

Syntheses of α -Pyrones Using Gold-Catalyzed Coupling Reactions

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I. Material and Methods:

Dry solvents (anhydrous CH₂Cl₂ and toluene) were purchased from Sigma-Aldrich. Unless otherwise stated, all reagents were obtained from commercial sources and used without further purification. All propiolic acids and alkynes are commercially available except **3c** and **3d**, the synthesis of which was described herein. Infrared spectra were recorded on a Nicolet Avatar 370 DTGS FTIR. ¹H NMR spectra were recorded on Varian Unity/Inova 500 (500 MHz), or Bruker Ultrashield 300 (300 MHz) spectrometers. ¹H NMR data are reported as follows: chemical shift in parts per million relative to CHCl₃ (7.27 ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened), coupling constant (Hz), and integration. ¹³C NMR spectra were recorded on Varian Unity/Inova 500 (125 MHz) or Bruker Ultrashield 300 (75 MHz) spectrometers. ¹³C NMR chemical shifts are reported in parts per million relative to solvent. All ¹³C NMR spectra were determined with broadband decoupling. High-resolution mass spectra (HRMS) were obtained through the Harvard University mass spectrometry facility. All reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using E. Merck silica gel 60 F254 precoated plates (0.25 mm). Flash chromatography was performed either on EM Science silica gel 60 (230–400 mesh) or using a CombiFlash companion system (Teledyne ISCO, Inc.) with pre-packed FLASH silica gel columns (Biotage, Inc.).

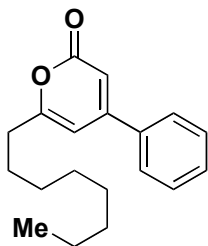
II. General experimental procedure and spectra data

General procedure of gold-catalyzed synthesis of α -pyrone from propiolic acid and alkyne (synthesis of **6l** as an example):

In a 4 mL vial with a threaded cap, phenylpropiolic acid (50 mg, 0.34 mmol, 1.0 equiv), 3-phenyl-1-propyne (199 mg, 0.213 mL, 1.71 mmol, 5.0 equiv), and $[(\text{Ph}_3\text{P})\text{AuCl}]$ (8.5 mg, 0.017 mmol, 0.05 equiv) were dissolved in 1.5 mL anhydrous CH_2Cl_2 . AgOTf (4.4 mg, 0.017 mmol, 0.05 equiv) was added to the solution in one portion. The reaction mixture was stirred in the sealed vial under air at room temperature for 12 h. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (hexane / EtOAc = 94 / 6) to give 85 mg desired product **6l** in 95% yield.

Compounds **6l** and **6c** were also produced in relatively large scale via the following described procedure.

In a 25 mL vial with a threaded cap, phenylpropiolic acid (0.5 g, 3.4 mmol, 1.0 equiv), 3-phenyl-1-propyne (1.98 g, 2.13 mL, 17.1 mmol, 5.0 equiv) or 1-heptyne (1.65 g, 2.24 mL, 17.1 mmol, 5.0 equiv), and $[(\text{Ph}_3\text{P})\text{AuCl}]$ (85 mg, 0.17 mmol, 0.05 equiv) were dissolved in 15 mL anhydrous CH_2Cl_2 . AgOTf (44 mg, 0.17 mmol, 0.05 equiv) was added to the solution in one portion. The reaction mixture was stirred in the sealed vial under air at room temperature for 24 h. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (hexane / EtOAc = 94 / 6) to give 0.68 g **6l** (76%) or 0.686 g **6c** (83%) respectively.



6-octyl-4-phenyl-2H-pyran-2-one (**6a**)

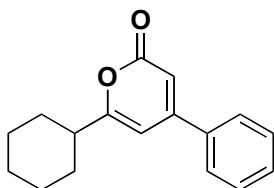
Phenylpropiolic acid: 30 mg, 0.20 mmol; 1-decyne: 142 mg, 1.03 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.0 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 49 mg; yield: 83%.

Compound **6a** was also prepared from **5a**:

In a 4 mL vial with a threaded cap, dec-1-en-2-yl 3-phenylpropiolate **5a** (15 mg, 0.053 mmol, 1.0 equiv), and $[(\text{Ph}_3\text{P})\text{AuCl}]$ (1.3 mg, 0.0026 mmol, 0.05 equiv) were dissolved in 0.26 mL anhydrous CH_2Cl_2 . AgOTf (0.9 mg, 0.0026 mmol, 0.05 equiv) was added to the solution in one portion. The reaction mixture was stirred in the sealed vial under air at room temperature for 3 h. The solvent was evaporated and the residue was purified by

flash chromatography on silica gel (hexane / EtOAc = 95 / 5) to give 15 mg desired product **6a** in 99% yield.

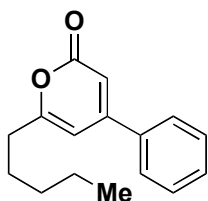
IR (neat, cm^{-1}): 2920, 2850, 1713, 1635, 1546, 1448, 1134, 853, 765, 686, 538; ^1H NMR (500 MHz, CDCl_3) δ 0.80-0.93 (m, 3 H), 1.21-1.43 (m, 12 H), 1.72 (t, $J = 7.3$ Hz, 2 H), 2.56 (t, $J = 7.6$ Hz, 2 H), 6.30 (s, 1 H), 6.36 (s, 1 H), 7.42-7.53 (m, 3 H), 7.59 (dd, $J = 6.6, 3.2$ Hz, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.0, 163.5, 155.4, 135.9, 130.5, 129.1, 126.6, 108.2, 102.7, 34.0, 31.8, 29.2, 29.1, 29.0, 26.9, 22.6, 14.0; HRMS (EI) calcd. for $[\text{C}_{19}\text{H}_{25}\text{O}_2]$ ($\text{M}+\text{H}$) $^+$ 285.18491, found 285.18559.



6-cyclohexyl-4-phenyl-2H-pyran-2-one (**6b**)

Phenylpropionic acid: 54 mg, 0.37 mmol; 1-cyclohexylacetylene: 199 mg, 1.84 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.6 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 58 mg; yield: 62%.

IR (neat, cm^{-1}): 3059, 2926, 2852, 1713, 1633, 1580, 1545, 1497, 1448, 1331, 1143, 849, 785, 696; ^1H NMR (300 MHz, CDCl_3) δ 7.56-7.59 (m, 2H), 7.46-7.48 (m, 3H), 6.34 (s, 1H), 6.27 (s, 1H), 2.40-2.55 (m, 1H), 2.00-2.04 (m, 2H), 1.83-1.88 (m, 2H), 1.72-1.76 (m, 1H), 1.18-1.54 (m, 5H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.8, 163.6, 155.5, 136.1, 130.4, 129.1, 126.6, 108.3, 100.8, 42.5, 30.5, 25.8, 25.7; HRMS (EI) calcd. for $[\text{C}_{17}\text{H}_{18}\text{O}_2\text{Na}]$ ($\text{M}+\text{Na}$) $^+$ 277.11990, found 277.11926.

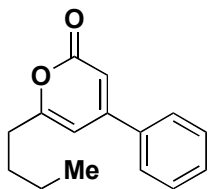


6-pentyl-4-phenyl-2H-pyran-2-one (**6c**)

Phenylpropionic acid: 50 mg, 0.34 mmol; 1-heptyne: 164 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 66 mg; yield: 80%.

IR (neat, cm^{-1}): 3061, 2954, 2928, 2859, 1711, 1635, 1581, 1545, 1497, 1448, 1402, 1332, 1138, 1103, 1050, 991, 851, 765, 695; ^1H NMR (300 MHz, CDCl_3) δ 7.59-7.56 (m, 2H), 7.49-7.46 (m, 3H), 6.35 (s, 1H), 6.30 (s, 1H), 2.55 (t, $J = 9$ Hz, 2H), 1.74-1.70 (m, 2H), 1.36-1.26 (m, 4H), 0.91 (t, $J = 6$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 163.4, 155.4, 135.9, 130.5, 129.1, 126.6, 108.2, 102.7, 34.0, 31.1, 26.6, 22.2, 13.8; HRMS (EI)

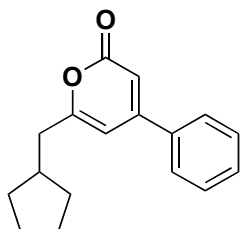
calcd. for $[C_{16}H_{18}O_2Na]$ $(M+Na)^+$ 265.11990, found 265.11928.



6-pentyl-4-phenyl-2H-pyran-2-one (6d)

Phenylpropionic acid: 50 mg, 0.34 mmol; 1-hexyne: 141 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 60 mg; yield: 77%.

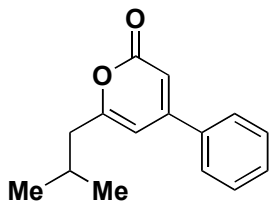
IR (neat, cm^{-1}): 3061, 2957, 2929, 2971, 1713, 1636, 1546, 1497, 1449, 1402, 1335, 1279, 1139, 1102, 989, 888, 852, 766, 696; 1H NMR (300 MHz, $CDCl_3$) δ 7.59-7.56 (m, 2H), 7.49-7.46 (m, 3H), 6.35 (s, 1H), 6.30 (s, 1H), 2.56 (t, $J = 9$ Hz, 2H), 1.75-1.65 (m, 2H), 1.44-1.35 (m, 2H), 0.95 (t, $J = 9$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 163.4, 155.4, 135.8, 130.5, 129.0, 126.6, 108.1, 102.7, 33.6, 28.9, 22.0, 13.6; HRMS (EI) calcd. for $[C_{15}H_{12}O_2Na]$ $(M+Na)^+$ 251.10425, found 251.10422.



6-(cyclopentylmethyl)-4-phenyl-2H-pyran-2-one (6e)

Phenylpropionic acid: 50 mg, 0.34 mmol; 3-cyclopentyl-1-propyne: 185 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 78 mg; yield: 90%.

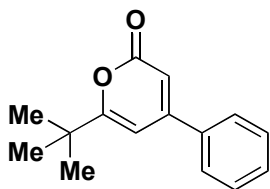
IR (neat, cm^{-1}): 3060, 2946, 2864, 1709, 1634, 1580, 1544, 1496, 1448, 1401, 1334, 1125, 990, 901, 851, 764, 692; 1H NMR (300 MHz, $CDCl_3$) δ 7.59-7.56 (m, 2H), 7.49-7.46 (m, 3H), 6.35 (s, 1H), 6.30 (s, 1H), 2.55 (d, $J = 9$ Hz, 2H), 2.36-2.25 (m, 1H), 1.88-1.75 (m, 2H), 1.68-1.52 (m, 4H), 1.27-1.15 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 163.4, 155.3, 135.9, 130.5, 129.0, 126.6, 108.1, 103.0, 40.0, 37.8, 32.3, 24.8; HRMS (EI) calcd. for $[C_{17}H_{18}O_2Na]$ $(M+Na)^+$ 277.11990, found 277.11955.



6-isobutyl-4-phenyl-2H-pyran-2-one (6f)

Phenylpropionic acid: 50 mg, 0.34 mmol; 4-methyl-1-pentyne: 140 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 47 mg; yield: 61%.

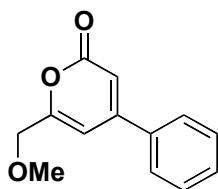
IR (neat, cm⁻¹): 3061, 2957, 2929, 2971, 1709, 1635, 1545, 1464, 1449, 1325, 989, 903, 852, 764, 695; ¹H NMR (300 MHz, CDCl₃) δ 7.59-7.56 (m, 2H), 7.49-7.47 (m, 3H), 6.36 (s, 1H), 6.29 (s, 1H), 2.42 (d, *J* = 6 Hz, 2H), 2.16 (hept., *J* = 6 Hz, 1H), 0.99 (d, *J* = 6 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 165.0, 163.2, 155.3, 135.9, 130.5, 129.1, 126.6, 108.2, 103.7, 43.2, 26.9, 22.2; HRMS (EI) calcd. for [C₁₅H₁₆O₂Na] (M+Na)⁺ 251.10425, found 251.10464.



6-(tert-butyl)-4-phenyl-2H-pyran-2-one (6g)

Phenylpropionic acid: 50 mg, 0.34 mmol; 3,3-dimethyl-1-butyne: 140 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 24 mg; yield: 31%.

IR (neat, cm⁻¹): 2967, 1729, 1708, 1630, 1580, 1547, 1389, 1366, 1324, 1105, 883, 846, 766, 699; ¹H NMR (300 MHz, CDCl₃) δ 7.59-7.56 (m, 2H), 7.49-7.47 (m, 3H), 6.35 (s, 1H), 6.34 (s, 1H), 1.34 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 172.6, 163.4, 155.5, 136.4, 130.5, 129.1, 126.7, 108.5, 99.5, 36.3, 28.0; HRMS (EI) calcd. for [C₁₅H₁₆O₂Na] (M+Na)⁺ 251.10425, found 251.10459.

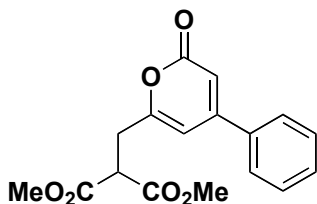


6-(methoxymethyl)-4-phenyl-2H-pyran-2-one (6h)

Phenylpropionic acid: 50 mg, 0.34 mmol; Methyl propargyl ether: 120 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction

temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 45 mg; yield: 61%.

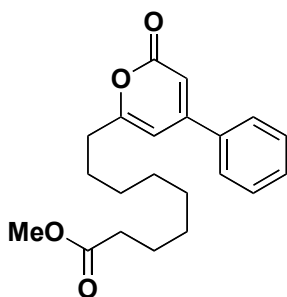
IR (neat, cm^{-1}): 2930, 1716, 1643, 1552, 1449, 1382, 1333, 1199, 1116, 1001, 853, 767, 694, 539; ^1H NMR (300 MHz, CDCl_3) δ 7.62-7.59 (m, 2H), 7.50-7.48 (m, 3H), 6.60 (s, 1H), 6.42 (s, 1H), 4.29 (s, 2H), 3.50 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 162.4, 161.2, 155.0, 135.5, 130.7, 129.1, 126.7, 109.3, 102.4, 70.3, 59.2; HRMS (EI) calcd. for $[\text{C}_{13}\text{H}_{12}\text{O}_3\text{Na}]$ ($\text{M}+\text{Na}$) $^+$ 239.06787, found 239.06817.



dimethyl 2-((2-oxo-4-phenyl-2H-pyran-6-yl)methyl)malonate (6i)

Phenylpropionic acid: 50 mg, 0.34 mmol; Dimethyl 2-(2-propynyl)malonate: 291 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 75 / 25; product mass: 38 mg; yield: 35%.

IR (neat, cm^{-1}): 2954, 1713, 1640, 1581, 1548, 1497, 1435, 1403, 1338, 1277, 1234, 1198, 1154, 1026, 929, 855, 767, 696, 583; ^1H NMR (300 MHz, CDCl_3) δ 7.57-7.55 (m, 2H), 7.49-7.47 (m, 3H), 6.41 (s, 1H), 6.39 (s, 1H), 3.95 (t, J = 6 Hz, 1H), 3.77 (s, 3H), 3.17 (d, J = 6 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 168.4, 162.5, 160.7, 155.0, 135.4, 130.7, 129.2, 126.6, 109.2, 104.5, 52.9, 49.0, 33.0; HRMS (EI) calcd. for $[\text{C}_{17}\text{H}_{16}\text{O}_6\text{Na}]$ ($\text{M}+\text{Na}$) $^+$ 339.08391, found 339.08515.

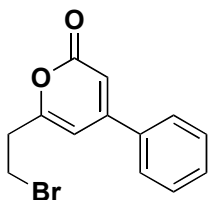


methyl 9-(2-oxo-4-phenyl-2H-pyran-6-yl)nonanoate (6j)

Phenylpropionic acid: 50 mg, 0.34 mmol; methyl undec-10-ynoate: 336 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 90 / 10; product mass: 59 mg; yield: 50%.

IR (neat, cm^{-1}): 2927, 2853, 1713, 1635, 1546, 1448, 1435, 1332, 1252, 1194, 1170, 851,

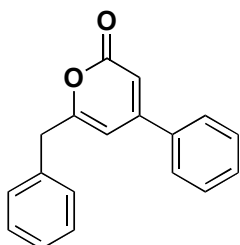
766; ^1H NMR (300 MHz, CDCl_3) δ 7.59-7.56 (m, 2H), 7.49-7.47 (m, 3H), 6.35 (s, 1H), 6.30 (s, 1H), 3.66 (s, 3H), 2.55 (t, $J = 6$ Hz, 2H), 2.30 (t, $J = 6$ Hz, 2H), 1.76-1.56 (m, 4H), 1.36-1.26 (m, 8); ^{13}C NMR (75 MHz, CDCl_3) δ 174.1, 165.8, 163.5, 155.4, 135.9, 130.5, 129.1, 126.6, 108.2, 102.7, 51.3, 34.0, 29.0, 28.9, 26.9, 24.8; HRMS (EI) calcd. for $[\text{C}_{21}\text{H}_{26}\text{O}_4\text{Na}]$ ($\text{M}+\text{Na}$) $^+$ 365.17233, found 365.17363.



6-(2-bromoethyl)-4-phenyl-2H-pyran-2-one (6k)

Phenylpropionic acid: 30 mg, 0.20 mmol; 4-bromo-1-butyne: 136 mg, 1.03 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.0 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 90 / 10; product mass: 37 mg; yield: 61%.

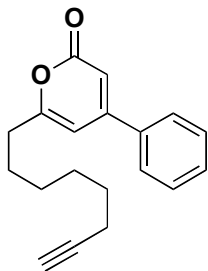
IR (neat, cm^{-1}): 3058, 1708, 1637, 1547, 1264, 1121, 851, 764, 692, 566, 538; ^1H NMR (300 MHz, CDCl_3) δ 7.54-7.65 (m, 2 H), 7.42-7.54 (m, 3 H), 6.43 (s, 2 H), 3.70 (t, $J = 6.6$ Hz, 2 H), 3.12 (t, $J = 6.6$ Hz, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 162.8, 161.0, 155.1, 135.6, 130.8, 129.2, 126.7, 109.4, 104.8, 37.2, 27.9; HRMS (EI) calcd. for $[\text{C}_{13}\text{H}_{12}\text{BrO}_2]$ ($\text{M}+\text{H}$) $^+$ 279.00152, found 279.00106.



6-benzyl-4-phenyl-2H-pyran-2-one (6l)

Phenylpropionic acid: 50 mg, 0.34 mmol; 3-phenyl-1-propyne: 199 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH_2Cl_2 (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 94 / 6; product mass: 85 mg; yield: 95%.

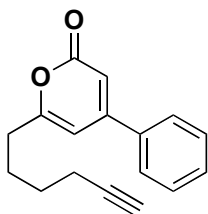
m.p.: 88.5-91.0 $^\circ\text{C}$; IR (neat, cm^{-1}): 3060, 3029, 2923, 1707, 1635, 1601, 1543, 1494, 1449, 1423, 1401, 1331, 1255, 1195, 1128, 1076, 991, 892, 852, 826, 763, 694; ^1H NMR (300 MHz, CDCl_3) δ 7.51-7.25 (m, 10H), 6.34 (s, 1H), 6.21 (s, 1H), 3.85 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 164.3, 163.0, 155.2, 135.7, 135.1, 130.5, 129.2, 129.0, 128.8, 127.3, 126.6, 108.5, 103.4, 40.2; HRMS (EI) calcd. for $[\text{C}_{18}\text{H}_{14}\text{O}_2\text{Na}]$ ($\text{M}+\text{Na}$) $^+$ 285.08860, found 285.08802.



6-(oct-7-yn-1-yl)-4-phenyl-2H-pyran-2-one (6m)

Phenylpropionic acid: 50 mg, 0.34 mmol; 1,9-decadiyne: 230 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 63 mg; yield: 66%.

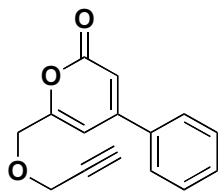
IR (neat, cm⁻¹): 3294, 2931, 2857, 1709, 1634, 1581, 1545, 1497, 1448, 1332, 1128, 990, 852, 766, 695, 630; ¹H NMR (300 MHz, CDCl₃) δ 7.59-7.56 (m, 2H), 7.49-7.48 (m, 3H), 6.35 (s, 1H), 6.30 (s, 1H), 2.56 (t, *J* = 6 Hz, 2H), 2.22-2.17 (m, 2H), 1.94 (m, 1H), 1.78-1.68 (m, 2H), 1.59-1.35 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 165.7, 163.4, 155.3, 135.8, 130.5, 129.1, 126.6, 108.2, 102.7, 84.2, 68.3, 33.9, 28.4, 28.2, 28.1, 26.8, 18.2; HRMS (EI) calcd. for [C₁₉H₂₀O₂Na] (M+Na)⁺ 303.13555, found 303.13596.



6-(hex-5-ynyl)-4-phenyl-2H-pyran-2-one (6n).

Phenylpropionic acid: 30 mg, 0.20 mmol; 1,7-octadiyne: 130 mg, 1.23 mmol, 6.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.0 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 30 mg; yield: 58%.

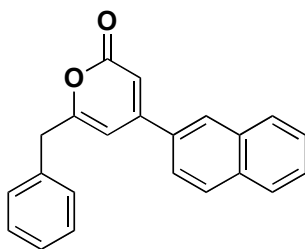
IR (neat, cm⁻¹): 3292, 2935, 1709, 1634, 1545, 1448, 1132, 852, 765, 694, 630; ¹H NMR (300 MHz, CDCl₃) δ 7.53-7.65 (m, 2 H), 7.38-7.53 (m, 3 H), 6.37 (s, 1 H), 6.33 (s, 1 H), 2.60 (t, *J* = 7.5 Hz, 2 H), 2.26 (td, *J* = 7.0, 2.6 Hz, 2 H), 1.99 (t, *J* = 2.6 Hz, 1 H), 1.80-1.93 (m, 2 H), 1.56-1.70 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 165.2, 163.3, 155.3, 135.8, 130.6, 129.1, 126.6, 108.4, 102.7, 83.7, 68.8, 33.5, 27.7, 25.9, 18.1; HRMS (EI) calcd. for [C₁₇H₁₇O₂] (M+H)⁺ 253.12231, found 253.12266.



4-phenyl-6-((prop-2-yn-1-yloxy)methyl)-2H-pyran-2-one (6o)

Phenylpropionic acid: 50 mg, 0.34 mmol; propargylether: 161 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 31 mg; yield: 38%.

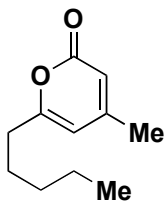
IR (neat, cm⁻¹): 3284, 3059, 2859, 1719, 1643, 1449, 1359, 1113, 1049, 907, 766, 696; ¹H NMR (300 MHz, CDCl₃) δ 7.61-7.59 (m, 2H), 7.50-7.48 (m, 3H), 6.62 (s, 1H), 6.43 (s, 1H), 4.45 (s, 2H), 4.32 (d, *J* = 3 Hz, 2H), 2.53 (t, *J* = 3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 162.3, 160.5, 154.9, 135.5, 130.7, 129.2, 126.7, 109.6, 103.0, 78.5, 75.7, 67.3, 58.4; HRMS (EI) calcd. for [C₁₅H₁₃O₃] (M+H)⁺ 241.08592, found 241.08590.



6-benzyl-4-(naphthalen-2-yl)-2H-pyran-2-one (6p)

3-(naphthalene-2-yl)propionic acid: 67 mg, 0.34 mmol; 3-phenyl-1-propyne: 199 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (3.0 mL, 0.1 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 85 mg; yield: 80%.

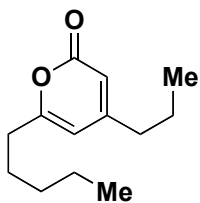
m.p.: 135.0-136.5 °C; IR (neat, cm⁻¹): 3089, 3059, 3031, 2925, 1700, 1632, 1546, 1497, 1312, 1131, 994, 907, 847, 820, 739, 701; ¹H NMR (300 MHz, CDCl₃) δ 7.97 (s, 1H), 7.88-7.82 (m, 3H), 7.54-7.50 (m, 3H), 7.38-7.24 (m, 5H), 6.46 (s, 1H), 6.35 (s, 1H), 3.87 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 164.22, 163.00, 155.05, 135.17, 134.05, 132.95, 132.80, 129.17, 128.98, 128.82, 128.61, 127.66, 127.51, 127.30, 126.90, 126.71, 123.40, 108.73, 103.41, 40.26; HRMS (EI) calcd. for [C₂₂H₁₆O₂Na] (M+Na)⁺ 335.10425, found 335.10485.



4-methyl-6-pentyl-2H-pyran-2-one (6q)

2-butynoic acid: 29 mg, 0.34 mmol; 1-heptyne: 164 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 93 / 7; product mass: 35 mg; yield: 57%.

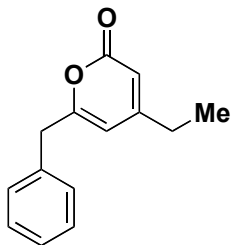
IR (neat, cm⁻¹): 2956, 2929, 2860, 1724, 1644, 1560, 1439, 1406, 1378, 1224, 1149, 1027, 957, 837; ¹H NMR (300 MHz, CDCl₃) δ 5.94 (s, 1H), 5.84 (s, 1H), 2.45 (t, *J* = 6 Hz, 2H), 2.12 (s, 3H), 1.68-1.63 (m, 2H), 1.34-1.25 (m, 4H), 0.90 (t, *J* = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 165.0, 163.3, 156.1, 110.5, 105.6, 33.6, 31.1, 26.5, 22.3, 21.4, 13.8; HRMS (EI) calcd. for [C₁₁H₁₇O₂] (M+H)⁺ 181.12231, found 181.12274.



6-pentyl-4-propyl-2H-pyran-2-one (6r)

2-hexynoic acid: 38 mg, 0.34 mmol; 1-heptyne: 164 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 41 mg; yield: 58%.

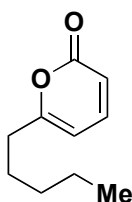
IR (neat, cm⁻¹): 2958, 2931, 2872, 1724, 1642, 1559, 1465, 838; ¹H NMR (300 MHz, CDCl₃) δ 5.93 (s, 1H), 5.84 (s, 1H), 2.45 (t, *J* = 9 Hz, 2H), 2.35 (t, *J* = 6 Hz, 2H), 1.68-1.54 (m, 4H), 1.34-1.32 (m, 4H), 0.96 (t, *J* = 9 Hz, 3H), 0.90 (t, *J* = 3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 165.1, 163.5, 160.1, 109.8, 104.8, 37.2, 33.6, 31.1, 26.5, 22.3, 21.4, 13.8, 13.5; HRMS (EI) calcd. for [C₁₃H₂₀O₂Na] (M+Na)⁺ 231.13555, found 231.13539.



6-benzyl-4-ethyl-2H-pyran-2-one (6s)

2-pentynoic acid: 34 mg, 0.34 mmol; 3-phenyl-1-propyne: 199 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 57 mg; yield: 77%.

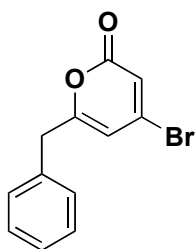
IR (neat, cm⁻¹): 3030, 2969, 2923, 1716, 1639, 1556, 1495, 1454, 1412, 1221, 1131, 1072, 986, 850, 758, 702; ¹H NMR (300 MHz, CDCl₃) δ 7.36-7.25 (m, 5H), 5.95 (s, 1H), 5.76 (s, 1H), 3.77 (s, 2H), 2.36 (q, *J* = 6 Hz, 2H), 1.13 (t, *J* = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 163.4, 163.1, 161.4, 135.2, 129.2, 128.7, 127.2, 109.2, 105.3, 39.9, 28.2, 12.1; HRMS (EI) calcd. for [C₁₄H₁₄O₂Na] (M+Na)⁺ 237.08860, found 237.08809.



