

## General Reagent Information

All reactions were set up on the benchtop and carried out in oven-dried Teflon seal screw-cap test-tubes stirring by magnetic stir bars under an atmosphere of nitrogen. Flash column chromatography was performed using silica gel purchased from Silicycle.  $\text{CuCl}_2$  (99%) was purchased from Acros and used as supplied. Amines were purchased from Acros Organics, Alfa Aesar, or Aldrich and purified by distillation before use. All ketones and alkynes were purchased from Acros Organics, Alfa Aesar or TCI America and purified by distillation before use.

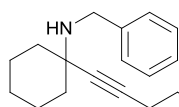
## General Analytical Information

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured on a Varian Inova 400 (400 MHz) spectrometer using  $\text{CDCl}_3$  as a solvent and tetramethylsilane as an internal standard. The following abbreviations are used singularly or in combination to indicate the multiplicity of signals: s - singlet, d - doublet, t - triplet, q - quartet, m - multiplet and br - broad. NMR spectra were acquired at 300 K. Gas chromatograph spectra were obtained on an Agilent Technologies 6850 Network GC System using dodecane as an internal standard. IR spectra were recorded on Perkin Elmer Spectrum One FT-IR Spectrometer. Attenuated total reflection infrared (ATR-IR) was used for analysis with selected absorption maxima reported in wavenumbers ( $\text{cm}^{-1}$ ). No sample preparation was necessary for ATR analysis. ATR-IR is based on the propagation of the infrared radiation through an internal reflection element (crystal) with a high refractive index, and its reflection at the interface between the crystal and the solid material. Mass spectrometric data was collected on a HP 5989A GC/MS quadrupole instrument. Exact masses were recorded on a Waters GCT Premier ToF instrument using direct injection of samples in acetonitrile into the electrospray source (ESI) and either positive or negative ionization.

## General Procedure

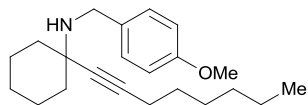
To an oven-dried test tube equipped with magnetic stir bar and Teflon-seal screw cap was added 5 mol %  $\text{CuCl}_2$ . The flask was purged with nitrogen for 5 minutes. Ketone (1.0 equiv), alkyne (1.0 equiv), and amine (1.0 equiv) were added, and the reaction was stirred at the designated temperature for the indicated time. Upon completion, as judged by GC, the mixture was cooled to room temperature and directly loaded atop a silica gel column. Chromatography with ethyl acetate (EtOAc) in hexanes as eluent afforded the desired product. The products were further identified by FT-IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and HRMS, which were all in good agreement with the assigned structures. References are provided for compounds matching those previously reported in the literature.

#### 4a: Synthesis of N-benzyl-1-(oct-1-yn-1-yl)cyclohexan-1-amine



Benzylamine (110  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 1-octyne (148  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 6 hours to afford the title compound as a clear light yellow oil in 91% yield (0.271 g, 0.91 mmol) after column chromatography on silica gel (20% EtOAc/hexanes). IR (film) 2928, 2854, 1740, 1605, 1495, 1452, 1115, 1028, 905, 732, 697  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 (d,  $J = 7.2$  Hz, 2H), 7.30 (t,  $J = 7.5$  Hz, 2H), 7.22 (t,  $J = 7.2$  Hz, 1H), 3.96 – 3.80 (m, 2H), 2.25 (t,  $J = 6.9$  Hz, 2H), 1.83 (d,  $J = 12.5$  Hz, 2H), 1.71 – 1.17 (m, 17H), 0.90 (t,  $J = 6.7$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  141.5, 128.7, 128.6, 127.0, 84.8, 84.1, 55.1, 48.2, 38.7, 31.6, 29.5, 28.8, 26.2, 23.3, 22.9, 18.0, 14.3. HRMS calculated requires  $[\text{M-H}]^-$ : 296.2373. Found  $m/z$ : 296.2376.

#### 4b: Synthesis of N-[(4-methoxyphenyl)methyl]-1-(oct-1-yn-1-yl)cyclohexan-1-amine

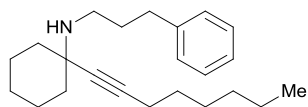


4-methoxybenzylamine (131  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 1-octyne (148  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 5 hours to afford the title compound as a clear light yellow oil in 87% yield (0.285 g, 0.87 mmol) after column chromatography on silica gel (20% EtOAc/hexanes). IR (film) 2928, 2854, 1715, 1612, 1511, 1455, 1244, 1171, 1106, 1037, 822, 732  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 (d,  $J = 8.6$  Hz, 2H), 6.84 (d,  $J = 8.6$  Hz, 2H), 3.89 – 3.71 (m, 5H), 2.26 (t,  $J = 6.9$  Hz, 2H), 1.81 (d,  $J = 12.4$  Hz, 2H), 1.68 – 1.17 (m, 16H), 0.88 (t,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  158.7, 133.7, 129.8, 114.0, 84.7, 84.1, 55.5, 55.0, 47.5, 38.6, 31.6, 29.4, 28.8, 26.2, 23.2, 22.8, 18.9, 14.3. HRMS calculated requires  $[\text{M-H}]^-$ : 326.2478. Found  $m/z$ : 326.2488.

3) O. P. Pereshivko, V. A. Peshkov and E. V. Van der Eycken, *Org. Lett.*, 2010, **12**, 2638.

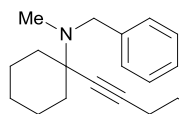
4) O.P. Pereshivko, V. A. Peshkov, D. S. Ermolatev, S. Van Hove, E. V. Van Der Eycken, K. Van Hecke, L. Van Meervelt, *Synthesis*, 2011, 1587.

#### 4c: Synthesis of 1-(oct-1-yn-1-yl)-N-(3-phenylpropyl)cyclohexan-1-amine



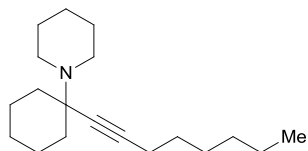
3-phenylpropylamine (  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 1-octyne (148  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 6 hours to afford the title compound as a brown oil in 82% yield (0.267 g, 0.82 mmol) after column chromatography on silica gel (15% EtOAc/hexanes). IR (film) 2927, 2854, 1715, 1603, 1496, 1453, 1121, 907, 733, 697  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 (m, 5H), 2.69 (m, 4H), 2.18 (t,  $J = 6.8$  Hz, 2H), 1.79 (dd,  $J = 16.4, 9.5$  Hz, 4H), 1.69 – 1.08 (m, 16H), 0.89 (t,  $J = 6.8$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  142.5, 128.6, 128.5, 125.9, 84.5, 84.0, 54.7, 43.0, 38.7, 34.1, 32.6, 31.5, 29.3, 28.7, 26.2, 23.3, 22.8, 18.9, 14.3. HRMS calculated requires  $[\text{M-H}]^-$ : 324.2686. Found  $m/z$ : 324.2679.

#### 4d: Synthesis of N-benzyl-N-methyl-1-(oct-1-yn-1-yl)cyclohexan-1-amine



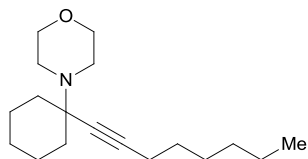
*N*-methylbenzylamine (129  $\mu$ L, 1.0 mmol), cyclohexanone (104  $\mu$ L, 1.0 mmol), 1-octyne (148  $\mu$ L, 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 4 hours to afford the title compound as a light yellow oil in 88% yield (0.274 g, 0.88 mmol) after column chromatography on silica gel (15% EtOAc/hexanes). IR (film) 2927, 2854, 2790, 1604, 1494, 1452, 1237, 959, 733, 697  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.25 (m, 4H), 7.21 (t,  $J = 7.1$  Hz, 1H), 3.58 (s, 2H), 2.27 (t,  $J = 6.8$  Hz, 2H), 2.12 (s, 3H), 2.02 – 1.85 (m, 2H), 1.70 (t,  $J = 10.3$  Hz, 2H), 1.60 – 1.42 (m, 8H), 1.37 – 1.21 (m, 6H), 0.92 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  141.6, 129.0, 128.3, 126.6, 85.5, 80.9, 58.9, 55.8, 37.1, 35.4, 31.6, 29.6, 28.7, 26.1, 23.0, 22.9, 18.9, 14.3. HRMS calculated requires  $[\text{M-H}]^-$ : 310.2529. Found  $m/z$ : 310.2543.

#### 4e: Synthesis of 1-[1-(oct-1-yn-1-yl)cyclohexyl]piperidine



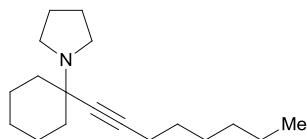
Piperidine (99  $\mu$ L, 1.0 mmol), cyclohexanone (104  $\mu$ L, 1.0 mmol), 1-octyne (148  $\mu$ L, 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 3 hours to afford the title compound as a light yellow oil in 91% yield (0.251 g, 0.91 mmol) after column chromatography on silica gel (10% EtOAc/hexanes). IR (film) 2928, 2853, 2819, 1720, 1453, 1269, 1119, 1034, 973, 921, 882, 791  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.86 – 3.53 (m, 4H), 2.73 – 2.43 (m, 4H), 2.19 (t,  $J = 7.0$  Hz, 2H), 1.86 (d,  $J = 12.5$  Hz, 2H), 1.74 – 1.00 (m, 18H), 0.86 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  86.5, 80.0, 67.7, 58.7, 46.6, 35.8, 31.5, 29.4, 28.7, 25.9, 23.0, 22.8, 18.8, 14.2. HRMS calculated requires  $[\text{M-H}]^-$ : 274.2529. Found  $m/z$ : 274.2530.

#### 4f: Synthesis of 4-[1-(oct-1-yn-1-yl)cyclohexyl]morpholine



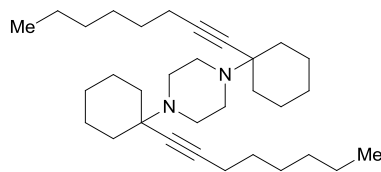
Morpholine (88  $\mu$ L, 1.0 mmol), cyclohexanone (104  $\mu$ L, 1.0 mmol), 1-octyne (148  $\mu$ L, 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 3 hours to afford the title compound as a clear light brown oil in 92% yield (0.255 g, 0.92 mmol) after column chromatography on silica gel (15% EtOAc/hexanes). IR (film) 2927, 2853, 1716, 1453, 1269, 1119, 973, 882, 791  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.81 – 3.62 (m, 4H), 2.70 – 2.49 (m, 4H), 2.19 (t,  $J = 7.0$  Hz, 2H), 1.86 (d,  $J = 12.5$  Hz, 2H), 1.69 – 1.15 (m, 16H), 0.86 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  86.5, 80.0, 67.7, 58.7, 46.6, 35.8, 31.5, 29.4, 28.7, 25.9, 23.0, 22.8, 18.8, 14.2. HRMS calculated requires  $[\text{M-H}]^-$ : 276.2322. Found  $m/z$ : 276.2322.

#### 4g: Synthesis of 1-[1-(oct-1-yn-1-yl)cyclohexyl]pyrrolidine



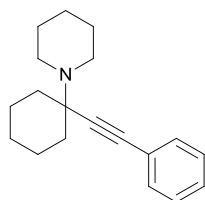
Pyrrolidine (84  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 1-octyne (148  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 2 hours to afford the title compound as a yellow oil in 88% yield (0.229 g, 0.88 mmol) after column chromatography on silica gel (30% EtOAc/hexanes). IR (film) 2927, 2855, 1716, 1678, 1446, 1125, 881, 808, 725  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.71 (t,  $J = 6.1$  Hz, 4H), 2.22 (t,  $J = 6.8$  Hz, 2H), 1.89 (d,  $J = 12.5$  Hz, 2H), 1.82 – 1.68 (m, 4H), 1.68 – 1.02 (m, 16H), 0.90 (t,  $J = 6.8$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  86.0, 80.2, 59.0, 47.0, 38.3, 31.5, 29.5, 28.6, 25.9, 23.6, 23.2, 22.8, 18.8, 14.2. HRMS calculated requires  $[\text{M}-\text{H}]^-$ : 260.2373. Found  $m/z$ : 260.2384.

#### 4h: Synthesis of 1,4-bis[1-(oct-1-yn-1-yl)cyclohexyl]piperazine



Piperazine (86.2 mg, 1.0 mmol), cyclohexanone (208  $\mu\text{L}$ , 2.0 mmol), 1-octyne (296  $\mu\text{L}$ , 2.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 16 hours to afford the title compound as a clear light brown oil in 68% yield (0.316 g, 0.68 mmol) after column chromatography on silica gel (20% EtOAc/hexanes). IR (film) 2927, 2855, 2186, 1720, 1455, 1284, 1128, 979, 907, 797, 731  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.69 (s, 8H), 2.20 (t,  $J = 6.8$  Hz, 4H), 1.93 (d,  $J = 12.1$  Hz, 4H), 1.76 – 1.08 (m, 32H), 0.89 (t,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  86.4, 80.3, 58.3, 46.5, 35.8, 31.4, 29.2, 28.6, 25.8, 23.0, 22.6, 18.8, 14.1. HRMS calculated requires  $[\text{M}-\text{H}]^-$ : 465.4203. Found  $m/z$ : 465.4217.

#### 4i: Synthesis of 1-[1-(2-phenylethynyl)cyclohexyl]piperidine

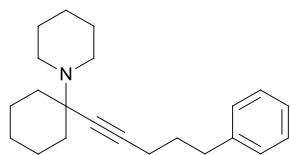


Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), phenylacetylene (110  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 2 hours to afford the title compound as a light yellow oil in 89% yield (0.238 g, 0.89 mmol) after column chromatography on silica gel (8% EtOAc/hexanes). IR (film) 2964, 2928, 2854, 2805, 2219, 1466, 1450, 1441, 1361, 1285, 1263, 1149, 1093, 962, 875, 800, 749, 668  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.38 (m, 2H), 7.32 – 7.23 (m, 3H), 2.66 (s, 4H), 2.08 (d,  $J = 12.3$  Hz, 2H), 1.74 – 1.57 (m, 8H), 1.54 – 1.41 (m, 4H), 1.25 (s, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  131.7, 128.2, 127.6, 123.8, 90.8, 86.1, 59.3, 47.2, 35.8, 26.6, 25.8, 24.8, 23.1. HRMS calculated requires  $[\text{M}+\text{H}]^+$ : 268.2060. Found  $m/z$ : 268.2071.

1) M. Cheng, Q. Zhang, X. Y. Hu, B. G. Li, J. X. Ji and A. S. C. Chan, *Adv. Synth. Catal.*, 2011, **353**, 1274.

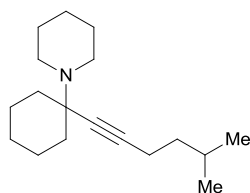
2) A. R. Katritzky, H. Yang, S. K. Singh, *J. Org. Chem.*, 2005, **70**, 286.

#### 4j: Synthesis of 1-[1-(5-phenylpent-1-yn-1-yl)cyclohexyl]piperidine



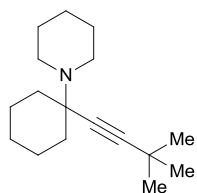
Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 5-phenyl-1-pentyne (152  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 4 hours to afford the title compound as a yellow oil in 78% yield (0.241 g, 0.78 mmol) after column chromatography on silica gel (15% EtOAc/hexanes). IR (film) 2928, 2854, 2800, 1717, 1603, 1495, 1453, 1443, 1244, 1151, 1098, 1077, 964, 908, 731, 697  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 – 7.15 (m, 5H), 2.84 – 2.69 (m, 2H), 2.69 – 2.46 (m, 4H), 2.32 – 2.13 (m, 2H), 1.94 (t,  $J = 15.7$  Hz, 2H), 1.89 – 1.74 (m, 2H), 1.71 – 1.34 (m, 12H), 1.31 – 1.10 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  142.2, 128.7, 128.5, 126.0, 85.5, 81.5, 59.1, 47.2, 36.2, 35.2, 31.4, 26.8, 26.0, 25.0, 23.4, 18.5. HRMS calculated requires  $[\text{M}+\text{Na}]^+$ : 332.2349. Found  $m/z$ : 332.2361.

