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Supporting Information For

Copper-catalyzed Highly Diastereoselective Cross-Dehydrogenative Coupling between 8-Hydroxyisochromanes and 1,3-Dicarbonyl Compounds

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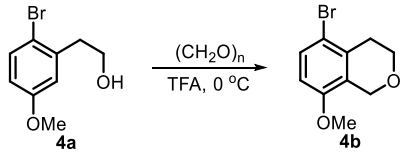
General Information:

All reactions under standard conditions were carried out under argon and monitored by thin-layer chromatography (TLC) on gel F254 plates. The silica gel (200-300 meshes) was used for column chromatography with light petroleum ether (b.p. 60~90 °C), dichloromethane and ethyl acetate used as eluents. All solvents were purified and dried by standard techniques and distilled prior to use. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on *Varian Mercury*-600MHz, *Bruker* AM-400 MHz or *Varian Mercury*-300 MHz instruments and the spectral data were reported in ppm relative to tetramethylsilane (0.00 ppm) or residual undeuterated solvent $CHCl_3$ (7.27 ppm) as internal standard for ^{1}H NMR and deuterated solvent $CDCl_3$ (77.0 ppm) as internal standard for ^{13}C NMR. The ratio of diastereoisomers was determined by ^{1}H NMR of the crude products. IR spectra were recorded on Nicolet FT-170SX spectrometer. The MS data were obtained with SHIMADZU GCMS-QP2010 SE by means of EI (70 eV) technique and signals were given in m/z with relative intensity (%) in brackets. High-resolution mass spectral analysis (HRMS) data were measured on a Bruker Daltonics APEXII 47e FT-ICR spectrometer by means of the ESI technique. The single crystal X-ray analysis was performed on an Agilent SuperNova Eos diffractometer. The substrates **4b**, **4c**, **4d**, and **1a** are known compounds. The substrates **4a** and **2a-2u** are commercially available.

1. Experimental details for substrates and products

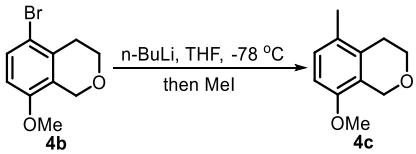
1.1 General procedure A: for the synthesis of 8-hydroxyisochromanes **1a-c**:



5-bromo-8-methoxyisochromane (4b)[1]:

To a mixture of paraformaldehyde (0.85 g, 4.4 mmol) in CF_3COOH (10 mL) which was stirred at 60 ℃ for 1.0 h was added 2-bromo-5-methoxyphenethyl alcohol **4a** (4.37 g, 19 mmol) dissolved in CF_3COOH (10 mL) dropwise carefully at 0 ℃. The resulting mixture was stirred at 0 °C for 2 h, and then concentrated in vacuo. Purification of the residue was diluted with water (10 mL) and extracted with dichloromethane (30 mL × 3). The organic layers were combined, washed with 2N NaOH (10 mL), H_2O (10 mL), and saturated brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by neutral silica gel column chromatography afforded the desired **4b** (2.57g, 56%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 6.99 (d, J = 8.8 Hz, 1H), 6.21 (d, J = 8.8 Hz, 1H), 4.31 (s, 2H), 3.55 (t, J = 5.8 Hz, 2H), 3.41 (s, 3H), 2.38 (t, J = 5.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 154.4, 133.9, 130.0, 126.1, 115.4, 108.7, 64.6, 64.1, 55.2, 29.1.

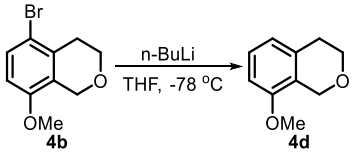


8-methoxy-5-methylisochromane (4c)[1]:

To a solution of 5-bromo-8-methoxyisochromane **4b** (1.07 g, 4.4 mmol) in dry THF (50 mL) at -78 °C was added 1.6M n-BuLi (4.4 mL, 6.6 mmol) under argon atmosphere. After the reaction

mixture was stirred at -78 °C for 2 h, the resulting solution was added MeI (0.42 mL, 5.3 mmol) and stirred at -78 °C for 4 h. The resulting solution was allowed to warm to room temperature and quenched by saturated aqueous NH_4Cl (5 mL) and H_2O (5 mL). The resulting mixture was extracted with ethyl acetate (20 mL × 3), washed with brine (5 mL), dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by neutral silica gel column chromatography afforded the desired **4c** (0.51 g, 65%) as a white solid.

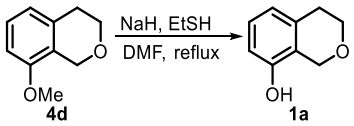
^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.15 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 4.81 (s, 2H), 3.87 (s, 3H), 3.69-3.64 (m, 2H), 3.26-3.21 (m, 2H), 2.32 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 156.2, 136.6, 131.8, 129.0, 124.8, 109.7, 55.9, 42.7, 38.0, 33.0, 19.2.



8-methoxyisochromane (4d)[1]:

To a solution of 5-bromo-8-methoxyisochromane **4b** (1.57 g, 6.5 mmol) in dry THF (50 mL) at -78 °C was added 1.6M n-BuLi (6.1 mL, 9.8 mmol) under argon atmosphere. After the reaction mixture was stirred at -78 °C for 4 h, the resulting solution was allowed to warm to room temperature and quenched by saturated aqueous NH_4Cl (5 mL) and H_2O (5 mL). The resulting mixture was extracted with ethyl acetate (20 mL × 3), washed with brine (5 mL), dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by neutral silica gel column chromatography afforded the desired **4d** (0.96 g, 90%) as a white solid.

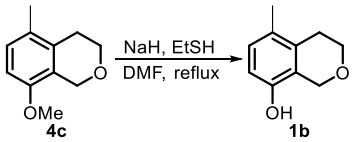
^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.19 (t, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.80 (s, 2H), 3.97 (t, *J* = 5.6 Hz, 2H), 3.84 (s, 3H), 2.87 (t, *J* = 5.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 155.2, 134.5, 126.7, 123.4, 120.8, 107.0, 64.6, 64.2, 54.9, 28.1.



isochroman-8-ol (1a)[2]:

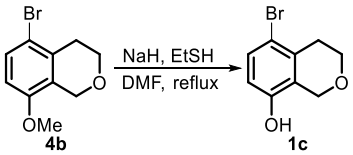
To a solution of NaH (0.5 g, 10.1 mmol) in dry DMF (20 mL) at 0 °C was added EtSH (0.91 mL, 10.1 mmol) dropwise carefully under argon atmosphere. After the mixture was stirred at 0 ℃ for 1.0 h, the solution was added 8-methoxyisochromane **4d** (1.1 g, 6.7 mmol) dissolved in dry DMF (10 mL) dropwise at 0 ℃. After the mixture was refluxed over 8 h, the resulting solution was allowed to cool to room temperature and quenched by H_2O (5 mL). The resulting mixture was added 4M HCl to adjust effectively pH within 1~2, extracted with ethyl ether (50 mL × 3), washed with H_2O (5 mL × 7), dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by neutral silica gel column chromatography afforded the desired **1a** (0.76 g, 76%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.46 (t, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.30 (s, 2H), 4.44 (t, *J* = 5.6 Hz, 2H), 3.29 (t, *J* = 5.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 151.9, 134.6, 127.0, 121.5, 120.6, 112.1, 64.9, 64.3, 28.1.



5-methylisochroman-8-ol (1b):

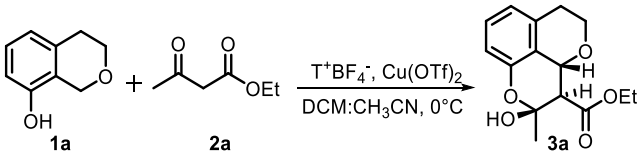
Prepared according to general procedure of **1a** to afford **1b** (73% yield) as a white solid. **mp**: 126-128 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 6.91 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 6.21 (s, 1H), 4.86 (s, 2H), 4.04 (t, *J* = 5.8 Hz, 2H), 2.71 (t, *J* = 5.8 Hz, 2H), 2.17 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 149.7, 132.9, 127.8 (2C), 121.6, 111.7, 64.9, 64.5, 26.2, 18.0; **MS** (EI) *m/z* (%) 164 (100), 149 (97), 134 (92), 91 (89); **HRMS** (ESI) Calcd. for $C_{10}H_{12}O_2$ $(M+Na)^+$: 187.0730, Found 187.0725.



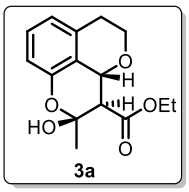
5-bromoisochroman-8-ol (1c):

Prepared according to general procedure of **1a** to afford **1c** (78% yield) as a white solid. **mp**: 126-128 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.26 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 8.4 Hz, 1H), 6.06 (brs, 1H), 4.76 (s, 2H), 3.99 (t, *J* = 5.8 Hz, 2H), 2.78 (t, *J* = 5.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 150.7, 134.3, 130.2, 124.5, 115.3, 113.7, 64.9, 64.1, 29.2; **IR** (neat) 3200, 1583, 1443, 1327, 1092, 799 cm^{-1}; **MS** (EI) *m/z* (%) 230 (14), 228 (13), 200 (9), 198 (8), 149 (100), 91 (45); **HRMS** (ESI) Calcd. for $C_9H_9BrO_2$ $(M+H)^+$: 228.9859, Found 228.9862.

1.2 General procedure B: Substrate scope of 8-hydroxyisochromanes **1a-1c** and 1,3-dicarbonyl compounds **2a-2u**:



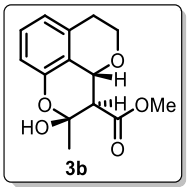
8-hydroxyisochromane **1a** (0.1 mmol) was dissolved in 0.5 mL of CH_2Cl_2 under argon atmosphere followed by addition of $T^+BF_4^-$ (0.11 mmol) at room temperature. The reaction mixture was stirred at room temperature and monitored by TLC. After the complete consumption of **1a**, the reaction mixture was cooled to 0 ºC and then added with **2a** (0.12 mmol), $Cu(OTf)_2$ (10%) and the additive solvent CH_3CN (1.5 mL). The reaction mixture was stirred at 0 ºC and monitored by TLC. After the complete consumption, the system was quenched by Et_3N (100 μL) and concentrated in vacuo. Purification of the residue by neutral silica gel column chromatography afforded the desired product **3a** (95% yield) as a colorless oil.



ethyl-2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3a):

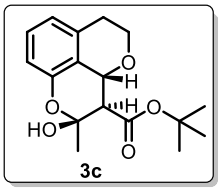
^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.03 (d, *J* = 11.2 Hz, 1H), 4.42-4.31 (m, 1H), 4.31-4.23 (m, 2H), 4.02 (dt, *J* = 11.4, 4.8 Hz, 1H), 3.12-3.04 (m, 1H), 2.88 (d, *J* = 11.6 Hz, 1H), 2.79 (dd, *J* = 17.2, 4.8 Hz, 1H), 1.67 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$, ppm): δ 172.6, 149.6, 133.2, 128.6, 121.0,

119.3, 113.5, 97.3, 70.2, 65.8, 61.8, 52.4, 28.0, 27.5, 14.2; **IR** (neat) 3440, 2930, 1730, 1465, 1259, 1179, 1094, 737 cm^{-1}; **MS** (EI) *m/z* (%) 278 (1), 235 (2), 187 (9), 148 (100), 91 (15); **HRMS** (ESI) Calcd. for $C_{15}H_{18}O_5$ $(M+Na)^+$: 301.1046, Found 301.1048.



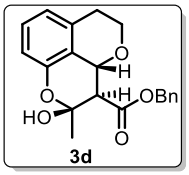
methyl-2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3b):

Prepared according to general procedure B from **2b** to afford **3b** (22.5 mg, 85% yield) as a white solid. **mp**: 137-140 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.03 (d, *J* = 11.6 Hz, 1H), 4.25 (dt, *J* = 10.4, 7.2 Hz, 1H), 4.04-3.97 (m, 1H), 3.87 (s, 3H), 3.80 (s, 1H), 3.13-3.03 (m, 1H), 2.89 (d, *J* = 11.6 Hz, 1H), 2.78 (dd, *J* = 17.0, 3.8 Hz, 1H), 1.65 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 173.1, 149.6, 133.2, 128.6, 121.1, 119.2, 113.5, 97.2, 70.2, 65.9, 52.7, 52.2, 28.0, 27.4; **IR** (neat) 3411, 2922, 1725, 1465, 1261, 1093, 737 cm^{-1}; **MS** (EI) *m/z* (%) 264 (1), 221 (2), 187 (6), 148 (100), 91 (21); **HRMS** (ESI) Calcd. for $C_{14}H_{16}O_5$ $(M+Na)^+$: 287.0890, Found 287.0898.



tert-butyl-2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3c):

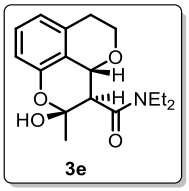
Prepared according to general procedure B from **2c** to afford **3c** (26.1 mg, 85% yield, d.r. = 11.1:1) as a white solid. **mp**: 131-134 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.12 (t, *J* = 7.8 Hz, 1H), 6.74 (d, *J* = 6.8 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 4.96 (d, *J* = 11.6 Hz, 1H), 4.29-4.23 (m, 1H), 4.09 (s, 1H), 4.00 (dt, *J* = 16.4, 4.8 Hz, 1H), 3.13-3.03 (m, 1H), 2.78-2.74 (m, 2H), 1.65 (s, 3H), 1.55 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$, ppm): δ 172.3, 149.7, 133.1, 128.5, 120.9, 119.5, 113.5, 97.4, 82.8, 70.5, 65.8, 52.9, 28.1, 28.0, 27.7, 27.5; **IR** (neat) 3437, 2927, 1723, 1465, 1260, 1156, 737 cm^{-1}; **MS** (EI) *m/z* (%) 306 (1), 250 (3), 187 (5), 148 (88), 91 (7), 57 (14) ; **HRMS** (ESI) Calcd. for $C_{17}H_{22}O_5$ $(M+Na)^+$: 329.1359, Found 329.1370.



benzyl-2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3d):

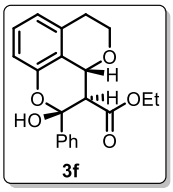
Prepared according to general procedure B **2d** to afford **3d** (28.9 mg, 85% yield, d.r. = 11.1:1) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.44-7.34 (m, 5H), 7.14 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.41 (d, *J* = 12.4 Hz, 1H), 5.23 (d, *J* = 12.0 Hz, 1H), 5.06 (d, *J* = 11.6 Hz, 1H), 4.27 (dd, *J* = 7.2, 1.6 Hz, 1H), 4.24 (dd, *J* = 7.2, 1.6 Hz, 1H), 4.00 (dd, *J*

= 11.4, 6.6 Hz, 1H), 3.67 (s, 1H), 3.09-3.05 (m, 1H), 2.93 (d, *J* = 11.6 Hz, 1H), 2.78 (dd, *J* = 17.2, 4.4 Hz, 1H), 1.57 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 172.3, 149.5, 135.3, 133.2, 128.6, 128.6, 128.4, 128.3, 121.1, 119.2, 113.5, 97.3, 70.2, 67.4, 65.8, 52.3, 28.0, 27.4; **IR** (neat) 3421, 2926, 1734, 1465, 1260, 1174, 1094, 737 cm^{-1}; **MS** (EI) *m/z* (%) 340 (1), 296 (4), 187 (10), 148 (100), 91 (83); **HRMS** (ESI) Calcd. for $C_{20}H_{20}O_5$ $(M+Na)^+$: 363.1203, Found 363.1198.



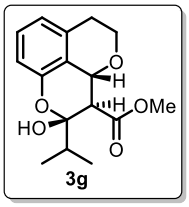
***N,N*-diethyl-2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxamide (3e)**:

Prepared according to general procedure B from **2e** to afford **3e** (27.8 mg, 91% yield) as a white solid. **mp**: 136-138 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$, ppm): δ 7.13 (t, *J* = 8.1 Hz, 1H), 6.74-6.72 (m, 2H), 6.44 (s, 1H), 4.96 (d, *J* = 11.4 Hz, 1H), 4.21-4.17 (m, 1H), 3.65 (dt, *J* = 15.0, 7.8 Hz, 1H), 3.56 (dt, *J* = 14.4, 7.2 Hz, 1H), 3.44 (dt, *J* = 13.8, 6.6 Hz, 1H), 3.28 (dt, *J* = 15.0, 7.2 Hz, 1H), 3.10 (d, *J* = 7.6 Hz, 1H), 2.76 (dd, *J* = 11.2, 4.8 Hz, 1H), 1.56 (s, 3H), 1.23-1.20 (m, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$, ppm): δ 172.7, 150.0, 133.1, 128.6, 120.8, 119.8, 113.7, 97.9, 71.5, 65.8, 47.0, 42.6, 41.5, 27.8, 27.5, 14.5, 13.0; **IR** (neat) 3364, 2922, 1593, 1097 cm^{-1}; **MS** (EI) *m/z* (%) 305 (1), 223 (6), 148 (100), 91 (98); **HRMS** (ESI) Calcd. for $C_{17}H_{23}NO_4$ $(M+Na)^+$: 328.1519, Found 328.1520.



ethyl-2-hydroxy-2-phenyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3f):

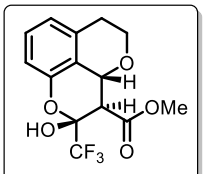
Prepared according to general procedure B from **2f** to afford **3f** (30.6 mg, 90% yield, d.r. = 8.3:1) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.59-7.55 (m, 2H), 7.43-7.38 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.81 (dd, *J* = 11.6, 8.0 Hz, 2H), 5.20 (d, *J* = 11.6 Hz, 1H),4.248 (s, 1H), 4.30-4.24 (m, 1H), 4.09-4.01 (m, 2H), 3.96-3.91 (m, 1H), 3.15-3.09 (m, 2H), 2.83 (dd, *J* = 16.8, 4.4 Hz, 1H),0.89 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 172.0, 150.0, 140.8, 133.3, 129.1, 128.7, 128.3, 125.7, 121.4, 119.4, 113.8, 98.6, 70.6, 65.9, 61.4, 53.6, 27.5, 13.7; **IR** (neat) 3406, 2980, 1737, 1467, 1252, 1028, 737 cm^{-1}; **MS** (EI) *m/z* (%) 340 (1), 249 (5), 192 (4), 148 (100), 105 (61), 91 (14); **HRMS** (ESI) Calcd. for $C_{20}H_{20}O_5$ $(M+Na)^+$: 363.1203, Found 363.1209.



methyl-2-hydroxy-2-isopropyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3g):

Prepared according to general procedure B from **2g** to afford **3g** (24.5 mg, 84% yield) as a white

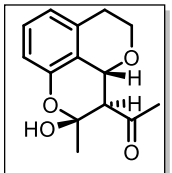
solid. **mp**: 178-180 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.13 (t, *J* = 8.0 Hz, 1H), 6.76-6.71 (m, 2H), 5.05 (d, *J* = 11.2 Hz, 1H), 4.28-4.22 (m, 1H), 4.00 (dt, *J* = 11.6, 4.8 Hz, 1H), 3.89 (s, 1H), 3.86 (s, 3H), 3.13-3.03 (m, 2H), 2.77 (dd, *J* = 16.8, 4.8 Hz, 1H), 1.93 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 173.7, 150.0, 132.9, 128.6, 120.8, 119.3, 113.6, 100.2, 71.0, 65.8, 52.7, 48.9, 37.5, 27.5, 17.1, 15.1; **IR** (neat) 3431, 2925, 1734, 1593, 1464, 1260, 774 cm^{-1}; **MS** (EI) *m/z* (%) 292 (2), 221 (4), 215 (4), 148 (100), 91 (15); **HRMS** (ESI) Calcd. for $C_{16}H_{20}O_5$ $(M+Na)^+$: 315.1203, Found 315.1194.



3h

methyl-2-hydroxy-2-(trifluoromethyl)-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3h):

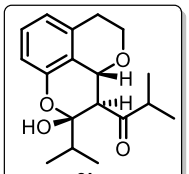
Prepared according to general procedure B from **2h** to afford **3h** (27.2 mg, 82% yield) as a white solid. **mp**: 123-126 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.20 (t, *J* = 8.0 Hz, 1H), 6.86-6.82 (m, 2H), 4.99 (d, *J* = 11.6 Hz, 1H), 4.31-4.25 (m, 1H), 3.97 (dt, *J* = 11.6, 4.4 Hz, 1H), 3.91 (s, 3H), 3.15-3.05 (m, 2H), 2.77 (dd, *J* = 17.0, 4.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 173.2, 148.3, 132.9, 129.2, 122.2, 118.5, 113.8, 94.8 (d, *J* = 34.2 Hz), 70.0, 65.9, 53.5, 45.8, 27.2; **IR** (neat) 3300, 2925, 1664, 1467, 1184, 777 cm^{-1}; **MS** (EI) *m/z* (%) 318 (2), 259 (3), 241 (63), 148 (100), 91 (30); **HRMS** (ESI) Calcd. for $C_{14}H_{13}F_3O_5$ $(M+Na)^+$: 341.0607, Found 341.0615.



3i

2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromen-3-yl)ethan-1-one (3i):

Prepared according to general procedure B from **2i** to afford **3i** (24.1 mg, 97% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 4.95 (d, *J* = 11.2 Hz, 1H), 4.26-4.21 (m, 1H), 3.96 (dt, *J* = 11.6, 4.8 Hz, 1H), 3.12-3.03 (m, 2H), 2.77 (dd, *J* = 16.8, 4.4 Hz, 1H), 2.44 (s, 3H), 1.59 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$, ppm): δ 211.8, 149.7, 132.8, 128.6, 120.9, 119.5, 113.5, 97.3, 71.3, 65.7, 57.7, 32.5, 27.9, 27.4; **IR** (neat) 3385, 2928, 1702, 1463, 1094, 737 cm^{-1}; **MS** (EI) *m/z* (%) 248 (1), 205 (8), 163 (17), 148 (100), 91 (84); **HRMS** (ESI) Calcd. for $C_{14}H_{16}O_4$ $(M+Na)^+$: 271.0941, Found 271.0932.

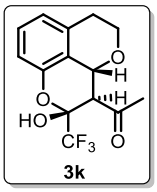


3j

2-hydroxy-2-isopropyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromen-3-yl)-2-methylpropan-1-one (3j):

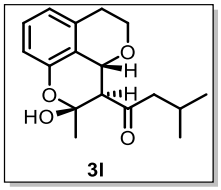
Prepared according to general procedure B from **2j** to afford **3j** (17.3 mg, 57% yield) as a white

solid. **mp**: 122-125 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.74-6.71 (m, 2H), 4.93 (d, *J* = 10.8 Hz, 1H), 4.71 (m, 1H), 4.23-4.17 (m, 1H), 3.91 (dt, *J* = 11.2, 4.4 Hz, 1H), 3.47 (d, *J* = 10.8 Hz, 1H), 3.12-3.02 (m, 1H), 2.95-2.87 (m, 1H), 2.74 (dd, *J* = 17.0, 4.6 Hz, 1H), 1.76-1.19 (m, 1H), 1.18 (d, *J* = 6.0 Hz, 9H), 1.03 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 219.8, 150.3, 132.7, 128.5, 120.7, 119.8, 113.6, 100.6, 72.9, 65.8, 52.1, 43.3, 37.3, 27.5, 17.8, 17.6, 17.4, 15.2; **IR** (neat) 3395, 2926, 1706, 1465, 1259, 1093, 779 cm^{-1}; **MS** (EI) *m/z* (%) 304 (1), 231 (12), 148 (100), 91 (9); **HRMS** (ESI) Calcd. for $C_{18}H_{24}O_4$ $(M+Na)^+$: 327.1567, Found 327.1561.



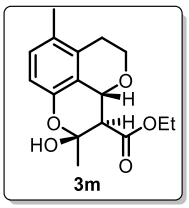
(2-hydroxy-2-(trifluoromethyl)-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromen-3-yl)ethan-1-one (**3k**):

Prepared according to general procedure B from **2k** to afford **3k** (16.0 mg, 53% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.20 (t, *J* = 8.0 Hz, 1H), 6.84-6.81 (m, 2H), 6.21 (s, 1H), 4.89 (d, *J* = 11.2 Hz, 1H), 4.28-4.22 (m, 1H), 3.91 (dt, *J* = 11.6, 4.4 Hz, 1H), 3.35 (d, *J* = 11.2 Hz, 1H), 3.14-3.04 (m, 1H), 2.76 (dd, *J* = 17.0, 4.2 Hz, 1H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 211.9, 148.4, 132.6, 129.2, 122.1, 118.8, 113.9, 95.4, 71.5, 65.8, 49.6, 33.7, 27.1; **IR** (neat) 3431, 2921, 1632, 1469, 1099, 619 cm^{-1}; **MS** (EI) *m/z* (%) 302 (80), 148 (100), 120 (15), 91 (12); **HRMS** (ESI) Calcd. for $C_{14}H_{13}F_3O_4$ $(M+Na)^+$: 325.0658, Found 325.0688.



2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromen-3-yl)-3-methylbutan-1-one (3l):

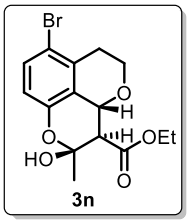
Prepared according to general procedure B from **2l** to afford **3l** (28.4 mg, 98% yield) as a a white solid. **mp**: 112-115 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.13 (t, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 4.90 (d, *J* = 11.6 Hz, 1H), 4.45 (s, 1H), 4.24-4.18 (m, 1H), 3.93 (dt, *J* = 11.6, 4.8 Hz, 1H), 3.04 (d, *J* = 11.2 Hz, 1H), 2.79-2.74 (m, 1H), 2.69 (dd, *J* = 18.0, 6.4 Hz, 1H), 2.55 (dd, *J* = 18.0, 6.8 Hz, 1H), 2.30-2.24 (m, 1H), 1.56 (s, 3H), 0.99-0.95 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 214.2, 149.8, 132.9, 128.6, 120.9, 119.6, 113.6, 97.3, 71.7, 65.8, 56.8, 55.2, 28.0, 27.4, 23.4, 22.6, 22.4; **IR** (neat) 3414, 2927, 1703, 1465, 1369, 1096, 779 cm^{-1}; **MS** (EI) *m/z* (%) 290 (1), 205 (31), 148 (100), 120 (17), 91 (11); **HRMS** (ESI) Calcd. for $C_{17}H_{22}O_4$ $(M+Na)^+$: 313.1410, Found 313.1410.



ethyl-2-hydroxy-2,7-dimethyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-

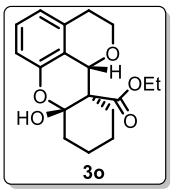
carboxylate (3m):

Prepared according to general procedure B from **1b** (16.4 mg) to afford **3m** (18.9 mg, 65% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ7.00 (d, *J* = 8.4 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 5.00(d, *J* = 11.6 Hz, 1H), 4.42-4.26 (m, 3H), 4.05-3.97 (m, 1H), 2.93-2.83 (m, 2H), 2.62 (dd, *J* = 17.2, 4.8 Hz, 1H), 2.15 (s, 3H), 1.64 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 172.9, 147.6, 131.1, 129.8, 128.6, 118.9, 113.2, 97.1, 70.7, 66.0, 61.8, 52.3, 28.0, 26.0, 18.0, 14.2; **IR** (neat) 3418, 2926, 1727, 1602, 1482, 1099, 738 cm^{-1}; **MS** (EI) *m/z* (%) 292 (2), 201 (4), 162 (100), 133 (21), 91 (16); **HRMS** (ESI) Calcd. for $C_{16}H_{20}O_5$ $(M+Na)^+$: 315.1203, Found 315.1208.



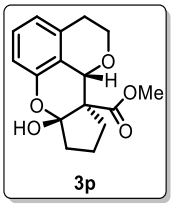
ethyl-7-bromo-2-hydroxy-2-methyl-3,3a,5,6-tetrahydro-2H-pyrano[2,3,4-de]chromene-3-carboxylate (3n):

Prepared according to general procedure B from **1c** (22.9 mg) to afford **3n** (32.1 mg, 90% yield) as a white solid. **mp**: 167-170 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ7.36 (t, *J* = 8.8 Hz, 1H), 6.64 (d, *J* = 8.8 Hz, 1H), 4.96 (d, *J* = 11.6 Hz, 1H), 4.43-4.25 (m, 3H), 4.02-3.94 (m, 1H), 2.98-2.88 (m, 1H), 2.83 (d, *J* = 11.6 Hz, 1H), 2.79-2.72 (m, 1H), 1.65 (s, 3H), 1.36 (t, *J* =7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 172.4, 148.8, 132.6, 132.0, 121.4, 115.7, 115.5, 97.4, 70.4, 65.9, 62.0, 51.8, 29.0, 27.9, 14.2; **IR** (neat) 3346, 2934, 1732, 1455, 1259, 1081, 813 cm^{-1}; **MS** (EI) *m/z* (%) 358 (5), 356 (6), 315 (8), 313 (8), 267 (13), 228 (100), 226 (98), 148(18), 91 (18); **HRMS** (ESI) Calcd. for $C_{15}H_{17}BrO_5$ $(M+Na)^+$: 379.0152, Found 379.0154.



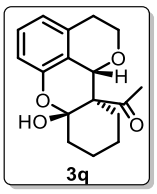
ethyl-7a-hydroxy-3,8,9,10,11,11b-hexahydro-2H-pyrano[4,3,2-kl]xanthene-11a(7aH)-carboxylate (3o):

Prepared according to general procedure B from **2o** to afford **3o** (22.3 mg, 70% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.14 (t, *J* = 8.0 Hz, 1H), 6.75-6.71 (m, 2H), 6.70 (d, *J* = 7.6 Hz, 1H), 5.54 (s, 1H), 5.13 (s, 1H), 4.70-4.39 (m, 1H), 4.37-4.28 (m, 1H), 4.26-4.20 (m, 1H), 3.94 (dt, *J* = 11.6, 4.4 Hz, 1H), 3.10-3.00 (m, 1H), 2.71 (dd, *J* = 16.8, 4.0 Hz, 1H), 2.74-2.72 (m, 1H), 2.24-2.20 (m, 1H), 1.65-1.54 (m, 5H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.21 (dt, *J* = 13.6, 4.4 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$, ppm): δ 176.9, 149.4, 133.6, 128.4, 120.9, 117.7, 113.5, 98.6, 74.3, 66.1, 62.1, 51.8, 37.3, 27.6, 23.9, 22.1, 21.4, 14.1; **IR** (neat) 3419, 2936, 1691, 1465, 1105, 737 cm^{-1}; **MS** (EI) *m/z* (%) 318 (33), 227 (66), 148 (100), 91(2); **HRMS** (ESI) Calcd. for $C_{18}H_{22}O_5$ $(M+Na)^+$: 341.1359, Found 341.1351.



