Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Synthesis of 1,3,4-Oxadiazoles from 1,2-Diacylhydrazines Using $[Et_2NSF_2]BF_4$ as a Practical Cyclodehydration Agent

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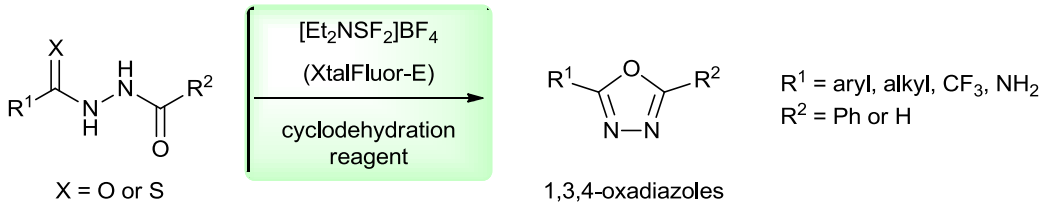
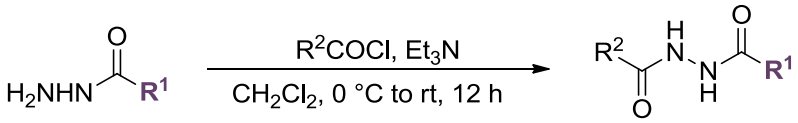


Table of Contents

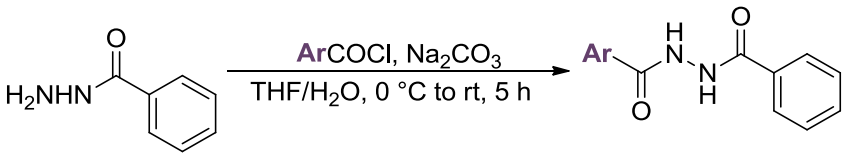
I. General information

The following includes general experimental procedures, specific details for representative reactions and spectroscopic information for the new compounds prepared. All reactions were carried out under a nitrogen or argon atmosphere with dry solvents under anhydrous conditions. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a VARIAN Inova 400 MHz or BRUKER Avance 300 MHz in $CDCl_3$ at ambient temperature using tetramethylsilane (^{1}H NMR) or residual $CHCl_3$ or DMSO (^{1}H and ^{13}C NMR) as the internal standard, or $CFCl_3$ (^{19}F NMR) as the external standard. Infrared spectra were recorded on a Thermo Scientific Nicolet 380 FT-IR spectrometer. High-resolution mass spectra were obtained on a LC/MS-TOF Agilent 6210 using electrospray ionization (ESI). Melting points were recorded on a Stanford Research System OptiMelt capillary melting point apparatus and are uncorrected.

II. General procedure for 1,2-diacylhydrazides synthesis



Method A - General protocol: To a stirred solution of the acyl hydrazine (1 mmol) in dry dichloromethane (15 mL) was added dry triethylamine (2 mmol) under N_2. The mixture was cooled to 0 °C and the acyl chloride (1 mmol) was added dropwise to the solution. The resulting mixture was stirred for 12 h at room temperature. The crude solution was then quenched by a saturated solution of $NaHCO_3$ and extracted with dichloromethane (3×). The combined organic extracts were washed with water (1×), brine (1×), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography to give the desired product.



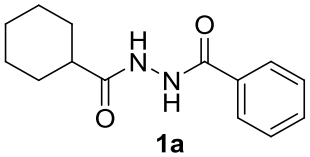
Method B - General Protocol:[1] To a stirred solution of the acyl chloride (1.8 mmol) in dry tetrahydrofuran (5 mL) at 0 °C was added a solution of benzoic hydrazine (1.8 mmol) and anhydrous sodium carbonate (1.8 mmol) in dry tetrahydrofuran (10 mL) and water (10 mL). The

[1] Hua, G.; Li, Y.; Fuller, A. L.; Slawin, A. M. Z.; Woollins, J. D. *Eur. J. Org. Chem.* **2009**, *15*, 1612-1618.

mixture was stirred at 0 °C for 1 h, and at room temperature for 4 h. Diethyl ether was then added and a precipitation was observed. The residue was collected by filtration, washed with cold diethyl ether and dried *in vacuo*.

The data for the 1,2-diacylhydrazides not described previously are given below.

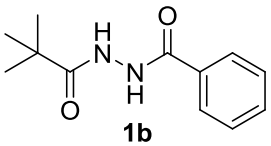
III. 1,2-Diacylhydrazines characterization



1a

***N'*-Benzoyl-2-cyclohexylhydrazide (1a).** Following the general **Method A** on a 3.7 mmol scale of benzoic hydrazine, the desired product (837 mg, 93%) was isolated as a white solid. The resulting crude product has been used directly without further purification.

mp 157-160 °C; IR (ATR, ZnSe) ν = 3228, 3022, 2927, 2856, 1688, 1636, 1516, 1487, 1452, 690 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68 (br s, 1H), 9.30 (br s, 1H), 7.82 (d, *J* = 7.6 Hz , 2H), 7.53-7.48 (m, 1H), 7.42-7.37 (m, 3H), 2.38-2.29 (m, 1H), 1.90-1.78 (m, 4H), 1.68 (m, 1H), 1.56-1.38 (m, 2H), 1.32-1.19 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 164.2, 132.4, 131.6, 128.8, 127.4, 43.3, 29.4, 25.7, 25.6; HRMS-ESI calcd for $C_{14}H_{19}N_2O_2$ $[M+H]^+$ 247.1441, found 247.1455.

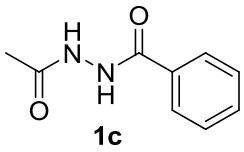


1b

***N'*-Benzoyl-1,1-dimethylethylhydrazide (1b).** Following the general **Method A** on a 3.7 mmol scale of benzoic hydrazine, the desired product (730 mg, 90%) was isolated as a white solid. The resulting crude has been directly used without purification.

mp 189-190 °C; IR (ATR, ZnSe) ν = 3223, 2970, 1645, 1519, 1284, 1224, 1143, 932, 710, 689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.98 (br s, 1H), 9.07 (br s, 1H), 7.84 (d, *J* = 7.4 Hz, 2H), 7.48 (t, *J* = 6.9 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0,

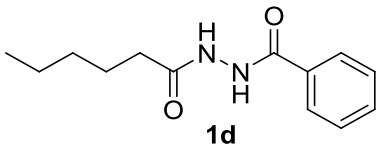
164.7, 132.3, 131.6, 128.7, 127.5, 38.4, 27.3; HRMS-ESI calcd for $C_{12}H_{17}N_2O_2$ $[M+H]^+$ 221.1285, found 221.1294.



1c

***N'*-Benzoylmethylhydrazide (1c).** Following the general **Method B** on a 1.8 mmol scale benzoic hydrazine, the desired product (318 mg, 97%) was isolated as a white solid by trituration using diethyl ether.

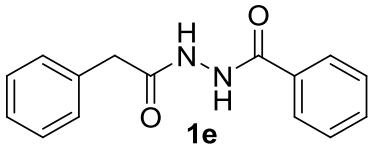
mp 174-175 °C; IR (ATR, ZnSe) ν = 3321, 3201, 1657, 1559, 1523, 1434, 1387, 710, 691, 676 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 10.30 (br s, 1H), 9.90 (br s, 1H), 7.88 (d, *J* = 7.5 Hz, 2H), 7.59-7.46 (m, 3 H), 1.93 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.59, 165.5, 132.6, 131.8, 128.5, 127.4, 20.6; HRMS-ESI calcd for $C_9H_{10}N_2O_2Na$ $[M+Na]^+$ 201.0634, found 201.0632.



1d

***N'*-Benzoylpentylhydrazide (1d).** Following the general **Method A** on a 1.8 mmol scale of benzoic hydrazine, the desired product (395 mg, 92%) was isolated as a white solid by flash chromatography using ethyl acetate/hexane (30/70).

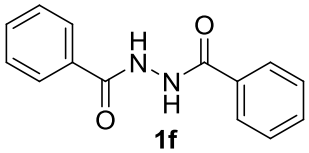
mp 105-106 °C; IR (ATR, ZnSe) ν = 3223, 3007, 2959, 2927, 1686, 1645, 1529, 1488, 1261, 715 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.11 (br s, 1H), 9.73 (br s, 1H), 7.83 (d, *J* = 7.5 Hz, 2H), 7,49 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 2.29 (t, *J* = 7.7 Hz, 2H), 1.65-1.61 (m, 2H), 1.29-1.25 (m, 4H), 0.87-0.84 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 165.1, 132.2, 131.4, 128.6, 127.6, 34.1, 31.4, 25.2, 22.4, 14.0; HRMS-ESI calcd for $C_{13}H_{19}N_2O_2$ $[M+H]^+$ 235.1441, found 235.1441.



1e

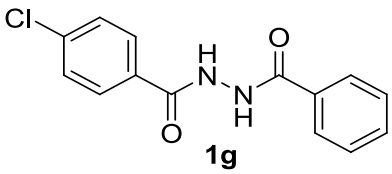
***N'*-Benzoyl-2-phenylmethylhydrazide (1e).** Following the general **Method A** on a 3.7 mmol scale of benzoic hydrazine, the desired product (926 mg, 95%) was isolated as a colorless solid by flash chromatography using methanol/dichloromethane (10/90).

mp 147-148 °C; IR (ATR, ZnSe) ν = 3263, 3029, 1688, 1653, 1599, 1484, 1469, 1247, 713, 690 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.38 (br s, 1H), 10.20 (br s, 1H), 7.87 (d, J = 7.2 Hz, 2H), 7.59-7.46 (m, 3H), 7.35-7.22 (m, 5H), 3.54 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.5, 165.5, 135.8, 132.5, 131.8, 129.1, 128.5, 128.3, 127.4, 126.5, 40.3; HRMS-ESI calcd for $C_{15}H_{15}N_2O_2$ $[M+H]^+$ 255.1128, found 255.1127.



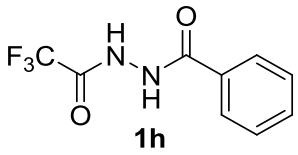
1f

***N'*-Benzoylbenzohydrazide (1f).** Following the general **Method B** on a 1.8 mmol scale of benzoic hydrazine, the desired product (349 mg, 79%) was isolated as a white solid by crystallization using diethyl ether. Spectral data for **1f** were identical with those previously reported.[1]



1g

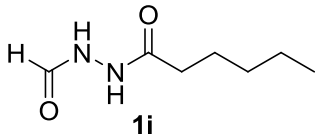
***N'*-Benzoyl-4-chlorobenzohydrazide (1g).** Following the general **Method B** on a 1.8 mmol scale of benzoic hydrazine, the desired product (396 mg, 78%) was isolated as a white solid by trituration using diethyl ether. Spectral data for **1g** were identical with those previously reported.[1]



1h

***N'*-Benzoyltrifluoromethylhydrazide (1h).** Following the general **Method A** on a 1.8 mmol scale of benzoic hydrazine and using triflic anhydride (1 equiv.) instead of an acyl chloride, the desired product (349 mg, 82%) was isolated as a white solid by flash chromatography using diethyl ether/ hexane (30/70).

mp 153-154 °C; IR (neat) ν = 3207, 1713, 1626, 1601, 1579, 1471, 1311, 1144, 958, 713 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.60 (br s, 1H), 10.77 (br s, 1H), 7.85 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.3, 155.9 (q, J_{C-F} = 36.6 Hz), 132.3, 131.7, 128.7, 127.5, 115.9 (q, J_{C-F} = 287.9 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ –75.1; HRMS-ESI calcd for $C_9H_8F_3N_2O_2$ $[M+H]^+$ 233.0532, found 233.0490.

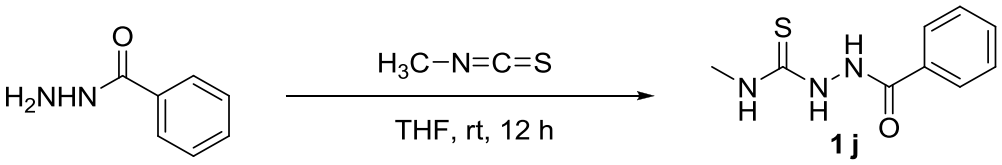


1i

***N'*-Pentylformylhydrazide (1i).** Following the general **Method A** on a 14.7 mmol scale of formic hydrazine, the desired product (664 mg, 29%) was isolated as a white solid by flash chromatography using methanol/hexane (5/95).

mp 93-95 °C; IR (ATR, ZnSe) ν = 3194, 2953, 2924, 1603, 1574, 1466, 1386, 1194, 1113, 661 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (br s, 1H), 8.96 (br s, 1H), 8.09 (s, 1H), 2.29 (t, J = 7.5 Hz, 2H), 1.66 (m, 2H), 1.34-1.32 (m, 4H), 0.91-0.88 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 157.1, 34.2, 31.4, 25.1, 22.5, 14.0; HRMS-ESI calcd for $C_7H_{14}N_2ONa$ $[M+Na]^+$ 181.0952, found 181.0947.

IV. Procedure for the synthesis of a thiosemicarbazide

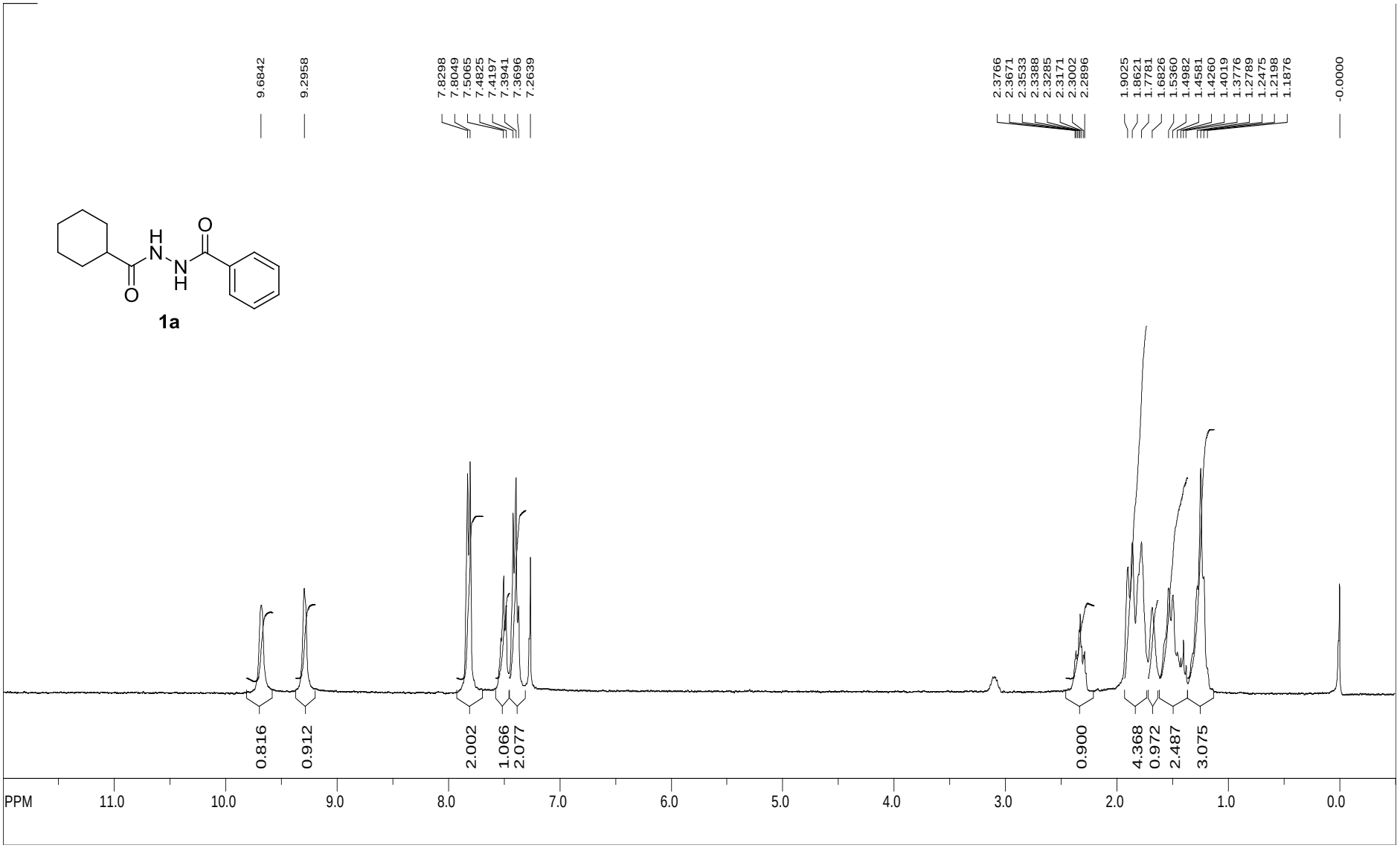


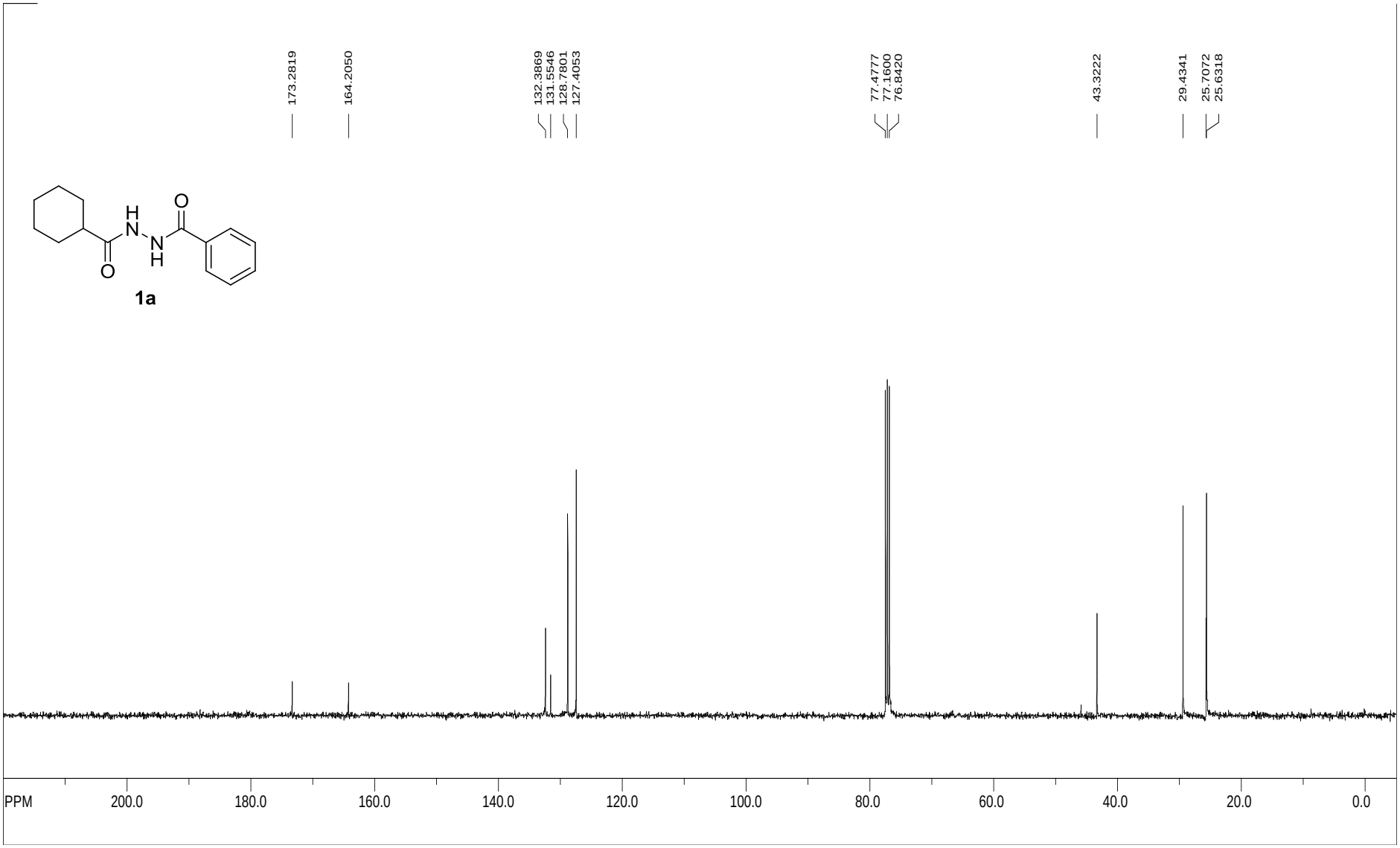
***N'*-Methylbenzoic acid thiosemicarbazide (1j).** Following the literature protocol[2] on a 1.8 mmol scale of benzoic hydrazine and 1.8 mmol scale of methyl isothiocyanate, the desired product (336 mg, 87%) was isolated as a white solid after trituration using Et_2O.

