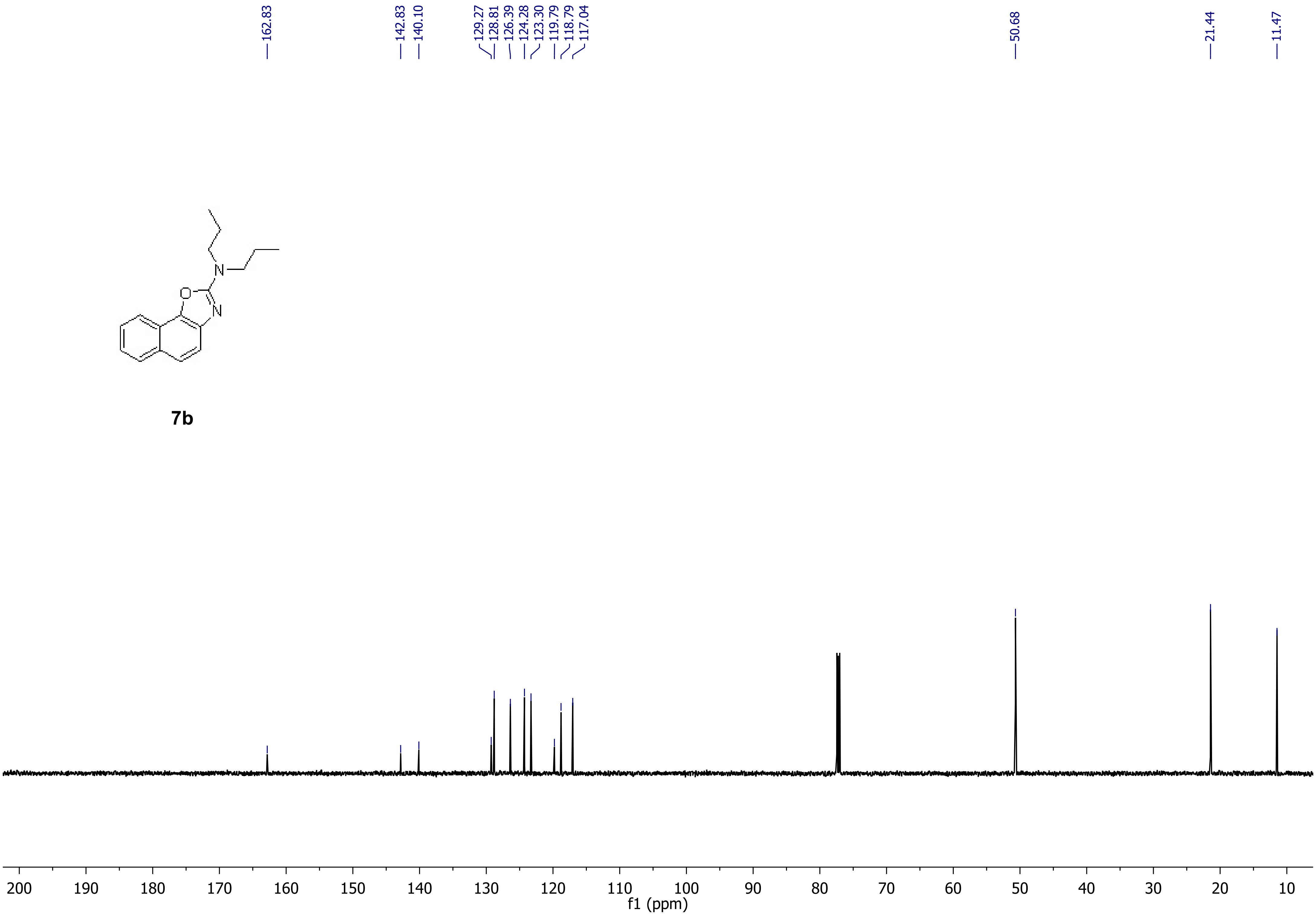
7a



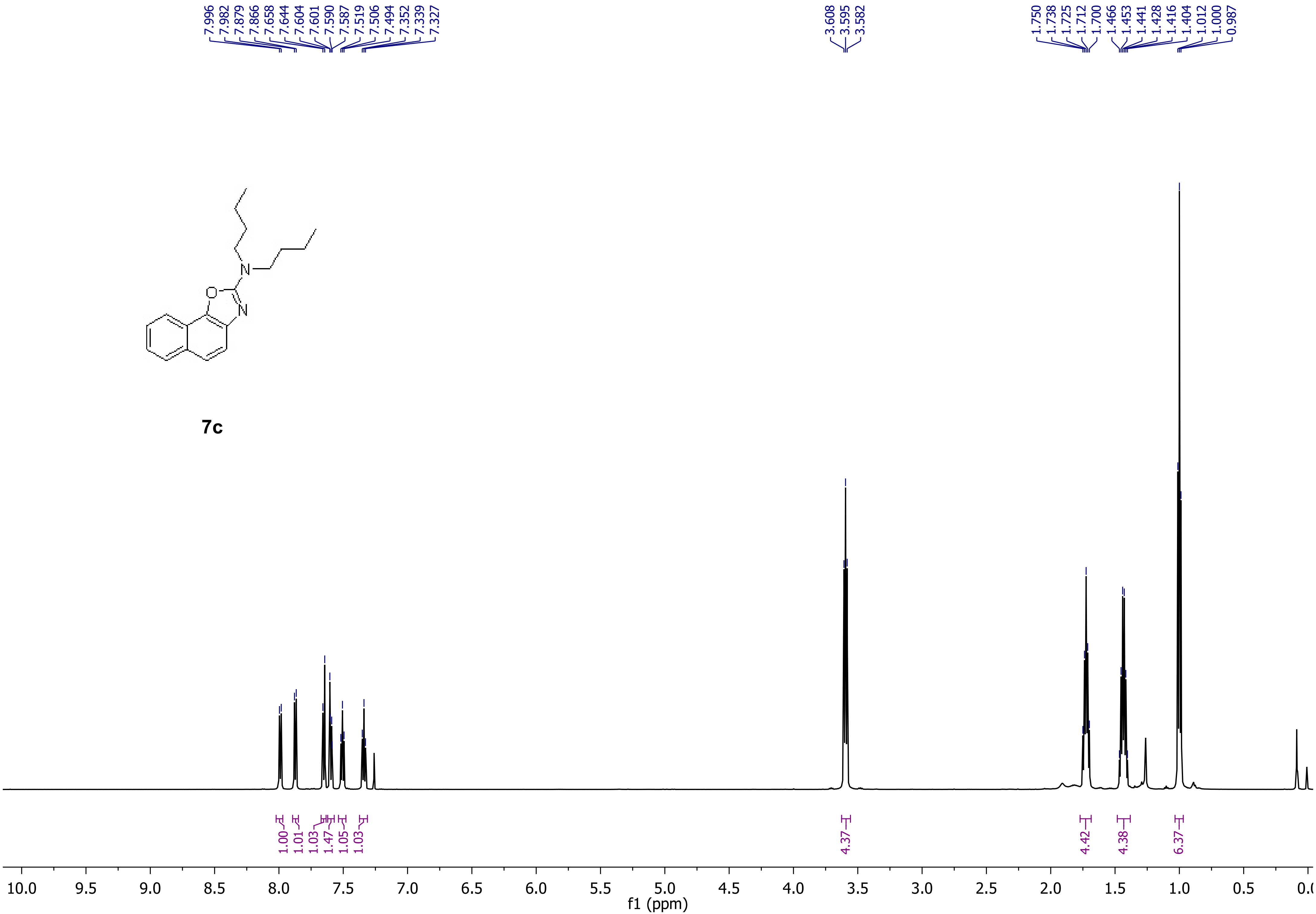
8.012
7.998
7.879
7.865
7.660
7.646
7.601
7.587
7.517
7.504
7.492
7.353
7.340
7.328
3.686
3.674
3.662
3.650
1.348
1.336
1.324
1.00
1.00
1.02
0.96
1.00
0.97
4.29
6.45
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.37
142.96
140.08
129.31
128.82
126.41
124.34
123.33
119.83
118.82
117.03
43.25
13.65
O
N
N
7a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

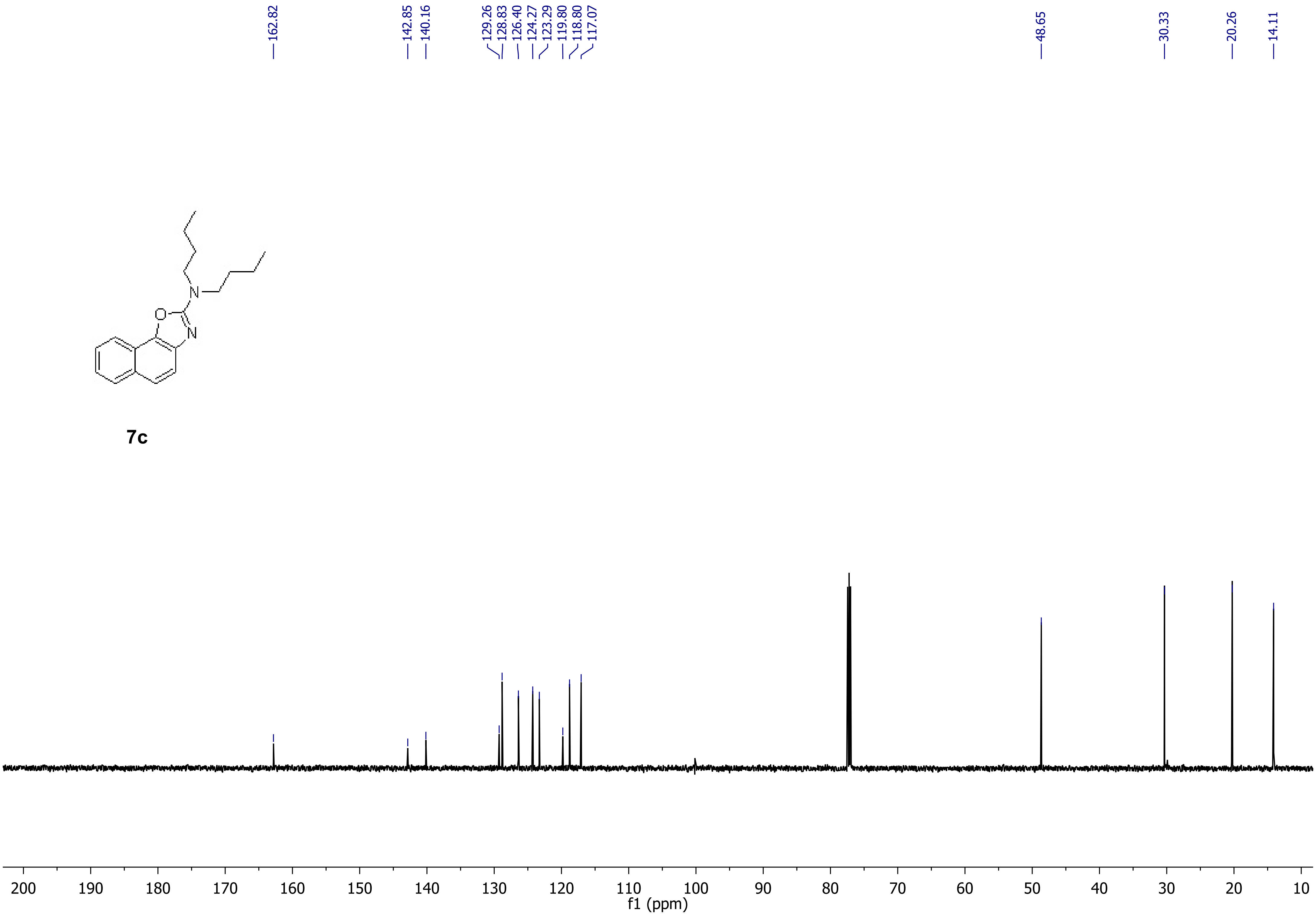

8.005
7.991
7.878
7.864
7.659
7.645
7.606
7.592
7.518
7.505
7.493
7.352
7.338
7.325
3.575
3.563
3.550
1.807
1.794
1.782
1.769
1.757
1.744
1.022
1.009
0.997
O
N
N
7b
1.00
1.00
0.99
0.95
1.02
0.97
4.33
4.40
6.42
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.83
142.83
140.10
129.27
128.81
126.39
124.28
123.30
119.79
118.79
117.04
50.68
21.44
11.47
N
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

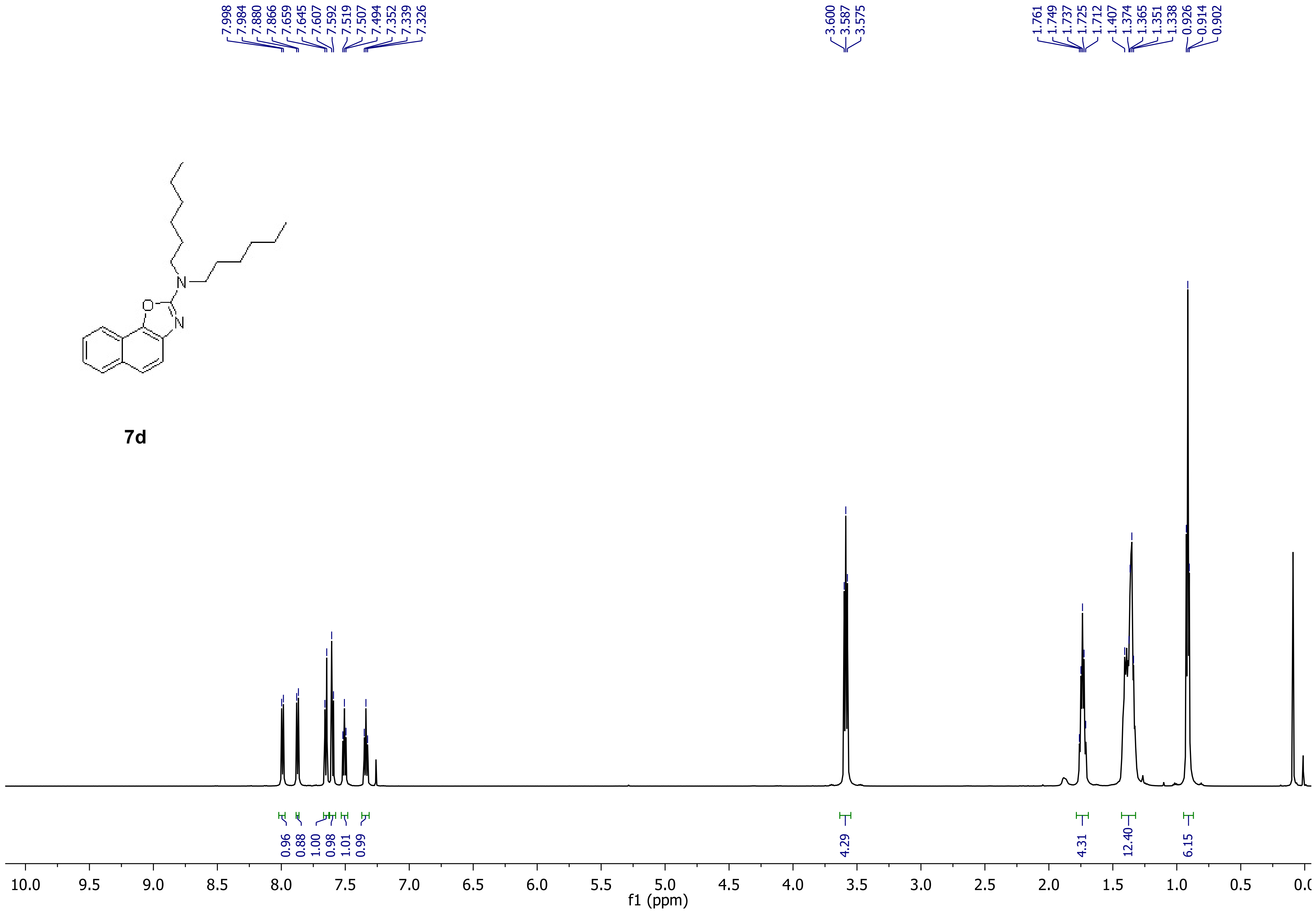
7b

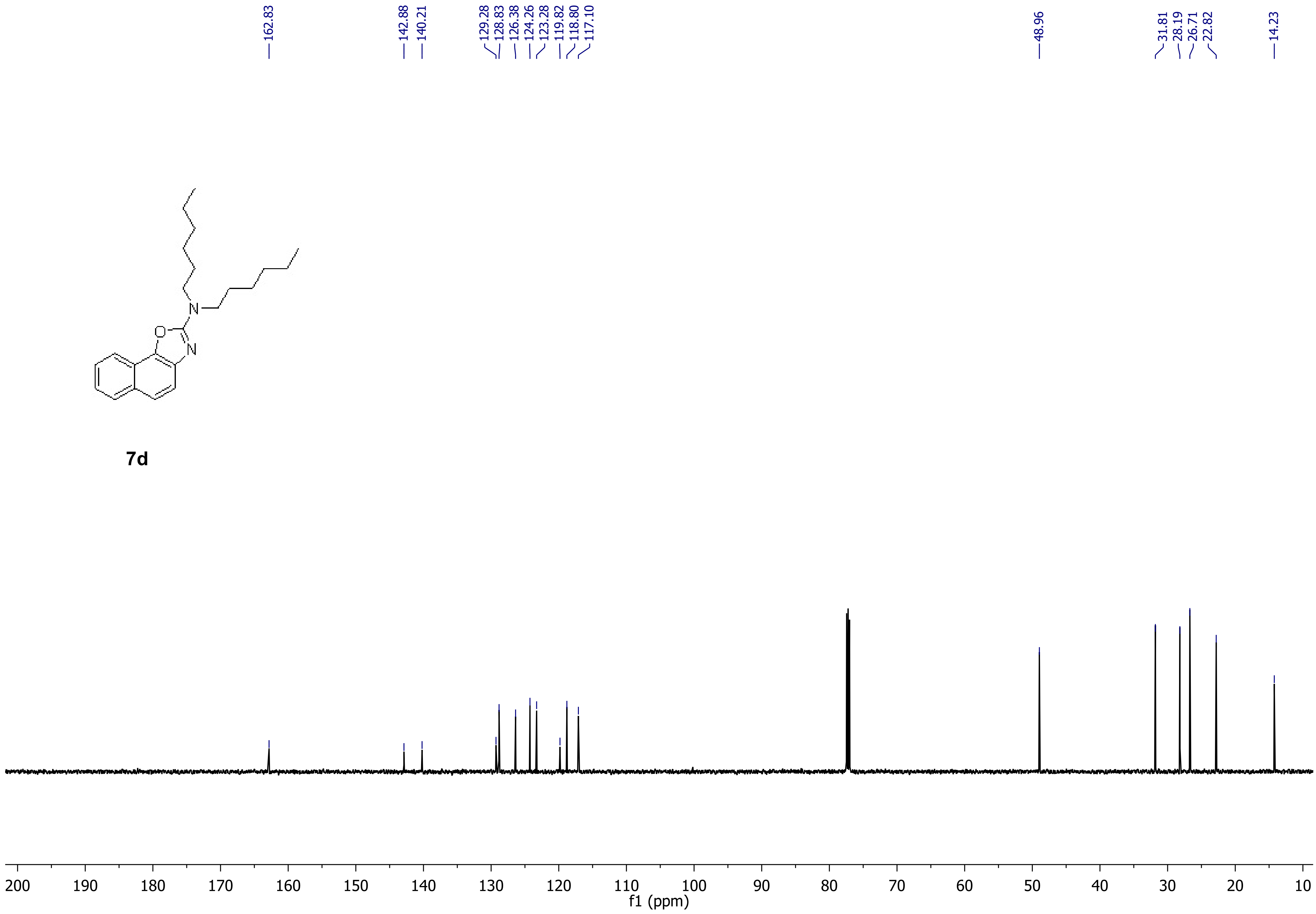


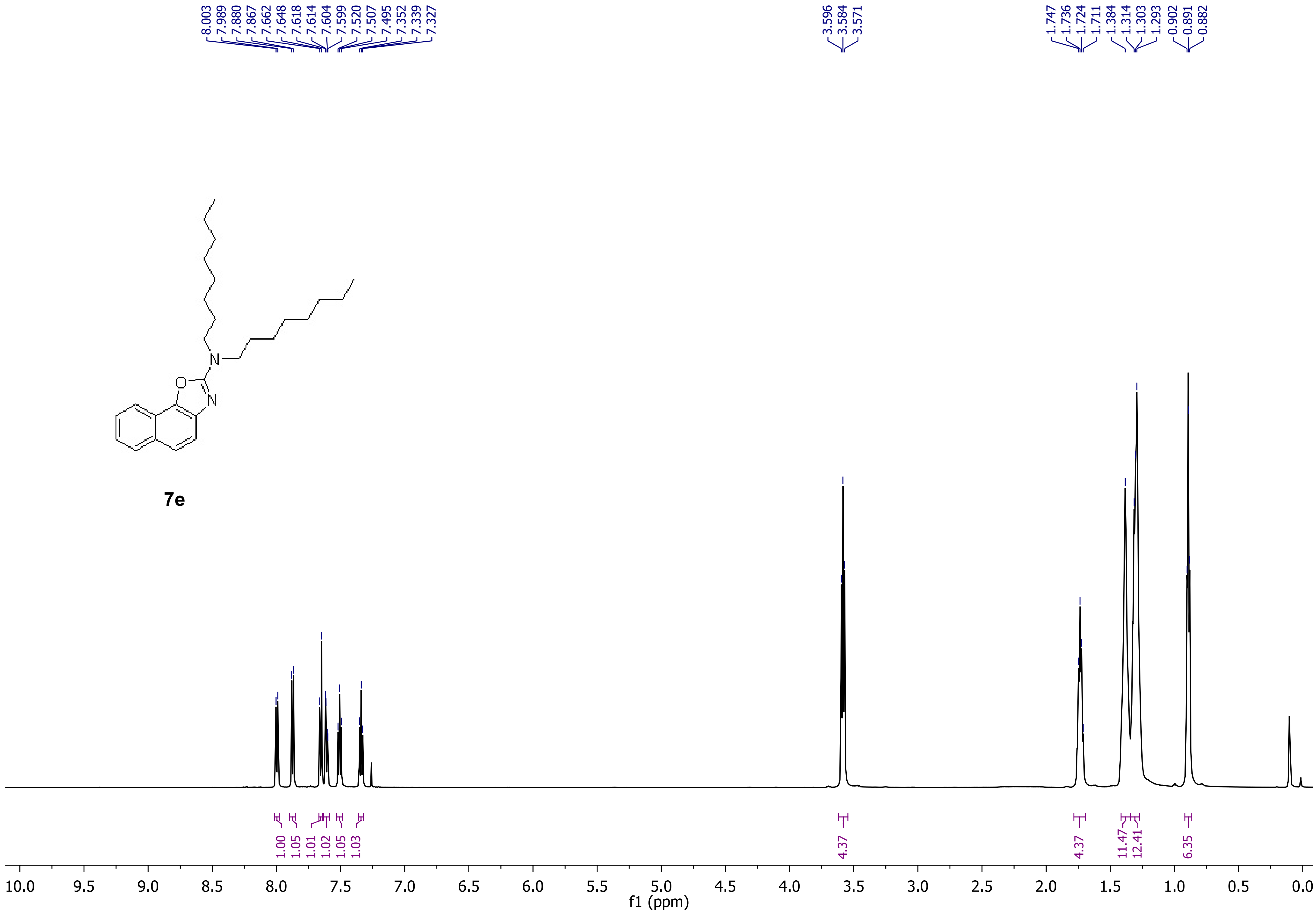
7.996
7.982
7.879
7.866
7.658
7.644
7.604
7.601
7.590
7.587
7.519
7.506
7.494
7.352
7.339
7.327
3.608
3.595
3.582
1.750
1.738
1.725
1.712
1.700
1.466
1.453
1.441
1.428
1.416
1.404
1.012
1.000
0.987
7c
1.00
1.01
1.03
1.47
1.05
1.03
4.37
4.42
4.38
6.37
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

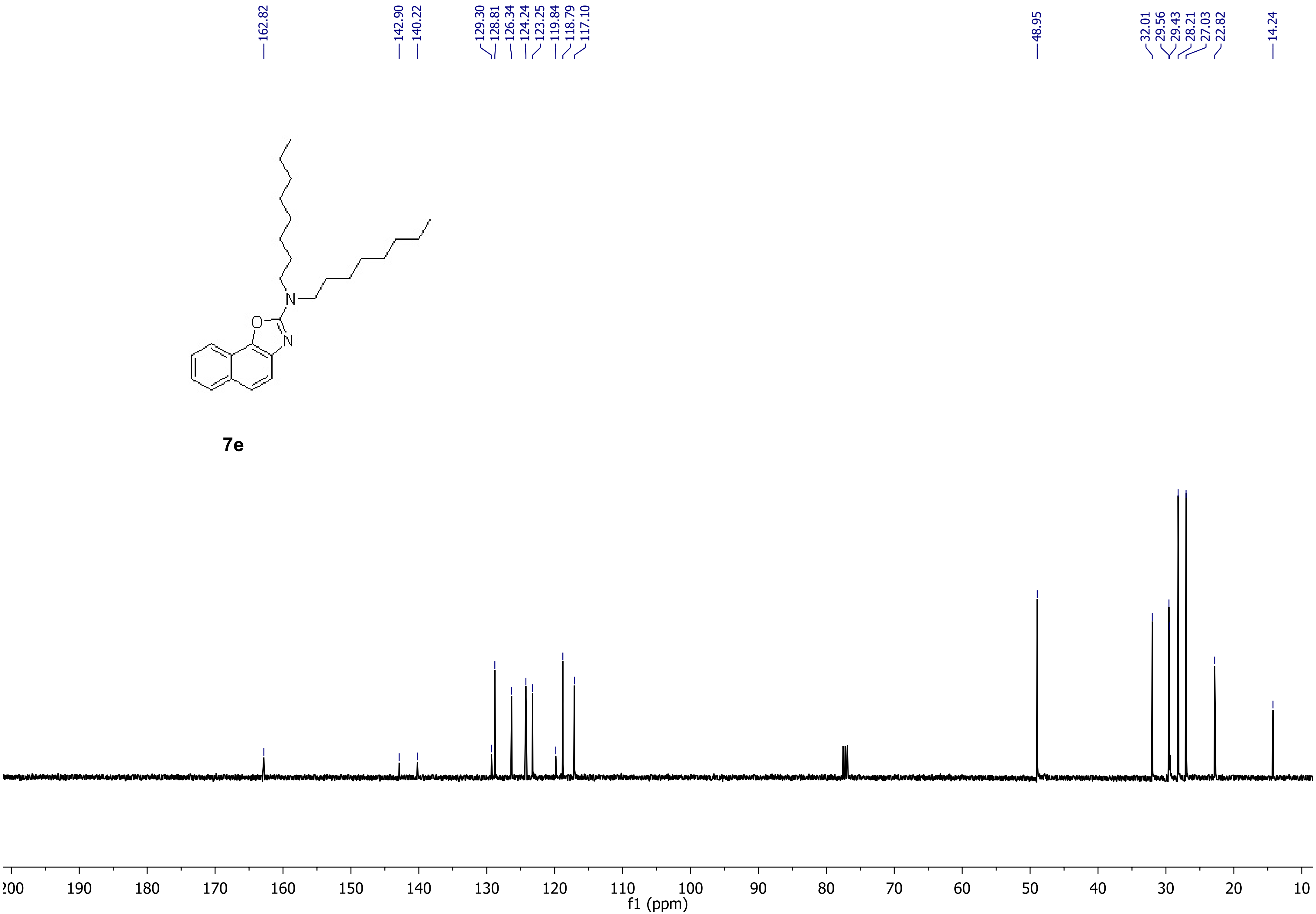


162.82
142.85
140.16
129.26
128.83
126.40
124.27
123.29
119.80
118.80
117.07
48.65
30.33
20.26
14.11
O
N
N
7c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

