

Supporting Information

Efficient Synthetic One-Pot Strategy for the Highly Regioselective Metal-Free Synthesis of 1,4-Disubstituted-1,2,3-Triazoles

Akbar Ali,^a Arlene G. Corrêa,^a Diego Alves,^b Julio Zukerman-Schpector,^a Bernhard Westermann,^c Marco A. B. Ferreira^a and Márcio W. Paixão^{*a}

Department of Chemistry, Federal University of São Carlos (UFSCar), São Carlos, SP, Brazil.

CEP:13565-905. Tel: +55 55 3351 8215

^b Department of Chemistry, Universidade Federal de Pelotas (UFPel), Pelotas, RS, Brazil.

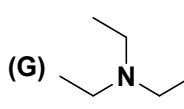
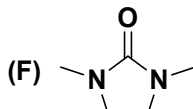
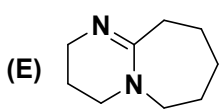
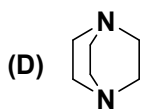
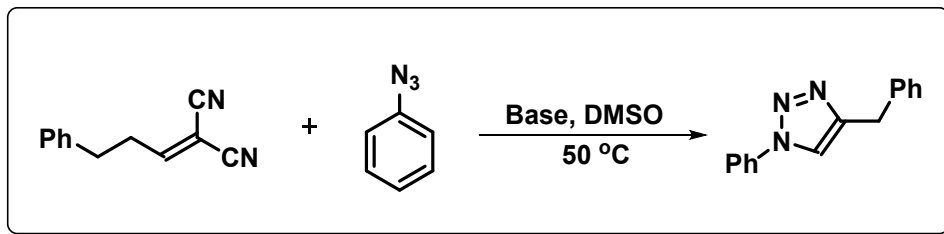
^c Department of Bioorganic Chemistry, Leibniz-Institute of Plant and Biochemistry, Halle, Germany.

Corresponding Author*: E-mail: mwpaixao@ufscar.br

General Experimental;

All solvents were dried and distilled prior to use by standard procedures. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz. for ^1H and 100 MHz for ^{13}C , respectively. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane (TMS), and coupling constants (J) are reported in hertz. High-resolution mass spectra (HRMS) were recorded using electron spray ionization (ESI) (Hybrid linear ion trap–orbitrap FT-MS and QqTOF/MS – Microtof – QII models). Melting points were determined using BUCHI melting point M-560 melting point meter. Flash column chromatography was carried out using silica gel 60 (230–400 mesh), and analytical thin-layer chromatography (TLC) was performed using silica gel aluminum sheets. HPLC chromatograms were obtained using apparatus with LC-10AT pump, a SPD-10A UV–vis detector, and an SCL-10A system controller using a Chiralcel OD-H column (4.6 mm diameter \times 250 mm length, particle size 5 μm). Optical rotations were measured with a Schmidt + Haensch Polartronic H Polarimeter, at 589 nm and 30 $^\circ\text{C}$ using a 1 mL cell with a 1 dm path length.

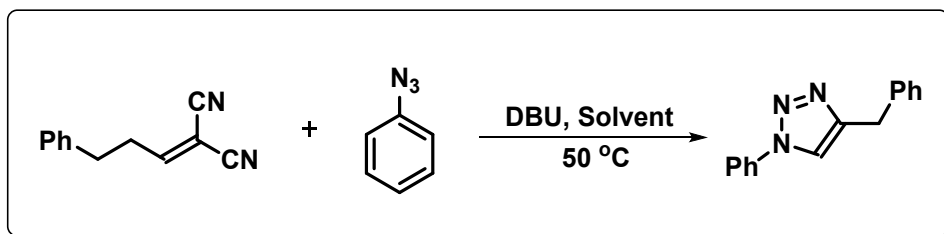
Optimization Table: (Base Screening)



Entry	Base	Time (hours)	Yield (%)
1	KF (A)	24	28
2	Guanidine carbonate (B)	24	23
3	CsCO ₃ (C)	24	41
4	DABCO (D)	24	05
5	DBU (E)	12	70
6	-----	24	----
7 ^a	DBU	24	40
8	DMI (F)	24	traces
9	TEA (G)	24	04

Unless otherwise noted, reactions were performed using alkydienenitrile (0.3 mmol), arylazide (0.6 mmol), and base (0.3 mmol) in 0.5 mL of DMSO. Yields are given for isolated products. ^a20 mol% of DBU was used.

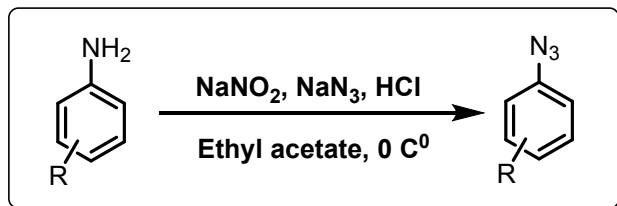
Optimization Table: (Solvent Screening)



Entry	Solvent	Yield (%)
1	CHCl ₃	14
2	CH ₃ OH	Traces
3	Toluene	24
4	DMSO	70
5	CH ₃ CN	34
6	DMF	42
7	THF	16
8	DMSO/H ₂ O (1:1)	35
9	DMSO/DMF (1:1)	49

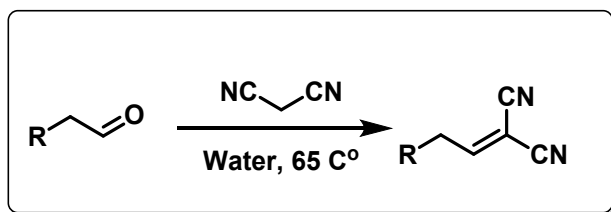
Unless otherwise noted, reactions were performed using alkylidene malononitrile (0.3 mmol), arylazide (0.6 mmol), and 1,8-diazabicyclo [5.4.0]undec-7-ene (0.3 mmol) in 0.5 mL of solvent. Yields are given for isolated products.

General method for the synthesis of aryl azides:



To a solution of arylamine (21.9 mmol) in ethyl acetate (40 mL) and water (5 mL) was added concentrated hydrochloric acid (12 mL) at $0\text{ }^\circ\text{C}$ for 10 min. Then a solution of sodium nitrite (37.0 mmol) in water (7.5 mL) was dropwise added. Upon completion of the addition, the reaction mixture was stirred for 30 min at the same reaction temperature. A solution of sodium azide (37.1 mmol) in water (8 mL) was subsequently added over a period of 5 min. After stirring at $0\text{ }^\circ\text{C}$ for 30 min, the reaction mixture was diluted with water (50 mL), and extracted with ethyl acetate (2x50 mL). The combined organic layer was washed with dilute sodium hydroxide solution, then with water, dried over anhydrous sodium sulfate and concentrated on a rotary evaporator. The crude compound was purified by column chromatography on silica gel with eluting with ethyl acetate/n-hexane as eluent (20:1 v/v).¹

General procedure for the synthesis of alkylidenemalononitrile:

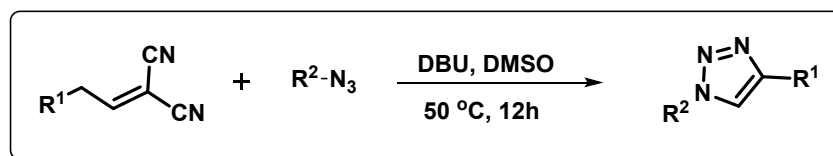


In a 50 mL round bottom flask containing a solution of aldehyde (10 mmol) in 10 mL of distilled water malononitrile (10 mmol) was dropwise added at $0\text{ }^\circ\text{C}$. The solution was vigorously stirred for 1 h at $65\text{ }^\circ\text{C}$. The reaction mixture was extracted with diethyl ether (2x50 mL). The combined organic layer was

dried over anhydrous sodium sulfate and concentrated on a rotary evaporator. The crude compound was purified by column chromatography on silica gel with eluting with ethyl acetate/n-hexane as eluent (10:1 to 5:1 vv).²

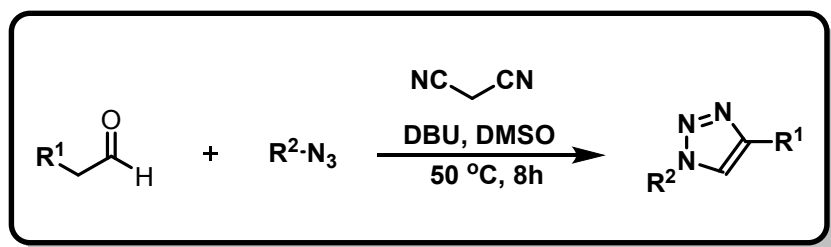
General procedure for the synthesis of substituted 1,2,3-triazoles:

Method (A): Using aromatic azides with preformed alkylidenemalononitrile;



In a 10 mL round bottom flask DBU (0.3 mmol) was added to a pre-stirred mixture of aryl azide (0.6 mmol) and alkylidenemalononitrile (0.3 mmol) in 0.5 mL of DMSO. The reaction mixture was then stirred for 12 hours at 50 °C. The reaction mixture was cooled to rt and extracted with ethyl acetate (2x20 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated on a rotary evaporator. The crude compound was purified by column chromatography on silica gel with eluting with ethyl acetate/n-hexane as eluent (10:1 to 5:1 vv).

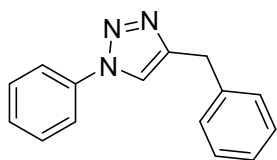
Method (B): One-pot strategy using aldehyde, malononitrile and aromatic azides.



In a 10 mL round bottom flask DBU (0.3 mmol) was added to a pre-stirred mixture of aldehyde (0.3 mmol), malononitrile (0.3 mmol) and aryl azide (0.6 mmol) and in 0.5 mL of DMSO. The reaction mixture was then stirred for 8 hours at 50 °C. The reaction mixture was cooled to rt and extracted with ethyl acetate (2x20 mL). The combined organic layer was dried over anhydrous sodium sulfate and

concentrated on a rotary evaporator. The crude compound was purified by column chromatography on silica gel with eluting with ethyl acetate/n-hexane as eluent (10:1 to 5:1 vv).

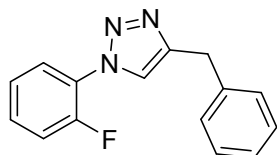
4-benzyl-1-phenyl-1*H*-1,2,3-triazole (3a):



Following general procedure, 4-benzyl-1-phenyl-1*H*-1,2,3-triazole was synthesized in 70% (method A) and 42% (method B) yield after column chromatography as white solid. Analytical data are in agreement with previous published data.³

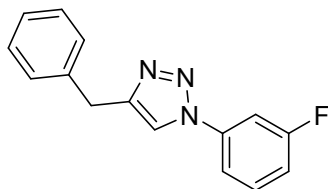
¹H NMR (400 MHz, CDCl₃) δ 7.72 – 7.64 (m, 2H), 7.59 (s, 1H), 7.49 – 7.45 (m, 2H), 7.41-7.22 (m, 6H), 4.17 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ = 148.5, 138.8, 137.2, 129.6, 128.8, 128.7, 128.5, 126.6, 120.4, 119.7, 32.3 ppm.

4-benzyl-1-(2-fluorophenyl)-1*H*-1,2,3-triazole (3b):



The title compound was synthesized according to the general procedure in 73% (method A) and 48% (method B) isolated yield as yellow solid (m.p: 59-61 °C). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (td, *J* = 7.8, 1.7 Hz, 1H), 7.73 (d, *J* = 2.9 Hz, 1H), 7.43 – 7.14 (m, 8H), 4.19 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ = 148.0, 138.7, 129.9, 129.8, 128.7, 126.6, 125.2, 124.8, 122.8, 122.7, 117.0, 116.8, 32.2 ppm. ESI-MS (*m/z*) calcd for C₁₅H₁₃N₃F [M + H]⁺ 254.1088, found 254.1082.

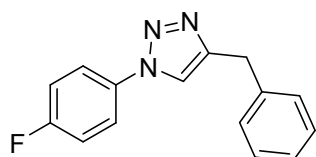
4-benzyl-1-(3-fluorophenyl)-1H-1,2,3-triazole (3c):



The title compound was synthesized according to the general procedure in 60% (method A) and 46% (method B) isolated yield as yellow solid (m.p: 71-73 °C).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.58 (s, 1H), 7.52 – 7.43 (m, 3H), 7.38 – 7.21 (m, 5H), 7.15 – 7.06 (m, 1H), 4.17 (s, 2H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 164.4, 161.9, 148.8, 138.6, 131.1, 128.8, 126.7, 119.5, 115.6, 115.3, 108.2, 107.9, 32.3 ppm. ESI-MS (m/z) calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{F}$ [M + H] $^+$ 254.1088, found 254.1082.

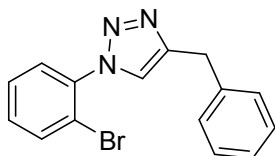
4-benzyl-1-(4-fluorophenyl)-1H-1,2,3-triazole (3d):



The title compound was synthesized according to the general procedure in 59% (method A) isolated yield as pale yellow solid (m.p: 81-83 °C).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.70 – 7.61 (m, 2H), 7.54 (s, 1H), 7.37 – 7.25 (m, 5H), 7.24 – 7.13 (m, 2H), 4.17 (s, 2H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 161.0, 148.6, 138.7, 128.7, 126.7, 122.4, 122.3, 119.8, 116.7, 116.6, 32.3 ppm. ESI-MS (m/z) calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{F}$ [M + H] $^+$ 254.1088, found 254.1085.

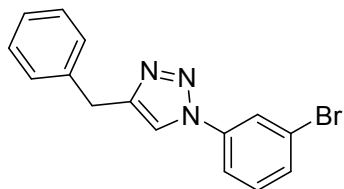
4-benzyl-1-(2-bromophenyl)-1H-1,2,3-triazole (3e):



The title compound was synthesized according to the general procedure in 48% (method A) isolated yield as red viscous oil.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.72 (dd, J = 8.0, 1.3 Hz, 1H), 7.61 – 7.43 (m, 3H), 7.43 – 7.27 (m, 5H), 7.23 (dd, J = 4.7, 3.8 Hz, 1H), 4.20 (s, 2H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 133.8, 131.0, 129.7, 129.2, 128.8, 128.7, 128.4, 128.2, 127.7, 126.6, 123.7, 118.6, 32.2 ppm. ESI-MS (m/z) calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{Br}$ [M + H] $^+$ 314.0287, found 314.0288.

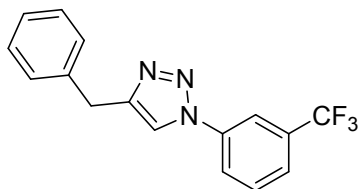
4-benzyl-1-(3-bromophenyl)-1*H*-1,2,3-triazole (3f):



The title compound was synthesized according to the general procedure in 71% (method A) and 45 % (method B) isolated yield as red solid (m.p: 67-69 °C).

¹H NMR (400 MHz, CDCl₃) δ 7.87 (t, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.60 – 7.49 (m, 2H), 7.32 (tt, *J* = 16.1, 5.1 Hz, 6H), 4.17 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ = 148.8, 138.6, 138.0, 131.5, 131.0, 128.8, 128.5, 126.7, 123.4, 123.2, 119.5, 118.8, 32.3 ppm. ESI-MS (m/z) calcd for C₁₅H₁₃N₃Br [M + H]⁺ 314.0287, found 314.0291.

