Supporting Information for

Exploring the chemical space of 1,2,3-triazolyl triclosan analogs for discovery of new antileishmanial chemotherapeutic agents

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List of Supporting Information

Material and Methods.

General Information.

All reactions progress was monitored on GP TLC plates. Column chromatography was performed with silica gel 60 (230-400 mesh) under a low pressure of nitrogen, using increasing EtOAc-hexane gradients as a solvent. All the solvents (hexane, ethyl acetate) were distilled before use. Chemical reagents were purchased from commercial suppliers and used without further purification, unless otherwise noted. Solvents were analytical grade or were purified by standard procedures prior to use. ^{1}H and ^{13}C NMR spectra were measured on a 300 MHz Bruker Avance II using $CDCl_3$ as a solvent. Chemical shifts were reported in ppm downfield from tetramethylsilane (δ) as the internal standards and coupling constants are in hertz (Hz). Assignments of proton resonances were confirmed by correlated spectroscopy (Heteronuclear Single Quantum Coherence, HSQC). The following abbreviations are used to indicate NMR signal multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet. High-resolution mass spectra (HRMS) were recorded on a Bruker MicroTOF II spray source. All the melting points were determined in open Pyrex capillaries with an Electrothermal 9000 melting point apparatus.

Synthesis of 2-(prop-2-yn-1-yloxy) phenol (3).

Catechol (1000 mg, 9.1 mmol) were dissolved in ethanol (10 ml). Afterwards potassium carbonate (1100 mg, 7.96 mmol) were added and the reaction were stirred for 30 minutes. Then the propargyl bromide (812 mg, 6.83 mmol) were added dropwise and the reaction were stirred at reflux overnight. The solvents were dried under vacuum and the residue was dissolved in dichloromethane. Brine was added and the solution was extracted with dichloromethane. Combined organic extracts were dried with sodium sulphate and evaporated. The resulting residue was purified by column chromatography over silica gel using an increasing AcOEt/hexane gradient to afford 624 mg of a white solid. (Isolated Yield: 46%). Spectral data of the product were coincident with previously reported by *Hamasaka et al*. [1]

Synthesis 1-methoxy-2-(prop-2-yn-1-yloxy)benzene (4).

2-Methoxyphenol (1000 mg, 8.1 mmol) were dissolved in ethanol (10 ml). Afterwards potassium carbonate (1448 mg, 10.5 mmol) were added and the reaction were stirred for 30 minutes. Then the propargyl bromide (1054 mg, 8.86 mmol) were added dropwise and the reaction were stirred at reflux overnight. The solvent were dried under vacuum and the residue was dissolved in dichloromethane. Brine was added and the solution was extracted with

dichloromethane. Combined organic extracts were dried with sodium sulphate and evaporated. The resulting residue was purified by column chromatography over silica gel using an increasing AcOEt/hexane gradient to afford 520 mg of a yellow oil. (Isolated Yield: 40%). Spectral data of the product were coincident with previously reported by *Irfan et al*.[2]

Synthesis of 2-(azidomethyl)phenol (8).

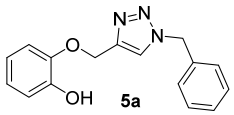
The procedure followed for the synthesis of 2-(azidomethyl)phenol intermediate were the reported by *Zhang et al*. [3] Spectral data of the product were coincident with the reported.

General procedure for the synthesis of 1,4-disubstituted 1,2,3-triazoles.

The respected alkyne (1 eq) and azide (1.5 eq) substract were suspended in 4 mL of ^{t}BuOH:H_2O (1:1). Afterwards, aqueous 1 M $CuSO_4$ (0.025 eq) solution and aqueous 1 M sodium ascorbate (0.1 eq) solution were added. The mixture was stirred overnight at room temperature. Brine was added and the solution was extracted with dichloromethane. Combined organic extracts were dried with sodium sulphate and evaporated. The resulting residue was purified by column chromatography over silica gel using an increasing AcOEt/hexane gradient to afford desired pure products.

Synthesis of compounds 5a to 9e.

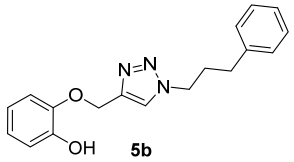
Synthesis of 2-((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)phenol (5a).



5a

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (40 mg; 0.27 mmol) and benzyl azide (60.0 mg; 0.40 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 57.7 mg of a colorless oil. (Isolated yield: 76%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.48 (s, 1H); 7.39 (d, *J* = 1.7 Hz, 1H); 7.37 (d, *J* = 2.1 Hz, 2H); 7.26 (m, 2H); 6.99 (dd, J_1 = 7.4 Hz, J_2 = 1.4 Hz, 1H); 6.92 (dd, J_1 = 7.7 Hz, J_2 = 2.2 Hz, 1H); 6.88 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H); 6.82 (ddd, J_1 = 7.4 Hz, J_2 = 1.4 Hz, J_3 = 1.4 Hz, 1H); 6.06 (s, 1H); 5.54 (s, 2H); 5.22 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.5 (C); 145.6 (C); 144.0 (C); 134.3 (C); 129.2 (CH); 128.9 (CH); 128.1 (CH); 122.7 (CH); 122.6 (CH); 120.1 (CH); 115.6 (CH); 113.7 (CH); 63.2 (CH_2); 54.3 (CH_2). **ESI-HRMS Calcd for ($M+Na^+$)** $C_{16}H_{15}N_3O_2Na$ 304.1056; found 304.1051.

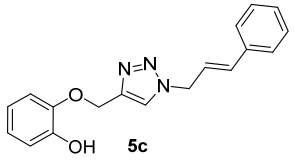
Synthesis of 2-((1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)methoxy)phenol (5b).



5b

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (40 mg; 0.27 mmol) and (3-azidopropyl)benzene (65.0 mg; 0.40 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 67.7 mg of a colorless oil. (Isolated yield: 81%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.50 (s, 1H); 7.30 (m, 1H); 7.23 (m, 2H); 7.15 (d, J = 6.8 Hz, 2H); 7.02 (dd, J_1 = 7.3 Hz, J_2 = 1.7 Hz, 1H); 6.92 (dd, J_1 = 8.0 Hz, J_2 = 2.4 Hz, 1H); 6.88 (dd, J_1 = 8.0 Hz, J_2 = 1.7 Hz, 1H); 6.82 (ddd, J_1 = 7.1 Hz, J_2 = 2.5 Hz, J_3 = 2.3 Hz, 1H); 6.13 (s, 1H); 5.26 (s, 2H); 4.35 (t, J = 7.6 Hz, 2H); 2.65 (t, J = 7.6 Hz, 2H); 2.26 (q, J = 7.6 Hz, 2H). **^{13}C ^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.7 (C); 145.7 (C); 143.6 (C); 140.0 (C); 128.6 (CH); 128.4 (CH); 126.4 (CH); 122.8 (CH); 122.6 (CH); 120.1 (CH); 115.7 (CH); 113.8 (CH); 63.2 (CH_2); 49.6 (CH_2); 32.4 (CH_2); 31.5 (CH_2). **ESI-HRMS Calcd for (M+Na$^+$)** $C_{18}H_{19}N_3NaO_2$ 332.1359; found 332.1387.

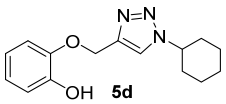
Synthesis of 2-((1-cinnamyl-1H-1,2,3-triazol-4-yl)methoxy)phenol (5c).



5c

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (40 mg; 0.27 mmol) and cinnamyl azide (64.0 mg; 0.40 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 58.9 mg of a colorless oil. (Isolated yield: 71%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.63 (s, 1H); 7.41-7.26 (m, 5H); 7.02 (dd, J_1 = 7.6 Hz, J_2 = 1.3 Hz, 1H); 6.96 (dd, J_1 = 7.8 Hz, J_2 = 2.2 Hz, 1H); 6.91 (dd, J_1 = 7.8 Hz, J_2 = 1.3 Hz, 1H); 6.84 (ddd, J_1 = 6.9 Hz, J_2 = 2.4 Hz, J_3 = 2.2 Hz, 1H); 6.67 (d, J = 15.7 Hz, 1H); 6.34 (dt, J_1 = 15.7 Hz, J_2 = 6.6 Hz, 1H); 6.12 (s, 1H); 5.26 (s, 1H); 5.14 (dd, J_1 = 6.7 Hz, J_2 = 1.3 Hz, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.6 (C); 145.7 (C); 143.9 (C); 135.6 (CH); 135.4 (C); 128.8 (CH); 126.8 (CH); 122.6 (CH); 122.5 (CH); 121.6 (CH); 120.1 (CH); 115.6 (CH); 113.7 (CH); 63.2 (CH_2); 52.5 (CH_2). **ESI-HRMS Calcd for (M+Na$^+$)** $C_{18}H_{17}N_3NaO_2$ 330.1213; found 330.1223.

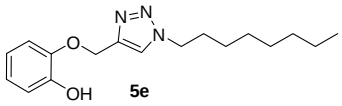
Synthesis of 2-((1-cyclohexyl-1H-1,2,3-triazol-4-yl)methoxy)phenol (5d).



5d

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (50 mg; 0.34 mmol) and cyclohexyl azide (63.0 mg; 0.51 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 62.7 mg of a colorless oil. (Isolated yield: 68%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.57 (s, 1H); 7.00 (dd, J_1 = 7.6 Hz, J_2 = 1.4 Hz, 1H); 6.94 (dd, J_1 =7.8 Hz, J_1 = 2.3 Hz, 1H); 6.89 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H); 6.82 (ddd, J_1 = 7.1 Hz, J_2 = 2.3 Hz, J_3 = 2.2 Hz, 1H); 6.20 (s, 1H); 5.24 (s, 2H); 4.45 (tt, J_1 = 11.4 Hz, J_2 = 3.9 Hz, 1H); 2.22 (dd, J_1 = 12.7 Hz, J_2 = 2.3 Hz, 2H); 1.93 (dt, J_1 = 13.7 Hz, J_2 = 3.6 Hz, 2H); 1.74 (dd, J_1 = 12.4 Hz, J_2 = 3.0 Hz, 2H); 1.70 (dd, J_1 = 12.7 Hz, J_2 = 3.7 Hz, 2H); 1.46 (qt, J_1 = 13.0 Hz, J_2 = 3.2 Hz, 1H); 1.28 (qt, J_1 = 12.5 Hz, J_2 = 3.2 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.6 (C); 145.8 (C); 143.1 (C); 122.5 (CH); 120.6 (CH); 120.1 (CH); 115.6 (CH); 113.8 (CH); 63.3 (CH_2); 60.3 (CH); 33.4 (CH_2); 25.1 (CH_2); 25.0 (CH_2).

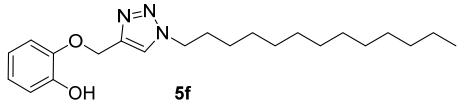
Synthesis of 2-((1-octyl-1H-1,2,3-triazol-4-yl)methoxy)phenol (5e)



5e

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (42 mg; 0.28 mmol) and octil azide (66.0 mg; 0.43 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 58.5 mg of a colorless oil. (Isolated yield: 65%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.54 (s, 1H); 7.01 (dd, J_1 = 7.7 Hz, J_2 = 1.4 Hz, 1H); 6.95 (dd, J_1 =7.9 Hz, J_2 = 2.3 Hz, 1H); 6.91 (dd, J_1 = 7.9 Hz, J_2 = 1.4 Hz, 1H); 6.83 (ddd, J_1 = 7.9 Hz, J_2 = 2.8 Hz, J_3 = 2.3 Hz, 1H); 6.10 (s, 1H); 5.27 (s, 2H); 4.35 (t, J = 7.2 Hz, 2H); 1.91 (q, J = 7.1 Hz, 2H); 1.37-1.22 (m, 10H); 0.88 (t, J = 7.1 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.6 (C); 145.6 (C); 143.5 (C); 122.5 (CH); 120.1 (CH); 115.5 (CH); 113.7 (CH); 63.3 (CH_2); 50.5 (CH_2); 31.7 (CH_2); 30.2 (CH_2); 29.0 (CH_2); 28.9 (CH_2); 26.4 (CH_2); 22.6 (CH_2); 14.0 (CH_3).

Synthesis of 2-((1-tridecyl-1H-1,2,3-triazol-4-yl)methoxy)phenol (5f).



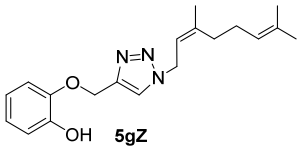
5f

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (35 mg; 0.24 mmol) and tridecanyl azide (80.0 mg; 0.35 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 72.4 mg of a colorless oil. (Isolated yield: 82%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.54 (s, 1H); 7.00 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H); 6.94 (dd, J_1 =7.8 Hz, J_2 = 2.1 Hz, 1H); 6.90 (dd, J_1 = 7.9 Hz, J_2 = 1.5 Hz, 1H); 6.82 (ddd,

J_1 = 7.8 Hz, J_2 = 2.5 Hz, J_3 = 2.3 Hz, 1H); 6.11 (s, 1H); 5.26 (s, 2H); 4.35 (t, J = 7.9 Hz, 2H); 1.09 (q, J = 7.6 Hz, 2H); 1.35-1.22 (m, 20H); 0.88 (t, J = 6.7 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.6 (C); 145.7 (C); 143.5 (C); 122.6 (CH); 122.5 (CH); 120.1 (CH); 115.6 (CH); 113.8 (CH); 63.2 (CH_2); 50.5 (CH_2); 31.9 (CH_2); 30.2 (CH_2); 29.6 (CH_2); 29.5 (CH_2); 29.4 (CH_2); 29.3 (CH_2); 29.0 (CH_2); 26.4 (CH_2); 22.7 (CH_2); 14.1 (CH_3).

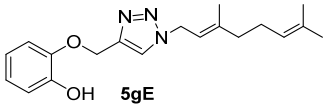
Synthesis of (Z)-2-((1-(3,7-dimethylocta-2,6-dien-1-yl)-1H-1,2,3-triazol-4-yl)methoxy)phenol (5gZ) and (E)-2-((1-(3,7-dimethylocta-2,6-dien-1-yl)-1H-1,2,3-triazol-4-yl)methoxy)phenol (5gE).

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (40 mg; 0.27 mmol) and geranyl azide (73.0 mg; 0.40 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 61.8 mg of the two isomers. (Isolated yield: 70%).



5gZ

(Z)-2-((1-(3,7-dimethylocta-2,6-dien-1-yl)-1H-1,2,3-triazol-4-yl)methoxy)phenol (5gZ). Colorless oil. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.54 (s, 1H); 7.02 (dd, J_1 = 7.7 Hz, J_2 = 1.5 Hz, 1H); 6.94 (dd, J_1 =7.9 Hz, J_2 = 2.4 Hz, 1H); 6.90 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H); 6.83 (ddd, J_1 = 7.0 Hz, J_2 = 2.4 Hz, J_3 = 2.1 Hz, 1H); 6.14 (s, 1H); 5.43 (tt, J_1 = 7.2 Hz, J_2 = 0.7 Hz, 1H); 5.23 (s, 2H); 5.08 (tq, J_1 = 7.0 Hz, J_2 = 1.5 Hz, 1H); 4.96 (dd, J_1 = 7.3 Hz, J_2 = 0.8 Hz, 2H); 2.24-2.07 (m, 4H); 1.81 (s, 3H); 1.68 (s, 3H); 1.60 (s; 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.6 (C); 145.7 (C); 143.5 (C); 143.4 (C); 132.7 (C); 123.1 (CH); 122.5 (CH); 122.0 (CH); 120.1 (CH); 117.5 (CH); 115.5 (CH); 113.6 (CH); 63.3 (CH_2); 47.9 (CH_2); 32.1 (CH_2); 26.2 (CH_2); 25.7 (CH_3); 23.4 (CH_3); 17.7 (CH_3). **ESI-HRMS Calcd for (M+Na$^+$)** $C_{19}H_{25}N_3NaO_2$ 350.1839; found 350.1845.

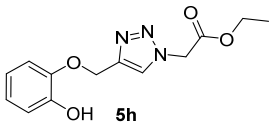


5gE

(E)-2-((1-(3,7-dimethylocta-2,6-dien-1-yl)-1H-1,2,3-triazol-4-yl)methoxy)phenol (5gE). Colorless oil. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.52 (s, 1H); 7.01 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H); 6.94 (dd, J_1 =8.1 Hz, J_1 = 2.3 Hz, 1H); 6.89 (dd, J_1 = 7.6 Hz, J_2 = 1.4 Hz, 1H); 6.82 (ddd, J_1 = 6.6 Hz, J_2 = 2.5 Hz, J_3 = 2.3 Hz, 1H); 6.10 (s, 1H); 5.43 (td, J_1 = 7.5 Hz, J_2 = 1.2 Hz, 1H); 5.23 (s, 2H); 5.05 (tq, J_1 = 6.5 Hz, J_2 = 1.4 Hz, 1H); 4.98 (d, J = 7.4 Hz, 2H); 2.11 (s, 4H); 1.78 (s, 3H); 1.67 (s, 3H); 1.59 (s; 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.6 (C); 145.7 (C); 143.6 (C); 143.5 (C); 132.1 (C); 123.4 (CH); 122.5 (CH); 122.0

(CH); 120.1 (CH); 116.7 (CH); 115.6 (CH); 113.7 (CH); 63.2 (CH_2); 48.0 (CH_2); 39.4 (CH_2); 26.1 (CH_2); 25.7 (CH_3); 17.7 (CH_3); 16.4 (CH_3). **ESI-HRMS Calcd for (M+Na$^+$)** $C_{19}H_{25}N_3NaO_2$ 350.1839; found 350.1845.

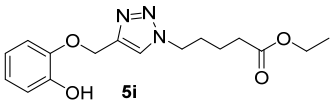
Synthesis of ethyl 2-(4-((2-hydroxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetate (5h).



5h

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (45 mg; 0.30 mmol) and ethyl 2-azidoacetate (59.0 mg; 0.46 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 66.5 mg of a colorless oil. (Isolated yield: 79%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.73 (s, 1H); 7.02 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H); 6.93 (dd, J_1 =7.5 Hz, J_2 = 2.1 Hz, 1H); 6.92 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H); 6.84 (ddd, J_1 = 6.9 Hz, J_2 = 2.6 Hz, J_3 = 2.4 Hz, 1H); 6.00 (s, 1H); 5.29 (s, 2H); 5.18 (s, 2H); 4.28 (q, J = 7.1 Hz, 2H); 1.31 (t, J = 7.3 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 166.3 (C); 146.5 (C); 145.5 (C); 143.9 (C); 124.5 (CH); 122.4 (CH); 120.1 (CH); 115.6 (CH); 113.6 (CH); 62.9 (CH2); 62.5 (CH2); 50.8 (CH2); 14.0 (CH3).

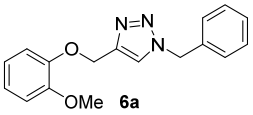
Synthesis of ethyl 5-(4-((2-hydroxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)pentanoate (5i).



5i

The 2-(prop-2-yn-1-yloxy) phenol (**3**) (40 mg; 0.27 mmol) and ethyl 5-azidopentanoate (95.0 mg; 0.54 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 67.3 mg of a colorless oil. (Isolated yield: 78%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:**7.58 (s, 1H); 6.98 (dd, J_1 = 7.6 Hz, J_2 = 1.3 Hz, 1H); 6.91 (dd, J_1 =7.8 Hz, J_1 = 1.9 Hz, 1H); 6.87 (dd, J_1 = 7.8 Hz, J_2 = 1.3 Hz, 1H); 6.80 (ddd, J_1 = 7.9 Hz, J_2 = 2.5 Hz, J_3 = 2.0 Hz, 1H); 6.10 (s, 1H); 5.26 (s, 2H); 4.39 (t, J = 7.1 Hz, 2H); 4.13 (q, J = 7.1 Hz, 2H); 2.34 (t, J = 7.0 Hz, 2H); 1.97 (q, J = 8.1 Hz, 2H); 1.65 (s, J = 8.1 Hz, 2H); 1.25 (t; J = 6.8 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 173.0 (C); 146.6 (C); 145.7 (C); 143.6 (C); 122.8 (CH); 122.5 (CH); 120.1 (CH); 115.6 (CH); 113.8 (CH); 63.2 (CH_2); 60.5 (CH_2); 50.0 (CH_2); 33.3 (CH_2); 29.4 (CH_2); 21.7 (CH_2); 14.2 (CH_3). **ESI-HRMS Calcd for (M+Na$^+$)** $C_{16}H_{21}N_3NaO_4$ 342.1424; found 342.1420.

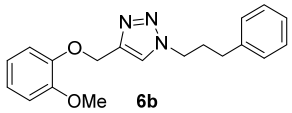
Synthesis of 1-benzyl-4-((2-methoxyphenoxy)methyl)-1H-1,2,3-triazole (6a).



6a

The 1-methoxy-2-(prop-2-yn-1-yloxy)benzene (**4**) (48 mg; 0.30 mmol) and benzyl azide (72.0 mg; 0.44 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 61.1 mg of a colorless oil. (Isolated yield: 70%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.55 (s, 1H); 7.37 (d, *J* = 1.9 Hz, 1H); 7.35 (d, *J* = 2.1 Hz, 2H); 7.25 (dd, J_1 = 7.6 Hz, J_2 = 2.4 Hz, 2H); 7.04 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H); 6.94 (ddd, J_1 = 8.1 Hz, J_2 = 1.9 Hz, 1H); 6.89 (dd, J_1 = 2.0 Hz, J_2 = 1.4 Hz, 1H); 6.88 (ddd, J_1 = 4.6 Hz, J_2 = 2.1 Hz, J_3 = 1.9 Hz, 1H); 5.51 (s, 2H); 5.27 (s, 2H); 3.83 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 149.7 (C); 147.6 (C); 144.7 (C); 134.5 (C); 129.1 (CH); 128.7 (CH); 128.1 (CH); 122.9 (CH); 121.9 (CH); 120.9 (CH); 114.6 (CH); 111.8 (CH); 63.3 (CH_2); 55.8 (CH_3); 54.1 (CH_2).

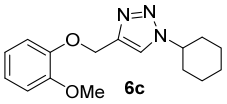
Synthesis of 4-((2-methoxyphenoxy)methyl)-1-(3-phenylpropyl)-1H-1,2,3-triazole (6b).



6b

The 1-methoxy-2-(prop-2-yn-1-yloxy)benzene (**4**) (50 mg; 0.31 mmol) and (3-azidopropyl)benzene (75.0 mg; 0.46 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 81.7 mg of a colorless oil. (Isolated yield: 82%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** δ = 7.59 (s, 1H); 7.28 (m, 2H); 7.20 (m, 1H); 7.15 (d, *J* = 7.1 Hz, 2H); 7.05 (dd, J_1 = 7.9 Hz, J_2 = 1.9 Hz, 1H); 6.93 (m, 1H); 6.91 (s, 1H); 6.90 (ddd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, J_3 = 2.3 Hz, 1H); 5.31 (s, 2H); 4.33 (t, *J* = 7.3 Hz, 2H); 3.87 (s, 3H); 2.64 (t, *J* = 7.5 Hz, 2H); 2.25 (q, *J* = 7.5 Hz, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 149.6 (C); 147.6 (C); 144.3 (C); 140.1 (C); 128.6 (CH); 128.4 (CH); 126.3 (CH); 122.9 (CH); 121.9 (CH); 120.9 (CH); 114.4 (CH); 111.9 (CH); 63.2 (CH_2); 55.9 (CH_3); 49.5 (CH_2); 32.4 (CH_2); 31.5 (CH_2).

Synthesis of 1-cyclohexyl-4-((2-methoxyphenoxy)methyl)-1H-1,2,3-triazole (6c).

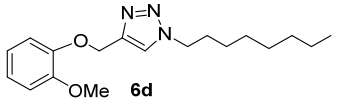


6c

The 1-methoxy-2-(prop-2-yn-1-yloxy)benzene (**4**) (58 mg; 0.36 mmol) and cyclohexyl azide (67.0 mg; 0.54 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 75.0 mg of a colorless oil. (Isolated yield: 73%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.63 (s, 1H); 7.07 (d, *J* = 7.6

Hz, 1H); 6.94 (m, 1H); 6.91 (s, 1H); 6.90 (m, 1H); 5.28 (s, 2H); 4.43 (tt, J_1 = 11.7 Hz, J_2 = 3.6 Hz, 1H); 3.87 (s, 3H); 2.20 (dd, J_1 = 12.7 Hz, J_2 = 2.2 Hz, 2H); 1.93 (dt, J_1 = 13.6 Hz, J_2 = 3.2 Hz, 2H); 1.75 (dd, J_1 = 11.9 Hz, J_2 = 3.2 Hz, 2H); 1.73 (dd, J_1 = 12.9 Hz, J_2 = 3.6 Hz, 2H); 1.45 (qt, J_1 = 13.4 Hz, J_2 = 3.5 Hz, 1H); 1.27 (qt, J_1 = 12.3 Hz, J_2 = 3.2 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 149.6 (C); 147.7 (C); 143.7 (C); 121.8 (CH); 120.9 (CH); 120.6 (CH); 114.3 (CH); 111.8 (CH); 63.4 (CH2); 60.1 (CH); 55.8 (CH_3); 33.5 (CH_2); 25.1 (CH_2); 25.0 (CH_2).

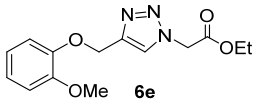
Synthesis of 4-((2-methoxyphenoxy)methyl)-1-octyl-1H-1,2,3-triazole (6d).



6d

The 1-methoxy-2-(prop-2-yn-1-yloxy)benzene (**4**) (50 mg; 0.31 mmol) and octyl azide (72.0 mg; 0.46 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 77.3 mg of a colorless oil. (Isolated yield: 79%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.61 (s, 1H); 7.04 (dd, *J1* = 7.0 Hz, *J2* = 2.2 Hz, 1H); 6.94 (m, 1H); 6.90 (s, 1H); 6.89 (dd, *J1* = 7.7 Hz, *J2* = 2.5 Hz, 1H); 5.30 (s, 2H); 4.32 (t, J = 7.3 Hz, 2H); 3.87 (s, 3H); 1.88 (q, *J* = 6.0 Hz, 2H); 1.37-1.20 (m, 10H); 0.87 (t, *J* = 6.0 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 149.6 (C); 147.6 (C); 144.3 (C); 122.6 (CH); 121.8 (CH); 120.9 (CH); 114.4 (CH); 111.8 (CH); 63.3 (CH_2); 55.9 (CH_3) 50.4 (CH_2); 31.7 (CH_2); 30.2 (CH_2); 29.0 (CH_2); 28.9 (CH_2); 26.4 (CH_2); 22.6 (CH_2); 14.0 (CH_3).

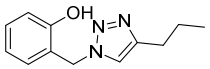
Synthesis of ethyl 2-(4-((2-methoxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetate (6e).



6e

The 1-methoxy-2-(prop-2-yn-1-yloxy)benzene (**4**) (55 mg; 0.34 mmol) and ethyl 2-azidoacetate (66.0 mg; 0.51 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, the reaction was work up and purified to afford 71.8 mg of a colorless oil. (Isolated yield: 80%). **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.79 (s, 1H); 7.06 (dd, J_1 = 8.3 Hz, J_2 = 1.9 Hz, 1H); 6.95 (m, 1H); 6.91 (s, 1H); 6.90 (m, 1H); 5.32 (s, 2H); 5.14 (s, 2H); 4.26 (q, *J* = 6.6 Hz, 2H); 3.87 (s, 3H); 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 166.27 (C); 149.6 (C); 147.6 (C); 144.5 (C); 124.6 (CH); 121.9 (CH); 120.9 (CH); 114.4 (CH); 111.9 (CH); 63.0 (CH_2); 62.3 (CH_2); 55.8 (CH_3); 50.8 (CH_2); 14.0 (CH_3).

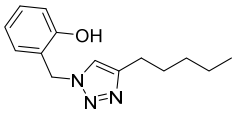
Synthesis of 2-((4-propyl-1H-1,2,3-triazol-1-yl)methyl)phenol. (9a).



9a

Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, 1-pentyne (79 µL; 0.8 mmol) and 2-(azidomethyl)phenol (60 µL; 0.4 mmol)was dissolved in 4 ml of H_2O:^{t}BuOH. The reaction was worked up and purified to afford 85.5 mg of a white solid. (Isolated yield: 98%).Mp: 97.3-98.1°C. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.39 (s, 1H), 7.24-7.18 (m, 2H), 6.97 (m, 1H), 6.89 (m, 1H), 5.47 (s, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.73-1.60 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H. **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 155.2 (C), 148.4 (C), 130.6 (CH), 130.4 (CH), 121.7 (CH), 121.3 (C), 120.7 (CH), 117.4 (CH), 50.1 (CH_2), 27.6 (CH_2), 22.6 (CH_2), 13.8 (CH_3).**ESI-HRMS Calcd for ($M+H^+$)** $C_{12}H_{16}N_3O$ 218.12294; found 252.1131.

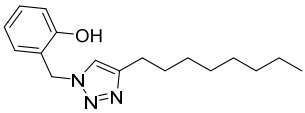
Synthesis of 2-((4-pentyl-1H-1,2,3-triazol-1-yl)methyl)phenol (9b).



9b

Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, 1-heptyne (106 µL; 0.8 mmol) and 2-(azidomethyl)phenol (60 µL; 0.4 mmol) was and dissolved in 4 ml of H_2O:^{t}BuOH. The reaction was worked up and purified to afford 38.9 mg of a white solid. (Isolated yield: 39%). Mp: 88.2-89.2°C. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.45 (s, 1H), 7.24 (s, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.86 (t, *J* = 7.3 Hz, 1H), 5.52 (s, 2H), 2.67 (t, *J* = 7.7 Hz, 2H), 1.63 (p, *J* = 7.5 Hz, 2H), 1.36-1.34(m, 4H), 0.85 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 155.4 (C), 148.4 (C), 130.4 (CH), 130.4 (CH), 121.6 (CH), 121.5 (C), 120.3 (CH), 116.9 (CH), 49.8 (CH_2), 31.4 (CH_2), 29.0 (CH_2), 25.5 (CH_2), 22.3 (CH_2), 13.9 (CH_3). **ESI-HRMS Calcd for ($M+H^+$)** $C_{14}H_{19}N_3O$ 246.16064, found 246.1601.

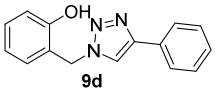
Synthesis of 2-((4-octyl-1H-1,2,3-triazol-1-yl)methyl)phenol (9c).



9c

Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, 1-decyne (37 µL; 0.4 mmol) and 2-(azidomethyl)phenol (60 µL; 0.4 mmol)was dissolved in 4 ml of H_2O:^{t}BuOH. The reaction was worked up and purified to afford 66.5 mg of a white solid. (Isolated yield: 57%). Mp: 77.3-77.9 °C.**^{1}H NMR (300 MHz, $CDCl_3$)** δ: 7.47 (s, 1H), 7.19 (d, *J*=7.8 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.4 Hz, 1H), 5.53 (s, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.63 (p, *J* = 7.7 Hz, 2H), 1.28-1.23 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H). **^{13}C RMN (75 MHz, $CDCl_3$)** δ : 155.4 (C), 148.4 (C), 130.4 (CH), 130.4 (CH), 121.5 (CH), 120.2 (CH), 116.7 (CH), 49.8 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 25.5 (CH_2), 22.6 (CH_2), 14.1 (CH_3).**ESI-HRMS Calcd for ($M+H^+$)** $C_{17}H_{25}N_3O$ 288.20459, found288.2070.

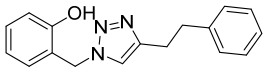
Synthesis of 2-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)phenol (9d).



9d

Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, 1-decyne (44 µL; 0.4 mmol) and 2-(azidomethyl)phenol (60 µL; 0.4 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. The reaction was worked up and purified to afford 89.2 mg of a white solid. (Isolated yield: 88%). Mp: 202.1-203.1°C.**^{1}H NMR (300 MHz, $CDCl_3$)** 7.69 (s, 1H), 7.55 (m, 2H), 7.22-6.88 (m, 5H), 6.80 -6.50 (m, 2H), 5.34 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 155.3 (C), 147.2 (C), 130.7 (C), 130.2 (CH), 130.0 (CH), 128.6 (CH), 127.8 (CH), 125.4 (CH), 121.2 (C), 120.1 (CH), 119.5 (CH), 115.8 (CH), 49.3 (CH_2).**ESI-HRMS Calcd for ($M+H^+$)** $C_{15}H_{14}N_3O$ 252.11359, found 252.1131.

Synthesis 2-((4-phenethyl-1H-1,2,3-triazol-1-yl)methyl)phenol (9e).



9e

Following the general procedure for the synthesis of 1,4-disubstituted-1,2,3-triazoles, 4-phenyl-1-butyne (52 µL; 0.4 mmol) and 2-(azidomethyl)phenol (60 µL; 0.4 mmol) was dissolved in 4 ml of H_2O:^{t}BuOH. The reaction was worked up and purified to afford 46.4 mg of a white solid. (Isolated yield: 41%). MP: 129.6-130.4°C.**^{1}H NMR (300 MHz, CDCl3) δ :** 7.24-7.11 (m, 8H); 6.95 (m, 1H); 6.89 (m, 1H); 5.46 (s, 2H); 2.97 (m, 4H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 155.0 (C); 147.4 (C); 141.0 (C); 130.6 (CH); 130.3 (CH); 128.4 (CH); 128.4 (CH); 126.1 (CH); 121.7 (CH); 121.6 (C); 120.8

(CH); 117.3 (CH); 50.0 (CH_2); 35.5 (CH_2); 27.5 (CH_2). **ESI-HRMS Calcd for ($M+H^+$)** $C_{17}H_{18}N_3O$ 280.14499; found 280.1444.

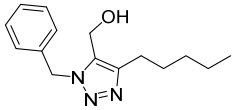
General procedure for synthesis of 1,2,3–triazoles by thermic cycloaddition.

Alkyne (1 eq) and the azide (1 eq) were suspended in 2 mL/eq of toluene. The mixture was stirred and heated under reflux for 35 hours. Then was allowed to go to room temperature. Brine was added and the solution was extracted with dichloromethane. Combined organic extracts were dried with sodium sulphate and evaporated. The resulting residue was purified by column chromatography over silica gel using an increasing AcOEt/hexane gradient to afford desired pure products.

Synthesis of compounds 11a to 15f.

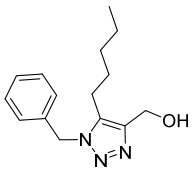
Synthesis of (1-benzyl-4-pentyl-1H-1,2,3-triazol-5-yl)methanol (11a) and (1-benzyl-5-pentyl-1H-1,2,3-triazol-4-yl)methanol (11b)

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, oct-2-yn-1-ol (95 µL; 0.75mmol) and benzyl azide (100 µL; 0.75 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 59.4 mg of a white solid corresponding to the compound **11a** and 42.2 mg of a white solid corresponding to the compound **11b**. (Isolated yield: 52%).



11a

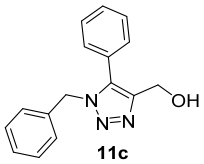
(1-benzyl-4-pentyl-1H-1,2,3-triazol-5-yl)methanol (11a). MP: 59.3-60.0°C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ : 7.29-7.30 (m, 3H); 7.22-7.19 (m, 2H); 5.59 (s, 2H); 4.53 (d, *J* = 4,7 Hz, 2H); 2.56 (t, *J* = 7,7 Hz, 2H); 1.60 (p , *J* = 7,0 Hz, 2H); 1.27 (m, 4H); 0.85 (t, *J* = 6,5 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 146.5 (C); 135.2 (C); 131.9 (C); 128.9 (CH); 128.3(CH); 127.5 (CH); 52.3 (CH_2); 52.1 (CH_2); 31.5 (CH_2); 29.6 (CH_2); 26.8 (CH_2); 22.4 (CH_2); 14.0 (CH_3). **ESI-HRMS Calcd for ($M+H^+$)** $C_{15}H_{21}N_3O$ 260.17629; found 260.1757.



11b

(1-benzyl-5-pentyl-1H-1,2,3-triazol-4-yl)methanol (11b). MP: 52.1-52.9°C.**^{1}H NMR (300 MHz, $CDCl_3$)** δ : 7.35-7.30 (m, 3H, H); 7.17- 7.15 (m, 2H); 5.49 (s, 2H); 4.71 (s, 2H); 2.57 (t, *J* = 7.6 Hz, 2H); 1.40-1.30 (m, 2H); 1.22-1.18 (m, 4H); 0.81 (t, *J* = 6.8 Hz, 3H). **ESI-HRMS Calcd for (M+H+)** $C_{15}H_{21}N_3O$ 260.17629; found 260.1757.

Synthesis of (1-benzyl-5-phenyl-1H-1,2,3-triazol-4-yl) methanol (11c)

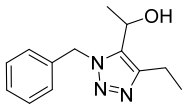


11c

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, 3-phenylprop-2-yn-1-ol (77 µL; 0.75 mmol) and benzyl azide (100 µL; 0.75 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 77.8 mg of a white solid. (Isolated yield: 76%). MP: 119,7-120,5 °C.**^{1}H NMR (300 MHz, $CDCl_3$):** δ : 7.45-7.43 (m, 3H,); 7.26-7.23 (m, 5H); 7.06-7.03 (m, 2H); 5.47 (s, 2H); 4.68 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ :** 145.0 (C), 135.9 (C), 135.3 (C), 129.7(CH), 129.0(CH), 128.8 (CH), 128.2 (CH), 127.3(CH), 126.4(C), 55.8 (CH_2), 52.1 (CH_2). **ESI-HRMS Calcd for (M+H$^+$)** $C_{17}H_{18}N_3O$ 266.12934; found 266.1288.

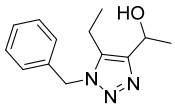
Synthesis of 1-(1-benzyl-4-ethyl-1H-1,2,3-triazol-5-yl)ethan-1-ol (11d) and 1-(1-benzyl-5-ethyl-1H-1,2,3-triazol-4-yl)ethan-1-ol (11e).

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, hex-3-yn-2-ol (90 µL; 0.90 mmol) and benzyl azide (120 µL; 0.90 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 46.5 mg of a white solid corresponding to compound **11d** and 56.5 mg of a colorless oil corresponding to compound **11e** (Isolated yield: 56%).



11d

1-(1-benzyl-4-ethyl-1H-1,2,3-triazol-5-yl)ethan-1-ol (11d). MP: 86,3-87,2°C.**^{1}H NMR (300 MHz, $CDCl_3$):** δ : 7.33-7.29 (m, 3H); 7.17-7.15 (m, 2H); 5.48 (s, 2H); 4.98 (s, 1H); 2.63 (q, *J* = 7.7 Hz, 2H); 1.62 (d, *J* = 7.7 Hz, 3H); 1.00 (t, *J* = 7,7 Hz, 3H).**^{13}C NMR (75 MHz, $CDCl_3$)** δ : 147.8 (C); 135.1 (C); 134.8 (C); 129.0 (CH); 128.3 (CH); 127.1 (CH); 63.1 (CH); 51.8 (CH_2); 23,6 (CH_3); 16,1 (CH_2); 13,5 (CH_3). **ESI-HRMS Calcd for ($M+H^+$)** $C_{13}H_{18}N_3O$ 232.14499; found 232.14444.

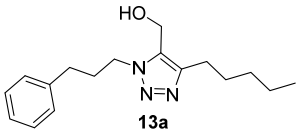


11e

1-(1-benzyl-5-ethyl-1H-1,2,3-triazol-4-yl)ethan-1-ol (11e). ^{1}H NMR (300 MHz, CDCl3): δ : 7.30-7.14 (m, 5H); 5.59 (q, *J* = 14.8 Hz, 2H); 5.04 (q, *J* = 7.1 Hz, 1H); 2.69-2.61 (m, 2H); 1.28-1.26 (d, *J* = 6.8 Hz, 3H); 1.24-1.21 (t, *J* = 3.5 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ : 146.0 (C); 135.9 (C); 135.2 (C); 128.8 (CH); 128.1 (CH); 127.2 (CH); 60.9 (CH); 52.5 (CH_2); 22.6 (CH_3); 18.7 (CH_2); 14.2 (CH_3). **ESI-HRMS Calcd for ($M+H^+$)** $C_{13}H_{18}N_3O$ 232.14499; found 232.1444.

Synthesis of (4-pentyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-5-yl)methanol (13a) y (5-pentyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)methanol (13b).

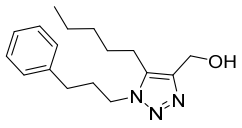
Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, oct-2-yn-1-ol (95 µL; 0,62 mmol) and phenyl propil azide (100 µL; 0,62 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 41 mg of a colorless oil corresponding to compound **13a** and 40. mg of a colorless oil corresponding to compound **13b** (Isolated yield: 46%).



13a

(4-pentyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-5-yl)methanol (13a). ^{1}H NMR (300 MHz, $CDCl_3$) δ : 7.31-7.17 (m, 5H); 4.62 (d, *J* = 4.3 Hz, 2H); 4.36 (t, *J* = 7.3 Hz, 2H); 2.69 (t, *J* = 7.3 Hz, 2H); 2.61 (t, *J* = 7.6 Hz, 2H); 2.29 (q, *J* = 7.1 Hz, 2H); 1.68-1.62 (m, 2H); 1.31 (m, 4H, C7-H); 0.88 (t, *J* = 7.0 Hz,

3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ : 146.1 (C); 140.6 (C); 131.3 (C); 128.5 (CH); 128.4 (CH); 126.2 (CH); 52.3 (CH_2); 47.9 (CH_2); 32.7 (CH_2); 31.5 (CH_2); 31.4 (CH_2); 29.7 (CH_2); 24.9 (CH_2); 22.4 (CH_2); 14.0 (CH_3).**ESI-HRMS Calcd for ($M+H^+$)** $C_{17}H_{26}N_3O$ 288.20759; found 288.2070.

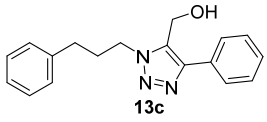


13b

(5-pentyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)methanol (13b). ^{1}H NMR (300 MHz, $CDCl_3$) δ : 7.31-7.17 (m, 5H); 4.62 (d, *J* = 4.3 Hz, 2H); 4.36 (t, *J* = 7.3 Hz, 2H); 2.69 (t, *J* = 7.3 Hz, 2H); 2.61 (t, *J* = 7.6 Hz, 2H); 2.29 (q, *J* = 7.1 Hz, 2H); 1.68-1.62 (m, 2H); 1.31 (m, 4H); 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ : 146.1 (C); 140.6 (C); 131.3 (C); 128.5 (CH); 128.4 (CH); 126.2 (CH); 52.3 (CH_2); 47.9 (CH_2); 32.7 (CH_2); 31.5 (CH_2); 31.4 (CH_2); 29.7 (CH_2); 24.9 (CH_2); 22.4 (CH_2); 14.0 (CH_3).**ESI-HRMS Calcd for ($M+H^+$)** $C_{17}H_{26}N_3O$ 288.20759; found 288.20704.

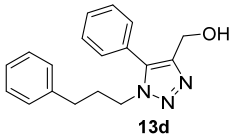
Synthesis of (4-phenyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-5-yl)methanol (13c) y (5-phenyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)methanol (13d).

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, 3-phenylprop-2-yn-1-ol (63 µL; 0,62 mmol) and phenyl propil azide (100 µL; 0,62 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 46.9 mg of a white solid corresponding to compound **13c** and 74.0 mg of a white solid corresponding to compound **13d** (Isolated yield: 66%).



13c

(4-phenyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-5-yl)methanol (13c). MP: 82.6-83.1°C.**^{1}H NMR (300 MHz, $CDCl_3$):** δ : 7.65 (d, *J* = 6.9 Hz, 2H); 7.44-7.28 (m, 5H); 7.22-7.17 (m, 3H); 4.76 (d, *J* = 4.2 Hz, 2H); 4.39 (d, *J* = 7.3 Hz, 2H); 2.71 (t, *J* = 7.3 Hz, 2H); 2.31 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ: δ : 145.9 (C); 140.4 (C); 131.5 (C); 130.7 (C); 128.8 (CH); 128.6 (CH); 128.4 (CH); 128.2 (CH); 127.7 (CH); 126.3 (CH); 52.6 (CH_2); 48.0 (CH_2); 32.7 (CH_2); 31.4 (CH_2).**ESI-HRMS Calcd for ($M+H^+$)** $C_{18}H_{20}N_3O$ 294.16064; found 294.1601.

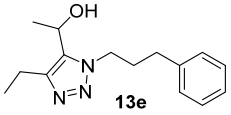


13d

(5-phenyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)methanol (13d). MP: 81.2-82.0 °C.**^{1}H NMR (300 MHz, $CDCl_3$):** δ : 7.49-7.47 (m, 3H); 7.36-7.33 (m, 2H); 7.23-7.19 (m, 3H); 7.04 (m, 2H); 4.67(s, 2H); 4.28 (t, *J* = 4.3 Hz, 2H); 2.57 (t, *J* = 7.3 Hz, 2H); 2.13 (p, *J* = 7,3 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ: 140.2 (C); 129.6 (C); 129.5 (C); 129.2 (C); 128.5 (CH); 128.5 (CH); 128.3 (CH); 128.3 (CH); 126.6 (CH); 126.2 (CH); 55.6 (CH_2); 47.8 (CH_2); 32.5 (CH_2); 31.3 (CH_2).**ESI-HRMS Calcd for ($M+H^+$)** $C_{18}H_{20}N_3O$ 294.16064; found 294.1601.

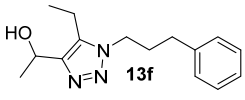
Synthesis of 1-(4-ethyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-5-yl)ethan-1-ol(13e) y 1-(5-ethyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)ethan-1-ol (13f).

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, hex-3-yn-2-ol (73 µL; 0.74 mmol) and phenyl propil azide (120 µL; 0.74 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 30.8 mg of a colorless oil corresponding to compound **13e** and 49.6 mg of a colorless oil corresponding to compound **13f.** (Isolated yield: 42%).



13e

1-(4-ethyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-5-yl)ethan-1-ol(13e). **^{1}H NMR (300 MHz, $CDCl_3$)** δ : 7.30-7.27 (m, 1H); 7.25 (m, 1H); 7.21-7.15 (m, 3H); 5.06 (q, *J* = 6.7 Hz, 1H); 4.36 (t, *J* = 7.4 Hz, 2H); 2.68 (t, *J* = 7.7 Hz, 2H); 2.63- 2.57 (m, 3H); 2.28-2.19 (m, 2H); 1.50 (t, *J* = 6.8 Hz, 3H); 1.19 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ : 145.4 (C); 140.7 (C); 134.8 (C); 128.5 (CH); 128.5 (CH); 128.4 (CH); 128.4 (CH); 126.2 (CH); 60.7 (CH); 48.3 (CH_3); 32.8 (CH_2); 31.7 (CH_2); 23.0 (CH_3); 18.6 (CH_2); 14.3 (CH_2). **ESI-HRMS Calcd for ($M+H^+$)** $C_{15}H_{22}N_3O$ 260.3467; found 260.1757.



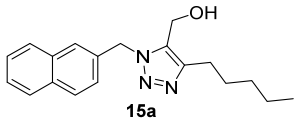
13f

1-(5-ethyl-1-(3-phenylpropyl)-1H-1,2,3-triazol-4-yl)ethan-1-ol (13f) **^{1}H NMR (300 MHz, $CDCl_3$)** δ : 7.31-7.27 (m, 2H); 7.22-7.17 (m, 3H); 4.98 (t, *J* = 5.8 Hz, 1H); 4.19 (t, *J* = 7.6 Hz, 3H); 2.69 (t, *J* =

7.4 Hz, 2H); 2.62 (t, *J* = 7.5 Hz, 2H); 2.23 (p , *J* = 7.3 Hz, 2H); 1.62 (d, *J* = 6.5 Hz, 3H); 1.14 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ : 147.6(C); 140.3 (C); 134.4 (C); 128.6 (CH); 128.4 (CH); 126.3 (CH); 63.1 (CH); 46.9 (CH_3); 32.7 (CH_2); 31.5 (CH_2); 23.6 (CH_3); 16.0 (CH_2); 14.0 (CH_2). **ESI-HRMS Calcd for ($M+H^+$)** $C_{15}H_{22}N_3O$ 260.3467; found 260.1757.

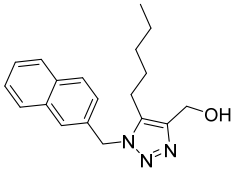
Synthesis of (1-(naphthalen-2-ylmethyl)-4-pentyl-1H-1,2,3-triazol-5-yl)methanol (15a) y (1-(naphthalen-2-ylmethyl)-5-pentyl-1H-1,2,3-triazol-4-yl)methanol (15b).

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, oct-2-yn-1-ol (73 µL; 0.38 mmol) and (3-azidopropyl)benzene (70 µL; 0.38 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 29.1 mg of a white solid corresponding to compound **15a** and 52.7 mg of a white solid corresponding to compound **15b.** (Isolated yield: 69%).



15a

(1-(naphthalen-2-ylmethyl)-4-pentyl-1H-1,2,3-triazol-5-yl)methanol (15a). MP: 90.5-91.3 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ **:** 7.82-7.77 (m, 3H); 7.68 (s, 1H); 7.50-7.47 (m, 2H); 7.34 (m, 1H); 5.78 (s, 2H); 4.54 (d, *J* = 5.4 Hz, 2H); 2.63 (t, *J* = 7.5 Hz, 2H); 1.66-1.62 (m, 2H); 1.32-1.30 (m, 4H); 0.87 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ **:** 133.2 (C); 133.1 (C); 132.6 (C); 129.0 (CH); 127.9 (CH); 127.8 (CH); 126.6 (CH); 126.5 (CH); 125.0 (CH); 52.7 (CH_2); 52.6 (CH_2); 31.5 (CH_2); 29.6 (CH_2); 24.9 (CH_2); 22.4 (CH_2); 14.0 (CH_3). **ESI-HRMS Calcd for ($M+H^+$)** $C_{19}H_{24}N_3O$ 310.18411; found 310.1904.



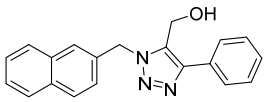
15b

(1-(naphthalen-2-ylmethyl)-5-pentyl-1H-1,2,3-triazol-4-yl)methanol (15b). MP: 79.2-80.2 °C. **^{1}H NMR (300 MHz, $CDCl_3$):** δ : 7.80 (m, 3H); 7.76 (s, 1H); 7.50-7.47 (m, 2H); 7.27 (m, 1H); 5.64 (s, 2H); 4.72 (d, *J* = 5.4 Hz, 2H); 2.59 (t, *J* = 7.5 Hz, 2H); 1.34 (p, *J* = 7.5 Hz, 2H); 1.14-1.12 (m, 4H); 0.72 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ : 144.9 (C); 135.2 (C); 133.2 (C); 133.0 (C); 132.4 (C); 129.0

(CH); 127.8 (CH); 127.8 (CH); 126.6 (CH); 126.5 (CH); 126.2 (CH); 124.7 (CH); 55.9 (CH_2); 52.2 (CH_2); 31.4 (CH_2); 28.5 (CH_2); 22.6 (CH_2); 22.1 (CH_2); 13.7 (CH_3). **ESI-HRMS Calcd for ($M+H^+$)** $C_{19}H_{24}N_3O$ 310.18411; found 310.1904.

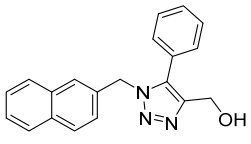
Synthesis of (1-(naphthalen-2-ylmethyl)-4-phenyl-1H-1,2,3-triazol-5-yl)methanol (15c) and (1-(naphthalen-2-ylmethyl)-5-phenyl-1H-1,2,3-triazol-4-yl)methanol (15d).

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, 3-phenylprop-2-yn-1-ol (39 µL; 0.38 mmol) and (3-azidopropyl)benzene (70 µL; 0.38 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 44.0 mg of a white solid corresponding to compound **15c** and 77.8 mg of a white solid corresponding to compound **15d.** (Isolated yield: 94%).



