Supporting Information for

Copper(I)-catalyzed access to 1,4,5-trisubstituted 1,2,3-triazoles via cycloaddition of azides and 1-iodoalkynes

Jason E. Hein, Jonathan C. Tripp, Larissa Krasnova, K. Barry Sharpless, Valery V. Fokin*

Department of Chemistry, The Scripps Research Institute,
10550 North Torrey Pines Road, La Jolla, California, 92037
Tel. 858.784.7515
Fax 858.784.7559
E-mail: jehein@scripps.edu
fokin@scripps.edu

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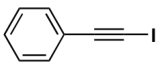
Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500, Bruker AMX-400 instruments and the chemical shifts (δ) are expressed in parts per million relative to residual $CHCl_3$, acetone, or DMSO as internal standards. Proton magnetic resonance (^{1}H NMR) spectra were recorded at 600, or 500 MHz. Carbon magnetic resonance (^{13}C NMR) spectra were recorded at 150, or 125 MHz. NMR acquisitions were performed at 295 K unless otherwise noted. Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet, p, pentet; br s, broad singlet. Infrared spectra were recorded as pure undiluted samples using ThermoNicolet Avatar 370 Fourier transform infrared spectrometer with a Smart MIRacle^{TM} HATR attachment. Melting points (mp) were determined using a Barnstead Electrothermal digital melting point apparatus (Model IA9300) and are uncorrected. GCMS data were recorded on an Agilent 7890A GC system with an Agilent 5975C Inert MSD system operating in the electron impact (EI+) mode. HPLC was performed on an Agilent 1100LC/MSD with an Agilent 1100 SL mass spectrometer (electrospray ionization, ES) eluting with 0.1% trifluoroacetic acid in H_2O and 0.05% trifluoroacetic acid in CH_3CN. High resolution mass spectrometry was performed on an Agilent ES-TOF instrument. All chromatography was performed using Merck silica gel (40−63 μM) with the indicated solvent mixtures. All starting materials were purchased from Aldrich, Acros, Fisher, Lancaster, or TCI chemical companies and used as received. Solvents were purchased from Fisher or Acros chemical companies and used as received (no extra drying, distillation or special handling practices were employed).

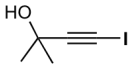
Synthesis of *N*-iodomorpholine-hydrogen iodide: Procedure adapted from Koyama, M.; Ohtani, N.; Kai, F.; Moriguchi, I.; Inouye, S. *J. Med. Chem.* **1987**, *30*, 552-562.

A solution of iodine (25.40 g, 0.10 mol) in MeOH (400 ml) was treated dropwise with morpholine (8.71 ml, 0.10 mol). On addition the solution rapidly changed from dark purple-brown to light orange and a fine orange precipitate was generated. The solution was stirred for ~45 min then solid was isolated by filtration. The solid was transferred to a round bottom flask and dried under vacuum. Once the material reached a free flowing consistency it was placed in a plastic bottle and stored in the fridge. This procedure gave *N*-iodomorpholine-hydrogen iodide as an orange crystalline powder (30.34 g, 0.09 mol, 89%) which was used without further purification or characterization.

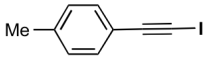
General procedure for the synthesis of 1-iodoalkynes - 1-iodo-phenylacetylene (1): Phenylacetylene (8.17 g, 80.00 mmol) was dissolved in THF (200 mL) and treated with CuI (0.76 g, 4.00 mmol) and *N*-iodomorpholine (30.00 g, 88.00 mmol). The reaction mixture was stirred at room temperature for 45 minutes, after which a fine white precipitate had formed. The suspension was poured onto a pad of neutral alumina (400 mL) and the filtrate was collected under vacuum. The solid phase was washed with DCM (4x100mL) and the combined organic fractions were pooled and concentrated by evaporation, giving **1** (16.61 g, 72.82 mmol, 91%) as a yellow oil. This material was used without further purification



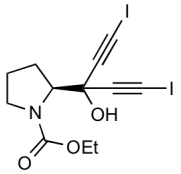
1-Iodo-phenylacetylene (1). yellow oil; IR (υ[cm^{-1}]) 3054, 2171, 1596, 1487, 1442, 1069, 1025, 915, 751, 687; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.45 – 7.40 (m, *J*=9.1, 3.9, 2H), 7.33 – 7.27 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 132.5, 129.0, 128.4, 123.6, 94.4, 6.4.



4-Iodo-2-methylbut-3-yn-2-ol (24). Synthesized from 2-methylbut-3-yn-2-ol (2.00 g, 23.78 mmol) using general procedure, 4.32 g, 20.57 mmol, 87%; clear oil; IR (υ[cm^{-1}])3359, 2981, 2933, 2179, 1697, 1363, 1219, 1161, 956, 903, 770; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.50 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 99.3, 67.0, 31.5, -0.4; HRMS (ESI-TOF) (*m/z*): $[M + Na]^+$ calcd for C_5H_7INaO, 232.9434; found 232.9443.

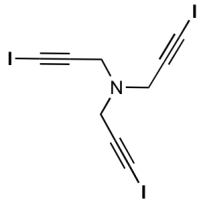


1-(Iodoethynyl)-4-methylbenzene (25). Synthesized from 1-ethynyl-4-methylbenzene (11.00g, 95.00 mmol) using general procedure, 19.70 g, 81.00 mmol, 89%; low melting solid; IR (υ[cm^{-1}]) 3027, 2164, 1904, 1505, 1446, 1178, 1116, 1019, 706; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.32 (d, *J*=8.1, 2H), 7.11 (d, *J*=8.0, 2H), 2.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 139.2, 132.4, 129.2, 120.5, 94.4, 21.7, 5.2.

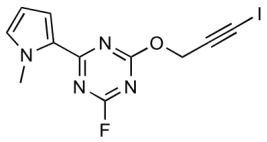


(S)-Ethyl 2-(3-hydroxy-1,5-diiodopenta-1,4-diyn-3-yl)pyrrolidine-1-carboxylate (26). Synthesized from (S)-ethyl 2-(3-hydroxypenta-1,4-diyn-3-yl)pyrrolidine-1-carboxylate[1] (1.00g, 4.52 mmol) using general procedure, 1.79 g, 3.78 mmol, 84%; white powder; mp = 124–129 °C (dec.); IR (υ[cm^{-1}]) 2975, 2884, 2182, 1643, 1422, 1382, 1348, 1202, 1127, 1028, 786; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.28 (s, 1H), 4.24 – 4.12 (m, 3H), 3.65 (br s, 1H), 3.42 – 3.32 (m, 1H), 2.24 (dt, *J*=14.5, 7.1, 1H), 2.20 – 2.09 (m, 1H), 2.09 – 2.00 (m, 1H), 1.80 – 1.69 (m, 1H), 1.28 (t, *J*=7.1, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 159.2, 93.0, 92.5, 72.0, 68.1, 62.9, 48.7, 30.1, 24.0,

14.8, 3.6, 2.8; HRMS (ESI-TOF) (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{13}I_2NNaO_3$, 495.8877; found 495.8870.

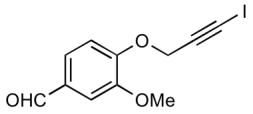


Tris(3-iodoprop-2-ynyl)amine (27). Synthesized from tripropargylamine (4.00 g, 30.50 mmol) using general procedure, 12.23 g, 24.03 mmol, 79%; white powder; **WARNING**: sample detonates when heated above 170 °C, use caution when handling this compound; IR (υ[cm^{-1}]) 2823, 2194, 1434, 1340, 1326, 1121, 1092, 1000, 970, 943; ^{1}H NMR (600 MHz, DMSO) δ = 3.46 (s, 6H); ^{13}C NMR (151 MHz, DMSO) δ = 88.1, 43.2, 10.1; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_9H_7I_3N$, 509.7707; found 509.7708.

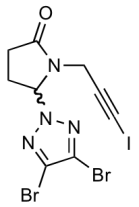


2-Fluoro-4-(3-iodoprop-2-ynyloxy)-6-(1-methyl-1H-pyrrol-2-yl)-1,3,5-triazine. 2,4-difluoro-6-(1-methyl-1H-pyrrol-2-yl)-1,3,5-triazine[2] (0.75 g, 3.82 mmol) was dissolved in acetonitrile (10 ml) and treated sequentially with 3-iodoprop-2-yn-1-ol[3] (0.63 g, 3.44 mmol) and DIPEA (0.67 ml, 3.82 mmol). The sample was stirred at r.t. for 25 min, after which a precipitate formed and was isolated by filtration. The solid was washed with hexanes and dried under vacuum to give **26** as a white solid, 1.31 g, 3.66 mmol, 96%; mp = 155–158 °C; IR (υ[cm^{-1}]) 3119, 2983, 2191, 1593, 1525, 1433, 1096, 986, 857, 755; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.45 (dd, *J*=3.9, 1.5, 1H), 6.91 (s, 1H), 6.22 (dd, *J*=3.8, 2.5, 1H), 5.18 (s, 2H), 4.09 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.3 (dd, *J*=328.6, 15.5), 171.3, 169.8, 133.1, 127.9, 121.6, 109.9, 87.6,

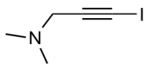
57.5, 38.9, 6.1; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{11}H_9FIN_4$, 358.9800; found 358.9796.



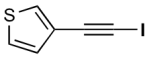
4-(3-Iodoprop-2-ynyloxy)-3-methoxybenzaldehyde. Synthesized from 3-methoxy-4-(prop-2-ynyloxy)benzaldehyde[4] (1.00 g, 5.26 mmol) using general procedure, 1.43 g, 4.52 mmol, 86%; yellow solid; mp = 121–127 °C; IR (υ[cm^{-1}]) 3003, 2849, 2206, 1686, 1584, 1506, 1280, 1157, 1027, 982, 803, 733, 663; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.85 (s, 1H), 7.44 (dd, *J*=8.2, 1.5, 1H), 7.40 (s, 1H), 7.09 (d, *J*=8.2, 1H), 4.96 (s, 2H), 3.92 (d, *J*=14.3, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.1, 152.3, 150.1, 131.1, 126.6, 112.6, 109.6, 88.1, 58.2, 56.2, 6.8; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{10}IO_3$, 316.9669; found 316.9677.



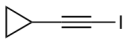
5-(4,5-Dibromo-2*H*-1,2,3-triazol-2-yl)-1-(3-iodoprop-2-ynyl)pyrrolidin-2-one. Synthesized from 5-(4,5-dibromo-2*H*-1,2,3-triazol-2-yl)-1-(prop-2-ynyl)pyrrolidin-2-one[5] (1.00 g, 2.87 mmol) using general procedure, 1.21 g, 2.55 mmol, 89%; waxy solid; IR (υ[cm^{-1}]) 2980, 2191, 1729, 1375, 1241, 1048, 824, 685; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.10 (d, *J*=7.6, 1H), 4.36 (d, *J*=17.8, 1H), 3.91 (d, *J*=17.8, 1H), 2.92 - 2.84 (m, 1H), 2.65-2.58 (m, 1H), 2.54 – 2.39 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 174.29, 126.4, 86.7, 73.1, 32.4, 28.6, 25.5, 1.0.; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_9H_8Br_2IN_4O$, 472.8104; found 472.8095.



3-Iodo-*N*,*N*-dimethylpropargylamine. Synthesized from *N*,*N*-dimethylpropargylamine (2.00 g, 24.06 mmol) using general procedure, 3.77 g, 18.04 mmol, 75%; white solid; mp = 135 °C (dec.); IR (υ[cm^{-1}]) 2975, 2944, 2876, 2787, 2162, 1471, 1326, 1040, 958, 809; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 3.40 (s, 2H), 2.27 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 89.0, 49.9, 44.3, 0.01; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for C_5H_9IN, 209.9774; found 209.9781.



3-(Iodoethynyl)thiophene. Synthesized from 3-ethylylthiophene (0.50 g, 4.62 mmol) using general procedure, 0.99 g, 4.21 mmol, 91%; brown oil; IR (υ[cm^{-1}]) 3100, 2174, 1570, 1355, 1222, 1160, 1078, 945, 767, 688; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.56 – 7.55 (m, 1H), 7.34 (dd, *J*=5.0, 2.9, 1H), 7.21 – 7.18 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 130.5, 130.2, 125.4, 122.7, 89.4, 6.2.



(Iodoethynyl)cyclopropane. Synthesized from ethynylcyclopropane (1.00 g, 15.13 mmol) using general procedure, 2.39 g, 12.45 mmol, 82%; yellow oil; IR (υ[cm^{-1}]) 3091, 3009, 2974, 2186, 1681, 1615, 1448, 1377, 1220, 1053, 1026, 962, 773; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.39 – 1.31 (m, 1H), 0.79 – 0.68 (m, 4H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 97.4, 8.4, 1.8, -11.5.

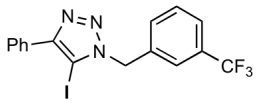
General procedure for the synthesis of 5-iodotriazoles using CuI-TEA –5-iodo-4-phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (3):

1 (0.23 g, 1.00 mmol) and **2** (0.20 g, 1.00 mmol) were dissolved in THF (5 mL). The solution was treated sequentially with CuI (9.52 mg, 0.05 mmol) and TEA (0.28 ml, 2.00 mmol) and then allowed to stir at room temperature for 6 hour. After this time the reaction was quenched by

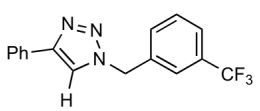
adding 1 mL of 10% NH_4OH solution. The volatile components were removed by evaporation, and the resulting residue was suspended in water and diethyl ether. A precipitate formed upon vigorous stirring and was isolated by filtration, giving **3** (0.39 g, 0.90 mmol, 90%) as a fine white powder.

General procedure for the synthesis of 5-iodotriazoles using CuI-TTTA –5-iodo-4-phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (3):

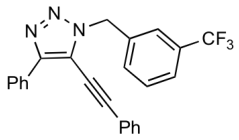
CuI (9.52 mg, 0.05 mmol) and TTTA (0.02 g, 0.05 mmol) were stirred in THF (4.5 mL) at room temperature for 20 min, after which a homogeneous solution was obtained. **1** (0.23 g, 1.00 mmol) and **2** (0.20 g, 1.00 mmol) were dissolved in THF (0.5 mL) and added in a single portion to the catalyst solution. The sample was allowed to stir for 45 min, and then quenched by adding 1 mL of 10% NH_4OH solution. The volatile components were removed by evaporation, and the resulting residue was suspended in water and diethyl ether. A precipitate formed upon vigorous stirring and was isolated by filtration, giving **3** (0.40 g, 0.93 mmol, 93%) as a fine white powder.



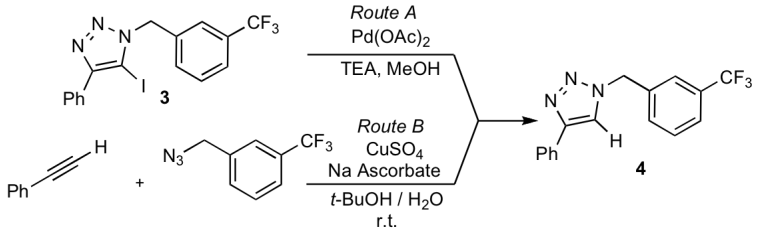
5-Iodo-4-phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (3). mp = 193–195 °C (dec.); IR (υ[cm^{-1}]) 3132, 1329, 1165, 1118, 1076, 767, 697; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.96 – 7.90 (m, 2H), 7.62 (s, 1H), 7.59 (d, *J*=7.5, 1H), 7.51 – 7.42 (m, 4H), 7.41 – 7.37 (m, 1H), 5.71 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 150.6, 135.5, 131.6 (q, *J*=32.7), 131.4, 130.2, 129.8, 129.0, 128.8, 127.6, 125.7 (q, *J*=3.7), 125.0 (q, *J*=3.8), 123.9 (q, *J*=272.4), 76.6, 54.0; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{12}F_3IN_3$, 430.0023; found 430.0026.



4-Phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (4). Isolated as a by-product from initial catalyst screening; mp = 126–127 °C; IR (υ[cm^{-1}]) 3073, 1323, 1153, 1075, 773, 699; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.81 – 7.76 (m, 2H), 7.70 (s, 1H), 7.61 (d, *J*=7.7, 1H), 7.57 (s, 1H), 7.50 (t, *J*=7.7, 1H), 7.46 (d, *J*=7.8, 1H), 7.39 (t, *J*=7.6, 2H), 7.34 – 7.29 (m, 1H), 5.62 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 148.8, 135.9, 131.8 (q, *J*=32.5), 131.5, 130.4, 130.0, 129.1, 128.6, 126.0, 125.9 (q, *J*=3.8), 124.9 (q, *J*=3.7), 123.9 (q, *J*=272.8), 119.7, 53.8; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{13}F_3N_3$, 304.1056; found 304.1059.



4-Phenyl-5-(phenylethynyl)-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (5). Isolated as a by-product from initial catalyst screening; mp = 115–118 °C; IR (υ[cm^{-1}]) 2963, 2219, 1504, 1453, 1328, 1161, 1071, 773, 690; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.17 (d, *J*=7.4, 2H), 7.71 (s, 1H), 7.59 (d, *J*=7.7, 1H), 7.55 (d, *J*=7.7, 1H), 7.51 – 7.34 (m, 9H), 5.71 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 148.5, 135.8, 131.8, 131.7, 131.5 (q, *J*=32.5), 130.3, 130.1, 129.8, 129.0, 128.9, 128.7 (q, *J*=165.0), 126.4, 125.7 (q, *J*=3.6), 125.2 (q, *J*=3.7), 124.9, 123.1, 121.3, 117.4, 103.0, 75.4, 52.6, 1.2; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{17}F_3N_3$, 404.1369; found 404.1372.

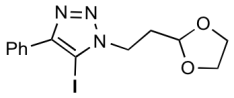


Assignment of regiochemistry for 5-iodo-4-phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (3): Iodotriazole **3** was reduced to give the corresponding 5-proto-triazole **4** (*Route A)*.

Concurrently, an authentic sample of 5-proto-triazole **4** was synthesized using the established CuAAC protocol (*Route B*). The physical and spectroscopic characteristics of the samples obtained via both routes were compared and found to be identical.

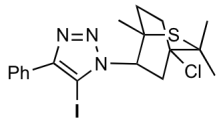
Route A: $Pd(OAc)_2$ (0.449 g, 2.000 mmol) was added to a solution of **3** (0.858 g, 2 mmol) and TEA (0.281 ml, 2.000 mmol) in MeOH (10 ml). The sample was warmed to 55 °C for 4h and monitored by LC-MS. Once the starting material had been consumed the sample was cooled and the volatile components were removed under vacuum. The crude residue was then purified by column chromatography (9:1 Hex:EtOAc - 4:1 Hex:EtOAc) to give **4** (0.59 g, 1.945 mmol, 97% yield) as a white solid.

Route B: Phenylacetylene (0.409 g, 4 mmol) and 3-(trifluoromethyl)benzyl azide (0.805 g, 4.00 mmol) were dissolved in 4:1 *t*-BuOH/H_2O (25 ml) and then treated sequentially with a 1M aq. solution of $CuSO_4$ (0.200 ml, 0.200 mmol) followed by solid sodium ascorbate (0.079 g, 0.400 mmol). The sample was stirred at r.t. for 4h. during which time a precipitate formed. The sample was quenched with 10 mL of 10% NH_4OH aq. and the solid was isolated by filtration. The solid was washed with water and dried under vacuum, giving **4** (1.112 g, 3.67 mmol, 92% yield) as a white solid.

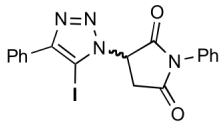


1-(2-(1,3-Dioxolan-2-yl)ethyl)-5-iodo-4-phenyl-1*H*-1,2,3-triazole (6). Synthesized from 1-iodo-phenylacetylene (2.28 g, 10.00 mmol) and 2-(2-azidoethyl)-1,3-dioxolane (1.43 g, 10.00 mmol) using general procedure, 3.64 g, 9.80 mmol, 98%; white powder; mp = 118–121 °C (dec.); IR (υ[cm^{-1}]) 3052, 2885, 1446, 1400, 1222, 1133, 1048, 900, 769, 714; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.94 – 7.88 (m, 2H), 7.44 (t, *J*=7.6, 2H), 7.38 (t, *J*=7.4, 1H), 5.01 (t, *J*=4.2, 1H), 4.61 – 4.55 (m, 2H), 4.05 – 3.96 (m, 2H), 3.93 – 3.84 (m, 2H), 2.40 – 2.31 (m, 2H); ^{13}C

NMR (151 MHz, $CDCl_3$) δ = 150.0, 130.5, 128.8, 128.7, 127.7, 101.7, 76.6, 65.4, 46.3, 33.8; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{15}IN_3O_2$, 372.0203; found 372.0203.

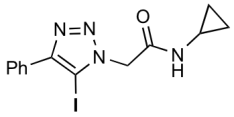


1-(4-chloro-1,3,3-trimethyl-2-thiabicyclo[2.2.2]octan-7-yl)-5-iodo-4-phenyl-1*H*-1,2,3-triazole (7). Synthesized from 1-iodo-phenylacetylene (0.10 g, 0.44 mmol) and 7-azido-4-chloro-1,3,3-trimethyl-2-thiabicyclo[2.2.2]octane (0.11 g, 0.44 mmol) using general procedure, 0.15 g, 0.32 mmol, 73%; mp = 157–159 °C (dec.); IR (υ[cm^{-1}]) 2979, 2103, 1447, 1387, 1326, 1240, 1160, 985, 772, 712, ; ^1H NMR (CDCl3, 600 MHz,) δ 7.94–7.92 (m, 2H), 7.48–7.46 (m, 2H), 7.42–7.39 (m, 1H), 5.25 (ddd, *J* = 11.2, 4.8, 2.1, 1H), 3.11 (ddd, *J* = 11.7, 11.2, 3.2, 1H), 2.73 (dd, *J* = 12.7, 5.3, 1H), 2.75–2.60 (m, 1H), 2.45–2.39 (m, 1H), 1.93–1.88 (m, 1H), 1.82 (s, 3H), 1.77 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 149.6, 130.4, 128.9, 128.8, 127.9, 79.4, 76.9, 72.4, 72.4, 68.8, 65.7, 42.5, 37.1, 36.4, 30.9, 30.5, 19.8; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{22}ClIN_3S$, 474.0262; found 474.0266.

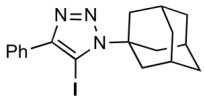


3-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-phenylpyrrolidine-2,5-dione (8). Synthesized from 1-iodo-phenylacetylene (0.30 g, 1.32 mmol) and 3-azido-1-phenylpyrrolidine-2,5-dione (0.28 g, 1.32 mol) using general procedure, 0.44 g, 1.00 mmol, 76%;. mp = 164–169 °C (dec.); IR (υ[cm^{-1}]) 2933, 1792, 1719, 1497, 1379, 1149, 786, 694; ^1H NMR ($CDCl_3$, 600 MHz,) δ 7.93–7.92 (m, 2H), 7.52–7.47 (m, 4H), 7.45–7.42 (m, 2H), 7.39–7.37 (m, 2H), 5.91 (dd, *J* = 9.4, 5.8, 1H), 3.71 (dd, *J* = 18.3, 5.8, 1H), 3.58 (dd, *J* = 18.3, 9.8, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz)

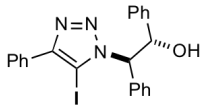
δ 172.4, 170.8, 151.6, 131.9, 130.4, 130.25, 130.1, 129.9, 129.5, 128.5, 127.2, 78.7, 58.4, 36.3; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{14}IN_4O_2$, 445.0156; found 445.0159.



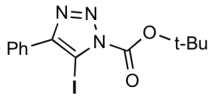
***N*-cyclopropyl-2-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)acetamide (9).** Synthesized from 1-iodo-phenylacetylene (0.25 g, 1.10 mmol) and 2-azido-*N*-cyclopropylacetamide (0.15 g, 1.10 mmol) using general procedure; 0.364 g, 0.989 mmol, 90%; mp = 197–198 °C (dec.); IR (υ[cm^{-1}]) 3287, 3071, 2971, 1661, 1557, 1407, 1269, 1129, 985, 952, 769, 686; ^{1}H NMR (DMSO-d_6, 600 MHz,) δ 8.53 (d, *J* = 3.6, 1H), 7.88–7.87 (m, 2H), 7.50–7.48 (m, 2H), 7.41–7.39 (m, 1H), 5.09 (s, 2H), 2.68– 2.63 (m, 1H), 0.64 (dt, *J* = 7.0, 5.0, 2H), 0.45 (dt, *J* = 6.9, 4.3, 2H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 167.1, 149.7, 131.9, 130.0, 129.6, 128.1, 84.1, 53.8, 23.7, 6.9; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{14}IN_4O$, 369.0207; found 369.0209.



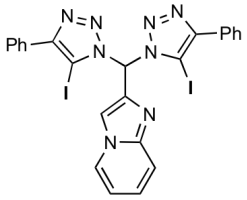
1-Adamantyl-5-iodo-4-phenyl-1*H*-1,2,3-triazole (10). Synthesized from 1-iodo-phenylacetylene (0.34 g, 1.50 mmol) and 1-azido-adamantane (0.27 g, 1.50 mmol) using general procedure; 0.28 g, 0.69 mmol, 46%, mp = 224–225 °C (dec.); IR (υ[cm^{-1}]) 2912, 2849, 1466, 1444, 1317, 1247, 1153, 1018, 983, 767, 692; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.78 – 7.74 (m, 2H), 7.43 (t, *J*=7.5, 2H), 7.38 (t, *J*=7.4, 1H), 2.59 (d, *J*=2.5, 6H), 2.29 (s, 3H), 1.83 – 1.74 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 152.0, 130.9, 129.0, 128.6, 128.5, 69.8, 64.4, 41.6, 36.0, 30.0; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{21}IN_3$, 406.0775; found 406.0771.



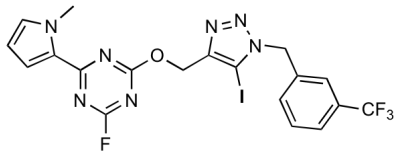
***trans*-2-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)-1,2-diphenylethanol (11).** Synthesized from 1-iodo-phenylacetylene (0.10g, 0.44 mmol) and *trans*-2-azido-1,2-diphenylethanol (0.11 g, 0.44 mmol) using general procedure; 0.196 g, 0.419 mmol, 96%; mp = 152–154 °C (dec.); IR (υ[cm^{-1}]) 3296, 2971, 1493, 1380, 1325, 1159, 1105, 950, 770, 744; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.83 – 7.79 (m, 2H), 7.41 (t, *J*=7.6, 2H), 7.37 – 7.34 (m, 1H), 7.33 – 7.22 (m, 10H), 5.86 (dd, *J*=5.6, 2.4, 1H), 5.66 (d, *J*=5.7, 1H), 3.75 (br s, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 149.4, 139.3, 134.1, 130.1, 129.2, 129.0, 128.9, 128.7, 128.6, 128.5, 128.5, 127.7, 126.9, 78.5, 75.6, 71.4; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{19}IN_3O$, 468.0567; found 468.0571.



***tert*-butyl 5-iodo-4-phenyl-1*H*-1,2,3-triazole-1-carboxylate (12).** Synthesized from 1-iodo-phenylacetylene (0.20 g, 0.88 mmol) and *tert*-butyl carbamoylazide (0.13 g, 0.88 mmol) using general procedure,sample purified by column chromatography (4:1 Hex:EtOAc); 0.21 g, 0.56 mmol, 77%; mp = 87–90 °C; IR (υ[cm^{-1}]) 2984, 1774, 1468, 1394, 1342, 1287, 1142, 959, 847, 752, 693; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.95 – 7.91 (m, 2H), 7.48 – 7.43 (m, 3H), 1.69 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 153.0, 145.0, 130.1, 128.8, 128.5, 128.5, 96.3, 88.0, 28.; HRMS (ESI-TOF) (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{14}IN_3NaO_2$, 394.0023; found 394.0024.

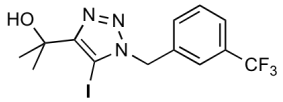


2-(bis(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)imidazo[1,2-α]pyridine (13). Synthesized from 1-iodo-phenylacetylene (0.25 g, 1.1 mmol) and 2-(diazidomethyl)imidazo[1,2-*a*]pyridine (0.12 g, 0.55 mmol) using general procedure; 0.62 g, 0.92 mmol, 84%; mp = 183–185 °C (dec.); IR (υ[cm^{-1}]) 3080, 1500, 1474, 1444, 1330, 1128,982, 809, 754, 739, 693,; ^{1}H NMR (DMSO-d_6, 600 MHz,) δ 8.60–8.59 (m, 1H), 8.46 (br s, 1H), 8.00 (br s, 1H), 7.92–7.90 (m, 4H), 7.60 (br s, 1H), 7.53–7.50 (m, 4H), 7.45–7.43 (m, 2H), 7.35–7.32 (m, 1H), 6.99–6.96 (m, 1H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 150.4, 131.2, 130.1, 130.05, 128.9, 128.4, 127.4, 118.4, 114.3, 84.0, 73.4; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{17}I_2N_8$, 670.9660; found 670.9657.

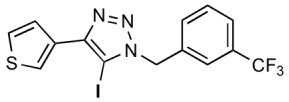


2-Fluoro-4-((5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-6-(1-methyl-1*H*-pyrrol-2-yl)-1,3,5-triazine (14). Synthesized from 2-fluoro-4-(3-iodoprop-2-ynyloxy)-6-(1-methyl-1H-pyrrol-2-yl)-1,3,5-triazine (0.25 g, 0.70 mmol) and 3-trifluoromethyl-benzylazide (0.14 g, 0.70 mmol) using general procedure; 0.31 g, 0.56 mmol, 80%; mp = 185–187 °C (dec.); IR (υ[cm^{-1}]) 3130, 3059, 1595, 1555, 1418, 1357, 1173, 1104, 1056, 911, 803, 756; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.61 – 7.58 (m, 2H), 7.50 – 7.41 (m, 3H), 6.90 (s, 1H), 6.21 (dd, *J*=3.9, 2.5, 1H), 5.64 (s, 2H), 5.56 (s, 2H), 4.09 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.5 (dd, *J*=361.1, 15.4), 171.3, 169.8, 135.0, 133.0, 131.6 (q, *J*=32.8), 131.5, 129.9, 125.9 (q,

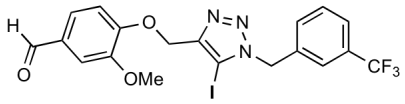
J=3.6), 125.1 (q, *J*=3.7), 123.9 (q, *J*=272.4), 121.5, 81.6, 61.7, 54.0, 39.0; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{15}F_4IN_7O$, 560.0313; found 560.0311.



