A 2-, 3-, and 4-Component Coupling To Form Isoquinolones Based on Directed Metalation.

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Supporting Information

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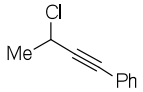
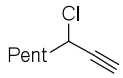
Method and Materials

General. Unless otherwise stated, reactions were performed using freshly purified solvents which were purified using solvent purification columns purchased from Glass Contour, Laguna Beach, CA. All reactions were monitored by thin-layer chromatography with E. Merck silica gel 60 F254 pre-coated plates (0.25 mm). Gas chromatography (GC) was performed on an HP 6890N autosampling GC with an HP-5 capillary column and equipped with a FID detector. Flash chromatography was performed with indicated solvents using silica gel (particle size 0.032-0.063m) purchased from Sorbent Technologies. ^{1}H and ^{13}C NMR spectra were recorded on Varian Inova-400 MHz or 500 MHz spectrometer. Chemical shift are reported relative to internal chloroform ($CDCl_3$: 1H, δ = 7.27, 13C, δ = 77.26). Coupling constants are in Hz and are reported as d (doublet), t (triplet), q (quartet). For signals having multiple coupling patterns, the coupling constant are listed in the same order as the pattern (e.g. dt, J = 2.0, 4.0; 2.0 is the coupling constant for the doublet and 4.0 is for the coupling constant for the triplet). HPLC analyses were carried out on a Shimadzu LC-2010A system. Mass spectra were acquired on a Shimadzu QP5000 GC/MS or Agilent technologies 1200 series LC/MS using indicated ionization methods.

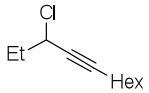
2. Procedure for the preparation of propargylic chlorides:



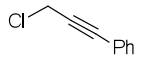
(3-Chlorobut-1-yn-1-yl)benzene (3a): yield 93 %. To a solution of 4-phenylbut-3-yn-2-ol (2.0 g, 13.7 mmol, 1.0 equiv.) in carbon tetrachloride (14 mL) was added triphenylphosphine (4.7 g, 17.8, 1.3 equiv.). The reaction mixture was heated at reflux for 1 h. After cooling to room temperature, hexanes was added and triphenylphosphine oxide was precipitated. Solvents were removed under reduced pressure and the crude product was purified by flash chromatography (Hexane/Ether : 95/5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.39 (m, 4H), 7.38 – 7.27 (m, 6H), 4.88 (q, J = 6.8, 2H), 1.84 (d, J = 6.8, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.04, 129.01, 128.98, 128.56, 122.42, 122.38, 88.66, 85.60, 44.82, 26.88.



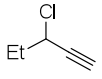
3-Chlorooct-1-yne (3c): As described for **3a**, but the reaction was stirred at room temperature for 3 days; yield 86 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (td, J = 6.7, 2.2, 1H), 2.58 (d, J = 2.3, 1H), 2.00 – 1.88 (m, 2H), 1.62 – 1.43 (m, 2H), 1.40 – 1.22 (m, 4H), 0.89 (t, J = 6.9, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.34, 74.14, 47.97, 39.17, 31.10, 25.86, 22.51, 13.92. ESI-MS (m/z): 167 $[M+Na]^+$



3-Chloroundec-4-yne (3b): As described for **3a**, but the reaction was stirred at room temperature for 3 days; yield 75 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.53 (tt, J = 6.2, 1.9, 1H), 2.23 (td, J = 7.1, 2.0, 2H), 1.94 (dt, J = 7.2, J = 7.2, 2H), 1.57 – 1.46 (m, 2H), 1.43 – 1.22 (m, 6H), 1.08 (t, J = 7.3, 3H), 0.89 (t, J = 6.8, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 87.63, 78.62, 51.25, 33.12, 31.48, 28.67, 28.62, 22.72, 18.98, 14.21, 10.77. ESI-MS (m/z): 187 $[M+H]^+$



(3-chloroprop-1-yn-1-yl)benzene (3d): As described for **3a**; yield 85 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.3, 2H), 7.39 – 7.28 (m, 3H), 4.38 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.14, 129.19, 128.65, 122.31, 86.62, 84.16, 31.48. ESI-MS (m/z): 151 $[M+H]^+$



3-Chloropent-1-yne was prepared according to the literature[1].

[1] D. J. Pasto, S. E. Warren, M. A. Morrison, *J. Org. Chem*. **1981**, *73*, 2837 - 2841

3. Procedure for the preparation of Benzamides:

N-Methylbenzamide, *N*-Benzylbenzamide, Benzanilide were purchased from Aldrich and used without further purification. *N*-isopropylbenzamide[1] and *N*-*tert*-butylbenzamide[2] were prepared from the corresponding acid chloride and amine. 4 - methoxy - *N* - methylbenzamide[3] and 4 - Chloro - *N* – methylbenzamide[3] *N*,3-dimethylbenzamide, 3-Methoxy-*N*-methylbenzamide, 3,4-Dimethoxy-N-Methylbenzamide were prepared from the corresponding acid chloride amine hydrochloride salt and matched the literature data.

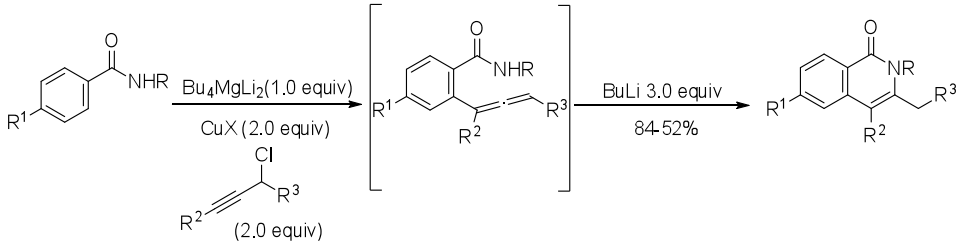
4. General Procedure for the Preparation of Isoquinolone Derivatives:

4.1 (Bu_4MgLi_2) was prepared according to literature.[4]

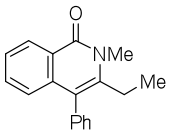
To a solution of $MgBr_2$ (0.5 mmol, 2.5 mL, 0.2 M) in THF was added dropwise *n*-butyllithium (2.0 mmol, 1.25 mL, 1.6 M in hexanes) at 0 °C and the resulting mixture was stirred at the same temperature for 1 h to give a solution of Bu_4MgLi_2.

Procedure for the preparation 0.2 M solution of $MgBr_2$ in THF

To a suspension of magnesium turning (0.0486g, 2.0 mmol) in THF (10 mL) was added 1,2-dibromoethane (0.17 mL, 2.0 mmol) under N_2. The mixture was refluxed for 1h to afford magnesium dibromide ($MgBr_2$, 2.0 mmol, 0.2 M) as a colorless solution.



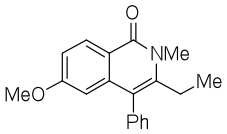
A solution of benzamide (0.5 mmol, 1.0 equiv) in THF (2.0 mL) was added to a freshly prepared solution of Bu_4MgLi_2 (0.5 mmol, 1.0 equiv) at room temperature. The resulting mixture was stirred at room temperature for 2 h before being cooled to between -50 and -60 °C. Prior to addition, copper salts and propargyl alcohols were weighed in a glove box to prevent oxygen-induced homocoupling of the benzamide. Thus, CuBr·Me_2S or CuCN·2LiCl (1.0 mmol, 2.0 equiv) in 5 mL of THF was added via canula. After 5-10 min propargyl chloride (1.0 mmol, 2.0 equiv) in 1.0 mL of THF was added. Stirring was continued for 1 h at -50 to -30 °C, and then *n*-butyllithium (1.5 mmol, 0.94 mL, 1.6 M in hexanes, 3.0 equiv) was then added dropwise at -50 °C. The reaction mixture was allowed to warm over 0.5-1.0 h while the cyclization of allenes to isoquinolone was monitored by TLC. Typically the reaction was completed between -10 and 10 °C. When competed, the reaction was quenched by the addition of 10 % NH_4OH in sat.NH_4Cl, diluted with EtOAc and washed with 10 % NH_4OH in sat.NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (Hexane/AcOEt :9/1).



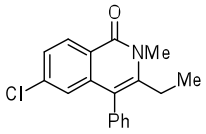
3-Ethyl-2-methyl-4-phenylisoquinolin-1(2*H*)-one (Table 1, Entry 1): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg , 2.0 equiv) and (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 84% isolated yield (111 mg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 7.7, 1H), 7.56 – 7.31 (m, 5H), 7.30 – 7.18 (m, 2H), 6.91 (d, *J* = 7.9, 1H), 3.72 (s, 3H), 2.54 (q, *J* = 7.4, 2H), 1.11 (t, *J* = 7.4, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.42, 142.27, 137.70,

[2] A. Rolfe, D. A. Probst, K. A.Volp, I. Omar, P. R. Hanson, D. L. Flynn, *J. Org. Chem*. **2008**, *73*, 8785
[3] T. K. Hyster, T. Rovis, *J. Am. Chem. Soc*, **2010**, *132*, 10569-10569
[4] E. Bellamy, O. Bayh, C. Hoarau, F. Trecourt, G. Queguiner, F. Marsais *Chem. Commun*. **2010**, *46*, 7043-7045

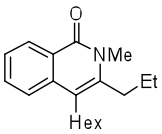
132.03, 131.15, 128.97, 127.88, 127.77, 126.07, 125.17, 124.23, 117.71, 31.51, 24.42, 13.85. IR (NaCl): 2973, 1644 $^{-1}$cm. ESI-MS (m/z): 264 $[M+H]^+$



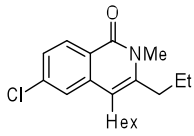
3-Ethyl-6-methoxy-2-methyl-4-phenylisoquinolin-1(2*H*)-one (Table 1, Entry 2): The title compound was prepared from 4-Methoxy-*N*-Methylbenzamide (0.5 mmol, 82 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 79% isolated yield (116 mg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.9, 1H), 7.54 – 7.37 (m, 3H), 7.25 – 7.23 (m, 2H), 6.98 (dd, *J* = 8.9, 2.5, 1H), 6.24 (d, *J* = 2.5, 1H), 3.69 (s, 3H), 3.65 (s, 3H), 2.52 (q, *J* = 7.4, 2H), 1.09 (t, *J* = 7.4, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 163.08, 162.55, 142.95, 139.77, 137.73, 131.09, 130.06, 129.01, 127.79, 118.33, 117.41, 114.93, 106.81, 55.33, 31.29, 24.53, 13.80. IR (NaCl): 2966, 1645 $^{-1}$cm. ESI-MS (m/z): 294 $[M+H]^+$



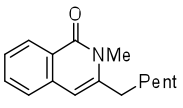
6-Chloro-3-ethyl-2-methyl-4-phenylisoquinolin-1(2*H*)-one (Table 1, Entry 3): The title compound was prepared from 4-Chloro-*N*-Methylbenzamide (0.5 mmol, 84 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 74% isolated yield (110 mg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.6, 1H), 7.44 – 7.27 (m, 3H), 7.21 (dd, *J* = 8.6, 2.0, 1H), 7.16 – 7.01 (m, 2H), 6.74 (d, *J* = 1.9, 1H), 3.58 (s, 3H), 2.41 (q, *J* = 7.5, 2H), 0.98 (t, *J* = 7.5, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.92, 143.97, 139.10, 138.74, 136.96, 131.12, 129.89, 129.29, 128.19, 126.69, 124.53, 122.61, 116.92, 31.65, 24.65, 13.81. IR (NaCl): 2975, 1645 $^{-1}$cm. ESI-MS (m/z): 298 $[M+H]^+$



4-Hexyl-2-methyl-3-propylisoquinolin-1(2*H*)-one (Table 1, Entry 6): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and 3-chloroundec-4-yne (1.0 mmol, 186 mg 2.0 equiv) in 72 % isolated yield (102 mg). The cyclization was completed at room temperature: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.0, 1H), 7.66 – 7.58 (m, 2H), 7.45 – 7.36 (m, 1H), 3.65 (s, 3H), 2.81 – 2.59 (m, 4H), 1.87 – 1.25 (m, 10H), 1.08 (t, *J* = 7.4, 3H), 0.90 (t, *J* = 7.0, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.15, 139.95, 136.70, 132.15, 128.50, 125.79, 125.02, 122.80, 114.28, 32.02, 31.89, 31.56, 30.67, 29.95, 27.98, 22.90, 22.85, 14.49, 14.31. IR (NaCl): 2957, 1650 $^{-1}$cm. ESI-MS (m/z): 286 $[M+H]^+$

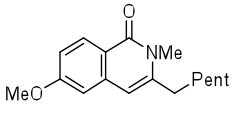


6-Chloro-4-hexyl-2-methyl-3-propylisoquinolin-1(2*H*)-one (Table 1, Entry 7) : The title compound was prepared from 4-Chloro-*N*-Methylbenzamide (0.5 mmol, 84 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and 3-chloroundec-4-yne (1.0 mmol, 186 mg 2.0 equiv) in 69 % isolated yield (110 mg). The cyclization was completed at room temperature: ^{1}H NMR (400 MHz, CDCl3) δ 8.36 (d, *J* = 8.6, 1H), 7.56 (d, *J* = 1.9, 1H), 7.34 (dd, J = 8.6, 1.9, 1H), 3.63 (s, 3H), 2.69 – 2.62 (m, 4H), 1.68 – 1.39 (m, 6H), 1.40 – 1.28 (m, 4H), 1.08 (t, *J* = 7.4, 3H), 0.91 (t, *J* = 7.0, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 162.56, 141.58, 138.78, 138.08, 130.38, 126.28, 123.33, 122.38, 113.45, 32.13, 31.81, 31.60, 30.49, 29.83, 27.89, 22.87, 22.75, 14.48, 14.29. IR (NaCl): 2928, 1651 $^{-1}$cm. ESI-MS (m/z): 298 $[M+H]^+$

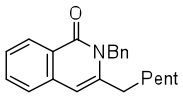


3-Hexyl-2-methylisoquinolin-1(2*H*)-one (Table 1, Entry 8): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 81 % isolated yield (98 mg): ^{1}H NMR (400 MHz, CDCl3) δ 8.36 (d, *J* = 8.1, 1H), 7.64 – 7.51 (m, 1H), 7.47 – 7.34 (m, 2H), 6.33 (s, 1H), 3.60 (s, 3H), 2.72 – 2.57 (m, 2H), 1.77 – 1.57 (m, 2H), 1.54 – 1.22 (m, 4H), 0.90 (t, *J* = 7.1, 3H). 13C NMR (101 MHz, CDCl3) δ 163.76, 143.65, 136.80, 132.21,

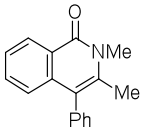
127.98, 126.01, 125.36, 124.36, 104.99, 33.88, 31.78, 30.88, 29.19, 28.51, 22.78, 14.27. IR (NaCl): 2933, 1646 $^{-1}$cm. ESI-MS (m/z): 244 $[M+H]^+$



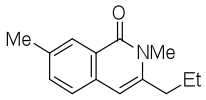
3-Hexyl-6-methoxy-2-methylisoquinolin-1(2*H*)-one (Table 1, Entry 9): The title compound was prepared from 4-Methoxy-*N*-Methylbenzamide (0.5 mmol, 82 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 73 % isolated yield (100 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.9, 1H), 6.97 (dd, *J* = 8.9, 2.5, 1H), 6.77 (d, *J* = 2.4, 1H), 6.26 (s, 1H), 3.88 (s, 3H), 3.57 (s, 3H), 2.63 (d, *J* = 7.8, 2H), 1.71 – 1.60 (m, 2H), 1.48 – 1.36 (m, 2H), 1.34 (m, 1.36 – 1.29, 4H), 0.90 (t, *J* = 7.0, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.41, 162.75, 144.37, 138.81, 130.04, 118.40, 115.75, 105.90, 104.78, 55.56, 33.92, 31.78, 30.65, 29.18, 28.48, 22.77, 14.26. IR (NaCl): 2934, 1644 $^{-1}$cm. ESI-MS (m/z): 274 $[M+H]^+$



2-Benzyl-3-hexylisoquinolin-1(2*H*)-one (Table 1, Entry 10): The title compound was prepared from N-benzylbenzamide (0.5 mmol, 105 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 52 % isolated yield (83 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.6, 1H), 7.61 (ddd, *J* = 8.2, 7.1, 1.3, 1H), 7.53 – 7.40 (m, 2H), 7.33 – 7.18 (m, 3H), 7.12 (d, *J* = 7.1, 2H), 6.37 (s, 1H), 5.43 (s, 2H), 2.57 (t, *J* = 7.8, 2H), 1.76 – 1.51 (m, 2H), 1.45 – 1.13 (m, 6H), 0.87 (t, *J* = 6.9, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.76, 143.80, 137.67, 137.02, 132.55, 128.94, 128.44, 127.31, 126.39, 126.21, 125.50, 124.59, 105.33, 46.67, 33.21, 31.73, 29.13, 29.02, 22.73, 14.26. IR (NaCl): 2929, 1654 $^{-1}$cm. ESI-MS (m/z): 320 $[M+H]^+$

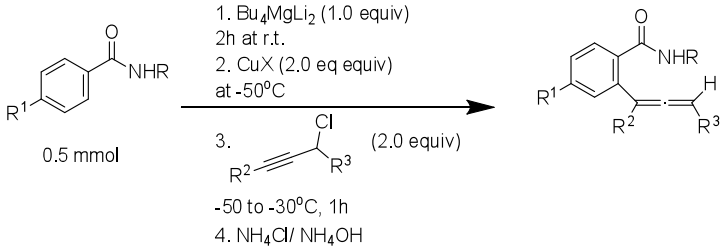


2,3-Dimethyl-4-phenylisoquinolin-1(2*H*)-one (Table 1, Entry 12): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 150 mg 2.0 equiv) in 46 % isolated yield (58 mg). The partial cyclization was observed after the addition of 3-chlorooct-1-yne at -50 ^{o}C. After addition of 3.0 equiv of *n*-BuLi, the cyclization was completed after 30 min at -30 ^{o}C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 8.0, 1.3, 1H), 7.53 – 7.37 (m, 5H), 7.26 – 7.20 (m, 2H), 6.98 (d, *J* = 8.0, 1H), 3.69 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.17, 137.88, 137.46, 137.11, 132.11, 131.33, 129.06, 128.02, 127.77, 126.07, 125.08, 124.20, 118.03, 31.84, 18.79. IR (NaCl): 1646 $^{-1}$cm. ESI-MS (m/z): 250 $[M+H]^+$

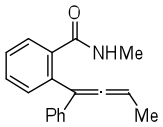


2,7-dimethyl-3-propylisoquinolin-1(2H)-one and **5-dimethyl-3-propylisoquinolin-1(2H)-one (Table 1, Entry 13).** The title compound was prepared from *N*,3-dimethylbenzamide (0.5 mmol, 74 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chloropent-1-yne (1.0 mmol, 105 mg 2.0 equiv) in 56 % isolated yield (60 mg) of non separable mixture of two regioisomers 2.8:1.
^{13}C NMR (101 MHz, cdcl$_3$) δ 163.75, 143.02, 142.31, 135.99, 135.63, 134.48, 133.79, 132.98, 132.44, 127.47, 126.01, 125.70, 125.34, 124.50, 124.32, 105.03, 101.88, 36.27, 35.81, 30.88, 22.01, 21.77, 21.65, 19.09, 13.99. IR (NaCl): 2961, 1644 $^{-1}$cm. ESI-MS (m/z): 316 $[M+H]^+$
2,7-dimethyl-3-propylisoquinolin-1(2H)-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.45 – 7.21 (m, 2H), 6.30 (s, 1H), 3.59 (s, 3H), 2.70 – 2.55 (m, 2H), 2.45 (s, 3H), 1.77 – 1.60 (m, 2H), 1.04 (t, *J* = 7.2, 3H),
2,5-dimethyl-3-propylisoquinolin-1(2H)-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.7, 1H), 7.45 – 7.20 (m, 2H), 6.42 (s, 1H), 3.59 (s, 3H), 2.71 – 2.57 (m, 2H), 2.48 (s, 3H), 1.78 – 1.62 (m, 2H), 1.04 (t, *J* = 7.2, 3H),

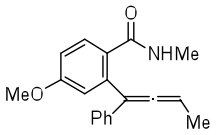
5. General Procedure for the Preparation of Allenes:



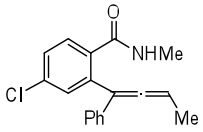
A solution of benzamide (0.5 mmol, 1.0 equiv) in THF (2.0 mL) was added to a freshly prepared solution of Bu_4MgLi_2 (0.5 mmol, 1.0 equiv) at room temperature. The resulting mixture was stirred at room temperature over a 2h period before being cooled to between -50 and -60 °C. Prior to addition, copper salts and propargyl alcohols were weighed in a glove box to prevent oxygen-induced homocoupling of the benzamide. Thus, CuBr·Me_2S or CuCN·2LiCl (1.0 mmol, 2.0 equiv) in 5 mL of THF was added, and, after 5-10 min, followed by the addition of propargyl chloride (1.0 mmol, 2.0 equiv) in 1.0 mL of THF. The reaction mixture was then allowed to warm to -30 °C over 1.0 h and quenched by the addition of 10 % NH_4OH in sat. NH_4Cl, diluted with EtOAc and washed with 10% NH_4OH in sat. NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel (Hexanes/EtOAc:7/3).



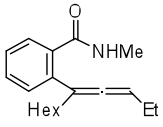
N-methyl-2-(1-phenylbuta-1,2-dien-1-yl)benzamide (Table 1, Entry 1): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg , 2.0 equiv) and (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 89% isolated yield (117 mg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.4, 1H), 7.51 – 7.26 (m, 5H), 7.21 (dd, *J* = 11.4, 4.3, 3H), 6.02 (bs, 1H), 5.68 (q, *J* = 7.1, 1H), 2.68 (d, *J* = 4.9, 3H), 1.84 (d, *J* = 7.1, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.72, 167.65, 135.05, 134.34, 132.87, 129.37, 128.62, 127.39, 126.84, 126.23, 125.43, 125.12, 106.18, 105.84, 87.81, 24.86, 12.45. ESI-MS (m/z): 264 $[M+H]^+$



4-methoxy-N-methyl-2-(1-phenylbuta-1,2-dien-1-yl)benzamide (Table 1, Entry 2): The title compound was prepared from 4-Methoxy-*N*-Methylbenzamide (0.5 mmol, 82 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 86% isolated yield (126 mg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.6, 1H), 7.32 – 7.23 (m, 2H), 7.23 – 7.16 (m, 3H), 6.91 (dd, *J* = 8.6, 2.6, 1H), 6.82 (d, *J* = 2.6, 1H), 6.03 (bs, 1H), 5.67 (q, *J* = 7.1, 1H), 3.81 (s, 3H), 2.65 (d, *J* = 4.9, 3H), 1.82 (d, *J* = 7.2, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.28, 168.99, 161.20, 136.61, 136.49, 131.48, 128.81, 128.39, 127.41, 126.89, 116.61, 113.38, 107.95, 89.96, 55.62, 26.78, 14.32. ESI-MS (m/z): 294 $[M+H]^+$

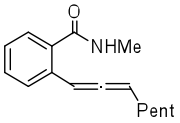


4-chloro-N-methyl-2-(1-phenylbuta-1,2-dien-1-yl)benzamide (Table 1, Entry 3): The title compound was prepared from 4-Chloro-*N*-Methylbenzamide (0.5 mmol, 84 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 76 % isolated yield (113 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3, 1H), 7.35 (dd, *J* = 8.3, 2.1, 1H), 7.32 – 7.26 (m, 3H), 7.26 – 7.13 (m, 3H), 5.94 (bs, 1H), 5.69 (q, *J* = 7.2, *J* = 7.2, 1H), 2.66 (d, *J* = 4.9, 3H), 1.83 (d, *J* = 7.2, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.61, 168.49, 136.69, 136.36, 136.32, 134.58, 131.07, 130.86, 128.88, 128.26, 127.60, 126.97, 106.98, 90.41 26.81, 14.28. EI-MS (m/z): 297 $[M]^+$

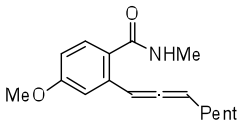


2-(Dodeca-4,5-dien-4-yl)-N-methylbenzamide (Table 1, Entry 6): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuBr·Me_2S (1.0 mmol, 205 mg, 2.0 equiv) and 3-chloroundec-4-yne (1.0 mmol, 186 mg 2.0 equiv) in 84% isolated yield (120 mg):^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.6, 1H), 7.40-7.36 (m, 1H), 7.34 – 7.22 (m, 2H), 6.25 (bs, 1H), 5.41 (tt, *J* = 6.0, 2.9, 1H), 2.99 (d, *J* = 4.9, 3H), 2.35 – 2.21 (m,

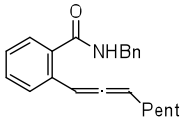
2H), 2.13 – 2.06 (m, 2H), 1.46 – 1.28 (m, 8H), 1.08 (t, *J* = 7.4, 3H), 0.89 (t, *J* = 6.7, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.70, 170.09, 137.36, 134.74, 130.33, 129.74, 129.08, 127.35, 106.88, 94.63, 33.98, 31.91, 29.11, 28.27, 27.01, 22.84, 22.39, 14.28, 13.74. EI-MS(*m/z*): 285 $[M]^+$



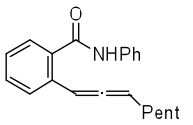
N-methyl-2-(octa-1,2-dien-1-yl)benzamide (Table 1, Entry 8): The title compound was prepared from *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 84 % isolated yield (102 mg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.8, 1H), 7.41 – 7.28 (m, 2H), 7.18 – 7.08 (m, 1H), 6.50 (dt, *J* = 6.1, 2.9, 1H), 5.92 (bs, 1H), 5.54 (dt, *J* = 6.7, *J* = 6.7 1H), 2.95 (d, *J* = 4.9, 3H), 2.11 (ddt, *J* = 7.1, J = 7.1, 3.0, 2H), 1.56 – 1.39 (m, 2H), 1.39 – 1.19 (m, 6H), 0.87 (t, *J* = 7.0, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.26, 170.38, 134.78, 133.14, 130.09, 127.85, 127.57, 126.65, 95.22, 91.76, 31.60, 29.10, 28.75, 26.95, 22.67, 14.29. EI-MS(*m/z*): 244 $[M+H]^+$



4-Methoxy-N-methyl-2-(octa-1,2-dien-1-yl)benzamide (Table 1, Entry 9): The title compound was prepared from 4-Methoxy-*N*-Methylbenzamide (0.5 mmol, 82 mg, 1.0 equiv), CuCN.2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 74 % isolated yield (101 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.5, 1H), 6.99 (d, *J* = 2.5, 1H), 6.70 (dd, *J* = 8.5, 2.5, 1H), 6.59 (dt, *J* = 6.1, 2.9, 1H), 5.82 (bs, 1H), 5.55 (dt, *J* = 6.7, *J* = 6.7, 1H), 3.79 (s, 3H), 2.96 (d, *J* = 4.8, 3H), 2.12 (ddt, *J* = 7.2, 7.2, 3.0, 2H), 1.54 – 1.42 (m, 2H), 1.38 – 1.22 (m, 4H), 0.87 (t, *J* = 6.9, 3H). EI-MS(*m/z*): 273 $[M]^+$. ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.15, 170.08, 160.85, 135.32, 129.39, 127.54, 112.71, 112.36, 95.27, 91.97, 55.44, 31.60, 29.16, 28.76, 26.97, 22.69, 14.26. ESI-MS (m/z): 274 $[M+H]^+$

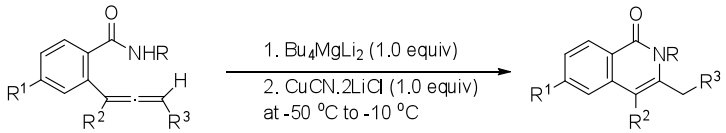


***N*-benzyl-2-(octa-1,2-dien-1-yl)benzamide (Table 1, Entry 10):** The title compound was prepared from N-benzylbenzamide (0.5 mmol, 105 mg, 1.0 equiv), CuCN2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 64 % isolated yield (104 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.6, 1H), 7.41 (dd, *J* = 7.6, 1.1, 1H), 7.38 – 7.26 (m, 6H), 7.18 (td, *J* = 7.5, 0.9, 1H), 6.58 (dt, *J* = 6.2, 3.0, 1H), 6.08 (bs, 1H), 5.55 (dt, *J* = 6.7, 6.7, *J* = 6.7, 1H), 4.63 (d, *J* = 5.7, 2H), 2.11 (ddt, *J* = 7.2, 7.2, 3.0, 2H), 1.53 – 1.41 (m, 2H), 1.40 – 1.23 (m, 4H), 0.87 (t, *J* = 7.1, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.34, 169.53, 138.28, 134.49, 133.40, 130.26, 128.99, 128.06, 127.95, 127.81, 127.56, 126.67, 95.21, 91.80, 44.27, 31.61, 29.10, 28.75, 22.68, 14.32. ESI-MS (m/z): 320 $[M+H]^+$



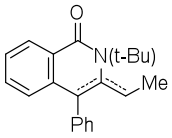
2-(Octa-1,2-dien-1-yl)-*N*-phenylbenzamide (Table 1, Entry 11): The title compound was prepared *N*-Phenylbenzamide (0.5 mmol, 98 mg, 1.0 equiv), CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) and 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 68 % isolated yield (102 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.9, 2H), 7.52 (t, *J* = 6.5, 2H), 7.44 – 7.32 (m, 2H), 7.31 – 7.21 (m, 2H), 7.15 (t, *J* = 7.4, 1H), 6.57 (dt, *J* = 6.0, 2.8, 1H), 5.55 (dt, *J* = 6.7, 6.7, 1H), 2.10 (ddt, *J* = 7.3, 7.3, 3.0, 2H), 1.53 – 1.41 (m, 2H), 1.37 – 1.22 (m, 6H), 0.87 (t, *J* = 7.0, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.48, 167.77, 138.22, 134.77, 133.44, 130.55, 129.30, 128.18, 127.72, 126.83, 124.75, 120.07, 95.32, 91.71, 31.61, 29.08, 28.73, 22.68, 14.31. ESI-MS (m/z): 306 $[M+H]^+$

6. General Procedure for the Preparation of Isoquinolone Derivatives from Allenes:

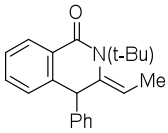


A solution of CuCN·2LiCl (0.2 mmol, 35 mg, 1.0 equiv) in THF (2.0 mL) was added to a freshly prepared solution of Bu_4MgLi_2 (0.2 mmol, 1.0 equiv) cooled to between -50 and -60 °C, followed by the addition of allene (0.3 mmol) in 2 mL of THF. The reaction was then allowed to warm to -10 °C during 30-50 min. The cyclization was monitored by TLC, and typically started at -30 and was completed at -10 °C. After completion, the reaction mixture was quenched with 10 % NH_4OH sat. NH_4Cl, diluted in EtOAc and washed with 10 % NH_4OH in sat. NH_4Cl. The organic layer was dried over magnesium sulfate and the

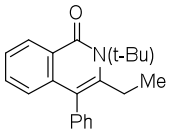
solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel (Hexanes/EtOAc: 1/1).



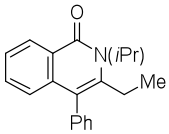
2-(*tert*-butyl)-3-ethyl-4-phenylisoquinolin-1(2*H*)-one (Table 1, Entry 4): A solution of *N*-*tert*-Butylbenzamide (0.5 mmol, 88 mg, 1.0 equiv) in THF (2.0 mL) was added to a freshly prepared solution of Bu_4MgLi_2 (0.5 mmol, 1.0 equiv) at room temperature. The mixture was stirred at room temperature for 2 h before being cooled to between -50 and -60°C. $CuBr{\cdot}Me_2S$ (1.0 mmol, 205 mg, 2.0 equiv) in 5 mL of THF was added. After 5-10 min (3-Chlorobut-1-yn-1-yl)benzene (1.0 mmol, 164 mg 2.0 equiv) in 1.0 mL of THF was added. The reaction mixture was allowed to warm to room temperature. After stirring overnight at room temperature, the reaction was quenched by the addition of 10 % NH_4OH in sat. NH_4Cl, diluted with EtOAc and washed with 10% NH_4OH in sat. NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel (Hexanes/EtOAc : 7/3) to give 135 mg of mixture of allene (87 %) and starting benzamide (13%). The mixture was dissolved in 2 mL of THF treated under the conditions described above for cyclization. The crude product was purified by using column chromatography on silica gel to give 110 mg (72 %) non separable mixture of alkylidene-dihydroisoquinolone (73%) and isoquinolone (27%).



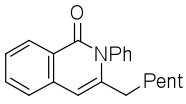
2-(*tert*-butyl)-3-ethylidene-4-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.5, 1.6, 1H), 7.51 – 7.31 (m, 4H), 7.29 – 7.19 (m, 3H), 6.94 (d, *J* = 6.3, 1H), 5.30 (q, *J* = 7.1, 1H), 5.16 (s, 1H), 1.98 (d, *J* = 7.1, 3H), 1.18 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.70, 140.53, 139.56, 131.98, 131.52, 128.76, 128.52, 128.41, 127.55, 127.22, 127.10, 126.12, 124.85, 116.13, 58.13, 45.21, 29.27, 12.63. IR (NaCl): 2974, 1650 $^{-1}$cm. ESI-MS (m/z): 306 $[M+H]^+$



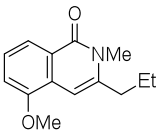
2-(*tert*-butyl)-3-ethyl-4-phenylisoquinolin-1(2*H*)-one: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 7.8, 1.3, 1H), 7.52 – 7.31 (m, 3H), 7.29 – 7.12 (m, 4H), 6.84 (d, *J* = 8.1, 1H), 2.74 (q, *J* = 7.3, 2H), 1.75 (s, 9H), 0.84 (t, *J* = 7.3, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.02, 138.02, 137.41, 131.83, 131.14, 128.90, 128.76, 128.61, 128.32, 127.52, 126.88, 126.56, 125.67, 125.33, 122.61, 61.45, 31.67, 27.45, 15.11. ESI-MS (m/z): 306 $[M+H]^+$



3-Ethyl-2-isopropyl-4-phenylisoquinolin-1(*2H*)-one (Table 1, Entry 5): The same procedure as described for entry 4 was followed. The crude product was purified by using column chromatography on silica gel to give 89 mg (61 %) of isoquinolone: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 8.0, 1.4, 1H), 7.55 – 7.32 (m, 5H), 7.30 – 7.18 (m, 2H), 6.81 (d, *J* = 7.6, 1H), 4.53 (m, 1H), 2.52 (q, *J* = 7.4, 2H), 1.75 (d, *J* = 6.7, 6H), 1.12 (t, *J* = 7.4, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.43, 142.25, 138.42, 137.67, 131.84, 131.10, 128.98, 127.66, 127.46, 125.99, 125.87, 125.12, 118.01, 51.33, 24.60, 20.10, 14.57. IR (NaCl) 2968, 1648 $^{-1}$cm. ESI-MS (m/z): 292 $[M+H]^+$

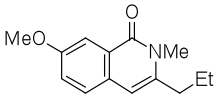


3-Hexyl-2-phenylisoquinolin-1(2*H*)-one (Table 1, Entry 11): 59 % isolated yield. The title compound was prepared from 2-(octa-1,2-dien-1-yl)-*N*-phenylbenzamide (0.3 mmol, 91 mg, 1.0 equiv) in 59 % (54 mg) isolated yield. The cyclization was monitored by TLC: started at 0 °C and was not complete after stirring overnight at room temperature. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.0, 1H), 7.63 (t, *J* = 7.5, 1H), 7.58 – 7.36 (m, 5H), 7.24 (d, *J* = 8.1, 1H), 6.42 (s, 1H), 2.30 – 2.20 (t, *J* = 7.8, 2H), 1.53 – 1.40 (m, 2H), 1.30 – 1.07 (m, 6H), 0.82 (t, *J* = 7.0, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.84, 143.93, 138.93, 137.36, 132.75, 129.65, 129.06, 128.73, 128.33, 126.30, 125.57, 124.99, 104.64, 33.82, 31.58, 28.97, 28.39, 22.62, 14.21. IR (NaCl) 1662 $^{-1}$cm. ESI-MS (m/z): 306 $[M+H]^+$

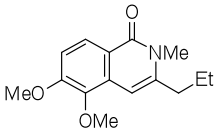


5-methoxy-2-methyl-3-propylisoquinolin-1(2H)-one (Table 1, Entry 14). A solution of 3,4-dimethoxy-*N*-methylbenzamide (0.5 mmol, 97 mg, 1.0 equiv) in THF (2.0 mL) was

added to a freshly prepared solution of Bu_4MgLi_2 (0.5 mmol, 1.0 equiv) at room temperature. The mixture was stirred at room temperature for 2 h before being cooled to between -50 and -60°C. CuCN·2LiCl (1.0 mmol, 174 mg, 2.0 equiv) in 5 mL of THF was added. After 5-10 min 3-chloropent-1-yne (1.0 mmol, 102 mg 2.0 equiv) in 1.0 mL of THF was added. The reaction mixture was then allowed to warm to -30 °C over 1.0 h and quenched by the addition of 10 % NH_4OH in sat. NH_4Cl, diluted with EtOAc and washed with 10% NH_4OH in sat. NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was dissolved in 2 mL of THF treated under the conditions described above for cyclization. The crude product was purified by using column chromatography on silica gel to give of product. The same procedure as described above was followed. The crude product was purified by using column chromatography on silica gel to give 84 mg (73 %) of isoquinolone: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.1, 1H), 7.32 (dd, J = 8.0, J = 8.0, 1H), 6.99 (dd, J = 7.9, 0.7, 1H), 6.70 (s, 1H), 3.92 (s, 3H), 3.60 (s, 3H), 2.72 – 2.56 (m, 2H), 1.80 – 1.63 (m, 2H), 1.04 (t, J = 7.4, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.48, 154.02, 142.78, 127.92, 126.13, 125.38, 119.65, 111.10, 99.25, 55.86, 36.13, 30.95, 21.89, 14.00. IR (NaCl): 2937, 1653 $^{-1}$cm. ESI-MS (m/z): 232 $[M+H]^+$

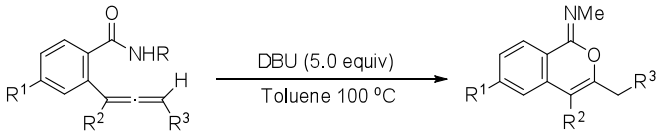


Minor regioisomer: **7-Methoxy-2-methyl-3-propylisoquinolin-1(2H)-one** (86 % purity) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 2.7, 1H), 7.36 (d, J = 8.7, 1H), 7.21 (dd, J = 8.7, 2.7, 1H), 6.31 (s, 1H), 3.91 (s, 3H), 3.62 (s, 3H), 2.77 – 2.48 (m, 2H), 1.87 – 1.64 (m, 2H), 1.05 (dd, J = 8.2, 6.5, 3H).

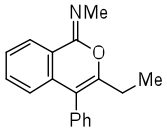


5,6-dimethoxy-2-methyl-3-propylisoquinolin-1(2H)-one (Table 1, Entry 15). The same procedure as described above was followed. The crude product was purified by using column chromatography on silica gel to give 100 mg (77 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.9, 1H), 7.05 (d, J = 8.9, 1H), 6.59 (s, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.56 (s, 3H), 2.71 – 2.58 (m, 2H), 1.81 – 1.65 (m, 2H), 1.04 (t, J = 7.3, 3H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 163.44, 154.50, 143.74, 141.52, 131.95, 124.98, 119.10, 111.72, 99.06, 61.23, 56.21, 36.21, 30.70, 21.91, 13.99. IR (NaCl): 2961, 1651 $^{-1}$cm. ESI-MS (m/z): 262 $[M+H]^+$

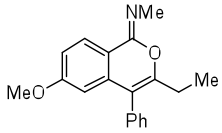
General Procedure for the Preparation of Azaisocoumarins Derivatives (Scheme 2):



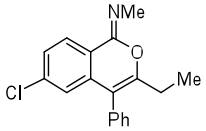
A solution of allene (0.3 mmol, 1.0 equiv) and DBU (1.5 mmol, 225 μL, 5.0 equiv) in 2 mL of toluene was stirred at 100 °C overnight. Toluene was then removed under reduced pressure and crude product was purified using column chromatography on silica gel (Hexanes/EtOAC: 9/1).