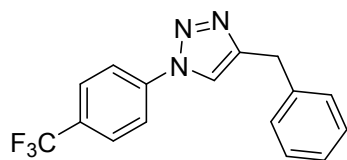
4-benzyl-1-(3-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (3g):



The title compound was synthesized according to the general procedure in 62% (method A) isolated yield as red viscous oil.

¹H NMR (400 MHz, CDCl₃) δ 7.93 (ddd, *J* = 9.2, 6.9, 1.1 Hz, 2H), 7.69 – 7.60 (m, 3H), 7.37 – 7.30 (m, 4H), 7.29 – 7.24 (m, 1H), 4.18 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ = 149.1, 138.5, 137.4, 132.5, 132.2, 130.5, 128.8, 126.8, 125.1, 123.4, 119.5, 117.3, 117.2, 32.3 ppm. ESI-MS (m/z) calcd for C₁₆H₁₃N₃F₃ [M + H]⁺ 304.1056, found 304.1051

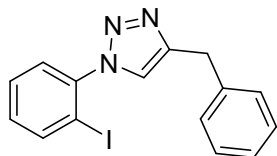
4-benzyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (3h):



The title compound was synthesized according to the general procedure in 57% (method A) and 43% (method B) isolated yield as yellow solid (m.p: 74-76 °C).

¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.6 Hz, 2H), 7.65 (s, 1H), 7.41 – 7.21 (m, 5H), 4.19 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ = 139.5, 138.4, 128.9, 128.8, 127.3, 127.0, 127.0, 126.8, 120.3, 120.2, 119.4, 116.0, 32.3 ppm. ESI-MS (m/z) calcd for C₁₆H₁₃N₃F₃ [M + H]⁺ 304.1056, found 304.1055.

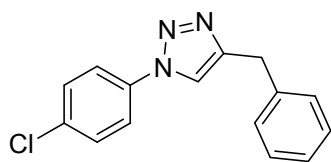
4-benzyl-1-(2-iodophenyl)-1*H*-1,2,3-triazole (3i):



The title compound was synthesized according to the general procedure in 44% (method A) isolated yield as red viscous oil.

¹H NMR (400 MHz, CDCl₃) δ 7.97 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.52 – 7.40 (m, 3H), 7.40 – 7.16 (m, 6 H), 4.21 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ = 147.5, 140.2, 138.8, 131.3, 129.8, 129.2, 128.8, 128.7, 127.8, 126.6, 123.6, 93.9, 32.2 ppm. ESI-MS (*m/z*) calcd for C₁₅H₁₃N₃I [M + H]⁺ 362.0148, found 362.0141.

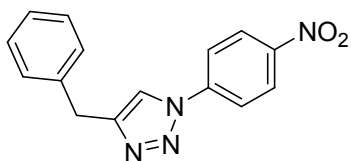
4-benzyl-1-(3-chlorophenyl)-1*H*-1,2,3-triazole (3j):



The title compound was synthesized according to the general procedure in 58% (method A) isolated yield as yellow solid (m.p: 110-112 °C).

¹H NMR (400 MHz, CDCl₃) δ 7.71 – 7.54 (m, 2H), 7.56 (s, 1H), 7.47 – 7.43 (m, 2H), 7.36 – 7.22 (m, 5H), 4.16 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ = 148.8, 138.6, 135.6, 134.3, 129.8, 128.8, 128.6, 126.7, 121.5, 119.5, 32.3 ppm. ESI-MS (*m/z*) calcd for C₁₅H₁₃N₃Cl [M + H]⁺ 270.0792, found 270.0782.

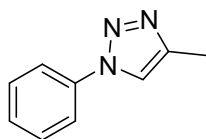
4-benzyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole (3k):



The title compound was synthesized according to the general procedure in 58% (method A) isolated yield as pale yellow solid (m.p: 98-100 °C).

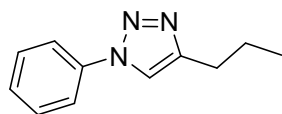
¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.65 (m, 2H), 7.59 (s, 1H), 7.51 – 7.45 (m, 2H), 7.42 – 7.32 (m, 3H), 7.31 – 7.21 (m, 2H), 4.17 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ = 148.5, 138.8, 137.2, 129.6, 128.8, 128.7, 128.5, 126.6, 120.42, 119.6, 32.3 ppm. ESI-MS (*m/z*) calcd for C₁₅H₁₃N₄O₂ [M + H]⁺ 281.1038, found 281.1039.

4-methyl-1-phenyl-1*H*-1,2,3-triazole (3l):



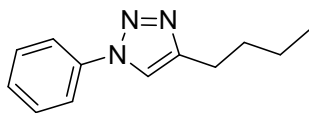
The title compound was synthesized according to the general procedure in 89% (method B) and 61% (method A) isolated yield as yellow solid. Analytical data are in agreement with previous published data.⁴ **¹H NMR** (400 MHz, CDCl₃) δ 7.68 – 7.60 (m, 3H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 2.37 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 143.0, 136.2, 128.6, 127.4, 119.4, 118.3, 9.4 ppm.

4-propyl-1-phenyl-1*H*-1,2,3-triazole (3m):



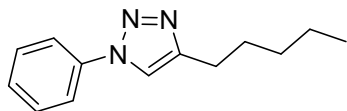
The title compound was synthesized by following the general procedure in 86% (method B) and 55% (method A) isolated yield as brown solid. Analytical data are in agreement with previous published data.⁴ **¹H NMR** (400 MHz, CDCl₃) δ 7.77 – 7.67 (m, 3H), 7.56 – 7.38 (m, 3H), 2.78 (t, *J* = 7.6 Hz, 2H), 1.84 – 1.70 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 148.9, 137.3, 129.6, 128.4, 120.4, 118.8, 27.8, 22.6, 13.8 ppm.

4-butyl-1-phenyl-1*H*-1,2,3-triazole (3n):



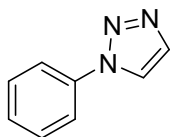
The title compound was prepared by using the general procedure in 75% (method B) and 55% (method A) isolated yield as yellow viscous oil. Analytical data are in agreement with previous published data.⁵ **¹H NMR** (400 MHz, CDCl₃) δ 7.77 – 7.68 (m, 3H), 7.57 – 7.47 (m, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 2.85 – 2.76 (m, 2H), 1.73 (dt, *J* = 15.4, 7.5 Hz, 2H), 1.44 (dq, *J* = 14.7, 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 149.2, 137.3, 129.6, 128.4, 120.4, 118.8, 31.5, 25.3, 22.3, 13.8 ppm.

4-pentyl-1-phenyl-1*H*-1,2,3-triazole (3o):



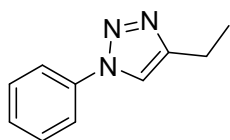
The title compound was synthesized by the general procedure in 86% (method B) and 65% (method A) isolated yield as yellow oil. Analytical data are in agreement with previous published data.⁴ **¹H NMR** (400 MHz, CDCl₃) δ 7.77 – 7.68 (m, 3H), 7.55 – 7.34 (m, 3H), 2.84 – 2.75 (m, 2H), 1.87 – 1.65 (m, 2H), 1.55 – 1.30 (m, 4H), 0.91 (t, J = 7.1 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 149.2, 137.3, 129.6, 128.4, 120.4, 118.8, 31.4, 29.1, 25.6, 22.4, 14.0 ppm.

1-phenyl-1*H*-1,2,3-triazole (3p):



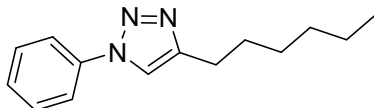
The title compound was prepared according to the general procedure in 64 % (method B) and 35% (method A) isolated yield as pale brown solid. Analytical data are in agreement with previous published data.⁴ **¹H NMR** (400 MHz, CDCl₃) δ 8.00 (d, J = 1.1 Hz, 1H), 7.86 (d, J = 1.1 Hz, 1H), 7.77 – 7.74 (m, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.47 (dt, J = 4.1, 1.6 Hz, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ = 137.0, 134.5, 129.8, 128.8, 12.7, 120.7 ppm.

4-ethyl-1-phenyl-1*H*-1,2,3-triazole (3q):



The title compound was synthesized according to the general procedure in 96% (method B) and 61% (method A) isolated yield as yellow liquid. Analytical data are in agreement with previous published data.⁴ **¹H NMR** (400 MHz, CDCl₃) δ 7.72 (ddd, J = 4.6, 3.6, 1.9 Hz, 3H), 7.56 – 7.37 (m, 3H), 2.85 (q, J = 7.3 Hz, 2H), 1.35 (t, J = 7.6 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 150.6, 137.3, 129.7, 128.4, 120.4, 118.4, 19.1, 13.6 ppm.

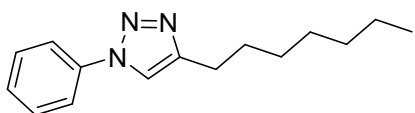
4-hexyl-1-phenyl-1*H*-1,2,3-triazole (3r):



The title compound was synthesized using the general procedure in 98% (method B) and 70% (method A) isolated yield as white solid.

Analytical data are in agreement with previous published data.⁵ **¹H NMR** (400 MHz, CDCl₃) δ 7.77 – 7.69 (m, 3H), 7.65 – 7.47 (m, 2H), 7.46 – 7.37 (m, 1H), 2.84 – 2.75 (m, 2H), 1.74 (dt, *J* = 15.4, 7.5 Hz, 2H), 1.69 – 1.01 (m, 6H), 0.90 (t, *J* = 6.1 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 149.2, 137.3, 129.7, 128.4, 120.4, 118.8, 31.5, 29.4, 28.9, 25.7, 22.6, 14.1 ppm

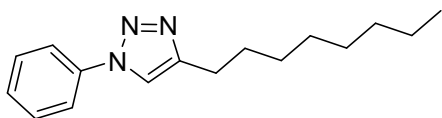
4-heptyl-1-phenyl-1*H*-1,2,3-triazole (3s):



The title compound was prepared according to the general procedure in 90% (method B) isolated yield as reddish viscous oil.

¹H NMR (400 MHz, CDCl₃) δ 7.77 – 7.67 (m, 3H), 7.57 – 7.36 (m, 3H), 2.84 – 2.75 (m, 2H), 1.73 (dt, *J* = 15.3, 7.6 Hz, 2H), 1.60 – 1.09 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 149.2, 137.3, 129.6, 128.4, 120.4, 118.8, 31.7, 29.4, 29.2, 29.0, 25.7, 22.6, 14.1 ppm. ESI-MS (*m/z*) calcd for C₁₅H₂₂N₃ [M + H]⁺ 244.1808, found 244.1804.

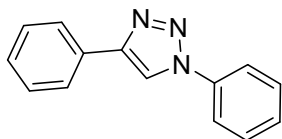
4-octyl-1-phenyl-1*H*-1,2,3-triazole (3t):



The title compound was synthesized according to the general procedure in 97% (method B) isolated yield as reddish viscous oil. Analytical data are in agreement with previous published

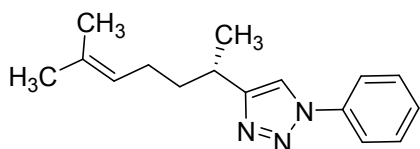
data.⁶ **¹H NMR** (400 MHz, CDCl₃) δ 7.76 – 7.66 (m, 3H), 7.56 – 7.37 (m, 3H), 2.84 – 2.75 (m, 2H), 1.73 (dt, *J* = 15.4, 7.6 Hz, 2H), 1.61 – 1.11 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 149.2, 137.3, 129.6, 128.4, 120.4, 118.7, 31.8, 29.4, 29.3, 29.3, 29.2, 25.7, 22.6, 14.1 ppm.

1,4-diphenyl-1*H*-1,2,3-triazole (3u):

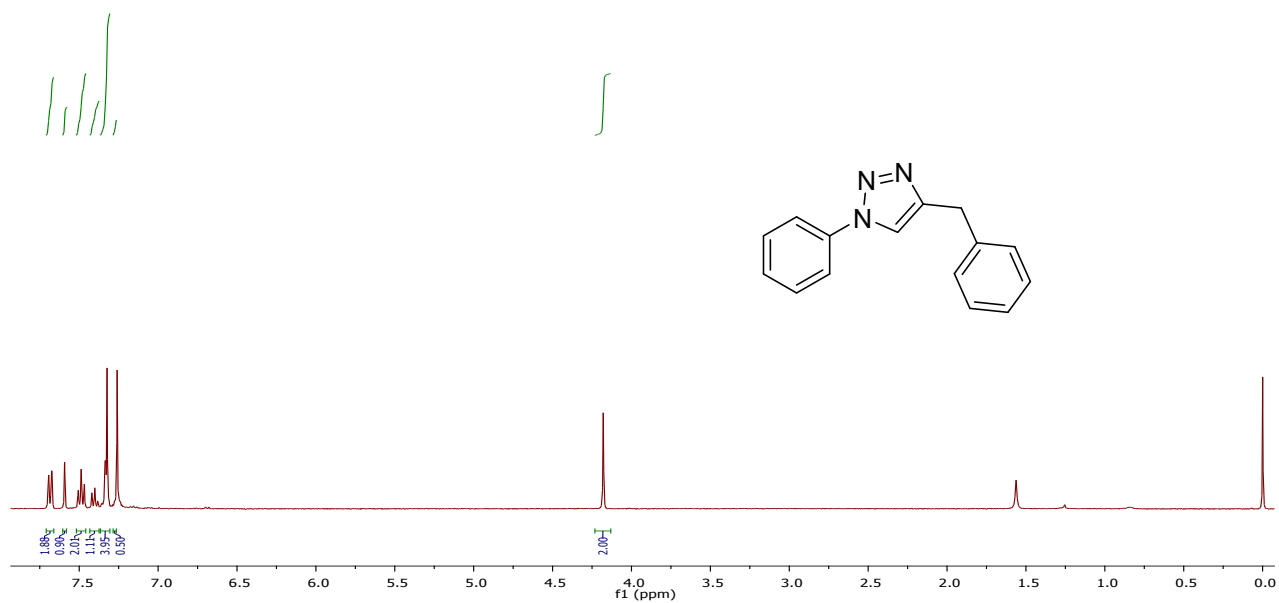


The title compound was synthesized according to the general procedure in 56% (method B) isolated yield as white solid. Analytical data are in agreement with previous published data.⁷ **¹H NMR** (400 MHz, CDCl₃) δ 8.20 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 6.9 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 3H), 7.37 (t, *J* = 6.8 Hz, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ = 148.4, 137.0, 130.2, 129.8, 128.9, 128.8, 128.4, 125.9, 120.6, 117.6 ppm.