15c

(1-(naphthalen-2-ylmethyl)-4-phenyl-1H-1,2,3-triazol-5-yl)methanol (15c). MP: 138.1-139.0 °C. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.83-7.66 (s, 6H); 7.51-7.36 (s, 6H); 5.82 (s, 2H); 4.71 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ:** 146.6 (C); 133.2 (C); 133.2 (C); 133.1 (C); 132.3 (C); 131.6 (C); 130.6 (CH); 129.2 (CH); 128.8 (CH); 128.3 (CH); 128.0 (CH); 127.8 (CH); 127.7 (CH); 126.7 (CH); 126.6 (CH); 126.6 (CH); 124.9 (CH); 52.8 (CH_2); 52.7(CH_2). **ESI-HRMS Calcd for ($M+H^+$)** $C_{20}H_{17}N_3O$ 316.14499; found 316.1437.



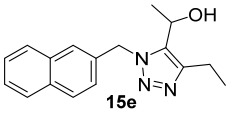
15d

(1-(naphthalen-2-ylmethyl)-5-phenyl-1H-1,2,3-triazol-4-yl)methanol (15d) MP: 170.2-171.1 °C. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.79-7.69 (s, 3H); 7.49-7.42 (s, 6H); 7.24-7.20 (s, 3H); 5.63 (s, 2H); 4.70 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ:** 144.9 (C); 133.1 (C); 132.9 (C); 132.7 (C); 132.7 (C); 131.9(C);

129,7 (CH); 129.7 (CH); 129.0 (CH); 128.8 (CH); 127.9 (CH); 127.9 (CH); 127.7 (CH); 126.5 (CH); 126.4 (CH); 124.8 (CH); 56.0 (CH_2); 52.3 (CH_2).**ESI-HRMS Calcd for (M+H$^+$)** $C_{20}H_{17}N_3O$ 316.14499; found 316.1437.

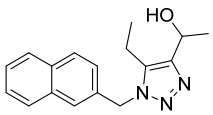
Synthesis of 1-(4-ethyl-1-(naphthalen-2-ylmethyl)-1H-1,2,3-triazol-5-yl)ethan-1-ol (15e) and 1-(5-ethyl-1-(naphthalen-2-ylmethyl)-1H-1,2,3-triazol-4-yl)ethan-1-ol (15f).

Following the general procedure for the synthesis of 1,2,3–triazoles by thermic cycloaddition, hex-3-yn-2-ol (43 µL; 0.44 mmol) and (3-azidopropyl)benzene (80 µL; 0.44 mmol) were added in 2 ml of toluene. The reaction is heated under reflux for 35 hours. The reaction was worked up and purified to afford 43.3 mg of a white solid corresponding to compound **15e** and 49.3 mg of a white solid corresponding to compound **15f.** (Isolated yield: 75%).



15e

1-(4-ethyl-1-(naphthalen-2-ylmethyl)-1H-1,2,3-triazol-5-yl)ethan-1-ol (15e). MP: 93.4-94.3 °C. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.89-7.45 (m, 3H); 7.61 (s, 1H); 7.45 (m, 2H); 7.30 (m, 1H); 5.76 (dd, J_1= 15.4 Hz, J_2= 8.5 Hz, 2H); 5.08 (q, J = 6.7 Hz, 2H); 2.69 (m, 2H); 1.28 (t, J = 6.9 Hz, 3H); 1.23 (t, J_1= 7.3 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ:** 146.2 (C); 134.9 (C); 133.3 (C); 133.2 (C); 133.0 (C); 128.8 (CH); 127.9 (CH); 127.7 (CH); 126.5 (CH); 126.4 (CH); 126.2 (CH); 124.9 (CH); 61.2 (CH); 52.7 (CH_2); 22.7 (CH_3); 18.8 (CH_2); 14.3 (CH_3). **ESI-HRMS Calcd for (M+H$^+$)** $C_{20}H_{17}N_3O$ 282.16064; found 282.1601.



15f

1-(5-ethyl-1-(naphthalen-2-ylmethyl)-1H-1,2,3-triazol-4-yl)ethan-1-ol (15f). MP: 105.2-106.0 °C. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.83-7.77 (m, 3H); 7.61 (s, 1H); 7.50-7.47 (m, 2H); 7.29 (m, 1H); 5.64 (s, 2H); 5.00 (q, J= 6.7 Hz, 2H); 2.65 (q, J = 7.7 Hz, 2H); 1.64 (d, J_1= 6.7 Hz, 3H); 1.01 (t, J = 7.6 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ:** 147.9 (C); 134.9 (C); 133.2 (C); 133.0 (C); 132.5 (C); 129.0 (CH); 127.9 (CH); 127.8 (CH); 126.6 (CH); 126.5 (CH); 126.2 (CH); 124.7 (CH); 63.2 (CH); 52.0 (CH_2); 23.6 (CH_3); 16.1 (CH_2); 13.6 (CH_3).**ESI-HRMS Calcd for (M+H$^+$)** $C_{20}H_{17}N_3O$ 282.16064; found 282.1601.

References:

(1) Hamasaka, G.; Uozumi, Y. *Chem. Commun.* **2014**, *50*, 14516.

(2) Irfan, M.; Aneja, B.; Yadava, U.; Khan, S. I.; Manzoor, N.; Daniliuc, C. G.; Abid, M. *Eur. J. Med. Chem.* **2015**, *93*, 246.

(3) Zhang, Q.; Takacs, J. M. *Org. Lett.* **2008**, *10*, 545.

Figures and Tables.

SMILES of compounds.

Table S1. SMILES of compounds tested.

Paper ID	Smiles
5a	OC1=CC=CC=C1OCC2=CN(CC3=CC=CC=C3)N=N2
5b	OC1=CC=CC=C1OCC2=CN(CCCC3=CC=CC=C3)N=N2
5c	OC1=CC=CC=C1OCC2=CN(C/C=C/C3=CC=CC=C3)N=N2
5d	OC1=CC=CC=C1OCC2=CN(C3CCCCC3)N=N2
5e	OC1=CC=CC=C1OCC2=CN(CCCCCCCC)N=N2
5f	OC1=CC=CC=C1OCC2=CN(CCCCCCCCCCCCCC)N=N2
5gZ	C/C(C)=C/CC/C(C)=C\CN1N=NC(COC2=CC=CC=C2O)=C1
5gE	OC1=CC=CC=C1OCC2=CN(C/C=C(C)/CC/C=C(C)/C)N=N2
5h	OC1=CC=CC=C1OCC2=CN(CC(OCC)=O)N=N2
5i	OC1=CC=CC=C1OCC2=CN(CCCCC(OCC)=O)N=N2
6a	COC1=CC=CC=C1OCC2=CN(CC3=CC=CC=C3)N=N2
6b	COC1=CC=CC=C1OCC2=CN(CCCC3=CC=CC=C3)N=N2
6c	COC1=CC=CC=C1OCC2=CN(C3CCCCC3)N=N2
6d	CCCCCCCCN1C=C(COC2=CC=CC=C2OC)N=N1
6e	O=C(OCC)CN1C=C(COC2=CC=CC=C2OC)N=N1
9a	OC1=C(CN2N=NC(CCC)=C2)C=CC=C1
9b	OC1=C(CN2N=NC(CCCCC)=C2)C=CC=C1
9c	OC1=C(CN2N=NC(CCCCCCCC)=C2)C=CC=C1
9d	OC1=C(CN2N=NC(C3=CC=CC=C3)=C2)C=CC=C1
9e	OC1=C(CN2N=NC(CCC3=CC=CC=C3)=C2)C=CC=C1
11a	OCC1=C(CCCCC)N=NN1CC2=CC=CC=C2
11b	OCC1=C(C2=CC=CC=C2)N(N=N1)CC3=CC=CC=C3
11c	OCC1=C(C2=CC=CC=C2)N(N=N1)CC3=CC=CC=C3
11d	OC(C)C1=C(CC)N=NN1CC2=CC=CC=C2
11e	CC(O)C1=C(CC)N(N=N1)CC2=CC=CC=C2
13a	CCCCCC1=C(N(N=N1)CCCC2=CC=CC=C2)CO
13b	CCCCCC(N(N=N1)CCCC2=CC=CC=C2)=C1CO
13c	OCC(N(N=N1)CCCC2=CC=CC=C2)=C1C3=CC=CC=C3
13d	OCC1=C(N(N=N1)CCCC2=CC=CC=C2)C3=CC=CC=C3
13e	CC(C(N(N=N1)CCCC2=CC=CC=C2)=C1CC)O
13f	CC(C1=C(N(N=N1)CCCC2=CC=CC=C2)CC)O
15a	CCCCCC1=C(CO)N(CC2=CC=C3C(C=CC=C3)=C2)N=N1
15b	OCC1=C(CCCCC)N(CC2=CC=C3C(C=CC=C3)=C2)N=N1
15c	OCC1=C(C2=CC=CC=C2)N=NN1CC3=CC=C4C(C=CC=C4)=C3
15d	OCC1=C(C2=CC=CC=C2)N(CC3=CC=C4C(C=CC=C4)=C3)N=N1
15e	CC(C1=C(CC)N=NN1CC2=CC=C3C(C=CC=C3)=C2)O
15f	CC(C1=C(CC)N(CC2=CC=C3C(C=CC=C3)=C2)N=N1)O

Multisequence alignment of :enoyl-[acyl-carrier-protein] reductases.

>CBZ37546.1 enoyl-[acyl-carrier-protein] reductase, putative [*Leishmania donovani*]
MQANRVTSLFGVQYPIVQGGMVWCSGWRLASAVSNAGGLGLVGAGSMSFDVFQHHVRRCKEAAKKPFGVN
VPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPSCKLALKCEAAGVNAVVAEGFEAGGH
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GEGDTYLTLKQYMPTRVMLNDYGKEARRLSESGATKAQLKEFRGKGRTKKGMFDGDVTNGELEIGQIVSACKD
VPTAAEVVERMVKEFRTRNAQLAKMNL

>CAC5433624.1 enoyl-[acyl-carrier-protein]_reductase_putative|GeneDB:LmjF.34.0610
[*Leishmania donovani*]
MQANRVTSLFGVQYPIVQGGMVWCSGWRLASAVSNAGGLGLVGAGSMSFDVFQHHVRRCKEAAKKPFGVN
VPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPSCKLALKCEAAGVNAVVAEGFEAGGH
NGLEEITTMALVPQVRKALAPEVPLLAAGGIASGEAMLAAMALGAEGVQVGTRFAVTQESSAAEEKKRCTAAG
EGDTYLTLKQYMPTRVMLNDYGKEARRLSESGATKAQLKEFRGKGRTKKGMFDGDVTNGELEIGQIVSACKDV
PTAAEVVERMVKEFRTRNAQLAKMNL

>XP_001686152.1 putative enoyl-[acyl-carrier-protein reductase[*Leishmania major* strain Friedlin]
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VPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPSCKLALKCEAAGVNAVVAEGFEAGGH
NGLEEITTMALIPQVRKALAPEIPLLAAGGIASGEAMLATMALGAEGVQVGTRFAVTQESSAAEEFKKRCTAAGE
GDTYLTLKQSMPTRVMLNDYGKEARRLSESGATKAQLEEFRGKGRTKKGIFDGDVTNGELEIGQIVSACKDVPT
AAEVVERMVKEFHTRKAQLAKMNL

>XP_001468450.1 putative enoyl-[acyl-carrier-protein reductase[*Leishmania infantum* JPCM5]
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VPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPSCKLALKCEAAGVNAVVAEGFEAGGH
NGLEEITTMALVPQVRKALAPEVPLLAAGGIASGEAMLAAMALGAEGVQVGTRFAVTQESSAAEEFKKRCTAA
GEGDTYLTLKQYMPTRVMLNDYGKEARRLSESGATKAQLKEFRGKGRTKKGMFDGDVTNGELEIGQIVSACKD
VPTAAEVVERMVKEFRTRNAQLAKMNL

>sp|P0AEK4|FABI_ECOLI Enoyl-[acyl-carrier-protein] reductase [NADH] FabI OS=*Escherichia coli*
(strain K12) OX=83333 GN=fabI PE=1 SV=2
MGFLSGKRILVTGVASKLSIAYGIAQAMHREGAELAFTYQNDKLKGRVEEFAAQLGSDIVLQCDVAEDASIDTMF
AELGKVWPKFDGFVHSIGFAPGDQLDGDYVNAVTREGFKIAHDISSYSFVAMAKACRSMLNPGSALLTLSYLGA
ERAIPNYNVMGLAKASLEANVRYMANAMGPEGVRVNAISAGPIRTLAASGIKDFRKMLAHCEAVTPIRRTVTIE
DVGNSAAFLCSDLSAGISGEVVHVDGGFSIAAMNELELK

>sp|P9WGR1|INHA_MYCTU Enoyl-[acyl-carrier-protein reductase [NADH] OS=*Mycobacterium tuberculosis* (strain ATCC 25618 / H37Rv) OX=83332 GN=inhA PE=1 SV=1
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VTEAIGAGNKLDGVVHSIGFMPQTGMGINPFFDAPYADVSKGIHISAYSYASMAKALLPIMNPGGSIVGMDFD
PSRAMPAYNWMTVAKSALESVNRFVAREAGKYGVRSNLVAAGPIRTLAMSAIVGGALGEEAGAQIQLLEEGW
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CLUSTAL 2.1 multiple sequence alignment


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XP_001468450.1          MQANRVTSLFGVQYPIVQGGMVWCSGWRLASAVSNAGGLGLVGAGSMSFD-VFQHHVRRC 59
CBZ37546.1              MQANRVTSLFGVQYPIVQGGMVWCSGWRLASAVSNAGGLGLVGAGSMSFD-VFQHHVRRC 59
XP_001686152.1          MQANRVTSLFGVQYPIVQGGMVWCSGWRLASAVSNAGGLGLVGAGSMNFD-IFQHHVRRC 59
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sp|P9WGR1|INHA_MYCTU    ----MTGLLDGKRILVSGIITDSSIAFHIARVAQEQG-------AQLVLTGFDRLRLIQR 49
                               * * :  :       . .: :* .  . *       ..: :    . ::

CAC5433624.1            KEAAKKPFGVNVPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPS 119
XP_001468450.1          KEAAKKPFGVNVPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPS 119
CBZ37546.1              KEAAKKPFGVNVPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPS 119
XP_001686152.1          KEASKKPFGVNVPLSRDMAQYMDFIIEEKVPIVFTSAGSPKLWTQKLQSHGIKVVHVVPS 119
sp|P0AEK4|FABI_ECOLI    VEEFAAQLGSDIVLQCDVAE------DASIDTMFAELG--KVWPKFDG-----FVHSIG- 93
sp|P9WGR1|INHA_MYCTU    ITDRLPAKAPLLELDVQNEE----HLASLAGRVTEAIG---AGNKLDG-----VVHSIGF 97
                                .  : *. :  :            :    *      :        .** :

CAC5433624.1            CKLALKCEAAGVNAVVAEGFEAGGHNGLEEITTMALVPQVRKALAPEVPLLAAGGIASGE 179
XP_001468450.1          CKLALKCEAAGVNAVVAEGFEAGGHNGLEEITTMALVPQVRKALAPEVPLLAAGGIASGE 179
CBZ37546.1              CKLALKCEAAGVNAVVAEGFEAGGHNGLEEITTMALVPQVRKALAPEVPLLAAGGIASGE 179
XP_001686152.1          CKLALKCEAAGVNAVVAEGFEAGGHNGLEEITTMALIPQVRKALAPEIPLLAAGGIASGE 179
sp|P0AEK4|FABI_ECOLI    FAPGDQLDGDYVNAVTREGFKIA--HDISSYSFVAMAKACRSMLNPGSALLTLSYLGAER 151
sp|P9WGR1|INHA_MYCTU    MPQTGMGINPFFDAPYAD---VSKGIHISAYSYASMAKALLPIMNPGGSIVGMD-FDPSR 153
                                  .:*   :    .    :.  :  ::       : *  .::  . : . .

CAC5433624.1            AMLAAMALGAEGVQVGTRFAVTQESSAAEE-KKRCTAAGEGDTYLTLKQYMPTRVMLNDY 238
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CBZ37546.1              AMLAAMALGAEGVQVGTRFAVTQESSAAEEFKKRCTAAGEGDTYLTLKQYMPTRVMLNDY 239
XP_001686152.1          AMLATMALGAEGVQVGTRFAVTQESSAAEEFKKRCTAAGEGDTYLTLKQSMPTRVMLNDY 239
sp|P0AEK4|FABI_ECOLI    AIPNYNVMGLAKASLEANVRYMANAMGPEGVRVNAISAG------------PIRTLAASG 199
sp|P9WGR1|INHA_MYCTU    AMPAYNWMTVAKSALESVNRFVAREAGKYGVRSNLVAAG------------PIRTLAMSA 201
                        *:     :      : :      .  .    : .  :**           * *.:  .

CAC5433624.1            GKEARRLSESGATKAQLKEFRGKGRTKKGMFDGDVTNGELEIGQIVSACKDVPTAAEVVE 298
XP_001468450.1          GKEARRLSESGATKAQLKEFRGKGRTKKGMFDGDVTNGELEIGQIVSACKDVPTAAEVVE 299
CBZ37546.1              GKEARRLSESGATKAQLKEFRGKGRTKKGMFDGDVTNGELEIGQIVSACKDVPTAAEVVE 299
XP_001686152.1          GKEARRLSESGATKAQLEEFRGKGRTKKGIFDGDVTNGELEIGQIVSACKDVPTAAEVVE 299
sp|P0AEK4|FABI_ECOLI    IKDFRKMLAHCEAVTPIRRTVTIEDVGN---SAAFLCSDLSAG-ISGEVVHVDGGFSIAA 255
sp|P9WGR1|INHA_MYCTU    IVGGALGEEAGAQIQLLEEGWDQRAPIGWNMKDATPVAKTVCALLSDWLPATTGDIIYAD 261
                                    :..           .     ..   . : .    .      .