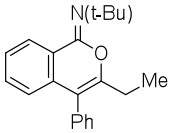
(Z)-N-(3-ethyl-4-phenyl-1H-isochromen-1-ylidene)methanamine (Scheme 2, 7a): 94% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, J = 7.6, 1.5, 1H), 7.57 – 7.34 (m, 3H), 7.35 – 7.14 (m, 4H), 6.73 (d, J = 7.5, 1H), 3.22 (s, 3H), 2.28 (q, J = 7.5, 2H), 1.16 (t, J = 7.5, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.18, 152.29, 135.53, 134.79, 131.45, 130.92, 128.98, 127.85, 127.23, 126.22, 124.36, 123.70, 113.82, 33.59, 25.01, 12.28. IR (NaCl): 2869, 1663 $^{-1}$cm. ESI-MS (m/z): 264 $[M+H]^+$



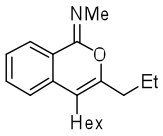
(Z)-N-(3-ethyl-6-methoxy-4-phenyl-1H-isochromen-1-ylidene)methanamine (Scheme 2): 95 % isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.8, 1H), 7.49 – 7.34 (m, 3H), 7.29 – 7.19 (m, 2H), 6.82 (dd, J = 8.8, 2.5, 1H), 6.19 (d, J = 2.5, 1H), 3.66 (s, 3H), 3.19 (s, 3H), 2.27 (q, J = 7.5, 2H), 1.15 (t, J = 7.5, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.23, 154.74, 152.20, 136.69, 135.49, 130.88, 128.98, 128.26, 127.87, 116.94, 113.77, 113.62, 108.63, 55.39, 33.41, 25.09, 12.24. IR (NaCl): 2930, 1606 $^{-1}$cm. ESI-MS (m/z): 294 $[M+H]^+$



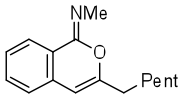
(Z)-N-(6-chloro-3-ethyl-4-phenyl-1H-isochromen-1-ylidene)methanamine (Scheme 2): 92% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5, 1H), 7.60 – 7.38 (m, 3H), 7.23 – 7.18 (m, 3H), 6.68 (d, *J* = 2.0, 1H), 3.20 (s, 3H), 2.27 (q, *J* = 7.5, 2H), 1.15 (t, *J* = 7.5, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.68, 151.46, 138.01, 136.56, 134.89, 130.92, 129.33, 128.29, 128.06, 127.57, 124.09, 122.30, 113.19, 33.69, 25.22, 12.29. IR (NaCl): 2972, 1670 $^{-1}$cm. ESI-MS (m/z): 298 $[M+H]^+$



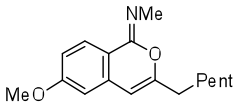
(Z)-N-(3-ethyl-4-phenyl-1H-isochromen-1-ylidene)-2-methylpropan-2-amine (Scheme 2): 74% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.6, 1.7, 1H), 7.47 – 7.27 (m, 3H), 7.27 – 7.11 (m, 4H), 6.62 (d, *J* = 7.3, 1H), 2.19 (q, *J* = 7.5, 2H), 1.38 (s, 9H), 1.10 (t, *J* = 7.5, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.40, 147.67, 135.81, 134.82, 131.06, 130.98, 128.95, 127.76, 127.23, 127.09, 124.82, 124.14, 113.60, 53.55, 30.26, 25.15, 12.87. IR (NaCl): 2967, 1669 $^{-1}$cm. ESI-MS (m/z): 306 $[M+H]^+$



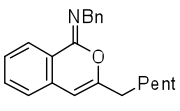
(Z)-N-(4-heptyl-3-propyl-1H-isochromen-1-ylidene)methanamine (Scheme 2): 93 % isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.9, 1H), 7.35 – 7.27 (m, 2H), 3.15 (s, 3H), 2.49 (t, *J* = 7.5, 4H), 1.72 (dd, *J* = 14.8, 7.4, 2H), 1.64 – 1.19 (m, 9H), 1.01 (t, *J* = 7.4, 3H), 0.90 (t, *J* = 6.3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.75, 152.05, 133.86, 131.56, 126.90, 126.57, 124.41, 122.20, 110.29, 33.46, 32.63, 31.92, 29.78, 29.71, 26.42, 22.90, 21.00, 14.30, 14.10. IR (NaCl): 2929, 1667 $^{-1}$cm. ESI-MS (m/z): 286 $[M+H]^+$



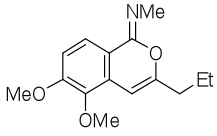
(Z)-N-(3-Hexyl-1H-isochromen-1-ylidene)methanamine (Scheme 2): 75% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.9, 1H), 7.44 – 7.35 (m, 1H), 7.31 – 7.20 (m, 1H), 7.10 (d, *J* = 7.7, 1H), 5.86 (s, 1H), 3.16 (s, 3H), 2.40 (t, *J* = 7.5, 2H), 1.71 – 1.59 (m, 2H), 1.44 – 1.22 (m, 6H), 0.89 (t, *J* = 6.6, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.53, 152.58, 133.42, 131.61, 127.32, 126.35, 124.66, 123.82, 101.27, 33.58, 33.49, 31.81, 28.95, 26.83, 22.78, 14.30. IR (NaCl): 2929, 1673 $^{-1}$cm. ESI-MS (m/z): 244 $[M+H]^+$



(Z)-N-(3-hexyl-6-methoxy-1H-isochromen-1-ylidene)methanamine (Scheme 2): 95 % isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.8, 1H), 6.81 (dd, *J* = 8.8, 2.5, 1H), 6.55 (d, *J* = 2.4, 1H), 5.82 (s, 1H), 3.82 (s, 3H), 3.13 (s, 3H), 2.39 (t, *J* = 7.5, 2H), 1.80 – 1.55 (m, 2H), 1.49 – 1.16 (m, 6H), 0.88 (t, *J* = 6.5, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.34, 157.10, 152.61, 135.23, 128.32, 116.90, 114.58, 107.82, 101.37, 56.47, 33.50, 33.37, 31.79, 28.93, 26.81, 22.76, 14.28. IR (NaCl): 2930, 1606 $^{-1}$cm. ESI-MS (m/z): 274 $[M+H]^+$

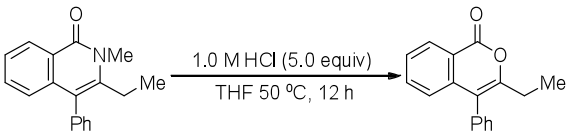


(Z)-N-(3-hexyl-1H-isochromen-1-ylidene)-1-phenylmethanamine: 73 % isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.0, 1H), 7.51 – 7.39 (m, 3H), 7.37 – 7.18 (m, 4H), 7.12 (d, *J* = 7.6, 1H), 5.90 (s, 1H), 4.70 (s, 2H), 2.40 (t, *J* = 7.5, 2H), 1.71 – 1.54 (m, 2H), 1.44 – 1.22 (m, 6H), 0.89 (t, *J* = 6.8, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.53, 151.72, 141.42, 133.55, 131.77, 128.46, 127.91, 127.35, 126.93, 126.53, 124.63, 123.83, 121.67, 101.51, 50.13, 33.53, 31.82, 28.96, 26.88, 22.80, 14.33. IR (NaCl): 2929, 1672 $^{-1}$cm. ESI-MS (m/z): 320 $[M+H]^+$

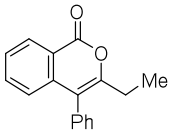


(Z)-N-(5,6-dimethoxy-3-propyl-1H-isochromen-1-ylidene)methanamine: 73 % isolated yiled; ^{1}H NMR (400 MHz, cdcl$_3$) δ 7.84 (d, *J* = 8.8, 1H), 6.85 (d, *J* = 8.8, 1H), 6.19 (s, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 3.13 (s, 3H), 2.40 (t, *J* = 7.4, 2H), 1.77 –

1.64 (m, 2H), 0.99 (t, *J* = 7.4, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 156.57, 154.85, 152.41, 141.95, 128.29, 123.07, 117.39, 111.42, 95.57, 61.27, 56.04, 35.76, 33.41, 20.31, 13.83. IR (NaCl): 2932, 1678 $^{-1}$cm. ESI-MS (m/z): 262 [M+H]$^+$

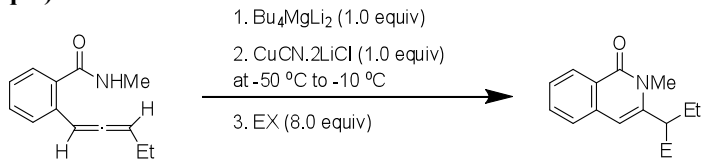


92 % isolated yield

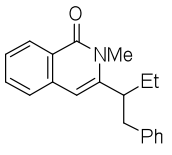


3-Ethyl-4-phenyl-1H-isochromen-1-one (Scheme 2, 8a): A solution of (Z)-N-(3-ethyl-6-methoxy-4-phenyl-1H-isochromen-1-ylidene)methanamine (0.06 mmol, 15 mg, 1.0 equiv) and 1.0 M of HCl (0.3 mmol, 300 µL, 5.0 equiv) in 2 mL of THF was heated at 50 °C. After 12 h the reaction mixture was diluted with EtOAc and washed with sat. NaCl solution. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure to give product in 92 % yield (13 mg). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.33 (dd, *J* = 7.9, 0.9, 1H), 7.56 (ddd, *J* = 8.1, 7.4, 1.4, 1H), 7.53 – 7.40 (m, 4H), 7.32 – 7.22 (m, 2H), 6.95 (d, *J* = 7.7, 1H), 2.37 (q, *J* = 7.5, 2H), 1.18 (t, *J* = 7.5, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.04, 156.38, 139.02, 134.72, 134.54, 130.72, 129.63, 129.16, 128.32, 127.59, 124.95, 120.28, 115.90, 25.19, 12.67. IR (NaCl): 1723 $^{-1}$cm. ESI-MS (m/z): 251 [M+H]$^+$

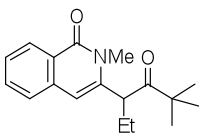
8. The Synthesis Functionalized Isoqunolone From Benzamides and Allenes:
8.1. From Allene (Eq. 3)



A solution of CuCN·2LiCl (0.2 mmol, 35 mg, 1.0 equiv) in THF (2.0 mL) was added to a freshly prepared solution of Bu_4MgLi_2 (0.2 mmol, 1.0 equiv) cooled to between -50 and -60 °C, followed by the addition of N-methyl-2-(penta-1,2-dien-1-yl)benzamide (0.2 mmol, 40 mg, 1.0 equiv) in 2 mL of THF. The reaction was then allowed to warm to -10 °C over 30-50 min and the cyclization was monitored by TLC. After the completion, the reaction mixture was cooled to -50 °C and the electrophile (8.0 equiv) was then added. The reaction was slowly warmed up to 0 °C, quenched with 10% NH_4OH in sat. NH_4Cl, diluted in EtOAc and washed with sat. NH_4Cl/10%NH_4OH : 1/1. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel (Toluene/EtOAc: 9/1).



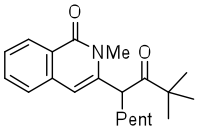
2-Methyl-3-(1-phenylbutan-2-yl)isoquinolin-1(2*H*)-one (Eq. 3, 1d): 71% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 8.37 (d, *J* = 8.1, 1H), 7.69 – 7.55 (m, 1H), 7.52 – 7.35 (m, 2H), 7.31 – 7.14 (m, 3H), 7.12 – 7.04 (m, 2H), 6.42 (s, 1H), 3.47 (s, 3H), 3.20 – 3.07 (m, 1H), 2.93 (dd, *J* = 7.0, 3.0, 2H), 1.88 – 1.64 (m, 2H), 0.91 (t, *J* = 7.4, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.68, 146.90, 139.37, 136.63, 132.28, 129.14, 128.69, 128.12, 126.73, 126.20, 125.59, 124.45, 103.95, 44.55, 42.50, 30.69, 27.94, 11.89. ESI-MS (m/z): 292 [M+H]$^+$



3-(5,5-Dimethyl-4-oxohexan-3-yl)-2-methylisoquinolin-1(2*H*)-one (Eq. 3, 1e): 72% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.36 (d, *J* = 7.5, 1H), 7.66 – 7.53 (m, 1H), 7.46 – 7.35 (m, 2H), 6.23 (s, 1H), 4.08 (dd, *J* = 10.1, 3.7, 1H), 3.75 (s, 3H), 2.17 – 2.09 (m, 1H), 1.76 – 1.59 (m, 1H), 1.10 (s, 9H), 0.92 (t, *J* = 7.3, 3H). ^{13}C NMR (101

MHz, $CDCl_3$) δ 212.14, 163.89, 140.62, 136.12, 132.57, 128.04, 126.85, 126.05, 124.64, 104.85, 49.77, 44.94, 30.84, 26.84, 13.05. IR (NaCl): 2966, 1705, 1652 $^{-1}$cm. ESI-MS (m/z): 286 $[M+H]^+$

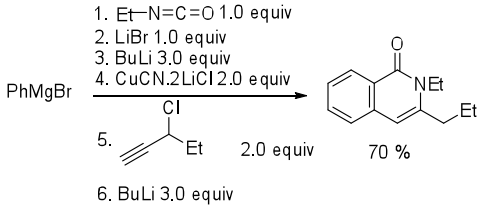
8.2. From benzamide (Eq. 4):

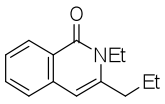


3-(2,2-Dimethyl-3-oxononan-4-yl)-2-methylisoquinolin-1(2*H*)-one (Eq. 4, 1f): A solution of *N*-Methylbenzamide (0.5 mmol, 67 mg, 1.0 equiv) in THF (2.0 ml) was added to a freshly prepared solution of Bu_4MgLi_2 (0.5 mmol) at room temperature. The resulted mixture was stirred at room temperature for 2 h before being cooled to between -50 and -60 °C. Prior to addition, copper salts and propargyl alcohols were weighed in a glove box to prevent oxygen-induced homocoupling of the benzamide. Thus, CuCN·2LiCl (1.0 mmol, 175 mg, 2.0 equiv) in 5 mL of THF was added, and after 5-10 min, 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) in 2.0 mL of THF was added. The stirring was continued for another 1 h at -50 to -30 °C and *n*-butyllithium (1.5 mmol, 0.94 mL, 1.6 M in hexanes, 3.0 equiv) was then added at -50 °C. The reaction mixture was then warmed to -20 °C and stirred at this same temperature for 1.5 h, before was cooled down again to -50 °C. Pivaloyl chloride (7.5 mmol, 0.92 mL, 15 equiv) was then added. The reaction was allowed to warm to room temperature, stirred overnight and then quenched by addition of NH_4Cl/10%NH_4OH, diluted in EtOAc and washed with 10% NH_4OH in sat. NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified using column chromatography on silica gel (Toluene/EtOAc: 95/5) to give 62% (101 mg) of 3-(2,2-Dimethyl-3-oxononan-4-yl)-2-methylisoquinolin-1(2*H*)-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.8, 1H), 7.62 – 7.51 (m, 1H), 7.47 – 7.33 (m, 2H), 6.02 (s, 1H), 4.14 (dd, *J* = 10.3, 3.4, 1H), 3.73 (s, 3H), 2.23 – 2.03 (m, 1H), 1.62 – 1.46 (m, 1H), 1.37 – 1.11 (m, 8H), 1.08 (s, 9H), 0.85 (t, *J* = 6.8, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.21, 163.84, 140.76, 136.13, 132.55, 128.03, 126.80, 126.01, 124.59, 104.77, 48.35, 48.28, 48.25, 45.01, 33.63, 31.91, 30.76, 28.22, 26.89, 22.64, 14.18. IR (NaCl): 2960, 1707, 1654 $^{-1}$cm. ESI-MS (m/z): 328 $[M+H]^+$

9. The Synthesis Functionalized Isoquinolone from Isocyanate in four Component Coupling:

3- Component Coupling (Eq. 5):

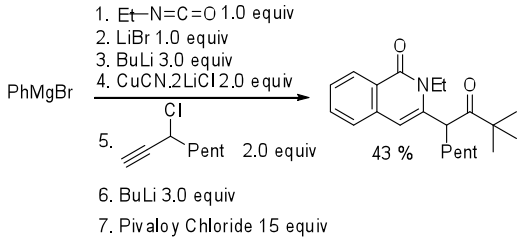


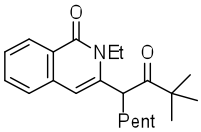


2-Ethyl-3-propylisoquinolin-1(2*H*)-one (Eq. 5, 1e): To a solution of PhMgBr (0.5 mmol, 0.5 mL, 1.0 M solution in THF, 1.0 equiv) in 2 mL of THF was added dropwise a solution of EtNCO (0.5 mmol, 40 μL, 1.0 equiv) in 2 mL of THF at -30 °C. The reaction mixture was warmed up to -10 °C over 30 min and dry LiBr (0.5 mmol, 43 mg, 1.0 equiv) in 1 mL of THF was added. After 5 min of stirring at -10 °C, the cold bath was removed and *n*-butyllithium (1.5 mmol, 0.94 mL, 1.6 M in hexanes, 3.0 equiv) was added. After the addition was complete, the reaction was heated at 60 °C for 1.5 h and then cooled to between -50 and -60 °C before the solution of CuCN·2LiCl (1.0 mmol, 174 mg, 2.0 equiv) in 5 mL THF was added. Prior to addition, copper salts and propargyl alcohols were weighed in a glove box to prevent oxygen-induced homocoupling of the benzamide. After 10 min, 3-chloropent-1-yne (1.0 mmol, 102 mg 2.0 equiv) was added in 2 mL THF. The stirring was continued for another 1 h at -55 to -30 °C and then *n*- butyllithium (1.5 mmol, 0.94 mL, 1.6 M in hexanes, 3.0 equiv) was added dropwise at -55 °C. The reaction mixture was then warmed up to -10 °C over 1.0 h and quenched by the addition of 10% NH_4OH in sat. NH_4Cl, diluted with EtOAc and washed with 10% NH_4OH in sat.

NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel (Hexanes/EtOAc 90:10) to give 75 mg (70 %) of 2-ethyl-3-propylisoquinolin-1(*2H*)-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.0, 1H), 7.64 – 7.51 (m, 1H), 7.46 – 7.35 (m, 2H), 6.33 (s, 1H), 4.17 (q, *J* = 7.0, 2H), 2.75 – 2.53 (m, 2H), 1.85 – 1.64 (m, 2H), 1.32 (t, *J* = 7.1, 3H), 1.06 (t, *J* = 7.3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.18, 142.86, 136.82, 132.20, 127.96, 126.01, 125.36, 124.75, 104.44, 48.41, 35.12, 22.46, 14.51, 14.08. IR (NaCl): 2933, 1646 $^{-1}$cm. ESI-MS (m/z): 217 $[M+H]^+$

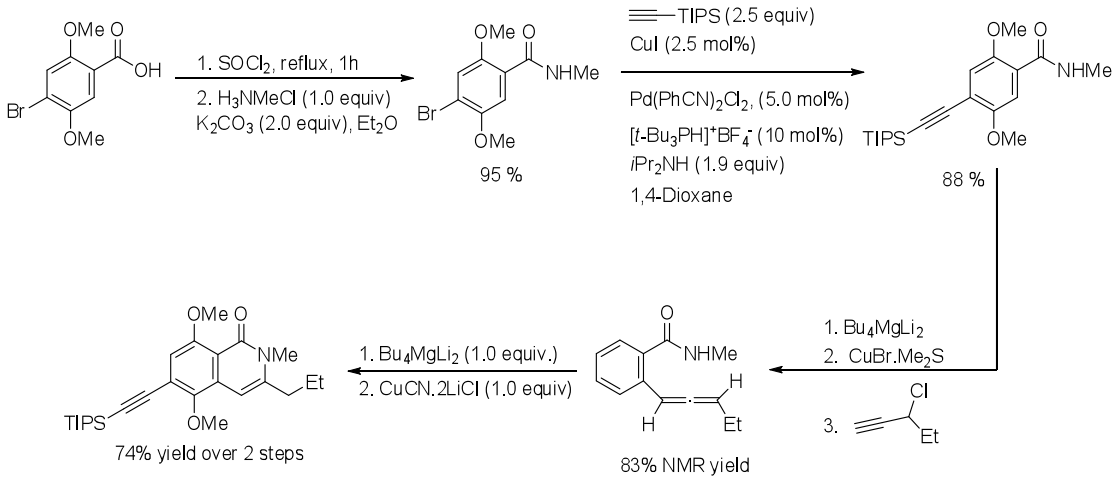
4- Component Coupling (Eq. 6):

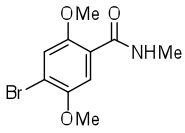




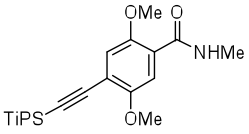
3-(2,2-Dimethyl-3-oxononan-4-yl)-2-ethylisoquinolin-1(2*H*)-one (Eq. 6, 1h): To a solution of PhMgBr (0.5 mmol, 0.5 mL, 1.0 M solution in THF, 1.0 equiv) in 2 mL of THF was added dropwise a solution of EtNCO (0.5 mmol, 40 µL, 1.0 equiv) in 2 mL of THF at -30 °C. The reaction mixture was warmed to -10 °C over 30 min and LiBr (0.5 mmol, 43 mg, 1.0 equiv) in 1 mL of THF was added. After 5 min of stirring at -10 °C, the cold bath was removed and *n*-butyllithium (1.5 mmol, 0.94 mL, 1.6 M in hexanes, 3.0 equiv) was added. After the addition was complete, the reaction was heated at 60 °C for 1.5 h and then cooled to between -50 and -60 °C, before a solution of CuCN·2LiCl (1.0 mmol, 174 mg, 2.0 equiv) in 5 mL THF was added. Prior to addition, copper salts and propargyl alcohols were weighed in a glove box to prevent oxygen-induced homocoupling of the benzamide. After 10 min 3-chlorooct-1-yne (1.0 mmol, 144 mg 2.0 equiv) was added in 2 mL THF. The stirring was continued for another 1h at -55 to -30 °C and *n*-butyllithium (1.5 mmol, 0.94 mL, 1.6 M in hexanes, 3.0 equiv) was added dropwise at -55 °C. The reaction mixture was then warmed to -30 °C and stirred at this same temperature for 1.5 h, before being cooled again to -55 °C at which point pivaloy chloride (7.5 mmol, 0.92 mL, 15 equiv) was added. The reaction was allowed to warm to room temperature, stirred overnight and then quenched by addition of 10 % NH_4OH in sat. NH_4Cl, diluted with EtOAc and washed with 10 % NH_4OH in sat. NH_4Cl. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel (Toluene/EtOAc 95:5) to give 73 mg (43 %) of 3-(2,2-Dimethyl-3-oxononan-4-yl)-2-ethylisoquinolin-1(2H)-one: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.0, 1H), 7.58 – 7.54 (m, 1H), 7.42 – 7.36 (m, 2H), 6.17 (s, 1H), 4.42 (tdd, *J* = 7.2, 7.2, 14.2, 1H), 4.17 – 3.97 (m, 2H), 2.27 – 2.18 (m, 1H), 1.60 – 1.50 (m, 1H), 1.47 (t, *J* = 7.1, 3H), 1.36 – 1.16 (m, 6H), 1.12 (s, 9H), 0.86 (t, *J* = 6.6, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.25, 163.45, 140.47, 136.14, 132.47, 127.86, 126.71, 125.98, 124.90, 104.66, 48.16, 45.29, 39.30, 34.33, 31.86, 28.55, 27.04, 22.63, 14.60, 14.17. IR (NaCl): 2966, 1705, 1653 $^{-1}$cm. ESI-MS (m/z): 342 $[M+H]^+$

10. Synthesis of the AB ring of (-)-Kibdelone (Eq. 2, 1c) [5]:



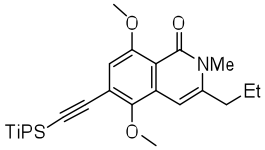


4-bromo-2,5-dimethoxy-N-methylbenzamide. The solution of 4-bromo-2,5-dimethoxybenzoic acid (3.84 mmol, 1.0 g) in 25 mL of $SOCl_2$ was stirred at reflux for 1 h. After the reaction mixture was cooled down to room temperature and $SOCl_2$ was removed under reduced pressure, the crude benzoyl chloride was dissolved in 30 mL of THF and K_2CO_3 (7.69 mmol, 1.06 g) was added followed by methylamine hydrochloride (3.84 mmol, 0.26 g). After the reaction mixture was stirred overnight at room temperature, it was diluted with EtOAc and water. The organic phase was separated and the aqueous layer was extracted twice with ethyl acetate. The combined extractions were then washed with a saturated NaCl solution. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by using column chromatography on silica gel to give 1.0 g of 4-bromo-2,5-dimethoxy-N-methylbenzamide (95 %) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.80 (s, 1H), 7.17 (s, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 2.99 (d, J = 4.8, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.24, 151.56, 150.72, 121.47, 117.21, 115.52, 114.90, 56.96, 56.95, 26.87. ESI-MS (m/z): 273 $[M]^+$.

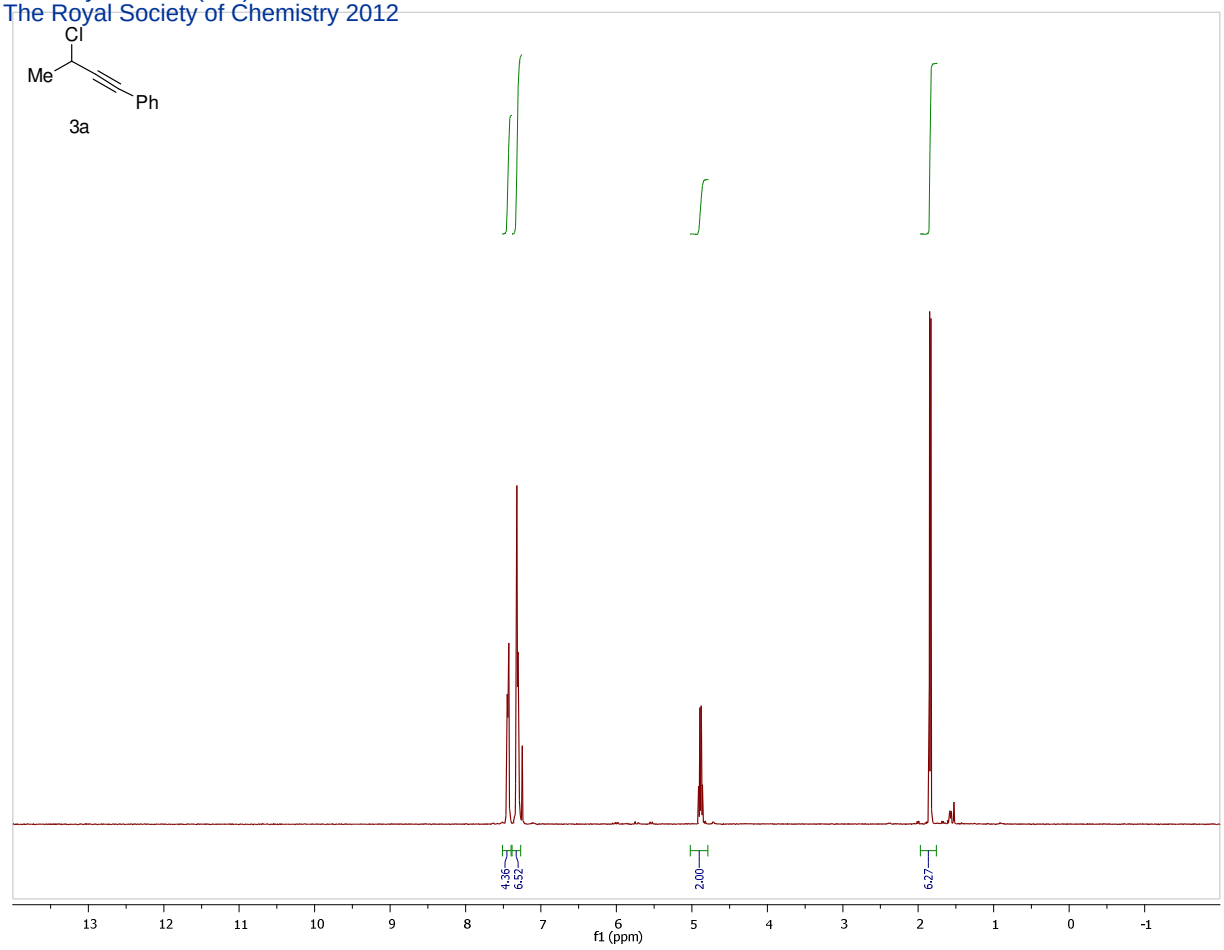


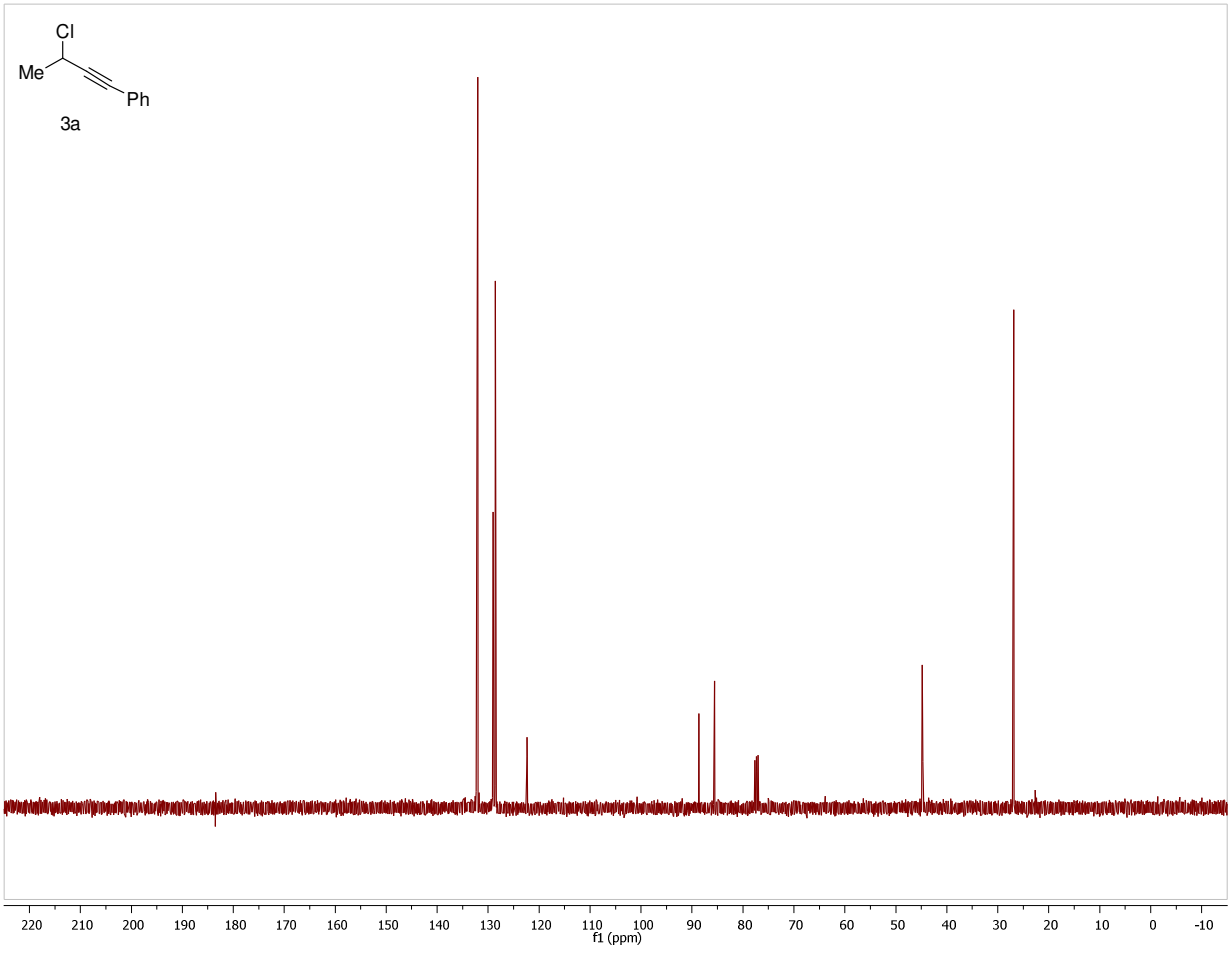
2,5-Dimethoxy-N-methyl-4-((triisopropylsilyl)ethynyl)benzamide was synthesized according to literature procedure.[4] 4-bromo-2,5-dimethoxy-N-methylbenzamide (1.0 g, 3.66 mmols) was combined with $Pd(PhCN)_2Cl_2$ (70 mg, 5 mol%), CuI (17 mg, 2.5 mol%), and [t-Bu_3PH][BF_4] (106 mg, 10 mol%) in a vial fitted with an efficient stir bar. The vial was purged with a stream of nitrogen for ~15 minutes. 1,4-dioxane (3.7 mL) was then added and the solution was sparged for 10 minutes and diisopropyl amine (1.0 mL, 1.9 eq.) was added while sparging continued. Finally triisopropylsilylacetylene (2.0 mL, 1.67 g, 9.15 mmol, 2.5 eq.) was added and sparging was continued for 10 additional minutes. The vial was then heated to 45 °C in an aluminum block with vigorous stirring for 12-18 hours under nitrogen. When the reaction was complete as judged by TLC, the reaction mixture was filtered through a plug of silica gel, washing with ethyl acetate. The combined extractions were then washed with a saturated NaCl solution, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue obtained was then purified by flash chromatography to give 1.2 g of alkyne. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.75 (s, 1H), 7.00 (s, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.00 (d, J = 4.7, 3H), 1.14 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.47, 155.47, 151.09, 122.26, 116.74, 116.66, 114.37, 102.45, 98.10, 56.75, 56.62, 26.83, 18.86, 11.54. IR (NaCl): 2941, 1646 $^{-1}$cm. ESI-MS (m/z): 376 $[M+H]^+$.

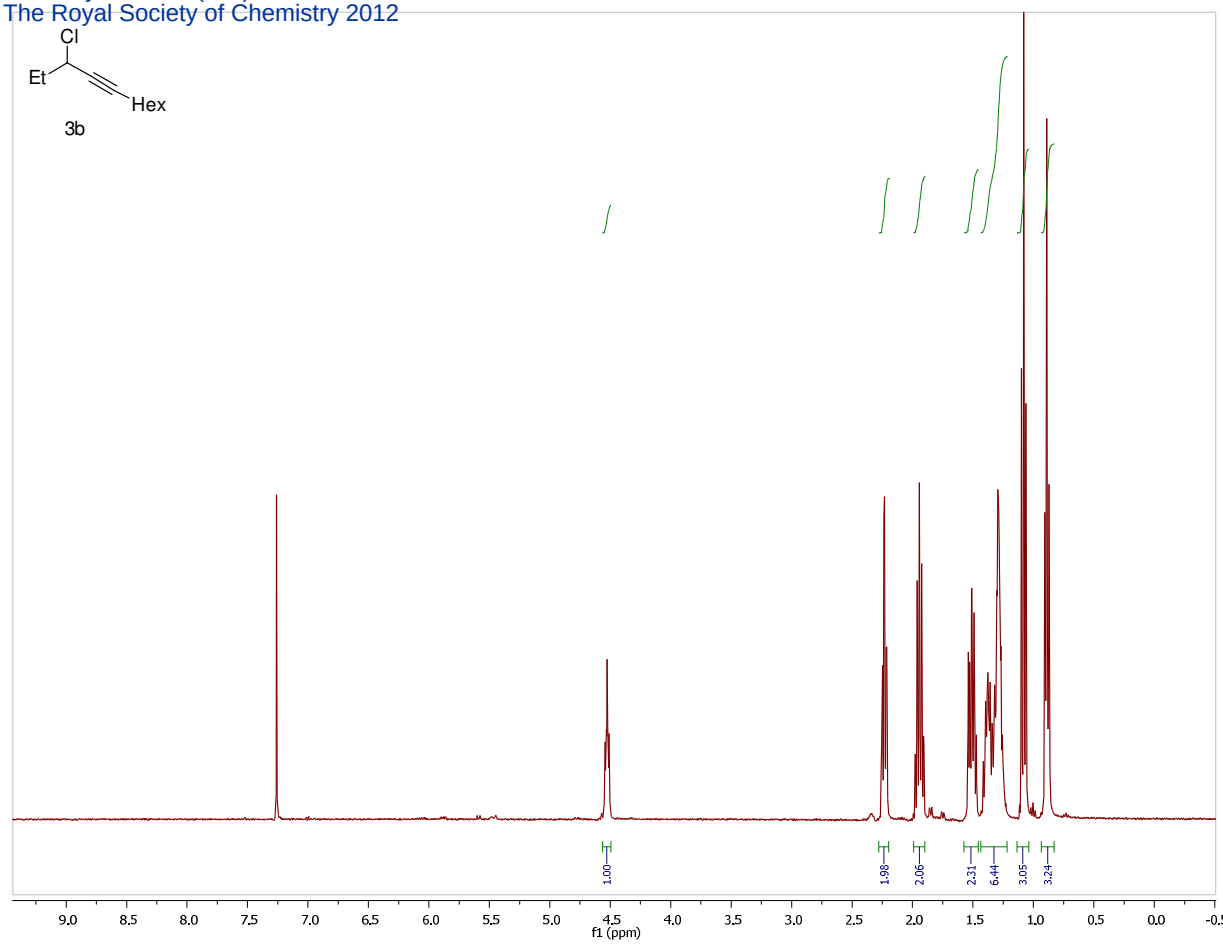
[5] J. R. Butler, C. Wang, J. Bian, J. M. Ready, *J. Am. Chem. Soc.* **2011**, *133*, 9956-9955

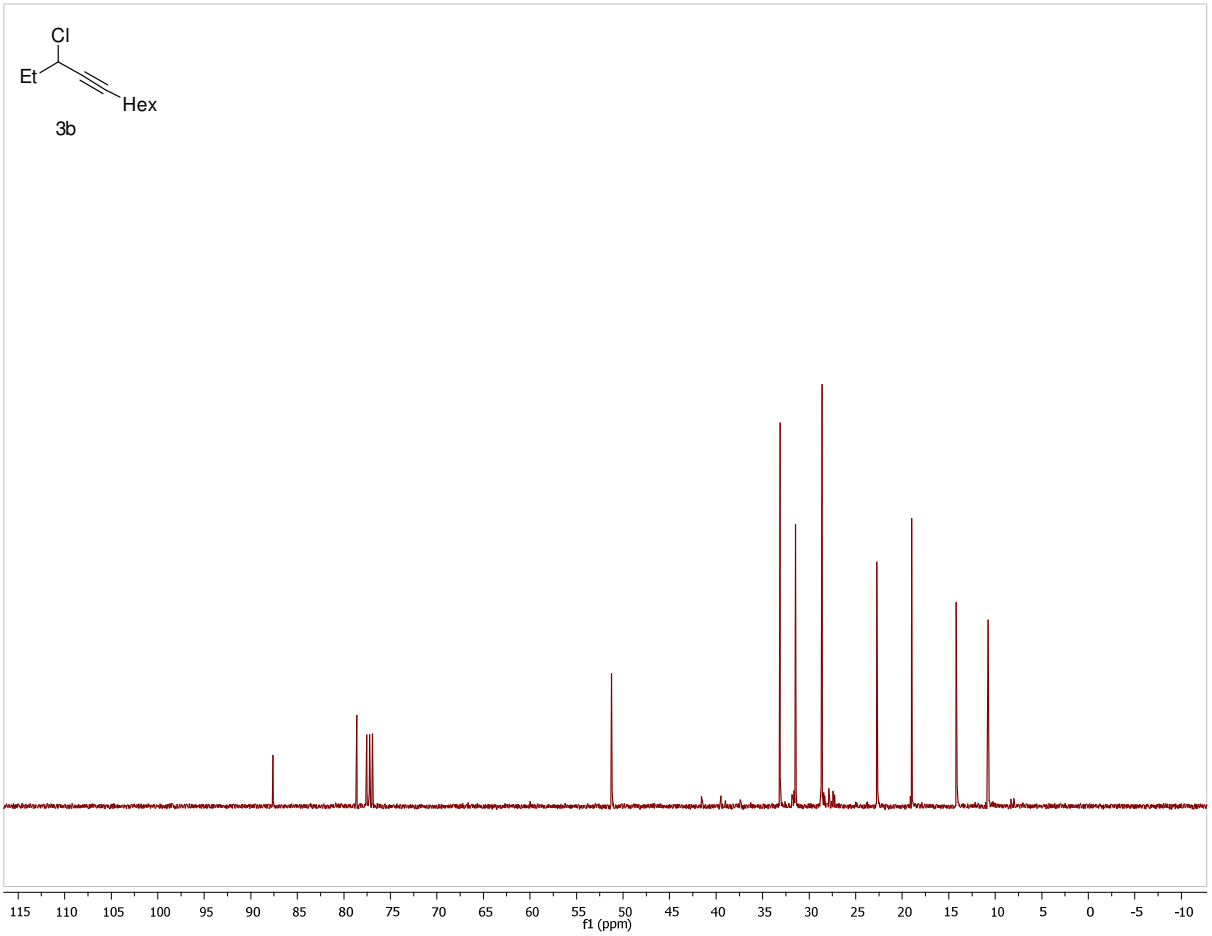


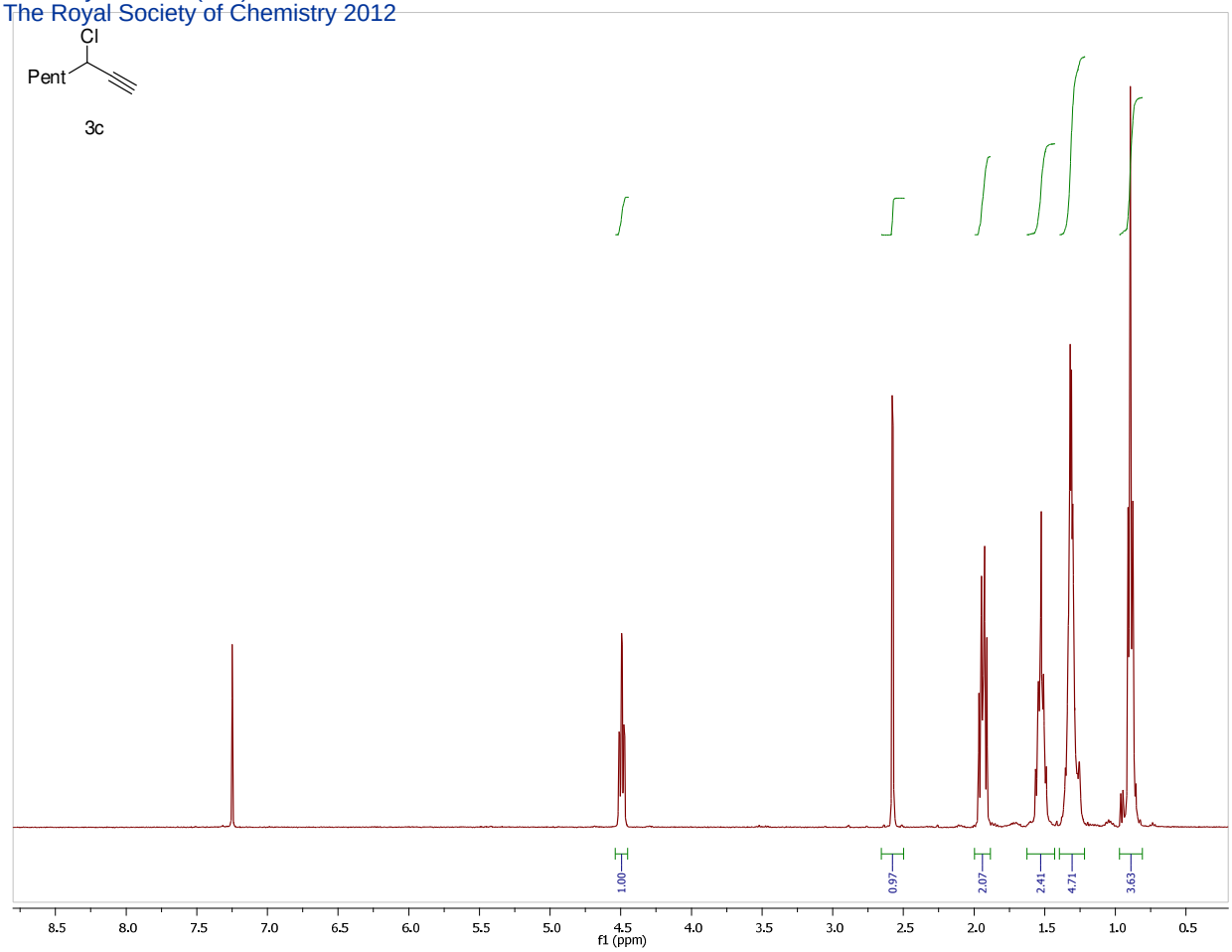
5,8-dimethoxy-2-methyl-3-propyl-6-((triisopropylsilyl)ethynyl) isoquinolin-1(2*H*)-one (Eq.2, 1c). 2,5-dimethoxy-N-methyl-4-((triisopropylsilyl)ethynyl)benzamide (0.25 mmol, 93 mg, 1.0 equiv) was condensed with 3-chloropent-1-yne as described above to give crude product as a mixture of allene (83 % ^{1}HNMR yield) and staring banzamide (17 % ^{1}HNMR). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (s, 1H), 6.27 (dt, *J* = 6.8, 3.3, 1H), 5.62 (s, 1H), 5.42 (dt, *J* = 6.4, *J* = 6.4, 1H), 3.85 (s, 3H), 3.75 (s, 3H), 2.93 (d, *J* = 4.9, 3H), 2.22 – 2.00 (m, 2H), 1.13 (s, 18H), 1.04 (t, *J* = 7.4, 3H). The crude allene was then cyclized as described above. The crude product was purified by using column chromatography on silica gel to give 82 mg (74 %) of isoquinolone: ^{1}H NMR (400 MHz $CDCl_3$) δ 6.74 (s, 1H), 6.51 (s, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.50 (s, 3H), 2.61 (t, *J* = 7.8, 2H), 1.77 – 1.60 (m, 2H), 1.15 (s, 18H), 1.02 (t, *J* = 7.3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.74, 156.36, 149.97, 144.95, 133.61, 119.65, 114.79, 110.54, 102.74, 98.57, 98.27, 61.67, 56.56, 36.20, 30.85, 21.63, 18.88, 13.93, 11.54. IR (NaCl): 1648 $^{-1}$cm.ESI-MS (m/z): 442 $[M+H]^+$