6-pentyl-2H-pyran-2-one (6t)

propionic acid: 48 mg, 0.68 mmol; heptyne: 328 mg, 3.41 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (3.0 mL, 0.2 M); reaction temperature: 50 °C; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 74 mg; yield: 65%.

IR (neat, cm⁻¹): 2956, 2931, 2871, 1725, 1701, 1629, 1557, 1459, 1213, 1089, 906, 805; ¹H NMR (300 MHz, CDCl₃) δ 7.27 (dd, *J* = 9, 6 Hz, 1H), 6.15 (d, *J* = 9 Hz, 1H), 5.99 (d, *J* = 6 Hz, 1H), 2.48 (d, *J* = 6 Hz, 2H), 1.69-1.64 (m, 2H), 1.35-1.30 (m, 4H), 0.90 (t, *J* = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.7, 162.8, 143.7, 112.9, 102.5, 33.7, 31.0, 26.5, 22.2, 13.8; HRMS (EI) calcd. for [C₁₀H₁₅O₂] (M+H)⁺ 167.10666, found 167.10717.

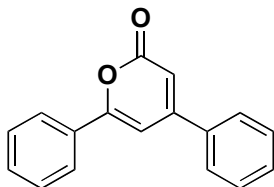


6-benzyl-4-bromo-2H-pyran-2-one (6u)

3-bromopropionic acid: 51 mg, 0.34 mmol; 3-phenyl-1-propyne: 199 mg, 1.71 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.2 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 70 mg; yield: 77%.

IR (neat, cm⁻¹): 3088, 3029, 1724, 1613, 1539, 1495, 1454, 1422, 1379, 1305, 1196, 1123, 989, 879, 834, 801, 752, 700; ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.24 (m, 5H), 6.45 (s, 1H), 6.04 (s, 1H), 3.78 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 164.3, 160.3, 141.0, 134.1,

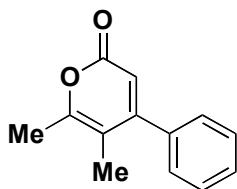
129.2, 129.0, 127.6, 115.2, 108.3, 39.8; HRMS (EI) calcd. for $[C_{12}H_{10}BrO_2]$ $(M+H)^+$ 264.98587, found 264.98595.



4,6-diphenyl-2H-pyran-2-one (6v)

Phenylpropionic acid: 27 mg, 0.18 mmol; phenylacetylene: 120 mg, 1.2 mmol, 6.3 equiv; reaction solvent and concentration: CH_2Cl_2 (1.8 mL, 0.1 M); reaction temperature: 60 °C; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 92 / 8; product mass: 10 mg; yield: 22% (note: phenyl propionic acid was slowly added to the reaction mixture over 2 h via a syringe pump).

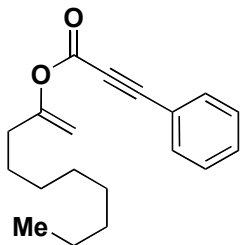
IR (neat, cm^{-1}): 3059, 2922, 2360, 1705, 1628, 1536, 1495, 849, 762, 688; 1H NMR (300 MHz, $CDCl_3$) δ 7.85-7.98 (2 H, m), 7.63-7.72 (2 H, m), 7.42-7.58 (6 H, m), 6.99 (1 H, s), 6.50 (1 H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5, 160.4, 155.6, 136.0, 131.6, 130.9, 130.7, 129.2, 129.0, 126.7, 125.8, 109.3, 101.4; HRMS (EI) calcd. for $[C_{17}H_{13}O_2]$ $(M+H)^+$ 249.09101, found 249.09394.



5,6-dimethyl-4-phenyl-2H-pyran-2-one (6w)

Phenylpropionic acid: 30 mg, 0.20 mmol; 2-butyne: 111 mg, 2.05 mmol, 10.0 equiv; reaction solvent and concentration: toluene (1.0 mL, 0.2 M); reaction temperature: 60 °C; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 95 / 5; product mass: 8 mg; yield: 20%.

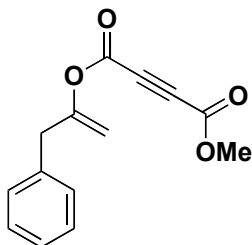
IR (neat, cm^{-1}): 2926, 1712, 1530, 1445, 1395, 1207, 899, 856, 770, 701; 1H NMR (300 MHz, $CDCl_3$) δ 7.26-7.42 (m, 3 H), 7.09-7.24 (m, 2 H), 6.02 (s, 1 H), 2.24 (s, 3 H), 1.78 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 160.2, 158.3, 137.4, 128.9, 128.5, 127.6, 112.3, 110.2, 18.1, 13.9; HRMS (EI) calcd. for $[C_{13}H_{13}O_2]$ $(M+H)^+$ 201.09101, found 201.09122.



dec-1-en-2-yl 3-phenylpropiolate (**5a**)

In a 4 mL vial with a threaded cap, phenylpropionic acid (30 mg, 0.20 mmol, 1.0 equiv), dec-1-yne (142 mg, 1.03 mmol, 5.0 equiv), and [(Ph₃P)AuCl] (5.1 mg, 0.01 mmol, 0.05 equiv) were dissolved in 1.0 mL anhydrous toluene. AgPF₆ (2.6 mg, 0.01 mmol, 0.05 equiv) was added to the solution in one portion. The reaction mixture was stirred in the sealed vial under air at room temperature for 12 h. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (hexane / EtOAc = 95 / 5) to give 17 mg **5a** in 29% yield and 21 mg **6a** in 35% yield.

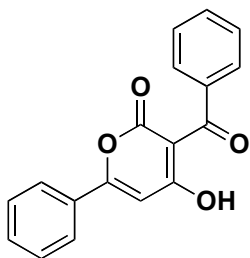
¹H NMR (300 MHz, CDCl₃) δ = 7.54-7.68 (m, 2 H), 7.47 (d, *J* = 7.2 Hz, 1 H), 7.33-7.44 (m, 2 H), 4.84 (d, *J* = 12.4 Hz, 2 H), 2.28 (t, *J* = 7.5 Hz, 2 H), 1.44-1.60 (m, 2 H), 1.37 (br. s., 2 H), 1.28 (br. s., 11 H), 0.75-0.94 (m, 4 H); ¹³C NMR (75 MHz, CDCl₃) δ 156.3, 152.0, 133.1, 130.8, 128.6, 119.5, 101.9, 87.4, 80.5, 33.2, 31.9, 29.3, 29.2, 29.0, 26.4, 22.7, 14.1.



6-benzyl-4-bromo-2H-pyran-2-one (**5b**)

4-methoxy-4-oxobut-2-ynoic acid: 25 mg, 0.20 mmol; 3-phenyl-1-propyne: 117 mg, 1.01 mmol, 5.0 equiv; reaction solvent and concentration: CH₂Cl₂ (1.5 mL, 0.18 M); reaction temperature: room temperature; reaction time: 12 h; eluent for flash chromatography on silica gel: Hexane / EtOAc = 70 / 30; product mass: 29 mg; yield: 59%.

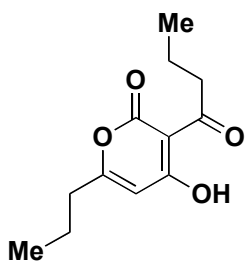
IR (neat, cm⁻¹): 3030, 2957, 1726, 1670, 1496, 1435, 1264, 1210, 1154, 1031, 889, 746, 700; ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.21 (m, 5H), 4.97 (s, 1H), 4.78 (s, 1H), 3.84 (s, 3H), 3.55 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 154.7, 152.0, 149.5, 135.7, 129.1, 128.6, 127.05, 104.3, 75.4, 74.4, 53.4, 39.4; HRMS (EI) calcd. for [C₁₄H₁₂O₄Na] (M+Na)⁺ 267.06278, found 267.06300.



3-benzoyl-4-hydroxy-6-phenyl-2H-pyran-2-one (7a)

In a 4 mL vial with a threaded cap, phenylpropionic acid (30 mg, 0.20 mmol, 1.0 equiv), and 5 mol% [(Ph₃P)AuCl] (5.1 mg, 0.01 mmol, 0.05 equiv) were dissolved in dry toluene. AgSbF₆ (5 mol%) (3.5 mg, 0.01 mmol, 0.05 equiv) was added to the solution at room temperature. The reaction mixture was stirred in the sealed vial under air at room temperature for 12 h. The solvent was evaporated to dryness and the residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 60 / 40) to give 24 mg product **7a** in 81% yield.

m.p.: 161.0-162.0 °C; IR (neat, cm⁻¹): 3097, 2920, 1717, 1623, 1537, 1224, 1056, 929, 853, 685, 590, 503; ¹H NMR (500 MHz, CDCl₃) δ 15.97 (s, 1 H), 7.92-7.96 (m, 2 H), 7.69-7.75 (m, 2 H), 7.51-7.62 (m, 5 H), 7.48 (t, *J* = 7.6 Hz, 2 H), 6.69 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 200.3, 180.9, 166.1, 160.1, 138.1, 132.7, 132.3, 130.2, 129.2, 128.3, 127.8, 126.6, 99.6, 98.1; HRMS (EI) calcd. for [C₁₈H₁₃O₄] (M+H)⁺ 293.08084, found 293.08189.

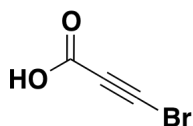


3-butyryl-4-hydroxy-6-propyl-2H-pyran-2-one (7b)

In a 4 mL vial with a threaded cap, 2-hexynoic acid (45 mg, 0.40 mmol, 1.0 equiv), and 5 mol% [(Ph₃P)AuCl] (9.9 mg, 0.02 mmol, 0.05 equiv) were dissolved in dry toluene. AgSbF₆ (5 mol%) (6.9 mg, 0.02 mmol, 0.05 equiv) was added to the solution at room temperature. The reaction mixture was stirred in the sealed vial under air at room temperature for 12 h. The solvent was evaporated to dryness and the residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 60 / 40) to give 25 mg product **7b** in 56% yield.

IR (neat, cm⁻¹): 2964, 2875, 1727, 1635, 1550, 1445, 987, 983, 824, 705, 502; ¹H NMR (500 MHz, CDCl₃) δ 16.86 (s, 1 H), 5.94 (s, 1 H), 3.07 (t, *J* = 7.3 Hz, 2 H), 2.48 (t, *J* = 7.6 Hz, 3 H), 1.64-1.80 (m, 5 H), 1.01 (td, *J* = 7.4, 2.2 Hz, 8 H); ¹³C NMR (75 MHz, CDCl₃) δ 207.8, 181.3, 172.3, 161.1, 100.9, 99.7, 43.5, 36.2, 19.8, 17.4, 13.8, 13.4;

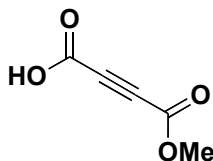
HRMS (EI) calcd. for [C₁₂H₁₇O₄] (M+H)⁺ 225.11214, found 225.11319.



3-Bromopropiolic acid (3c)

The title compound was prepared according to the reaction condition for the preparation of ethyl 3-bromopropiolate.¹ The NMR of product is consistent with reported data.² In a 25 mL vial with a threaded cap, propiolic acid (619 mg, 8.84 mmol, 1.0 equiv) was dissolved in 17.7 mL acetone. To the stirred solution at room temperature was added silver nitrate (150 mg, 0.88 mmol, 0.1 equiv). After 5 min, N-bromosuccinimide (1888 mg, 10.61 mmol, 1.2 equiv) was added at once. Stirring was continued overnight at room temperature. The reaction mixture was filtered through a short column of Celite, which is rinsed with EtOAc. After careful rotary evaporation of organic solvent, the residue was allowed to stay at room temperature for 24 h, during which most succinimide crashed out. The oil residue was further purified by flash chromatography on silica gel (AcOH / CH₂Cl₂ / MeOH = 2 / 90 / 8) to give 301 mg product in 23% yield.

¹H NMR (300 MHz, CDCl₃) δ 9.80-10.40 (brs, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 156.1, 72.1, 56.0.



4-methoxy-4-oxobut-2-ynoic acid (3d)

The title compound was prepared following a previous report.³ In a flame-dried round bottle flask under nitrogen equipped with a stir bar and a septum, methyl propiolate (0.84 mL, 10 mmol) was dissolved in 25 mL dry THF and cooled to -78°C. *n*-Butyl lithium solution (2.5 M in hexanes, 4.0 mL, 10 mmol) was added dropwise via syringe. The reaction was continued under -78°C for 1 hour followed by the addition of dry ice powder. The reaction was allowed to warm to room temperature, and subsequently stirred for 1 hour. The solvent was removed in vacuo. Water (25 mL) and hexane (25 mL) were added. The layers were separated, and the aqueous layer was acidified by HCl (2 M, aq.) to pH~2. The aqueous layer was then back-extracted with ethyl acetate (25 mL × 3). The organic layers were combined and washed with brine (25 mL). The upper layer was dried

¹ Poulsen, T. B.; Bernardi, L.; Alemán, J.; Overgaard, J.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *129*, 441-449.

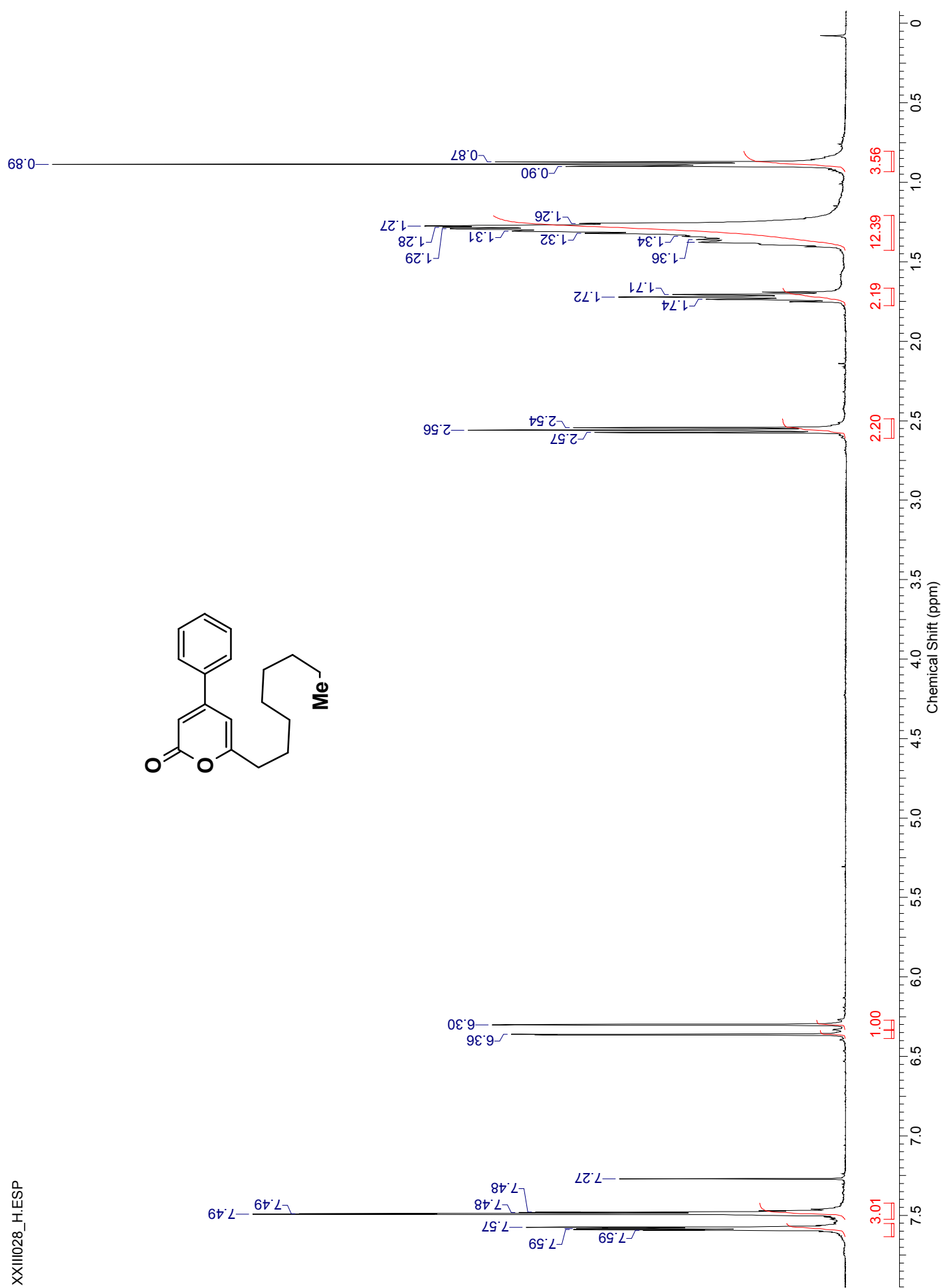
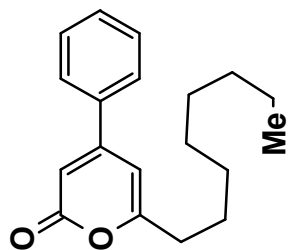
² Andersen, N. G.; Maddaford, S. P.; Keay, B. A. *J. Org. Chem.* **1996**, *61*, 2885-2887.

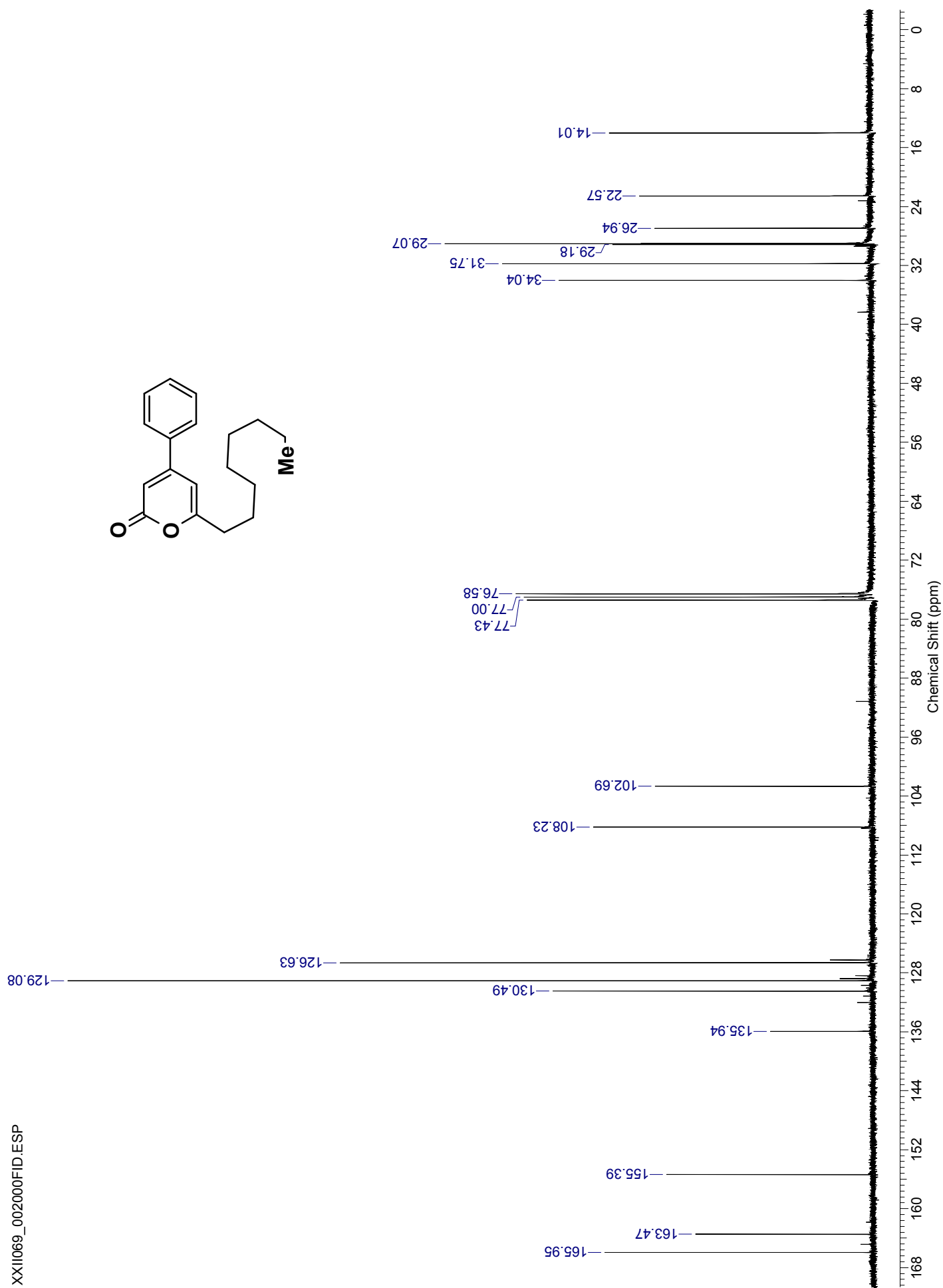
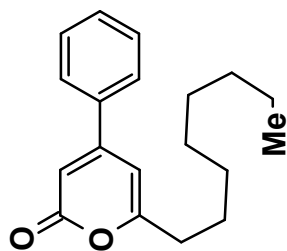
³ Zheng, H.; McDonald, R.; Hall, G. D. *Chem. Eur. J.* **2010**, *16*, 5454-5460.

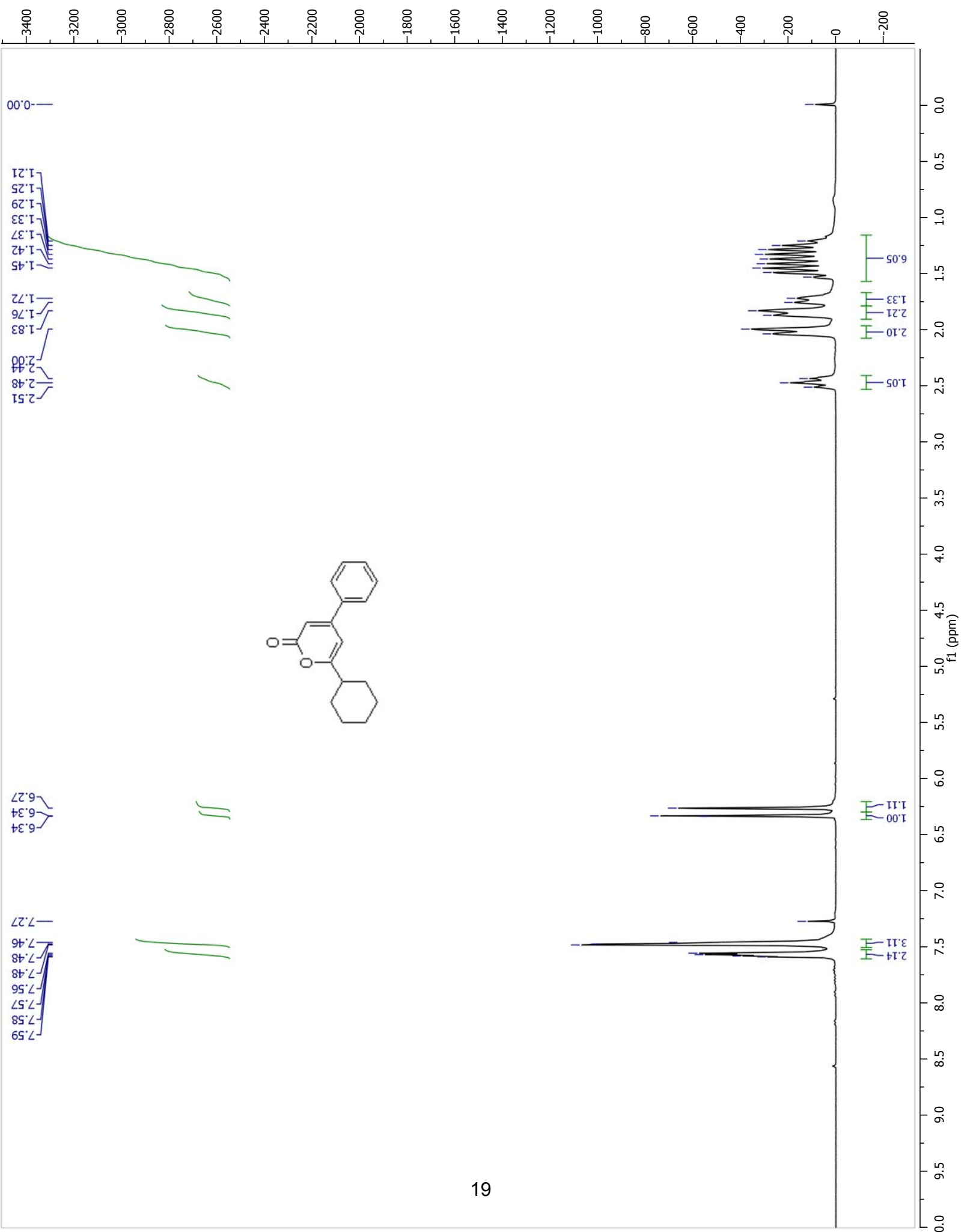
over Na₂SO₄ and filtered. The crude product was added to a silica gel column and was eluted with 10% MeOH in CH₂Cl₂ (0.5% AcOH) to give 650 mg desired product in 51% yield as a light brown oil.

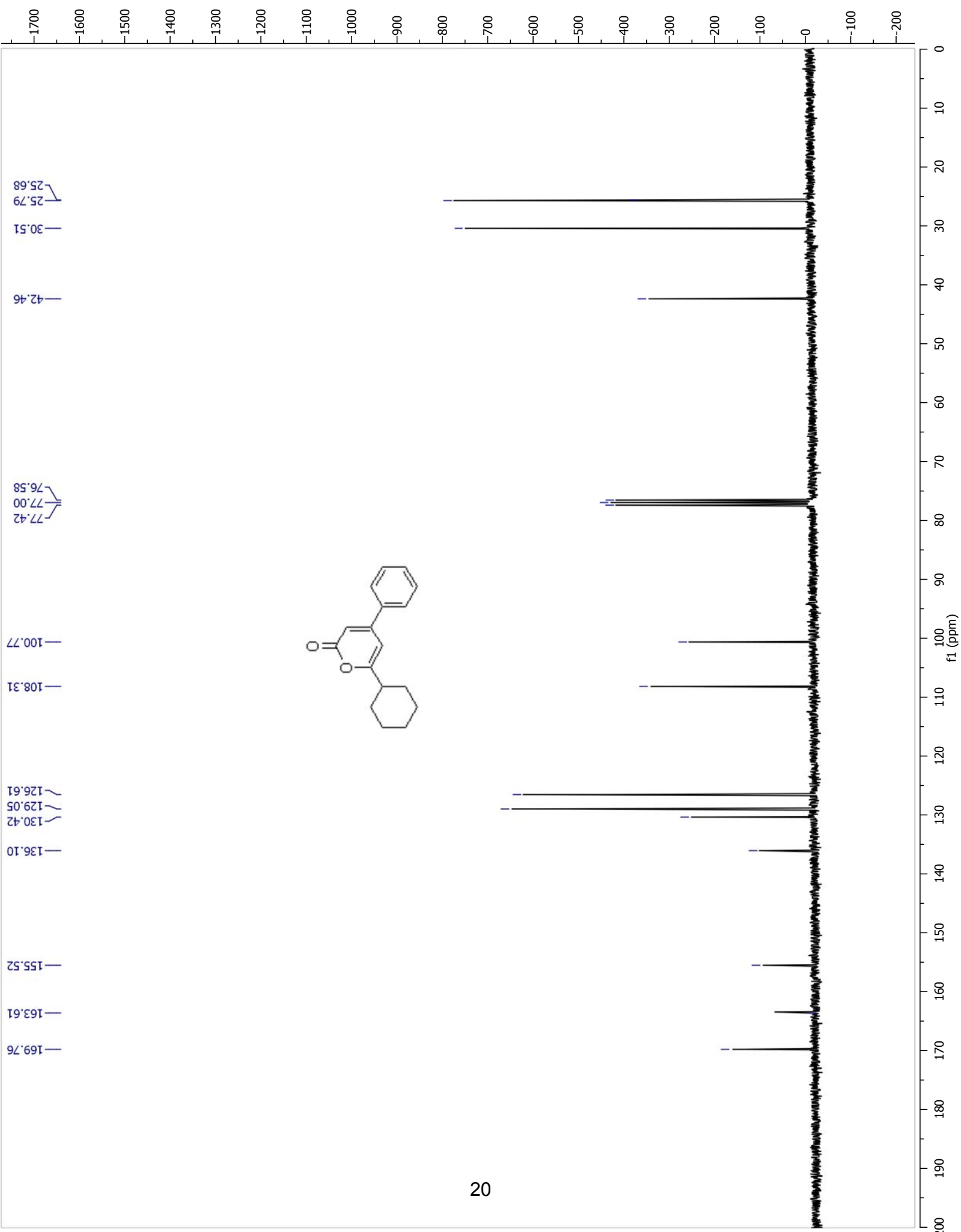
IR (neat, cm⁻¹): 2961, 1698, 1436, 1247, 1024, 910, 756, 635; ¹H NMR (300 MHz, CDCl₃) δ 10.15 (s, brs, 1 H), 3.89 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 155.1, 152.1, 76.5, 74.1, 53.7.

