Thermolysis of Geminal Diazides: Reagent-free Synthesis of 3-Hydroxypyridines

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Supporting Information

General remarks: All commercial reagents were used as received. Thin-layer chromatography (TLC) was conducted with precoated glass-backed plates (silica gel 60 F254) and visualized by exposure to UV light (254 nm) or stained with ceric ammonium molybdate (CAM), kalium permanganate stain ($KMnO_4$), or by putting the TLC plates in an iodine-chamber. Flash chromatography was performed with silica gel (43-60 μm); the eluent used is reported in parentheses. ^{1}H-NMR spectra were recorded at 400 MHz or 600 MHz spectrometers. ^{13}C-NMR spectra were recorded at 101 MHz or 151 MHz. Chemical shifts are reported in ppm relative to the solvent signal. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); p (pentet); hept (heptet); dd (doublet of doublets); dt (doublet of triplets); qd (quartet of doublets); pd (pentet of doublets); ddd (doublet of doublet of doublets); tt (triplet of triplets); m (multiplet). IR spectra were recorded using ATR technique. High resolution mass spectra of the derivatized geminal diazides were obtained using ESI ionization

methods on a MicroTOF. The NMR data for the β-ketocarbonyl compounds are always reported for the predominant keto form.

Microwave Experiments: All microwave irradiation experiments were carried out in a Bioatage Initiator^{+} microwave system, operating at a frequency of 2.45 GHz with an irradiation power from 0 to 400 W. The reactions were carried out in 20 mL glass tubes, sealed with Teflon septum under continuous stirring with a magnetic stirrer. The reaction mixture was irradiated at the indicated temperature and time. Then, the mixture was cooled to ambient temperature with pressurized air.

Cautionary note

Organic azides are potentially explosive compounds and should be handled with appropriate care and safety equipment.

General procedure **A** for the nucleophilic substitution at C1 of β-ketoesters/amides:

Diisopropylamine (2.20 eq.) was dissolved in dry tetrahydrofuran (c = 0.25 M) and the solution cooled to 0 °C. *n*-Butyllithium (2.20 eq., 2.5 M solution in *n*-hexane) was slowly added and the reaction mixture was stirred at room temperature for 30 minutes and afterwards cooled to 0 °C. β–ketoester/amide was dissolved in dry tetrahydrofuran (in a threefold volume with respect to the β-ketoester/amide) and slowly added to the solution. The reaction mixture was stirred for 15 minutes after which alkyl/allyl halide (1.20 eq.) was added. The solution was allowed to stir at 0 °C for 30 minutes and at room temperature for 90 minutes. A saturated, aqueous solution of ammonium chloride was added and the separated aqueous layer extracted with ethyl acetate (2x). The combined organic layers were washed with brine, dried over magnesium sulfate and the solvent was evaporated *in vacuo*. Column chromatography afforded the pure products.

General procedure **B** for the azidation of β-ketoesters/amides:

The respective β–ketoester/amide was dissolved in a 2:1 mixture of dimethylsulfoxide and water (c = 0.1 M). Sodium azide (4.0 eq.), sodium bicarbonate (3.0 eq.) and iodine (2.05 eq.) were added to the solution and the mixture was stirred at room temperature until thin layer chromatography indicated complete consumption of the starting material. A saturated, aqueous solution of sodium thiosulfate was added and the aqueous layer extracted with ethyl acetate (3x). The combined organic layers were washed with brine, dried over magnesium sulfate and the solvent was evaporated *in vacuo*. Column chromatography afforded the geminal diazides.

General procedure **C** for the reaction of geminal diazides with cyclooctyne:

Geminal diazide was dissolved in chloroform (c = 0.1 M) and treated with cyclooctyne (2.20 eq.). The solution was stirred at room temperature until thin layer chromatography indicated complete consumption of the starting material. Afterwards, the solvent was removed *in vacuo* and the product obtained after column chromatography.

This reaction was performed to obtain more stable derivatives of the geminal diazides **1**: We were not able to obtain the accurate masses of the diazido compounds. Upon derivatization with cyclooctyne, full characterization was easily possible, and accurate masses of the derivatives having the bistriazole units were obtained through standard ESI ionization.

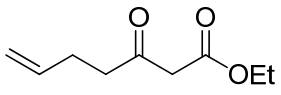
General procedure **D** for the thermolysis of geminal diazides:

Geminal diazide was dissolved in xylene (mixture of isomers, 0.05 M) and the solution was heated at 140 °C under microwave irradiation until thin layer chromatography indicated complete consumption of the starting material (typically after two hours if not indicated otherwise). The reaction mixture was allowed to cool to room temperature and the solution was concentrated *in vacuo* to a volume of approximately 2 mL. The crude product was directly subjected to column chromatography, whereby excess of xylene was removed by eluting the column with cyclohexane or petrolether.

Experimental data

Synthesis of the starting materials

ethyl 3-oxohept-6-enoate

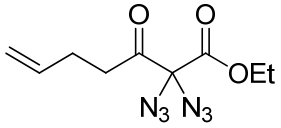


$C_9H_{14}O_3$
170.21 g/mol

Following the general procedure **A** with allyl bromide (5.00 mL of ethyl acetoacetate), the product was obtained as a yellowish liquid (4.881 g, 28.68 mmol, 73%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10). The analytical data corresponds with the previously published data.[1]

TLC: R_f = 0.31 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 5.79 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.03 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.98 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.42 (s, 2H), 2.64 (t, *J* = 7.3 Hz, 2H), 2.37 – 2.31 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 202.1, 167.3, 136.7, 115.7, 61.5, 49.5, 42.5, 27.5, 14.2; **IR** (ATR): ϑ [cm^{-1}] 3080, 2982, 2931, 1740, 1715, 1642, 1411, 1367, 1314, 1325, 1154, 1095, 1030, 914, 842, 803, 738, 636, 583, 559, 443; **HRMS** (ESI): [m/z] calculated for [$C_9H_{14}O_3Na$] 193.0835, found 193.0836.

ethyl 2,2-diazido-3-oxohept-6-enoate (**1a**)



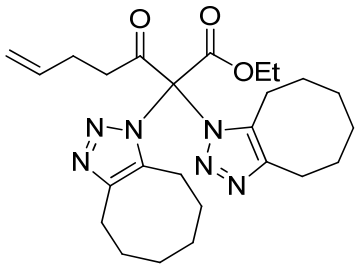
$C_9H_{12}N_6O_3$
252.23 g/mol

Following the general procedure **B** (805 mg of ethyl 3-oxohept-6-enoate, 0.1 M, 1 h), the product was obtained as a yellowish liquid (728 mg, 2.89 mmol, 61%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.67 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.78 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.06 (dq, *J* = 17.1, 1.4 Hz, 1H), 5.02 (dq, *J* = 10.2, 1.4 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.68 (t, *J* = 7.2 Hz, 2H), 2.39 – 2.35 (m, 2H), 1.35 (t, *J* = 7.1

Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 197.6, 164.4, 136.1, 116.2, 83.2, 64.3, 36.9, 27.3, 14.2; **IR** (ATR): ϑ [cm^{-1}] 3082, 2984, 2926, 2855, 2113, 1744, 1643, 1446, 1398, 1369, 1222, 1097, 1047, 1016, 998, 947, 918, 853, 759, 719, 623, 555, 451.

ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

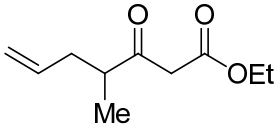


$C_{25}H_{36}N_6O_3$
468.59 g/mol

Following the general procedure **C** (24 mg of **1a**, 16 h), the product was obtained as a yellowish liquid (35 mg, 0.07 mmol, 78%) upon purification by column chromatography (CH:EtOAc = 75:25).

TLC: R_f = 0.23 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.85 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.07 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.2, 1.4 Hz, 1H), 4.51 (q, *J* = 7.2 Hz, 2H), 3.01 – 2.92 (m, 2H), 2.91 – 2.83 (m, 4H), 2.66 – 2.54 (m, 2H), 2.23 – 2.12 (m, 4H), 1.77 – 1.68 (m, 4H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.40 – 1.30 (m, 12H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 191.8, 161.8, 146.1, 136.7, 136.6, 115.8, 86.3, 64.9, 41.0, 29.5, 27.6, 26.2, 25.7, 25.1, 24.4, 22.0, 13.9; **IR** (ATR): ϑ [cm^{-1}] 2928, 2856, 1747, 1444, 1371, 1255, 1014, 911, 848, 459; **HRMS** (ESI): [m/z] calculated for [$C_{25}H_{36}N_6O_3Na$] 491.2747 found 491.2741.

ethyl 4-methyl-3-oxohept-6-enoate

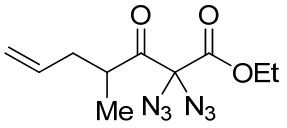


$C_{10}H_{16}O_3$
184.23 g/mol

Following the general procedure **A** with methyl iodide (1.310 g of ethyl 3-oxohept-6-enoate), the product was obtained as a yellow liquid (861 mg, 4.56 mmol, 77%) upon purification by column chromatography (CH:EtOAc = 90:10).

TLC: R_f = 0.87 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.80 – 5.64 (m, 1H), 5.11 – 5.00 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H) 3.47 (s, 2H), 2.73 (sext, *J* = 6.9 Hz, 1H), 2.49 – 2.36 (m, 1H), 2.19 – 2.06 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.8, 167.3, 135.2, 117.4, 61.5, 48.1, 46.3, 36.9, 15.8, 14.3; **IR** (ATR): ῡ [cm^{-1}] 3079, 2979, 2936, 2911, 2878, 1743, 1712, 1642, 1626, 1458, 1413, 1368, 1307, 1231, 1154, 1114, 1096, 1025, 917, 841, 804, 652, 632; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_{16}O_3Na$] 207.0997, found 207.0992.

ethyl 2,2-diazido-4-methyl-3-oxohept-6-enoate (**1b**)

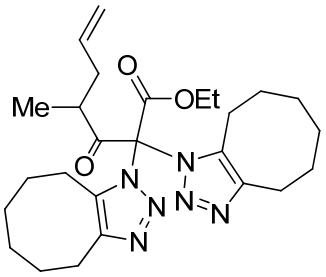


$C_{10}H_{14}N_6O_3$
266.26 g/mol

Following the general procedure **B** (163 mg of ethyl 4-methyl-3-oxohept-6-enoate, 0.1 M, 4 h), the product was obtained as a colorless liquid (145 mg, 0.54 mmol, 61%) upon purification by column chromatography (CH:EtOAc = 90:10 → 96:4).

TLC: R_f = 0.48 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 5.73 – 5.63 (m, 1H), 5.10 – 5.02 (m, 2H), 4.36 (qd, *J* = 7.1, 2.7 Hz, 2H), 3.03 – 2.94 (m, 1H), 2.47 – 2.39 (m, 1H), 2.17 – 2.08 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 201.7, 164.4, 134.7, 117.8, 83.3, 64.2, 41.5, 37.6, 17.0, 14.2; **IR** (ATR): ῡ [cm^{-1}] 2977, 2105, 1423, 1373, 1347, 1192, 1125, 1055, 1013, 994, 682, 637.

ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-4-methyl-3-oxohept-6-enoate

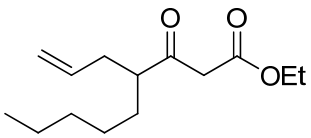


$C_{26}H_{38}N_6O_3$
482.62 g/mol

Following the general procedure **C** (29 mg of ethyl 2,2-diazido-4-methyl-3-oxohept-6-enoate, 16 h), the product was obtained as a yellow liquid (18 mg, 0.03 mmol, 29%) upon purification by column chromatography (CH:EtOAc = 75:25).

TLC: R_f = 0.34 (PE:EtOAc / 70:30, [UV, $KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 5.81 – 5.71 (m, 1H), 5.14 – 5.05 (m, 2H), 4.57 – 4.47 (m, 2H), 3.09 – 3.00 (m, 1H), 2.91 – 2.84 (m, 5H), 2.37 – 2.28 (m, 1H), 2.24 – 2.11 (m, 3H), 1.76 – 1.70 (m, 5H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.41 – 1.30 (m, 12H), 1.35 (d, *J* = 6.7 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 196.9, 161.5, 146.1, 146.1, 136.6, 136.5, 135.4, 117.7, 86.8, 64.9, 45.0, 39.4, 27.68, 27.66, 26.3, 26.2, 25.7, 25.12, 25.09, 24.4, 22.1, 18.8, 14.3, 13.8; **IR** (ATR): ϑ [cm^{-1}] 2929, 2857, 2252, 1763, 1741, 1640, 1567, 1457, 1443, 1371, 1254, 1240, 1144, 1133, 1016, 939, 906, 849, 720; **HRMS** (ESI): [m/z] calculated for [$C_{26}H_{38}N_6O_3Na$] 505.2903, found 505.2898.

ethyl 4-allyl-3-oxononanoate

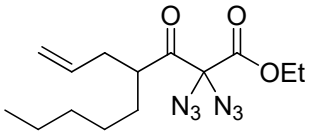


$C_{14}H_{24}O_3$
240.34 g/mol

Following the general procedure **A** with 1-bromo pentane (303 mg of ethyl 3-oxohept-6-enoate), the product was obtained as an orange liquid (146 mg, 0.60 mmol, 34%) upon purification by column chromatography (CH:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.56 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 5.80 – 5.63 (m, 1H), 5.10 – 4.98 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.44 (s, 2H), 2.67 (tt, *J* = 7.6, 5.9 Hz, 1H), 2.42 – 2.28 (m, 1H), 2.26 – 2.13 (m, 1H), 1.70 – 1.55 (m, 1H), 1.51 – 1.37 (m, 1H), 1.32 – 1.21 (m, 6H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 205.8, 167.2, 135.3, 117.3, 61.4, 52.2, 49.0, 35.5, 32.0, 30.9, 26.9, 22.6, 14.3, 14.1; **IR** (ATR): ϑ [cm^{-1}] 2959, 2929, 2858, 1742, 1717, 1642, 1465, 1411, 1367, 1313, 1235, 1204, 1154, 1031, 915, 587; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{24}O_3Na$] 263.1623, found 263.1618.

ethyl 4-allyl-2,2-diazido-3-oxononanoate (**1c**)

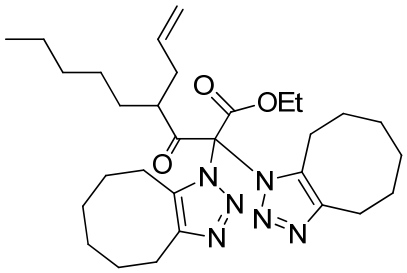


$C_{14}H_{22}N_6O_3$
322.36 g/mol

Following the general procedure **B** (140 mg of ethyl 4-allyl-3-oxononanoate, 0.1 M, 1 h), the product was obtained as a yellow liquid (115 mg, 0.35 mmol, 61%) upon purification by column chromatography (CH:EtOAc = 90:10 → 96:4).

TLC: R_f = 0.54 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.67 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.10 – 5.02 (m, 1H), 5.06 – 5.00 (m, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.03 – 2.96 (m, 1H), 2.44 – 2.36 (m, 1H), 2.24 – 2.18 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.30 – 1.22 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 201.5, 164.4, 134.8, 117.7, 83.3, 64.2, 46.7, 35.8, 31.9, 31.3, 26.7, 22.6, 14.14, 14.10; **IR** (ATR): ϑ [cm^{-1}] 2957, 2930, 2860, 2120, 1754, 1738, 1642, 1446, 1369, 1223, 1152, 1097, 1054, 1020, 919, 855, 833, 778, 727, 620, 547.

ethyl 4-allyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxononanoate

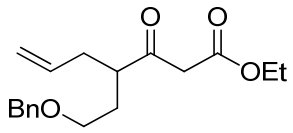


$C_{30}H_{46}N_6O_3$
538.72 g/mol

Following the general procedure **C** (15 mg of ethyl 4-allyl-2,2-diazido-3-oxononanoate, 1 h), the product was obtained as a yellow liquid (8 mg, 0.01 mmol, 30%) upon purification by column chromatography (CH:EtOAc = 90:10).

TLC: R_f = 0.14 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.85 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.16 – 5.07 (m, 2H), 4.60 – 4.45 (m, 2H), 3.15 – 3.09 (m, 1H), 2.94 – 2.86 (m, 4H), 2.75 – 2.52 (m, 2H), 2.32 – 2.16 (m, 4H), 1.81 – 1.70 (m, 4H), 1.44 (t, *J* = 7.2 Hz, 3H), 1.46 – 1.33 (m, 12H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.36 – 1.21 (m, 8H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 195.5, 161.6, 146.08, 146.06, 136.6, 136.5, 135.3, 117.5, 86.9, 64.9, 49.5, 36.2, 32.10, 32.08, 27.7, 26.33, 26.29, 26.0, 25.72, 25.70, 25.20, 25.17, 24.5, 22.7, 22.2, 14.4, 14.2, 13.8; **IR** (ATR): ϑ [cm^{-1}] 3926, 2856, 1763, 1739, 1457, 1444, 1255, 1238, 1131, 1016, 941, 723; **HRMS** (ESI): [m/z] calculated for [$C_{30}H_{46}N_6O_3Na$] 561.3529, found 561.3524.

ethyl 4-(2-(benzyloxy)ethyl)-3-oxohept-6-enoate



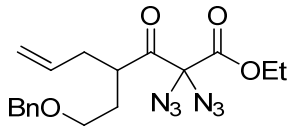
$C_{18}H_{24}O_4$
304.38 g/mol

Following the general procedure **A** with ((bromomethoxy)methyl)benzene (307 mg of ethyl 3-oxohept-6-enoate), the product was obtained as a colorless liquid (317 mg, 1.04 mmol, 57%) upon purification by column chromatography (PE:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.21 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.37 – 7.27 (m, 5H), 5.71 (ddt, *J* = 16.2, 10.4, 7.1 Hz, 1H), 5.09 – 5.01 (m, 2H), 4.45 (d, *J* =

2.3 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.47 (d, *J* = 4.0 Hz, 2H), 2.92 – 2.83 (m, 1H), 2.43 – 2.34 (m, 1H), 2.24 – 2.15 (m, 1H), 2.04 – 1.93 (m, 1H), 1.80 – 1.71 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.6, 167.2, 138.4, 135.0, 128.5, 127.9, 127.82, 127.78, 117.6, 73.1, 67.8, 61.3, 49.3, 49.0, 35.8, 31.1, 14.3; **IR** (ATR): ῡ [cm^{-1}] 3065, 2980, 2936, 2870, 1802, 1739, 1710, 1641, 1496, 1453, 1410, 1367, 1309, 1235, 1204, 1156, 1097, 1073, 1026, 918, 843, 807, 739, 714, 699, 648, 609, 462; **HRMS** (ESI): [m/z] calculated for [$C_{18}H_{24}O_4Na$] 327.1572 found 327.1567.

ethyl 2,2-diazido-4-(2-(benzyloxy)ethyl)-3-oxohept-6-enoate (**1d**)

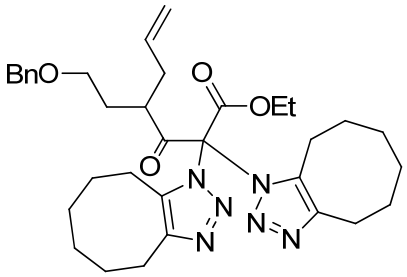


$C_{18}H_{22}N_6O_4$
386.41 g/mol

Following the general procedure **B** (301 mg of ethyl 4-(2-benzyloxy)ethyl)-3-oxohept-6-enoate, 0.1 M, 1 h), the product was obtained as a yellowish liquid (182 mg, 0.60 mmol, 61%) upon purification by column chromatography (CH:EtOAc = 100:0 → 80:20).

TLC: R_f = 0.42 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.34 – 7.30 (m, 5H), 5.72 – 5.61 (m, 1H), 5.08 – 5.02 (m, 2H), 4.46 (d, *J* = 2.6 Hz, 2H), 4.30 (q, *J* = 7.2 Hz, 2H), 3.48 – 3.37 (m, 2H), 3.26 – 3.19 (m, 1H), 2.46 – 2.38 (m, 1H), 2.26 – 2.20 (m, 1H), 2.05 – 1.98 (m, 1H), 1.80 – 1.74 (m, 1H), 1.32 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 201.3, 164.4, 138.4, 134.4, 128.5, 127.9, 127.81, 127.76, 118.0, 83.1, 73.0, 67.4, 64.2, 43.7, 36.0, 31.2, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3031, 2981, 2929, 2861, 2117, 1751, 1641, 1496, 1454, 1415, 1366, 1225, 1155, 1095, 1025, 916, 853, 736, 697, 612, 546, 462.

ethyl 4-(2-(benzyloxy)ethyl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

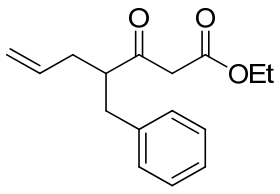


$C_{34}H_{46}N_6O_4$
602.77 g/mol

Following the general procedure **C** (24 mg of ethyl 2,2-diazido-4-(2-benzyloxy)ethyl)-3-oxohept-6-enoat, 1 h), the product was obtained as a yellow liquid (13 mg, 0.02 mmol, 34%) upon purification by column chromatography (CH:EtOAc = 90:10 → 70:30).

TLC: R_f = 0.08 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.34 – 7.26 (m, 5H), 5.88 – 5.76 (m, 1H), 5.11 – 5.03 (m, 2H), 4.52 – 4.43 (m, 4H), 3.61 – 3.51 (m, 2H), 3.28 – 3.22 (m, 1H), 2.91 – 2.85 (m, 4H), 2.74 – 2.65 (m, 1H), 2.63 – 2.54 (m, 1H), 2.29 – 2.11 (m, 4H), 2.07 – 1.93 (m, 2H), 1.77 – 1.70 (m, 4H), 1.44 – 1.31 (m, 12H), 1.38 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 195.5, 161.4, 146.14, 146.09, 138.6, 136.7, 136.5, 135.1, 128.4, 127.8, 127.7, 117.7, 86.9, 73.0, 67.5, 65.0, 46.6, 36.6, 32.1, 27.68, 27.65, 26.3, 25.73, 25.71, 25.2, 24.5, 22.1, 13.7; **IR** (ATR): ῡ [cm^{-1}] 2927, 2856, 1763, 1739, 1454, 1370, 1255, 12399, 1096, 1015, 942, 916, 884, 848, 735, 698; **HRMS** (ESI): [m/z] calculated for [$C_{34}H_{46}N_6O_4Na$] 625.3478, found 625.3473.

ethyl 4-benzyl-3-oxononanoate

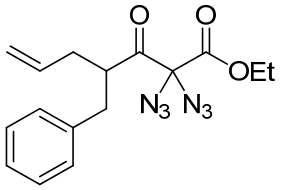


$C_{16}H_{20}O_3$
260.32 g/mol

Following the general procedure **A** with benzyl bromide (500 mg of ethyl 3-oxohept-6-enoate), the product was obtained as a yellowish liquid (458 mg, 1.76 mmol, 60%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.57 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.29 – 7.21 (m, 2H), 7.21 – 7.15 (m, 1H), 7.15 – 7.10 (m, 2H), 5.77 – 7.65 (m, 1H), 5.08 – 5.04 (m, 1H), 5.04 – 4.98 (m, 1H), 4.16 – 4.05 (m, 2H), 3.23 (d, *J* = 2.9 Hz, 2H), 3.05 – 2.97 (m, 1H), 2.93 – 2.86 (m 1H), 2.77 – 2.68 (m, 1H), 2.42 – 2.32 (m, 1H), 2.26 – 2.17 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.5, 166.9, 139.1, 134.9, 129.1, 128.7, 126.6, 117.8, 61.4, 53.7, 50.2, 37.3, 36.6, 14.2; **IR** (ATR): ῡ [cm^{-1}] 3078, 3028, 2981, 2931, 2860, 1743, 1711, 1641, 1497, 1444, 1420, 1367, 1305, 1232, 1150, 1095, 1074, 1029, 994, 916, 842, 803, 751, 699, 651, 558, 499; **HRMS** (ESI): [m/z] calculated for [$C_{16}H_{20}O_3Na$] 283.1305, found 283.1308.

ethyl 2,2-diazido-4-benzyl-3-oxohept-6-enoate (**1e**)

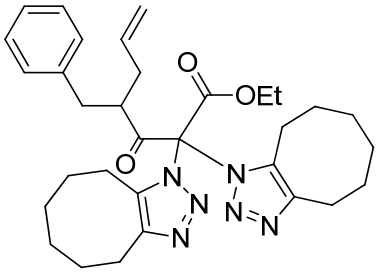


$C_{16}H_{18}N_6O_3$
342.35 g/mol

Following the general procedure **B** (400 mg of ethyl 4-benzyl-3-oxononanoate, 0.1 M, 1 h), the product was obtained as a yellowish liquid (211 mg, 0.62 mmol, 40%) upon purification by column chromatography (CH:EtOAc = 90:10 → 90:10).

TLC: R_f = 0.78 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 7.32 – 7.25 (m, 2H), 7.23 – 7.19 (m, 1H), 7.16 – 7.13 (m, 2H), 5.72 – 5.65 (m, 1H), 5.08 – 5.08 (m, 1H), 5.06 – 5.04 (m, 1H), 4.23 – 4.17 (m, 1H), 4.17 – 4.11 (m, 1H), 3.36 – 3.31 (m, 1H), 3.00 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.68 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.46 – 2.41 (m, 1H), 2.24 – 2.18 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 200.7, 164.1, 138.6, 134.3, 129.3, 128.6, 126.8, 118.2, 83.4, 64.2, 48.8, 37.2, 36.7, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3080, 3029, 2983, 2929, 2860, 2118, 1752, 1738, 1641, 1604, 1497, 1454, 1368, 1223, 1096, 1059, 1021, 919, 853, 747, 699, 621, 545, 504.

ethyl 4-benzyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

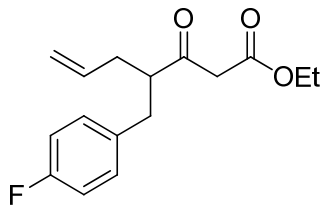


$C_{32}H_{42}N_6O_3$
558.71 g/mol

Following the general procedure **C** (48 mg of ethyl 2,2-diazido-4-benzyl-3-oxohept-6-enoate, 1 h), the product was obtained as a yellow liquid (32 mg, 0.05 mmol, 66%) upon purification by column chromatography (CH:EtOAc = 75:25).

TLC: R_f = 0.72 (PE:EtOAc / 70:30, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.30 – 7.25 (m, 2H), 7.25 – 7.18 (m, 3H), 5.80 – 5.70 (m, 1H), 5.08 – 4.99 (m, 2H), 4.57 – 4.40 (m, 2H), 3.50 – 3.38 (m, 2H), 2.98 – 2.93 (m, 1H), 2.92 – 2.87 (m, 4H), 2.48 – 2.12 (m, 6H), 1.79 – 1.71 (m, 4H), 1.43 – 1.36 (m, 15H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 194.6, 161.5, 146.2, 146.1, 138.9, 136.7, 136.6, 134.3, 129.7, 128.5, 126.6, 118.1, 87.0, 65.0, 51.4, 37.3, 35.0, 27.68, 27.65, 26.32, 26.26, 25.71, 25.70, 25.19, 25.15, 24.48, 24.46, 22.2, 13.8; **IR** (ATR): ῡ [cm^{-1}] 2931, 2857, 2252, 1763, 1741, 1560, 1507, 1496, 1474, 1455, 1443, 1395, 1371, 1399, 1255, 1172, 1144, 1083, 1013, 968, 949, 918, 881, 848, 821, 793, 745, 701, 655, 628, 567, 504, 461, 429; **HRMS** (ESI): [m/z] calculated for [$C_{32}H_{42}O_3N_6Na$] 581.3216, found 581.3211.

ethyl 4-(4-fluorobenzyl)-3-oxohept-6-enoate

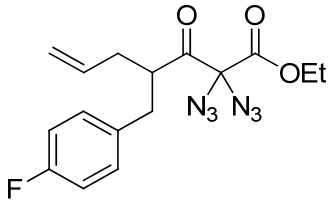


$C_{16}H_{19}FO_3$
278.32 g/mol

Following the general procedure **A** with 4-fluorobenzyl bromide (307 mg of ethyl 3-oxohept-6-enoate), the product was obtained as a yellow liquid (282 mg, 1.30 mmol, 72%) upon purification by column chromatography (CH:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.18 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.13 – 7.07 (m, 2H), 7.00 – 6.92 (m, 2H), 5.78 – 5.66 (m, 1H), 5.10 – 5.04 (m, 2H), 4.11 (qd, *J* = 7.1, 2.2 Hz, 2H), 3.27 (d, *J* = 2.9 Hz, 2H), 3.04 – 2.96 (m, 1H), 2.94 – 2.87 (m, 1H), 2.74 – 2.66 (m, 1H), 2.42 – 2.34 (m, 1H), 2.27 – 2.18 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.3, 166.8, 134.6, 130.6, 130.5, 118.0, 115.6, 115.4, 61.4, 53.7, 50.2, 36.3, 35.6, 14.2; **IR** (ATR): ῡ [cm^{-1}] 3078, 2981, 2932, 2871, 1743, 1411, 1642, 1509, 1445, 1417, 1367, 1307, 1220, 1157, 1094, 1030, 994, 919, 822, 761, 739, 646, 537, 498; **HRMS** (ESI): [m/z] calculated for [$C_{16}H_{19}FO_3Na$] 301.1216, found 301.1210.

ethyl 2,2-diazido-4-(4-fluorobenzyl)-3-oxohept-6-enoate (**1f**)

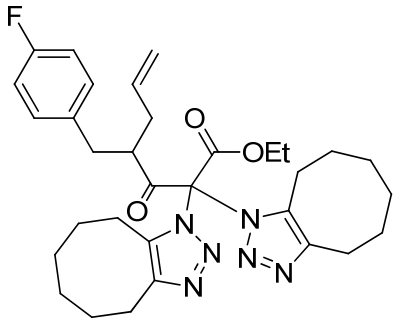


$C_{16}H_{17}FN_6O_3$
360.34 g/mol

Following the general procedure **B** (866 mg of ethyl 3-(4-fluorobenzyl)-3-oxohept-6-enoate, 0.1 M, 1 h), the product was obtained as a yellowish liquid (423 mg, 1.17 mmol, 38%) upon purification by column chromatography (CH:EtOAc = 90:10 → 80:20).

TLC: R_f = 0.61 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.13 – 7.07 (m, 2H), 7.00 – 6.93 (m, 2H), 5.68 (ddt, *J* = 16.7, 10.4, 7.1 Hz, 1H), 5.10 – 5.07 (m, 1H), 5.07 – 5.03 (m, 1H), 4.20 (dq, *J* = 9.0, 7.1 Hz, 2H), 3.33 – 3.26 (m, 1H), 3.00 – 2.93 (m, 1H), 2.69 – 2.63 (m, 1H), 2.48 – 2.38 (m, 1H), 2.23 – 2.15 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 200.6, 164.1, 134.1, 130.8, 130.7, 118.3, 115.5, 115.3, 83.3, 64.3, 48.8, 36.3, 35.7, 14.1; **IR** (ATR): ῡ [cm^{-1}] 2985, 2102, 1676, 1514, 1410, 1346, 1272, 1223, 1195, 1150, 1018, 965, 860, 805, 780, 696, 637, 587, 518, 486, 416.

ethyl 4-(4-fluorobenzyl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

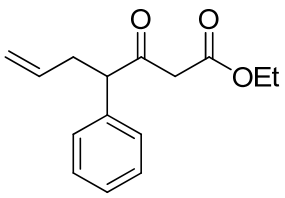


$C_{32}H_{41}FN_6O_3$
576.70 g/mol

Following the general procedure **C** (22 mg of ethyl 2,2-diazido-4-(4-fluorobenzyl)-3-oxohept-6-enoate, 1 h), the product was obtained as a yellow liquid (11 mg, 0.01 mmol, 31%) upon purification by column chromatography (CH:EtOAc = 90:10 → 70:30).

TLC: R_f = 0.16 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.22 – 7.17 (m, 2H), 6.99 – 6.93 (m, 2H), 5.78 – 5.66 (m, 1H), 5.11 – 5.04 (m, 1H), 5.01 (dq, *J* = 17.0, 1.6 Hz, 1H), 4.55 (dq, *J* = 10.7, 7.2 Hz, 1H), 4.43 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.45 – 3.35 (m, 2H), 2.98 – 2.84 (m, 5H), 2.43 – 2.22 (m, 4H), 2.23 – 2.05 (m, 2H), 1.81 – 1.70 (m, 4H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.51 – 1.31 (m, 12H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 194.5, 161.4, 146.3, 146.2, 136.8, 136.5, 134.5, 134.1, 131.24, 131.16, 118.2, 115.4, 115.2, 87.0, 65.1, 51.5, 36.4, 35.0, 25.7, 24.5, 22.2, 13.8; **IR** (ATR): ῡ [cm^{-1}] 2927, 2856, 1763, 1740, 1509, 1443, 1371, 1255, 1221, 1158, 1144, 1093, 1014, 941, 921, 881, 844, 815, 793, 545; **HRMS** (ESI): [m/z] calculated for [$C_{32}H_{41}FN_6O_3Na$] 599.3122, found 599.3116.

ethyl 3-oxo-4-phenylhept-6-enoate

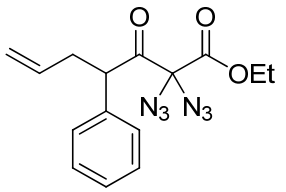


$C_{15}H_{18}O_3$
246.30 g/mol

Following the general procedure **A** with allyl bromide (956 mg of ethyl 3-oxo-4-phenylbutanoat), the product was obtained as a colorless liquid (783 mg, 3.18 mmol, 69%) upon purification by column chromatography (PE:EtOAc = 100:0 → 80:20). The analytical data corresponds with the previously published data.[2]

TLC: R_f = 0.35 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.36 – 7.26 (m, 3H), 7.22 – 7.18 (m, 2H), 5.66 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.04 – 4.99 (m, 1H), 4.96 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.15 – 4.07 (m, 1H), 3.86 (t, *J* = 7.4 Hz, 2H), 3.41 (d, *J* = 15.4 Hz, 1H), 3.28 (d, *J* = 15.4 Hz, 1H), 2.83 (ddt, *J* = 14.3, 7.1, 1.2 Hz, 1H), 2.49 – 2.40 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 201.8, 167.1, 137.4, 135.5, 129.2, 128.7, 127.8, 117.0, 61.4, 58.9, 48.3, 36.3, 14.2; **IR** (ATR): ῡ [cm^{-1}] 3064, 3029, 2981, 2937, 2913, 1742, 1713, 1642, 1494, 1454, 1409, 1367, 1311, 1234, 1148, 1096, 1075, 1030, 997, 916, 846, 749, 700, 644, 581, 540, 495, 450; **HRMS** (ESI): [m/z] calculated for [$C_{15}H_{18}O_3Na$] 269.1148, found 269.1141.

ethyl 2,2-diazido-3-oxo-4-phenylhept-6-enoate (1g)

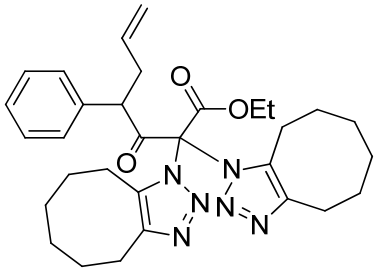


$C_{15}H_{16}N_6O_3$
328.33 g/mol

Following the general procedure **B** (605 mg of ethyl 3-oxo-4-phenylhept-6-enoate, 0.1 M, 4 h), the product was obtained as a colorless liquid (445 mg, 1.38 mmol, 69%) upon purification by column chromatography (PE:EtOAc = 100:0 → 95:5).

TLC: R_f = 0.64 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.35 – 7.29 (m, 2H), 7.29 – 7.21 (m, 3H), 5.66 – 5.55 (m, 1H), 5.04 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.99 (dq, *J* = 10.1, 1.6 Hz, 1H), 4.20 (t, *J* = 7.5 Hz, 1H), 4.06 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.80 (dq, *J* = 10.7, 7.1 Hz, 1H), 2.82 – 2.74 (m, 1H), 2.53 – 2.44 (m, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 197.8, 163.9, 136.4, 134.6, 129.0, 128.7, 128.0, 117.8, 83.3, 64.0, 53.4, 38.4, 13.8; **IR** (ATR): ῡ [cm^{-1}] 3066, 3031, 2983, 2940, 2117, 1754, 1739, 1642, 1600, 1493, 1455, 1368, 1223, 1097, 1056, 1030, 994, 918, 854, 824, 743, 698, 645, 617, 553, 507, 462.

ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxo-4-phenylhept-6-enoate

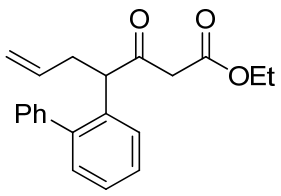


$C_{31}H_{40}N_6O_3$
544.69 g/mol

Following the general procedure **C** (67 mg of ethyl 2,2-diazido-3-oxo-4-phenylhept-6-enoate, 16 h), the product was obtained as a viscous liquid (102 mg, 0.19 mmol, 92%) upon purification by column chromatography (CH:EtOAc = 80:20).

TLC: R_f = 0.34 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.27 – 7.20 (m, 5H), 5.49 (ddt, *J* = 17.1, 10.1, 7.2 Hz, 1H), 5.00 – 4.93 (m, 1H), 4.89 – 4.84 (m, 1H), 4.17 (dq, *J* = 10.1, 3.4 Hz, 1H), 4.13 – 4.03 (m, 1H), 3.33 – 3.25 (m, 1H), 3.07 – 2.97 (m, 1H), 2.96 – 2,87 (m, 2H), 2.87 – 2.77 (m, 4H), 2.58 – 2.48 (m, 1H), 2.46 – 2.37 (m, 1H), 2.18 – 2.10 (m, 1H), 2.01 – 1.94 (m, 1H), 1.82 – 1.54 (m, 6H), 1.54 – 1.38 (m, 5H), 1.37 – 1.26 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 193.7, 160.8, 146.2, 145.9, 139.2, 136.9, 136.3, 134.7, 128.6, 128.0, 127.5, 117.7, 86.4, 64.3, 60.5, 57.0, 40.7, 27.6, 25.6, 25.2, 24.42, 24.39, 22.0, 14.3, 13.0; **IR** (ATR): ῡ [cm^{-1}] 2928, 2856, 1764, 1740, 1641, 1568, 1455, 1443, 1371, 1237, 1133, 1116, 1078, 1045, 1019, 999, 945, 916, 849, 805, 748, 722, 700, 649, 606, 561, 504, 462; **HRMS** (ESI): [m/z] calculated for [$C_{31}H_{40}O_3N_6Na$] 567.3054, found 567.3055.

ethyl 4-([1,1'-biphenyl]-2-yl)-3-oxohept-6-enoate

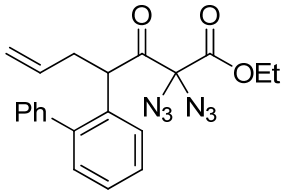


$C_{21}H_{22}O_3$
322.40 g/mol

Following the general procedure **A** allyl bromide (560 mg of ethyl 4-([1,1'-biphenyl]-2-yl)-3-oxobutanoate), the product was obtained as a yellow liquid (445 mg, 31.38 mmol, 69%) upon purification by column chromatography (PE:EtOAc = 100:0 → 95:5).

TLC: R_f = 0.49 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.49 – 7.37 (m, 3H), 7.38 – 7.26 (m, 5H), 7.23 – 7.16 (m, 1H), 5.62 (ddt, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.00 – 4.88 (m, 2H), 4.04 (t, *J* = 7.2 Hz, 1H), 4.02 (qd, *J* = 7.1, 0.9 Hz, 2H), 3.16 (d, *J* = 5.2 Hz, 2H), 2.87 – 2.74 (m, 1H), 2.49 – 2.37 (m, 1H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 201.7, 166.9, 142.9, 141.0, 135.6, 135.2, 130.8, 129.5, 128.5, 128.4, 127.58, 127.56, 127.5, 17.0, 61.3, 54.3, 48.3, 36.5, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3061, 2980, 2935, 1742, 1714, 1641, 1478, 1307, 1246, 1147, 1032, 915, 752, 703, 556, 528**;** **HRMS (ESI):** [m/z] calculated for [$C_{21}H_{22}O_3Na$] 345.1467, found 345.1461.

ethyl 4-([1,1'-biphenyl]-2-yl)-2,2-diazido-3-oxohept-6-enoate (**1h**)

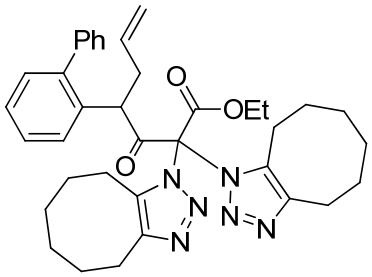


$C_{21}H_{20}N_6O_3$
404.42 g/mol

Following the general procedure **B** (445 mg of ethyl 4-([1,1'-biphenyl]-2-yl)-3-oxohept-6-enoate, 0.1 M, 1 h), the product was obtained as a yellow liquid (280 mg, 0.69 mmol, 50%) upon purification by column chromatography (PE:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.36 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.50 – 7.28 (m, 8H), 7.22 – 7.18 (m, 1H), 5.57 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.00 – 4.92 (m, 2H), 4.41 (dd, *J* = 9.4, 5.0 Hz, 1H), 4.05 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.90 (dq, *J* = 10.7, 7.1 Hz, 1H), 2.88 – 2.78 (m, 1H), 2.44 – 2.35 (m, 1H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 198.4, 163.7, 142.8, 140.9, 134.8, 133.9, 131.1, 129.4, 128.3, 127.8, 127.7, 127.6, 127.3, 117.5, 83.0, 63.9, 49.2, 38.5, 13.9; **IR** (ATR): ῡ [cm^{-1}] 3062, 2983, 2123, 1736, 1641, 1478, 1438, 1393, 1372, 1232, 1097, 1045, 1010, 918, 850, 775, 754, 703, 634, 607, 545, 507, 462.

ethyl 4-([1,1'-biphenyl]-2-yl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

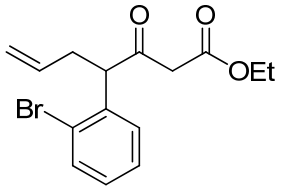


$C_{37}H_{44}N_6O_3$
620.78 g/mol

Following the general procedure **C** (21 mg of ethyl 4-([1,1'-biphenyl]-2-yl)-2,2-diazido-3-oxohept-6-enoate, 16 h), the product was obtained as a yellow liquid (20 mg, 0.03 mmol, 61%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.38 (PE:EtOAc / 80:20, [UV, $KmnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 7.58 (d, *J* = 8.0 Hz, 1H), 7.33 (td, J = 7.6, 1.6 Hz, 1H), 7.29 – 7.17 (m, 6H), 7.11 – 7.09 (m, 1H), 5.53 (ddt, *J* = 17.3, 10.1, 7.3 Hz, 1H), 4.88 – 4.83 (m, 2H), 4.19 – 4.10 (m, 2H), 2.95 – 2.79 (m, 6H), 2.78 – 2.72 (m, 1H), 2.52 – 2.40 (m, 1H), 2.32 – 2.23 (m, 1H), 2.14 – 2.06 (m, 1H), 2.01 – 1.92 (m, 1H), 1.78 – 1.51 (m, 8H), 1.49 – 1.40 (m, 3H), 1.40 – 1.23 (m, 8H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 193.9, 160.8, 146.0, 145.9, 136.9, 136.6, 136.2, 135.1, 130.5, 129.8, 127.9, 127.8, 127.2, 127.0, 117.3, 86.5, 64.3, 51.6, 41.6, 27.8, 27.7, 26.6, 26.4, 25.72, 25.67, 25.23, 25.20, 24.4, 22.2, 22.0, 13.3; **IR** (ATR): ῡ [cm^{-1}] 2927, 2856, 2236, 1764, 1736, 1477, 1440, 1256, 1238, 908, 727, 702, 646; **HRMS** (ESI): [m/z] calculated for [$C_{37}H_{45}N_6O_3$] 621.3553, found 621.3548.

ethyl 4-(2-bromophenyl)-3-oxohept-6-enoate

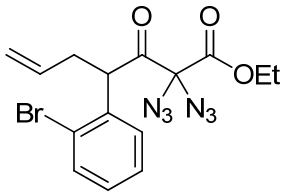


$C_{15}H_{17}BrO_3$
325.20 g/mol

Following the general procedure **A** allyl bromide (3.000 g of ethyl 4-(2-bromophenyl)-3-oxobutanoate), the product was obtained as an orange liquid (2.073 g, 6.37 mmol, 61%) upon purification by column chromatography (PE:EtOAc = 100:0 → 94:6).

TLC: R_f = 0.43 (PE:EtOAc / 95:5, [UV, KmnO4]); **^{1}H-NMR** (400 MHz, CDCl3): δ [ppm] 7.61 - 7.58 (m, 1H), 7.30 - 7.26 (m, 1H), 7.15 - 7.10 (m, 2H), 5.73 - 5.63 (m, 1H), 5.00 (ddd, *J* = 17.1, 3.2, 1.5 Hz, 1H), 4.94 (ddd, *J* = 10.2, 2.8, 1.1 Hz, 1H), 4.48 (t, *J* = 7.3 Hz, 1H), 4.11 (qd, *J* = 7.2, 0.8 Hz, 2H), 3.42 (d, *J* = 15.7 Hz, 1H), 3.29 (d, *J* = 15.7 Hz, 1H), 2.84 - 2.77 (m, 1H), 2.43 (dtt, *J* = 14.6, 7.4, 1.2 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, CDCl3): δ [ppm] 201.6, 166.9, 137.0, 134.8, 133.5, 129.32, 129.26, 128.2, 125.6, 117.3, 61.4, 57.0, 48.4, 35.8, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3076, 2981, 2935, 1743, 1715, 1642, 1470, 1438, 1367, 1308, 1230, 1147, 1111, 1096, 995, 846, 751, 664, 582, 452**; HRMS (ESI):** [m/z] calculated for [$C_{15}H_{17}O_3NaBr$] 347.0253, found 347.0252.

ethyl 2,2-diazido-4-(2-bromophenyl)-3-oxohept-6-enoate (**1i**)

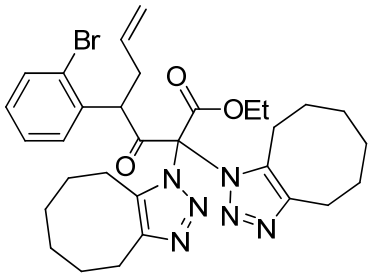


$C_{15}H_{15}BrN_6O_3$
407.22 g/mol

Following the general procedure **B** (1.500 g of ethyl 4-(2-bromophenyl)-3-oxohept-6-enoate, 0.1 M, 90 min), the product was obtained as a yellow liquid (1.321 g, 3.24 mmol, 70%) upon purification by column chromatography (PE:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.48 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.60 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.30 - 7.28 (m, 1H), 7.22 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.15 - 7.10 (m, 1H), 5.68 (ddt, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.07 - 5.03 (m, 1H), 5.02 - 4.99 (m, 1H), 4.84 (dd, *J* = 8.2, 6.5 Hz, 1H), 4.16 (dqd, *J* = 10.7, 7.1, 0.6 Hz, 1H), 4.02 (dqd, *J* = 10.7, 7.1, 0.6 Hz, 1H), 2.76 - 2.68 (m, 1H), 2.46 - 2.39 (m, 1H), 1.17 (td, *J* = 7.2, 0.8 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 197.9, 163.7, 136.1, 134.0, 133.6, 129.3, 128.7, 127.9, 125.3, 118.1, 83.2, 64.2, 51.8, 38.1, 13.9; **IR** (ATR): ῡ [cm^{-1}] 3078, 2984, 2940, 2115, 1741, 1642, 1471, 1439, 1223, 1021, 99,, 821, 653, 452.

ethyl 4-(2-bromophenyl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

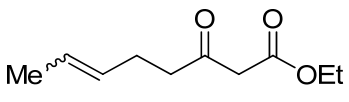


$C_{31}H_{39}BrN_6O_3$
623.58 g/mol

Following the general procedure **C** (50 mg of ethyl 2,2,-diazido-4-(2-bromophenyl)-3-oxohept-6-enoate, 16 h), the product was obtained as a viscous liquid (61 mg, 0.10 mmol, 80%) upon purification by column chromatography (CH:EtOAc = 100:0 → 80:20).

TLC: R_f = 0.52 (PE:EtOAc / 80:20, [UV, KmnO4]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.67 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.52 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.27 (td, *J* = 7.8, 1.3 Hz, 1H), 7.05 (ddd, *J* = 8.0, 7.8, 1.5 Hz, 1H), 5.64 (td, *J* = 17.0, 10.1, 7.3, 1H), 4.99 (dd, *J* = 10.1, 3.5 Hz, 1H), 4.94 - 4.86 (m, 2H), 4.29 (dq, *J* = 10.6, 7.2 Hz, 1H), 3.42 - 3.33 (m, 2H), 2.95 - 2.82 (m, 4H), 2.60 - 2.53 (m, 1H), 2.33 (ddd, *J* = 16.1, 9.1, 4.0 Hz, 1H), 2.08 (ddd, *J* = 16.2, 7.6, 3.9 Hz, 1H), 1.92 - 1.61 (m, 8H), 1.51 - 1.21 (m, 8H), 1.17 - 1.09 (m, 1H), 0.98 - 0.93 (m, 1H), 0.80 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 139.8, 160.4, 146.4, 146.0, 138.7, 137.1, 136.4, 133.8, 132.7, 128.7, 128.1, 125.0, 118.0, 86.8, 64.6. 54.0, 41.7, 27.63, 27.58, 26.21, 26.16, 25.8, 25.7, 25.2, 25.1, 24.5, 22.1, 22.0, 12.9; **IR** (ATR): ῡ [cm^{-1}] 2928, 2856, 1769, 1743, 1458, 1370, 1238, 1144, 1020, 850, 728, 659, 457; **HRMS** (ESI): [m/z] calculated for [$C_{31}H_{40}N_6O_3Br$] 623.2340, found 623.2359.

ethyl 3-oxooct-6-enoate

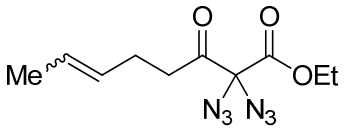


$C_{10}H_{16}O_3$
184.23 g/mol

Following the general procedure **A** (3.000 mL of ethyl acetoacetate), the product was obtained as an amber colored liquid (2.868 g, 15.57 mmol, 66%) upon purification by column chromatography (PE:EtOAc = 100:0 → 88:12).

TLC: R_f = 0.36 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.49 – 5.32 (m, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.39 (s, 2H), 2.57 (t, *J* = 7.3 Hz, 2H), 2.28 – 2.21 (m, 2H), 1.63 – 1.57 (m, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 202.4, 167.3, 129.1, 126.3, 61.4, 49.4, 42.9, 26.5, 17.9, 14.2; **IR** (ATR): ῡ [cm^{-1}] 2982, 2937, 2920, 2858, 1741, 1714, 1647, 1444, 1410, 1367, 1310, 1234, 1188, 1150, 1095, 1032, 967, 843, 803, 739, 704, 650, 587, 507, 443, 431; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_{16}O_3Na$] 207.0992, found 207.0989.

ethyl 2,2-diazido-3-oxooct-6-enoate (**1j**)

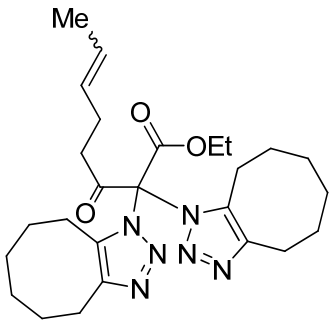


$C_{10}H_{14}N_6O_3$
266.26 g/mol

Following the general procedure **B** with crotyl bromide (500 mg of ethyl 3-oxooct-6-enoate, 0.1 M, 45 min), the product was obtained as a colorless liquid (684 mg, 8.14 mmol, 60%) upon purification by column chromatography (PE:EtOAc = 100:0 → 97:3).

TLC: R_f = 0.85 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.53 – 5.43 (m, 1H), 5.41 – 5.32 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.62 (t, *J* = 7.2 Hz, 2H), 2.32 – 2.25 (m, 2H), 1.65 – 1.60 (m, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 197.7, 164.4, 128.6, 126.9, 83.2, 64.2, 37.6, 26.4, 18.0, 14.1; **IR** (ATR): ῡ [cm^{-1}] 2985, 2969, 2940, 2920, 2858, 2113, 1744, 1446, 1398, 1369, 1222, 1097, 1046, 1014, 966, 853, 749, 699, 627, 555, 508, 447.

ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxooct-6-enoate

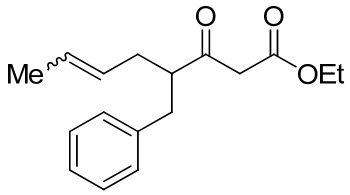


$C_{26}H_{38}N_6O_3$
482.62 g/mol

Following the general procedure **C** (100 mg of ethyl 2,2-diazido-3-oxooct-6-enoate, 4 h), the product was obtained as a viscous liquid (147 mg, 0.30 mmol, 81%) upon purification by column chromatography (CH:EtOAc = 100:0 → 80:20).

TLC: R_f = 0.62 (PE:EtOAc / 80:20, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.54 – 5.37 (m, 2H), 4.50 (q, *J* = 7.1 Hz, 2H), 2.95 – 2.84 (m, 6H), 2.55 – 2.47 (m, 2H), 2.21 – 2.13 (m, 4H), 1.75 – 1.68 (m, 4H), 1.65 – 1-60 (m, 3H), 1.41 – 1.28 (m, 15H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 191.9, 161.8, 146.1, 136.6, 129.1, 126.6, 86.3, 64.8, 41.7, 28.5, 27.6, 26.2, 25.7, 25.0, 24.4, 22.0, 17.9, 13.8; **IR** (ATR): ῡ [cm^{-1}] 2927, 2856, 1769, 1566, 1443, 1341, 1254, 1173, 1143, 1128, 1086, 1045, 1017, 966, 939, 915, 848, 794, 757, 731, 708, 687, 635, 607, 556, 502, 462; **HRMS** (ESI): [m/z] calculated for [$C_{26}H_{38}O_3N_6Na$] 505.2898, found 505.2904.

ethyl 4-benzyl-3-oxooct-6-enoate

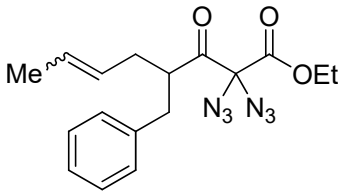


$C_{17}H_{22}O_3$
274.35 g/mol

Following the general procedure **A** with benzyl bromide (1.000 g of ethyl 3-oxooct-6-enoate), the product was obtained as a red liquid (1.057 g, 3.85 mmol, 71%) upon purification by column chromatography (PE:EtOAc = 95:5 → 92:8).

TLC: R_f = 0.51 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.30 – 7.24 (m, 2H), 7.22 – 7.18 (m, 1H), 7.17 – 7.13 (m, 2H), 5.53 – 5.45 (m, 1H), 5.38 – 5.32 (m, 1H), 4.18 – 4.08 (m, 2H), 3.26 (q, *J* = 15.4 Hz, 2H), 3.01 – 2.96 (m, 1H), 2.93 – 2.87 (m, 1H), 2.74 – 2.69 (m, 1H), 2.35 – 2.29 (m, 1H), 2.21 – 2.16 (m, 1H), 1.67 – 1.63 (m, 3H), 1.23 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.7, 166.9, 139.3, 129.1, 128.6, 128.5, 127.2, 126.5, 61.3, 54.1, 50.2, 37.2, 34.5, 18.0, 14.2; **IR** (ATR): ῡ [cm^{-1}] 3086, 3063, 3027, 2981, 2936, 2918, 2856, 1744, 1711, 1645, 1627, 1604, 1496, 1454, 1444, 1422, 1367, 1305, 1231, 1148, 1114, 1095, 1075, 1030, 967, 916, 841, 803, 750, 699, 655, 590, 561, 492; **HRMS** (ESI): [m/z] calculated for [$C_{17}H_{22}O_3Na$] 297.1461, found 297.1462.

ethyl 2,2-diazido-4-benzyl-3-oxooct-6-enoate (1k)

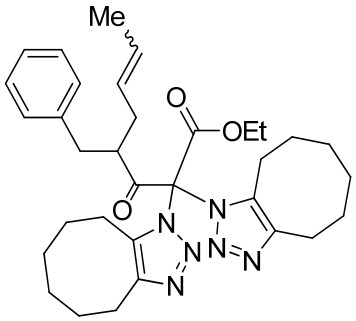


$C_{17}H_{20}N_6O_3$
356.38 g/mol

Following the general procedure **B** (500 mg of ethyl 4-benzyl-3-oxooct-6-enoate, 0.1 M, 2 h), the product was obtained as a yellowish liquid (459 mg, 1.15 mmol, 63%) upon purification by column chromatography (PE:EtOAc = 100:0 → 94:6).

TLC: R_f = 0.80 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.30 – 7.25 (m, 2H), 7.22 – 7.17 (m, 1H), 7.16 – 7.11 (m, 2H), 5.53 – 5.42 (m, 1H), 5.35 – 5.25 (m, 1H), 4.24 – 4.08 (m, 2H), 3.33 – 3.25 (m, 1H), 2.97 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.67 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.41 – 2.32 (m, 1H), 2.19 – 2.10 (m, 1H), 1.65 (dd, *J* = 6.8, 1.4 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 200.8, 164.1, 138.9, 129.3, 129.0, 128.6, 126.70, 126.66, 83.3, 64.2, 49.2, 37.1, 34.7, 18.1, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3028, 2983, 2939, 2919, 2857, 2118, 1752, 1738, 1604, 1497, 1445, 1368, 1223, 1096, 1077, 1056, 1022, 966, 923, 854, 834, 746, 699, 545, 496.

ethyl 4-benzyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxooct-6-enoate

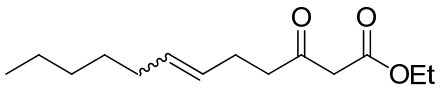


$C_{33}H_{44}N_6O_3$
572.74 g/mol

Following the general procedure **C** (53 mg of ethyl 2,2-diazido-4-benzyl-3-oxooct-6-enoate, 16 h), the product was obtained as a viscous liquid (59 mg, 0.10 mmol, 69%) upon purification by column chromatography (CH:EtOAc = 90:10 → 80:20).

TLC: R_f = 0.37 (PE:EtOAc / 80:20, [UV, $KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 7.29 – 7.25 (m, 2H), 7.24 – 7.21 (m, 2H), 7.21 – 7.17 (m, 1H), 5.45 – 5.38 (m, 1H), 5.36 – 5.30 (m, 1H), 4.55 – 4.49 (m, 1H), 4.47 – 4.39 (m, 1H), 3.45 – 3.35 (m, 2H), 2.98 – 2.86 (m, 5H), 2.38 – 2.26 (m, 4H), 2.25 – 2.17 (m, 1H), 1.80 – 1.69 (m, 4H), 1.63 (dd, *J* = 6.3, 1.1 Hz, 3H), 1.46 – 1.33 (m, 13H), 1.27 – 1.15 (m, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 194.7, 161.5, 146.2, 146.1, 139.1, 136.7, 136.5, 129.8, 128.7, 128.4, 126.7, 126.5, 87.0, 64.9, 51.7, 37.3, 34.0, 27.7, 27.6, 26.31, 26.25, 25.7, 25.19, 25.16, 24.5, 24.4, 22.2, 22.1, 18.1, 13.8; **IR** (ATR): ῡ [cm^{-1}] 2928, 2855, 1763, 1739, 1559, 1507, 1455, 1371, 1255, 1237, 1144, 1077, 1045, 1014, 967, 951, 935, 900, 848, 743, 700, 570; **HRMS** (ESI): [m/z] calculated for [$C_{33}H_{44}O_3N_6Na$] 595.3367, found 595.3364.

ethyl 3-oxododec-6-enoate

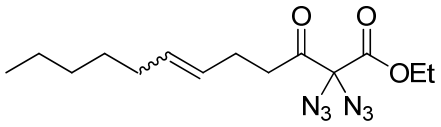


$C_{14}H_{24}O_3$
240.34 g/mol

Following the general procedure **A** (1.350 g of ethyl acetoacetate), the product was obtained as a yellow liquid (1.802 g, 7.49 mmol, 69%) upon purification by column chromatography (PE:EtOAc = 90:10 → 80:20).

TLC: R_f = 0.34 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 5.48 - 5.42 (m, 1H), 5.40 - 5.34 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.42 (s, 2H), 2.60 (t, *J* = 7.4 Hz, 2H), 2.31 - 2.26 (m, 2H), 1.98 - 1.93 (m, 2H), 1.30 - 1.23 (m, 9H), 0.87 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 202.3, 167.2, 132.0, 127.8, 61.4, 49.4, 43.0, 32.5, 31.4, 29.2, 26.6, 22.6, 14.2, 14.1; **IR** (ATR): ῡ [cm^{-1}] 2957, 2926, 2856, 1742, 1716, 1648, 1466, 1444, 1410, 1367, 1312, 1232, 1182, 1150, 1096, 1032, 969; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{24}O_3Na$] 263.1623, found 263.1618.

ethyl 2,2-diazido-3-oxododec-6-enoate (1l)

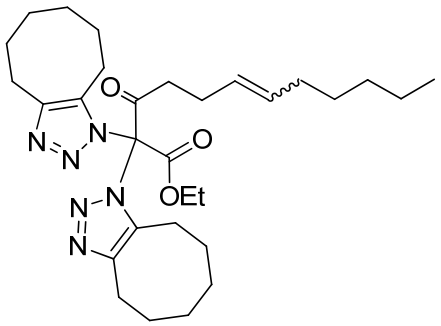


$C_{14}H_{22}N_6O_3$
322.36 g/mol

Following the general procedure **B** 1-bromooct-2-ene (253 mg of ethyl 3-oxododec-6-enoate, 0.1 M, 1 h), the product was obtained as a yellow liquid (214 mg, 0.66 mmol, 63%) upon purification by column chromatography (PE:EtOAc = 100:0 → 94:6).

TLC: R_f = 0.50 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.51 – 5.42 (m, 1H), 5.39 – 5.29 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.63 (t, *J* = 7.2 Hz, 2H), 2.31 – 2.28 (m, 1H), 1.97 – 1.94 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.38 – 1.20 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 197.7, 164.4, 132.6, 127.2, 83.2, 64.2, 37.7, 32.6, 31.5, 29.2, 27.3, 26.4, 22.7, 14.2; **IR** (ATR): ῡ [cm^{-1}] 2958, 2927, 2857, 2114, 1745, 1488, 1465, 1457, 1446, 1396, 1369, 1226, 1097, 1048, 1017, 969, 853, 727, 608, 555, 444.

ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxododec-6-enoate



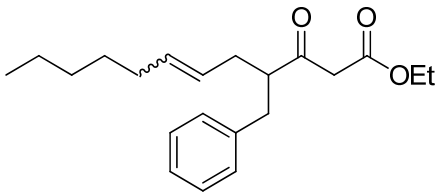
$C_{30}H_{46}N_6O_3$
538.72 g/mol

Following the general procedure **C** (17 mg of ethyl 2,2-diazido-3-oxododec-6-enoate, 1 h), the product was obtained as a yellow liquid (3 mg, 0.006 mmol, 11%) upon purification by column chromatography (CH:EtOAc = 90:10 → 70:30).

TLC: R_f = 0.20 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.52 – 5.45 (m, 1H), 5.44 – 5.39 (m, 1H), 4.51 (q, *J* = 7.1 Hz, 2H), 2.96 – 2.89 (m, 2H), 2.87 (dd, *J* = 7.6, 5.8 Hz, 5H), 2.52 (dd, *J* = 14.5, 7.1 Hz, 2H), 2.18 (s, 4H), 1.95 (td, *J* = 7.4, 0.8

Hz, 2H), 1.72 (sb, 5H), 1.41 – 1.29 (m, 19H), 0.86 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 191.9, 161.8, 146.1, 136.7, 132.3, 127.8, 86.4, 64.8, 41.8, 32.6, 31.5, 29.2, 28.6, 27.7, 26.2, 25.8, 25.1, 24.4, 22.7, 22.0, 14.2, 13.9; **IR** (ATR): ῡ [cm^{-1}] 2927, 2855, 2240, 1770, 1748, 1565, 1458, 1444, 1371, 1256, 1133, 1090, 1019, 906, 849, 727, 647; **HRMS** (ESI): [m/z] calculated for [$C_{30}H_{46}N_6O_3Na$] 561.3529, found 561.3524.

ethyl 4-benzyl-3-oxododec-6-enoate

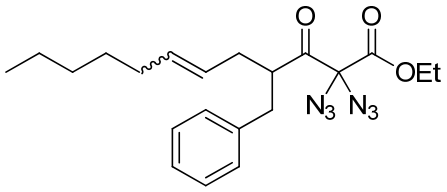


$C_{21}H_{30}O_3$
330.46 g/mol

Following the general procedure **A** with benzyl bromide (302 mg of ethyl 4-benzyl-3-oxooct-6-enoate), the product was obtained as an orange liquid (359 mg, 1.08 mmol, 92%) upon purification by column chromatography (PE:EtOAc = 100:0 → 95:5).

TLC: R_f = 0.53 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.29 - 7.25 (m, 2H), 7.22 - 7.21 (m, 1H), 7.19 - 7.13 (m, 2H), 5.51 - 5.42 (m, 1H), 5.35 - 5.27 (m, 1H), 4.16 - 4.08 (m, 2H), 3.26 (d, *J* = 3.8 Hz, 1H), 2.99 - 2.88 (m, 2H), 2.72 (dd, *J* = 13.3, 6.1 Hz, 1H), 2.35 - 2.28 (m, 1H), 2.22 – 2.15 (m, 1H), 2.02 – 1.94 (m, 2H), 1.37 - 1.21 (m, 10H), 0.88 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.7, 167.0, 139.4, 134.4, 129.1, 128.7, 126.5, 125.9, 61.3, 54.2, 50.2, 37.1, 34.6, 32.6, 31.5, 29.2, 22.6, 14.21, 14.17; **IR** (ATR): ῡ [cm^{-1}] 3028, 2956, 2925, 2872, 1745, 1713, 1646, 1627, 1605, 1496, 1455, 1367, 1304, 1230, 1148, 1095, 1075, 1030, 970, 842, 802, 750, 736, 699, 497; **HRMS** (ESI): [m/z] calculated for [$C_{21}H_{30}O_3Na$] 353.2093, found 353.2087.

ethyl 2,2-diazido-3-oxododec-6-enoate (1m)

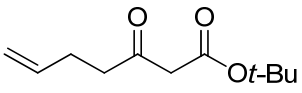


$C_{21}H_{28}N_6O_3$
412.49 g/mol

Following the general procedure **B** (1.369 g of ethyl 4-benzyl-3-oxododec-6-enoate, 0.1 M, 1 h), the product was obtained as a yellow liquid (1.329 g, 3.00 mmol, 73%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.54 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.30 – 7.26 (m, 2H), 7.22 – 7.18 (m, 1H), 7.16 – 7.13 (m, 2H), 5.51 – 5.44 (m, 1H), 5.33 – 5.25 (m, 1H), 4.23 – 4.07 (m, 2H), 3.33 – 3.27 (m, 1H), 2.97 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.70 (dd, *J* = 13.7, 6.7 Hz, 1H), 2.42 – 2.35 (m, 1H), 2.19 – 2.12 (m, 1H), 2.02 – 1.96 (m, 2H), 1.38 – 1.24 (m, 9H), 0.89 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 200.7, 164.1, 138.9, 134.8, 129.3, 128.6, 126.6, 125.3, 83.3, 64.2, 49.3, 37.0, 34.8, 32.7, 31.5, 29.1, 22.6, 14.2, 14.1; **IR** (ATR): ϑ [cm^{-1}] 2957, 2926, 2856, 2124, 1741, 1715, 1647, 1604, 1497, 1455, 1368, 1228, 1152, 1095, 1029, 970, 922, 852, 803, 746, 699, 545, 502.

***tert*-butyl 3-oxohept-6-enoate**



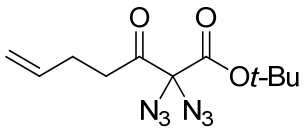
$C_{11}H_{18}O_3$
198.26 g/mol

Following the general procedure **A** with allyl bromide (3.37 mL of ethyl *tert*-butyl acetoacetate), the product was obtained as a yellowish liquid (3.101 g, 15.64 mmol, 77%) upon purification by column chromatography (PE:EtOAc = 100:0 → 90:10). The analytical data corresponds with the previously published data.[3]

TLC: R_f = 0.57 (PE:EtOAc / 95:5, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.77 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.00 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.95 (dq, *J* = 10.2, 1.6 Hz, 1H), 3.31 (s, 2H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.35 – 2.27 (m, 2H), 1.43 (s, 9H); **^{13}C-NMR** (101

MHz, $CDCl_3$): δ [ppm] 202.5, 166.4, 136.8, 115.5, 82.0, 50.7, 42.0, 28.0, 27.5; **IR** (ATR): ῡ [cm^{-1}] 3080, 2980, 2933, 1734, 1713, 1642, 1368, 1318, 1251, 1145, 1090, 914, 837; **HRMS** (ESI): [m/z] calculated for [$C_{11}H_{18}O_3Na$] 221.1148, found 221.1153.

***tert*-butyl 2,2-diazido-3-oxohept-6-enoate (1n)**

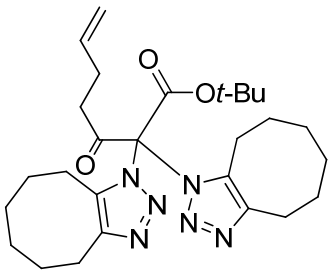


$C_{11}H_{16}N_6O_3$
280.28 g/mol

Following the general procedure **B** (1.500 g of *tert*-butyl 3-oxohept-6-enoate, 0.1 M, 1 h), the product was obtained as a yellowish liquid (1.236 g, 4.41 mmol, 58%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.87 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 5.78 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.06 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.2, 1.6 Hz, 1H), 2.64 (t, *J* = 7.2 Hz, 2H), 2.38 – 2.34 (m, 2H), 1.52 (s, 9H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 197.7, 163.1, 136.2, 116.1, 86.9, 83.4, 36.8, 27.9, 27.4; **IR** (ATR): ῡ [cm^{-1}] 3081, 2983, 2936, 2113, 1742, 1643, 1476, 1459, 1397, 1372, 1238, 1149, 1053, 995, 947, 918, 832, 750, 705, 621, 554, 467, 436.

***tert*-butyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate**

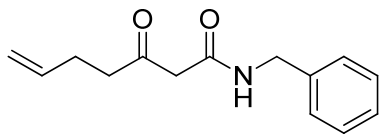


$C_{27}H_{40}N_6O_3$
496.64 g/mol

Following the general procedure **C** (15 mg of *tert*-butyl 2,2-diazido-3-oxohept-6-enoate, 16 h), the product was obtained as a yellow liquid (20 mg, 0.04 mmol, 65%) upon purification by column chromatography (CH:EtOAc = 90:10 → 75:25).

TLC: R_f = 0.20 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.89 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.10 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.03 (dq, *J* = 10.2, 1.4 Hz, 1H), 3.02 (d, *J* = 8.8 Hz, 2H), 2.88 (td, *J* = 6.1, 1.1 Hz, 4H), 2.63 (q, *J* = 7.3 Hz, 2H), 2.25 – 2.11 (m, *J* = 8.0 Hz, 4H), 1.78 – 1.69 (m, *J* = 7.4 Hz, 4H), 1.61 (s, 9H), 1.58 (s, 4H), 1.42 – 1.35 (m, 8H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 192.2, 160.2, 146.0, 136.8, 136.7, 115.8, 87.9, 86.8, 41.0, 29.7, 27.8, 27.7, 26.1, 25.8, 25.1, 24.5, 22.0; **HRMS** (ESI): [m/z] calculated for [$C_{27}H_{40}N_6O_3Na$] 519.3060, found 519.3054.

***N*-benzyl-3-oxohept-6-enamide**

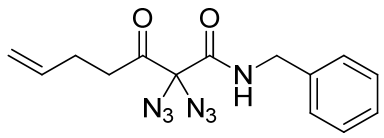


$C_{14}H_{17}NO_2$
231.29 g/mol

tert-Butyl 3-oxohept-6-enoate (1.000 g, 5.04 mmol) and *N*-benzylamide (606 µl, 5.55 mmol, 1.10 eq.) were dissolved in 12 mL xylene (mixture of isomers) in a microwave reaction vial and heated at 160 °C for 8 hours under microwave irradiation. The reaction mixture was washed with water, a 10% aqueous solution of citric acid, brine and then dried over magnesium sulfate. The solvent was removed *in vacuo* and the product obtained as a yellow solid (521 mg, 2.25 mmol, 45%) after column chromatography (CH:EtOAc = 90:10 → 65:35).