#### 4k: Synthesis of 1-[1-(5-methylhex-1-yn-1-yl)cyclohexyl]piperidine



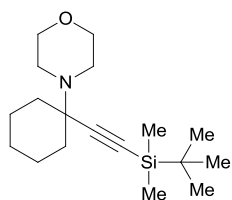
Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 5-methyl-1-hexyne (112  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 3 hours to afford the title compound as an orange crystalline solid in 92% yield (0.240 g, 0.92 mmol) after column chromatography on silica gel (5% EtOAc/hexanes). IR (film) 2927, 2853, 2795, 1722, 1467, 1453, 1442, 1259, 1244, 1152, 1109, 965, 859, 782  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.54 (s, 4H), 2.18 (dt,  $J = 9.4, 7.4$  Hz, 2H), 1.91 (d,  $J = 12.3$  Hz, 2H), 1.75 – 1.45 (m, 10H), 1.44 – 1.29 (m, 6H), 1.20 – 1.11 (m, 1H), 0.92 – 0.84 (m, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  85.9, 80.6, 59.0, 47.1, 38.6, 36.1, 27.4, 26.8, 26.0, 25.0, 23.3, 22.4, 16.9. HRMS calculated requires  $[\text{M}-\text{H}]^-$ : 260.2373. Found  $m/z$ : 260.2371.

#### 4l: Synthesis of 1-[1-(3,3-dimethylbut-1-yn-1-yl)cyclohexyl]piperidine



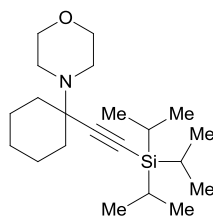
Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 3,3-dimethyl-1-butyne (124  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 2 hours to afford the title compound as a yellow solid in 81% yield (0.200 g, 0.81 mmol) after column chromatography on silica gel (10% EtOAc/hexanes). IR (film) 2964, 2854, 2806, 2748, 2218, 1466, 1451, 1441, 1361, 1285, 1263, 1150, 1093, 1019, 962, 876, 800, 749, 668  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.51 (s, 4H), 1.88 (d,  $J = 12.3$  Hz, 2H), 1.73 – 1.42 (m, 10H), 1.42 – 1.23 (m, 4H), 1.18 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  95.1, 78.7, 58.8, 47.0, 36.1, 31.8, 27.6, 26.8, 26.0, 25.0, 23.4. HRMS calculated requires  $[\text{M}-\text{H}]^-$ : 246.2216. Found  $m/z$ : 246.2226.

#### 4m: Synthesis of 4-{1-[2-(tert-butyldimethylsilyl)ethynyl]cyclohexyl}morpholine



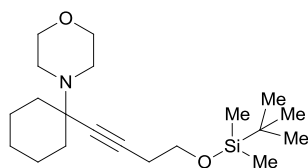
Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), (*tert*-butyldimethylsilyl)acetylene (187  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 5 hours to afford the title compound as a white crystalline solid in 91% yield (0.279 g, 0.91 mmol) after column chromatography on silica gel (4% EtOAc/hexanes). IR (film) 2947, 2927, 2890, 2850, 2153, 1467, 1447, 1270, 1255, 1247, 1168, 1118, 961, 882, 852, 836, 823, 806, 771, 683  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.75 – 3.64 (m, 4H), 2.68 – 2.52 (m, 4H), 1.91 (d,  $J = 12.5$  Hz, 2H), 1.66 (dd,  $J = 8.4, 4.0$  Hz, 2H), 1.54 (dd,  $J = 13.7, 5.4$  Hz, 2H), 1.39 – 1.30 (m, 2H), 1.27 – 1.11 (m, 2H), 0.92 (s, 9H), 0.08 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  106.9, 88.3, 67.7, 59.1, 46.7, 35.7, 26.3, 25.9, 22.9, 16.7, -4.1. HRMS calculated requires  $[\text{M}-\text{H}]^-$ : 306.2248. Found  $m/z$ : 306.2259.

#### 4n: Synthesis of 4-(1-{2-[tris(propan-2-yl)silyl]ethynyl}cyclohexyl)morpholine

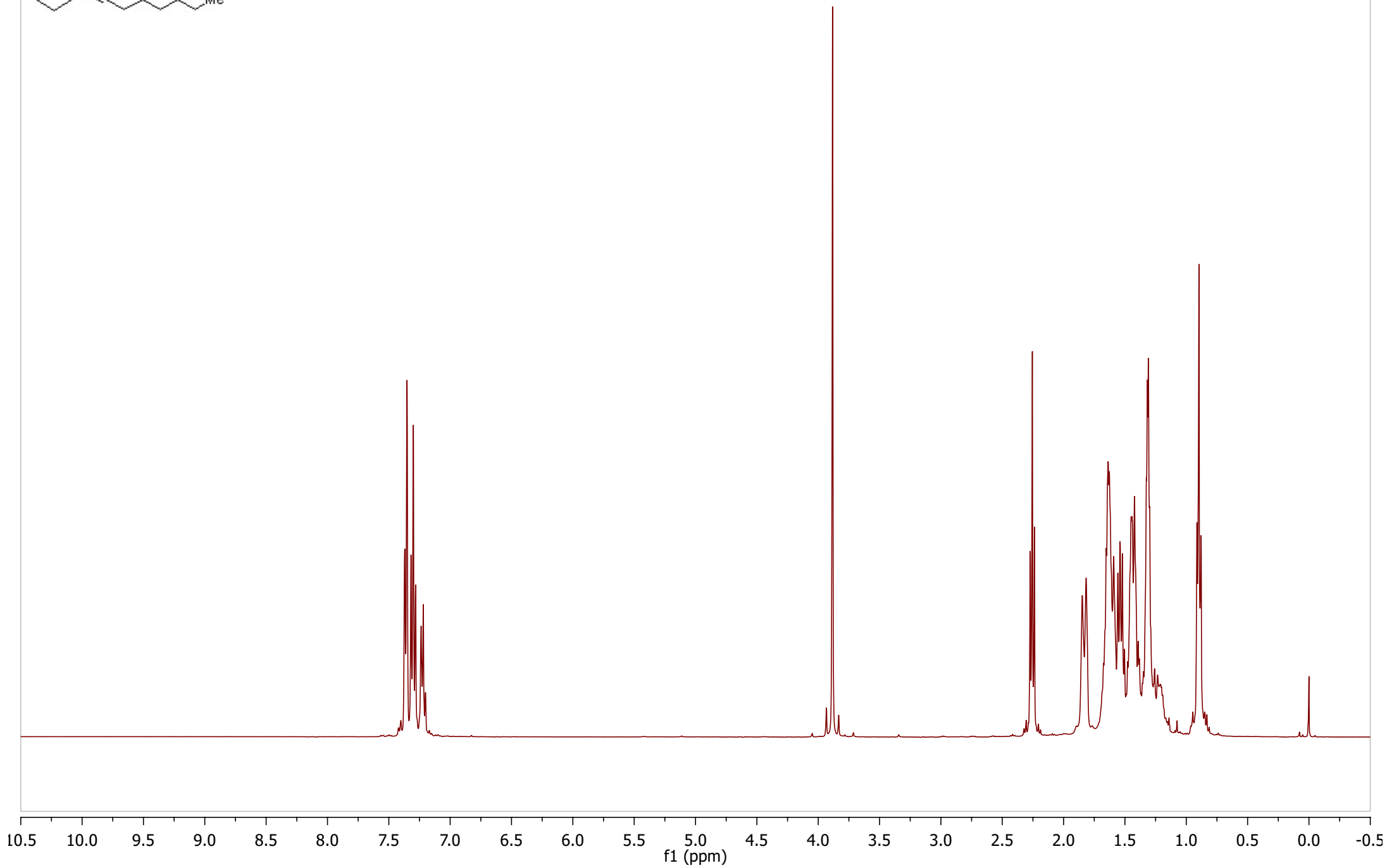
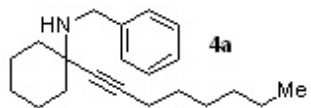


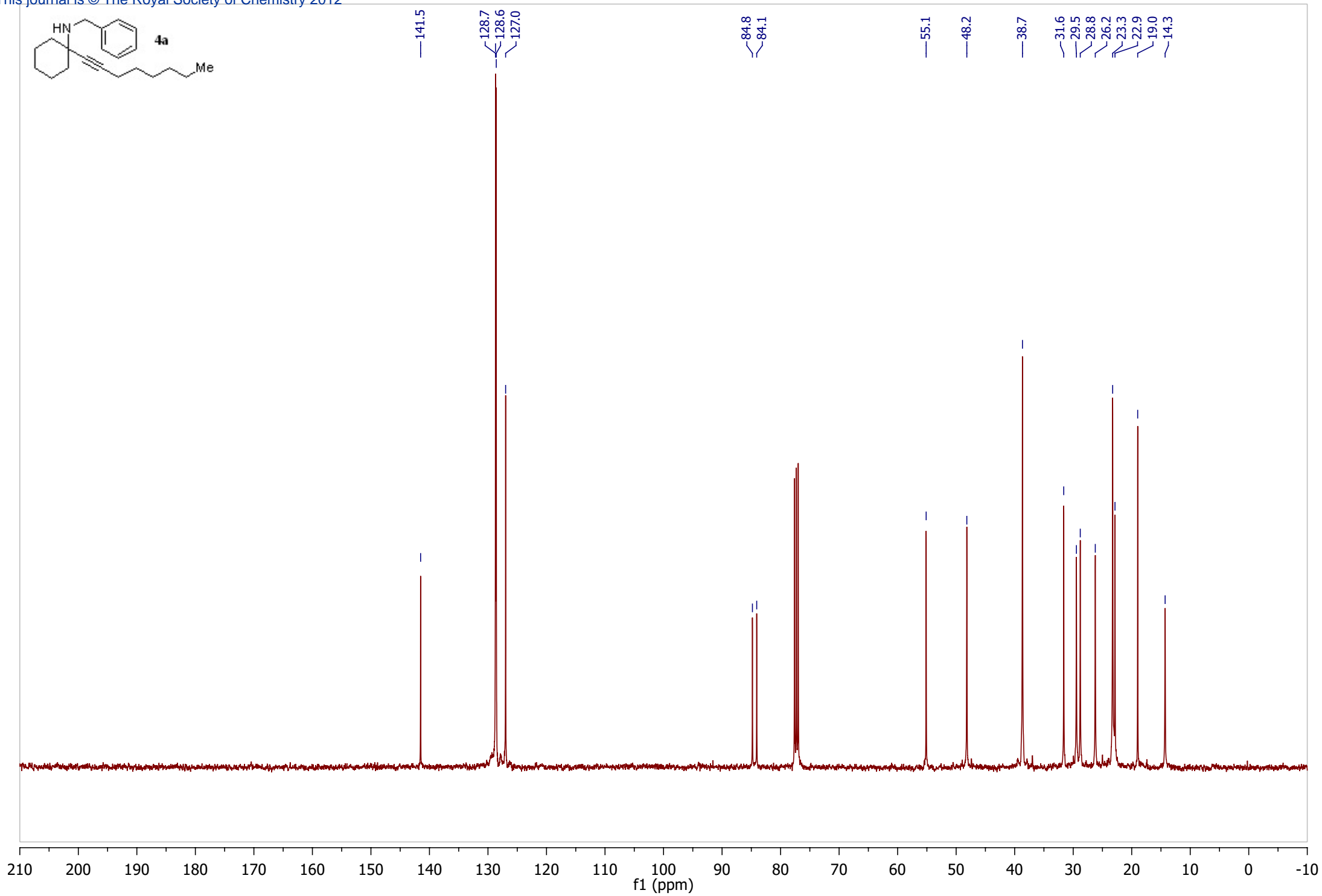
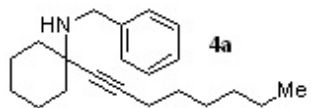
Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), triisopropylsilylacetylene (225  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 6 hours to afford the title compound as a clear oil in 73% yield (0.253 g, 0.73 mmol) after column chromatography on silica gel (3% EtOAc/hexanes). IR (film) 2931, 2861, 2819, 2156, 1454, 1383, 1269, 1119, 973, 920, 881, 846, 734, 674  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.77 – 3.61 (m, 4H), 2.67 – 2.52 (m, 4H), 1.94 (d,  $J = 12.5$  Hz, 2H), 1.74 – 1.40 (m, 6H), 1.32 (td,  $J = 12.2, 3.6$  Hz, 2H), 1.17 – 0.98 (m, 21H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  108.1, 86.0, 67.7, 59.2, 46.8, 35.9, 25.9, 23.0, 18.9, 11.4. HRMS calculated requires  $[\text{M}-\text{H}]^-$ : 348.2717. Found  $m/z$ : 348.2710.

#### 4o: Synthesis of 4-(1-{4-[(*tert*-butyldimethylsilyloxy)but-1-yn-1-yl]cyclohexyl)morpholine

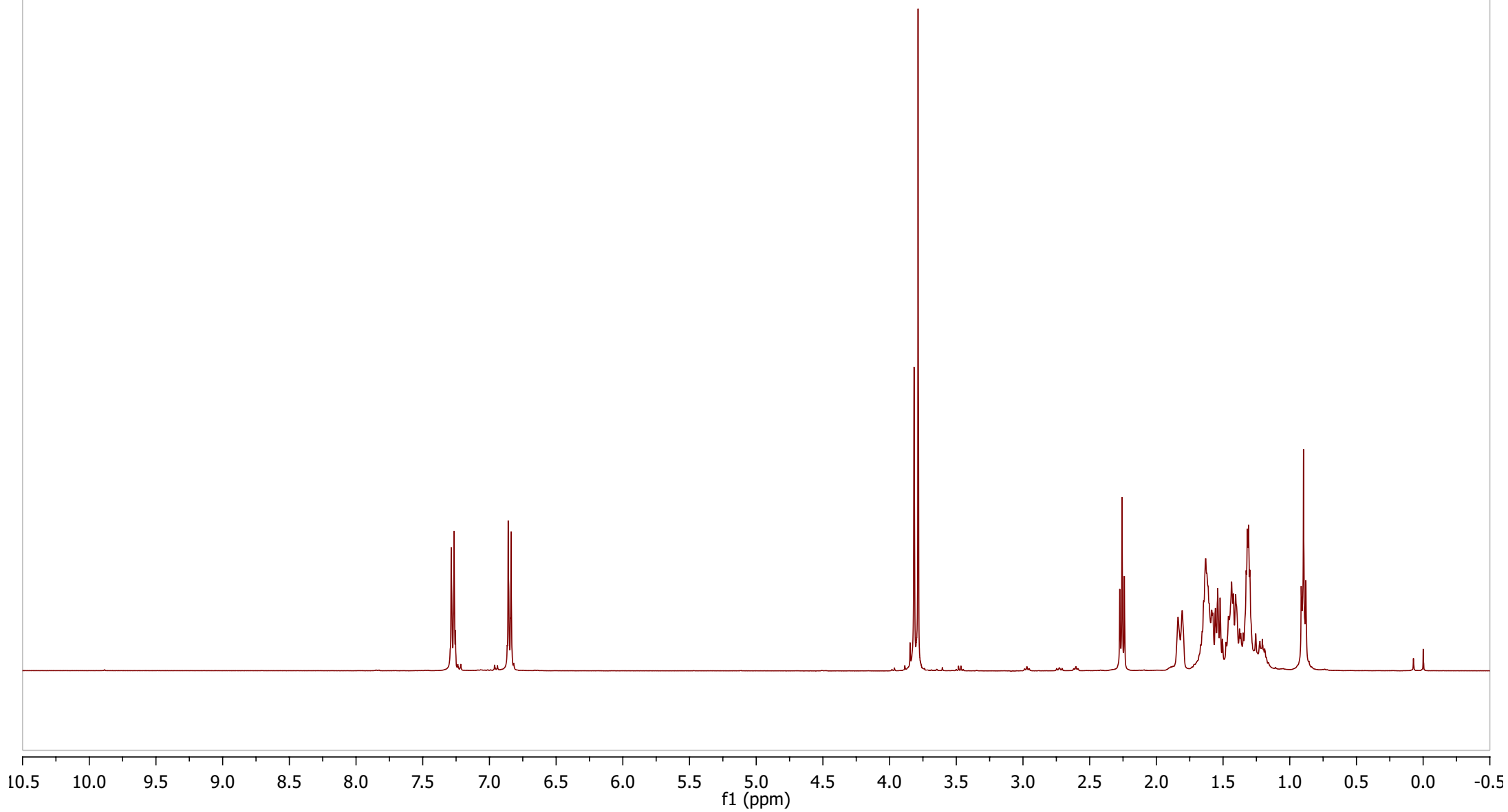
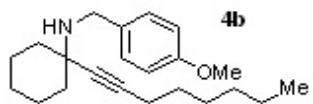