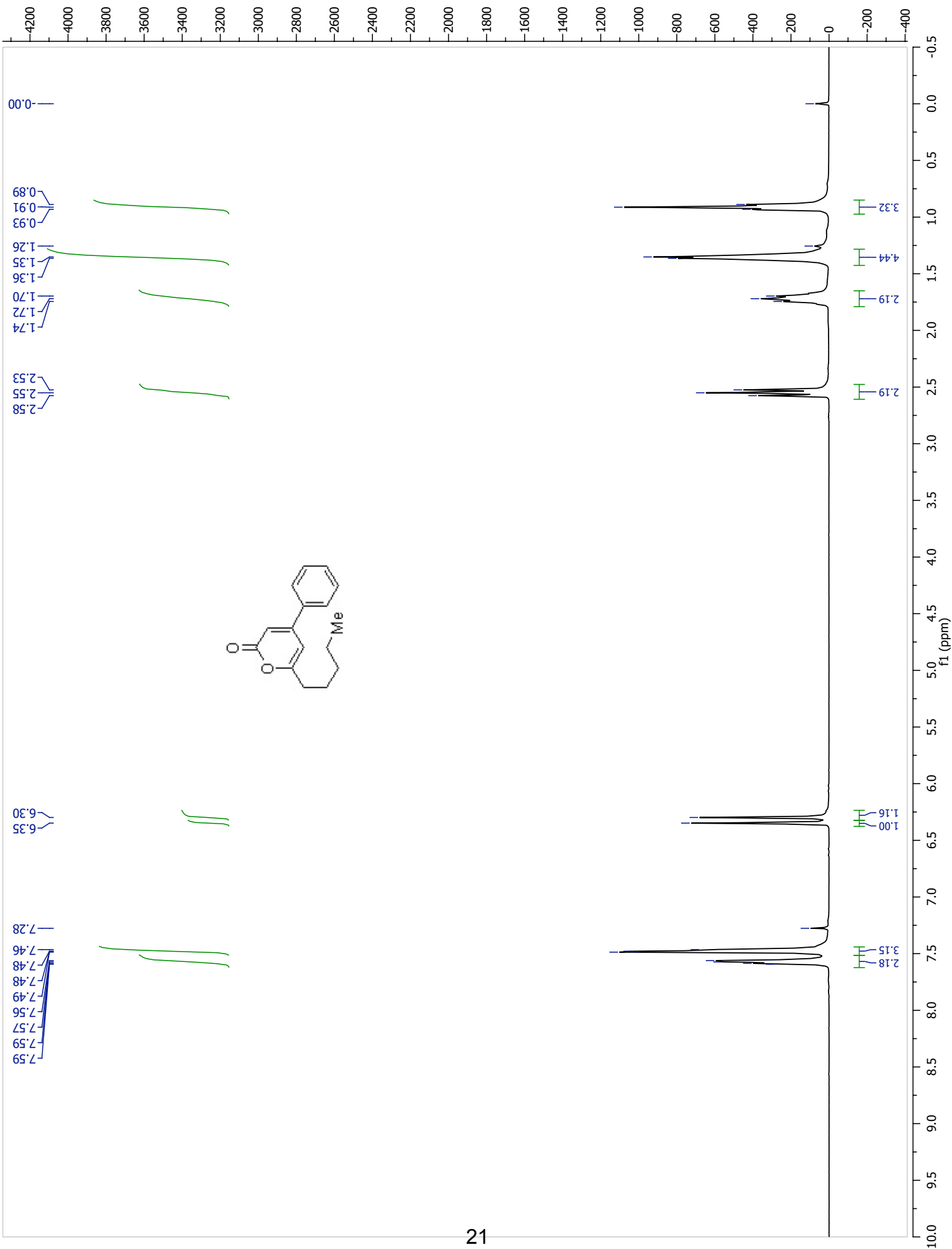
***III.* ¹H NMR and ¹³C NMR spectra of all the compounds.**