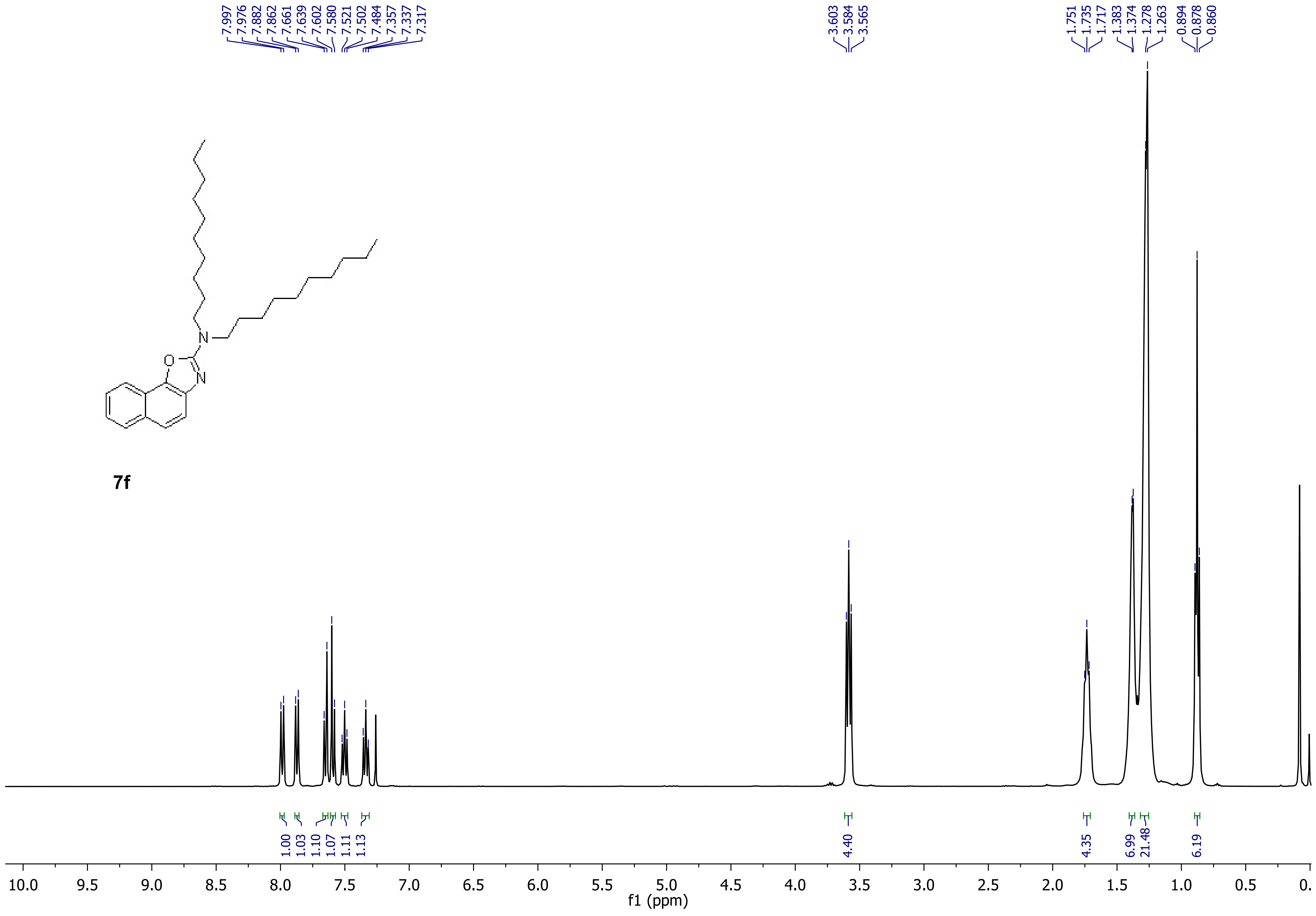

7.998
7.984
7.880
7.866
7.659
7.645
7.607
7.592
7.519
7.507
7.494
7.352
7.339
7.326
3.600
3.587
3.575
1.761
1.749
1.737
1.725
1.712
1.407
1.374
1.365
1.351
1.338
0.926
0.914
0.902
7d
0.96
0.88
1.00
0.98
1.01
0.99
4.29
4.31
12.40
6.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

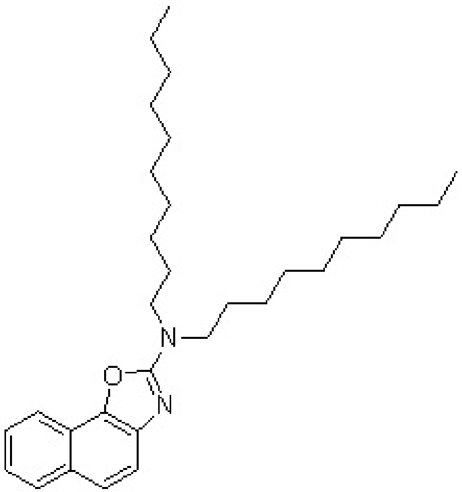

162.83
142.88
140.21
129.28
128.83
126.38
124.26
123.28
119.82
118.80
117.10
48.96
31.81
28.19
26.71
22.82
14.23
O
N
N
7d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.003
7.989
7.880
7.867
7.662
7.648
7.618
7.614
7.604
7.599
7.520
7.507
7.495
7.352
7.339
7.327
3.596
3.584
3.571
1.747
1.736
1.724
1.711
1.384
1.314
1.303
1.293
0.902
0.891
0.882
N
O
N
7e
1.00
1.05
1.01
1.02
1.05
1.03
4.37
4.37
11.47
12.41
6.35
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
f1 (ppm)

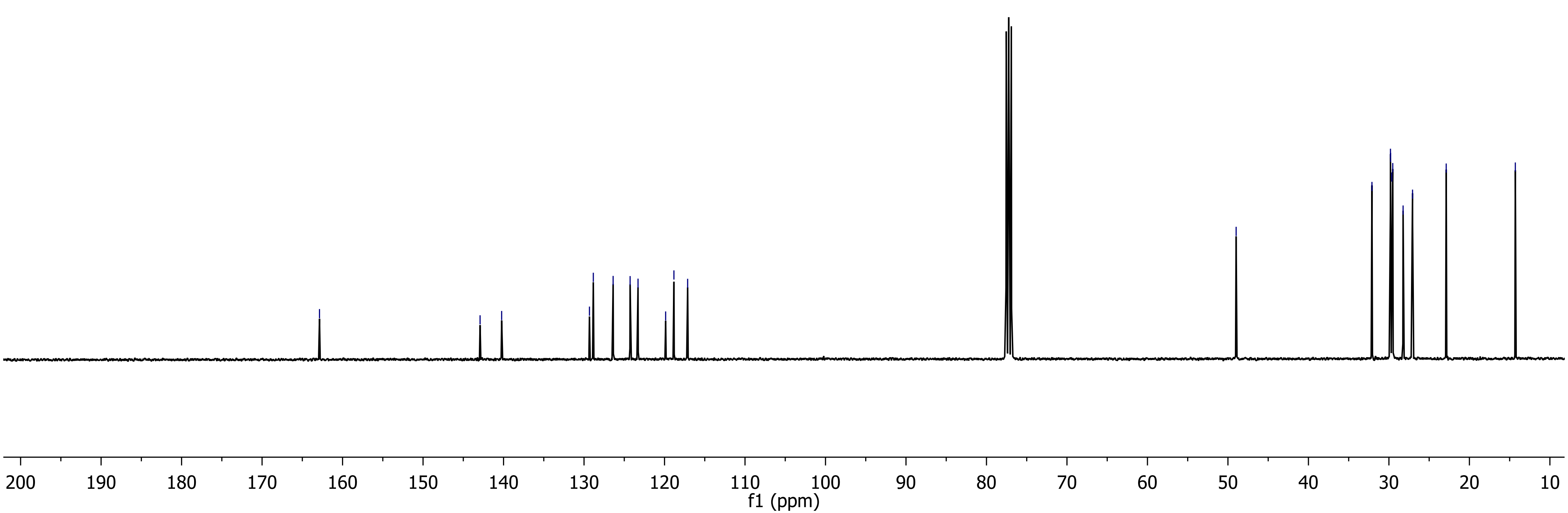


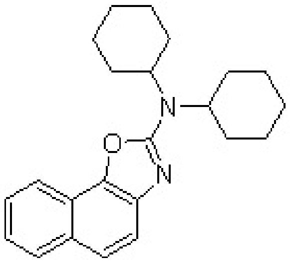
162.82
142.90
140.22
129.30
128.81
126.34
124.24
123.25
119.84
118.79
117.10
48.95
32.01
29.56
29.43
28.21
27.03
22.82
14.24
O
N
N
7e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.997
7.976
7.882
7.862
7.661
7.639
7.602
7.580
7.521
7.502
7.484
7.357
7.337
7.317
3.603
3.584
3.565
1.751
1.735
1.717
1.383
1.374
1.278
1.263
0.894
0.878
0.860
O
N
N
7f
1.00
1.03
1.10
1.07
1.11
1.13
4.40
4.35
6.99
21.48
6.19
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.
f1 (ppm)

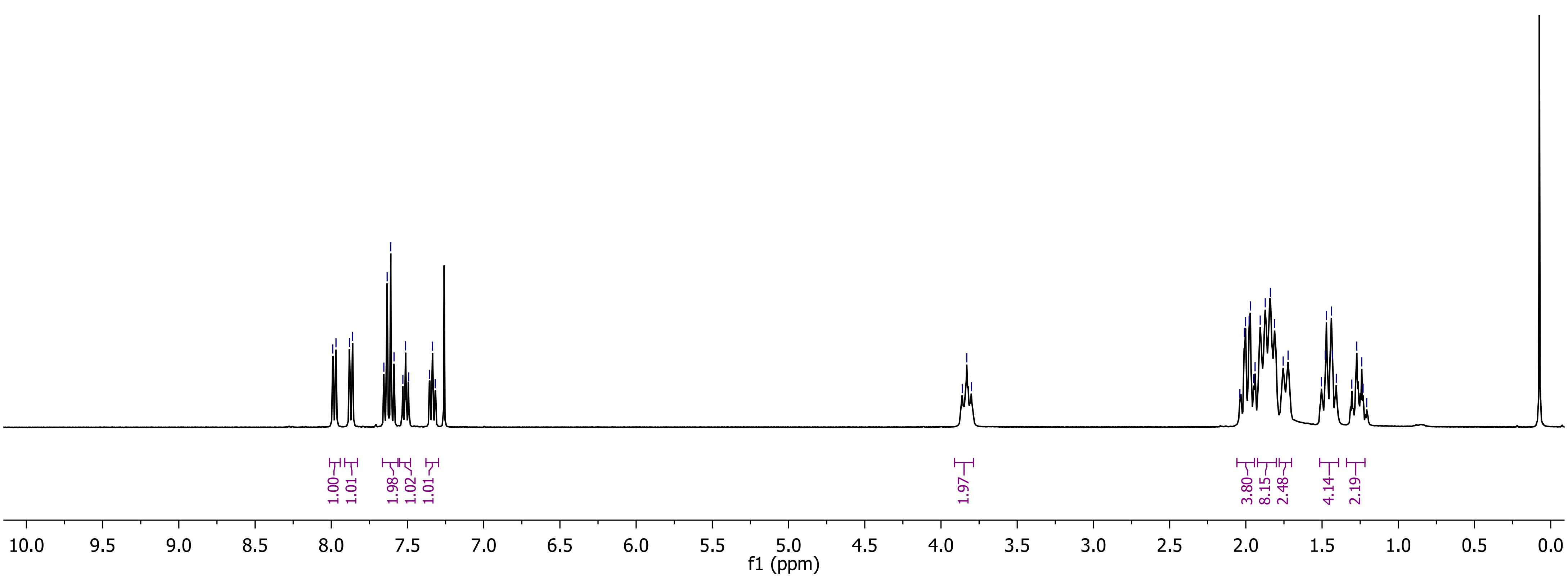


7f

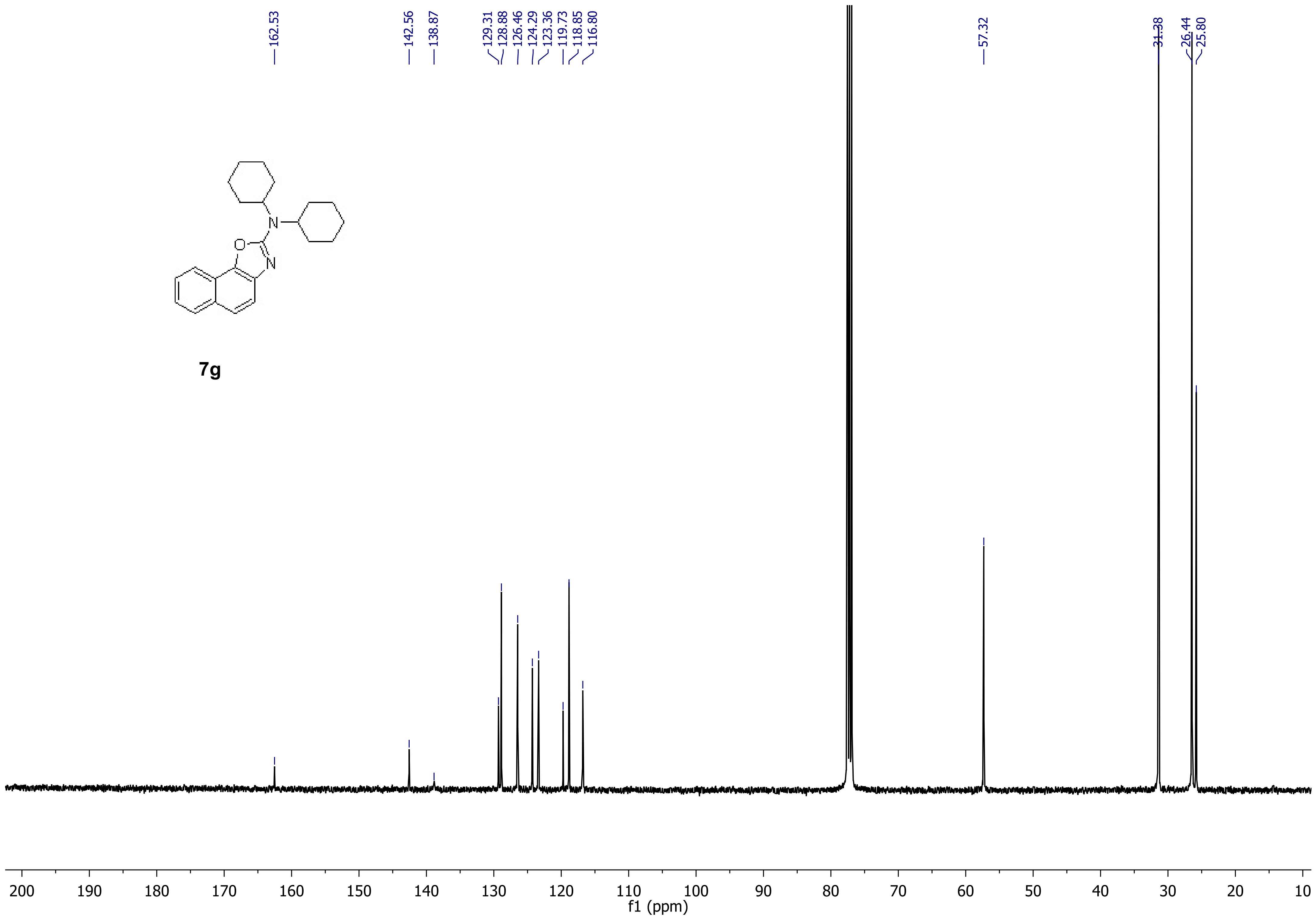

162.86
142.92
140.23
129.33
128.85
126.38
124.27
123.29
119.86
118.83
117.13
48.98
32.11
29.81
29.79
29.63
29.52
28.24
27.06
22.88
14.30
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

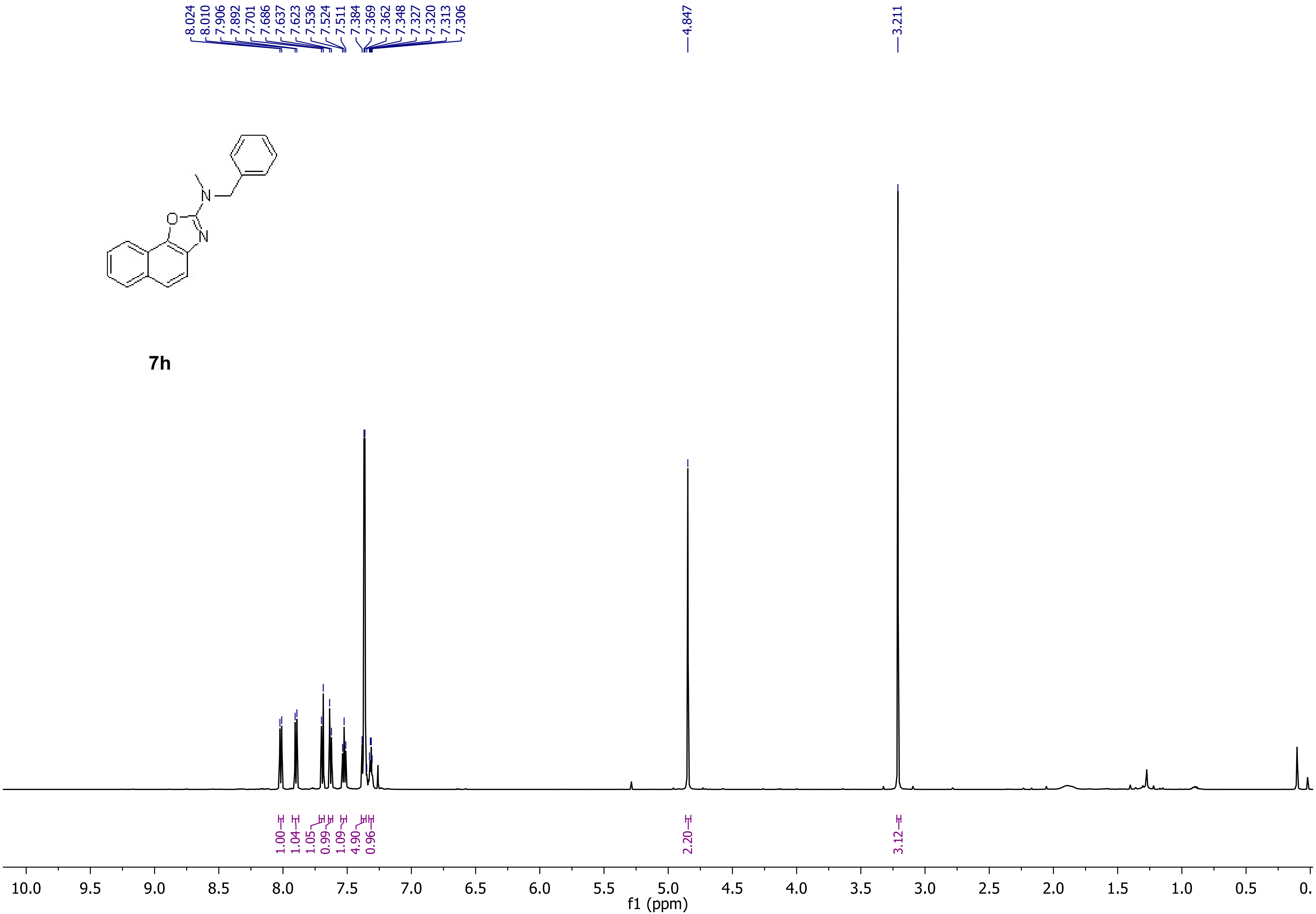


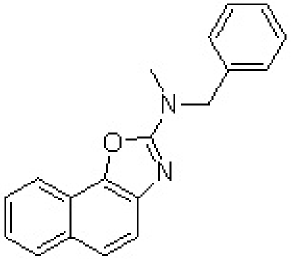
7g



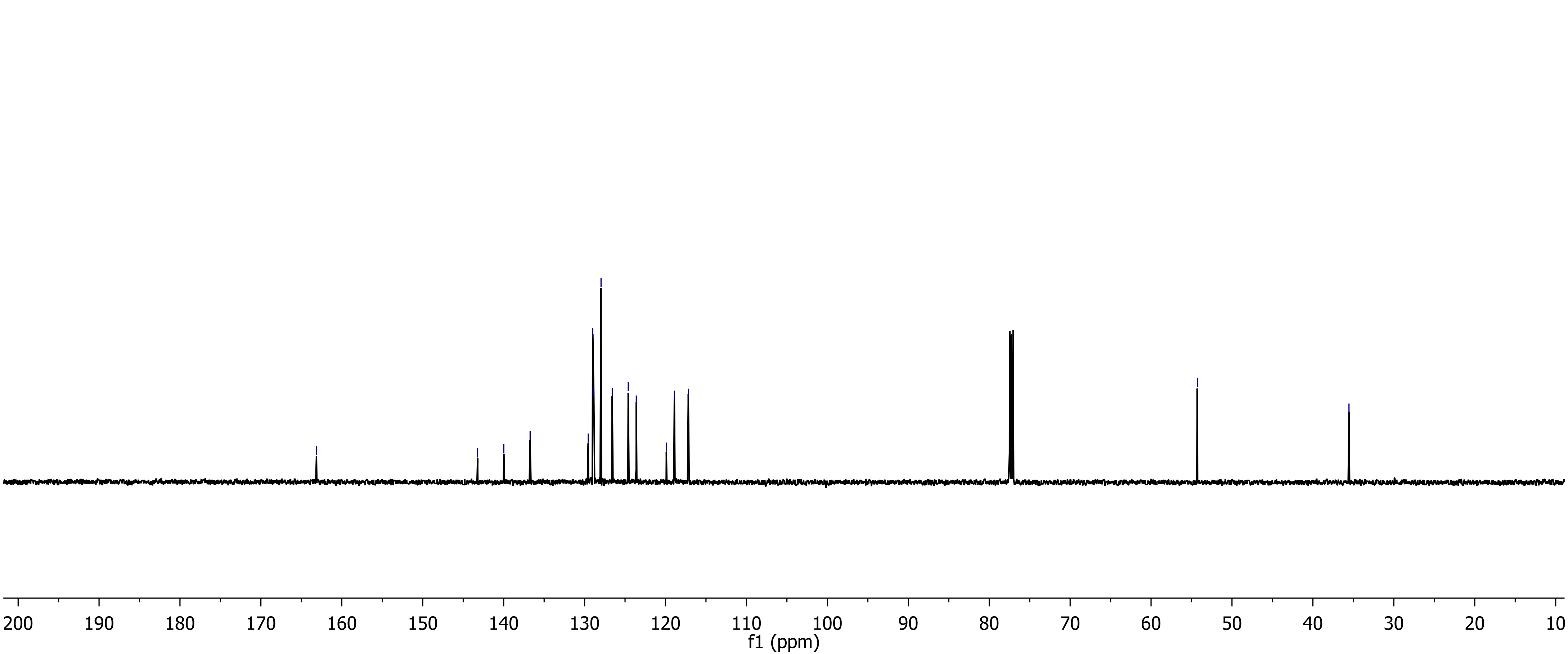
7.990
7.969
7.881
7.860
7.655
7.634
7.610
7.588
7.530
7.513
7.492
7.356
7.336
7.318
3.861
3.831
3.801
2.039
2.009
2.002
1.979
1.971
1.948
1.939
1.906
1.873
1.839
1.812
1.755
1.723
1.504
1.480
1.472
1.439
1.431
1.407
1.305
1.272
1.240
1.231
1.207
1.00
1.01
1.98
1.02
1.01
1.97
3.80
8.15
2.48
4.14
2.19
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
f1 (ppm)

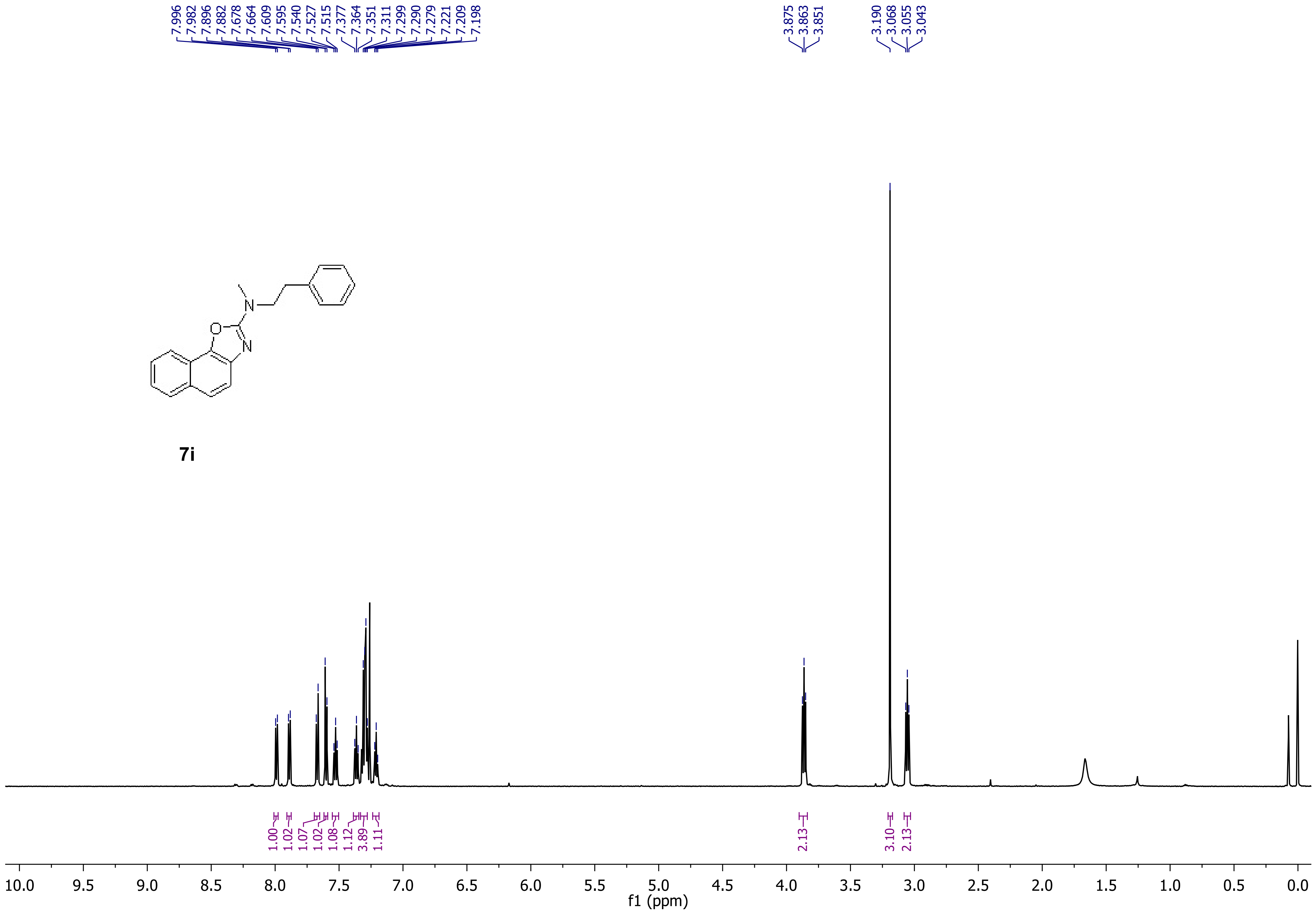

162.53
142.56
138.87
129.31
128.88
126.46
124.29
123.36
119.73
118.85
116.80
57.32
31.38
26.44
25.80
O
N
N
7g
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