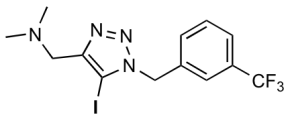
2-(5-Iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)propan-2-ol (15). Synthesized from 4-iodo-2-methylbut-3-yn-2-ol (2.10 g, 10.00 mmol) and 3-trifluoromethyl-benzylazide (2.01 g, 10.00 mmol) using general procedure; 3.82 g, 9.30 mmol, 93%; mp = 77–80 °C; IR (υ[cm^{-1}]) 3385, 2981, 2938, 1326, 1170, 1120, 1074, 763, 699; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.58 – 7.57 (m, 2H), 7.48 – 7.45 (m, 1H), 7.42 – 7.41 (m, 1H), 5.62 (s, 2H), 1.66 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 156.4, 135.4, 131.5 (q, *J*=33.2), 131.4, 129.8, 125.7 (q, *J*=3.7), 125.1 (q, *J*=3.8), 123.9 (q, *J*=272.4), 74.2, 69.7, 53.8, 30.1; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{14}F_3IN_3O$, 412.0128; found 412.0126.



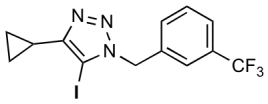
5-Iodo-4-(thiophen-3-yl)-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (16). Synthesized from 3-(iodoethynyl)thiophene (0.54 g, 2.31 mmol) and 3-trifluoromethyl-benzylazide (0.46 g, 2.31 mmol) using general procedure; 0.99 g, 2.28 mmol, 99%; mp = 153–158 °C (dec.); IR (υ[cm^{-1}]) 3121, 1326, 1194, 1163, 1096, 1075, 853, 792, 702; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.97 – 7.93 (m, 1H), 7.75 (d, *J*=5.0, 1H), 7.59 (d, *J*=7.7, 2H), 7.58 (s, 1H), 7.47 (t, *J*=7.7, 1H), 7.45 – 7.38 (m, 2H), 5.69 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 147.5, 135.4, 131.6 (q, *J*=32.7), 131.3, 131.0, 129.8, 126.7, 126.2, 125.7 (q, *J*=3.7), 124.9 (q, *J*=3.8), 123.9 (q, *J*=272.4), 123.5, 76.0, 53.9; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{14}H_{10}F_3IN_3S$, 435.9587; found 435.9586.



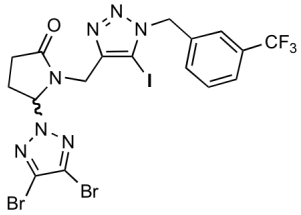
4-((5-Iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3-methoxy benzaldehyde (17). Synthesized from 4-(3-iodoprop-2-ynyloxy)-3-methoxybenzaldehyde (0.25 g, 0.79 mmol) and 3-trifluoromethyl-benzylazide (0.16 g, 0.79 mmol) using general procedure; 0.40 g, 0.77 mmol, 97%; mp = 130–134 °C (dec.); IR (υ[cm^{-1}]) 3123, 1702, 1689, 1588, 1506, 1329, 1262, 1133, 1123,994, 792; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.83 (s, 1H), 7.59 (d, *J*=7.6, 1H), 7.56 (s, 1H), 7.47 (t, *J*=7.7, 1H), 7.41 (dd, *J*=15.8, 6.7, 2H), 7.39 (s, 1H), 7.21 (d, *J*=8.1, 1H), 5.62 (s, 2H), 5.27 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.2, 153.1, 150.5, 147.5, 135.0, 131.6, 131.6 (q, *J*=32.7), 131.1, 129.9, 126.7, 125.9 (q, *J*=3.6), 125.1 (q, *J*=3.7), 123.9 (q, *J*=272.4), 113.5, 109.7, 81.2, 62.9, 56.3, 54.0; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{16}F_3IN_3O_3$, 518.0183; found 518.0186.



1-(5-Iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)-*N*,*N*-dimethylmethanamine (18). Synthesized from 3-iodo-*N*,*N*-dimethylpropargylamine (0.25 g, 1.20 mmol) and 3-trifluoromethyl-benzylazide (0.24 g, 1.20 mmol) using general procedure, sample purified by column chromatography (30:1 $CHCl_3$: MeOH); 0.39 g, 0.95 mmol, 80%; mp = 117–119 °C (dec.); IR (υ[cm^{-1}]) 2973, 2827, 1455, 1326, 1164, 1118, 1020, 757; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.57 (d, *J*=7.7, 1H), 7.52 (s, 1H), 7.45 (t, *J*=7.7, 1H), 7.39 (d, *J*=7.7, 1H), 5.63 (s, 2H), 3.54 (s, 2H), 2.29 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 149.1, 135.5, 131.5 (q, *J*=32.6), 131.3, 129.9, 125.7 (q, *J*=3.7), 124.9 (q, *J*=3.7), 123.9 (q, *J*=272.5), 81.0, 53.9 (d, *J*=37.0), 45.3, 30.3; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{15}F_3IN_4$, 411.0288; found 411.0287.

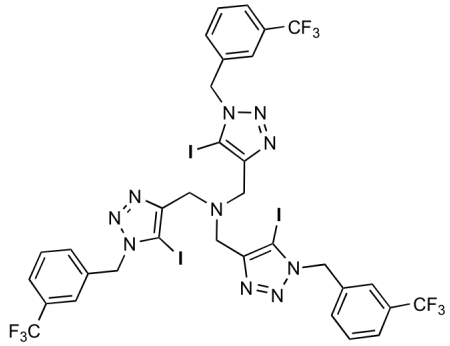


4-Cyclopropyl-5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (19). Synthesized from (iodoethynyl)cyclopropane (0.30 g, 1.56 mmol) and 3-trifluoromethyl-benzylazide (0.31 g, 1.56 mmol) using general procedure; 0.59 g, 1.50 mmol, 96%; mp = 129–134 °C (dec.); IR (υ[cm^{-1}]) 3087, 3011, 1453, 1325, 1165, 1122, 1074, 777, 701; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.57 – 7.56 (m, 2H), 7.45 (t, *J*=7.7, 1H), 7.39 (d, *J*=7.7, 1H), 5.57 (s, 2H), 1.78 – 1.72 (m, 1H), 1.06 – 1.01 (m, 2H), 0.99 – 0.93 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 153.8, 135.6, 131.7 (q, *J*=32.6), 131.4, 129.7, 125.6 (q, *J*=3.7), 125.0 (q, *J*=3.9), 124.0 (q, *J*=272.3), 77.9, 53.7, 7.8, 7.5; HRMS (ESI-TOF) (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{11}F_3IN_3Na$, 415.9847; found 415.9847.

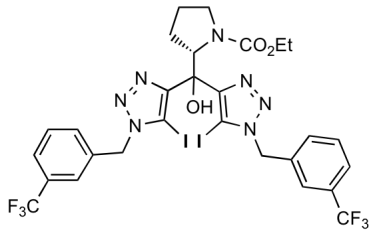


5-(4,5-Dibromo-2*H*-1,2,3-triazol-2-yl)-1-((5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methyl)pyrrolidin-2-one (20). Synthesized from 5-(4,5-dibromo-2*H*-1,2,3-triazol-2-yl)-1-(3-iodoprop-2-ynyl)pyrrolidin-2-one (0.50 g, 1.06 mmol) and 3-trifluoromethyl-benzylazide (0.21 g, 1.06 mmol) using general procedure; 0.66 g, 0.98 mmol, 93%; mp = 105–110 °C (dec.); IR (υ[cm^{-1}]) 3002, 2104, 1696, 1415,1327, 1166, 1123, 1074, 921, 829, 753, 702; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.59 (d, *J*=7.8, 1H), 7.56 (s, 1H), 7.48 (t, *J*=7.7, 1H), 7.40 (d, *J*=7.7, 1H), 6.16 (d, *J*=7.6, 1H), 5.59 (d, *J*=3.3, 2H), 4.88 (d, *J*=15.7, 1H), 3.92 (d, *J*=15.7, 1H), 2.95 – 2.86 (m, 1H), 2.65 – 2.56 (m, 1H), 2.49 (dd, *J*=17.1, 9.9, 1H), 2.43 – 2.36 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 175.0, 147.0, 135.1, 131.6 (m), 131.5, 129.9, 126.1, 125.8 (m),

125.1 (m), 123.9 (m), 79.6, 78.3, 53.9, 36.4, 28.6, 25.6; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{14}Br_2F_3IN_7O$, 673.8618; found 673.8613.

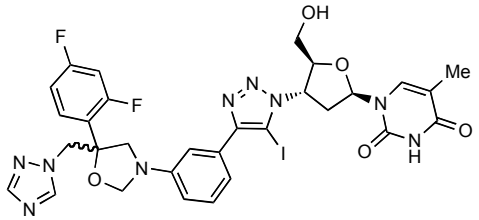


Tris((5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methyl)amine (21). Synthesized from tris(3-iodoprop-2-ynyl)amine (0.22 g, 0.43 mmol) and 3-trifluoromethyl-benzylazide (0.27 g, 1.34 mmol) using general procedure, sample triturated with MeCN; 0.39 g, 0.35 mmol, 81%; mp = 171–173 °C (dec.); IR (υ[cm^{-1}]) 3072, 1445, 1328, 1162, 1123, 1095, 756; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.62 (s, 3H), 7.59 (d, *J*=7.7, 3H), 7.51 (d, *J*=7.6, 3H), 7.44 (t, *J*=7.7, 3H), 5.48 (s, 6H), 3.64 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 149.4, 135.4, 132.3, 131.6 (q, *J*=32.7), 129.8, 125.9 (q, *J*=3.6), 125.8 (q, *J*=3.5), 123.8 (q, *J*=272.5), 81.2, 53.6, 48.2; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{33}H_{25}F_9I_3N_{10}$, 1112.9249; found 1112.9249.



(*S*)-Ethyl 2-(hydroxybis(5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methyl)pyrrolidine-1-carboxylate (22). Synthesized from (*S*)-ethyl 2-(3-hydroxy-1,5-diiodopenta-1,4-diyn-3-yl)pyrrolidine-1-carboxylate (0.30 g, 0.63 mmol) and 3-trifluoromethyl-benzylazide (0.29 g, 1.46 mmol) using general procedure, sample purified by column chromatography (2:1 Hex:EtOAc); 0.41 g, 0.47 mmol, 73%; mp = 185–189 °C (dec.); IR (υ[cm$^-$

[1]) 3537, 3075, 2978, 1675, 1453, 1328, 1159, 1111, 1077, 701; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.55 (d, *J*=5.4, 3H), 7.50 – 7.36 (m, 5H), 6.60 (br s, 1H, OH), 5.74 – 5.50 (m, 4H), 5.21 (dd, *J*=8.5, 4.0, 1H), 4.07 (br s, 2H), 3.46 (br s, 1H), 2.99 (br s, 1H), 2.38 (br s, 1H), 2.35 – 2.23 (m, *J*=8.3, 1H), 1.61 (br s, 1H), 1.19 (br s, 3H), 1.13 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 159.1, 153.2, 150.4, 133.1 (m), 131.5 (m), 129.7, 129.6, 125.6 (m), 125.9 (m), 124.6 (m, *J*=3.7), 124.2 (m), 79.8, 79.7, 75.6, 65.2, 62.2, 53.8, 53.7, 48.2, 29.0, 23.9, 15.0; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{28}H_{26}F_6I_2N_7O_3$, 876.0085; found 876.0083.

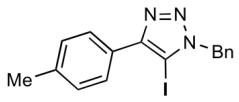


1-((2*R*,4*S*,5*S*)-4-(4-(3-(5-((1*H*-1,2,4-triazol-1-yl)methyl)-5-(2,4-difluorophenyl)oxazolidin-3-yl)phenyl)-5-iodo-1*H*-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (T.O.C. graphic) Synthesized from 5-((1*H*-1,2,4-triazol-1-yl)methyl)-5-(2,4-difluorophenyl)-3-(3-(iodoethynyl)phenyl)oxazolidine (0.90g, 1.83 mmol) and azidothymidine (0.49, 1.83 mmol) using general procedure, sample purified by column chromatography (EtOAc – 10:1 EtOAc:MeOH) on Biotage KP-NH functionalize silica gel, isolated as a 1:1 mixture of diastereomers; 1.18 g, 1.55 mmol, 85%; mp = 201–210 °C (dec.); IR (υ[cm^{-1}]) 3300, 3061, 3011, 2930, 2859, 1686, 1608, 1500, 1473, 1272, 1102, 964, 852, 692; H NMR (600 MHz, $CDCl_3$) δ = 9.76 (s, 1H), 8.08 (s, 1H), 7.75 (s, 1H), 7.47 (s, 1H), 7.36 (dd, *J*=15.1, 8.6, 1H), 7.31 – 7.24 (m, 2H), 7.01 (s, 1H), 6.87 – 6.81 (m, 1H), 6.81 – 6.76 (m, 1H), 6.52 (d, *J*=7.6, 1H), 6.34 (t, *J*=6.8, 1H), 5.55 – 5.49 (m, 1H), 5.14 (s, 1H), 4.95 (s, 1H), 4.64 (dd, *J*=76.3, 14.6, 2H), 4.49 (d, *J*=3.0, 1H), 4.30 (s, 1H), 4.03 – 3.95 (m, 2H), 3.85 (d, *J*=10.2, 1H),

3.67 (d, *J*=9.0, 1H), 3.05 – 2.96 (m, 1H), 2.96 – 2.86 (m, 1H), 2.12 (s, 1H), 2.01 (s, 1H), 1.86 (s, 3H);^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.4, 164.2, 164.0 (d, *J*=12.1), 162.3 (d, *J*=12.1), 160.0 (d, *J*=11.8), 158.4 (d, *J*=11.9), 151.4, 150.8, 150.1, 145.1, 144.6, 138.4, 131.0, 129.8, 128.7 – 128.2(m), 123.7 – 123.4 (m), 118.0, 113.9, 112.6, 111.9 (d, *J*=21.1), 111.4, 104.8 (t, *J*=25.9), 89.6, 85.7, 83.2 (d, *J*=3.6), 81.4, 78.2 (d, *J*=2.6), 62.3, 60.8, 55.4, 54.7 (d, *J*=5.3), 37.5, 14.4, 12.7; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{30}H_{28}F_2IN_9O_5$, 760.1299; found 760.1293.

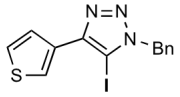
One-pot/two-step procedure for the synthesis of 5-iodotriazoles using *N*-iodomorpholine and CuI-TTTA– 1-Benzyl-5-iodo-4-*p*-tolyl-1*H*-1,2,3-triazole (28):

4-methyl-phenylacetylene (0.50 g, 4.30 mmol) was dissolved in THF (15 ml) and treated with *N*-iodomorpholine (2.20 g, 6.46 mmol) followed by CuI (0.04 g, 0.22 mmol). Sample was monitored by GC-MS. After 45 min the reaction had gone to completion and a fine white precipitate had formed. The suspension was placed on a pad of neutral alumina (~25 mL) and the solution was collected under vacuum. The pad was then washed 3 times with THF (4.50 ml) (final volume ~30mL, including original reaction). This solution was charged with benzyl azide (0.57 g, 4.30 mmol), followed by TTTA (0.09 g, 0.22 mmol) and finally CuI (0.04 g, 0.22 mmol). The reaction was stirred for 3h, and then the solvent was removed under a stream of compressed air, and the residue was triturated with MeCN/Et_2O. Product was isolated by filtration, giving **28** as a white solid. (1.26 g, 3.36 mmol, 78%)

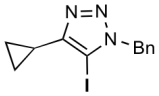


1-Benzyl-5-iodo-4-*p*-tolyl-1*H*-1,2,3-triazole (28). mp = 119–120 °C (dec.); IR (υ[cm^{-1}]) 3033, 1541, 1497, 1357, 1229, 1079, 984, 819, 695; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.75 (d, *J*=8.1, 2H), 7.31 – 7.26 (m, 3H), 7.25 – 7.22 (m, 2H), 7.19 (d, *J*=8.1, 2H), 5.59 (s, 2H), 2.32 (s, 3H); ^{13}C

NMR (151 MHz, $CDCl_3$) δ = 150.5, 138.7, 134.6, 129.4, 129.1, 128.7, 128.0, 127.5, 76.3, 54.5, 21.6; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{15}IN_3$, 376.0305; found 376.0307.



5-Iodo-4-(thiophen-3-yl)-1-benzyl-1*H*-1,2,3-triazole (29). Synthesized from 3-ethynylthiophene (0.45 g, 4.16 mmol) and benzylazide (0.55 g, 4.16 mmol) using one-pot/two-step general procedure, 1.24 g, 3.38 mmol, 81%; mp = 125–127 °C (dec.); IR (υ[cm^{-1}]) 3025, 1496, 1455, 1354, 1318, 1230, 1211, 1072, 1008, 783, 717; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.94 (d, *J*=1.6, 1H), 7.75 (d, *J*=4.7, 1H), 7.39 (dd, *J*=4.7, 3.0, 1H), 7.36 – 7.29 (m, 3H), 7.29 – 7.25 (m, 2H), 5.64 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 147.3, 134.5, 131.2, 129.1, 128.7, 127.9, 126.8, 126.1, 122.9, 76.0, 54.5; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{11}IN_3S$, 367.9713; found 367.9713.

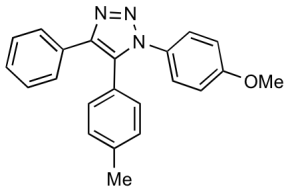


4-Cyclopropyl-5-iodo-1-benzyl-1*H*-1,2,3-triazole (30). Synthesized from ethynylcyclopropane (0.25 g, 3.78 mmol) and benzylazide (0.50 g, 3.78 mmol) using one-pot/two-step general procedure, 0.843 g, 2.59 mmol, 69%; mp = 114–116 °C (dec.); IR (υ[cm^{-1}]) 3028, 1544, 1495, 1451, 1421, 1359, 1333, 1290, 1217, 1145, 1074, 1033, 724; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.31 – 7.25 (m, 3H), 7.22 – 7.18 (m, 2H), 5.49 (s, 2H), 1.72 (dq, *J*=8.4, 5.0, 1H), 1.01 – 0.97 (m, 2H), 0.91 (ddd, *J*=10.8, 6.5, 4.1, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 153.4, 134.7, 129.0, 128.5, 127.9, 77.9, 54.2, 7.7, 7.4; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{13}IN_3$, 326.0149; found 326.0151.

One-pot, three-step procedure for the synthesis of 1,4,5-triaryltriazoles –

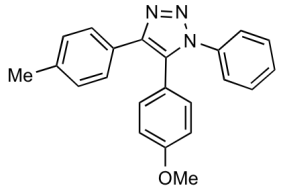
1-(4-methoxyphenyl)-4-phenyl-5-*p*-tolyl-1*H*-1,2,3-triazole (31):

Phenylacetylene (0.51 g, 5.00 mmol) was dissolved in THF (20 ml) and treated with N-iodomorpholine (2.56 g, 7.50 mmol) followed by CuI (0.05 g, 0.25 mmol). Sample was stirred for 45 min and monitored by GC-MS. After this time the suspension was poured onto a pad of neutral alumina (~30 mL) and the solution was collected under vacuum. The pad was then washed 3 times with THF (7.5 ml) (final volume ~42 mL, including original reaction). This solution was charged with 4-methoxyphenylazide (0.75 g, 5.00 mmol), followed by TTTA (0.11 g, 0.25 mmol) and finally CuI (0.05 g, 0.25 mmol). The reaction was stirred for 2h and monitored by LC-MS. After this time the starting materials had been consumed. The reaction was then charged with *p*-tolylboronic acid (1.36 g, 10.00 mmol) and TEA (2.11 ml, 15.00 mmol) and then warmed to 65°C. $Pd(OAc)_2$ (0.02 g, 0.10 mmol) was added to the heated solution and the reaction mixture was stirred for 4h. After this time the volatile components were removed under vacuum and the residue was purified by column chromatography (4:1 Hex:EtOAc). This gave **31** as a white solid. (1.25 g, 3.66 mmol, 73%)

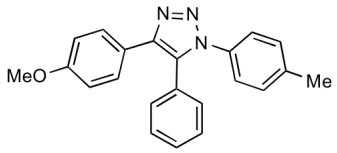


1-(4-methoxyphenyl)-4-phenyl-5-*p*-tolyl-1*H*-1,2,3-triazole (31). mp = 162–166 °C (dec.); IR (υ[cm^{-1}]) 2967, 1512, 1484, 1253, 1182, 994, 832, 780, 697; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.59 (d, *J*=7.9, 2H), 7.31 – 7.25 (m, 3H), 7.21 (d, *J*=8.6, 2H), 7.09 (dd, *J*=45.5, 7.6, 4H), 6.85 (d, *J*=8.6, 2H), 3.80 (s, 3H), 2.35 (s, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 160.0, 144.6, 139.5,

134.1, 131.3, 130.2, 129.9, 129.9, 128.7, 128.0, 127.5, 126.8, 124.9, 114.4, 55.7, 21.6; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{20}N_3O$, 342.1601; found 342.1601.



5-(4-methoxyphenyl)-1-phenyl-4-*p*-tolyl-1*H*-1,2,3-triazole (32). Synthesized from 4-methyl-phenylacetylene (0.58 g, 5.00 mmol), phenylazide (0.60 g, 5.00 mmol), and 4-methoxy-phenylboronic (1.52 g, 10.00mmol) acid using one-pot/three-step general procedure, 1.22 g, 3.57 mmol, 71%; mp = 172–174 °C (dec.); IR (υ[cm^{-1}]) 3064, 2922, 1611, 1523, 1499, 1250, 1177, 995, 847, 820, 760, 687; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.49 (d, *J*=8.0, 2H), 7.38 – 7.33 (m, 3H), 7.32 – 7.27 (m, 2H), 7.10 (dd, *J*=13.0, 8.2, 4H), 6.85 (d, *J*=8.5, 2H), 3.80 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 160.4, 144.9, 137.8, 136.9, 133.4, 131.7, 129.4, 129.3, 129.0, 128.3, 127.4, 125.4, 119.9, 114.7, 55.5, 21.5; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{20}N_3O$, 342.1601; found 342.1600.



4-(4-methoxyphenyl)-5-phenyl-1-*p*-tolyl-1*H*-1,2,3-triazole (33). Synthesized from 4-methoxy-phenylacetylene (0.66 g, 5.00 mmol), 4-methyl-phenylazide (0.67 g, 5.00 mmol), and phenylboronic acid (1.22 g, 10.00 mmol) using one-pot/three-step general procedure, 1.19 g, 3.50 mmol, 70%; mp = 192–195 °C (dec.); IR (υ[cm^{-1}]) 3019, 2937, 1619, 1517, 1481, 1370, 1247, 1177, 1027, 997, 842, 820, 747; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.50 (d, *J*=8.4, 2H), 7.39 – 7.30 (m, 3H), 7.20 – 7.11 (m, 6H), 6.83 (d, *J*=8.5, 2H), 3.78 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 159.5, 144.8, 139.2, 134.3, 133.1, 130.4, 129.9, 129.4, 129.2, 128.8,

128.2, 125.2, 123.6, 114.1, 55.4, 21.4; HRMS (ESI-TOF) (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{20}N_3O$, 342.1601; found 342.1605.

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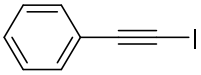
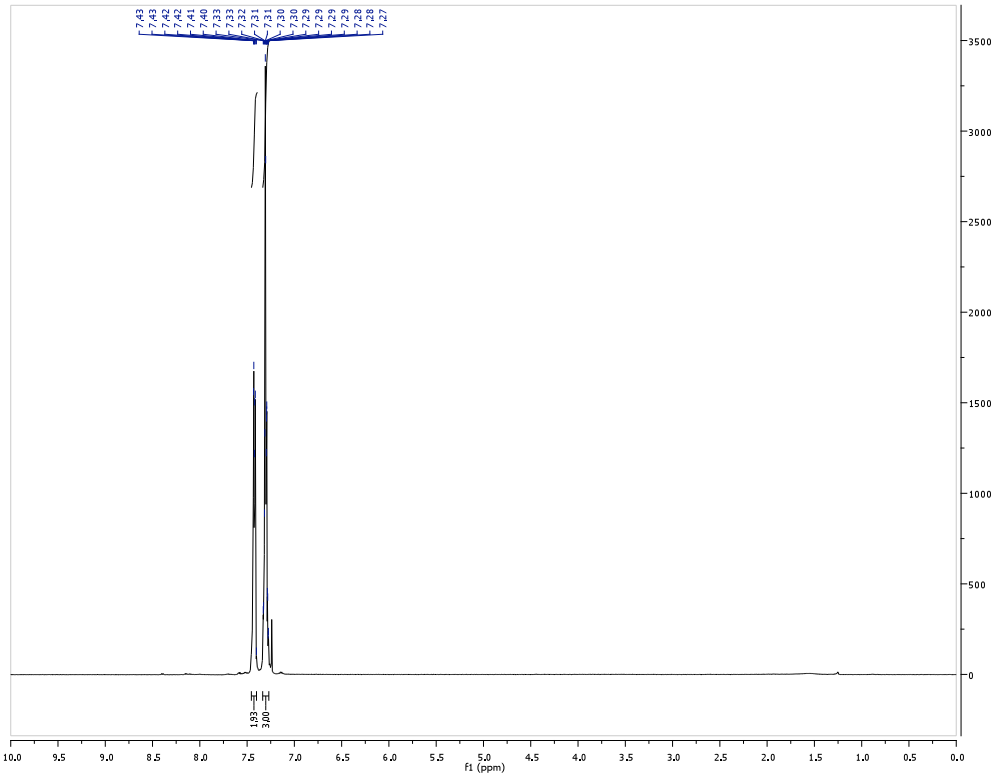
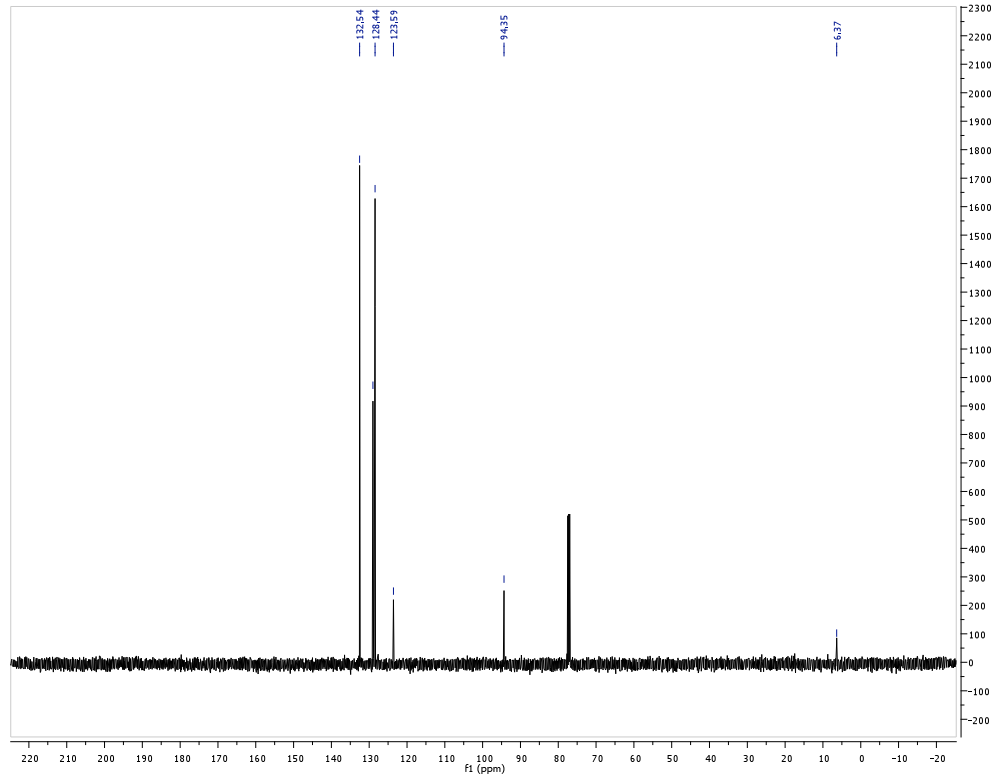
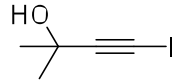
1-iodo-phenylacetylene (1)

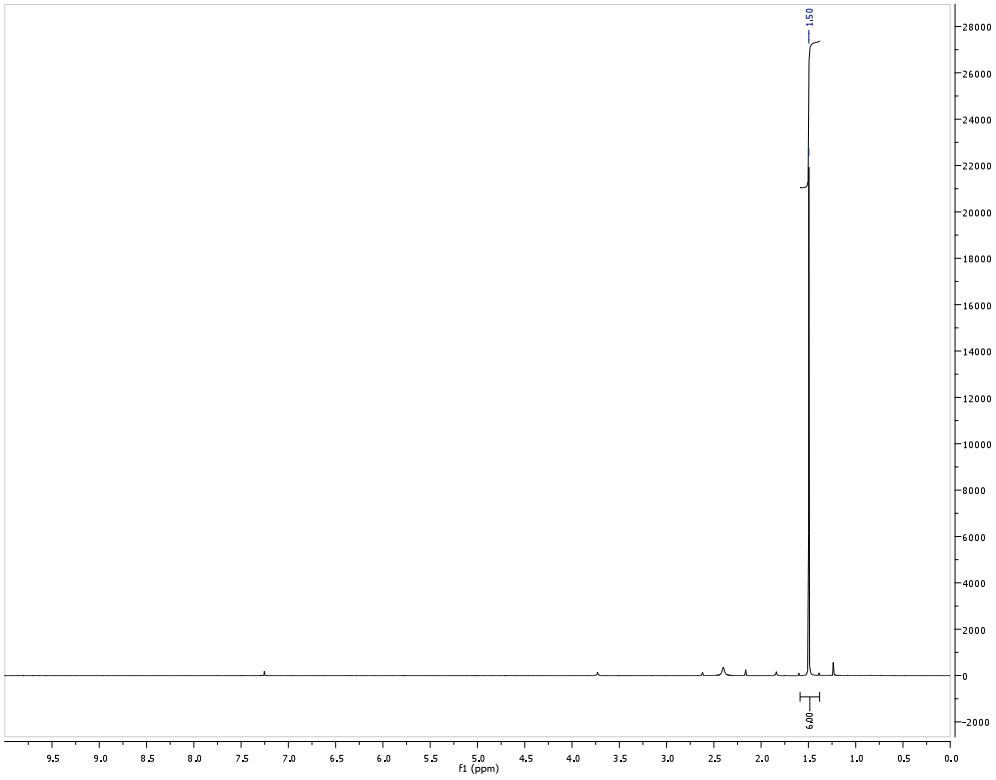


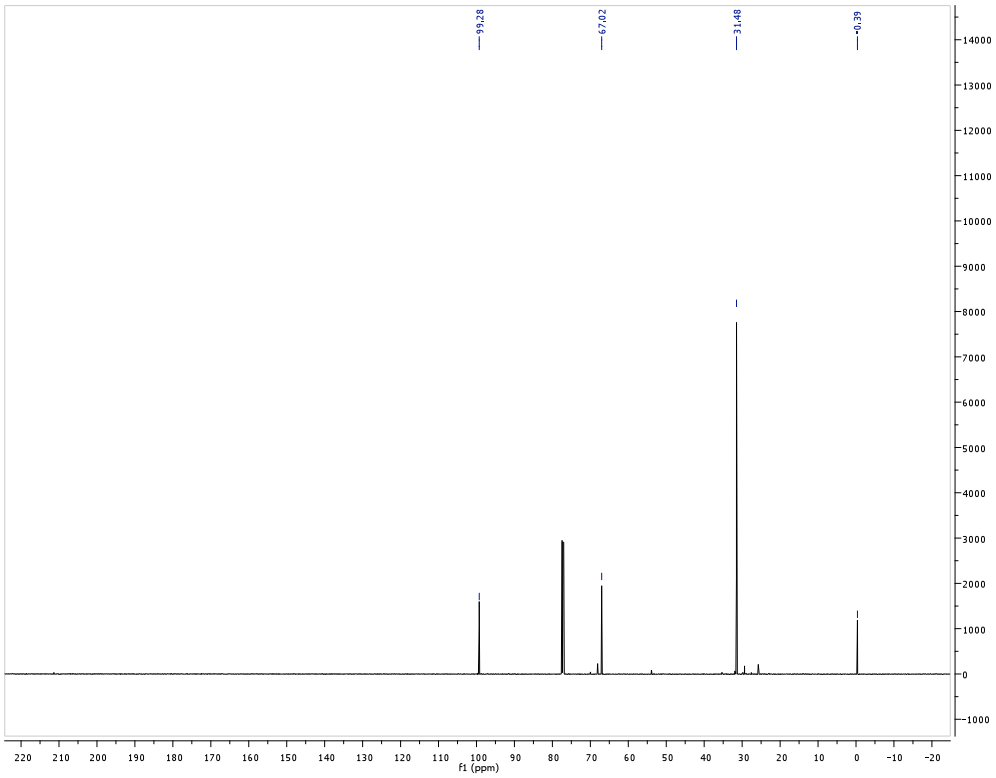




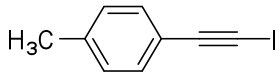
4-Iodo-2-methylbut-3-yn-2-ol (24)