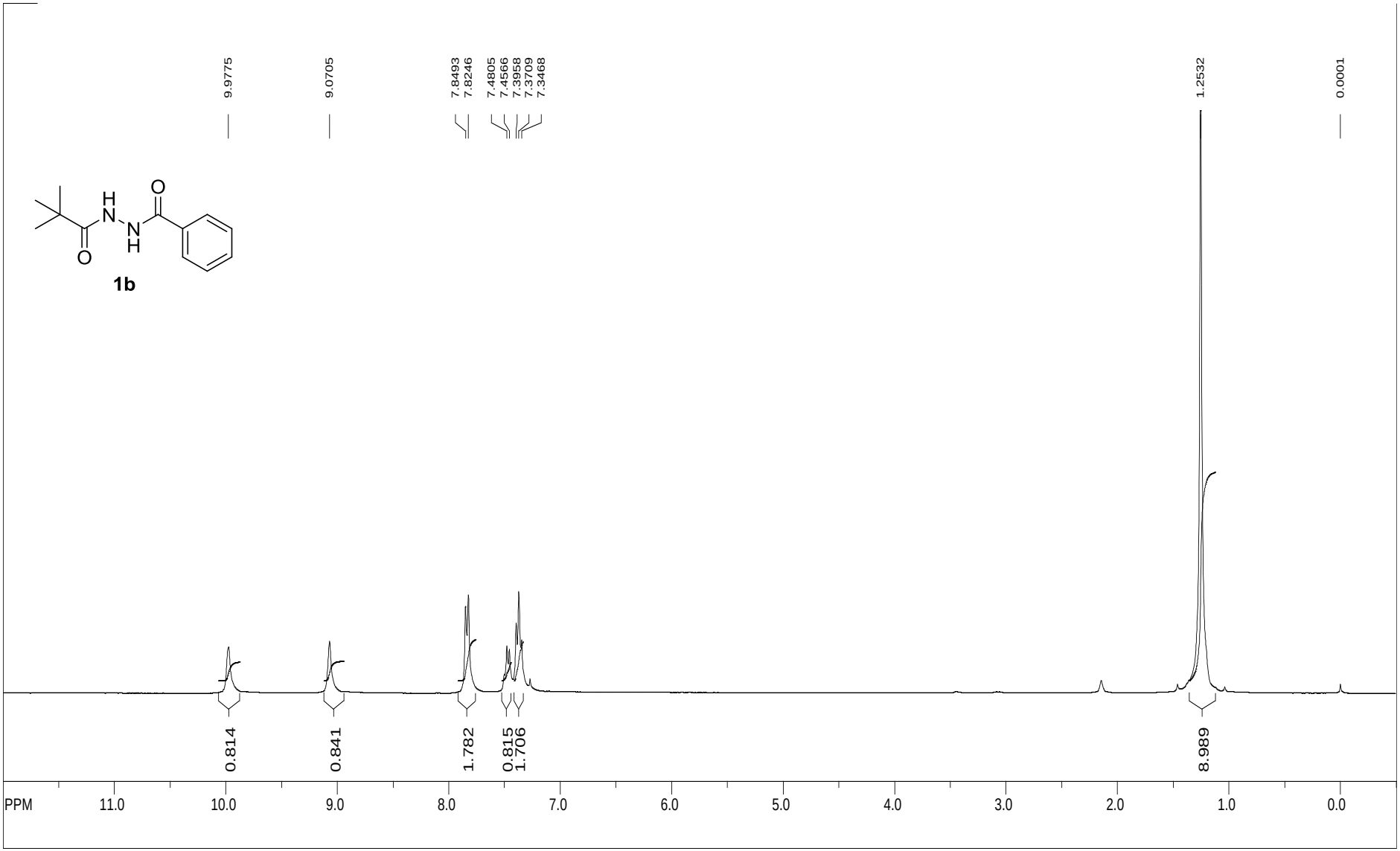
mp 187-189 °C; IR (ATR, ZnSe) ν = 3293, 3165, 2938, 1677, 1559, 1456, 1408, 1238, 1062, 692 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 10.34 (br s, 1H), 9.33 (br s, 1H), 8.04 (br s, 1H), 7.92 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 2.87 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.3, 166.0, 132.5, 131.9, 127.8, 127.9, 31.0; HRMS-ESI calcd for $C_9H_{12}N_3OS$ $[M+H]^+$ 210.0701, found 210.0696.

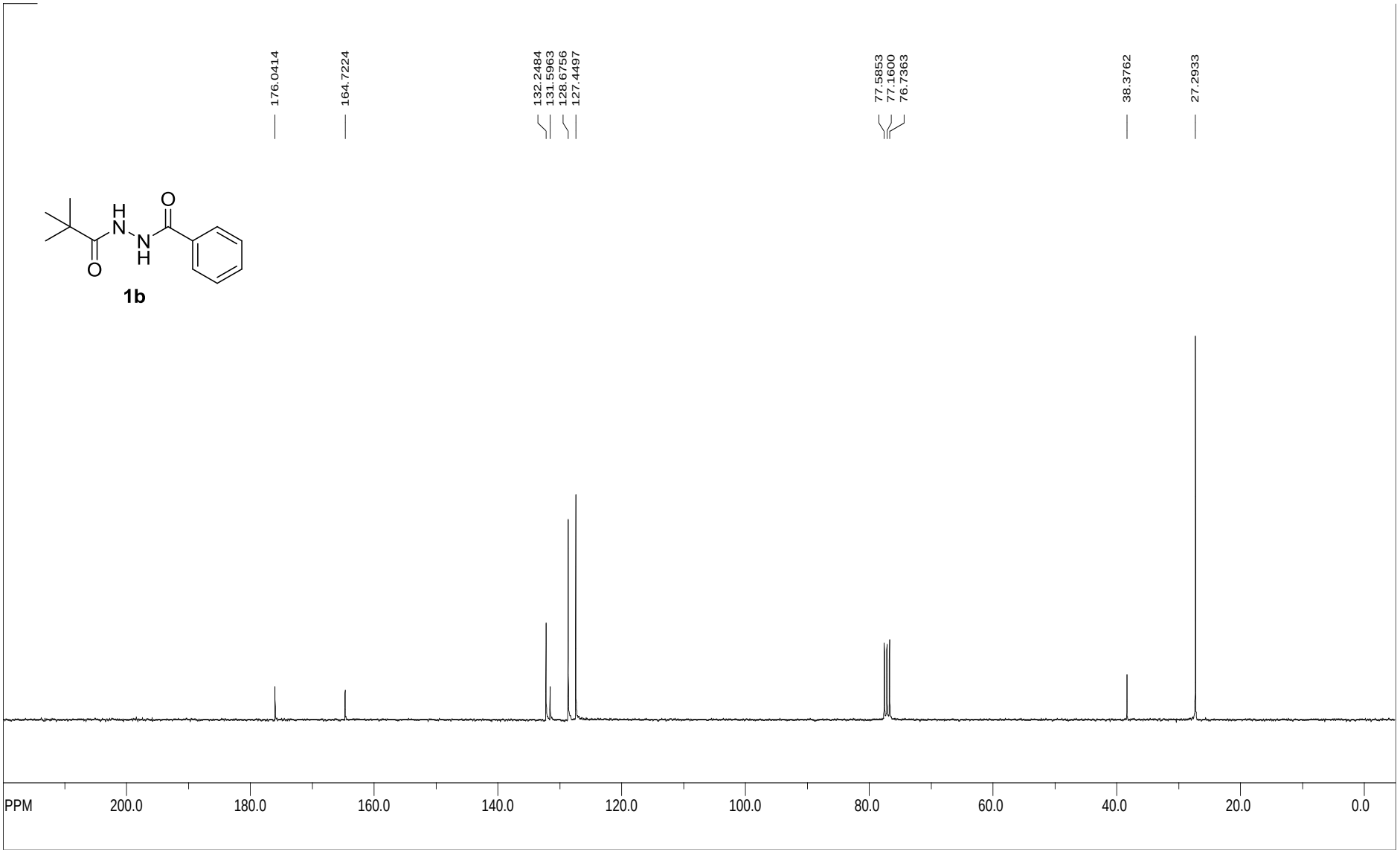
V. ^1H and ^{13}C spectrum

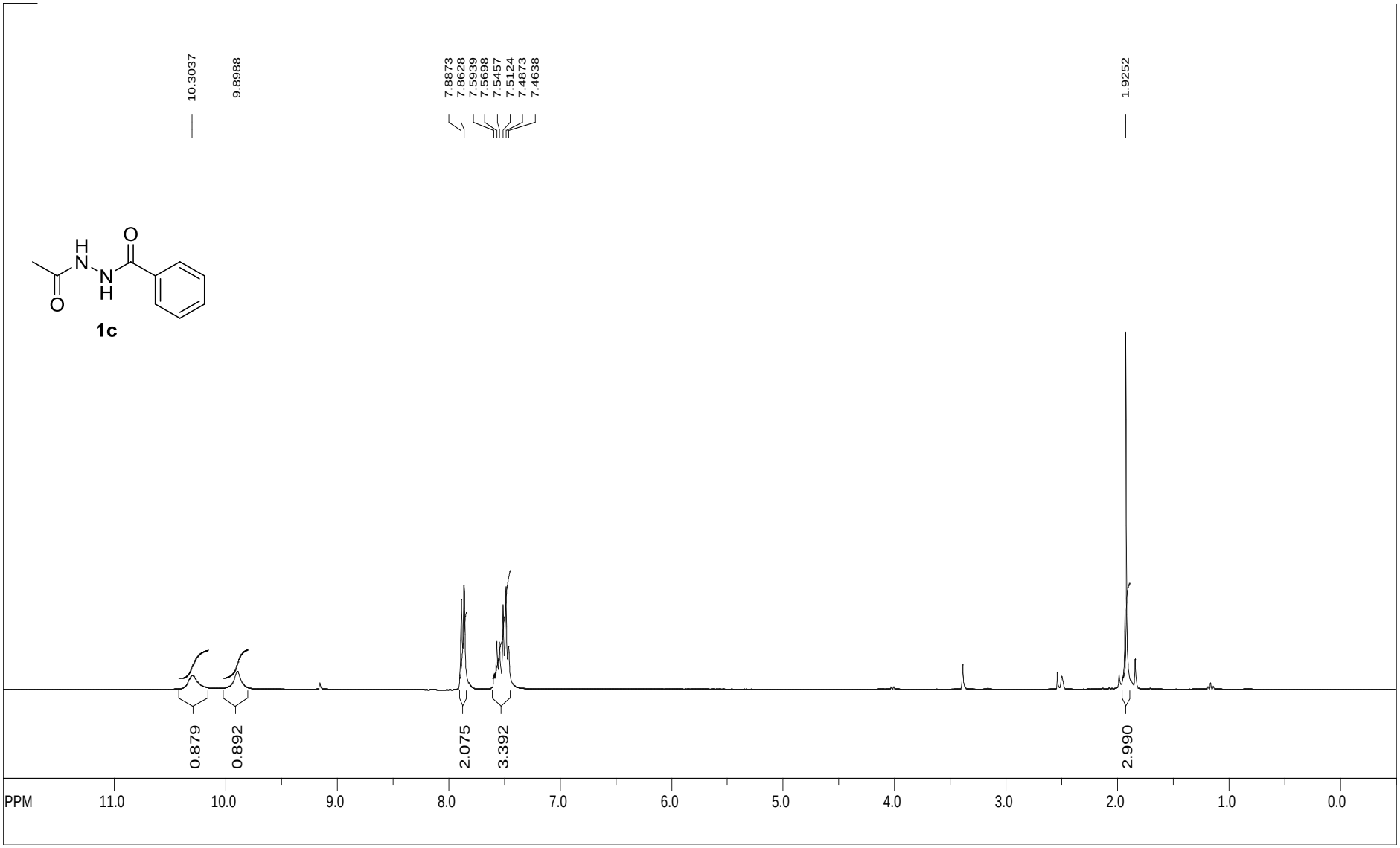
[2] Dolman, S. J.; Gosselin, F.; O'Shea, P. D.; Davies, I. W. *J. Org. Chem.* **2006**, *71*, 9548-9551.