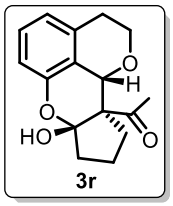
methyl-7a-hydroxy-3,7a,8,9,10,10b-hexahydrocyclopenta[b]pyrano[2,3,4-de]chromene-10a(2H)-carboxylate (3p):

Prepared according to general procedure B from **2p** to afford **3p** (24.4 mg, 84% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.15 (t, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.19 (s, 1H), 4.25-4.19 (m, 2H), 3.92 (dd, *J* = 11.6, 3.6 Hz, 1H), 3.88 (s, 3H), 3.10-3.01 (m, 1H), 2.67 (dd, *J* = 16.8, 3.2 Hz, 1H), 2.41-2.35 (m, 1H), 2.06-1.99 (m, 2H), 1.82-1.74 (m, 1H), 1.58-1.44 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$, ppm): δ 174.3, 149.7, 134.0, 128.1, 121.5, 119.9, 114.2, 109.5, 73.2, 65.5, 60.4, 52.9, 38.4, 27.6, 27.5, 20.4; **IR** (neat) 3369, 2926, 1733, 1466, 1255, 1099, 780 cm^{-1}; **MS** (EI) *m/z* (%) 304 (5), 287 (4), 148 (100), 91 (61); **HRMS** (ESI) Calcd. for $C_{16}H_{18}O_5$ $(M+Na)^+$: 313.1046, Found 313.1054.



1-(7a-hydroxy-3,8,9,10,11,11b-hexahydro-2H-pyrano[4,3,2-kl]xanthen-11a(7aH)-yl)ethan-1-one (3q):

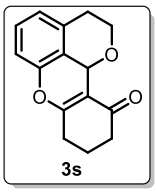
Prepared according to general procedure B from **2q** to afford **3q** (23.0 mg, 80% yield) as a white solid. **mp**: 178-181 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.14 (t, *J* = 8.0 Hz, 1H), 6.74-6.71 (m, 2H), 5.39 (s, 1H), 4.95 (s, 1H), 4.27-4.21 (m, 1H), 3.92 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.11-3.01 (m, 1H), 2.72 (dd, *J* = 16.8, 4.4 Hz, 1H), 2.51 (s, 3H), 2.29-2.25 (m, 1H), 2.04-2.00 (m, 1H), 1.68-1.62 (m, 4H), 1.41 (dd, *J* = 14.4, 3.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 218.3, 149.4, 133.5, 128.5, 120.9, 117.9, 113.6, 99.0, 74.3, 66.0, 55.8, 36.6, 30.5, 27.4, 25.0, 22.3, 22.0; **IR** (neat) 3442, 2927, 1736, 1591, 1462, 1262, 1098, 737 cm^{-1}; **MS** (EI) *m/z* (%) 288 (3), 227 (100), 148 (79), 91 (2); **HRMS** (ESI) Calcd. for $C_{17}H_{20}O_4$ $(M+Na)^+$: 311.1254, Found 311.1252.



1-(7a-hydroxy-3,7a,8,9,10,10b-hexahydrocyclopenta[b]pyrano[2,3,4-de]chromen-10a(2H)-yl)ethan-1-one (3r):

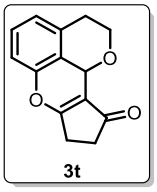
Prepared according to general procedure B from **2r** to afford **3r** (23.6 mg, 86% yield) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, ppm): δ 7.12 (t, *J* = 7.8 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.10 (s, 1H), 4.37 (s, 1H), 4.21-4.17 (m, 1H), 3.94 (dd, *J* = 7.6, 4.2 Hz, 1H), 3.08-3.03 (m, 1H), 2.75-2.73 (m, 1H), 2.50-2.44 (m, 2H), 2.19-2.16 (m, 1H), 1.89-1.86 (m, 2H), 1.49 (s, 3H), 1.41 (dd, *J* = 14.4, 3.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 224.1, 150.0, 133.9, 128.4, 121.0, 118.6, 113.4, 99.7, 74.4, 65.7, 55.5, 40.2, 27.4, 25.8, 25.1, 19.3; **IR** (neat) 3449, 2927, 1737,

1590, 1427, 1098, 737 cm^{-1}; **MS** (EI) *m/z* (%) 274 (8), 231 (16), 186 (20), 150 (100), 120 (18), 91 (12); **HRMS** (ESI) Calcd. for $C_{16}H_{18}O_4$ $(M+Na)^+$: 297.1097, Found 297.1089.



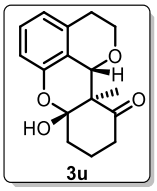
2,3,8,9,10,11b-hexahydro-11H-pyrano[4,3,2-kl]xanthen-11-one (3s):

Prepared according to general procedure B from **2s** to afford **3s** (14.5 mg, 60% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.28-7.24 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 5.23 (s, 1H), 3.81-3.78 (m, 1H), 3.55-3.49 (m, 2H), 3.08-3.01 (m, 1H), 2.82-2.77 (m, 1H), 2.62-2.56 (m, 1H), 2.47-2.44 (m, 1H), 2.37-2.27 (m, 1H), 2.14-1.94 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 198.8, 153.3, 139.4, 131.9, 130.0, 127.8, 123.5, 119.23, 115.9, 95.6, 63.5, 38.8, 35.6, 35.4, 18.1; **IR** (neat) 3392, 2922, 1642, 1400, 1244, 1048, 786 cm^{-1}; **MS** (EI) *m/z* (%) 242 (6), 212 (5), 84 (88), 71 (80), 57 (100); **HRMS** (ESI) Calcd. for $C_{15}H_{14}O_3$ $(M+Na)^+$: 265.0835, Found 265.0842.



3,8,9,10b-tetrahydrocyclopenta[b]pyrano[2,3,4-de]chromen-10(2H)-one (3t):

Prepared according to general procedure B from **2t** to afford **3t** (14.2 mg, 62% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.28 (t, *J* = 8.0 Hz, 1H), 7.05-7.00 (m, 2H), 5.35 (s, 1H), 4.30 (dd, *J* = 10.4, 6.8 Hz, 1H), 4.04 (dd, *J* = 10.8, 6.8 Hz, 1H), 3.01-2.97 (m, 2H), 2.84-2.80 (m, 2H), 2.61-2.57 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 202.5, 180.0, 148.5, 136.7, 128.8, 124.4, 120.3, 114.7, 113.9, 64.4, 61.7, 33.7, 27.5, 25.8; **IR** (neat) 3371, 2928, 1647, 1401, 1248, 1057, 734 cm^{-1}; **MS** (EI) *m/z* (%) 227 (32), 198(13), 101 (21), 86 (100), 58 (23); **HRMS** (ESI) Calcd. for $C_{14}H_{12}O_3$ $(M+Na)^+$: 251.0679, Found 251.0682.



7a-hydroxy-11a-methyl-2,3,7a,8,9,10,11a,11b-octahydro-11H-pyrano[4,3,2-kl]xanthen-11-one (3u):

Prepared according to general procedure B from **1u** (21.0 mg) to afford **3u** (18.6 mg, 68% yield) as a white solid. **mp**: 164-166 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.78 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 5.12 (s, 1H), 4.26-4.17 (m, 2H), 3.05-3.02 (m, 1H), 2.68-2.74 (m, 2H), 2.50-2.36 (m, 1H), 2.35-2.33 (m, 2H), 2.20-1.86 (m, 3H), 1.24 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 208.8, 148.4, 135.4, 128.0, 121.7, 113.2, 102.2, 69.3, 65.3, 52.0, 36.5, 32.5, 27.7, 19.9, 14.2; **IR** (neat) 3373, 2927, 1713, 1463, 1250, 1053, 784 cm^{-1}; **MS** (EI) *m/z* (%) 274 (2), 259 (11), 187 (5), 148 (100), 91 (25); **HRMS** (ESI) Calcd. for $C_{16}H_{18}O_4$ $(M+Na)^+$: 297.1097, Found 297.1103.

1.3 General procedure C: for the synthesis of oxoammonium salts[3]:

Synthesis of $TEMPO^+BF_4^-$:

TEMPO (1.5 g, 9.5 mmol) was slurried with H_2O (20.0 mL) and 42% HBF_4 (5.0 mL, 13.5 mmol) was slowly added dropwise over 1.0 h at room temperature. After the solution turned to amber color, NaOCl (2.2 mL, 4.5 mmol) was added over 1.0 h at 0 ℃ and stirred for additional 1.0 h at 0 ℃. The reaction mixture was filtered and the yellow crystalline precipitate was washed with ice-cold 5% $NaHCO_3$ (2.0 mL), water (20 mL) and ice-cold Et_2O (500 mL). The solid was dried over 24 h at 50 ℃ in vacuo to yield $TEMPO^+BF_4^-$;

Synthesis of $TEMPO^+ ClO_4^-$:

TEMPO (5.0 g, 32 mmol) was slurried with H_2O (20.0 mL) and 70% $HClO_4$ (2.58 mL, 32 mmol) was slowly added dropwise over 1.0 h at room temperature. After the solution turned to amber color, NaOCl (17.1 mL, 16 mmol) was added over 1.0 h at 0 ℃ and stirred for additional 1.0 h at 0 ℃. The reaction mixture was filtered and the yellow crystalline precipitate was washed with ice-cold 5% $NaHCO_3$ (10.0 mL), water (20 mL) and ice-cold Et_2O (500 mL). The solid was dried over 24 h at 50 ℃ in vacuo to yield $TEMPO^+ ClO_4^-$;

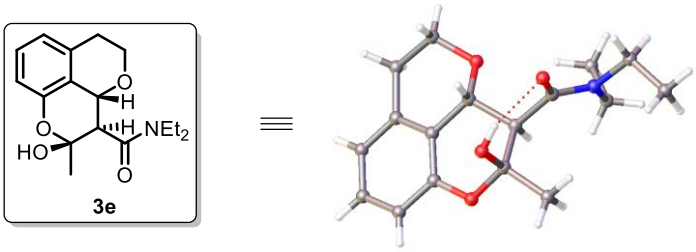
Synthesis of $TEMPO^+ PF_6^-$:

TEMPO (3.0 g, 19.2 mmol) was slurried with H_2O (20.0 mL) and 60% HPF_6 (4.0 mL, 28.8 mmol) was slowly added dropwise over 1.0 h at room temperature. After the solution turned to amber color, NaOCl (10.3 mL, 9.6 mmol) was added over 1.0 h at 0 ℃ and stirred for additional 1.0 h at 0 ℃. The reaction mixture was filtered and the yellow crystalline precipitate was washed with ice-cold 5% $NaHCO_3$ (10.0 mL), water (20 mL) and ice-cold Et_2O (500 mL). The solid was dried over 24 h at 50 ℃ in vacuo to yield $TEMPO^+PF_6^-$;

Synthesis of $TEMPO^+ OTf^-$:

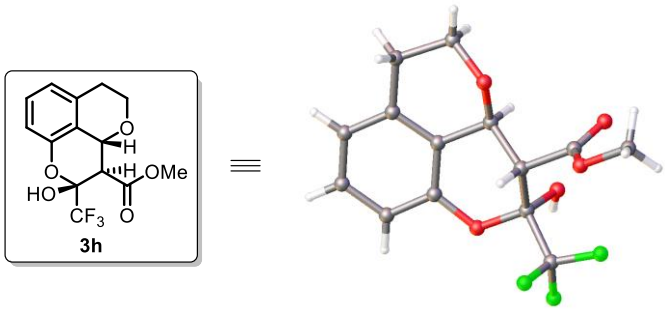
TEMPO (2.0 g, 12.8 mmol) was slurried with H_2O (20.0 mL) and TfOH (2.25 mL, 25.6 mmol) was slowly added dropwise over 1.0 h at room temperature. After the solution turned to amber color, NaOCl (10.3 mL, 9.6 mmol) was added over 1.0 h at 0 ℃ and stirred for additional 1.0 h at 0 ℃. The reaction mixture was filtered and the yellow crystalline precipitate was washed with ice-cold 5% $NaHCO_3$ (10.0 mL), water (20 mL) and ice-cold Et_2O (500 mL). The solid was dried over 24 h at 50 ℃ in vacuo to yield $TEMPO^+OTf^-$;

2. X-Ray ellipsoid plots of 3e, 3h, 3q, 3u



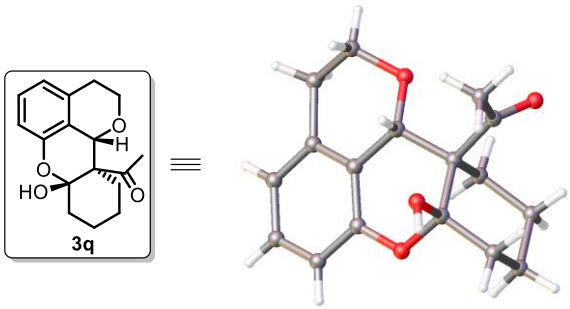
X-ray structure of **3e**

The structure of compound **3e** was corroborated by single-crystal. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: 1899674.



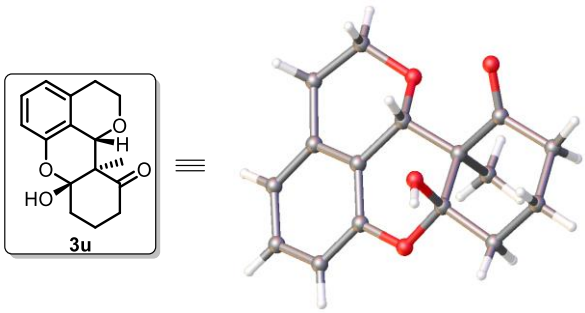
X-ray structure of **3h**

The structure of compound **3h** was corroborated by single-crystal. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: 1899677.



X-ray structure of **3q**

The structure of compound **3q** was corroborated by single-crystal. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: 1899676.



X-ray structure of **3u**

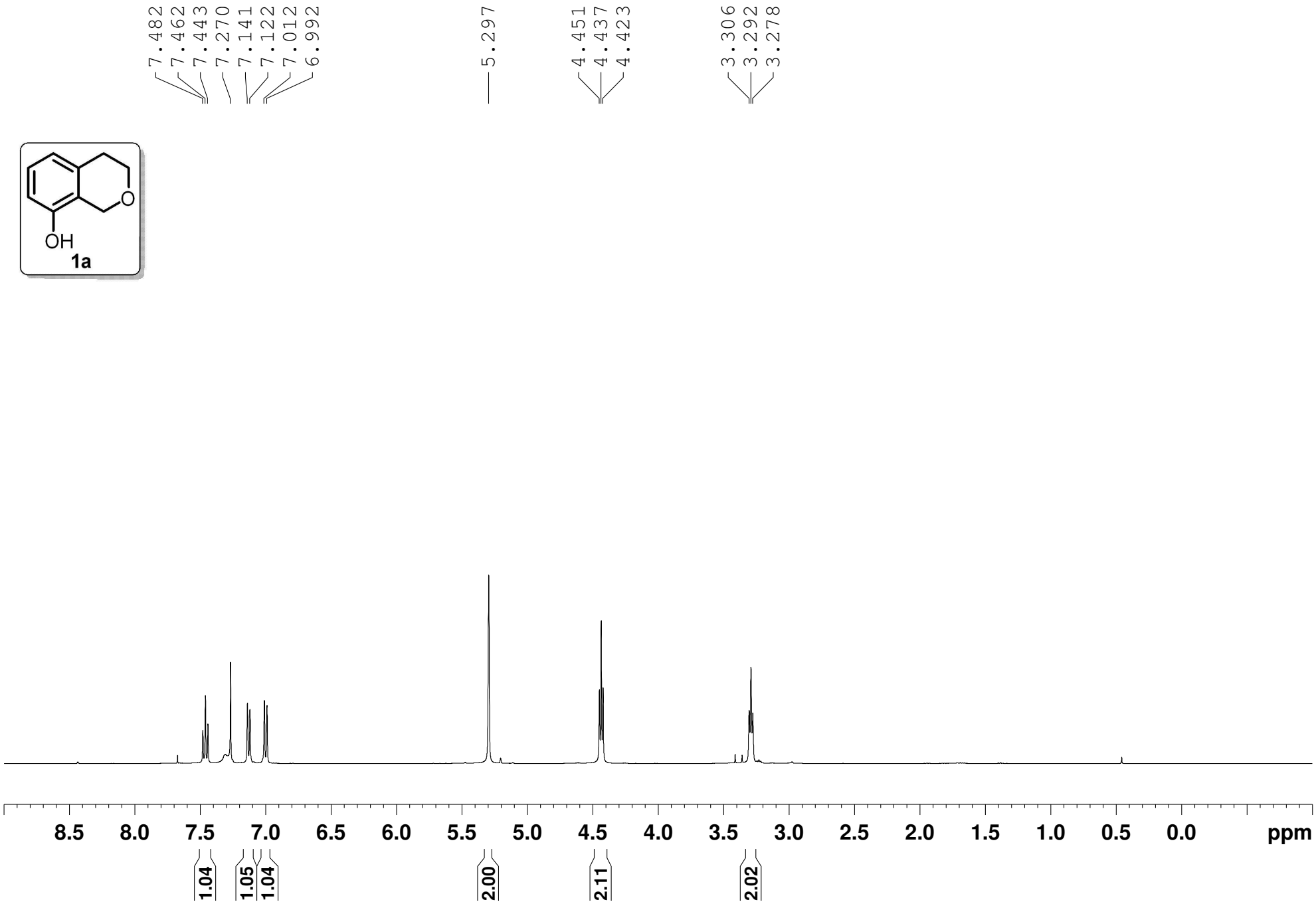
The structure of compound **3u** was corroborated by single-crystal. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: 1899675.

References:

(1) A. L. Meyer, R. B. Turner, *Tetrahedron*, 1971, **27**, 2609-2615.

(2) e-EROS Encyclopedia of Reagents for Organic Synthesis, 2015, 1-24.