TLC: R_f = 0.23 (PE:EtOAc / 70:30, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.35 – 7.23 (m, 5H), 5.77 (ddt, *J* = 16.8, 10.2, 6.8 Hz, 1H), 5.06 – 5.00 (m, 1H), 5.00 – 4.97 (m, 1H), 4.44 (d, *J* = 5.8 Hz, 2H), 3.41 (s, 2H), 2.63 (t, *J* = 7.3 Hz, 2H), 2.35 – 2.29 (m, 2H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 206.1, 165.5, 138.0, 136.4, 128.8, 127.8, 127.6, 115.9, 49.1, 43.7, 43.0, 27.4; **IR** (ATR): ϑ [cm^{-1}] 3282, 3077, 3064, 3034, 2998, 2977, 2919, 1712, 1660, 1638, 1562, 1497, 1453, 1417, 1369, 1345, 1279, 1253, 1212, 1172, 1082, 1038, 1017, 997, 907, 857, 798, 729, 698, 636, 609, 566, 483, 464, 448; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{17}NO_2Na$] 254.1151, found 254.1150.

2,2-diazido-*N*-benzyl-3-oxohept-6-enoate (1o)

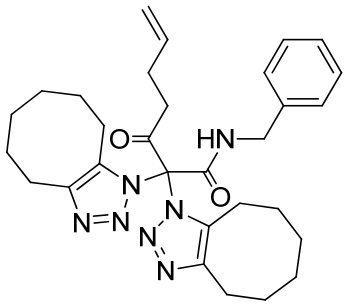


$C_{14}H_{15}N_7O_2$
313.31 g/mol

Following the general procedure **B** (472 mg of *N*-benzyl-3-oxohept-6-enamide, 0.1 M, 30 min), the product was obtained as a colorless liquid (401 mg, 1.28 mmol, 63%) upon purification by column chromatography (PE:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.56 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 7.38 – 7.34 (m, 2H), 7.34 – 7.30 (m, 1H), 7.27 – 7.24 (m, 2H), 6.87 – 6.82 (m, 1H), 5.76 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.04 (dq, *J* = 16.8, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.47 (d, *J* = 5.9 Hz, 2H), 2.78 (t, *J* = 7.2 Hz, 2H), 2.39 – 2.31 (m, 2H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 198.4, 163.0, 136.7, 136.1, 129.1, 128.2, 127.9, 116.1, 84.8, 44.3, 36.8, 27.4; **IR** (ATR): ῡ [cm^{-1}] 3338, 3079, 3033, 2980, 2929, 2110, 1736, 1674, 1642, 1517, 1455, 1435, 1401, 1359, 1226, 1110, 1080, 1047, 1029, 994, 956, 917, 789, 752, 726, 697, 640, 544, 495, 461.

***N*-benzyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enamide**

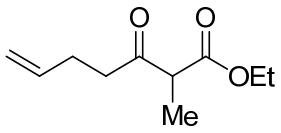


$C_{30}H_{39}N_7O_2$
529.68 g/mol

Following the general procedure **C** (50 mg of 2,2-diazido-*N*-benzyl-3-oxohept-6-enoate, 16 h), the product was obtained as a colorless (43 mg, 0.08 mmol, 51%) upon purification by column chromatography (CH:EtOAc = 90:10 → 80:20).

TLC: R_f = 0.29 (PE:EtOAc / 80:20, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 8.63 (t, *J* = 5.8 Hz, 1H), 7.33 (d, *J* = 4.4 Hz, 4H), 7.31 – 7.26 (m, 1H), 5.71 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.02 – 4.96 (m, 1H), 4.96 – 4.92 (m, 1H), 4.59 (d, *J* = 5.8 Hz, 2H), 2.98 (t, *J* = 7.4 Hz, 2H), 2.88 (t, *J* = 6.5 Hz, 4H), 2.43 – 2.35 (m, 2H), 2.25 – 2.06 (m, 4H), 1.78 – 1.67 (m, 4H), 1.44 – 1.22 (m, 12H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 194.4, 160.9, 146.2, 136.9, 136.7, 136.4, 129.0, 128.1, 128.0, 115.9, 87.8, 45.5, 38.9, 29.0, 27.9, 26.0, 25.8, 25.0, 24.5, 22.1; **IR** (ATR): ϑ̃ [cm^{-1}] 3228, 3065, 3031, 2925, 2854, 2123, 1739, 1702, 1642, 1517, 1455, 1440, 1371, 1355, 1309, 1253, 1145, 1081, 1047, 1028, 1000, 948, 908, 793, 753, 729, 699, 633, 493, 463, 411; **HRMS** (ESI): [m/z] calculated for [$C_{30}H_{39}N_7O_2Na$] 552.3057, found 552.3058.

ethyl 2-methyl-3-oxohept-6-enoate

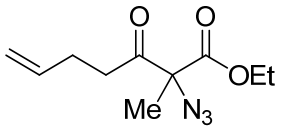


$C_{10}H_{16}O_3$
184.23 g/mol

Following the general procedure **A** with allyl bromide (811 mg of ethyl 2-methyl-3-oxobutanoate), the product was obtained as a yellow liquid (238 mg, 1.29 mmol, 39%) upon purification by column chromatography (PE:EtOAc = 90:10 → 88:12). The analytical data corresponds with the previously published data.[3]

TLC: R_f = 0.52 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.79 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.03 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.98 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.18 (qd, *J* = 7.1, 0.7 Hz, 2H), 3.51 (q, *J* = 7.1 Hz, 1H), 2.75 – 2.52 (m, 2H), 2.37 – 2.31 (m, 2H), 1.33 (d, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 205.1, 170.7, 136.9, 115.6, 61.5, 53.1, 40.6, 27.7, 14.2, 12.9; **IR** (ATR): ϑ̃ [cm^{-1}] 2983, 2941, 1740, 1714, 1642, 1451, 1407, 1375, 1322, 1239, 1191, 1118, 1069, 1035, 997, 913, 860, 635; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_{16}O_3Na$] 207.0997, found 207.0992.

ethyl 2-azido-3-methyl-3-oxohept-6-enoate (**3**)

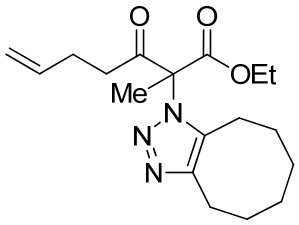


$C_{10}H_{15}N_3O_3$
225.24 g/mol

Following the general procedure **B** (207 mg of ethyl 2-methyl-3-oxohept-6-enoate, 2.3 eq. NaN_3, 2.0 eq. $NaHCO_3$, 1.2 eq. I_2, 1 h), the product was obtained as a yellow liquid (148 mg, 0.65 mmol, 58%) upon purification by column chromatography (PE:EtOAc = 100:0 → 96:4).

TLC: R_f = 0.63 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.78 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.04 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.99 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.28 (dq, *J* = 7.1, 2.2 Hz, 2H), 2.76 – 2.54 (m, 2H), 2.40 – 2.29 (m, 2H), 1.58 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 201.9, 168.6, 135.5, 116.0, 73.0, 63.0, 37.1, 27.6, 19.4, 14.2; **IR** (ATR): ῡ [cm^{-1}] 2980, 2936, 2874, 2112, 1742, 1719, 1640, 1505, 1472, 1447, 1388, 1368, 1318, 1224, 1156, 1128, 1095, 1071, 1038, 1017, 911, 851, 758, 648, 619, 553, 456.

ethyl-2-(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-2-methyl-3-oxohept-6-enoate



$C_{18}H_{27}N_3O_3$
333.43 g/mol

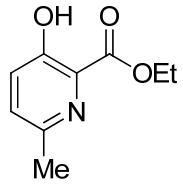
Following the general procedure **C** (22 mg ethyl 2-azido-3-methyl-3-oxohept-6-enoate, 1 h), the product was obtained as a yellow liquid (84 mg, 0.08 mmol, 85%) upon purification by column chromatography (PE:EtOAc = 50:50 → 25:75).

TLC: R_f = 0.21 (PE:EtOAc / 90:10, [CAM]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 5.77 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1H), 5.02 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.99 – 4.95 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.76 – 2.66 (m, 1H), 2.64 – 2.59 (m, 1H), 2.59 – 2.55 (m, 2H), 2.43 – 2.36 (m, 2H), 2.08 (s, 3H), 1.82 – 1.68 (m, 5H), 1.58 – 1.38 (m, 5H), 1.29 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 200.2, 167.9, 145.7, 136.6, 134.5, 115.9, 74.9, 63.1, 38.0, 28.1, 28.0, 26.7, 25.9, 25.2, 24.5, 23.1, 21.6, 14.0; **IR** (ATR): ῡ [cm^{-1}] 2930, 2856, 1730,

1642, 1445, 1375, 1253, 1197, 1128, 1093, 1038, 1001, 952, 915, 864, 794, 756, 732, 690, 639, 558, 526, 504, 450; **HRMS** (ESI): [m/z] calculated for [$C_{18}H_{28}N_3O_3$] 334.2131, found 334.2125.

Synthesis of the 3-hydroxypyridines

ethyl 3-hydroxy-6-methylpicolinate (**2a**)



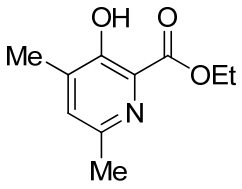
$C_9H_{11}NO_3$
181.18 g/mol

Method A: Following the general procedure **D** (200 mg of **1a**, 0.05 M, 2 h), the product was obtained as a yellow liquid (140 mg, 0.77 mmol, 97%) upon purification by column chromatography (CH:EtOAc = 90:10 → 70:30).

Method B: Ethyl 2,2-diazido-3-oxohept-6-enoate (5.050 g, 20.02 mmol) was dissolved in 400 mL xylene and stirred at 140 °C for two hours. The solvent was evaporated *in vacuo* and the product obtained as a yellow liquid (2.533 g, 13.98 mmol, 70%) after column chromatography (CH:EtOAc = 90:10 → 70:30).

TLC: R_f = 0.16 (PE:EtOAc / 70:30, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.68 (s, 1H), 7.28 (s, 2H), 4.55 (q, *J* = 7.1 Hz, 2H), 2.56 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 169.9, 157.3, 150.1, 129.9, 129.1, 126.7, 62.6, 24.0, 14.4; **IR** (ATR): ϑ [cm^{-1}] 3153, 2982, 2960, 2927, 2856, 1668, 1586, 1465, 1406, 1381, 1340, 1294, 1199, 1099, 1018, 923, 864, 834, 807, 718, 667, 558, 541, 488, 457, 440, 416; **HRMS** (ESI): [m/z] calculated for [$C_9H_{11}NO_3Na$] 204.0631, found 204.0632.

ethyl 3-hydroxy-4,6-methylpicolinate (**2b**)

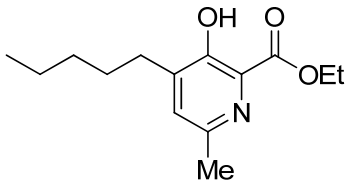


$C_{10}H_{13}NO_3$
195.22 g/mol

Following the general procedure **D** (199 mg of **1b**, 0.05 M, 2 h), the product was obtained as an orange liquid (69 mg, 0.35 mmol, 69%) upon purification by column chromatography (CH:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.28 (PE:EtOAc / 70:30, [UV]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.90 (s, 1H), 7.13 (s, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 3H), 2.27 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.3, 156.6, 149.4, 137.2, 130.7, 128.0, 62.6, 23.9, 15.5, 14.4; **IR** (ATR): ϑ [cm^{-1}] 3029, 2985, 2921, 1676, 1579, 1502, 1477, 1452, 1411, 1381, 1346, 1329, 1271, 1232, 1195, 1149, 1109, 1019, 967, 928, 864, 835, 804, 755, 724, 704, 591, 543, 498, 486, 453, 412; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_{14}NO_3$] 196.0974, found 196.0968.

ethyl 3-hydroxy-6-methyl-4-pentylpicolinate (**2c**)

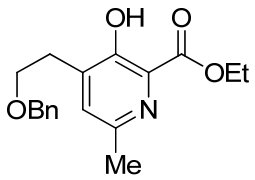


$C_{14}H_{21}NO_3$
251.32 g/mol

Following the general procedure **D** (98 mg of **1c**, 0.05 M, 2 h), the product was obtained as an orange liquid (39 mg, 0.15 mmol, 48%) upon purification by column chromatography (PE:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.12 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.92 (s, 1H), 7.12 (s, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.65 – 1.60 (m, 2H), 1.46 (t, *J* = 7.1 Hz, 3H), 1.40 – 1.29 (m, 6H), 0.91 (t, *J* = 6.7 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.4, 156.3, 149.5, 141.7, 129.6, 128.1, 62.6, 31.7, 29.3, 28.4, 24.0, 22.6, 14.4, 14.1; **IR** (ATR): ϑ [cm^{-1}] 3338, 2969, 2931, 2882, 1672, 1465, 1409, 1378, 1305, 1203, 1160, 1128, 1107, 950, 816, 638, 487, 423; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{22}NO_3$] 252.1600, found 252.1594.

ethyl (2-(benzyloxy)ethyl)-3-hydroxy-6-methylpicolinate (**2d**)

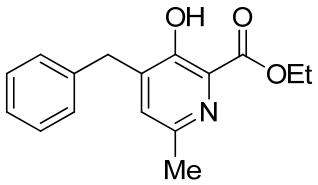


$C_{18}H_{21}NO_4$
315.36 g/mol

Following the general procedure **D** (99 mg of **1d**, 0.05 M, 2 h), the product was obtained as an orange liquid (39 mg, 0.12 mmol, 48%) upon purification by column chromatography (PE:EtOAc = 75:25 → 70:30).

TLC: R_f = 0.18 (PE:EtOAc / 90:10, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.93 (s, 1H), 7.33 – 7.25 (m, 4H), 7.28 (s, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 4.52 (s, 2H), 3.75 (t, *J* = 6.5 Hz, 2H), 2.97 (td, *J* = 6.5, 0.7 Hz, 2H), 2.50 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 4H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.3, 156.2, 149.4, 138.3, 137.8, 130.5, 128.5, 127.8, 127.7, 127.0, 73.1, 68.2, 62.6, 29.9, 24.0, 14.4; **IR** (ATR): ϑ [cm^{-1}] 3351, 3027, 2923, 2869, 2104, 1703, 1609, 1516, 1491, 1454, 1417, 1378, 1364, 1273, 1251, 1203, 1157, 1097, 1076, 1027, 1011, 897, 775, 739, 697, 607, 561, 541, 471, 439; **HRMS** (ESI): [m/z] calculated for [$C_{18}H_{22}NO_4$] 316.1549, found 316.1543.

ethyl 4-benzyl-3-hydroxy-6-methylpicolinate (**2e**)



$C_{16}H_{17}NO_3$
271.31 g/mol

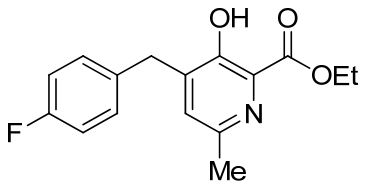
Method A: Following the general procedure **D** (198 mg of **1e**, 0.05 M, 2 h), the product was obtained as a yellow solid (137 mg, 0.52 mmol, 72%) upon purification by column chromatography (CH:EtOAc = 100:0 → 70:30).

Method B: Ethyl 4-benzyl-2,2-diazido-3-oxononanoate (2.444 g, 7.13 mmol) was dissolved in 140 mL xylene and stirred at 140 °C for two hours. The solvent was evaporated *in vacuo*

and the product obtained as a yellow solid (951 mg, 3.505 mmol, 53%) after column chromatography (CH:EtOAc = 100:0 → 70:30).

TLC: R_f = 0.28 (PE:EtOAc / 70:30, [UV]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 11.02 (s, 1H), 7.35 – 7.29 (m, 2H), 7.25 – 7.21 (m, 3H), 7.00 (s, 1H), 4.53 (q, *J* = 7.1 Hz, 2H), 4.00 (s, 2H), 2.47 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.3, 155.9, 149.7, 140.0, 138.6, 129.9, 129.3, 128.8, 128.5, 126.7, 62.6, 35.1, 24.1, 14.4; **IR** (ATR): ῡ [cm^{-1}] 3029, 2985, 2921, 1676, 1579, 1502, 1477, 1452, 1411, 1381, 1346, 1329, 1271, 1232, 1195, 1149, 1109, 1019, 967, 928, 864, 835, 804, 755, 724, 704, 591, 543, 498, 486, 453, 412; **HRMS** (ESI): [m/z] calculated for [$C_{16}H_{18}NO_3$] 272.1281, found 272.1279.

ethyl 4-(4-fluorobenzyl)-3-hydroxy-6-methylpicolinate (2f)

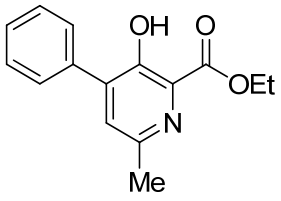


$C_{16}H_{16}FNO_3$
289.30 g/mol

Following the general procedure **D** (300 mg of **1f**, 0.05 M, 2 h), the product was obtained as an orange liquid (163 mg, 0.56 mmol, 68%) upon purification by column chromatography (PE:EtOAc = 100:0 → 70:30).

TLC: R_f = 0.63 (PE:EtOAc / 70:30, [UV, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 11.04 (s, 1H), 7.24 – 7.20 (m, 2H), 7.04 – 6.99 (m, 3H), 4.55 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 2H), 2.50 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.3, 163.0, 160.6, 155.8, 149.7, 139.8, 134.22, 134.19, 130.73, 130.65, 129.7, 128.6, 116.7, 115.5, 62.7 34.3, 24.0, 14.4; **IR** (ATR): ῡ [cm^{-1}] 3074, 2985, 2914, 1675, 1616, 1601, 1579, 1513, 1477, 1454, 1410, 1381, 1345, 1329, 1272, 1223, 1195, 1162, 1149, 1109, 1012, 965, 933, 859, 845, 829, 805, 780, 760, 724, 696, 623, 587, 518, 486, 455, 416; **HRMS** (ESI): [m/z] calculated for [$C_{16}H_{17}FNO_3$] 290.1192, found 290.1187.

ethyl 3-hydroxy-6-methyl-phenylpicolinate (2g)

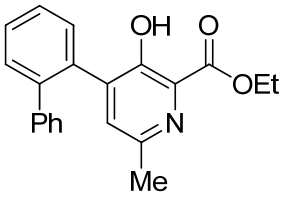


$C_{15}H_{15}NO_3$
257.28 g/mol

Following the general procedure **D** (252 mg of **1g**, 0.05 M, 2 h), the product was obtained as a yellow liquid (122 mg, 0.47 mmol, 62%) upon purification by column chromatography (CH:EtOAc = 90:0 → 70:30).

TLC: R_f = 0.32 (PE:EtOAc / 70:30, [UV]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 11.25 (s, 1H), 7.64 – 7.61 (m, 2H), 7.48 – 7.39 (m, 3H), 7.32 (s, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 2.58 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.3, 154.9, 149.8, 139.0, 135.0, 129.7, 129.5, 129.3, 128.8, 128.5, 62.7, 24.0, 14.4; **IR** (ATR): ῡ [cm^{-1}] 3058, 2981, 2929, 2105, 1738, 1663, 1564, 1455, 1432, 1407, 1379, 1342, 1272, 1250, 1187, 1087, 1018, 949, 892, 873, 811, 737, 695, 642, 612, 538, 495, 477, 455; **HRMS** (ESI): [m/z] calculated for [$C_{15}H_{16}NO_3$] 258.1125, found 258.1127.

ethyl 4-([1,1'-biphenyl]-2-yl)-3-hydroxy-6-methylpicolinate (2h)



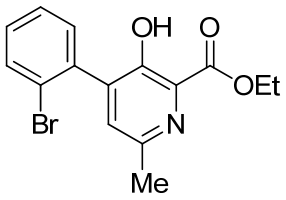
$C_{21}H_{19}NO_3$
333.38 g/mol

Following the general procedure **D** (262 mg of **1h**, 0.05 M, 2 h), the product was obtained as a yellow liquid (176 mg, 0.52 mmol, 81%) upon purification by column chromatography (CH:EtOAc = 90:0 → 70:30).

TLC: R_f = 0.22 (PE:EtOAc / 80:20, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.84 (s, 1H), 7.49 – 7.46 (m, 2H), 7.44 – 7.39 (m, 2H), 7.21 – 7.17 (m, 3H), 7.17 – 7.14 (m, 2H), 6.96 (s, 1H), 4.51 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H)**; ^{13}C-NMR**

(101 MHz, $CDCl_3$): δ [ppm] 170.1, 155.2, 149.2, 141.7, 141.0, 140.0, 133.6, 131.4, 130.43, 130.41, 129.3, 129.0, 128.9, 128.1, 127.2, 127.0, 62.7, 23.9, 14.4**; IR** (ATR): ϑ [cm^{-1}] 3057, 3023, 2981, 2929, 2104, 1664, 1571, 1432, 1406, 1379, 1344, 1274, 1187, 1084, 1018, 1009, 744, 699, 642, 612**; HRMS (ESI):** [m/z] calculated for [$C_{21}H_{20}NO_3$] 334.1443, found 334.1438.

ethyl 4-(2-bromophenyl)-3-hydroxy-6-methylpicolinate (2i)

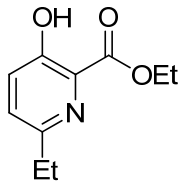


$C_{15}H_{14}BrNO_3$
336.18 g/mol

Following the general procedure **D** (400 mg of **1i**, 0.05 M, 2 h), the product was obtained as a yellow liquid (255 mg, 0.76 mmol, 77%) upon purification by column chromatography (CH:EtOAc = 100:0 → 75:25).

TLC: Rf = 0.24 (PE:EtOAc / 80:20, [UV, KmnO4]); **^{1}H-NMR** (400 MHz, CDCl3): δ [ppm] 11.00 (s, 1H), 7.70 - 7.67 (m, 1H), 7.41 - 7.37 (m, 1H), 7.30 - 7.26 (m, 2H), 7.21 (s, 1H), 4.56 (q, *J* = 7.1 Hz, 2H), 2.59 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H)**; ^{13}C-NMR** (101 MHz, CDCl3): δ [ppm] 170.1, 154.8, 149.5, 139.0, 136.3, 133.1, 131.0, 130.6, 130.1, 129.5, 17.4, 123.1, 62.8, 24.0, 14.4**; IR** (ATR): ϑ [cm^{-1}] 6056, 2981, 2931, 2861, 1665, 1572, 1445, 1406, 1379, 1344, 1277, 1187, 1096, 1017, 910, 811, 724, 634, 613, 493, 455, 441, 417**; HRMS (ESI):** [m/z] calculated for [C15H15NO3Br] 336.0230, found 336.0231.

ethyl 6-ethyl-3-hydroxypicolinate (2j)

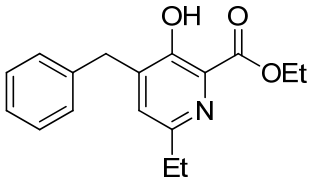


$C_{10}H_{13}NO_3$
195.22 g/mol

Following the general procedure **D** (200 mg of **1j**, 0.05 M, 2 h), the product was obtained as a yellow liquid (26 mg, 0.13 mmol, 18%) upon purification by column chromatography (CH:EtOAc = 90:10 → 84:16).

TLC: R_f = 0.35 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.68 (s, 1H), 7.31 – 7.29 (m, 2H), 4.53 (q, *J* = 7.1 Hz, 2H), 2.83 (q, *J* = 7.6 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.6 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.0, 157.3, 155.3, 129.1, 128.5, 126.8, 62.6, 30.8, 14.4, 14.2; **IR** (ATR): ῡ [cm^{-1}] 3194, 2971, 2934, 2874, 1719, 1669, 1589, 1468, 1411, 1379, 1343, 1297, 1255, 1195, 1099, 1016, 843, 808, 738, 700, 665, 594, 542, 500, 457, 440, 417; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_{14}NO_3$] 196.0968, found 196.0963.

ethyl 4-benzyl-6-ethyl-3-hydroxypicolinate (2k)

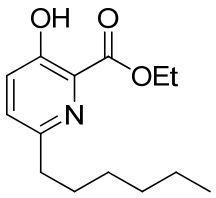


$C_{17}H_{19}NO_3$
285.34 g/mol

Following the general procedure **D** (250 mg of **1k**, 0.05 M, 2 h), the product was obtained as a yellow liquid (88 mg, 0.31 mmol, 44%) upon purification by column chromatography (CH:EtOAc = 90:10 → 84:16).

TLC: R_f = 0.40 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 11.02 (s, 1H), 7.34 – 7.29 (m, 2H), 7.26 – 7.22 (m, 3H), 7.05 (s, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 2H), 2.75 (q, *J* = 7.6 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.6 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.4, 156.0, 154.9, 139.9, 138.6, 129.2, 128.7, 128.6, 128.5, 126.7, 62.5, 35.2, 30.9, 14.4, 14.3; **IR** (ATR): ῡ [cm^{-1}] 3087, 3062, 3028, 2969, 2934, 2873, 1748, 1665, 1602, 1577, 1495, 1464, 1412, 1379, 1348, 1317, 1273, 1196, 1147, 1095, 1068, 1021, 925, 863, 807, 738, 698, 588, 555, 510, 488, 450, 417; **HRMS** (ESI): [m/z] calculated for [$C_{17}H_{20}NO_3$] 286.1438, found 286.1443.

ethyl 6-hexyl-3-hydroxypicolinate (2l)

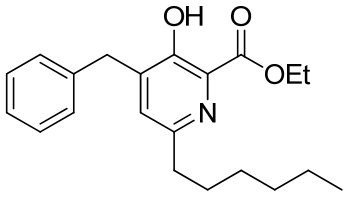


$C_{14}H_{21}NO_3$
251.32 g/mol

Following the general procedure **D** (335 mg of ethyl **1l**, 0.05 M, 2 h), the product was obtained as an orange liquid (87 mg, 0.35 mmol, 33%) upon purification by column chromatography (CH:EtOAc = 90:10 → 80:20).

TLC: R_f = 0.39 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.67 (s, 1H), 7.25 (s, 2H), 4.53 - 4.48 (q, *J* = 7.1 Hz, 2H), 2.78 - 2.74 (m, 2H), 1.70 - 1.62 (m, 2H), 1.46 - 1.43 (t, *J* = 7.1 Hz, 3H), 1.34 - 1.27 (m, 6H), 0.87 - 0.84 (m, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.0, 157.3, 154.3, 129.1, 129.0, 126.5, 62.5, 37.7, 31.8, 30.0, 29.1, 22.7, 14.3, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3157, 3257, 2928, 2857, 1672, 1467, 1203, 1100, 905, 726; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{22}NO_3$] 252.1600, found 252.1594.

ethyl 4-benzyl-6-hexyl-3-hydroxypicolinate (2m)



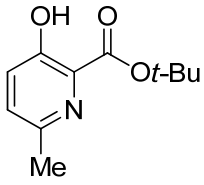
$C_{21}H_{27}NO_3$
341.44 g/mol

Following the general procedure **D** (400 mg of **1m**, 0.05 M, 2 h), the product was obtained as a yellow solid (166 mg, 0.49 mmol, 50%) upon purification by column chromatography (CH:EtOAc = 100:0 → 85:15).

TLC: R_f = 0.37 (PE:EtOAc / 90:10, [UV, $KmnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 11.03 (s, 1H), 7.33 - 7.29 (m, 2H), 7.25 - 7.22 (m, 3H), 7.03 (s, 1H), 4.55 - 4.50 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 2.73 - 2.69 (m, 2H), 1.67 - 1.61 (m, 2H), 1.48 - 1.44 (t, *J* = 7.1 HZ, 3H), 1.34 - 1.26 (m ,6H), 0.89 - 0.86 (m, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 170.4,

156.0, 153.8, 139.7, 138.6, 129.2, 129.1, 128.7, 128.6, 126.6, 62.5, 37.8, 35.2, 31.8, 30.1, 29.1, 22.7, 14.4, 14.2; **IR** (ATR): ϑ [cm^{-1}] 2955, 2924, 2855, 2100, 1738, 1713, 1495, 1454, 1376, 1232, 1157, 1115, 1097, 1030, 969, 737, 698**; HRMS (ESI):** [m/z] calculated for [$C_{21}H_{28}NO_3$] 342.2069, found 342.2064.

***tert*-butyl 3-hydroxy-6-methylpicolinate (2n)**

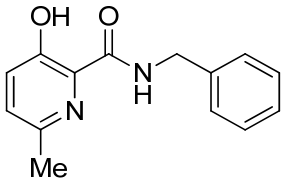


$C_{11}H_{15}NO_3$
209.24 g/mol

Following the general procedure **D** (250 mg of **1n**, 0.05 M, 1 h), the product was obtained as a pale yellow liquid (92 mg, 0.44 mmol, 49%) upon purification by column chromatography (CH:EtOAc = 90:10 → 75:25).

TLC: R_f = 0.57 (PE:EtOAc / 80:20, [UV]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 10.79 (s, 1H), 7.20 (s, 2H), 2.50 (s, 3H), 1.66 (s, 9H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 169.3, 157.1, 149.7, 130.2, 129.3, 126.5, 84.1, 28.2, 23.9; **IR** (ATR): ϑ [cm^{-1}] 3149, 3117, 2981, 2931, 1663, 1585, 1465, 1394, 1366, 1296, 1279, 1217, 1149, 1099, 1036, 1004, 927, 843, 810, 776, 741, 718, 667, 558, 535, 491, 473, 445, 415; **HRMS** (ESI): [m/z] calculated for [$C_{11}H_{15}NO_3Na$] 232.0944, found 232.0942.

***N*-benzyl 3-hydroxy-6-methylpicolinate (2o)**

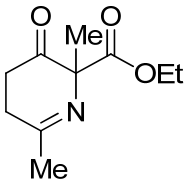


$C_{14}H_{14}N_2O_2$
242.27 g/mol

Following the general procedure **D** (58 mg of **1o**, 0.05 M, 6 h), the product was obtained as a yellow solid (18 mg, 0.07 mmol, 40%) upon purification by column chromatography (CH:EtOAc = 100:0 → 90:10).

TLC: R_f = 0.52 (PE:EtOAc / 90:10, [366 nm, $KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 11.93 (s, 1H), 8.39 (sb, 1H), 7.39 – 7.35 (m, 4H), 7.34 – 7.29 (m, 1H), 7.22 (d, *J* = 8.6 Hz, 1H), 7.18 (d, *J* = 8.6 Hz, 1H), 4.65 (d, *J* = 6.3 Hz, 2H), 2.43 (s, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 169.0, 155.9, 148.2, 137.9, 130.1, 128.94, 128.85, 127.9, 127.8, 126.7, 43.0, 23.4; **IR** (ATR): ῡ [cm^{-1}] 3314, 2951, 2922, 2852, 1639, 1585, 1496, 1467, 1429, 1396, 1358, 1316, 1306, 1278, 1237, 1199, 1179, 1140, 1116, 1077, 1031, 1008, 970, 898, 815, 793, 766, 741, 694, 664, 603, 544, 477, 456, 436; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{15}N_2O_2$] 243.1128, found 243.1127.

ethyl 2,6-dimethyl-3-oxo-2,3,4,5-tetrahydropyridin-2-carboxylate (4)



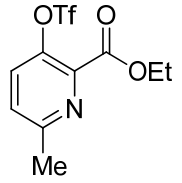
$C_{10}H_{15}NO_3$
197.23 g/mol

Following the general procedure **D** (80 mg of **3**, 0.05 M, 2 h), the product was obtained as a brown liquid (12 mg, 0.06 mmol, 18%) upon purification by column chromatography (CH:EtOAc = 100:0 → 80:20). Compound **4** was characterized using IR- and NMR-techniques. Due to the presumably highly unstable nature of this entity, acquisition of high resolution mass analytical data was rendered challenging and the structure assignment based on the spectroscopic data at hand.

TLC: R_f = 0.13 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 4.20 - 4.14 (m, 2H), 2.88 – 2.80 (m, 1H), 2.75 – 2.67 (m, 1H), 2.65 – 2.58 (m, 1H), 2.47 – 2.39 (m, 1H), 2.17 (s, 3H), 1.58 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 207.4, 171.1, 169.4, 72.1, 62.1, 32.9, 31.8, 27.6, 22.5, 14.1; **IR** (ATR): ῡ [cm^{-1}] 3306, 2982, 2936, 1719, 1663, 1584, 1523, 1444, 1368, 1232, 1105, 1015, 858, 767.

Modifications of 3-hydroxypyridines

ethyl 6-methyl-3-(((trifluoromethyl)sulfonyl)oxy)picolinate (5)

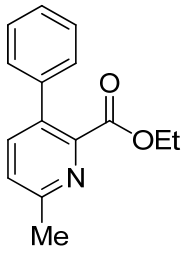


$C_{10}H_{10}F_3NO_5S$
313.25 g/mol

2a (266 mg, 1.47) and triethylamine (407 µl, 2.94 mmol, 2.0 eq.) were dissolved in 15 mL dry dichloromethane under a nitrogen atmosphere and cooled to 0 °C. Triflic anhydride (493 µL, 2.94 mmol, 2.0 eq.) was slowly added to the cooled solution and the reaction mixture stirred for one hour at 0 °C. The reaction was stopped by addition of an aqueous solution of sodium bicarbonate. The solution was stirred until the evolution of gas bubbles has stopped and afterwards extracted with dichloromethane. The combined organic phases were washed with a saturated aqueous solution of sodium bicarbonate, brine and dried over magnesium sulfate. The solvent was evaporated *in vacuo* and the product obtained after column chromatography (CH:EtOAc = 100:0 → 85:15) as a pale yellow liquid (378 mg, 1.21 mmol, 82%).

TLC: R_f = 0.19 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.56 (d, *J* = 8.6 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 4.50 (q, *J* = 7.1 Hz, 2H), 2.66 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 163.0, 159.1, 144.2, 141.7, 131.1, 127.6, 118.7 (q, *J* = 320.7 Hz, 1C), 62.9, 24.2, 14.1; **IR** (ATR): ϑ [cm^{-1}] 3081, 2987, 2942, 1730, 1587, 1457, 1426, 1386, 1305, 1251, 1205, 1135, 1073, 1020, 925, 871, 800, 771, 723, 700, 661, 646, 617, 582, 505, 456; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_{10}NO_5SF_3Na$] 336.0124, found 336.0116.

ethyl 6-methyl-3-phenylpicolinate (**6**)

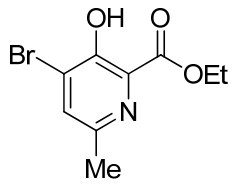


$C_{15}H_{15}NO_2$
241.29 g/mol

Tris(dibenzylidene)dipalladium(0) (15 mg, 0.02 mmol, 5 mol%) was dissolved in 3 mL 1,4-dioxane in a microwave vial and the solution rapidly stirred while a steam of nitrogen was passed through the solution. Triphenylphosphine (17 mg, 0.06 mmol, 20 mol%) was added and the solution was stirred for 15 minutes. Afterwards, caesium carbonate (312 mg, 0.96 mmol, 3.0 eq.), **5** (100 mg, 0.32 mmol) and phenylboronic acid (55 mg, 0.45 mmol, 1.40 eq.) were added successively. The microwave vial was sealed and the reaction mixture was stirred at 100 °C for four hours under microwave irradiation. After the reaction has reached completion, the organic phase was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered over Celite® and the solvent was evaporated *in vacuo*. The product was obtained after column chromatography (CH:EtOAc = 100:0 → 90:10) as a colorless liquid (74 mg, 0.31 mmol, 96%).

TLC: R_f = 0.24 (PE:EtOAc / 90:10, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.62 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.35 (m, 3H), 7.34 – 7.30 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.63 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 167.5, 157.4, 148.9, 138.4, 134.0, 128.5, 128.4, 127.9, 124.8, 61.6, 24.2, 13.7; **IR** (ATR): ῦ [cm^{-1}] 3081, 2987, 2942, 1730, 1587, 1457, 1426, 1386, 1305, 1251, 1205, 1135, 1073, 1020, 925, 871, 800, 771, 723, 700, 661, 646, 617, 582, 505, 456; **HRMS** (ESI): [m/z] calculated for [$C_{15}H_{15}NO_2Na$] 264.0995, found 264.0992.

ethyl 4-bromo-3-hydroxy-6-methylpicolinate (**7**)

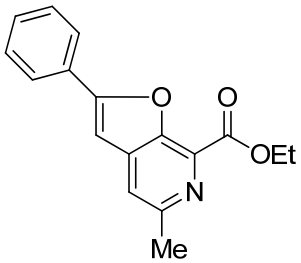


$C_9H_{10}BrNO_3$
260.08 g/mol

2a (441 mg, 2.43 mmol) and *N*-bromosuccinimide (476 mg, 2.68 mmol, 1.10 eq.) were dissolved in 10 mL acetonitrile and stirred under reflux for three hours. The reaction was stopped by addition of a saturated aqueous solution of sodium thiosulfate and the aqueous layer extracted with ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate and the solvent was concentrated *in vacuo*. The product was obtained after column chromatography (CH:EtOAc = 100:0 80:20) as a white solid (485 mg, 1.86 mmol, 77%).

TLC: R_f = 0.50 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 11.32 (s, 1H), 7.56 (s, 1H), 4.54 (q, *J* = 7.1 Hz, 2H), 2.52 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 169.6, 154.6, 150.2, 133.1, 129.7, 122.7, 63.2, 23.6, 14.3; **IR** (ATR): ῡ [cm^{-1}] 3073, 2989, 2920, 2856, 1652, 1571, 1470, 1439, 1412, 1380, 1339, 1281, 1203, 1015, 947, 890, 866, 802, 785, 745, 726, 595, 490, 454, 419; **HRMS** (ESI): [m/z] calculated for [$C_9H_{11}NO_3Br$] 259.9917, found 259.9918.

ethyl 5-methyl-2-phenylfuro[2,3-*c*]pyridine-7-carboxylate (**8a**)



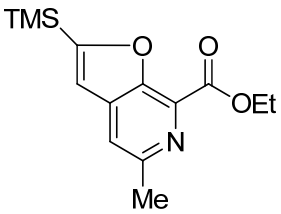
$C_{17}H_{15}NO_3$
281.31 g/mol

Tris(dibenzylideneacetone)dipalladium(0) (18 mg, 0.02 mmol, 5 mol%) was dissolved in 3 mL dry acetonitrile in a microwave vial and the mixutre vigorously stirred while a constant

steam of nitrogen was passed through the solution. Triphenylphosphine (20 mg, 0.08 mmol, 20 mol%) was added and the resulting solution was stirred for 15 minutes. **7** (100 mg, 0.38 mmol) was added, followed by phenylacetylene (51 µL, 0.46 mmol, 1.20 eq.) and copper(I) iodide (7 mg, 0.04 mmol, 10 mol%). The microwave vial was sealed and then stirred at 70 °C under microwave irradiation for twelve hours. After the reaction has reached completion, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic phases were washed with brine, dried over magnesium sulfate and filtered over a pad of Celite®. The solvent was removed *in vacuo* and the product was obtained after column chromatography (CH:EtOAc = 90:10 → 60:40) as a yellow solid (92 mg, 0.33 mmol, 85%).

TLC: R_f = 0.31 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.97 - 7.94 (m, 2H), 7.52 (s, 1H), 7.51 - 7.42 (m, 3H), 7.00 (s, 1H), 4.60 (q, *J* = 7.1 Hz, 2H), 2.72 (s, 3H), 1.54 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 164.1, 160.3, 151.5, 150.5, 139.3, 131.3, 130.3, 129.2, 129.1, 126.1, 118.6, 99.7, 62.0, 24.5, 14.6; **IR** (ATR): ῡ [cm^{-1}] 3112, 3058, 2976, 2920, 2866, 1725, 1599, 1489, 1471, 1426, 1391, 1364, 1260, 1117, 1037, 949, 925, 864, 828, 797, 759, 690, 655, 625, 550, 509, 486, 456; **HRMS** (ESI): [m/z] calculated for [$C_{17}H_{16}NO_3$] 282.1125, found 282.1124.

ethyl 5-methyl-2-(trimethylsilyl)furo[2,3-*c*]pyridine-7-carboxylate (**8b**)



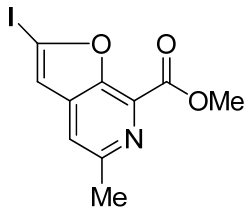
$C_{14}H_{19}NO_3Si$
277.39 g/mol

Tris(dibenzylideneacetone)dipalladium(0) (149 mg, 0.16 mmol, 5 mol%).was dissolved in 12 mL dry acetonitrile in a microwave vial and the mixture was vigorously stirred while a constant steam of nitrogen was passed through the solution. Triphenylphosphine (166 mg, 0.63 mmol, 20 mol%) was added and the resulting solution stirred for 15 minutes. **7** (822 mg, 3.16 mmol) was added, followed by trimethylsilylacetylene (542 µl, 3.79 mmol, 1.20 eq.) and copper(I) iodide (60 mg, 0.32 mmol, 10 mol%). The microwave vial was sealed and the reaction mixture was stirred at 100 °C under microwave irradiation for twelve hours. After the reaction has reached completion, the reaction mixture was filtered through a pad of Celite®,

diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine and dried over magnesium sulfate. The solvent was removed *in vacuo* and the product was obtained after column chromatography (CH:EtOAc = 90:10 → 60:40) as a yellow solid (490 mg, 1.77 mmol, 56%).

TLC: R_f = 0.18 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] 7.49 (s, 1H), 6.90 (s, 1H), 4.53 (q, *J* = 7.1 Hz, 2H), 2.68 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H), 0.37 (s, 9H); **^{13}C-NMR** (101 MHz, $CDCl_3$): δ [ppm] 169.6, 164.2, 153.4, 150.6, 138.2, 131.4, 118.8, 114.4, 61.7, 24.2, 14.4, -1.9; **IR** (ATR): ῡ [cm^{-1}] 2959, 2932, 2903, 1725, 1602, 1525, 1421, 1380, 1337, 1247, 1212, 1190, 1130, 1066, 1038, 911, 839, 799, 757, 702, 632, 542, 514, 484; **HRMS** (ESI): [m/z] calculated for [$C_{14}H_{20}NO_3Si$] 278.1207, found 278.1208.

methyl 2-iodo-5-methylfuro[2,3-*c*]pyridine-7-carboxylate (**9**)



$C_{10}H_8INO_3$
317.08 g/mol

8b (100 mg, 0.36 mmol) was dissolved in 2 mL dry methanol. *N*-Iodosuccinimide (162 mg, 0.72 mmol, 2.0 eq.) and potassium fluoride (42 mg, 0.72 mmol, 2.0 eq.) were added to the solution and the reaction mixture was stirred at 60 °C for 16 hours. The reaction was stopped by the addition of a saturated aqueous solution of sodium thiosulfate and the aqueous phase extracted with dichloromethane. The combined organic phases were washed with brine, dried over magnesium sulfate and the solvent was evaporated *in vacuo*. The product was obtained after column chromatography (CH:EtOAc = 100:0 → 70:30) as a pale yellow solid (90 mg, 0.28 mmol, 79%).

TLC: R_f = 0.14 (PE:EtOAc / 80:20, [$KMnO_4$]); **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] 7.48 (s, 1H), 6.99 (s, 1H), 4.07 (s, 3H), 2.70 (s, 3H); **^{13}C-NMR** (151 MHz, $CDCl_3$): δ [ppm] 164.0, 153.9, 151.8, 138.9, 130.5, 117.5, 116.5, 104.1, 53.1, 24.4; **IR** (ATR): ῡ [cm^{-1}] 3122, 29952, 1922, 2851, 1724, 1596, 1513, 1435, 1419, 1378, 1343, 1246, 1219, 1177, 1131, 1048, 1030,

995, 901, 877, 808, 795, 774, 739, 651, 629, 552, 503, 486; **HRMS** (ESI): [m/z] calculated for [$C_{10}H_9NO_3I$] 317.9622, found 317.9633

Literature

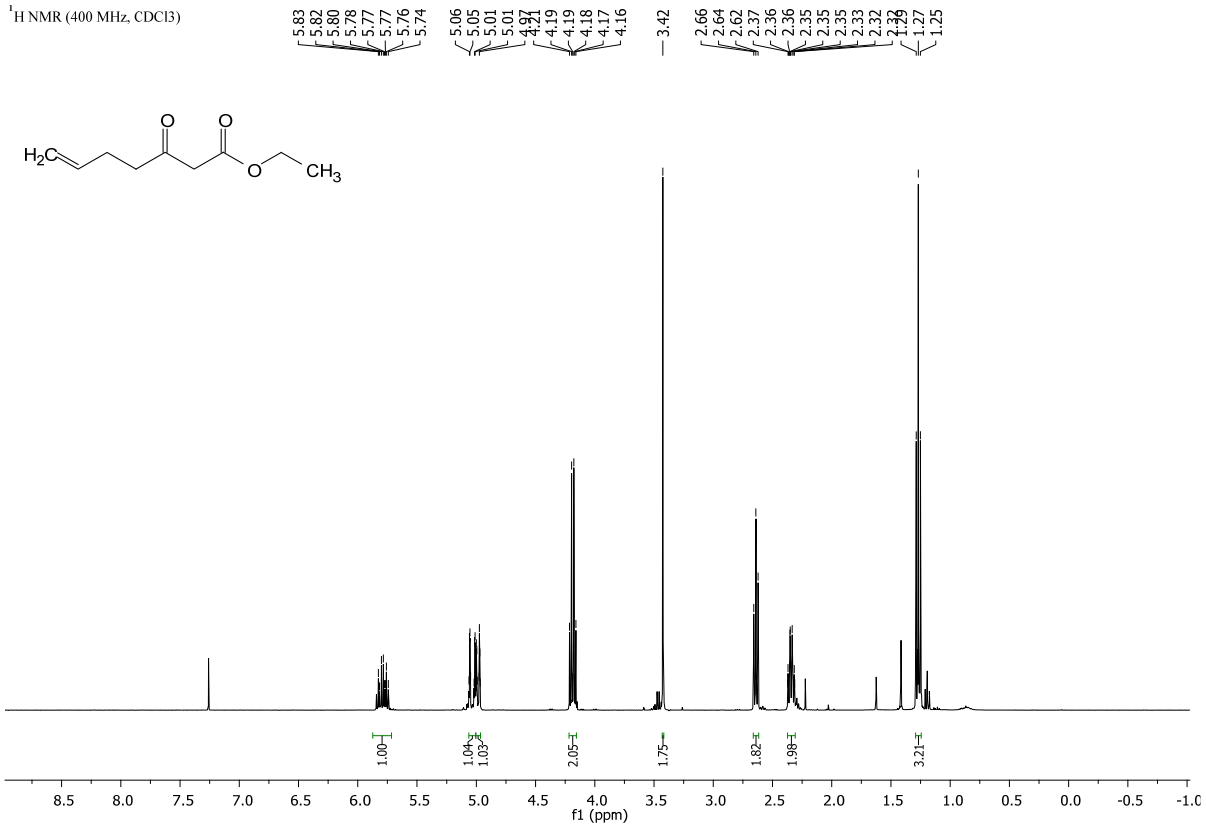
[1] Bargiggia, F. C.; Murray, W. V. *J. Org. Chem.* **2005**, *70*, 9636.

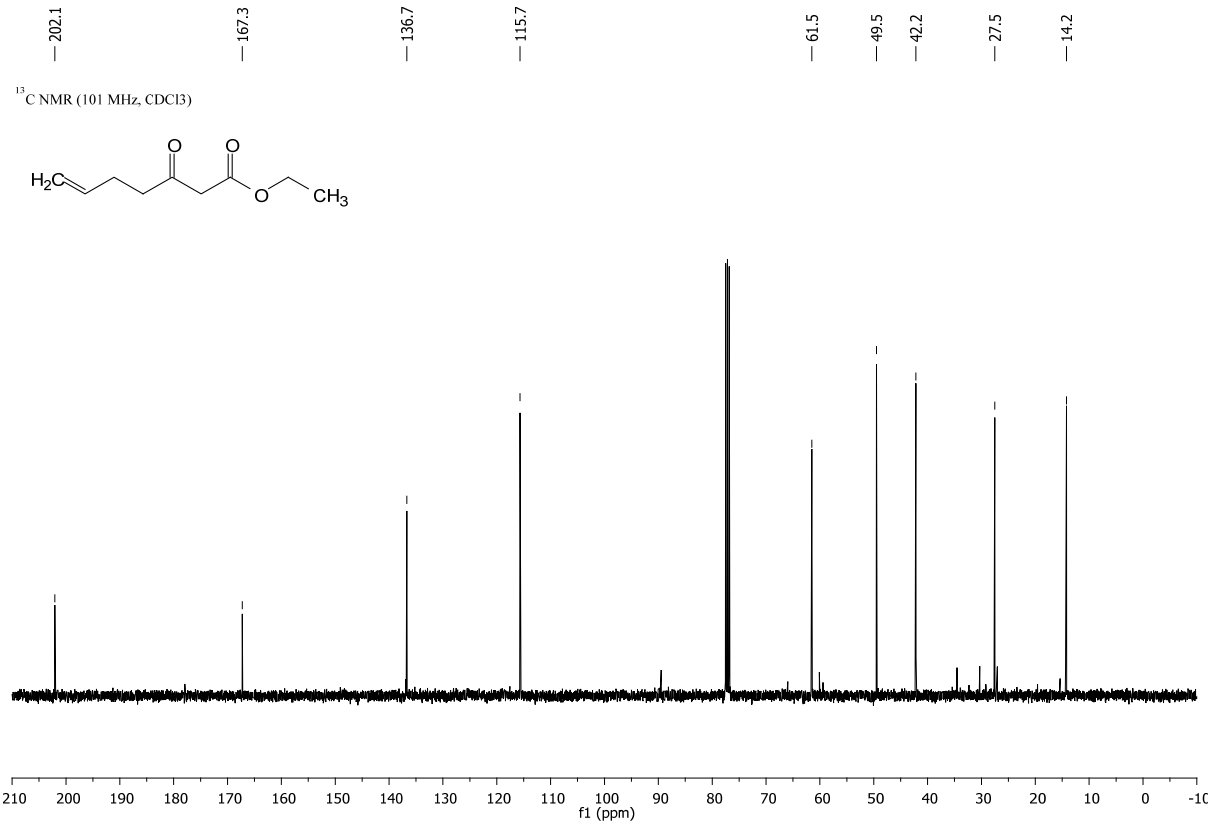
[2] Therkelsen, F. D.; Hansen, A.-L. L.; Pedersen, E. B.; Nielsen, C. *Org. Biomol. Chem.* **2003**, *1*, 2908.

[3] Graalfs, H.; Fröhlich, R.; Wolff, C.; Mattay, J. *Eur. J. Org. Chem.* **1999**, 1057.

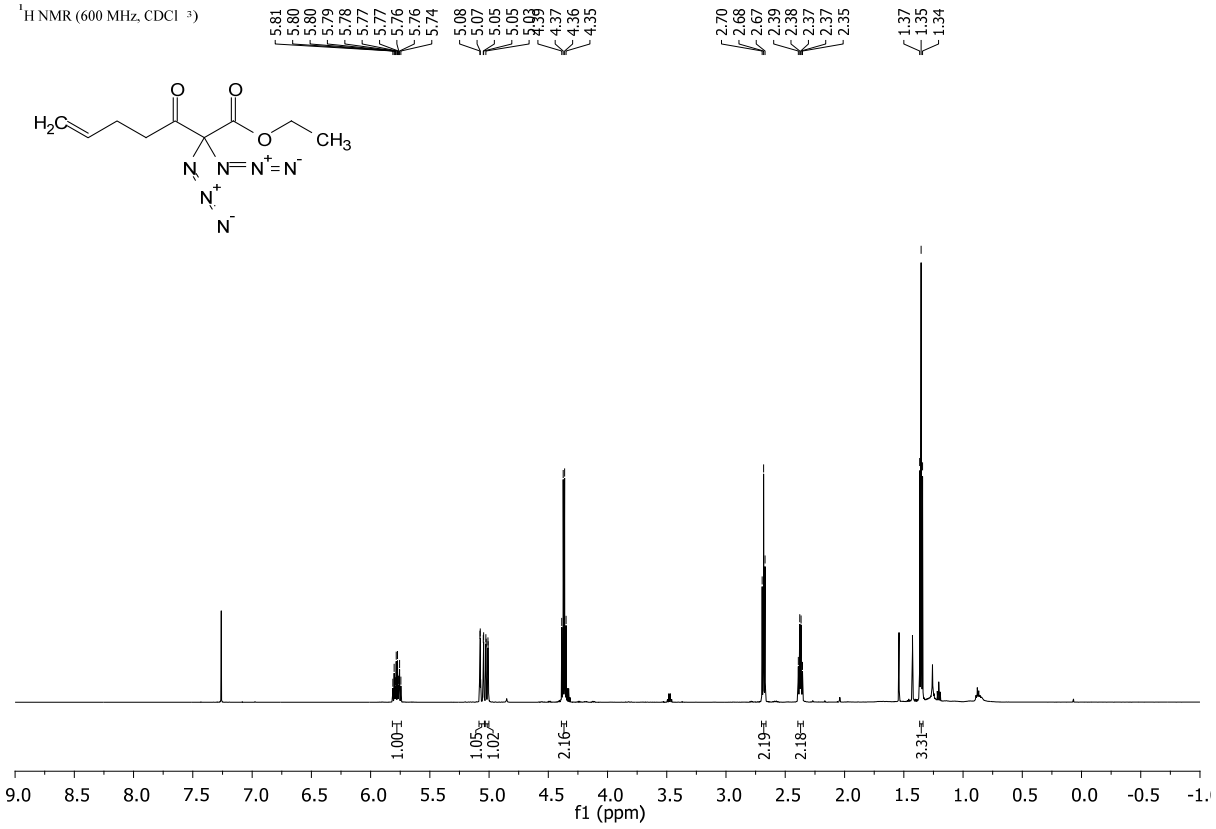
Spectra (^{1}H-NMR, ^{13}C-NMR, IR)

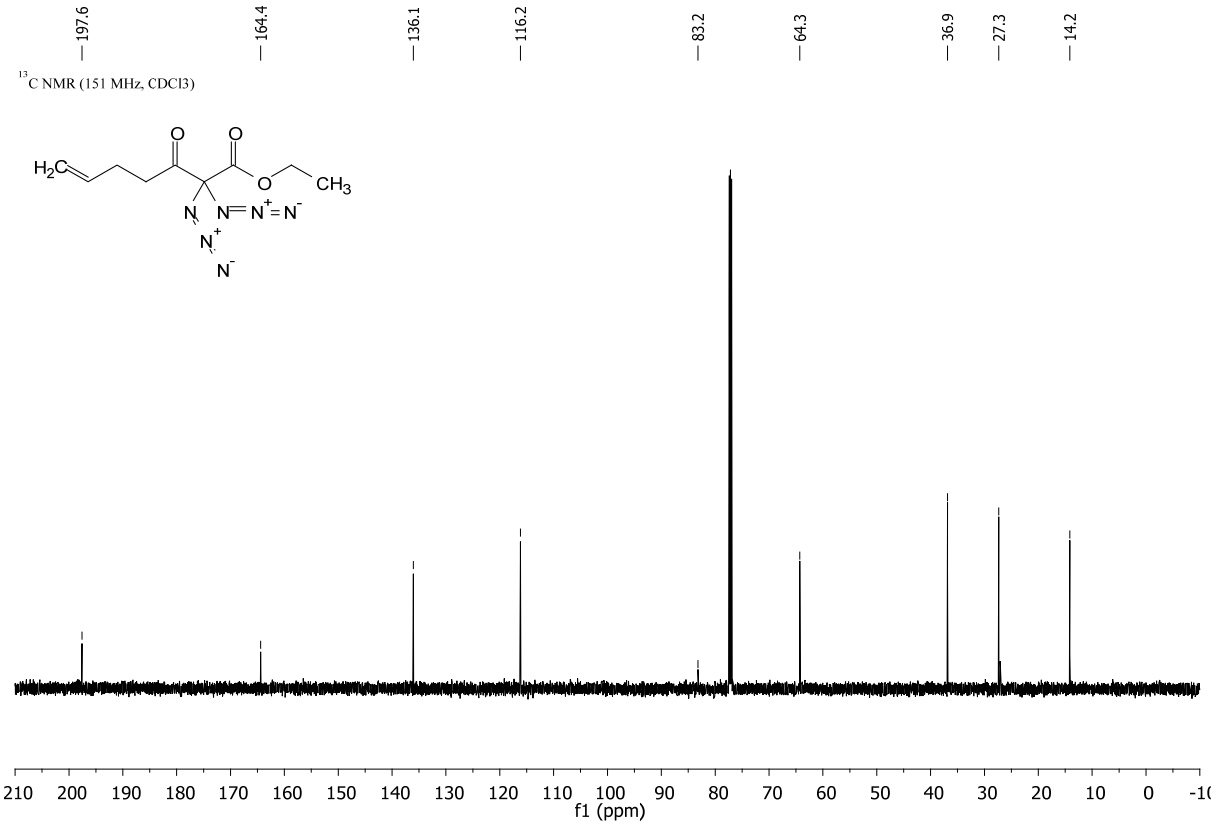
ethyl 3-oxohept-6-enoate

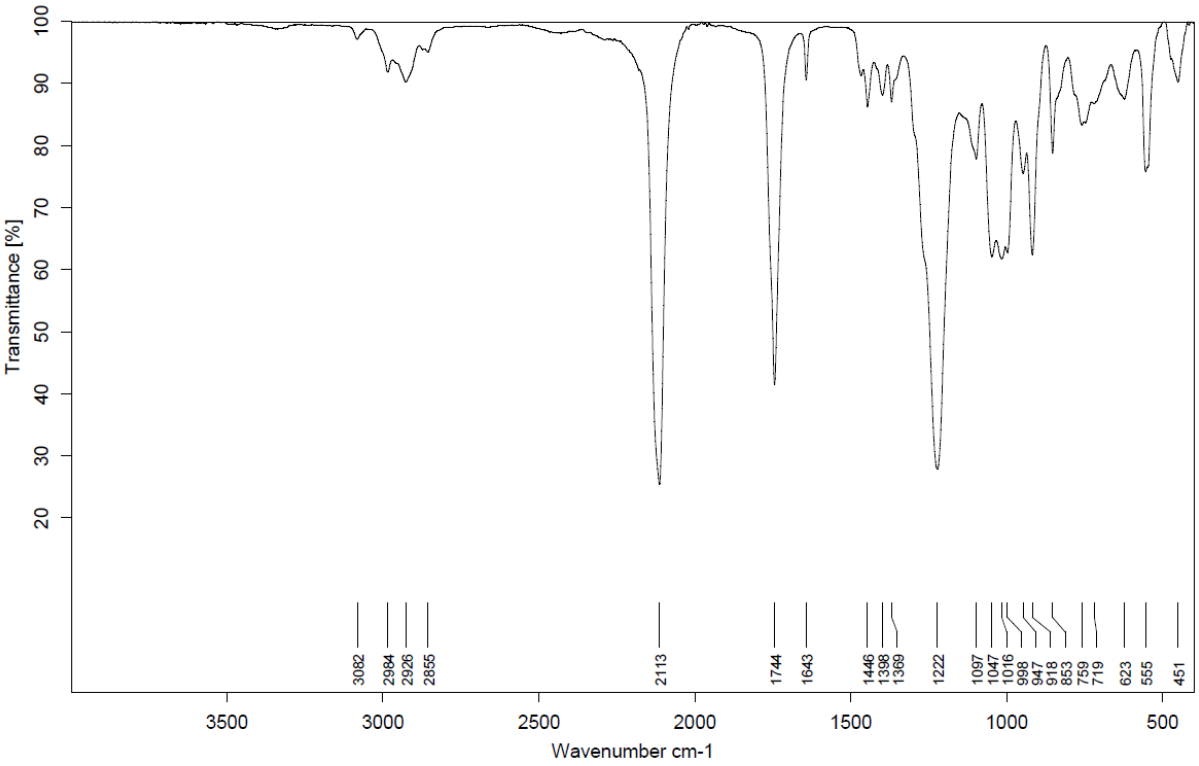




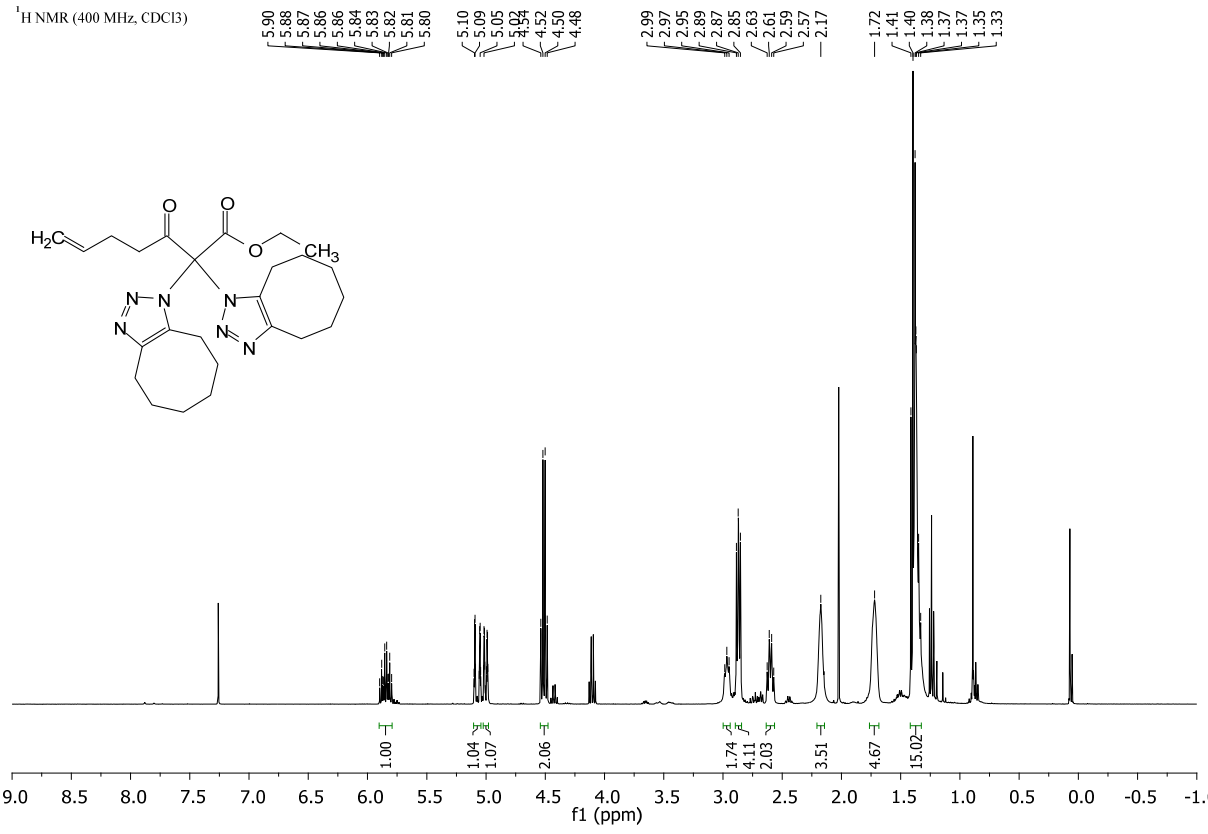
ethyl 2,2-diazido-3-oxohept-6-enoate (1a)

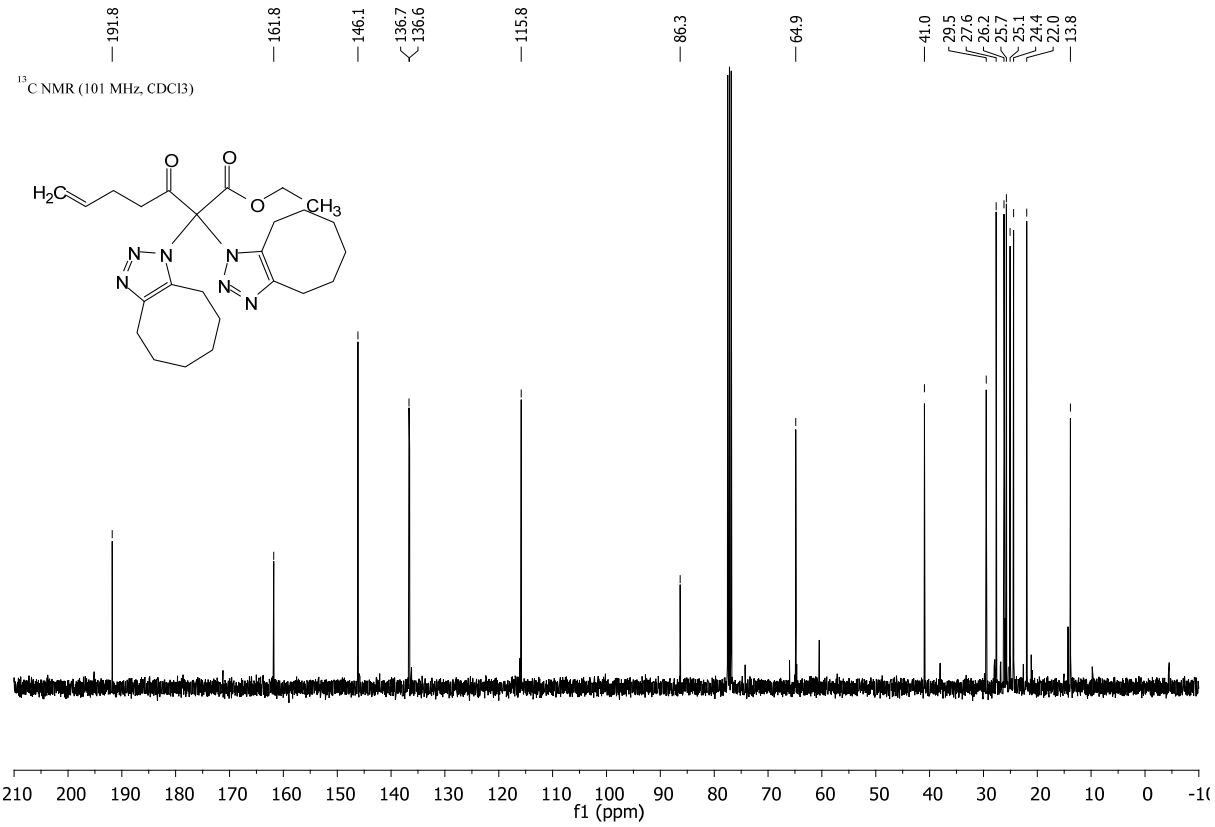




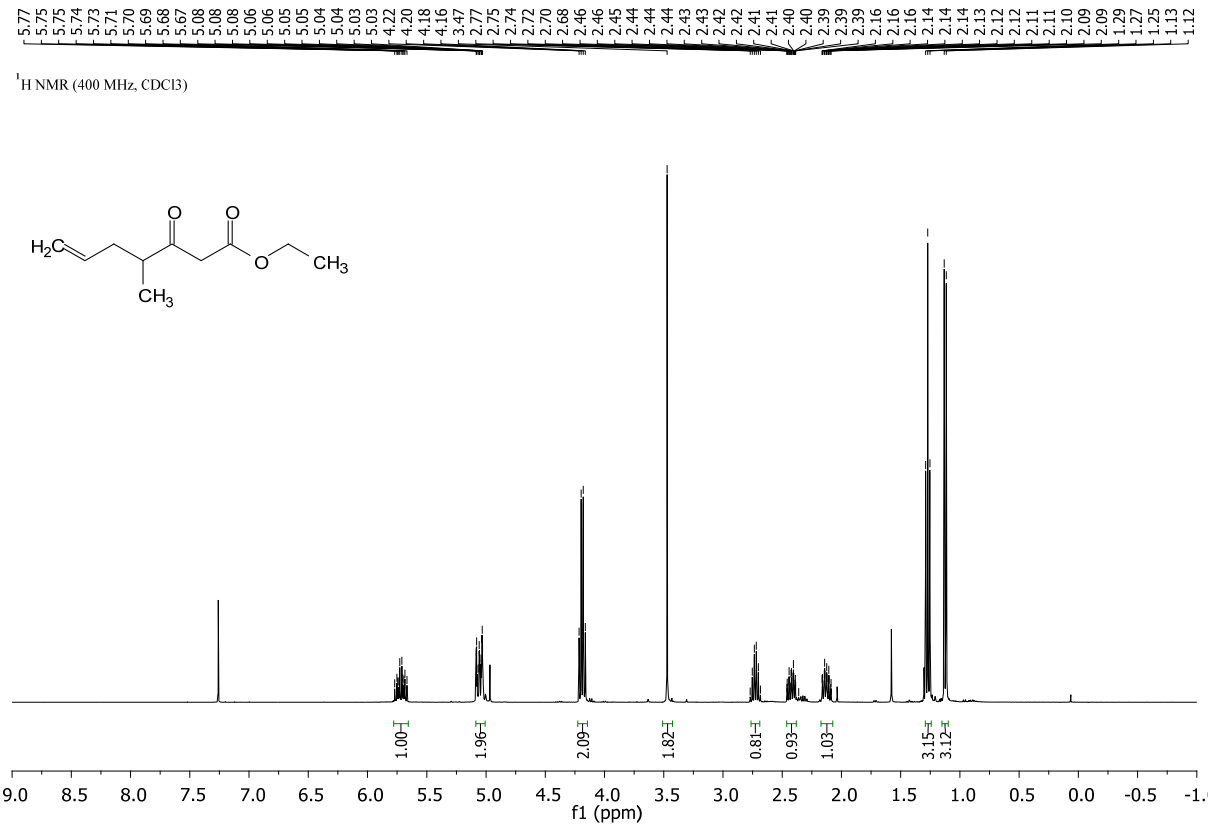


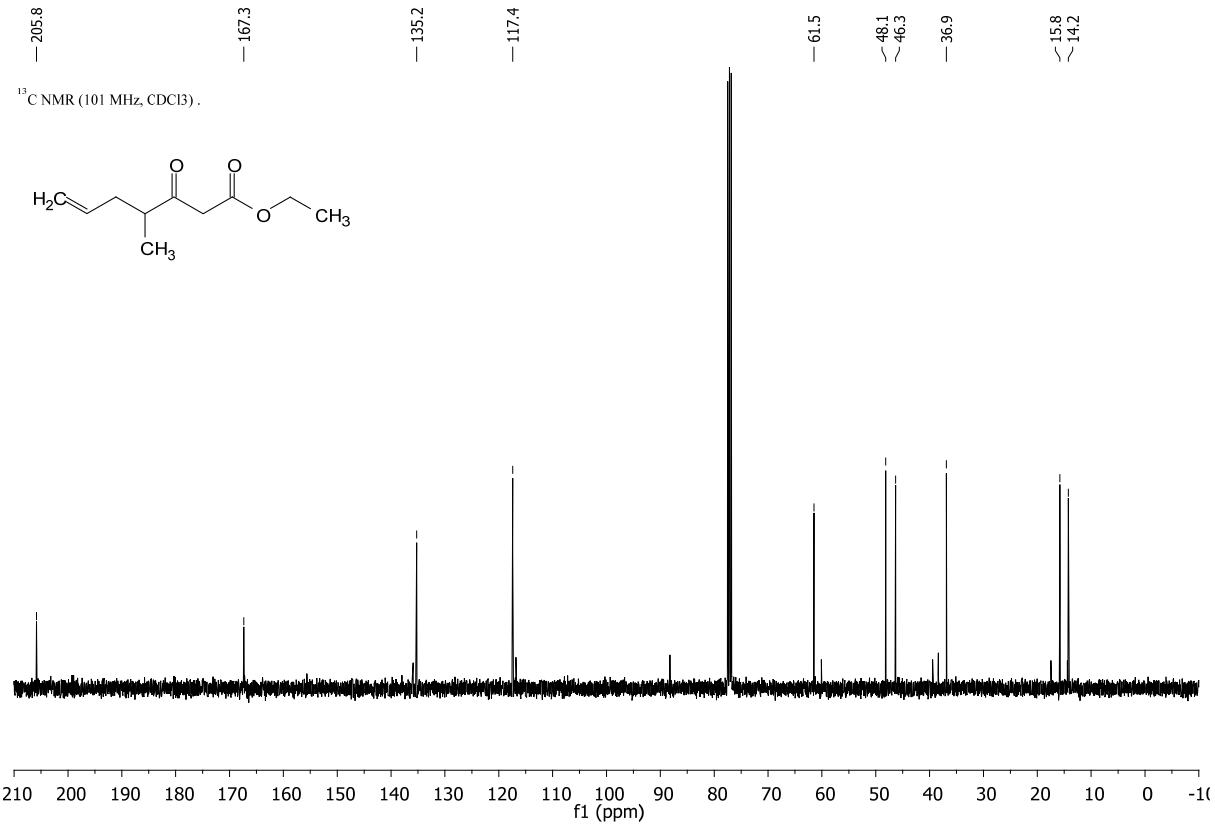
ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate



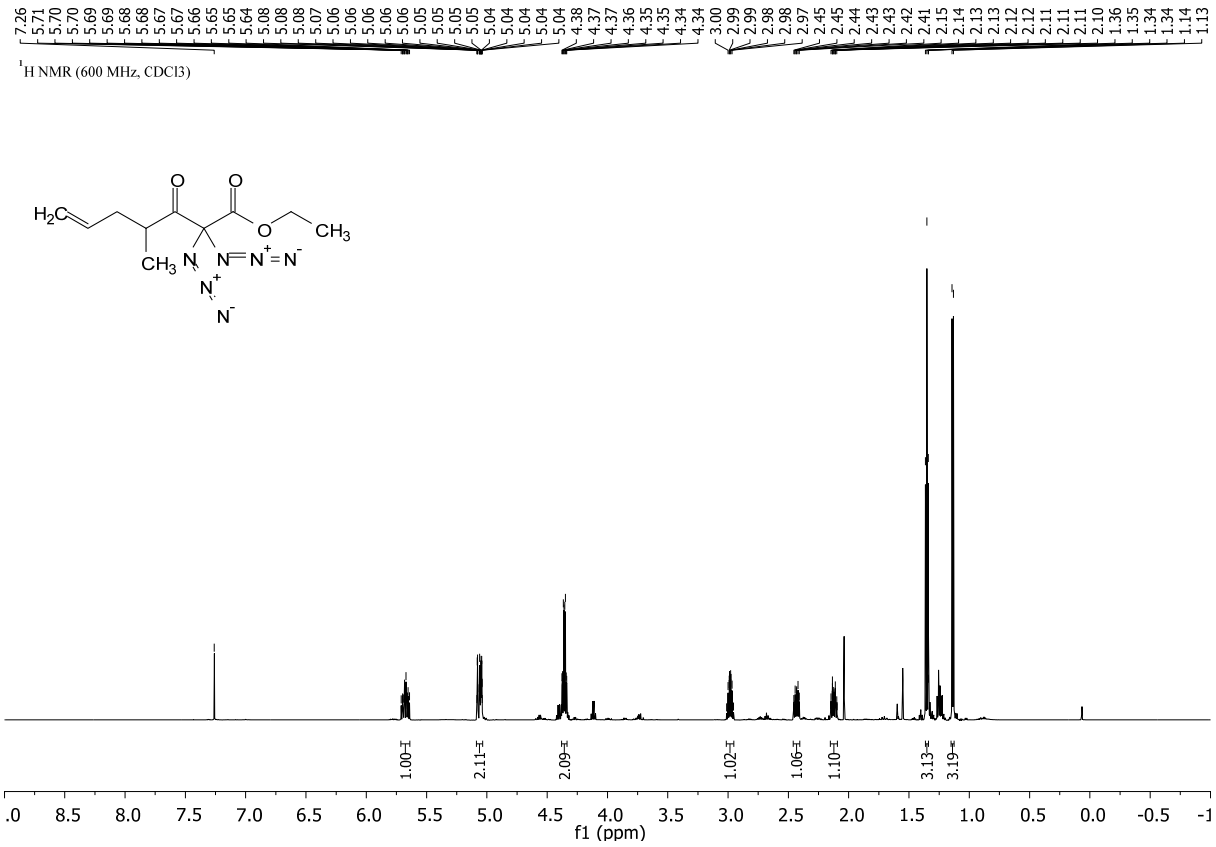


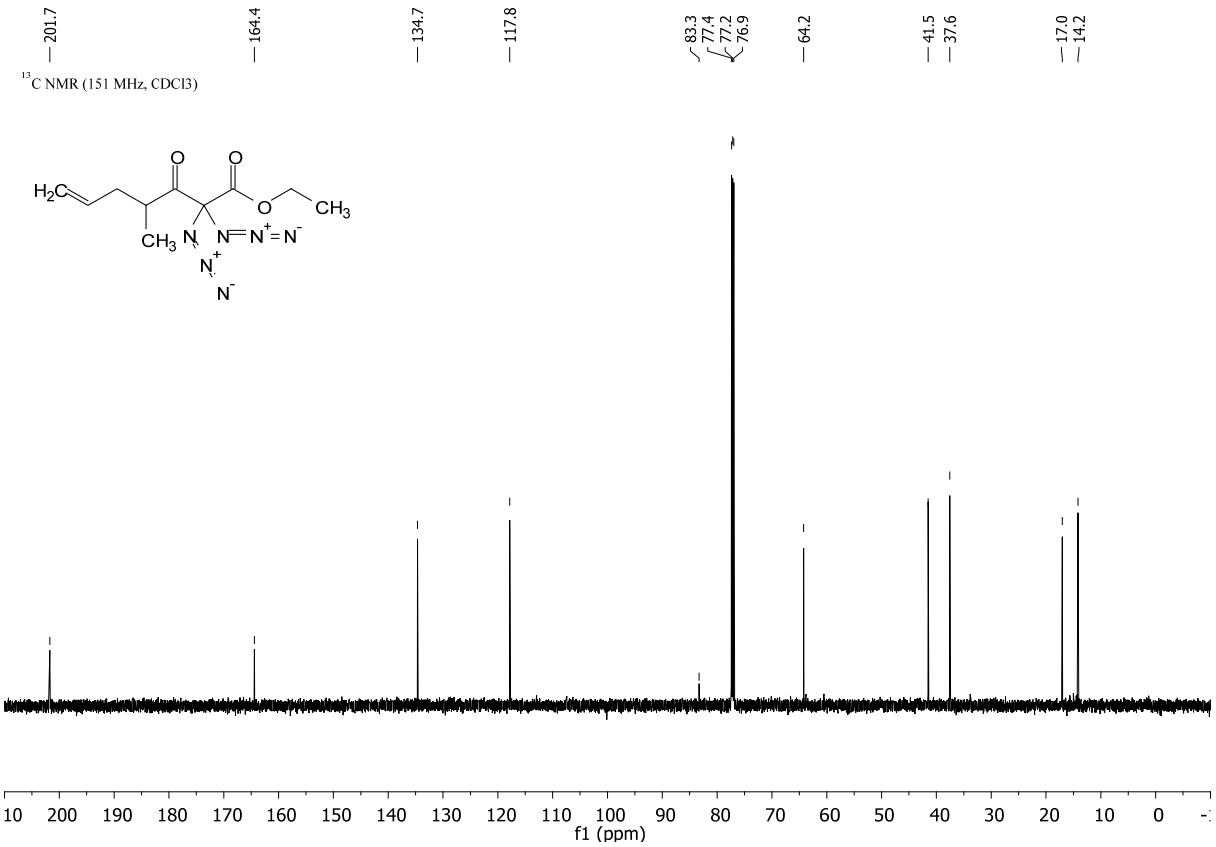
ethyl 4-methyl-3-oxohept-6-enoate





ethyl 2,2-diazido-4-methyl-3-oxohept-6-enoate (1b)

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76.9
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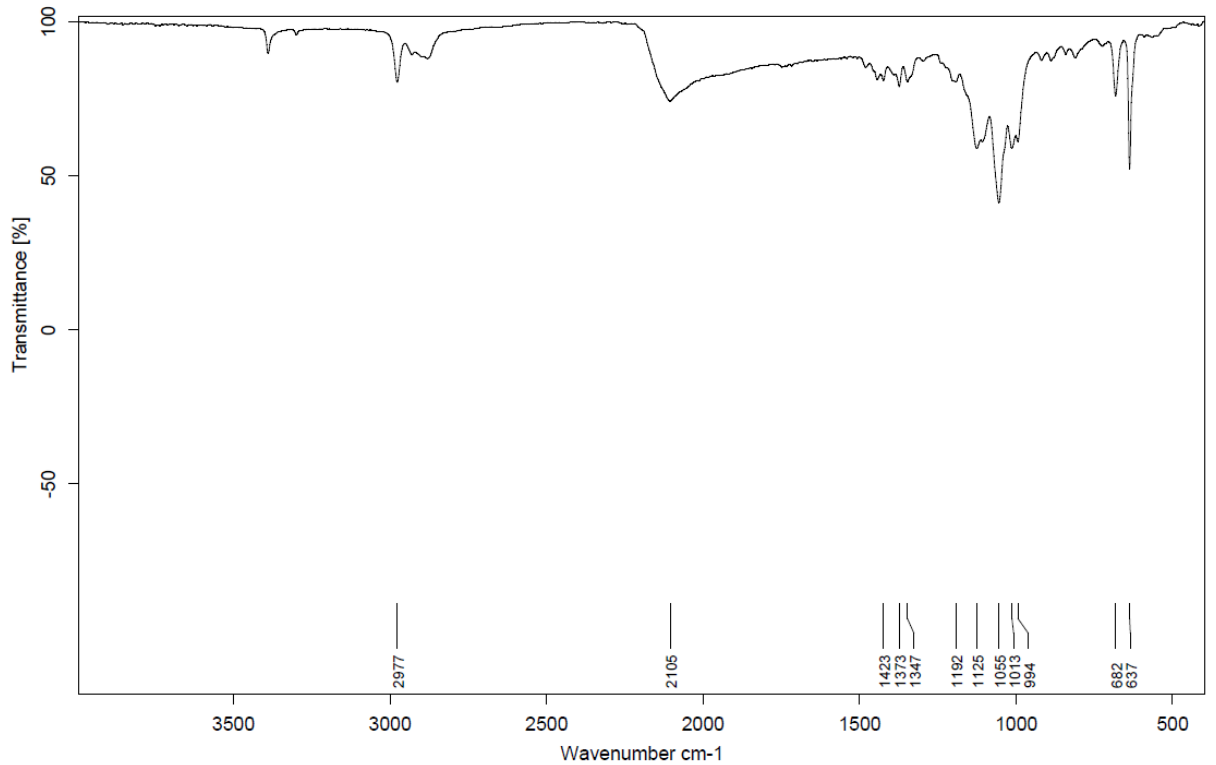
41.5
37.6
17.0
14.2
13C NMR (151 MHz, CDCl3)
f1 (ppm)


Transmittance [%]
Wavenumber cm-1
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1373
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1192
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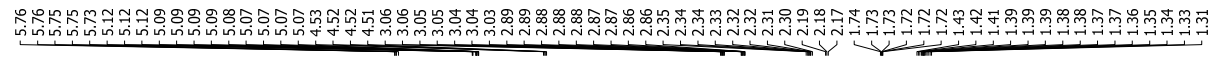
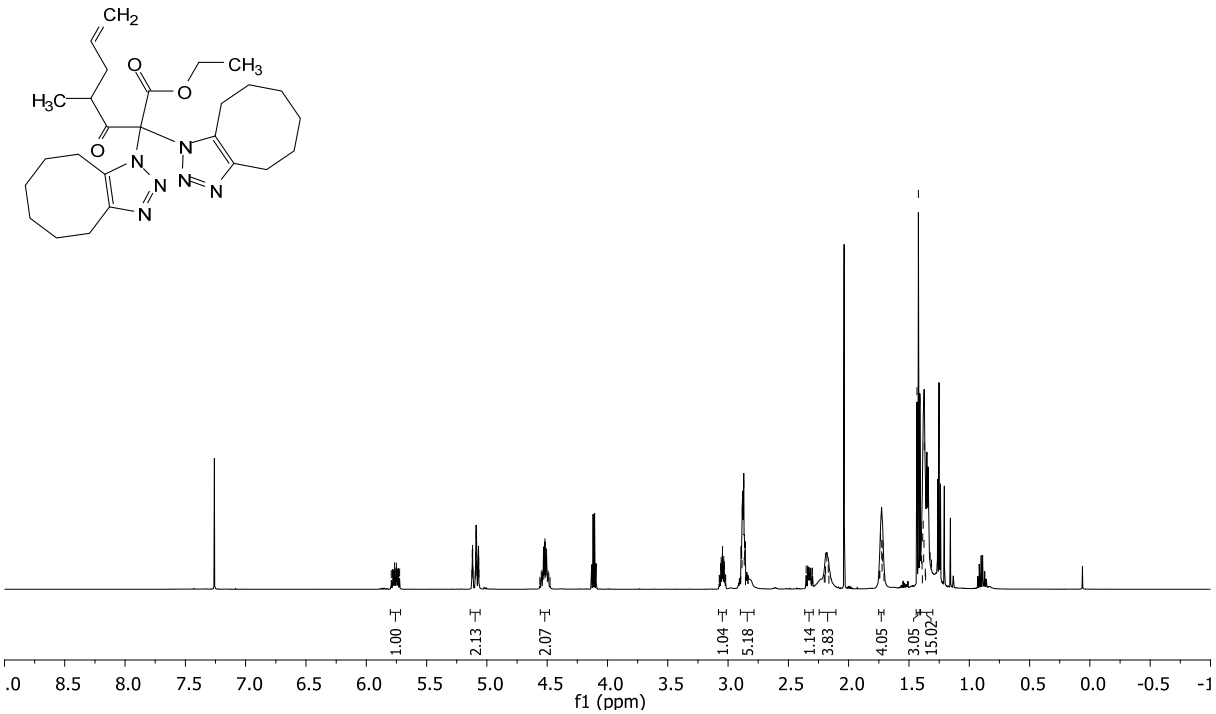
1055
1013
994
682
637

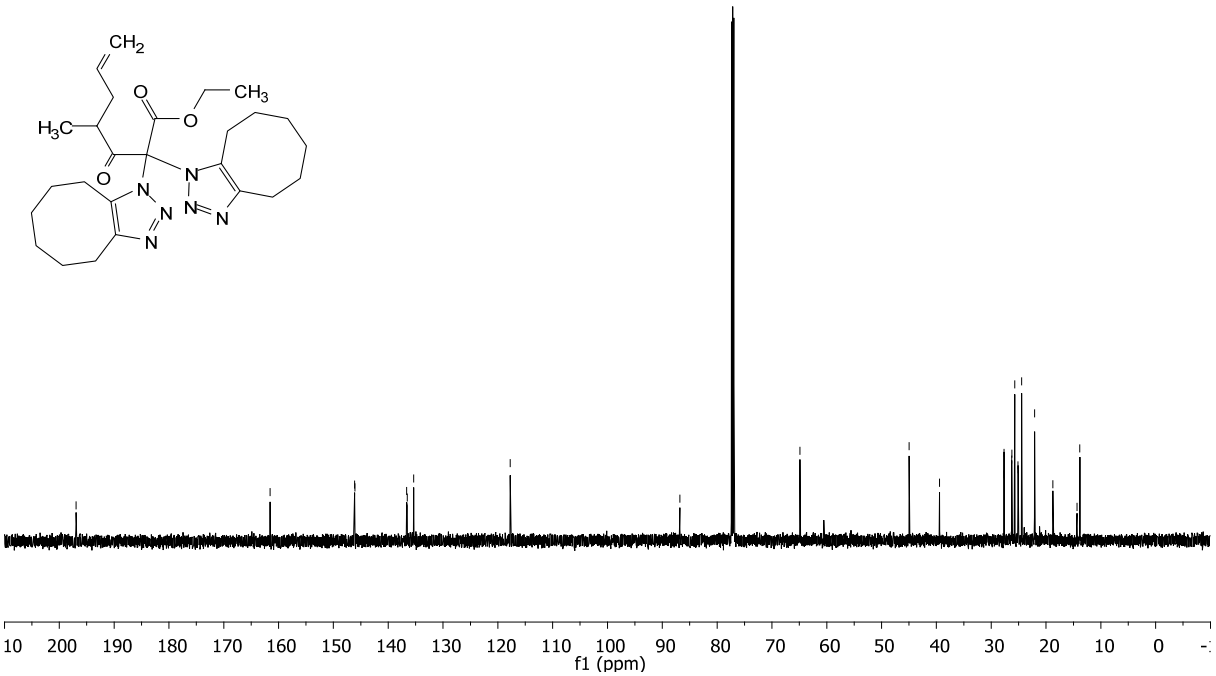
ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-4-methyl-3-oxohept-6-enoate



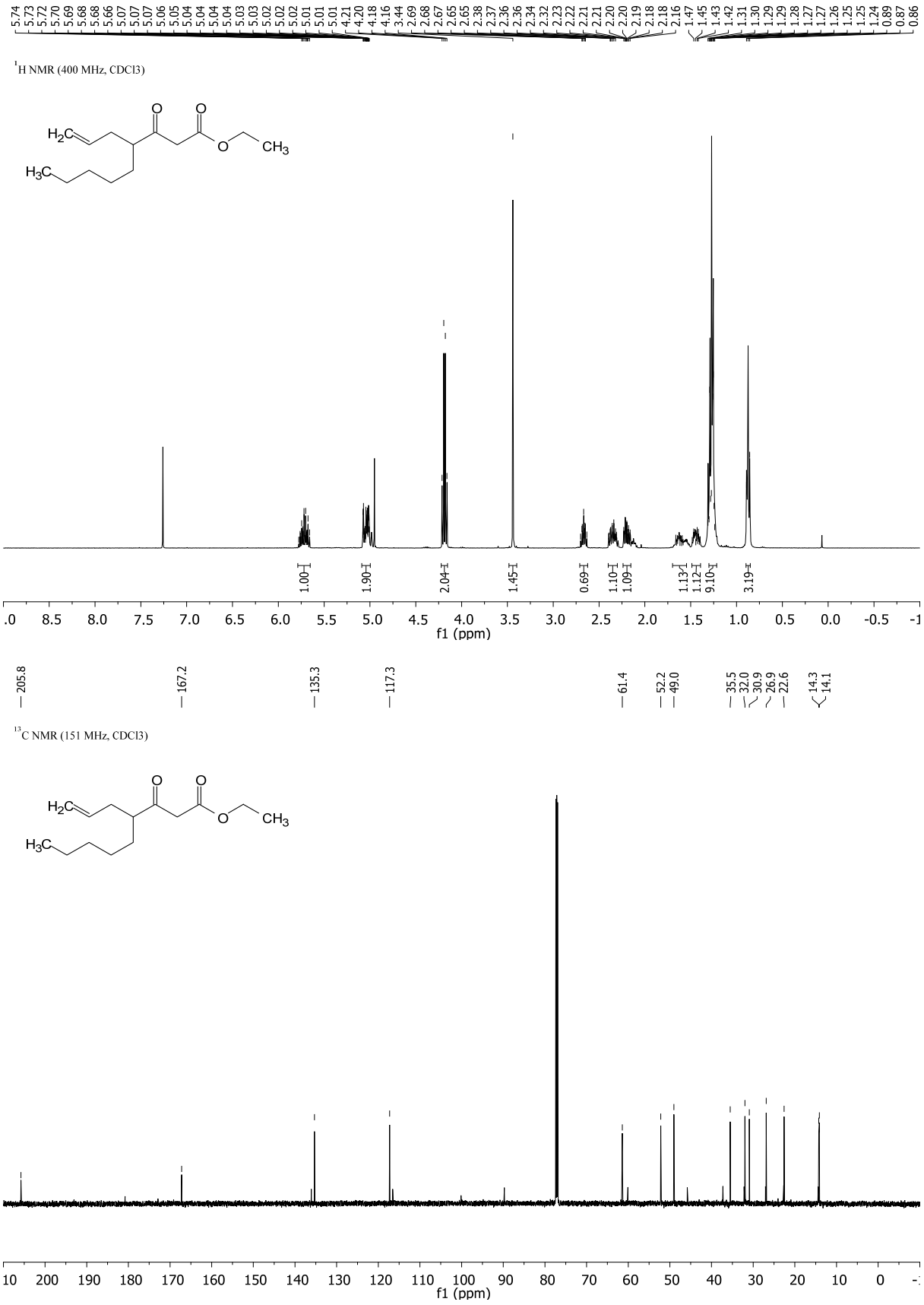
^{1}H NMR (600 MHz, CDCl3)



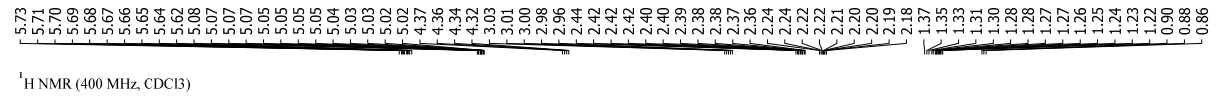
^{13}C NMR (151 MHz, CDCl3)



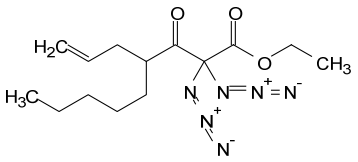
ethyl 4-allyl-3-oxononanoat

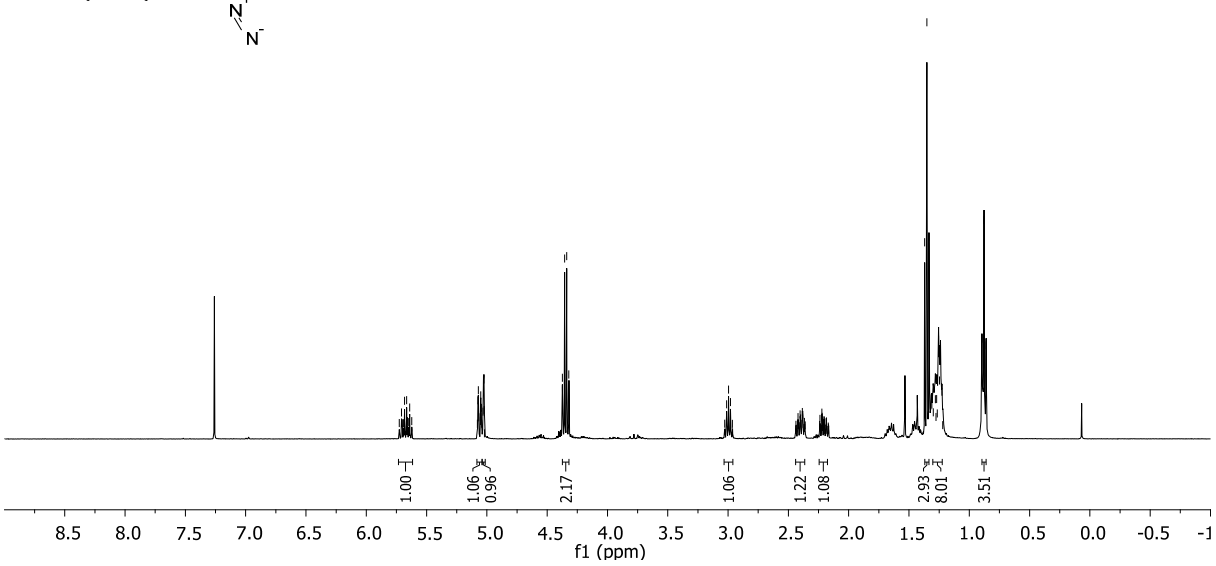


ethyl 4-allyl-2,2-diazido-3-oxononanoate (1c)

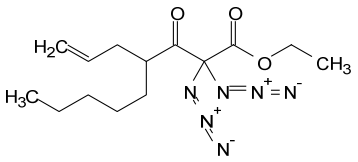


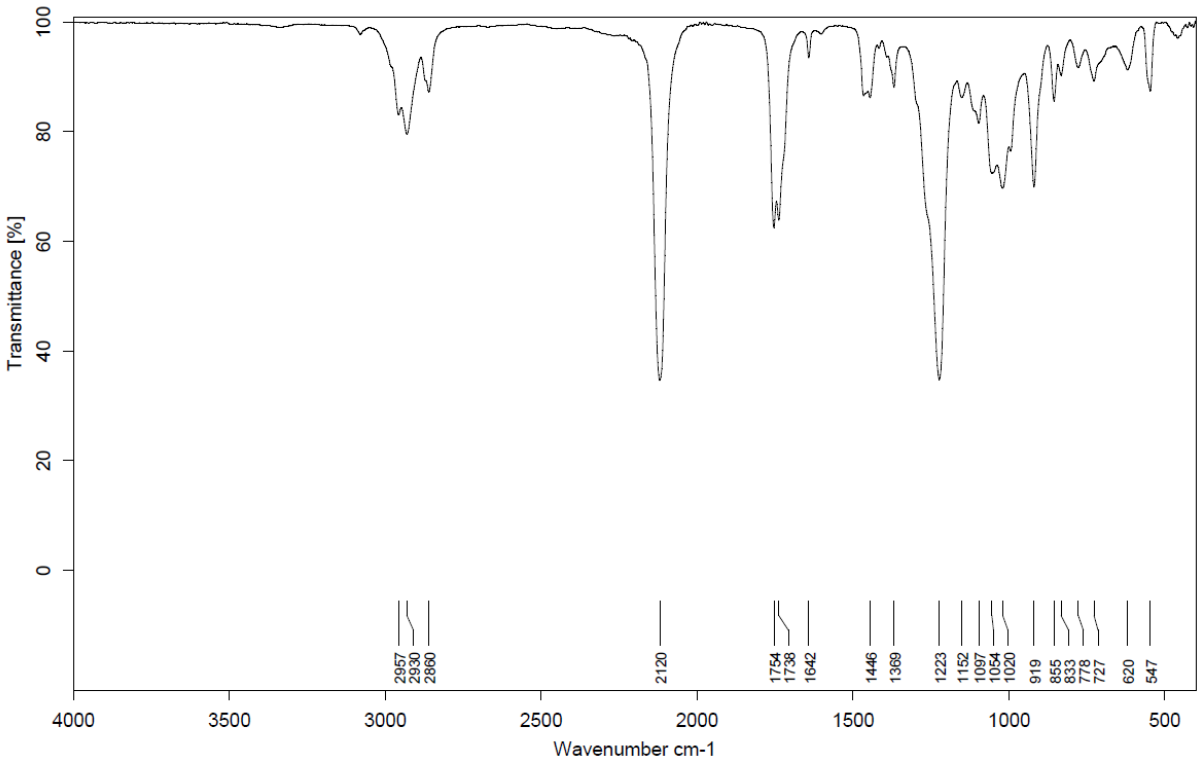
^{1}H NMR (400 MHz, CDCl3)



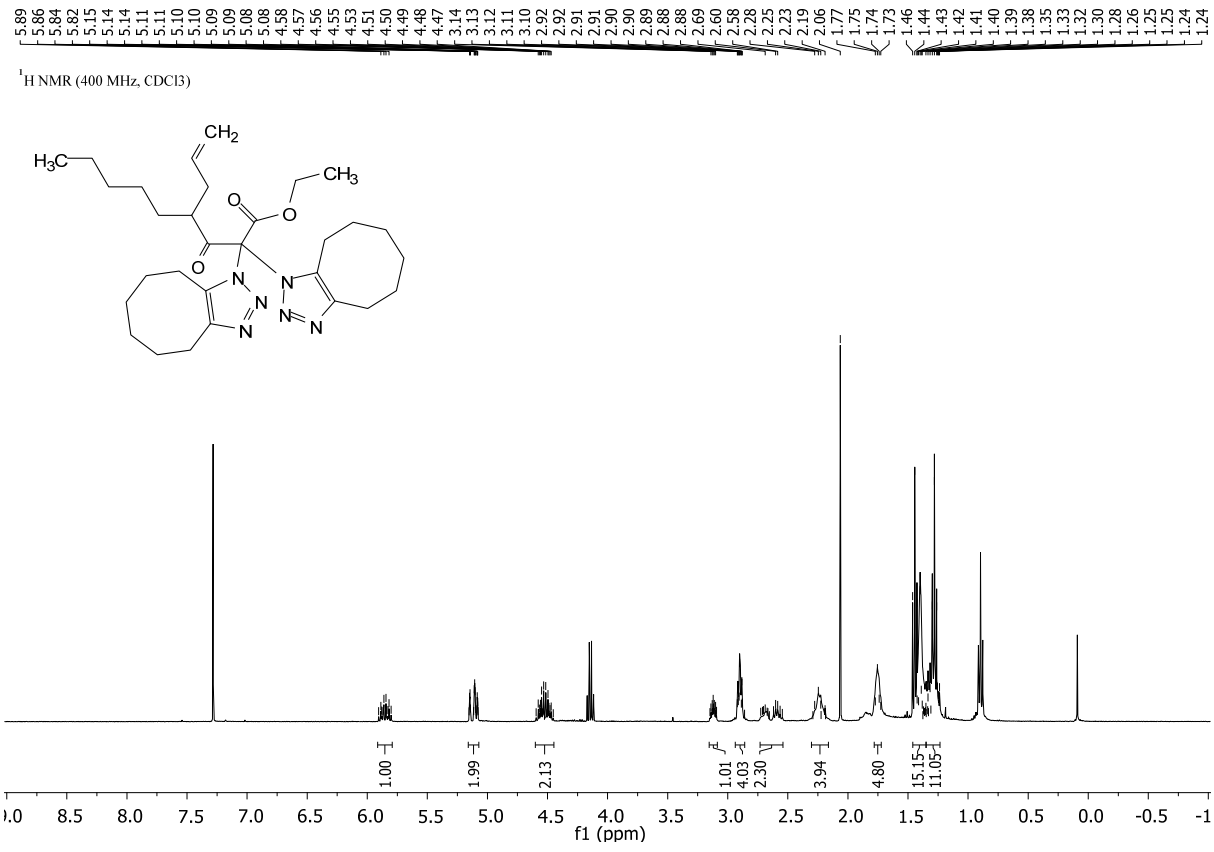


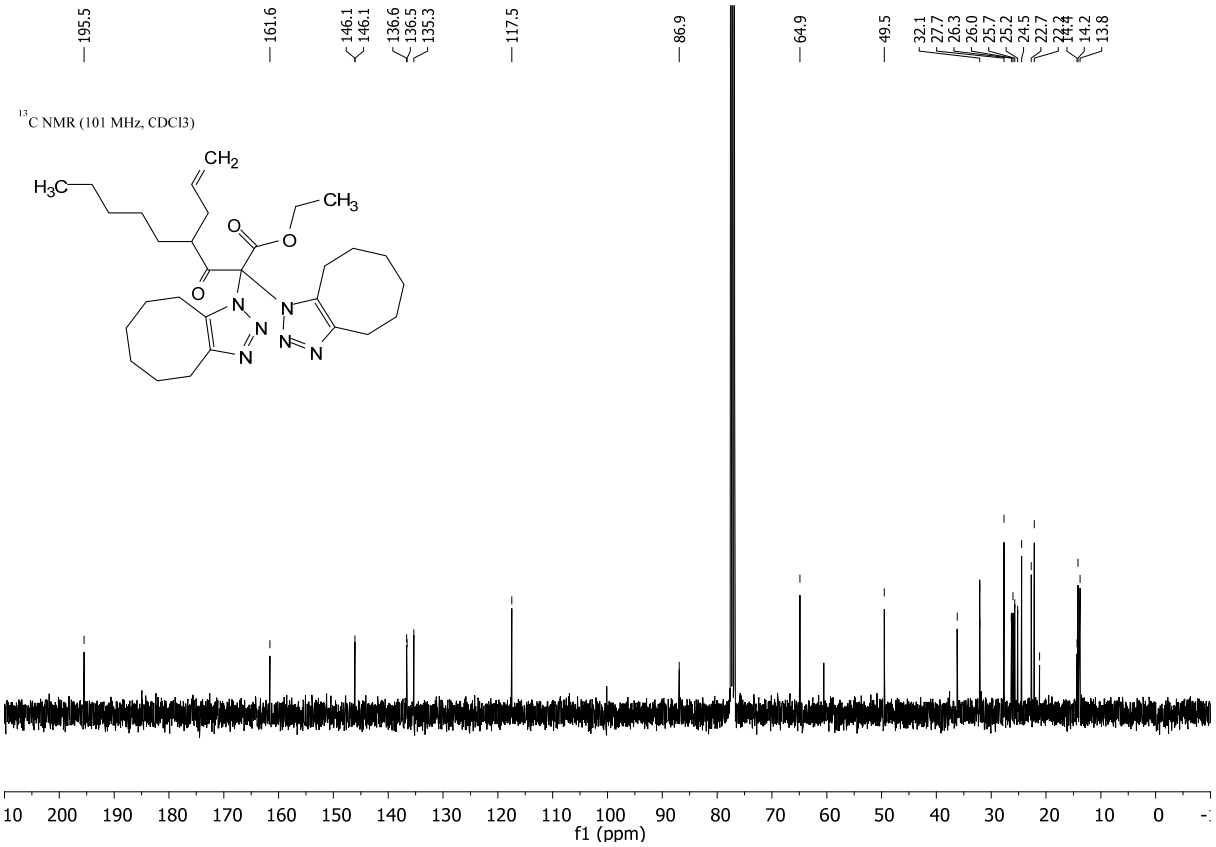
^{13}C NMR (151 MHz, CDCl3)



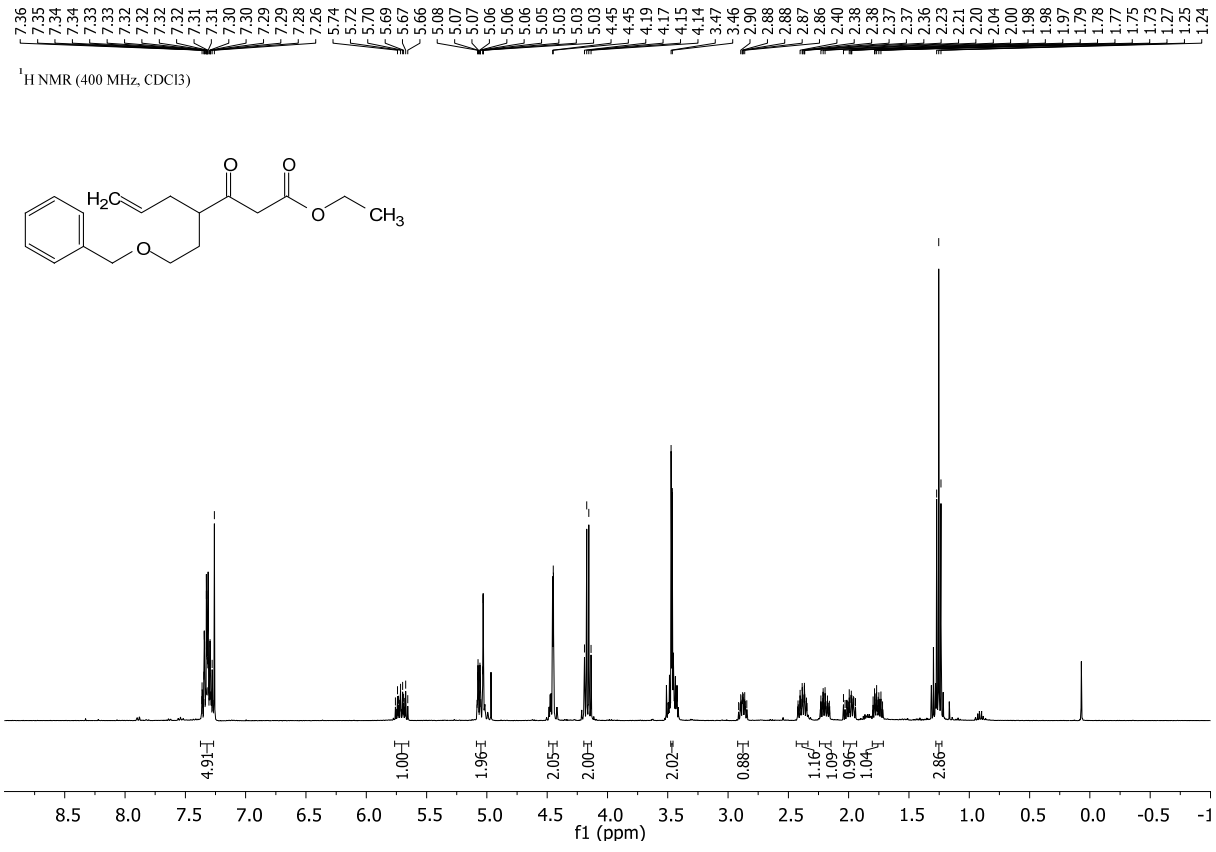


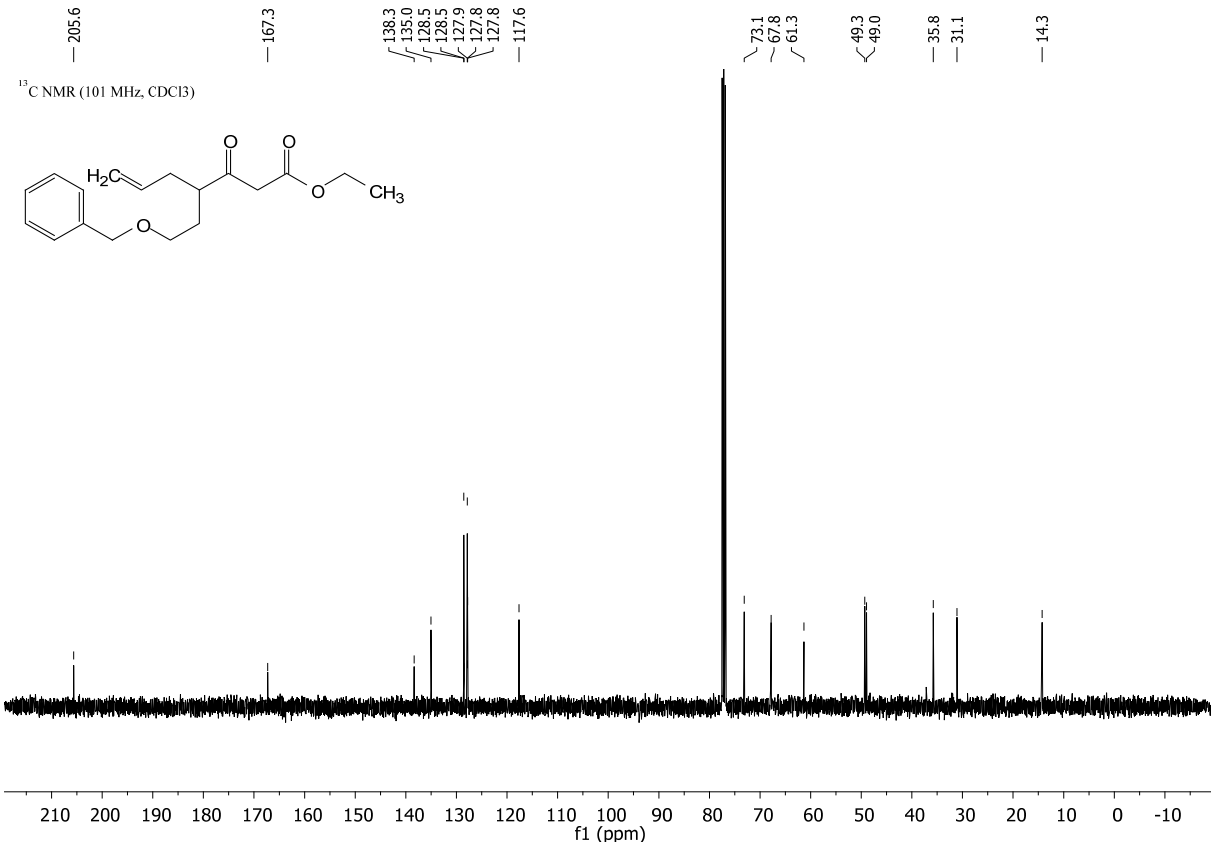
ethyl 4-allyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxononanoate



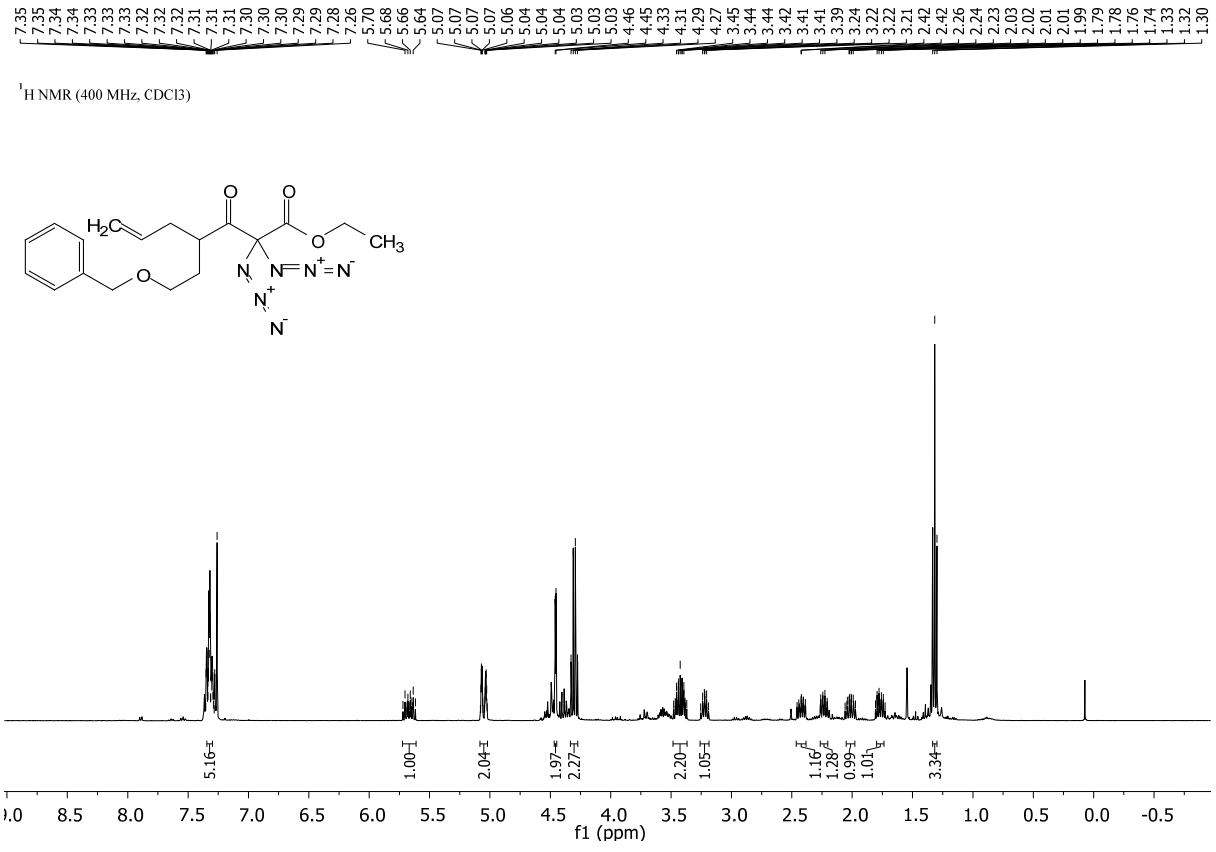


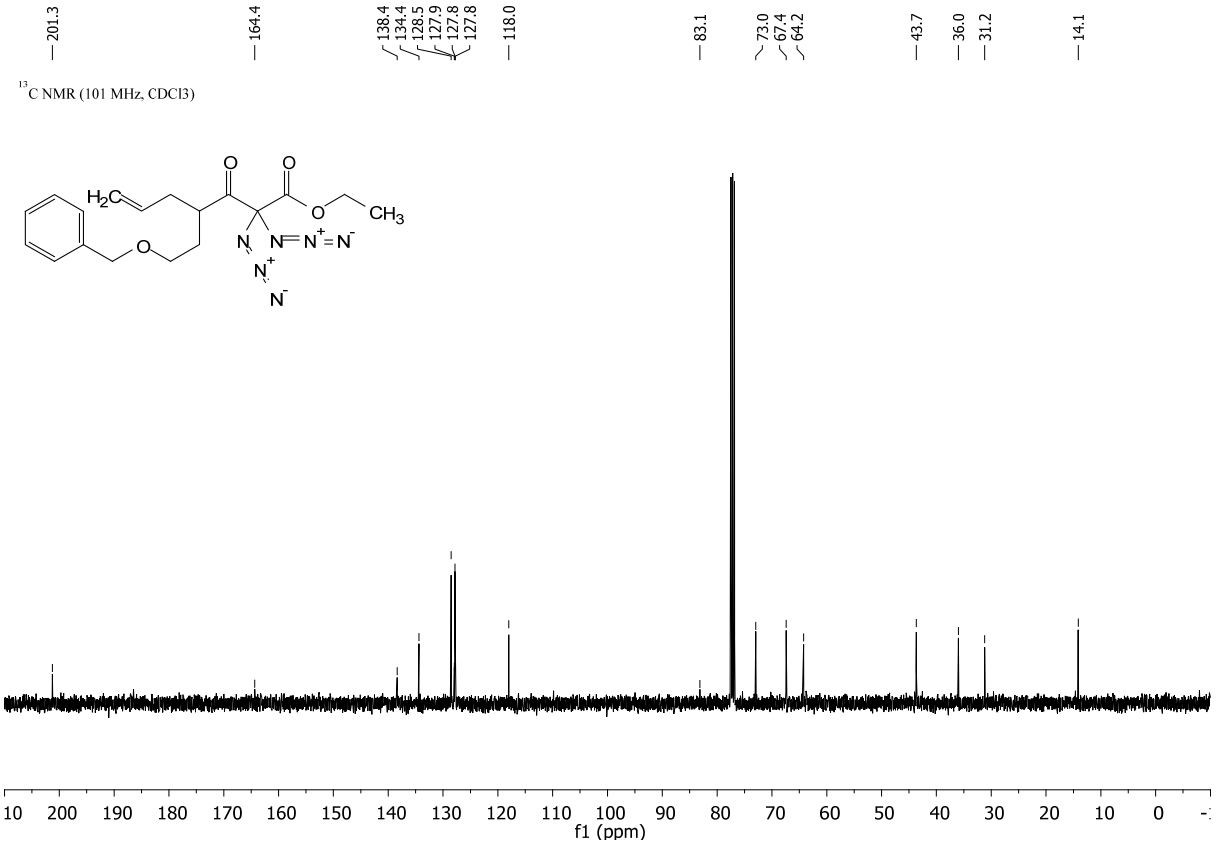
ethyl 4-(2-(benzyloxy)ethyl)-3-oxohept-6-enoate





ethyl 2,2-diazido-4-(2-(benzyloxy)ethyl)-3-oxohept-6-enoate (1d)

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127.8
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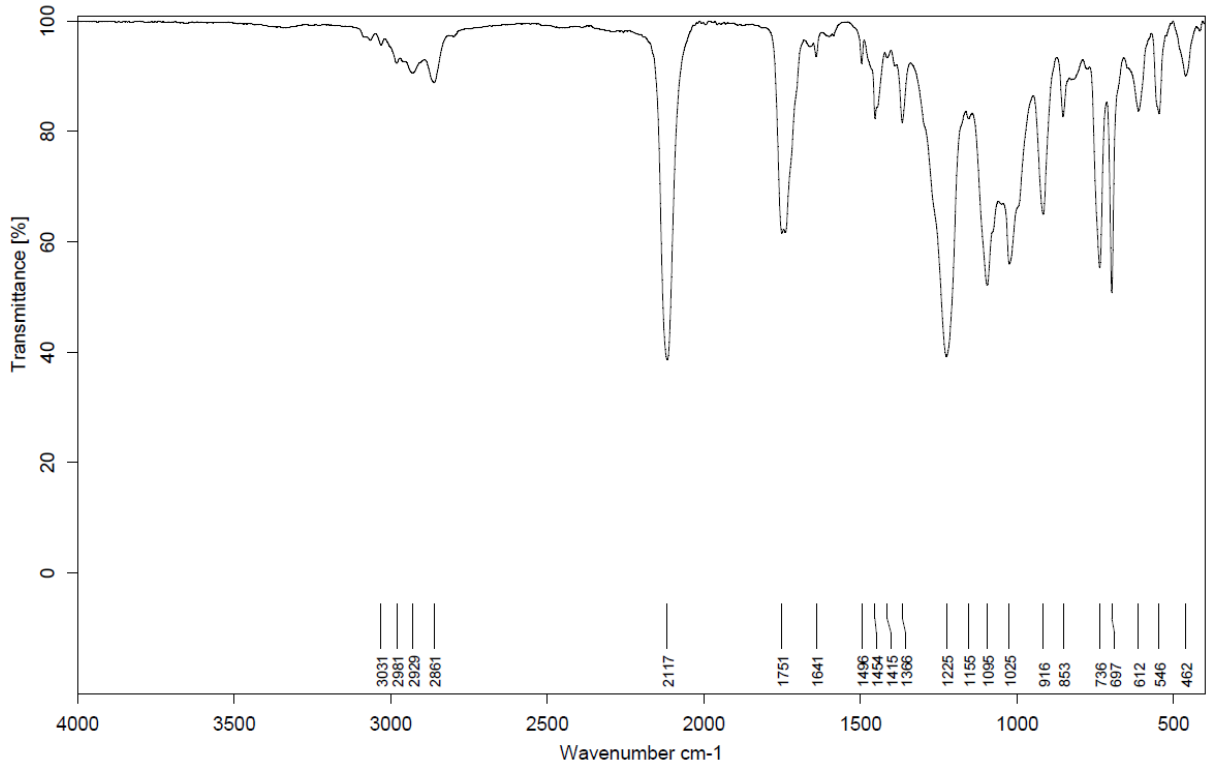
31.2
14.1
13C NMR (101 MHz, CDCl3)
f1 (ppm)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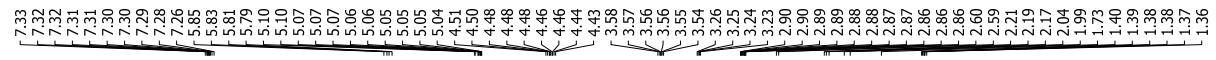
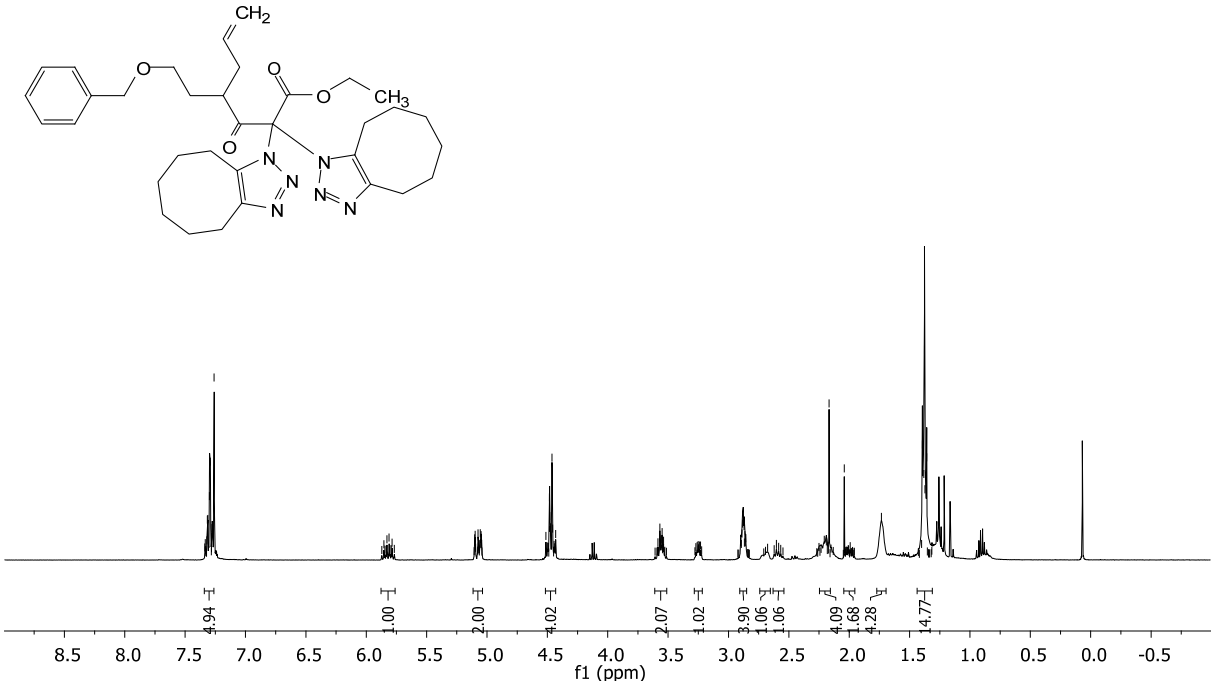
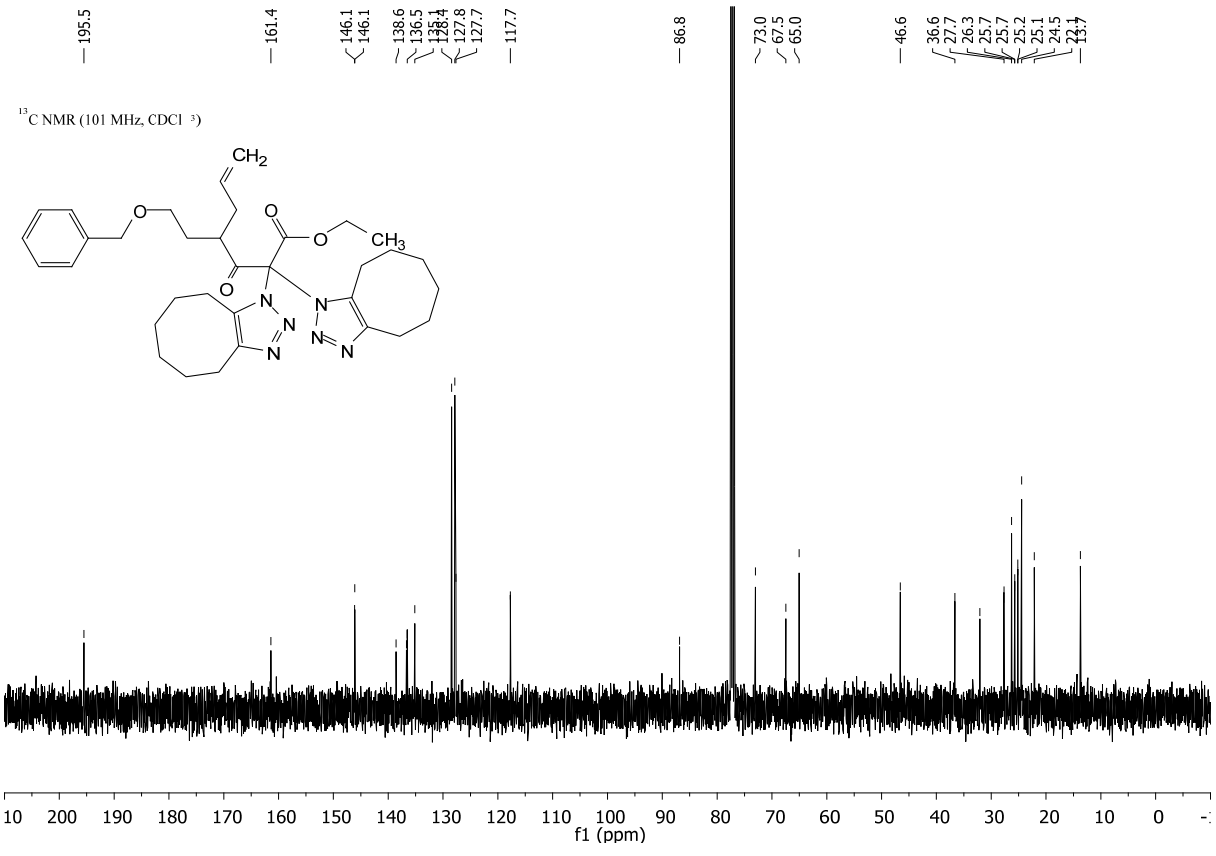
853
736
697
612
546
462

ethyl 4-(2-(benzyloxy)ethyl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate



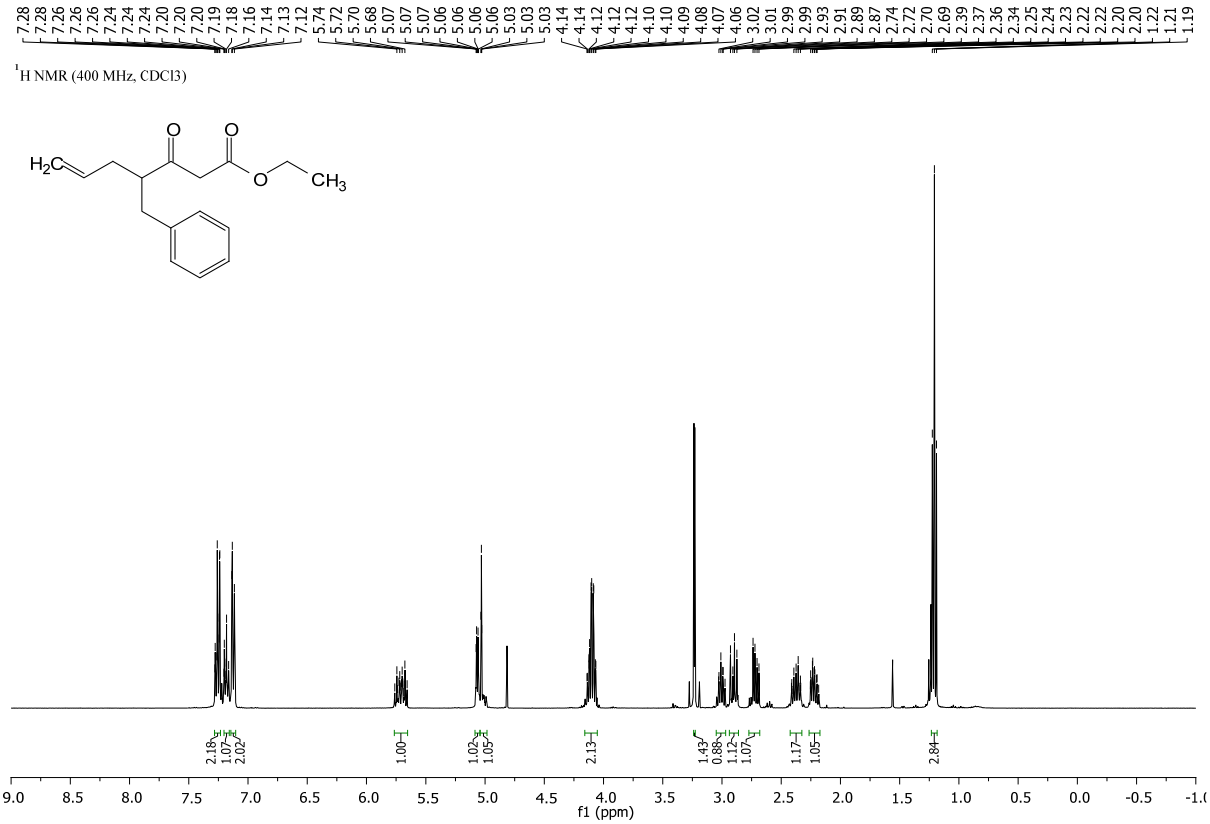
^{1}H NMR (400 MHz, CDCl3)

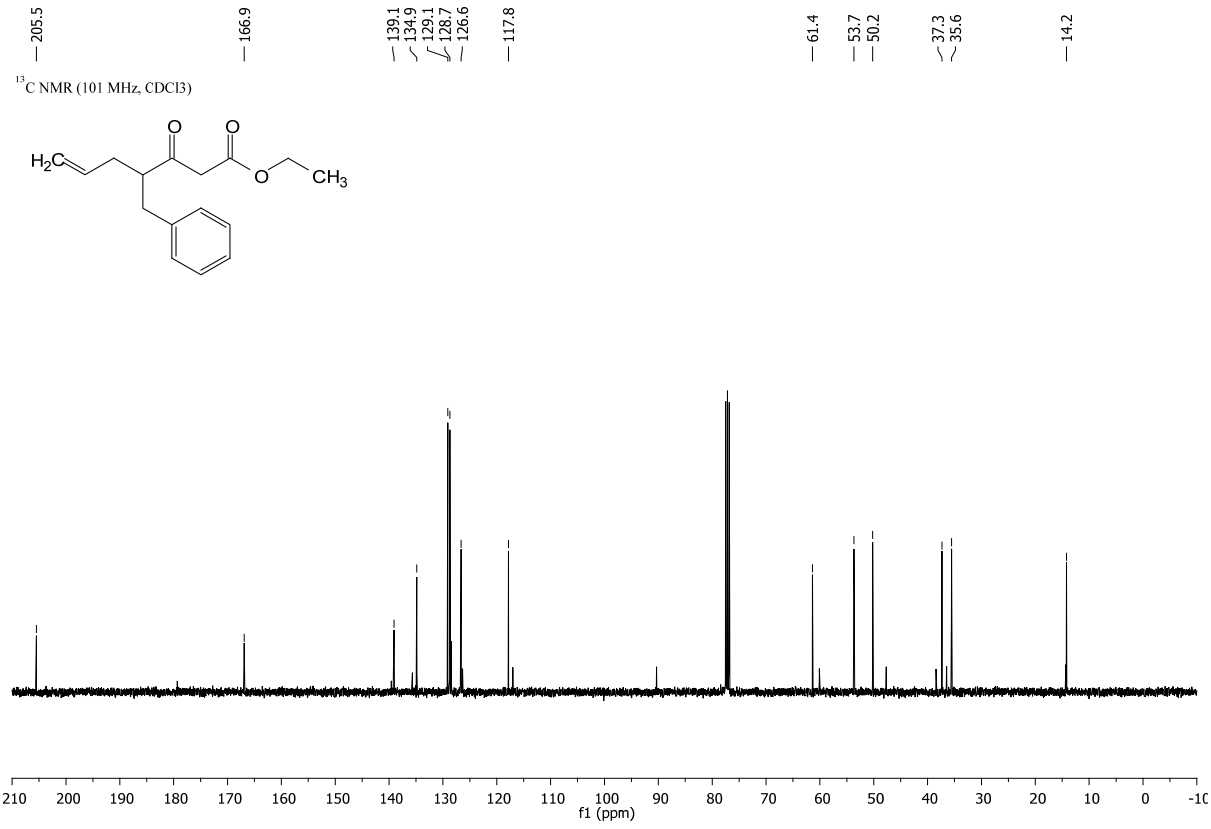




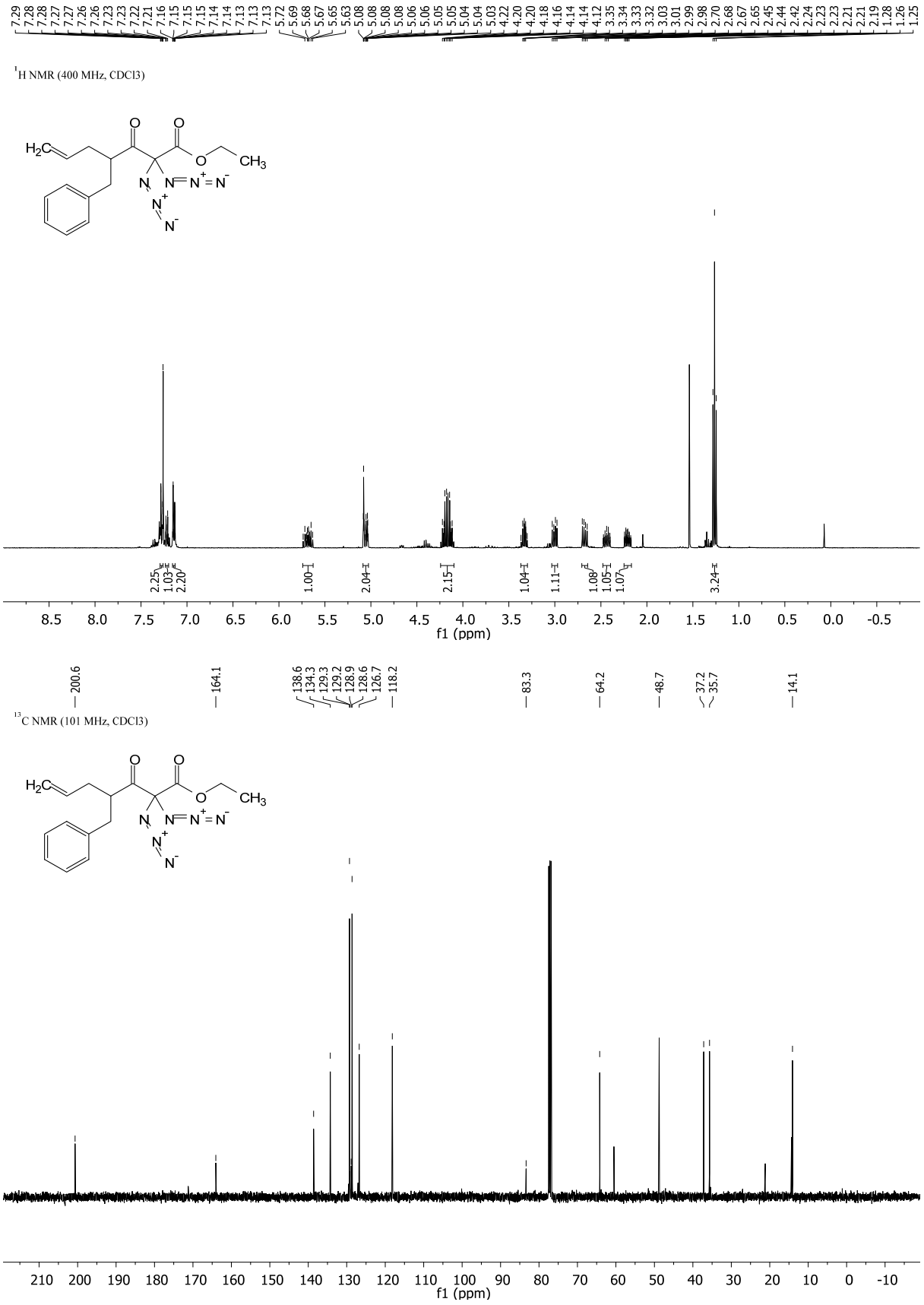
^{13}C NMR (101 MHz, CDCl 3)

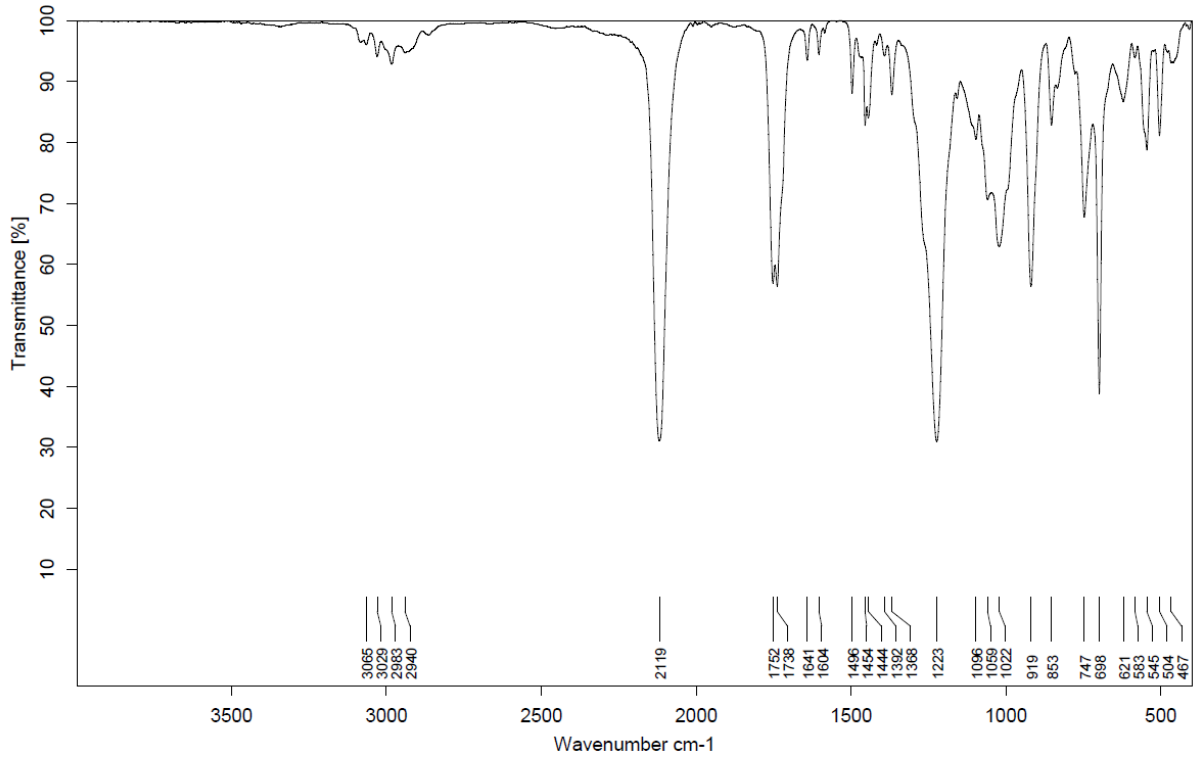
ethyl 4-benzyl-3-oxononanoate



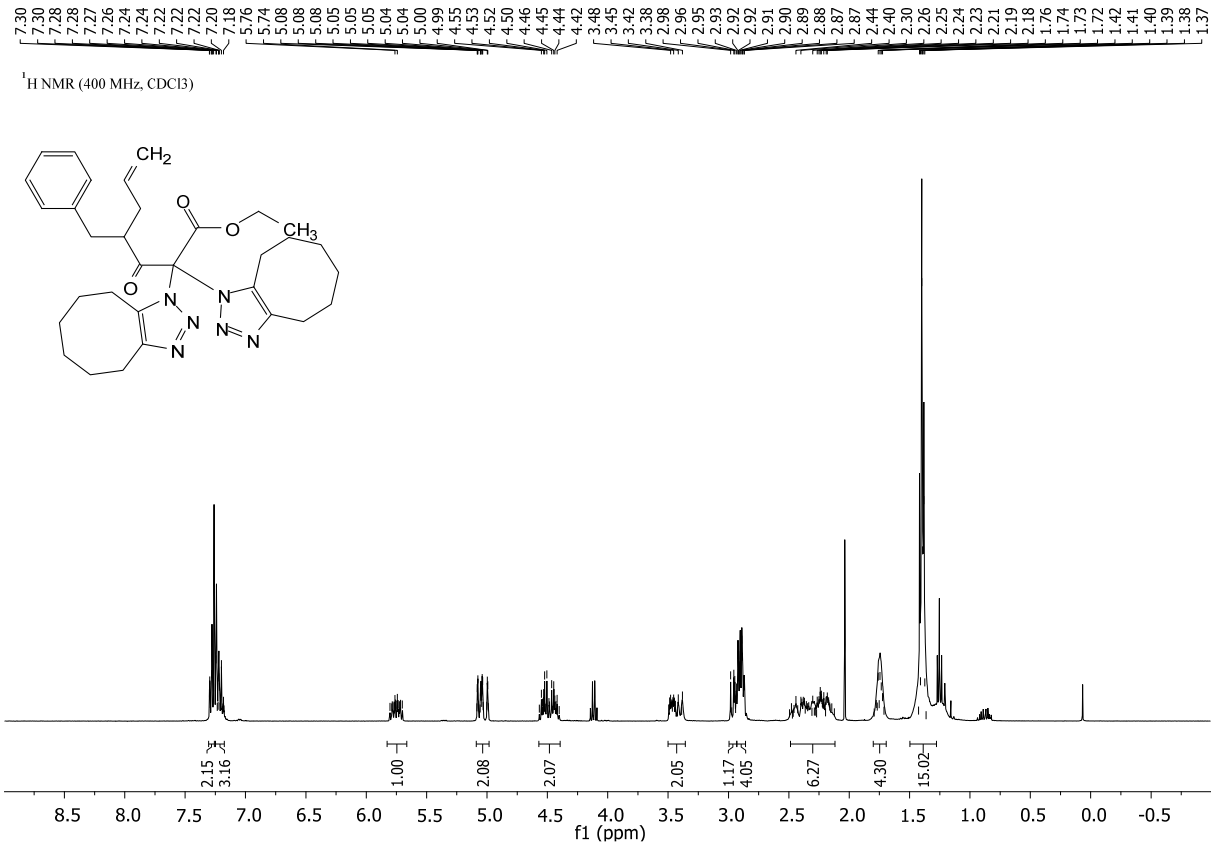


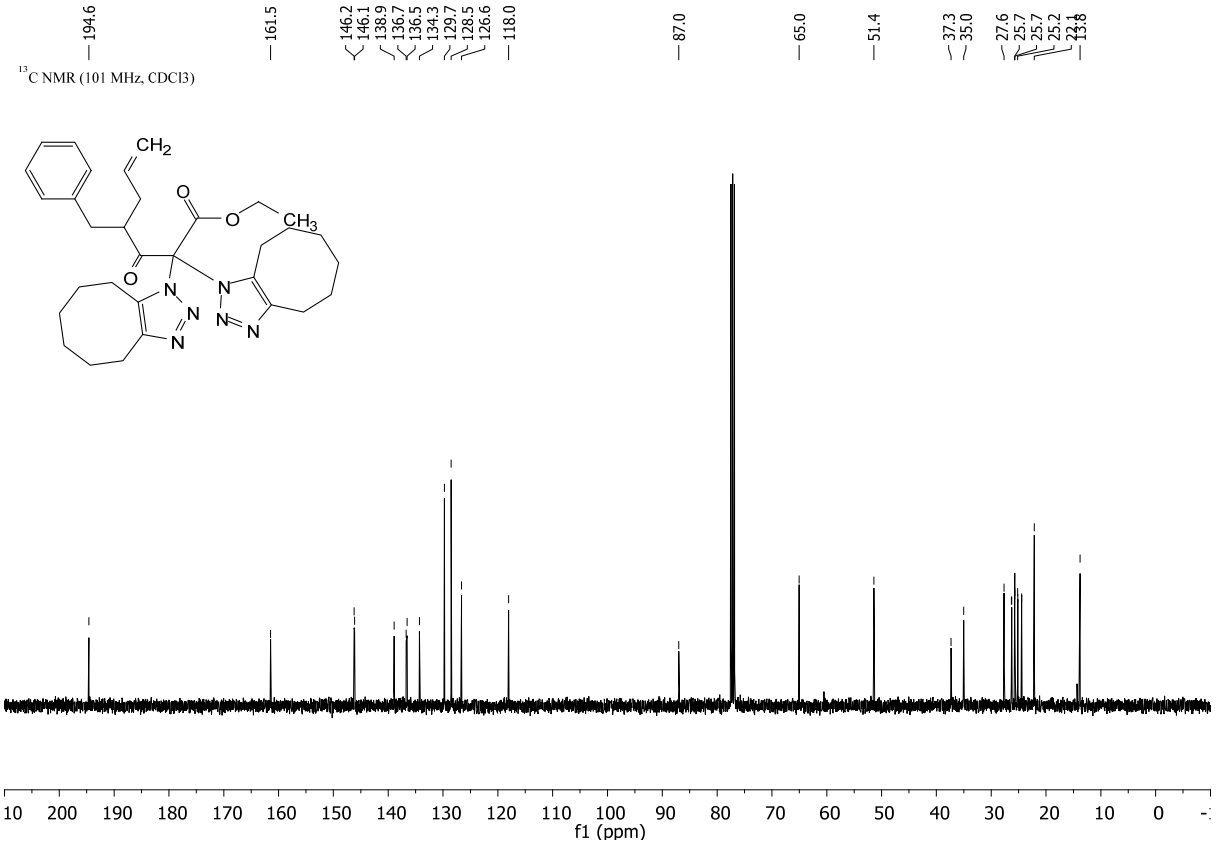
ethyl 2,2-diazido-4-benzyl-3-oxohept-6-enoate (1e)