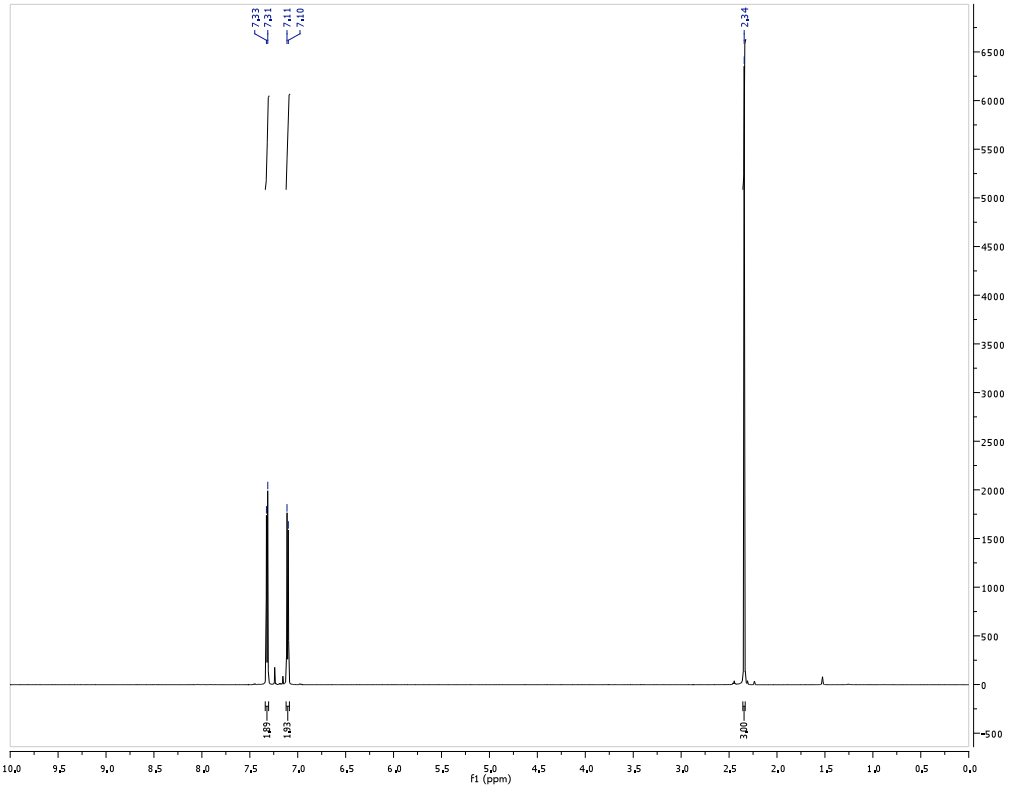


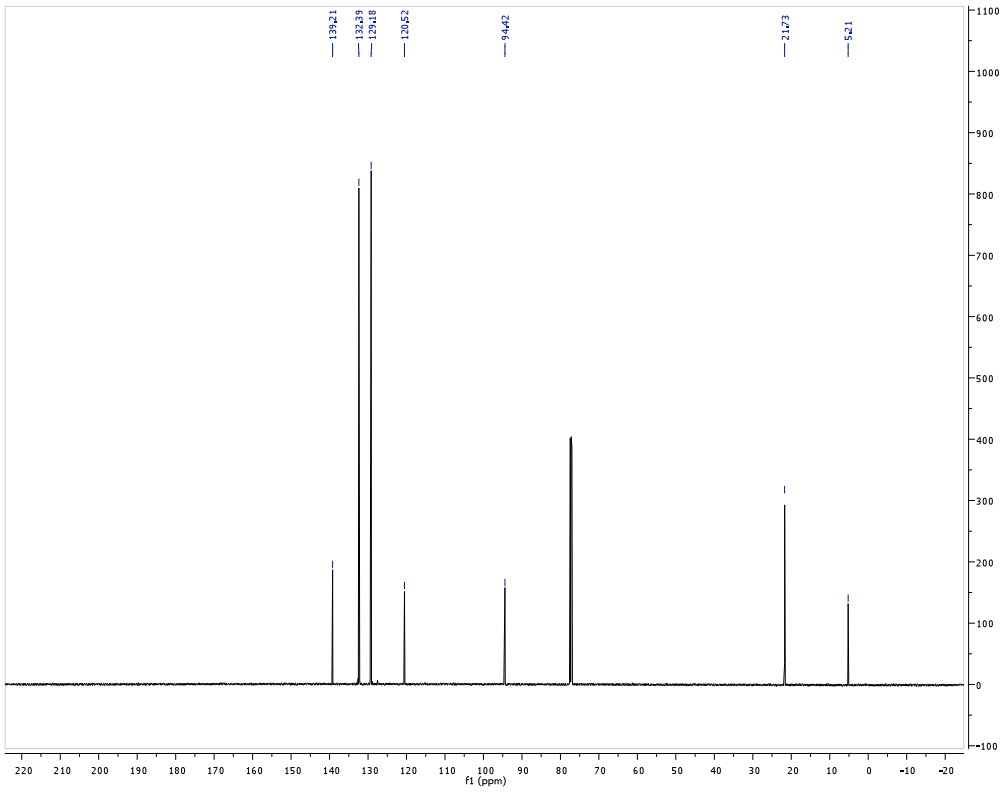




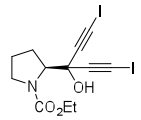
1-(Iodoethynyl)-4-methylbenzene (25)

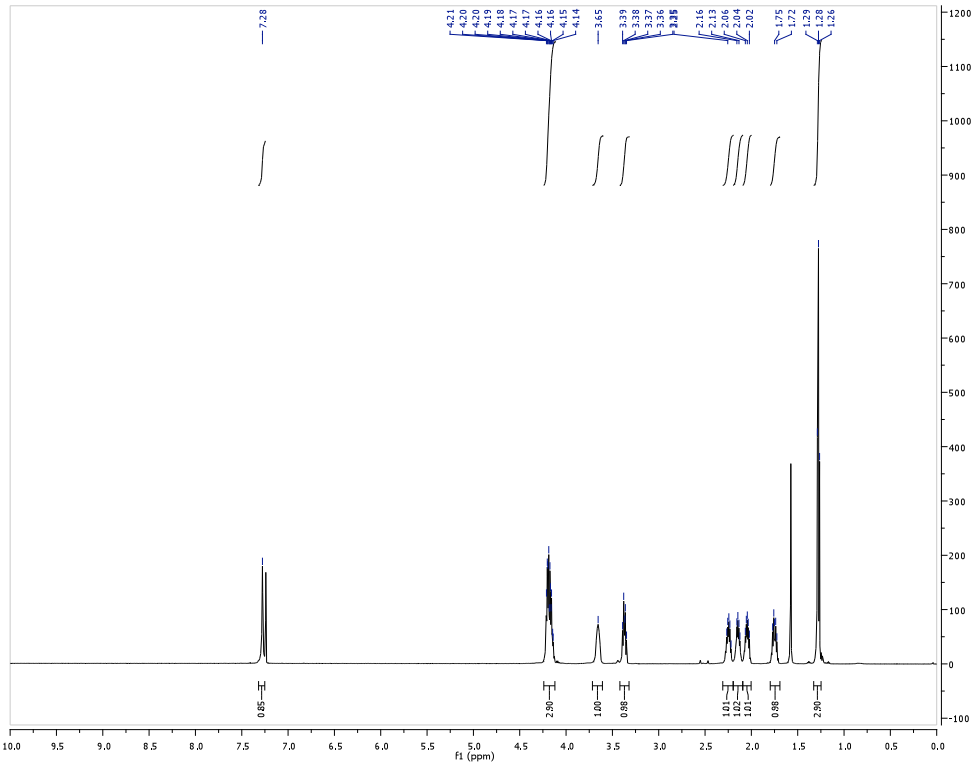


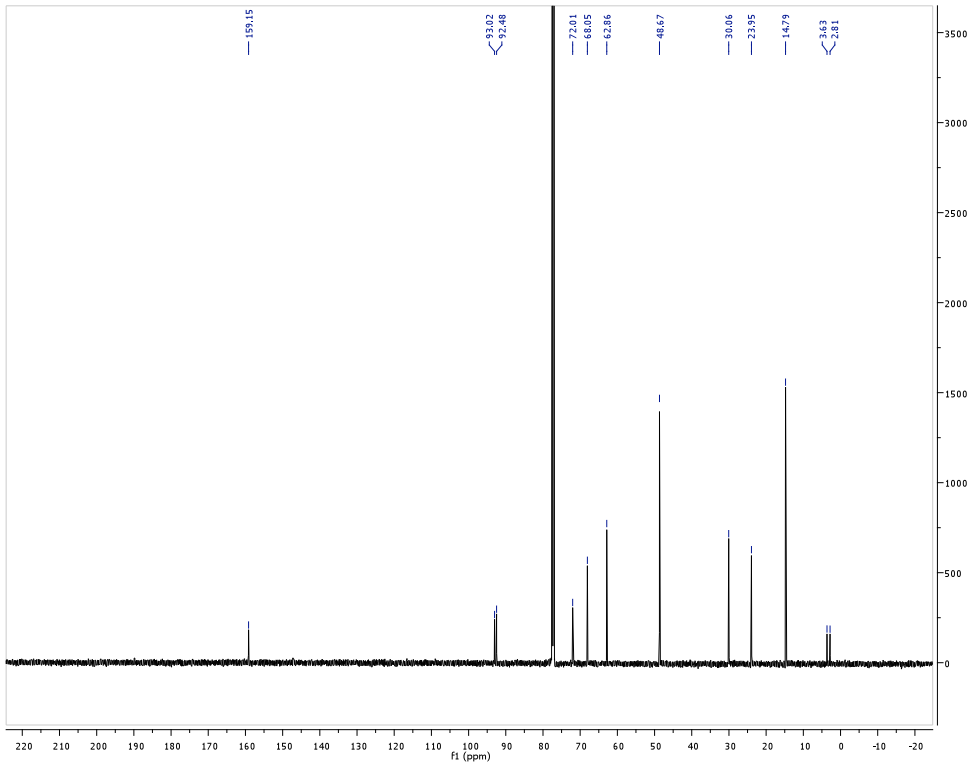




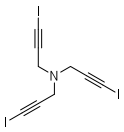
(*S*)-Ethyl 2-(3-hydroxy-1,5-diiodopenta-1,4-diyn-3-yl)pyrrolidine-1-carboxylate (26)

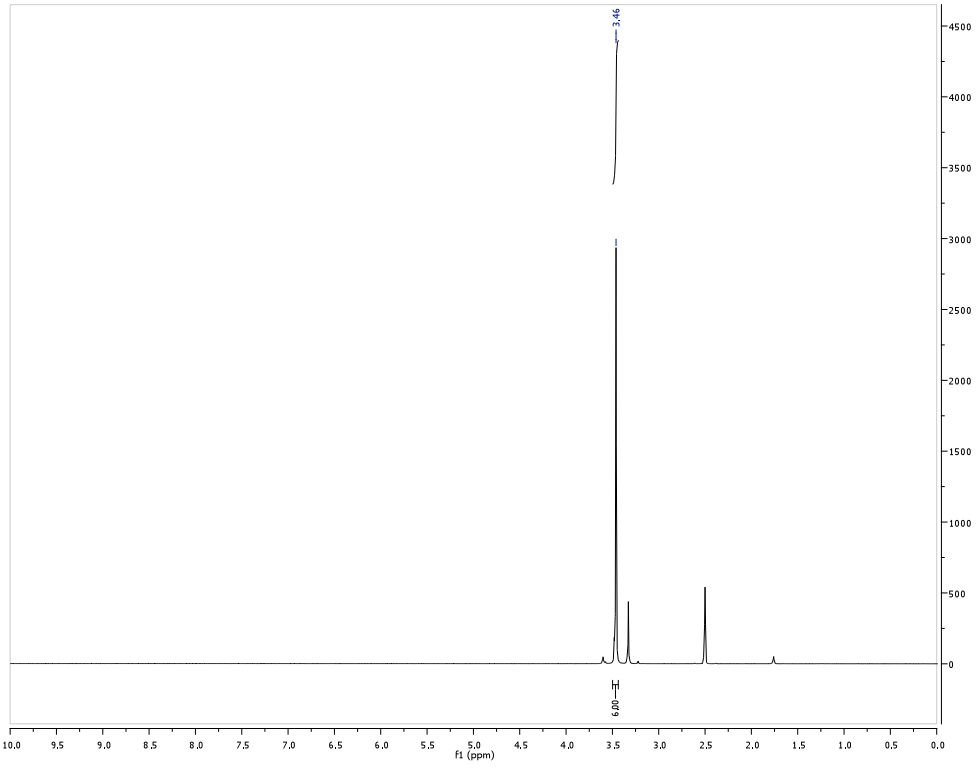


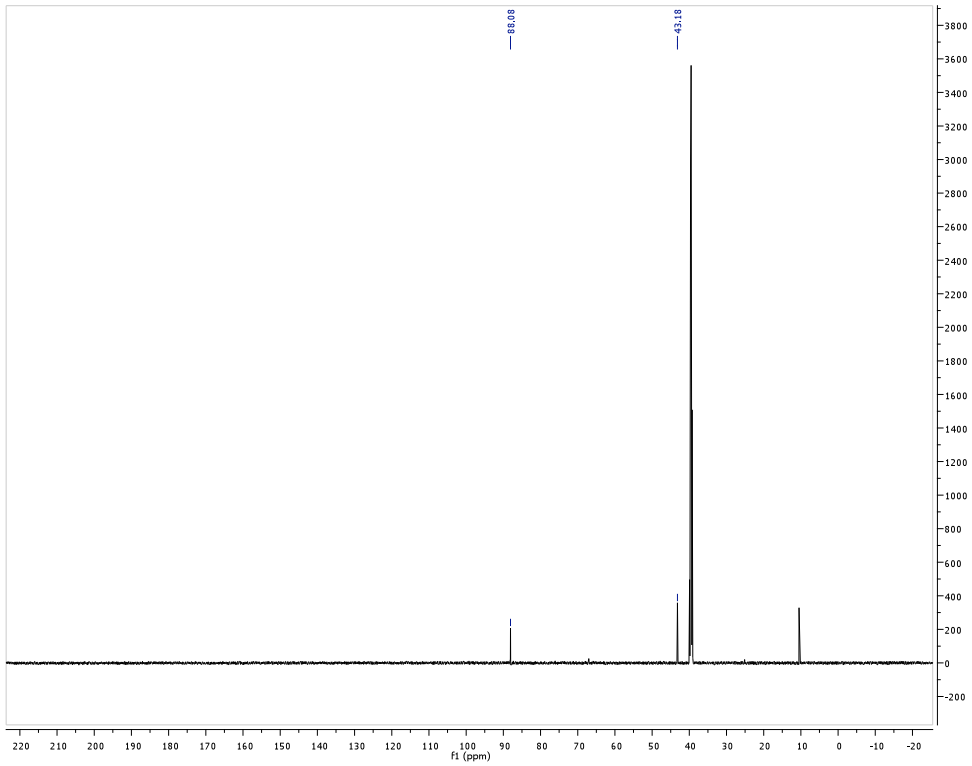




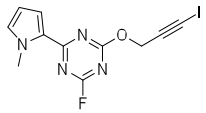
Tris(3-iodoprop-2-ynyl)amine (27)

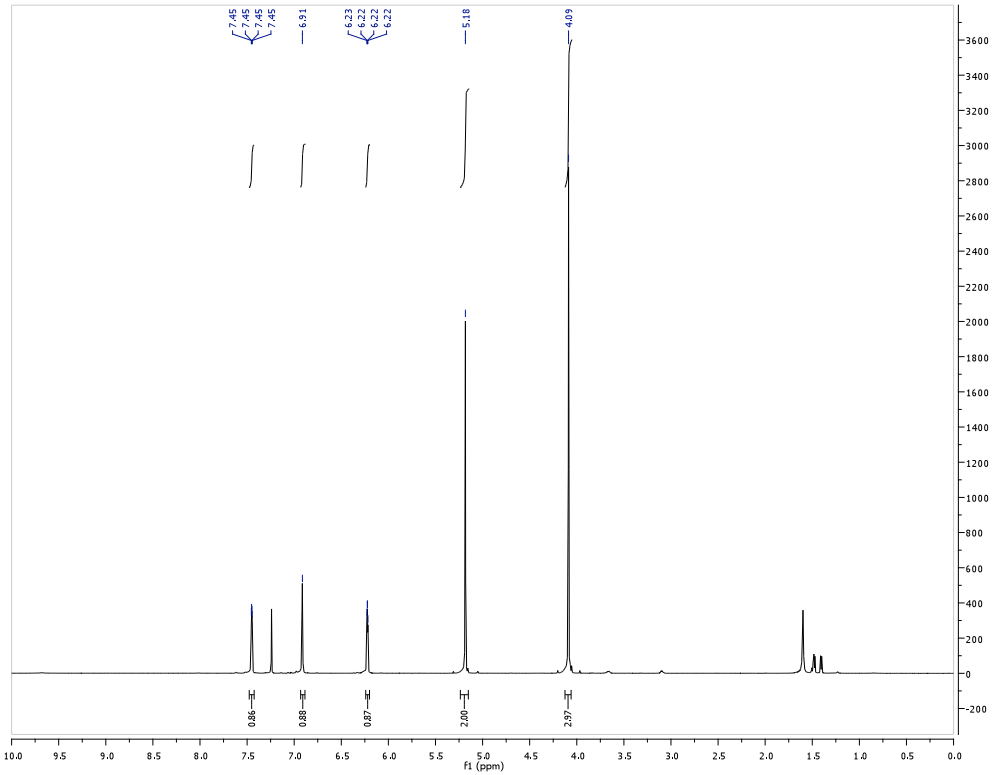


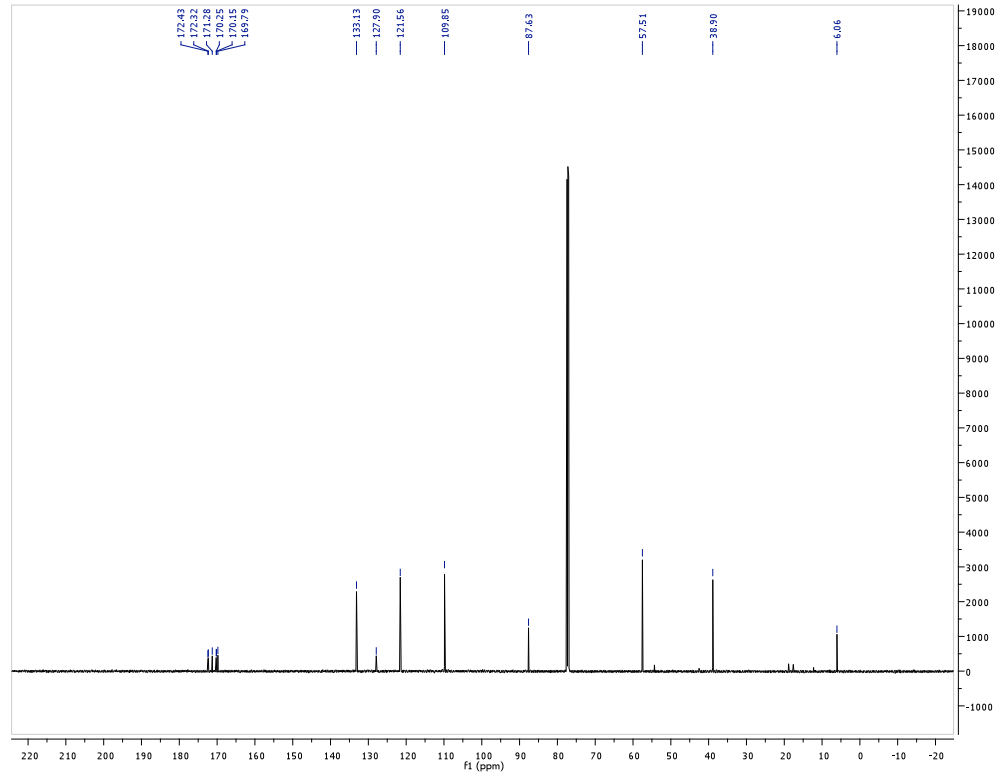




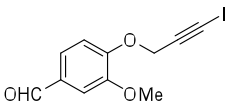
2-Fluoro-4-(3-iodoprop-2-ynyloxy)-6-(1-methyl-1*H*-pyrrol-2-yl)-1,3,5-triazine

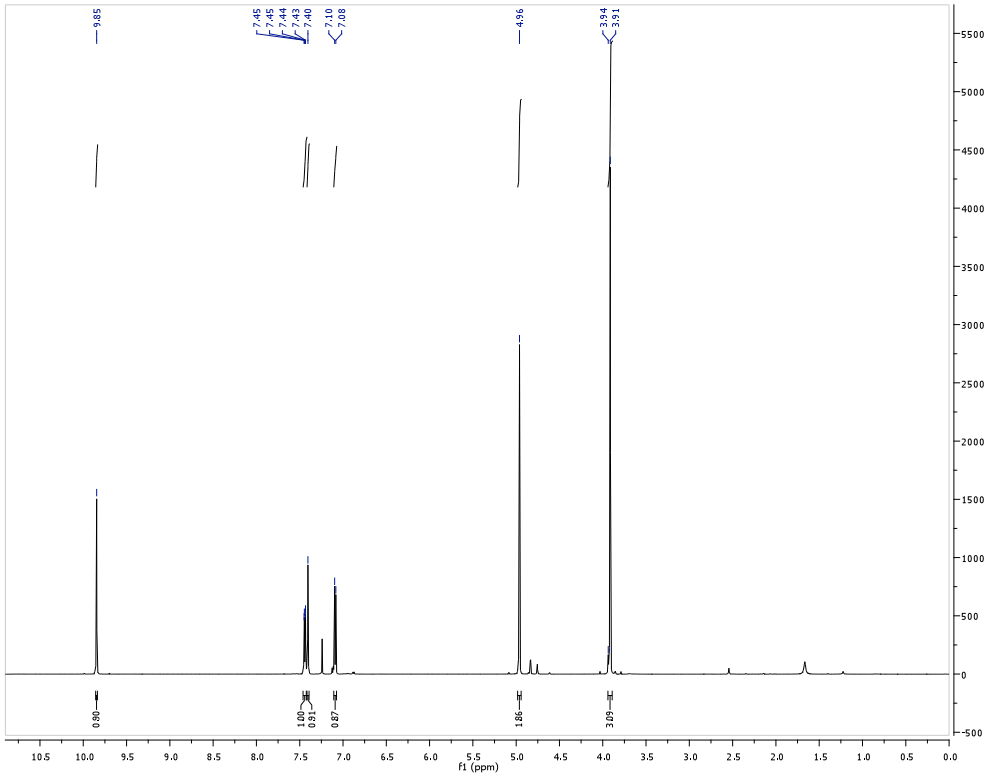


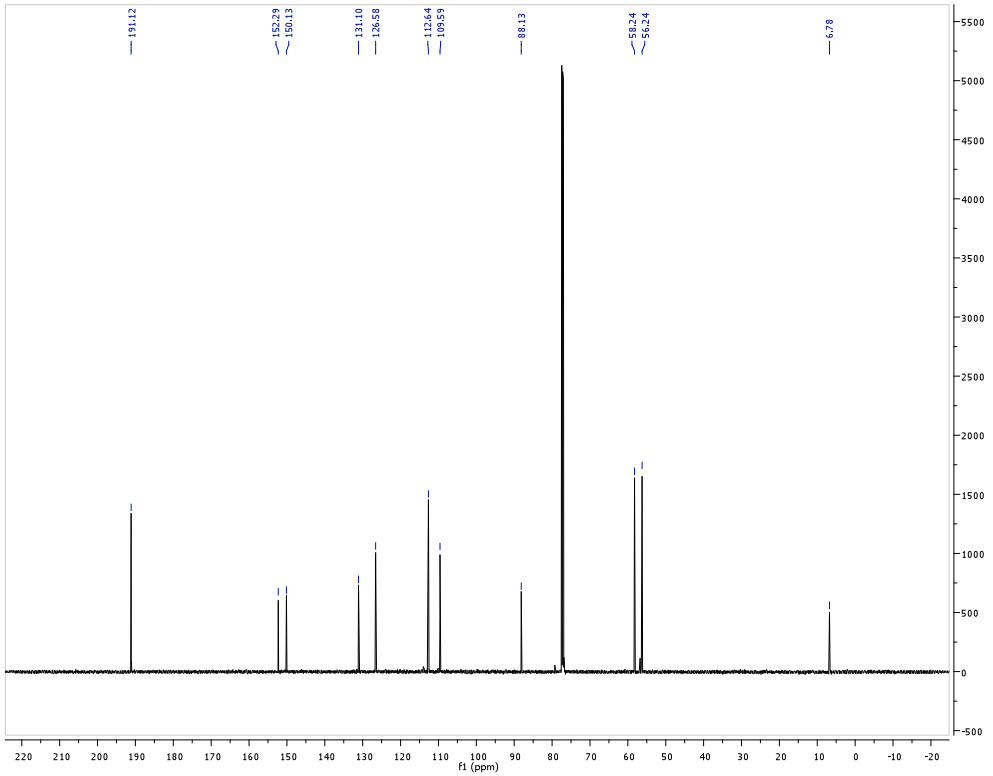




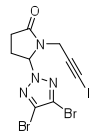
4-(3-Iodoprop-2-ynyloxy)-3-methoxybenzaldehyde

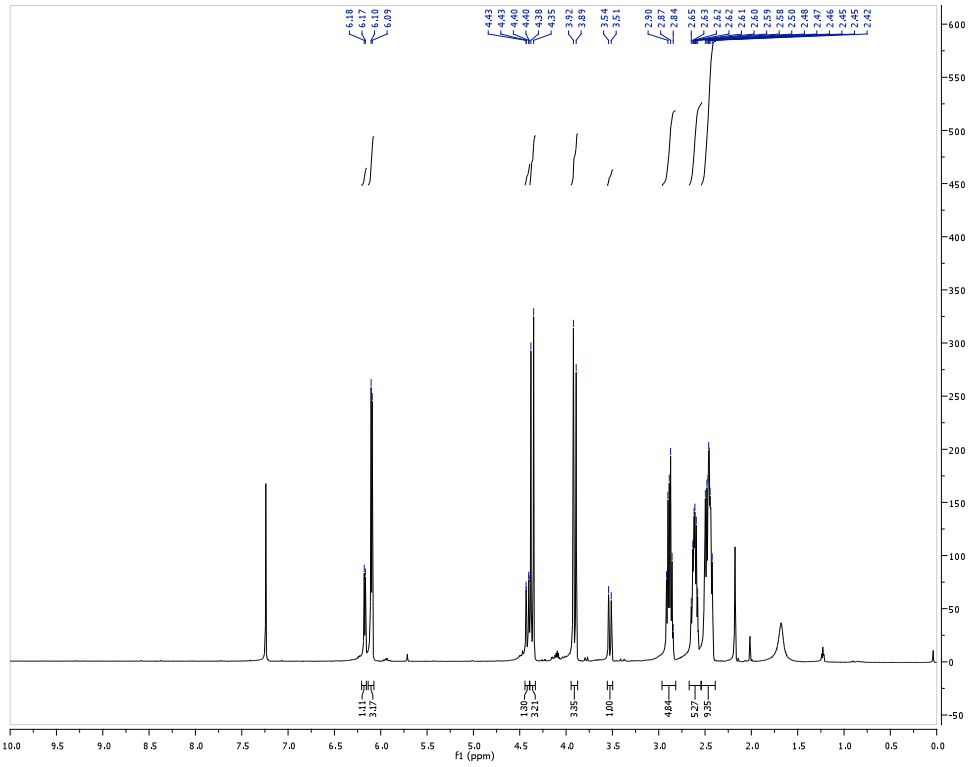


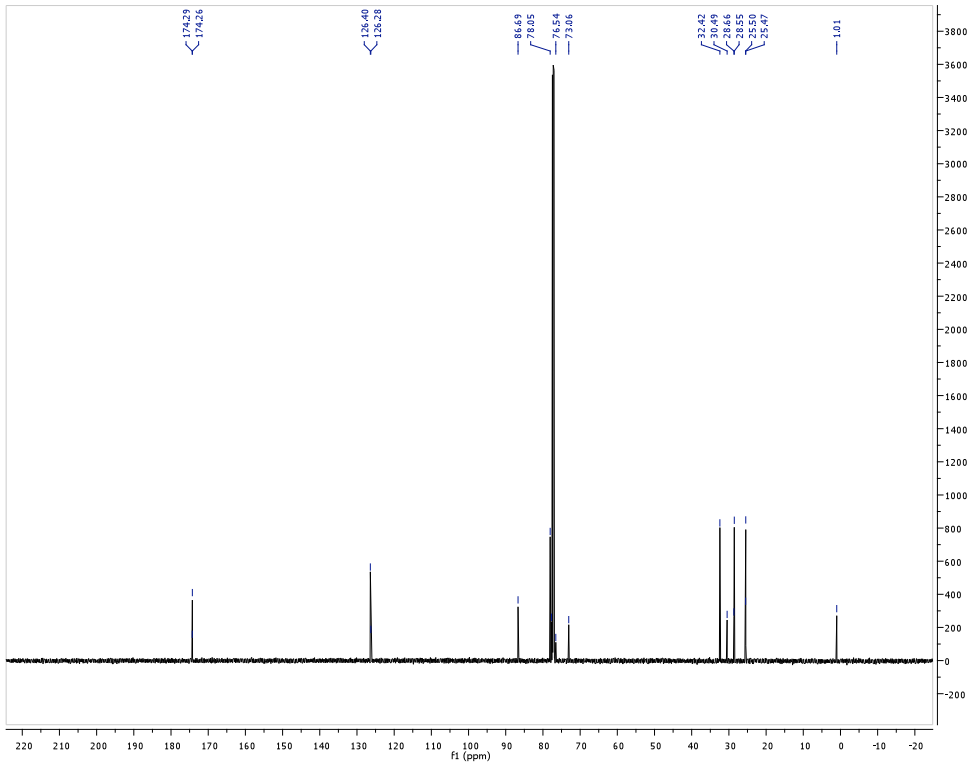




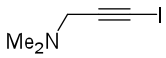
5-(4,5-Dibromo-2*H*-1,2,3-triazol-2-yl)-1-(3-iodoprop-2-ynyl)pyrrolidin-2-one

