Electronic Supplementary Material (ESI) for Green Chemistry.

A Molar Efficient Synthesis of Amides from Acid Chlorides and Amines in the Bioavailable Solvent Cyrene

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I. General Experimental Information

Unless otherwise indicated, all commercially available reagents and solvents were used directly from the supplier without further purification. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR were recorded at ambient temperature in $CDCl_3$ (7.27 ppm). Chemical shift values are expressed as parts per million (ppm) and J values are in Hertz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, q: quartet or combination, br.s broad singlet or m: multiplet. The melting points reported are uncorrected. All reactions were performed in 5 mL microwave vials with Teflon coated caps.

II. Cyrene Hydration Study

A. NMR analysis of Cyrene in $CDCl_3$ at 1 M concentration

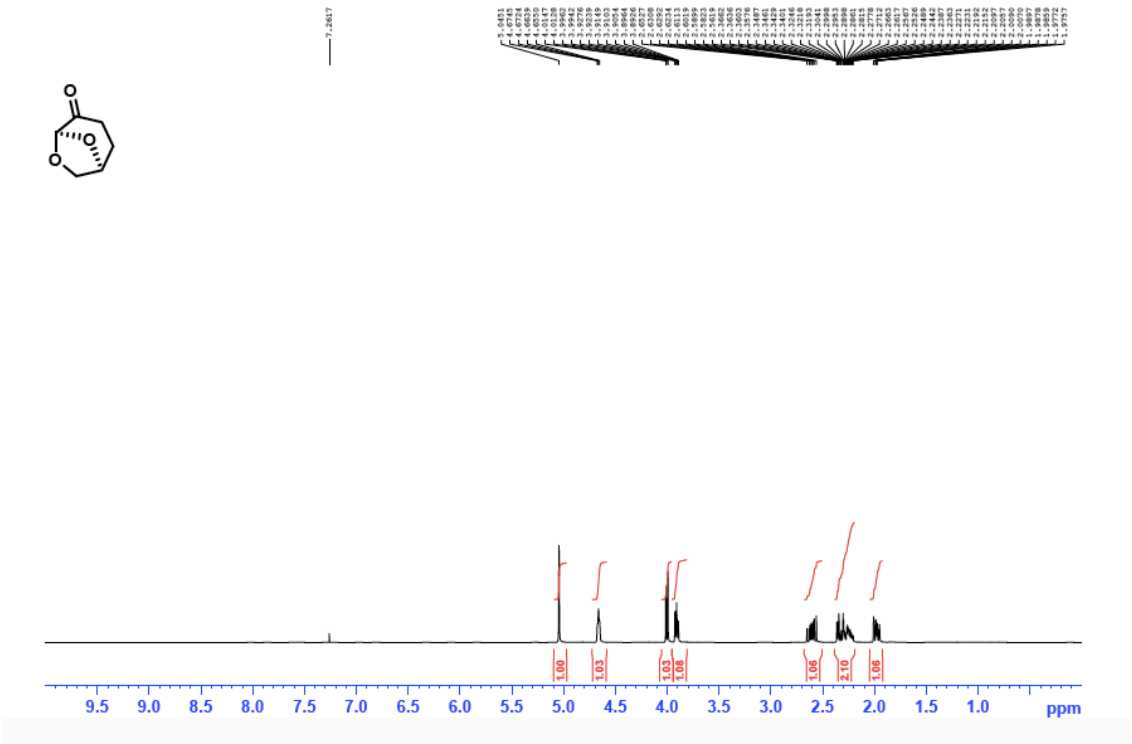


Figure S1 Proton NMR of Cyrene in $CDCl_3$ at 1 M concentration

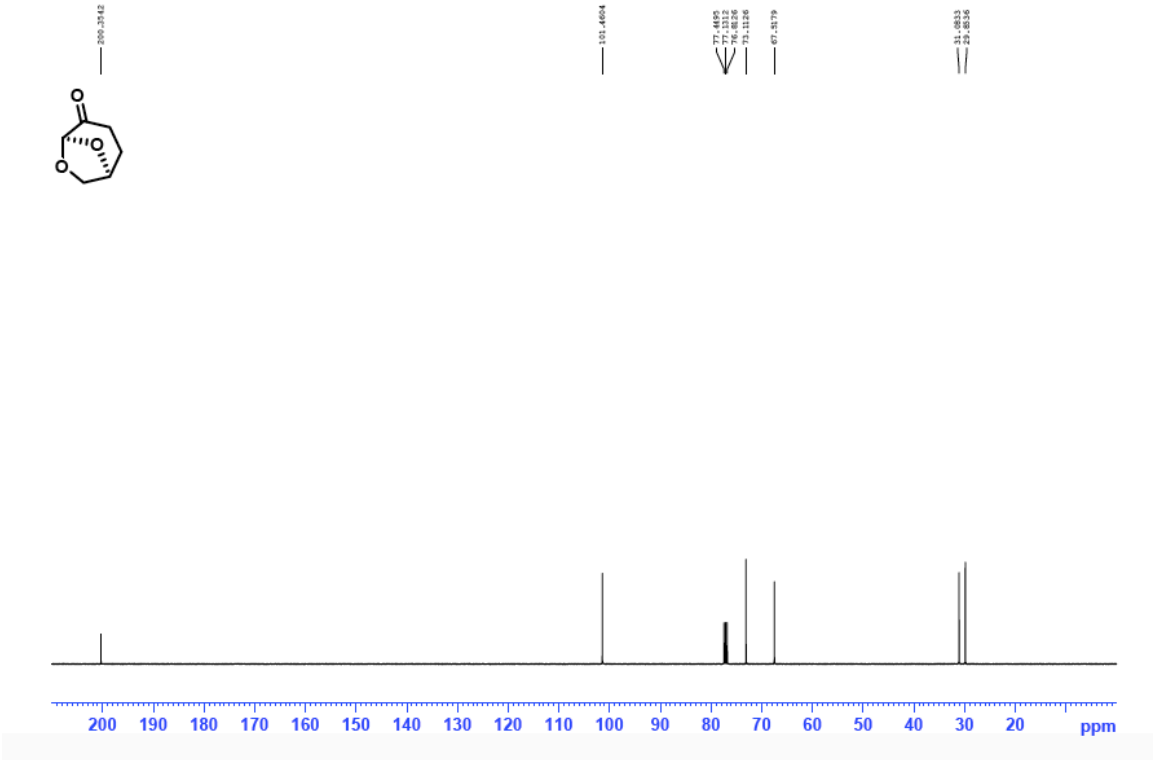


Figure S2 Carbon 13 NMR of Cyrene in $CDCl_3$ at 1 M concentration

B. NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture.

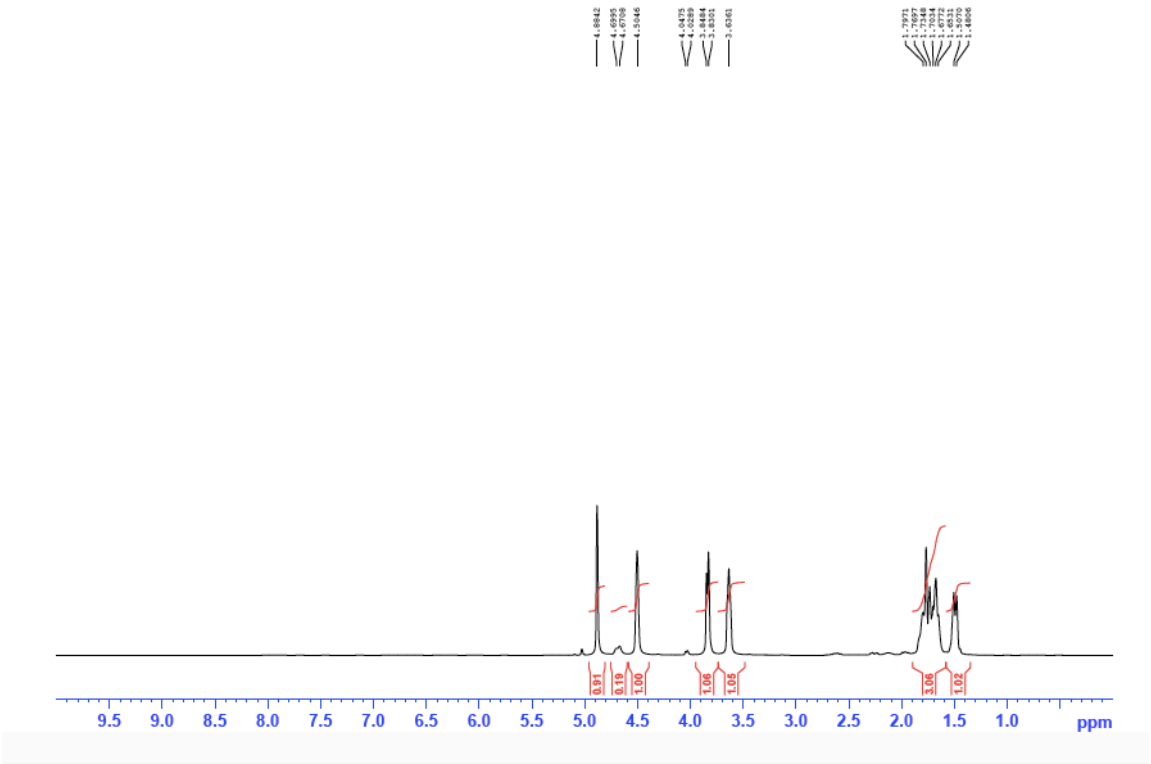


Figure S3 Proton NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

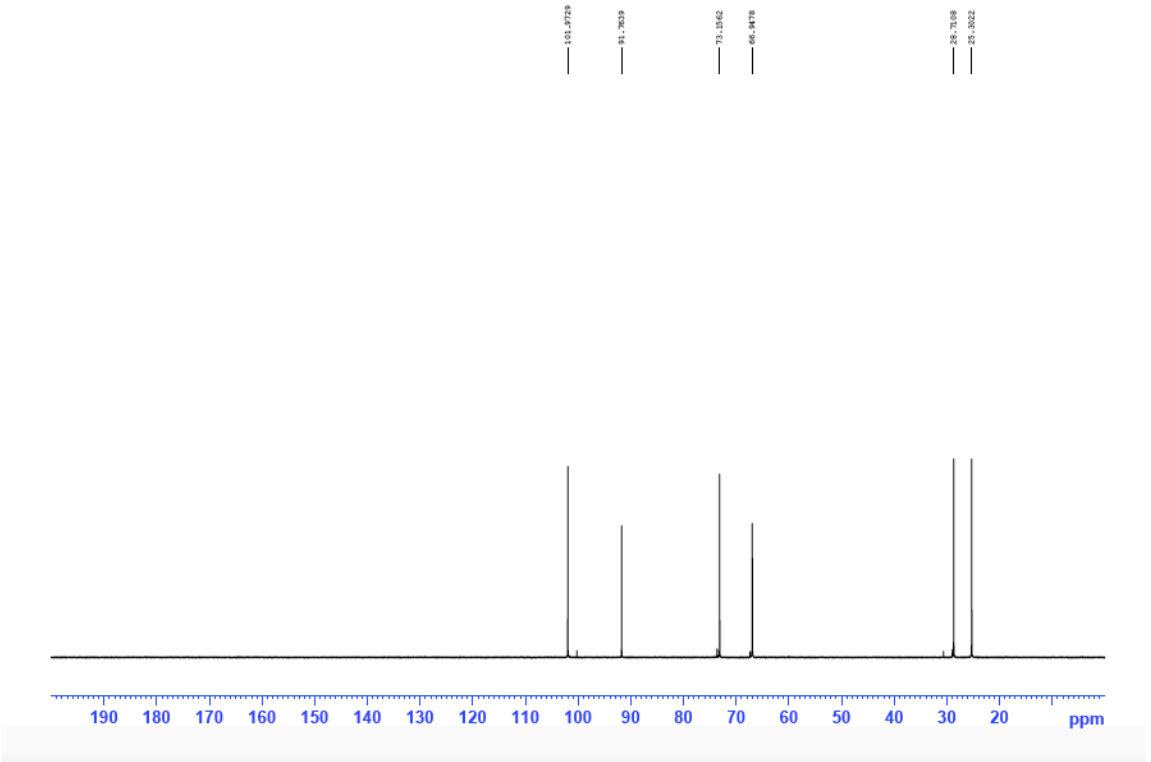


Figure S4 Carbon 13 NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

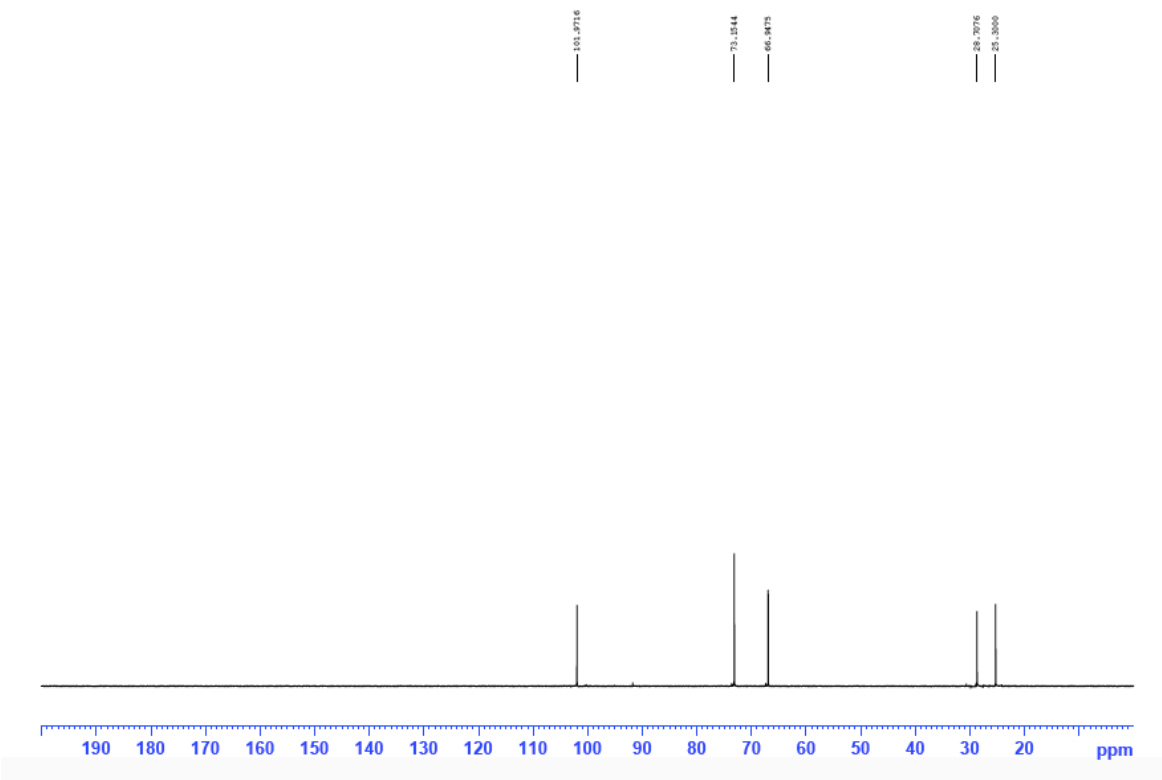


Figure S5 13C DEPT90 NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

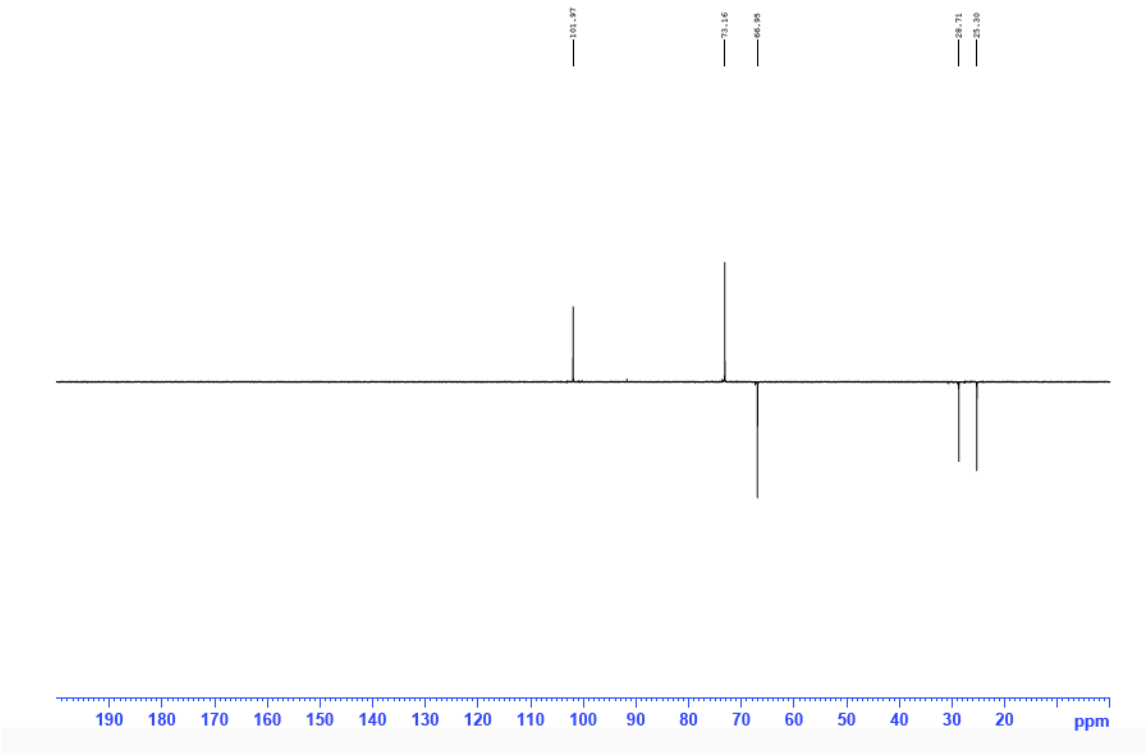


Figure S6 13C DEPT135 NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

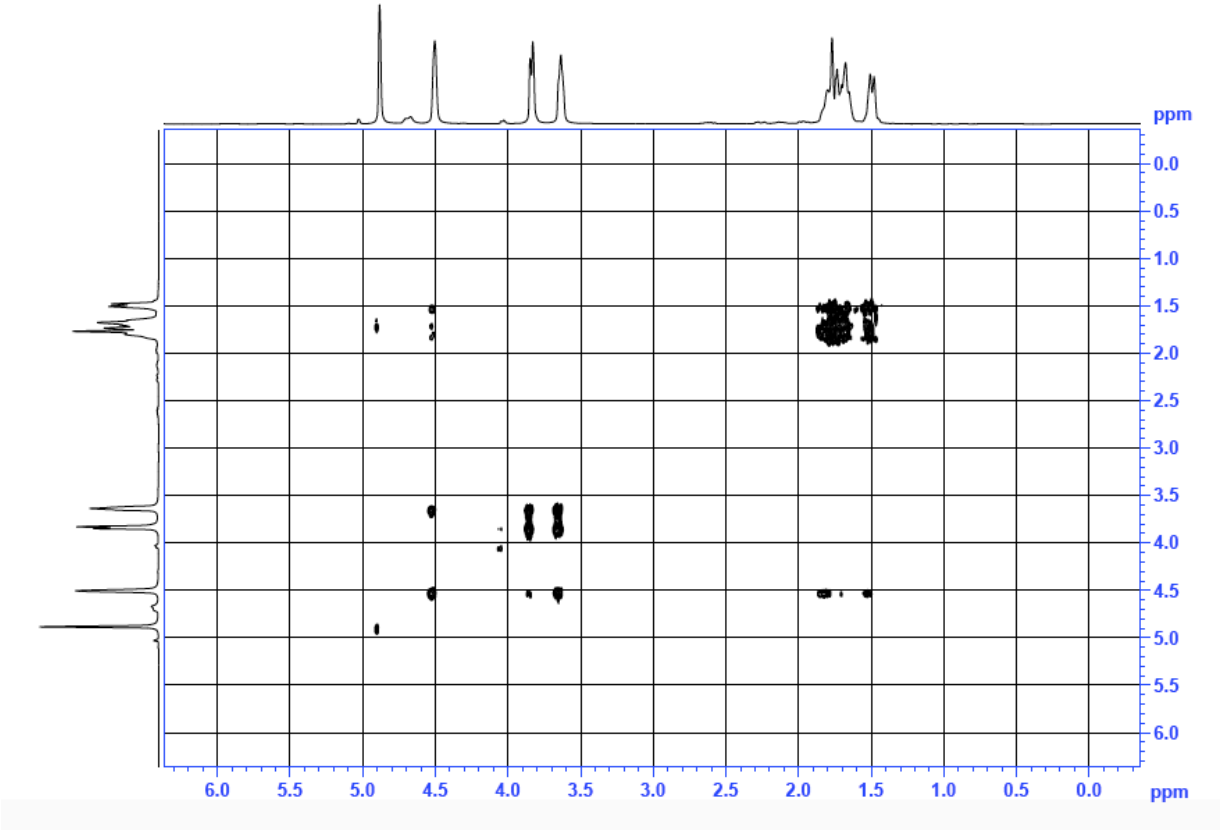


Figure S7 COSY NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

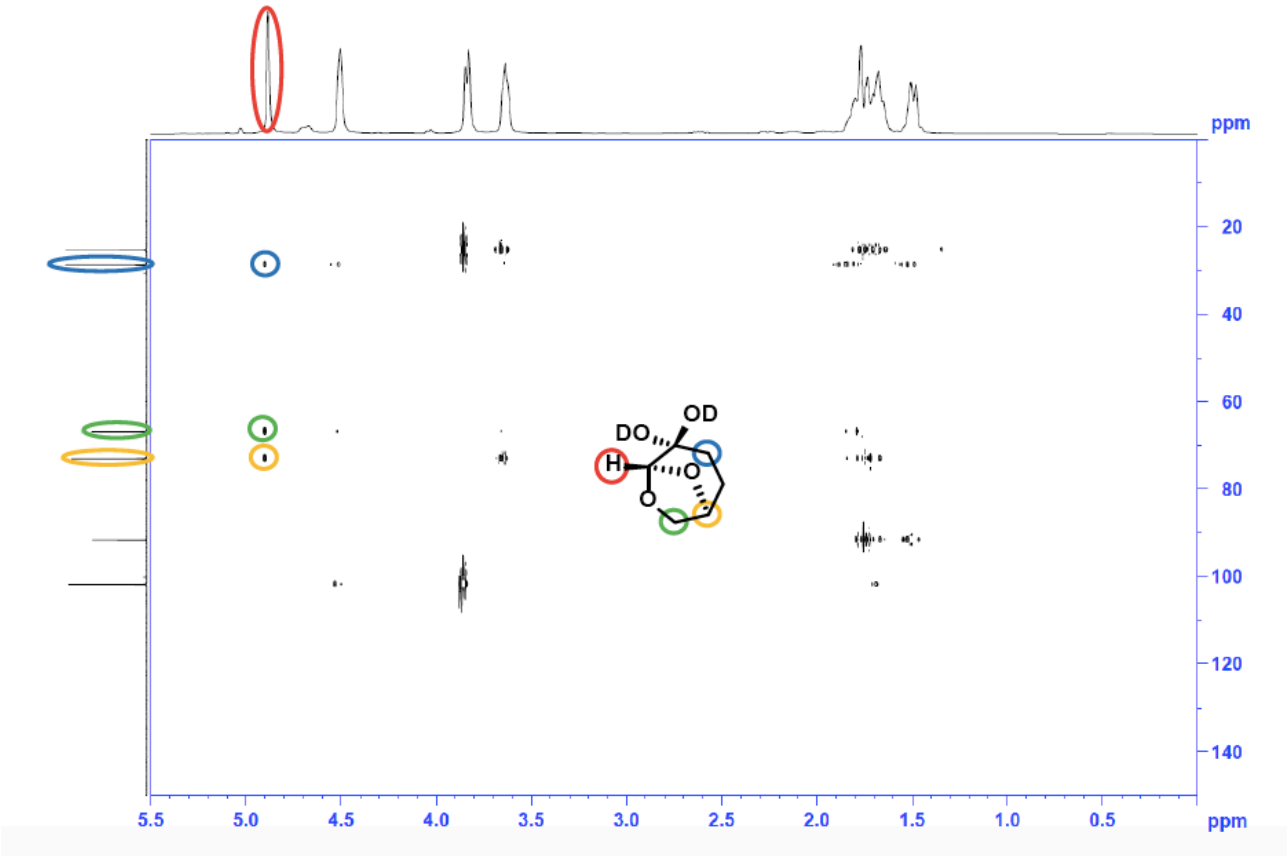


Figure S8 HMBC NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

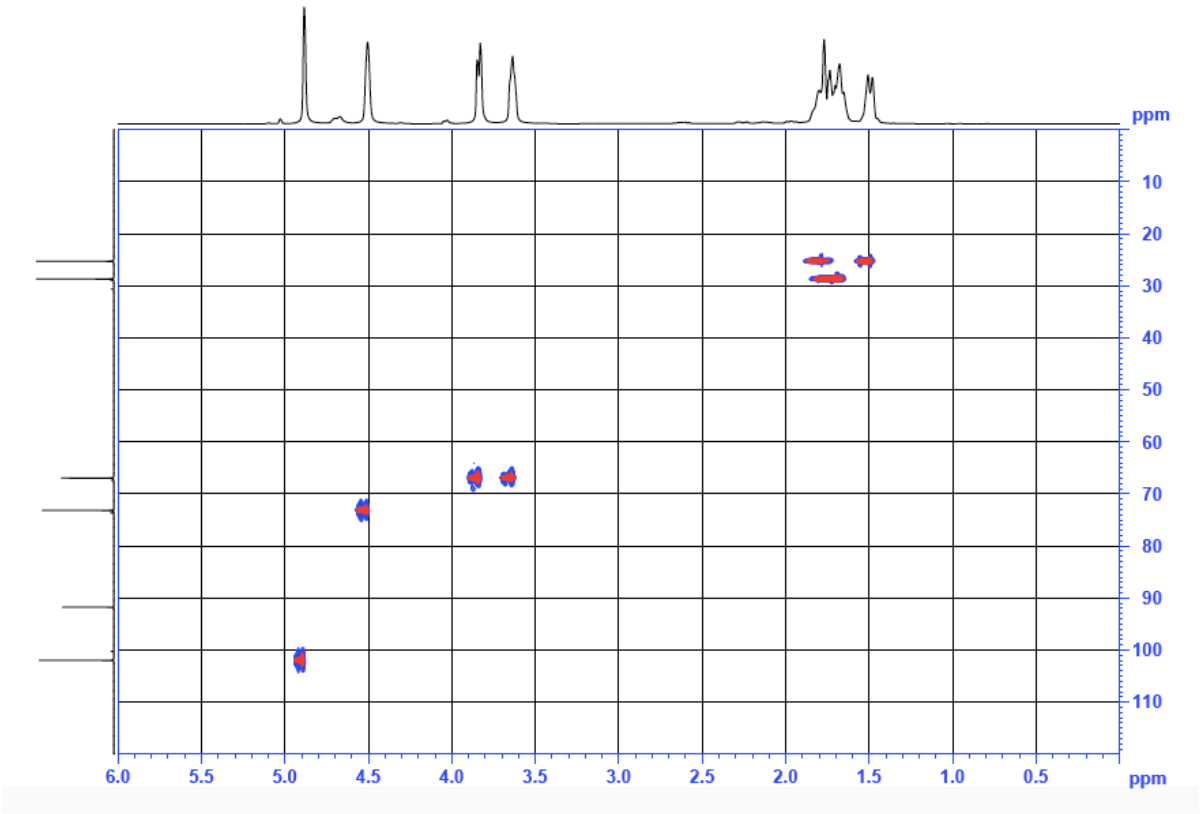


Figure S9 HSQC NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

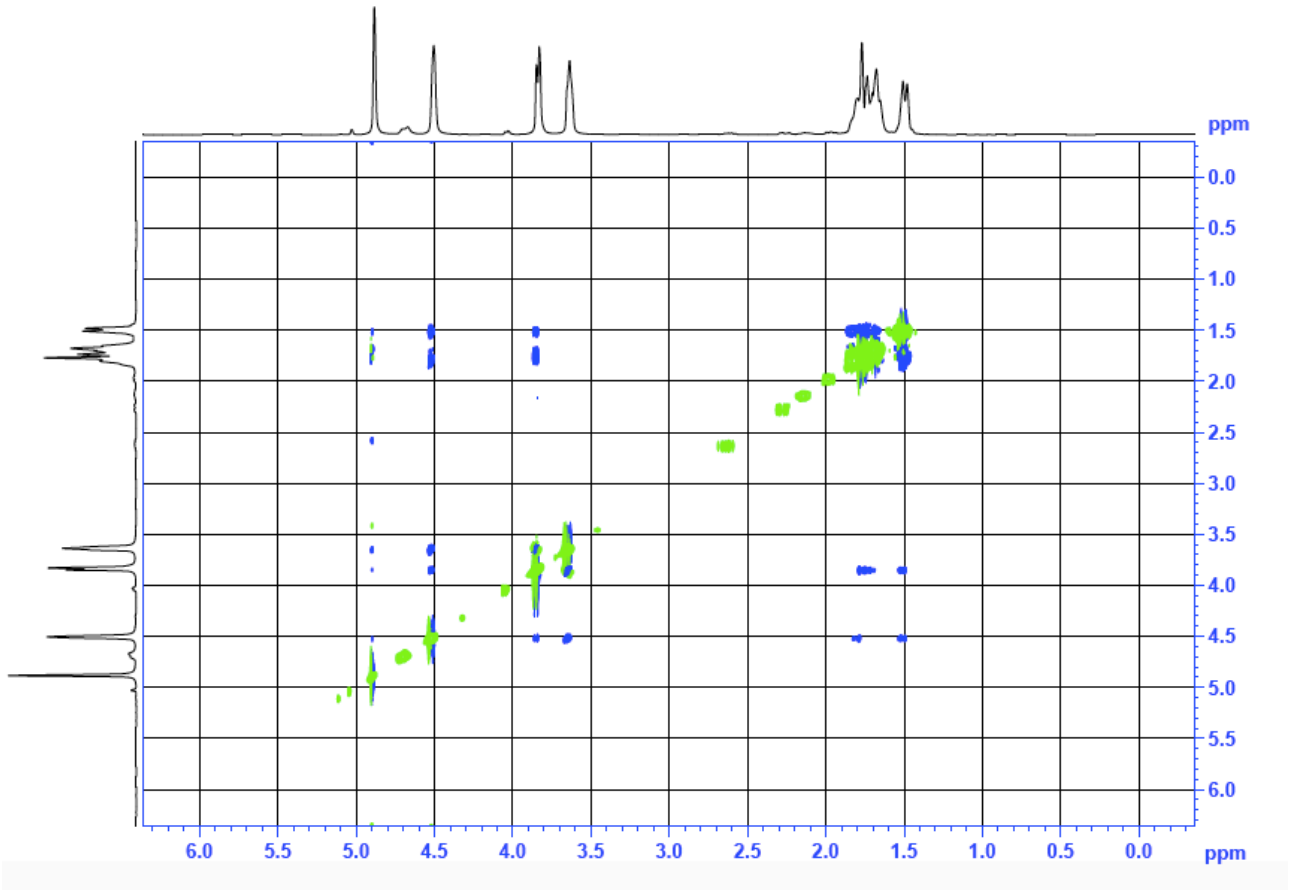


Figure S10 NOESY NMR analysis of a 10:1 v/v mixture of D_2O:Cyrene mixture

B. A series of D_2O:Cyrene mixture were made up in an NMR tube at rt and subjected to proton analysis. Peaks at approximately 4.6 *vs* 4.8 ppm and 4.9 *vs* 5.1 ppm were integrated and the average difference in peak area use to create Figure 2 in the main text (also see, Figure S11).