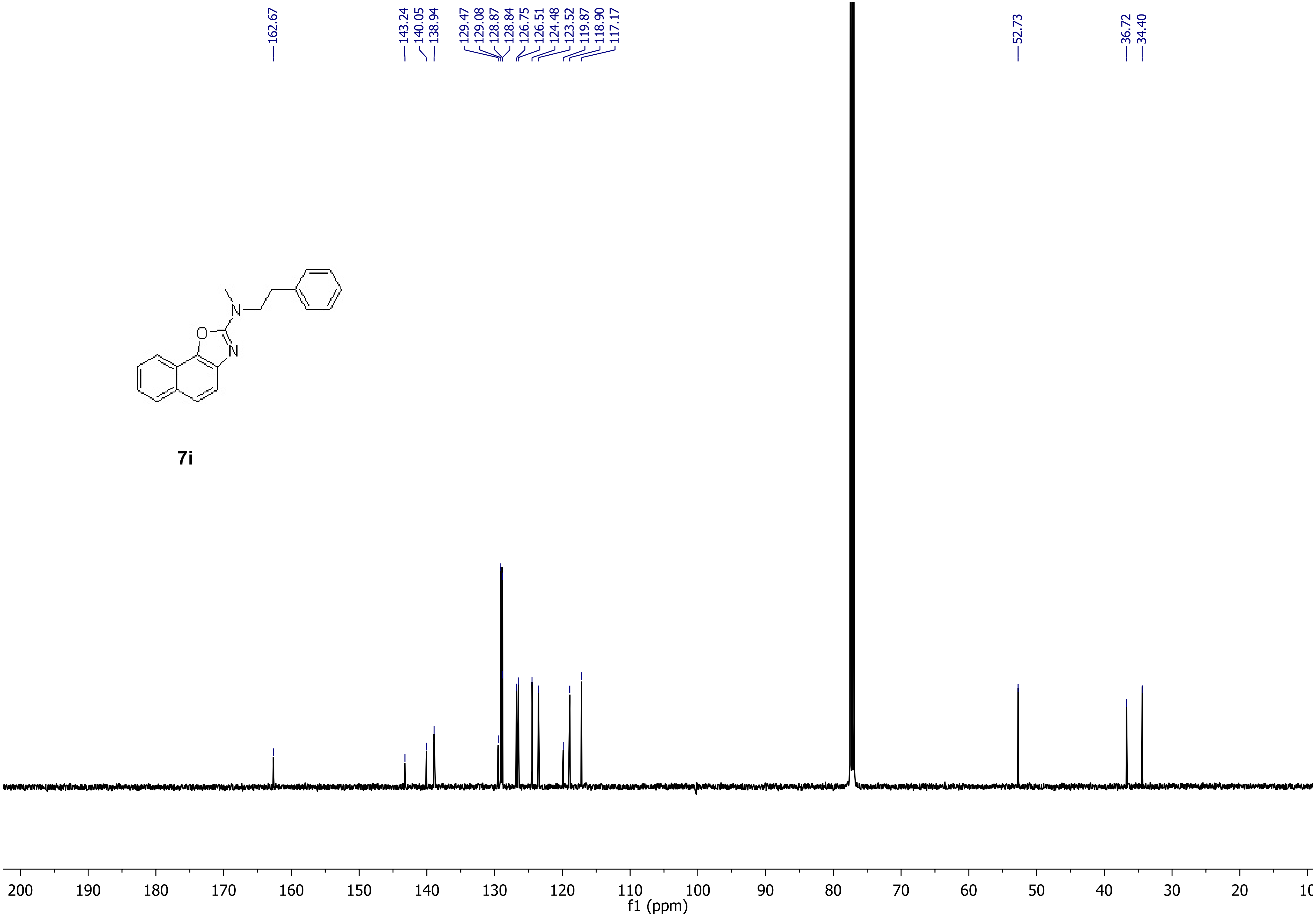

8.024
8.010
7.906
7.892
7.701
7.686
7.637
7.623
7.536
7.524
7.511
7.384
7.369
7.362
7.348
7.327
7.320
7.313
7.306
4.847
3.211
O
N
N
7h
1.00
1.04
1.05
0.99
1.09
4.90
0.96
2.20
3.12
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


O
N
N

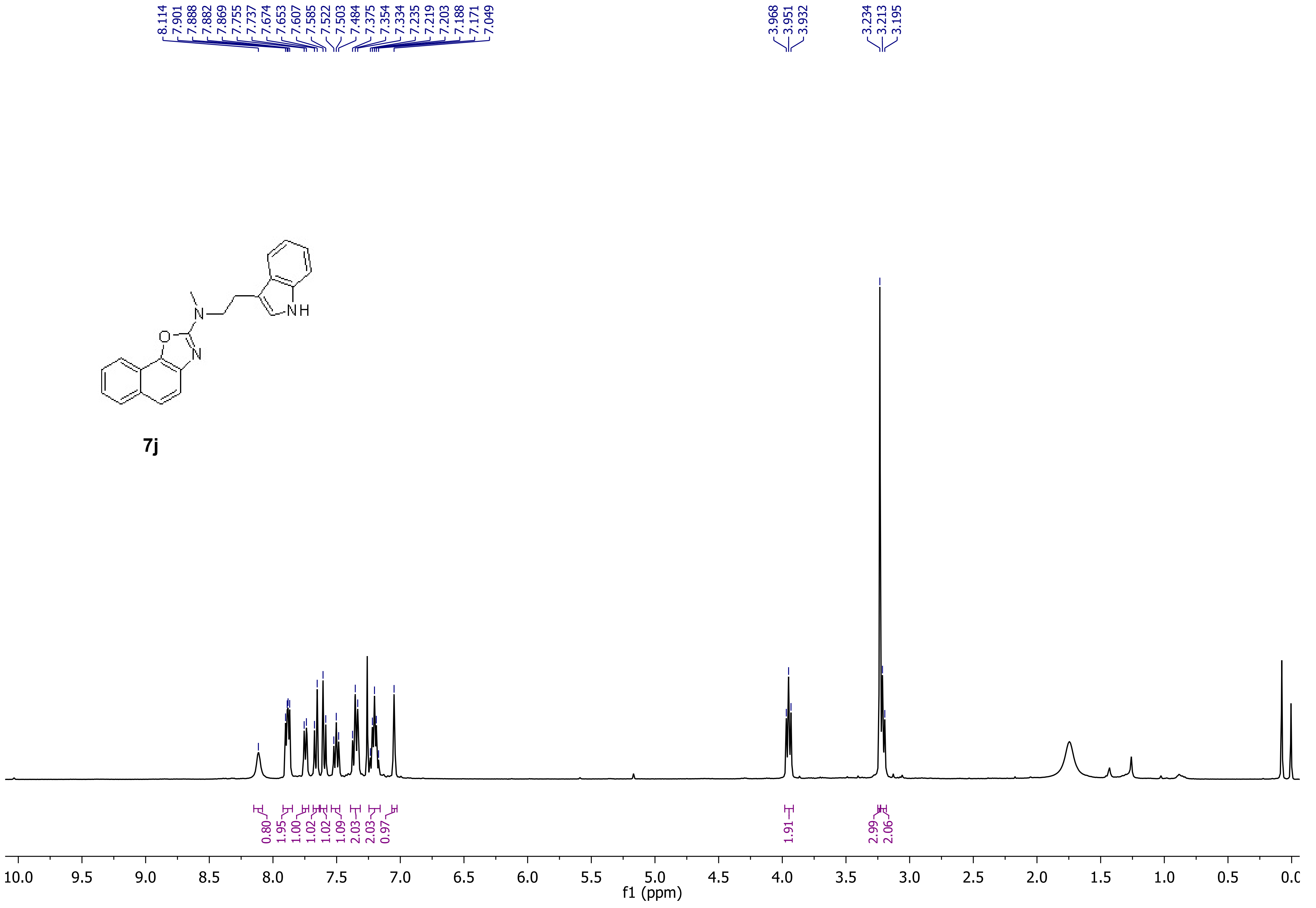
7h

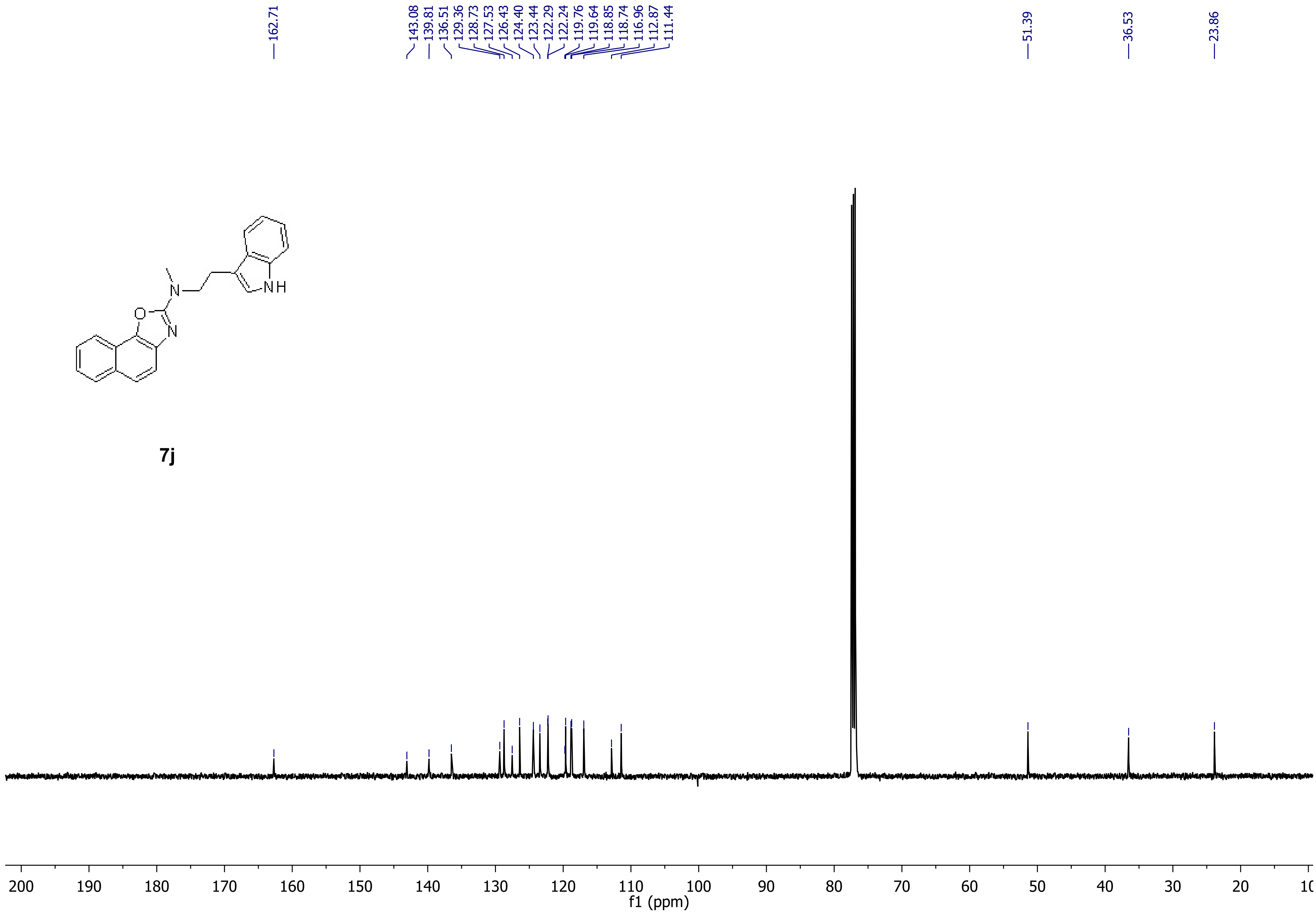

163.13
143.22
139.98
136.73
129.56
128.99
128.87
127.97
126.58
124.61
123.61
119.89
118.90
117.18
54.28
35.54
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.996
7.982
7.896
7.882
7.678
7.664
7.609
7.595
7.540
7.527
7.515
7.377
7.364
7.351
7.311
7.299
7.290
7.279
7.221
7.209
7.198
3.875
3.863
3.851
3.190
3.068
3.055
3.043
O
N
N
7i
1.00
1.02
1.07
1.02
1.08
1.12
3.89
1.11
2.13
3.10
2.13
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
f1 (ppm)

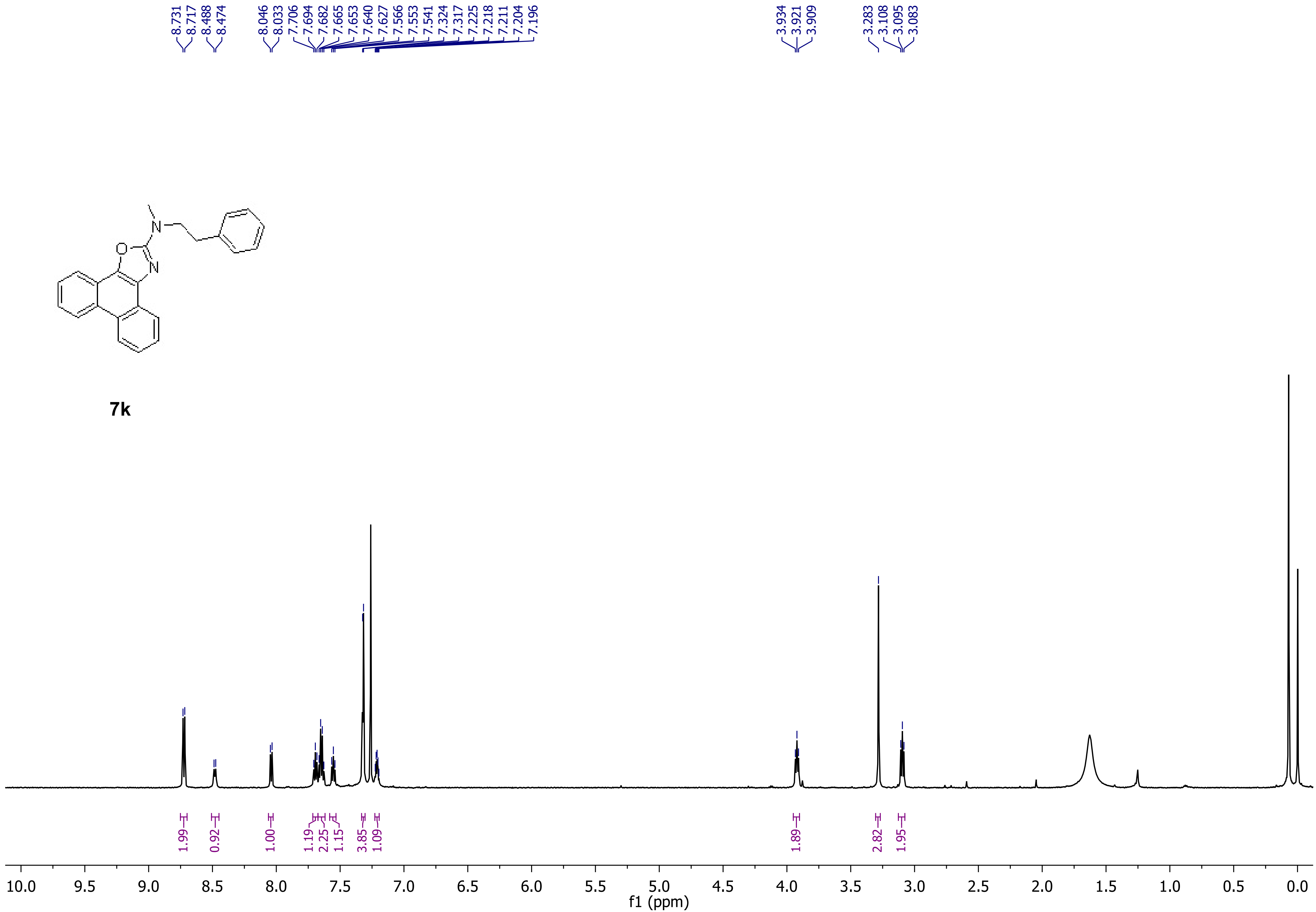

162.67
143.24
140.05
138.94
129.47
129.08
128.87
128.84
126.75
126.51
124.48
123.52
119.87
118.90
117.17
52.73
36.72
34.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

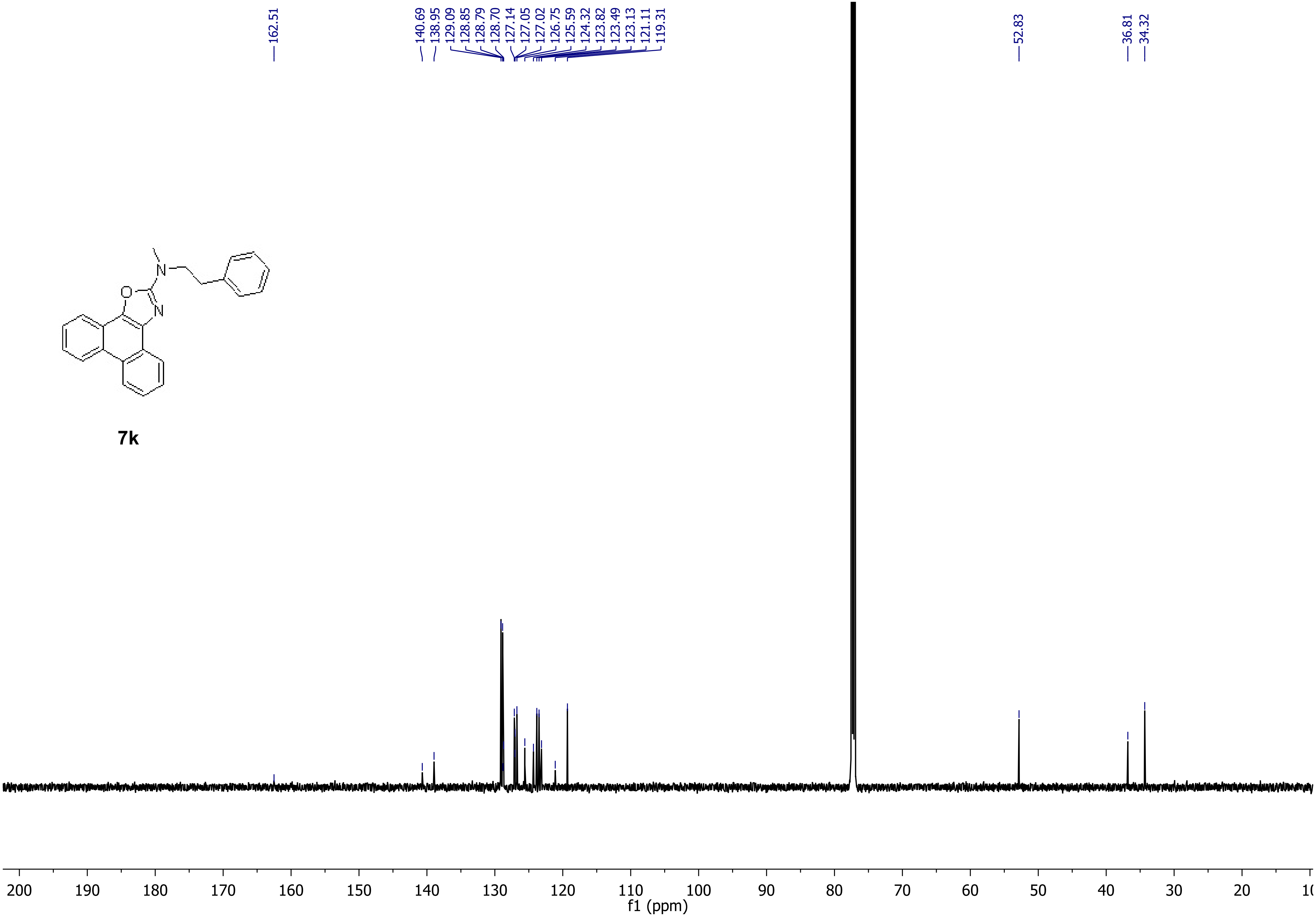
7i

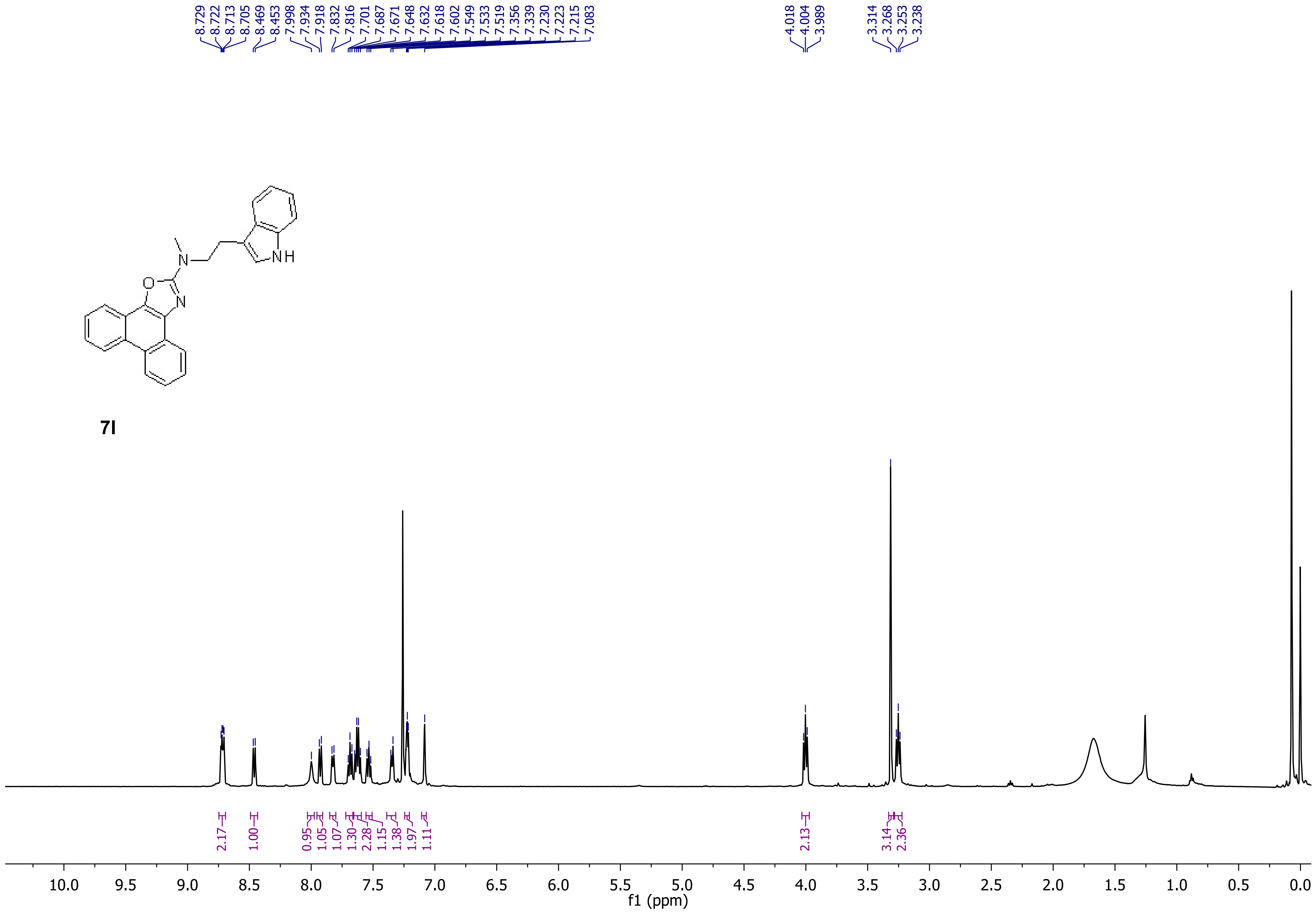

8.114
7.901
7.888
7.882
7.869
7.755
7.737
7.674
7.653
7.607
7.585
7.522
7.503
7.484
7.375
7.354
7.334
7.235
7.219
7.203
7.188
7.171
7.049
3.968
3.951
3.932
3.234
3.213
3.195
O
N
N
NH
7j
0.80
1.95
1.00
1.02
1.02
1.09
2.03
2.03
0.97
1.91
2.99
2.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


162.71
143.08
139.81
136.51
129.36
128.73
127.53
126.43
124.40
123.44
122.29
122.24
119.76
119.64
118.85
118.74
116.96
112.87
111.44
51.39
36.53
23.86
O
N
N
NH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

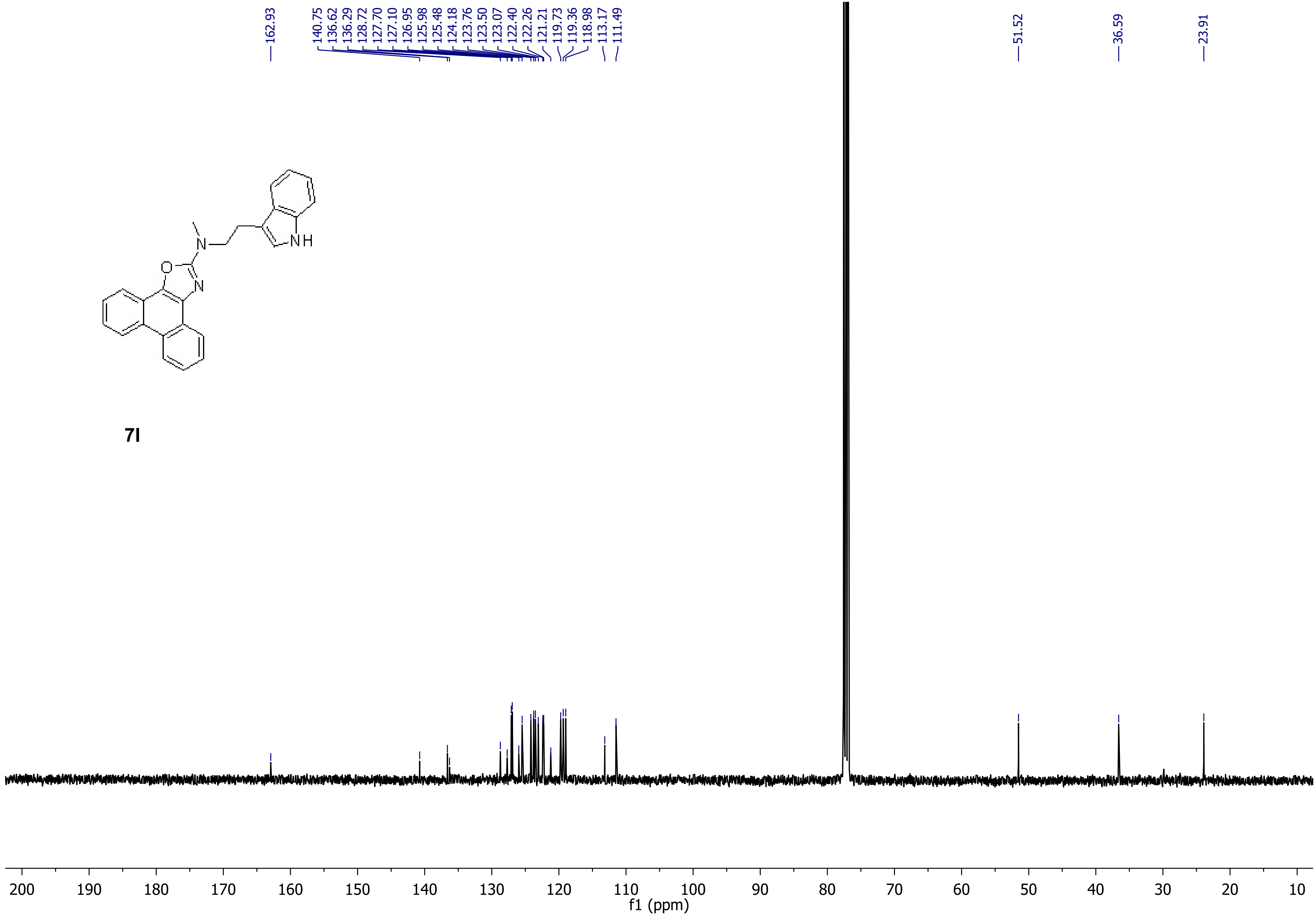
7j


8.731
8.717
8.488
8.474
8.046
8.033
7.706
7.694
7.682
7.665
7.653
7.640
7.627
7.566
7.553
7.541
7.324
7.317
7.225
7.218
7.211
7.204
7.196
3.934
3.921
3.909
3.283
3.108
3.095
3.083
O
N
N
7k
1.99
0.92
1.00
1.19
2.25
1.15
3.85
1.09
1.89
2.82
1.95
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
f1 (ppm)

