Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Ring-opening hydroarylation of monosubstituted cyclopropanes enabled by hexafluoroisopropanol

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Contents

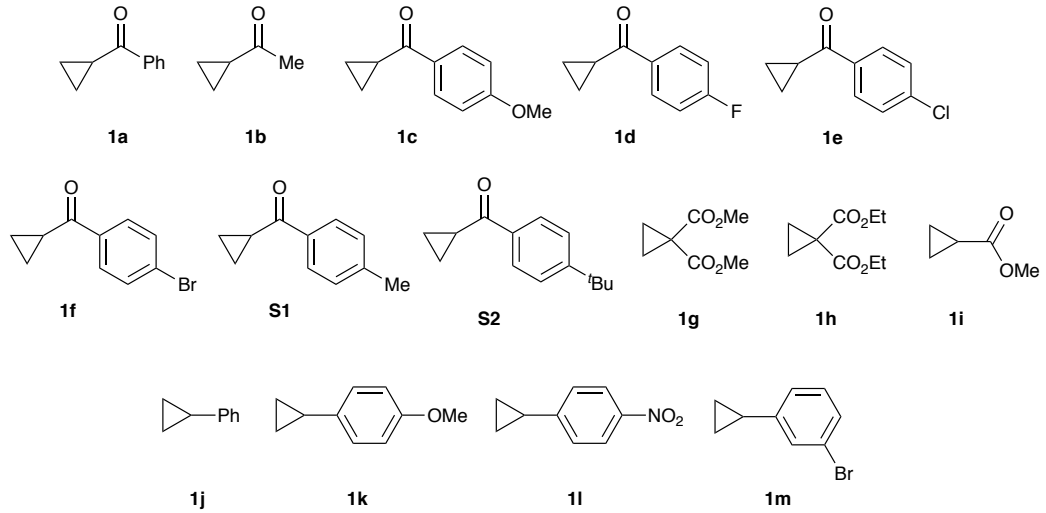
1. General Information

All Friedel-Crafts reactions were performed in 10 mL Pyrex pressure tubes under an atmosphere of air. Elevated temperatures were achieved by way of a stirrer-hotplate, metal heating block and thermocouple. Purification of reaction products was carried out by flash column chromatography using Merck silica gel (40-63 μm). Analytical thin layer chromatography (TLC) was performed on aluminum sheets pre-coated with silica gel 60 F254 (Merck), cut to size. Visualization was accomplished with UV light followed by staining with basic $KMnO_4$ solution and heating.

^{1}H-NMR spectra were recorded on a Bruker UltraShield 400 (400 MHz) spectrometer at ambient temperature and are reported in ppm using solvent as internal standard ($CDCl_3$ at 7.26 ppm). ^{13}C-NMR spectra were recorded on a Bruker UltraShield Plus 400 (100 MHz) spectrometer at ambient temperature and are reported in ppm using solvent as internal standard ($CDCl_3$ at 77.16 ppm). ^{19}F-NMR spectra were recorded on a Bruker UltraShield 400 (376.5 MHz) spectrometer at ambient temperature and are reported in ppm using trifluoroacetic acid as external standard (at –76.55 ppm) or hexafluorobenzene as an internal standard (at -164.9 ppm). Data are reported as: multiplicity (ap = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, qd = quartet of doublets, dt = doublet of triplets, dm = doublet of multiplets, td = triplet of doublets, quintd = quintet of doublets), coupling constants (in Hz) and integration. In cases where compounds were isolated as mixtures of regioisomers, signals corresponding to protons of the major regioisomer were integrated as integer values matching the number of protons in the molecule. Non-integer integration values correspond to signals of protons of minor regioisomers or to overlapping signals of regioisomers. Melting points were obtained on a Büchi Melting Point B-450 apparatus. High resolution mass spectrometry (HRMS) analysis was performed on instruments GCT 1er Waters (EI and CI) and MicroTOF-Q Bruker (ESI).

2. Materials

All commercial materials were purchased from Sigma-Aldrich, Alfa Aesar and FluoroChem, and were used as received, without further purification. Triflic acid (TfOH) *ReagentPlus*®, ≥99% (CAS: 1493-13-6) was purchased from Sigma Aldrich, and HFIP (CAS: 920-66-1) from FluoroChem. The cyclopropane substrates employed in this study are as follows:



3. General Procedures

General Procedure A*: *Arylative Cyclopropane Ring-Opening

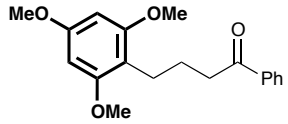
A 10 mL Pyrex tube was charged with a stir bar, followed by the requisite cyclopropane (0.25 mmol), nucleophile (0.25-0.75 mmol), HFIP (0.125-0.250 mL) and finally TfOH (2.2 µL, 10 mol%). The reaction was then heated at the requisite temperature for the necessary amount of time. At completion, the crude reaction mixture was concentrated *in vacuo* onto silica gel and purified by flash column chromatography over silica in the eluent system stated to give the desired ring-opened product.

General procedure B: Suzuki-Miyaura Cross Coupling for cyclopropane synthesis

To a solution of cyclopropylboronic acid (0.286 g, 3.40 mmol, 1.30 equiv), bromoarene (2.6 mmol), tricyclohexyl phosphine (0.072 g, 0.30 mmol, 0.10 equiv) in toluene (10 mL) and water (0.5 mL) was added potassium phosphate (1.64 g, 7.70 mmol, 3.00 equiv) and $Pd(OAc)_2$ (28.6 mg, 5 mol%) in one portion. The mixture was heated to 100 °C for 3-16 h under Ar. After the reaction was cooled to ambient temperature, water was added and the mixture was extracted with EtOAc. The desired product was purified by flash column chromatography (10 % of EtOAc in petroleum ether).

4. Characterization Data of Ring Opened Hydroarylation Products

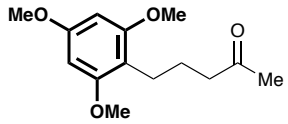
1-Phenyl-4-(2,4,6-trimethoxyphenyl)butan-1-one 2a



The title compound was prepared according to General Procedure A from cyclopropylphenyl ketone (0.035 mL, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (5% EtOAc in petroleum ether) gave **2a** as a white solid.

Yield: 0.053 g, 67%; **mp:** 84-85 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.93-7.91 (2H, m), 7.52 (1H, dd, J = 8.3, 6.4 Hz), 7.43 (2H, t, J = 7.6 Hz), 6.11 (2H, s), 3.80 (3H, s), 3.71 (6H, s), 2.92 (2H, t, J = 7.4 Hz), 2.69 (2H, t, J = 7.1 Hz), 1.94 (2H, quint. J = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 200.8, 159.4, 159.0, 137.5, 132.7, 128.5, 128.1, 110.6, 90.5, 55.6, 55.4, 38.0, 23.9, 21.7; **HRMS:** (ESI^+) $[M+H]^+$ $C_{19}H_{23}O_4$ Found: 315.1569, requires 315.1591.

5-(2,4,6-Trimethoxyphenyl)pentan-2-one 2b

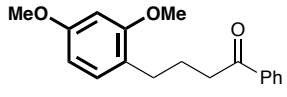


The title compound was prepared according to General Procedure A from cyclopropylmethyl ketone (0.025 mL, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (0-10% EtOAc in petroleum ether) gave **2b** as a pale-yellow liquid.

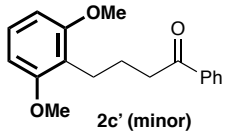
Yield: 0.048 g, 76%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 6.11 (2H, s), 3.79 (3H, s), 3.77 (6H, s), 2.57 (2H, t, J = 7.3 Hz), 2.38 (2H, t, J = 7.5 Hz), 2.10 (3H, s), 1.75 (2H, quint. J = 7.4 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 209.9, 159.4, 158.9, 110.5, 90.5, 55.6, 55.4, 43.4, 29.7, 23.7, 21.7; **HRMS:** (ESI^+) $[M+H]^+$ $C_{14}H_{21}O_4$ Found: 253.1408, requires 253.1434.

4-(2,4-Dimethoxyphenyl)-1-phenylbutan-1-one 2c and

4-(2,6-Dimethoxyphenyl)-1-phenylbutan-1-one 2c'



2c (major)



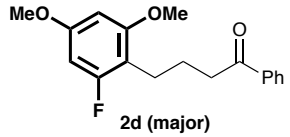
2c' (minor)

The title compounds were prepared according to General Procedure A from cyclopropylphenyl ketone (0.035 mL, 0.25 mmol) and 1,3-dimethoxybenzene (0.065 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (0-10% EtOAc in petroleum ether) gave **2c** and **2c'** as a colourless oil (ca. 2:1 mixture of regioisomers).

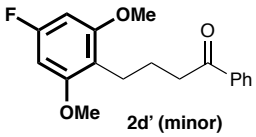
Yield: 0.068 g, 69%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.95 (2H, dd, J = 8.3, 1.2 Hz), 7.59-7.53 (1H, m), 7.48-7.44 (2H, m), 7.15 (0.4H, t, J = 8.3 Hz), 7.07 (0.7H, d, J = 7.9 Hz), 6.54 (0.8H, d, J = 8.3 Hz), 6.47-6.43 (1.3H, m), 3.83-3.82 (2H, m), 3.76-3.75 (4H, m), 2.98 (2H, q, J = 7.1 Hz), 2.80 (0.75H, t, J = 7.1 Hz), 2.69 (1.25H, t, J = 7.3 Hz), 2.08-1.98 (2H, m); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 200.6, 200.5, 159.2, 158.4, 137.3, 137.2, 132.8, 132.6, 130.2, 128.5, 128.4, 128.0, 126.9, 122.5, 118.2, 103.8, 103.5, 98.5, 55.5, 55.4, 55.2, 37.9, 28.9, 24.6, 23.5, 22.0; **HRMS:** (ESI^+) $[M+H]^+$ $C_{18}H_{21}O_3$ Found: 285.1468, requires 285.1485.

4-(2-Fluoro-4,6-dimethoxyphenyl)-1-phenylbutan-1-one 2d and

4-(4-Fluoro-2,6-dimethoxyphenyl)-1-phenylbutan-1-one 2d'



2d (major)



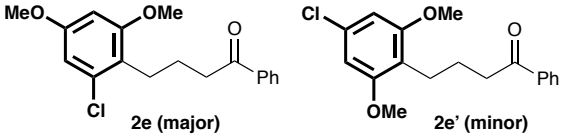
2d' (minor)

The title compounds were prepared according to General Procedure A from cyclopropylphenyl ketone (0.034 g, 0.25 mmol) and 1-fluoro-3,5-dimethoxybenzene (0.078 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (0-30% EtOAc in petroleum ether) gave **2d** and **2d'** as a colourless oil (ca. 2:1 mixture of regioisomers).

Yield: 0.062 g, 82%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.92 (2H, d, J = 7.3 Hz), 7.53 (1H, t, J = 7.3 Hz), 7.44 (2H, t, J = 7.6 Hz), 6.26 (0.4H, s), 6.23 (0.8H, s), 6.21 (0.8H, s), 3.76 (1.5H, s), 3.70 (1.5H, s), 3.69 (3H, s), 2.93 (2H, app. dt, J = 11.6, 7.4 Hz), 2.71-2.69 (2H, m), 1.95 (2H, app. dquint, J = 15.5, 7.7 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 200.6 (major), 200.4 (minor), 162.6 (d, J = 240.8 Hz – major), 162.2 (d, J = 240.6 Hz – minor), 159.3 (d, J = 12.5 Hz), 158.9 (d, J = 12.5 Hz), 137.4, 137.3, 132.9, 132.8, 128.6, 128.5, 128.1, 113.5 (d, J = 3.5 Hz – minor), 109.6 (d, J = 19.8 Hz), 94.3 (d, J = 2.3 Hz – major), 92.9 (d, J = 28.1 Hz), 91.7 (d, J = 25.7 Hz), 55.7, 55.6, 37.9, 24.0, 23.6, 21.8, 21.5, 21.5; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ -113.4 (minor), -116.2 (major); **HRMS:** (ESI^+) $[M+H]^+$ $C_{18}H_{18}FO_3$ Found: 303.1386, requires 303.1391.

4-(2-Chloro-4,6-dimethoxyphenyl)-1-phenylbutan-1-one 2e and

4-(4-Chloro-2,6-dimethoxyphenyl)-1-phenylbutan-1-one 2e'



The title compounds were prepared according to General Procedure A from cyclopropylphenyl ketone (0.034 g, 0.25 mmol) and 5-chloro-1,3-dimethoxybenzene (0.086 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (0-30% EtOAc in petroleum ether) gave **2e** and **2e'** as a colourless oil (ca. 2:1 mixture of regioisomers).

Yield: 0.055 g, 70%

Major regioisomer 2e

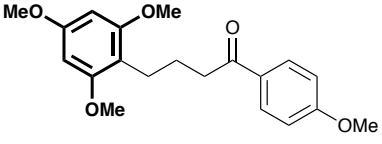
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.96 (2H, d, J = 7.2 Hz), 7.56 (1H, t, J = 7.4 Hz), 7.46 (2H, t, J = 7.6 Hz), 6.53 (1H, d, J = 2.3 Hz), 6.34 (1H, d, J = 2.3 Hz), 3.79 (3H, s), 3.70 (3H, s), 3.00 (2H, t, J = 7.4 Hz), 2.85 (2H, t, J = 7.3 Hz), 2.00 (2H, quint. J = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 200.4, 159.2, 158.8, 137.3, 135.2, 132.9, 128.6, 128.1, 121.0, 105.5, 97.5, 55.7, 55.6, 37.9, 25.7, 23.4; **HRMS:** (ESI^+) $[M+Na]^+$ $C_{18}H_{19}{}^{35}ClO_3Na$ Found: 341.0926, requires 341.0915.

Minor regioisomer 2e'

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.91 (2H, d, J = 7.1 Hz), 7.53 (1H, t, J =7.4 Hz), 7.44 (2H, t, J – 7.6 Hz), 6.50 (2H, s), 3.70 (6H, s), 2.91 (2H, t, J = 7.3 Hz), 2.70 (2H, t, J = 7.2 Hz), 1.93 (2H, quint. J = 7.2 Hz).

^{13}C NMR: (100 MHz, $CDCl_3$) δ 200.4, 158.6, 137.3, 132.7, 132.3, 128.4, 128.0, 116.6, 104.4, 55.7, 37.7, 23.3, 21.7; **HRMS:** (ESI^+) $[M+H]^+$ $C_{18}H_{20}{}^{35}ClO_3$ Found: 319.1090, requires 319.1095.

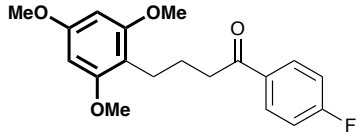
1-(4-Methoxyphenyl)-4-(2,4,6-trimethoxyphenyl)butan-1-one 2f



The title compound was prepared according to General Procedure A from cyclopropyl 4-methoxyphenylmethanone (0.044 g, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (0-15% EtOAc in petroleum ether) gave **2f** as a colourless oil.

Yield: 0.046 g, 61%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.90 (2H, d, J = 8.9 Hz), 6.90 (2H, d, J = 8.9 Hz), 6.11 (2H, s), 3.86 (3H, s), 3.80 (3H, s), 3.71 (6H, s), 2.87 (2H, t, J = 7.4 Hz), 2.67 (2H, t, J = 7.2 Hz), 1.91 (2H, quint. J = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 199.5, 163.2, 159.4, 159.0, 130.6, 130.4, 113.6, 110.8, 90.5, 55.6, 55.5, 55.4, 37.8, 24.2, 21.8; **HRMS:** (ESI^+) $[M+Na]^+$ $C_{20}H_{24}O_5Na$ Found: 367.1524, requires 367.1516.

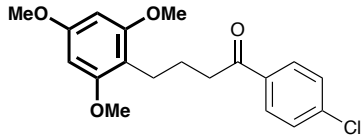
1-(4-Fluorophenyl)-4-(2,4,6-trimethoxyphenyl)butan-1-one 2g



The title compound was prepared according to General Procedure A from cyclopropyl 4-fluorophenylketone (0.036 mL, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (0-15% EtOAc in petroleum ether) gave **2g** as a colourless oil.

Yield: 0.080 g, 98%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.96-7.91 (2H, m), 7.12-7.07 (2H, m), 6.10 (2H, s), 3.80 (3H, s), 3.71 (6H, s), 2.88 (2H, t, J = 7.4 Hz), 2.67 (2H, t, J = 7.1 Hz), 1.92 (2H, quint. J = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 199.2, 165.6 (d, J = 253.7 Hz), 159.5, 159.0, 133.9 (d, J = 2.6 Hz), 130.7 (d, J = 9.3 Hz), 115.6 (d, J = 21.9 Hz), 110.6, 90.5, 55.6, 55.5, 37.9, 23.9, 21.7; **^{19}F NMR:** (376 MHz, $CDCl_3$) δ -106.3; **HRMS:** (ESI^+) $[M+H]^+$ $C_{19}H_{22}O_4F$ Found: 333.1485, requires 333.1497.

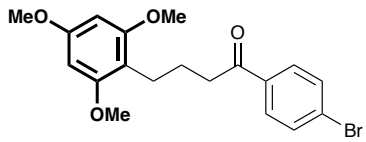
1-(4-Chlorophenyl)-4-(2,4,6-trimethoxyphenyl)butan-1-one 2h



The title compound was prepared according to General Procedure A from cyclopropyl 4-chlorophenylketone (0.045 g, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (0-15% EtOAc in petroleum ether) gave **2h** as a white solid.

Yield: 0.079 g, 91%; **mp:** 88-89 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.85 (2H, d, J = 8.5 Hz), 7.40 (2H, d, J = 8.4 Hz), 6.10 (2H, s), 3.80 (3H, s), 3.70 (6H, s), 2.88 (2H, t, J = 7.3 Hz), 2.67 (2H, t, J = 7.0 Hz), 1.92 (2H, quint., J = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 199.5, 159.5, 159.0, 139.0, 135.8, 129.6, 128.8, 110.5, 90.5, 55.6, 55.4, 37.9, 23.8, 21.6; **HRMS:** (ESI^+) $[M+H]^+$ $C_{19}H_{22}O_4{}^{35}Cl$ Found: 349.1191, requires 349.1201.

1-(4-Bromophenyl)-4-(2,4,6-trimethoxyphenyl)butan-1-one 2i

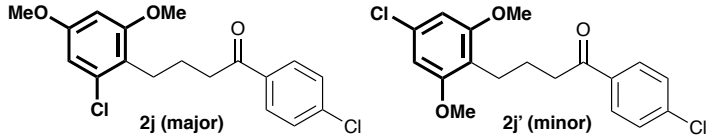


The title compound was prepared according to General Procedure A from cyclopropyl 4-bromophenylketone (0.050 g, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (0-15% EtOAc in petroleum ether) gave **2i** as a white solid.

Yield: 0.068 g, 69%; **mp:** 96-97 °C; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.77 (2H, d, J = 8.6 Hz), 7.57 (2H, d, J = 8.6 Hz), 6.10 (2H, s), 3.80 (3H, s), 3.70 (6H, s), 2.87 (2H, t, J = 7.3 Hz), 2.67 (2H, t, J = 7.1 Hz), 1.91 (2H, quint. J = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 199.7, 159.5, 159.0, 136.2, 131.8, 129.7, 127.8, 110.5, 90.5, 55.6, 55.4, 37.9, 23.8, 21.6; **HRMS:** (ESI^+) $[M+H]^+$ $C_{19}H_{22}O_4{}^{79}Br$ Found: 393.0676, requires 393.0696.

4-(2-Chloro-4,6-dimethoxyphenyl)-1-(4-chlorophenyl)butan-1-one 2j and

4-(4-Chloro-2,6-dimethoxyphenyl)-1-(4-chlorophenyl)butan-1-one 2j'



The title compounds were prepared according to General Procedure A from cyclopropyl 4-chlorophenyl ketone (0.045 g, 0.25 mmol) and 5-chloro-1,3-dimethoxybenzene (0.086 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (0-30% EtOAc in petroleum ether) gave **2j** and **2j'** as a colourless oil (ca. 2:1 mixture of regioisomers).

Yield: 0.066 g, 74%

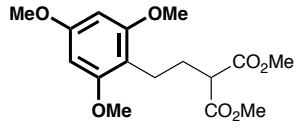
Major regioisomer 2j

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.86 (2H, d, J = 8.6 Hz), 7.41 (2H, d, J = 8.6 Hz), 6.50 (1H, d, J = 2.4 Hz), 6.32 (1H, d, J = 2.4 Hz), 3.77 (3H, s), 3.68 (3H, s), 2.93 (2H, t, J = 7.3 Hz), 2.81 (2H, t, J = 7.3 Hz), 1.97 (2H, quint. J = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 199.1, 159.2, 158.9, 139.3, 135.6, 135.2, 129.6, 128.9, 120.8, 105.6, 97.5, 55.7, 55.6, 37.9, 25.7, 23.3; **HRMS:** (ESI^+) $[M+K]^+$ $C_{18}H_{18}{}^{35}Cl_2O_3K$ Found: 391.0273, requires 391.0265.

Minor regioisomer 2j'

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.87 (2H, d, J = 8.5 Hz), 7.43 (2H, d, J = 8.5 Hz), 6.53 (2H, s), 3.72 (6H, s), 2.90 (2H, t, J = 7.3 Hz), 2.71 (2H, t, J = 7.2 Hz), 1.94 (2H, quint. J = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 199.1, 158.6, 139.1, 132.4, 129.4, 128.7, 116.5, 106.9, 104.4, 55.7, 37.7, 23.2, 21.7; **HRMS:** (ESI^+) $[M+H]^+$ $C_{18}H_{19}{}^{35}Cl_2O_3$ Found: 353.0702, requires 353.0706.

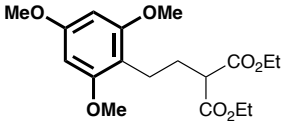
Dimethyl 2-(2,4,6-trimethoxyphenethyl)malonate 2k



The title compound was prepared according to General Procedure A from dimethyl cyclopropane-1,1-dicarboxylate (0.034 g, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (10-30% EtOAc in petroleum ether) gave **2k** as a colourless liquid.

Yield: 0.079 g, 98%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 6.09 (2H, s), 3.78 (3H, s), 3.75 (6H, s), 3.70 (6H, s), 3.31 (1H, t, J = 7.5 Hz), 2.63 (2H, t, J = 7.1 Hz), 2.08 (2H, q, J = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 170.2, 159.7, 159.0, 109.3, 20.4, 55.6, 55.4, 52.4, 51.2, 28.5, 20.1; **HRMS:** (ESI^+) $[M+H]^+$ $C_{16}H_{23}O_7$ Found: 327.1413, requires 327.1438.

Diethyl 2-(2,4,6-trimethoxyphenethyl)malonate 2l

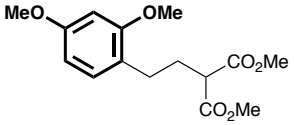


The title compound was prepared according to General Procedure A from diethyl cyclopropane-1,1-dicarboxylate (0.044 mL, 0.25 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (25% EtOAc in petroleum ether) gave **2l** as a colourless liquid.

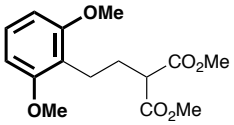
Yield: 0.063 g, 71%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 6.10 (2H, s), 4.16 (4H, app. qq, J = 10.5, 7.1 Hz), 3.79 (3H, s), 3.76 (6H, s), 3.28 (1H, t, J = 7.5 Hz), 2.64 (2H, t, J = 7.2 Hz), 2.06 (2H, q, J = 7.3 Hz), 1.25 (6H, t, J = 7.1 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 169.8, 159.6, 159.0, 109.6, 90.4, 61.2, 55.6, 55.4, 51.7, 28.4, 20.2, 14.2; **HRMS:** (ESI^+) $[M+Na]^+$ $C_{18}H_{26}O_7Na$ Found: 377.1552, requires 377.1571.

Dimethyl 2-(2,4-dimethoxyphenethyl)malonate 2m and

Dimethyl 2-(2,6-dimethoxyphenethyl)malonate 2m'



2m (major)



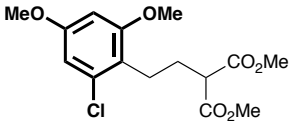
2m' (minor)

The title compounds were prepared according to General Procedure A from dimethyl cyclopropane-1,1-dicarboxylate (0.034 g, 0.25 mmol) and 1,3-dimethoxybenzene (0.065 mL, 0.50 mmol) in HFIP (0.125mL) and stirred at 100 °C. Purification by flash column chromatography over silica (0-30% EtOAc in petroleum ether) gave **2m** and **2m'** as a colourless oil (ca. 2:1 mixture of regioisomers).

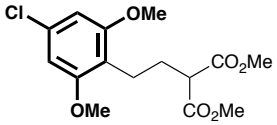
Yield: 0.057 g, 77%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.15 (0.4H, dd, J = 9.9, 6.8 Hz), 7.02 (0.6H, d, J = 8.0 Hz), 6.55-6.42 (2H, m), 3.81-3.79 (7H, m), 3.75-3.73 (5H, m), 3.38 (1H, app. q, J = 7.9 Hz), 2.75 (0.8H, t, J = 7.1 Hz), 2.61 (1.2H, t, J = 7.4 Hz), 2.25-2.12 (2H, m); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 170.1, 170.0, 161.0, 159.4, 158.4, 157.0, 130.4, 130.1, 127.2, 121.2, 116.8, 107.8, 106.2, 103.8, 103.5, 101.5, 98.5, 55.5, 55.4, 55.2, 52.4, 52.3, 51.2, 51.1, 29.1, 28.1, 27.2, 20.4; **HRMS:** (ESI^+) $[M+Na]^+$ $C_{15}H_{20}O_6Na$ Found: 319.1138, requires 319.1152.

Dimethyl 2-(2-chloro-4,6-dimethoxyphenethyl)malonate 2n and

Dimethyl 2-(4-chloro-2,6-dimethoxyphenethyl)malonate 2n'



2n (major)



2n' (minor)

The title compound was prepared according to General Procedure A from dimethyl cyclopropane-1,1-dicarboxylate (0.034 g, 0.25 mmol) and 5-chloro-1,3-dimethoxybenzene (0.086 g, 0.50 mmol) in HFIP (0.125mL) and stirred at 100 °C. Purification by flash column chromatography over silica (0-30% EtOAc in petroleum ether) gave **2n** and **2n'** as a colourless oil (ca. 2:1 mixture of regioisomers).

Yield: 0.046 g, 56%

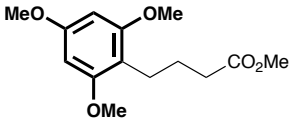
Major regioisomer 2n

^{1}H NMR: (400 MHz, $CDCl_3$) δ 6.52 (1H, d, J = 2.4 Hz), 6.35 (1H, d, J = 2.4 Hz), 3.79 (3H, s), 3.78 (3H, s), 3.75 (6H, s), 3.38 (1H, t, J = 7.5 Hz), 2.79 (2H, t, J = 7.5 Hz), 2.14 (2H, q, J = 7.5 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 169.8, 159.0, 158.9, 135.1, 119.7, 105.5, 97.3, 55.6, 55.5, 52.4, 51.2, 27.8, 24.0; **HRMS:** (ESI$^+$) $[M+H]^+$ $C_{15}H_{20}{}^{35}ClO_6$ Found: 331.0958, requires 331.0943.

Minor regioisomer 2n'

^{1}H NMR: (400 MHz, $CDCl_3$) δ 6.53 (2H, s), 3.79 (6H, s), 3.73 (6H, s), 3.32 (1H, t, J = 7.5 Hz), 2.69 (2H, t, J = 7.1 Hz), 2.11 (2H, q, J = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 170.0, 158.6, 132.7, 115.3, 104.4, 55.7, 55.4, 51.1, 27.9, 20.2.

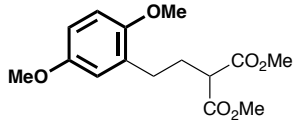
Methyl 4-(2,4,6-trimethoxyphenyl)butanoate 2o



The title compound was prepared according to General Procedure A from methyl cyclopropanecarboxylate (0.025 g, 0.025 mmol) and 1,3,5-trimethoxybenzene (0.084 g, 0.50 mmol) in 1,2-DCE (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (10% EtOAc in petroleum ether) gave **2o** as a colourless oil.

Yield: 0.010 g, 15%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 6.11 (2H, s), 3.80 (3H, s), 3.77 (6H, s), 3.64 (3H, s), 2.61 (2H, t, J = 7.2 Hz), 2.28 (2H, t, J = 7.8 Hz), 1.80 (2H, quint. J = 7.5 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 174.7, 159.5, 159.0, 110.4, 90.5, 55.7, 55.4, 51.4, 33.8, 24.7, 21.8; **HRMS:** (ESI$^+$) $[M+H]^+$ $C_{14}H_{21}O_5$ Found: 269.1388, requires 269.1384.

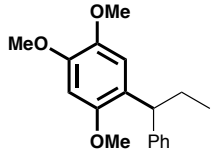
Dimethyl 2-(2,5-dimethoxyphenethyl)malonate 2r



The title compound was prepared according to General Procedure A from dimethyl cyclopropane-1,1-dicarboxylate (0.034 g, 0.25 mmol) and 1,4-dimethoxybenzene (0.069 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at 100 °C. Purification by flash column chromatography over silica (0-20% EtOAc in petroleum ether) gave **2r** as a colourless oil.

Yield: 0.014 g, 19%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 6.75 (1H, d, J = 9.7 Hz), 6.72-6.69 (2H, m), 3.76 (3H, s), 3.76 (3H, s), 3.73 (6H, s), 3.38 (1H, t, J = 7.5 Hz), 2.63 (2H, t, J = 7.5 Hz), 2.19 (2H, q, J = 7.5 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 170.0, 153.5, 151.9, 130.1, 116.5, 111.7, 111.3, 55.9, 55.8, 52.6, 51.2, 29.0, 28.1; **HRMS:** (ESI^+) $[M+Na]^+$ $C_{15}H_{20}O_6Na$ Found: 319.1119, requires 319.1152.

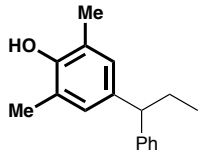
1,2,4-Trimethoxy-5-(1-phenylpropyl)benzene 3a



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.031 mL, 0.25 mmol) and 1,2,4-trimethoxybenzene (0.075 mL, 0.50 mmol) in HFIP (0.0125 mL) and stirred at 80 °C. Purification by flash column chromatography over silica (1% EtOAc petroleum ether) allowed for partial separation of **3a** from excess nucleophile to provide an analytical sample of **3a** in 90% purity.

Yield (NMR relative to CH_2Br_2): 79 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.28-7.27 (4H, m), 7.16 (1H, app. dd, J = 8.3, 4.3 Hz), 6.80 (1H, s), 6.52 (1H, s), 4.25 (1H, t, J = 7.8 Hz), 3.88 (3H, s), 3.83 (3H, s), 3.76 (3H, s), 2.08-1.96 (2H, m), 0.92 (3H, t, J = 7.4 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 151.5, 147.7, 145.4, 143.1, 128.1, 128.0, 125.7, 125.4, 112.2, 98.2, 56.8, 56.7, 56.1, 44.7, 28.0, 12.7; **HRMS:** ($APCI^+$) $[M]^+$ $C_{18}H_{22}O_3$ Found: 286.1577, requires 286.1563.

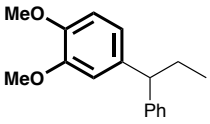
2,6-Dimethyl-4-(1-phenylpropyl)phenol 3b



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.031 mL, 0.25 mmol) and 2,6-dimethylphenol (0.061g, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (2% EtOAc in petroleum ether) gave **3b** as a yellow oil.

Yield: 0.041 g, 68 %; **^{1}H NMR:** (400 MHz, $CDCl_3$): δ 7.35-7.19 (5H, m), 6.90 (2H, s), 4.51 (1H, s), 3.72 (1H, t, J = 7.7 Hz), 2.26 (6H, s), 2.08 (2H, quint, J = 7.3 Hz), 0.95 (3H, t, J = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 150.4, 145.9, 136.9, 128.4, 128.3, 127.9, 125.9, 122.8, 52.6, 28.8, 16.1, 13.0; **HRMS:** (ESI^-) $[M-H]^-$ $C_{17}H_{19}O$ Found: 239.1440, requires: 239.1441.

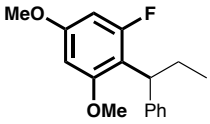
1,2-Dimethoxy-4-(1-phenylpropyl)benzene 3c



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.132 mL, 1.00 mmol) and 1,2-dimethoxybenzene (0.252 mL, 0.500 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by filtration through Celite (CH_2Cl_2) followed by bulb-to-bulb distillation under vacuum (3 mm Hg, 60.4 °C), gave **3c** as a yellow oil.

Yield: 0.045 g, 70 %; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 7.32-7.15 (5H, m), 6.82 (2H, s), 6.76 (1H, s), 3.87 (3H, s), 3.86 (3H, s), 3.76 (1H, t, *J* = 7.9 Hz), 2.07 (2H, quint, *J* = 7.5 Hz), 0.92 (3H, t, *J* = 7.5 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 148.8, 147.3, 145.4, 137.9, 128.4, 128.0, 127.8, 126.1, 119.8, 111.5, 111.2, 55.9, 52.9, 28.8, 12.9; **HRMS:** (APCI$^+$) $[M]^+$ $C_{17}H_{20}O_2$ Found: 256.1455, requires 256.1456.

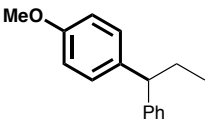
1-Fluoro-3,5-dimethoxy-2-(1-phenylpropyl)benzene 3d



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.031 mL, 0.25 mmol) and 1-fluoro-3,5-dimethoxybenzene (0.067 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Attempted purification could not separate the product regioisomers from excess nucleophile (ca. 2:1 mix of regioisomers).

Yield (NMR relative to CH_2Br_2): 83 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.38-7.36 (0.7H, m), 7.30-7.23 (2.3H, m), 7.20-7.11 (2.0H, m), 6.30-6.29 (2H, m), 3.81 (4H, s), 3.79-3.78 (2H, m), 2.23-2.01 (2H, m), 0.94-0.86 (3H, m).

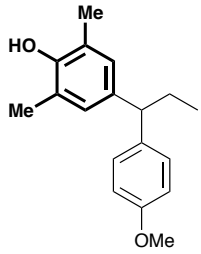
1-Methoxy-4-(1-phenylpropyl)benzene 3e



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.031 mL, 0.25 mmol) and anisole (0.054 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Attempted purification by flash column chromatography over silica (100 % petroleum ether) gave **3e** as a colourless liquid (ca. 3:1 mix of regioisomers), however not all anisole could be removed from the product.

Yield (NMR relative to CH_2Br_2): 93 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.36-7.12 (7H, m), 7.01-6.93 (0.62H, m), 6.87-6.83 (1.35H, m), 3.85 (1.5H, s), 3.80 (2.5H, s), 3.79-3.73 (1H, m), 2.11-2.02 (2H, m), 0.92 (3H, t, *J* = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 157.8, 145.6, 137.4, 128.8, 128.3, 127.8, 125.9, 113.7, 55.1, 52.4, 28.8, 12.8; **HRMS:** (APCI$^+$) $[M]^+$ $C_{16}H_{18}O$ Found: 226.1356, requires 226.1352.

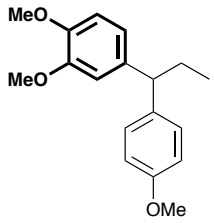
4-(1-(4-Methoxyphenyl)propyl)-2,6-dimethylphenol 3f



The title compound was prepared according to General Procedure A from cyclopropane S3 (0.037 mg, 0.25 mmol) and 2,6-dimethylphenol (0.061 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (2% EtOAc in petroleum ether) gave **3f** as a yellow oil.

Yield: 0.034 g, 50 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.15 (2H, d, *J* = 8.7 Hz), 6.84 (2H, d, *J* = 4.7 Hz), 6.83 (2H, d, *J* = 4.2 Hz), 4.461 (1H, s) 3.79 (3H, s) 3.62 (1H, t, *J* = 7.8 Hz), 2.22 (6H, s), 2.0 (2H, quint, *J* = 7.6 Hz), 0.89 (3H, t, *J* = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 157.7, 150.3, 138.0, 137.3, 128.7, 127.9, 122.7, 113.7, 55.2, 51.7, 29.0, 16.1, 12.9; **HRMS:** ($APCI^+$) $[M+H]^+$ $C_{18}H_{23}O_2$ Found: 271.1642, requires 271.1614.

1,2-Dimethoxy-4-(1-(4-methoxyphenyl)propyl)benzene 3g

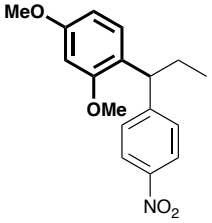


The title compound was prepared according to General Procedure A from cyclopropane S3 (0.037 g, 0.25 mmol) and 1,2-dimethoxybenzene (0.063 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (1-7% EtOAc in petroleum ether) gave **3g** as a colourless liquid.

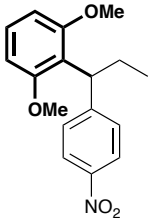
Yield: 0.035 g, 49 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.16 (2H, d, *J* = 8.7 Hz), 6.85 (2H, d, *J* = 8.7 Hz), 6.80 (2H, d, *J* = 2.7 Hz), 6.74 (1H, s), 3.86 (6H, d, *J* = 3.8 Hz), 3.80 (2H, s), 3.71 (1H, t, *J* = 7.8 Hz), 2.03 (2H, quint, *J* = 7.6 Hz), 1.28 (1H, s), 0.91 (3H, t, *J* = 7.4 Hz); **^{13}C NMR:** (400 MHz, $CDCl_3$) δ 157.8, 148.8, 147.2, 138.3, 137.6, 128.7, 119.6, 113.7, 111.3, 111.1, 55.9, 55.8, 55.2, 52.0, 29.0, 12.9; **HRMS:** (ESI^+) $[M+Na]^+$ $C_{18}H_{22}O_3Na$ Found: 309.1464, requires 309.1461.

2,4-Dimethoxy-1-(1-(4-nitrophenyl)propyl)benzene 3h and

1,3-dimethoxy-2-(1-(4-nitrophenyl)-propyl)benzene 3h'



3h (major)



3h' (minor)

The title compound was prepared according to General Procedure A from cyclopropane S2 (0.041 g, 0.25 mmol) and 1,3-dimethoxybenzene (0.065 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (100 % petroleum ether) gave **3h** and **3h'** as a colourless oil (a ca. 3:1 mix of regioisomers).
Yield: 0.024 g, 32 %.

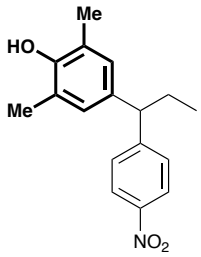
Major Regioisomer 3h

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.09 (2H, d, *J* = 8.7 Hz), 7.36 (2H, d, *J* = 8.7 Hz), 7.13 (1H, d, *J* = 8.4 Hz), 6.48 (1H, dd, *J* = 8.4, 2.4 Hz), 6.41 (1H, d, *J* = 2.4 Hz), 4.23 (1H, t, *J* = 7.8 Hz), 3.79 (3H, s), 3.72 (3H, s), 2.09-1.96 (2H, m), 0.90 (3H, t, *J* = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 159.6, 158.1, 153.9, 146.1, 128.9, 127.8, 124.3, 123.5, 104.2, 98.8, 55.5, 55.4, 45.1, 27.6, 12.7; **HRMS:** (APCI$^+$) $[M]^+$ $C_{17}H_{19}NO_4$ Found: 301.1304, requires 301.1309.

Minor Regioisomer 3h'

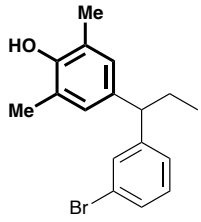
^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.06 (2H, d, *J* = 8.9 Hz), 7.50 (2H, dd, *J* = 8.9, 0.6 Hz), 7.16 (1H, t, *J* = 8.3 Hz), 6.53 (2H, d, *J* = 8.3 Hz), 4.67 (1H, t, *J* = 7.9 Hz), 3.73 (6H, s), 2.26-2.17 (2H, m), 0.87 (3H, t, *J* = 7.4 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 158.5, 153.8, 145.6, 128.7, 128.0, 122.8, 119.8, 104.4, 55.6, 41.4, 24.1, 12.7.