(3) M. Shibuya, M. Tomizawa, and Y. Iwabuchi, *J. Org. Chem.*, 2008, **73**, 4750-4752.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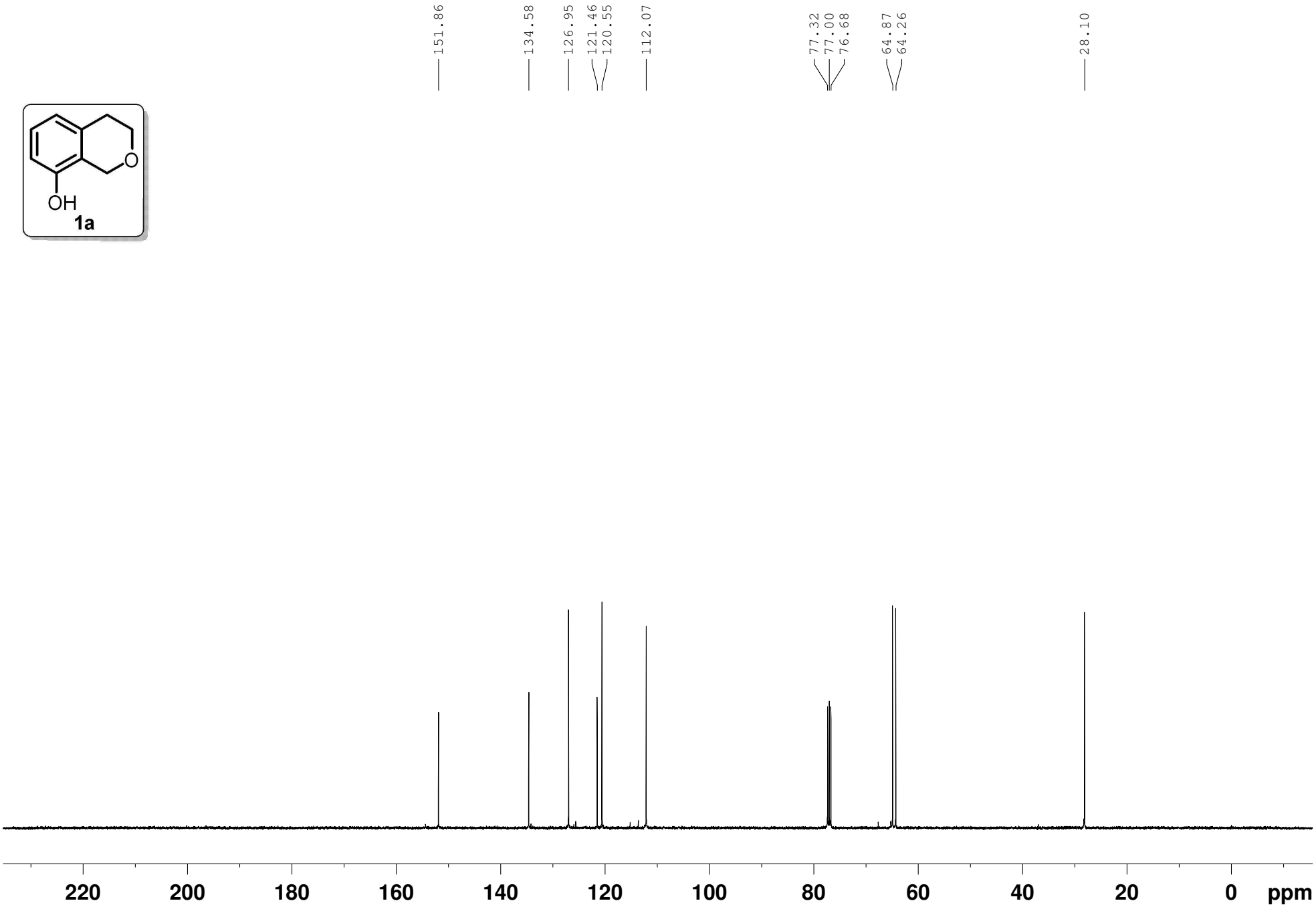
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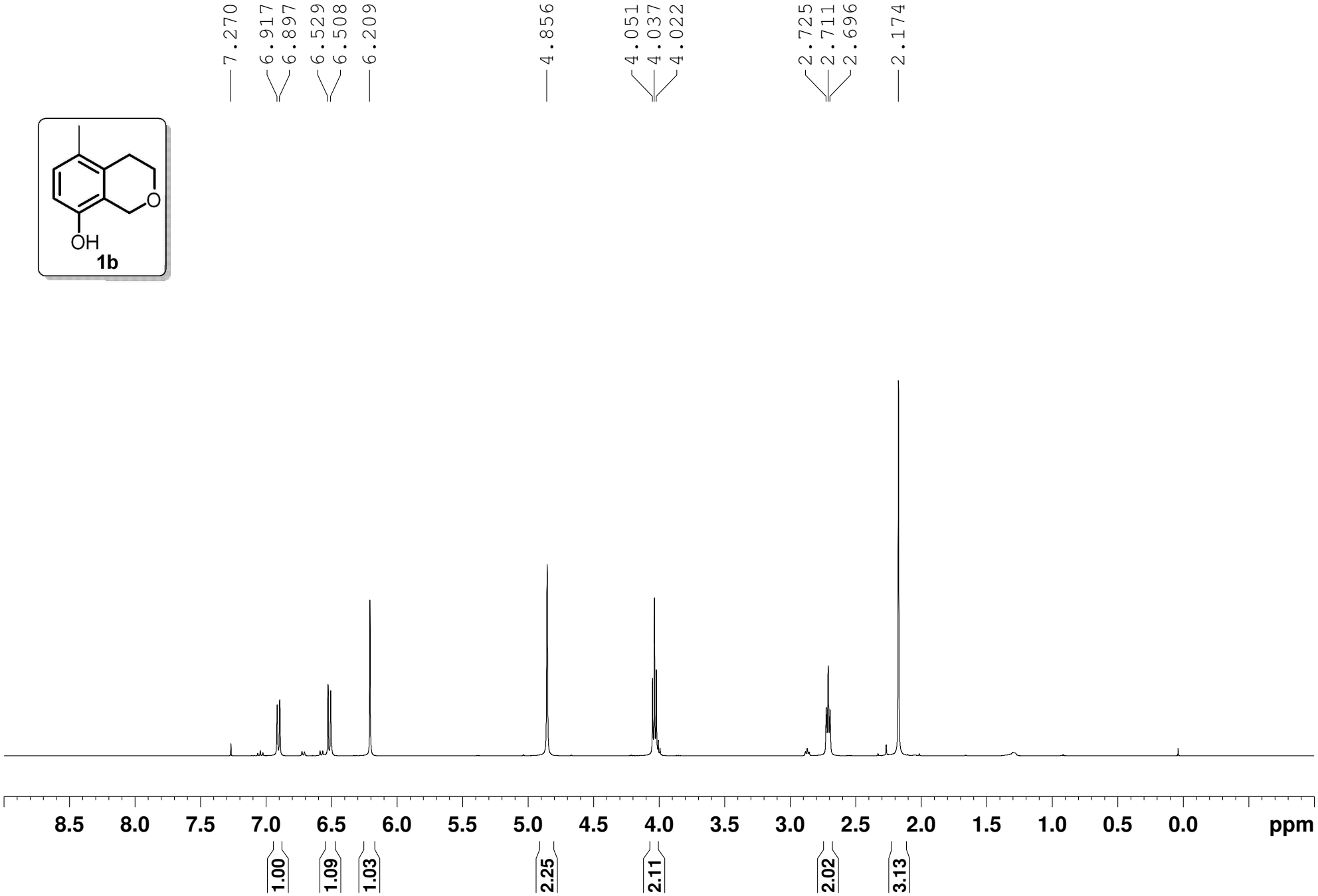
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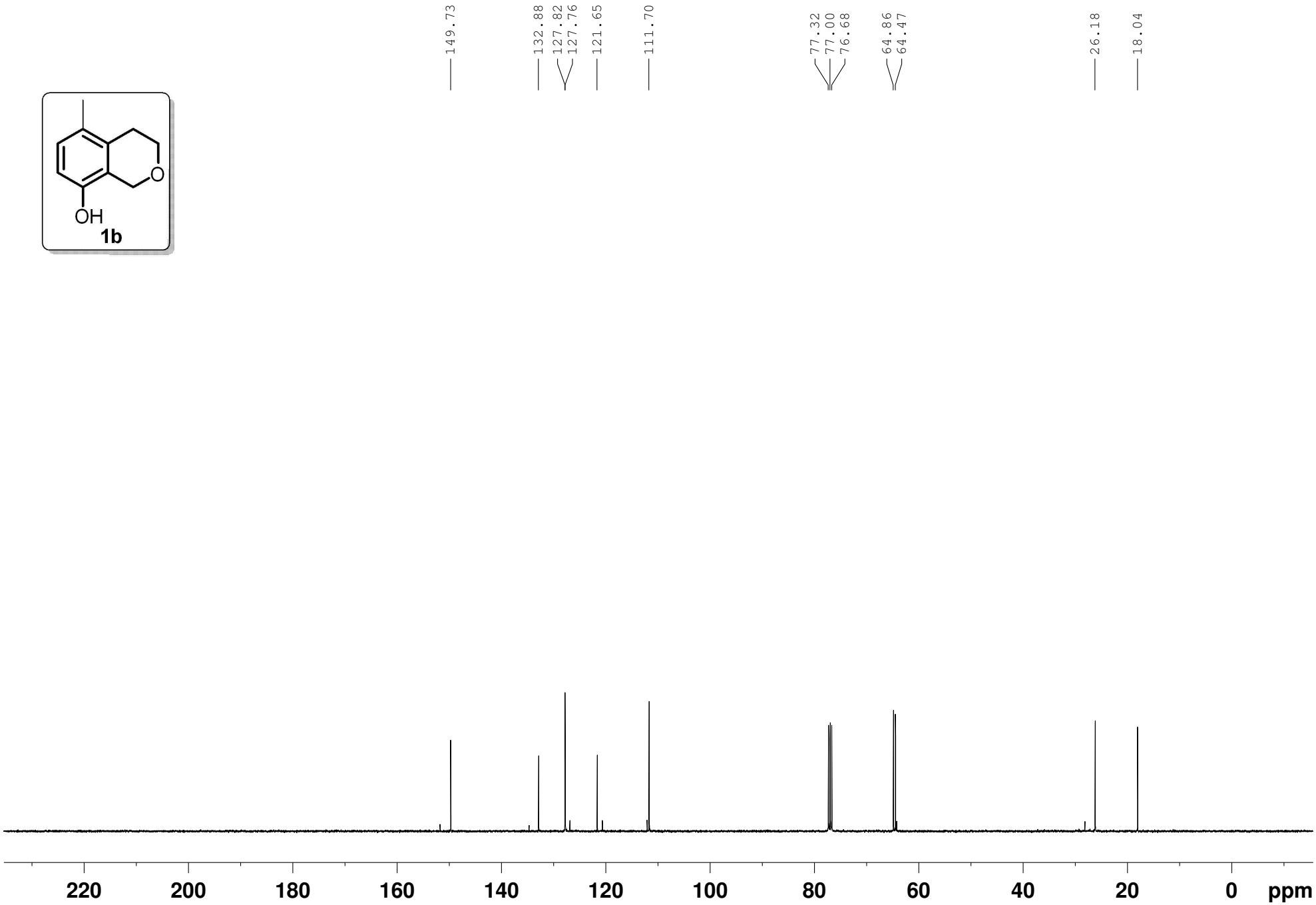
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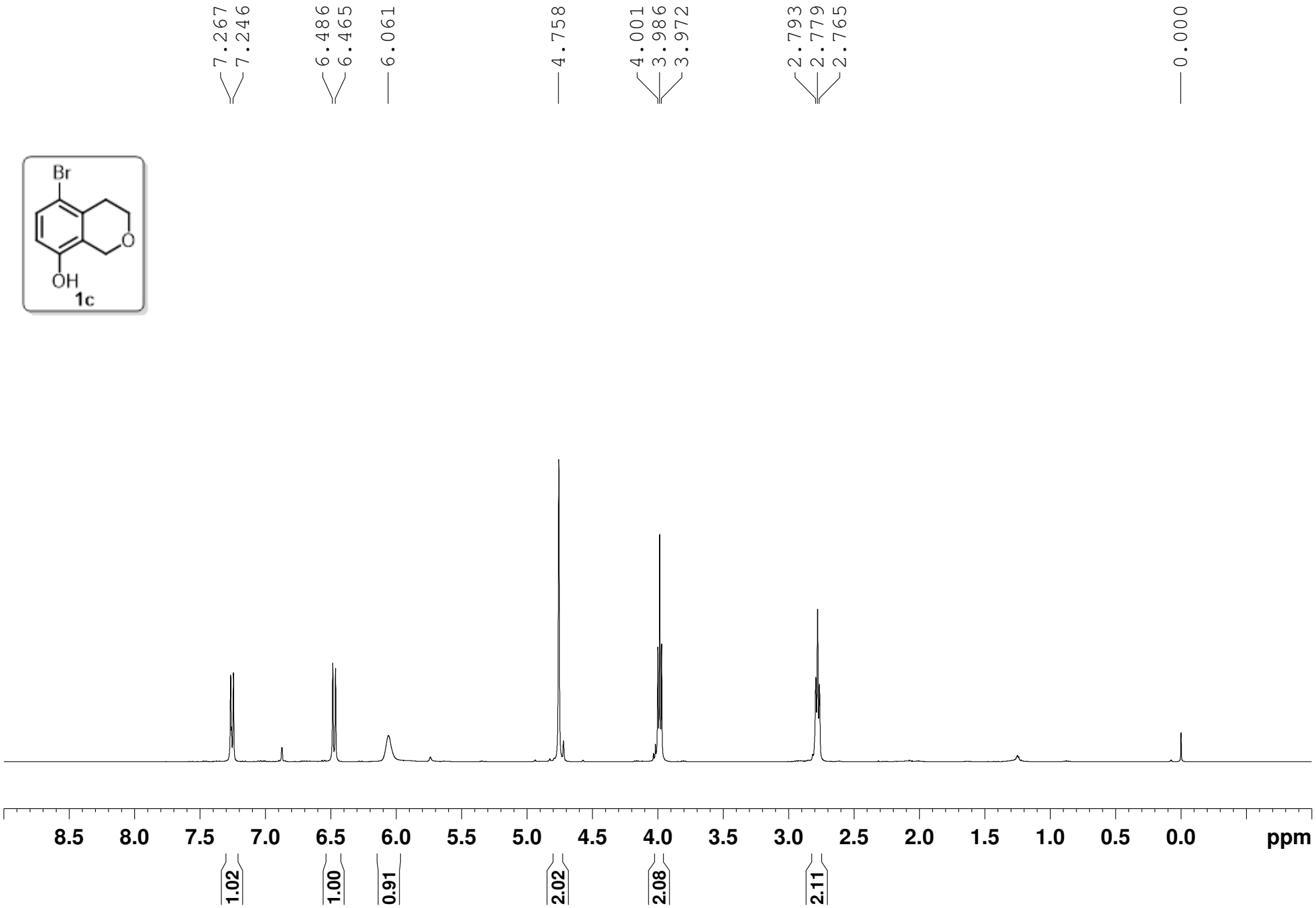
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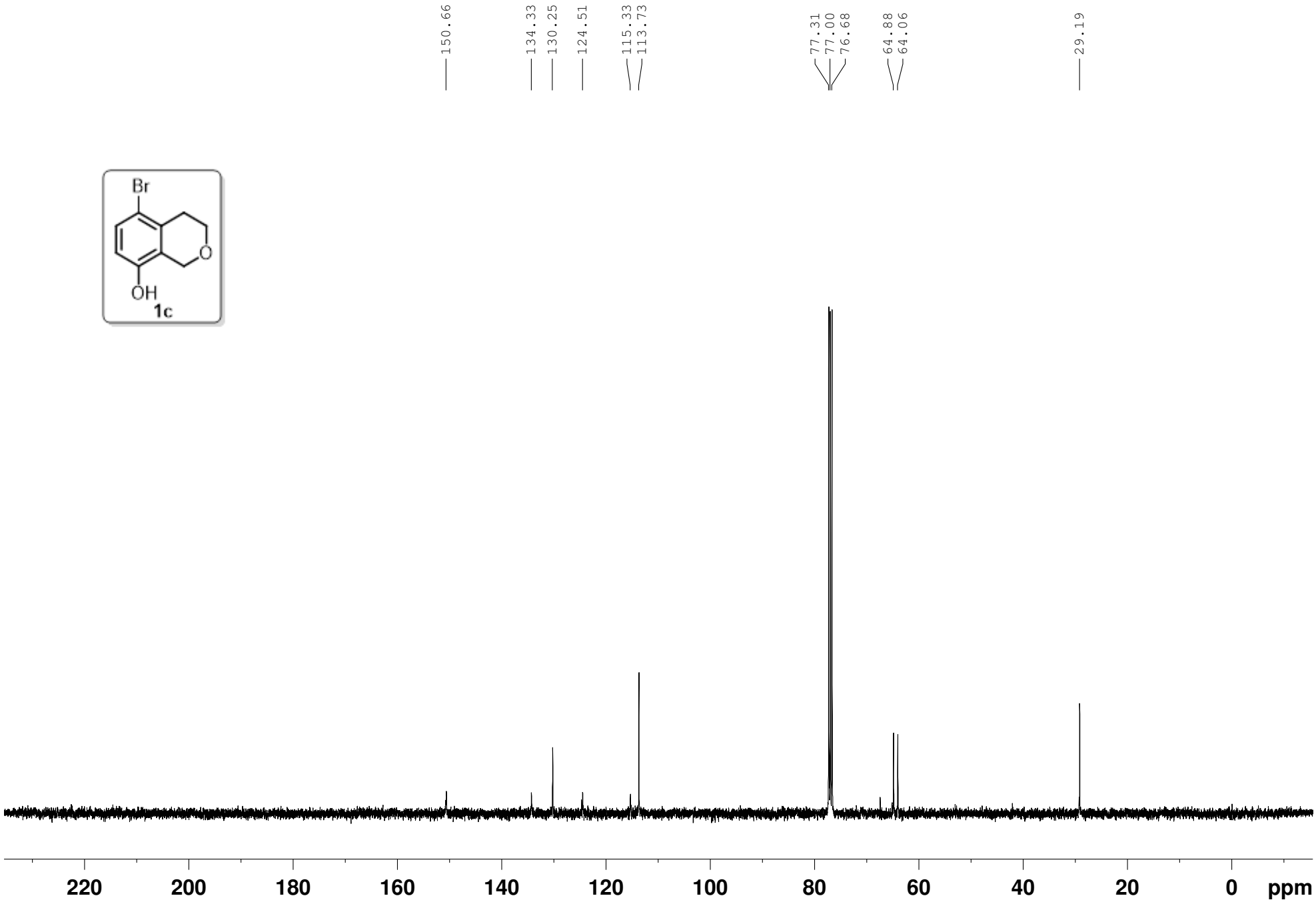
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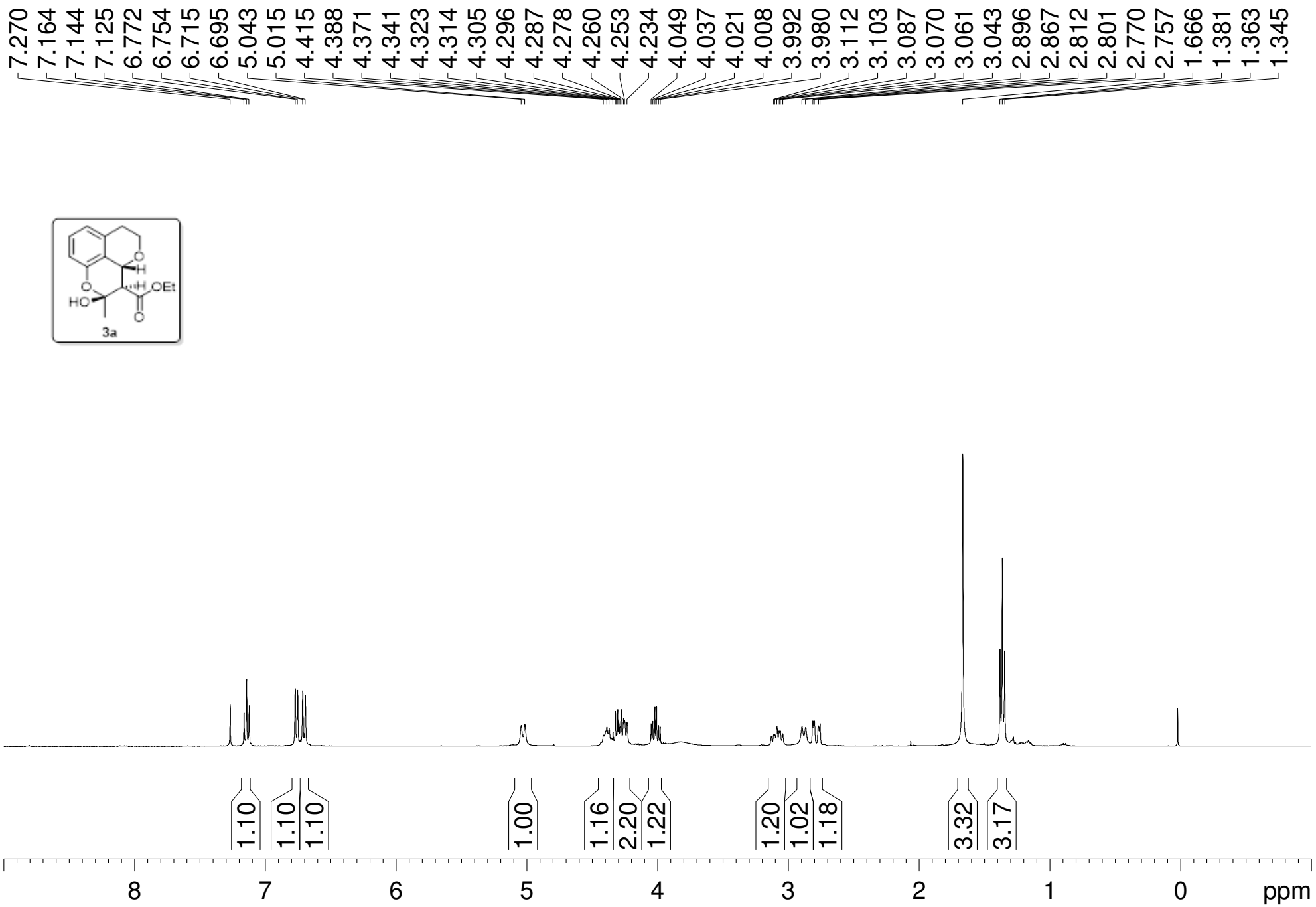
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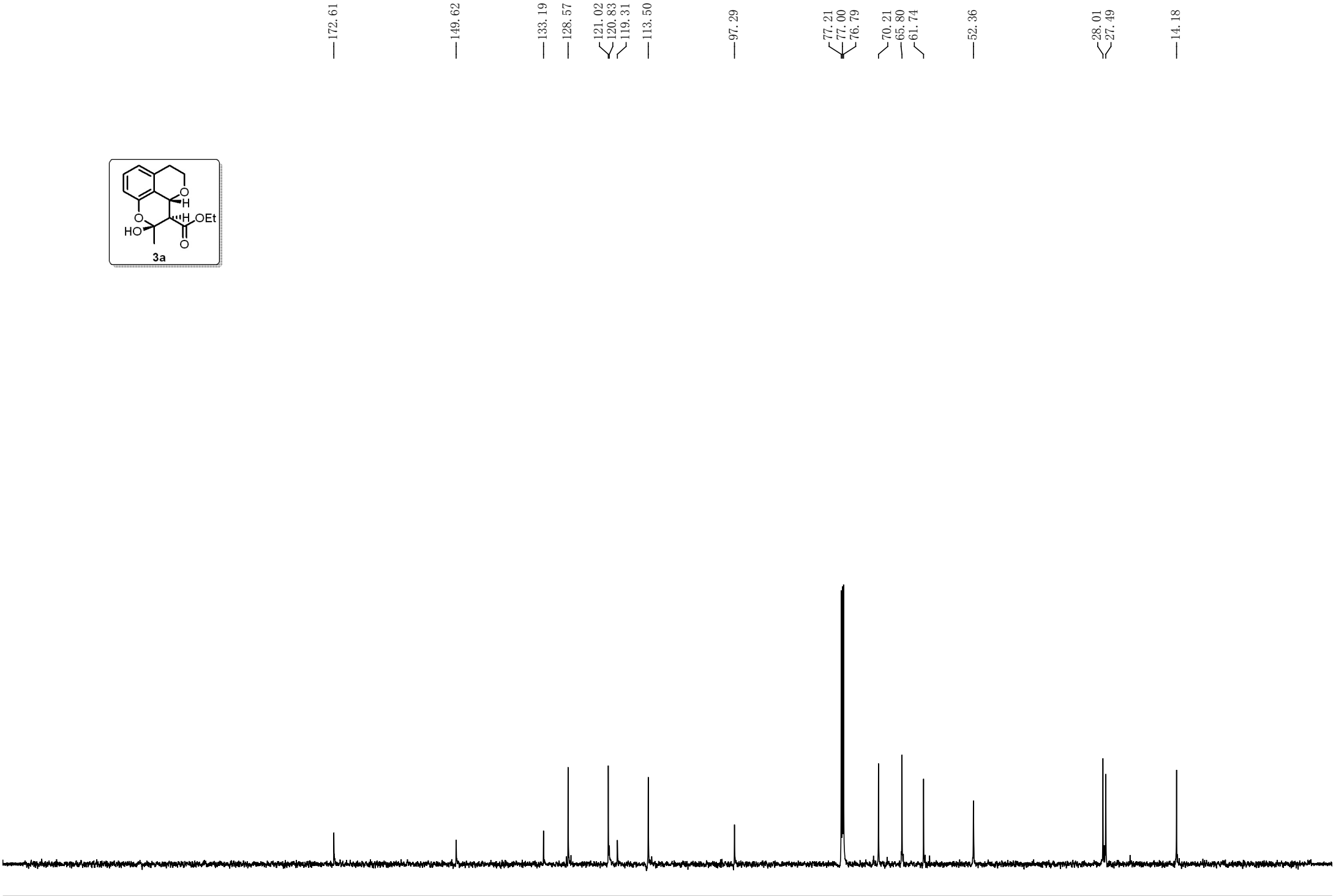
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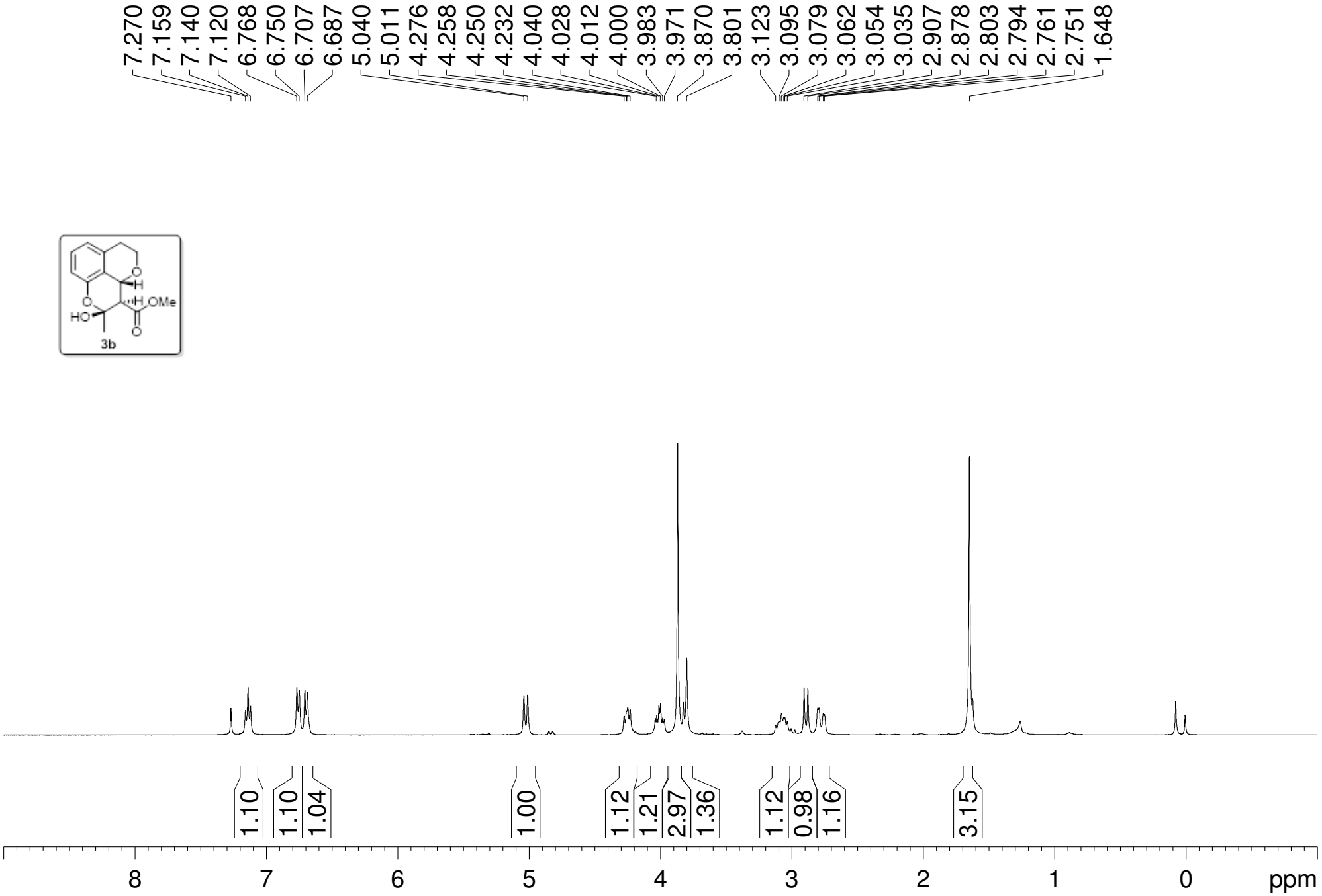
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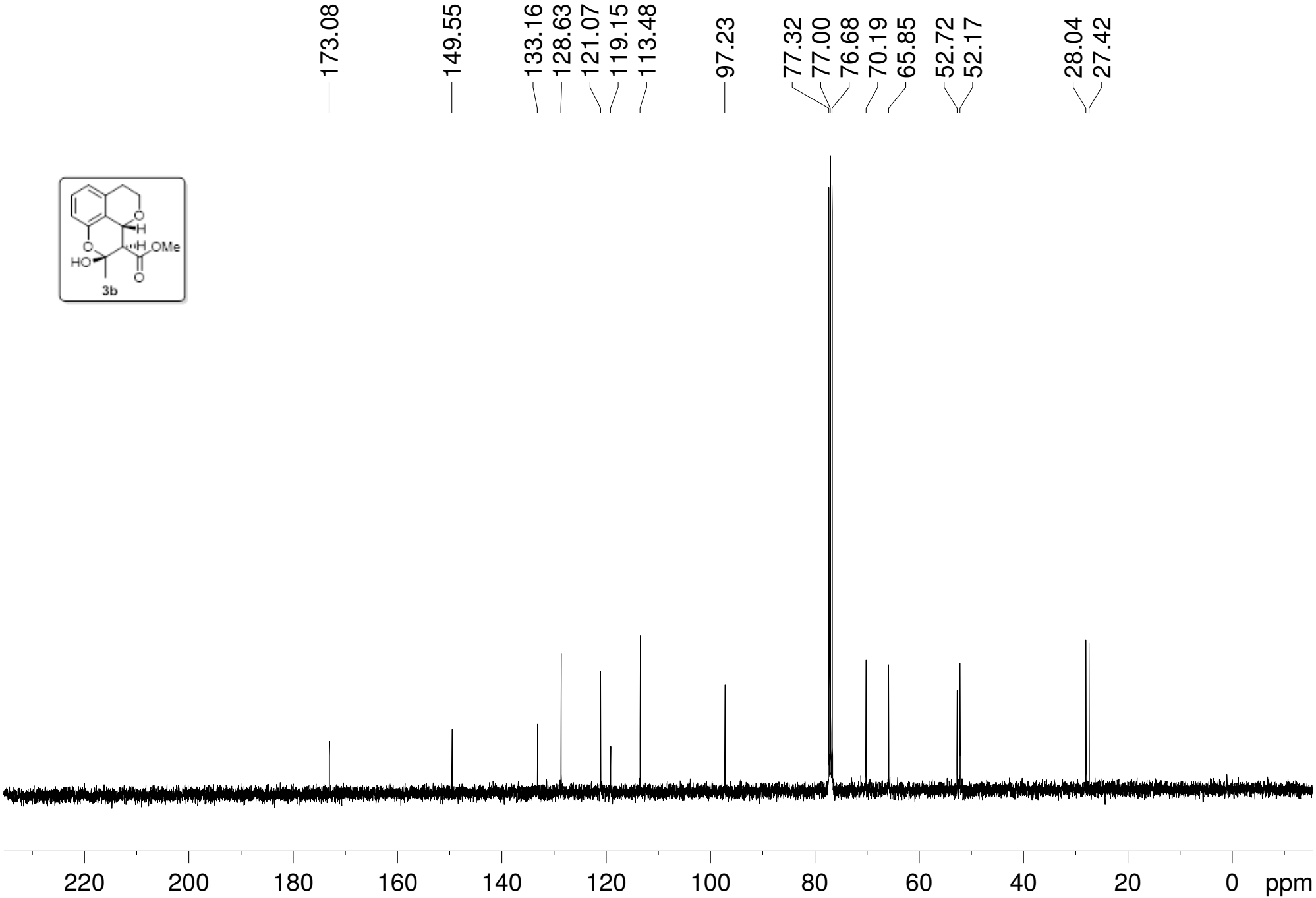
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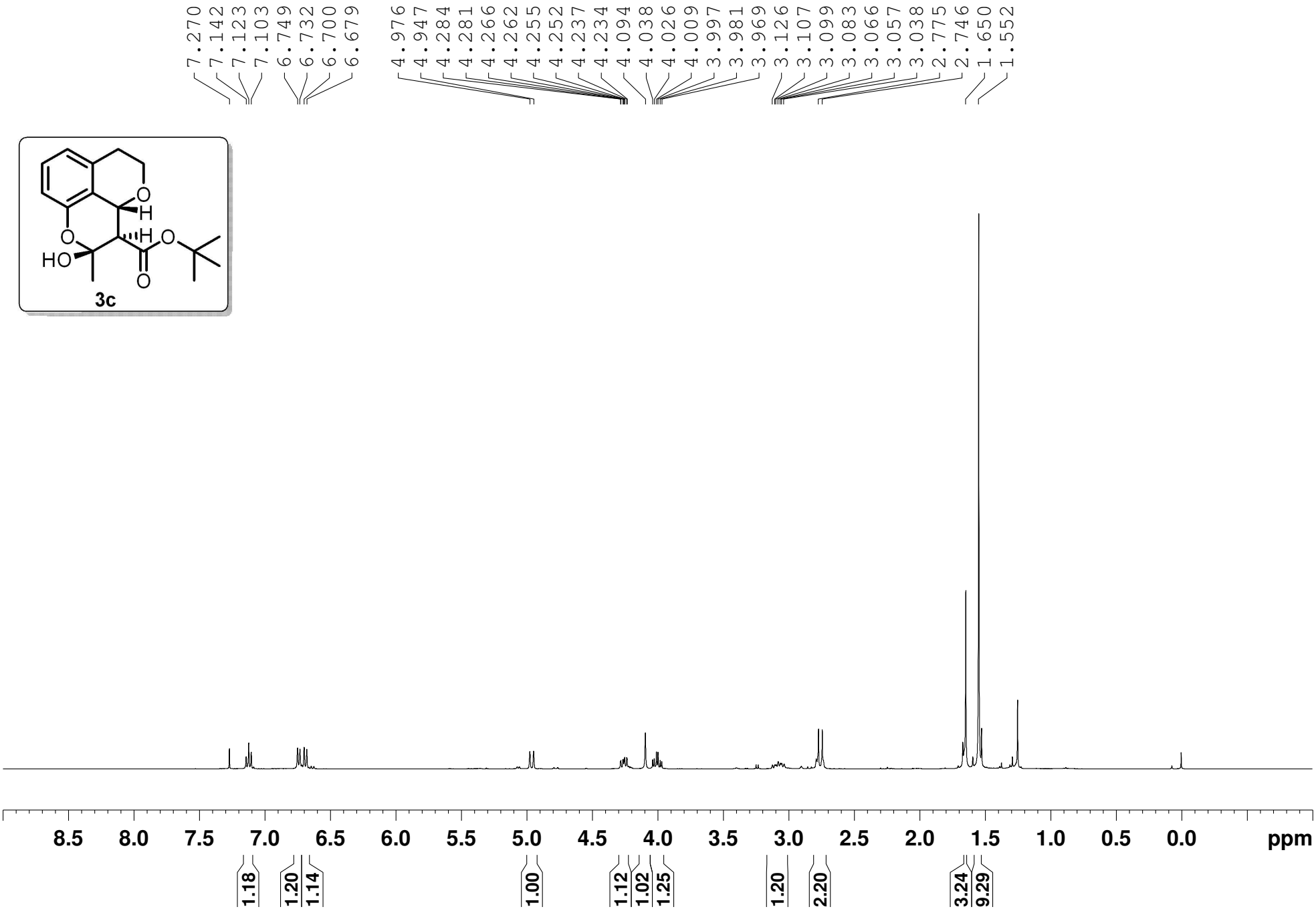
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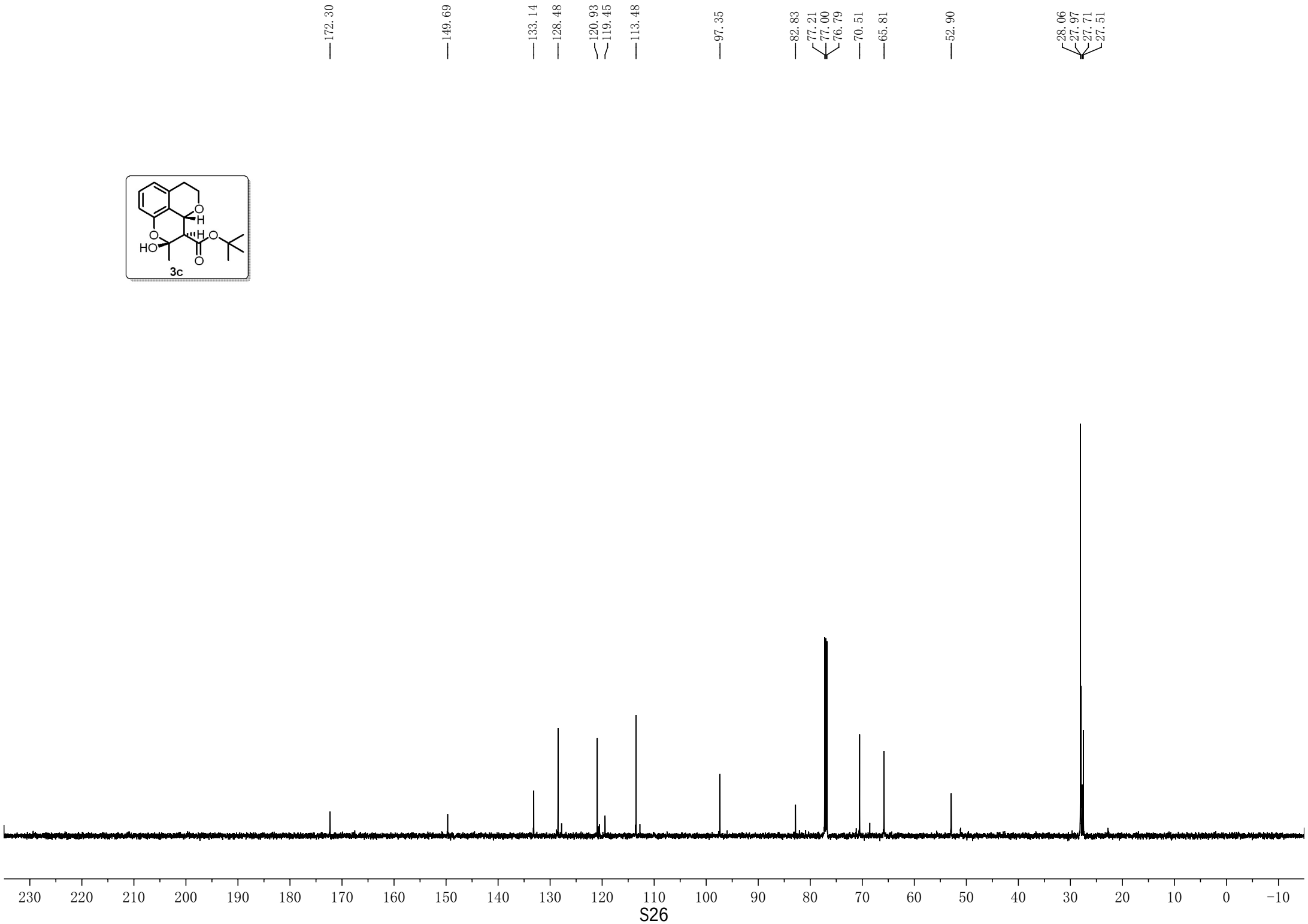
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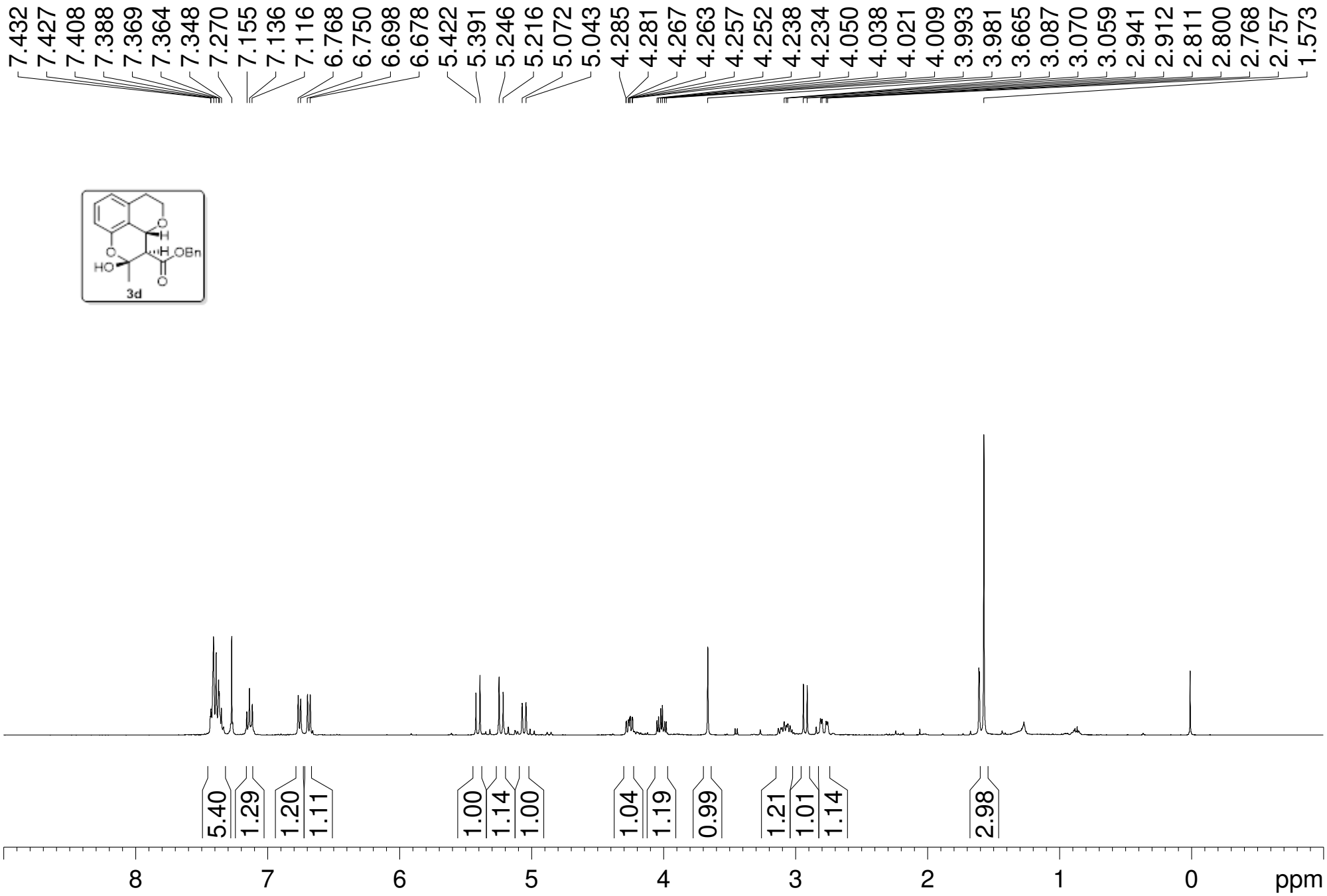
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O