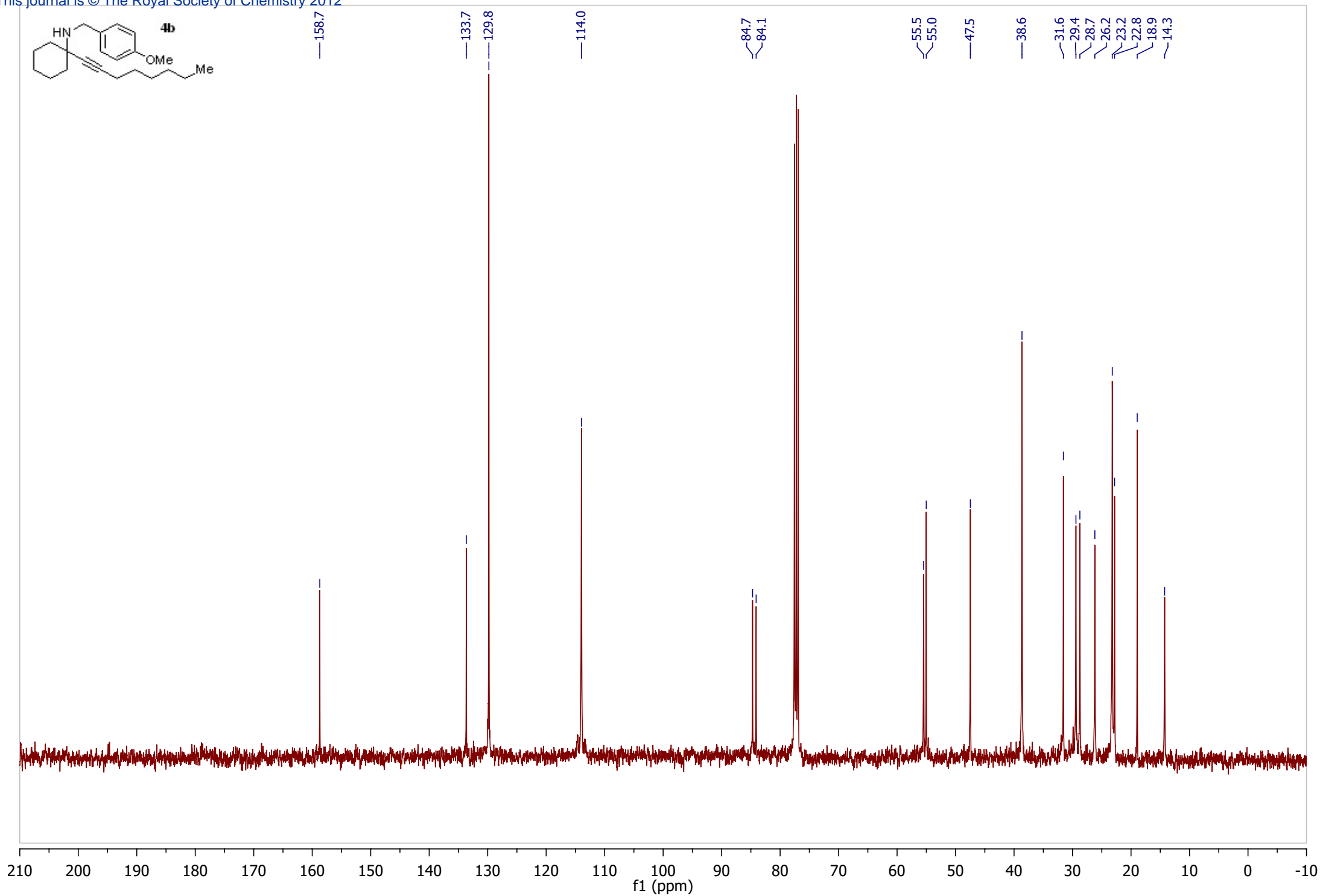
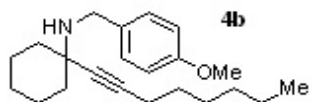
Piperidine (99  $\mu\text{L}$ , 1.0 mmol), cyclohexanone (104  $\mu\text{L}$ , 1.0 mmol), 4-(*tert*-butyldimethylsilyloxy)-1-butyne (207  $\mu\text{L}$ , 1.0 mmol),  $\text{CuCl}_2$  (6.8 mg, 0.05 mmol) was stirred at 110  $^\circ\text{C}$  for 6 hours to afford the title compound as a light brown oil in 84% yield (0.295 g, 0.84 mmol) after column chromatography on silica gel (15% EtOAc/hexanes). IR (film) 2928, 2854, 2820, 1716, 1453, 1269, 1256, 1118, 1104, 974, 920, 882, 834, 774, 732, 664  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.69 (m, 6H), 2.67 – 2.47 (m, 4H), 2.41 (t,  $J = 7.1$  Hz, 2H), 1.84 (d,  $J = 12.6$  Hz, 2H), 1.63 (d,  $J = 4.8$  Hz, 2H), 1.54 – 1.47 (m, 2H), 1.40 – 1.30 (m, 2H), 1.28 – 1.07 (m, 2H), 0.86 (s, 9H), 0.04 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  83.1, 81.0, 67.7, 62.6, 58.6, 46.6, 35.7, 26.1, 26.0, 25.9, 23.3, 22.8, 18.5, -5.1. HRMS calculated requires  $[\text{M}+\text{H}]^+$ : 352.2672. Found  $m/z$ : 352.3046.

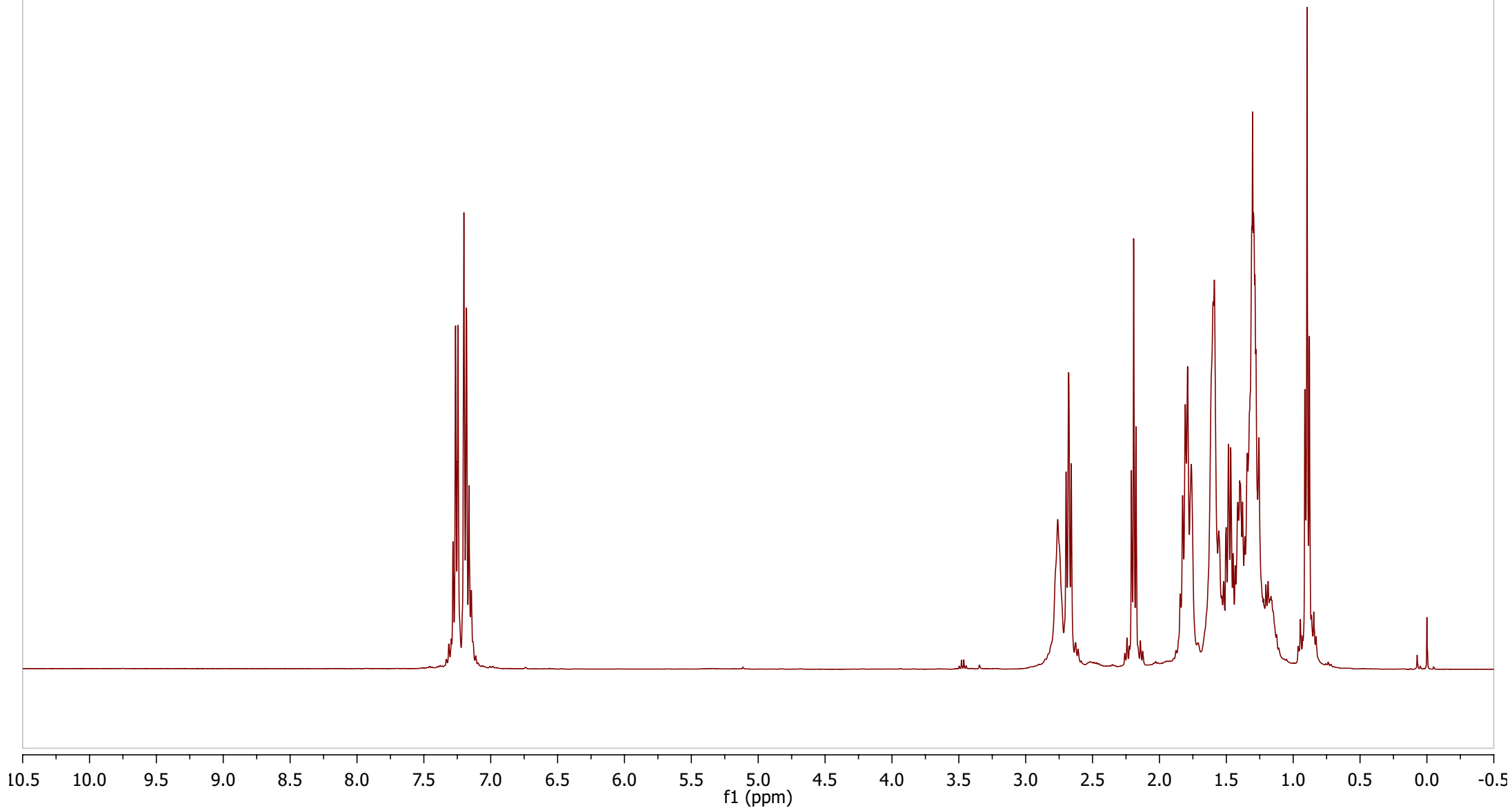
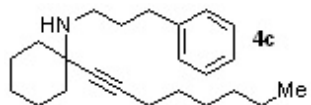


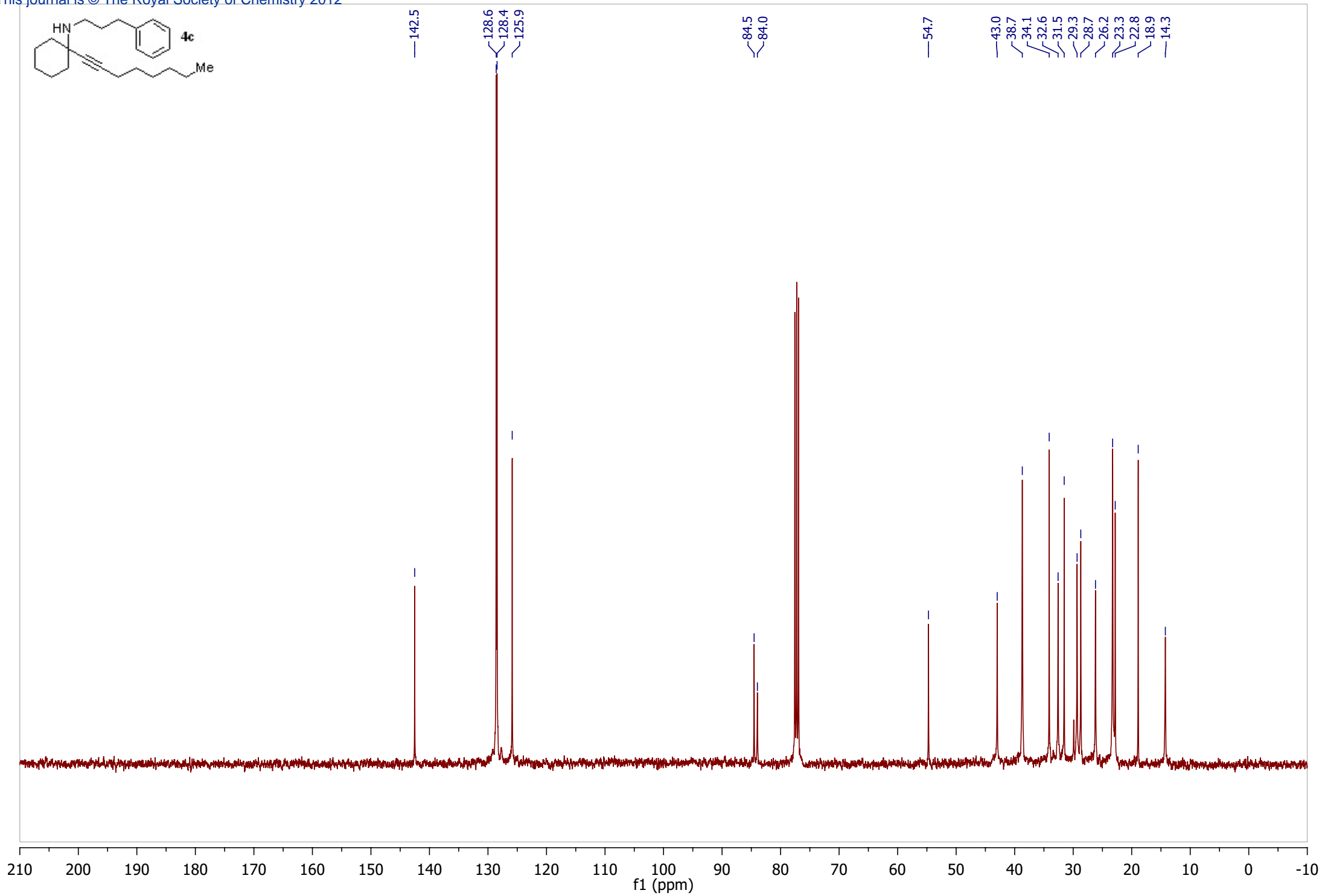
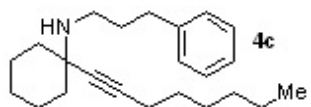


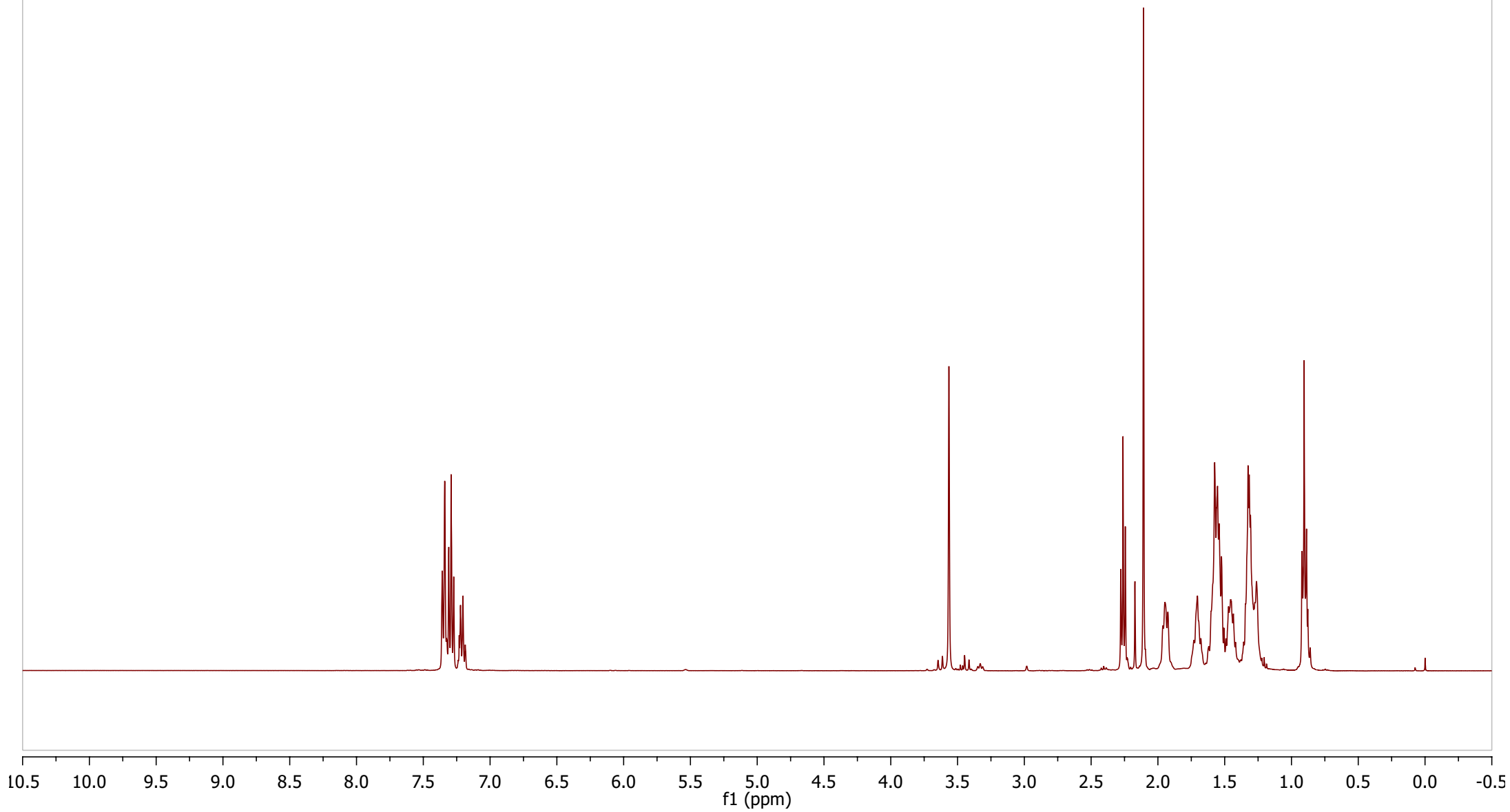
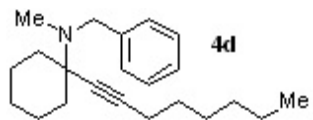