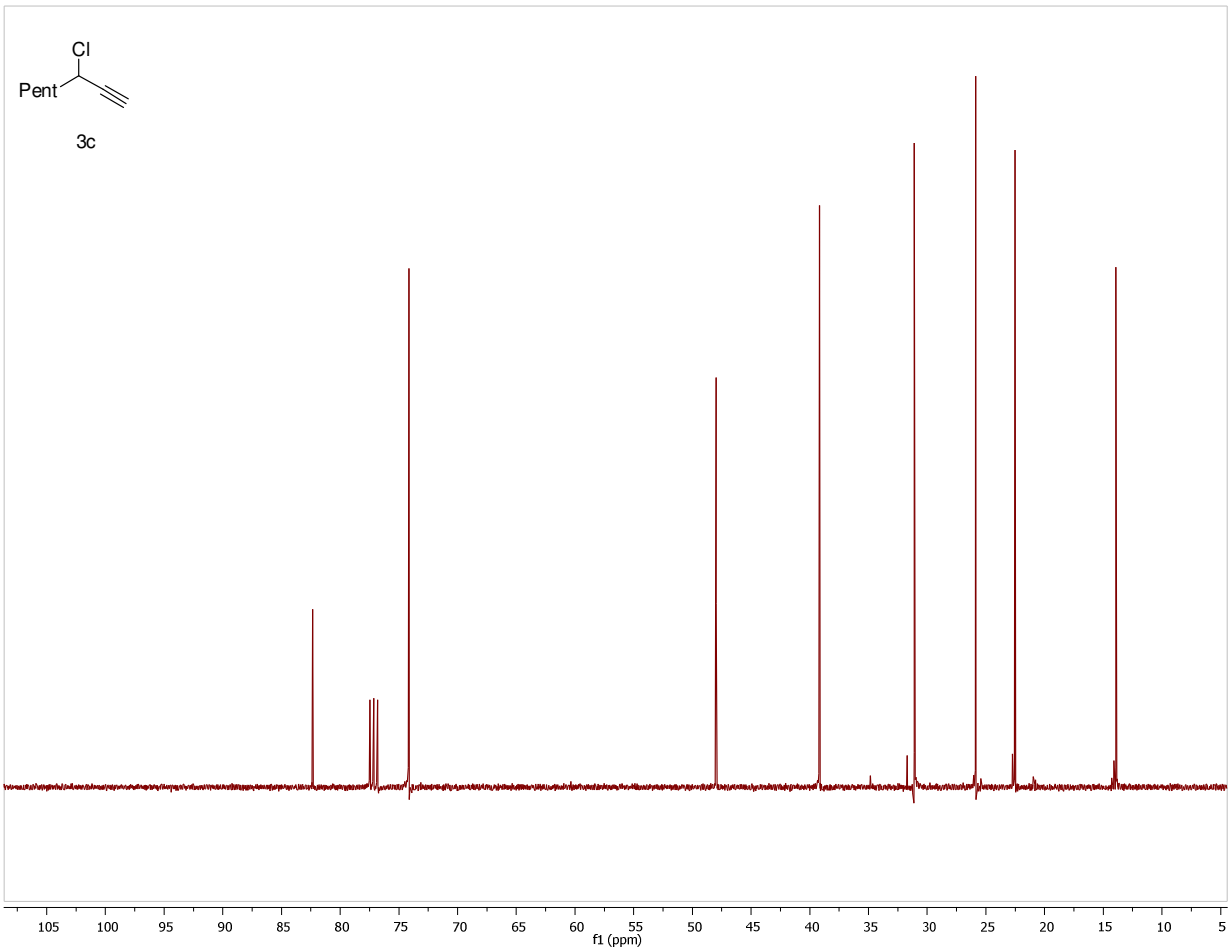


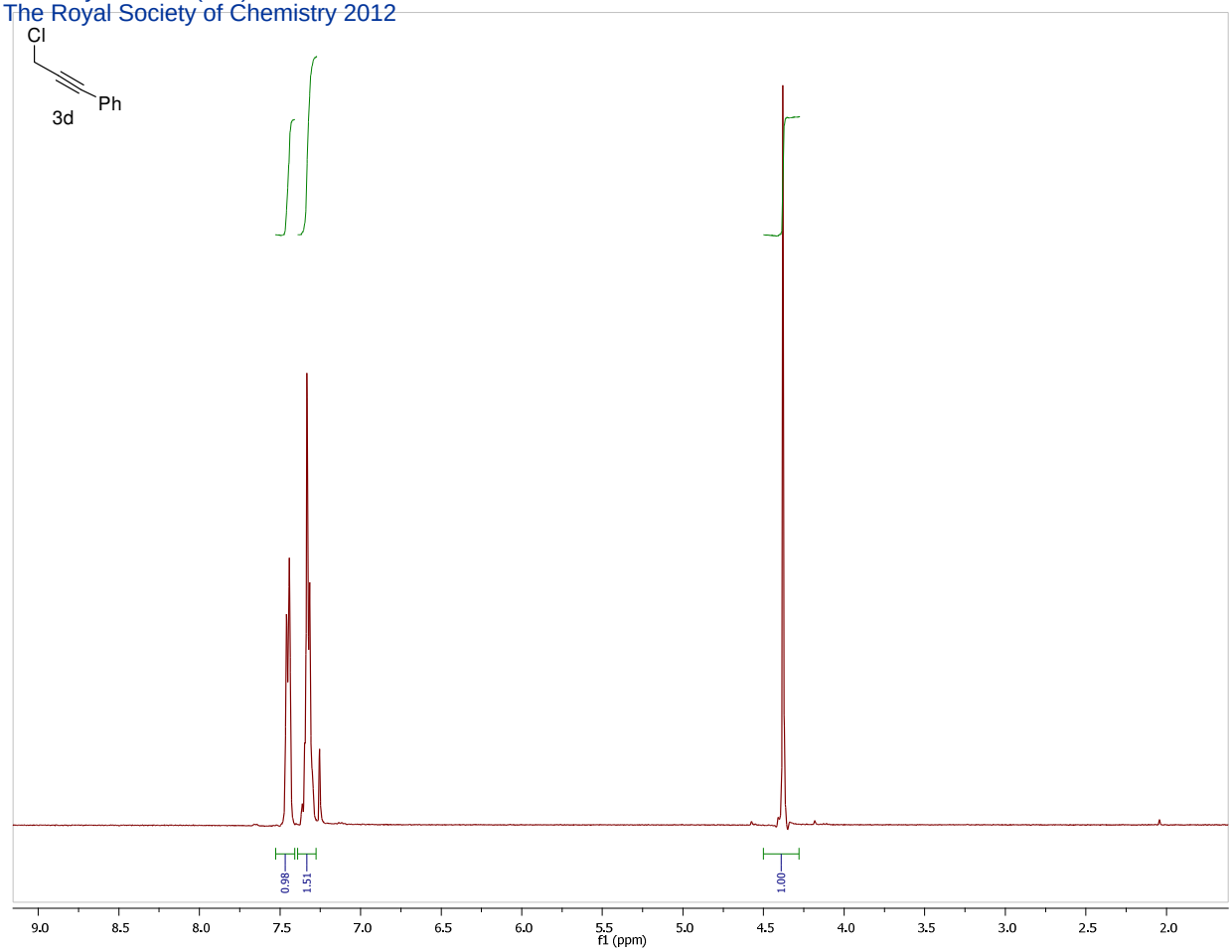


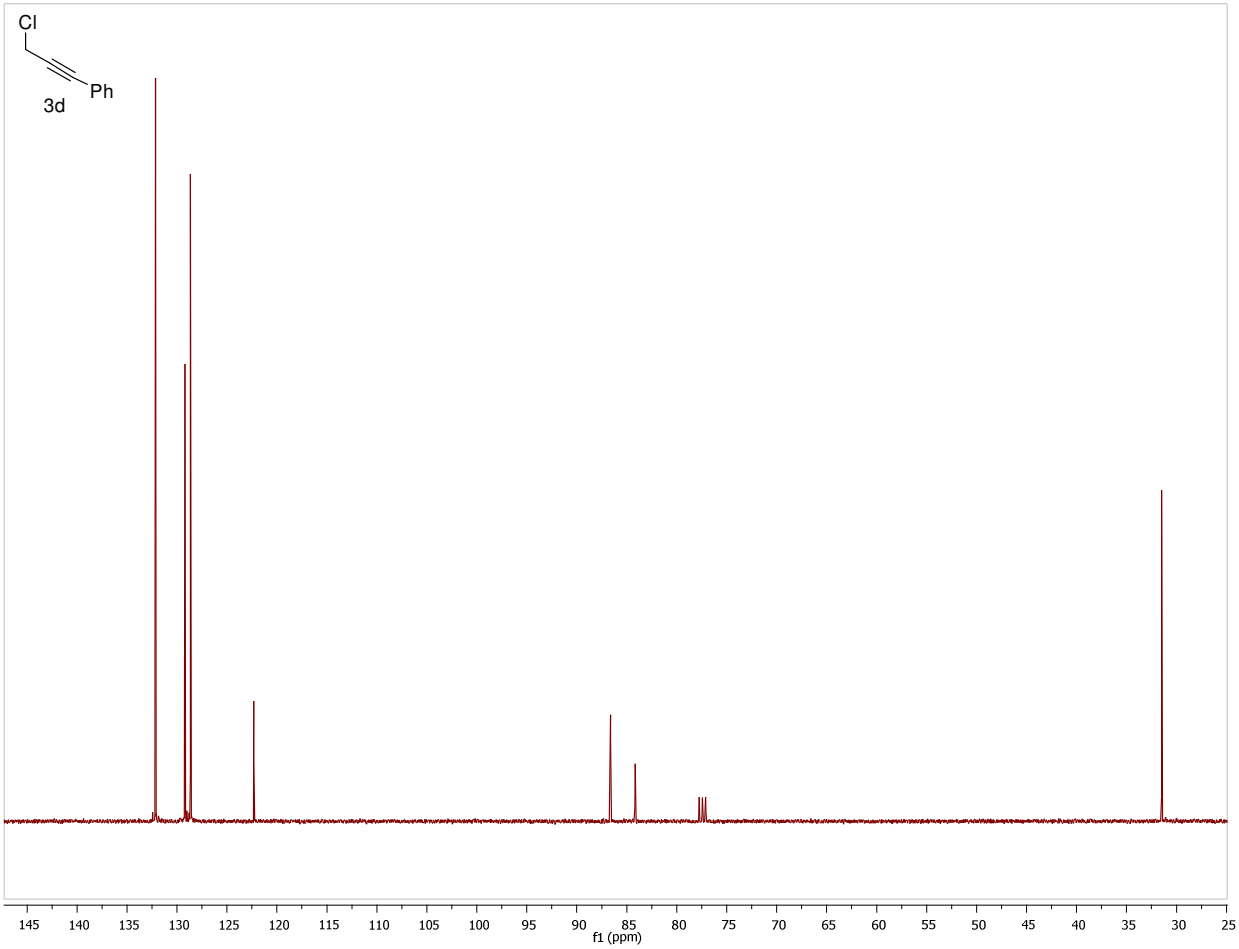


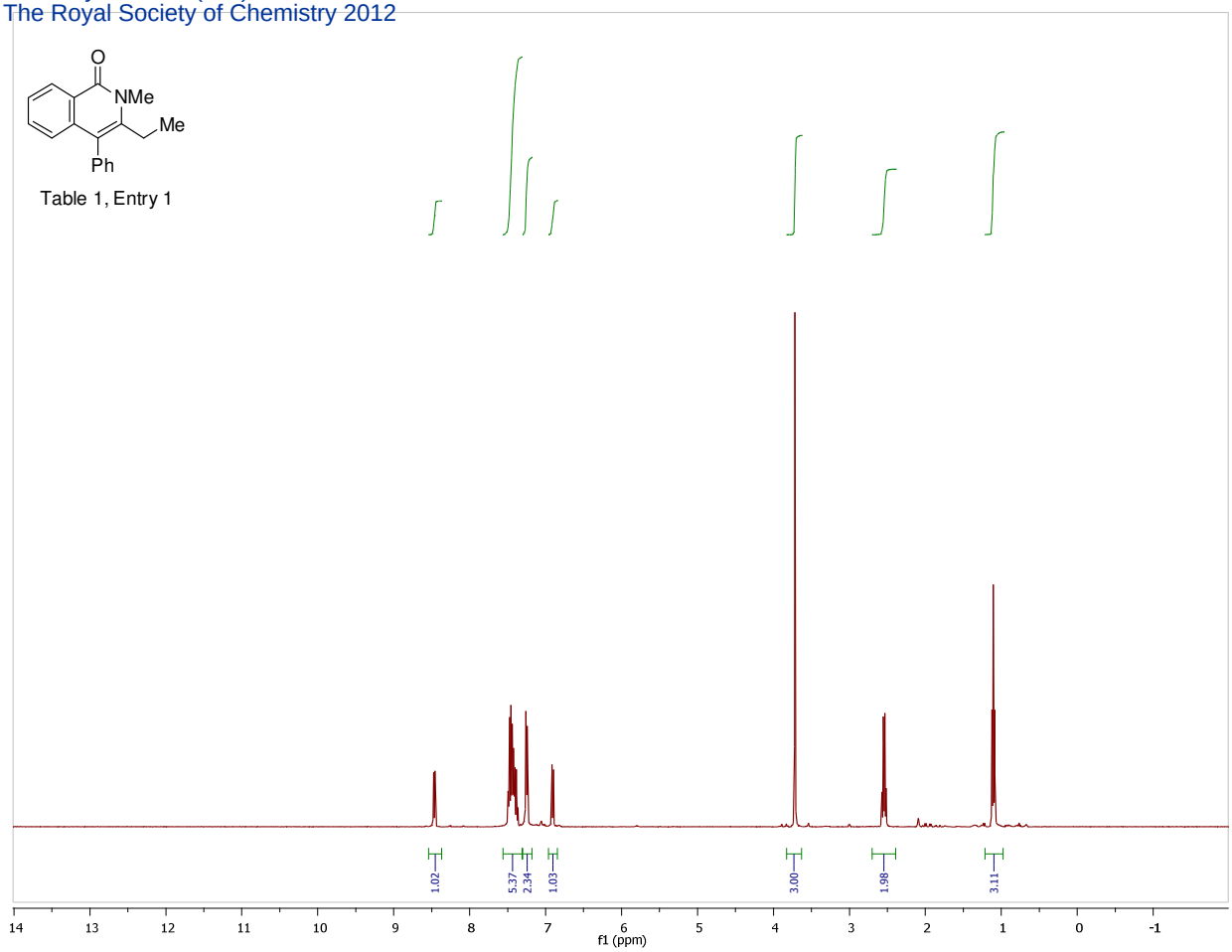


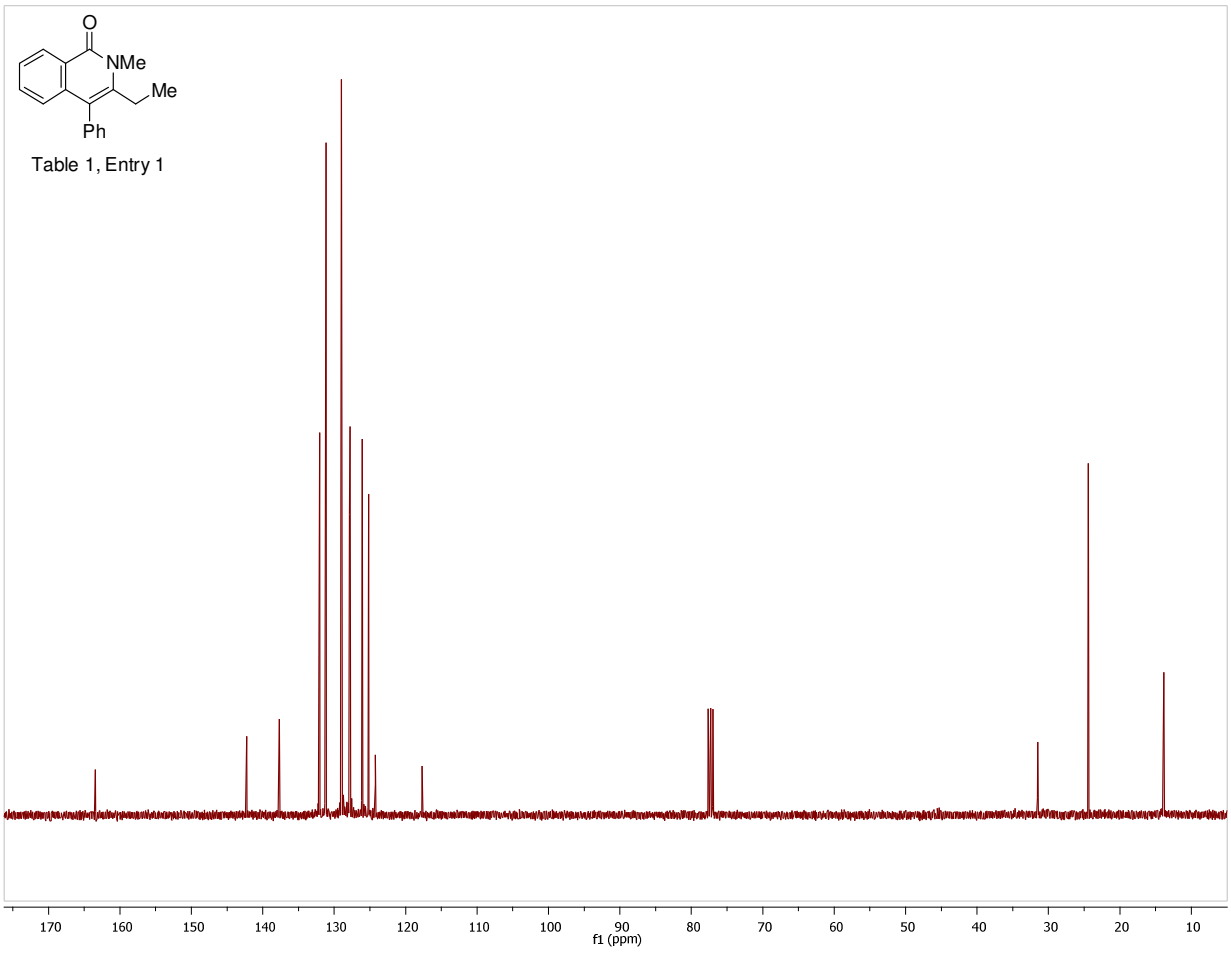


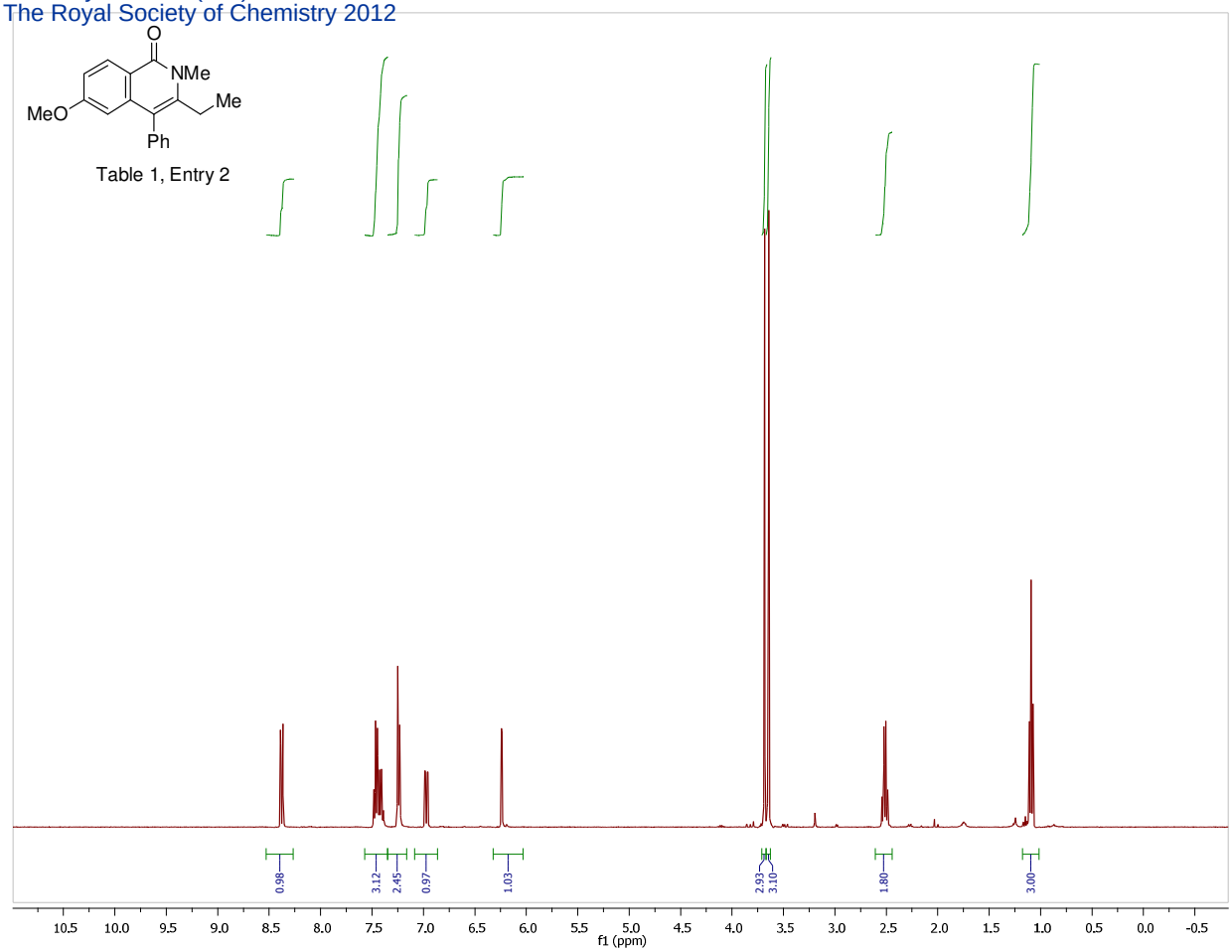


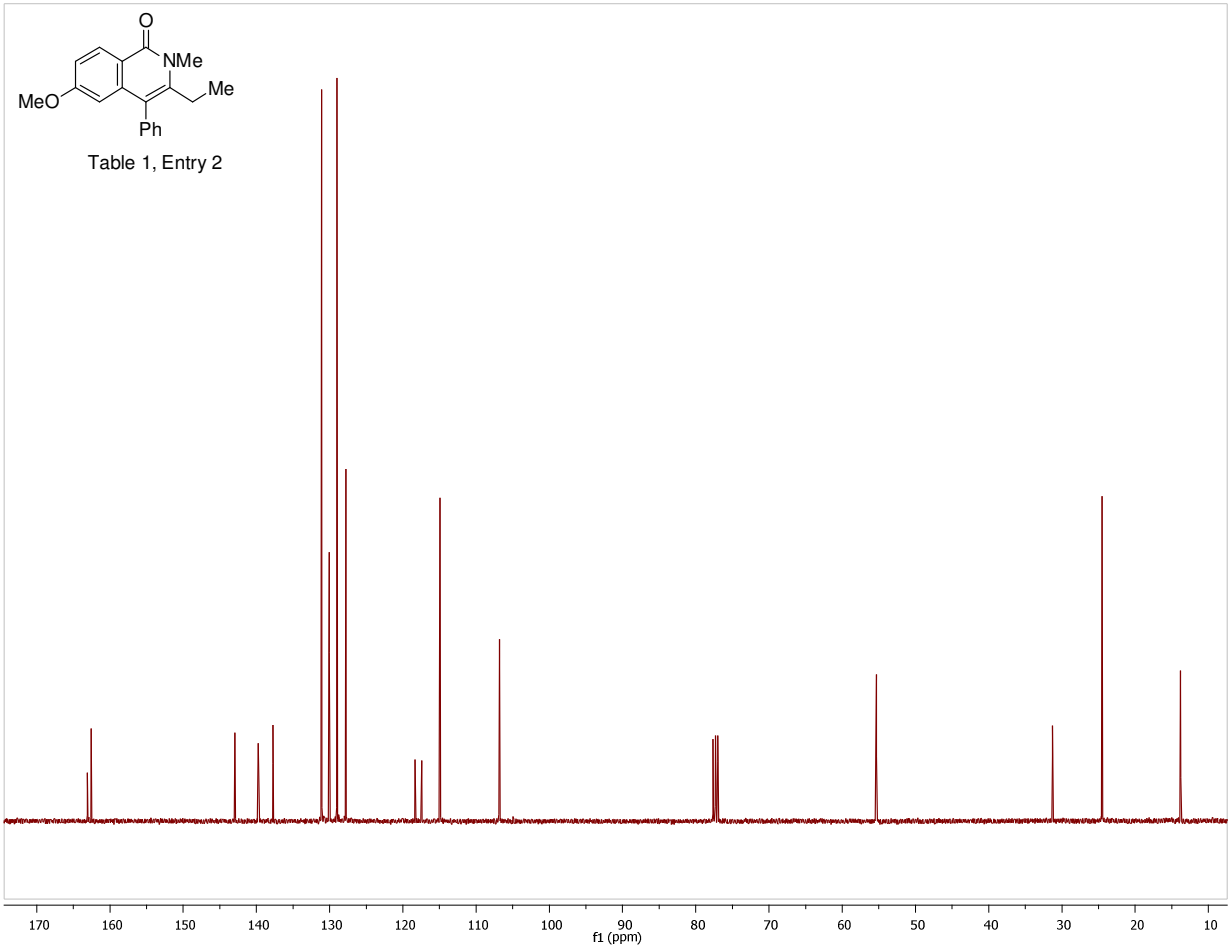


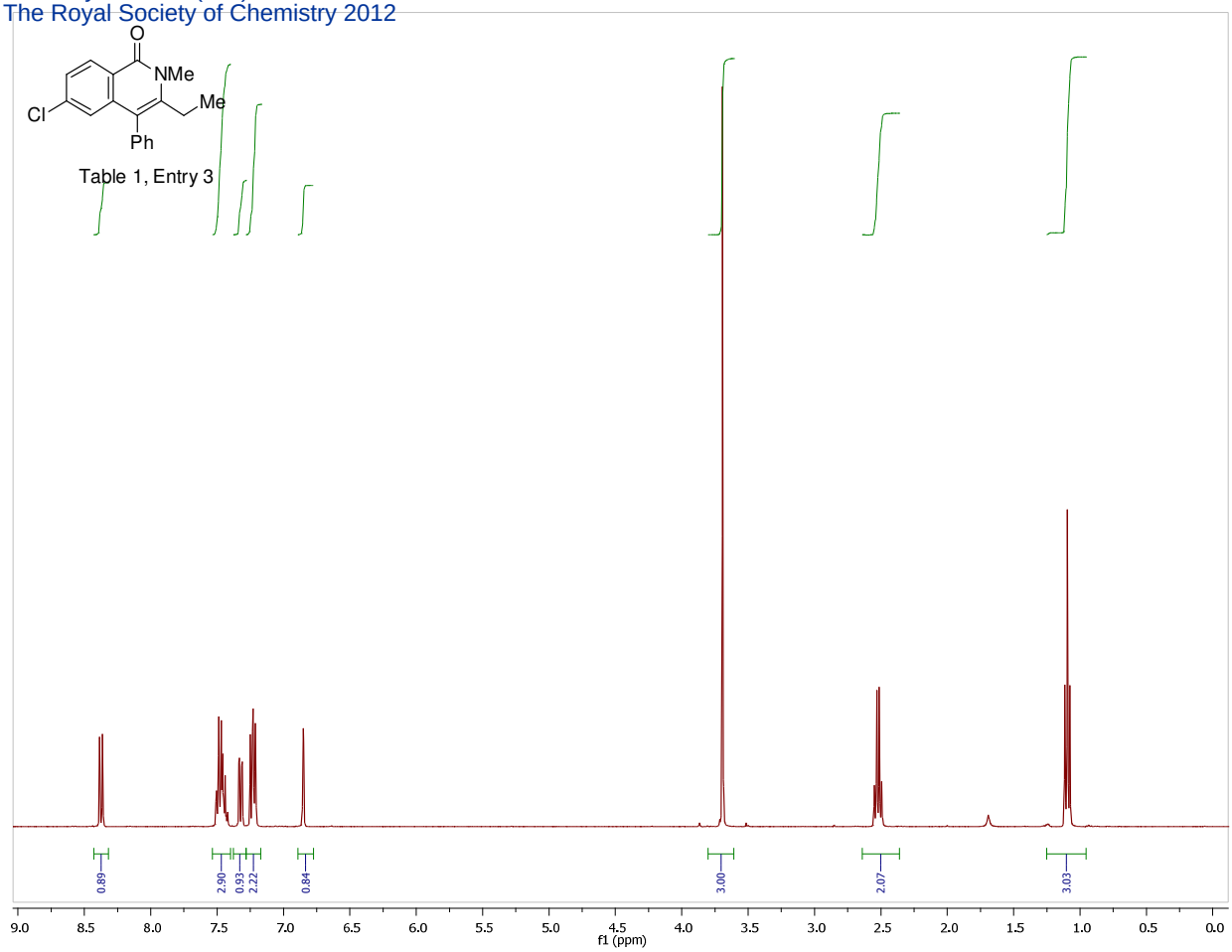


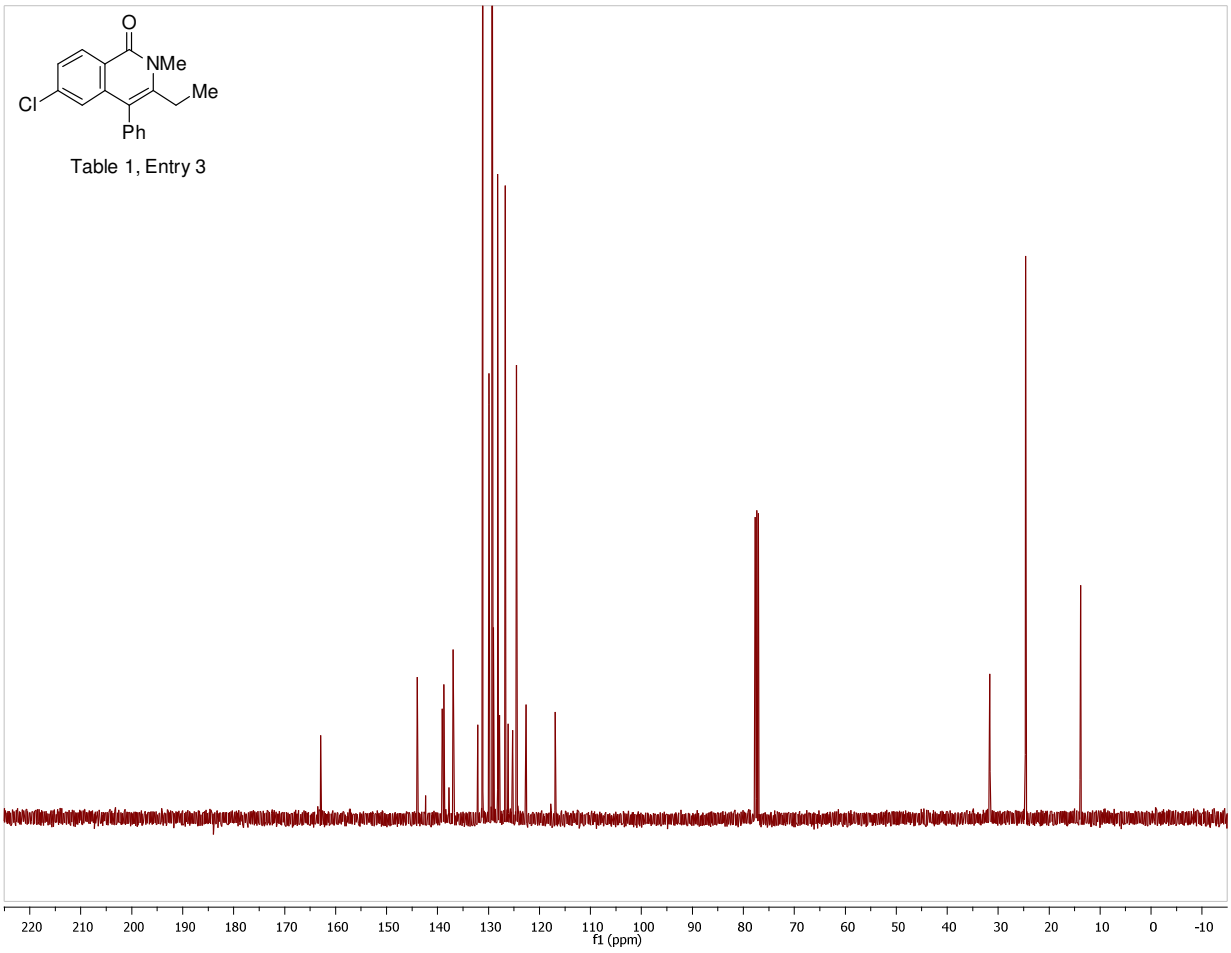


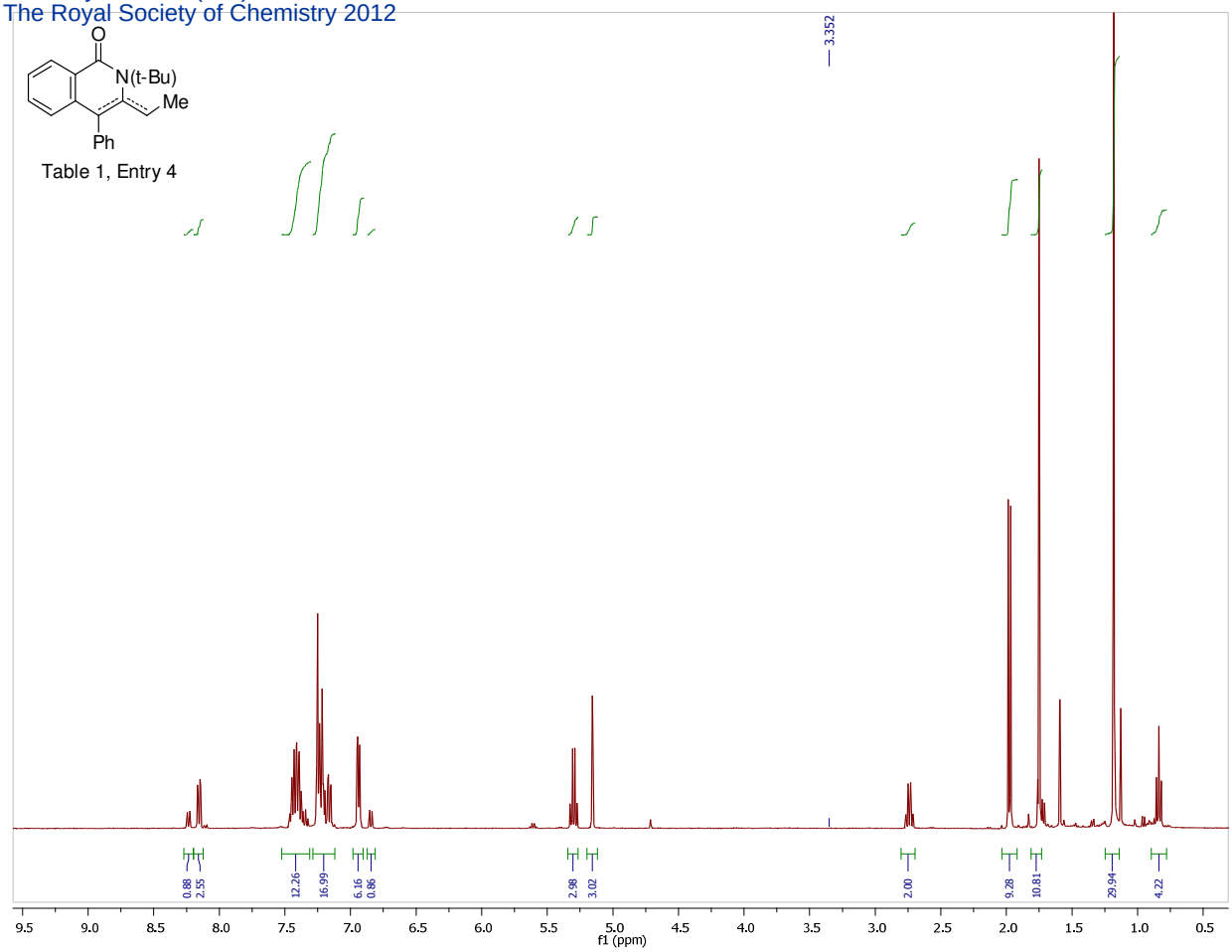


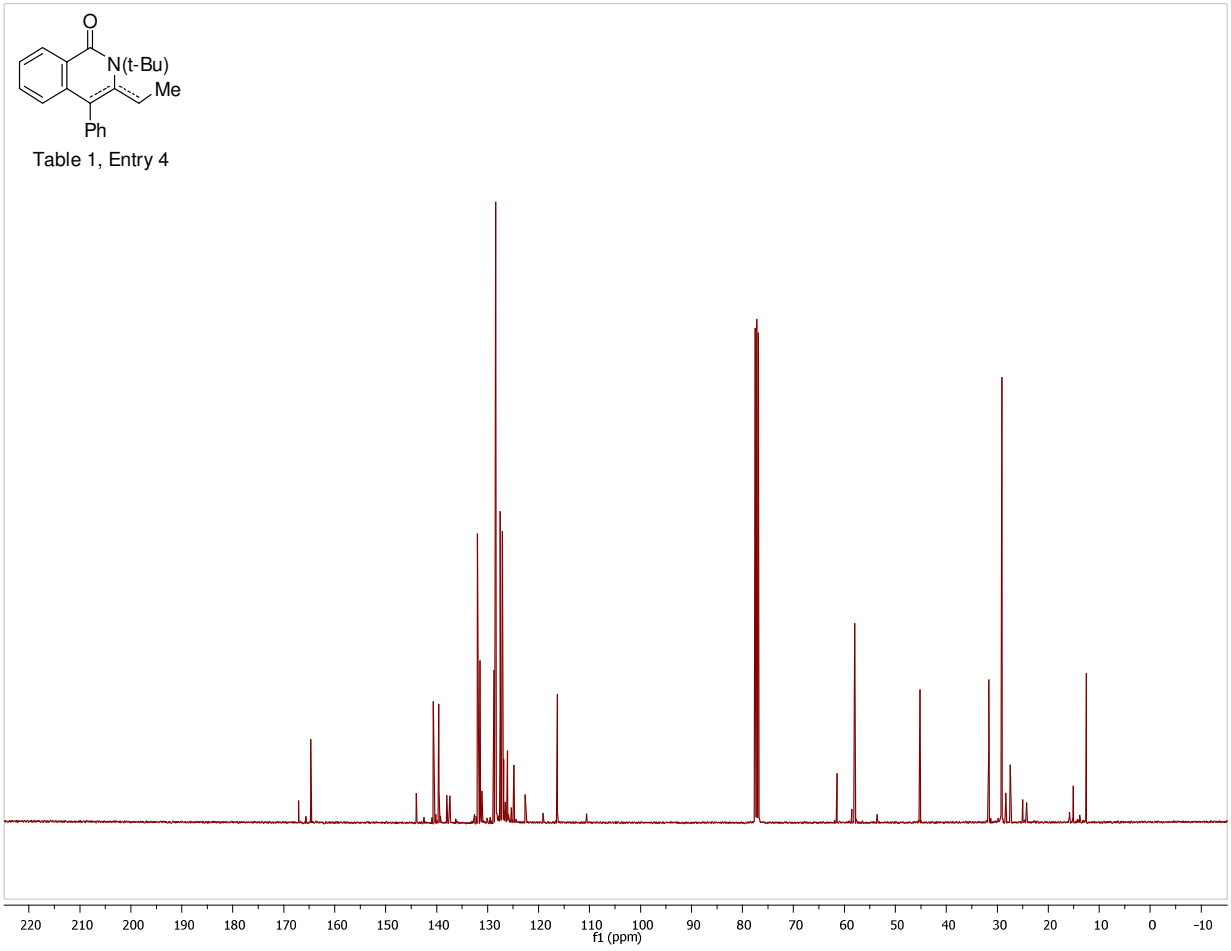


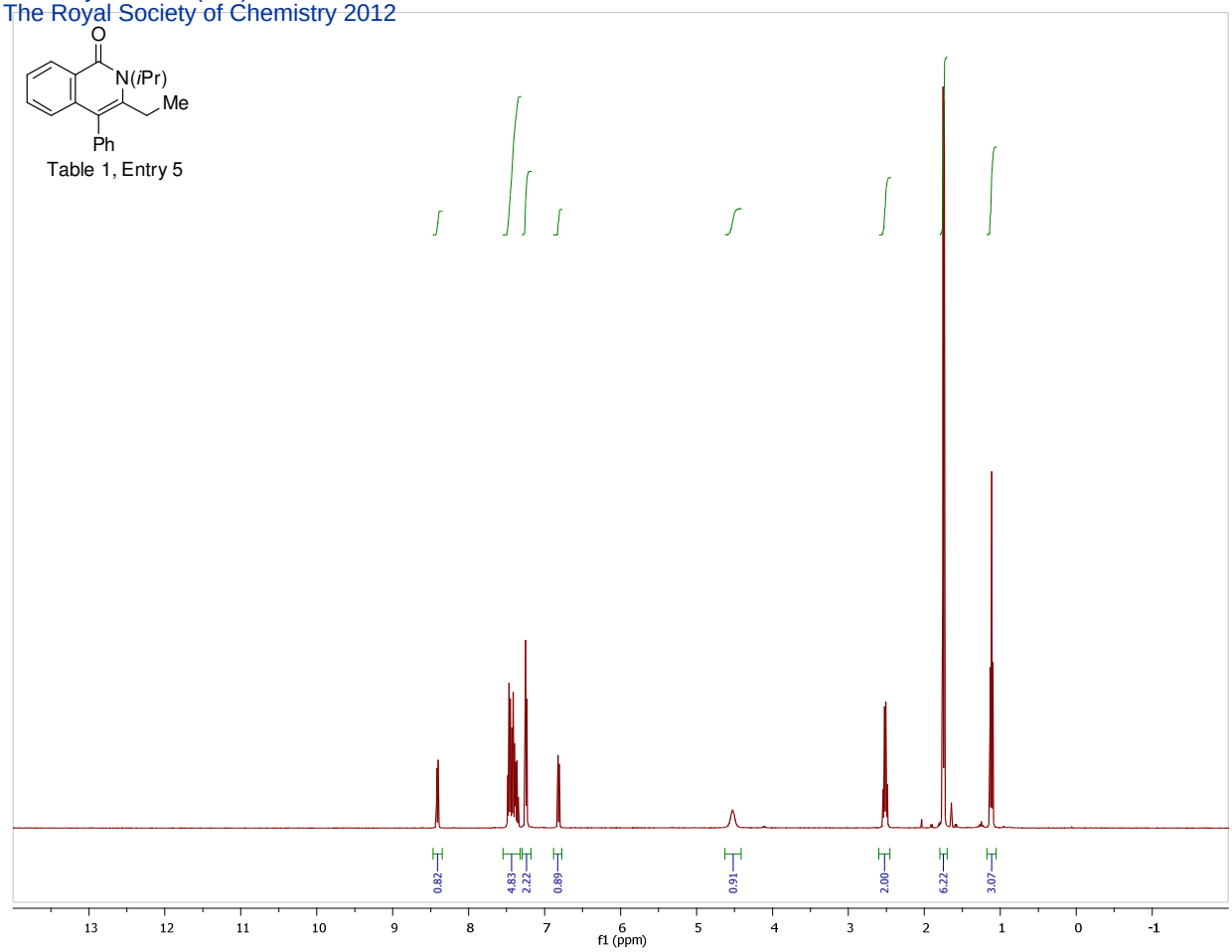


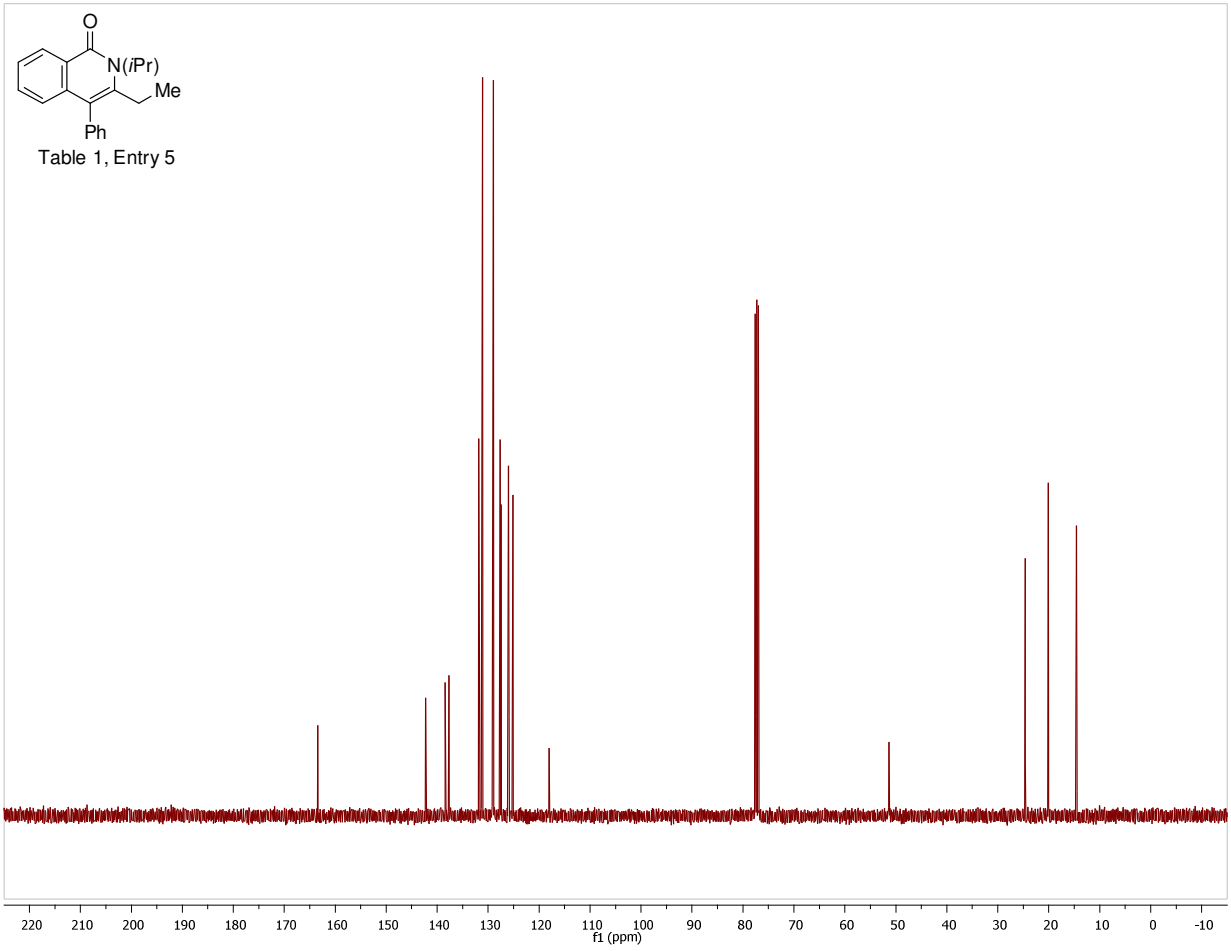


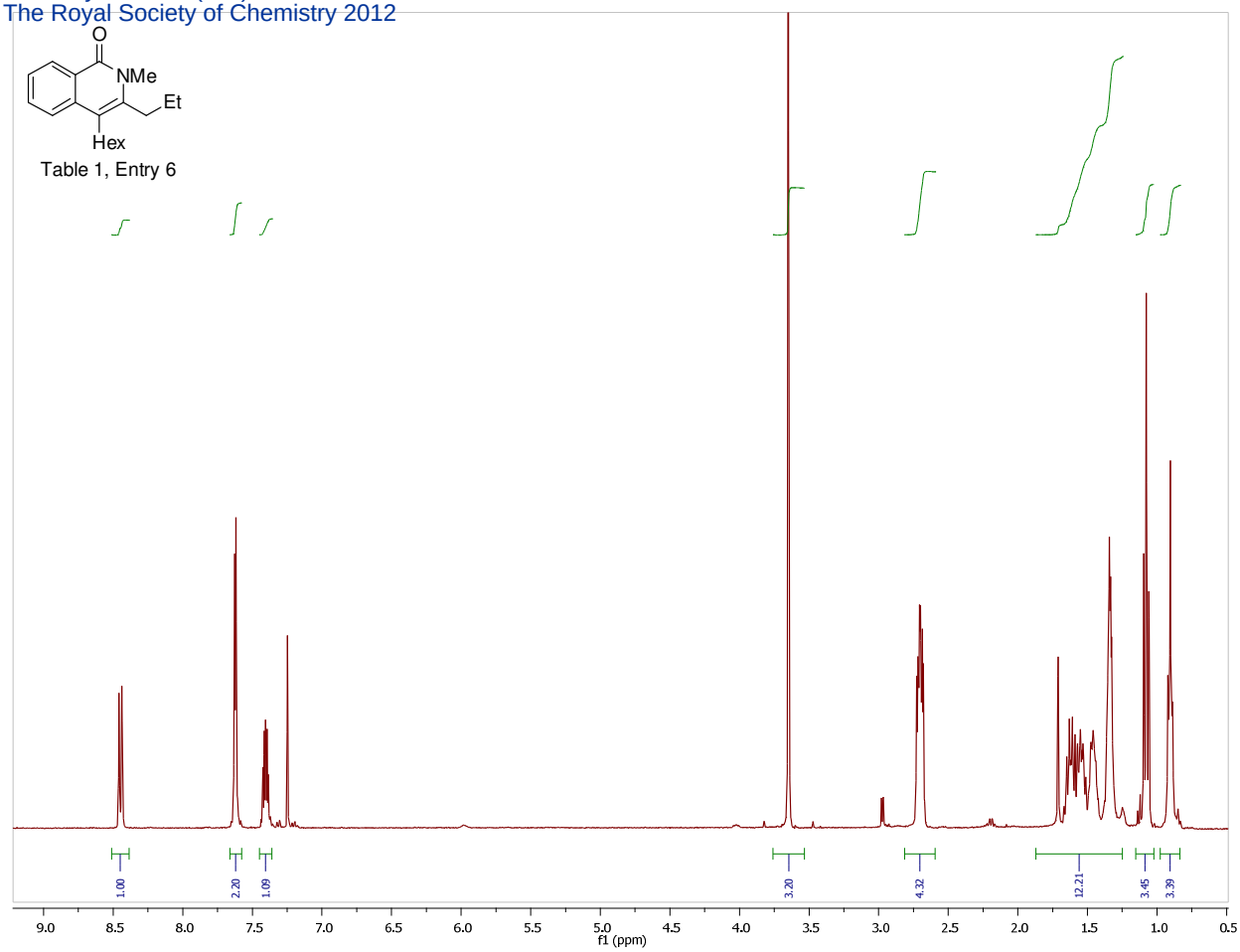