HO
H
OBn
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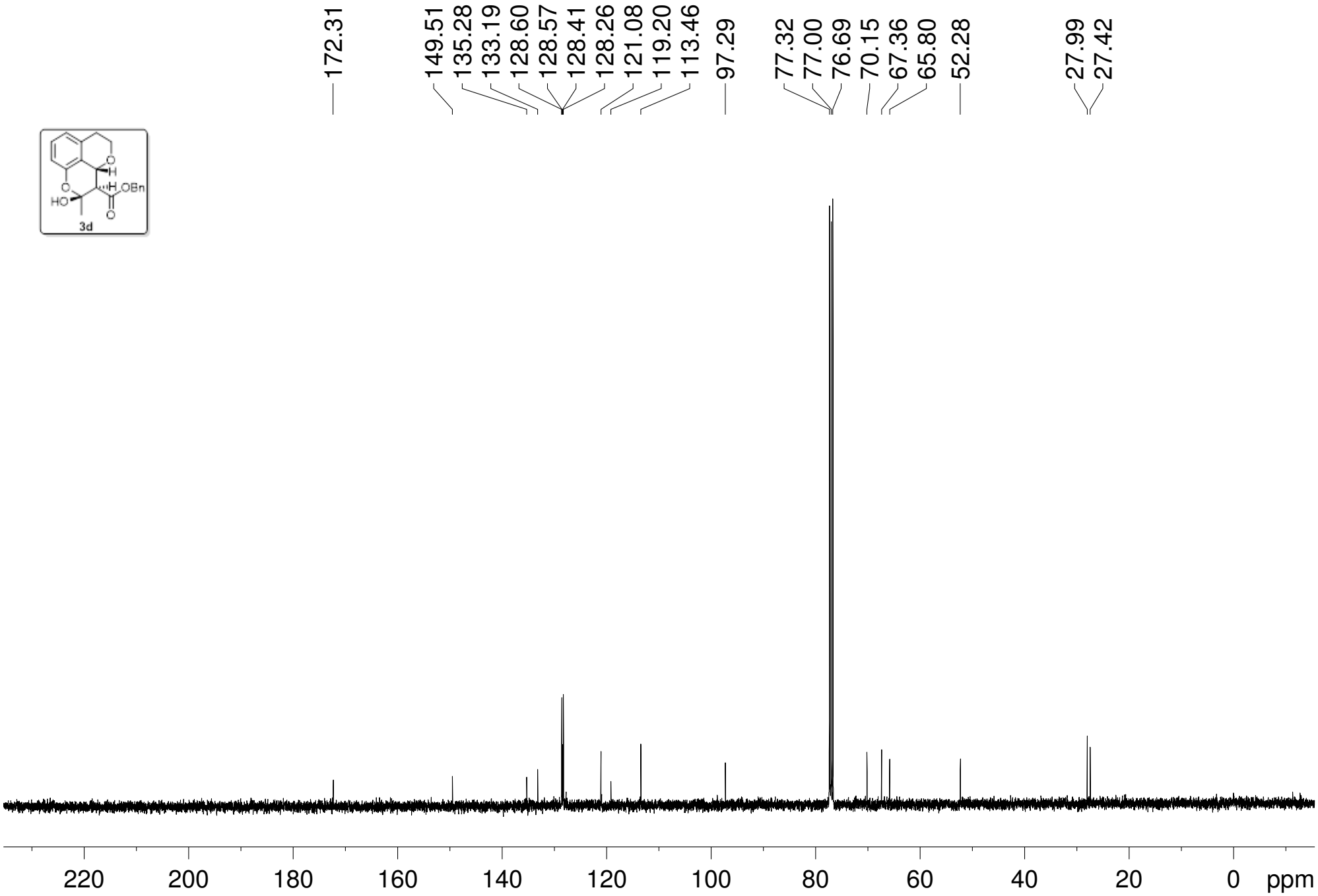
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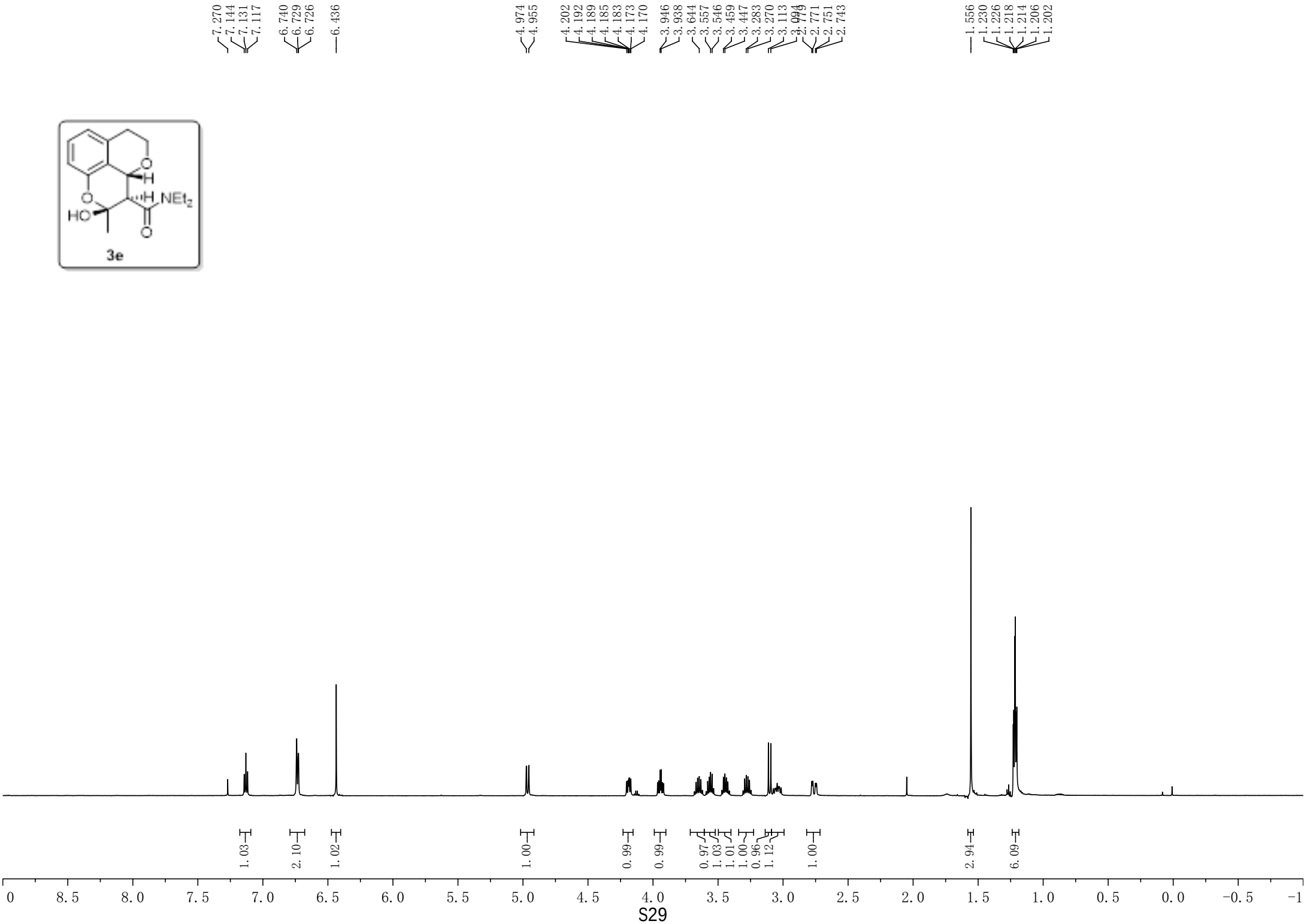
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O
H
NEt2
HO
O
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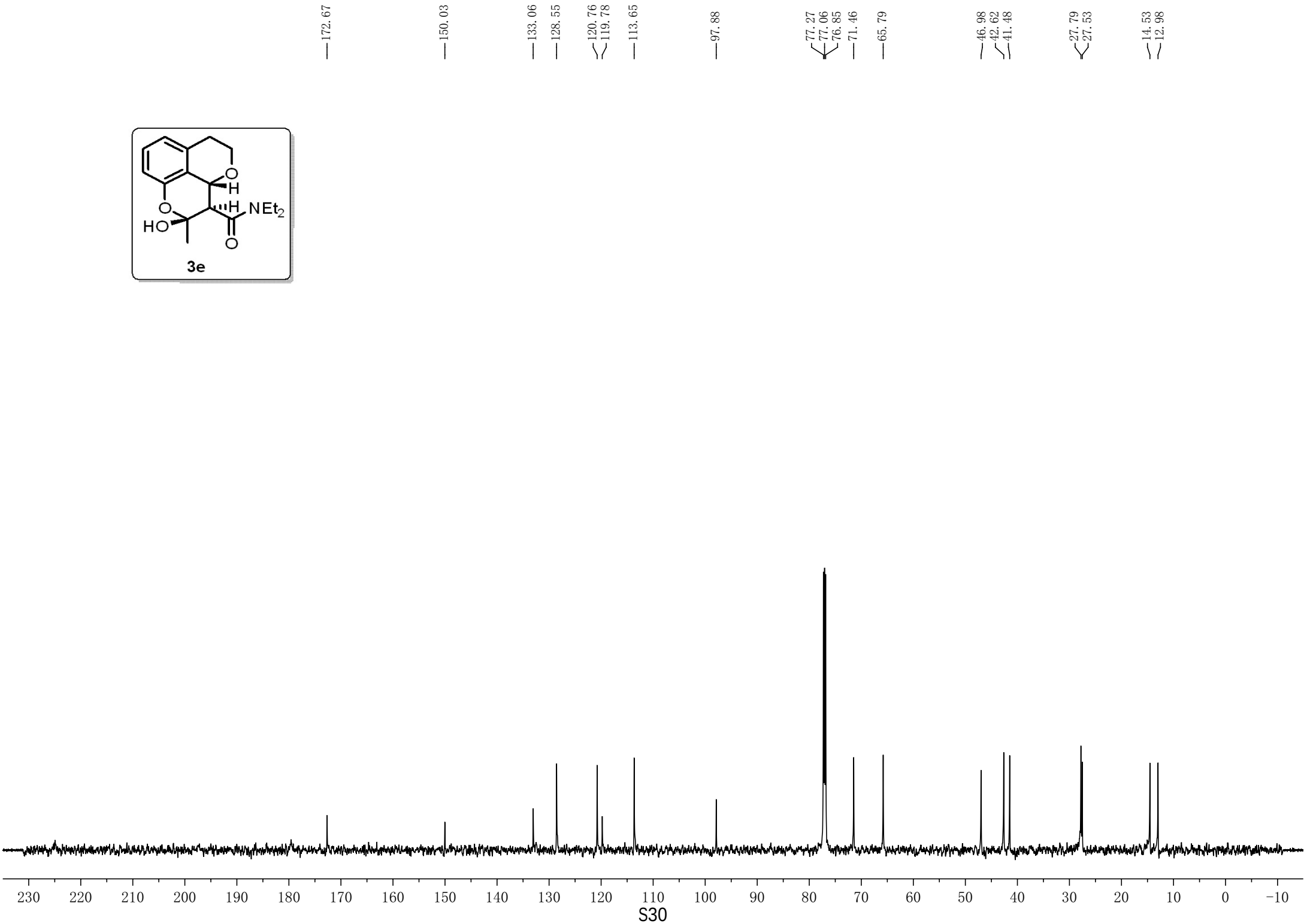
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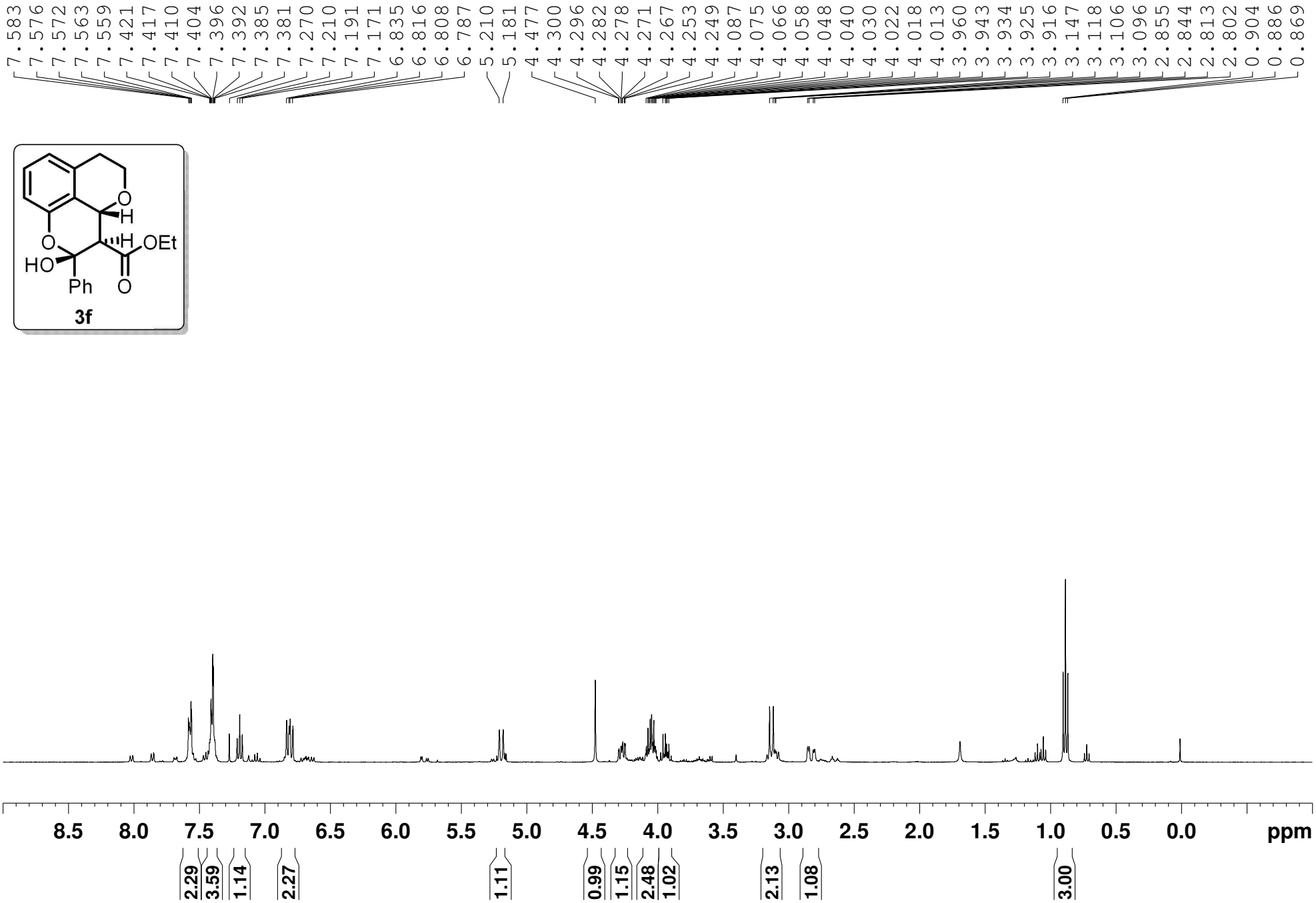
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Ph
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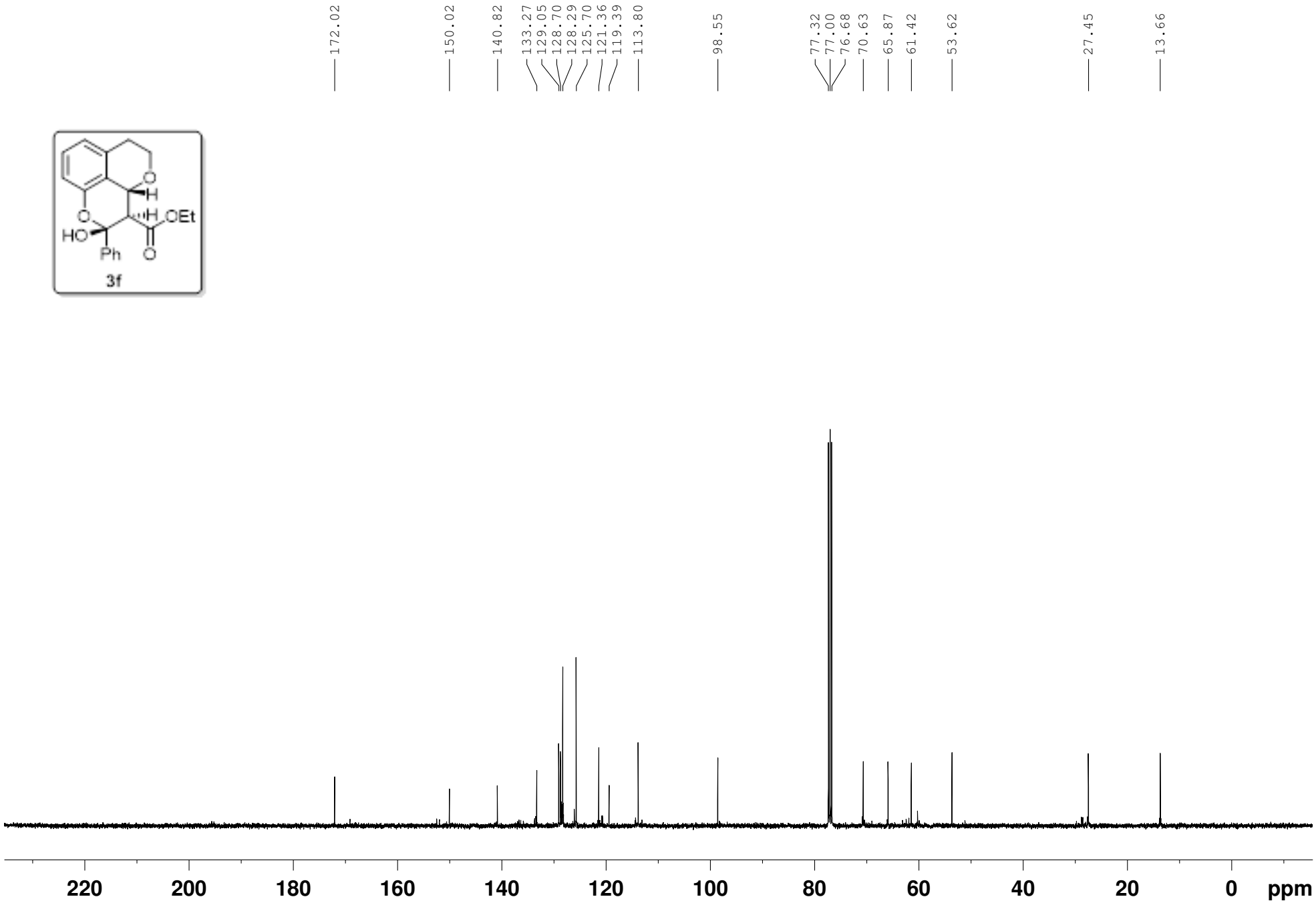
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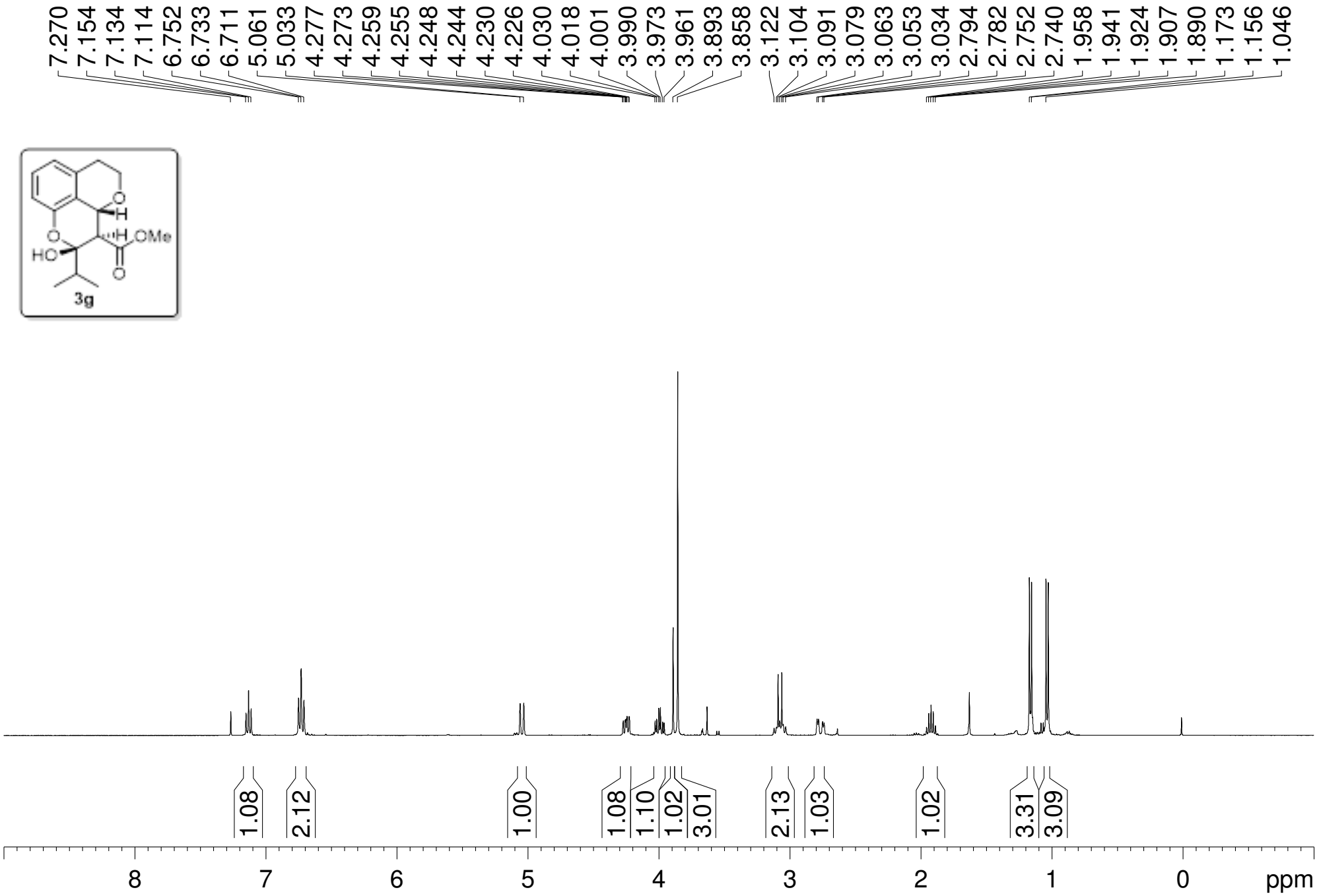
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4.018
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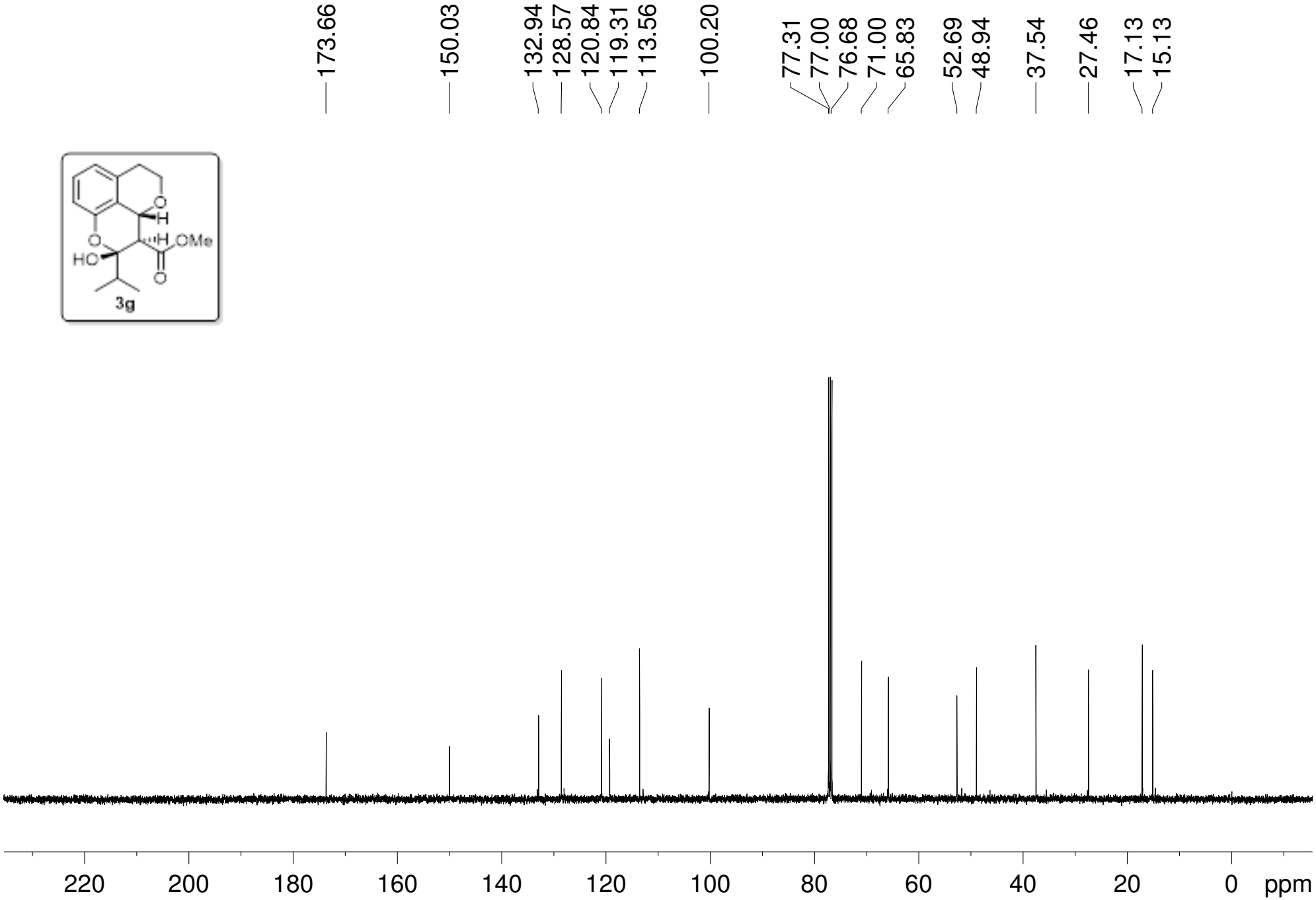
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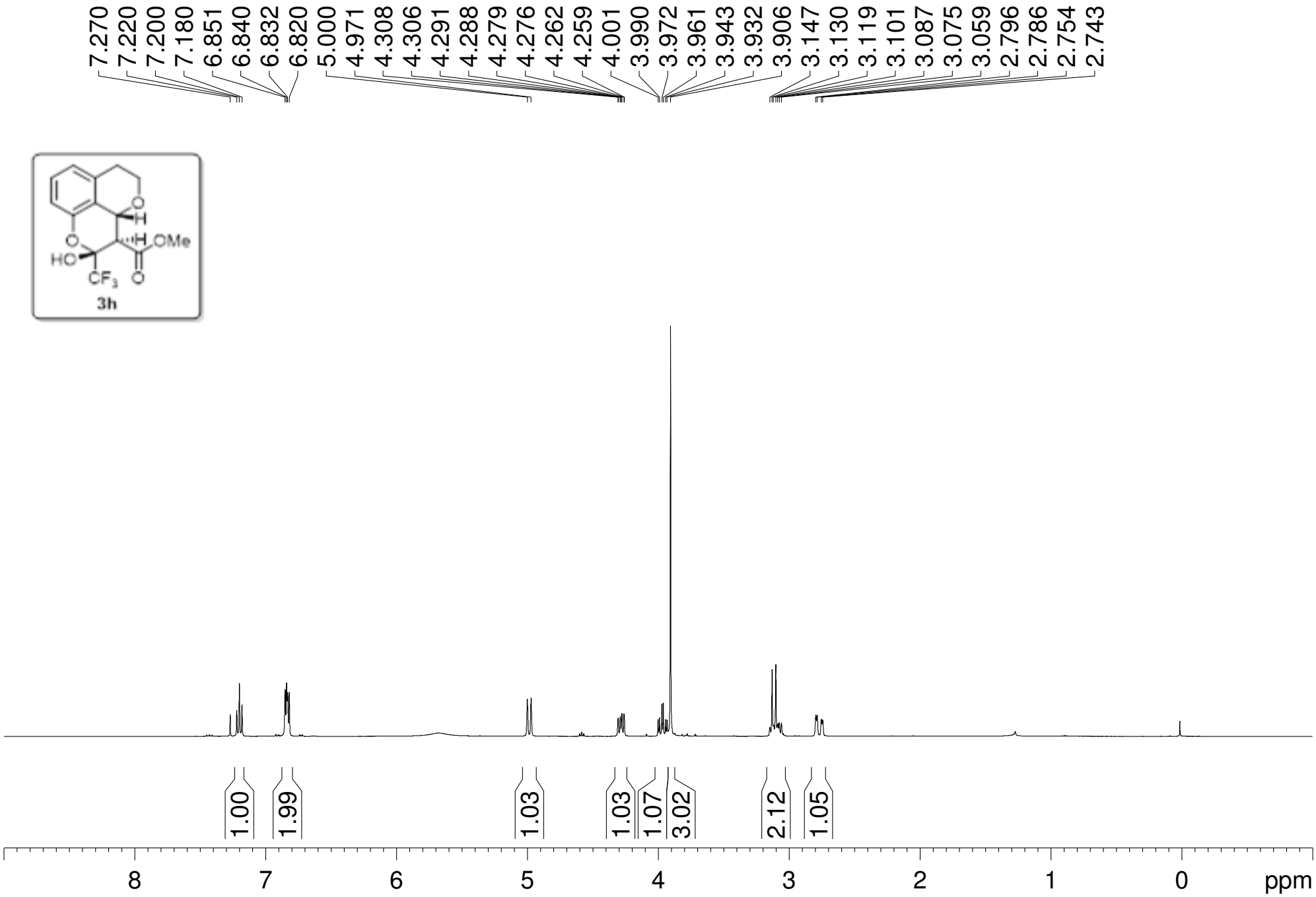
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3.119
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3.087
3.075
3.059
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2.786
2.754
2.743
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HO
CF3
3h
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1.99