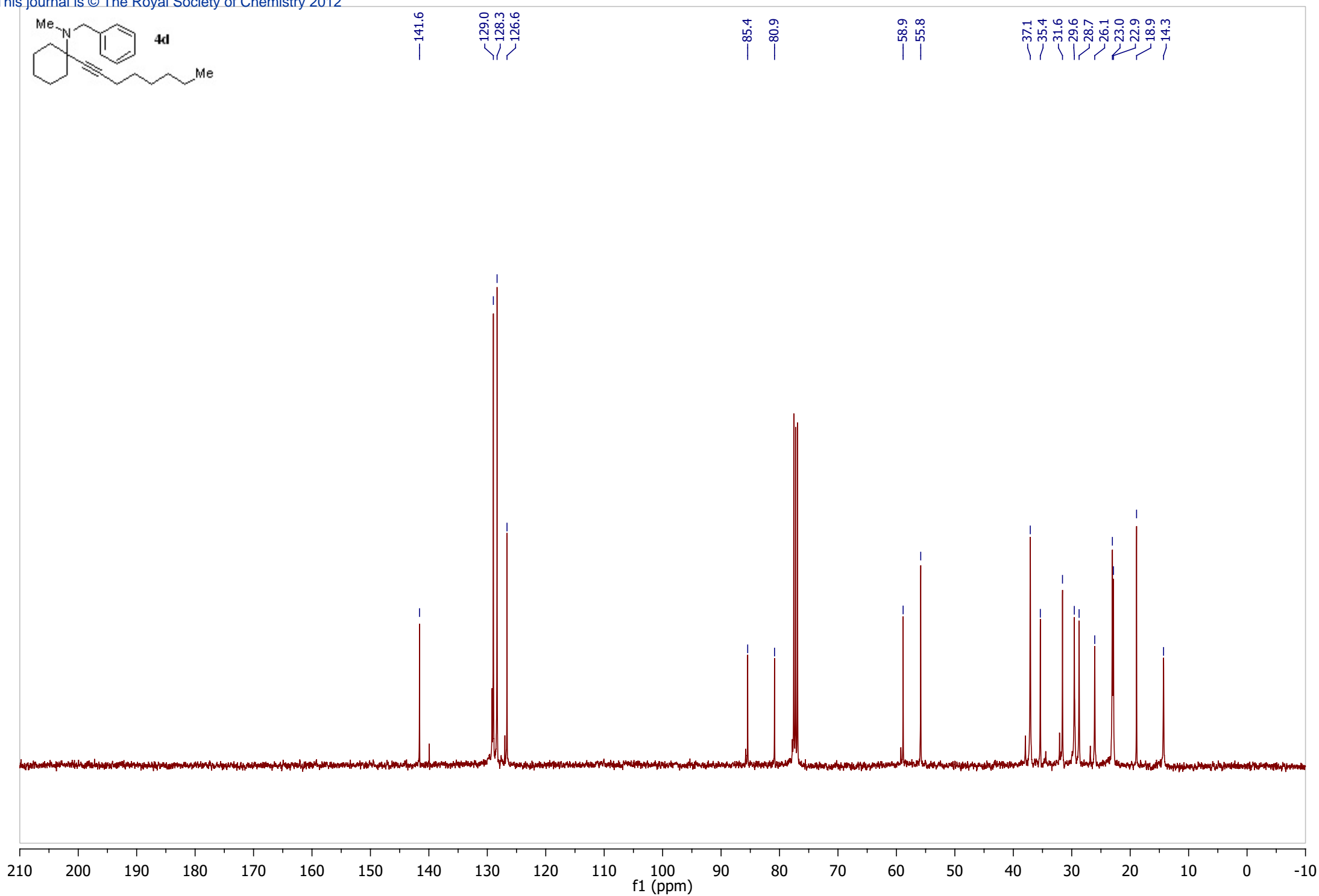
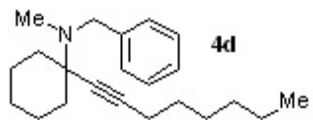


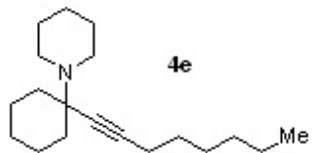






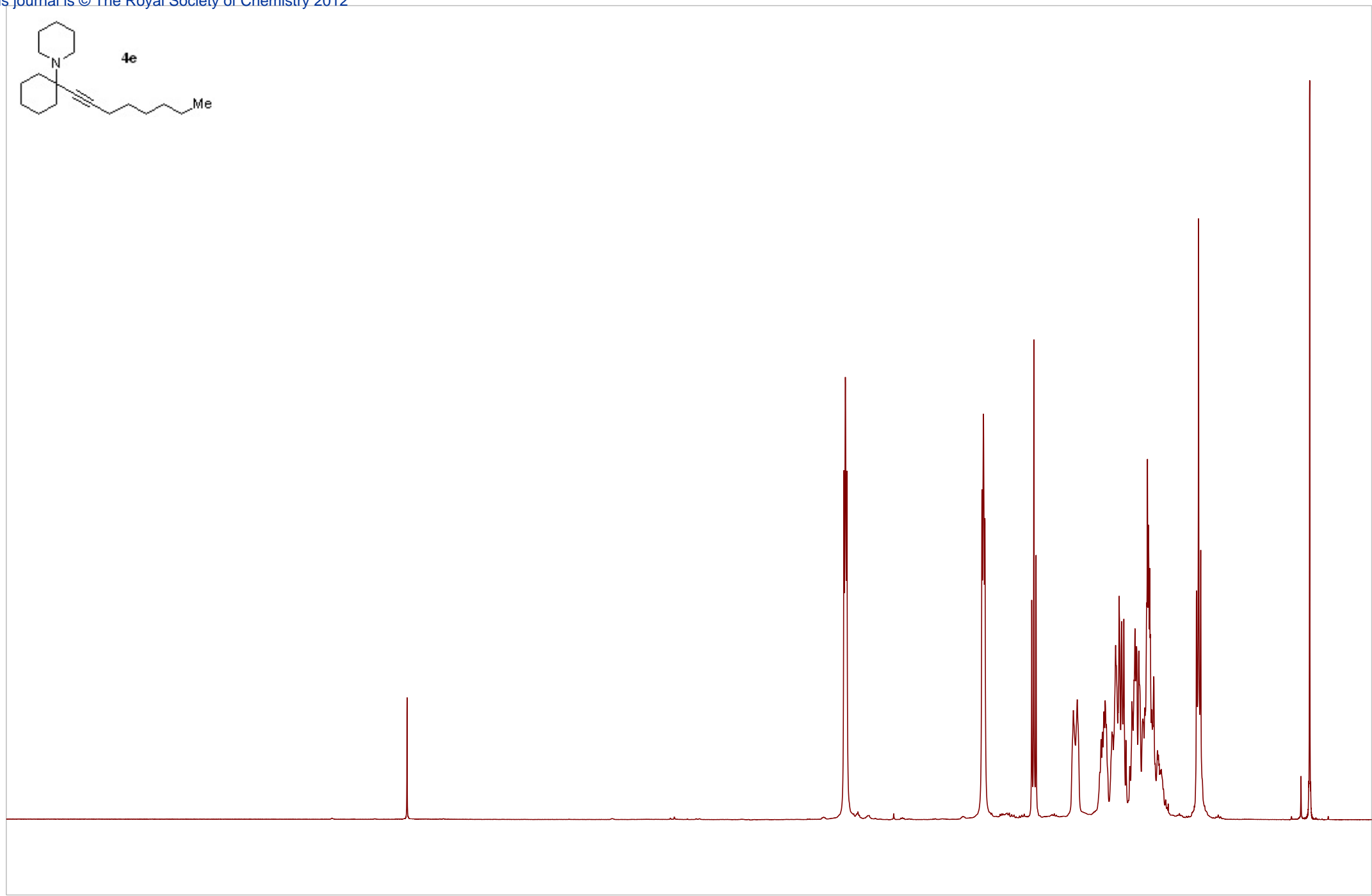


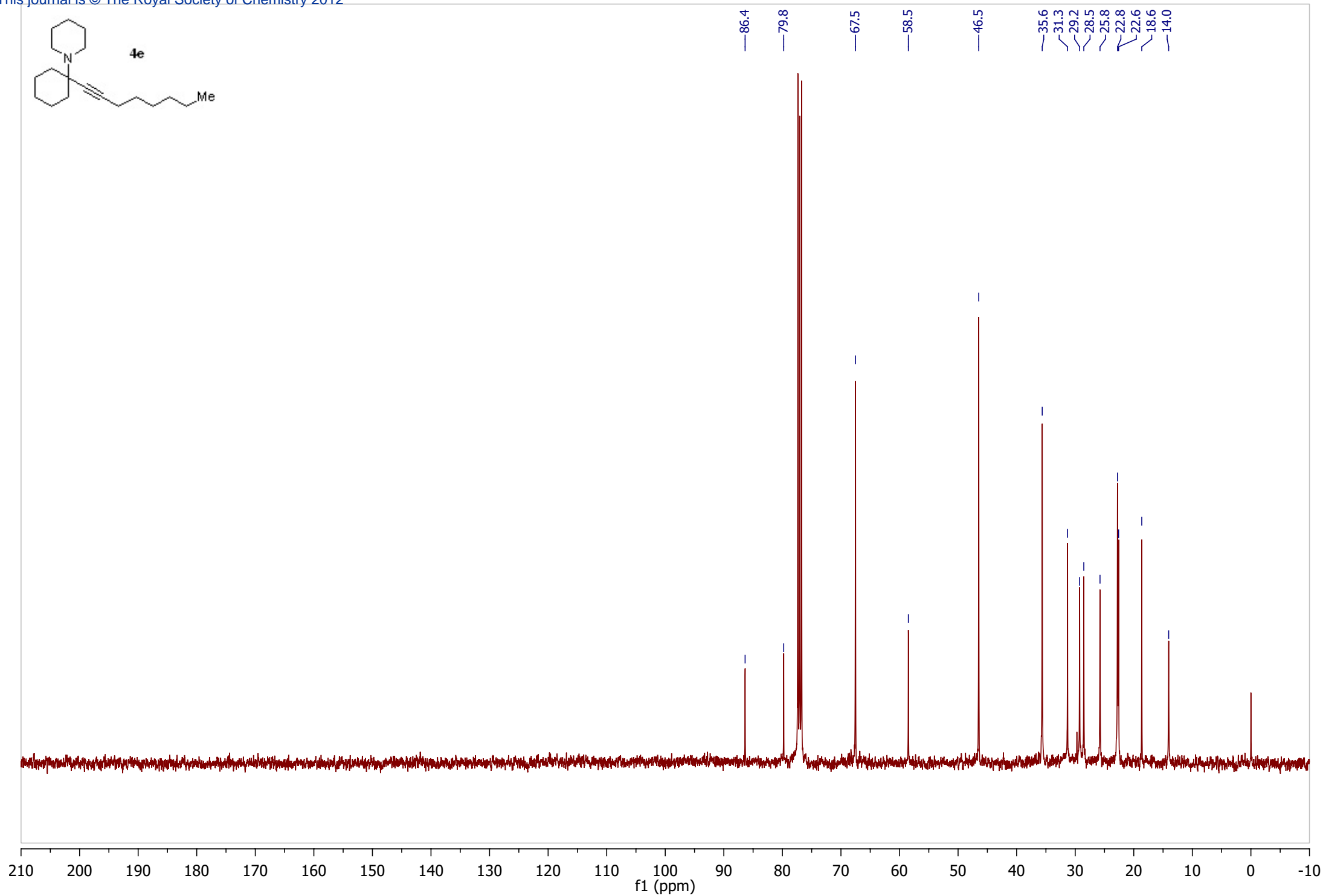
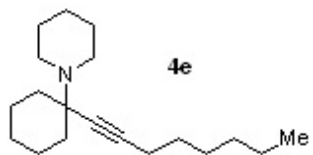