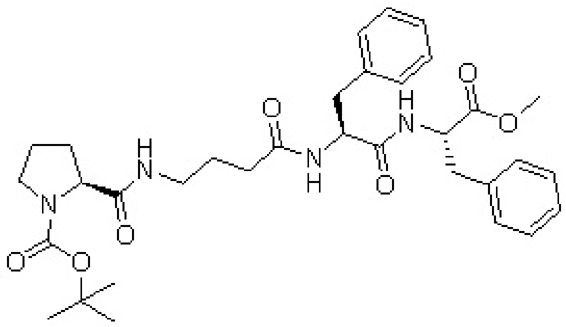

162.51
140.69
138.95
129.09
128.85
128.79
128.70
127.14
127.05
127.02
126.75
125.59
124.32
123.82
123.49
123.13
121.11
119.31
52.83
36.81
34.32
O
N
N
7k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


8.729
8.722
8.713
8.705
8.469
8.453
7.998
7.934
7.918
7.832
7.816
7.701
7.687
7.671
7.648
7.632
7.618
7.602
7.549
7.533
7.519
7.356
7.339
7.230
7.223
7.215
7.083
4.018
4.004
3.989
3.314
3.268
3.253
3.238
N
O
N
NH
2.17
1.00
0.95
1.05
1.07
1.30
2.28
1.15
1.38
1.97
1.11
2.13
3.14
2.36
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
f1 (ppm)

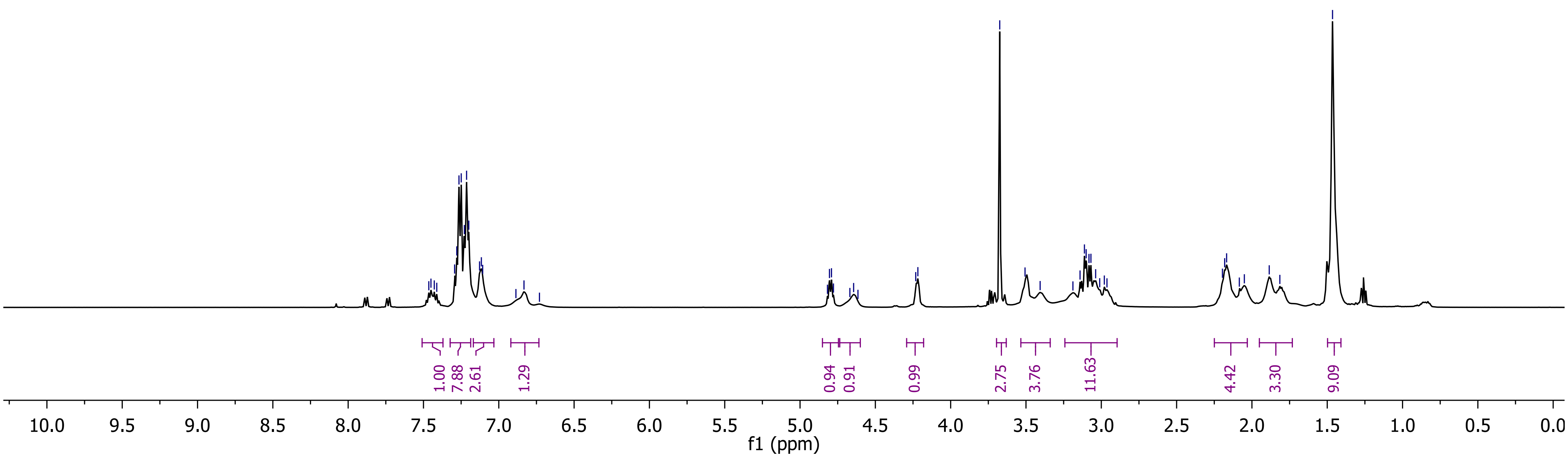
7l

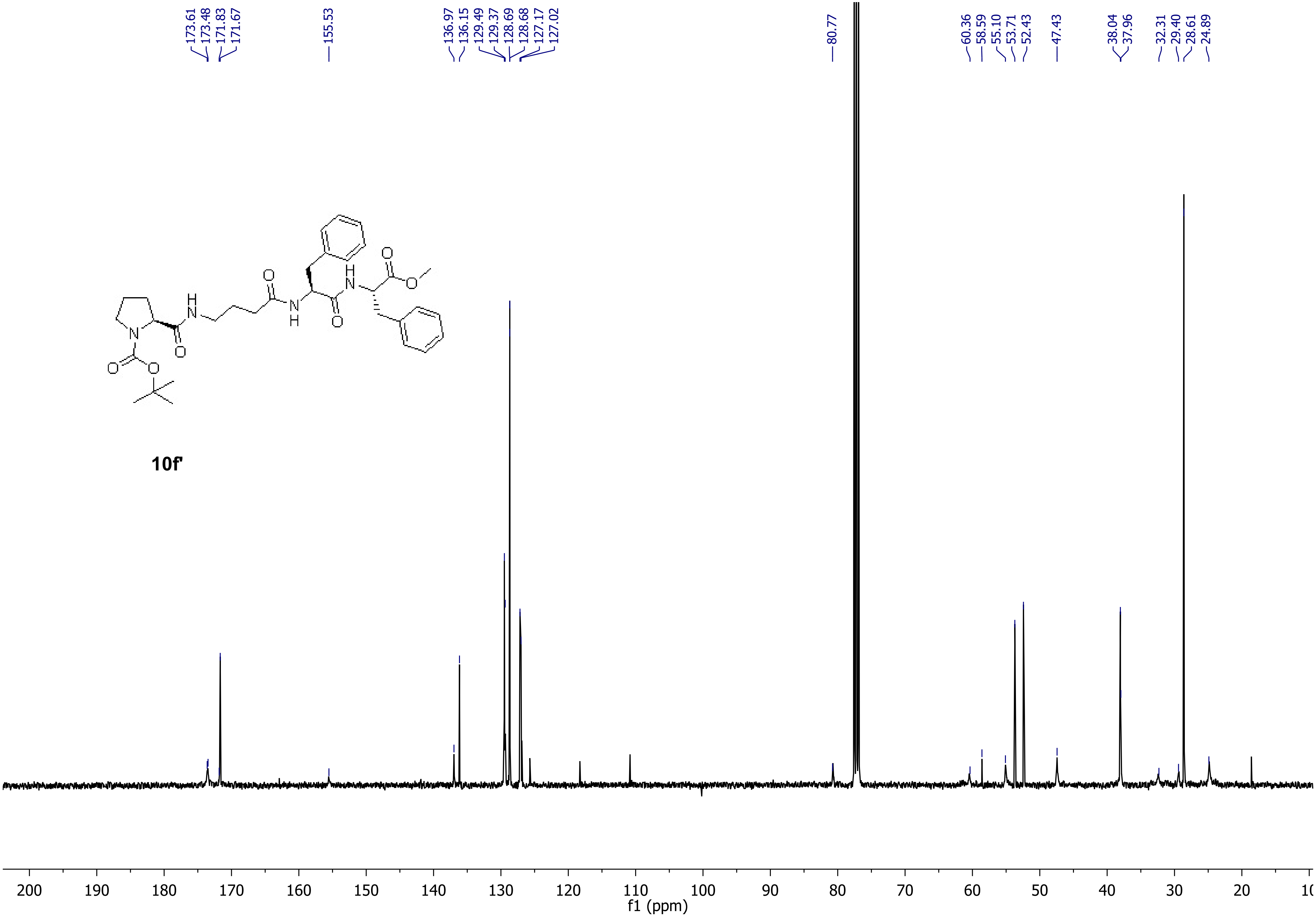


162.93
140.75
136.62
136.29
128.72
127.70
127.10
126.95
125.98
125.48
124.18
123.76
123.50
123.07
122.40
122.26
121.21
119.73
119.36
118.98
113.17
111.49
51.52
36.59
23.91
O
N
N
NH
7l
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

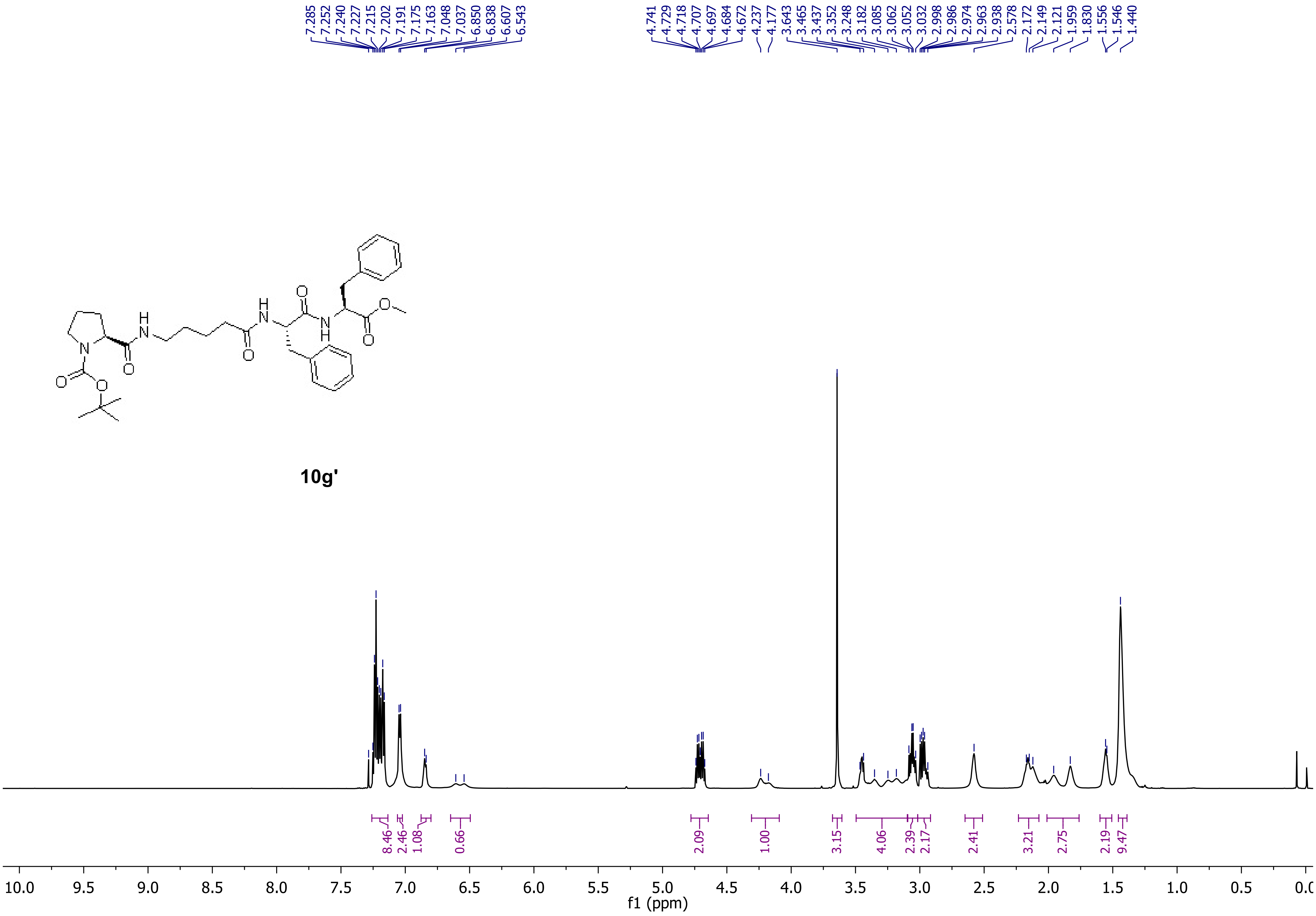


10f'

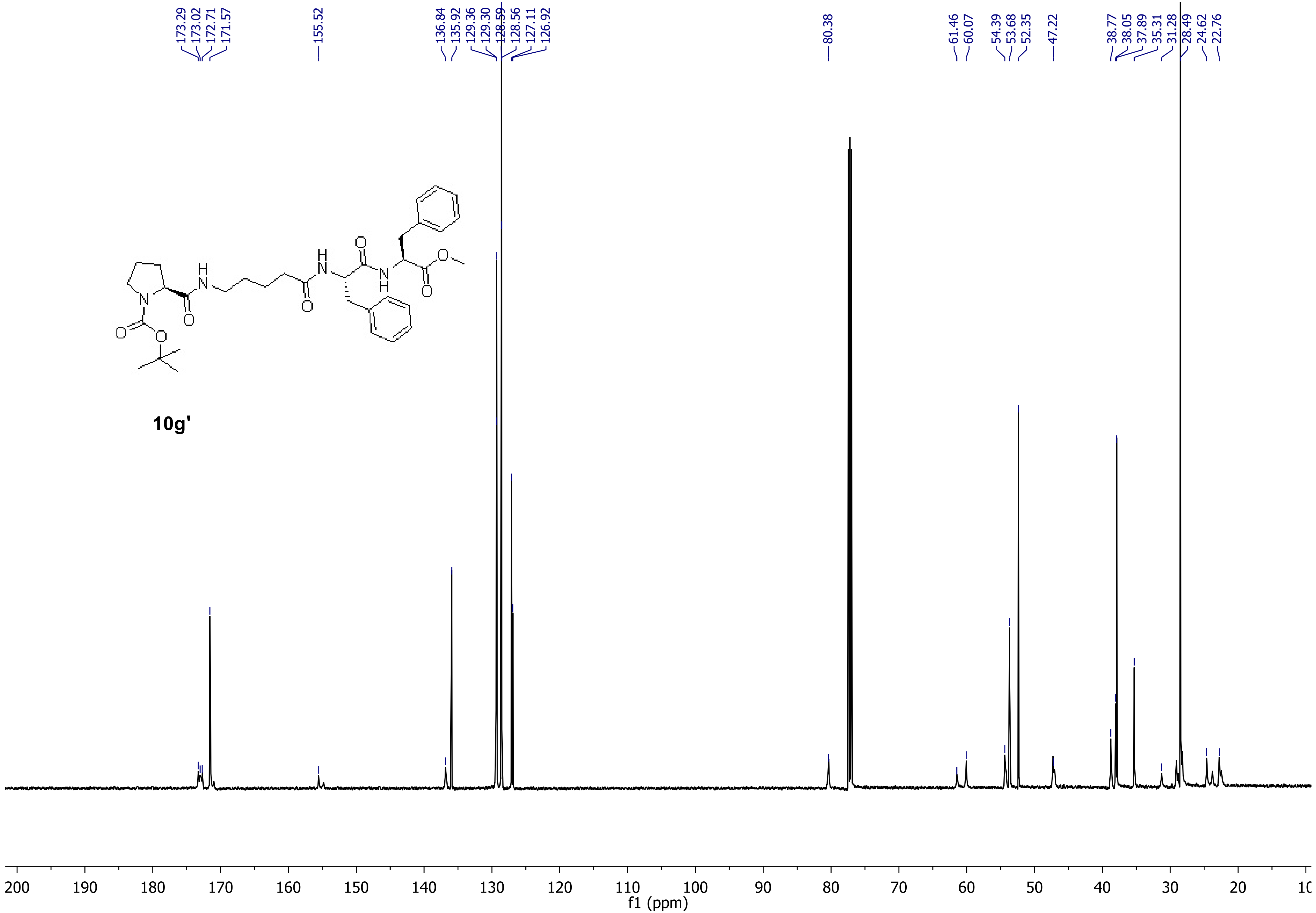

7.465
7.450
7.428
7.412
7.293
7.279
7.264
7.249
7.229
7.214
7.199
7.128
7.116
7.107
6.886
6.833
6.730
4.818
4.805
4.791
4.778
4.669
4.644
4.616
4.232
4.218
3.674
3.506
3.406
3.188
3.141
3.112
3.101
3.082
3.069
3.038
3.010
2.980
2.962
2.196
2.181
2.168
2.084
2.050
1.885
1.815
1.465
1.00
7.88
2.61
1.29
0.94
0.91
0.99
2.75
3.76
11.63
4.42
3.30
9.09
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
f1 (ppm)

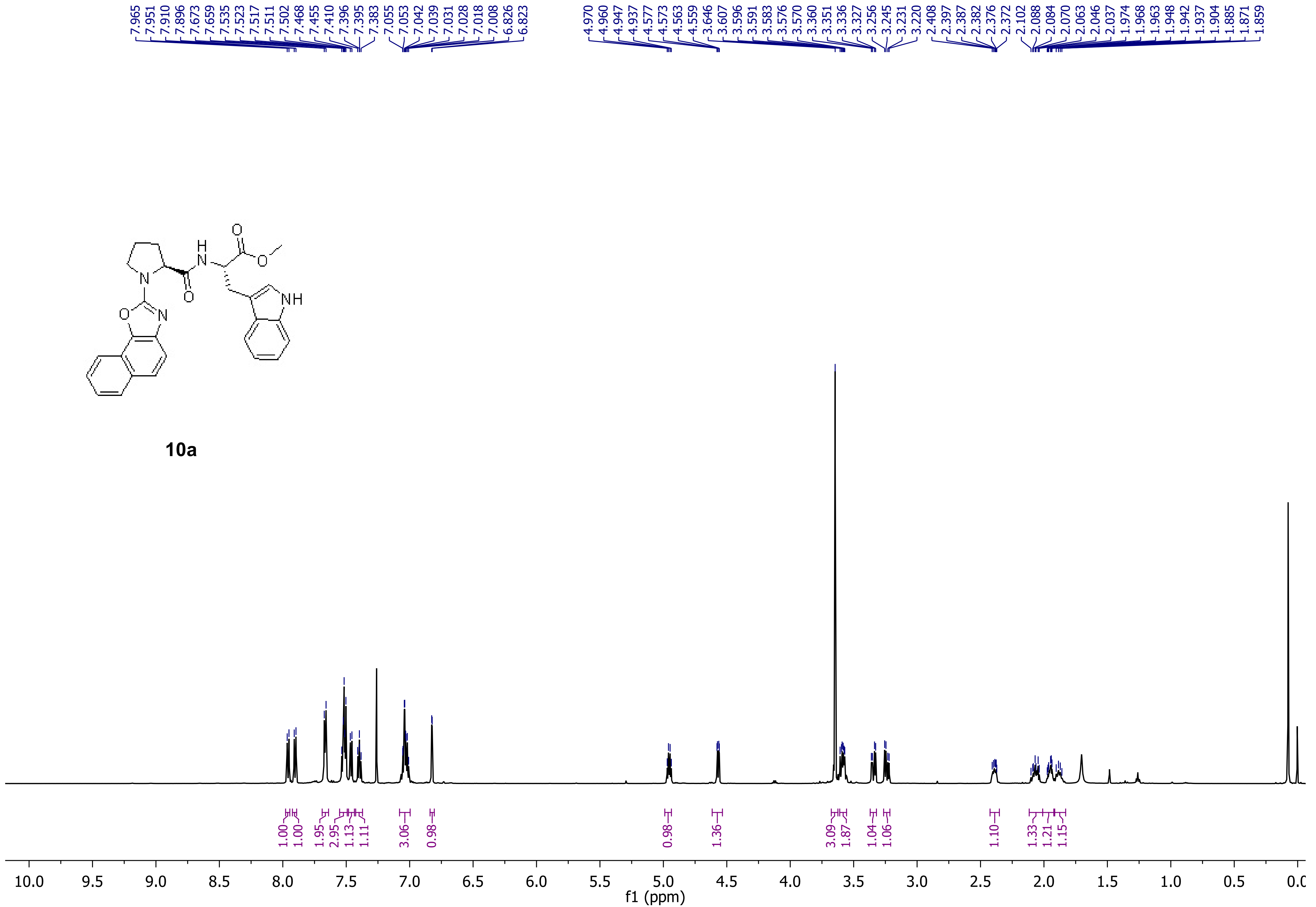


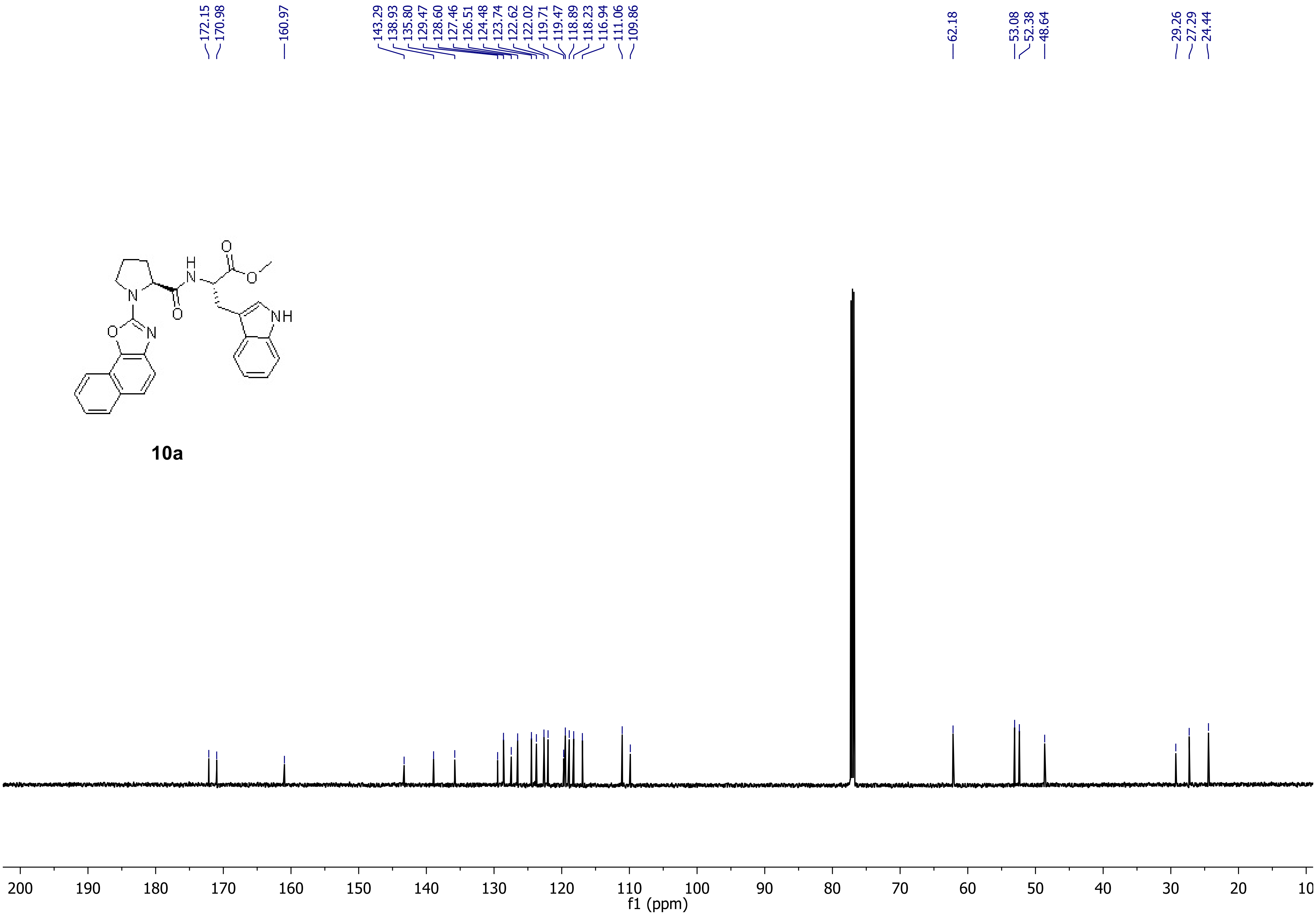
173.61
173.48
171.83
171.67
155.53
136.97
136.15
129.49
129.37
128.69
128.68
127.17
127.02
80.77
60.36
58.59
55.10
53.71
52.43
47.43
38.04
37.96
32.31
29.40
28.61
24.89
10f'
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.285
7.252
7.240
7.227
7.215
7.202
7.191
7.175
7.163
7.048
7.037
6.850
6.838
6.607
6.543
4.741
4.729
4.718
4.707
4.697
4.684
4.672
4.237
4.177
3.643
3.465
3.437
3.352
3.248
3.182
3.085
3.062
3.052
3.032
2.998
2.986
2.974
2.963
2.938
2.578
2.172
2.149
2.121
1.959
1.830
1.556
1.546
1.440
8.46
2.46
1.08
0.66
2.09
1.00
3.15
4.06
2.39
2.17
2.41
3.21
2.75
2.19
9.47
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
f1 (ppm)