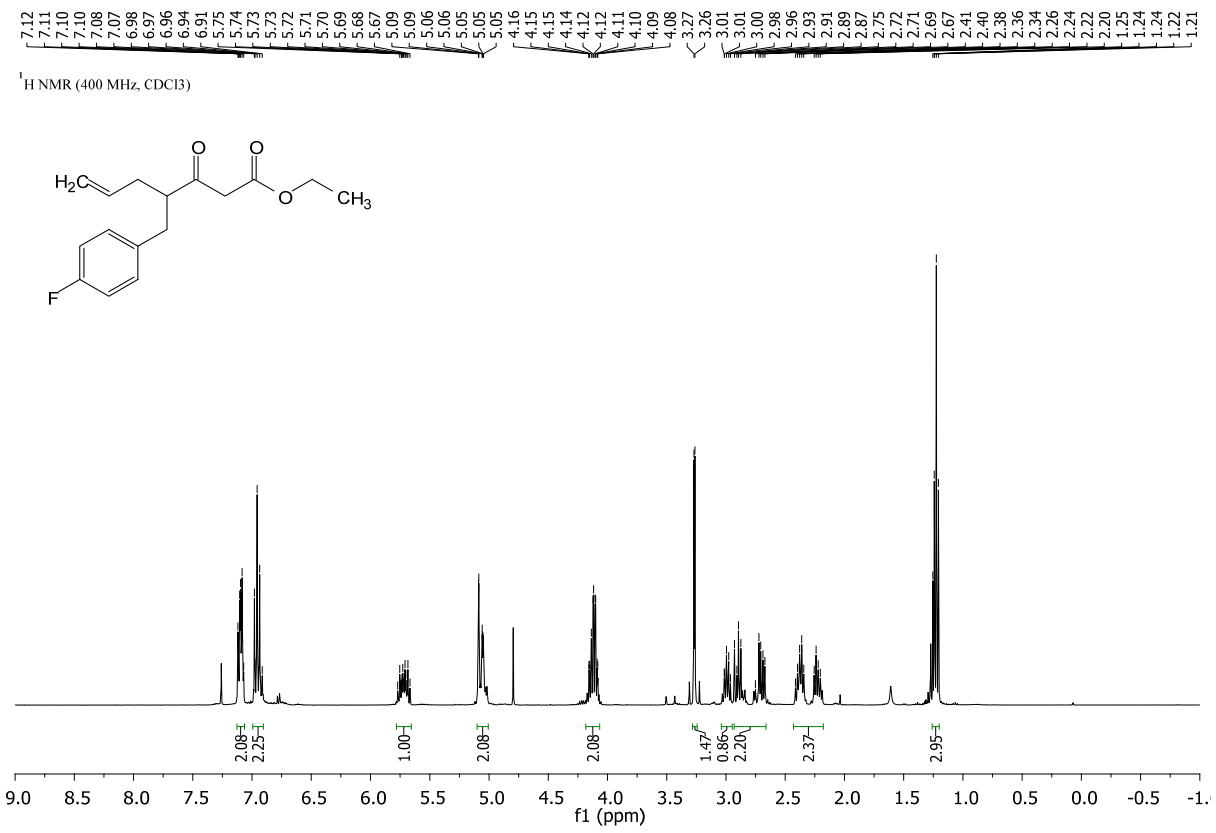


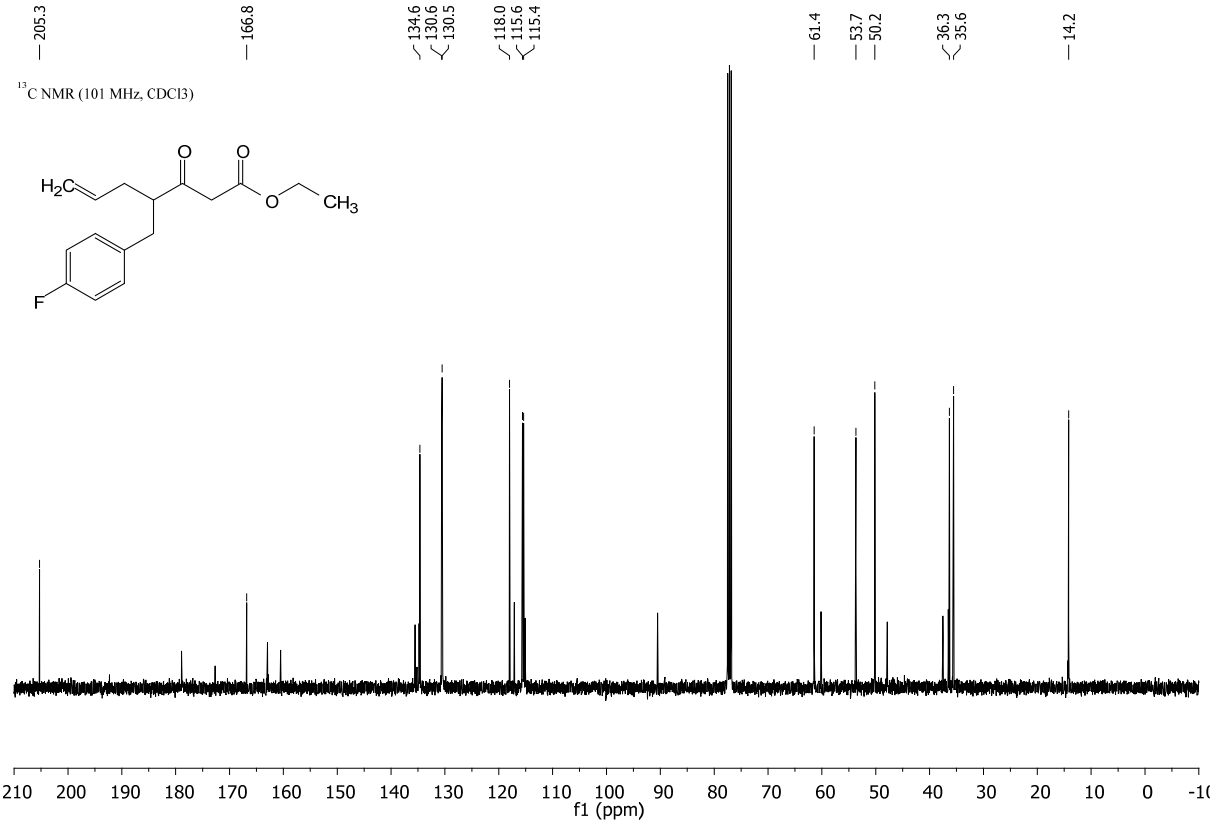
ethyl 4-benzyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate



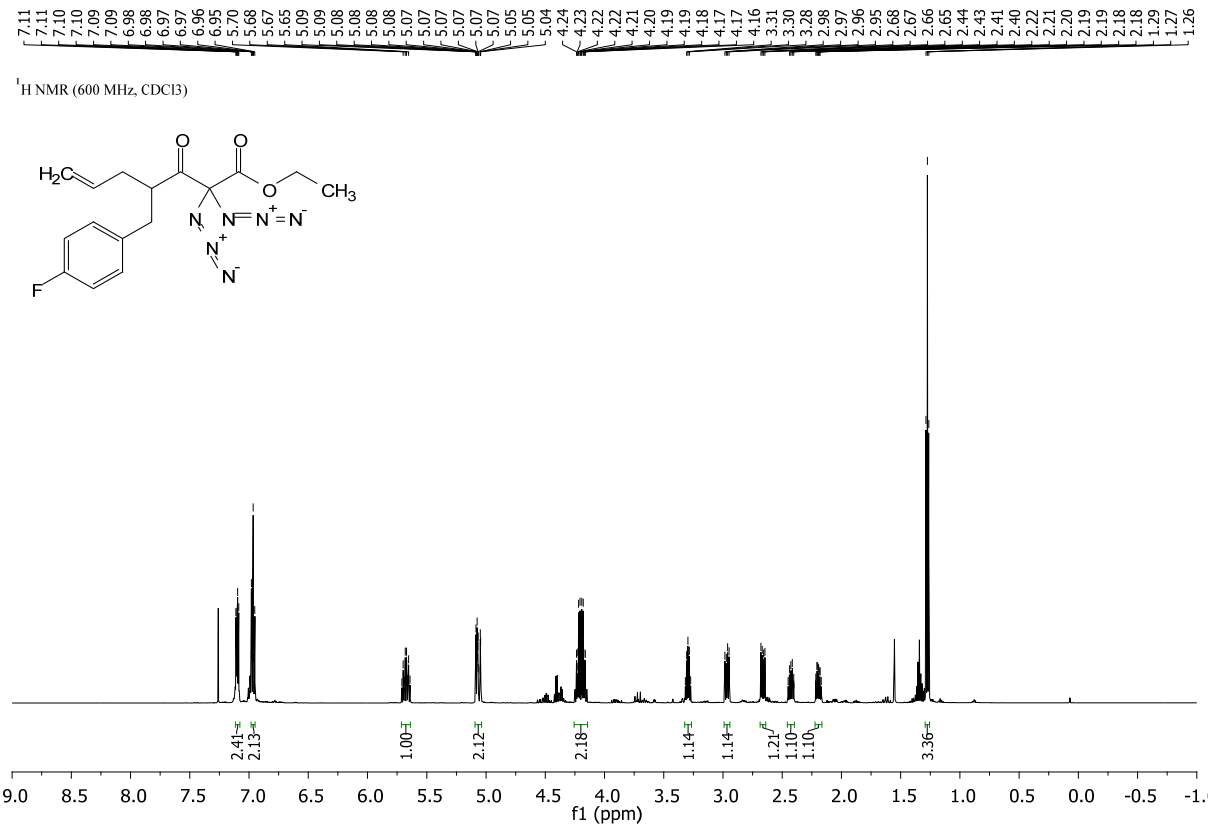


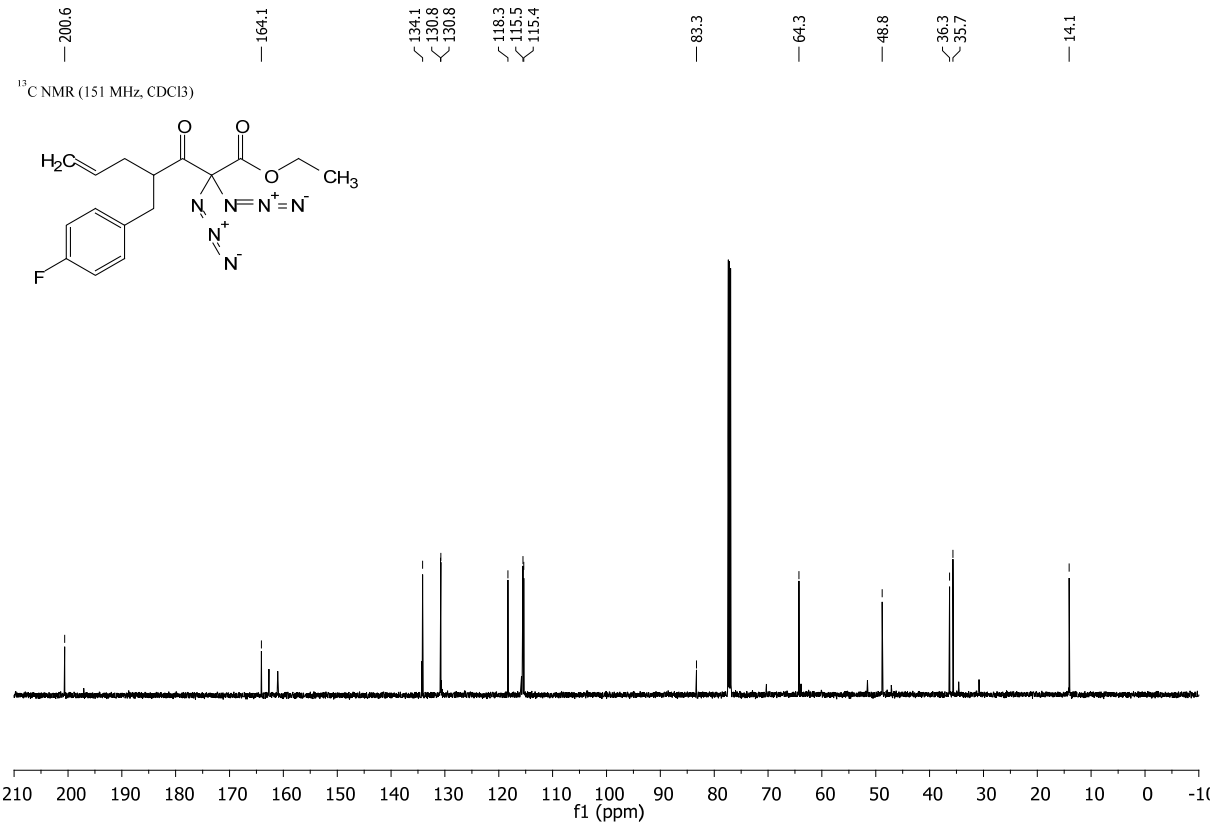
ethyl 4-(4-fluorobenzyl)-3-oxohept-6-enoate





ethyl 2,2-diazido-4-(4-fluorobenzyl)-3-oxohept-6-enoate (1f)

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134.1
130.8
130.8
118.3
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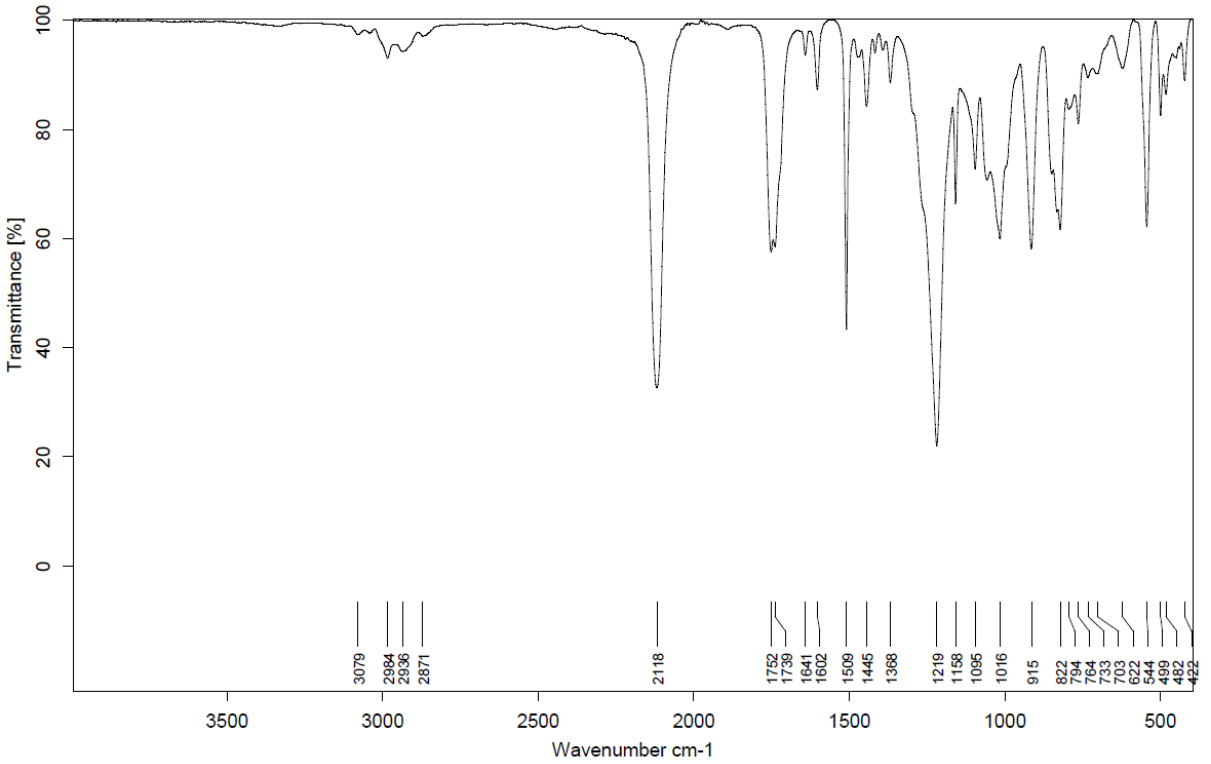
83.3
64.3
48.8
36.3
35.7
14.1
13C NMR (151 MHz, CDCl3)
f1 (ppm)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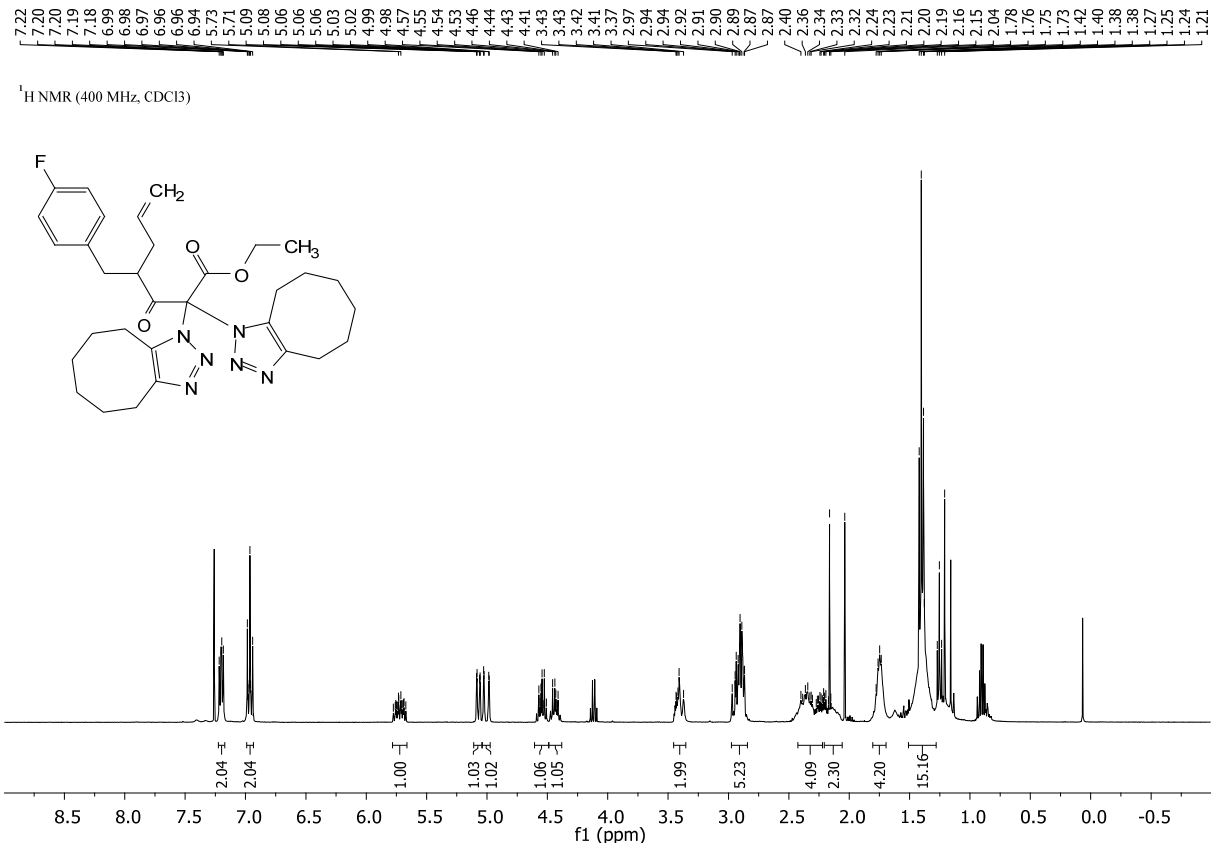
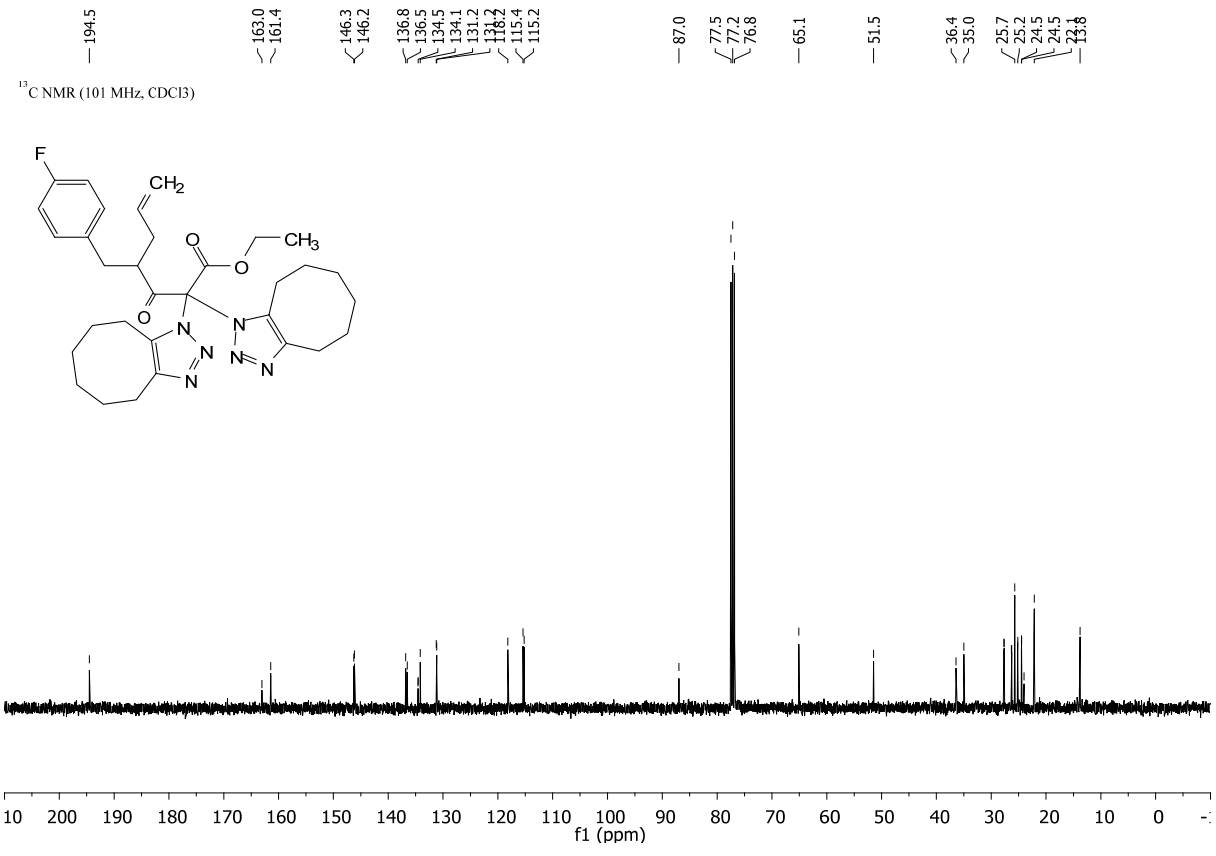
1095
1016
915
822
794
764
733
703
622
544
499
482
422

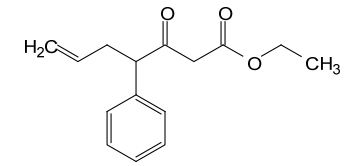
ethyl 4-(4-fluorobenzyl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

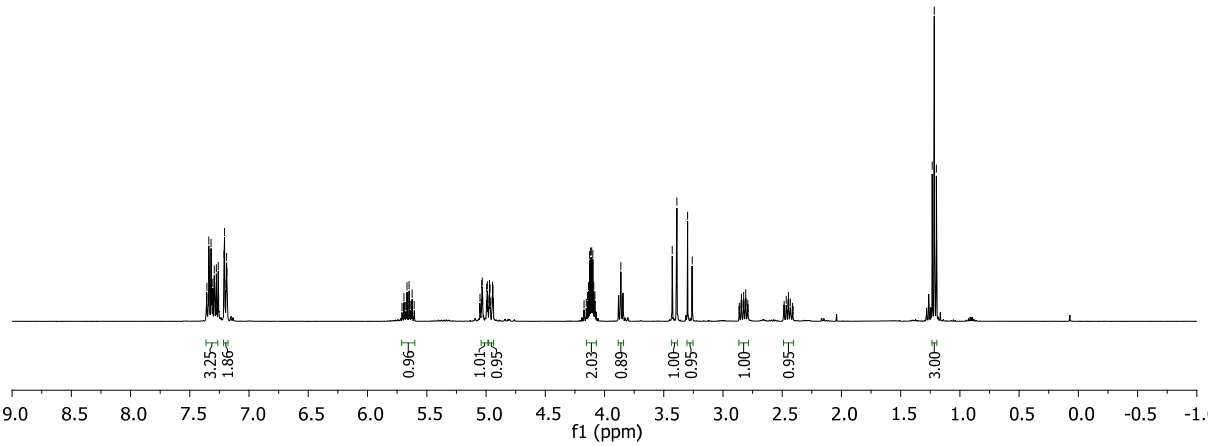




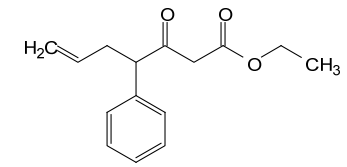
ethyl 3-oxo-4-phenylhept-6-enoate

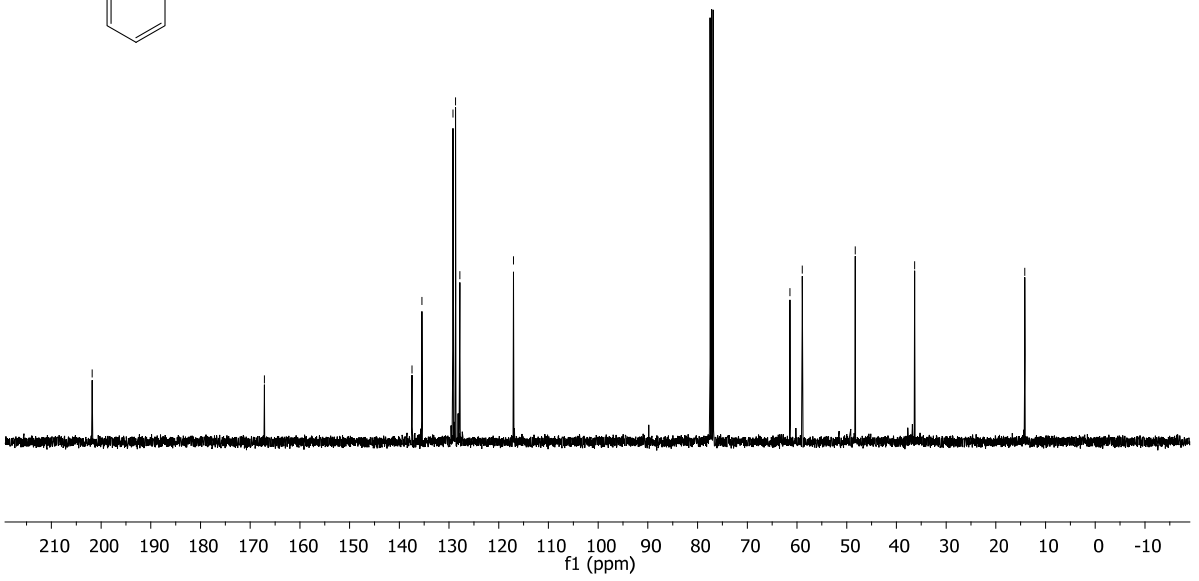
^{1}H NMR (400 MHz, CDCl3)



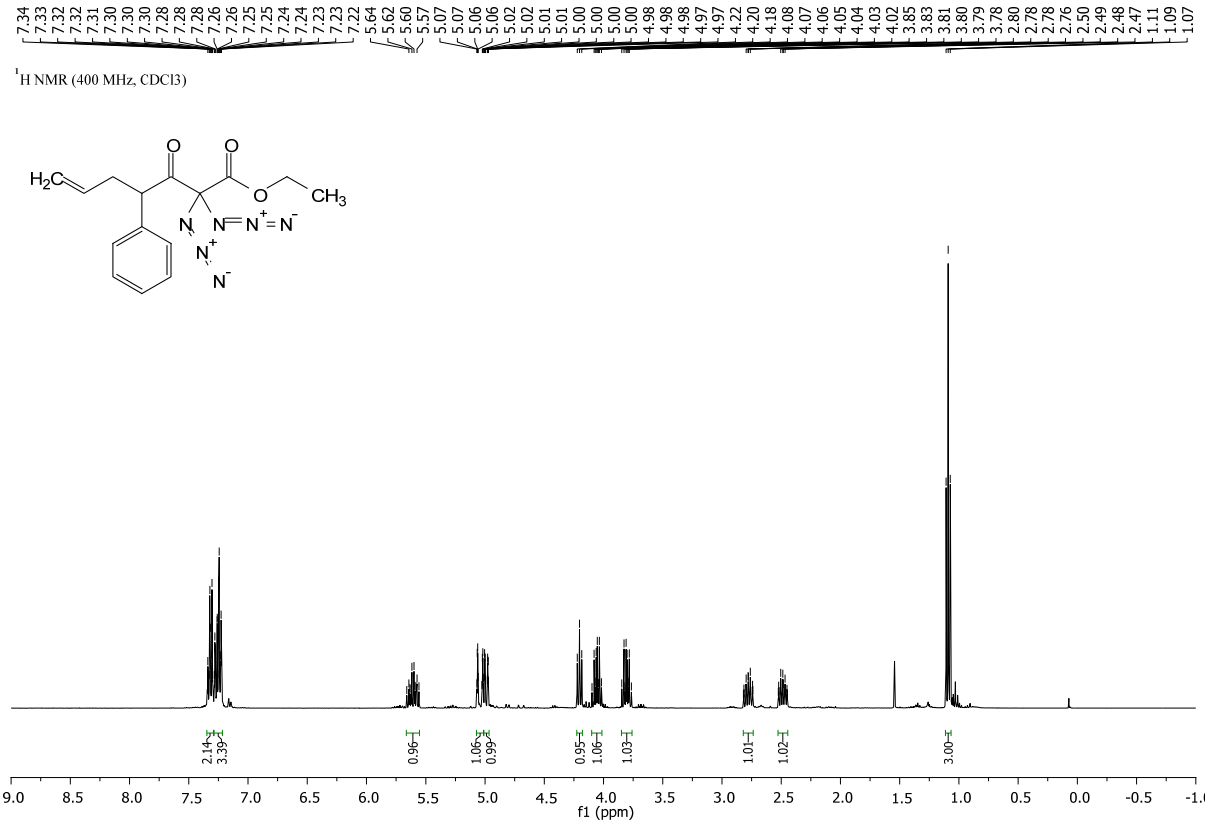


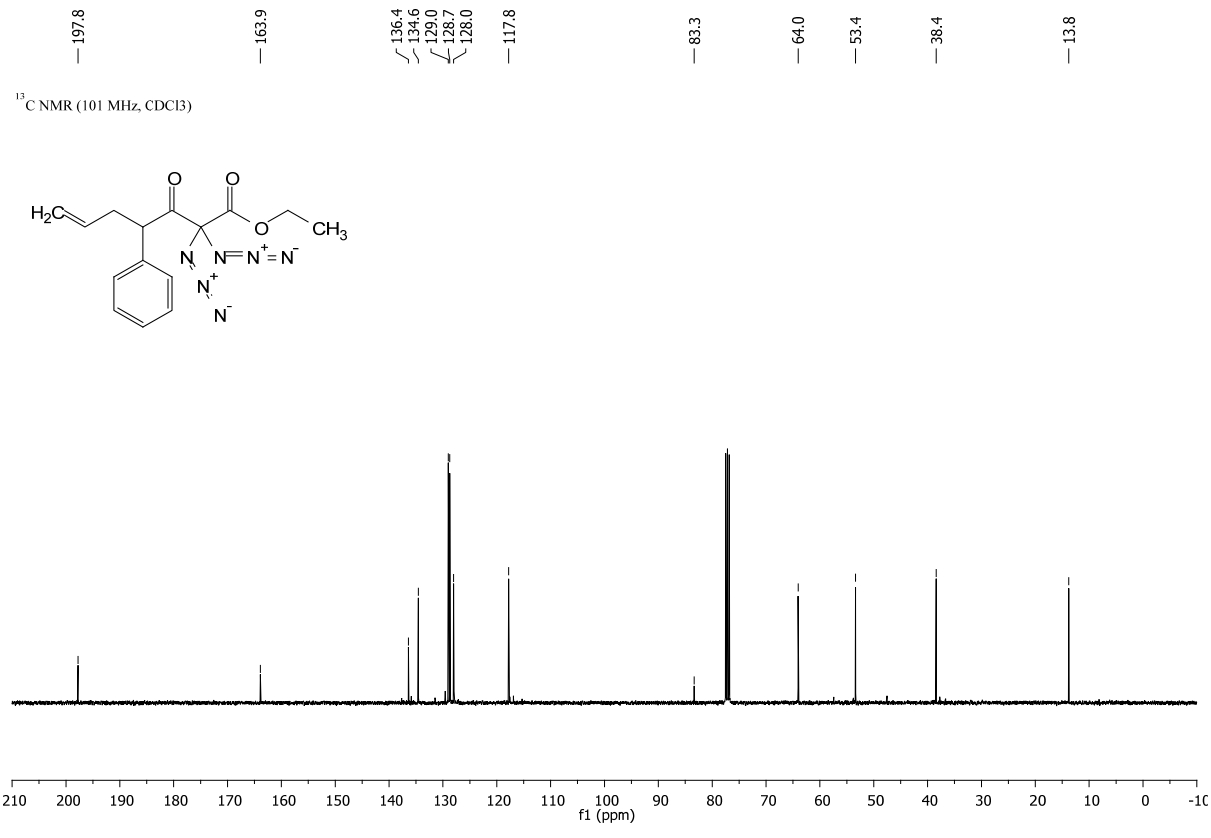
^{13}C NMR (101 MHz, CDCl3)

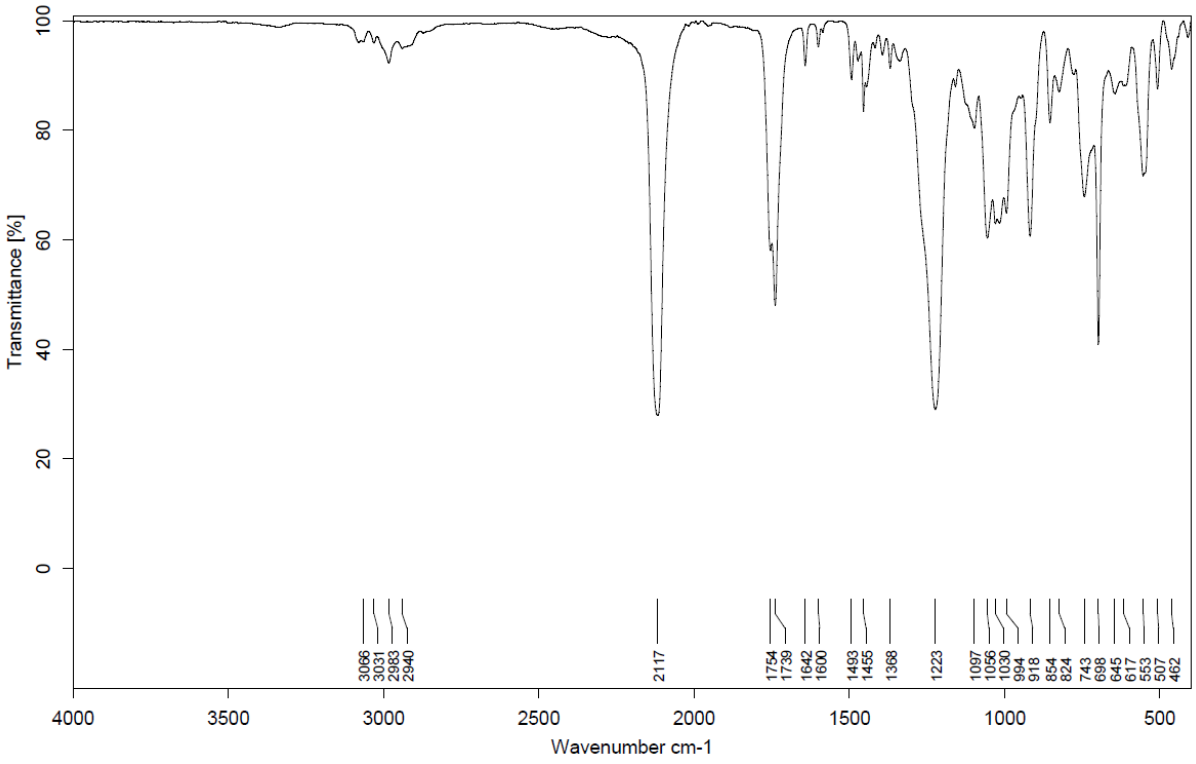




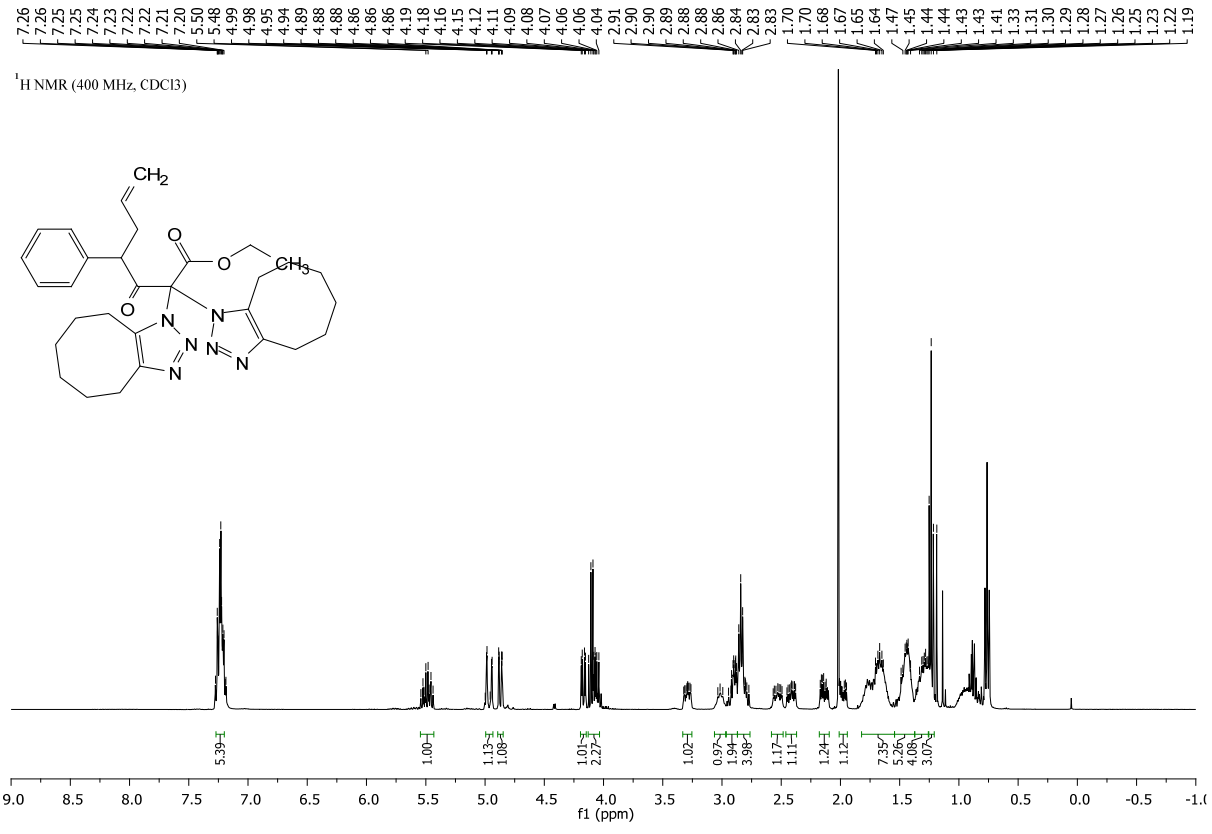
ethyl 2,2-diazido-3-oxo-4-phenylhept-6-enoate (1g)

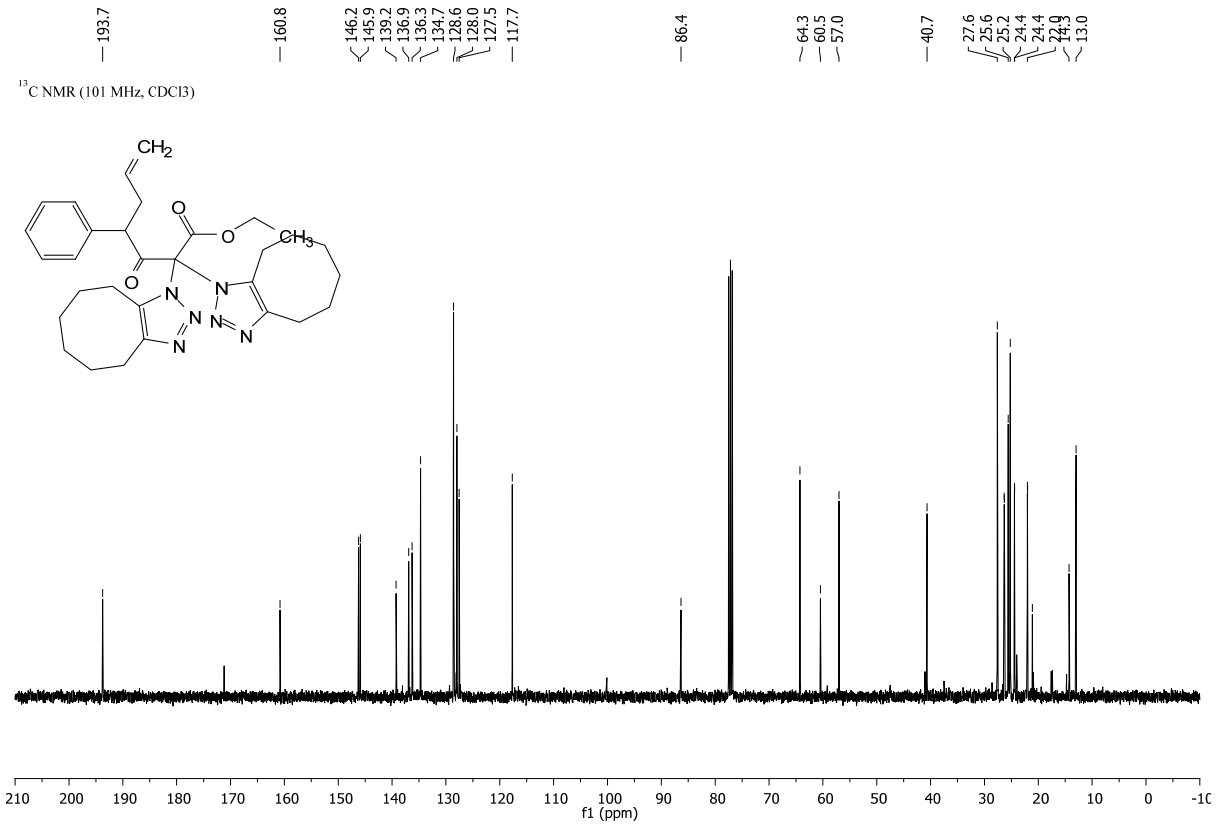




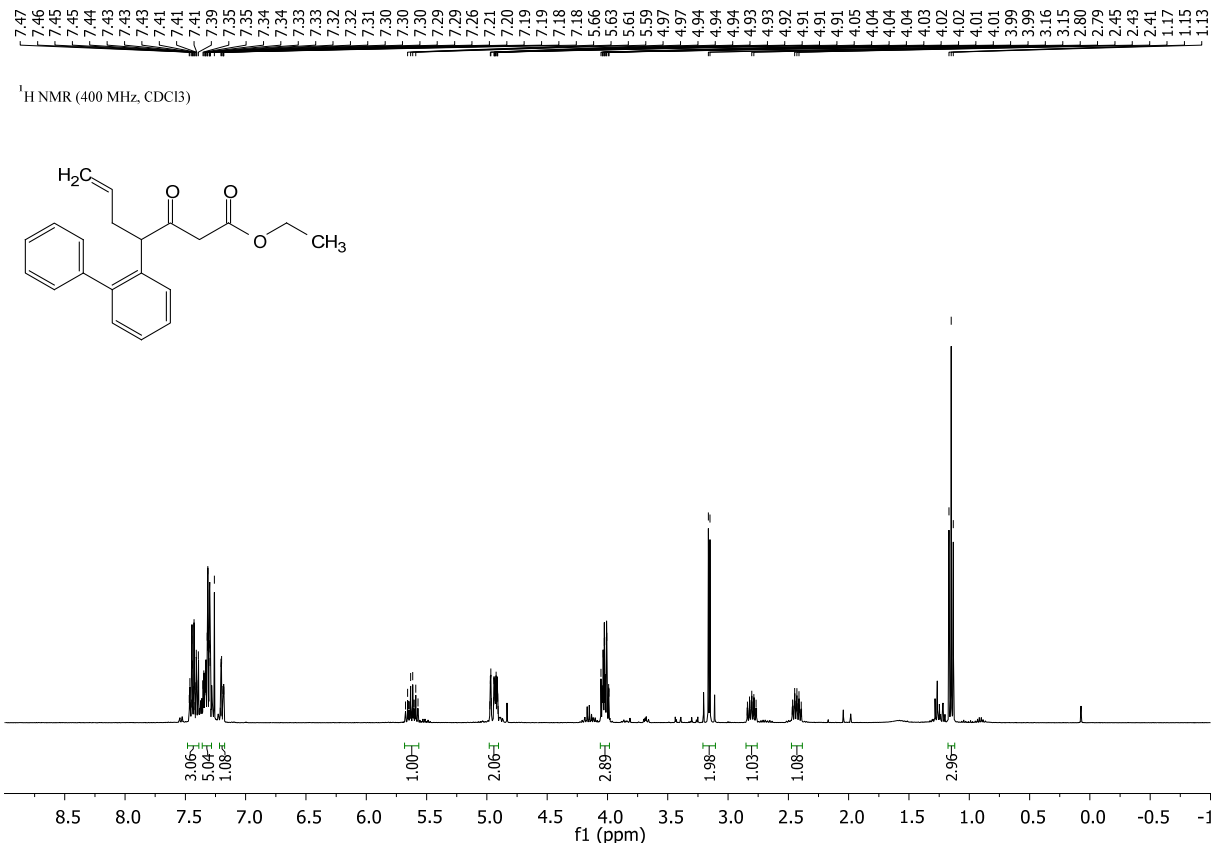


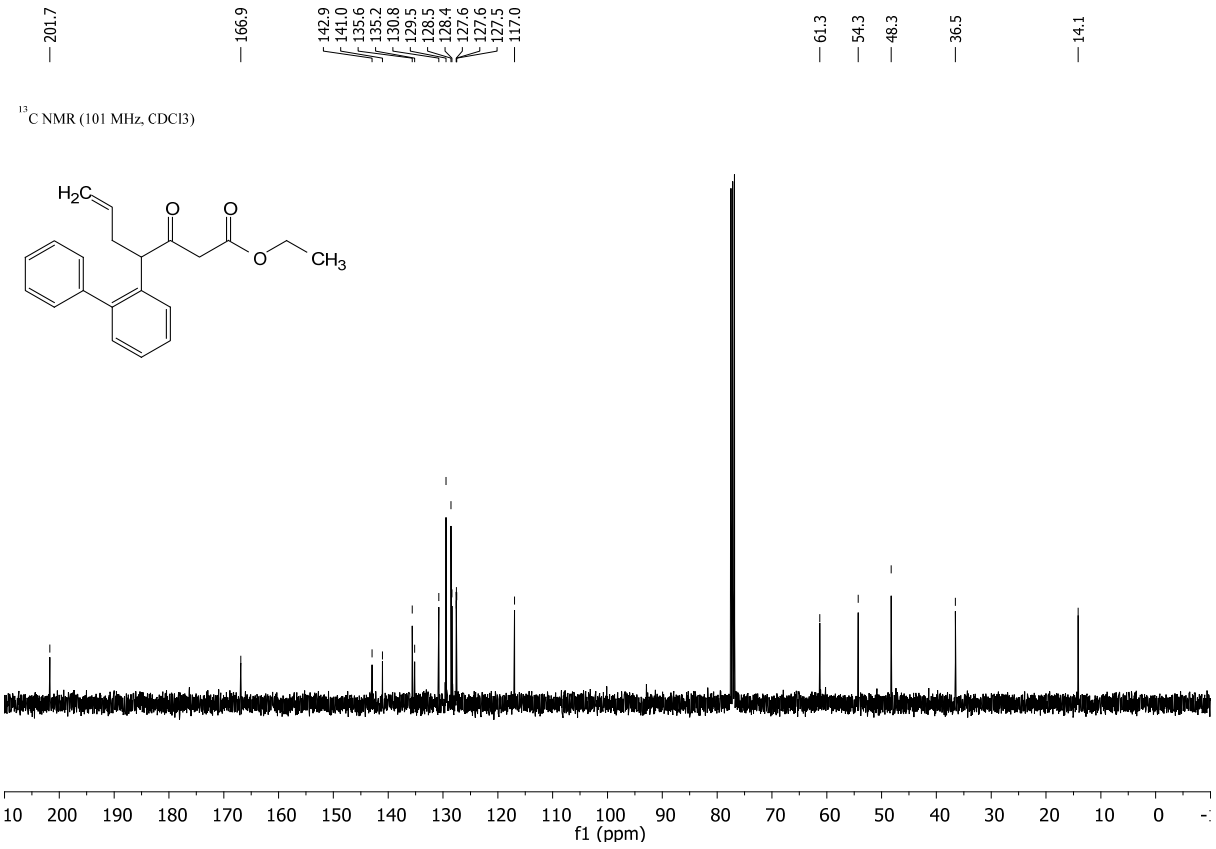
ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxo-4-phenylhept-6-enoate



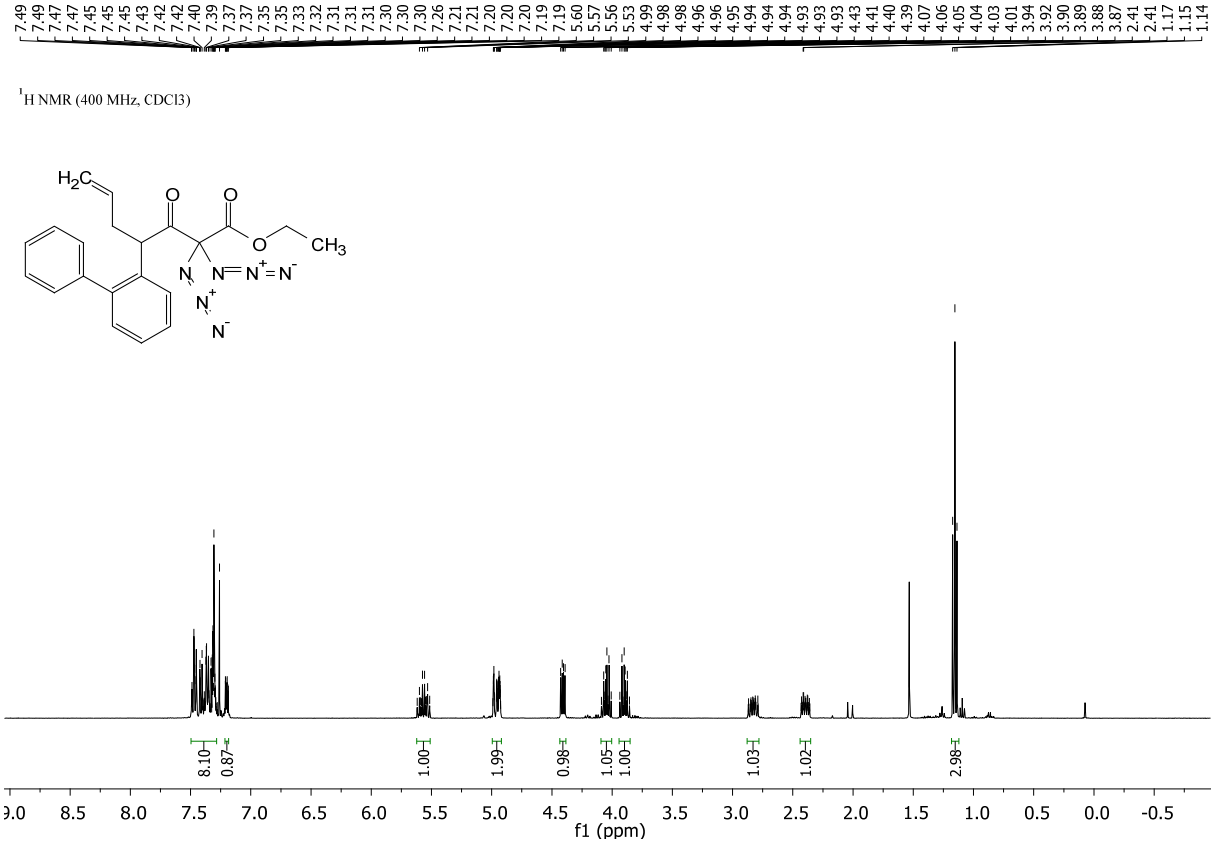


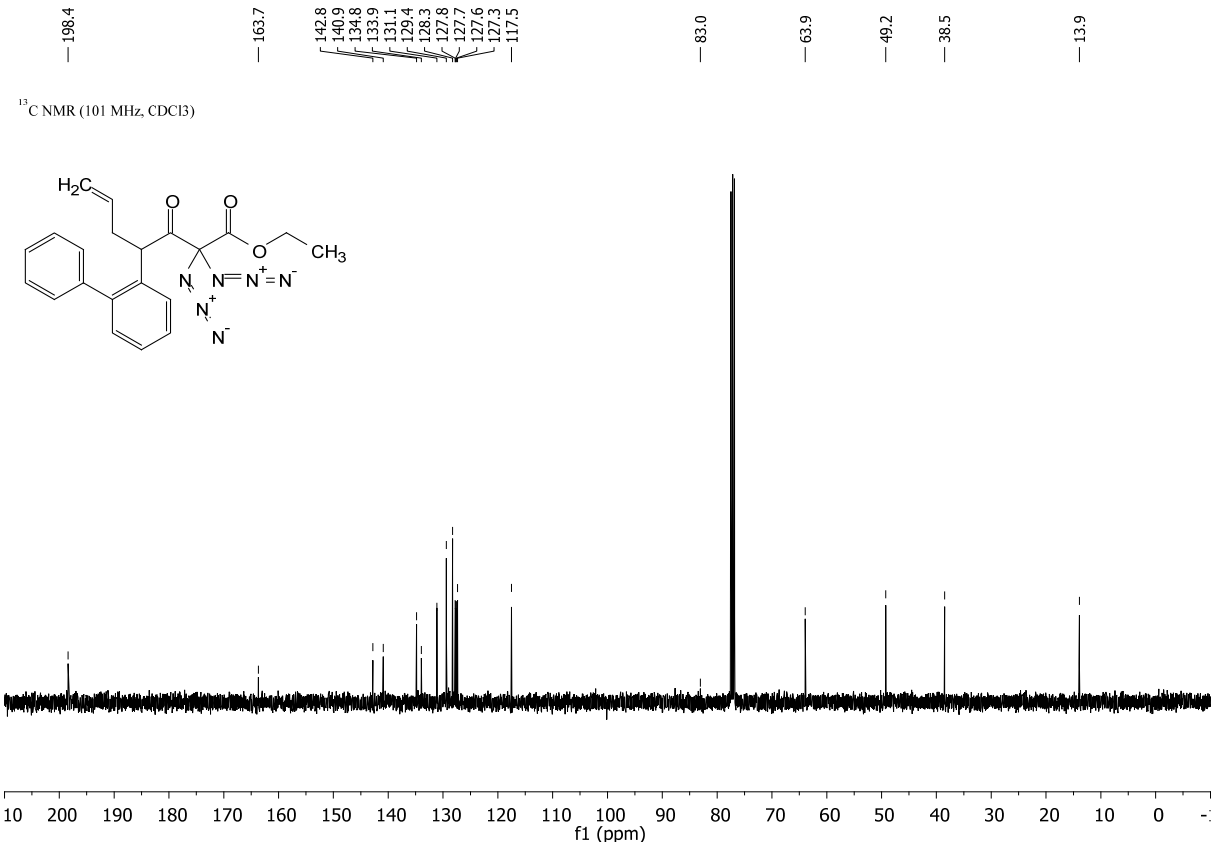
ethyl 4-([1,1'-biphenyl]-2-yl)-3-oxohept-6-enoate

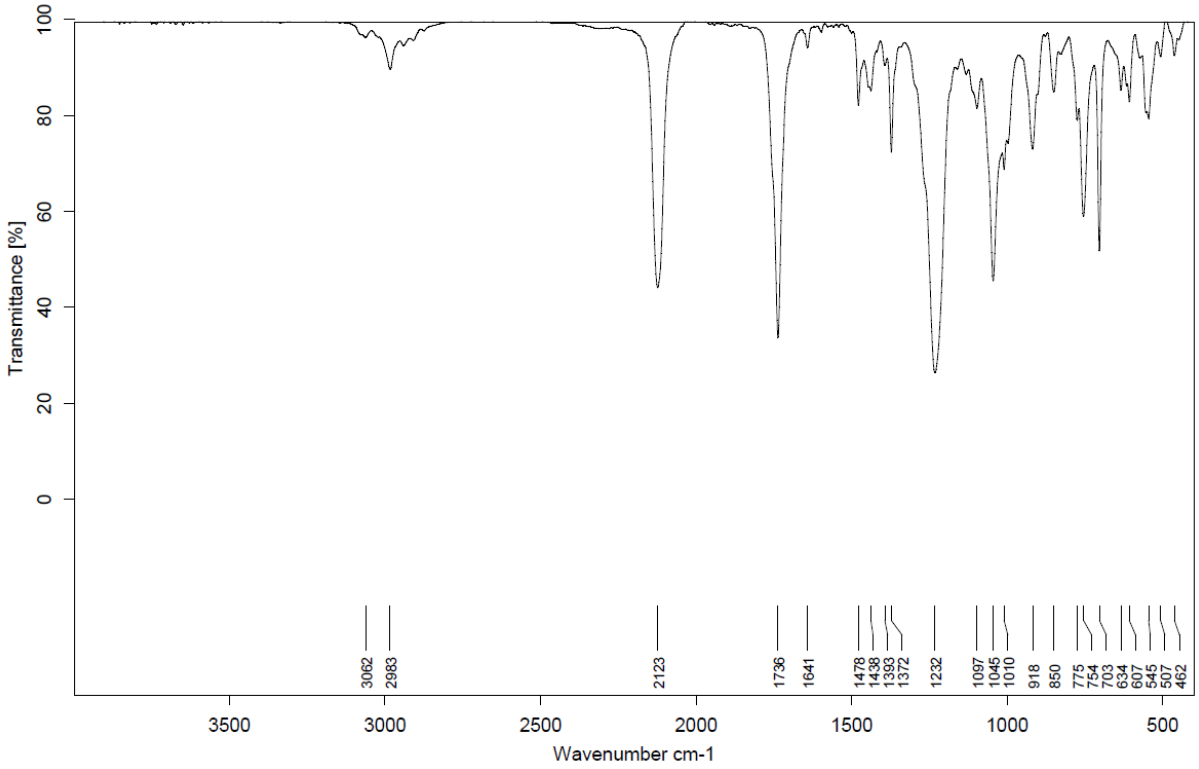




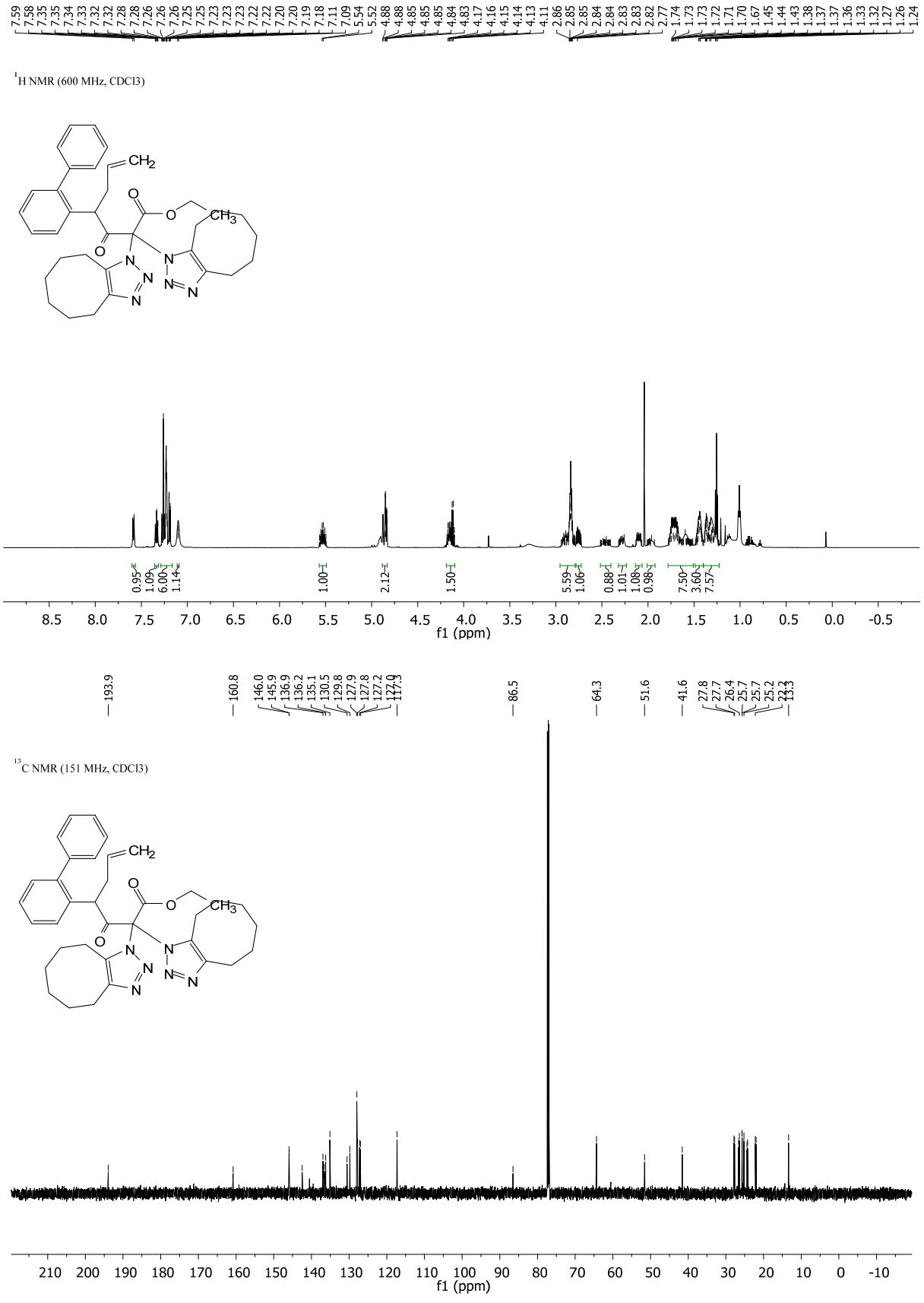
ethyl 4-([1,1'-biphenyl]-2-yl)-2,2-diazido-3-oxohept-6-enoate (1h)



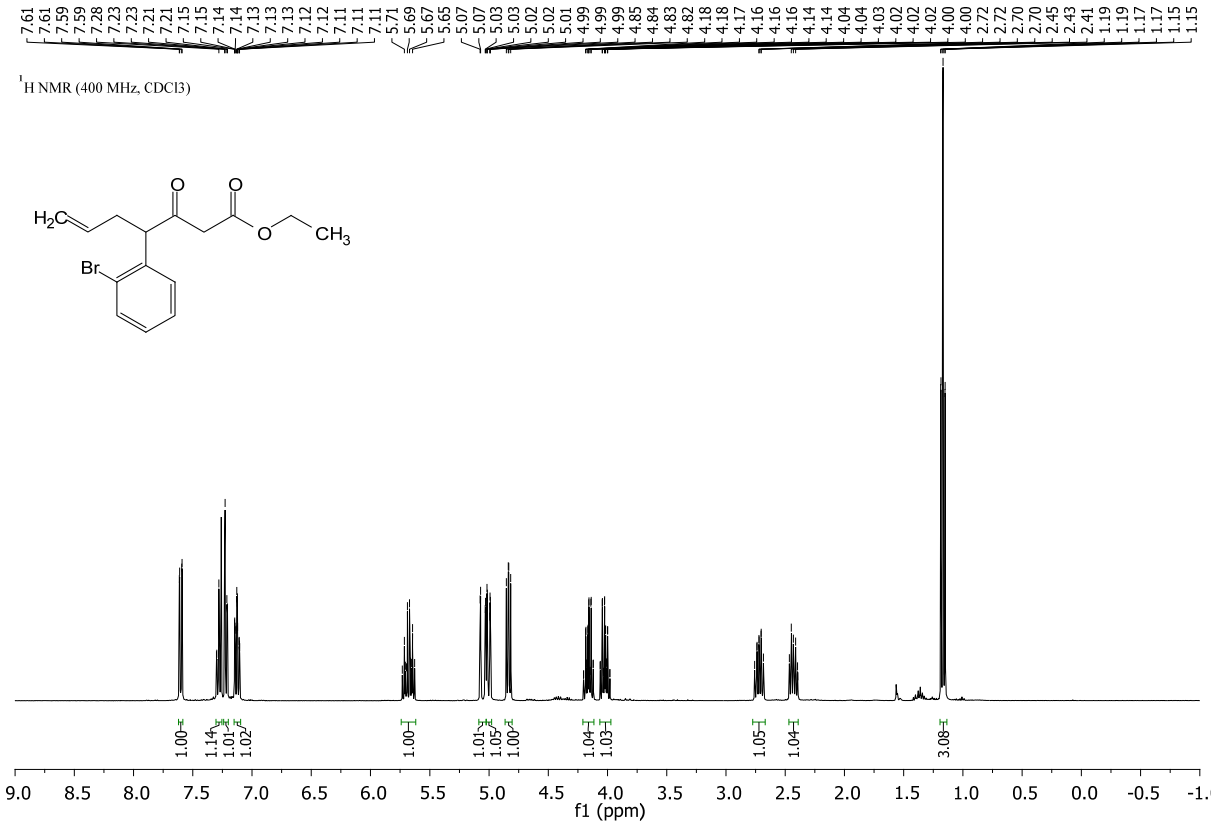

198.4
163.7
142.8
140.9
134.8
133.9
131.1
129.4
128.3
127.8
127.7
127.6
127.3
117.5
83.0
63.9
49.2
38.5
13.9
13C NMR (101 MHz, CDCl3)
H2C
O
O
O
CH3
N
N
N+
N-
N+
N-
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

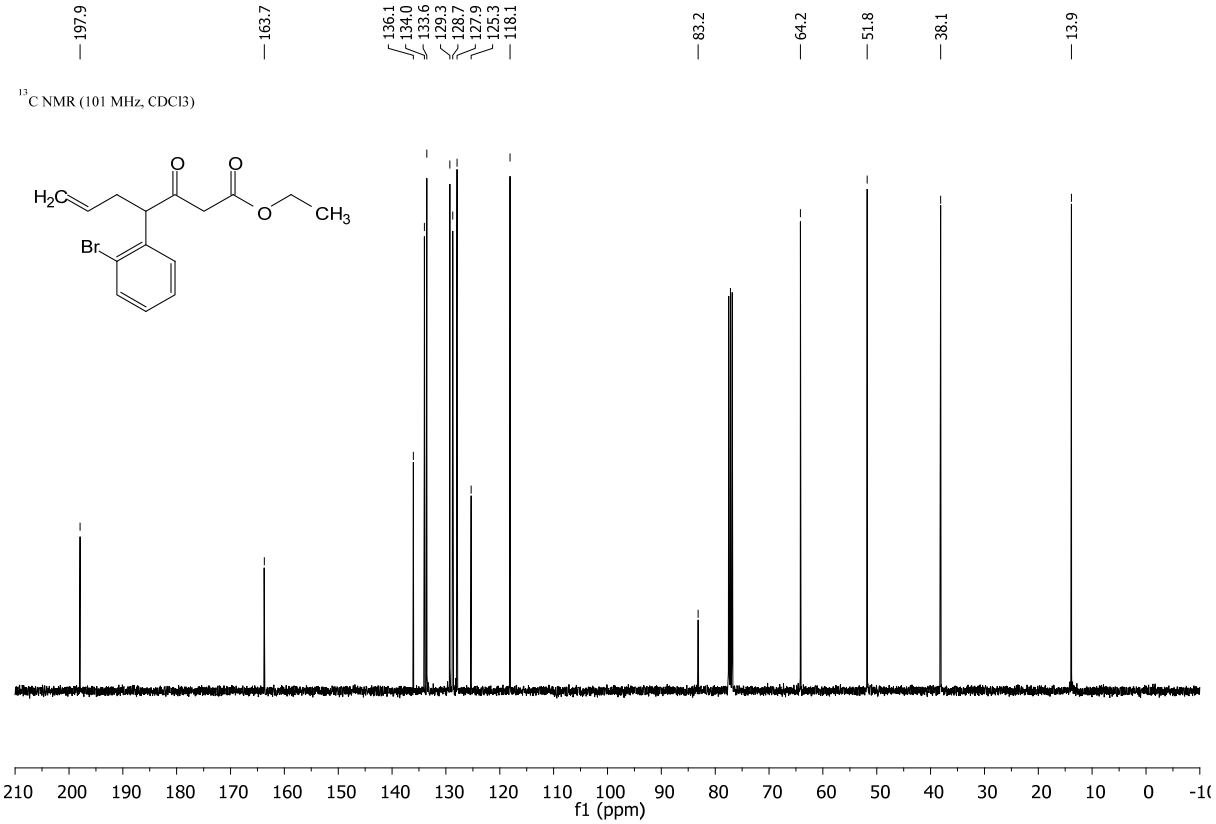

Transmittance [%]
100
80
60
40
20
0
3062
2983
2123
1736
1641
1478
1438
1393
1372
1232
1097
1045
1010
918
850
775
754
703
634
607
545
507
462
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

ethyl 4-([1,1'-biphenyl]-2-yl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