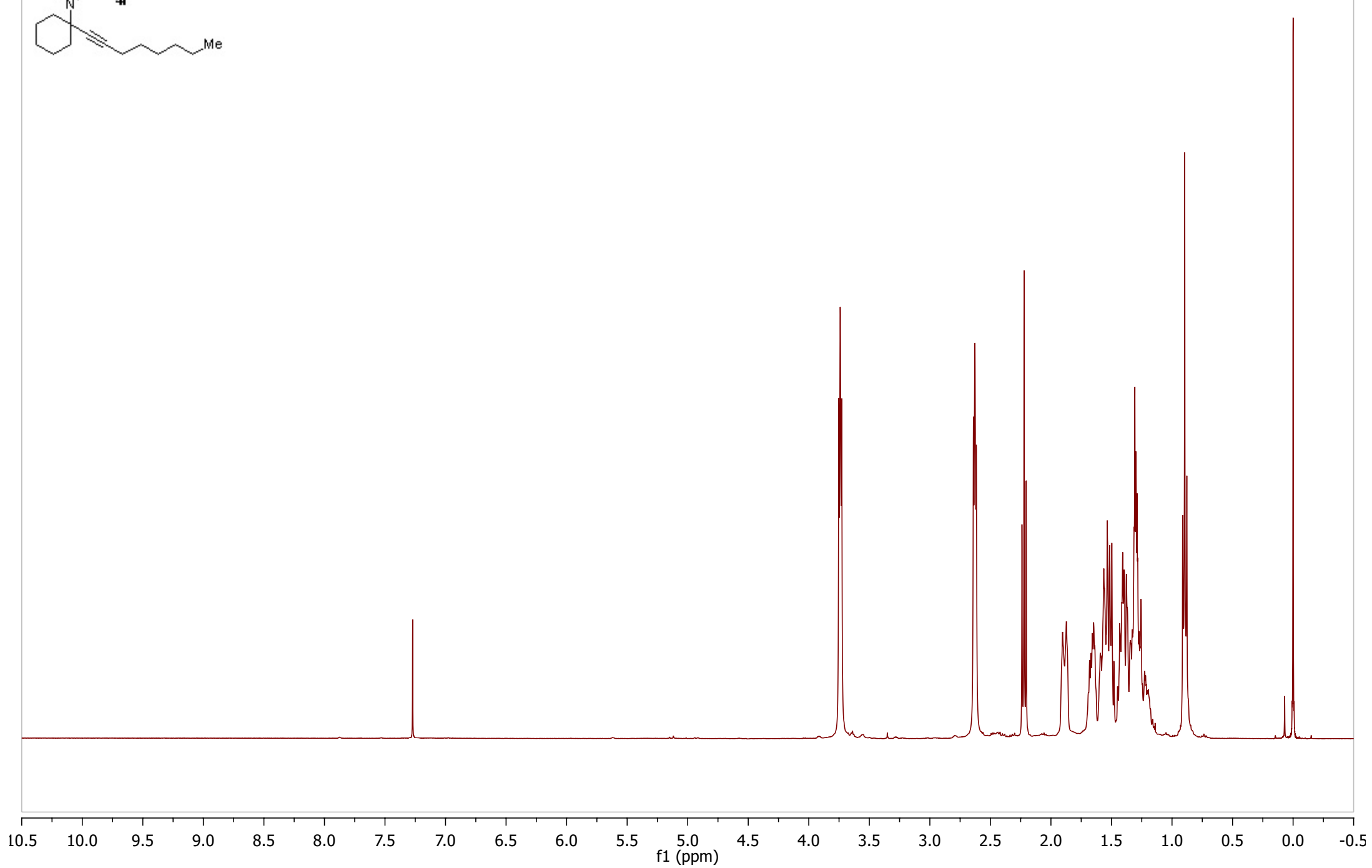
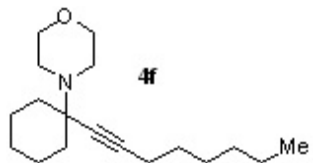
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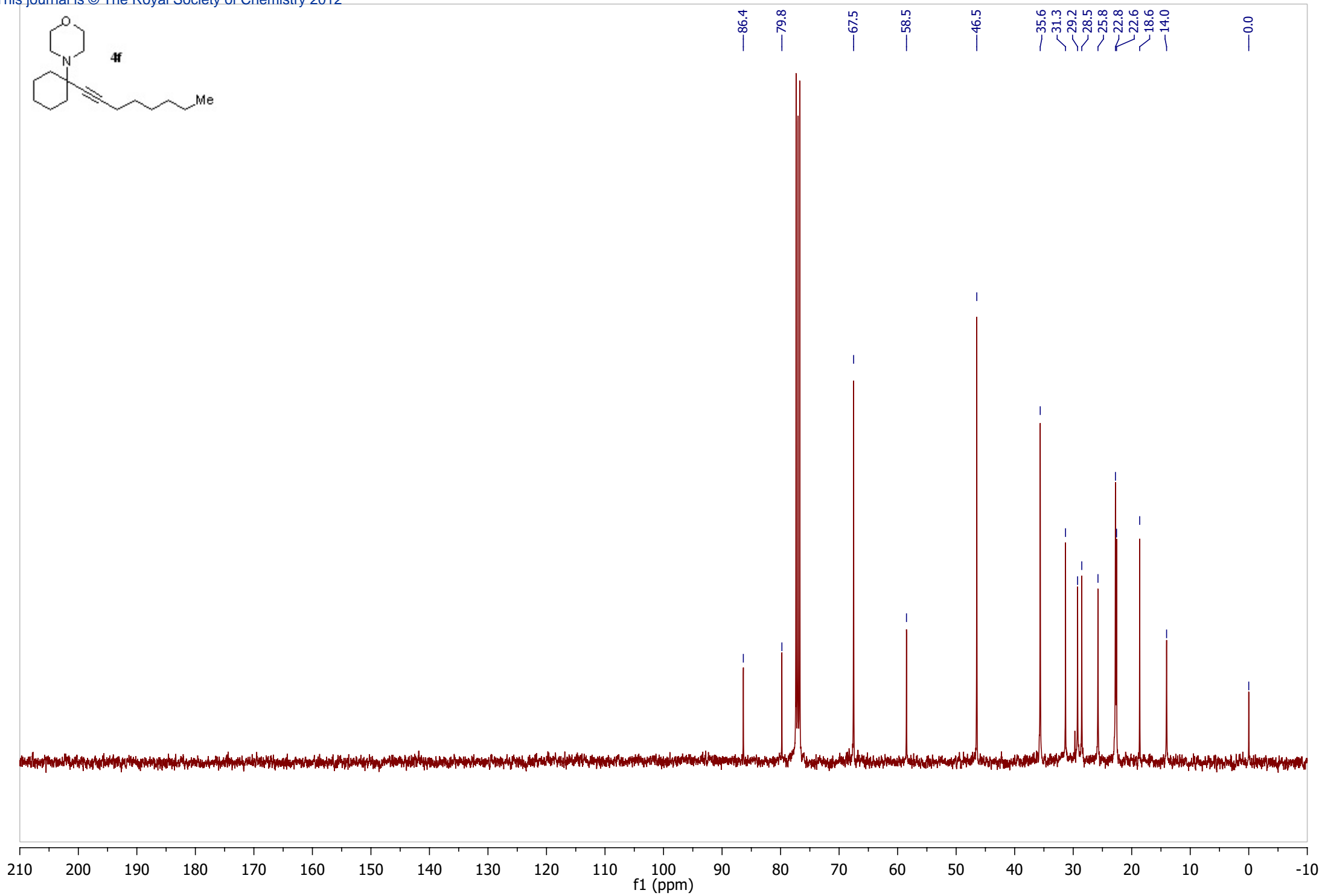
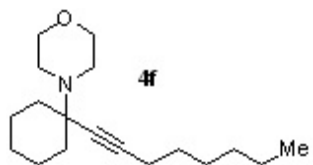
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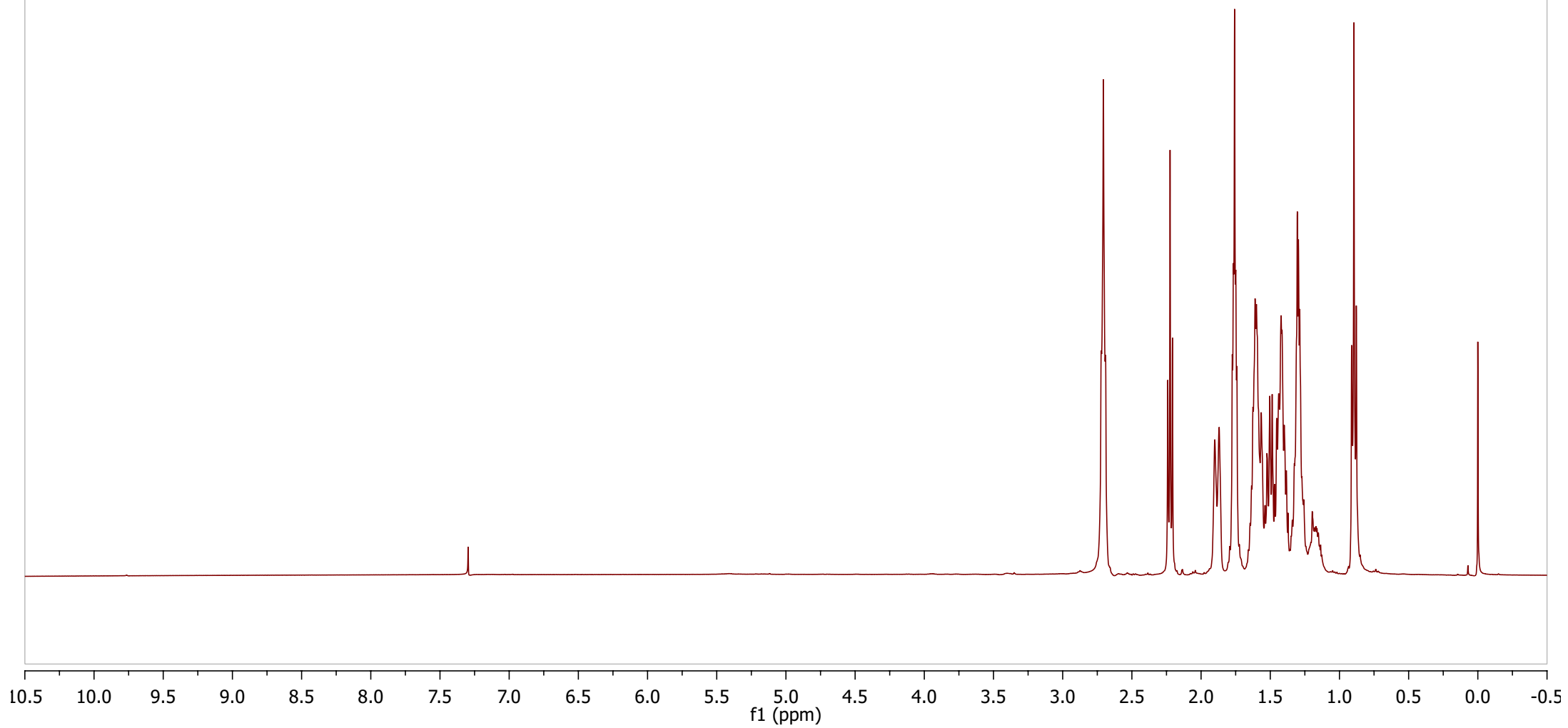
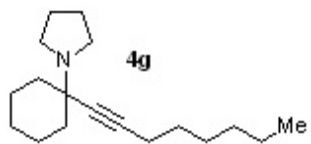


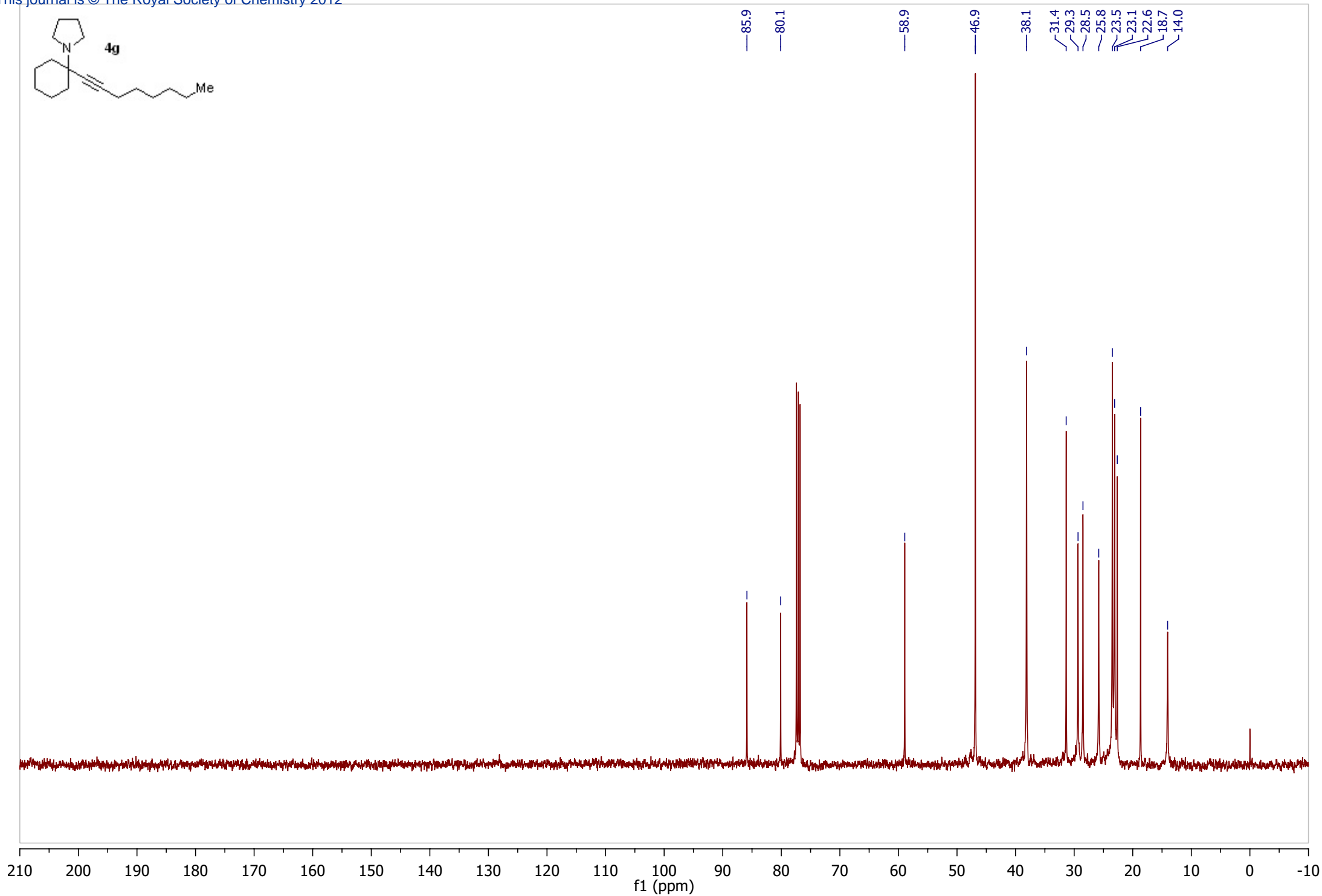
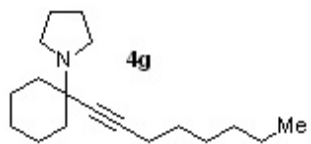


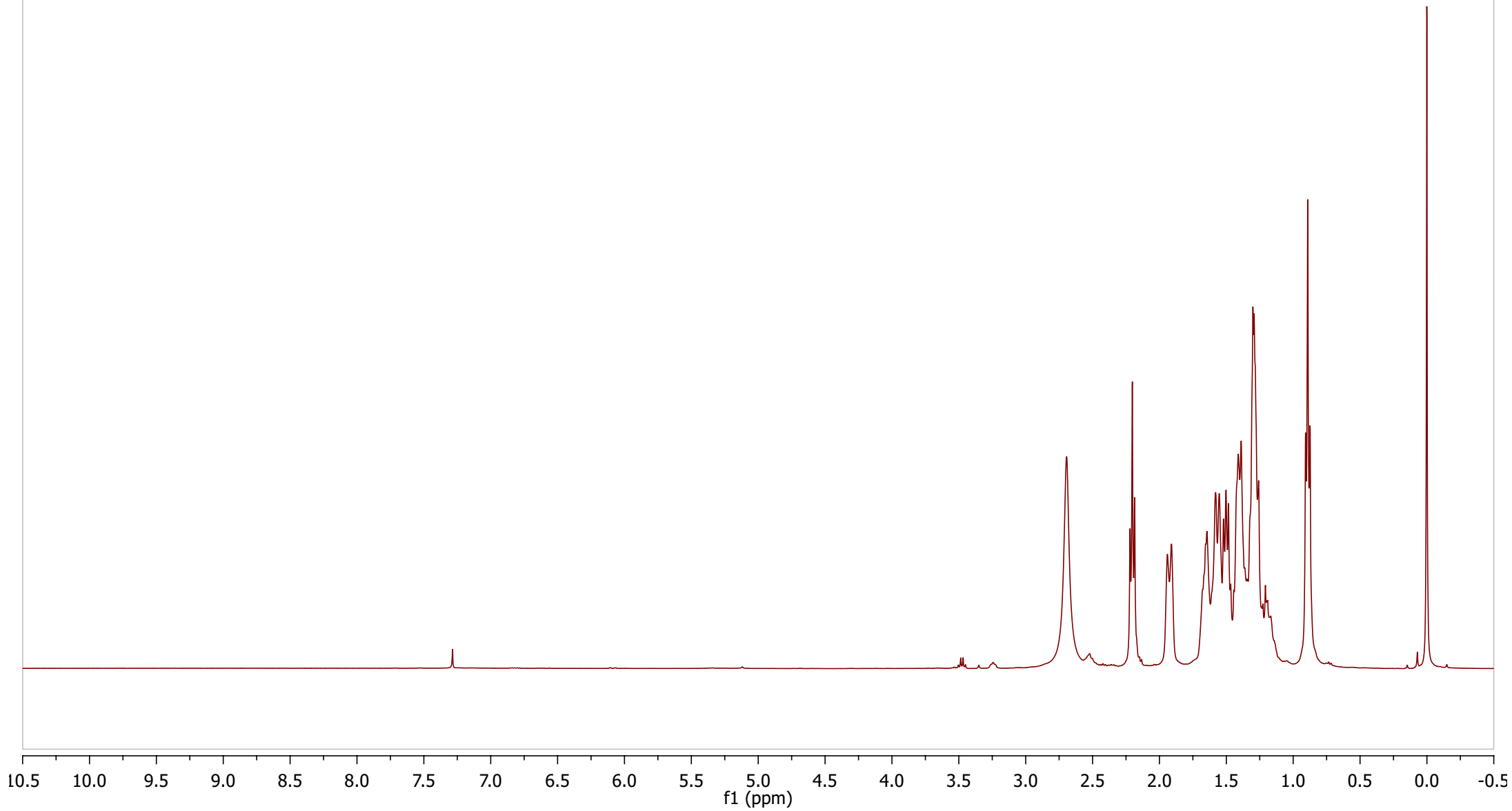
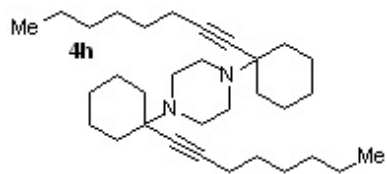