1.03
1.03
1.07
3.02
2.12
1.05
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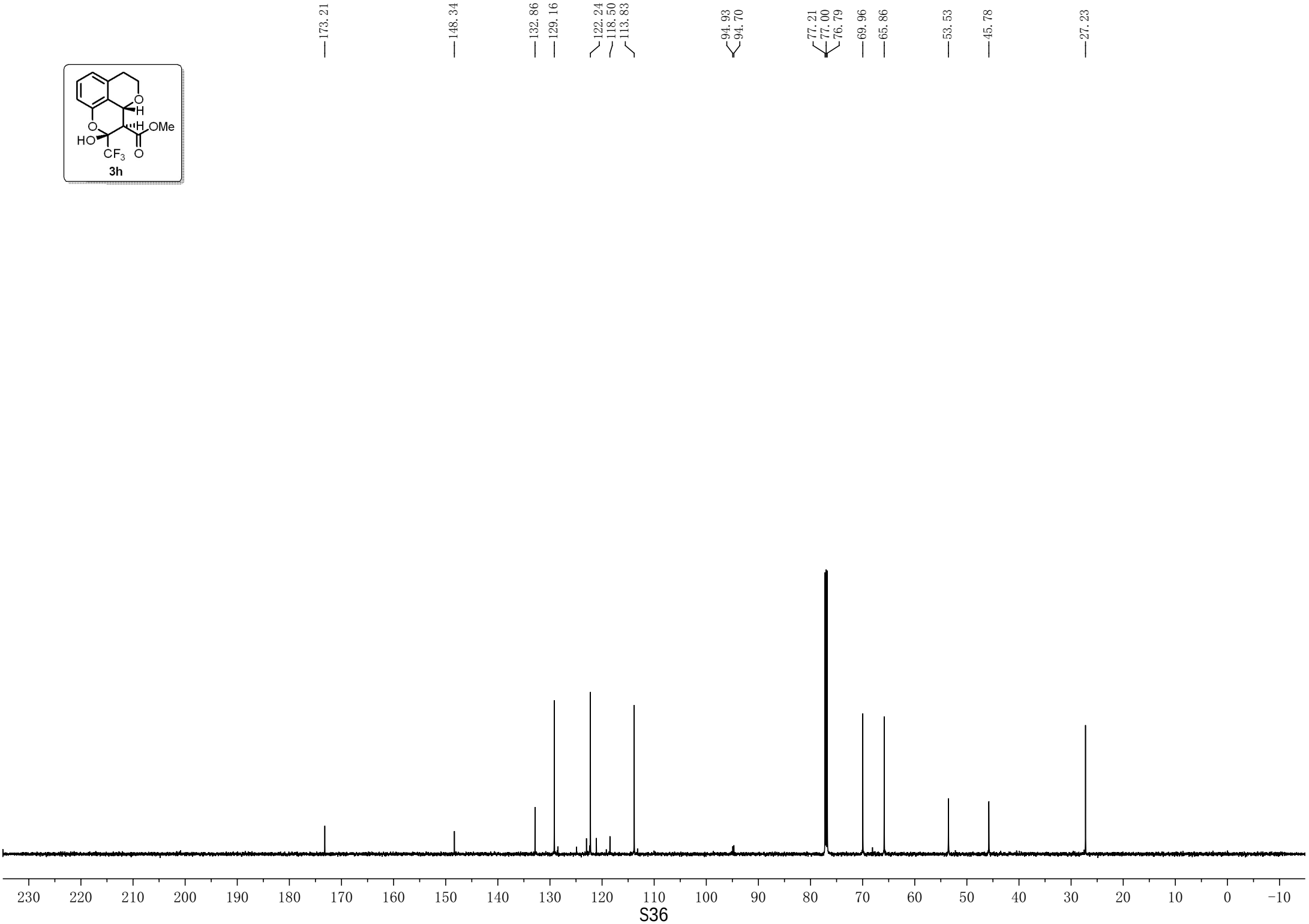
O
H
OMe
HO
CF3
O
3h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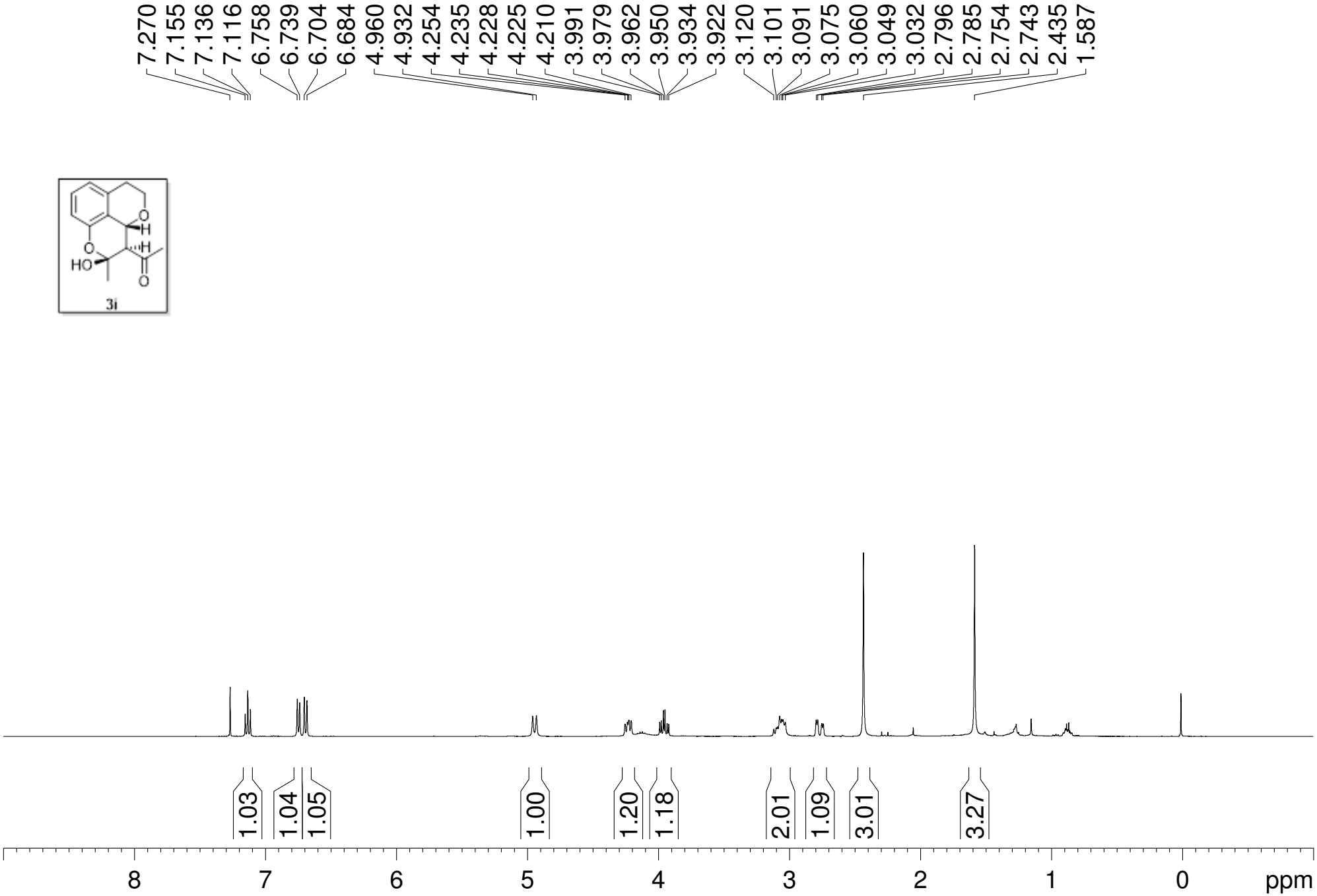
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H
O
HO
O
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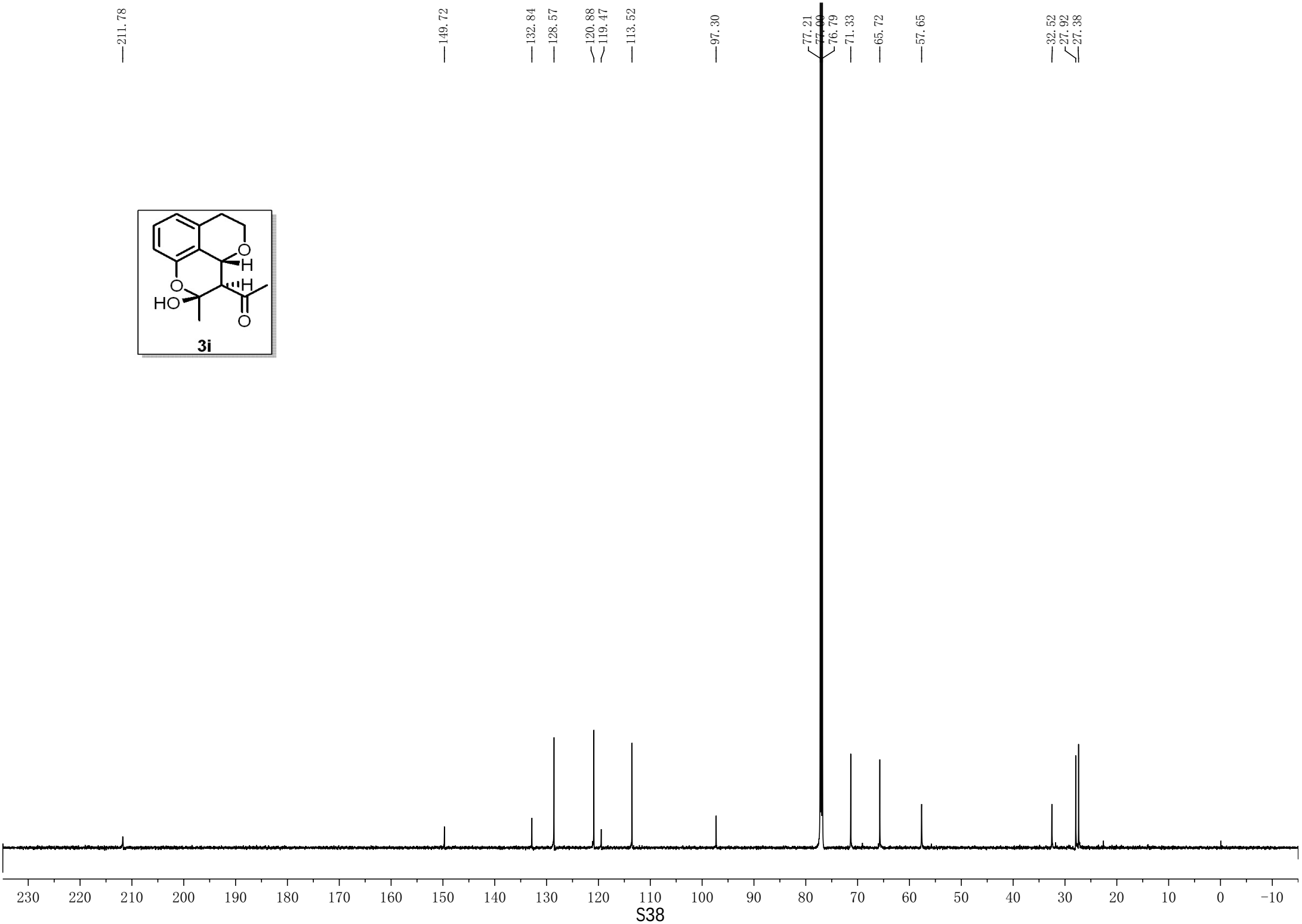
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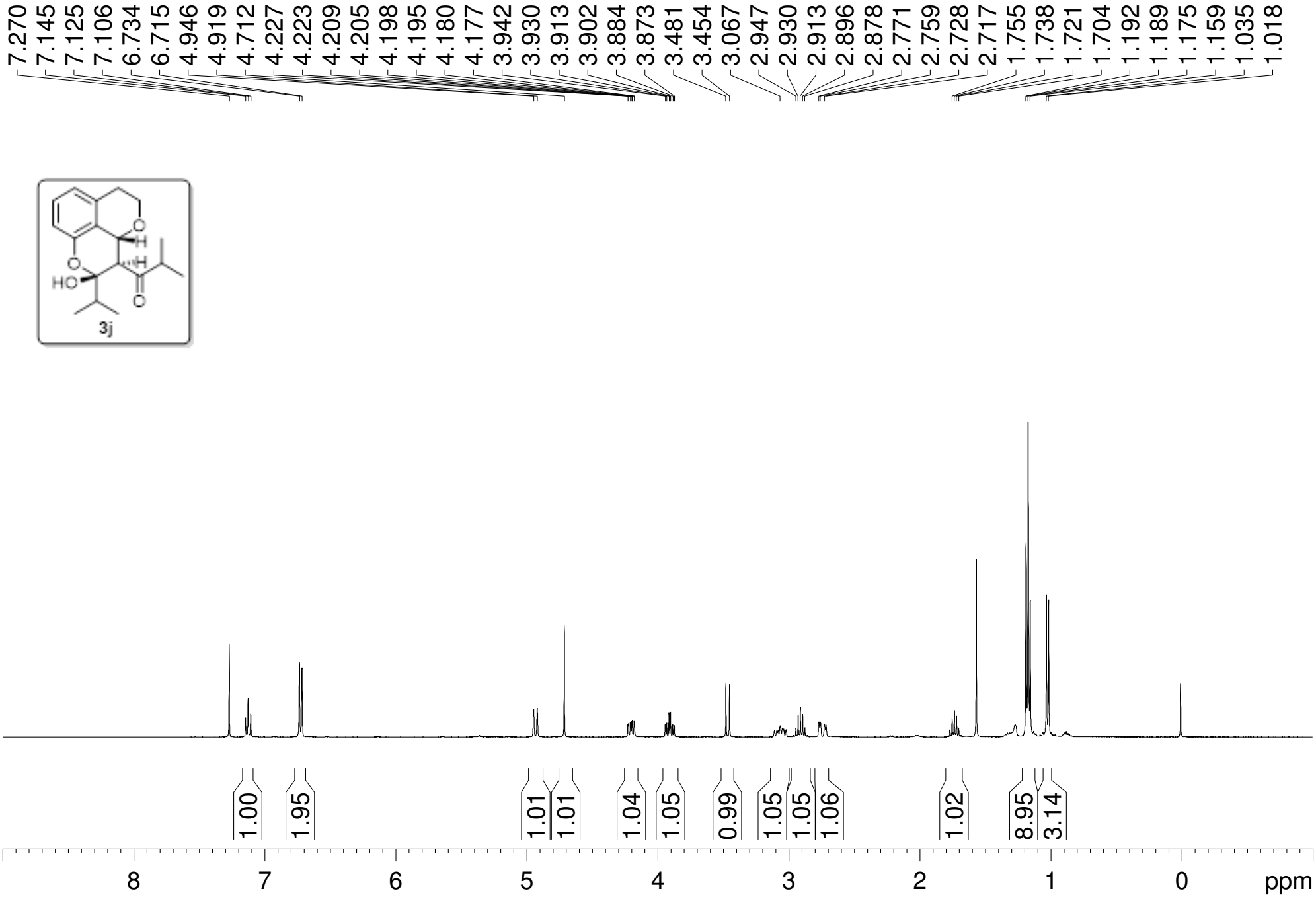
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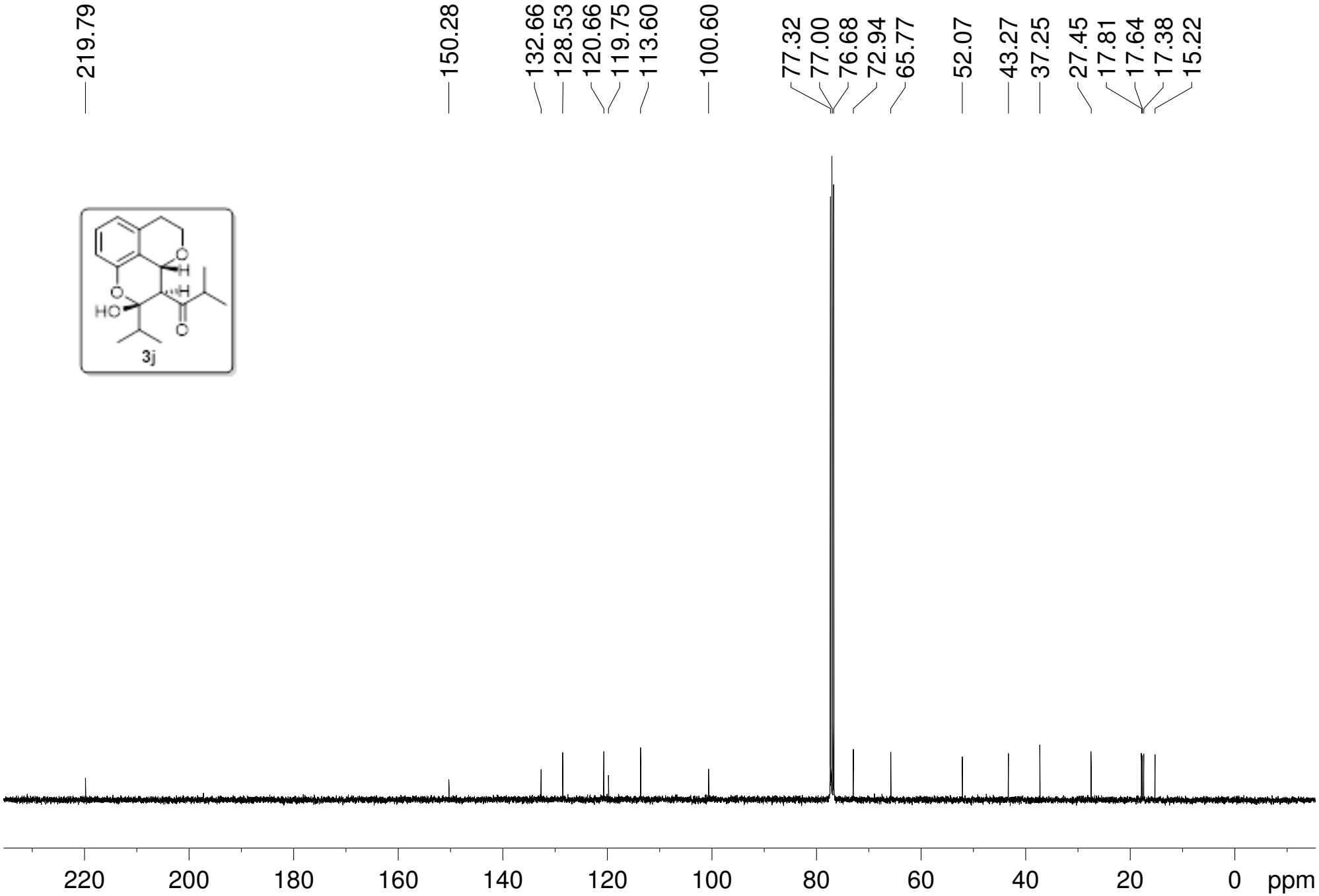
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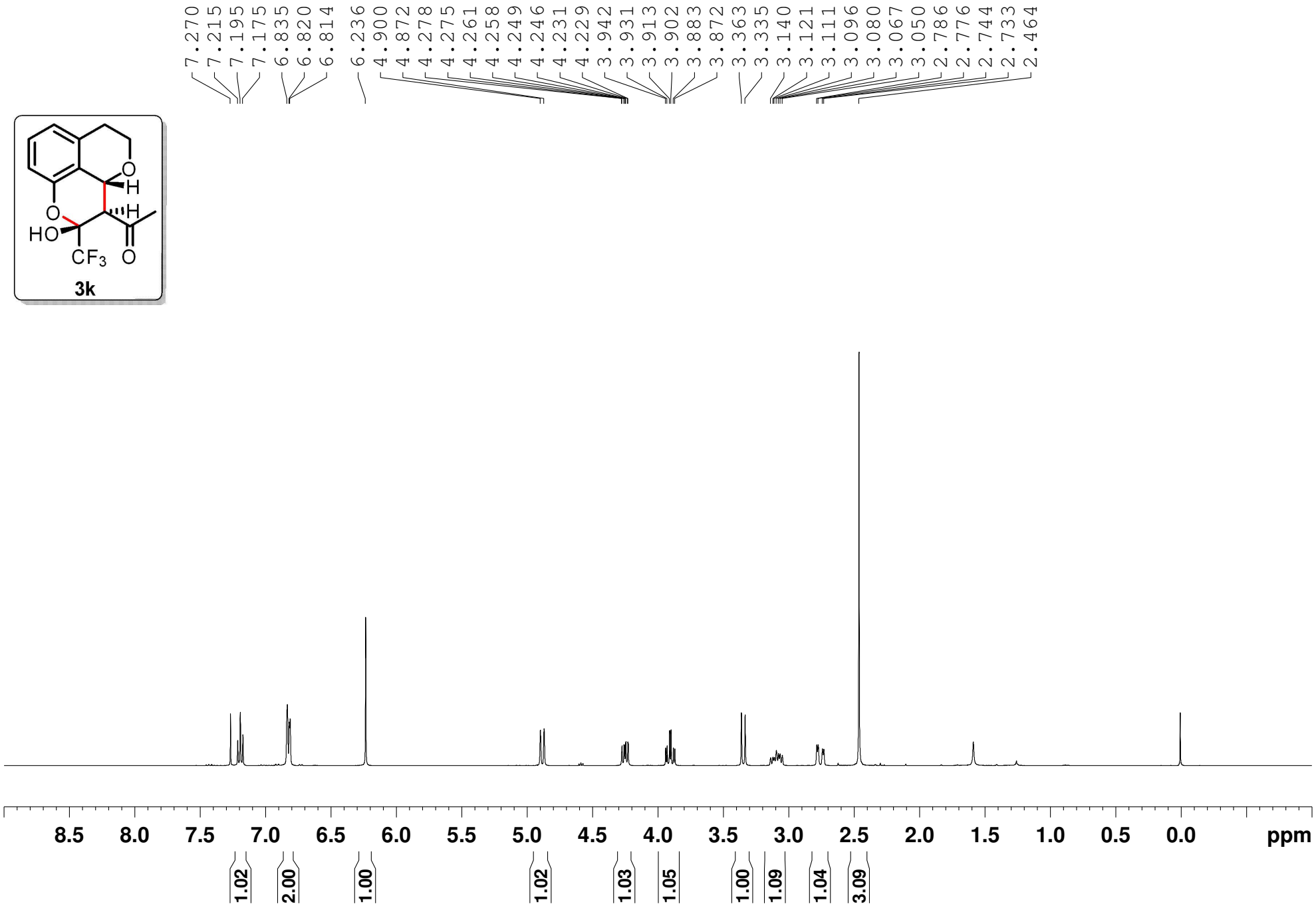
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O
H
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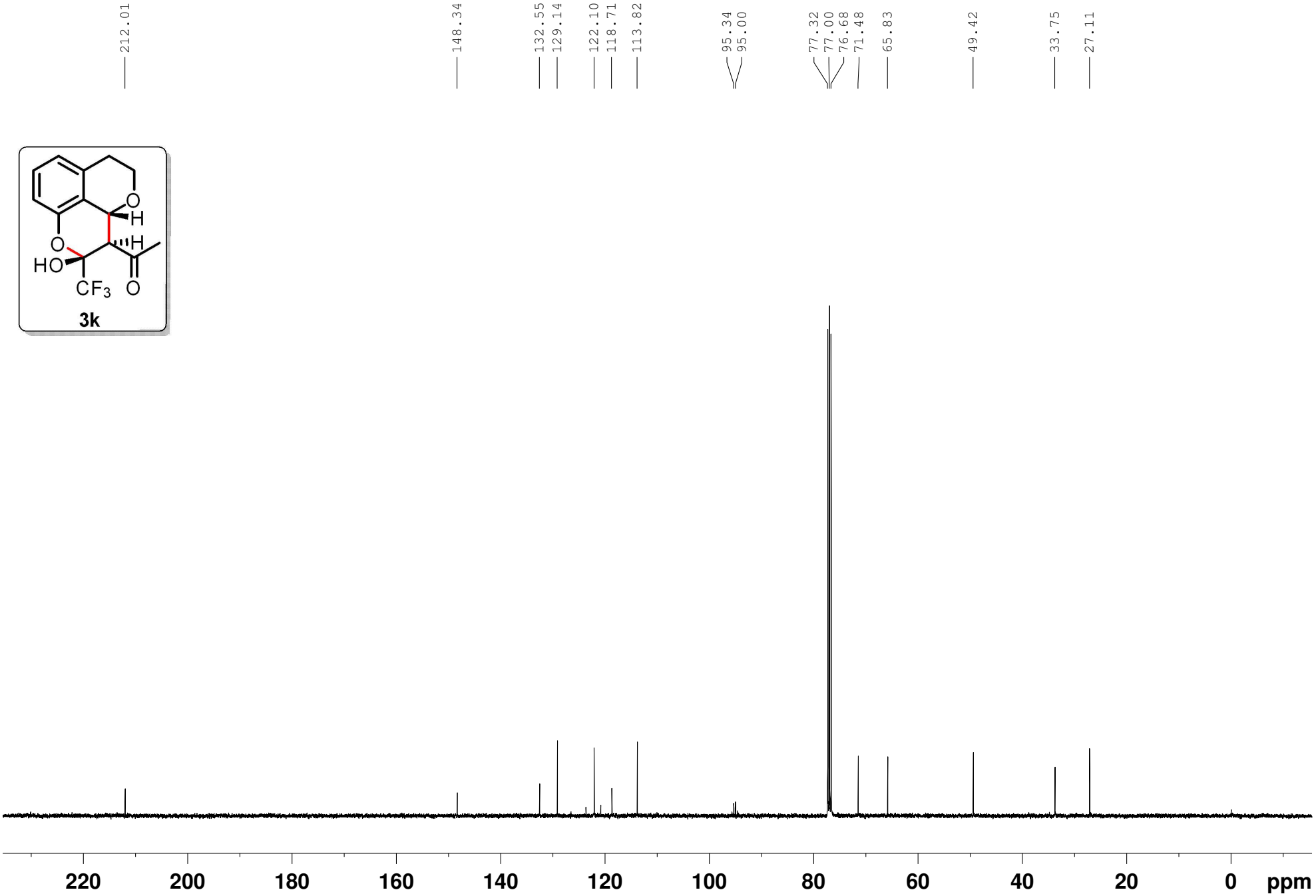
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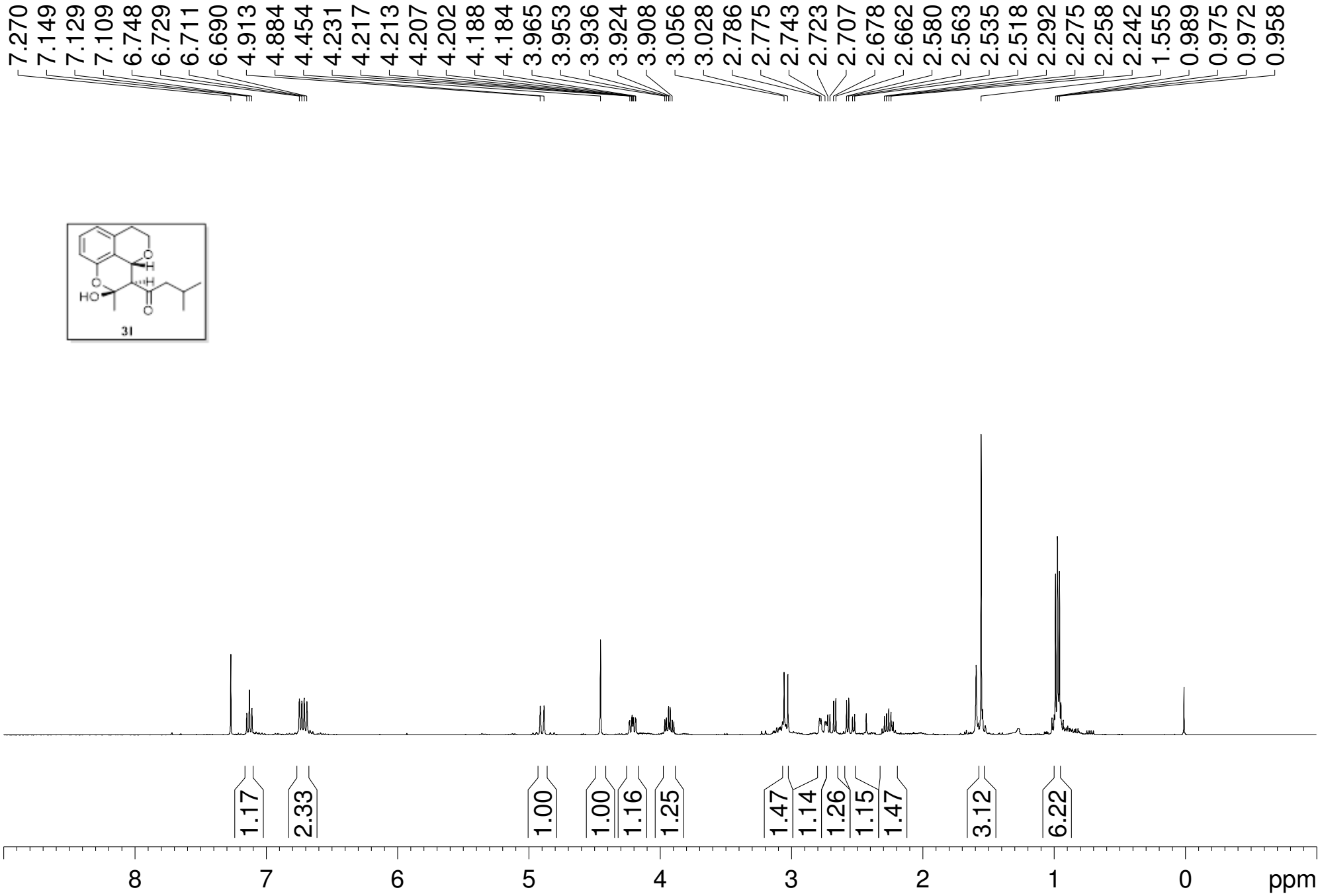
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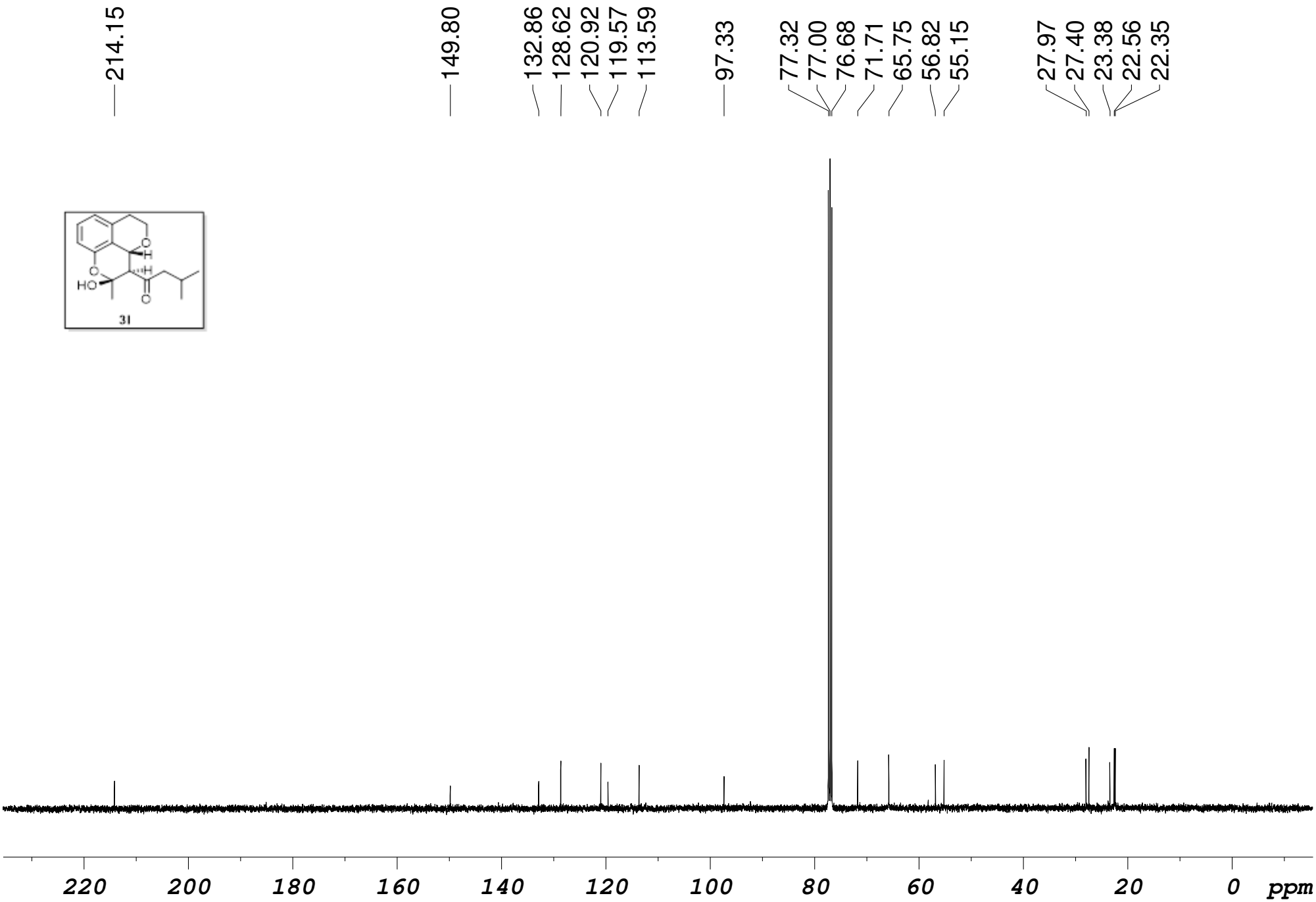
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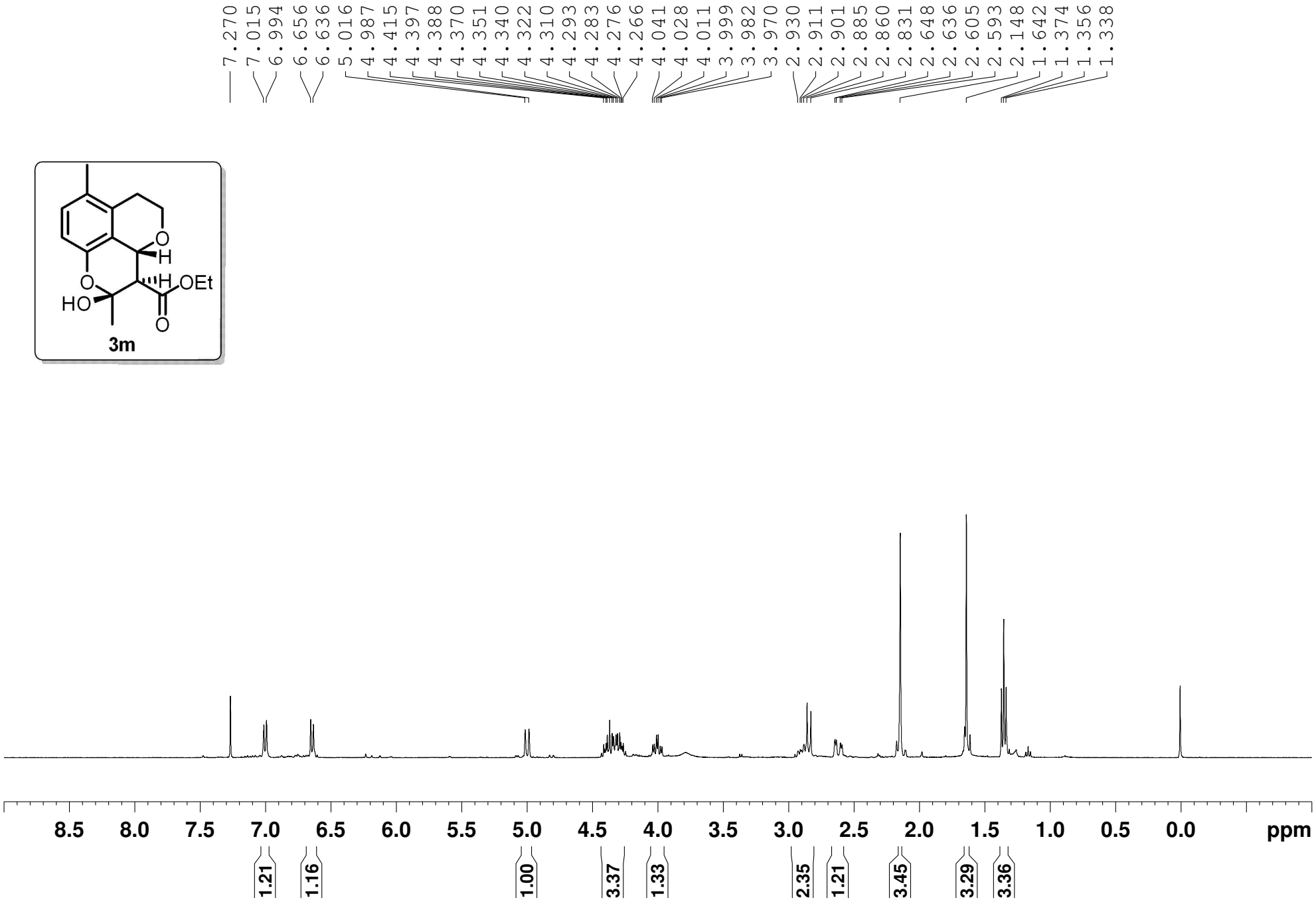
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H
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HO