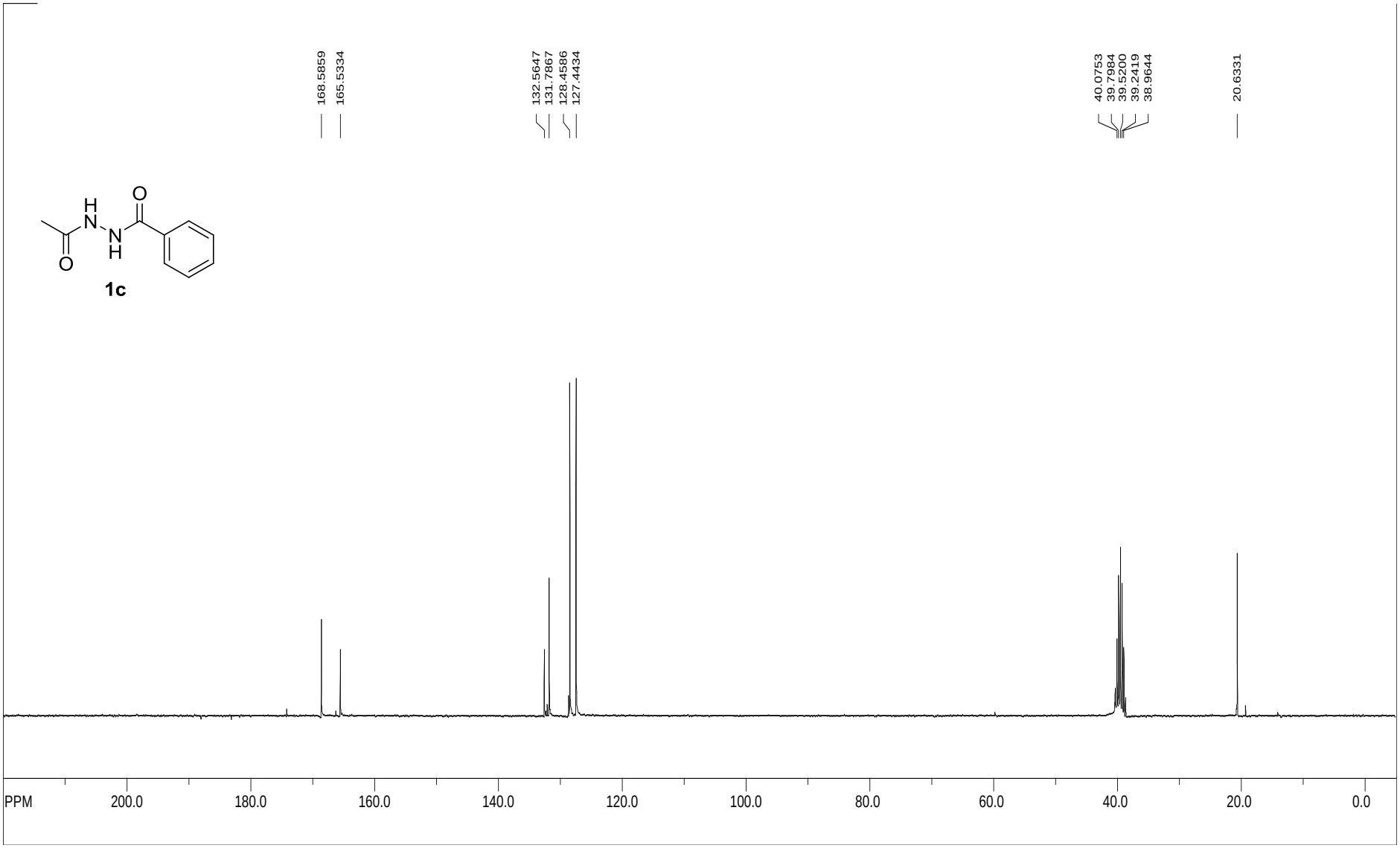


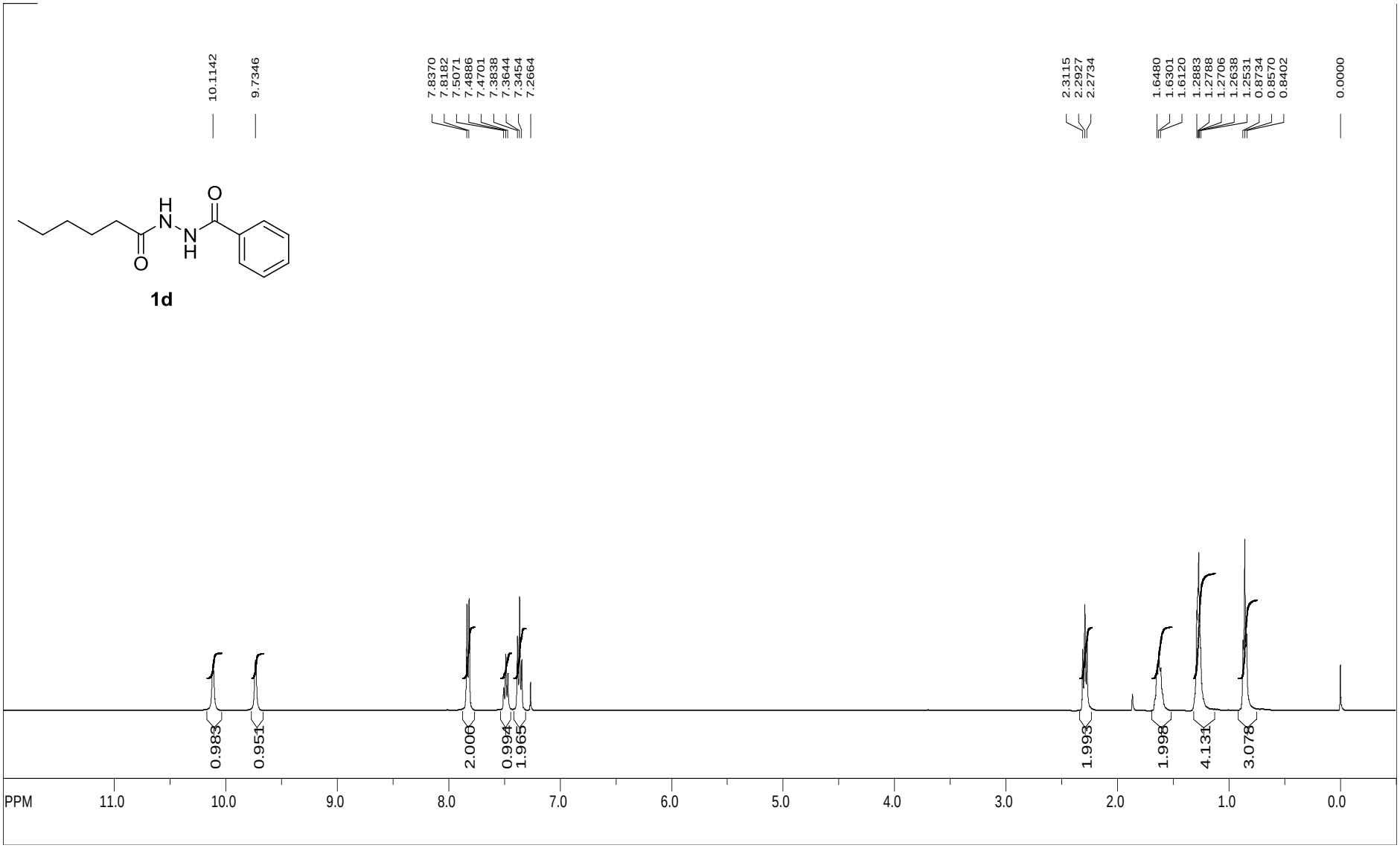












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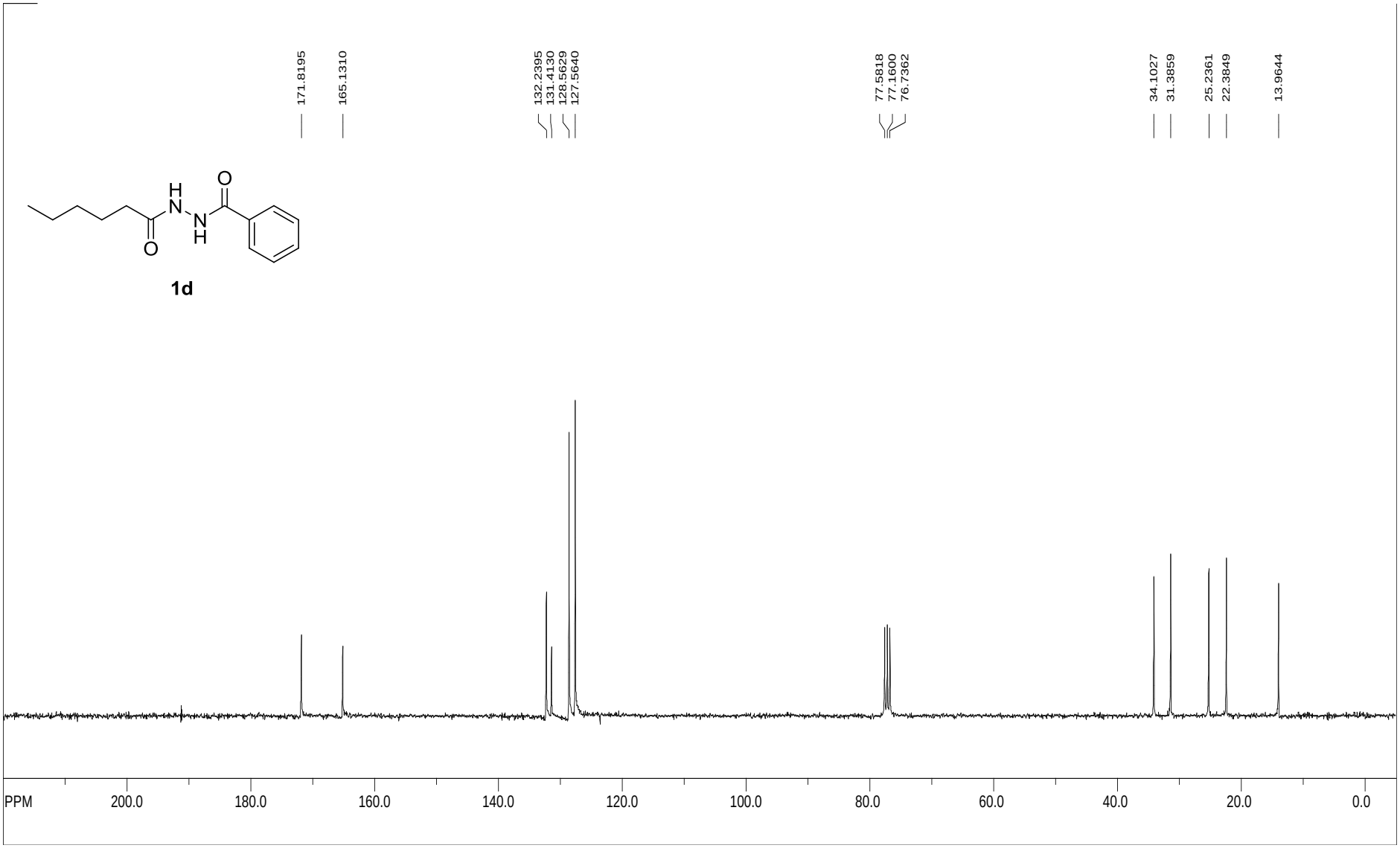