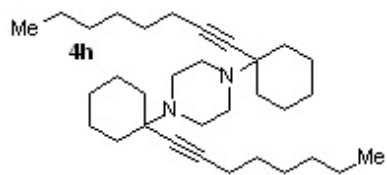




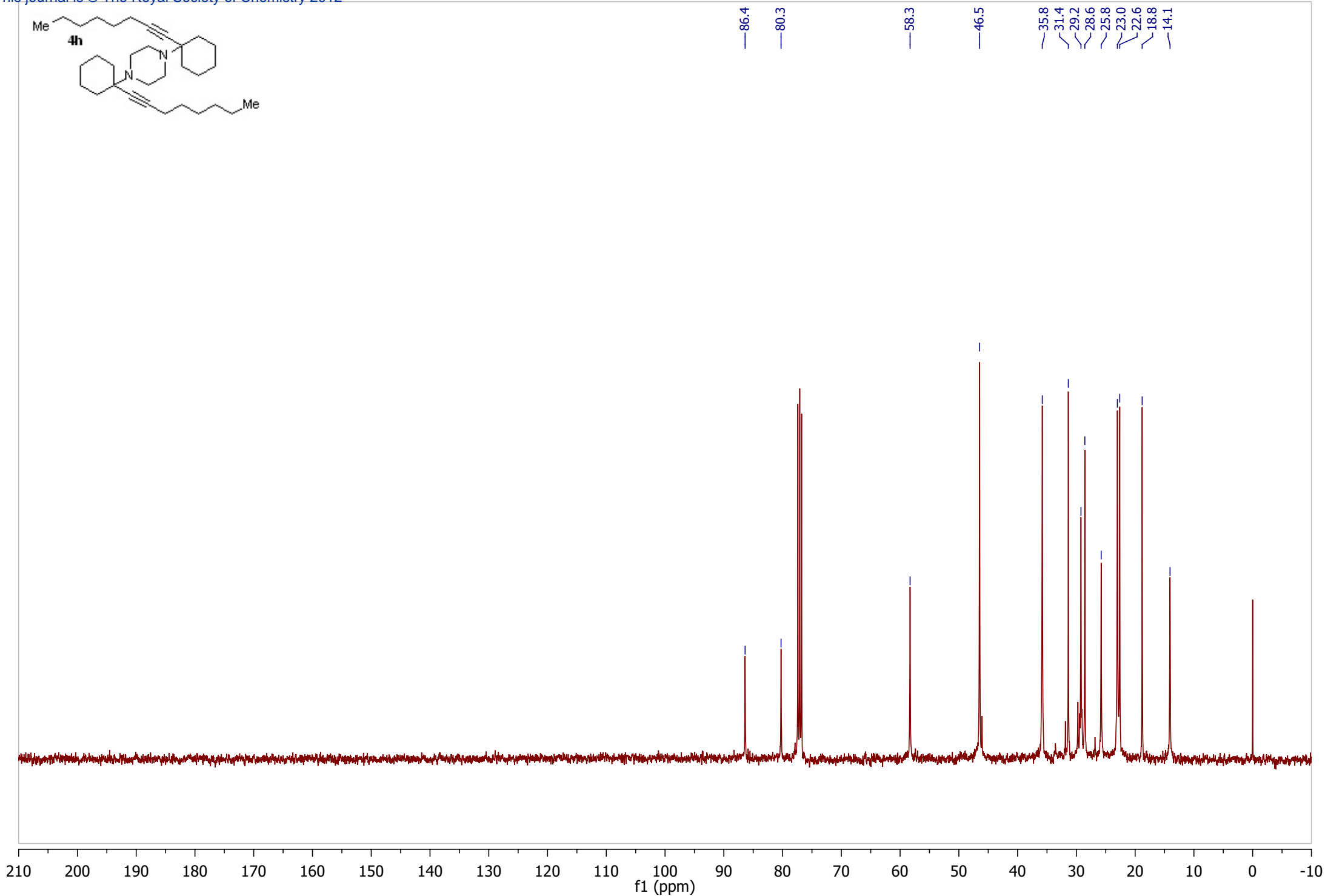


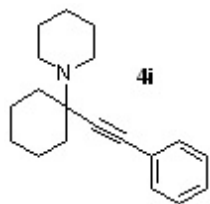




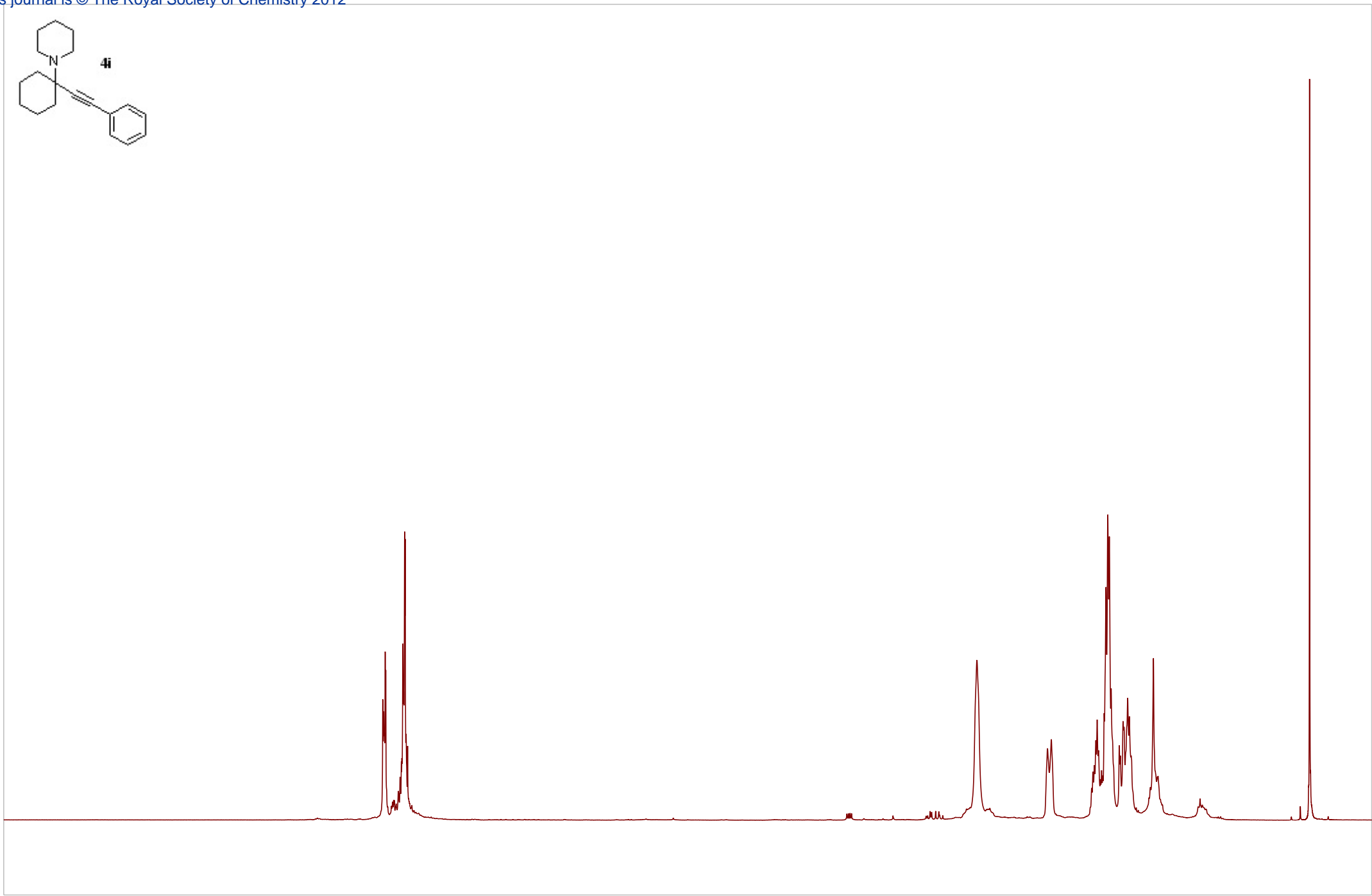


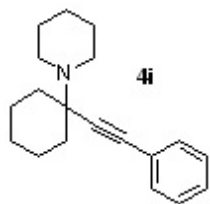
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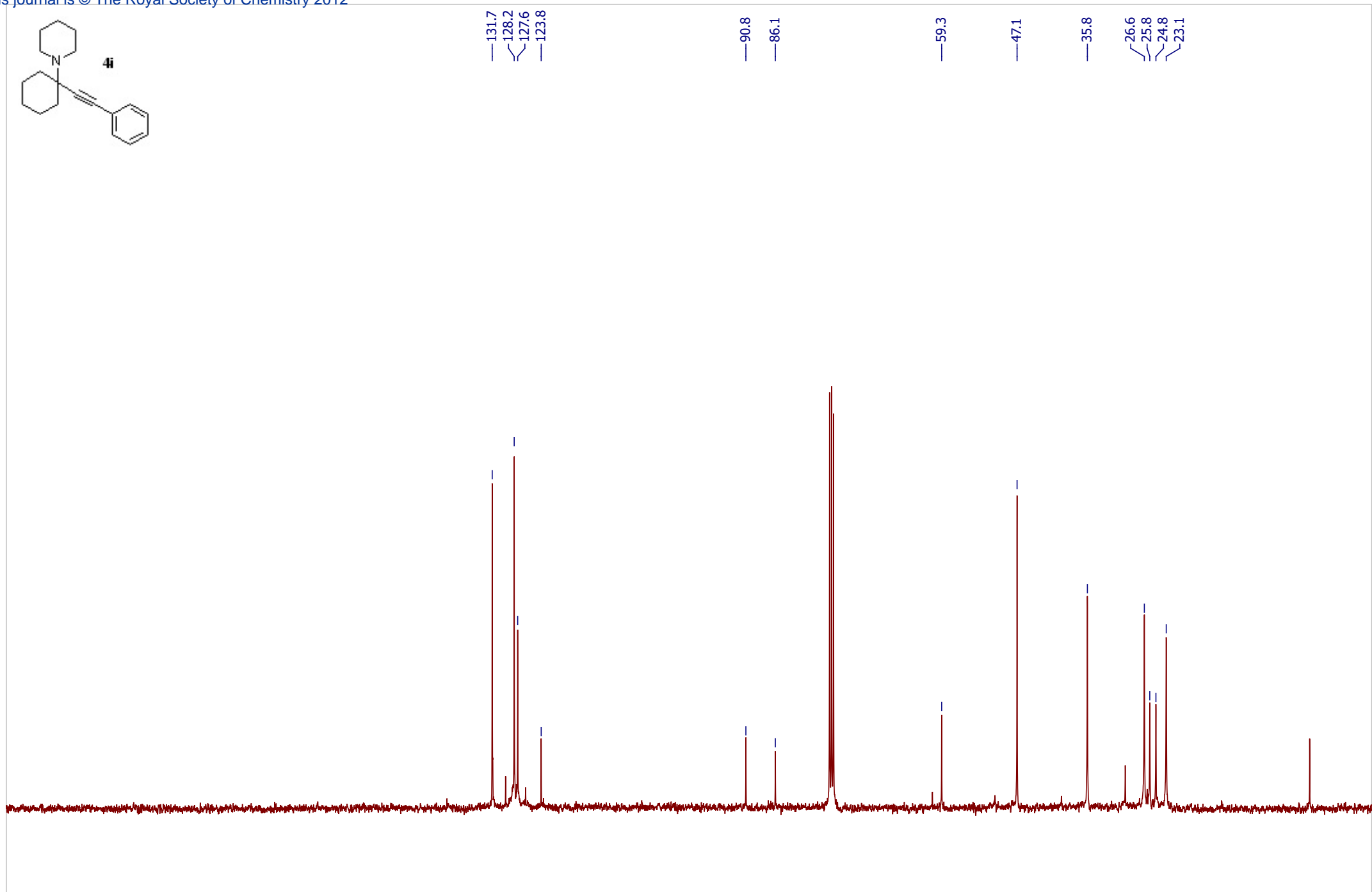
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f1 (ppm)



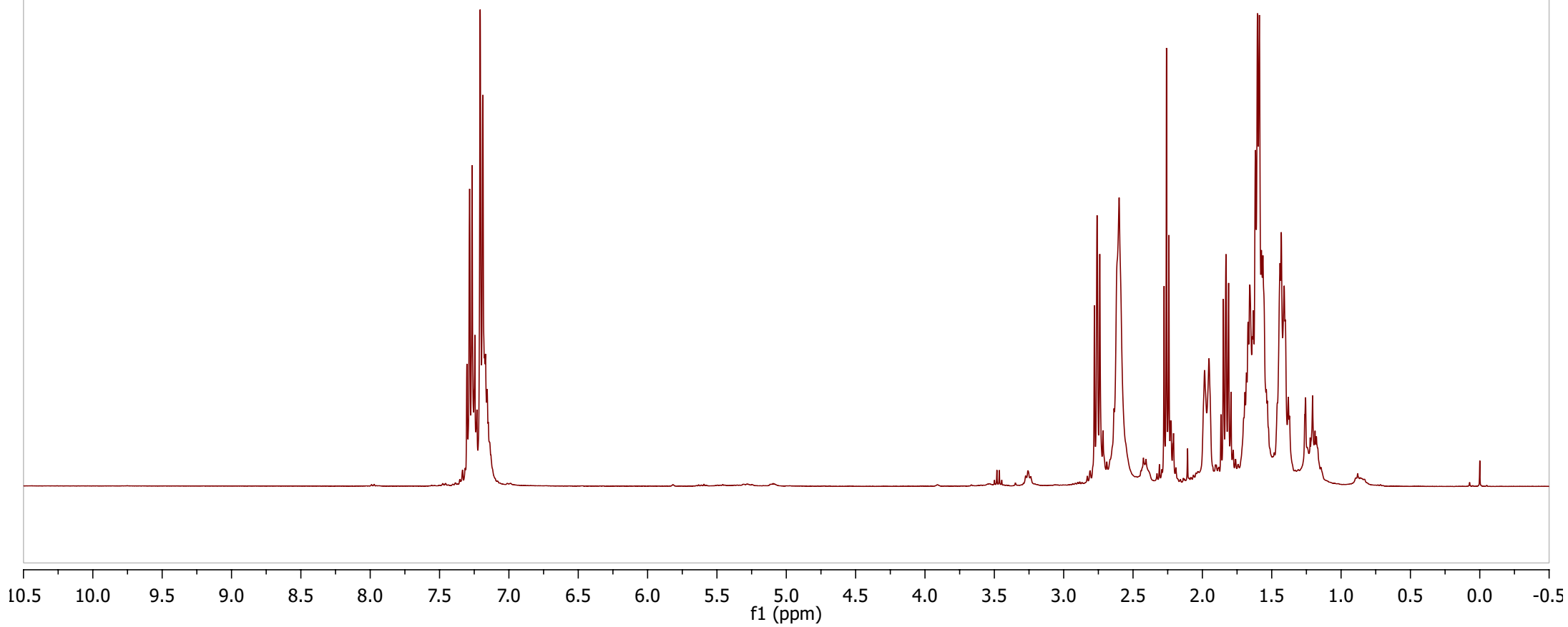
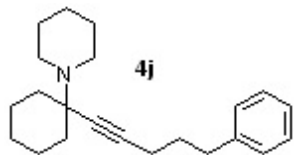