CAC5433624.1            RMVKEFRTRNAQLAKMNL 316
XP_001468450.1          RMVKEFRTRNAQLAKMNL 317
CBZ37546.1              RMVKEFRTRNAQLAKMNL 317
XP_001686152.1          RMVKEFHTRKAQLAKMNL 317
sp|P0AEK4|FABI_ECOLI    MNELELK----------- 262
sp|P9WGR1|INHA_MYCTU    GGAHTQLL---------- 269
```

Figure S1. Multisequence alignment of :enoyl-[acyl-carrier-protein] reductases.

Physicochemical parameters of active compounds.

The physicochemical parameters were calculated using the free software Data Warrior.

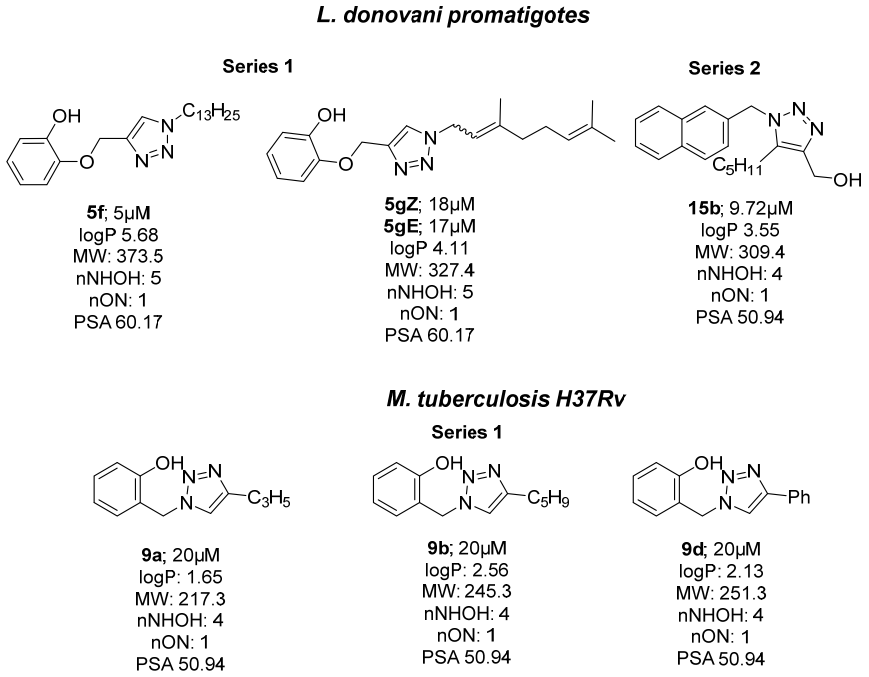
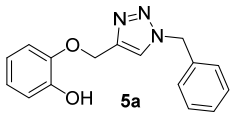


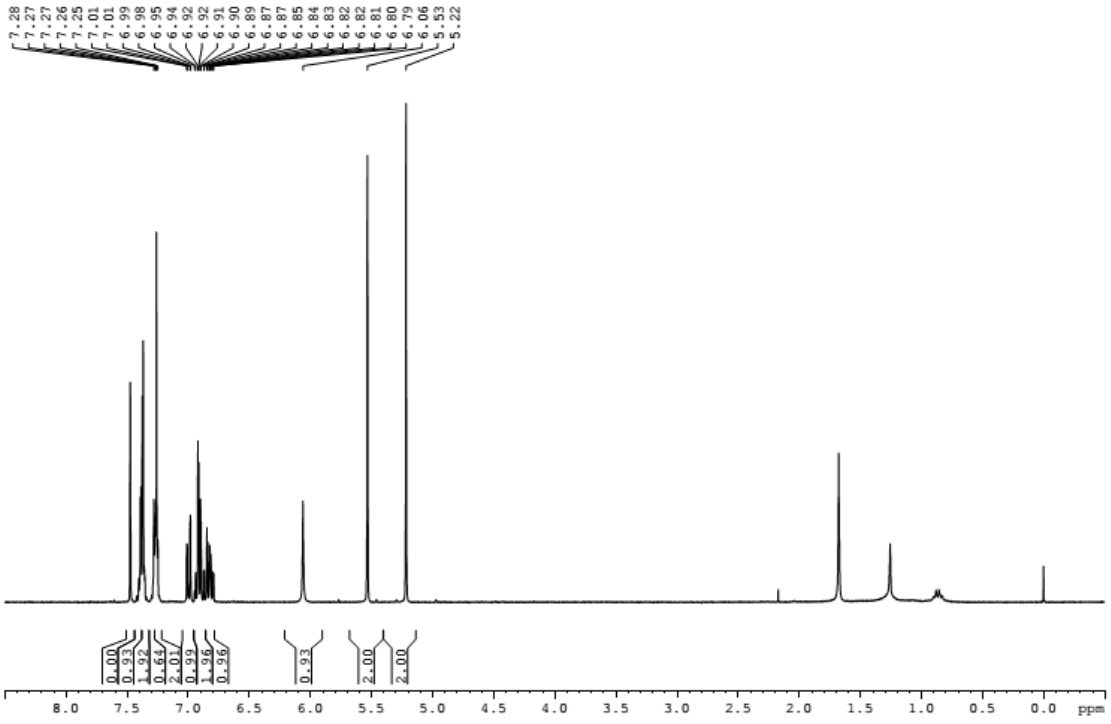
Figure S2. Physicochemical parameters of the active compounds of the library.

Spectral Data of compounds.

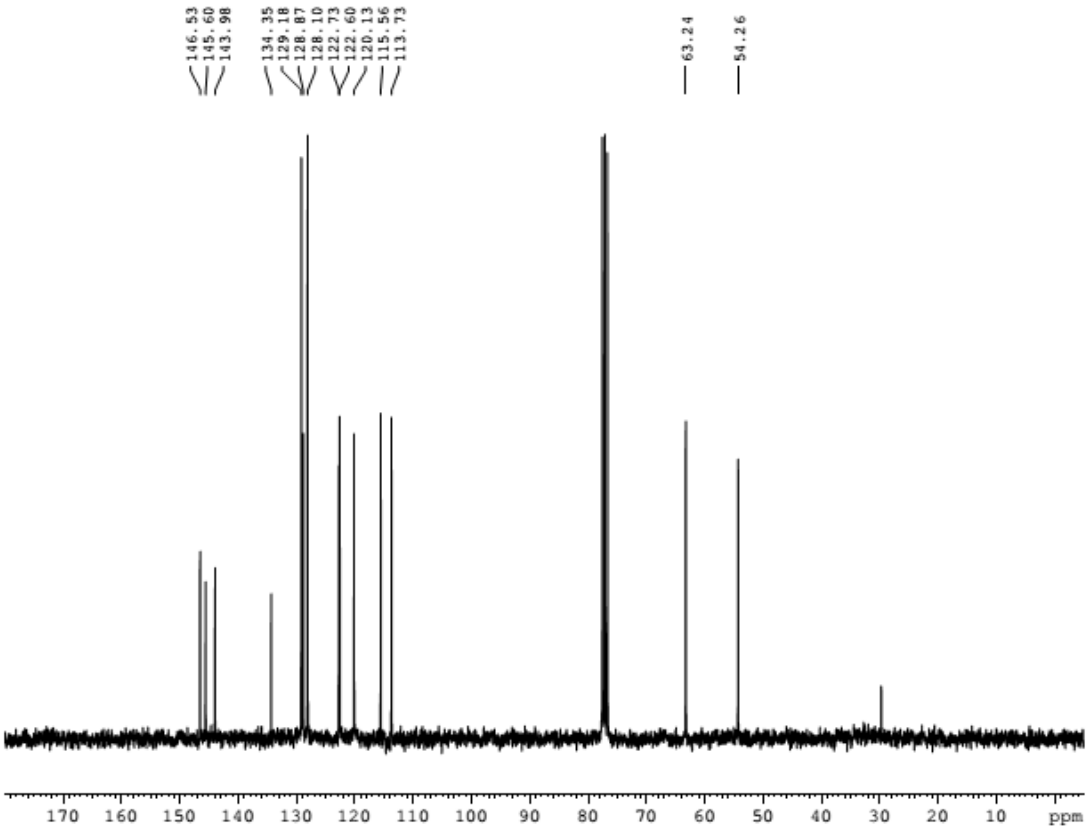
Compound 5a



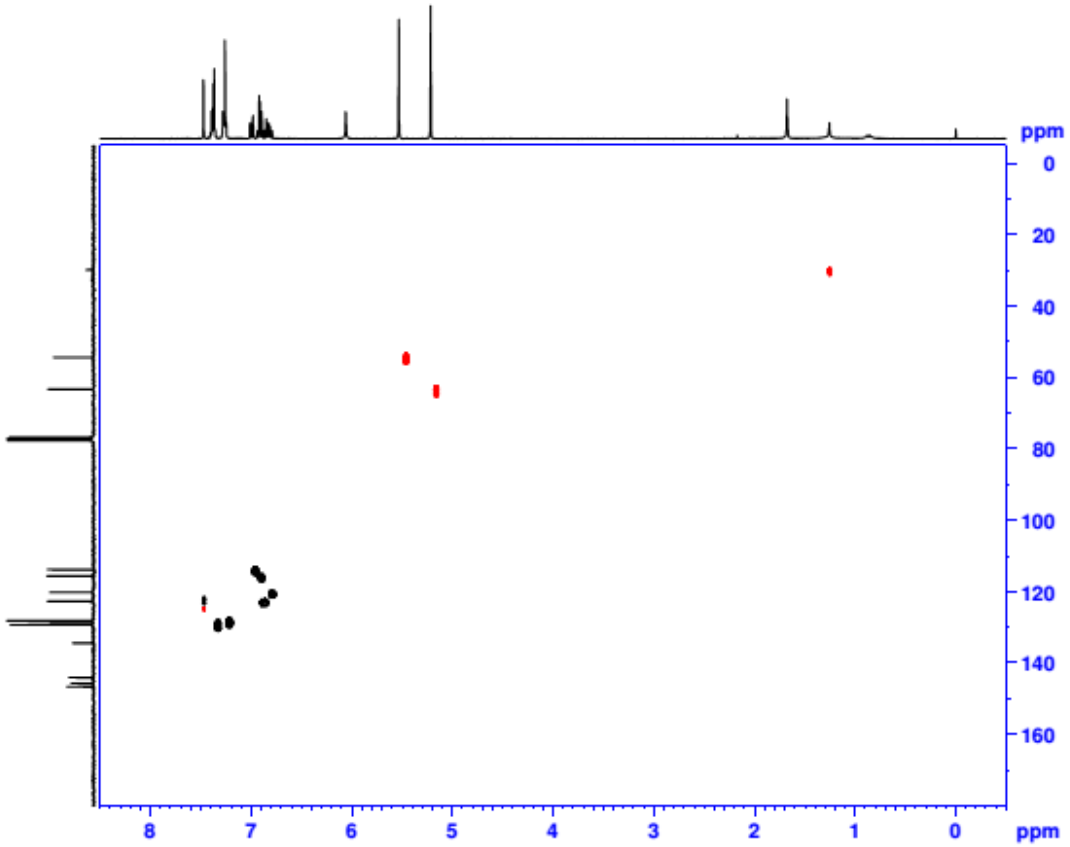
^{1}H NMR (300 MHz, $CDCl_3$)



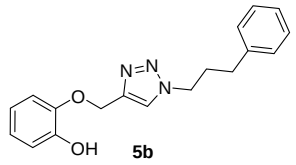
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

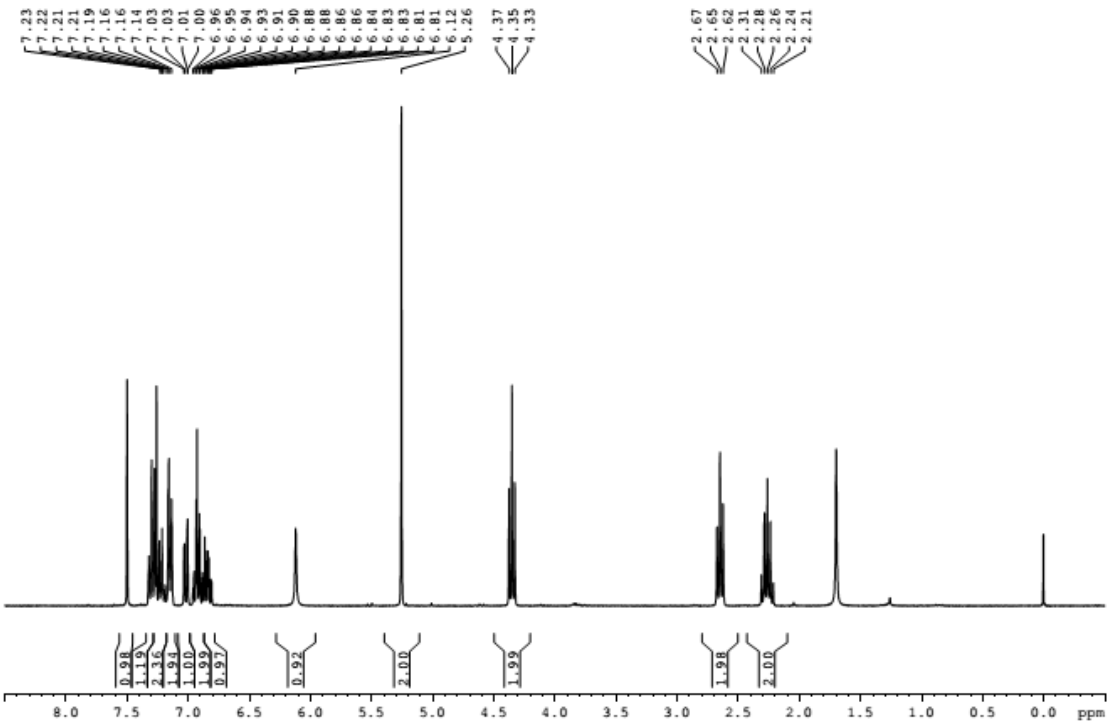


Compound 5b

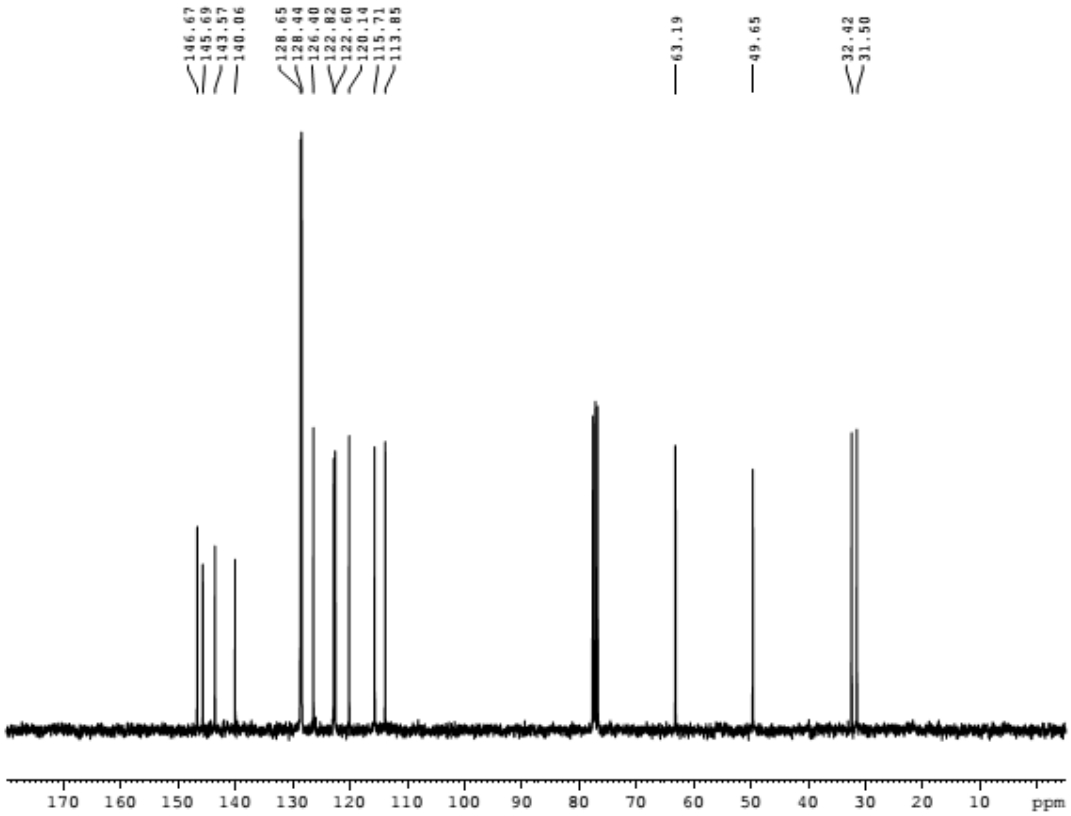


5b

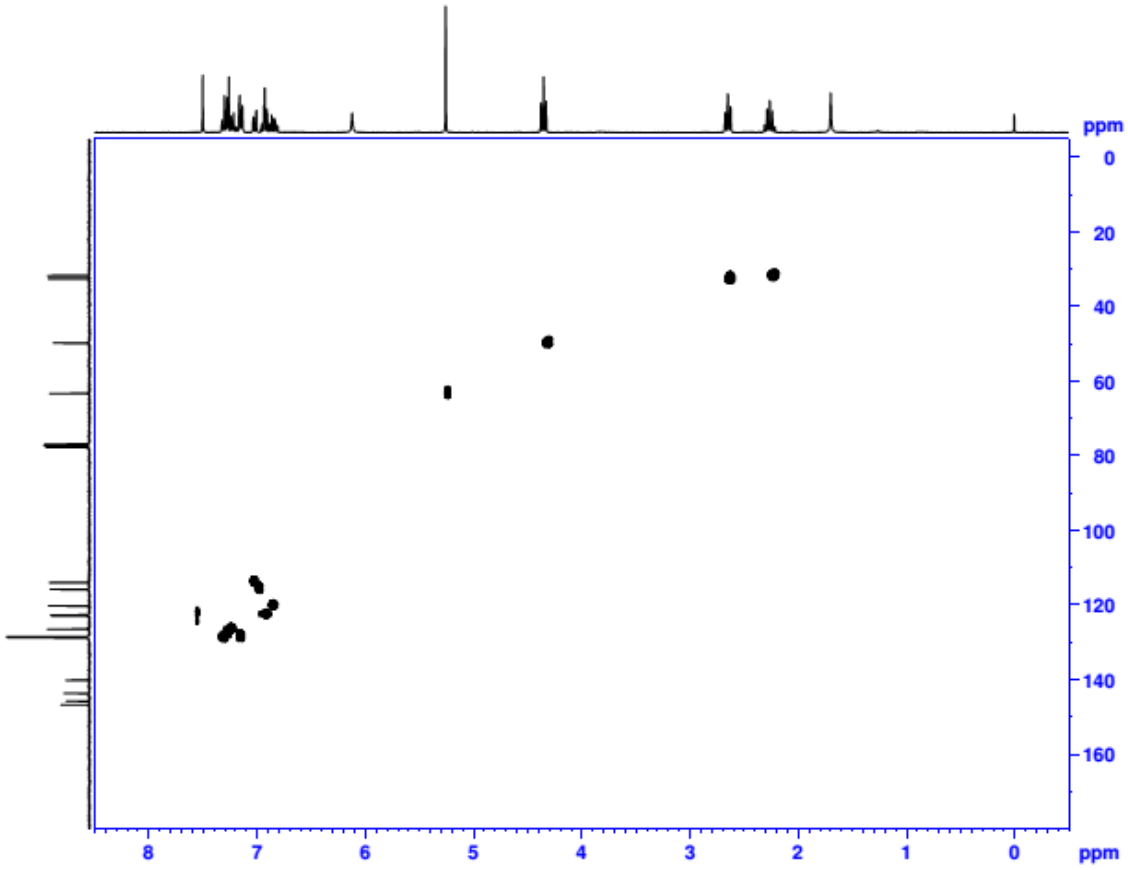
^{1}H NMR (300 MHz, $CDCl_3$)



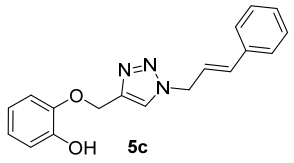
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

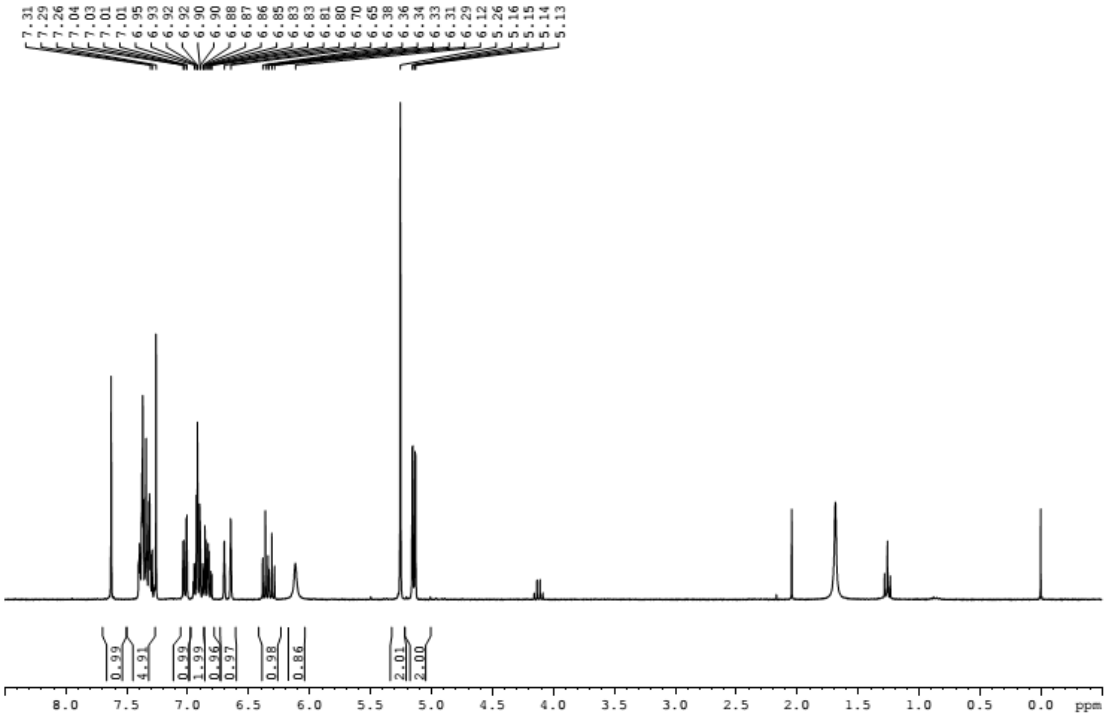


Compound 5c

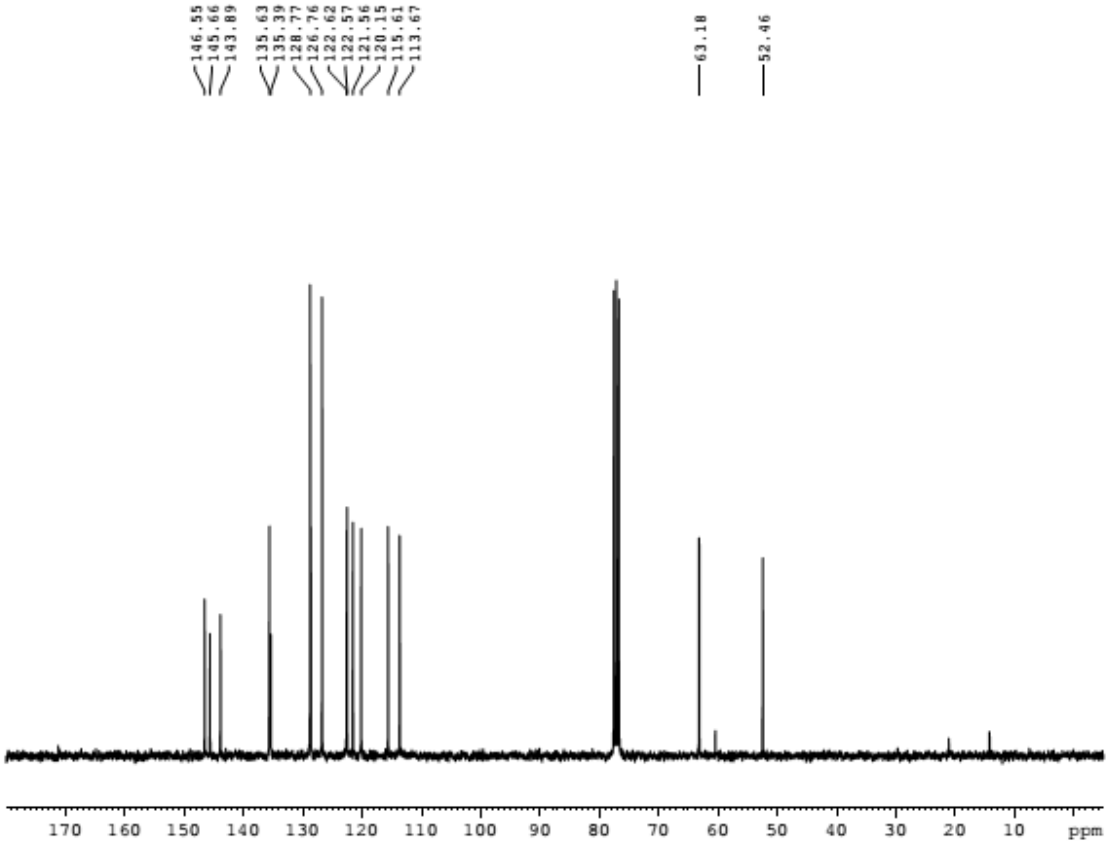


5c

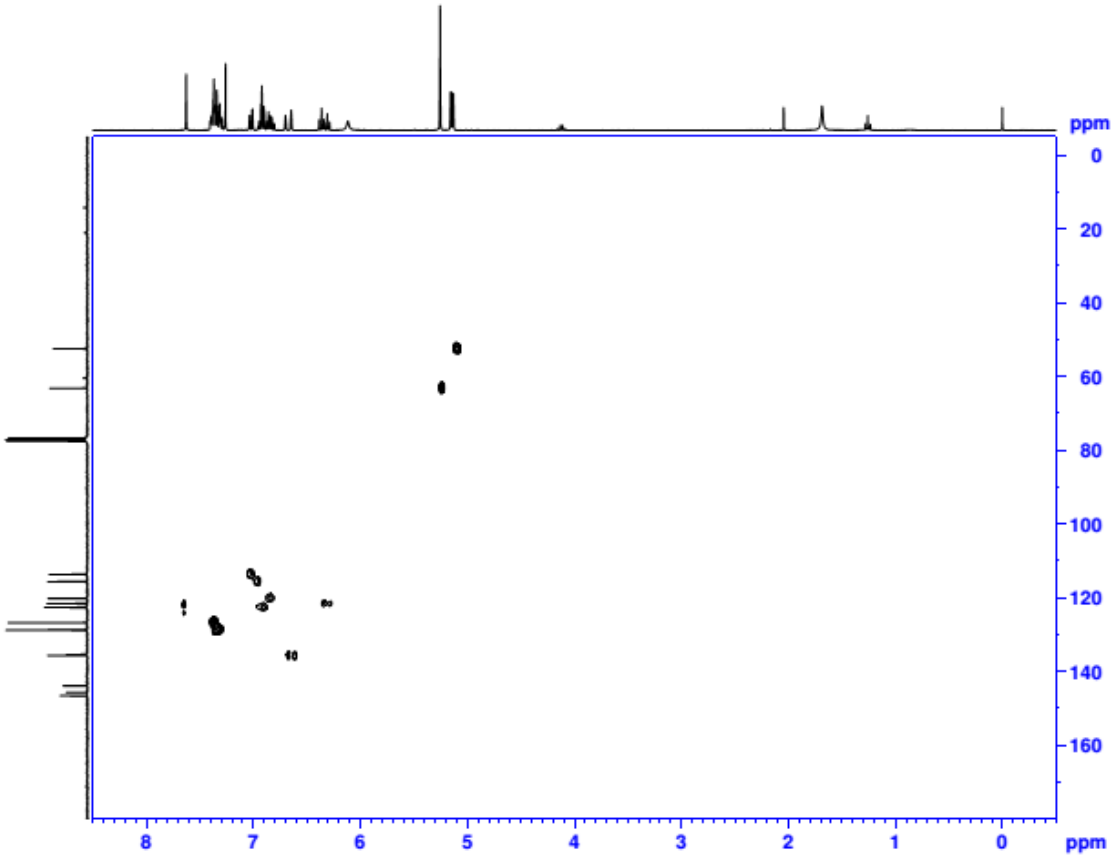
^{1}H NMR (300 MHz, $CDCl_3$)



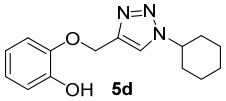
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

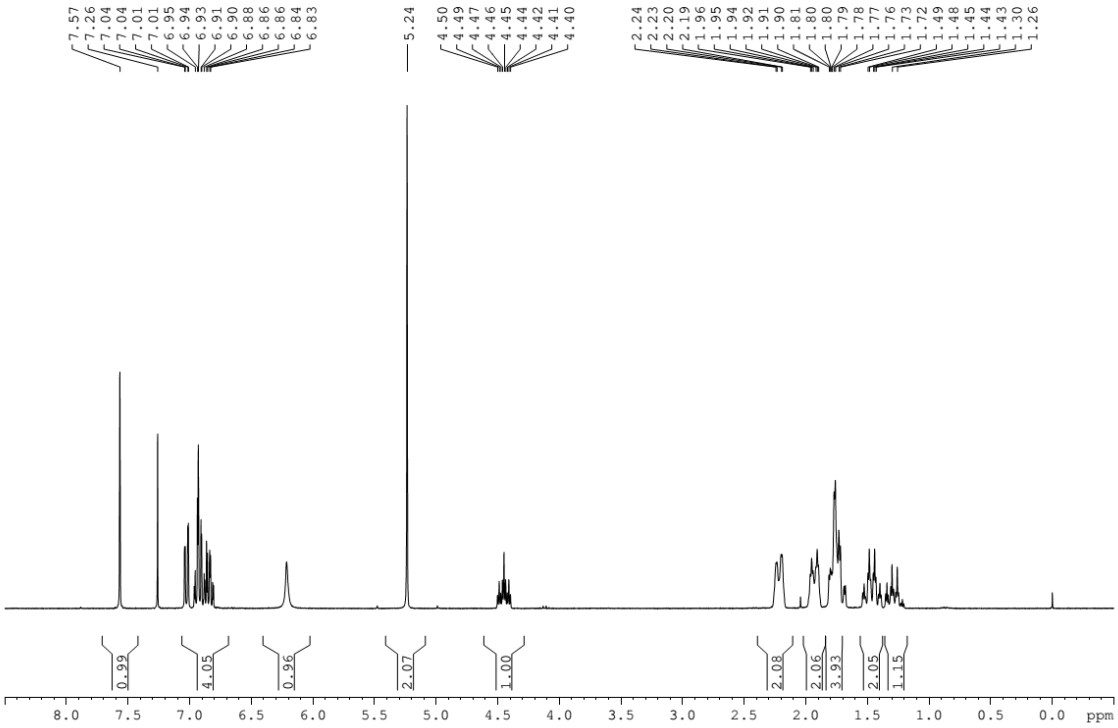


Compound 5d

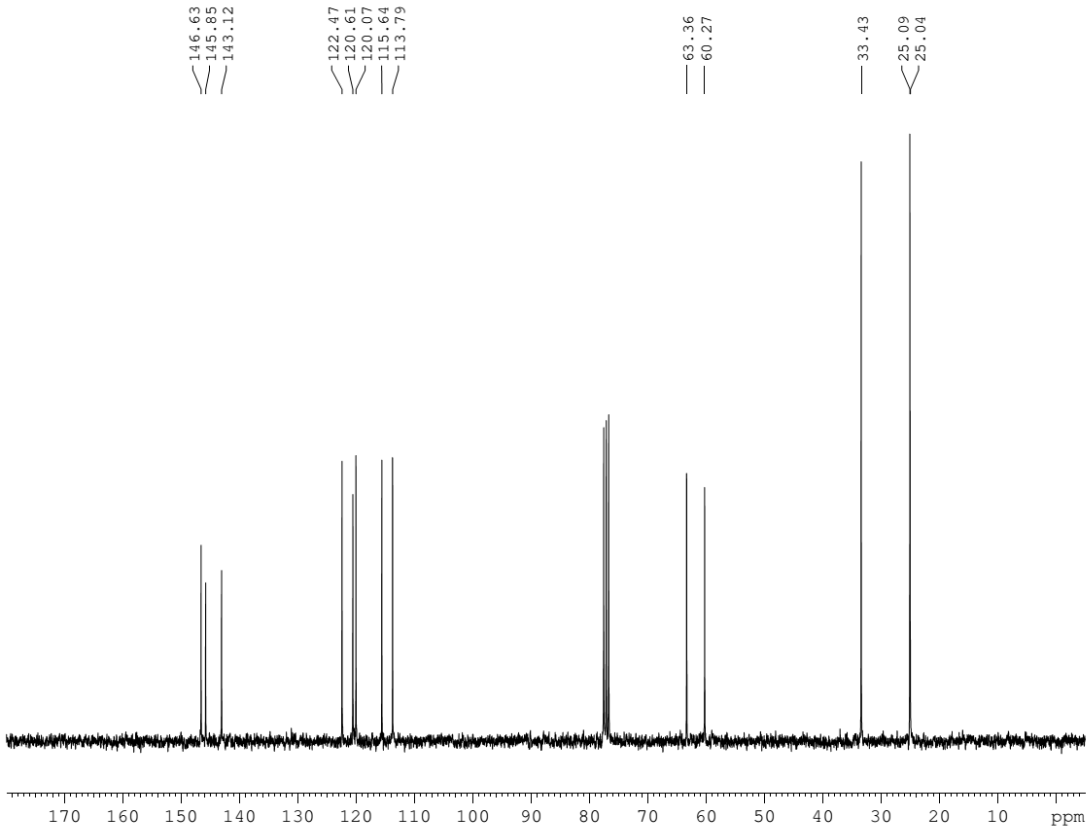


5d

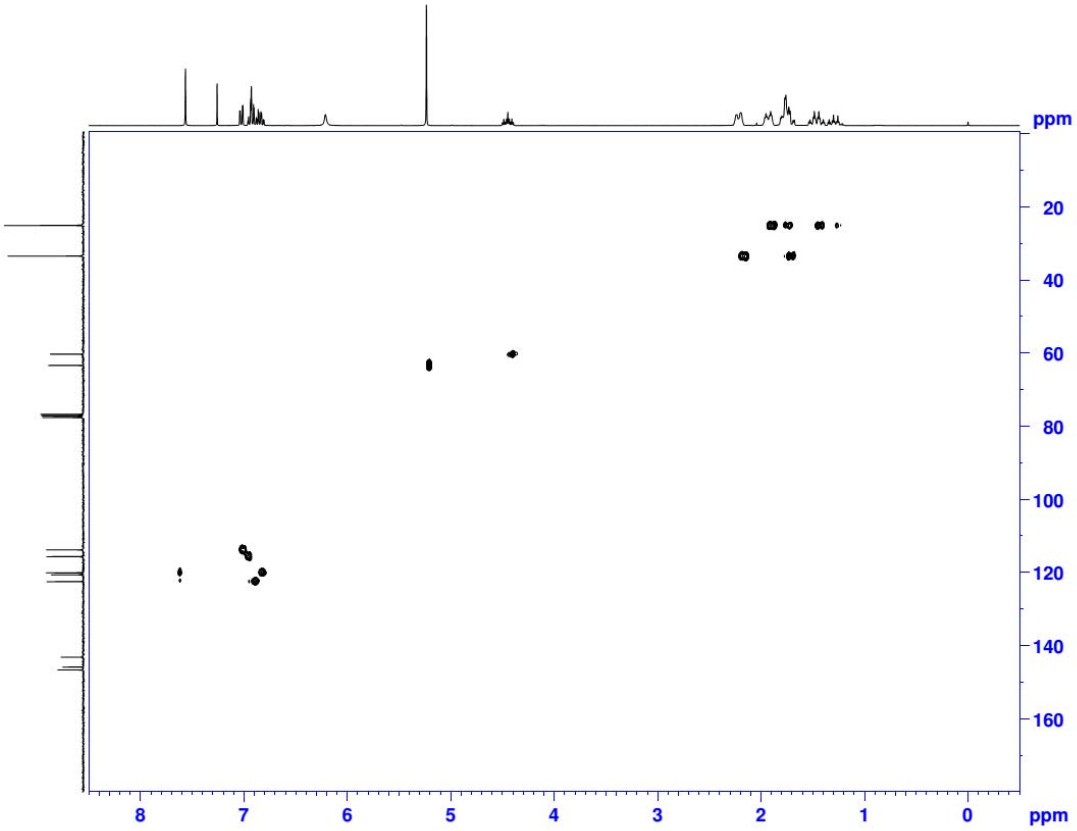
^{1}H NMR (300 MHz, $CDCl_3$)



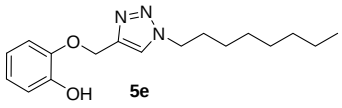
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

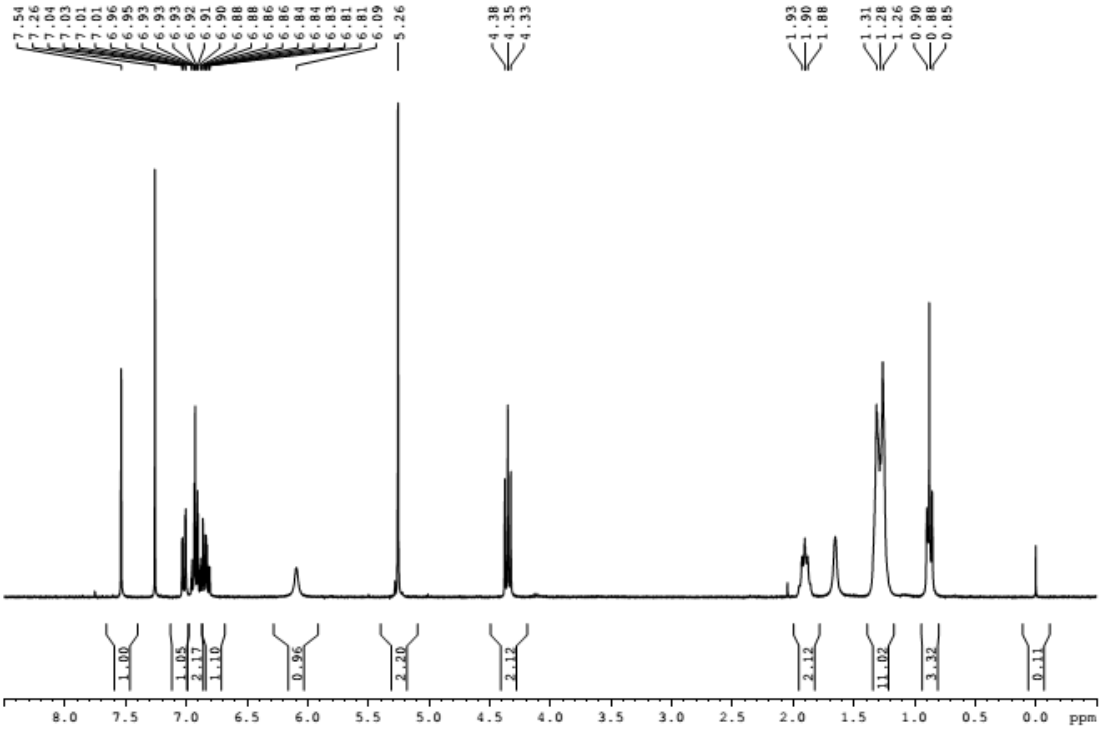


Compound 5e

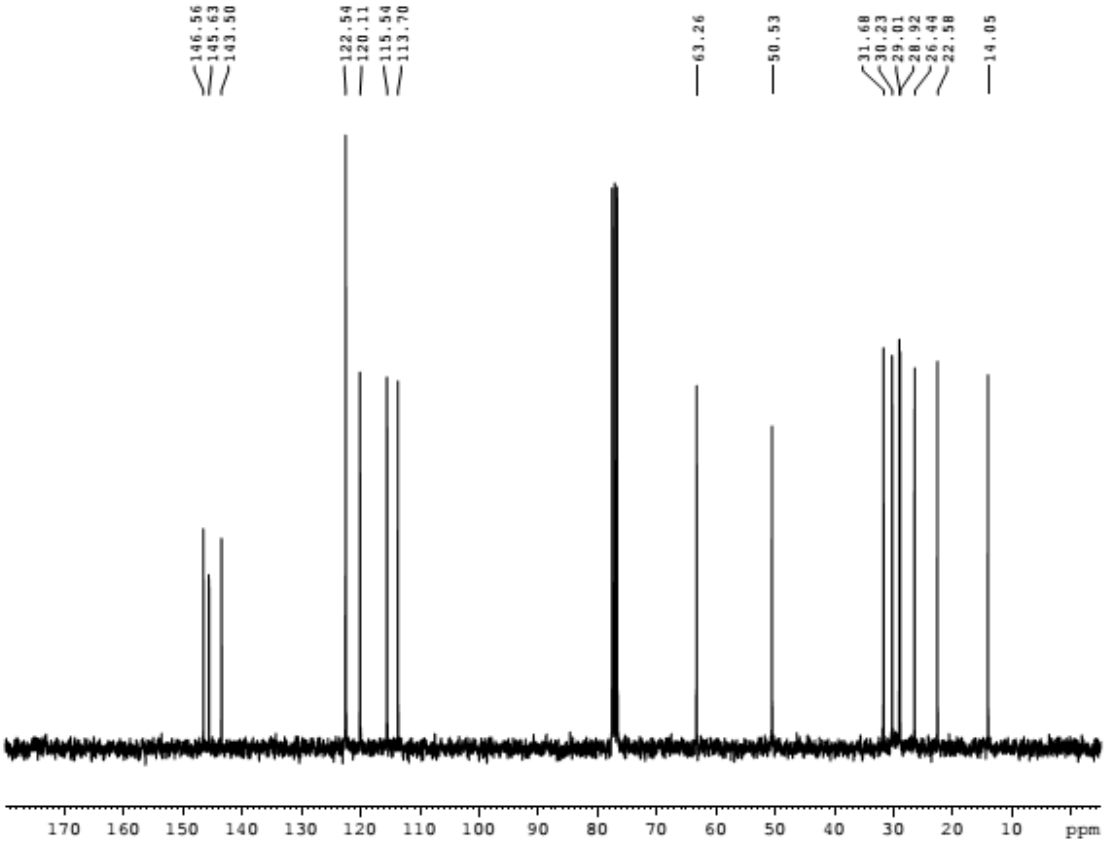


5e

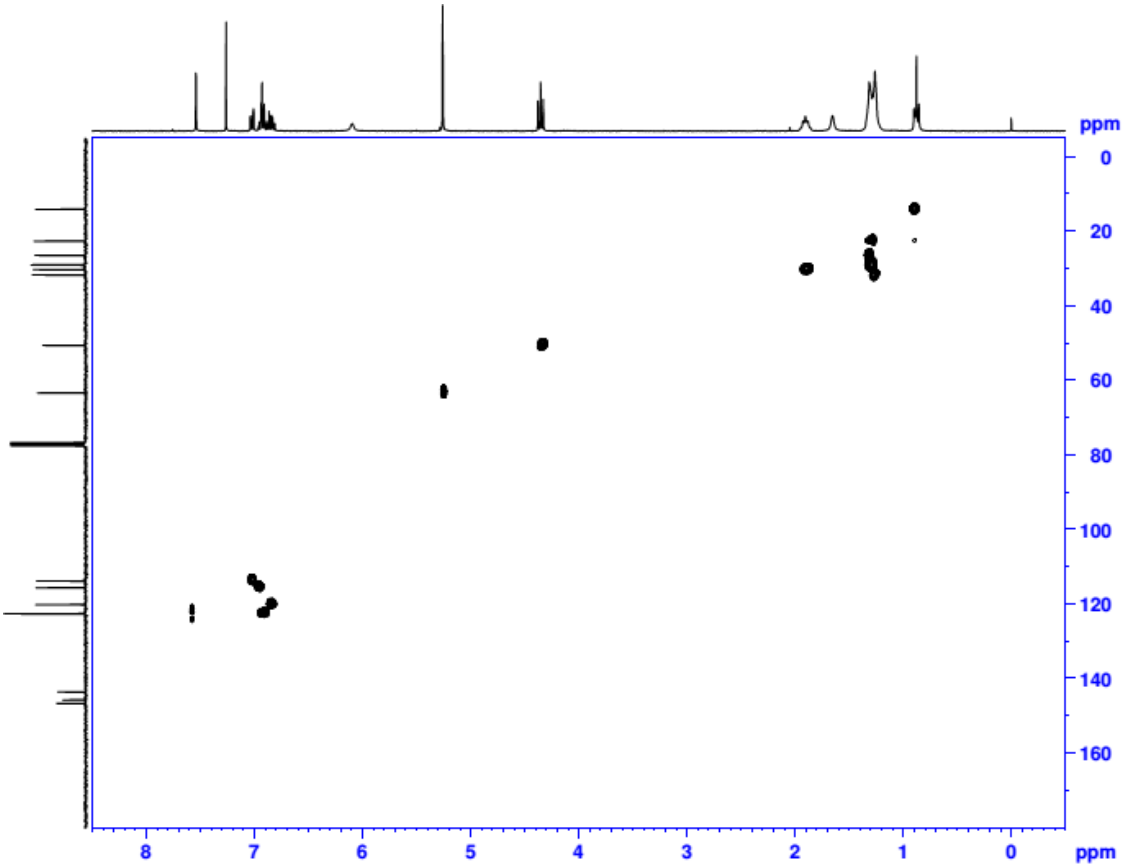