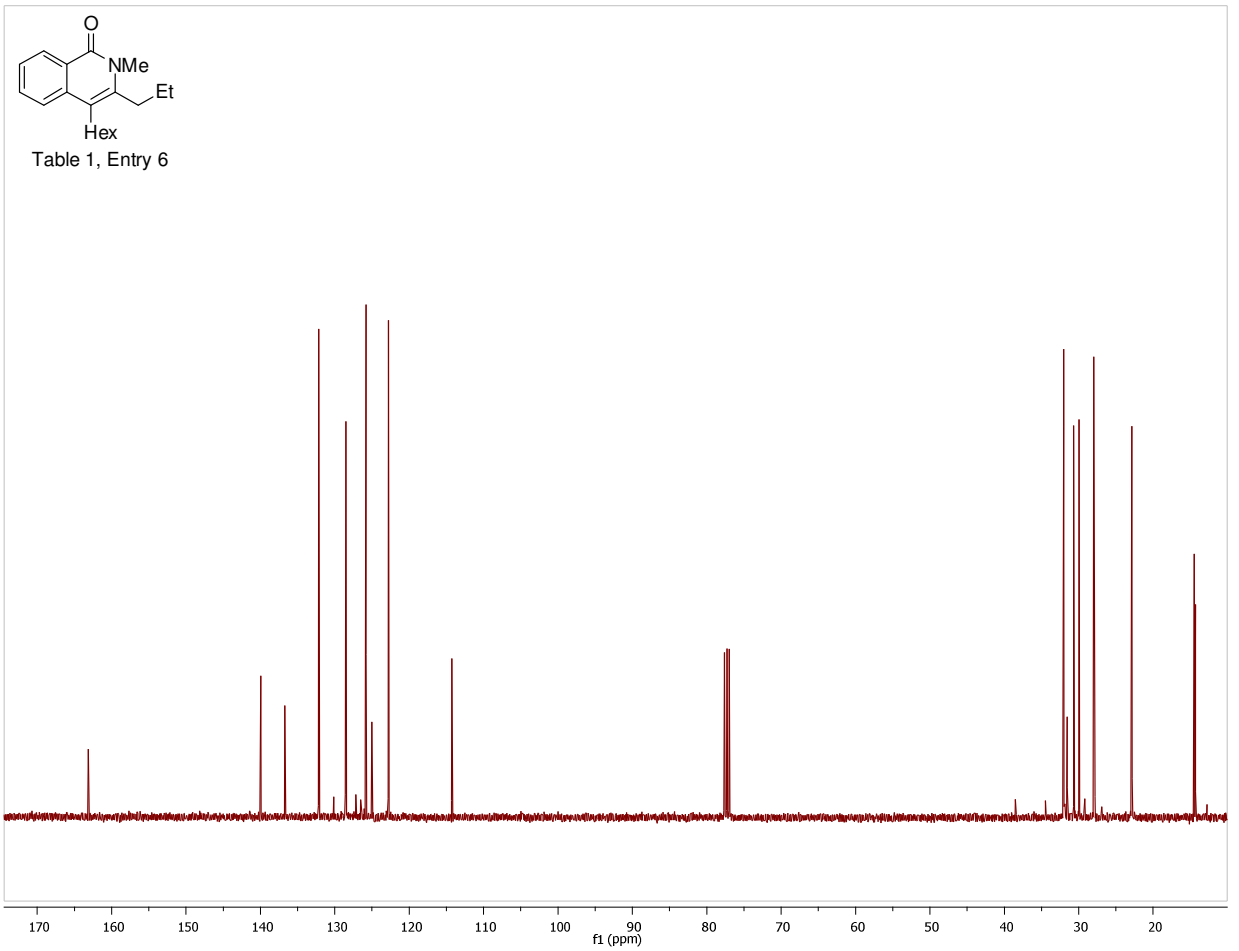


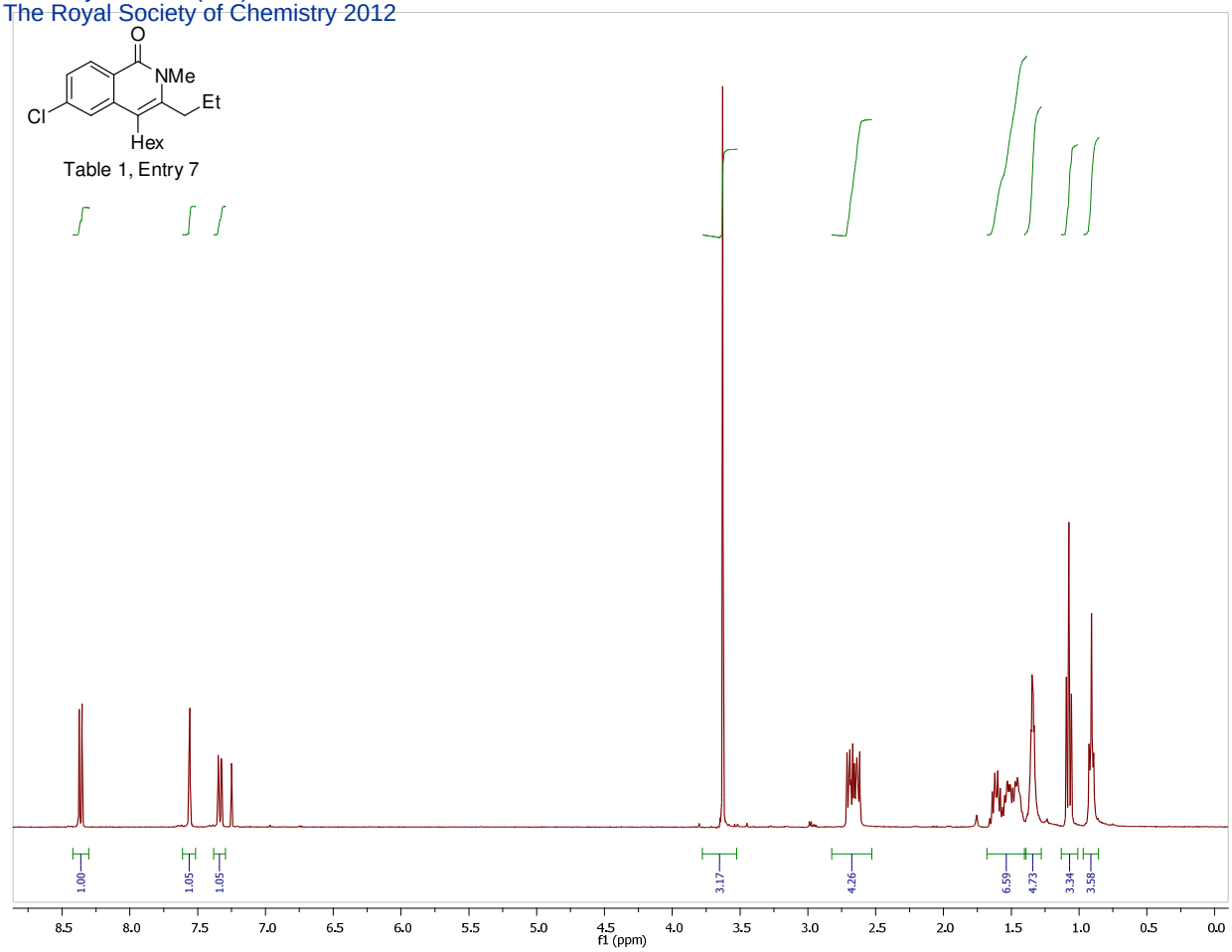


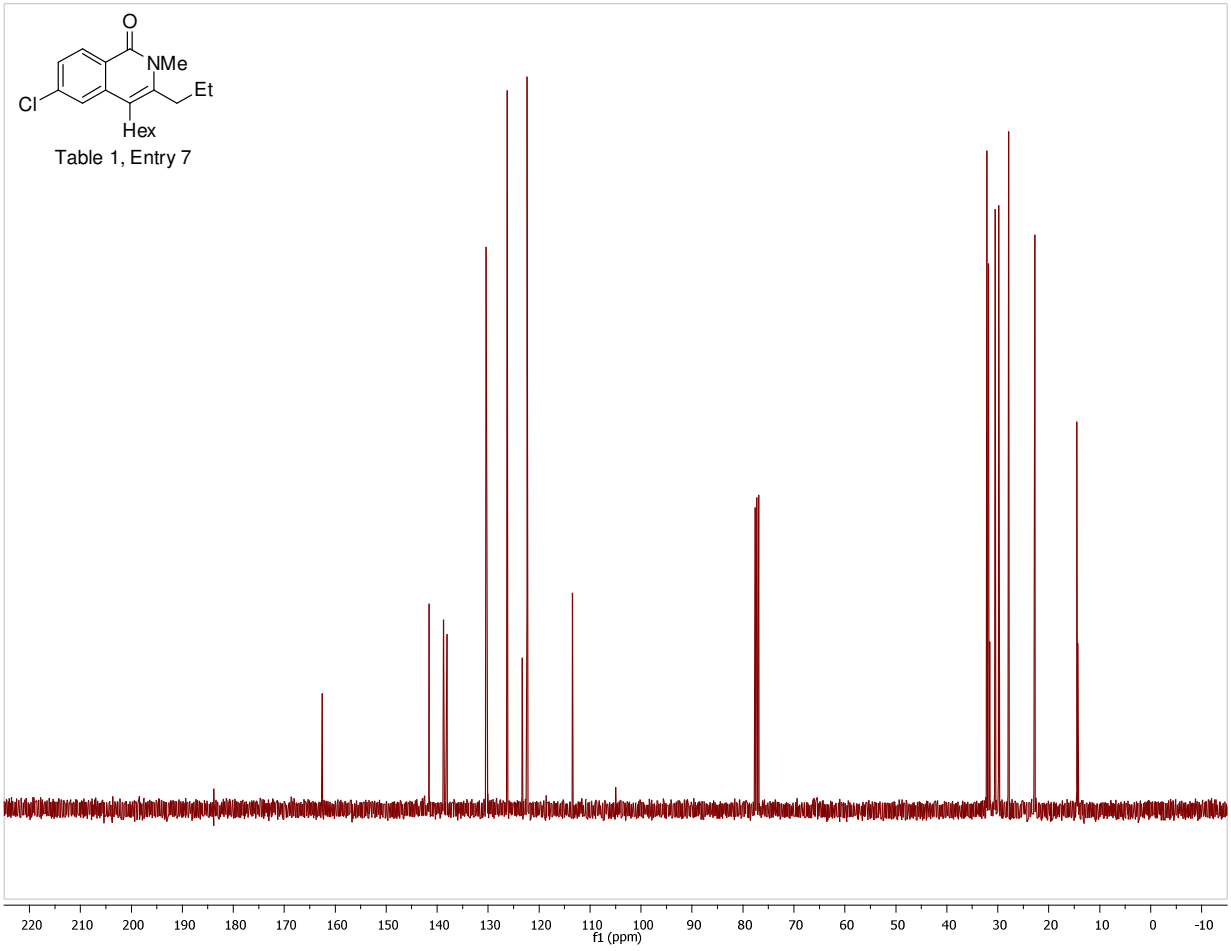


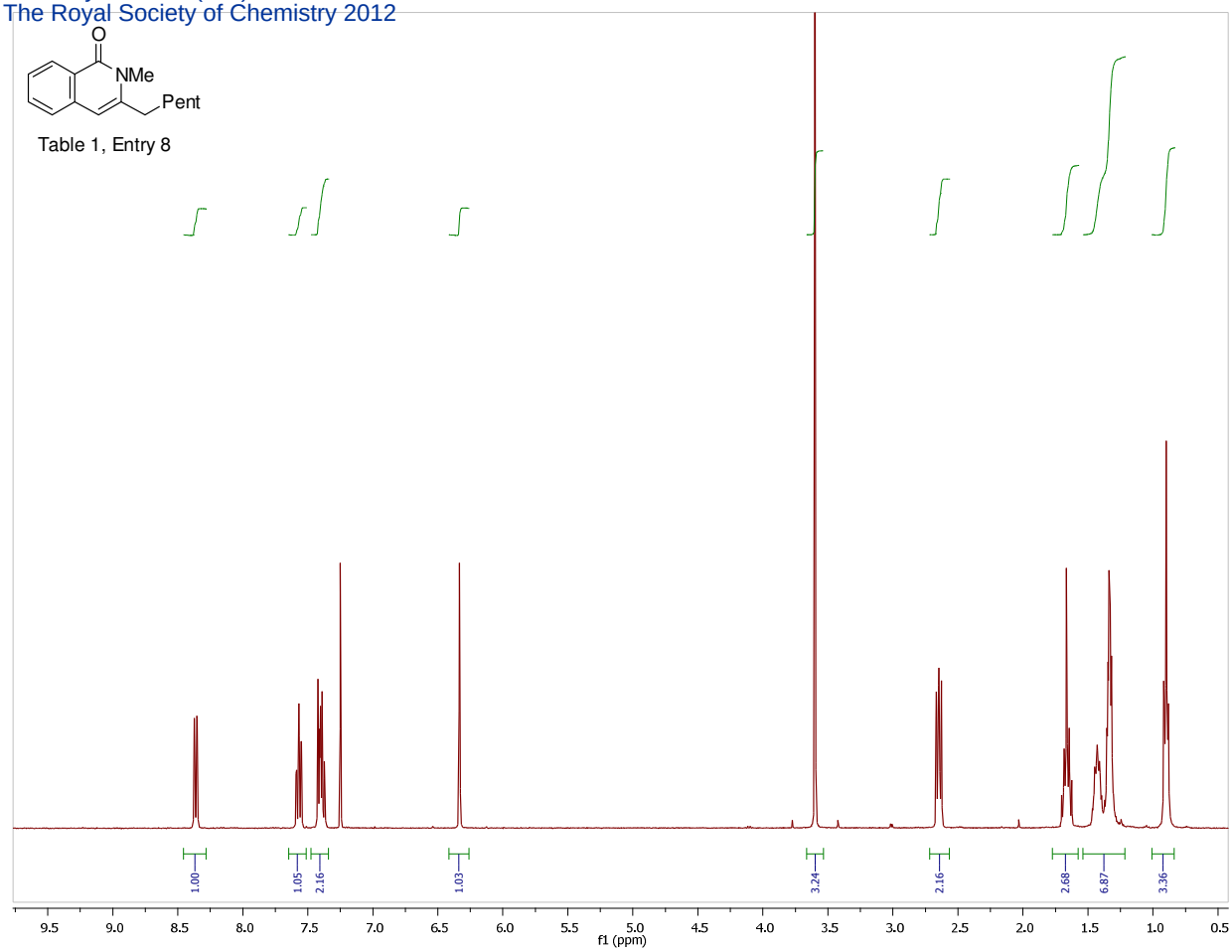


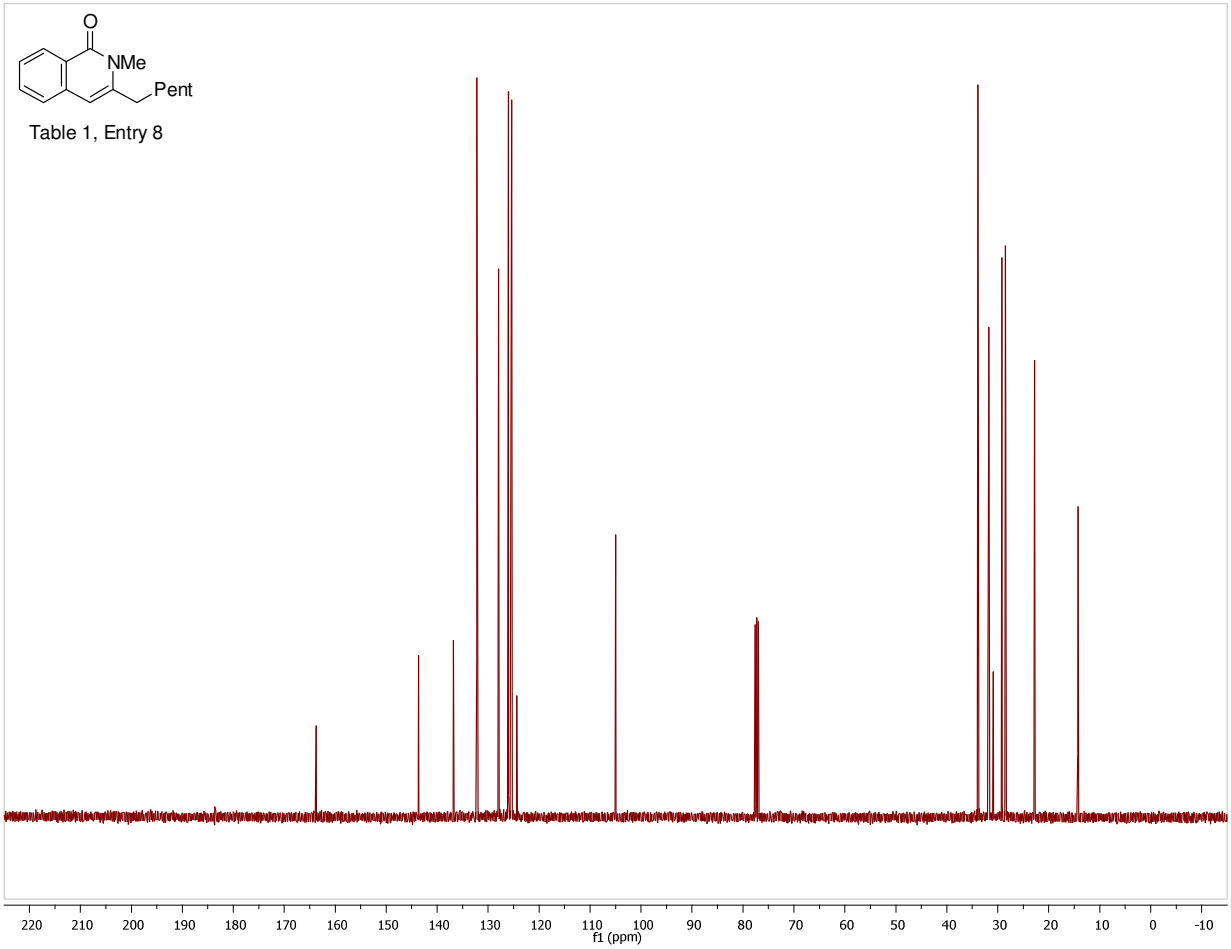


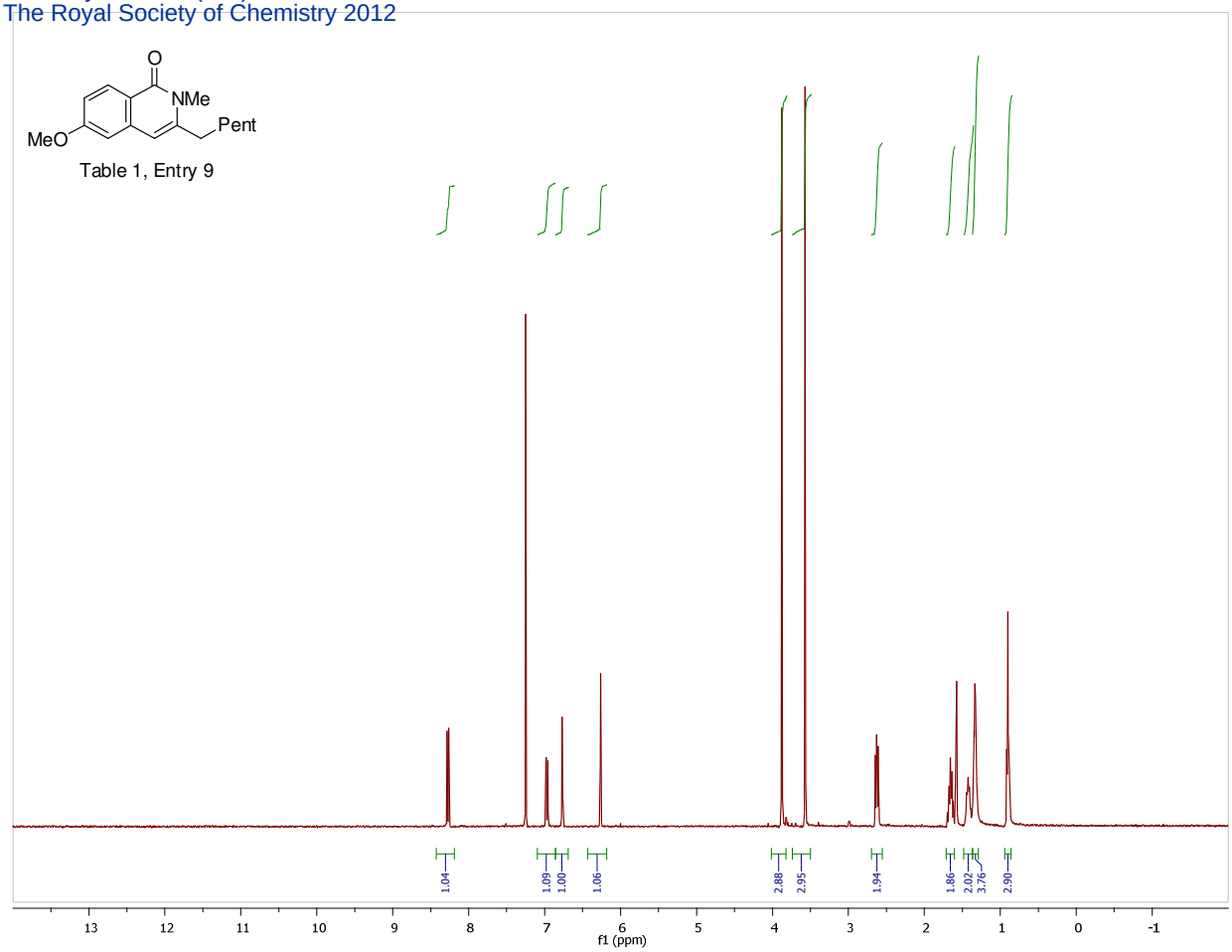


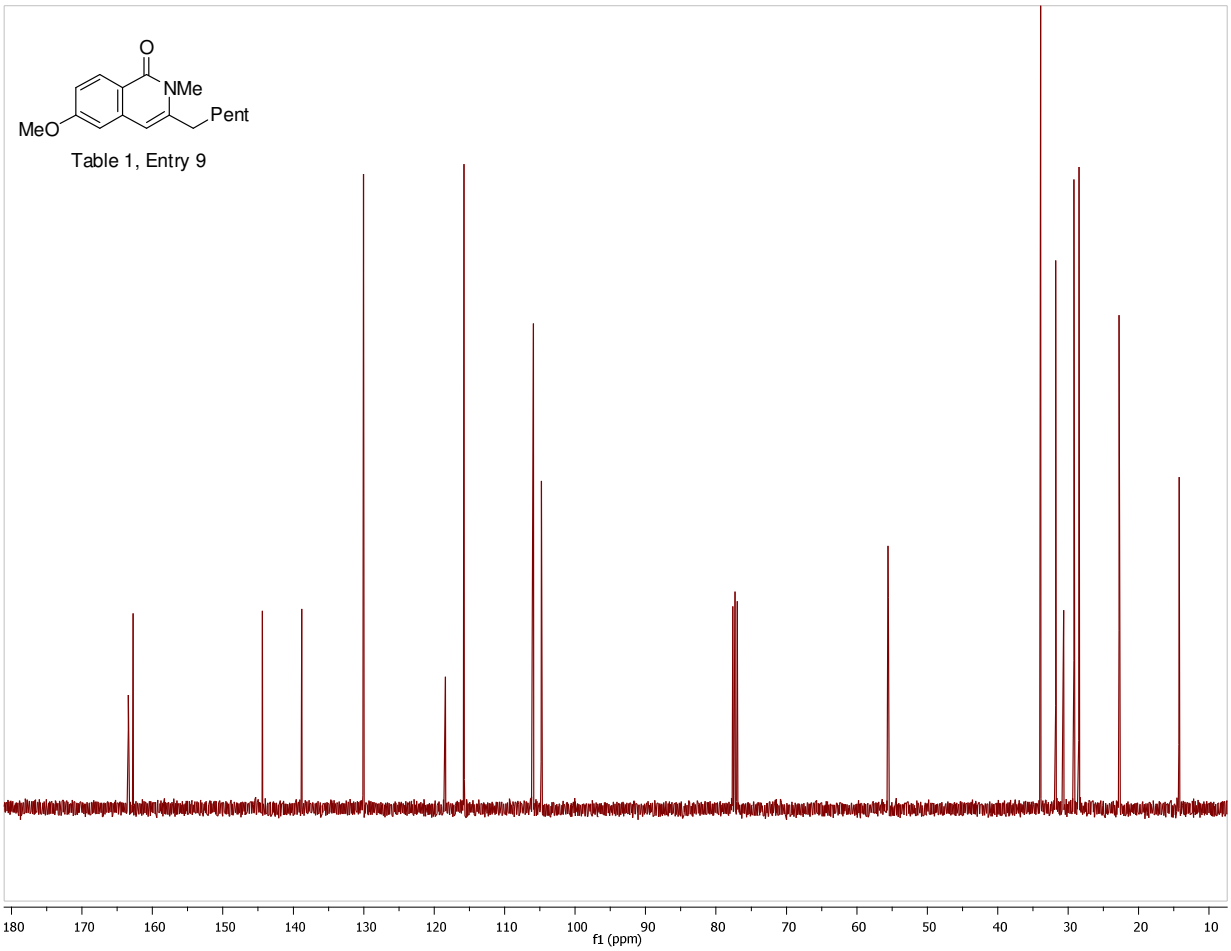


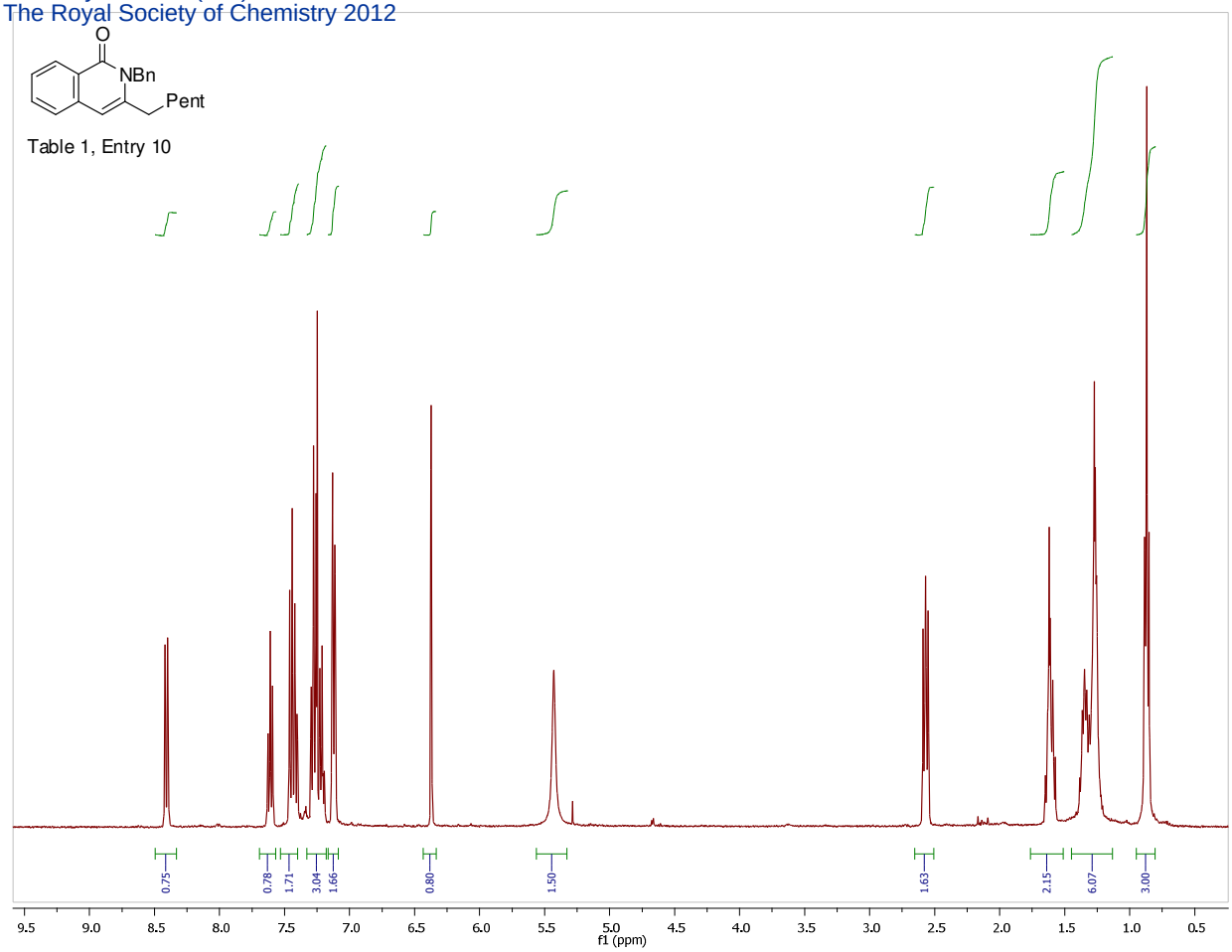


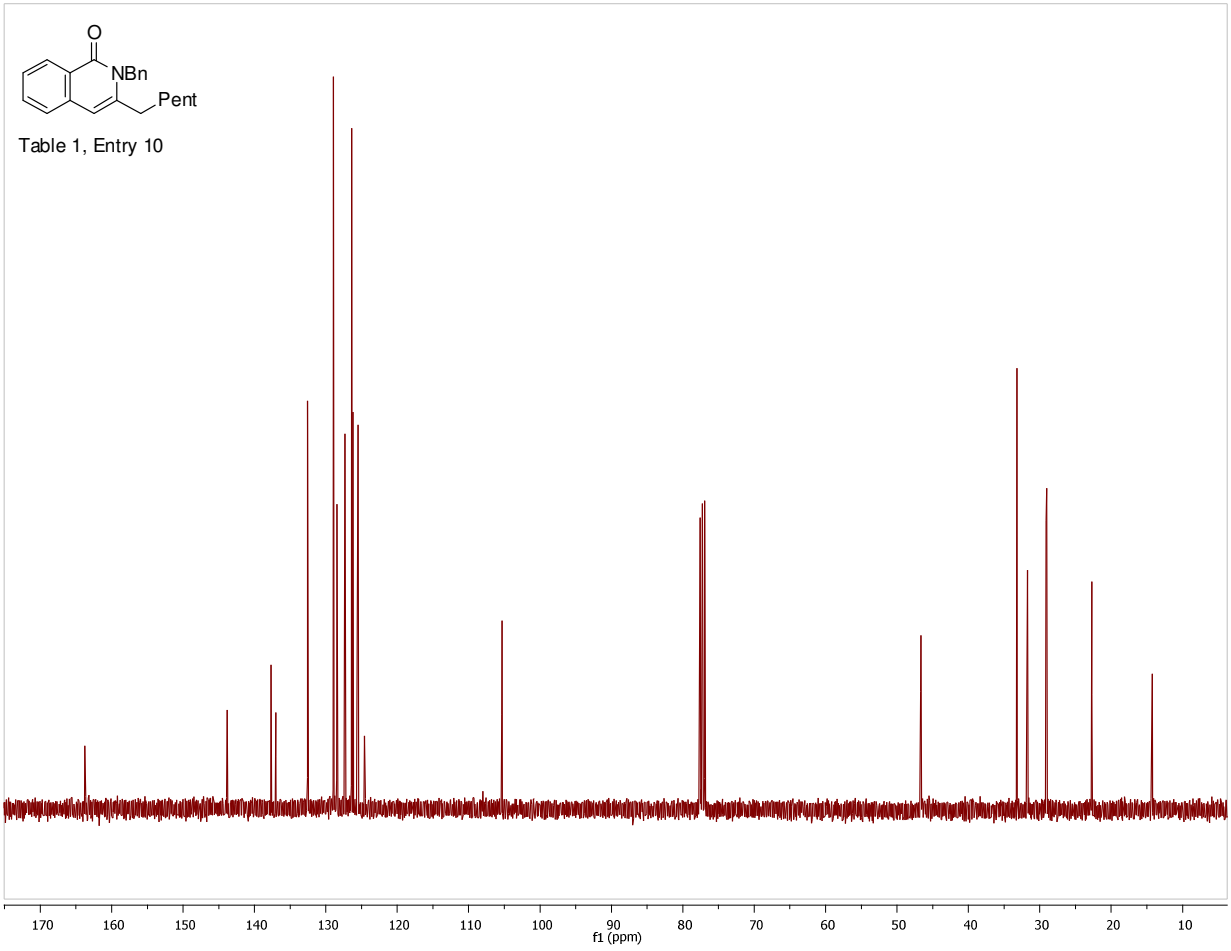


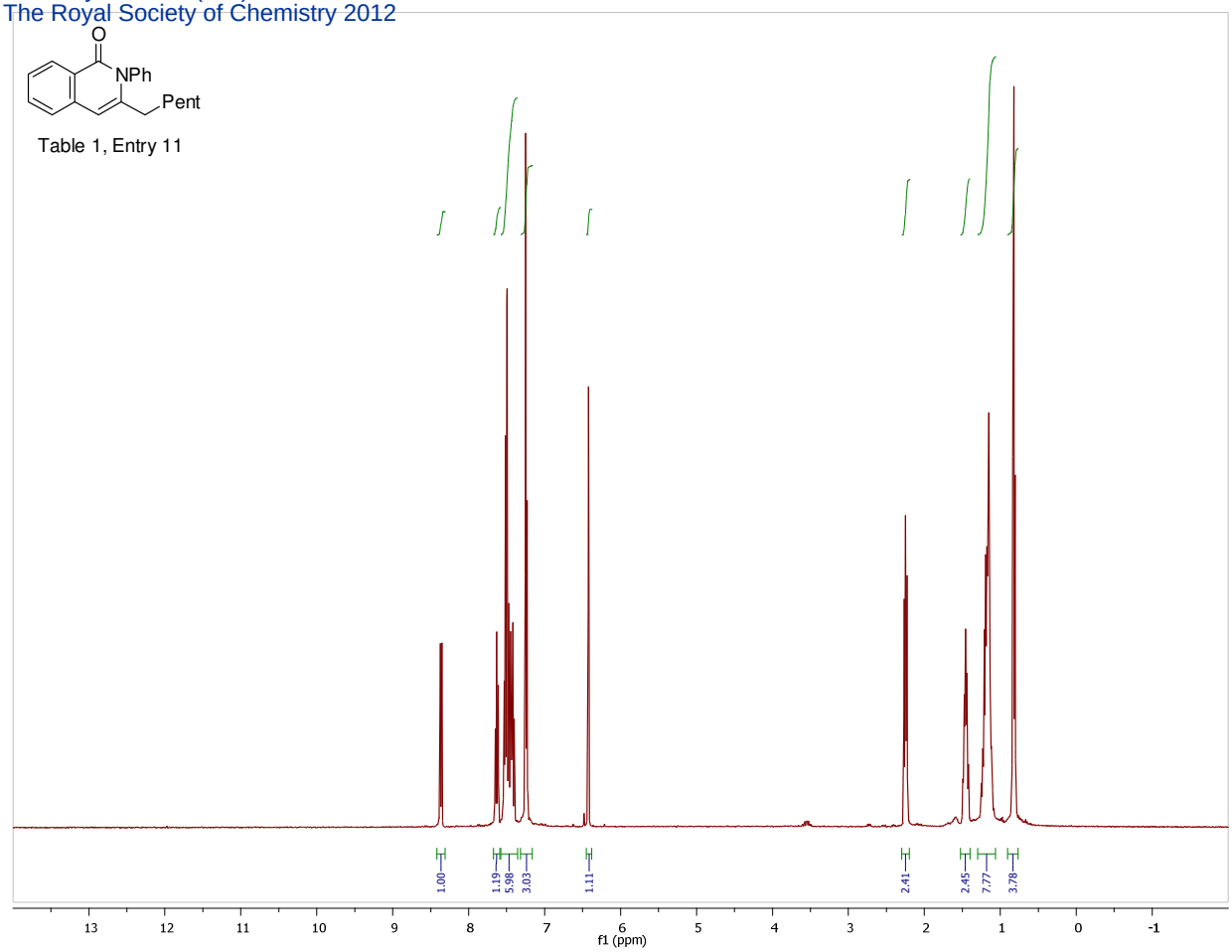


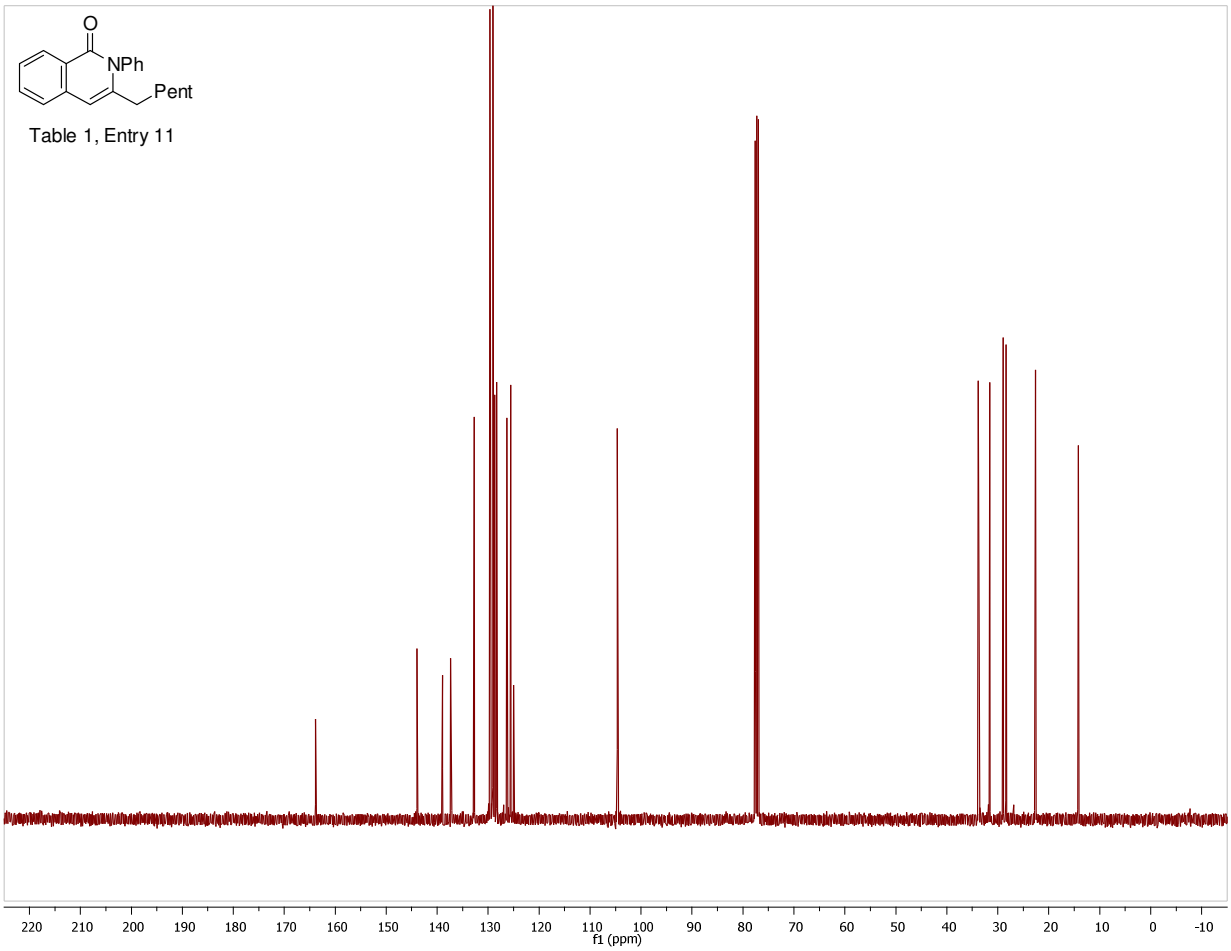


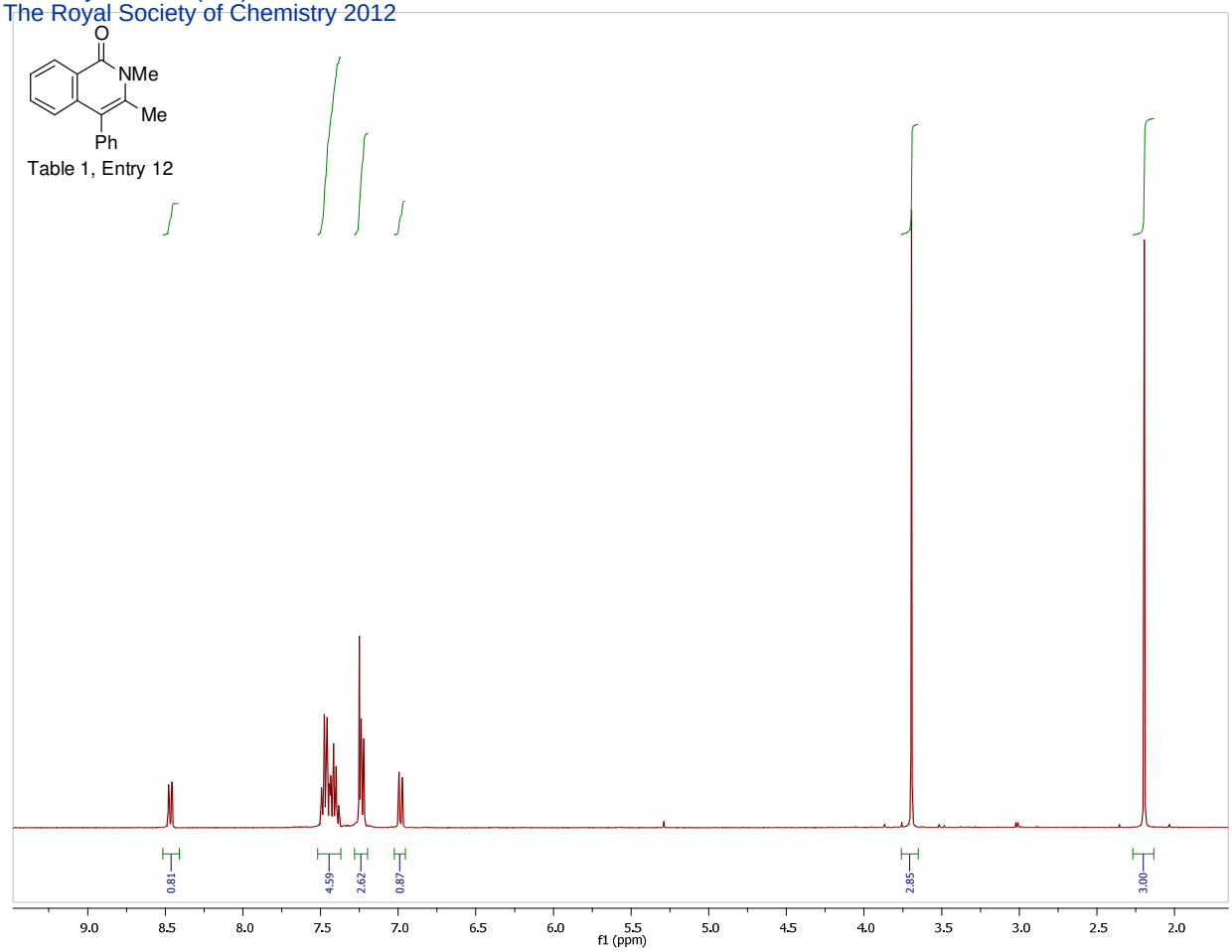


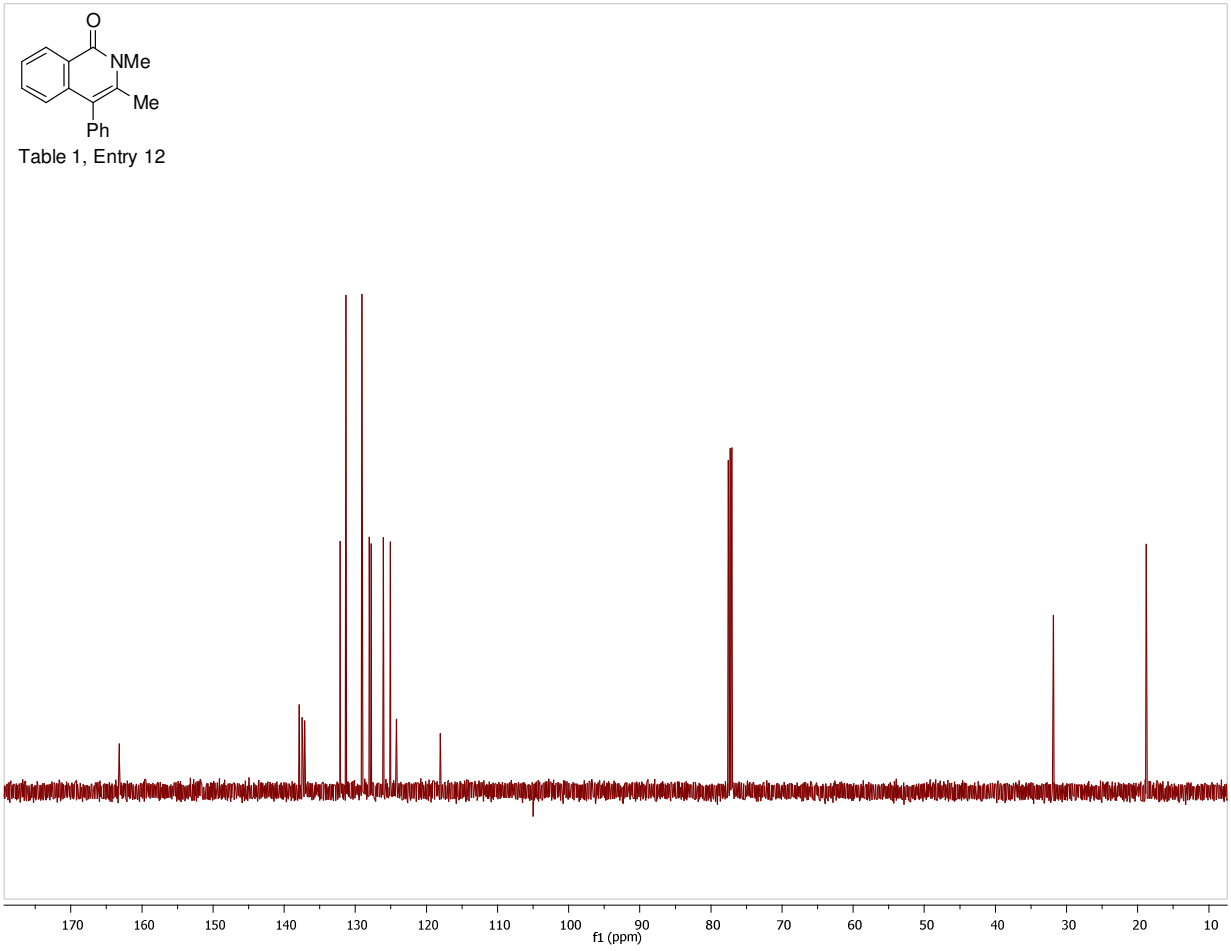


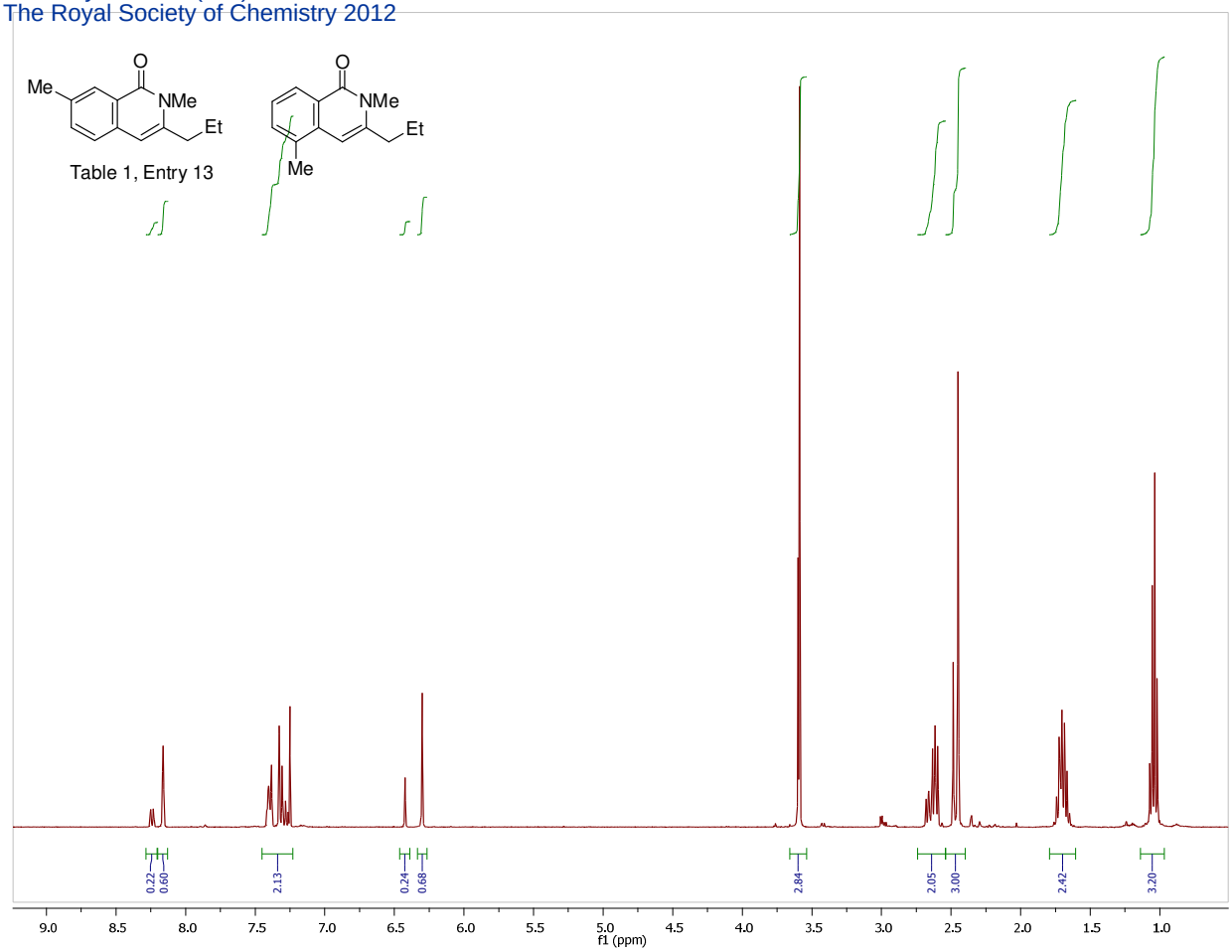