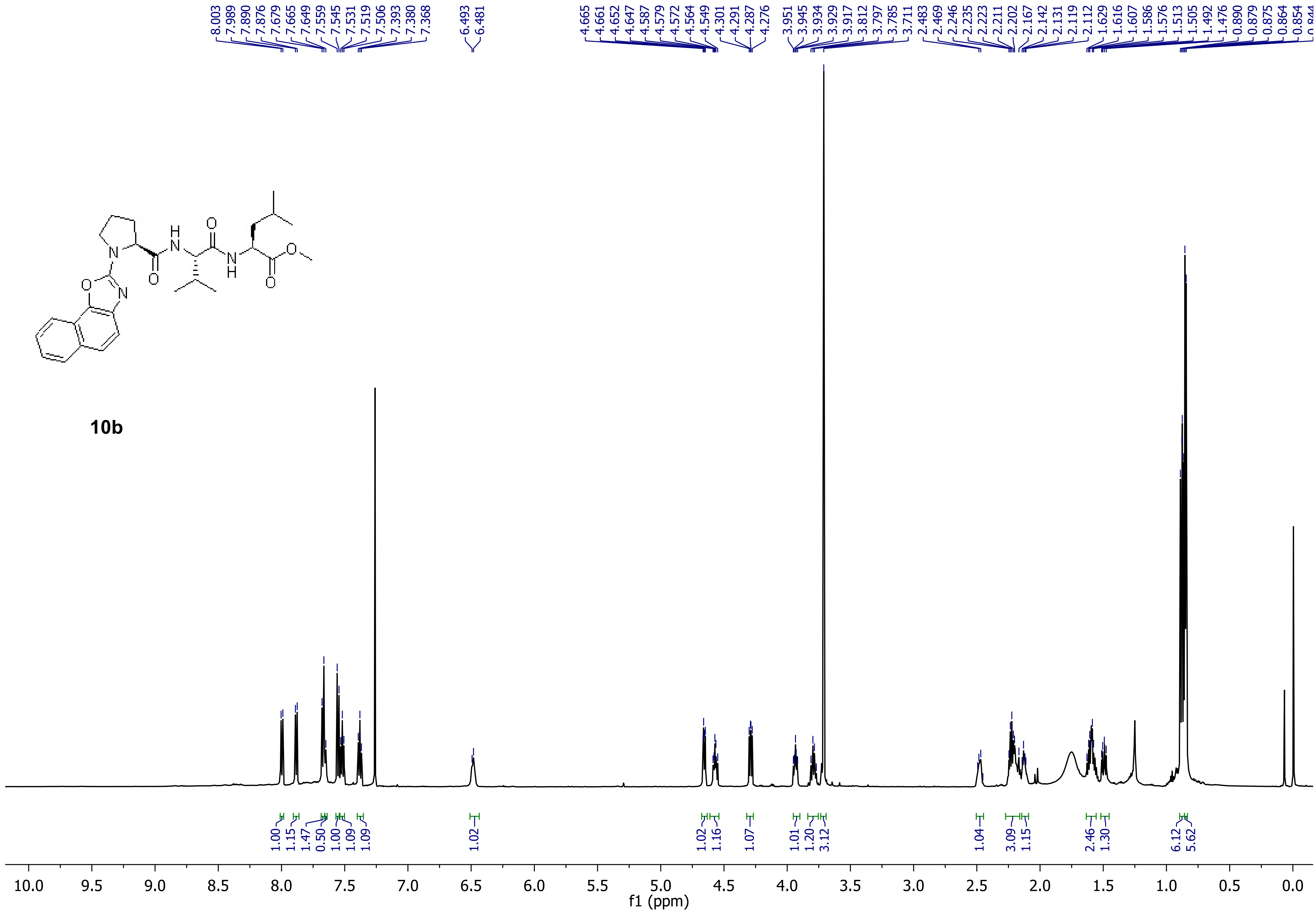
10g'

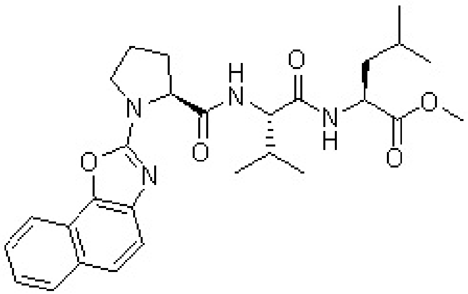

173.29
173.02
172.71
171.57
155.52
136.84
135.92
129.36
129.30
128.59
128.56
127.11
126.92
80.38
61.46
60.07
54.39
53.68
52.35
47.22
38.77
38.05
37.89
35.31
31.28
28.49
24.62
22.76
O
H
N
O
N
H
N
O
O
N
O
O
O
10g'
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.965 7.951 7.910 7.896 7.673 7.659 7.535 7.523 7.517 7.511 7.502 7.468 7.455 7.410 7.396 7.395 7.383 7.055 7.053 7.042 7.039 7.031 7.028 7.018 7.008 6.826 6.823
4.970 4.960 4.947 4.937 4.577 4.573 4.563 4.559 3.646 3.607 3.596 3.591 3.583 3.576 3.570 3.360 3.351 3.336 3.327 3.256 3.245 3.231 3.220 2.408 2.397 2.387 2.382 2.376 2.372 2.102 2.088 2.084 2.070 2.063 2.046 2.037 1.974 1.968 1.963 1.948 1.942 1.937 1.904 1.885 1.871 1.859
H
N
O
O
N
O
N
NH
10a
1.00 1.00 1.95 2.95 1.13 1.11 3.06 0.98 0.98 1.36 3.09 1.87 1.04 1.06 1.10 1.33 1.21 1.15
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
f1 (ppm)

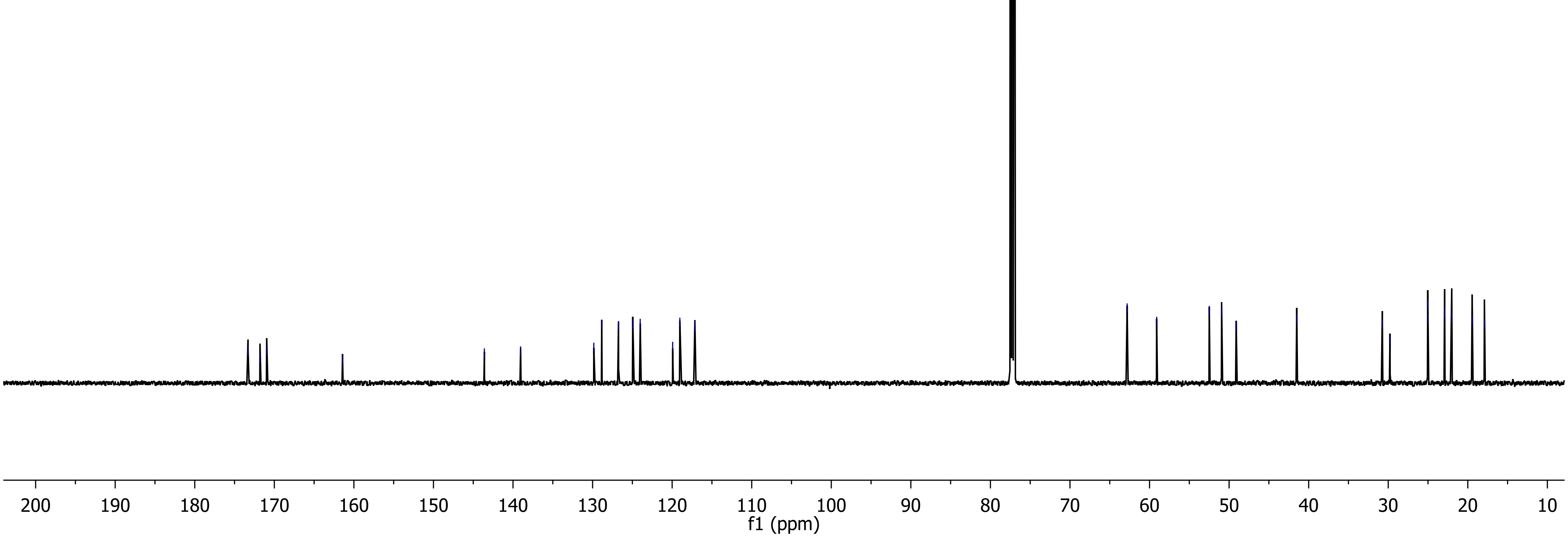


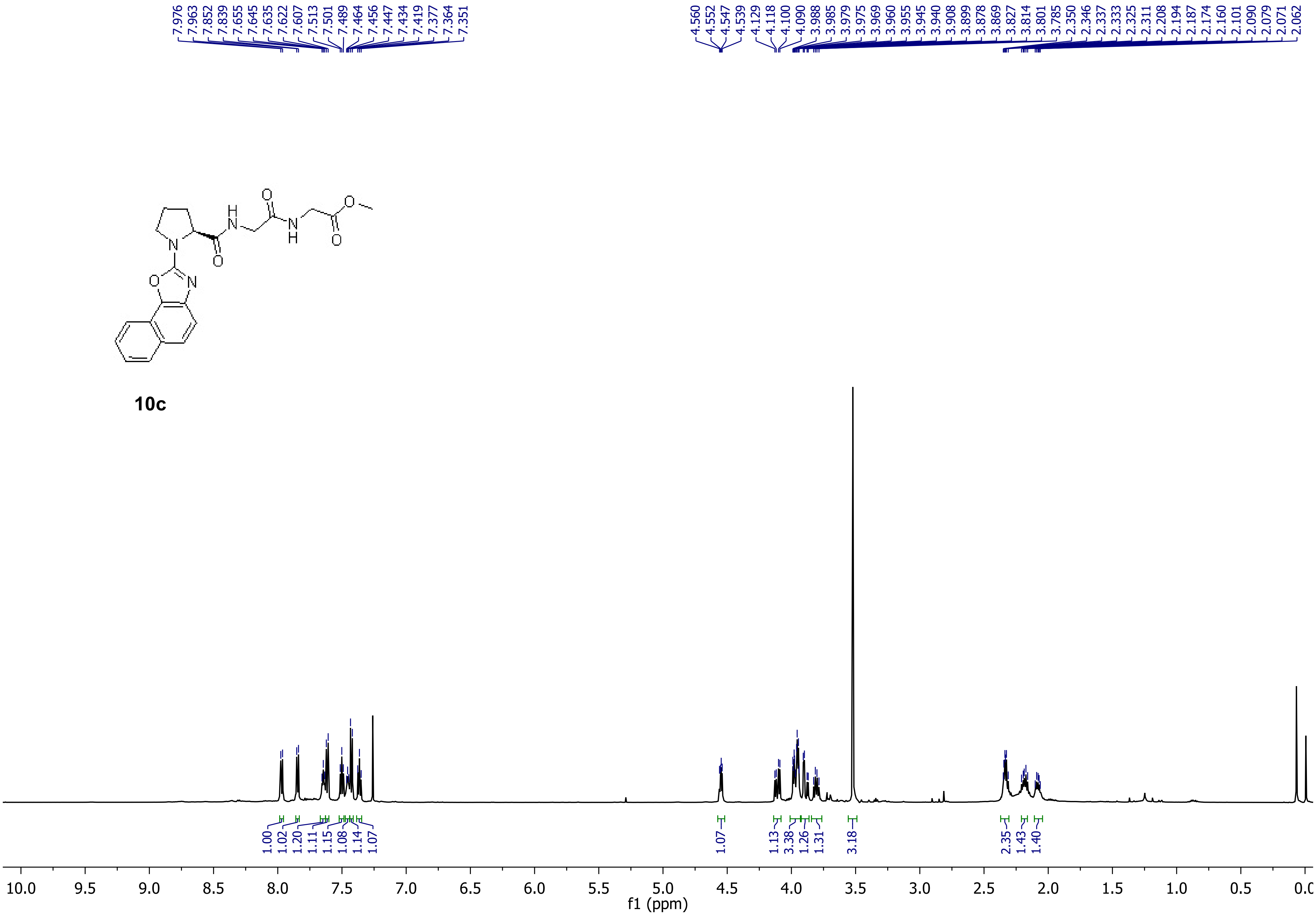
172.15
170.98
160.97
143.29
138.93
135.80
129.47
128.60
127.46
126.51
124.48
123.74
122.62
122.02
119.71
119.47
118.89
118.23
116.94
111.06
109.86
62.18
53.08
52.38
48.64
29.26
27.29
24.44
O
H
N
O
N
O
NH
O
N
10a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

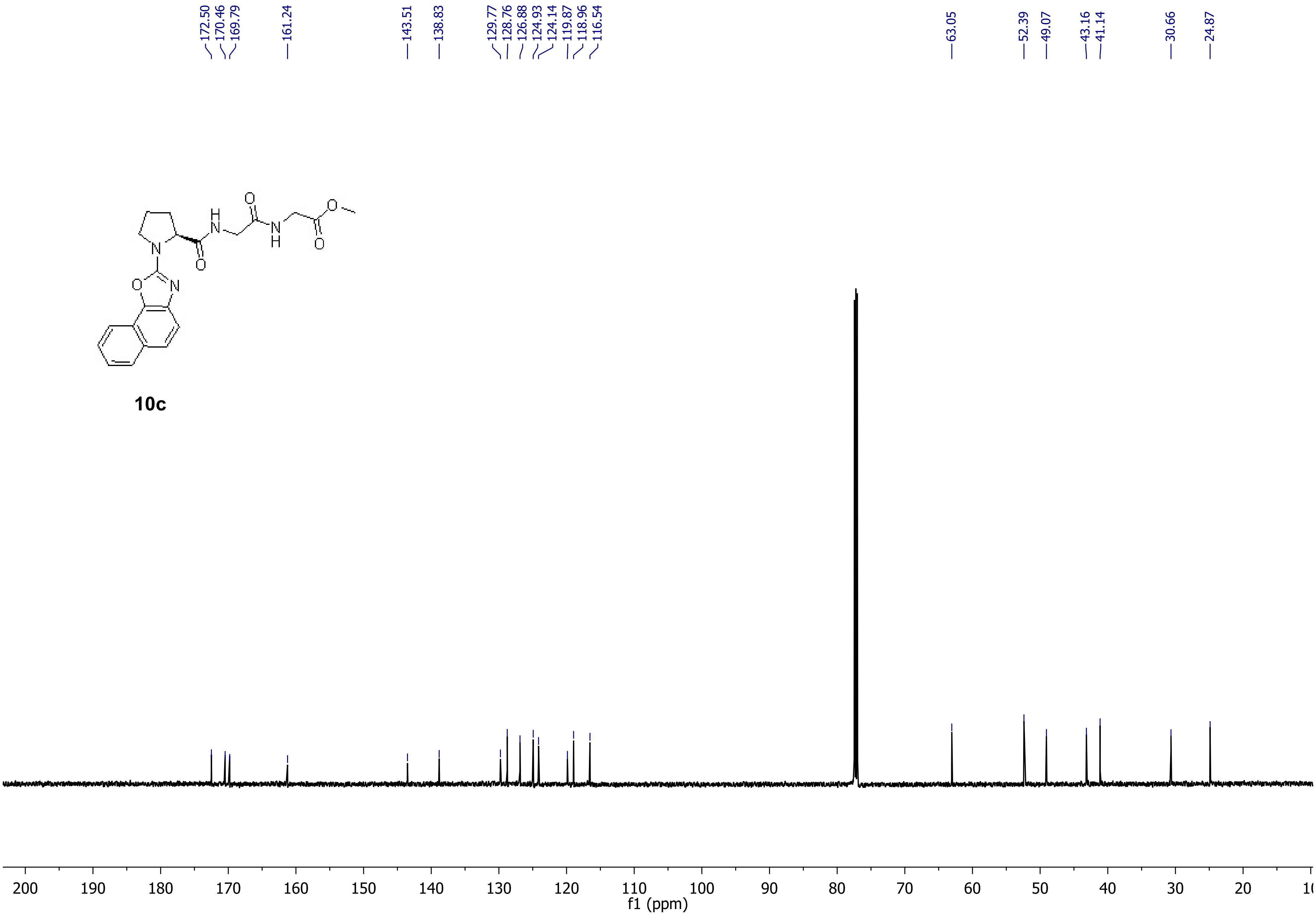

8.003
7.989
7.890
7.876
7.679
7.665
7.649
7.559
7.545
7.531
7.519
7.506
7.393
7.380
7.368
6.493
6.481
4.665
4.661
4.652
4.647
4.587
4.579
4.572
4.564
4.549
4.301
4.291
4.287
4.276
3.951
3.945
3.934
3.929
3.917
3.812
3.797
3.785
3.711
2.483
2.469
2.246
2.235
2.223
2.211
2.202
2.167
2.142
2.131
2.119
2.112
1.629
1.616
1.607
1.586
1.576
1.513
1.505
1.492
1.476
0.890
0.879
0.875
0.864
0.854
10b
1.00
1.15
1.47
0.50
1.00
1.09
1.09
1.02
1.02
1.16
1.07
1.01
1.20
3.12
1.04
3.09
1.15
2.46
1.30
6.12
5.62
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
f1 (ppm)

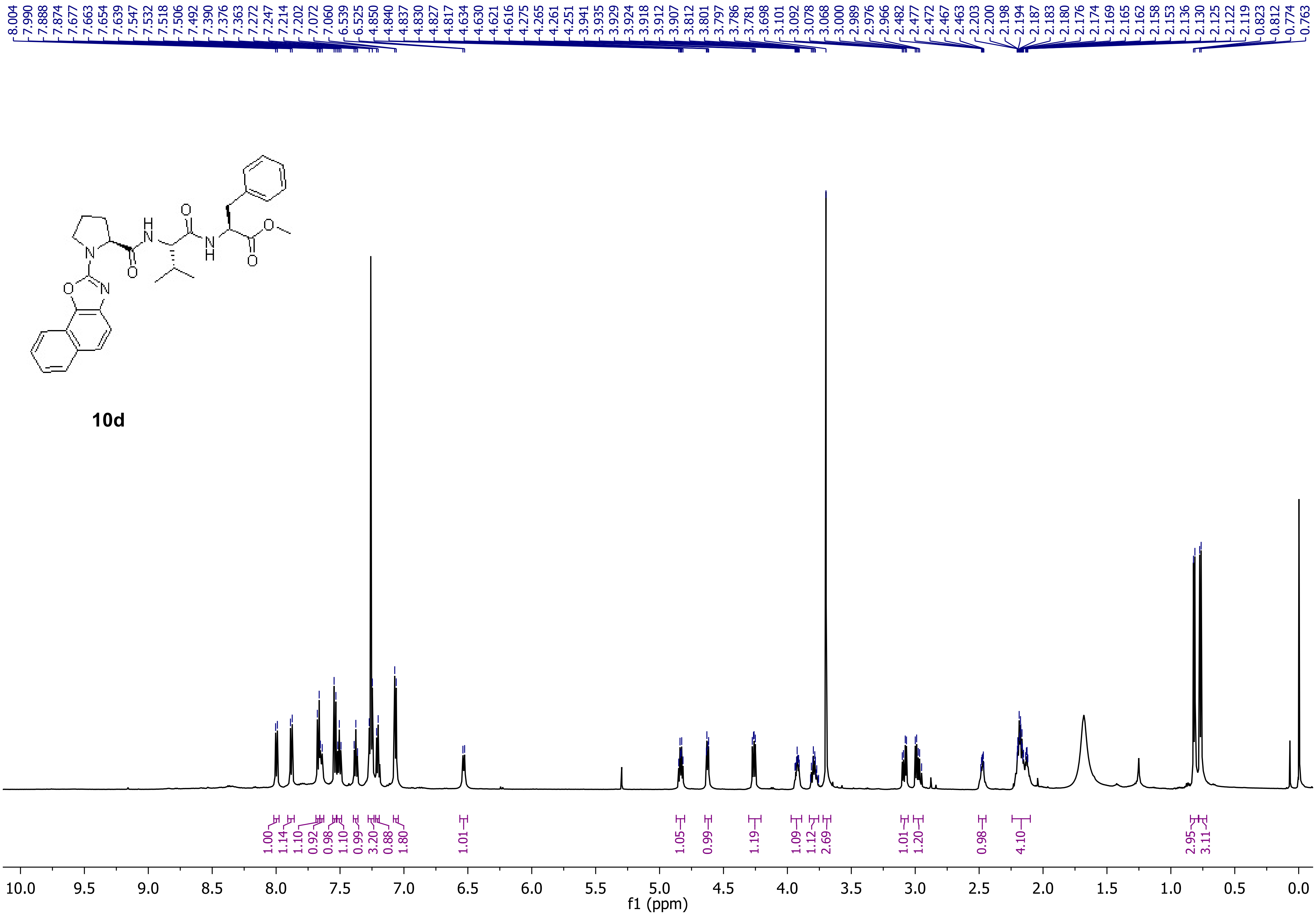


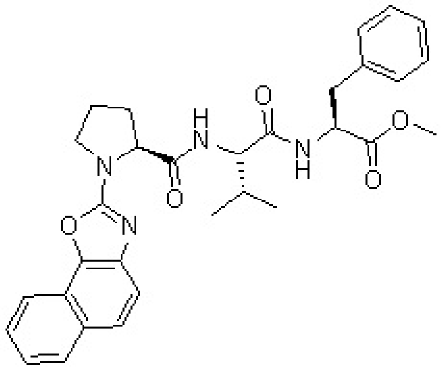
10b


173.31
171.81
170.96
161.43
143.60
139.05
129.85
128.85
126.74
124.96
124.02
119.94
119.03
117.15
62.82
59.10
52.49
50.94
49.11
41.50
30.74
29.77
25.03
25.00
22.91
22.01
19.45
17.91
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

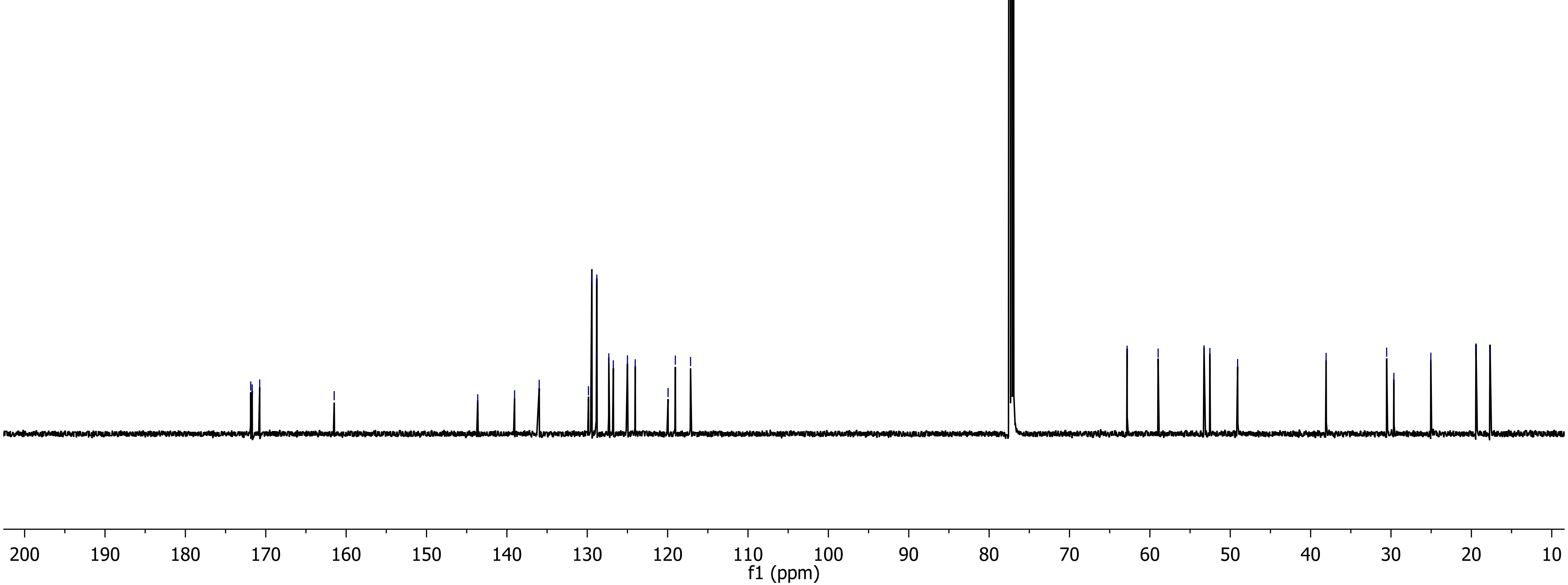

7.976 7.963 7.852 7.839 7.655 7.645 7.635 7.622 7.607 7.513 7.501 7.489 7.464 7.456 7.447 7.434 7.419 7.377 7.364 7.351
4.560 4.552 4.547 4.539 4.129 4.118 4.100 4.090 3.988 3.985 3.979 3.975 3.969 3.960 3.955 3.945 3.940 3.908 3.899 3.878 3.869 3.827 3.814 3.801 3.785 2.350 2.346 2.337 2.333 2.325 2.311 2.208 2.194 2.187 2.174 2.160 2.101 2.090 2.079 2.071 2.062
10c
1.00 1.02 1.20 1.11 1.15 1.08 1.14 1.07
1.07
1.13 3.38 1.26 1.31
3.18
2.35 1.43 1.40
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
f1 (ppm)

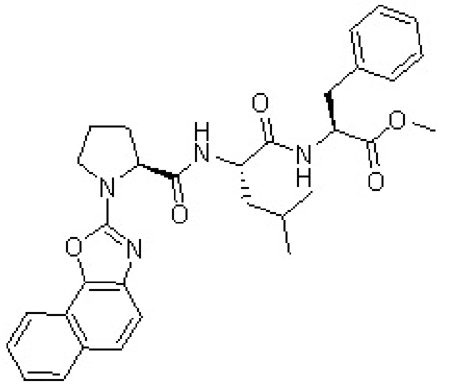

172.50
170.46
169.79
161.24
143.51
138.83
129.77
128.76
126.88
124.93
124.14
119.87
118.96
116.54
63.05
52.39
49.07
43.16
41.14
30.66
24.87
10c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


8.004 7.990 7.888 7.874 7.677 7.663 7.654 7.639 7.547 7.532 7.518 7.506 7.492 7.390 7.376 7.363 7.272 7.247 7.214 7.202 7.072 7.060 6.539 6.525 4.850 4.840 4.837 4.830 4.827 4.817 4.634 4.630 4.621 4.616 4.275 4.265 4.261 4.251 3.941 3.935 3.929 3.924 3.918 3.912 3.907 3.812 3.801 3.797 3.786 3.781 3.698 3.101 3.092 3.078 3.068 3.000 2.989 2.976 2.966 2.482 2.477 2.472 2.467 2.463 2.203 2.200 2.198 2.194 2.187 2.183 2.180 2.176 2.174 2.169 2.165 2.162 2.158 2.153 2.136 2.130 2.125 2.122 2.119 0.823 0.812 0.774 0.763
10d
1.00 1.14 1.10 0.92 0.98 1.10 0.99 3.20 0.88 1.80 1.01 1.05 0.99 1.19 1.09 1.12 2.69 1.01 1.20 0.98 4.10 2.95 3.11
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
f1 (ppm)