^{1}H NMR (300 MHz, $CDCl_3$)



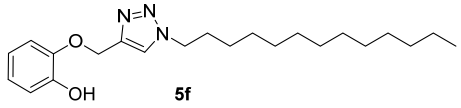
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

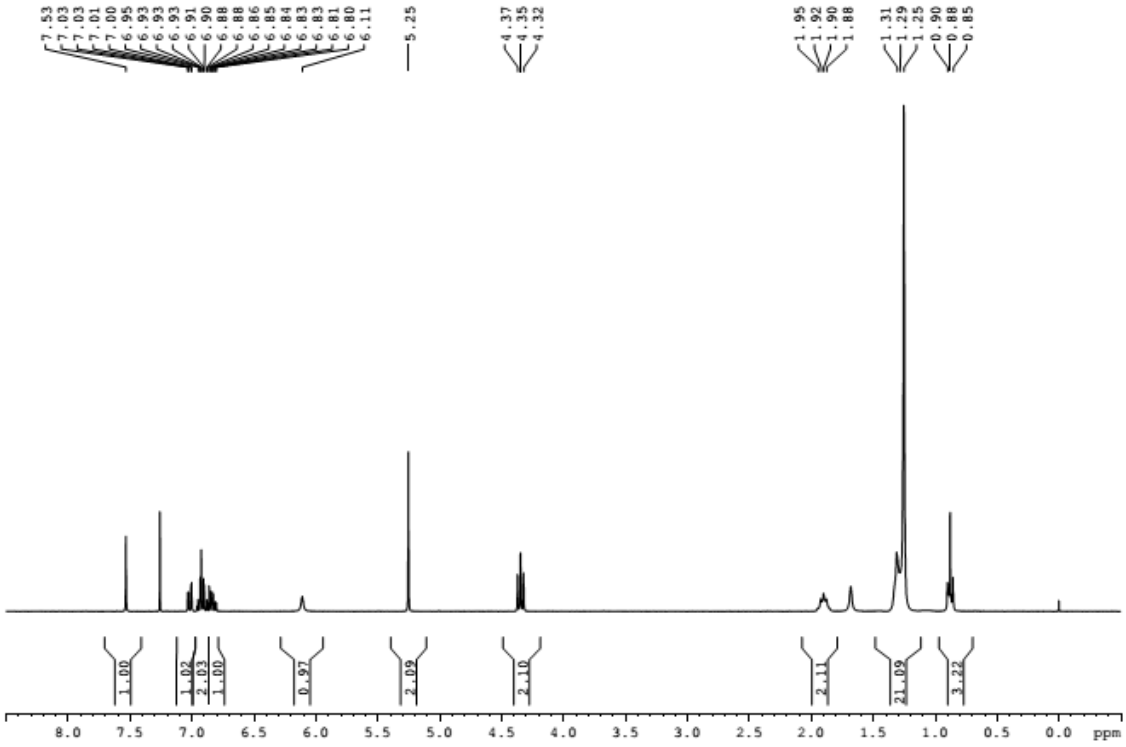


Compound 5f

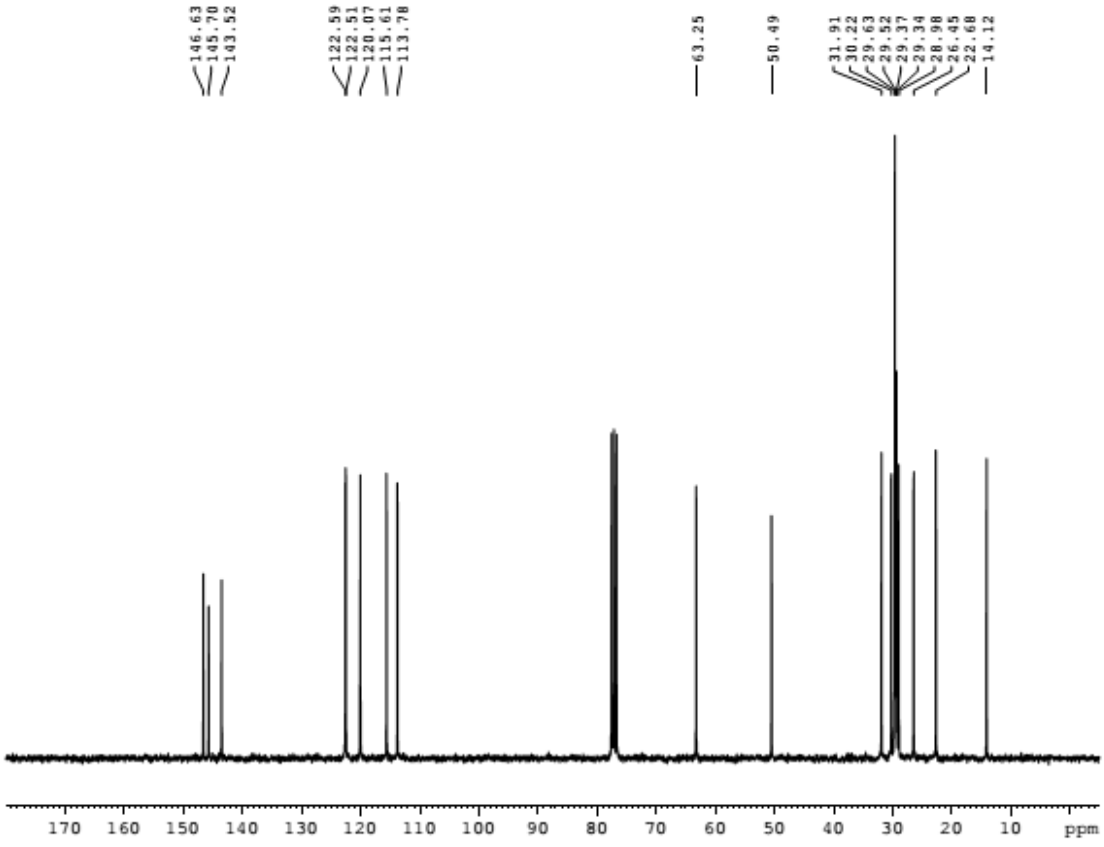


5f

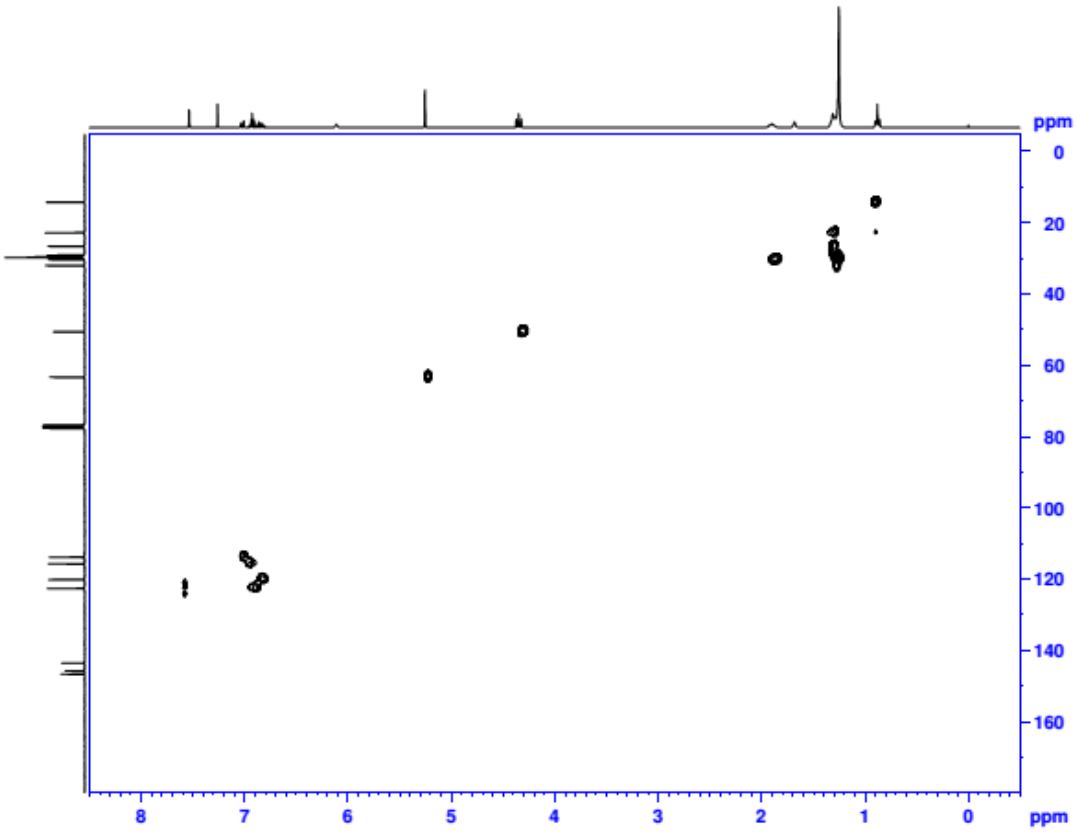
^{1}H NMR (300 MHz, $CDCl_3$)



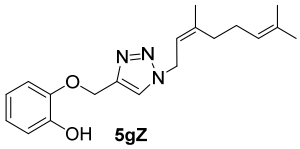
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

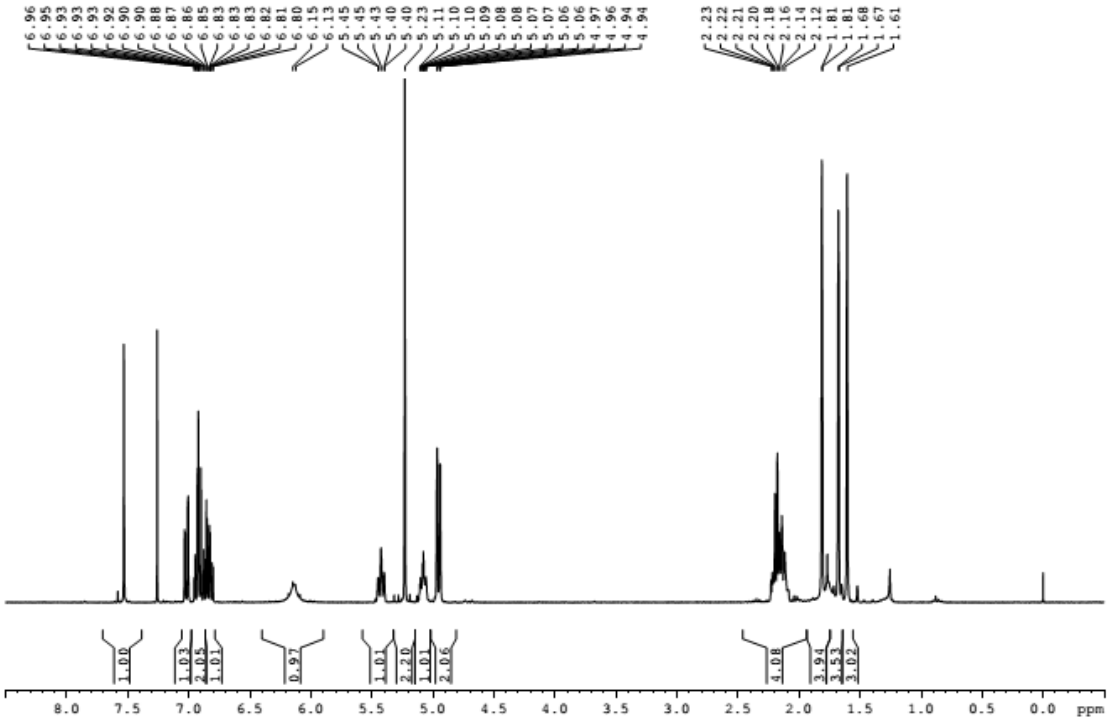


Compound 5gZ

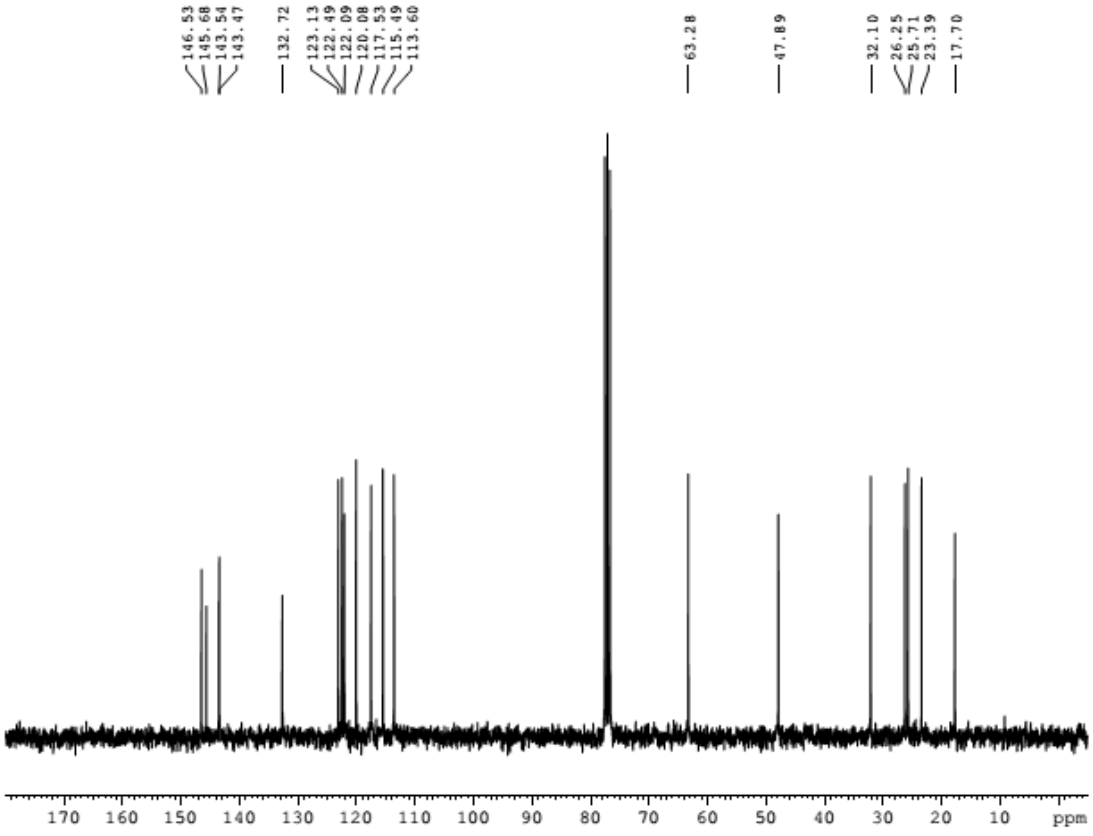


5gZ

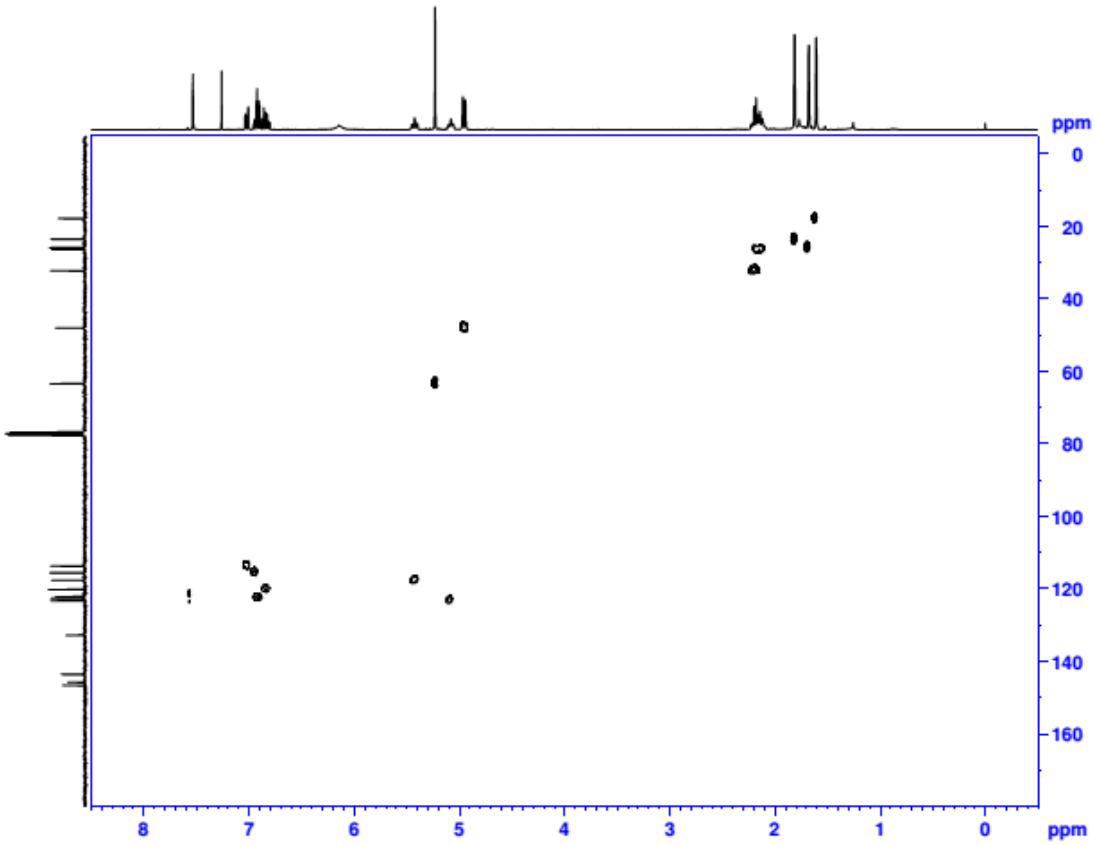
^{1}H NMR (300 MHz, $CDCl_3$)



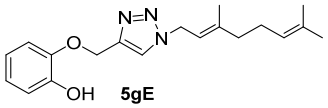
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

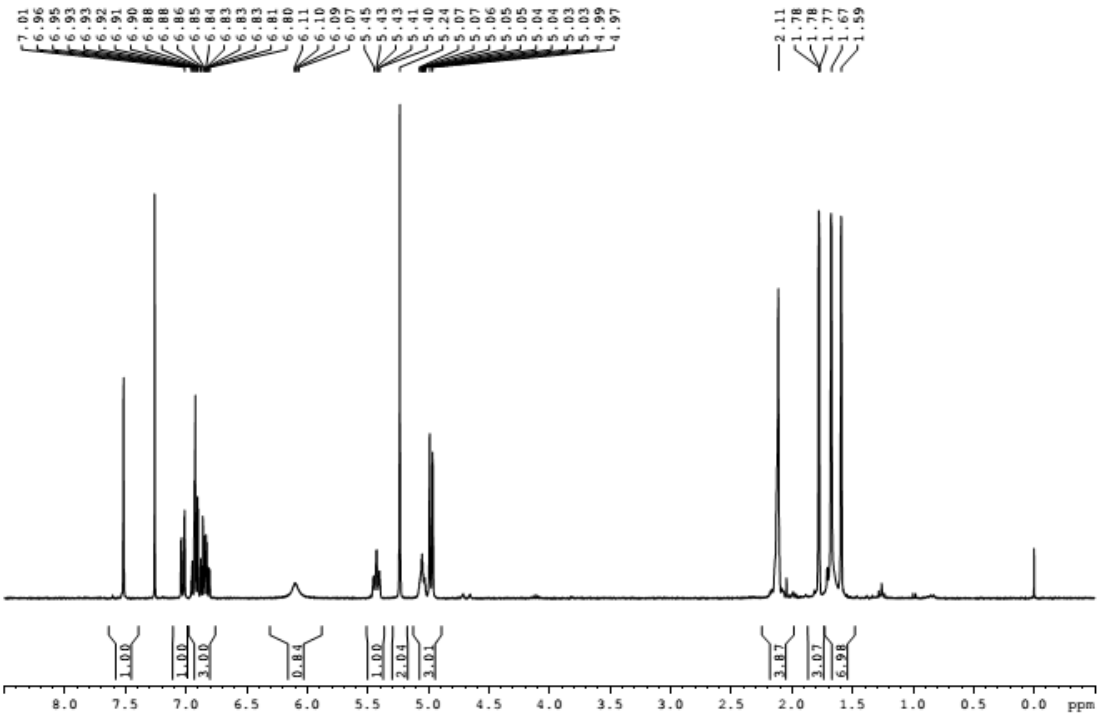


Compound 5gE

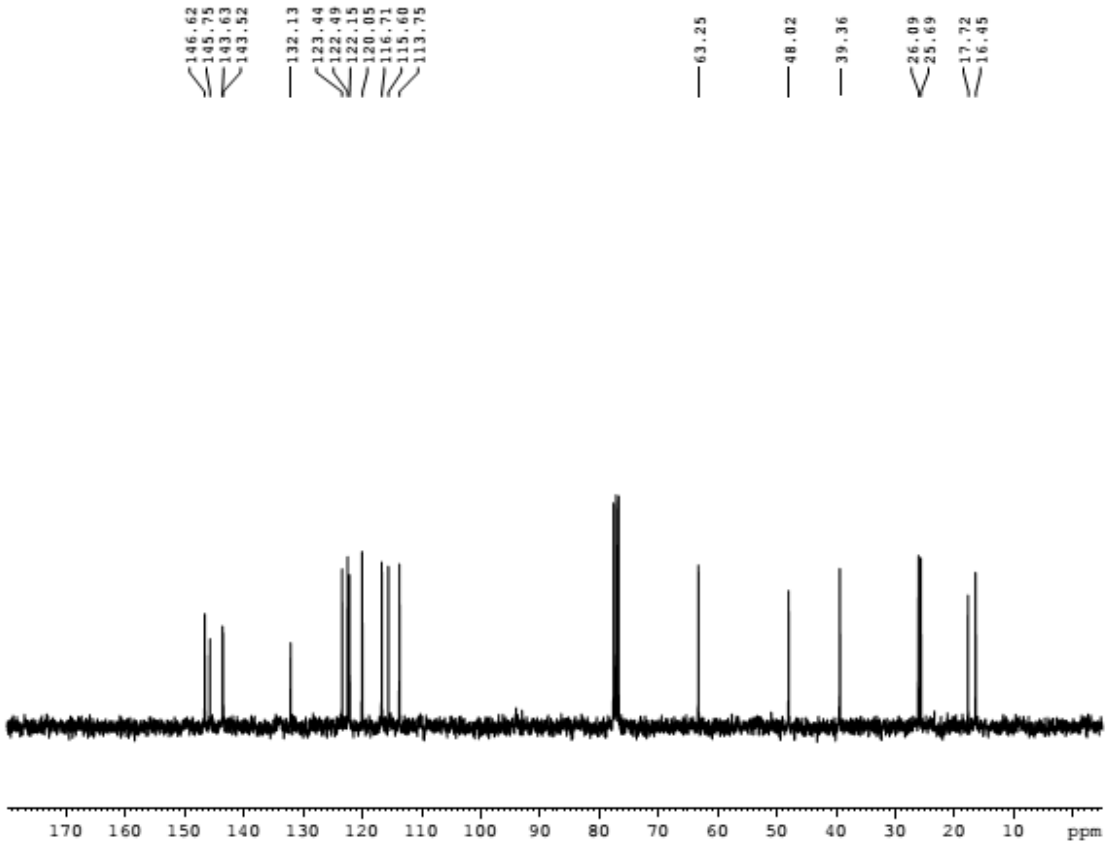


5gE

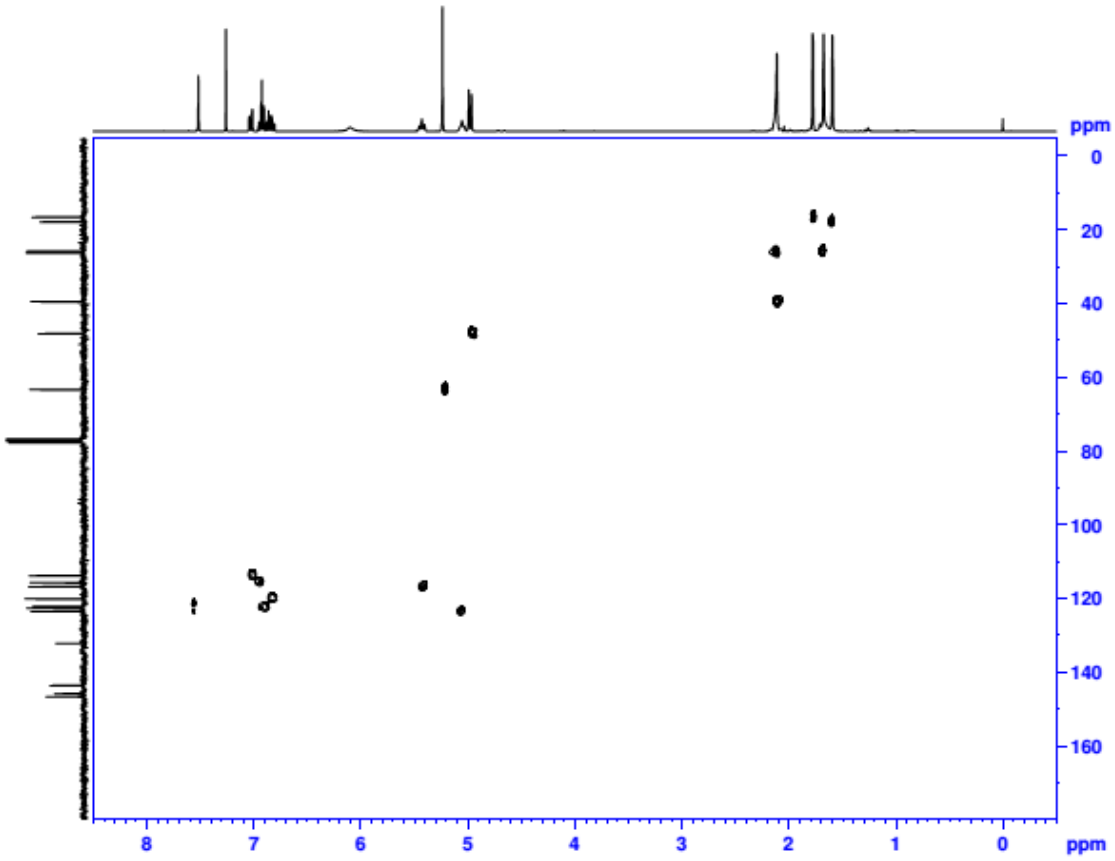
^{1}H NMR (300 MHz, $CDCl_3$)



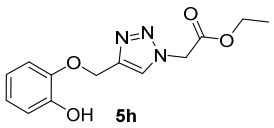
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

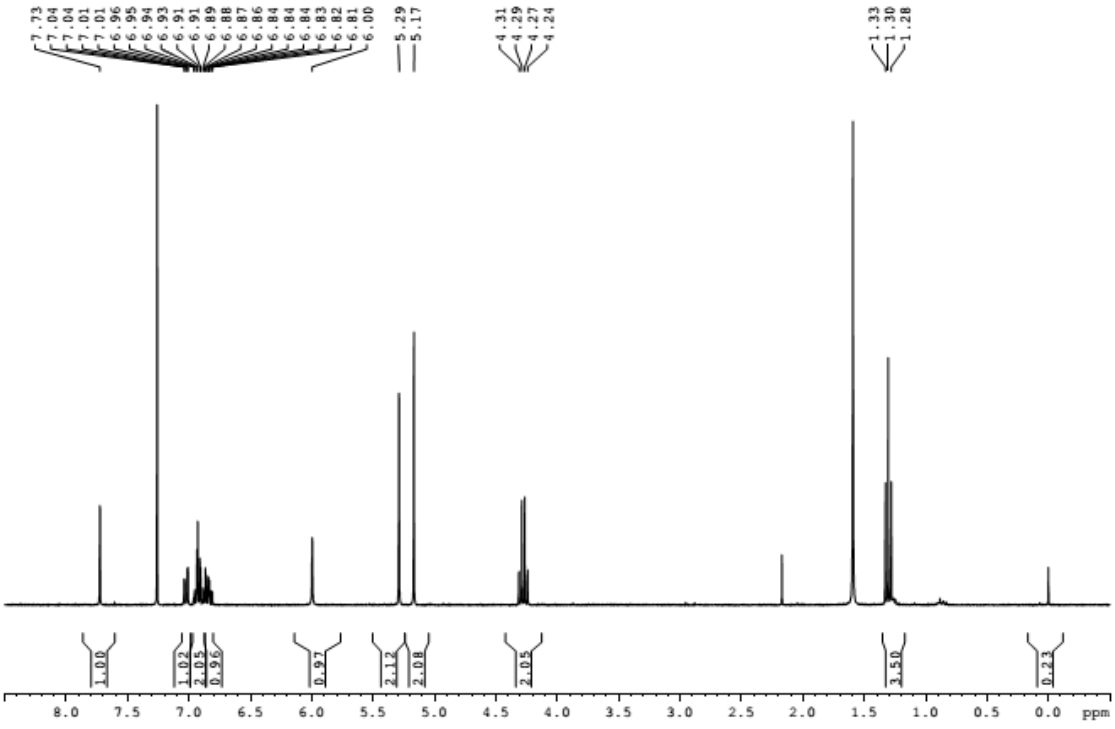


Compound 5h

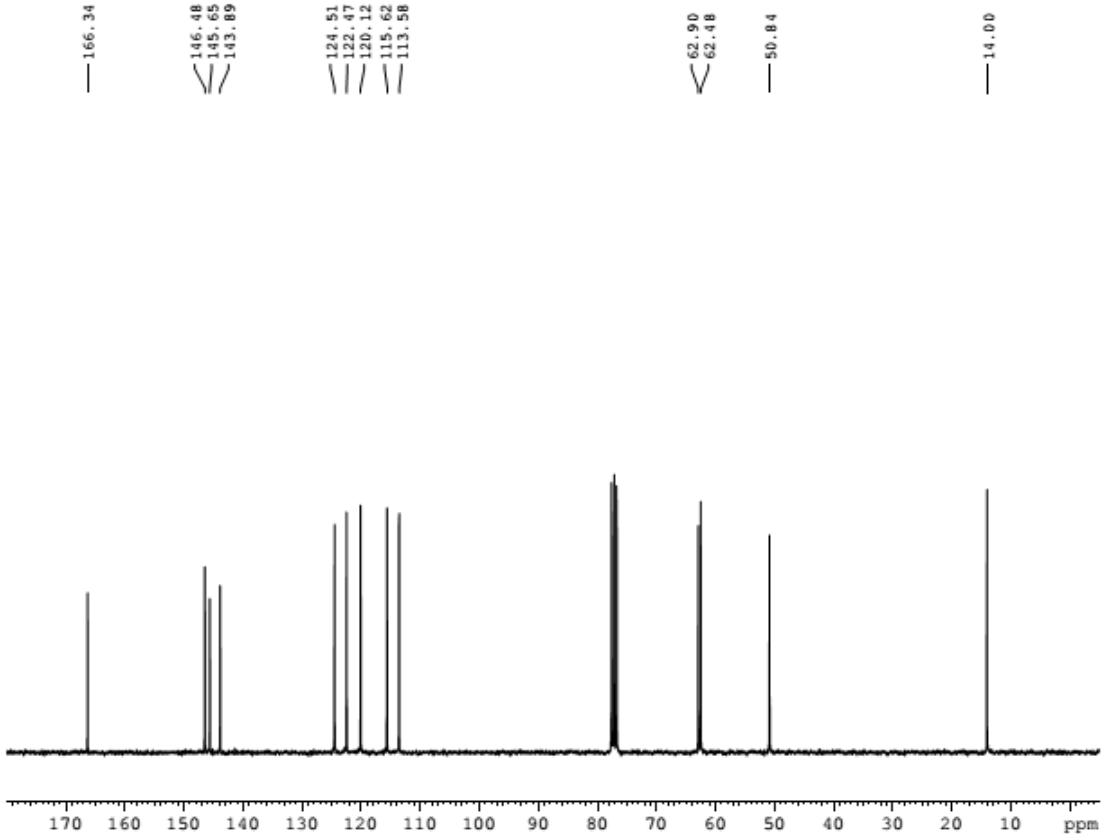


5h

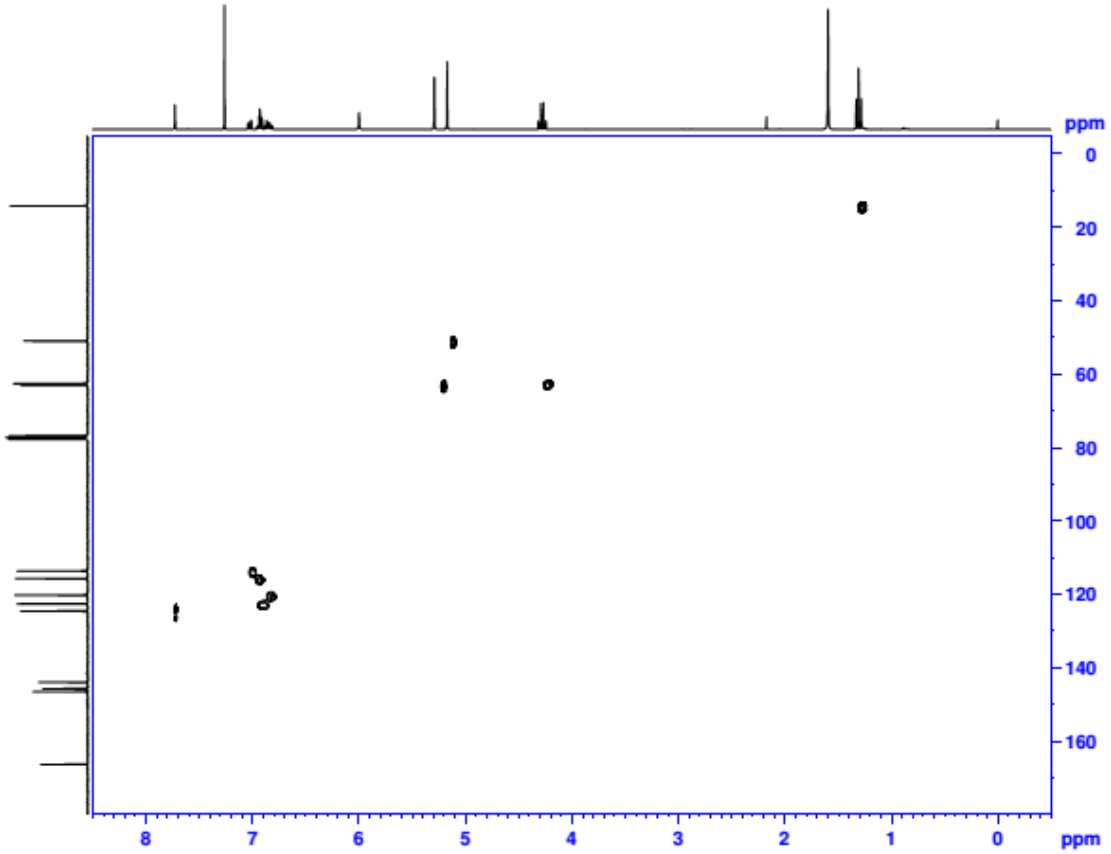
^{1}H NMR (300 MHz, $CDCl_3$)



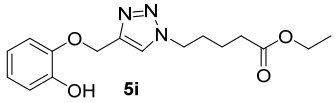
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

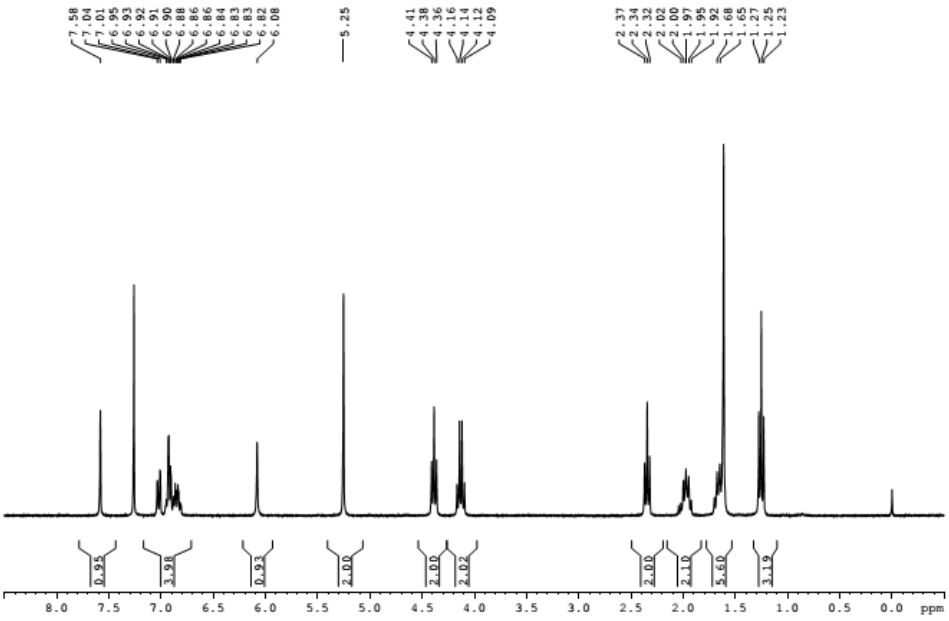


Compound 5i

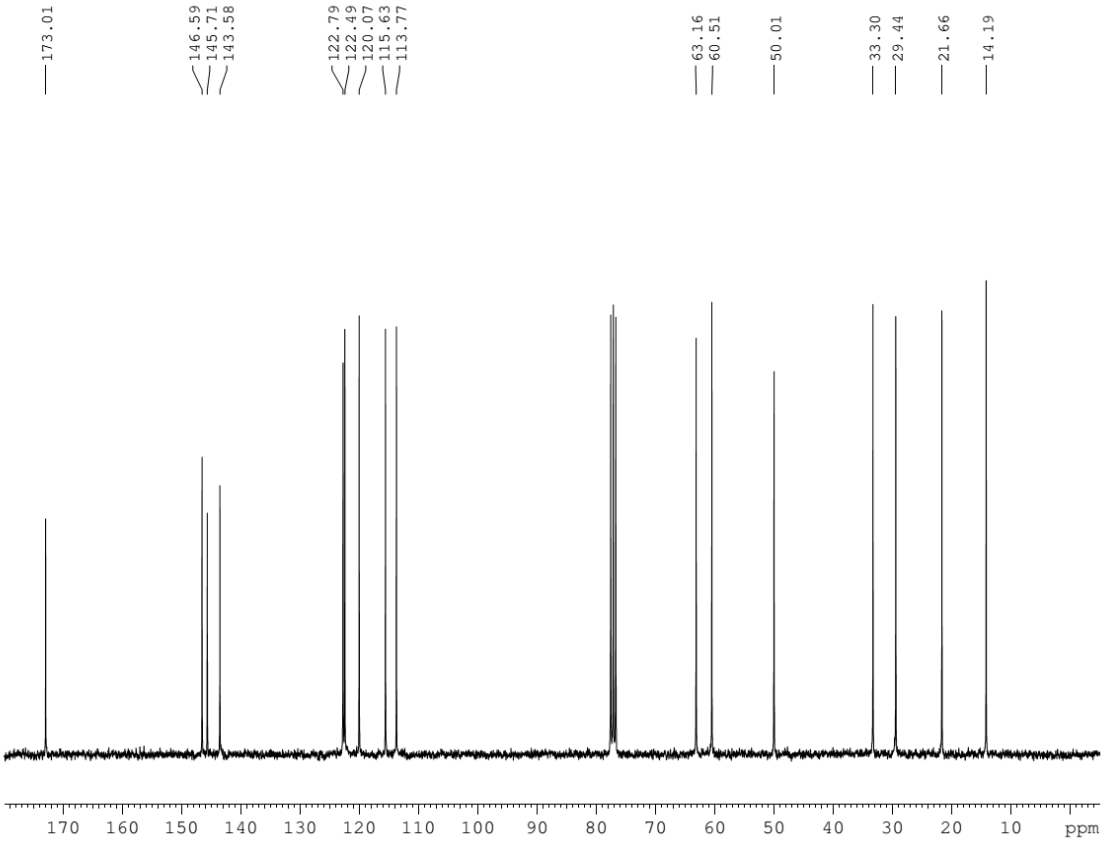


5i

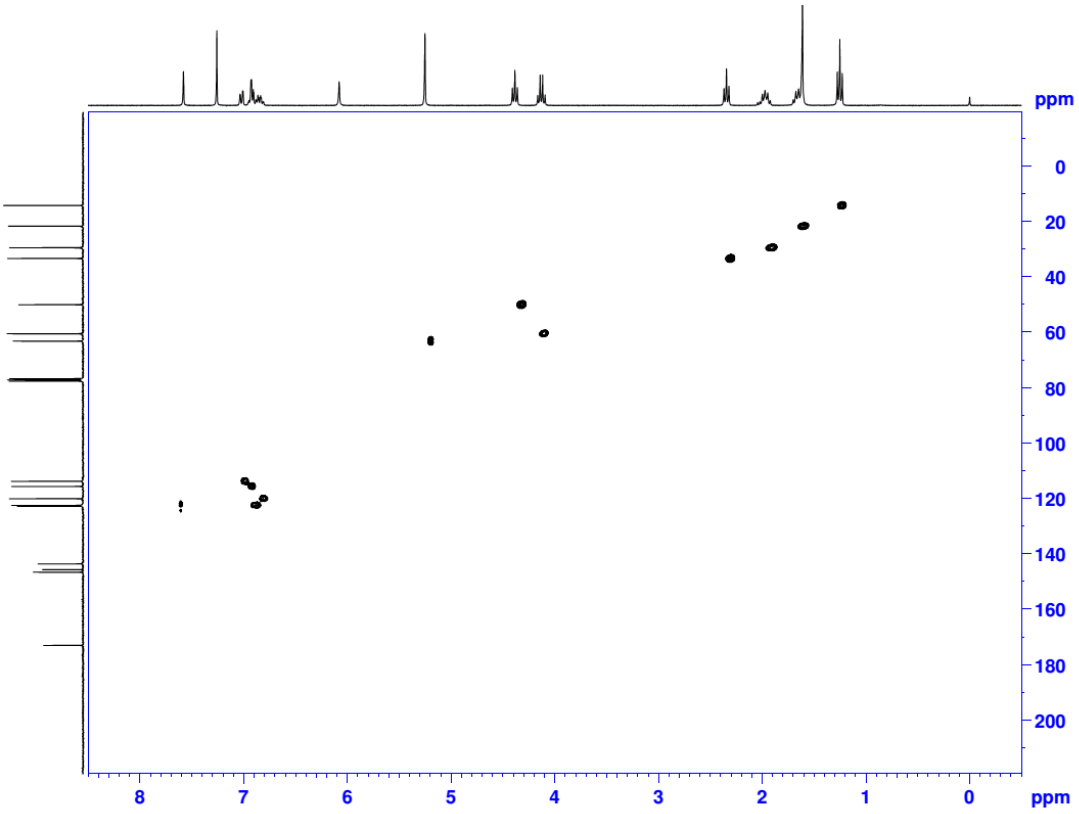
^{1}H NMR (300 MHz, $CDCl_3$)



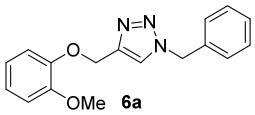
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

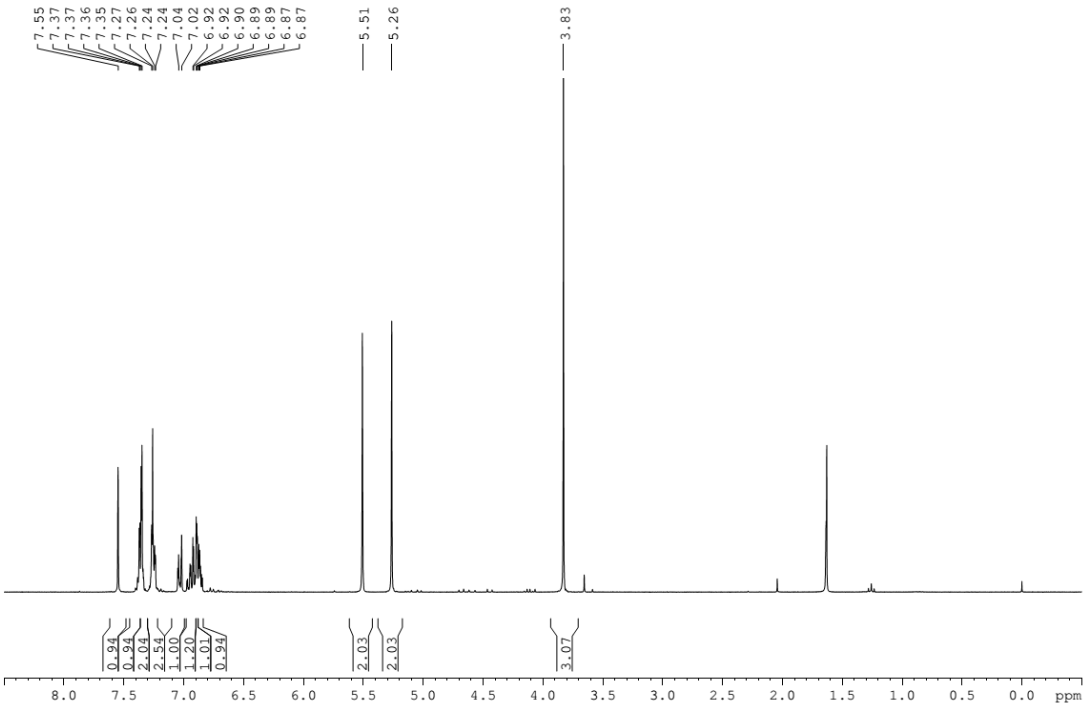


Compound 6a

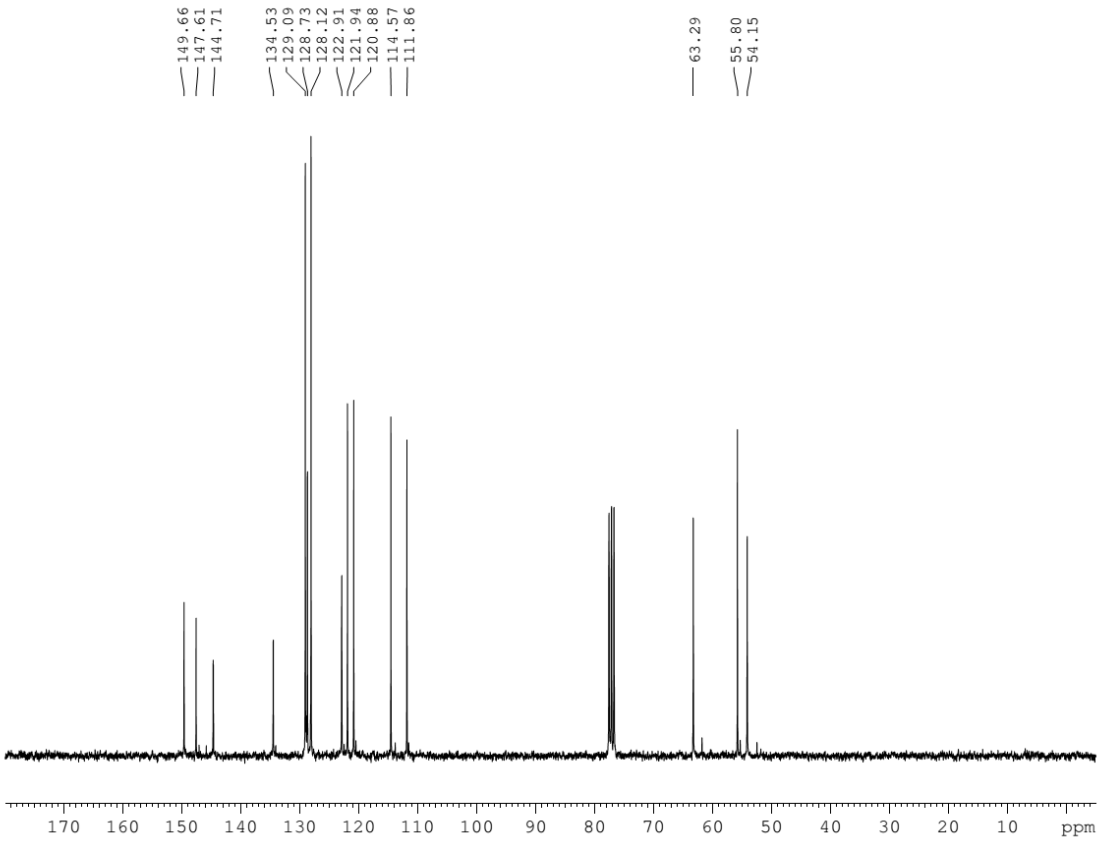


6a

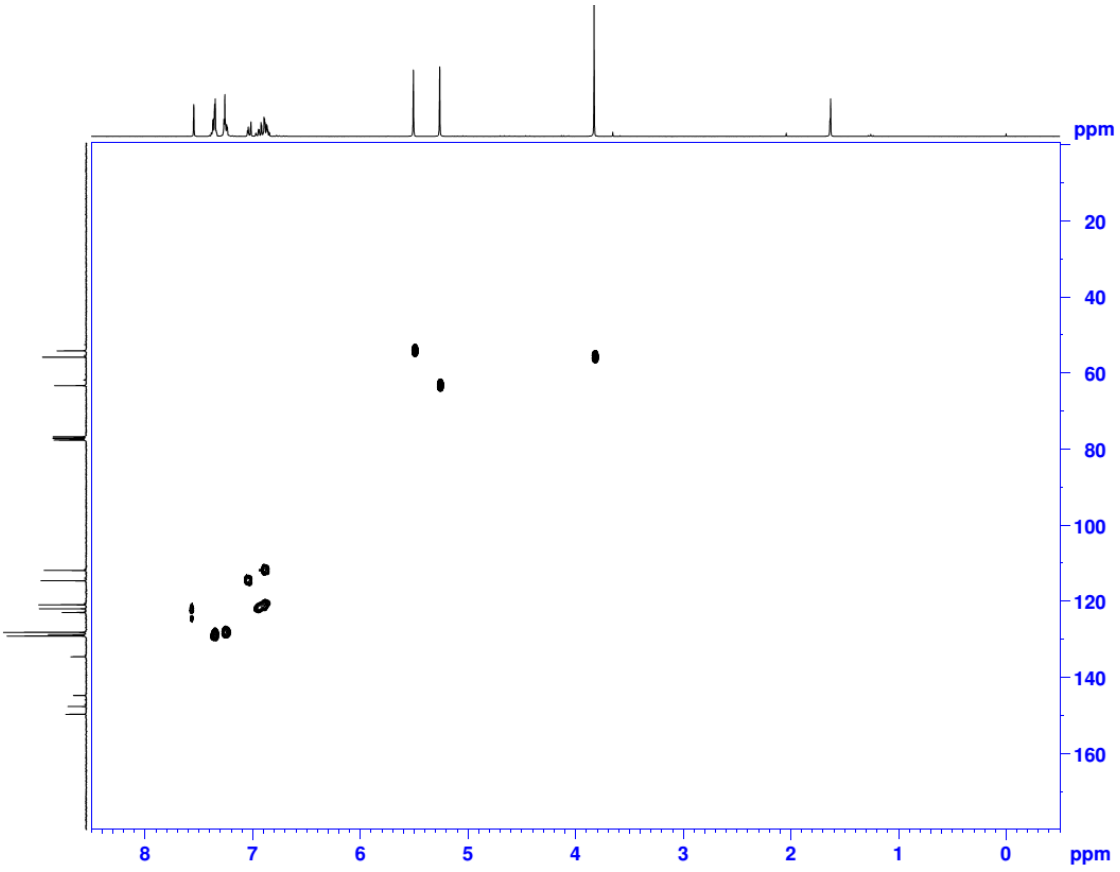
^{1}H NMR (300 MHz, $CDCl_3$)



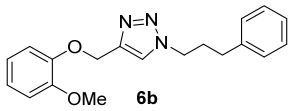
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

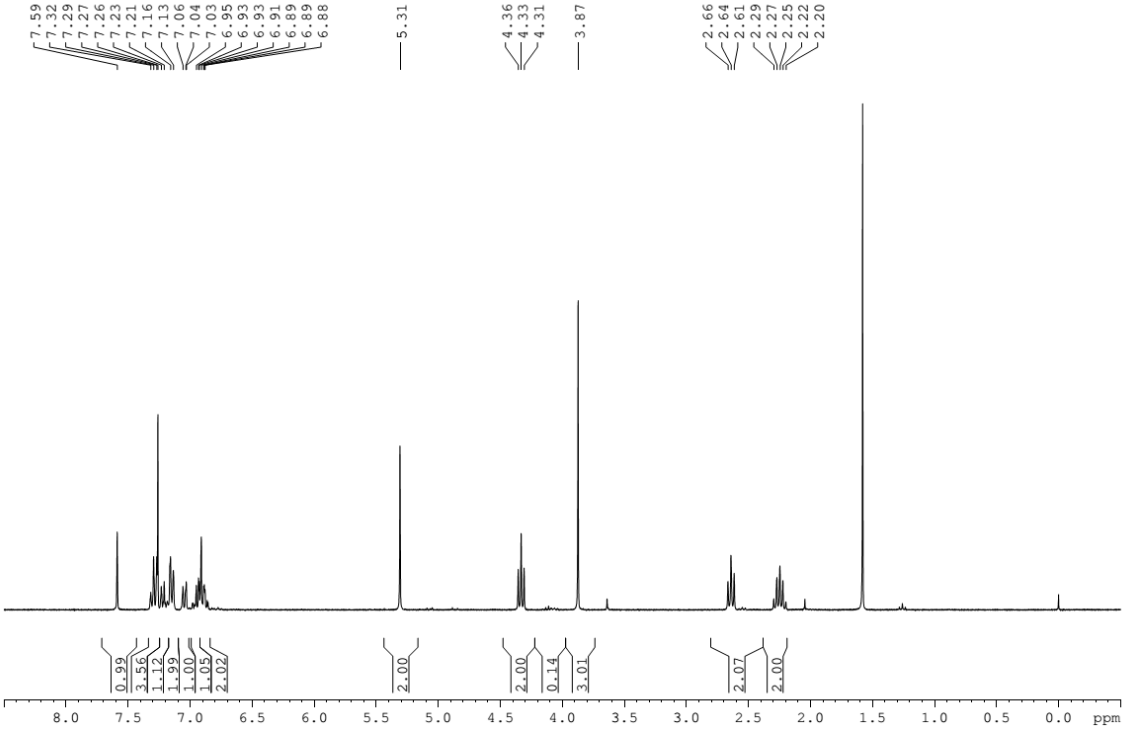


Compound 6b

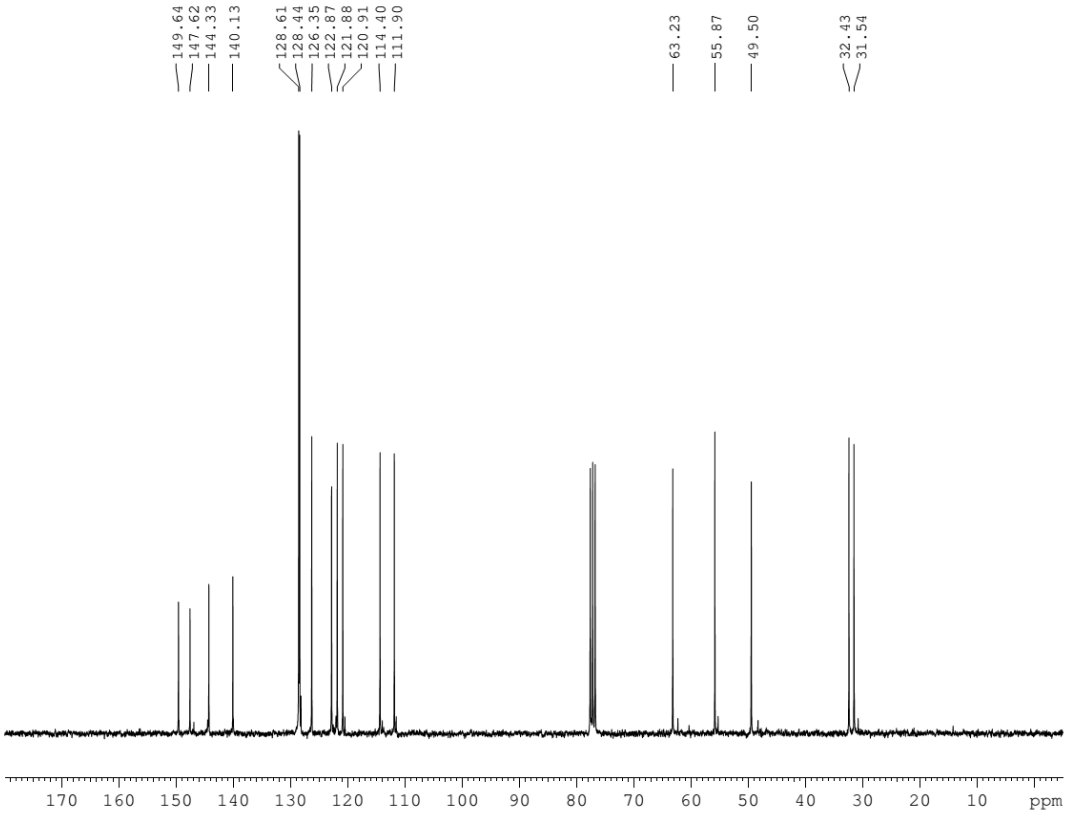


6b

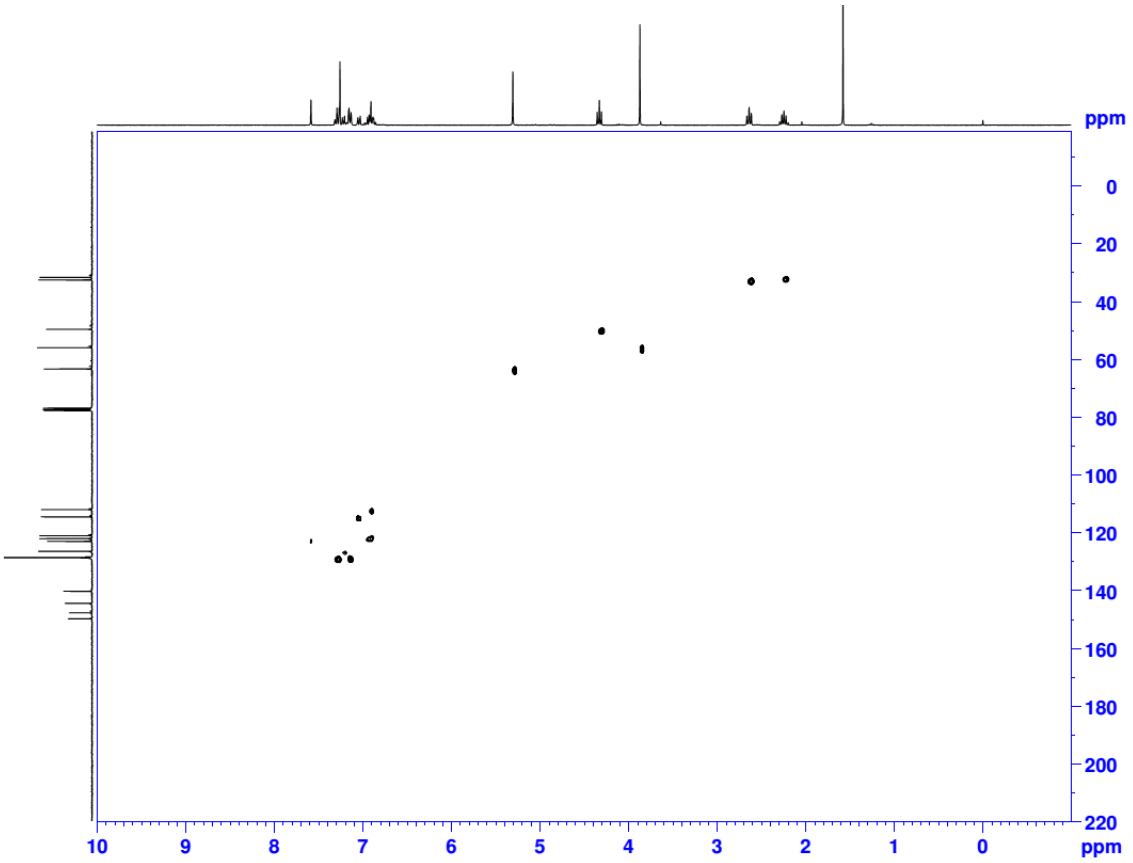