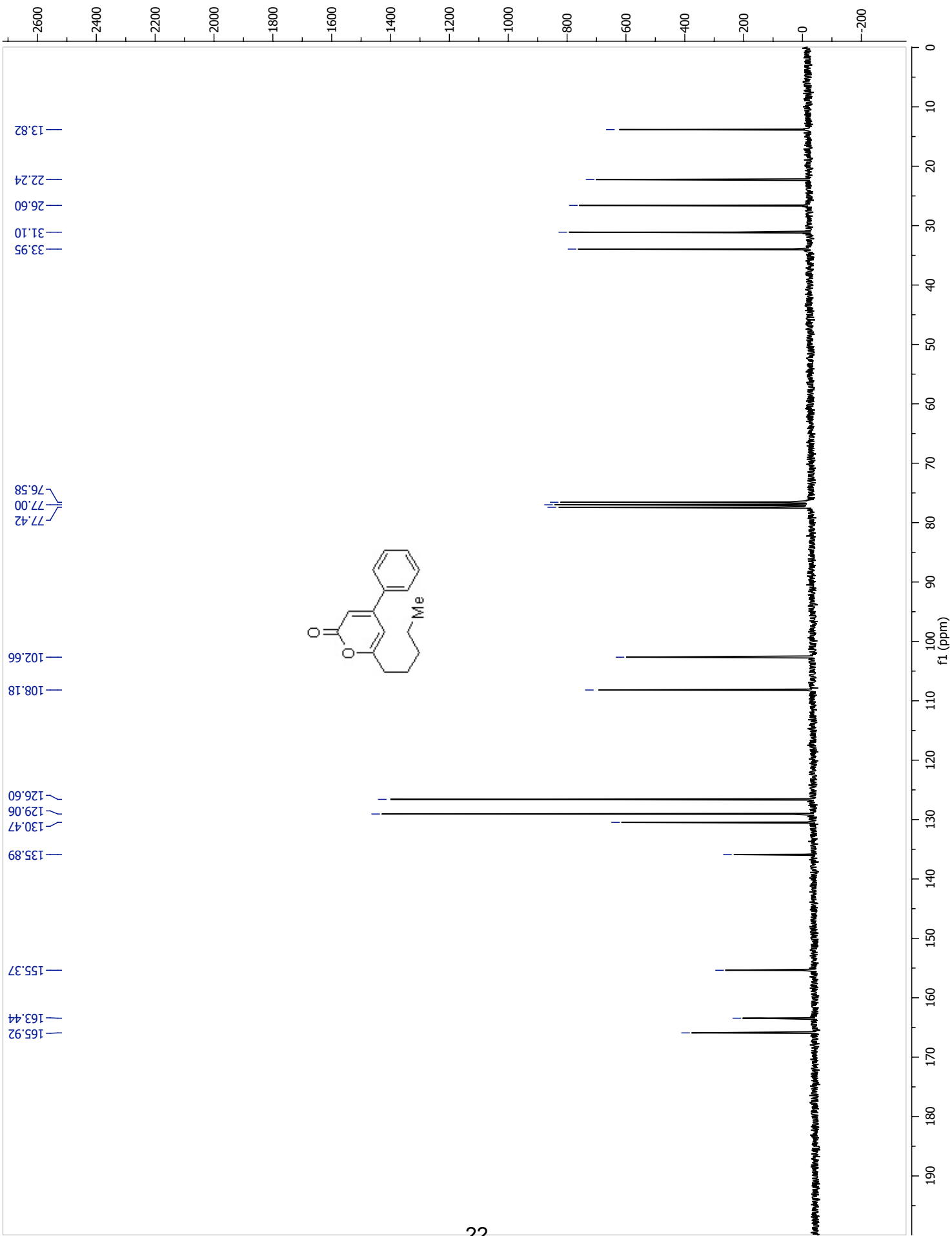


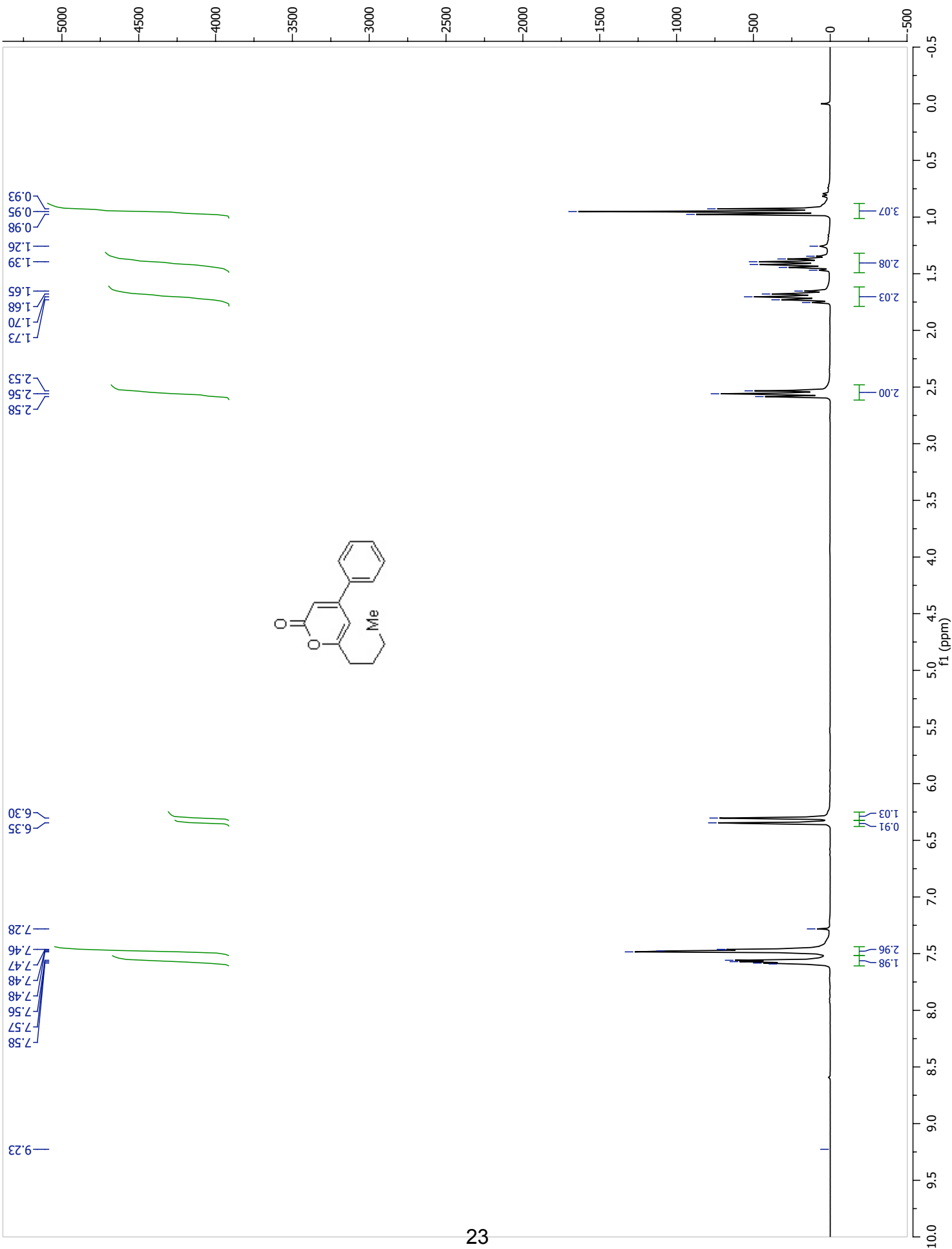


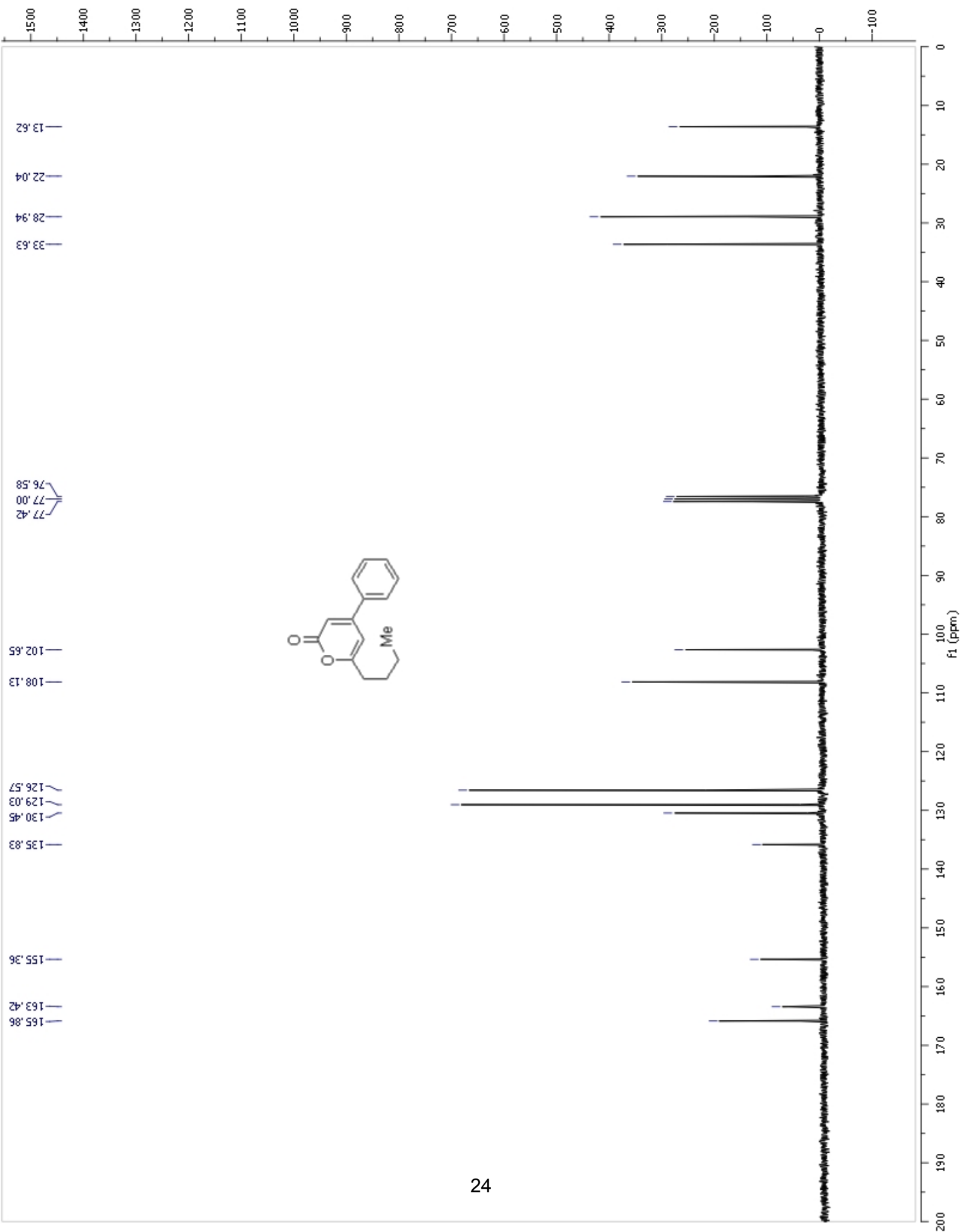


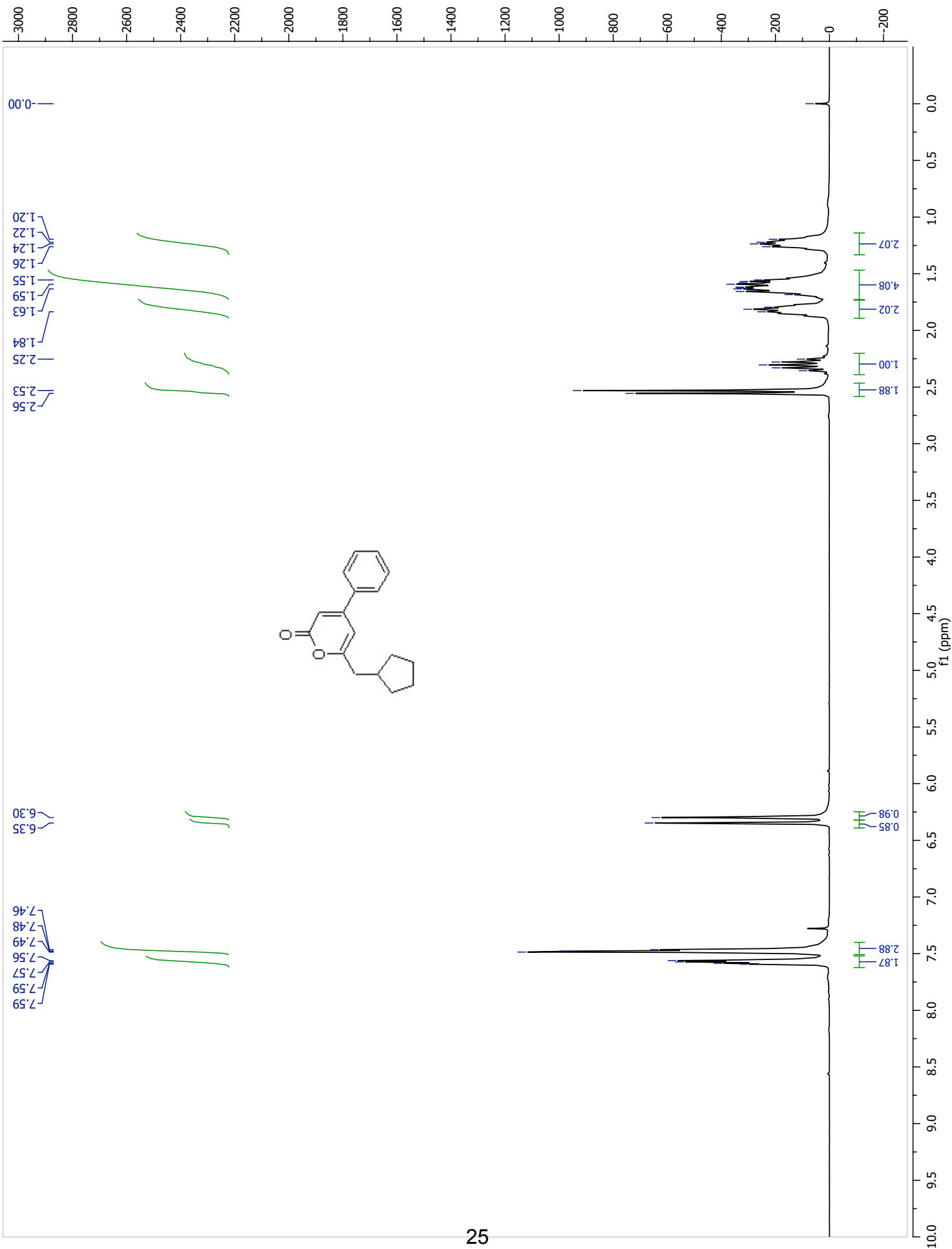


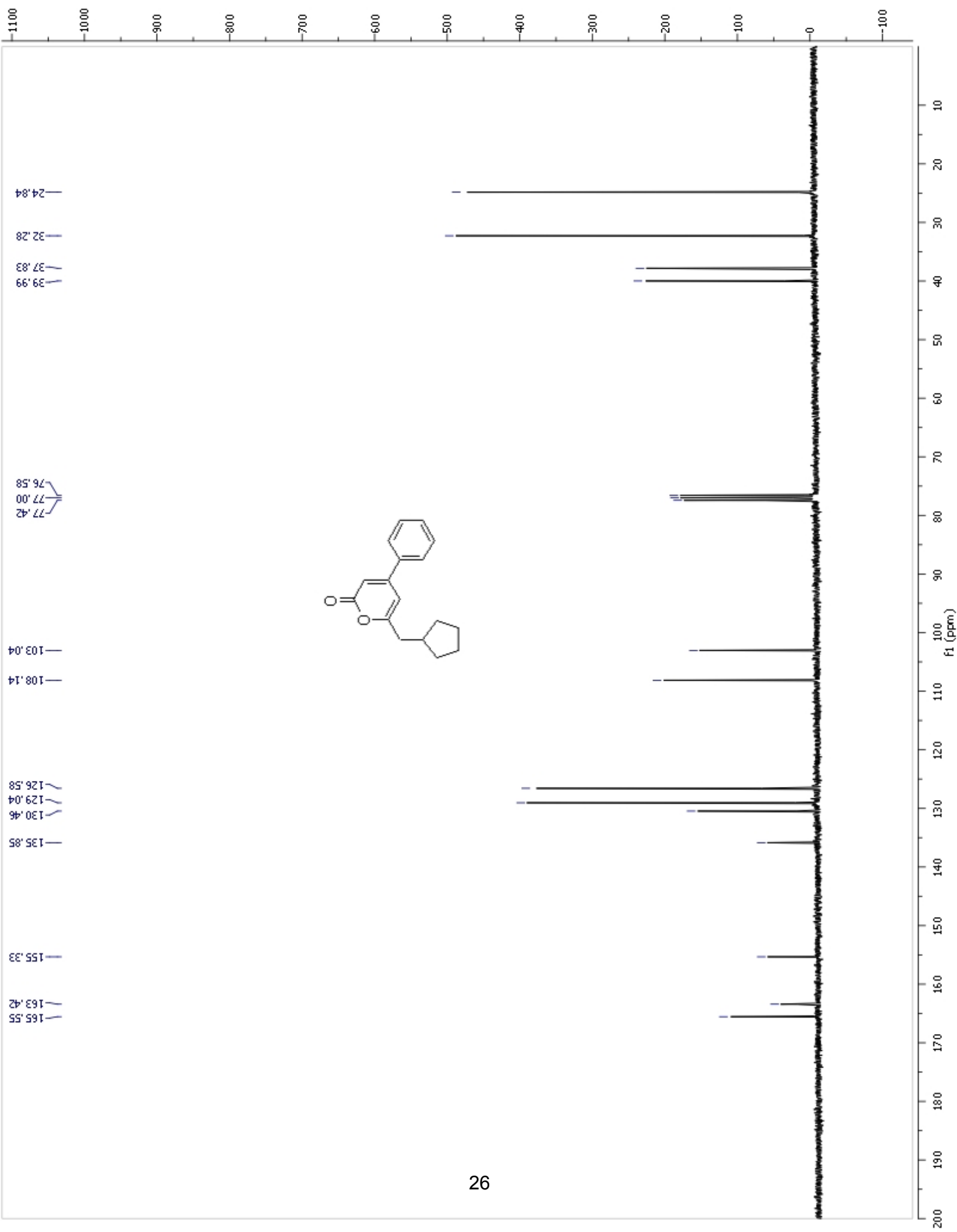


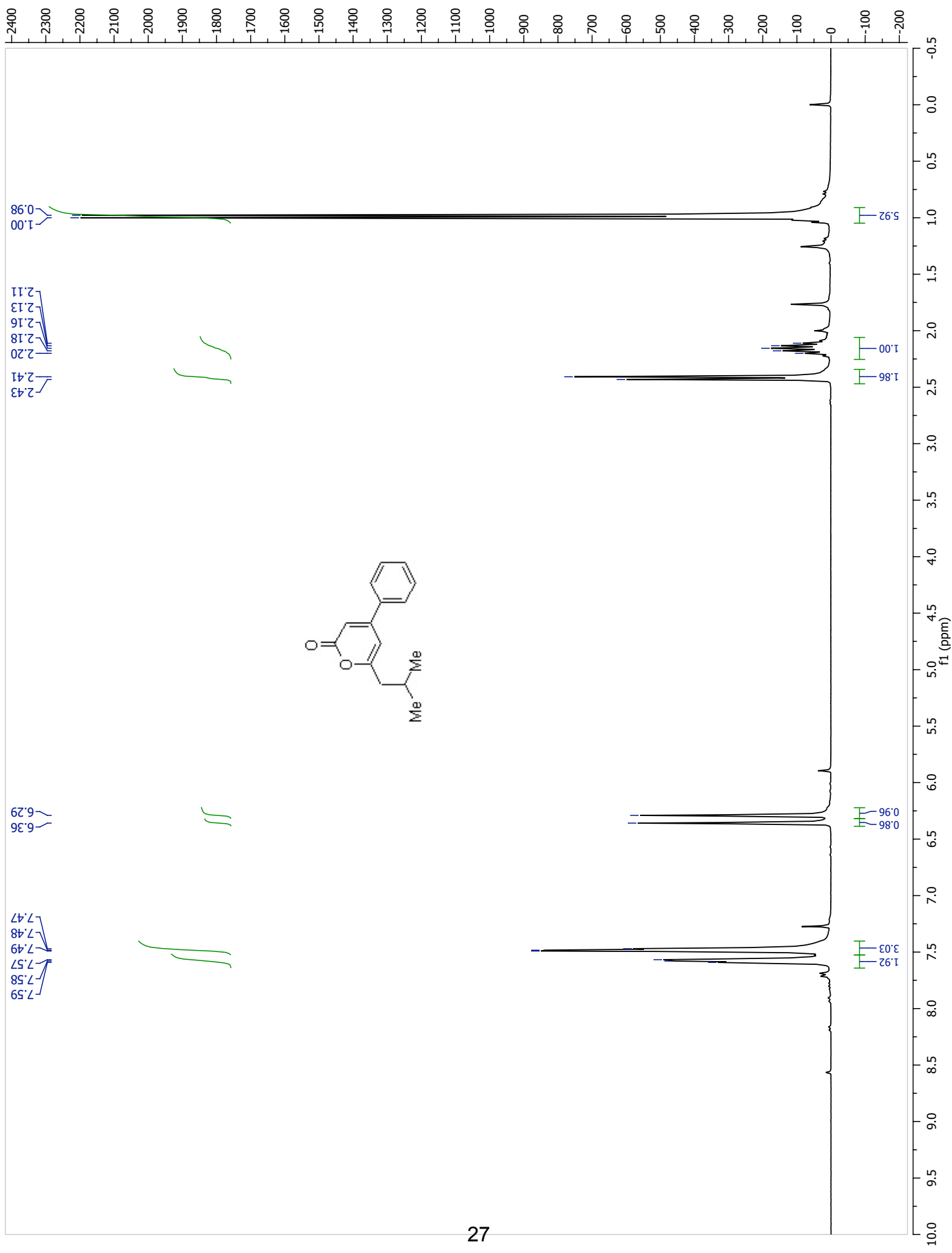


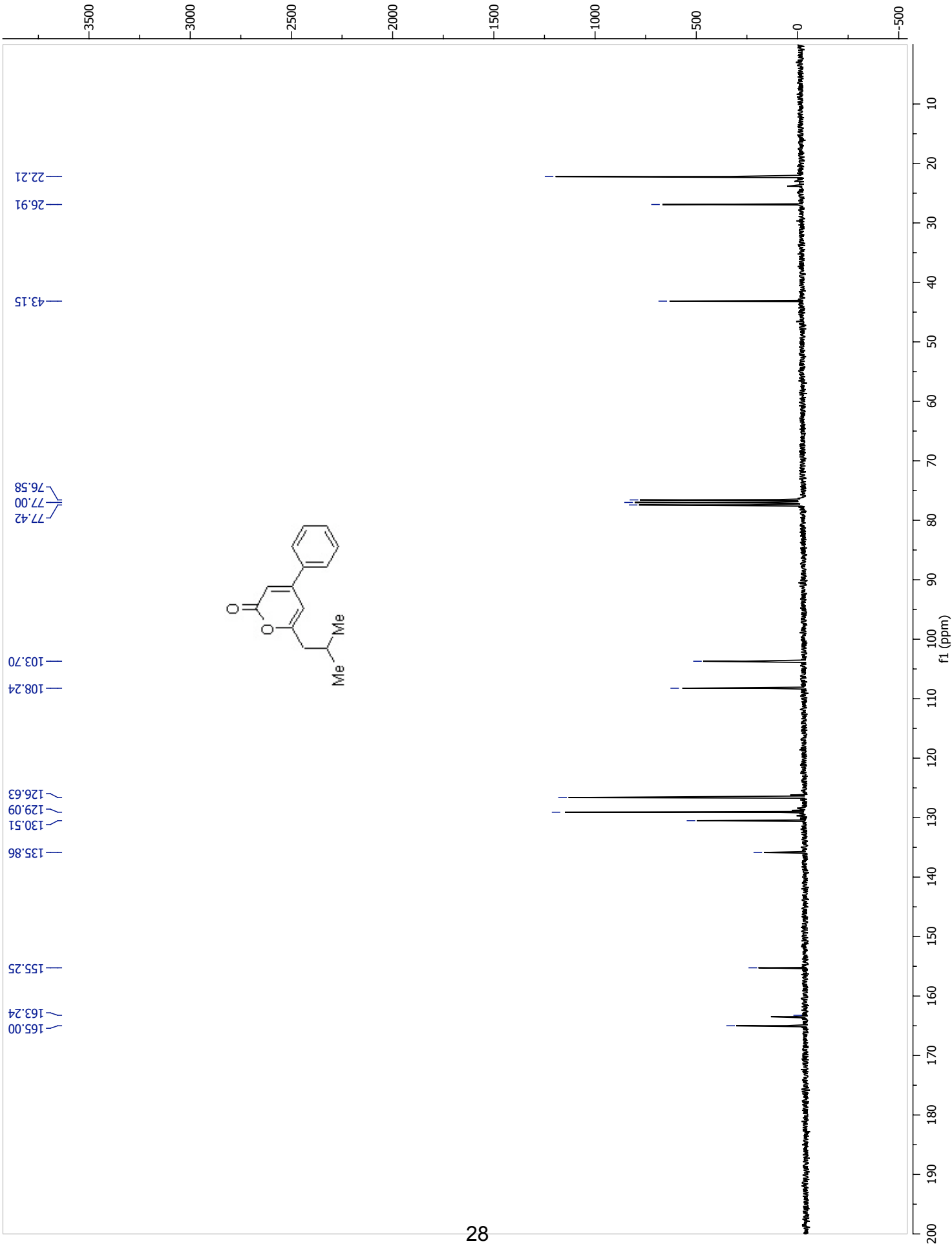


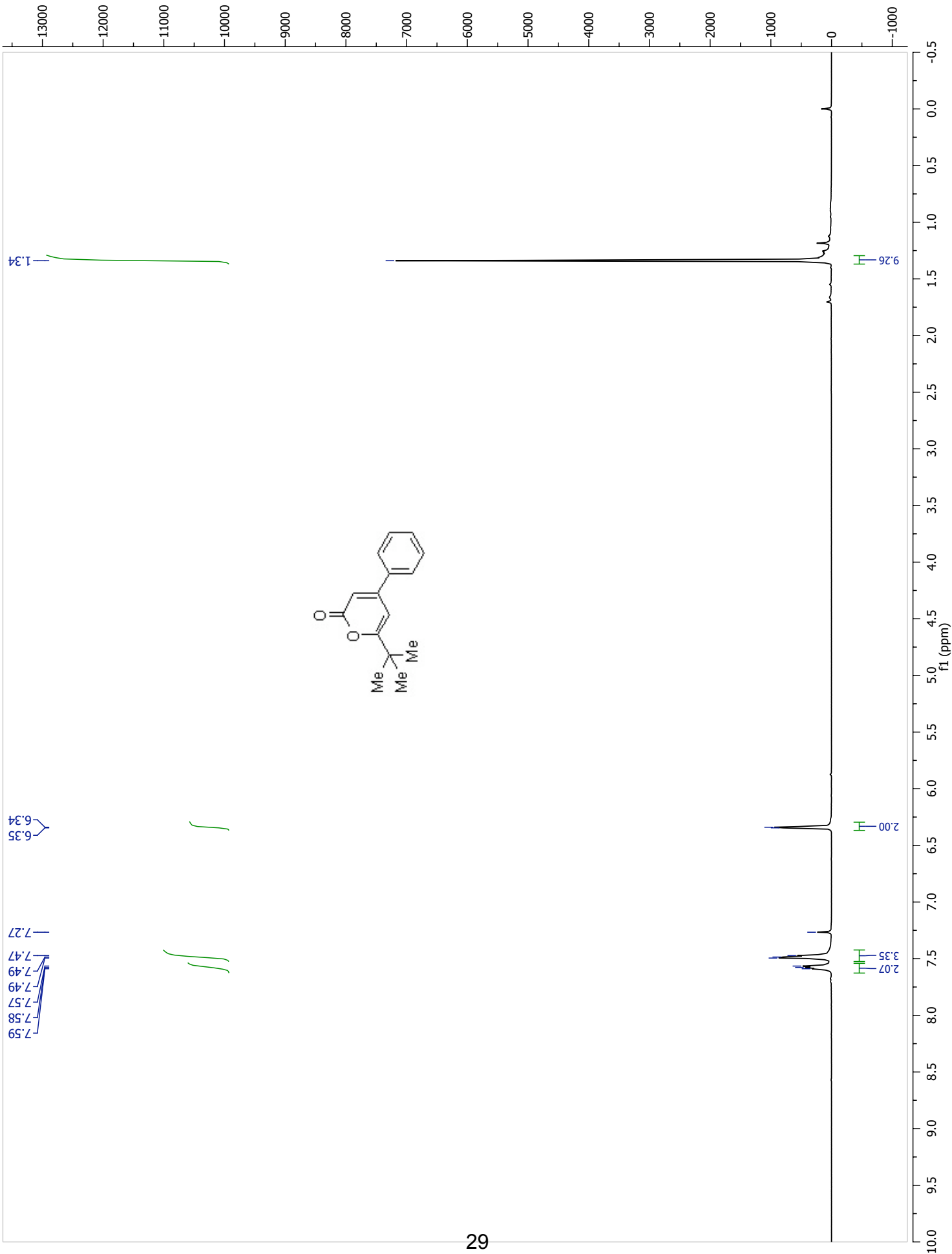


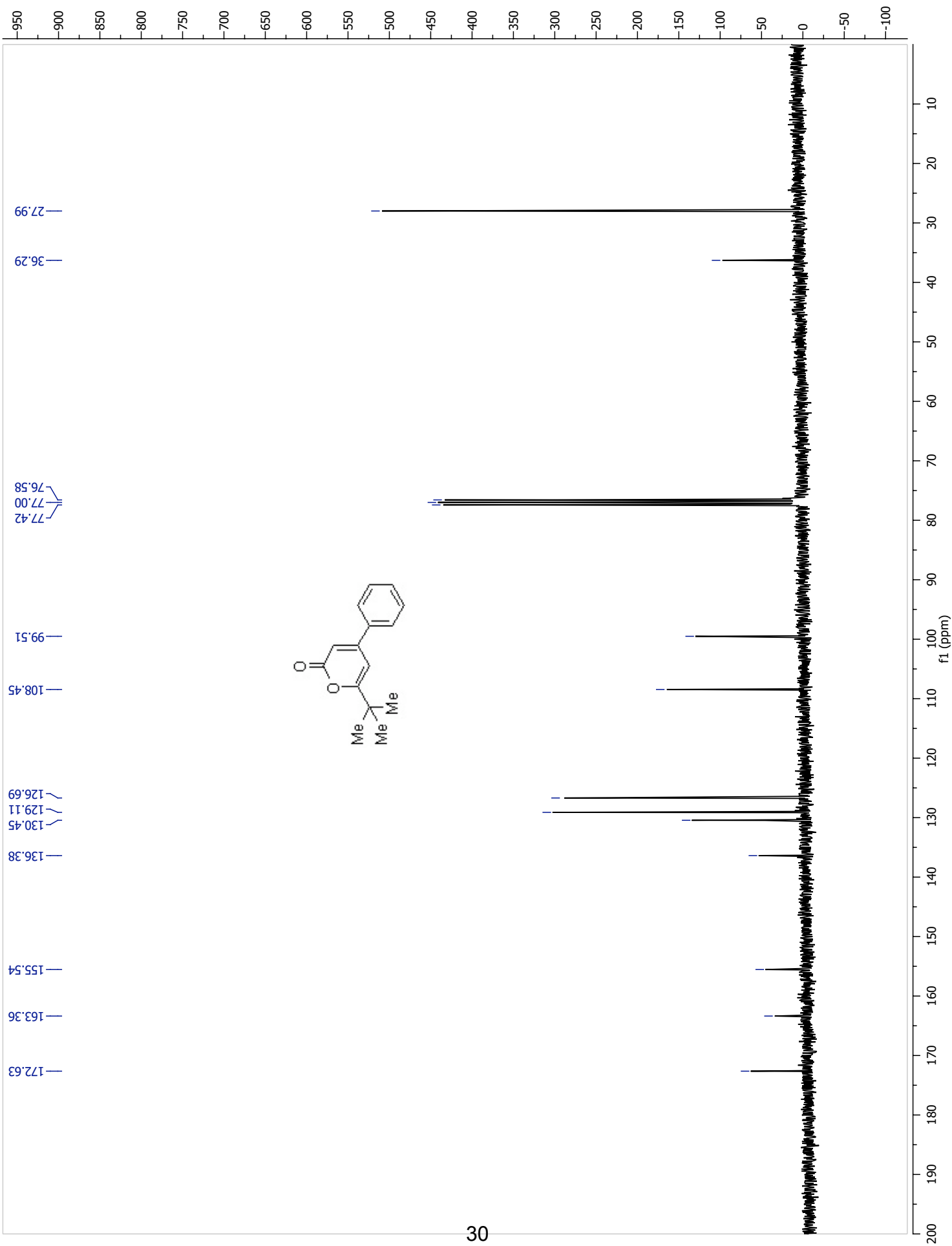


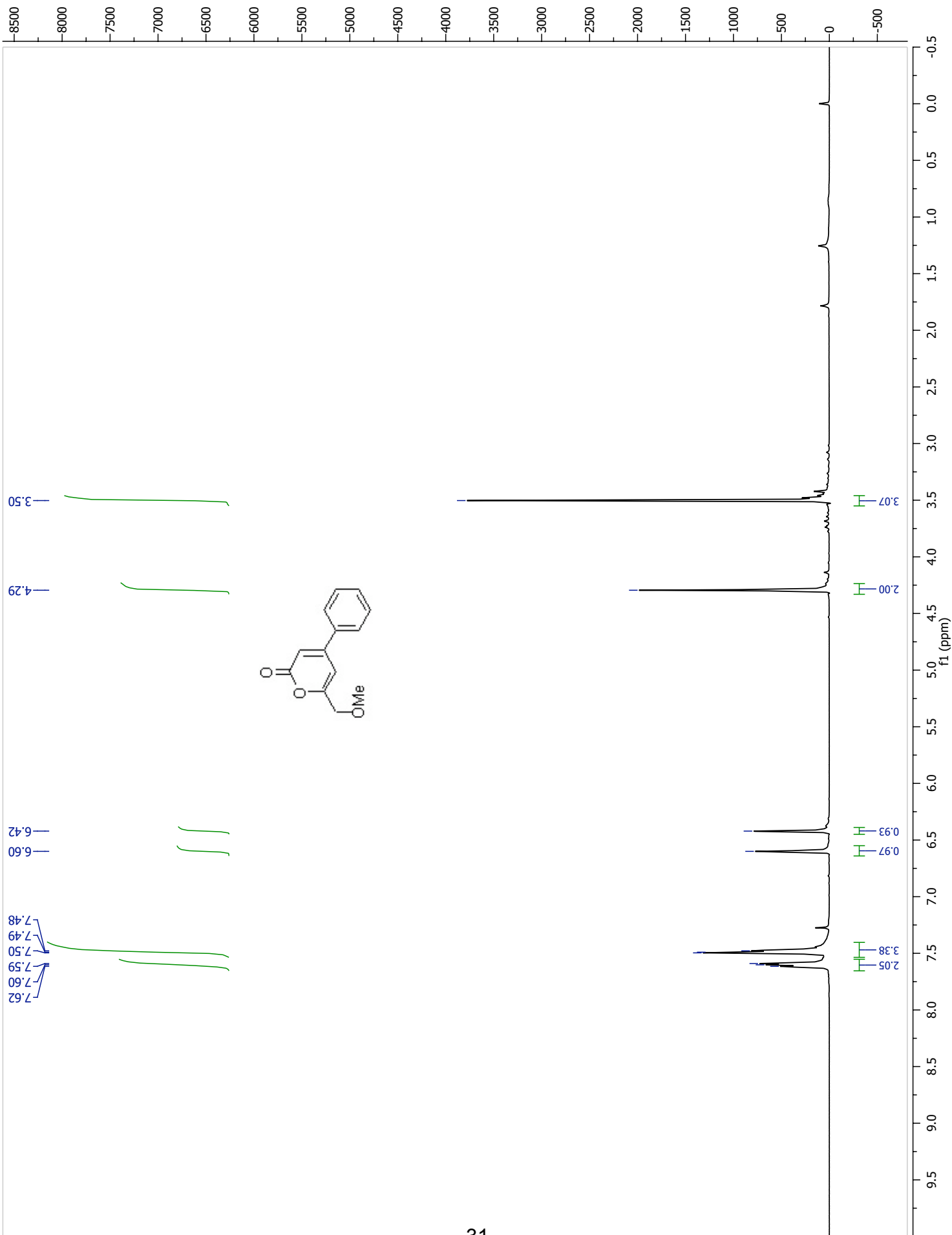


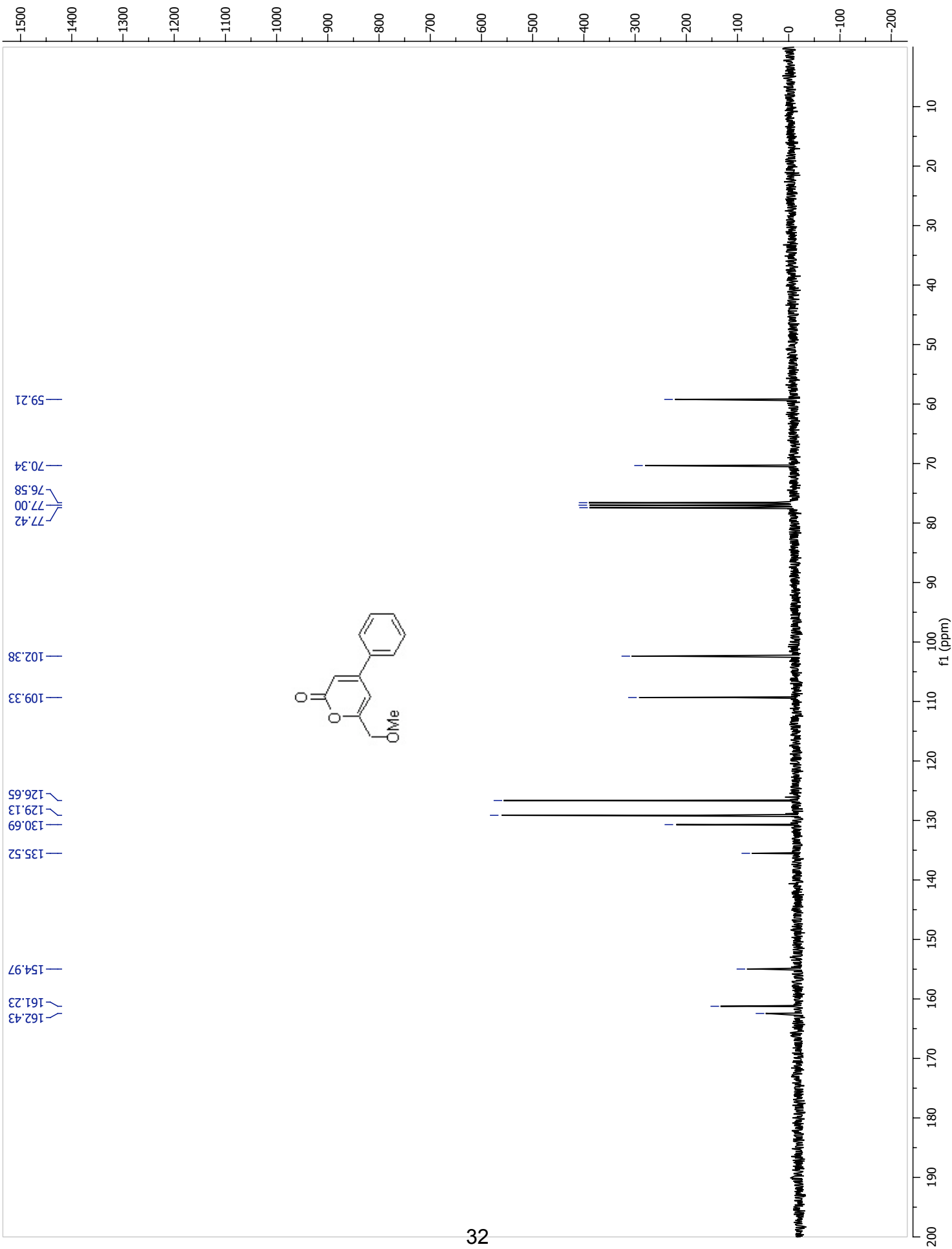