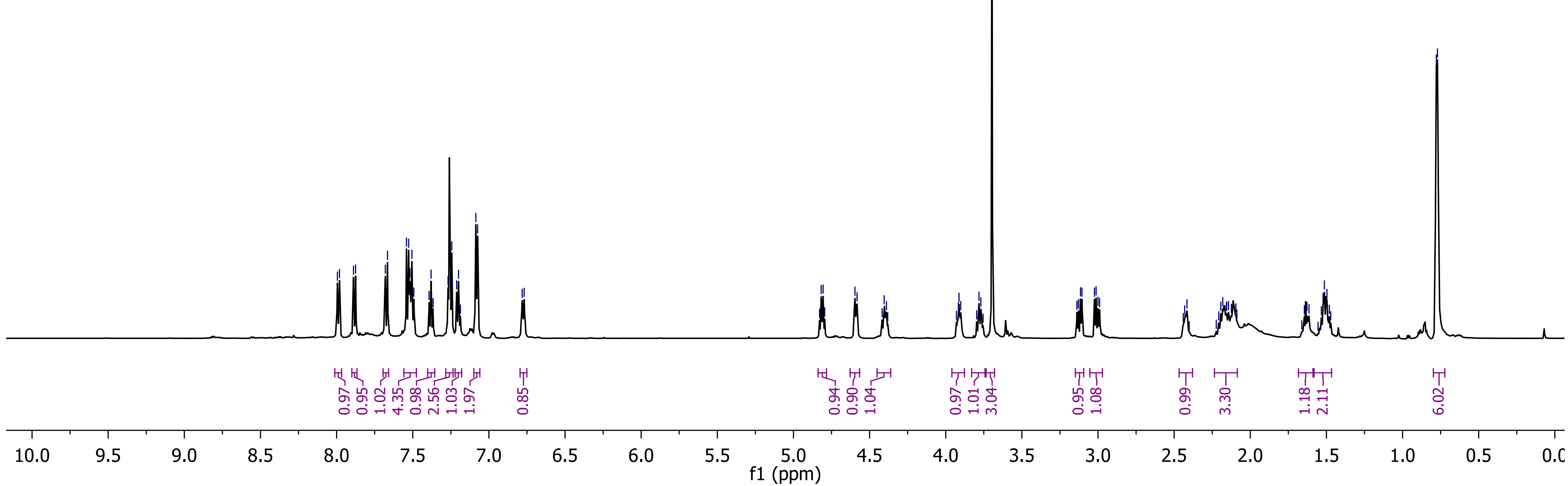
10d


171.87
171.69
170.76
161.49
143.63
139.04
135.98
129.85
129.43
128.86
128.81
127.32
126.76
125.00
124.03
119.95
119.04
117.15
62.83
58.97
53.26
52.54
49.08
38.07
30.54
29.64
25.04
19.42
17.68
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

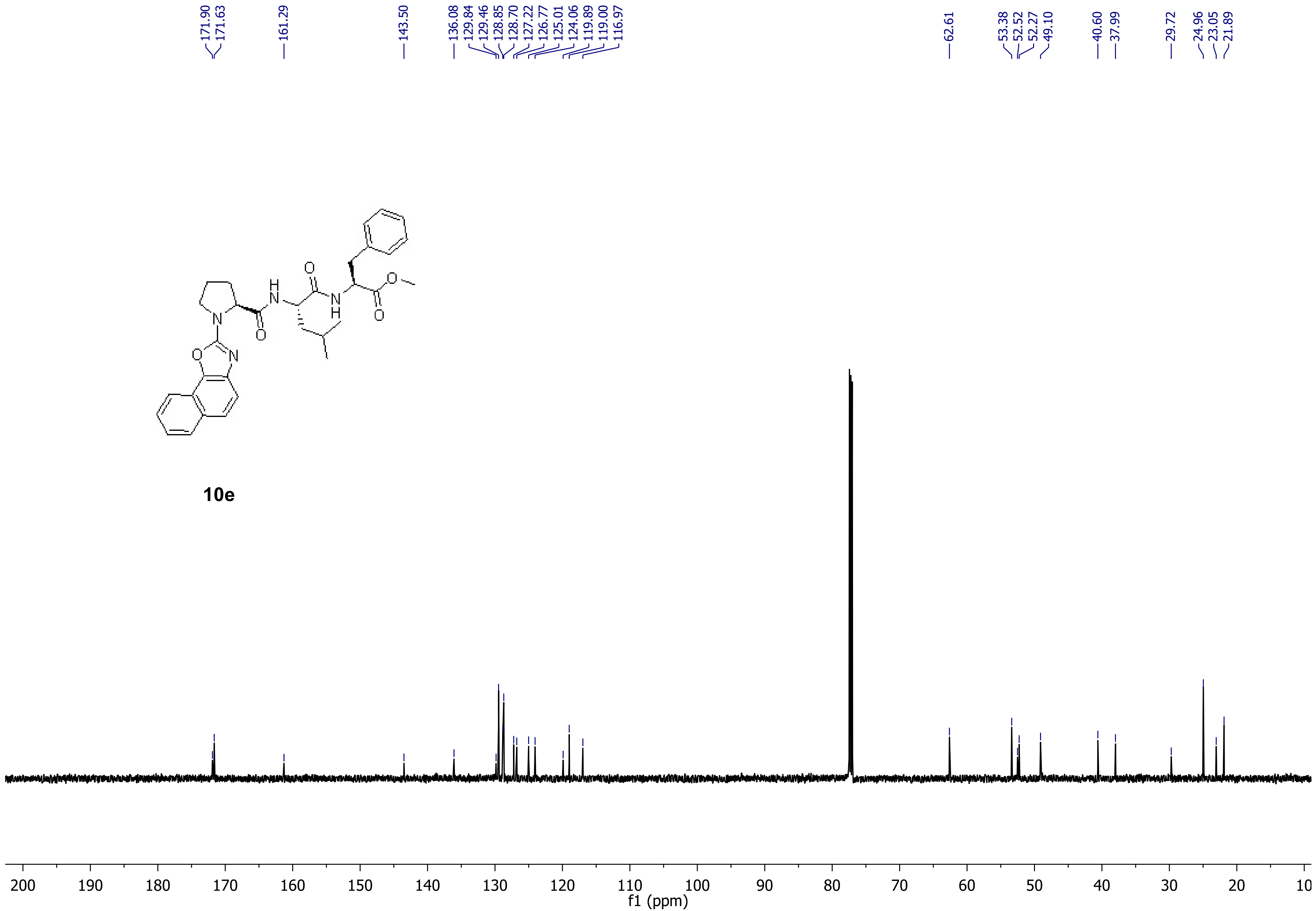


O
H
N
N
H
O
O
N
O
O
N

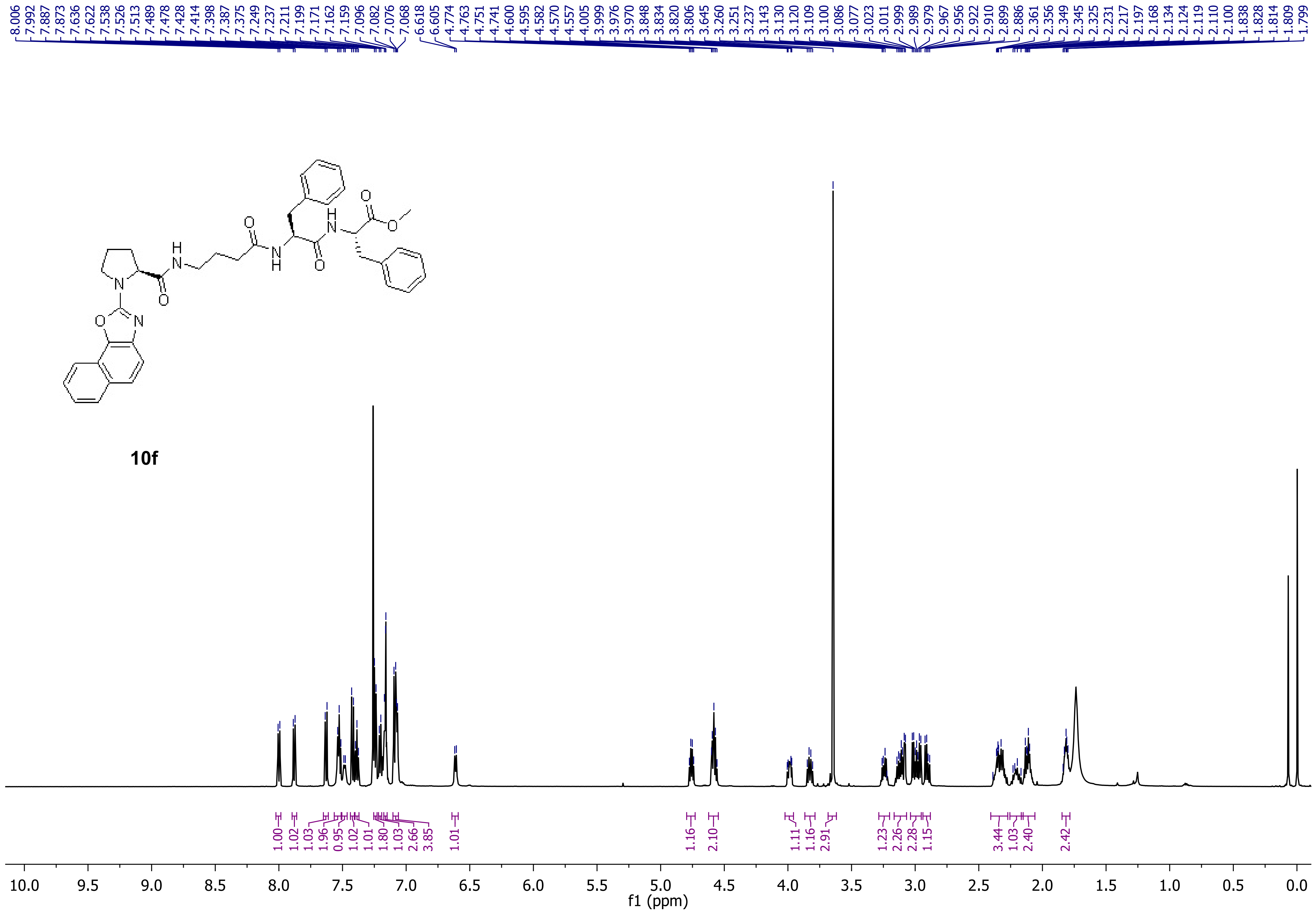
10e

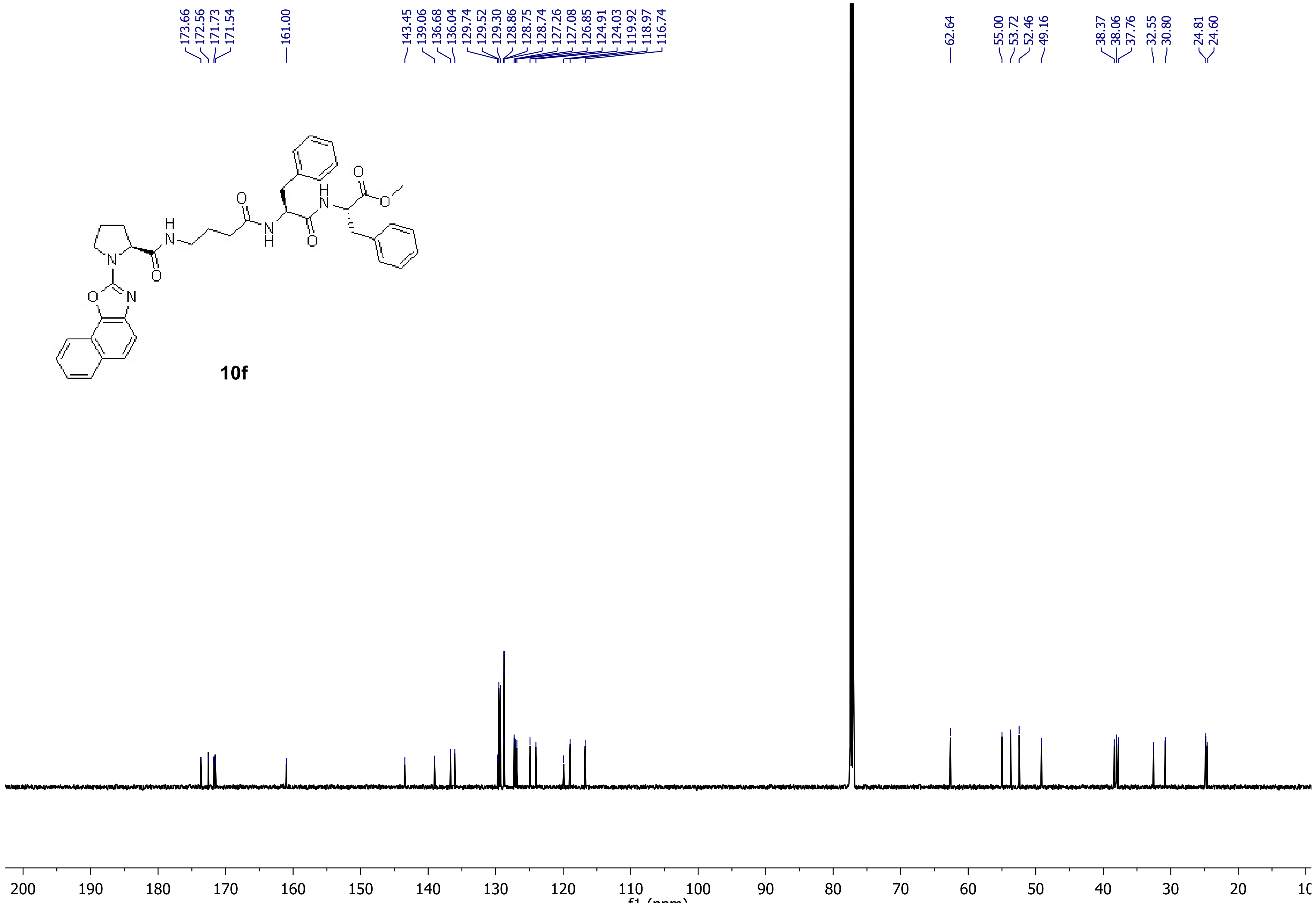


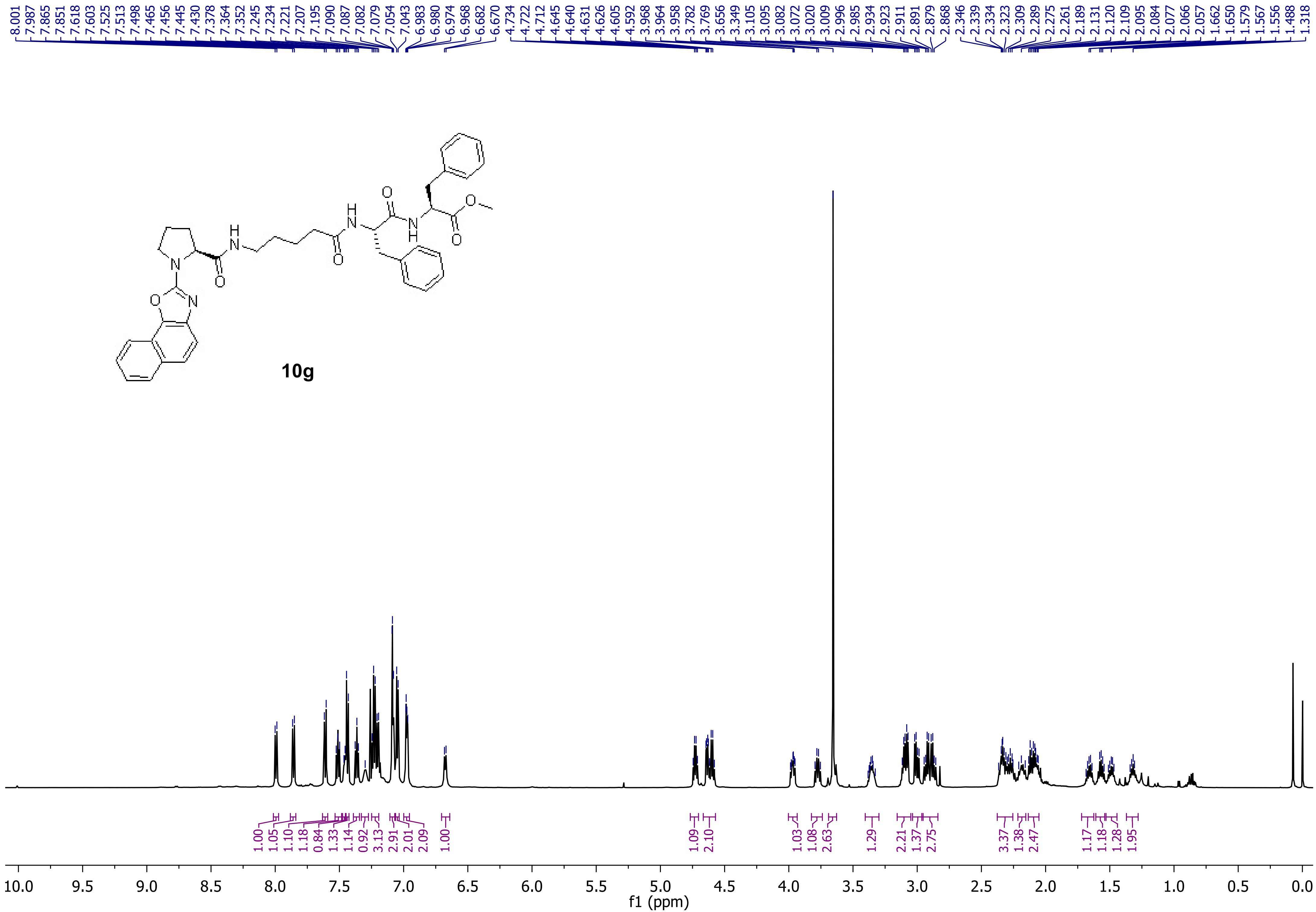
7.995
7.981
7.889
7.875
7.680
7.666
7.541
7.527
7.518
7.505
7.493
7.393
7.380
7.366
7.268
7.244
7.212
7.199
7.187
7.086
7.074
6.781
6.768
4.828
4.818
4.805
4.795
4.596
4.582
4.418
4.404
4.389
4.381
3.930
3.917
3.913
3.901
3.797
3.782
3.770
3.755
3.696
3.138
3.129
3.115
3.105
3.023
3.012
3.000
2.989
2.440
2.431
2.416
2.401
2.224
2.207
2.194
2.181
2.157
2.155
2.143
2.124
2.094
2.088
1.662
1.645
1.628
1.614
1.555
1.533
1.522
1.513
1.497
1.481
1.472
0.778
0.771
0.97
0.95
1.02
4.35
0.98
2.56
1.03
1.97
0.85
0.94
0.90
1.04
0.97
1.01
3.04
0.95
1.08
0.99
3.30
1.18
2.11
6.02
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
f1 (ppm)

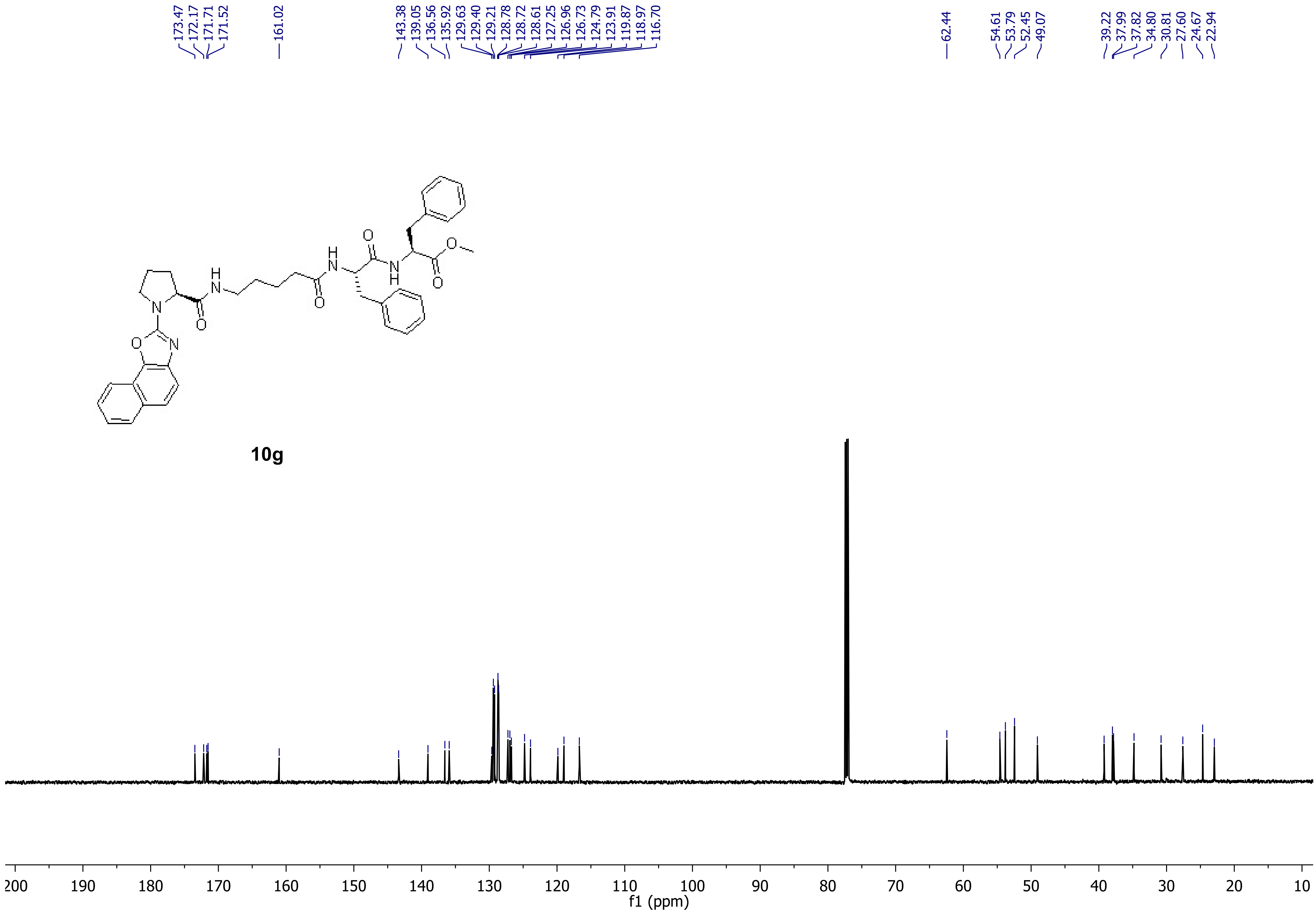

171.90
171.63
161.29
143.50
136.08
129.84
129.46
128.85
128.70
127.22
126.77
125.01
124.06
119.89
119.00
116.97
62.61
53.38
52.52
52.27
49.10
40.60
37.99
29.72
24.96
23.05
21.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

10e

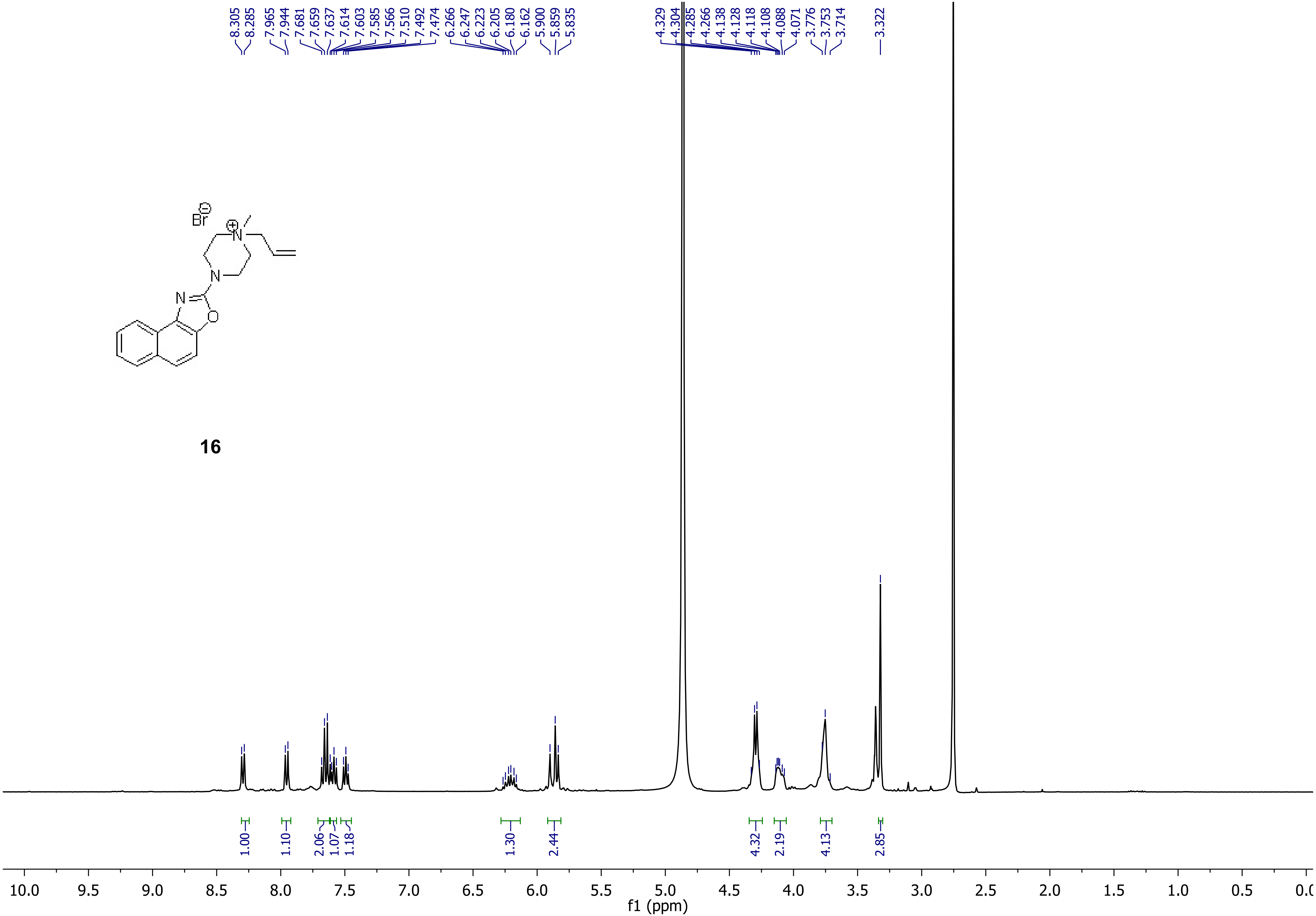

8.006 7.992 7.887 7.873 7.636 7.622 7.538 7.526 7.513 7.489 7.478 7.428 7.414 7.398 7.387 7.375 7.249 7.237 7.211 7.199 7.171 7.162 7.159 7.096 7.082 7.076 7.068 6.618 6.605 4.774 4.763 4.751 4.741 4.600 4.595 4.582 4.570 4.557 4.005 3.999 3.976 3.970 3.848 3.834 3.820 3.806 3.645 3.260 3.251 3.237 3.143 3.130 3.120 3.109 3.100 3.086 3.077 3.023 3.011 2.999 2.989 2.979 2.967 2.956 2.922 2.910 2.899 2.886 2.361 2.356 2.349 2.345 2.325 2.231 2.217 2.197 2.168 2.134 2.124 2.119 2.110 2.100 1.838 1.828 1.814 1.809 1.799
10f
1.00 1.02 1.03 1.96 0.95 1.02 1.01 1.80 1.03 2.66 3.85 1.01 1.16 2.10 1.11 1.16 2.91 1.23 2.26 2.28 1.15 3.44 1.03 2.40 2.42
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
f1 (ppm)