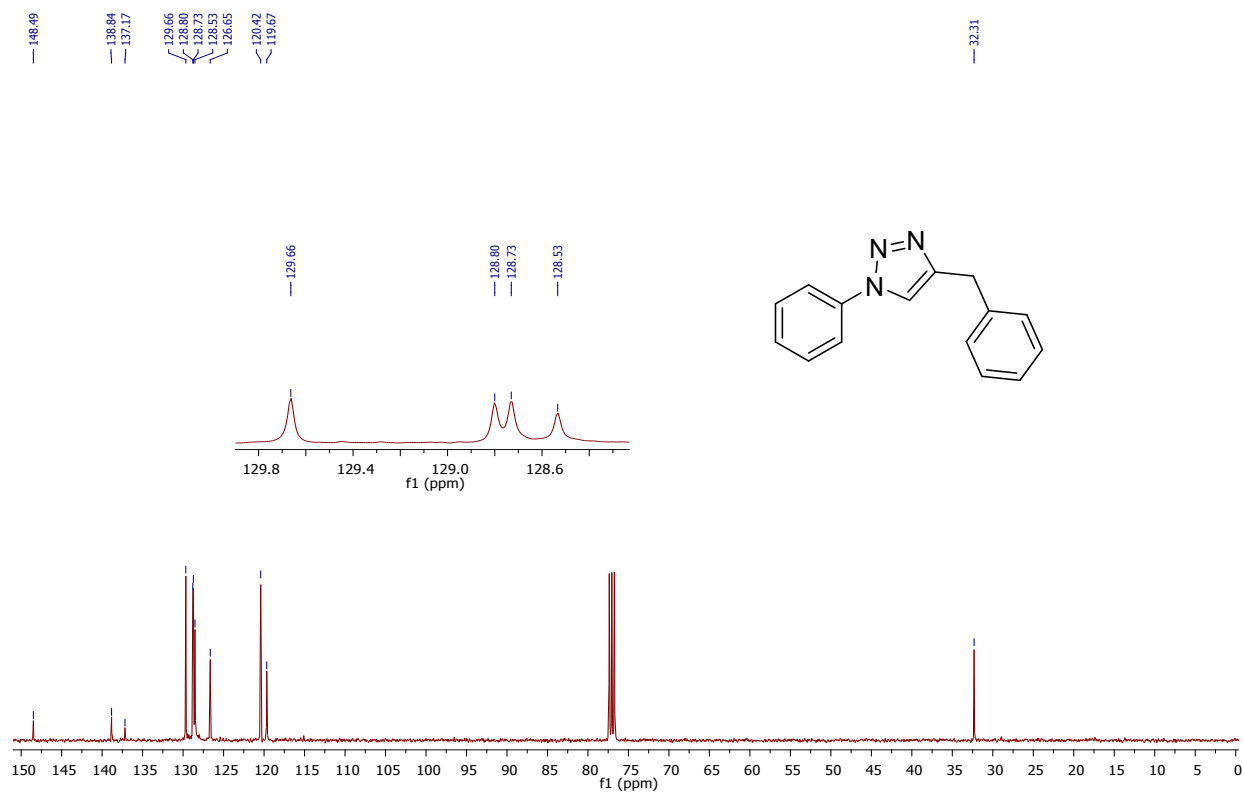
(*S*)-4-(6-methylhept-5-en-2-yl)-1-phenyl-1*H*-1,2,3-triazole (3v):



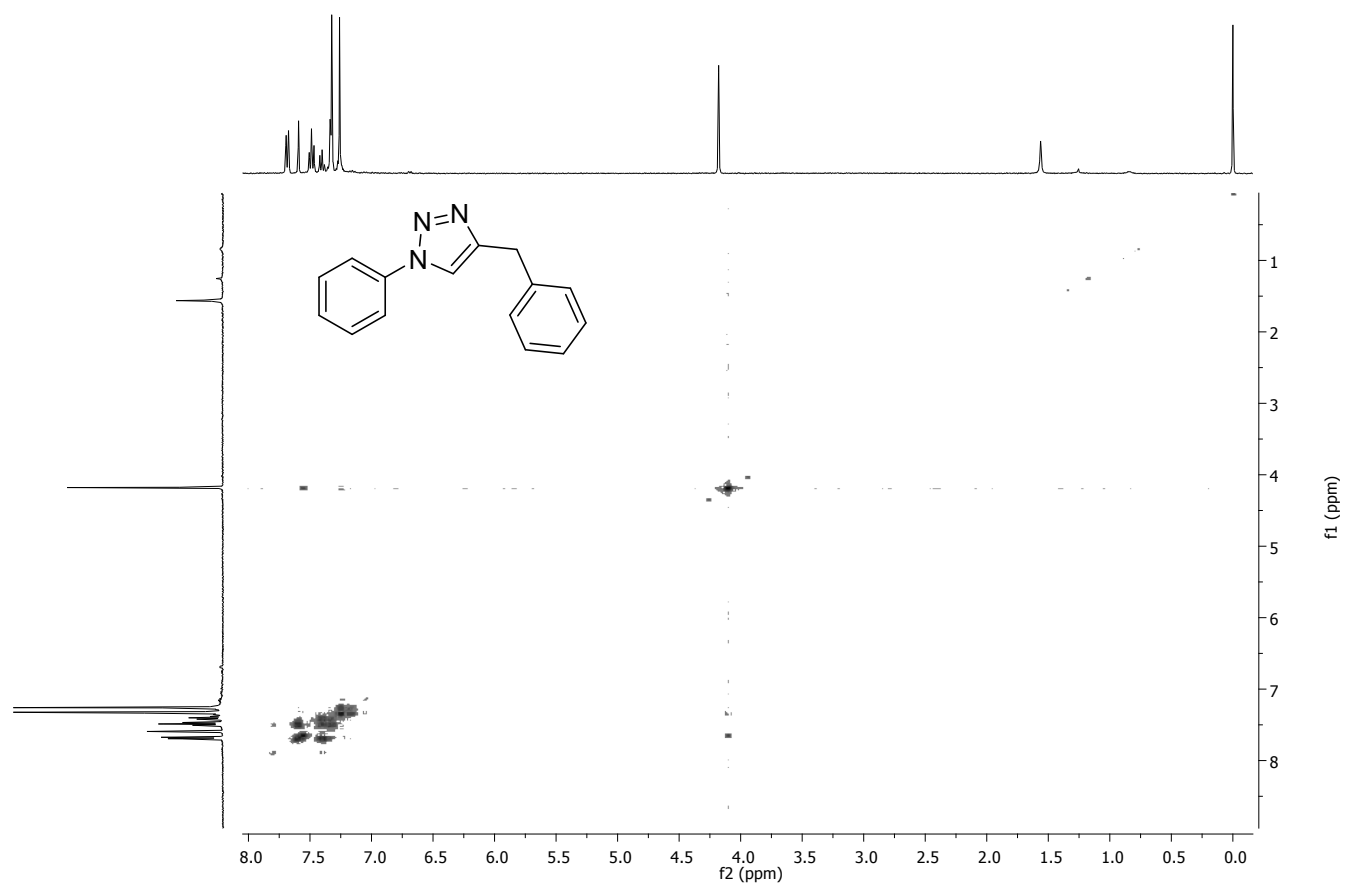
The title compound was synthesized according to the general procedure (B) in 86% isolated yield. **¹H NMR** (400 MHz, CDCl₃) δ 7.77 – 7.67 (m, 3H), 7.54 – 7.47 (m, 2H), 7.44 – 7.38 (m, 1H), 5.21 – 5.08 (m, 1H), 3.05 (d, *J* = 7.0 Hz, 1H), 2.09 – 1.98 (m, 2H), 1.84 (ddt, *J* = 19.8, 8.6, 6.7 Hz, 1H), 1.71 – 1.62 (m, 4H), 1.58 (s, 3H), 1.36 (d, *J* = 7.0 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 154.3, 137.3, 131.8, 129.6, 128.2, 124.1, 120.4, 117.86, 37.0, 30.7, 25.7, 20.5, 17.7. ppm. [α]_D²⁵ = + 46.423 (*c* 0.0052 g. mL⁻¹, C₂H₅OH); ESI-MS (*m/z*) calcd for C₁₆H₂₂N₃[M + H]⁺ 256.1813 found 256.1809



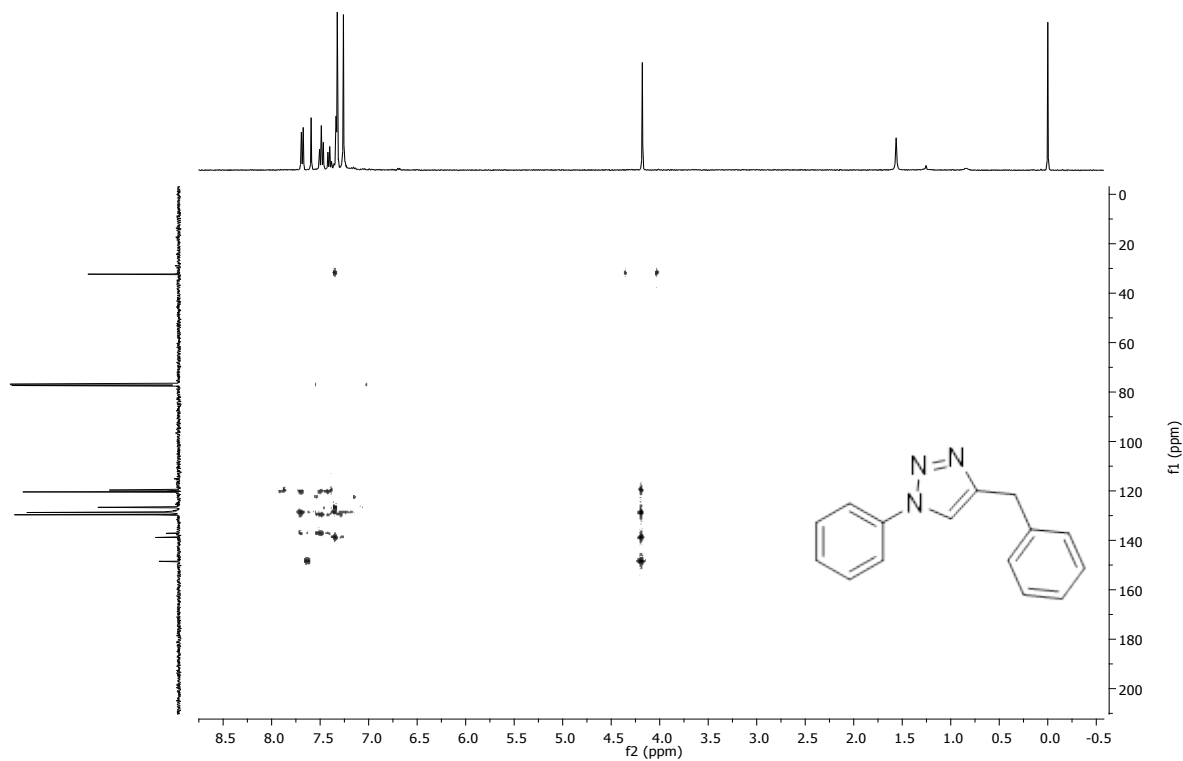
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3a)



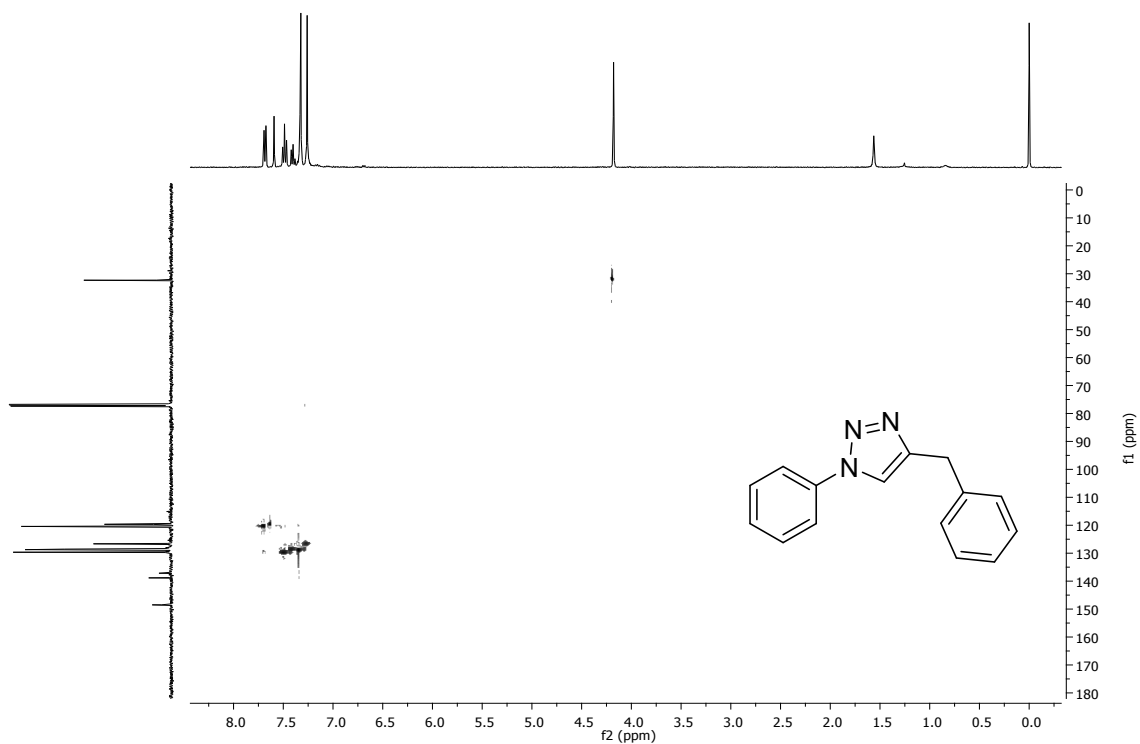
^{13}C NMR spectra at 100 MHz in CDCl_3 for compound (3a)



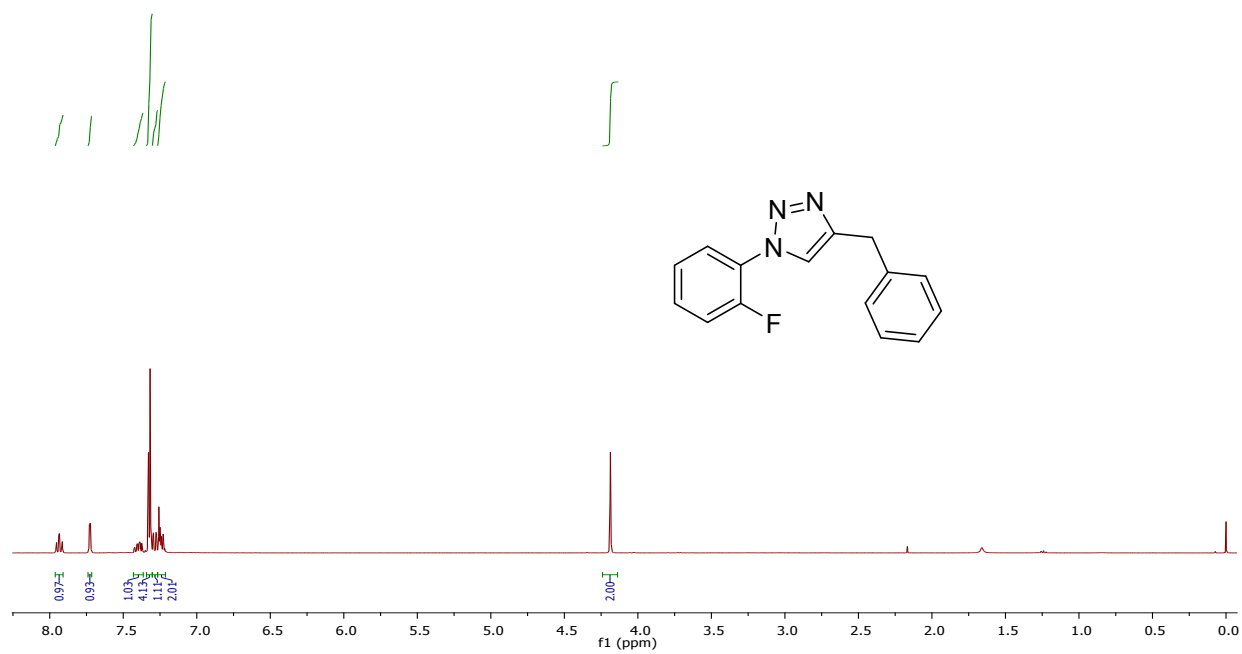
COSY spectra at 400 MHz in CDCl_3 for compound (3a)