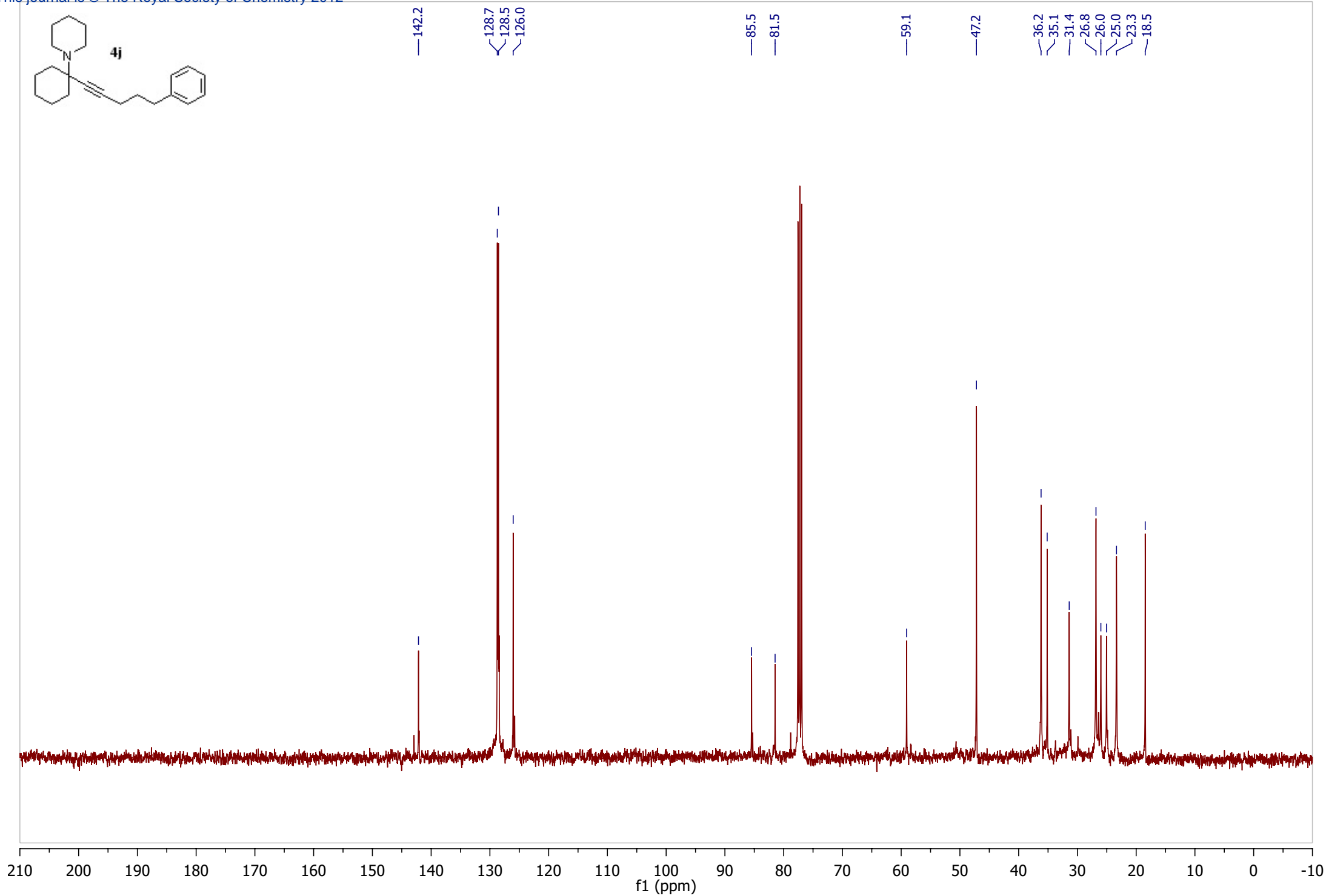
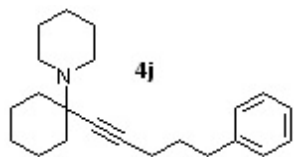
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24.8  
23.1

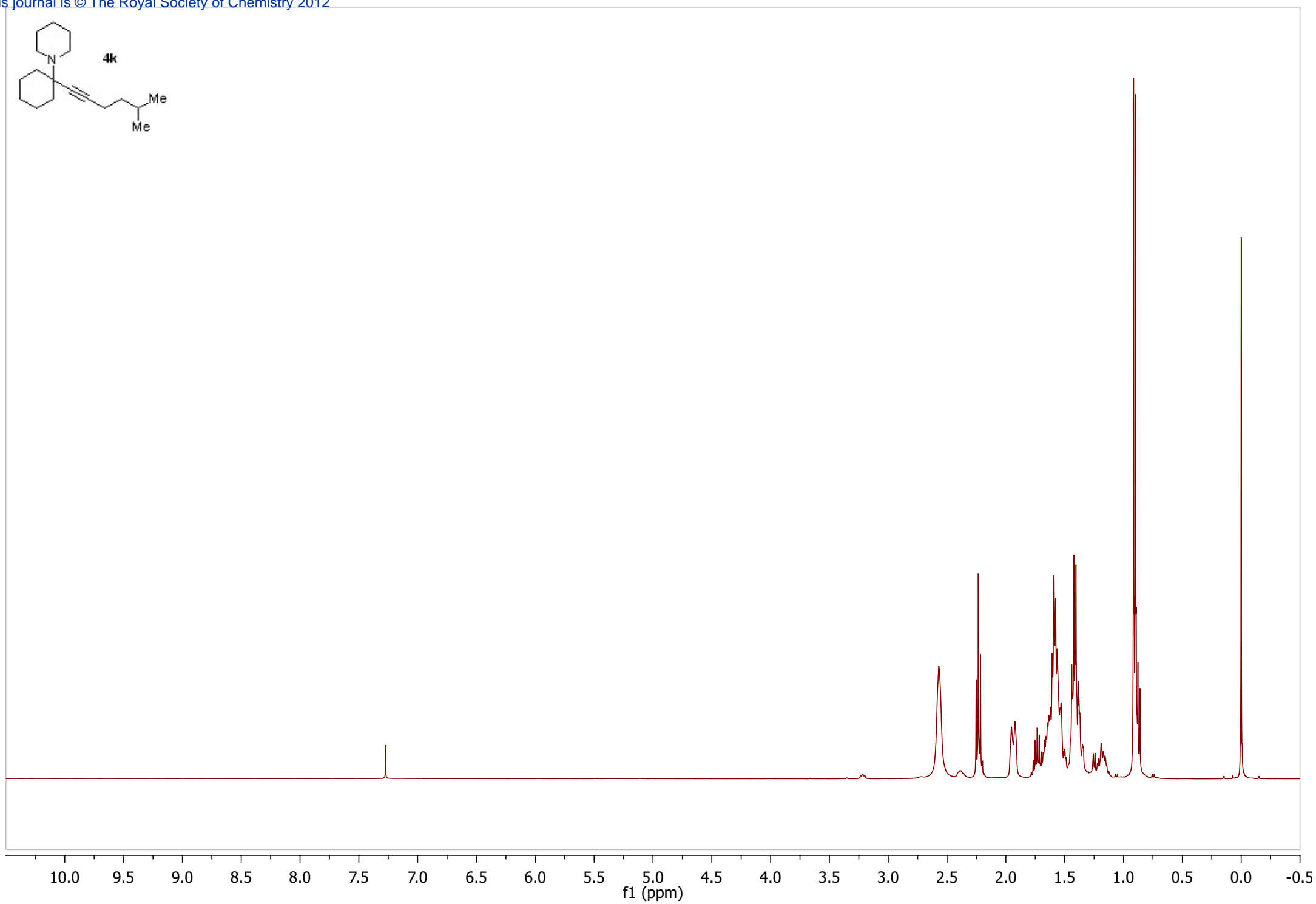
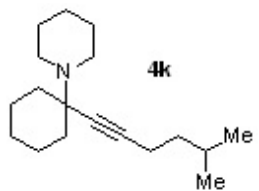
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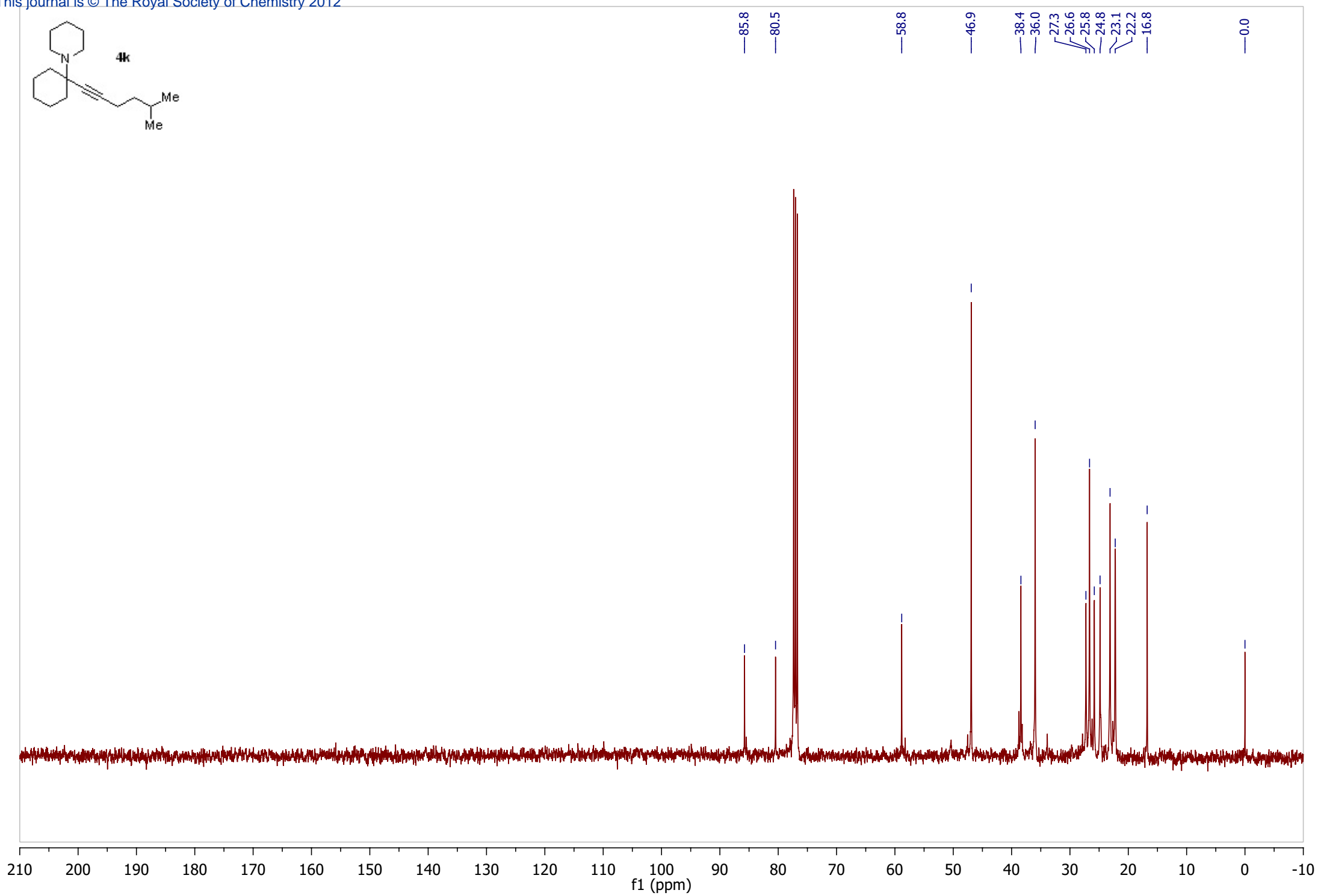
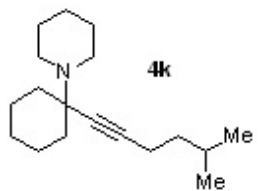