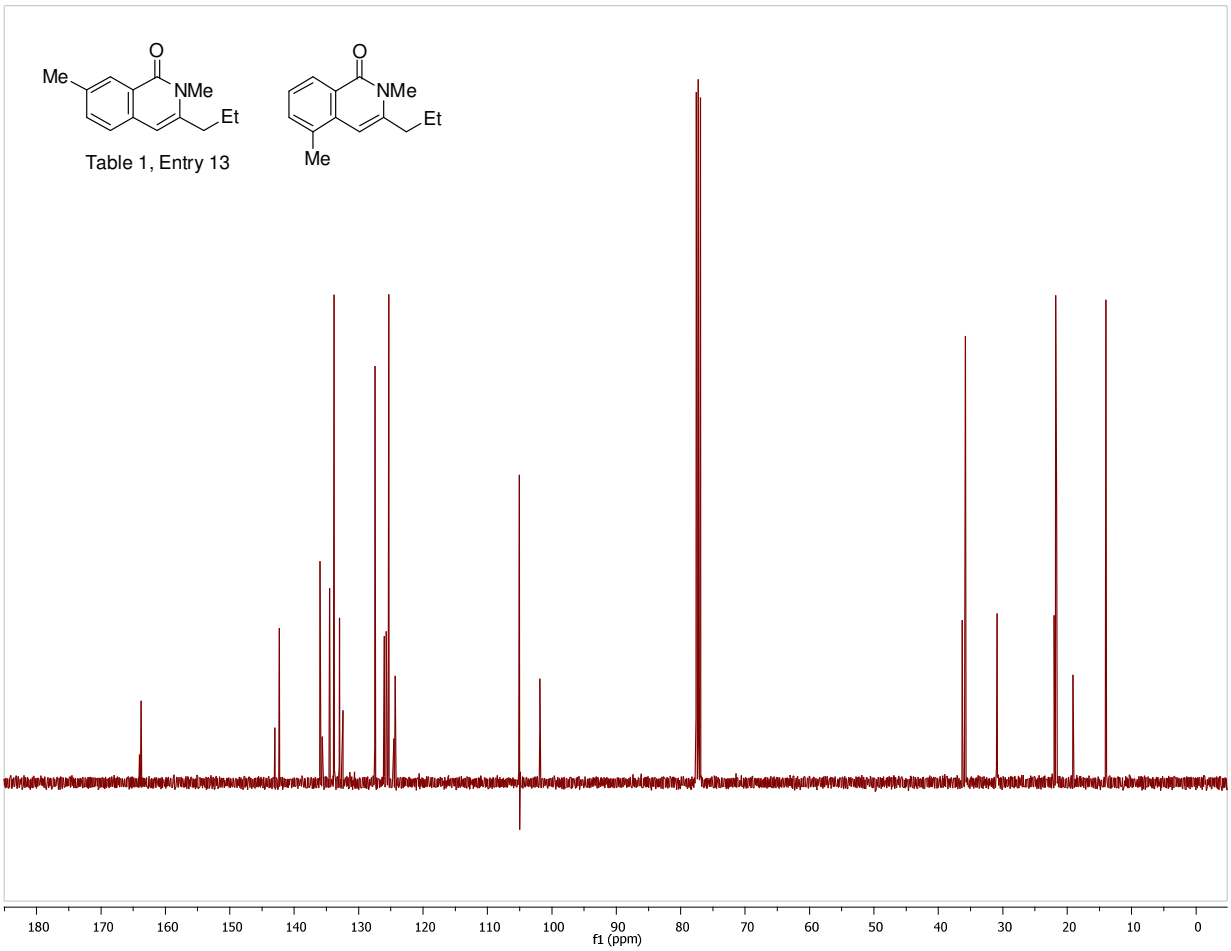


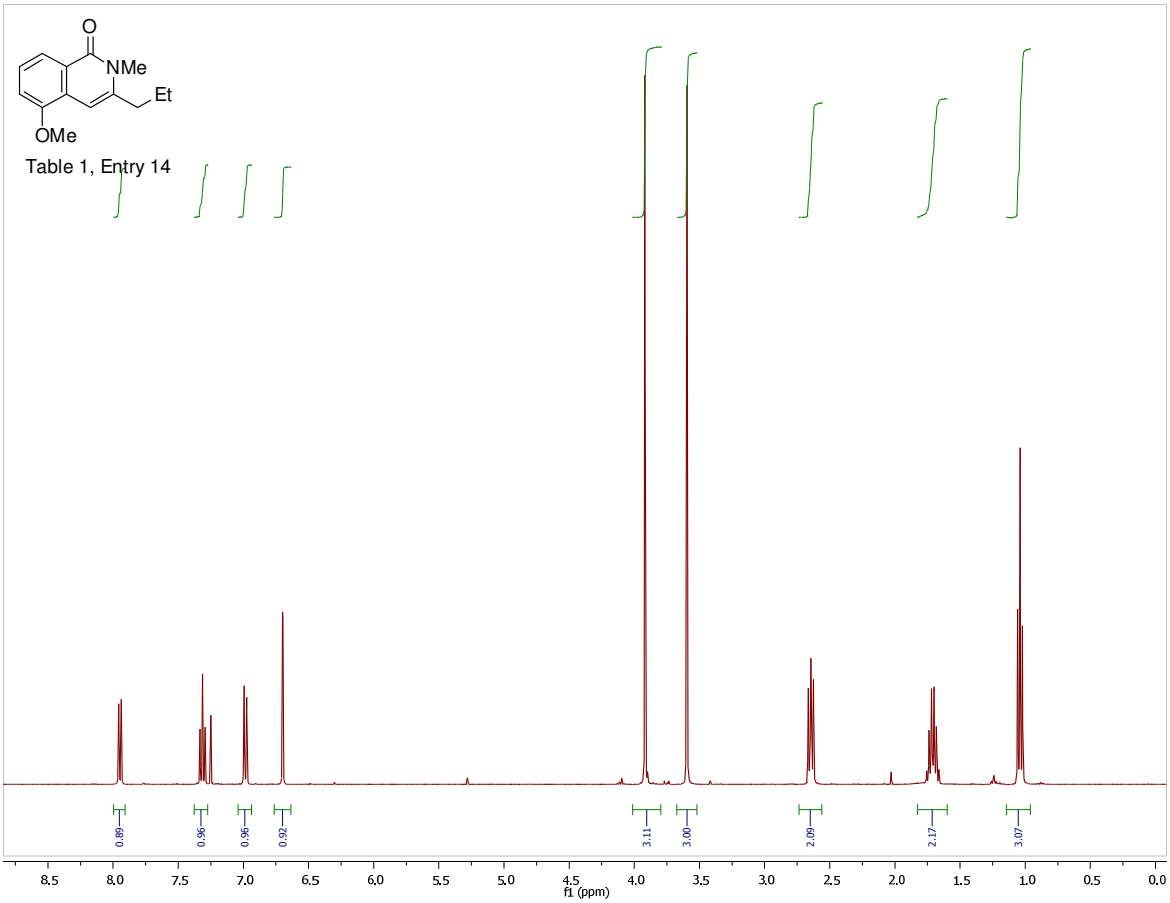


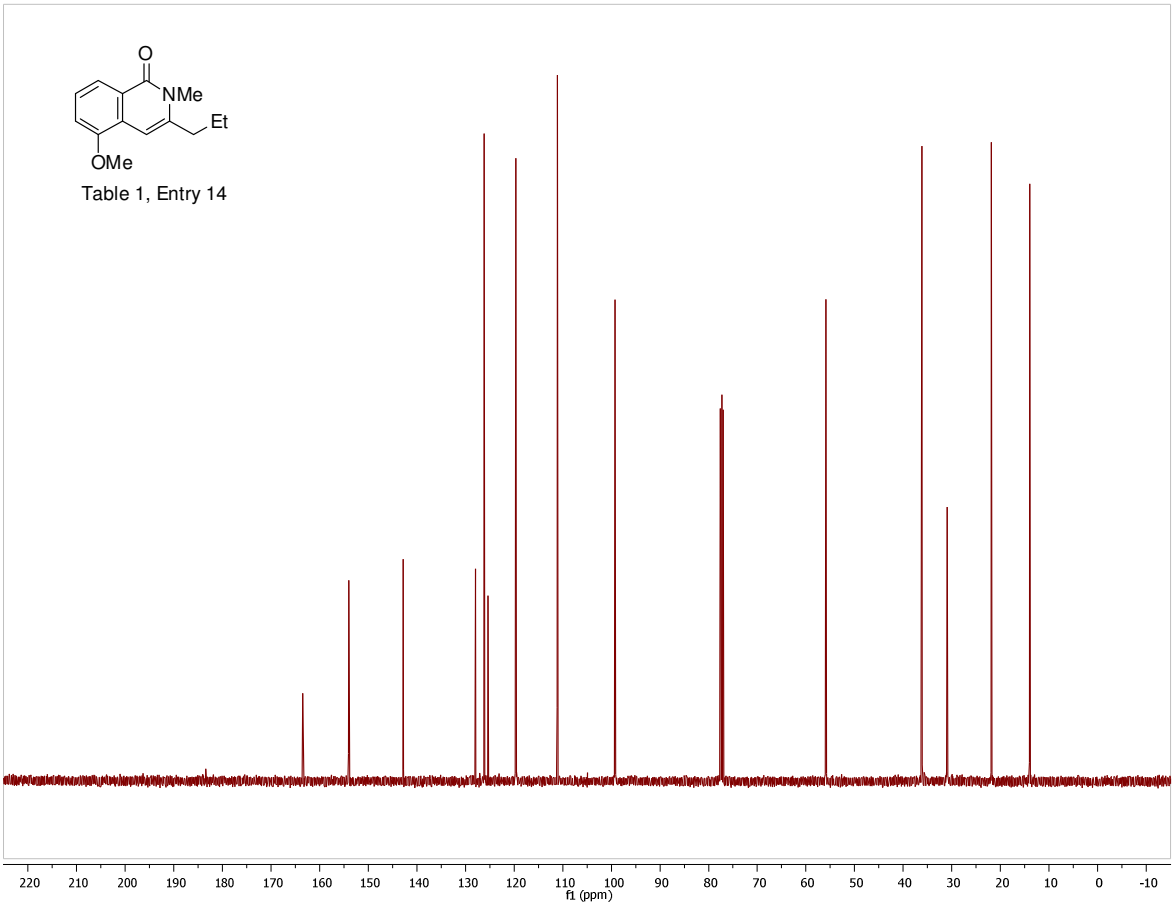


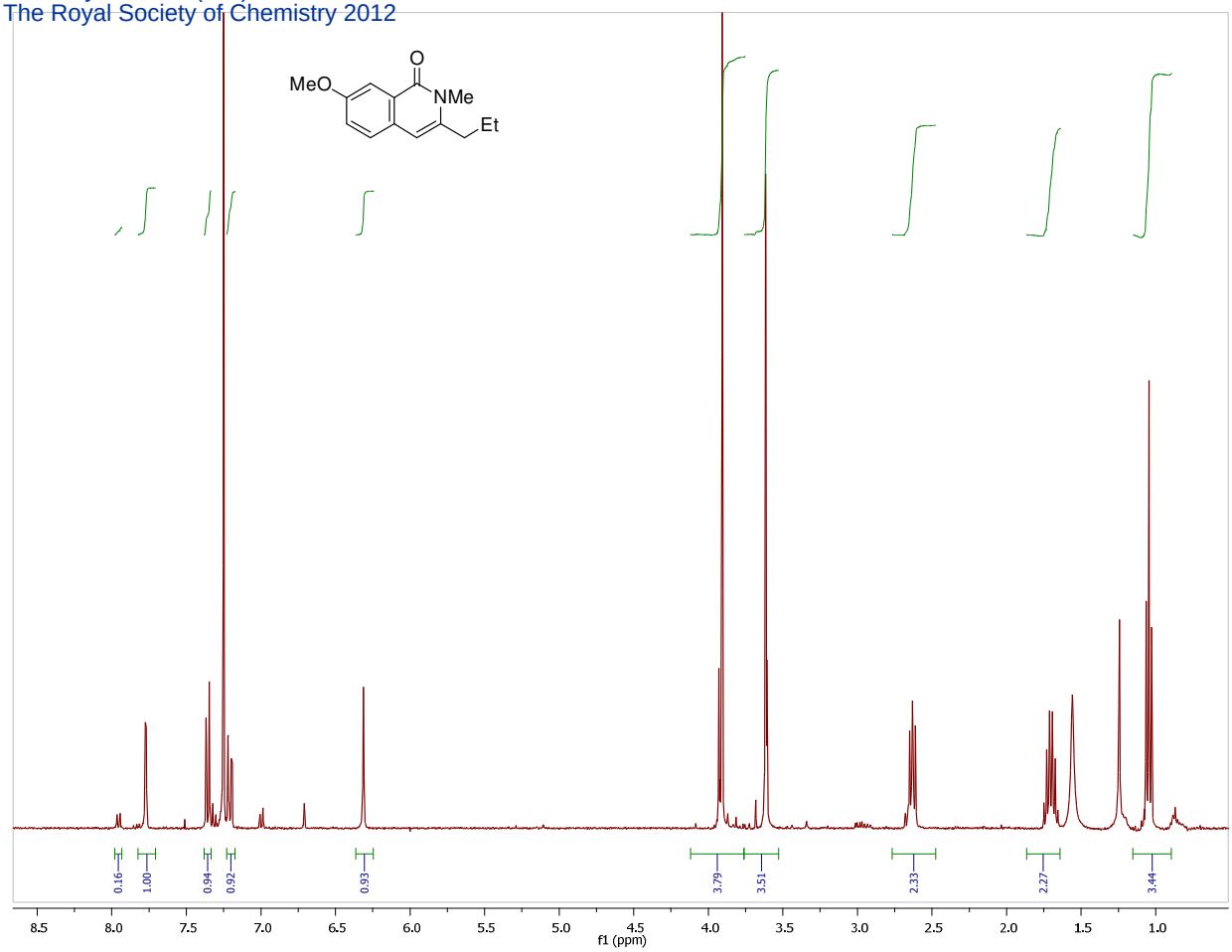


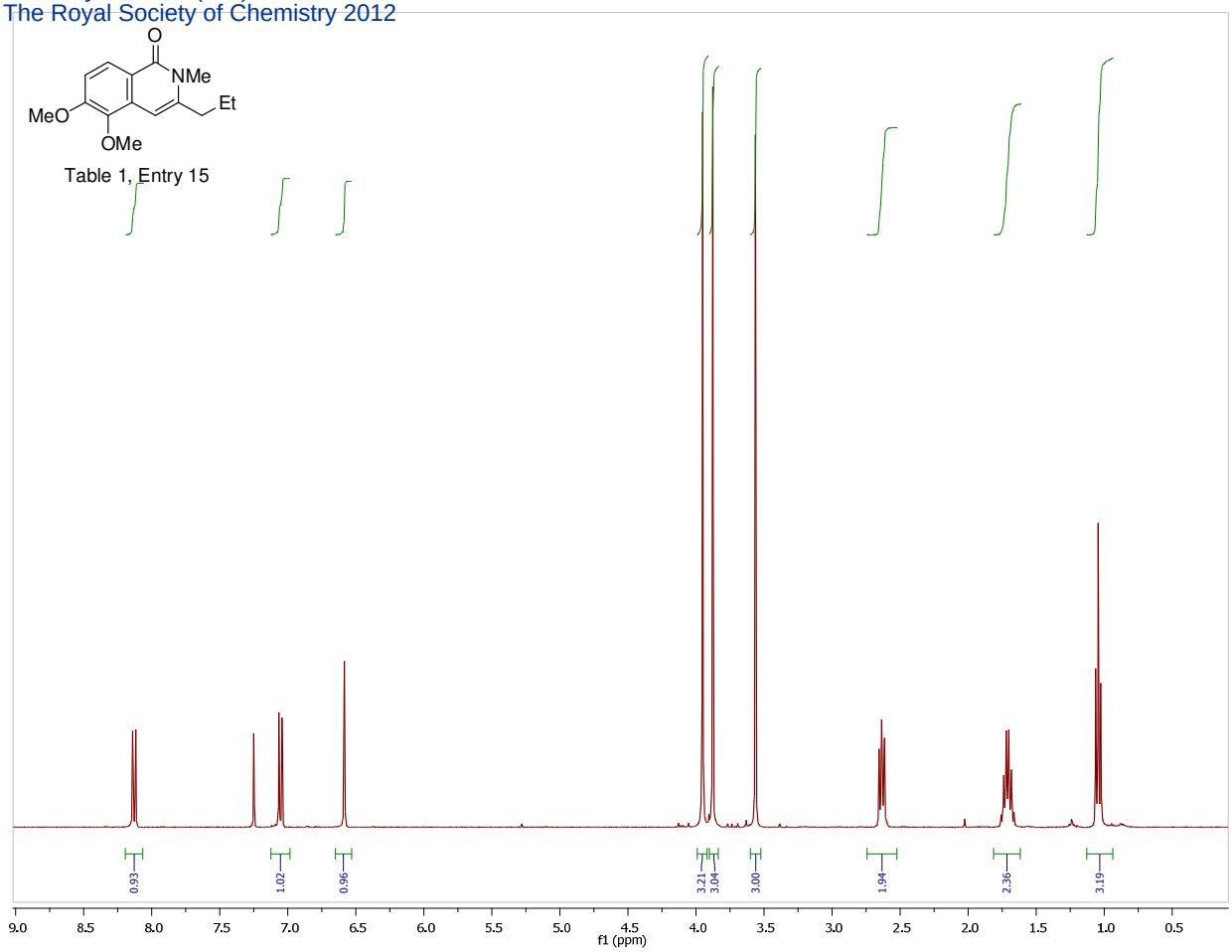


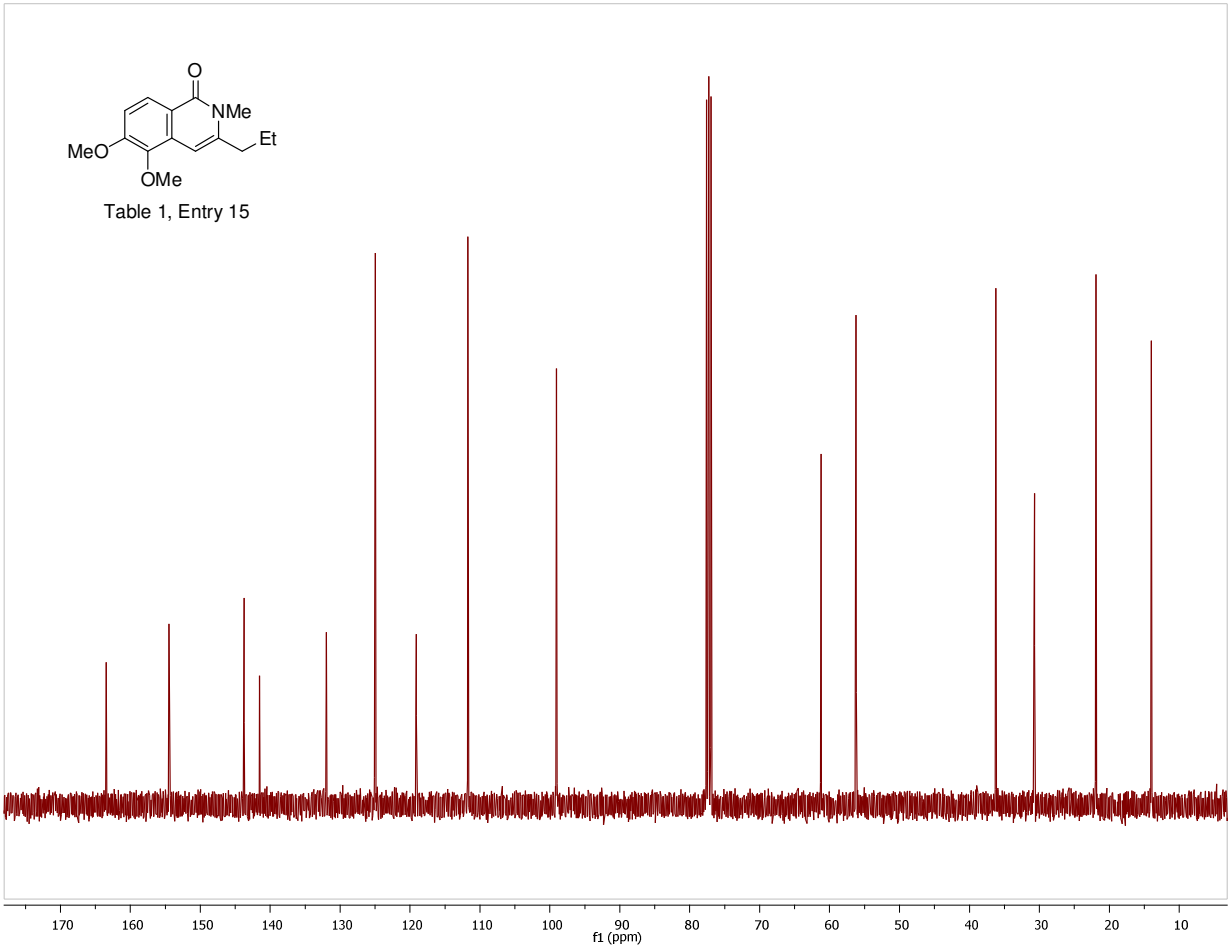


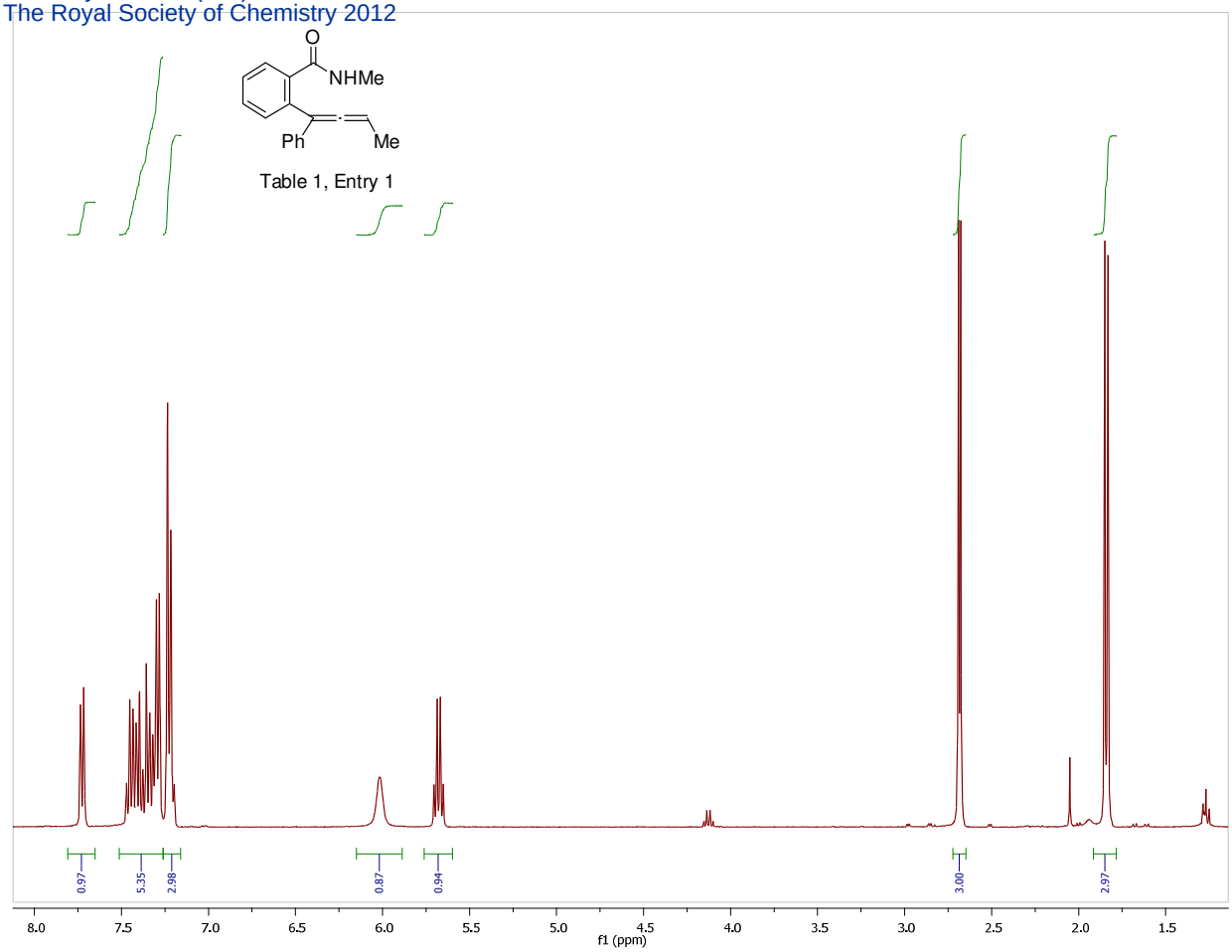


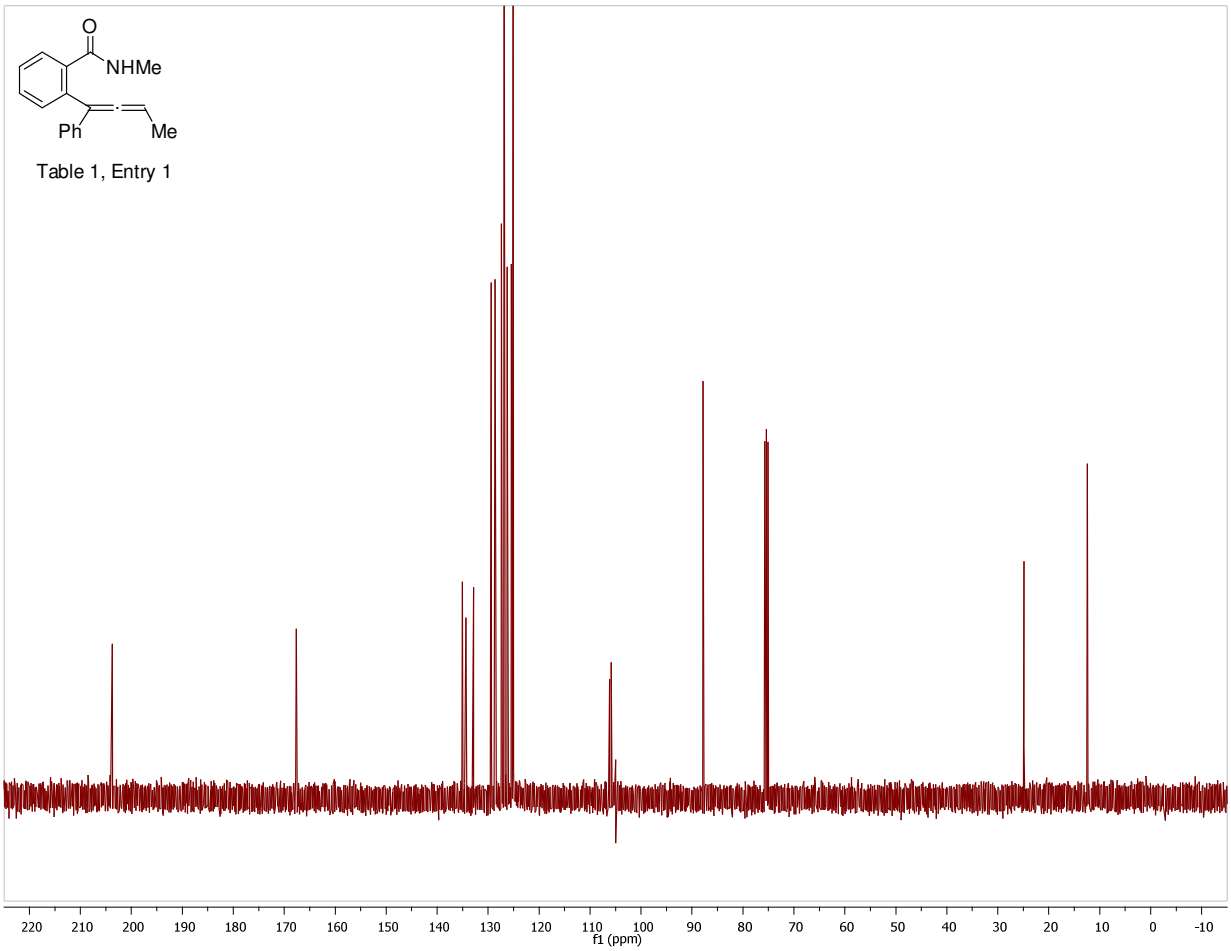


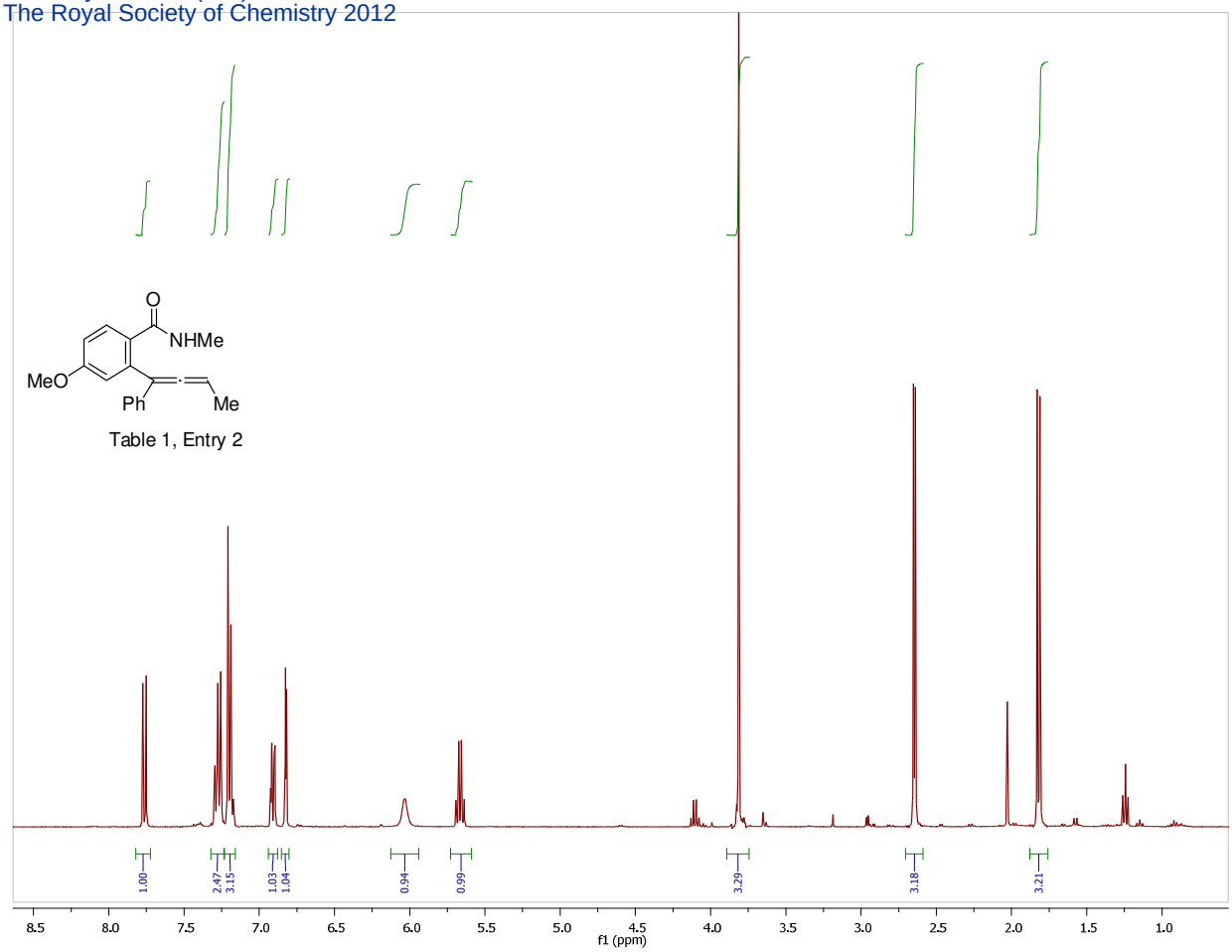


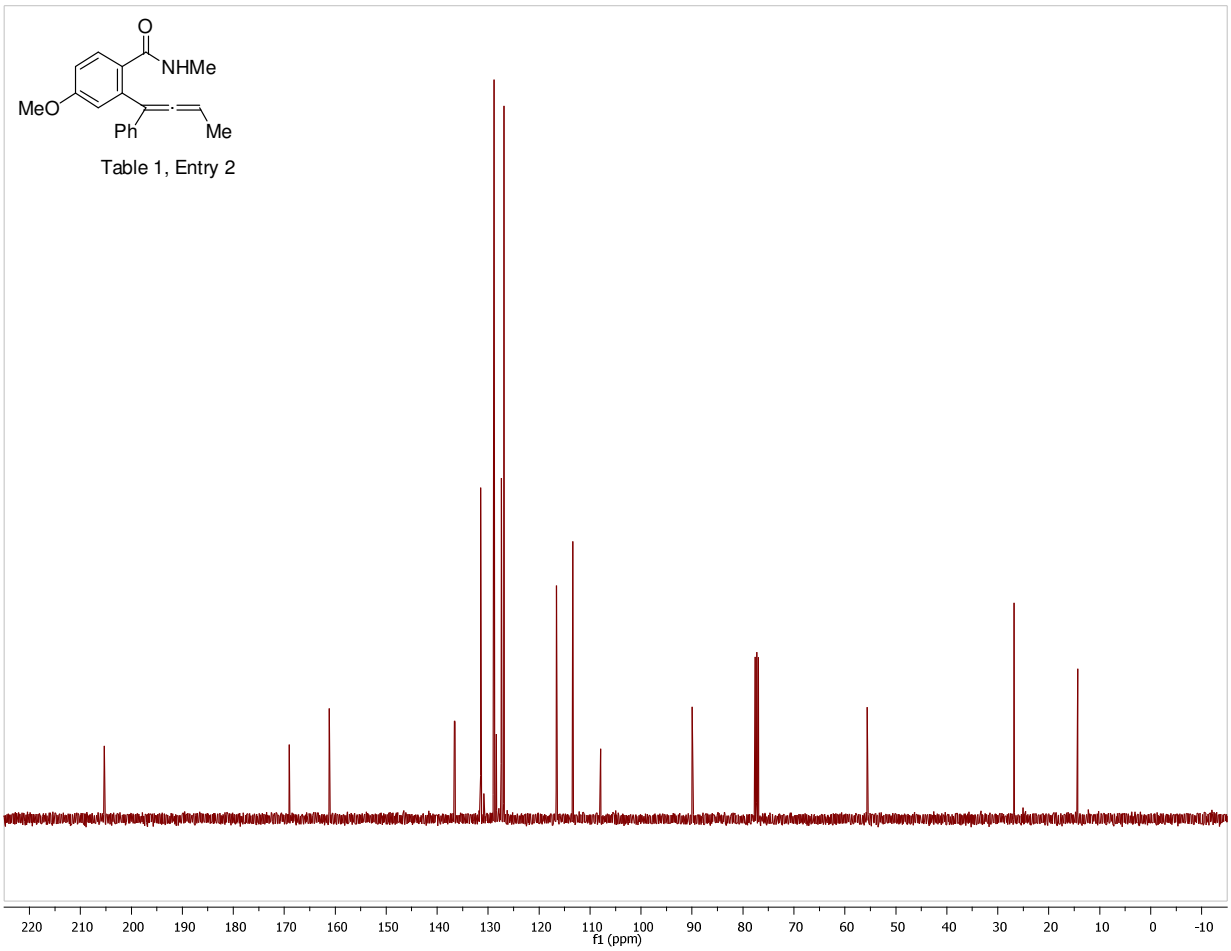


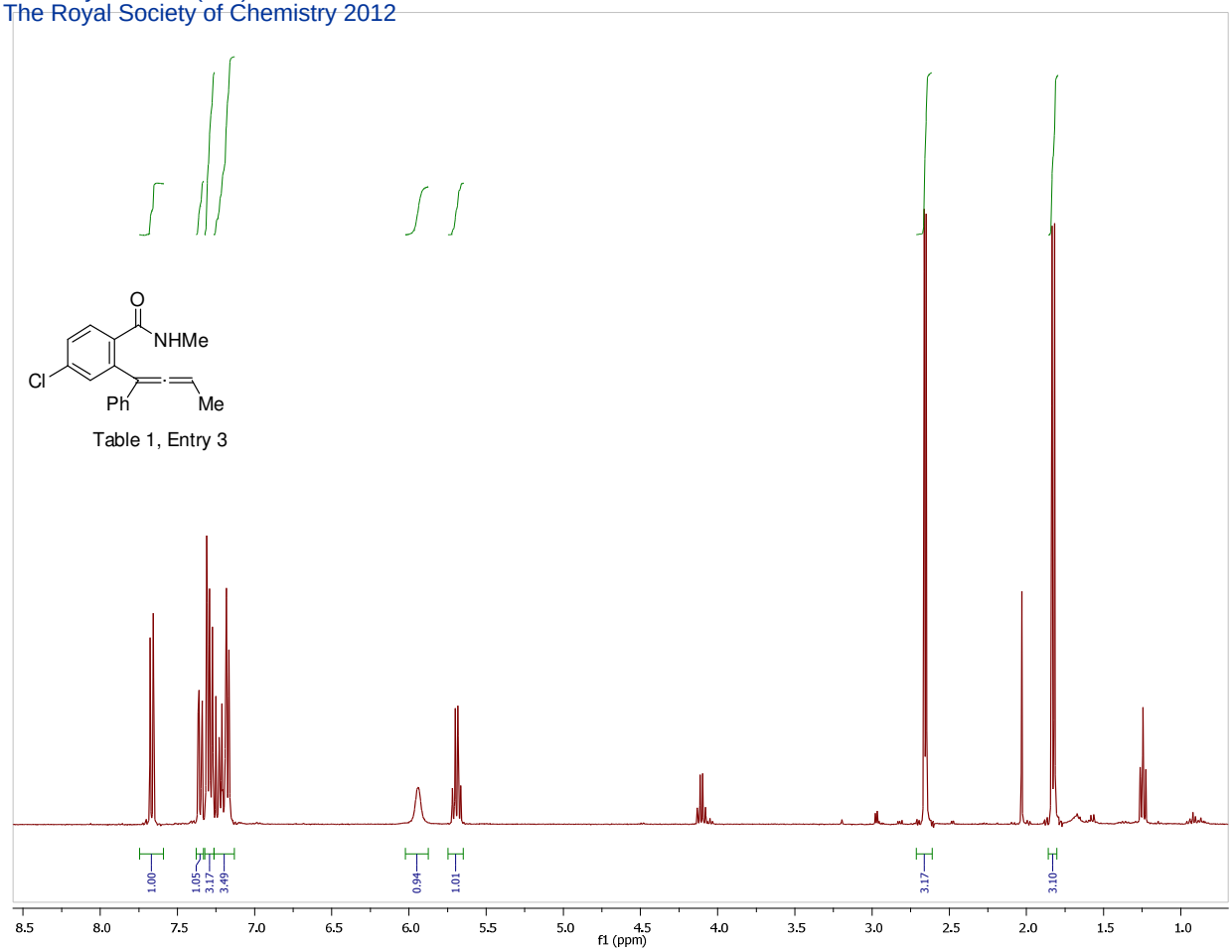


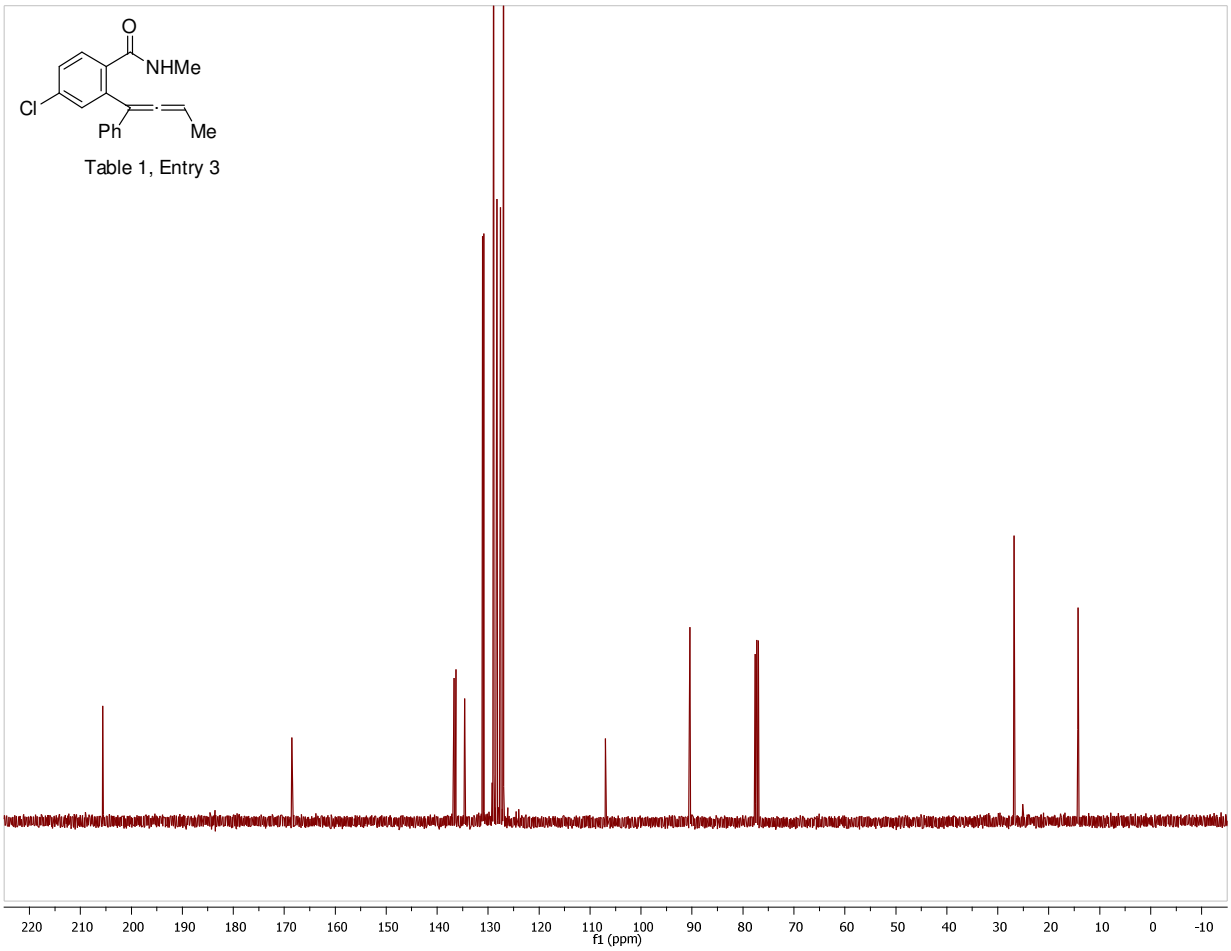


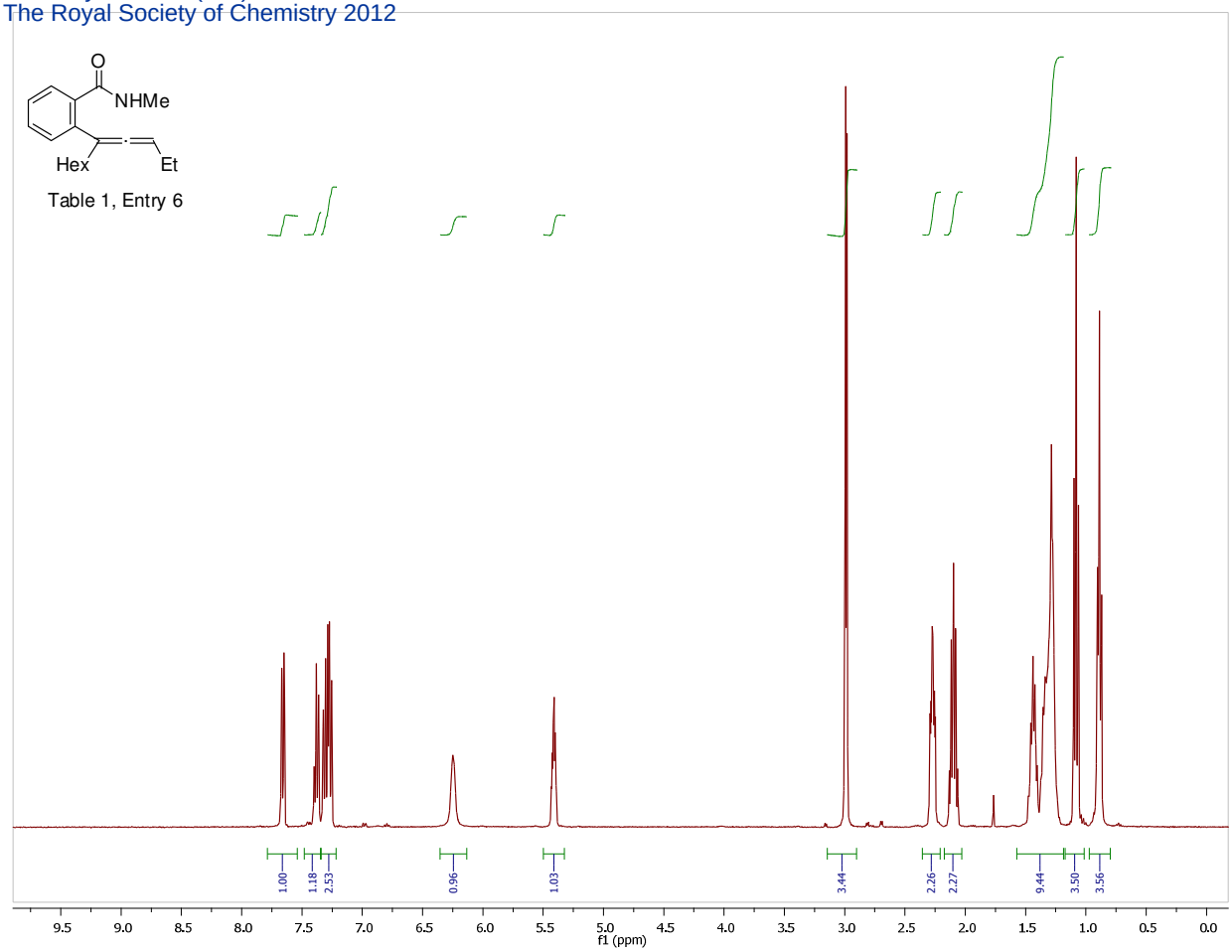


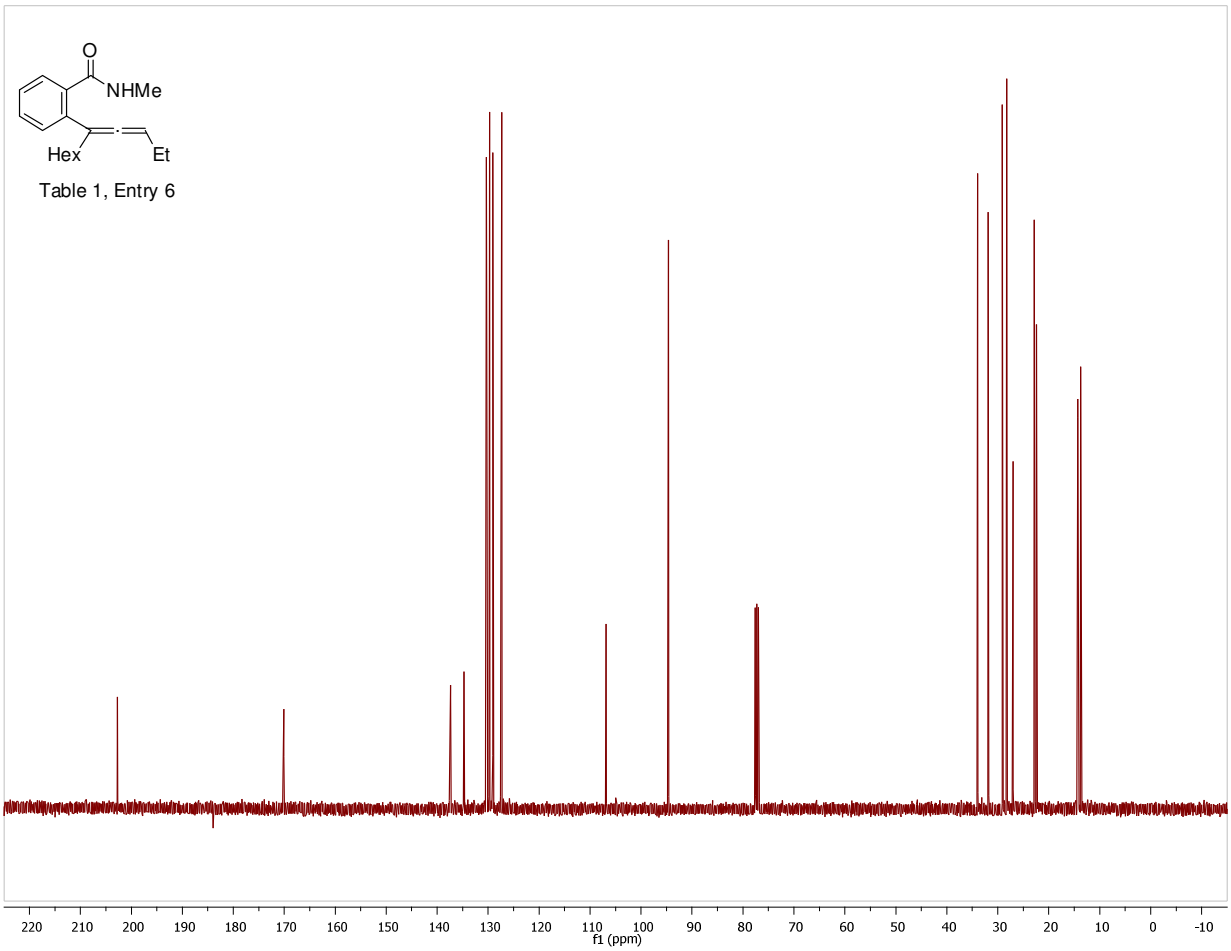