2,6-Dimethyl-4-(1-(4-nitrophenyl)propyl)phenol 3i



The title compound was prepared according to General Procedure A from cyclopropane S2 (0.041 g, 0.25 mmol) and 2,6-dimethylphenol (0.061 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (100 % petroleum ether) gave **3i** and **3i'** as a yellow oil (a ca. 3:1 mix of regioisomers).
Yield: 0.043 g, 60 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) (*only data for the major regioisomer are reported*) δ 8.13 (2H, d, *J* = 8.7 Hz), 7.37 (2H, d, *J* = 8.7 Hz), 6.80 (2H, s), 4.51 (1H, s), 3.76 (1H, t, *J* = 7.8 Hz), 2.21 (6H, s), 2.08-2.01 (2H, m), 0.90 (3H, t, *J* = 7.4 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) (*only data for the major regioisomer are reported*) δ 153.7, 150.9, 134.9, 128.9, 128.6, 127.9, 123.7, 123.2, 52.4, 28.4, 16.0, 12.7; **HRMS:** (APCI$^+$) $[M]^+$ $C_{17}H_{19}NO_3$ Found: 285.1353, requires 285.1359.

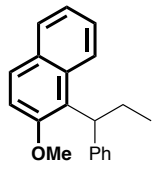
2,6-Dimethyl-4-(1-(3-bromophenyl)propyl)phenol 3j



The title compound was prepared according to General Procedure A from cyclopropane (0.147 g, 0.750 mmol) and 2,6-dimethylphenol (0.091 g, 0.75 mmol) in HFIP (0.250 mL) and stirred at room temperature. Purification by flash column chromatography over silica (10% EtOAc in petroleum ether) gave **3j** as a yellow oil.

Yield: 0.233 g, 97 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) 7.44 (1H, br s), 7.36-7.34 (1H, m), 7.21-7.17 (2H, m), 6.88 (2H, s), 4.64 (1H, s), 3.68 (1H, t, *J* = 7.8 Hz), 2.27 (6H, s), 2.06 (2H, quint. *J* = 7.4 Hz), 0.95 (3H, t, *J* = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) 150.7, 148.4, 136.0, 130.9, 130.0, 129.1, 128.0, 126.5, 123.1, 122.6, 52.3, 28.7, 16.2, 12.9; **HRMS:** ($APCI^+$) $[M]^+$ $C_{17}H_{19}{}^{79}BrO$ Found: 318.0620, requires 318.0614.

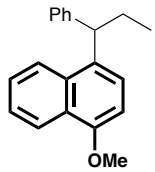
2-Methoxy-1-(1-phenylpropyl)naphthalene 3k



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.033 mL, 0.25 mmol) and 2-methoxynaphthalene (0.079 g, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (100% petroleum ether) gave **3k** as an off-white solid.

Yield: 0.065 g, 94 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.78-7.71 (3H, m), 7.39-1.16 (8H, m), 4.00 (1H, t, *J* = 7.9 Hz), 3.95 (3H, s), 2.26-2.12 (2H, m), 1.02 (3H, t, *J* = 7.3 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 157.4, 145.3, 140.4, 133.2, 129.3, 129.1, 128.4, 128.1, 127.4, 126.9, 126.1, 125.9, 118.7, 105.7, 55.3, 53.1, 28.5, 12.9; **HRMS:** (ESI^+) $[M+H]^+$ $C_{20}H_{21}O$ Found: 277.1578, requires 277.1587.

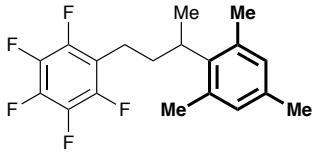
1-Methoxy-4-(1-phenylpropyl)naphthalene 3l



The title compound was prepared according to General Procedure A from cyclopropylbenzene (0.033 mL, 0.25 mmol) and 1-methoxynaphthalene (0.072 mL, 0.50 mmol) in HFIP (0.125 mL) and stirred at room temperature. Purification by flash column chromatography over silica (100% petroleum ether) gave **3l** as a colourless oil (ca. 4:1 mix of regioisomers).

Yield: 0.065 g, 94 %; **^{1}H NMR:** (400 MHz, $CDCl_3$) (*only data for the major regioisomer are reported*) δ 8.29 (1H, s), 7.79 (1H, d, *J* = 8.5 Hz), 7.45-7.34 (8H, m), 6.88 (1H, d, *J* = 7.7 Hz), 4.10-4.03 (1H, m), 4.07 (3H, s), 2.32-2.26 (2H, m), 1.04 (3H, t, *J* = 6.7 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) (*only data for the major regioisomer are reported - one carbon resonance is not observed/overlaps with other resonances*) δ 155.3, 145.3, 142.1, 133.2, 128.4, 128.1, 127.7, 127.3, 126.0, 125.3, 120.1, 120.0, 103.9, 55.5, 53.6, 28.5, 12.9; **HRMS:** (ESI^+) $[M+K]^+$ $C_{20}H_{20}KO$ Found: 315.1159, requires 315.1146.

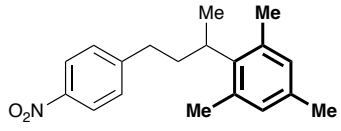
1,2,3,4,5-Pentafluoro-6-(3-mesitylbutyl)benzene 3m



The title compound was prepared according to General Procedure B from (cyclopropylmethyl)pentafluorobenzene **S5** (60.2 mg, 0.244 mmol, 90% pure), mesitylene (67.9 μL, 0.488 mmol) and TfOH (2.2 µL, 0.025 mmol) in 0.125 mL of HFIP (24 h, 100 °C). Purification by flash column chromatography over silica (100% petroleum ether) gave **3m** as an off-white solid.

Yield: 0.082 g, 88%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 6.84 (2H, s), 3.31 (1H, sext, *J* = 7.6 Hz), 2.74–2.62 (1H, m), 2.62–2.50 (1H, m), 2.40 (3H, s), 2.35–2.28 (3H, s), 2.26 (3H, s), 2.18–2.04 (1H, m), 2.04–1.89 (1H, m), 1.37 (3H, d, *J* = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 145.1 (dm, *J* = 244.0 Hz), 139.5 (dm, *J* = 249.6 Hz), 137.5 (dm, *J* = 244.9 Hz), 138.6, 136.3 (br), 135.4, 131.4 (broad), 130.5, 129.4 (br), 115.6 (td, *J* = 18.7, 3.6 Hz), 35.0, 35.0, 21.6 (br, 2C), 21.4 (br), 20.7, 19.1; **^{19}F NMR:** (376.5 MHz, $CDCl_3$, CF_3CO_2H - ext. std.) δ –143.4 (2F, dd, *J* = 22.4, 8.4 Hz), –157.2 (1F, t, *J* = 20.6 Hz), 162.0 (2F, dq, *J* = 21.1, 10.8 Hz); **HRMS:** (APCI$^+$) $[M+H]^+$ $C_{19}H_{20}F_5$ found 342.1416; requires 342.1407.

1,3,5-Trimethyl-2-(4-(4-nitrophenyl)butan-2-yl)benzene 3n

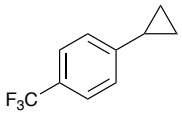


The title compound was prepared according to General Procedure B from 1-cyclopropylmethyl-4-nitrobenzene **S6** (45.3 mg, 0.256 mmol), mesitylene (71.1 μL, 0.511 mmol) and TfOH (2.3 μL, 0.026 mmol) in 0.125 mL of HFIP (24 h, 100 °C). Purification by flash column chromatography over silica (100% petroleum ether) gave **3m** as a yellow oil (mixture of two regioisomers in the ratio 4:1, according to the ^{1}H NMR spectrum). Only data for the major regioisomer is reported.

Yield: 0.068 g, 88%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.11 (2H, d, *J* = 8.8 Hz), 7.25 (2H, d, *J* = 8.4 Hz), 6.81 (2H, s), 3.21 (1H, sext, *J* = 7.6 Hz), 2.72–2.53 (2H, m), 2.34 (3H, s), 2.24 (3H, s), 2.20–2.07 (4H, s), 2.07–1.97 (1H, m), 1.32 (3H, d, *J* = 7.2 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 150.7, 146.4, 138.9, 136.4, 131.4, 129.3, 129.3, 123.7, 36.7, 34.7, 34.4, 21.6, 20.8, 19.2; **HRMS:** (APCI$^+$) $[M]^+$ $C_{19}H_{23}NO_2$, found 297.1731; requires 297.1723.

5. Preparation of Non-Commercial Cyclopropanes

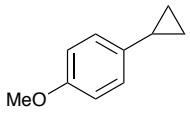
1-Cyclopropyl-4-(trifluoromethyl)benzene S3



Prepared according to General Procedure B with corresponding analytical data.[1]

Yield: 96 %; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 1.98-1.95 (m, 1H), 1.09-1.05 (m, 2H), 0.79-0.76 (m, 2H).

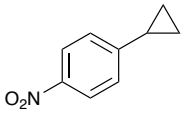
1-Cyclopropyl-4-methoxybenzene 1k



Prepared according to General Procedure B with corresponding analytical data.[2]

Yield: 20 %; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 7.04 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 3.81 (s, 3H), 1.89-1.86 (m, 1H), 0.93-0.91 (m, 2H), 0.65-0.63 (m, 2H).

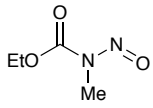
1-Cyclopropyl-4-nitrobenzene 1l



Prepared according to General Procedure B with corresponding analytical data.[3]

Yield: 74 %; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 8.12 (d, *J*=8.9 Hz, 2H), 7.18 (d, *J*=8.9 Hz, 2H), 2.05-1.99 (m, 1H), 1.16-1.13 (m, 2H), 0.88-0.81 (m, 2H).

Ethyl *N*-methyl-*N*-nitrosocarbamate S4

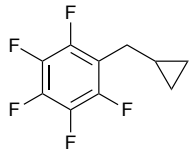


The title compound was prepared according to a literature procedure with corresponding spectral data.[4] To stirring ethyl *N*-methylcarbamate (0.41 g, 4.00 mmol), a solution of H_3PO_4 (0.340 g, 3.44 mmol) in H_2O (0.34 mL) was added carefully. Then, a solution of $NaNO_2$ (0.340 g, 4.90 mmol) in H_2O (0.79 mL) was added slowly, over 1 h, under stirring, and the reaction mixture stirred at room temperature for 16 h. The mixture was extracted with toluene (2 x 5 mL) and used as a crude solution for the preparation of the following cyclopropanes (**S5** and **S6**).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.56 (2H, q, *J* = 7.2 Hz), 3.16 (3H, s), 1.47 (3H, t, *J* = 7.2 Hz).

[1] Y-Y. Zhou, C. Uyeda, *Angew. Chem. Int. Ed.*, 2016, *55*, 3171-3175.
[2] L. Ackermann, A. R. Kapdi and C. Schulzke, *Org. Lett.*, 2010, *12*, 2298-2301.
[3] G. A. Somorjai, *J. Am. Chem. Soc.*, 2016, *138*, 8533-8537.
[4] F. Shroeder, Ruethi, F. WO2015059290 (A1), 2015.

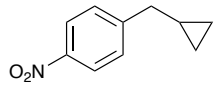
(Cyclopropylmethyl)pentafluorobenzene S5



In a 100 mL round bottom flask, allyl pentafluorobenzene (766 µL, 5.00 mmol) was dissolved in 5 mL of toluene, together with 2.5 mL of 40% KOH(aq) solution and $Pd(acac)_2$ (30 mg, 0.10 mmol) and cooled to 0 °C. Then, 10 mL of crude ethyl *N*-methyl-*N*-nitrosocarbamate **S4** in toluene solution was added, the reaction mixture stirred at 0 °C for 1 h, and then at ambient temperature for 16 h. At completion, the organic layer was decanted, dried over anhydrous Na_2SO_4, and the solvent removed under reduced pressure. The crude residue was filtered through a celite plug and concentrated to give **S4** as a yellow oil, which was used without further purification.

Yield: 0.621 g, 56%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 2.61 (2H, d, *J* = 6.8 Hz), 1.05–0.89 (1H, m), 0.50 (2H, d, *J* = 7.6 Hz), 0.25 (2H, d, *J* = 4.4 Hz); **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 145.2 (dm, *J* = 243.0 Hz), 139.7 (dm, *J* = 249.5 Hz), 137.6 (dm, *J* = 248.4 Hz), 117.3, 115.2 (td, *J* = 19.4, 3.7 Hz), 27.2, 11.0, 4.9; **^{19}F NMR:** (376.5 MHz, $CDCl_3$, CF_3CO_2H - ext. std.) δ –143.1 (2F, dd, *J* = 22.5, 8.4 Hz), –157.0 (1F, t, *J* = 21.0 Hz), –161.9 (2F, dq, *J* = 21.0, 10.8 Hz); **HRMS:** (ESI) *m/z* for $C_{10}H_7F_5$ ($[M+H]^+$) calculated 222.0462; found 222.0454.

1-Cyclopropylmethyl-4-nitrobenzene S6



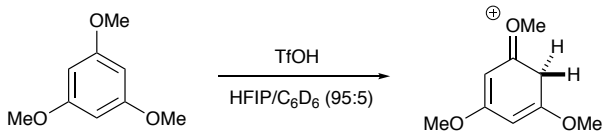
The title compound was prepared from 4-nitrobenzyl chloride (346 mg, 2.01 mmol), potassium cyclopropyltrifluoroborate (452 mg, 3.05 mmol), $Pd_2(dba)_3$ (94 mg, 0.10 mmol), RuPhos (100 mg, 0.21 mmol) and K_2CO_3 (556 mg, 4.02 mmol). The reactants were dissolved in a degassed mixture of toluene/water (19:1, mL/mL) under an argon atmosphere. The reaction was stirred for 9 h at 120 ^{o}C. After cooling to room temperature, the reaction mixture was filtered through celite and $MgSO_4$, and the solvent was removed under reduced pressure. Purification by automated flash column chromatography over silica (with a mixture of petroleum ether and ethyl acetate) gave **S6** as a pale yellow oil.

Yield: 0.225 g, 63%; **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 2.65 (d, *J* = 6.8 Hz, 2H), 1.06–0.93 (m, 1H), 0.63–0.51 (m, 2H), 0.24 (q, J = 5.2 Hz, 2H). Spectral data are in agreement with the literature.[5]

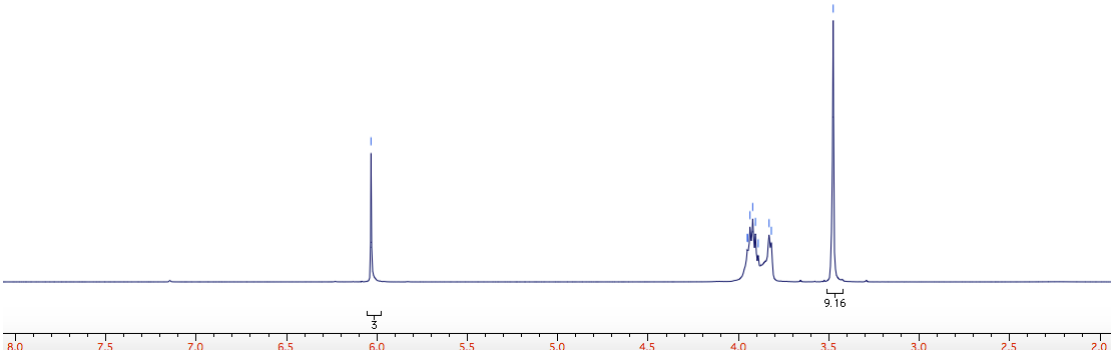
[5] V. Colombel, F. Rombouts, D. Oehlrich, G. A. Molander *J. Org. Chem.* **2012**, *77*, 2966.

6. ^{1}H-NMR Titration Data

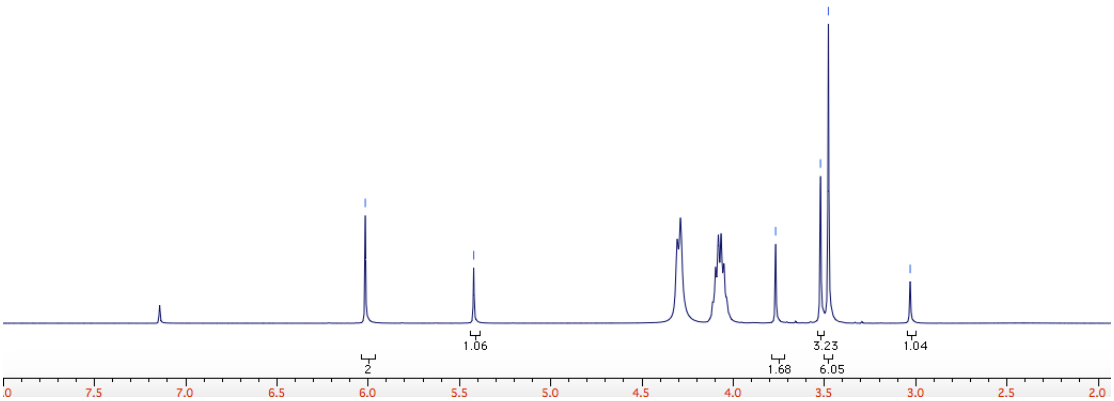
1,3,5-Trimethoxybenzene and TfOH in HFIP/C_6D_6 (95:5)



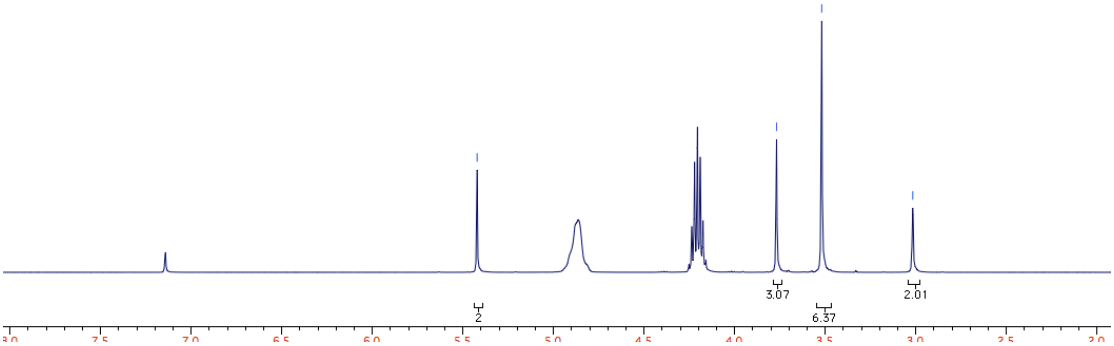
0% TfOH



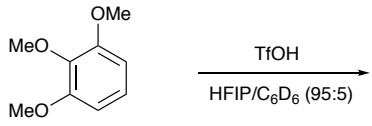
50 mol% TfOH



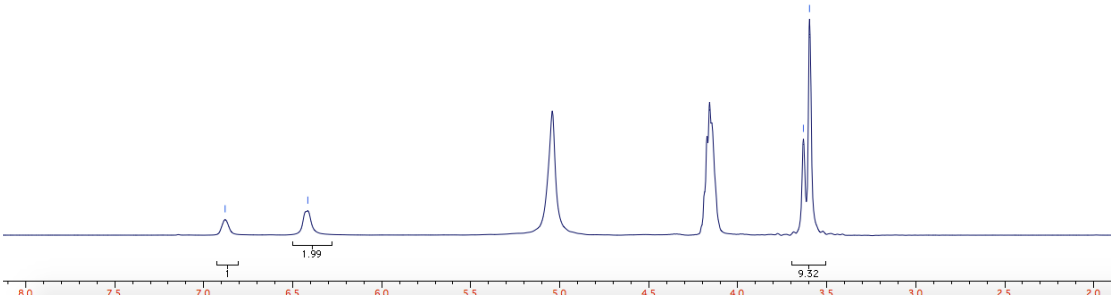
100 mol% TfOH



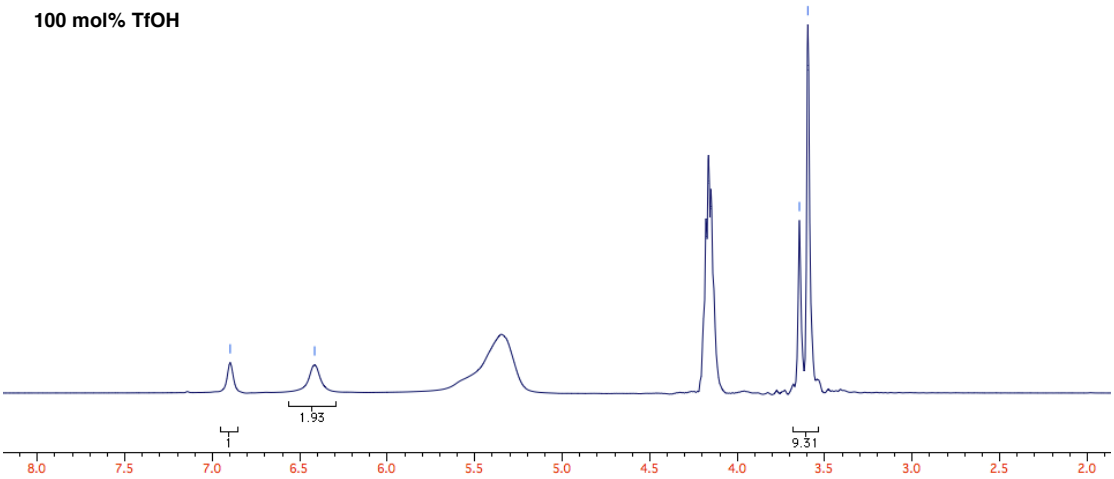
1,2,3-Trimethoxybenzene and TfOH in HFIP/C_6D_6 (95:5)



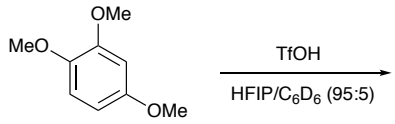
50 mol% TfOH



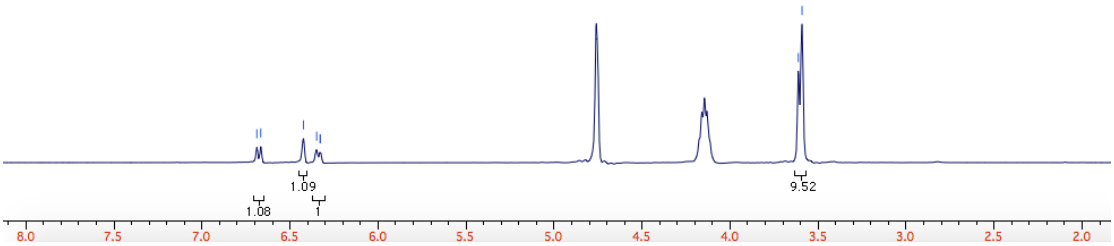
100 mol% TfOH



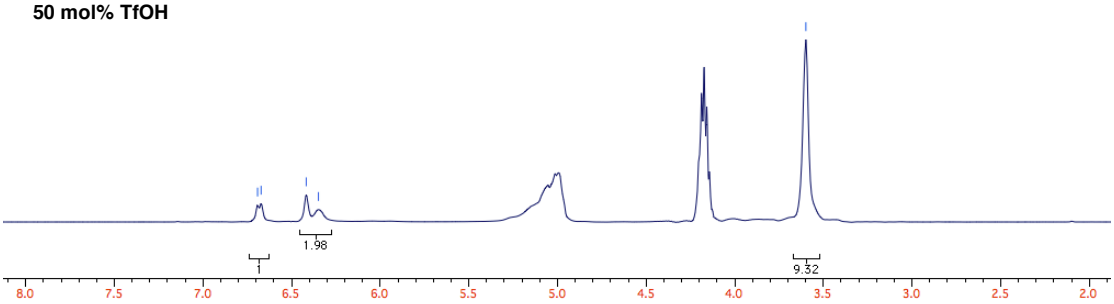
1,2,4-Trimethoxybenzene and TfOH in HFIP/C_6D_6 (95:5)



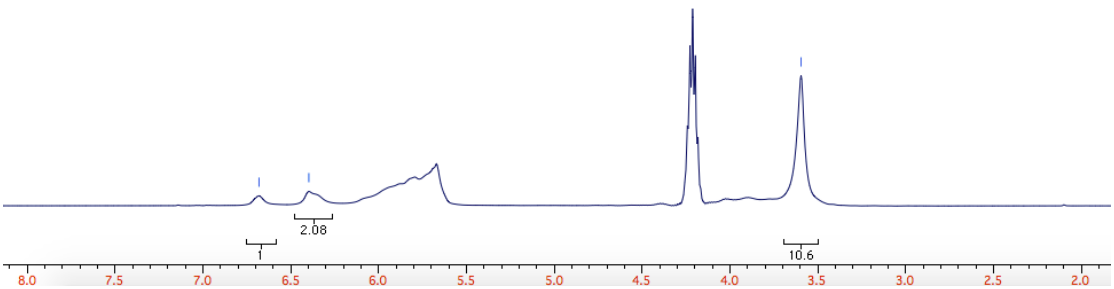
0% TfOH



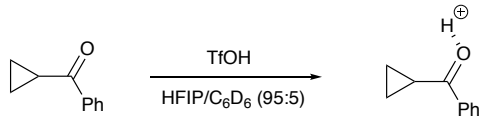
50 mol% TfOH



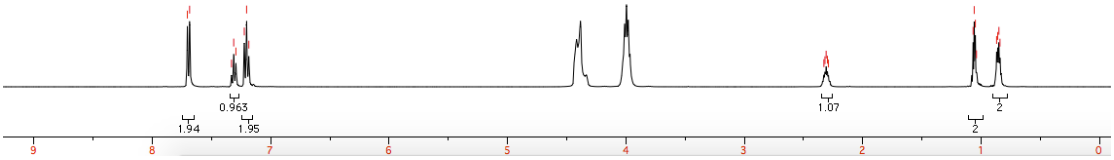
100 mol% TfOH



Cyclopropyl phenyl ketone and TfOH in HFIP/C_6D_6 (95:5)



0% TfOH



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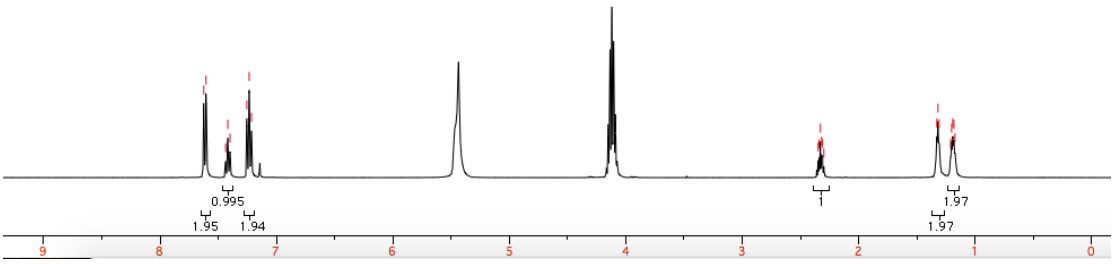

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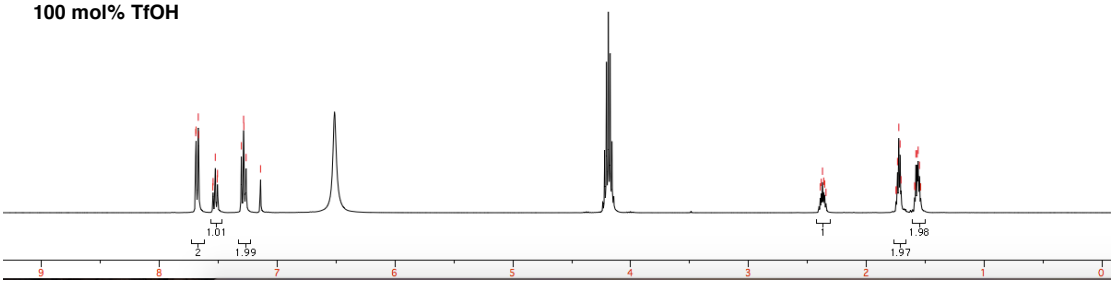
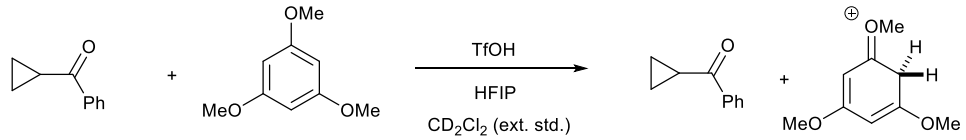
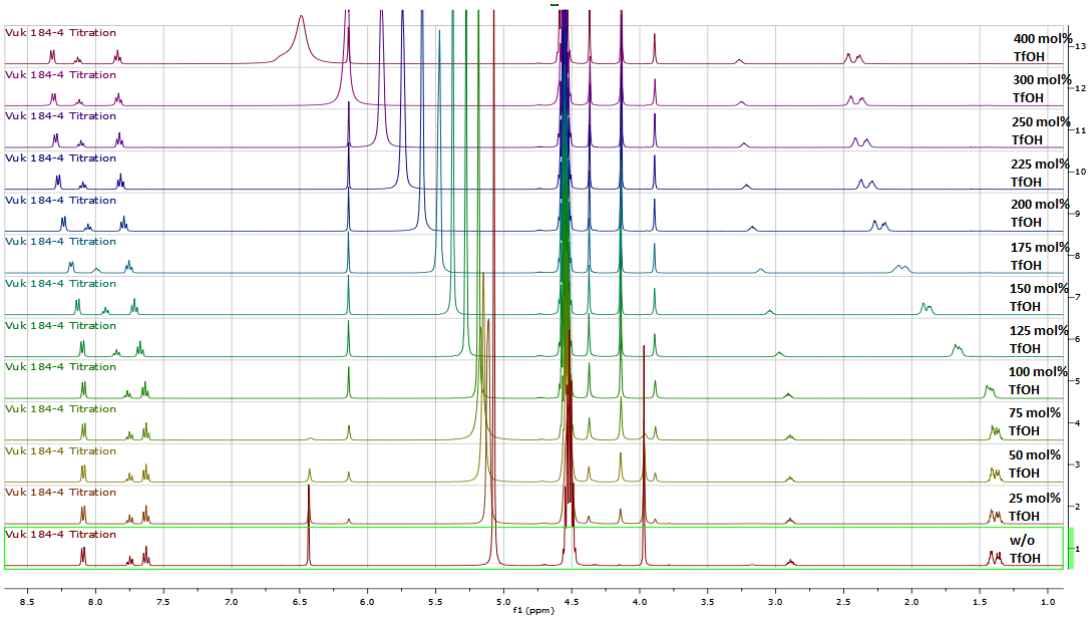


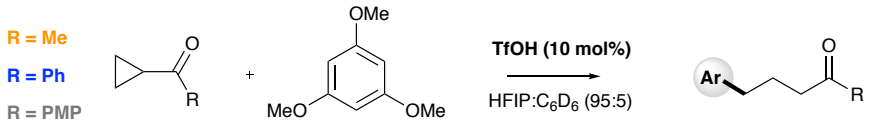
Cyclopropyl phenyl ketone and 1,3,5-Trimethoxybezene (1:1, molar ratio) with TfOH in HFIP (CD_2Cl_2 – external standard)

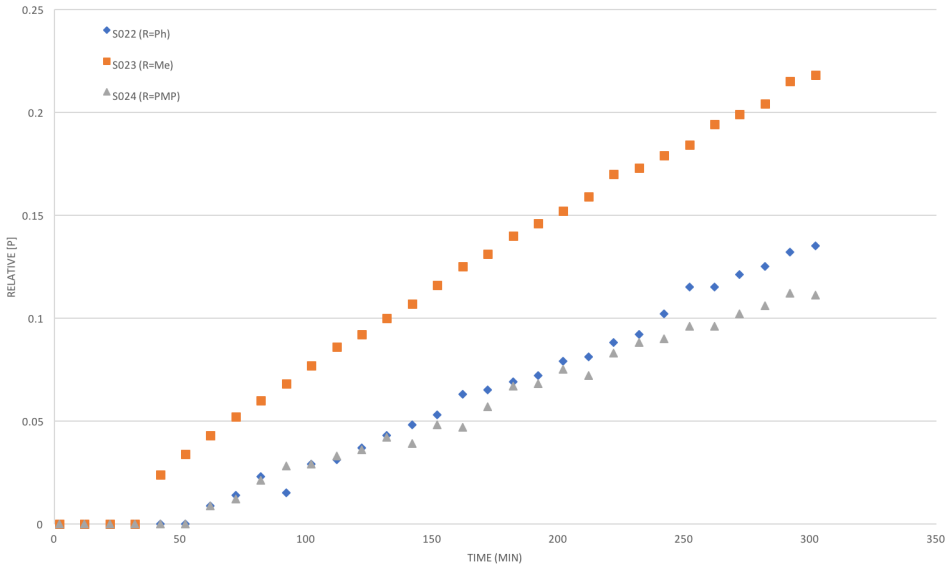




7. Relative Rate Experiments & Hammett Analysis

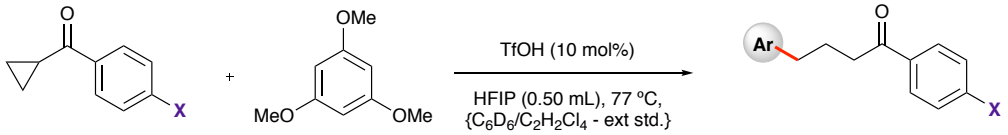
A comparison of the relative rates (determined *via* [product] formation/time) of the arylation of the following cyclopropyl ketones was undertaken and monitored by ^{1}H NMR spectroscopy at 65 °C.





As indicated on the chart above, methyl cyclopropyl ketone exhibited the fastest rate of arylation. The phenyl and 4-methoxyphenyl ketone derivatives displayed much slower rates of arylation, suggesting that mesomeric stabilization of nascent positive charge retards this arylation reaction. This observation strongly suggests that a mechanism involving direct protonation of the cyclopropane ring is not a contributing mechanistic pathway and that protonation initially occurs on the carbonyl group side-chain.

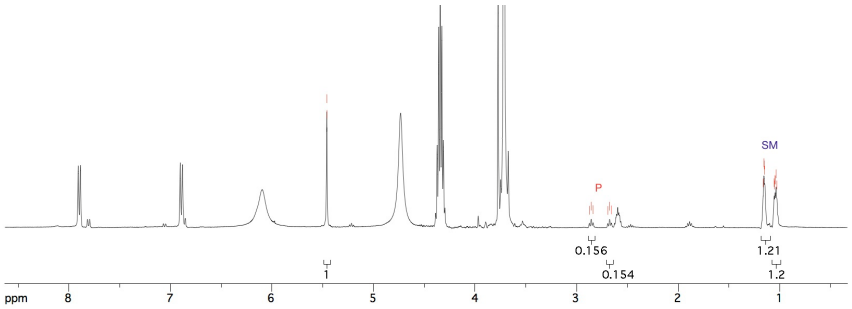
Standard Procedure for ^{1}H NMR Time Course Experiments



0.50 mmol [1M] 1.0 mmol [2M] **X** = H, Me-, MeO-, Cl, F

A screw-top NMR tube containing capillaries of external standard C_6D_6 and tetrachloroethane was charged with a 1M solution of the requisite cyclopropane (0.50 mmol) in HFIP (0.500 mL) followed by 1,3,5-trimethoxybenzene (1.0 mmol, 0.168 g). After introduction to the NMR probe, this sample was heated at 77 °C and allowed to rest at this temperature for 5 min. The sample was then locked and shimmed. After removing the NMR tube, TfOH (4.4 µL, 10 mol%) was added to the mixture, the tube capped, inverted 3 times, reintroduced into the machine and acquisition begun after 120 seconds. The reaction was then followed by ^{1}H NMR over time (ns = 4, 300 s/36 experiments or every 600s/24 experiments). Conversion to product was calculated relative to the internal standard as below and plotted between 2-10% conversion to determine initial rates.

$$[\mathrm{P}] = \frac{\text{Average } \mathbf{P} \text{ integration}}{\text{Average } \mathbf{P} \text{ integration} + \text{Average } \mathbf{SM} \text{ Integration}} \times \text{Conc.}$$



Average initial rates were determined via the average of at least 3 congruent values – the values being given in Table **S1** below.

	Ph	p-F	p-Cl	p-Me	p-MeO
Run 1	0.000286082	0.000225879	0.000411375	0.000385802	0.000230652
Run 2	0.000481448		0.000211763	0.000434392	0.000172799
Run 3	Poorly Shimmed	0.000209991	0.000243308	0.000331549	0.00030776
Run 4	0.000242146	0.000221579	Poorly Shimmed		0.000256576
Run 5	0.000264584	0.000287866	0.000127467		0.000242874
Run 6	0.000322052		0.000385617		
Run 7	0.000333308		0.000218328		
Run 8	0.000429073				
Run 9	0.000292829				
Average	**0.00033144**	**0.000236329**	**0.00026631**	**0.000383914**	**0.000242132**
log kobs	**-3.479594916**	**-3.62648358**	**-3.574613259**	**-3.4157659**	**-3.615947344**
log (kobs/KH)	**0**	**-0.146888664**	**-0.095018343**	**0.063829016**	**-0.136352428**
s value	**0**	**0.34**	**0.23**	**-0.17**	**-0.27**
s+ value	-0.18	-0.07	0.11	-0.31	-0.78

Table S1: Initial rates data for Hammett Analysis. Average initial rates are shown in purple, log(kobs) are given in blue and the relative rates for Hammett analysis are shown in red.

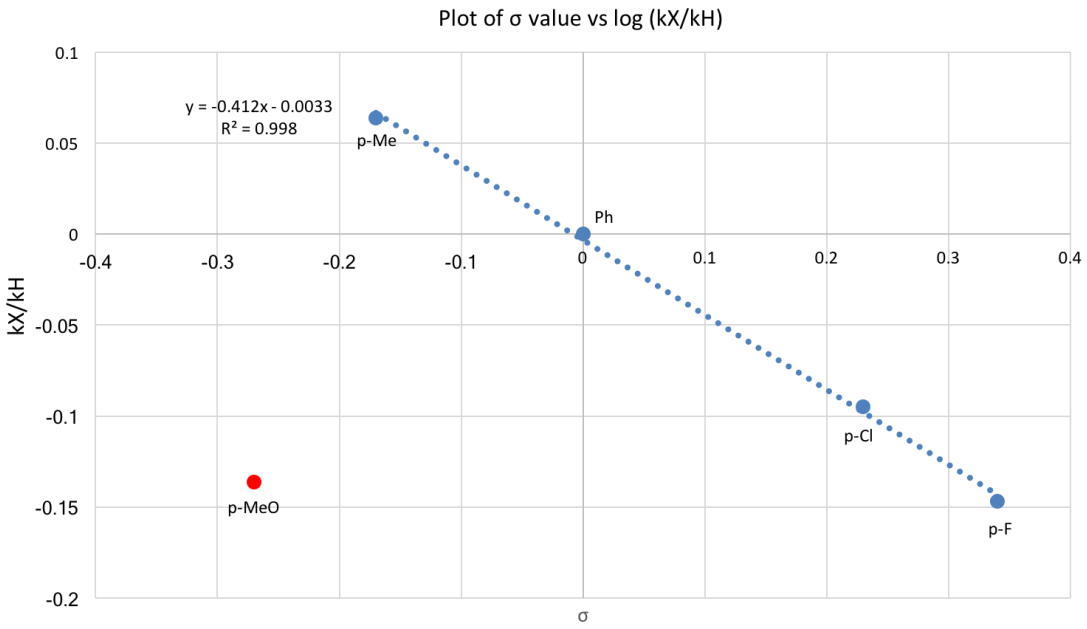


Figure S1: Hammett Plot.

8. DFT Calculations

DFT calculations were performed using Gaussian 16 A03.[1] The ωB97X-D exchange-correlation functional [2] and the def2-TZVP basis set [3] was used in all calculations. The SMD solvent model [4] was used with parameters adapted for HFIP. An absolute Gibbs energy of solvation for the proton of -267 kcal/mol was included in calculations involving charged species.

1. Gaussian 16, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

2. J.-D. Chai and M. Head-Gordon, “Long-range corrected hybrid density functionals with damped atom-atom dispersion corrections,” *Phys. Chem. Chem. Phys.*, 10 (2008) 6615-20. DOI: 10.1039/B810189B

3. F. Weigend and R. Ahlrichs, “Balanced basis sets of split valence, triple zeta valence and quadruple zeta valence quality for H to Rn: Design and assessment of accuracy,” *Phys. Chem. Chem. Phys.*, 7 (2005) 3297-305. DOI: 10.1039/B508541A

4. V. Marenich, C. J. Cramer, and D. G. Truhlar, “Universal solvation model based on solute electron density and a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions,” J. Phys. Chem. B, 113 (2009) 6378-96. DOI: 10.1021/jp810292n

Table S2. Reaction energies for all reactions modelled according to Path B. All values are Gibbs energies in kcal/mol, calculated using ωB97X-D/def2-TZVP with an SMD solvation correction.

