

Supporting Information for:

One-pot Oxidation and Rearrangement of Propargylamines and *in situ* Pyrazole Synthesis

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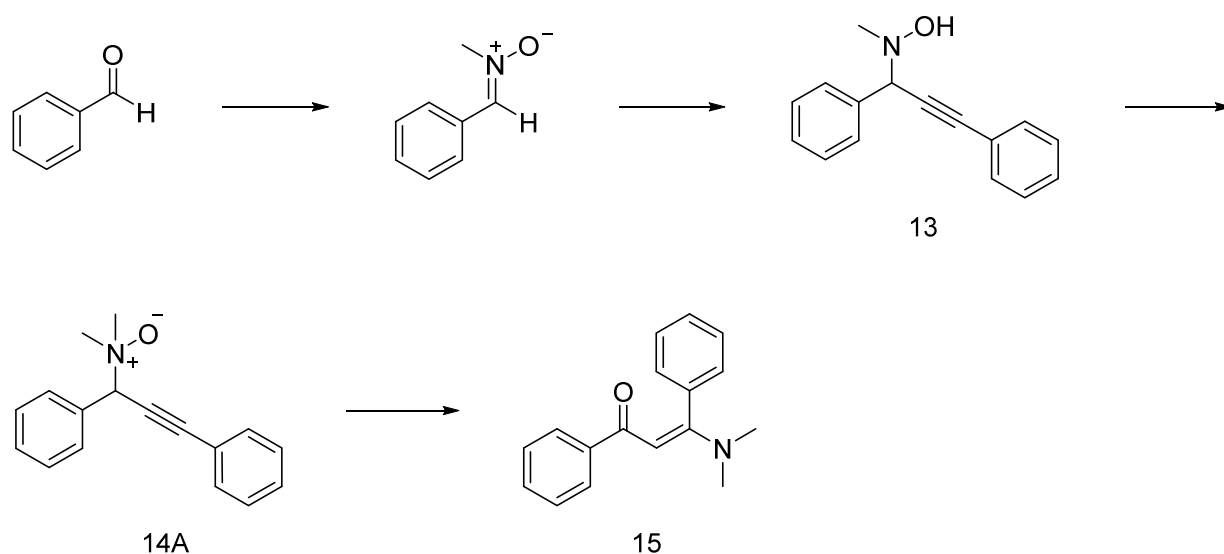
General analytical methods:

Catalysts, reagents and solvents were obtained from commercial sources and used without further purification. Flash silica gel chromatography was conducted on a Biotage Isolera One purification system using pre-packed Silicycle or Biotage brand silica gel cartridges.

Nuclear magnetic resonance (NMR) spectra were acquired on 400 MHz Agilent VNMR-5 console using an AutoX-DB probe or a 500 MHz Bruker Avance III console using a Prodigy cryoprobe spectrometers. Chemical shifts are reported in ppm and referenced to residual solvent peaks as internal standards. Coupling constants are reported in hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublets of doublets, dt = doublet of triplets, dq = doublet of quartets, t = triplet, td = triplet of doublets, q = quartet, qd = quartet of doublets, sxt = sextet, m = multiplet, br = broad. High-resolution mass spectroscopy (HRMS) was obtained using an Agilent 6220 TOF with an Agilent 1200 uHPLC. Elemental analysis was obtained at The University of Camerino, Via S. Agostino 1, 62032, Camerino (MC).

Isoxazolinium Ion a Viable Precursor to Enaminones (Scheme 4):

(2E)-3-(dimethylamino)-1,3-diphenylprop-2-en-1-one, 15



Step 1: To a solution of benzaldehyde (1.0 g, 9.5 mmol, 1.0 equiv) in ethanol (10 mL, 0.9 M) was added *N*-methylhydroxylamine hydrochloride (1.8 g, 20.7 mmol, 2.2 equiv) and sodium bi-

carbonate (1.1 g, 13.2 mmol, 1.4 equiv). The resulting mixture was stirred at 60 °C for 18 hours, cooled to room temperature, and then diluted with dichloromethane (10 ml). The organic phase was washed with water (15 mL), brine (10 mL), dried over sodium sulfate, filtered and concentrated in vacuo. The crude material was recrystallized from hot diethyl ether (25 mL) and isolated by filtration to afford *N*-methyl-*N*-[(*E*)-phenylmethylidene]amine oxide as white solid (910 mg, 71%). ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.16 - 8.22 (m, 2 H), 7.36 - 7.43 (m, 3 H), 7.34 (s, 1 H), 3.84 (s, 3 H); ¹³C-NMR (100 MHz, CDCl₃) δ 135.13, 130.47, 130.38, 128.45, 128.37, 54.39; HRMS (m/z): calculated for C₈H₉NO, [M + H]⁺ 136.0757; found 136.0753.

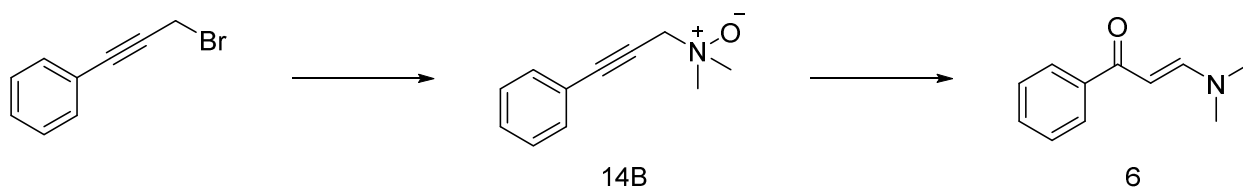
Step 2: To a solution of *N*-methyl-*N*-[(*E*)-phenylmethylidene]amine oxide (330 mg, 2.4 mmol, 1.0 equiv) in toluene (15 mL, 0.16 M) was added phenylacetylene (353 μL, 3.2 mmol, 1.3 equiv) and a 1.0 M solution of diethylzinc in hexanes (485 μL, 0.5 mmol, 0.2 equiv). The mixture was degassed by bubbling nitrogen gas, stirred at room temperature for 3 hours and then diluted with a saturated sodium hydrogencarbonate solution (5 mL). The resulting mixture was extracted with diethyl ether (3 x 10 mL), the combined organic layers were washed with water (5 mL), brine (5 mL), dried over sodium sulfate, filtered and concentrated in vacuo. The residue was triturated with *n*-pentane. The solid thus obtained was filtered and dried to afford *N*-hydroxy-*N*-methyl-1,3-diphenylprop-2-yn-1-amine, **13** as a white solid (463 mg, 81%). ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.59 (d, *J*=7.01 Hz, 2 H), 7.53 (dd, *J*=6.62, 2.72 Hz, 2 H), 7.30 - 7.42 (m, 6 H), 4.92 (br. s., 1 H), 2.70 (br. s., 3 H); ¹³C NMR (100 MHz, CHLOROFORM-*d*) δ = 137.36, 131.89, 129.04, 128.43, 128.40, 128.29, 128.23, 122.74, 88.28, 84.76, 65.81; HRMS (m/z): calculated for C₁₆H₁₅NO [M + H]⁺ 238.1226; found 238.1226.

Step 3: To a solution of **13** (200 mg, 0.8 mmol, 1.0 equiv) in dichloromethane (5 mL, 0.08 M) was added methyl trifluoromethanesulfonate (170 mg, 1.0 mmol, 1.2 equiv). The solution was stirred at room temperature for 2 hours and concentrated in vacuo to afford the desired crude (1,3-diphenylprop-2-yn-1-yl)dimethylamine oxide, **14A**. ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.67 - 7.71 (m, 2 H), 7.45 - 7.50 (m, 3 H), 7.40 - 7.45 (m, 2 H), 7.34 - 7.40 (m, 1 H), 7.29 - 7.34 (m, 2 H), 5.90 (s, 1 H), 3.64 (s, 3 H), 3.36 (s, 3 H); ¹³C NMR (100 MHz, CHLOROFORM-*d*) δ = 132.13, 131.77, 131.72, 130.32, 129.15, 128.69, 128.43, 119.90, 93.71, 78.74,

75.40, 54.88, 52.00; HRMS (m/z): calculated for C₁₇H₁₇NO [M + H]⁺ 252.1383, found 252.1384.

Step 4: To a solution of crude **14A** in ethanol (5 mL, 0.08 M) and added sodium carbonate (179 mg, 1.7 mmol, 2.0 equiv) and the mixture was stirred at room temperature for 18 hours. The mixture was then heated at 85 °C for 1 hour and cooled to room temperature to afford the desired crude (2*E*)-3-(dimethylamino)-1,3-diphenylprop-2-en-1-one, **15**. ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.88 (dd, *J*=8.19, 1.35 Hz, 2 H), 7.40 - 7.46 (m, 5 H, chloroform-*d* under peak), 7.35 - 7.39 (m, 2 H), 7.26 - 7.30 (m, 3 H), 5.92 (s, 1 H), 2.97 (br. s., 6 H); ¹³C NMR (126 MHz, CHLOROFORM-*d*) δ = 187.46, 164.82, 141.81, 137.03, 130.59, 128.59, 128.51, 128.04, 127.92, 127.67, 94.28, 40.52. HRMS (m/z): calculated for C₁₇H₁₇NNaO [M + Na]⁺ 274.1202; found 274.1205.

3-(dimethylamino)-1-phenylprop-2-en-1-one, **6**



Step 1: To a solution of N,N-dimethylhydroxylamine hydrochloride (204 mg, 2.1 mmol, 2.1 equiv) in methanol (3 mL) and added a solution of sodium methoxide (116 mg, 2.1 mmol) in methanol (2 mL). A white solid precipitated immediately and after stirring at room temperature for 30 minutes the reaction was filtered through a small pad of celite, and rinsing with methanol. To the solution of N,N-dimethylhydroxylamine was added the (3-bromoprop-1-yn-1-yl)benzene¹ (200 mg, 1.0 mmol, 1.0 equiv). The reaction was stirred at room temperature for 1 hour and the solvent was concentrated in vacuo to afford the desired crude dimethyl(3-phenylprop-2-yn-1-yl)amine oxide, **14B**² as a white solid. ¹H NMR (500 MHz, DMSO-*d*₆) δ ppm 7.62 - 7.70 (m, 1 H), 7.50 - 7.58 (m, 2 H), 7.38 - 7.45 (m, 3 H), 4.84 (s, 1 H), 4.51 (d, *J*=6.60 Hz, 1 H), 3.45 - 3.48

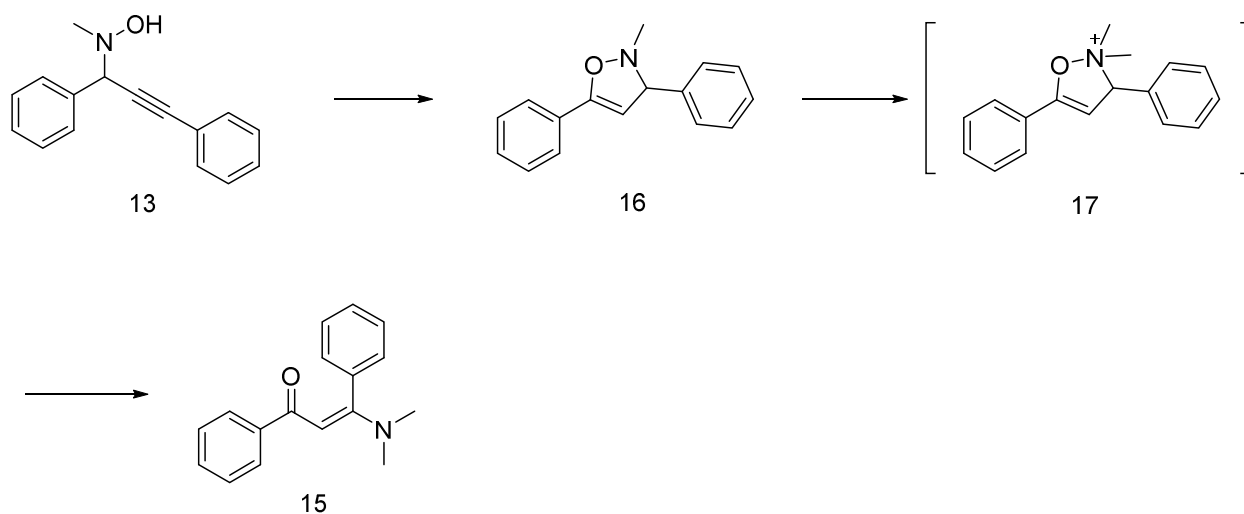
¹ Bera, K.; Sarkar, S.; Biswas, S.; Maiti, S.; Jana, U. *J. Org. Chem.* **2011**, 76, 3539-3544

² Compound was unstable and a HRMS could not be obtained.

(m, 6 H); ^{13}C NMR (101 MHz, DMSO- d_6) δ = 132.19, 129.24, 129.18, 129.10, 128.10, 121.31, 79.88, 60.69, 56.80, 56.51.

Step 2: To a solution of **14B** in ethanol (5 mL, 0.2 M) was added sodium carbonate (218 mg, 2.1 mmol, 2.0 equiv). The reaction mixture was stirred at 85 °C for 2 hours and the reaction was cooled to room temperature to afford the desired crude 3-(dimethylamino)-1-phenylprop-2-en-1-one **6**³. ^1H NMR (400 MHz, CHLOROFORM- d) δ ppm 7.83 (d, J =5.84 Hz, 2 H), 7.69 (d, J =12.46 Hz, 1 H), 7.33 (d, J =7.40 Hz, 3 H), 5.63 (d, J =12.46 Hz, 1 H), 2.98 (br. s., 3 H), 2.78 (br. s., 3 H); ^{13}C NMR (100 MHz, CHLOROFORM- d) δ = 188.38, 154.16, 140.49, 130.80, 128.06, 127.39, 92.03, 44.90, 37.17.

(2E)-3-(dimethylamino)-1,3-diphenylprop-2-en-1-one, **15**



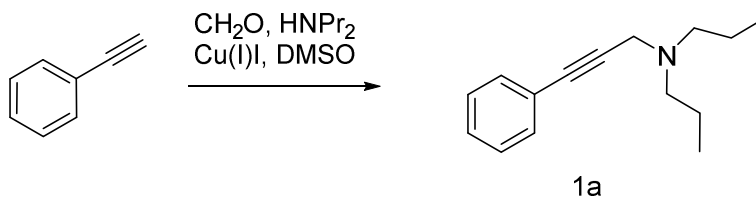
Step 1: To a solution of *N*-hydroxy-*N*-methyl-1,3-diphenylprop-2-yn-1-amine, **13** (60 mg, 0.3 mmol, 1.0 equiv) in dichloromethane (3 mL, 0.02 M) were added sodium tetrachloroaurate (III) dihydrate ($\text{Na}_2\text{AuCl}_4 \cdot 2\text{H}_2\text{O}$) (5 mg, 0.01 mmol, 5 mol %) and 4-dimethylaminopyridine (10 mg, 0.08 mmol, 0.3 equiv). The reaction mixture was stirred at room temperature for 3 hours. The

³ Data are consistent with the literature. Larina, N.; Lokshin, V.; Berthet, J.; Delbaere, S.; Vermeersch, G.; Khodorkovsky, V. *Tetrahedron* **2010**, *66*, 8291-8299.

mixture was filtered over a short pad of celite and the solvent was concentrated in vacuo to afford the desired 2-methyl-3,5-diphenyl-2,3-dihydro-1,2-oxazole, **16**. ^1H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.62 - 7.66 (m, 2 H), 7.36 - 7.45 (m, 8 H), 7.28 - 7.35 (m, 1 H), 5.42 (d, $J=2.69$ Hz, 1 H), 4.90 (br. s., 1 H), 3.03 (s, 3 H); ^{13}C NMR (100 MHz, CHLOROFORM-*d*) δ = 152.43, 129.06, 128.98, 128.81, 128.65, 128.53, 128.41, 127.79, 127.07, 125.75, 95.82, 47.20; HRMS (m/z): calculated for $\text{C}_{16}\text{H}_{15}\text{NO}$ $[\text{M} + \text{H}]^+$ 238.1226, found 238.1227.

Step 2: To a solution of the crude oxazole **16** in dichloromethane (3.0 mL, 0.02 M) was added methyl trifluoromethanesulfonate (35 μL , 0.3 mmol, 1.2 equiv). The reaction was stirred at room temperature for 10 minutes. The solvent was concentrated in vacuo and the residue (**17**) was taken up in ethanol (2.0 mL, 0.03 M) and sodium carbonate (54 mg, 0.5 mmol, 2.0 equiv) was added. The mixture was stirred at room temperature for 18 hours to afford the desired crude (2*E*)-3-(dimethylamino)-1,3-diphenylprop-2-en-1-one, **15**.

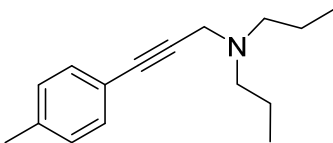
General procedure for propargylic amine formation (GP1, Table 1 & 2 starting materials):



To a solution of ethynylbenzene (1.5 g, 14.0 mmol, 1.0 equiv) in dimethylsulfoxide (15 mL, 0.96 M) was added a 38% aqueous formaldehyde solution (1.0 mL, 14.0 mmol, 1.0 equiv), dipropylamine (2.2 mL, 15.8 mmol, 1.1 equiv) and copper (I) iodide (59 mg, 0.3 mmol, 2 mol %). The reaction was stirred at 30 °C for 5 hours. The reaction mixture was treated with a 1N sodium hydroxide solution (10 mL) and extracted with diethyl ether (2 x 75 mL). The combined organic layers were dried over sodium sulfate, filtered and the solvent was concentrated in vacuo to afford 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** as a clear oil (2.7 g, 87%). ^1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.40 - 7.48 (m, 2 H), 7.25 - 7.34 (m, 3 H), 3.62 (s, 2 H), 2.46 - 2.56 (m, 4 H), 1.53 (sxt, $J=7.40$ Hz, 4 H), 0.94 (t, $J=7.40$ Hz, 6 H); ^{13}C NMR (101 MHz,

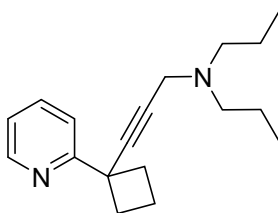
CHLOROFORM-*d*) δ = 131.68, 128.19, 127.81, 123.51, 84.92, 84.86, 55.87, 42.71, 20.80, 11.97; GC-MS: m/z 215.2 [M⁺].

3-(4-methylphenyl)-*N,N*-dipropylprop-2-yn-1-amine, 1c



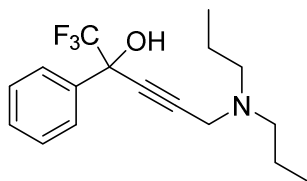
Following GP1, the title compound was prepared as a clear oil (1.78 g, 61%) starting from 1-ethynyl-4-methylbenzene. ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.33 (m, J =8.07 Hz, 2 H), 7.09 - 7.13 (m, 2 H), 3.61 (s, 2 H), 2.61 (s, 2 H, residual DMSO in sample), 2.48 - 2.53 (m, 4 H), 2.35 (s, 3 H), 1.53 (sxt, J =7.43 Hz, 4 H), 0.93 (t, J =7.34 Hz, 6 H); ¹³C NMR (101 MHz, CHLOROFORM-*d*) δ = 137.83, 131.56, 128.94, 120.39, 84.93, 84.03, 55.86, 42.76, 21.40, 20.76, 11.97; GC-MS: m/z 229.2 [M⁺].

***N,N*-dipropyl-3-[1-(pyridin-2-yl)cyclobutyl]prop-2-yn-1-amine, 1g**



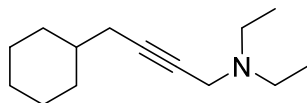
Following GP1, the title compound was prepared as a clear oil (2.3 g, 67%) starting from 2-(1-ethynylcyclobutyl)pyridine. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.57 (d, J =4.67 Hz, 1 H), 7.52 - 7.62 (m, 2 H), 7.08 (ddd, J =6.71, 4.96, 1.56 Hz, 1 H), 3.47 (s, 2 H), 2.74 - 2.85 (m, 2 H), 2.37 - 2.50 (m, 6 H), 2.24 - 2.37 (m, 1 H), 1.91 - 2.03 (m, 1 H), 1.47 (sxt, J =7.47 Hz, 4 H), 0.81 - 0.93 (m, 6 H); ¹³C NMR (100 MHz, CHLOROFORM-*d*) δ = 163.40, 148.93, 136.17, 121.27, 120.68, 90.40, 77.97, 55.86, 42.86, 42.38, 35.96, 20.68, 16.77, 11.95; HRMS (m/z): calculated for C₁₈H₂₆N₂Na [M + Na]⁺ 293.1988, found 293.2001.

5-(dipropylamino)-1,1,1-trifluoro-2-phenylpent-3-yn-2-ol, 1h



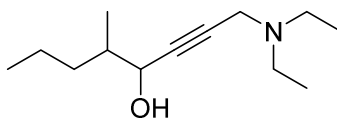
Following GP1, the title compound was prepared as a yellow solid (1.15 g, 74%) starting from 1,1,1-trifluoro-2-phenylbut-3-yn-2-ol. ^1H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.77 (dd, $J=5.99, 3.06$ Hz, 2 H), 7.40 - 7.44 (m, 3 H), 3.55 (s, 2 H), 2.47 - 2.53 (m, 4 H), 1.49 - 1.57 (m, 4 H), 0.92 (t, $J=7.46$ Hz, 6 H); ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ = 136.16, 129.26, 128.04, 123.54 (q, $J = 286.84$ Hz), 127.21, 82.93, 82.21, 72.52 (q, $J = 32.32$ Hz), 55.83, 41.86, 20.08, 11.86; ^{19}F NMR (470 MHz, CHLOROFORM-*d*) δ = -80.48; HRMS (*m/z*): calculated for $\text{C}_{17}\text{H}_{22}\text{F}_3\text{NNaO}$ [$\text{M} + \text{Na}$] $^+$ 336.1546, found 336.1535.

4-Cyclohexyl-*N,N*-diethylbut-2-yn-1-amine, **1i**



Following GP1, the title compound was prepared as a yellow oil (0.6 g, 89%) starting from prop-2-yn-1-ylcyclohexane. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 3.33-3.31 (m, 2H), 2.46 (qd, $J = 7.18, 1.63$ Hz, 4H), 2.03-1.98 (m, 2H), 1.76-1.52 (m, 5H), 1.44-1.28 (m, 1H), 1.24-0.75 (m, 5H), 0.99 (dt, $J = 7.18, 1.62$ Hz, 3H); ^{13}C NMR (100 MHz, CHLOROFORM-*d*) δ = 83.83, 75.25, 47.30, 41.08, 37.67, 32.85, 26.73, 26.49, 26.32, 12.77. Elemental analysis: calculated for $\text{C}_{14}\text{H}_{25}\text{N}$ (%): C, 81.09; H, 12.15; N, 6.75. Found: C, 80.95; H, 11.78; N, 6.44.

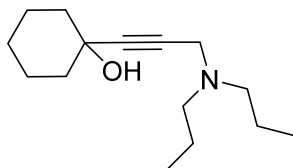
1-(Diethylamino)-5-methyloct-2-yn-4-ol, **1j**



Following GP1, the title compound was prepared as a yellow oil (0.6 g, 90%) starting from 4-methylhept-1-yn-3-ol. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.27-4.18 (m, 1H), 3.46-3.42 (m, 2H), 2.91 (br s, 1H), 2.55-2.48 (m, 4H), 1.74-1.09 (m, 5H), 1.07-1.01 (m, 6H), 0.97-0.92 (m, 3H), 0.90-0.84 (m, 3H). ^{13}C NMR (100 MHz, CHLOROFORM-*d*) δ = 85.71, 85.05, 79.82, 79.60, 66.98, 66.94, 66.85, 66.84, 47.60, 47.40, 40.80, 40.76, 39.57, 39.29, 35.28, 34.42,

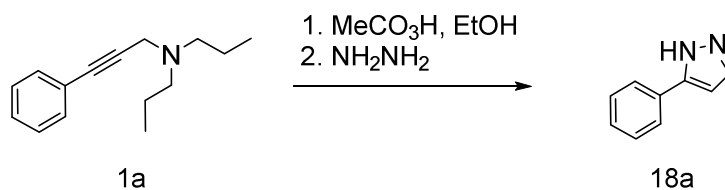
20.47, 20.38, 15.35, 14.82, 14.53, 14.50, 14.44, 12.64. Elemental analysis: calculated for $C_{13}H_{25}NO$ (%): C, 73.88; H, 11.92; N, 6.63. Found: C, 73.52; H, 11.46; N, 6.35.

1-[3-(dipropylamino)prop-1-yn-1-yl]cyclohexanol, **22**



Following GP1, the title compound was prepared as a yellow oil (1.7 g, 89%) starting from 1-ethynylcyclohexanol, except the reaction was stirred for 18 hours. 1H NMR (500 MHz, $DMSO-d_6$) δ ppm 5.17 (s, 1 H), 3.34 (s, 2 H), 2.32 - 2.39 (m, 4 H), 1.69 - 1.78 (m, 2 H), 1.56 - 1.65 (m, 2 H), 1.35 - 1.52 (m, 9 H), 1.10 - 1.21 (m, 1 H), 0.85 (t, $J=7.46$ Hz, 6 H).

General procedure for the two-step, one-pot preparation of pyrazole from propargylic amines (GP2, Table 1):

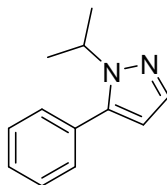


Step 1: To a solution of **1a** (100 mg, 0.46 mmol, 1.0 equiv) in ethanol (2 mL, 0.2 M) was added peroxyacetic acid (0.1 mL, 0.5 mmol, 1.1 equiv). The reaction was stirred at 85 °C for 1 hour.

Step 2: Hydrazine (19 μ L, 0.6 mmol, 1.3 equiv) was added and the resulting mixture was stirred at 85 °C for 30 minutes. The reaction was quenched with a 4 N hydrochloric acid (2 mL), diluted with a saturated sodium bicarbonate solution, extracted with dichloromethane (2 x 25 mL), the combined organic extract was dried over sodium sulfate, filtered and the solvent was concentrated in vacuo. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-80% of ethyl acetate in heptanes to afford 5-phenyl-1H-pyrazole, **18a** as a white solid (28 mg, 42%). 1H NMR (500 MHz, $CHCl_3-d$) δ ppm 7.67 - 7.71 (m, 2 H), 7.56 (d, $J=2.20$ Hz, 1 H), 7.33 - 7.38 (m, 2 H), 7.24 - 7.30 (m, 1 H), 6.56 (d, $J=1.96$ Hz, 1 H); ^{13}C NMR (126 MHz, $CHCl_3-d$) δ = 133.19, 133.17, 131.93, 128.85,

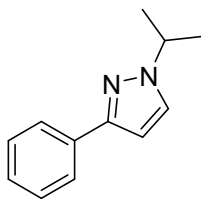
128.18, 125.78, 102.78; HRMS (m/z): calculated for C₉H₈N₂ [M + H]⁺ 147.0819, found 147.0817.

5-phenyl-1-(propan-2-yl)-1*H*-pyrazole, 18b-1



Following GP2, the title compound was prepared as a white solid (25 mg, 19%) starting from 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** and isopropylhydrazine (2.0 equiv). Silica gel column chromatography separated the two regioisomers. ¹H NMR (500 MHz, CHLOROFORM-*d*) δ = 7.76 - 7.71 (m, 2H), 7.37 (d, *J*=2.2 Hz, 1H), 7.34 - 7.28 (m, 2H), 7.23 - 7.17 (m, 1H), 6.46 (d, *J*=2.4 Hz, 1H), 4.48 (td, *J*=6.6, 13.4 Hz, 1H), 1.47 (d, *J*=6.6 Hz, 6H); ¹³C NMR (126 MHz, CHLOROFORM-*d*) δ = 150.73, 133.92, 128.56, 127.35, 127.29, 125.61, 102.29, 77.25, 53.86, 23.07; HRMS (m/z): calculated for C₁₂H₁₄N₂ [M + H]⁺ 189.1291, found 189.1293; 1D-NOE experiment confirmed interaction between isopropyl methyl groups and ortho phenyl protons, supporting regiochemical assignment.