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HO
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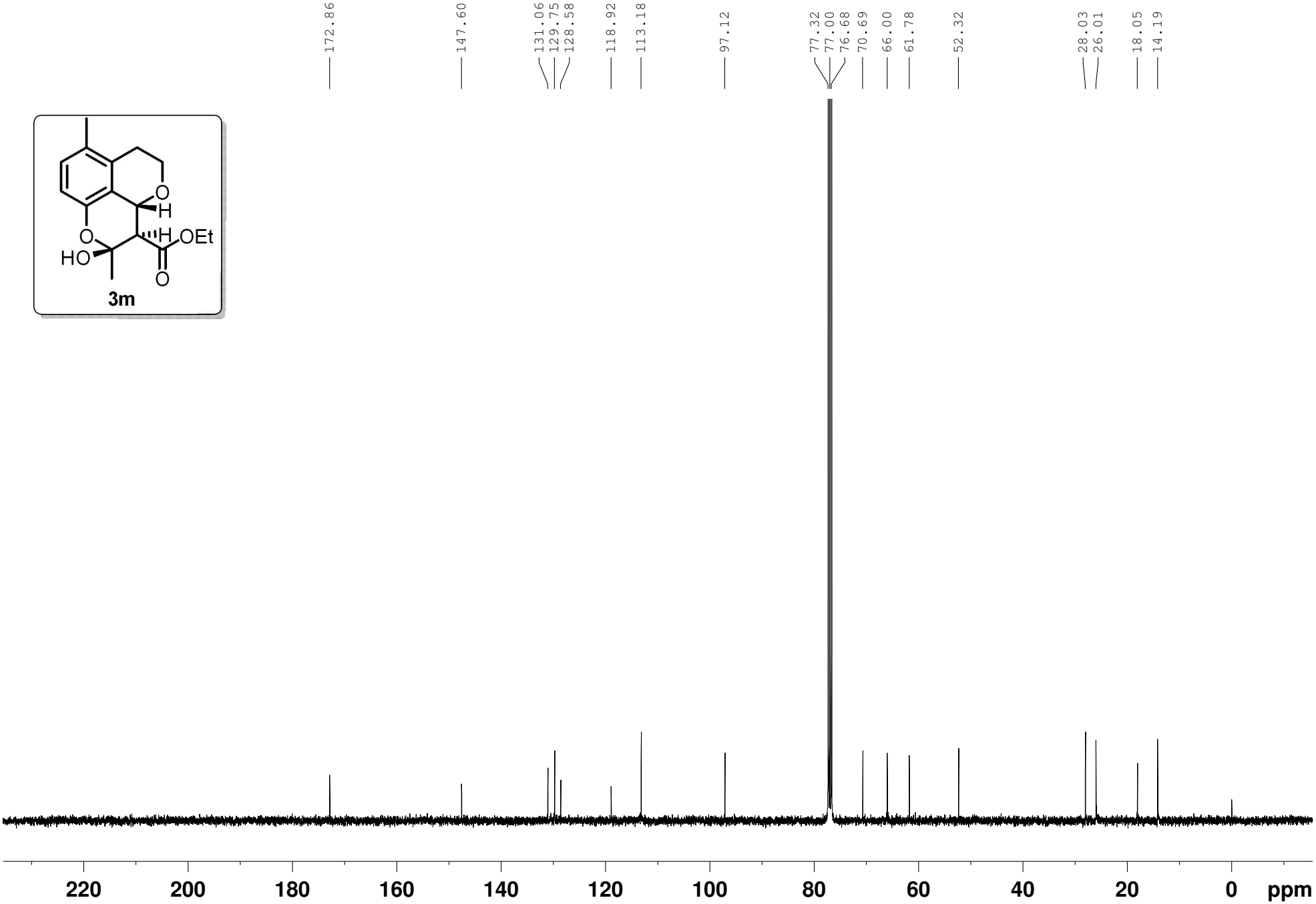
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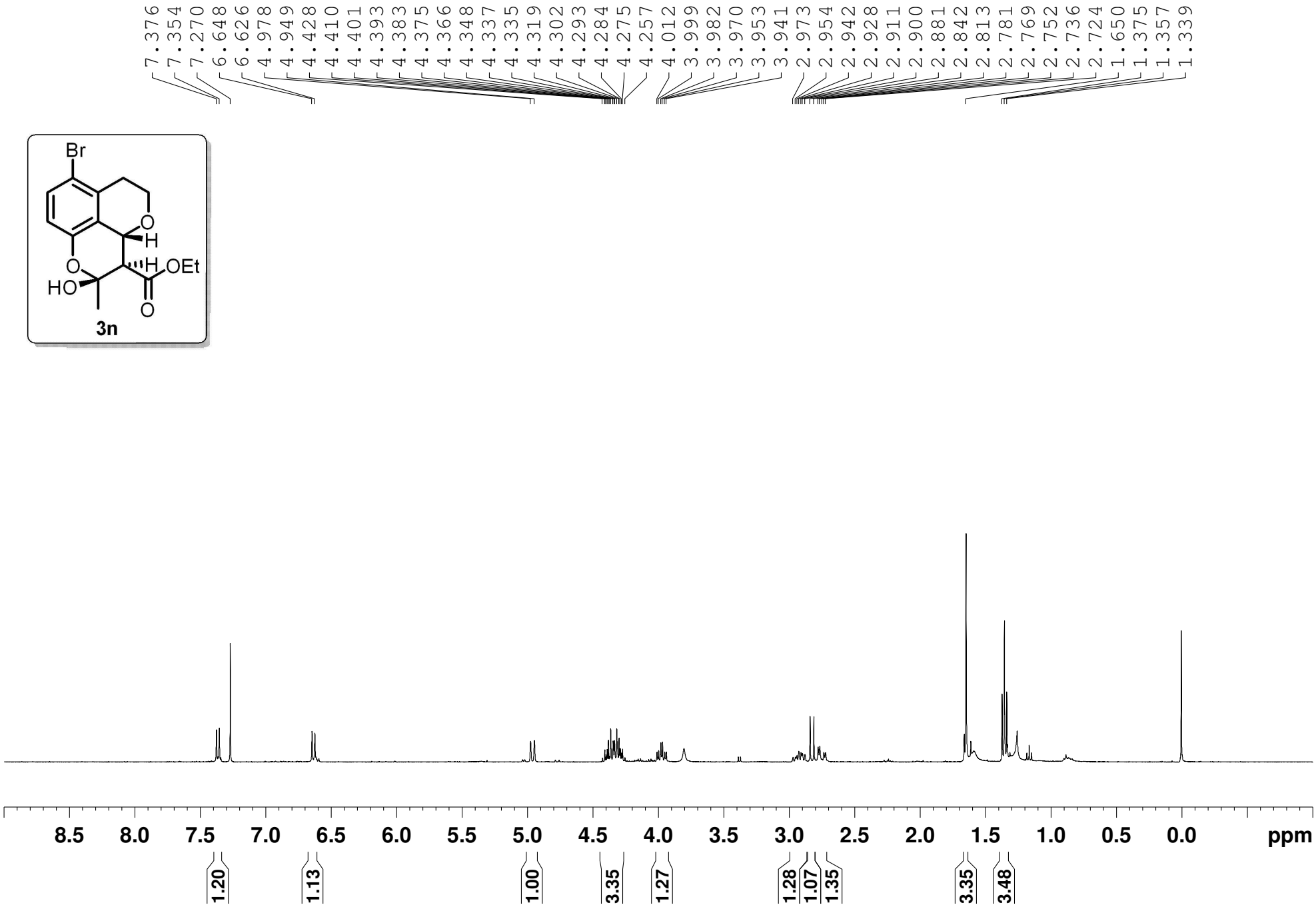
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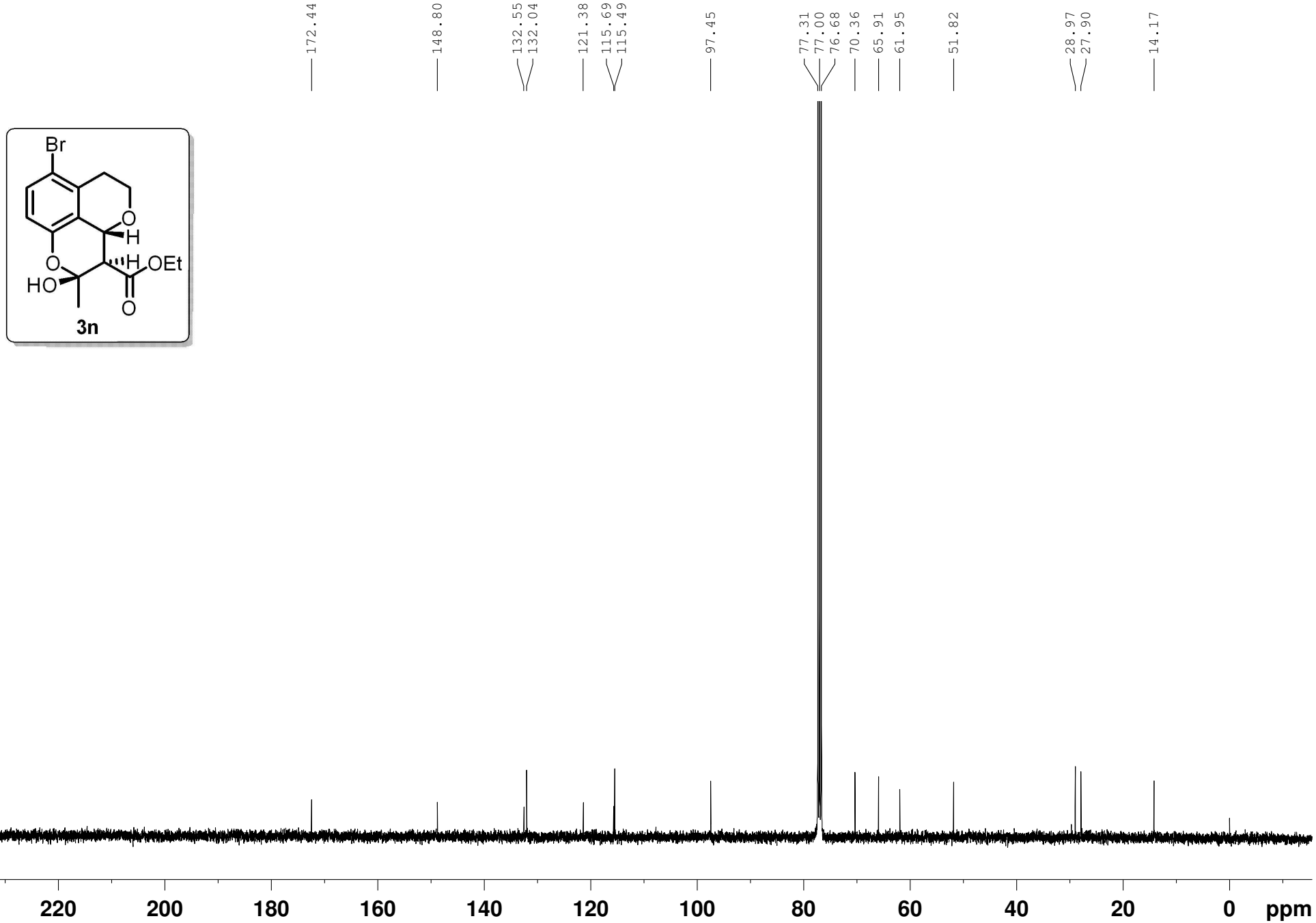
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Br
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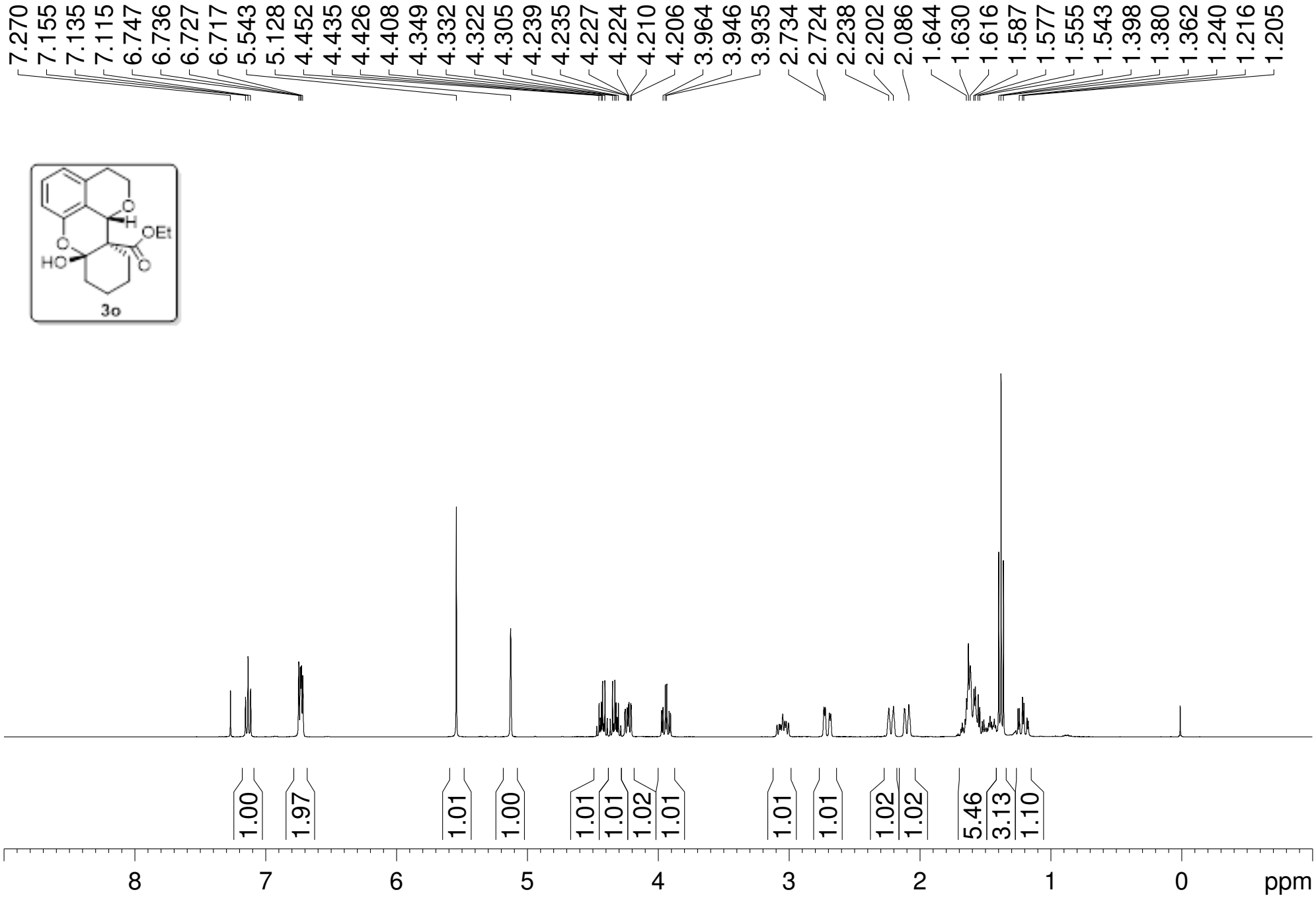
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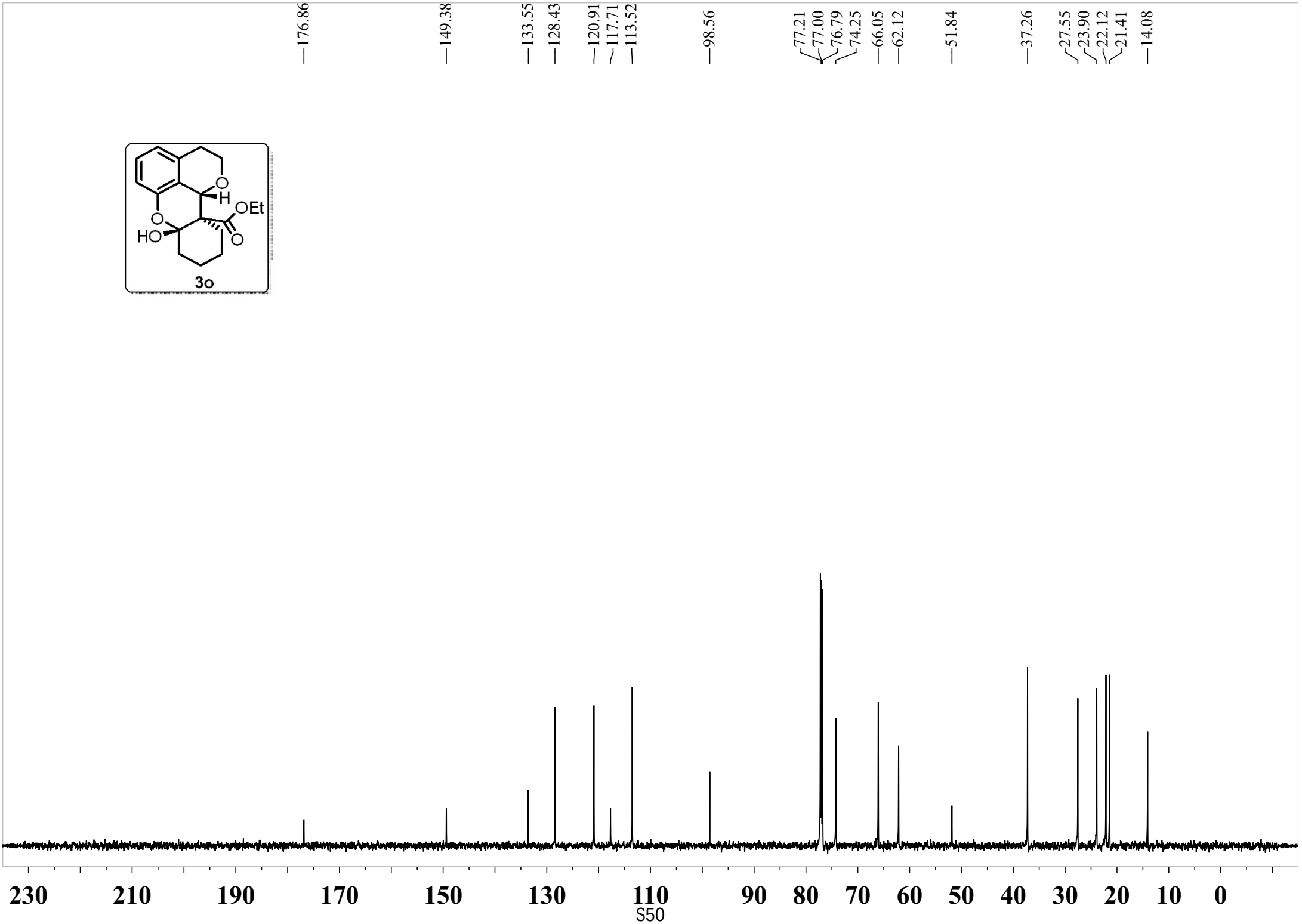
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H
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O
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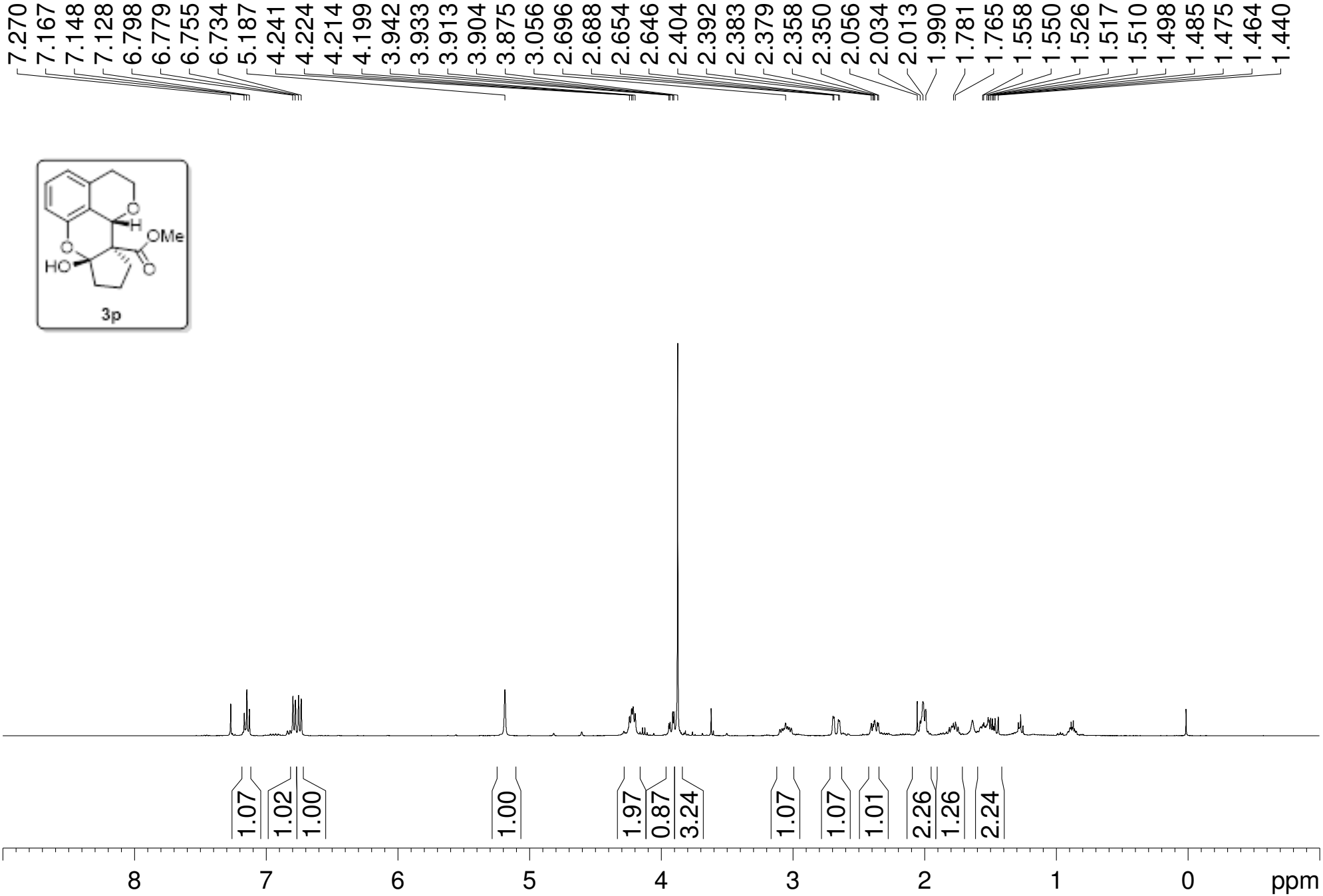
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1.510
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HO
3p
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1.02
1.00
1.00
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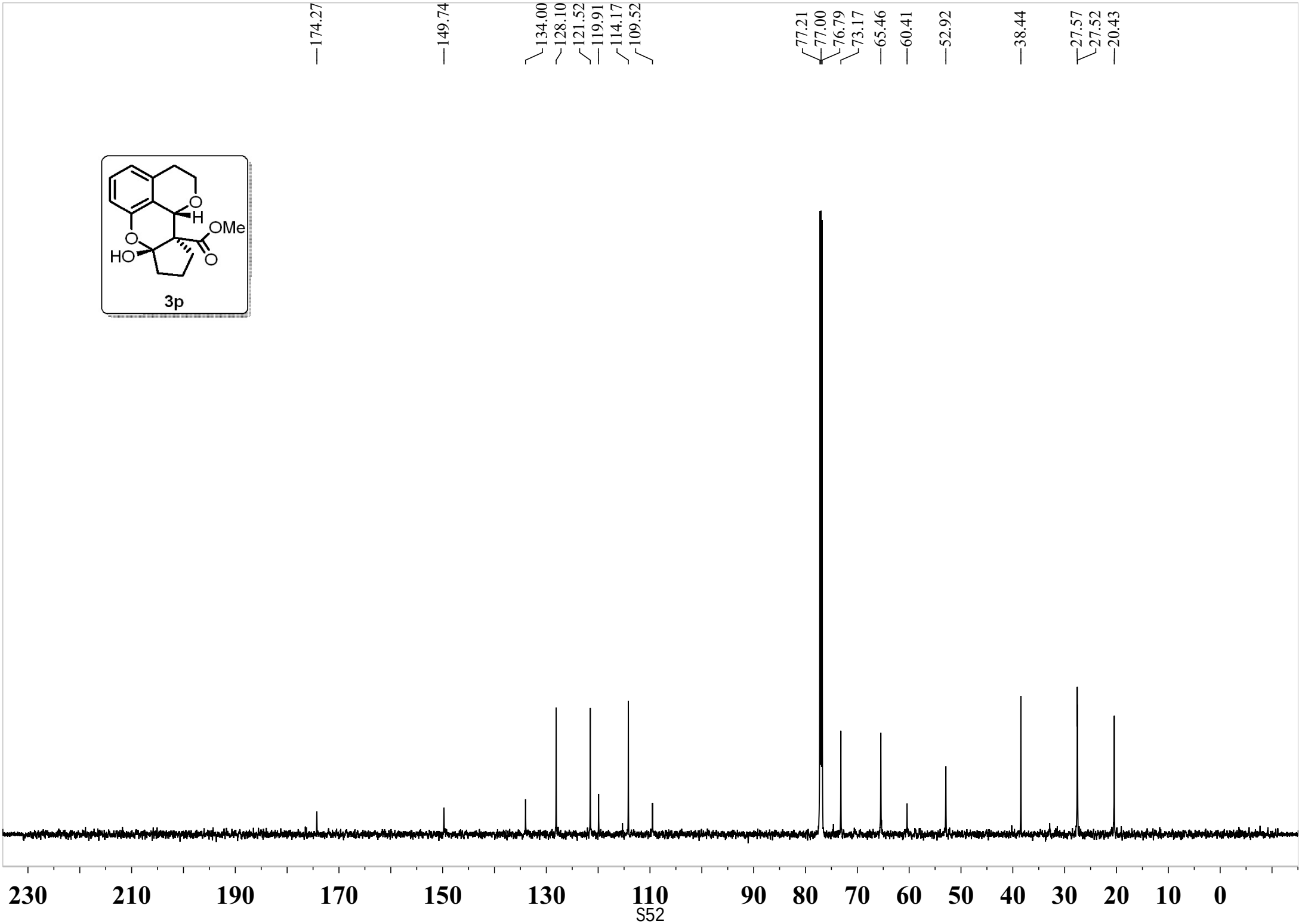
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H
OMe
O
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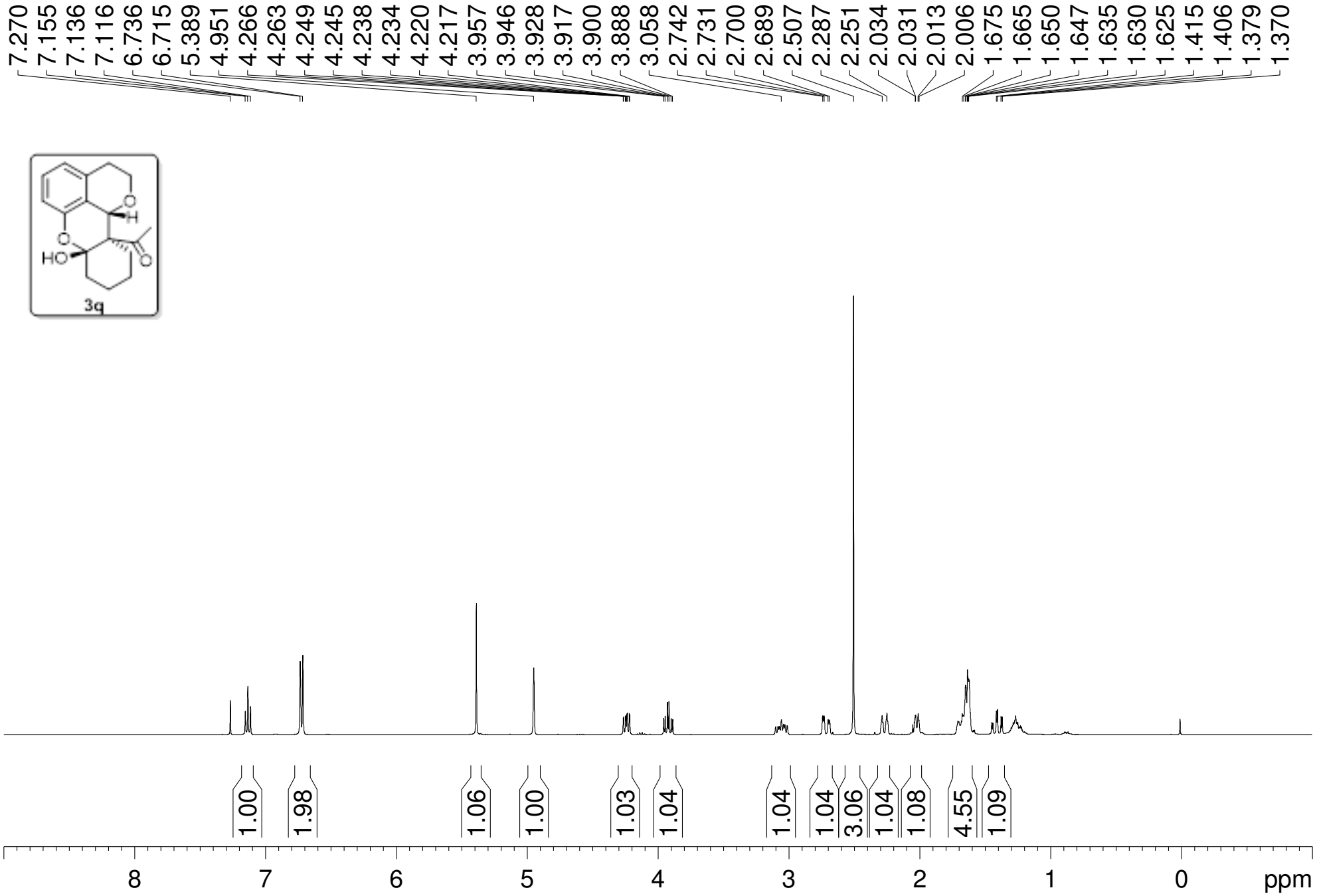
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4.220