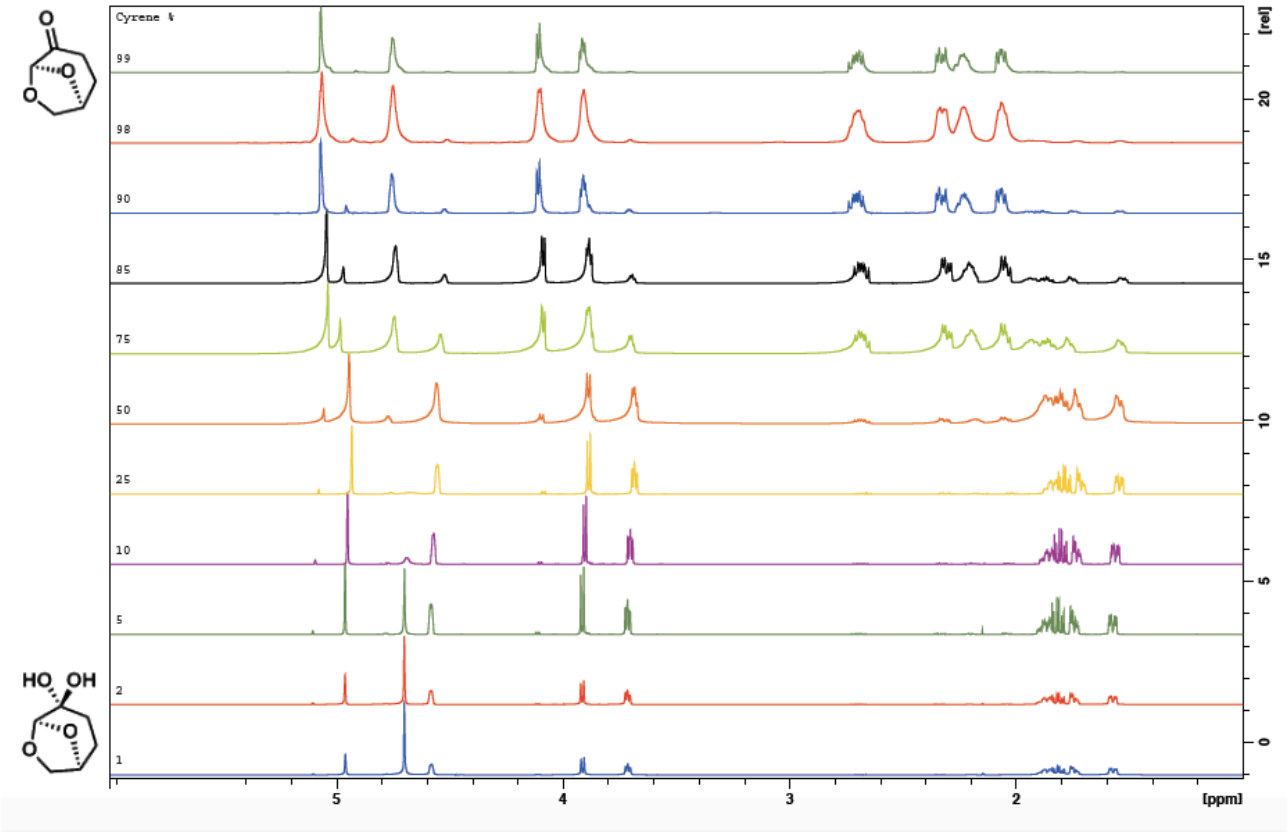


Figure S11 Stacked proton NMRs of various D_2O to Cyrene mixtures.

III. Cyrene / Water Temperature Study

A. Water (2.5 mL) was added to Cyrene (2.5 mL) with stirring at room temperature.

Entry	Time (min)	Temperature (°C)		Av. Temp (°C)
		Exp 1	Exp 2	
1	0	27.0	27.0	27.0
2	1	35.5	40.0	37.8
3	2	41.0	41.5	41.3
4	3	40.0	40.0	40.0
5	4	38.5	38.8	38.7
6	5	37.0	37.5	37.3
7	6	36.0	36.2	36.1
8	7	34.9	35.2	35.1
9	8	34.0	34.8	34.4
10	9	33.0	34.0	33.5
11	10	32.5	33.2	32.9
12	11	32.0	32.7	32.4

13	12	31.4	32.0	31.7
14	13	30.8	31.7	31.3
15	14	30.2	31.2	30.7
16	15	30.0	30.9	30.5
17	16	30.0	30.5	30.3
18	17	29.8	30.2	30.0
19	18	29.2	30.0	29.6
20	19	29.0	29.9	29.5
21	20	28.8	29.8	29.3
22	21	28.7	29.7	29.2
23	22	28.5	29.4	29.0
24	23	28.3	29.1	28.7
25	24	28.1	29.0	28.6
26	25	28.0	28.9	28.5

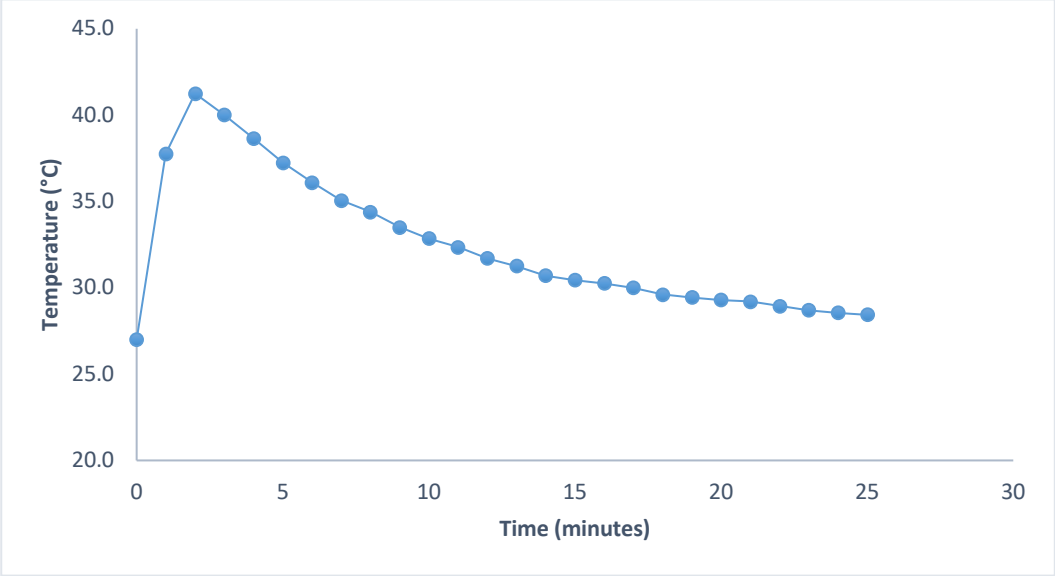
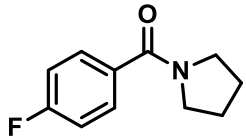


Figure S12 Change in temperature *vs.* time when water (2.5 mL) was added to Cyrene (**1**, 2.5 mL)

IV. Preparation of Amides 4a,b,d,e,h, 5a-k and 6a-k

* Note – isolated yields for compounds that were directly precipitated from the aqueous Cyrene solution, **5a-k and 6a-k**, were obtained by the following protocol: To the solid was added ethyl acetate (5 mL) and the resultant solution was dried over sodium sulphate and the solvent was removed under reduced pressure.

(4-Fluorophenyl)(pyrrolidin-1-yl)methanone[14] **4a**

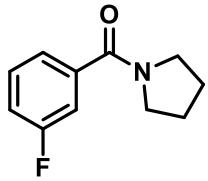


Method 1: To a stirred solution of 4-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford (4-fluorophenyl)(pyrrolidin-1-yl)methanone (**4a**, 72 mg, 75%) as a colourless solid.

Method 2: Method To a stirred solution of 4-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was diluted with EtOAc (5 mL) and added to water (10 mL). The mixture was extracted with EtOAc (2 x 10 mL) and the organic extracts were combined and dried over Na_2SO_4 and the solvent was removed under reduced pressure and the residue purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford (4-fluorophenyl)(pyrrolidin-1-yl)methanone (**4a**, 88 mg, 91%) as a colourless solid.

mp: 87-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-7.47 (m, 2H), 7.05-7.01 (m, 2H), 3.58 (t, J = 6.8 Hz, 2H), 3.38 (t, J = 6.6 Hz, 2H), 1.95-1.80 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -110.41 (s, 1F); ^{13}C (100 MHz, $CDCl_3$): δ 168.6, 163.4 (d, $J_{C\text{-}F}$ = 248 Hz), 133.2 (d, $J_{C\text{-}F}$ = 3 Hz), 129.4 (d, $J_{C\text{-}F}$ = 8 Hz), 115.2 (d, $J_{C\text{-}F}$ = 22 Hz), 49.7, 46.3, 26.4, 24.4; IR 3064, 2980, 2956, 2886, 1621, 1601, 1425 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{13}FNO]^+$ 194.0976; found 194.0975.

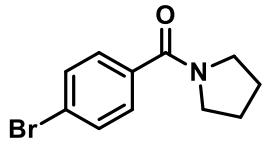
(3-Fluorophenyl)(pyrrolidin-1-yl)methanone[14] **4b**



To a stirred solution of 3-fluorobenzoyl chloride (61 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford (3-fluorophenyl)(pyrrolidin-1-yl)methanone (**4b**, 73 mg, 76%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.31 (m, 1H), 7.26-7.24 (m, 1H), 7.20-7.16 (m, 1H), 7.09-7.04 (m, 1H), 3.59 (t, J = 6.9 Hz, 2H), 3.38 (t, J = 6.5 Hz, 2H), 1.96-1.81 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.30 (s, 1F); ^{13}C (100 MHz, $CDCl_3$): δ 168.2 (d, $J_{C\text{-}F}$ = 2 Hz), 162.4 (d, $J_{C\text{-}F}$ = 246 Hz), 139.2 (d, $J_{C\text{-}F}$ = 7 Hz), 130.0 (d, $J_{C\text{-}F}$ = 8 Hz), 122.8 (d, $J_{C\text{-}F}$ = 3 Hz), 116.7 (d, $J_{C\text{-}F}$ = 21 Hz), 114.3 (d, $J_{C\text{-}F}$ = 23 Hz), 49.5, 46.2, 26.4, 24.4; IR 3067, 2973, 2876, 1621, 1581, 1445 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{13}FNO]^+$ 194.0976; found 194.0976.

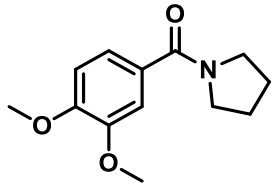
4-Bromo-*N*-phenylbenzamide[14] **4d**



To a stirred solution of 4-bromobenzoyl chloride (110 mg, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford 4-bromo-*N*-phenylbenzamide (**4d**, 64 mg, 50%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.52 (m, 2H), 7.41-7.39 (m, 2H), 3.62 (t, *J* = 6.9 Hz, 2H), 3.40 (t, *J* = 6.6 Hz, 2H), 1.99-1.84 (m, 4H); ^{13}C (100 MHz, $CDCl_3$): δ 168.6, 136.0, 131.5, 128.9, 124.1, 49.6, 46.3, 26.4, 24.4; IR 2970, 2874, 162, 1417 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{13}BrNO]^+$ 254.0175; found 254.0176.

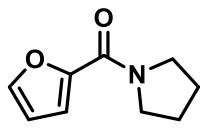
(3,4-Dimethoxyphenyl)(pyrrolidin-1-yl)methanone[15] **4e**



To a stirred solution of 3,4-dimethoxybenzoyl chloride (100 mg, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford (3,4-dimethoxyphenyl)(pyrrolidin-1-yl)methanone (**4e**, 81 mg, 68%) as a white oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06-7.02 (m, 2H), 6.77 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 6H), 3.54 (t, *J* = 6.8 Hz, 2H), 3.41 (t, *J* = 6.4 Hz, 2H), 1.88-1.77 (m, 4H); ^{13}C (100 MHz, $CDCl_3$): δ 169.3, 150.2, 148.6, 129.5, 120.22, 110.9, 110.1, 55.9, 49.8, 46.3, 26.4, 24.4; IR 3430, 2970, 2935, 2878, 1610, 1578, 1510, 1453 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{13}H_{17}NO_3Na]^+$ 258.1101; found 258.1104.

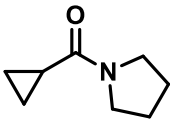
Furan-2-yl(pyrrolidin-1-yl)methanone[16] **4h**



To a stirred solution of furoyl chloride (49 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford furan-2-yl(pyrrolidin-1-yl)methanone (**4h**, 64 mg, 68%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 0.7 Hz, *J* = 1.6 Hz, 1H), 7.01 (dd, *J* = 0.6 Hz, *J* = 3.5 Hz, 1H), 6.44 (dd, *J* = 1.7 Hz, *J* = 3.5 Hz, 1H), 3.78 (t, *J* = 6.8 Hz, 2H), 3.60 (t, *J* = 6.9 Hz, 2H), 1.98-1.81 (m, 4H); ^{13}C (100 MHz, $CDCl_3$): δ 158.1, 148.7, 144.0, 115.7, 111.3, 47.8, 47.0, 26.6, 23.7; IR 3486, 3110, 2971, 2877, 1611, 1479, 1413 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_9H_{11}NO_2Na]^+$ 188.0682; found 188.0683.

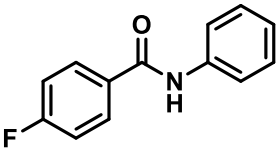
cyclopropyl(pyrrolidin-1-yl)methanone[17] **5j**



To a stirred solution of cyclopropanecarbonyl chloride (45 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and pyrrolidine (42 µL, 0.5 mmol) and the resultant mixture was stirred at r.t. for 1 h. The solution was purified by flash chromatography column on silica gel (30% EtOAc in hexane → 70% EtOAc in hexane) to afford cyclopropyl(pyrrolidin-1-yl)methanone (**4j**, 11 mg, 16%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.60 (t, *J* = 6.8 Hz, 2H), 3.45 (t, *J* = 6.9 Hz, 1H), 1.98 (quin, *J* = 6.6 Hz, 2H), 1.85 (quin, *J* = 6.8 Hz, 2H), 1.64-1.58 (m, 1H), 1.00-0.97 (m, 2H); ^{13}C (100 MHz, $CDCl_3$): δ 170.1, 46.5, 46.0, 26.1, 24.5, 12.5, 7.3; IR 3438, 1615, 1451 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_8H_{14}NO]^+$ 140.1070; found 140.1071.

4-Fluoro-*N*-phenylbenzamide[1] **5a**

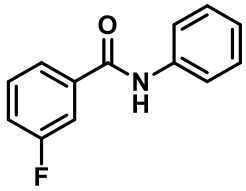


Method 1: To a stirred solution of 4-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford 4-fluoro-*N*-phenylbenzamide (**5a**, 77 mg, 72%) as an off white solid.

Method 2: To a stirred solution of 4-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford 4-fluoro-*N*-phenylbenzamide (**5a**, 98 mg, 91%) as an off white solid.

mp: 183-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.87 (m, 2H), 7.75 (br. s, 1H), 7.63 (d, *J* = 7.7 Hz, 2H), 7.40-7.36 (m, 2H), 7.20-7.15 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -107.37 (s, 1F); ^{13}C (100 MHz, $CDCl_3$): δ 166.2, 164.2 (d, $J_{C\text{-}F}$ = 97 Hz), 137.7, 131.2 (d, $J_{C\text{-}F}$ = 3 Hz), 129.4 (d, $J_{C\text{-}F}$ = 9 Hz), 129.2, 120.2, 115.9 (d, $J_{C\text{-}F}$ = 22 Hz); IR 3347, 3082, 2919, 1654, 1587, 1524 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{13}H_{11}FNO]^+$ 216.0819; found 216.0825.

3-Fluoro-*N*-phenylbenzamide[2] **5b**

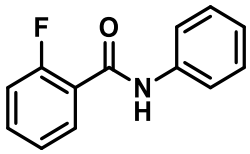


Method 1: To a stirred solution of 3-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford 3-fluoro-*N*-phenylbenzamide (**5b**, 82 mg, 76%) as a white solid.

Method 2: To a stirred solution of 3-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford 3-fluoro-*N*-phenylbenzamide (**5b**, 81 mg, 75%) as a white solid.

mp: 144-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (br. s, 1H), 7.64-7.58 (m, 4H), 7.47 (dt, J = 5.5 Hz, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 2H), 7.28-7.23 (m, 1H), 7.20-7.16 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -111.21 (s, 1F); ^{13}C (100 MHz, $CDCl_3$): δ 164.4, 162.9 (d, $J_{C\text{-}F}$ = 247 Hz), 137.6, 137.3 (d, $J_{C\text{-}F}$ = 7 Hz), 130.5 (d, $J_{C\text{-}F}$ = 8 Hz), 129.2, 124.9, 122.4 (d, $J_{C\text{-}F}$ = 3 Hz), 120.3, 118.9 (d, $J_{C\text{-}F}$ = 21 Hz), 114.6 (d, $J_{C\text{-}F}$ = 23 Hz); IR 3349, 3061, 1654, 1595, 1530, 1503 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{13}H_{11}FNO]^+$ 216.0819; found 216.0825.

2-Fluoro-*N*-phenylbenzamide[3] **5c**

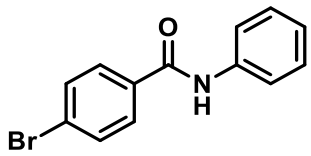


Method 1: To a stirred solution of 2-fluorobenzoyl chloride (60 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 2-fluoro-*N*-phenylbenzamide (**5c**, 79 mg, 73%) as a white solid.

Method 2: To a stirred solution of 2-fluorobenzoyl chloride (60 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 2-fluoro-*N*-phenylbenzamide (**5c**, 75 mg, 70%) as a white solid.

mp. (°C) 94-98; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.46 (br. d, J = 14.7, 1H), 8.19 (td, J = 8.0, J = 3.9, 1H), 7.67 (d, J = 7.6Hz, 2H), 7.56-7.50 (m, 1H), 7.40-7.31 (m, 3H), 7.22-7.15 (m, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -113.16; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.3 (d, J_{C-F} = 3.5 Hz), 160.4 (d, J_{C-F} = 245 Hz), 137.7, 133.7 (d, J_{C-F} = 9.4 Hz), 132.2 (d, J_{C-F} = 1.8 Hz), 129.1, 125.1 (d, J_{C-F} = 3.2 Hz), 124.8, 121.4 (d, J_{C-F} = 11.2 Hz), 120.6, 116.2 (d, J_{C-F} = 24.9 Hz); IR (neat): 3376, 3065, 2981, 1657 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{13}H_{11}FNO]^+$ 216.0819; found 216.0825.

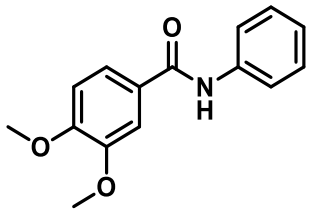
4-Bromo-*N*-phenylbenzamide[1] **5d**



To a stirred solution of 4-bromobenzoyl chloride (110 mg, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 4-bromo-*N*-phenylbenzamide (**5d**, 118 mg, 85%) as an off white solid.

mp. (°C) 178-181; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, J = 8.4, 3H), 7.65-7.62 (m, 4H), 7.39 (t, J = 7.9, 2H), 7.18 (t, J = 7.4, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.7, 137.6, 133.8, 132.1, 129.2, 128.6, 126.6, 124.8, 120.2; IR (neat): 3347, 3094, 3056, 2916, 1651 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{13}H_{11}BrNO]^+$ 276.0019; found 276.0025.

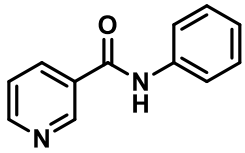
3,4-Dimethoxy-*N*-phenylbenzamide[4] **5e**



To a stirred solution of 3,4-dimethylbenzoyl chloride (102 mg, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (78 µL, 0.56 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 3,4-dimethoxy-*N*-phenylbenzamide (**5e**, 108 mg, 83%) as a white solid.

mp. (°C) 171-175; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (br. s, 1H), 7.64 (d, J = 7.6 Hz, 2H), 7.49 (d, J = 2.0 Hz, 1H), 7.41-7.34 (m, 3H), 7.14 (t, J = 7.4 Hz, 1H), 6.87 (d, J = 8.3 Hz, 1H), 3.93 (s, 3H) , 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.3, 152.1, 149.2, 138.1, 129.1, 127.5, 124.4, 120.2, 119.5, 110.7, 110.3, 56.1, 56.0; IR (neat): 3314, 2941, 2846, 1640 cm^{-1}; HRMS (DUALESI-TOFMS) *m/z* Calcd. for $[C_{15}H_{15}NO_3]^+$ 258.1125; found 258.1129.

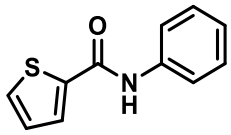
N-Phenylnicotinamide[5] **5f**



To a stirred solution of pyridine-3carbonyl chloride hydrochloride (89 mg, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford *N*-phenylnicotinamide (**5f**, 32 mg, 32%) as a white solid.

mp: 118-119°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.10 (d, *J* = 1.8 Hz, 1H), 8.79 (dd, *J* = 1.6 Hz, *J* = 4.8 Hz, 1H), 8.23-8.20 (m, 1H), 7.85 (br. s, 1H), 7.65 (d, *J* = 7.9 Hz, 2H), 7.46 (dd, *J* = 4.8 Hz, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.0 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H); ^{13}C (100 MHz, $CDCl_3$): δ 163.8, 152.7, 147.8, 137.4, 135.3, 130.8, 129.2, 125.1, 123.7, 120.4; IR 3349, 3055, 2919, 2850, 1653, 1601, 1584, 1529 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{12}H_{11}N_2O]^+$ 199.0866; found 199.0871.

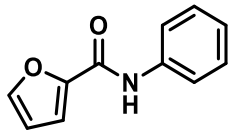
N-Phenyl-2-thiophenecarboxamide[4] **5g**



To a stirred solution of 2-thiophenecarbonyl chloride (53 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-phenyl-2-thiophenecarboxamide (**5g**, 56 mg, 55%) as a white solid.

mp. (°C) 144-148; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (br. s, 1H), 7.64-7.61 (m, 3H), 7.52 (dd, *J* = 1.0 Hz, *J* = 5.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.17-7.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.0, 139.3, 137.6, 130.8, 129.1, 128.5, 127.8, 124.6, 120.3; IR (neat): 3292, 3087, 3032, 2931, 1628 cm^{-1}; HRMS (DUALESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{10}NOS]^+$ 204.0478; found 204.0482.

N-Phenyl-2-furancarboxamide[6] **5h**

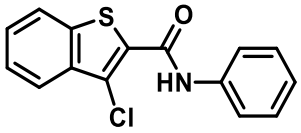


To a stirred solution of 2-furoyl chloride (49 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over

sodium sulfate and the solvent was removed under reduced pressure to give *N*-phenyl-2-furancarboxamide (**5h**, 64 mg, 68%) as an off white solid.

mp. (°C) 120-125; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.16 (br. s, 1H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.49 (d, *J* = 0.9 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 3.4 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.54 (dd, *J* = 1.7 Hz, *J* = 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.1, 147.8, 144.2, 137.4, 129.1, 124.5, 120.0, 115.3, 112.6; IR (neat): 3292, 3129, 3057, 2980, 1654 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{10}NO_2]^+$ 188.0706; found 188.0714.

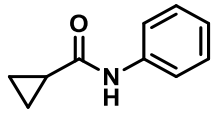
3-Chloro-*N*-phenylbenzo[b]thiophene-2-carboxamide[7] **5i**



To a stirred solution of 3-chlorobenzothiophene-2-carbonyl chloride (118 mg, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (71 µL, 0.56 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 3-chloro-n-phenylbenzo[b]thiophene-2-carboxamide (**5i**, 66 mg, 45%) as a white solid.

mp. (°C) 178-182; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.96 (br. s, 1H), 7.96-7.89 (m, 2H), 7.72 (d, *J* = 7.6 Hz, 2H), 7.58-7.53 (m, 2H), 7.43 (d, *J* = 2.0 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.7, 138.2, 137.2, 137.0, 129.2, 127.7, 125.6, 125.1, 123.3, 122.9, 120.4, 118.5; IR (neat): 3323, 3053, 1642 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{15}H_{11}ClNOS]^+$ 288.0244; found 288.0245.

N-Phenylcyclopropanecarboxamide[5] **5j**

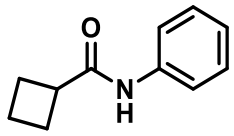


Method 1: To a stirred solution of cyclopropancarbonyl chloride (45 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-phenylcyclopropanecarboxamide (**5j**, 37 mg, 46%) as a white solid.

Method 2: To a stirred solution of cyclopropancarbonyl chloride (45 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-phenylcyclopropanecarboxamide (**5j**, 39 mg, 49%) as a white solid.

mp. (°C) 110-114; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (br. s, 1H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.08 (t, *J* = 7.2 Hz, 2H), 1.55-1.50 (m, 1H), 1.09-1.05 (m, 2H), 0.84-0.79 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 138.2, 129.0124.0, 119.8, 15.7, 7.9; IR (neat): 3284, 3253, 3131, 2980, 1656 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{10}H_{12}NO]^+$ 162.0913; found 162.0916.

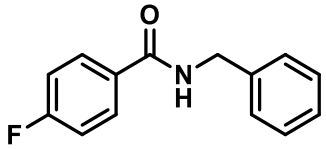
N-Phenylcyclobutanecarboxamide **5k**



To a stirred solution of cyclobutanecarbonyl chloride (57 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and aniline (46 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-phenylcyclobutanecarboxamide (**5k**, 67 mg, 76%) as an off white solid.

mp. (°C) 109-113; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, *J* = 7.9 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.16 (br. s, 1H), 7.09 (t, *J* = 5.4 Hz, 1H), 3.16 (quin, *J* = 8.5 Hz, 1H), 2.45-2.35 (m, 2H), 2.26-2.18 (m, 2H), 2.06-1.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.2, 138.0, 129.0, 124.1, 119.7, 40.9, 25.3, 18.1; IR (neat): 3294, 3137, 2982, 2942, 2865, 1657 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{14}NO]^+$ 176.1070; found 176.1074.

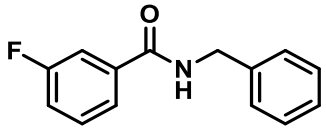
N-Benzyl-4-fluorobenzamide[8] **6a**



To a stirred solution of 4-fluorobenzoyl chloride (59 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (55 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-benzyl-4-fluorobenzamide (**6a**, 93 mg, 81%) as a white solid.

mp. (°C) 140-145; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82-7.78 (m, 2H), 7.38-7.28 (m, 5H), 7.12-7.07 (m, 2H), 6.44 (br. s, 1H) 4.63 (d, *J* = 5.6 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -108.08; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 164.8 (d, $J_{C\text{-}F}$ = 250.4 Hz), 138.0, 130.5 (d, $J_{C\text{-}F}$ = 3.1 Hz), 129.3 (d, $J_{C\text{-}F}$ = 8.9 Hz), 128.8, 128.0, 127.7, 115.6 (d, $J_{C\text{-}F}$ = 21.7 Hz), 44.2; IR (neat): 3317, 3066, 3032, 2931, 1640 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{14}H_{13}FNO]^+$ 230.0976; found 230.0976.

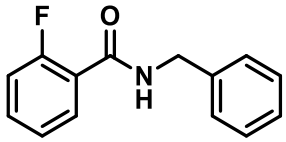
N-Benzyl-3-fluorobenzamide[9] **6b**



To a stirred solution of 3-fluorobenzoylchloride (61 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (55 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-benzyl-3-fluorobenzamide (**6b**, 78 mg, 73%) as an off white solid.

mp. (°C) 90-93; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54-7.49 (m, 2H), 7.54-7.49 (m, 2H), 7.38-7.26 (m, 6H), 7.20-7.15 (m, 1H), 6.85 (br. s, 1H), 4.58 (d, J = 5.7, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -111.79; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2 (d, $J_{C\text{-}F}$ = 2.4 Hz), 162.7 (d, $J_{C\text{-}F}$ = 246.1 Hz), 138.0, 136.6 (d, $J_{C\text{-}F}$ = 6.8 Hz), 130.2 (d, $J_{C\text{-}F}$ = 7.8 Hz), 128.8, 127.9, 127.7, 122.5 (d, $J_{C\text{-}F}$ = 3.0 Hz), 118.5 (d, $J_{C\text{-}F}$ = 21.1 Hz), 114.5 (d, $J_{C\text{-}F}$ = 22.7 Hz), 44.2; IR (neat): 3295, 3070, 3034, 2933, 1634 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{14}H_{13}FNO]^+$ 230.0976; found 230.0979.

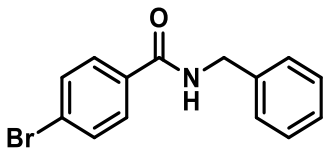
2-Fluoro-*N*-(phenylmethyl)benzamide[9] **6c**



To a stirred solution of 2-fluorobenzoyl chloride (60 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzyl amine (55 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 2-fluoro-*N*-(phenylmethyl)benzamide (**6c**, 89 mg, 76%) as a white solid.

mp. (°C) 39-40; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (td, J = 1.8, J = 7.9, 1H), 7.47-7.06 (m, 9H), 4.66 (d, J = 5.7, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -113.42; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.3 (d, $J_{C\text{-}F}$ = 3.1 Hz), 160.4 (d, $J_{C\text{-}F}$ = 245.7 Hz), 138.0, 133.4 (d, $J_{C\text{-}F}$ = 9.3 Hz), 132.2 (d, $J_{C\text{-}F}$ = 2.1 Hz), 128.8, 127.7, 127.6, 124.9 (d, $J_{C\text{-}F}$ = 3.2 Hz), 121.0 (d, $J_{C\text{-}F}$ = 11.4 Hz), 116.0 (d, $J_{C\text{-}F}$ = 24.6 Hz), 44.1; IR (neat): 3306, 3085, 29279, 1644 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{14}H_{13}FNO]^+$ 230.0976; found 229.0980.