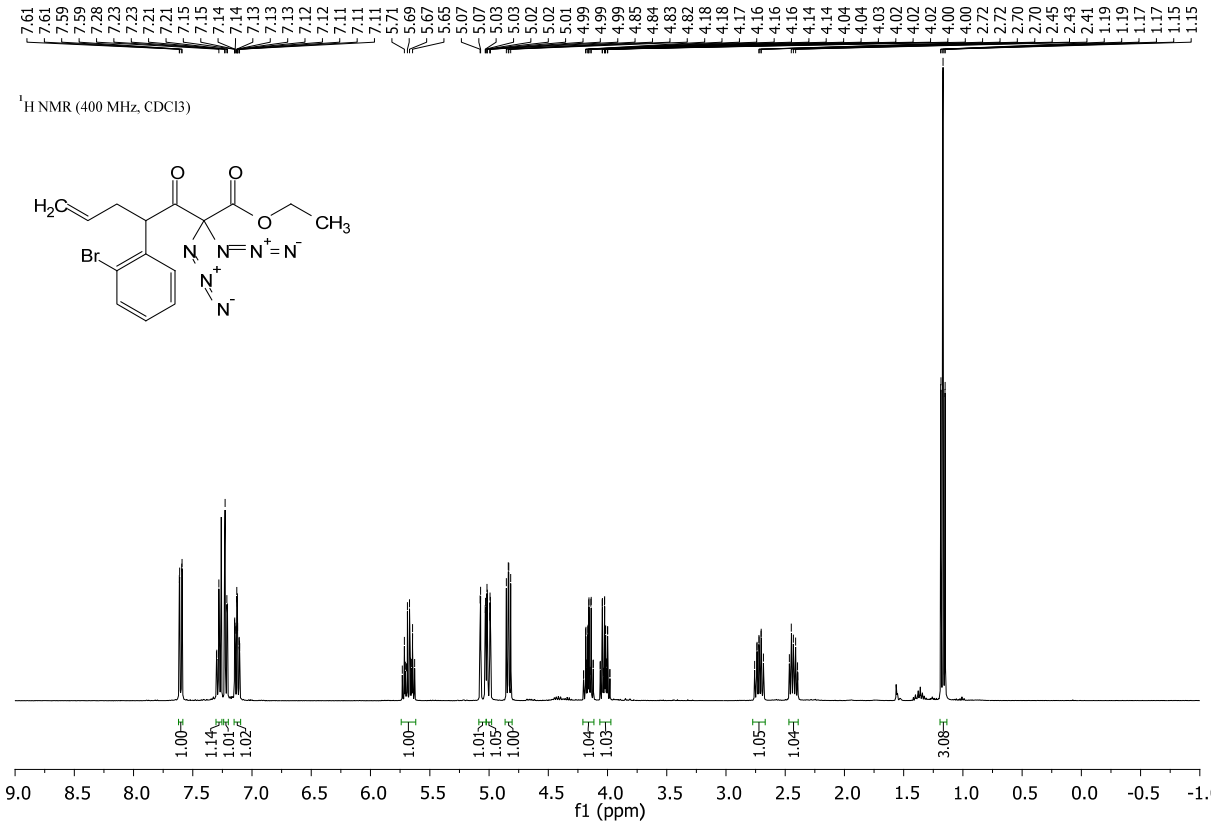


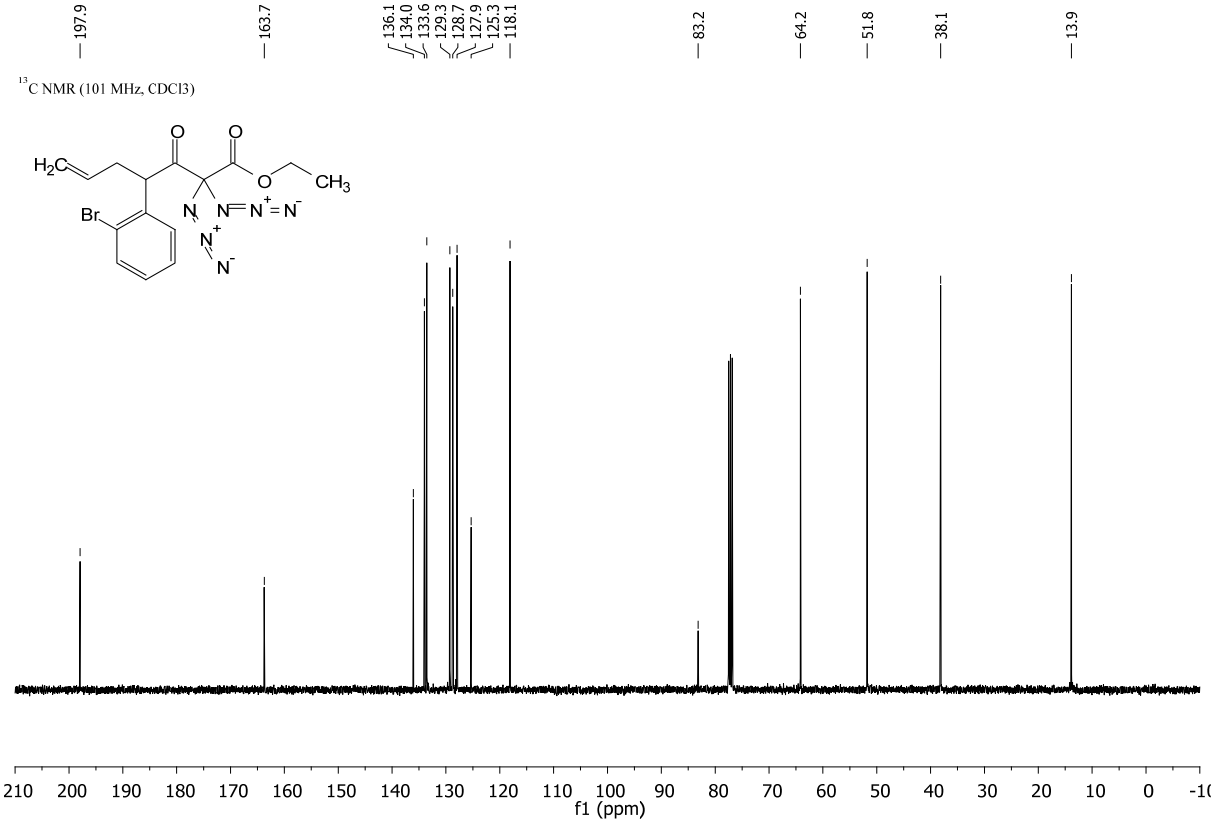
ethyl 4-(2-bromophenyl)-3-oxohept-6-enoate

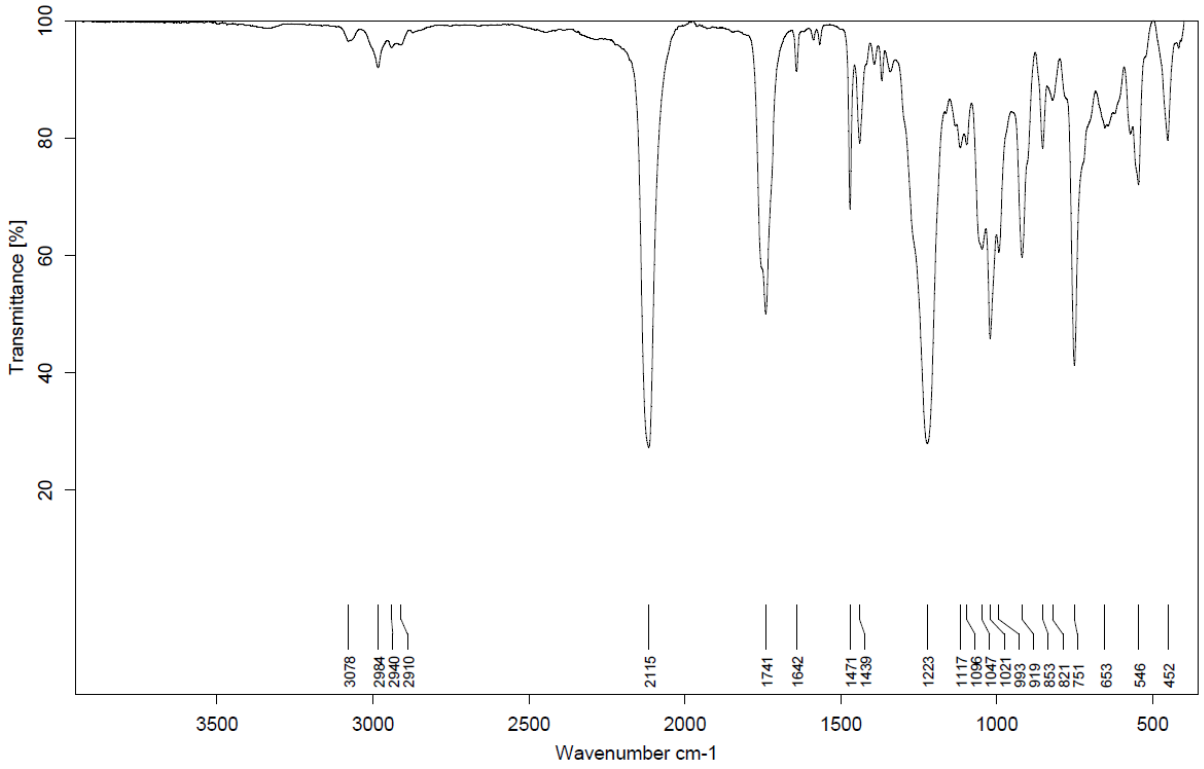




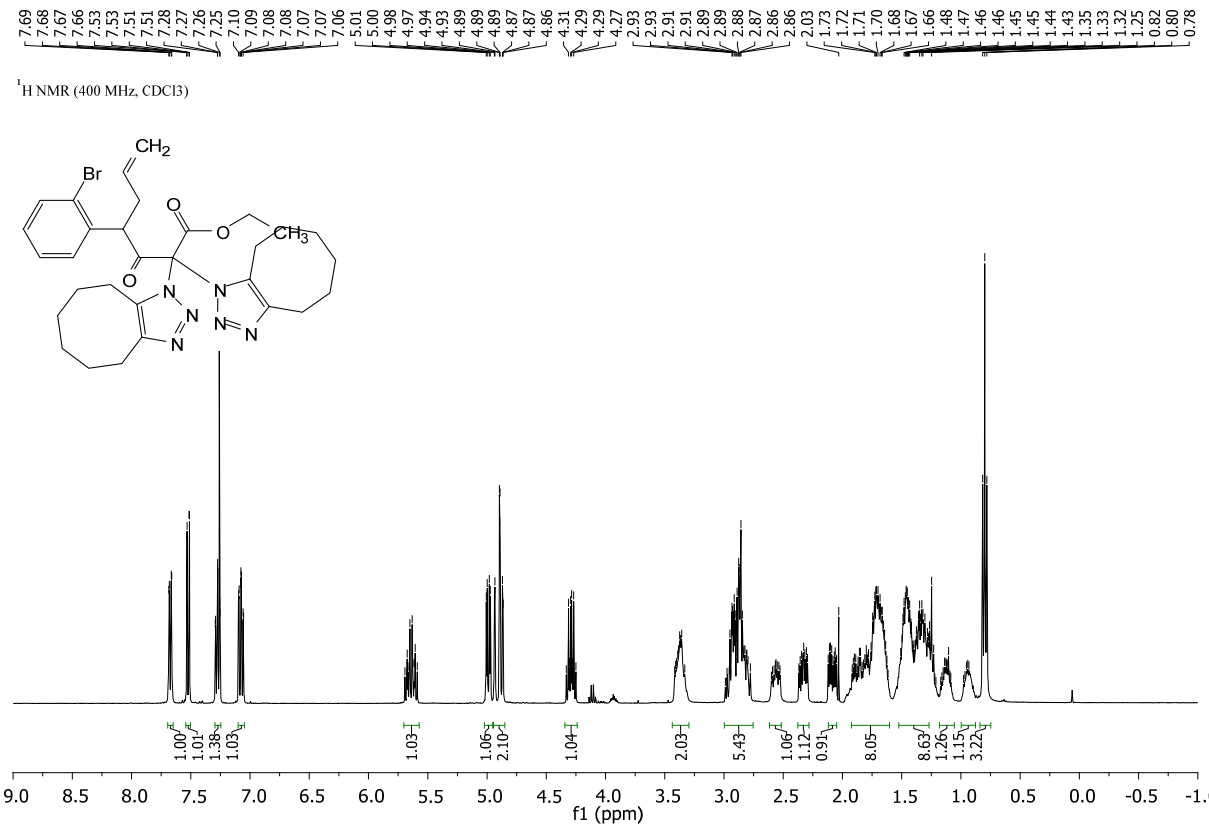
ethyl 2,2-diazido-4-(2-bromophenyl)-3-oxohept-6-enoate (1i)

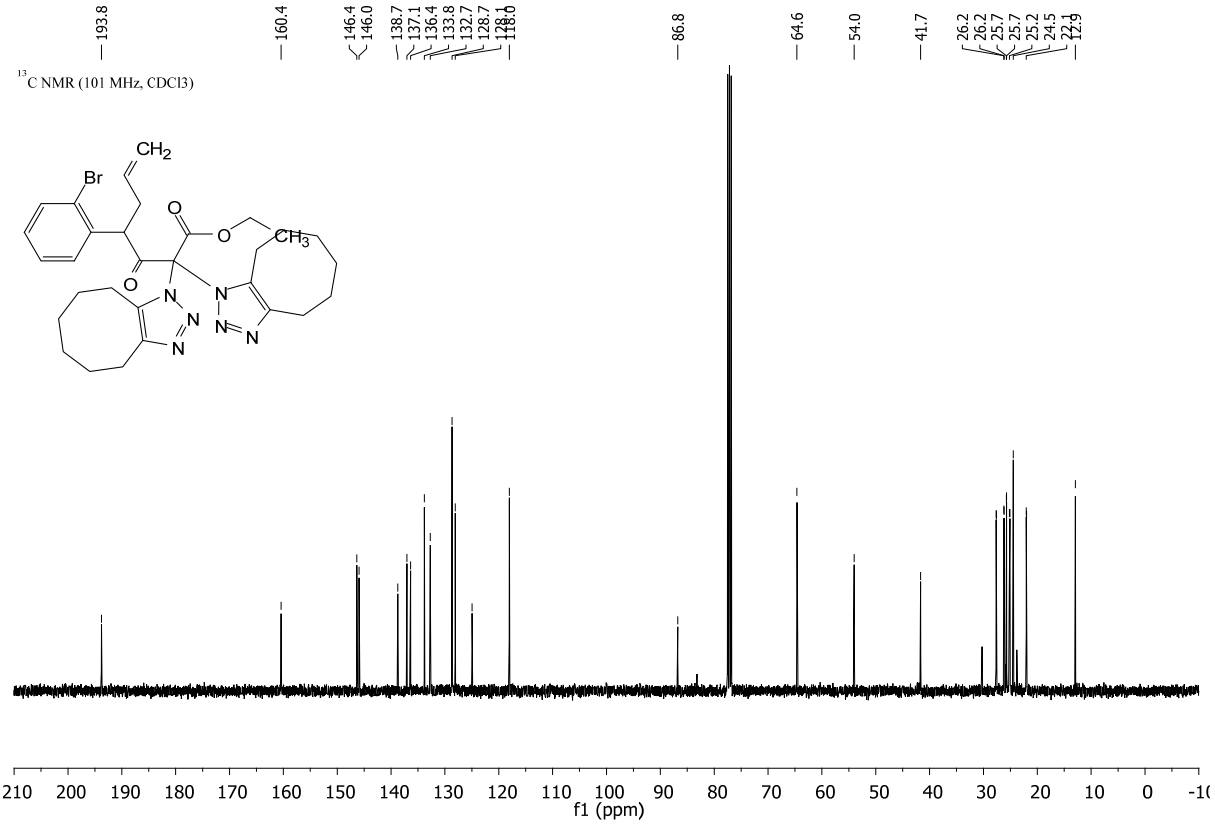




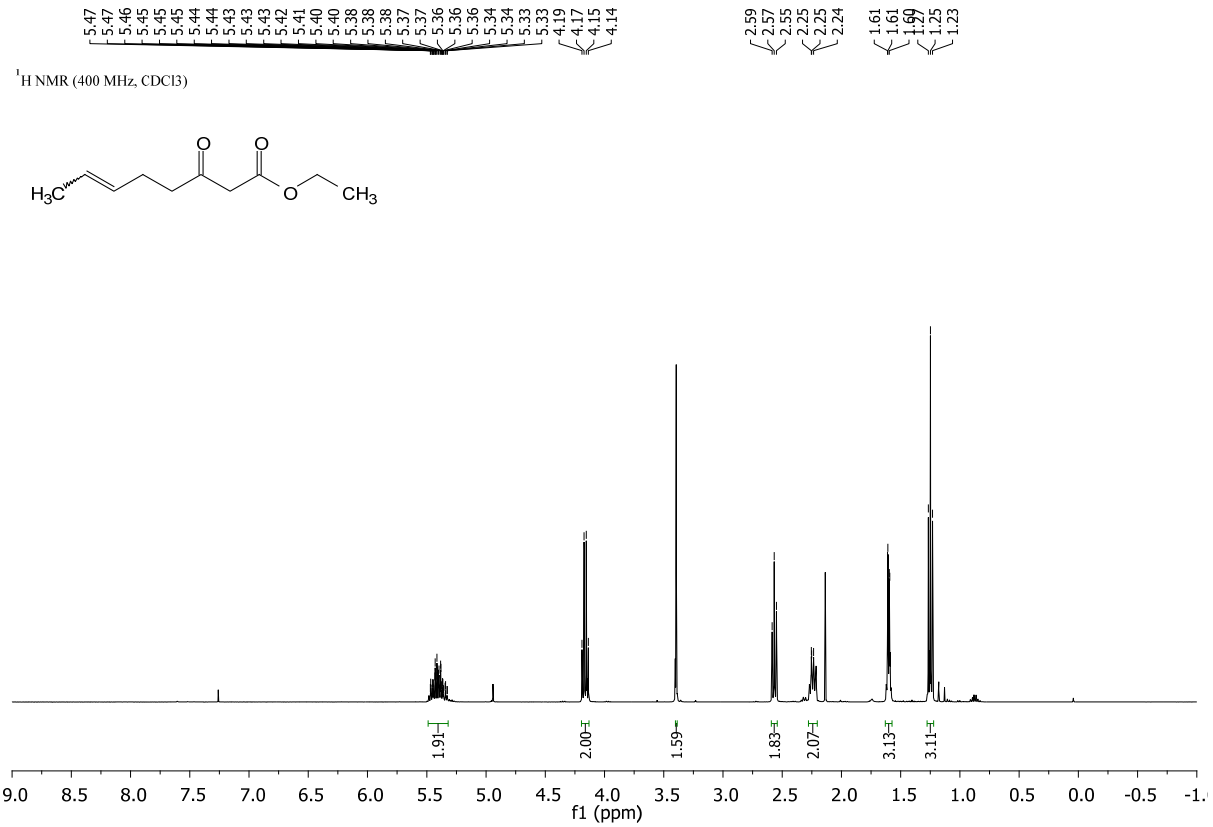


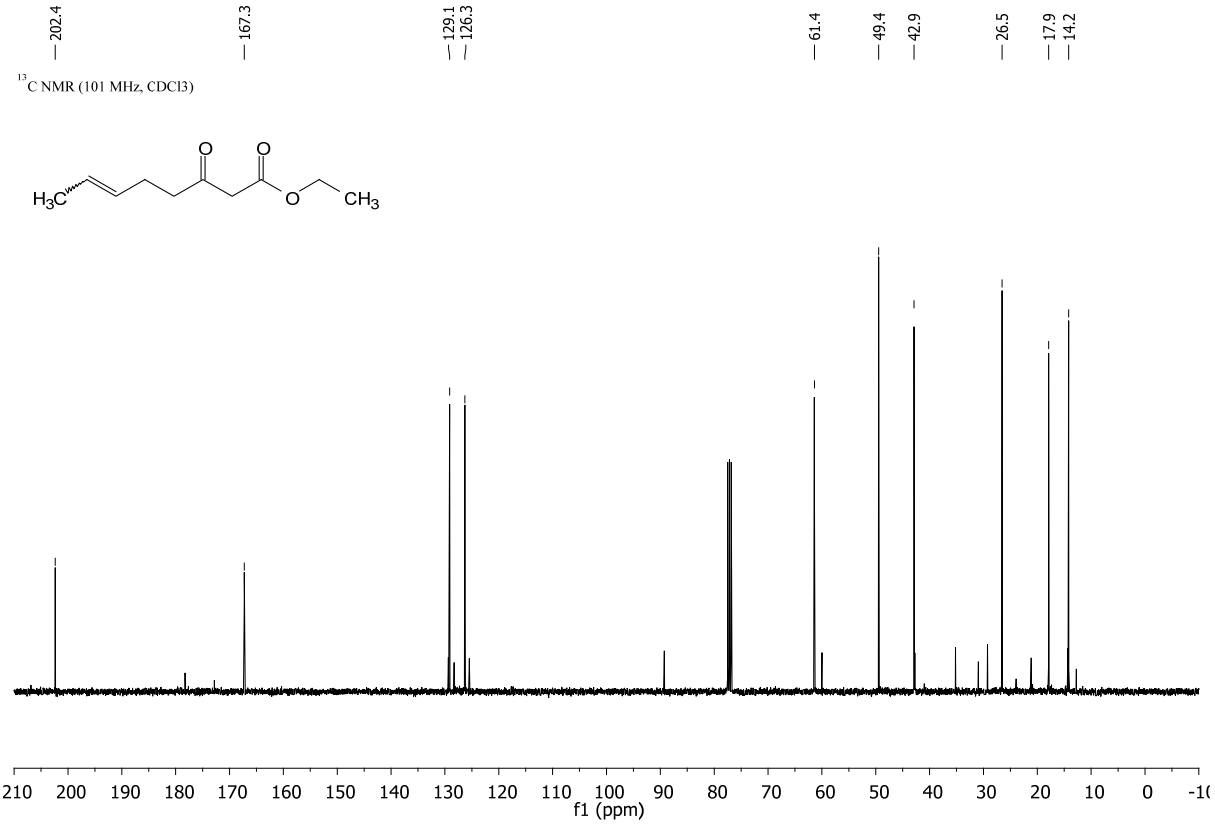
ethyl 4-(2-bromophenyl)-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate



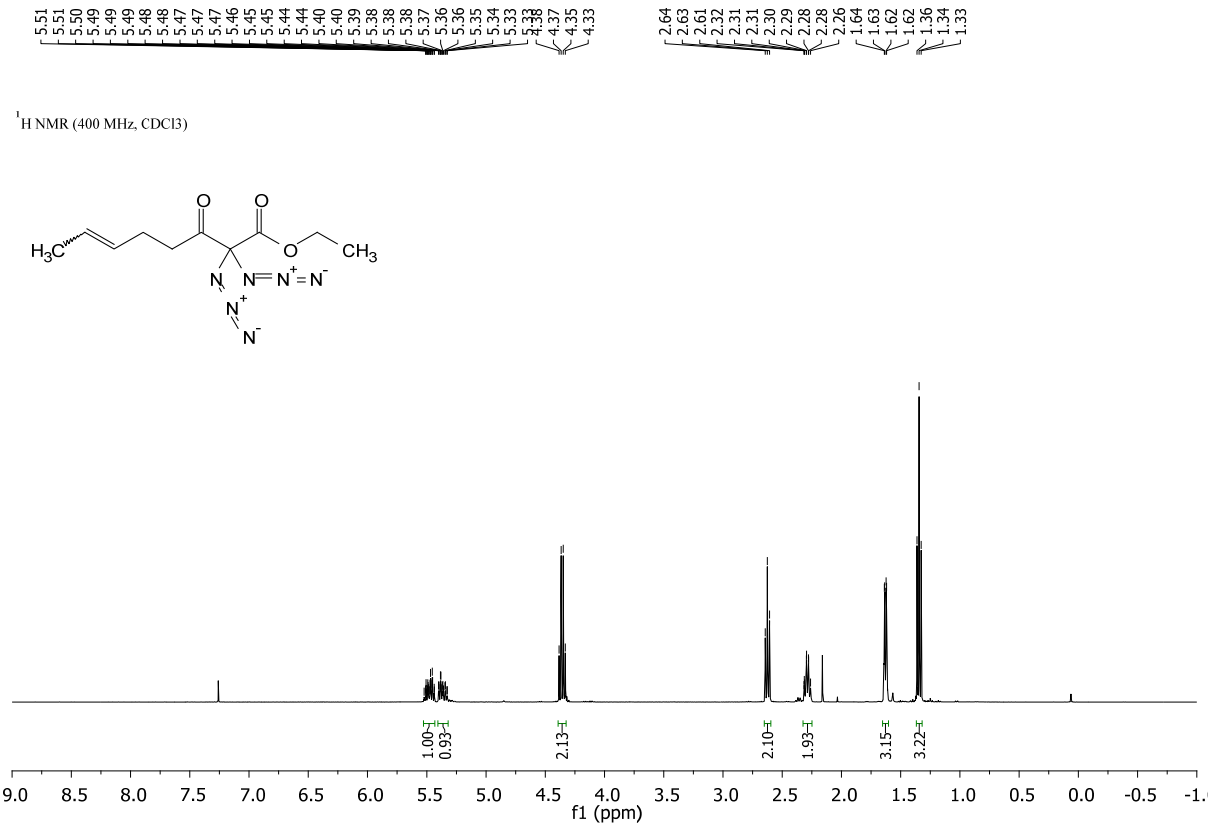


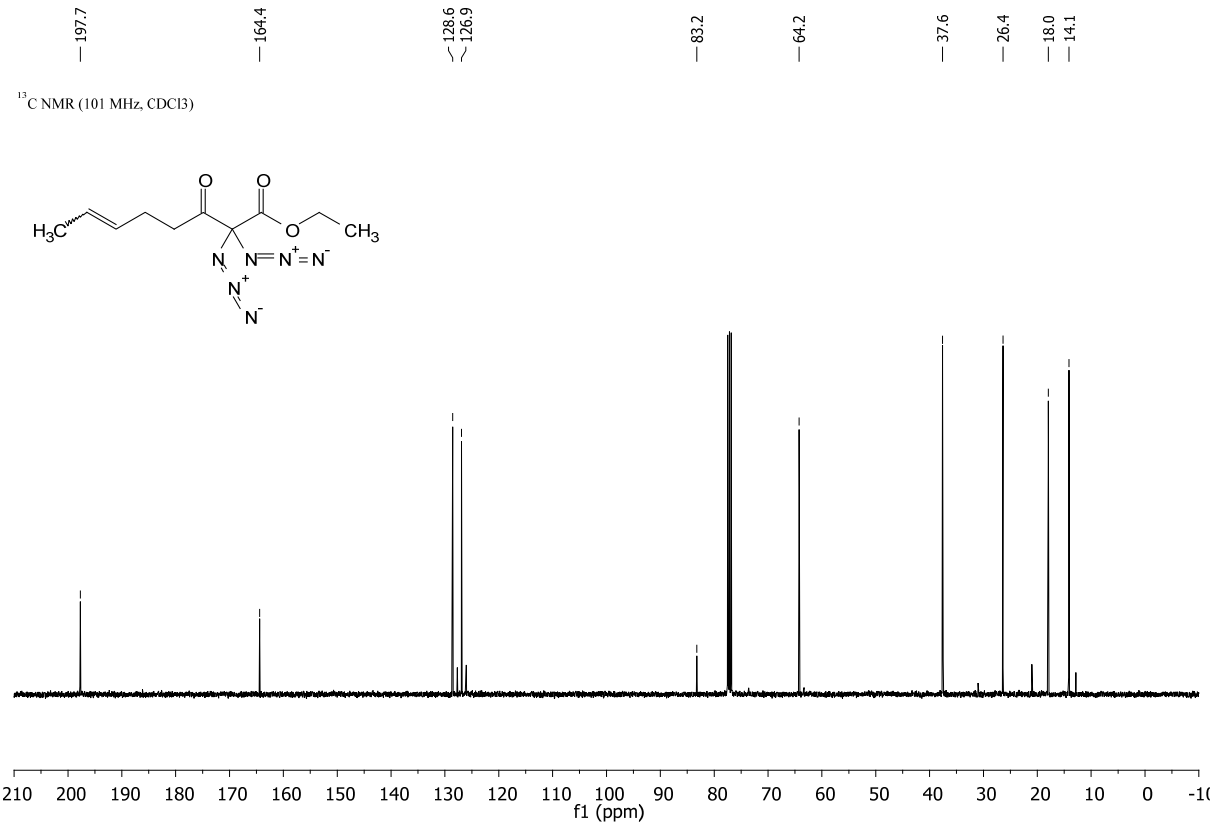
ethyl 3.oxooct-6-enoate

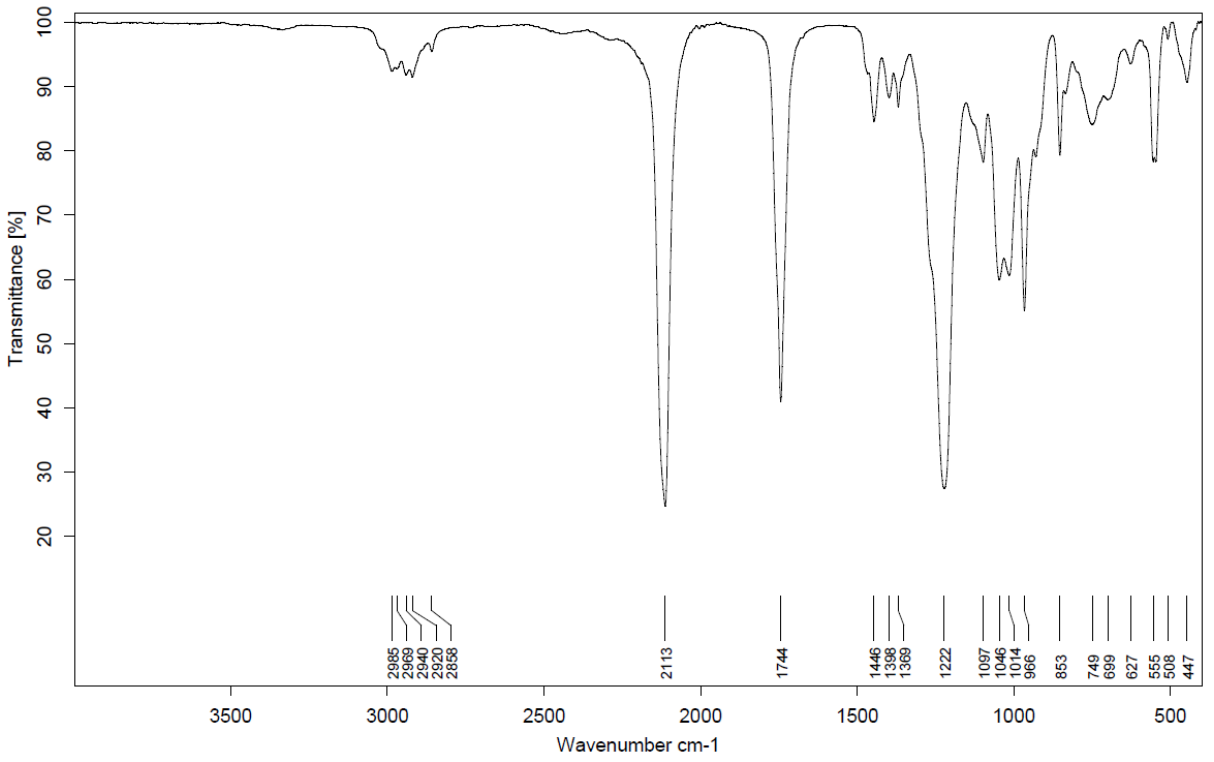




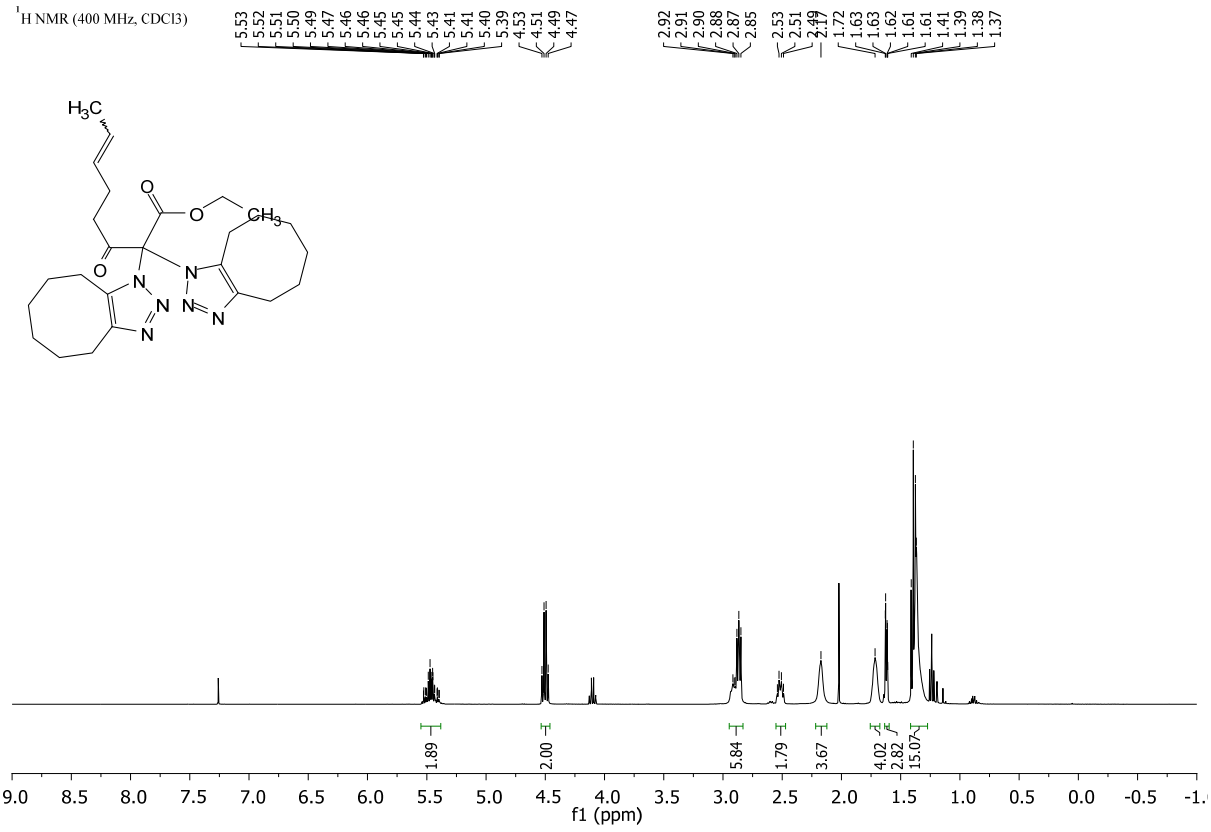
ethyl 2,2-diazido-3-oxooct-6-enoate (1j)

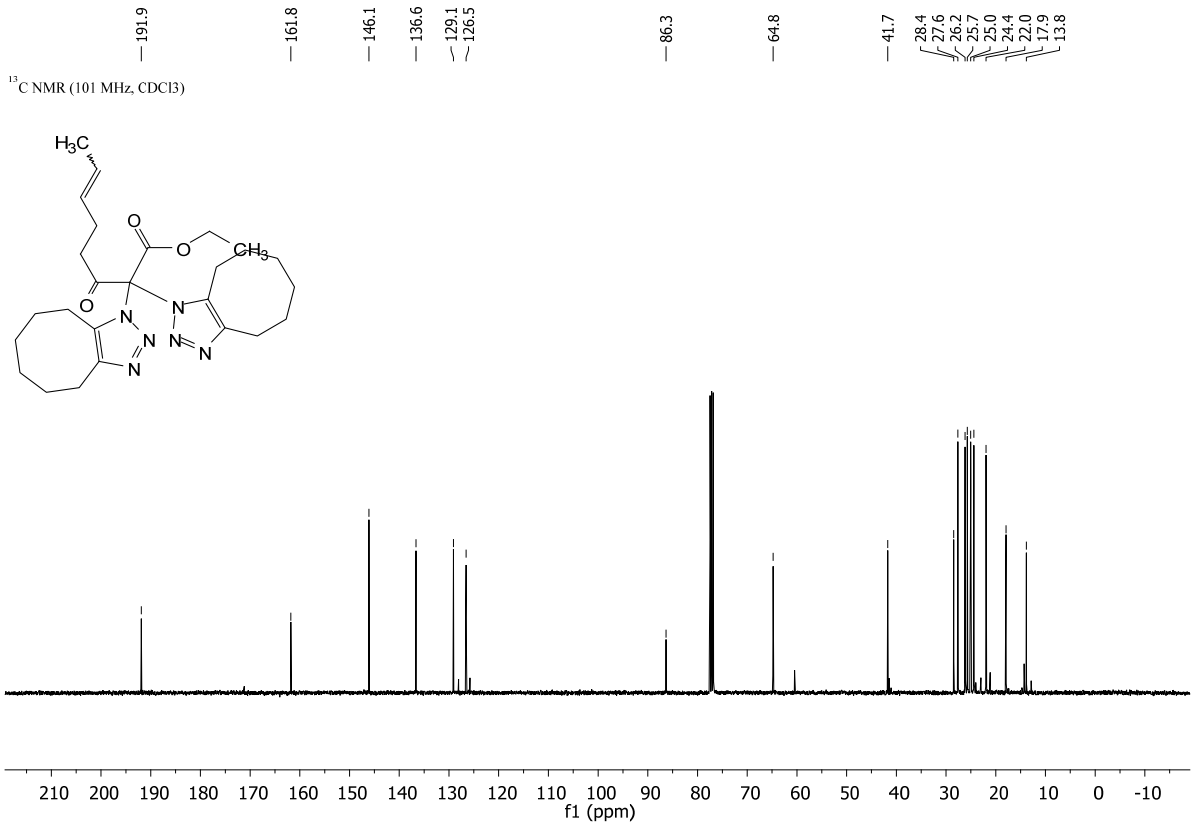



197.7
164.4
128.6
126.9
83.2
64.2
37.6
26.4
18.0
14.1
13C NMR (101 MHz, CDCl3)
f1 (ppm)

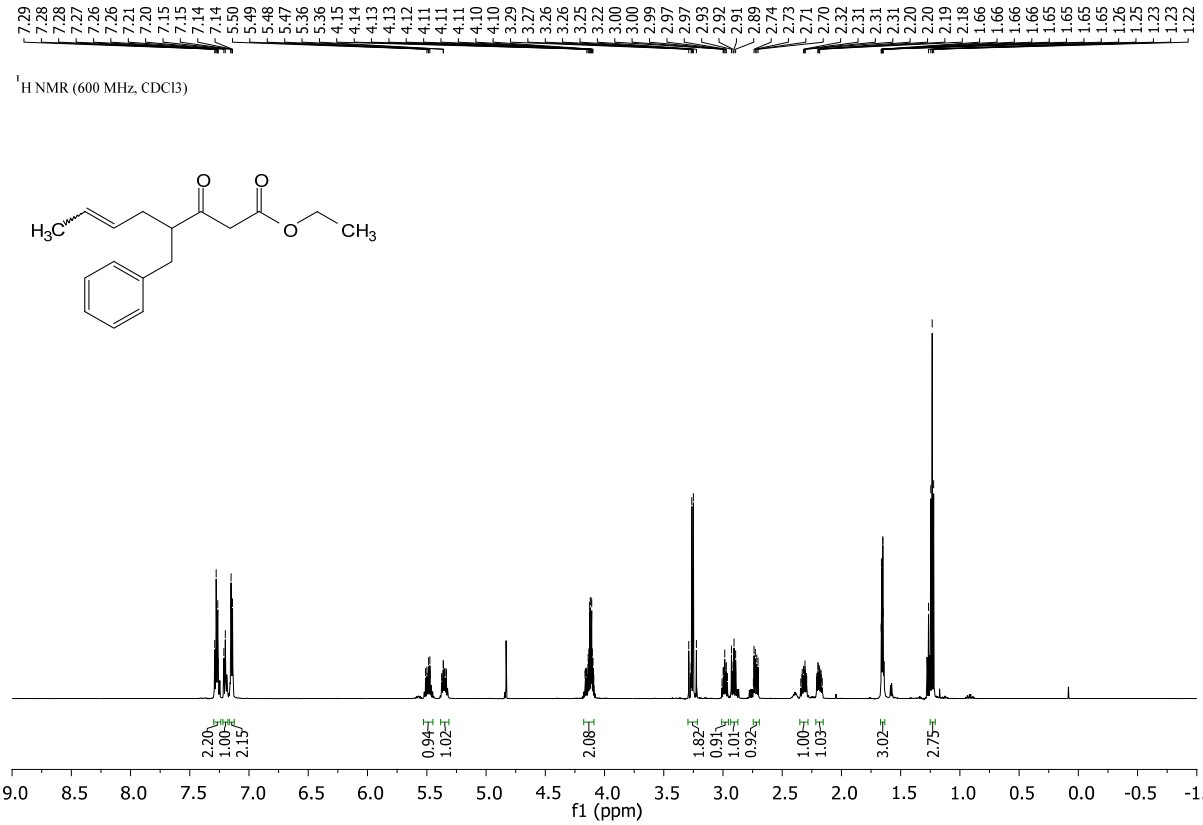

Transmittance [%]
Wavenumber cm-1
2985
2969
2940
2920
2858
2113
1744
1446
1398
1369
1222
1097
1046
1014
966
853
749
699
627
555
508
447

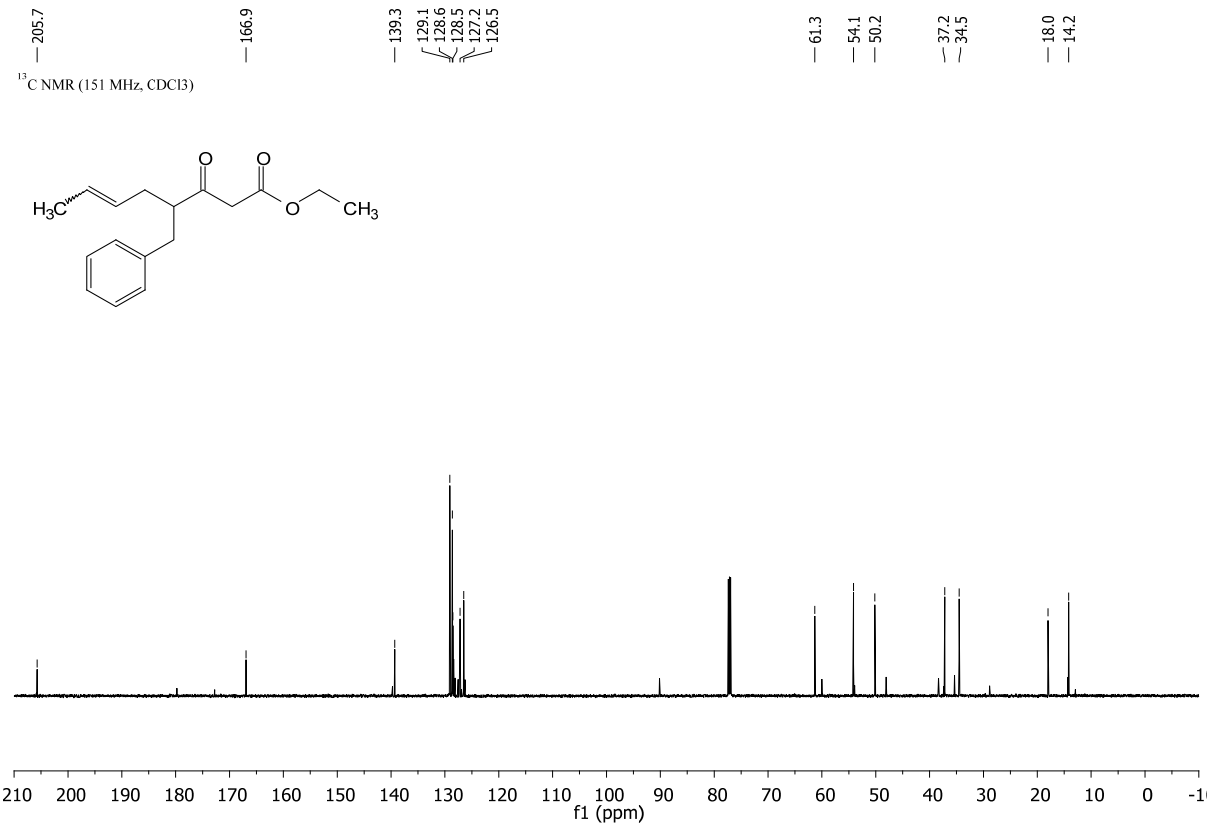
ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxooct-6-enoate



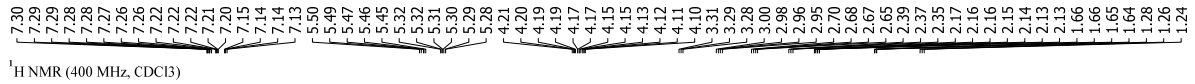


ethyl 4-benzyl-3-oxooct-6-enoate

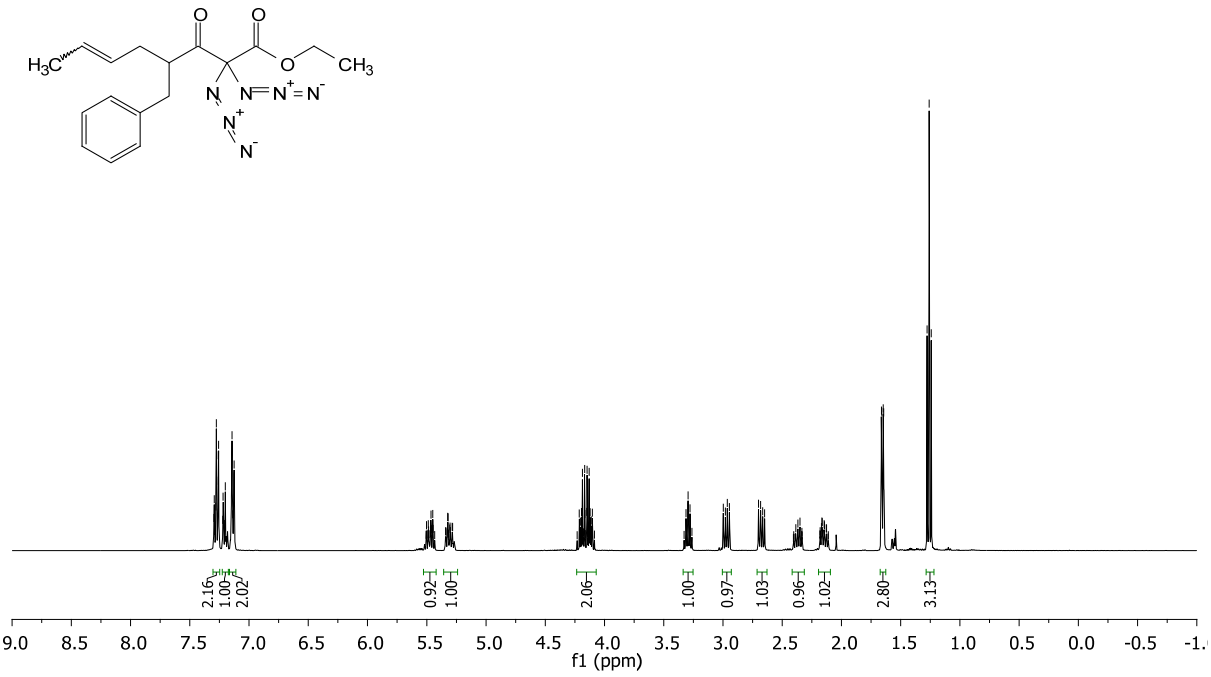




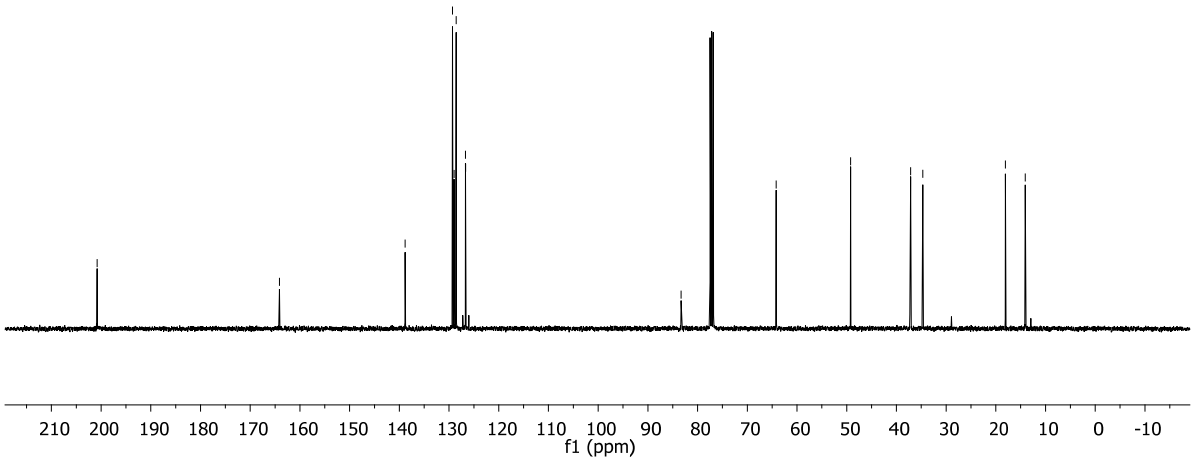
ethyl 2,2-diazido4-benzyl-3-oxooct-6-enoate (1k)

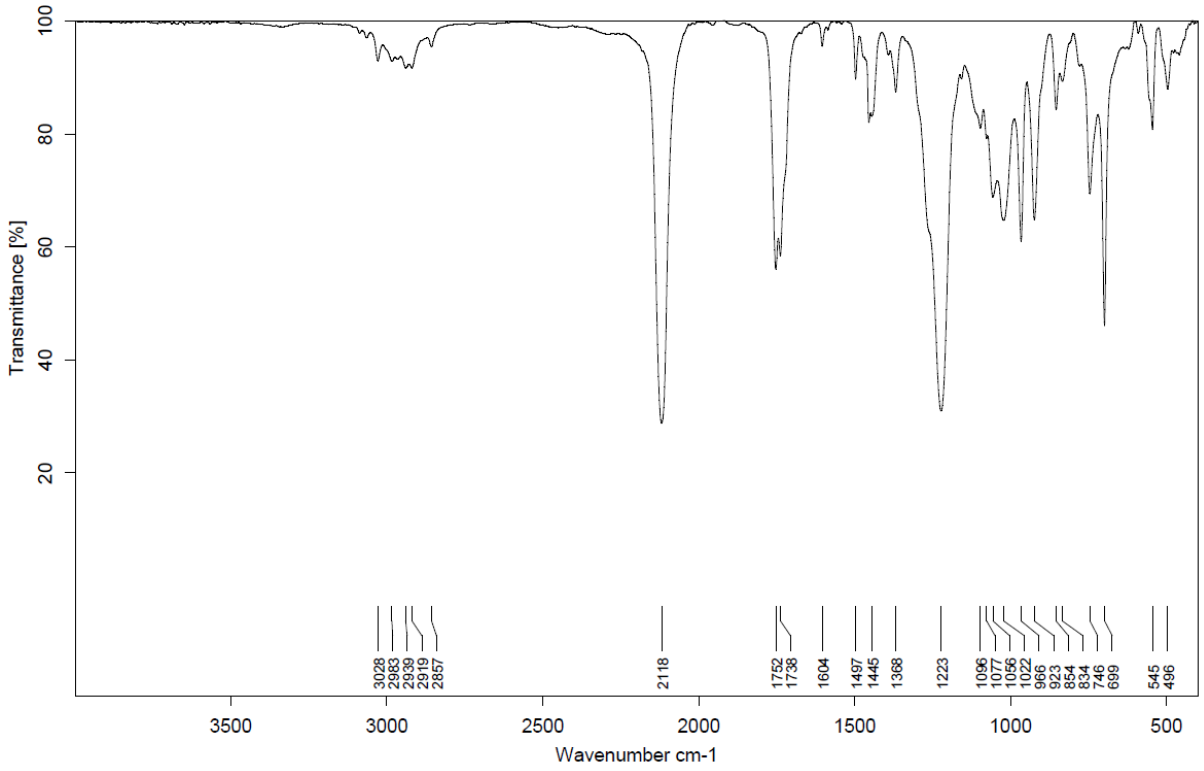


^{1}H NMR (400 MHz, CDCl3)

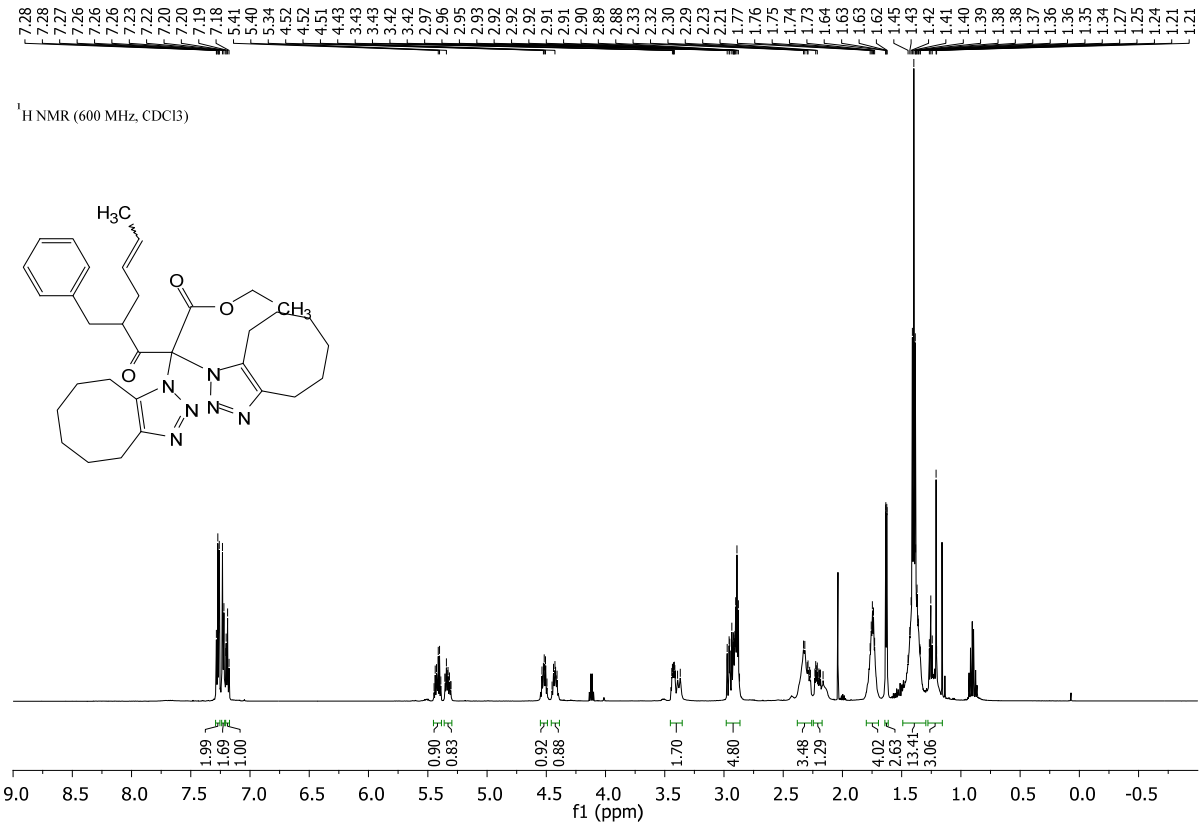


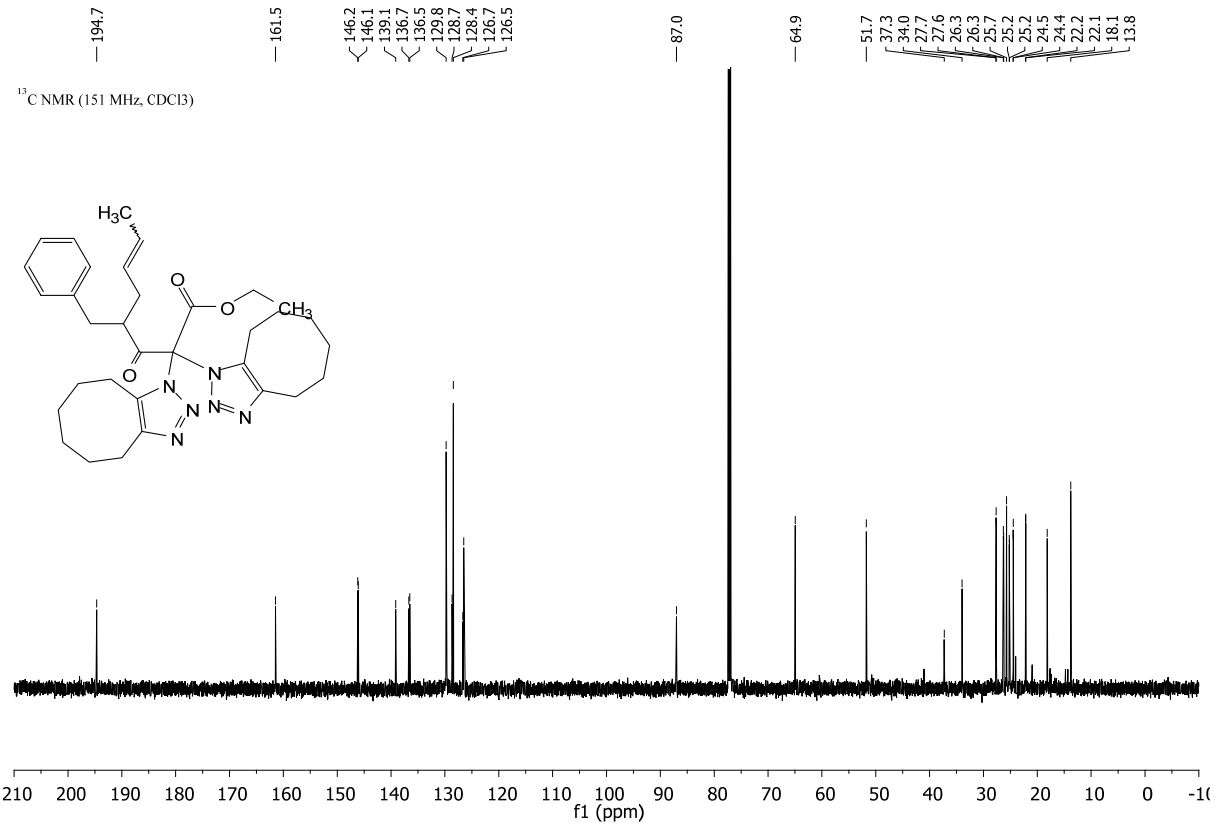
^{13}C NMR (101 MHz, CDCl3)



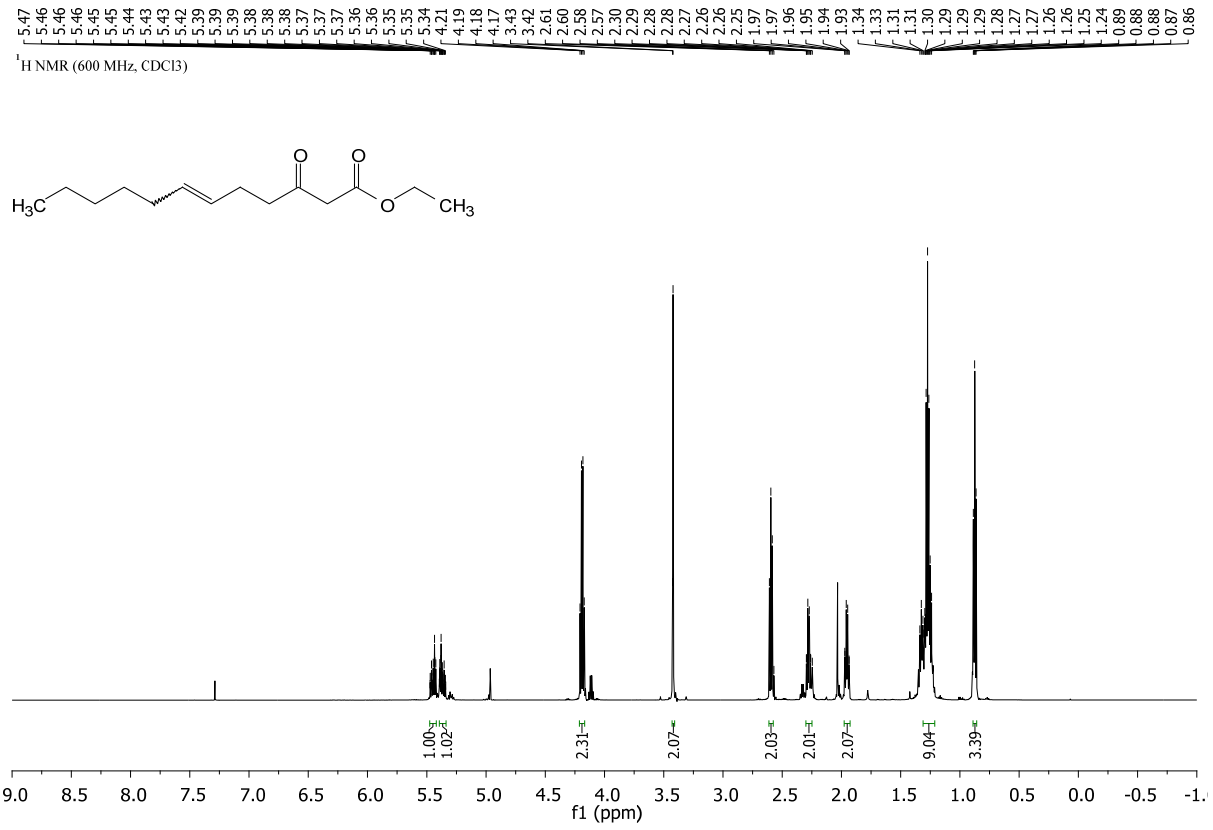


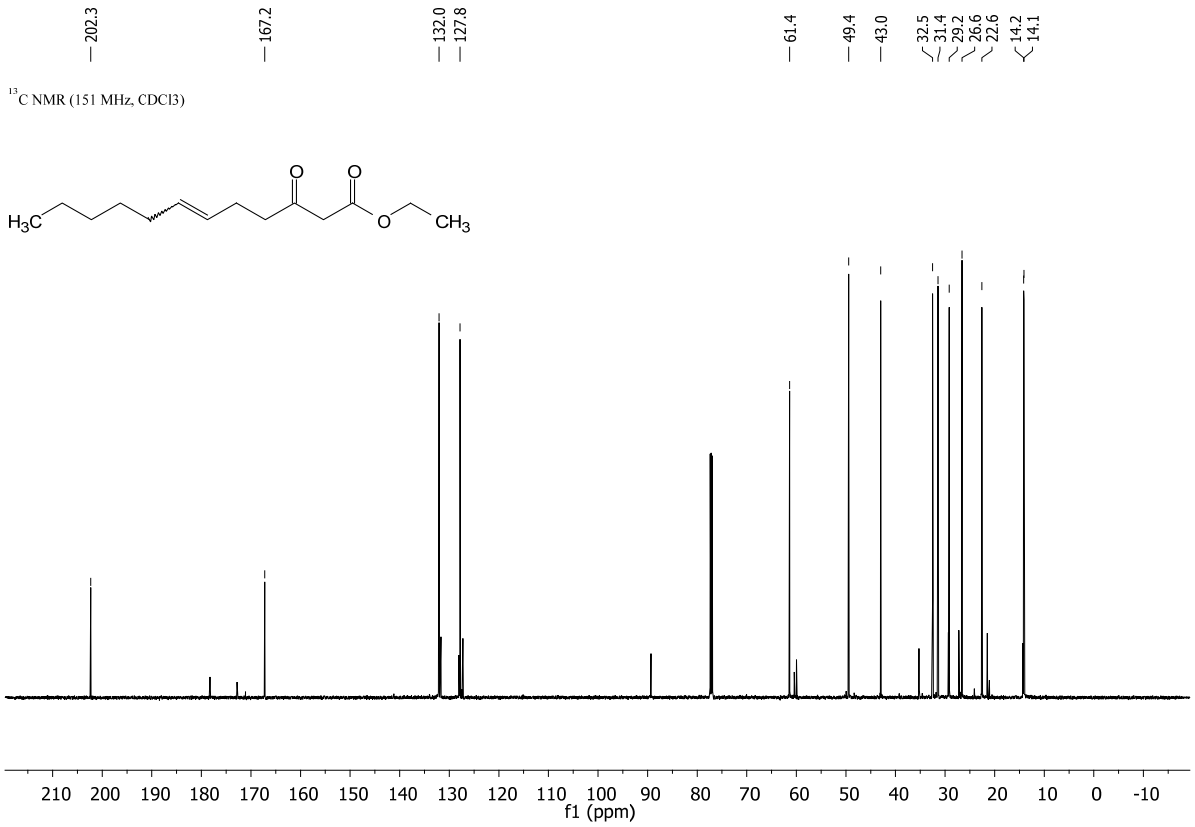
ethyl 4-benzyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxooct-6-enoate



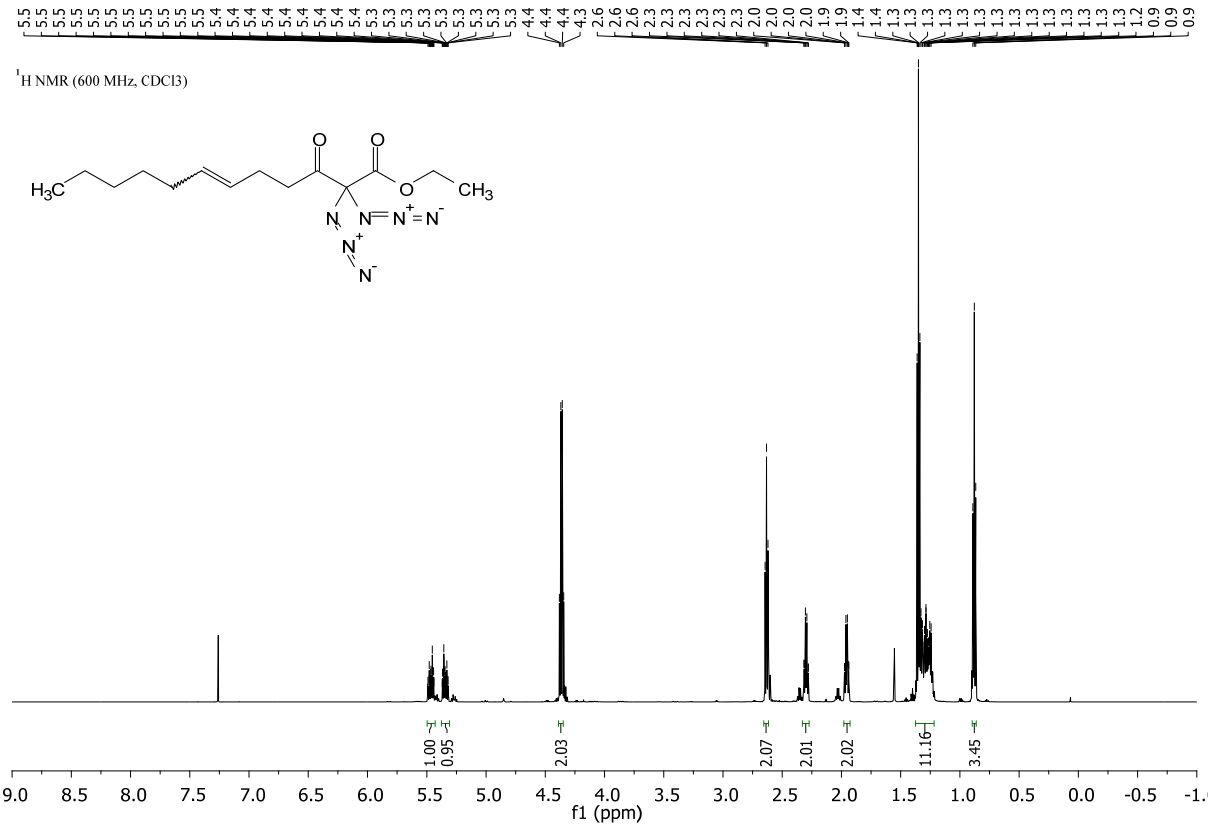


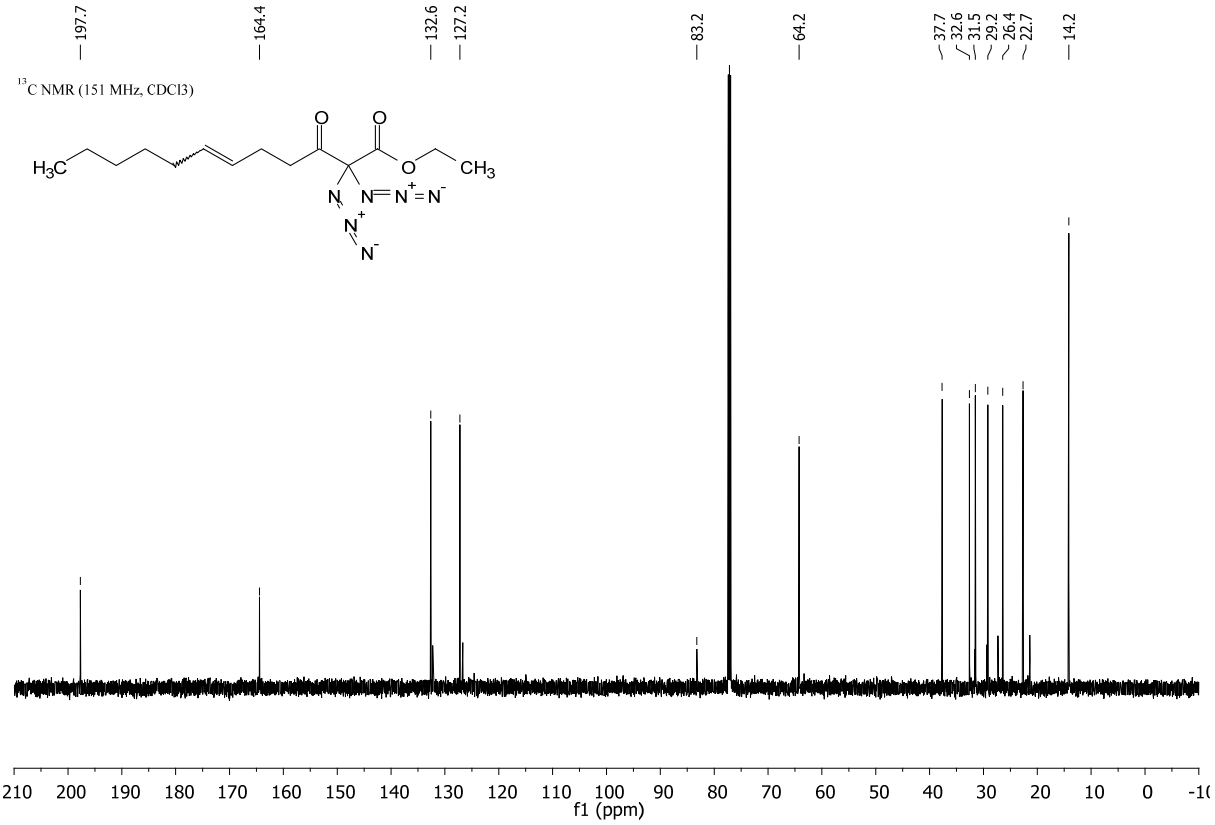
ethyl 3-oxododec-6-enoate

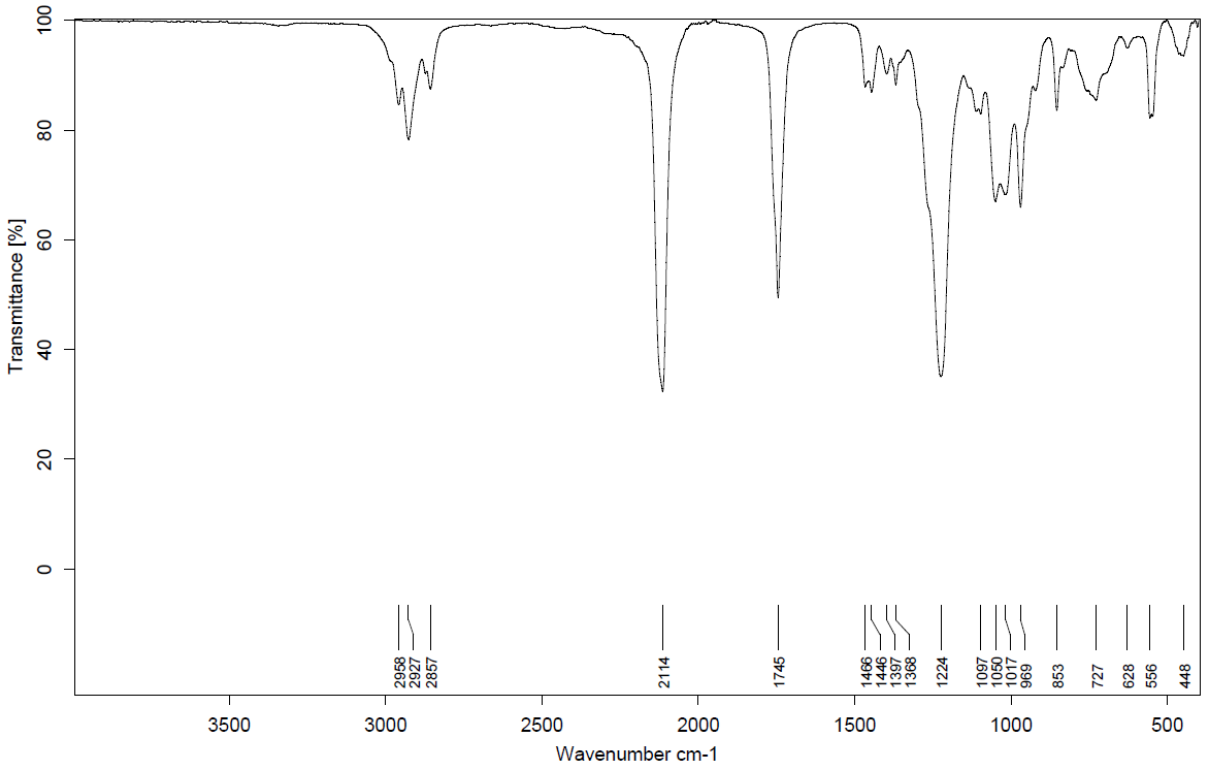




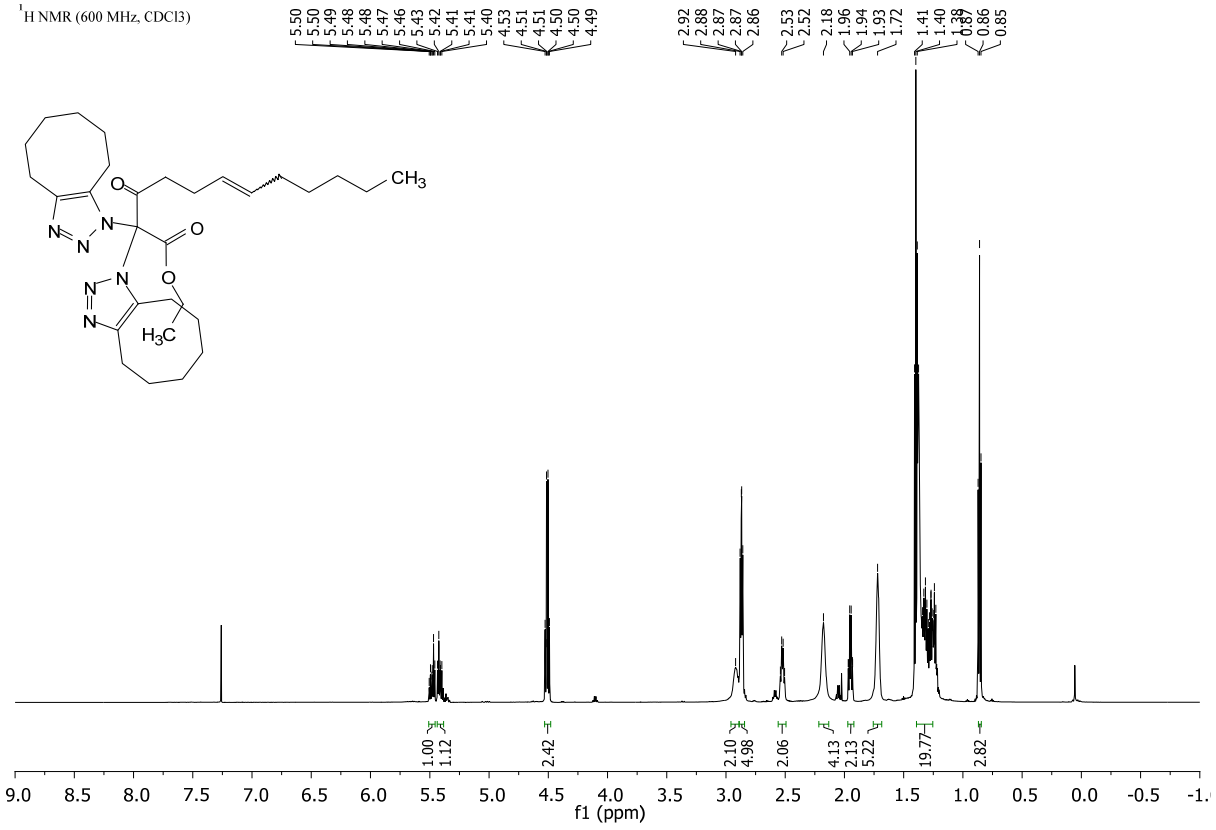
ethyl 2,2-diazido-3-oxododec-6-enoate (1l)