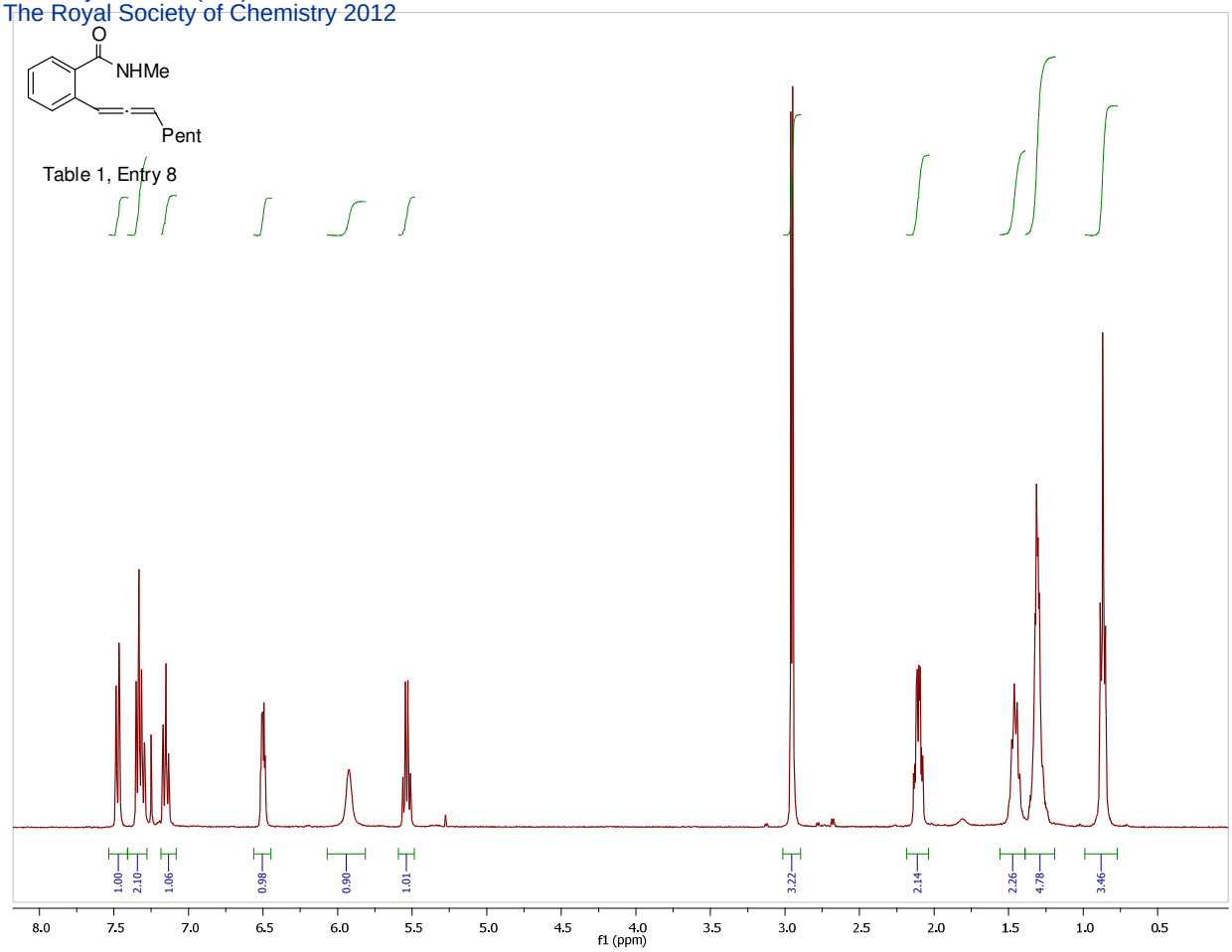


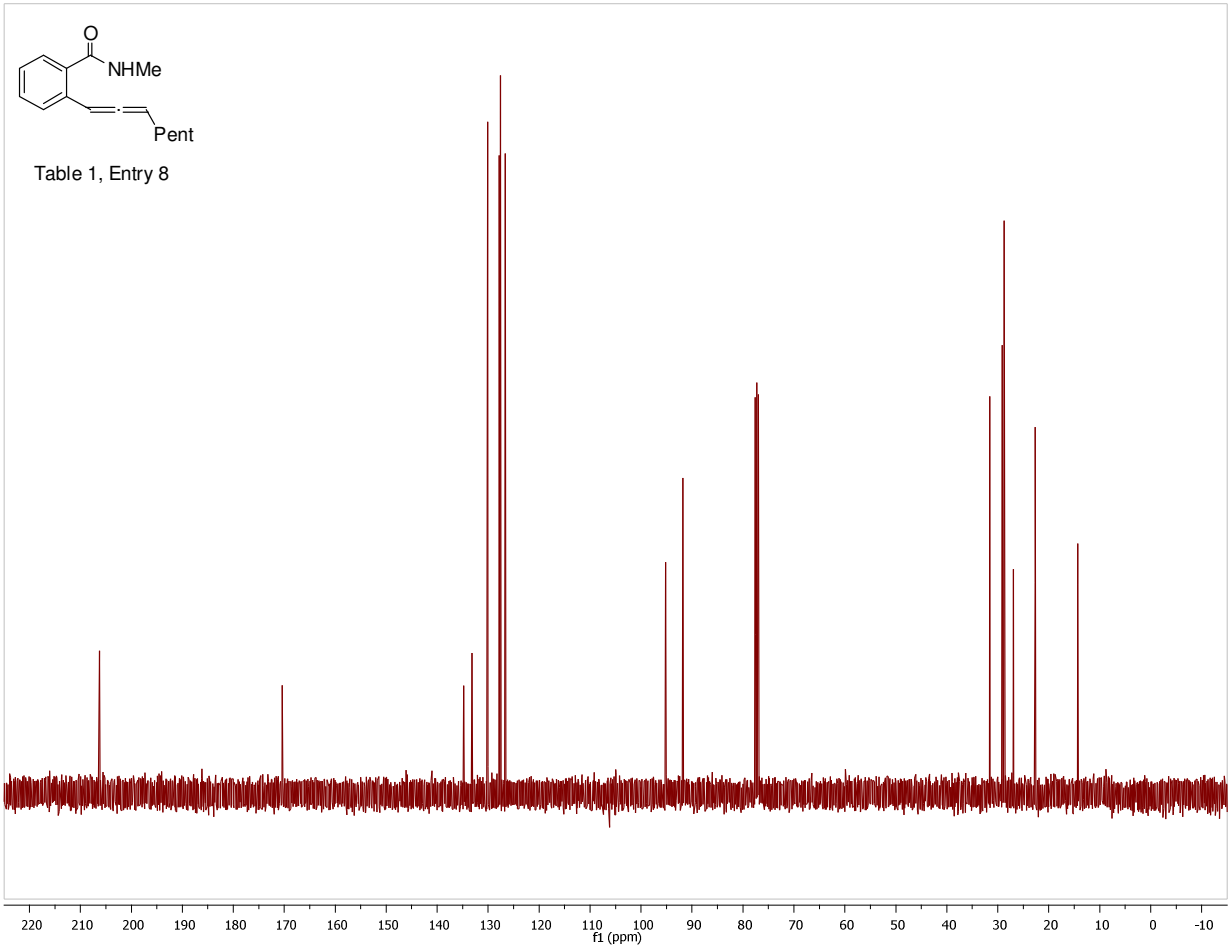


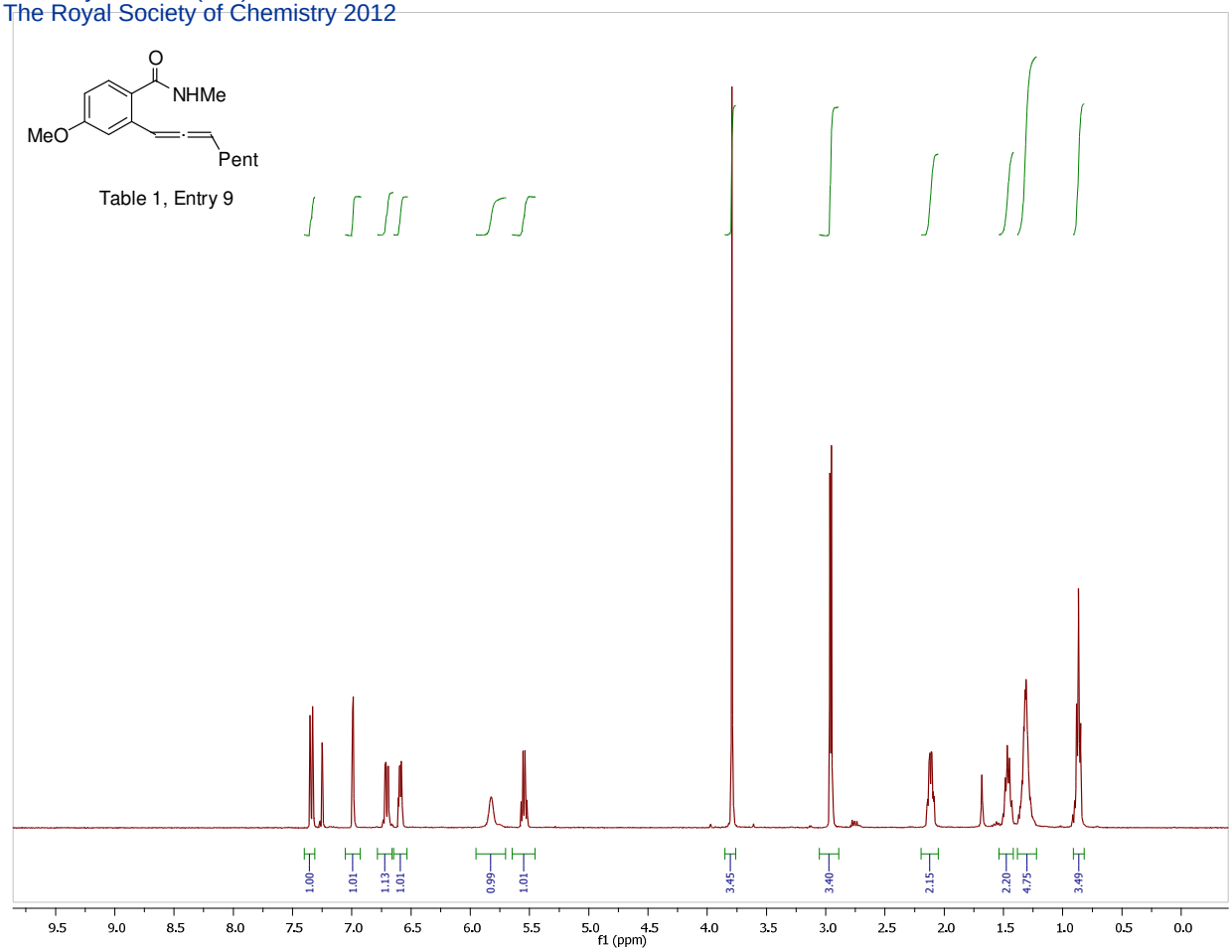


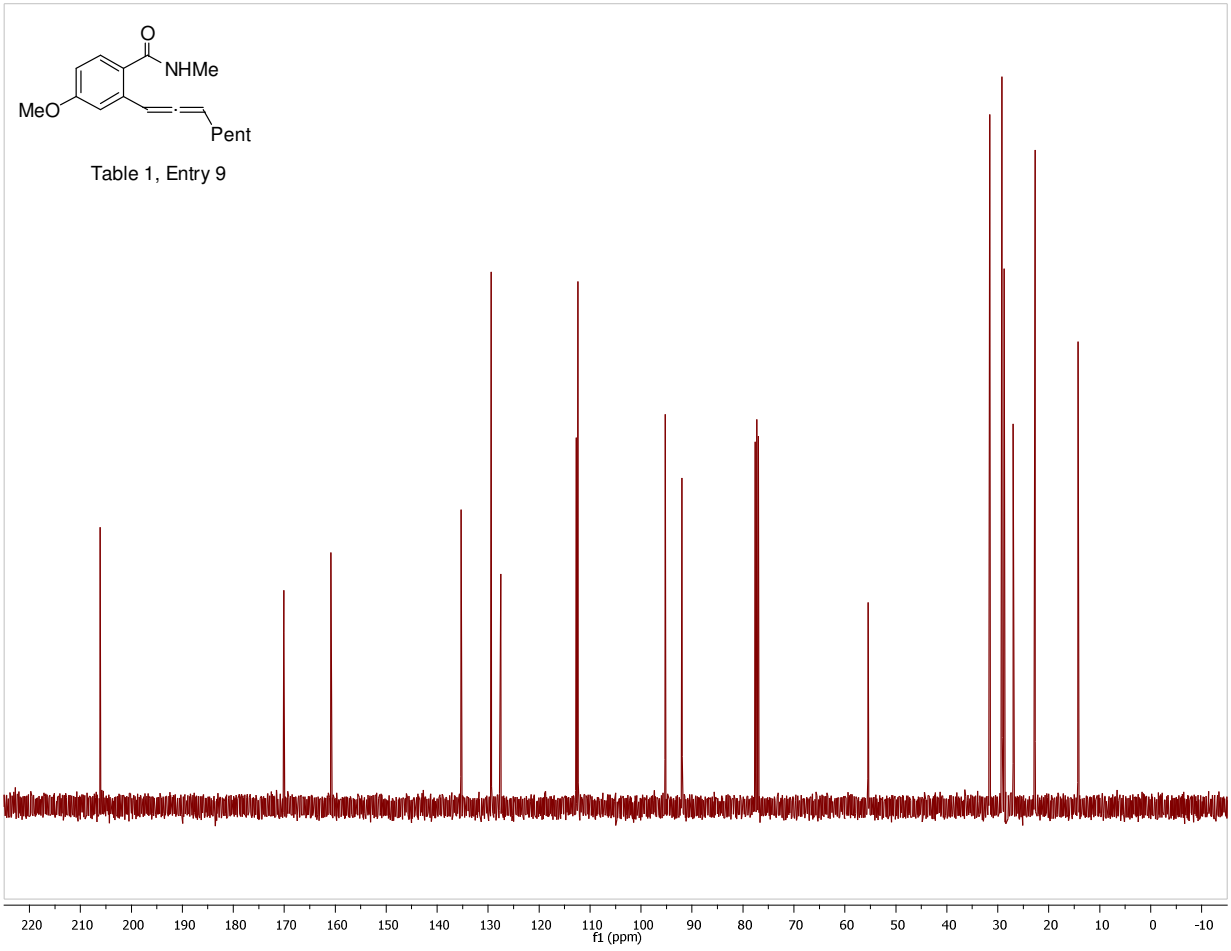


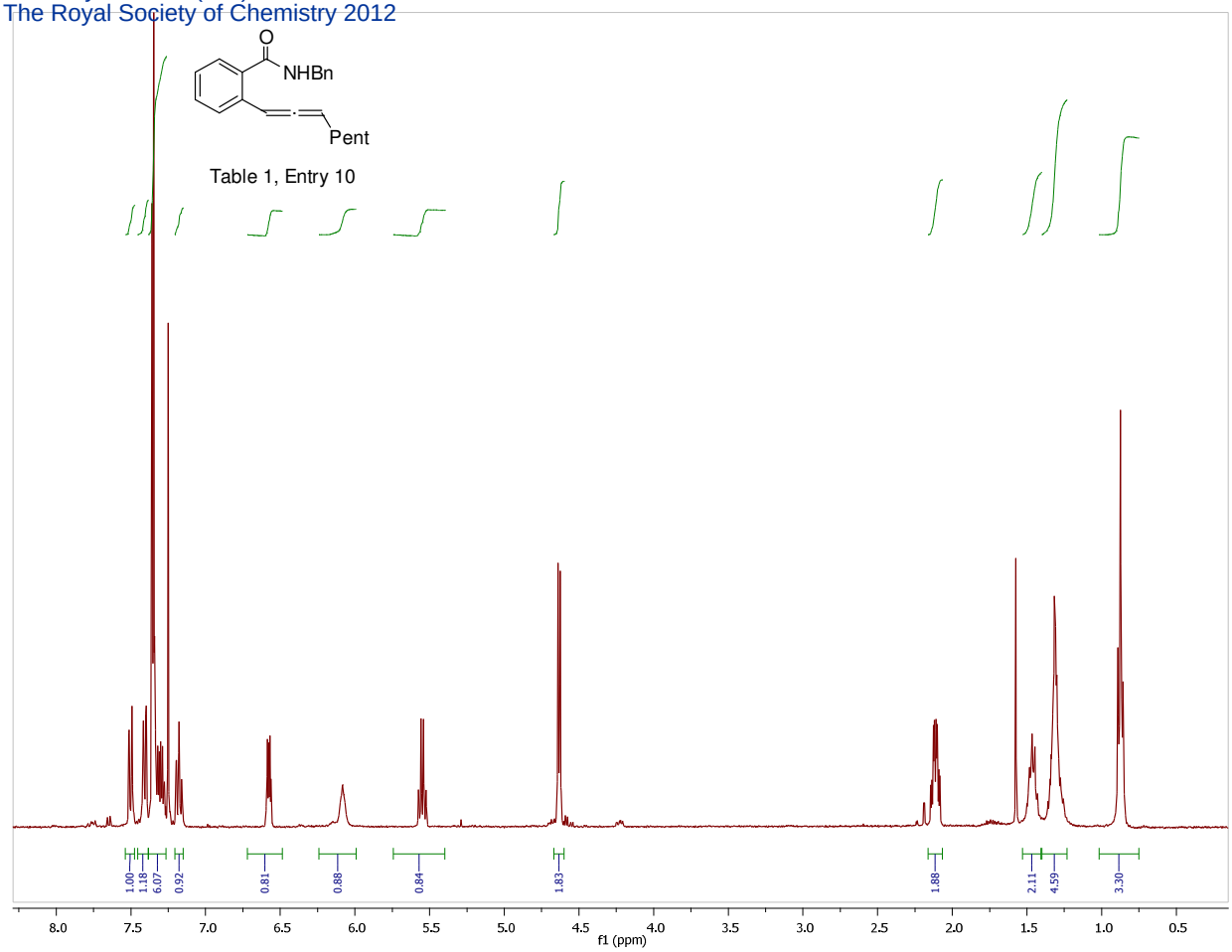


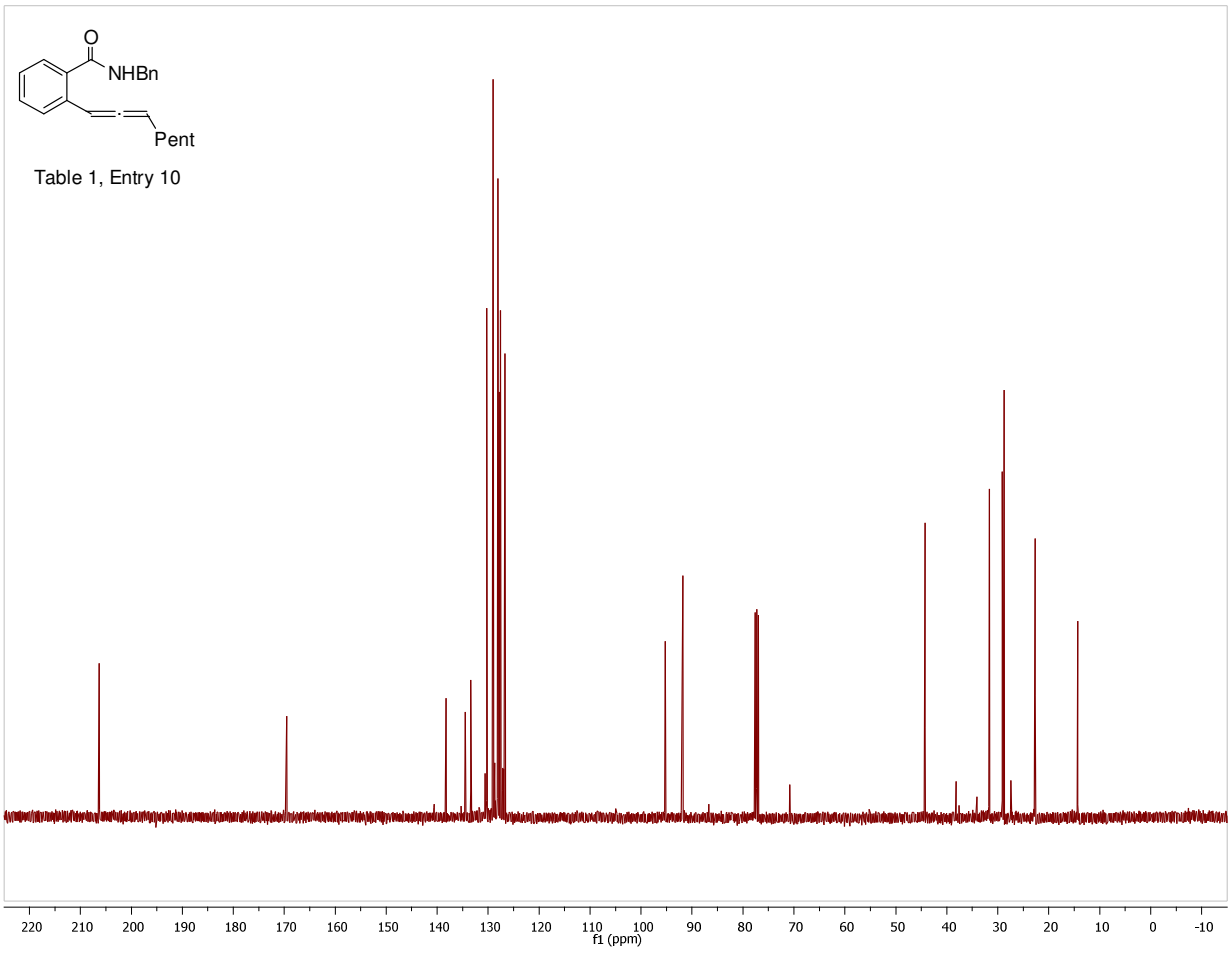


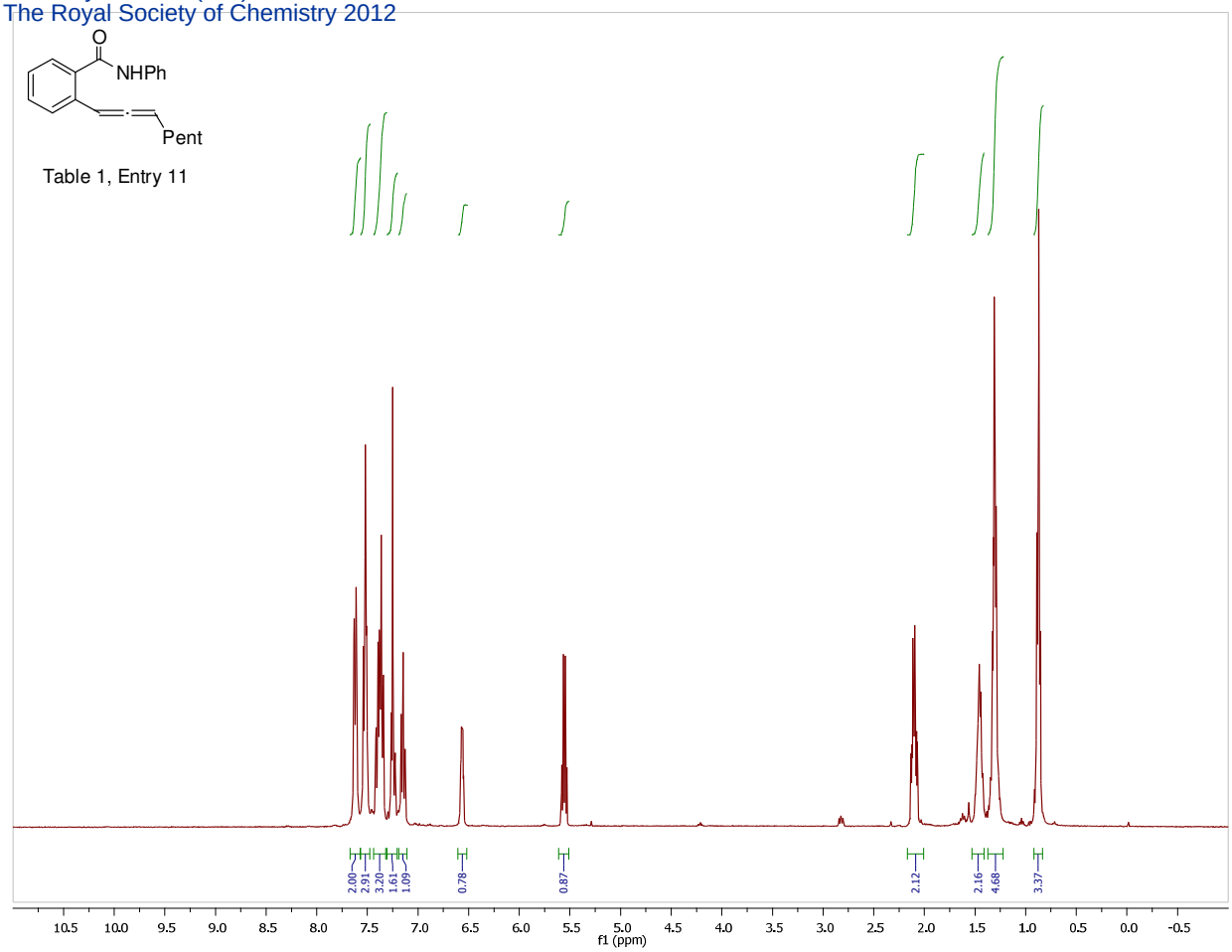


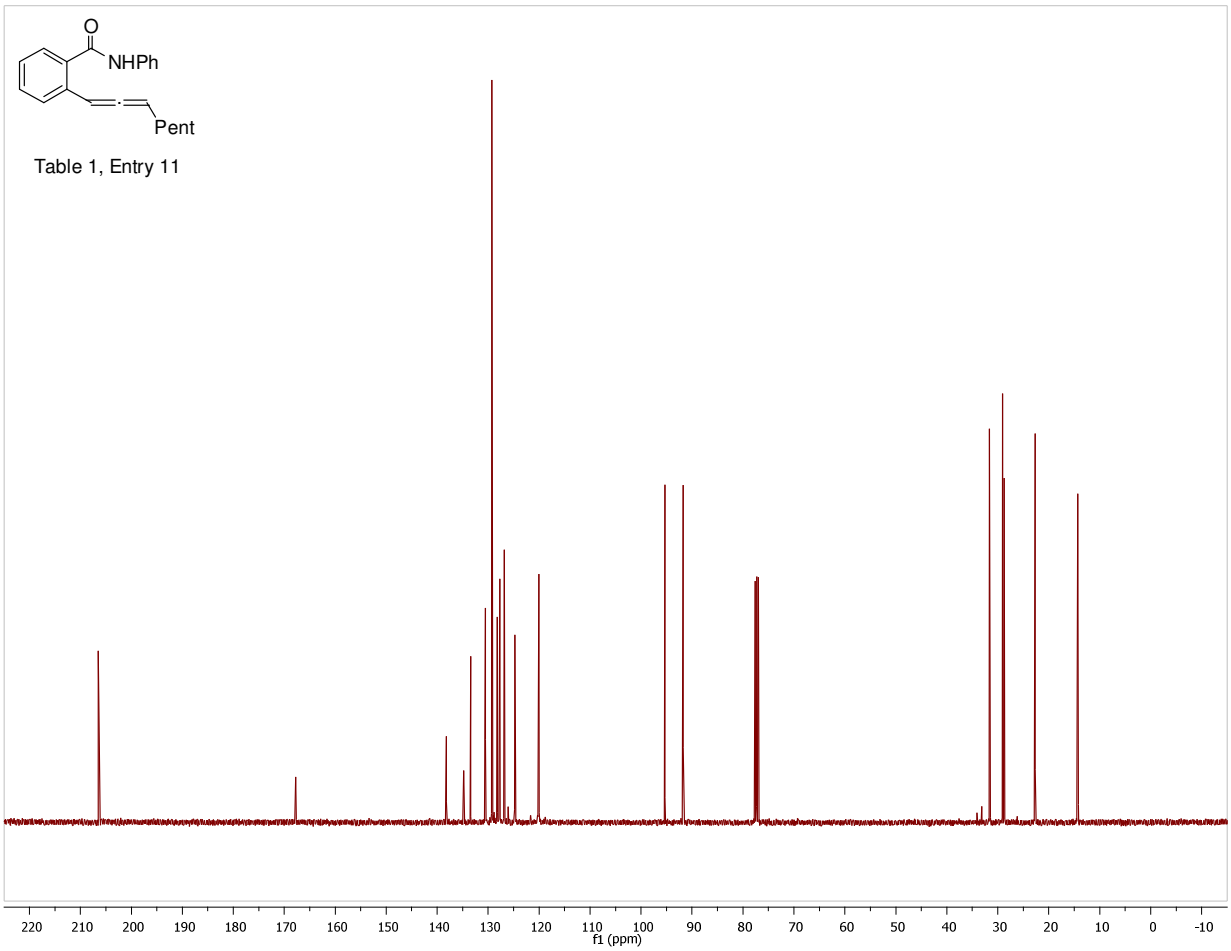


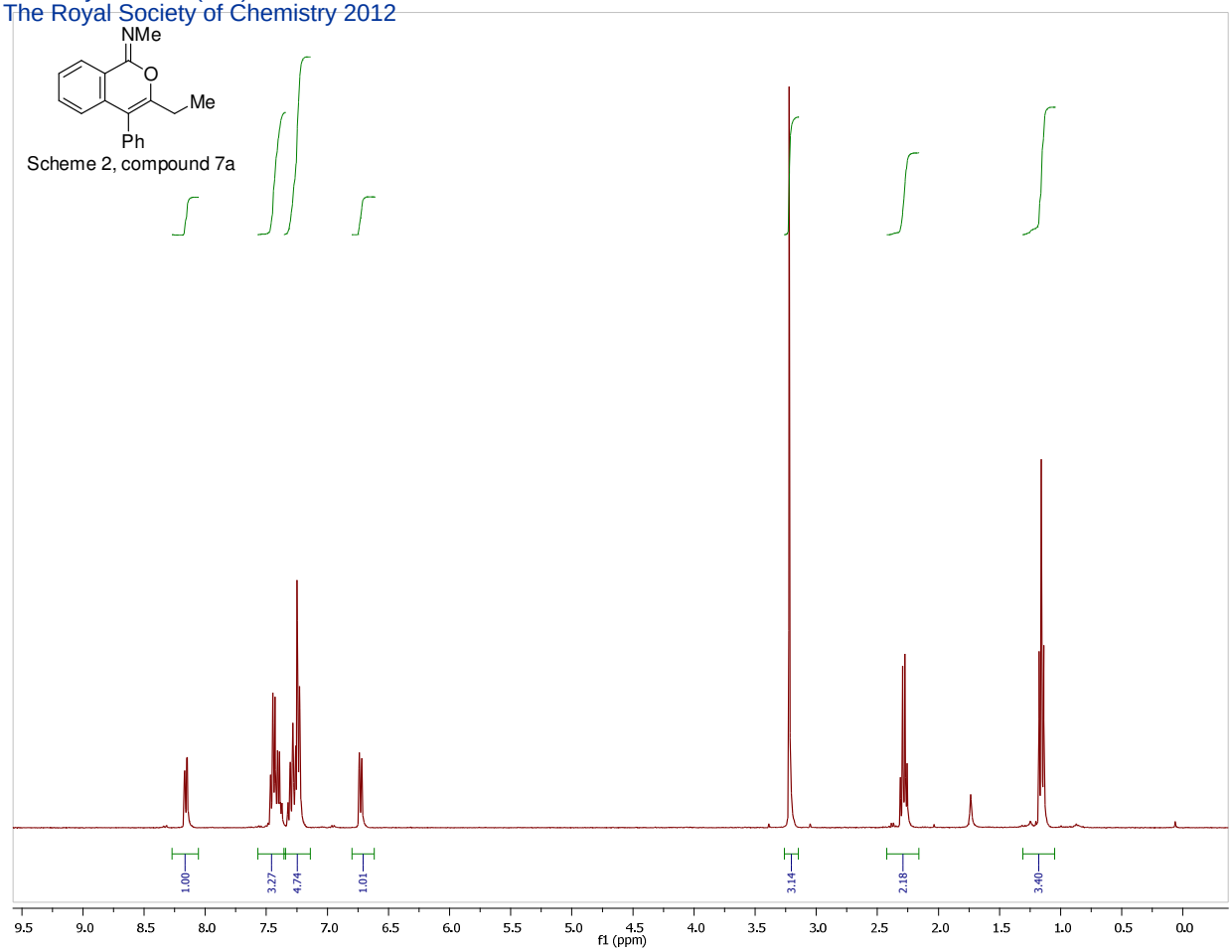


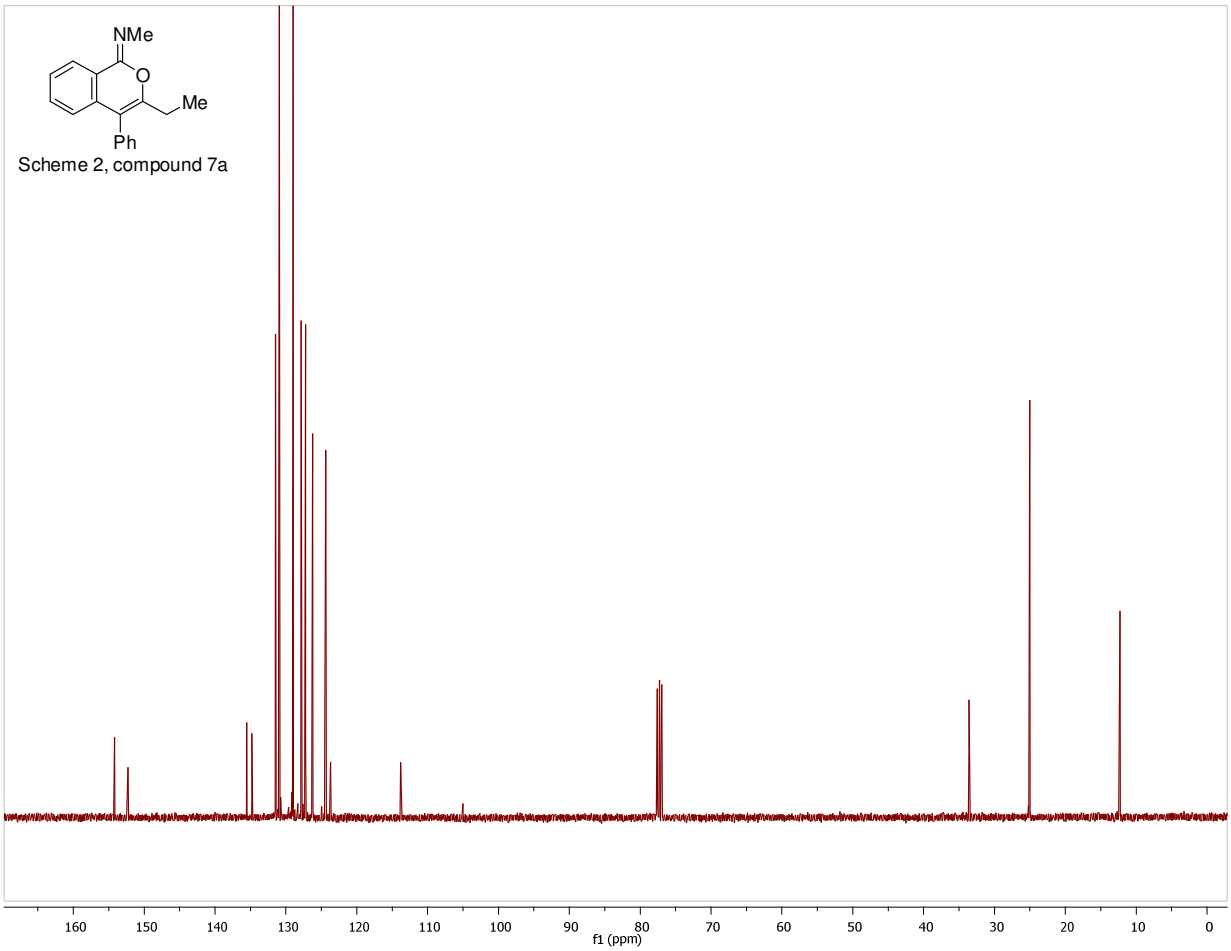


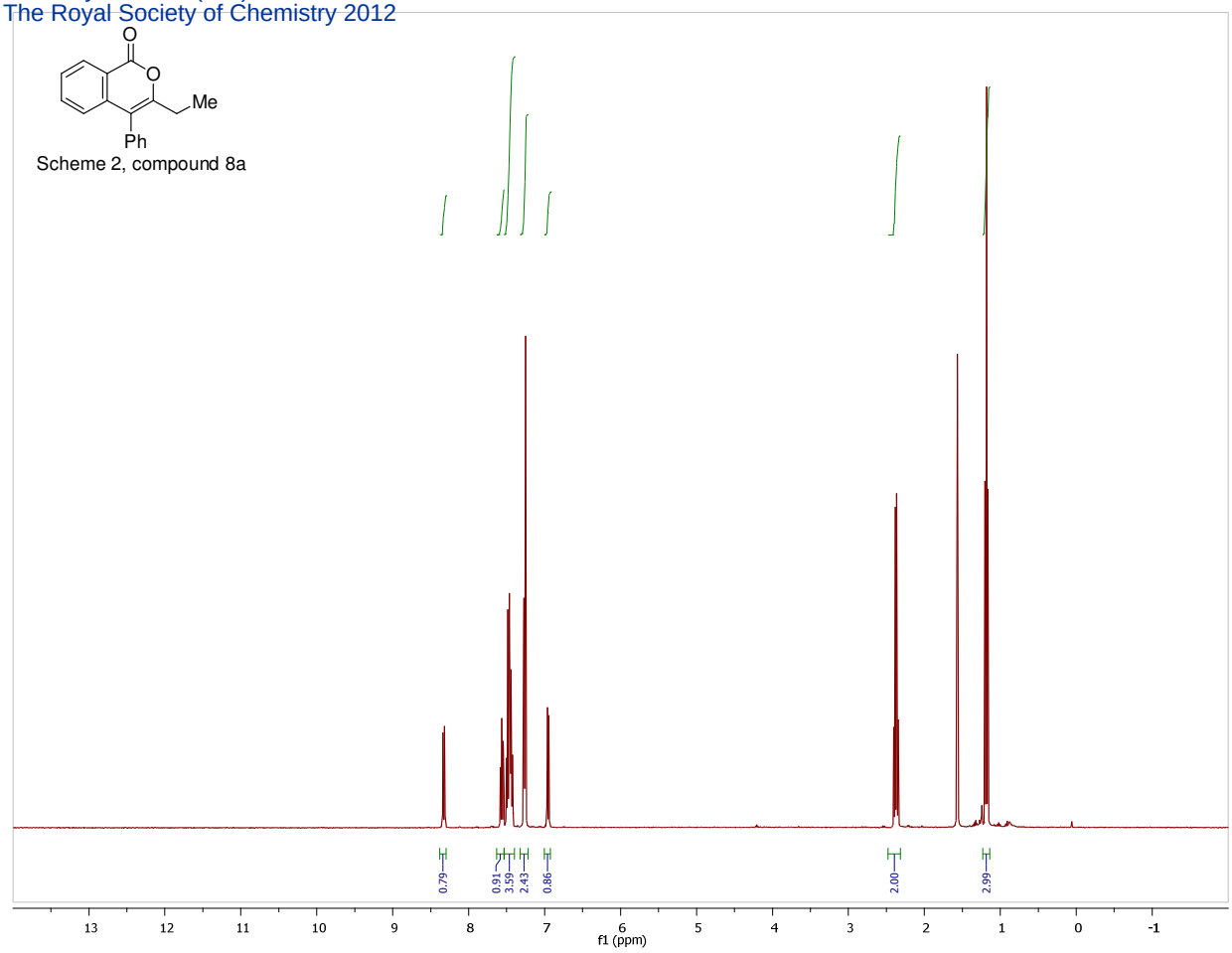




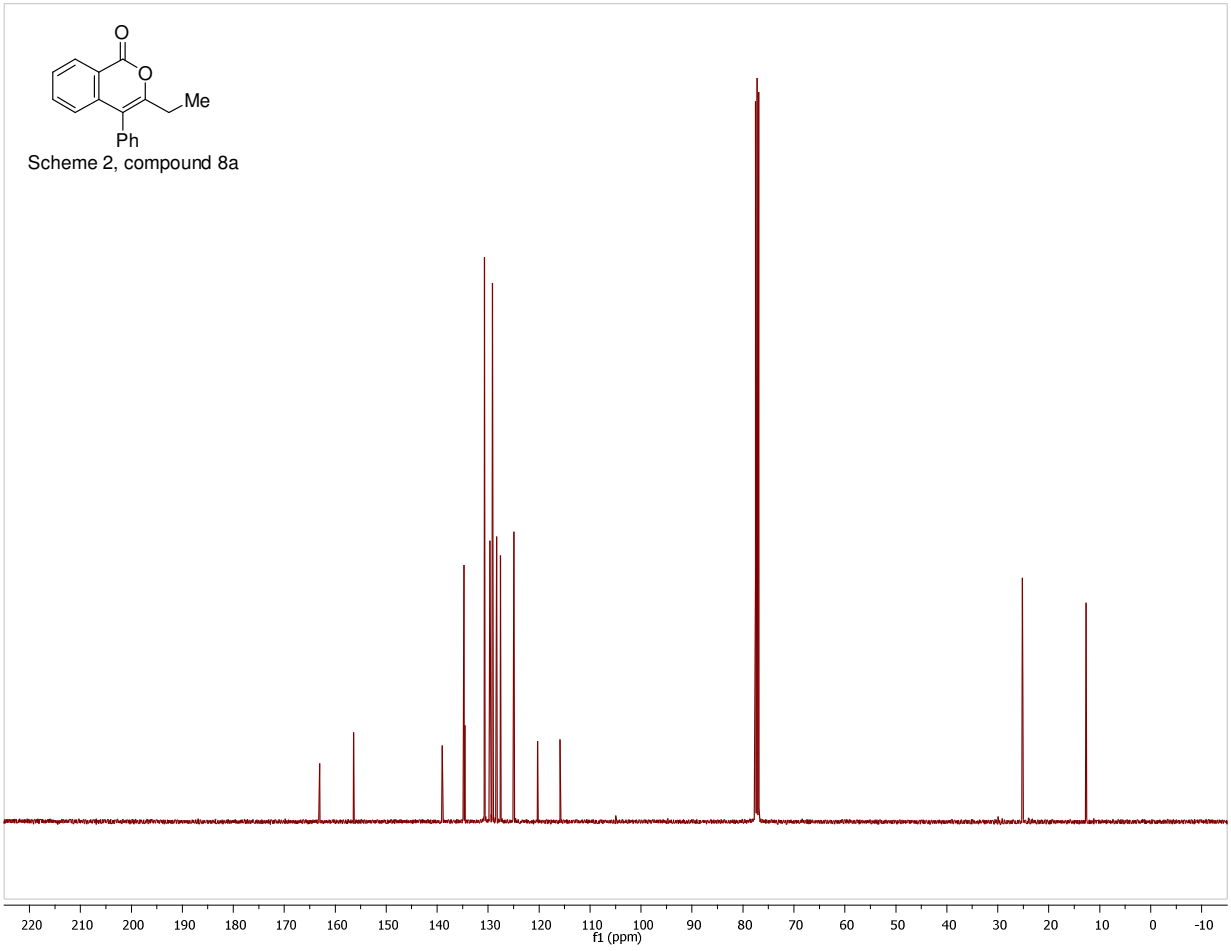




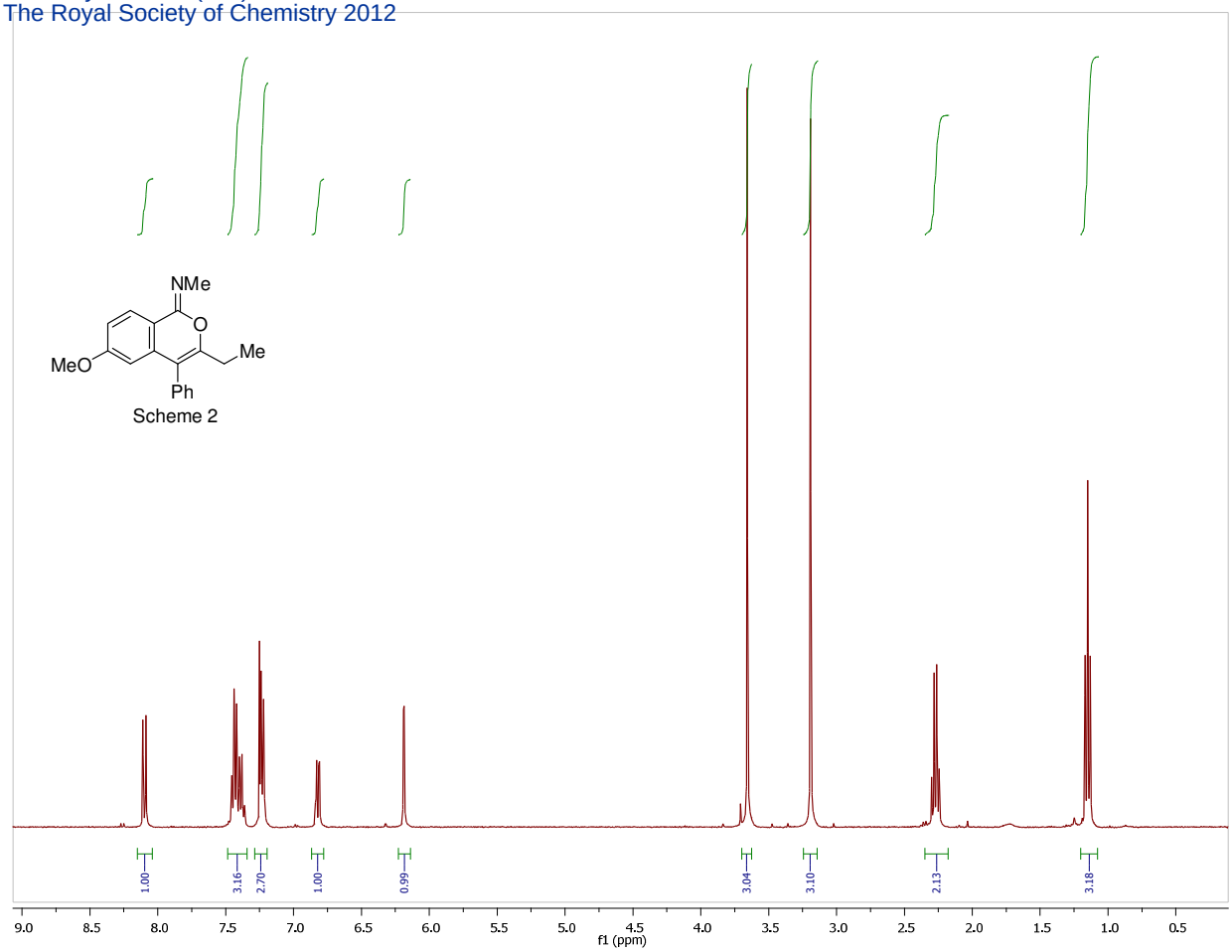