Arene	Ketone	Protonated Cyclopropane	Transition State	Intermediate	Enol	Product
1,3,5-trimethoxybenzene	-C(=O)Me	4.37	32.25	1.23	-0.09	-12.66
1,3,5-trimethoxybenzene	-C(=O)OCH_3	10.74	43.14	20.89	14.17	-13.07
1,3,5-trimethoxybenzene	-(C(=O)OCH_3)$_3$	10.21	33.45	2.99	0.03	-12.64
1,4-dimethoxybenzene	-C(=O)Me	4.37	37.49	17.63	-1.06	-15.02
1,3,5-trimethoxybenzene	-(C(=O)Ph	7.52	32.92	0.01	0.69	-12.94
1,3,5-trimethoxybenzene	-(C(=O)Ph-F)	8.23	34.00	1.48	1.73	-12.22
1,3,5-trimethoxybenzene	-(C(=O)Ph-OMe)	5.71	33.55	0.76	1.68	-12.51
1,3,5-trimethoxybenzene	-(C(=O)Ph-Cl)	8.75	33.88	-0.13	0.31	-12.53
1,3,5-trimethoxybenzene	-(C(=O)Ph-Me)	7.07	33.88	1.65	2.74	-11.73
1,2,3-trimethoxybenzene	-(C(=O)Ph	7.52	36.41	10.10	-1.92	-14.61
1,2,4-trimethoxybenzene	-(C(=O)Ph	7.52	33.71	5.20	-1.56	-14.30