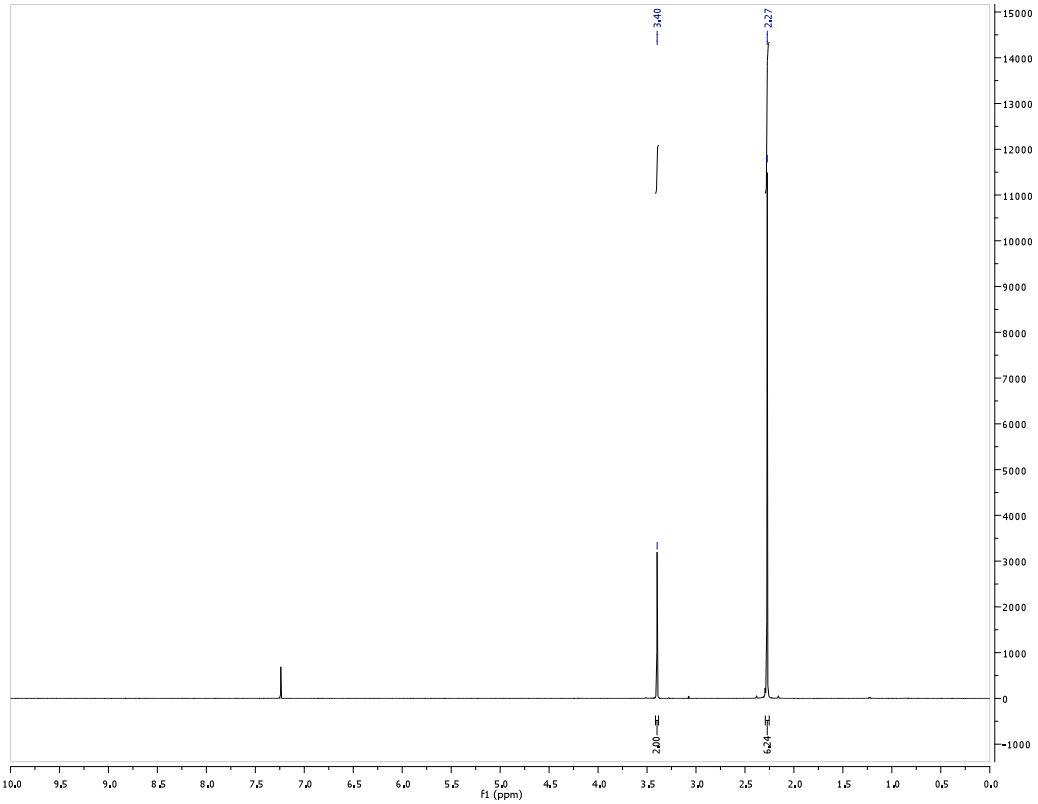


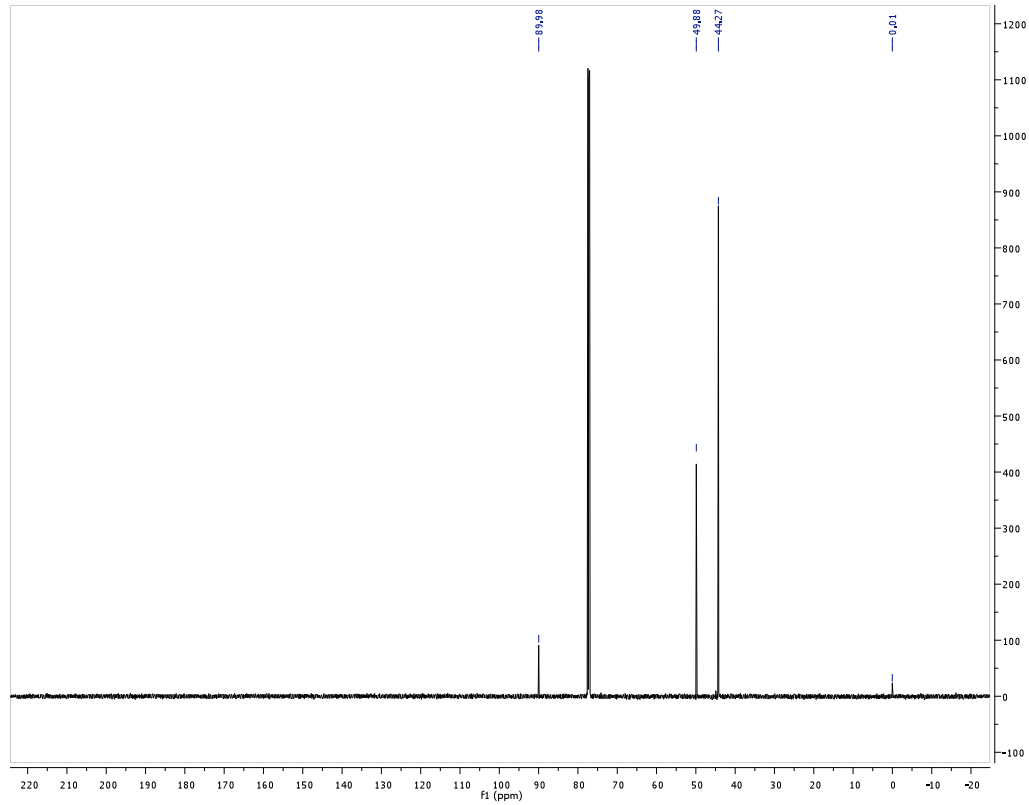




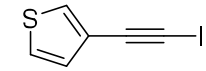
3-Iodo-*N*,*N*-dimethylpropargylamine

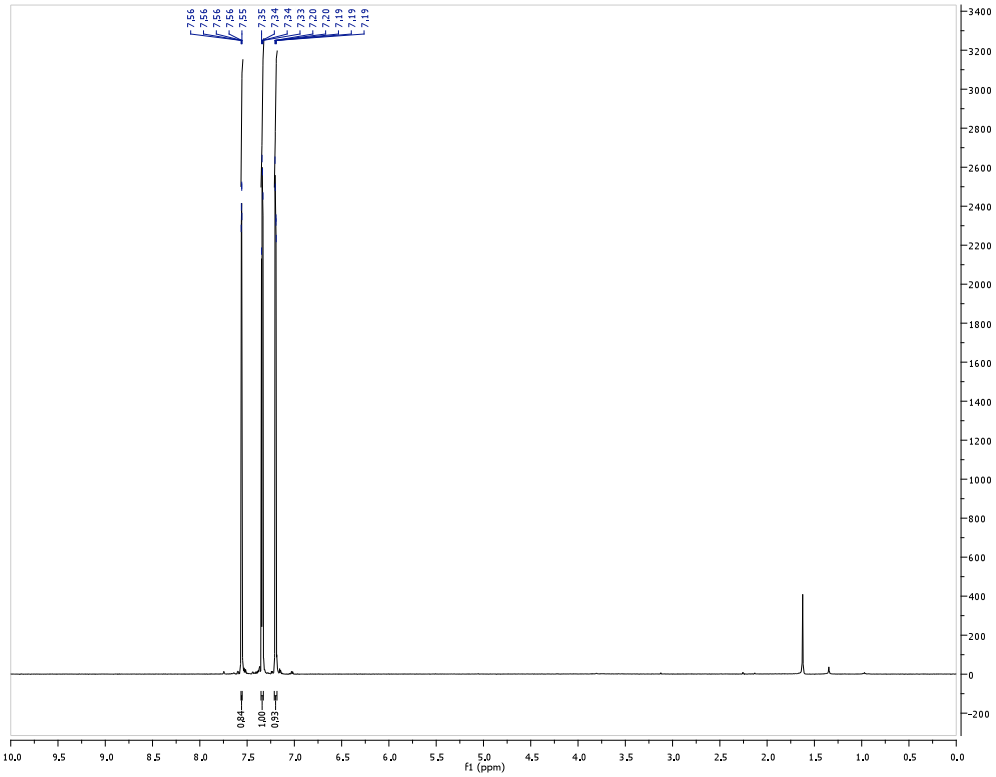


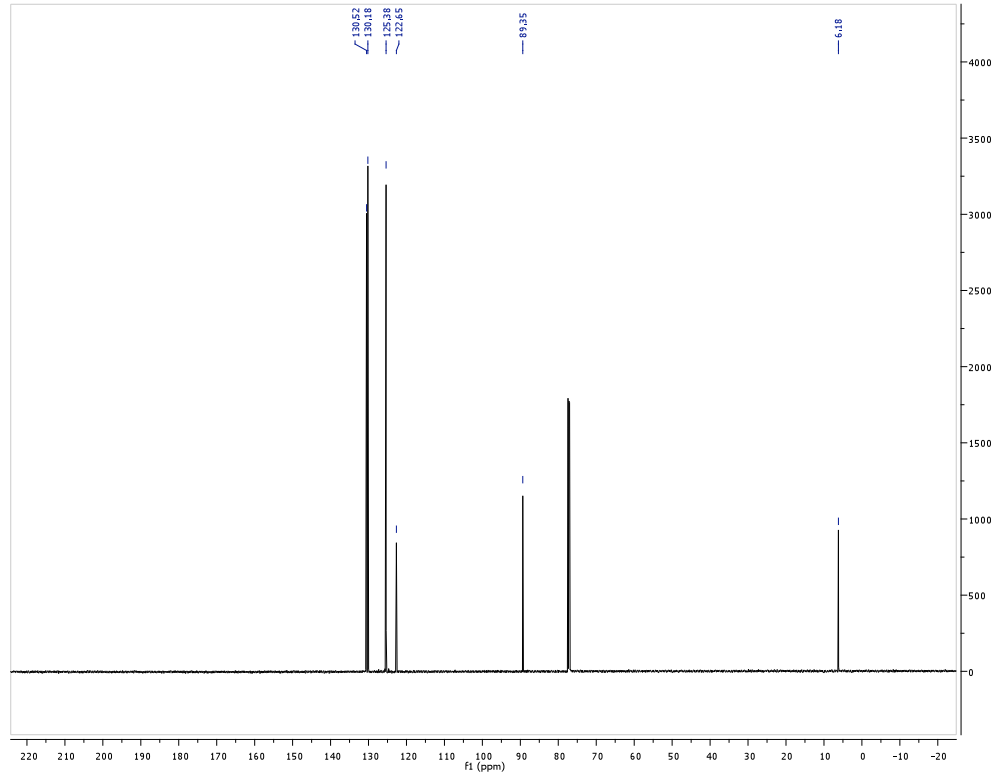




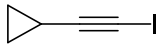
3-(Iodoethynyl)thiophene

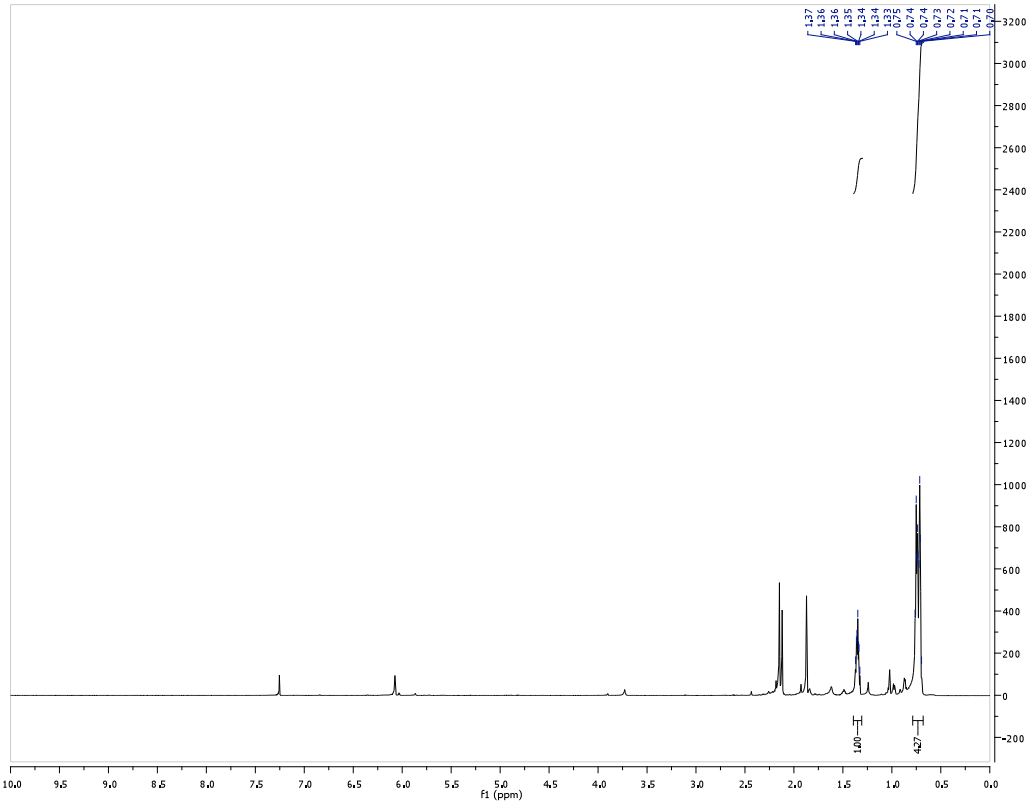


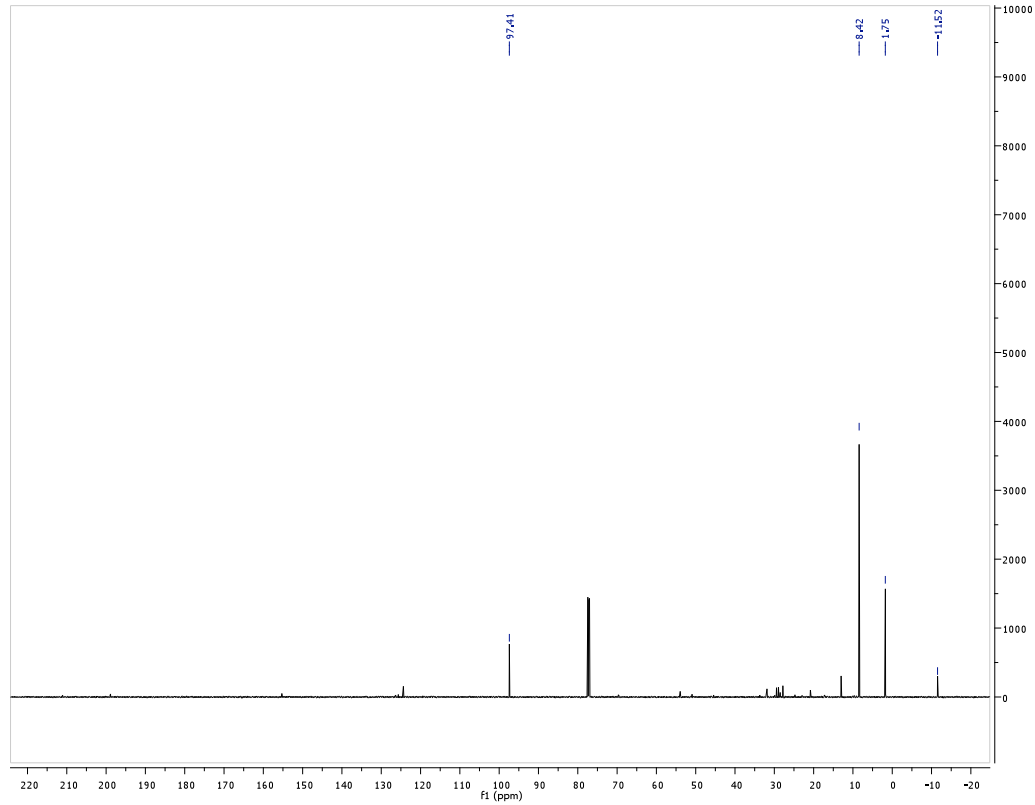




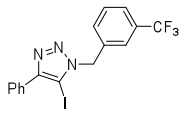
(Iodoethynyl)cyclopropane

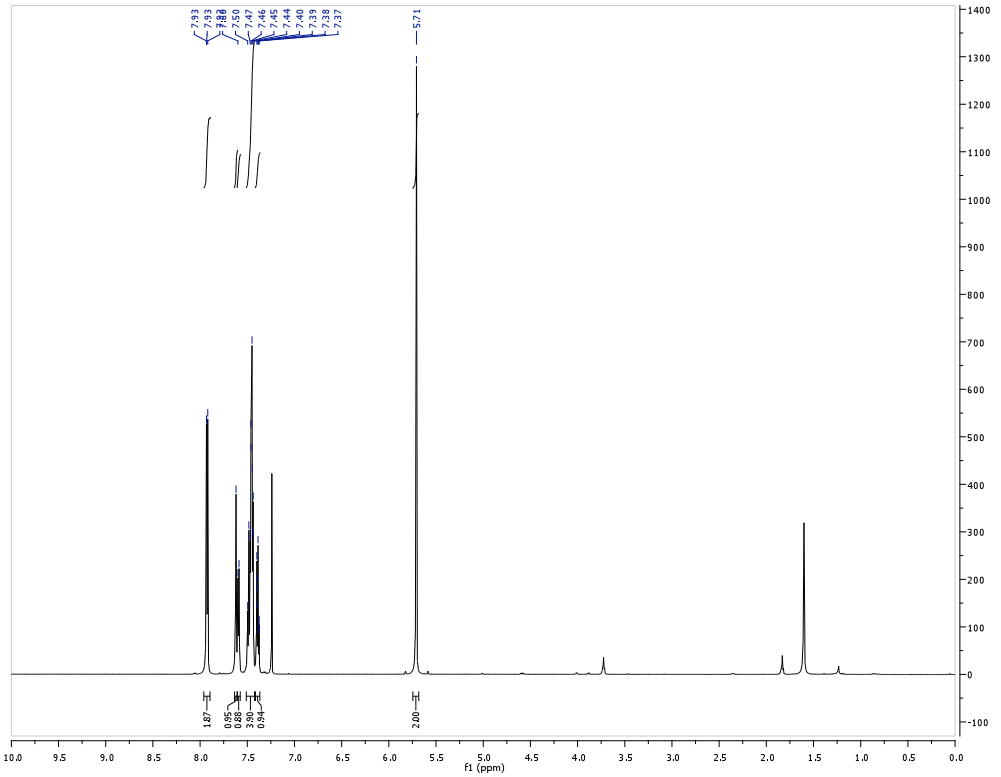


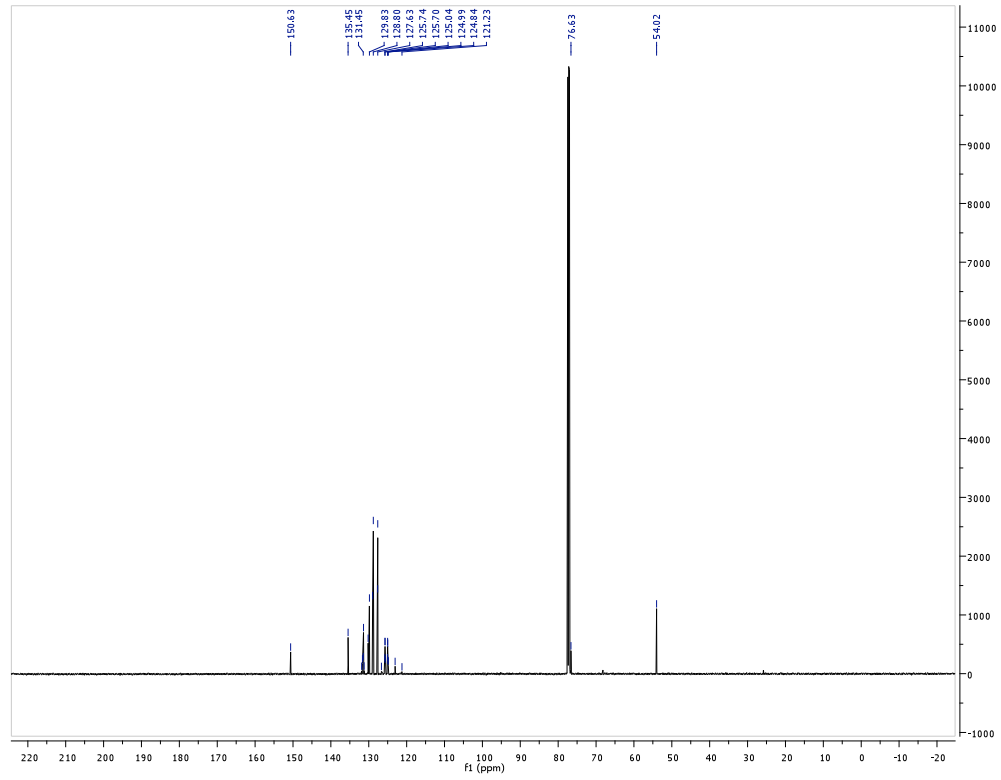




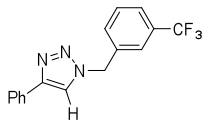
5-Iodo-4-phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (3)

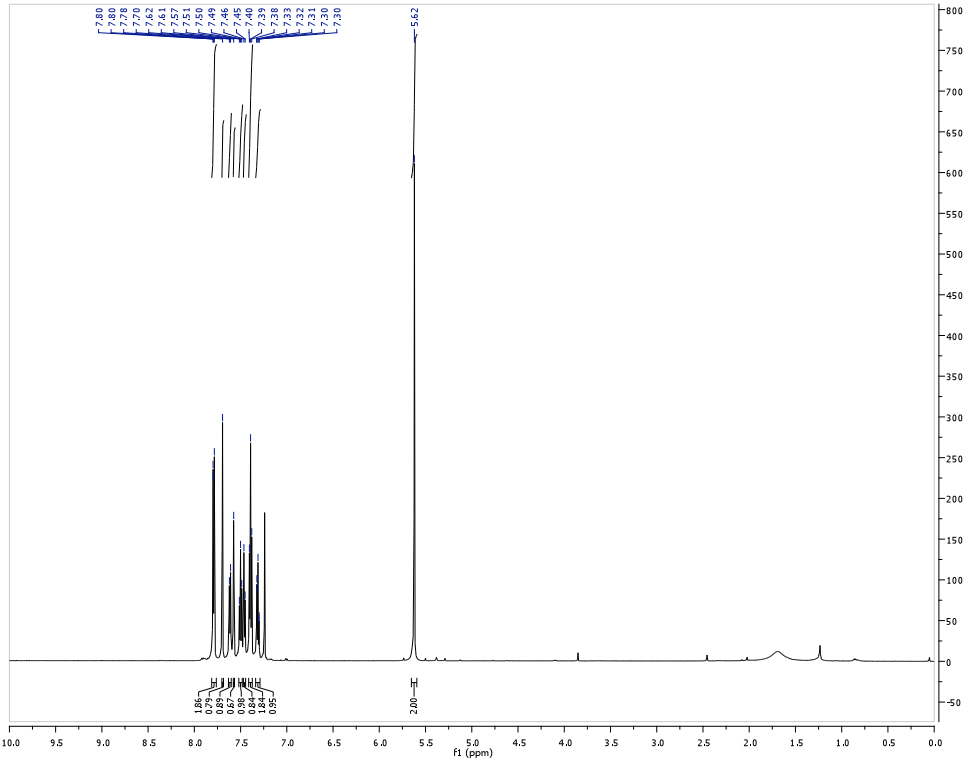


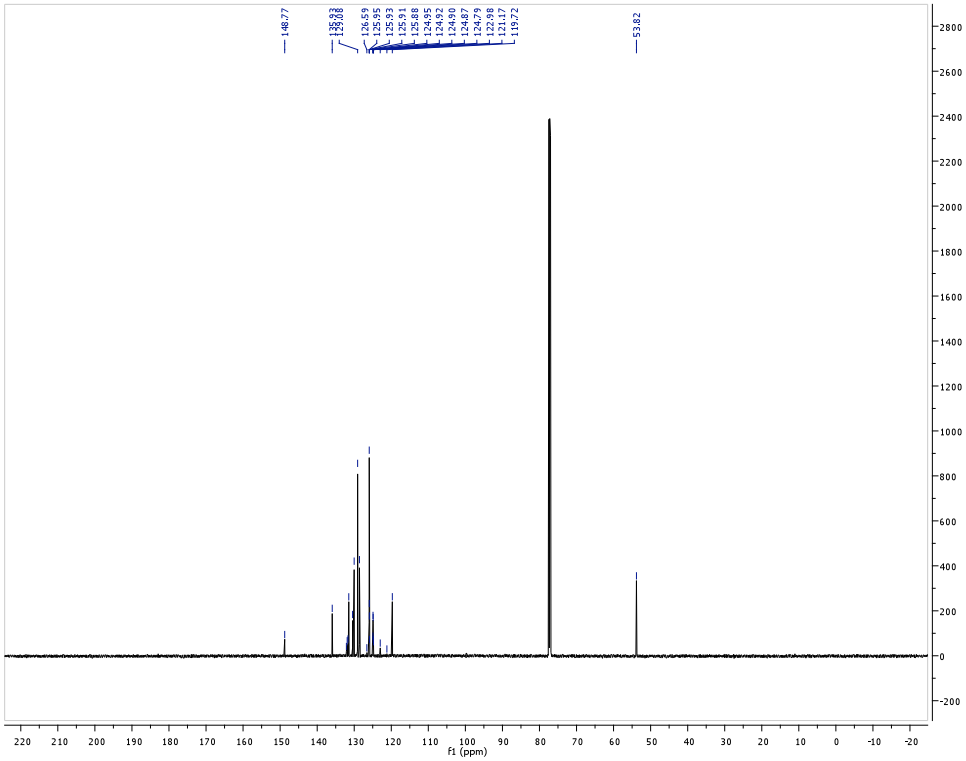




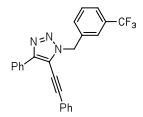
4-Phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (4)

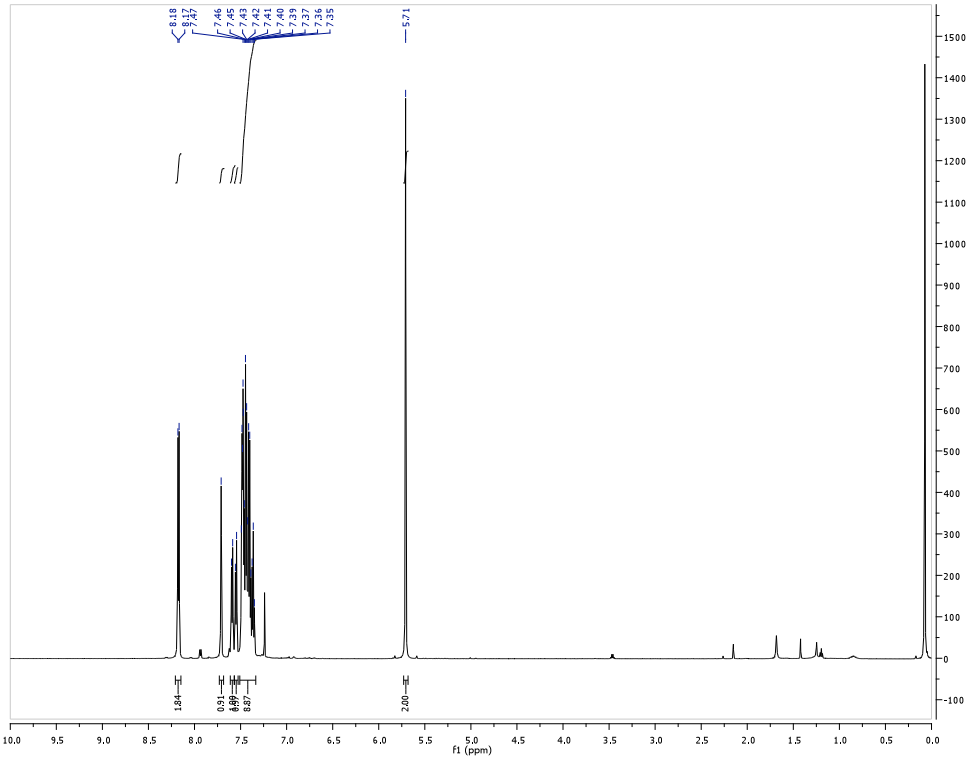


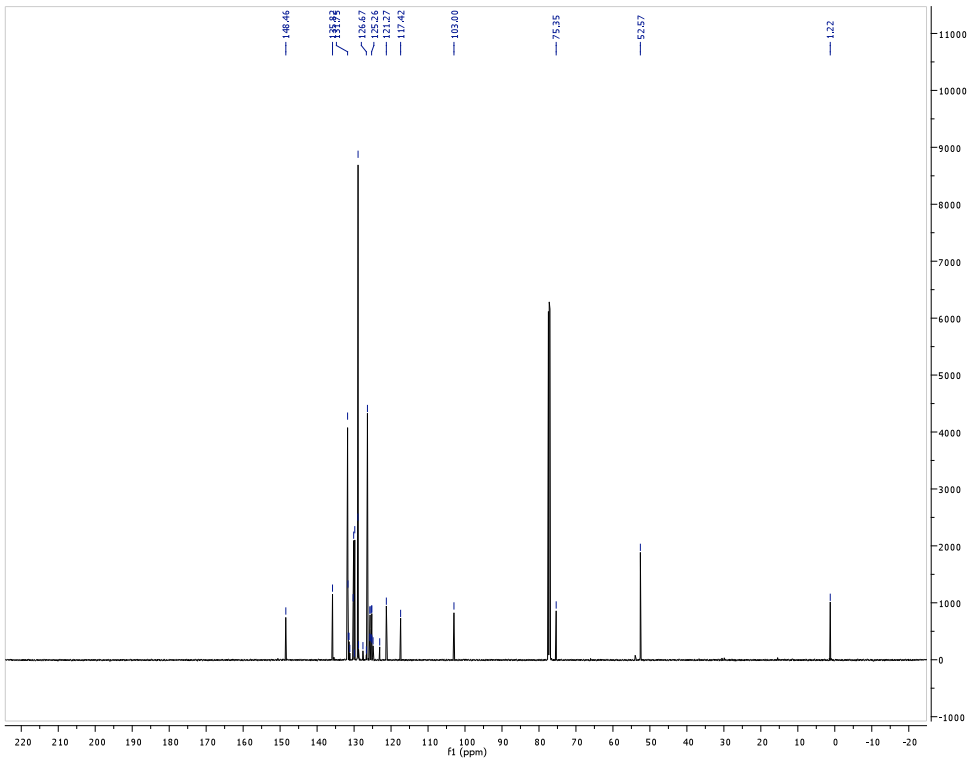




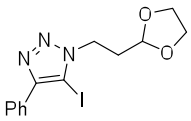
4-Phenyl-5-(phenylethynyl)-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (5)