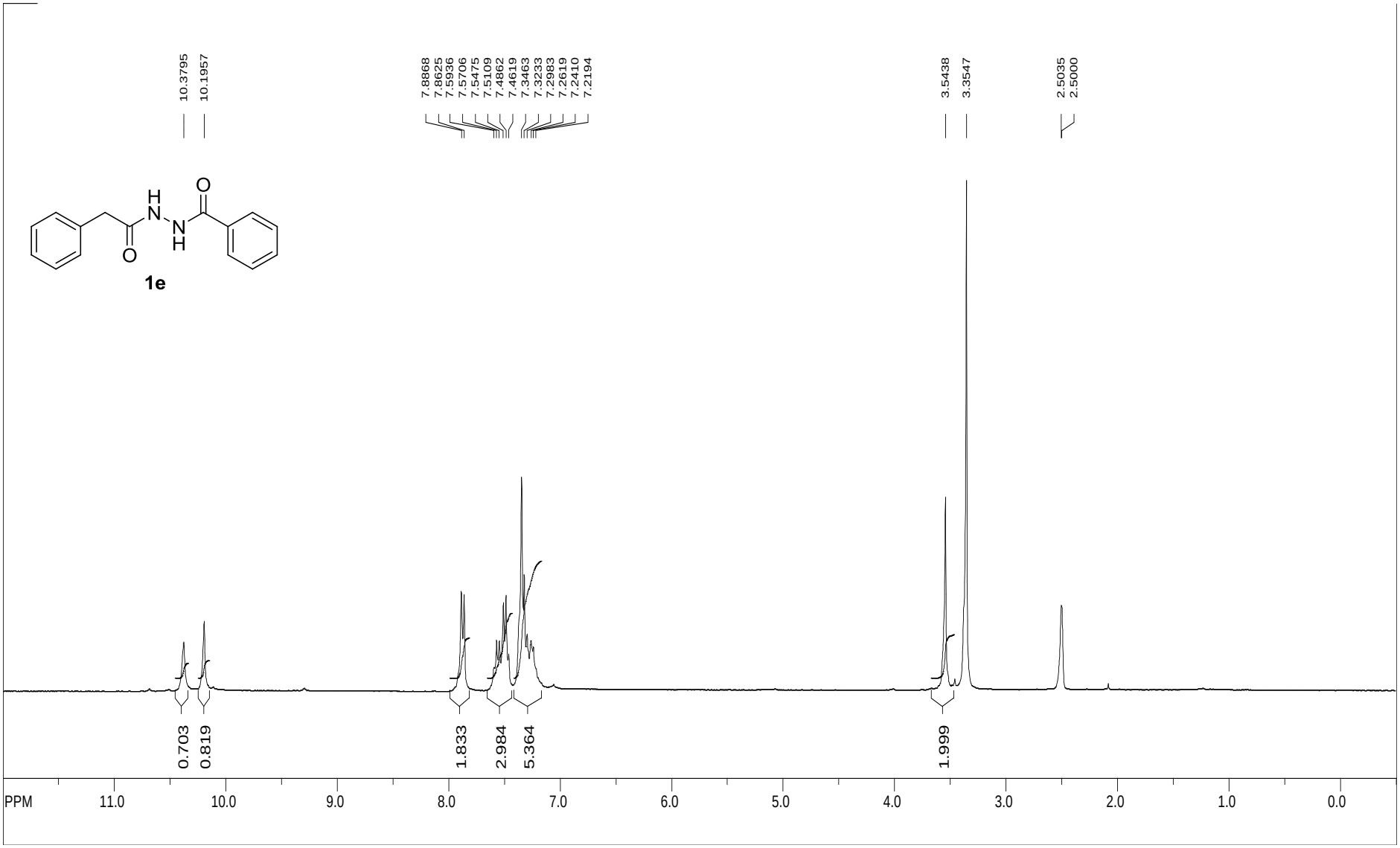

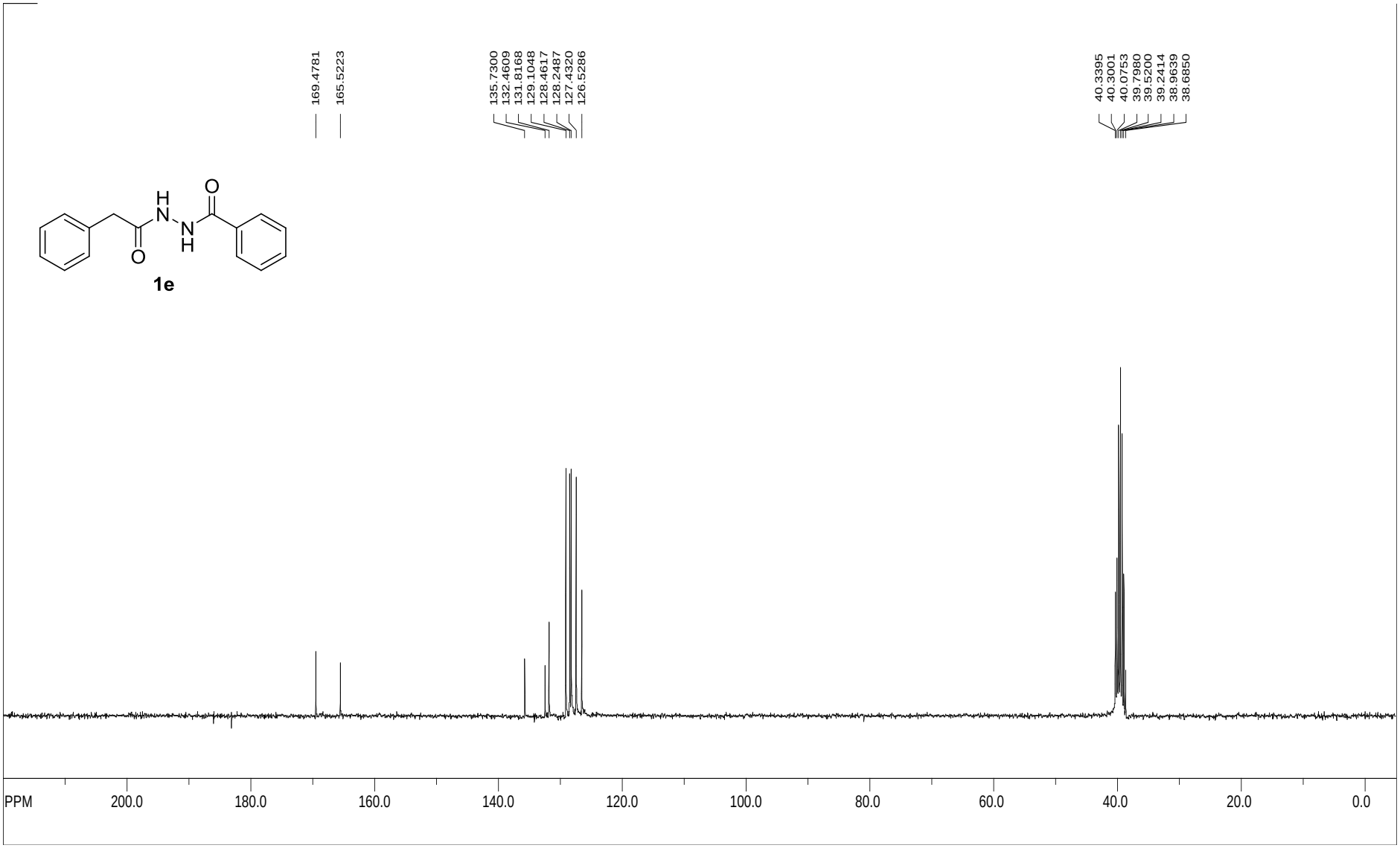

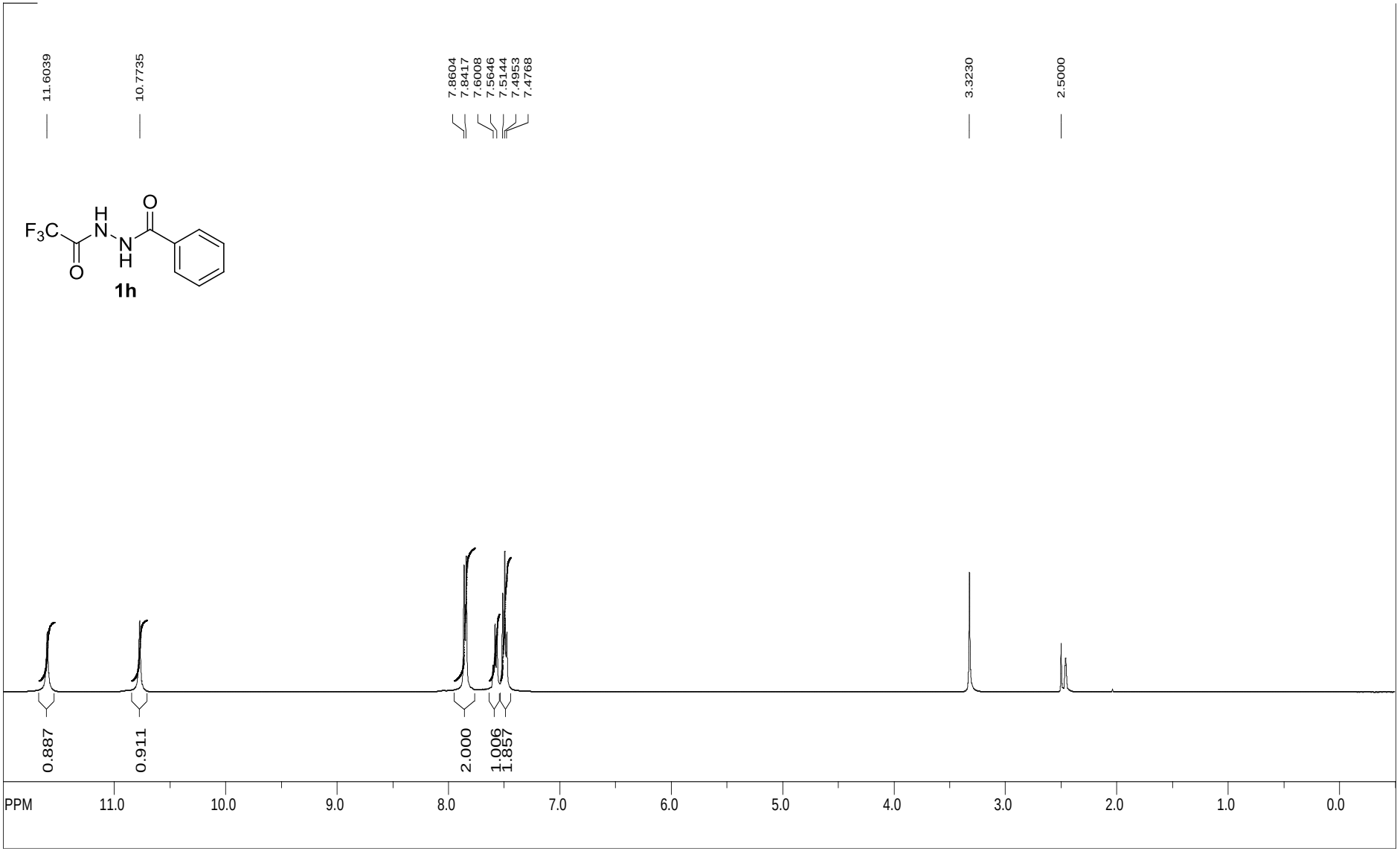

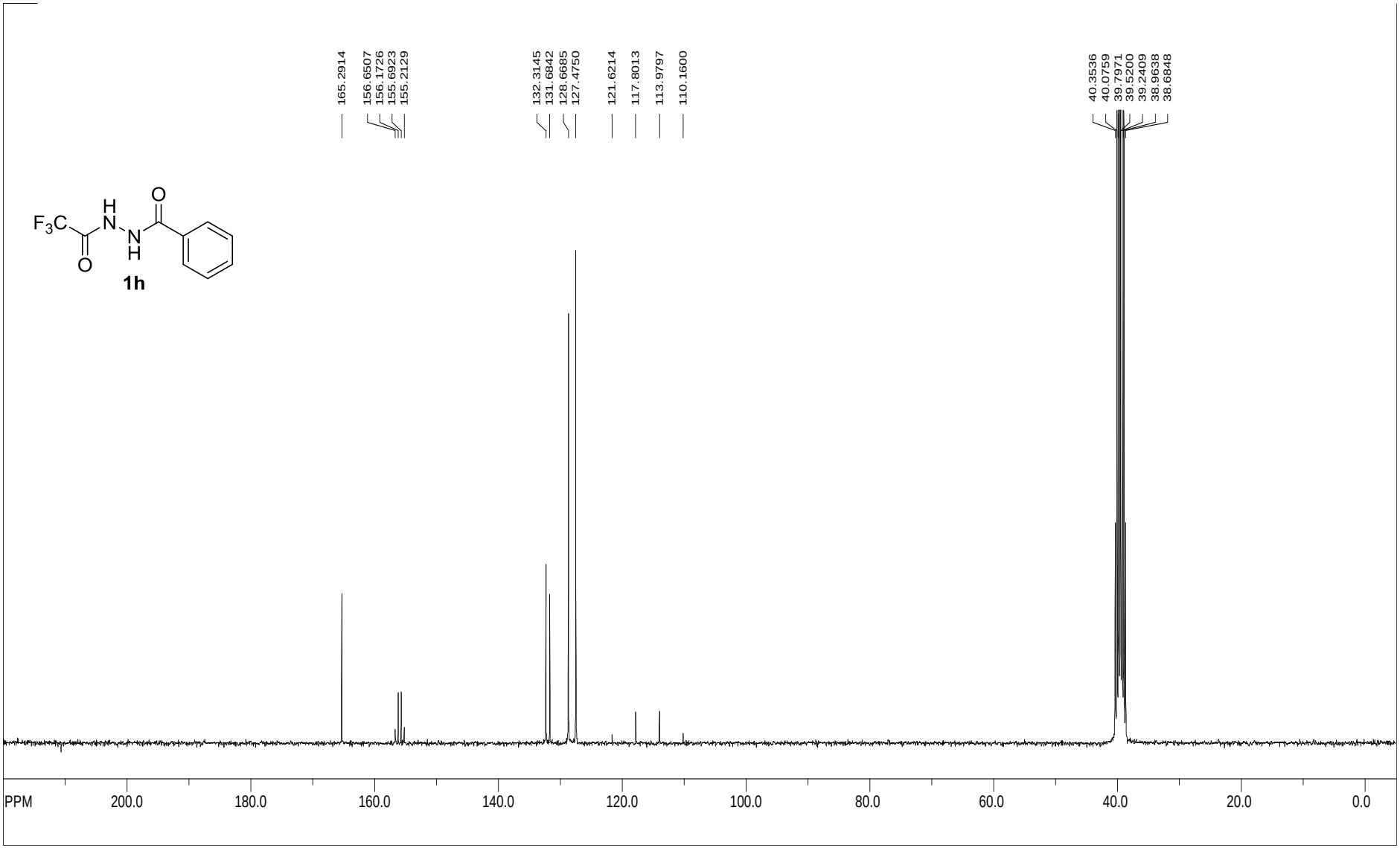

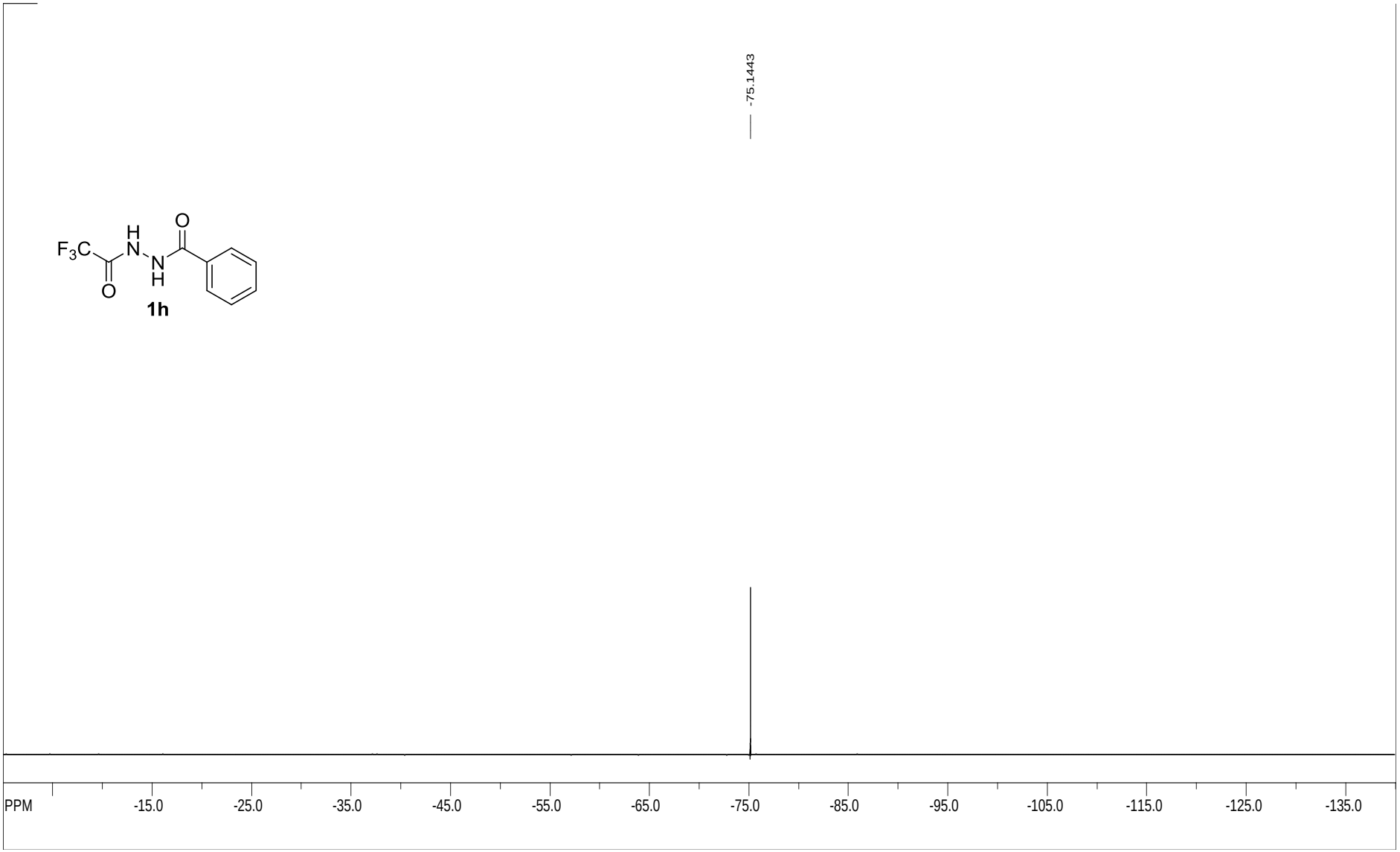

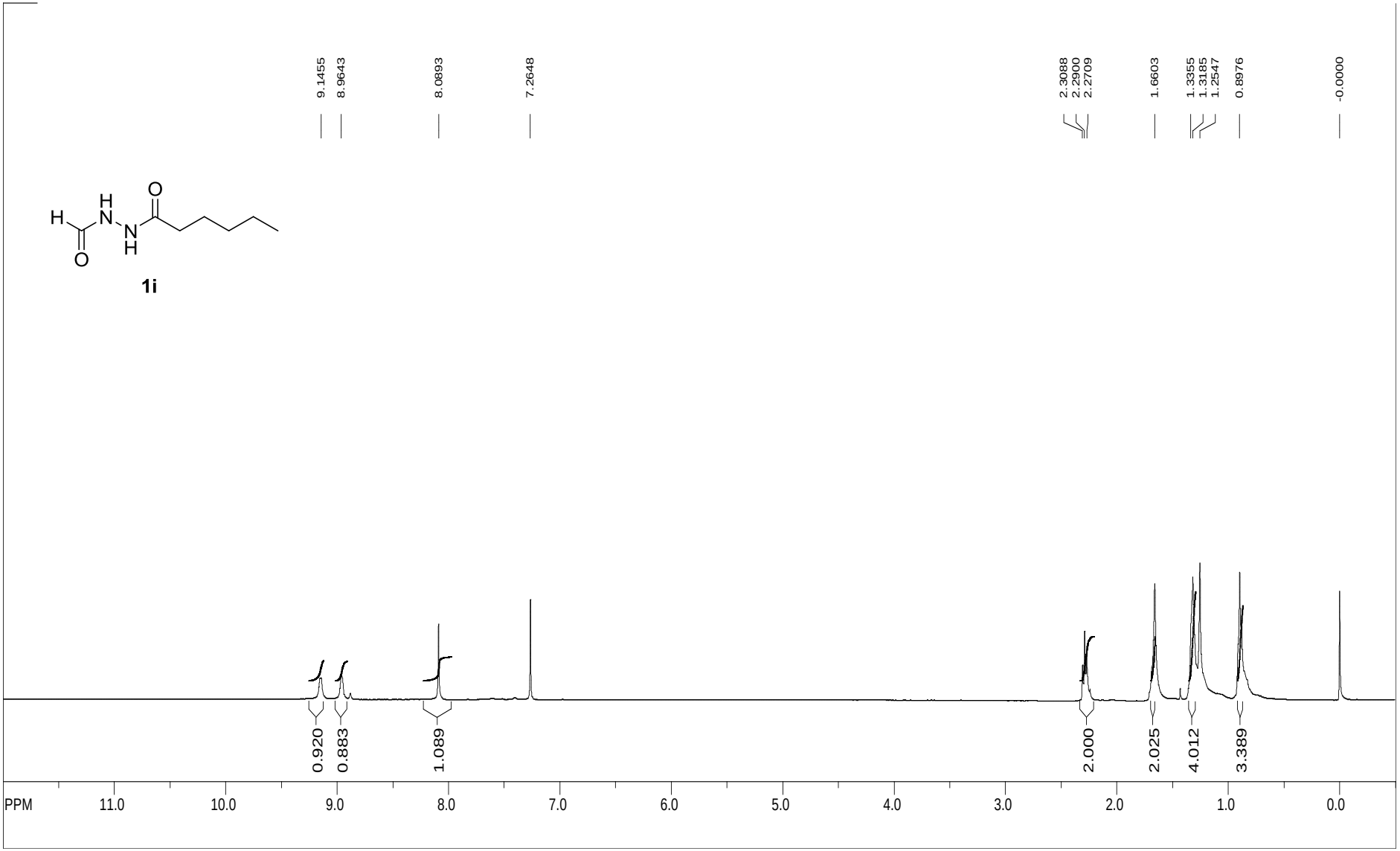

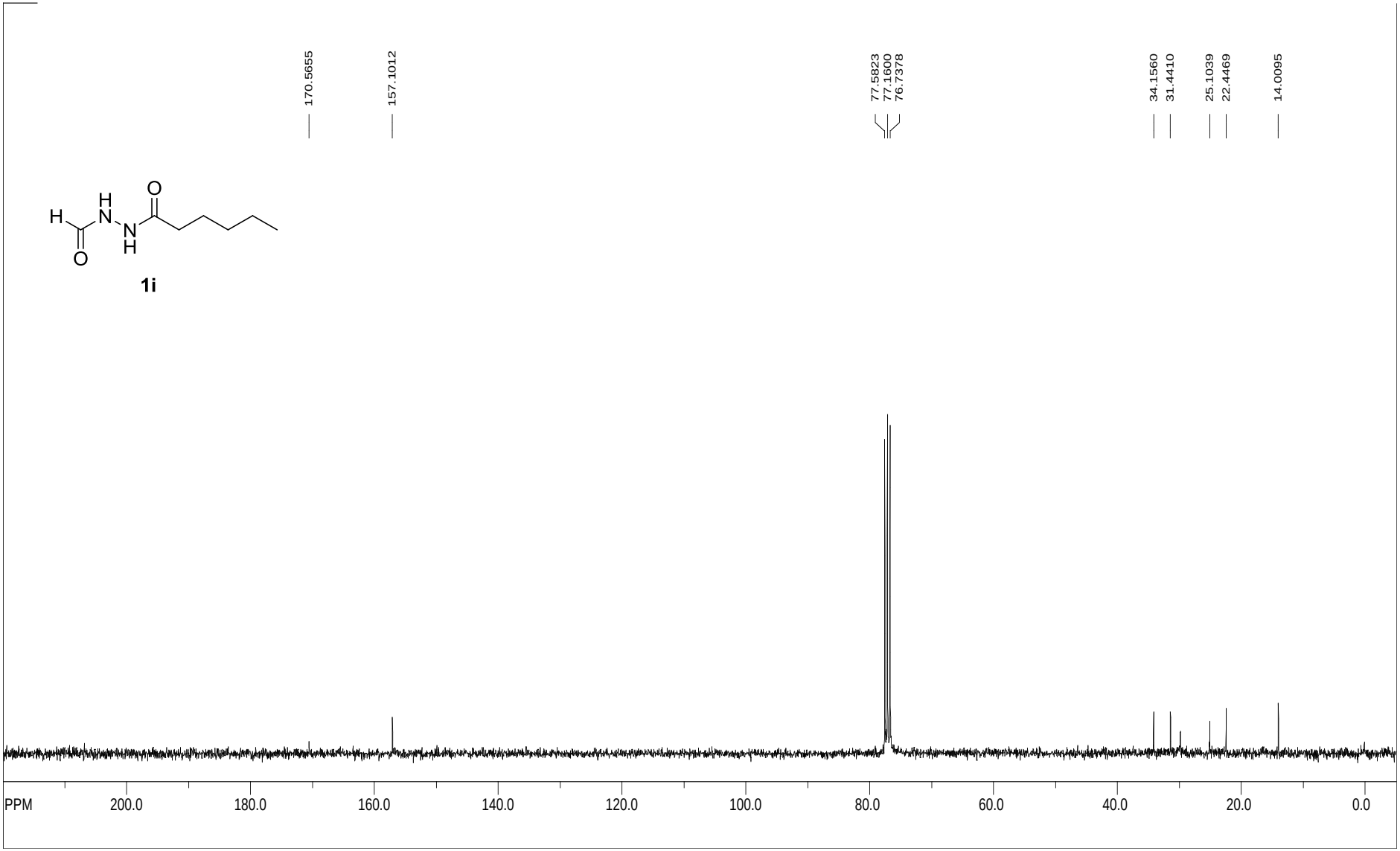