Sample Input File

```
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%mem=4000MB
%chk=TS.chk
#wb97xd scrf=(SMD,solvent=generic,read)  def2tzvp freq

Transition state - TMB plus MVK

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C,-1.5383033942,-0.8855814596,-0.9809255084
C,-0.5216755045,1.3088109006,-0.9946604833
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C,-1.2518454133,1.6658483416,0.1198162327
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H,-2.9640901569,-1.2563454706,0.5869233666
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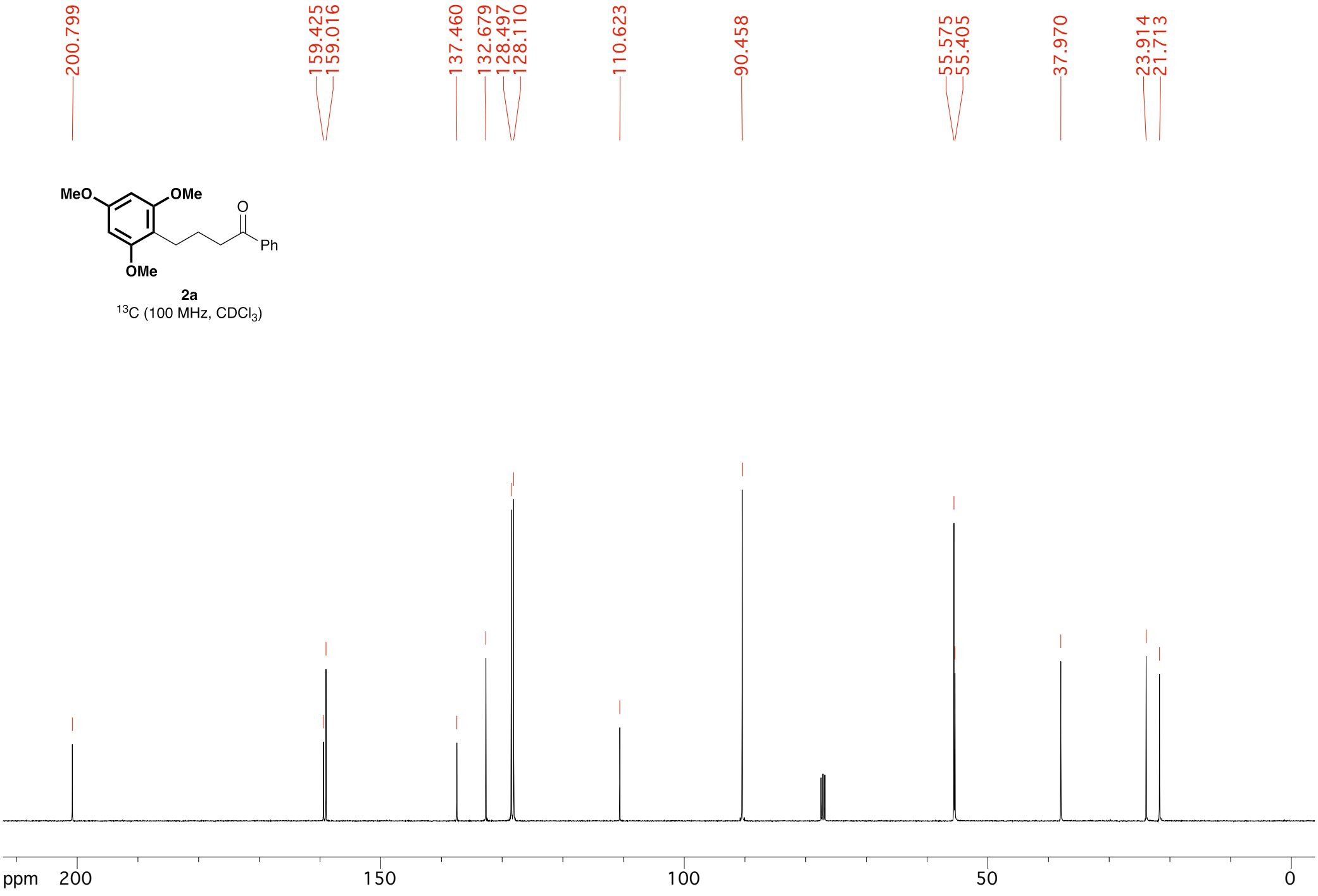
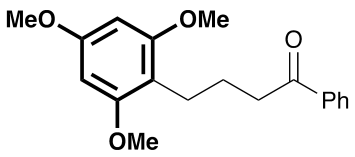
9. Spectral data for Products



2a

^{13}C (100 MHz, $CDCl_3$)



2a

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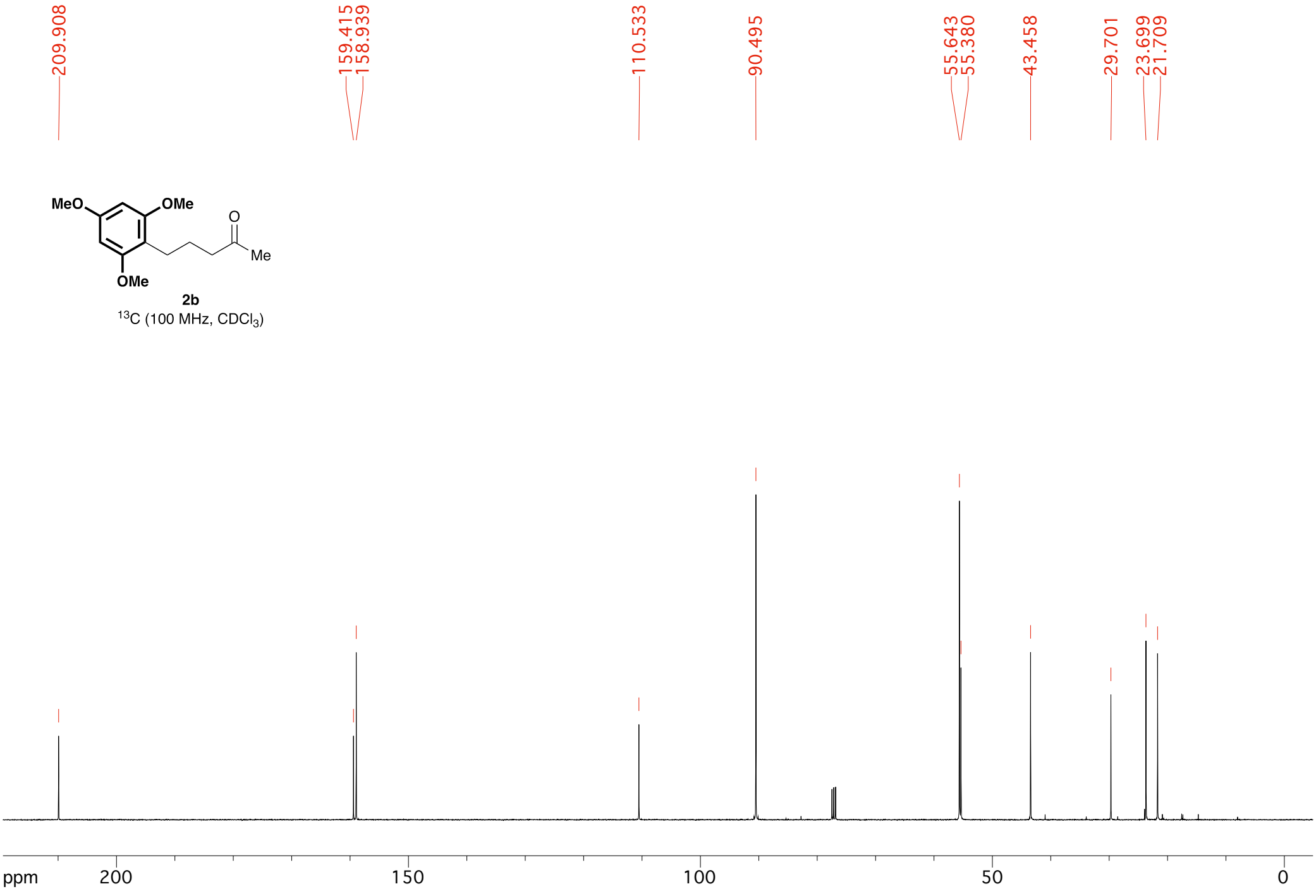
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OMe
2b
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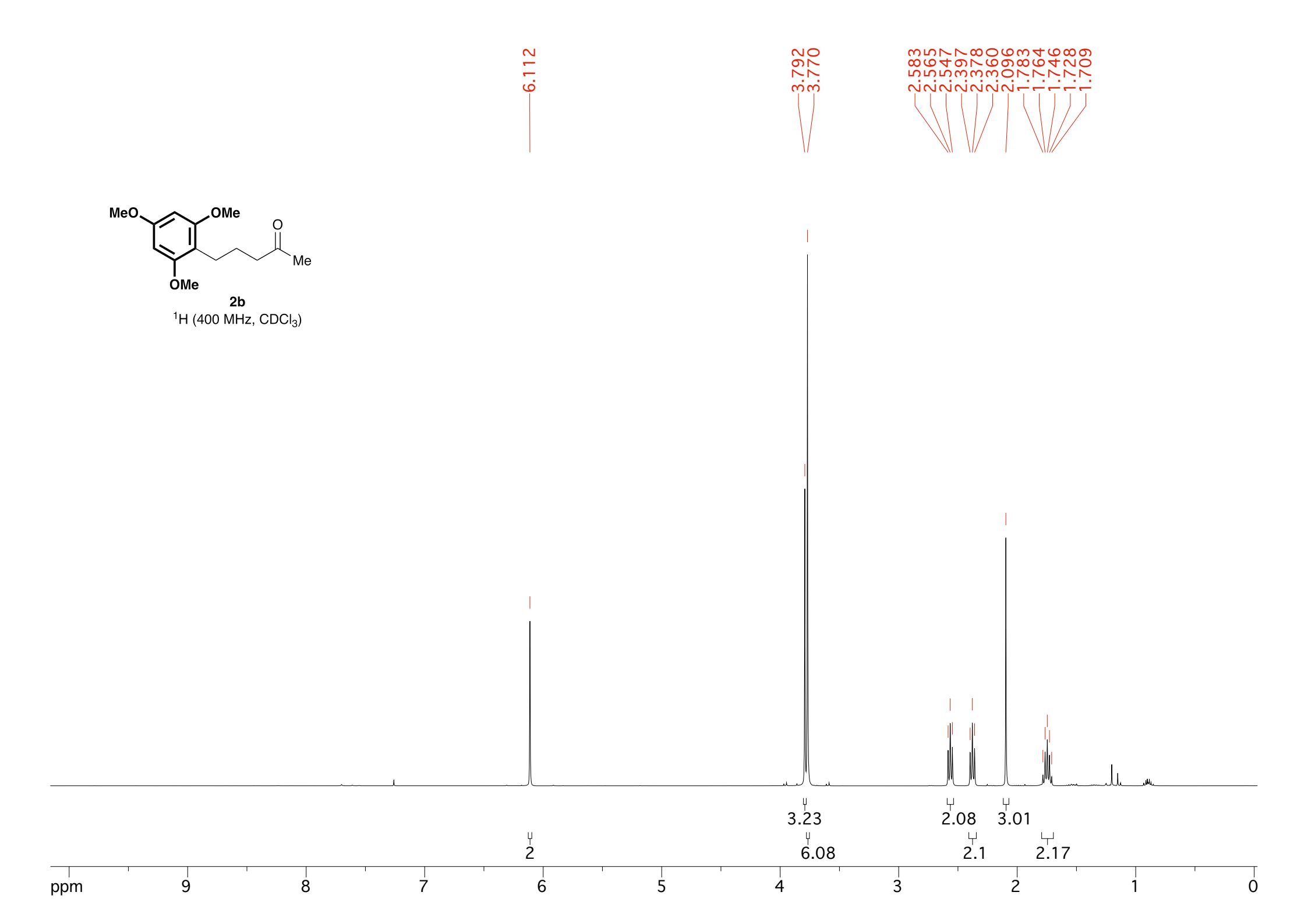
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OMe
O
Me
OMe
2b
1H (400 MHz, CDCl3)
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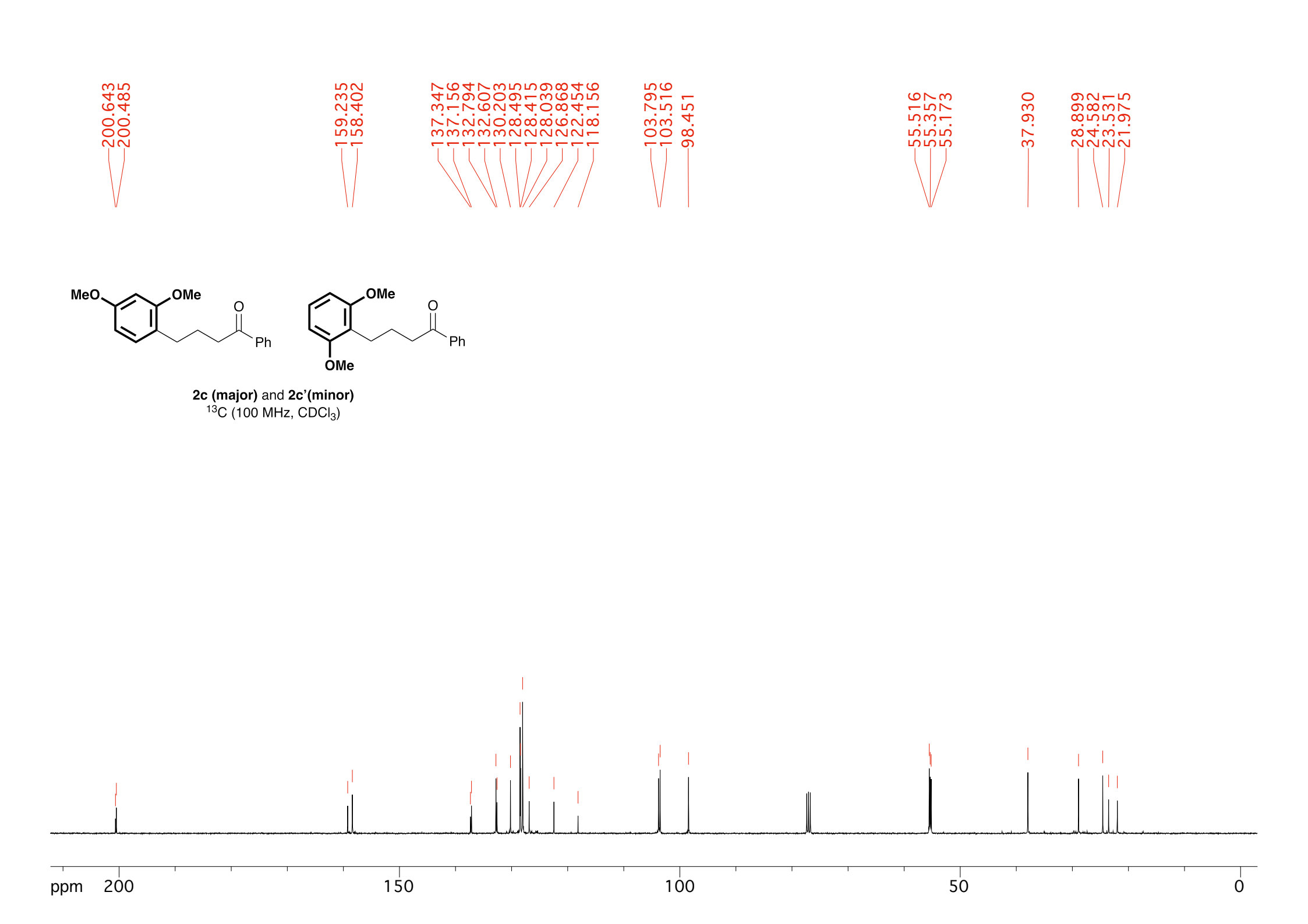

2c (major) and **2c'(minor)**
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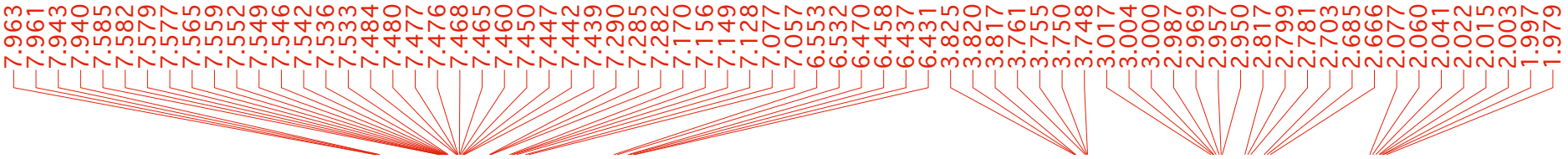

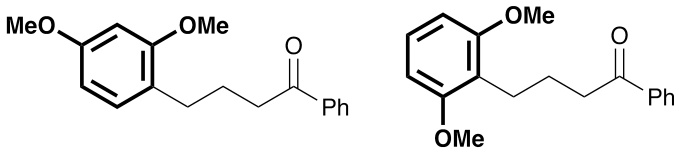

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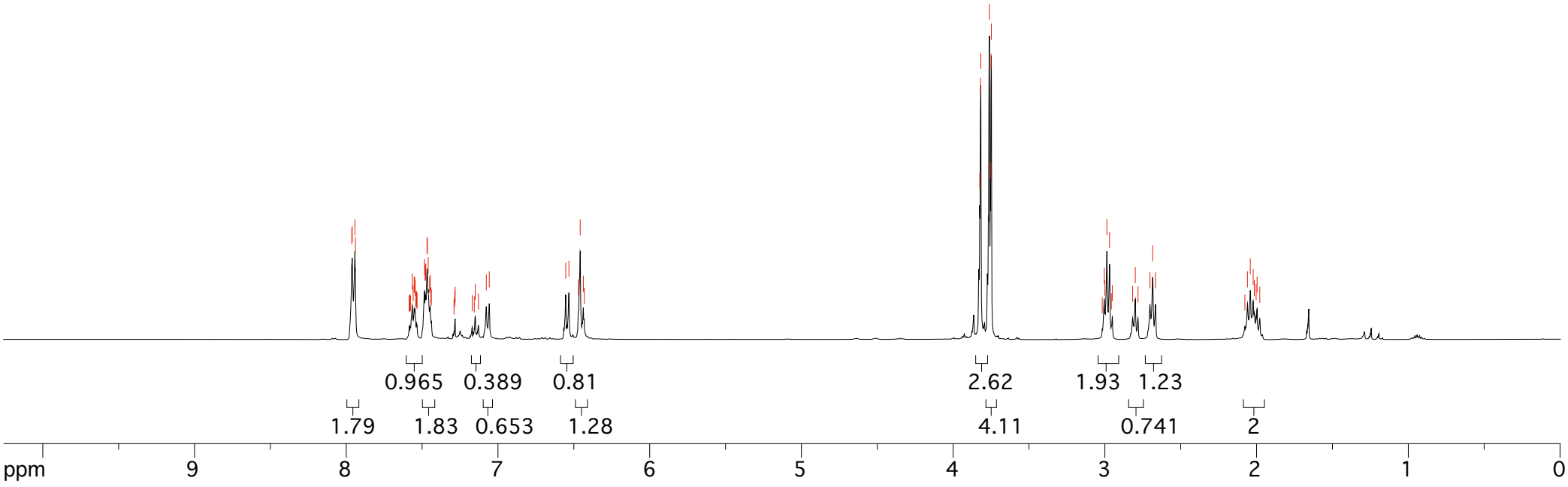

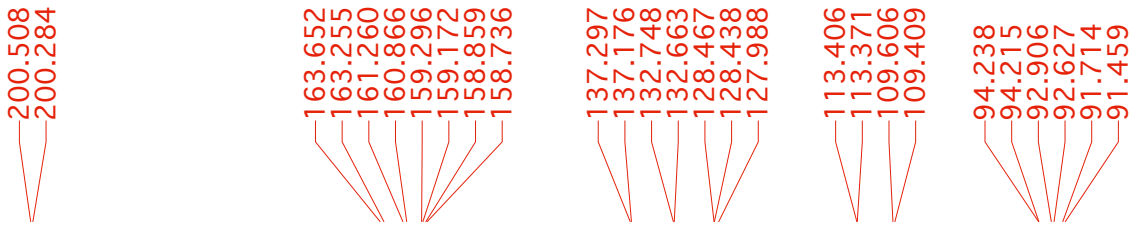

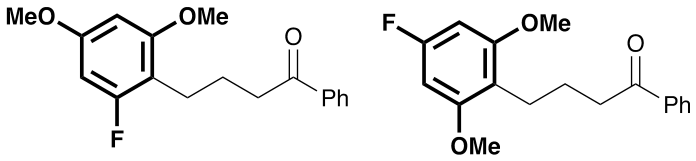

2d (major) and **2d'(minor)**
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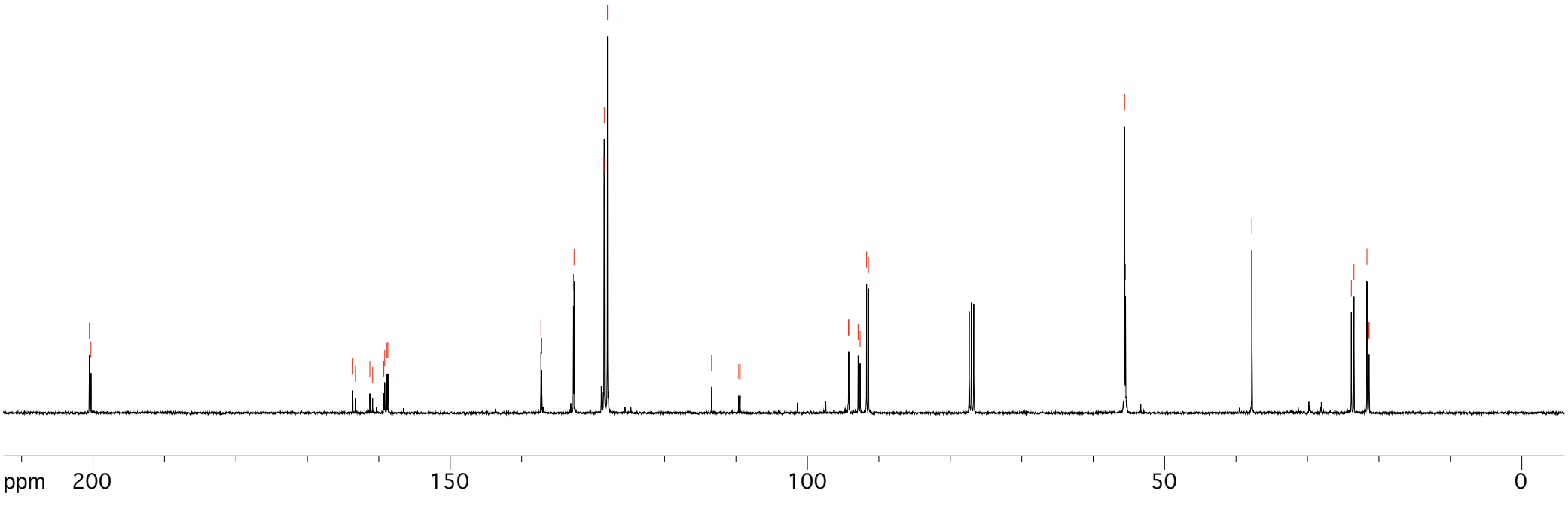

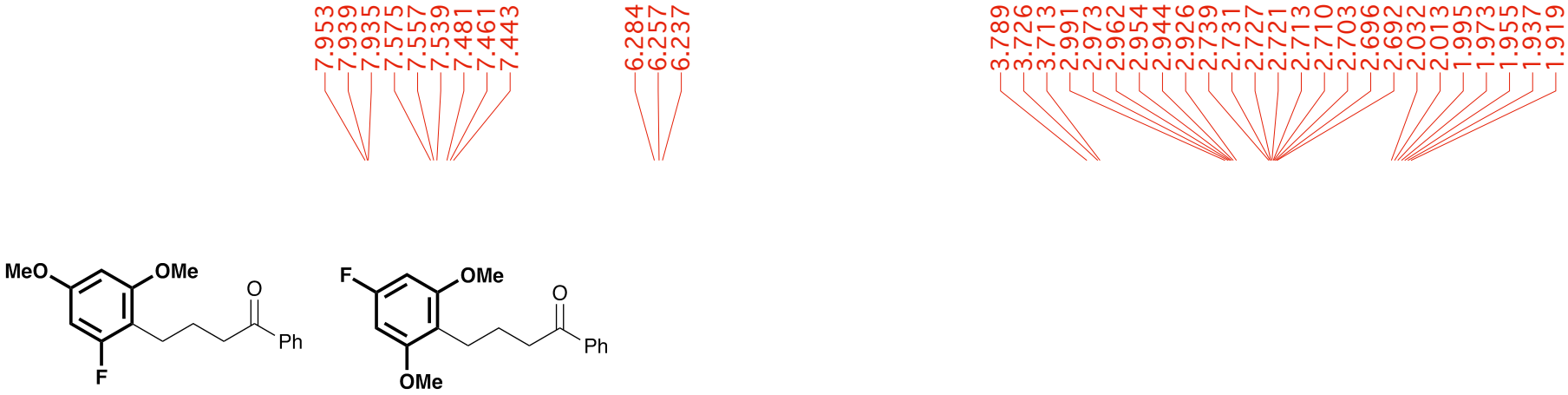

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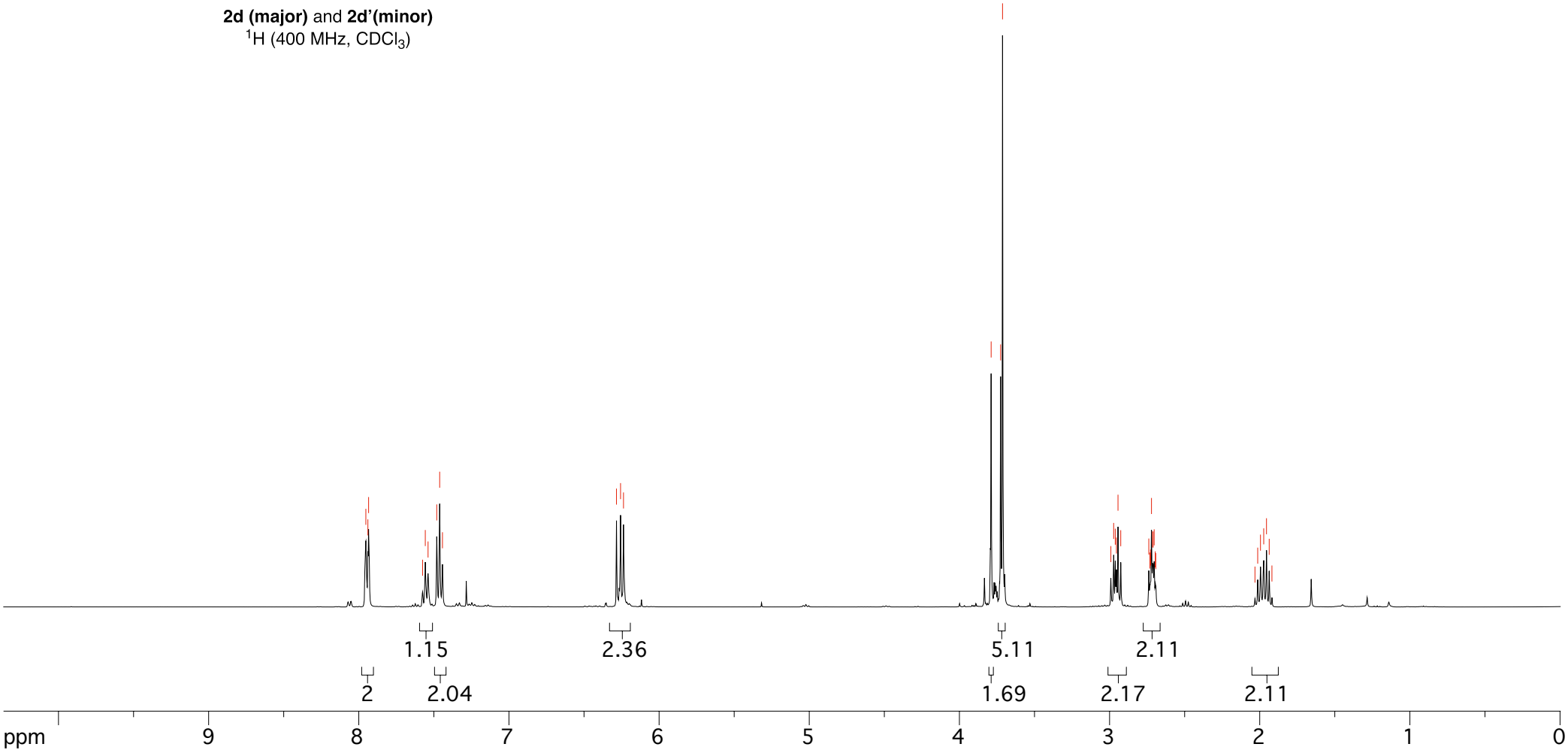

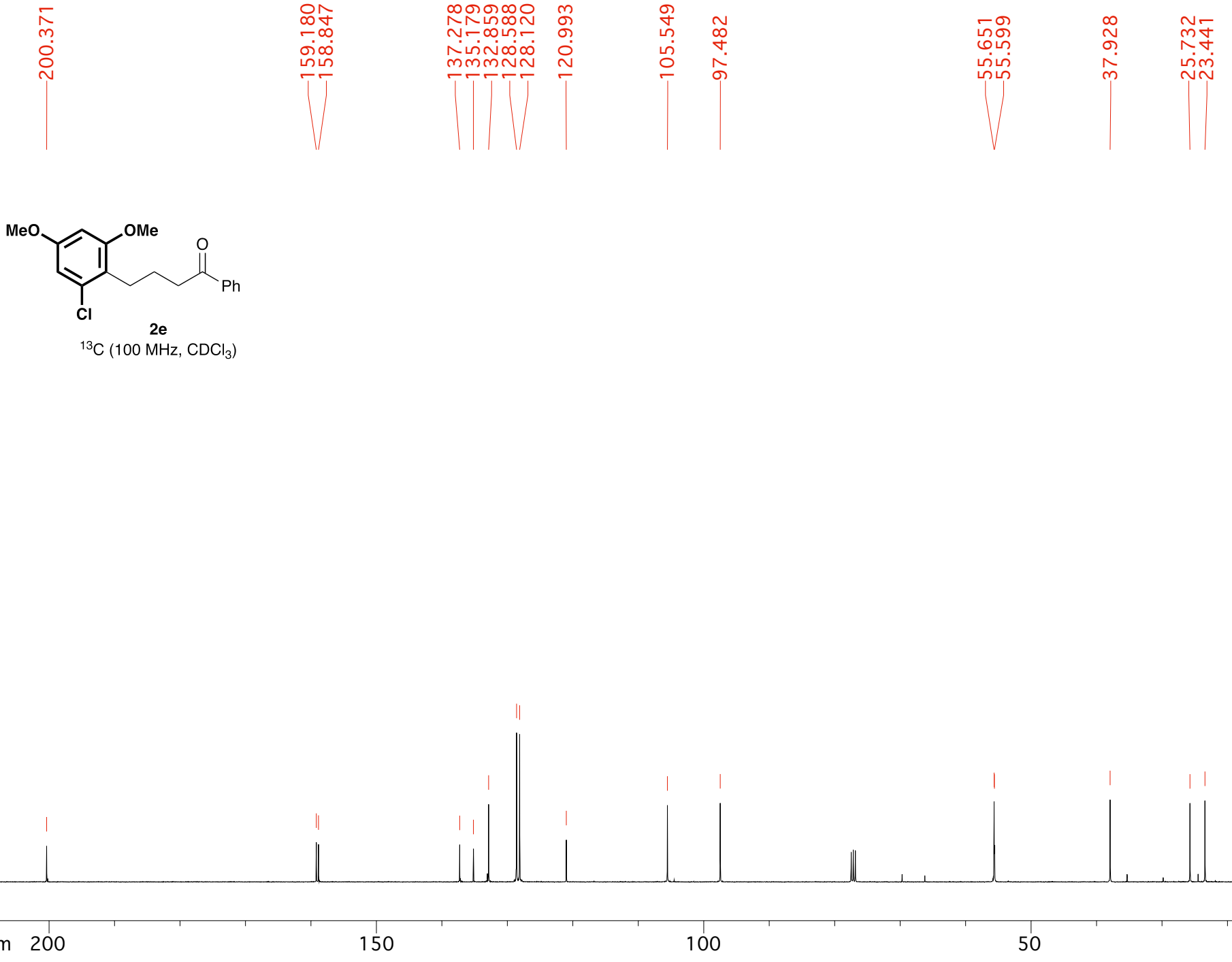
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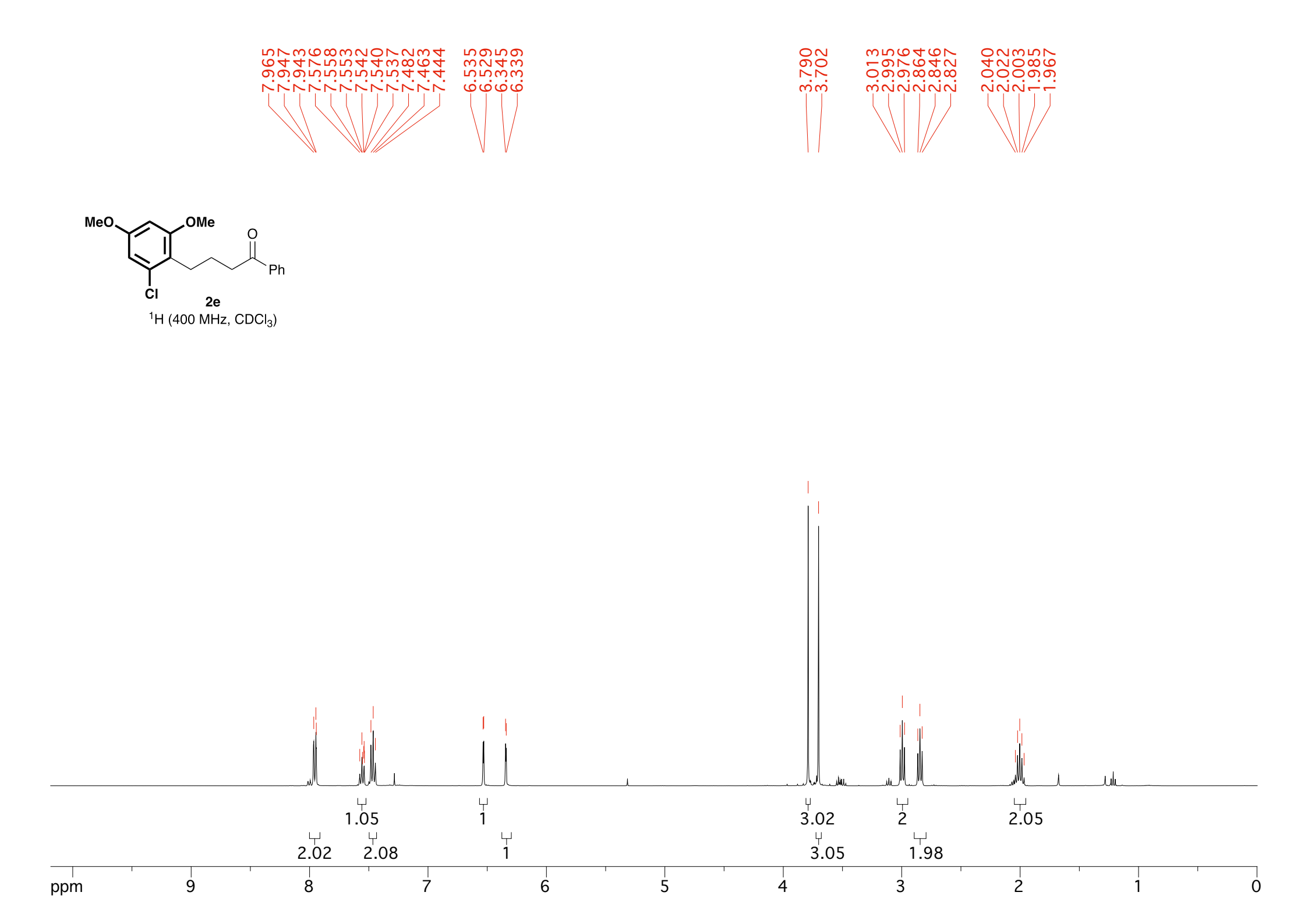
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OMe
O
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2
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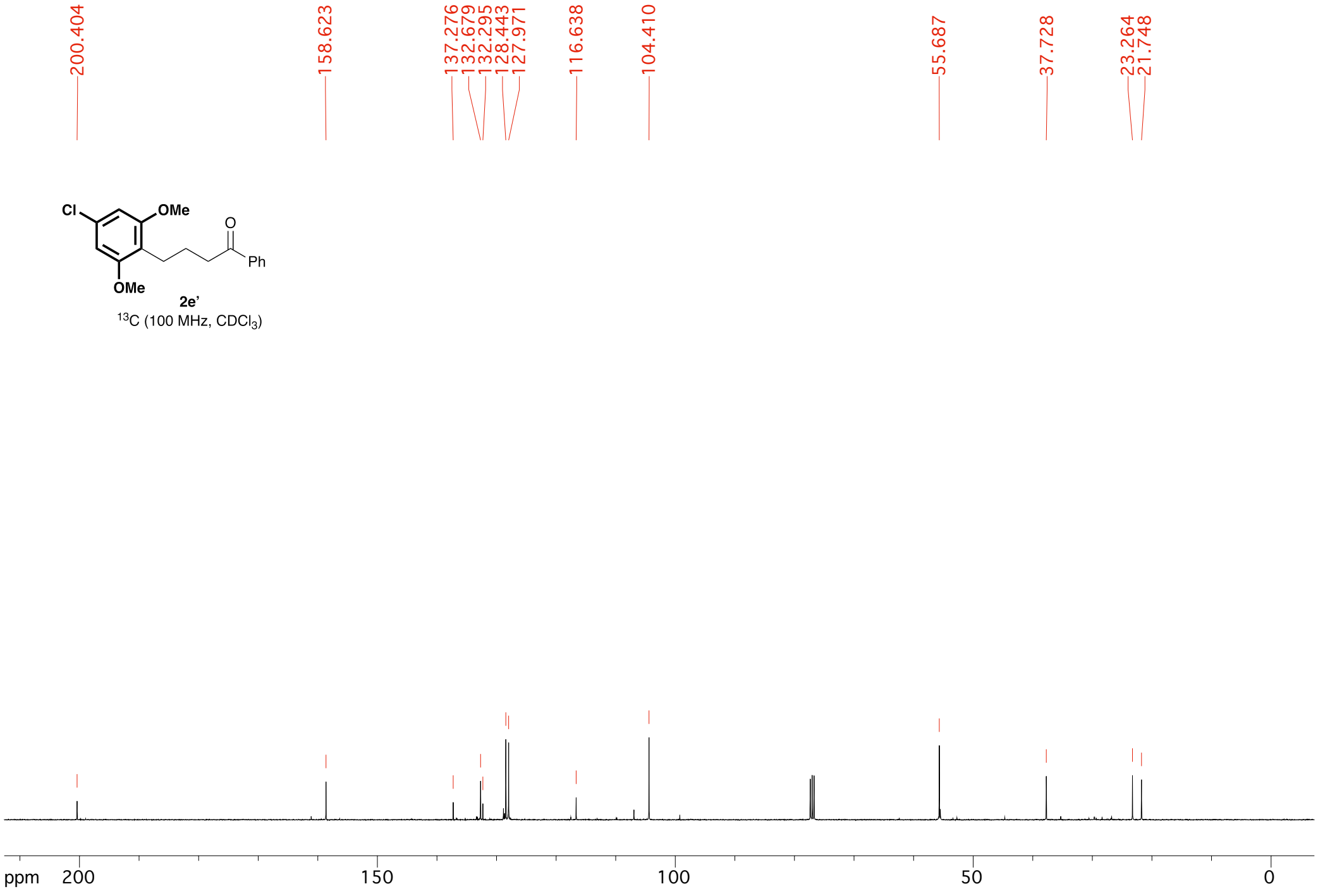
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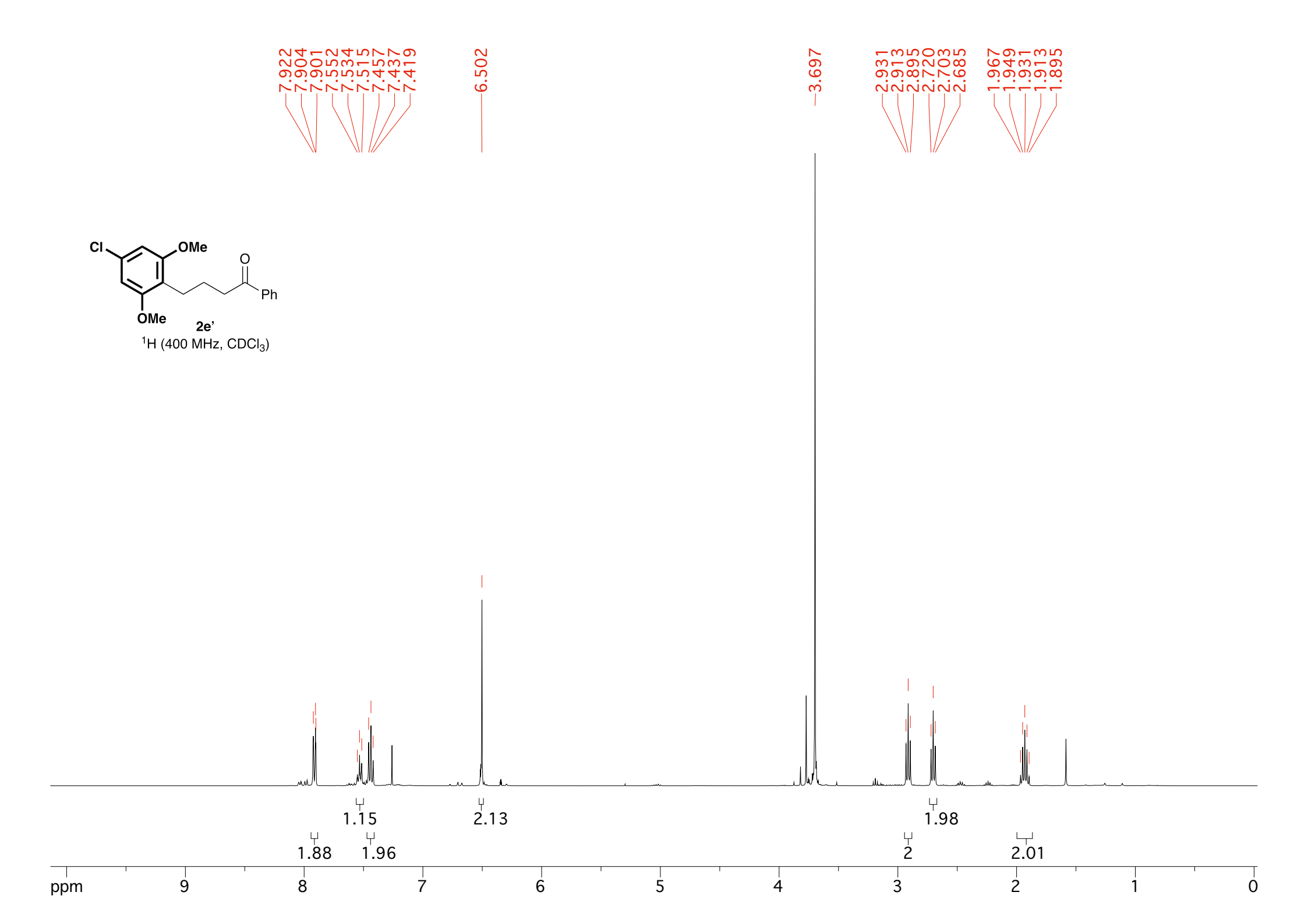