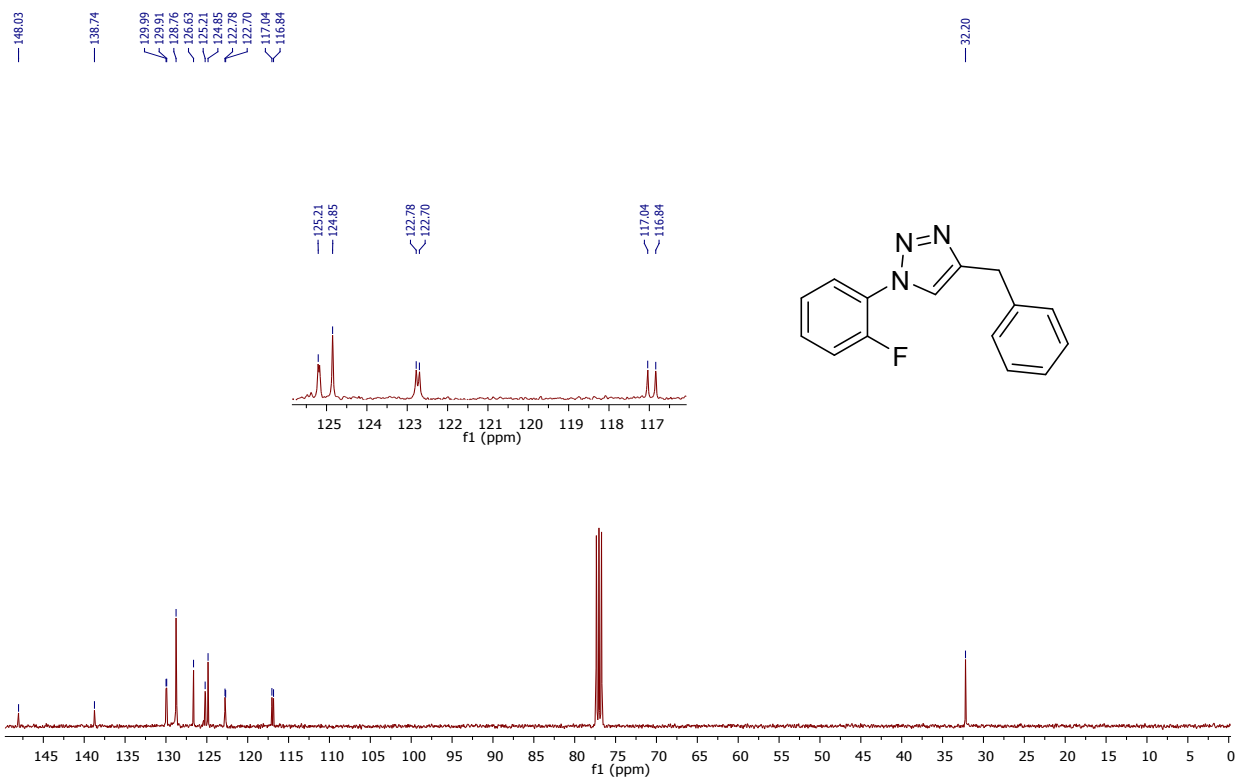
HMBC spectra at 400 MHz in CDCl_3 for compound (3a)



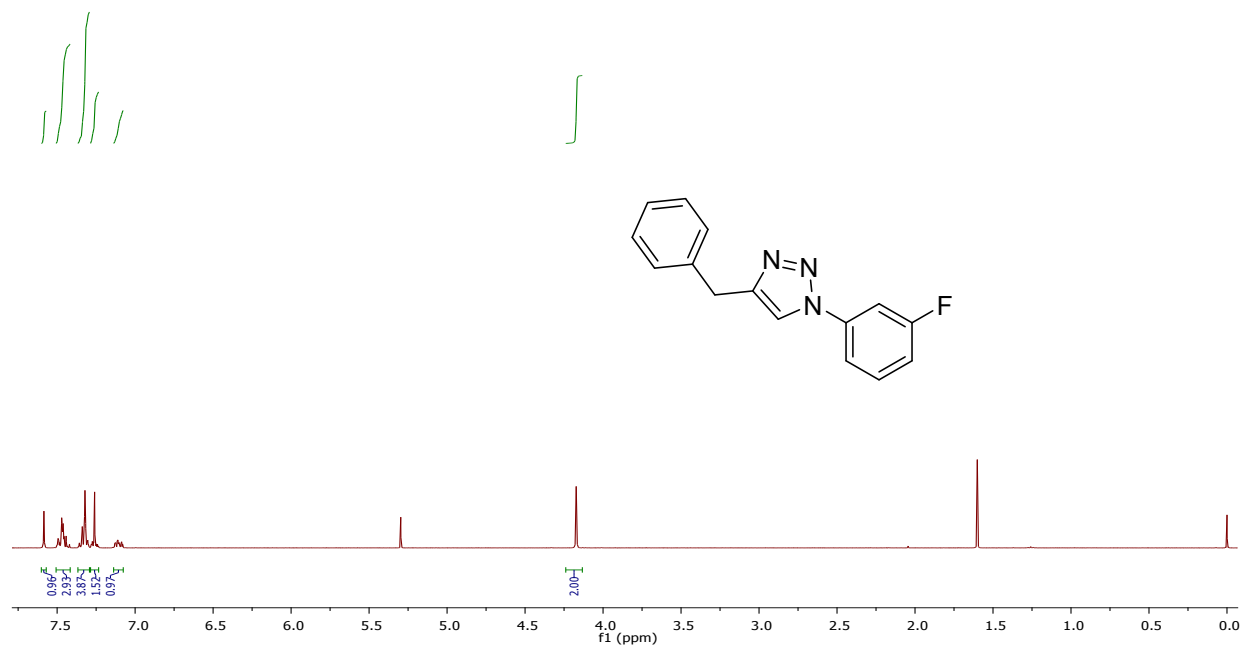
HSQC spectra at 400 MHz in CDCl_3 for compound (3a)



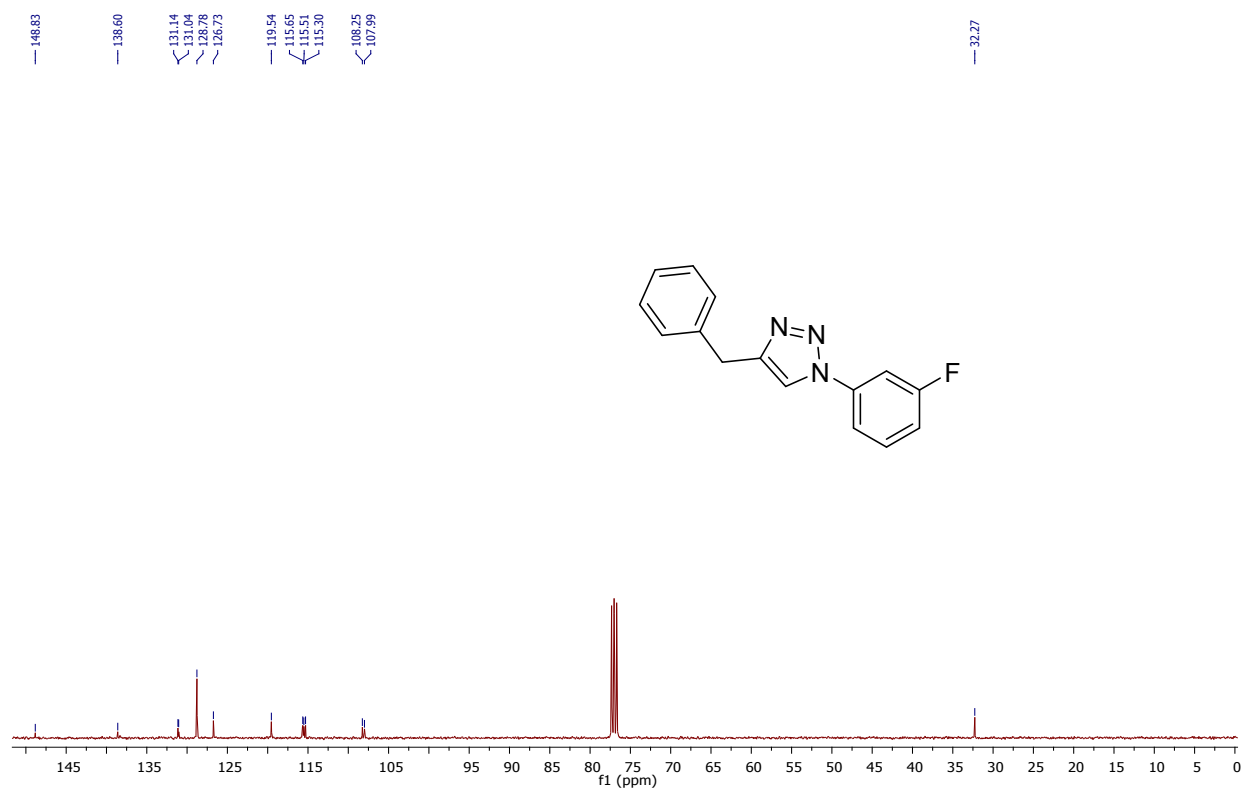
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3b)



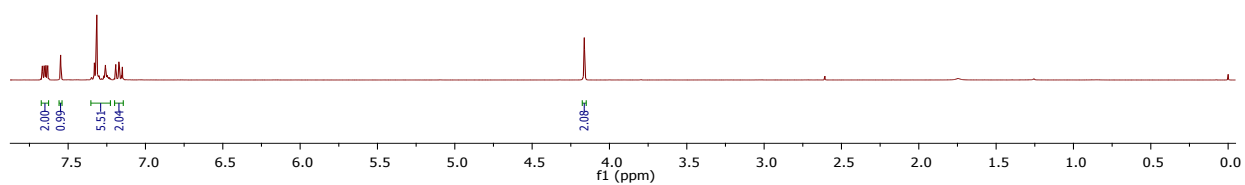
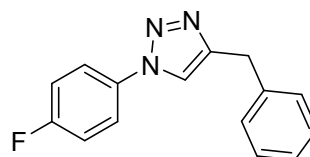
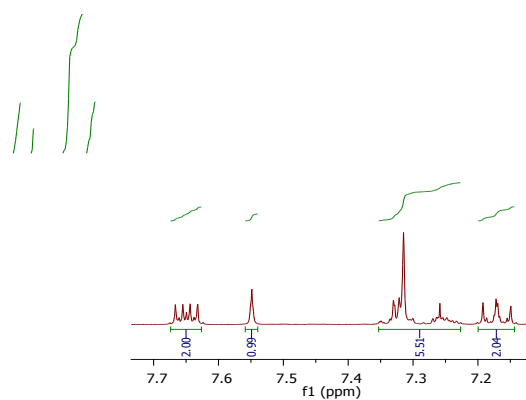
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3b)



¹H NMR spectra at 400 MHz in CDCl₃ for compound (3c)



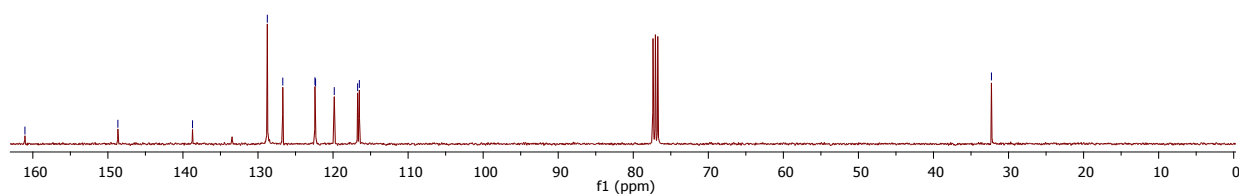
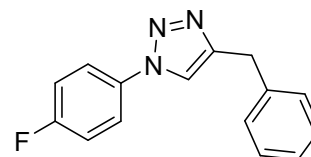
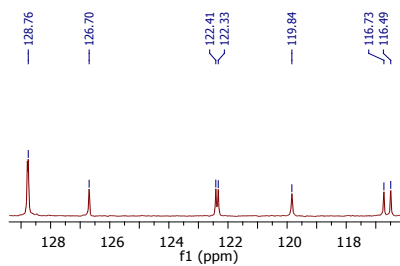
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3c)



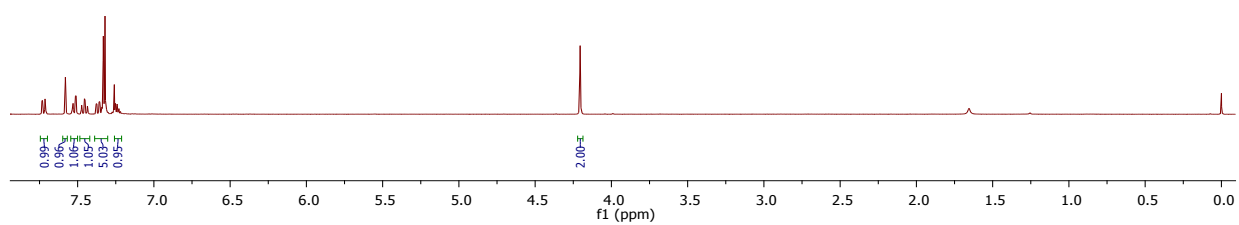
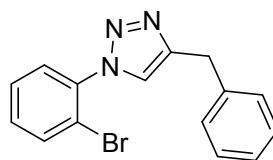
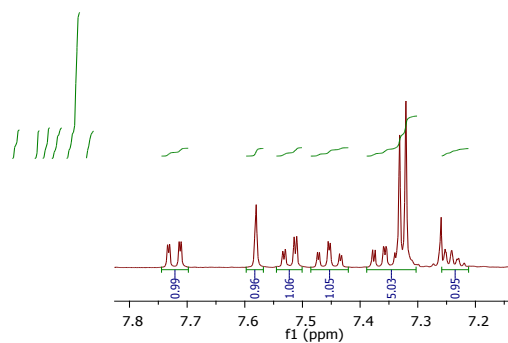
^1H NMR spectra at 400 MHz in CDCl_3 for compound (3d)

— 161.05
— 148.67
— 138.72
— 128.76
— 126.70
— 122.41
— 122.33
— 119.84
— 116.73
— 116.49