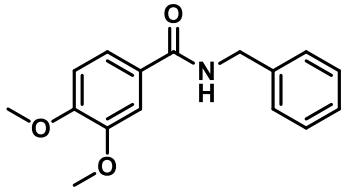
N-(4-bromobenzoyl)benzylamine[10] **6d**



To a stirred solution of 4-bromobenzoyl chloride (101.5 mg, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (71 µL, 0.51 mmol) and aniline (50 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-(4-bromobenzoyl)benzylamine (**6d**, 69 mg, 69%) as an off white solid.

mp. (°C) 165-169; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67-7.65 (m, 2H), 7.56-7.55 (m, 2H), 7.38-7.29 (m, 5H), 6.42 (br. s, 4.63 (d, J = 5.6, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 137.9, 133.2, 131.8, 128.9, 128.6, 128.0, 127.8, 126.3, 44.3; IR (neat): 3305, 3060, 3029, 1639 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{14}H_{12}BrNONa]^+$ 311.9994; found 311.9989.

N-benzyl-3,4-dimethoxybenzamide[11] **6e**

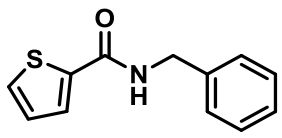


Method 1: To a stirred solution of 3,4-dimethoxybenzoyl chloride (100 mg, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (54 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford *N*-benzyl-3,4-dimethoxybenzamide (**6e**, 101 mg, 86%) as a white solid.

Method 2: To a stirred solution of 3,4-dimethoxybenzoyl chloride (1 g, 5 mmol) in Cyrene (5 mL) at 0 °C were added triethylamine (767 µL, 5.5 mmol) and benzylamine (546 µL, 5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford *N*-benzyl-3,4-dimethoxybenzamide (**6e**, 1.04 g, 77%) as a white solid.

mp: 124-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 1.9 Hz, 1H), 7.34 (dd, J = 1.9 Hz, J = 7.3 Hz, 1H), 7.28-7.22* (m, 5H), 7.06 (t, J = 5.5 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 4.5 (d, J = 5.8 Hz, 2H), 3.84 (s, 3H), 3.79 (s, 3H); ^{13}C (100 MHz, $CDCl_3$): δ 167.1, 151.7, 148.8, 138.6, 128.6, 127.8, 127.4, 126.9, 119.7, 110.6, 110.2, 55.9, 55.9, 44.0; IR 3276, 3085, 3013, 2933, 2838, 1627, 1581, 1505 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{16}H_{18}NO_3]^+$ 272.1281; found 272.1276.

N-Benzylthiophene-2-carboxamide[8] **6g**

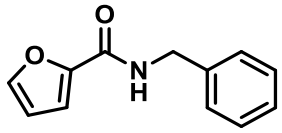


To a stirred solution of 2-thiophenecarbonyl chloride (53 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (55 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred

for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-benzylthiophene-2-carboxamide (**6g**, 80 mg, 74%) as an off white solid.

mp. (°C) 117-121; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 (dd, *J* = 1.1 Hz, *J* = 3.7 Hz, 1H), 7.47 (dd, *J* = 1.1 Hz, *J* = 5.0 Hz, 1H), 7.35-7.28 (m, 5H), 7.06 (dd, *J* = 3.7 Hz, *J* = 5.0 Hz, 1H), 6.39 (br. s, 1H), 4.61 (d, *J* = 5.8, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.8, 138.8, 138.0, 130.1, 128.8, 128.2, 128.0, 127.68, 127.67, 44.0; IR (neat): 3348, 3089, 3060, 3032, 1621 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{12}H_{12}NOS]^+$ 218.0634; found 218.0640.

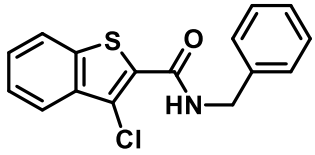
N-(phenylmethyl)-2-furancarboxamide[12] **6h**



To a stirred solution of furoyl chloride (49 µL, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (55 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give *N*-(phenylmethyl)-2-furancarboxamide (**6h**, 74 mg, 73%) as an off white solid.

mp. (°C) 109-110; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40-7.39 (m, 1H), 7.35-7.26 (m, 5H), 7.13-7.12 (m, 1H), 6.76 (br. s, 1H), 6.40 (dd, *J* = 1.7 Hz, *J* = 3.5 Hz, 1H), 4.59 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.3, 147.9, 144.0, 138.1, 128.8, 127.9, 127.6, 114.4, 112.2, 43.1; IR (neat): 3283, 3124, 3062, 3030, 1638 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{12}H_{12}NO_2]^+$ 202.0863; found 202.866.

3-Chloro-*N*-(phenylmethyl)benzo[b]thiophene-2-carboxamide **6i**



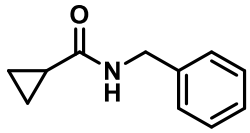
Method 1: To a stirred solution of 3-chlorobenzothiophene-2-carbonyl chloride (118 mg, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (79 µL, 0.56 mmol) and benzylamine (56 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to give 3-chloro-*N*-(phenylmethyl)benzo[b]thiophene-2-carboxamide (**6i**, 73 mg, 47%) as an off white solid.

Method 2: To a stirred solution of 3-chlorobenzothiophene-2-carbonyl chloride (118 mg, 0.5 mmol) in Cyrene (0.5 mL, 1 M) at 0 °C were added triethylamine (79 µL, 0.56 mmol) and benzylamine (56 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 24 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced

pressure to give 3-chloro-*N*-(phenylmethyl)benzo[b]thiophene-2-carboxamide (**6i**, 106 mg, 74%) as an off white solid.

mp. (°C) 122-126; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88-7.84 (m, 2H), 7.53-7.31 (m, 8H), 4.74 (d, *J* = 5.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.8, 138.0, 137.6, 137.0, 133.1, 128.9, 127.8, 127.4, 125.4, 123.1, 122.9, 118.7, 44.2; IR (neat): 3259, 3057, 1626 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{16}H_{12}ClNOSNa]^+$ 324.0220; found 324.0218.

N-Benzylcyclopropanecarboxamide[10] **6j**

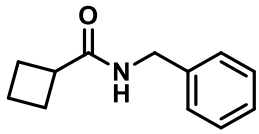


To a stirred solution of cyclopropanecarbonyl chloride (45 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (54 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford *N*-benzylcyclopropanecarboxamide (**6j**, 56 mg, 64%) as a white solid.

mp: 139-141°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.26* (m, 5H), 5.85 (br. s, 1H), 4.47 (d, *J* = 5.7 Hz, 2H), 1.38-1.32 (m, 1H), 1.04-1.00 (m, 2H), 0.78-0.74 (m, 2H); ^{13}C (100 MHz, $CDCl_3$): δ 170.8, 138.5, 128.7, 127.9, 127.5, 43.9, 14.8, 7.3; IR 3291, 1630, 1560, 1452, 1110 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{11}H_{14}NO]^+$ 176.1070; found 176.1073.

*Overlaps with residual $CHCl_3$

N-Benzylcyclobutanecarboxamide[13] **6k**



To a stirred solution of cyclobutanecarbonyl chloride (57 µL, 0.5 mmol) in Cyrene (0.5 mL) at 0 °C were added triethylamine (77 µL, 0.55 mmol) and benzylamine (54 µL, 0.5 mmol). The resultant mixture was allowed to warm to r.t. over 1 h. Water (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over sodium sulfate and the solvent was removed under reduced pressure to afford *N*-benzylcyclobutanecarboxamide (**6k**, 40 mg, 42%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.26* (m, 5H), 5.59 (br. s, 1H), 3.03 (quin, *J* = 8.5 Hz, 1H), 2.37-2.27 (m, 2H), 2.20-2.12 (m, 2H), 2.03-1.83 (m, 2H); ^{13}C (100 MHz, $CDCl_3$): δ 174.8, 138.5, 128.7, 127.8, 127.5, 43.5, 39.9, 28.4, 18.2; IR 3290, 2930, 1631, 1520, 1450 cm^{-1}; HRMS (DualESI-TOFMS) *m/z* Calcd. for $[C_{12}H_{15}NOK]^+$ 228.0785; found 228.0787.

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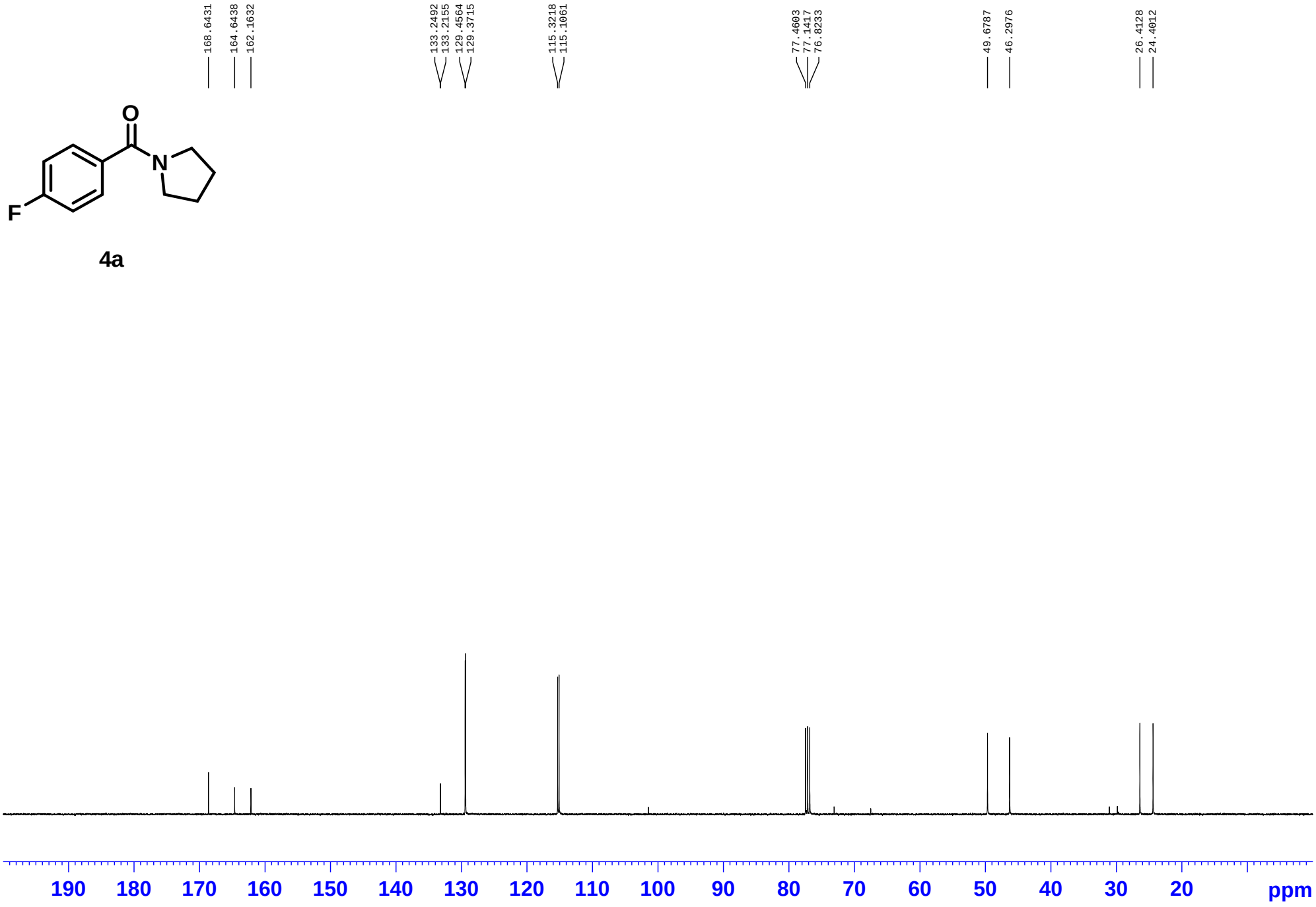
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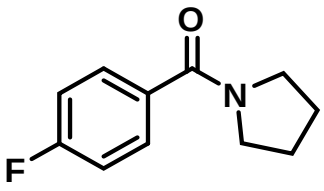

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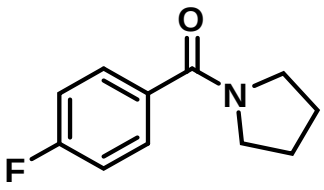
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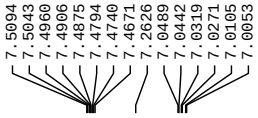
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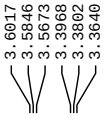
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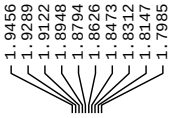
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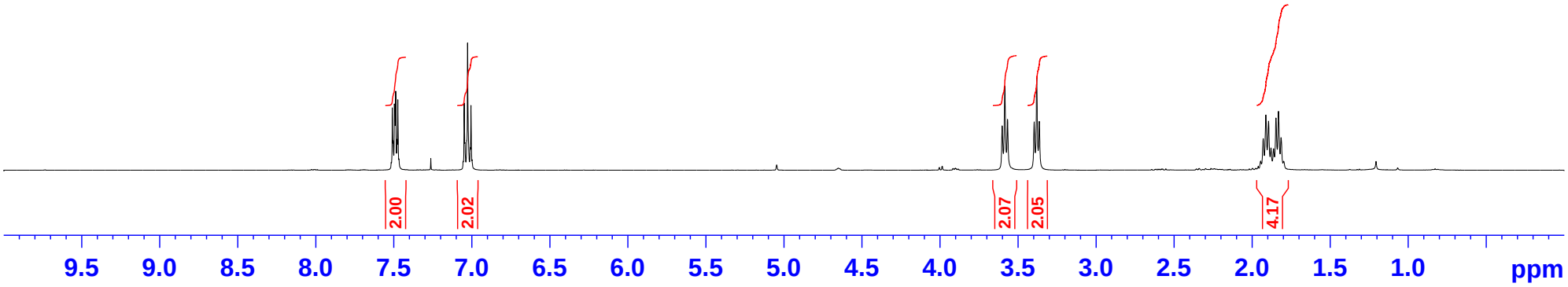
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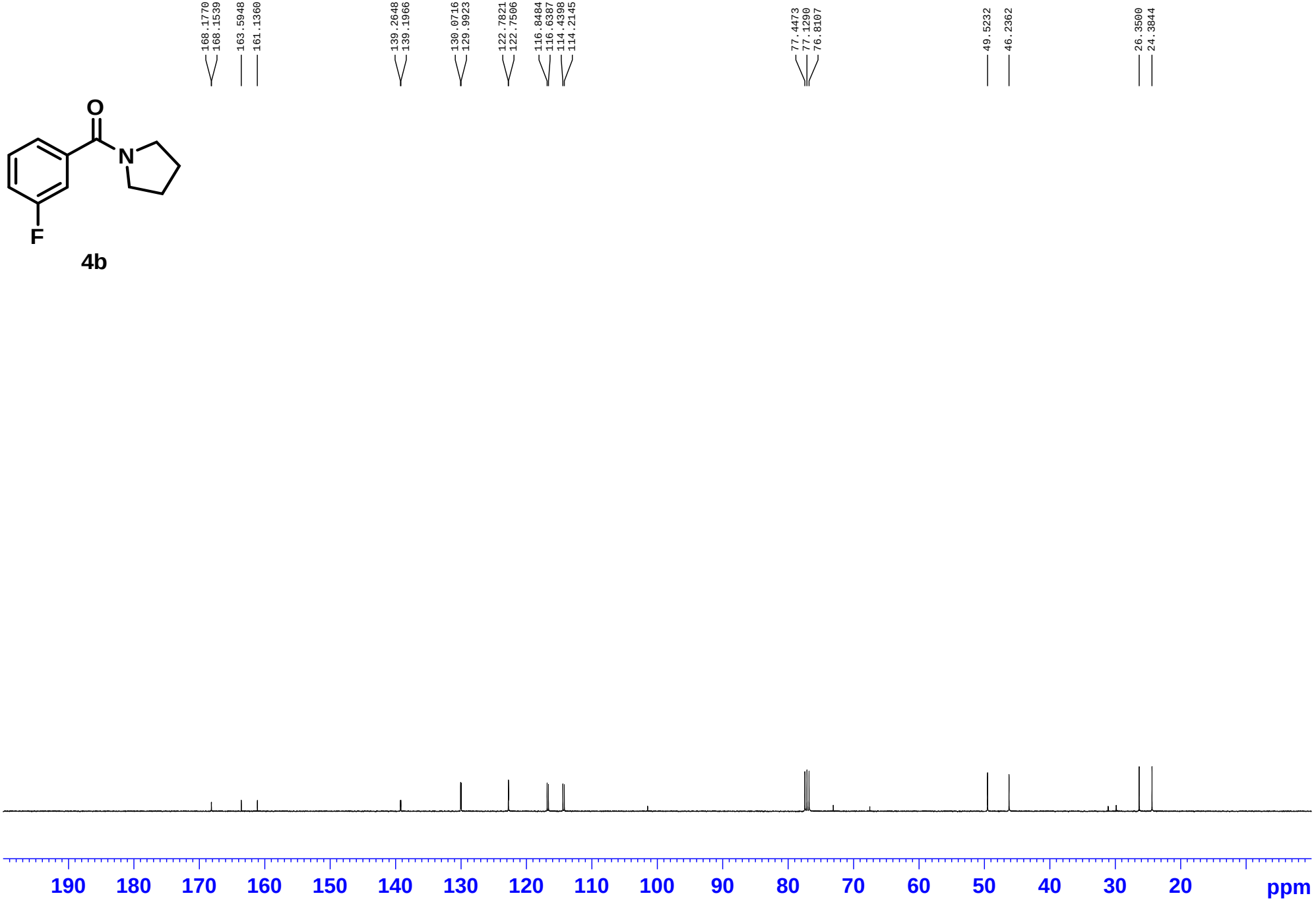
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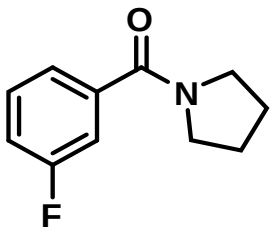

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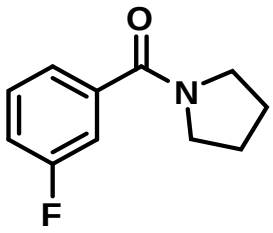
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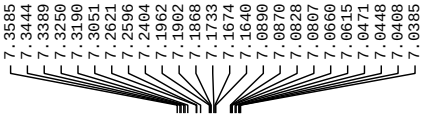
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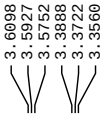
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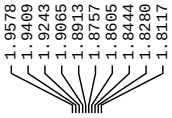
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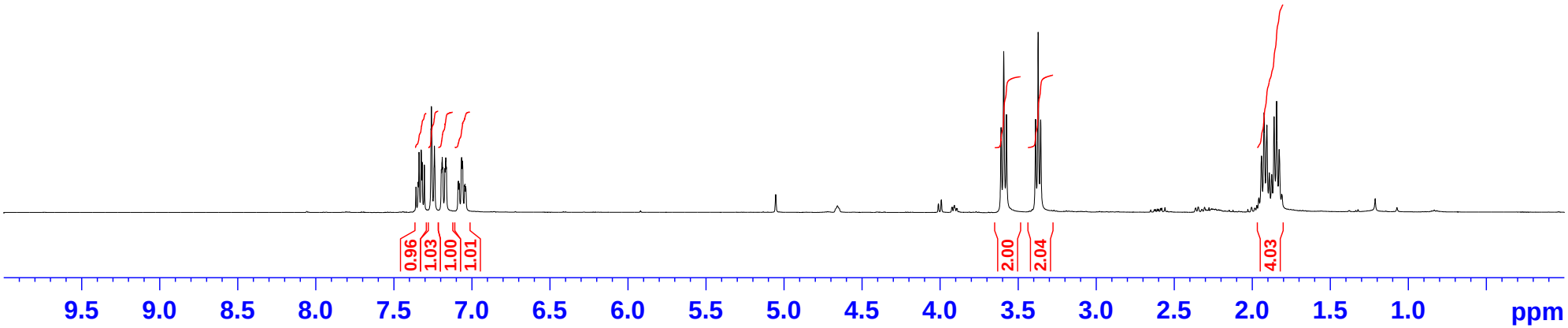
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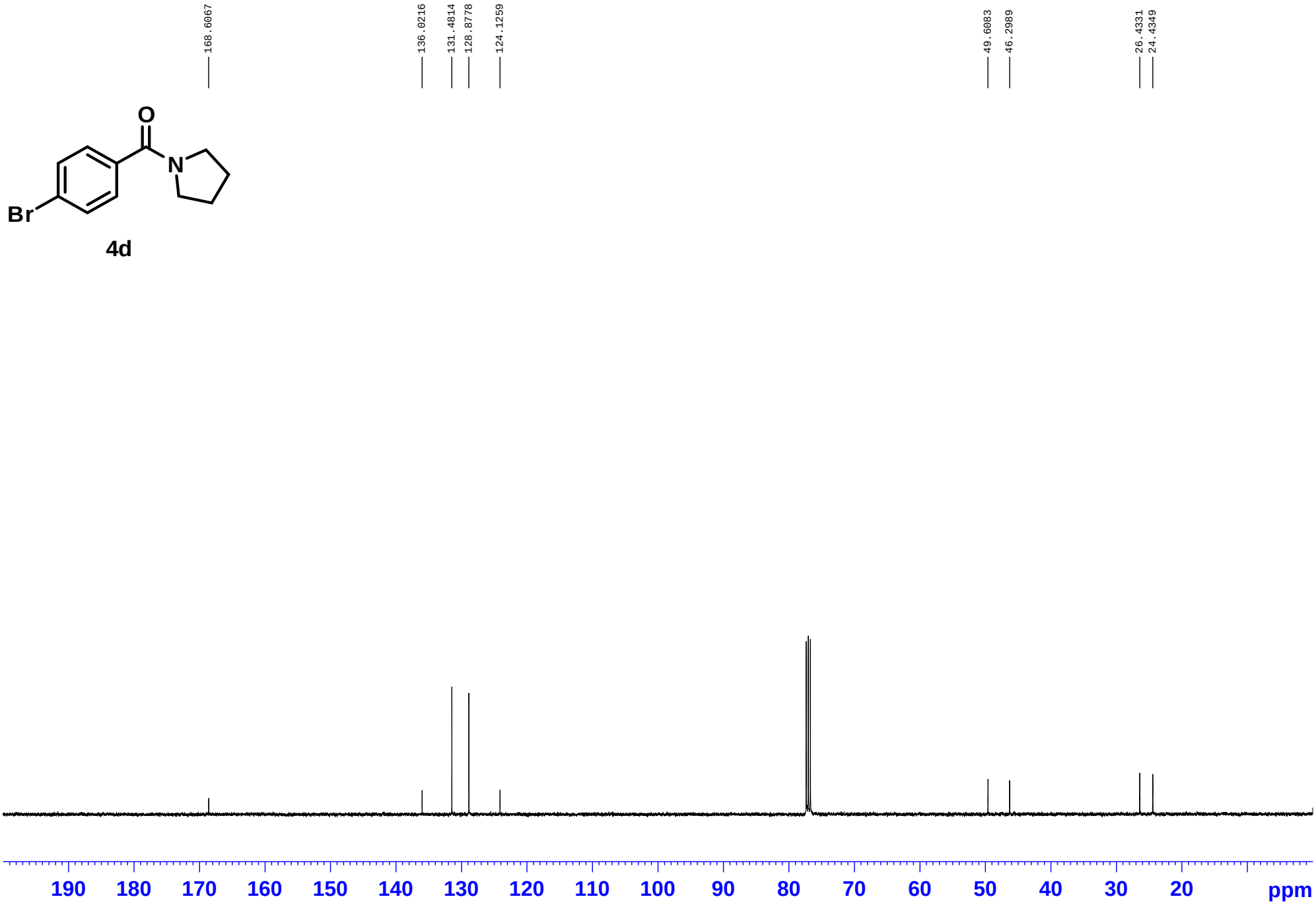
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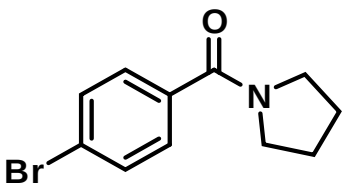
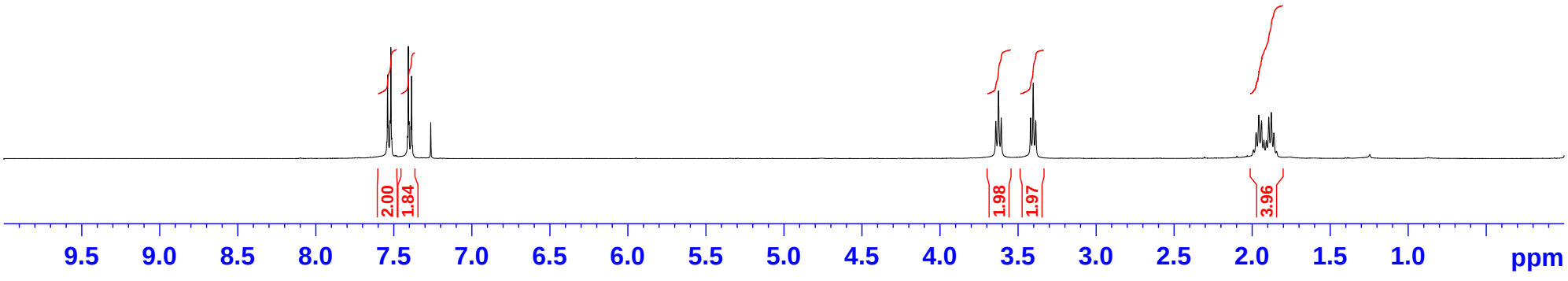

O
N
Br

4d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3.6253
3.6078
3.4195
3.4029
3.3867
1.9911
1.9741
1.9575
1.9398
1.9245
1.9086
1.8934
1.8774
1.8610
1.8446
2.00
1.84
1.98
1.97
3.96
9.5
9.0
8.5
8.0
7.5
7.0
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5.0
4.5
4.0
3.5
3.0
2.5
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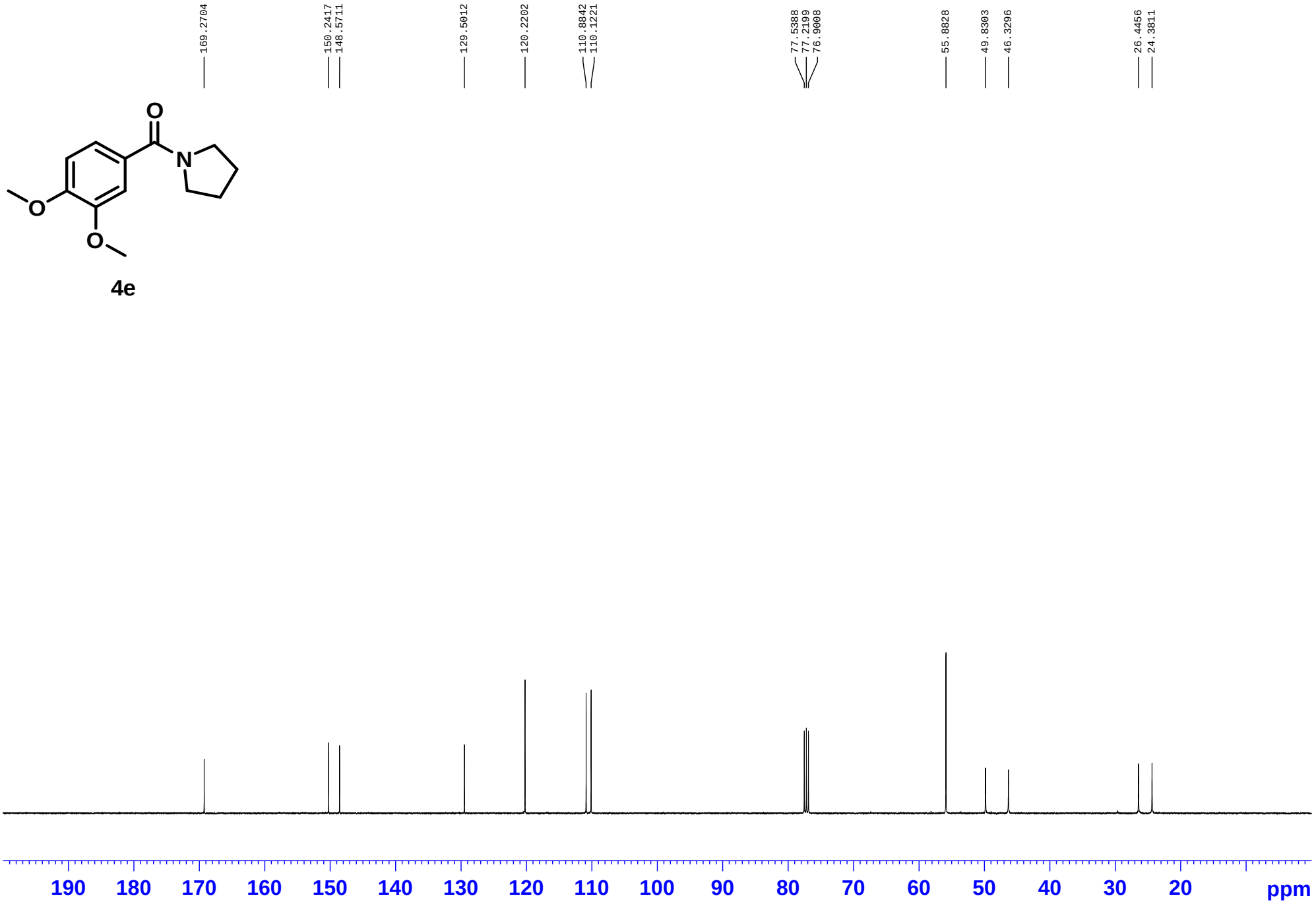
1.5
1.0
ppm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110.1221
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77.2199
76.9008
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46.3296
26.4456
24.3811
O
N
O
O
4e
190
180
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160
150
140
130
120
110
100
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80
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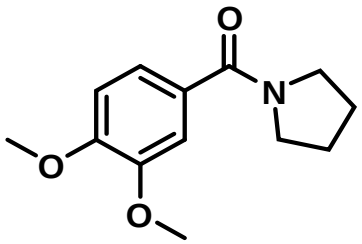
50
40
30
20
ppm