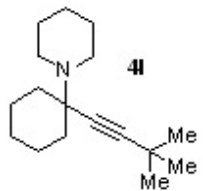




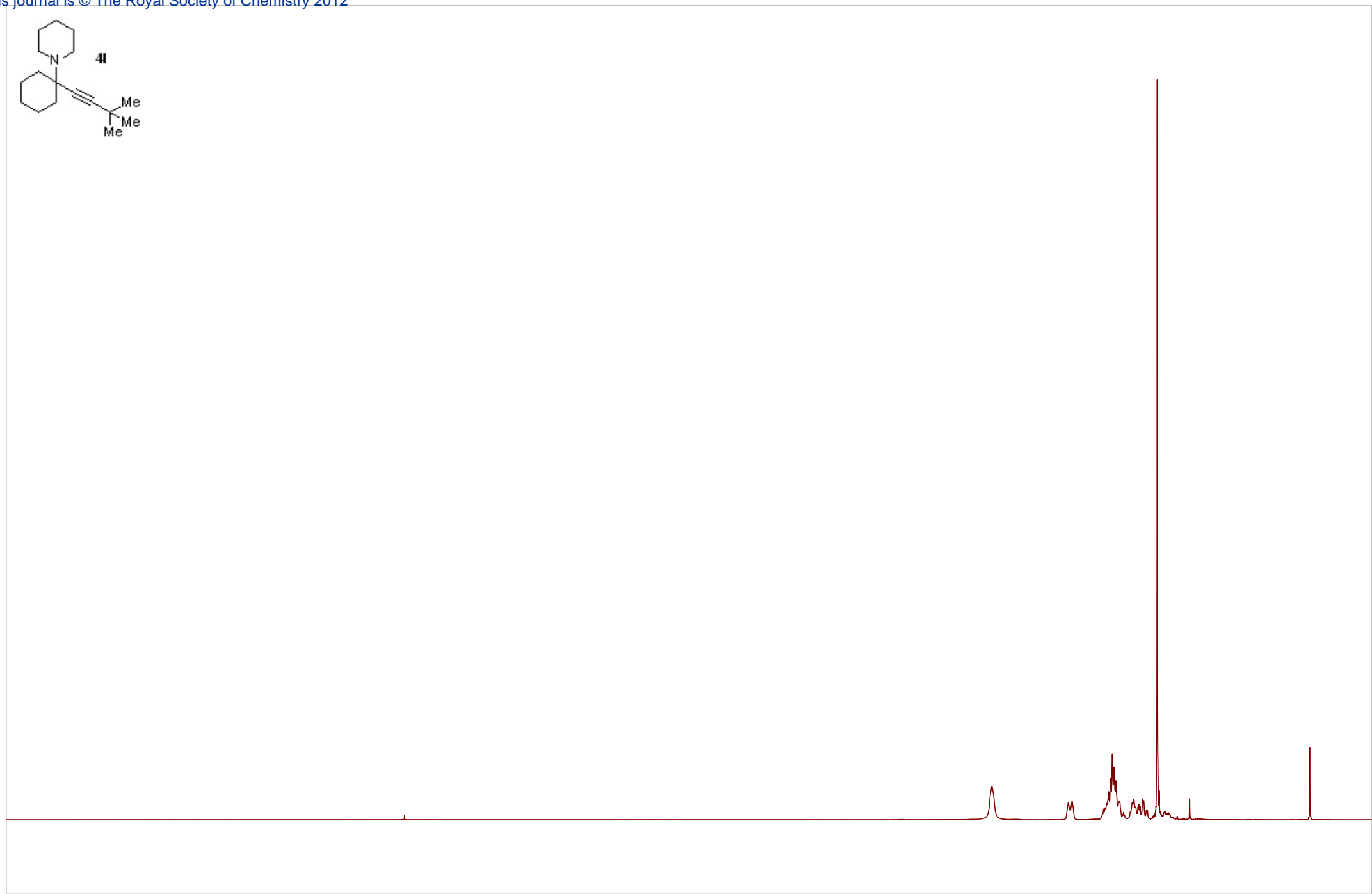


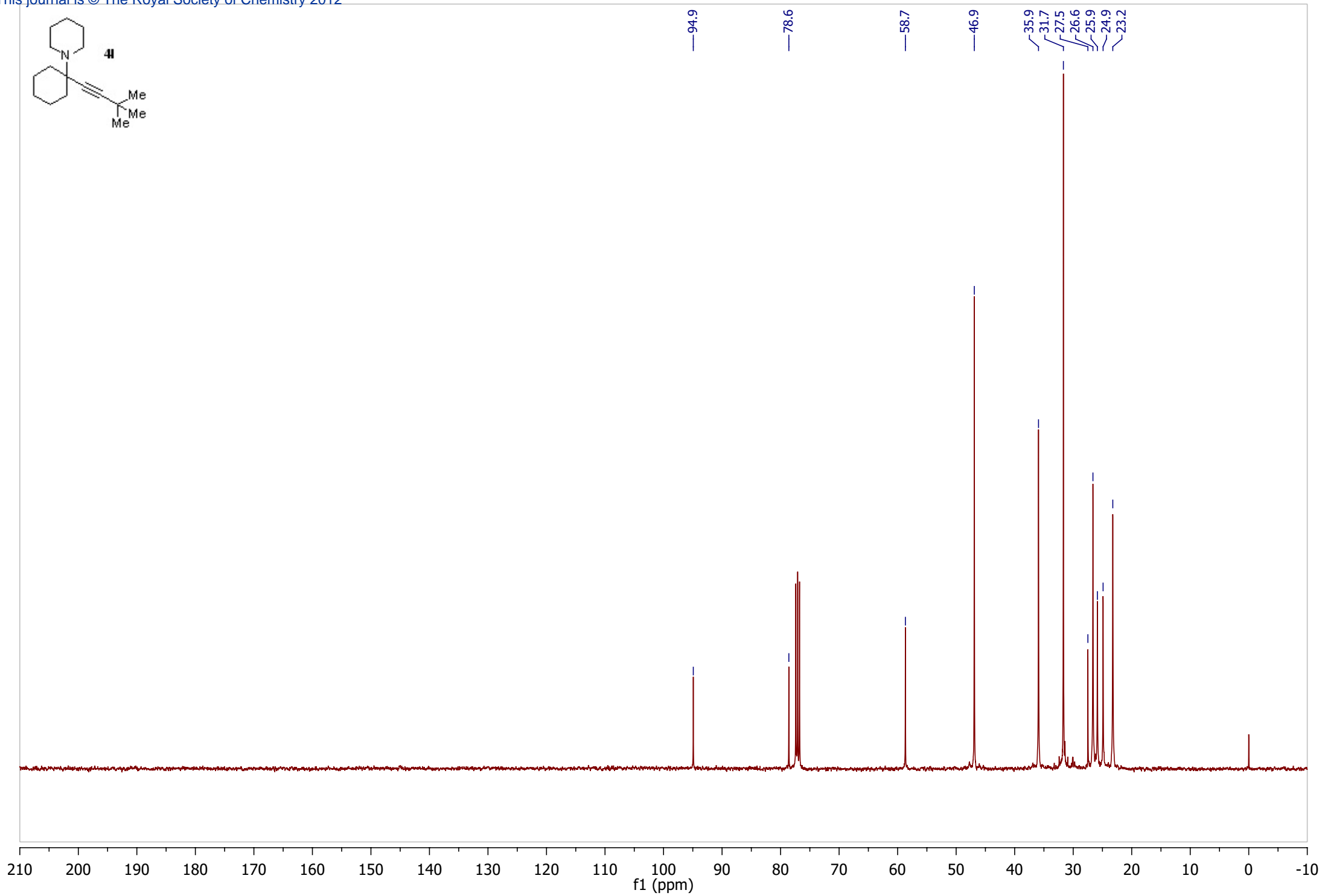
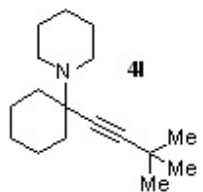


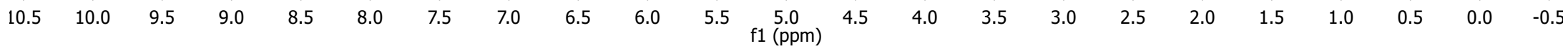
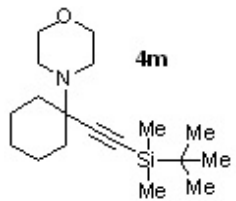


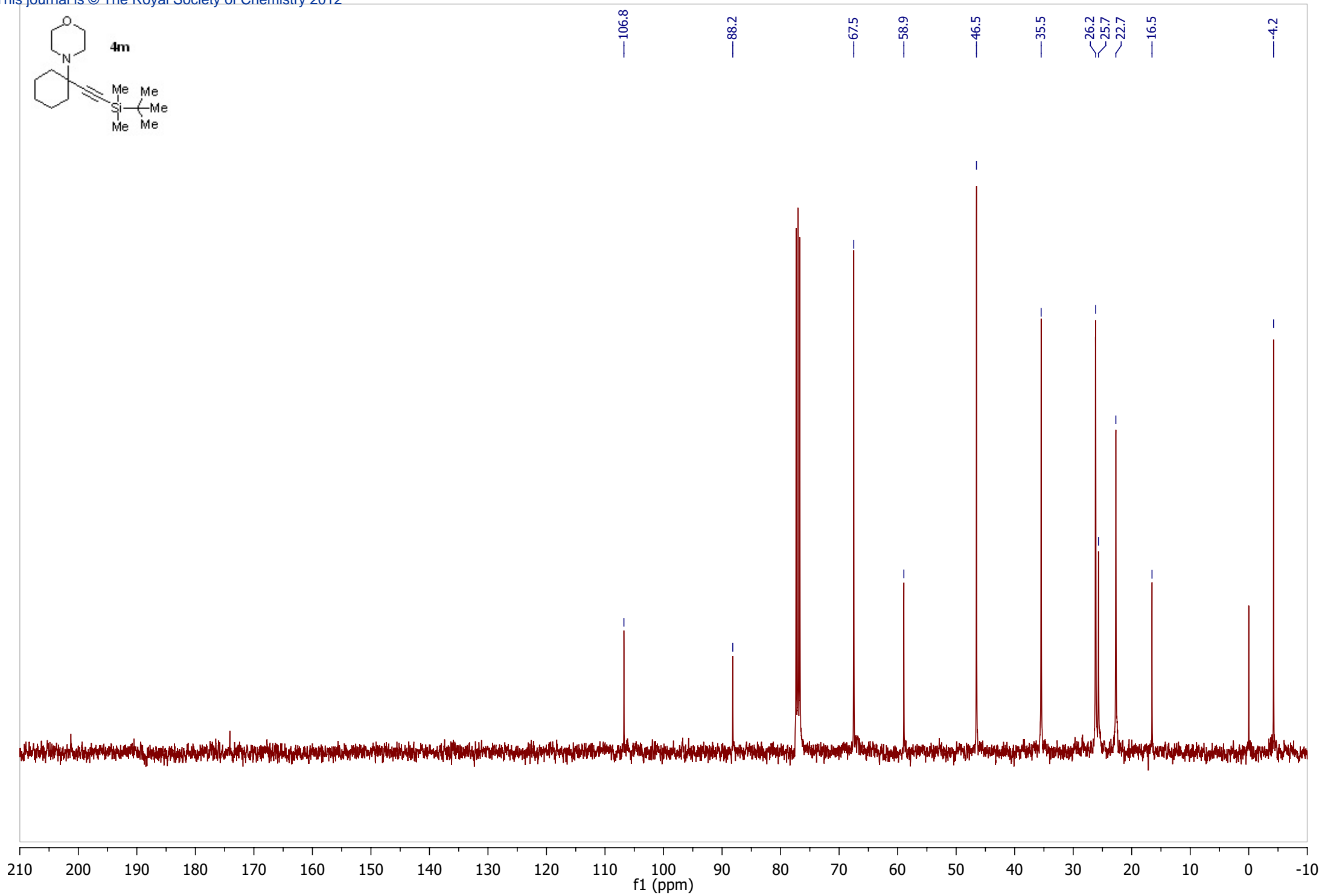
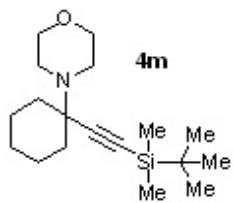


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f1 (ppm)

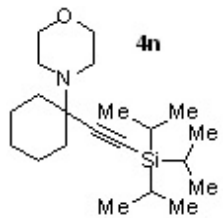




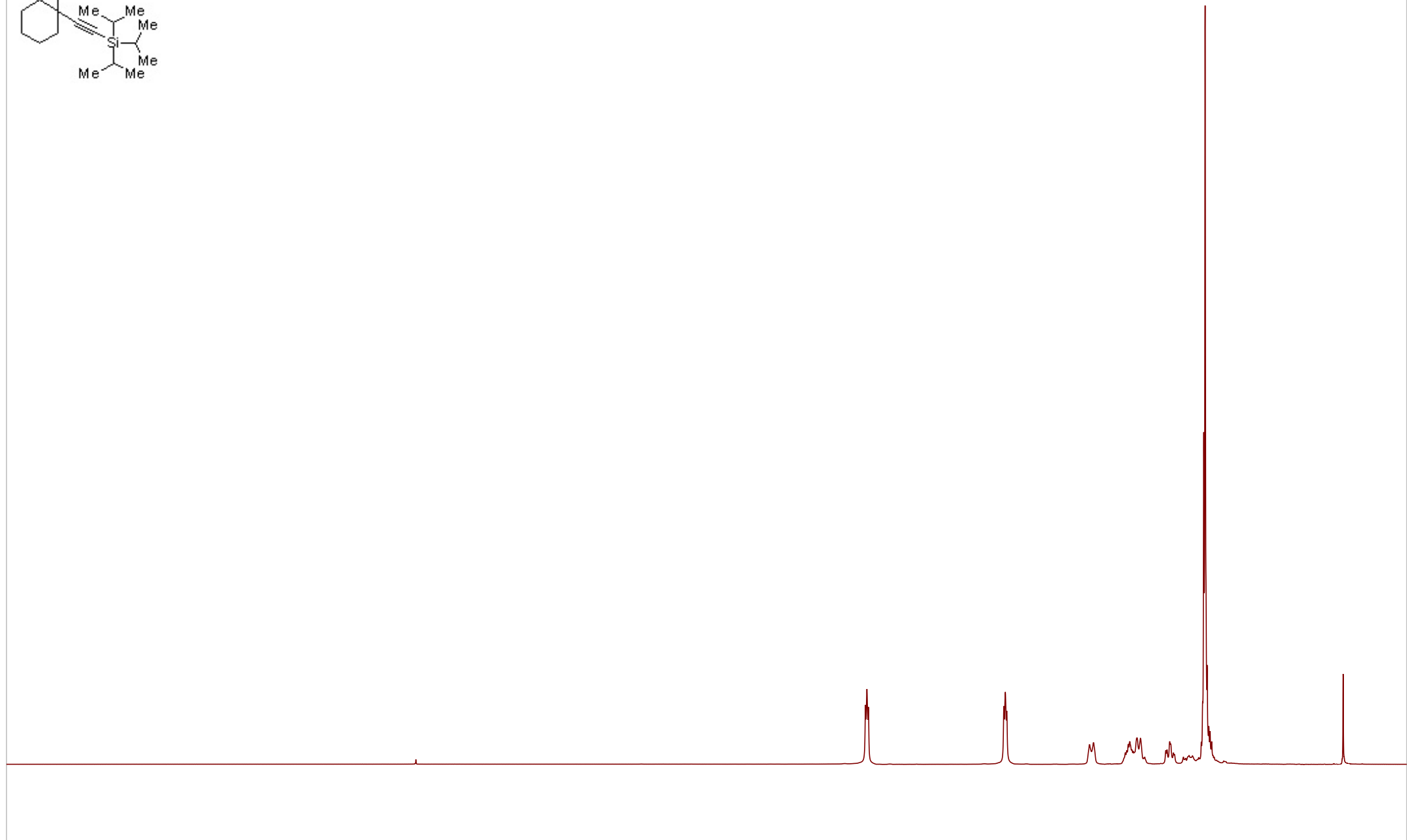


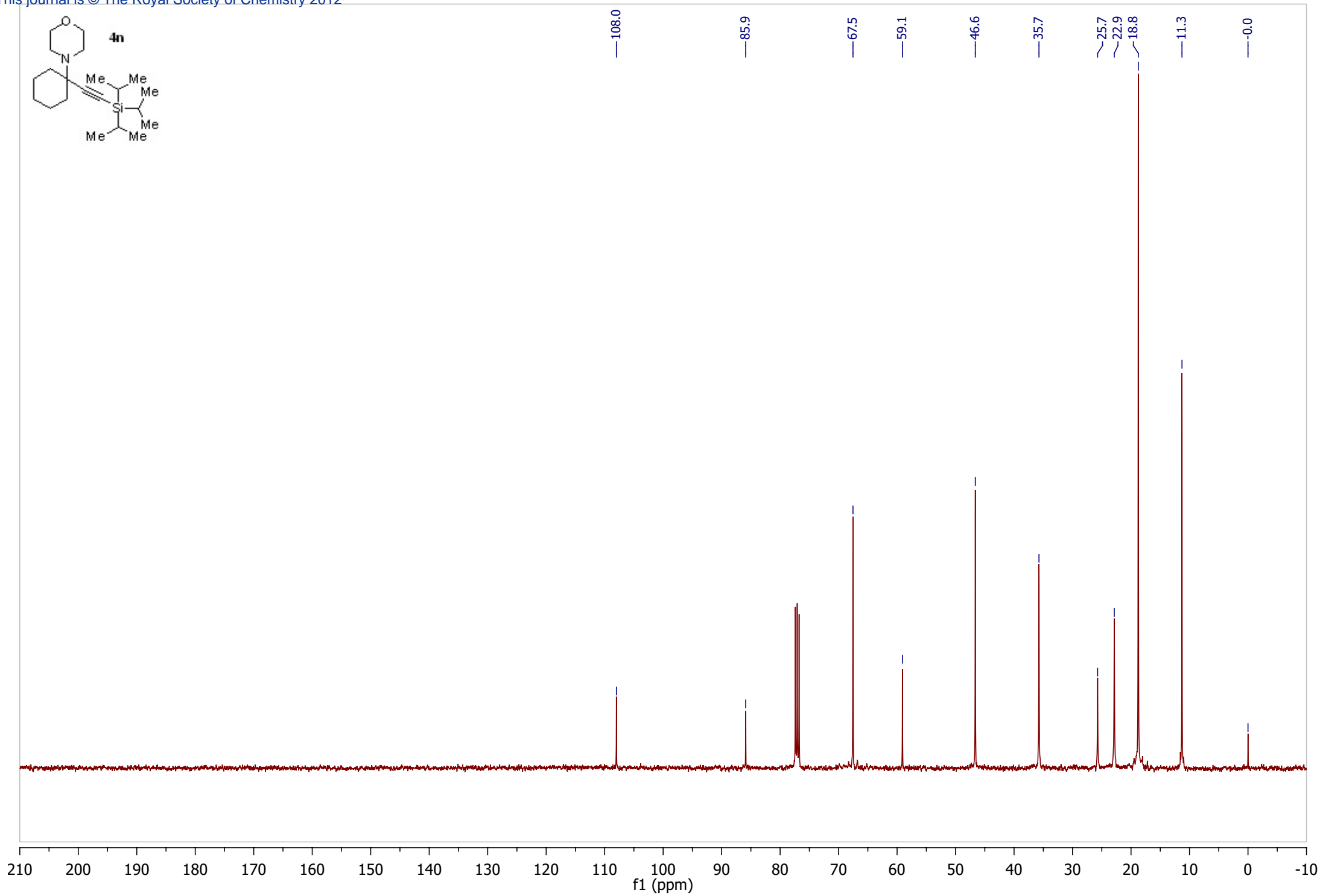
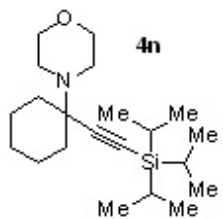


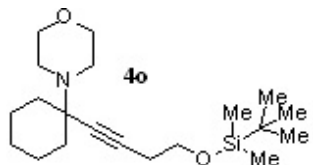




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f1 (ppm)







10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5  
f1 (ppm)