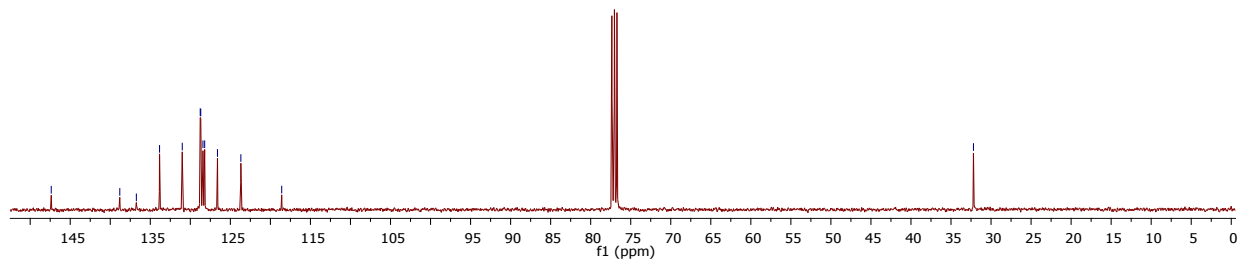
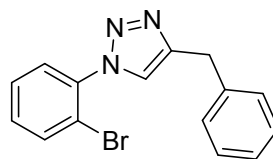
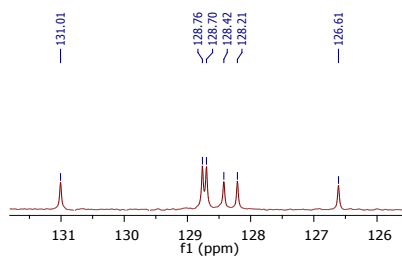
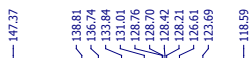
— 32.28



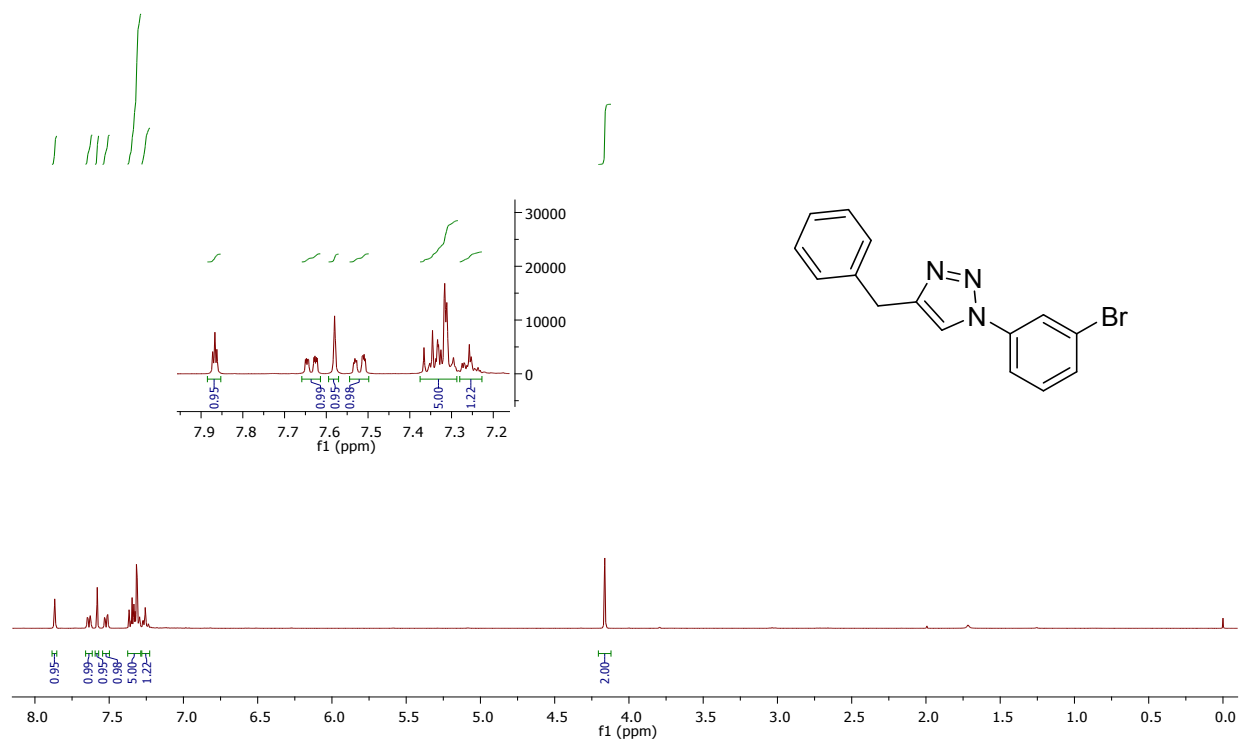
^{13}C NMR spectra at 100 MHz in CDCl_3 for compound (3d)



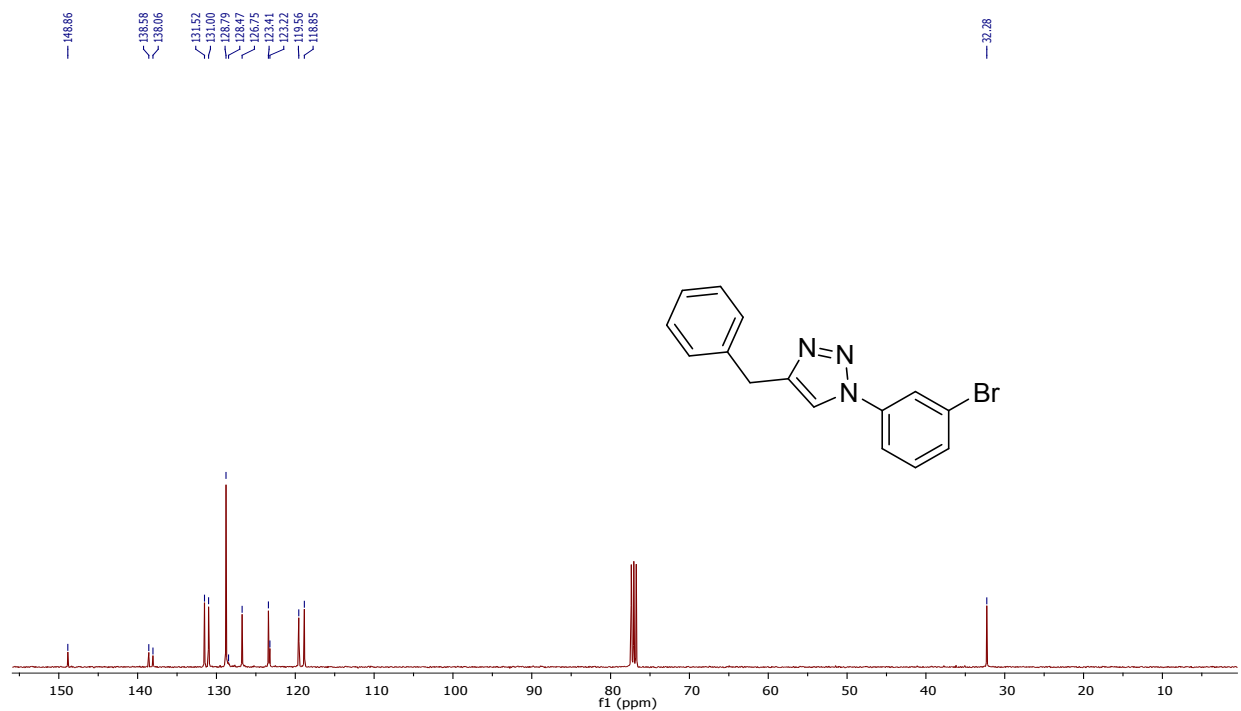
^1H NMR spectra at 400 MHz in CDCl_3 for compound (3e)



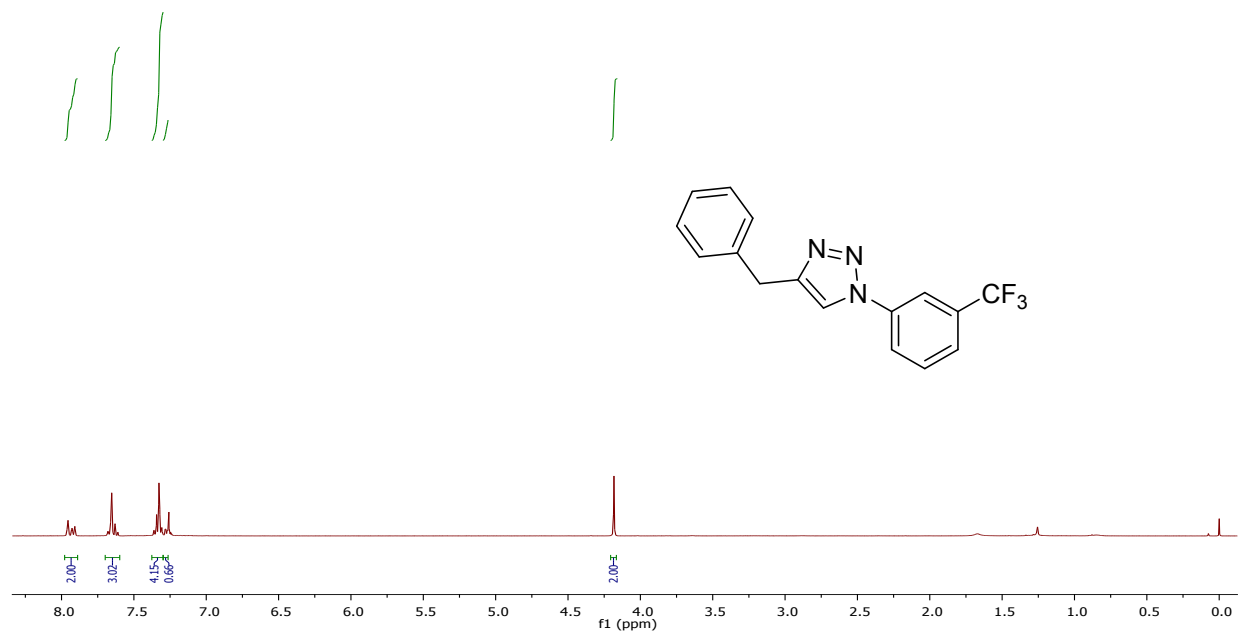
^{13}C NMR spectra at 100 MHz in CDCl_3 for compound (3e)



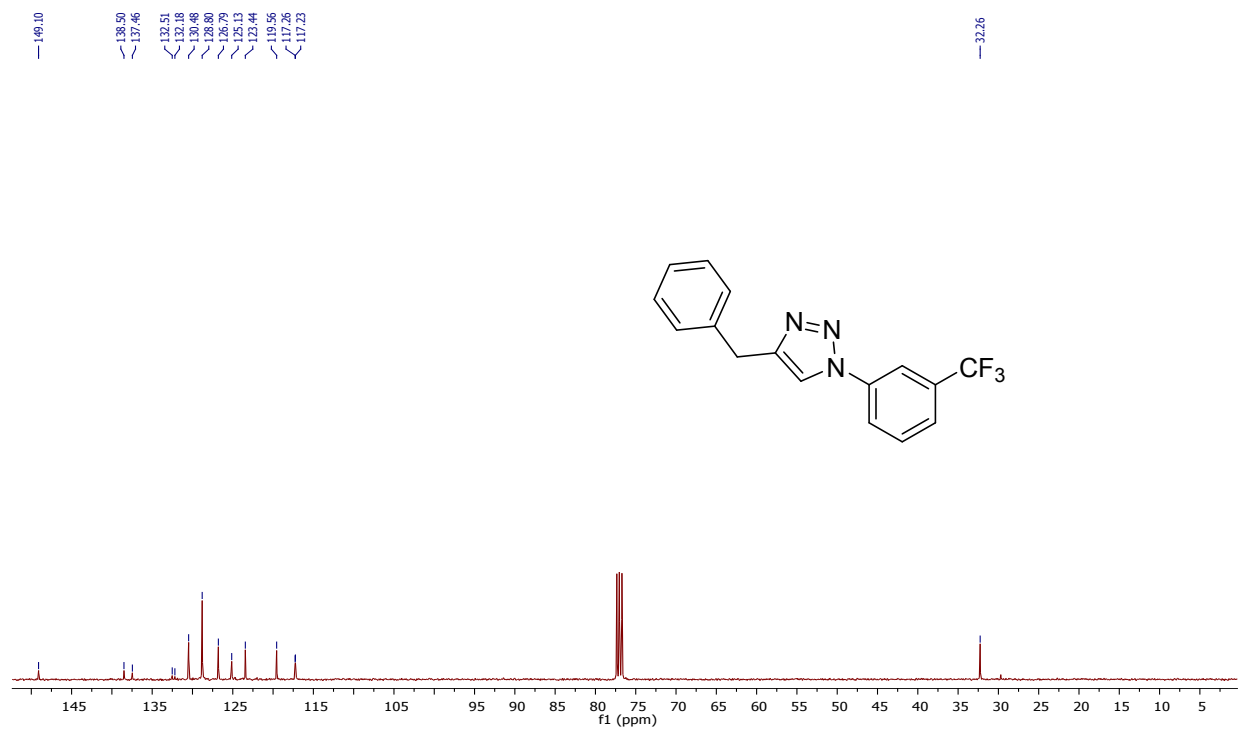
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3f)



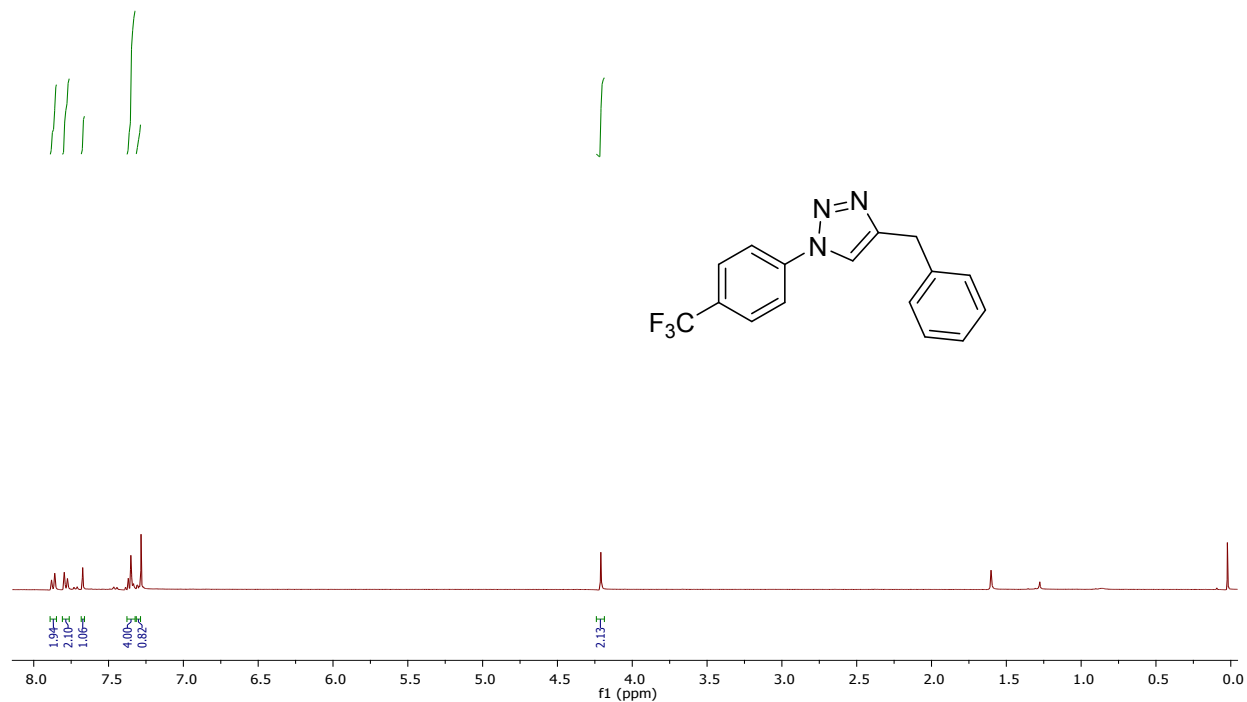
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3f)