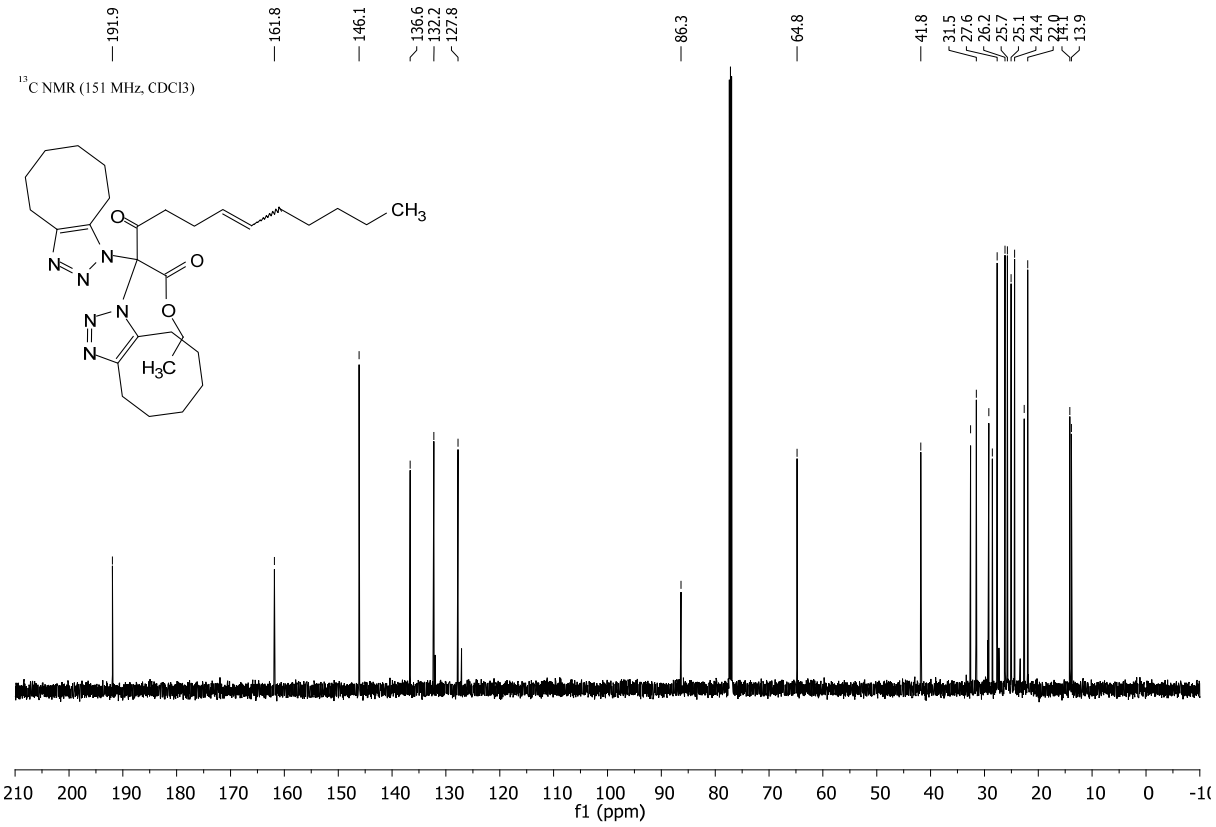



197.7
164.4
132.6
127.2
83.2
64.2
37.7
32.6
31.5
29.2
26.4
22.7
14.2
13C NMR (151 MHz, CDCl3)
f1 (ppm)

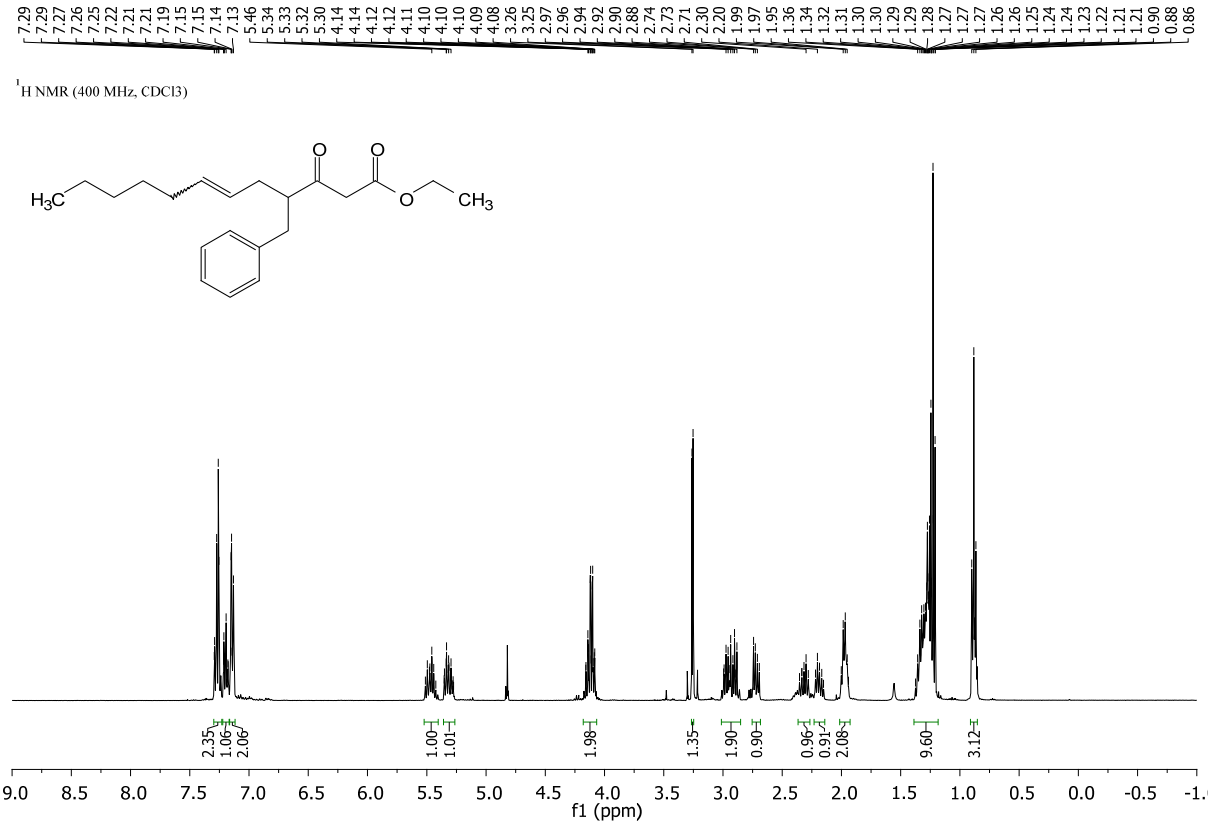

Transmittance [%]
Wavenumber cm-1
2958
2927
2857
2114
1745
1466
1446
1397
1368
1224
1097
1050
1017
969
853
727
628
556
448

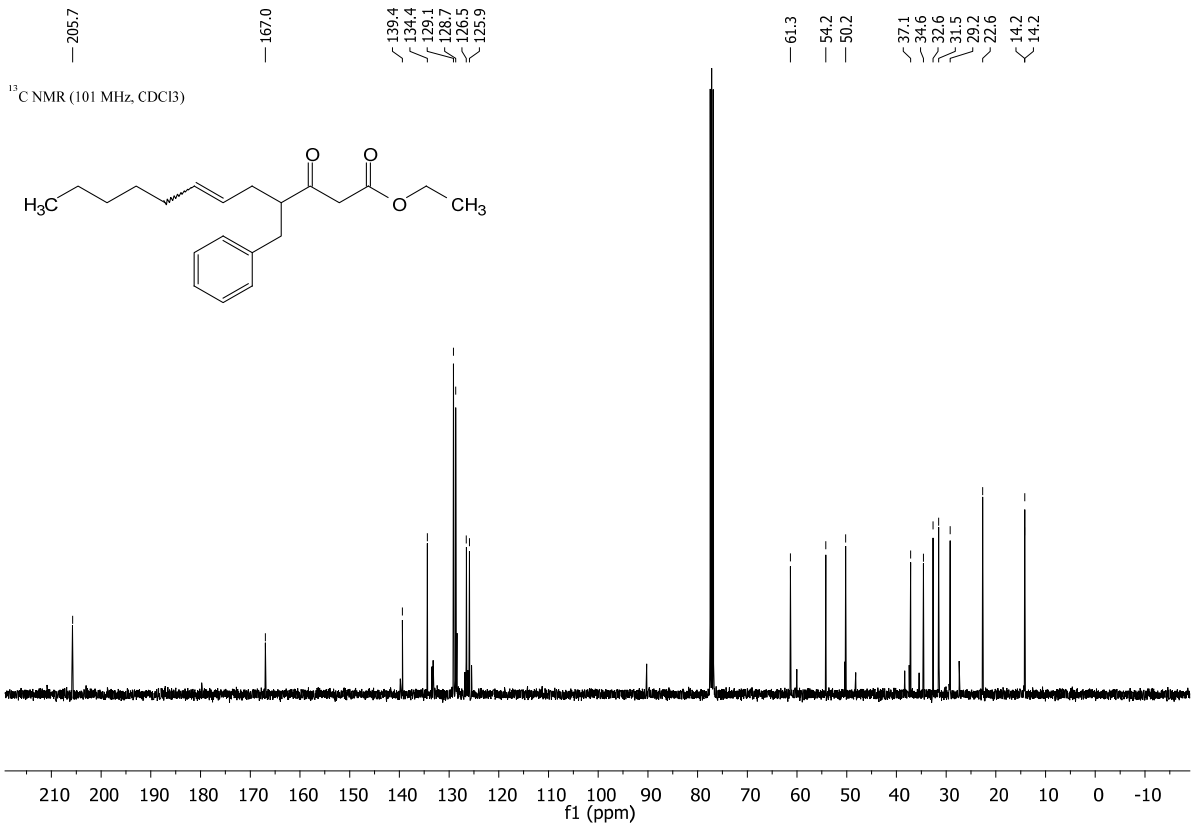
ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxododec-6-enoate



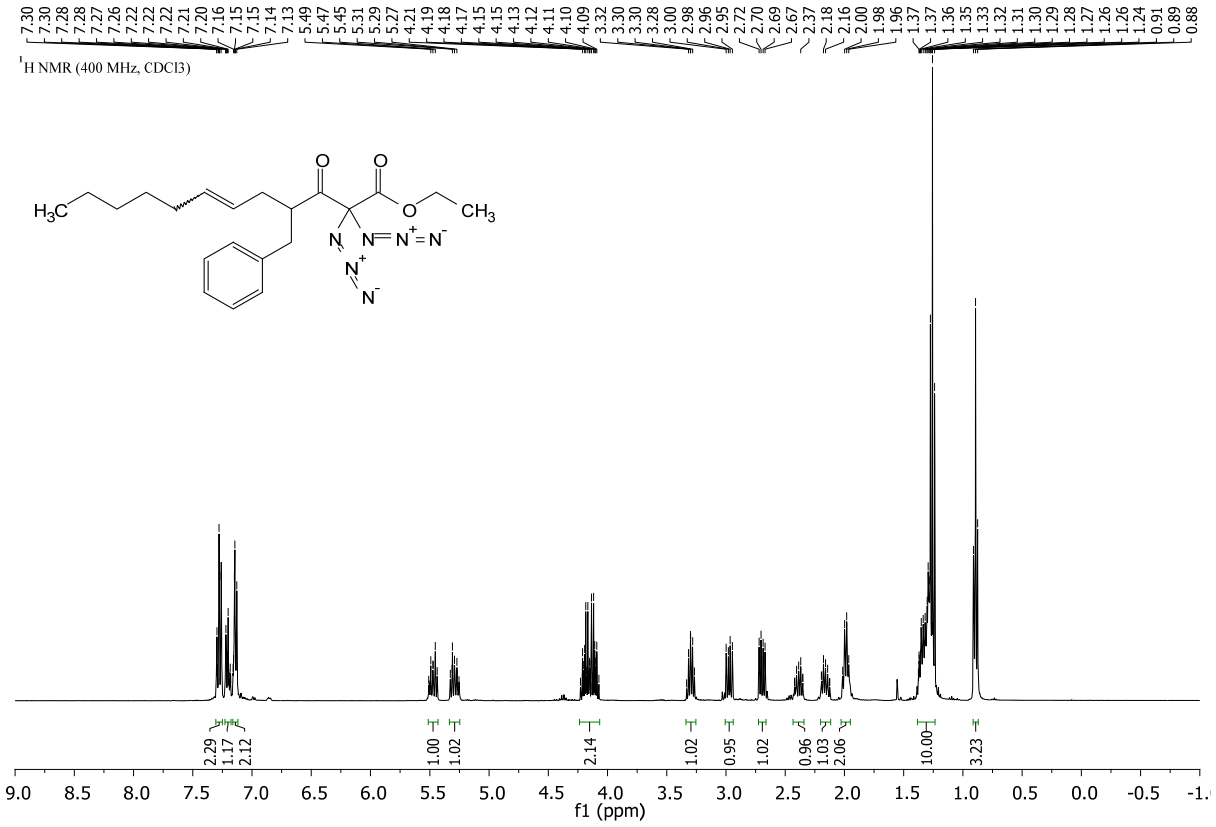


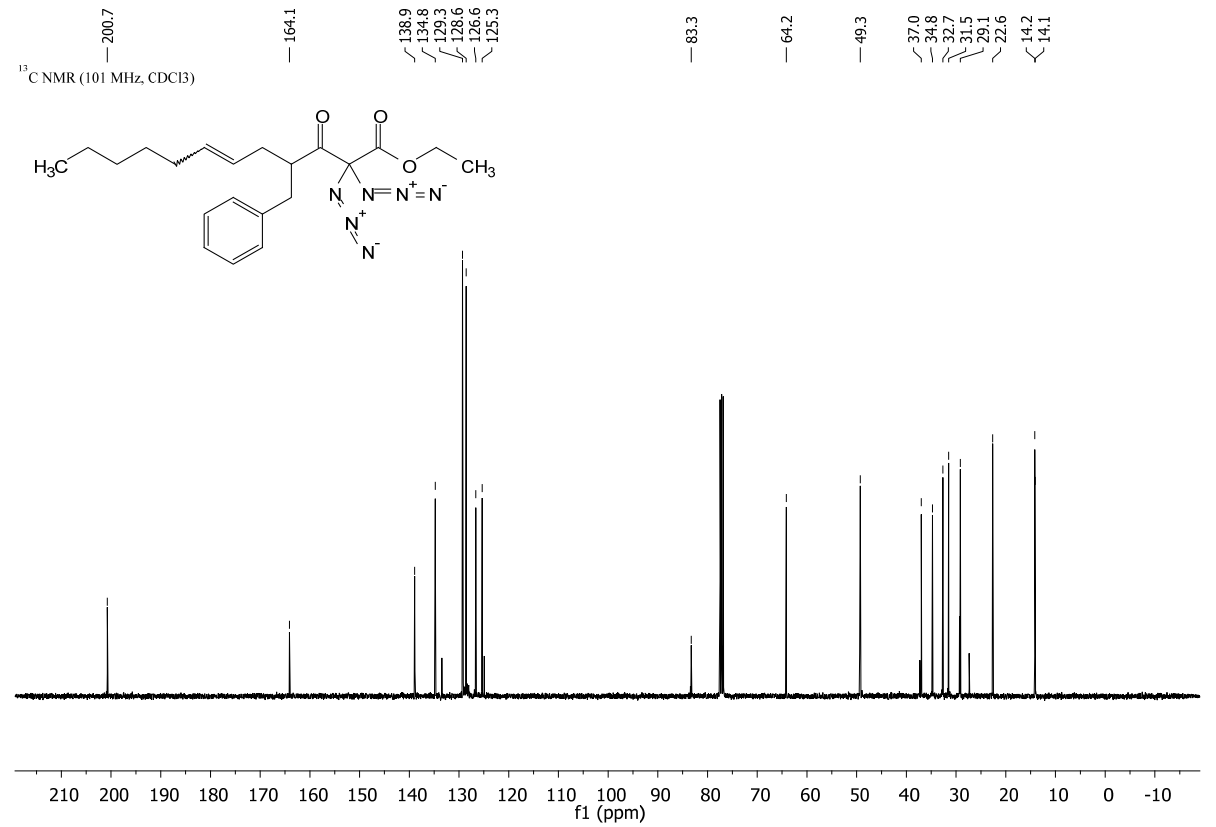
ethyl 4-benzyl-3-oxododec-6-enoate

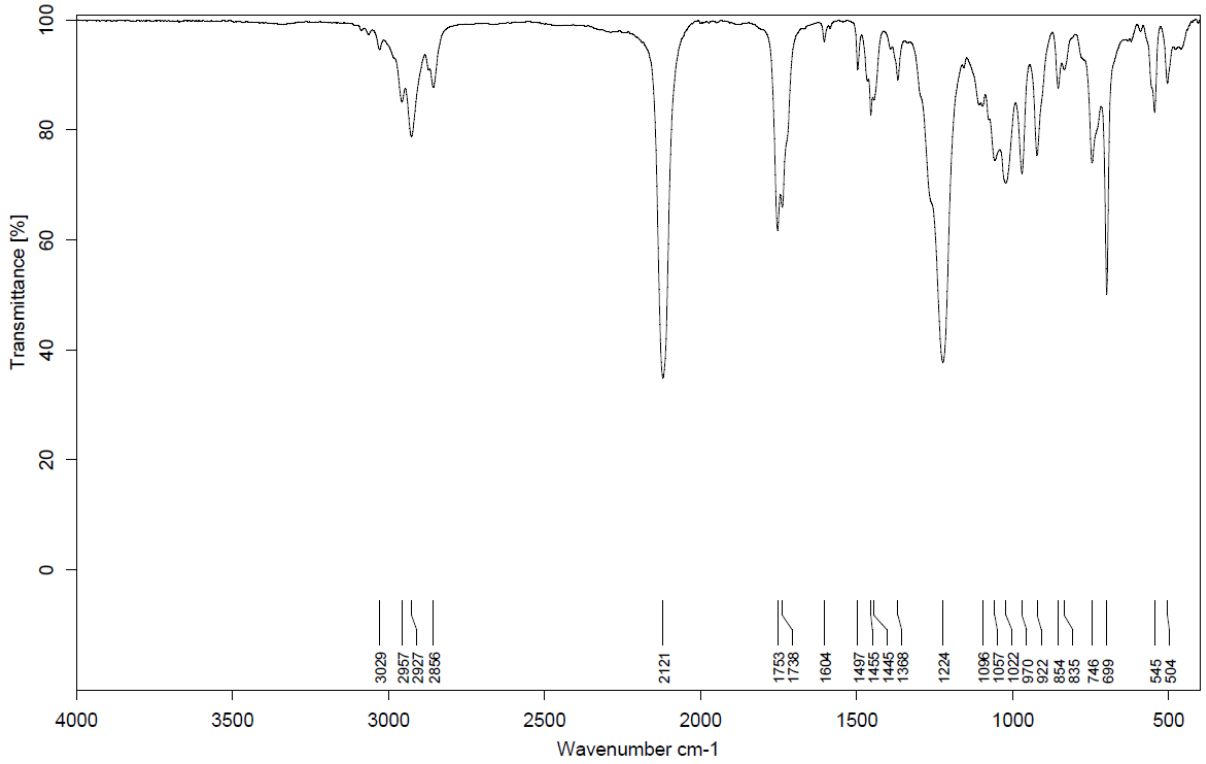




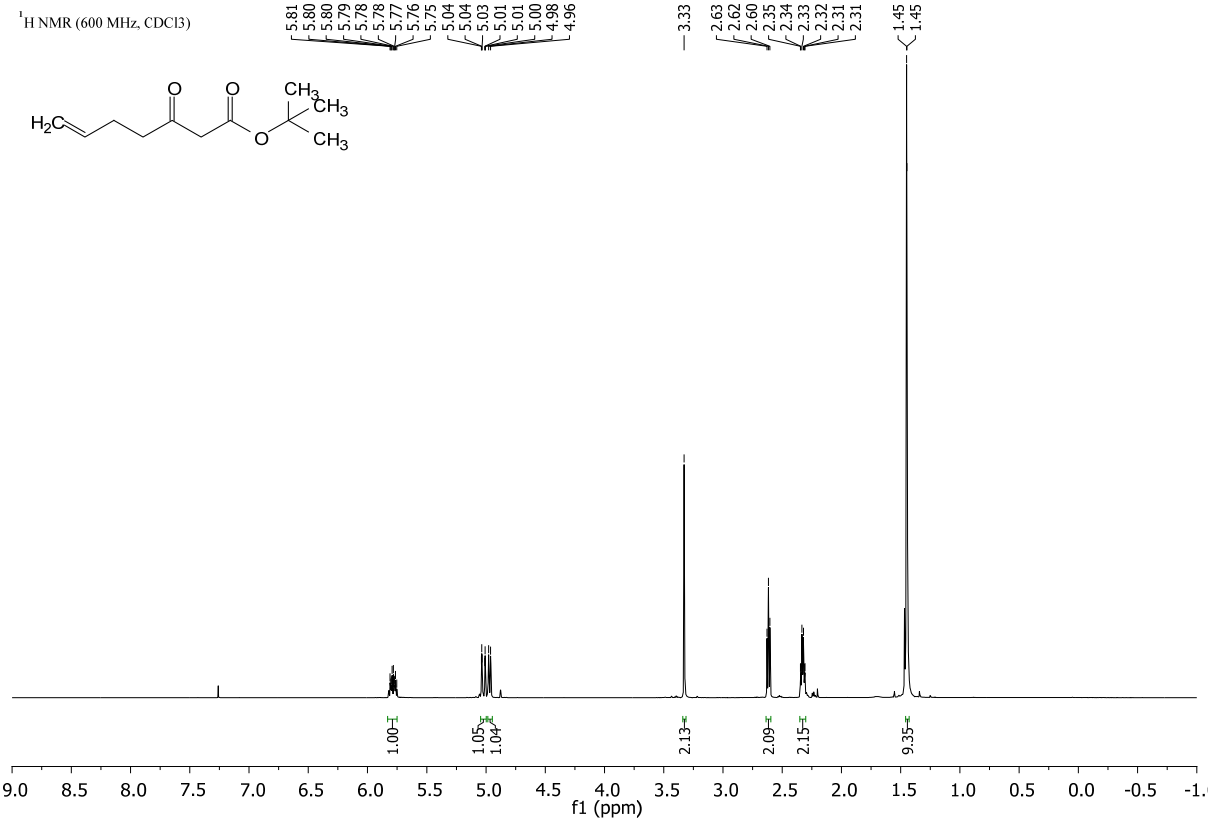
ethyl 2,2-diazido-3-oxododec-6-enoate (1m)

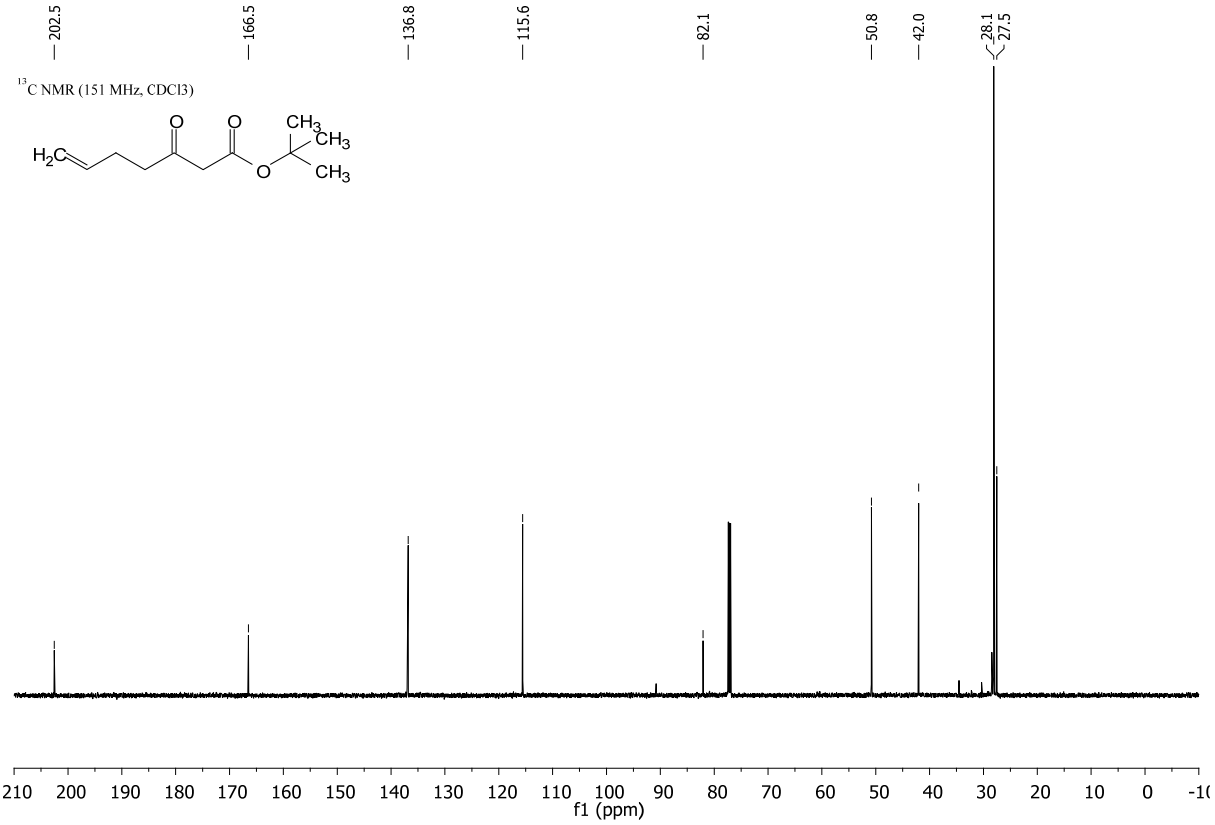




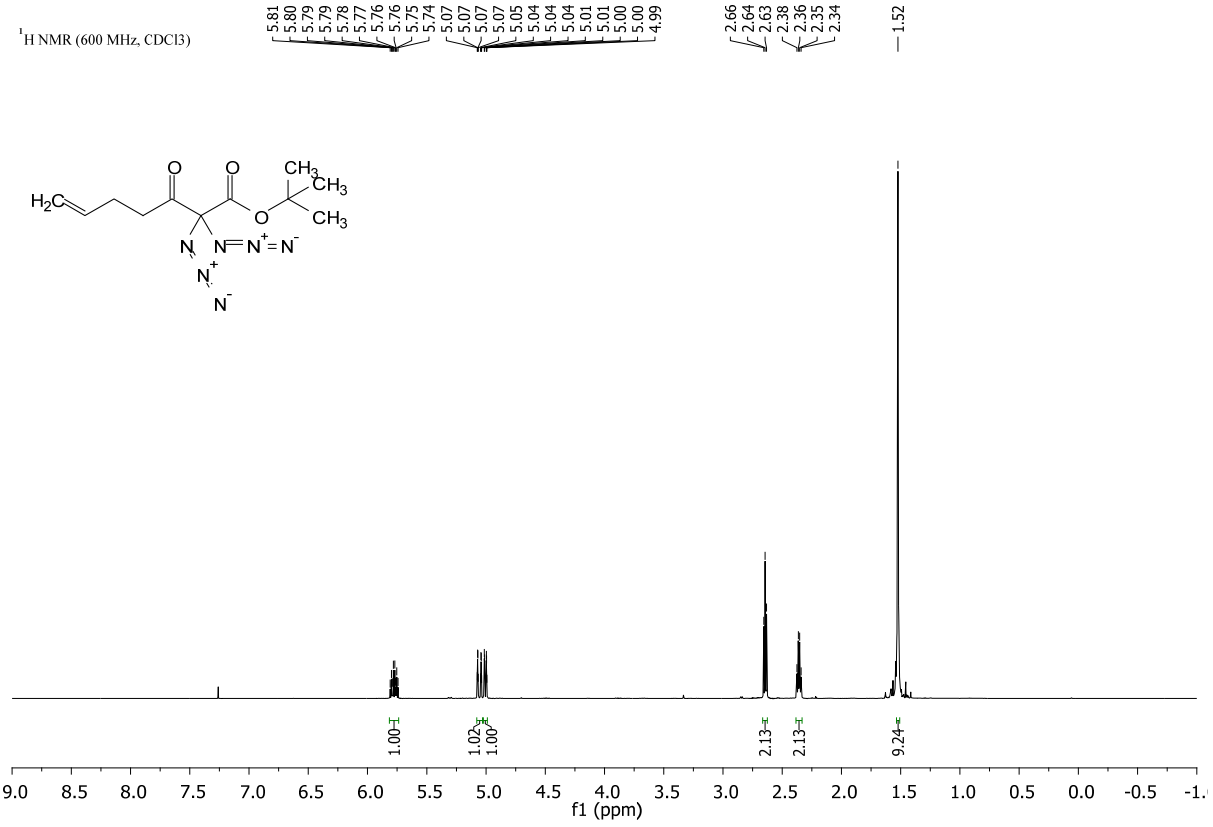


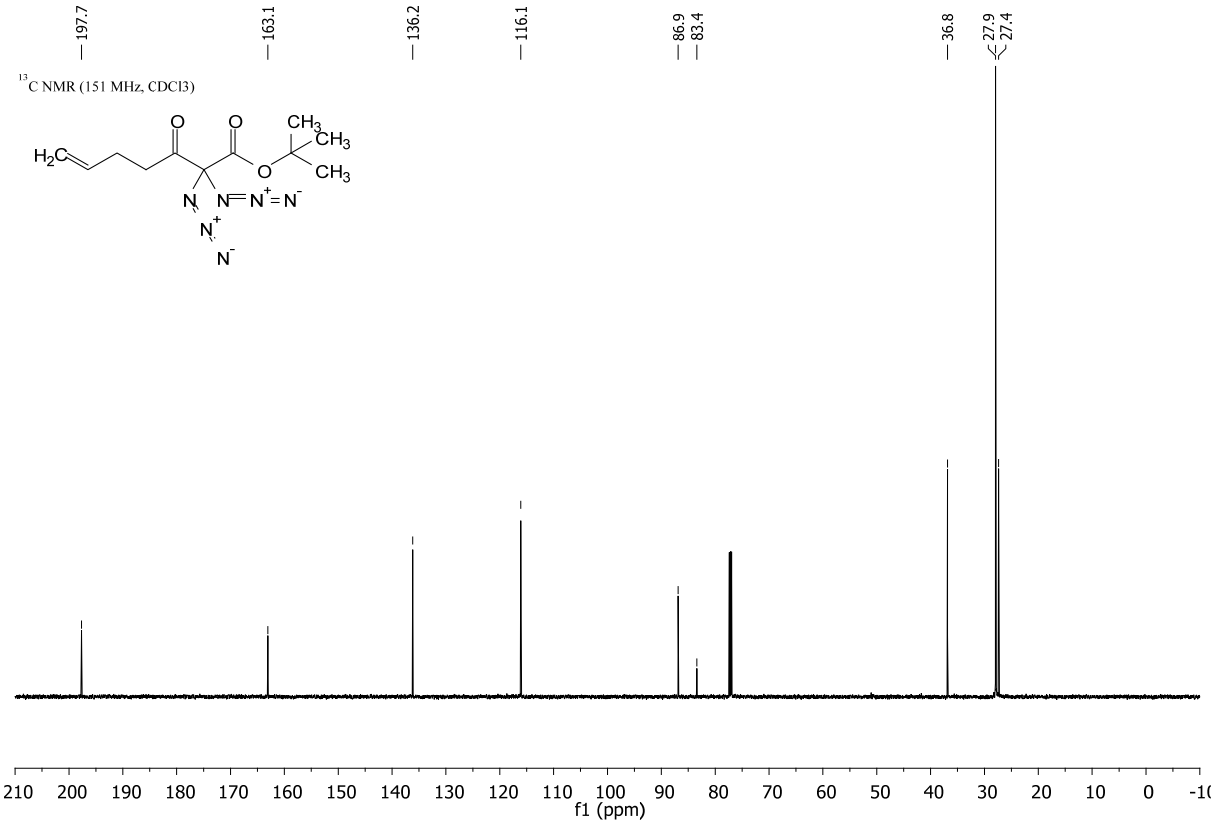
tert-butyl 3-oxohept-6-enoate





tert-butyl 2,2-diazido-3-oxohept-6-enoate (1n)

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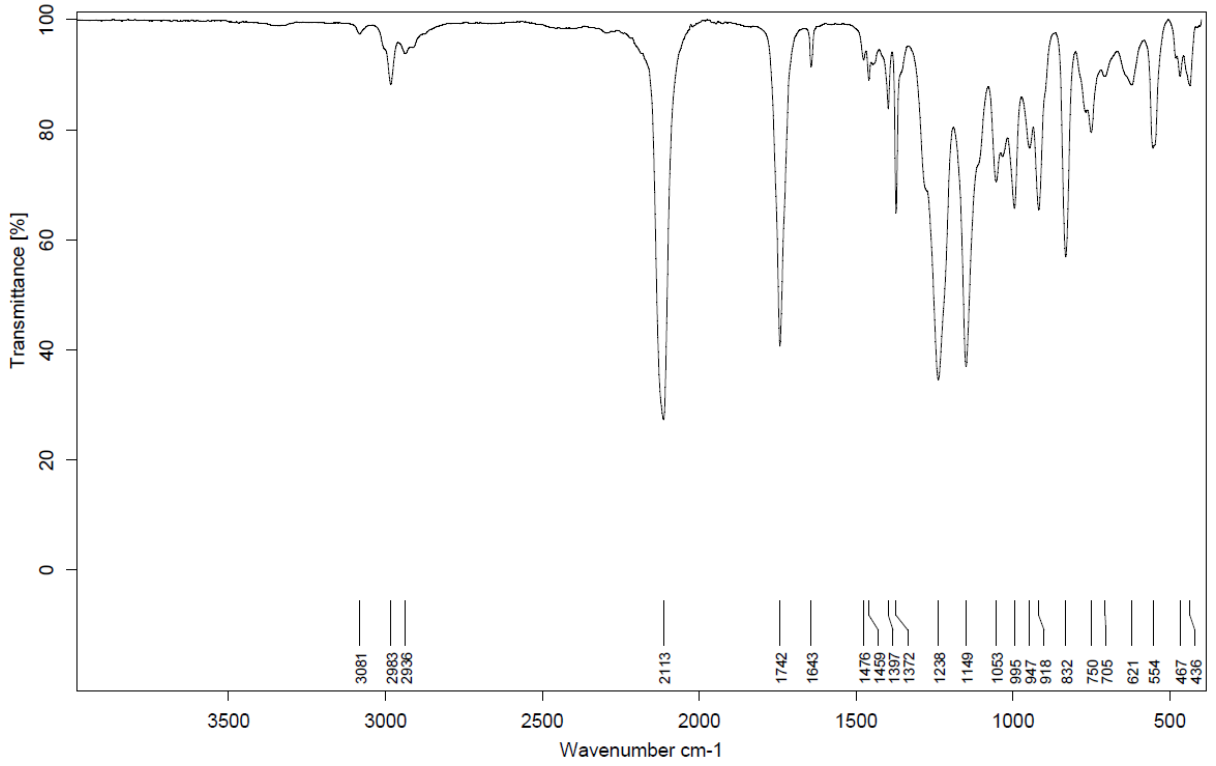
116.1
86.9
83.4
36.8
27.9
27.4
13C NMR (151 MHz, CDCl3)
f1 (ppm)


Transmittance [%]
Wavenumber cm-1
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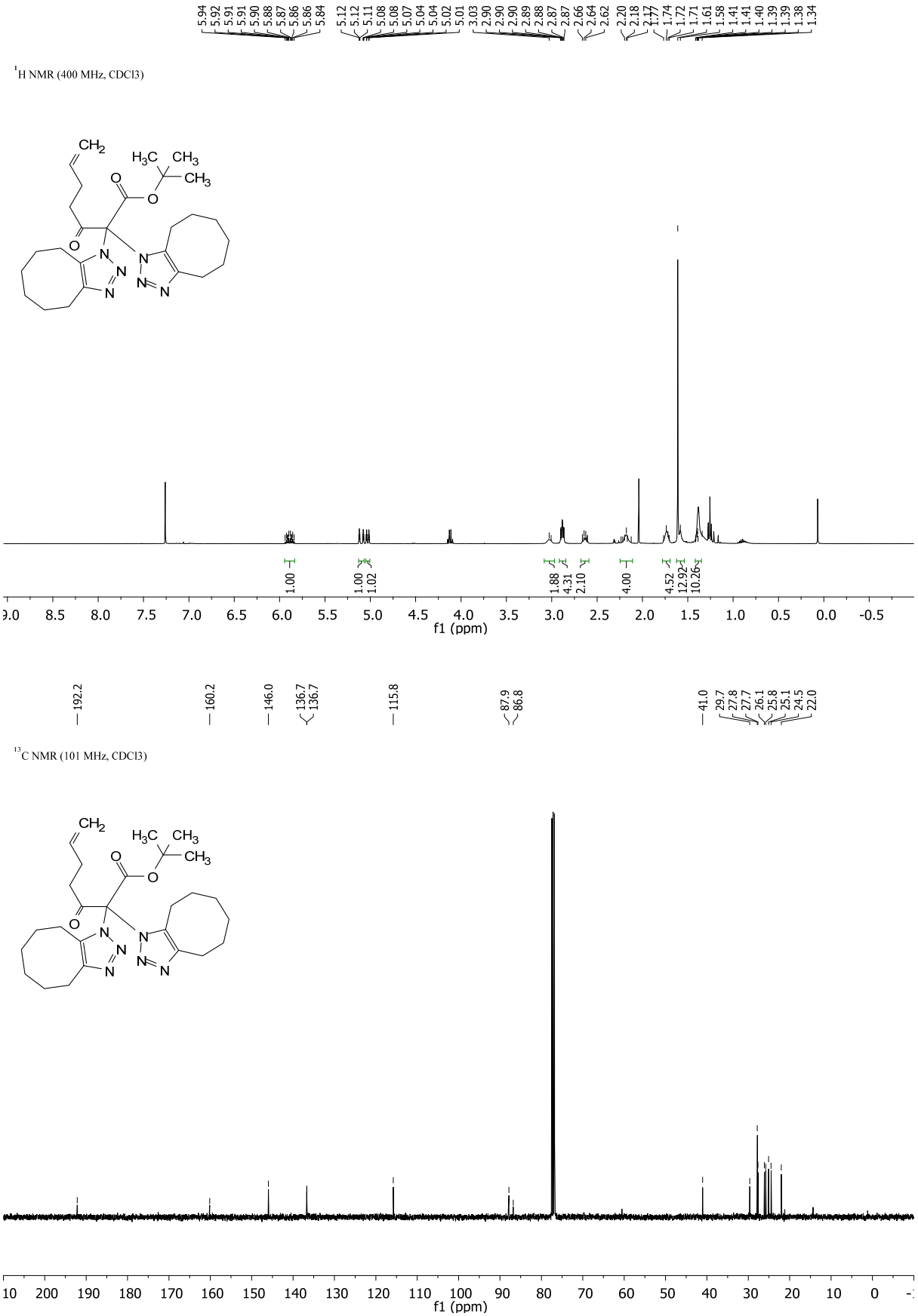
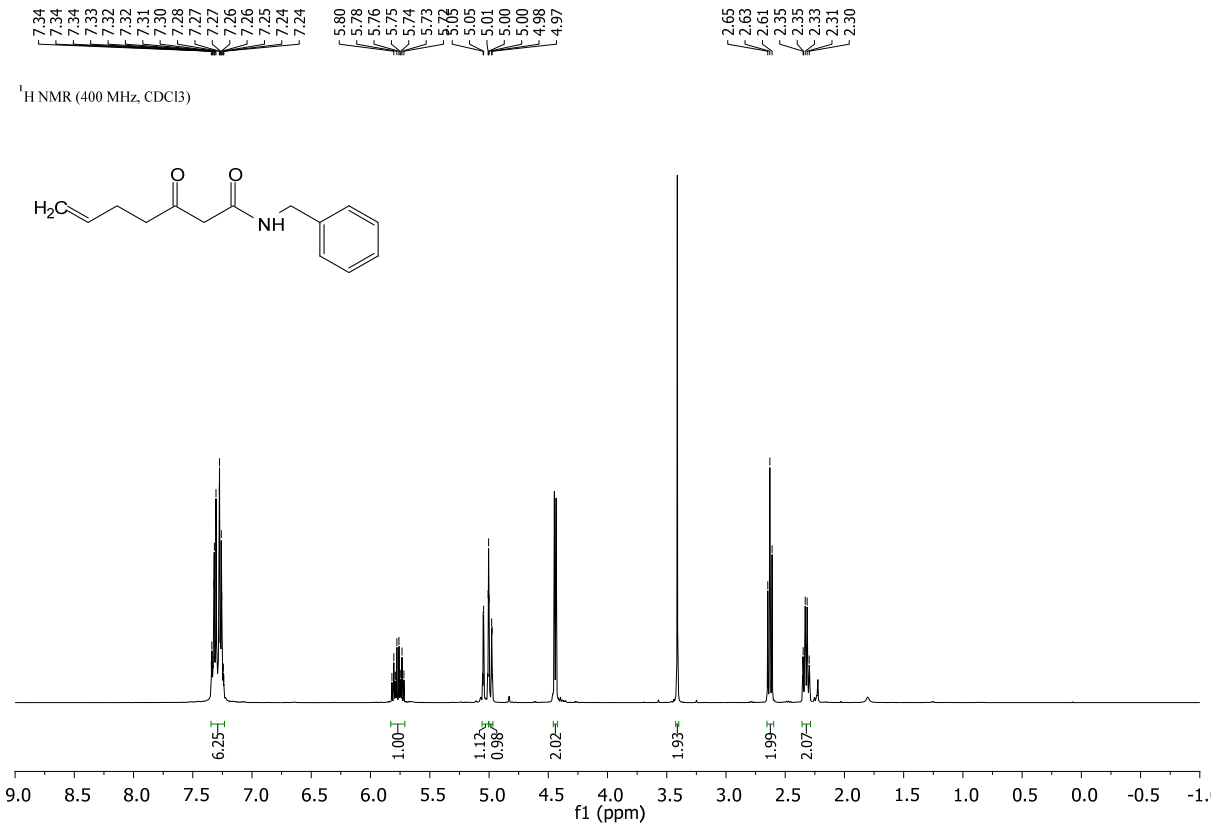
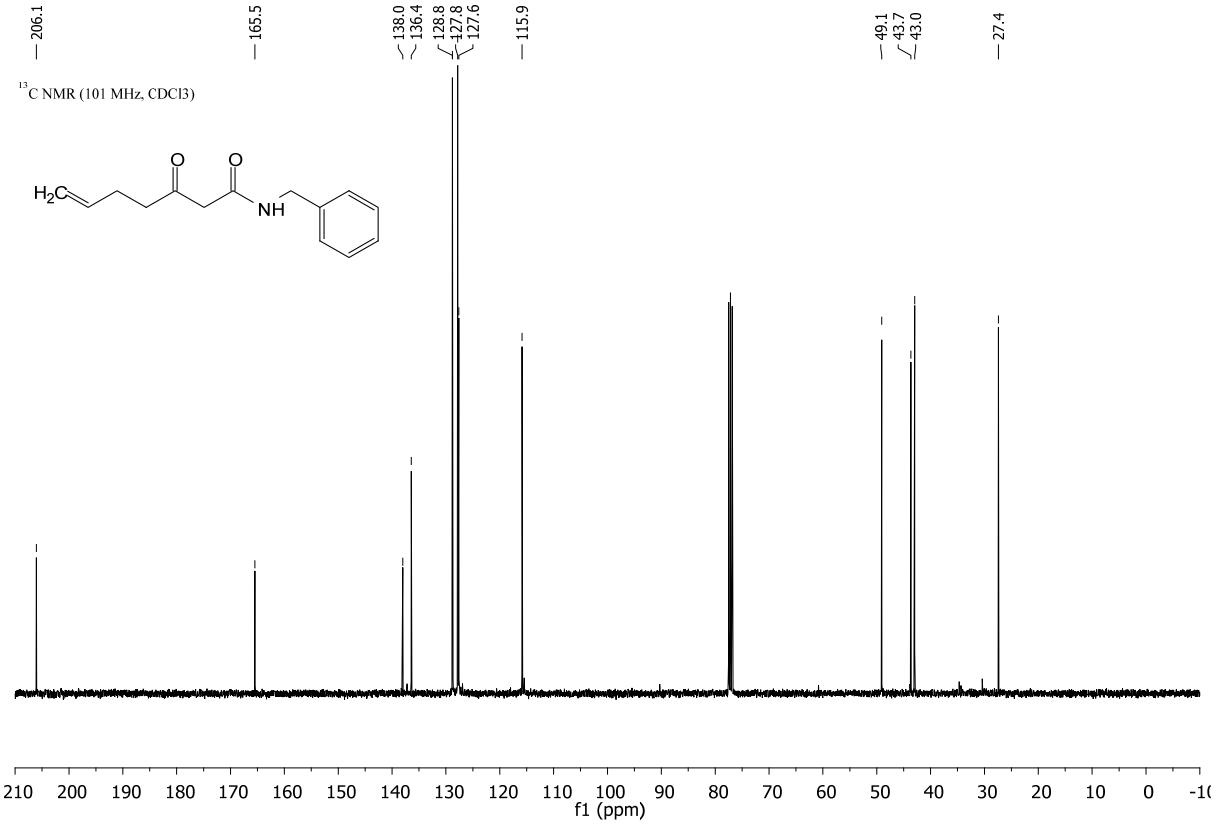
1053
995
947
918
832
750
705
621
554
467
436

tert-butyl 2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enoate

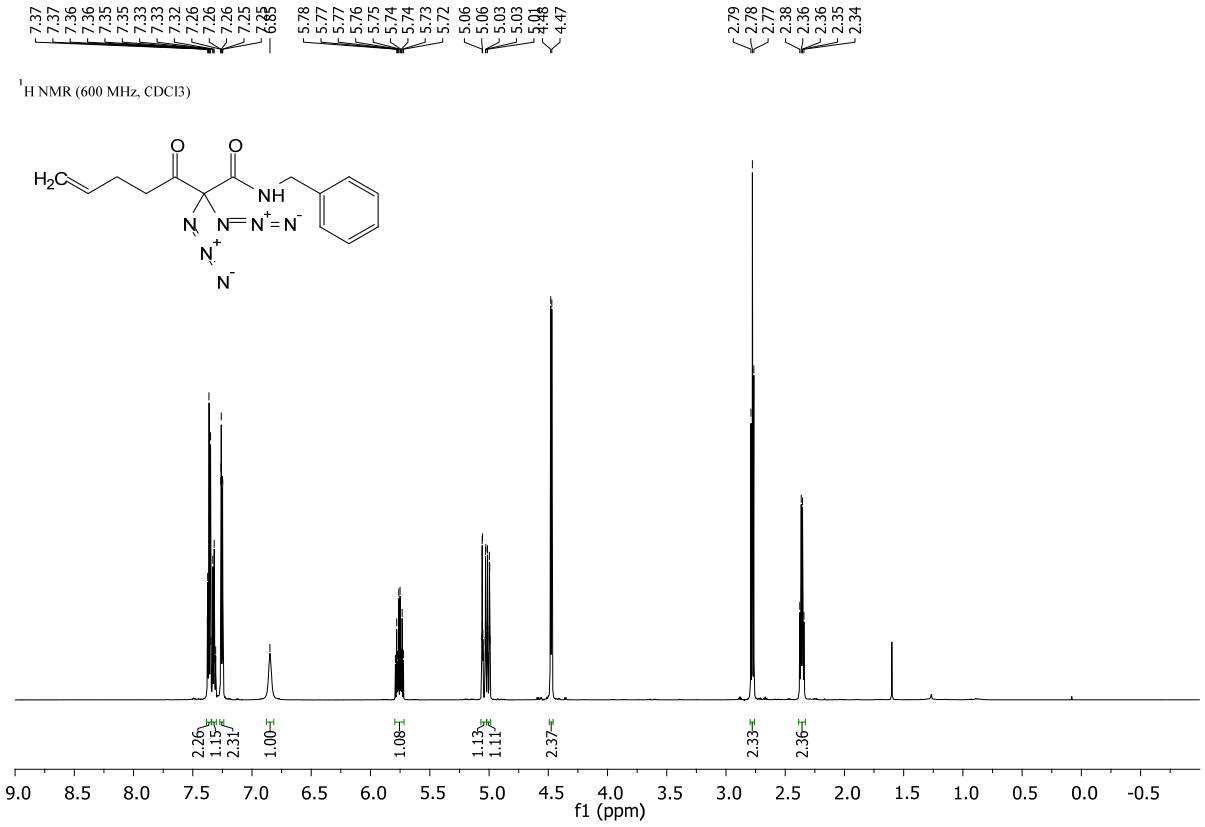


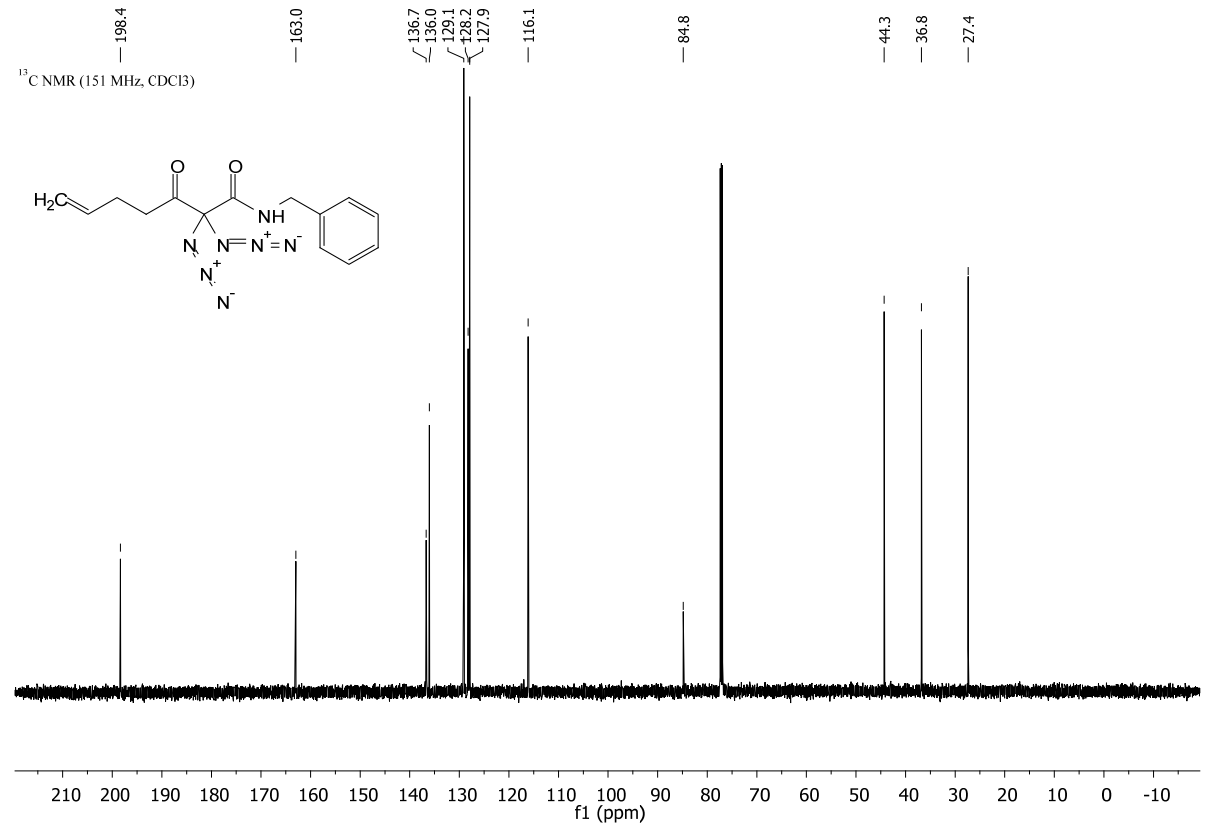
N-benzyl-3-oxohept-6-enamide

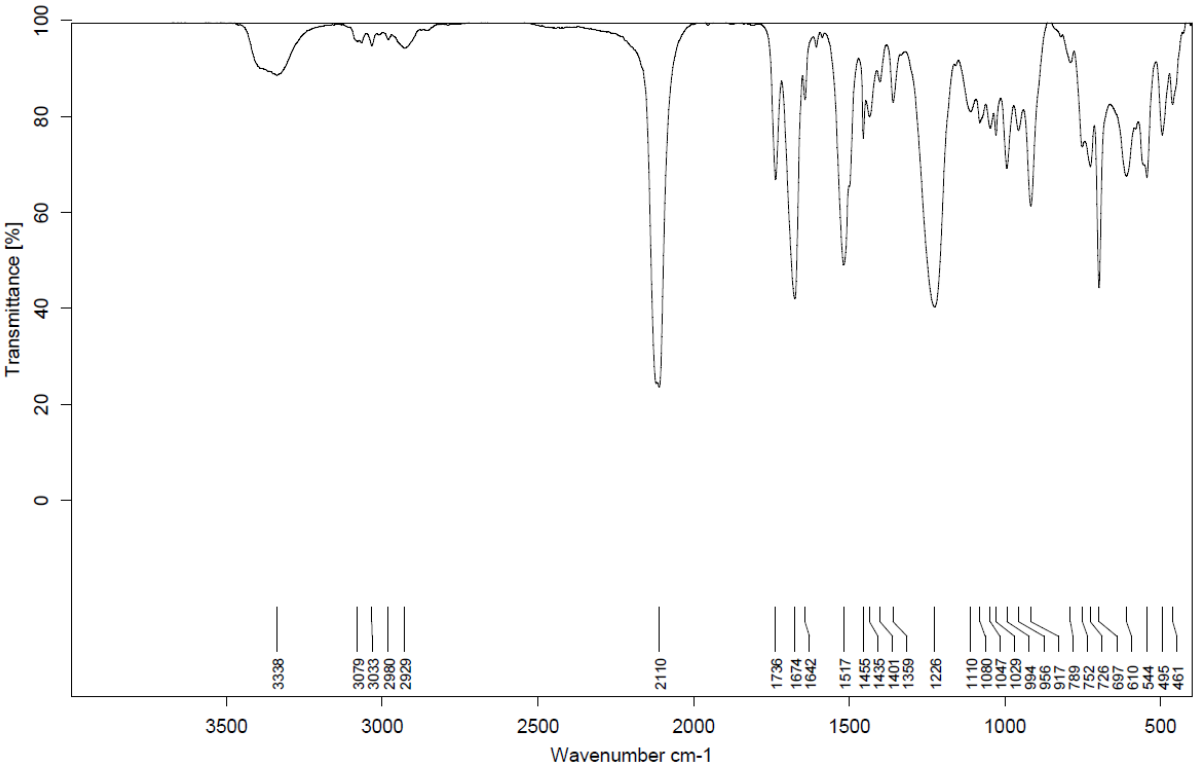




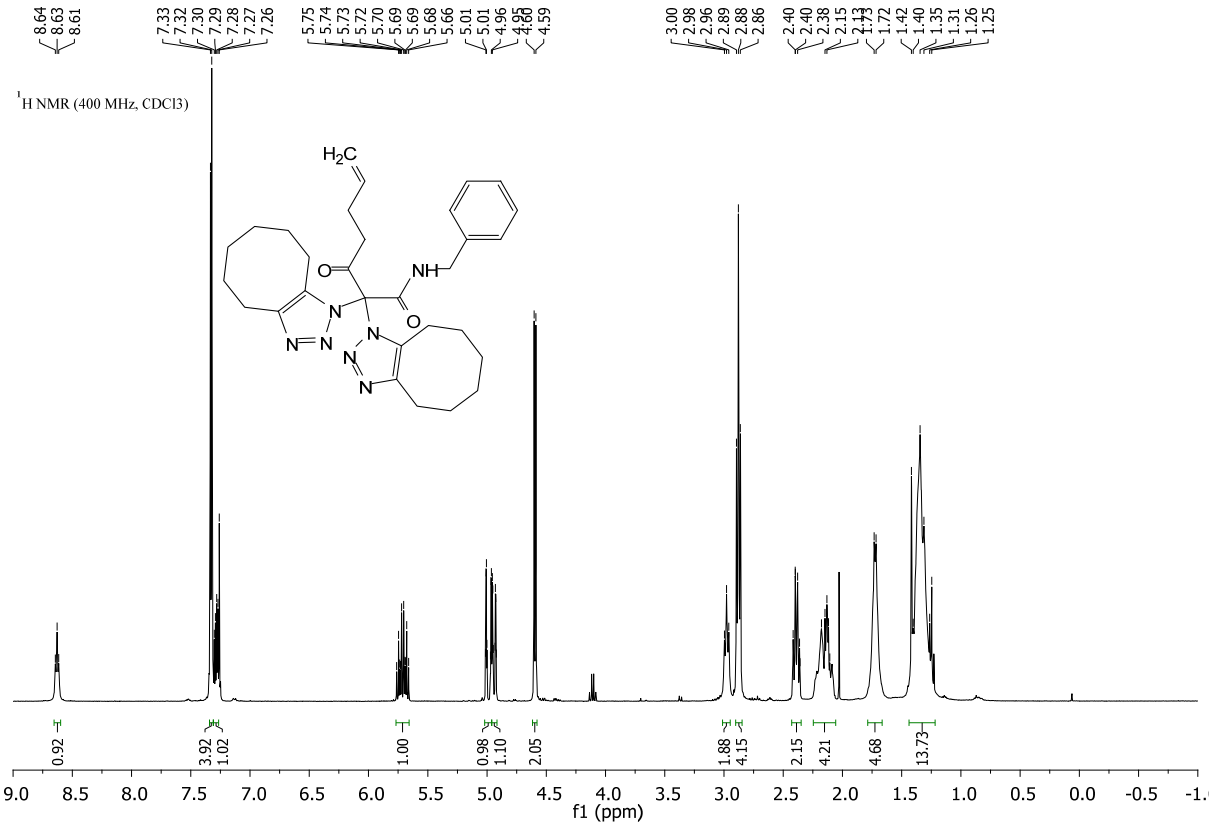
2,2-diazido-*N*-benzyl-3-oxohept-6-enoate (**1o**)

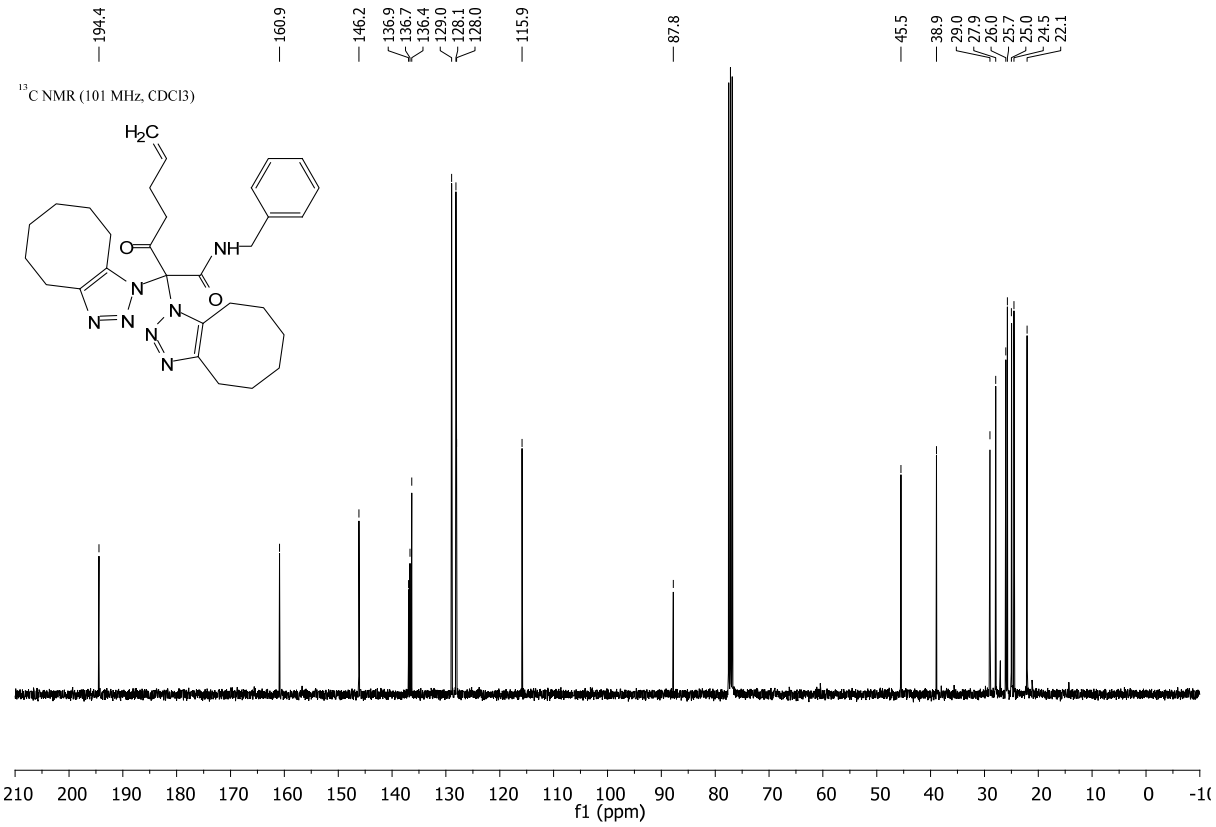




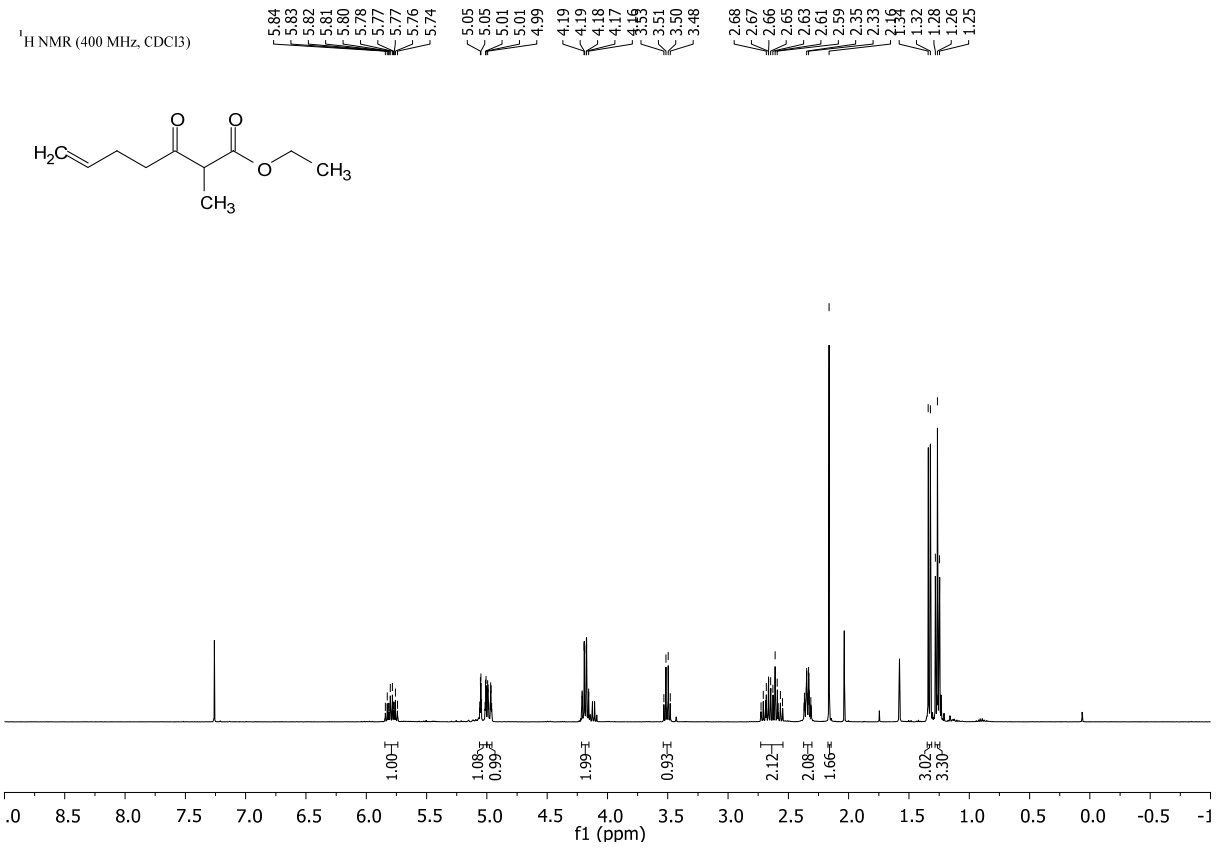


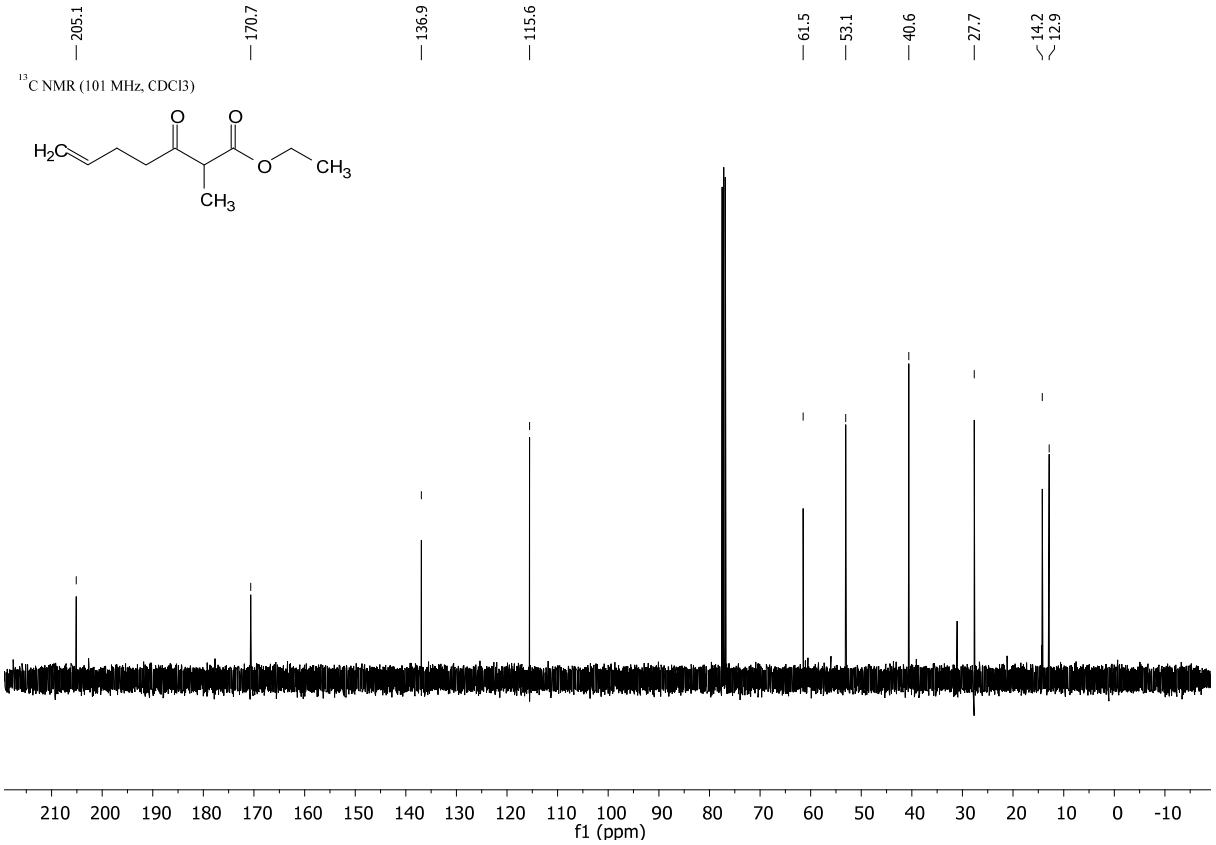
***N*-benzyl-2,2-bis(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-3-oxohept-6-enamide**