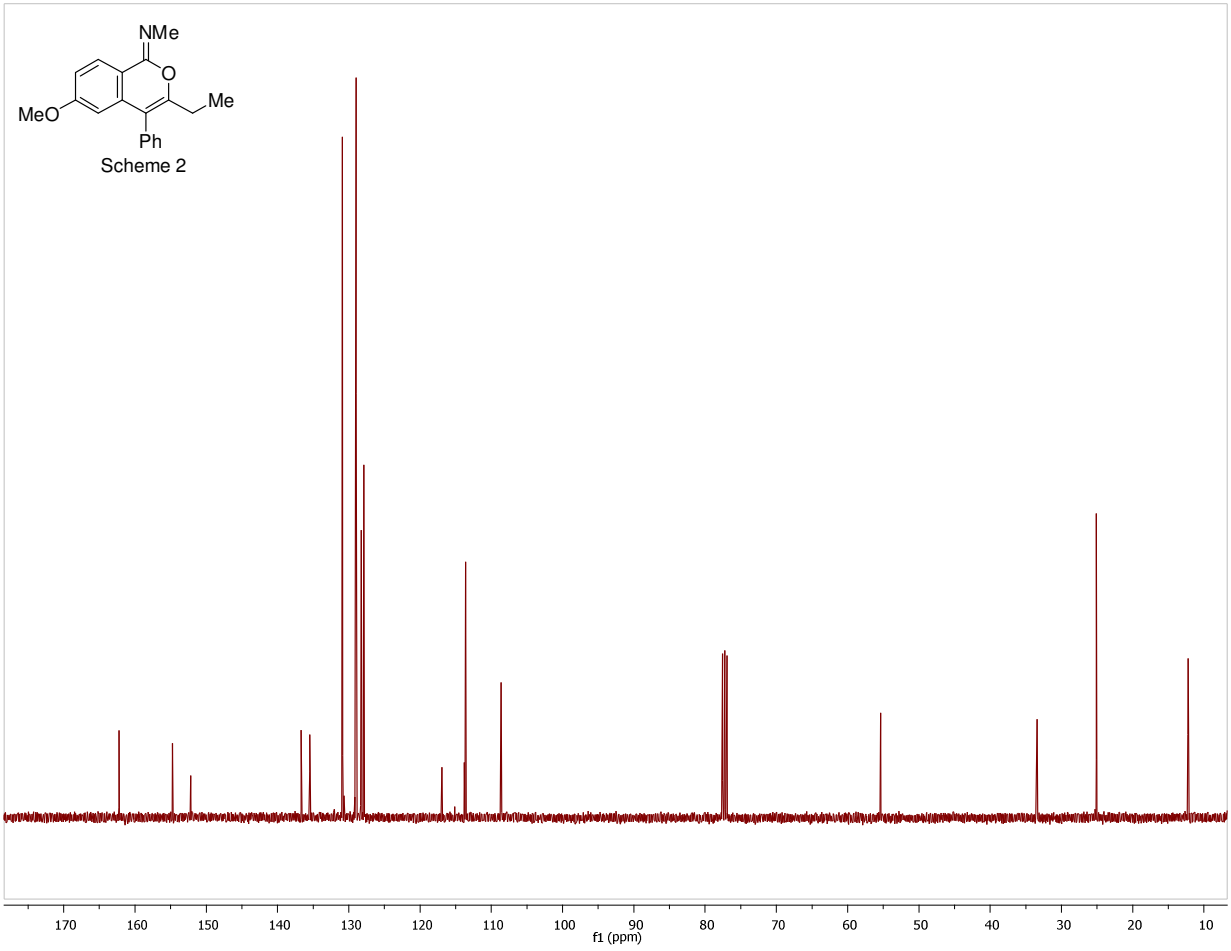
Scheme 2, compound 8a



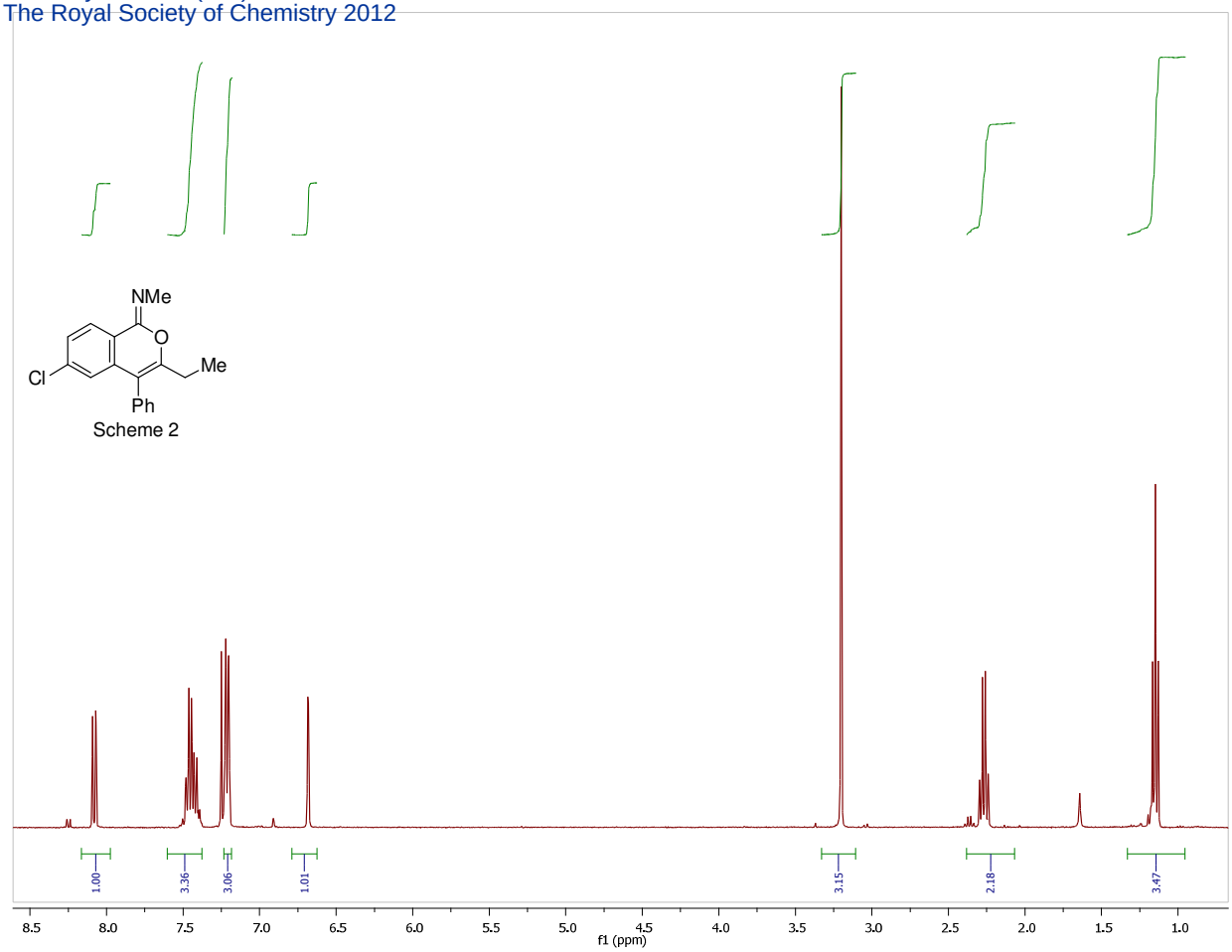
Scheme 2, compound 8a



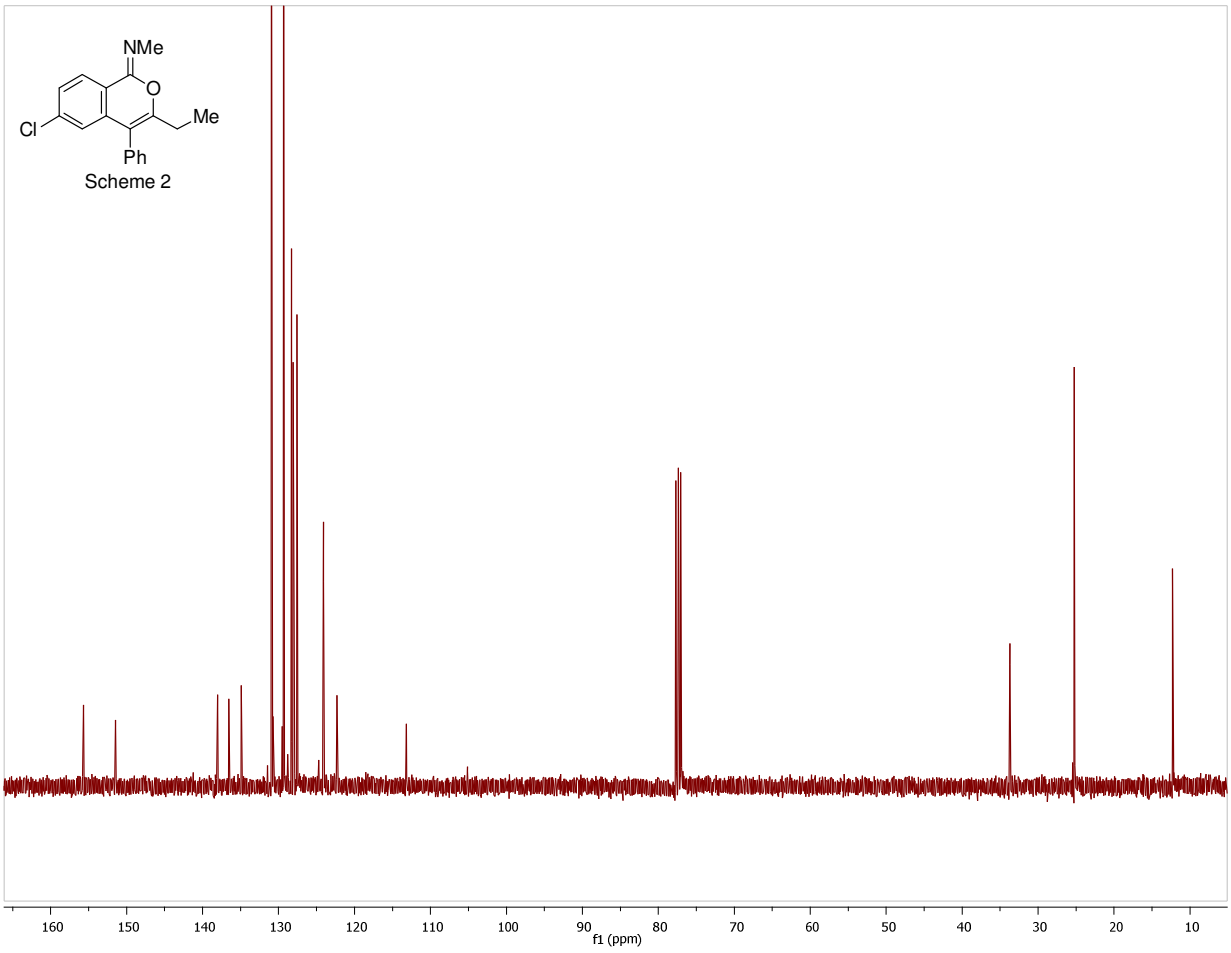
Scheme 2



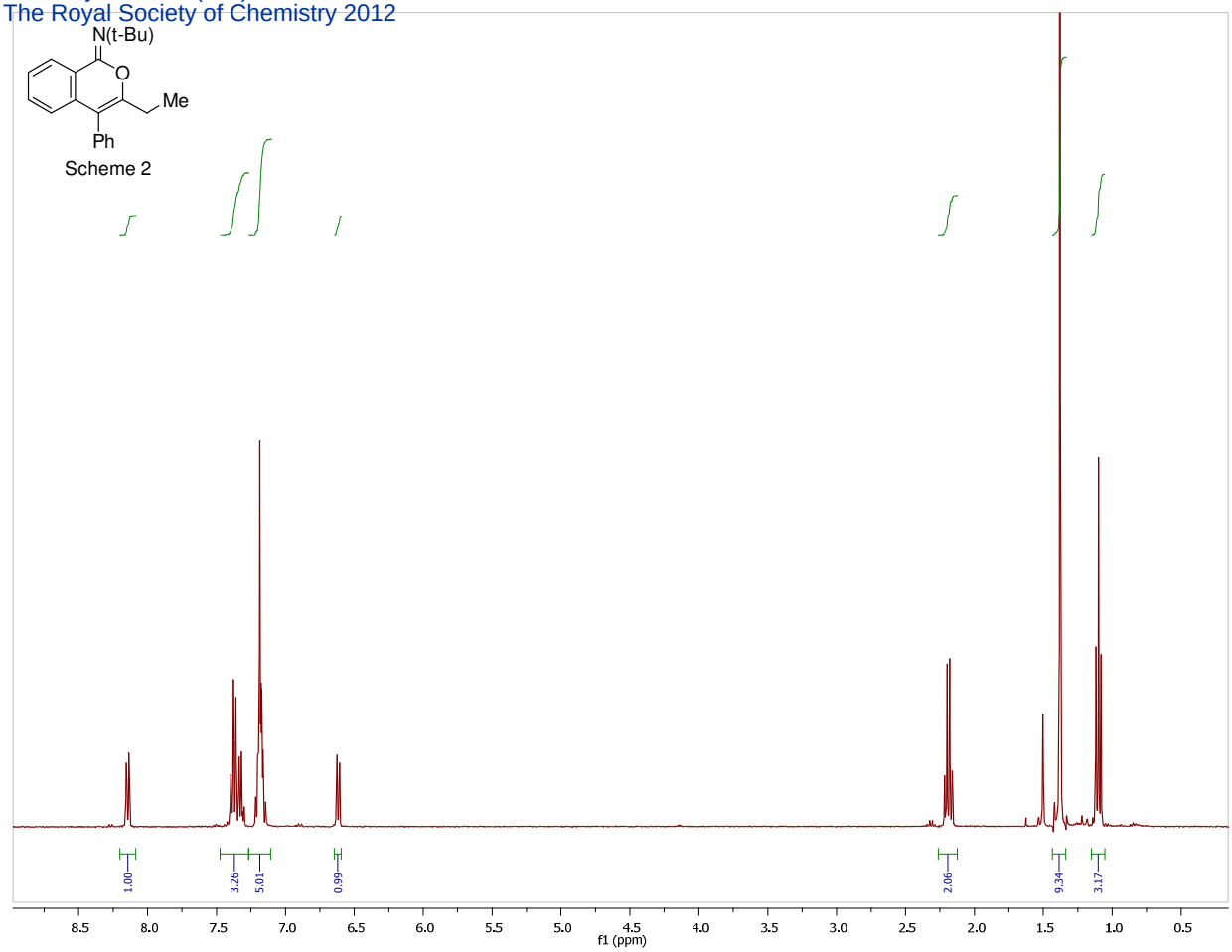
Scheme 2

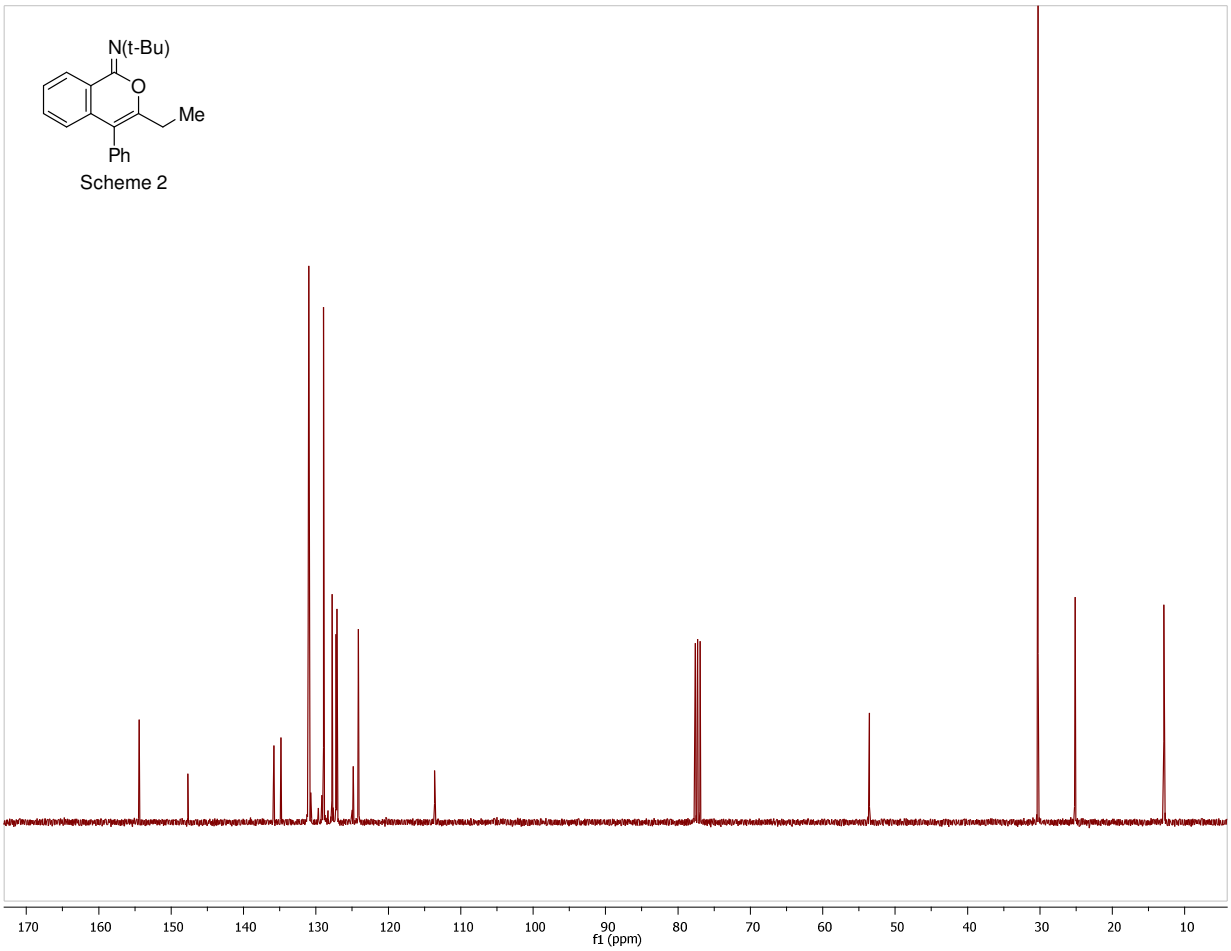


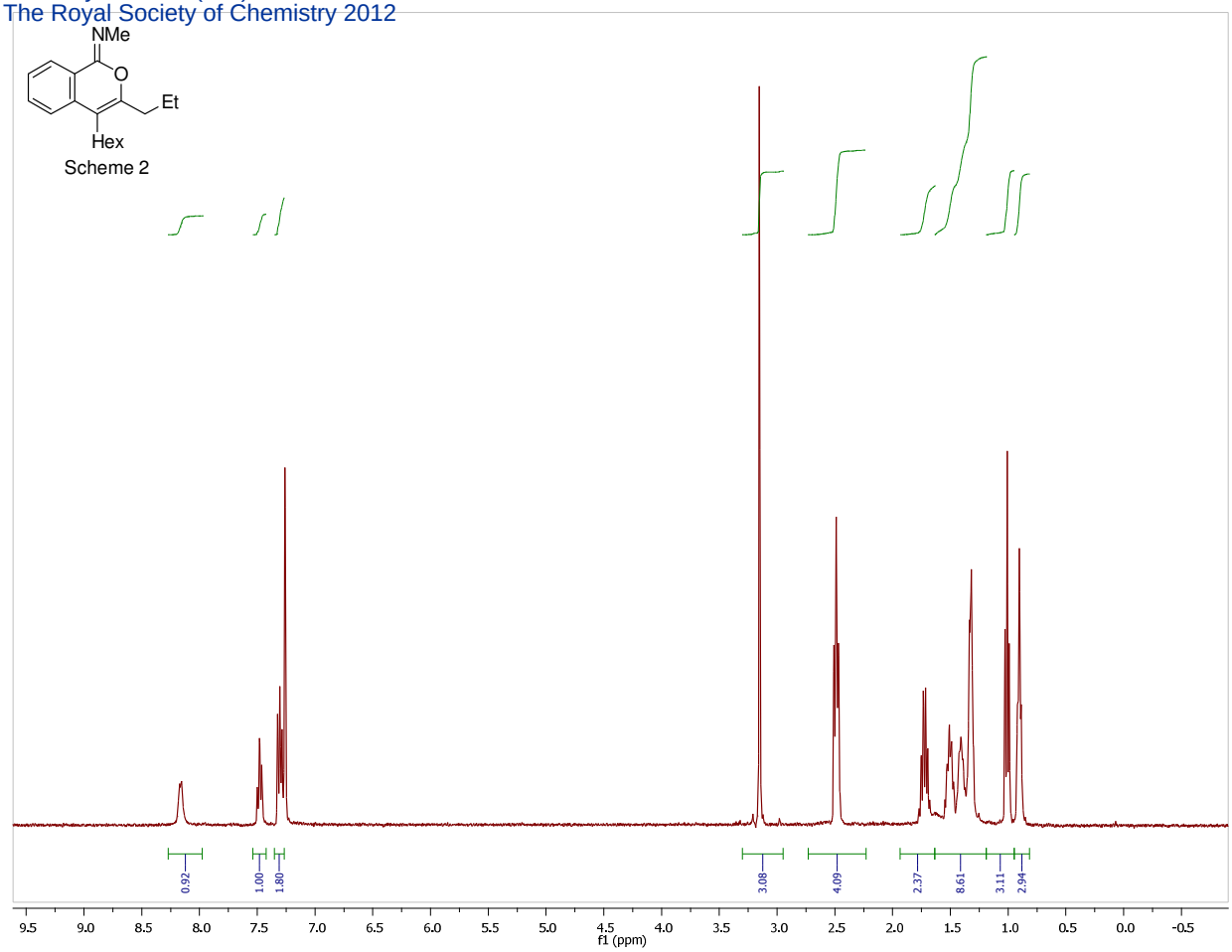
Scheme 2

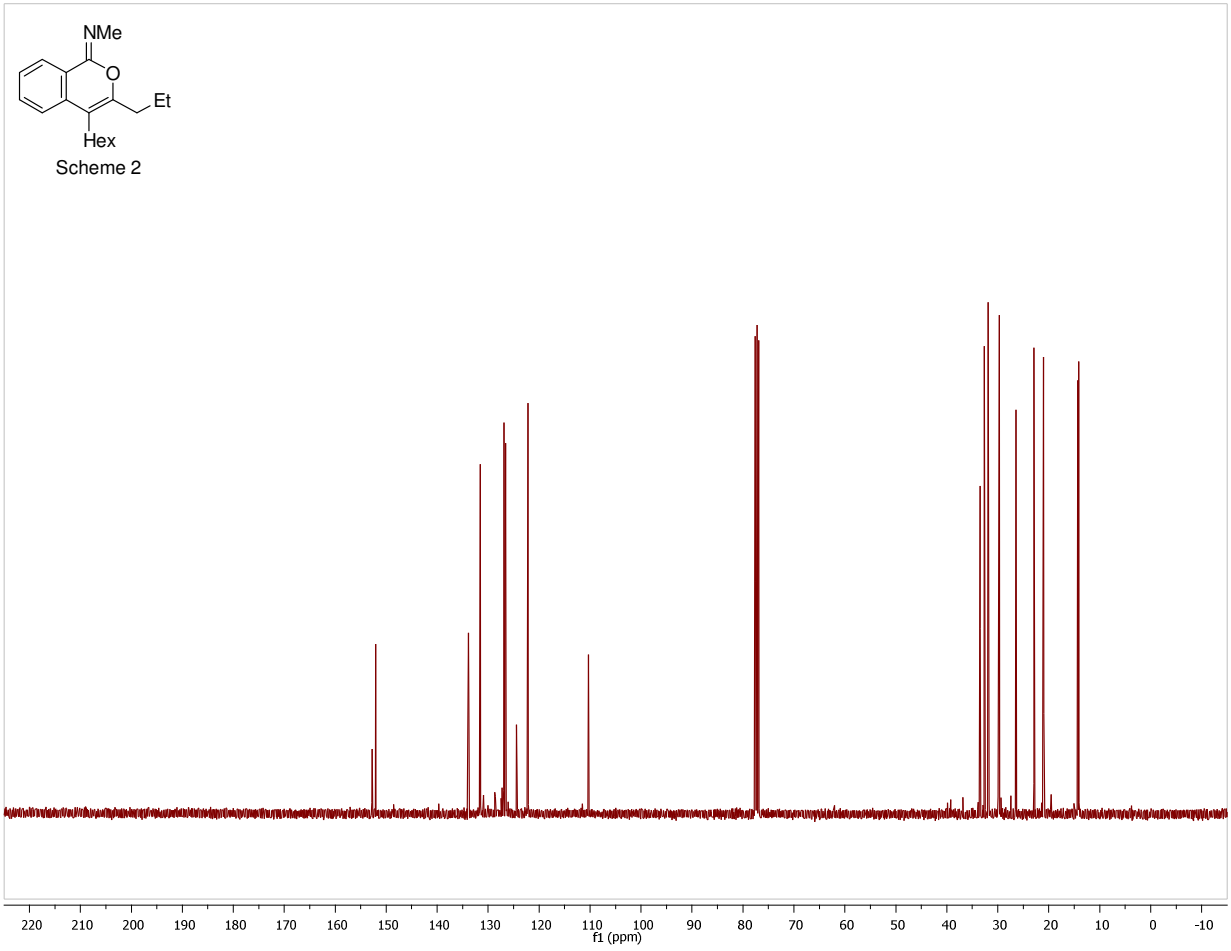


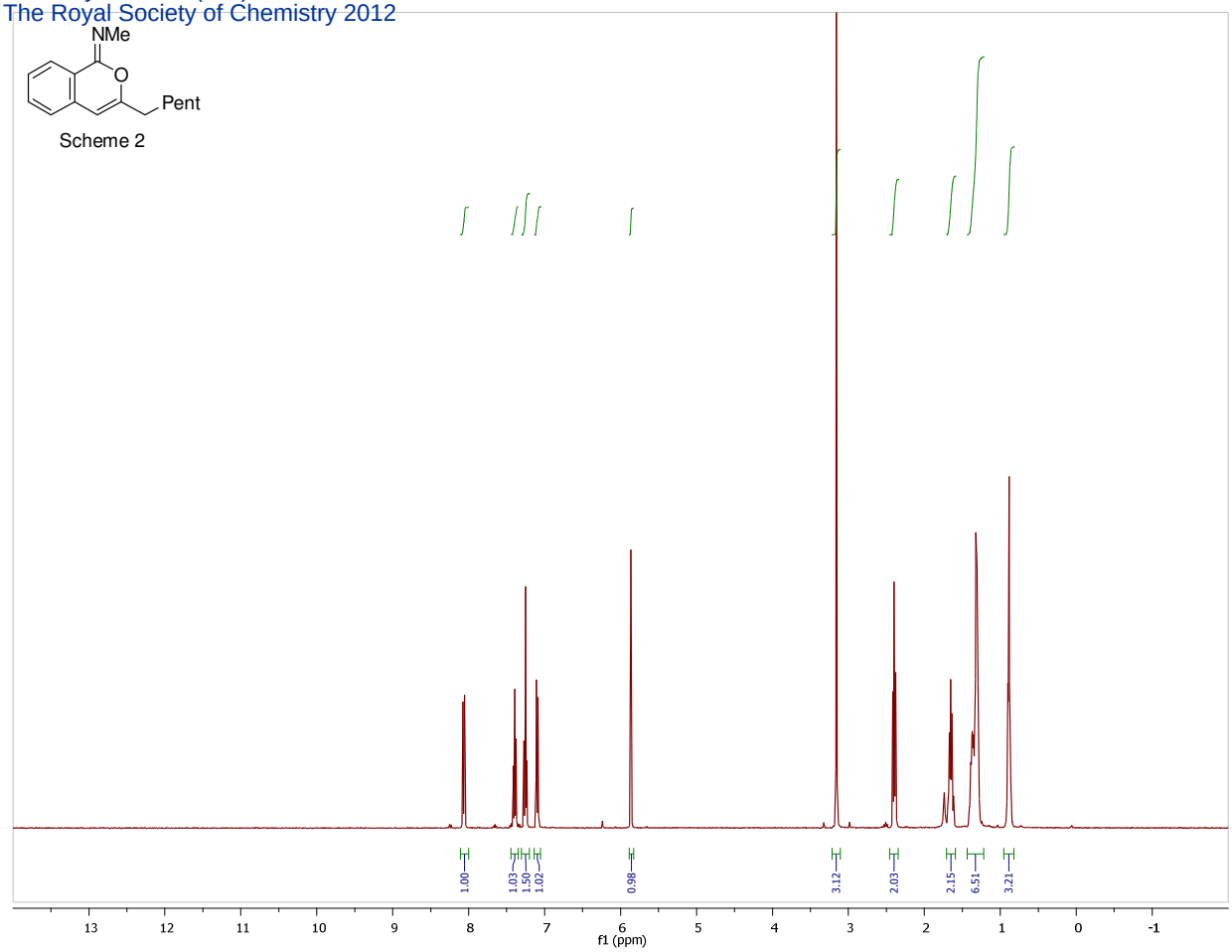
Scheme 2

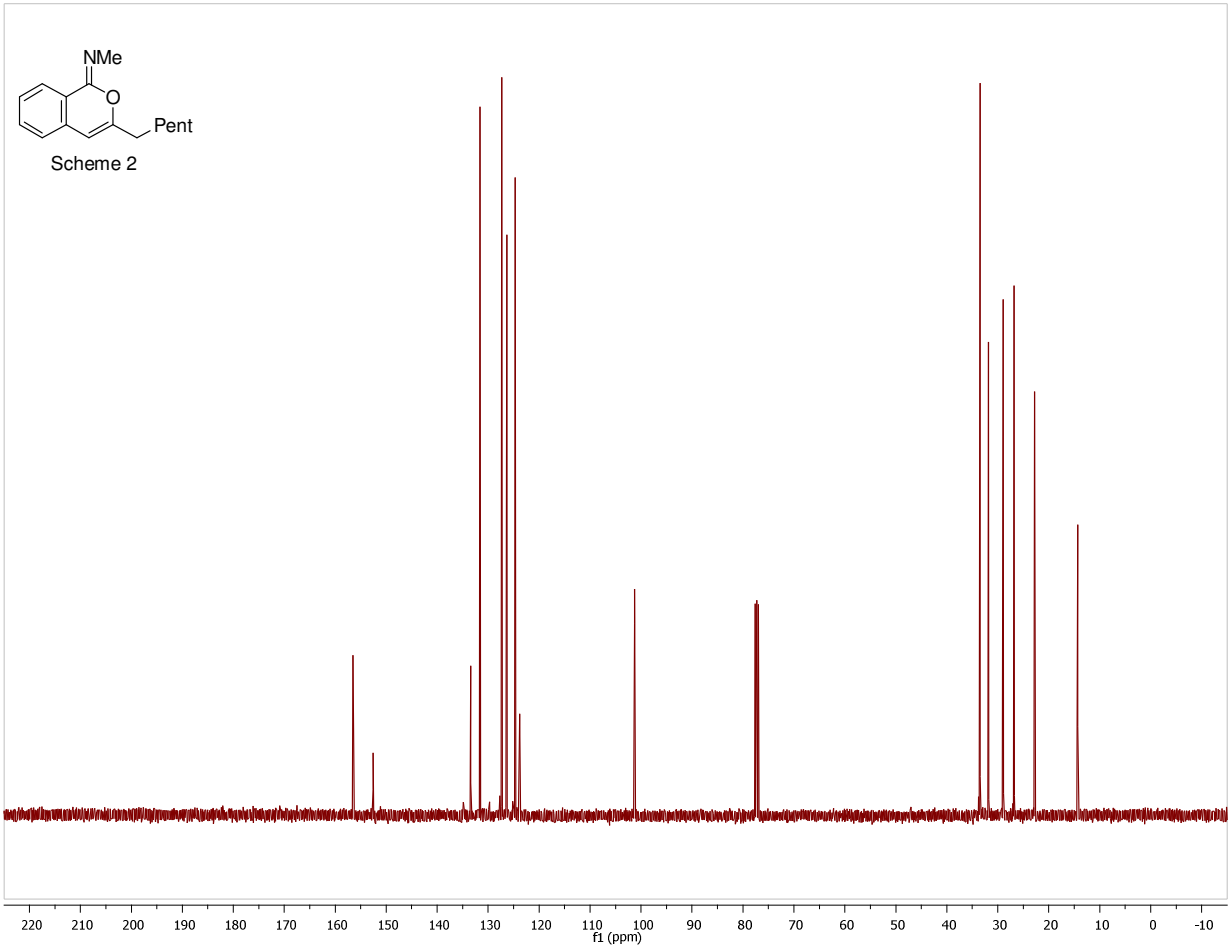


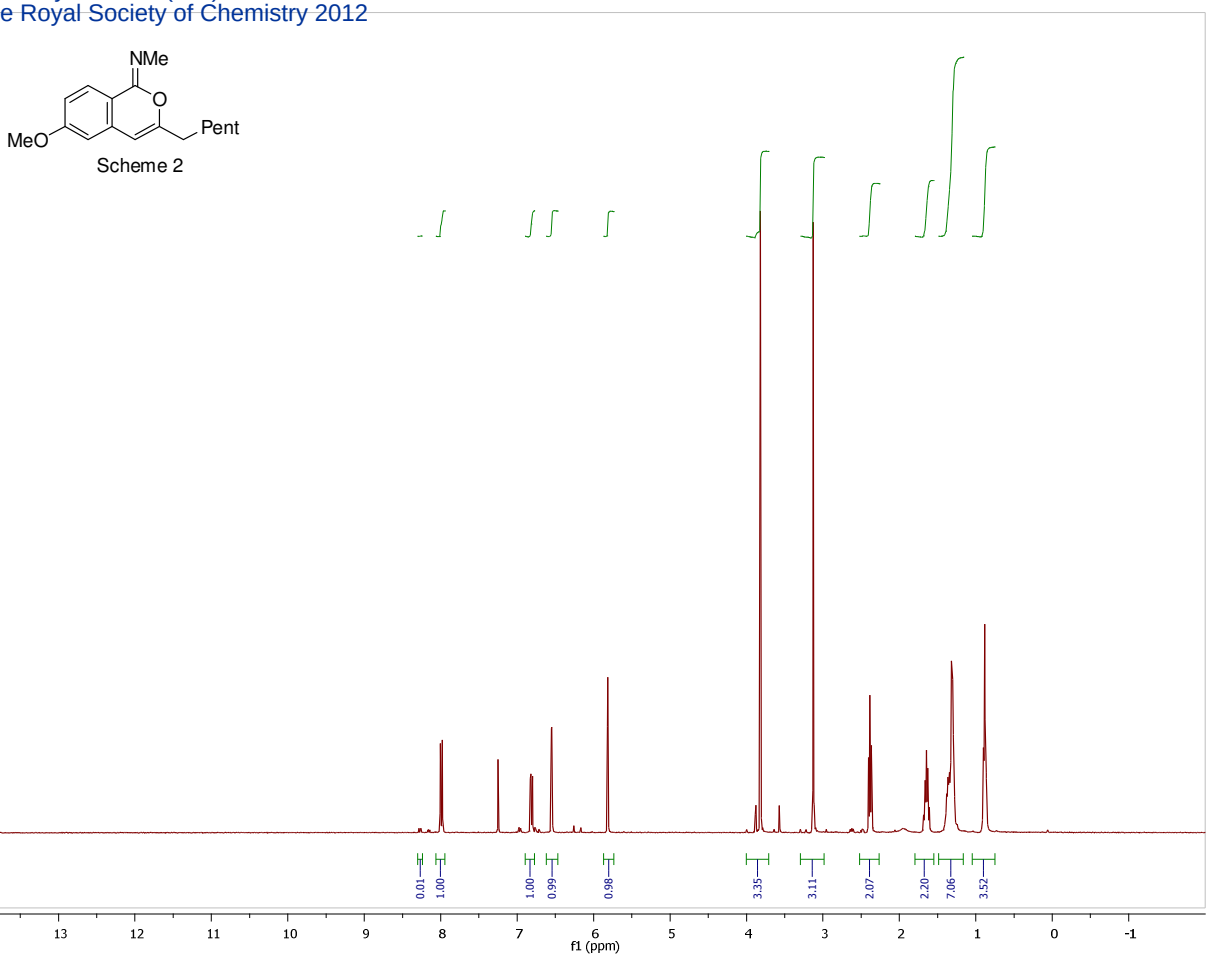


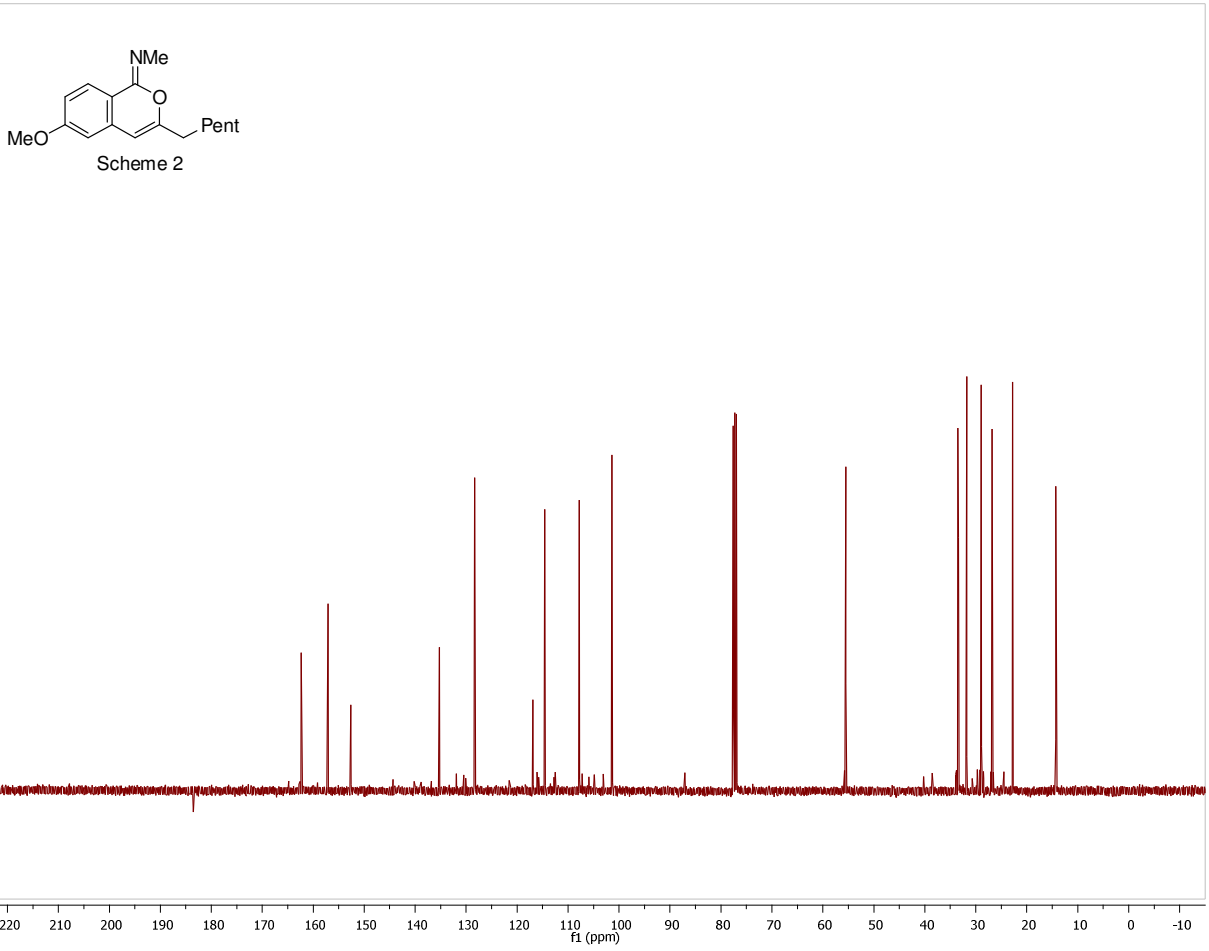


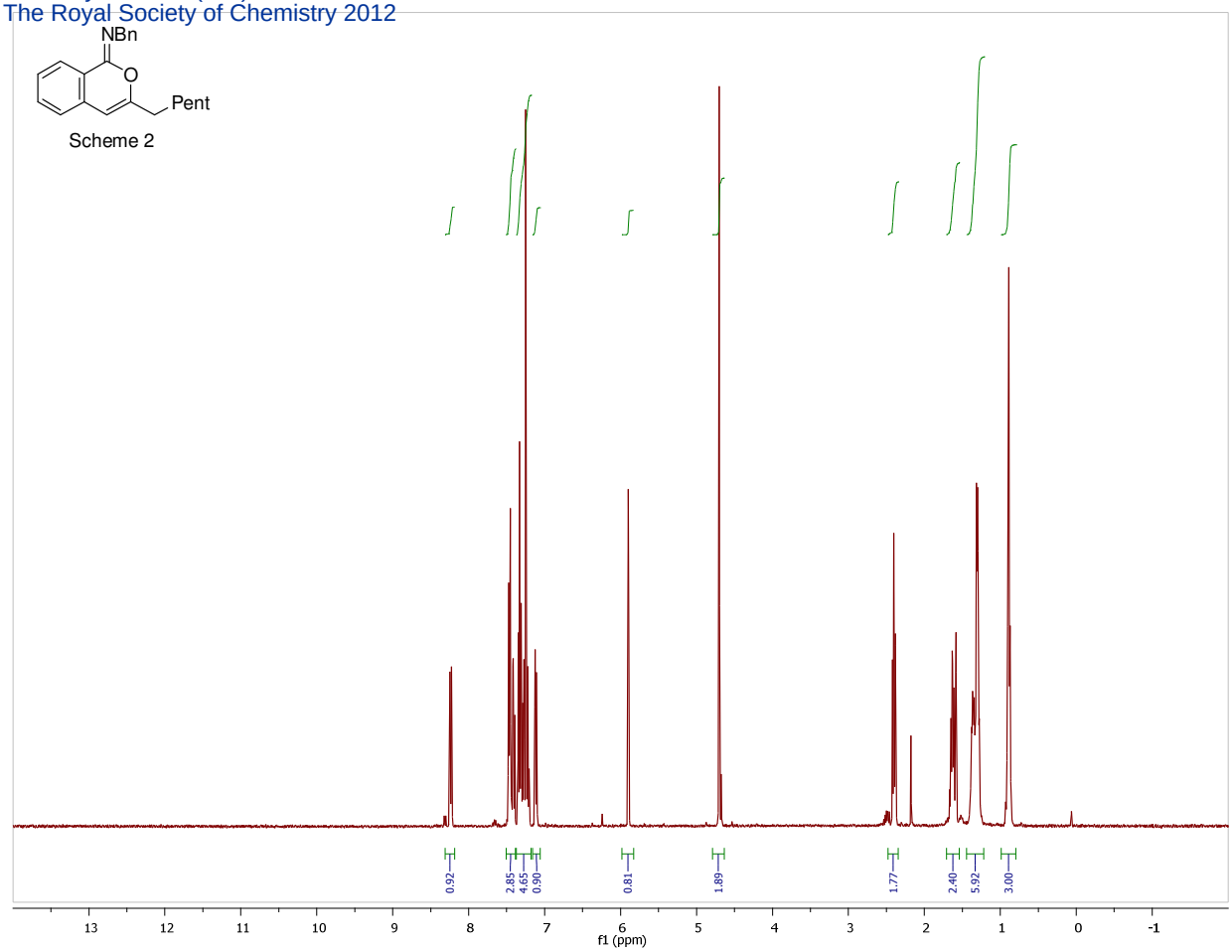