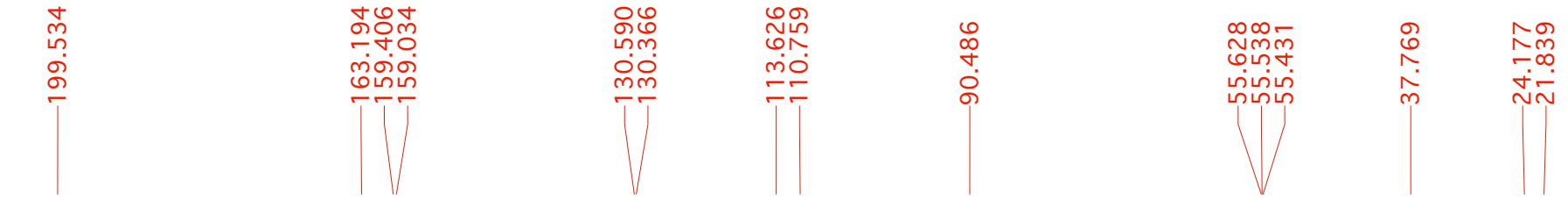
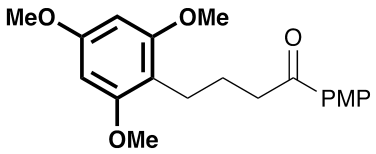
158.623
137.276
132.679
132.295
128.443
127.971
116.638
104.410
55.687
37.728
23.264
21.748
Cl
OMe
O
Ph
OMe
2e'
^{13}C (100 MHz, $CDCl_3$)
ppm
200
150
100
50
0

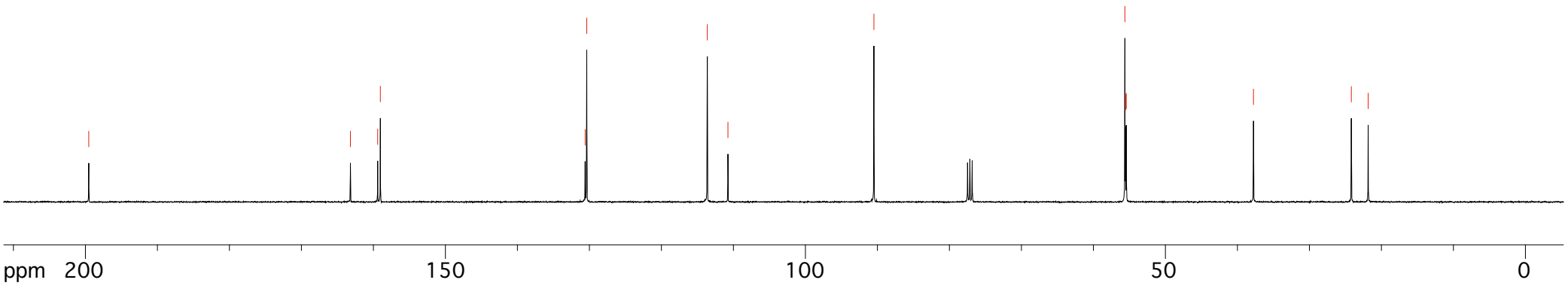

7.922
7.904
7.901
7.552
7.534
7.515
7.457
7.437
7.419
6.502
3.697
2.931
2.913
2.895
2.720
2.703
2.685
1.967
1.949
1.931
1.913
1.895
Cl
OMe
O
Ph
OMe
2e'
1H (400 MHz, CDCl3)
1.15
2.13
1.98
1.88
1.96
2
2.01
ppm
9
8
7
6
5
4
3
2
1
0

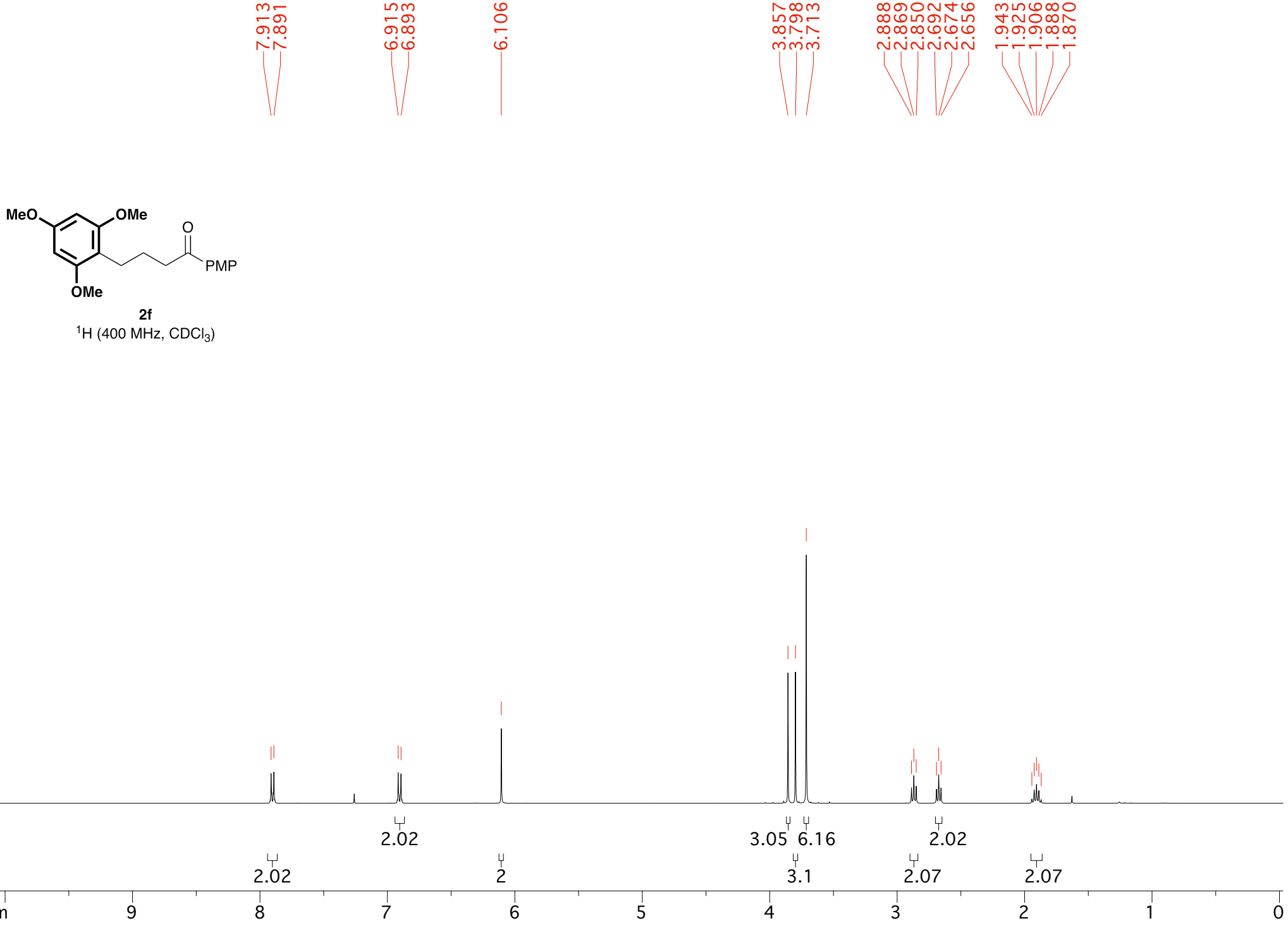




2f

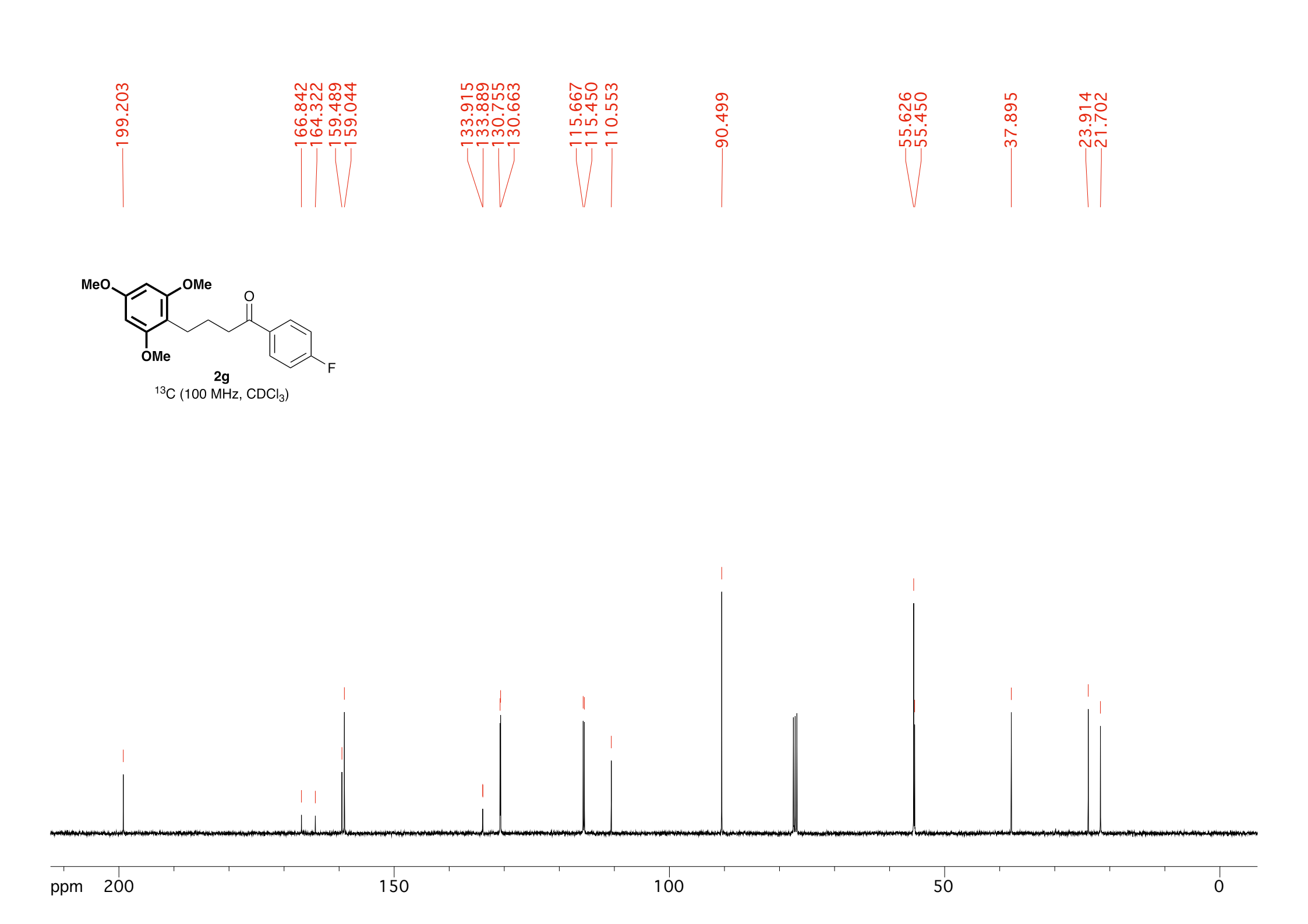
^{13}C (100 MHz, $CDCl_3$)

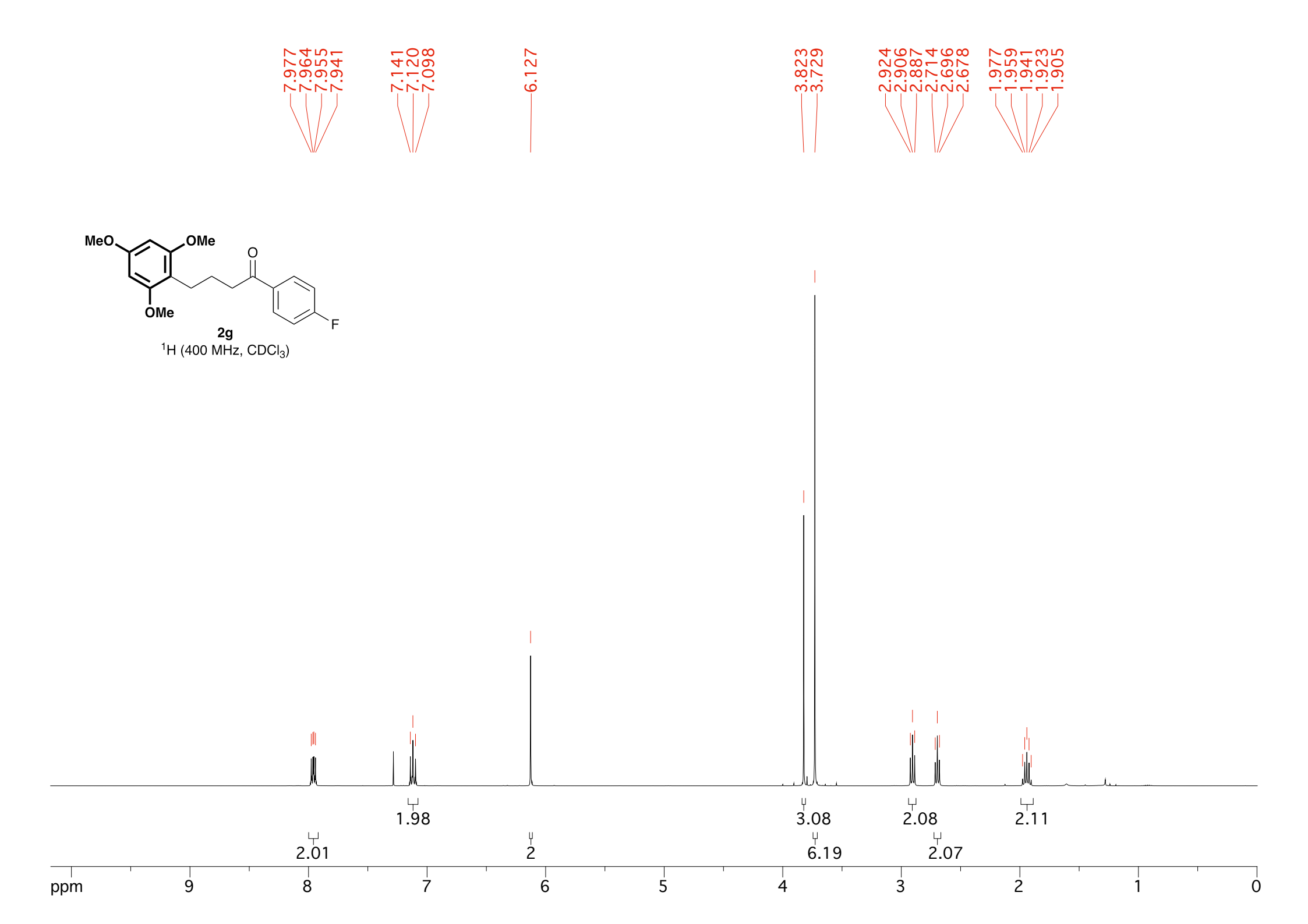


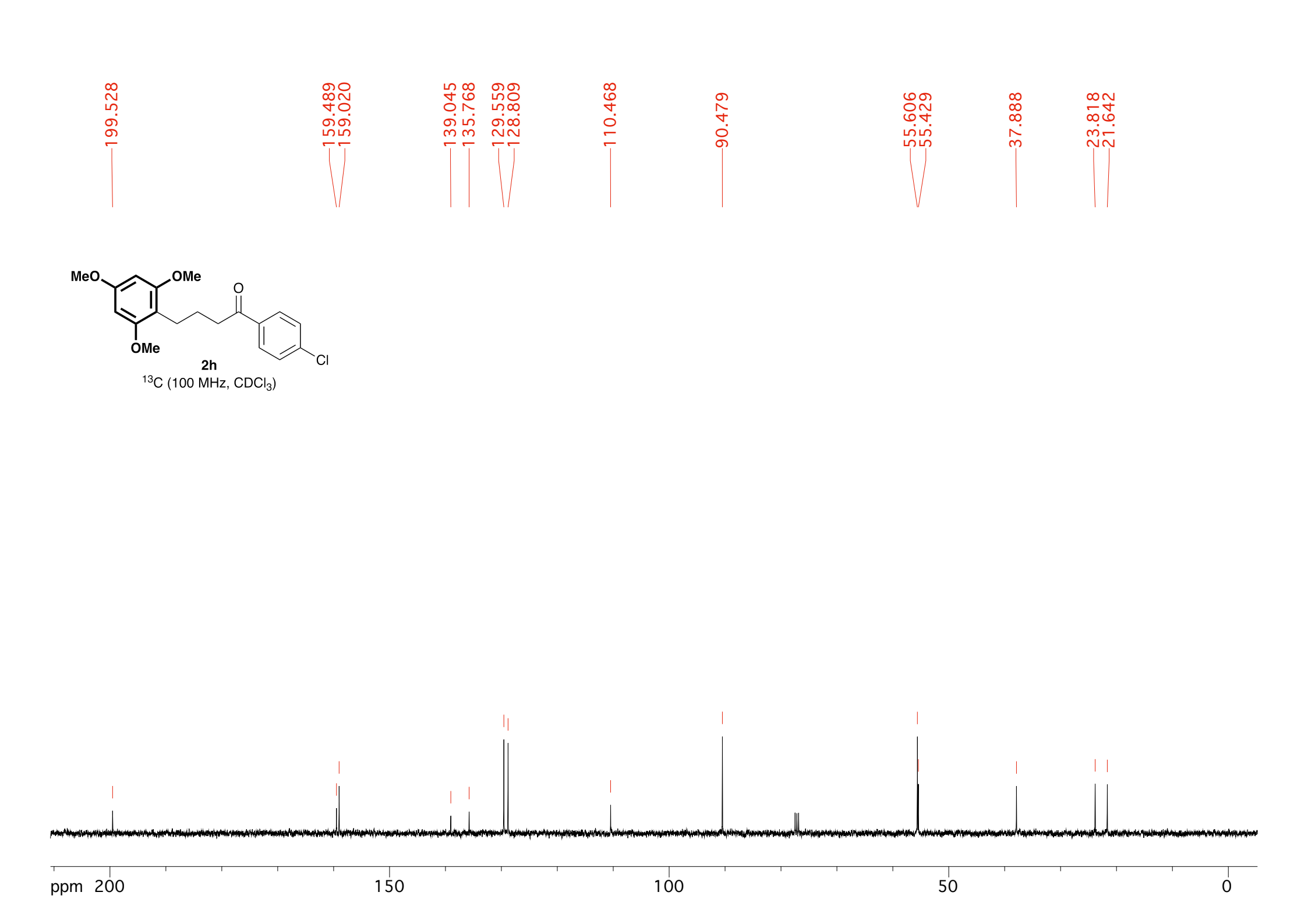


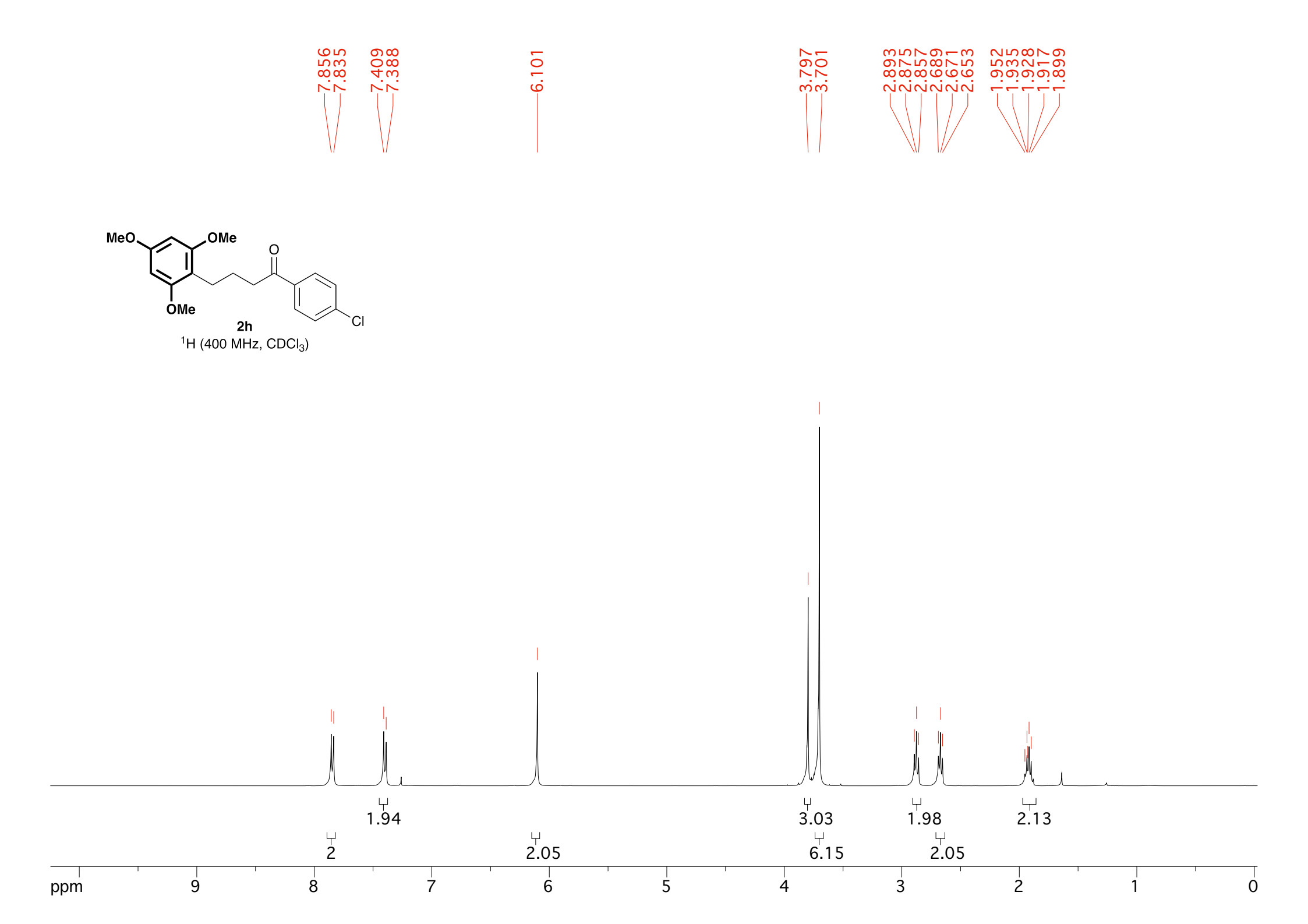
2f

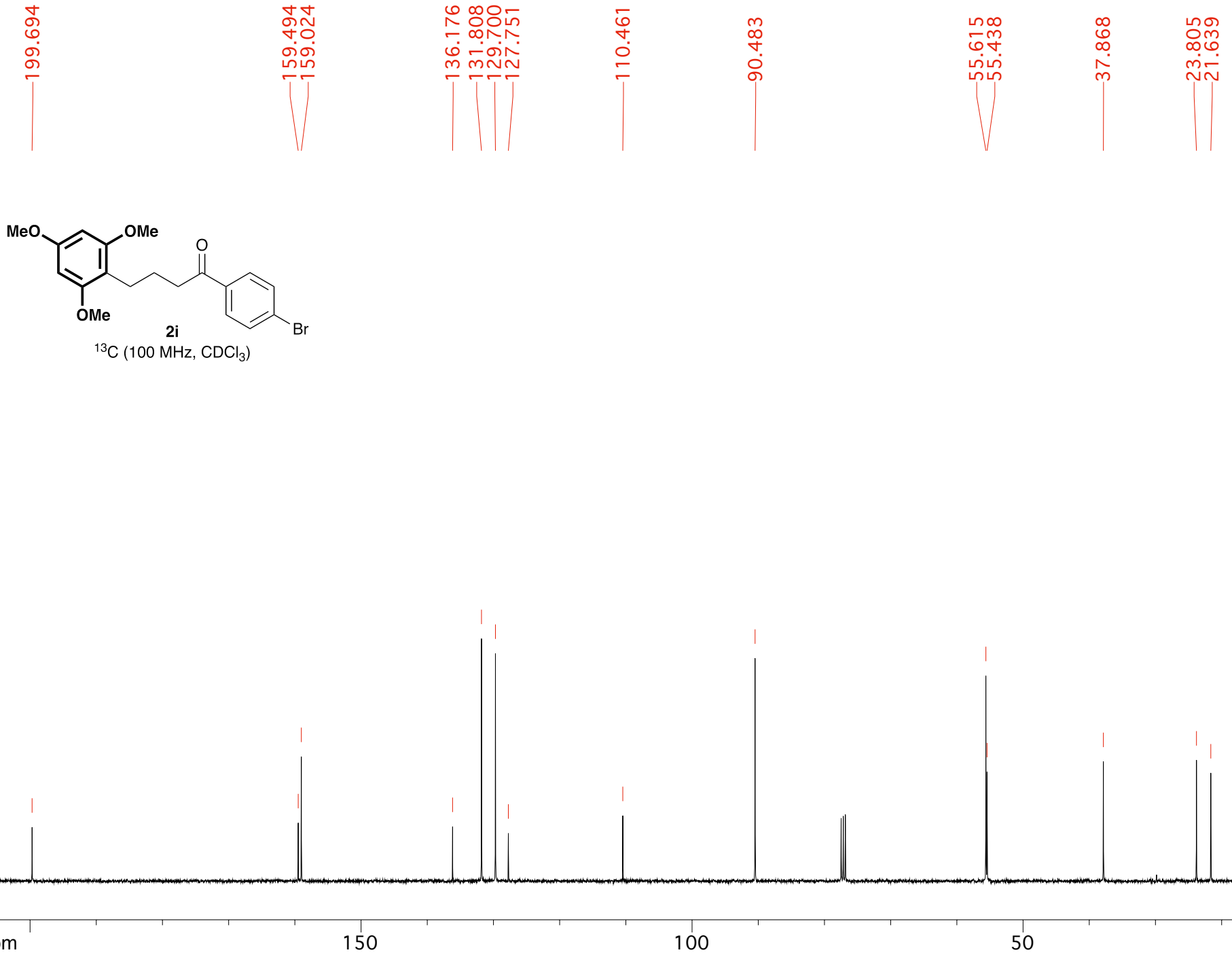
^{1}H (400 MHz, $CDCl_3$)

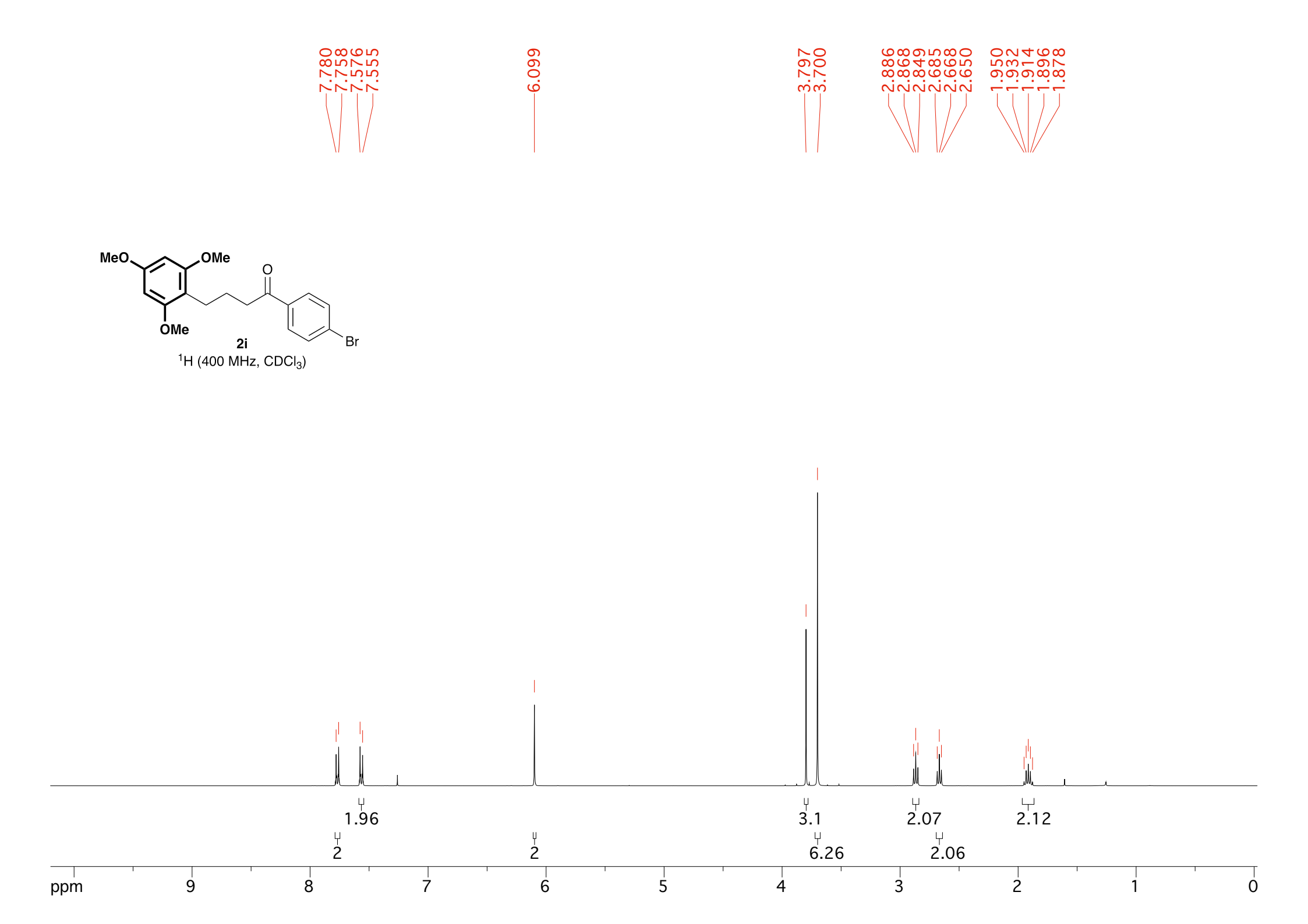

199.203
166.842
164.322
159.489
159.044
133.915
133.889
130.755
130.663
115.667
115.450
110.553
90.499
55.626
55.450
37.895
23.914
21.702
MeO
OMe
OMe
O
F
2g
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0

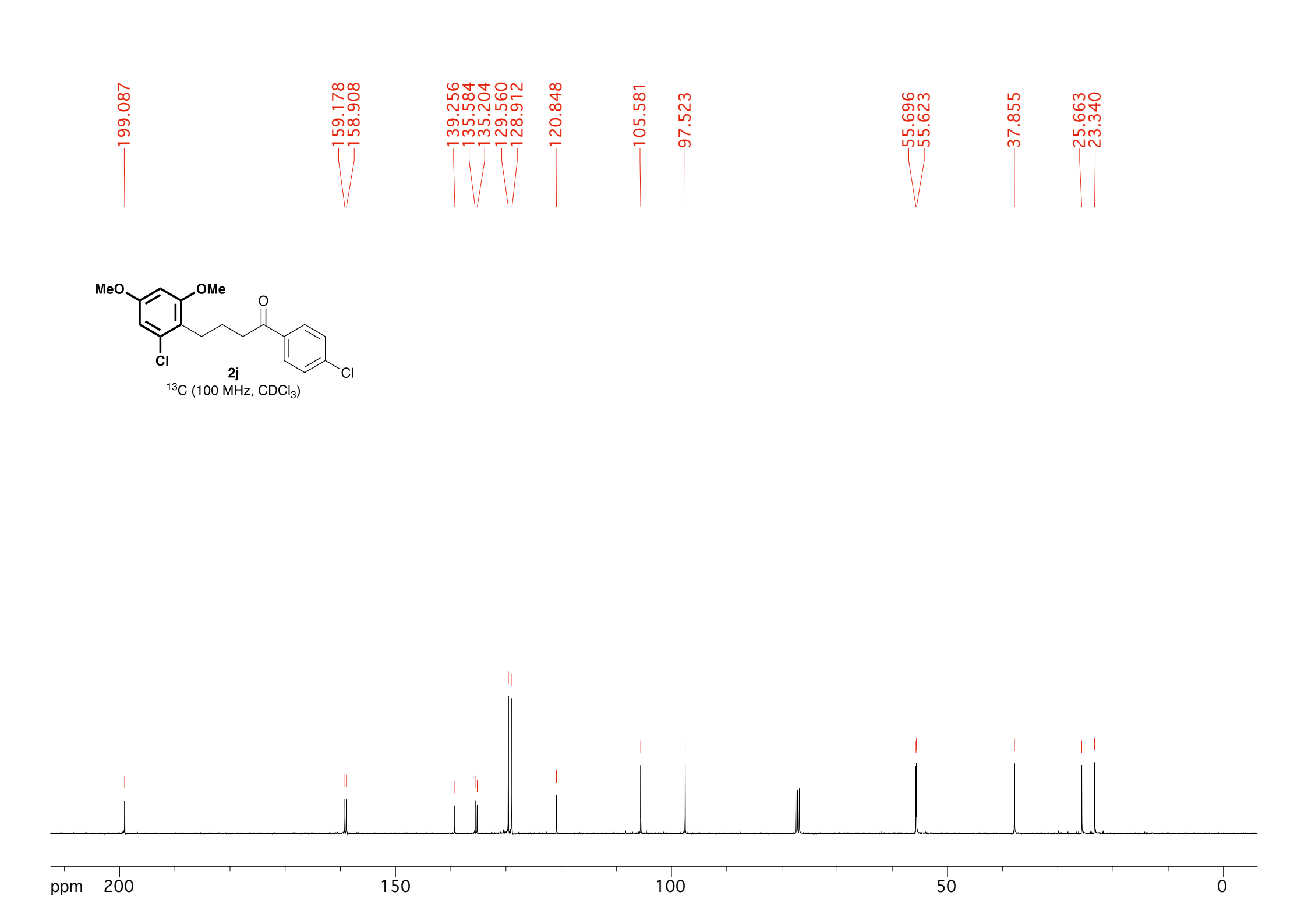

7.977
7.964
7.955
7.941
7.141
7.120
7.098
6.127
3.823
3.729
2.924
2.906
2.887
2.714
2.696
2.678
1.977
1.959
1.941
1.923
1.905
MeO
OMe
OMe
O
F
2g
1H (400 MHz, CDCl3)
1.98
3.08
2.08
2.11
2.01
2
6.19
2.07
ppm
9
8
7
6
5
4
3
2
1
0

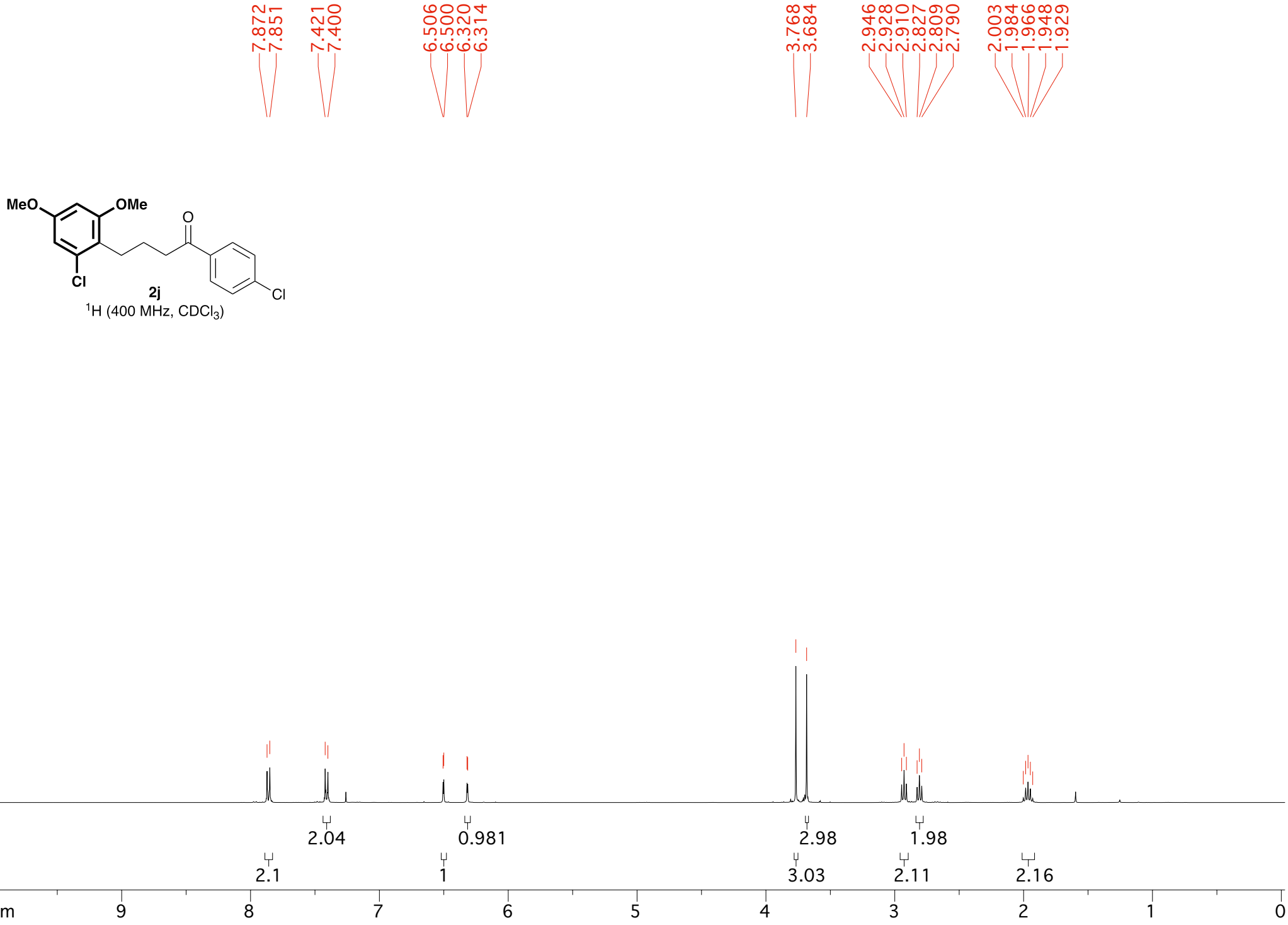

199.528
159.489
159.020
139.045
135.768
129.559
128.809
110.468
90.479
55.606
55.429
37.888
23.818
21.642
MeO
OMe
OMe
O
Cl
2h
13C (100 MHz, CDCl3)
ppm 200
150
100
50
0

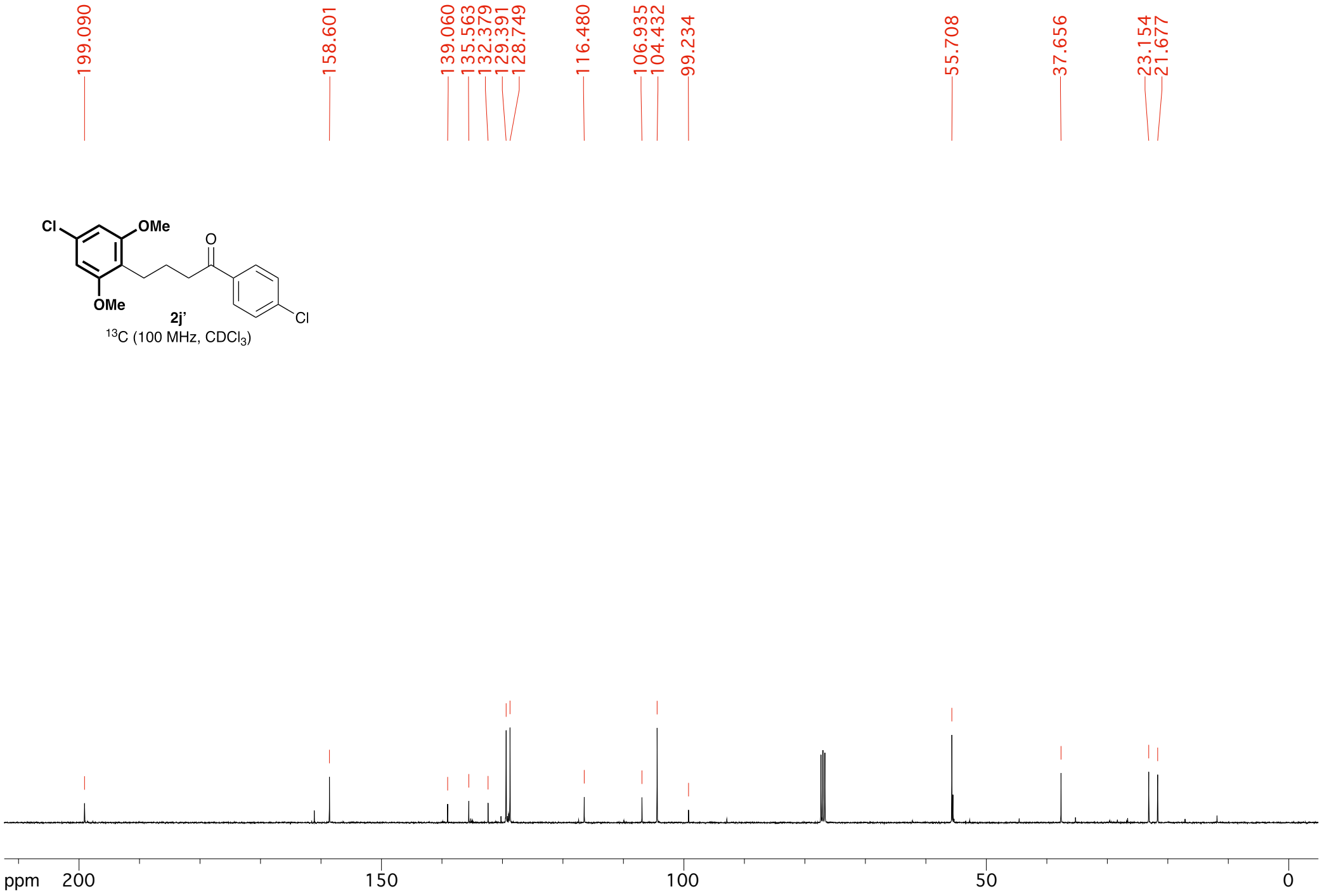

7.856
7.835
7.409
7.388
6.101
3.797
3.701
2.893
2.875
2.857
2.689
2.671
2.653
1.952
1.935
1.928
1.917
1.899
MeO
OMe
O
OMe
Cl
2h
^{1}H (400 MHz, $CDCl_3$)
1.94
3.03
1.98
2.13
2
2.05
6.15
2.05
ppm
9
8
7
6
5
4
3
2
1
0

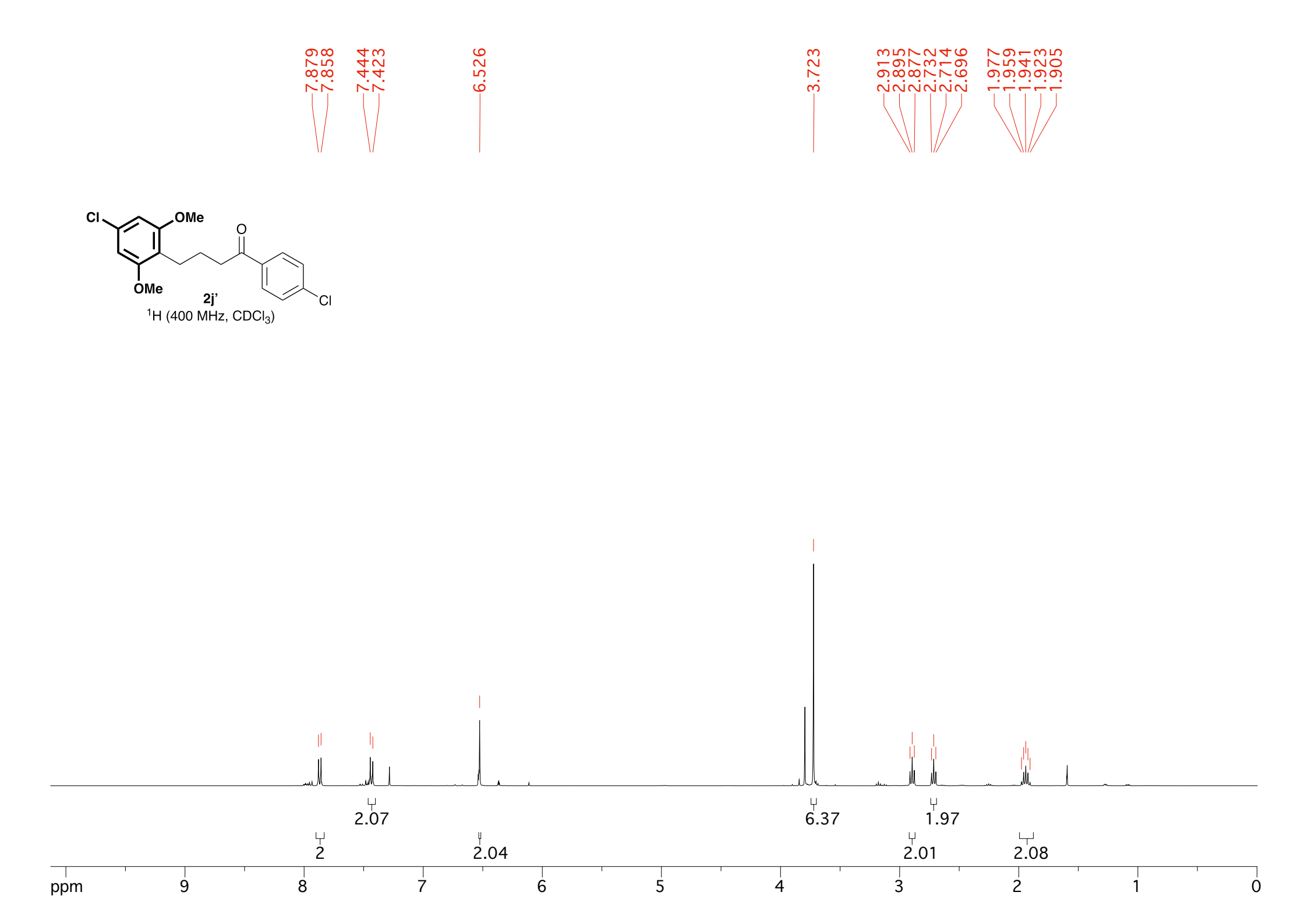

199.694
159.494
159.024
136.176
131.808
129.700
127.751
110.461
90.483
55.615
55.438
37.868
23.805
21.639
MeO
OMe
OMe
O
Br
2i
13C (100 MHz, CDCl3)
ppm
150
100
50
0


7.780
7.758
7.576
7.555
6.099
3.797
3.700
2.886
2.868
2.849
2.685
2.668
2.650