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3.928
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3.900
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1.625
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1.04
1.04
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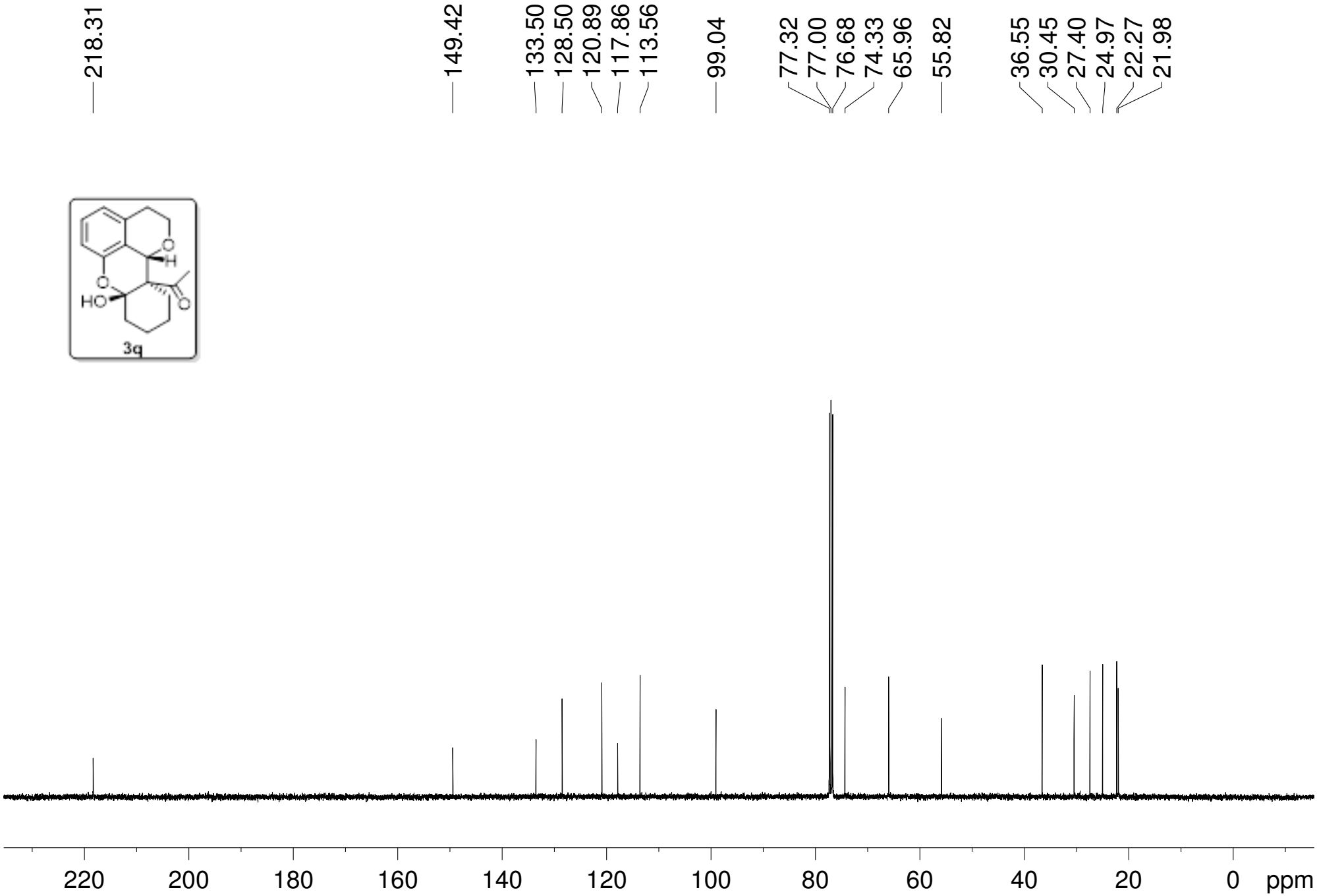
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36.55
30.45
27.40
24.97
22.27
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HO
O
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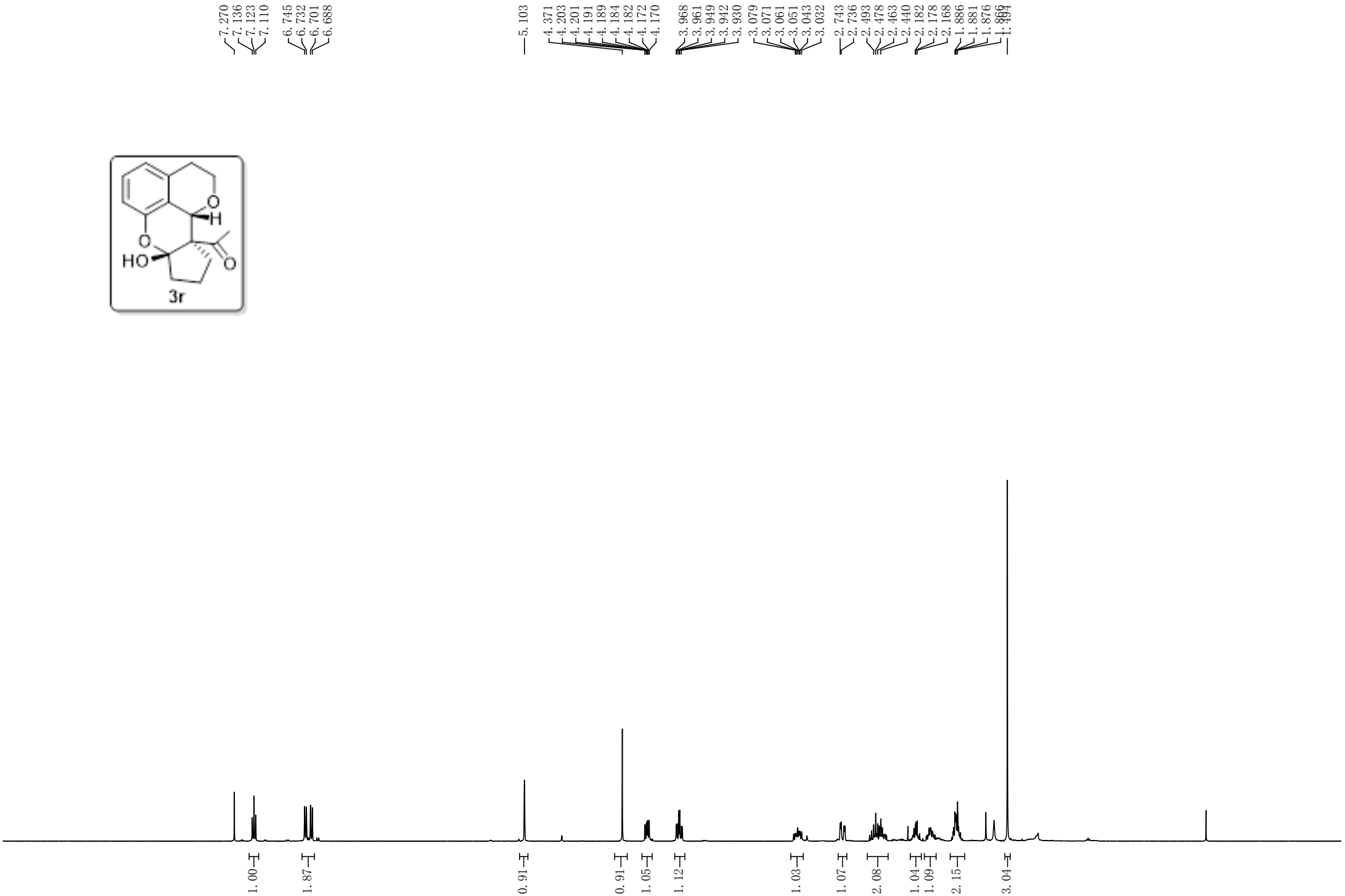
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1.866
1.494
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HO
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1.09
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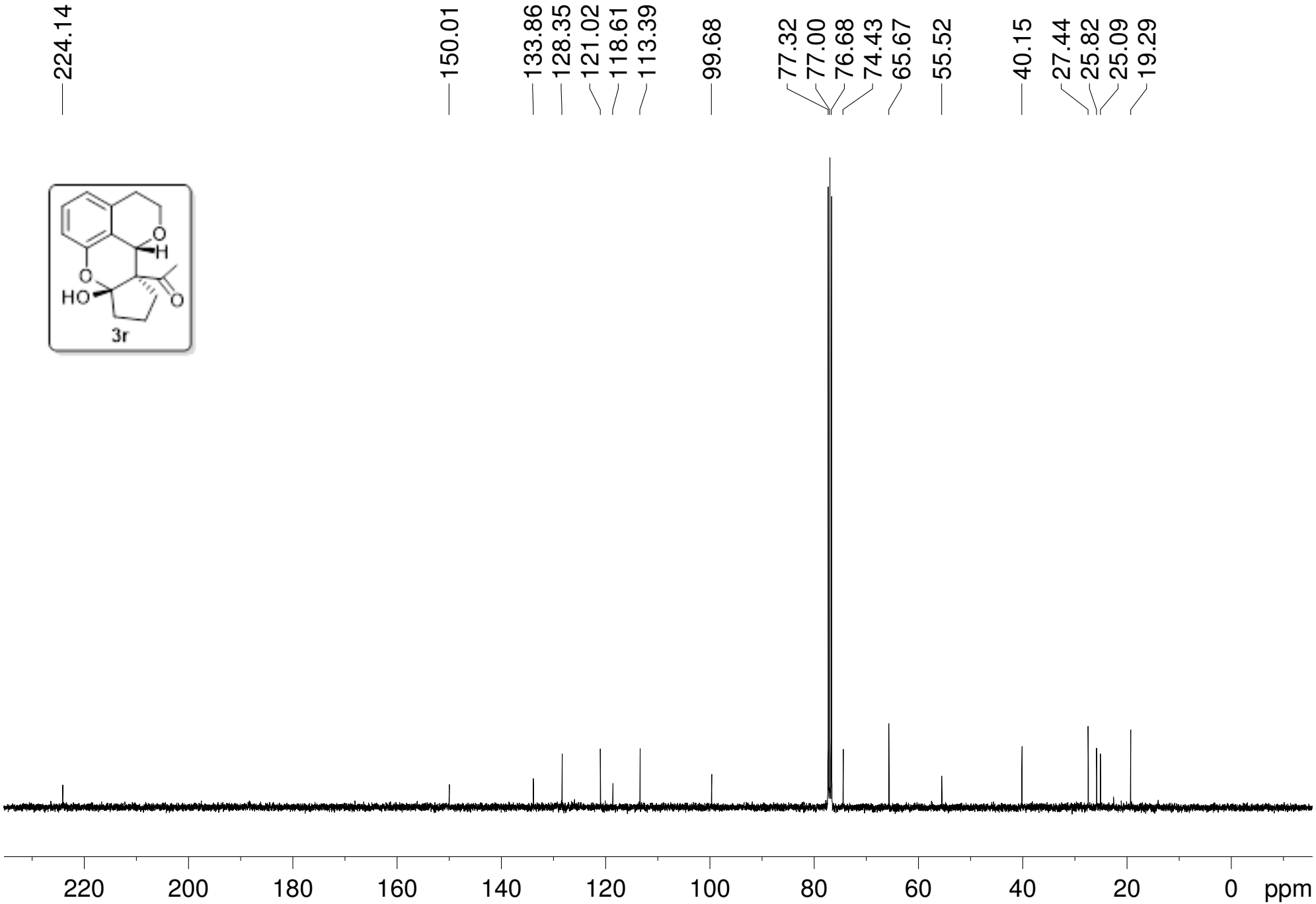
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25.09
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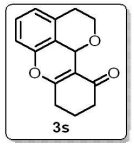
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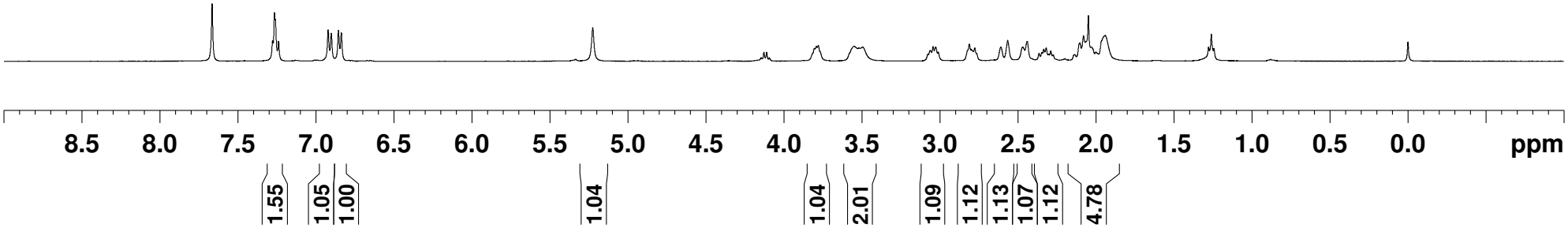
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3.011
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2.611
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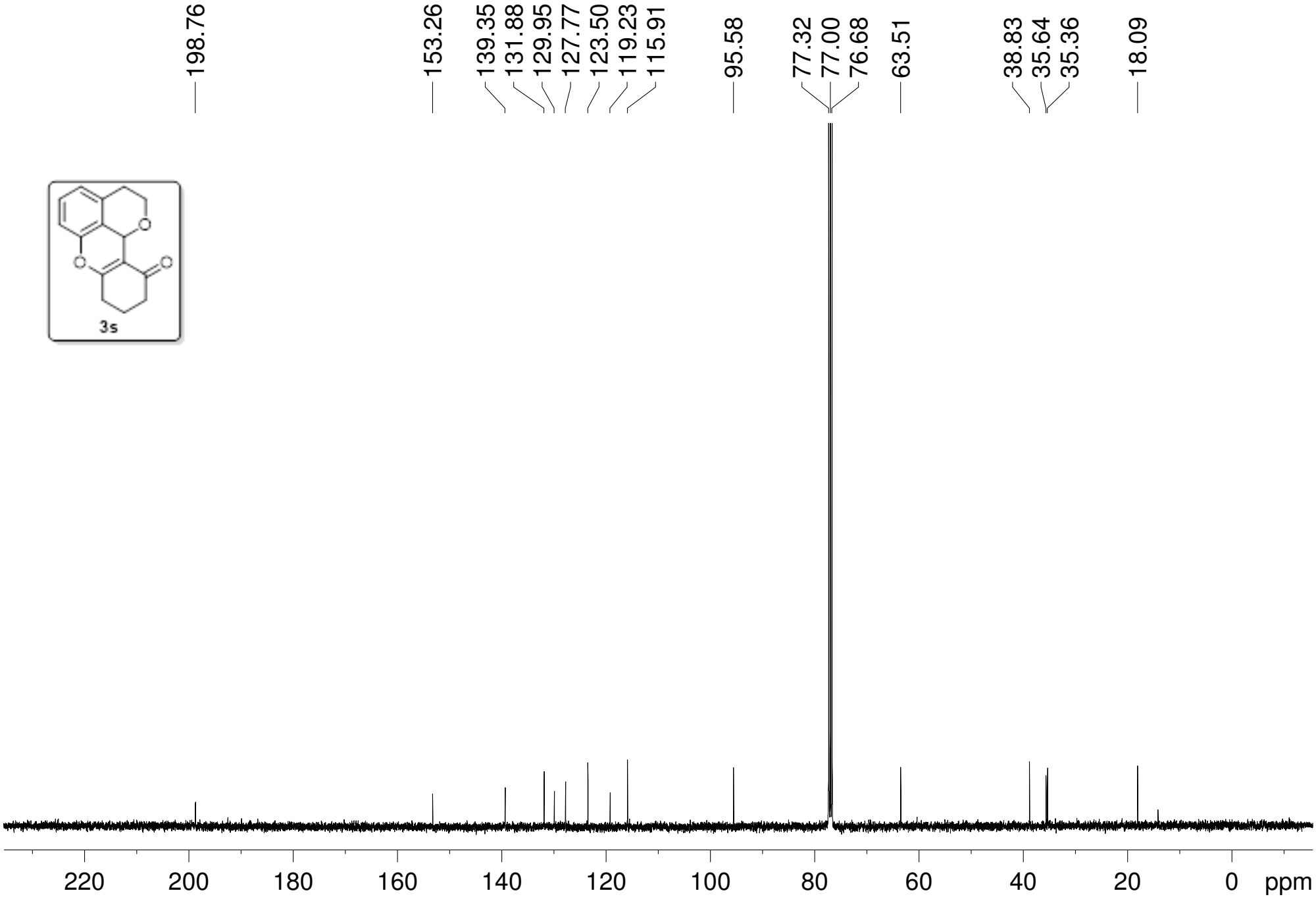