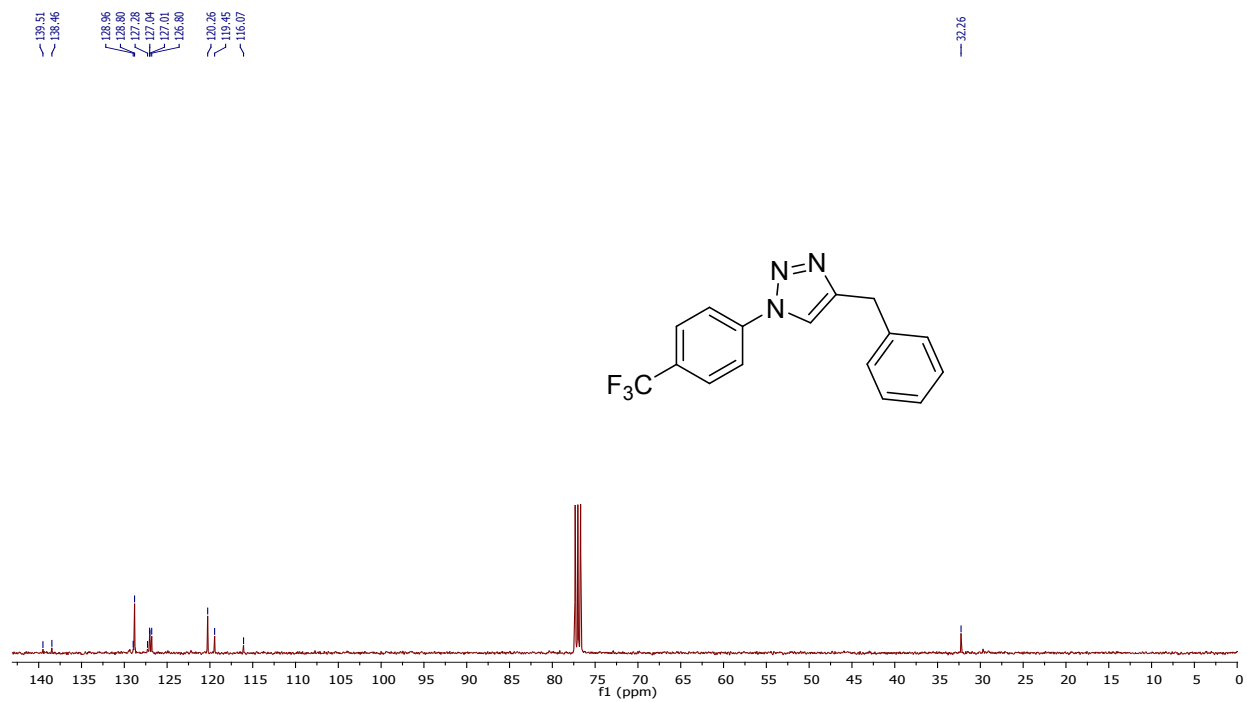
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3g)



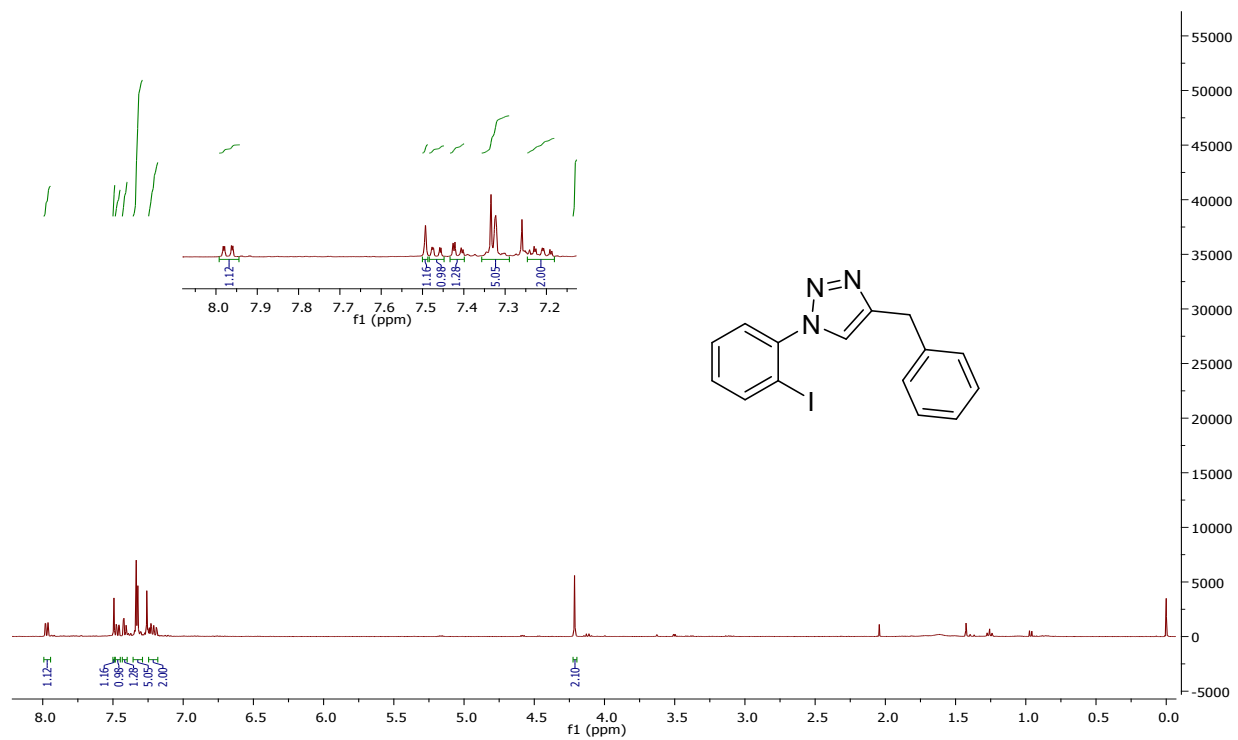
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3g)



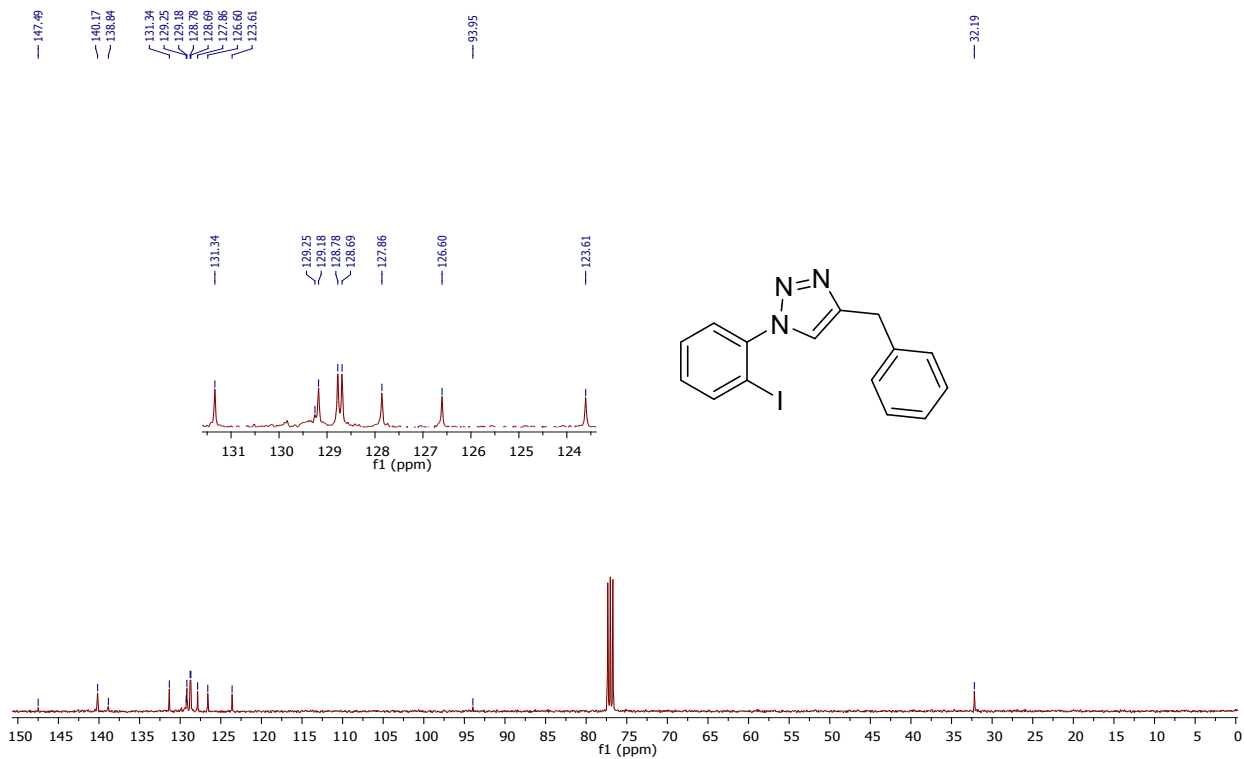
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3h)



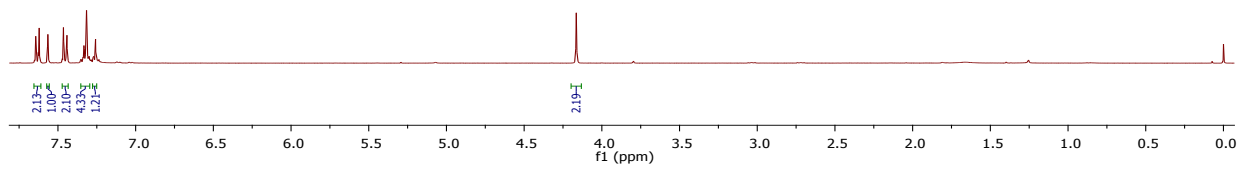
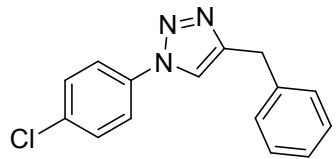
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3h)



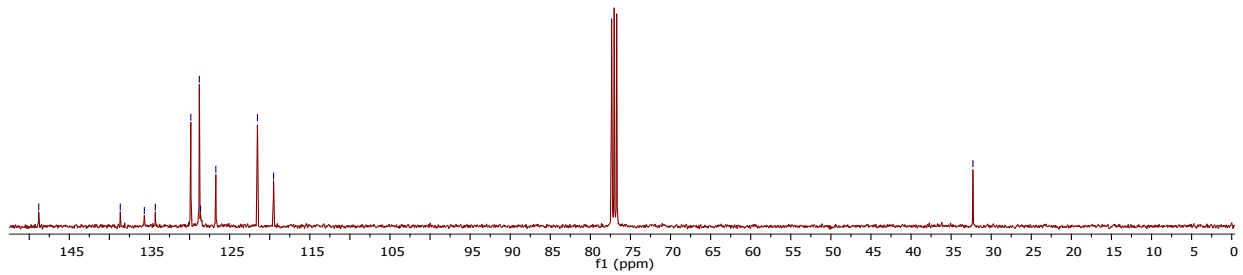
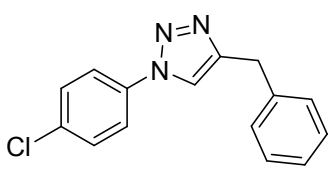
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3i)



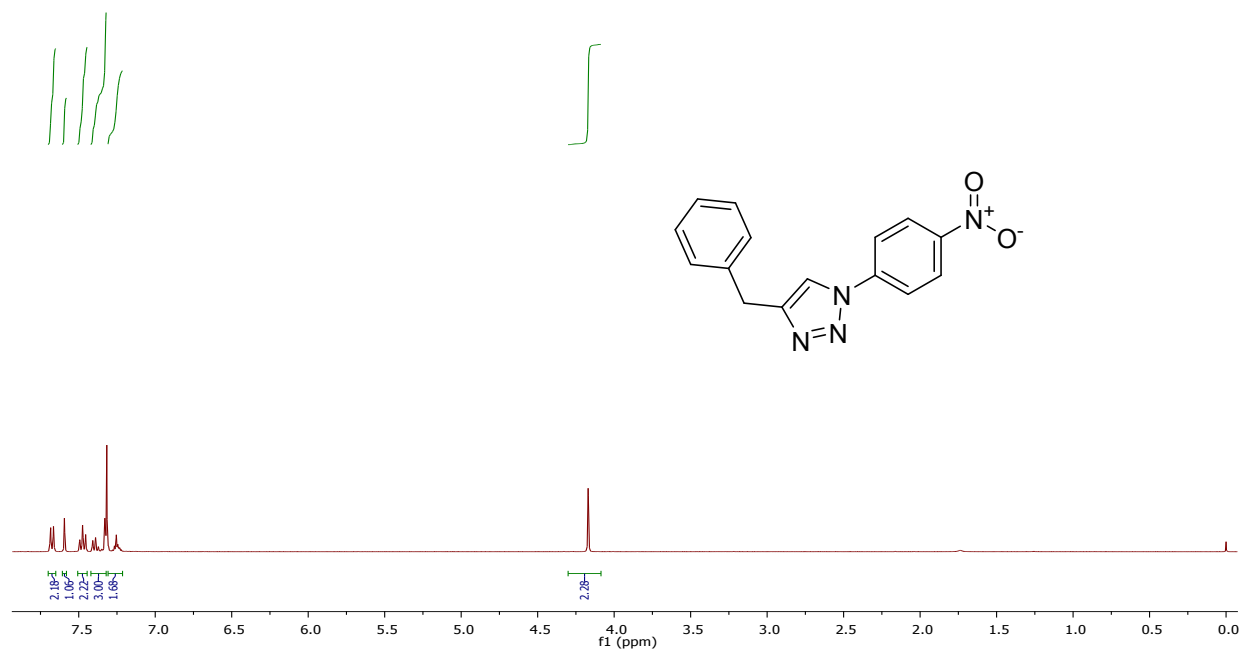
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3i)