1.950
1.932
1.914
1.896
1.878
MeO
OMe
O
OMe
Br
2i
^{1}H (400 MHz, $CDCl_3$)
1.96
2
2
3.1
6.26
2.07
2.06
2.12
ppm
9
8
7
6
5
4
3
2
1
0


199.087
159.178
158.908
139.256
135.584
135.204
129.560
128.912
120.848
105.581
97.523
55.696
55.623
37.855
25.663
23.340
MeO
OMe
O
Cl
Cl
2j
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0

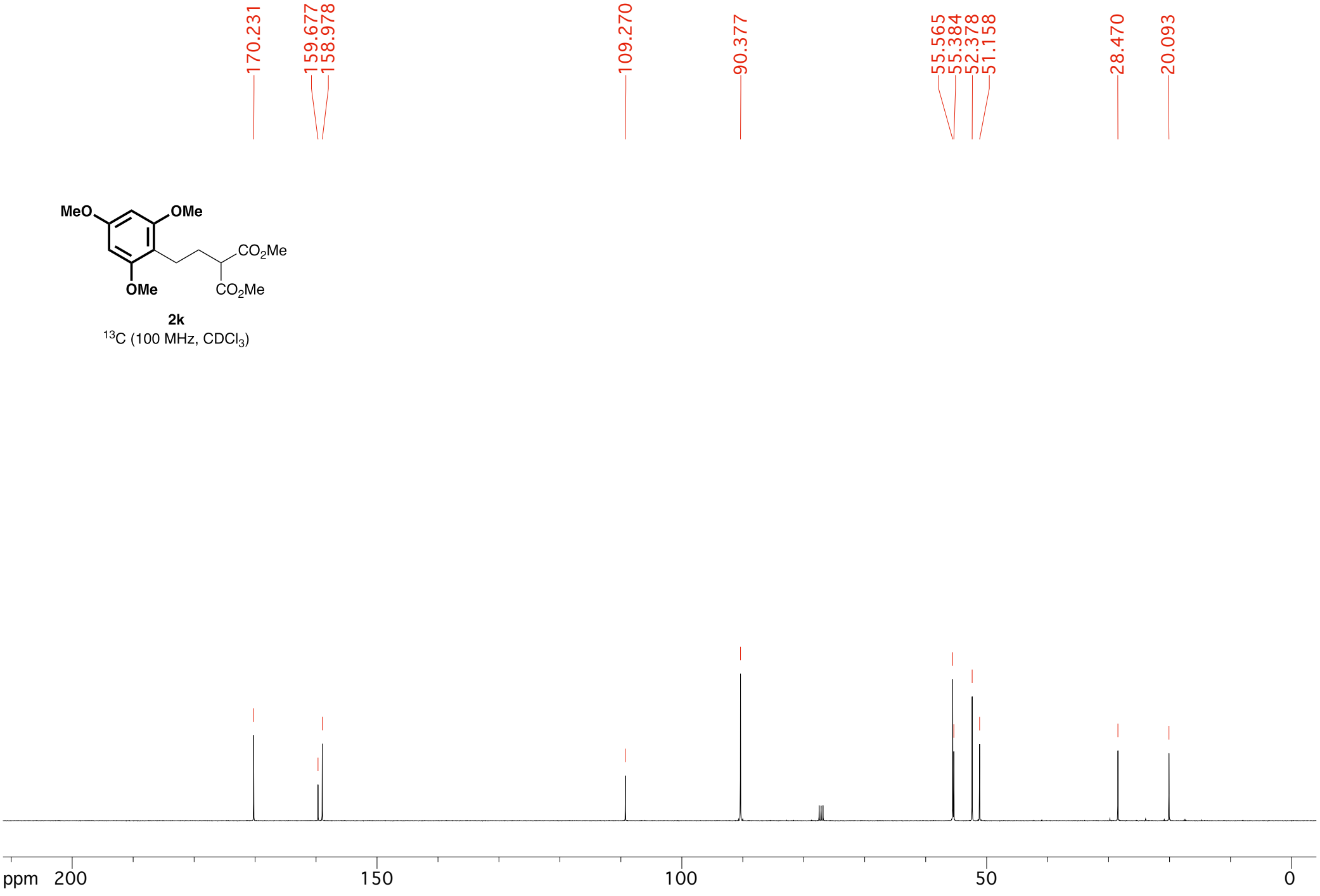

7.872
7.851
7.421
7.400
6.506
6.500
6.320
6.314
3.768
3.684
2.946
2.928
2.910
2.827
2.809
2.790
2.003
1.984
1.966
1.948
1.929
MeO
OMe
O
Cl
Cl
2j
1H (400 MHz, CDCl3)
2.04
0.981
2.98
1.98
2.1
1
3.03
2.11
2.16
ppm
9
8
7
6
5
4
3
2
1
0


199.090
158.601
139.060
135.563
132.379
129.391
128.749
116.480
106.935
104.432
99.234
55.708
37.656
23.154
21.677
Cl
OMe
O
OMe
Cl
2j'
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0


7.879
7.858
7.444
7.423
6.526
3.723
2.913
2.895
2.877
2.732
2.714
2.696
1.977
1.959
1.941
1.923
1.905
Cl
OMe
O
OMe
Cl
2j'
1H (400 MHz, CDCl3)
2.07
6.37
1.97
2
2.04
2.01
2.08
ppm
9
8
7
6
5
4
3
2
1
0

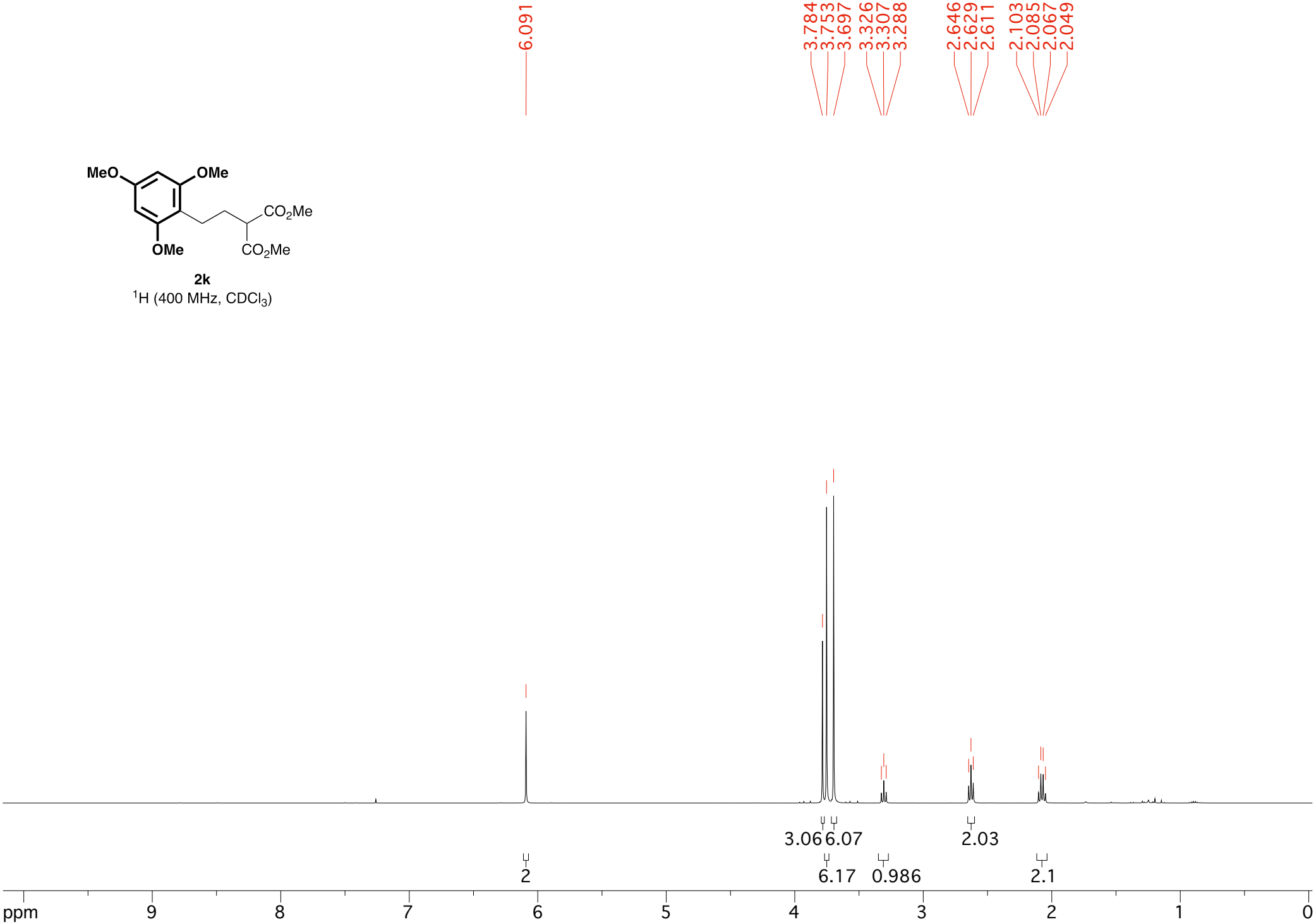
2k

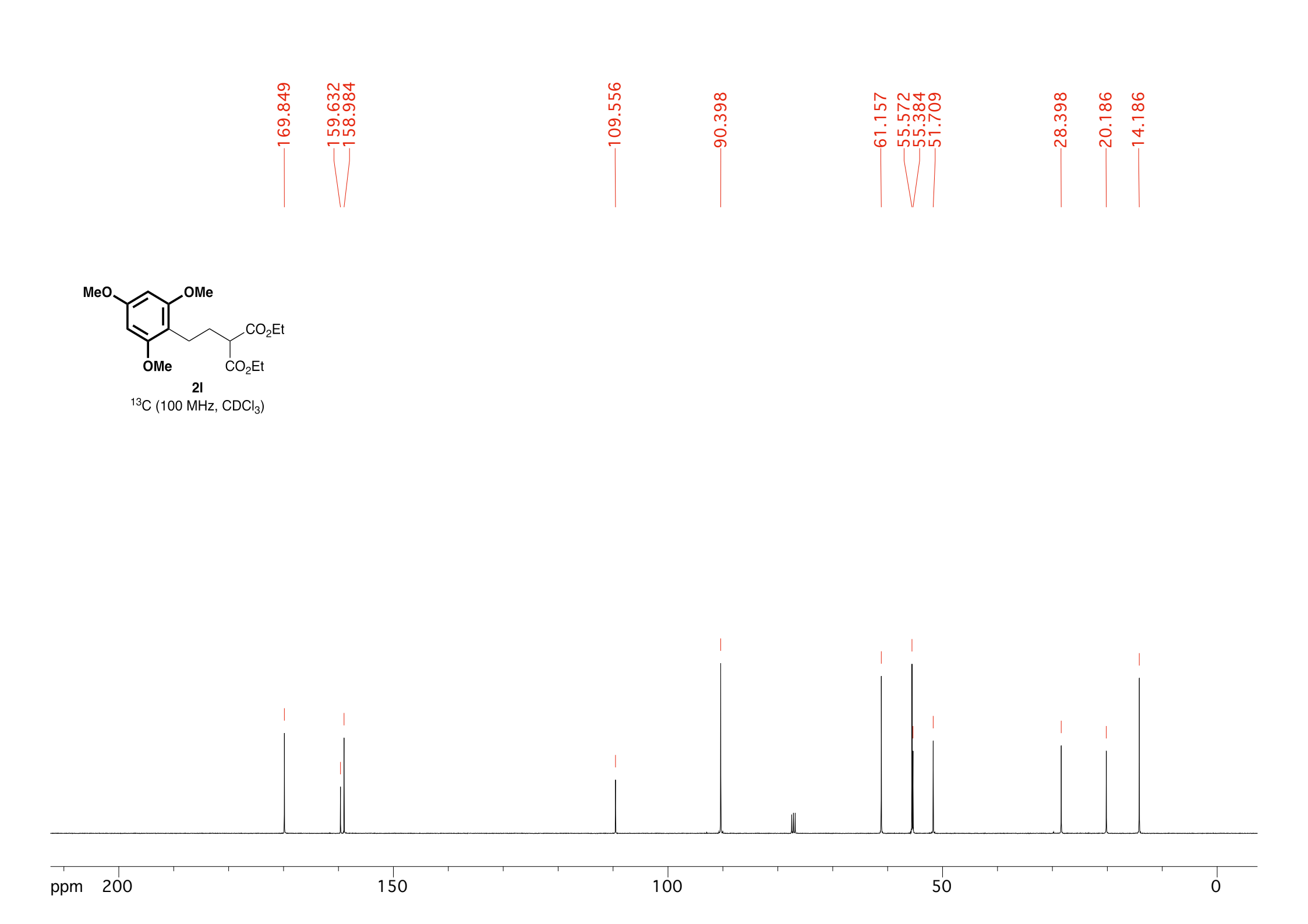
^{13}C (100 MHz, $CDCl_3$)



2k

^{1}H (400 MHz, $CDCl_3$)



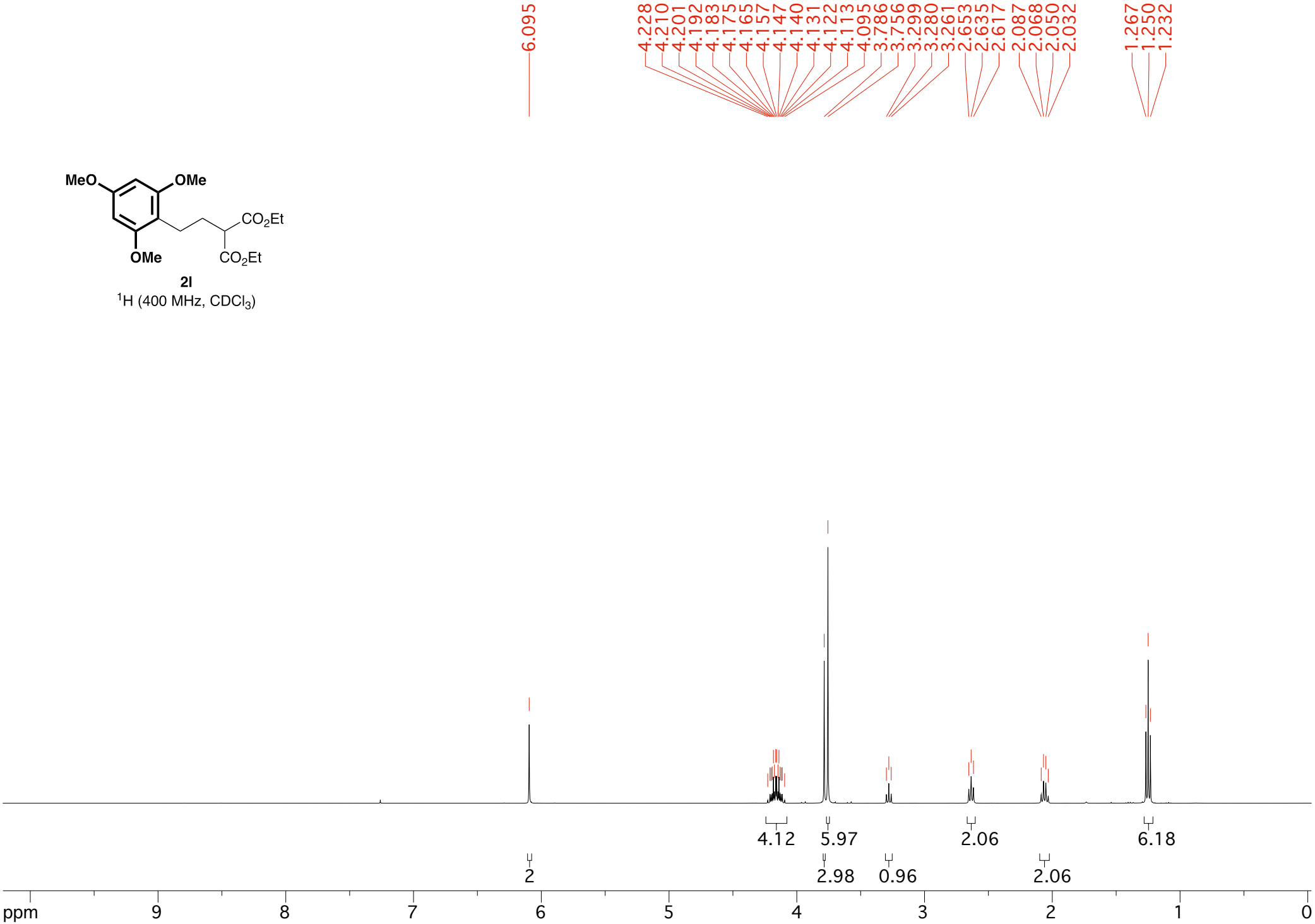


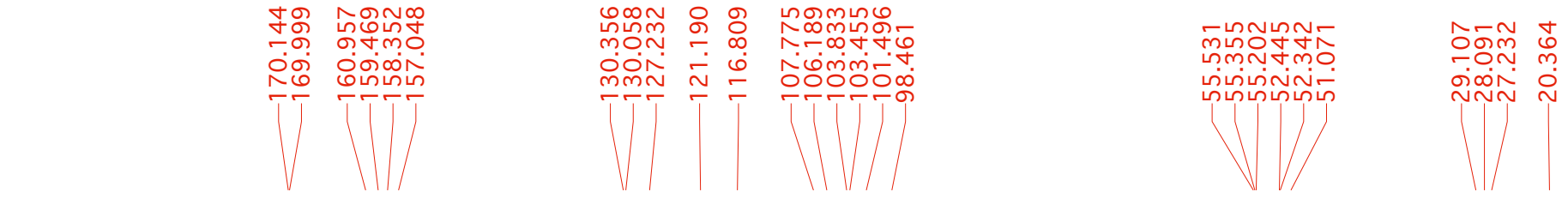
2l

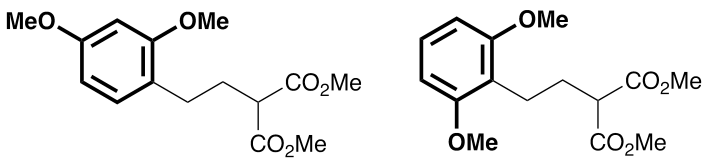
^{13}C (100 MHz, $CDCl_3$)

2l

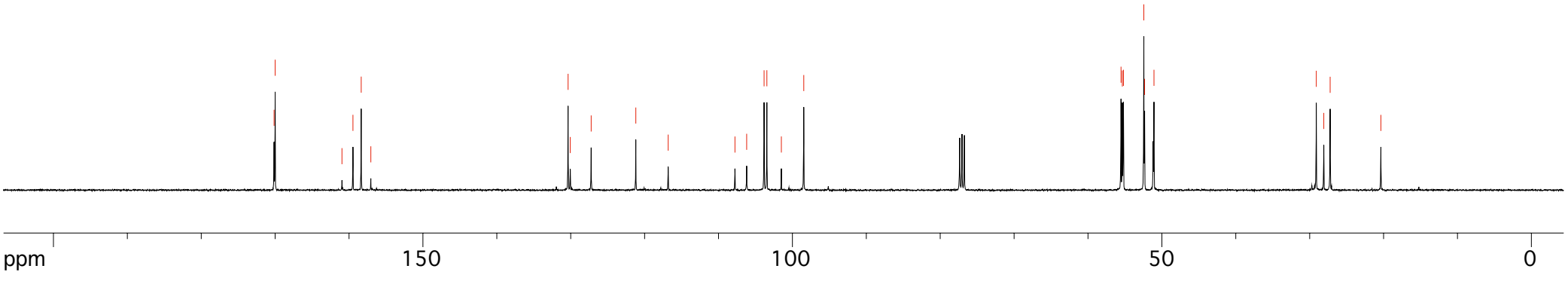
^{1}H (400 MHz, $CDCl_3$)

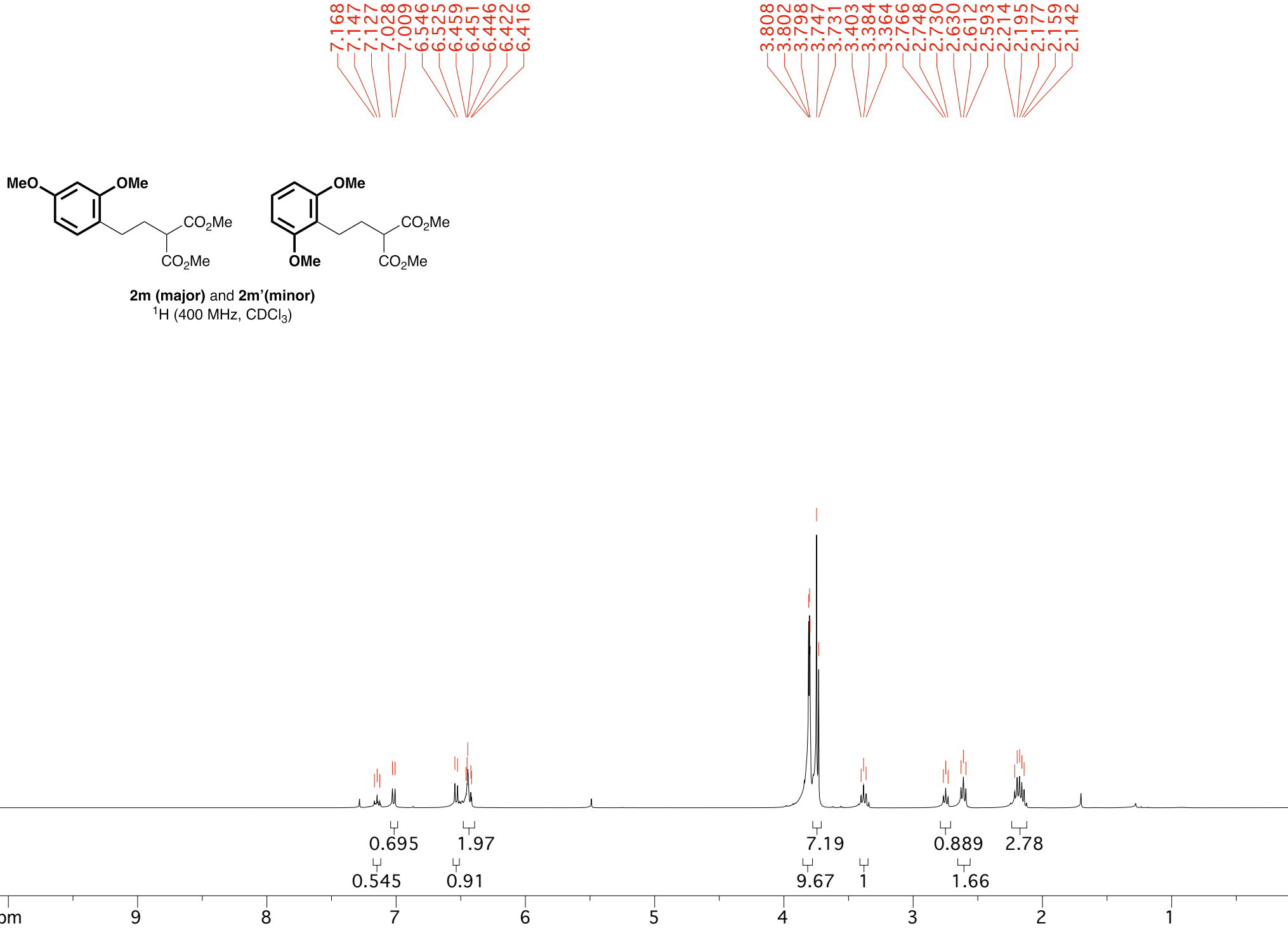




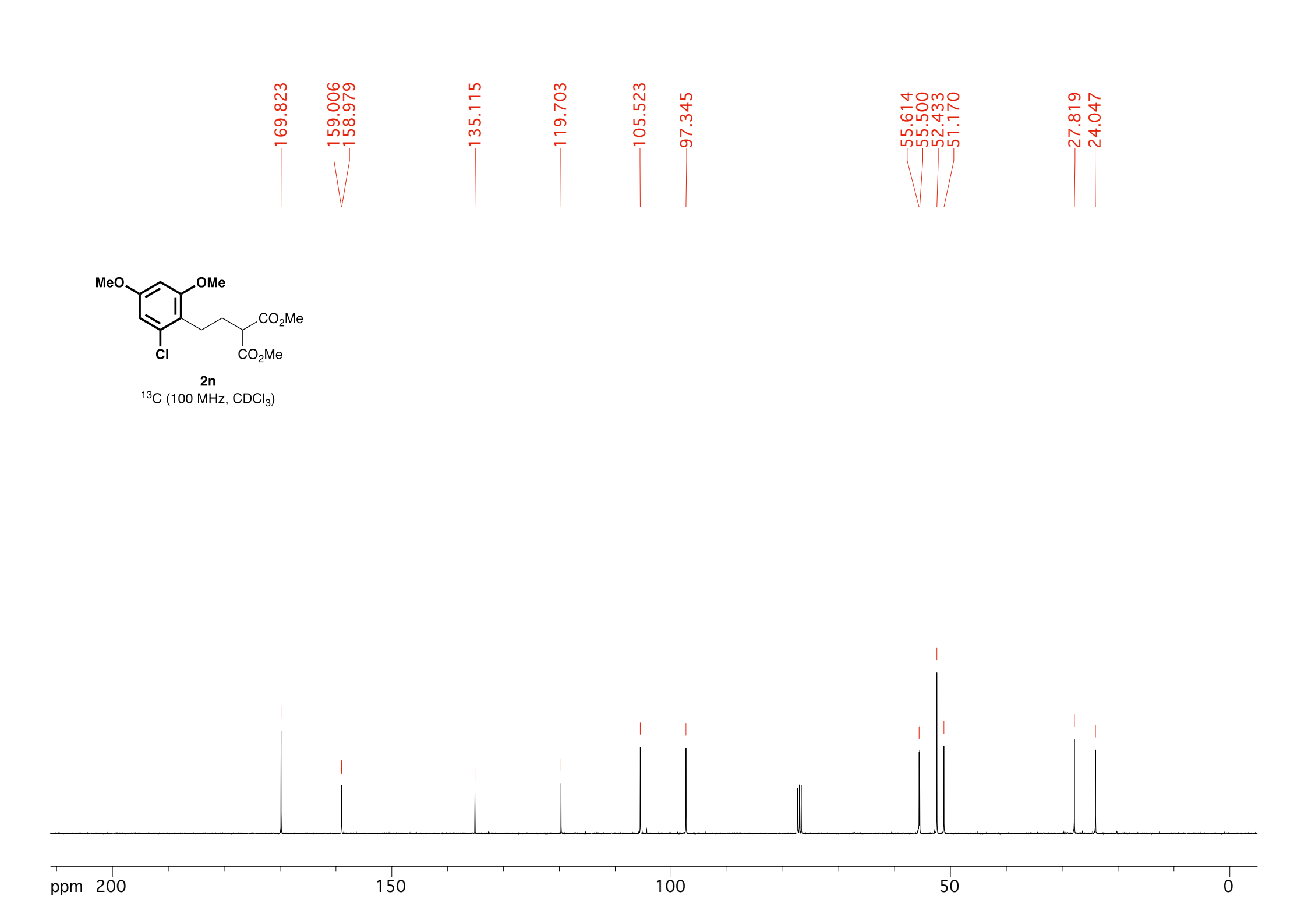


2m (major) and **2m'(minor)**
^{13}C (100 MHz, $CDCl_3$)



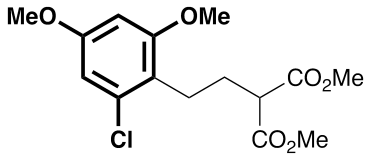


2m (major) and **2m'(minor)**
^{1}H (400 MHz, $CDCl_3$)



2n

^{13}C (100 MHz, $CDCl_3$)



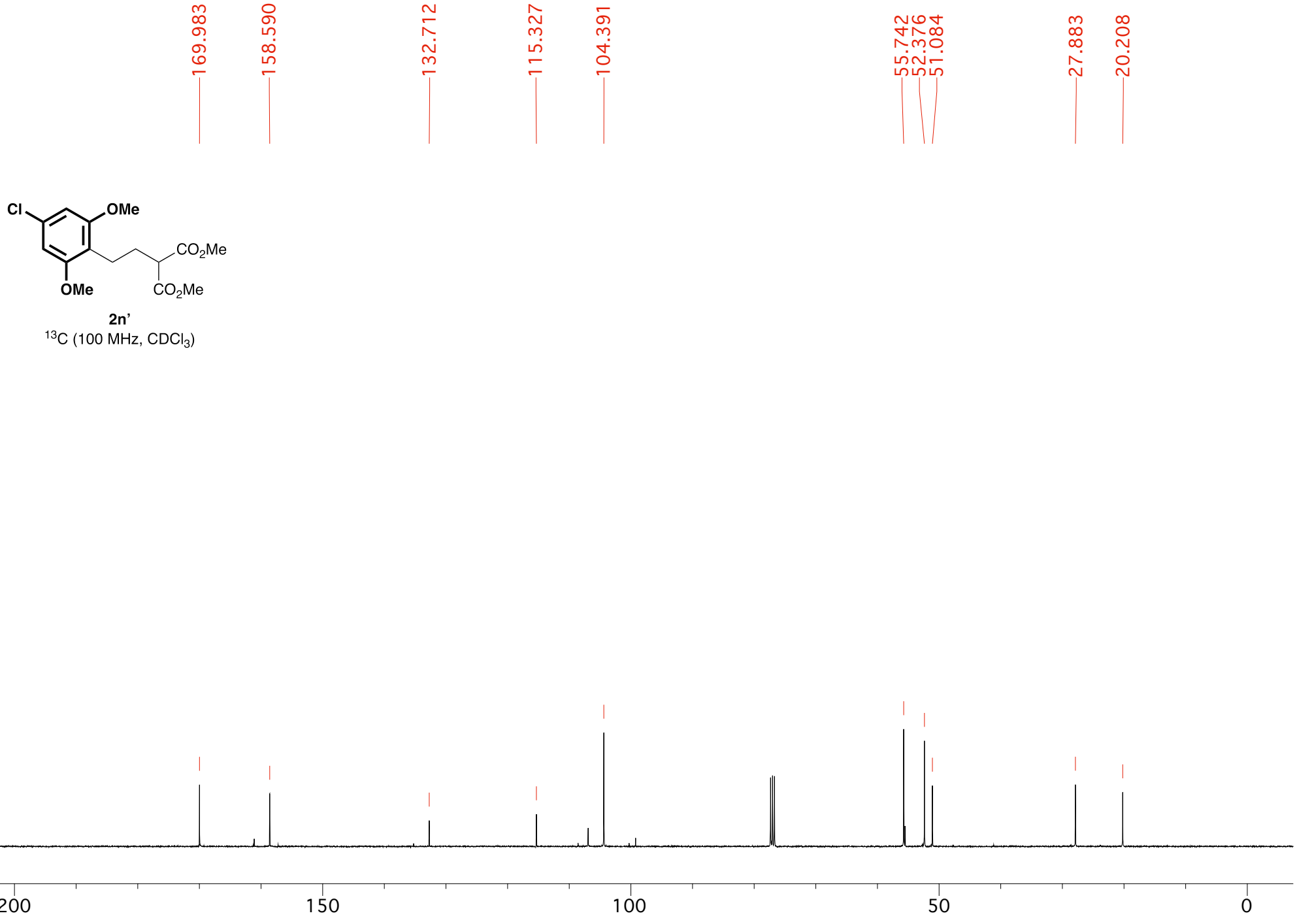
2n

^{1}H (400 MHz, $CDCl_3$)

6.524
6.518
6.350
6.344
3.788
3.782
3.747
3.403
3.384
3.365
2.803
2.785
2.766
2.171
2.152
2.133
2.115

0.971
6.08
2.1
1
6.24
1.02
2.16

ppm 9 8 7 6 5 4 3 2 1 0

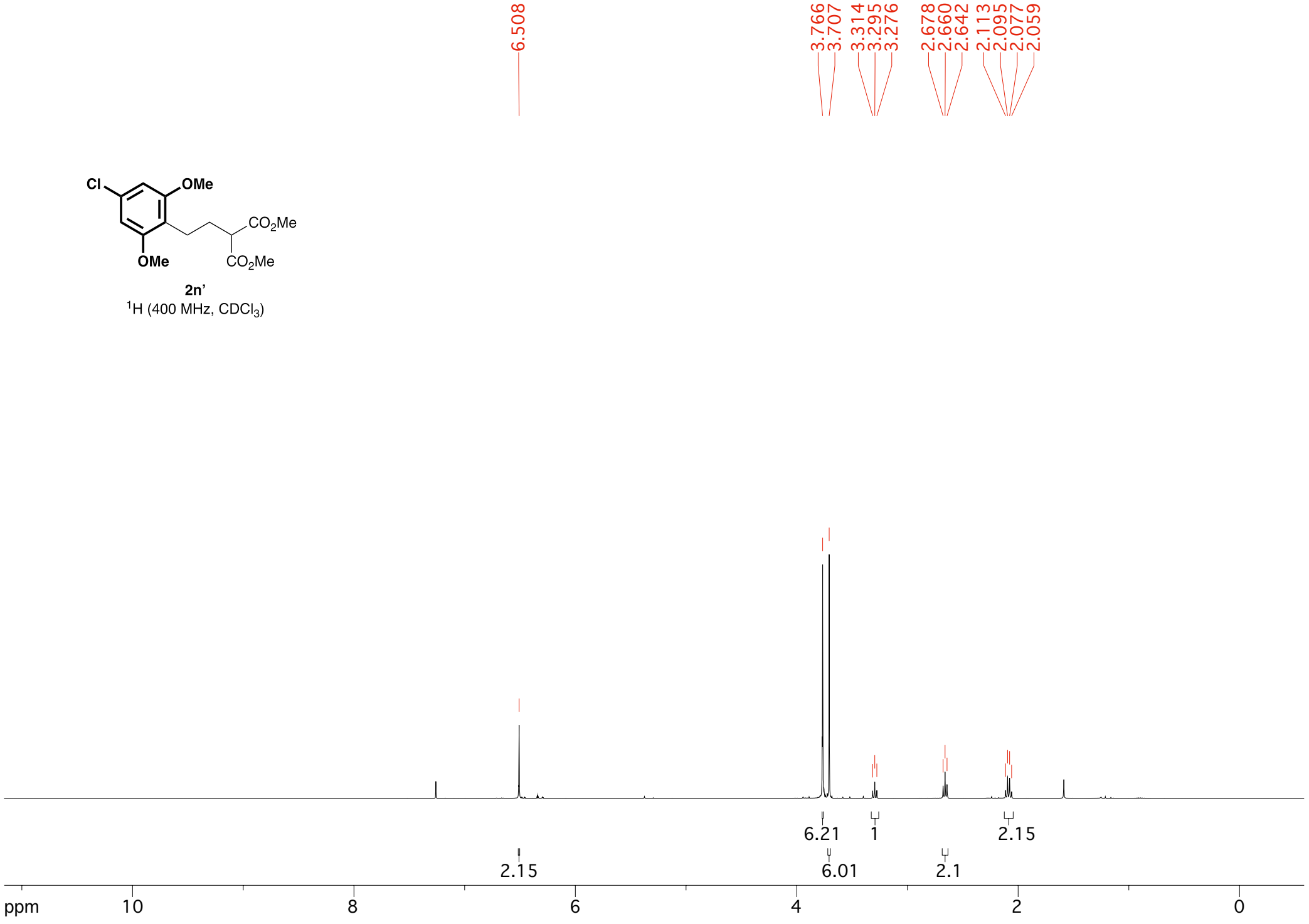


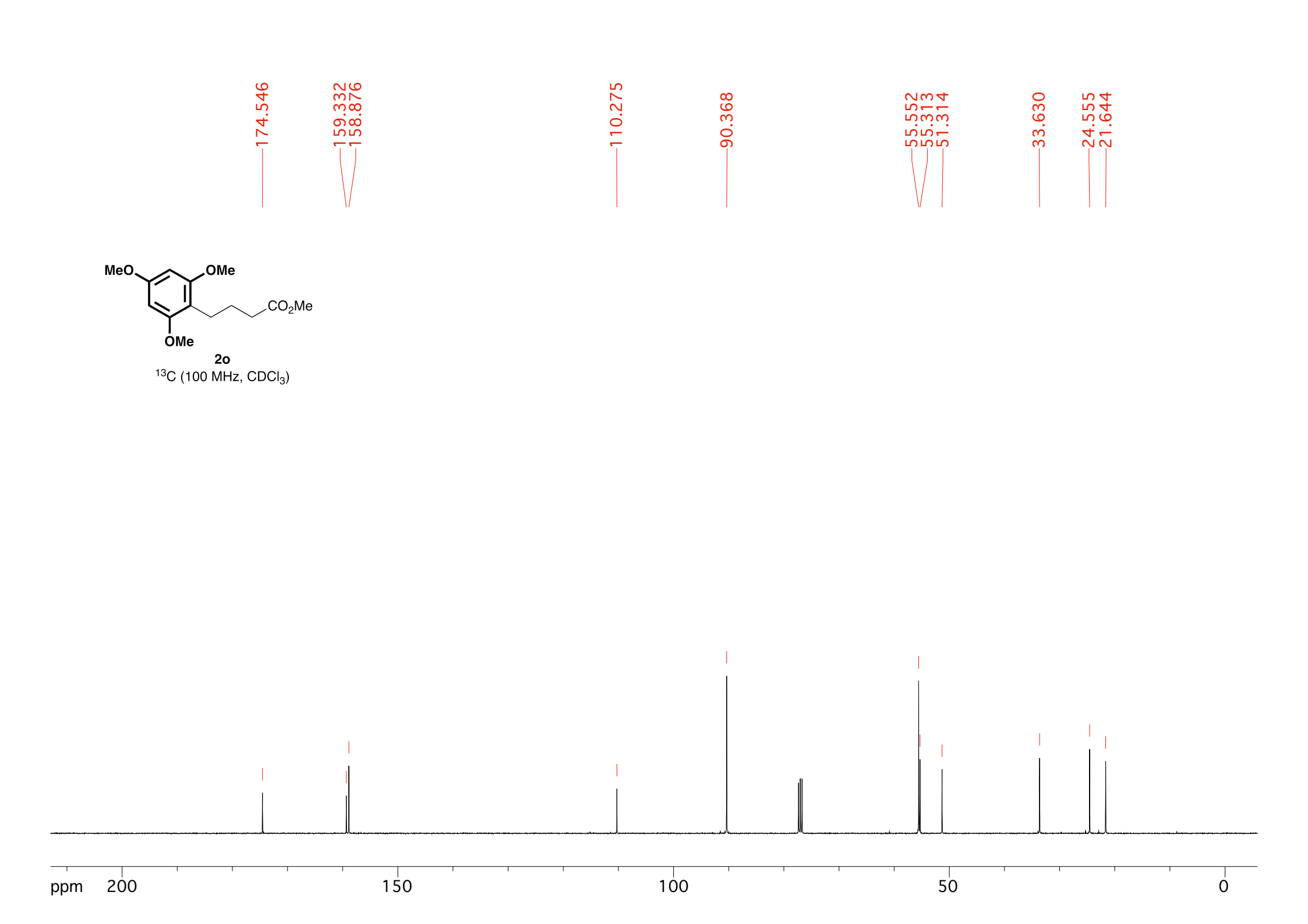
2n'

^{13}C (100 MHz, $CDCl_3$)

2n'

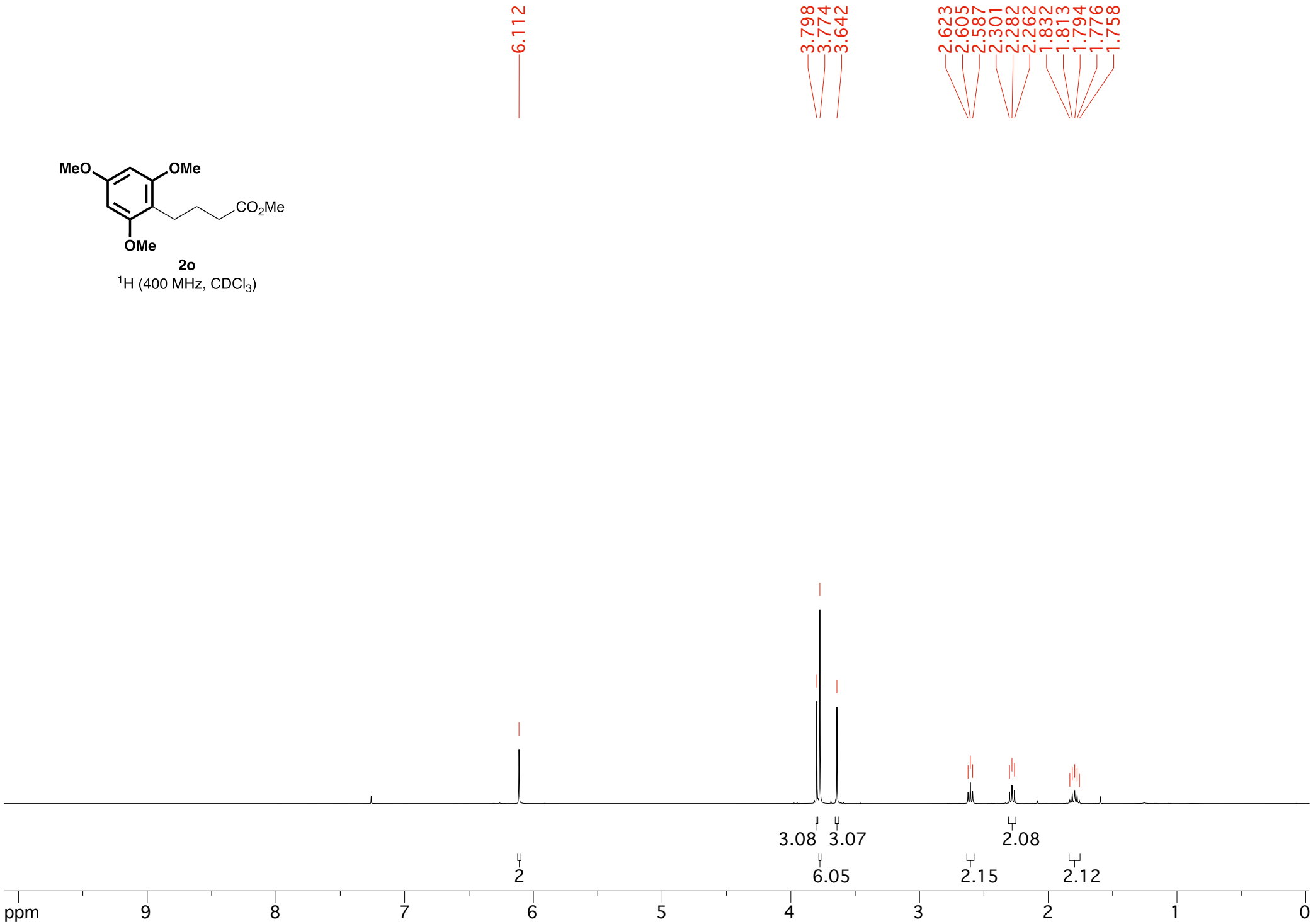
^{1}H (400 MHz, $CDCl_3$)

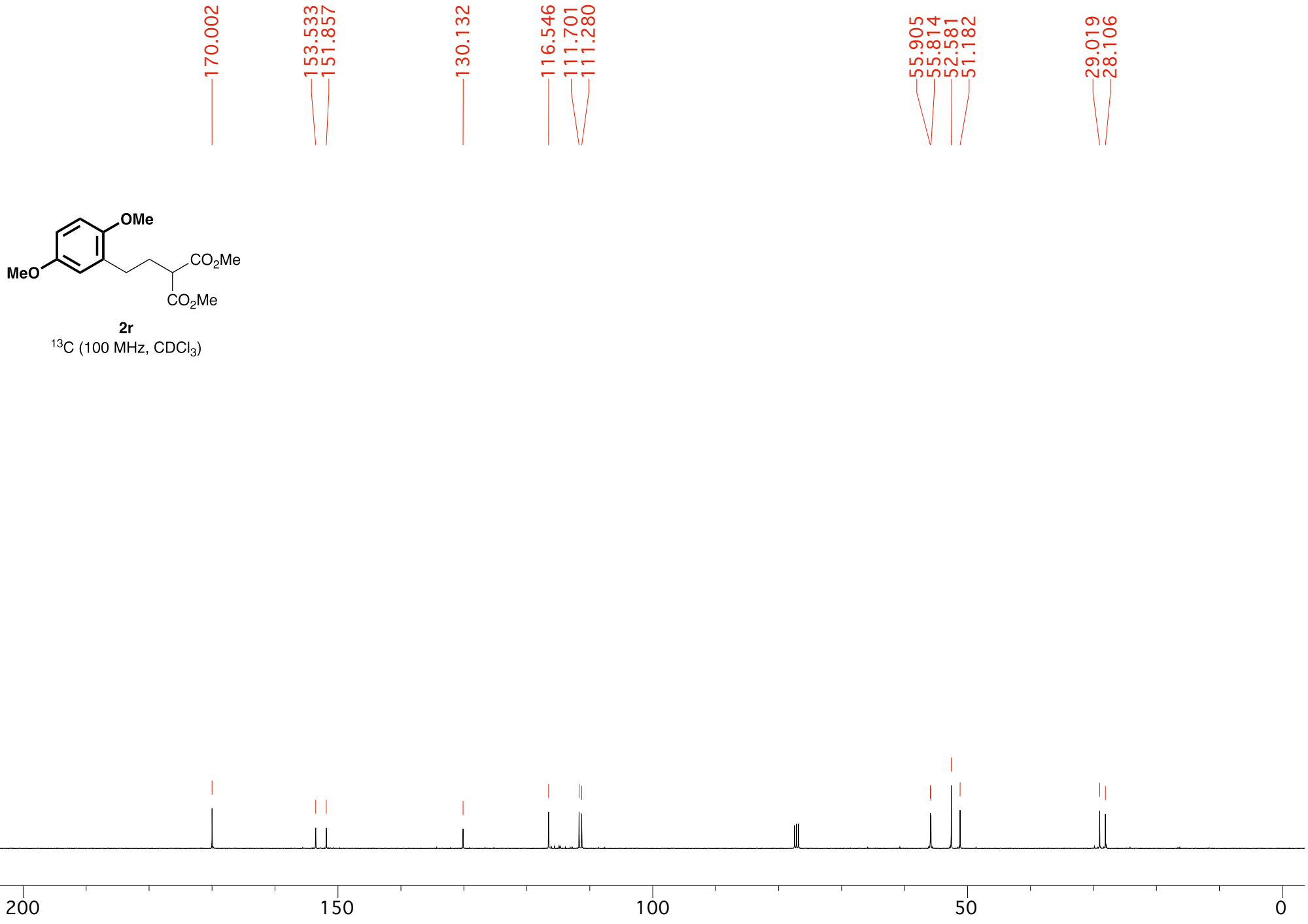



174.546
159.332
158.876
110.275