^{1}H NMR (300 MHz, $CDCl_3$)



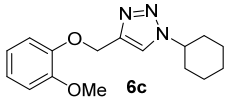
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

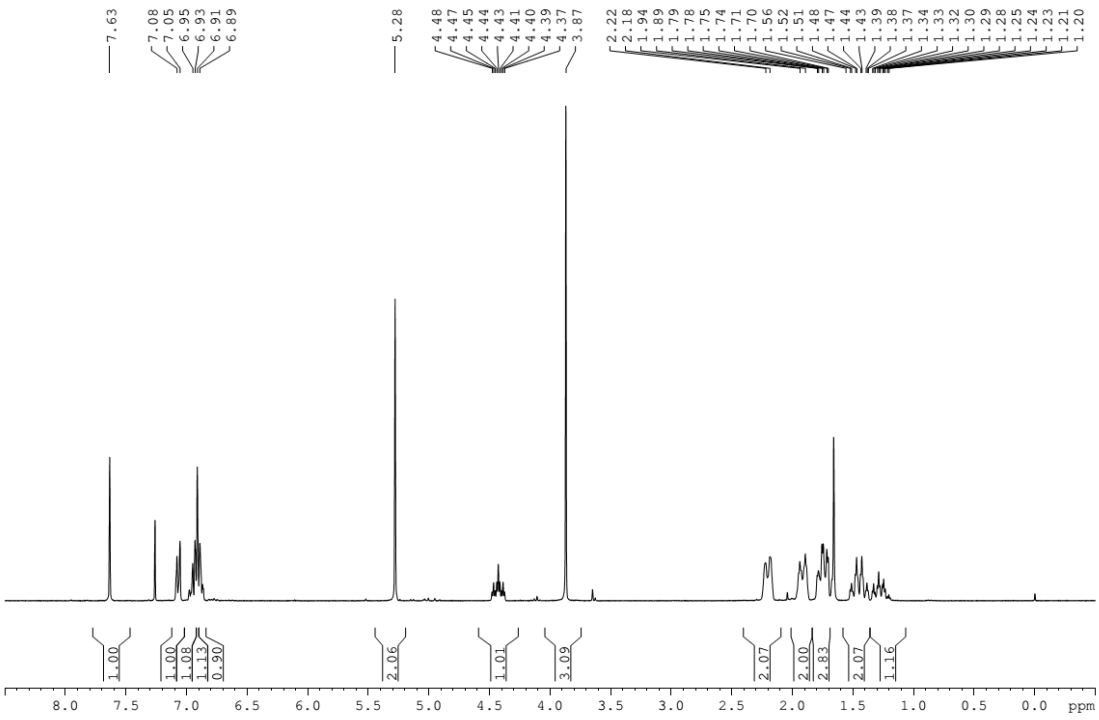


Compound 6c

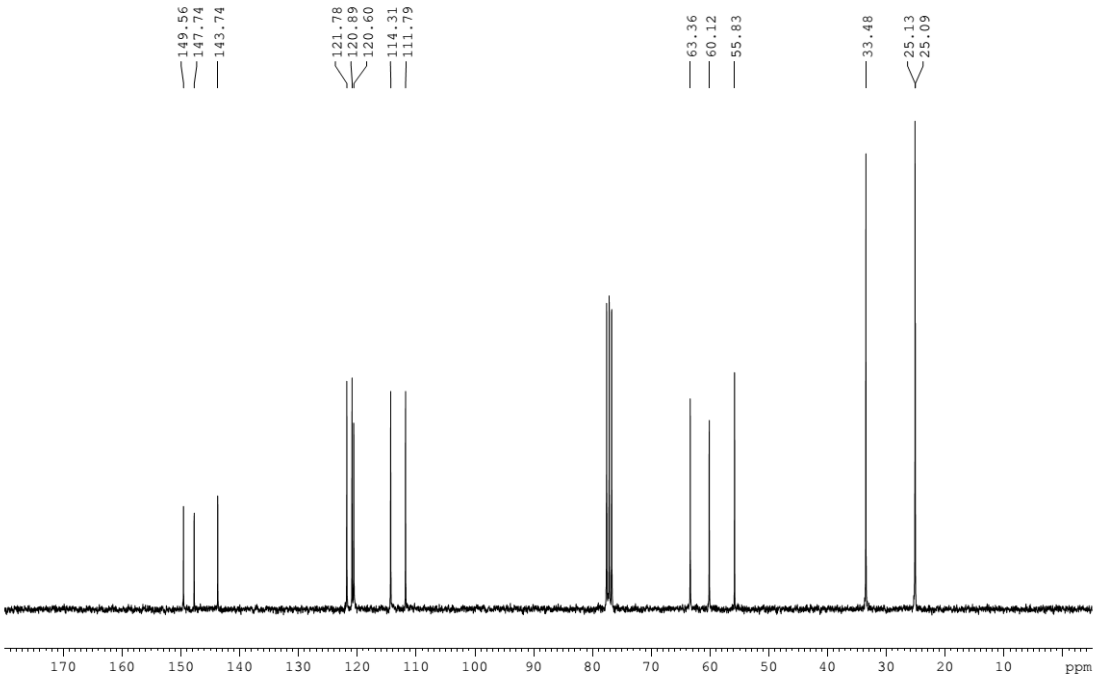


6c

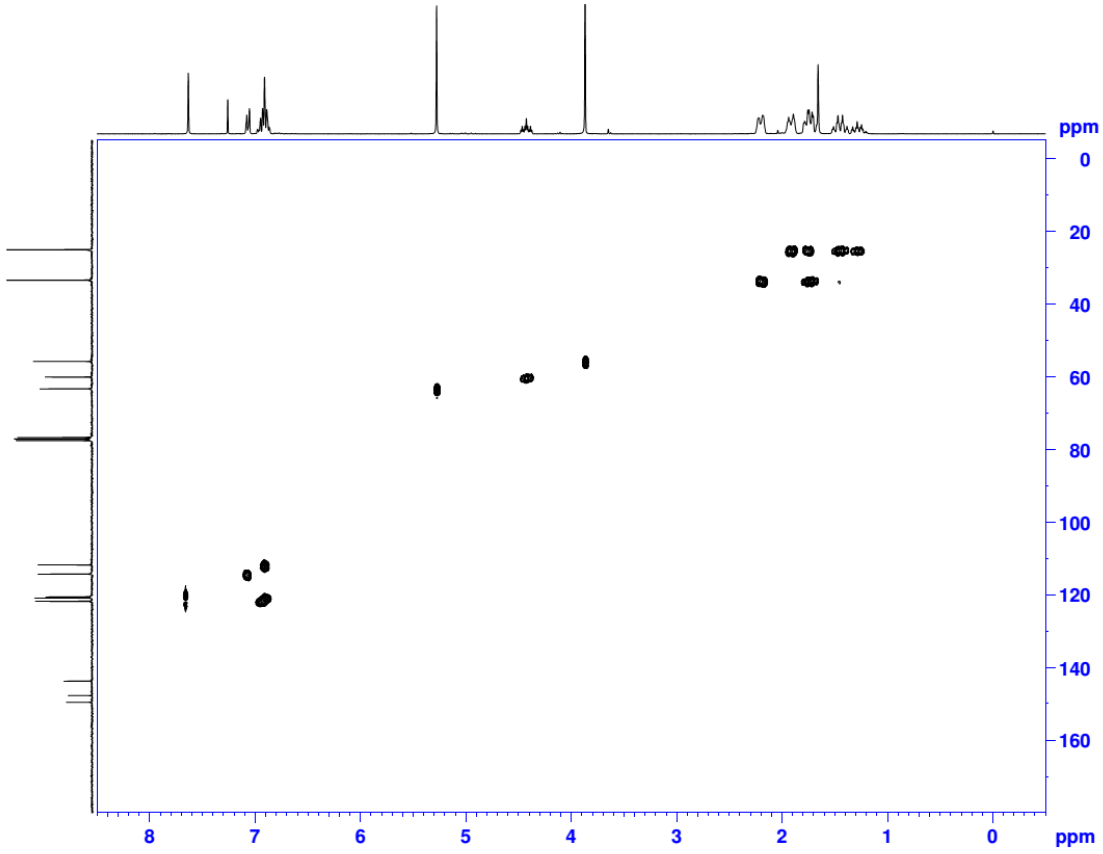
^{1}H NMR (300 MHz, $CDCl_3$)



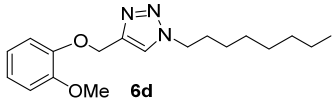
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

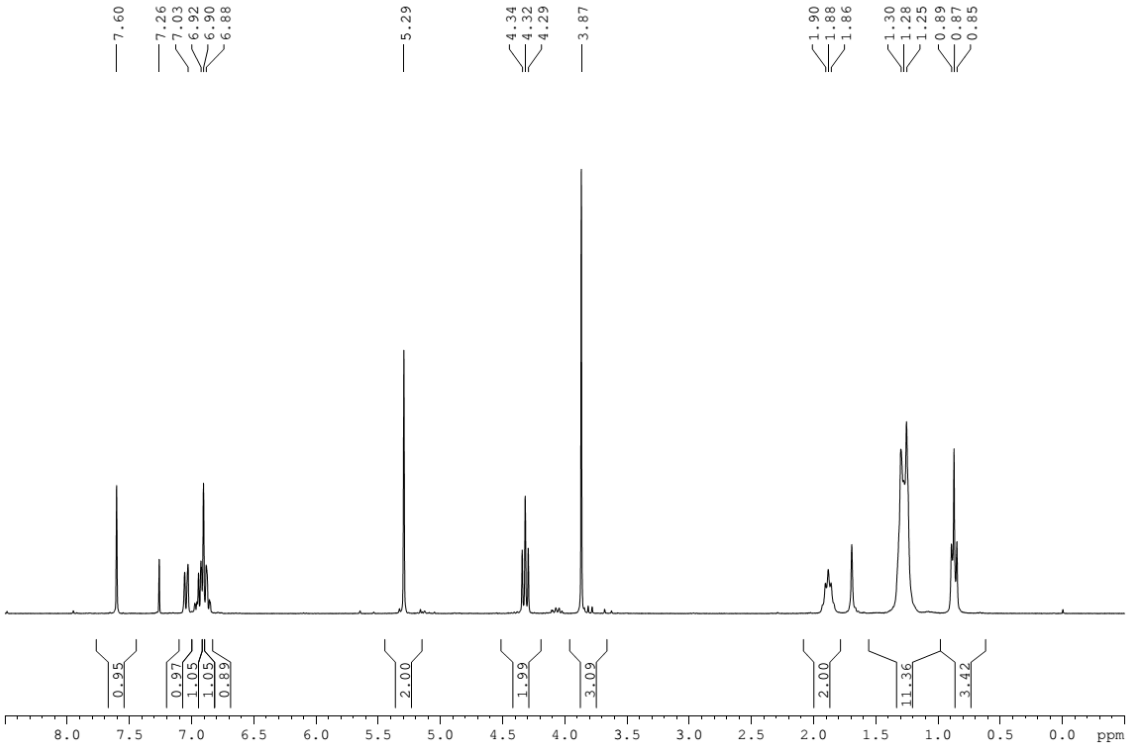


Compound 6d

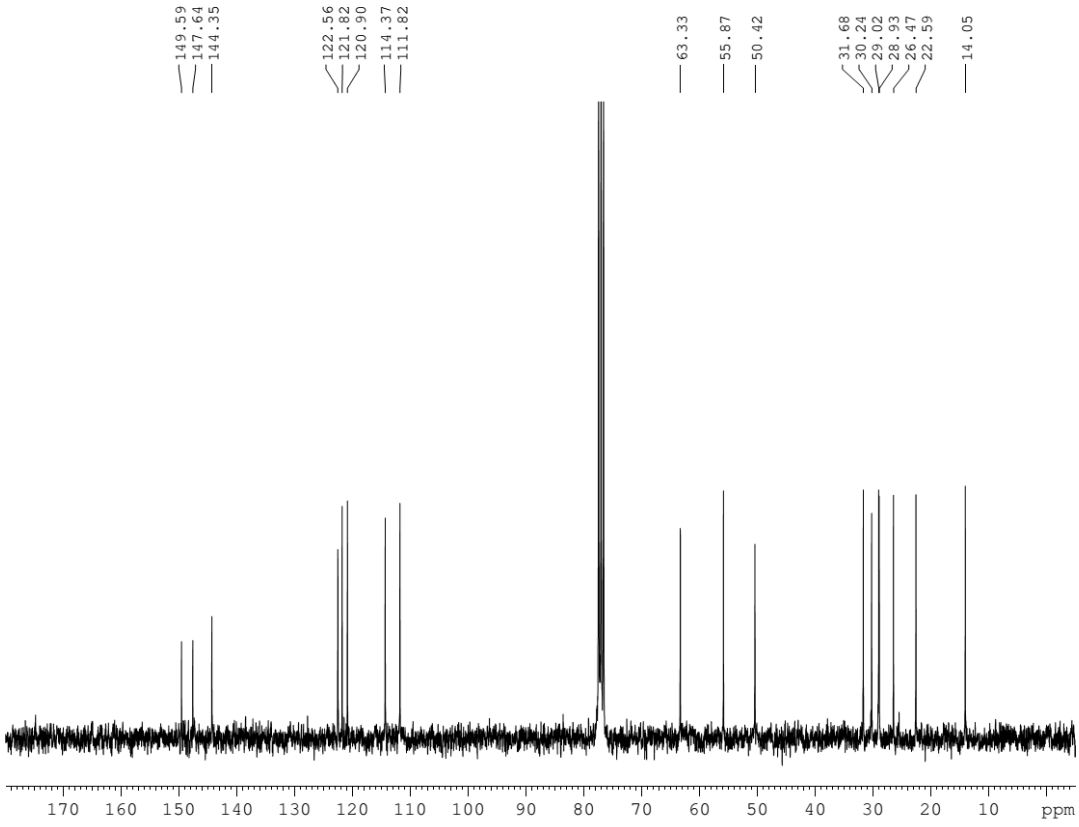


6d

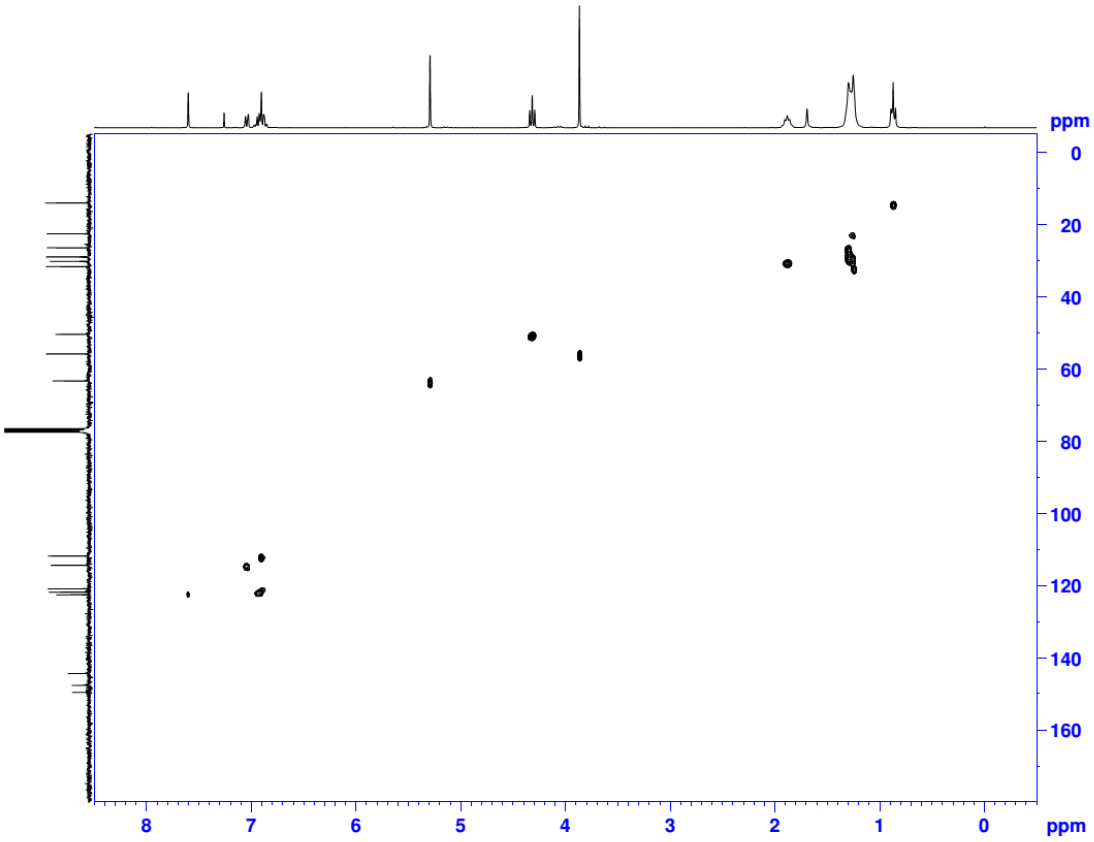
^{1}H NMR (300 MHz, $CDCl_3$)



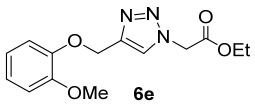
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

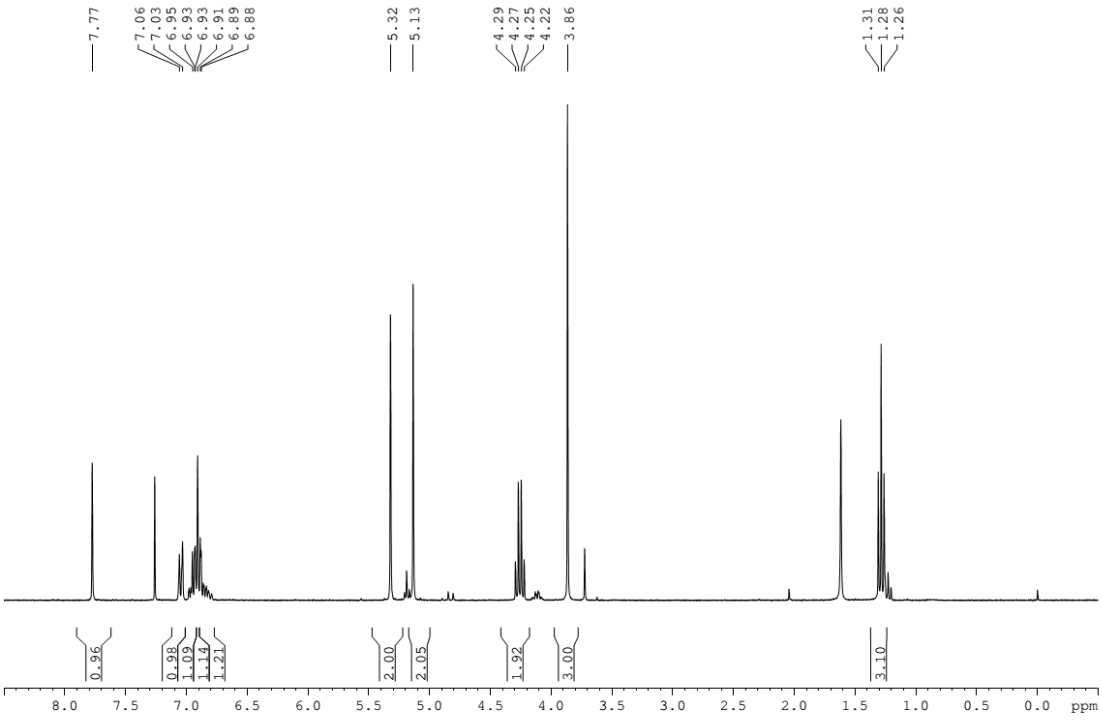


Compound 6e

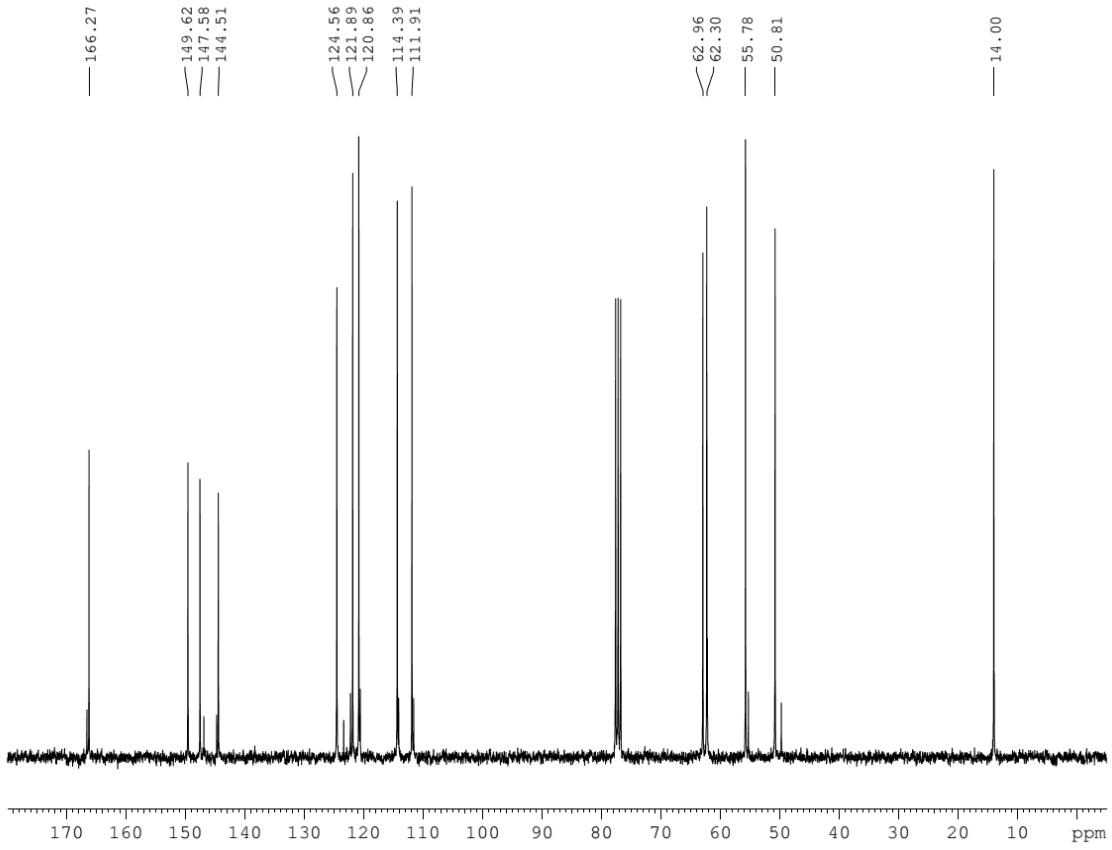


6e

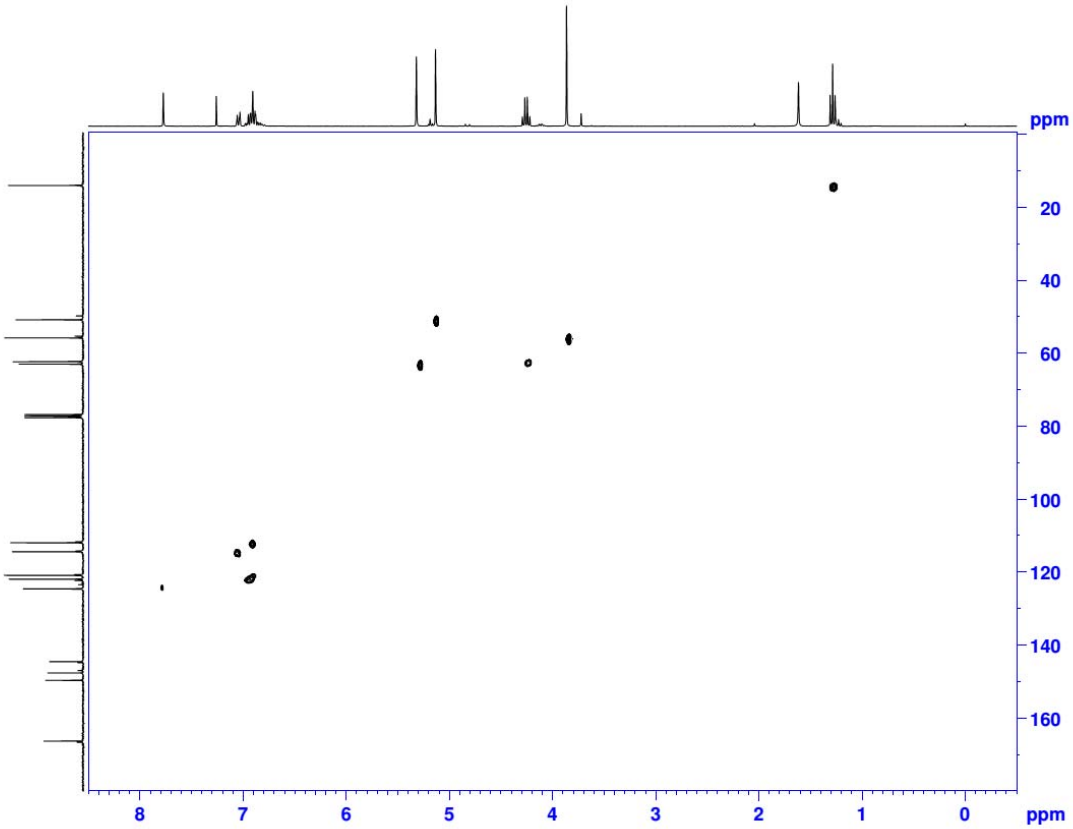
^{1}H NMR (300 MHz, $CDCl_3$)



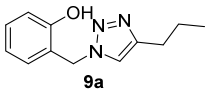
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

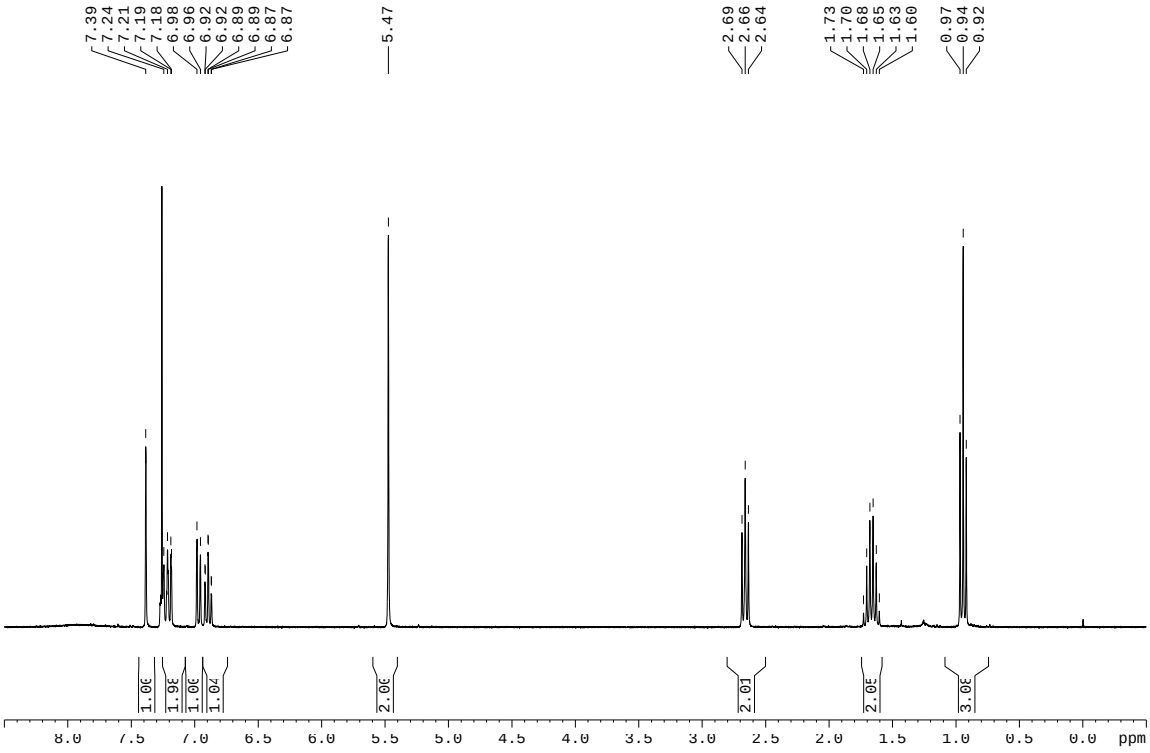


Compound 9a

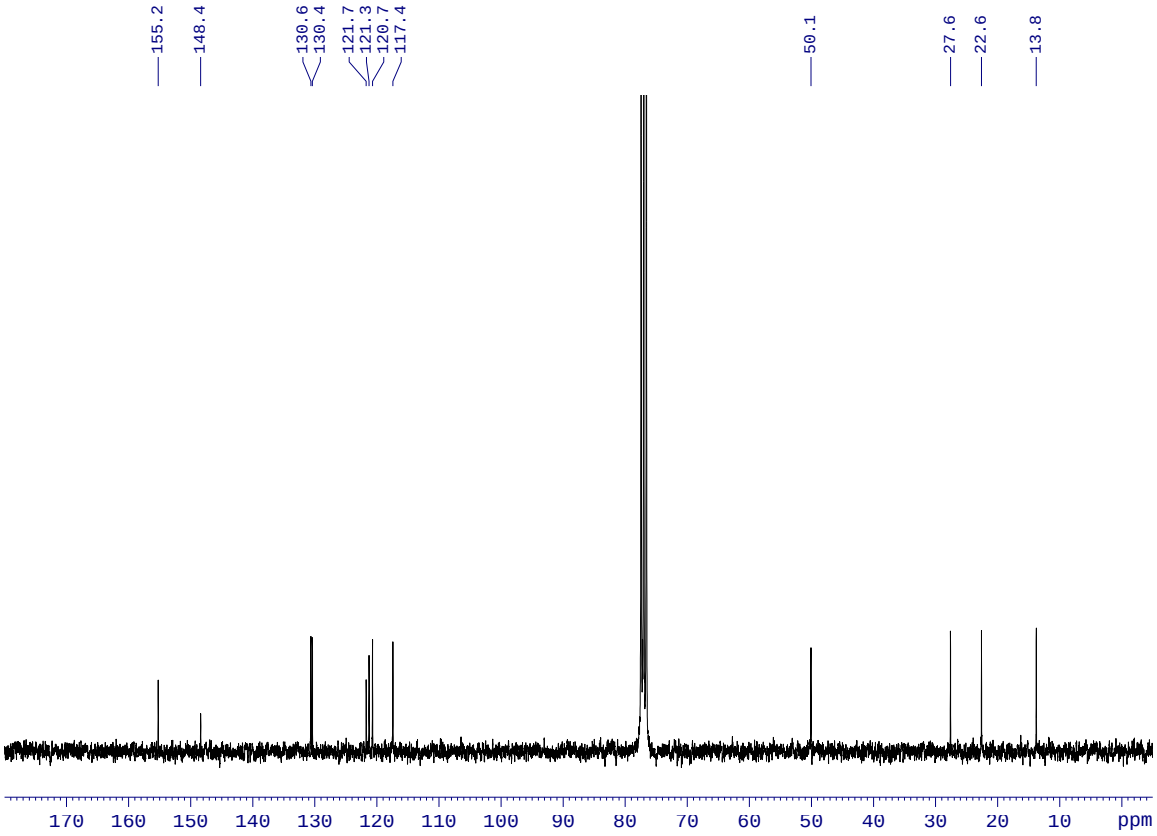


9a

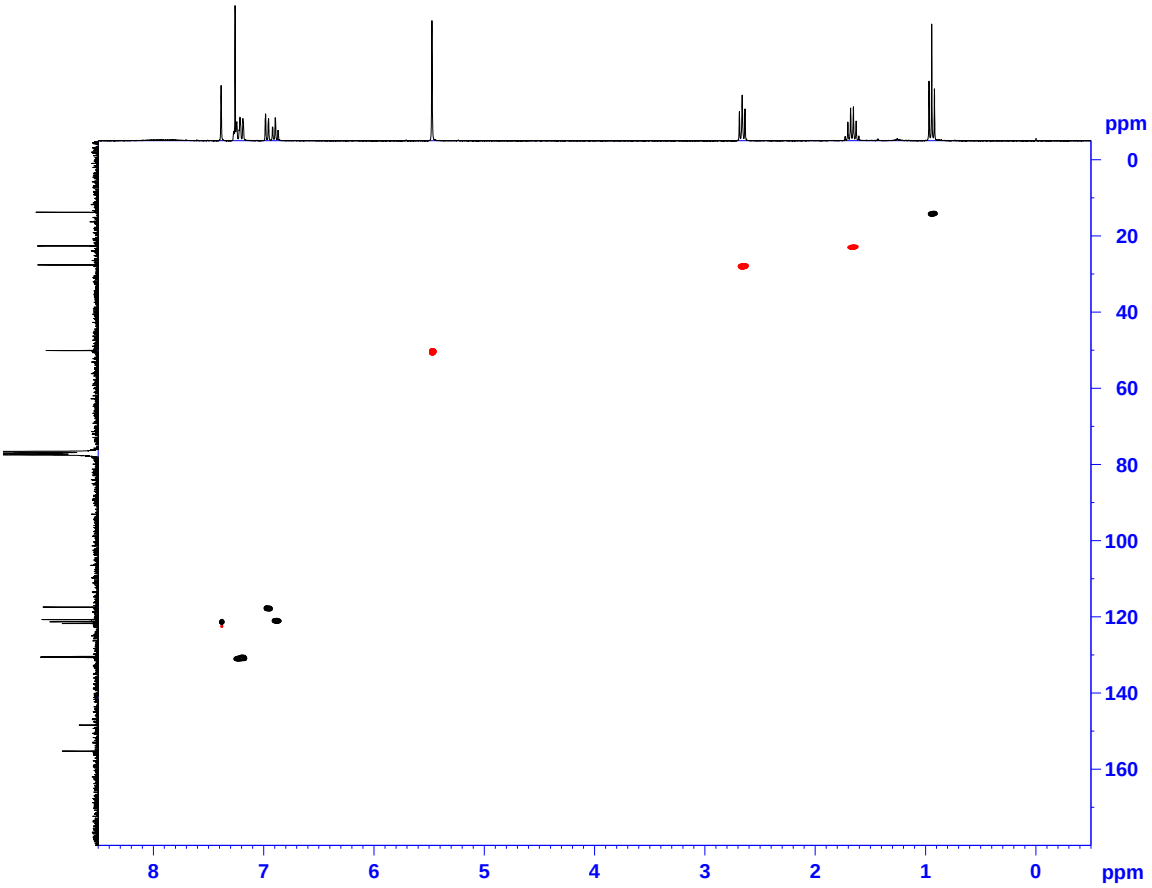
^{1}H NMR (300 MHz, $CDCl_3$)



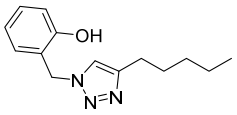
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

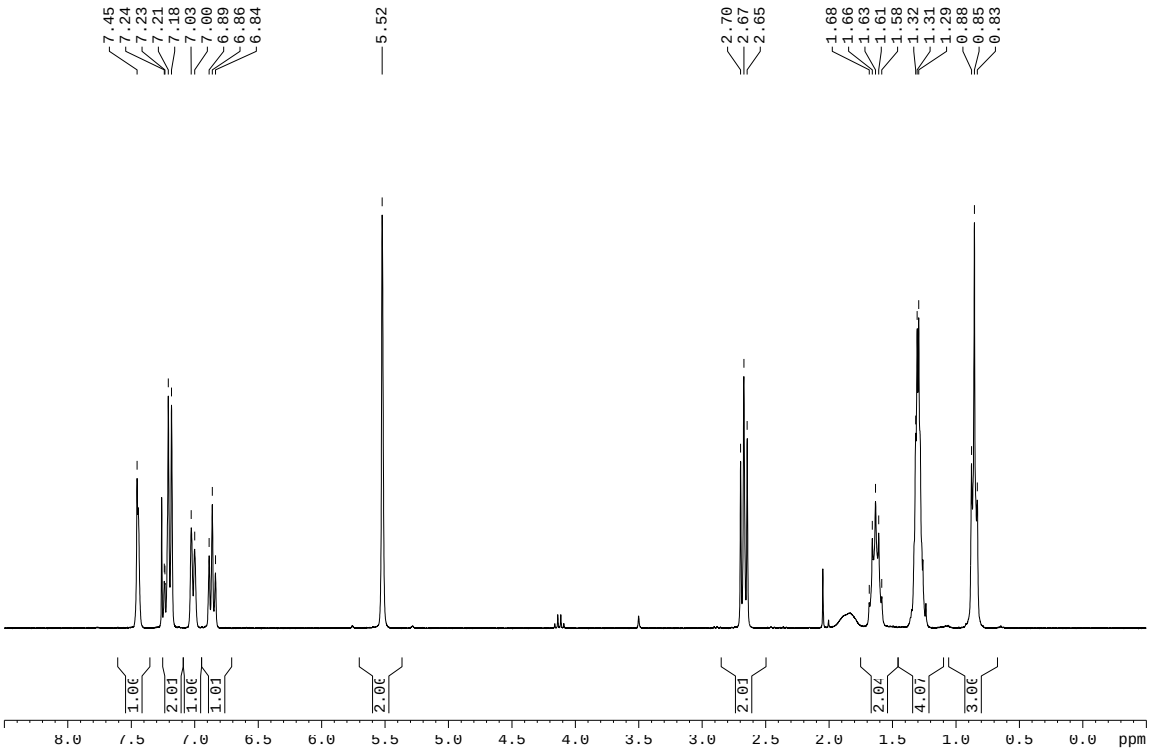


Compound 9b

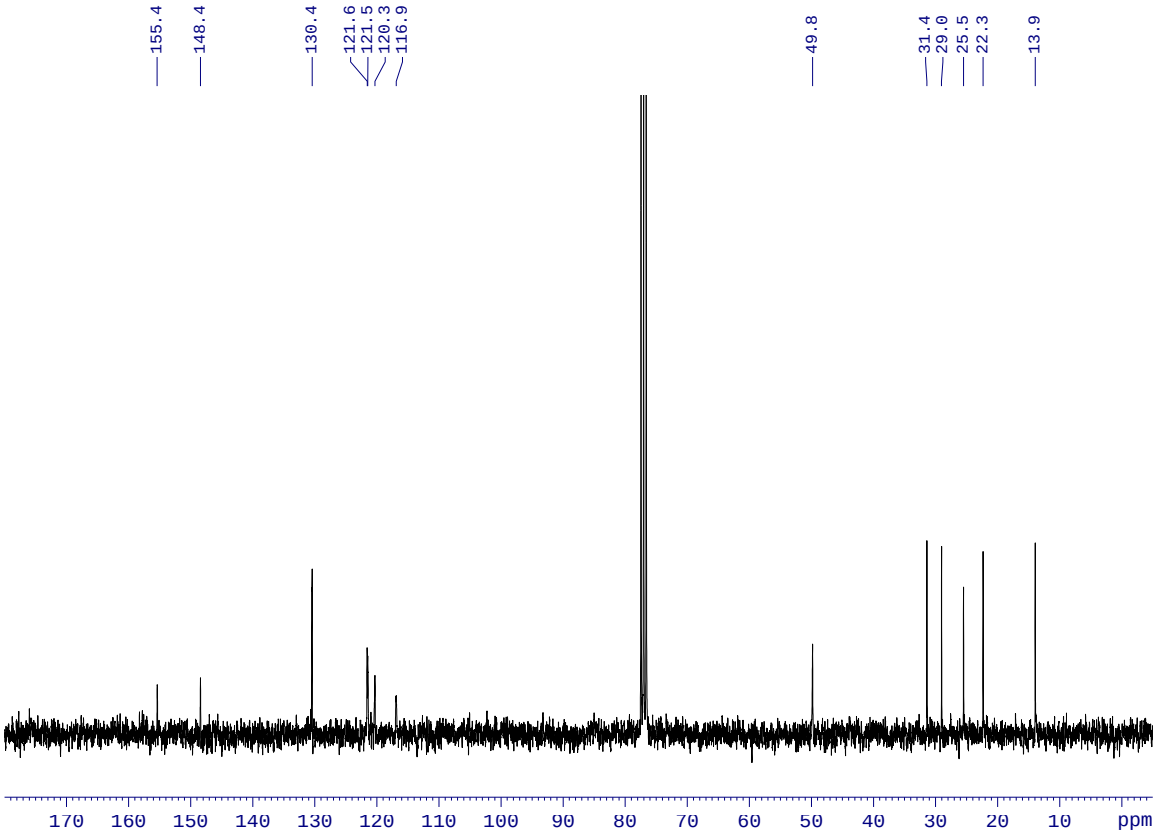


9b

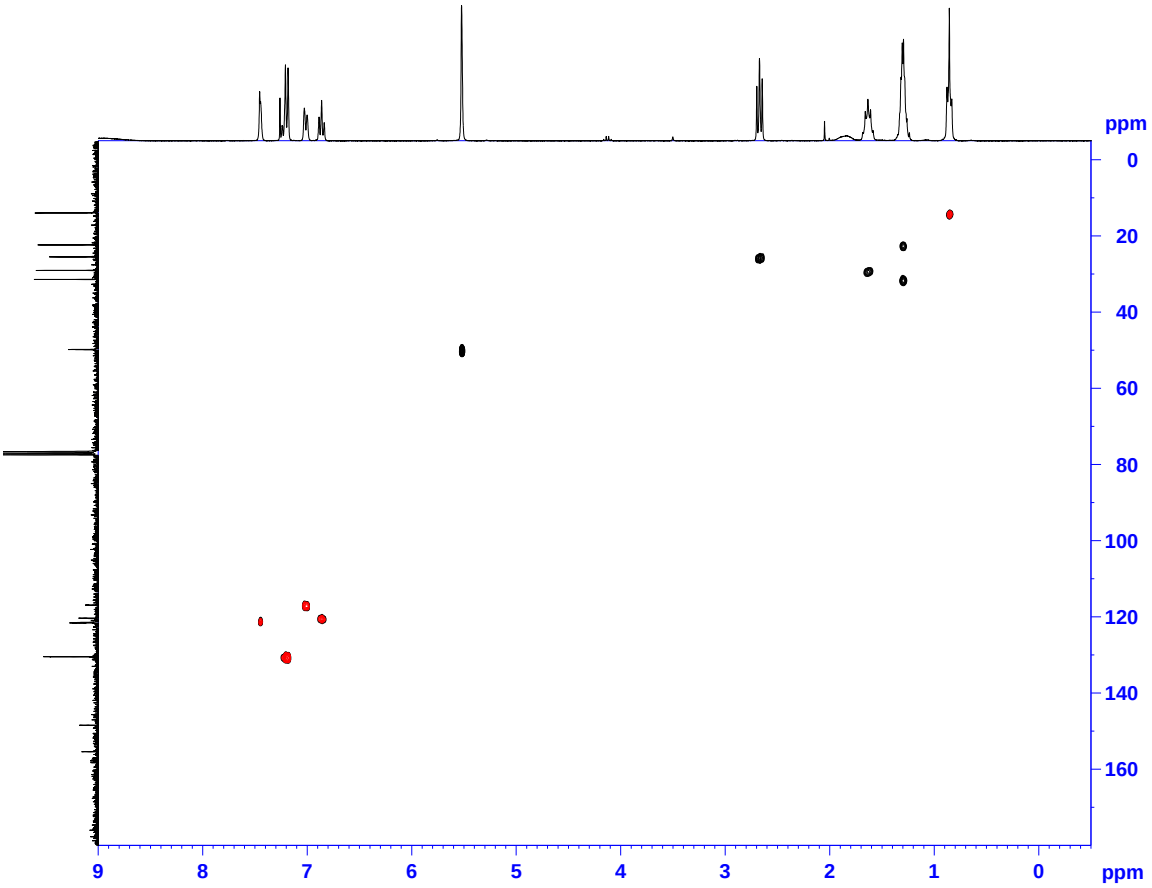
^{1}H NMR (300 MHz, $CDCl_3$)



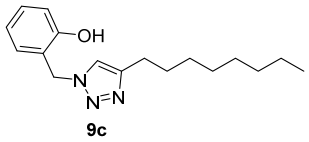
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

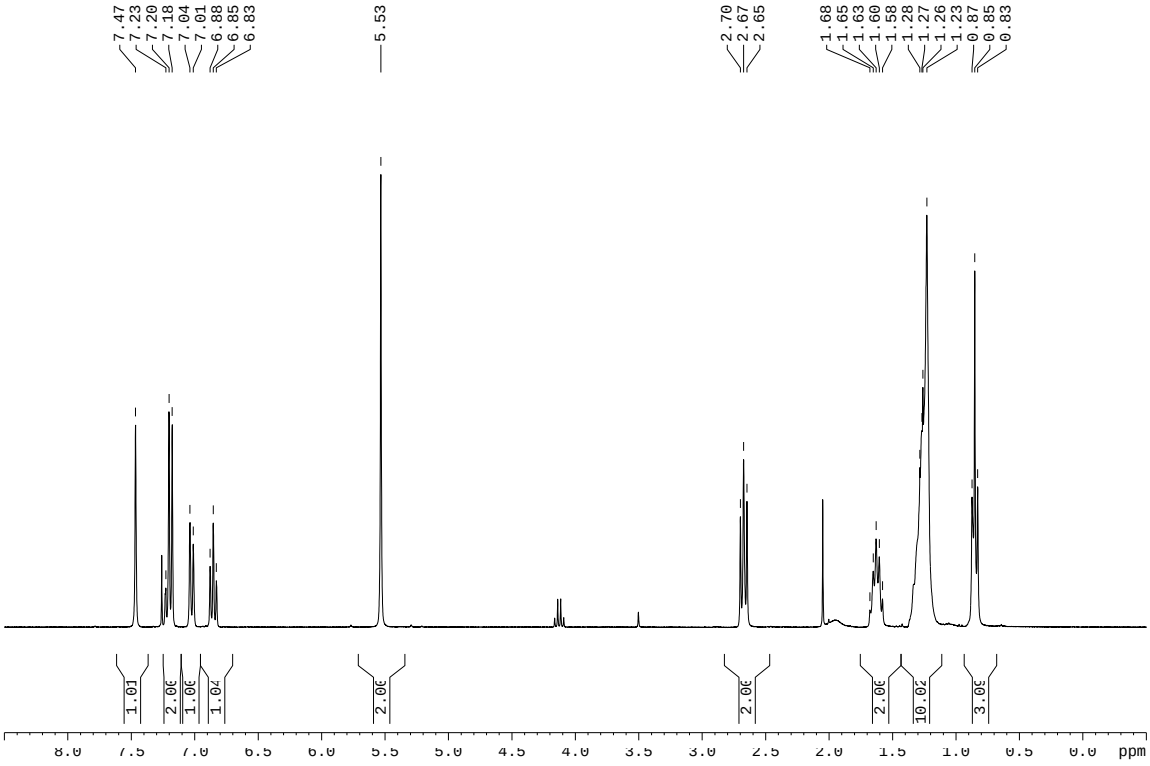


Compound 9c

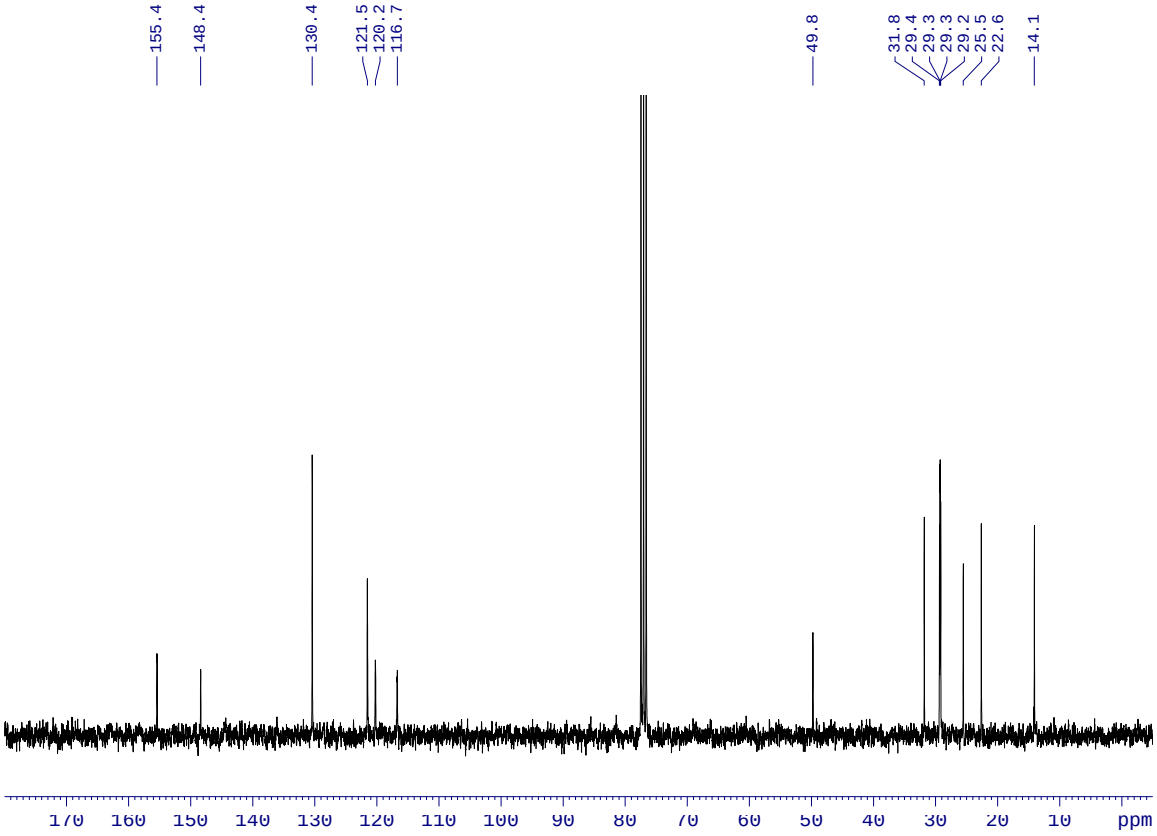


9c

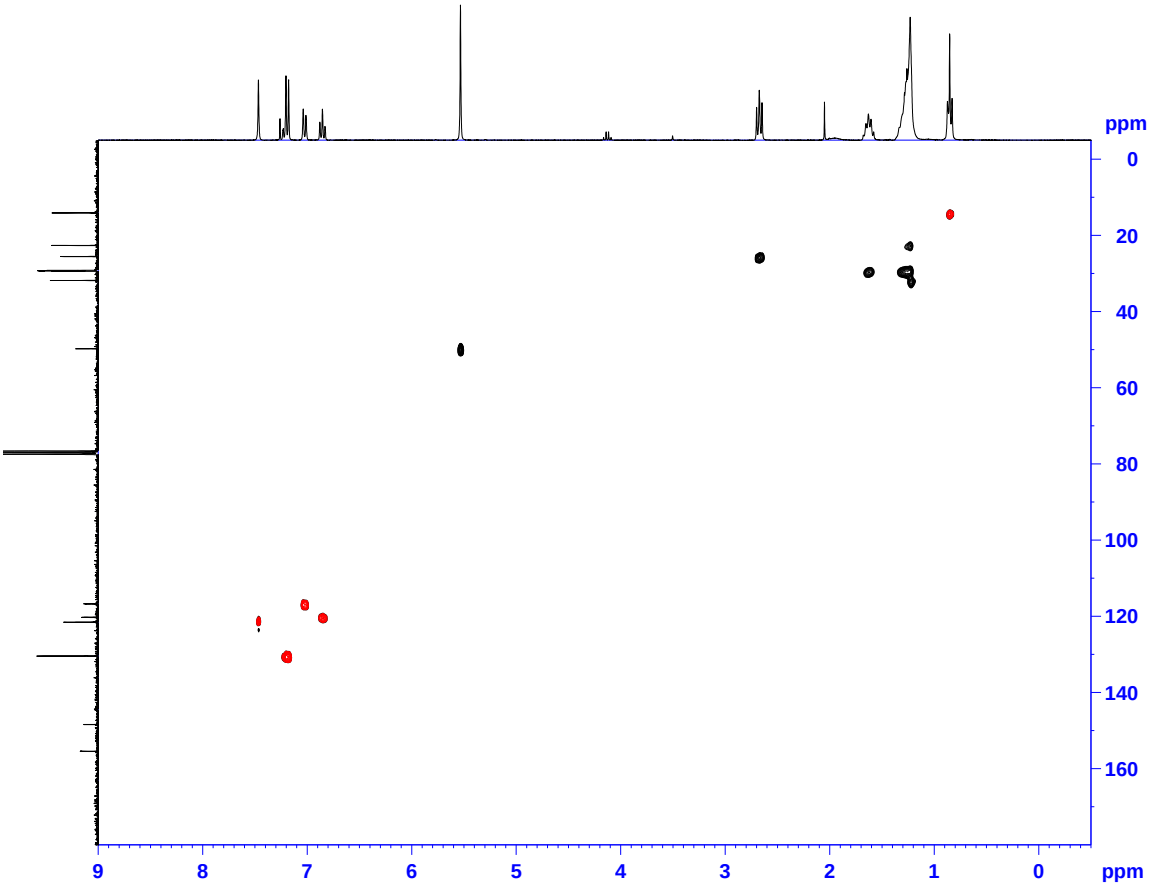
^{1}H NMR (300 MHz, $CDCl_3$)



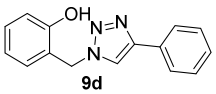
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

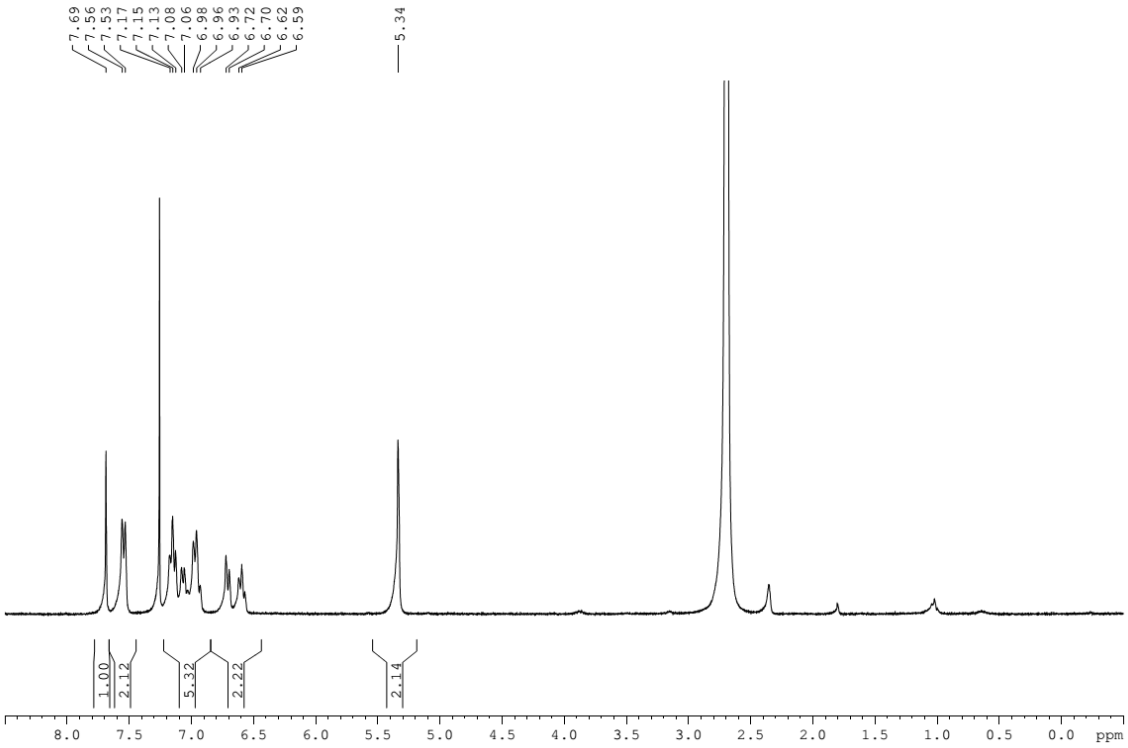


Compound 9d

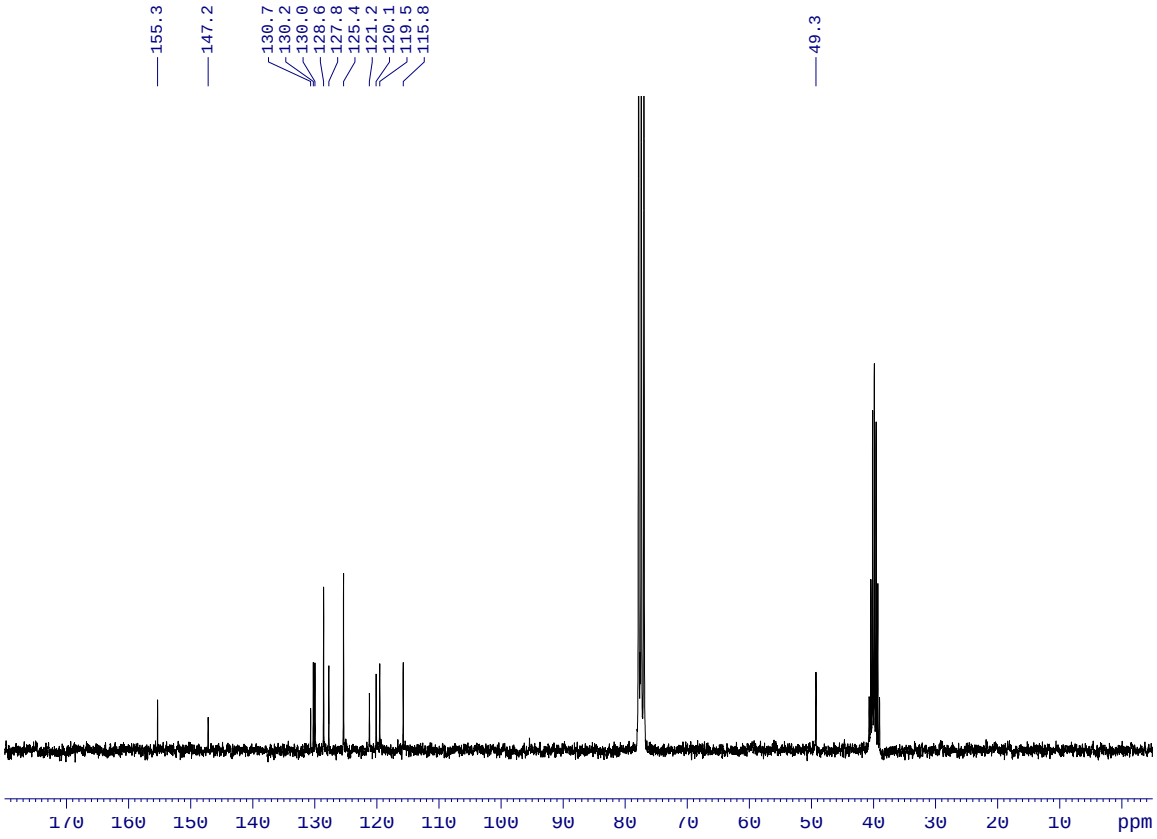


9d

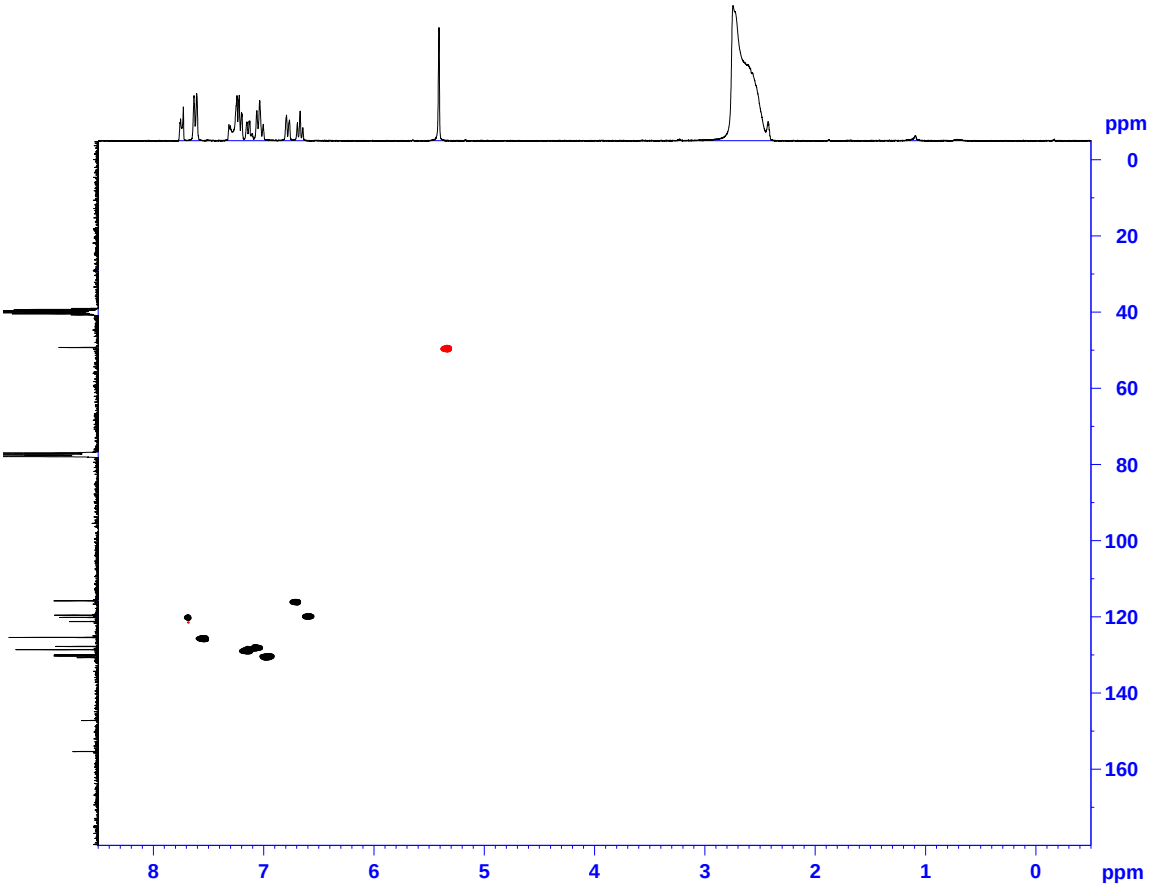