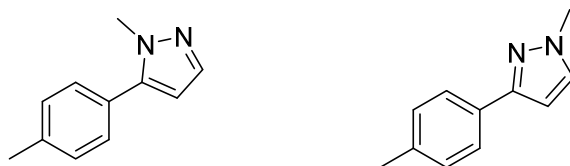
3-phenyl-1-(propan-2-yl)-1*H*-pyrazole, 18b-2



Following GP2, the title compound was prepared as a white solid (93 mg, 72%) starting from 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** and isopropylhydrazine (2.0 equiv). Silica gel column chromatography separated the two regioisomers. ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.60 (d, *J*=1.47 Hz, 1 H), 7.37 - 7.51 (m, 5 H), 6.26 (d, *J*=1.71 Hz, 1 H), 4.58 (dt, *J*=13.33, 6.54 Hz, 1 H), 1.50 (d, *J*=6.60 Hz, 6 H); ¹³C NMR (126 MHz, CHLOROFORM-*d*) δ = 142.58, 138.58, 131.25, 129.12, 128.67, 128.41, 105.73, 49.90, 22.98; HRMS (m/z): calculated for C₁₂H₁₄N₂ [M + H]⁺ 189.1291, found 189.1301; 1D-NOE experiment confirmed interaction

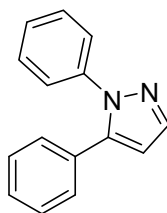
between isopropyl methyl groups and the 5-position pyrazole proton, supporting regiochemical assignment.

1-methyl-5-(4-methylphenyl)-1*H*-pyrazole, 18c-1 & 1-methyl-3-(4-methylphenyl)-1*H*-pyrazole, 18c-2



Following GP2, the title compounds were prepared as a mixture of regioisomers (88 mg, 59%) starting from 3-(4-methylphenyl)-*N,N*-dipropylprop-2-yn-1-amine, **1c** and methylhydrazine (1.2 equiv). Silica gel column chromatography could not separate the two regioisomers. Major regioisomer: ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.53 (d, *J*=1.71 Hz, 1 H), 7.32 - 7.35 (m, 2 H), 7.27 - 7.30 (m, 2 H), 6.31 (d, *J*=1.96 Hz, 1 H), 3.91 (s, 3 H), 2.44 (s, 3 H). Minor regioisomer: ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.70 - 7.73 (m, 2 H), 7.38 (d, *J*=2.20 Hz, 1 H), 7.21 - 7.24 (m, 2 H), 6.53 (d, *J*=2.20 Hz, 1 H), 3.97 (s, 3 H), 2.39 (s, 3 H). Mixture of regioisomers: ¹³C NMR (126 MHz, CHLOROFORM-*d*) δ = 151.69, 143.62, 138.48, 138.39, 137.22, 131.28, 130.80, 129.38, 129.31, 128.65, 127.87, 125.45, 105.84, 102.61, 38.99, 37.44, 21.29, 21.26; HRMS (*m/z*): calculated for C₁₁H₁₂N₂Na [M + Na]⁺ 195.0893, found 195.0897.

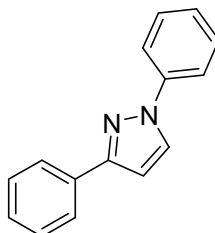
1,5-diphenyl-1*H*-pyrazole, 18d-1



Following GP2, the title compound was prepared as a white solid (80 mg, 26%) starting from 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** and phenylhydrazine (3.0 equiv). Silica gel column chromatography separated the two regioisomers. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.92 - 8.03 (m, 3 H), 7.77 - 7.85 (m, 2 H), 7.48 (m, 4 H), 7.28 - 7.45 (m, 3 H, chloroform

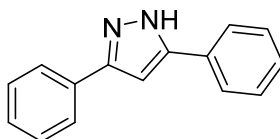
signal under peak), 6.79 (d, $J=2.34$ Hz, 1 H); ^{13}C NMR (100 MHz, CHLOROFORM- d) δ = 152.93, 133.18, 129.44, 128.70, 128.07, 128.01, 126.33, 125.88, 119.03, 112.97, 105.07; HRMS (m/z): calculated for $\text{C}_{15}\text{H}_{12}\text{N}_2$ $[\text{M} + \text{H}]^+$ 221.1073, found 221.1074.

1,3-diphenyl-1*H*-pyrazole, 18d-2



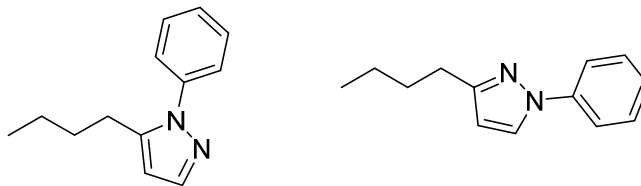
Following GP2, the title compound was prepared as a white solid (140 mg, 45%) starting from 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** and phenylhydrazine (3.0 equiv). Silica gel column chromatography separated the two regioisomers. ^1H NMR (400 MHz, CHLOROFORM- d) δ ppm 7.74 (d, $J=1.56$ Hz, 1 H), 7.20 - 7.38 (m, 11 H), 6.52 (d, $J=1.56$ Hz, 1 H); ^{13}C NMR (100 MHz, CHLOROFORM- d) δ = 143.00, 140.31, 140.14, 130.61, 128.89, 128.76, 128.46, 128.20, 127.41, 125.21, 107.87; HRMS (m/z): calculated for $\text{C}_{15}\text{H}_{12}\text{N}_2$ $[\text{M} + \text{H}]^+$ 221.1104, found 221.1106.

3,5-diphenyl-1*H*-pyrazole, 18e



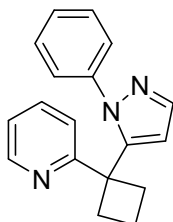
Following GP2 but only step 2, the title compound was prepared as a white solid (90 mg, 48%) starting from (2*E*)-3-(dimethylamino)-1,3-diphenylprop-2-en-1-one, **15** and hydrazine (3.0 equiv). ^1H NMR (400 MHz, DMSO- d_6) δ ppm 7.82 (d, $J=7.40$ Hz, 4 H), 7.44 (t, $J=7.59$ Hz, 4 H), 7.29 - 7.36 (m, 2 H), 7.17 (s, 1 H); ^{13}C NMR (100 MHz, CHLOROFORM- d) δ = 128.91, 128.35, 125.59, 100.19; HRMS (m/z): calculated for $\text{C}_{15}\text{H}_{12}\text{N}_2$ $[\text{M} + \text{H}]^+$ 221.1073; found 221.1073.

5-butyl-1-phenyl-1*H*-pyrazole, 18f-1 & 3-butyl-1-phenyl-1*H*-pyrazole, 18f-2



Following GP2, the title compounds were prepared as a mixture of regioisomers (37 mg, 41%) starting from *N,N*-dibutylhept-2-yn-1-amine and phenylhydrazine (1.0 equiv). Silica gel column chromatography could not separate the two regioisomers. Major regioisomer: ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ ppm 7.56 - 7.63 (m, 1 H), 7.36 - 7.51 (m, 5 H), 6.21 (s, 1 H), 2.61 - 2.70 (m, 2 H), 1.58 (dt, $J=15.47$, 7.64 Hz, 2 H), 1.33 (dq, $J=14.94$, 7.35 Hz, 2 H), 0.87 (t, $J=7.40$ Hz, 3 H). Minor regioisomer: ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ ppm 7.91 (br. s., 1 H), 7.33 (t, $J=7.79$ Hz, 2 H), 7.26 (s, 2 H), 7.21 (s, 1 H), 7.00 (t, $J=7.40$ Hz, 1 H), 2.53 (t, $J=7.40$ Hz, 2 H), 1.39 - 1.45 (m, 2 H), 1.20 - 1.27 (m, 2 H), 0.94 (t, $J=7.01$ Hz, 3 H). Mixture of regioisomers: ^{13}C NMR (100 MHz, $\text{CHLOROFORM-}d$) δ = 145.02, 143.81, 140.00, 139.77, 129.43, 129.01, 127.77, 125.40, 122.16, 113.85, 105.27, 30.95, 27.36, 25.90, 24.35, 22.28, 21.36, 13.88, 13.74; HRMS (m/z): calculated for $\text{C}_{15}\text{H}_{16}\text{N}_2$ [$\text{M} + \text{H}$] $^+$ 202.1417, found 202.1418.

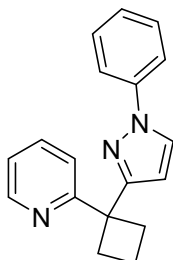
2-[1-(1-phenyl-1*H*-pyrazol-3-yl)cyclobutyl]pyridine, **18g-1**



Following GP2, the title compound was prepared as a yellow oil (13 mg, 6%) starting from *N,N*-dipropyl-3-[1-(pyridin-2-yl)cyclobutyl]prop-2-yn-1-amine, **1g** and phenylhydrazine (1.2 equiv). Silica gel column chromatography separated the two regioisomers. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ ppm 8.60 (d, $J=4.67$ Hz, 1 H), 7.81 (d, $J=2.73$ Hz, 1 H), 7.70 (d, $J=8.17$ Hz, 2 H), 7.55 - 7.64 (m, 1 H), 7.42 (t, $J=7.98$ Hz, 2 H), 7.19 - 7.29 (m, 3 H, chloroform signal under peak), 7.10 (dd, $J=7.01$, 5.45 Hz, 1 H), 6.24 (d, $J=2.34$ Hz, 1 H), 2.90 (dd, $J=8.17$, 7.01 Hz, 4 H), 2.10 - 2.27 (m, 1 H), 1.97 (dq, $J=17.86$, 6.76 Hz, 1 H); ^{13}C NMR (100 MHz, $\text{CHLOROFORM-}d$) δ = 166.41, 159.71, 148.34, 140.35, 136.65, 129.28, 127.32, 125.87, 121.40,

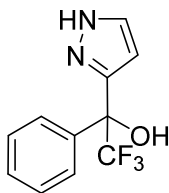
120.96, 118.90, 106.01, 48.76, 33.64, 16.72; HRMS (m/z): calculated for C₁₈H₁₇N₂ [M + H]⁺ 277.1495, found 277.1499.

2-[1-(1-phenyl-1*H*-pyrazol-5-yl)cyclobutyl]pyridine, 18g-2



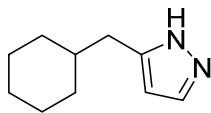
Following GP2, the title compound was prepared as a yellow oil (76 mg, 37%) starting from *N,N*-dipropyl-3-[1-(pyridin-2-yl)cyclobutyl]prop-2-yn-1-amine, **1g** and phenylhydrazine (1.2 equiv). Silica gel column chromatography separated the two regioisomers. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.46 (d, *J*=3.89 Hz, 1 H), 7.66 (d, *J*=1.95 Hz, 1 H), 7.45 (td, *J*=7.69, 1.75 Hz, 1 H), 7.10 - 7.25 (m, 3 H), 6.99 - 7.07 (m, 1 H), 6.93 (d, *J*=8.17 Hz, 1 H), 6.87 (d, *J*=7.01 Hz, 2 H), 6.53 (d, *J*=1.56 Hz, 1 H), 2.50 - 2.71 (m, 4 H), 1.88 - 2.12 (m, 2 H); ¹³C NMR (100 MHz, CHLOROFORM-*d*) δ = 164.34, 149.92, 148.73, 140.50, 139.46, 136.13, 128.35, 127.93, 126.20, 121.05, 120.95, 106.03, 47.24, 34.06, 16.49; HRMS (m/z): calculated for C₁₈H₁₇N₂ [M + H]⁺ 277.1495, found 277.1505.

2,2,2-trifluoro-1-phenyl-1-(1*H*-pyrazol-1-yl)ethanol, 18h



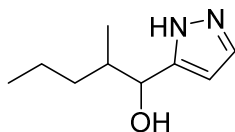
Following GP2, the title compound was prepared as a yellow solid (28 mg, 36%) starting from 5-(dipropylamino)-1,1,1-trifluoro-2-phenylpent-3-yn-2-ol, **1h** and isopropylhydrazine (2.0 equiv). ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.58 - 7.63 (m, 2 H), 7.50 - 7.57 (m, 2 H), 7.25 - 7.35 (m, 5 H), 6.43 (br. s., 1 H), 5.90 (br. s., 1 H); ¹³C NMR (101 MHz, CHLOROFORM-*d*) δ = 137.34, 128.98, 128.71, 128.33, 128.16, 126.84 (q, *J*=1.6 Hz, 7C), 126.34, 126.21; HRMS (m/z): calculated for C₁₁H₉F₃N₂O [M + H]⁺ 243.0796; found 245.0795.

5-(Cyclohexylmethyl)-1*H*-pyrazole, 18i



Following GP2, the title compound was prepared as a yellow oil (92 mg, 46%) starting from 4-cyclohexyl-*N,N*-diethylbut-2-yn-1-amine, **1i** with the following modifications: 2N solution of hydrochloric acid in methanol and an aqueous solution of hydrazine. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.88 (br s, 1H), 7.49 (br s, 1H), 6.06 (br s, 1H), 2.55 (d, J = 7.07 Hz, 2H), 1.75-1.51 (m, 7H), 1.28-1.10 (m, 3H), 1.00-0.89 (m, 2H); ¹³C NMR (100 MHz, CHLOROFORM-*d*) δ = 218.81, 146.43, 135.60, 104.41, 38.59, 34.72, 33.35, 26.60, 26.40, 26.34; Elemental analysis: calculated for C₁₀H₁₆N₂ (%): C, 73.13; H, 9.82; N, 17.06. Found: C, 72.48; H, 9.91; N, 16.92.

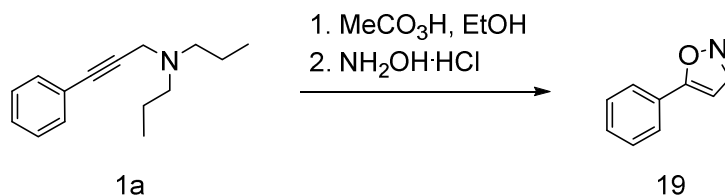
2-Methyl-1-(1*H*-pyrazol-5-yl)pentan-1-ol, 18j



Following GP2, the title compound was prepared as a yellow oil (47 mg, 40%) starting from 1-(diethylamino)-5-methyloct-2-yn-4-ol, **1j** with the following modifications: 2N solution of hydrochloric acid in methanol and an aqueous solution of hydrazine. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.45 (br s, 1H), 7.07 (br s, 1H), 6.11 (br s, 1H), 4.71-4.61 (m, 1H), 1.94-1.76 (m, 1H), 1.55-1.01 (m, 5H), 0.91-0.79 (m, 6H); ¹³C NMR (100 MHz, CHLOROFORM-*d*) δ = 150.79, 150.36, 134.44, 134.31, 102.80, 102.47, 72.55, 71.99, 39.25, 35.28, 34.39, 20.51, 20.36, 15.56, 14.55, 14.47; Elemental analysis: calculated for C₉H₁₆N₂O (%): C, 64.25; H, 9.59; N, 16.65. Found: C, 63.67; H, 9.57; N, 16.39.

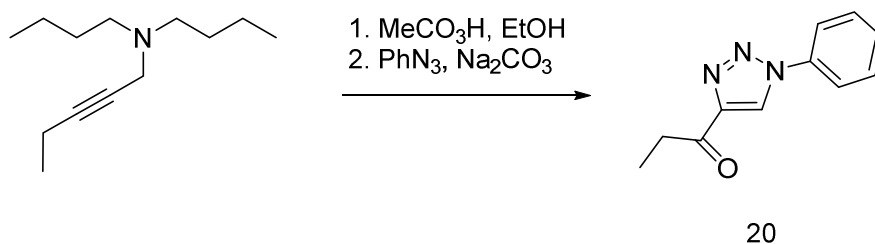
Extended One-pot Pyrazole Formation (Table 2)

5-phenyl-1,2-oxazole, **19**⁴



To a solution of 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** (100 mg, 0.46 mmol, 1.0 equiv) in ethanol (3 mL, 0.2 M) was added peroxyacetic acid (0.1 mL, 0.6 mmol, 1.3 equiv). The reaction was stirred at room temperature for 5 minutes and 85 °C for 30 minutes. To the resulting rearranged intermediate was added a 4N hydroxylamine hydrochloride solution in 1,4-dioxane (1 mL) and the reaction was stirred at 85 °C for 5 minutes. The reaction was treated with 1N sodium hydroxide (5 mL) and extracted with dichloromethane (2 x 50 mL). The combined organic layers were dried over sodium sulfate, filtered and the solvent was concentrated in vacuo. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-40% of ethyl acetate in heptanes to afford 5-phenyl-1,2-oxazole, **19** as an oil (36 mg, 53%). ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 8.32 (d, $J=1.96$ Hz, 1 H), 7.80 - 7.86 (m, 2 H), 7.44 - 7.54 (m, 3 H), 6.55 (d, $J=1.96$ Hz, 1 H); ¹³C NMR (126 MHz, CHLOROFORM-*d*) δ = 169.41, 150.85, 130.23, 129.03, 127.31, 125.91, 98.66; GC-MS: m/z 145.0 [M^+], retention time=2.527 minutes.

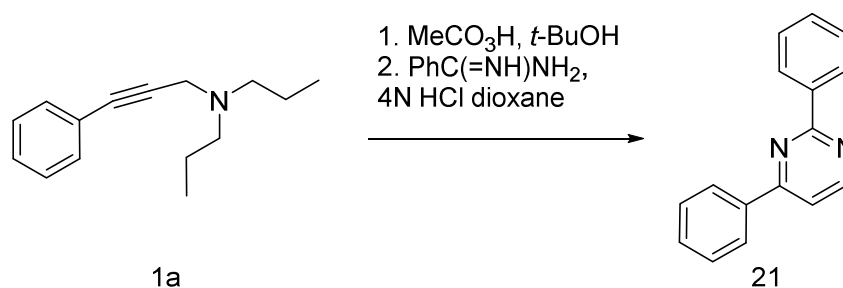
1-(1-phenyl-1*H*-1,2,3-triazol-4-yl)propan-1-one, **20**



⁴ Data are consistent with the literature. Rosa, F. A.; Machado, H.; Bonacorso, H. G.; Zanatta, N.; Martins, M. A. P. *J. Heterocyclic Chem.*, **2008**, *45*, 879-885.

To a solution of *N,N*-dibutylpent-2-yn-1-amine⁵ (195 mg, 1.0 mmol, 1.0 equiv) in ethanol (5 mL, 0.2 M) was added peroxyacetic acid (0.2 mL, 1.1 mmol, 1.1 equiv). The reaction was stirred at 85 °C for 1 hour. To the resulting rearranged intermediate was added phenyl azide (10.0 mL, 5.0 mmol, 5.0 equiv) and sodium carbonate (530 mg, 5.0 mmol, 5.0 equiv). The reaction was stirred at 85 °C for 18 hours. The reaction was diluted with a saturated ammonium chloride solution (5 mL) and extracted with dichloromethane (2 x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and the solvent was concentrated in vacuo. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-60% of ethyl acetate in heptanes to afford 1-(1-phenyl-1*H*-1,2,3-triazol-4-yl)propan-1-one, **20**⁶ as a white solid (67 mg, 33%). ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.49 (s, 1 H), 7.73 - 7.78 (m, 2 H), 7.46 - 7.59 (m, 3 H), 3.22 (q, *J*=7.43 Hz, 2 H), 1.26 (t, *J*=7.34 Hz, 3 H); ¹³C NMR (101 MHz, CHLOROFORM-*d*) δ = 195.83, 148.17, 129.95, 129.49, 123.27, 120.77, 33.00, 7.74; HRMS (*m/z*): calculated for C₁₁H₁₁N₃O [M + H]⁺ 202.0975, found 202.0973.

2,4-diphenylpyrimidine, **21**



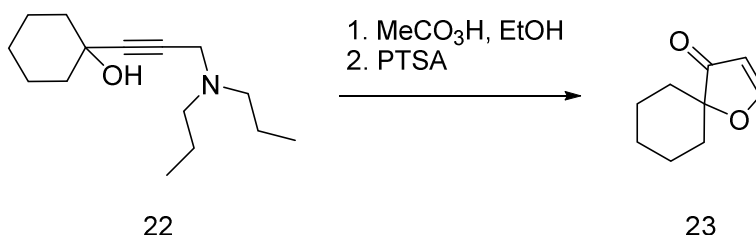
To a solution of 3-phenyl-*N,N*-dipropylprop-2-yn-1-amine, **1a** (108 mg, 0.5 mmol, 1.0 equiv) in *t*-butanol (2 mL, 0.2 M) was added peroxyacetic acid (0.1 mL, 0.55 mmol, 1.1 equiv). The reaction was stirred at room temperature for 5 minutes and 85 °C for 30 minutes. The solvent was concentrated in vacuo and fresh *t*-butanol (2 mL) was added along with benzenecarboximidamide (180 mg, 1.50 mmol, 3.0 equiv) and potassium *t*-butoxide (2.5 mL, 2.5 mmol, 5.0 equiv). The reaction was stirred at 85 °C for 48 hours and then a 4N hydrochloride solution in 1,4-dioxane (1 mL) and the reaction was stirred at 85 °C for 1 hour. The reaction was

⁵ Parcell, R.F.; Pollard, C.B. *J. Am. Chem. Soc.*, **1950**, 72, 3312-3313.

⁶ Data are consistent with the literature. Janreddy, D.; Kavala, V.; Kuo, C.; Chen, W.; Ramesh, C.; Kotipalli, T.; Kuo, T.; Chen, M.; He, C.; Yao, C. *Adv. Syn. Cat.* **2013**, 355, 2918-2927.

diluted with a saturated ammonium chloride solution (5 mL) and extracted with dichloromethane (2 x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and the solvent was concentrated in vacuo. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-40% of ethyl acetate in heptanes to afford 2,4-diphenylpyrimidine, **21**⁷ as a yellow solid (42 mg, 36%). ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 8.74 (d, *J*=5.14 Hz, 1 H), 8.47 - 8.54 (m, 2 H), 8.10 - 8.17 (m, 2 H), 7.49 (d, *J*=5.38 Hz, 1 H), 7.36 - 7.48 (m, 7 H); ¹³C NMR (126 MHz, CHLOROFORM-*d*) δ = 164.63, 163.90, 157.89, 137.92, 137.00, 131.00, 130.75, 128.97, 128.58, 128.33, 127.25, 114.55; HRMS (m/z): calculated for C₁₆H₁₂N₂ [M + H]⁺ 233.1073, found 233.1074.

1-oxaspiro[4.5]dec-2-en-4-one, **23**



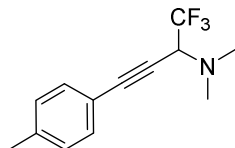
To a solution of 1-[3-(dipropylamino)prop-1-yn-1-yl]cyclohexanol, **22** (200 mg, 0.8 mmol, 1.0 equiv) in ethanol (3 mL, 0.3 M) was added peroxyacetic acid (0.2 mL, 0.9 mmol, 1.1 equiv). The reaction was stirred at room temperature for 5 minutes and 85 °C for 90 minutes. The reaction was cooled to room temperature and to the resulting rearranged intermediate was added p-toluene sulfonic acid (227 mg, 1.3 mmol, 1.5 equiv). The reaction was stirred at room temperature for 18 hours. The reaction was treated with a saturated sodium bicarbonate solution (5 mL) and extracted with diethyl ether (2 x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and the solvent was concentrated in vacuo. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-50% of ethyl acetate in heptanes to afford 1-oxaspiro[4.5]dec-2-en-4-one, **23** as an oil (56 mg, 44%). ¹H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 8.19 (s, 1 H), 5.64 (s, 1 H), 1.74 - 1.81 (m, 3 H), 1.55 - 1.72

⁷ Data are consistent with the literature. Lin, M.; Chen, Q.; Zhu, Y.; Chen, X.; Cai, J.; Pan, Y.; Zhan, Z. *Synlett*, **2011**, 8, 1179-1183.

(m, 7 H); ^{13}C NMR (126 MHz, CHLOROFORM- d) δ = 207.58, 176.26, 105.32, 89.46, 31.48, 24.41, 21.69; HRMS (m/z): calculated for $\text{C}_9\text{H}_{12}\text{O}_2$ $[\text{M} + \text{H}]^+$ 154.0944, found 154.0949.

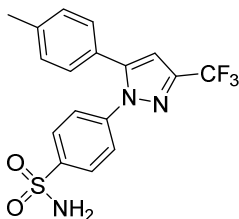
Celecoxib Synthesis:

1,1,1-trifluoro-*N,N*-dimethyl-4-(4-methylphenyl)but-3-yn-2-amine, **26**



Into a 25 mL flask equipped with a magnetic stirring bar was added the 1-ethynyl-4-methylbenzene, **24** (2090 mg, 18 mmol, 1.0 equiv.), 1,1-bis(dimethylamino)-2,2,2-trifluoroethane, **25** (3060 mg, 18 mmol, 1.0 equiv.), and zinc triflate (1640 mg, 4.5 mmol, 0.25 equiv.). The mixture was stirred at room temperature for 18 hours. The reaction mixture was diluted with diethylether (150 mL), washed with 10% aqueous ammonium hydroxide (50 mL). The diethylether layer was separated, dried over sodium sulfate and concentrated to afford a brown oil. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-10% ethyl acetate in heptanes to afford 1,1,1-trifluoro-*N,N*-dimethyl-4-(4-methylphenyl)but-3-yn-2-amine, **26** as a yellow oil (3.6 g, 83%). ^1H NMR (500 MHz, CDCl_3) δ ppm 7.40 (d, $J=8.2$ Hz, 2 H), 7.15 (d, $J=8.2$ Hz, 2 H), 4.14 (q, $J=7.7$ Hz, 1 H), 2.48 (s, 6 H), 2.37 (s, 3 H); ^{13}C NMR (126 MHz, CDCl_3) δ ppm 139.14, 131.88, 129.08, 123.90 (q, $J=283.10$ Hz, 1C), 118.72, 89.02, 76.48 (q, $J=2.01$ Hz, 1C), 60.38 (q, $J=32.12$ Hz, 1C), 42.65, 21.41; GCMS (EI): m/z 241.2, 197.1, 172.1, 129.1, 85.7. HRMS: observed ($m+H$)/ z 242.1150, expected: 242.1156.