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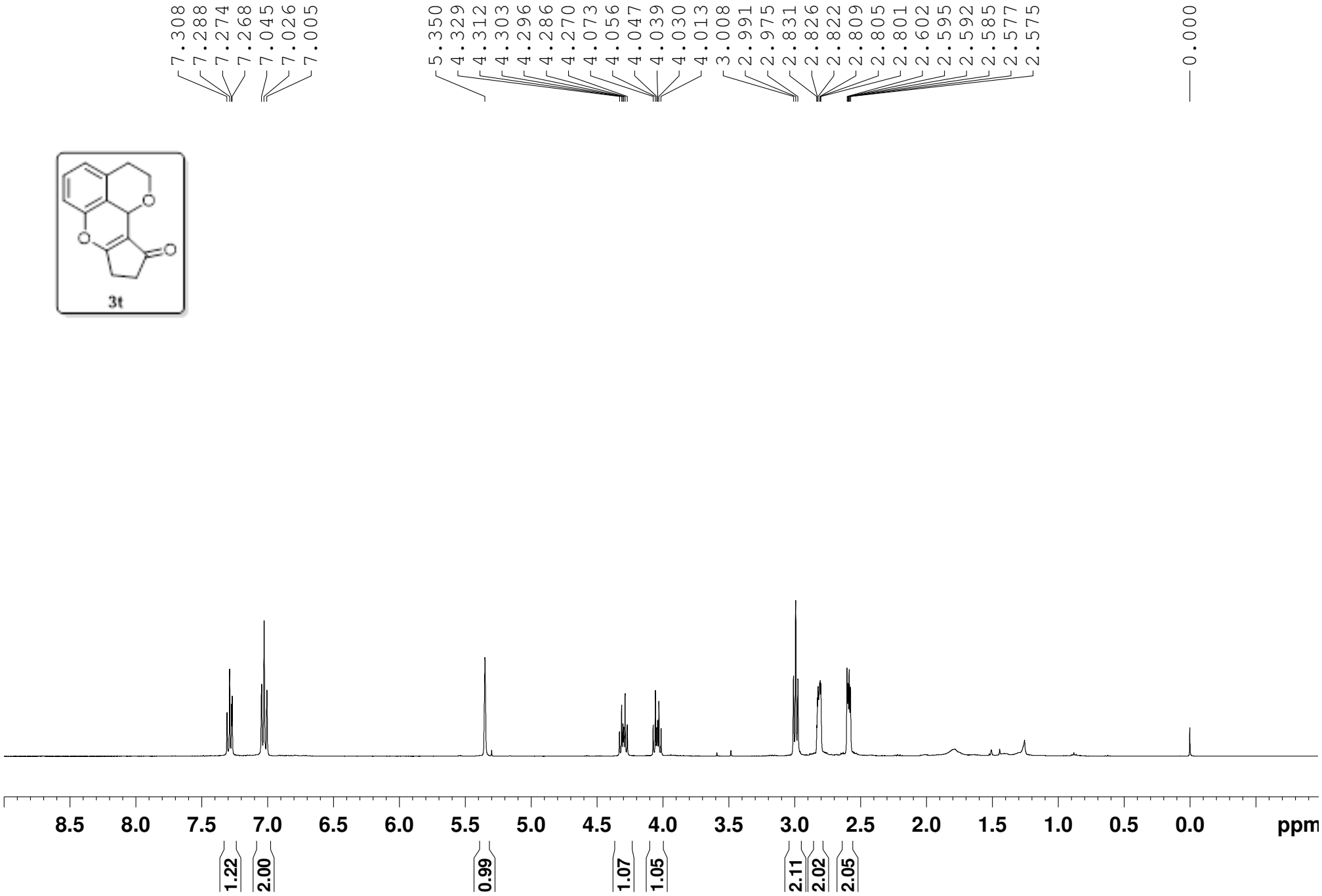
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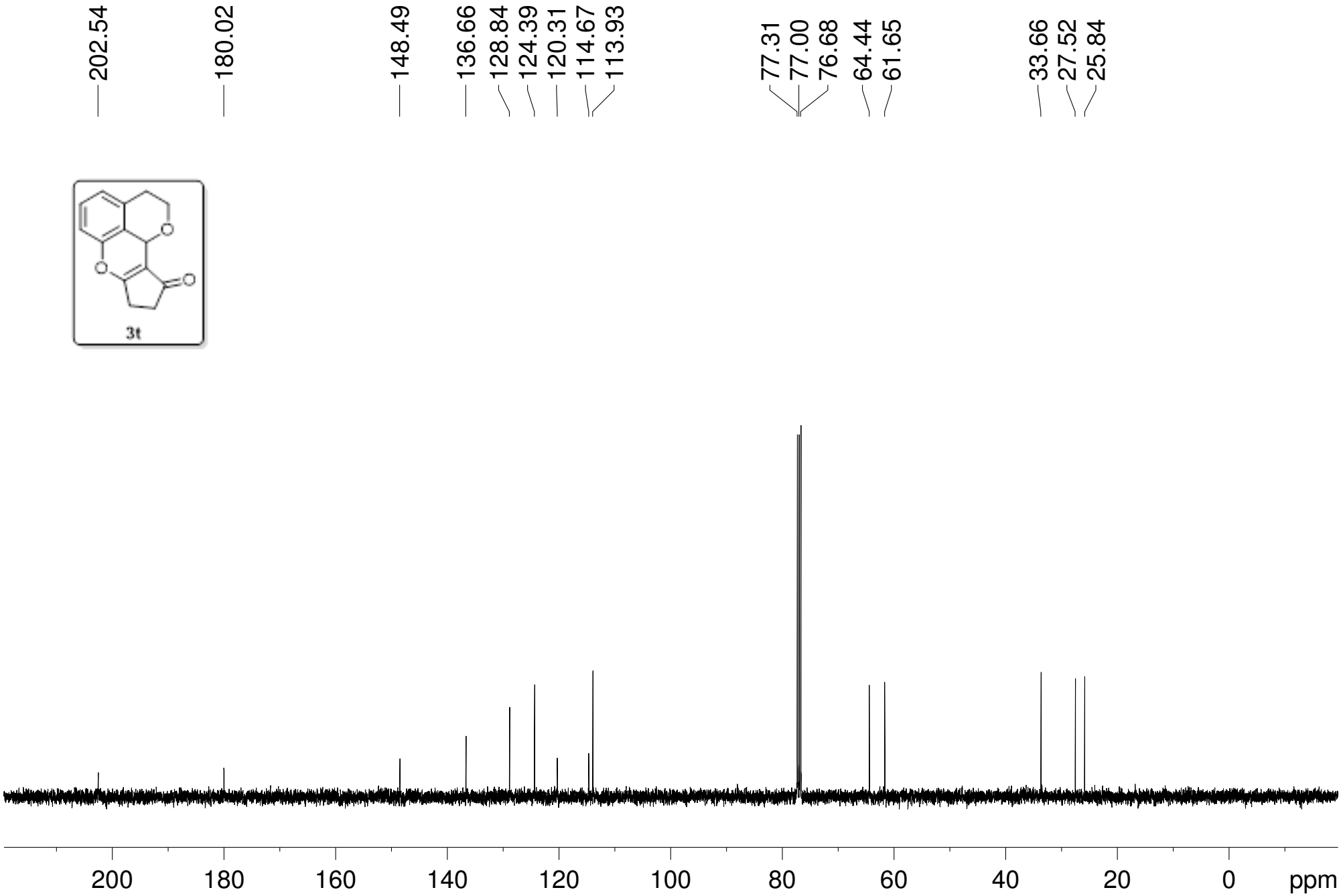
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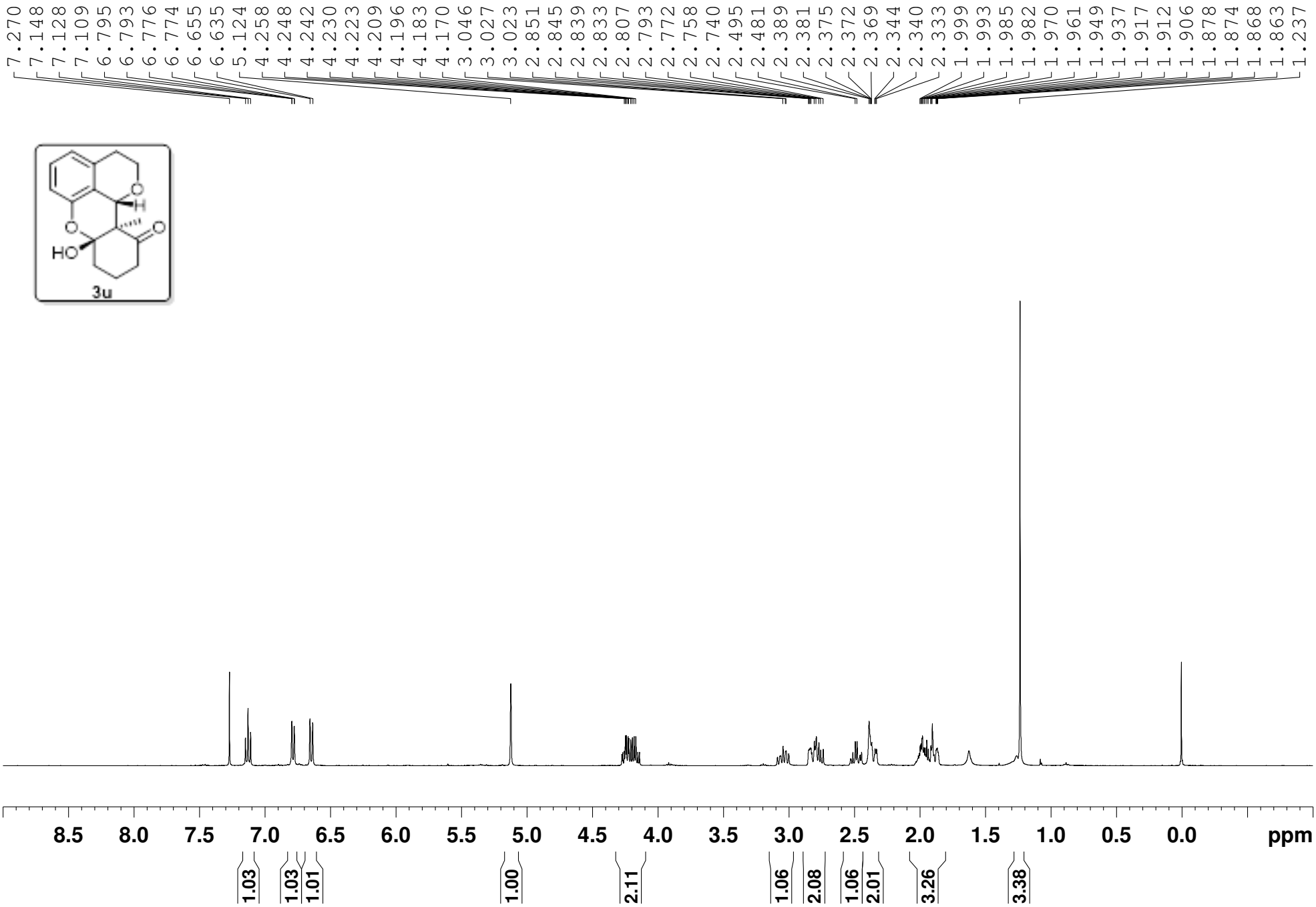
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H
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HO
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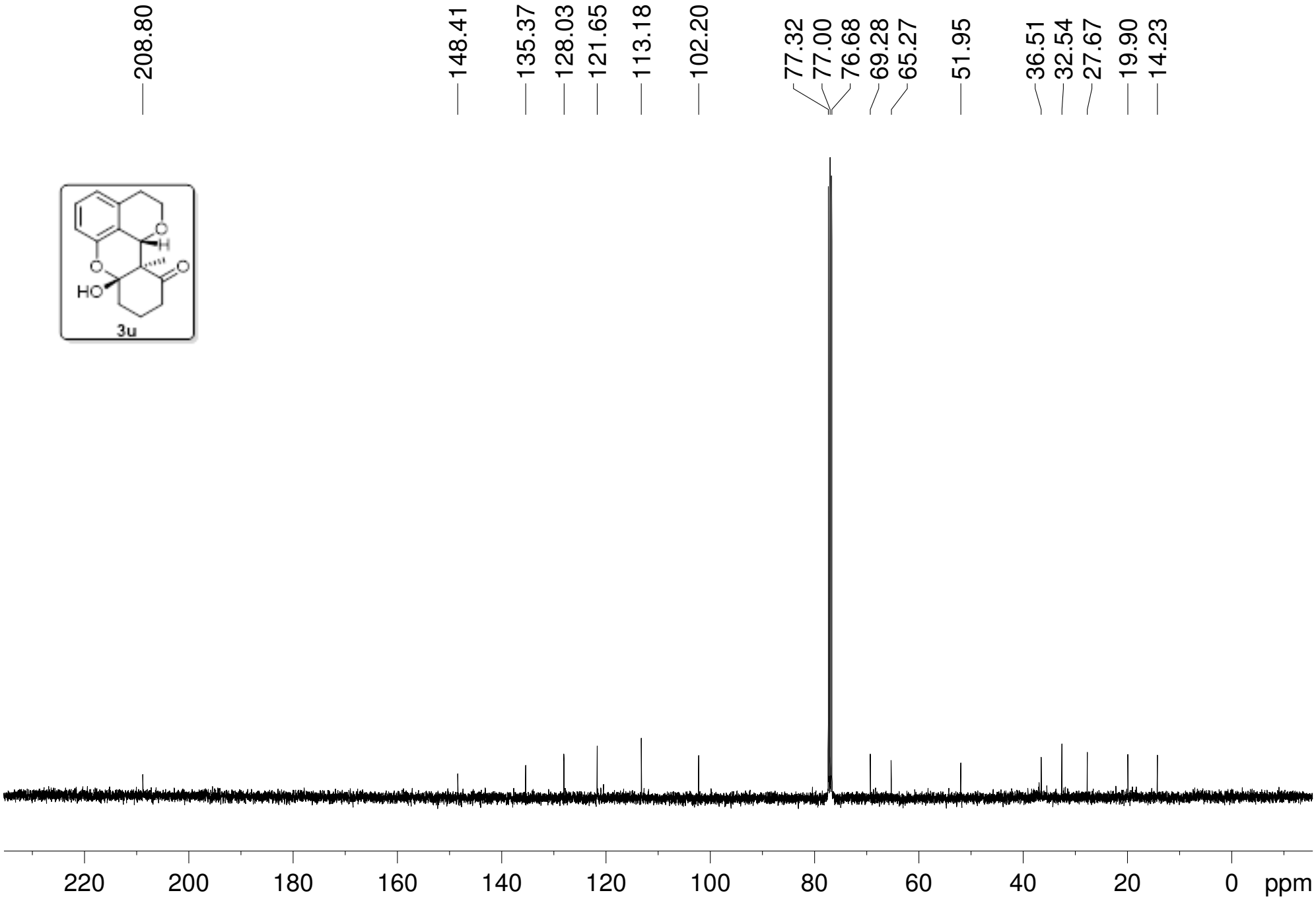
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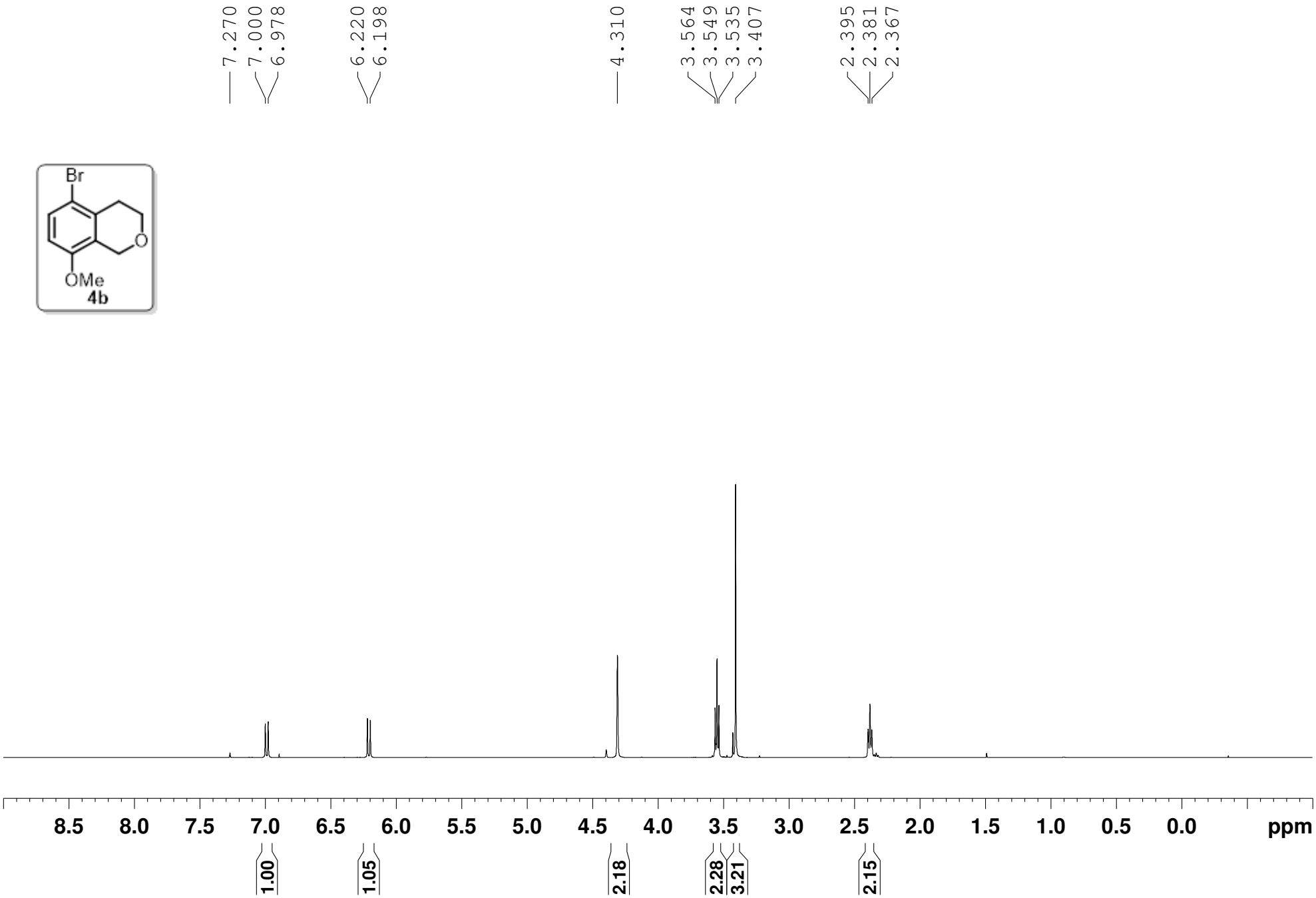
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OMe
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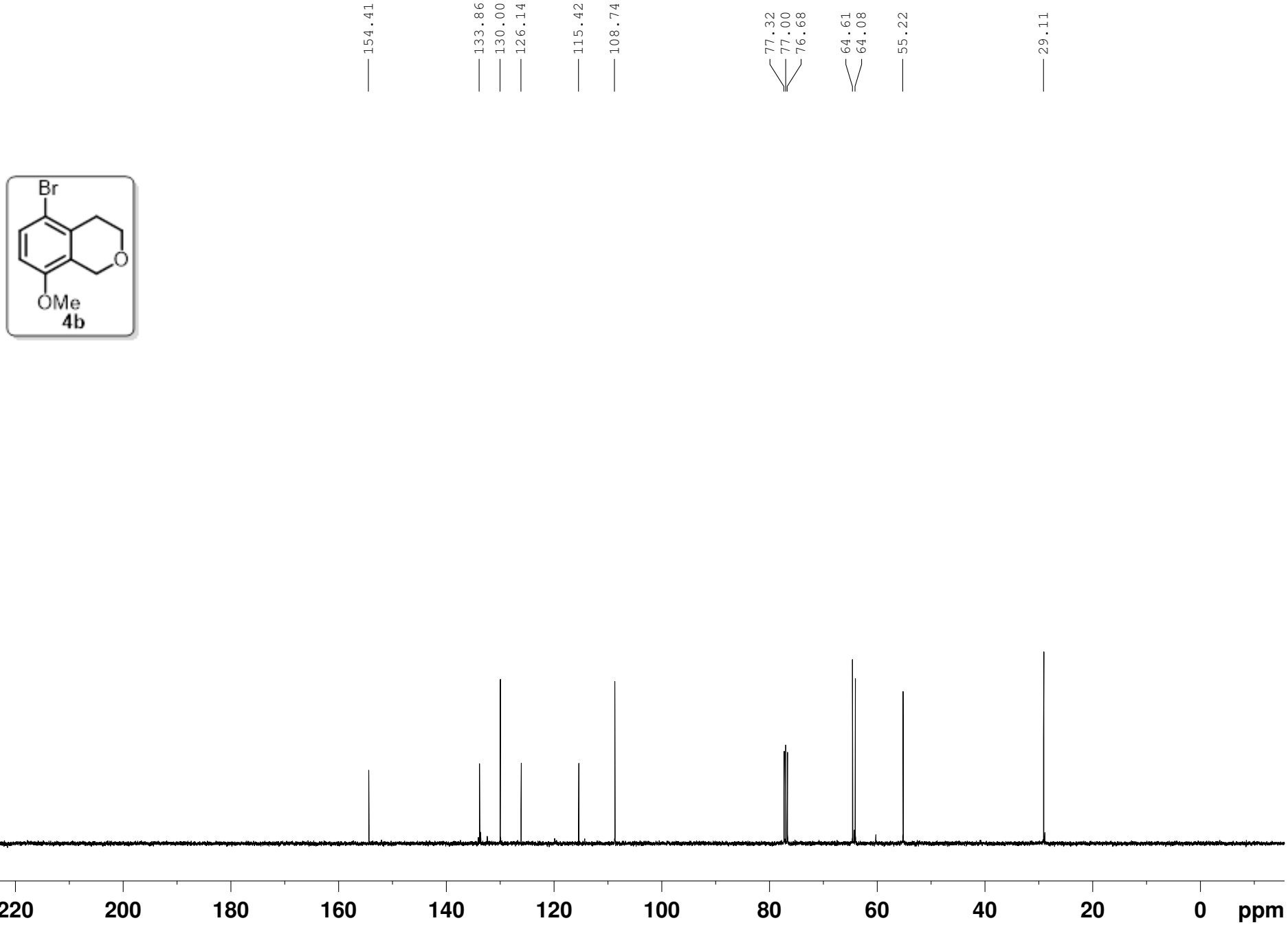
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OMe
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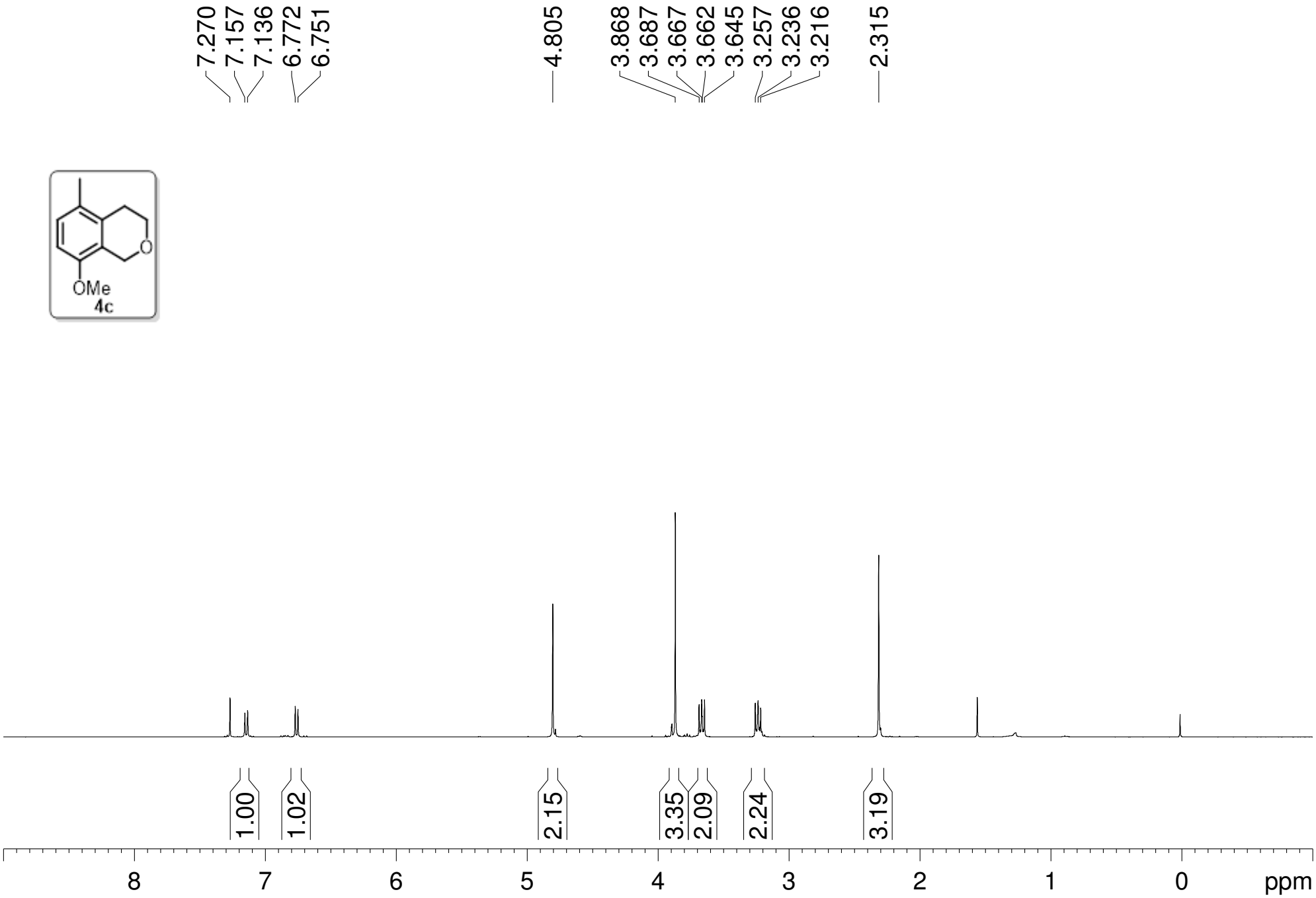
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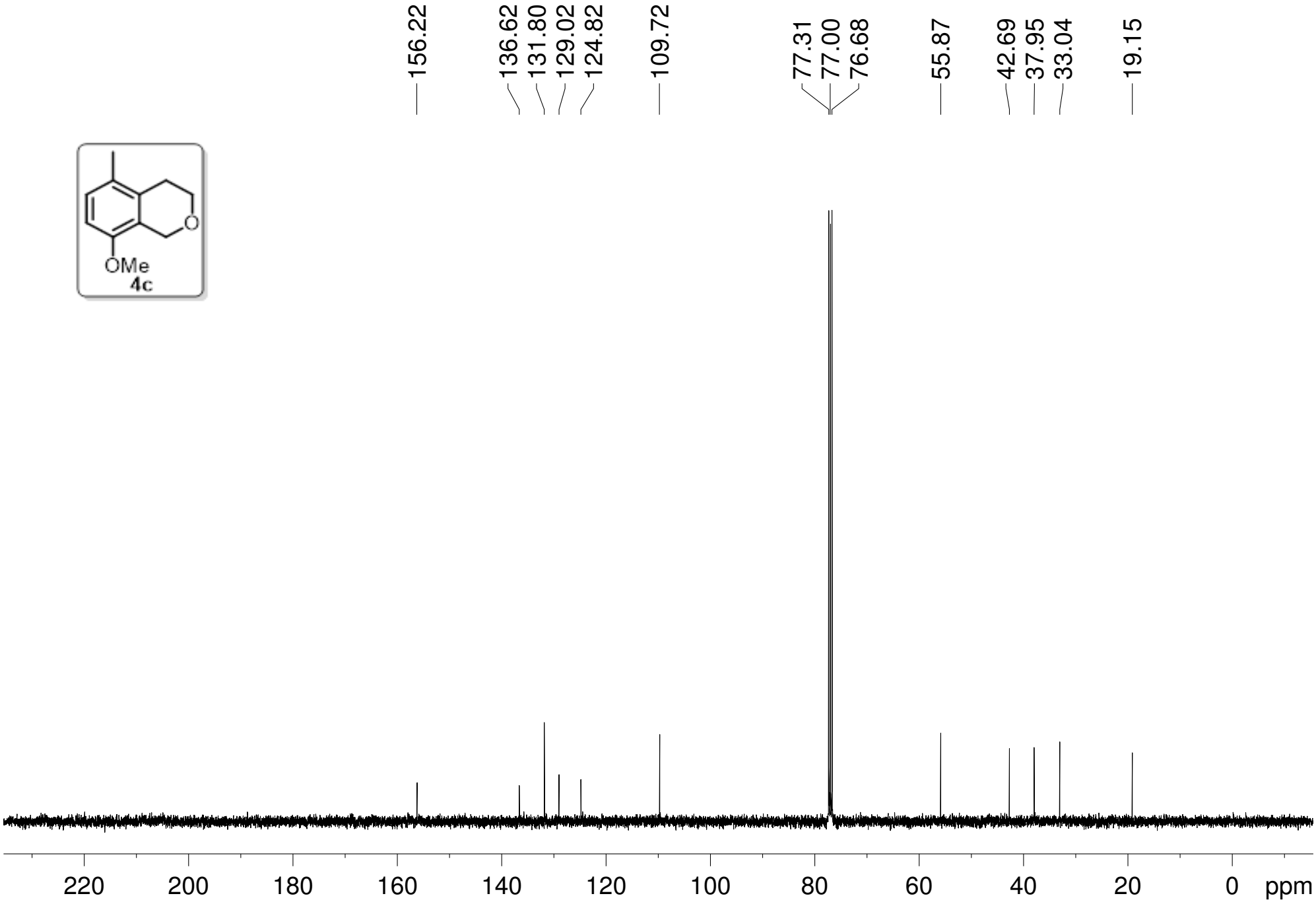
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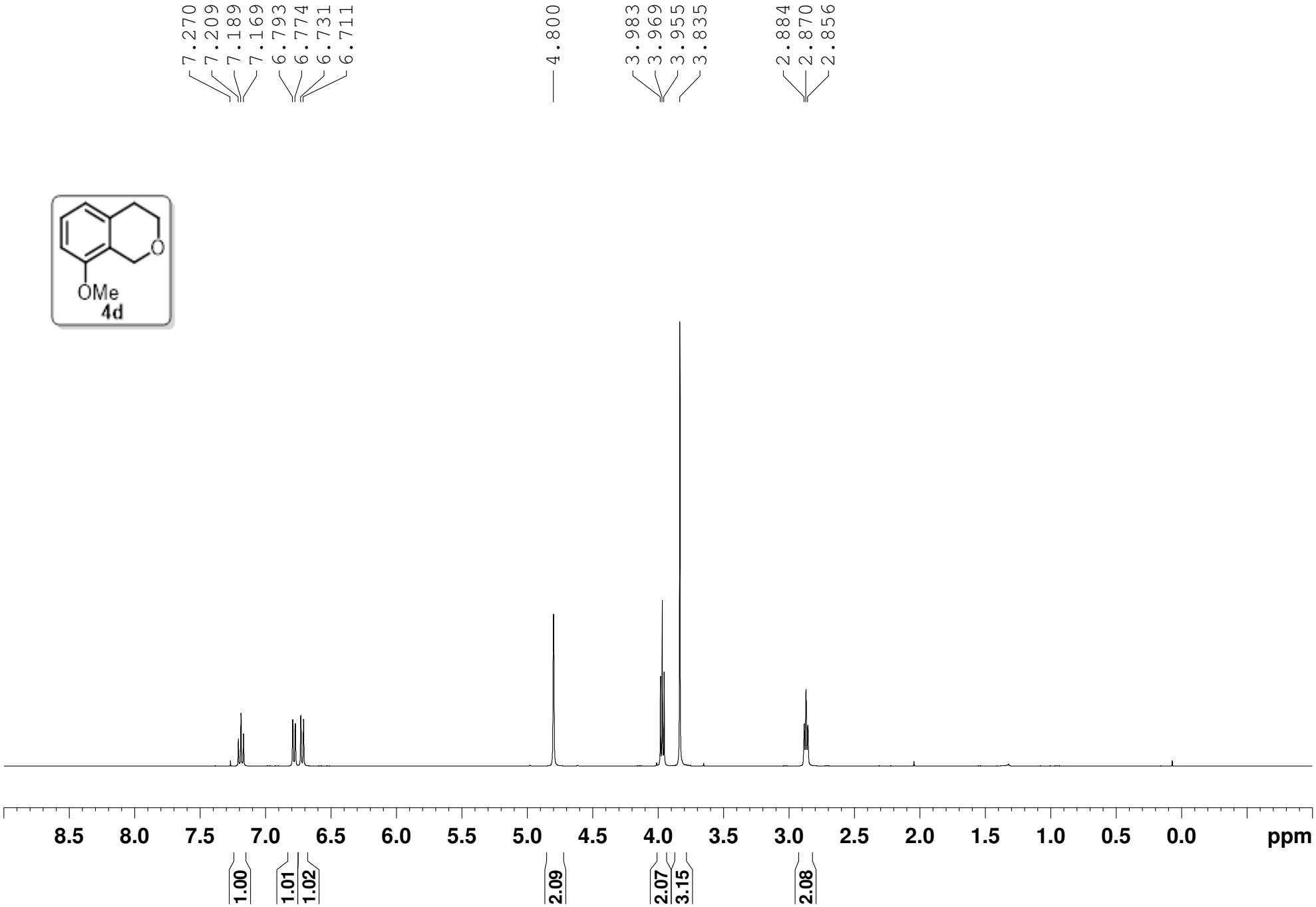
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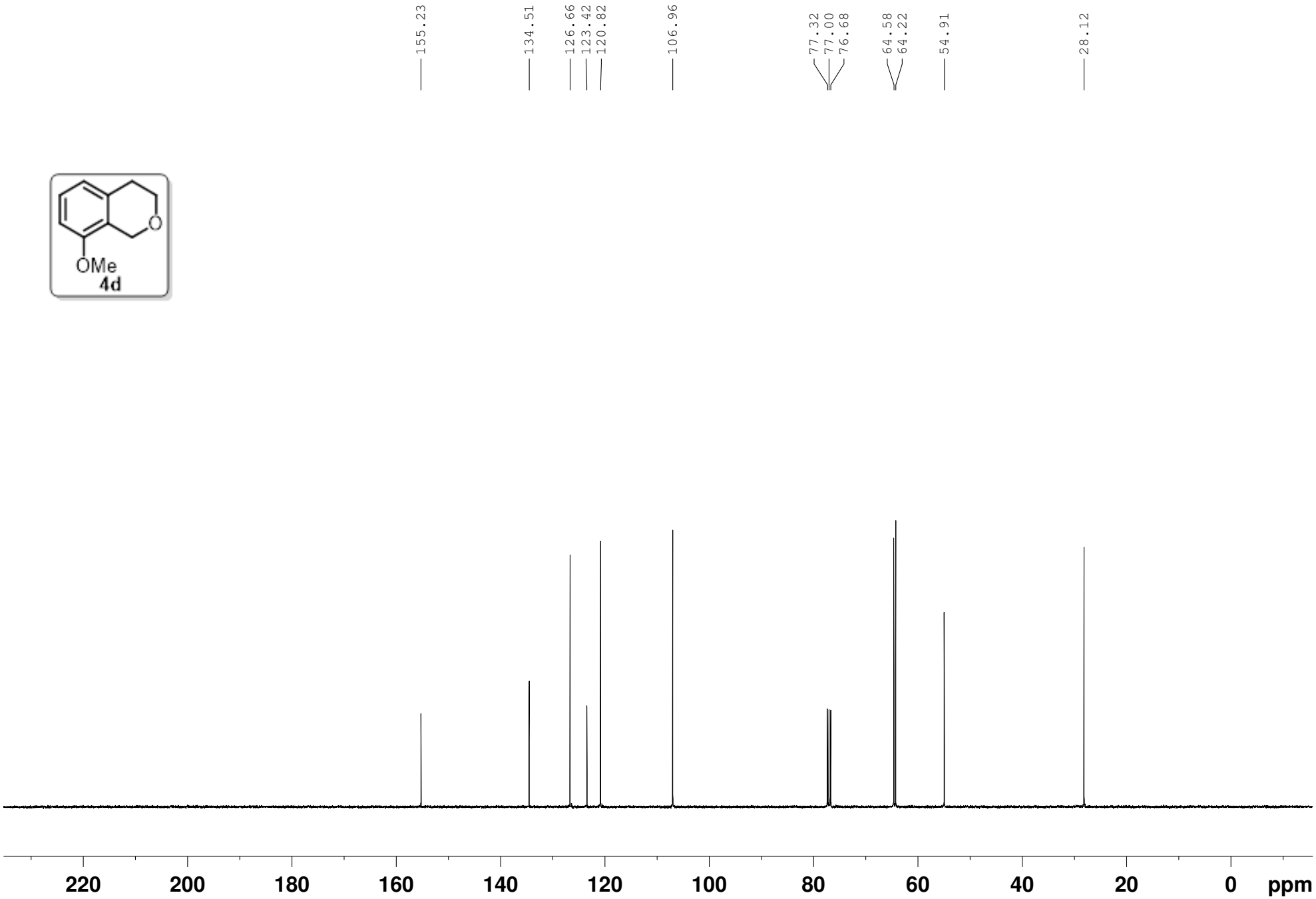
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