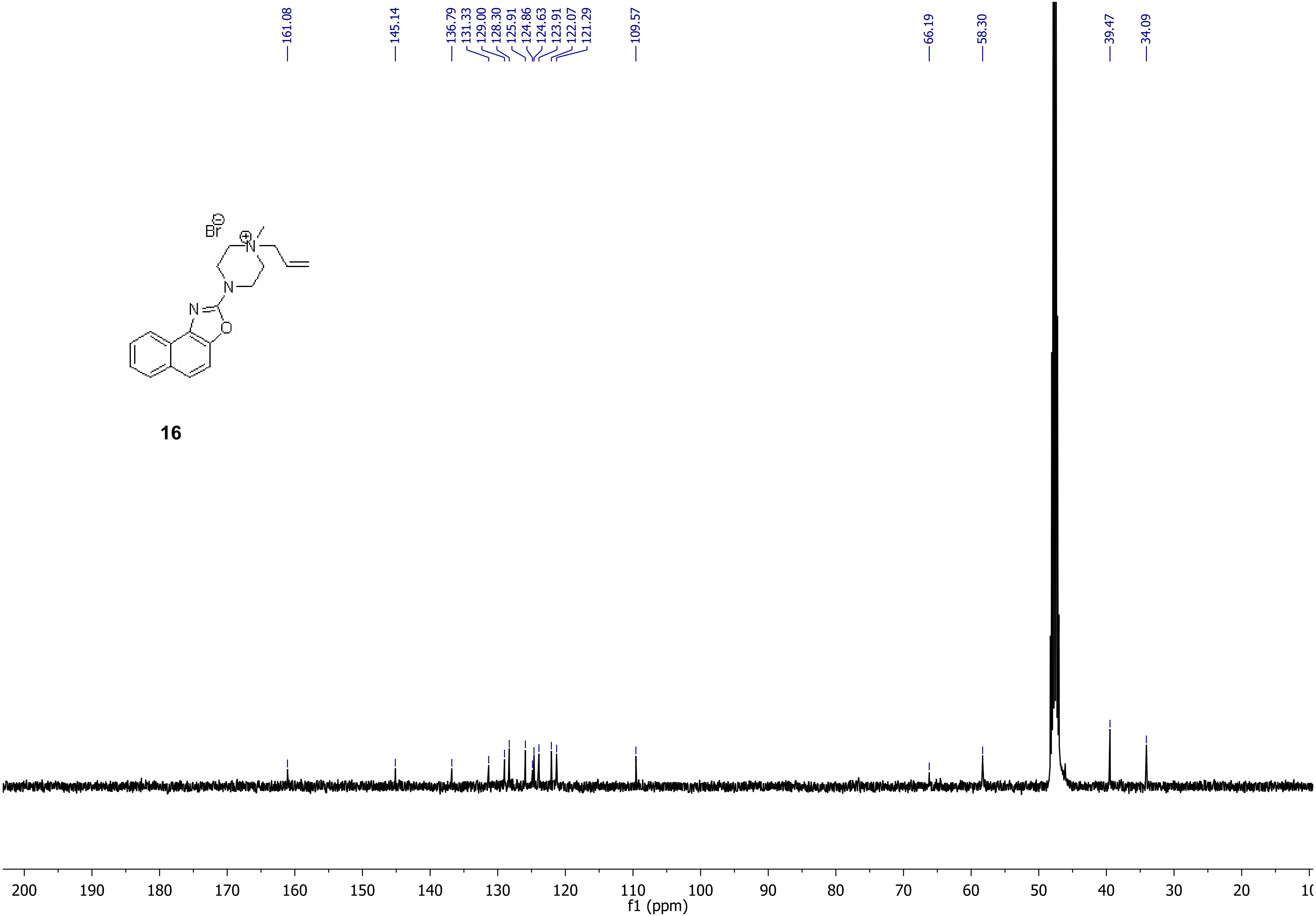

173.66
172.56
171.73
171.54
161.00
143.45
139.06
136.68
136.04
129.74
129.52
129.30
128.86
128.75
128.74
127.26
127.08
126.85
124.91
124.03
119.92
118.97
116.74
62.64
55.00
53.72
52.46
49.16
38.37
38.06
37.76
32.55
30.80
24.81
24.60
10f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


8.001 7.987 7.865 7.851 7.618 7.603 7.525 7.513 7.498 7.465 7.456 7.445 7.430 7.378 7.364 7.352 7.245 7.234 7.221 7.207 7.195 7.090 7.087 7.082 7.079 7.054 7.043 6.983 6.980 6.974 6.968 6.682 6.670 4.734 4.722 4.712 4.645 4.640 4.631 4.626 4.605 4.592 3.968 3.964 3.958 3.782 3.769 3.656 3.349 3.105 3.095 3.082 3.072 3.020 3.009 2.996 2.985 2.934 2.923 2.911 2.891 2.879 2.868 2.346 2.339 2.334 2.323 2.309 2.289 2.275 2.261 2.189 2.131 2.120 2.109 2.095 2.084 2.077 2.066 2.057 1.662 1.650 1.579 1.567 1.556 1.488 1.318
10g
1.00 1.05 1.10 1.18 0.84 1.33 1.14 0.92 3.13 2.91 2.01 2.09 1.00 1.09 2.10 1.03 1.08 2.63 1.29 2.21 1.37 2.75 3.37 1.38 2.47 1.17 1.18 1.28 1.95
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
f1 (ppm)

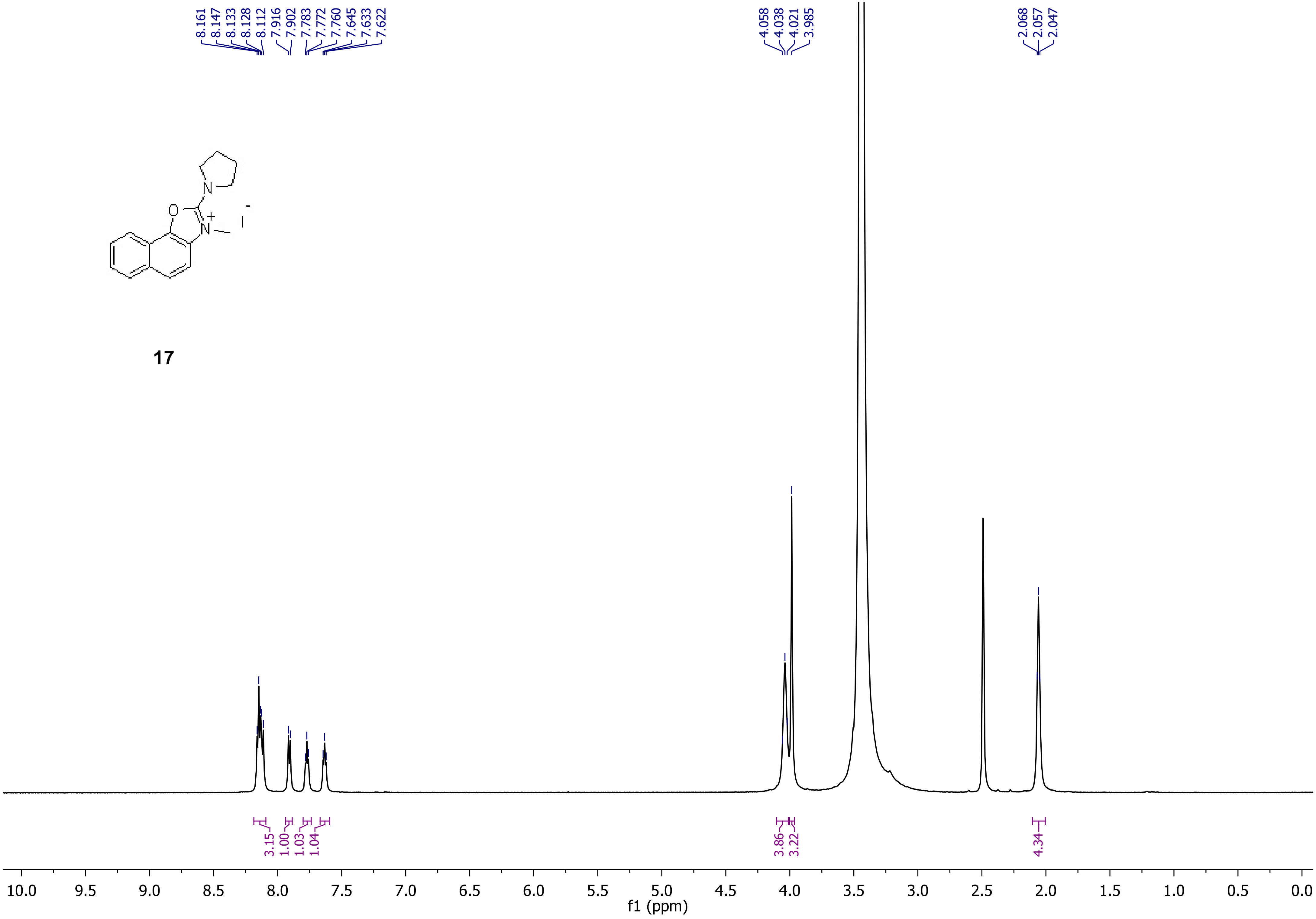

173.47
172.17
171.71
171.52
161.02
143.38
139.05
136.56
135.92
129.63
129.40
129.21
128.78
128.72
128.61
127.25
126.96
126.73
124.79
123.91
119.87
118.97
116.70
62.44
54.61
53.79
52.45
49.07
39.22
37.99
37.82
34.80
30.81
27.60
24.67
22.94
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

10g

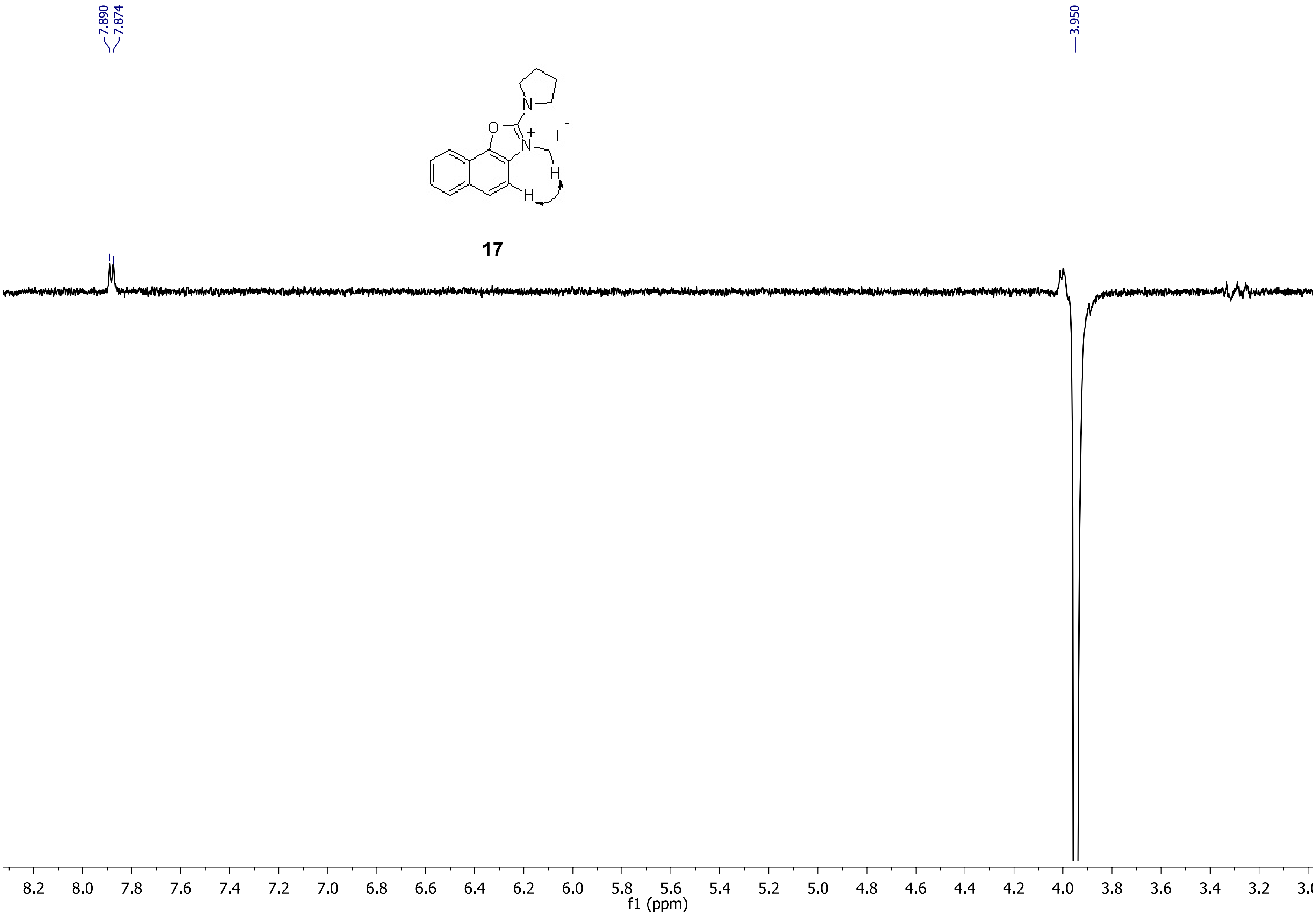

8.305
8.285
7.965
7.944
7.681
7.659
7.637
7.614
7.603
7.585
7.566
7.510
7.492
7.474
6.266
6.247
6.223
6.205
6.180
6.162
5.900
5.859
5.835
4.329
4.304
4.285
4.266
4.138
4.128
4.118
4.108
4.088
4.071
3.776
3.753
3.714
3.322
Br
N
N
N
O
16
1.00
1.10
2.06
1.07
1.18
1.30
2.44
4.32
2.19
4.13
2.85
10.0
9.5
9.0
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
f1 (ppm)

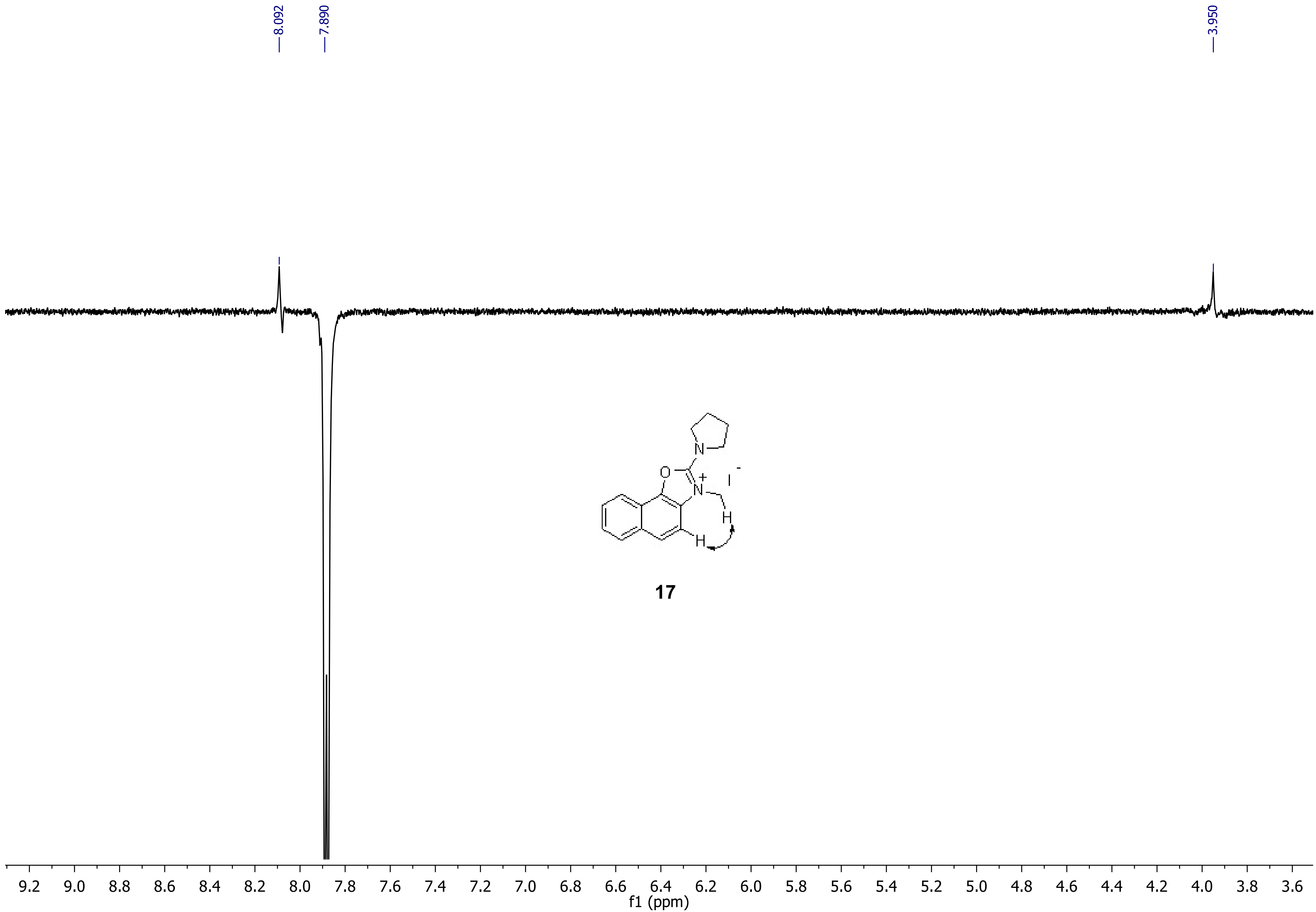

161.08
145.14
136.79
131.33
129.00
128.30
125.91
124.86
124.63
123.91
122.07
121.29
109.57
66.19
58.30
39.47
34.09
Br
N
N
N
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

16

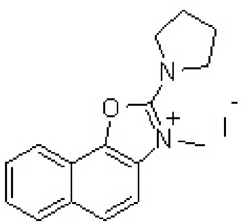


8.161
8.147
8.133
8.128
8.112
7.916
7.902
7.783
7.772
7.760
7.645
7.633
7.622
4.058
4.038
4.021
3.985
2.068
2.057
2.047
17
3.15
1.00
1.03
1.04
3.86
3.22
4.34
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

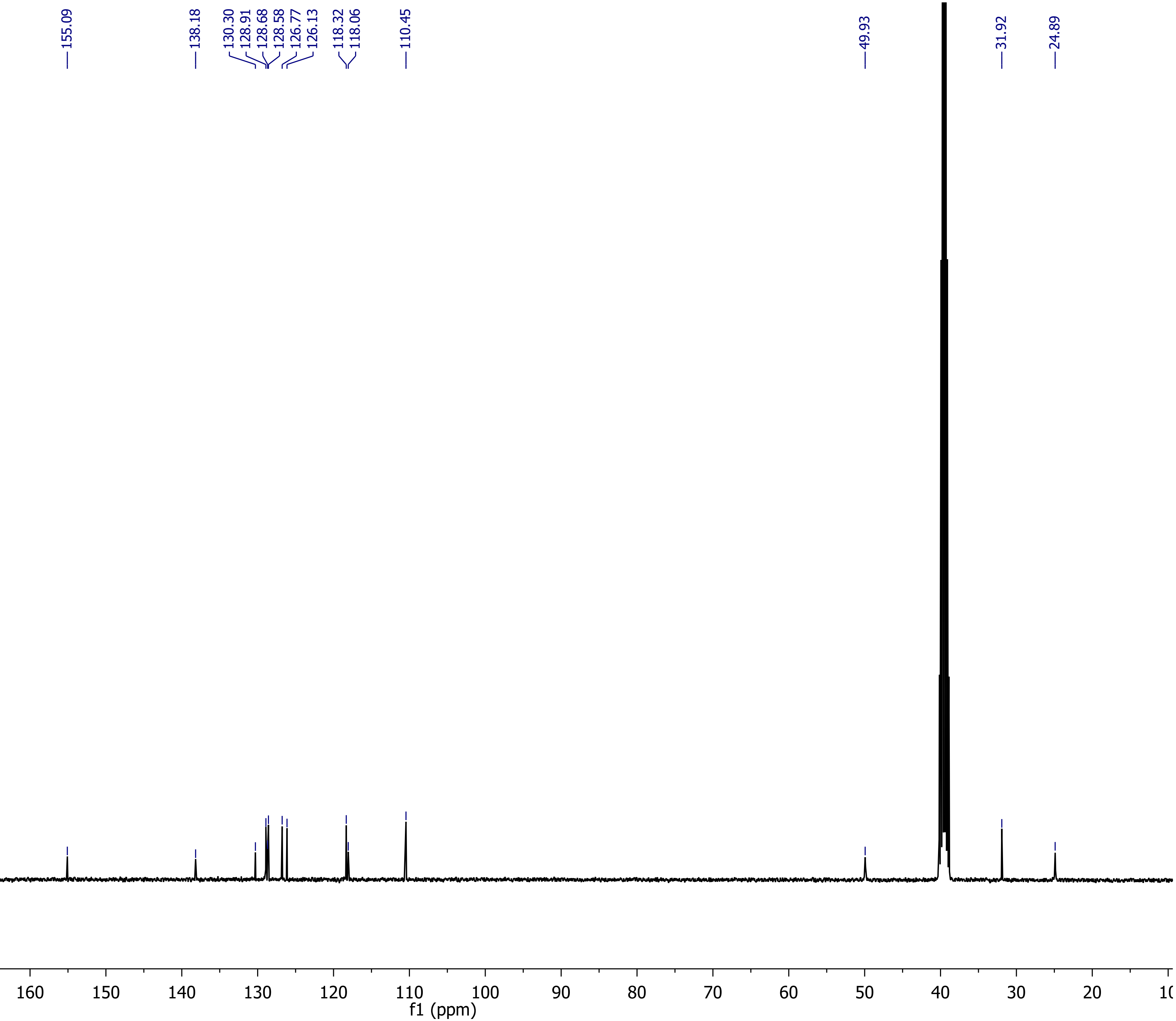

7.890
7.874
3.950
O
N
N
+
I
-
H
H
17
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
f1 (ppm)



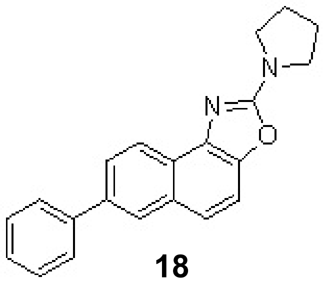
8.092
7.890
3.950
O
N
N
+
I
-
H
H
17
9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6
f1 (ppm)