4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide, **29**



One-pot three-step synthesis (Scheme 6)

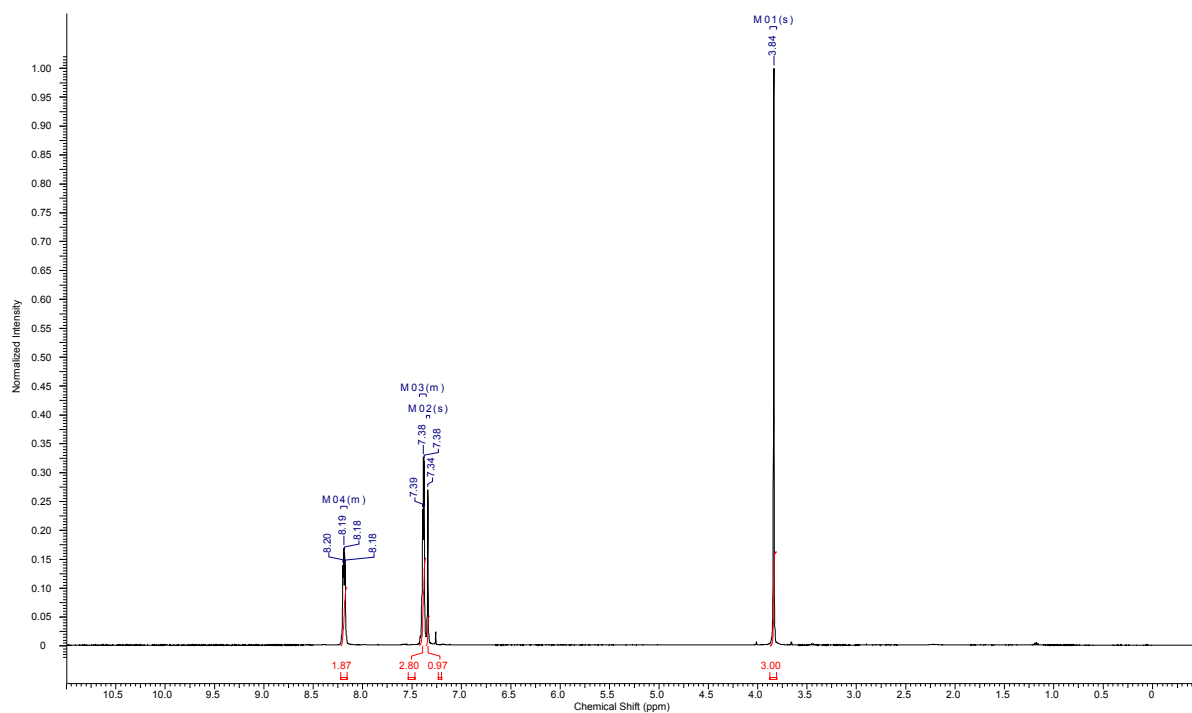
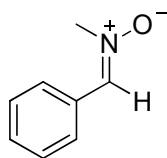
To a solution of 1,1,1-trifluoro-*N,N*-dimethyl-4-(4-methylphenyl)but-3-yn-2-amine, **26** (241 mg, 1.0 mmol) in ethanol (4 mL) was added *m*-chloroperoxybenzoic acid (263 mg, 1.1 mmol, 1.1 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 30 minutes while a steady stream of nitrogen was bubbled through the reaction mixture. The nitrogen line was then removed. Water (0.4 mL) was added to the reaction mixture and stirred at 85 °C for 30 minutes. The reaction mixture was cooled to room temperature and then a suspension of 4-hydrazinylbenzenesulfonamide (284 mg, 1.5 mmol, 1.5 equiv.) in a solution of 4 N hydrogen chloride in dioxane (2 mL) was added. The mixture was stirred at room temperature for 5 minutes and then 85 °C for 30 minutes (remained a suspension). The reaction was kept at room temperature for 1 hour. The solid (excess hydrazine) was removed via filtration. The filtrate was concentrated and redissolved in dichloromethane (75 mL) and washed with saturated sodium carbonate (50 mL). The aqueous layer was extracted with ethyl acetate (50 mL). The organic layer was dried over sodium sulfate and concentrated to afford a deep yellow solid. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-50% ethyl acetate in heptanes to afford 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide, **29** (140 mg, 37%). ¹H NMR (500 MHz, DMSO-*d*₆) δ ppm 7.89 (d, *J*=8.56 Hz, 2 H), 7.55 (d, *J*=8.80 Hz, 2 H), 7.53 (s, 2 H), 7.18 - 7.26 (m, 5 H), 2.32 (s, 3 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm 145.75, 144.48, 142.66 (q, *J*=38.2, 1C), 141.60, 139.59, 129.91, 129.26, 127.29, 126.48, 125.85, 121.79 (q, *J*=269.2 Hz, 1C), 106.63 (q, *J*=1.7 Hz, 1C), 21.28; HRMS: observed (*m*+*H*)/*z* 382.0826, expected: 382.0792.

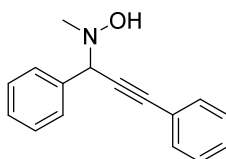
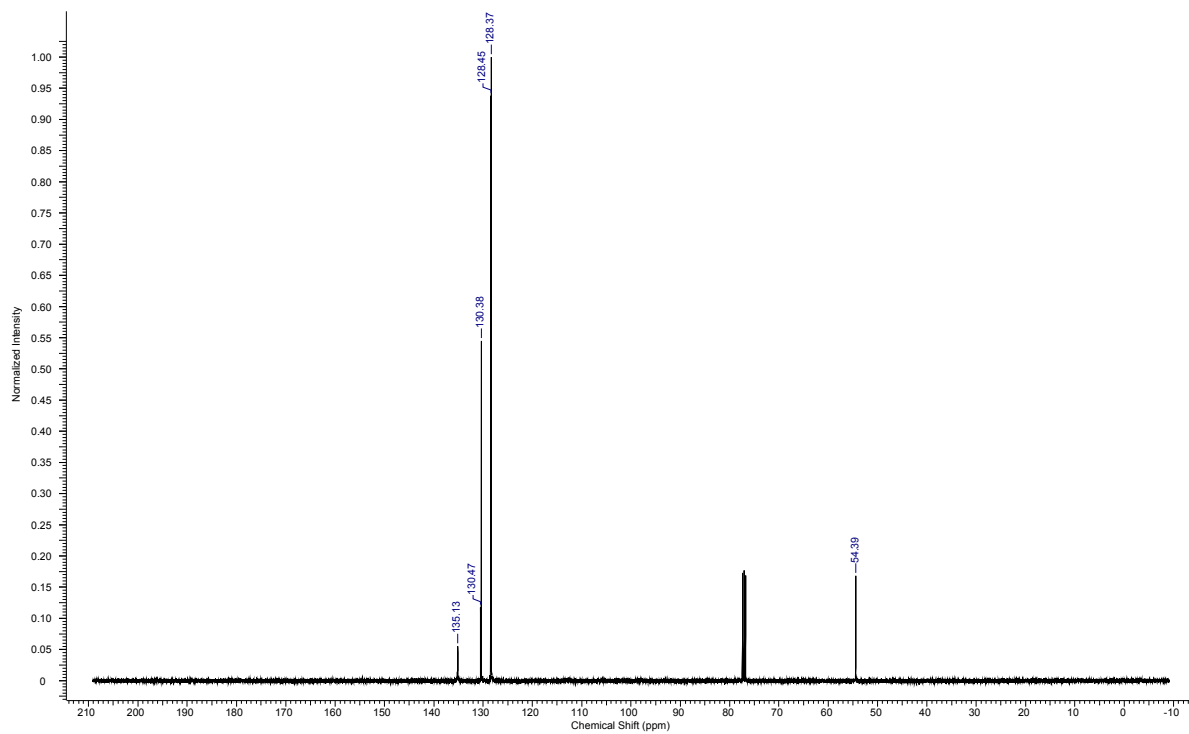
One-pot four-step synthesis (Scheme 7)

Into a 50 mL round-bottom-flask equipped with a magnetic stirring bar was added 1-ethynyl-4-methylbenzene, **24** (796 mg, 6.0 mmol), 1,1-bis(dimethylamino)-2,2,2-trifluoroethane, **25** (1020 mg, 6.0 mmol), and zinc triflate (436 mg, 1.2 mmol). The reaction mixture was stirred at 85 °C for 1 hour. To the mixture was added ethanol (12 mL) and cooled to 0 °C. A steady stream of nitrogen was bubbled through the mixture while stirring at 0 °C. *m*-chloroperoxybenzoic acid was added (1.44 g, 6 mmol) and the colorless mixture started to turn into light yellow. The reaction mixture was stirred at 0 °C for 30 minutes. Additional *m*-chloroperoxybenzoic acid (1.08 g, 4.5 mmol) was added and mixture stirred at 0 °C for 30 minutes. To the mixture was added wa-

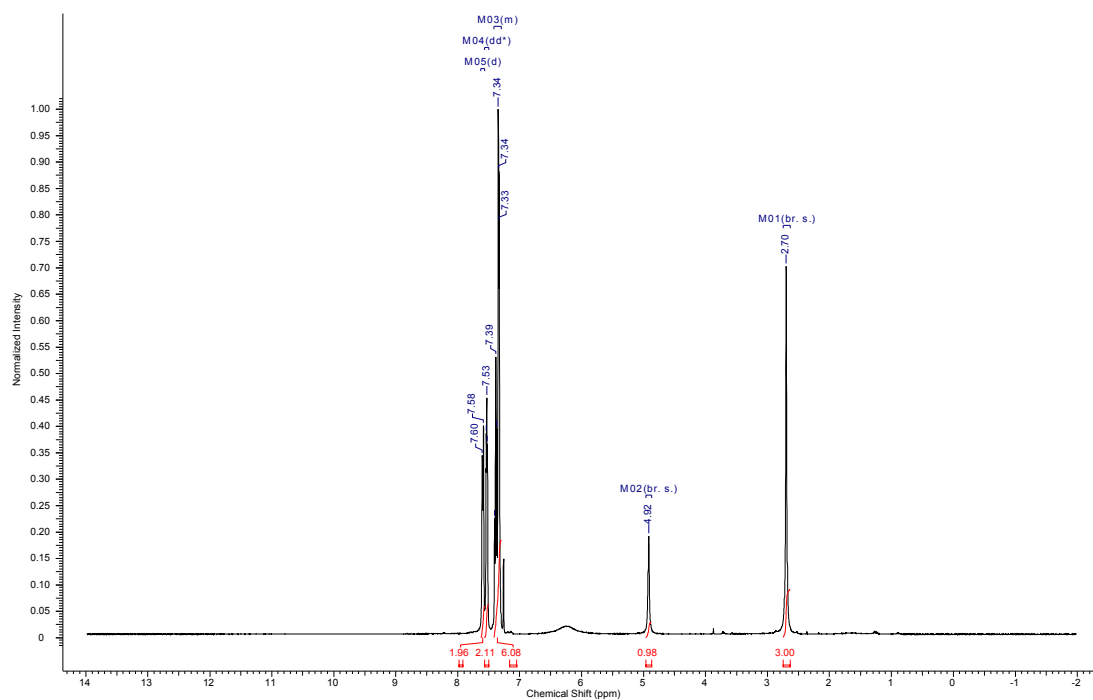
ter (1.2 mL). The reaction mixture was then stirred at 85 °C for 30 minutes, cooled to 0 °C and a suspension of 4-hydrazinylbenzenesulfonamide (562 mg, 3 mmol) in a solution of 4N hydrogen chloride in dioxane (6 mL) was added over a period of 5 minutes. The resulting mixture was stirred at 0 °C for another 5 minutes, then room temperature for 10 minutes, 85 °C for 16 h and then left standing at room temperature for 2 days. The mixture was then diluted with ethyl acetate (100 mL), extracted with 1 N sodium hydroxide. The aqueous layer extracted with ethyl acetate (70 mL) and the combined organic layers were concentrated. The crude residue was purified by chromatography on a silica gel column, eluting with a gradient from 0-75% ethyl acetate in heptanes to afford 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide, **29** (448 mg, 39%).

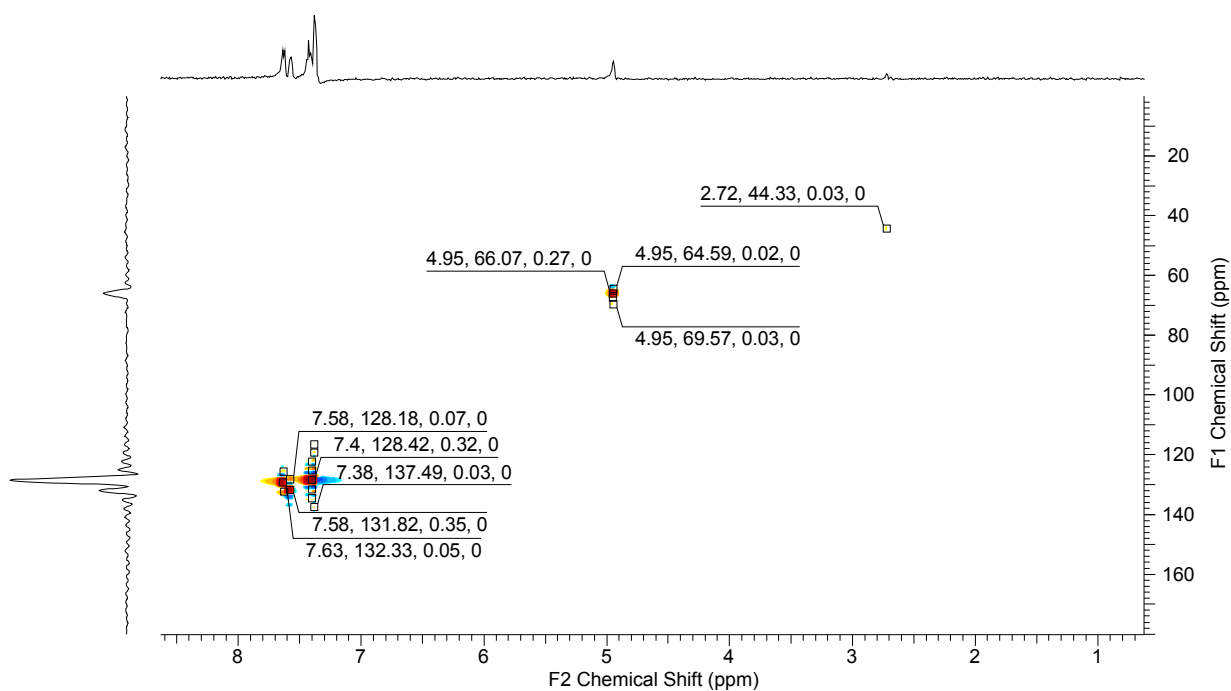
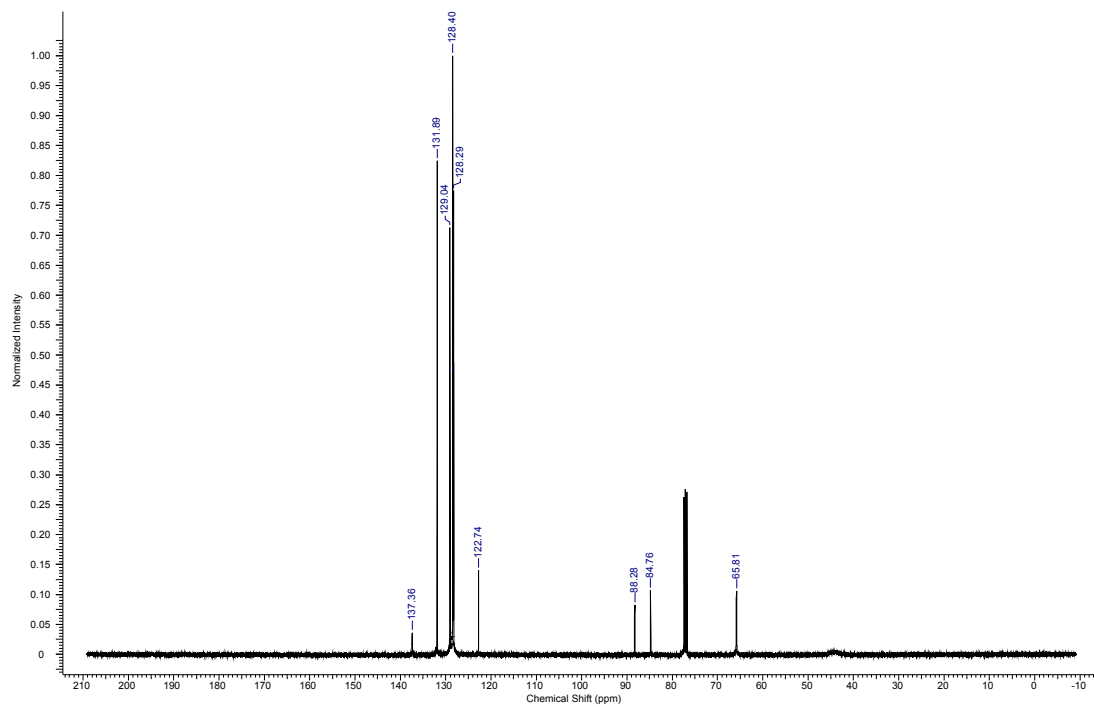
Spectral Data

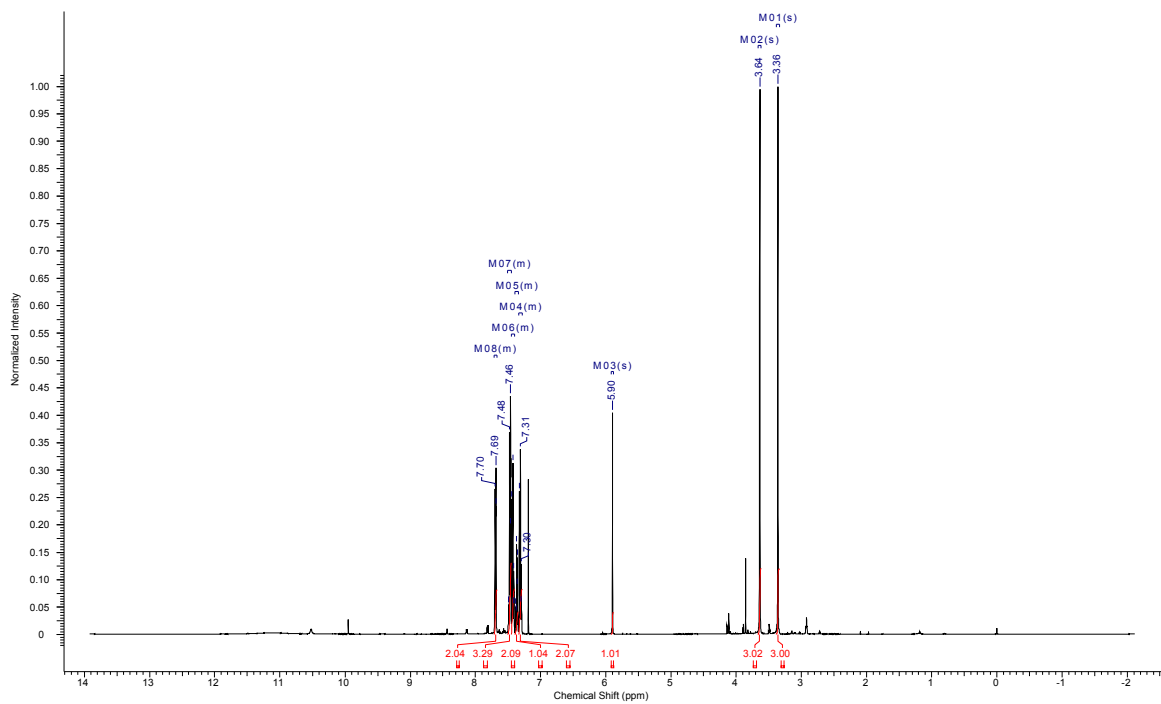
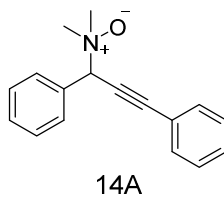


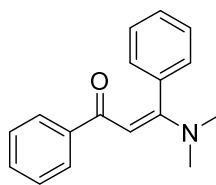
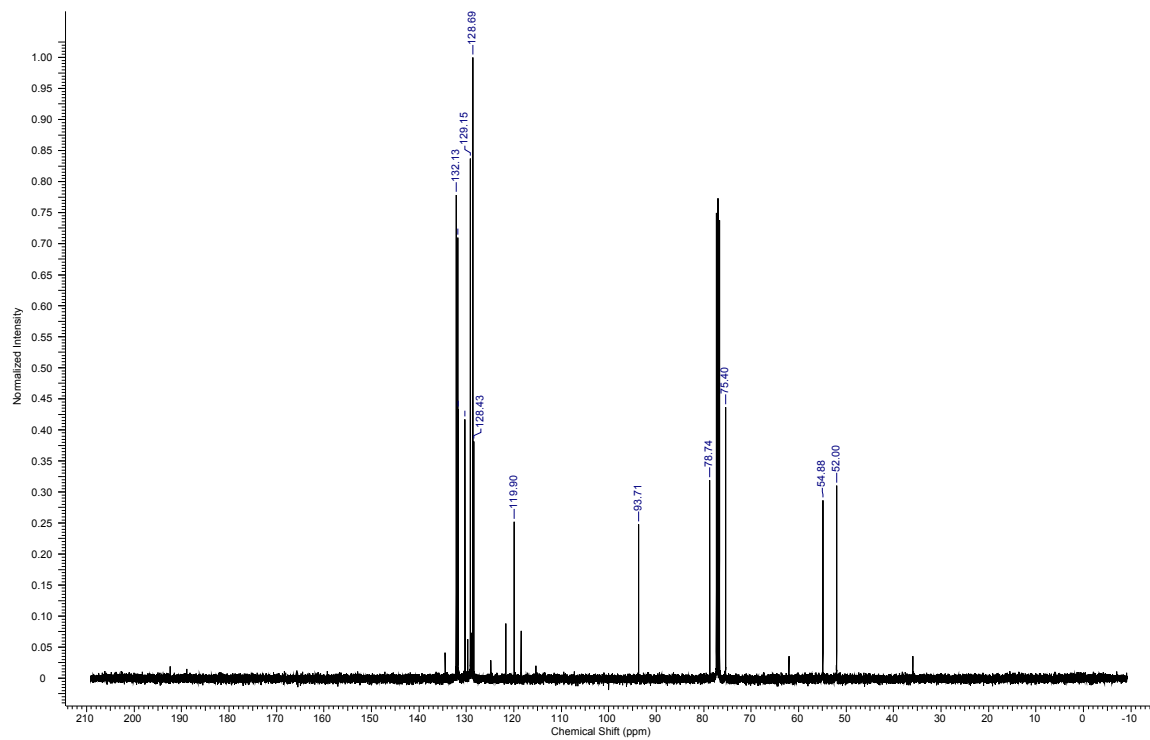


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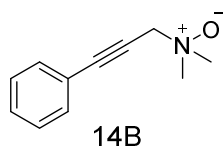
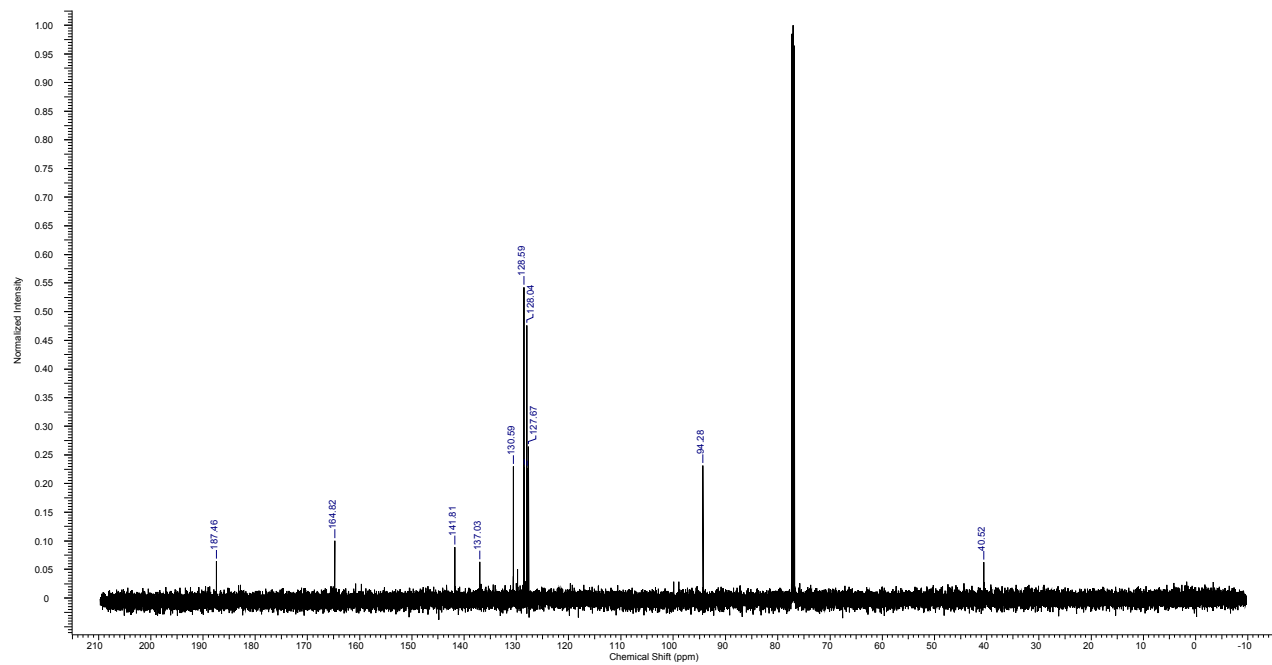
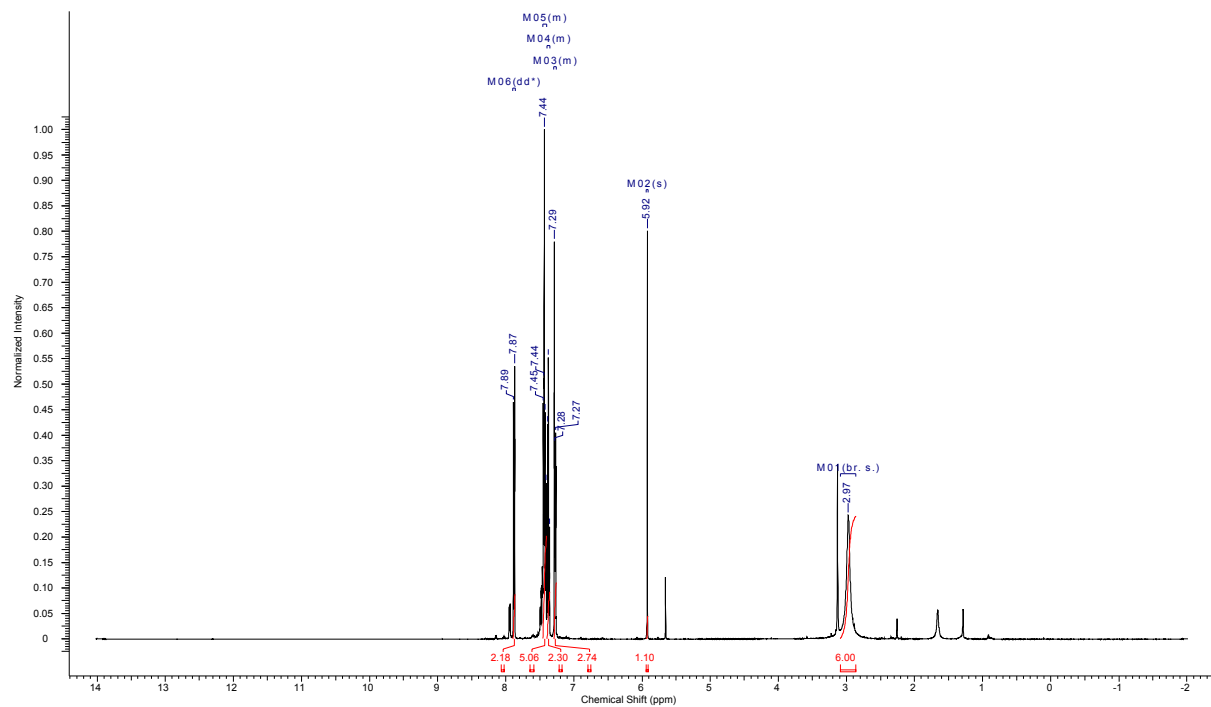