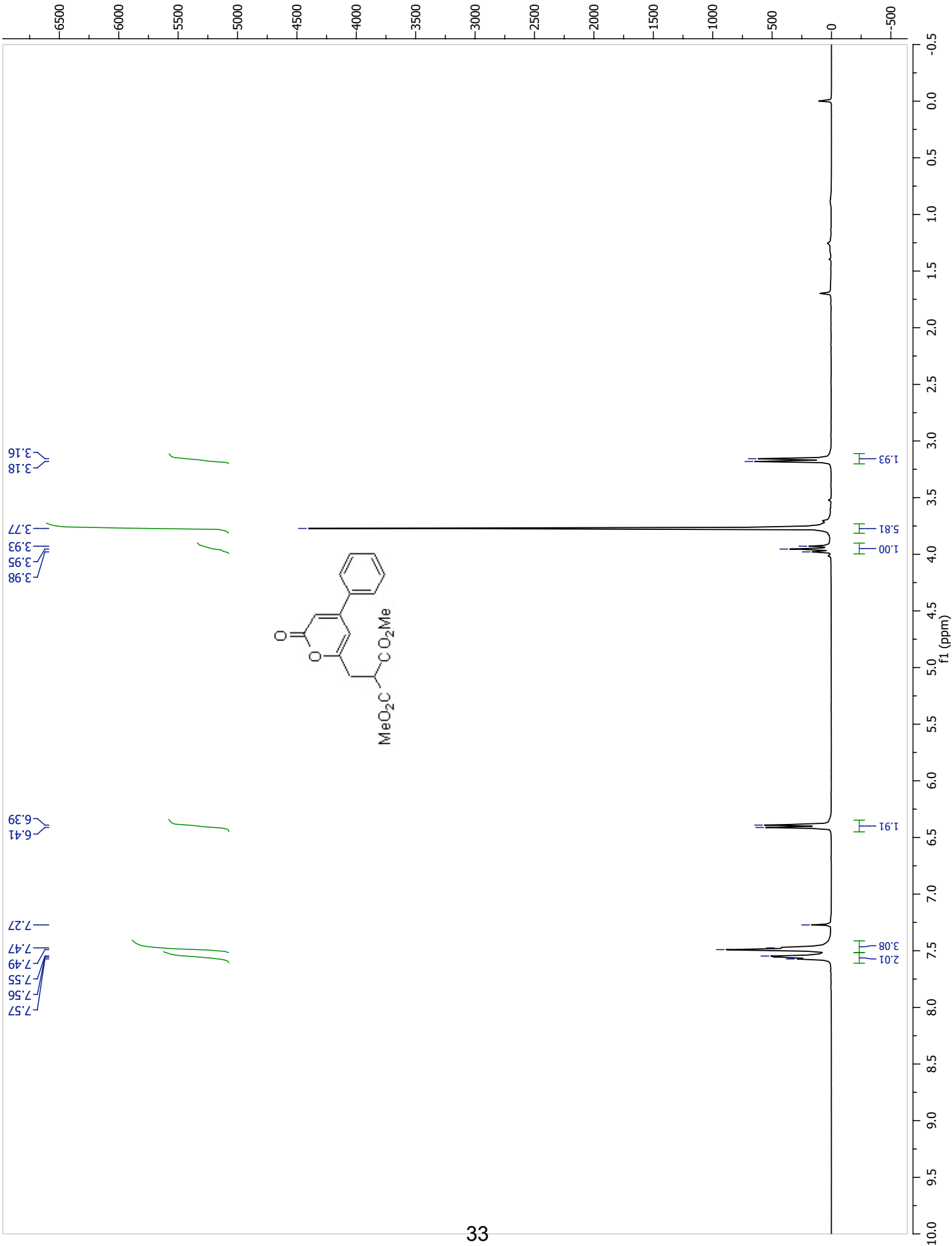


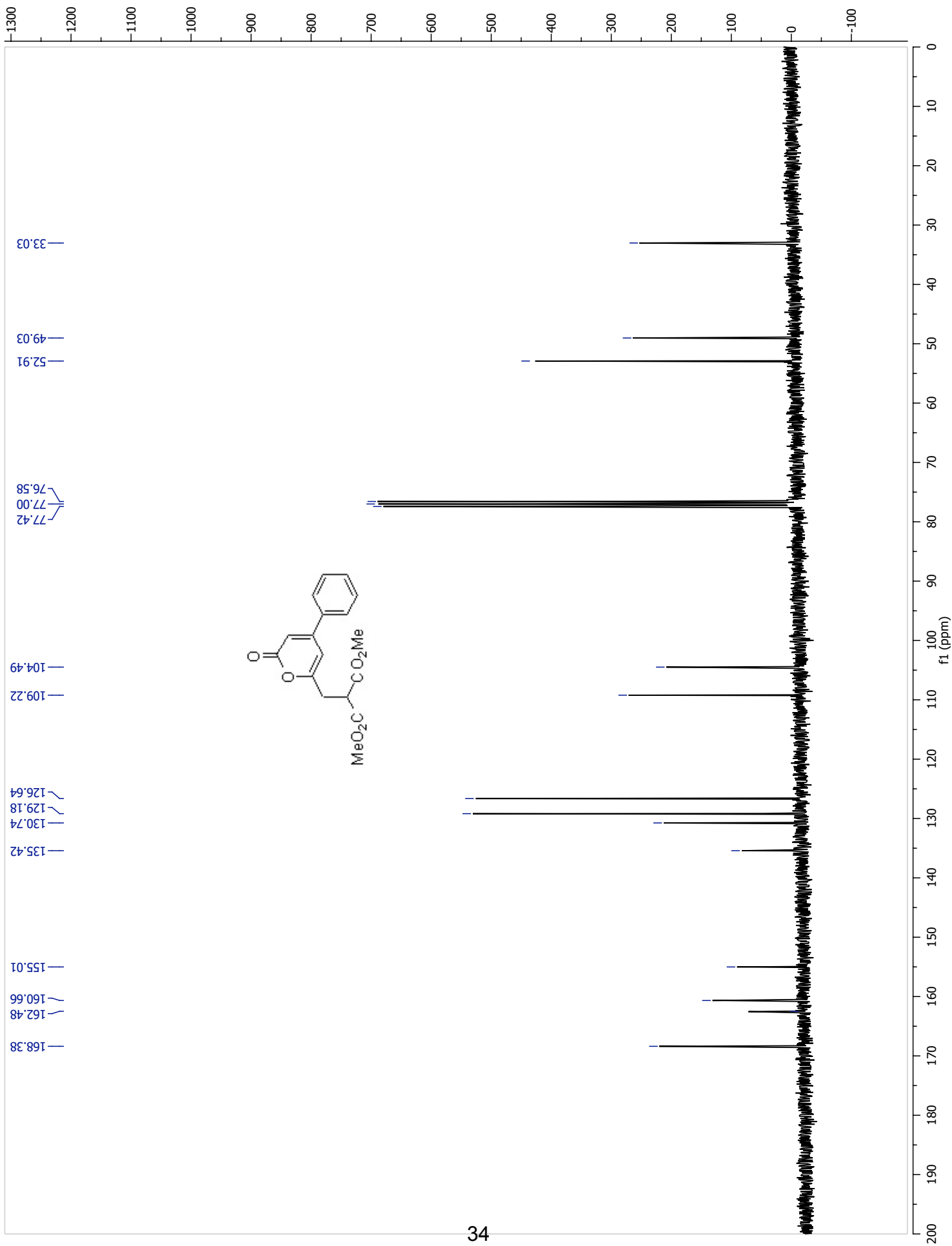


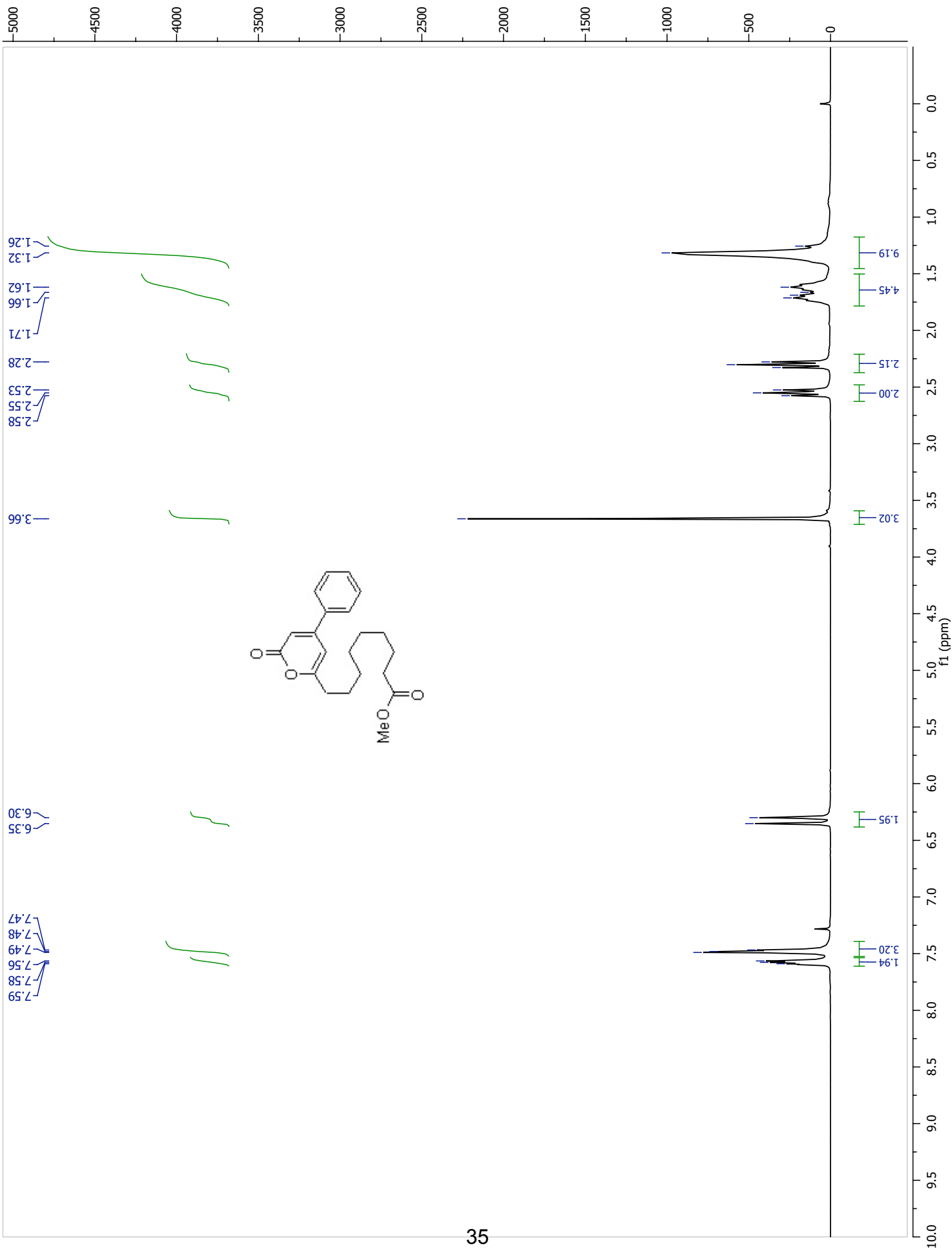


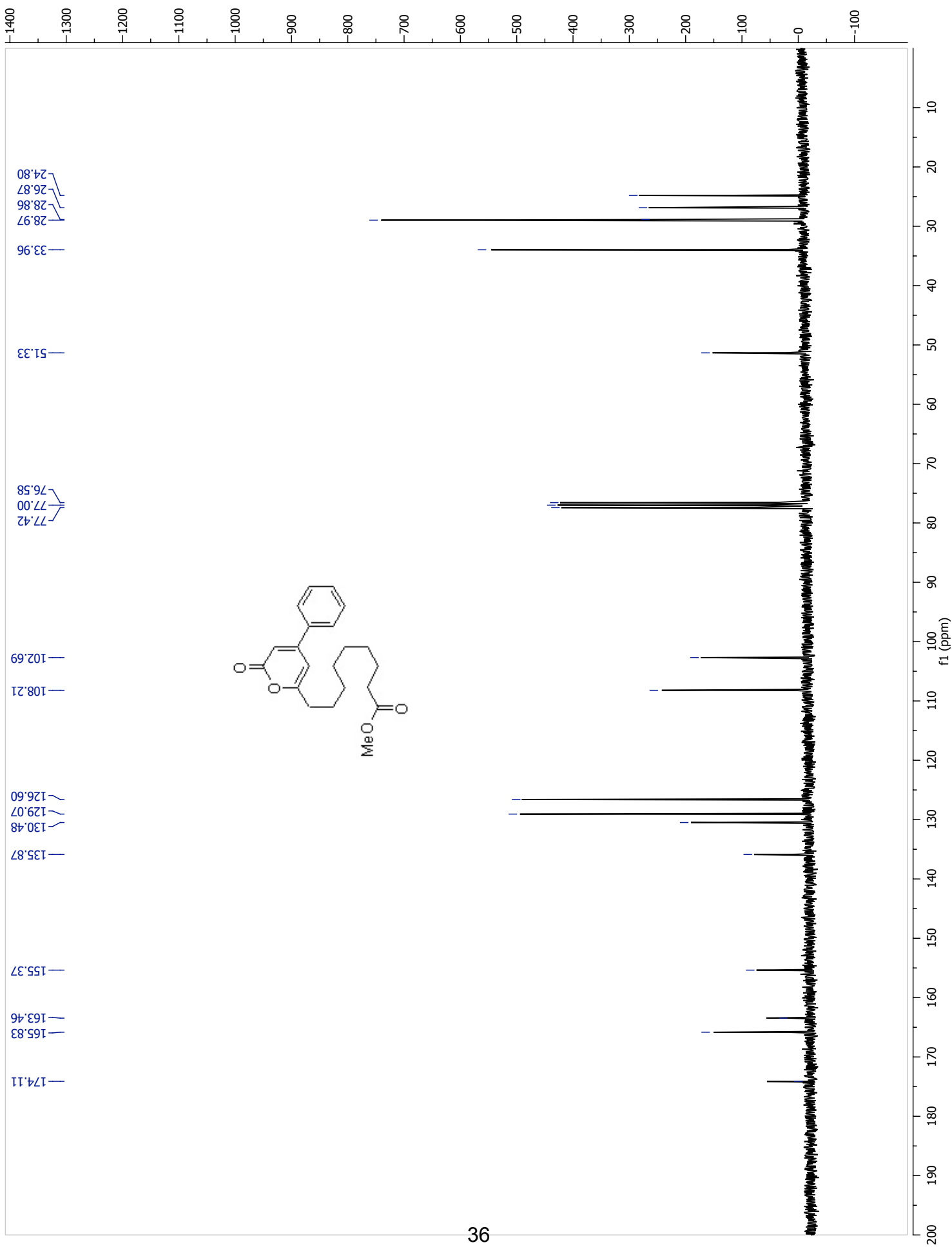


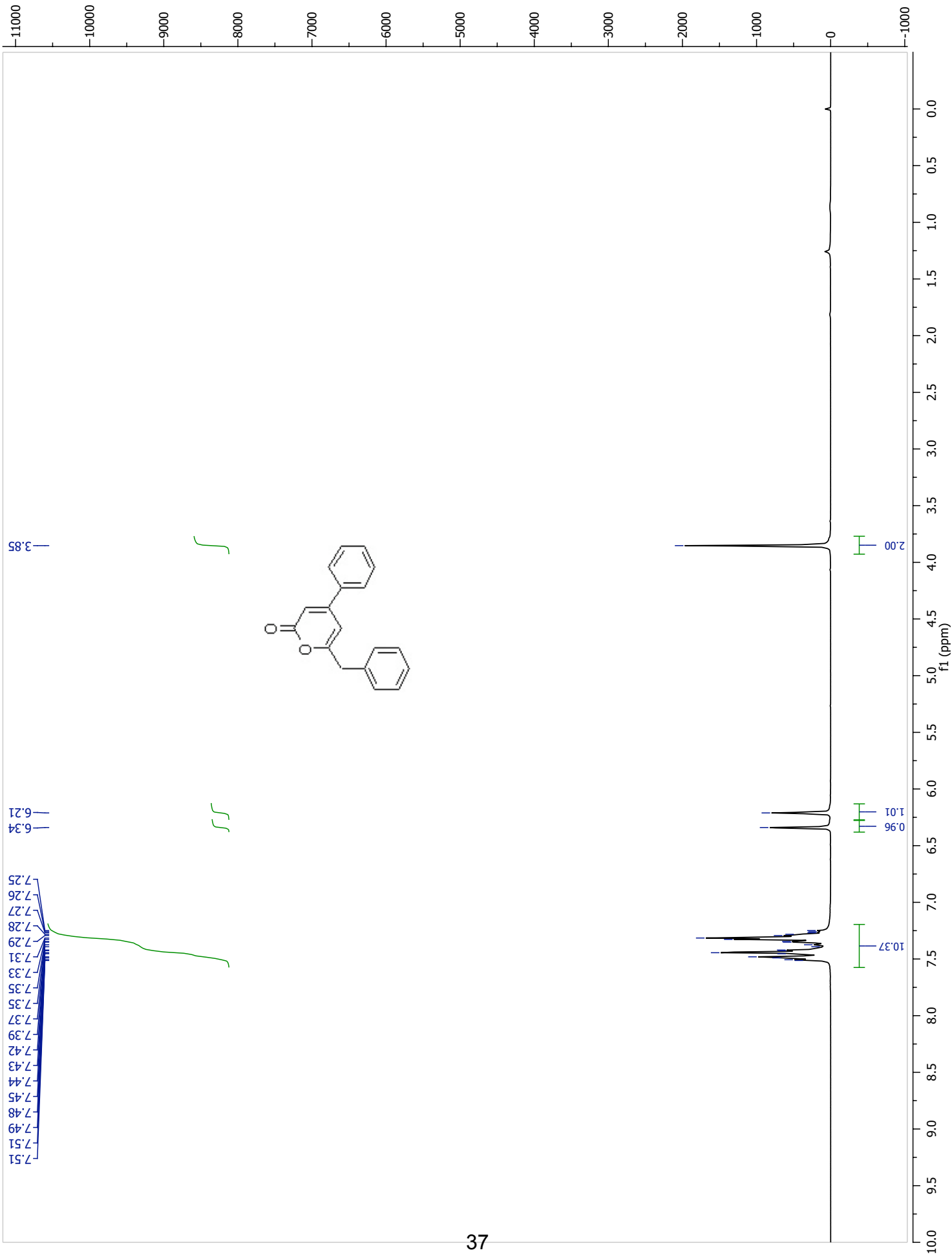


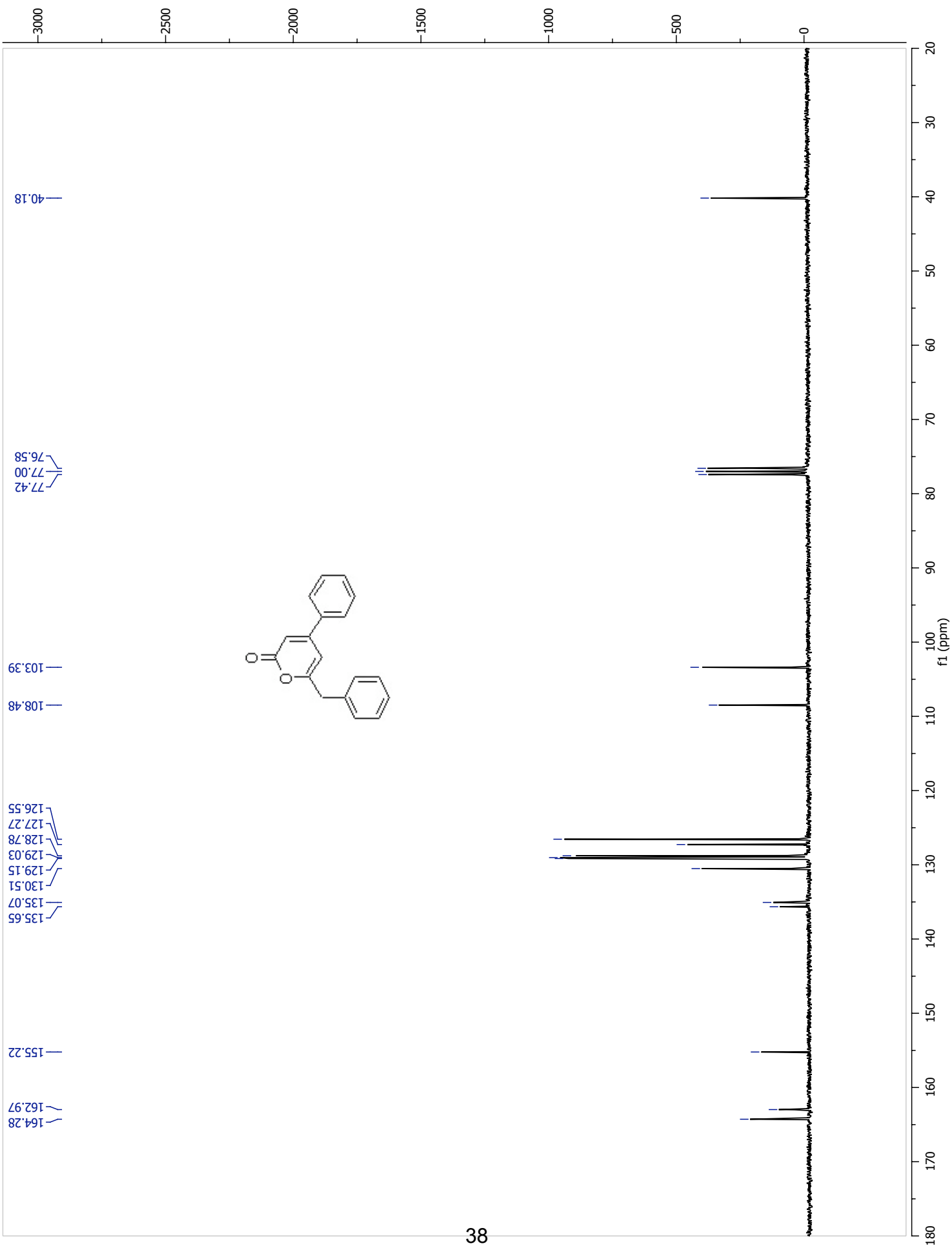


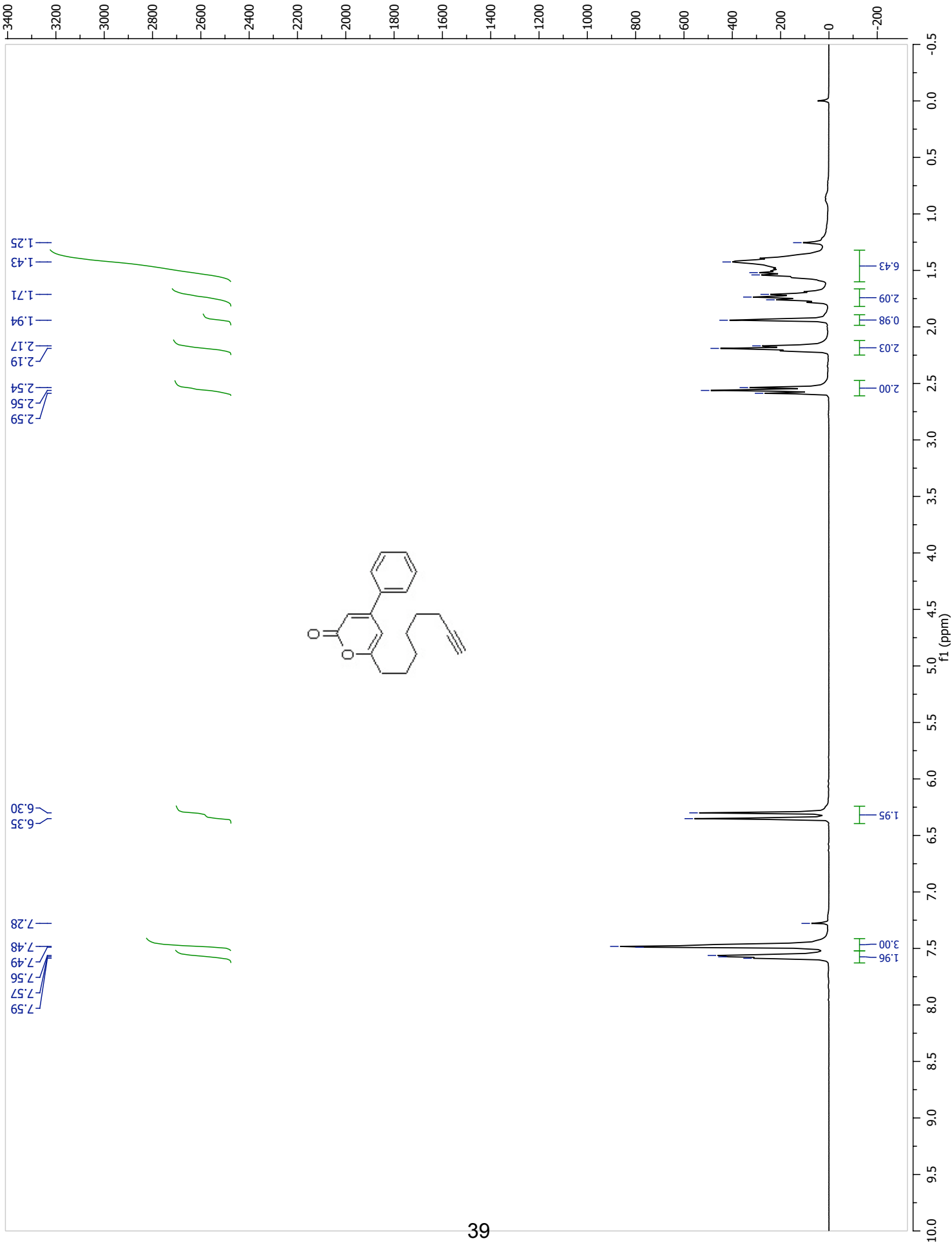


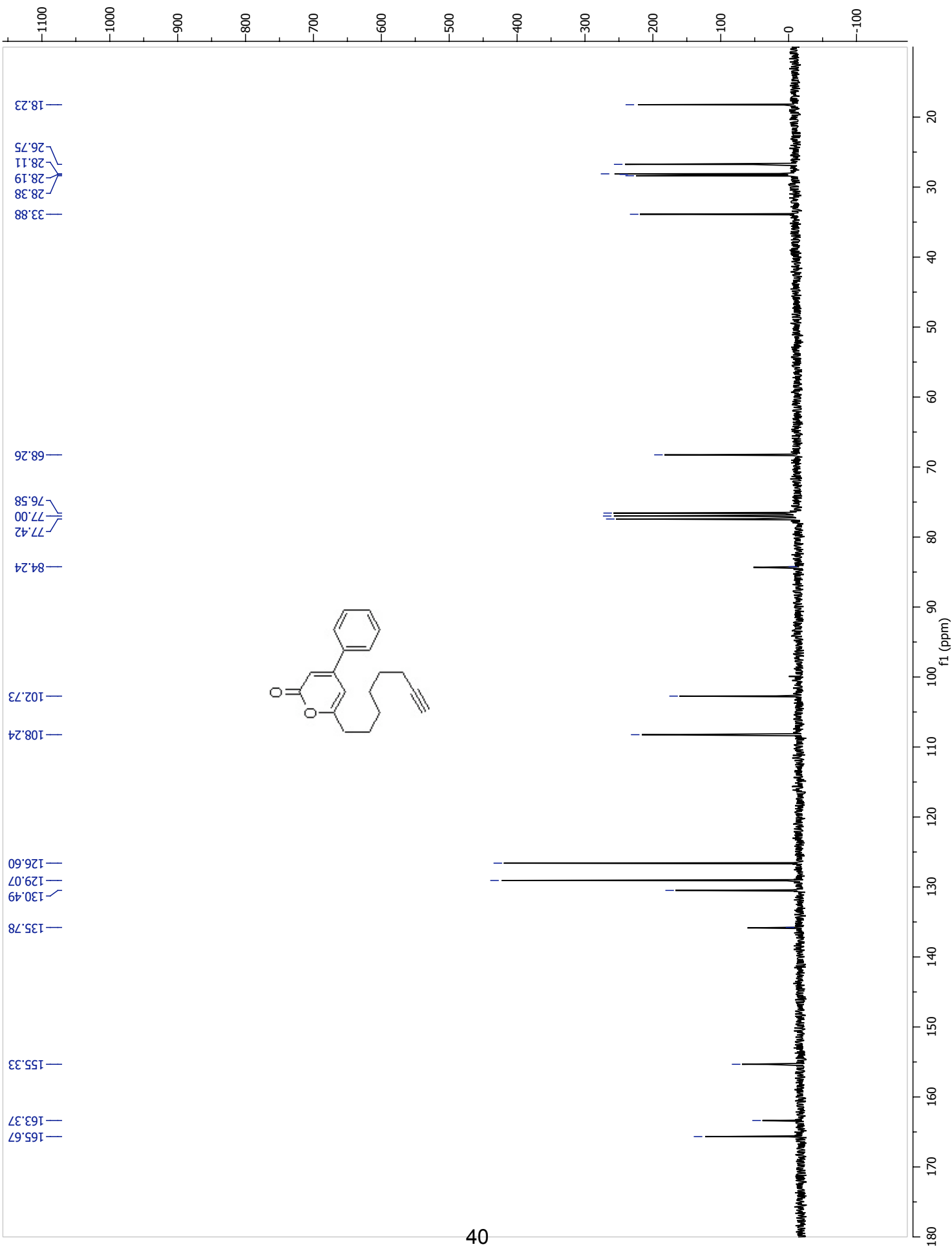




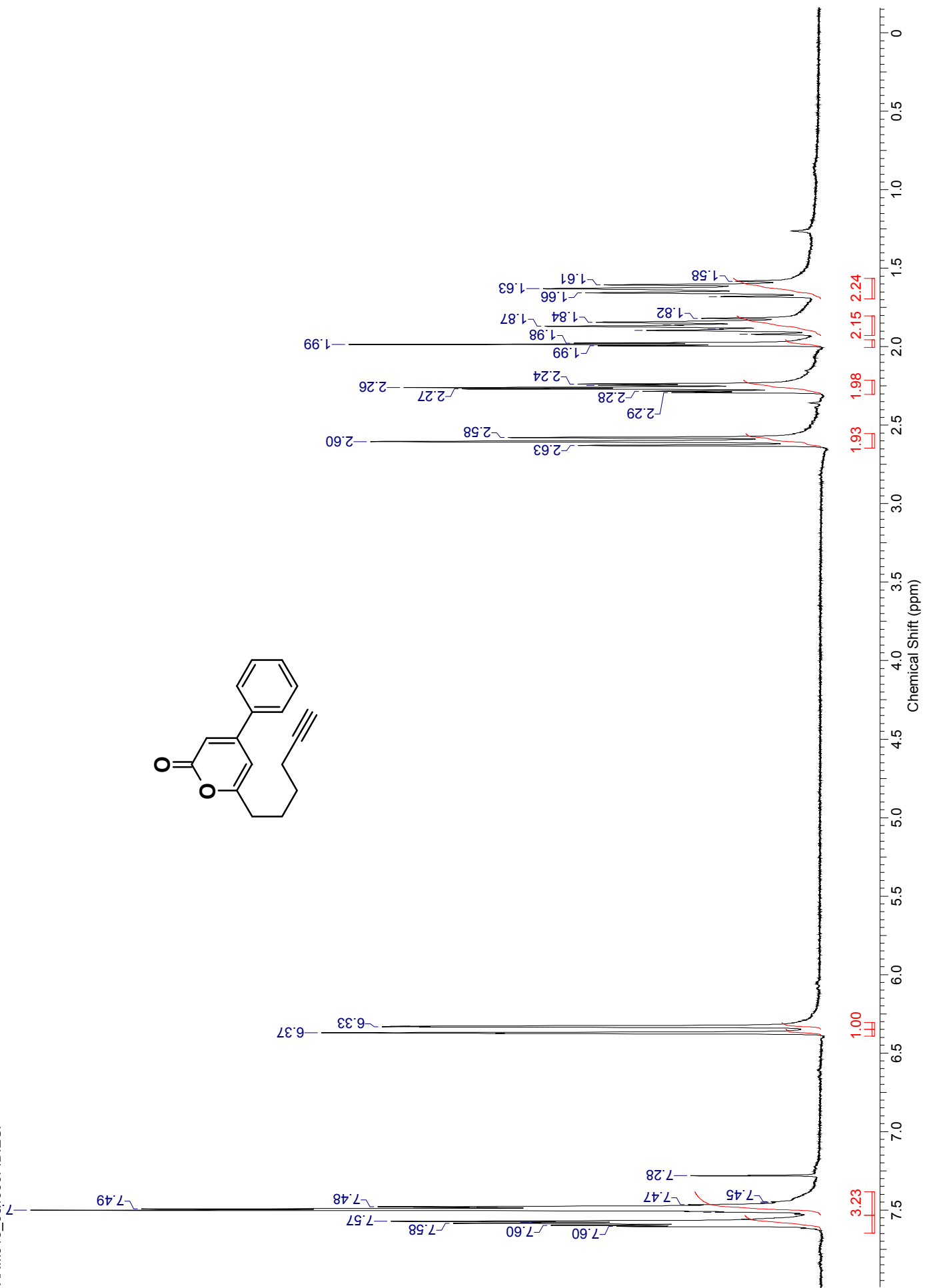
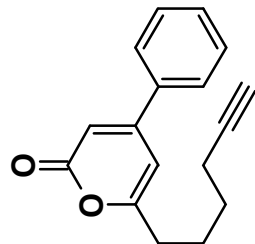


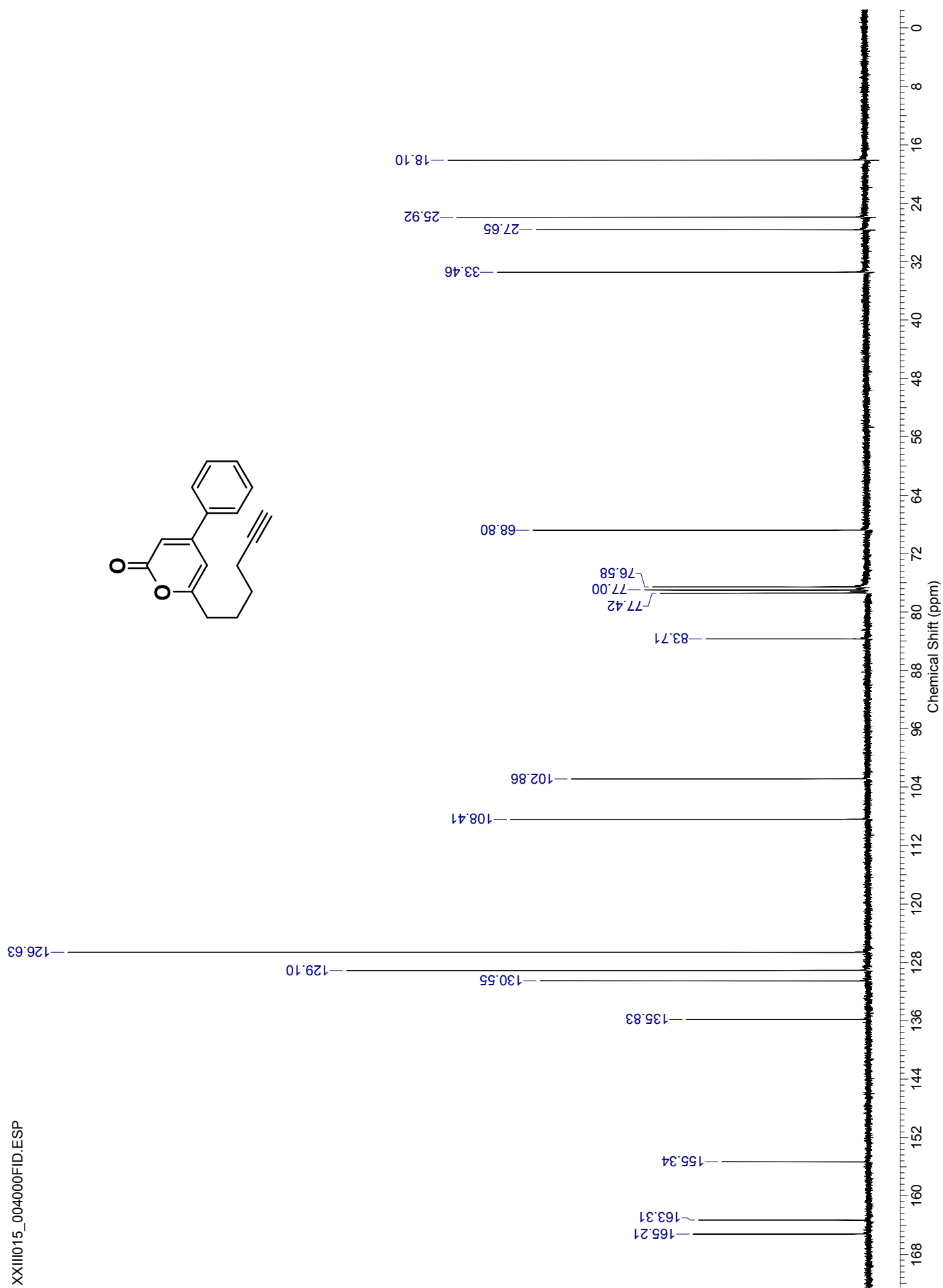
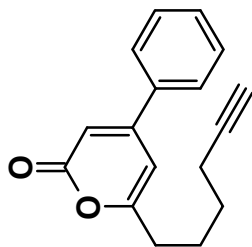