90.368
55.552
55.313
51.314
33.630
24.555
21.644
MeO
OMe
OMe
CO2Me
2o
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0

2o

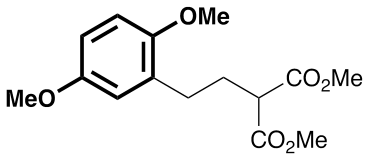
^{1}H (400 MHz, $CDCl_3$)





2r

^{13}C (100 MHz, $CDCl_3$)



2r

^{1}H (400 MHz, $CDCl_3$)

6.791
6.767
6.742
6.734
6.729
6.723
6.717

3.781
3.779
3.754
3.422
3.403
3.384

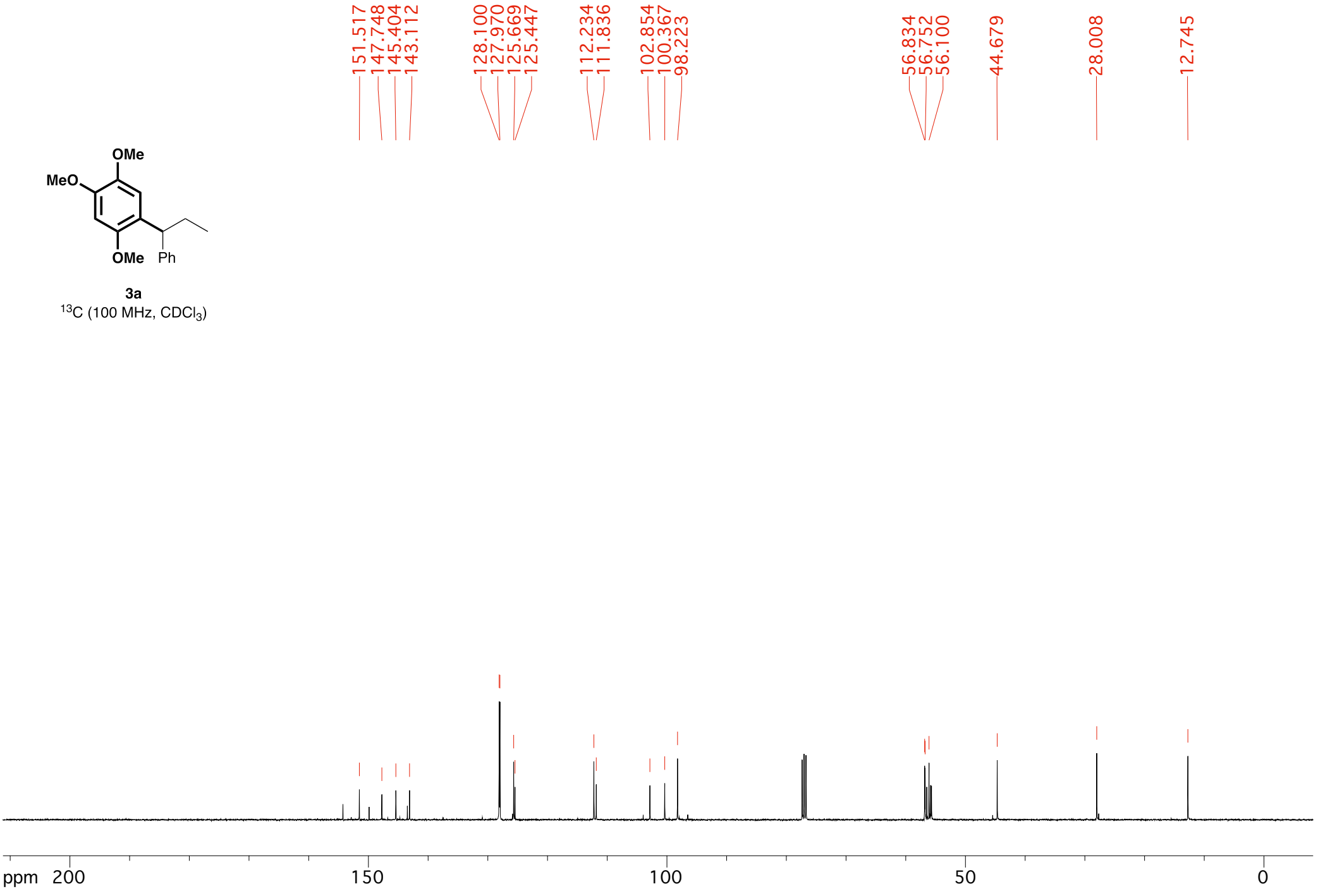
2.676
2.658
2.639
2.245
2.226
2.207
2.189

5.93
0.909
2.21
2.74
5.9
2

ppm 9 8 7 6 5 4 3 2 1 0

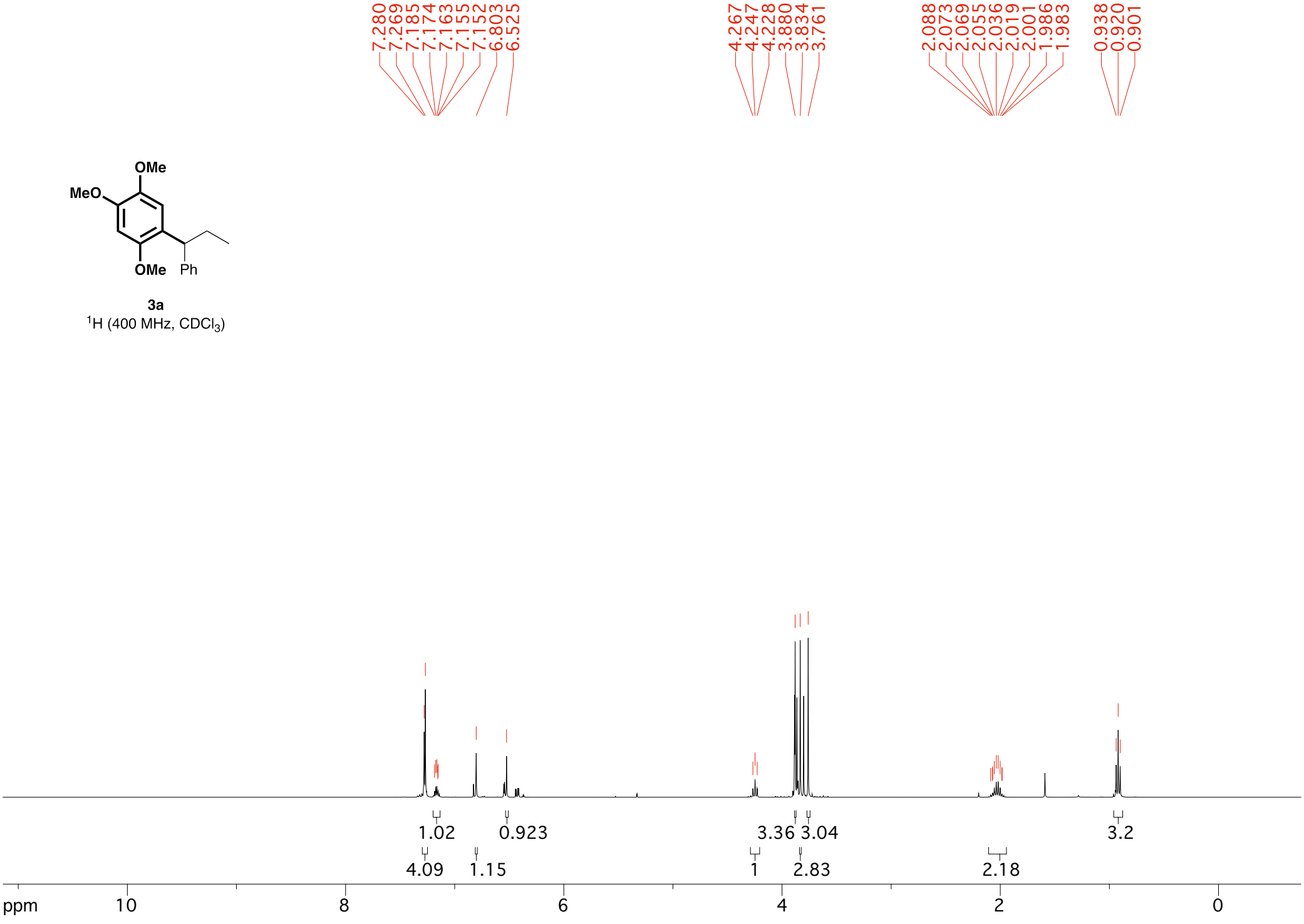
3a

^{13}C (100 MHz, $CDCl_3$)



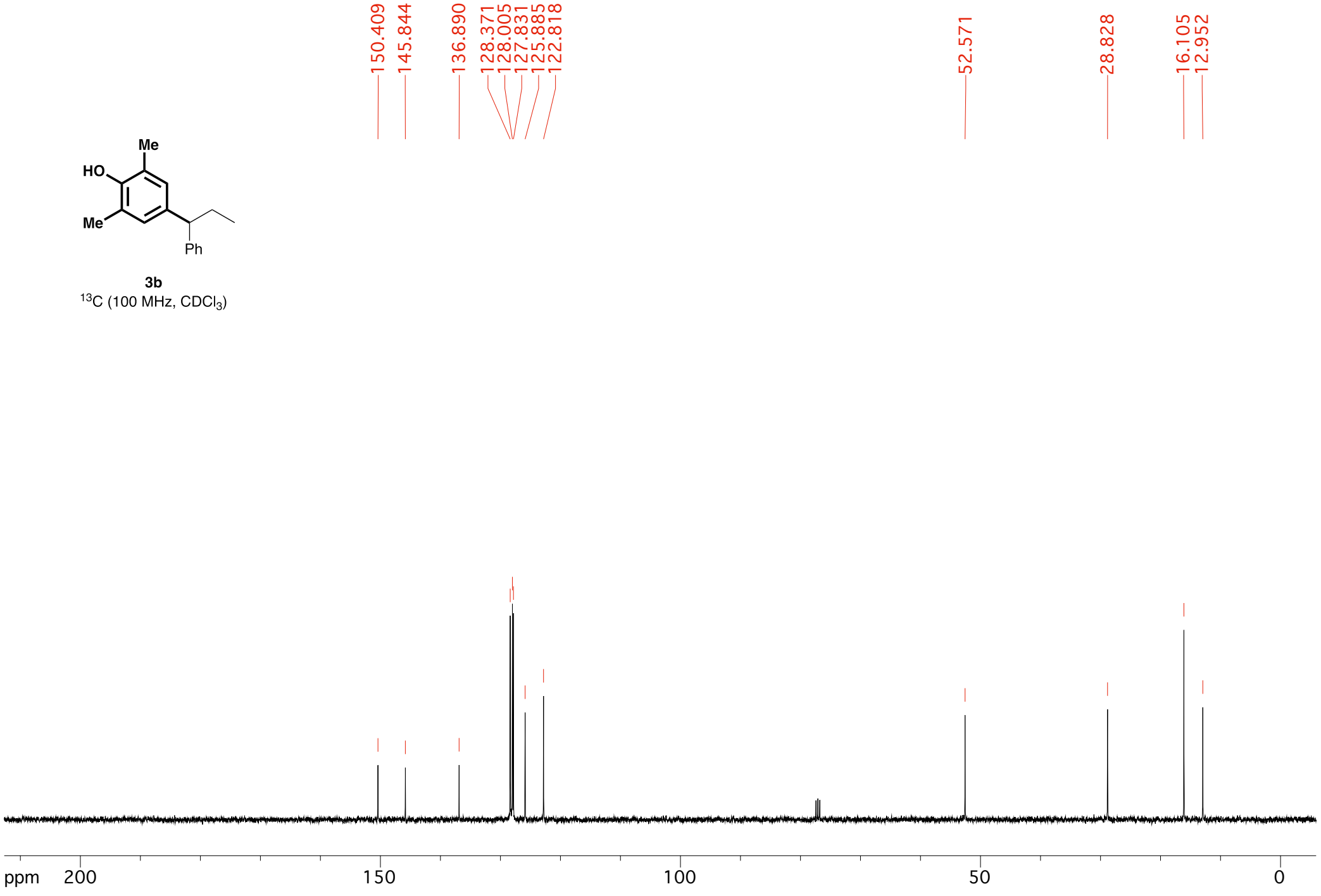
3a

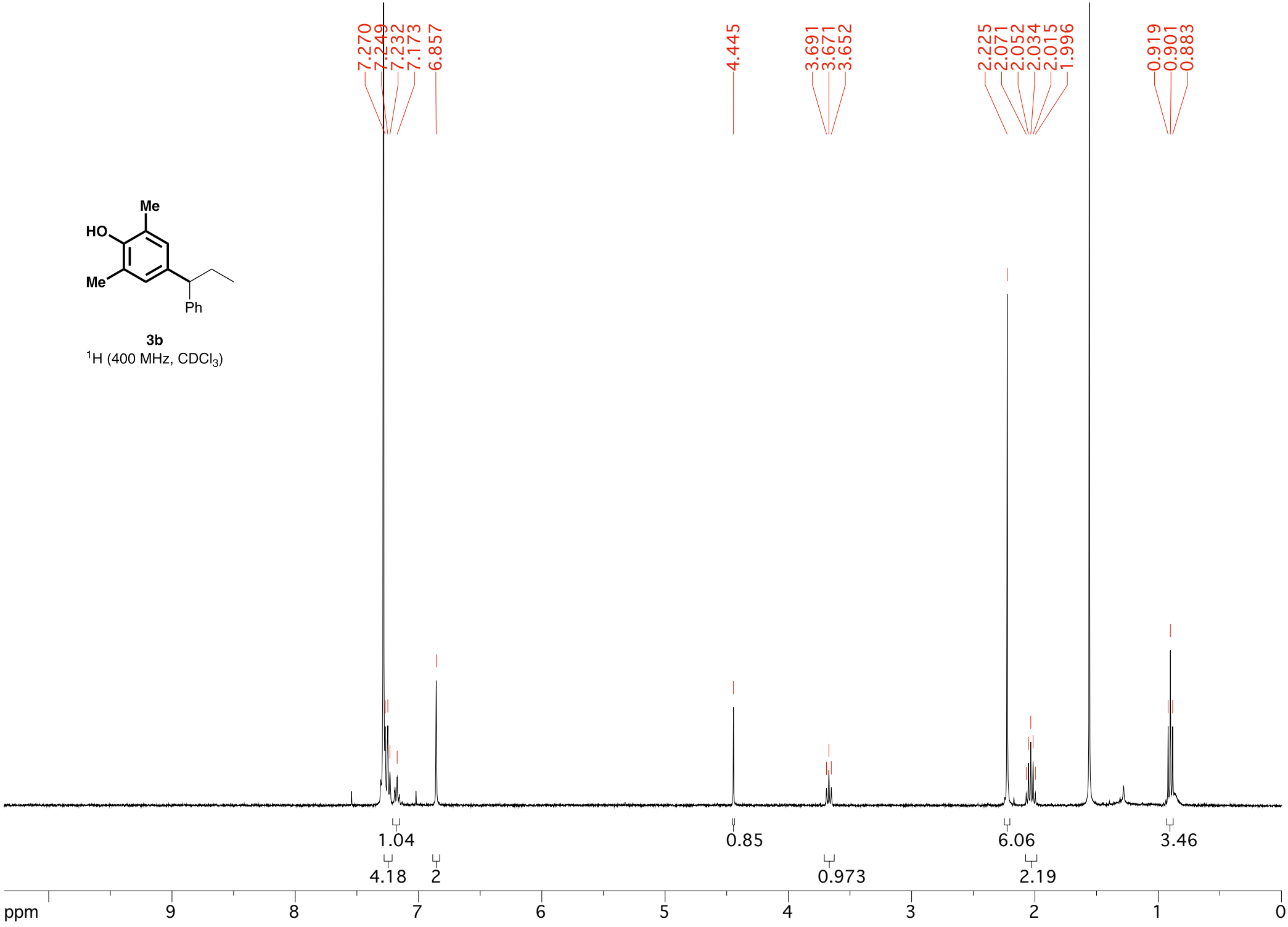
^{1}H (400 MHz, $CDCl_3$)



3b

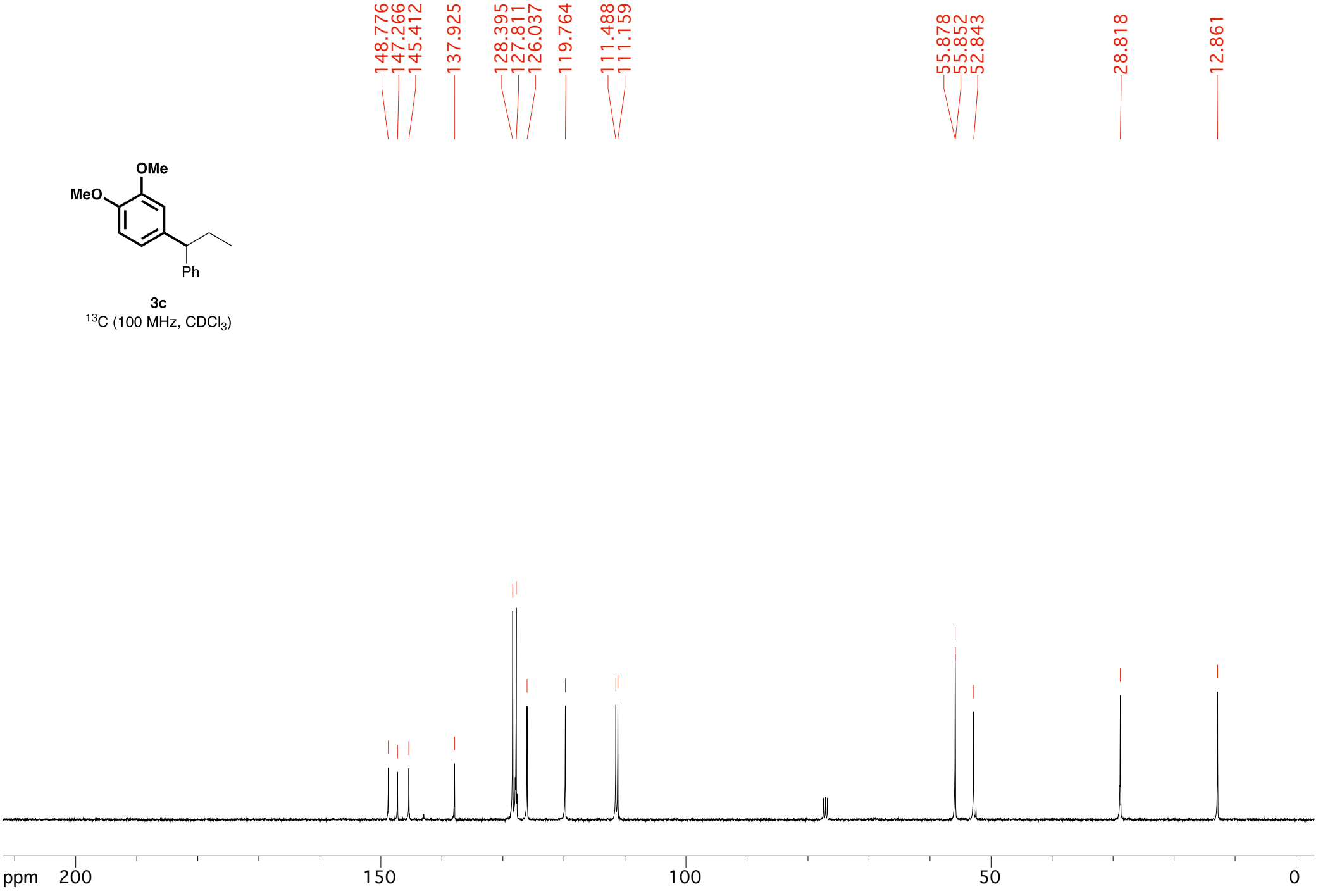
^{13}C (100 MHz, $CDCl_3$)




7.270
7.249
7.232
7.173
6.857
4.445
3.691
3.671
3.652
2.225
2.071
2.052
2.034
2.015
1.996
0.919
0.901
0.883
Me
HO
Me
Ph
3b
1H (400 MHz, CDCl3)
1.04
0.85
6.06
3.46
4.18
2
0.973
2.19
ppm
9
8
7
6
5
4
3
2
1
0

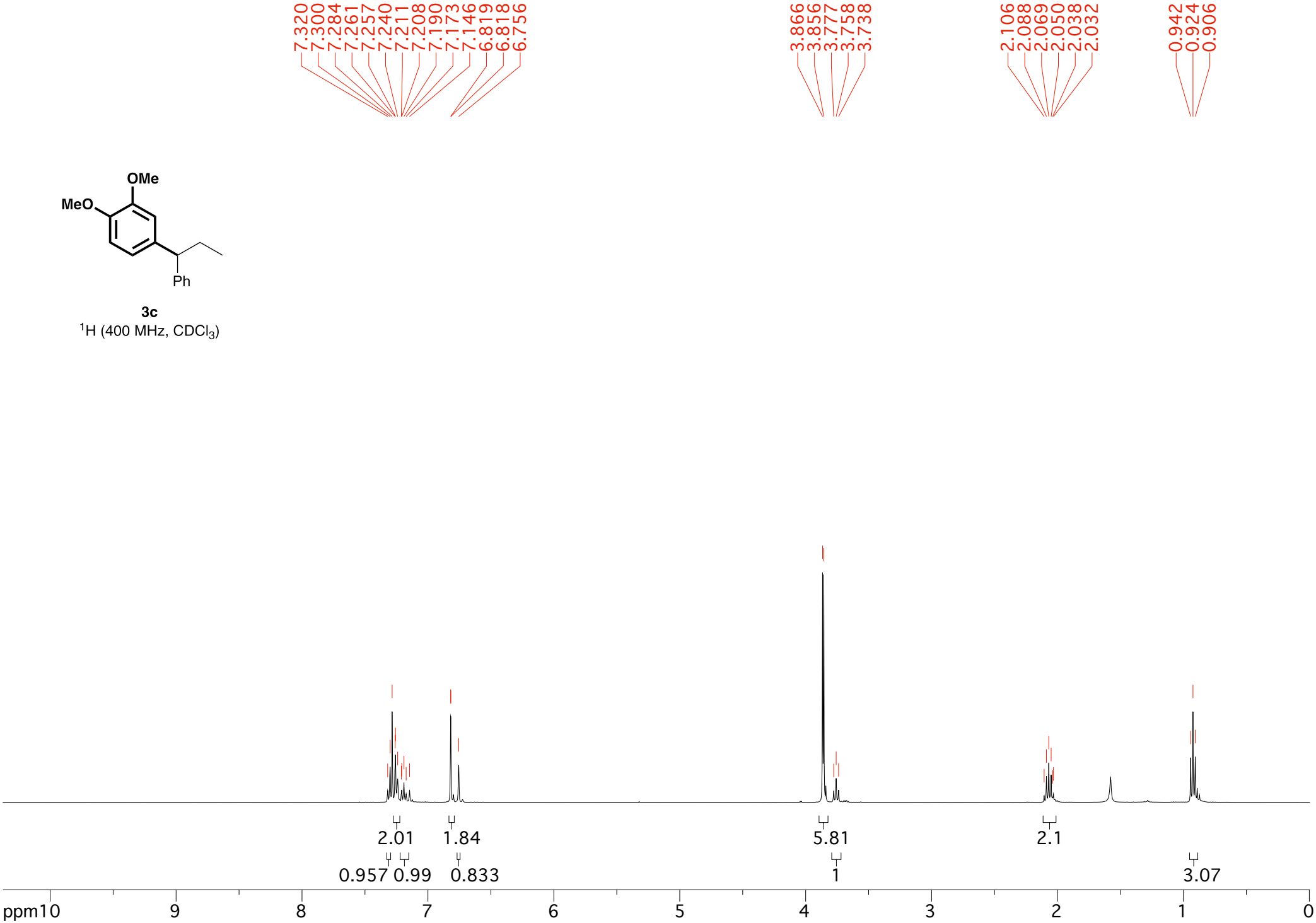
3c

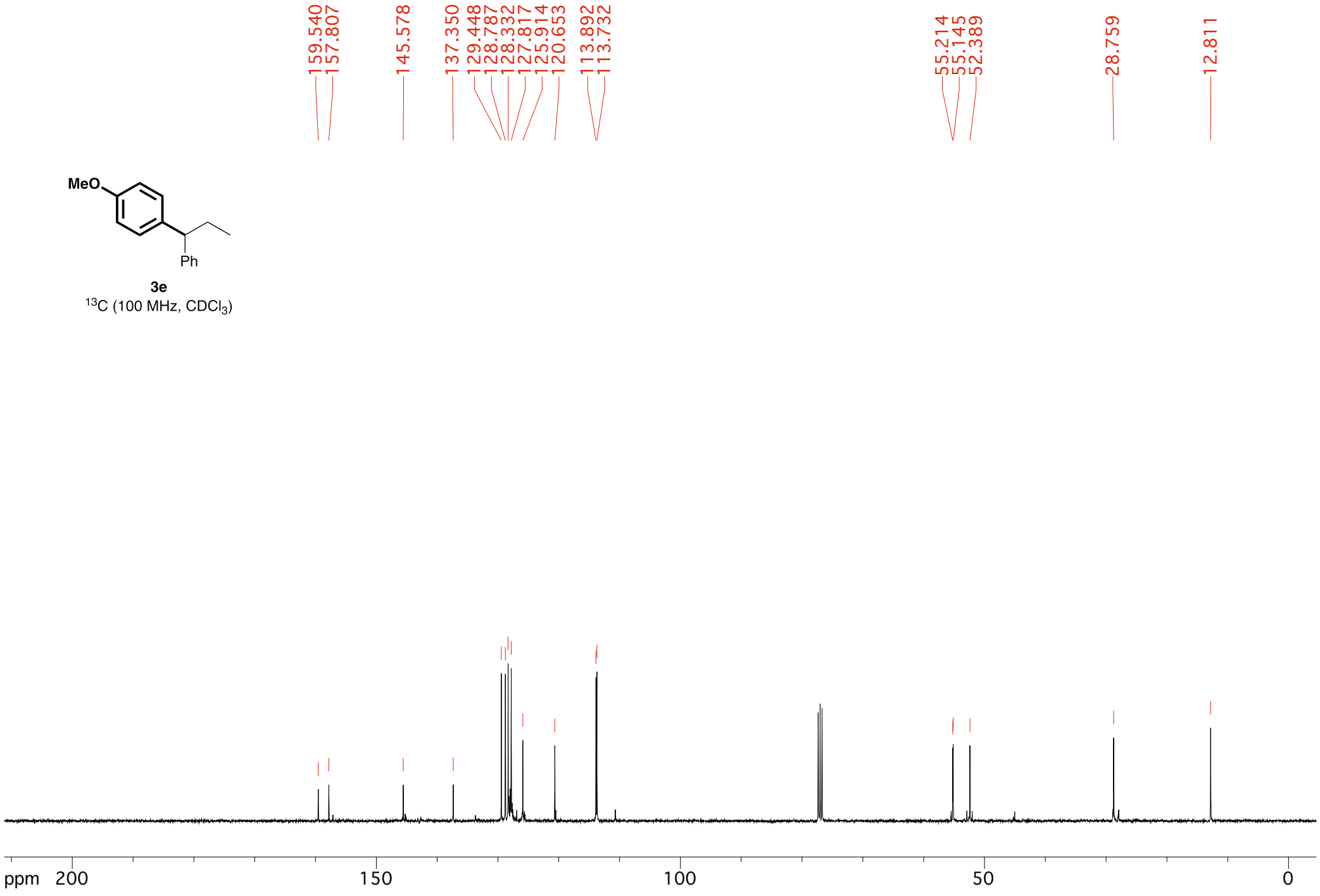
^{13}C (100 MHz, $CDCl_3$)



3c

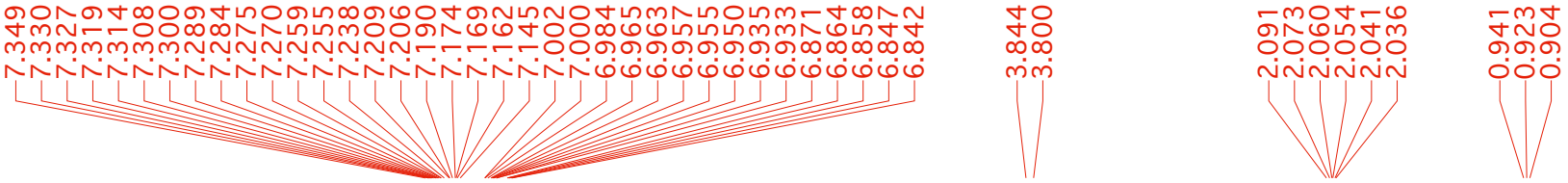
^{1}H (400 MHz, $CDCl_3$)

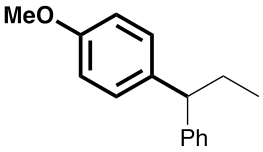




3e

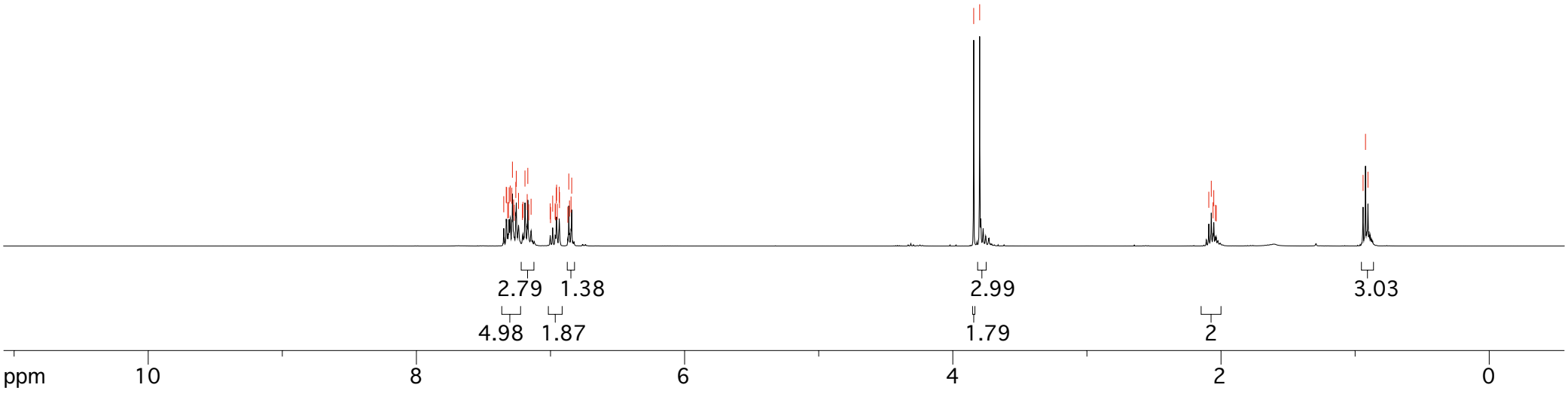
^{13}C (100 MHz, $CDCl_3$)

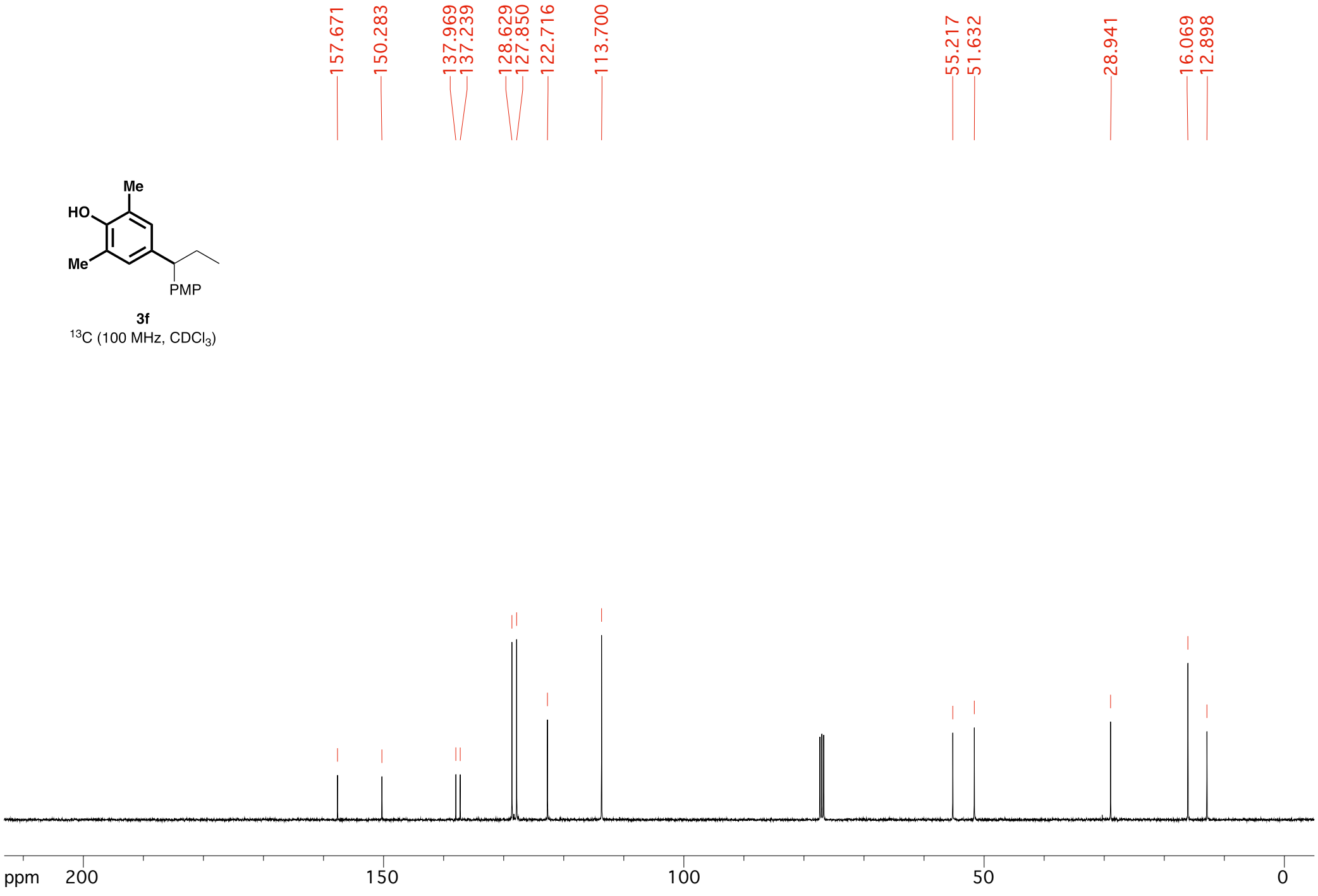




3e

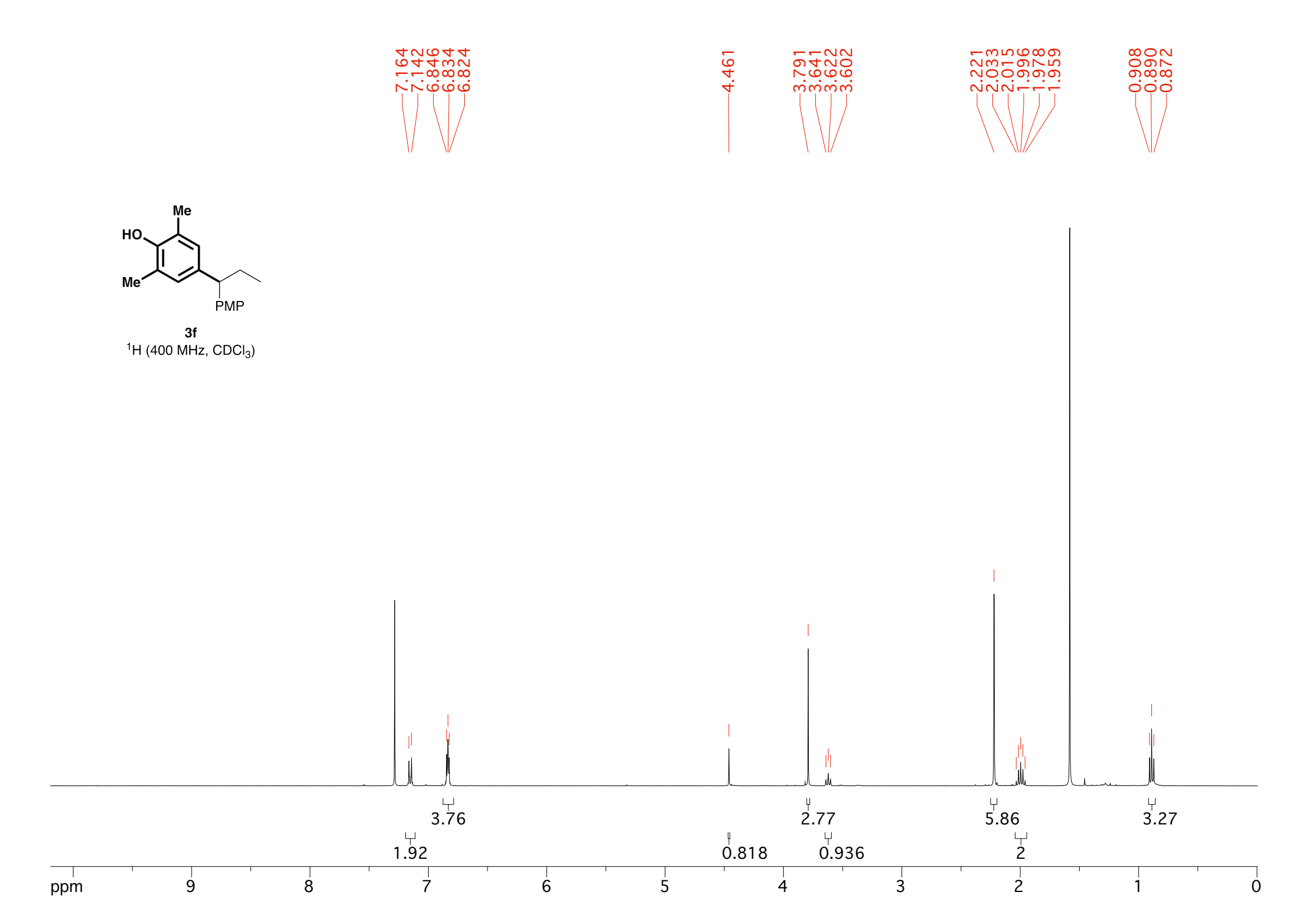
^{1}H (400 MHz, $CDCl_3$)





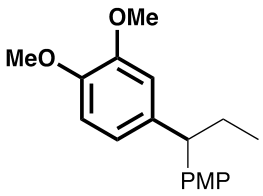
3f

^{13}C (100 MHz, $CDCl_3$)



3f

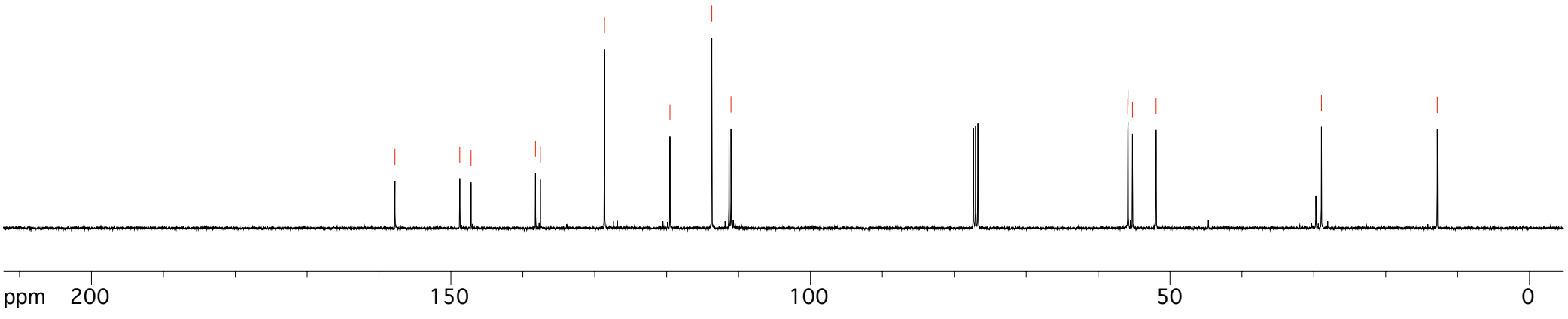
^{1}H (400 MHz, $CDCl_3$)



3g

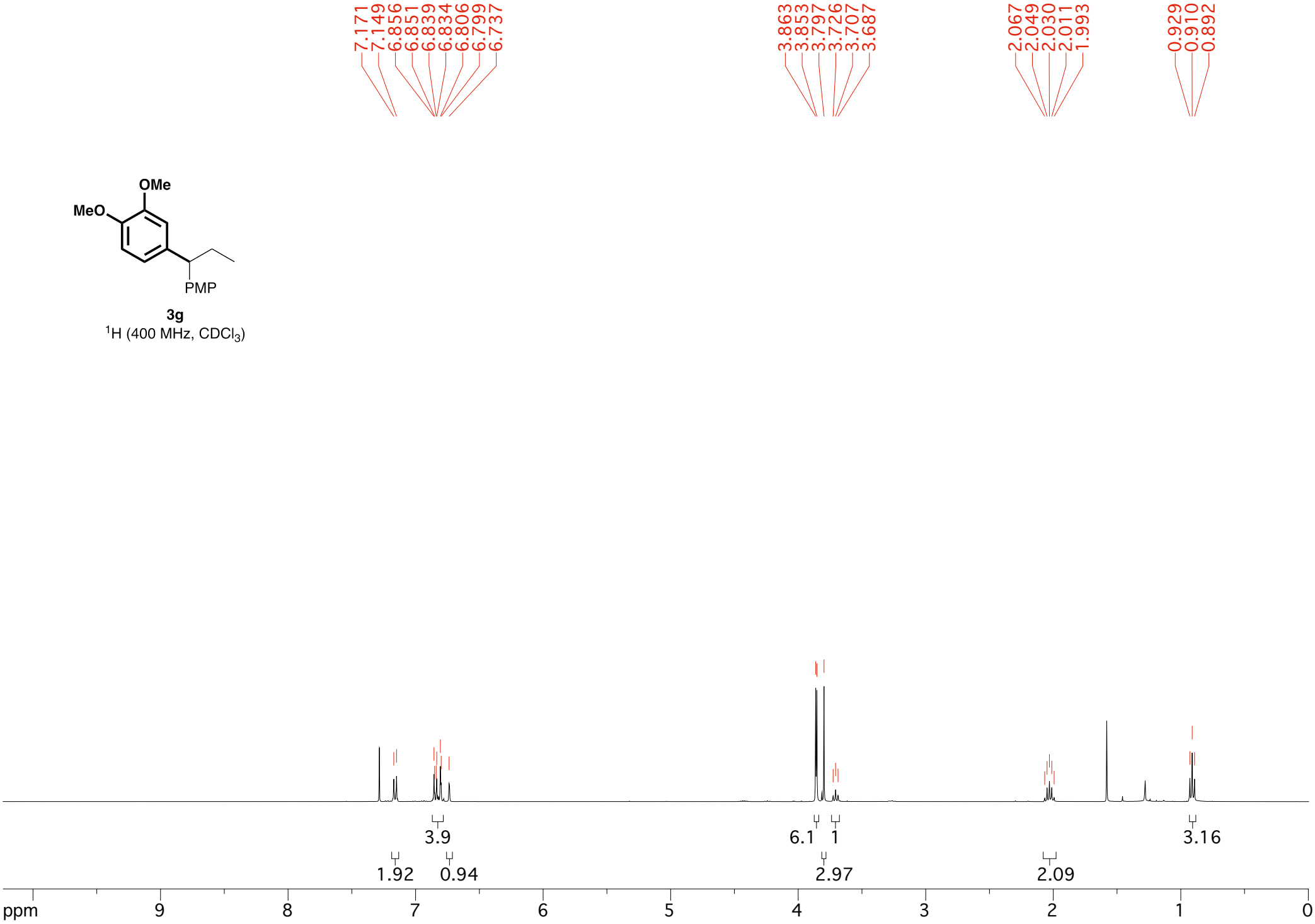
^{13}C (100 MHz, $CDCl_3$)

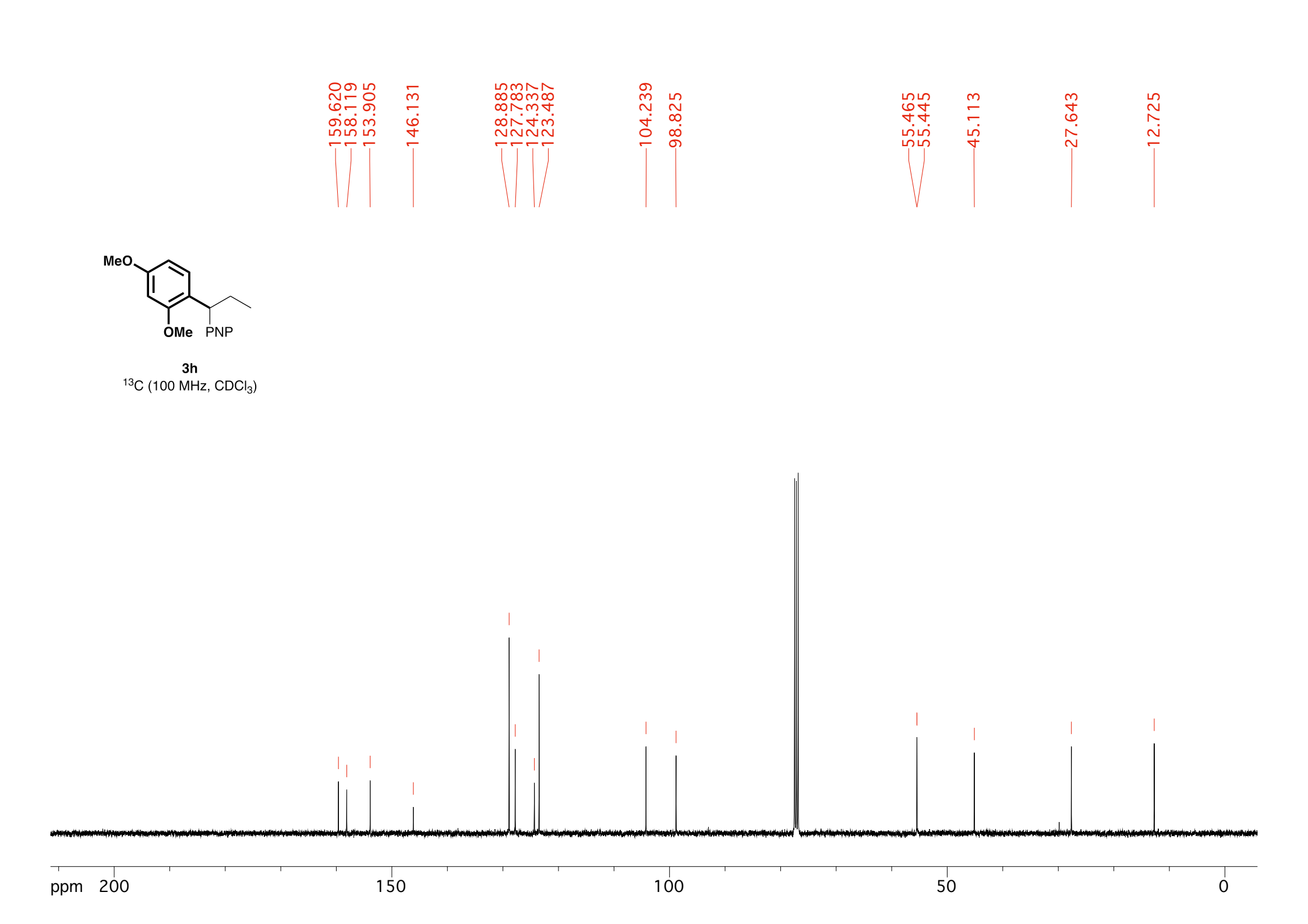
157.778
148.767
147.200
138.243
137.562
128.649
119.541
113.721
111.323
111.049
55.862
55.820
55.218
51.931
28.943
12.830

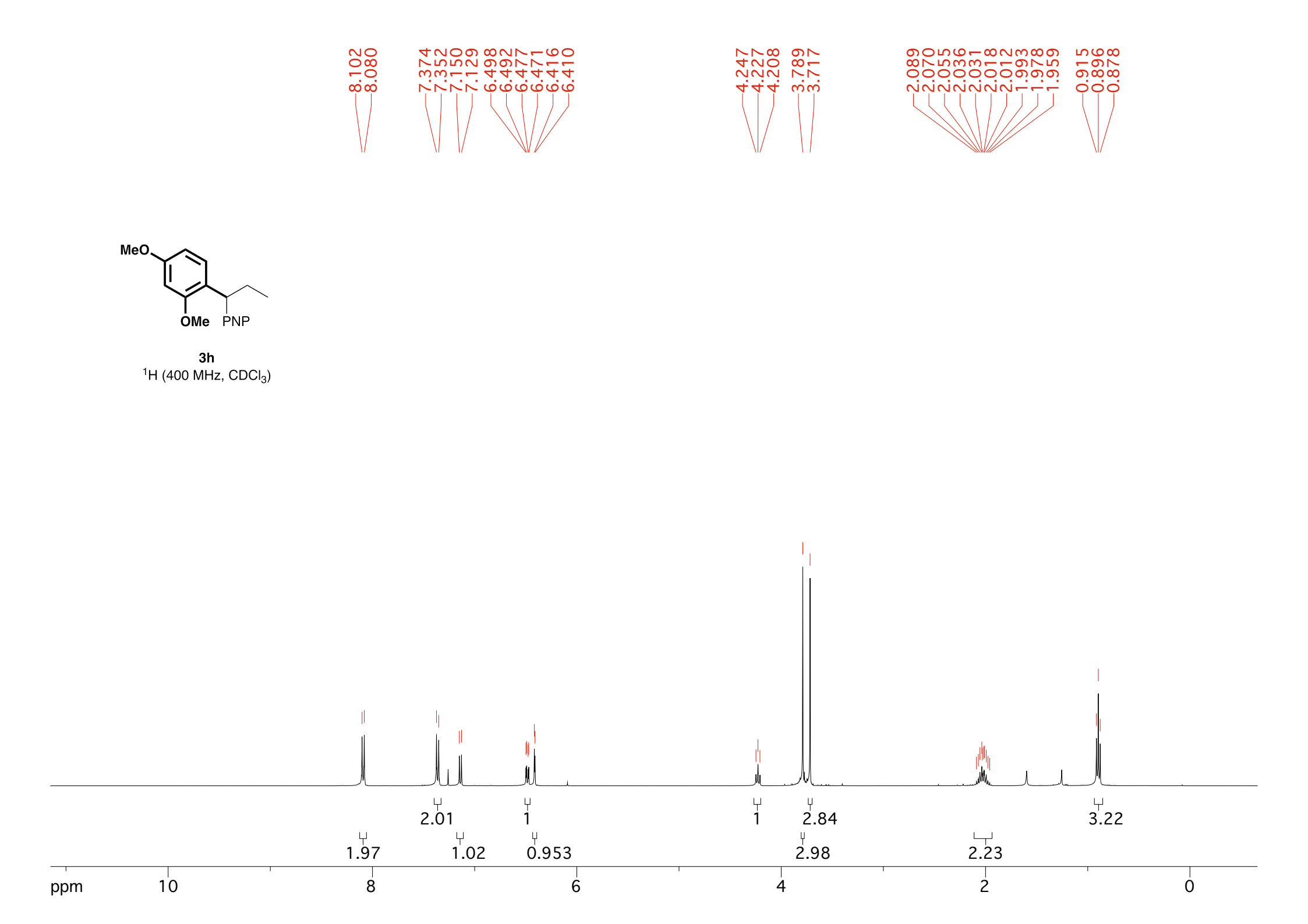


3g

^{1}H (400 MHz, $CDCl_3$)

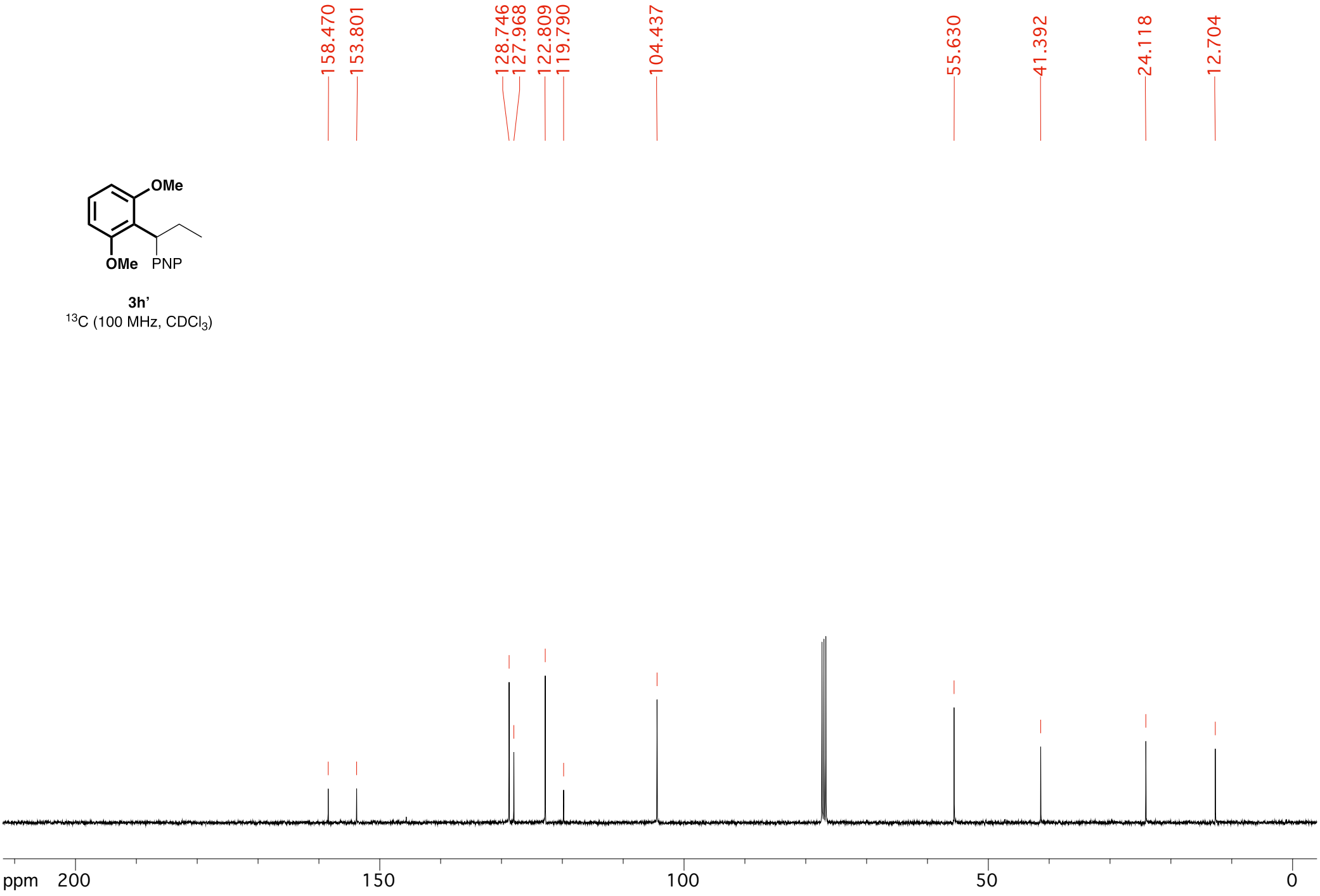



159.620
158.119
153.905
146.131
128.885
127.783
124.337
123.487
104.239
98.825
55.465
55.445
45.113
27.643
12.725
MeO
OMe
PNP
3h
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0



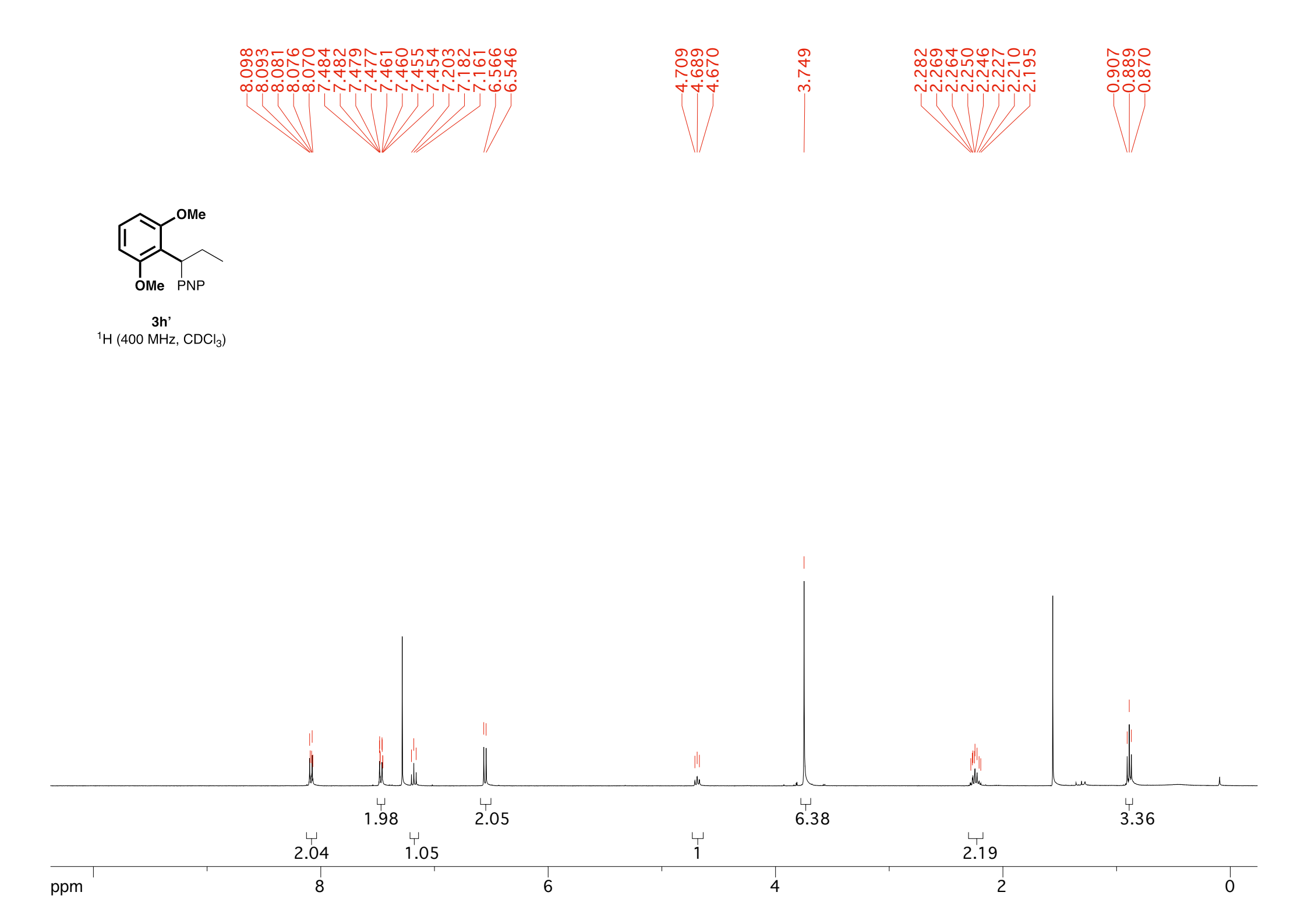
3h

^{1}H (400 MHz, $CDCl_3$)