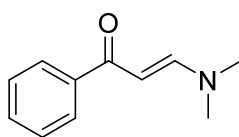
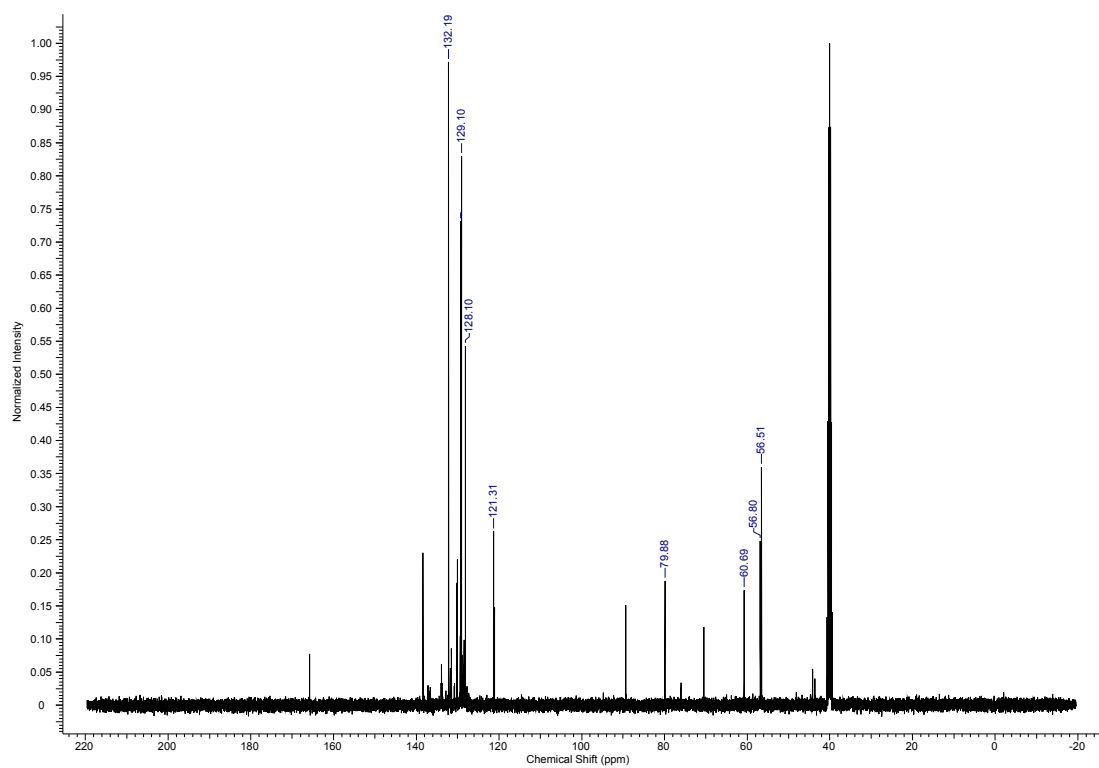
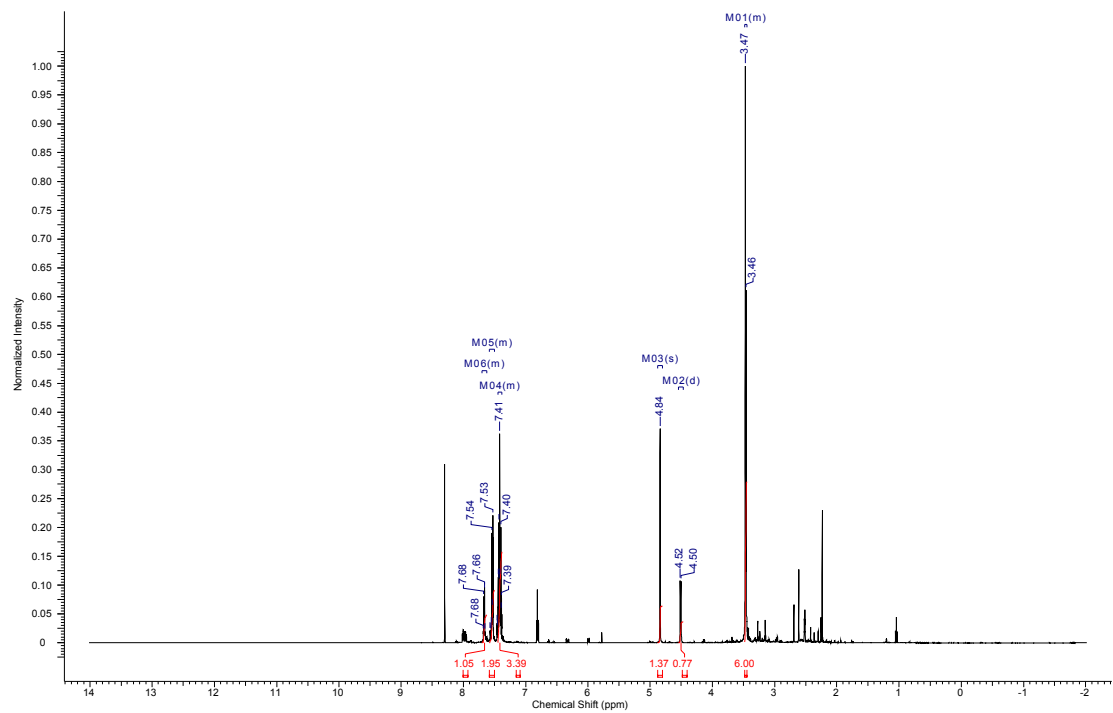






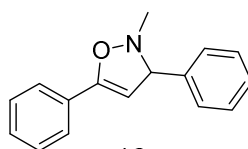
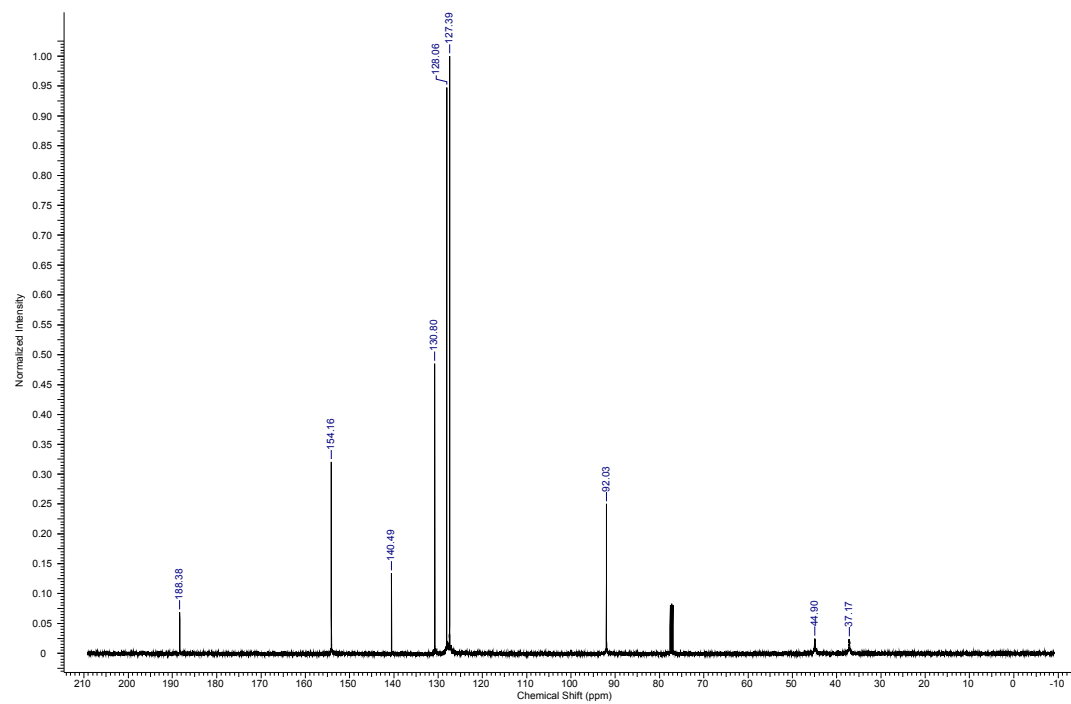
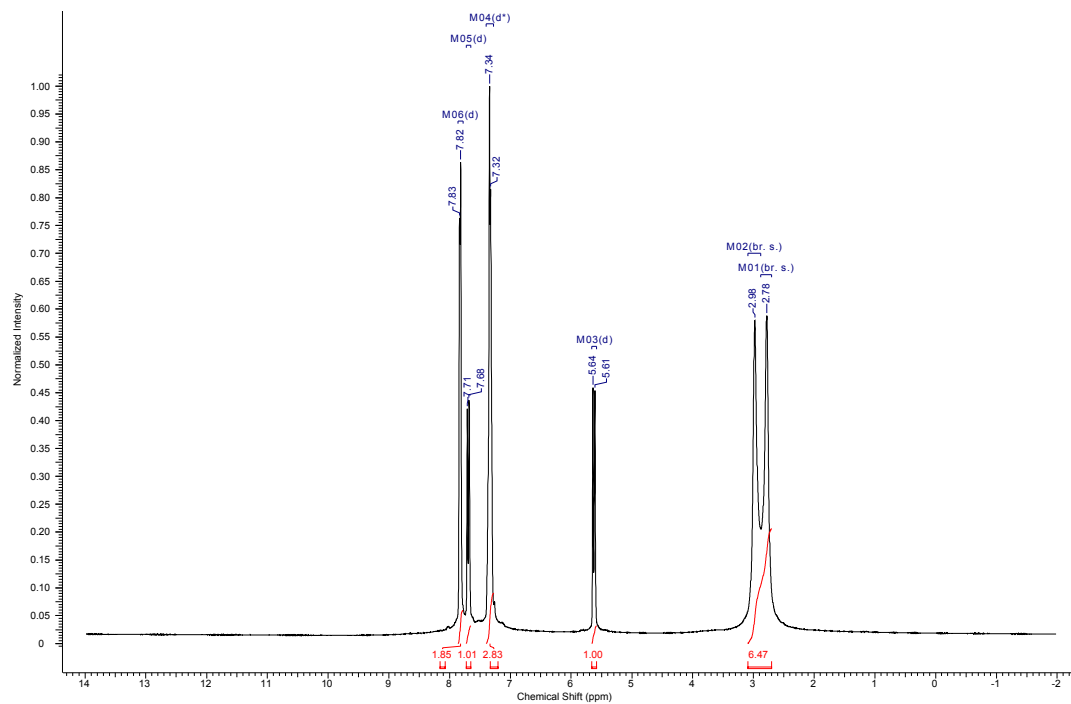
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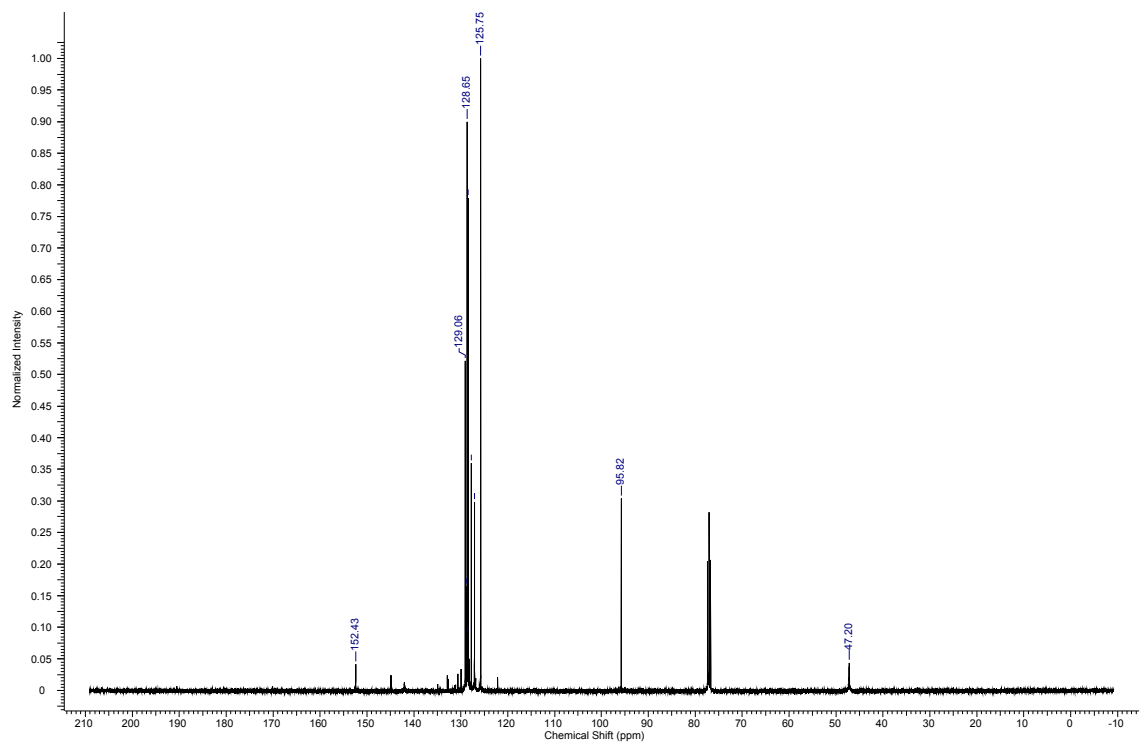
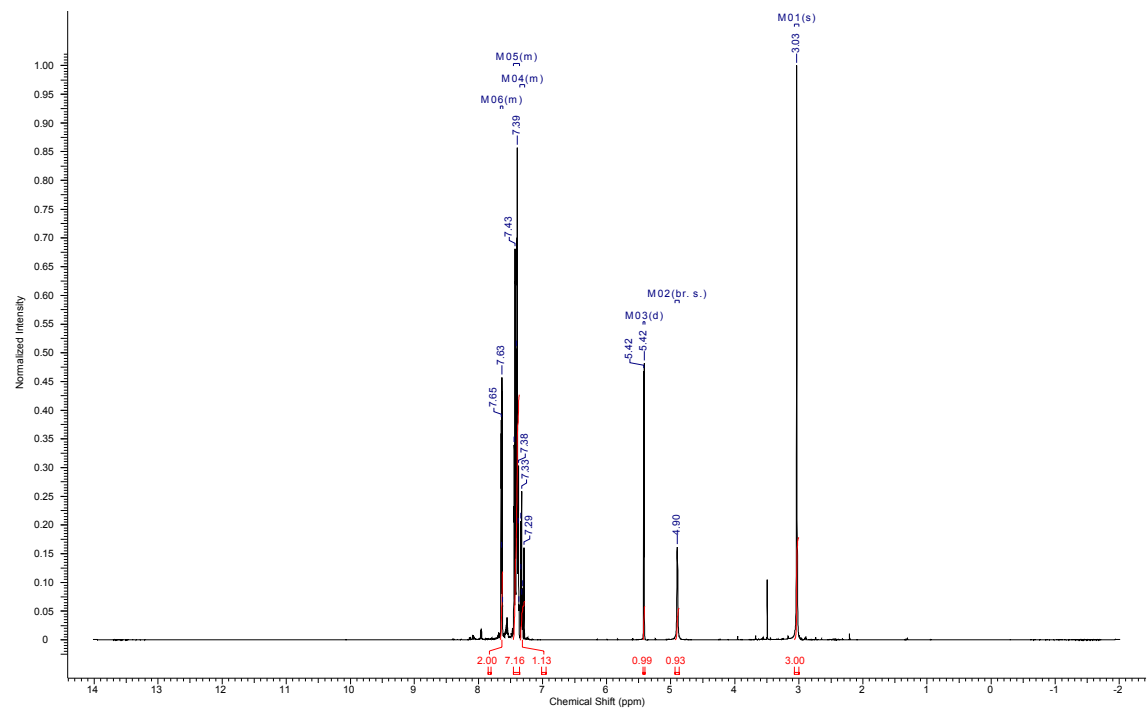


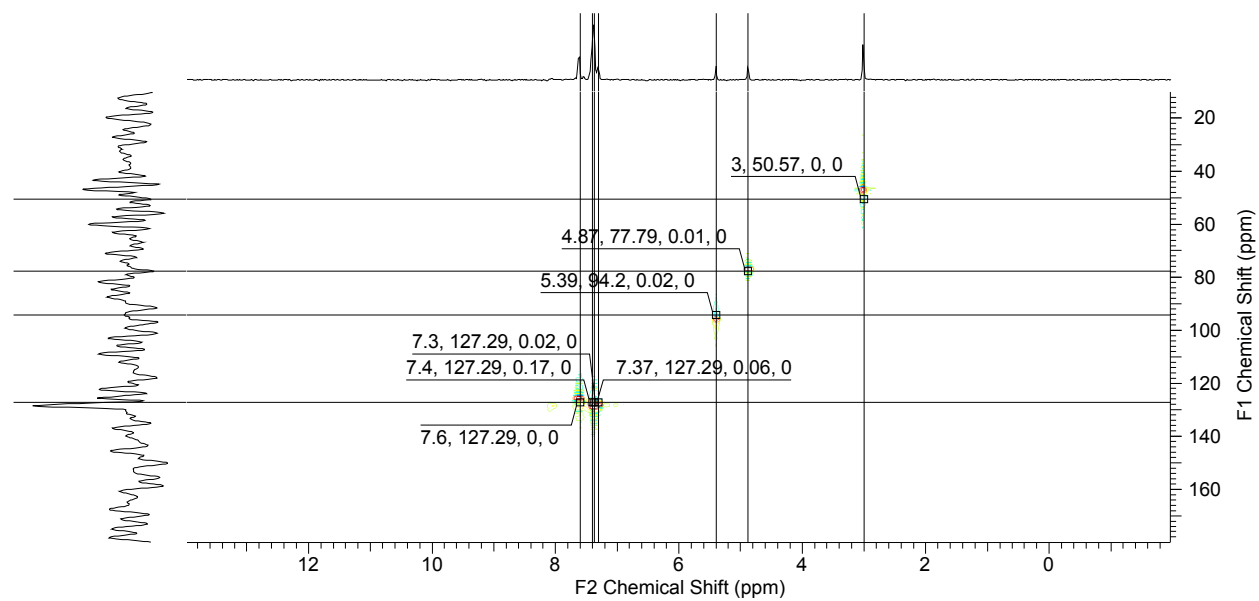
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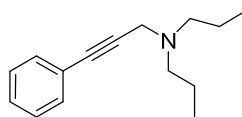
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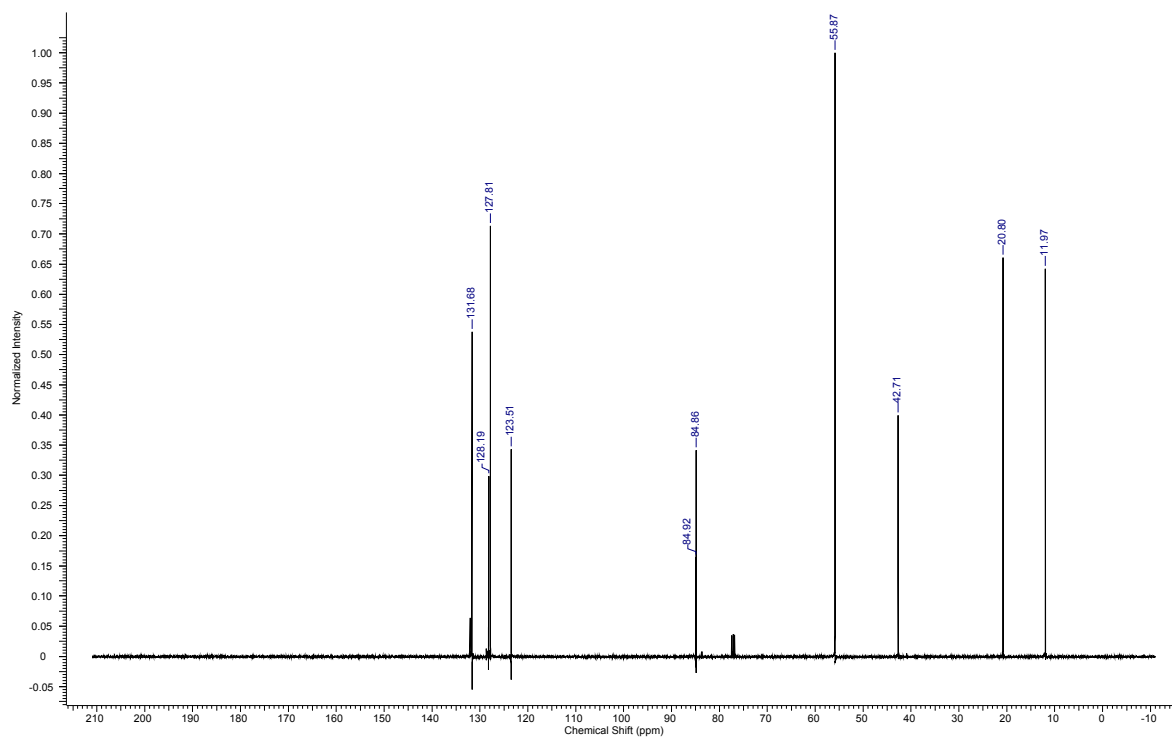
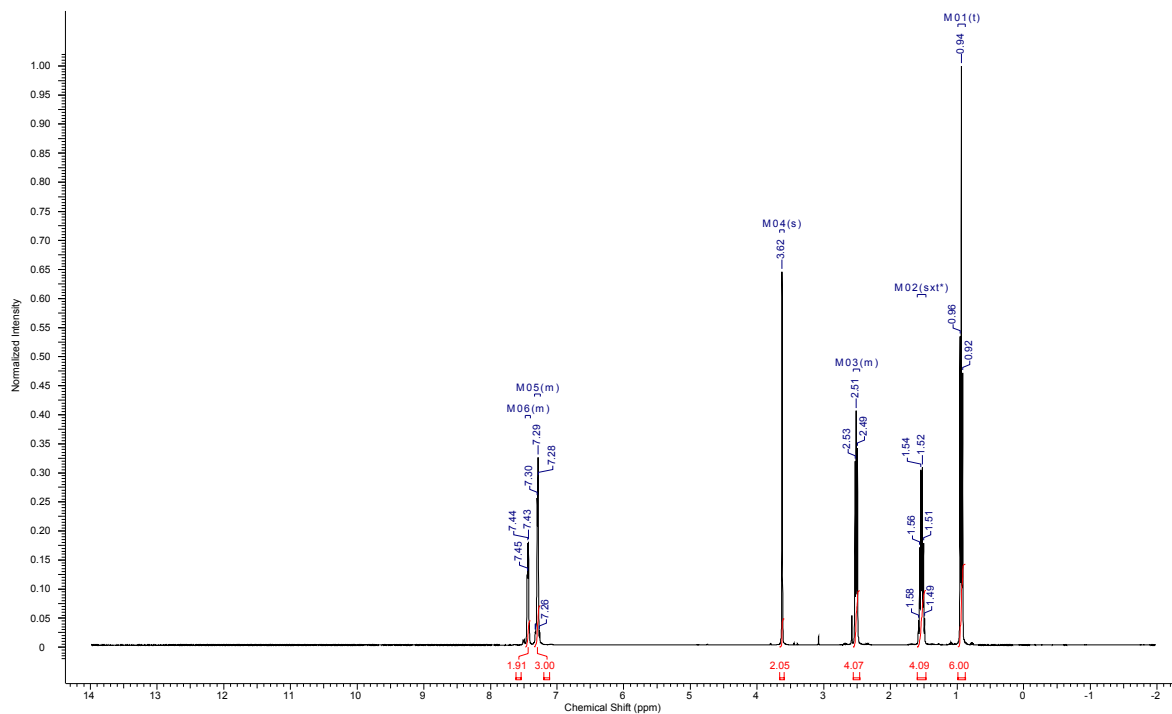
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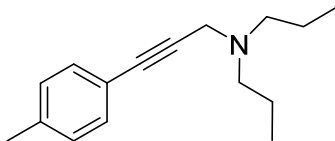




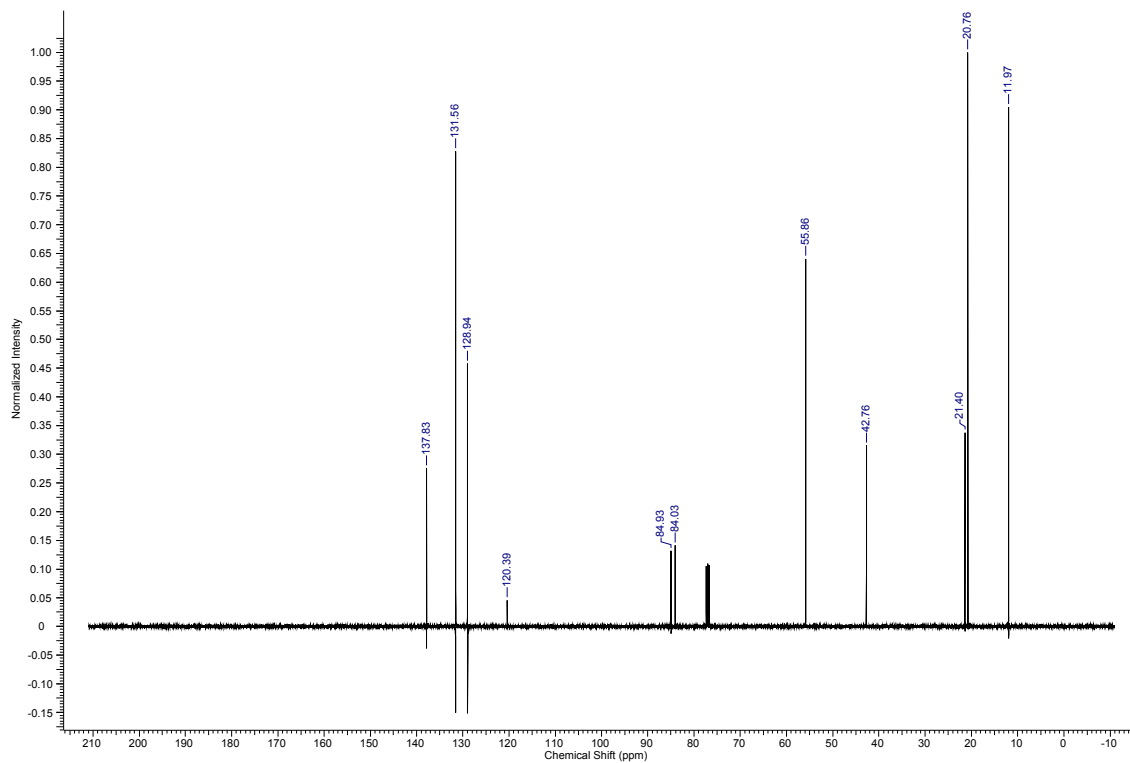
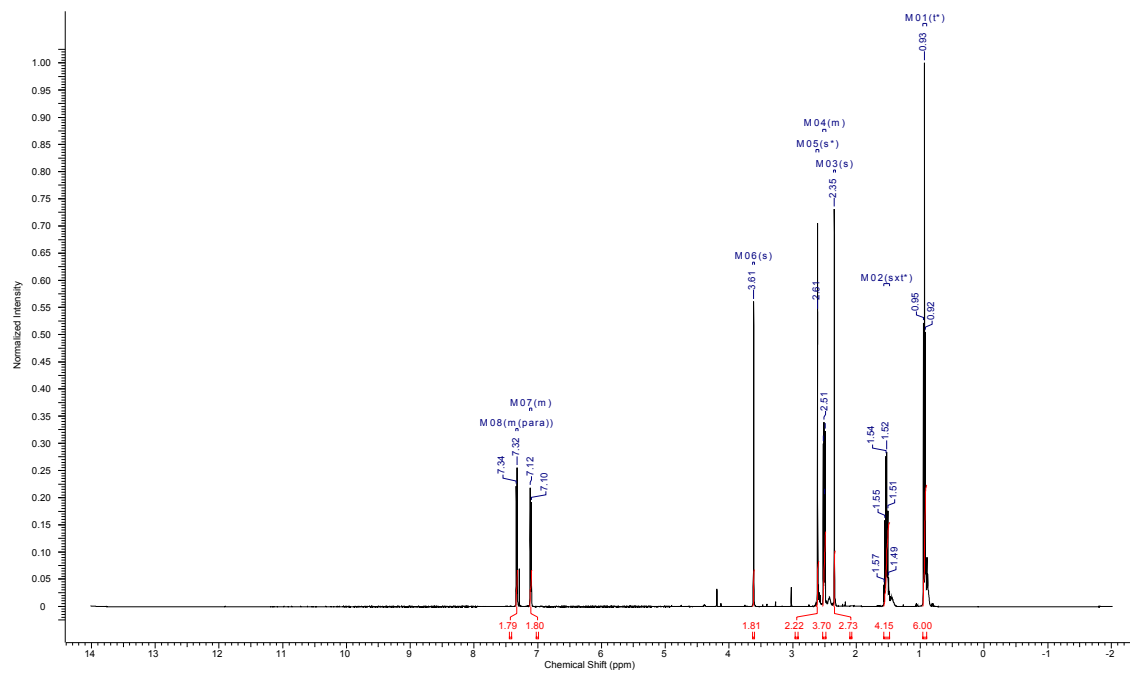