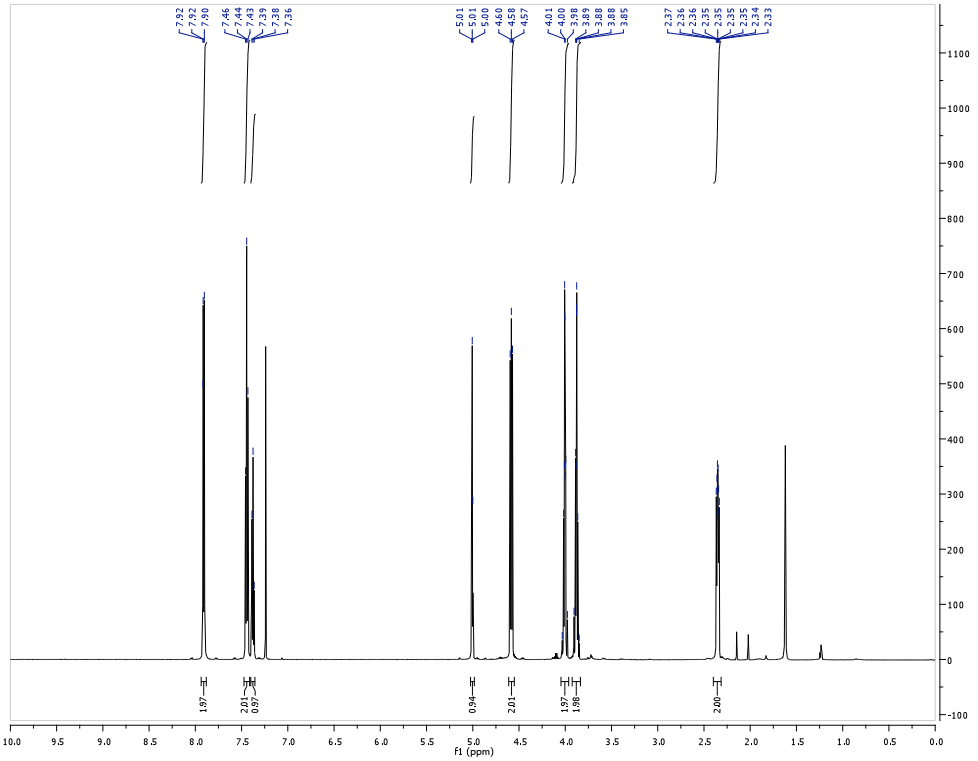


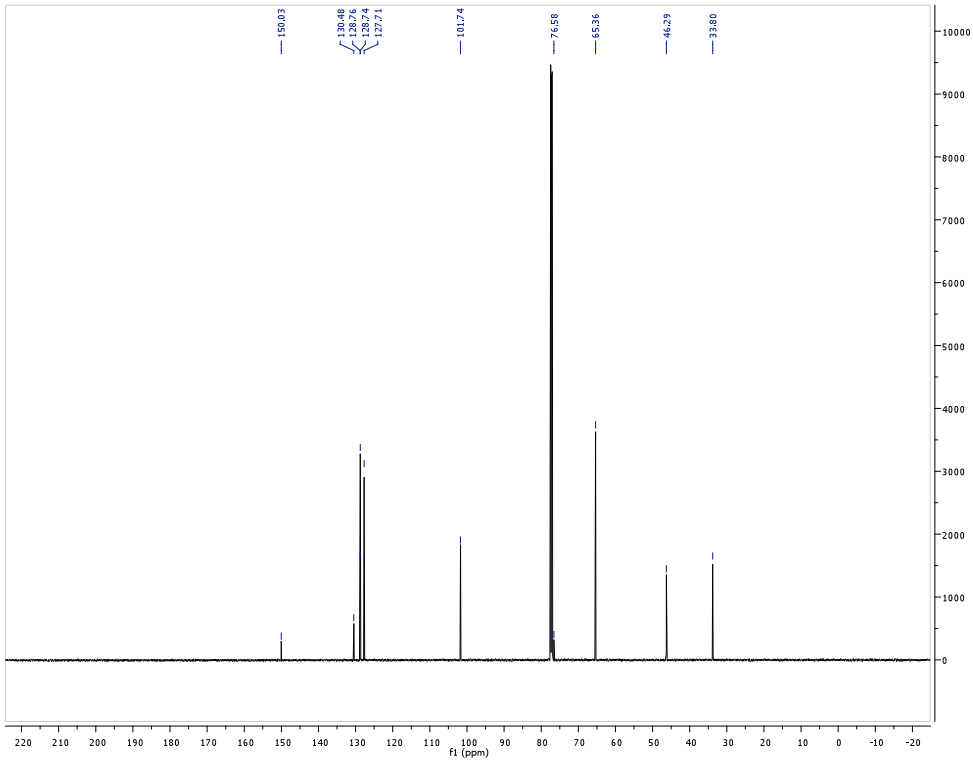




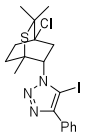
1-(2-(1,3-Dioxolan-2-yl)ethyl)-5-iodo-4-phenyl-1*H*-1,2,3-triazole (6)

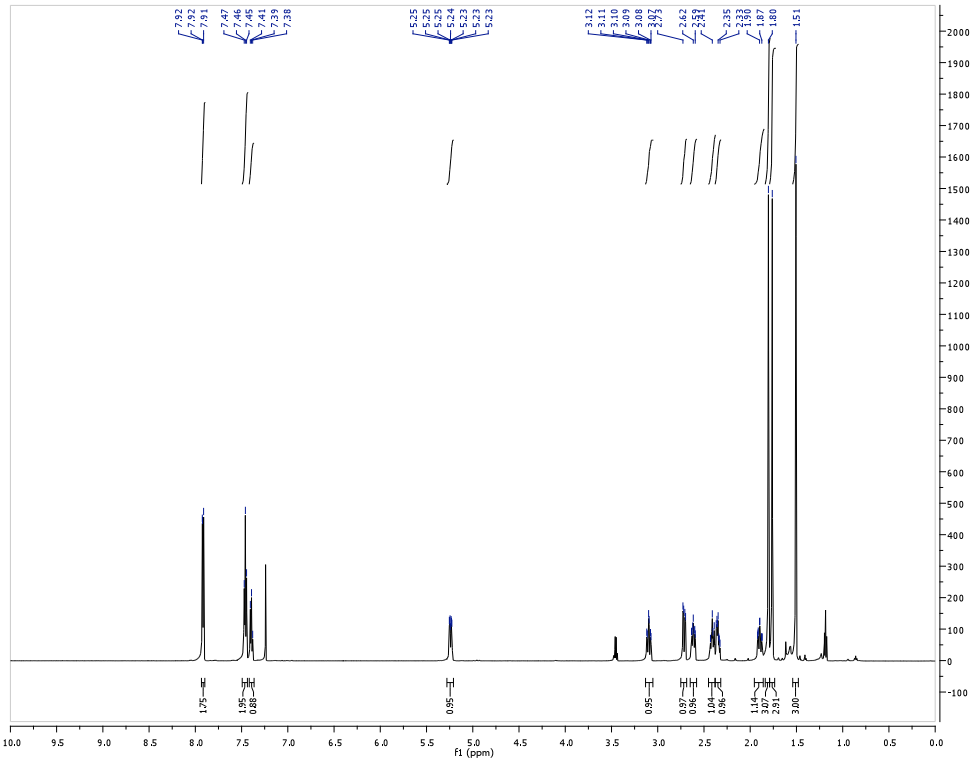


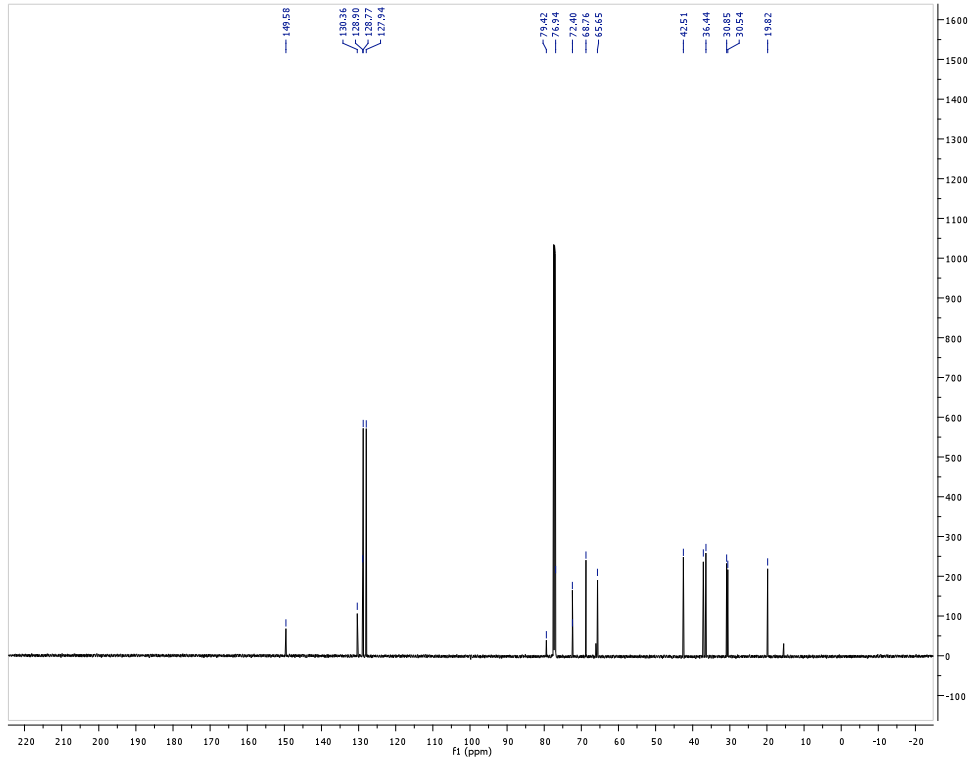




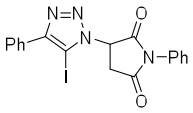
1-(4-chloro-1,3,3-trimethyl-2-thiabicyclo[2.2.2]octan-7-yl)-5-iodo-4-phenyl-1*H*-1,2,3-triazole (7)

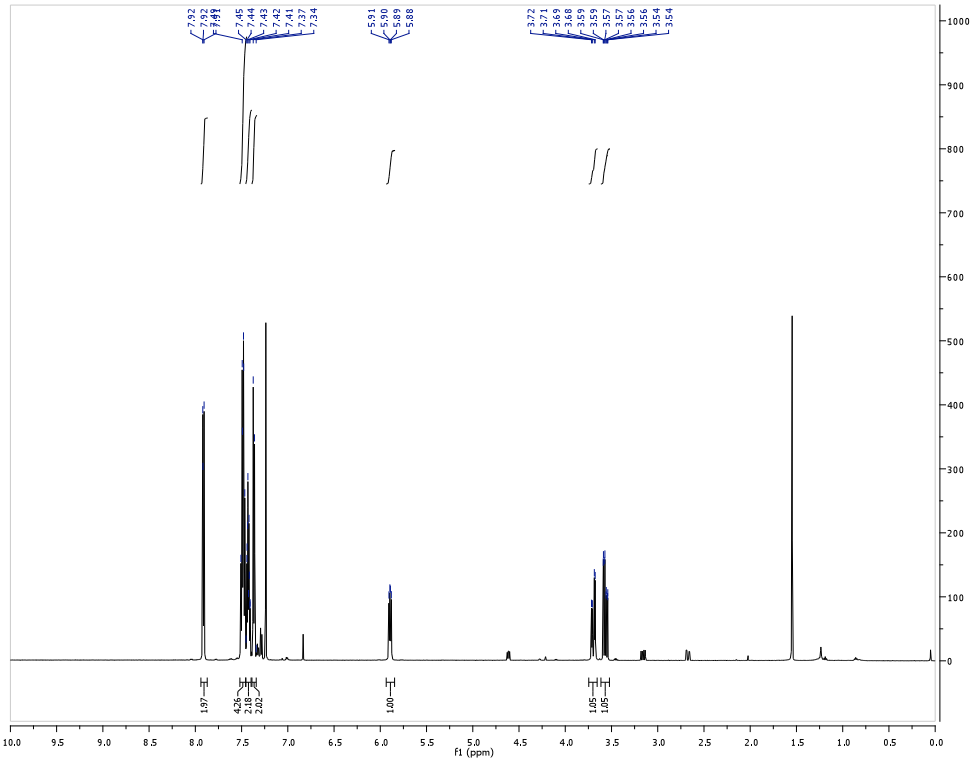


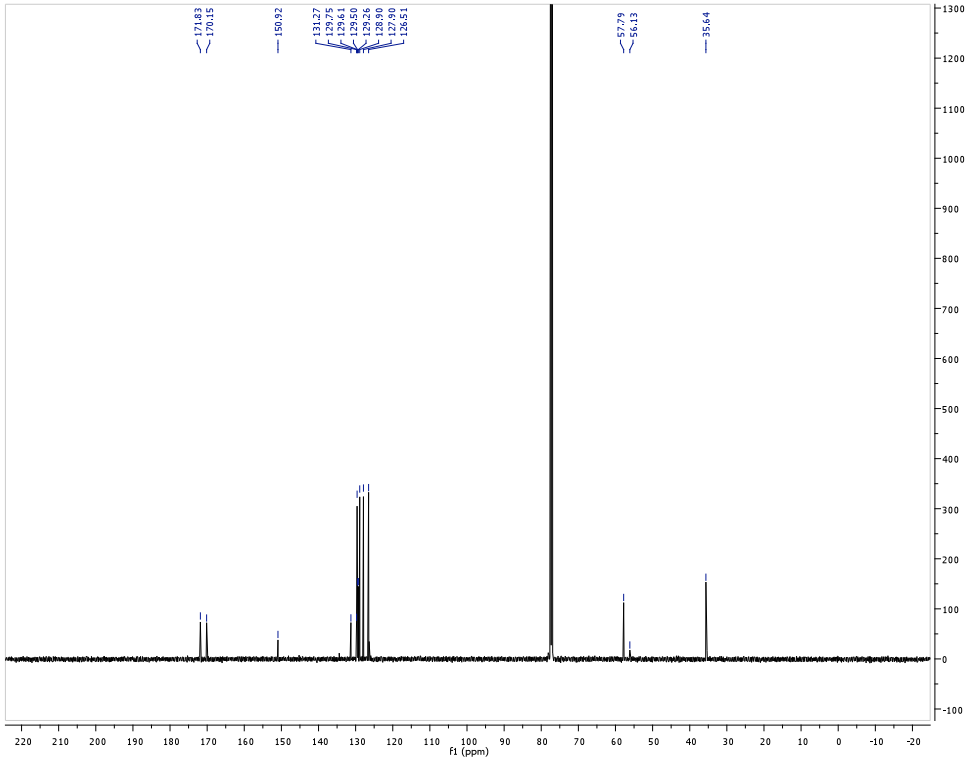




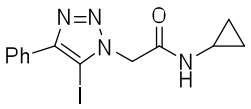
3-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-phenylpyrrolidine-2,5-dione (8)

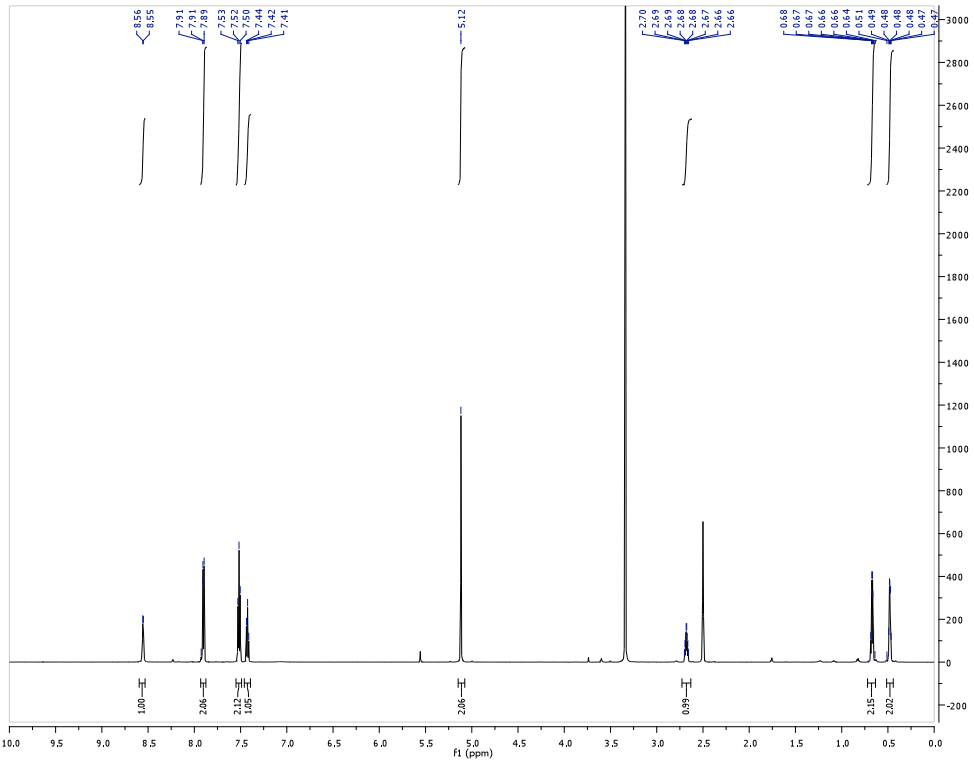


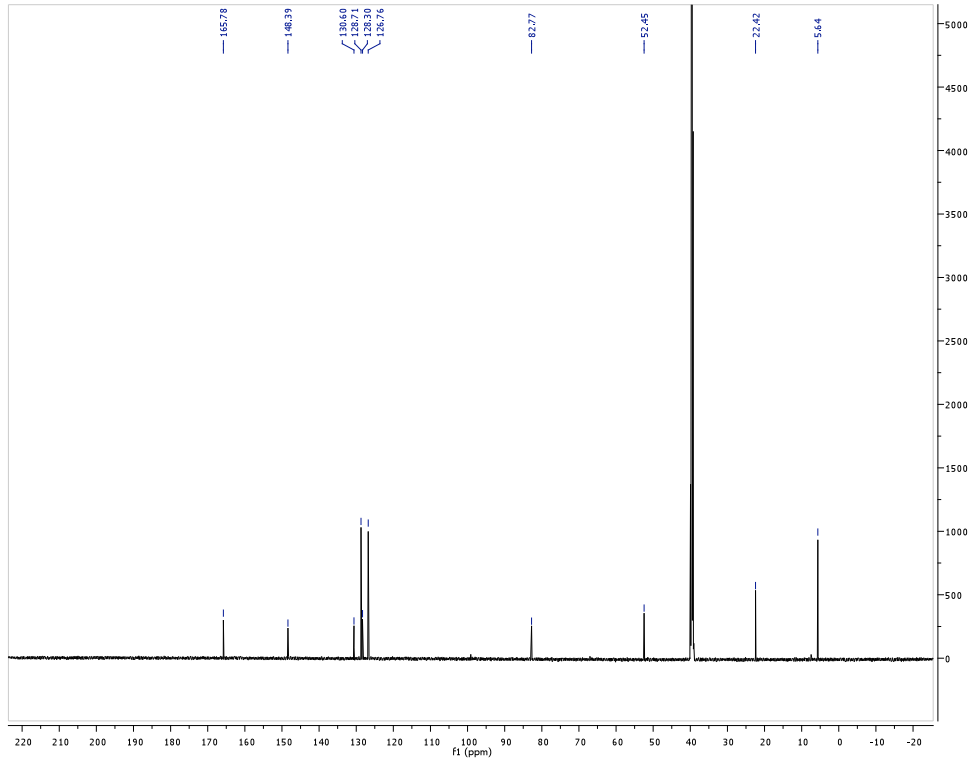




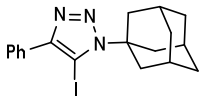
_N_-cyclopropyl-2-(5-iodo-4-phenyl-1_H_-1,2,3-triazol-1-yl)acetamide (9)

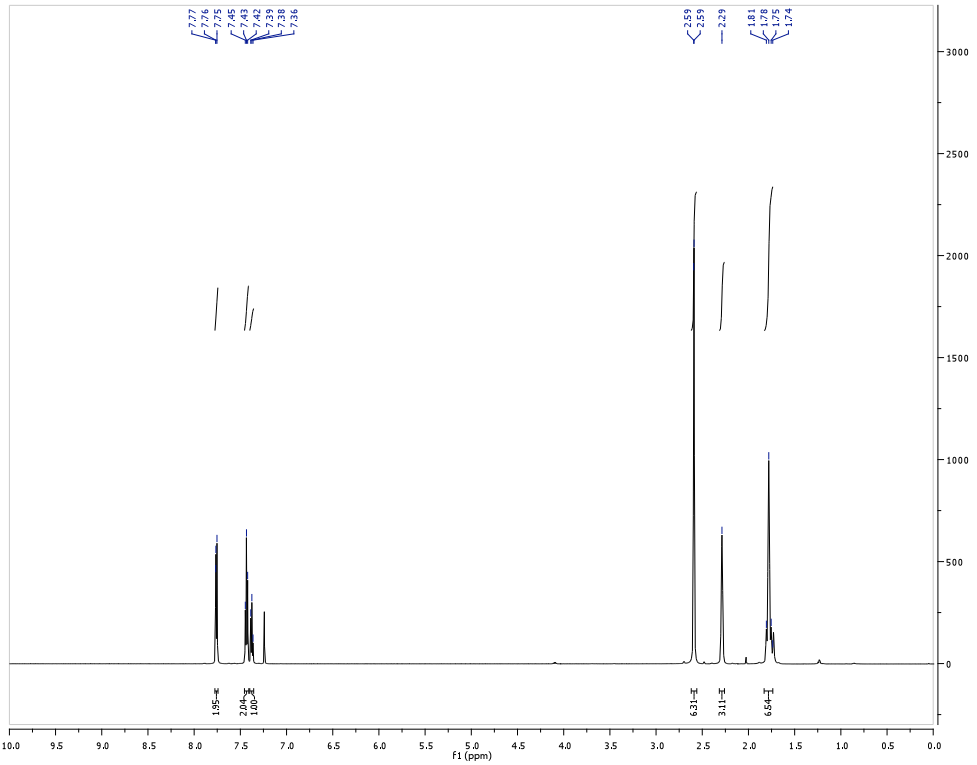


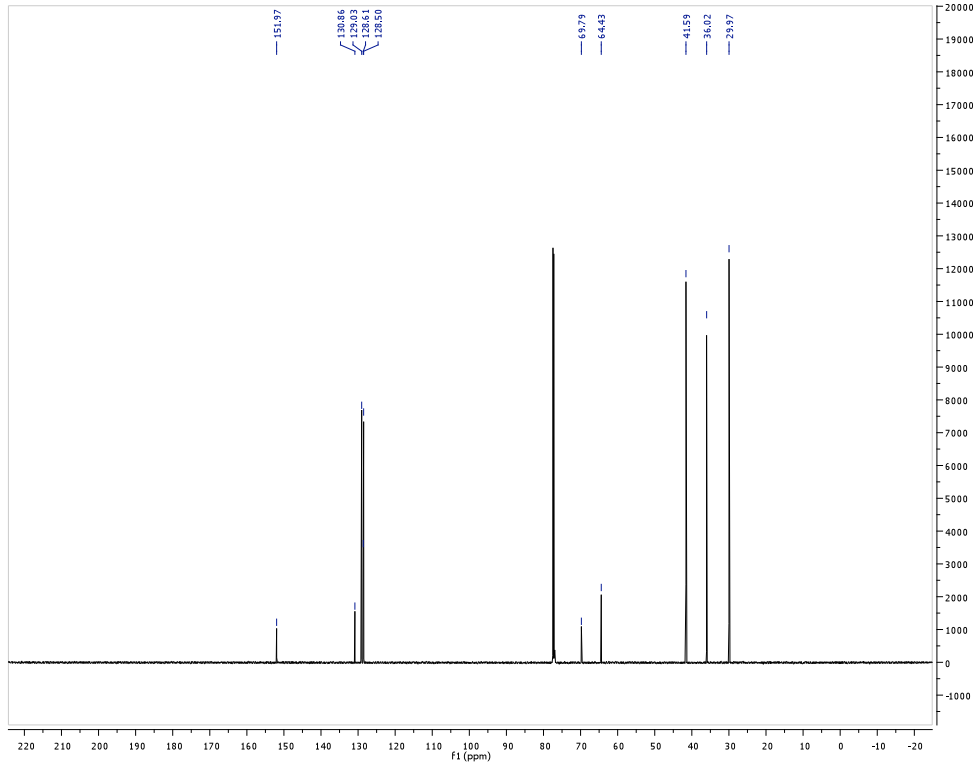




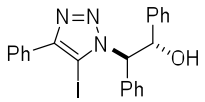
1-Adamantyl-5-iodo-4-phenyl-1*H*-1,2,3-triazole (10)

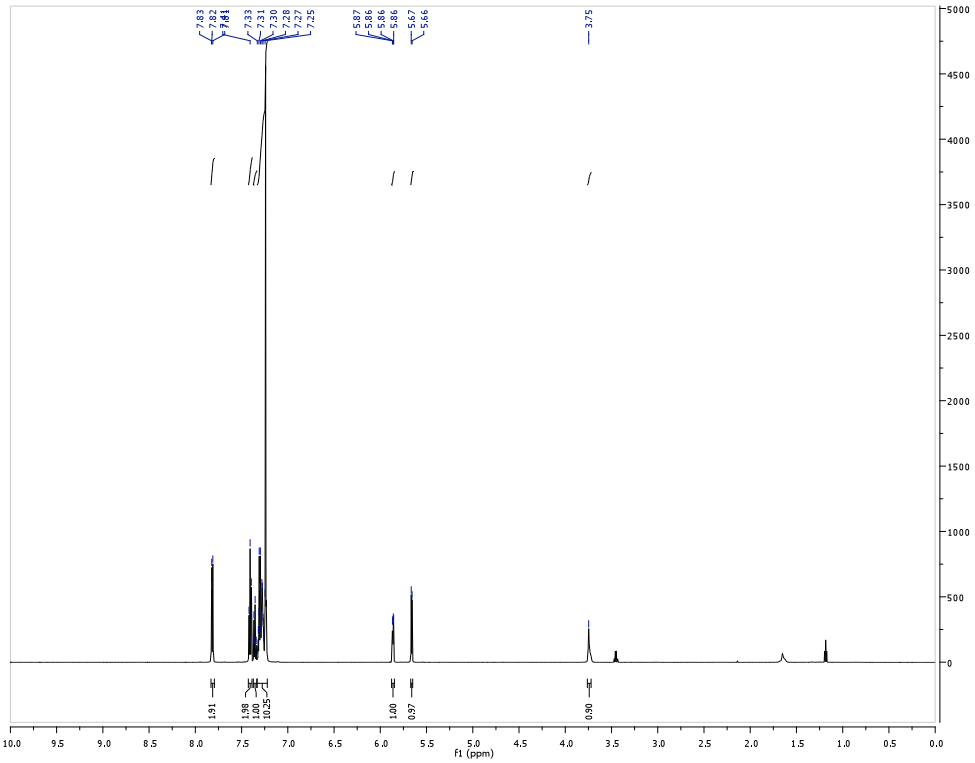


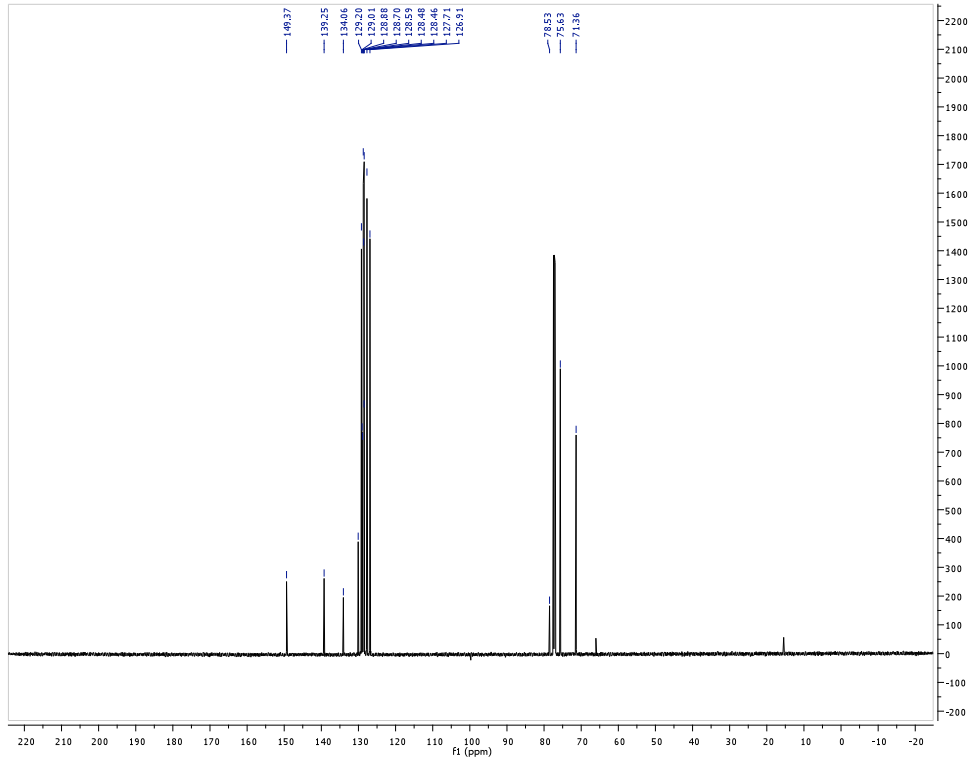




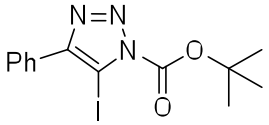
trans-2-(5-iodo-4-phenyl-1_H_-1,2,3-triazol-1-yl)-1,2-diphenylethanol (11)