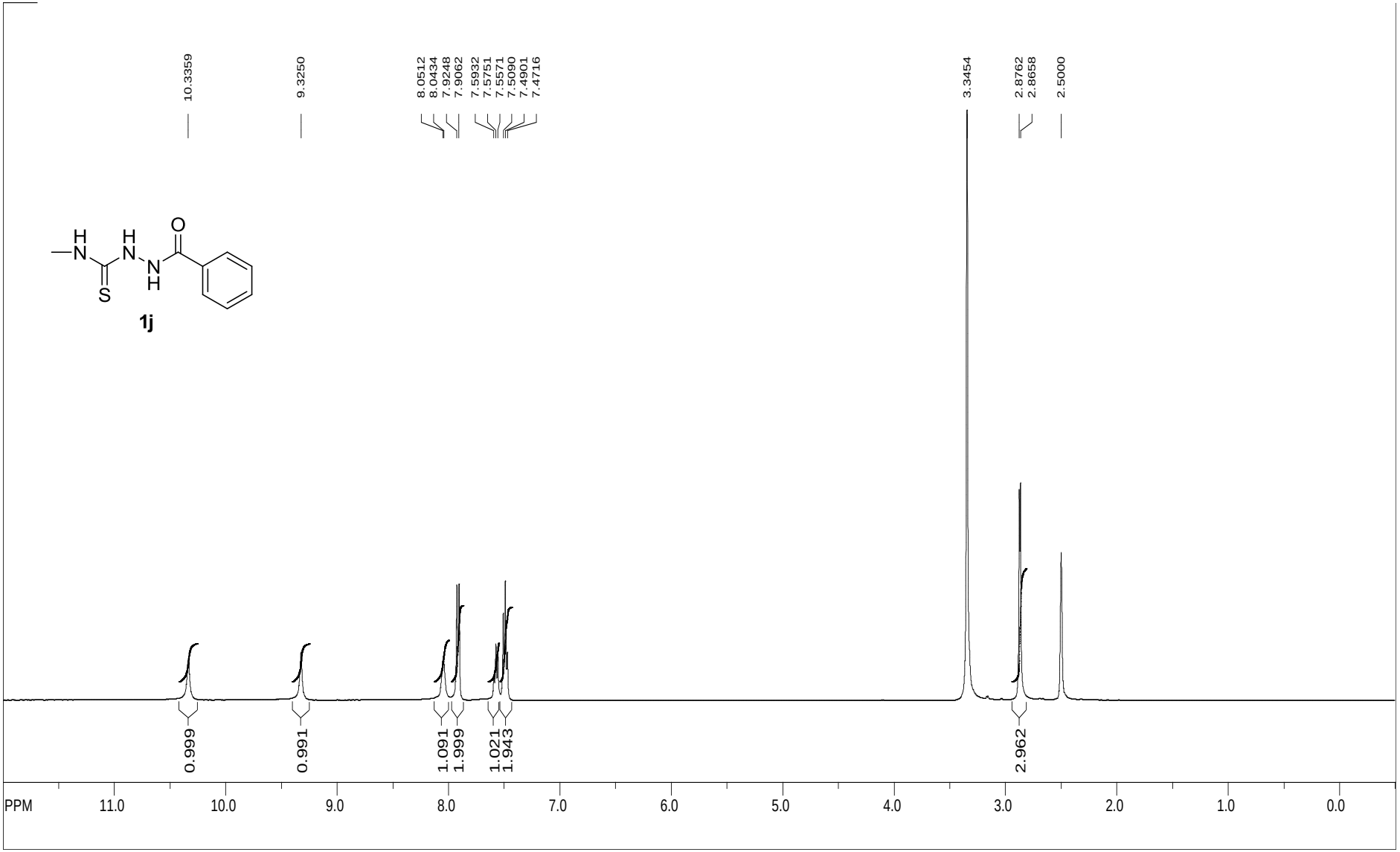

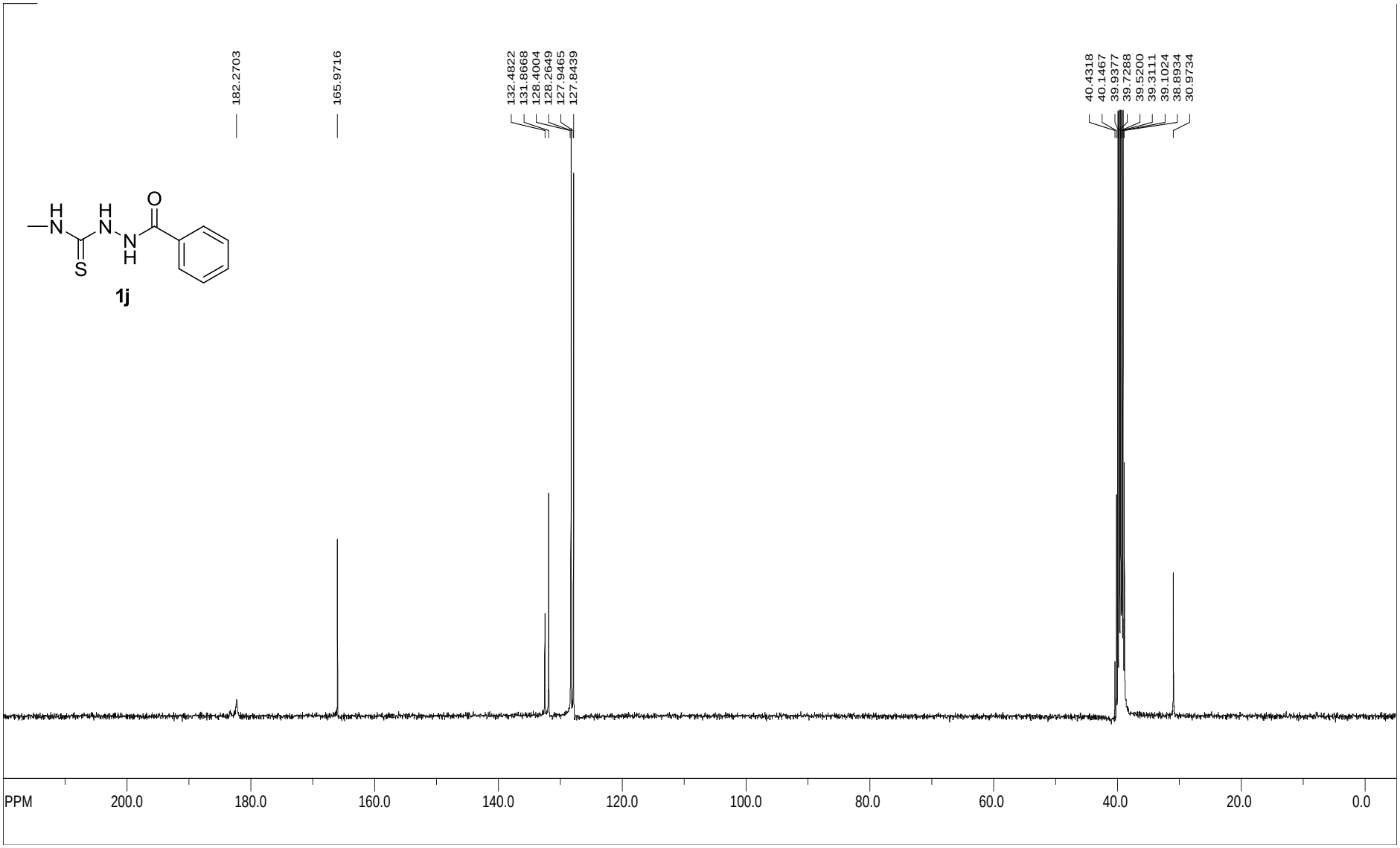

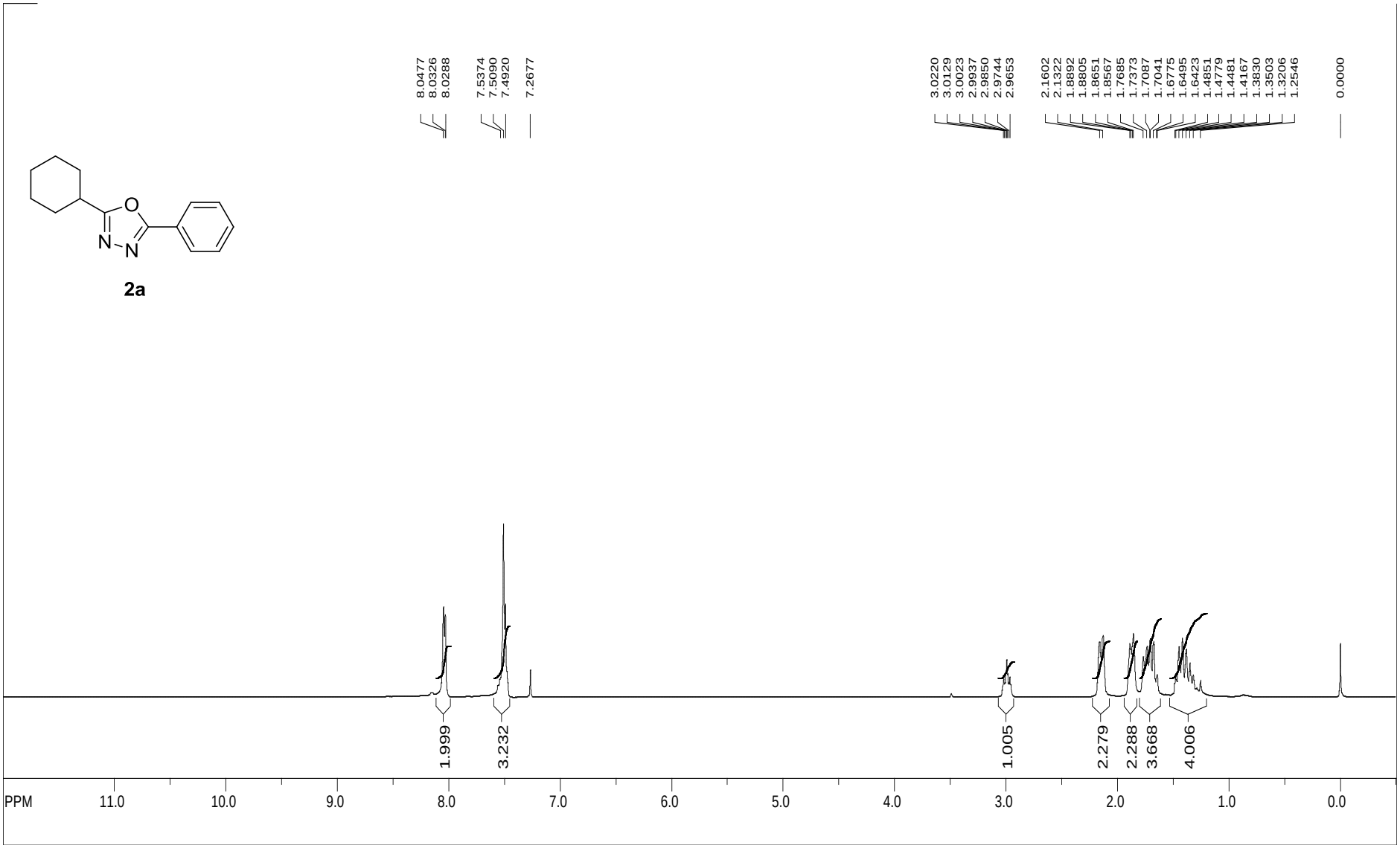

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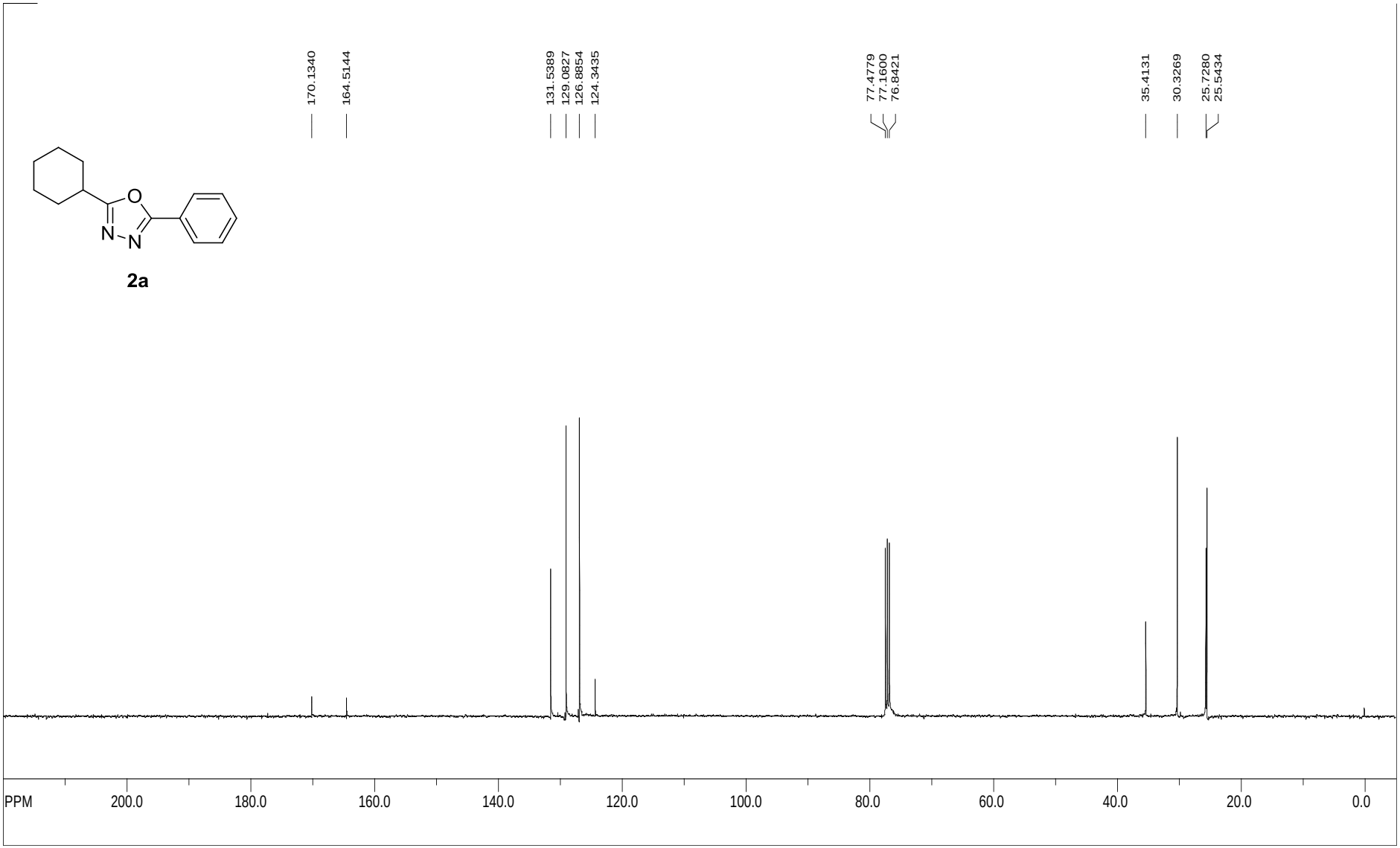

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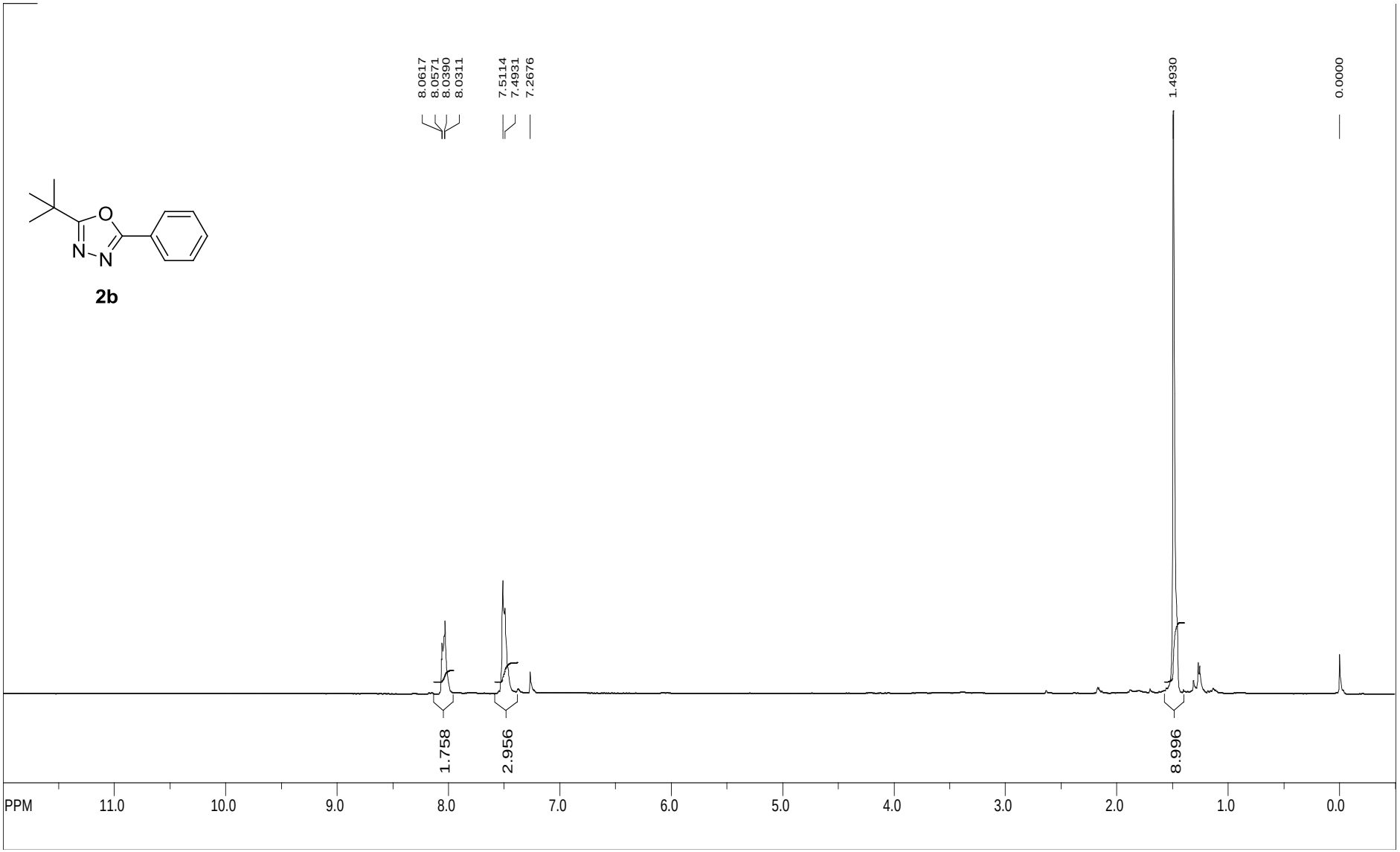