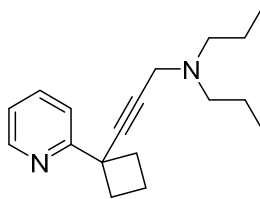
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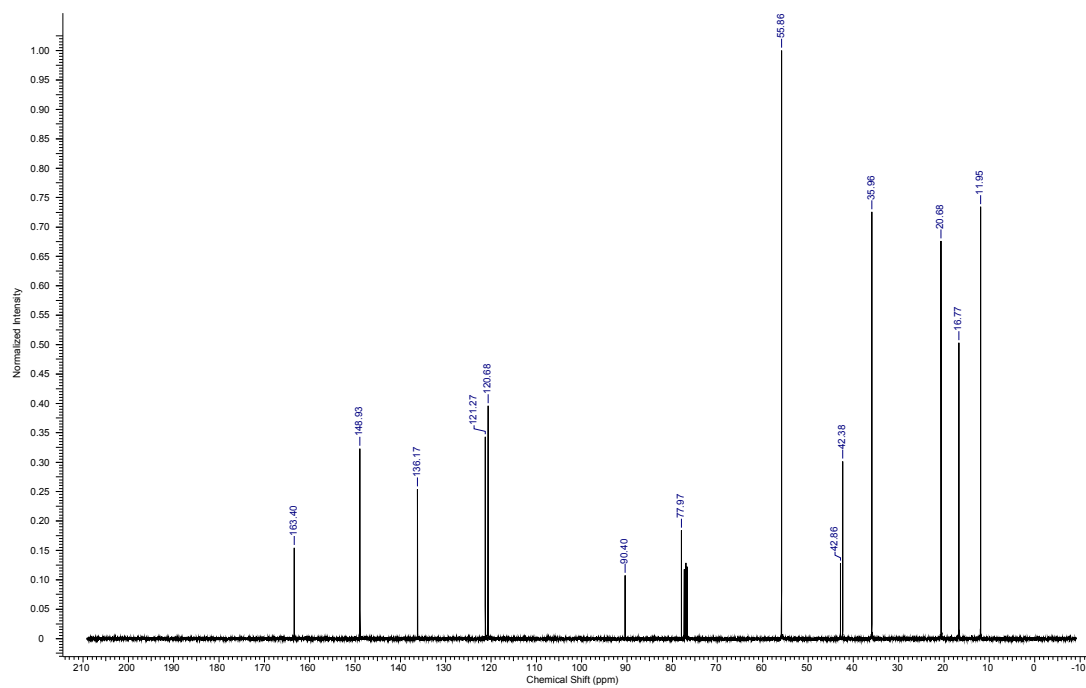
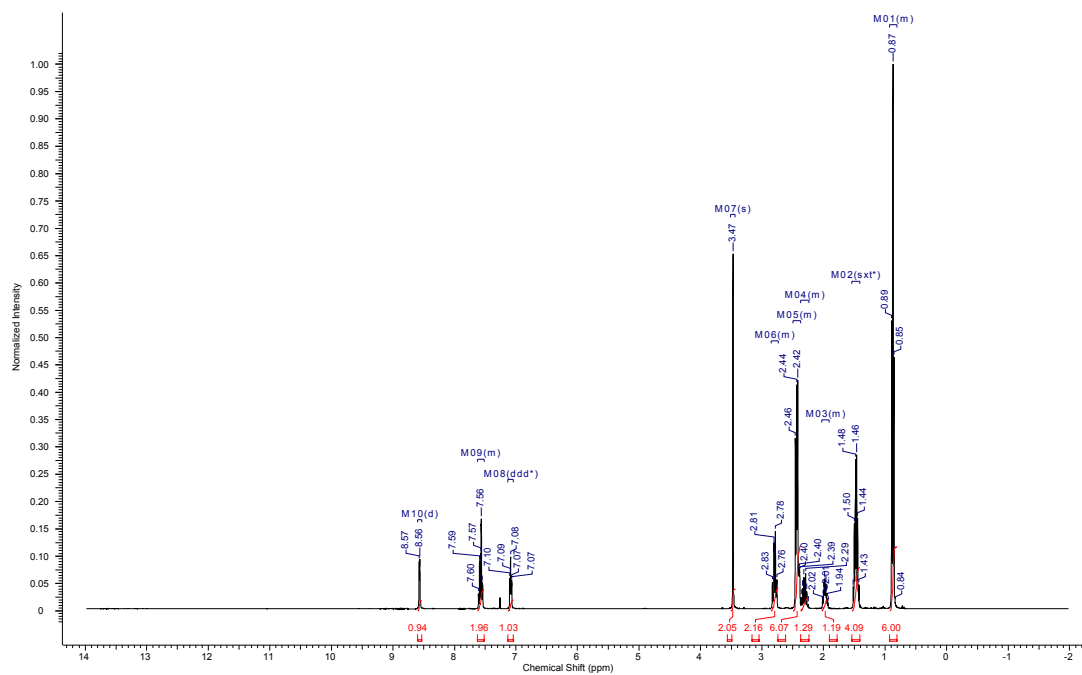


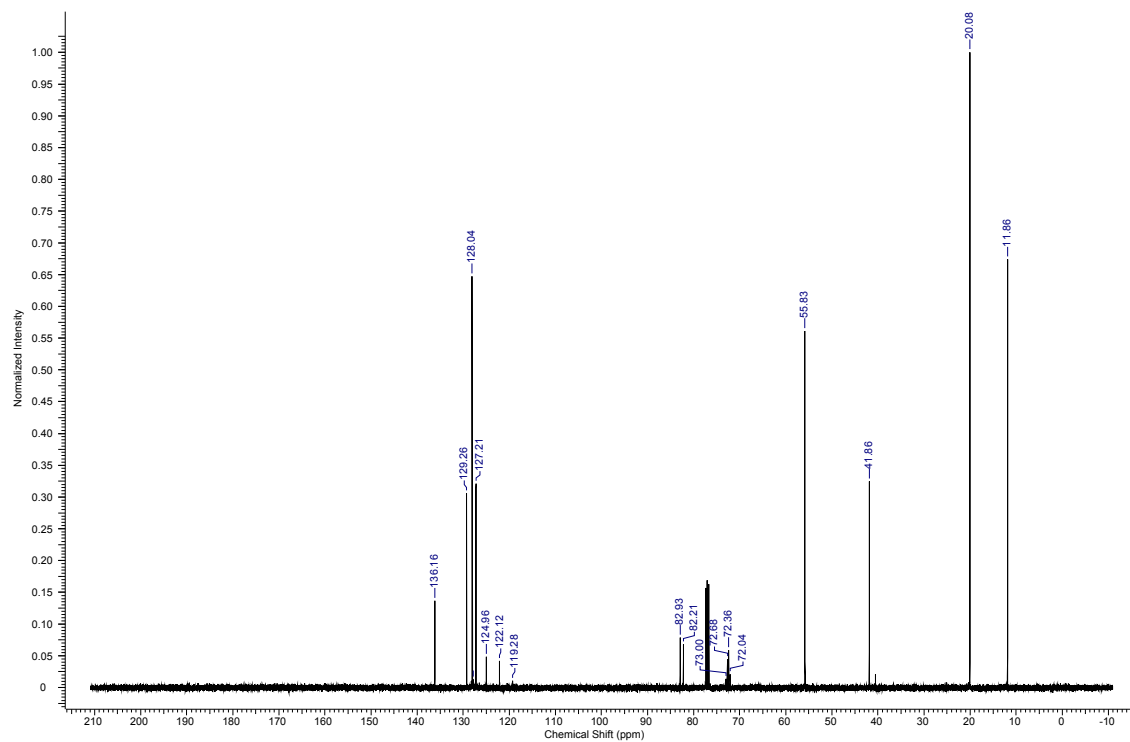
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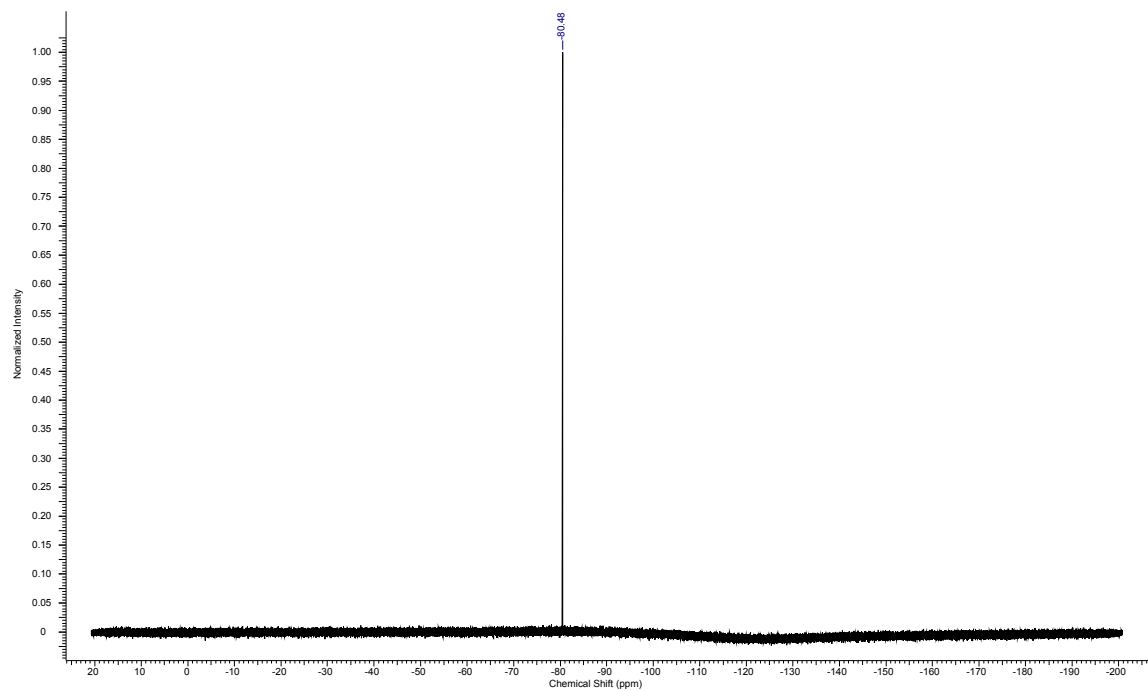


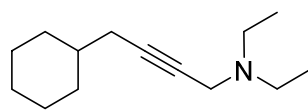


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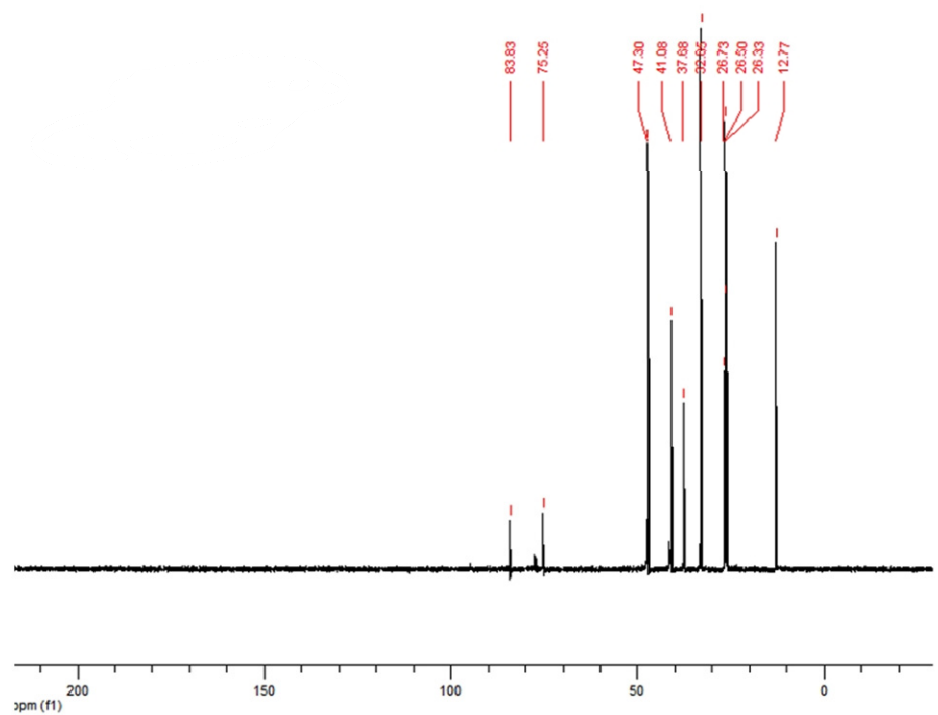
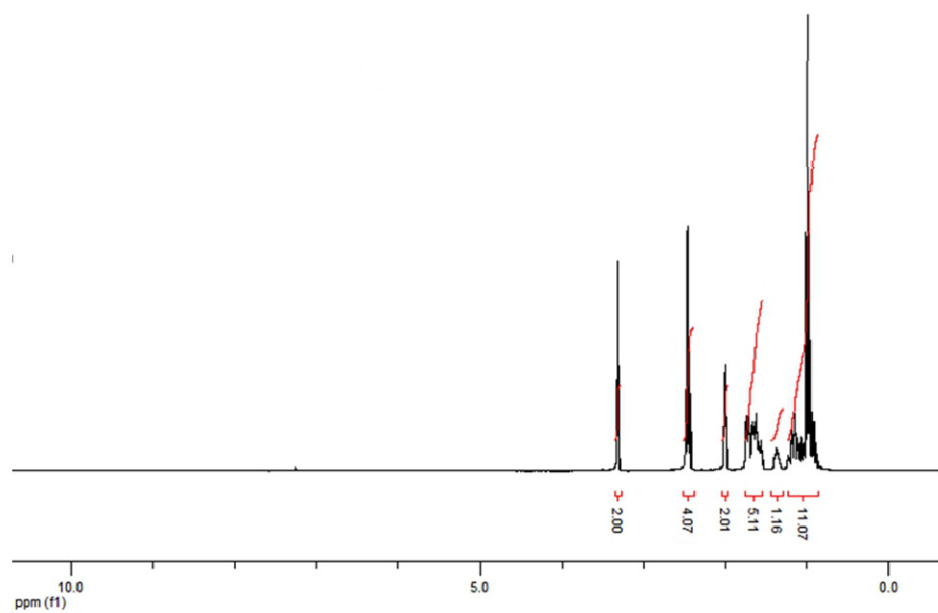


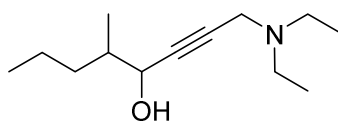




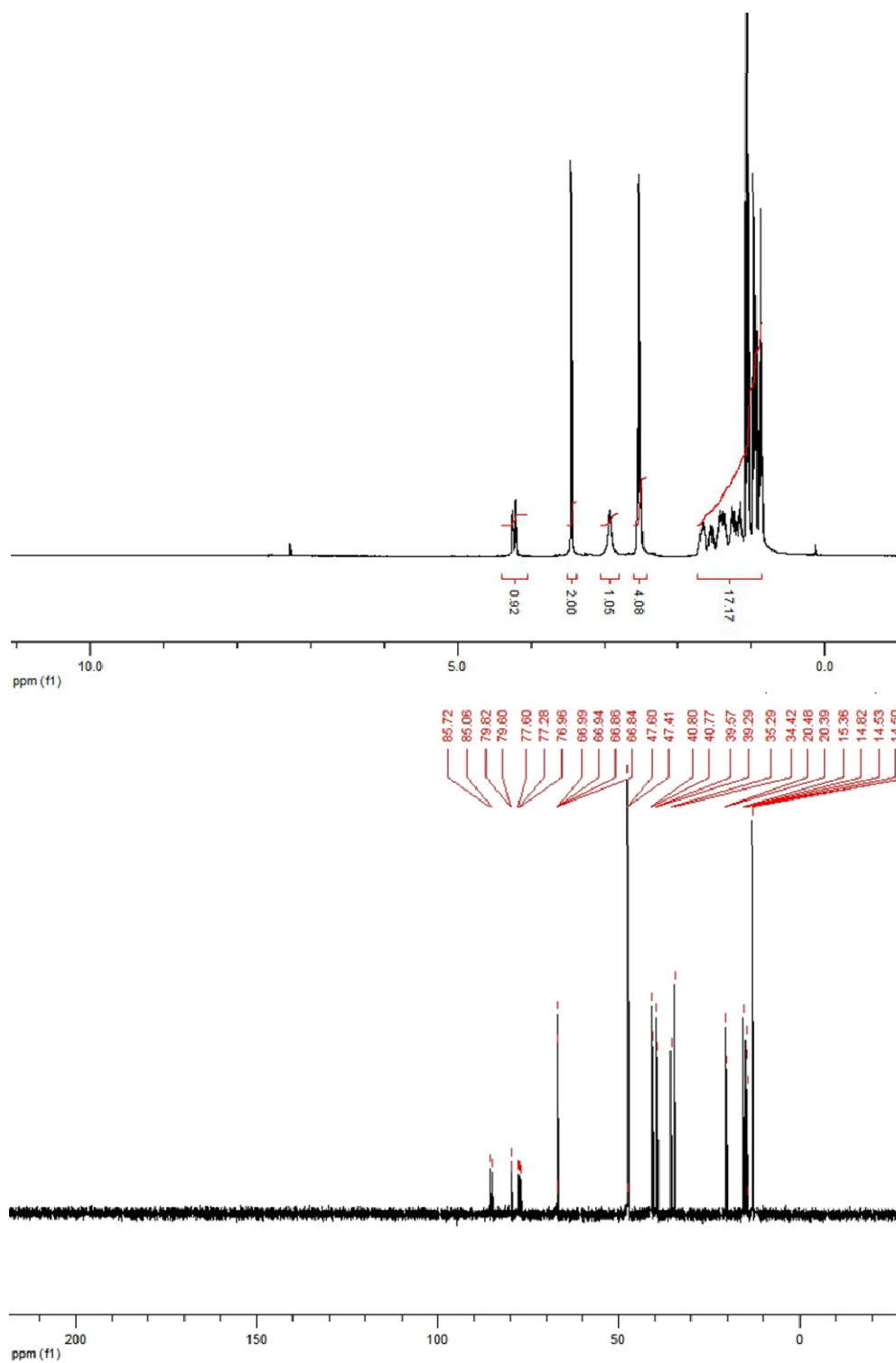


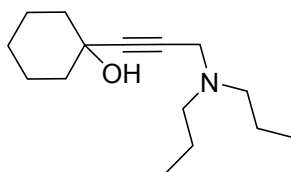
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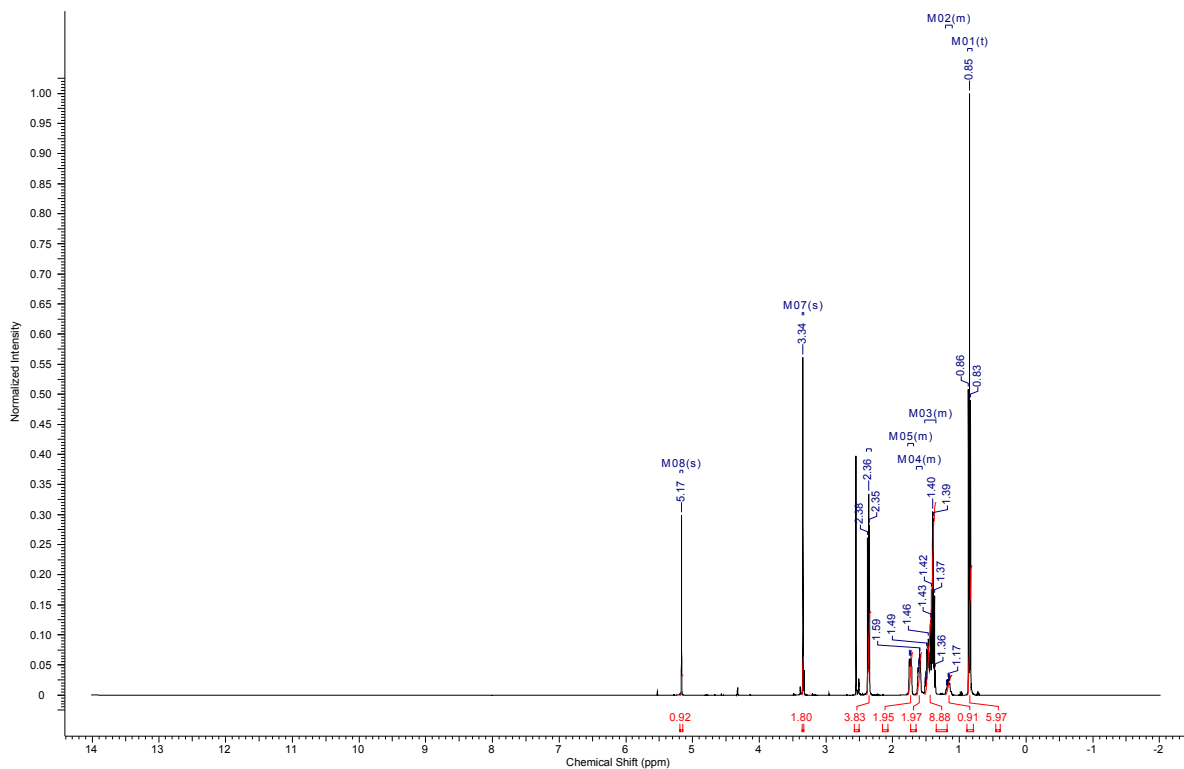


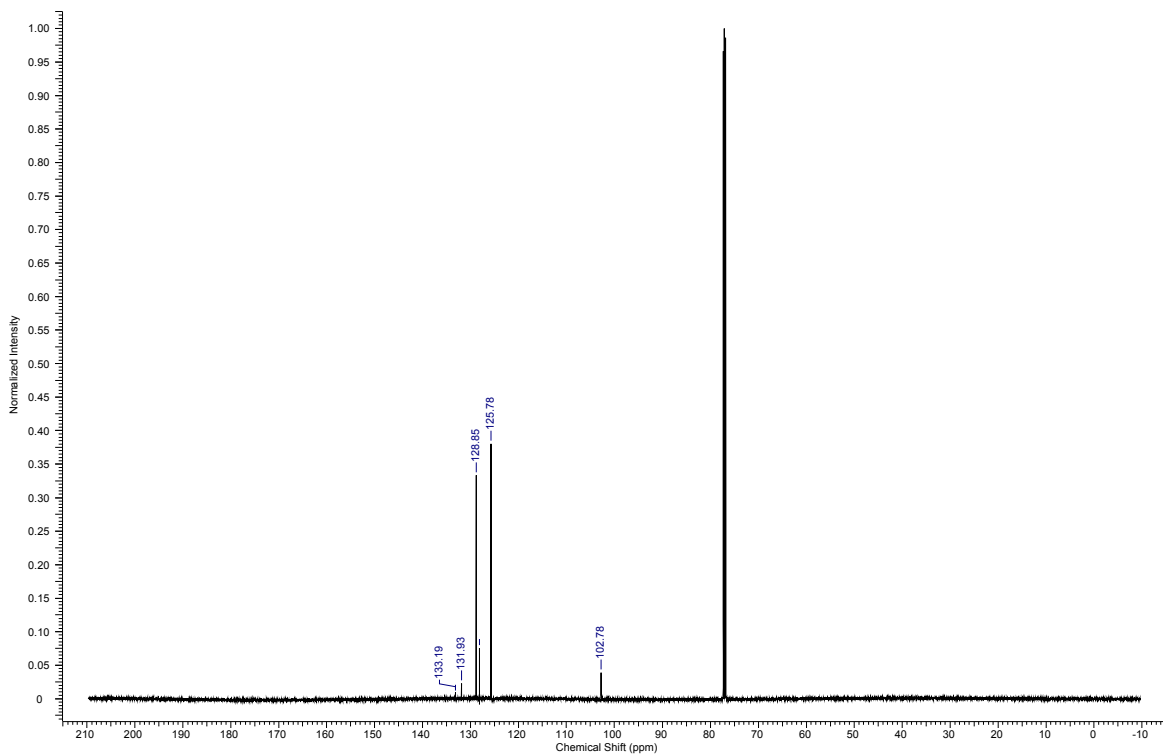
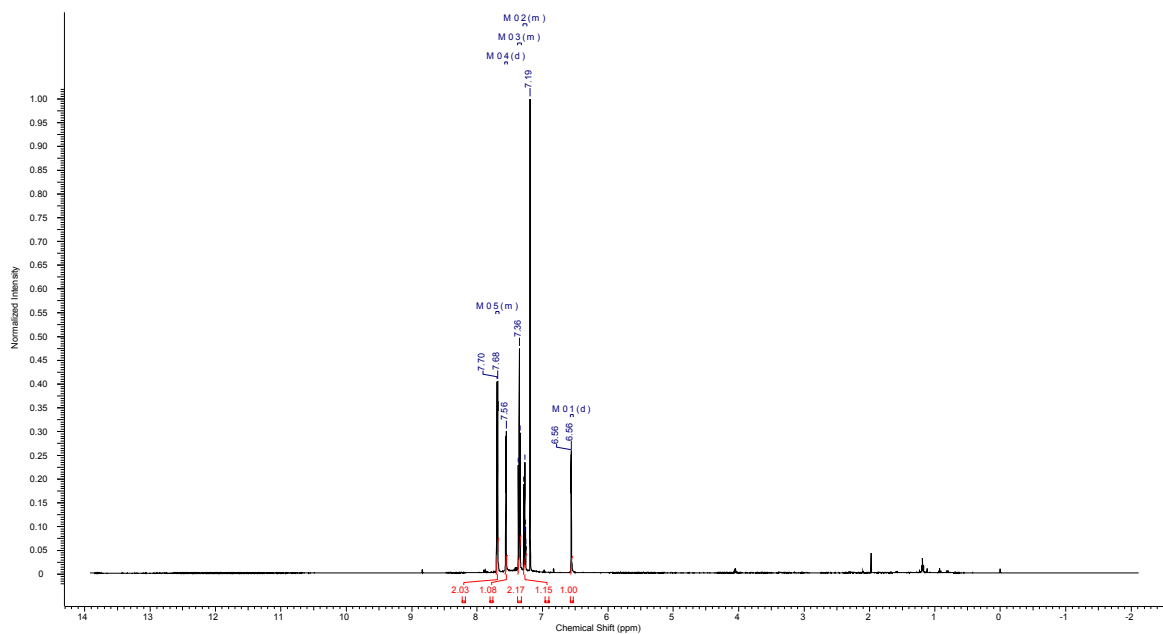
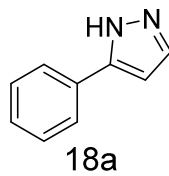
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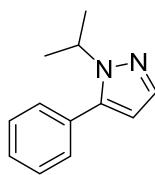