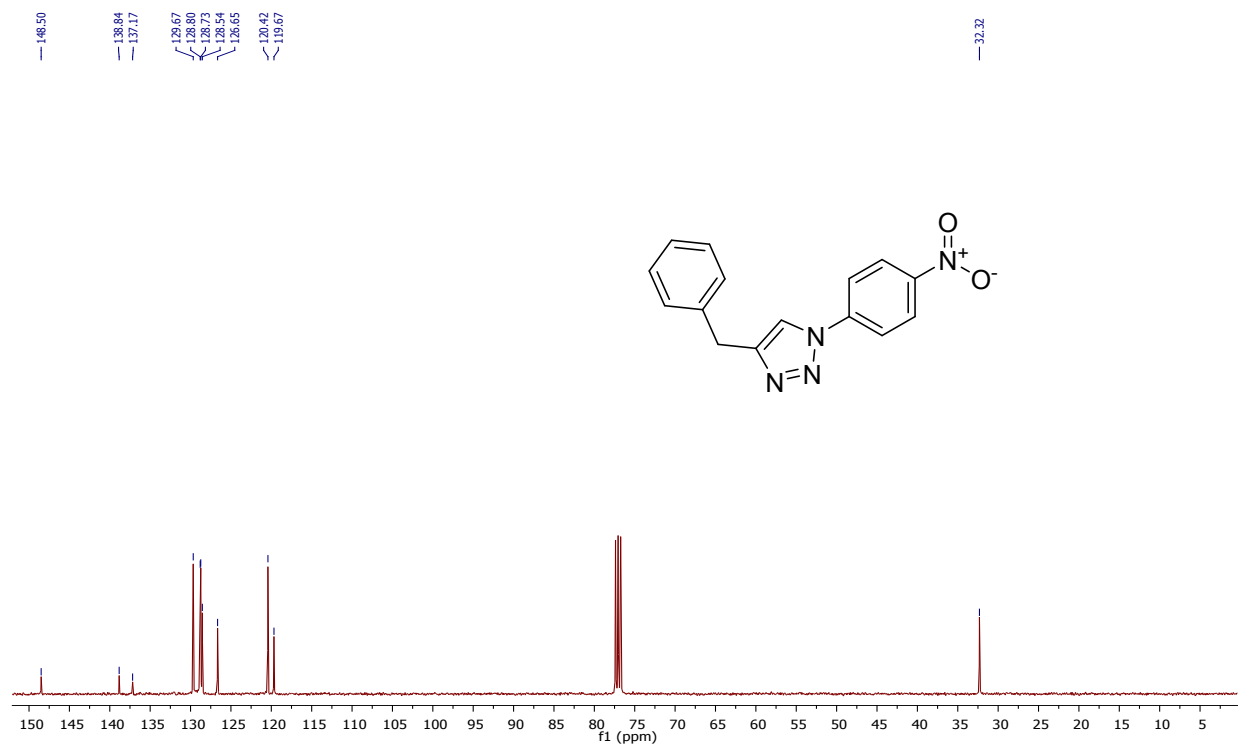
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3j)



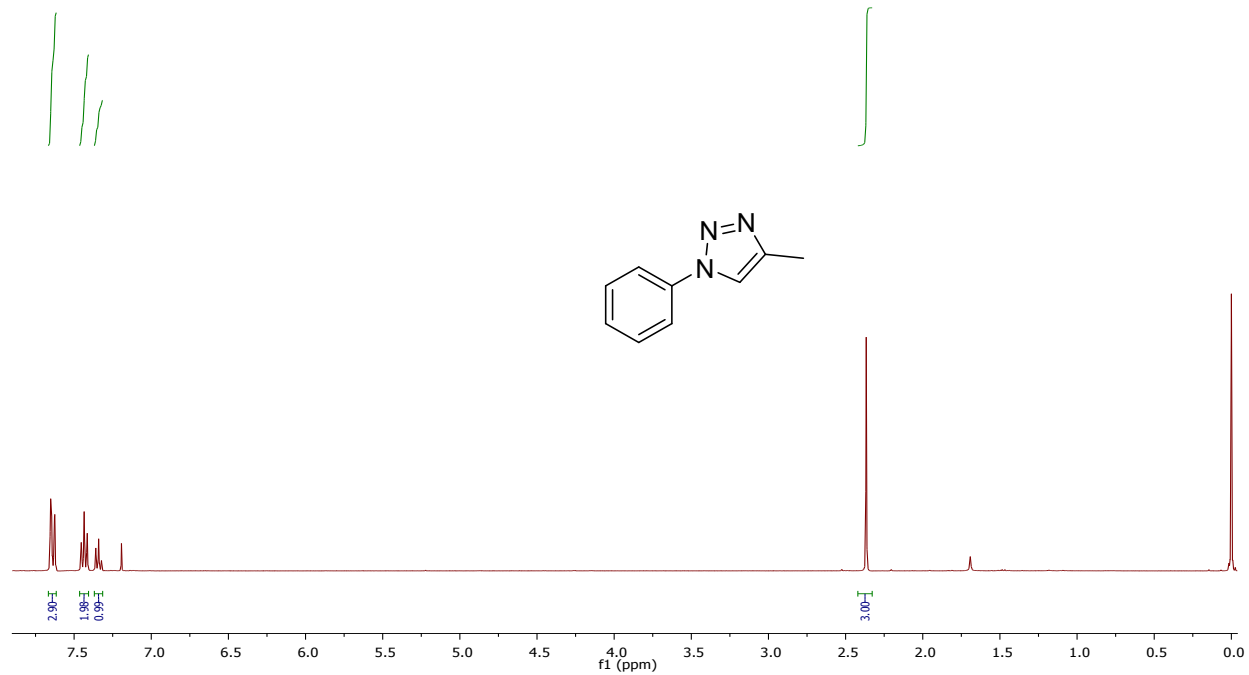
¹³CNMR spectra at 100 MHz in CDCl₃ for compound (3j)



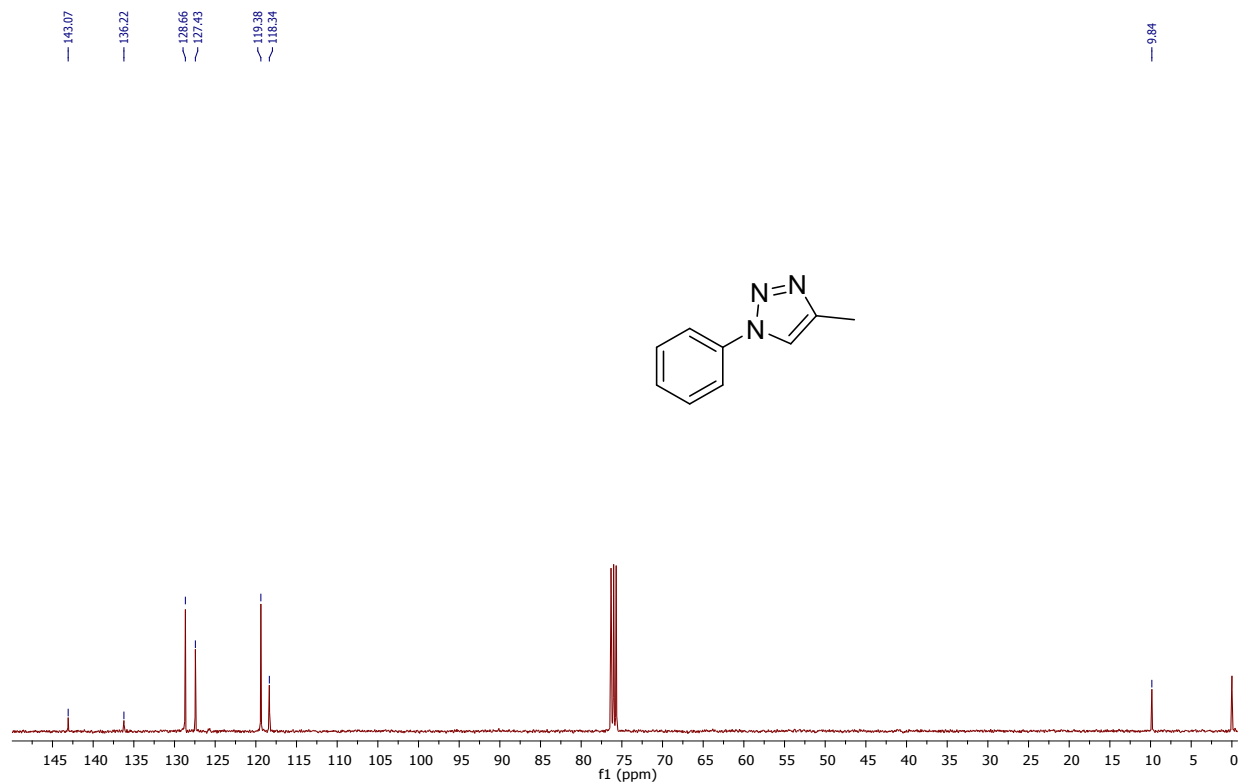
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3k)



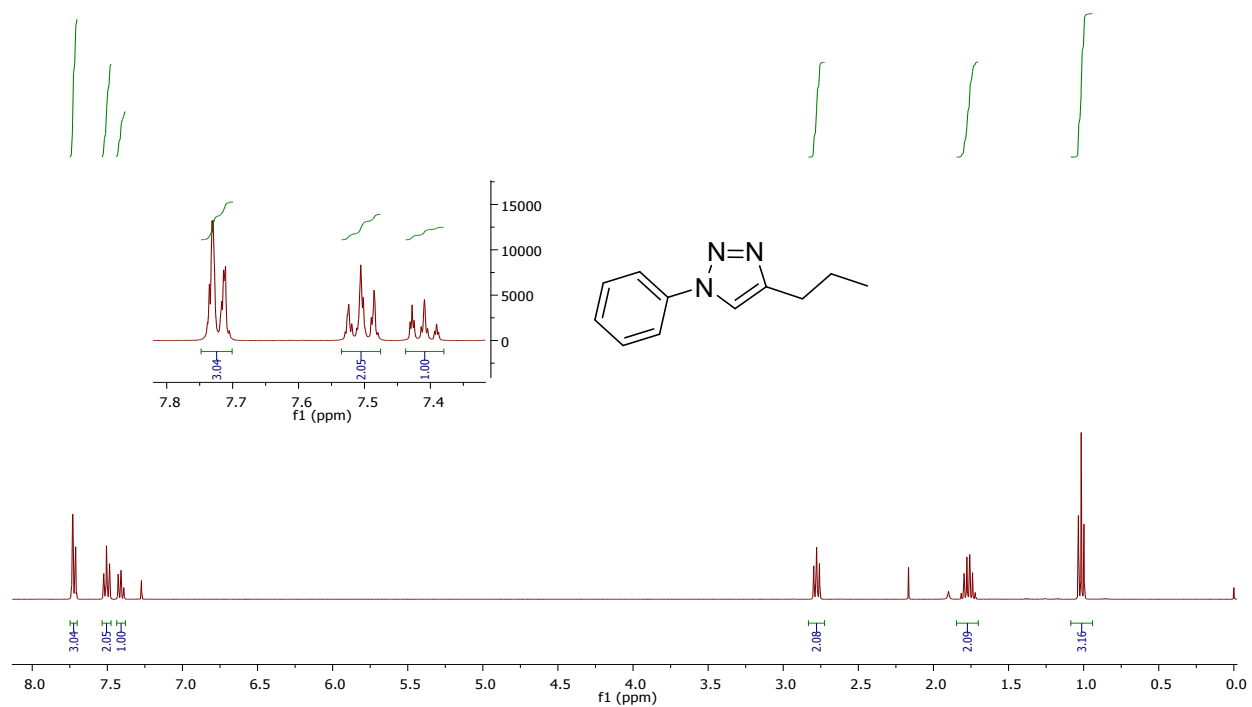
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3k)



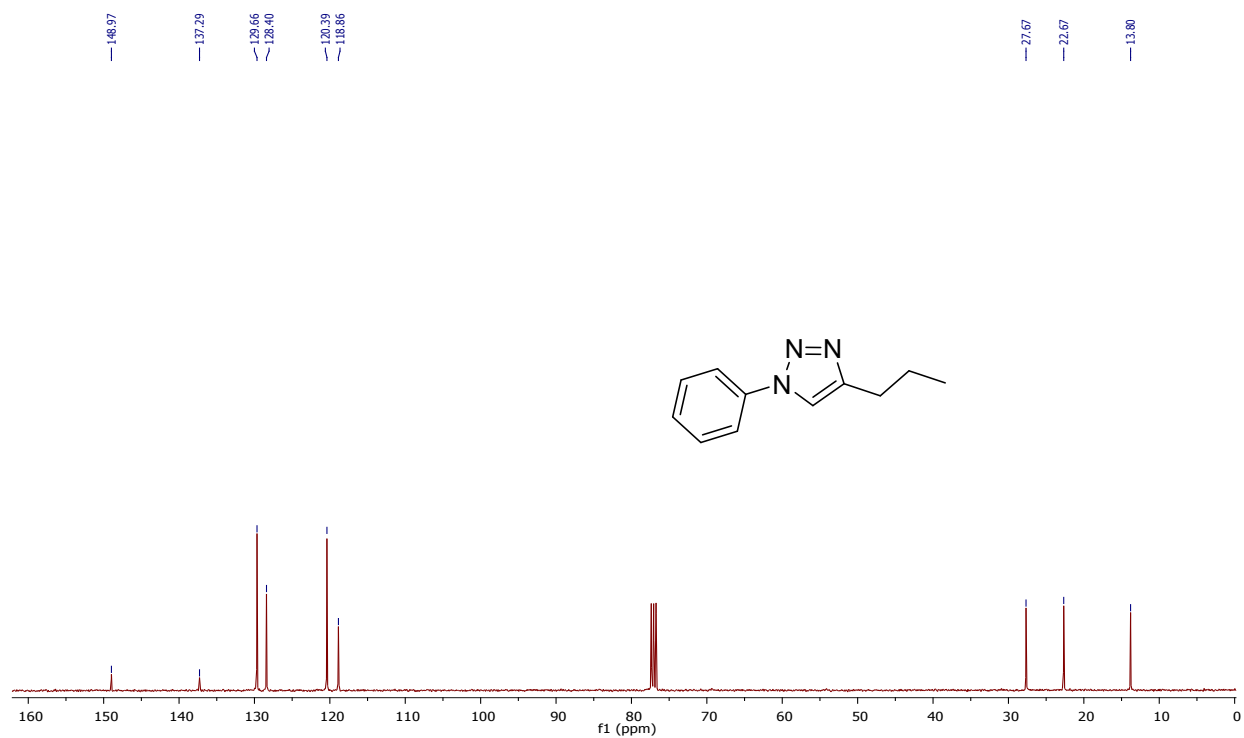
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3k)