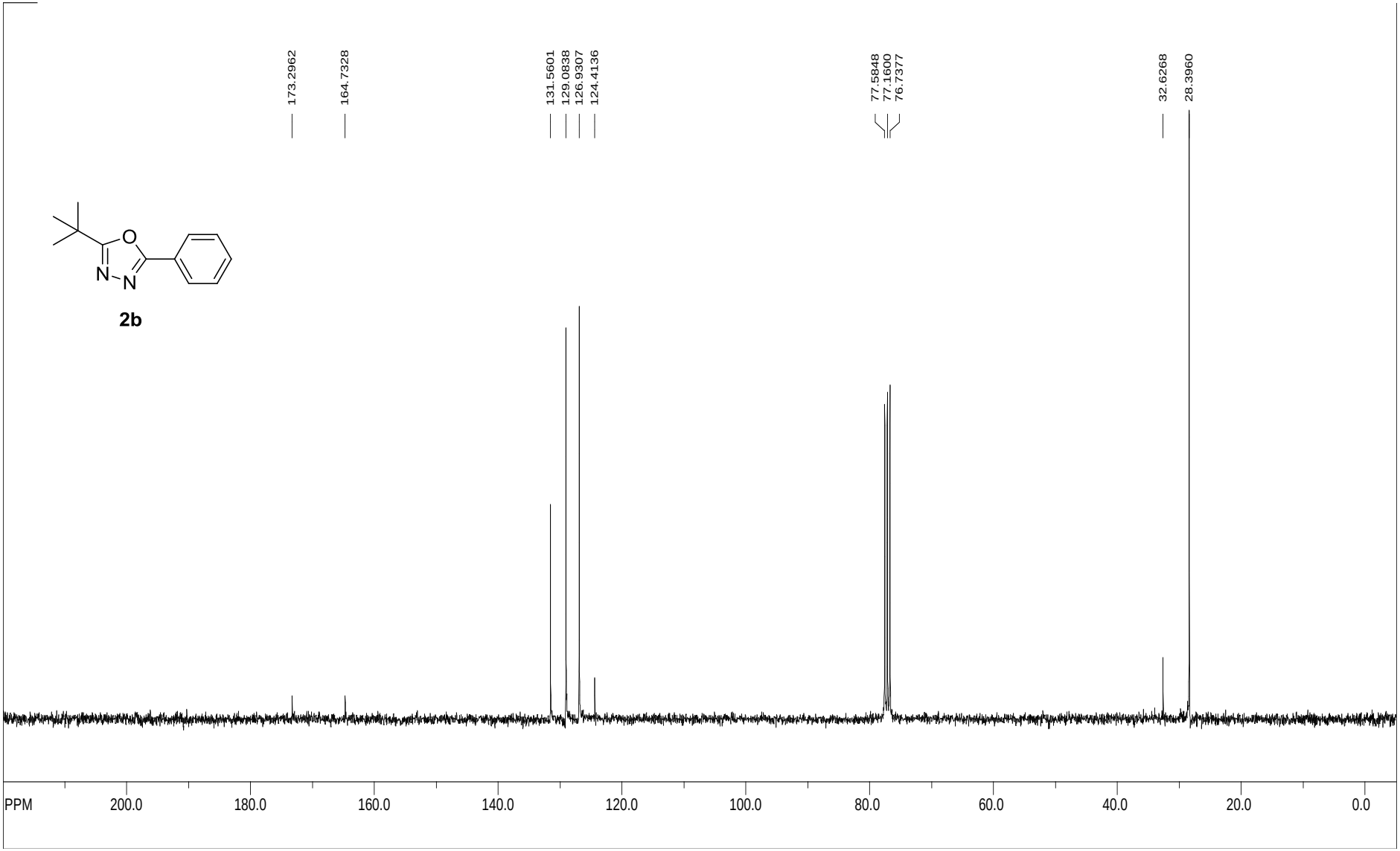

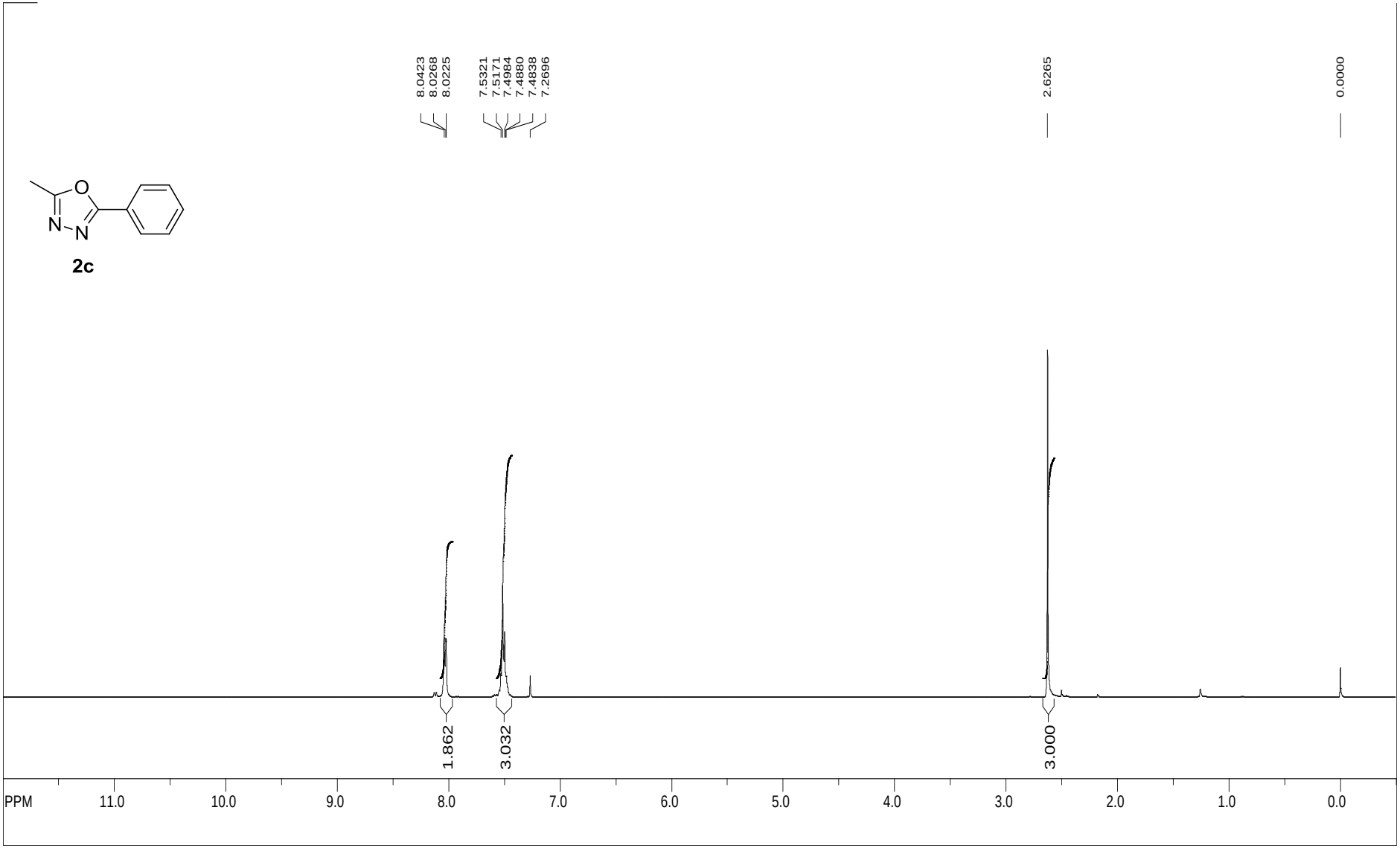

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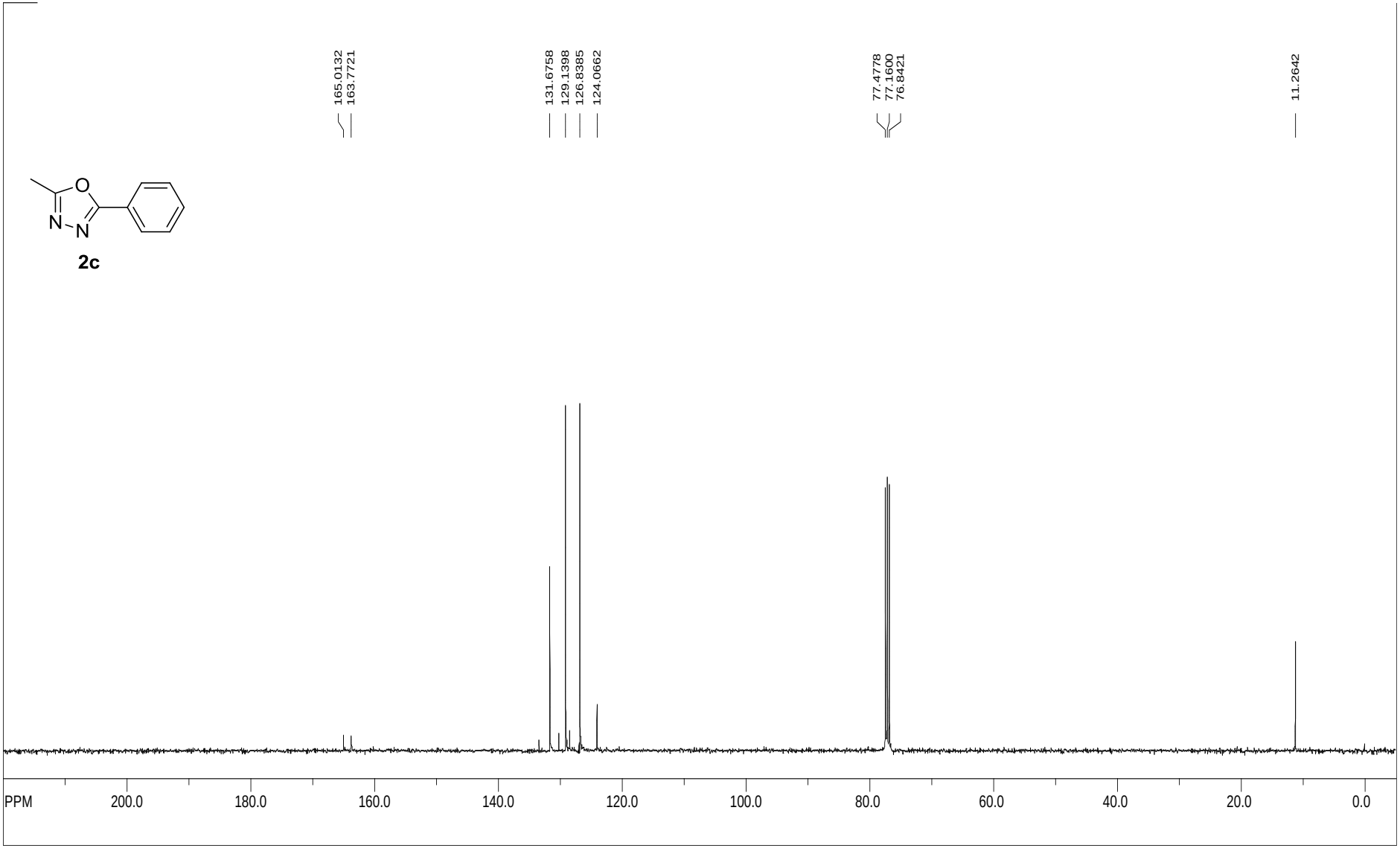

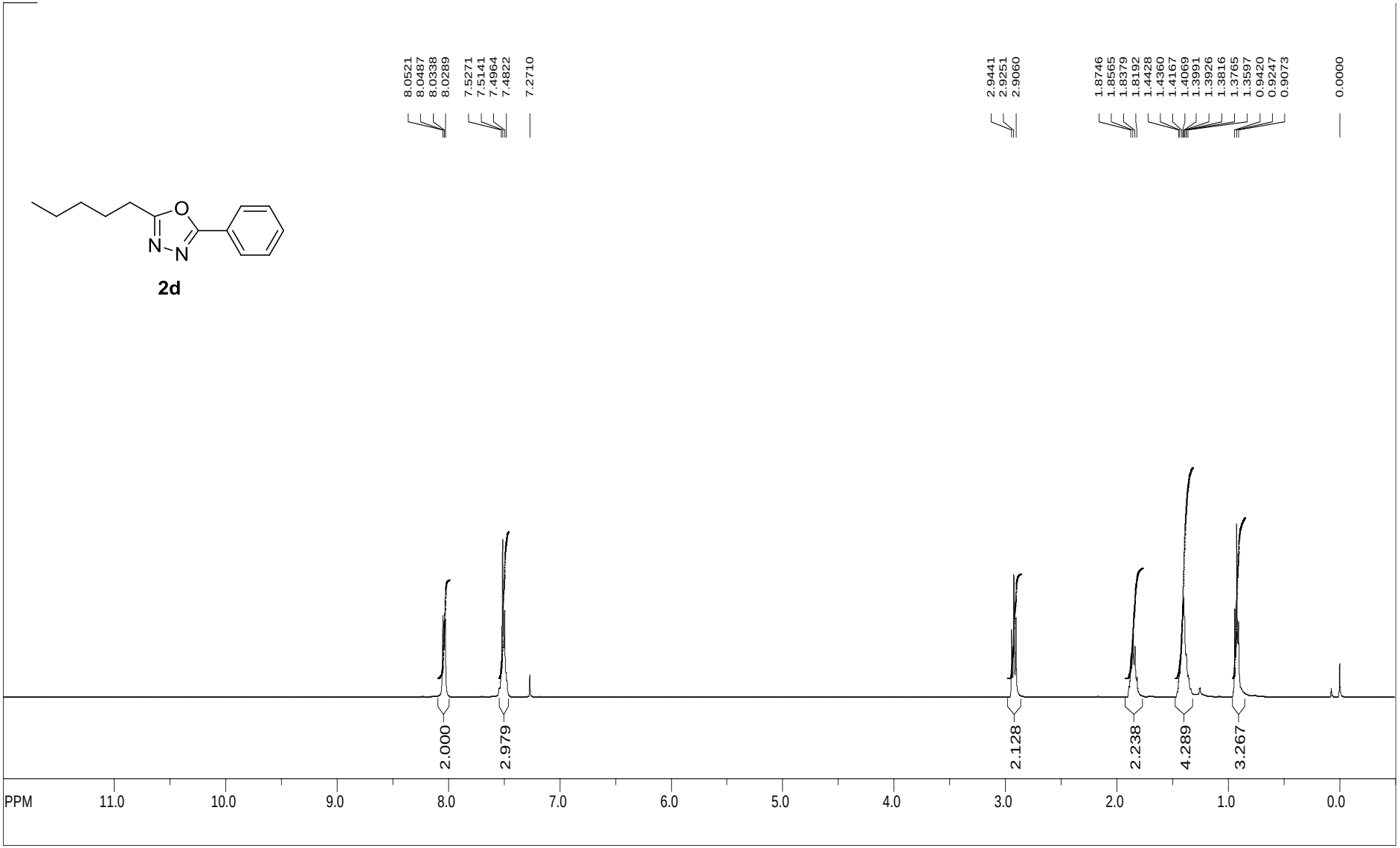

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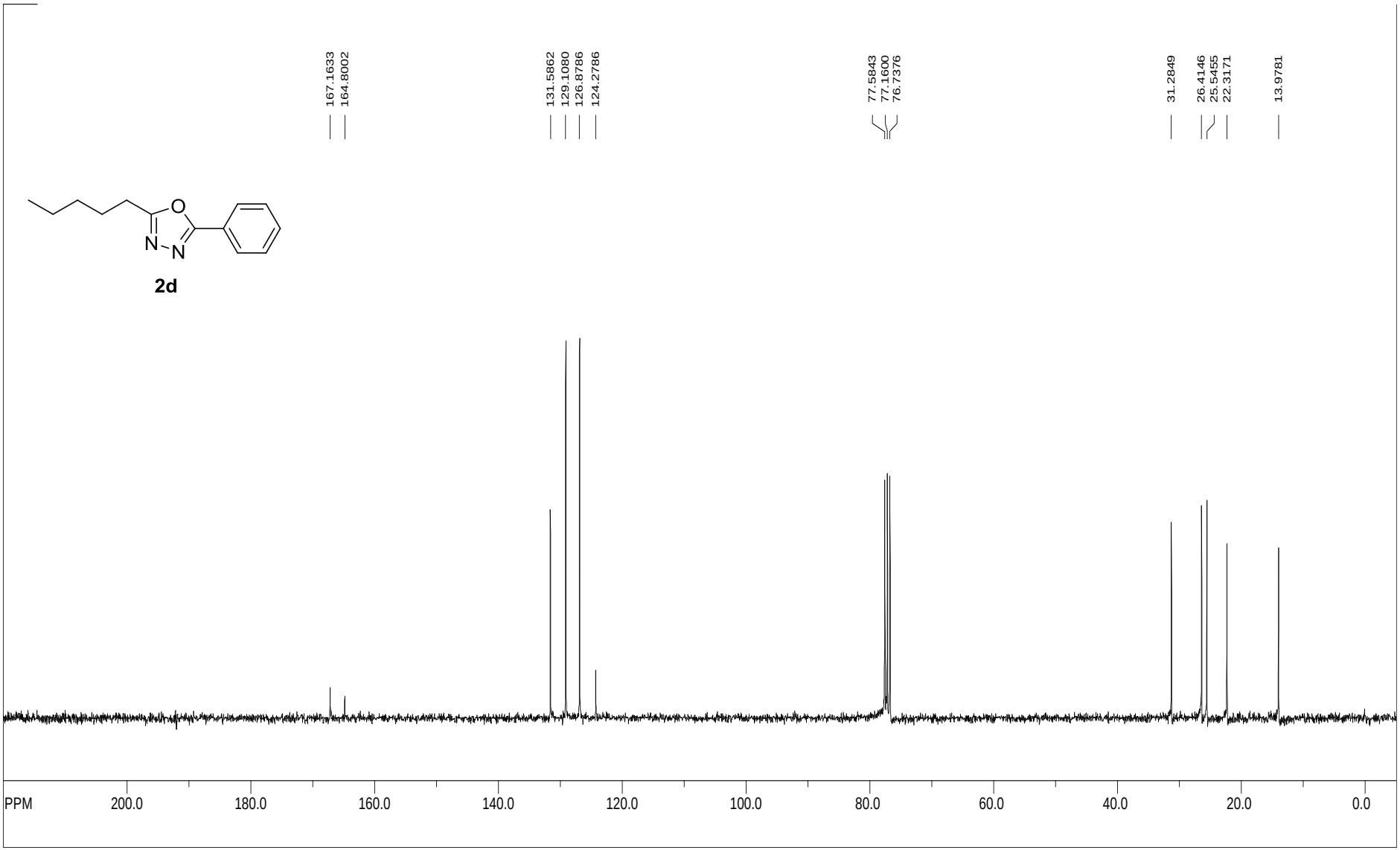