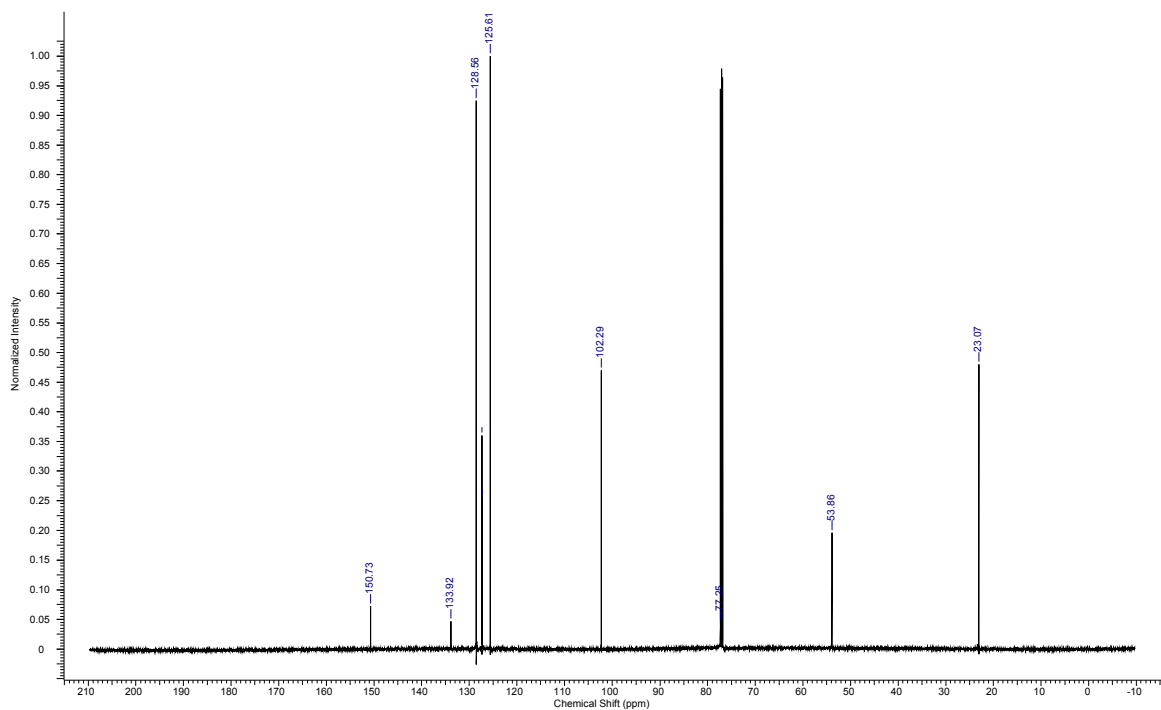
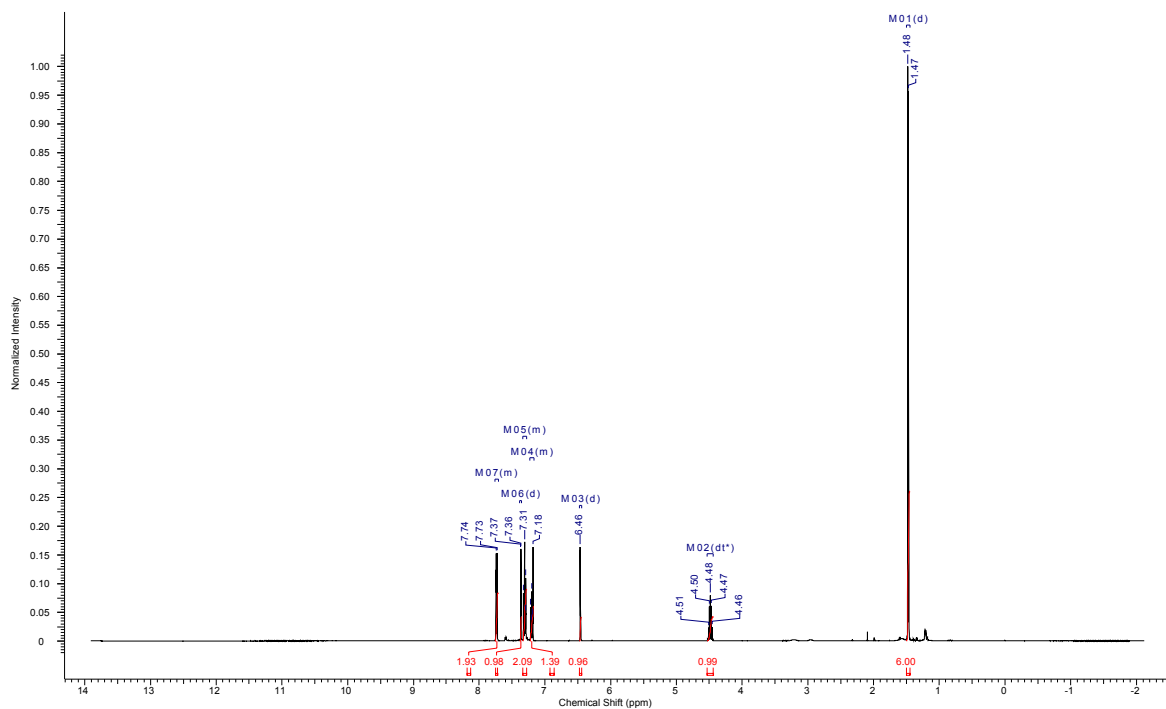
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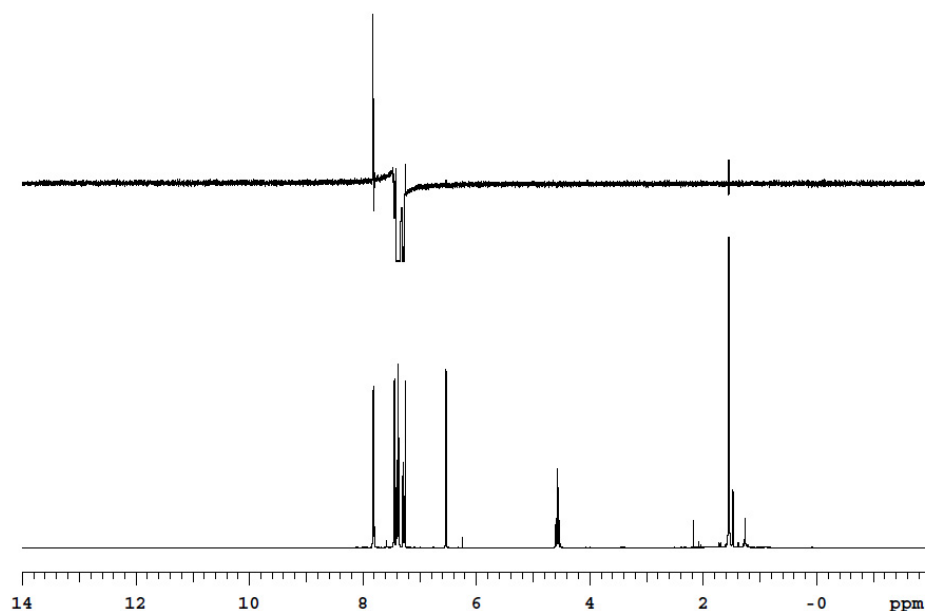
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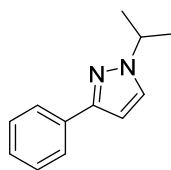


Pulse Sequence: NOESY1D
Solvent: CDCl3

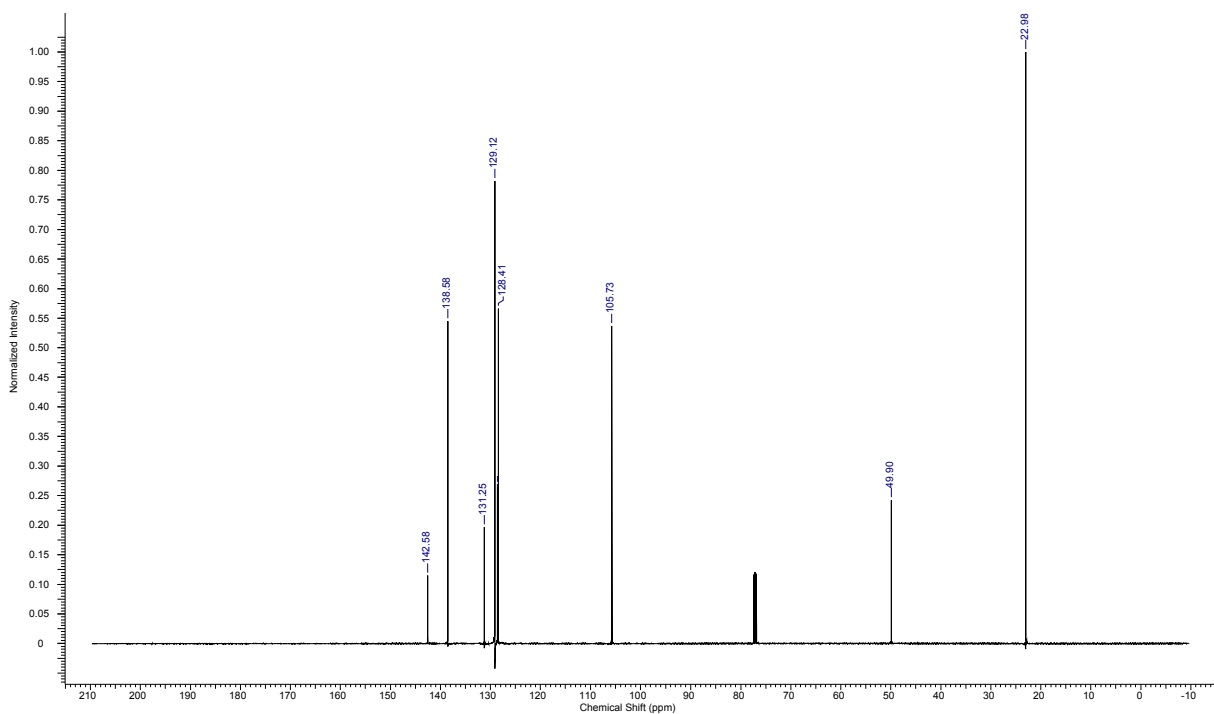
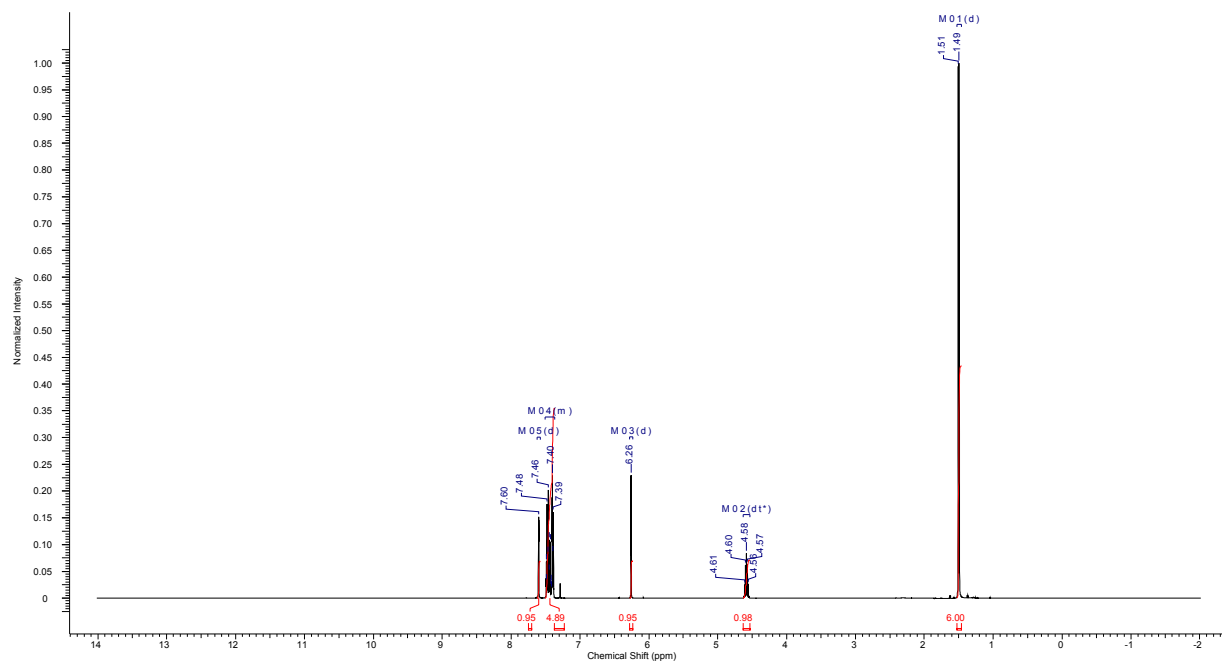
Temp. 25.0 C / 298.1 K
Sample #29, Operator: proper

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Pulse 90.0 degrees
NOE Mixing 0.800 sec
Acq. time 2.556 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 400.1994812 MHz
DATA PROCESSING
Gauss apodization 1.181 sec
FT size 65536
Total time 6 min 10 sec



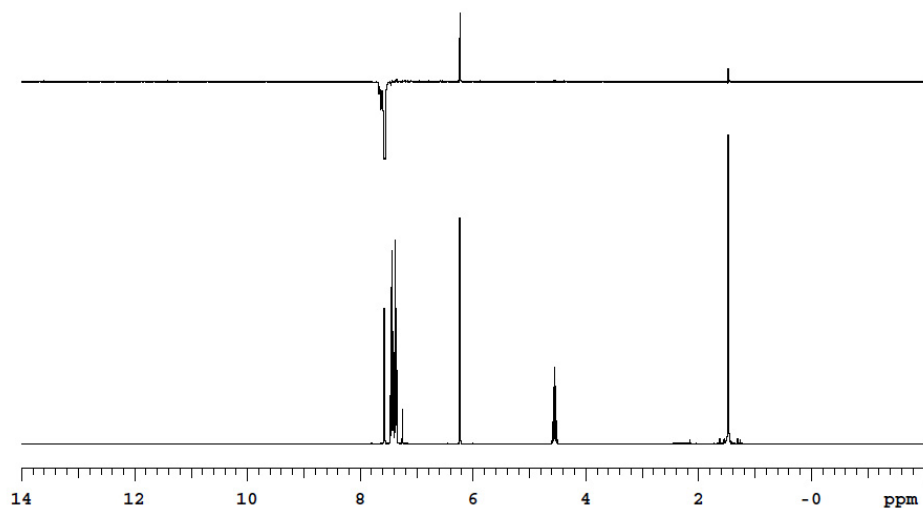


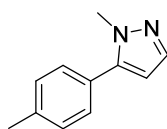
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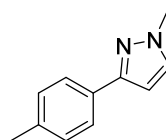
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DATA PROCESSING
Gauss apodization 1.181 sec
FT size 65536
Total time 6 min 10 sec

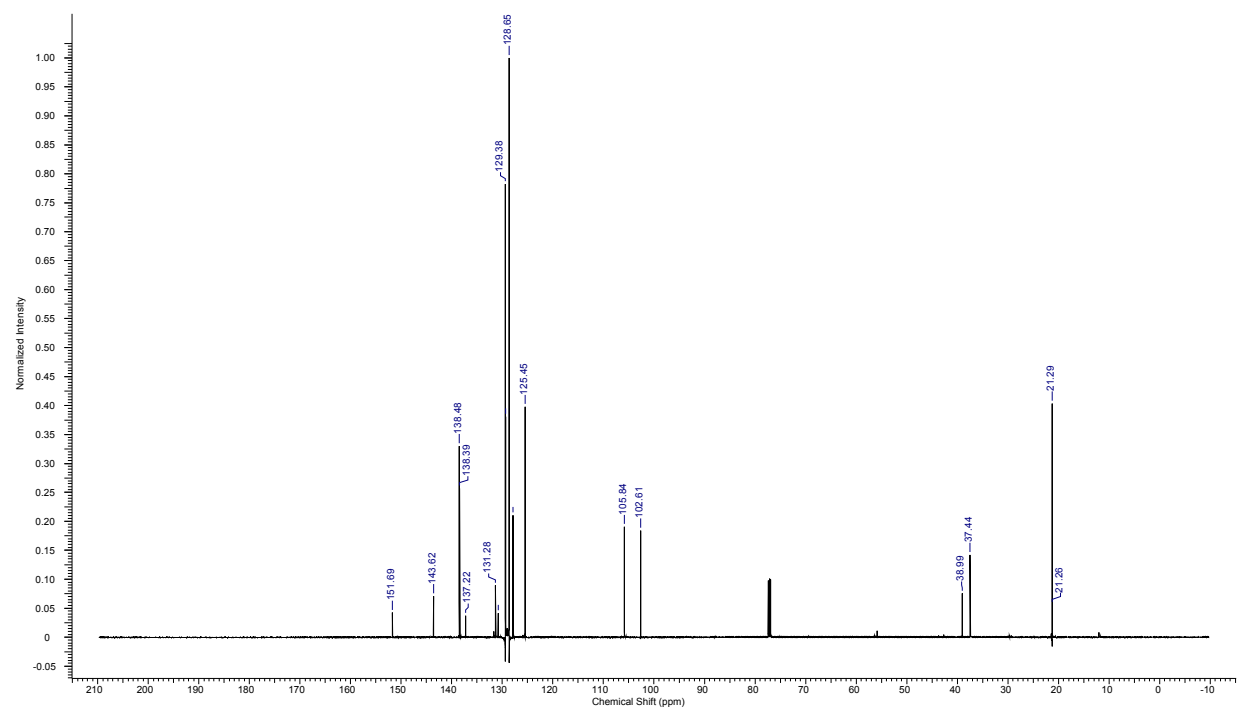
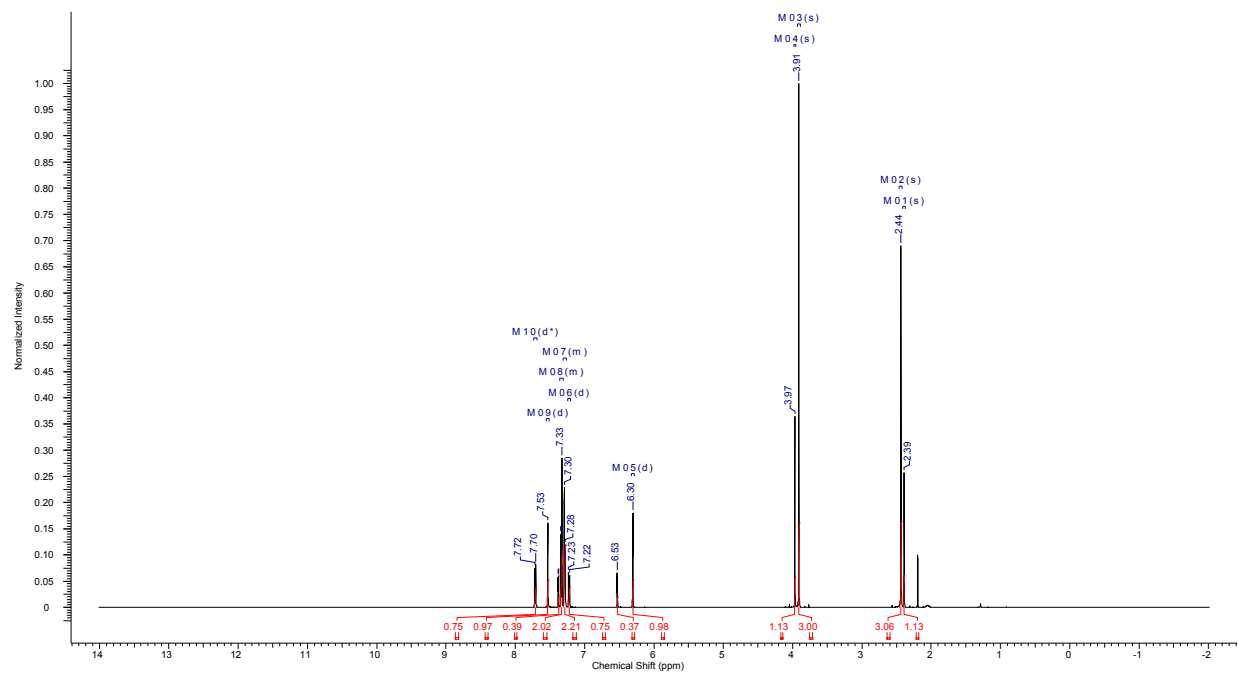


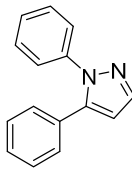


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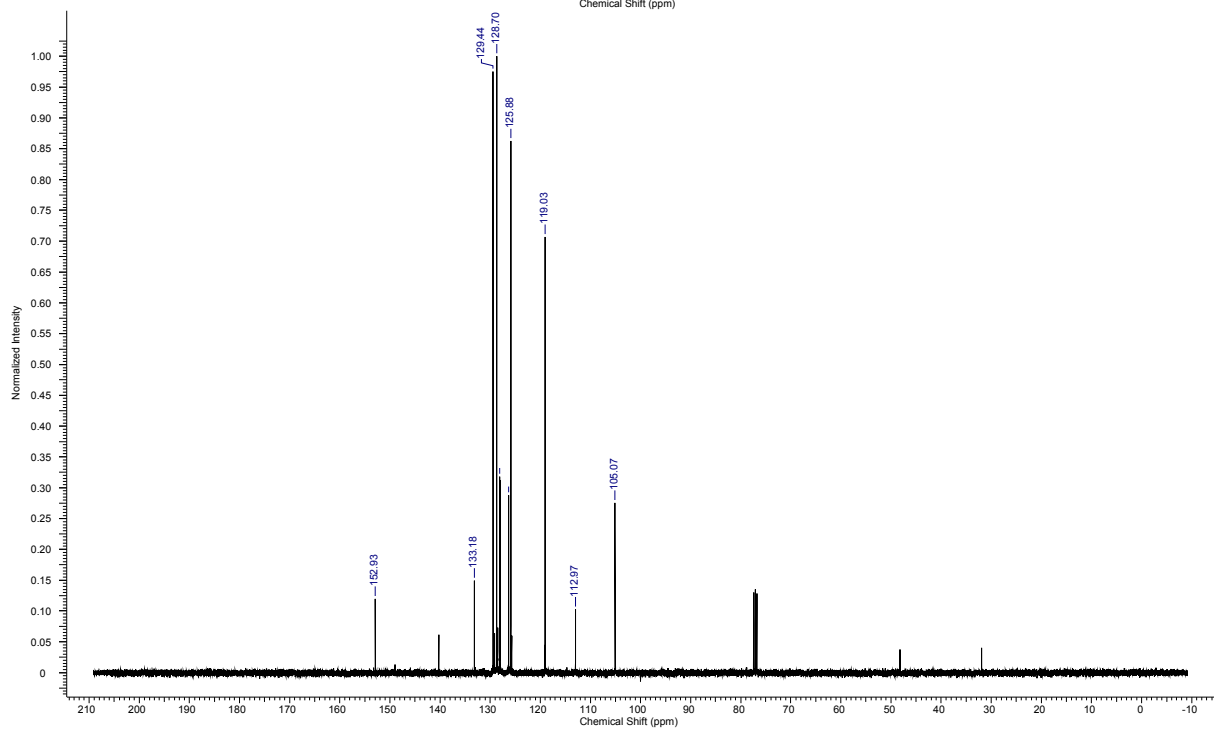
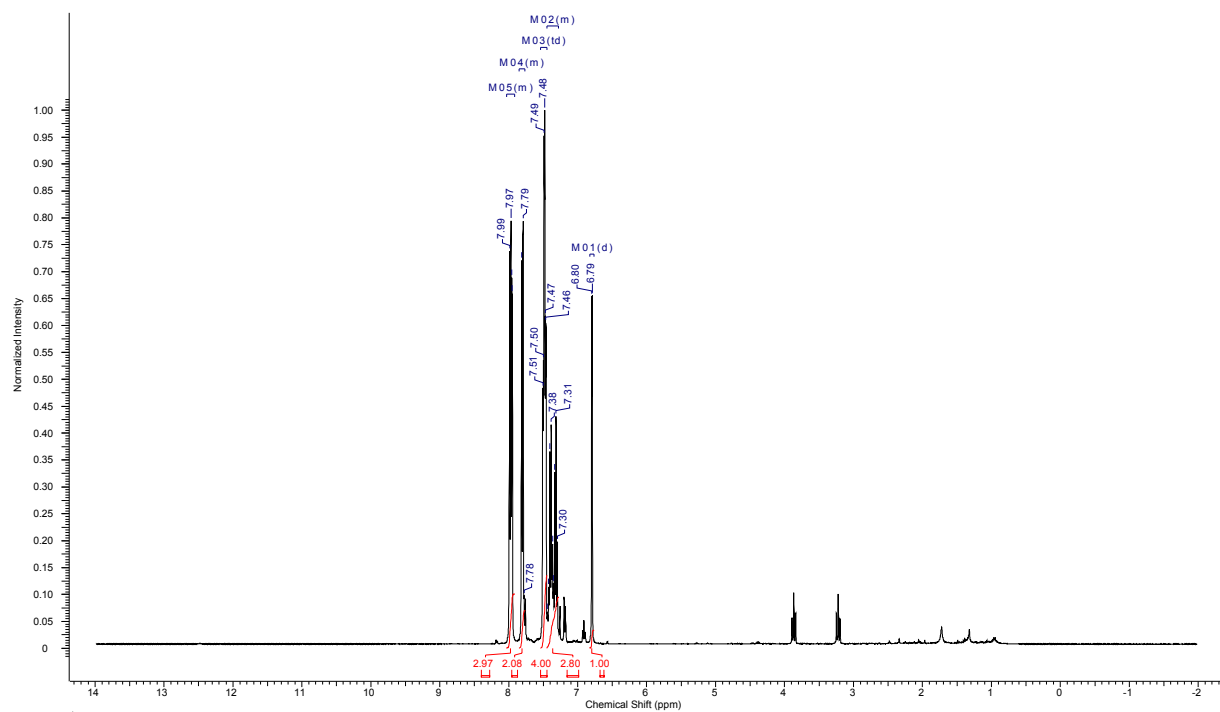


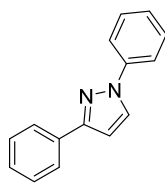
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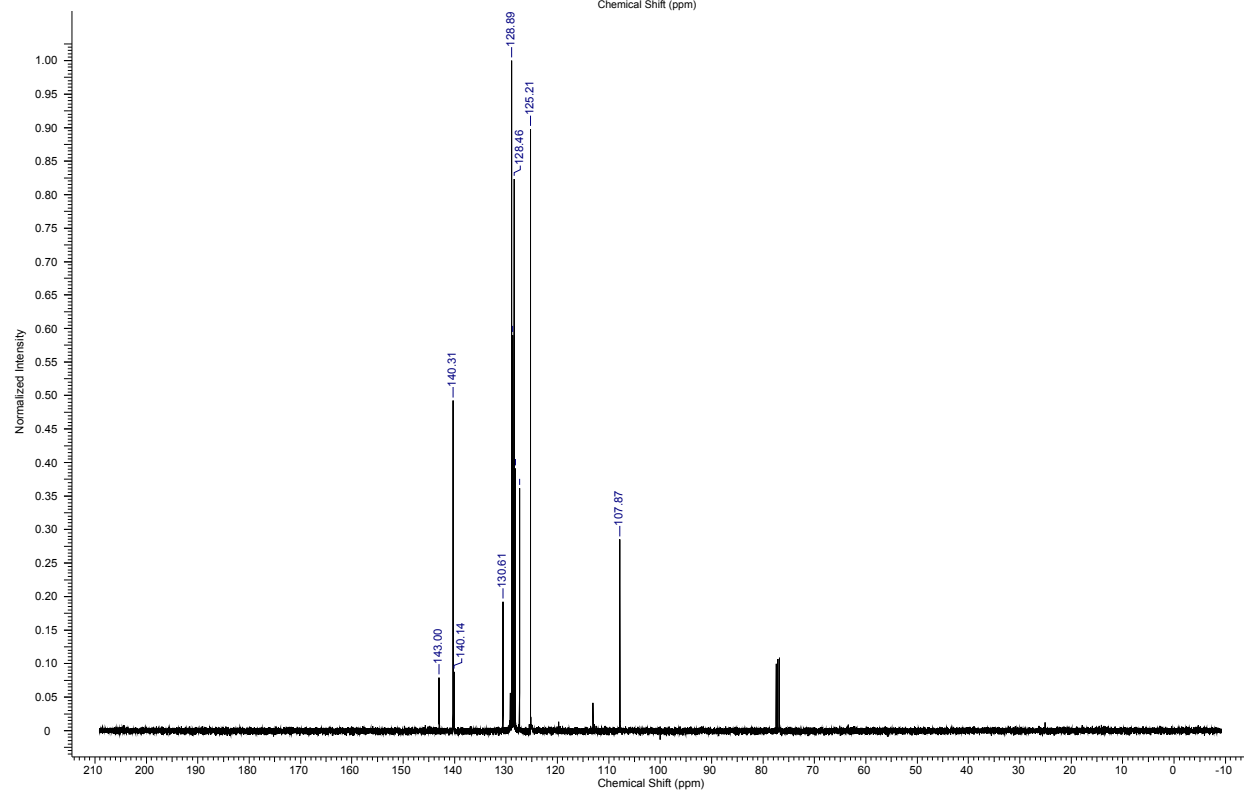
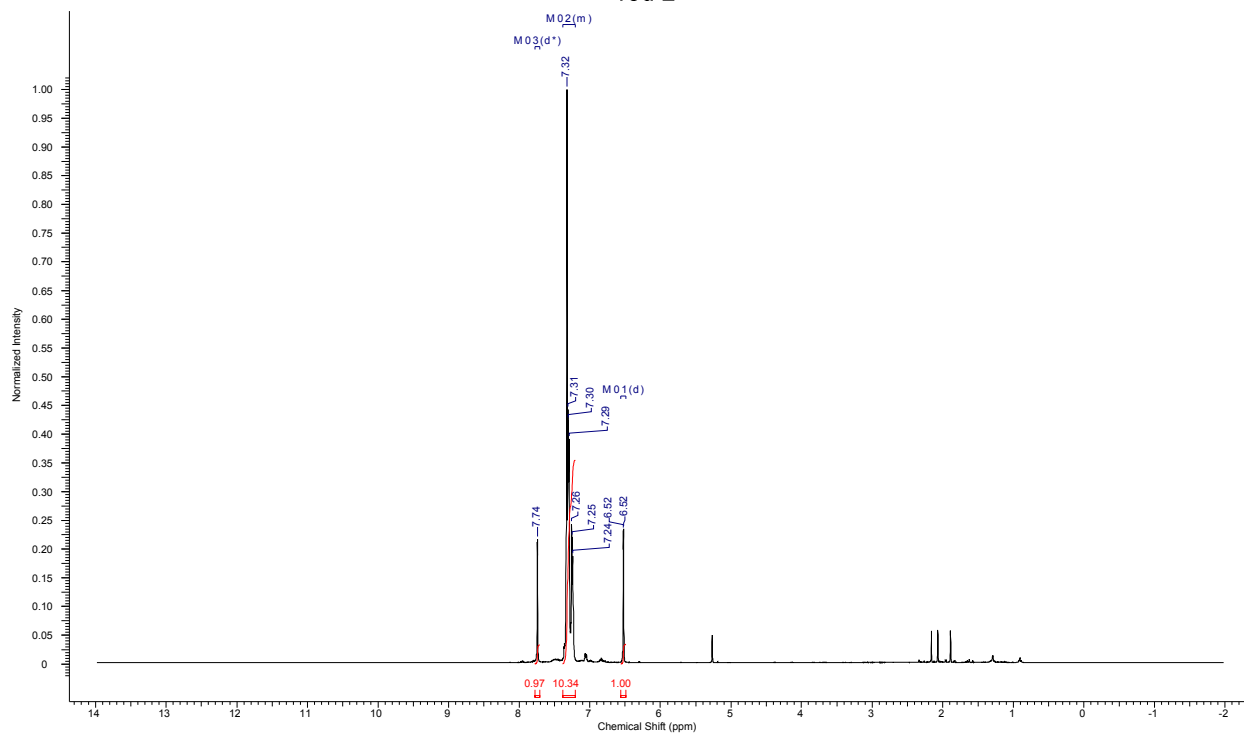