O
N
O
O

4e

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7.0567
7.0522
7.0438
7.0391
7.0234
7.0187
6.7780
6.7576
3.8131
3.5568
3.5400
3.5230
3.4243
3.4082
3.3925
1.8824
1.8658
1.8495
1.8340
1.8131
1.7983
1.7826
1.7665
1.91
0.97
5.93
1.94
2.00
3.96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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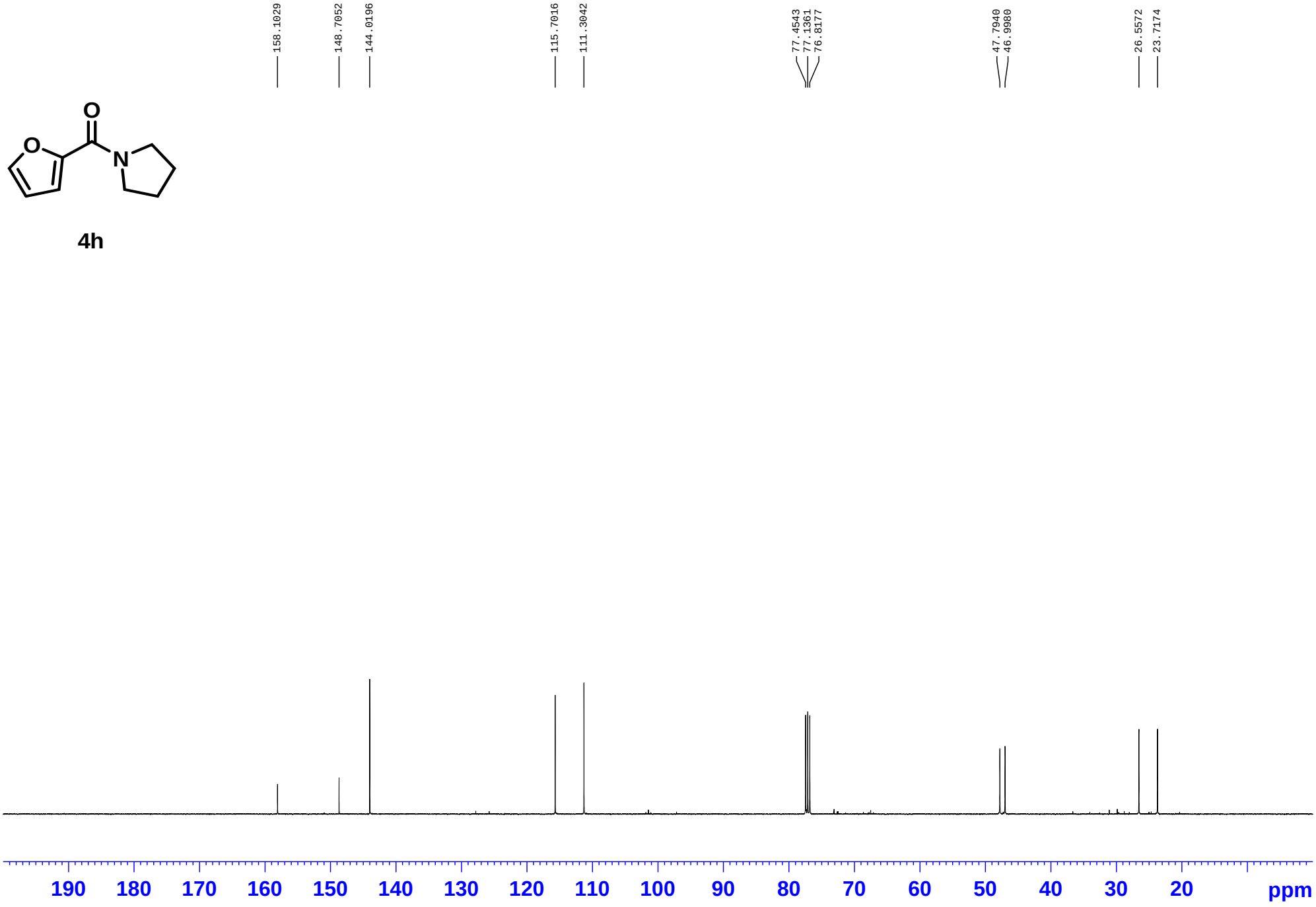
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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115.7016
111.3042
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77.1361
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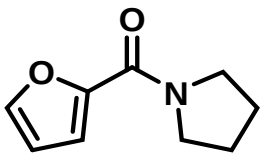
47.7940
46.9980
26.5572
23.7174
O
O
N
4h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
O
N

4h

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7.4614
7.4596
7.2618
7.0152
7.0136
7.0065
7.0050
6.4423
6.4379
6.4336
6.4293
3.7962
3.7794
3.7624
3.6163
3.5991
3.5820
1.9826
1.9660
1.9491
1.9326
1.9164
1.8814
1.8653
1.8478
1.8312
1.8147
0.93
0.95
0.94
2.04
2.00
1.97
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
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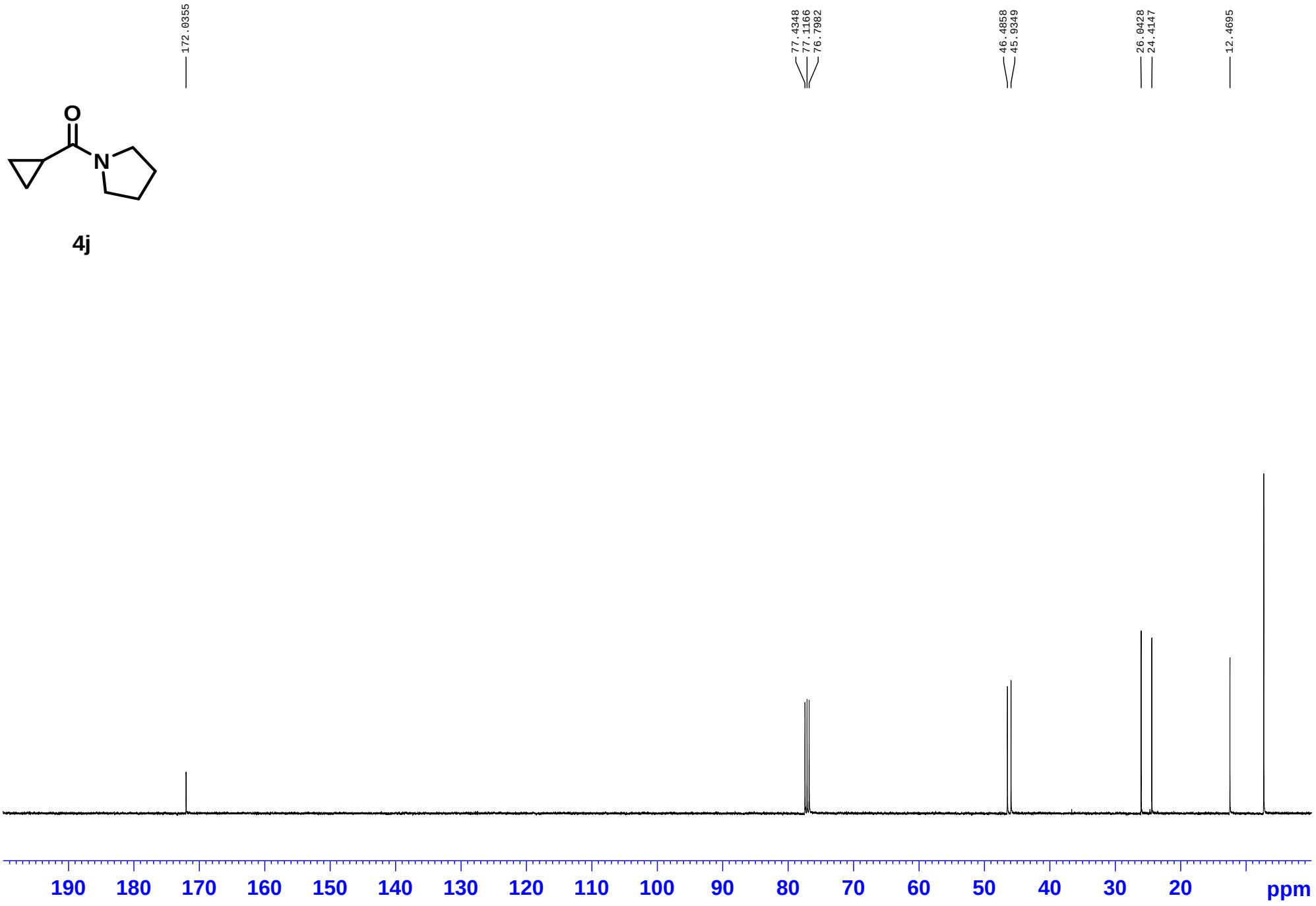
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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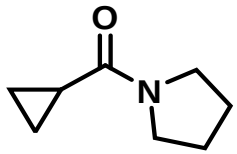
77.1166
76.7982
46.4858
45.9349
26.0428
24.4147
12.4695
O
N
4j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
N

4j

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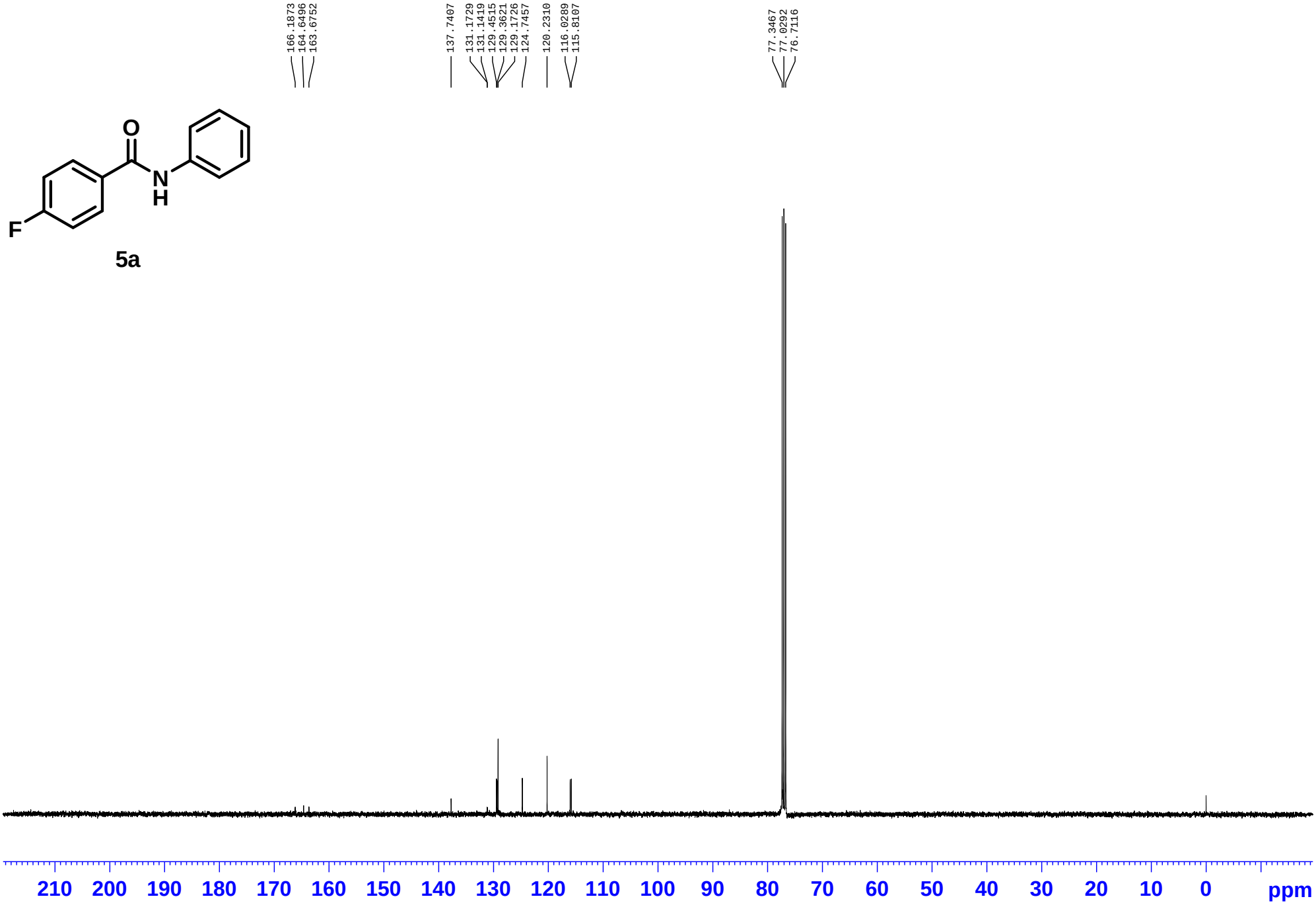
3.5927
3.5756
3.5585
3.4387
3.4215
3.4043
1.9764
1.9594
1.9424
1.9258
1.9087
1.8509
1.8344
1.8173
1.8000
1.7825
1.6123
1.6006
1.5923
1.5808
1.5692
1.5609
1.5493
0.9589
0.9490
0.9418
0.9378
0.9303
0.9213
0.7240
0.7153
0.7076
0.6954
0.6878
0.6782
2.00
2.00
2.05
2.04
1.01
1.91
1.96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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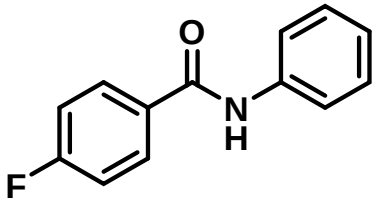
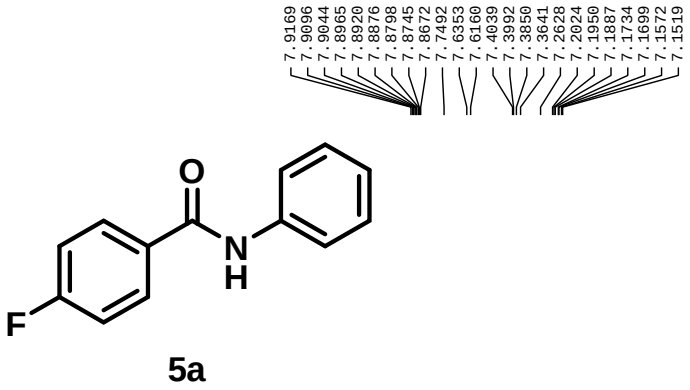
131.1419
129.4515
129.3621
129.1726
124.7457
120.2310
116.0289
115.8107
77.3467
77.0292
76.7116
O
N
H
F
5a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



5a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7.9044
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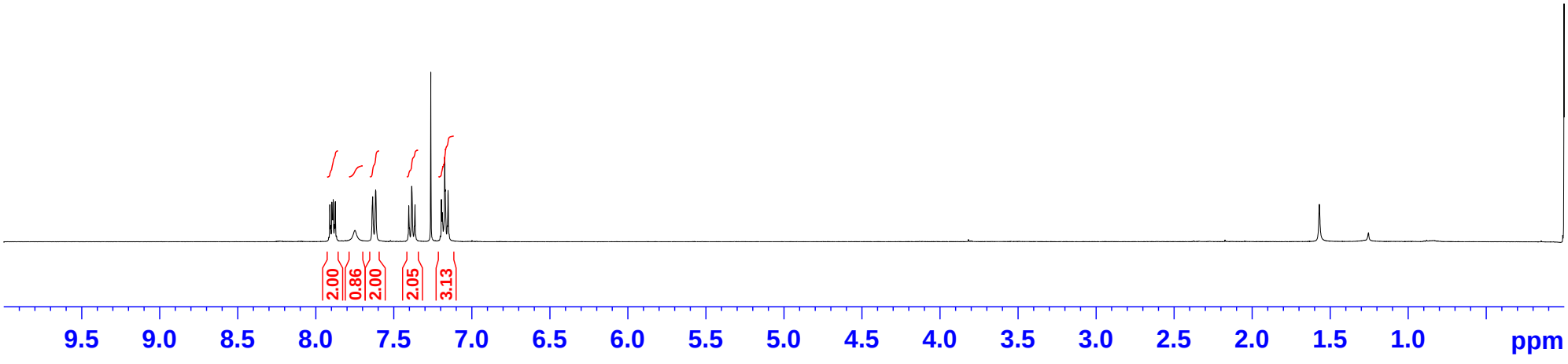
7.8920
7.8876
7.8798
7.8745
7.8672
7.7492
7.6353
7.6160
7.4039
7.3992
7.3850
7.3641
7.2628
7.2024
7.1950
7.1887
7.1734
7.1699
7.1572
7.1519
O
N
H
F

5a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0.86
2.00
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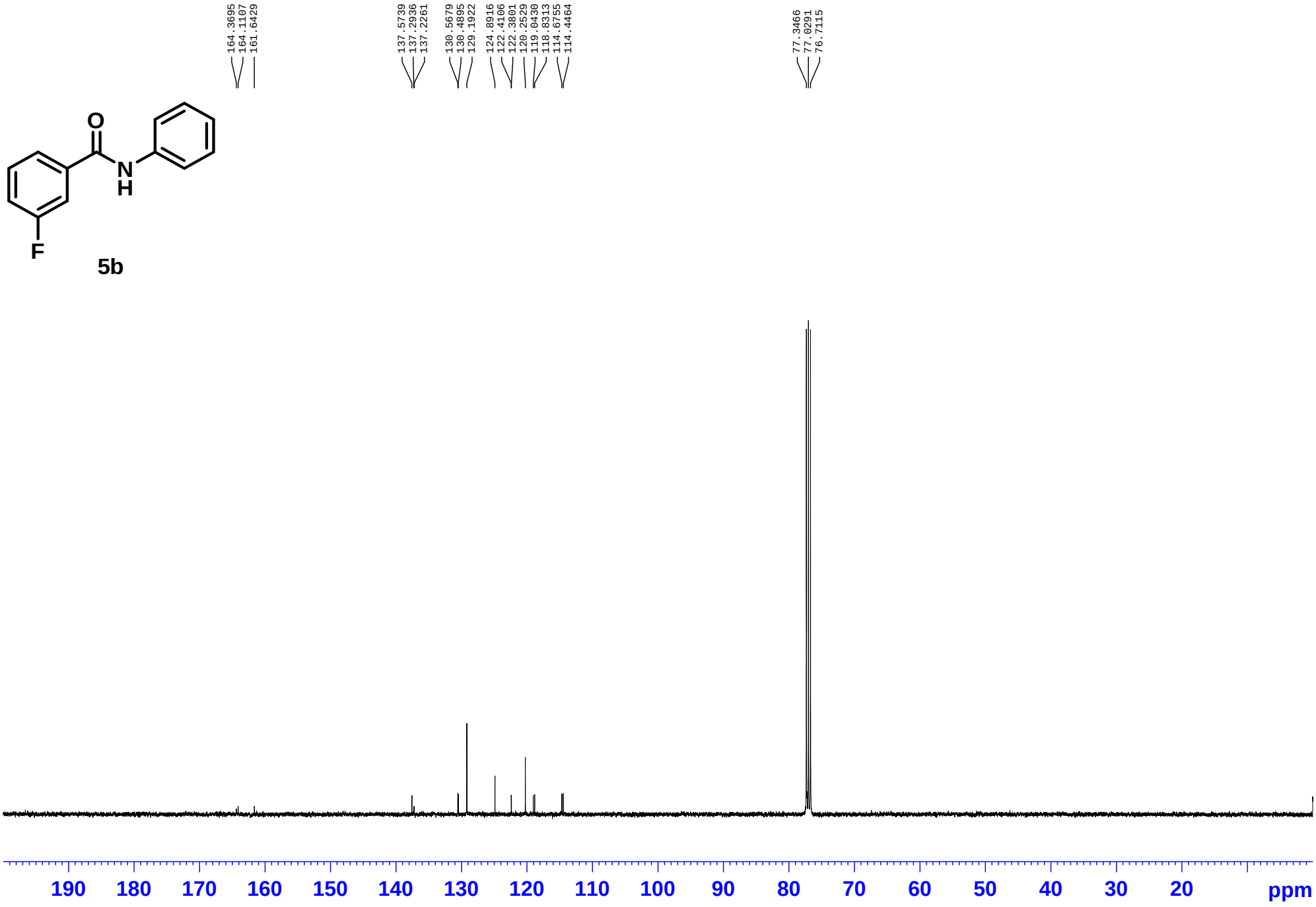
3.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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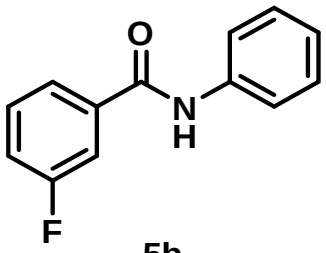
137.2936
137.2261
130.5679
130.4895
129.1922
124.8916
122.4106
122.3801
120.2529
119.8430
118.8313
114.6755
114.4464
77.3466
77.0291
76.7115
O
N
H
F
5b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



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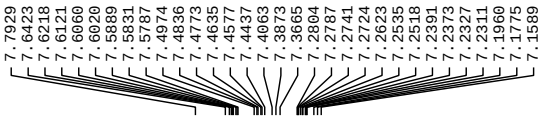
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7.6218
7.6121
7.6060
7.6020
7.5889
7.5831
7.5787
7.4974
7.4836
7.4773
7.4635
7.4577
7.4437
7.4063
7.3873
7.3665
7.2804
7.2787
7.2741
7.2724
7.2623
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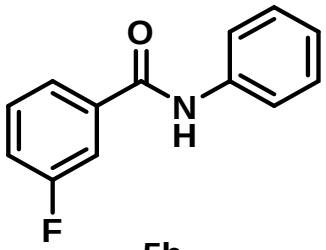
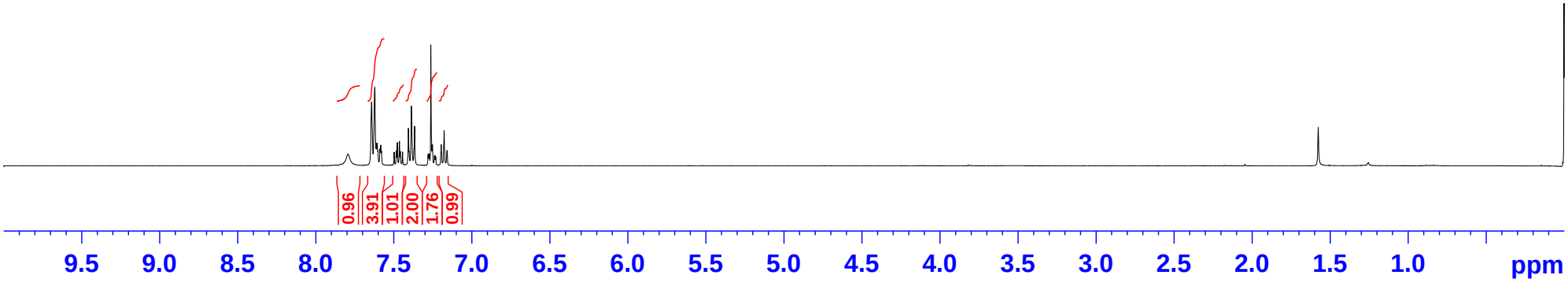
7.2518
7.2391
7.2373
7.2327
7.2311
7.1960
7.1775
7.1589


O
N
H
F

5b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3.91
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2.00
1.76
0.99
9.5
9.0
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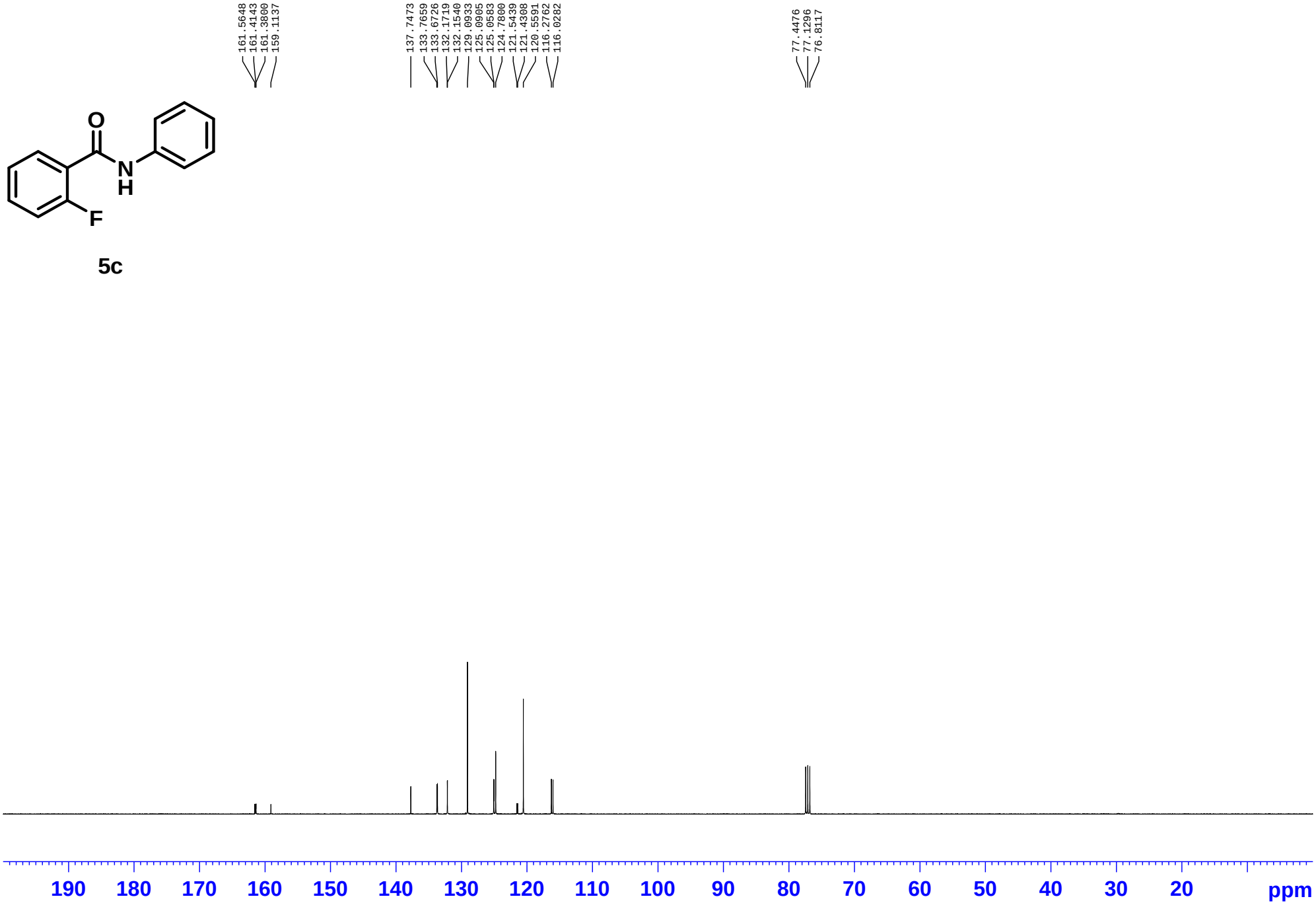
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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161.3800
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133.6726
132.1719
132.1540
129.0933
125.0905
125.0583
124.7800
121.5439
121.4308
120.5591
116.2762
116.0282
77.4476
77.1296
76.8117
O
N
H
F
5c
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180
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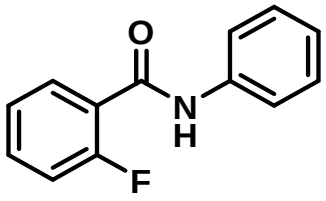
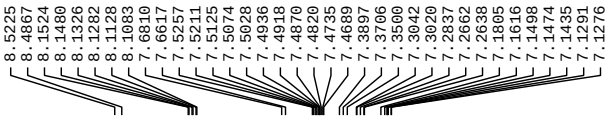
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



5c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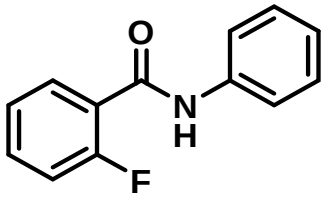
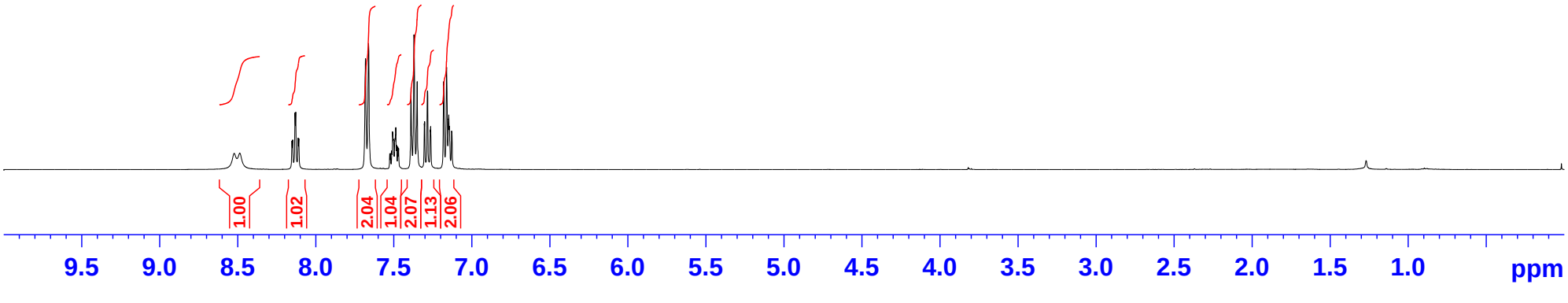
8.1480
8.1326
8.1282
8.1128
8.1083
7.6810
7.6617
7.5257
7.5211
7.5125
7.5074
7.5028
7.4936
7.4918
7.4870
7.4820
7.4735
7.4689
7.3897
7.3706
7.3500
7.3042
7.3020
7.2837
7.2662
7.2638
7.1805
7.1616
7.1498
7.1474
7.1435
7.1291
7.1276