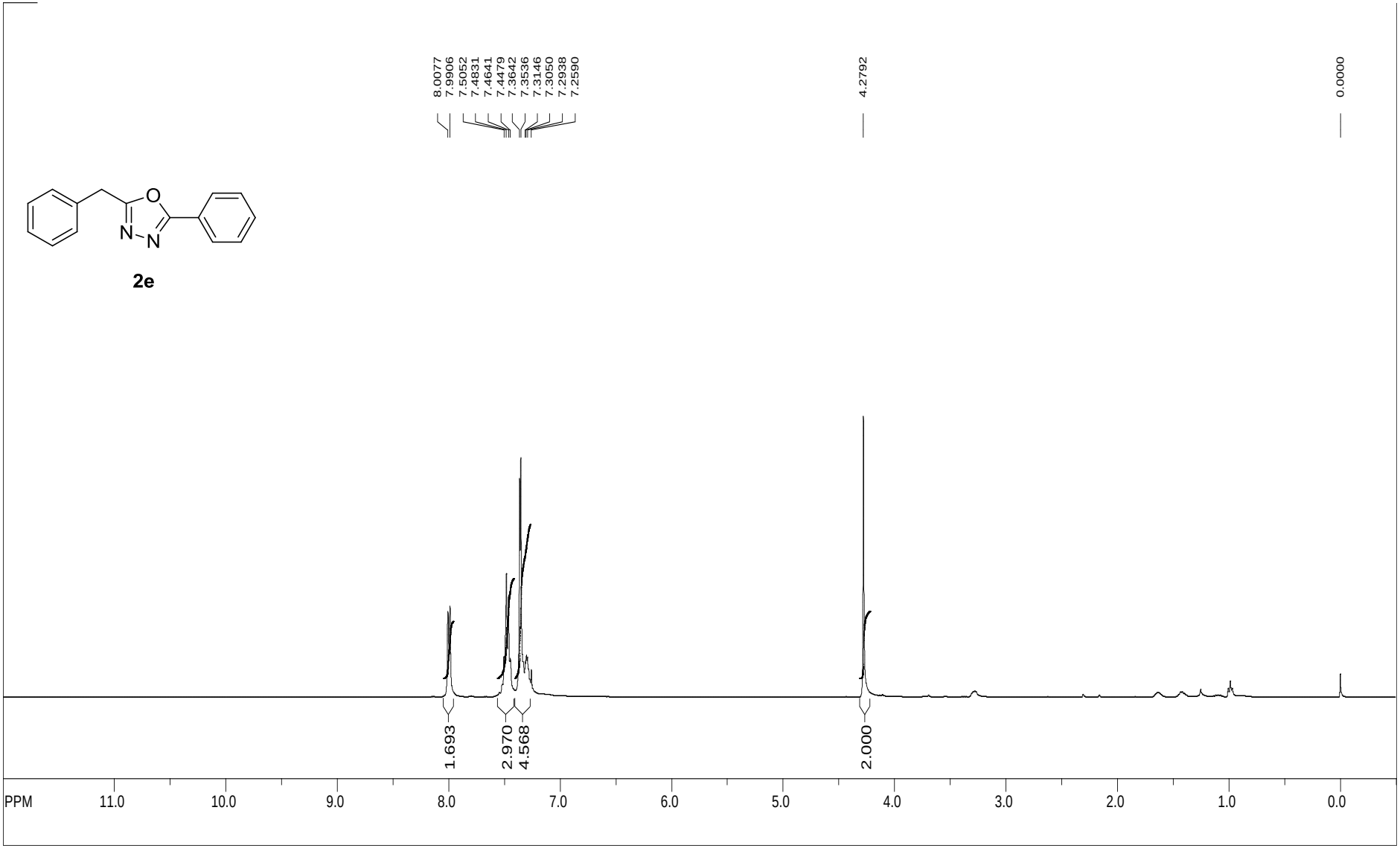

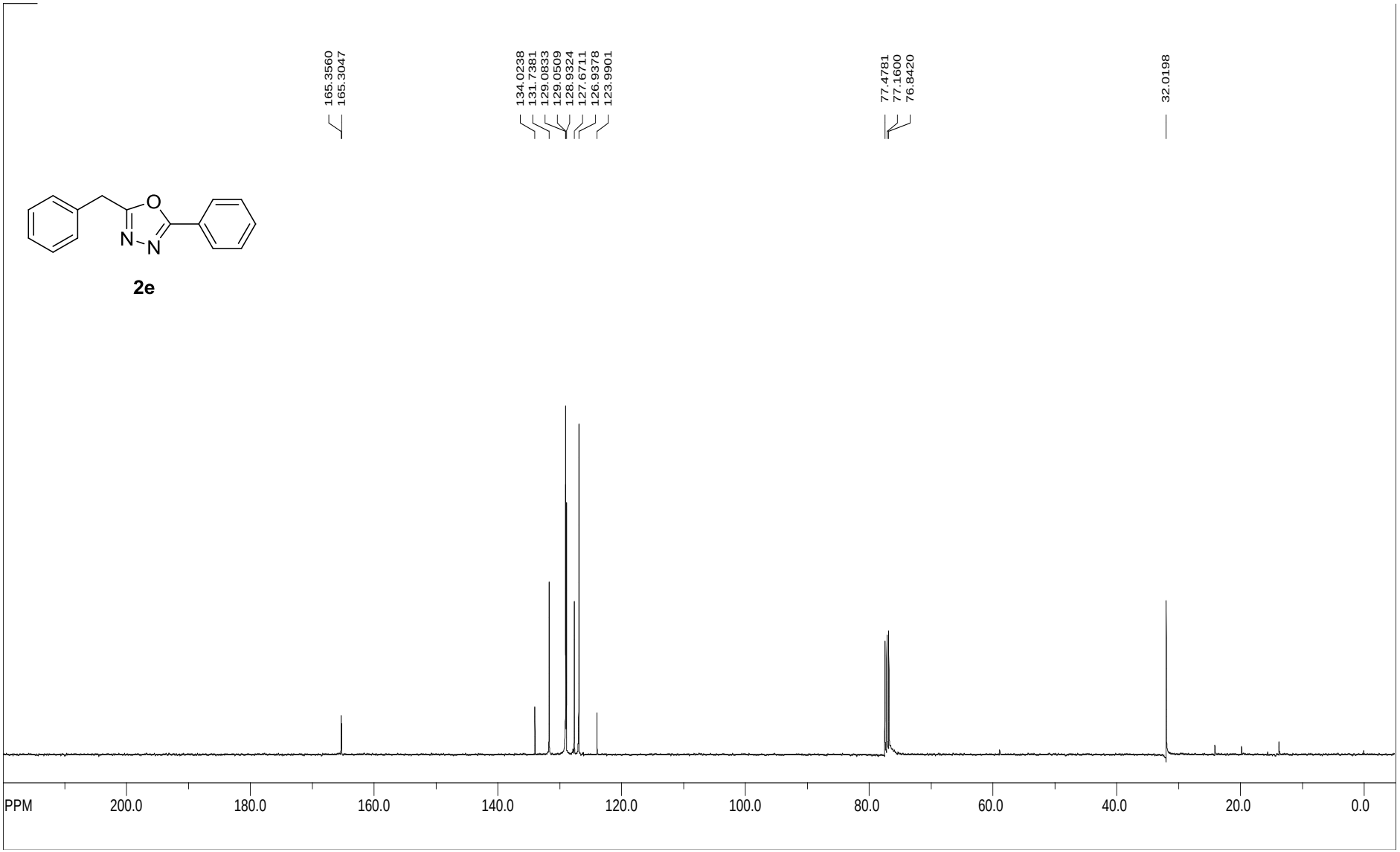

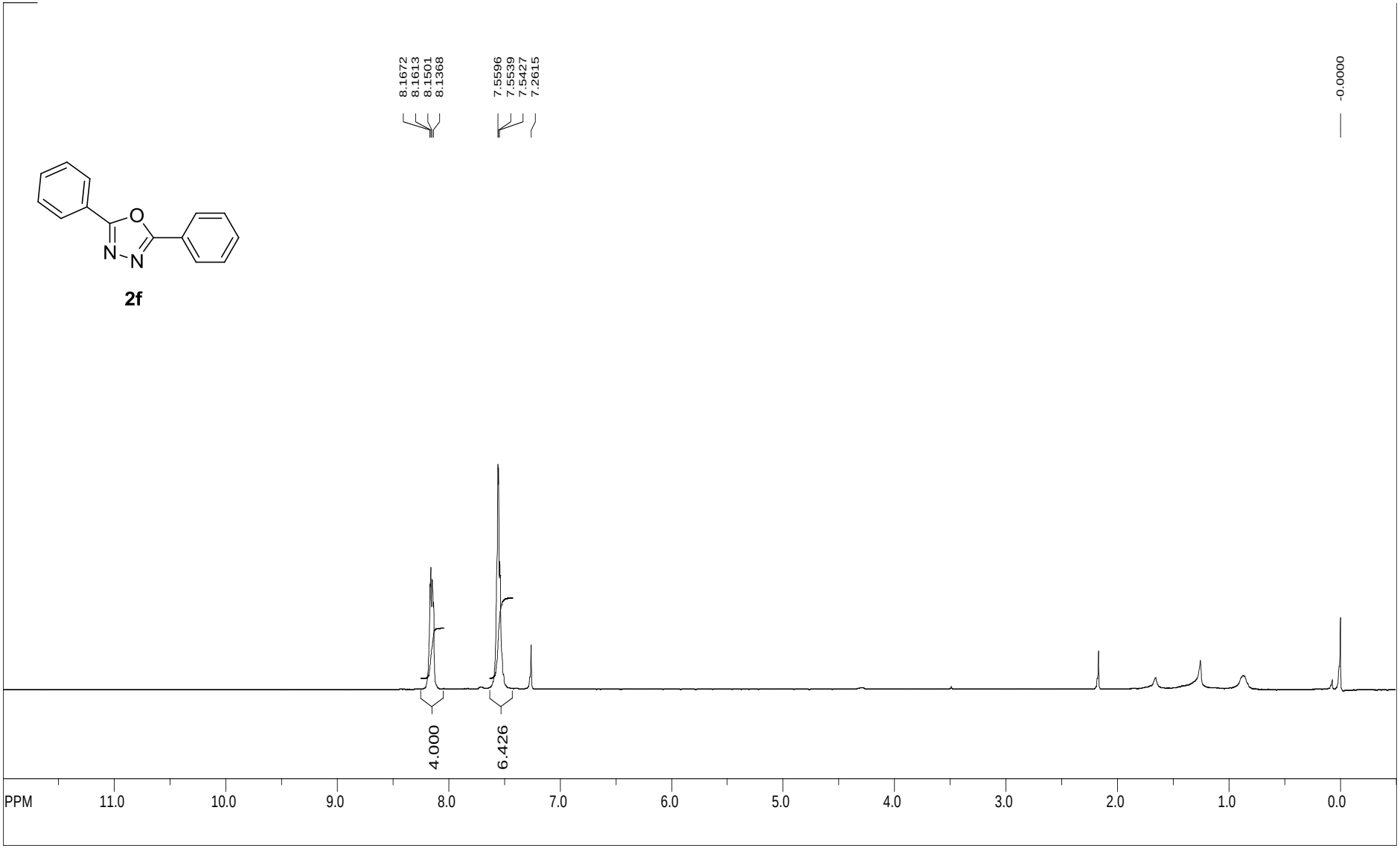

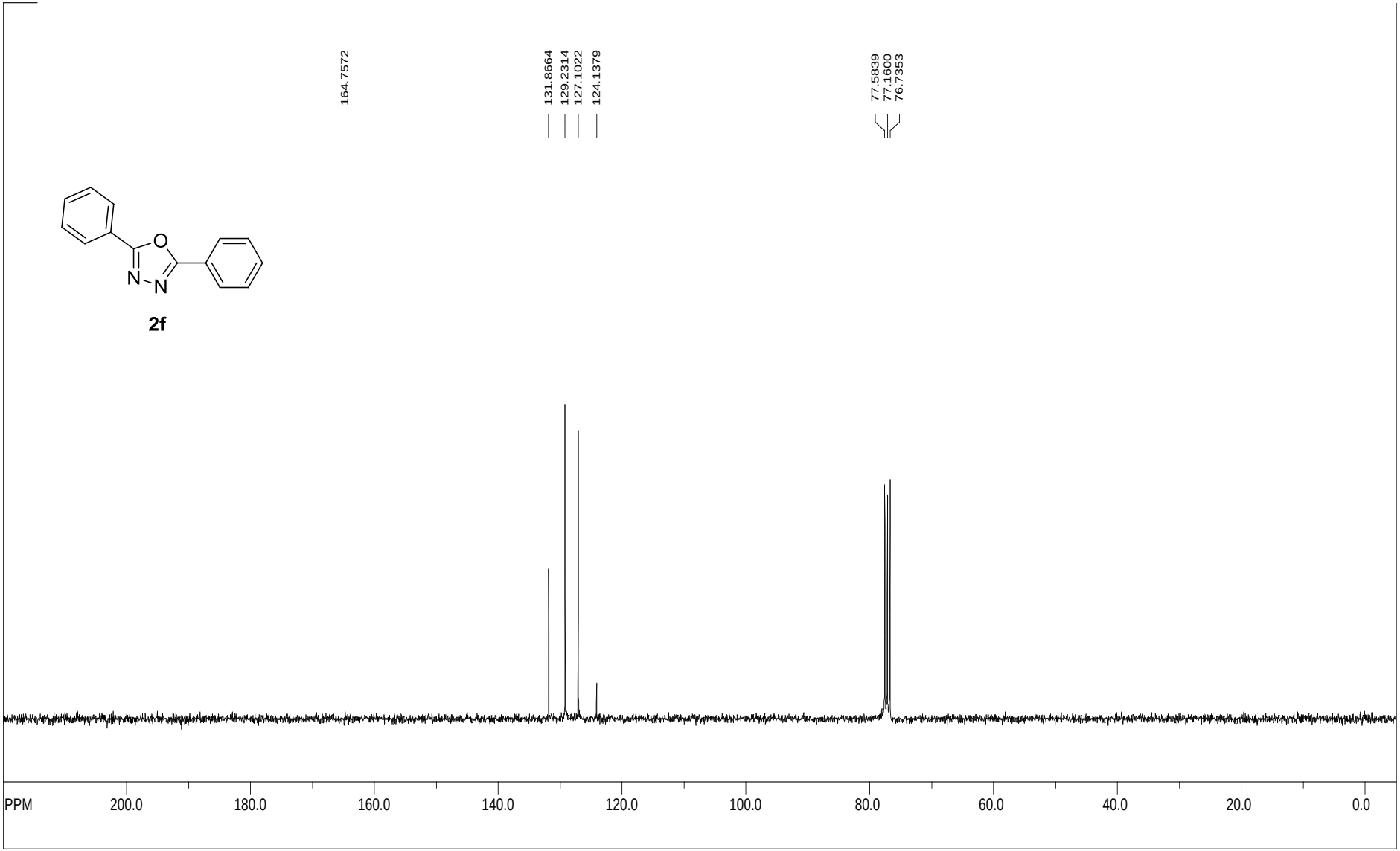

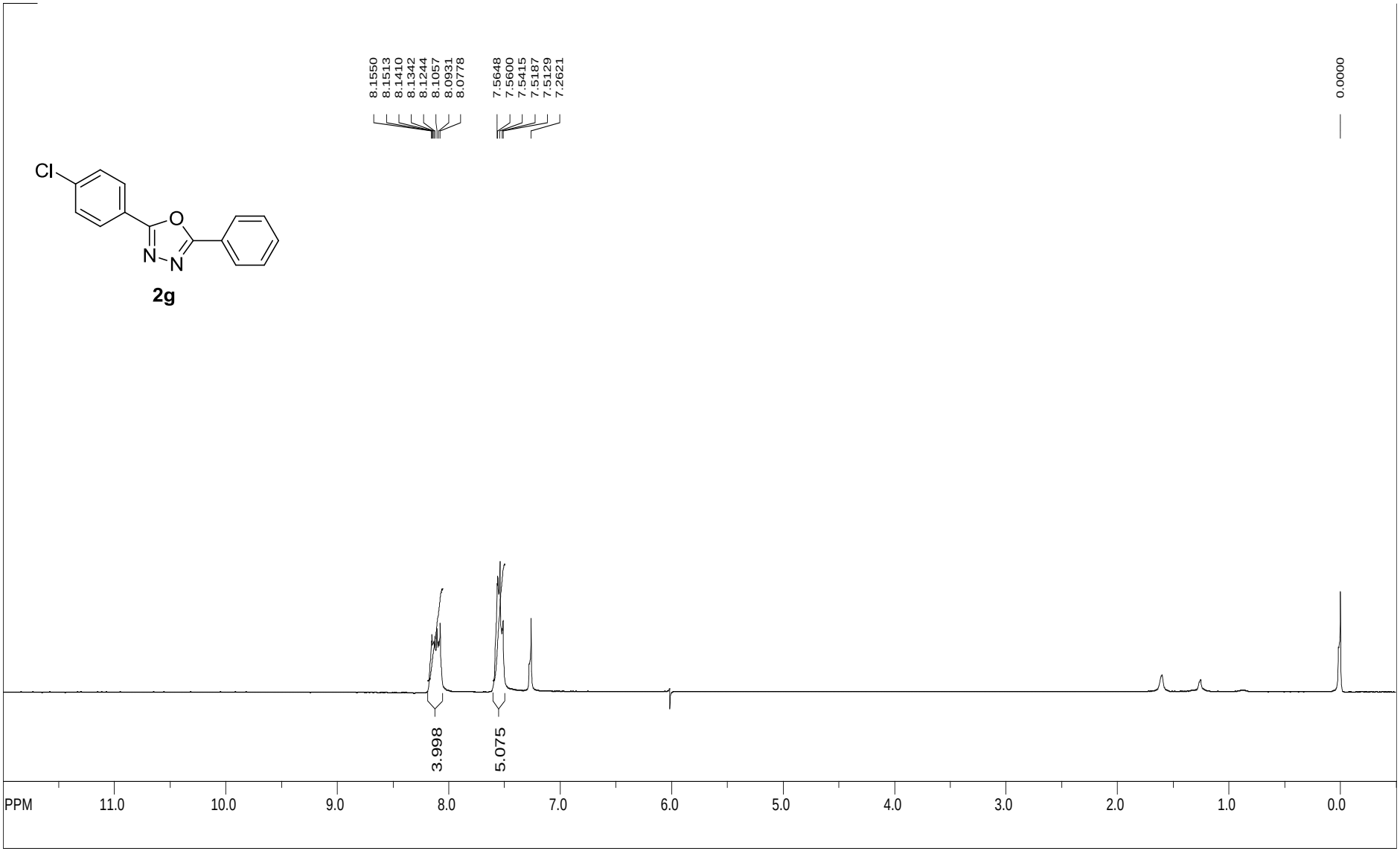

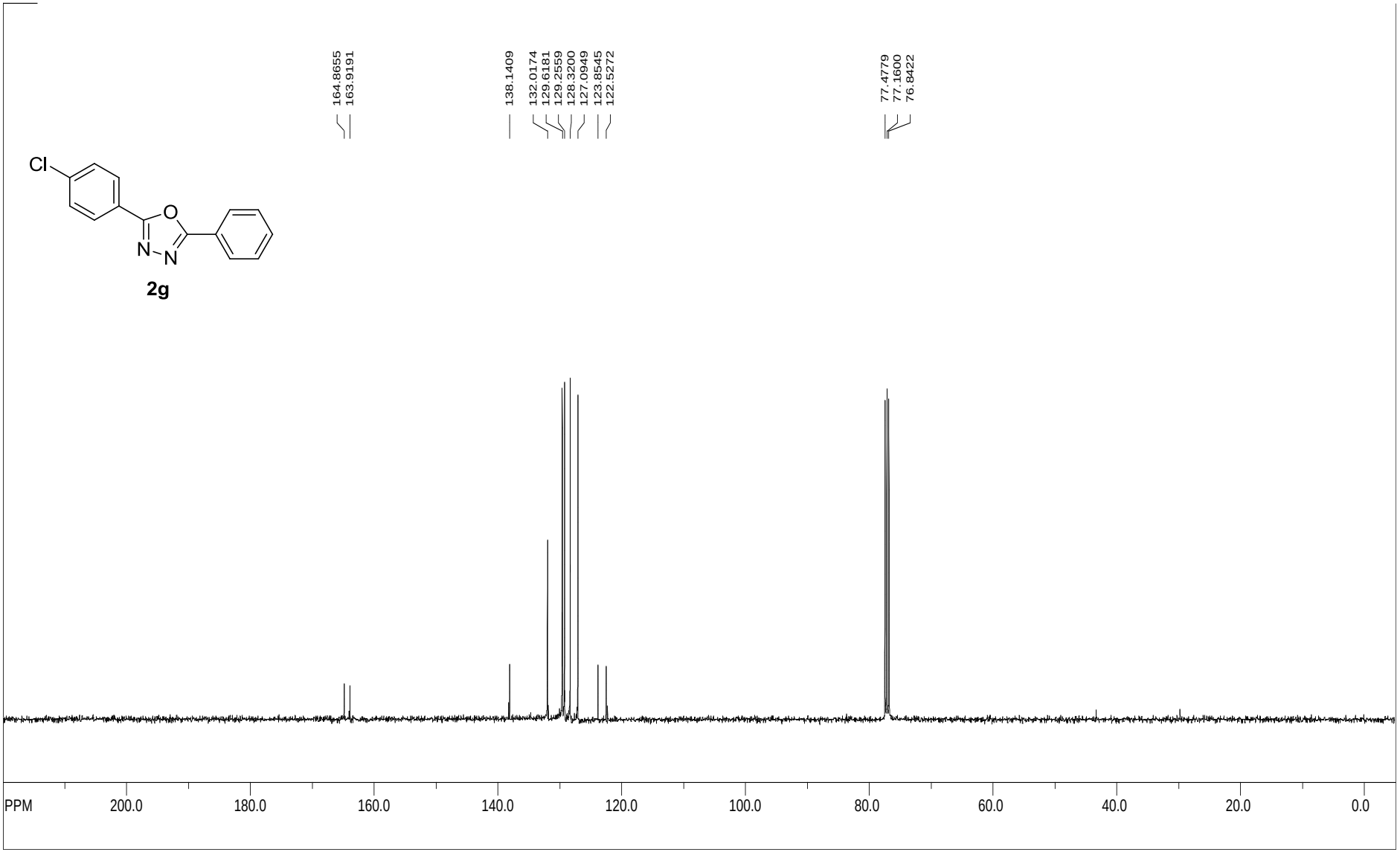