^{1}H NMR (300 MHz, $CDCl_3$)



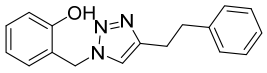
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

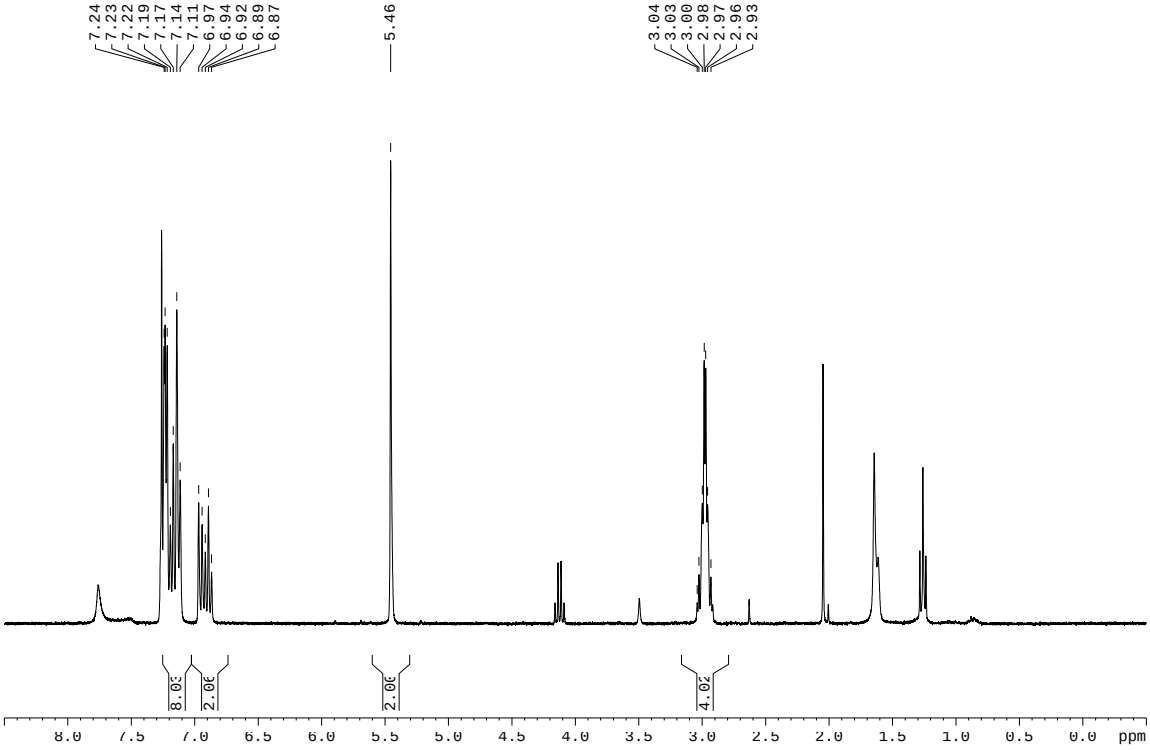


Compound 9e

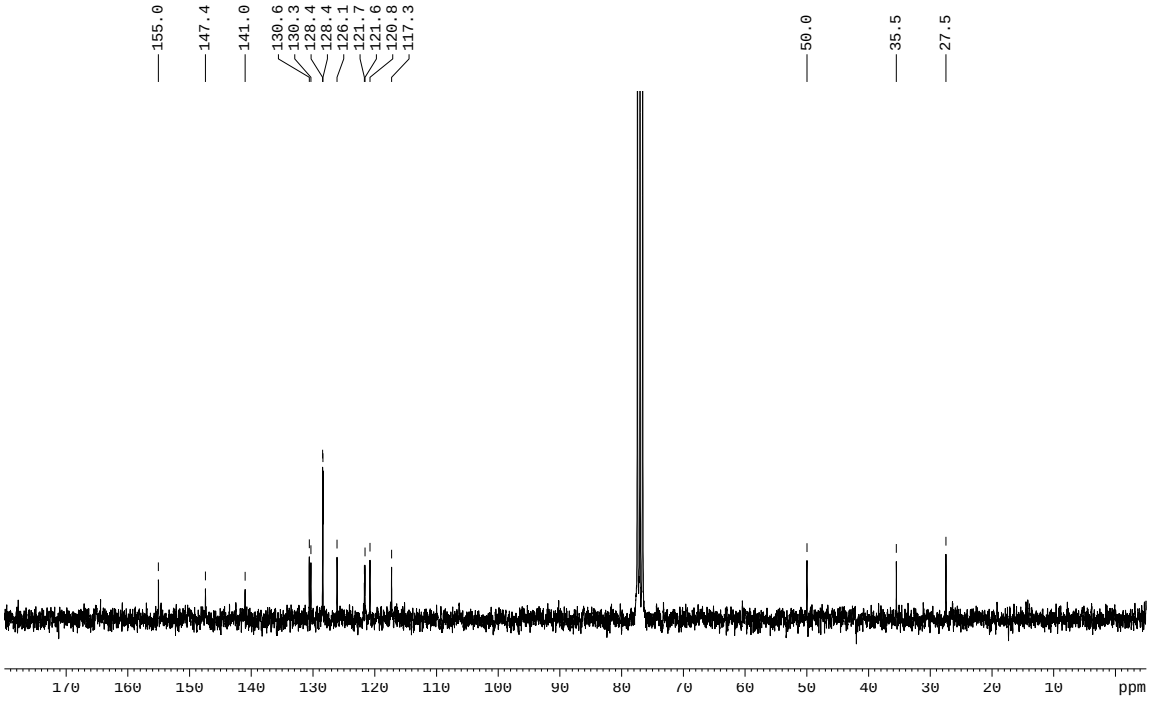


9e

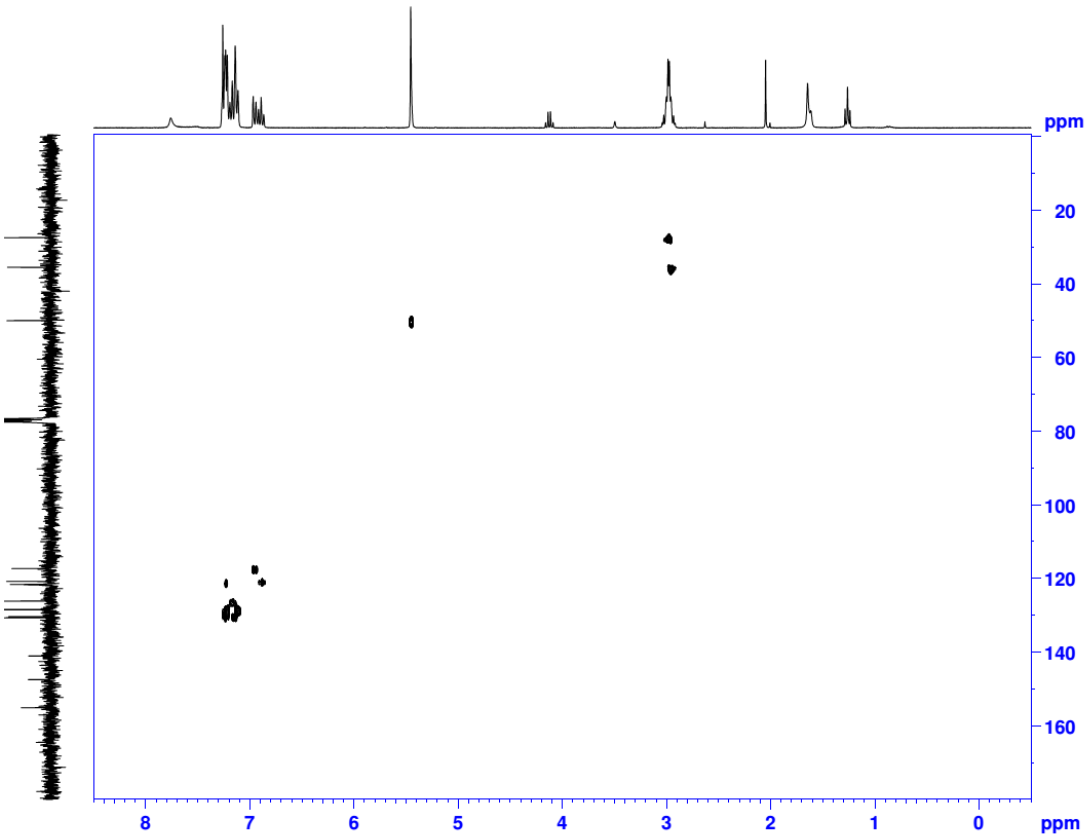
^{1}H NMR (300 MHz, $CDCl_3$)



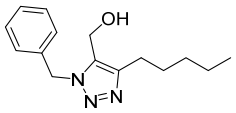
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

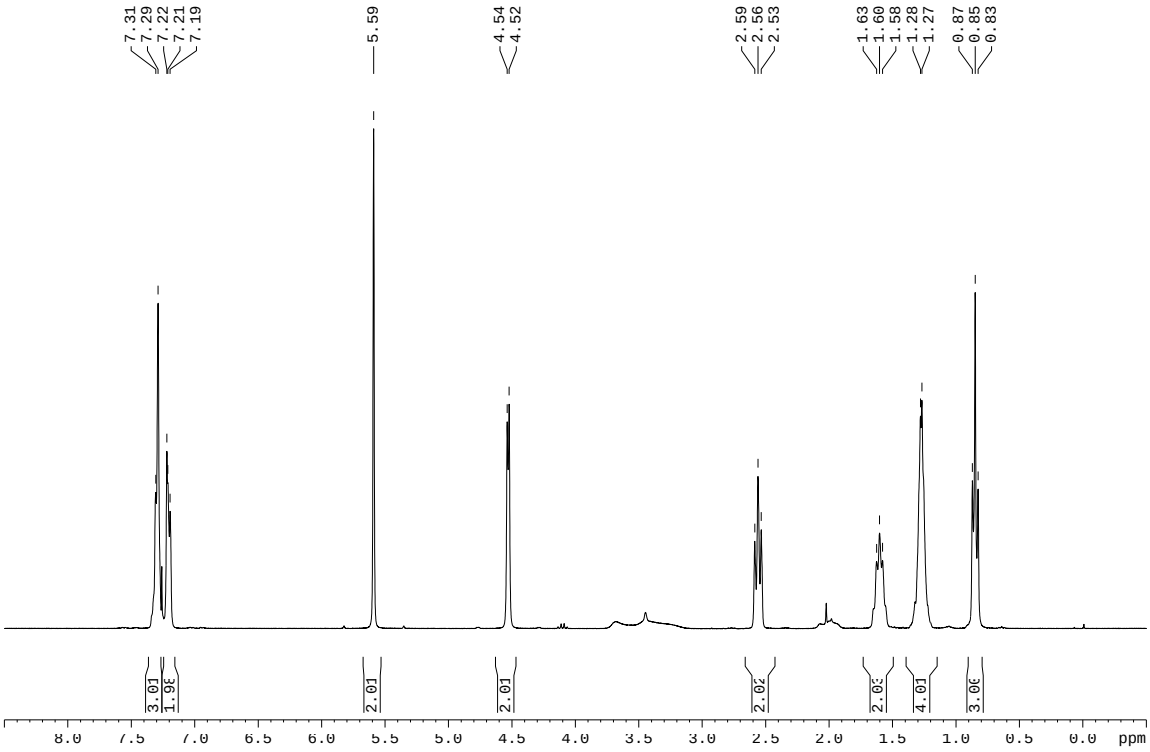


Compound 11a

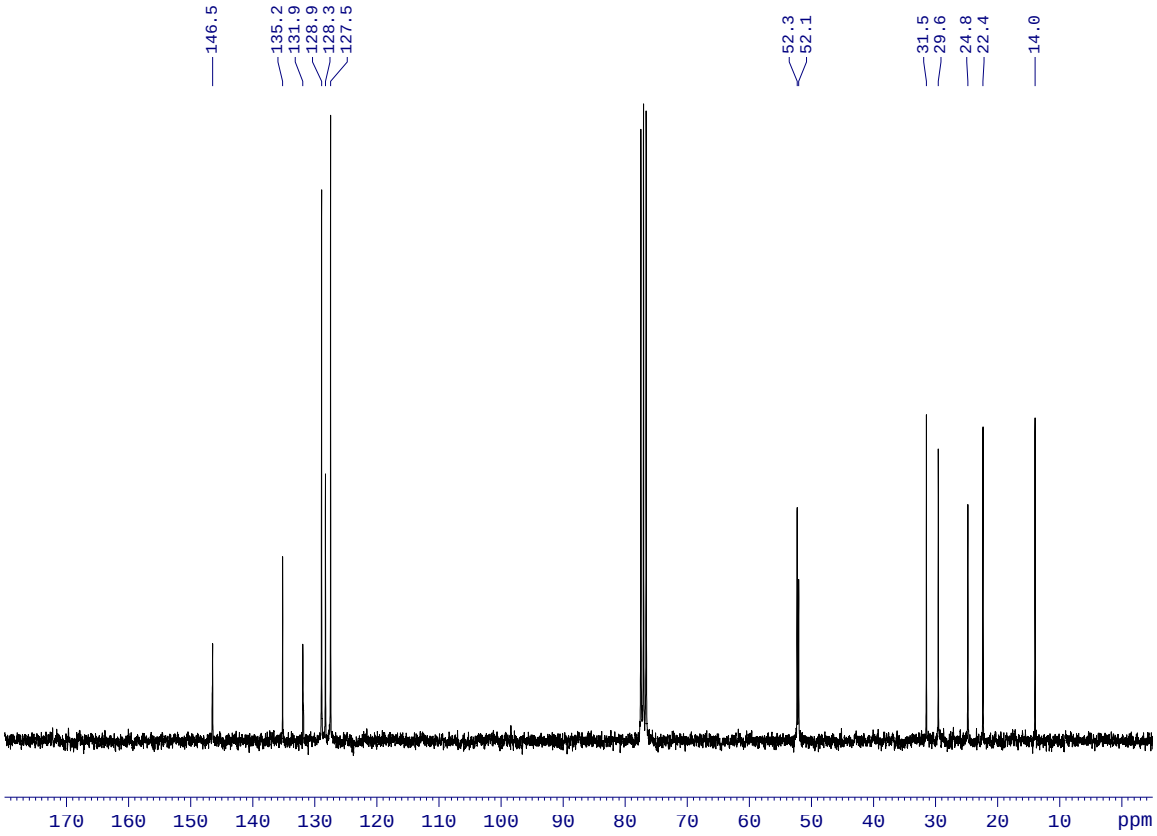


11a

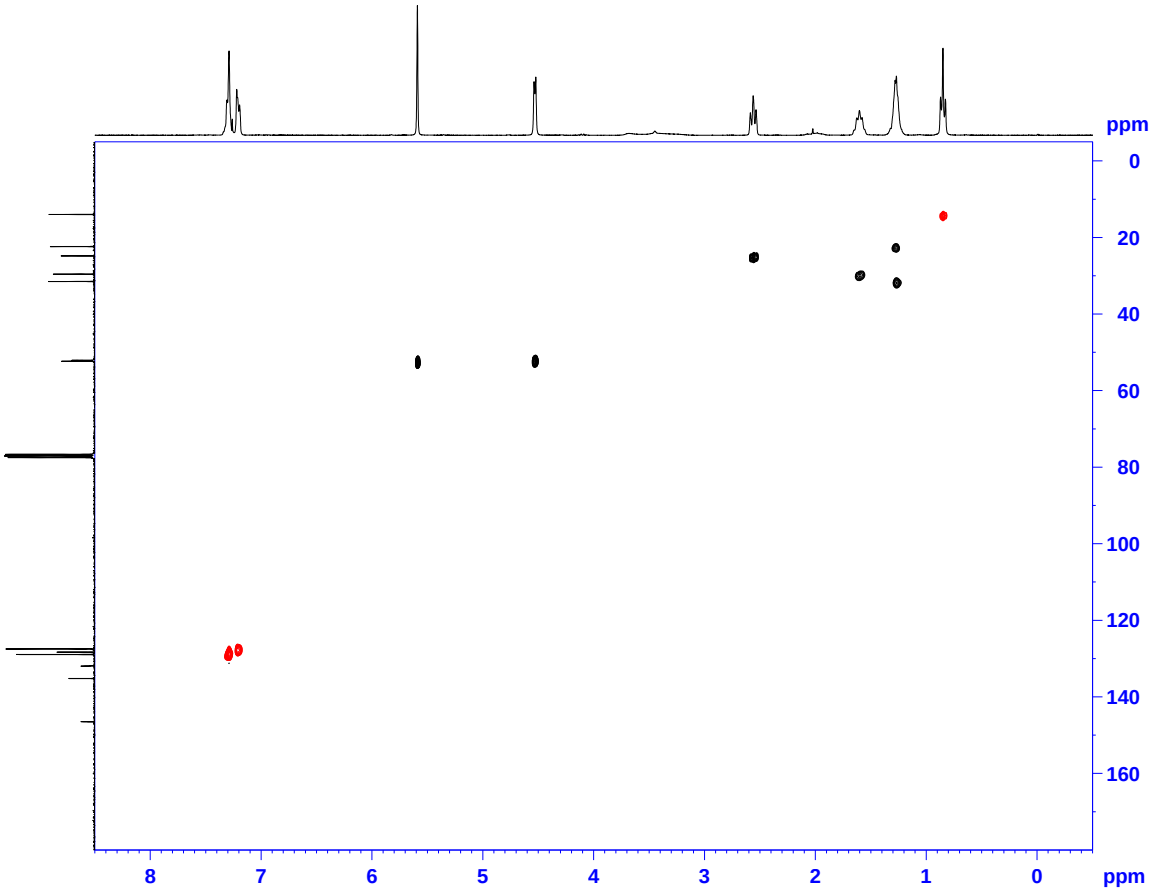
^{1}H NMR (300 MHz, $CDCl_3$)



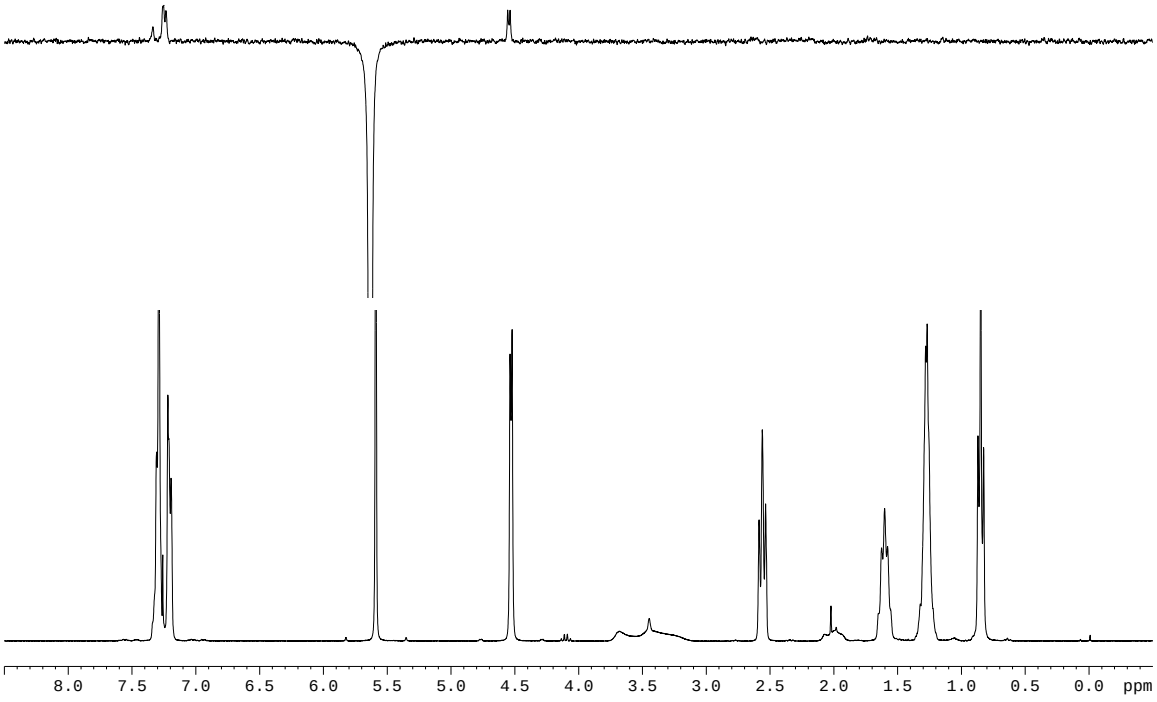
^{13}C NMR (75 MHz, $CDCl_3$)



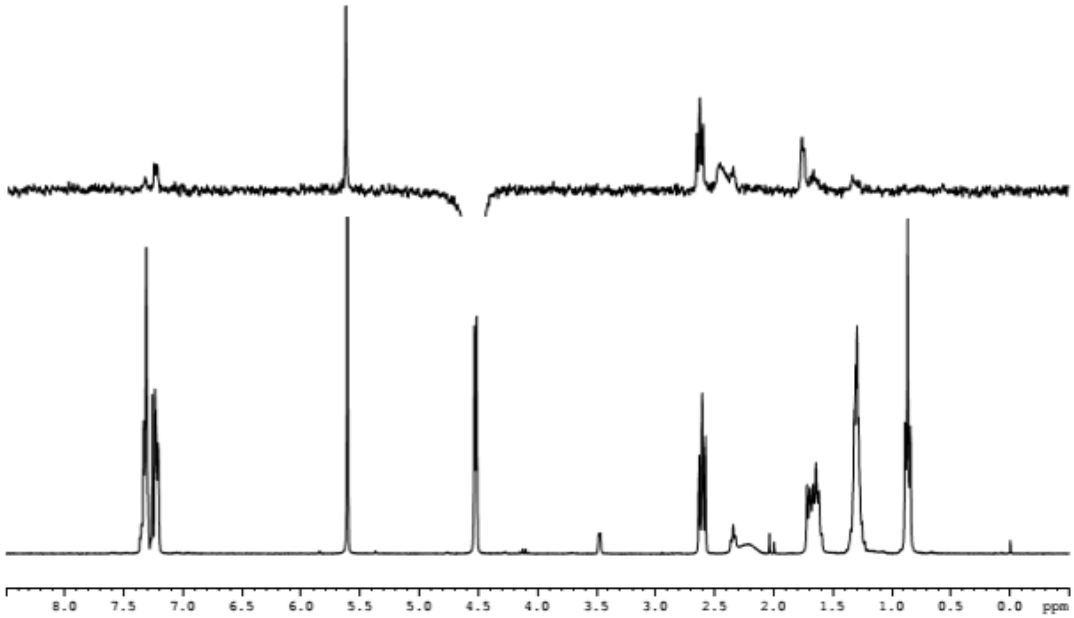
HSQC



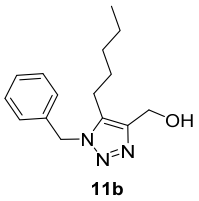
NOE


8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

NOE

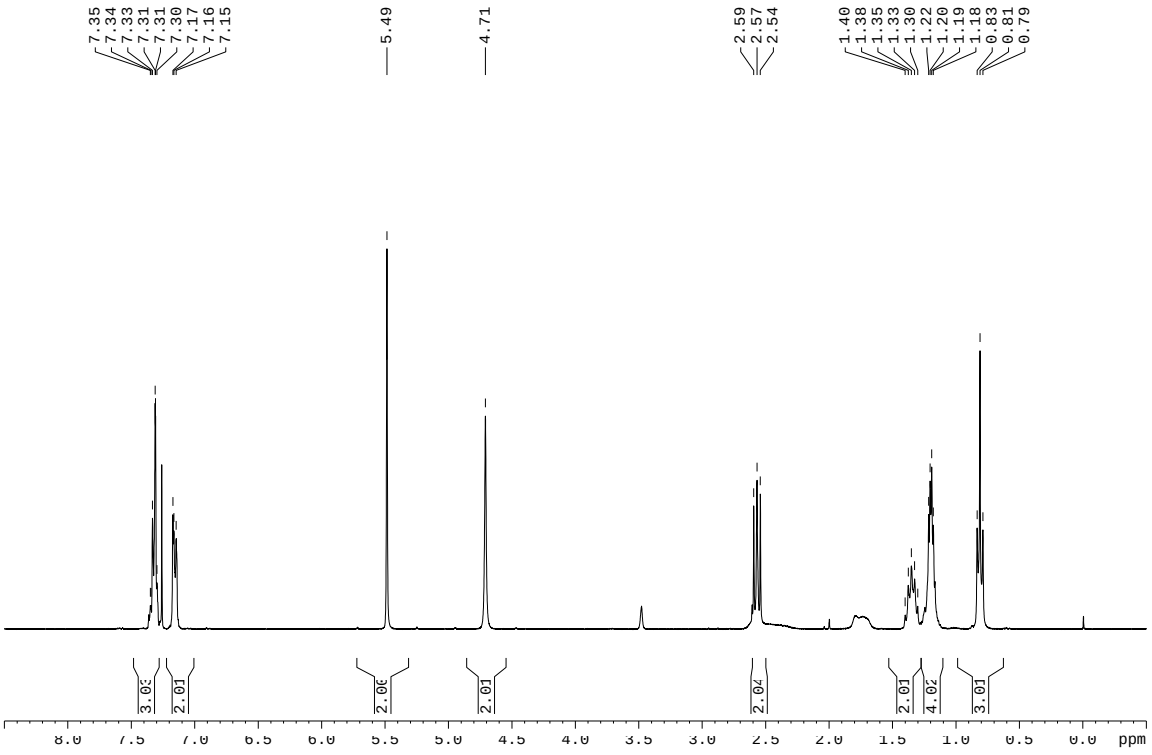

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

Compound 11b

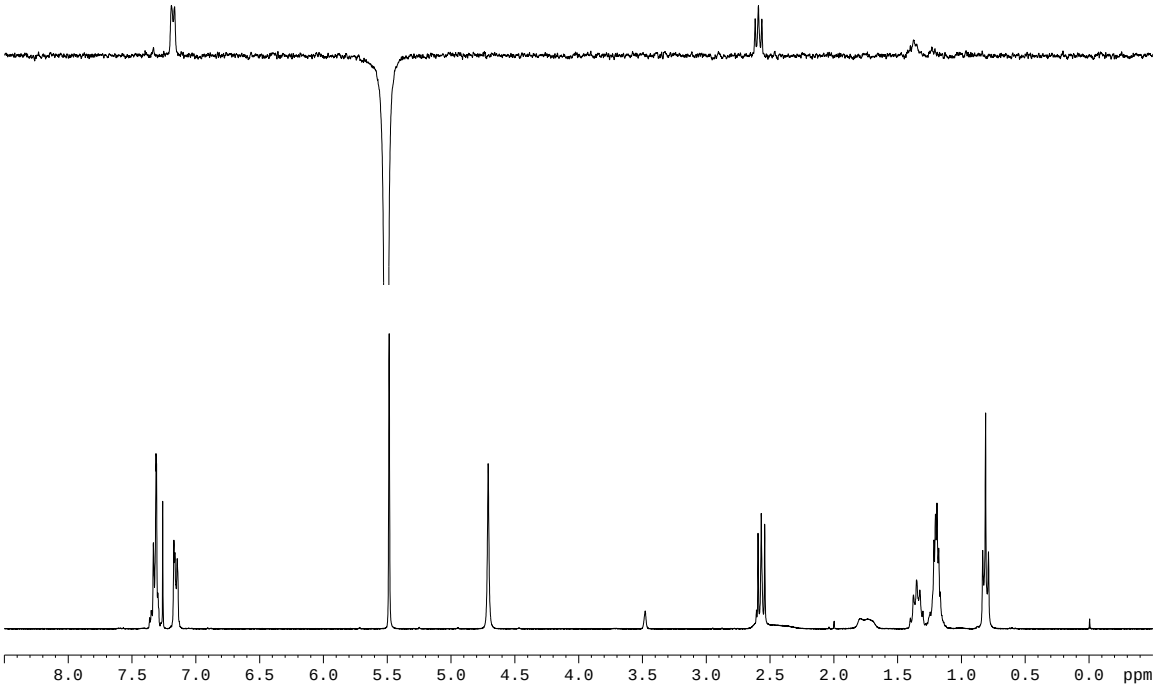


11b

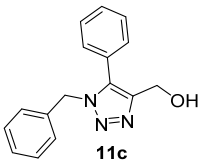
^{1}H NMR (300 MHz, $CDCl_3$)



NOE

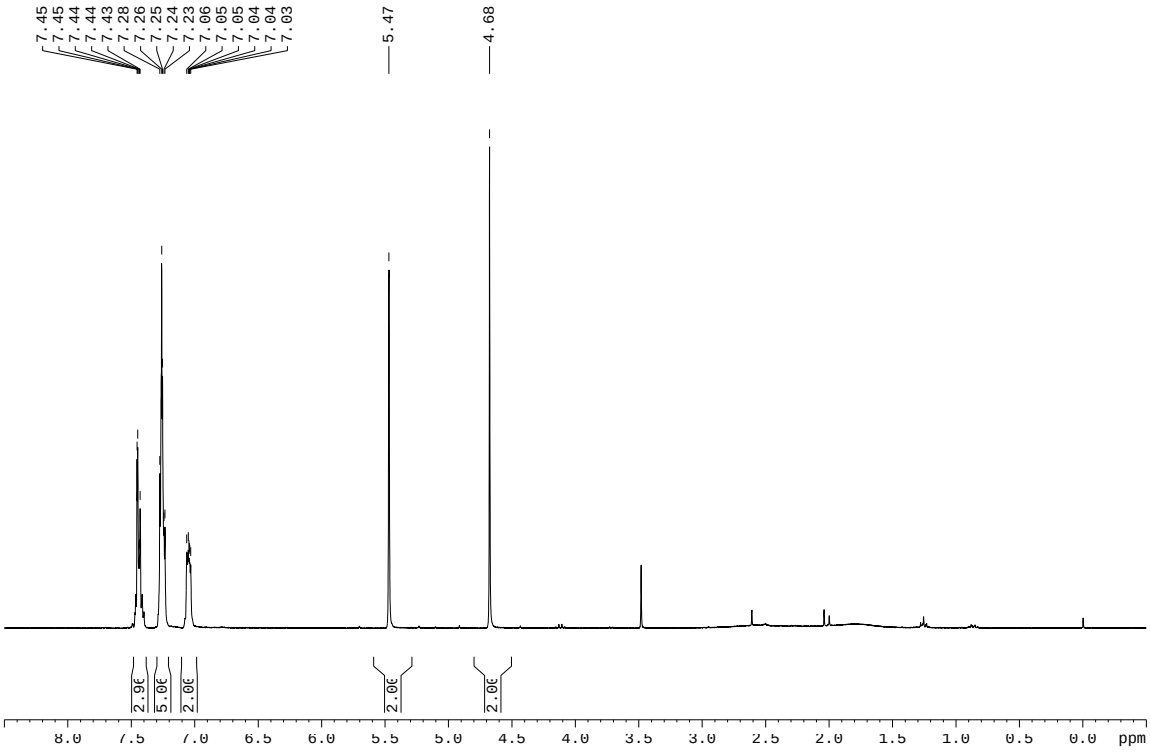


Compound 11c

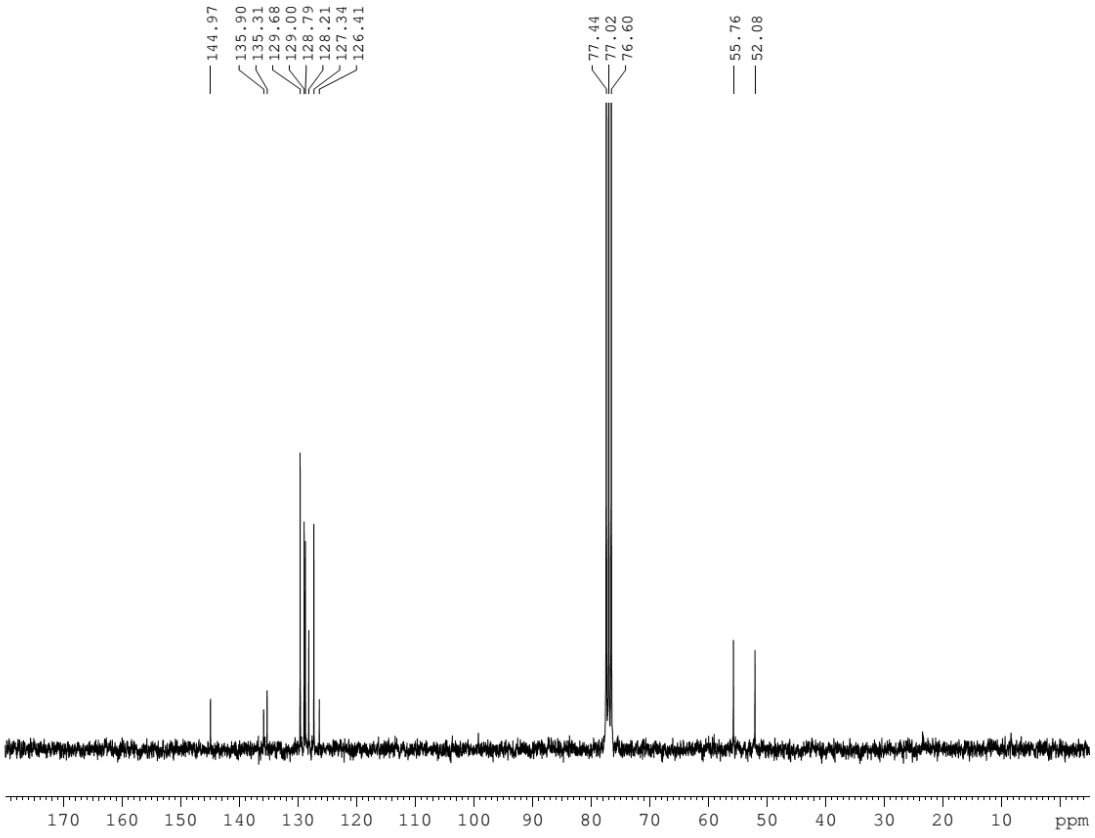


11c

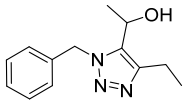
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)

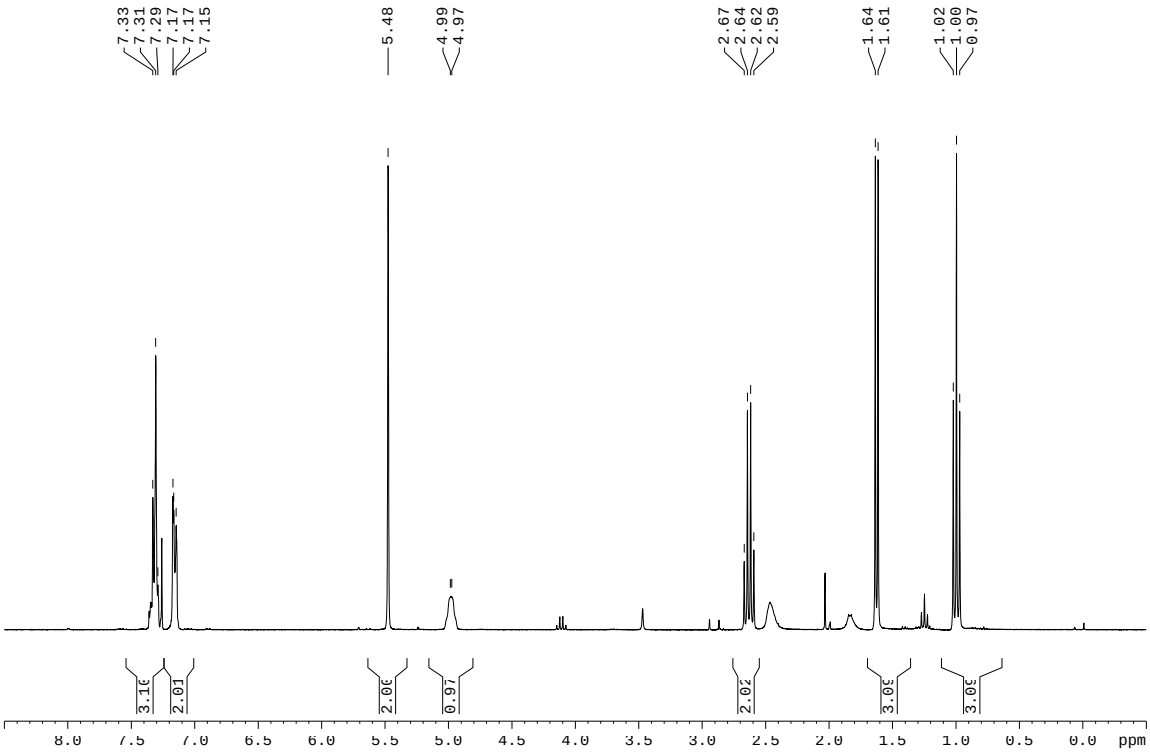


Compound 11d

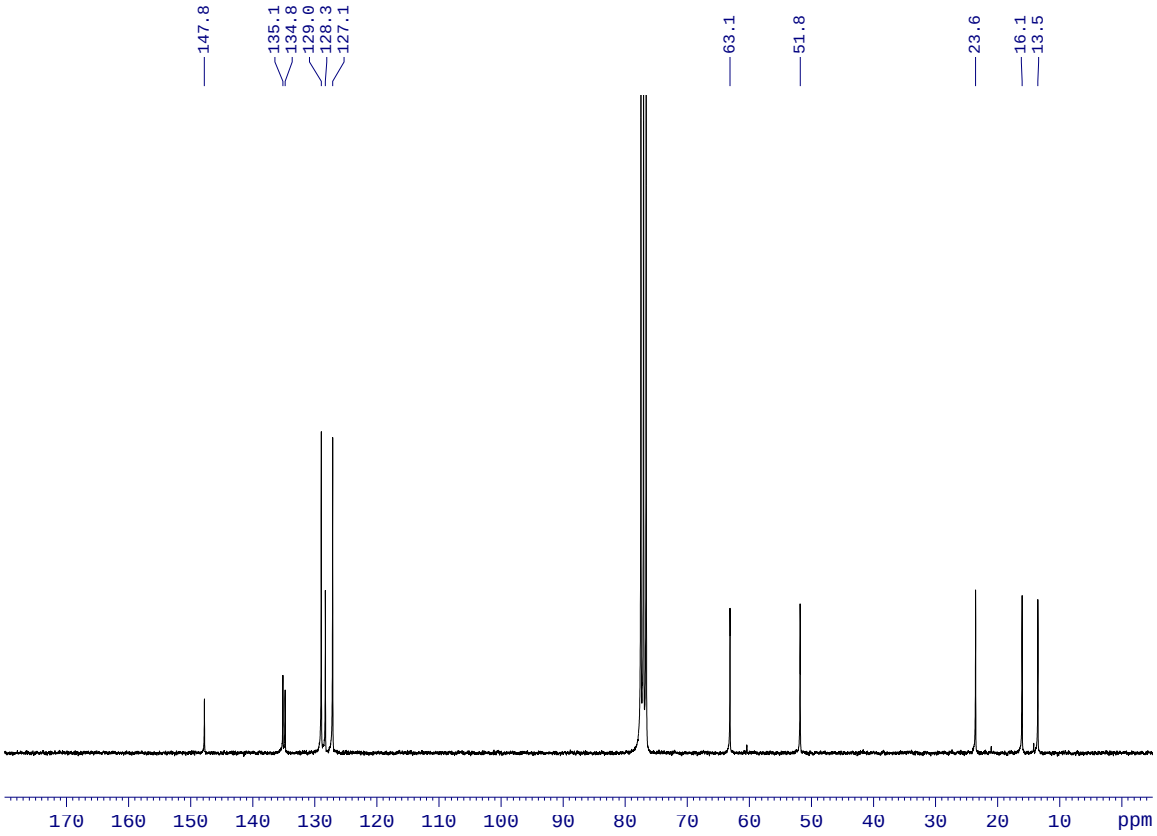


11d

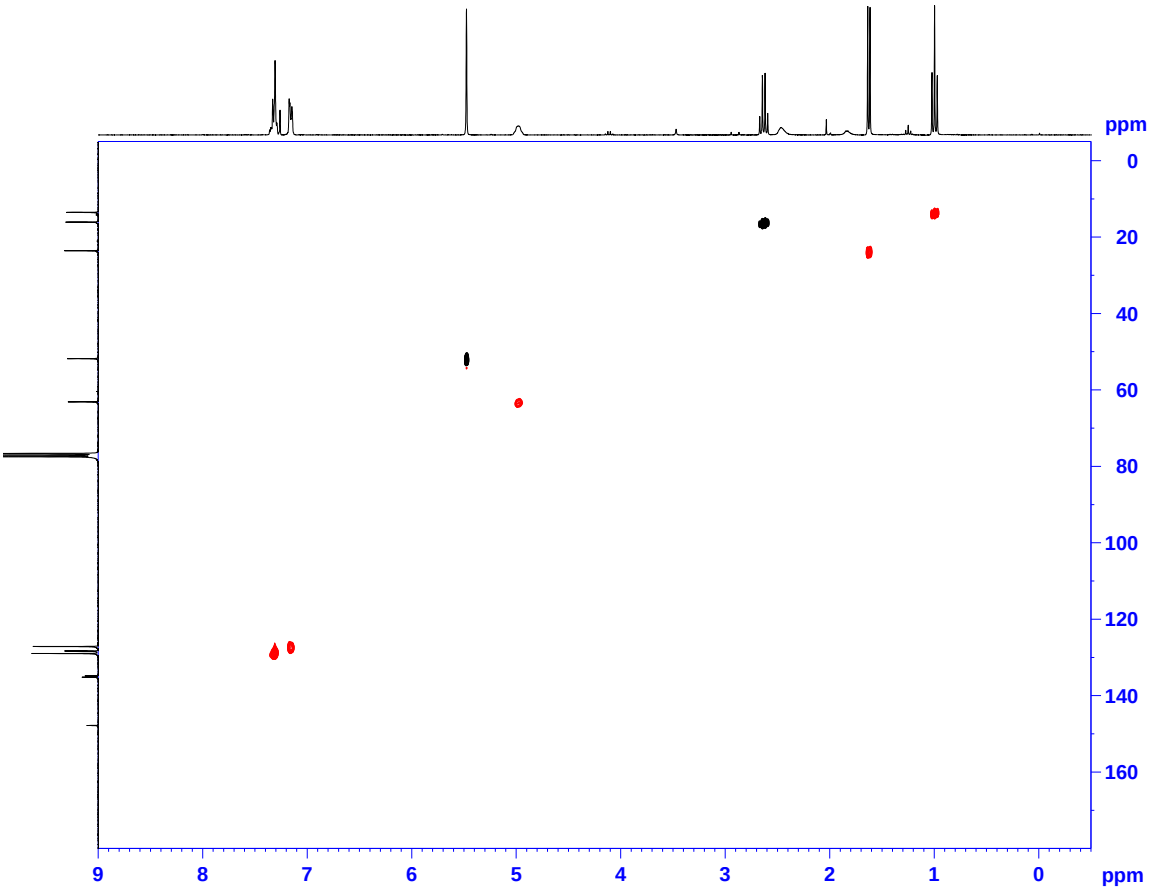
^{1}H NMR (300 MHz, $CDCl_3$)



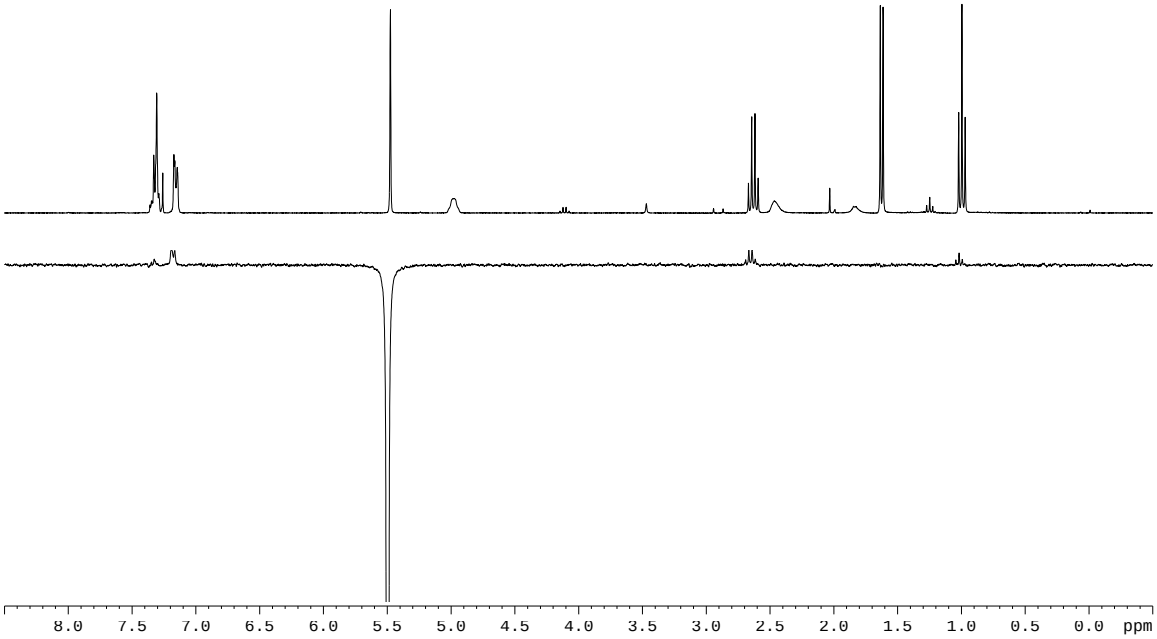
^{13}C NMR (75 MHz, $CDCl_3$)



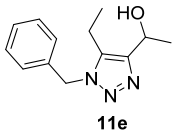
HSQC



NOE

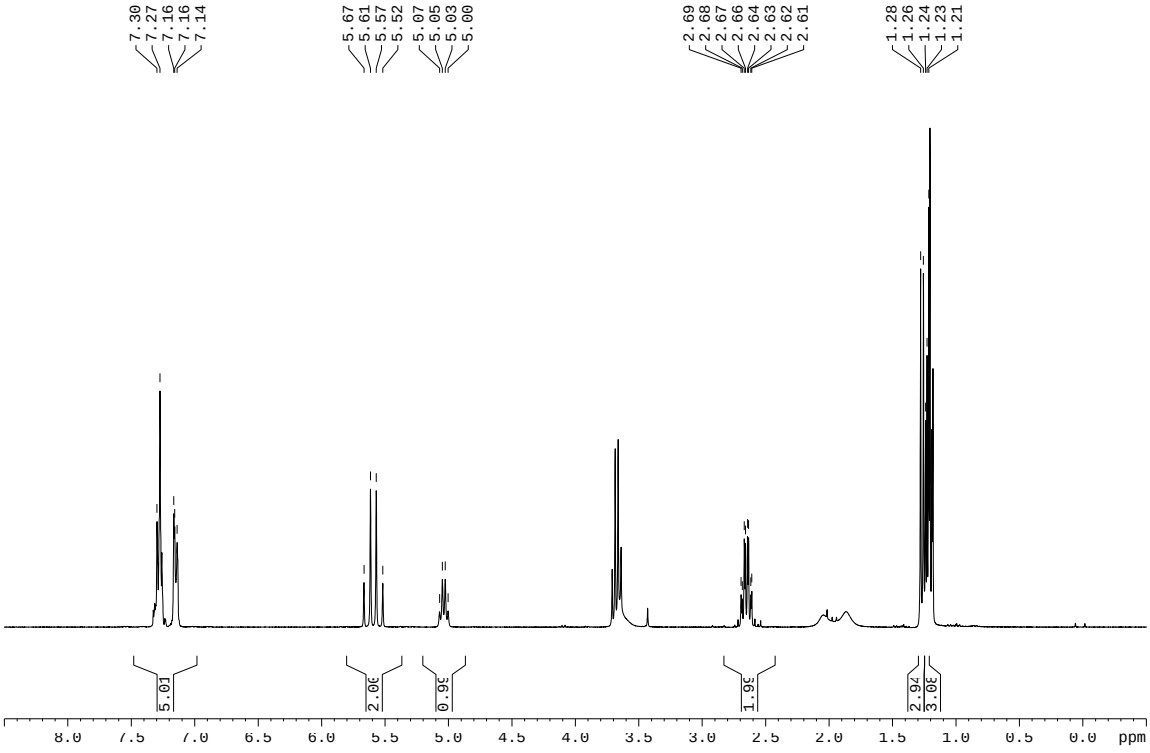


Compound 11e

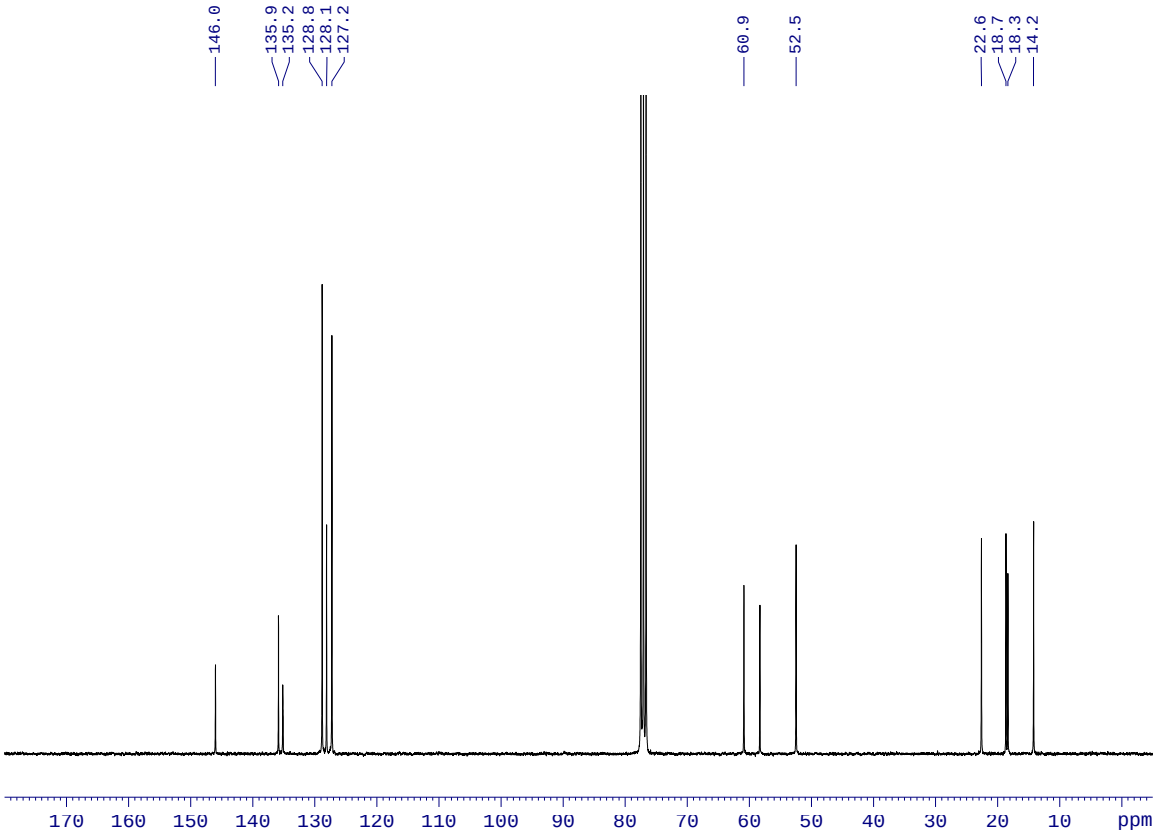


11e

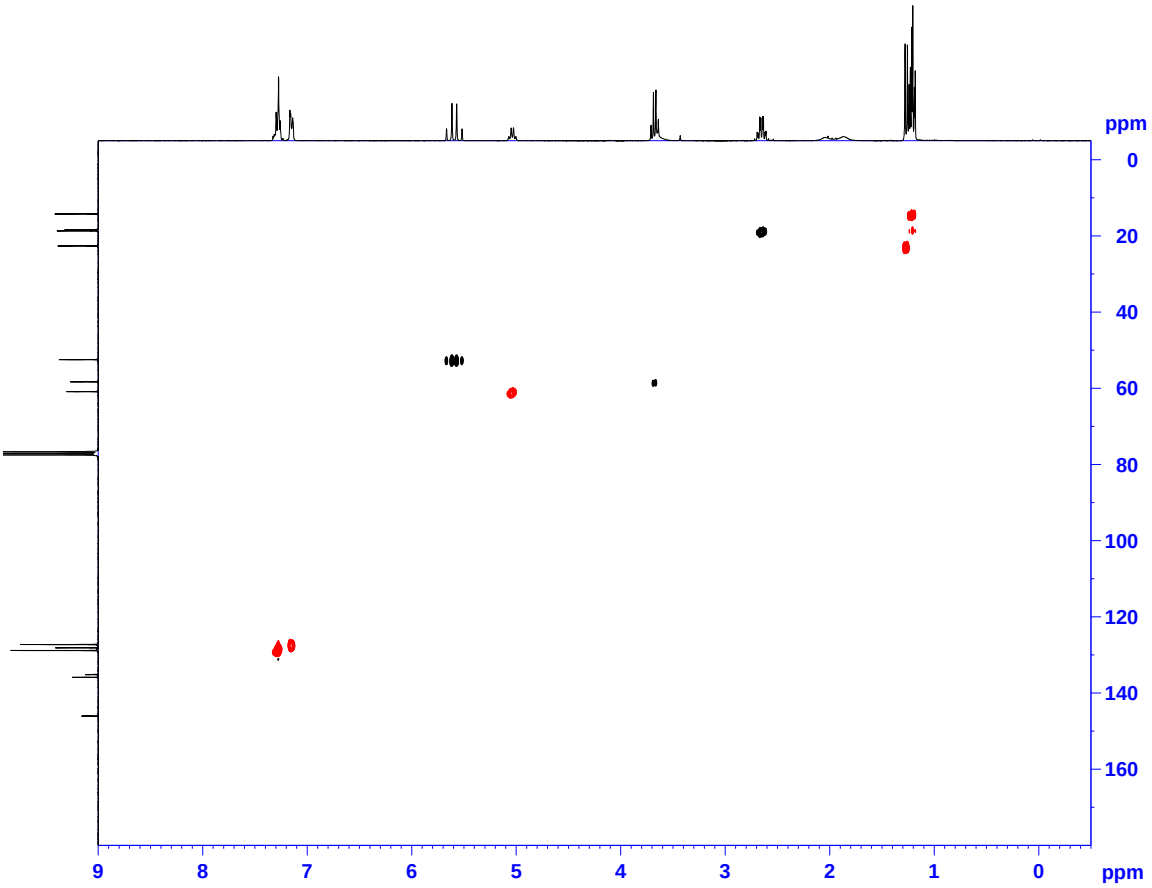
^{1}H NMR (300 MHz, $CDCl_3$)



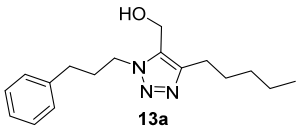
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

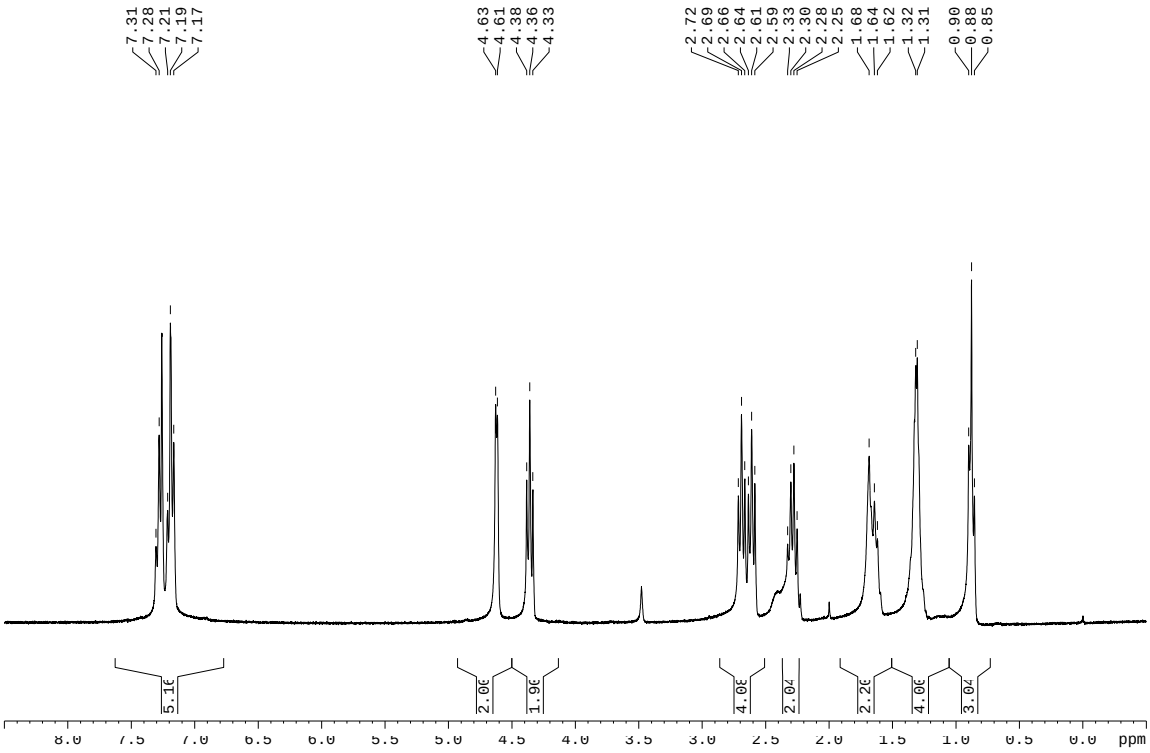


Compound 13a

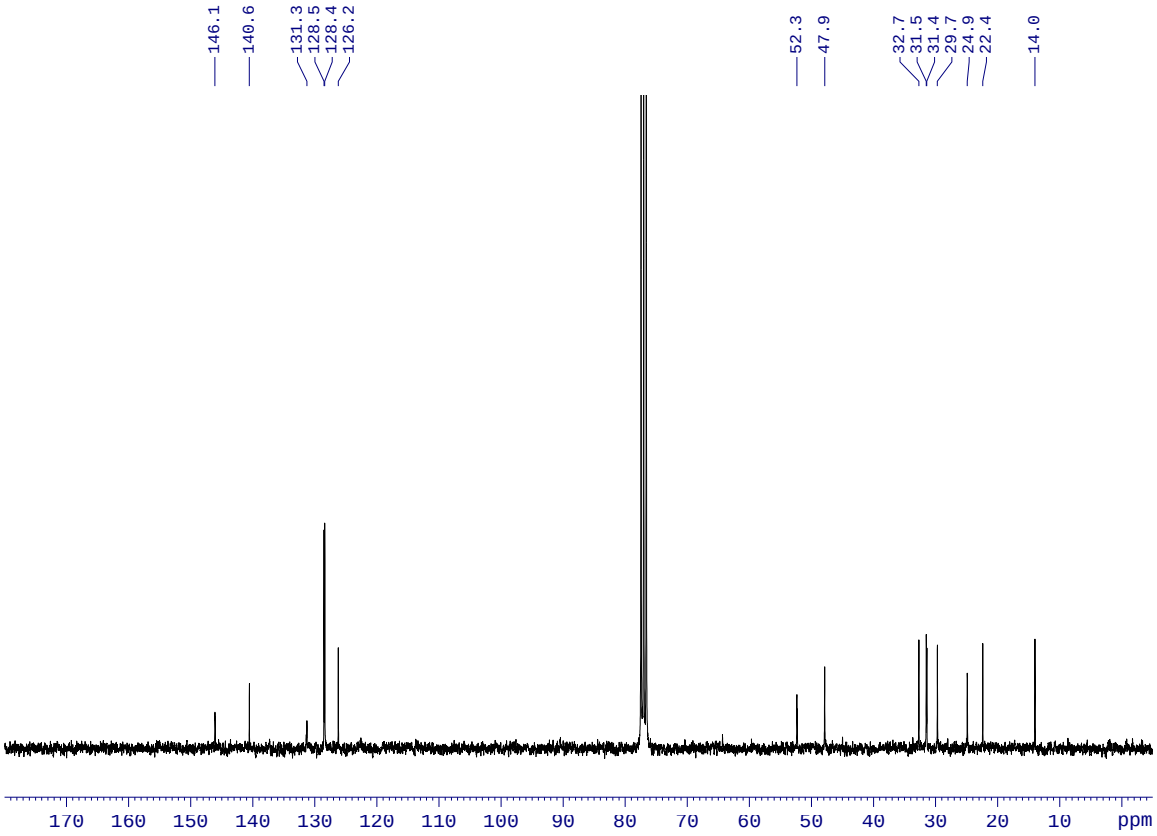