O
N
H
F

5c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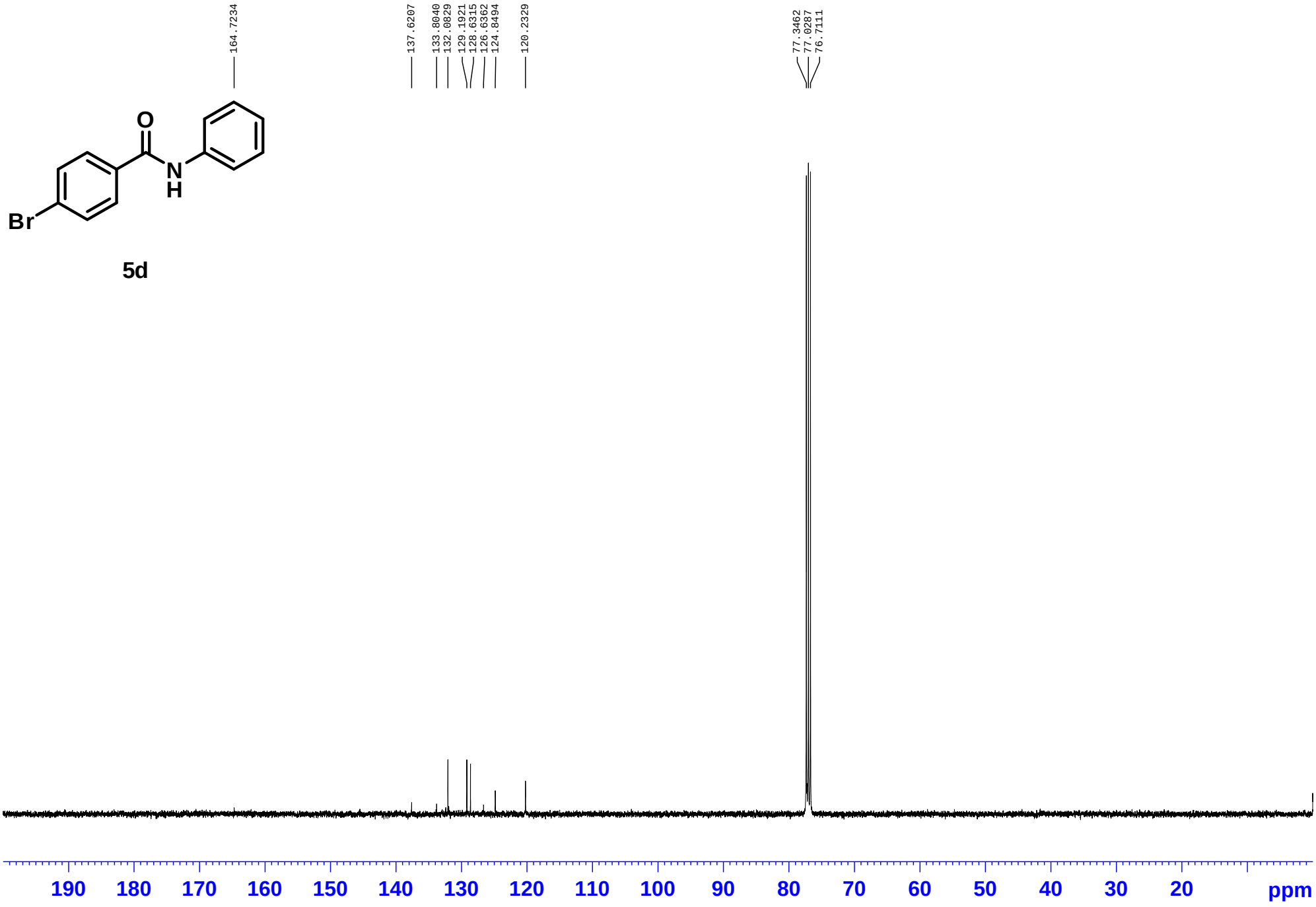
1.02
2.04
1.04
2.07
1.13
2.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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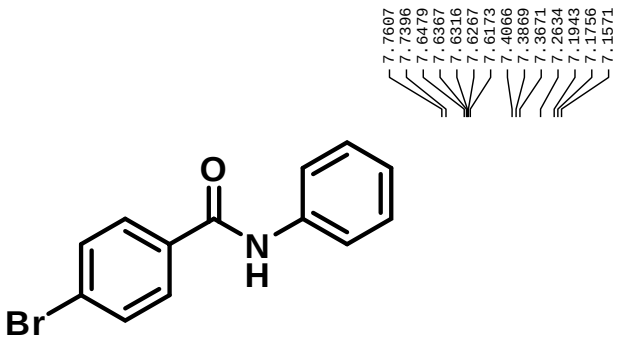
129.1921
128.6315
126.6362
124.8494
120.2329
77.3462
77.0287
76.7111
O
N
H
Br
5d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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7.6479
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7.6316
7.6267
7.6173
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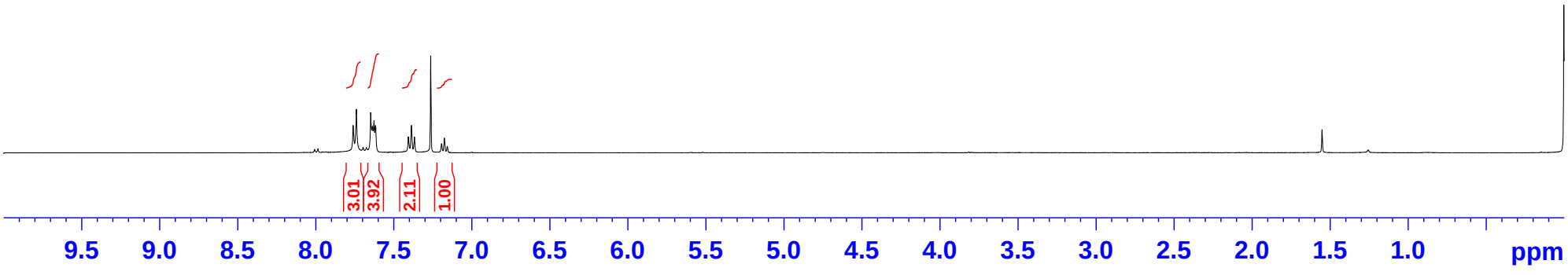
7.2634
7.1943
7.1756
7.1571
O
N
H
Br

5d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3.92
2.11
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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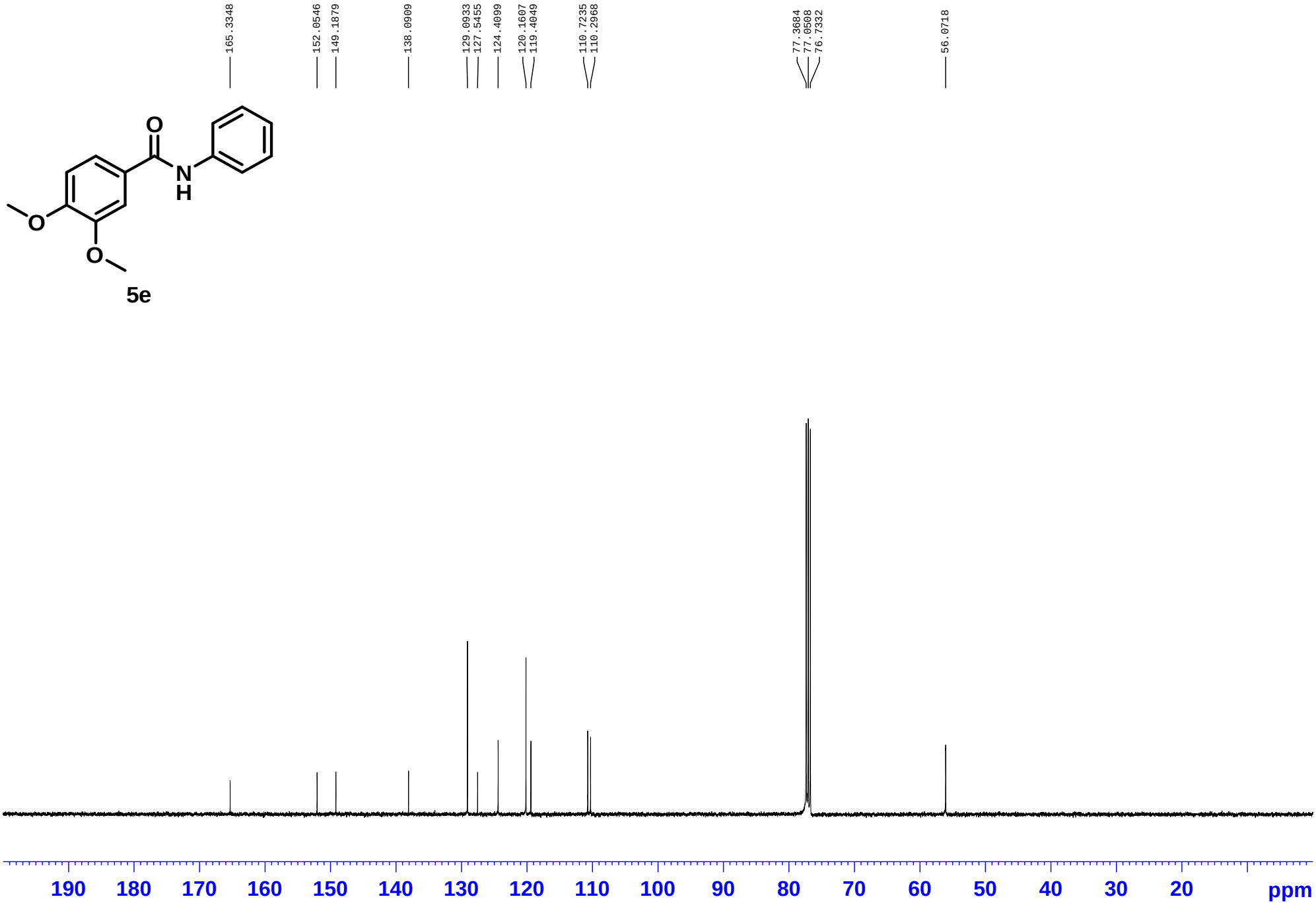
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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138.0909
129.0933
127.5455
124.4099
120.1607
119.4049
110.7235
110.2968
77.3684
77.0508
76.7332
56.0718
O
N
H
O
O
5e
190
180
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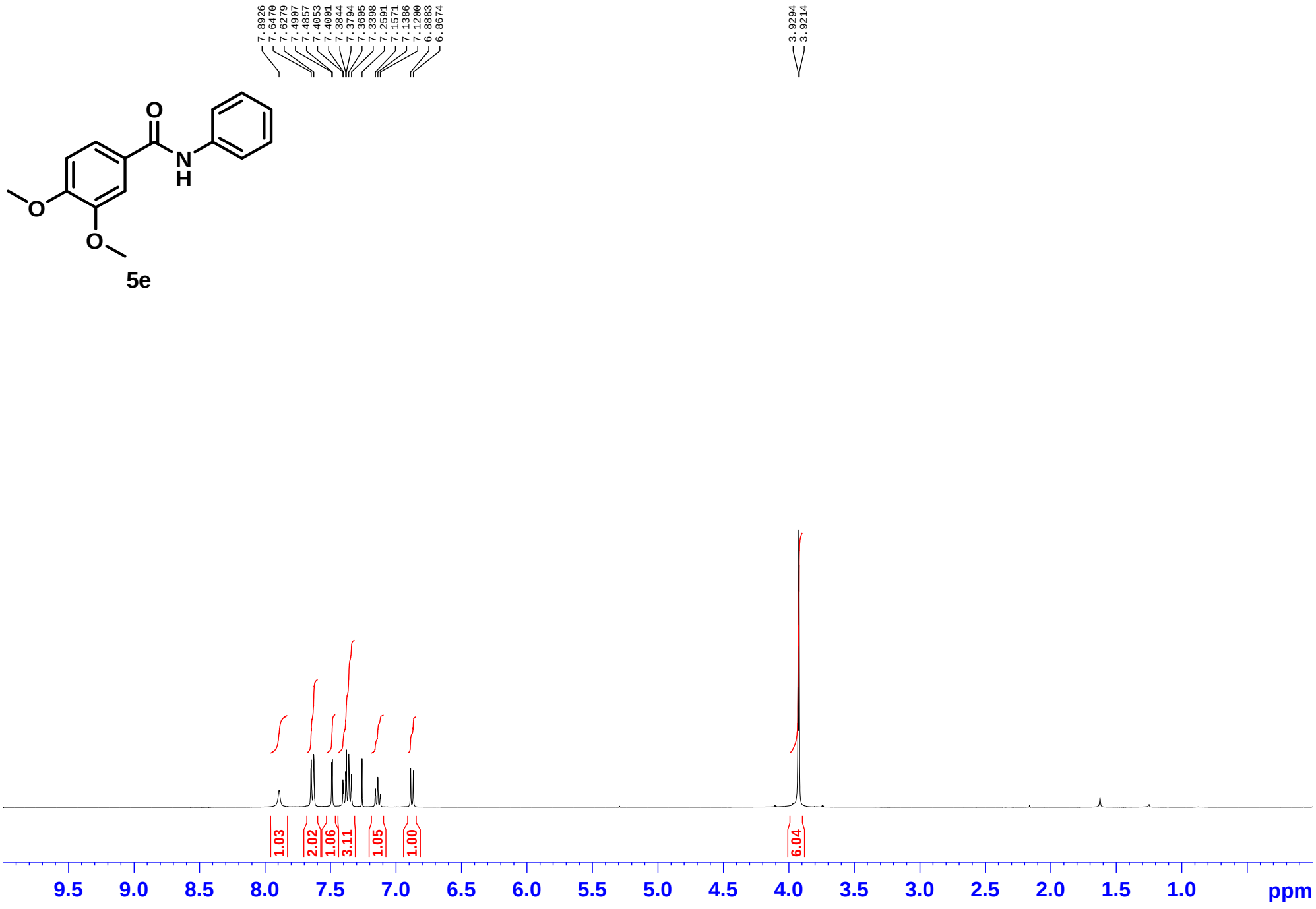
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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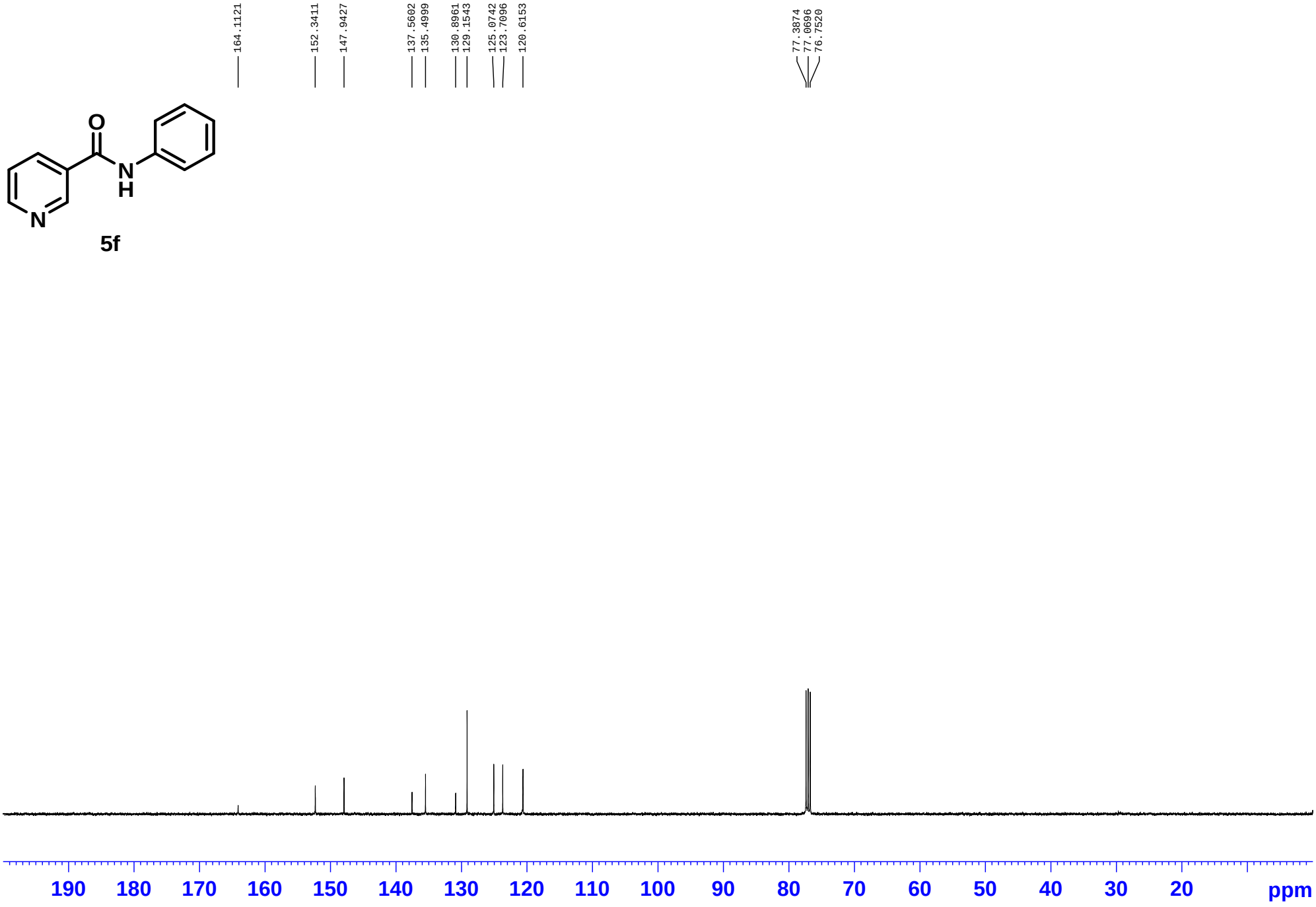
7.4857
7.4053
7.4001
7.3844
7.3794
7.3605
7.3398
7.2591
7.1571
7.1386
7.1200
6.8883
6.8674
3.9294
3.9214
O
N
H
O
O
5e
1.03
2.02
1.06
3.11
1.05
1.00
6.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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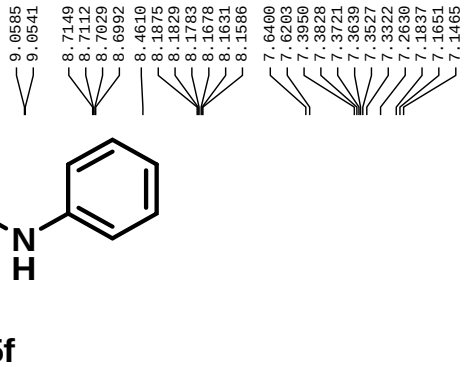
147.9427
137.5602
135.4999
130.8961
129.1543
125.0742
123.7096
120.6153
77.3874
77.0696
76.7520
O
N
H
N
5f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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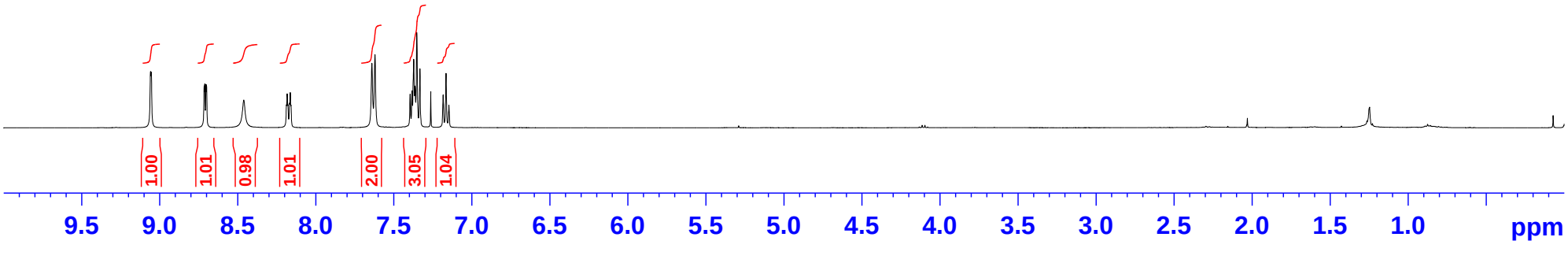
8.6992
8.4610
8.1875
8.1829
8.1783
8.1678
8.1631
8.1586
7.6400
7.6203
7.3950
7.3828
7.3721
7.3639
7.3527
7.3322
7.2630
7.1837
7.1651
7.1465
O
N
H
N

5f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1.01
0.98
1.01
2.00
3.05
1.04
9.5
9.0
8.5
8.0
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7.0
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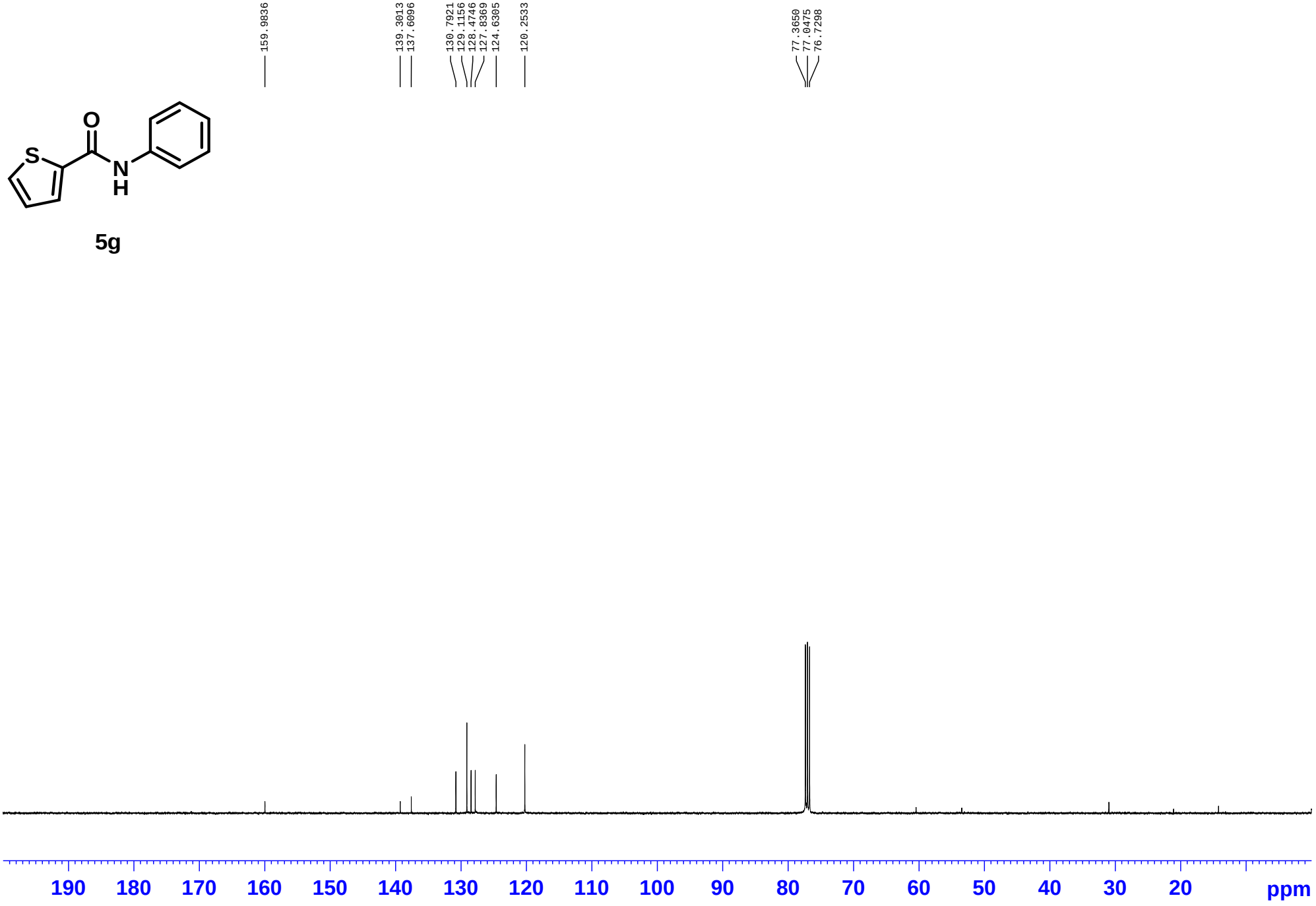
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77.3650
77.0475
76.7298
O
S
N
H
5g
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160
150
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120
110
100
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80
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40
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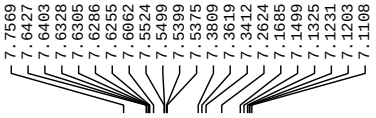
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7.6255
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7.5399
7.5375
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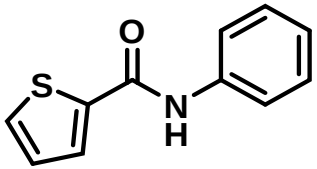
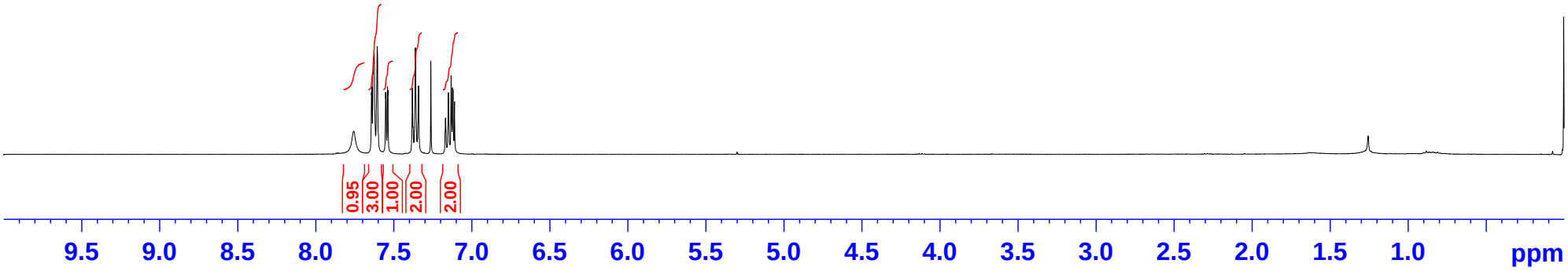
7.3412
7.2624
7.1685
7.1499
7.1325
7.1231
7.1203
7.1108