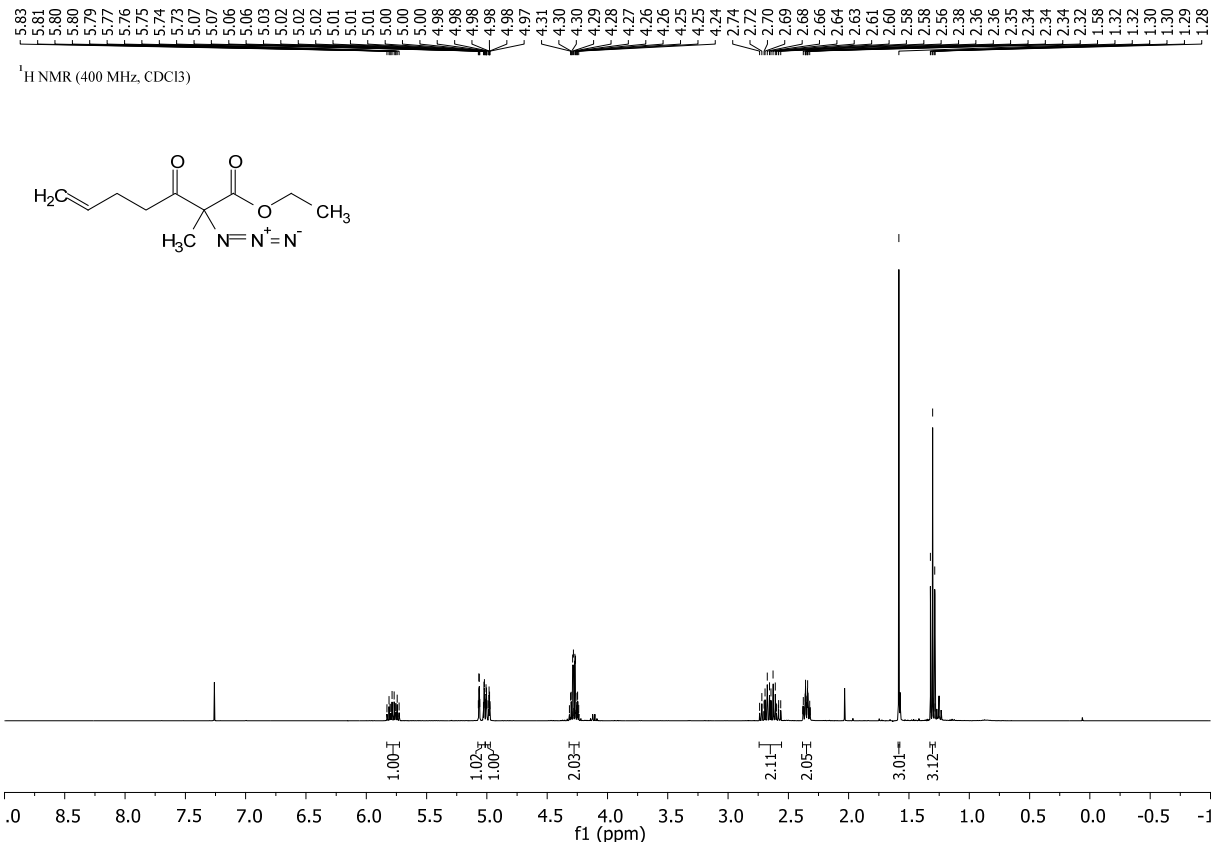


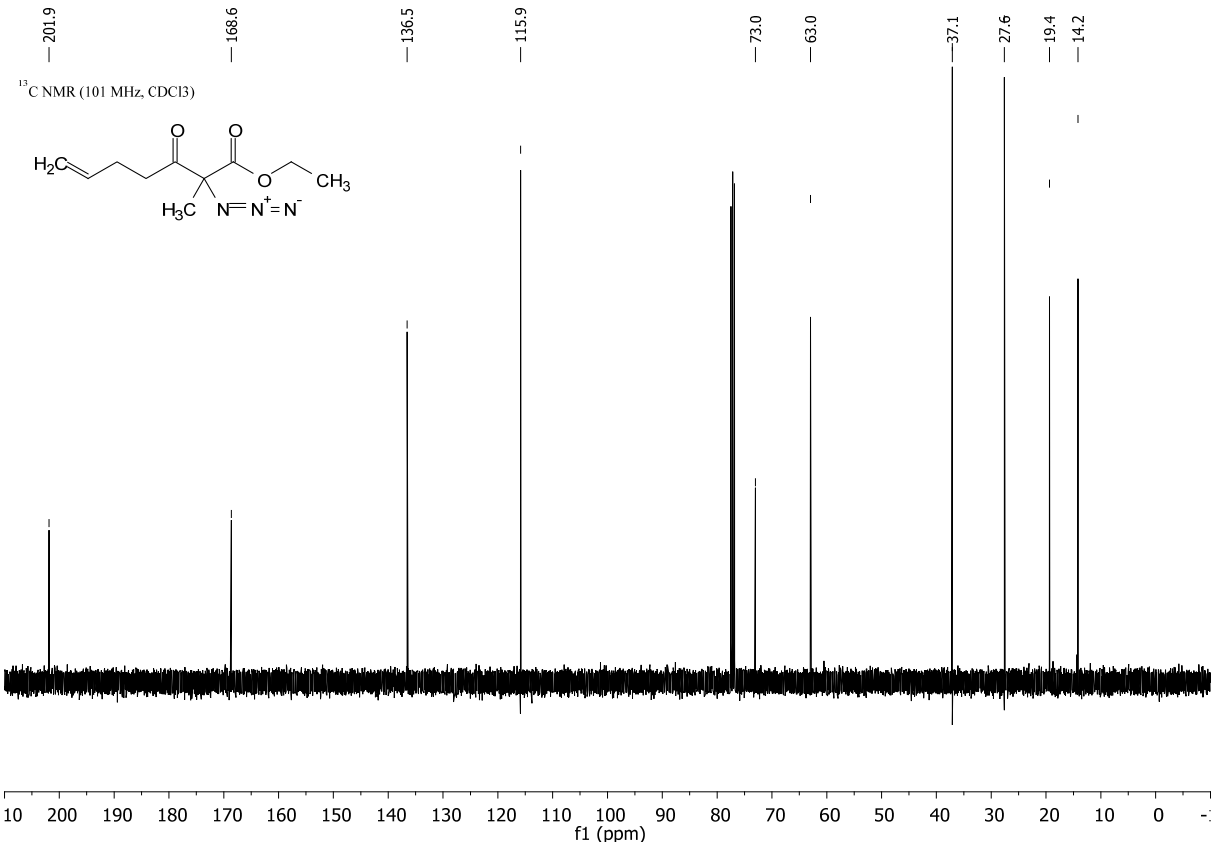
ethyl 2-methyl-3-oxohept-6-enoate

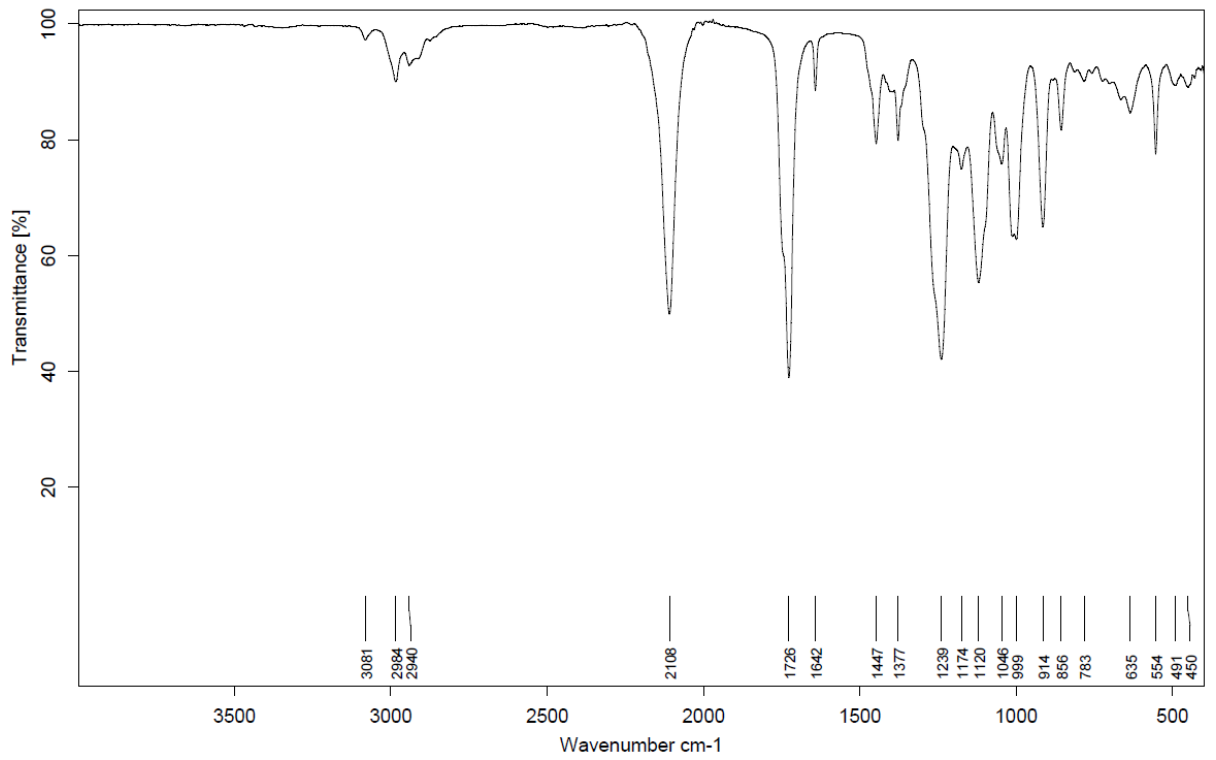




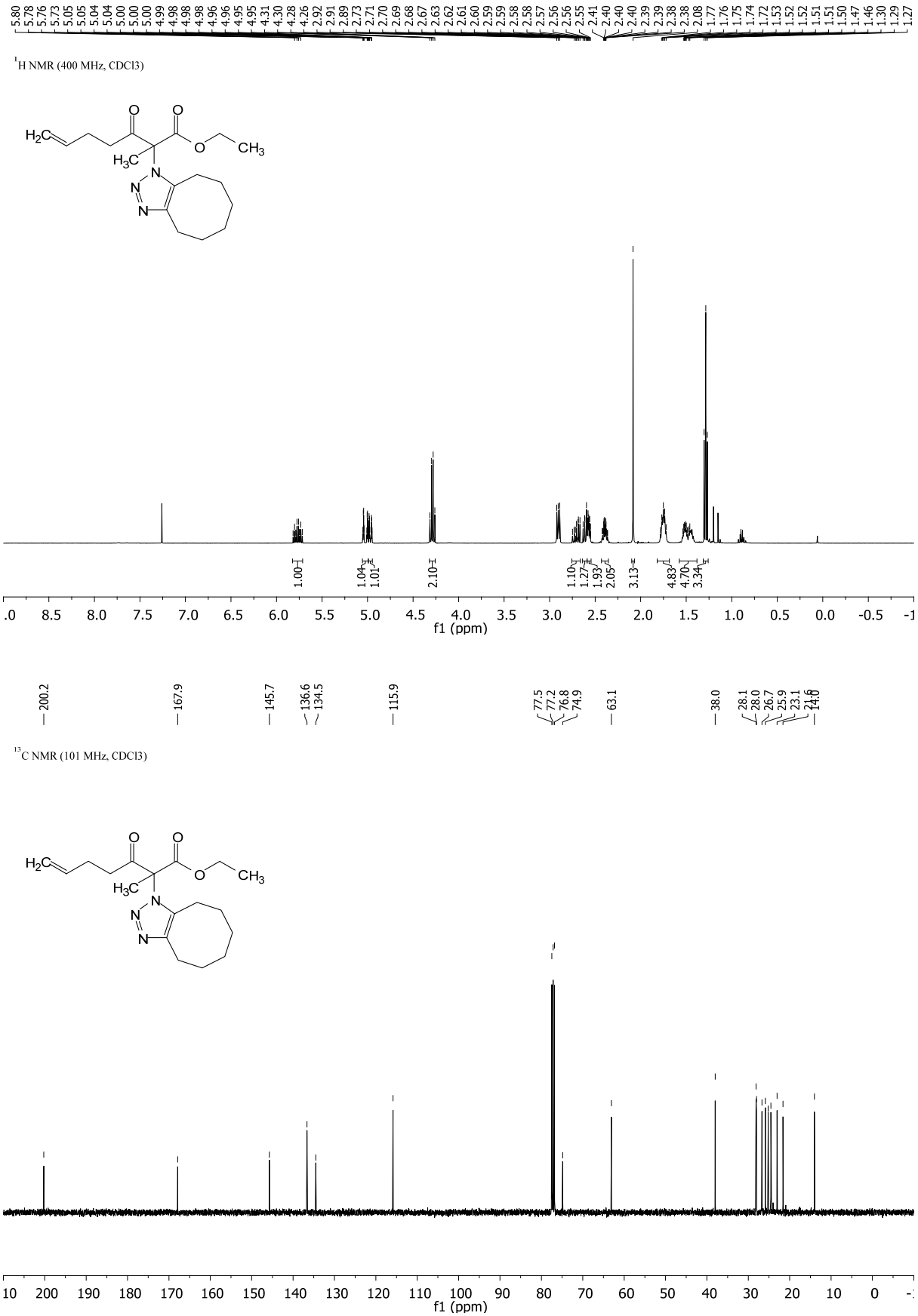
ethyl 2-azido-3-methyl-3-oxohept-6-enoate (3)



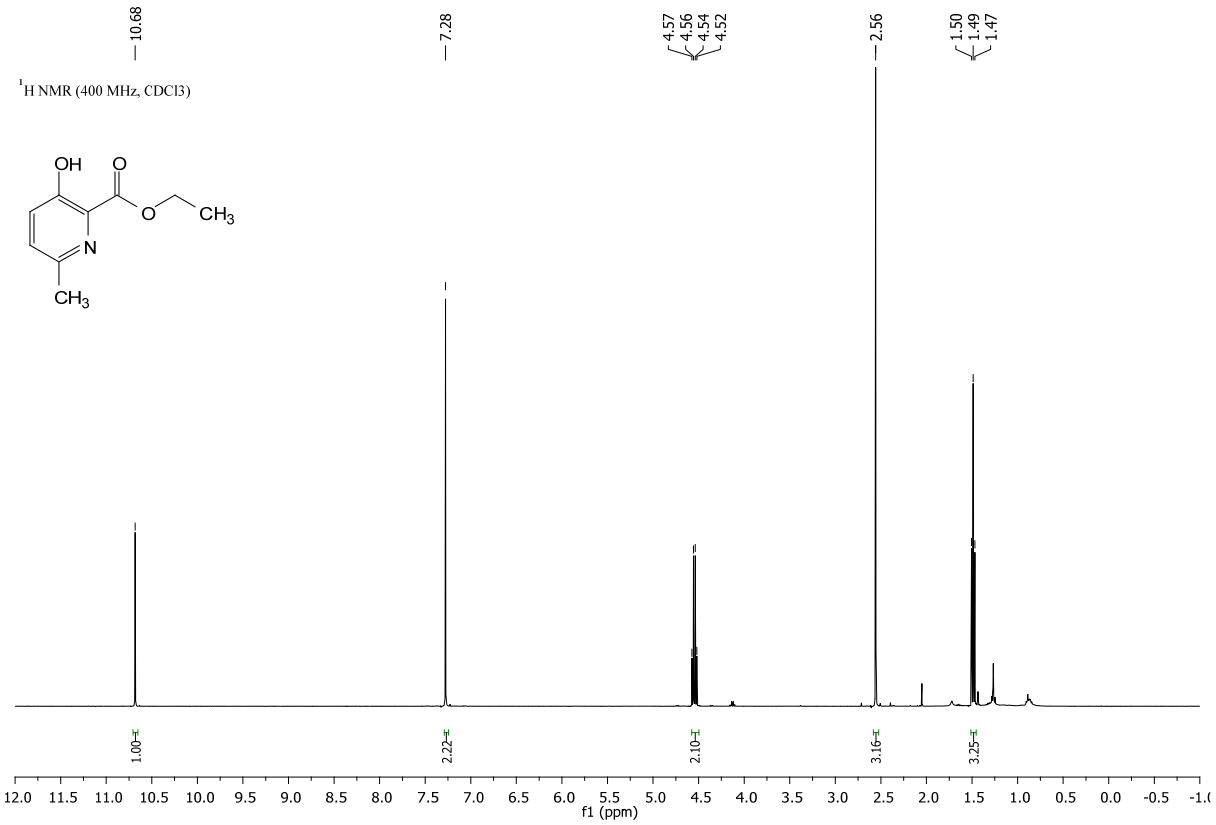

201.9
168.6
136.5
115.9
73.0
63.0
37.1
27.6
19.4
14.2
13C NMR (101 MHz, CDCl3)
f1 (ppm)

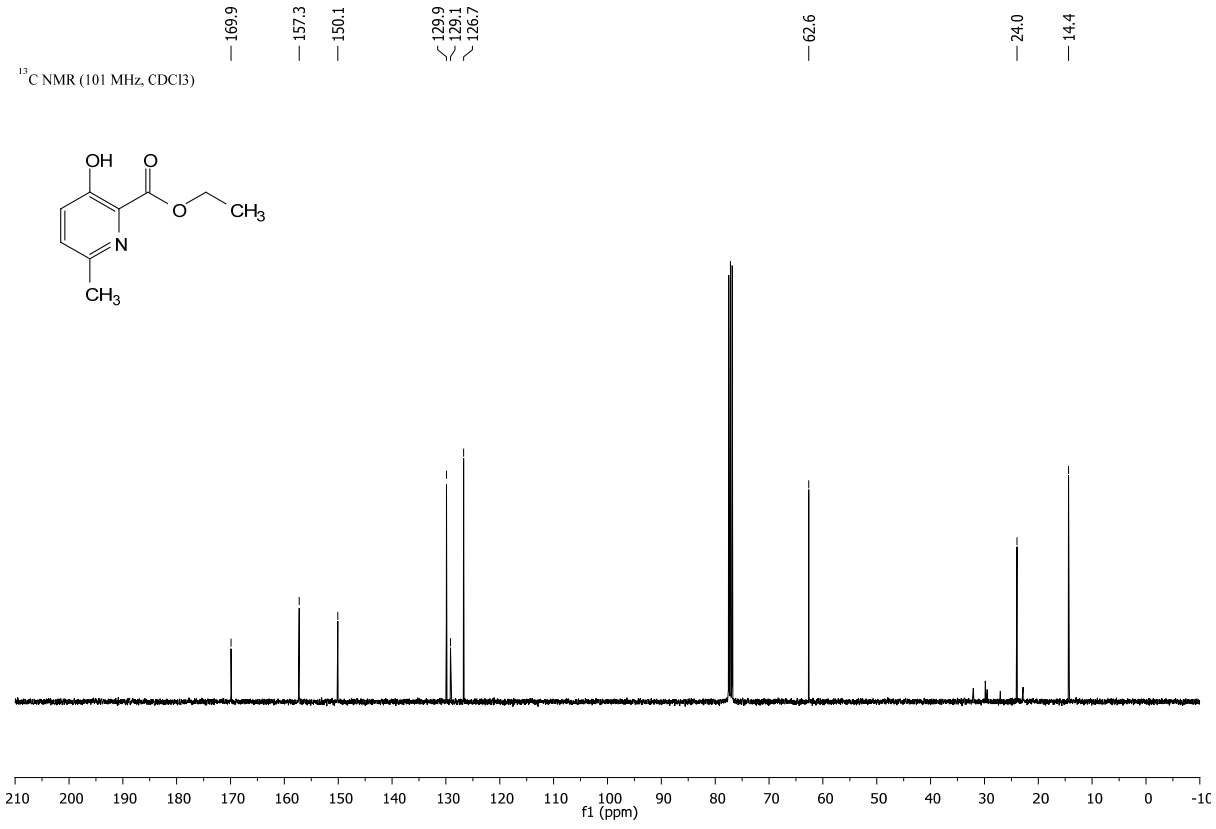

Transmittance [%]
Wavenumber cm-1
3081
2984
2940
2108
1726
1642
1447
1377
1239
1174
1120
1046
999
914
856
783
635
554
491
450

ethyl-2-(4,5,6,7,8,9-hexahydro-1*H*-cycloocta[*d*][1,2,3]triazol-1-yl)-2-methyl-3-oxohept-6-enoate

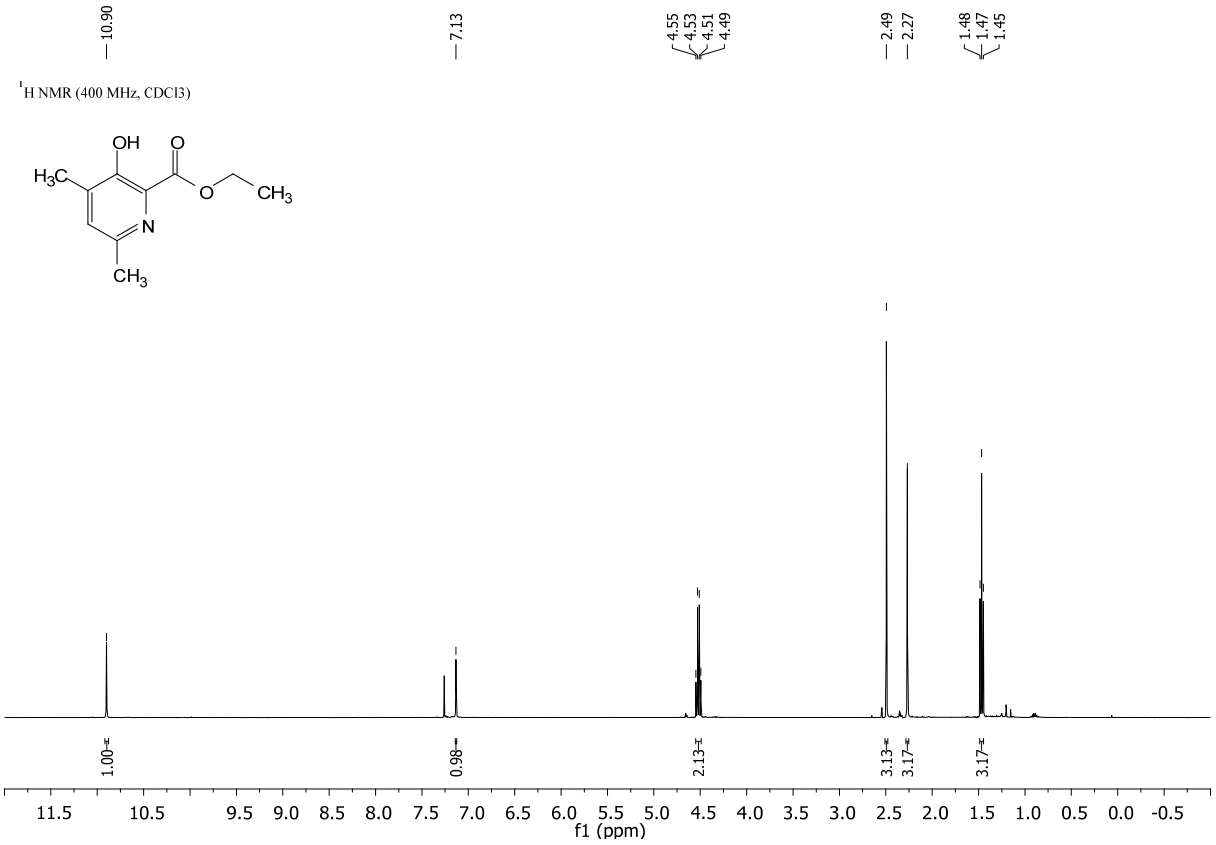


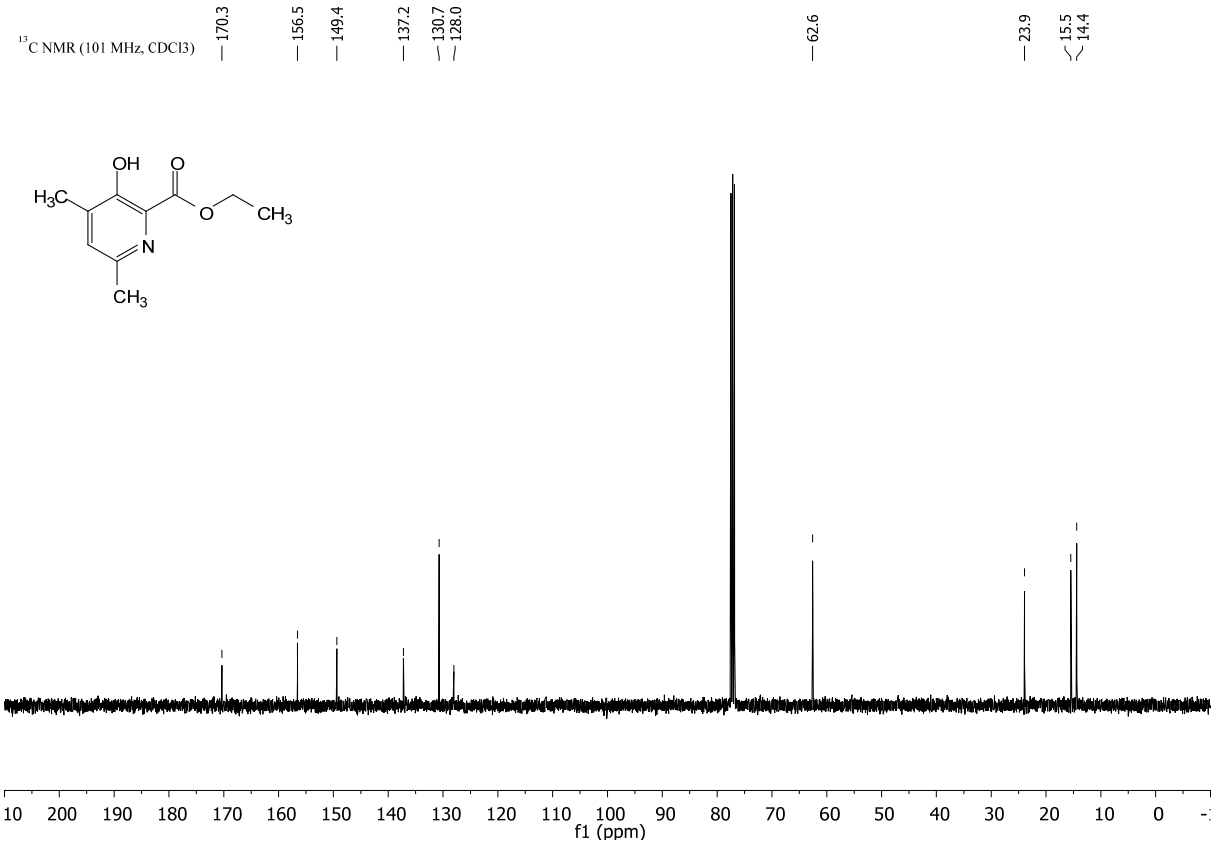
ethyl 3-hydroxy-6-methylpicolinate (2a)



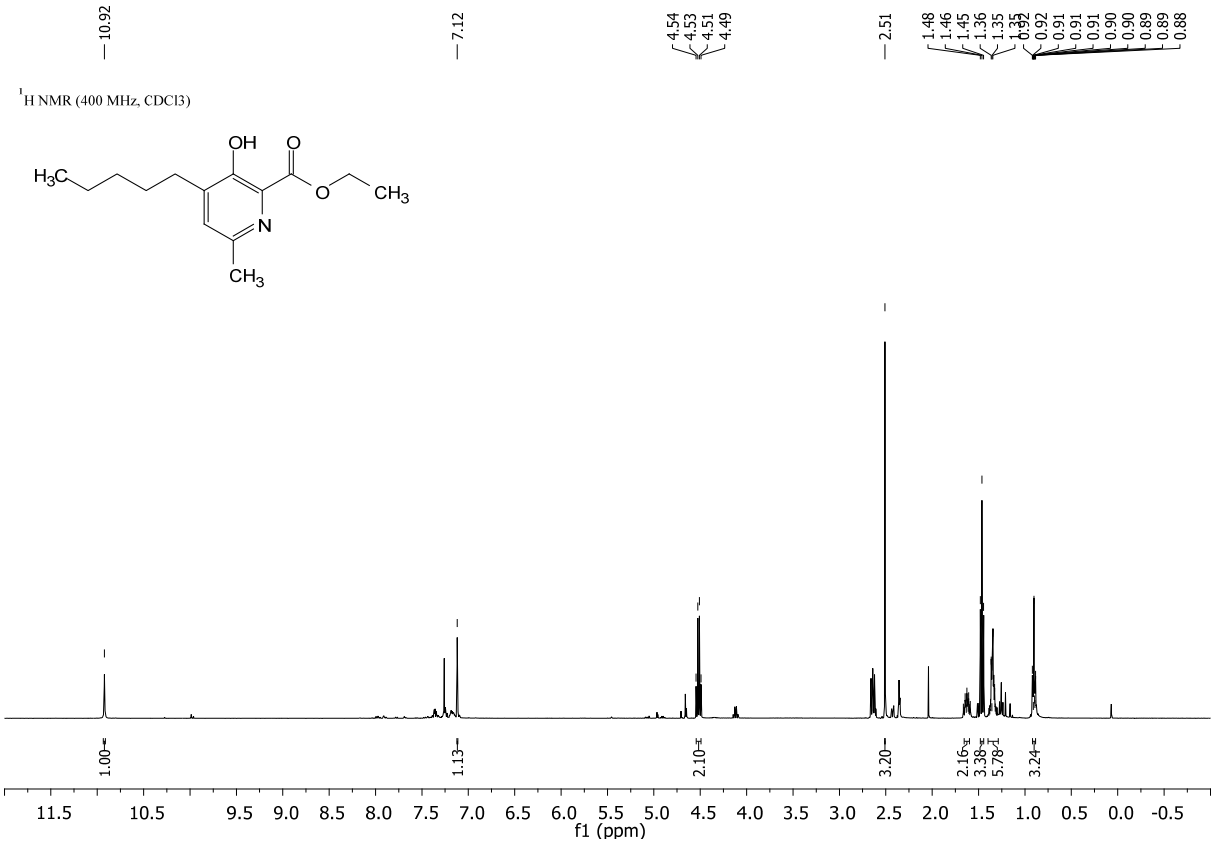


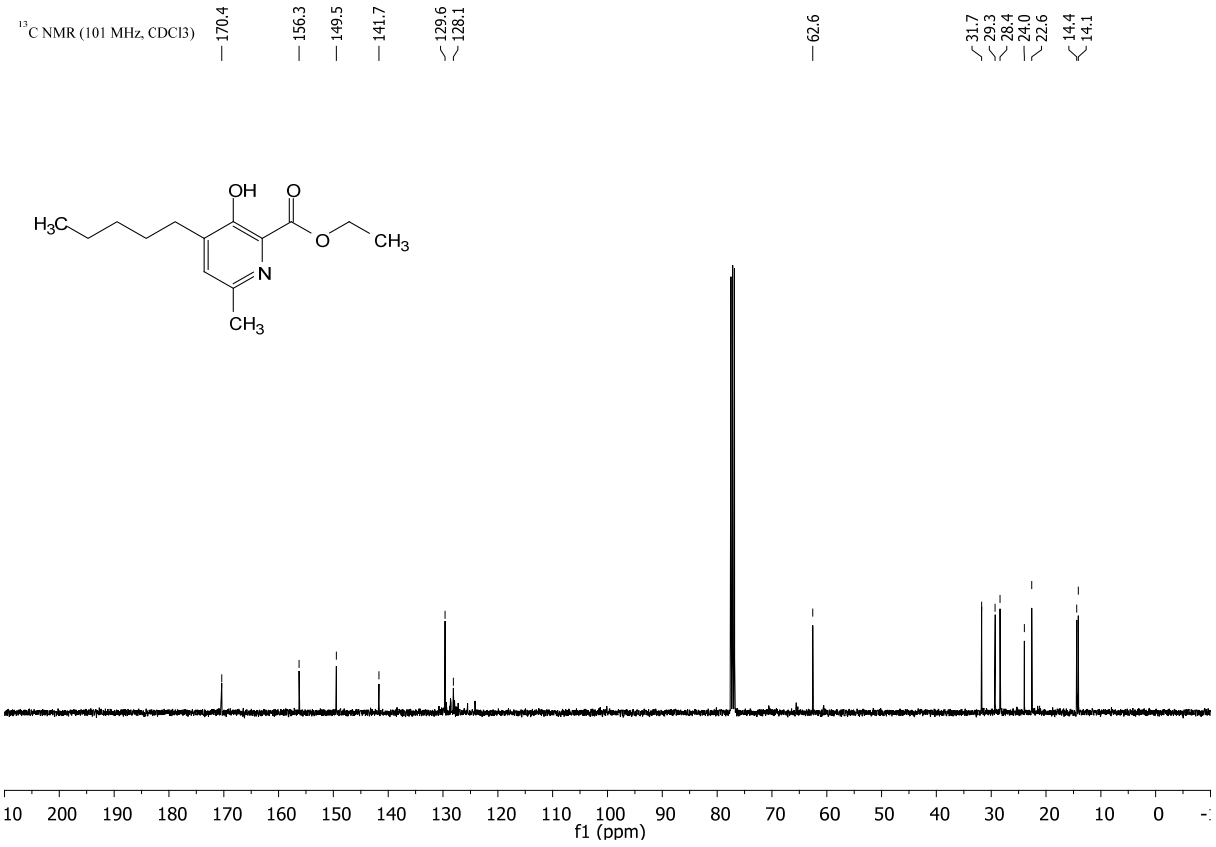
ethyl 3-hydroxy-4,6-methylpicolinate (2b)



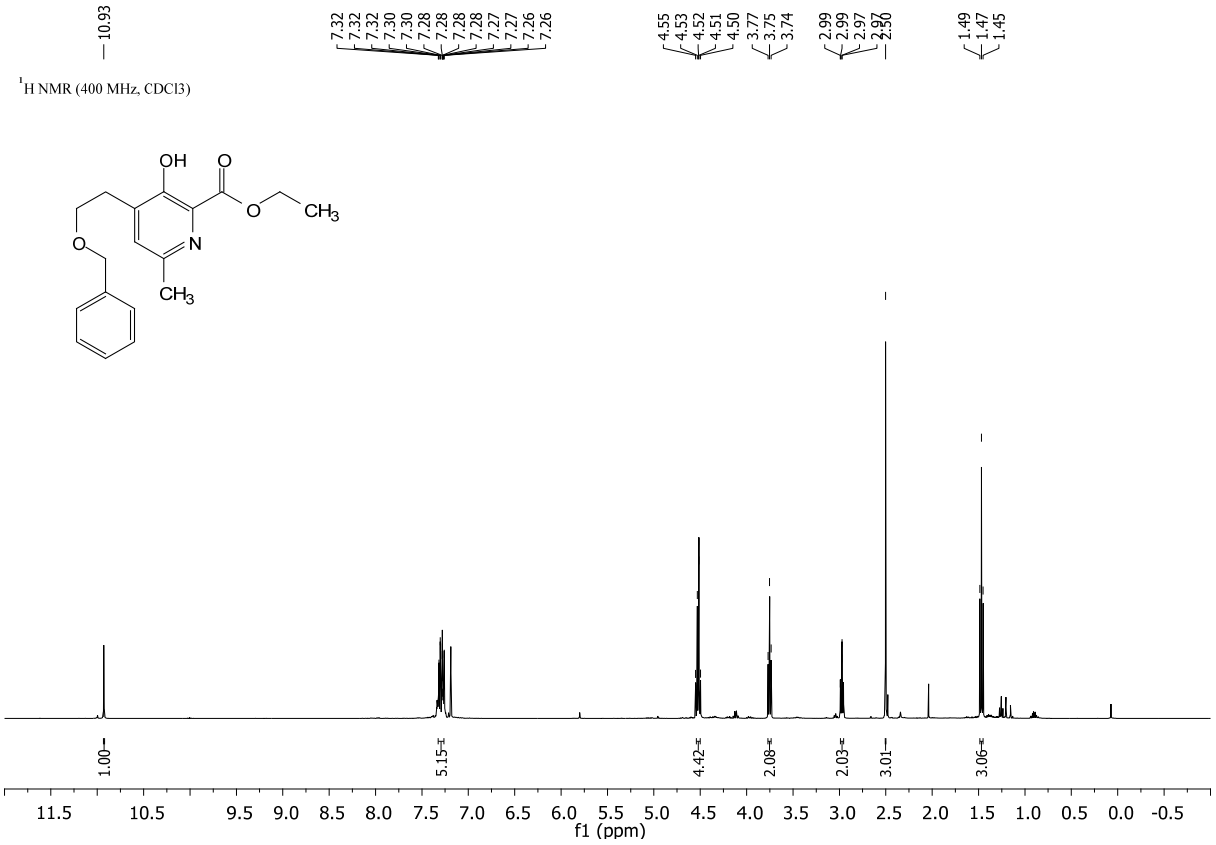


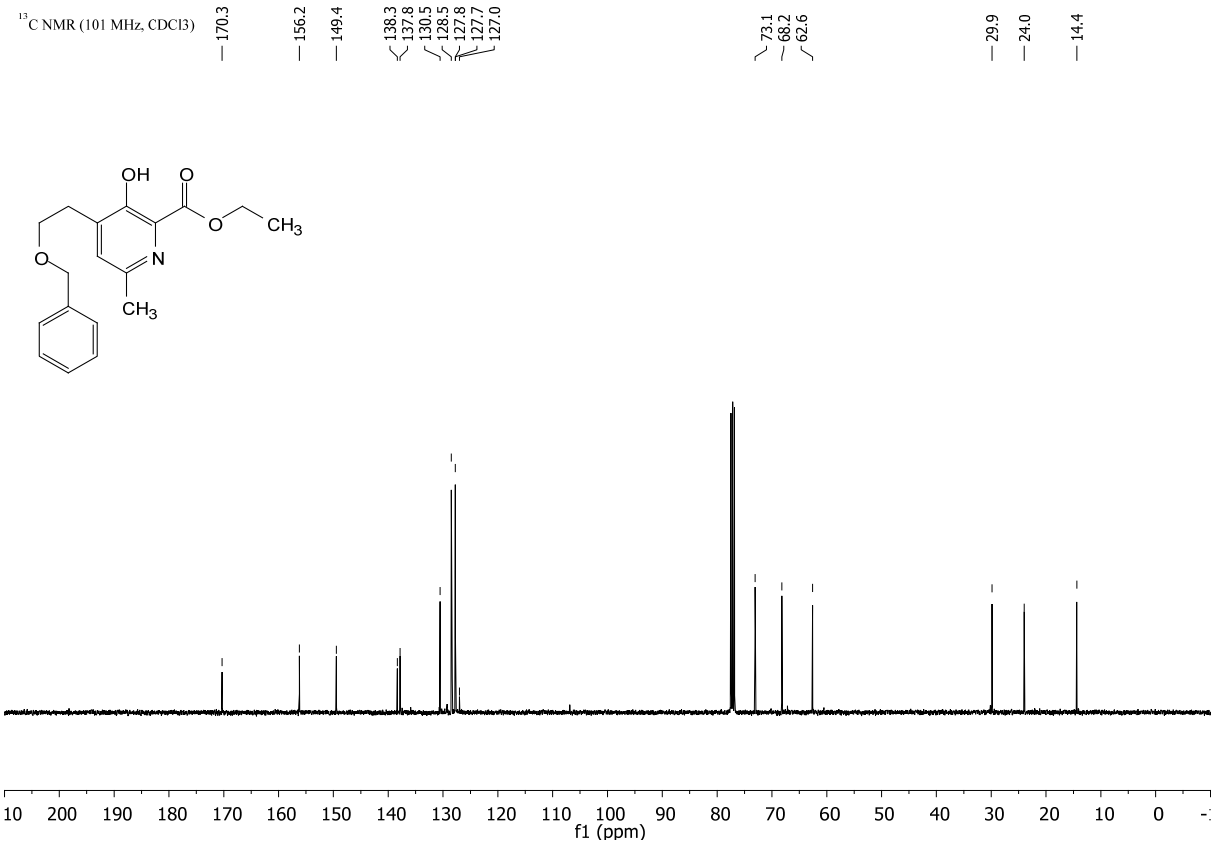
ethyl 3-hydroxy-6-methyl-4-pentylpicolinate (2c)



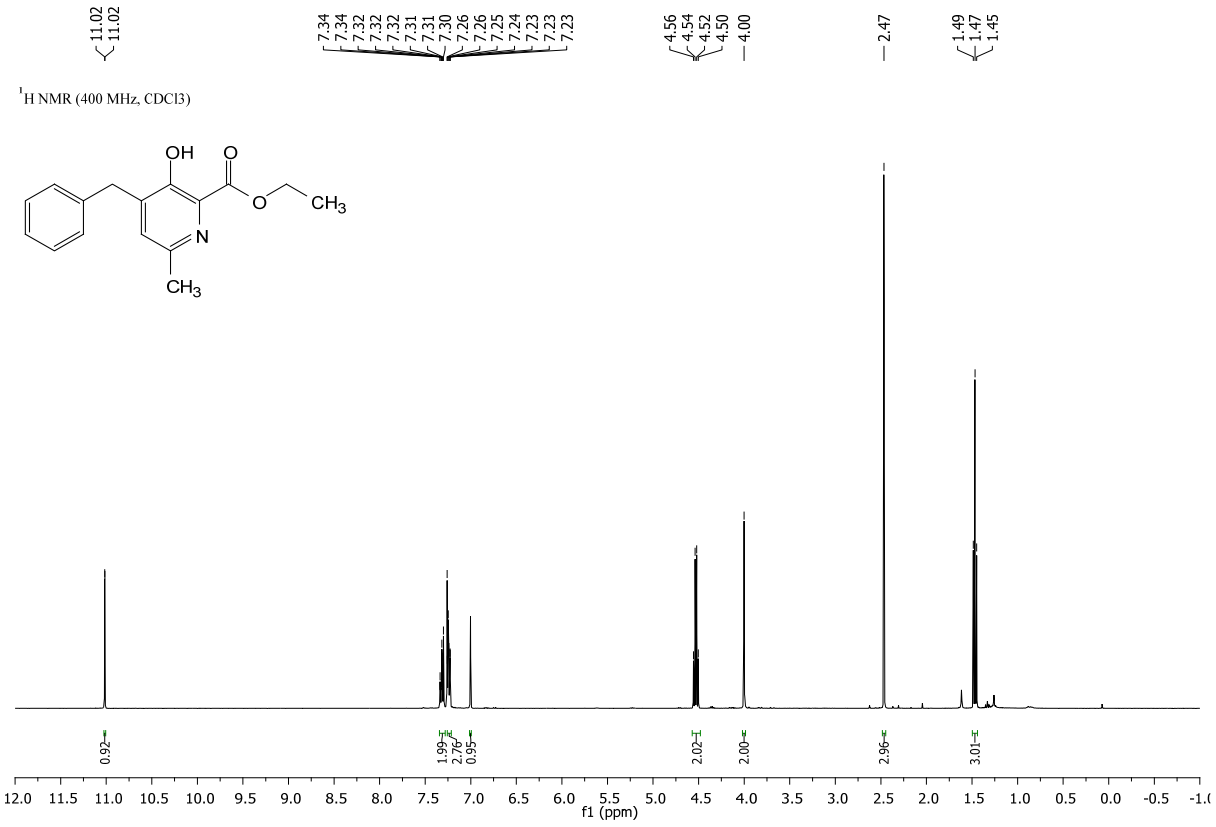


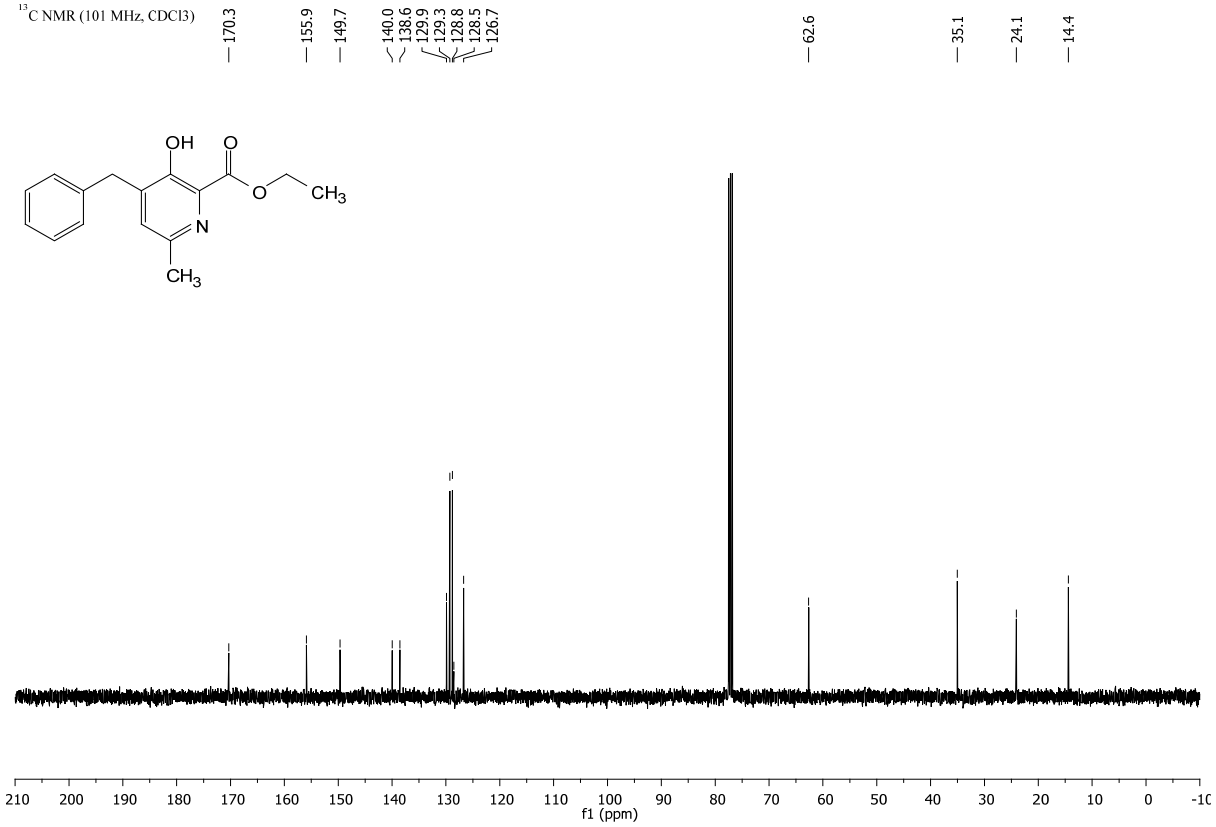
ethyl (2-(benzyloxy)ethyl)-3-hydroxy-6-methylpicolinate (2d)



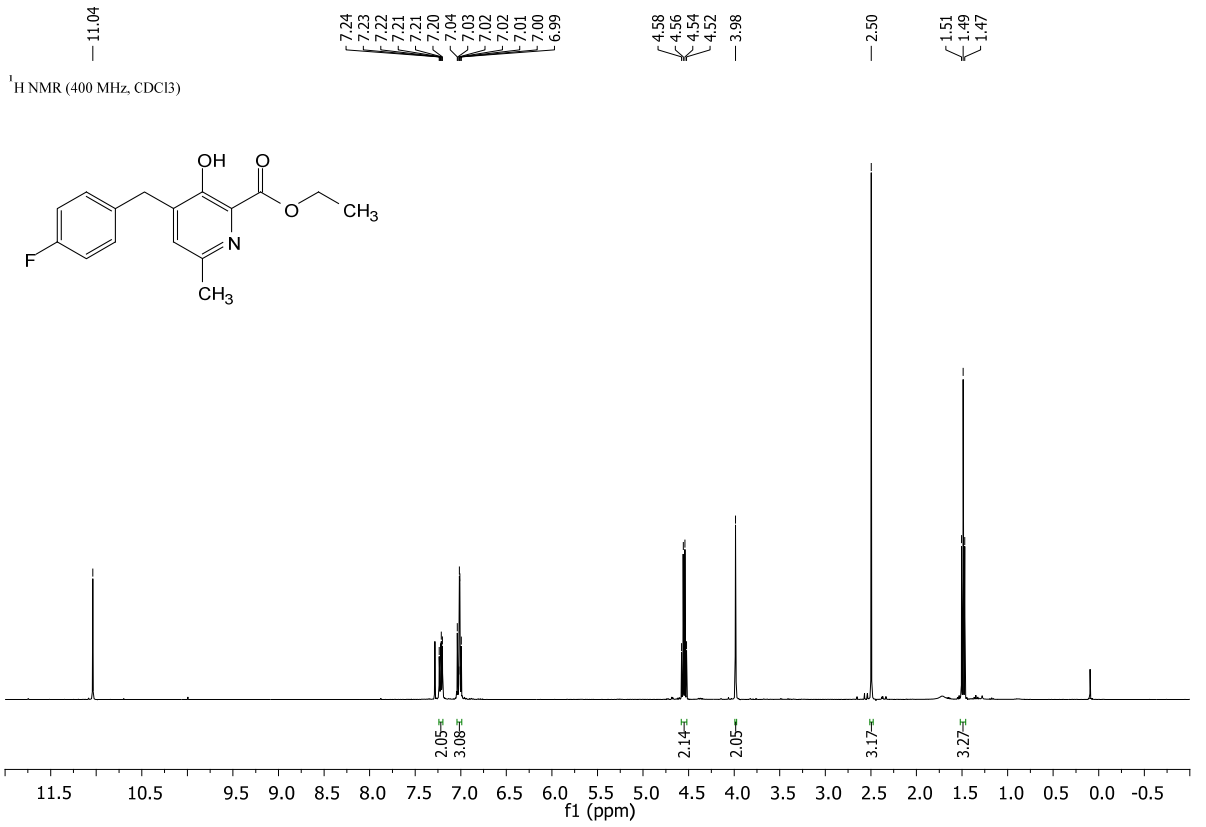


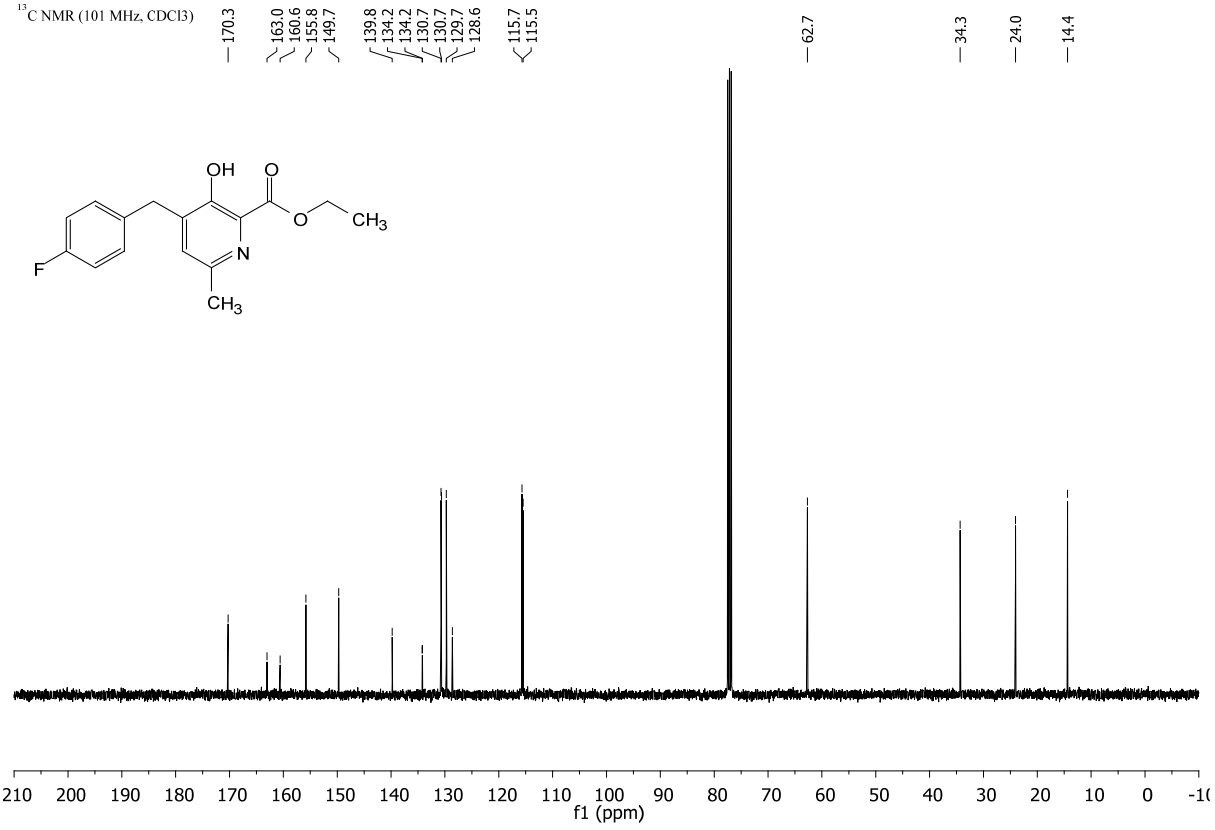
ethyl 4-benzyl-3-hydroxy-6-methylpicolinate (2e)



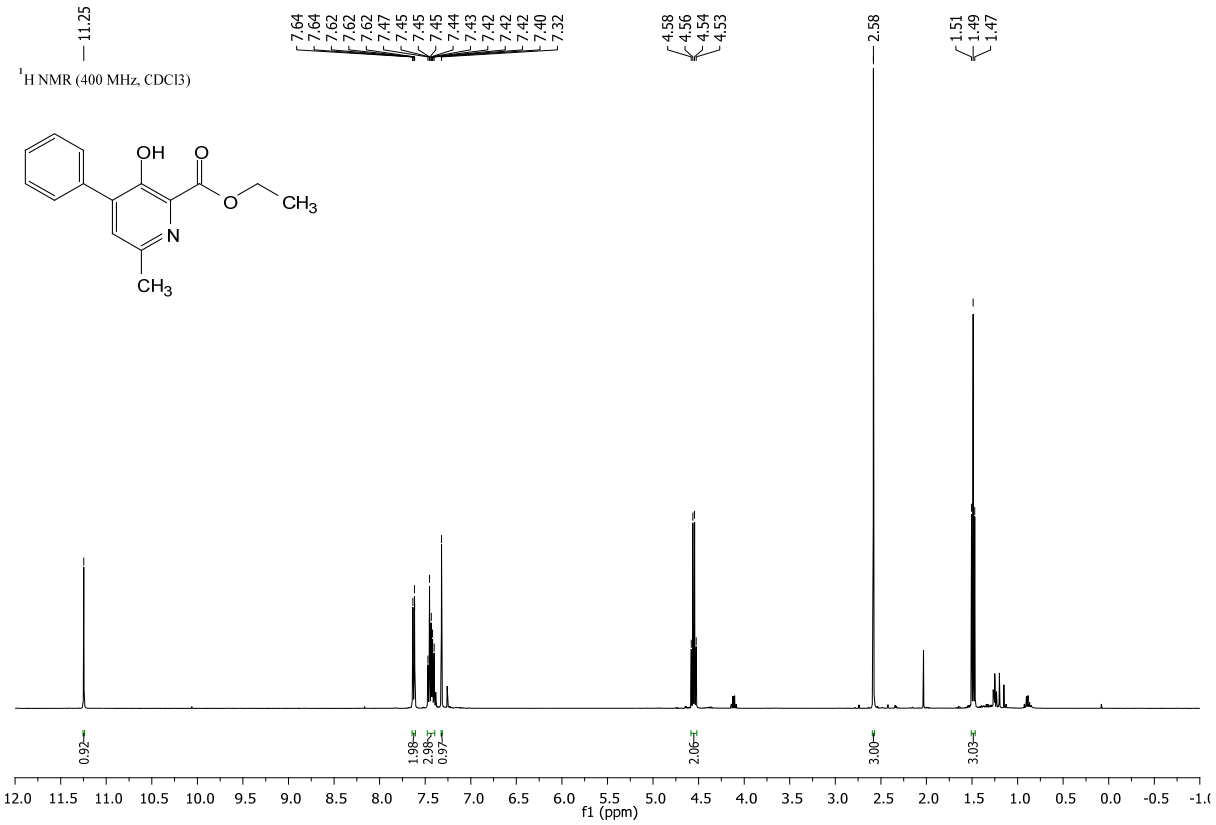


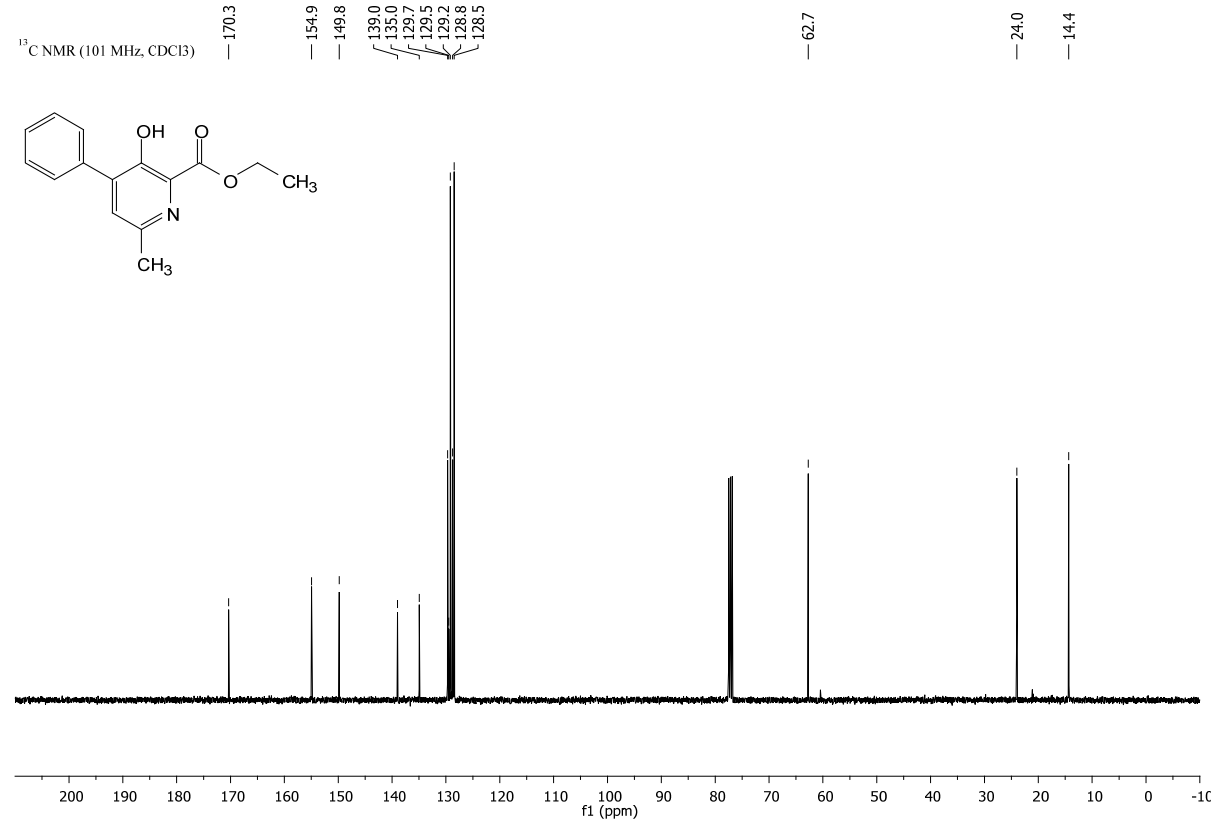
ethyl 4-(4-fluorobenzyl)-3-hydroxy-6-methylpicolinate (2f)



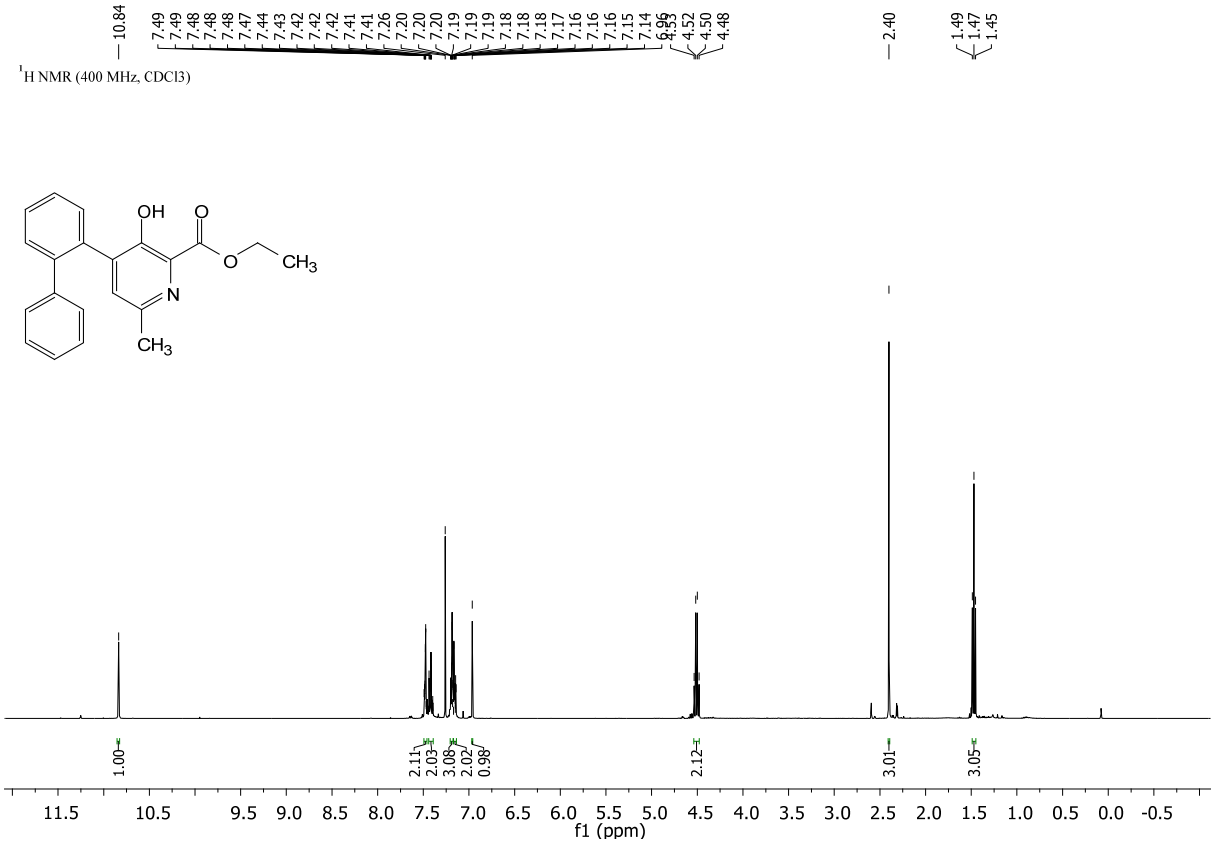


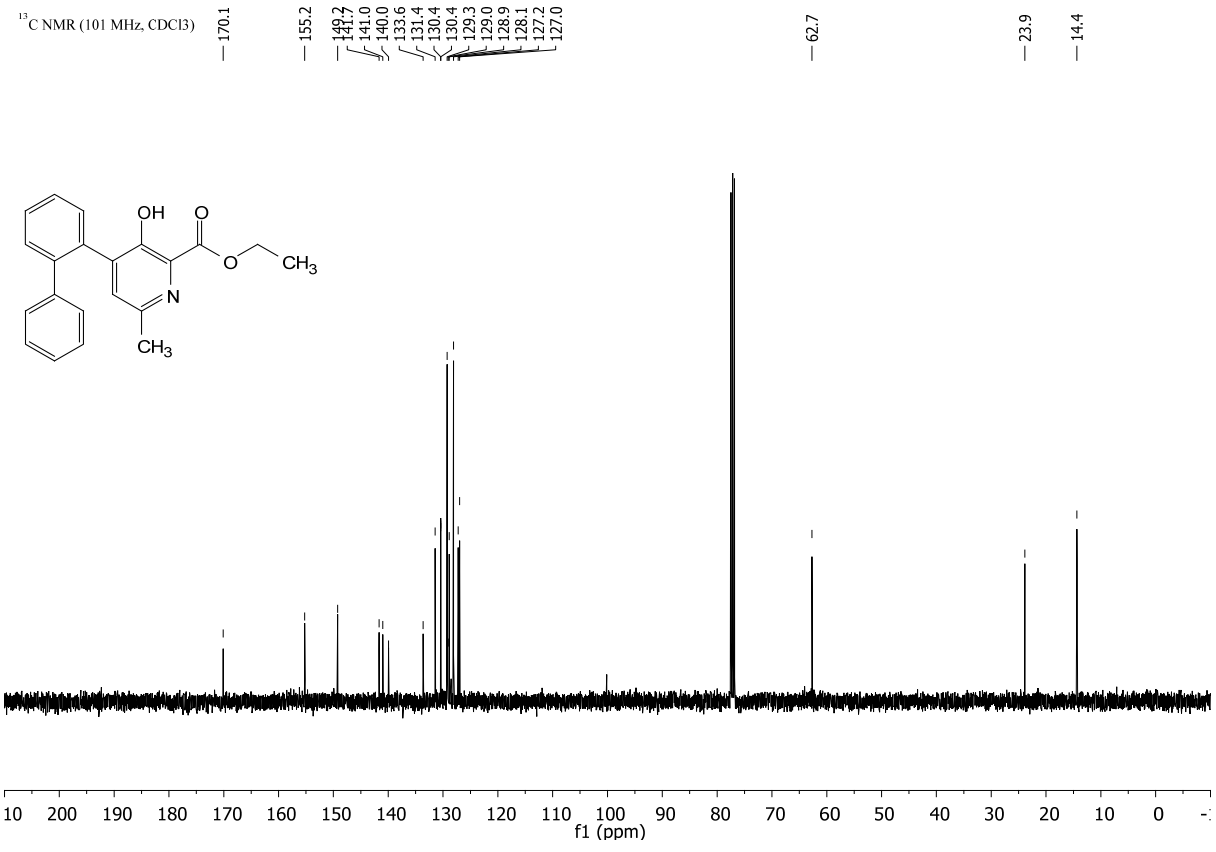
ethyl 3-hydroxy-6-methyl-phenylpicolinate (2g)



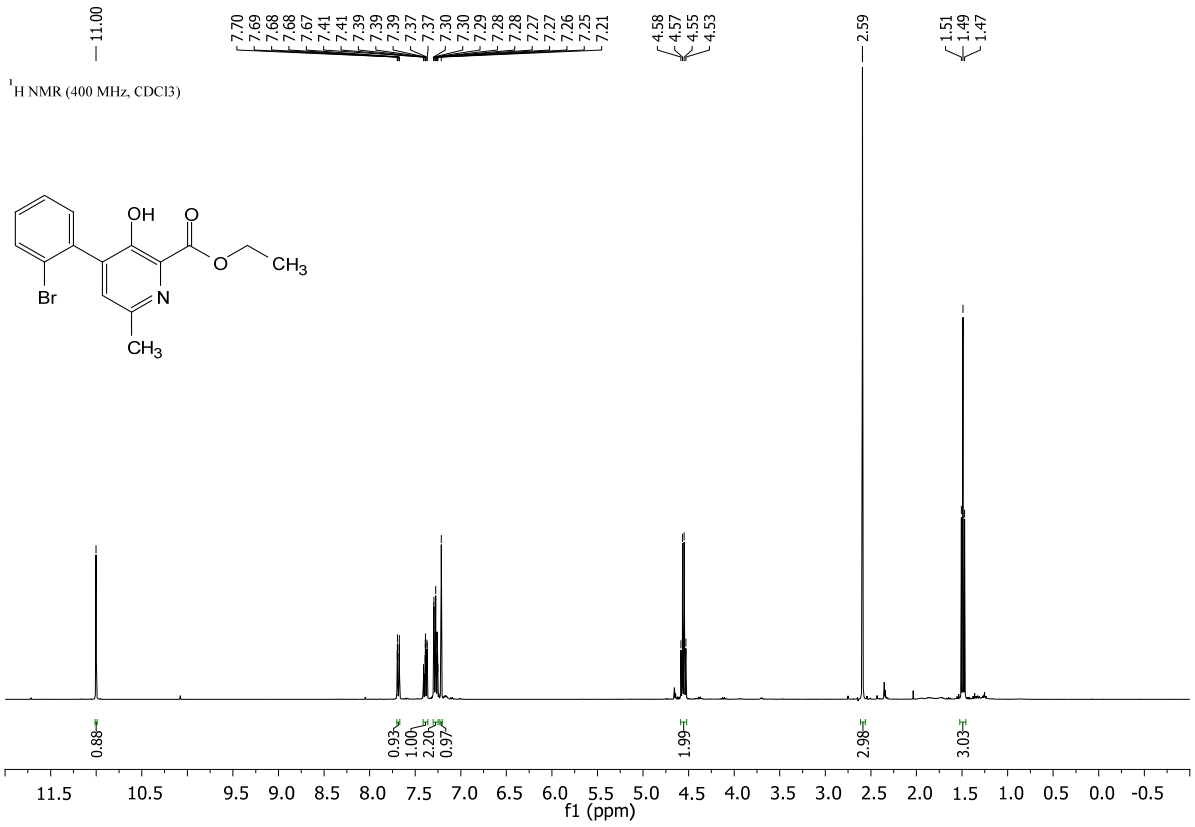


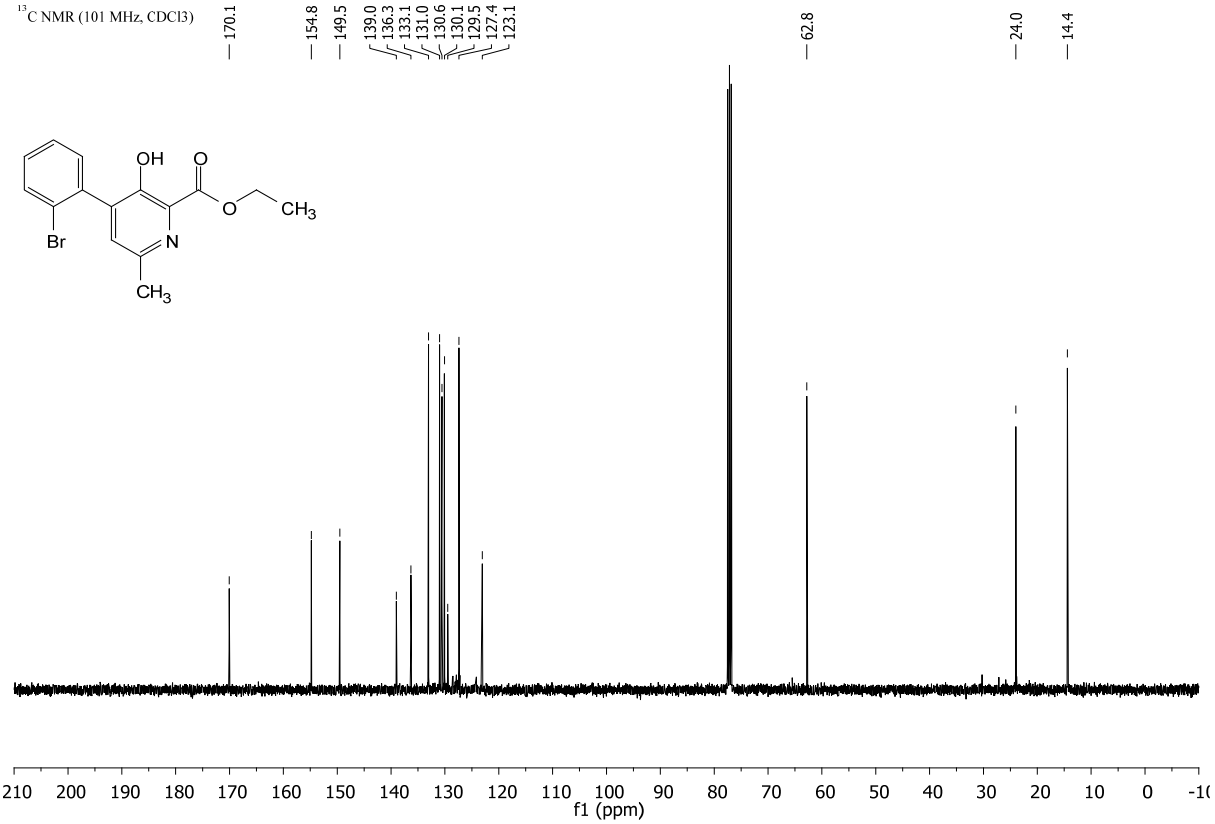
ethyl 4-([1,1'-biphenyl]-2-yl)-3-hydroxy-6-methylpicolinate (2h)



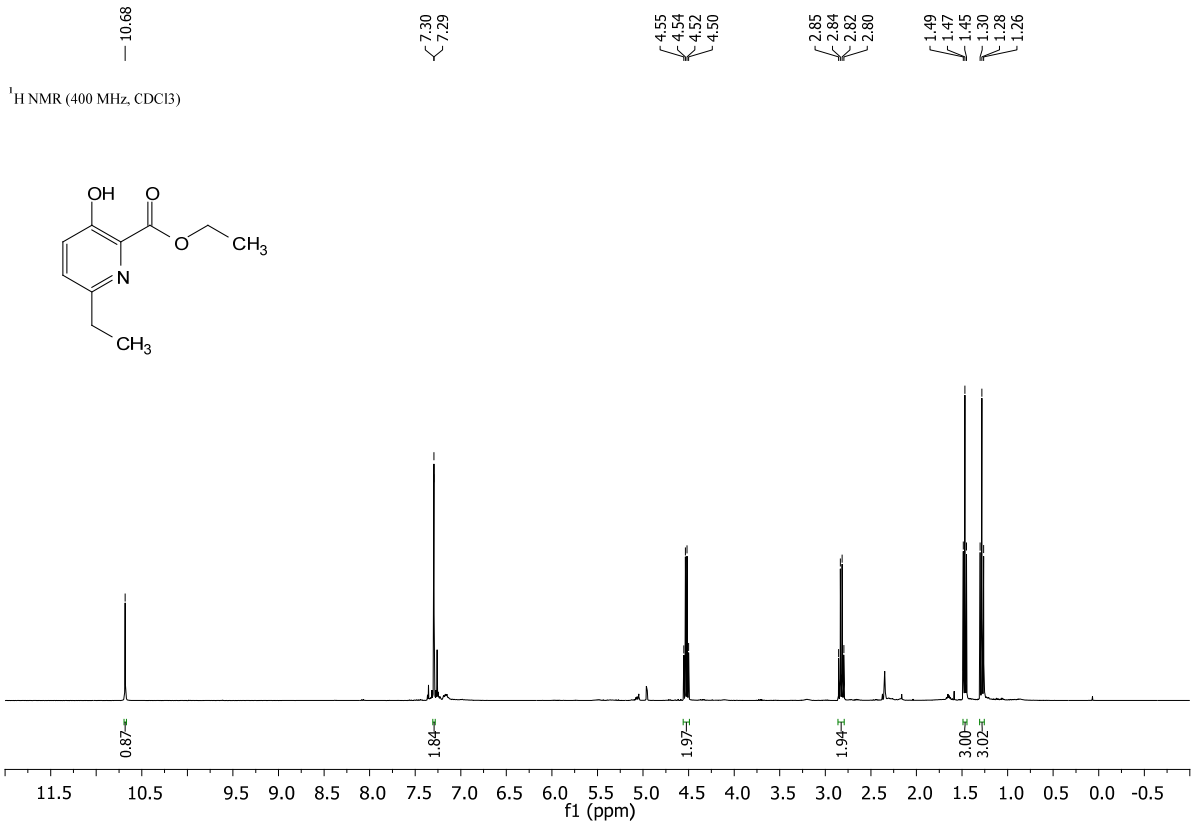


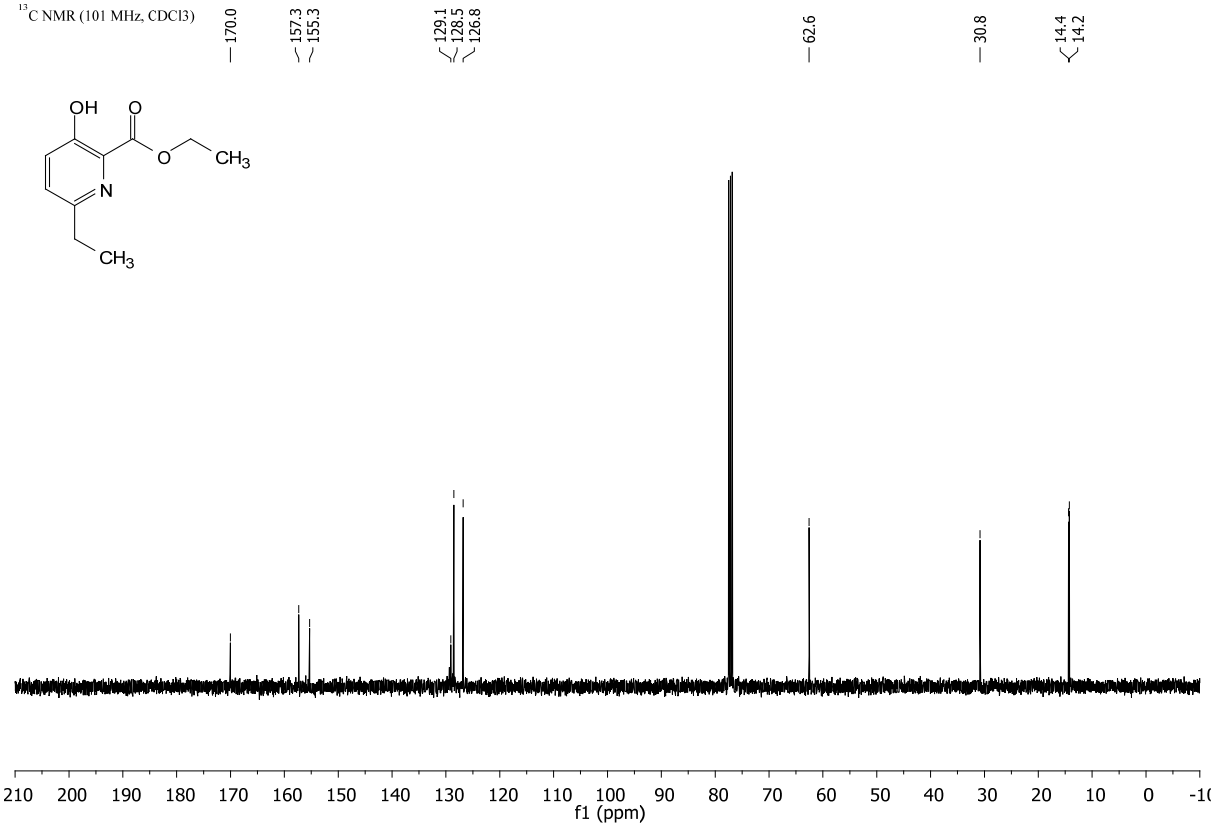
ethyl 4-(2-bromophenyl)-3-hydroxy-6-methylpicolinate (2i)