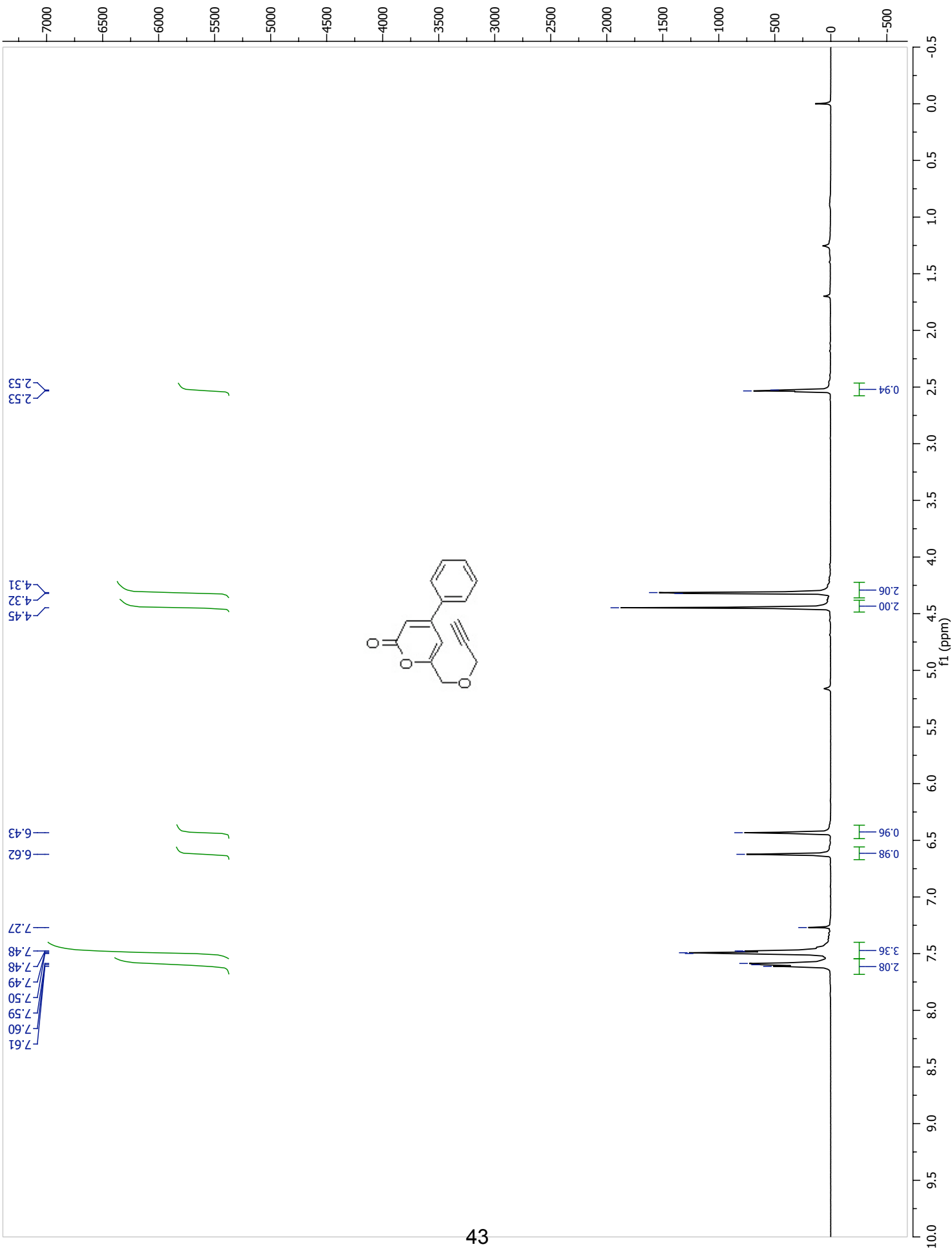


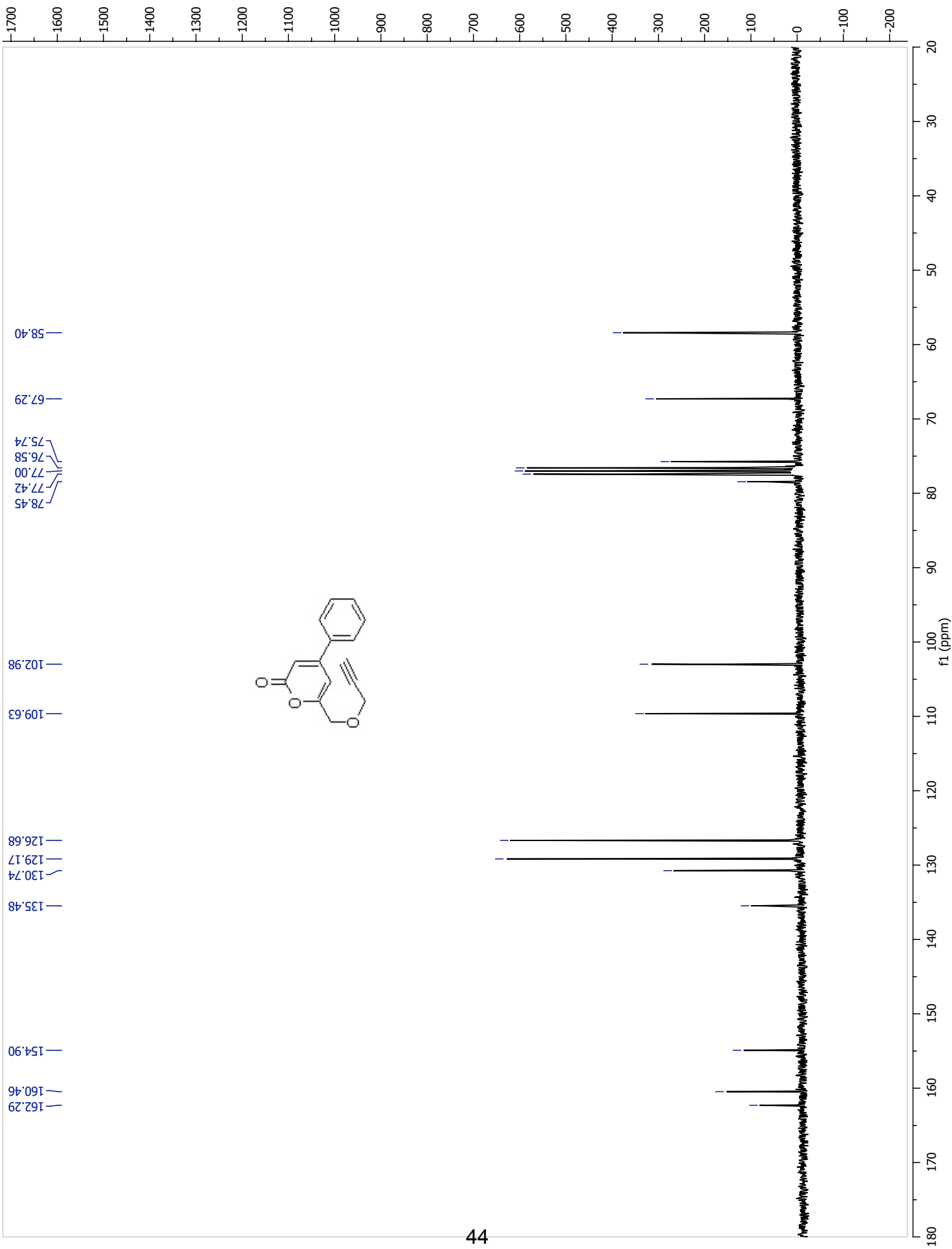


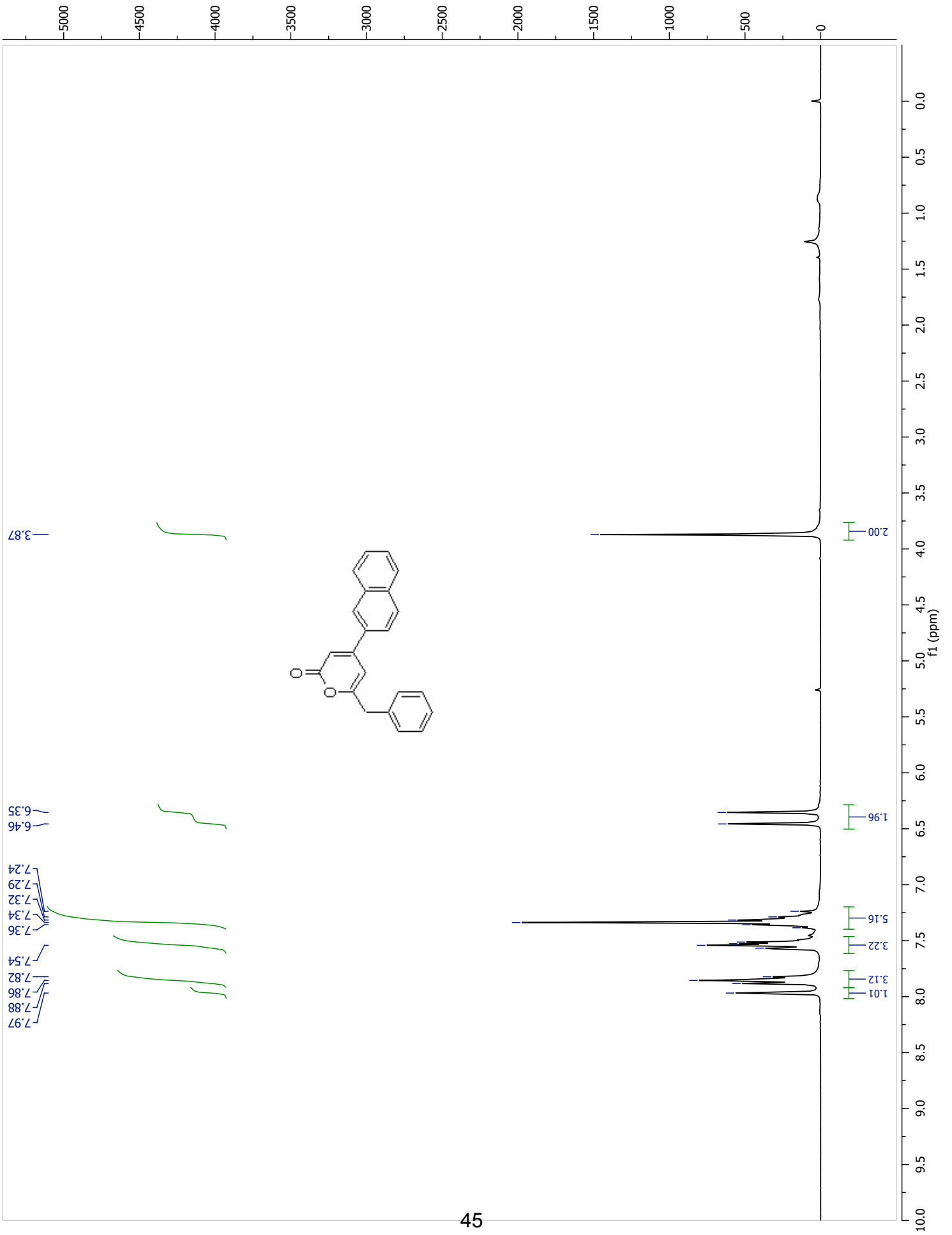
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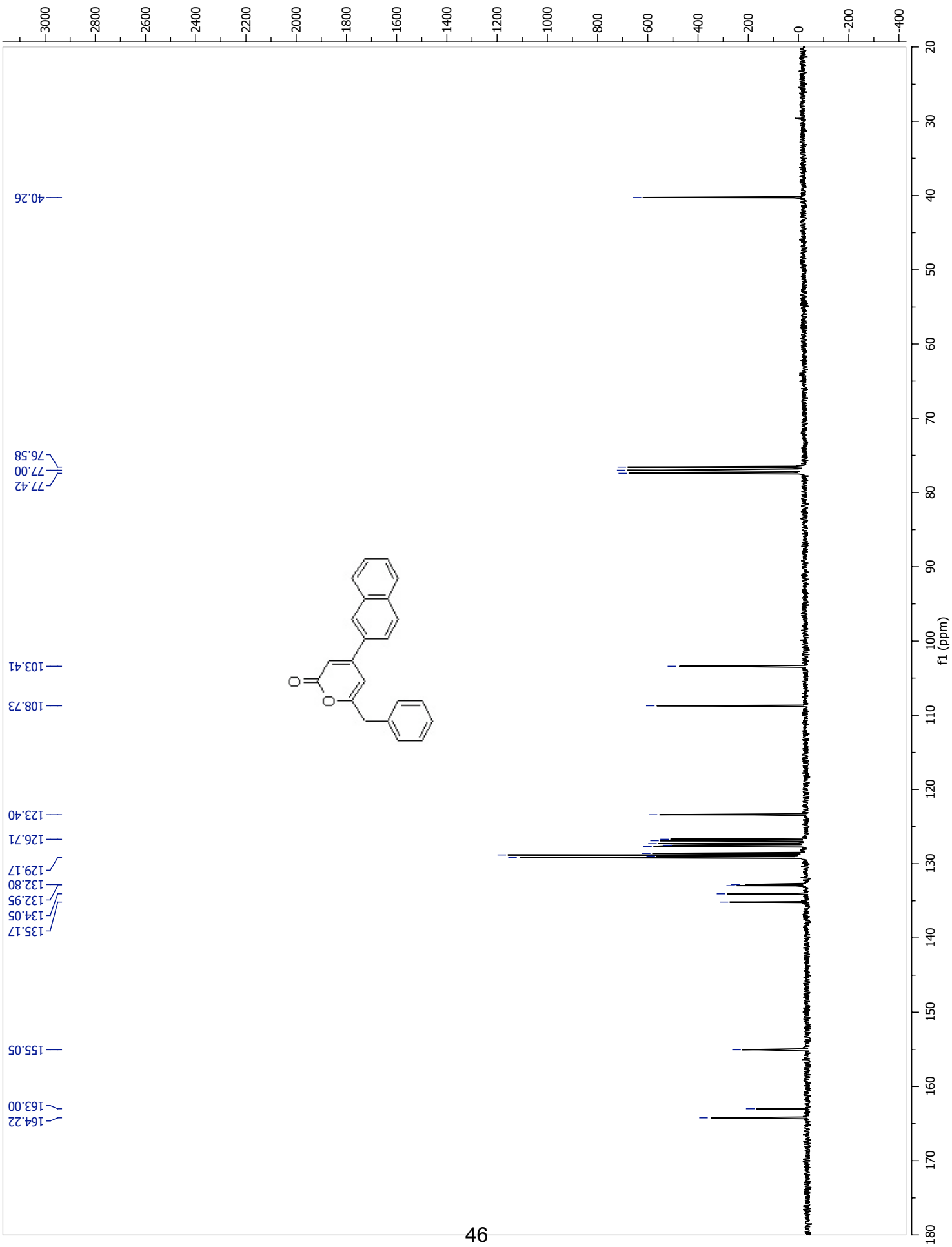