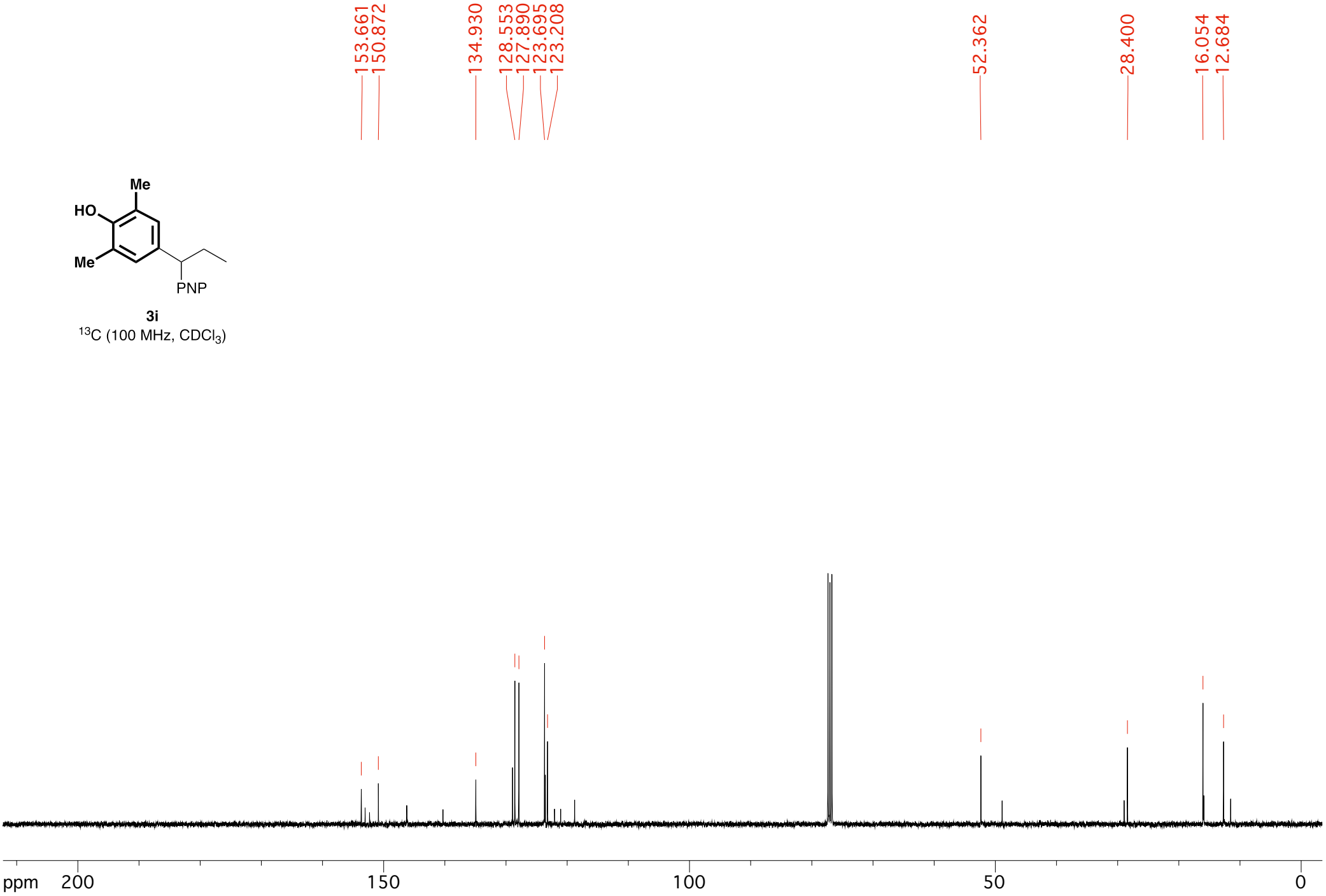
3h'

^{13}C (100 MHz, $CDCl_3$)


8.098
8.093
8.081
8.076
8.070
7.484
7.482
7.479
7.477
7.461
7.460
7.455
7.454
7.203
7.182
7.161
6.566
6.546
4.709
4.689
4.670
3.749
2.282
2.269
2.264
2.250
2.246
2.227
2.210
2.195
0.907
0.889
0.870
OMe
OMe
PNP
3h'
1H (400 MHz, CDCl3)
1.98
2.05
6.38
3.36
2.04
1.05
1
2.19
ppm
8
6
4
2
0

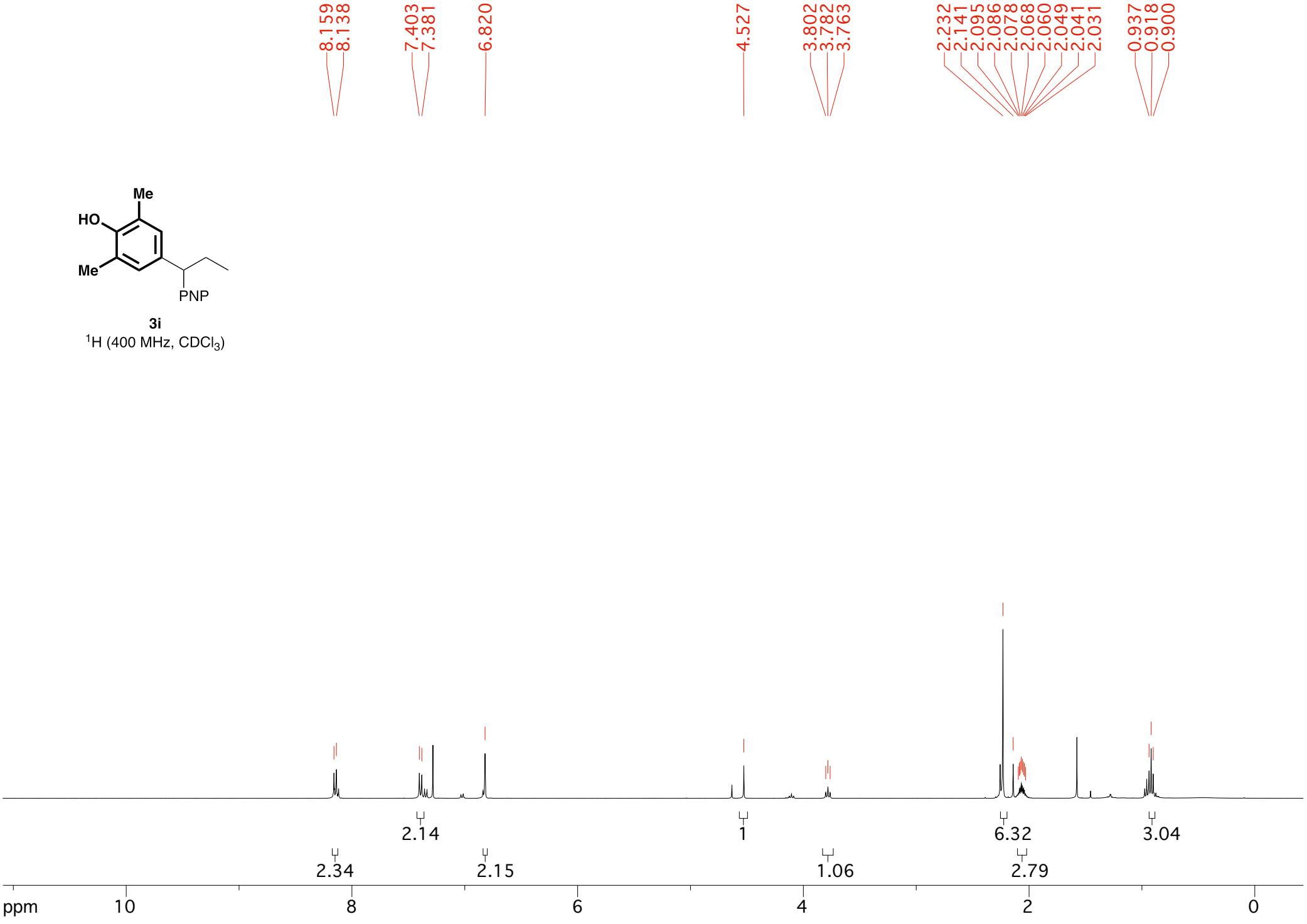
3i

^{13}C (100 MHz, $CDCl_3$)



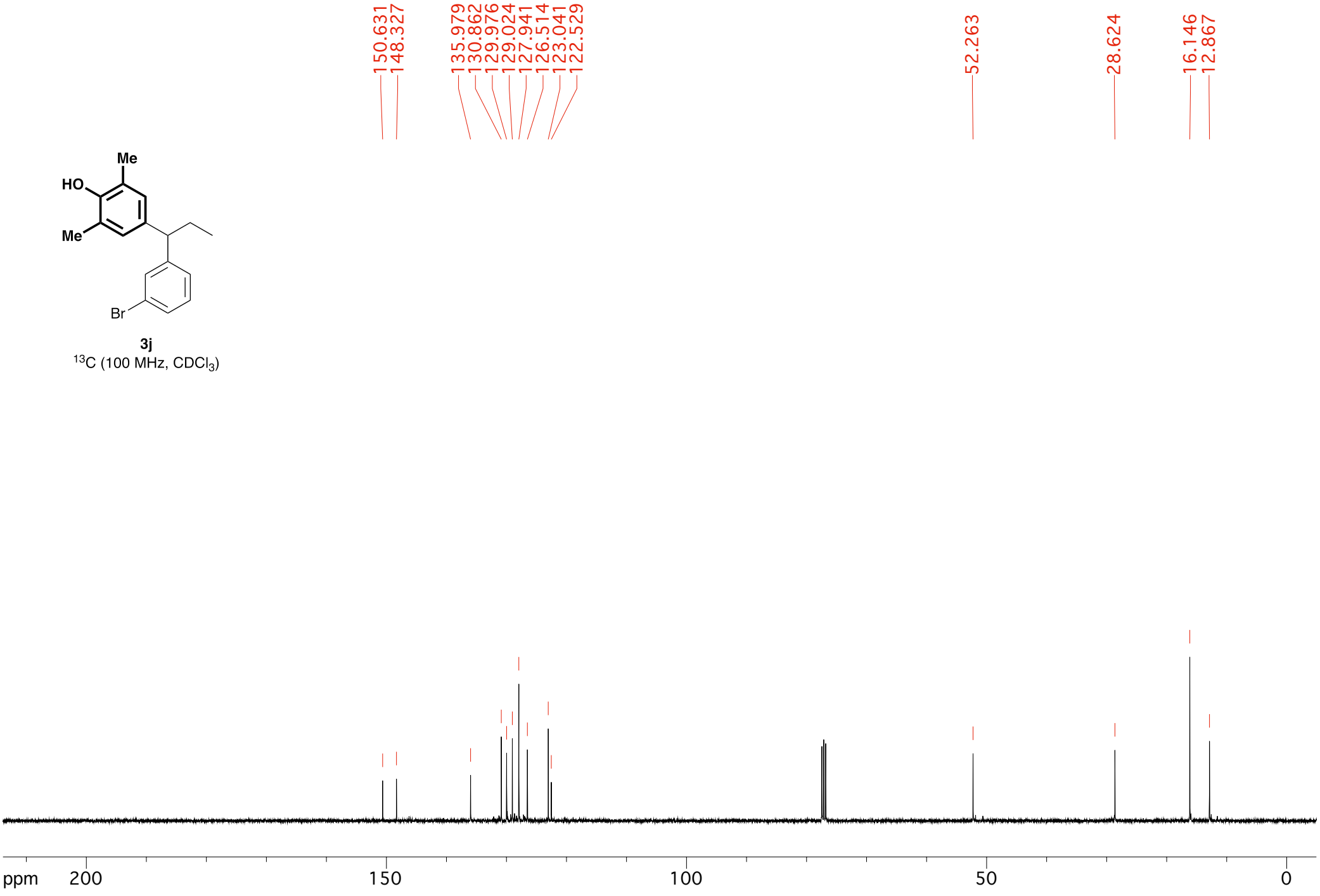
3i

^{1}H (400 MHz, $CDCl_3$)



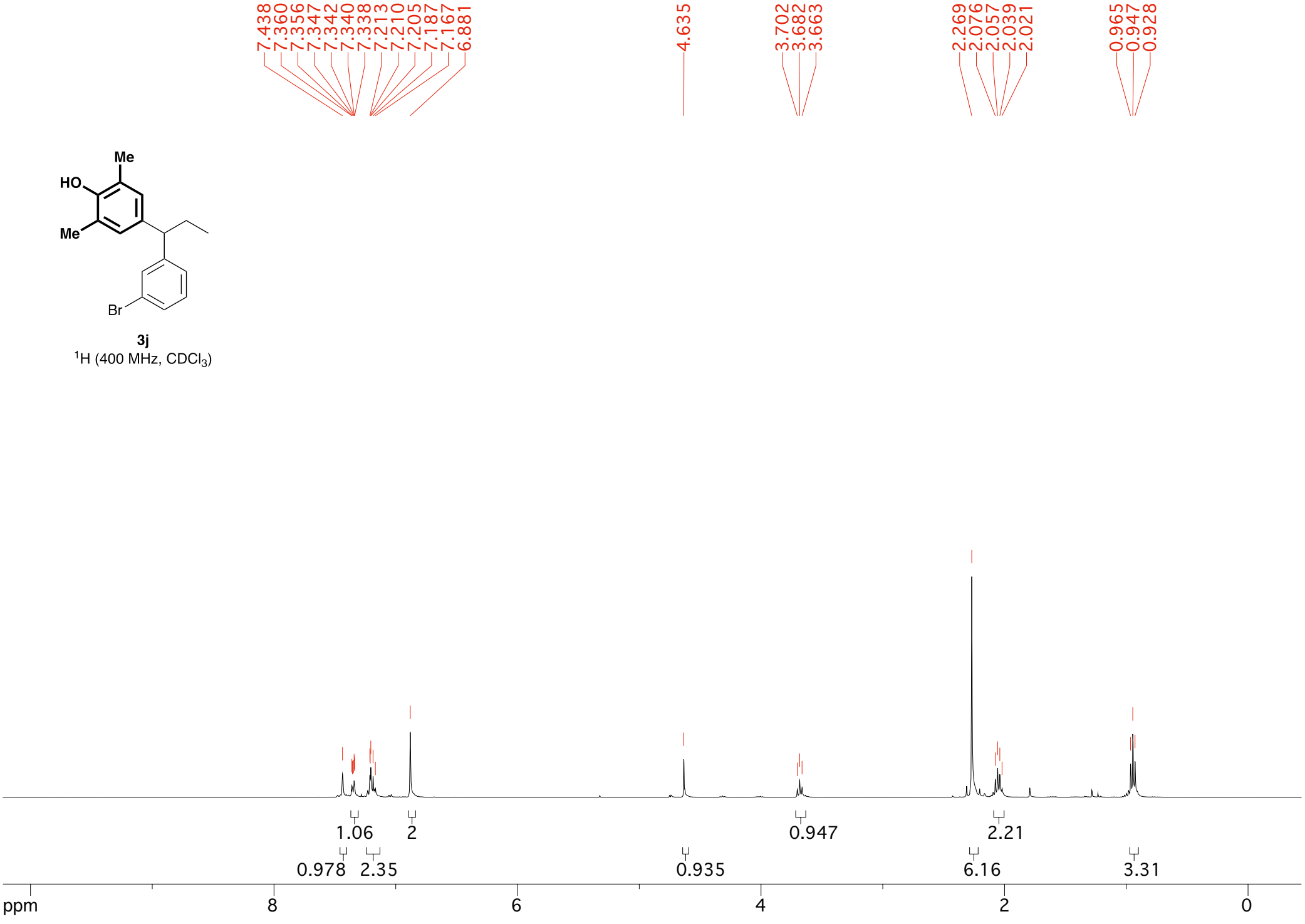
3j

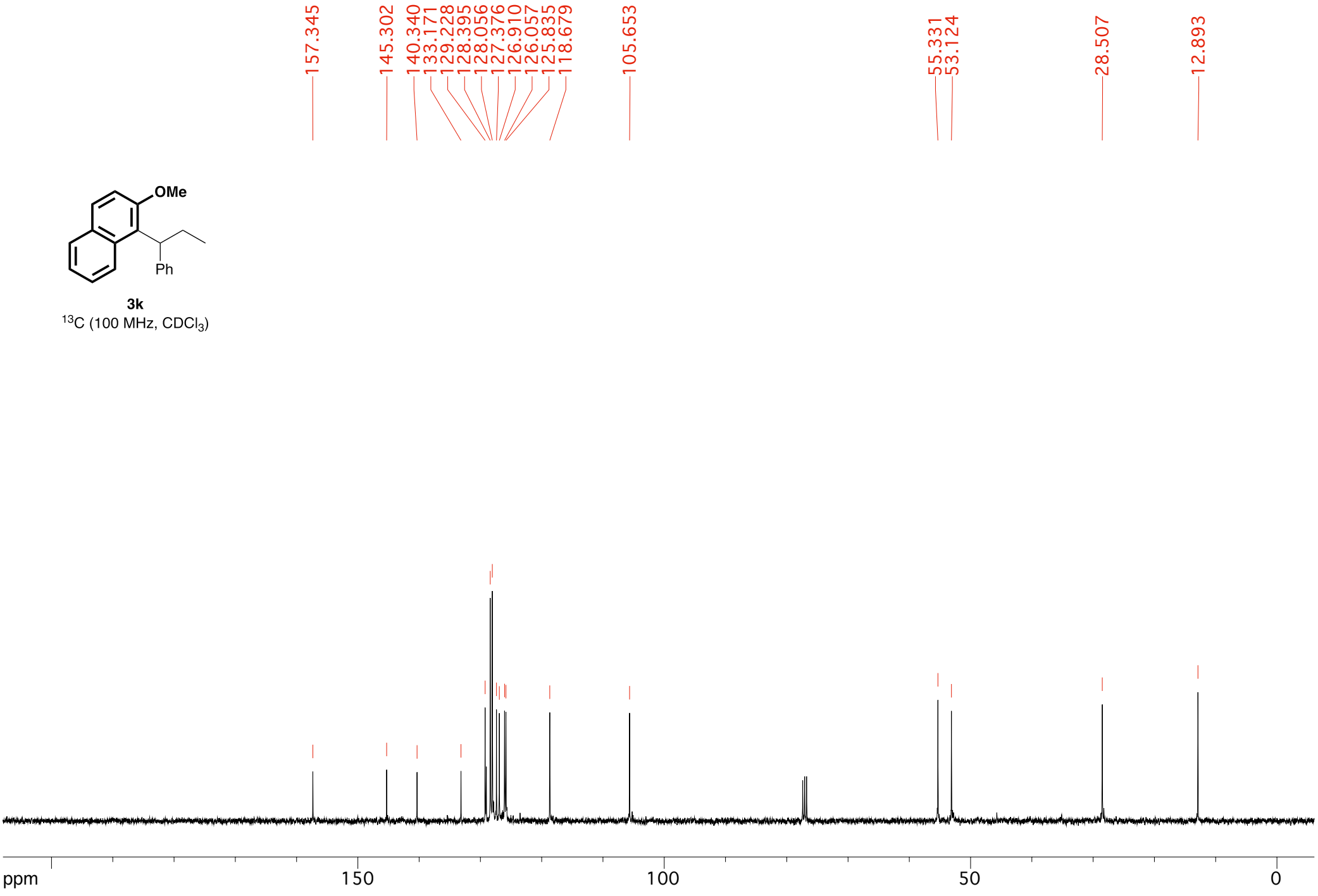
^{13}C (100 MHz, $CDCl_3$)



3j

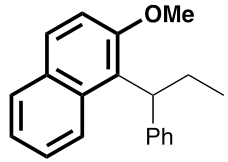
^{1}H (400 MHz, $CDCl_3$)





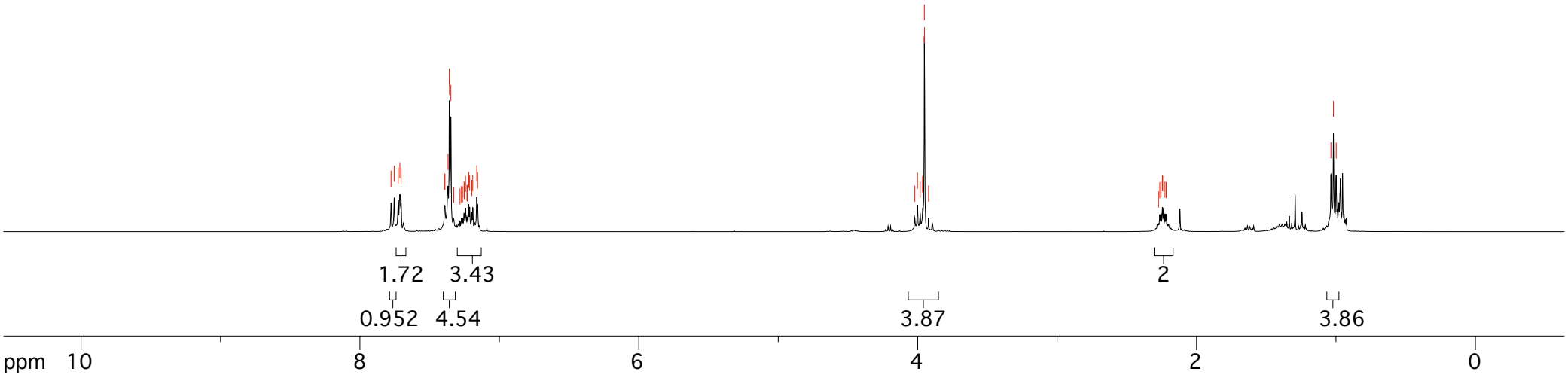
3k

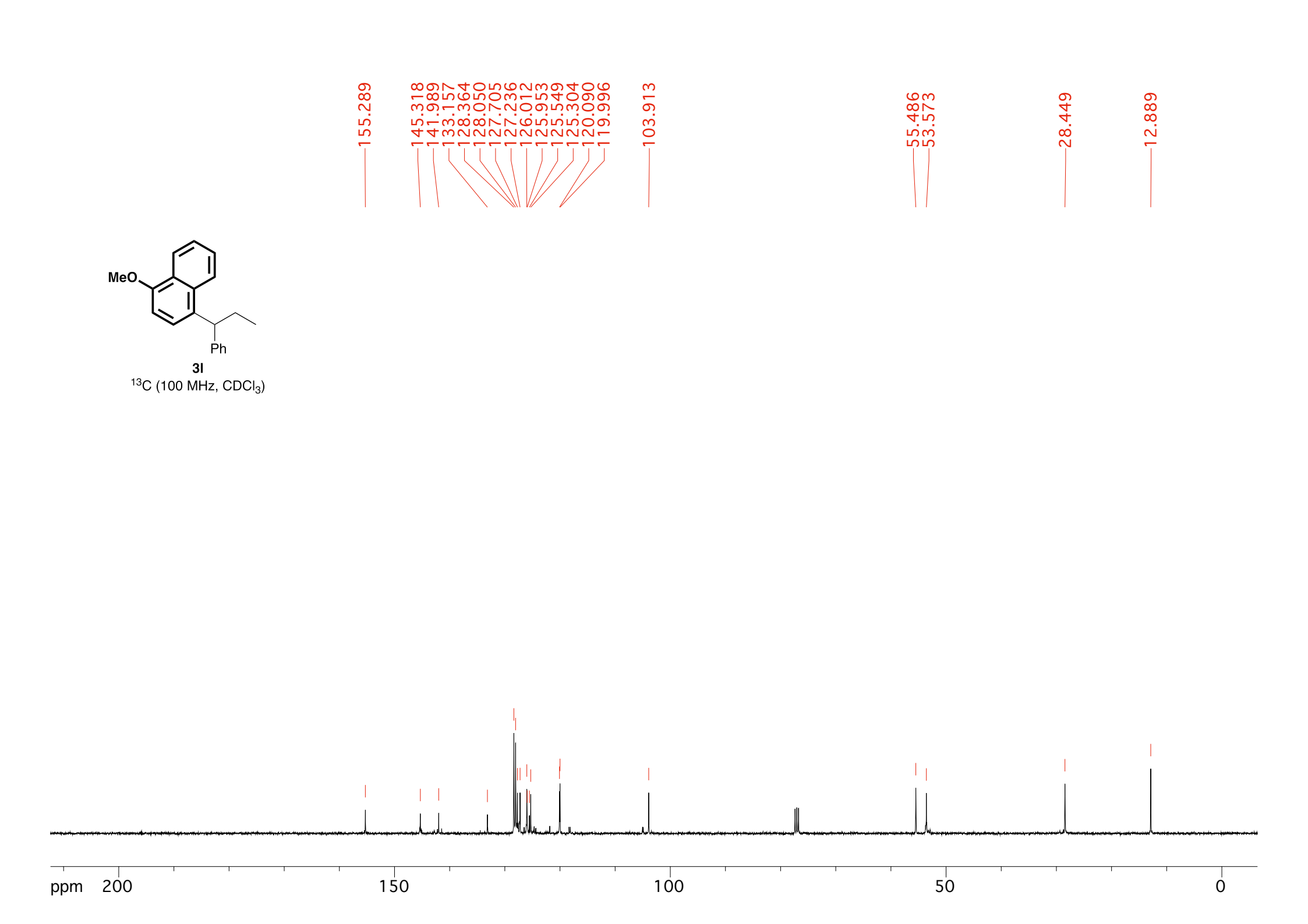
^{13}C (100 MHz, $CDCl_3$)

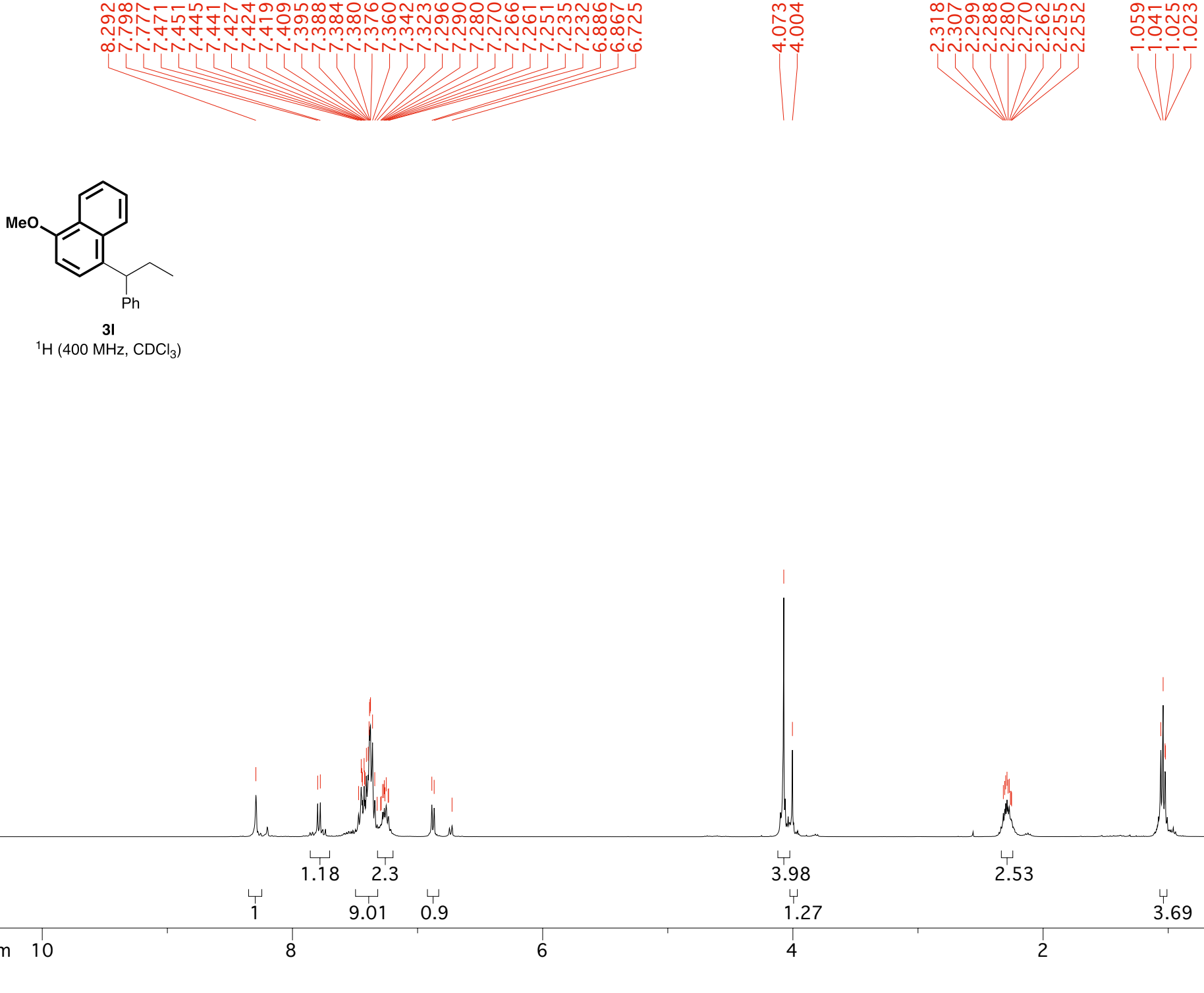


3k

^{1}H (400 MHz, $CDCl_3$)

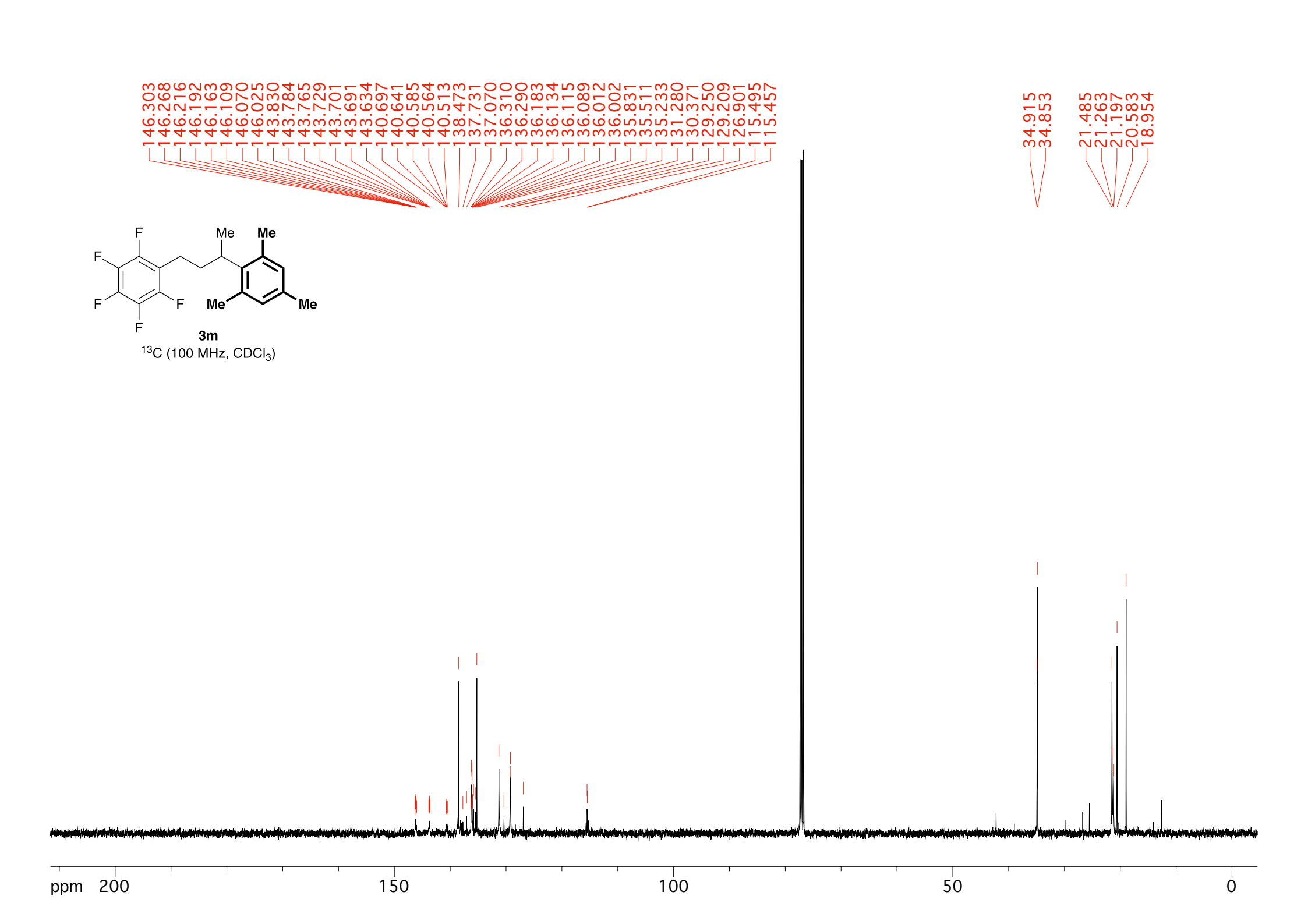


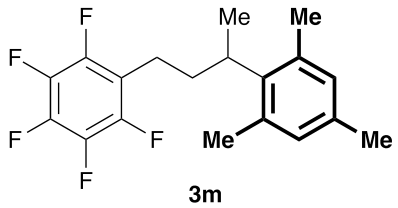

155.289
145.318
141.989
133.157
128.364
128.050
127.705
127.236
126.012
125.953
125.549
125.304
120.090
119.996
103.913
55.486
53.573
28.449
12.889
MeO
Ph
3l
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0



3l

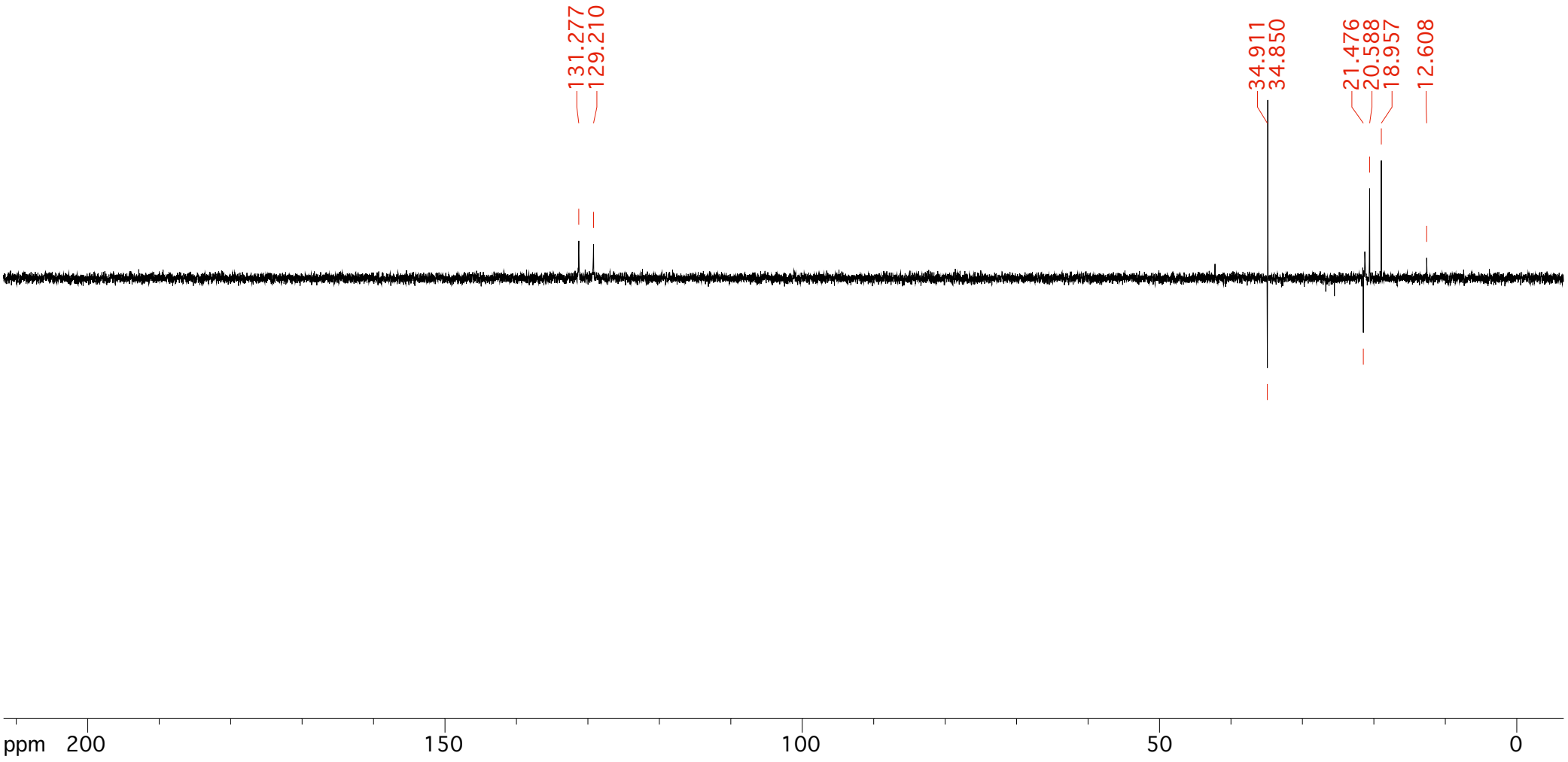
^{1}H (400 MHz, $CDCl_3$)

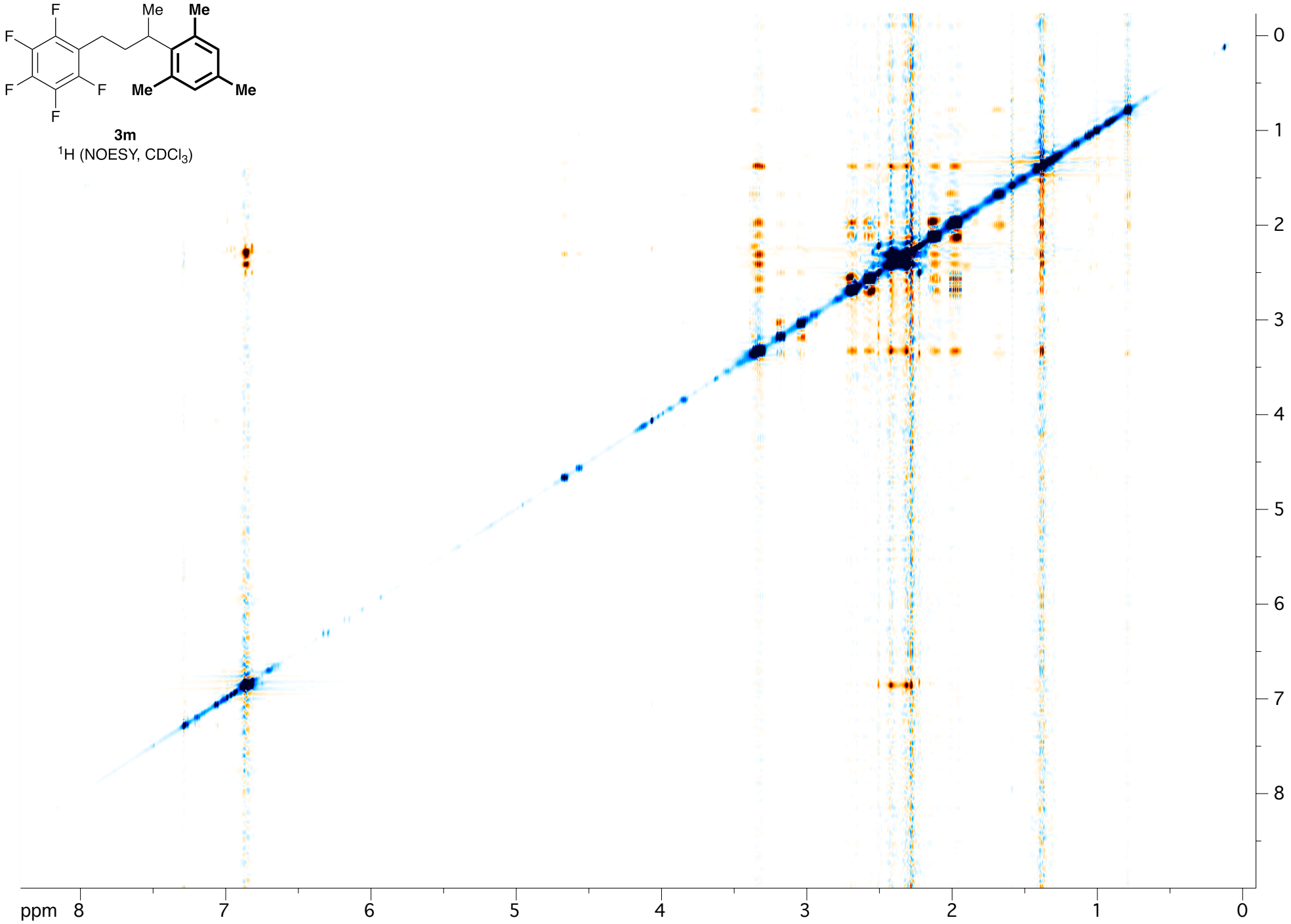

146.303
146.268
146.216
146.192
146.163
146.109
146.070
146.025
143.830
143.784
143.765
143.729
143.701
143.691
143.634
140.697
140.641
140.585
140.564
140.513
138.473
137.731
137.070
136.310
136.290
136.183
136.134
136.115
136.089
136.012
136.002
135.831
135.511
135.233
131.280
130.371
129.250
129.209
126.901
115.495
115.457
34.915
34.853
21.485
21.263
21.197
20.583
18.954
F
F
F
F
Me
Me
Me
Me
3m
13C (100 MHz, CDCl3)
ppm
200
150
100
50
0



3m

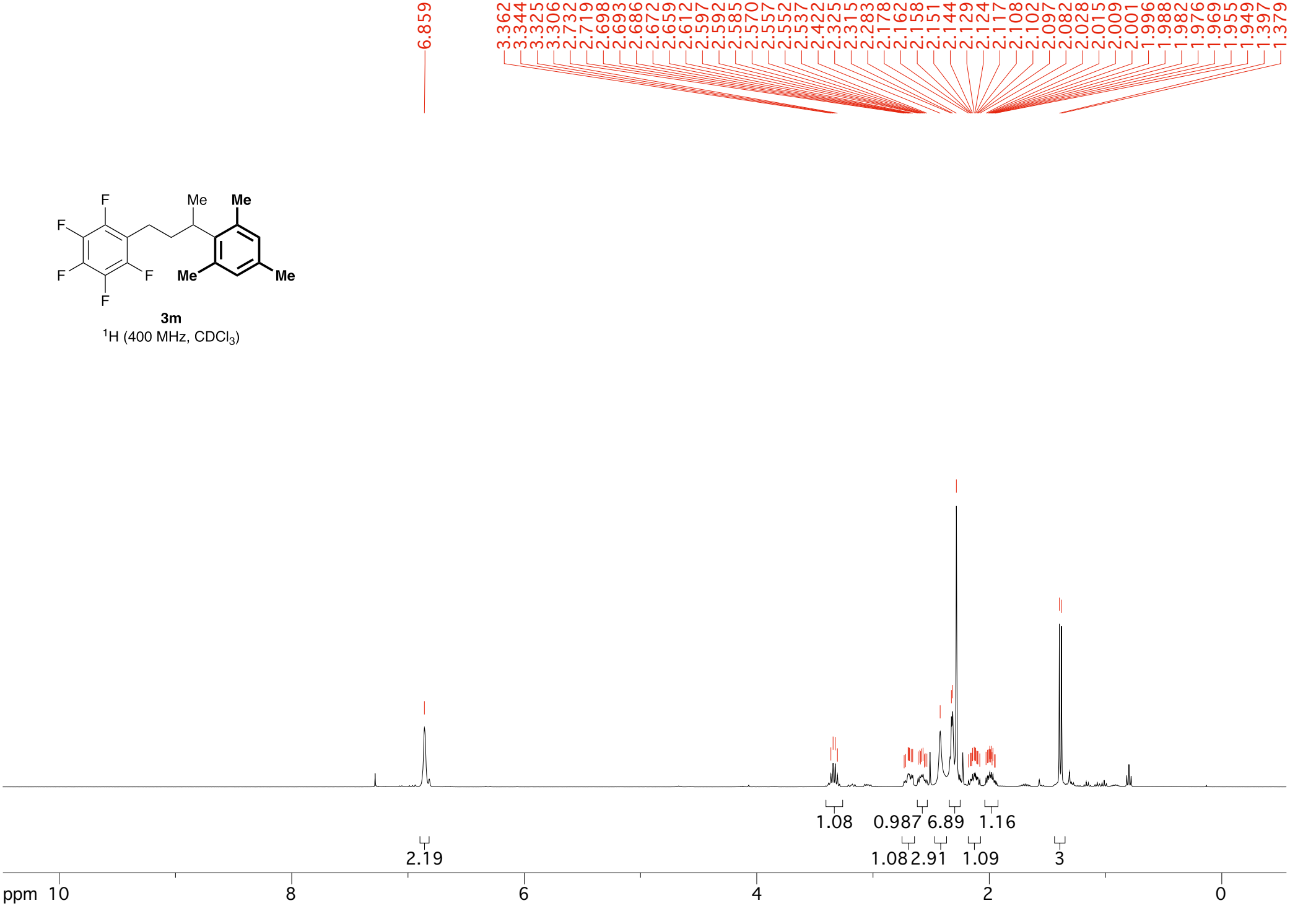
^{13}C DEPT135 (100 MHz, $CDCl_3$)

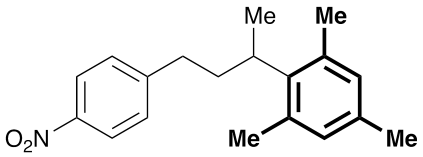



F
Me
Me
F
F
F
Me
Me
F
3m
^{1}H (NOESY, $CDCl_3$)
0
1
2
3
4
5
6
7
8
ppm
8
7
6
5
4
3
2
1
0

3m

^{1}H (400 MHz, $CDCl_3$)





3n

^{13}C (100 MHz, $CDCl_3$)

150.513
146.239
138.760
135.211
129.151
123.574
36.595
34.617
34.220
21.483
20.632
19.095

ppm
150
100
50
0

3n

^{1}H (400 MHz, $CDCl_3$)