O
S
N
H

5g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1.5
1.0
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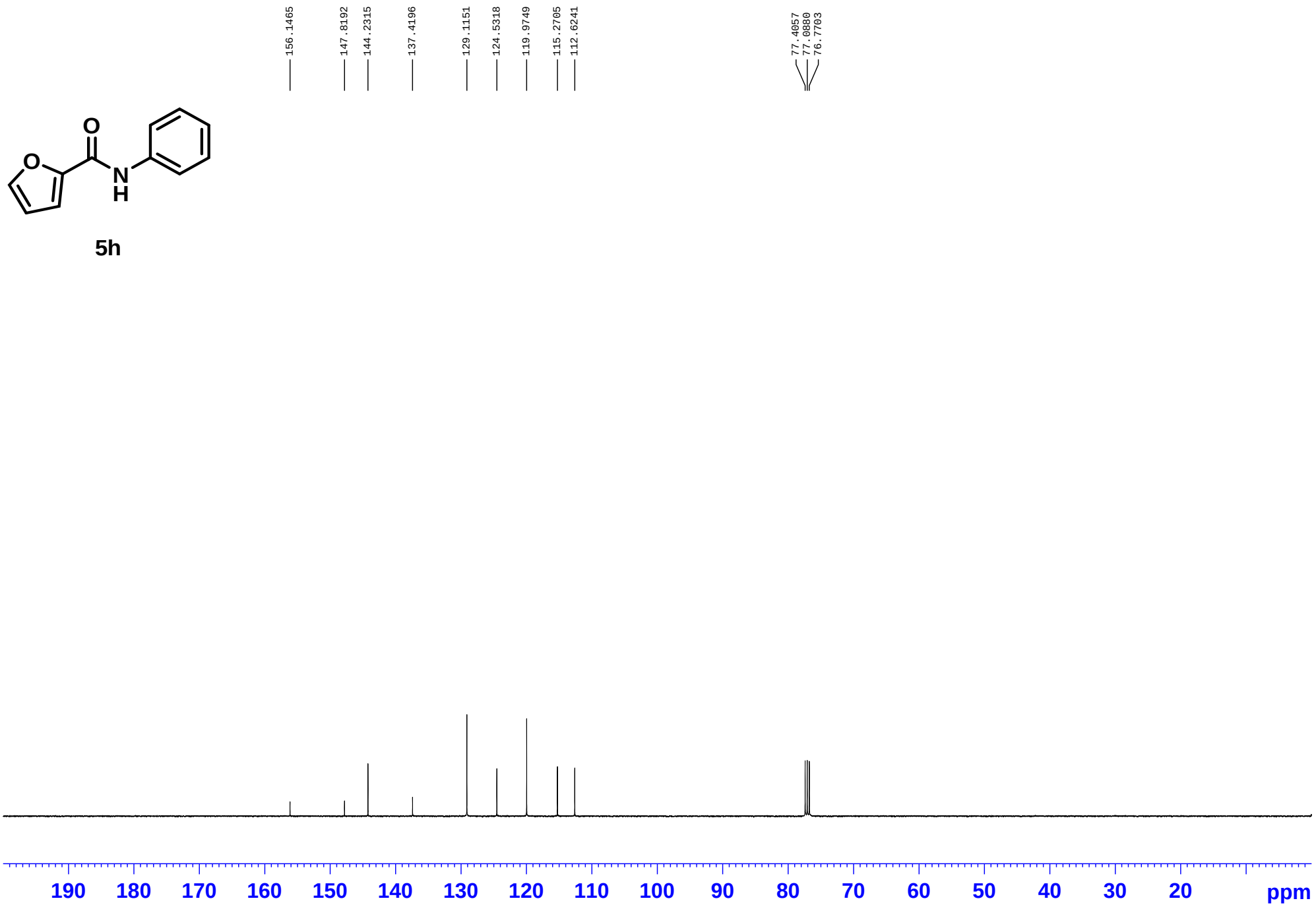
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119.9749
115.2705
112.6241
77.4057
77.0880
76.7703
O
O
N
H
5h
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180
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160
150
140
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120
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80
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40
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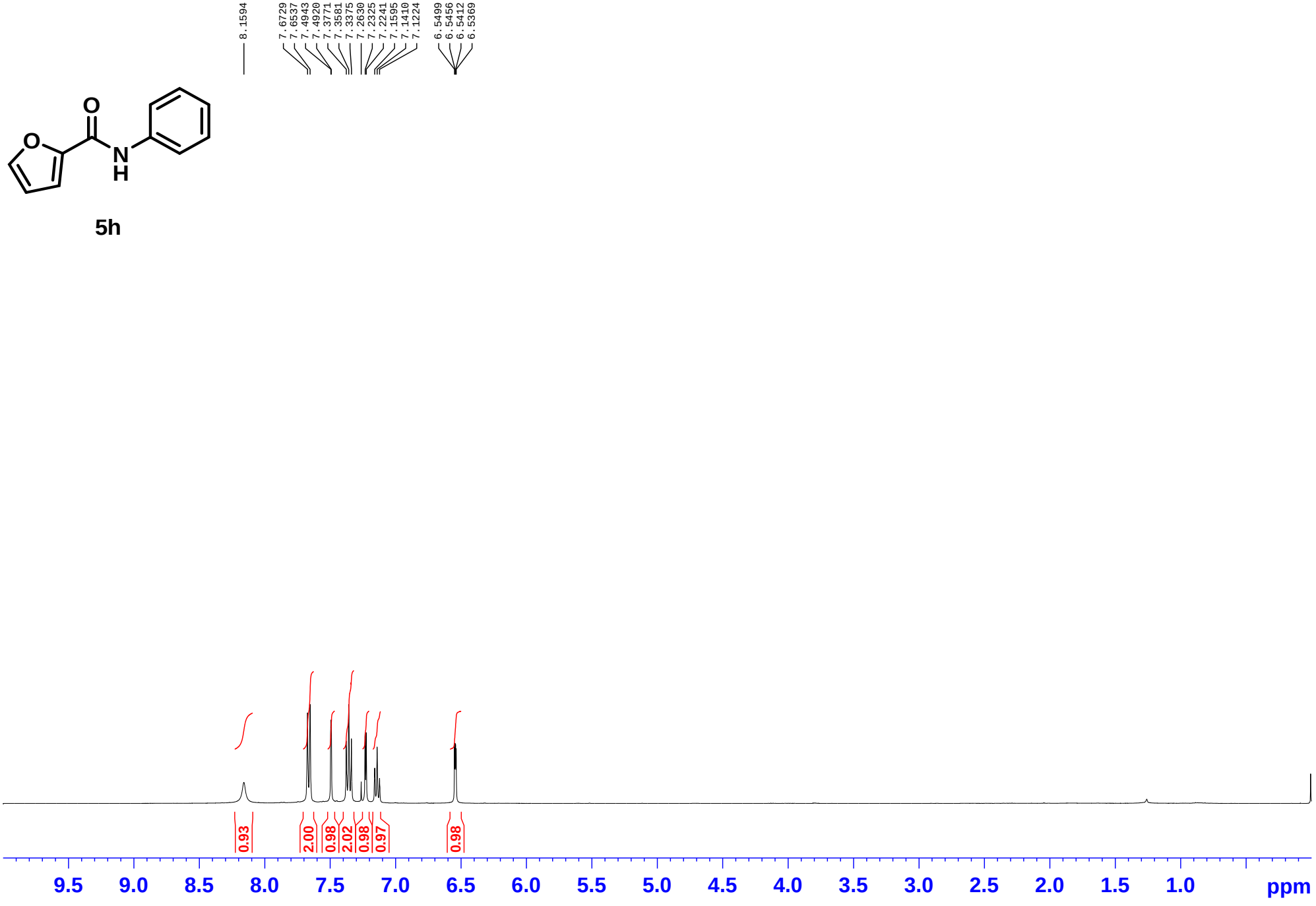
20
ppm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7.3771
7.3581
7.3375
7.2630
7.2325
7.2241
7.1595
7.1410
7.1224
6.5499
6.5456
6.5412
6.5369
O
O
N
H
0.93
2.00
0.98
2.02
0.98
0.97
0.98
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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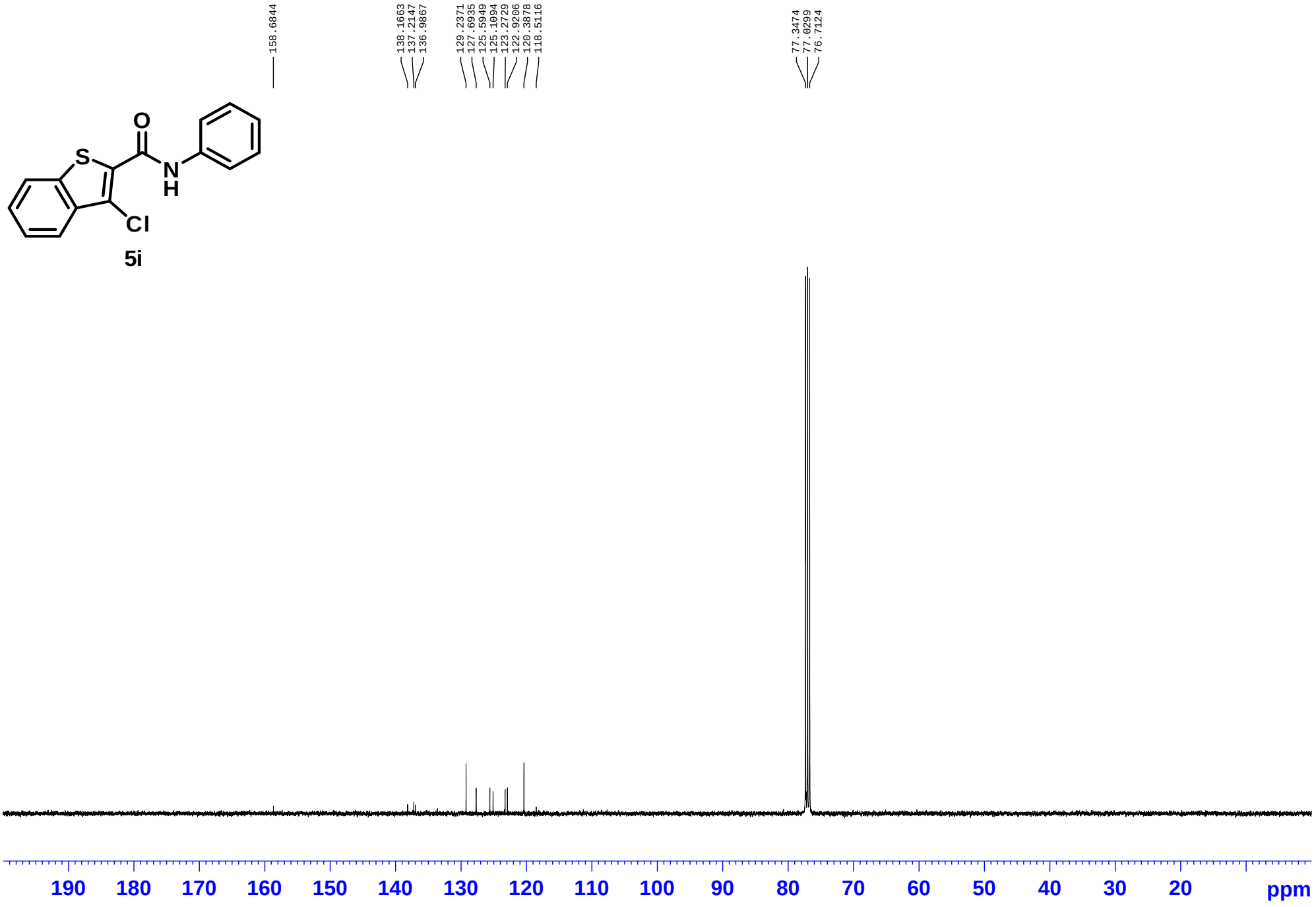
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

5h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77.3474
77.0299
76.7124
O
S
N
H
Cl
5i
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160
150
140
130
120
110
100
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80
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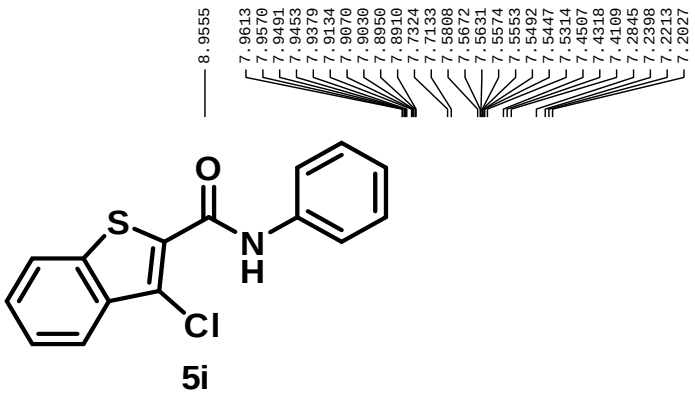
60
50
40
30
20
ppm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7.8910
7.7324
7.7133
7.5808
7.5672
7.5631
7.5574
7.5553
7.5492
7.5447
7.5314
7.4507
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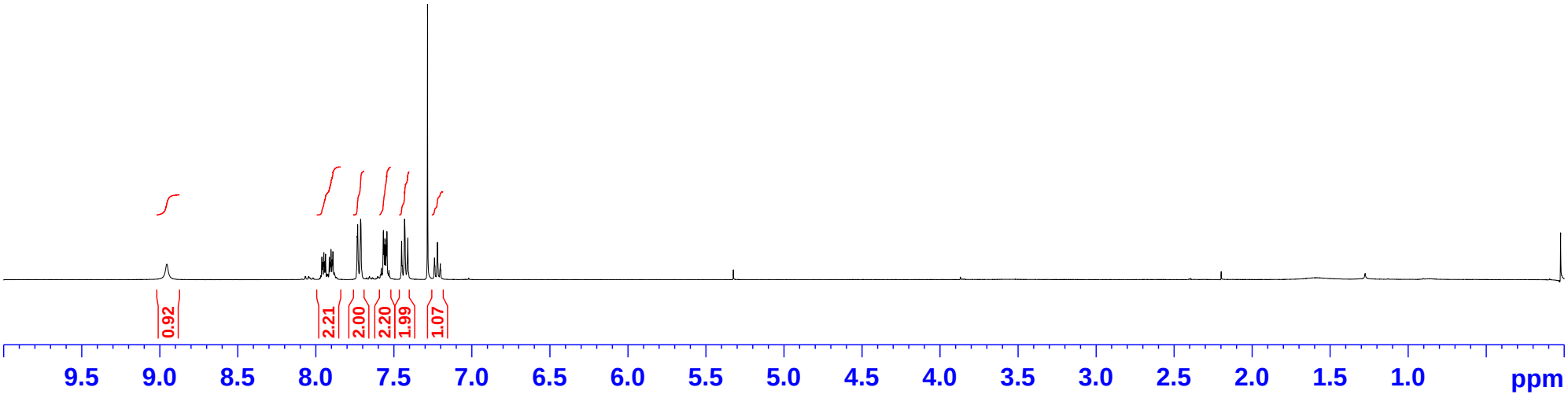
7.4109
7.2845
7.2398
7.2213
7.2027
O
S
N
H
Cl

5i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1.07
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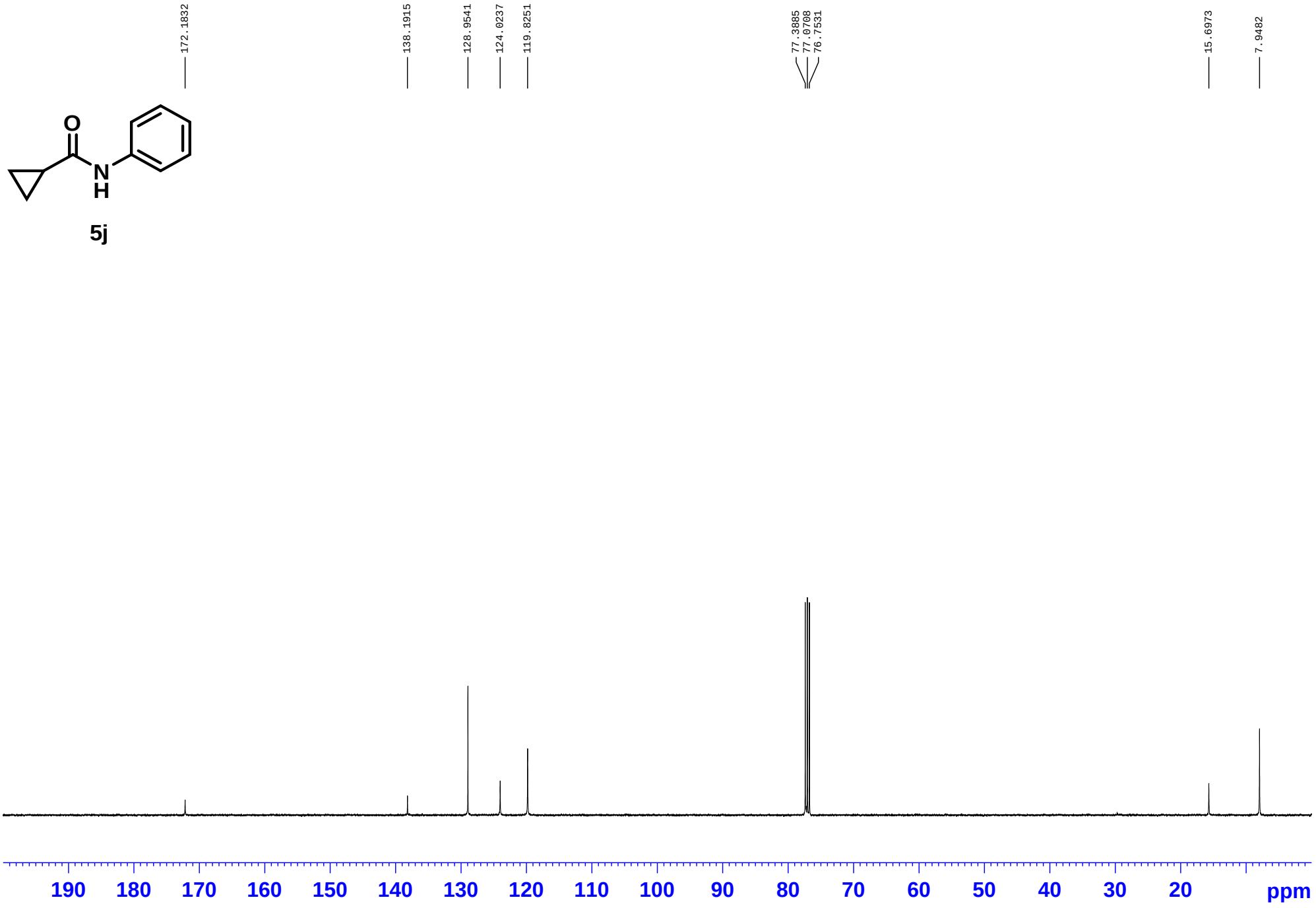
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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124.0237
119.8251
77.3885
77.0708
76.7531
15.6973
7.9482
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N
H
5j
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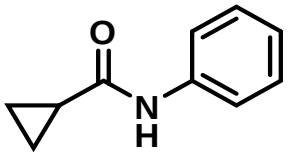
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
N
H

5j

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7.5013
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7.2624
7.0972
7.0791
7.0610
1.5333
1.5236
1.5135
1.5053
1.4940
1.0905
1.0800
1.0724
1.0695
1.0619
1.0523
0.8385
0.8291
0.8213
0.8096
0.8019
0.7916
0.96
2.00
2.19
0.99
1.03
2.06
2.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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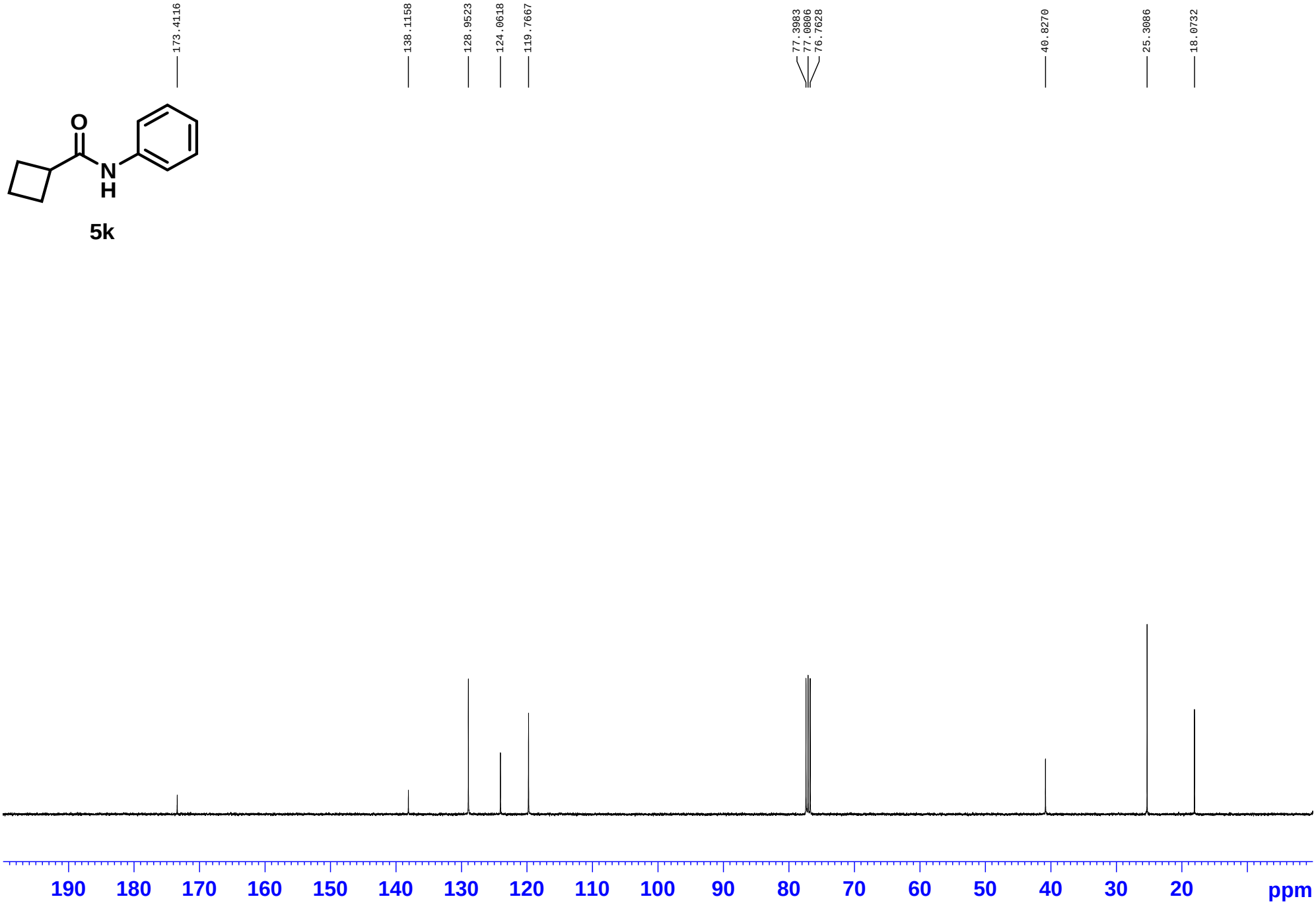
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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O
N
H
5k
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160
150
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130
120
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80
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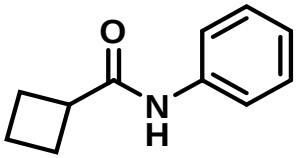
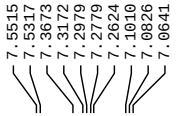
40
30
20
ppm


O
N
H

5k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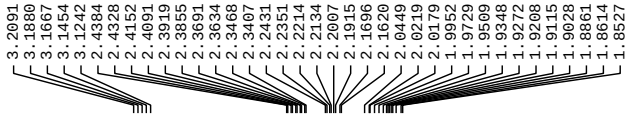
7.2624
7.1010
7.0826
7.0641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3.1242
2.4384
2.4328
2.4152
2.4091
2.3919
2.3855
2.3691
2.3634
2.3468
2.3407
2.2431
2.2351
2.2214
2.2134
2.2007
2.1915
2.1696
2.1620
2.0449
2.0219
2.0179
1.9952
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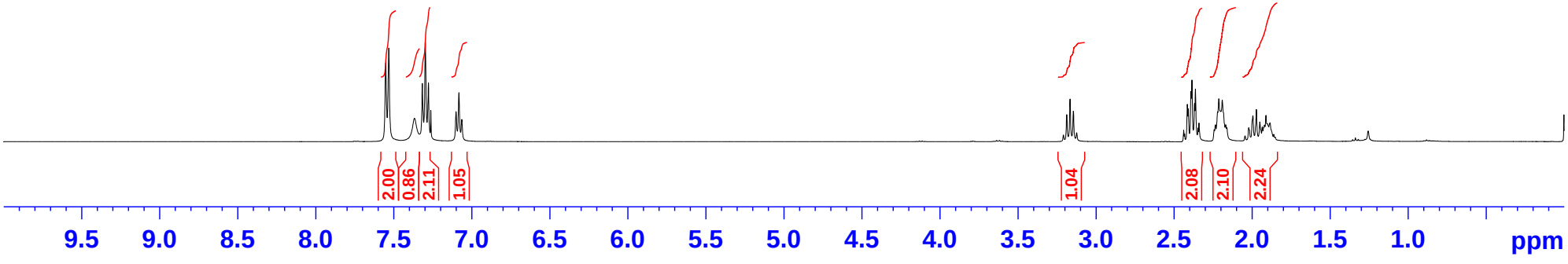
1.9348
1.9272
1.9208
1.9115
1.9028
1.8861
1.8614
1.8527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1.04
2.08
2.10
2.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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5.0
4.5
4.0
3.5
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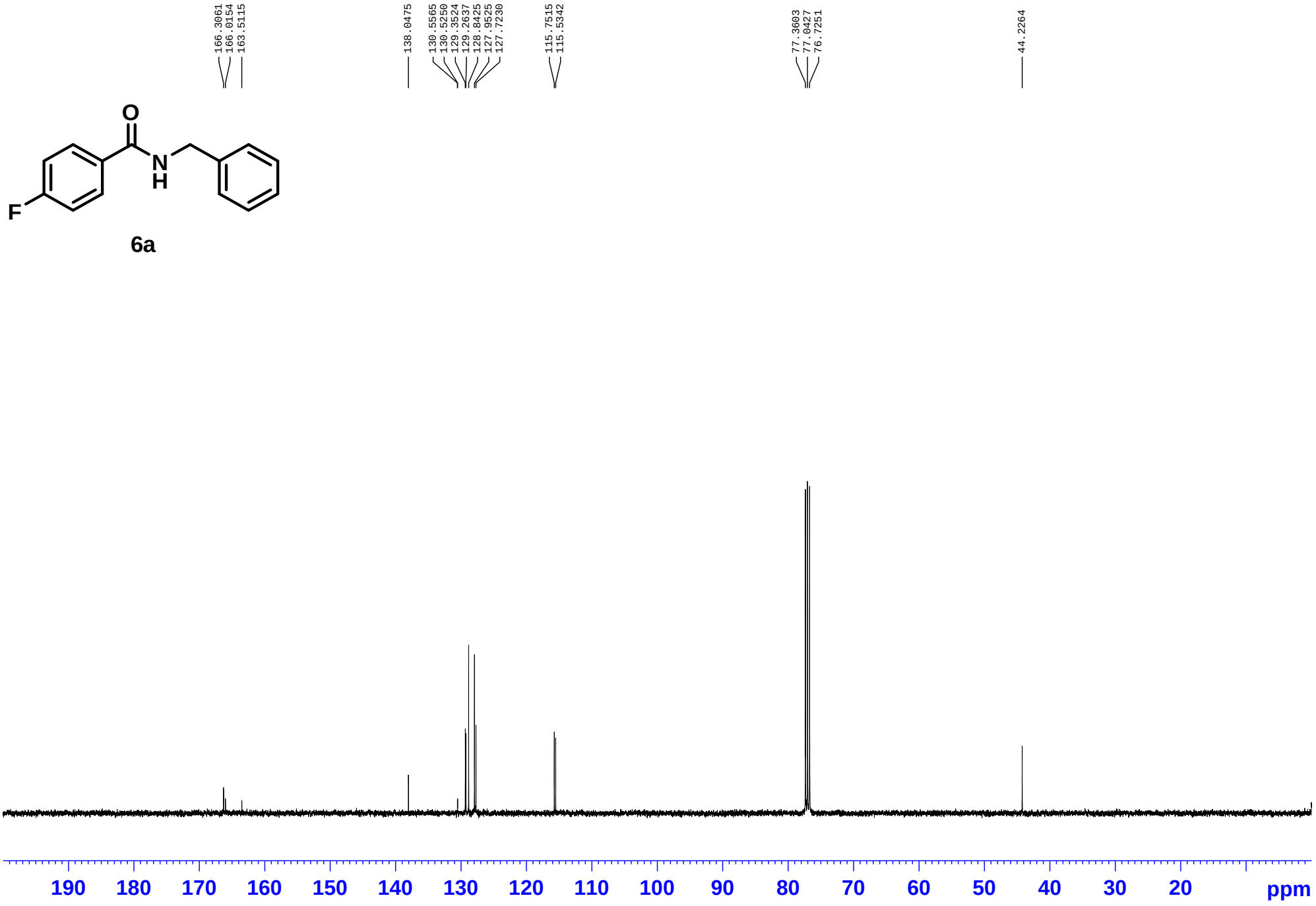
2.5
2.0
1.5
1.0
ppm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129.3524
129.2637
128.8425
127.9525
127.7230
115.7515
115.5342
77.3603
77.0427
76.7251
44.2264
O
N
H
F
6a
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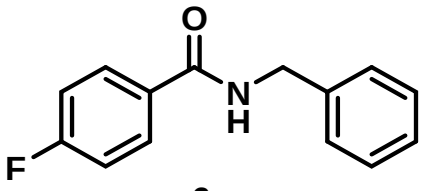
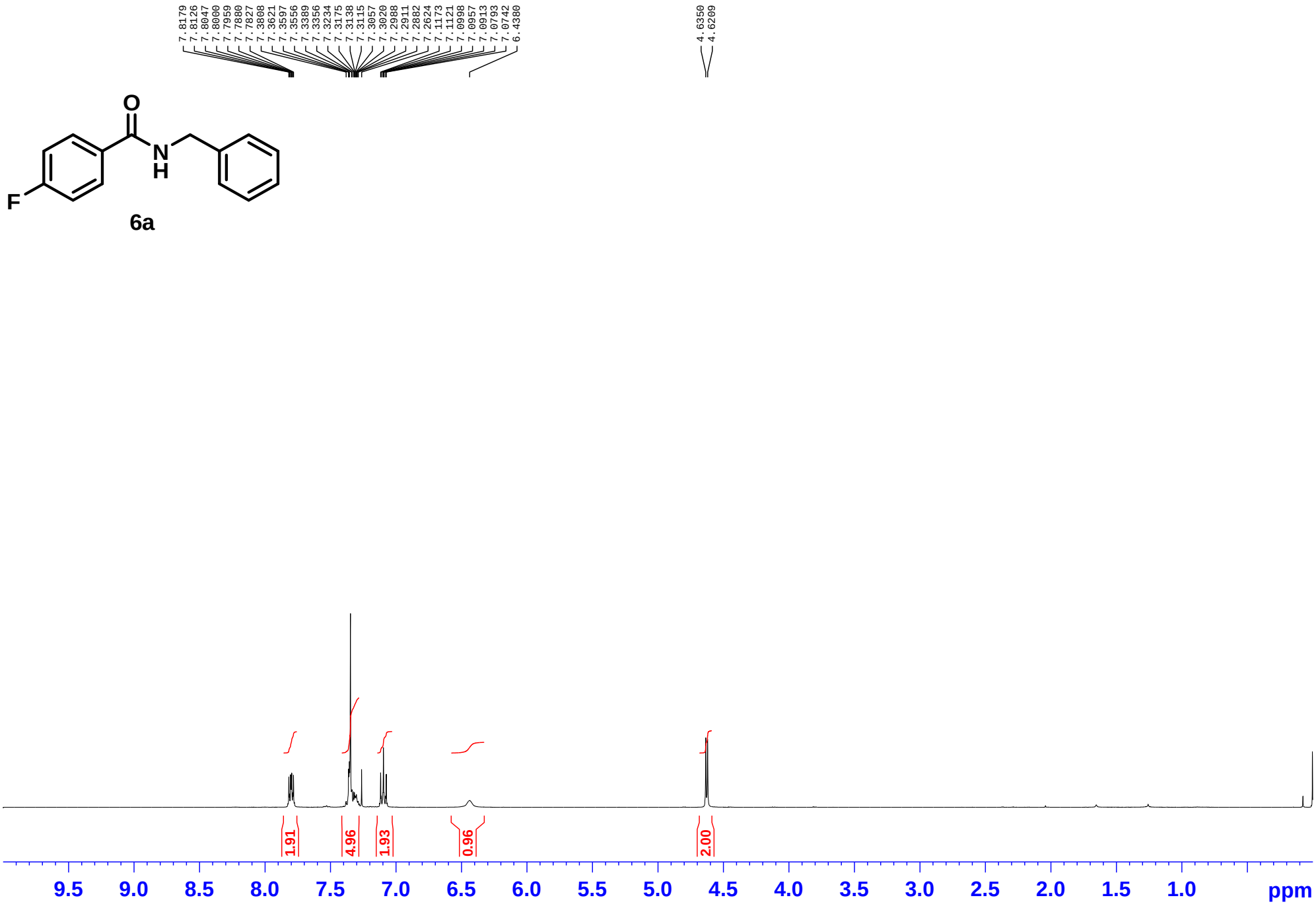
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