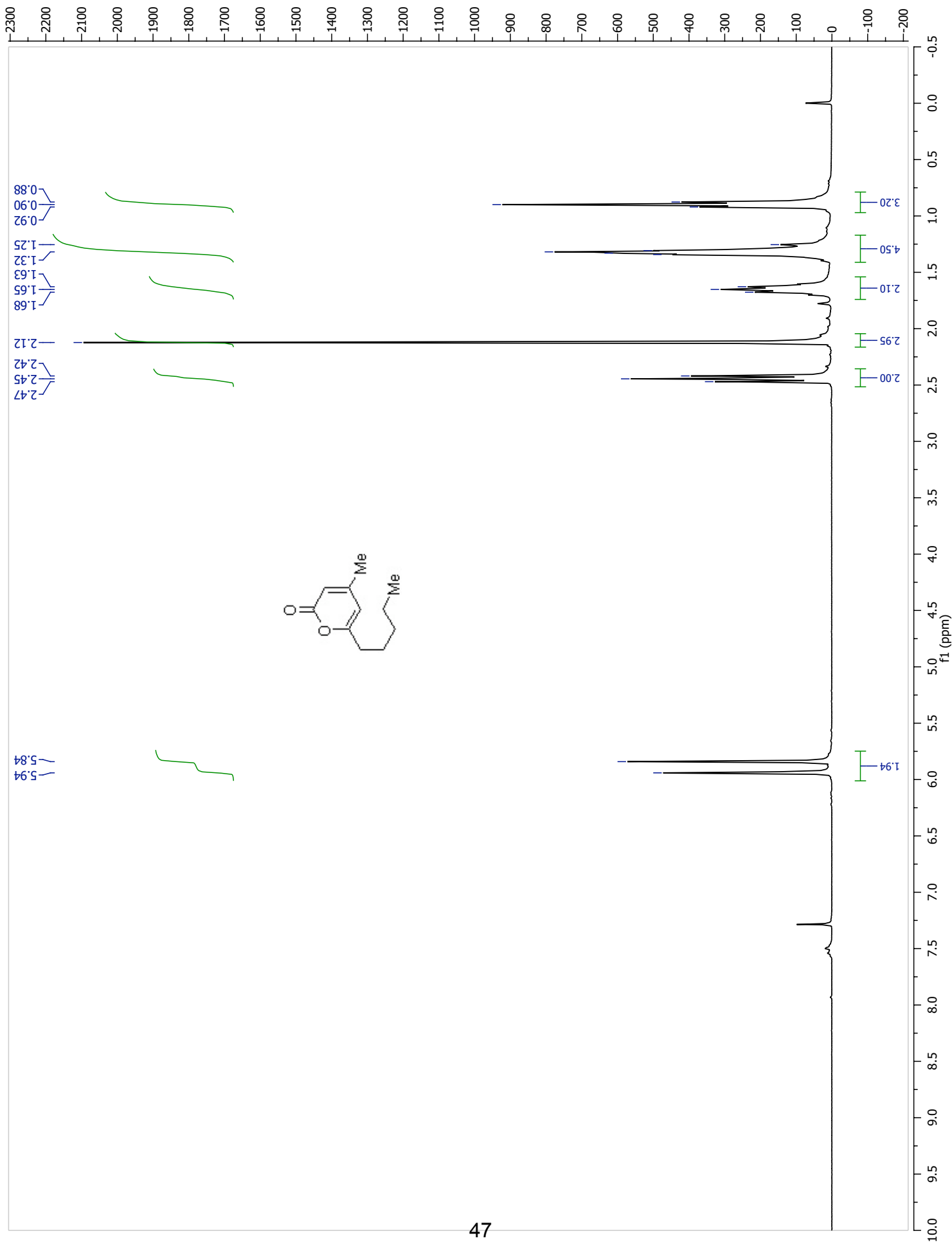


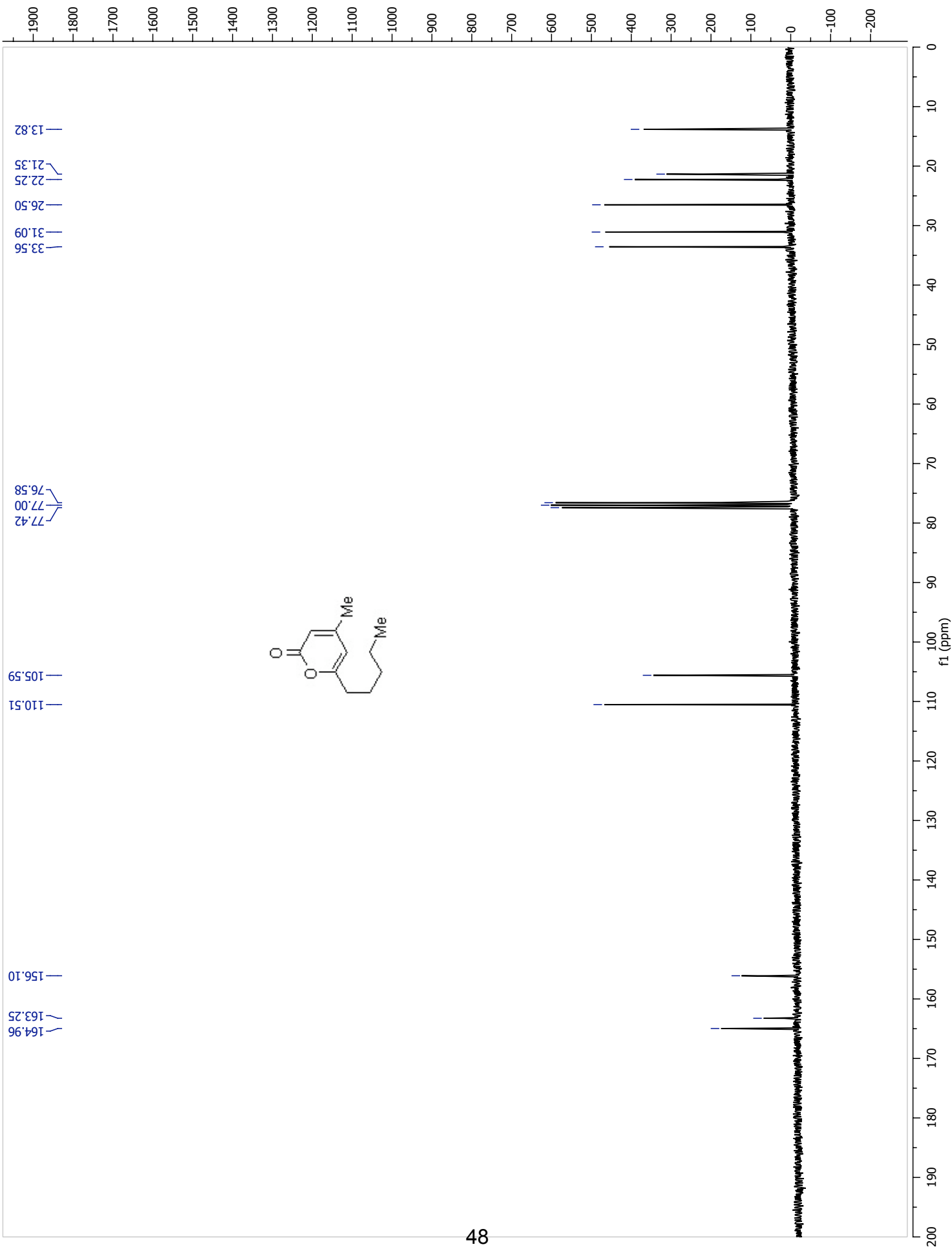


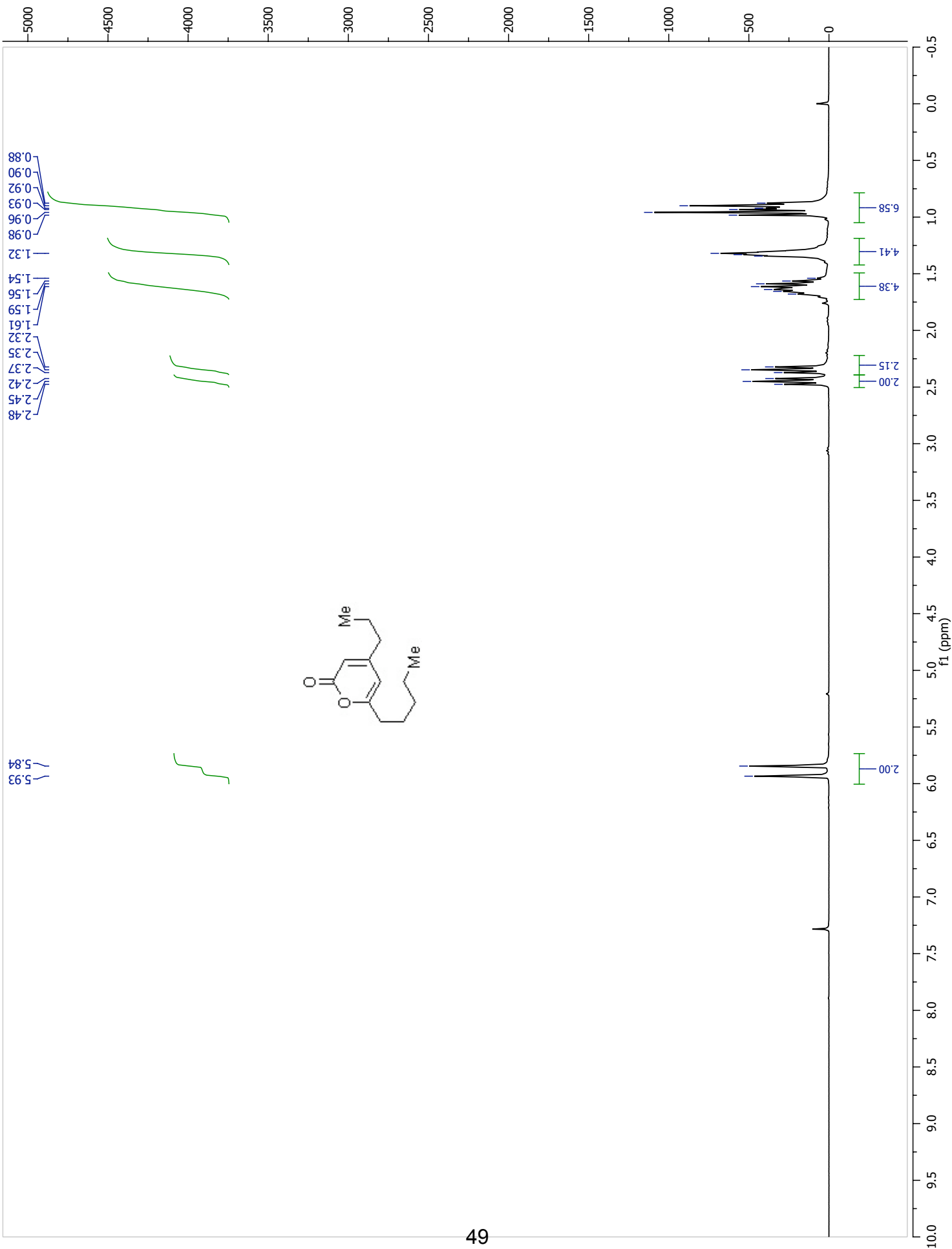


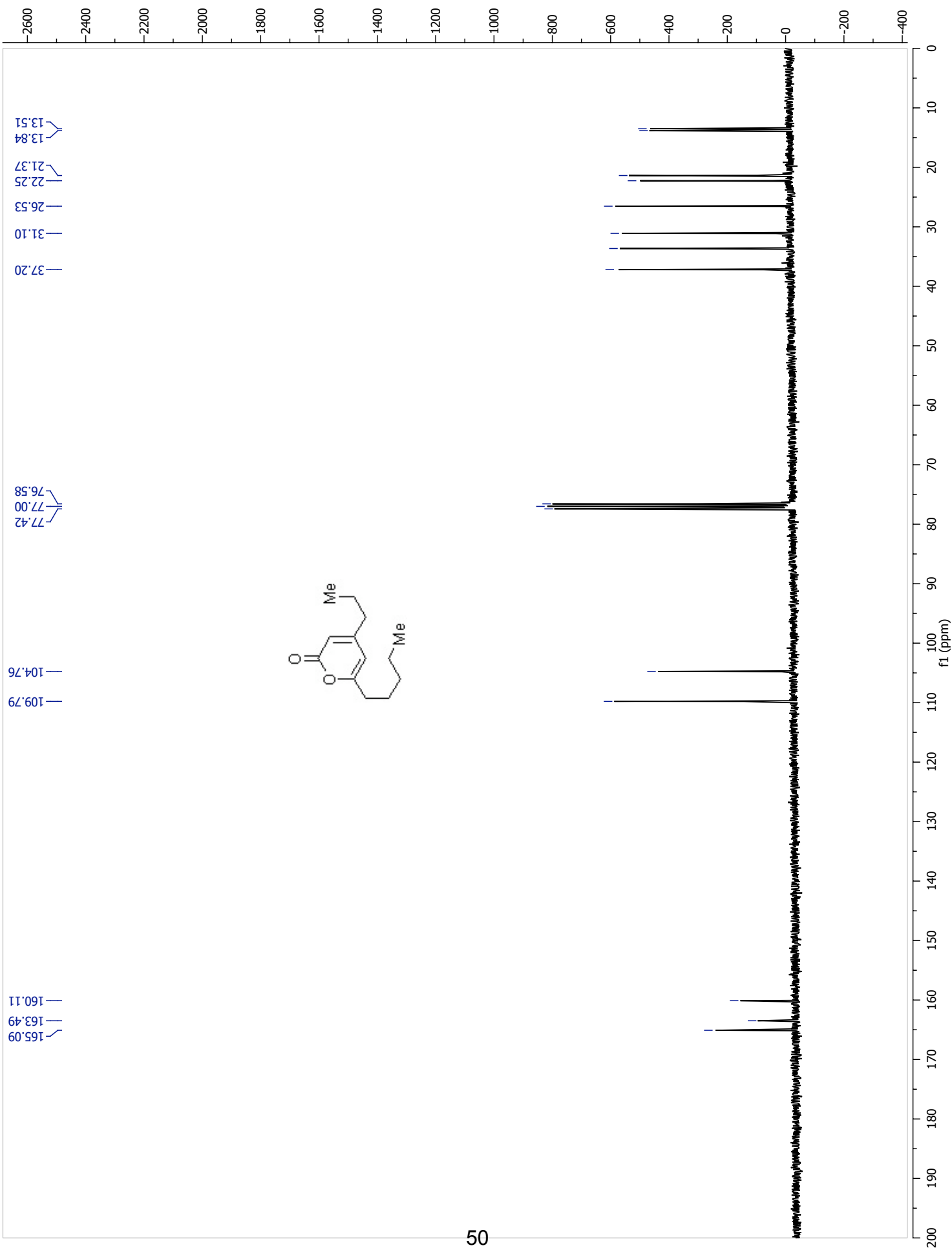


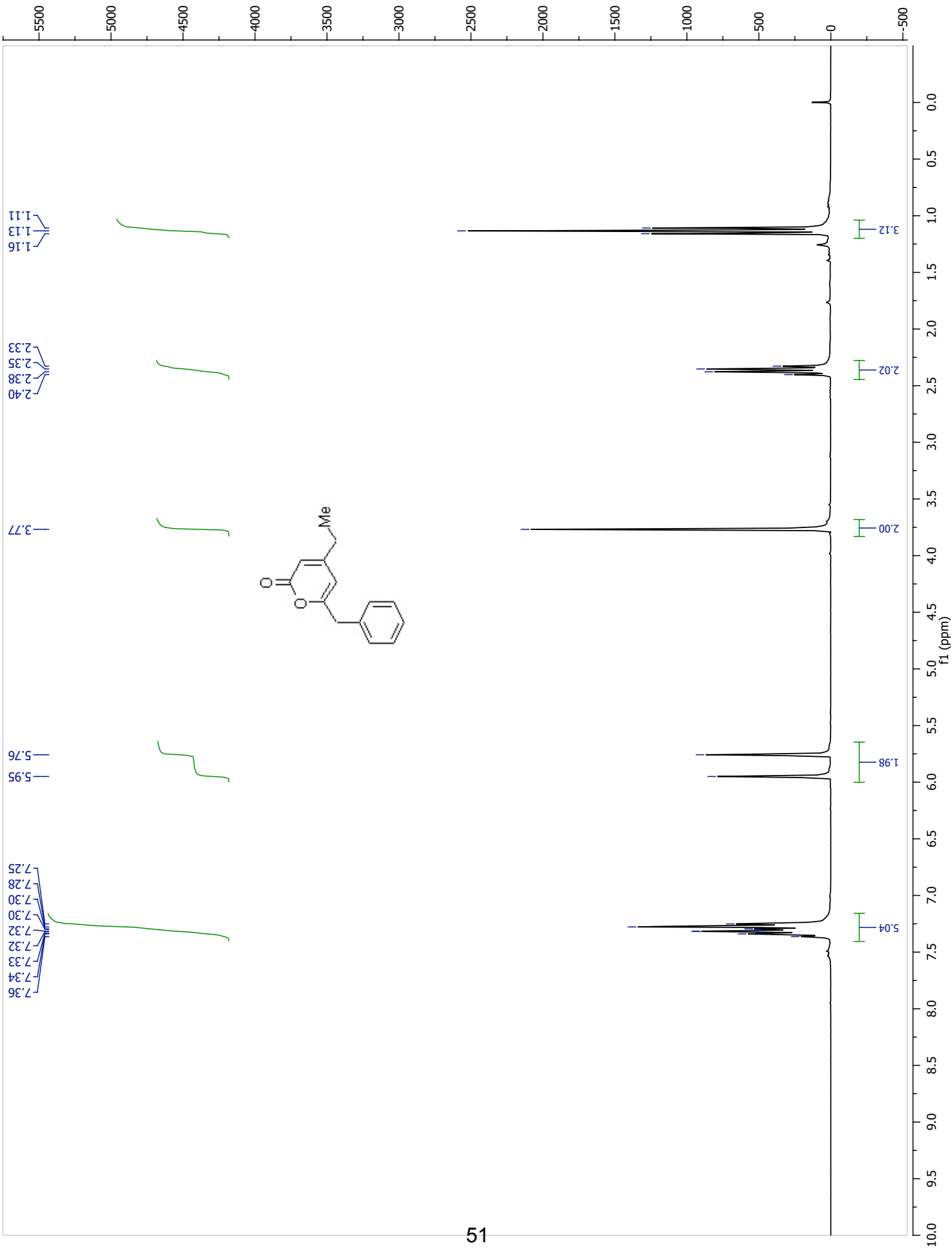


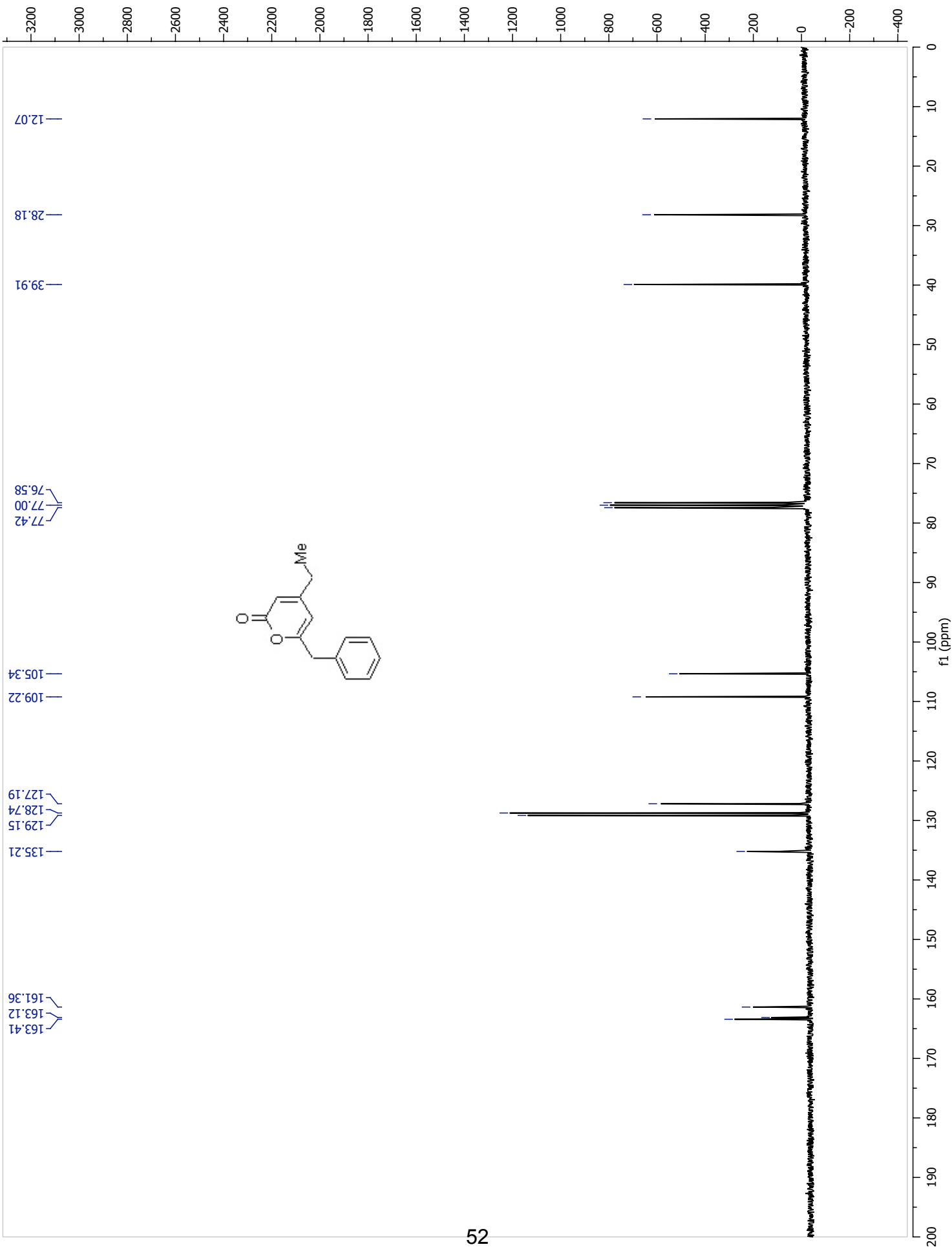


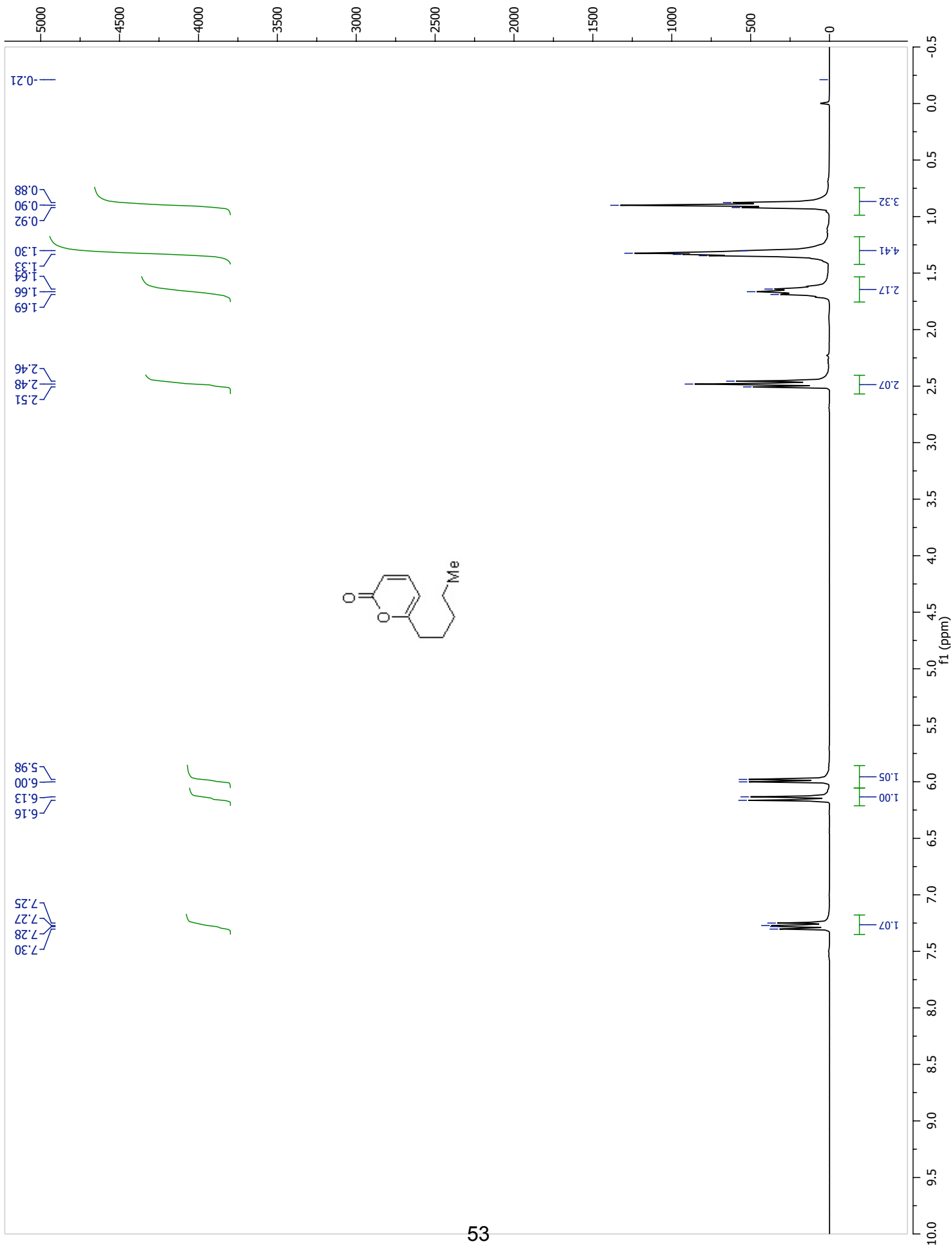


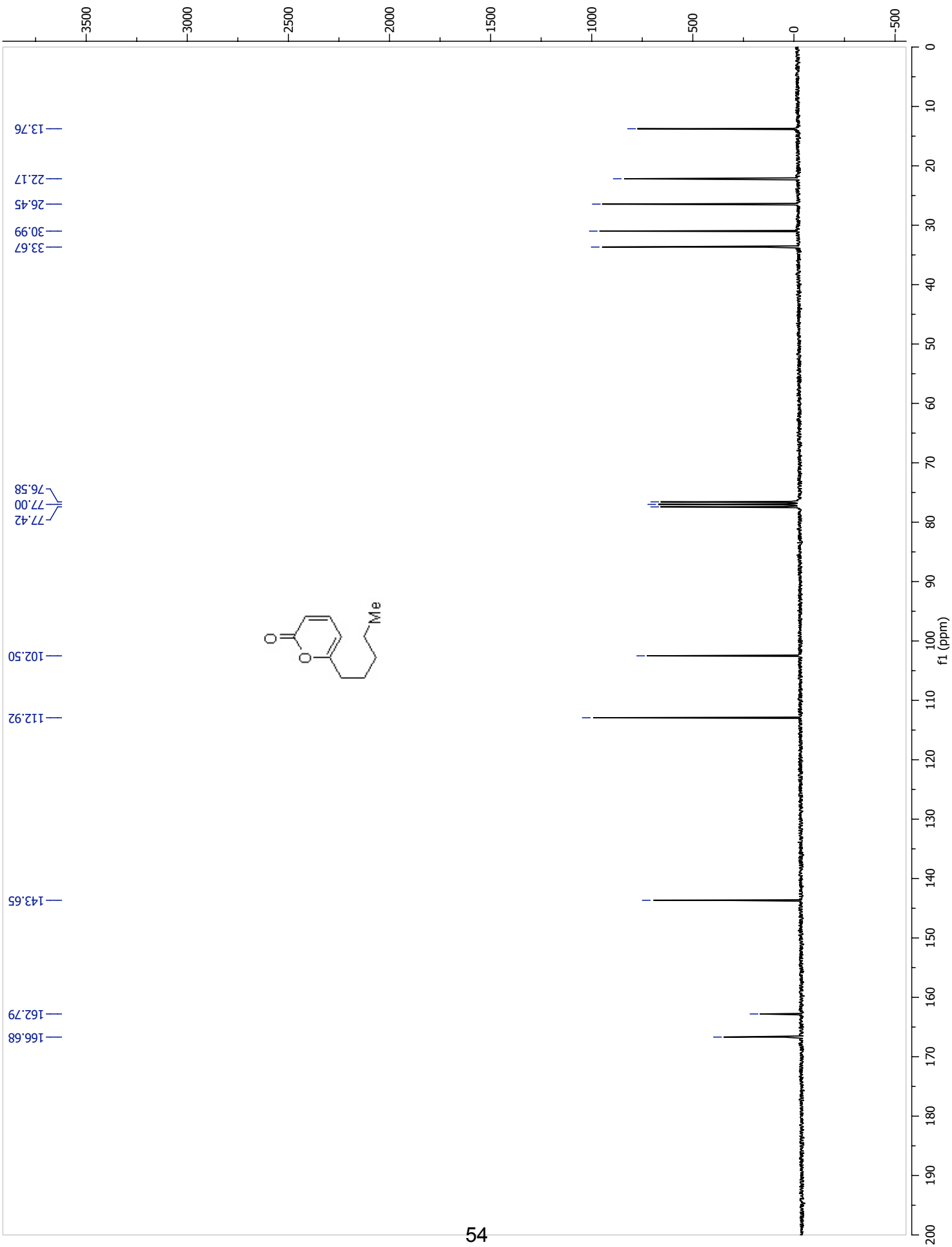


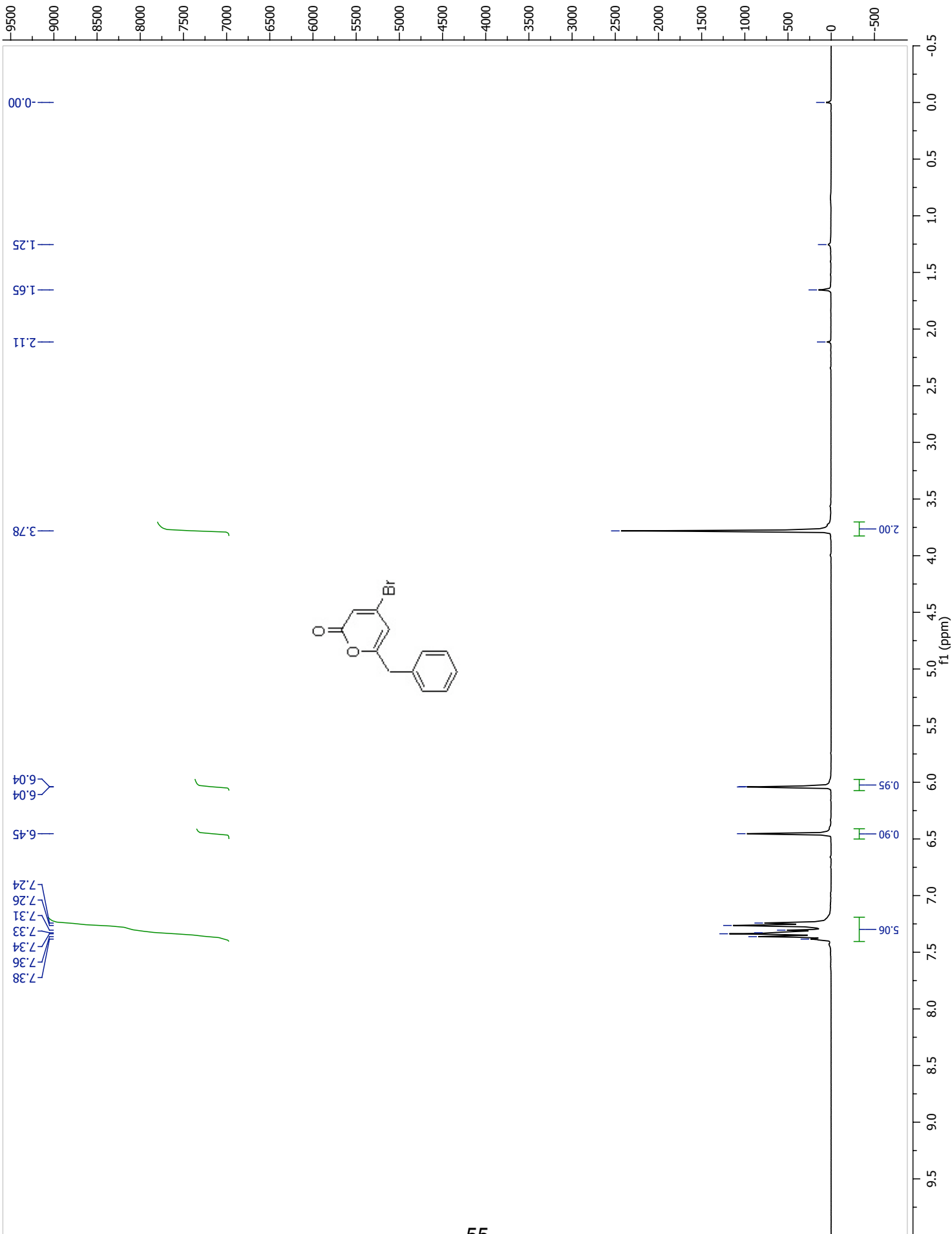


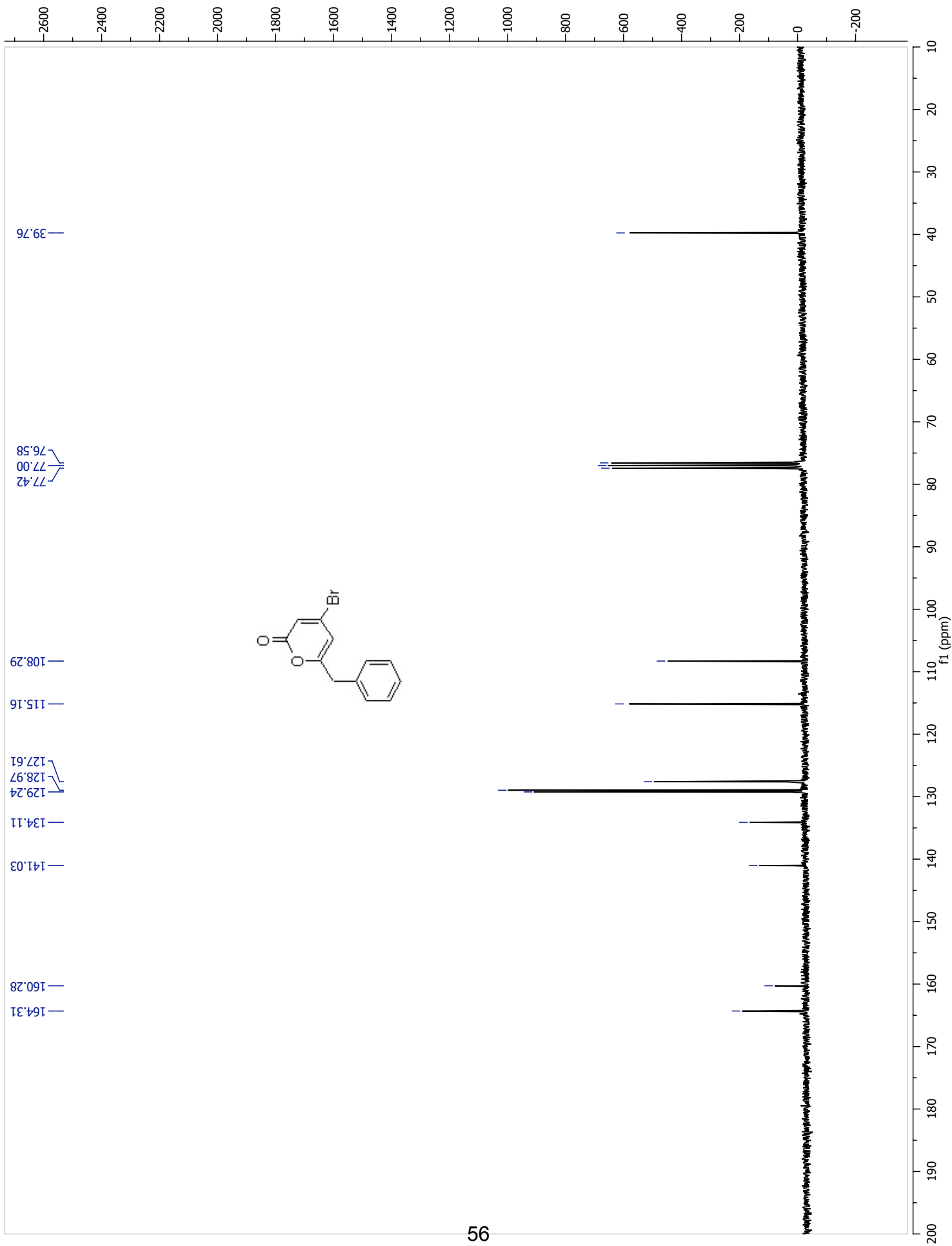


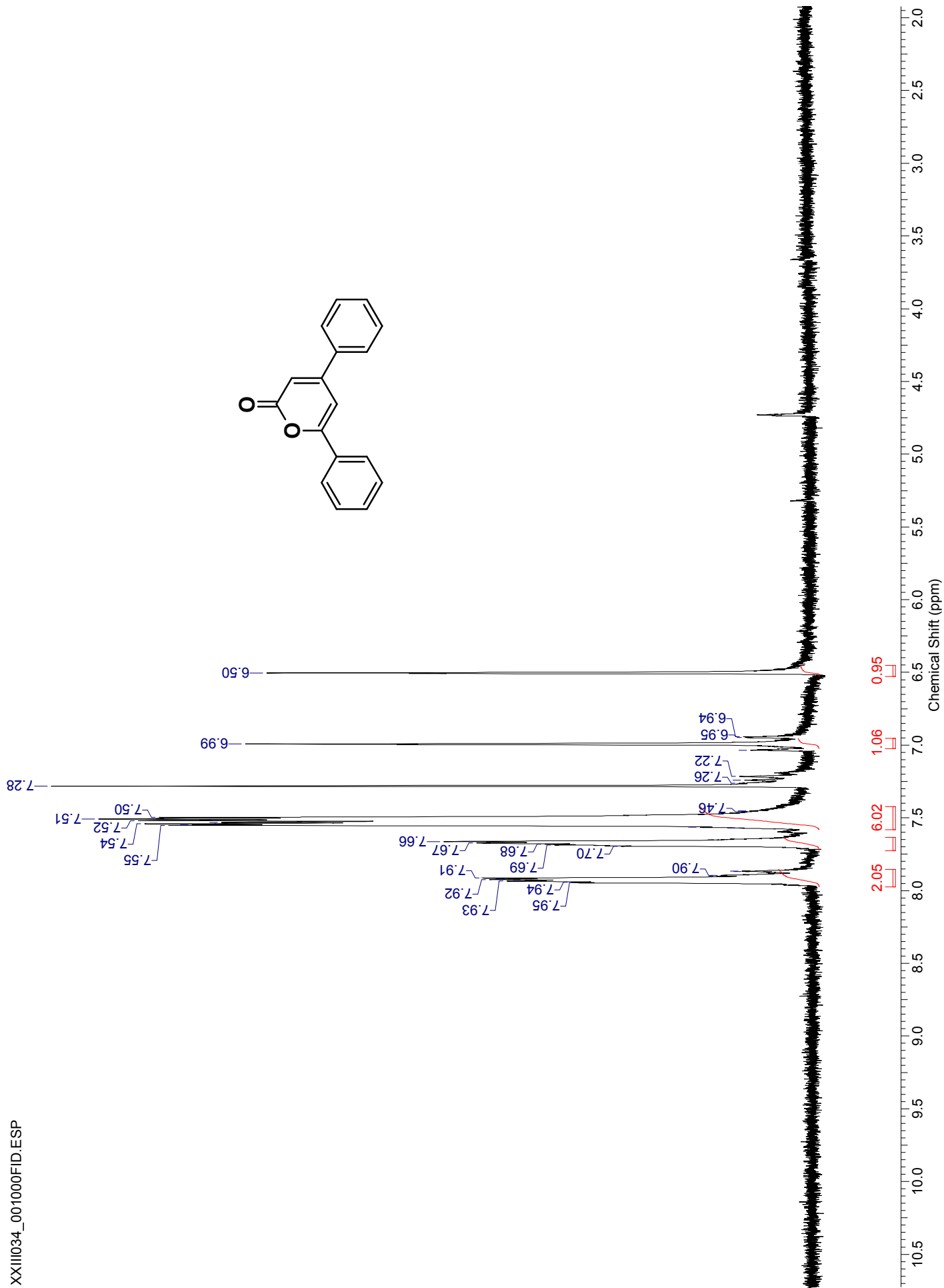
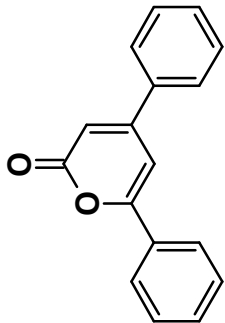