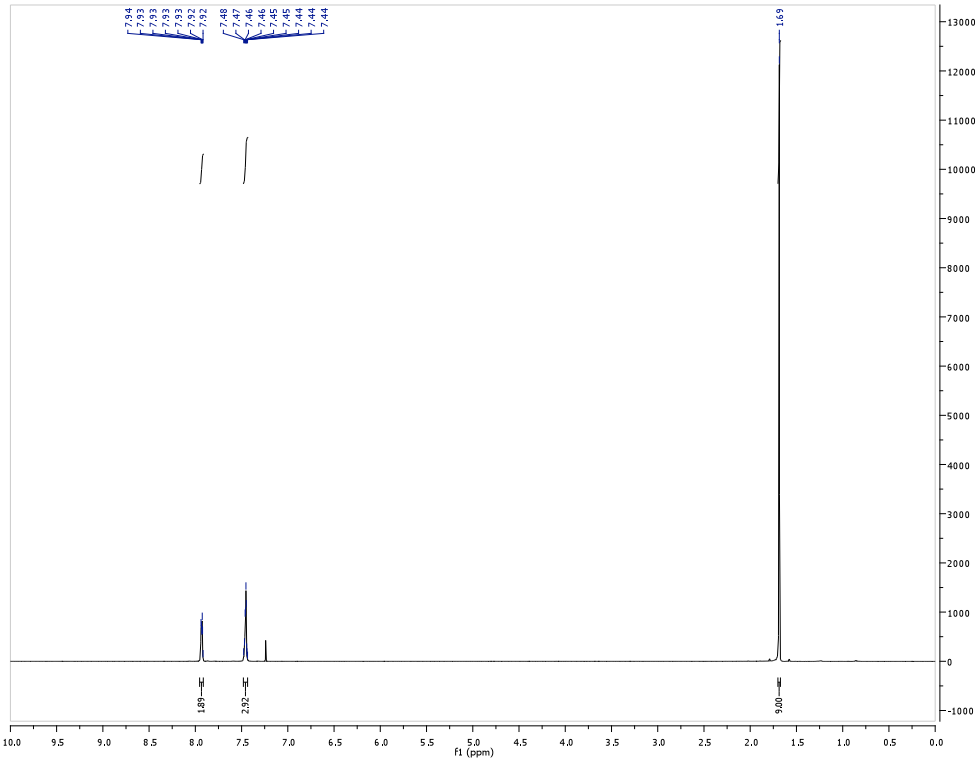


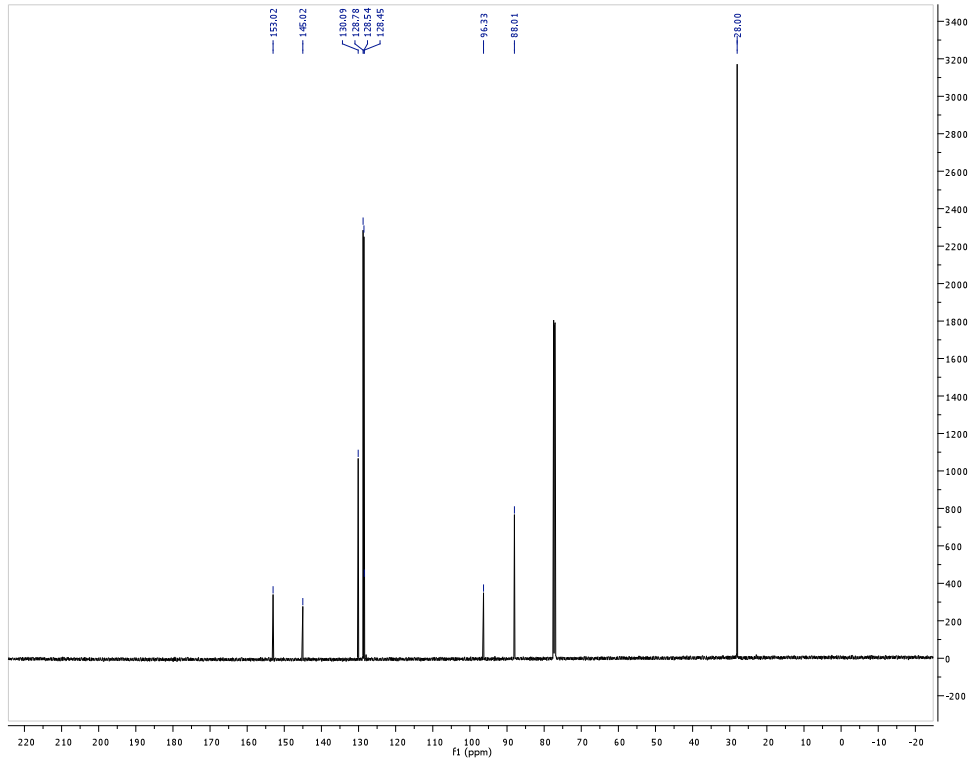




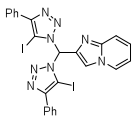
tert-butyl 5-iodo-4-phenyl-1_H_-1,2,3-triazole-1-carboxylate (12)

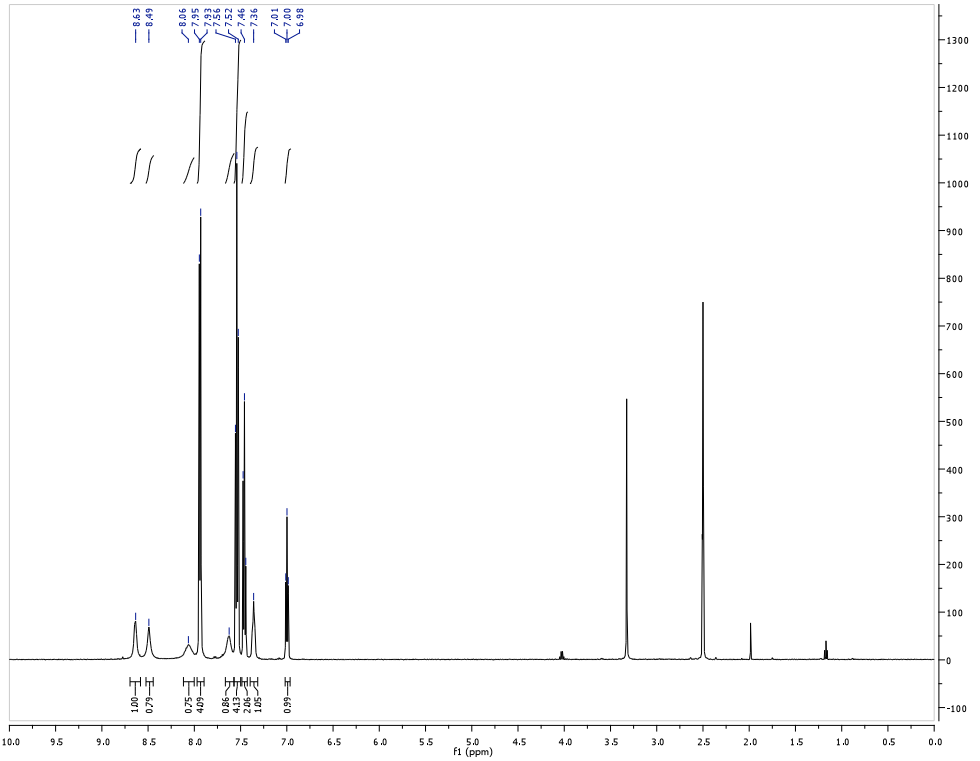


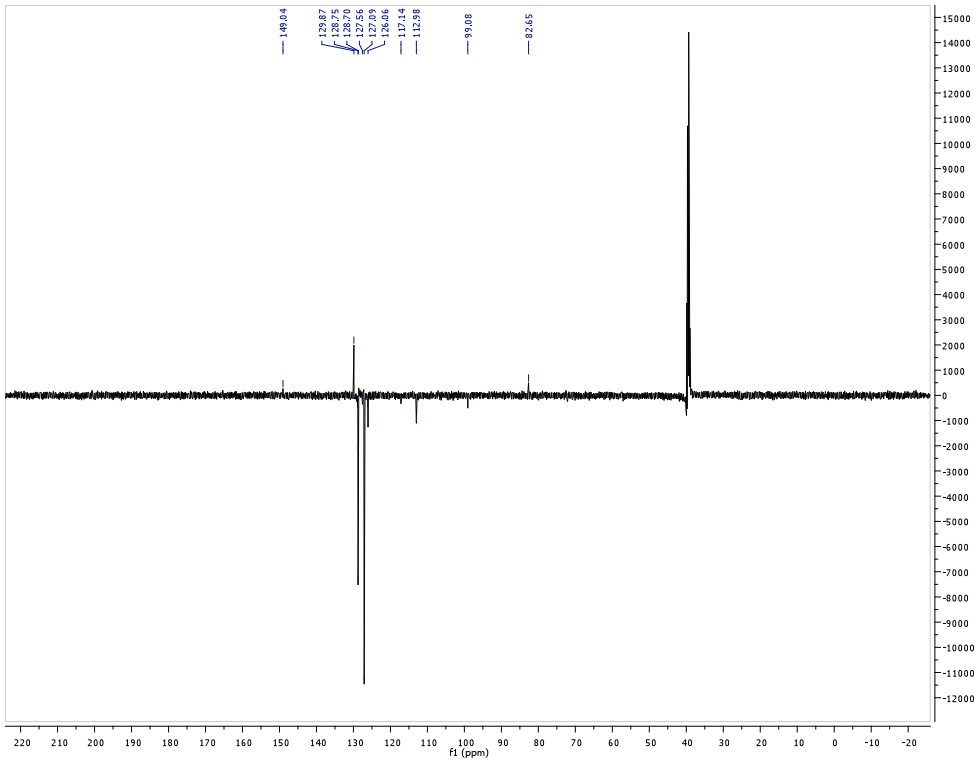




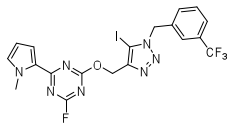
2-(Bis(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)imidazo[1,2-*α*]pyridine (13)

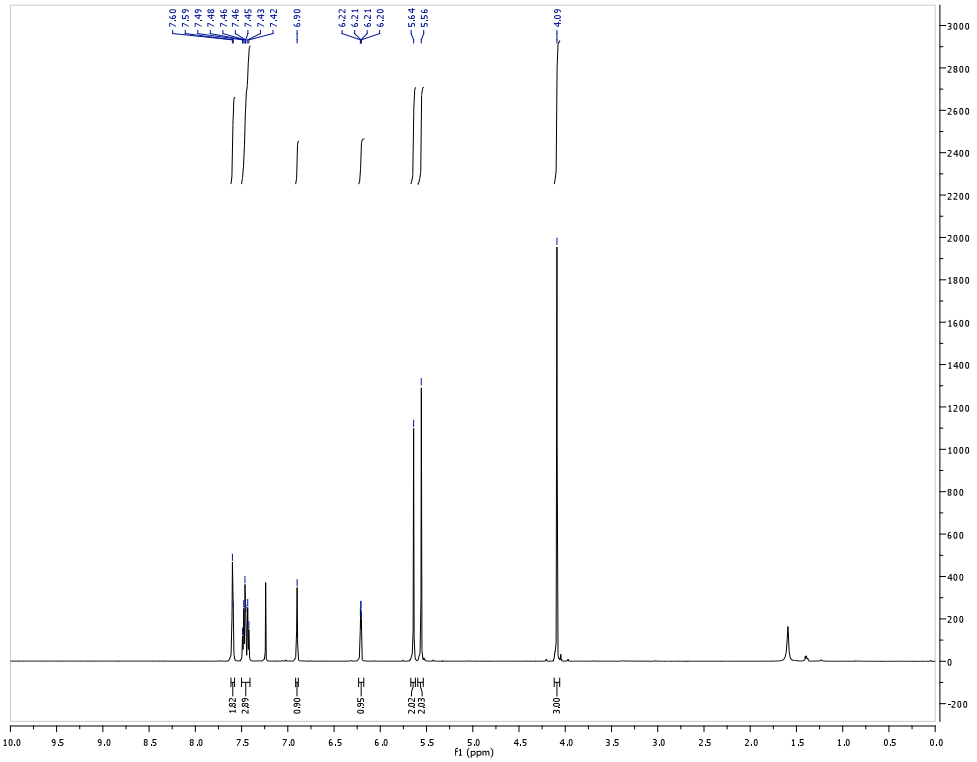


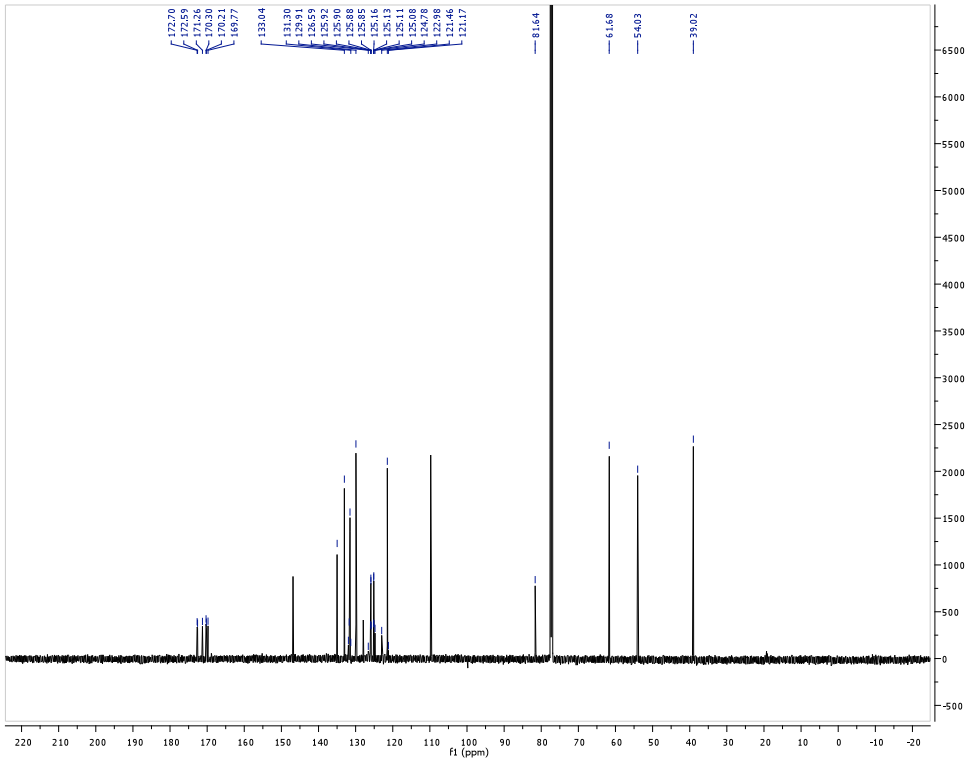




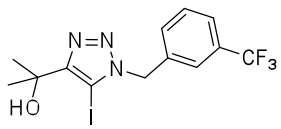
2-Fluoro-4-((5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-6-(1-methyl-1*H*-pyrrol-2-yl)-1,3,5-triazine (14)

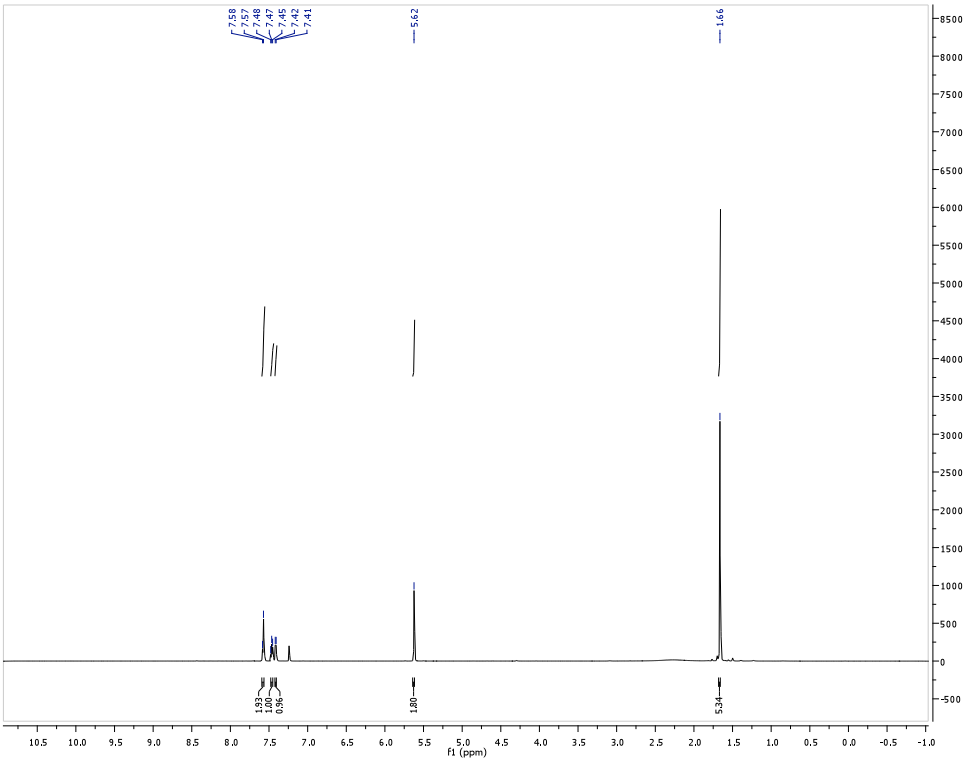


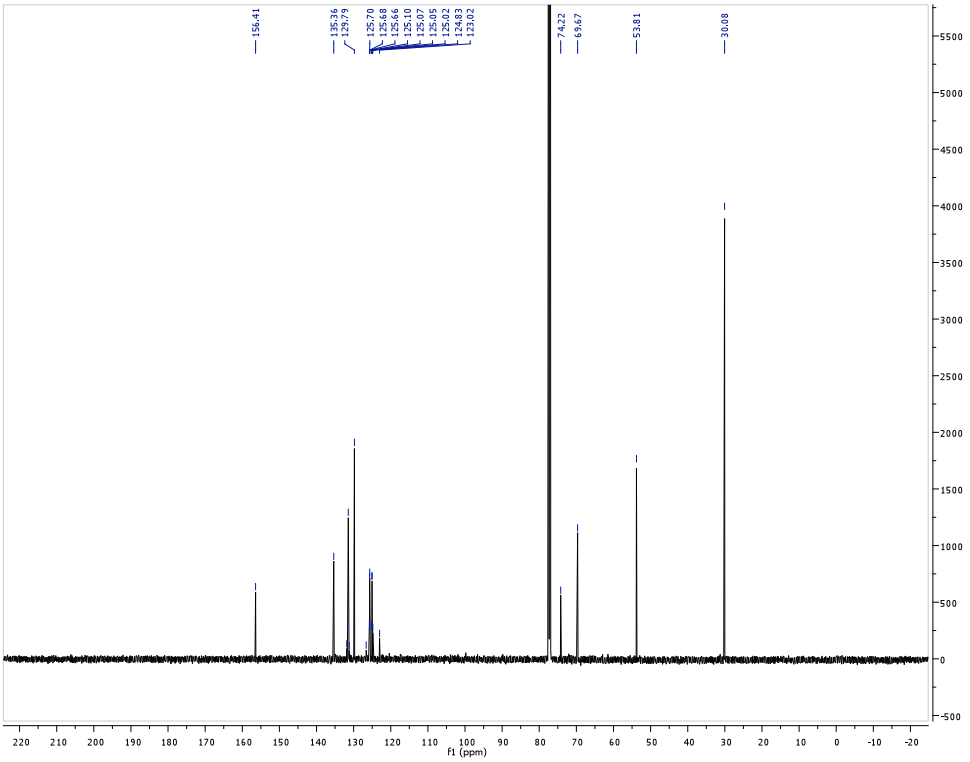




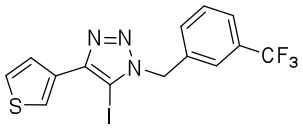
2-(5-Iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)propan-2-ol (15)

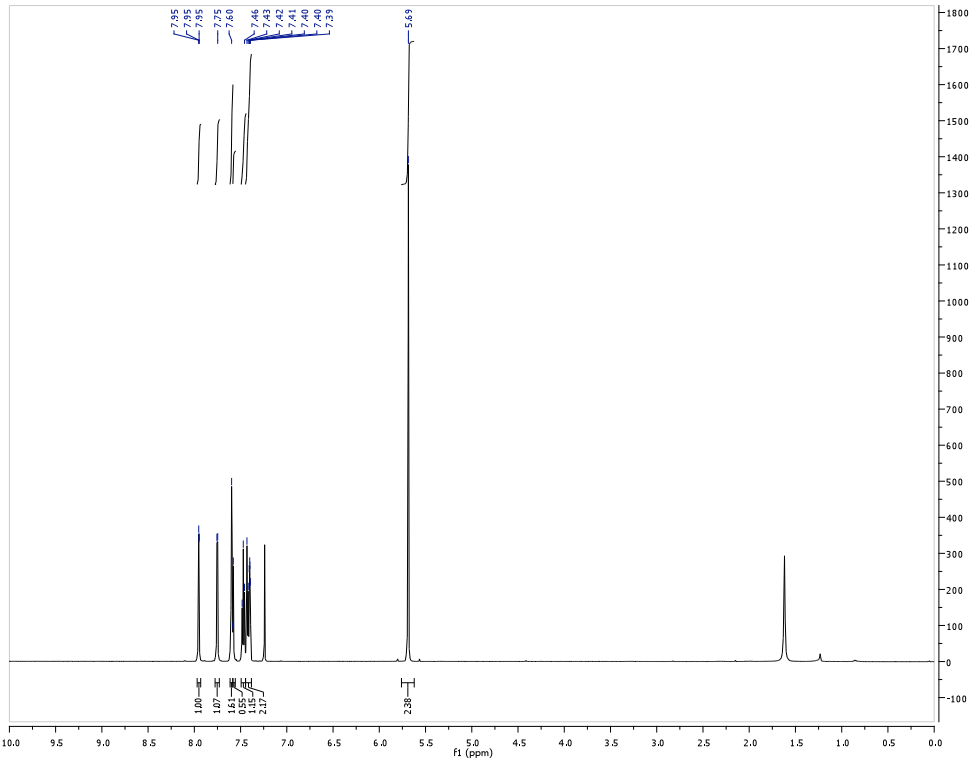


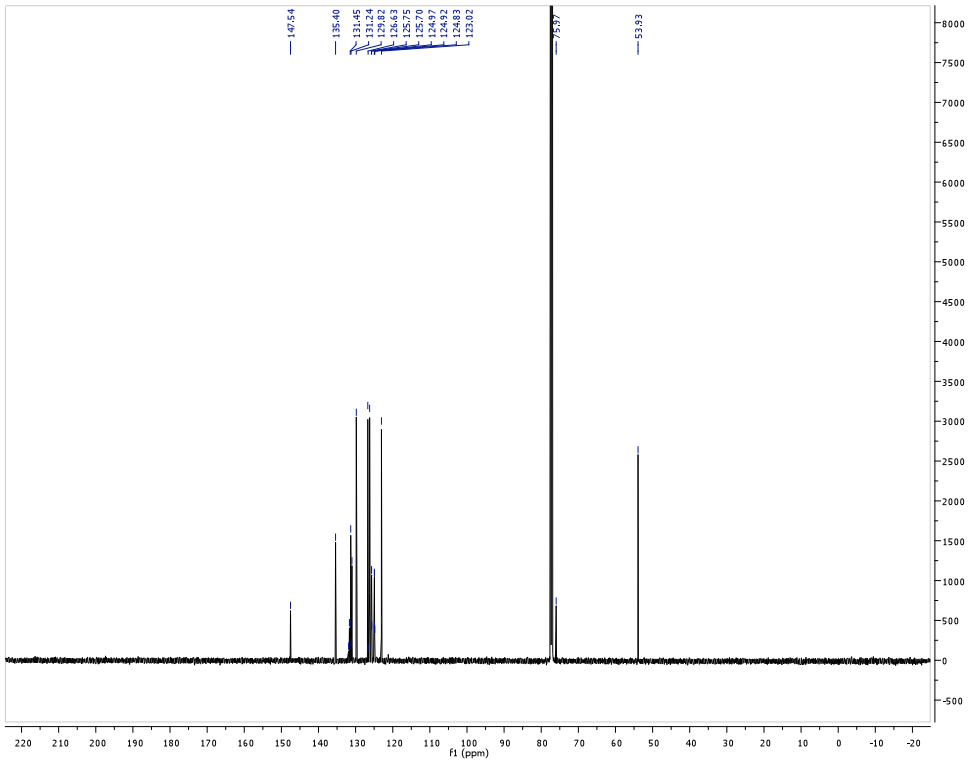




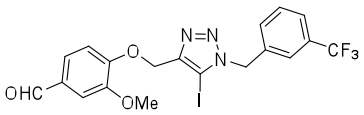
5-Iodo-4-(thiophen-3-yl)-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (16)

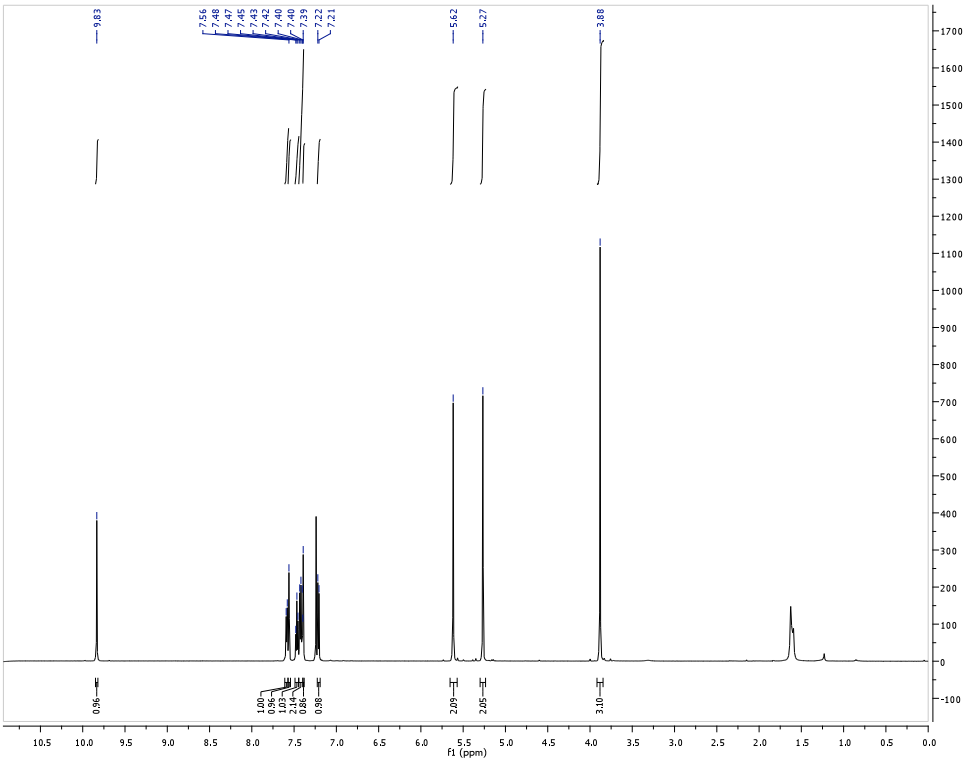


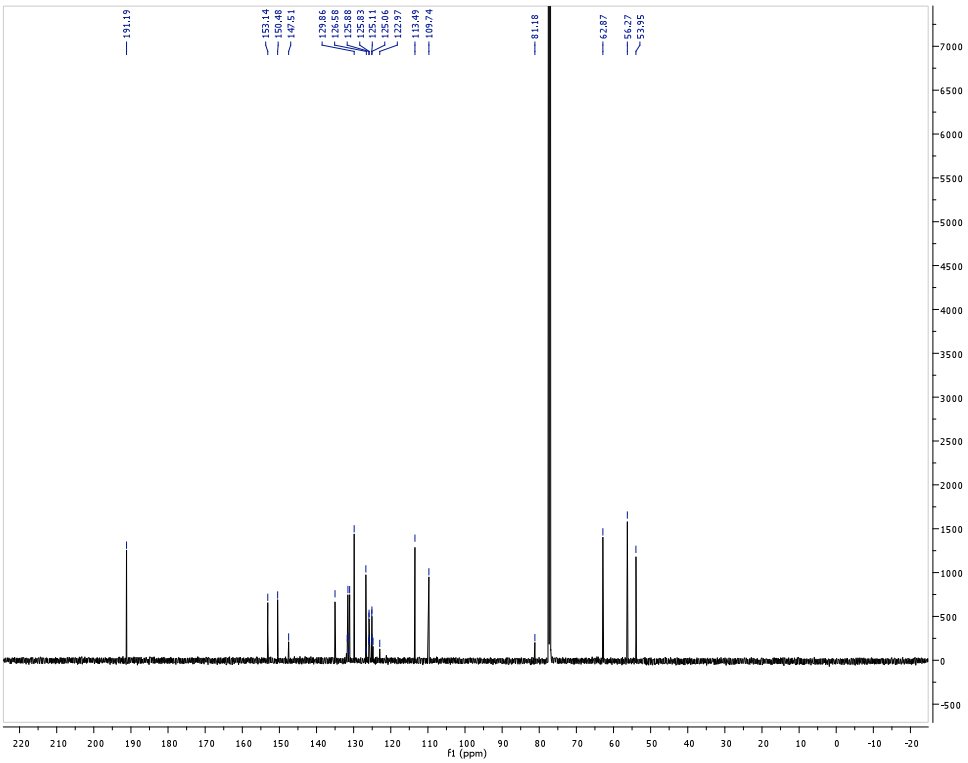




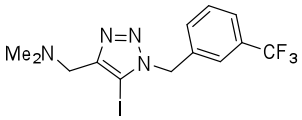
4-((5-Iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3-methoxybenzaldehyde (17)