6a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7.3556
7.3389
7.3356
7.3234
7.3175
7.3138
7.3115
7.3057
7.3020
7.2988
7.2911
7.2882
7.2624
7.1173
7.1121
7.0998
7.0957
7.0913
7.0793
7.0742
6.4380
4.6350
4.6209
O
N
H
F
6a
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4.96
1.93
0.96
2.00
9.5
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8.0
7.5
7.0
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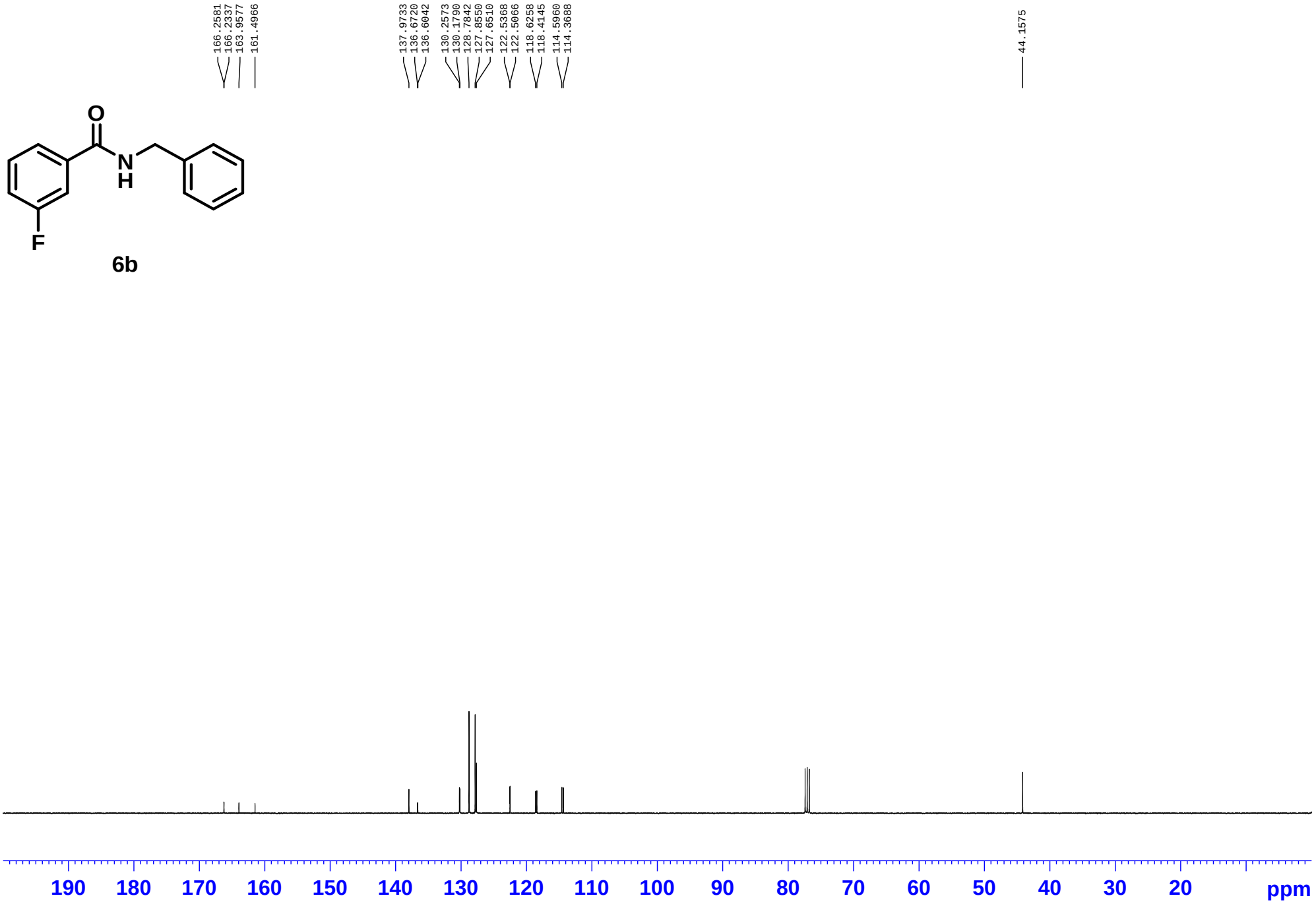
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127.6510
122.5368
122.5066
118.6258
118.4145
114.5960
114.3688
44.1575
O
N
H
F
6b
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160
150
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130
120
110
100
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80
70
60
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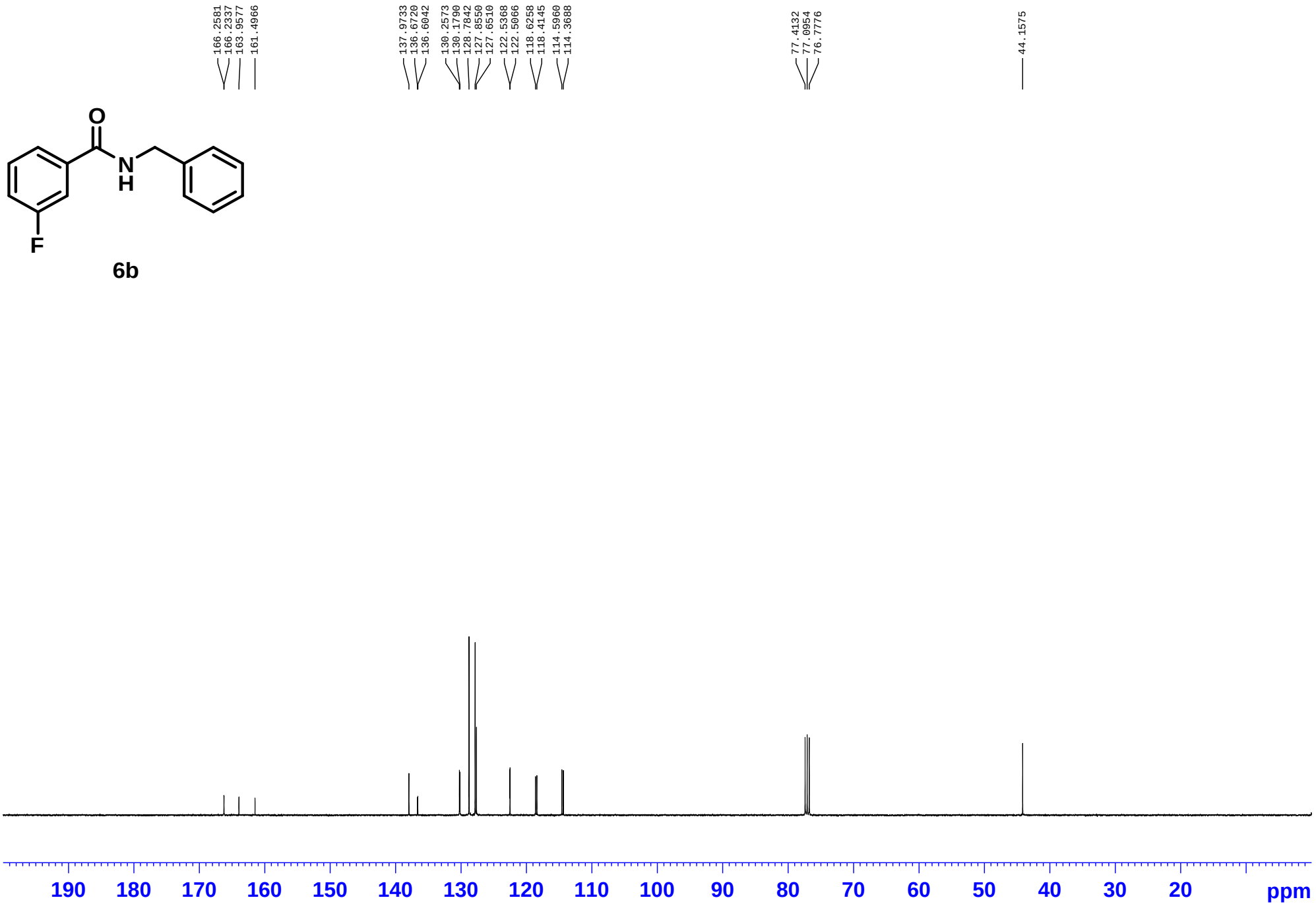
40
30
20
ppm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163.9577
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127.6510
122.5368
122.5066
118.6258
118.4145
114.5960
114.3688
77.4132
77.0954
76.7776
44.1575
O
N
H
F
6b
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160
150
140
130
120
110
100
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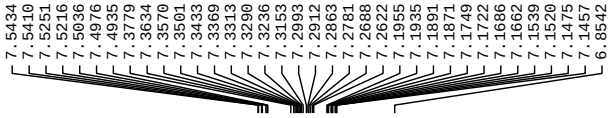
80
70
60
50
40
30
20
ppm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7.4935
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7.3570
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7.3433
7.3369
7.3313
7.3290
7.3236
7.3153
7.2993
7.2912
7.2863
7.2781
7.2688
7.2622
7.1955
7.1935
7.1891
7.1871
7.1749
7.1722
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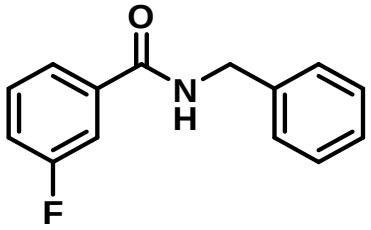
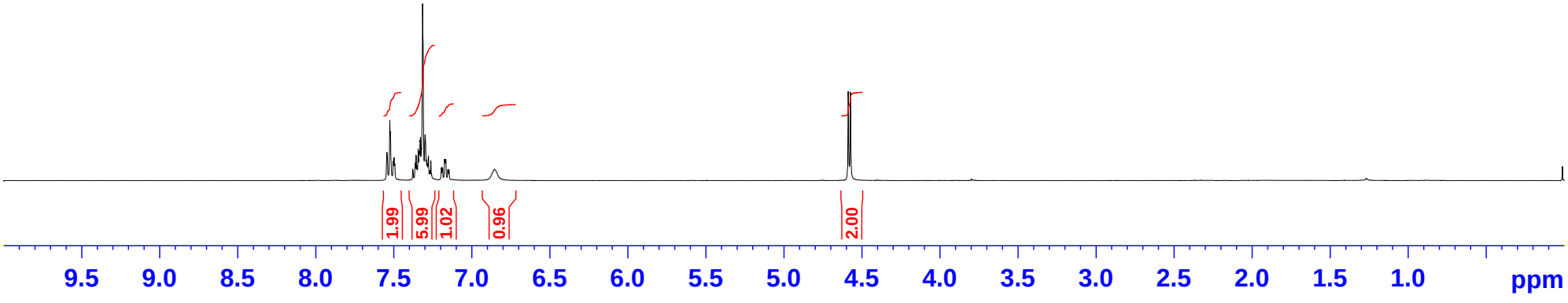
7.1539
7.1520
7.1475
7.1457
6.8542
4.5881
4.5738


O
N
H
F

6b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5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


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161.8390
159.3803
138.0862
133.3843
133.2919
132.0775
132.0561
128.7599
127.7316
127.5420
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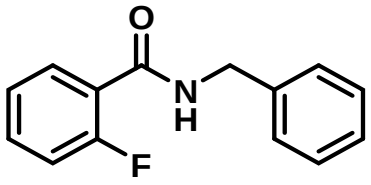
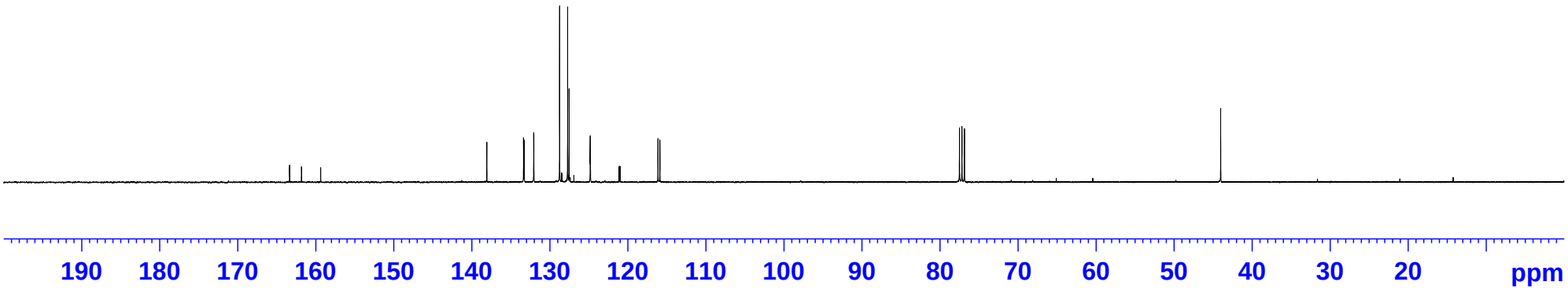
76.8720
44.0308


O
N
H
F

6c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150
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130
120
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100
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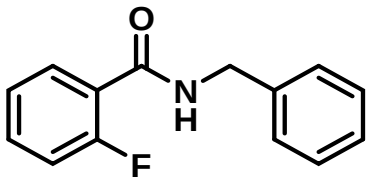
80
70
60
50
40
30
20
ppm



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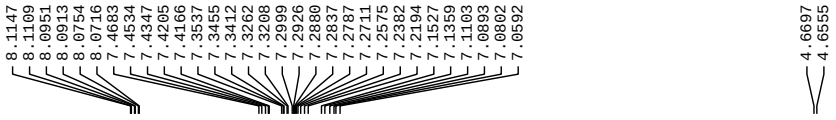
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8.0716
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7.4205
7.4166
7.3537
7.3455
7.3412
7.3262
7.3208
7.2999
7.2926
7.2880
7.2837
7.2787
7.2711
7.2575
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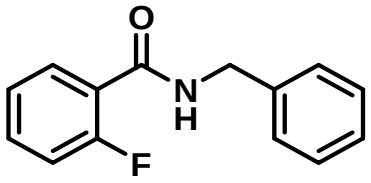
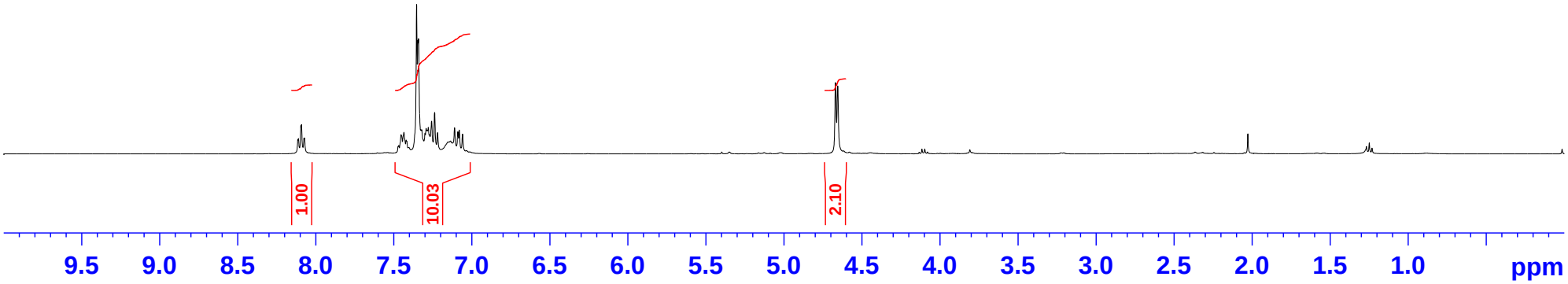
7.0802
7.0592
4.6697
4.6555


O
N
H
F

6c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2.5
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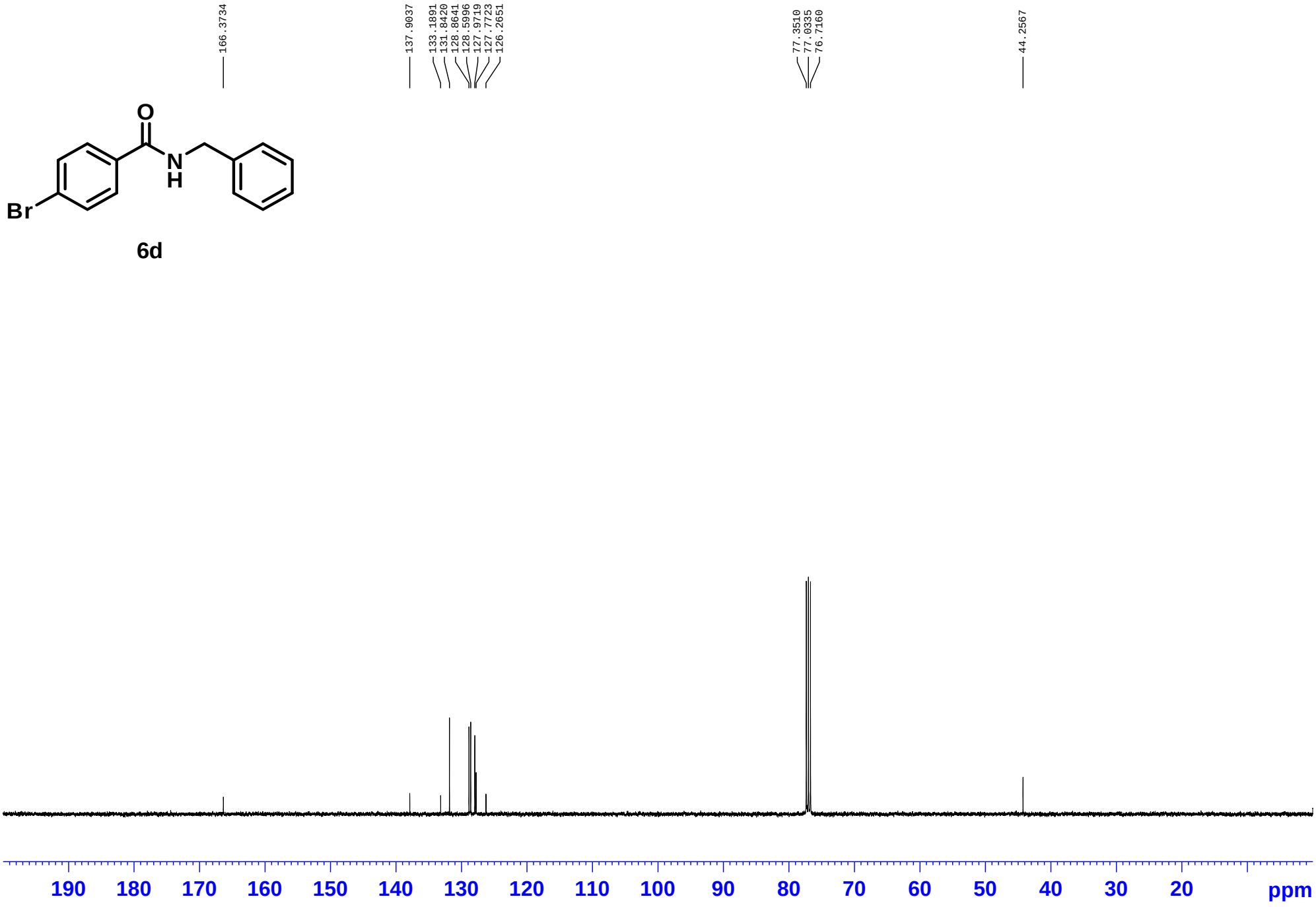
1.5
1.0
ppm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77.0335
76.7160
44.2567
O
N
H
Br
6d
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160
150
140
130
120
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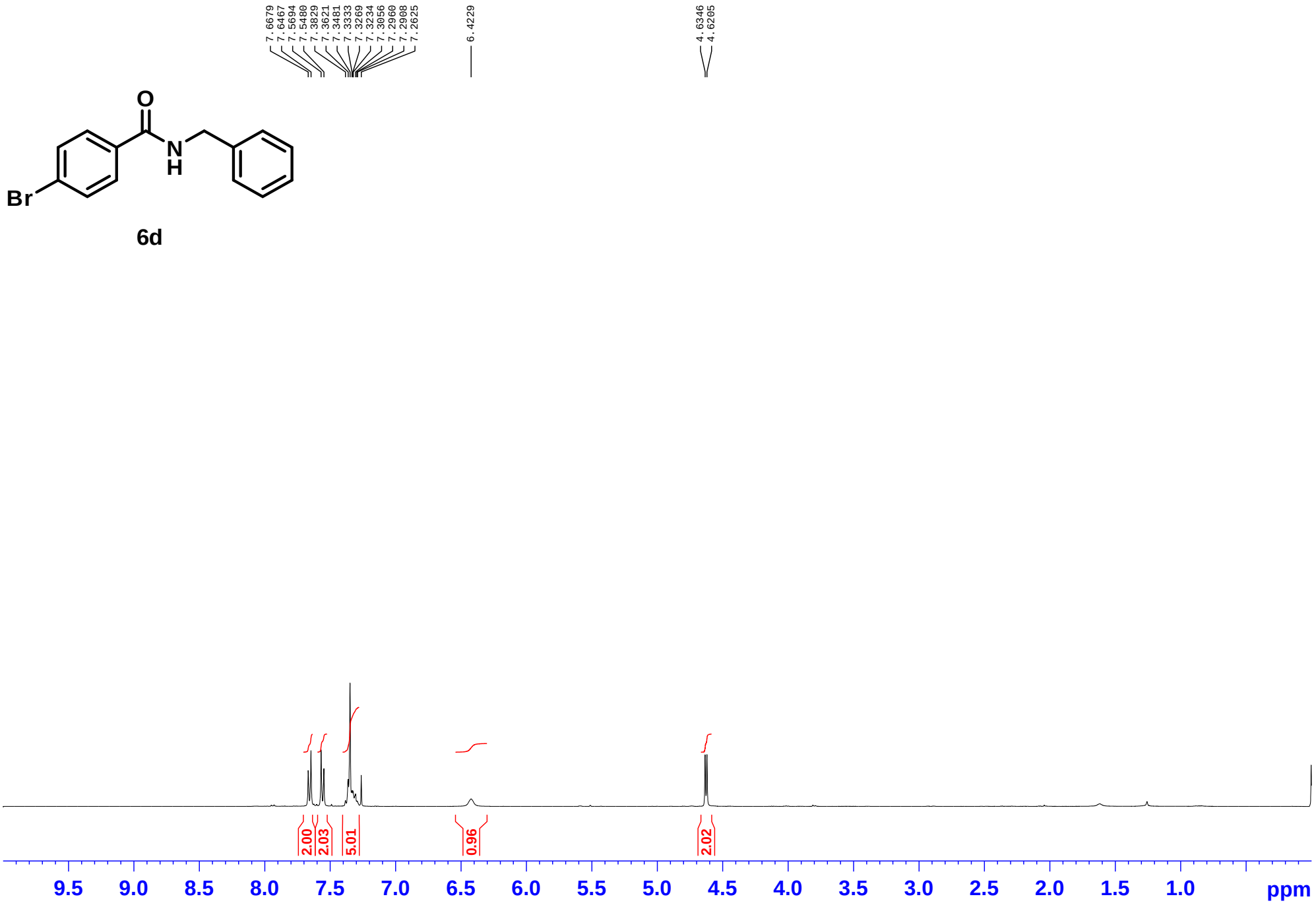
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7.2908
7.2625
6.4229
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4.6205
O
N
H
Br
6d
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2.03
5.01
0.96
2.02
9.5
9.0
8.5
8.0
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7.0
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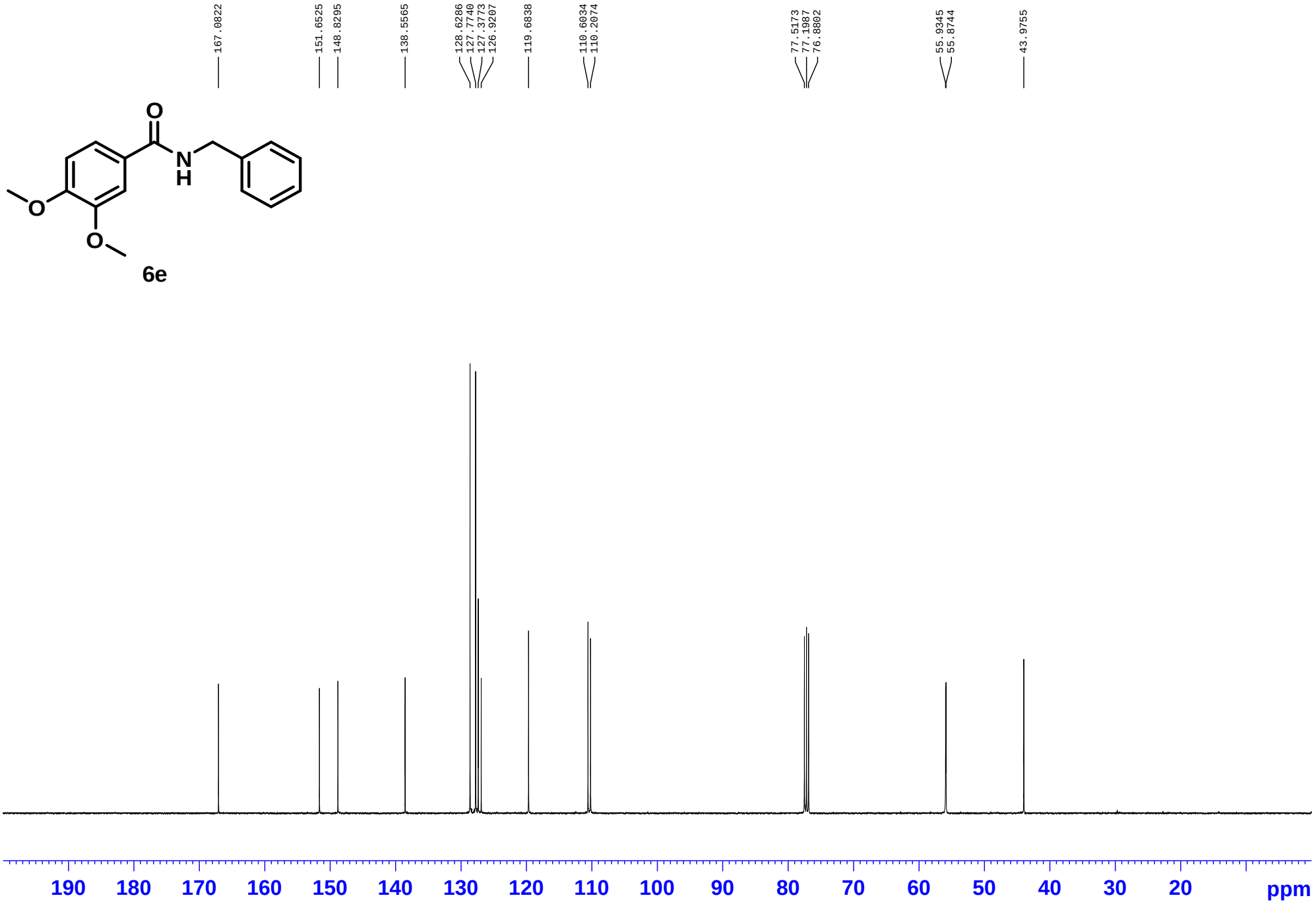
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O
N
H
O
O
6e
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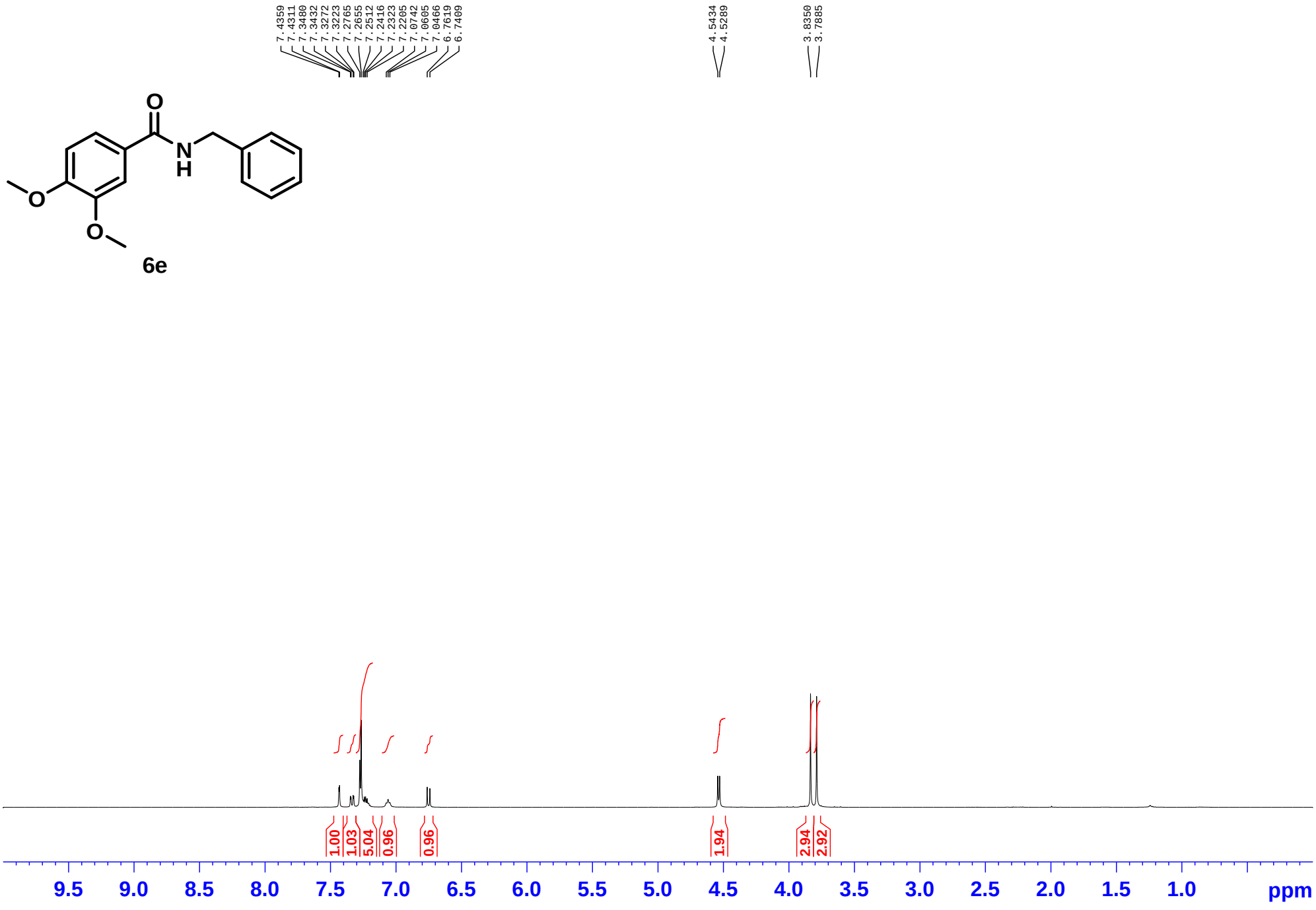
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7.2323
7.2205
7.0742
7.0605
7.0466
6.7619
6.7409
4.5434
4.5289
3.8350
3.7885
O
N
H
O
O
6e
1.00
1.03
5.04
0.96
0.96
1.94
2.94
2.92
9.5
9.0
8.5
8.0
7.5
7.0
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4.0
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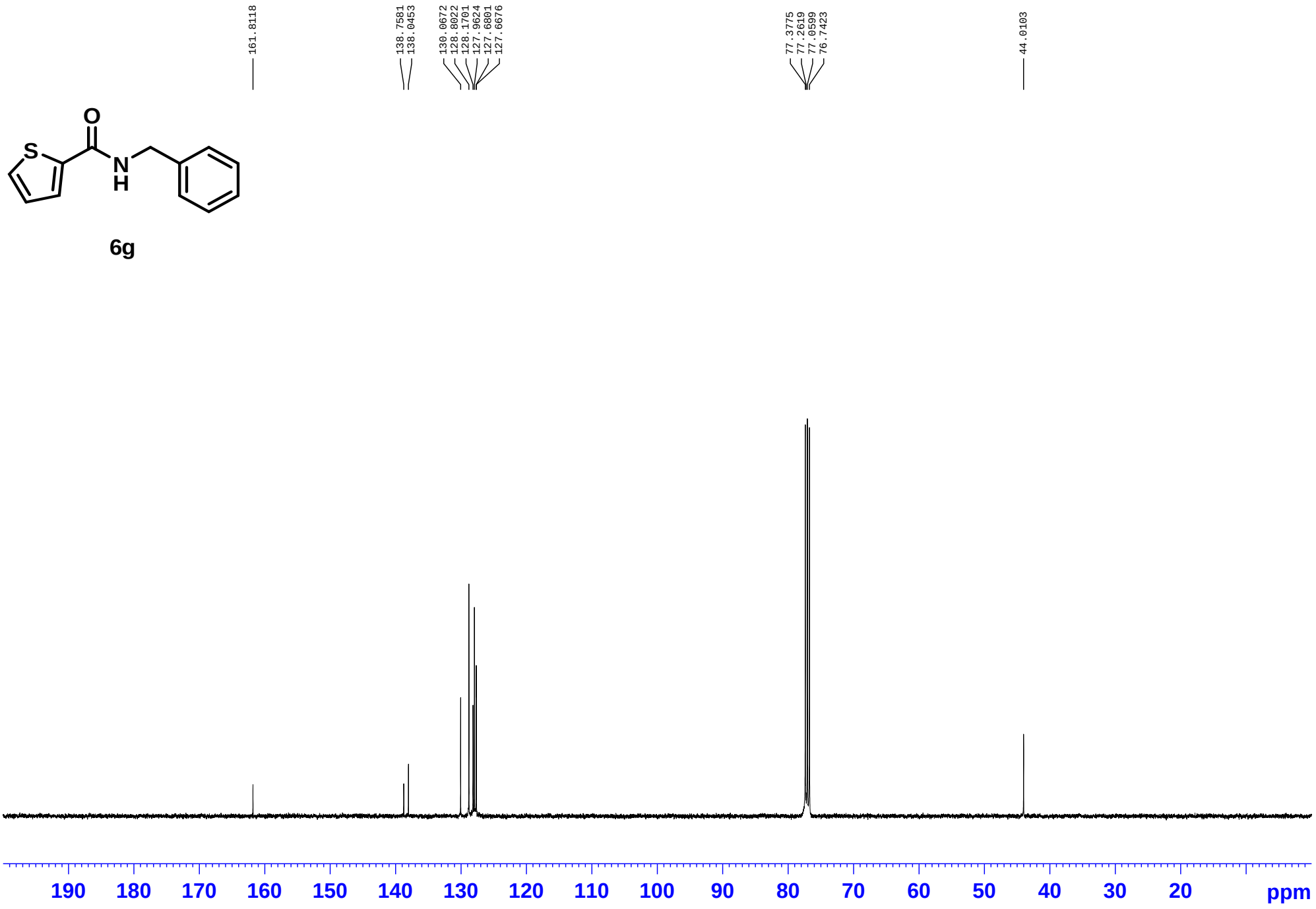
1.5
1.0
ppm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77.0599
76.7423
44.0103
O
S
N
H
6g
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150
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120
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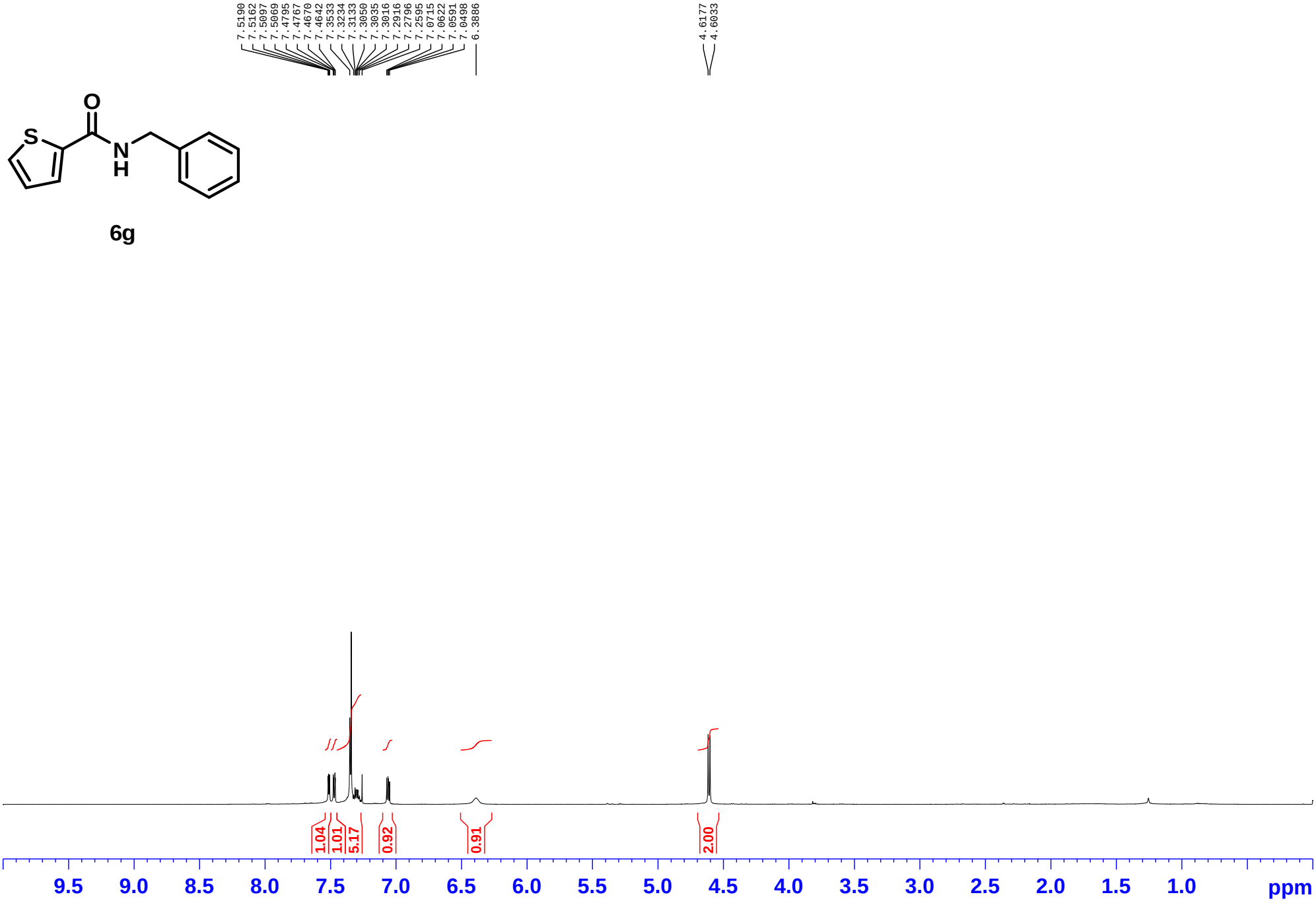
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7.2916
7.2796
7.2595
7.0715
7.0622
7.0591
7.0498
6.3886
4.6177
4.6033
O
S
N
H
6g
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1.01
5.17
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0.91
2.00
9.5
9.0
8.5
8.0
7.5
7.0
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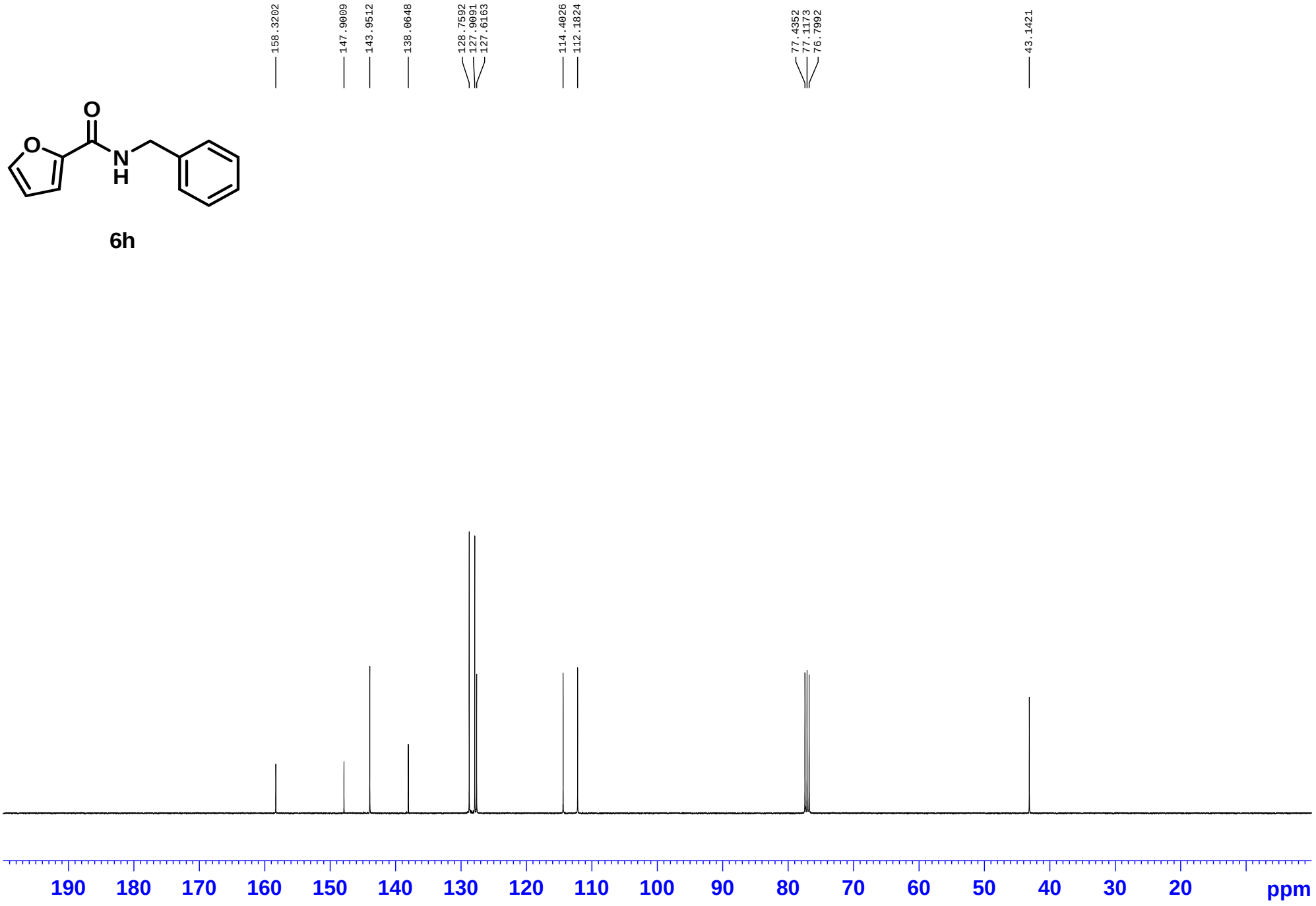
1.5
1.0
ppm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112.1824
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77.1173
76.7992
43.1421
O
O
N
H
6h
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180
170
160
150
140
130
120
110
100
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80
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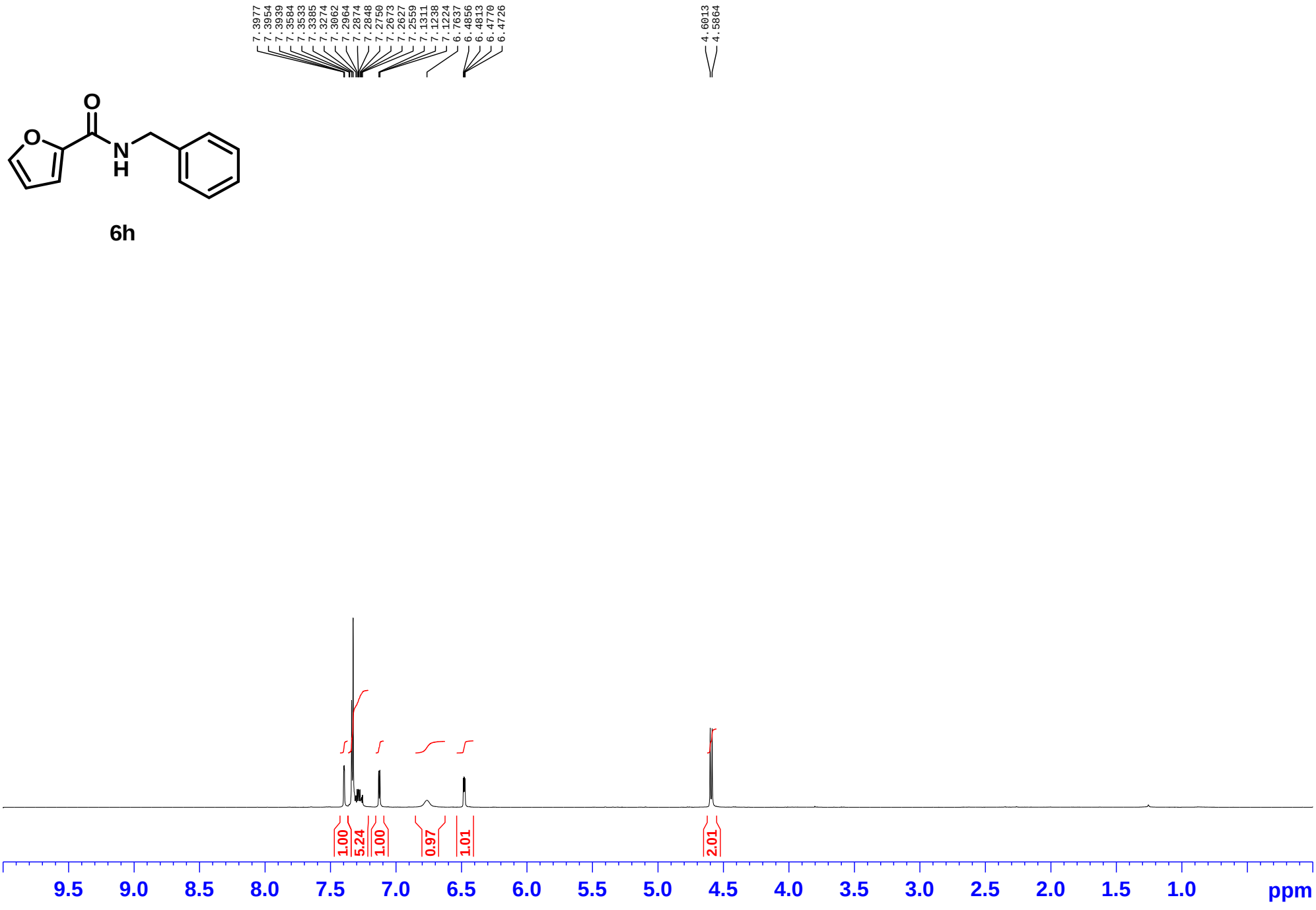
40
30
20
ppm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7.2750
7.2673
7.2627
7.2559
7.1311
7.1238
7.1224
6.7637
6.4856
6.4813
6.4770
6.4726
4.6013
4.5864
O
O
N
H
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1.00
0.97
1.01
2.01
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9.0
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7.0
6.5
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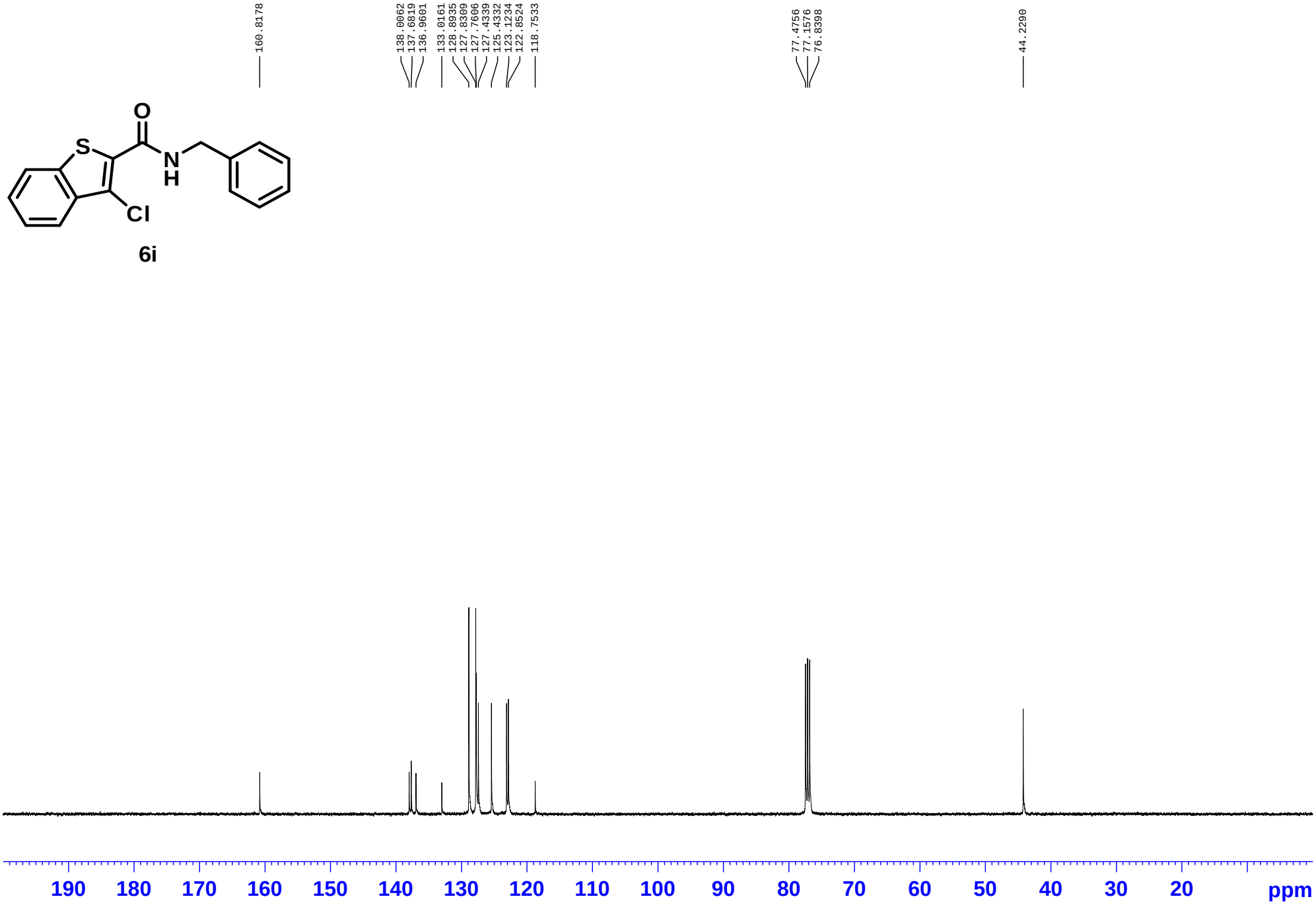
1.0
ppm