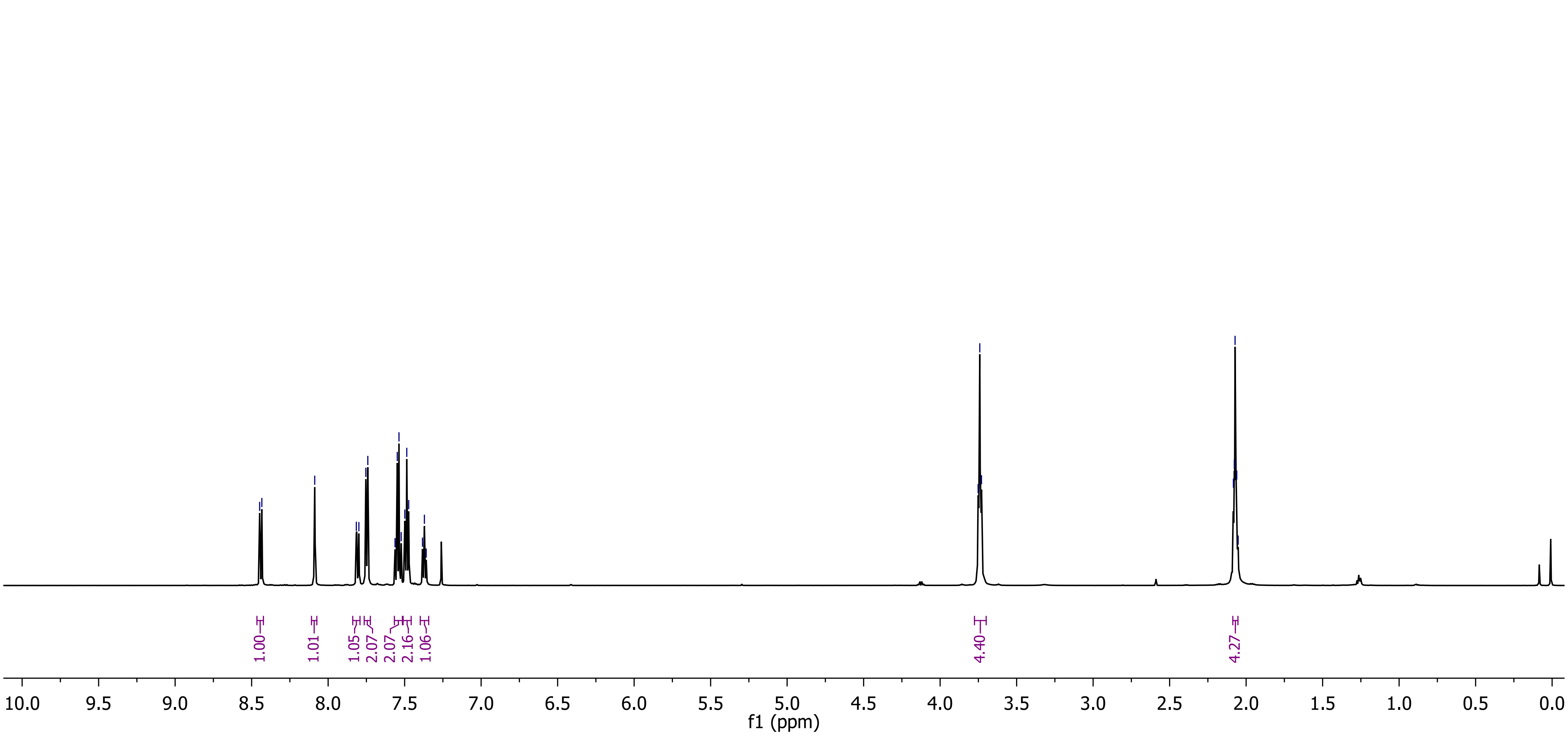
17

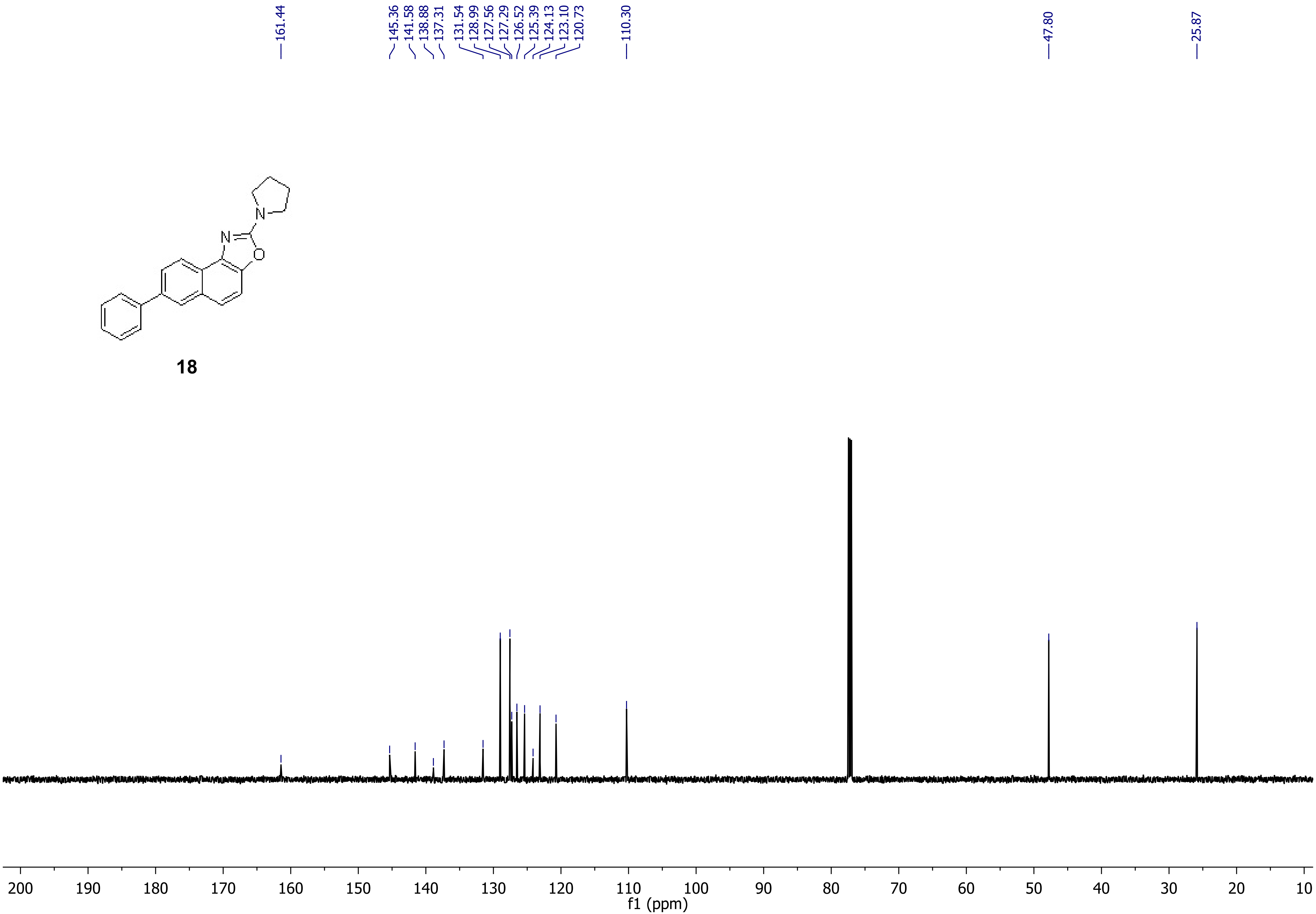


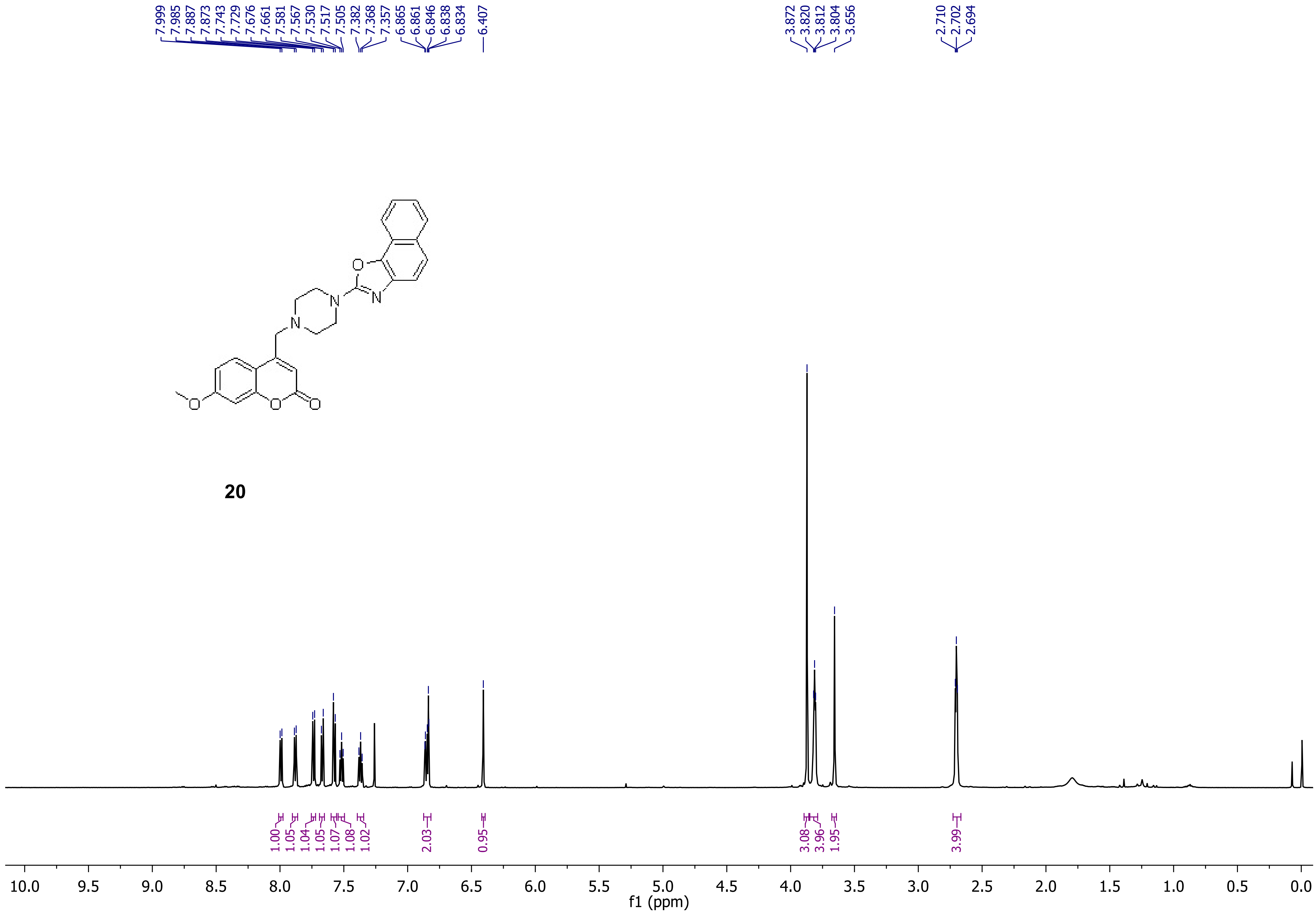
155.09
138.18
130.30
128.91
128.68
128.58
126.77
126.13
118.32
118.06
110.45
49.93
31.92
24.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



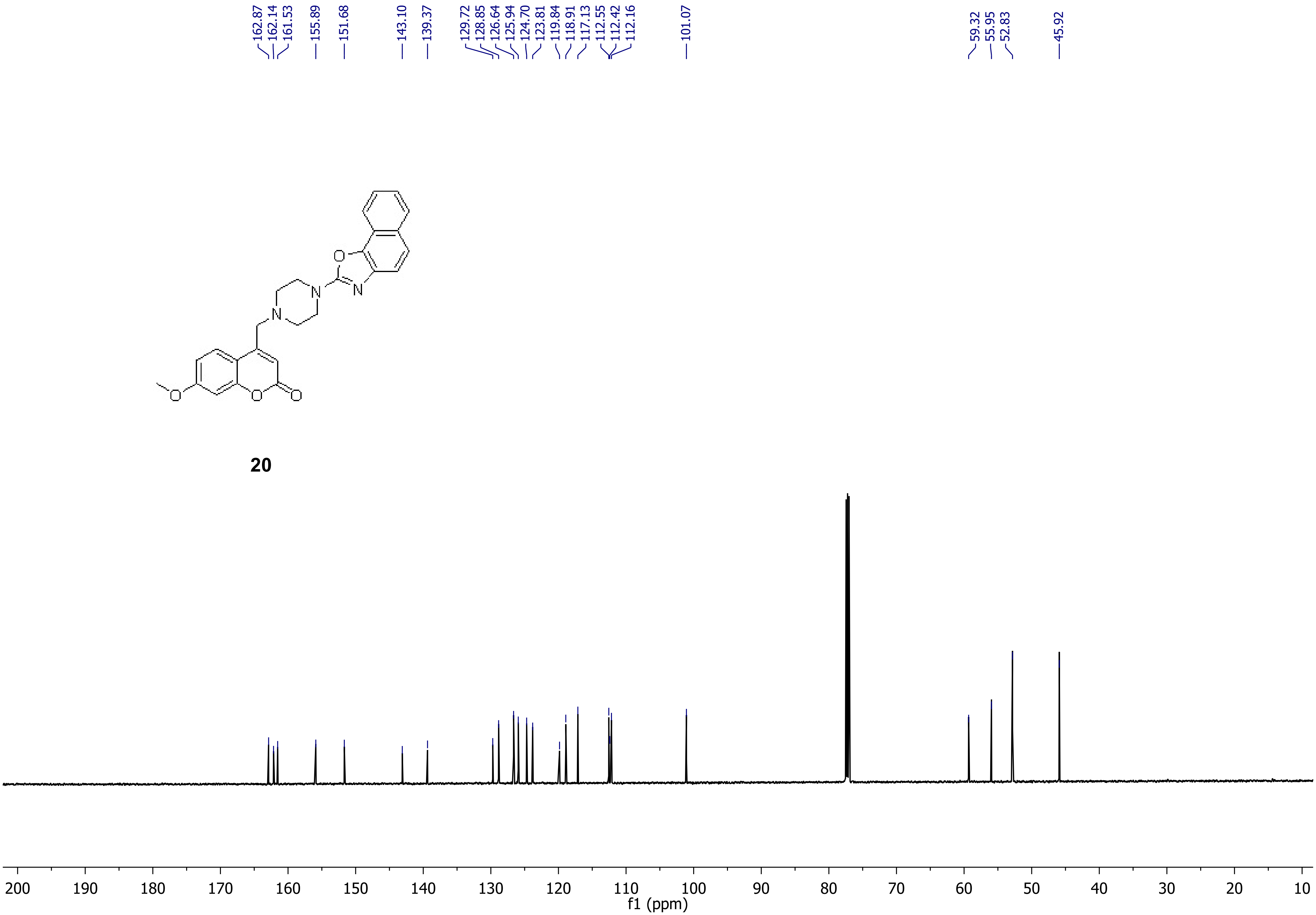
18

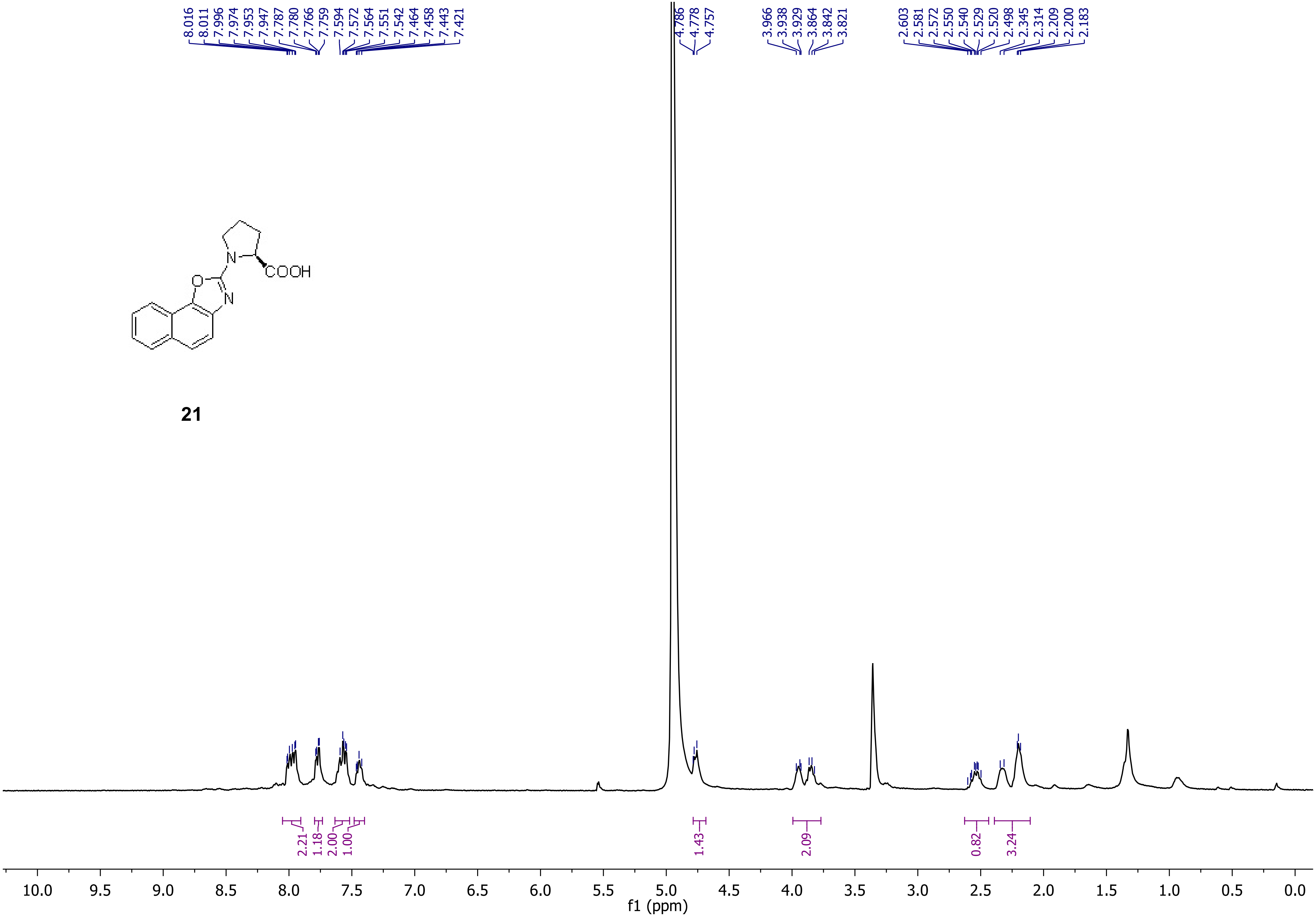

8.447
8.433
8.088
7.816
7.799
7.754
7.741
7.563
7.548
7.537
7.522
7.499
7.486
7.473
7.383
7.371
7.359
3.752
3.741
3.730
2.083
2.077
2.072
2.061
2.052
1.00
1.01
1.05
2.07
2.07
2.16
1.06
4.40
4.27
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

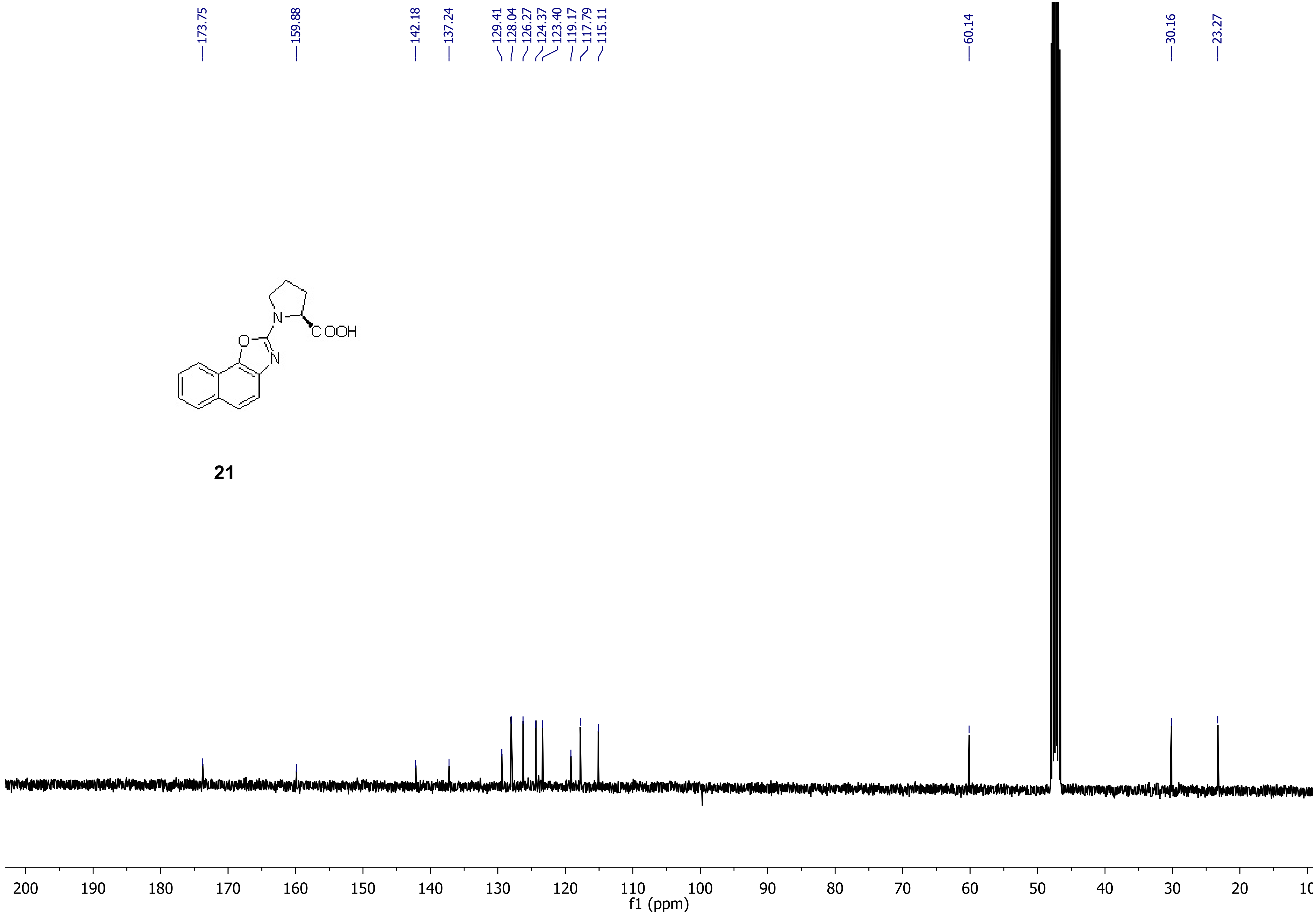

161.44
145.36
141.58
138.88
137.31
131.54
128.99
127.56
127.29
126.52
125.39
124.13
123.10
120.73
110.30
47.80
25.87
N
N
O
18
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

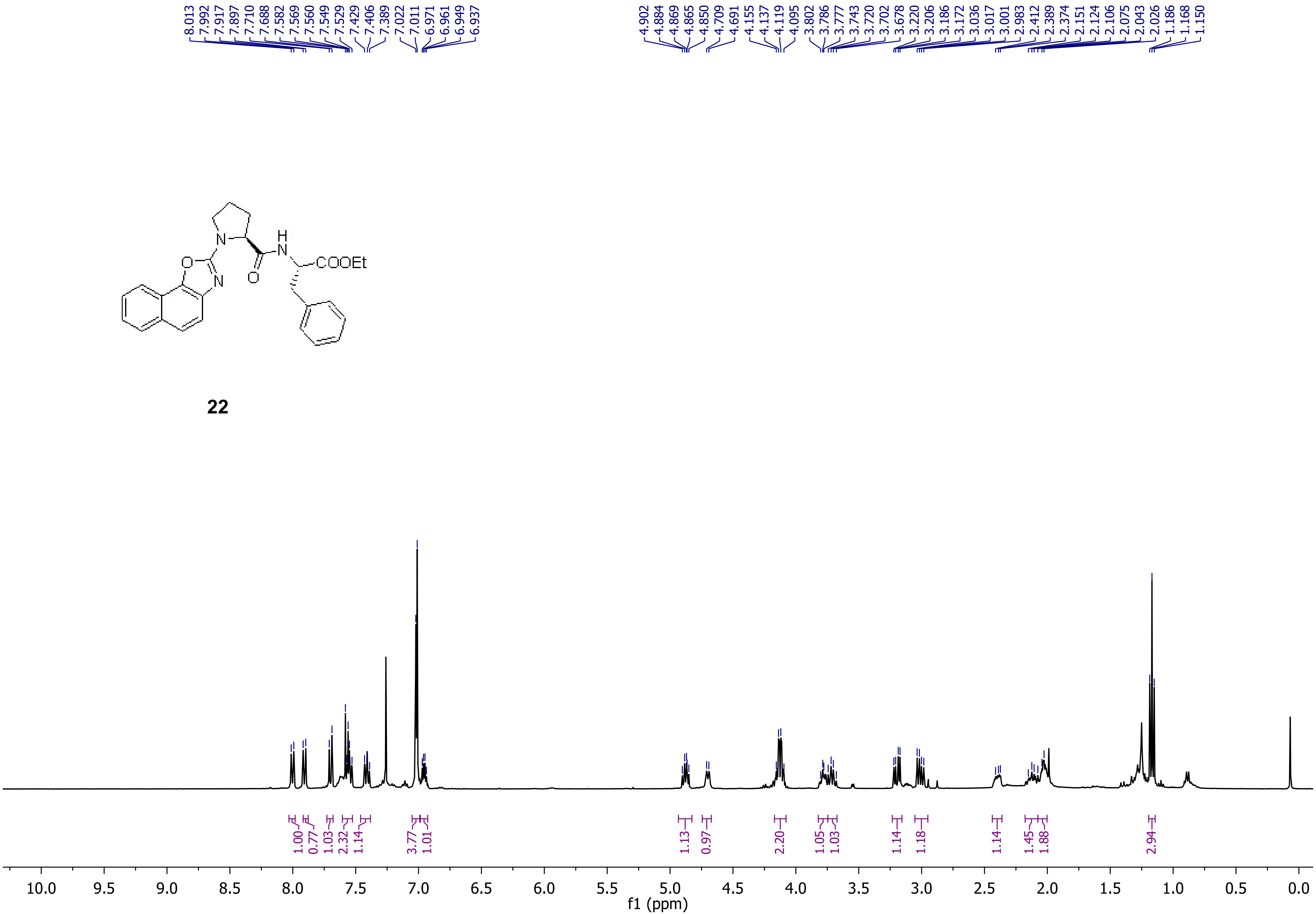

7.999
7.985
7.887
7.873
7.743
7.729
7.676
7.661
7.581
7.567
7.530
7.517
7.505
7.382
7.368
7.357
6.865
6.861
6.846
6.838
6.834
6.407
3.872
3.820
3.812
3.804
3.656
2.710
2.702
2.694
1.00
1.05
1.04
1.05
1.07
1.08
1.02
2.03
0.95
3.08
3.96
1.95
3.99
f1 (ppm)

20

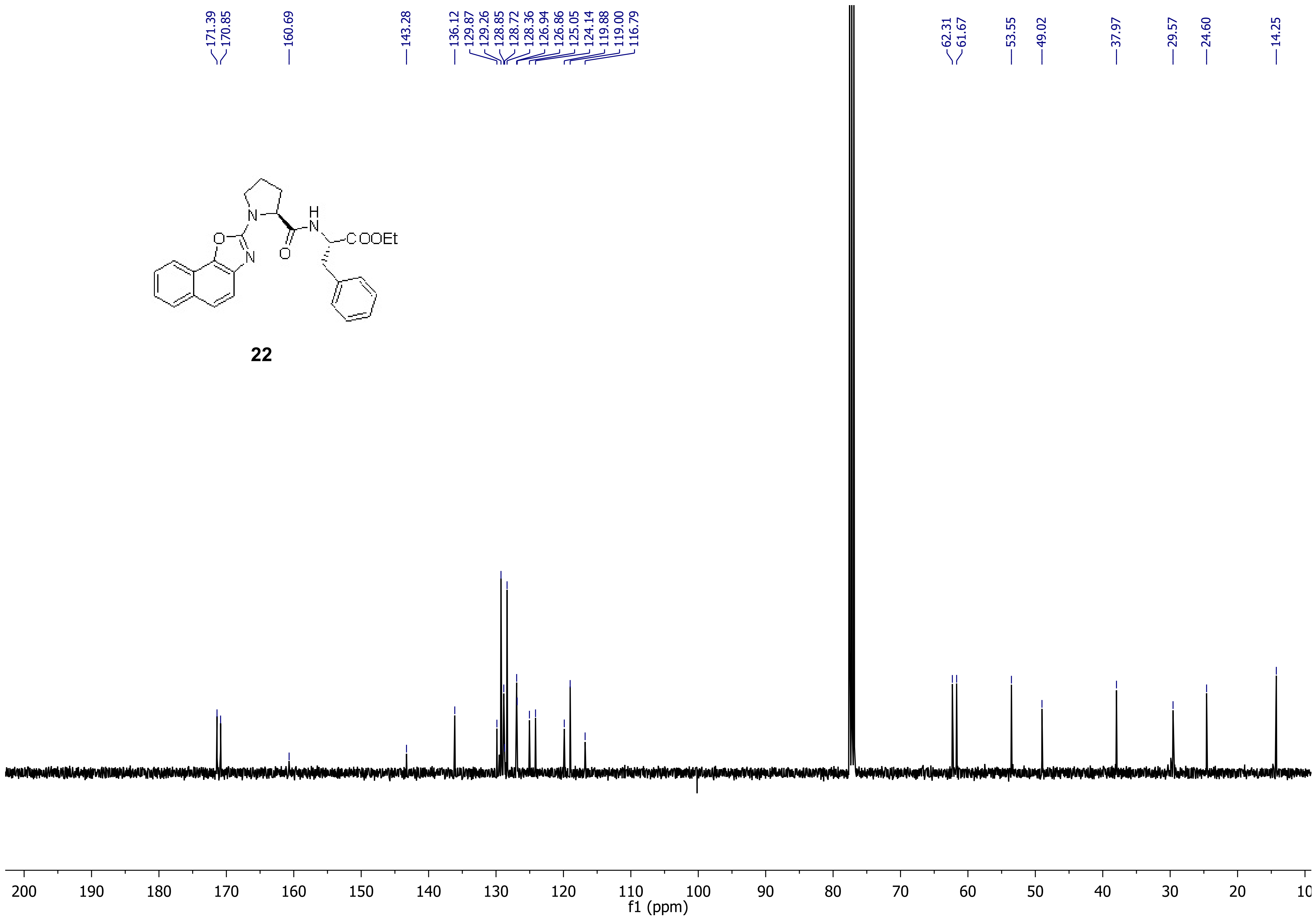

162.87
162.14
161.53
155.89
151.68
143.10
139.37
129.72
128.85
126.64
125.94
124.70
123.81
119.84
118.91
117.13
112.55
112.42
112.16
101.07
59.32
55.95
52.83
45.92
20
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.016
8.011
7.996
7.974
7.953
7.947
7.787
7.780
7.766
7.759
7.594
7.572
7.564
7.551
7.542
7.464
7.458
7.443
7.421
4.786
4.778
4.757
3.966
3.938
3.929
3.864
3.842
3.821
2.603
2.581
2.572
2.550
2.540
2.529
2.520
2.498
2.345
2.314
2.209
2.200
2.183
N
COOH
O
N
21
2.21
1.18
2.00
1.00
1.43
2.09
0.82
3.24
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
f1 (ppm)


173.75
159.88
142.18
137.24
129.41
128.04
126.27
124.37
123.40
119.17
117.79
115.11
60.14
30.16
23.27
N
O
N
COOH
21
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



8.013
7.992
7.917
7.897
7.710
7.688
7.582
7.569
7.560
7.549
7.529
7.429
7.406
7.389
7.022
7.011
6.971
6.961
6.949
6.937
4.902
4.884
4.869
4.865
4.850
4.709
4.691
4.155
4.137
4.119
4.095
3.802
3.786
3.777
3.743
3.720
3.702
3.678
3.220
3.206
3.186
3.172
3.036
3.017
3.001
2.983
2.412
2.389
2.374
2.151
2.124
2.106
2.075
2.043
2.026
1.186
1.168
1.150
N
H
N
O
COOEt
O
N
22
1.00
0.77
1.03
2.32
1.14
3.77
1.01
1.13
0.97
2.20
1.05
1.03
1.14
1.18
1.14
1.45
1.88
2.94
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
f1 (ppm)



171.39
170.85
160.69
143.28
136.12
129.87
129.26
128.85
128.72
128.36
126.94
126.86
125.05
124.14
119.88
119.00
116.79
62.31
61.67
53.55
49.02
37.97
29.57
24.60
14.25
N
O
N
H
N
O
COOEt
22
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)