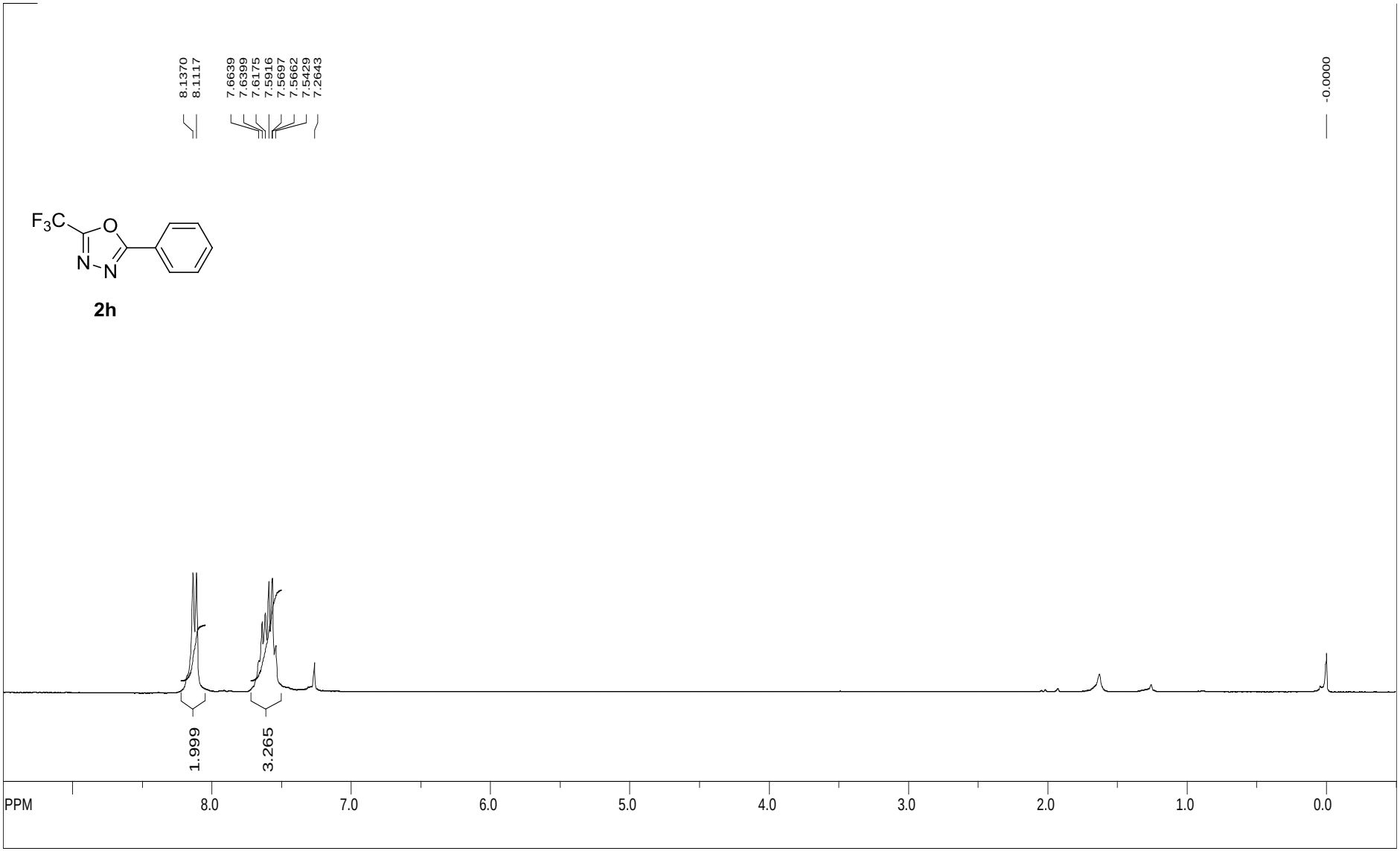

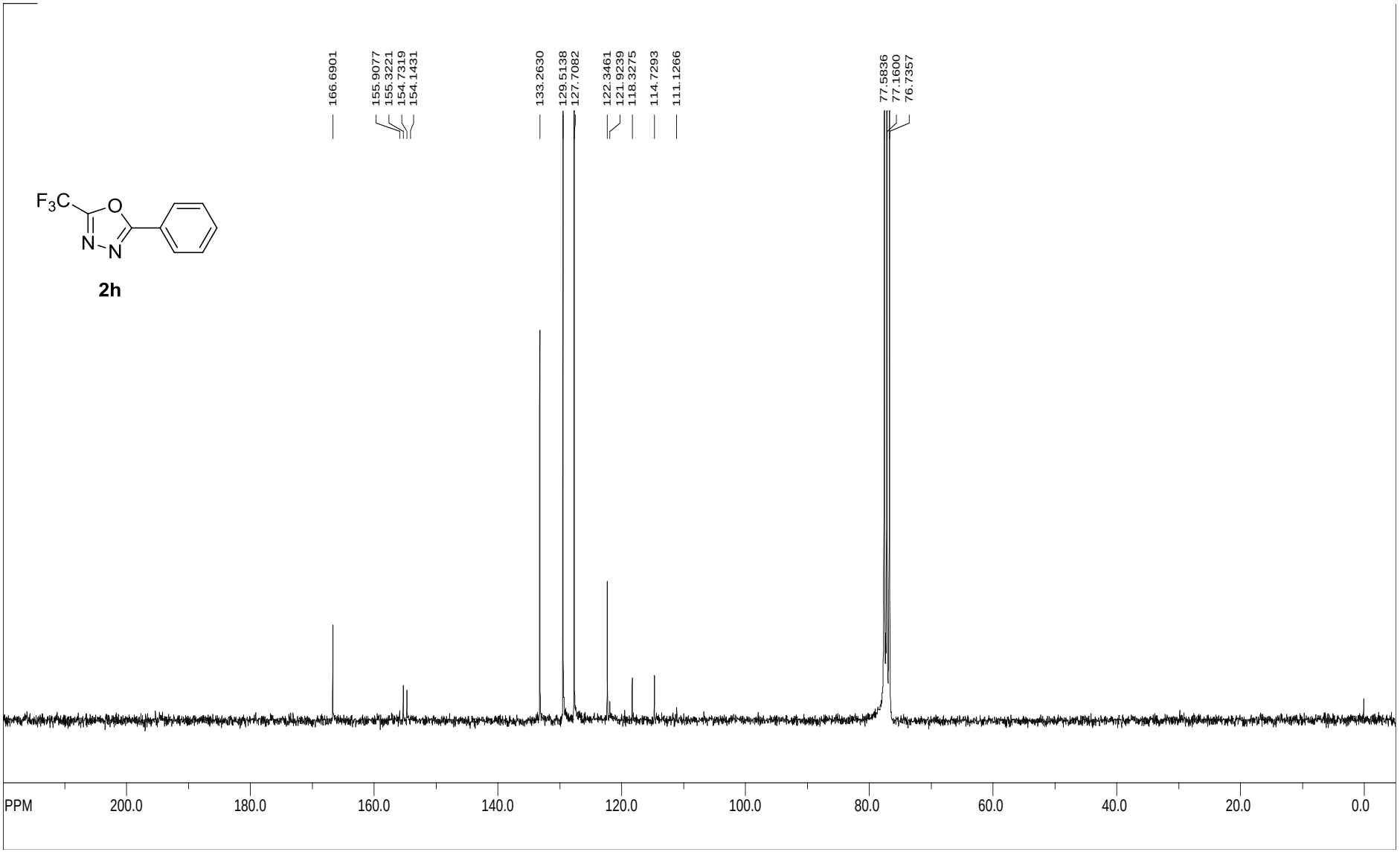

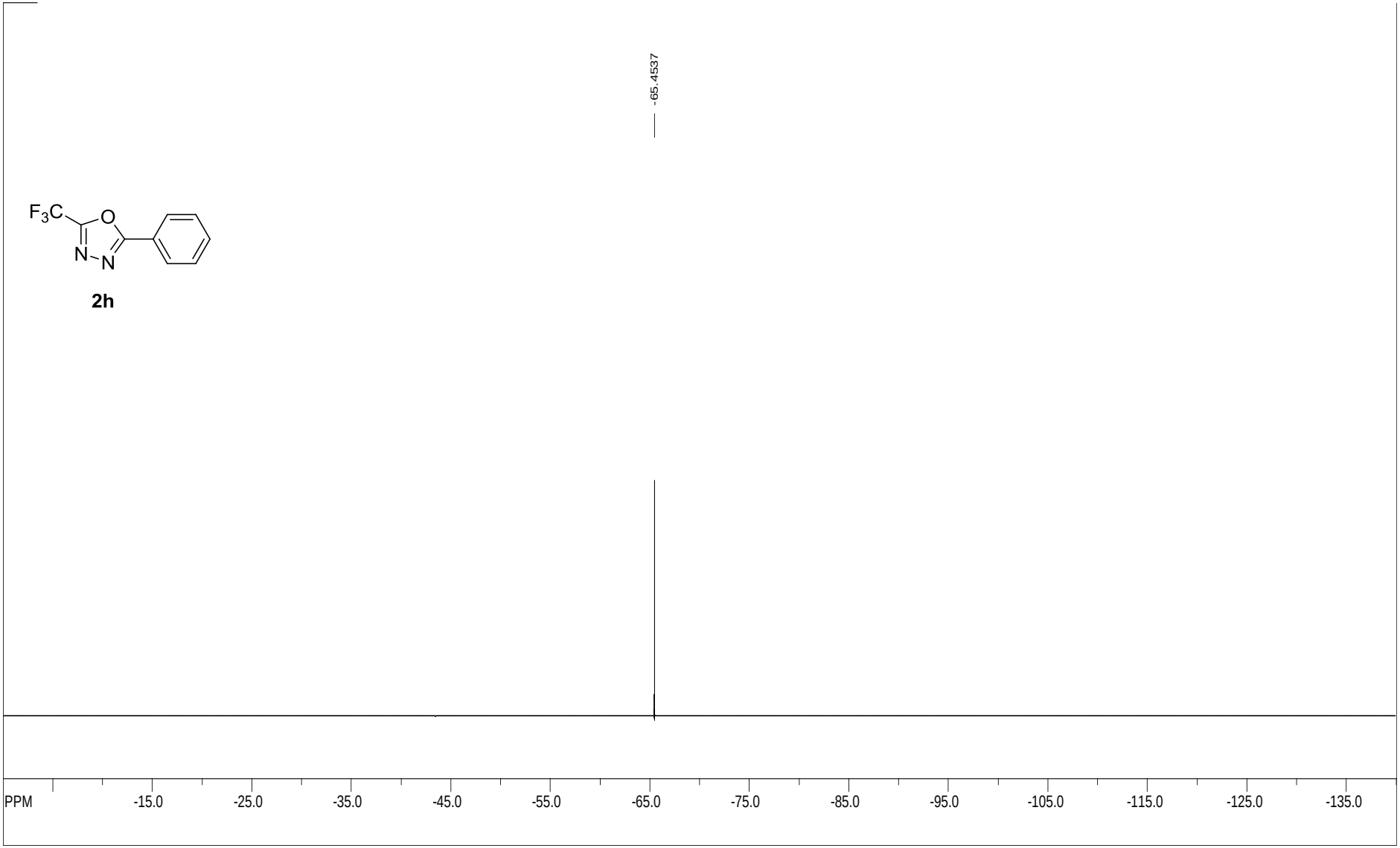

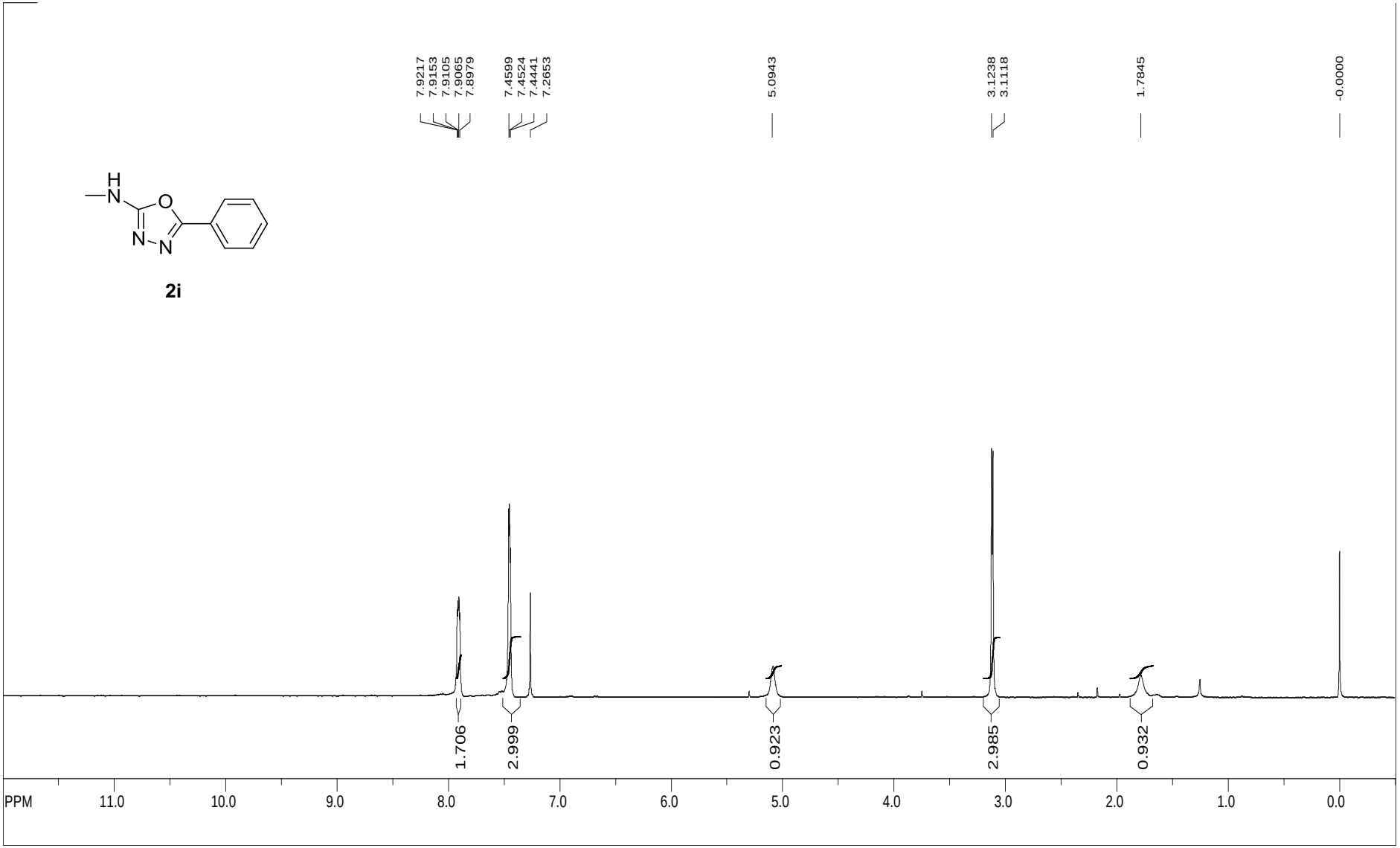

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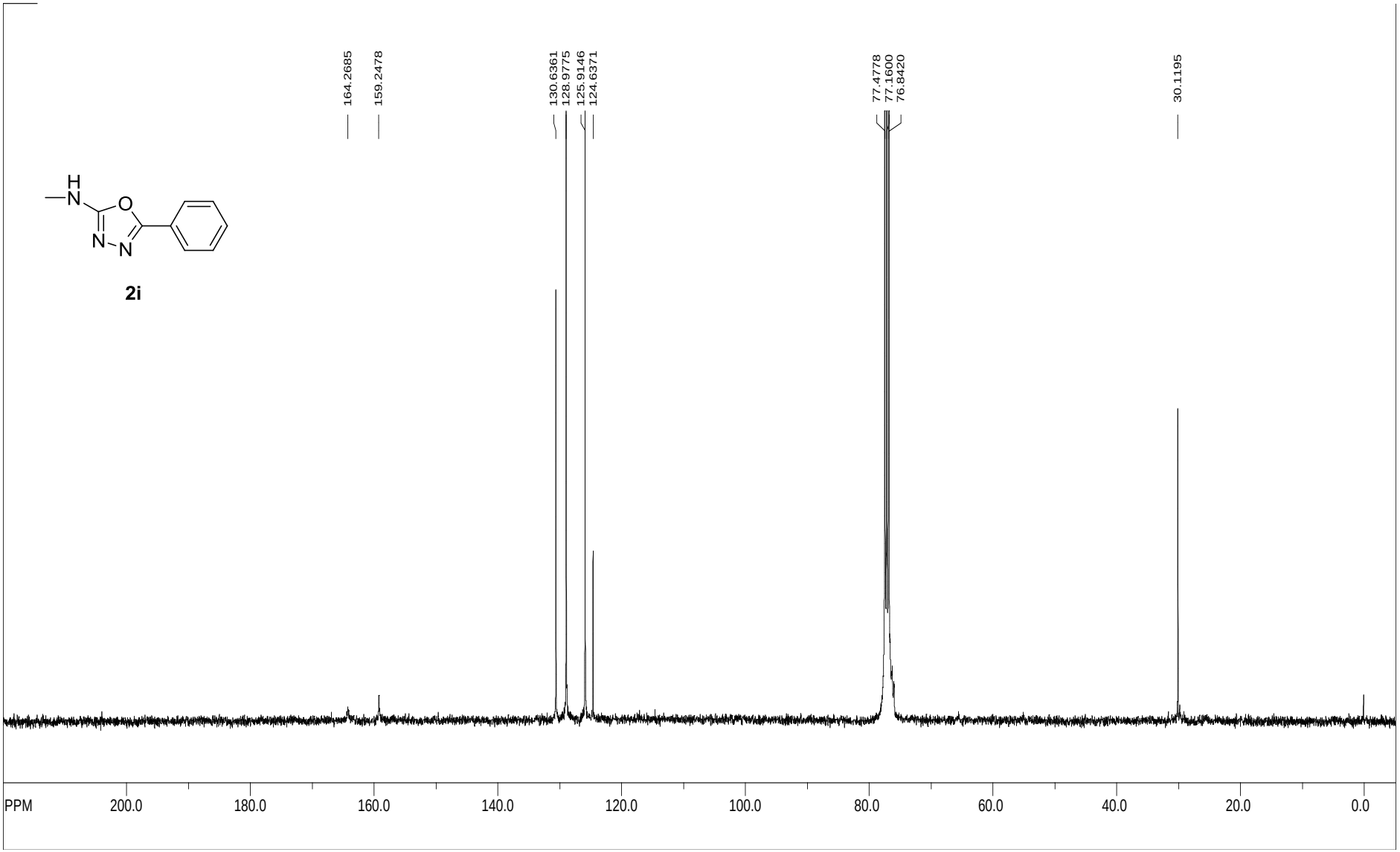

2i