6h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O
S
N
H
Cl
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160
150
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130
120
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100
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80
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40
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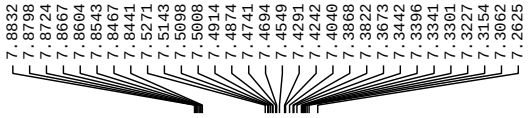
20
ppm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7.5008
7.4914
7.4874
7.4741
7.4694
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7.4242
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7.3868
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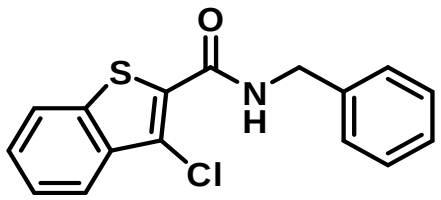
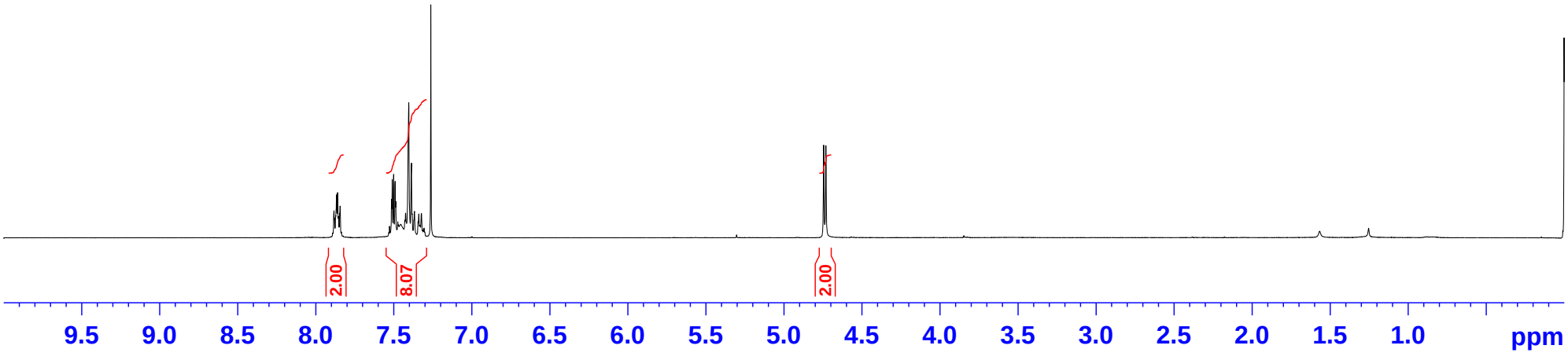
4.7311


O
S
N
H
Cl

6i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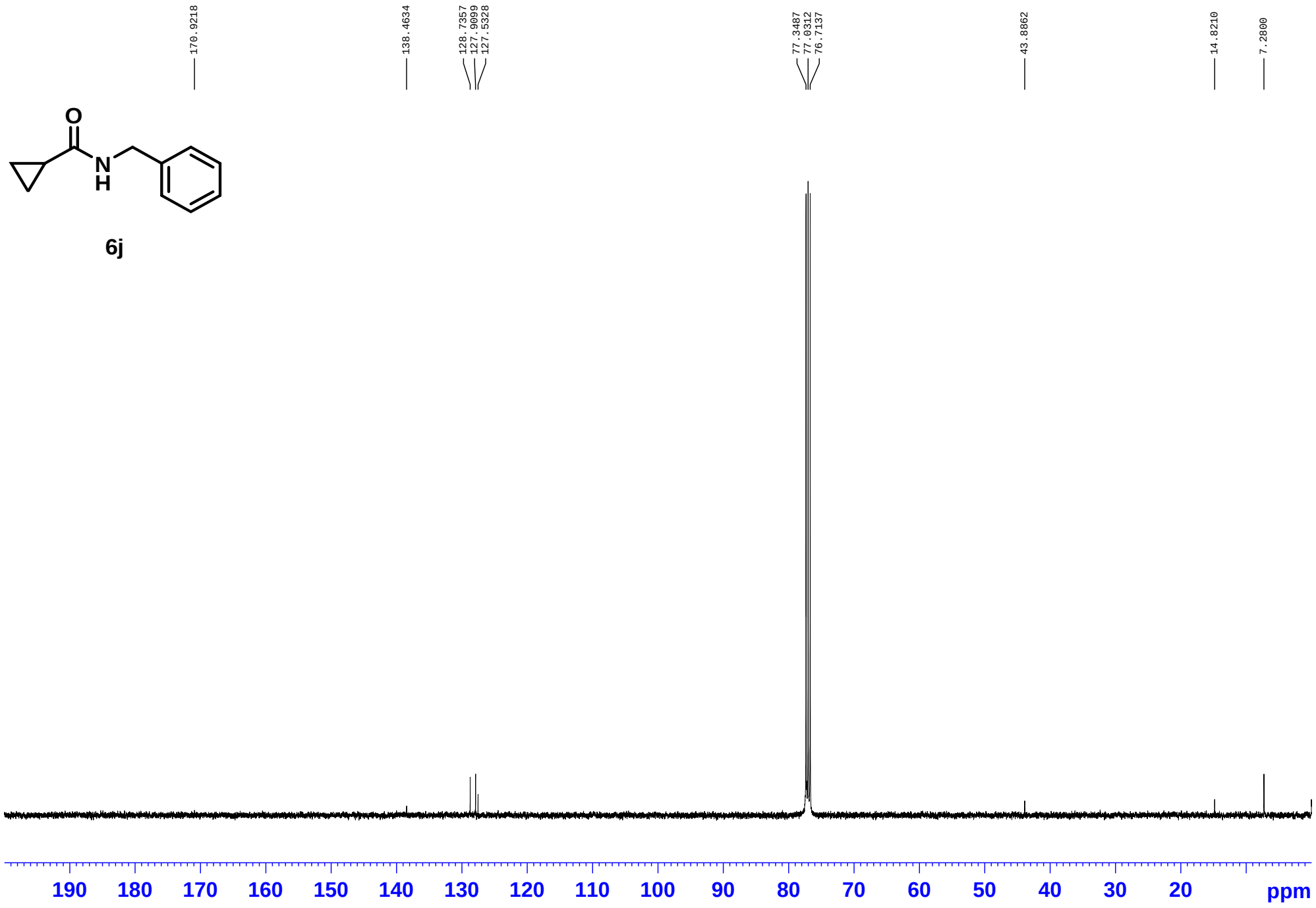
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O
N
H
6j
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110
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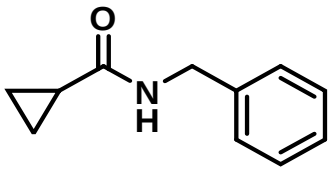
20
ppm


O
N
H

6j

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1.3612
1.3499
1.3385
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1.0327
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1.0215
1.0142
1.0048
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0.7745
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0.7372
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4.0
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3.0
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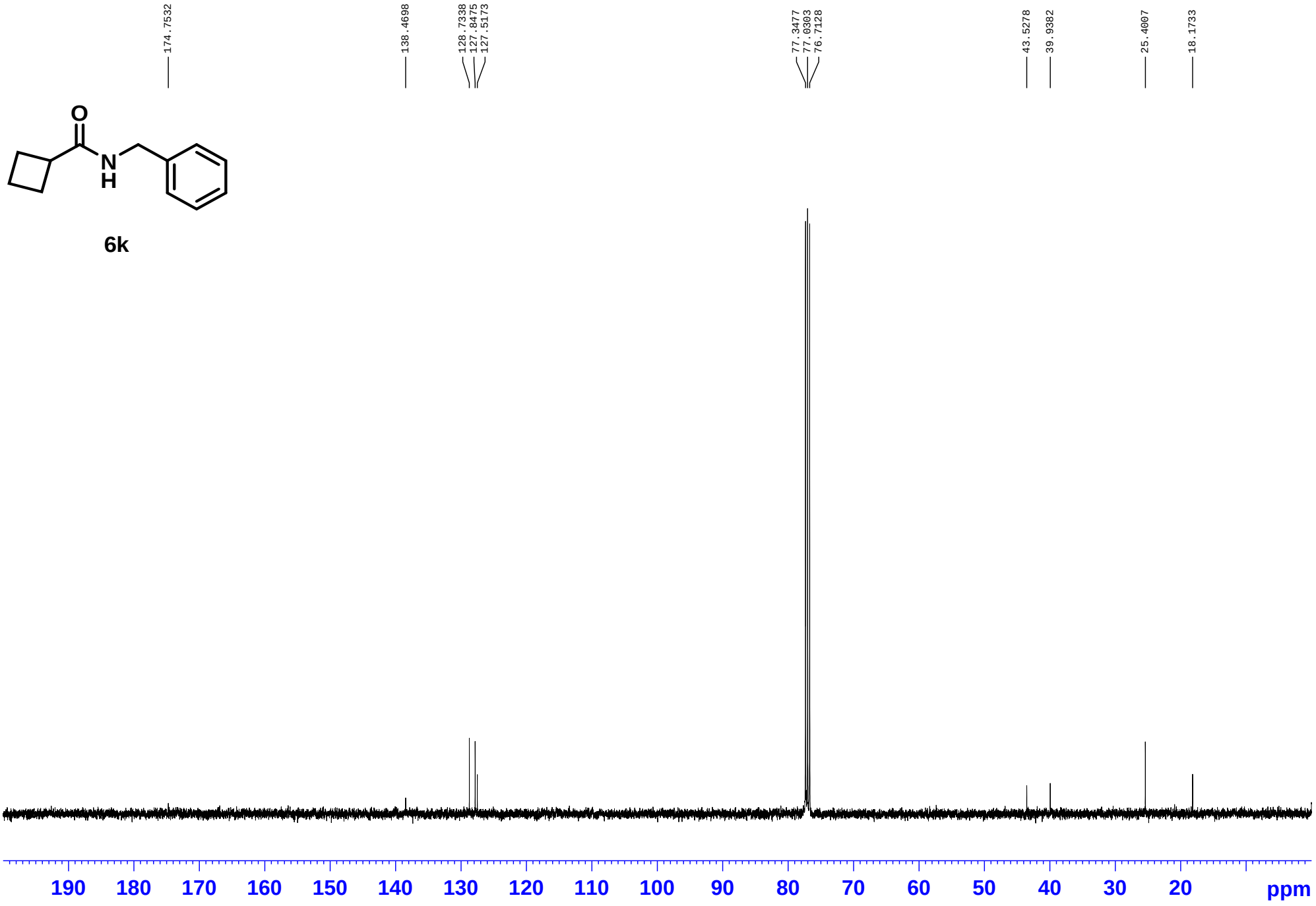
2.0
1.5
1.0
ppm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N
H
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120
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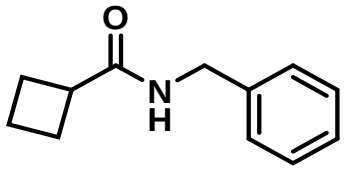
40
30
20
ppm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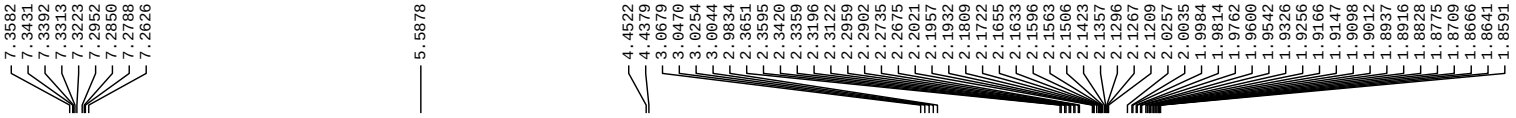
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3.0679
3.0470
3.0254
3.0044
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2.3595
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2.2902
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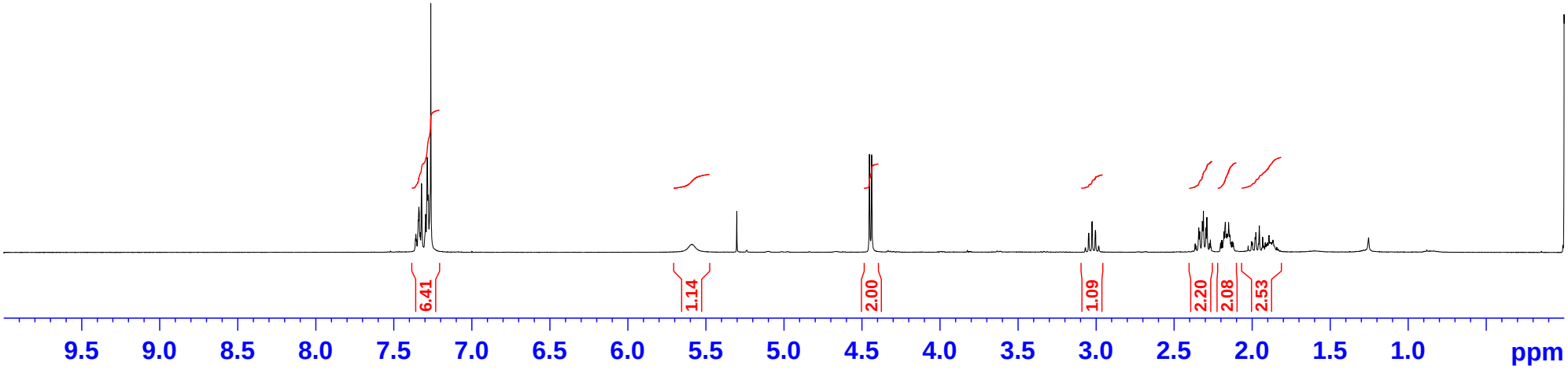
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1.5
1.0
ppm