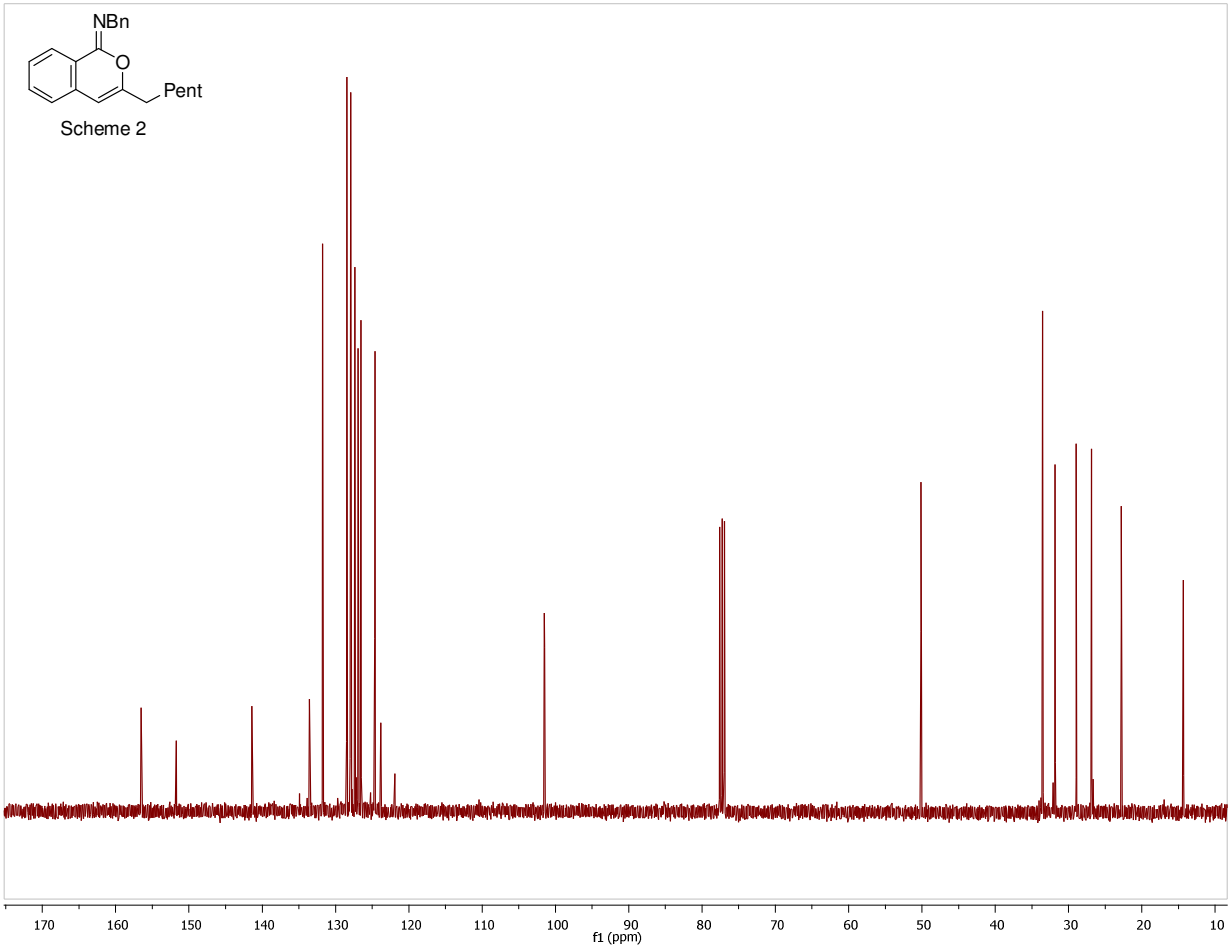


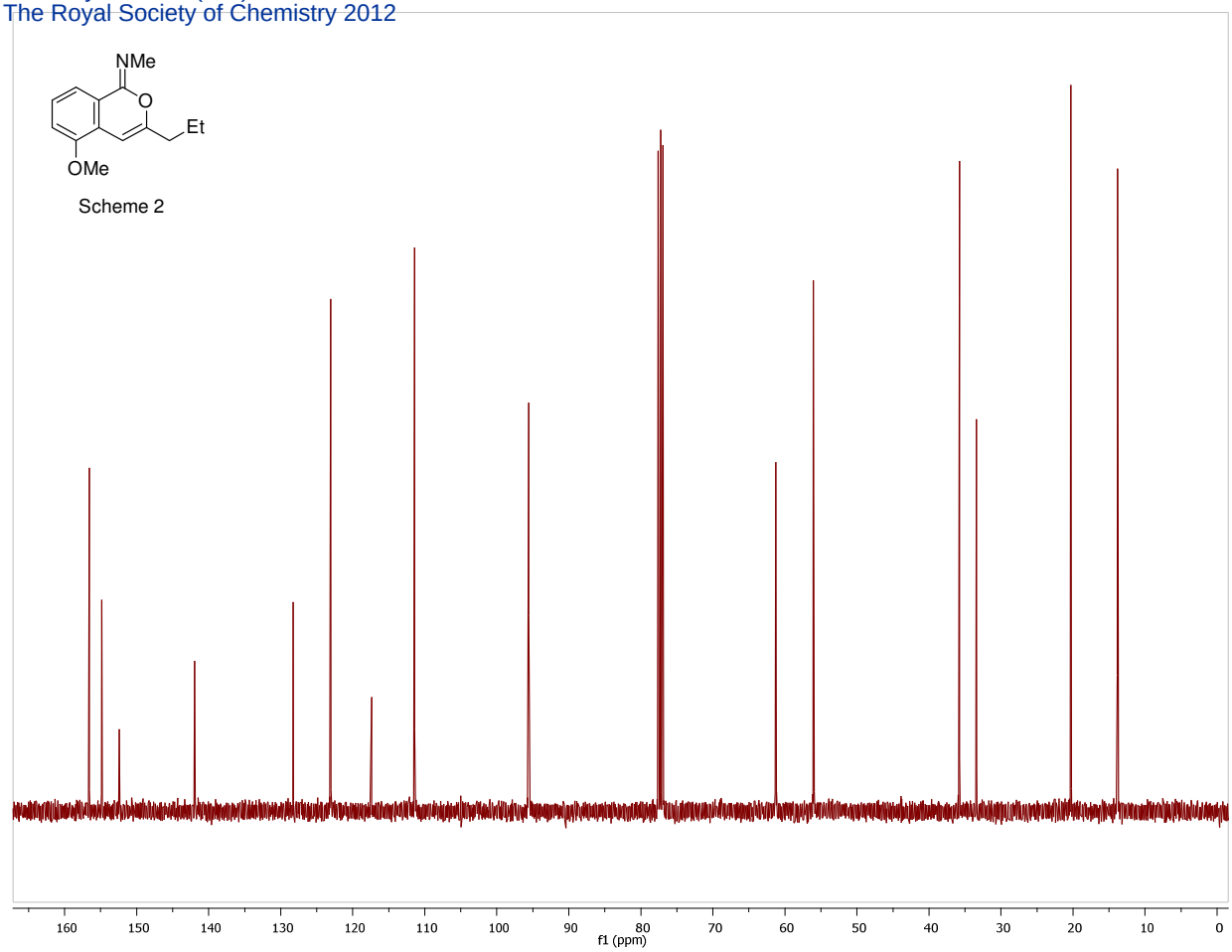




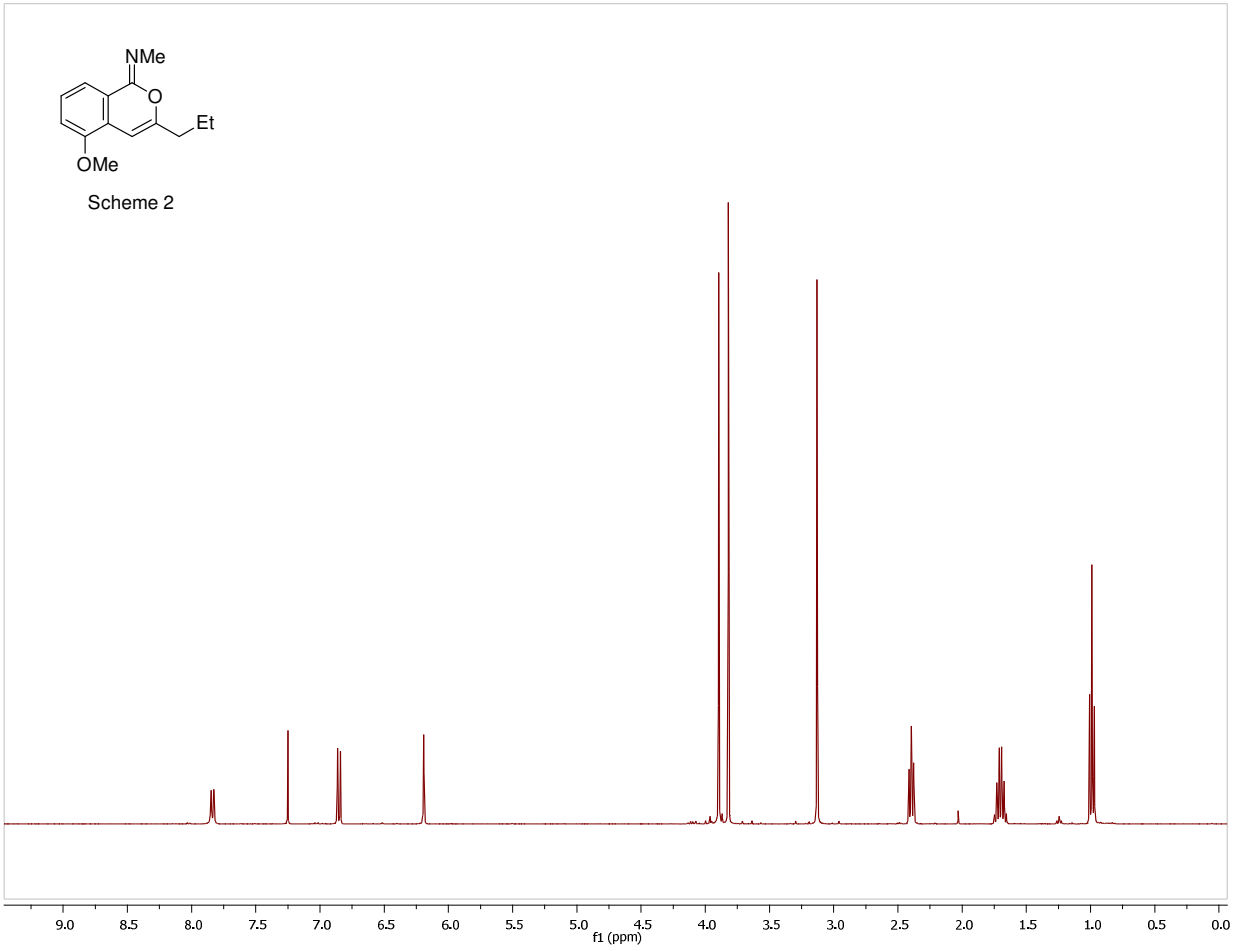




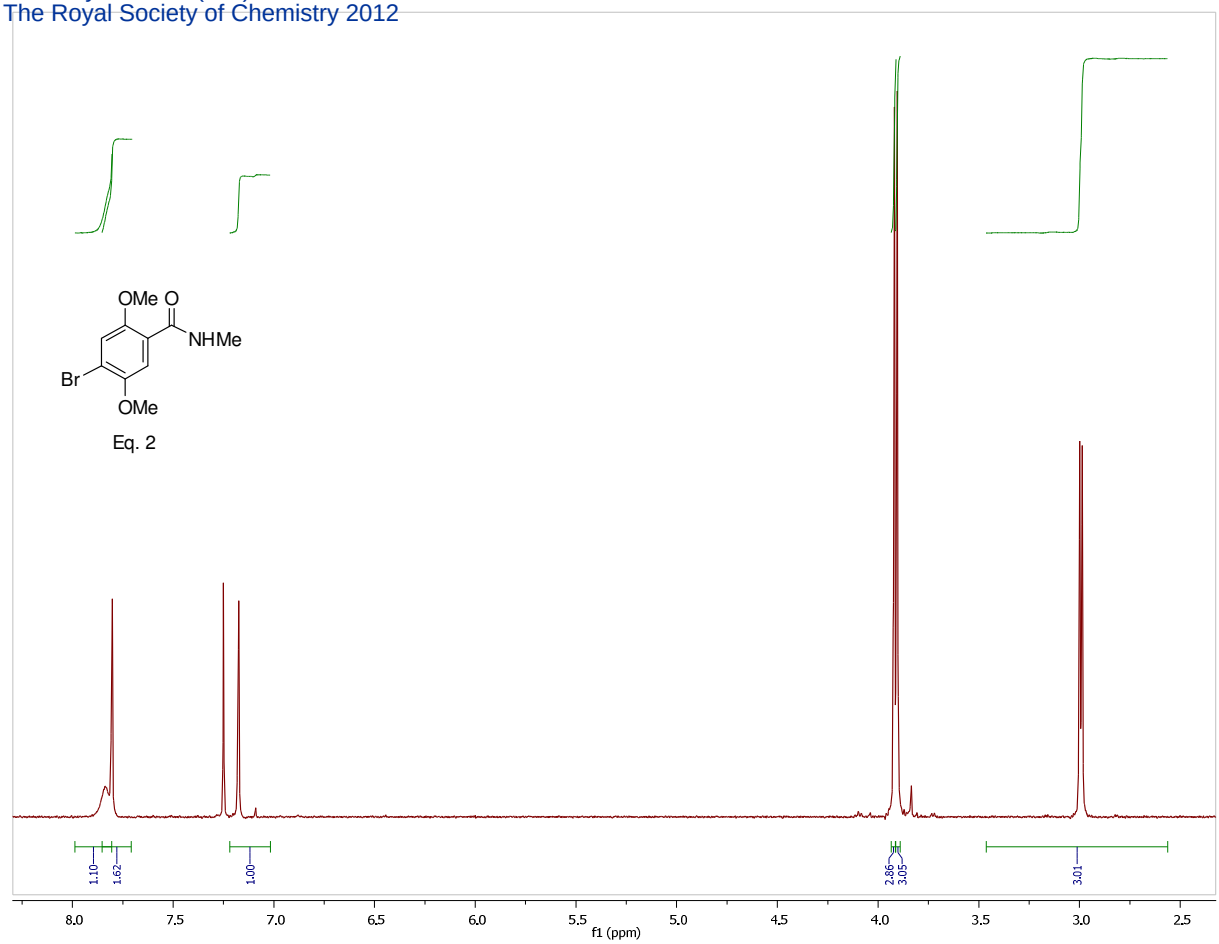


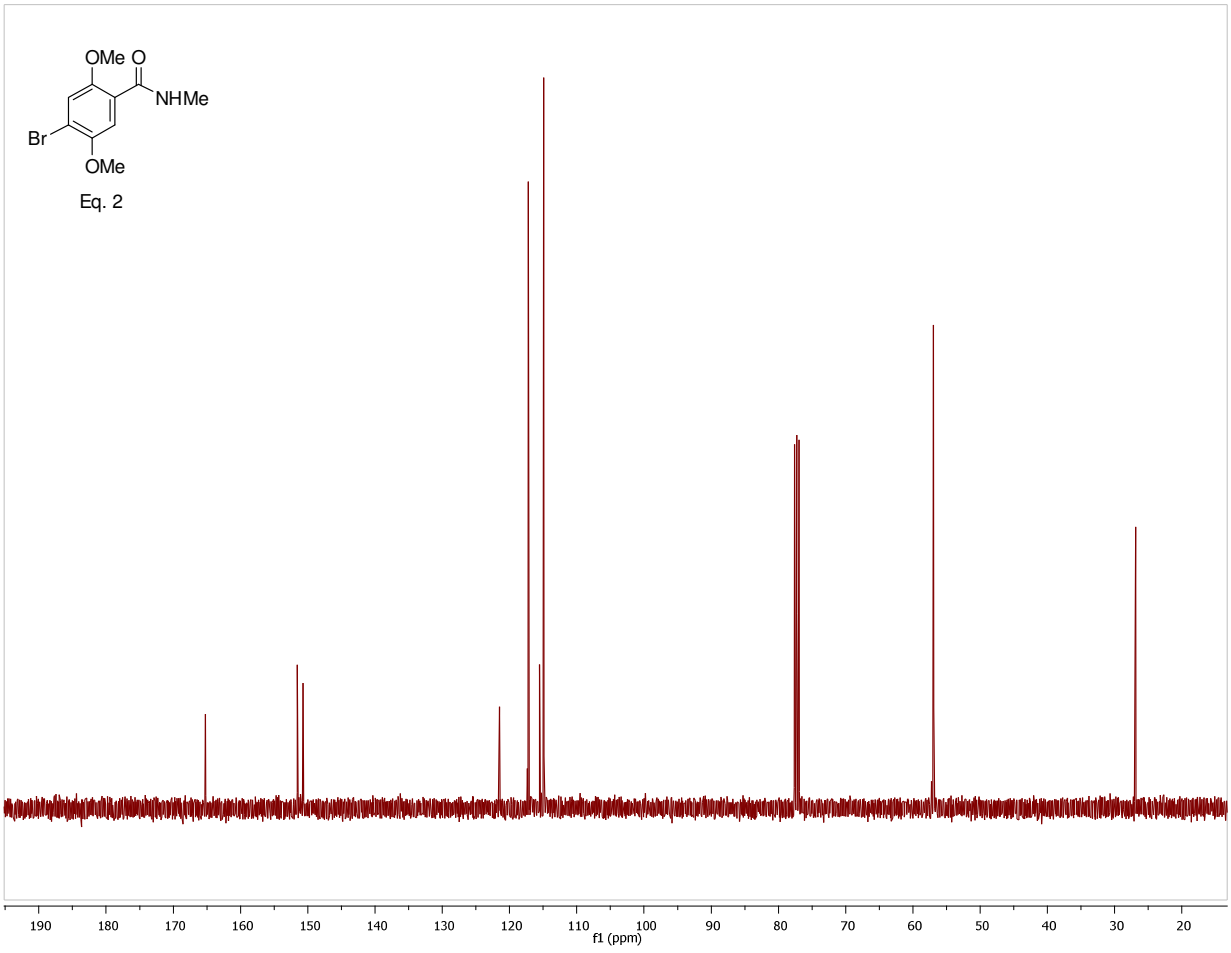


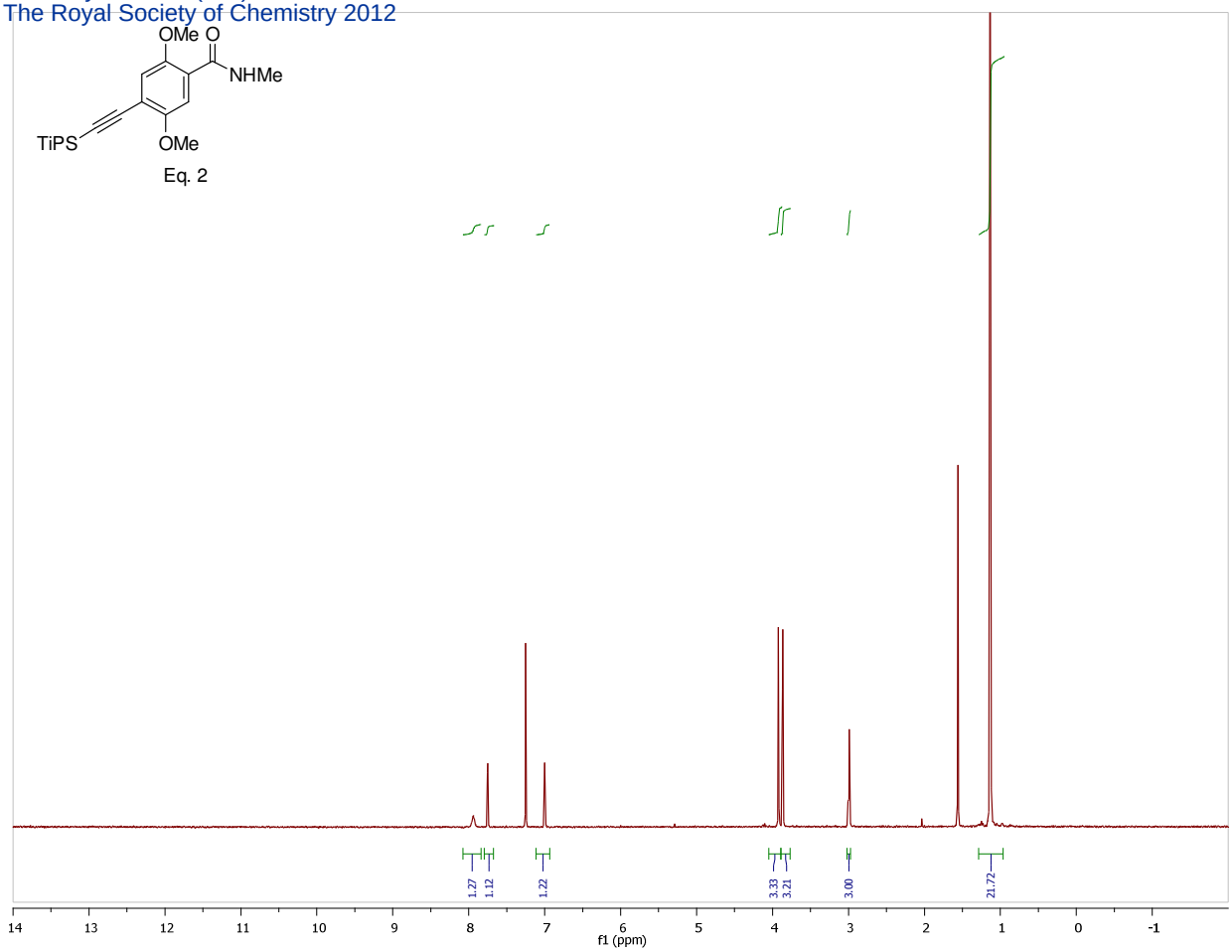
Scheme 2

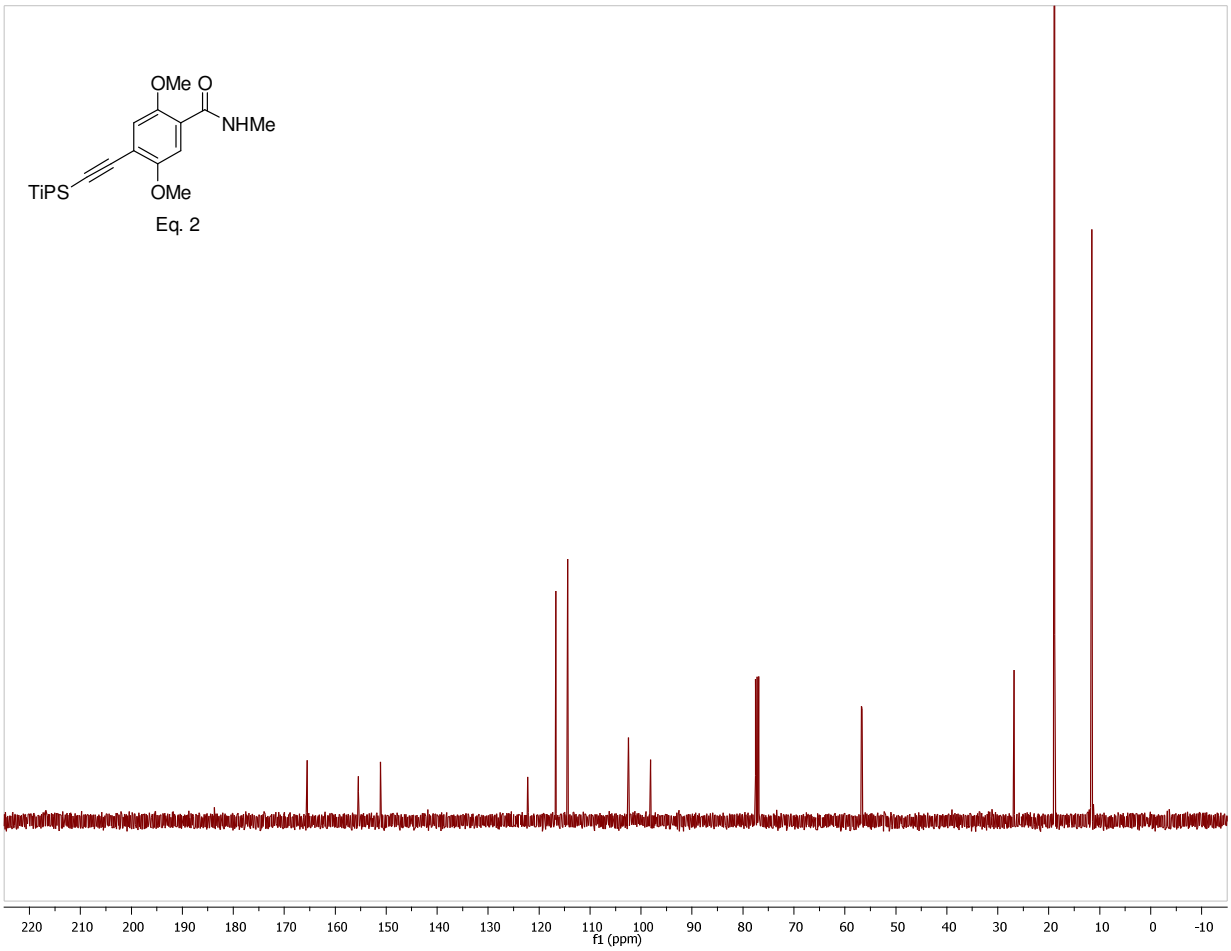


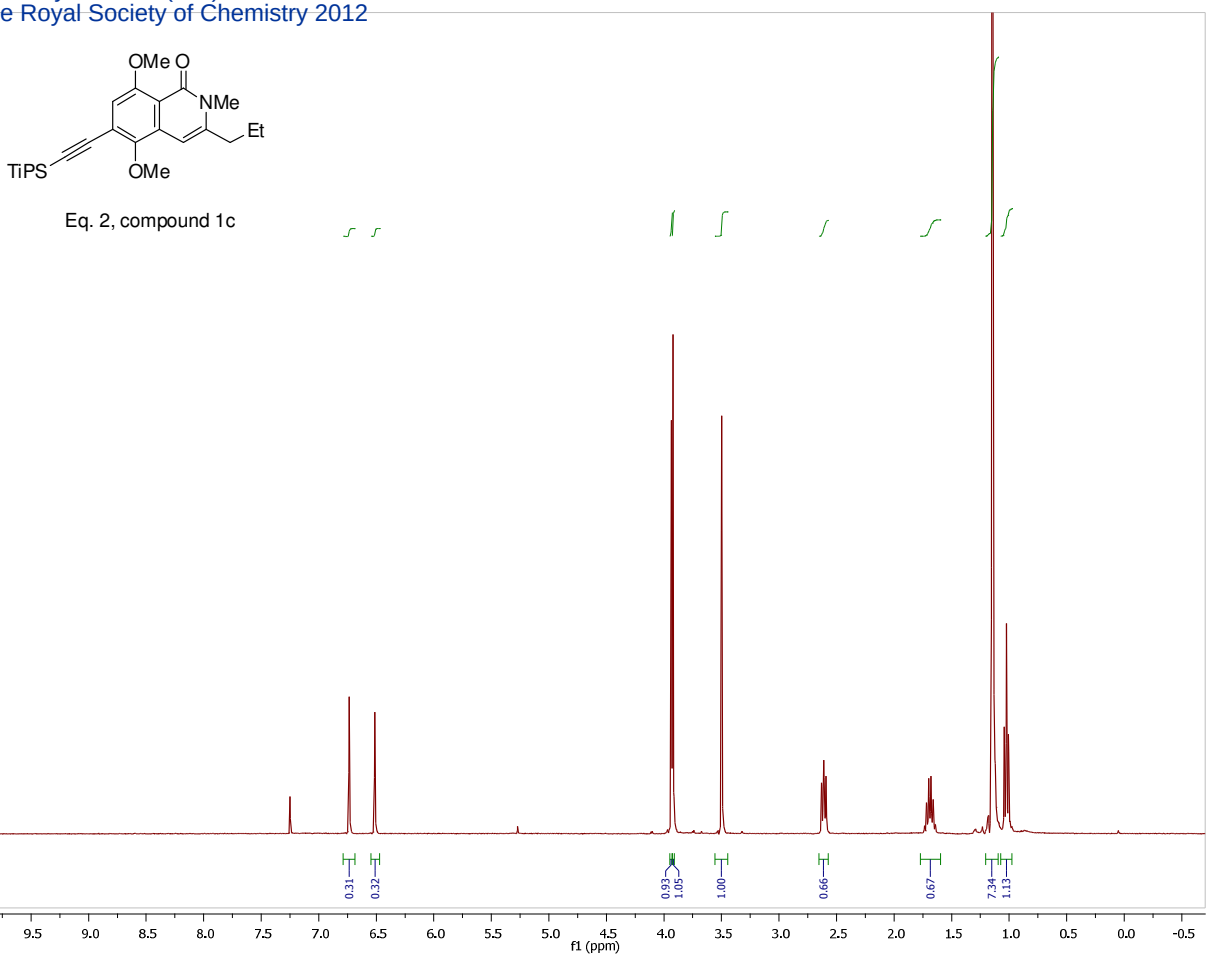
Scheme 2

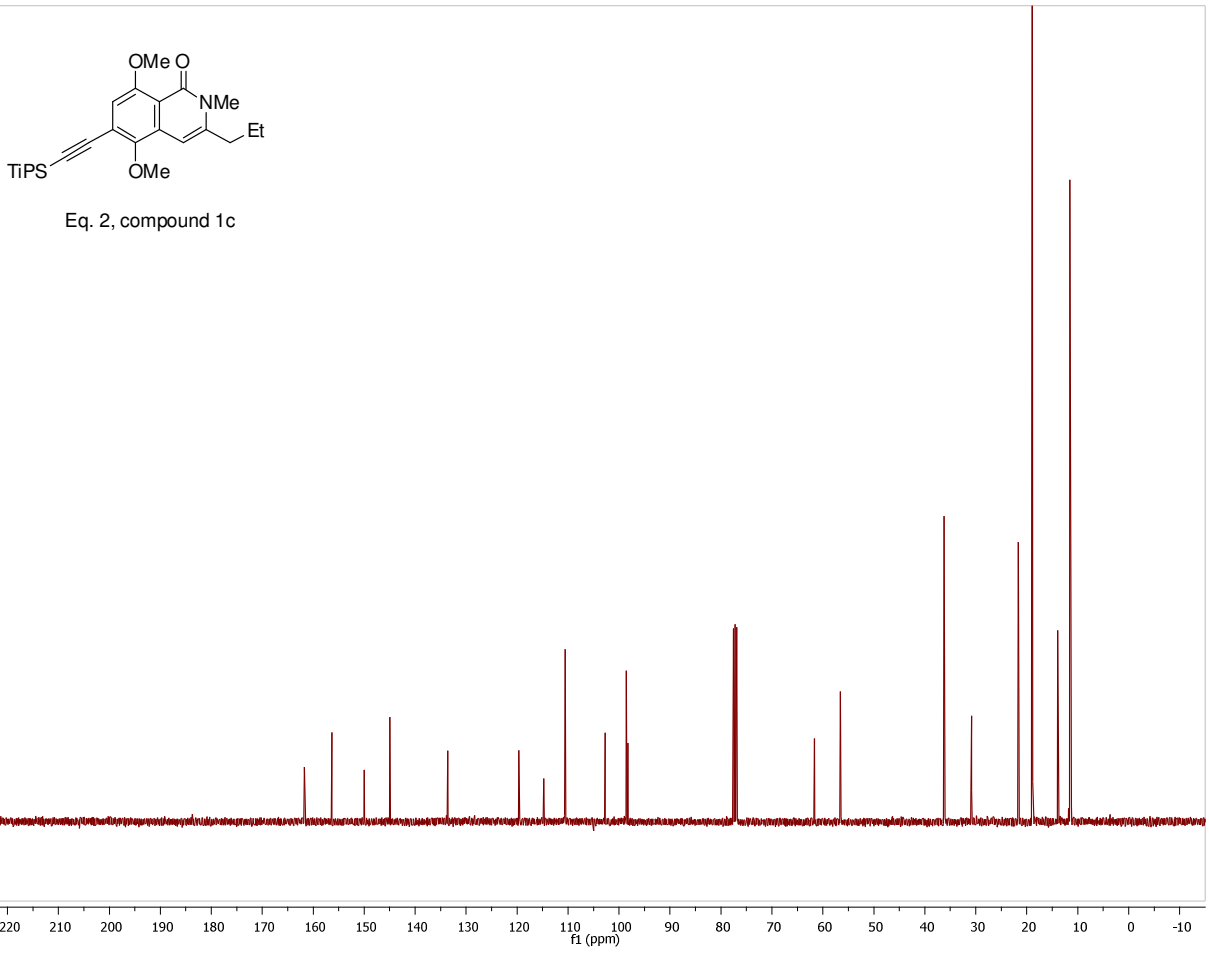


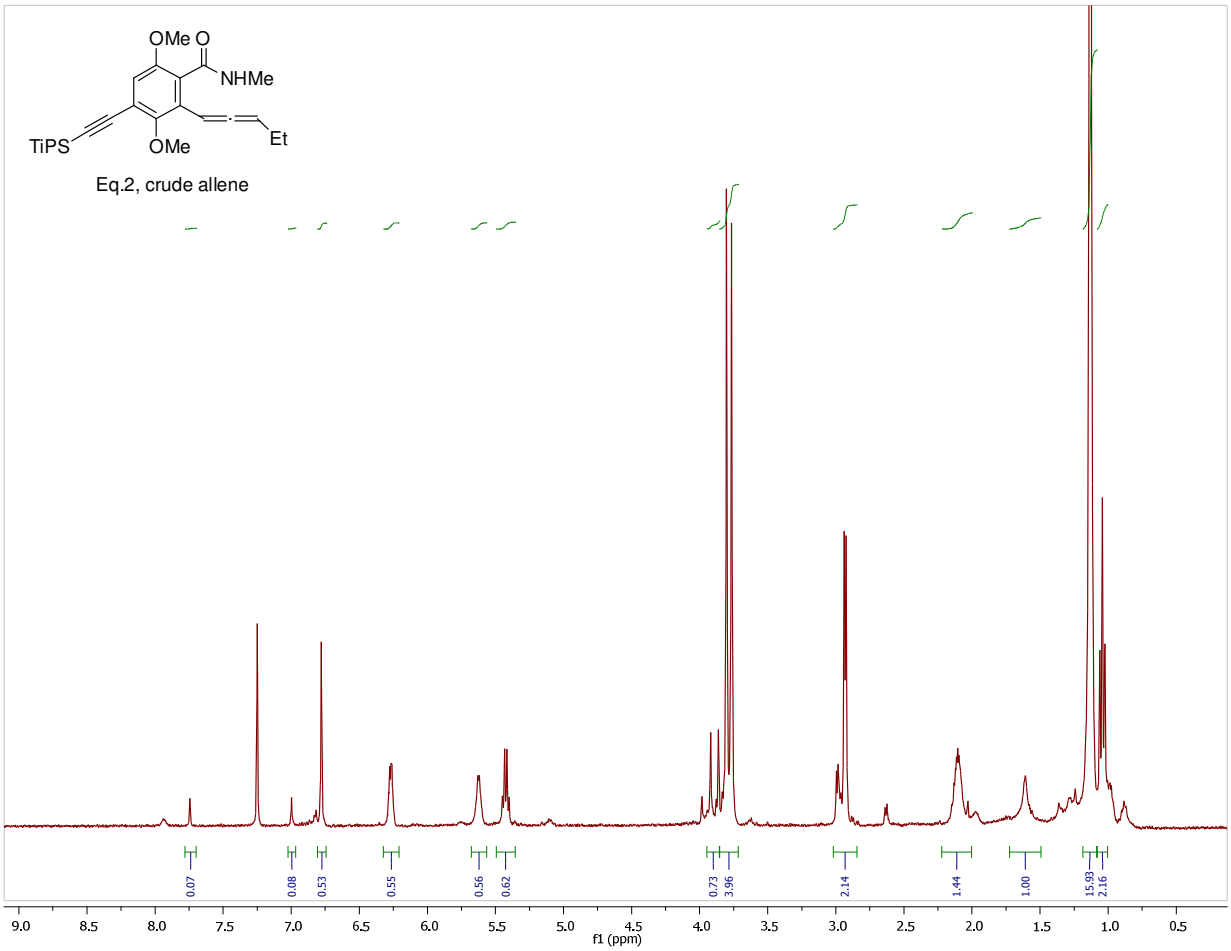











OMe O
NHMe
TiPS
OMe
Et
Eq.2, crude allene
0.07
0.08
0.53
0.55
0.56
0.62
0.73
3.96
2.14
1.44
1.00
15.93
2.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)