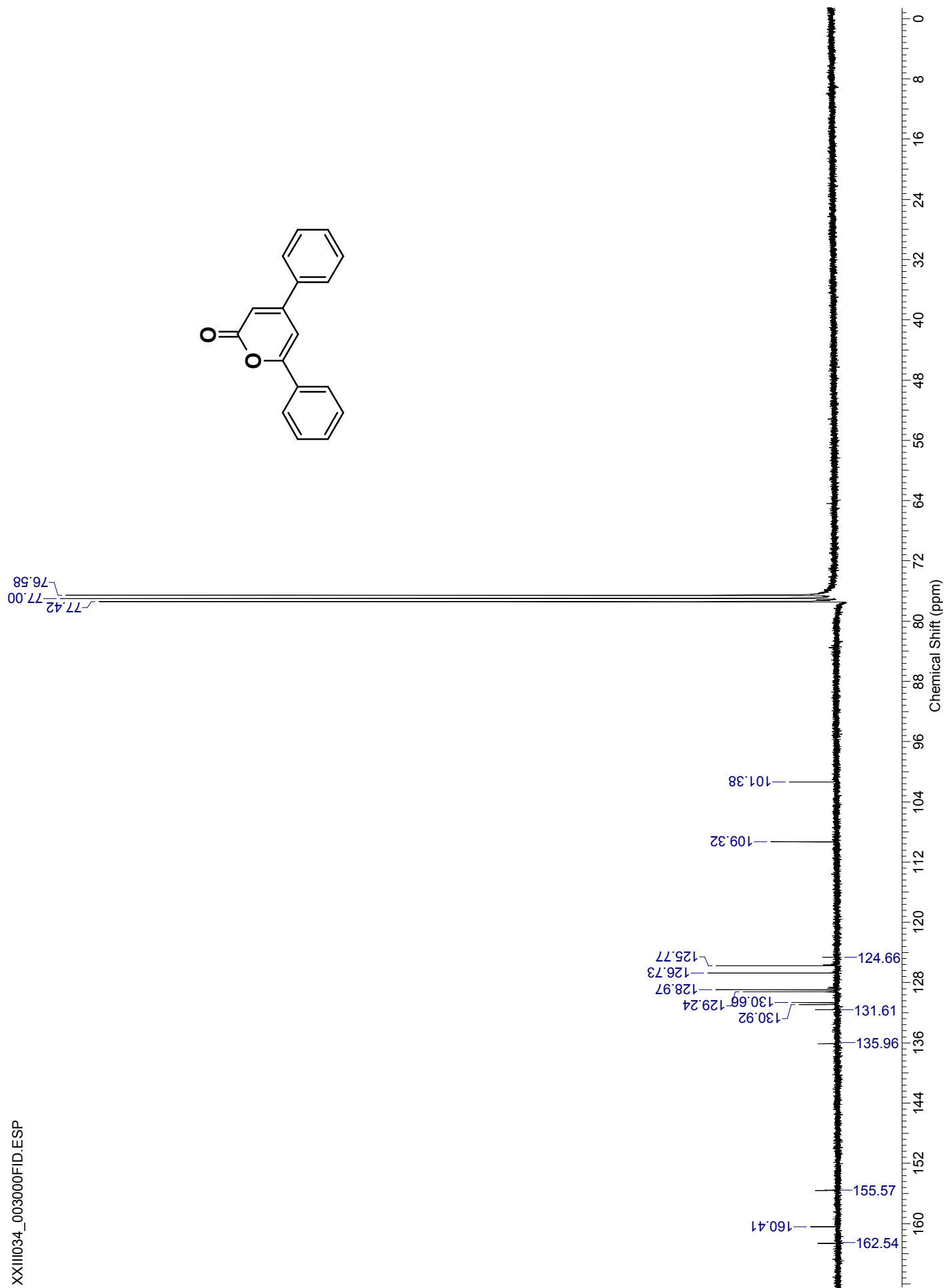
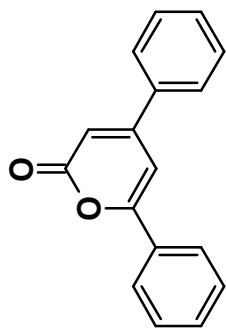


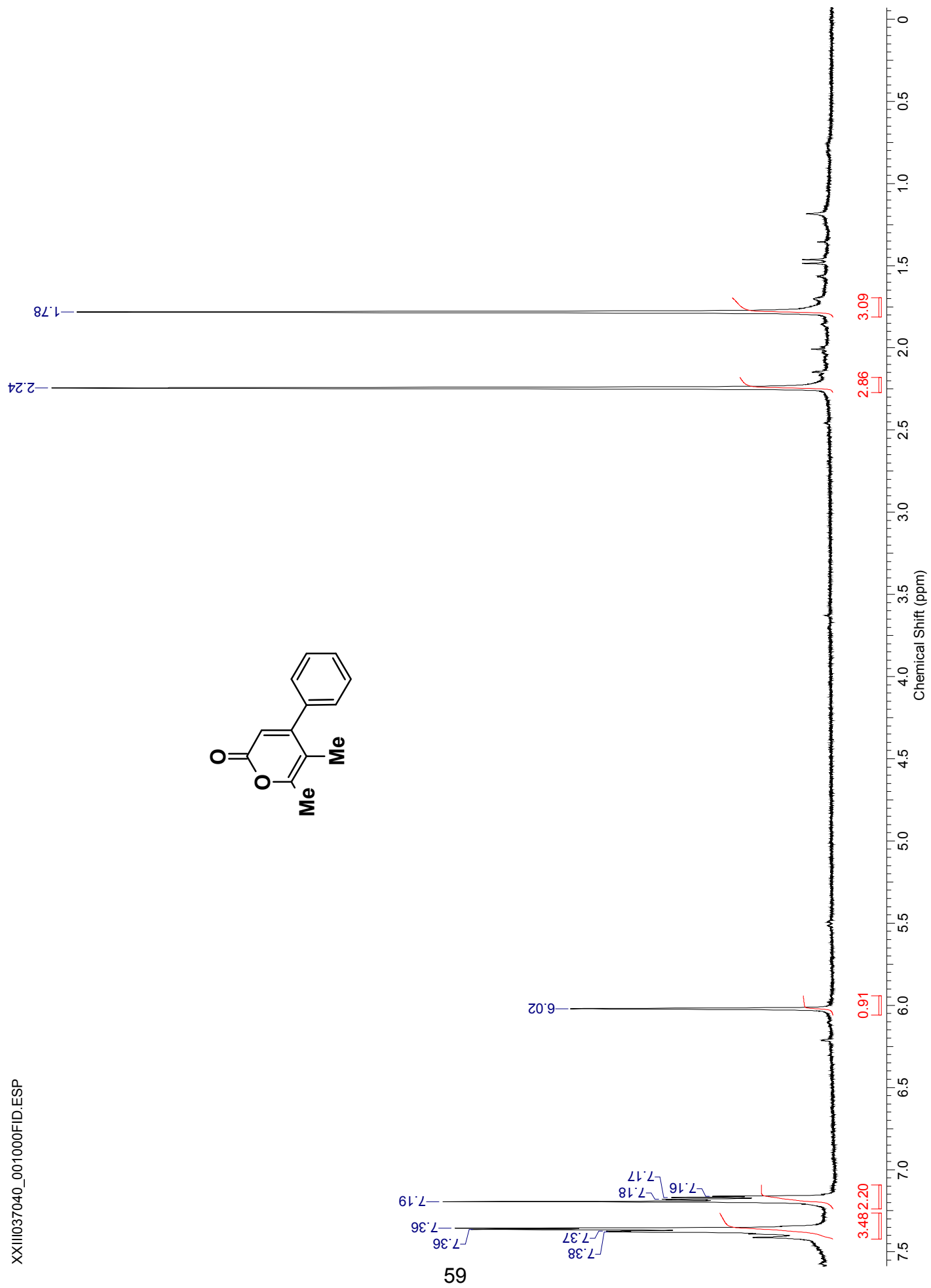
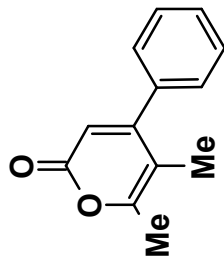


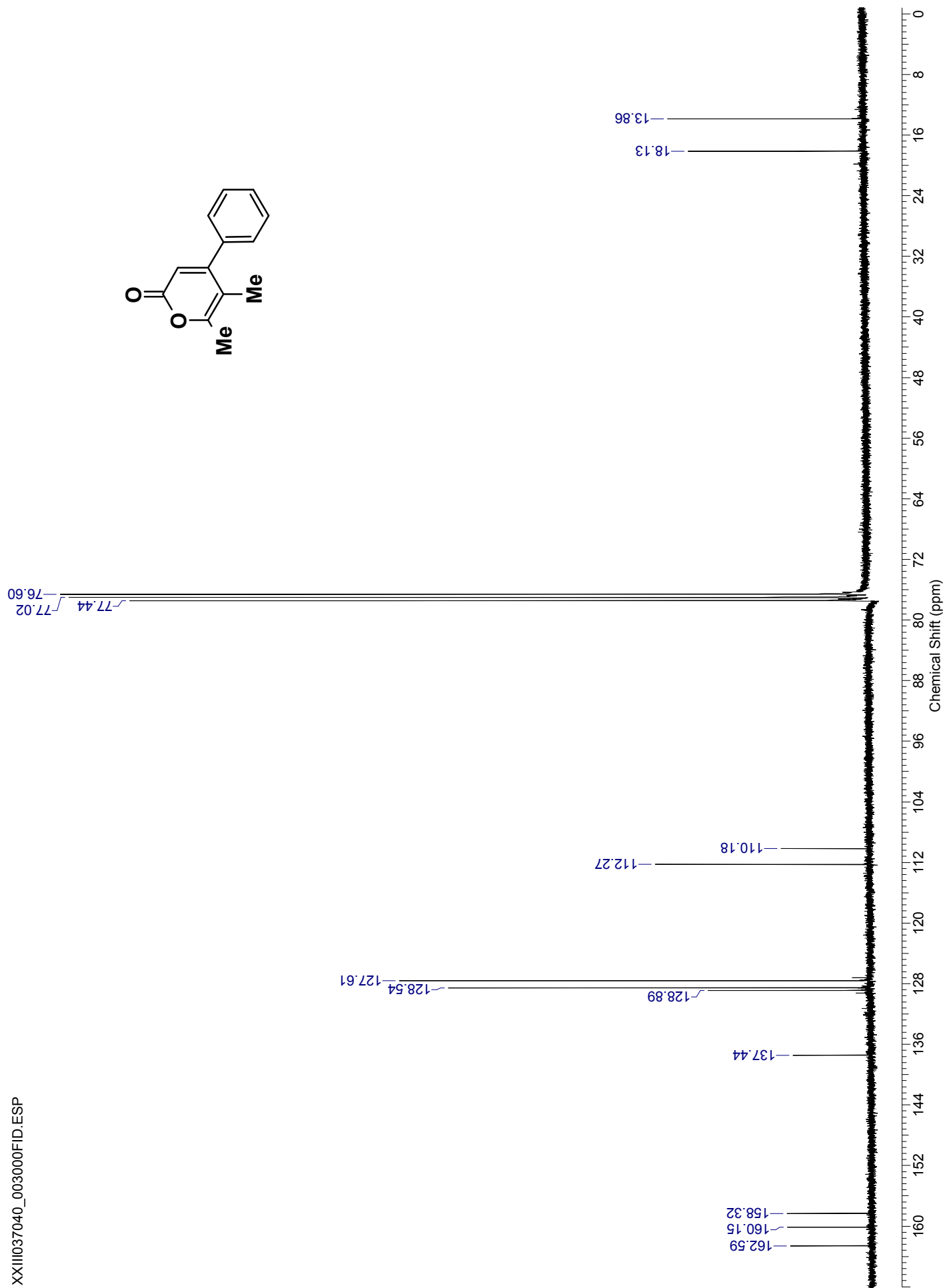
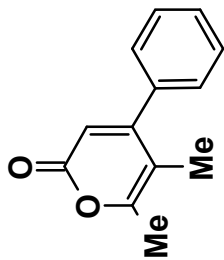


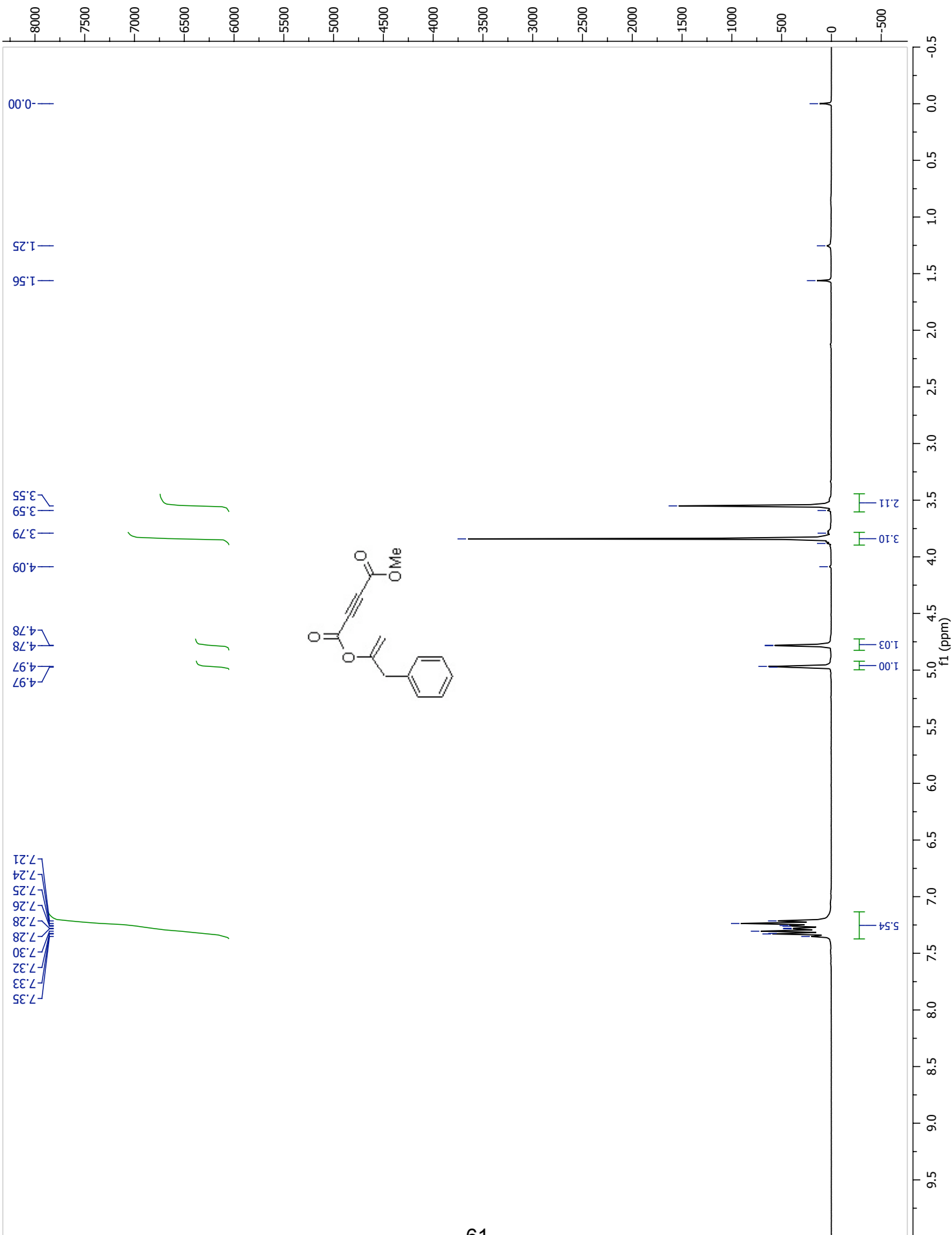


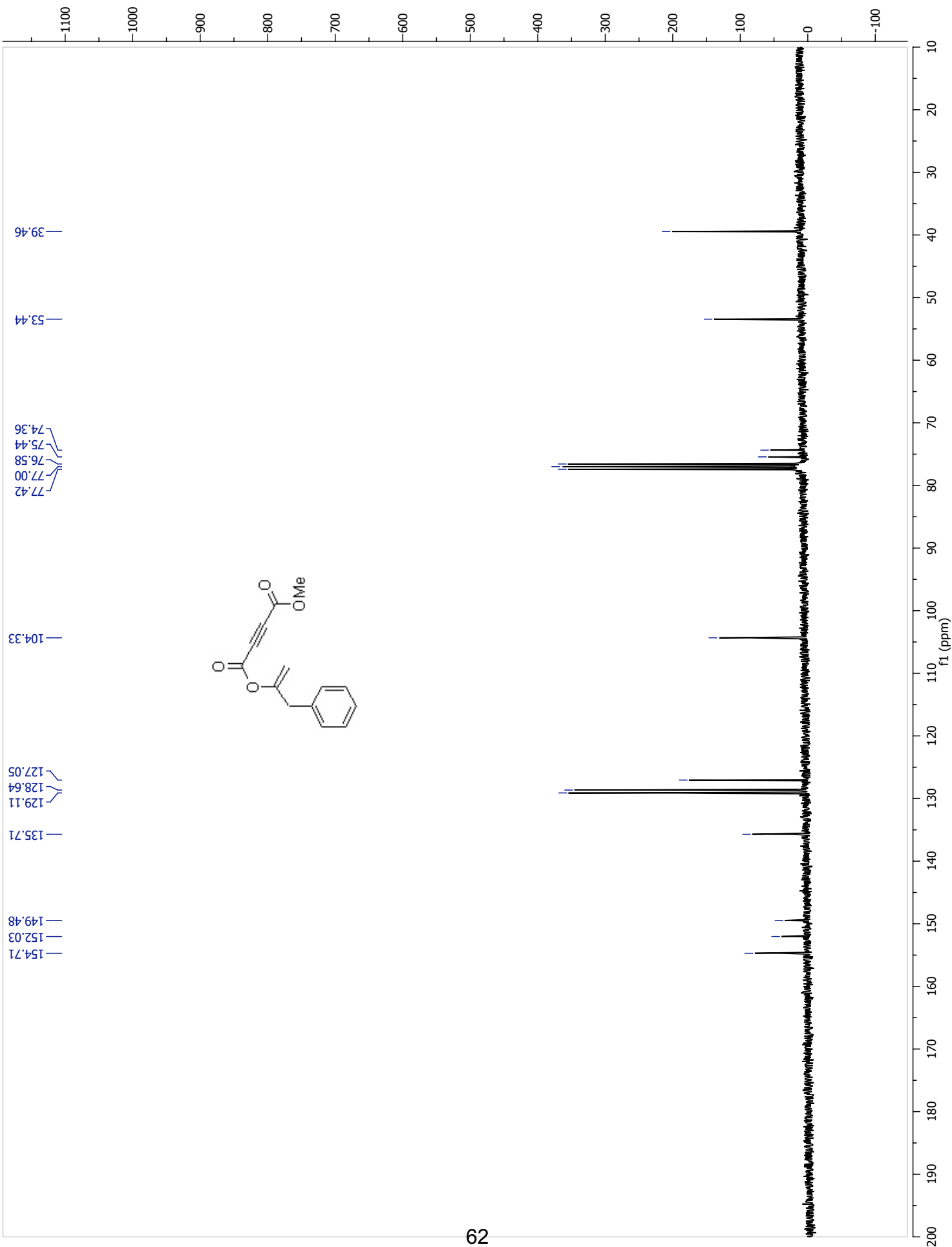


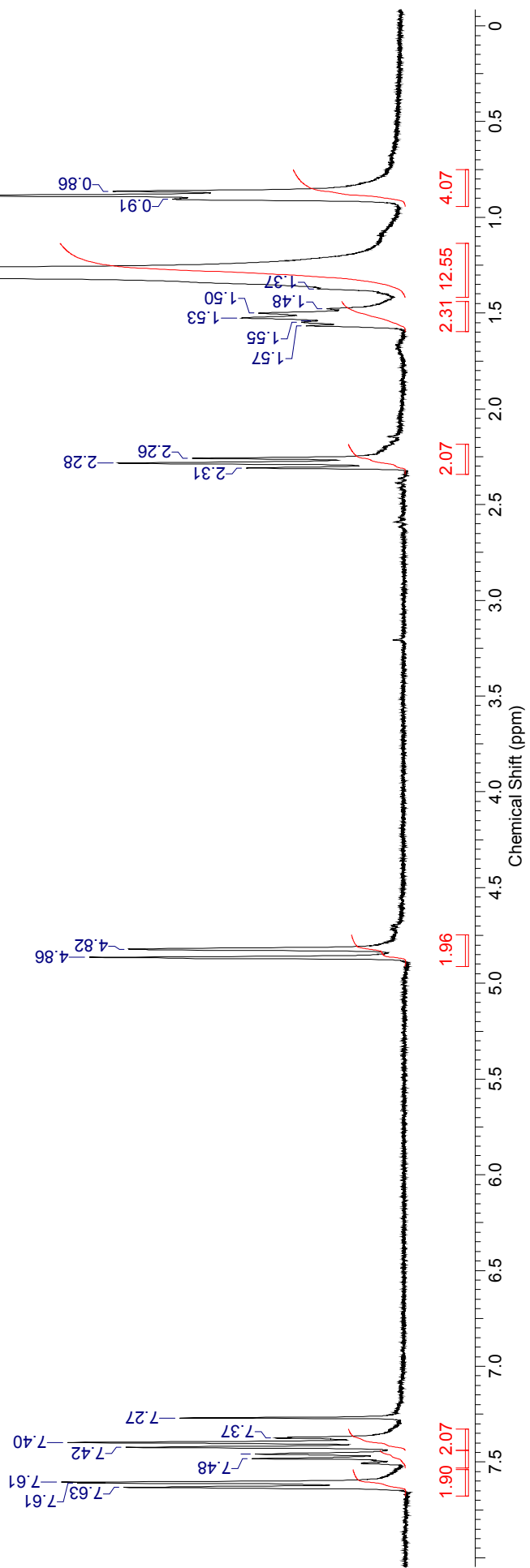
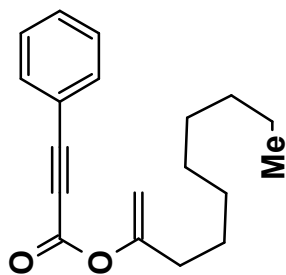


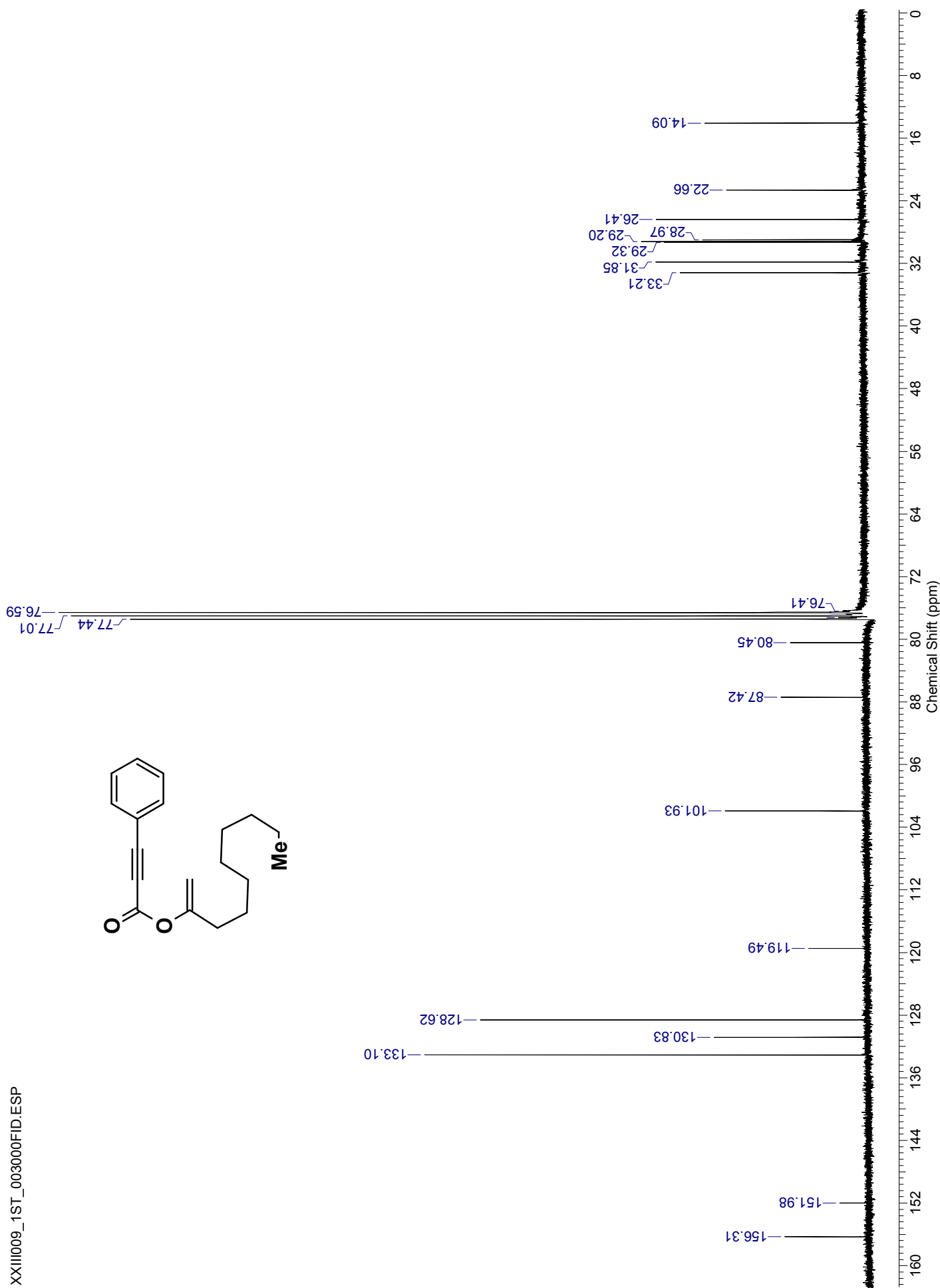
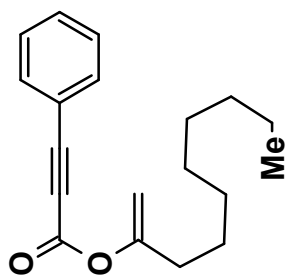


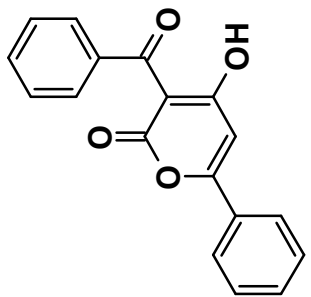












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