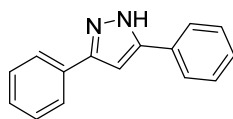
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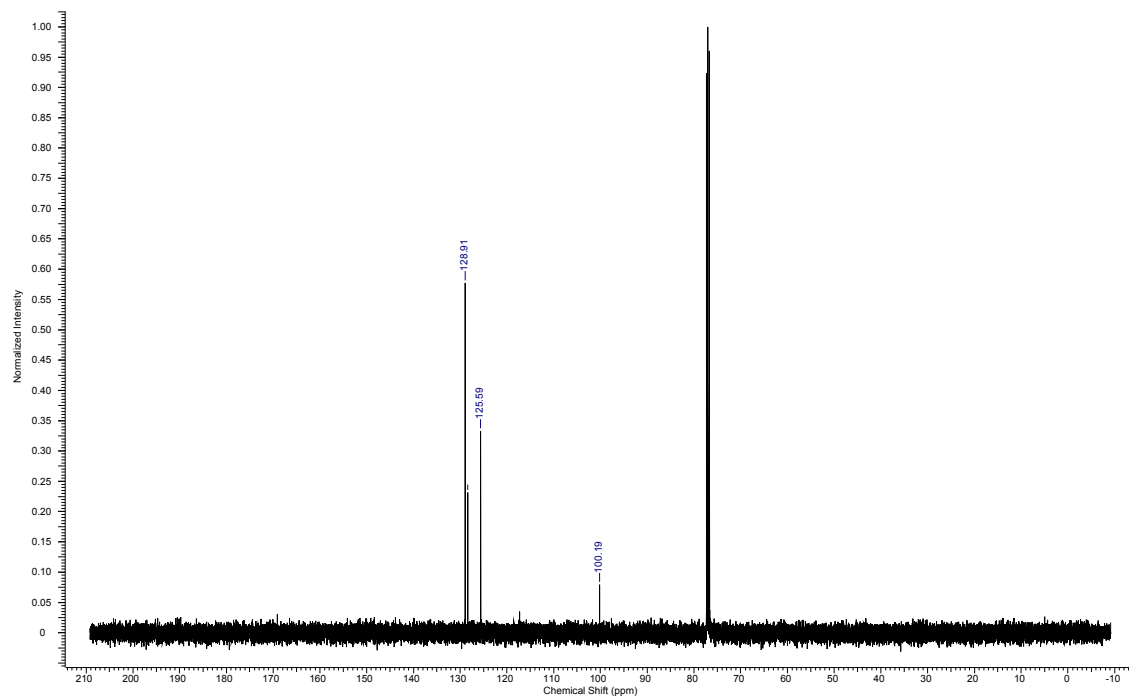
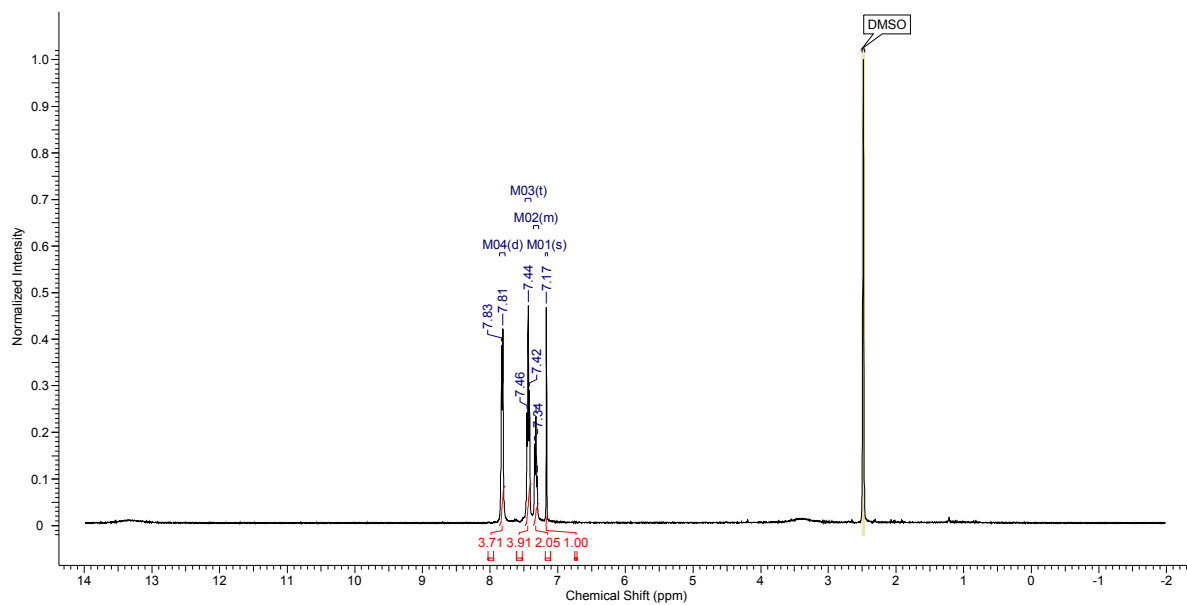


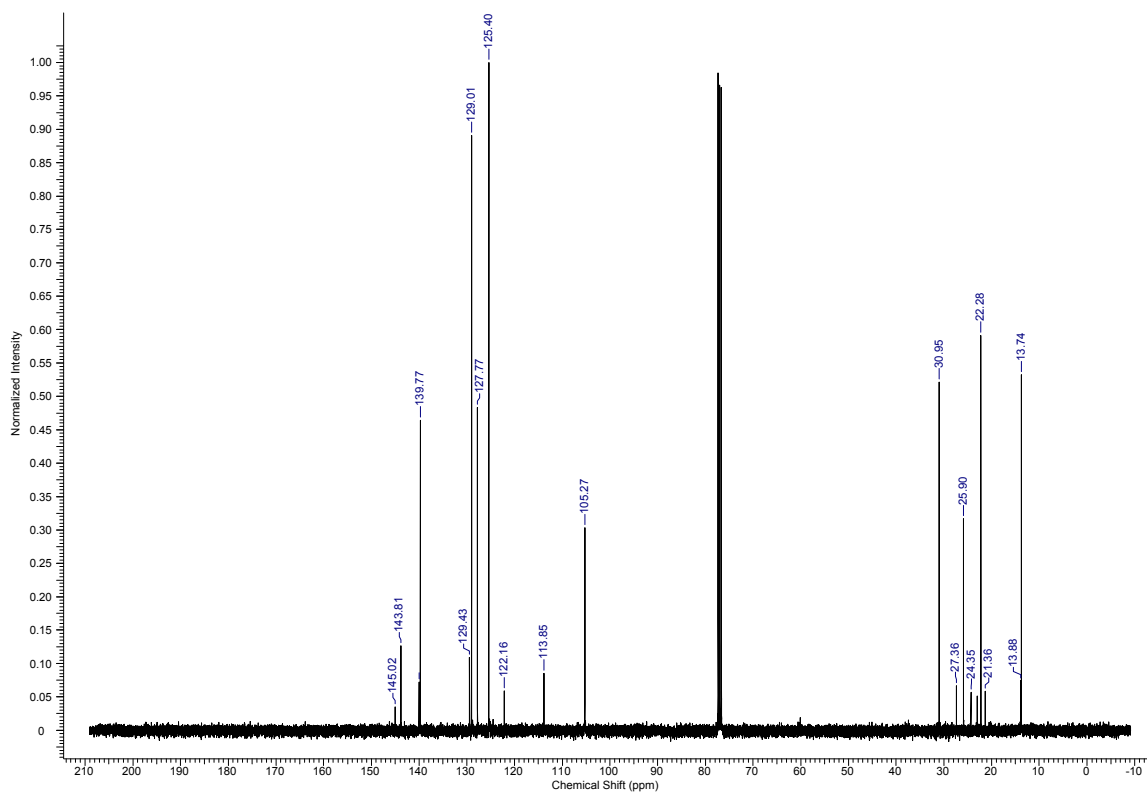
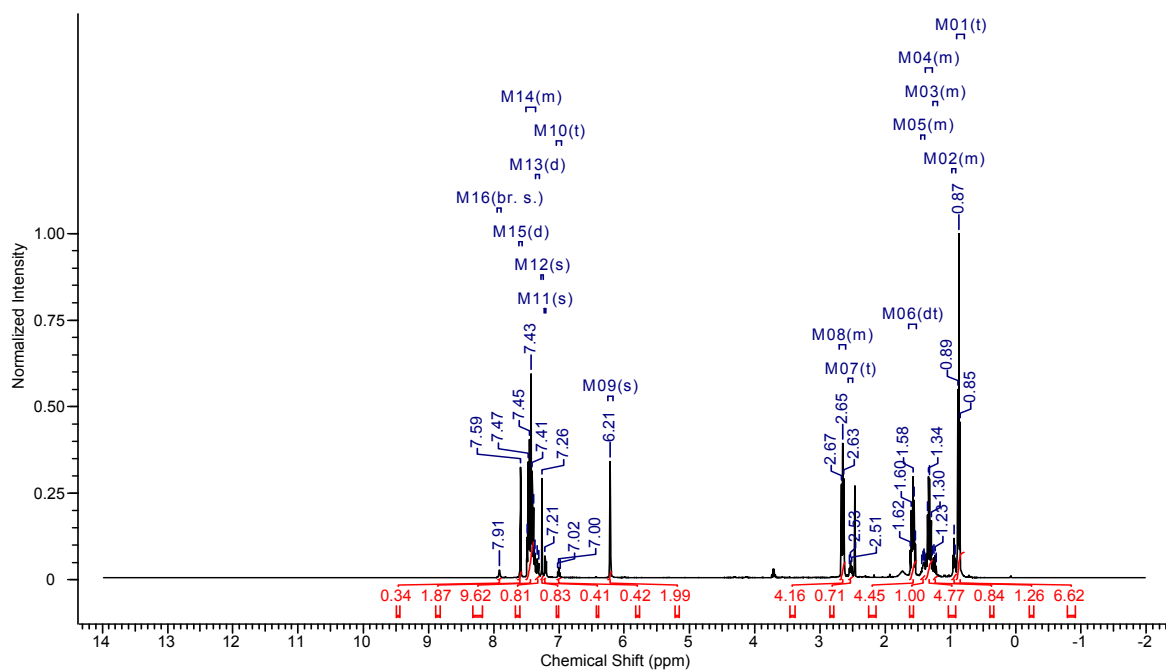
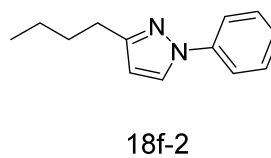
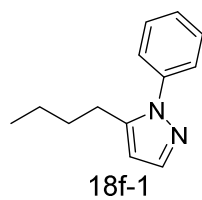
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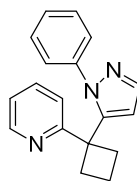




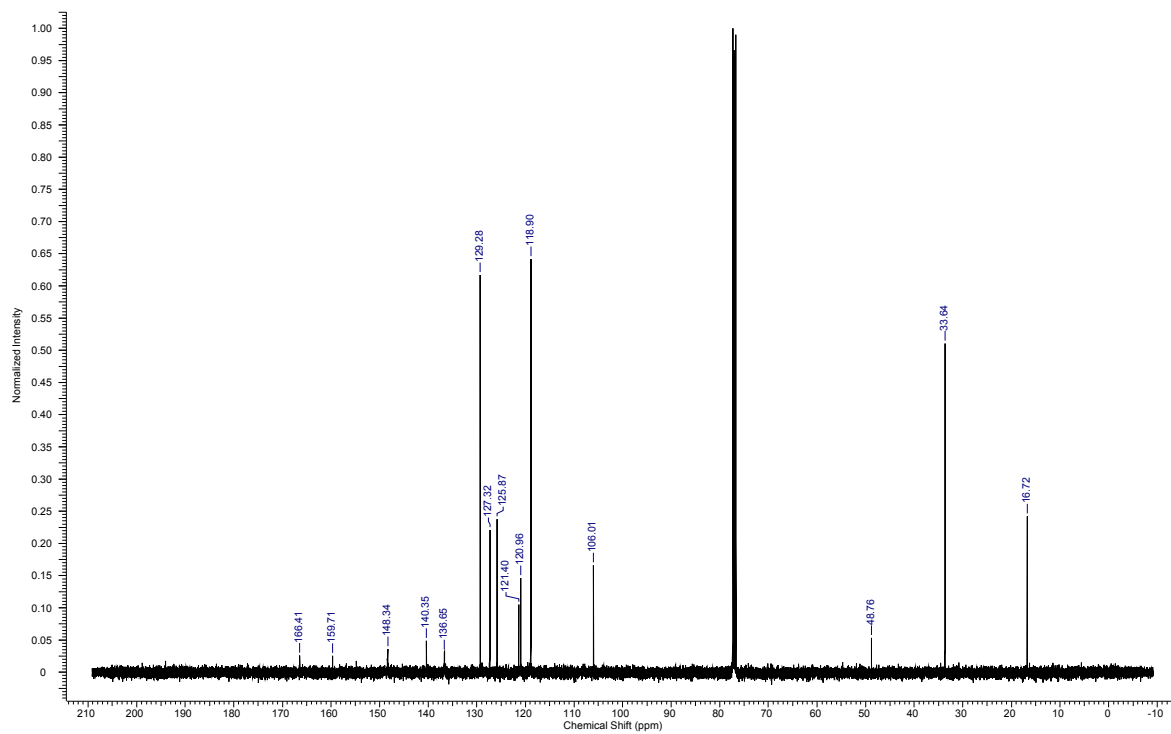
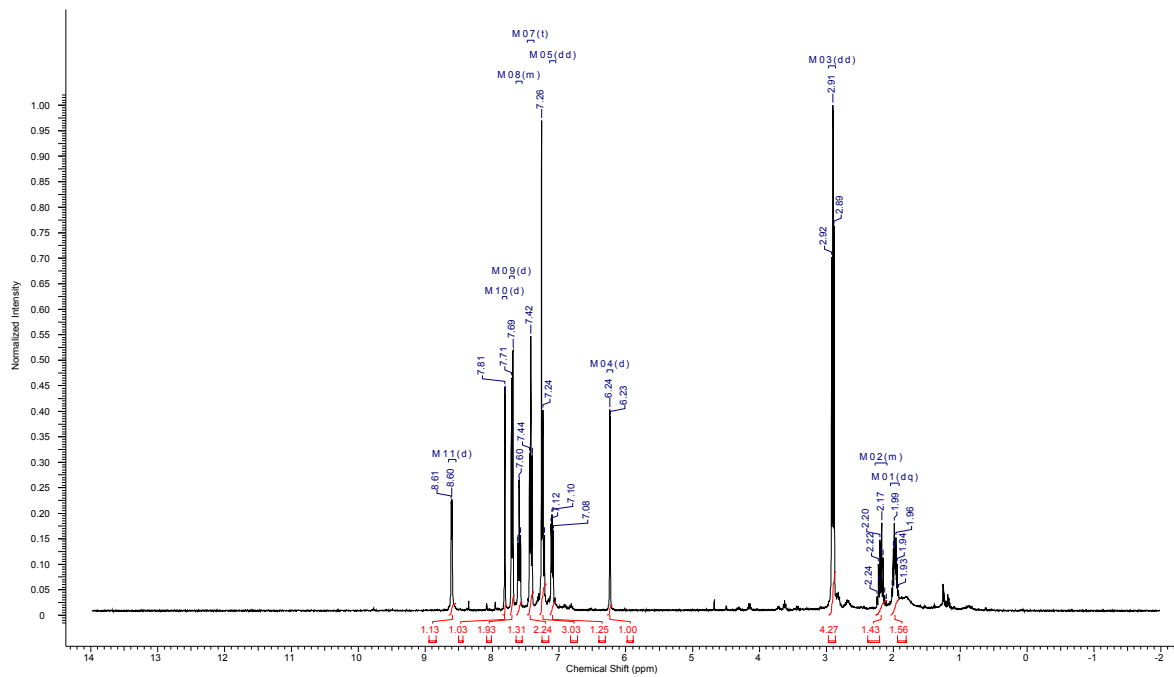
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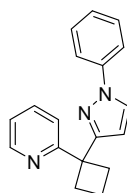




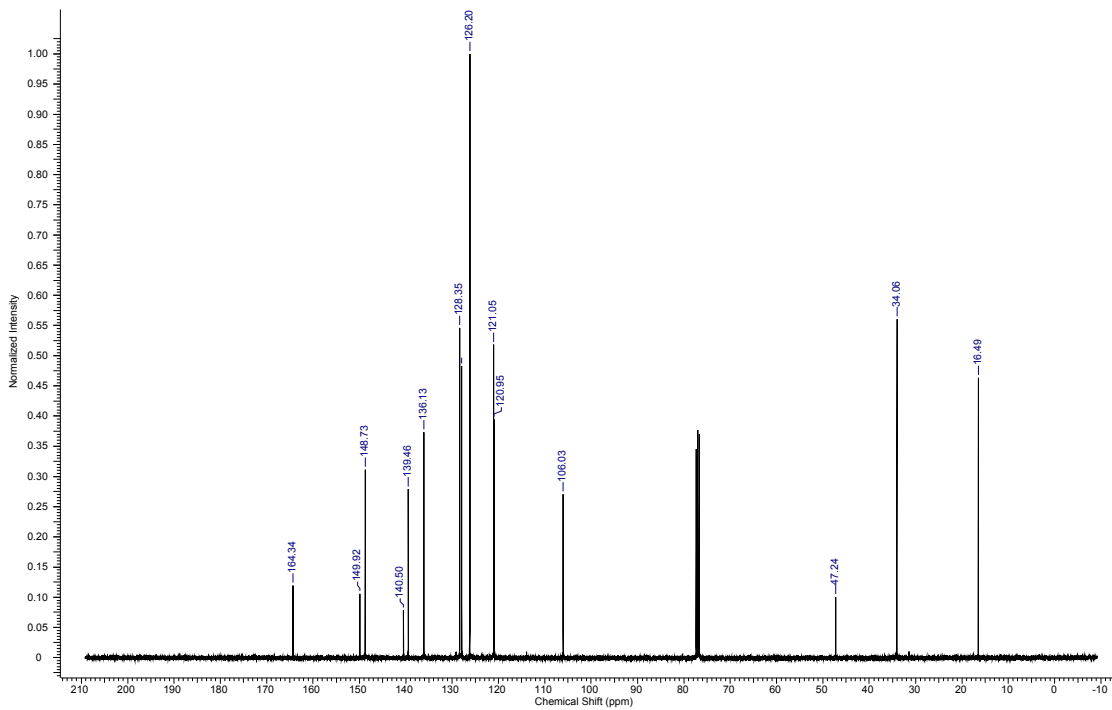
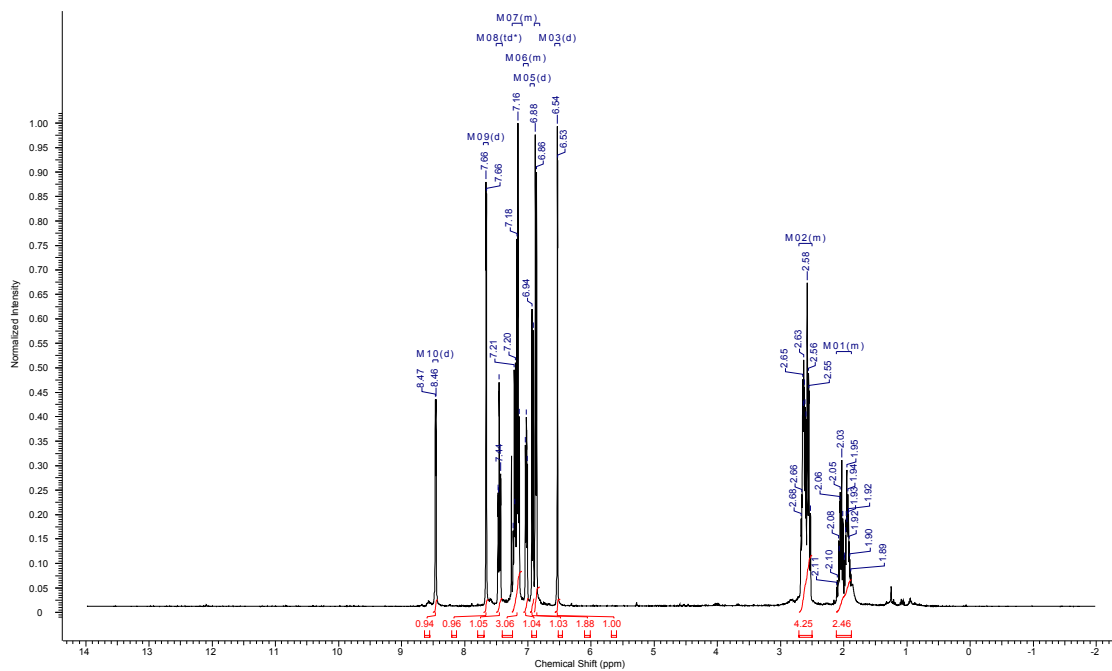


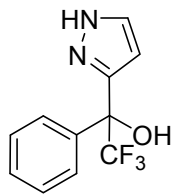
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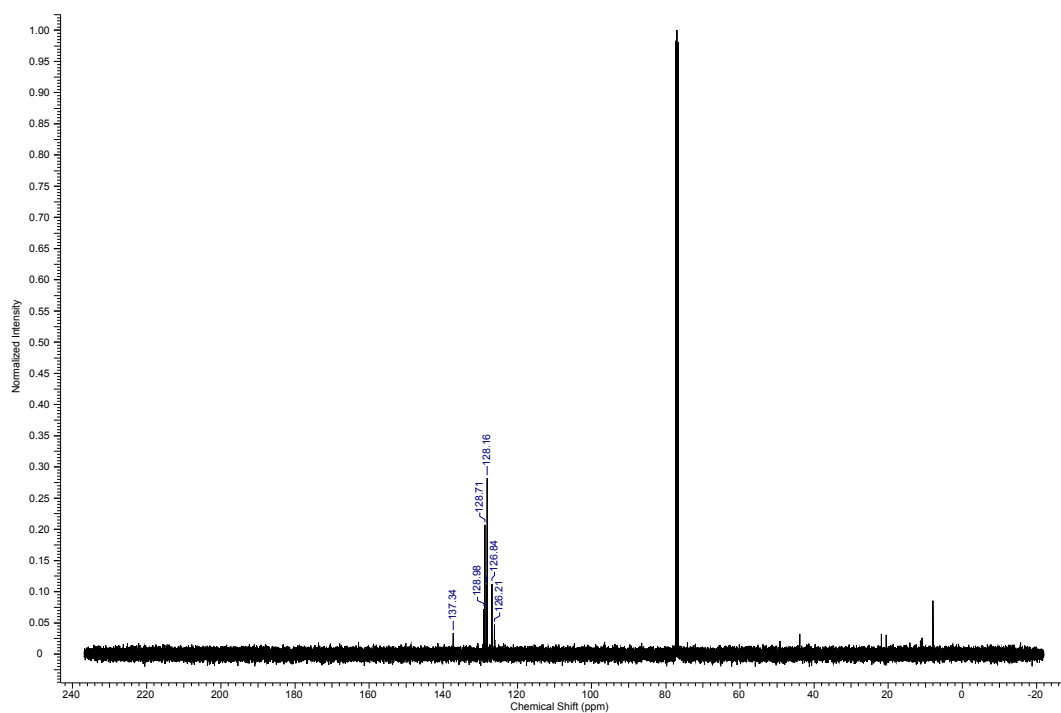
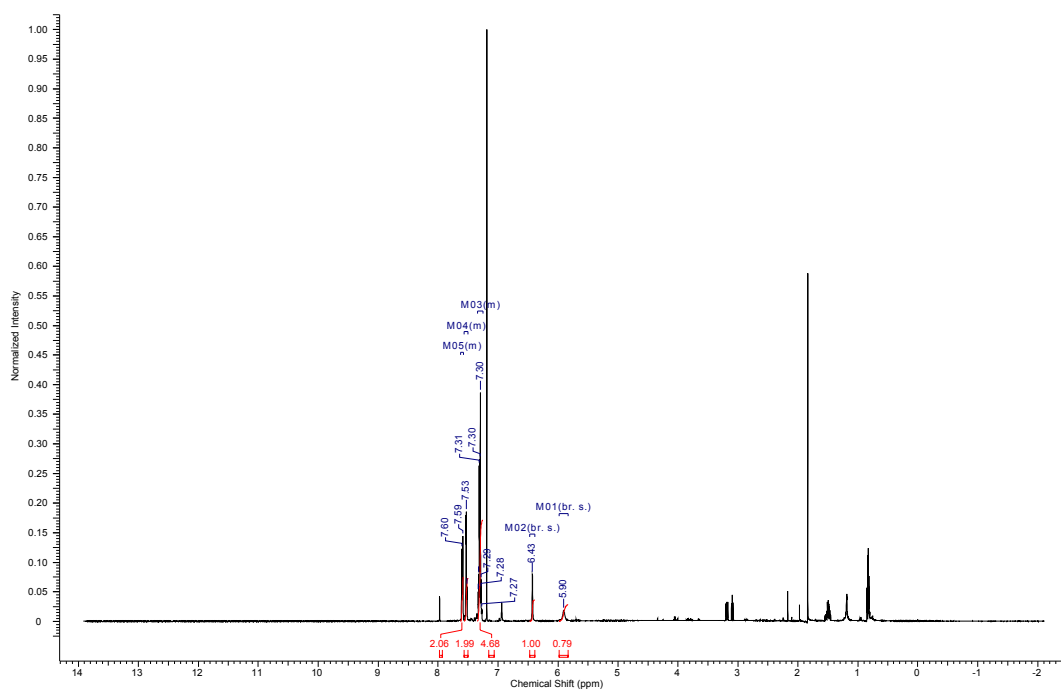


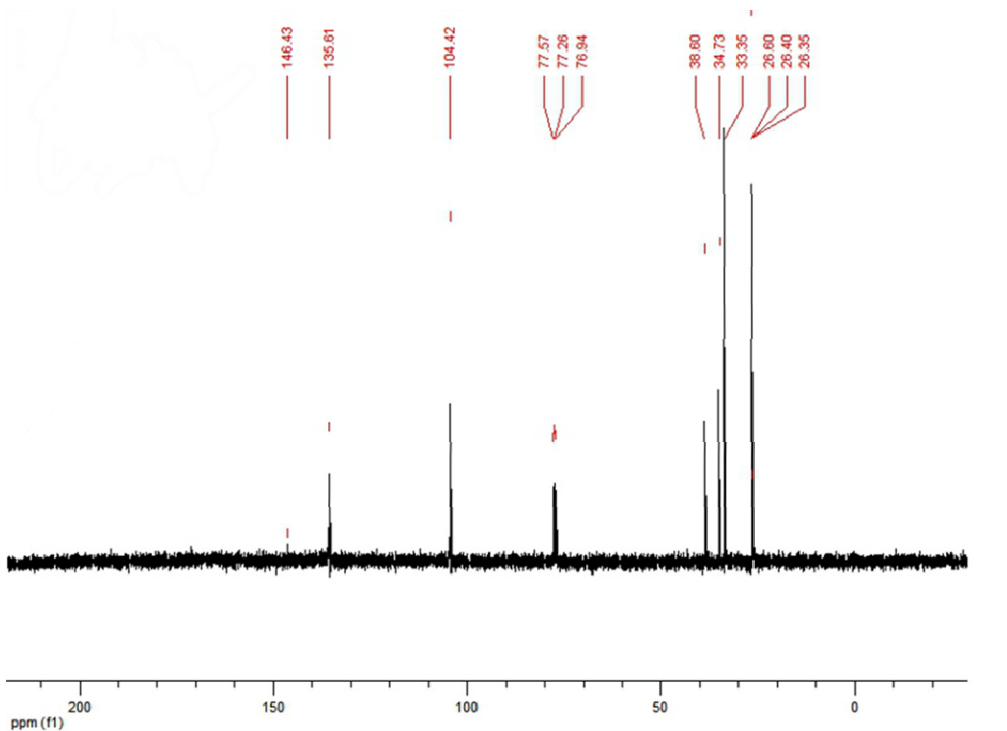
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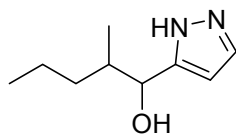