13a

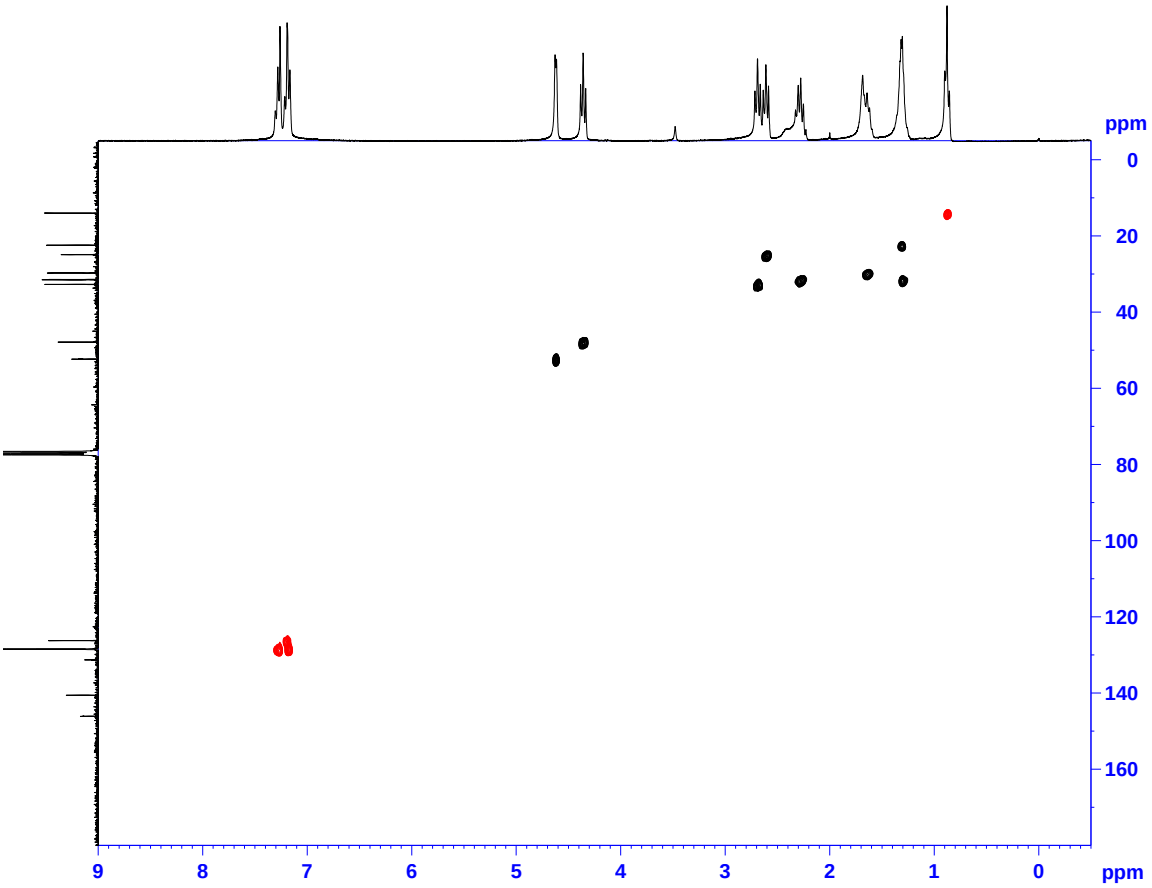
^{1}H NMR (300 MHz, $CDCl_3$)



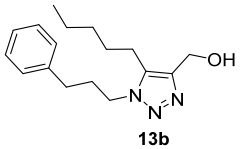
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

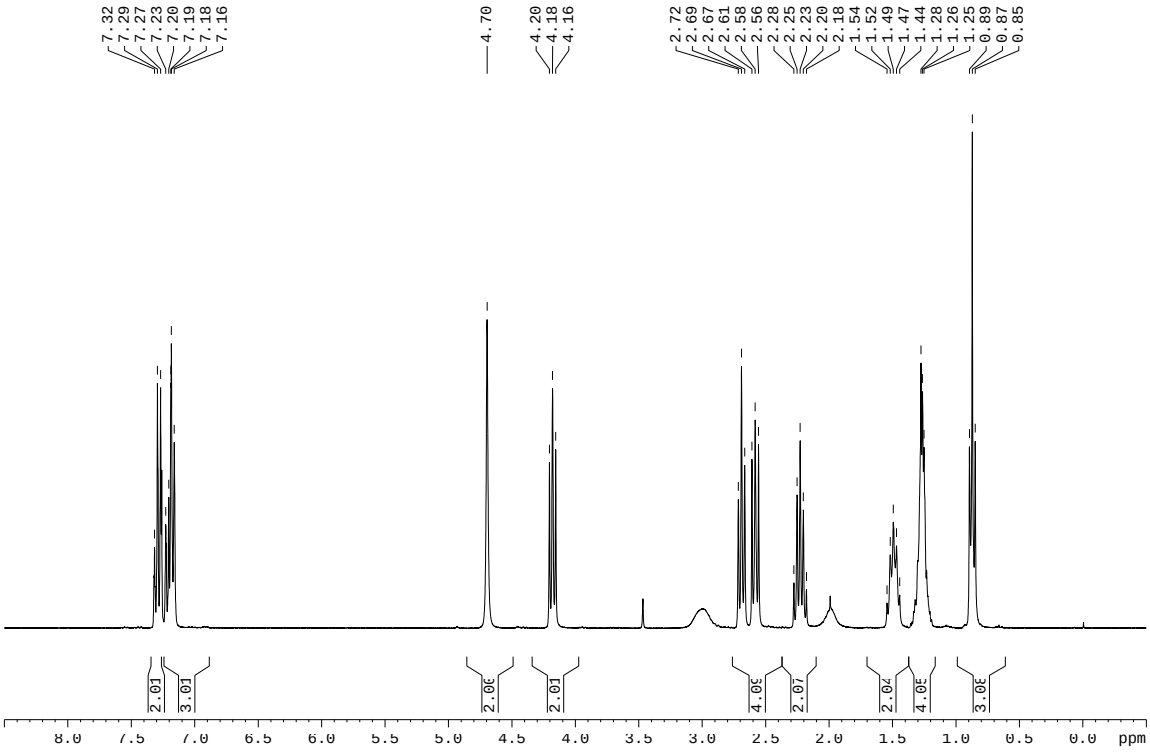


Compound 13b

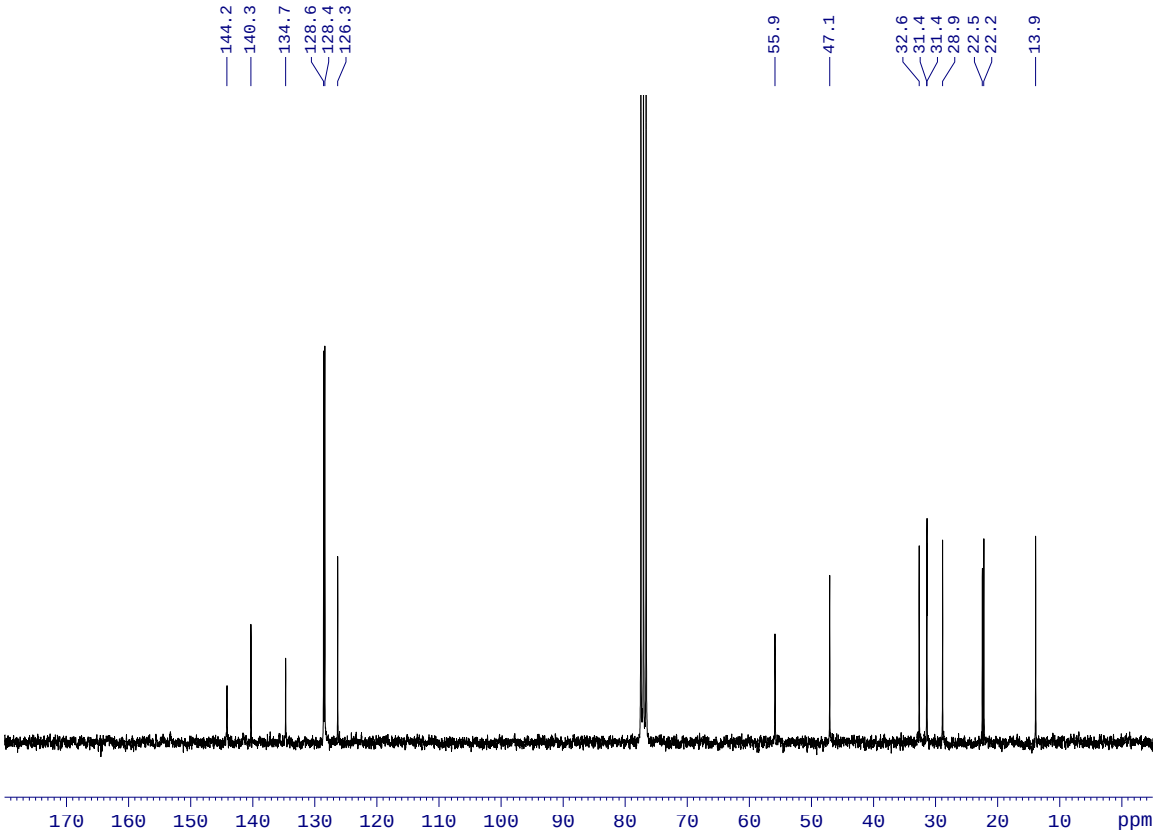


13b

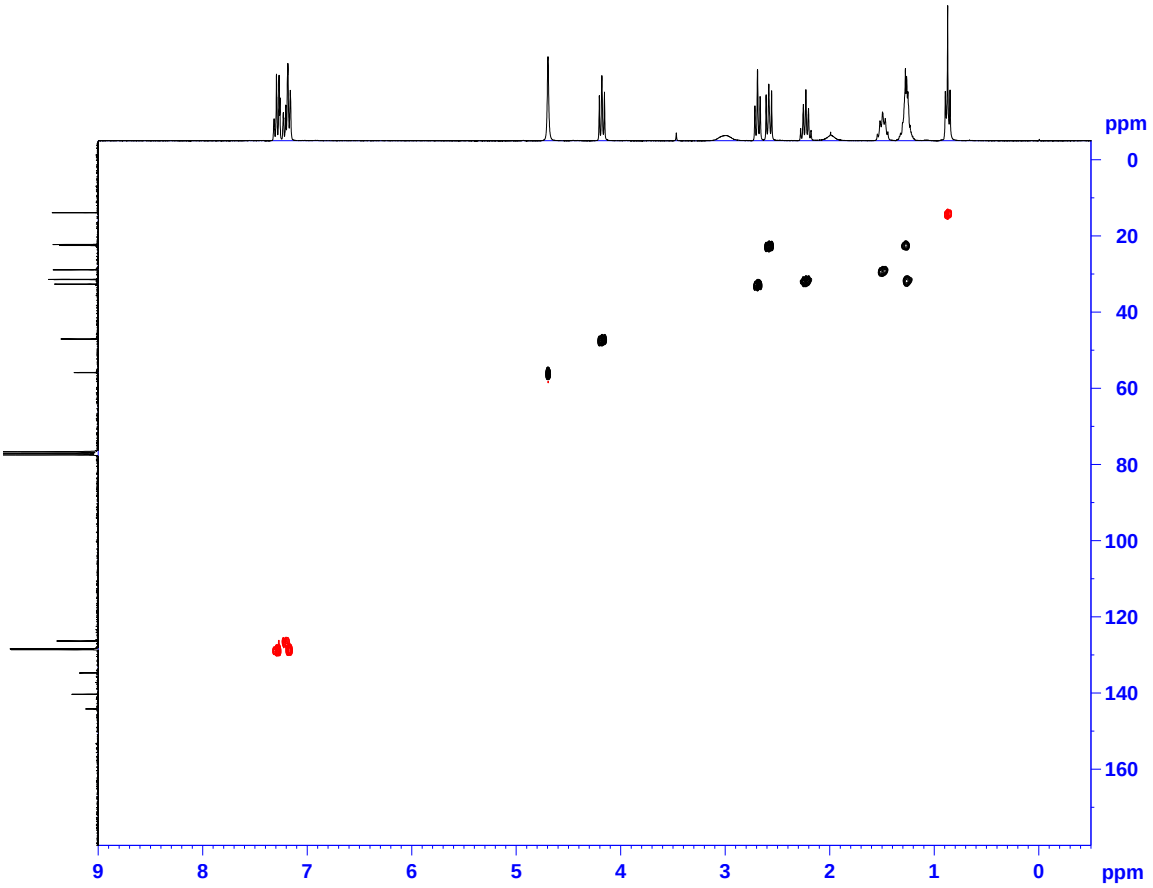
^{1}H NMR (300 MHz, $CDCl_3$)



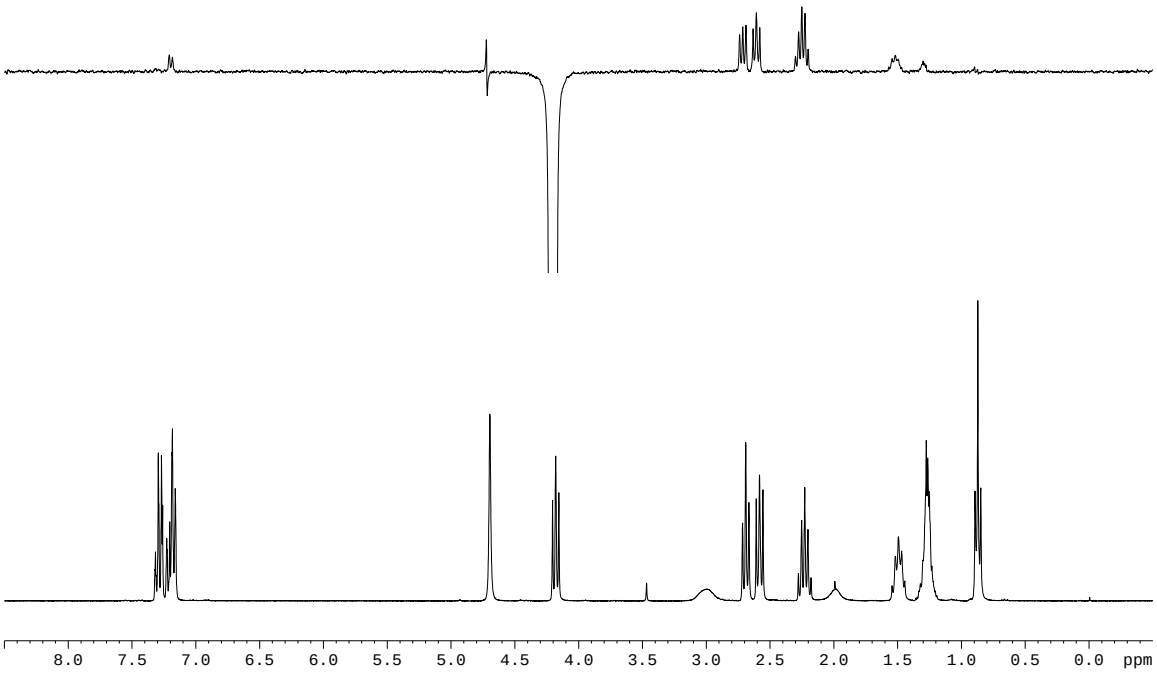
^{13}C NMR (75 MHz, $CDCl_3$)



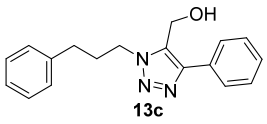
HSQC


ppm
0
20
40
60
80
100
120
140
160
9
8
7
6
5
4
3
2
1
0
ppm

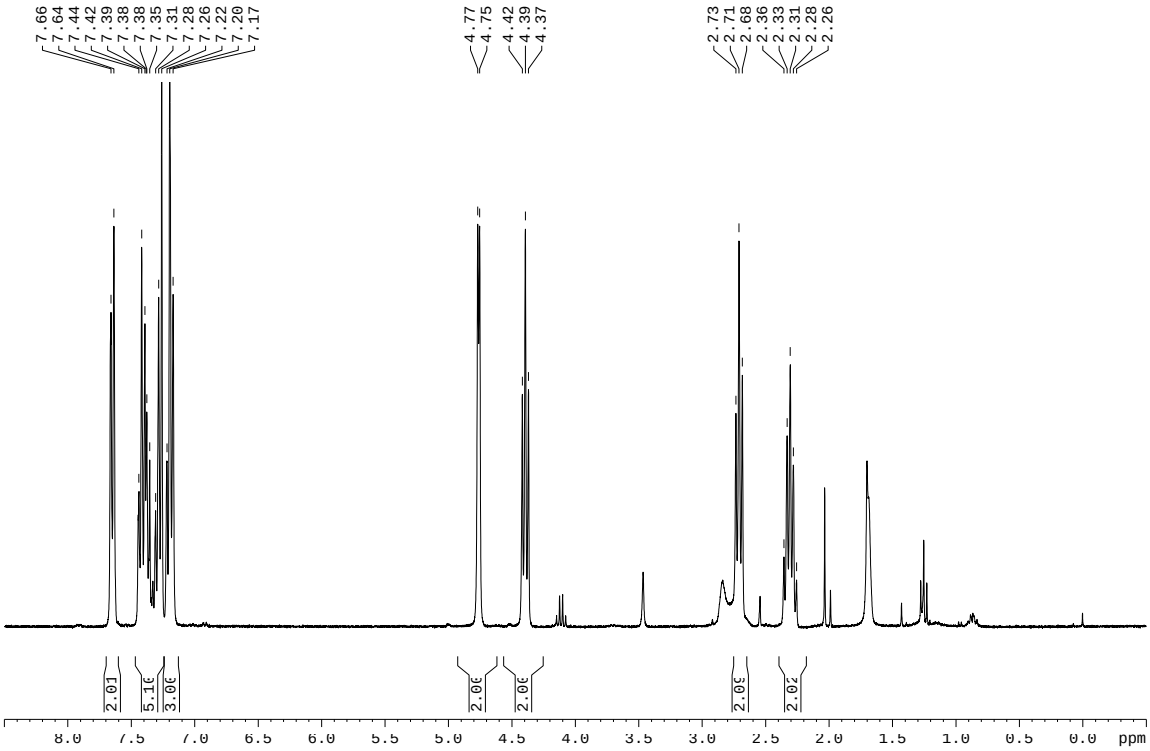
NOE


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

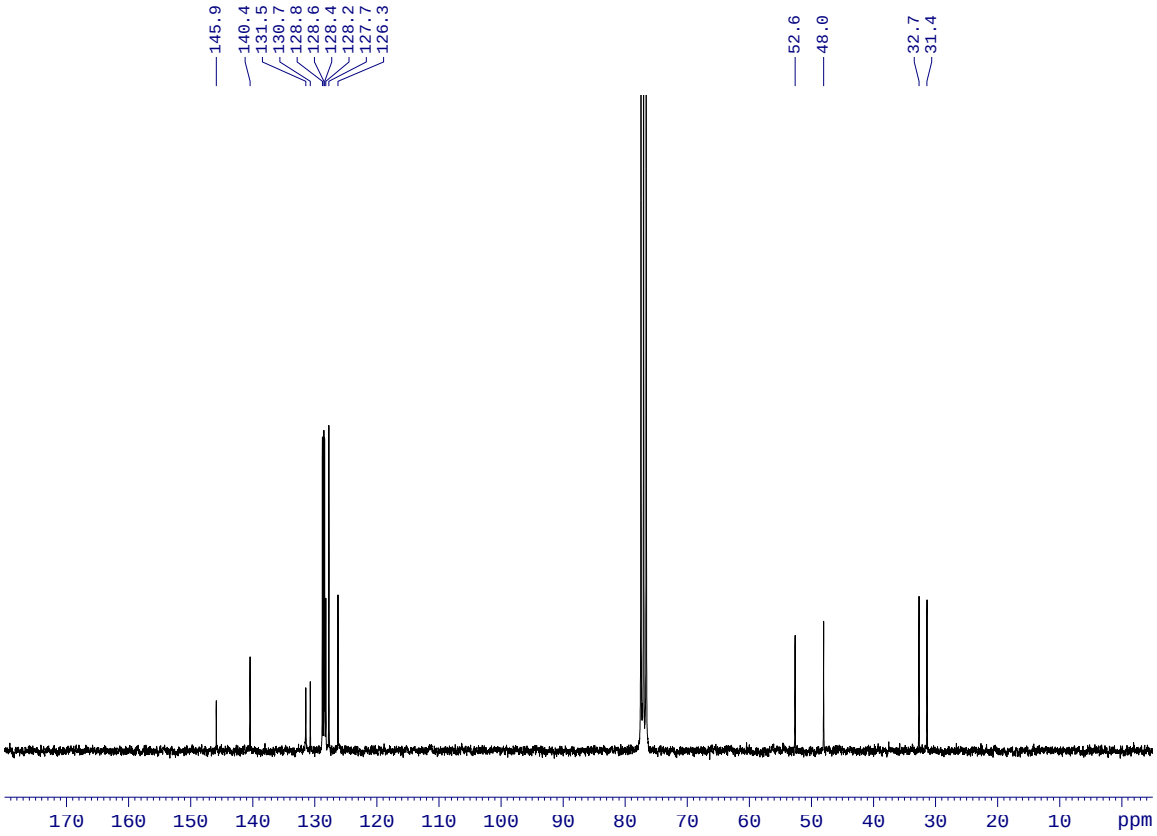
Compound 13c



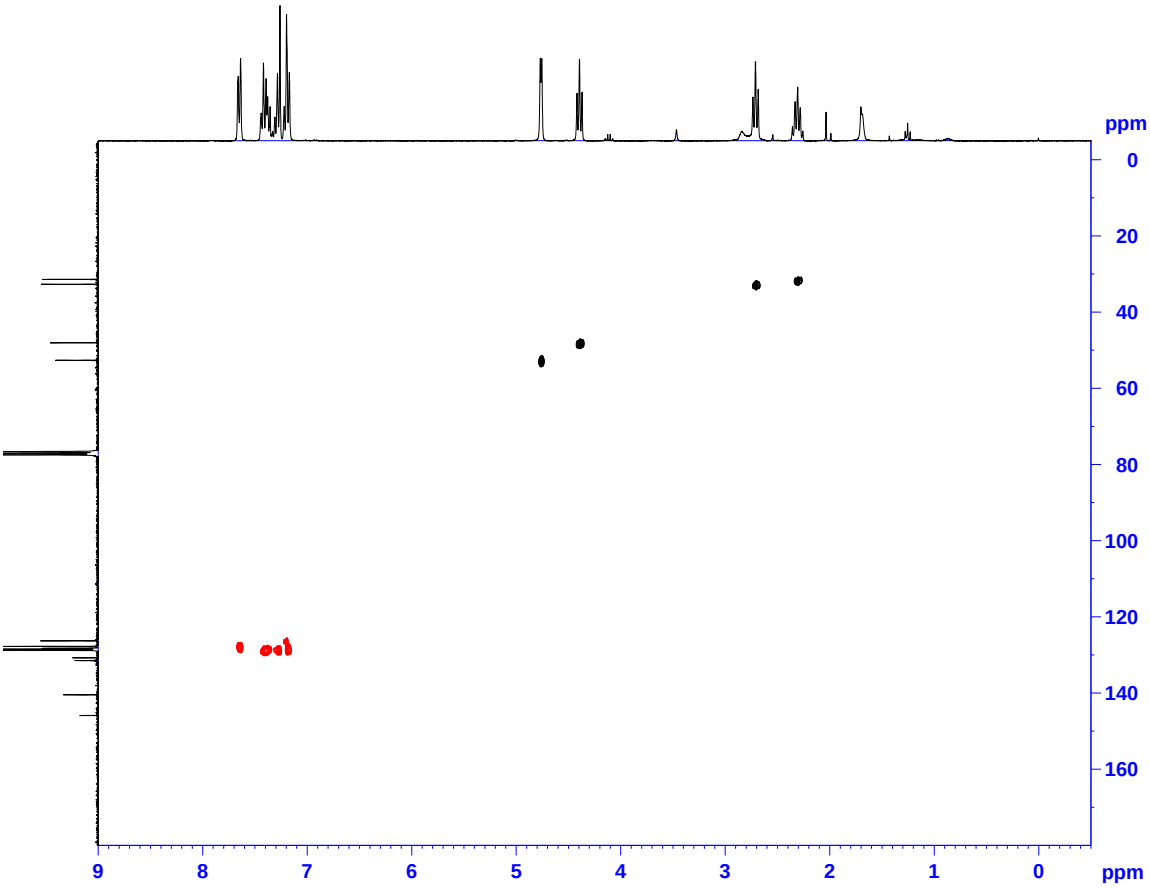
^{1}H NMR (300 MHz, $CDCl_3$)



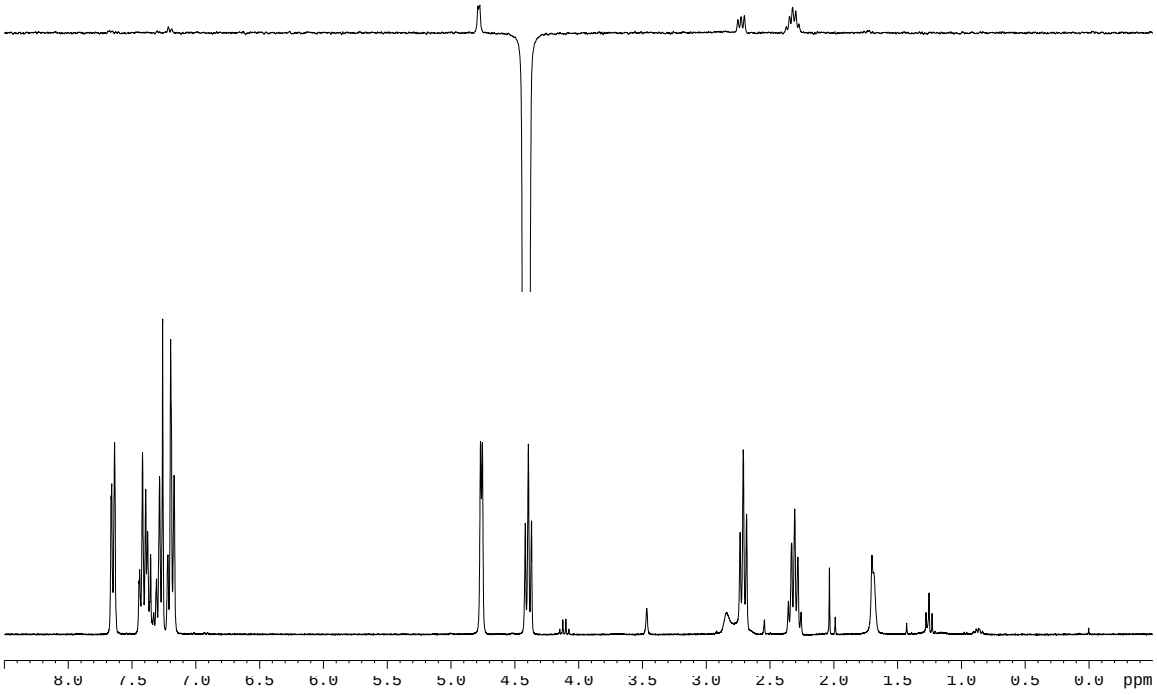
^{13}C NMR (75 MHz, $CDCl_3$)



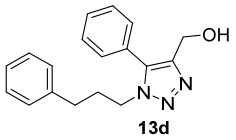
HSQC



NOE

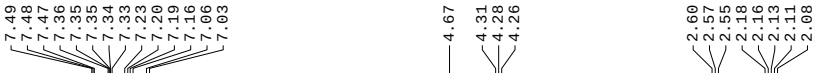


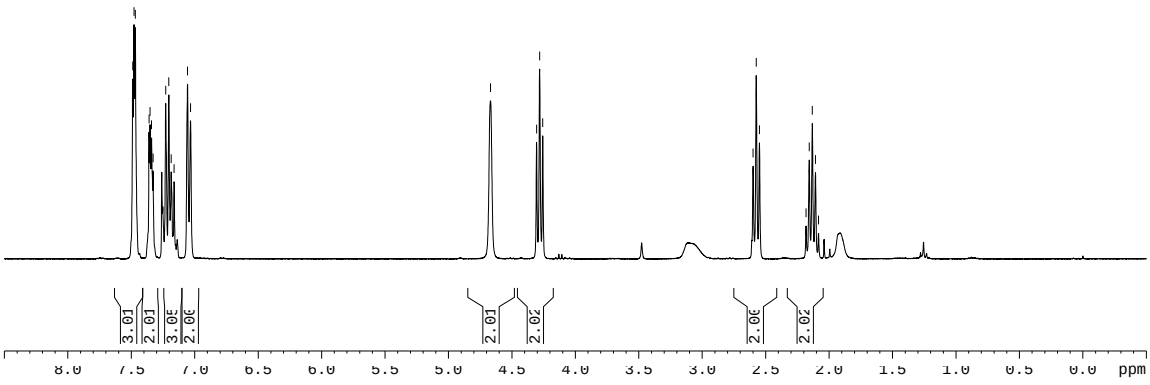
Compound 13d



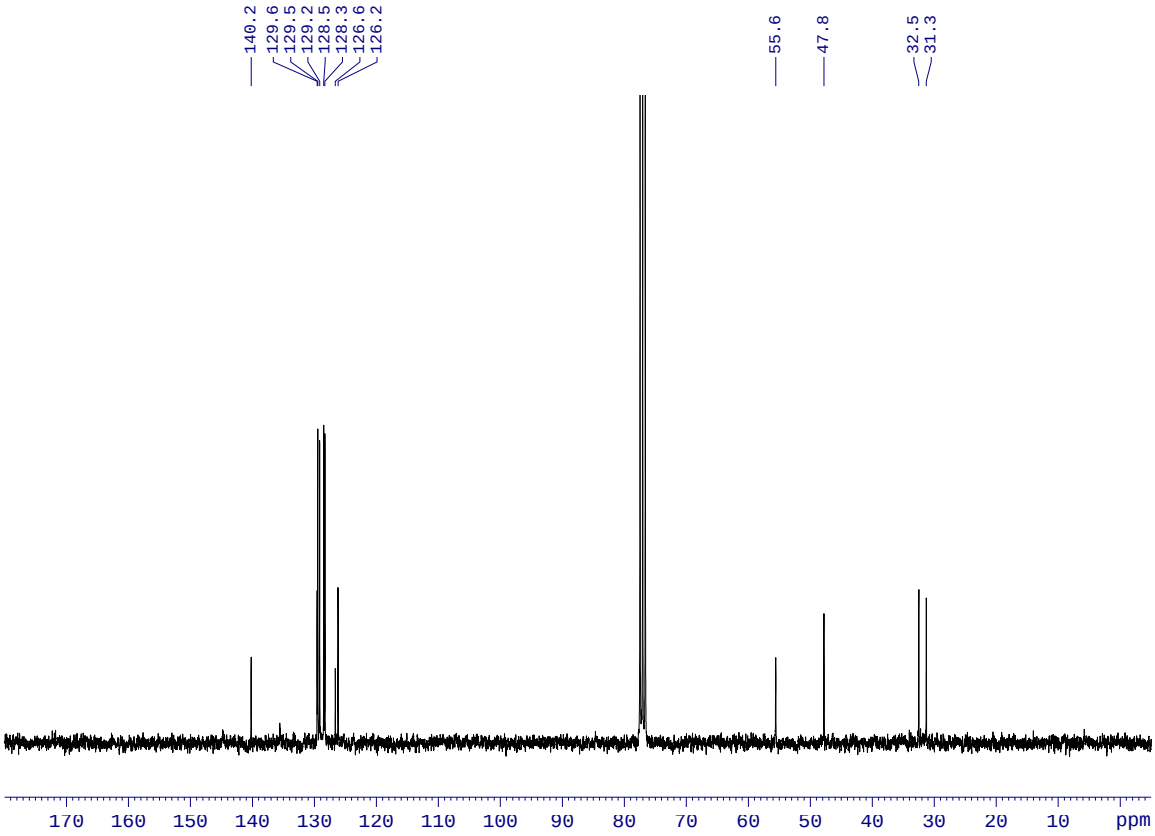
13d

^{1}H NMR (300 MHz, $CDCl_3$)

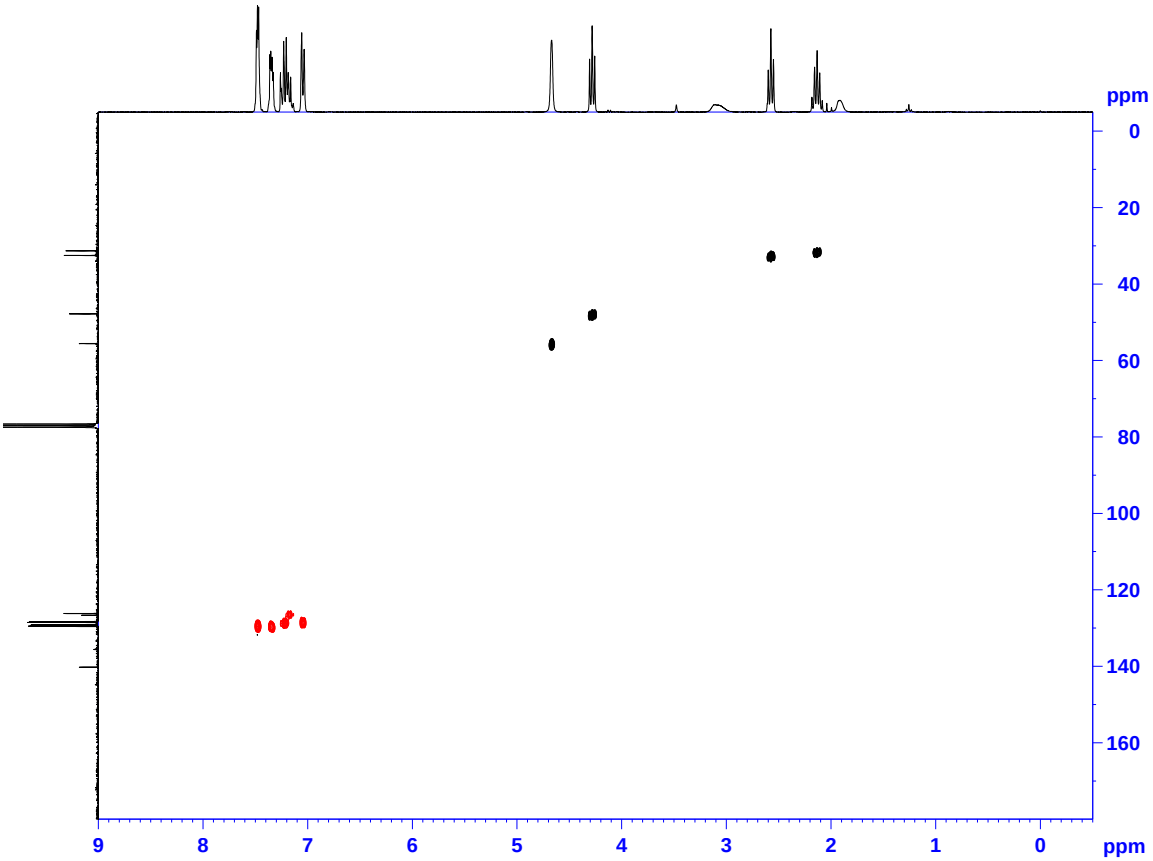




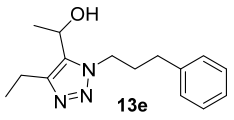
^{13}C NMR (75 MHz, $CDCl_3$)



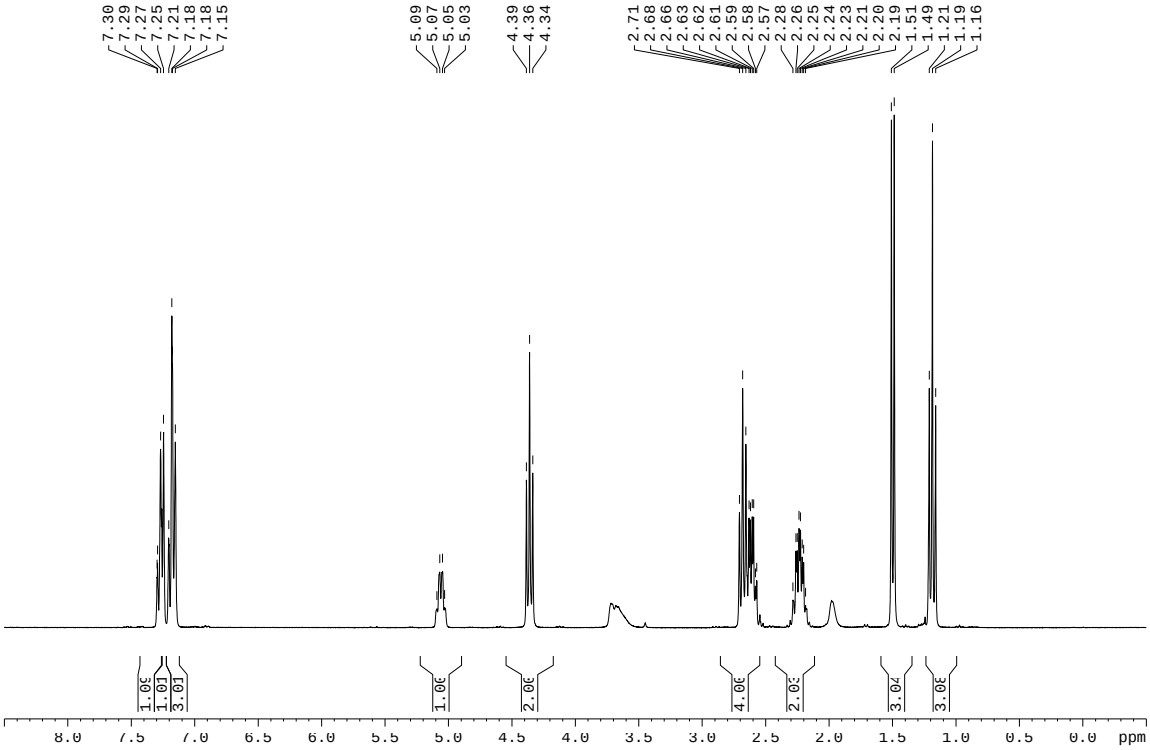
HSQC



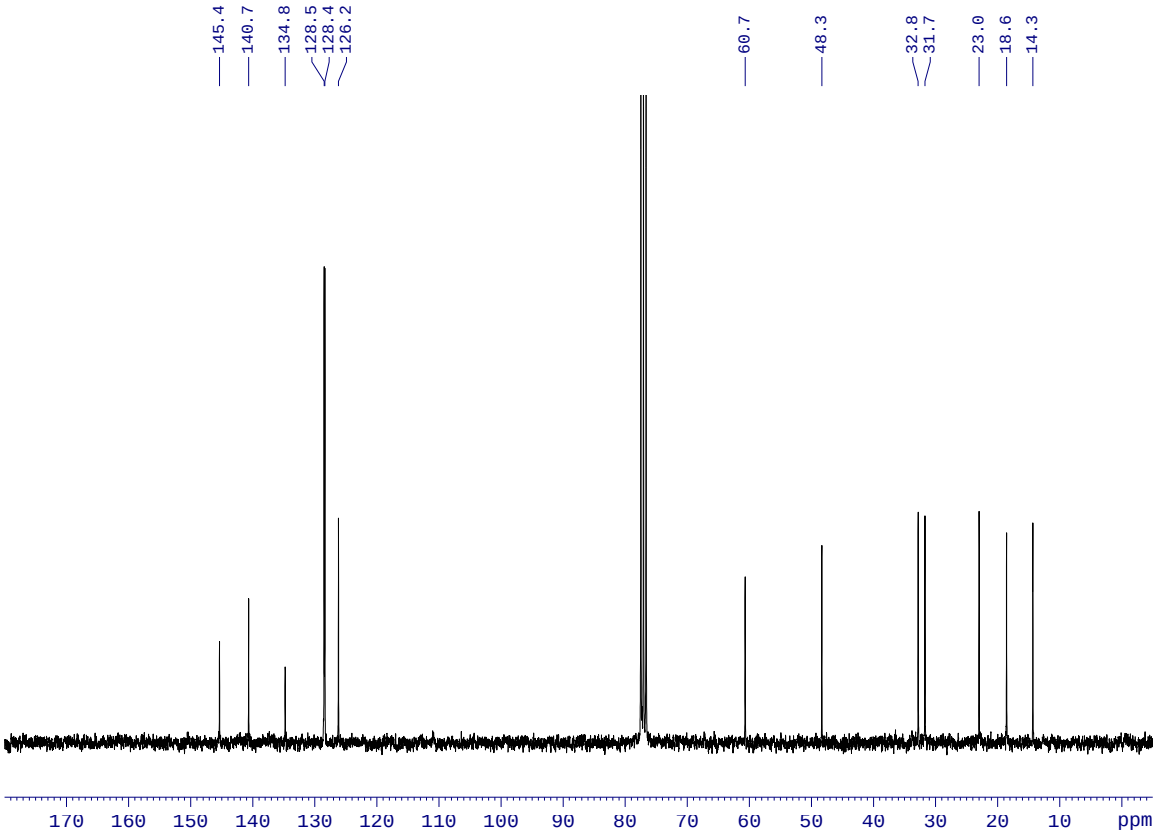
Compound 13e



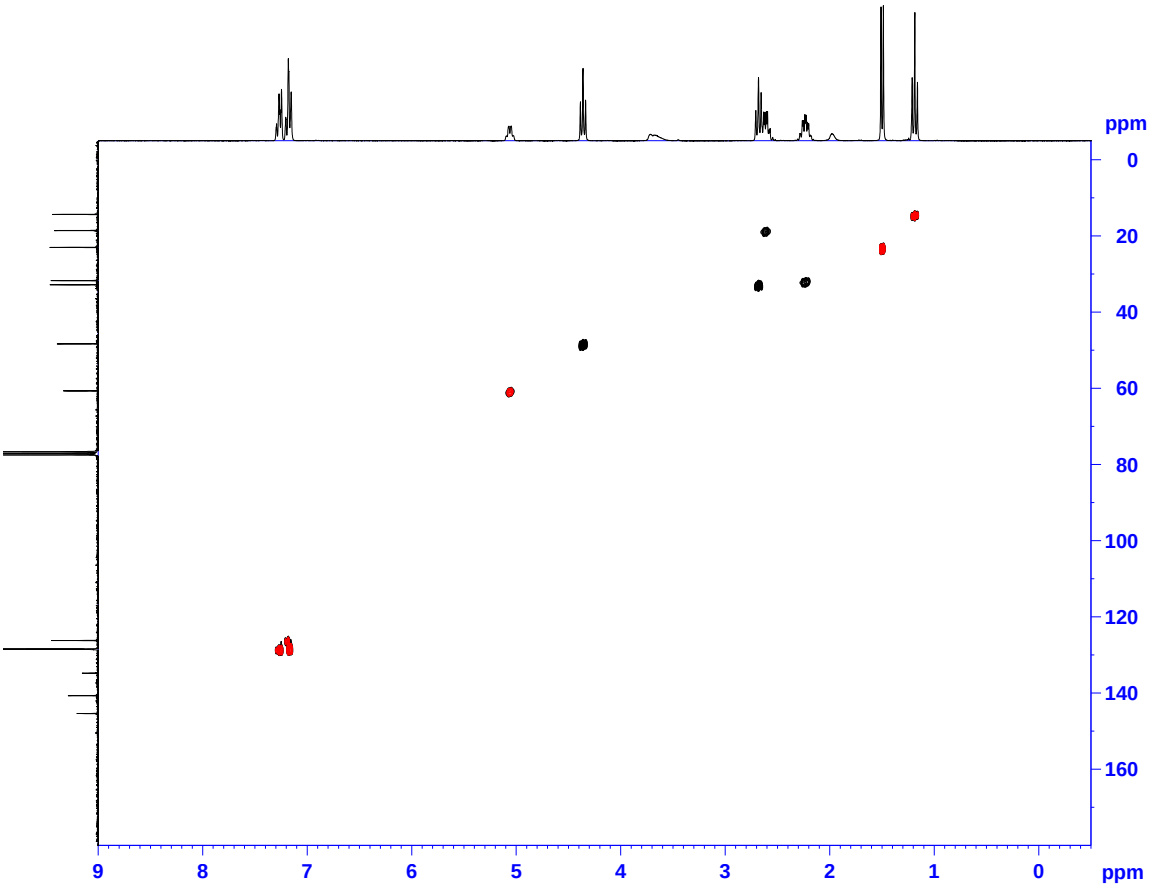
^{1}H NMR (300 MHz, $CDCl_3$)



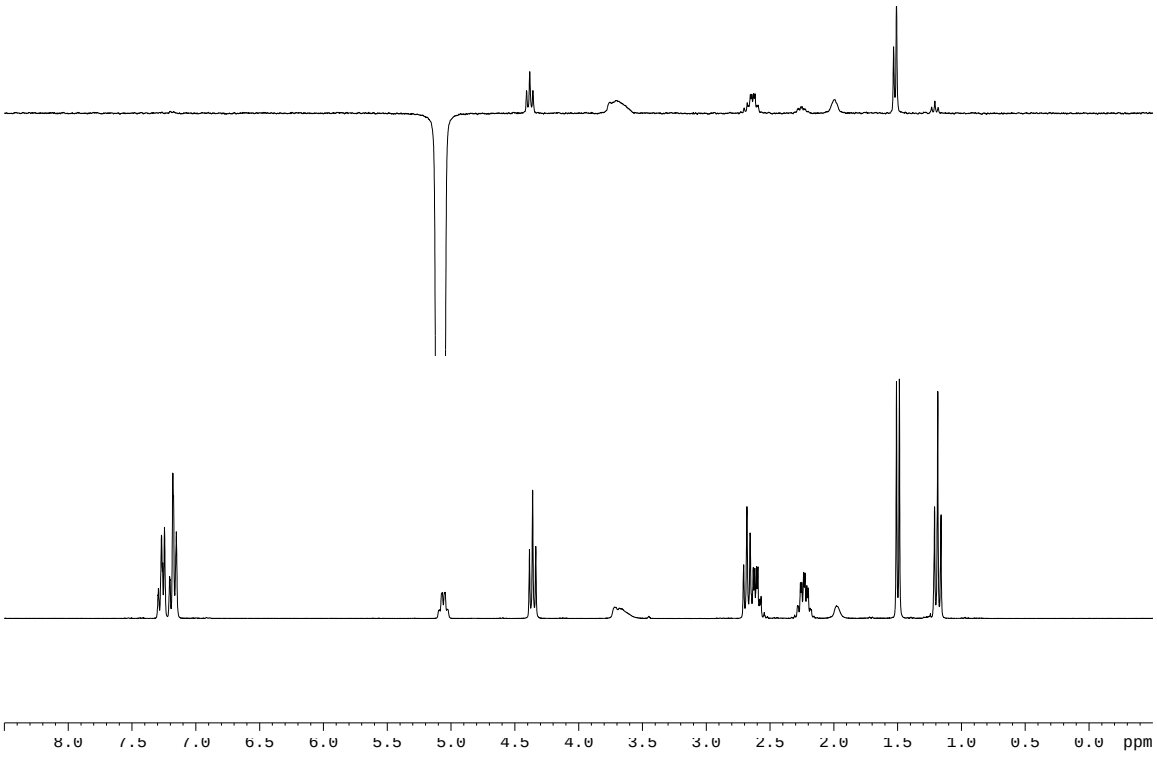
^{13}C NMR (75 MHz, $CDCl_3$)



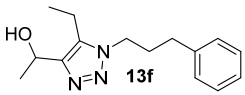
HSQC



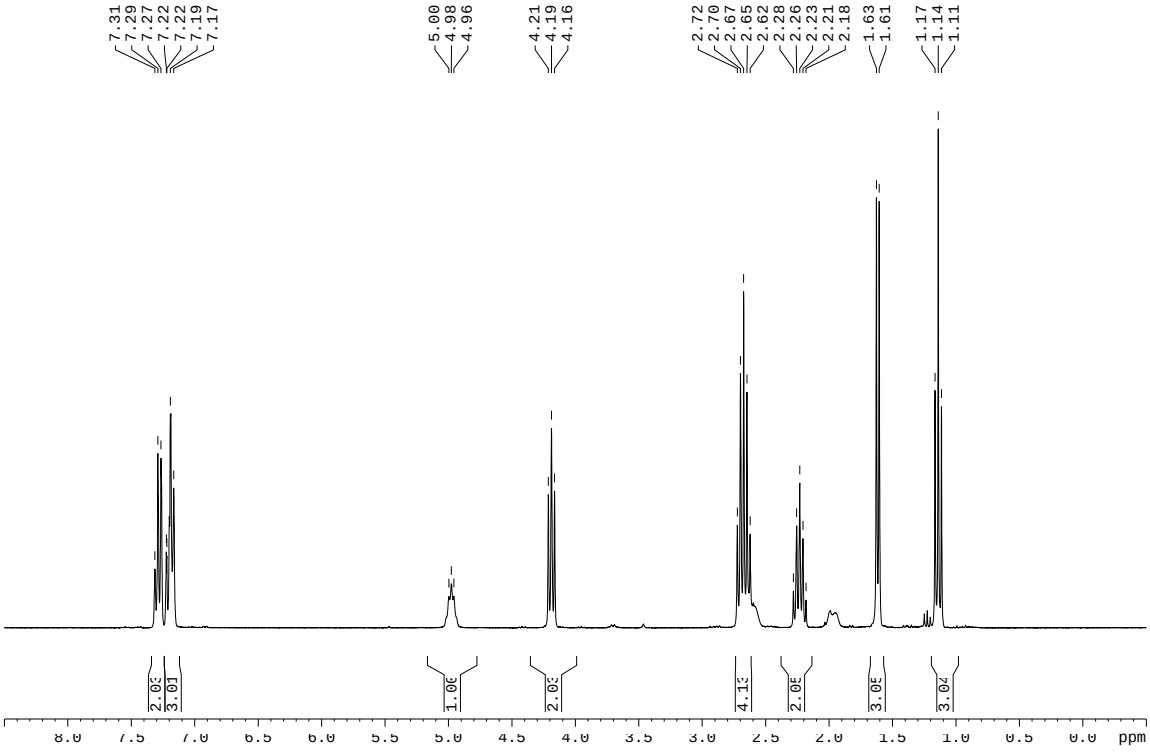
NOE



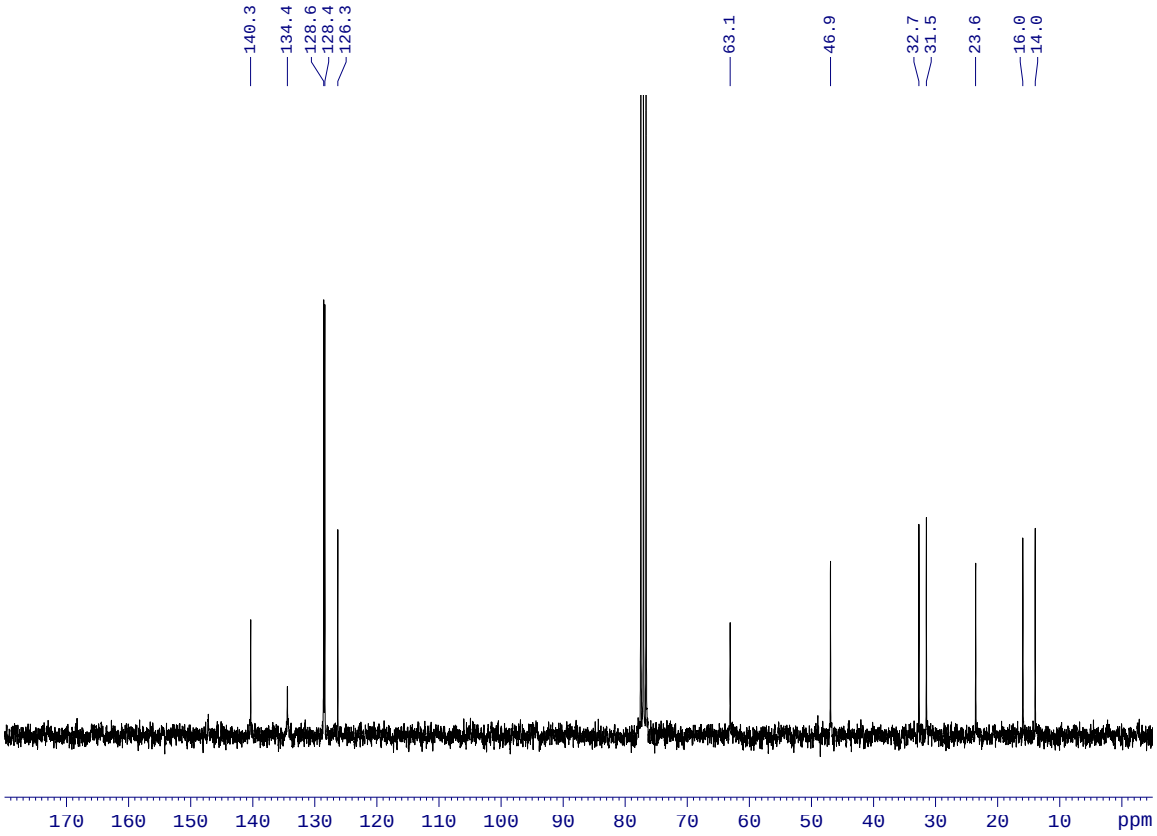
Compound 13f



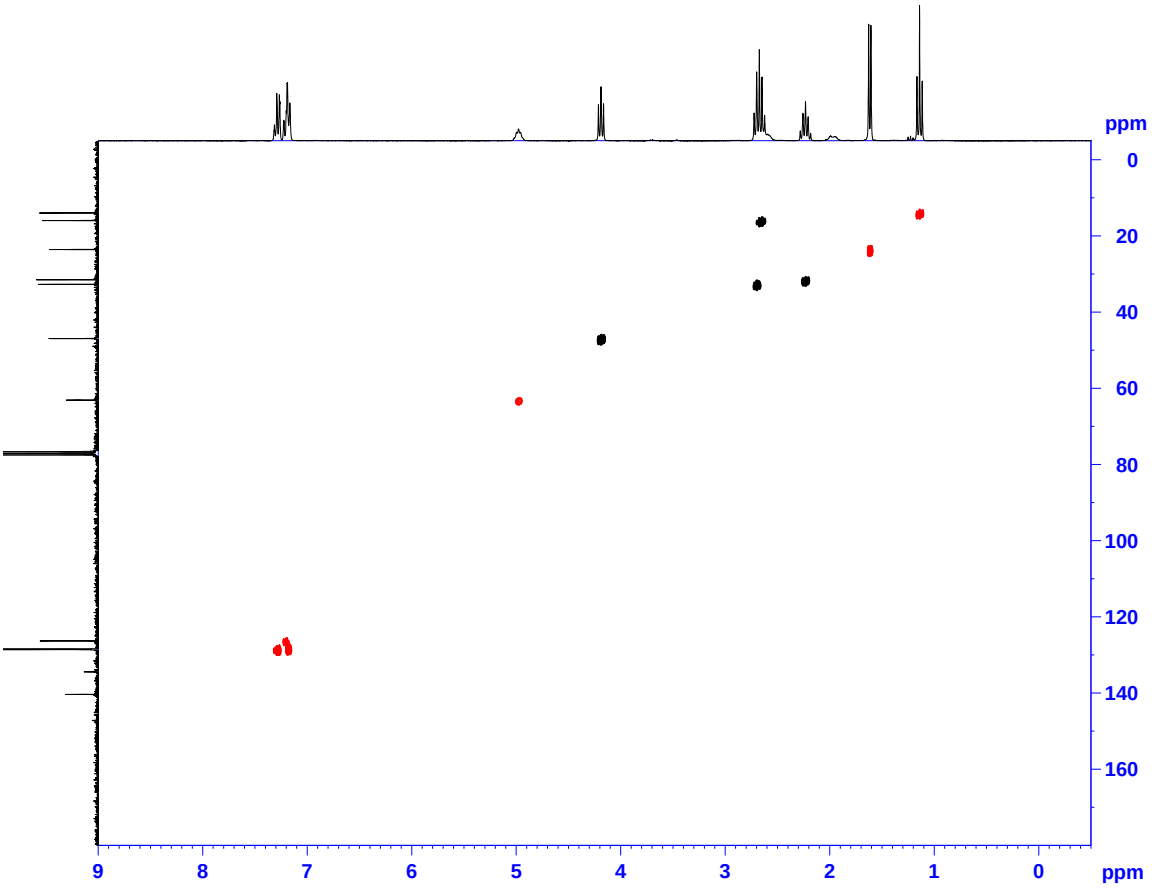
^{1}H NMR (300 MHz, $CDCl_3$)



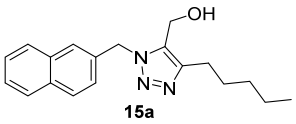
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

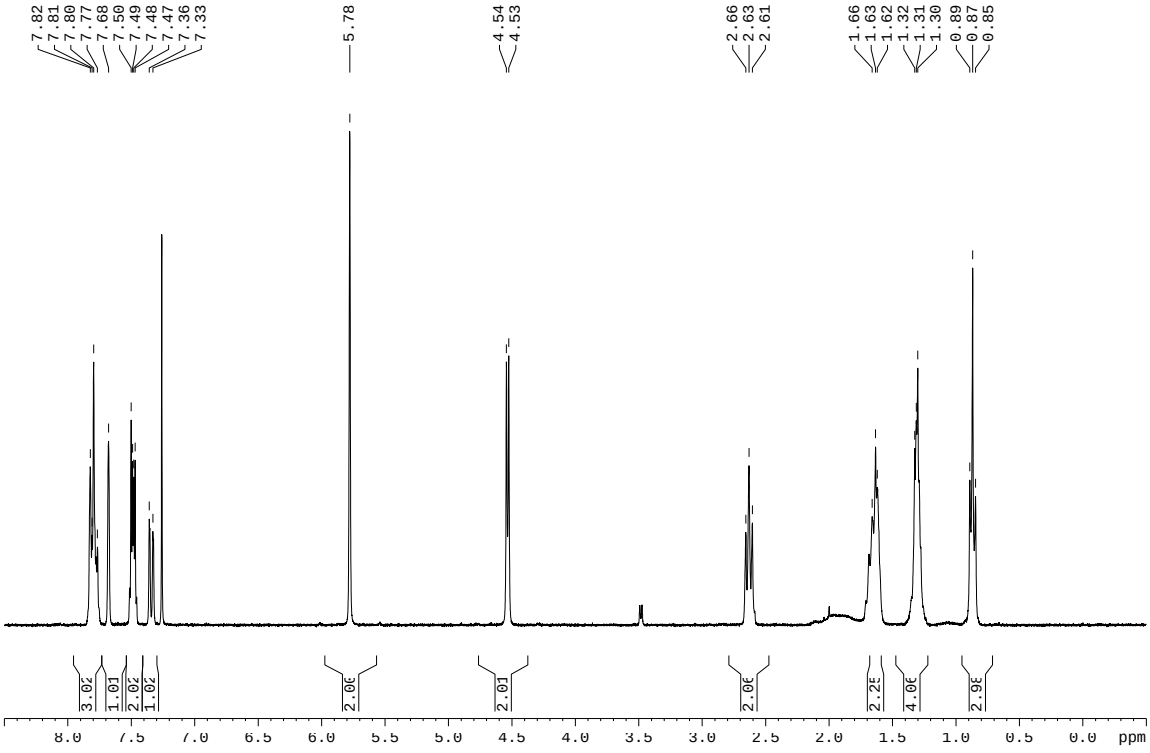


Compound 15a

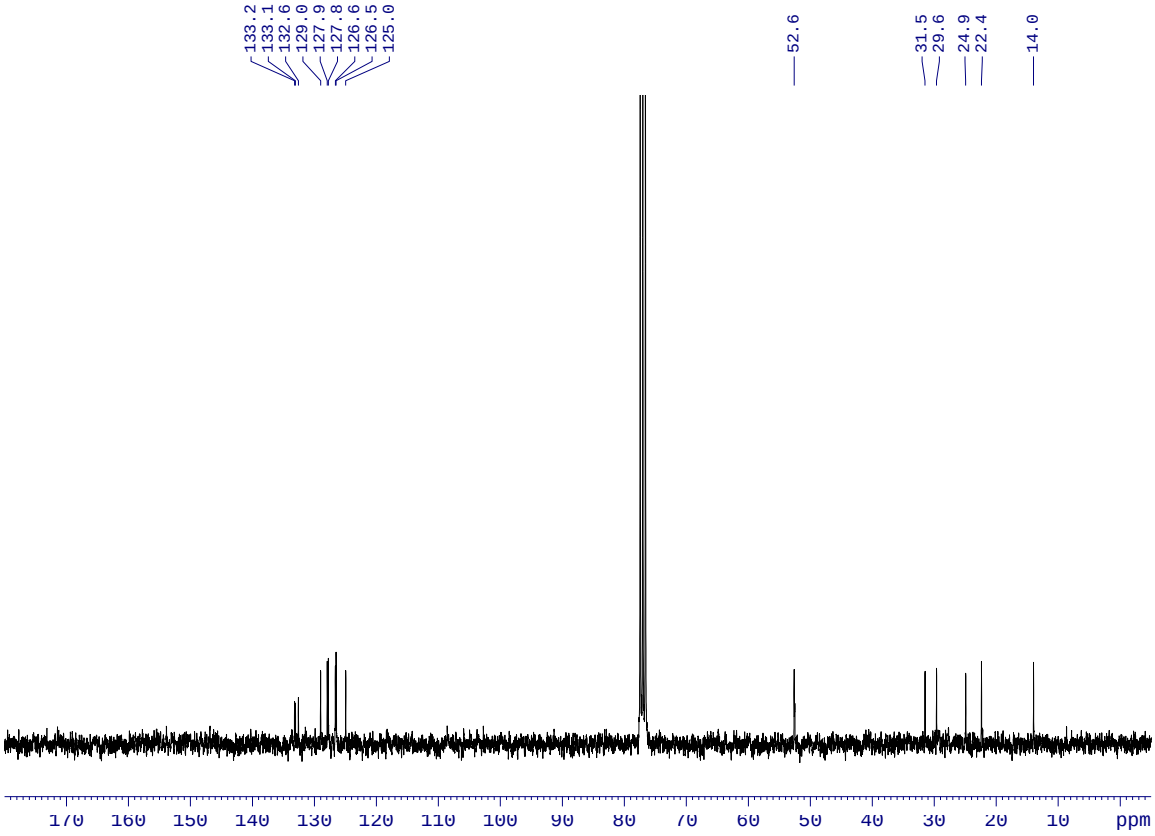


15a

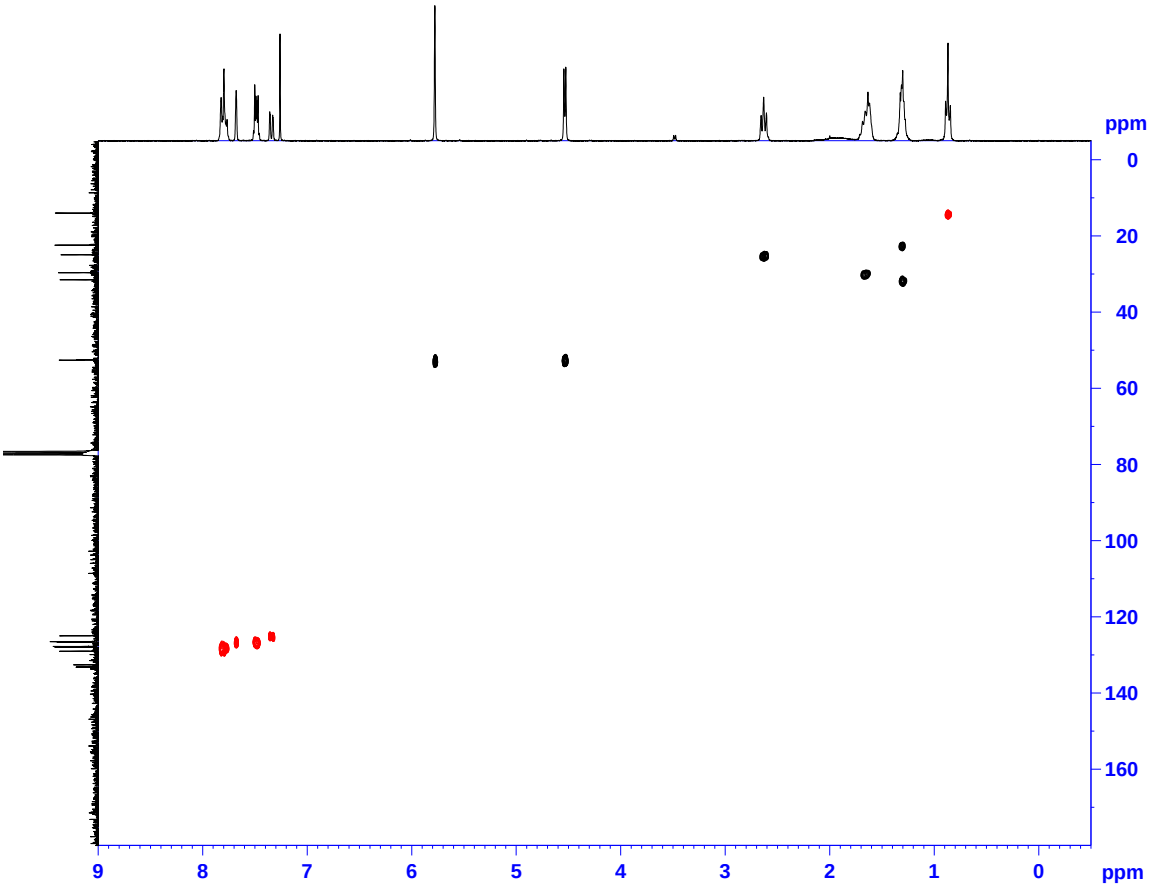