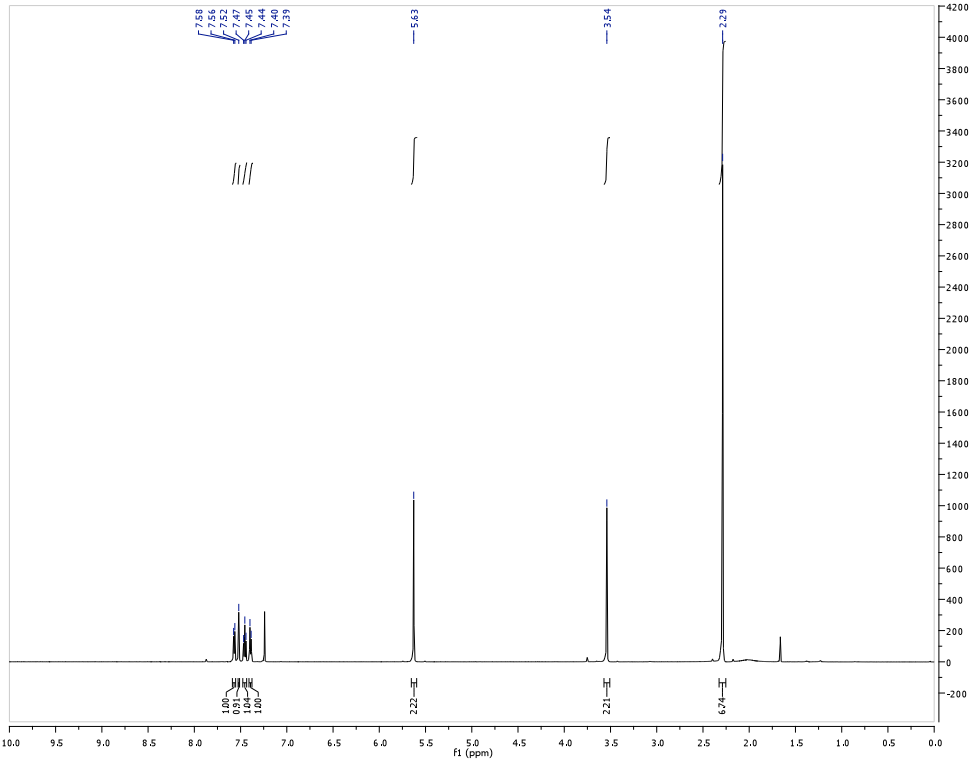


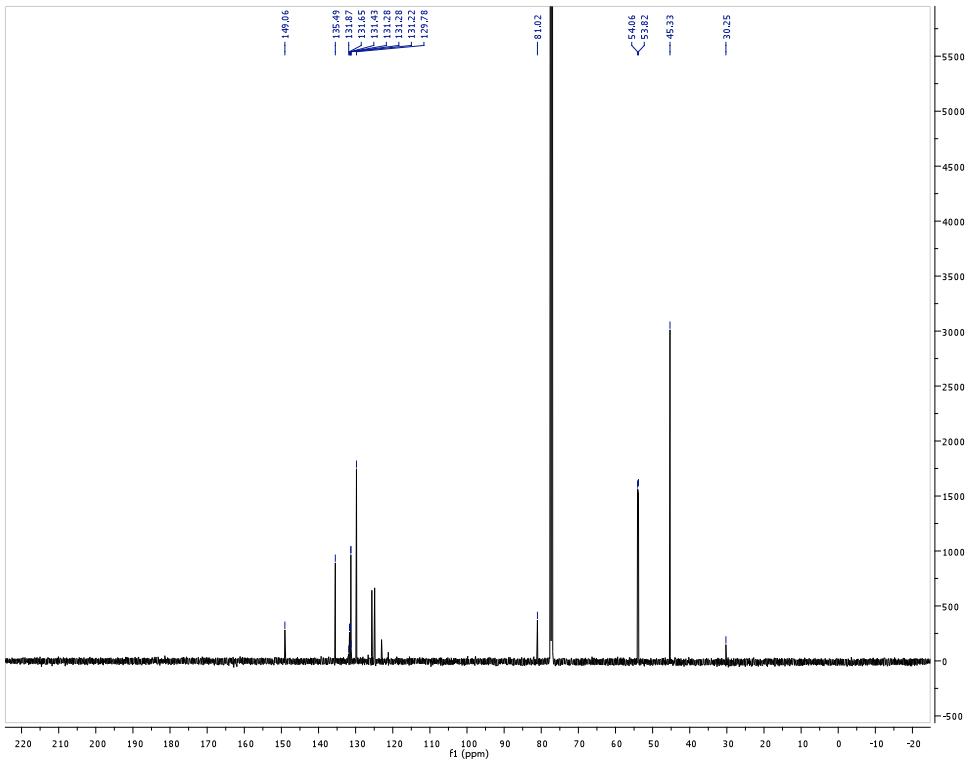




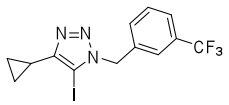
1-(5-Iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)-*N*,*N*-dimethylmethanamine (18)

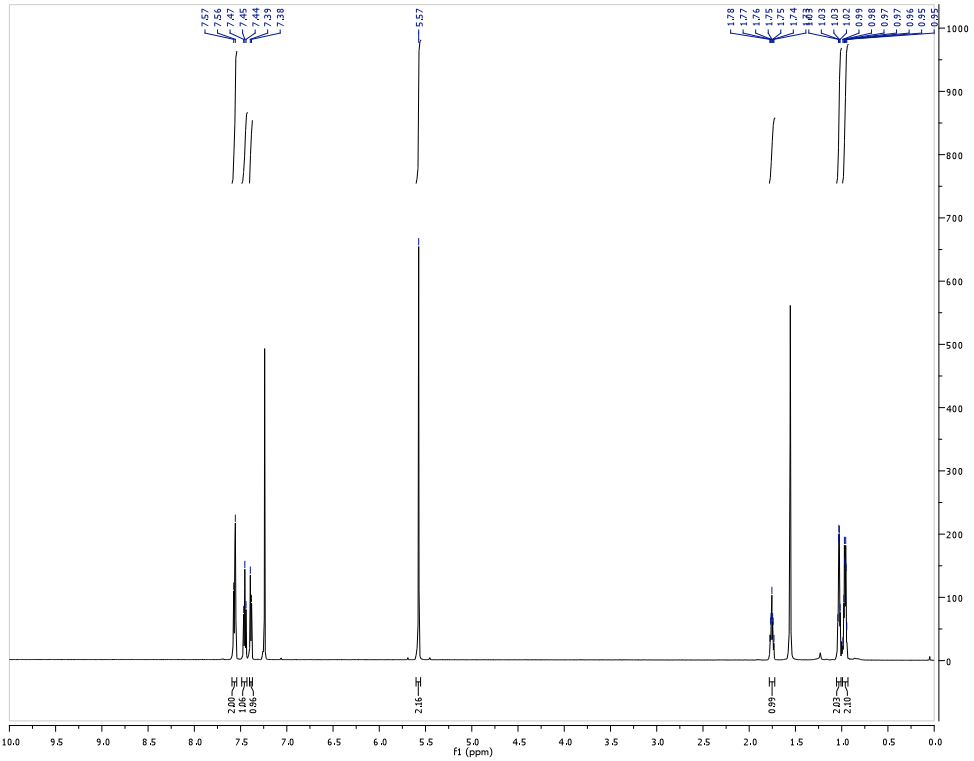


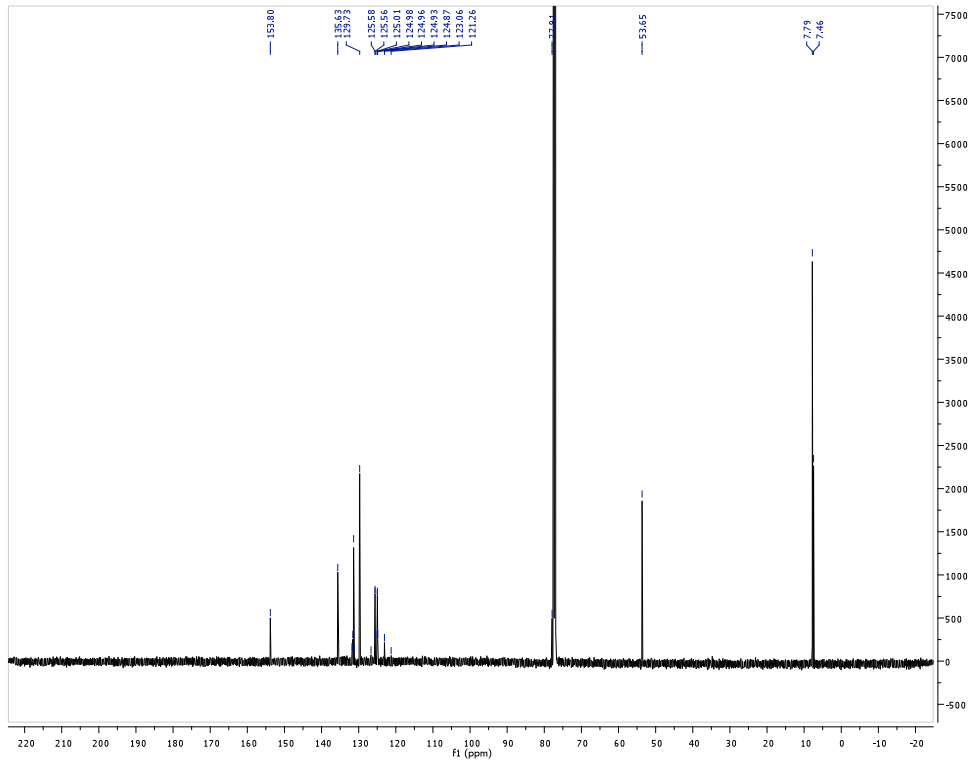




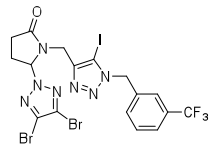
4-Cyclopropyl-5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole (19)

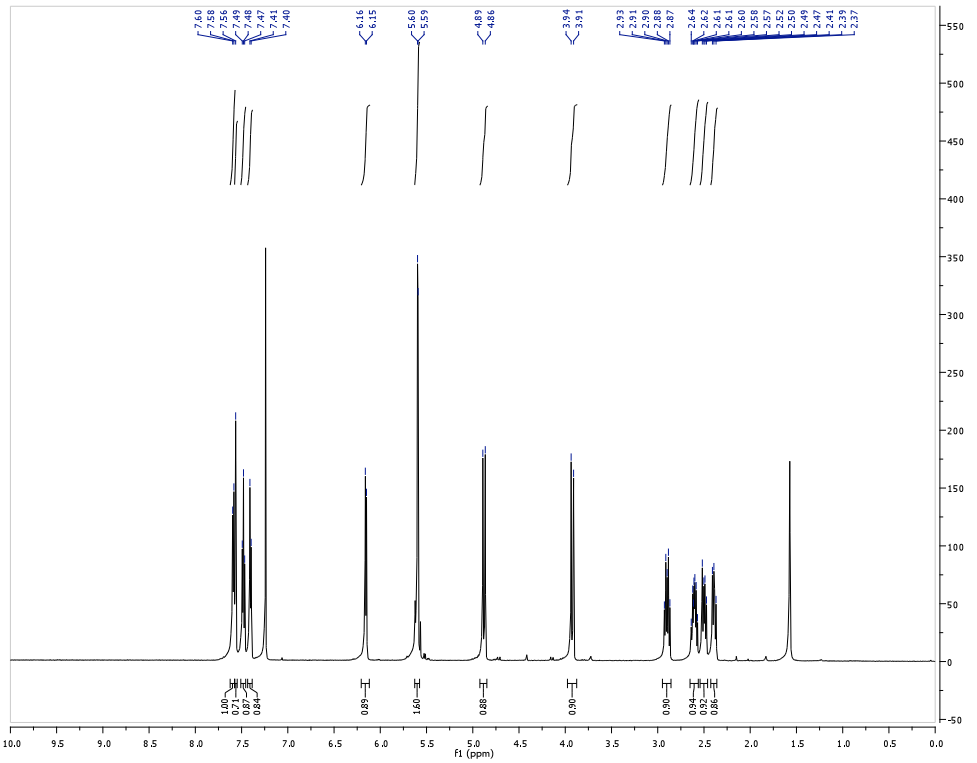


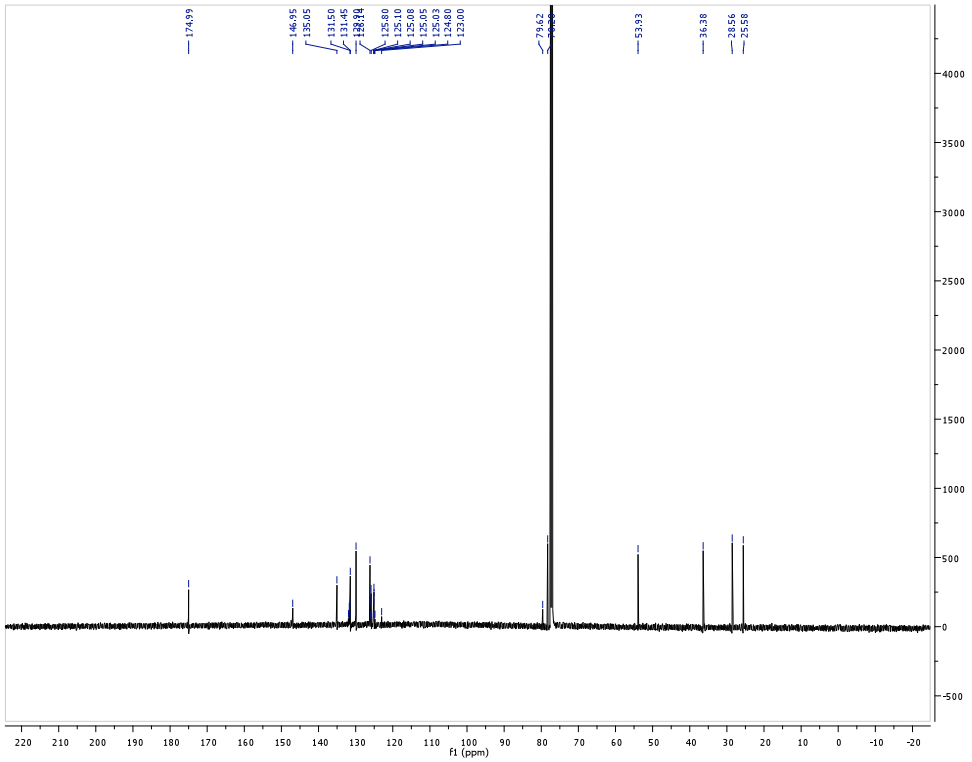




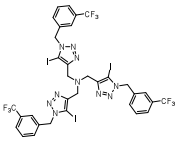
5-(4,5-Dibromo-2*H*-1,2,3-triazol-2-yl)-1-((5-iodo-1-(3-(trifluoro-methyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methyl)pyrrolidin-2-one (20)

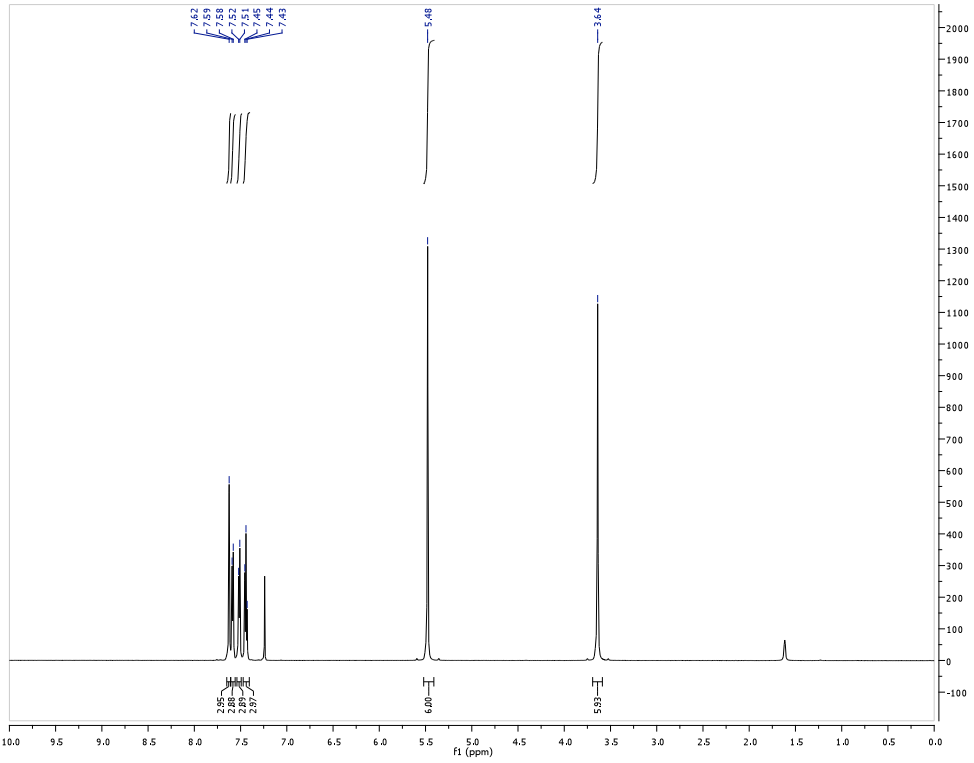


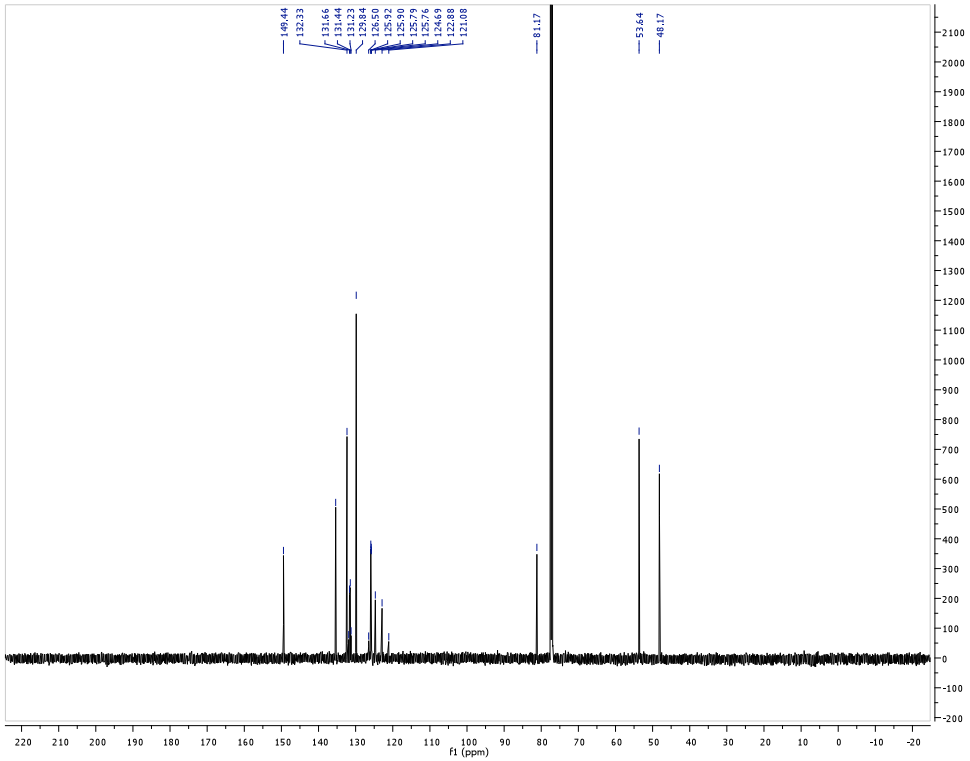




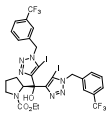
Tris((5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methyl)amine (21)

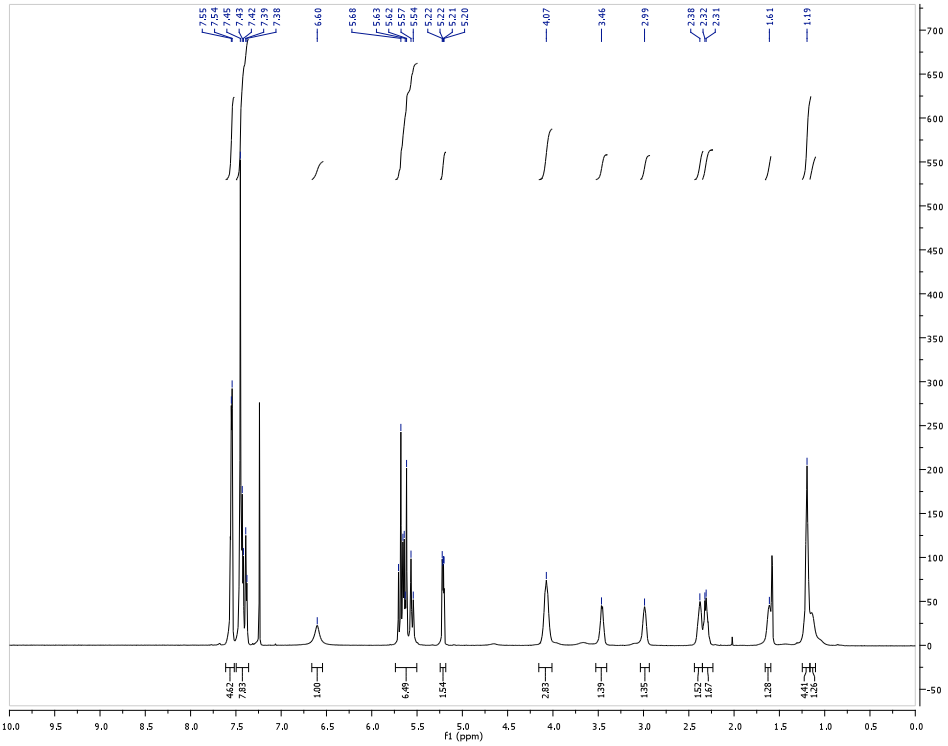


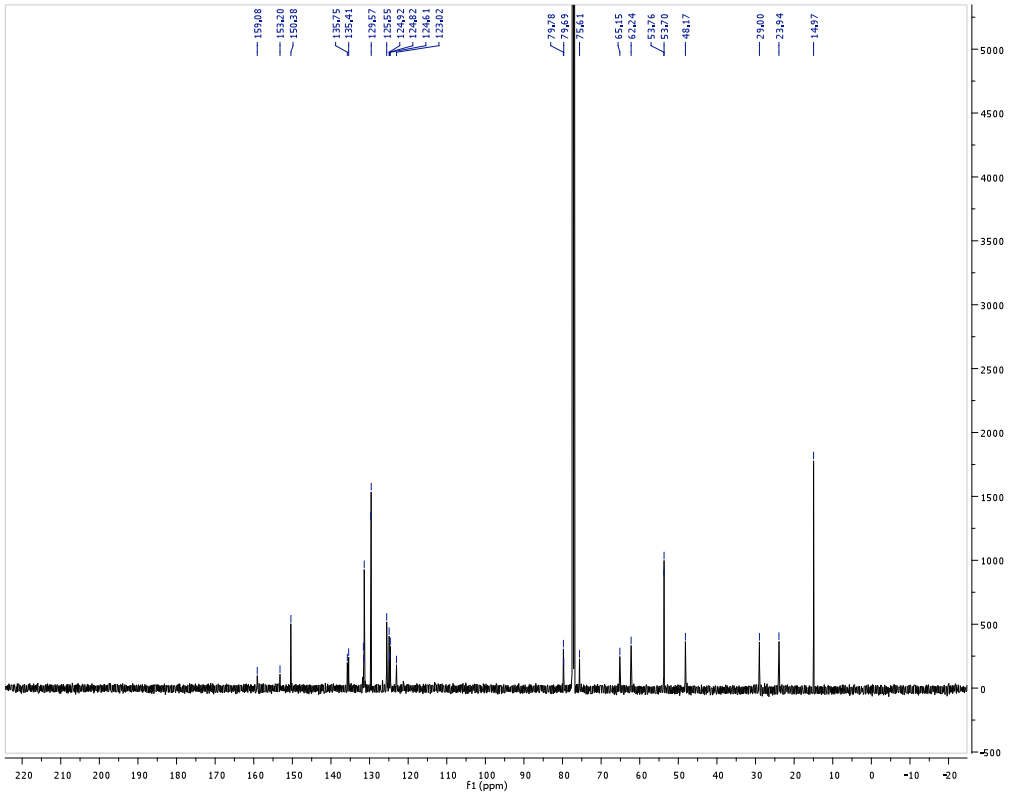




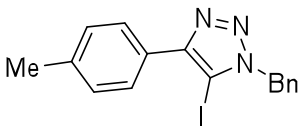
(*S*)-Ethyl 2-(hydroxybis(5-iodo-1-(3-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)meth yl)pyrrolidine-1-carboxylate (22)

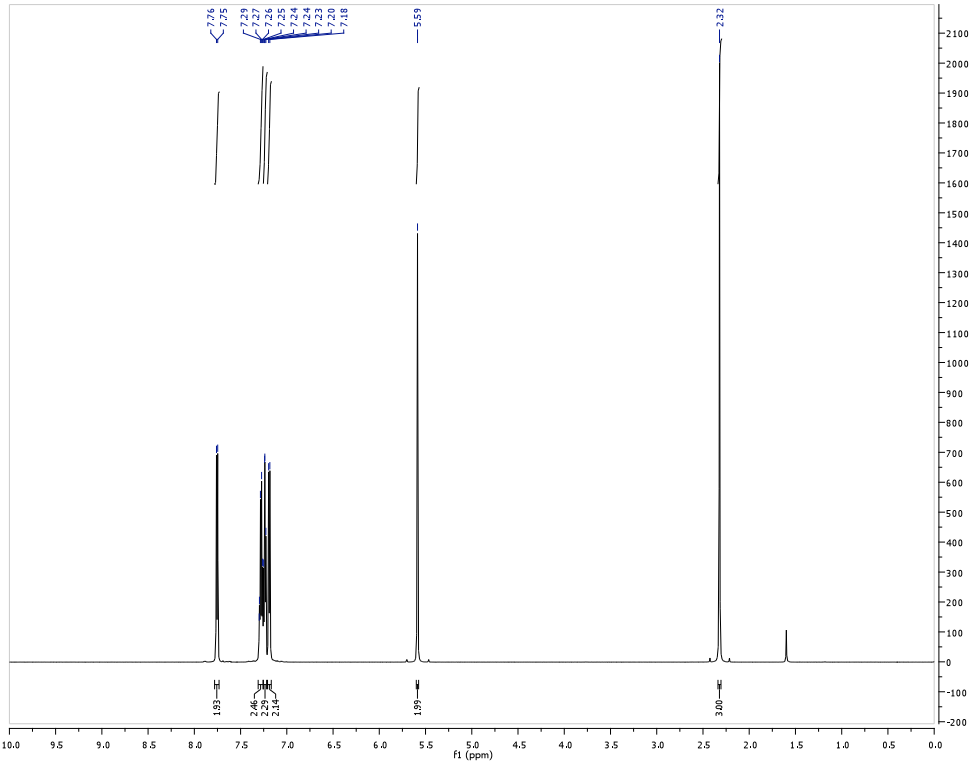


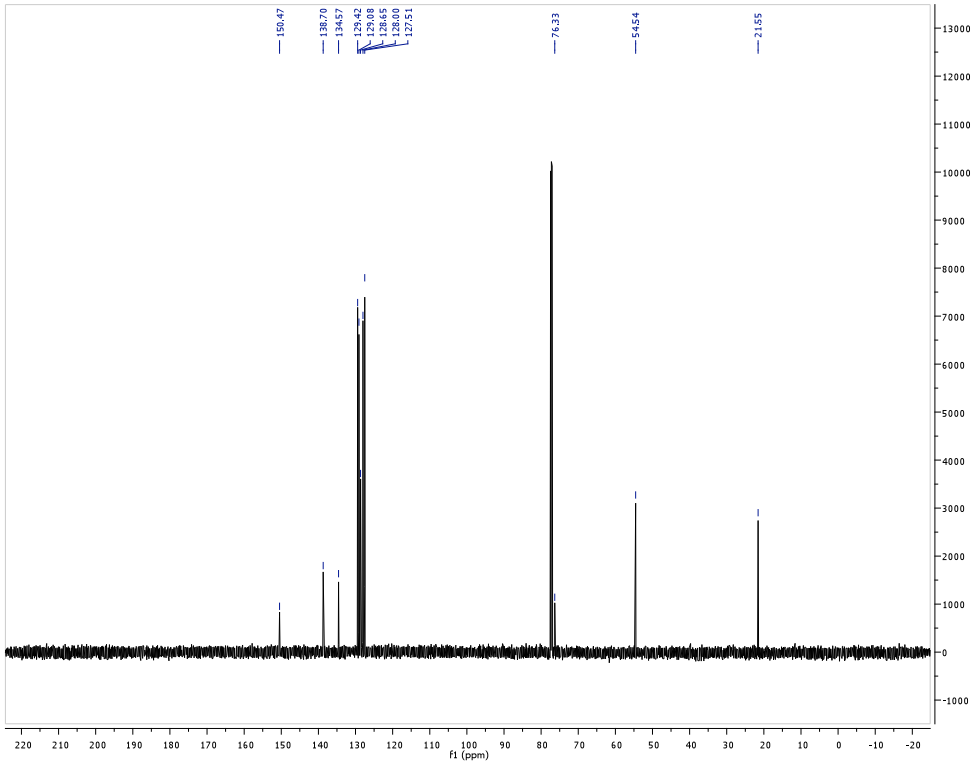




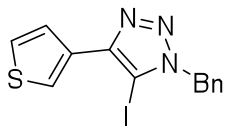
1-Benzyl-5-iodo-4-*p*-tolyl-1*H*-1,2,3-triazole (28)