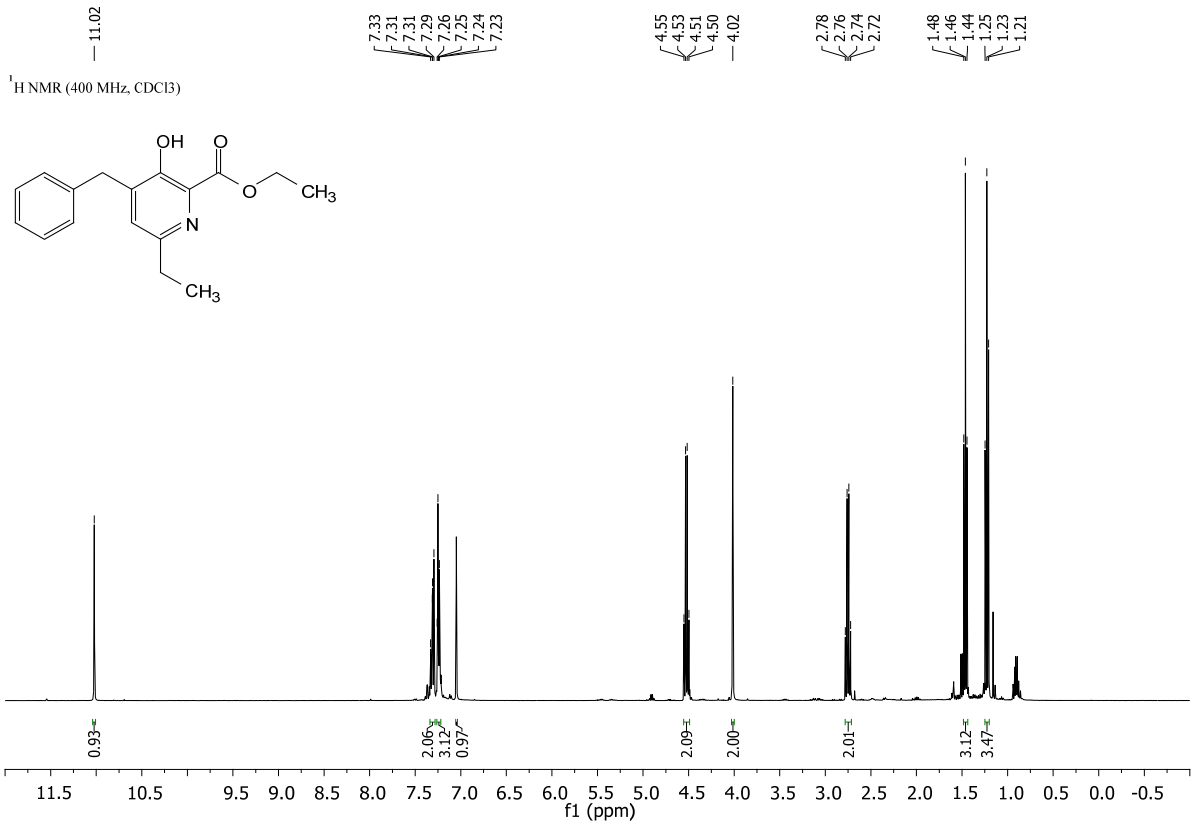


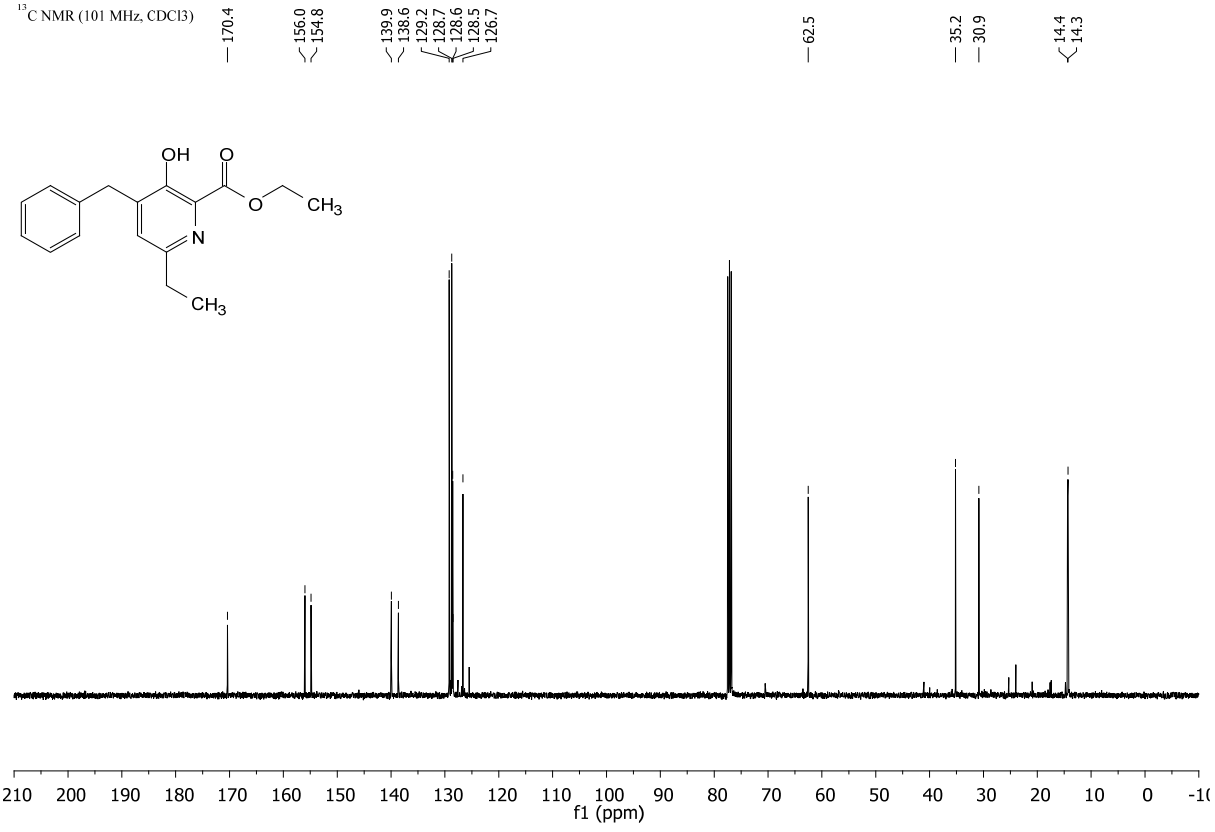
ethyl 6-ethyl-3-hydroxypicolinate (2j)



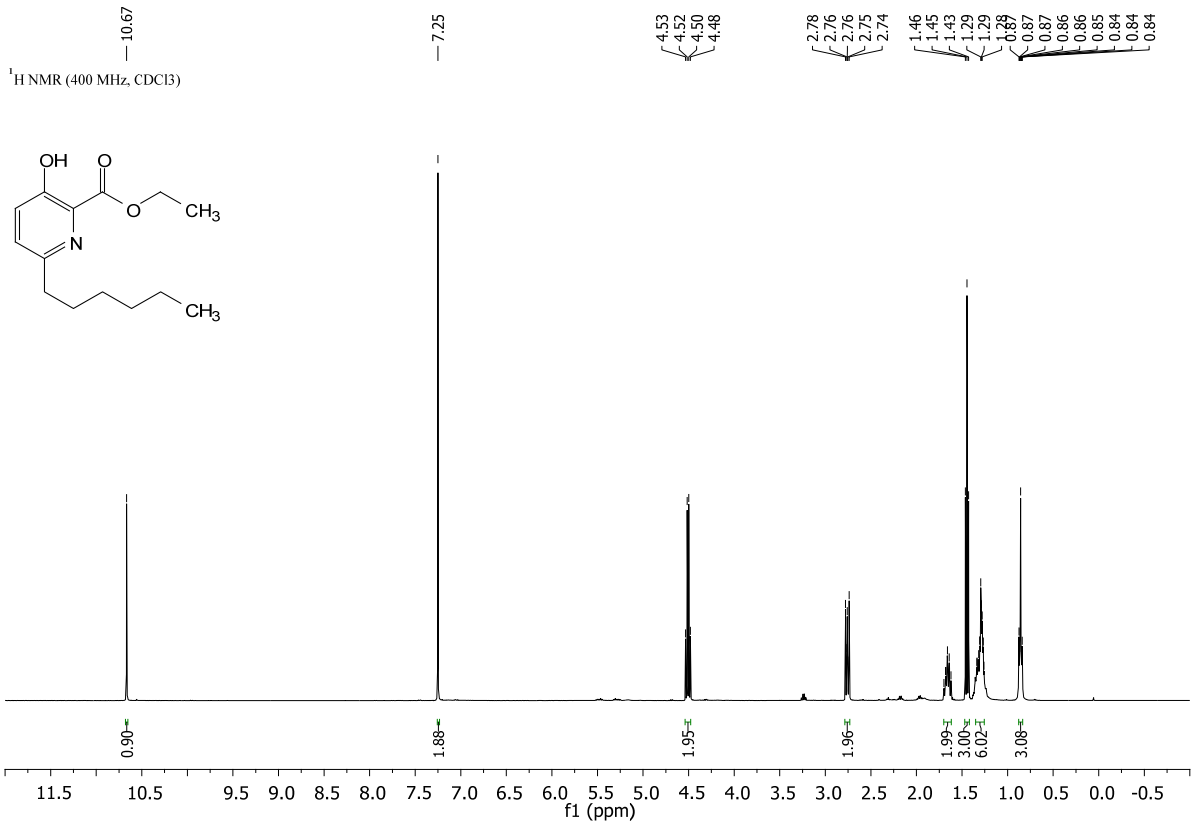


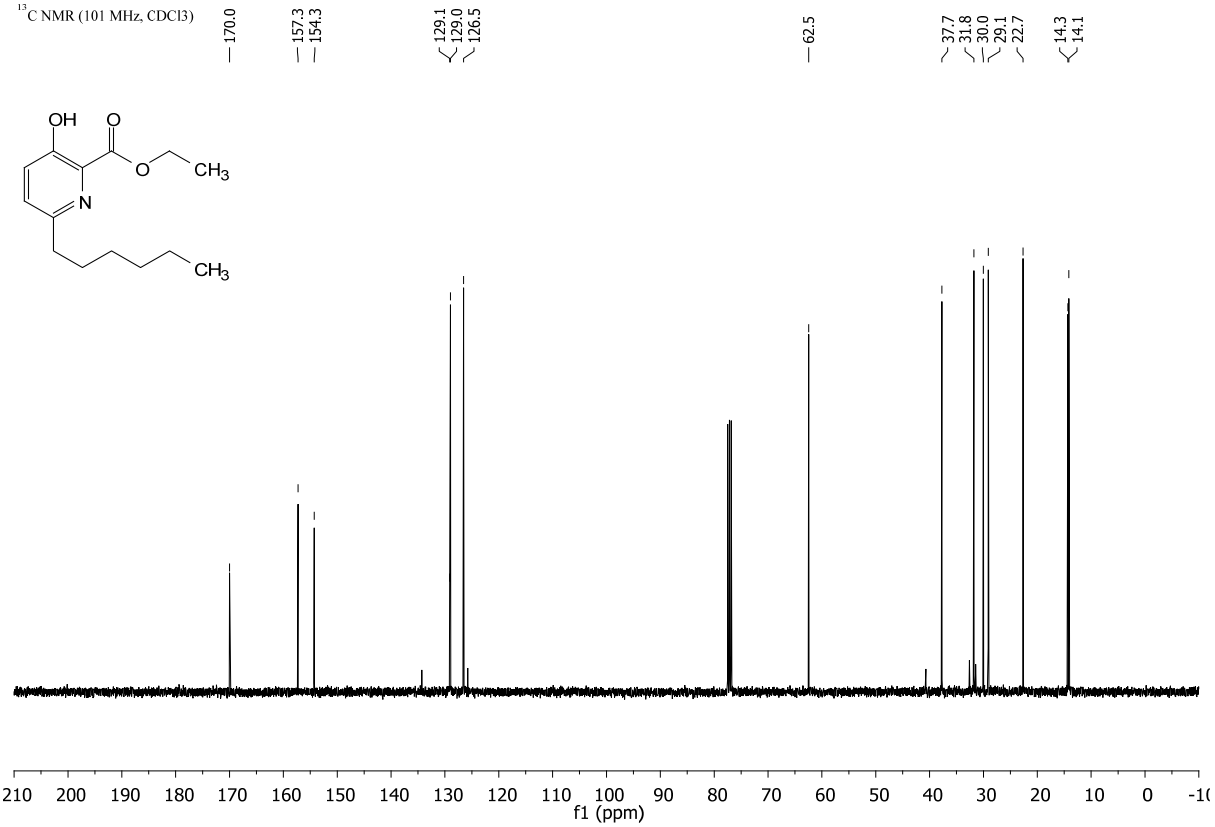
ethyl 4-benzyl-6-ethyl-3-hydroxypicolinate (2k)



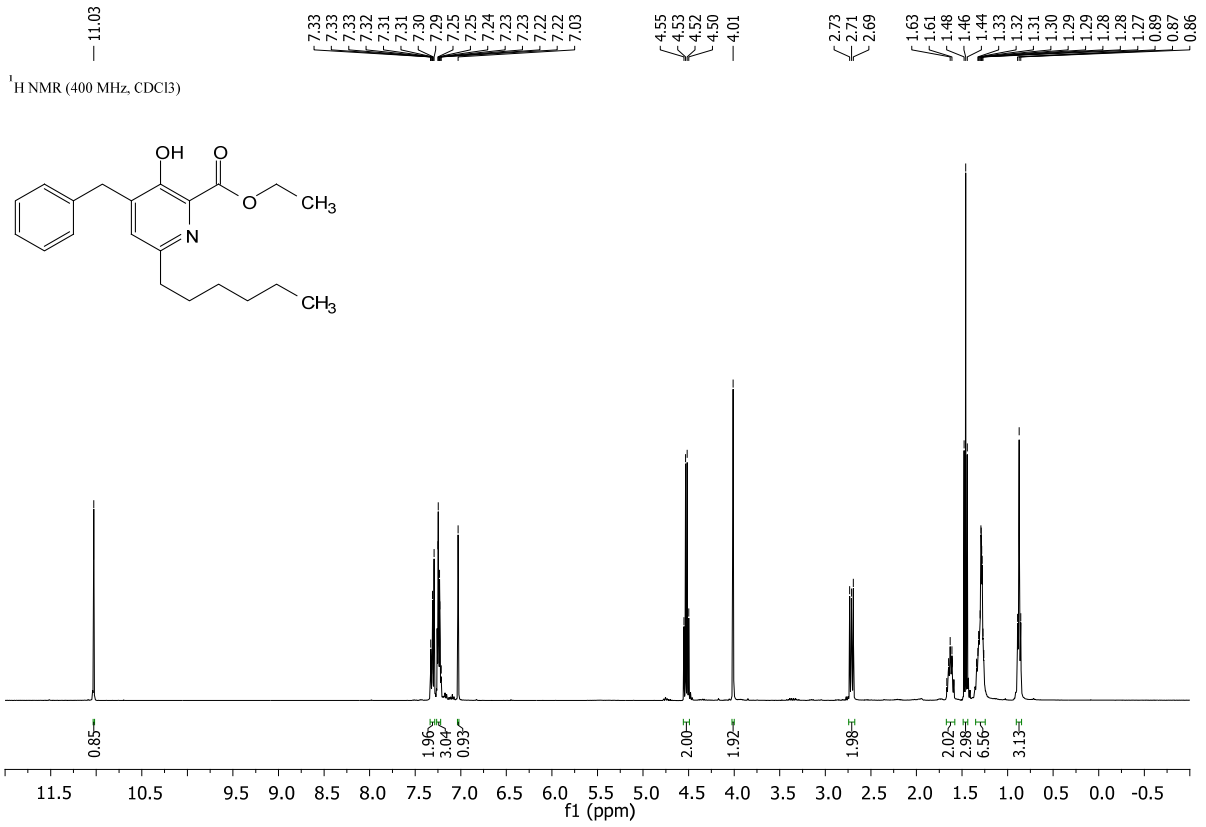


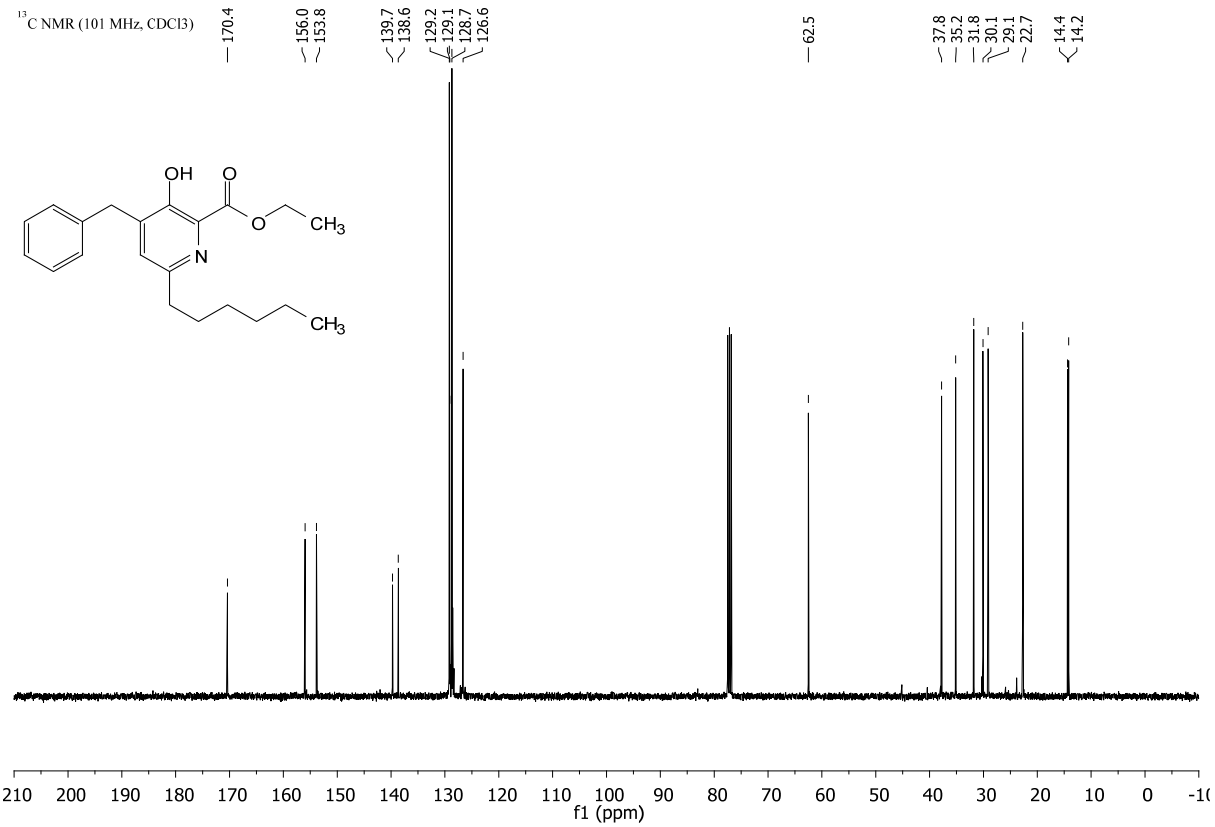
ethyl 6-hexyl-3-hydroxypicolinate (2l)



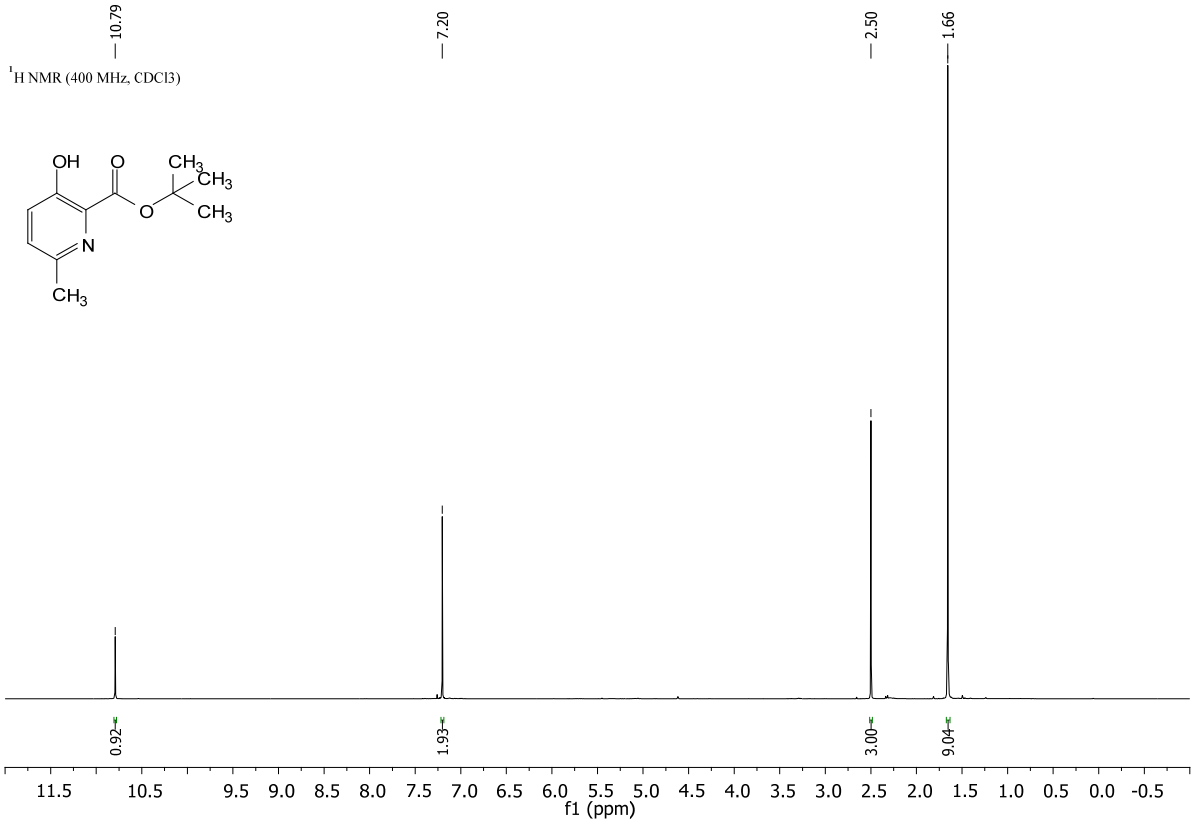


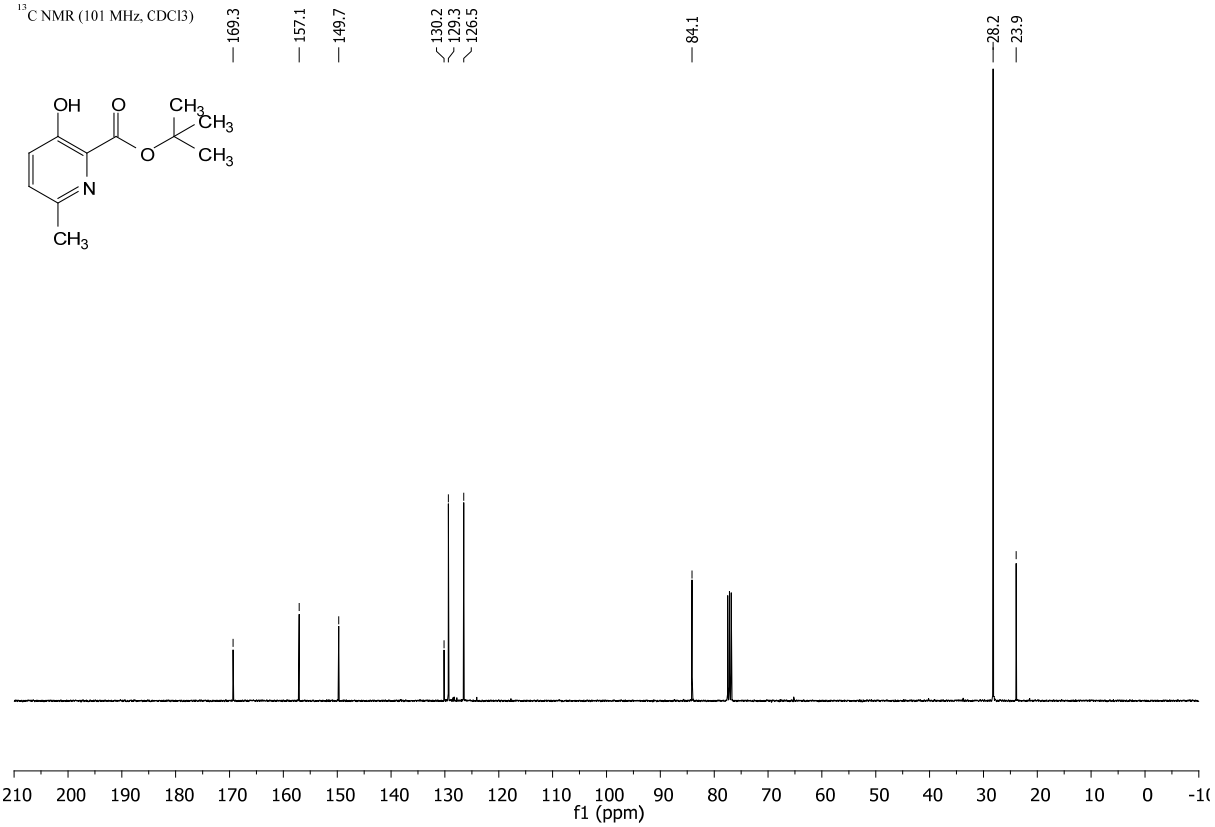
ethyl 4-benzyl-6-hexyl-3-hydroxypicolinate (2m)



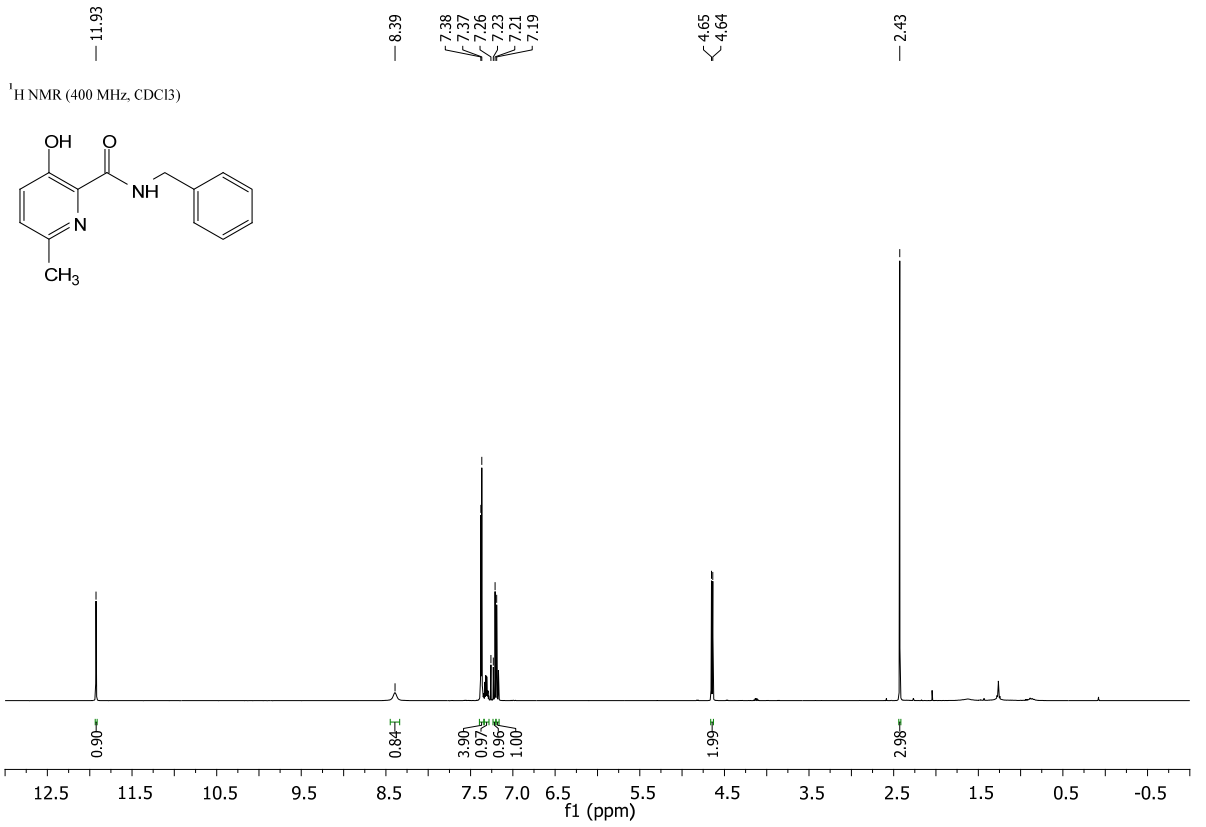


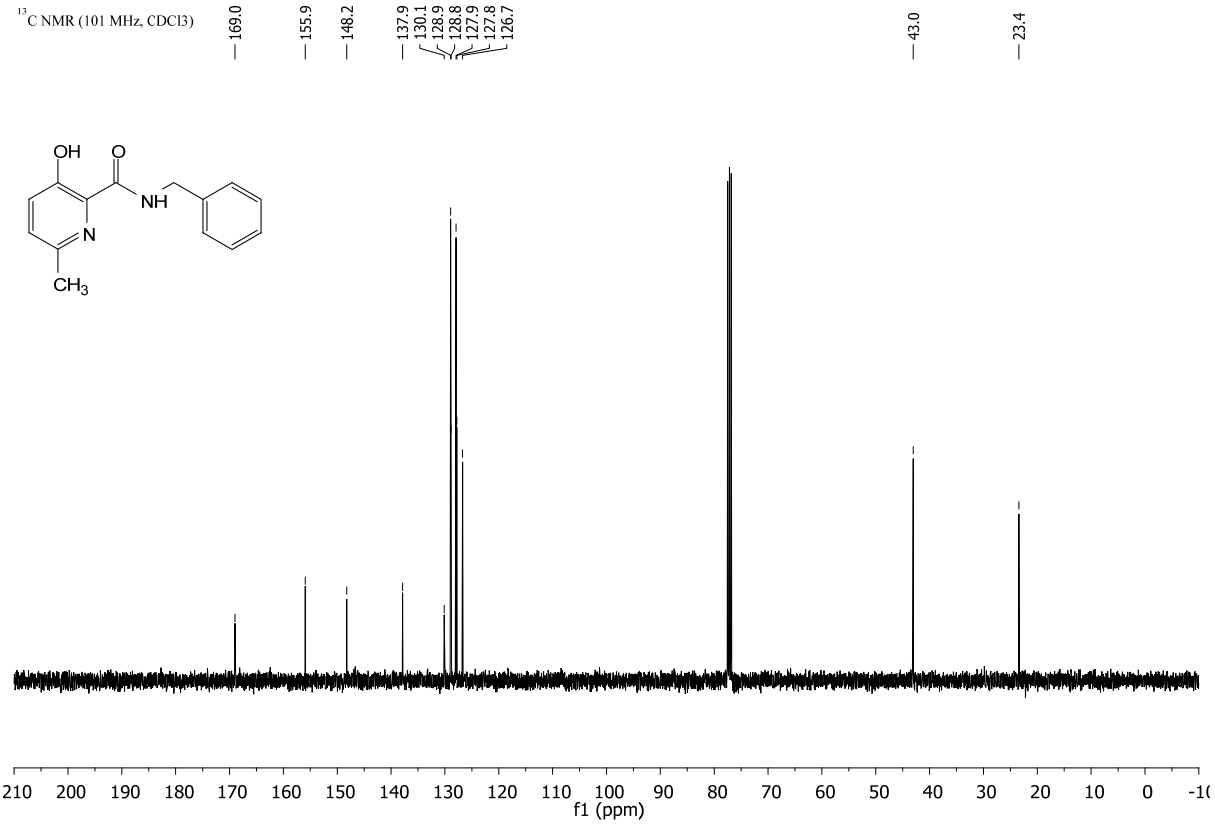
tert-butyl 3-hydroxy-6-methylpicolinate (2n)





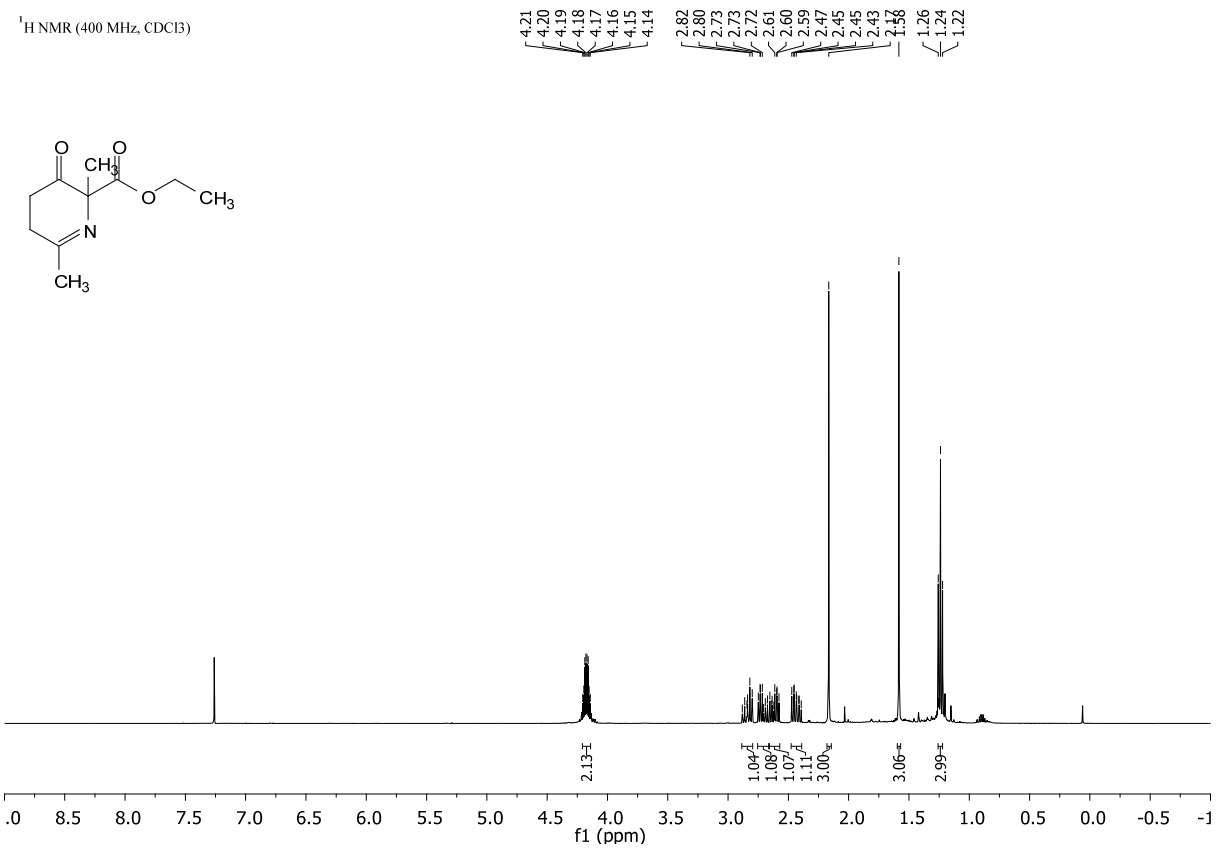
N-benzyl 3-hydroxy-6-methylpicolinate (2o)



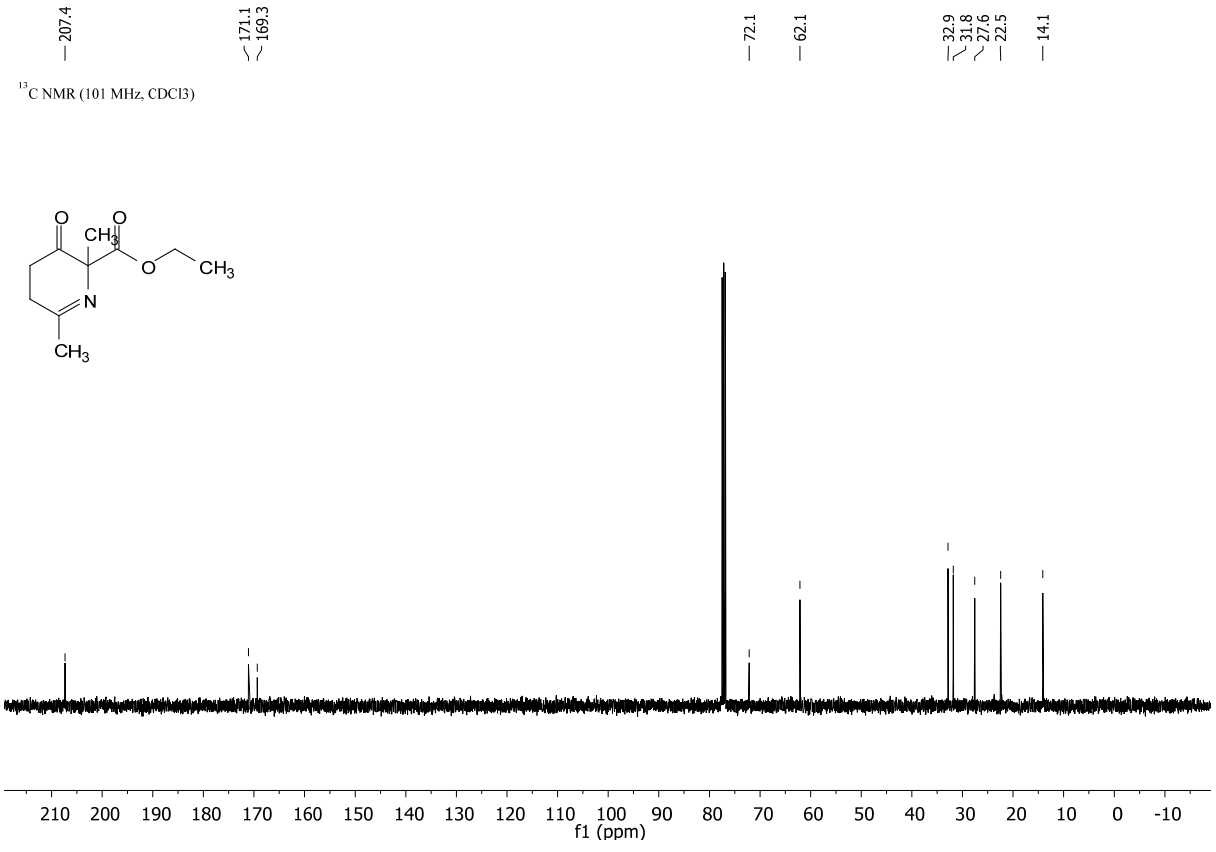


ethyl 2,6-dimethyl-3-oxo-2,3,4,5-tetrahydropyridin-2-carboxylate (4)

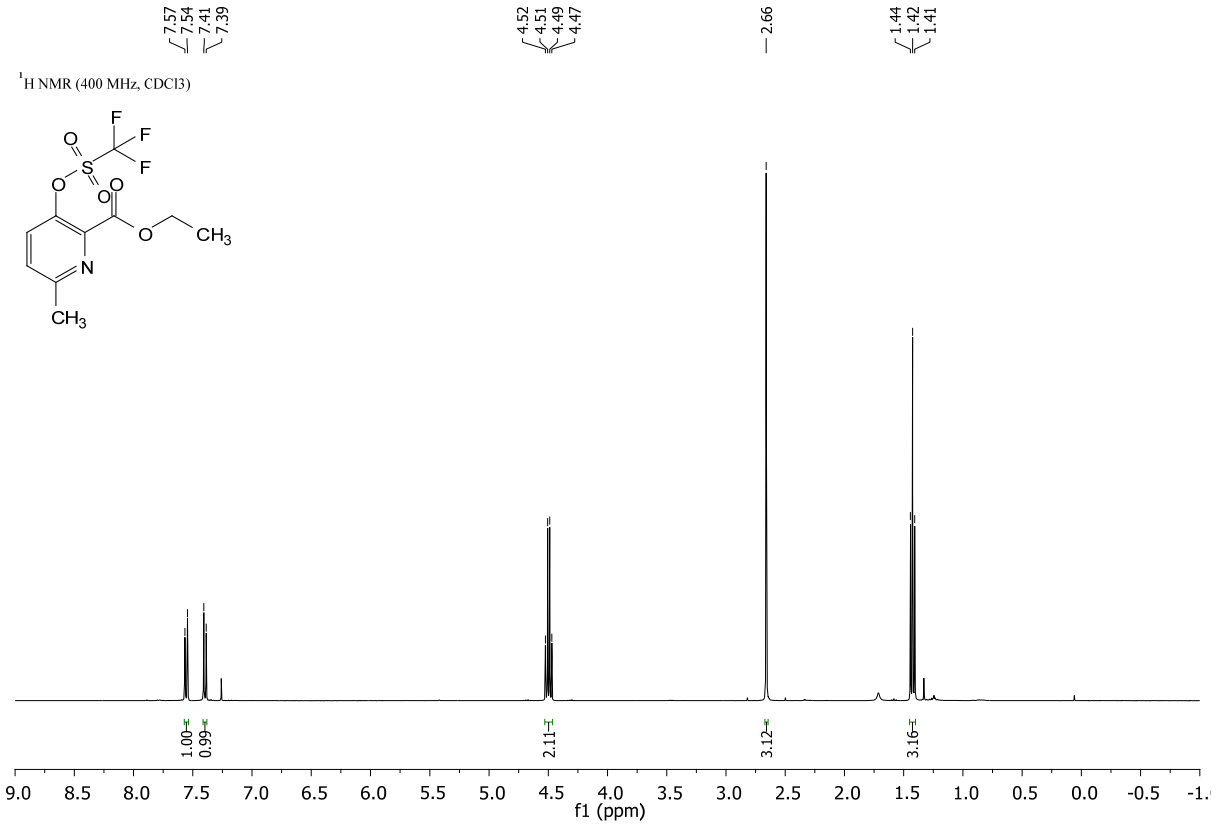
^{1}H NMR (400 MHz, CDCl3)

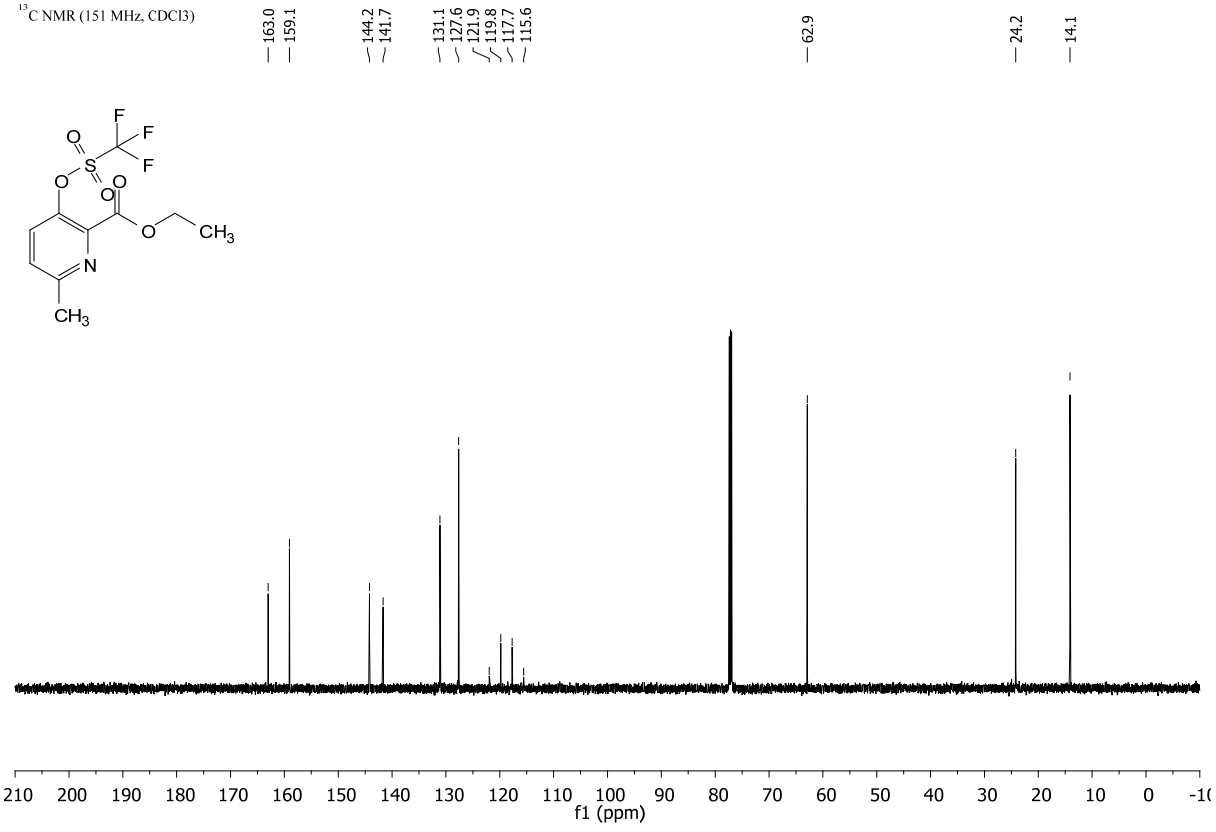


^{13}C NMR (101 MHz, CDCl3)

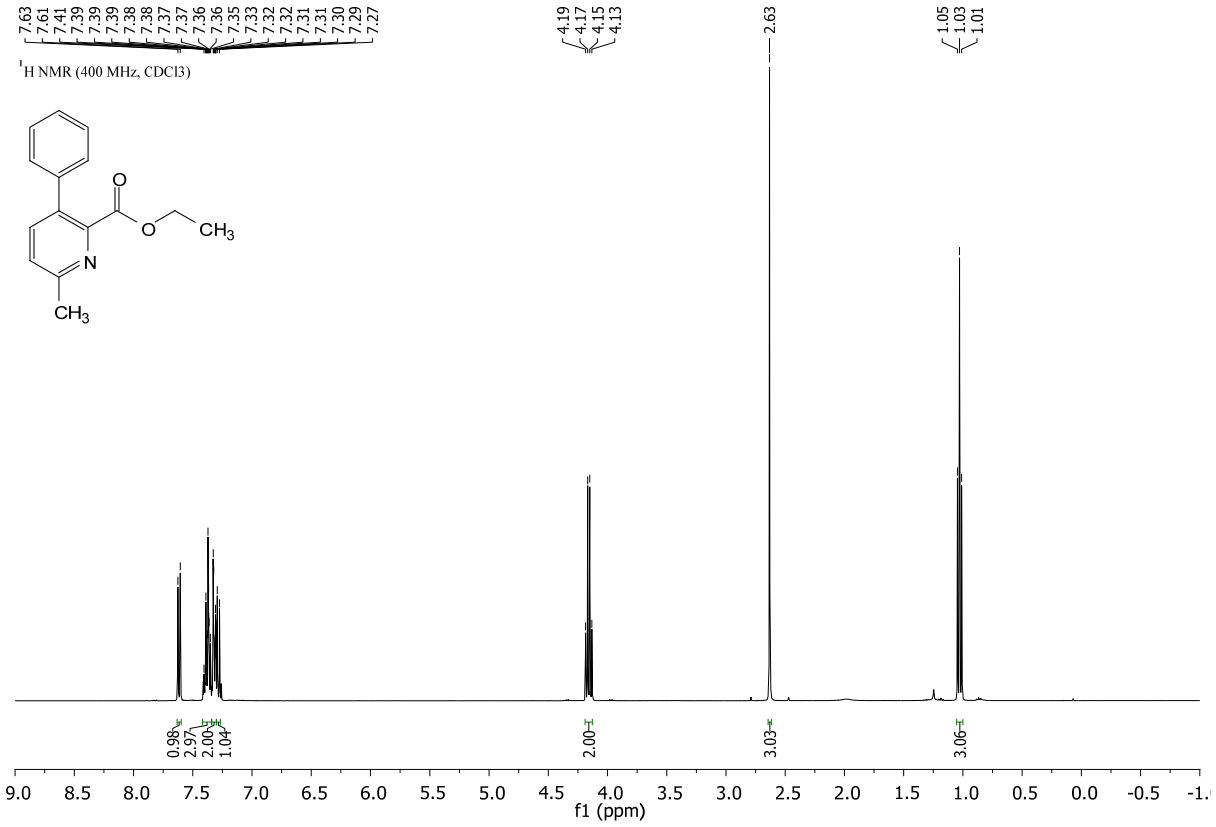


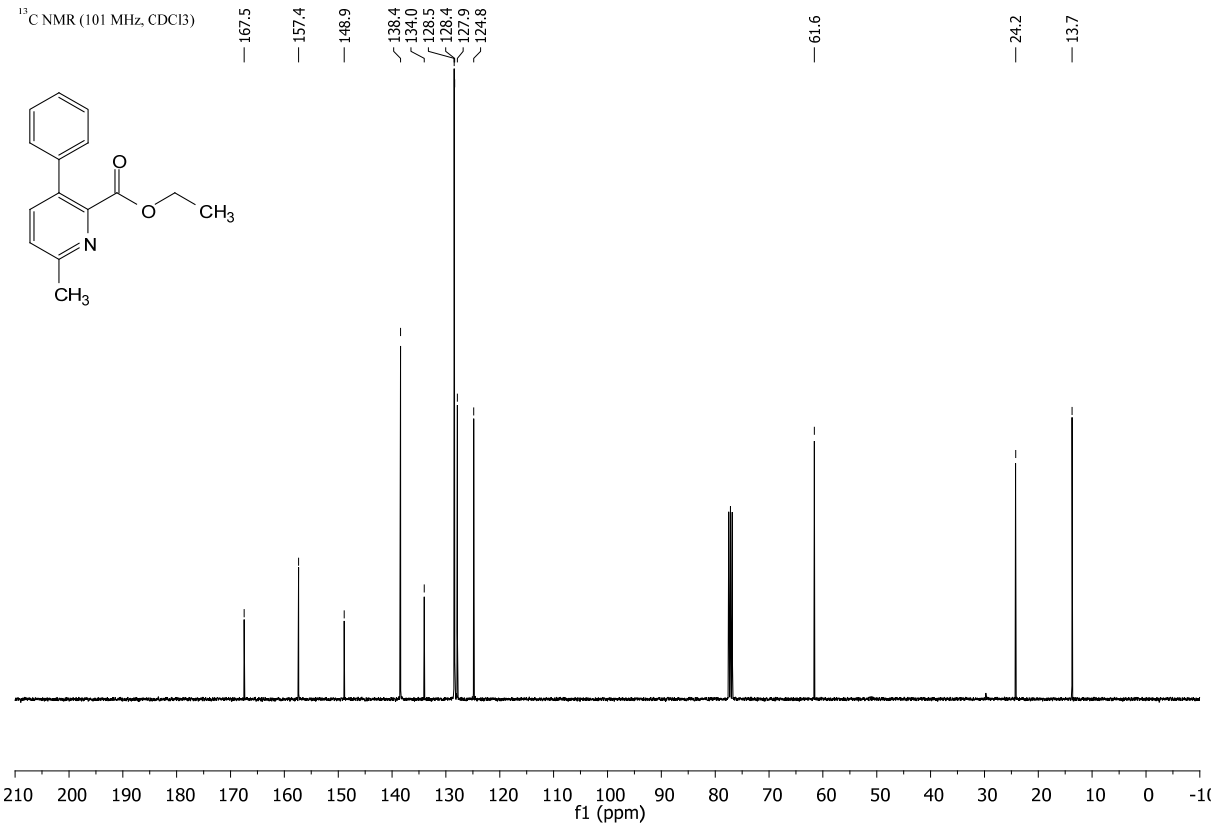
ethyl 6-methyl-3-(((trifluoromethyl)sulfonyl)oxy)picolinate (5)



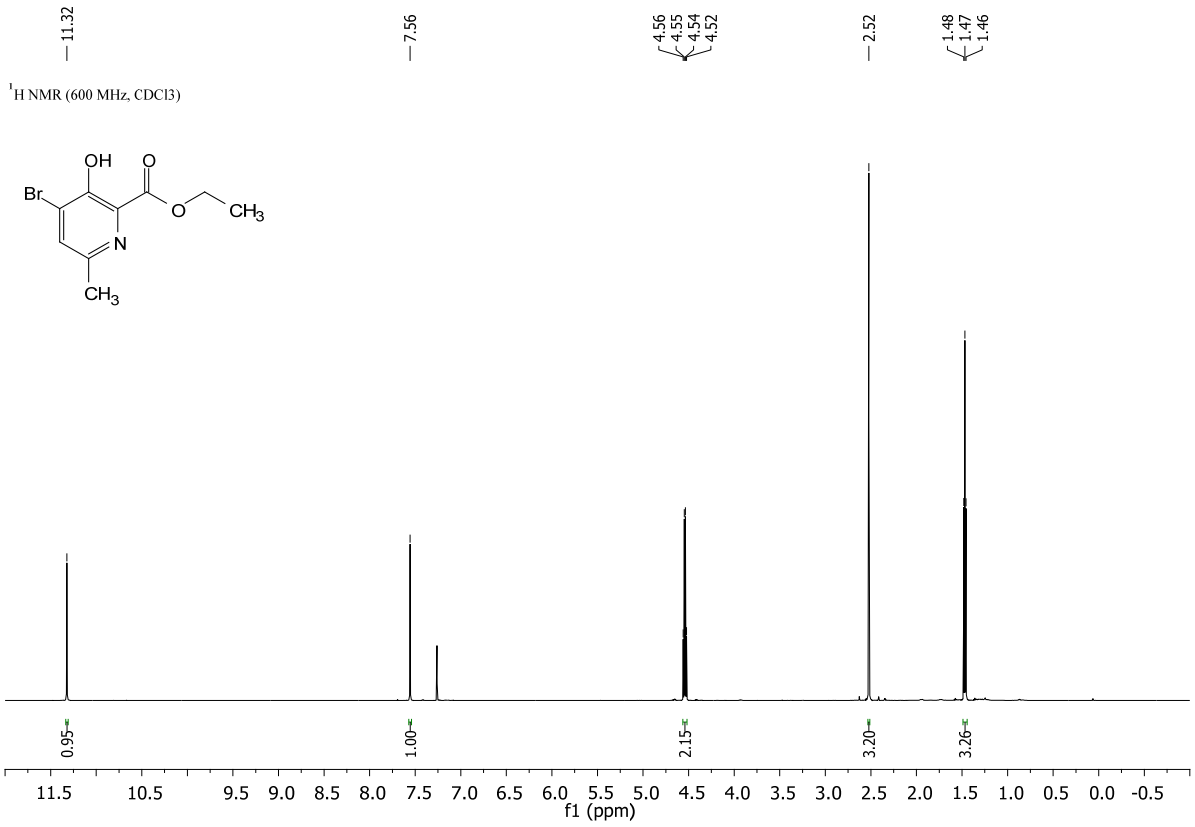


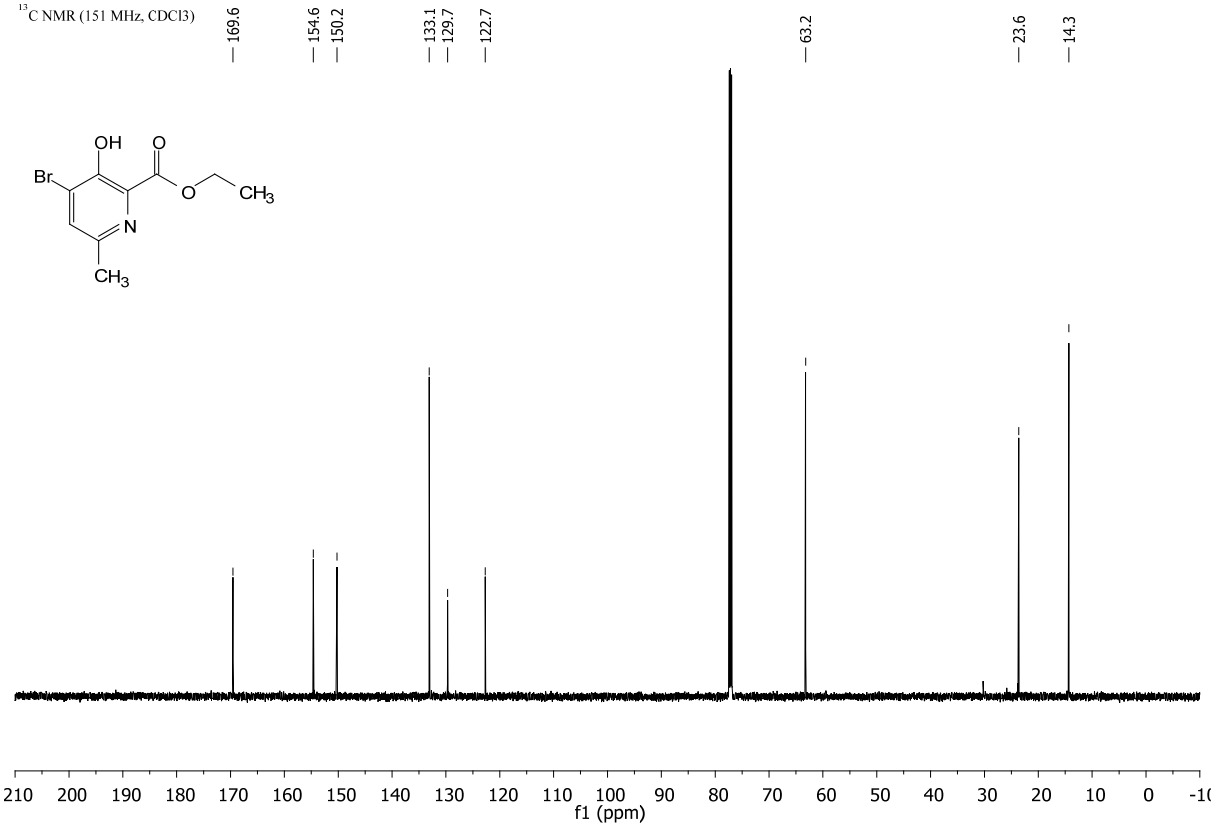
ethyl 6-methyl-3-phenylpicolinate (6)



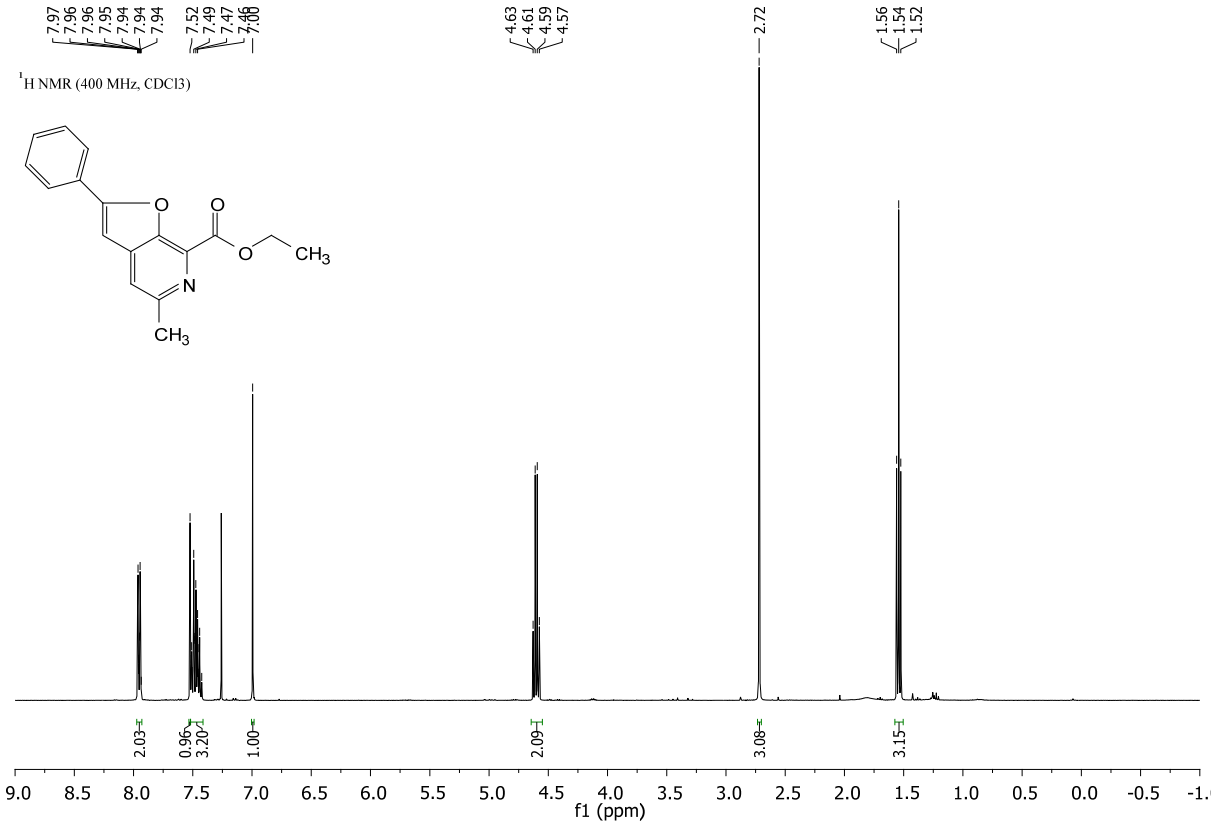


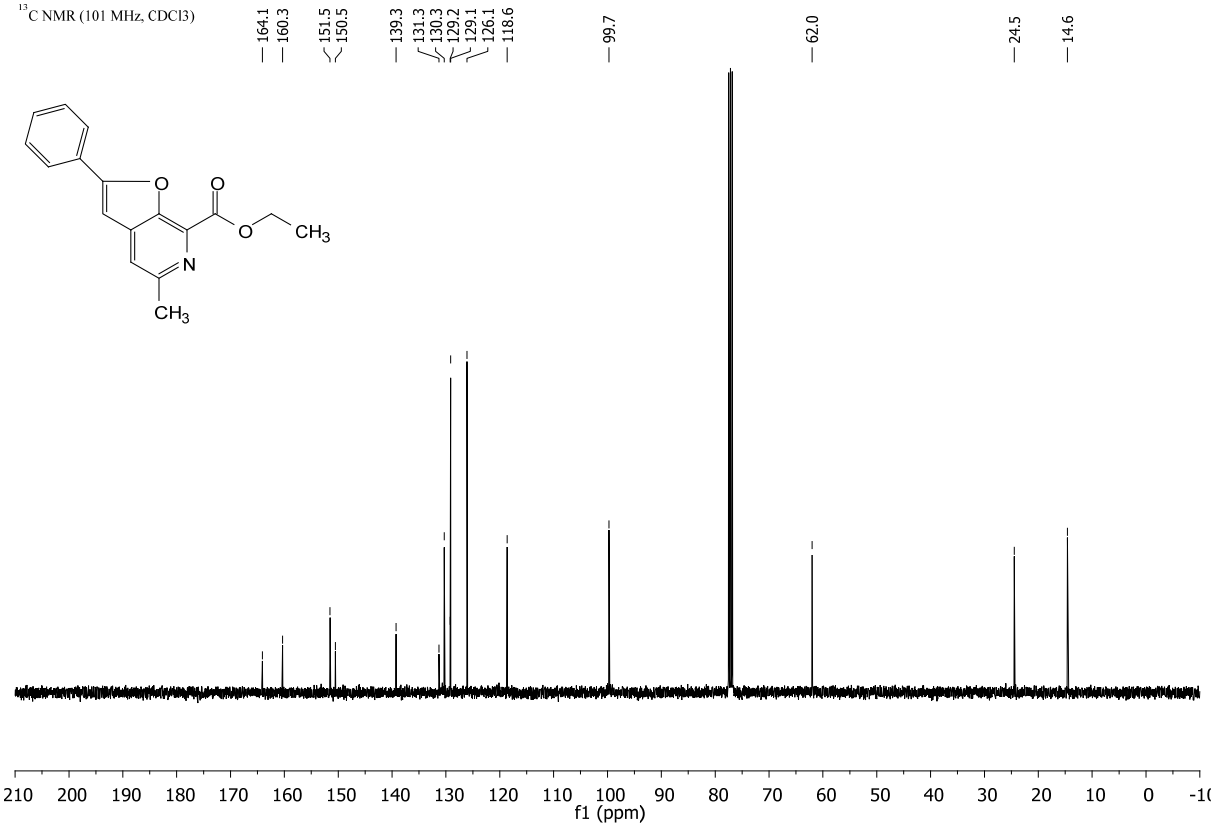
ethyl 4-bromo-3-hydroxy-6-methylpicolinate (7)



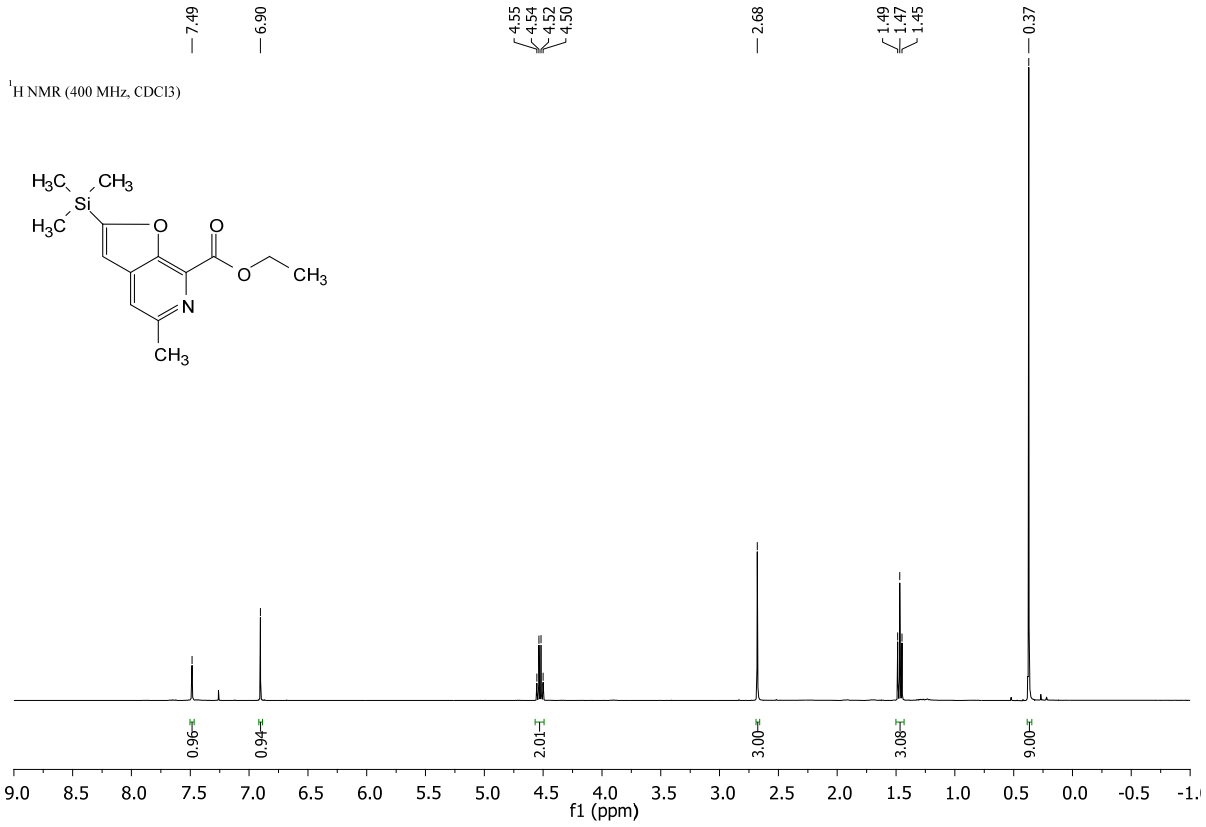


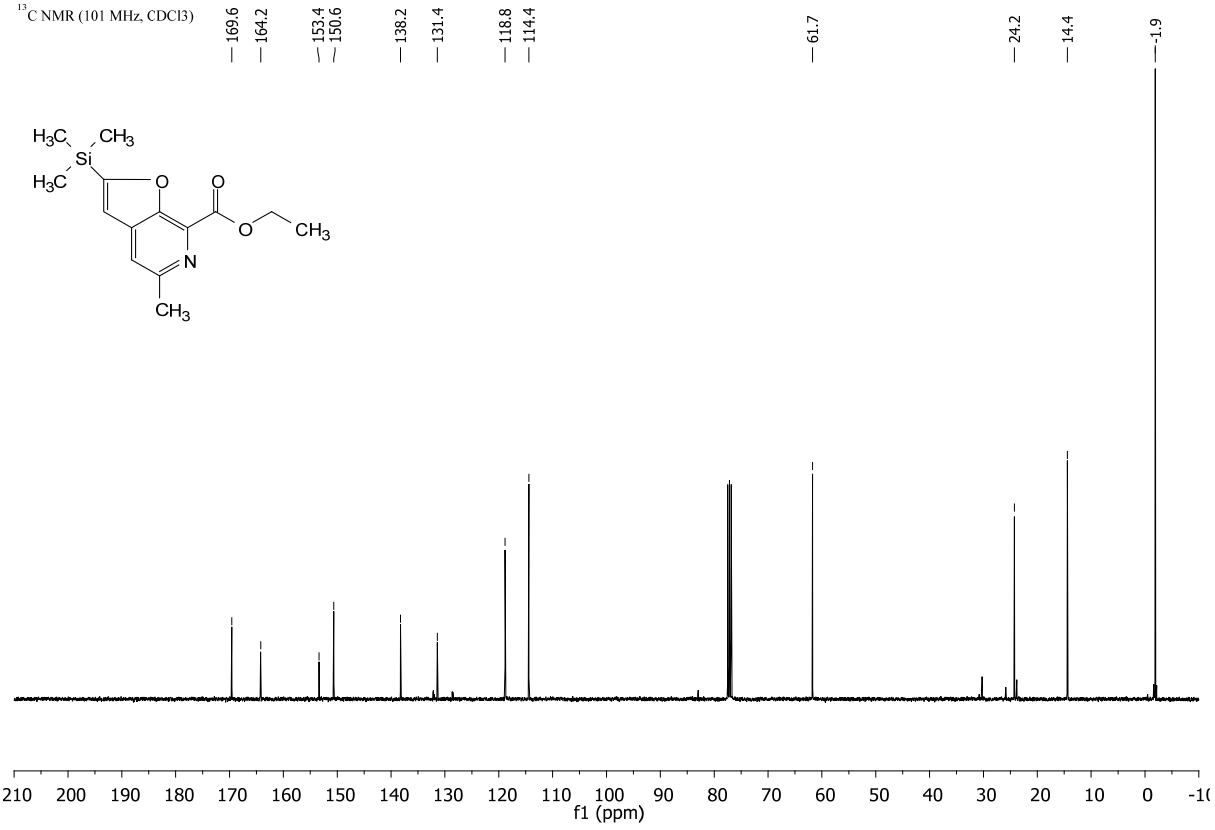
ethyl 5-methyl-2-phenylfuro[2,3-*c*]pyridine-7-carboxylate (8a)





ethyl 5-methyl-2-(trimethylsilyl)furo[2,3-*c*]pyridine-7-carboxylate (8b)





methyl 2-iodo-5-methylfuro[2,3-*c*]pyridine-7-carboxylate (9)