^{1}H NMR (300 MHz, $CDCl_3$)



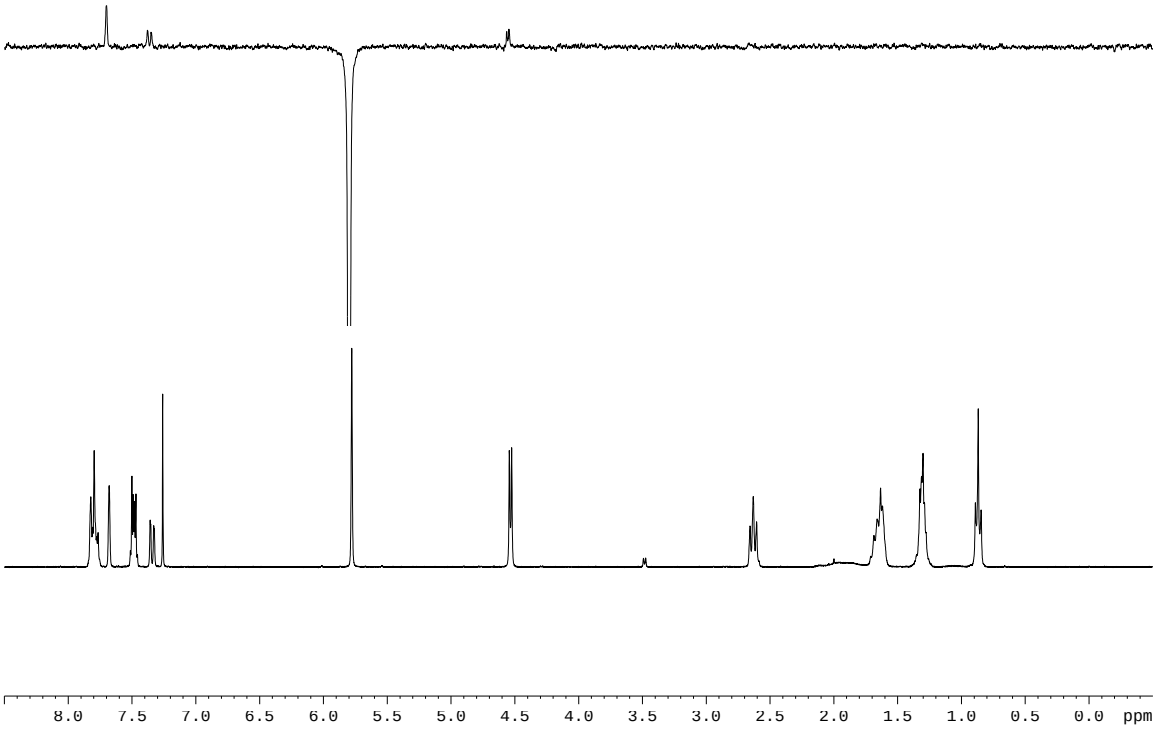
^{13}C NMR (75 MHz, $CDCl_3$)



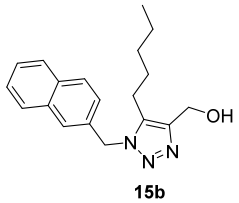
HSQC



NOE

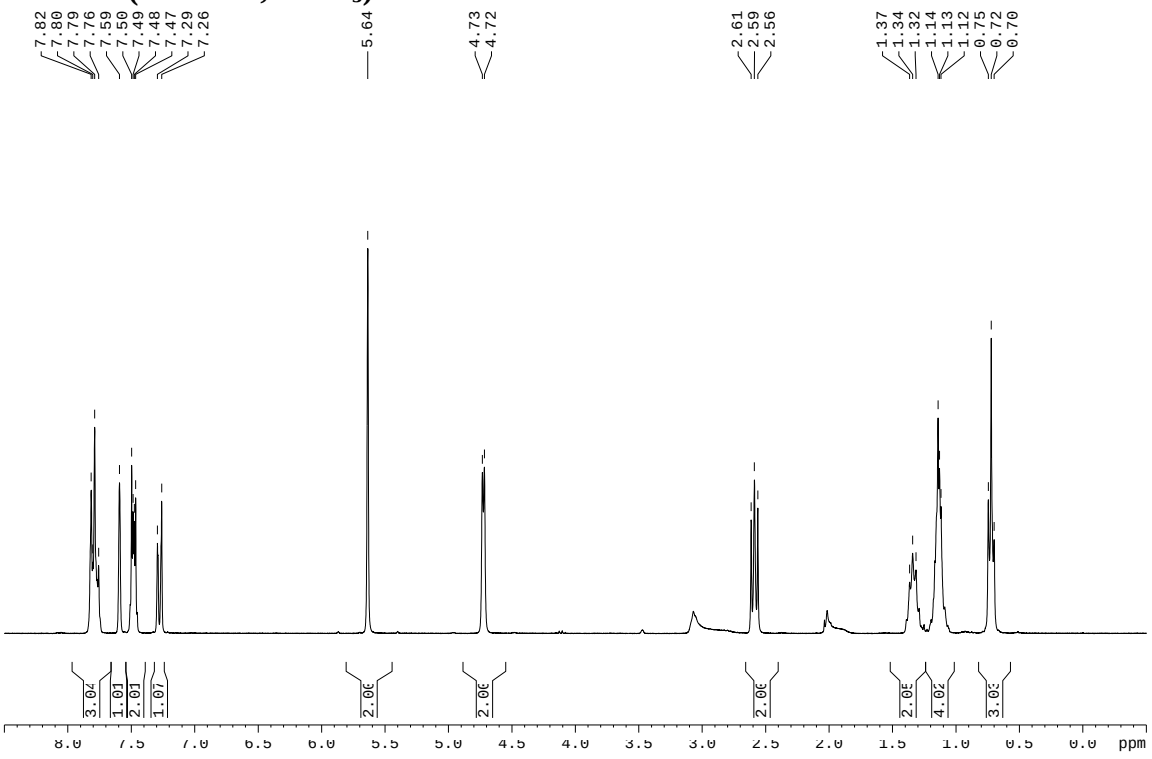


Compound 15b

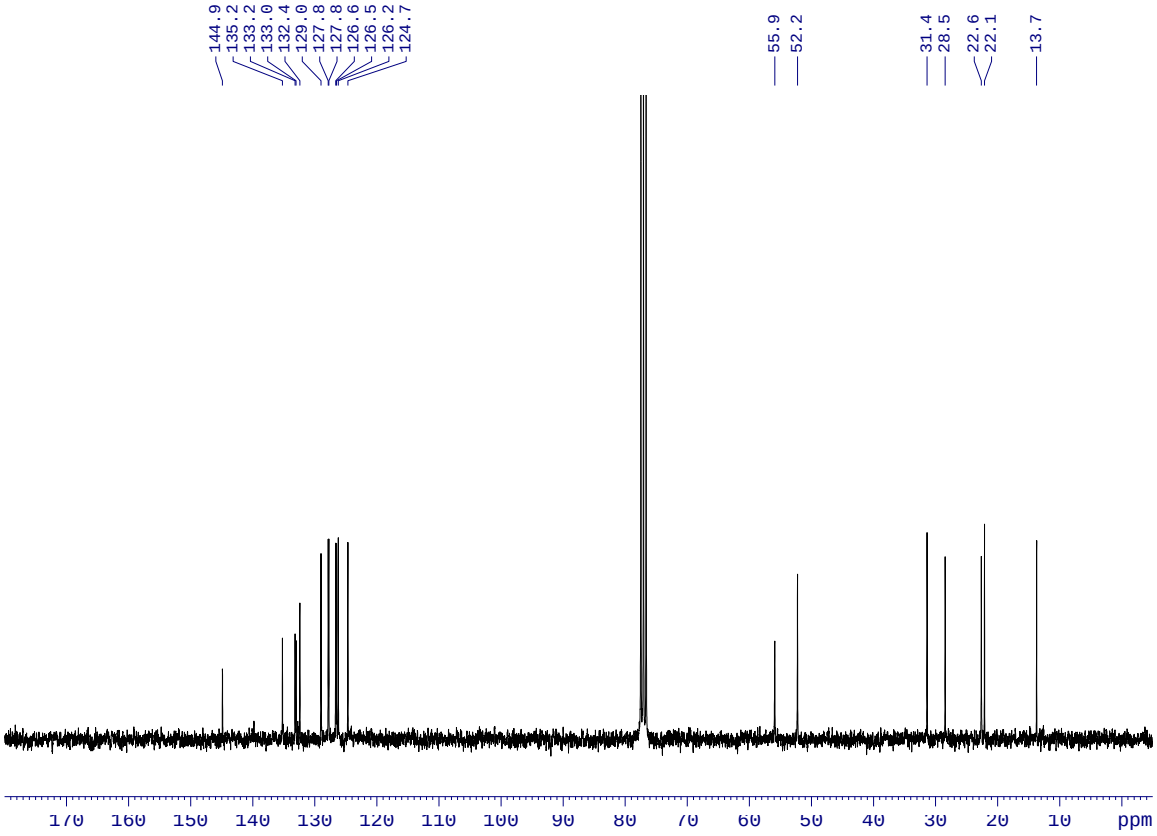


15b

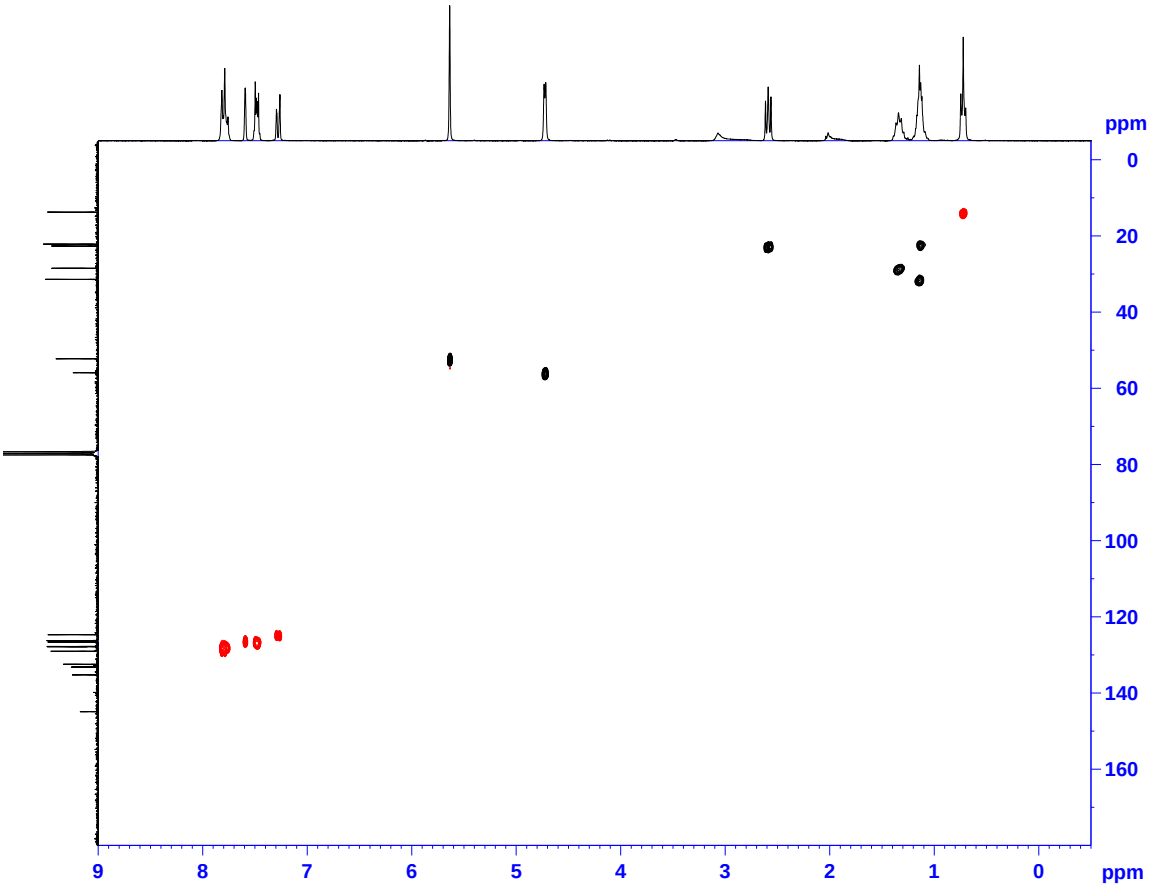
^{1}H NMR (300 MHz, $CDCl_3$)



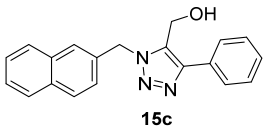
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

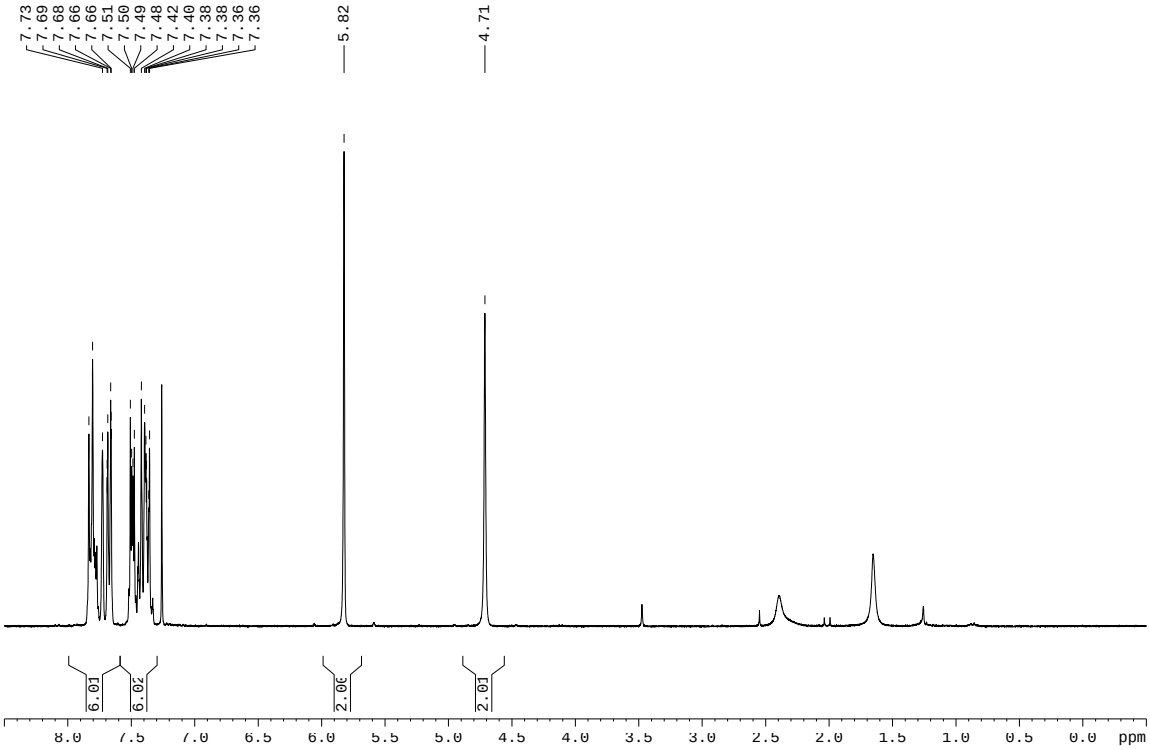


Compound 15c

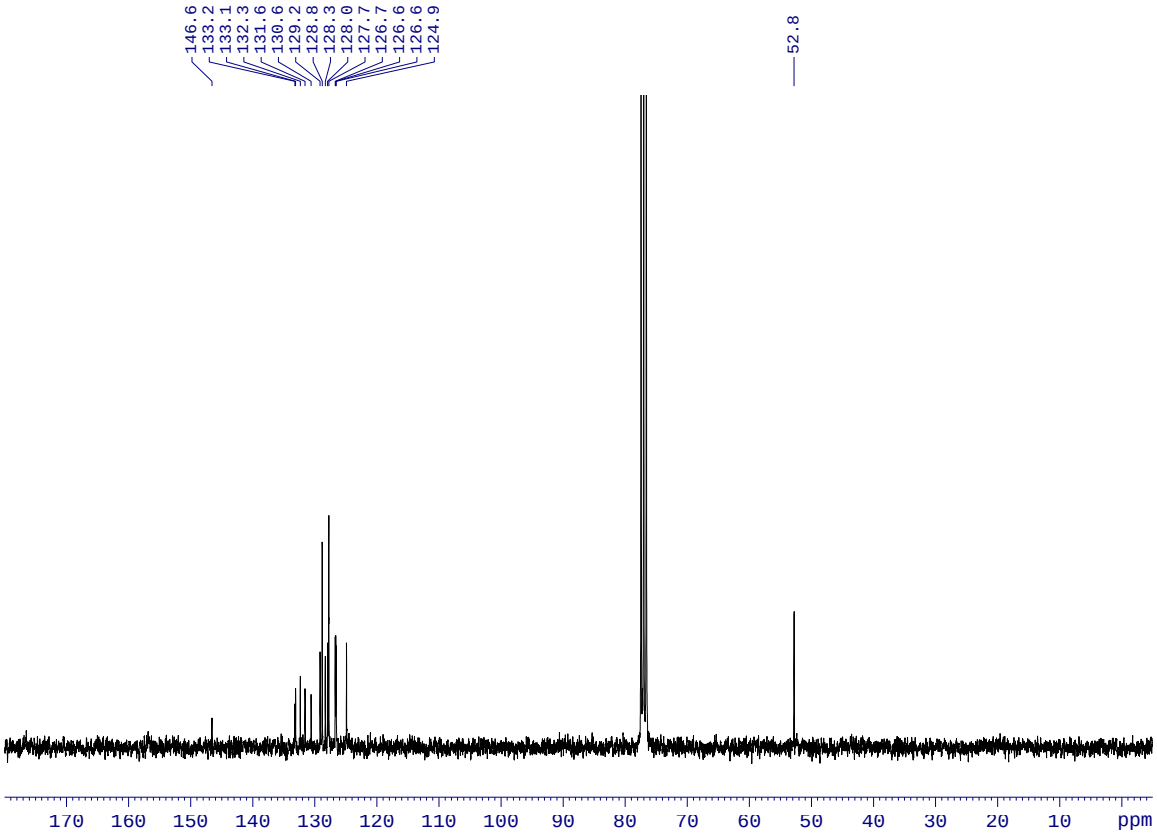


15c

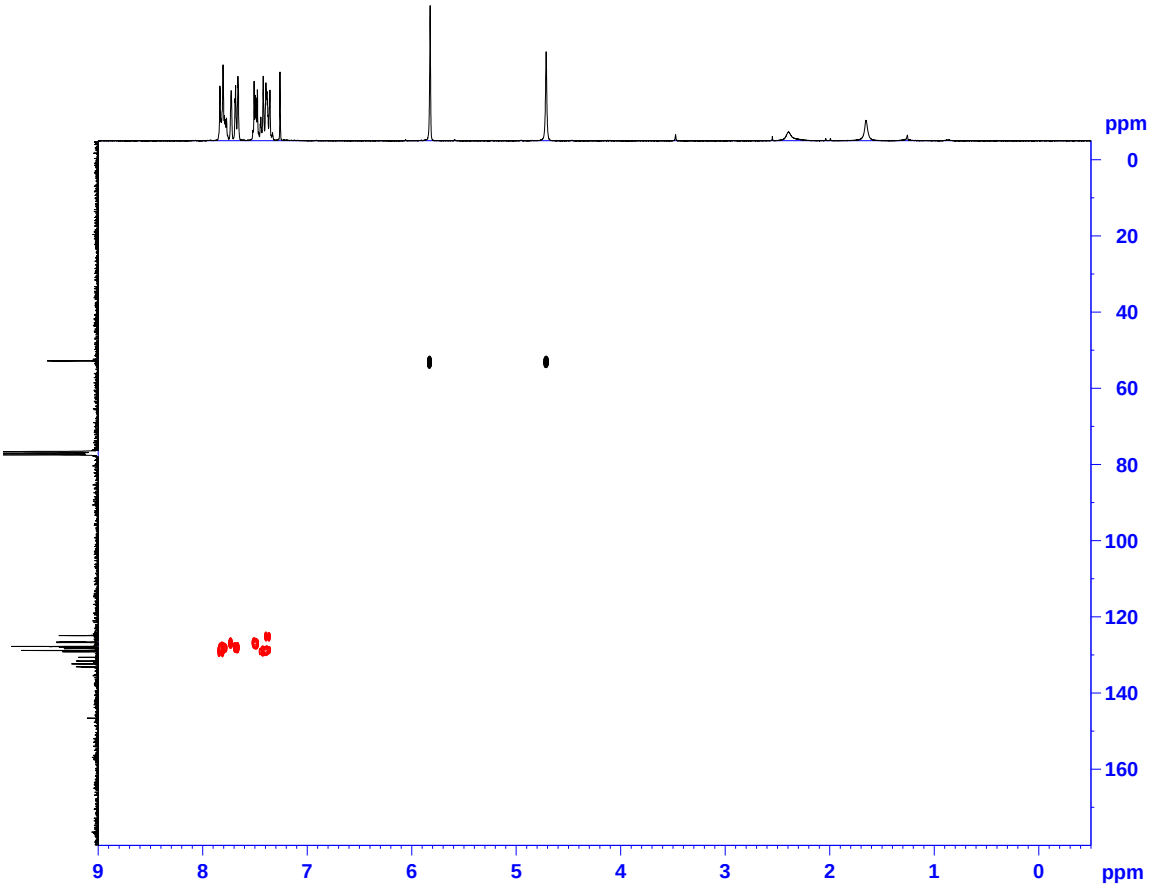
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



HSQC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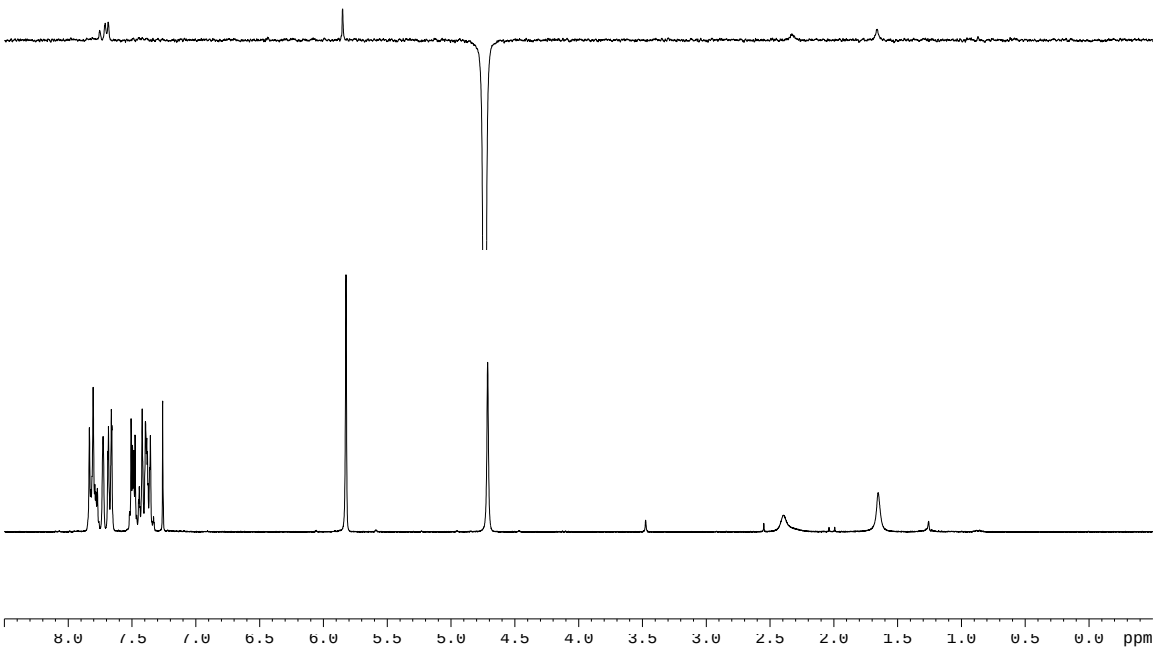
ppm

NOE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5.5
5.0
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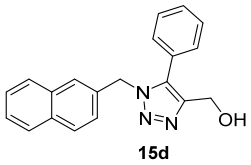
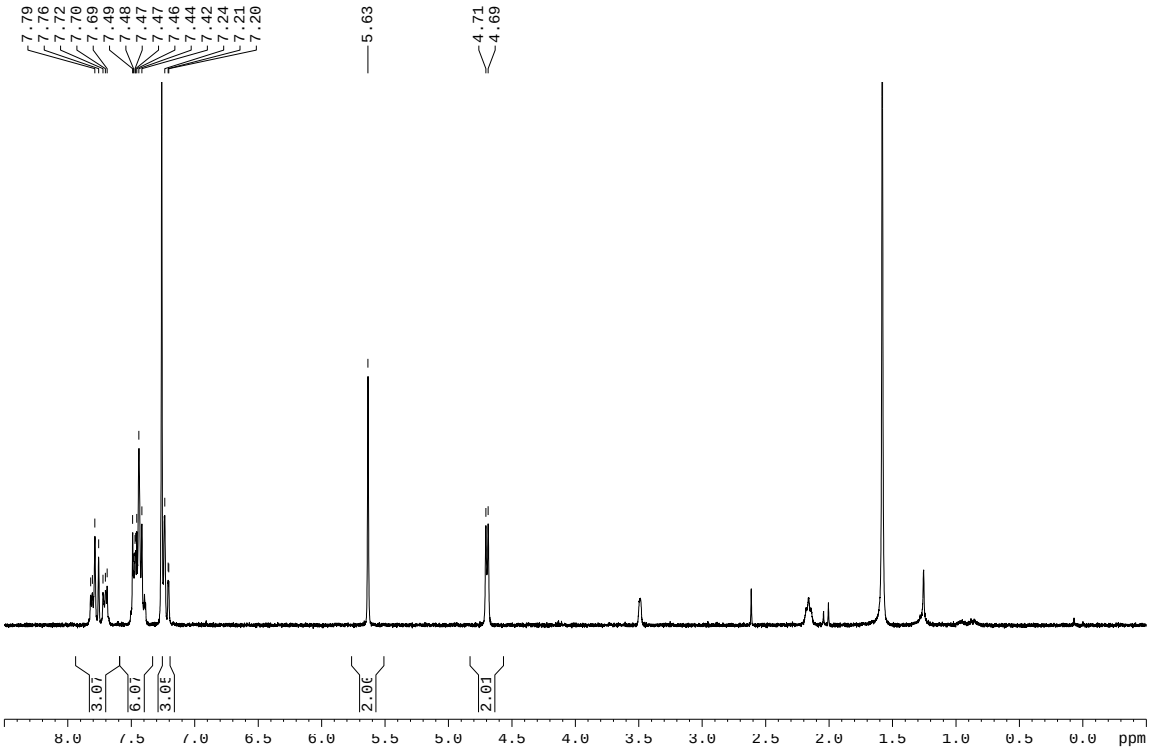
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

Compound 15d

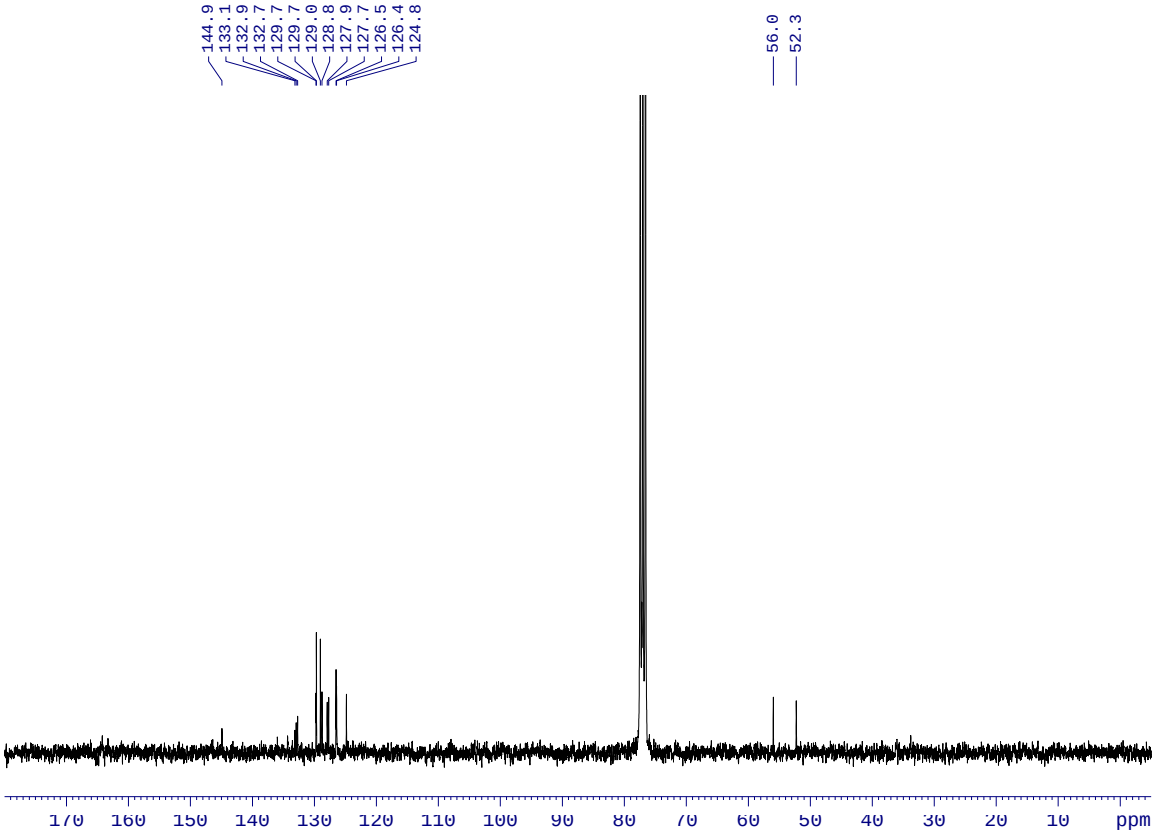


15d

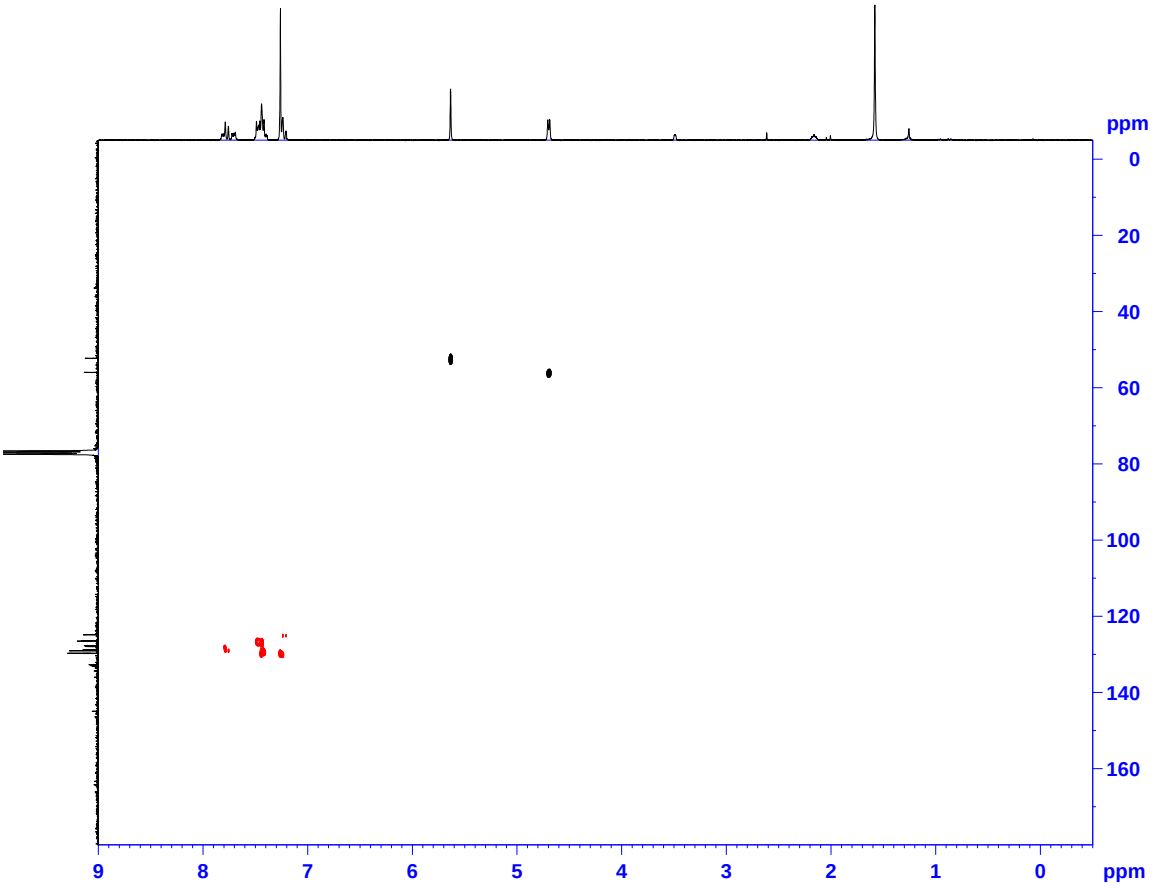
^{1}H NMR (300 MHz, $CDCl_3$)



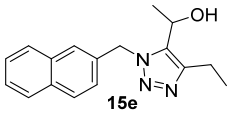
^{13}C NMR (75 MHz, $CDCl_3$)



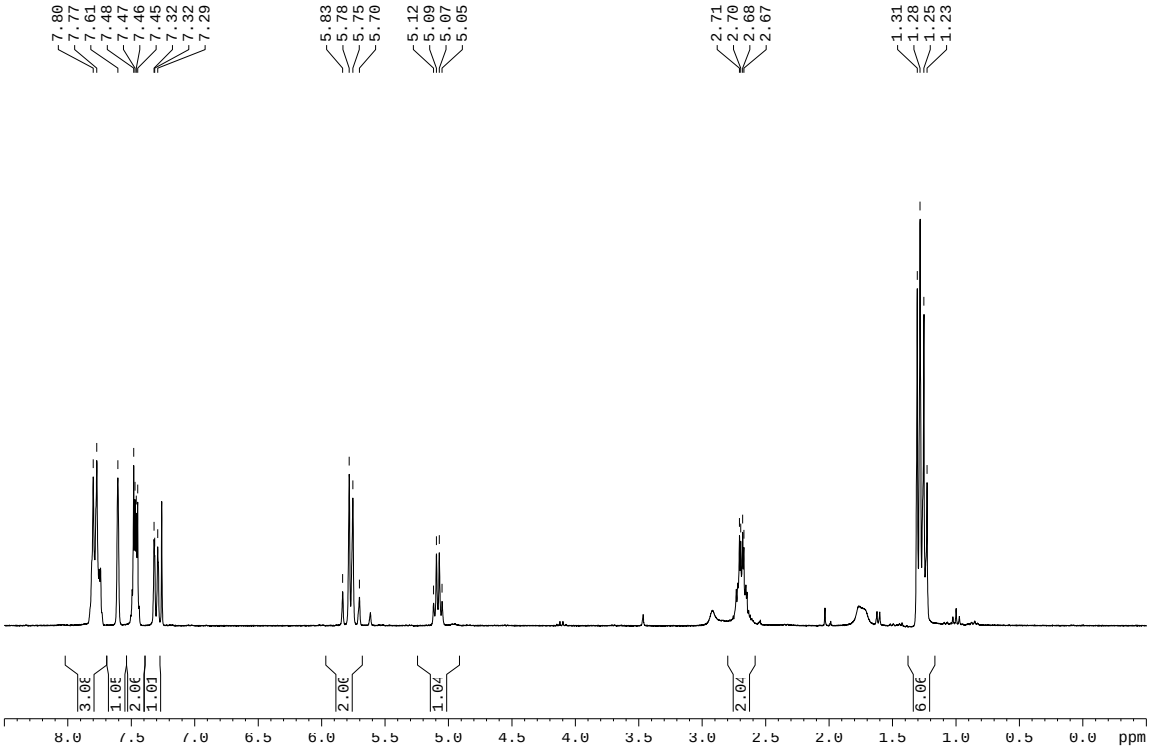
HSQC



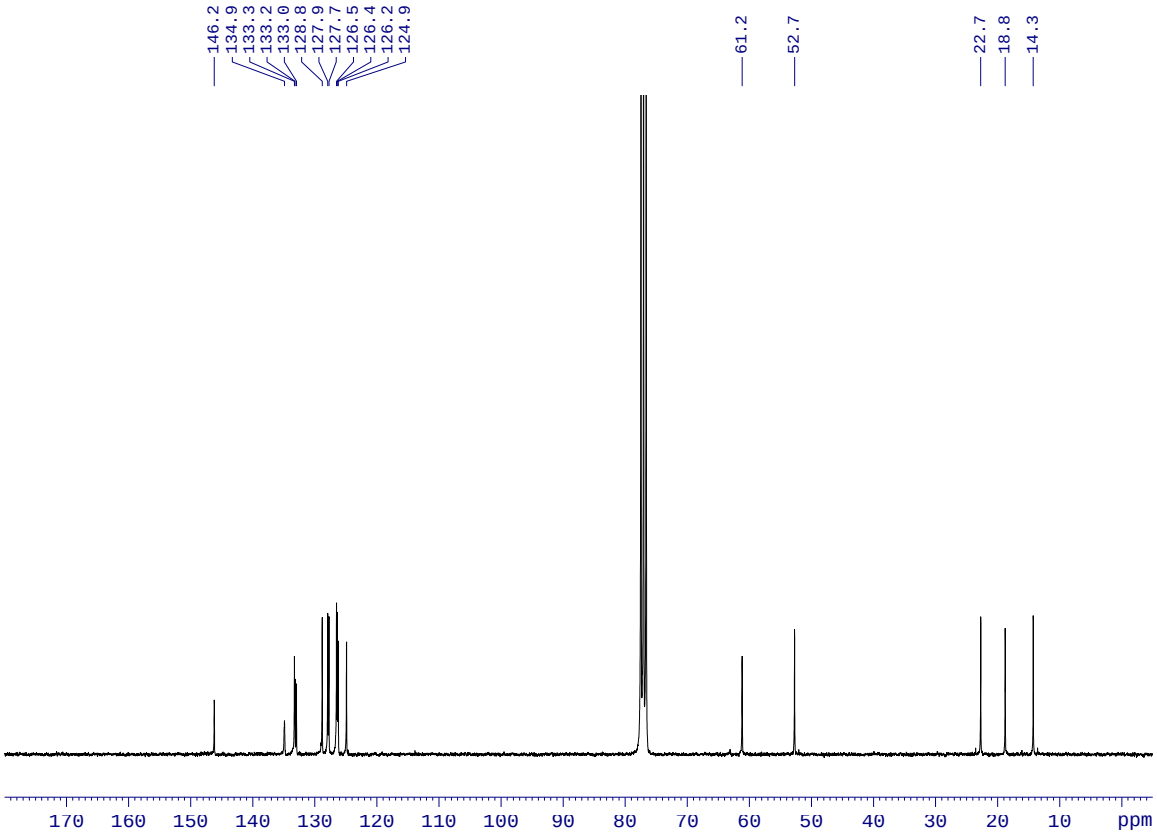
Compound 15e



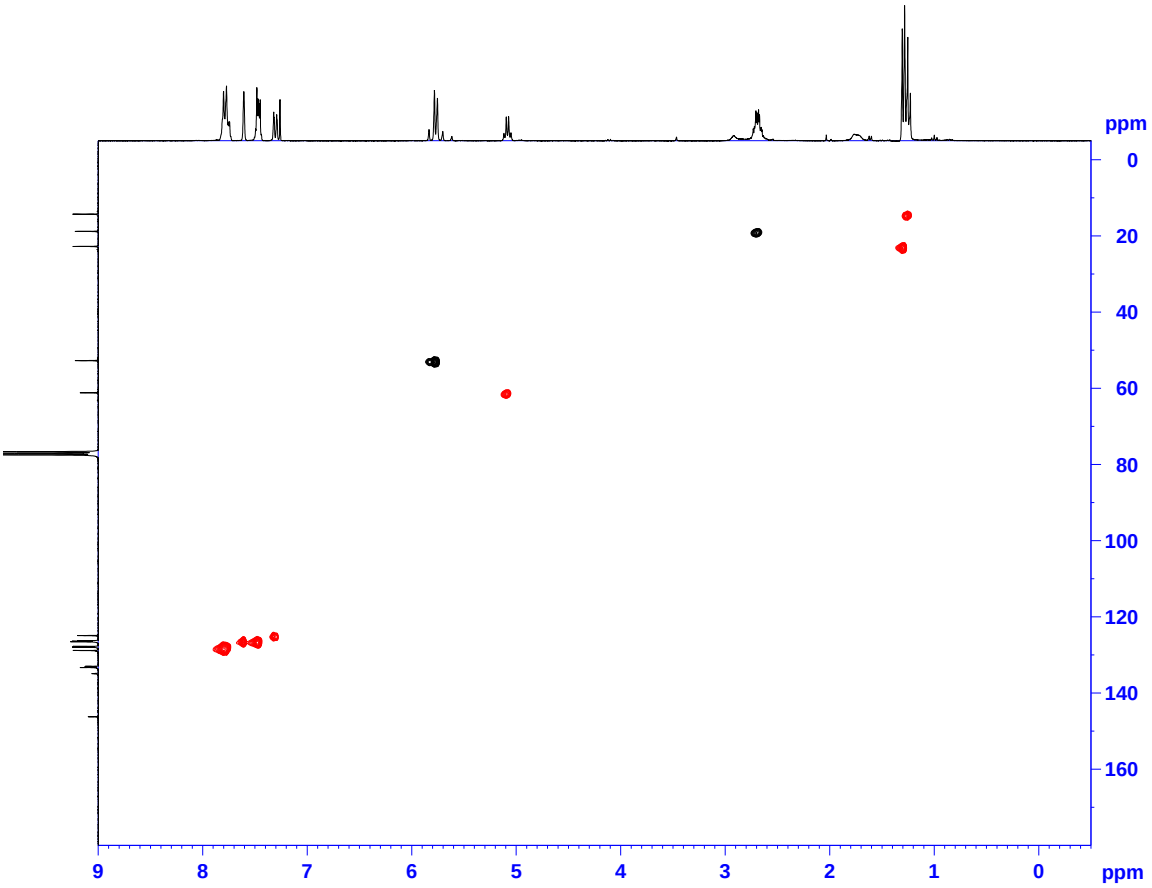
^{1}H NMR (300 MHz, $CDCl_3$)



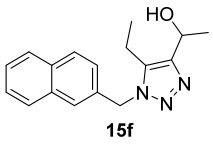
^{13}C NMR (75 MHz, $CDCl_3$)



HSQC

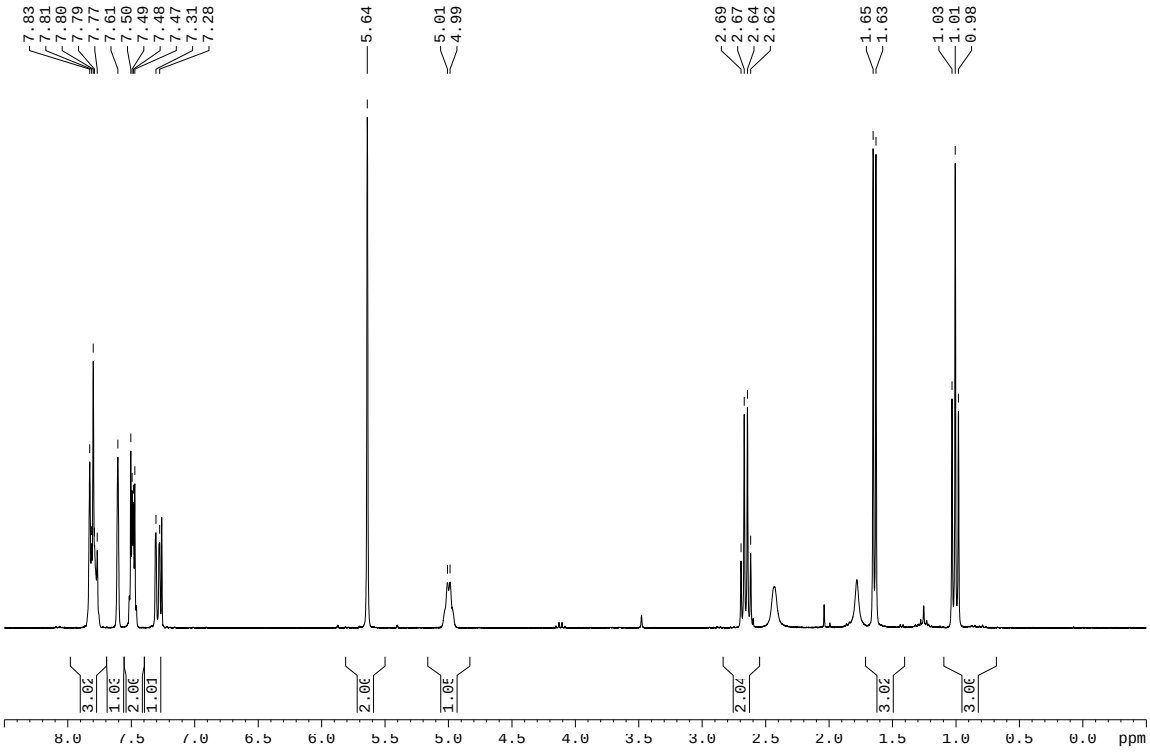


Compound 15f

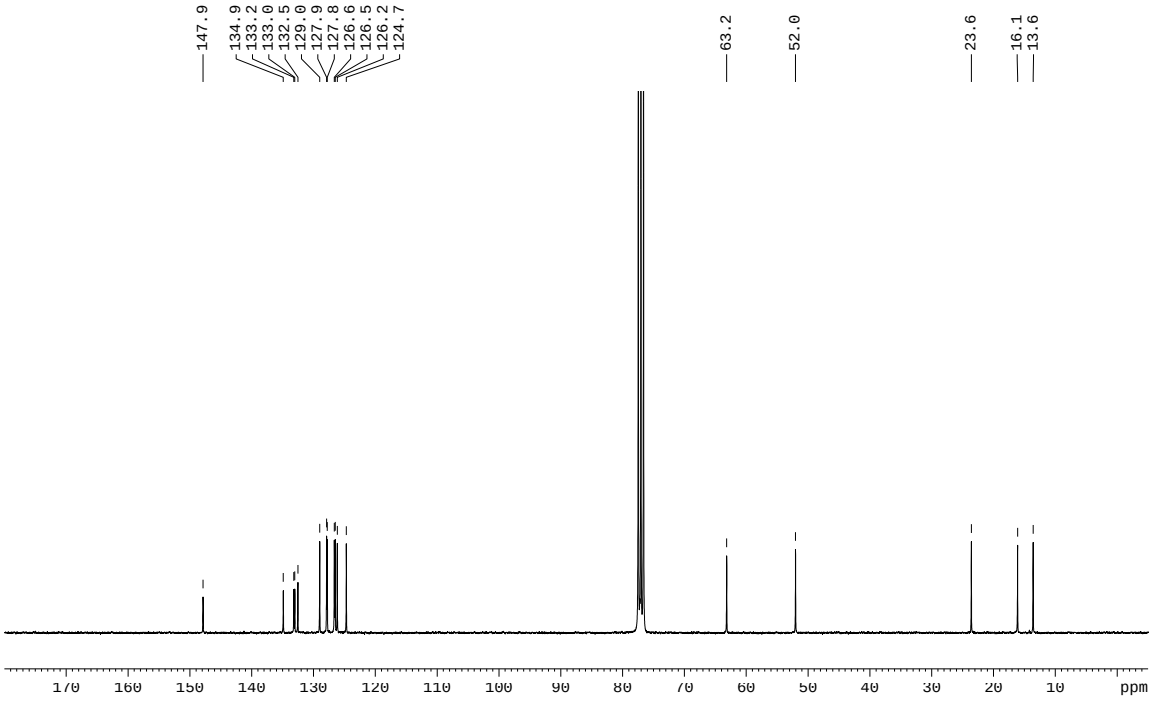


15f

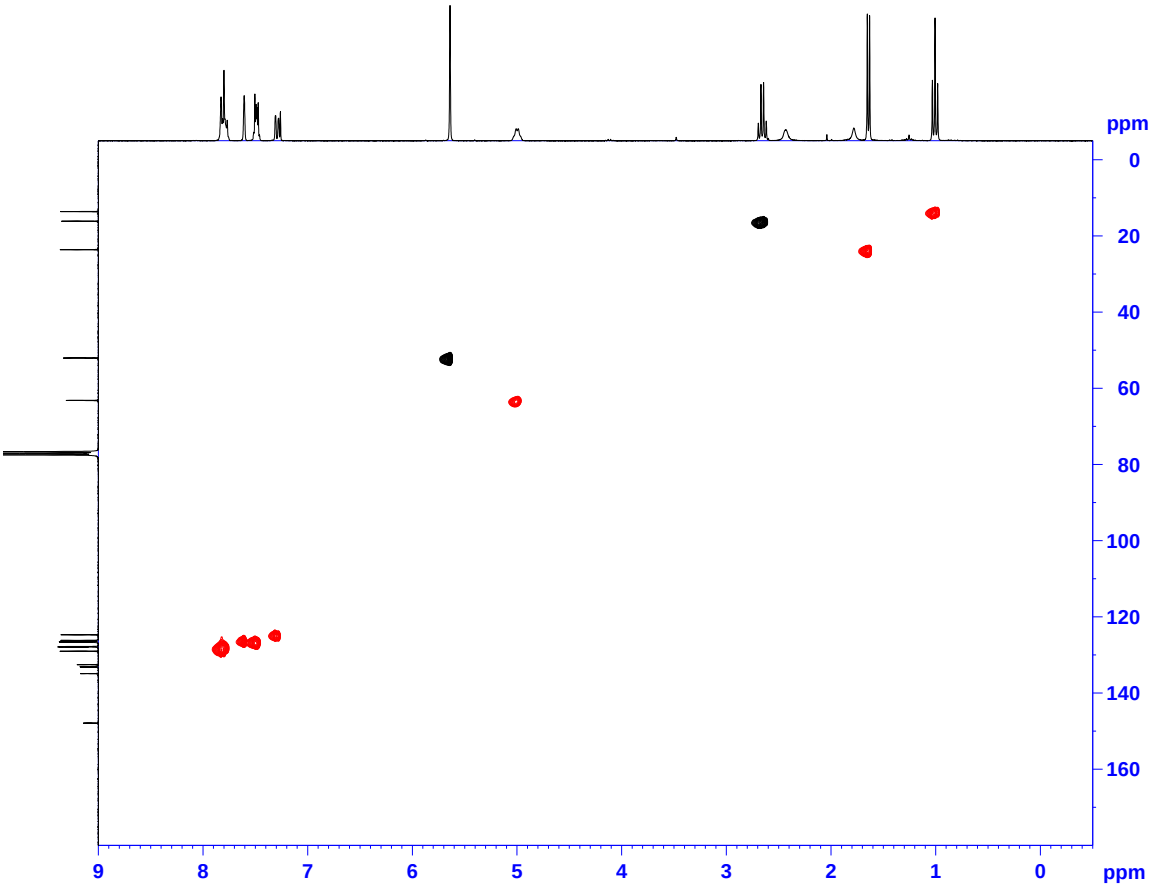
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



HSQC


ppm
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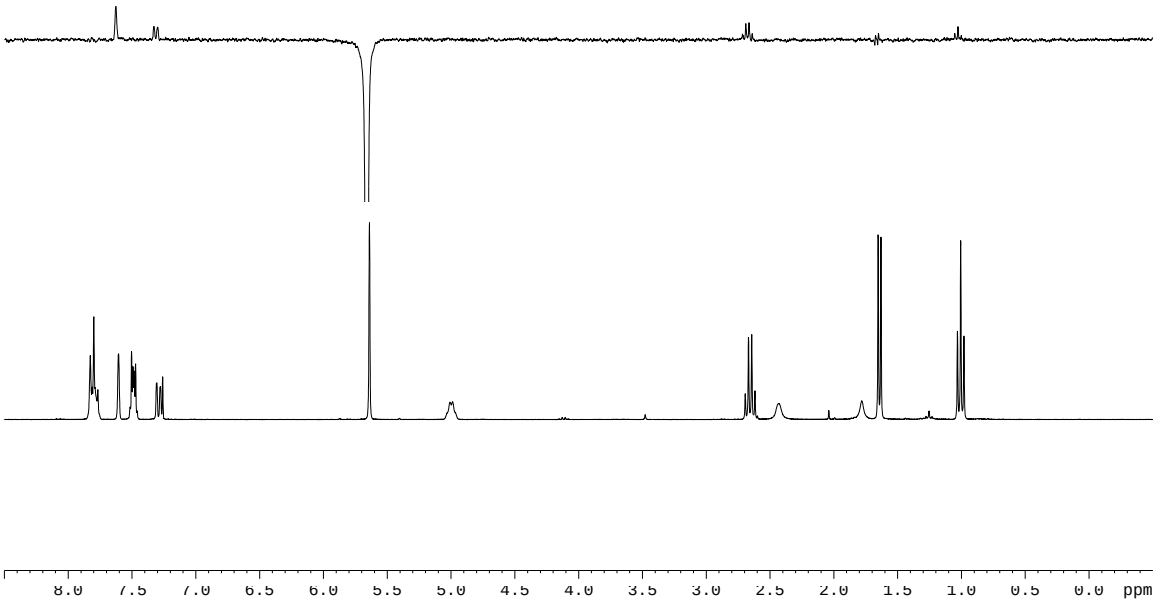
6
5
4
3
2
1
0
ppm

NOE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2.5
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1.0
0.5
0.0
ppm