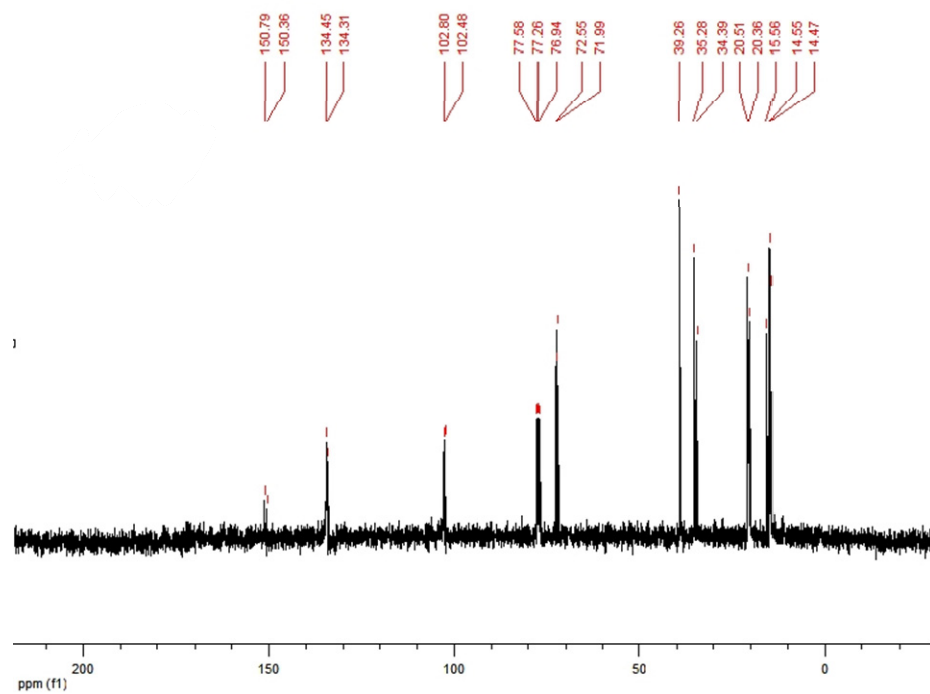
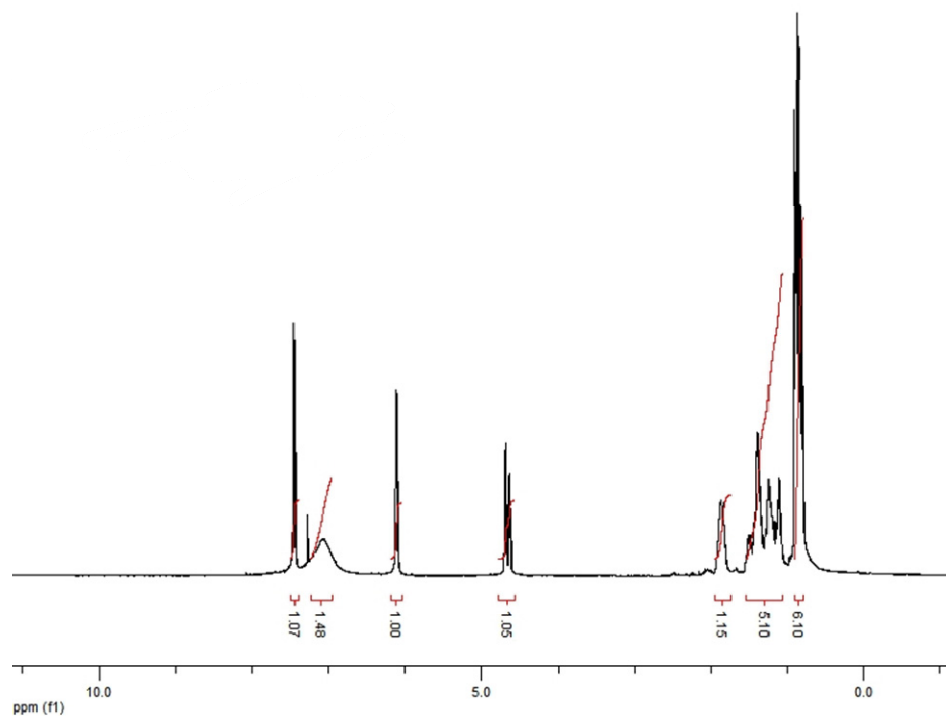
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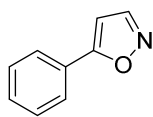




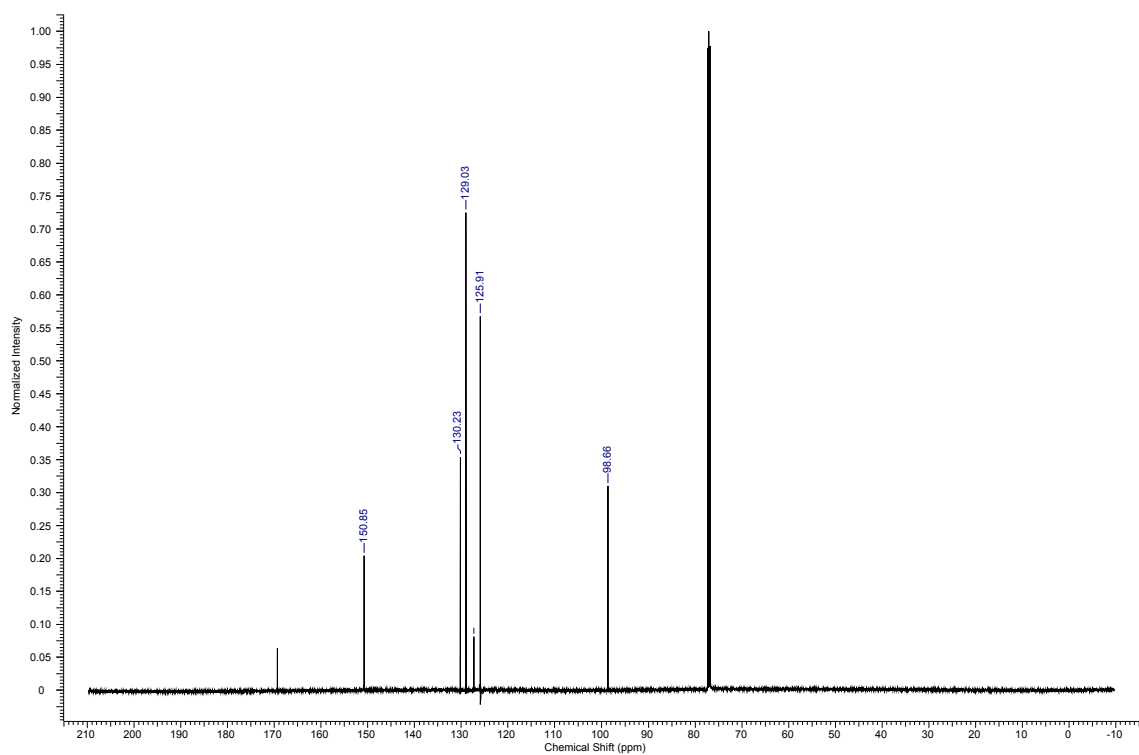
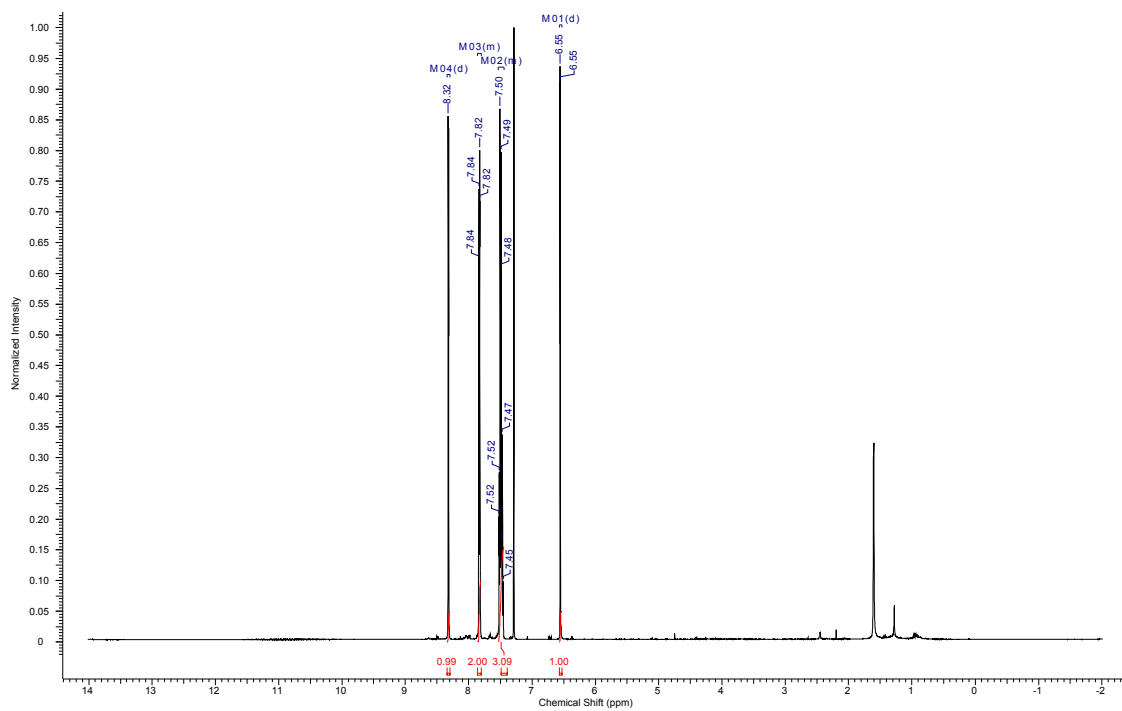


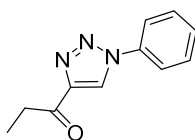
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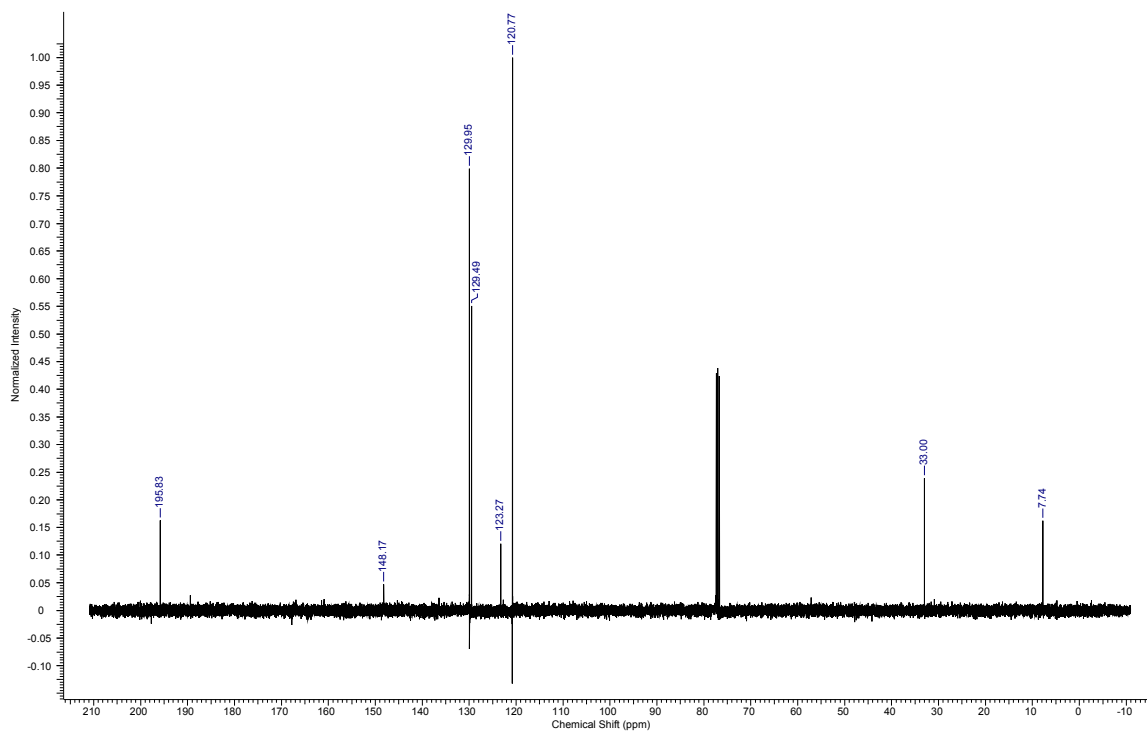
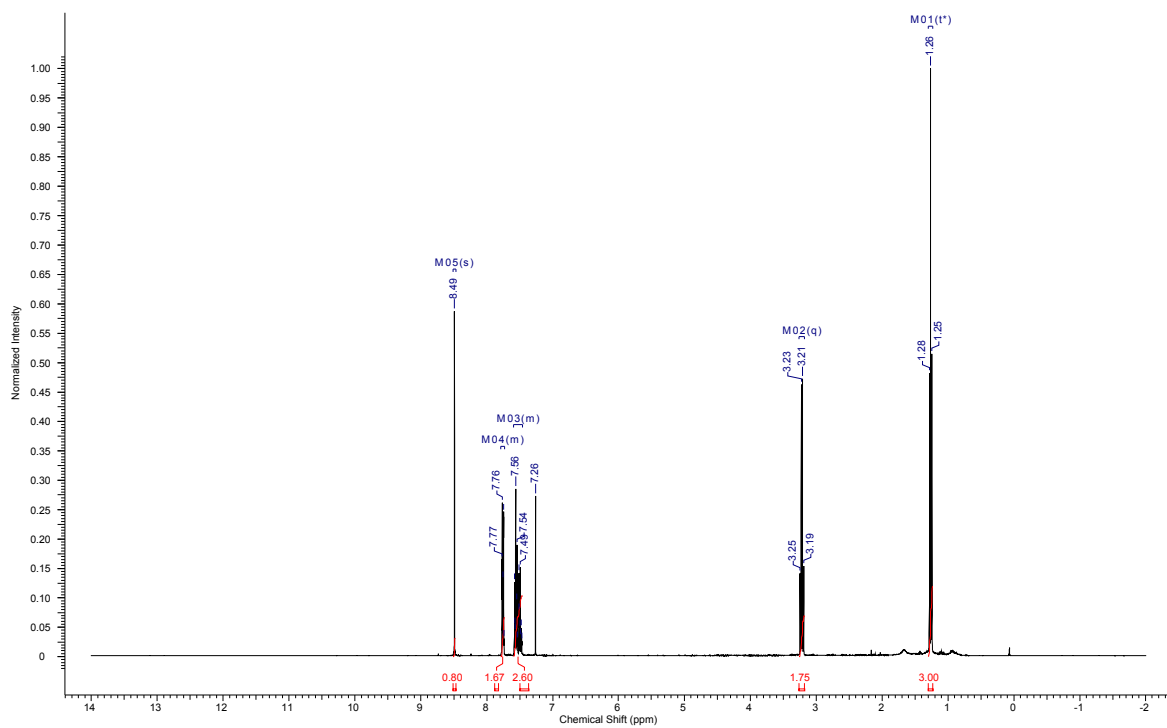


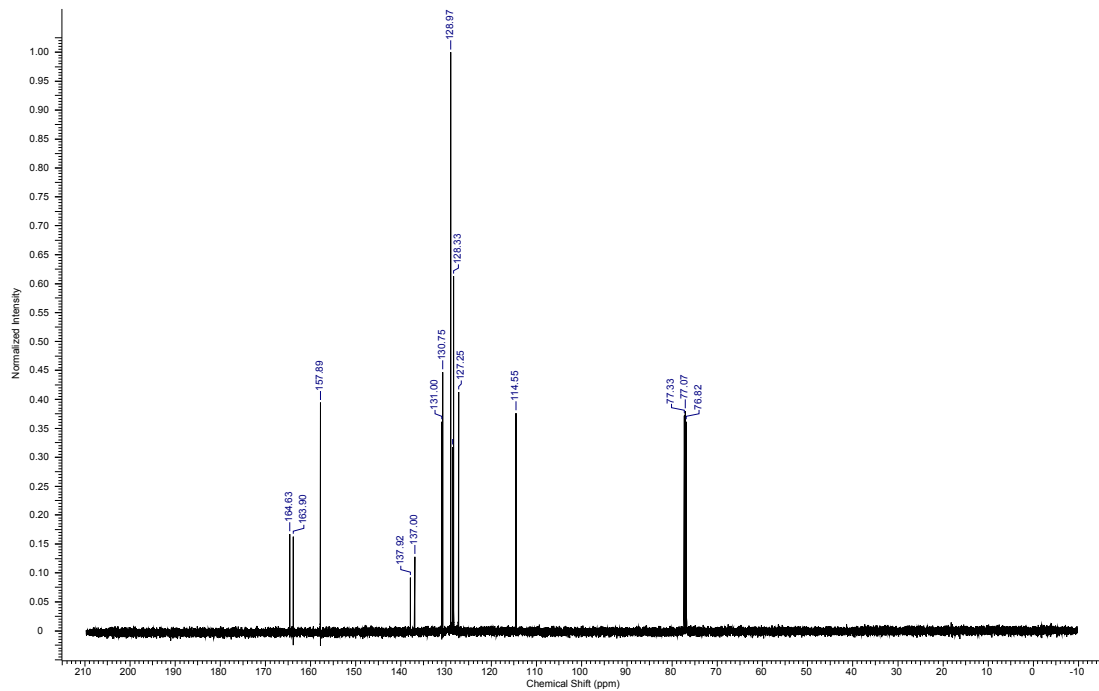
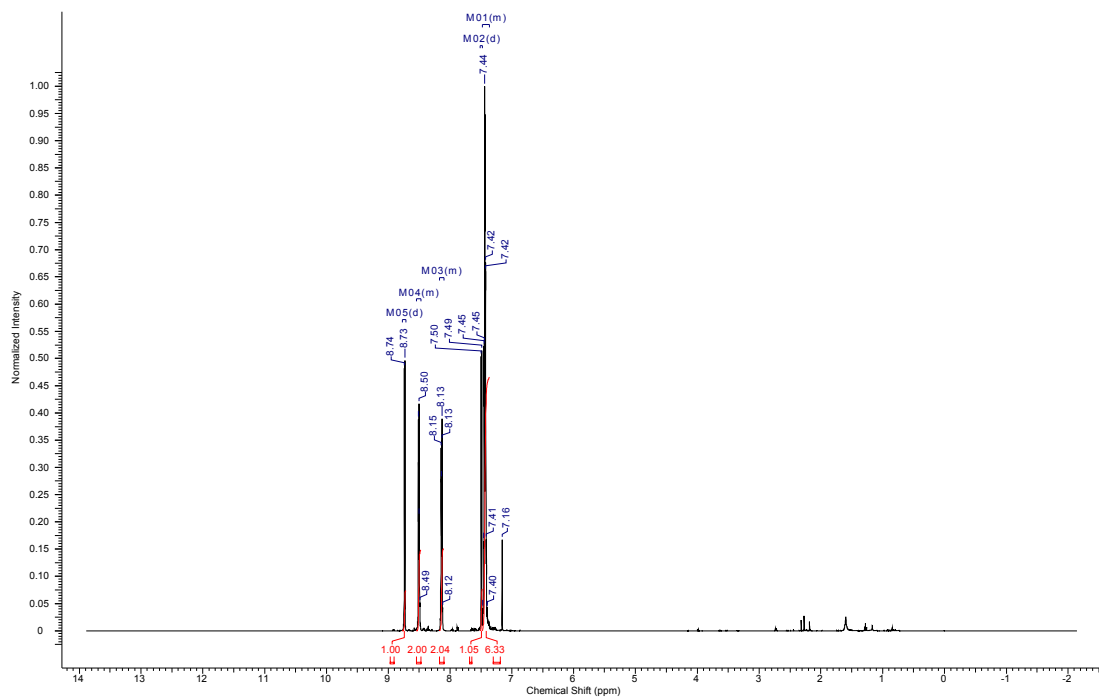
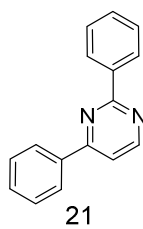
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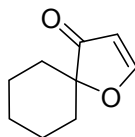




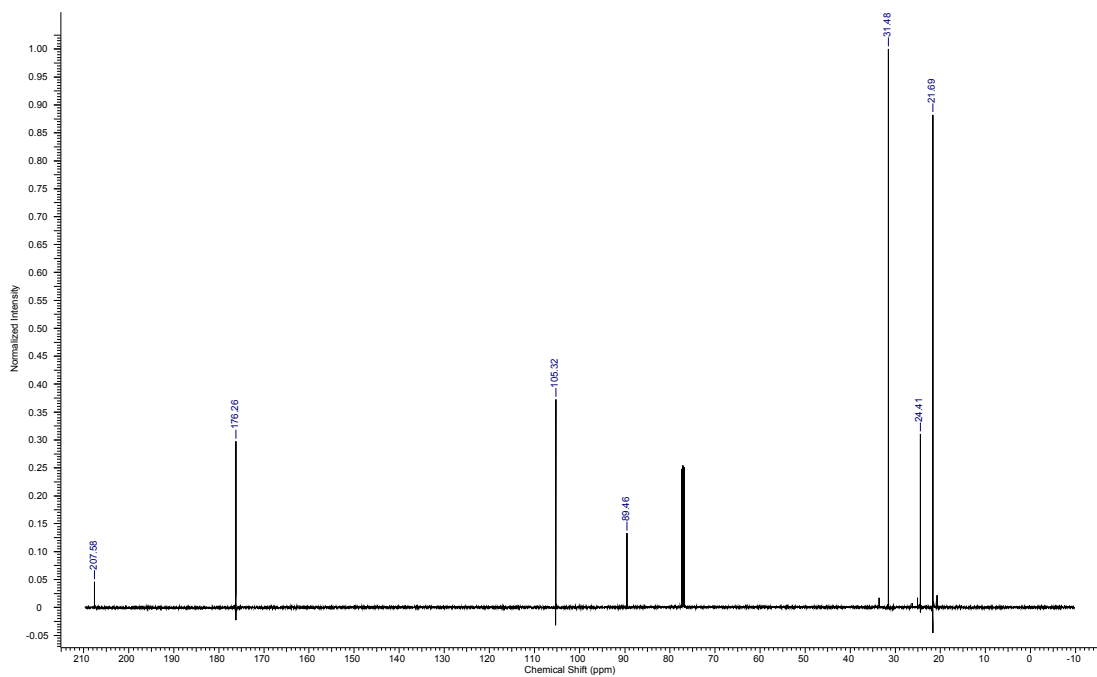
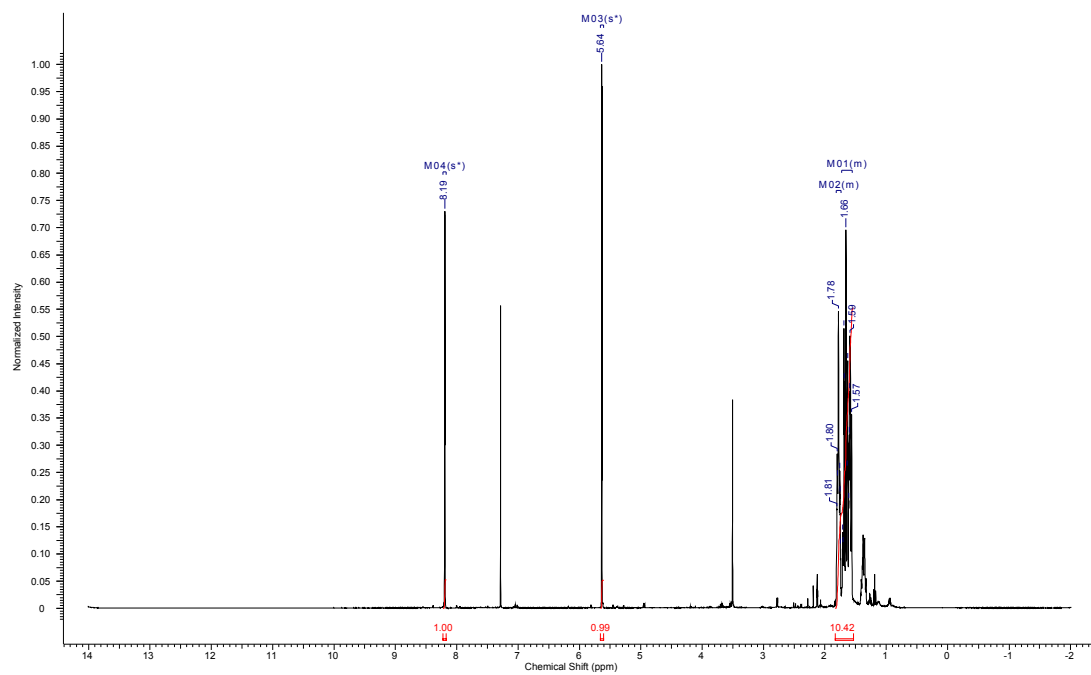
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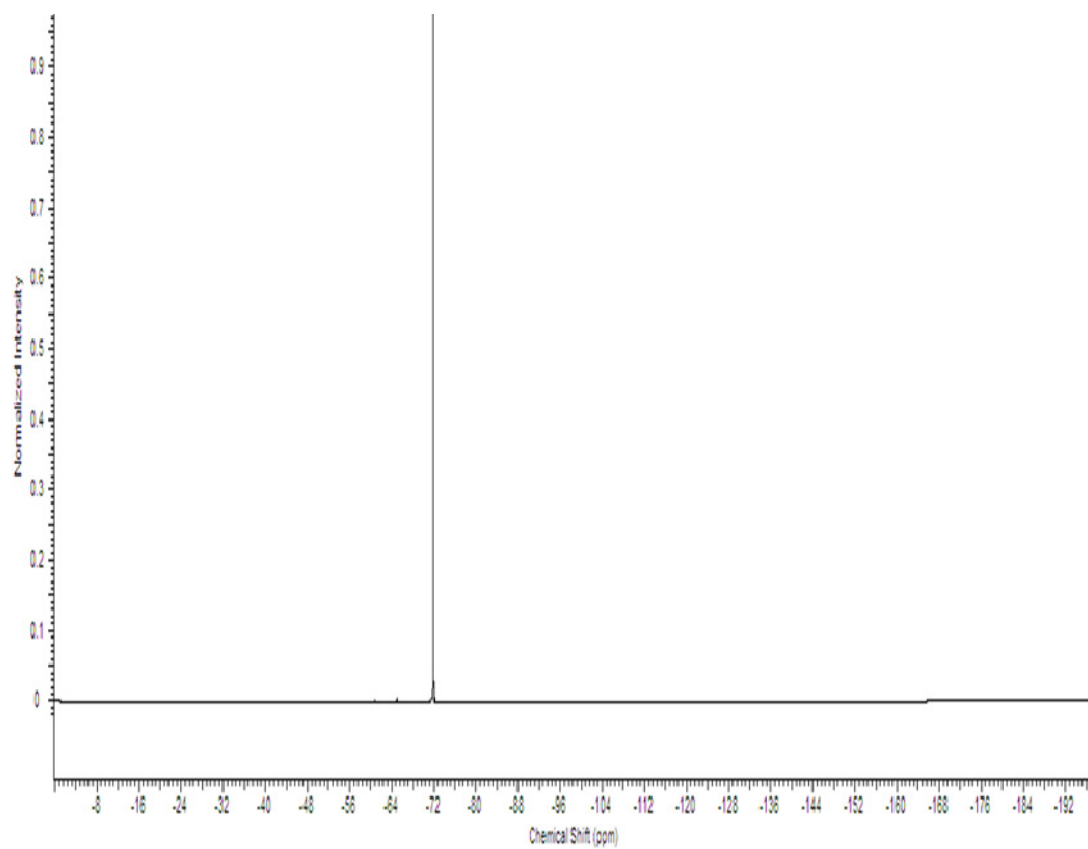


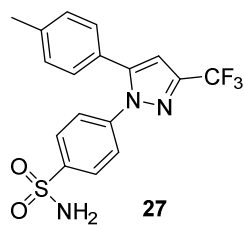




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LCMS chromatogram, ELSD ratio of **27** and regioisomer