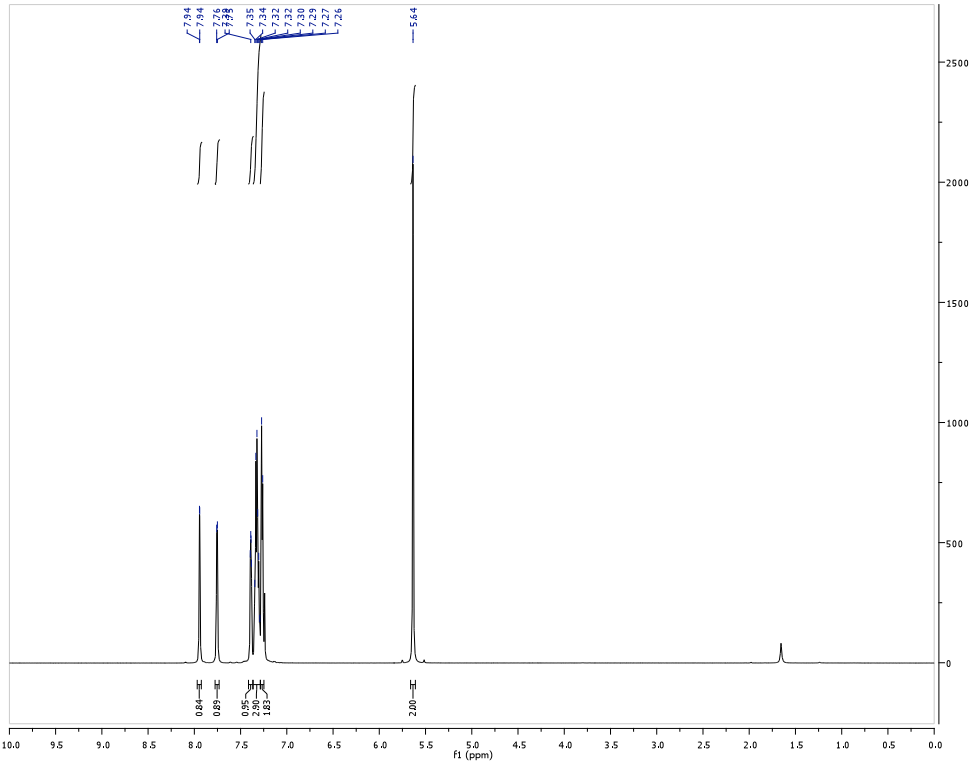


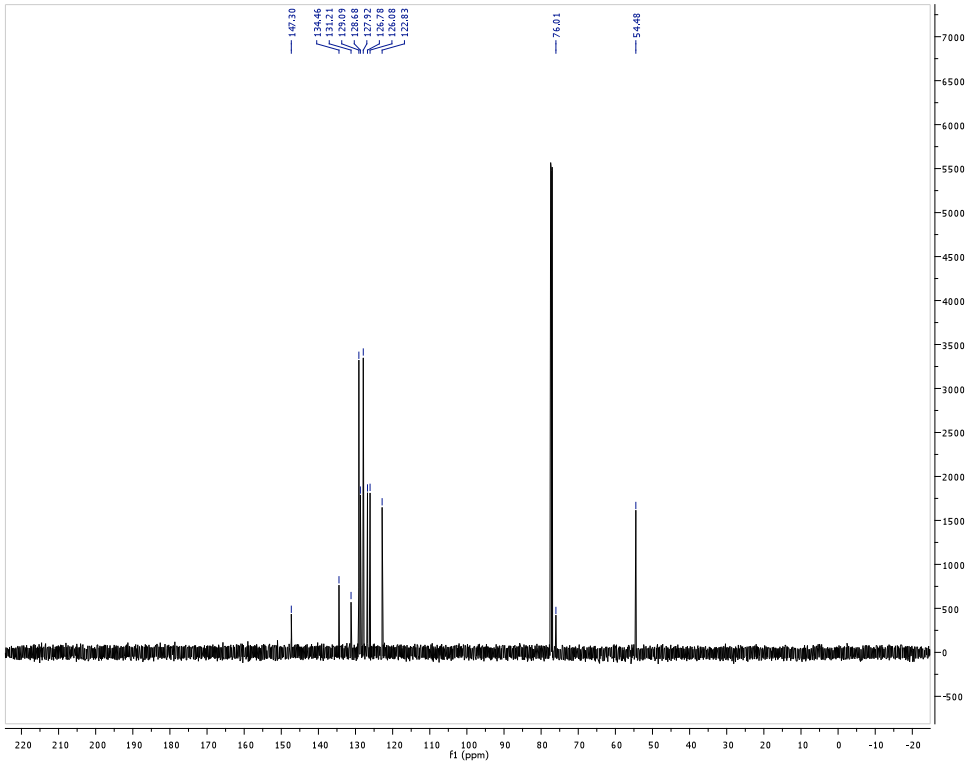




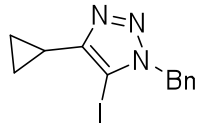
5-Iodo-4-(thiophen-3-yl)-1-benzyl-1*H*-1,2,3-triazole (29)

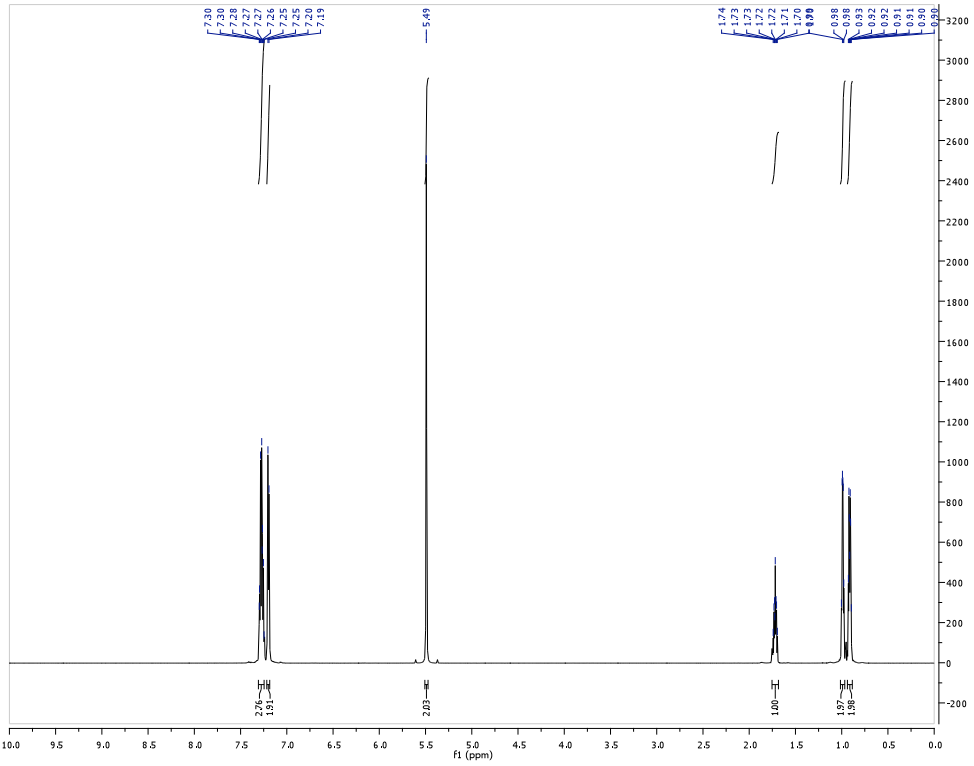


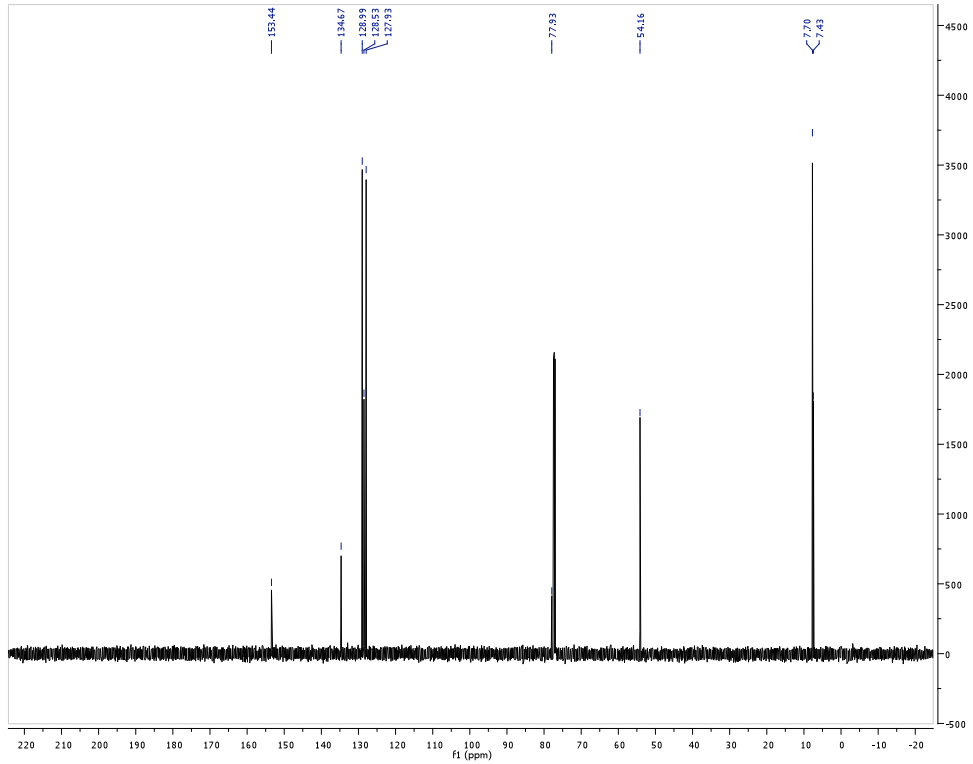




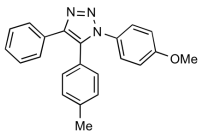
4-Cyclopropyl-5-iodo-1-benzyl-1*H*-1,2,3-triazole (30)

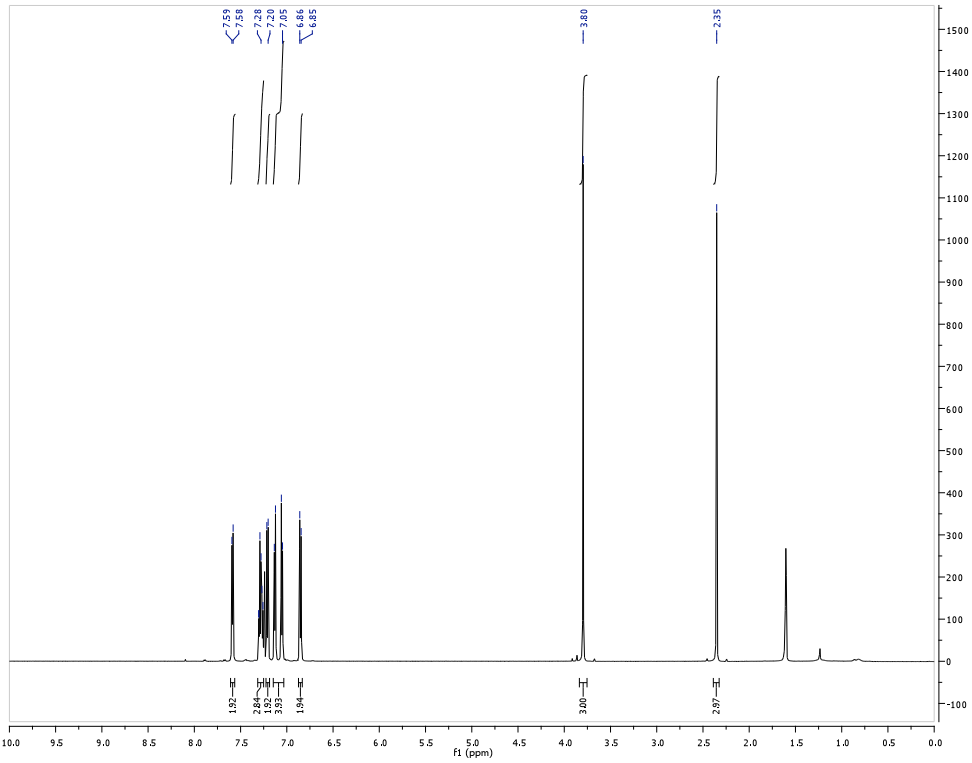


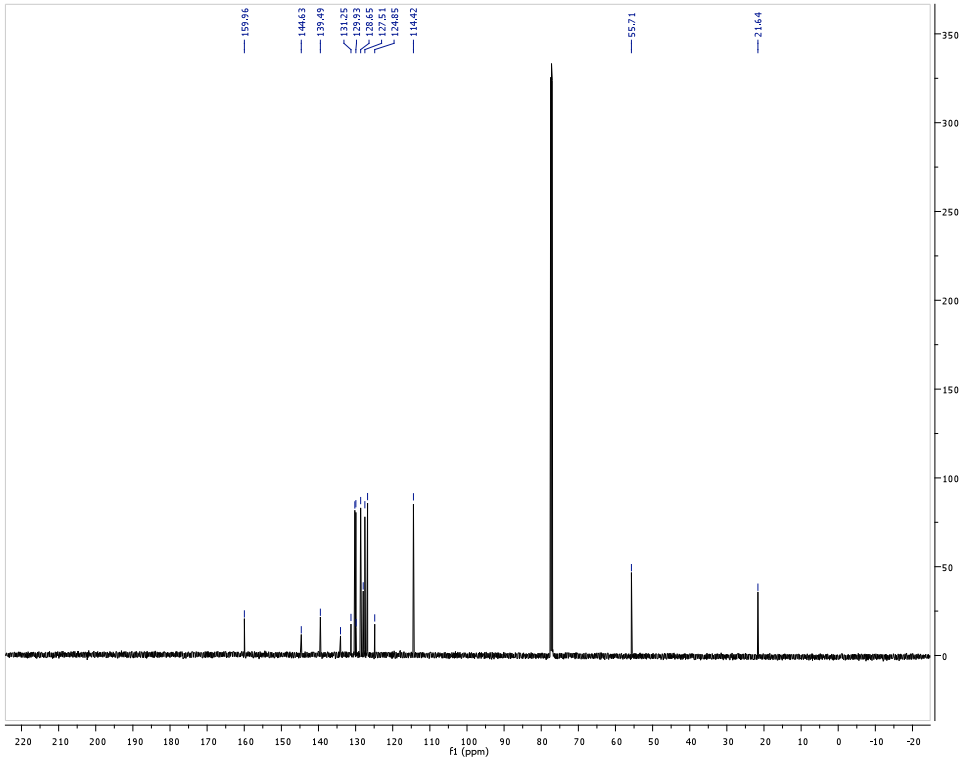




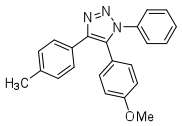
1-(4-methoxyphenyl)-4-phenyl-5-*p*-tolyl-1*H*-1,2,3-triazole (31)

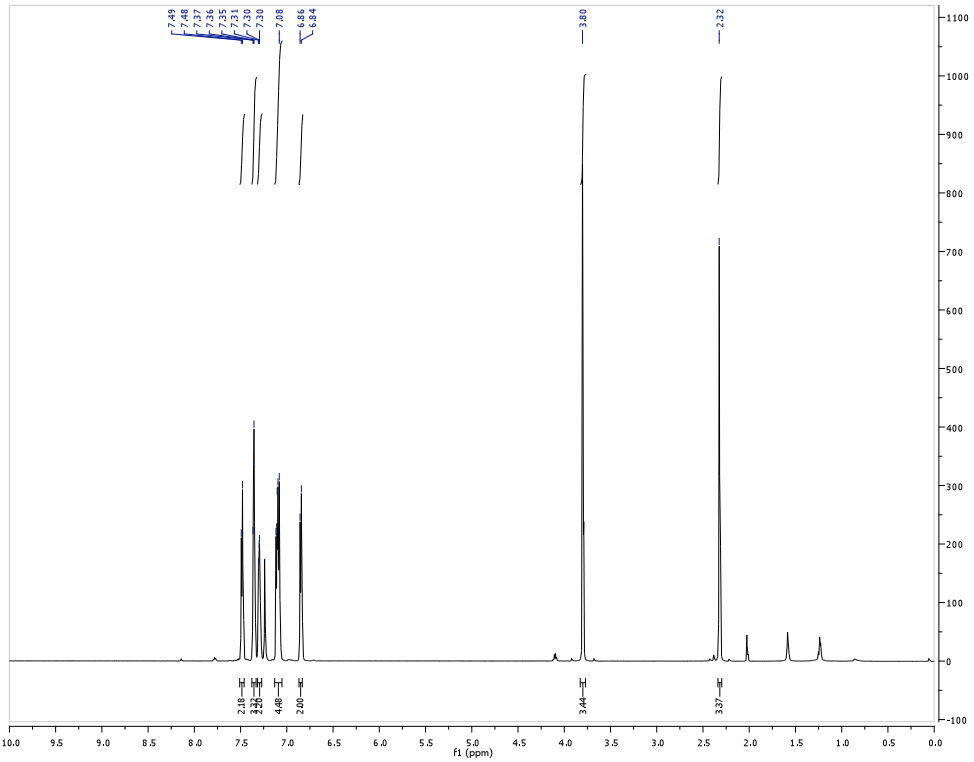


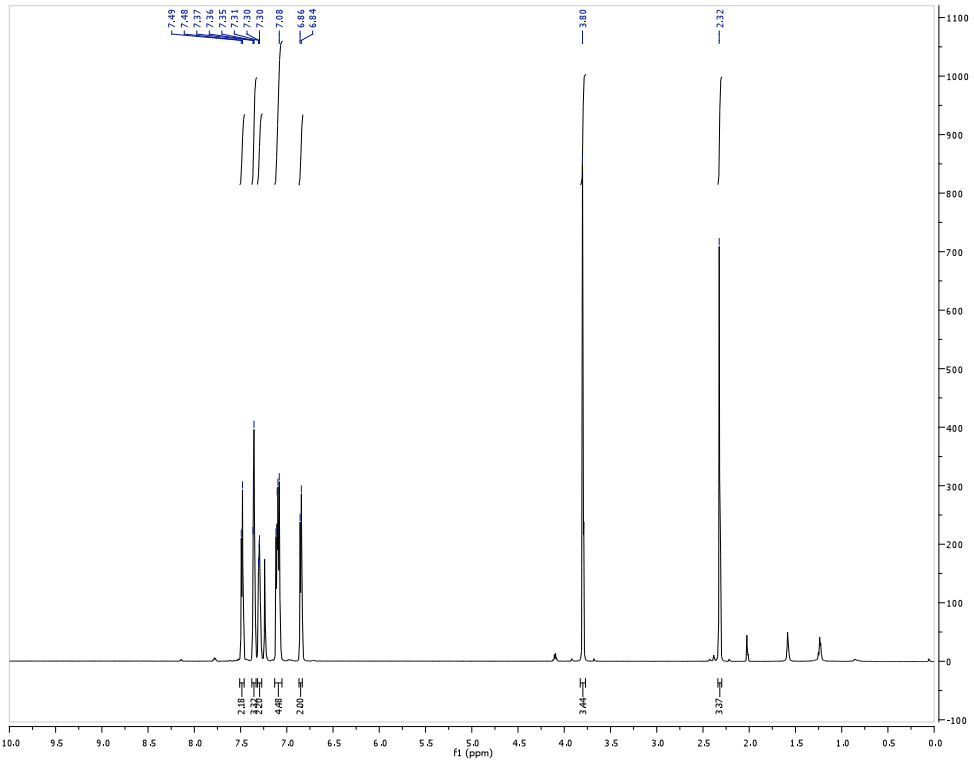




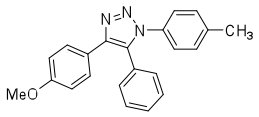
5-(4-methoxyphenyl)-1-phenyl-4-*p*-tolyl-1*H*-1,2,3-triazole (32)

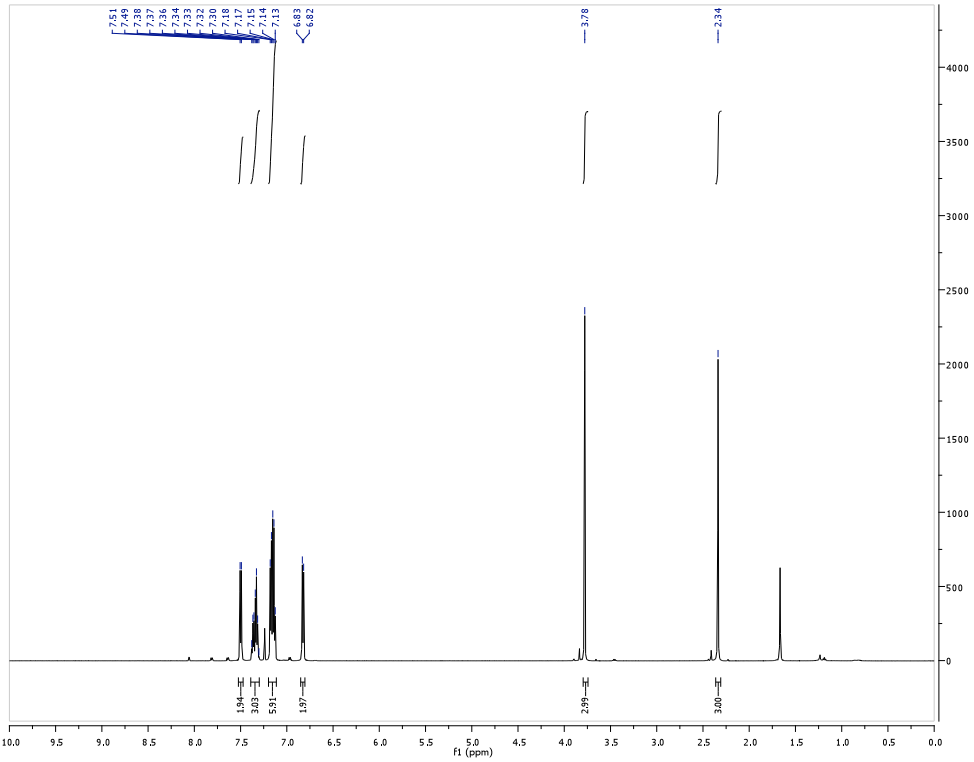


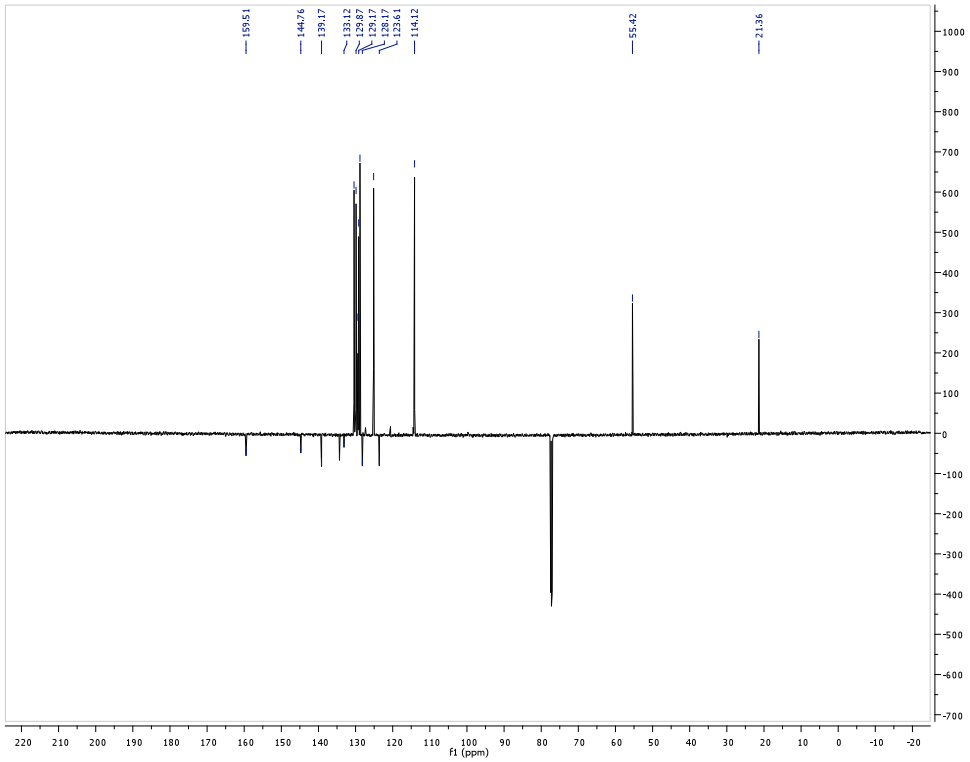




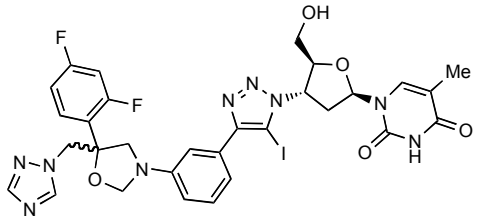
4-(4-methoxyphenyl)-5-phenyl-1-*p*-tolyl-1*H*-1,2,3-triazole (33)

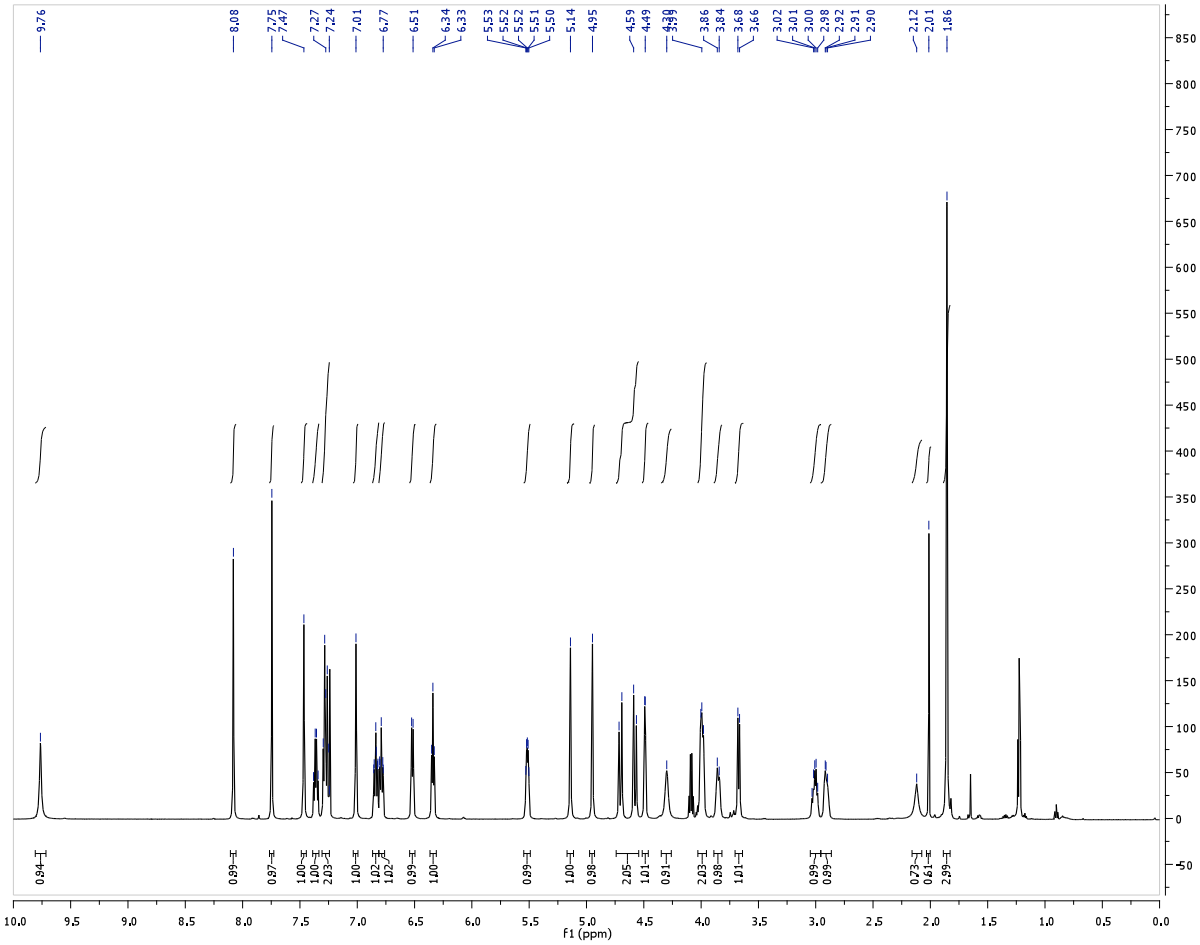


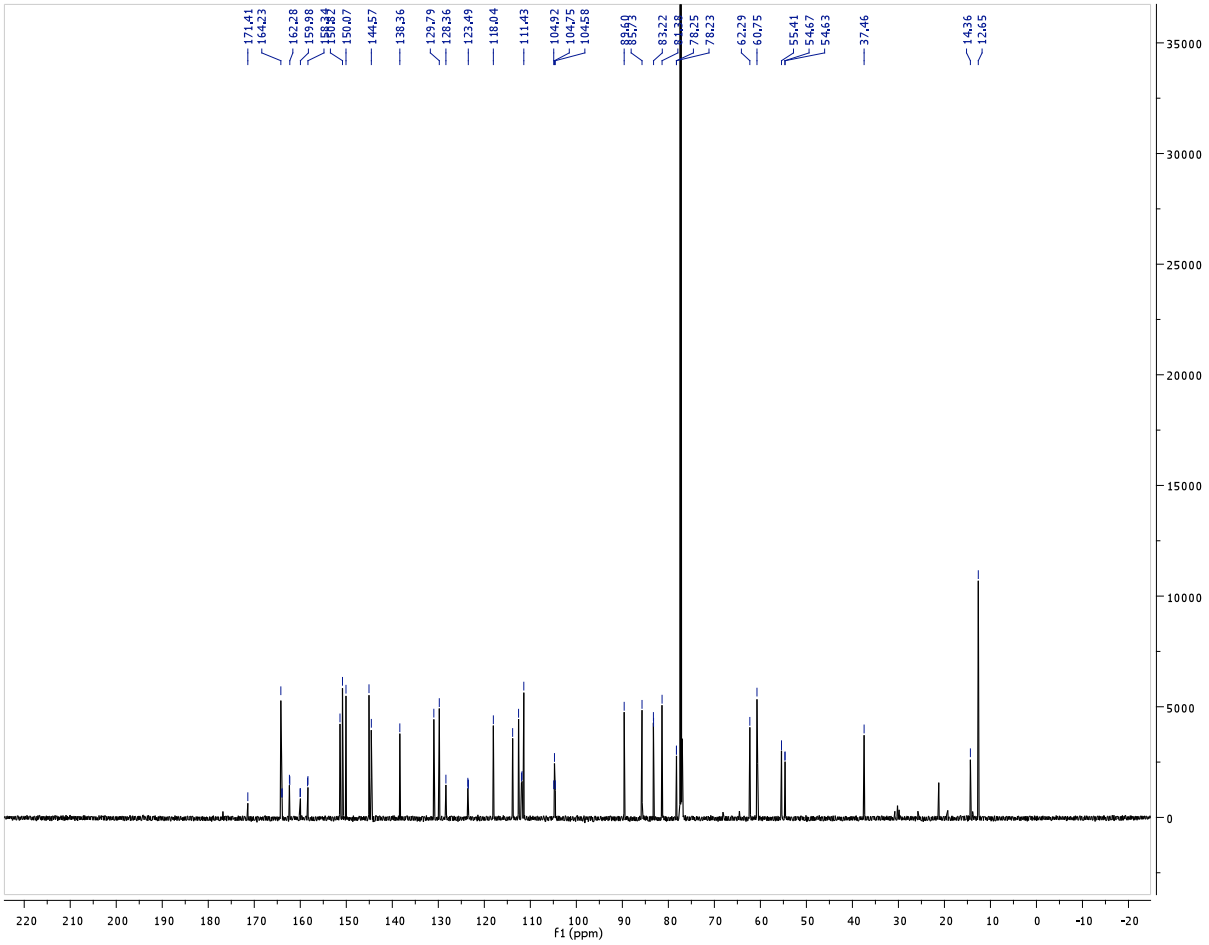




1-((2*R*,4*S*,5*S*)-4-(4-(3-(5-((1*H*-1,2,4-triazol-1-yl)methyl)-5-(2,4-difluorophenyl)oxazolidin-3-yl)phenyl)-5-iodo-1*H*-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (T.O.C. graphic)



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159.98
158.34
158.12
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150.07
144.57
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123.49
118.04
111.43
104.92
104.75
104.58
86.50
85.93
83.22
78.25
78.23
62.29
60.75
55.41
54.67
54.63
37.46
14.36
12.65
35000
30000
25000
20000
15000
10000
5000
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)