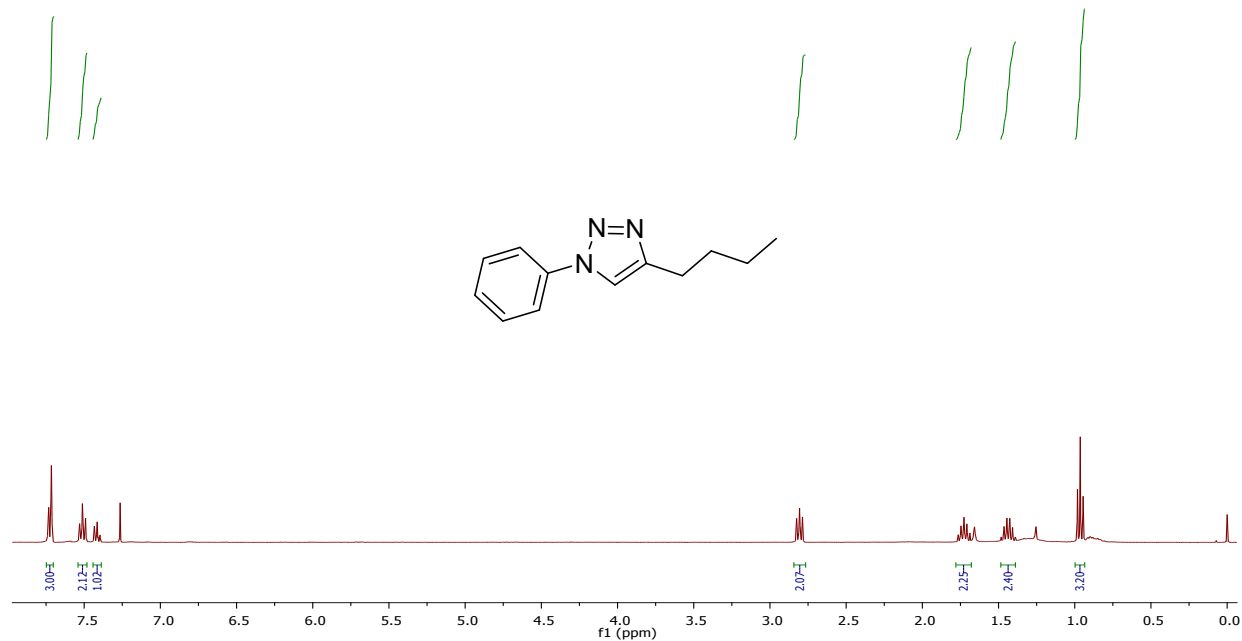
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3k)



¹H NMR spectra at 400 MHz in CDCl₃ for compound (3m)

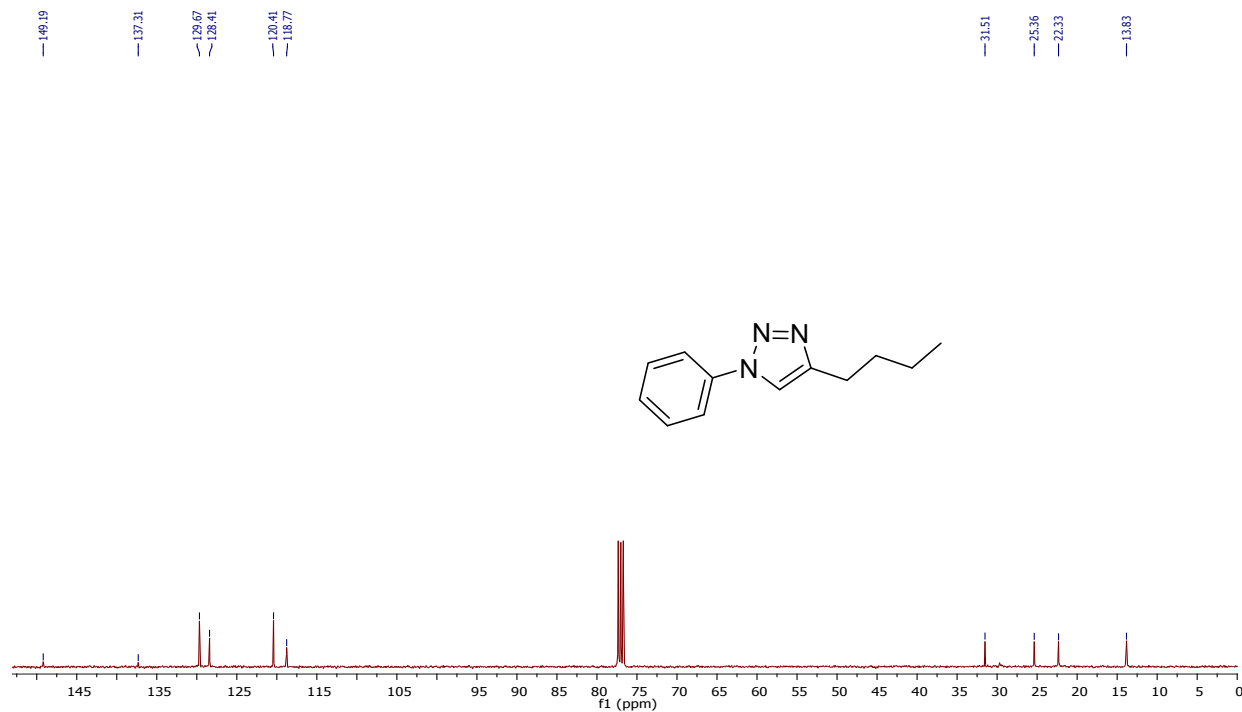


¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3m)

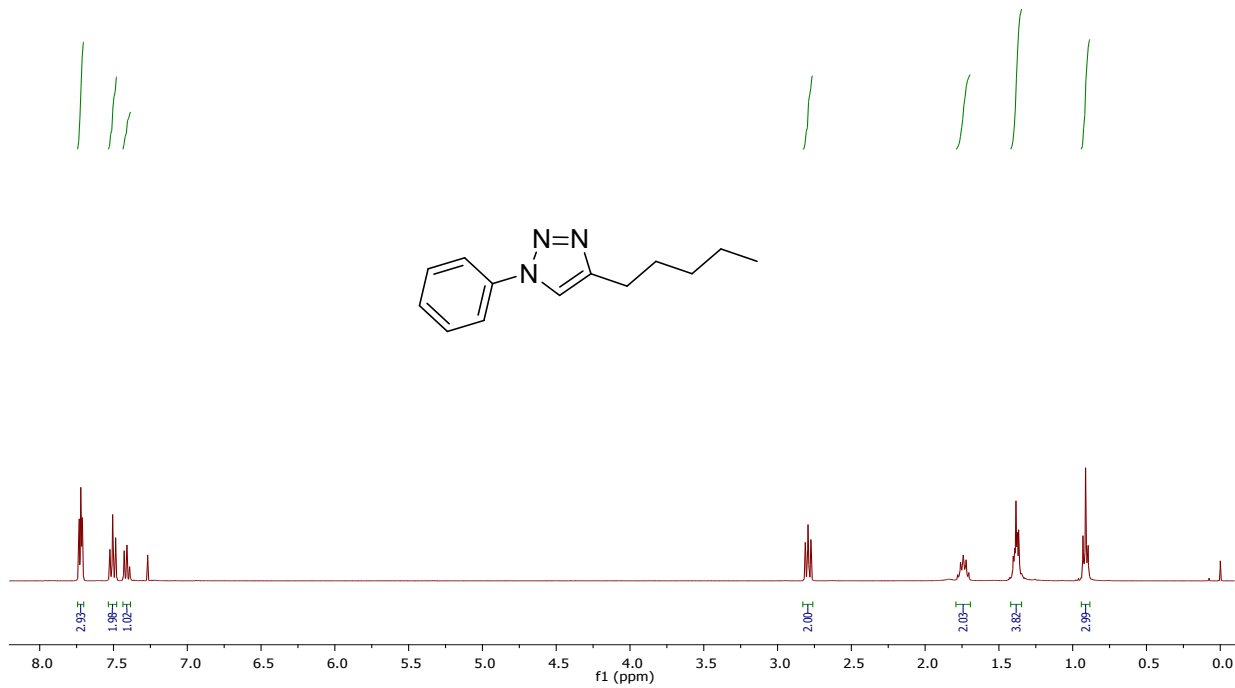


¹H NMR spectra at 400 MHz in CDCl₃ for compound (3n)

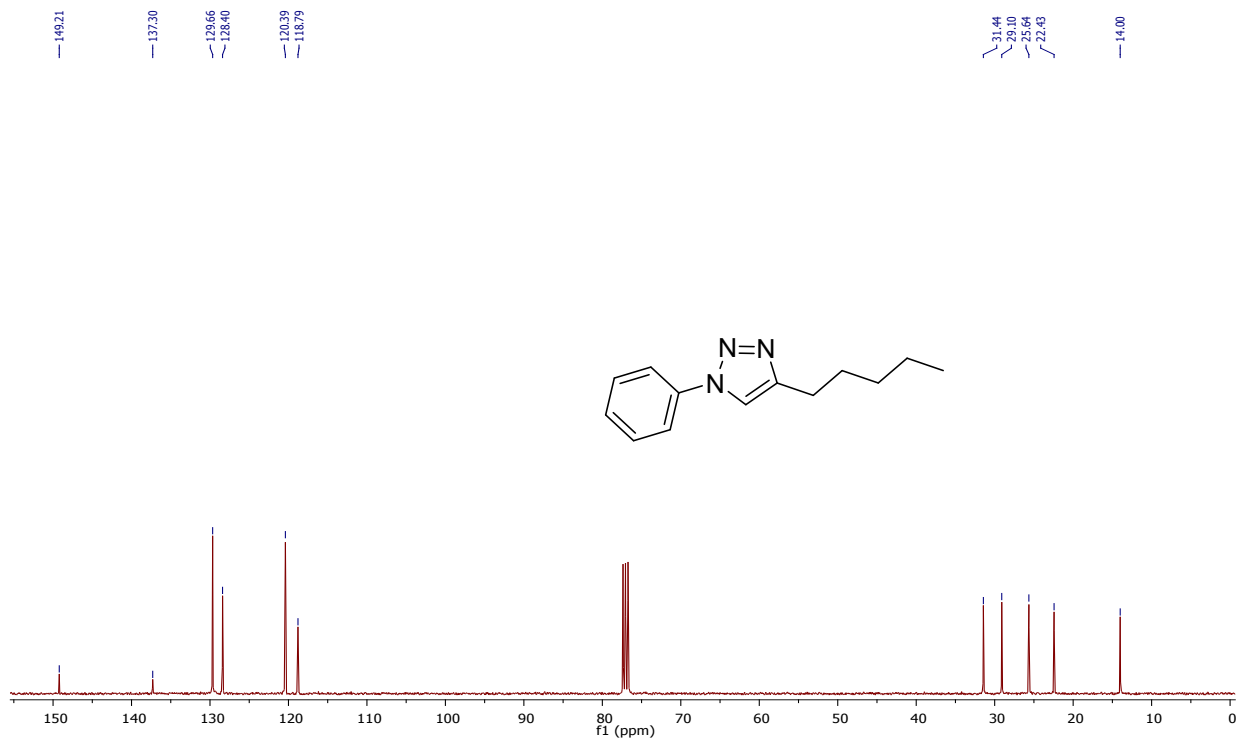
¹³C NMR of (3n)



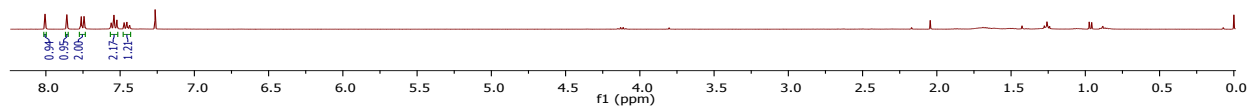
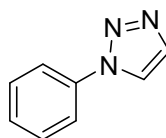
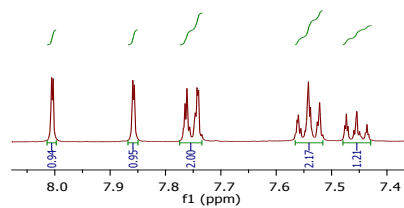
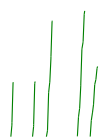
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3n)



¹H NMR spectra at 400 MHz in CDCl₃ for compound (3o)



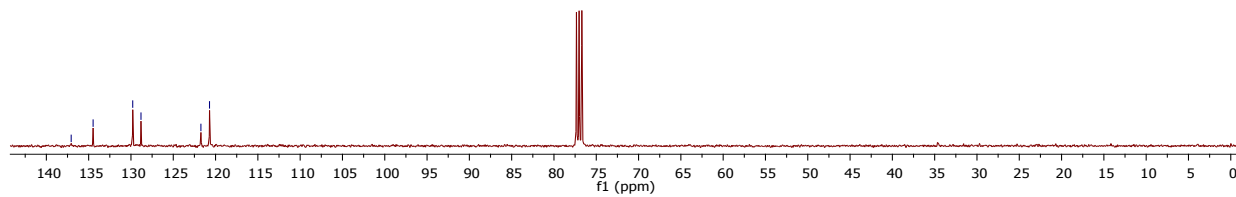
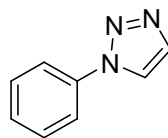
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3o)



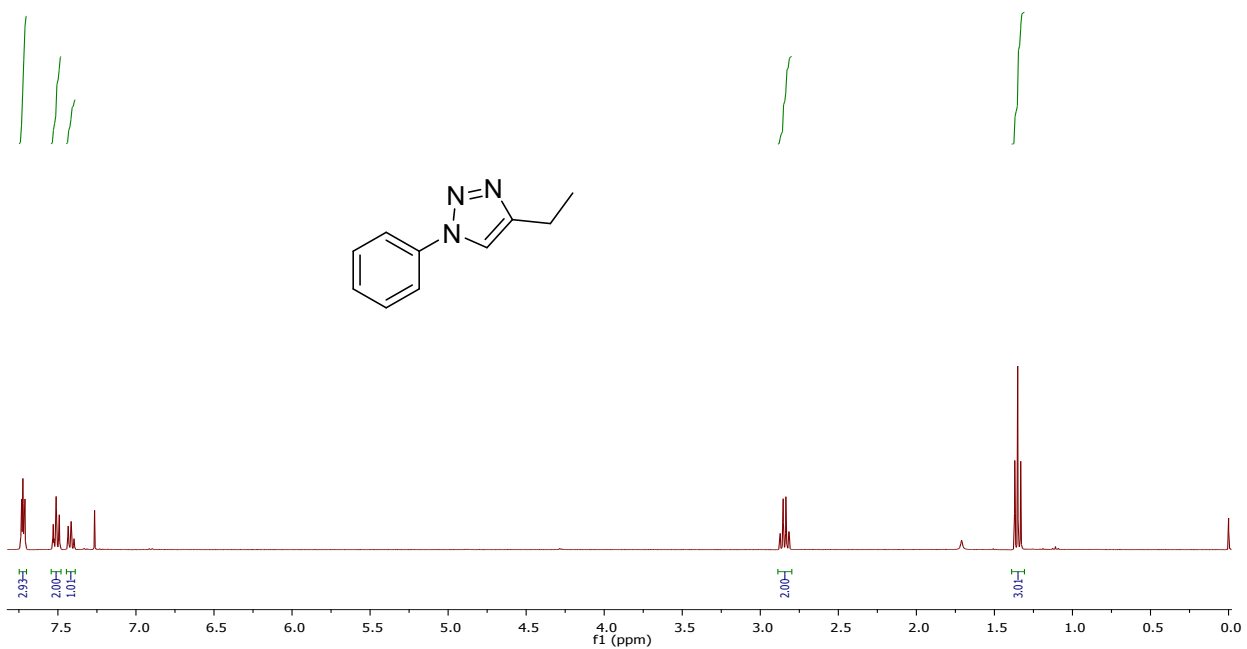
^1H NMR spectra at 400 MHz in CDCl_3 for compound (3p)

C^{13} NMR of (3p)

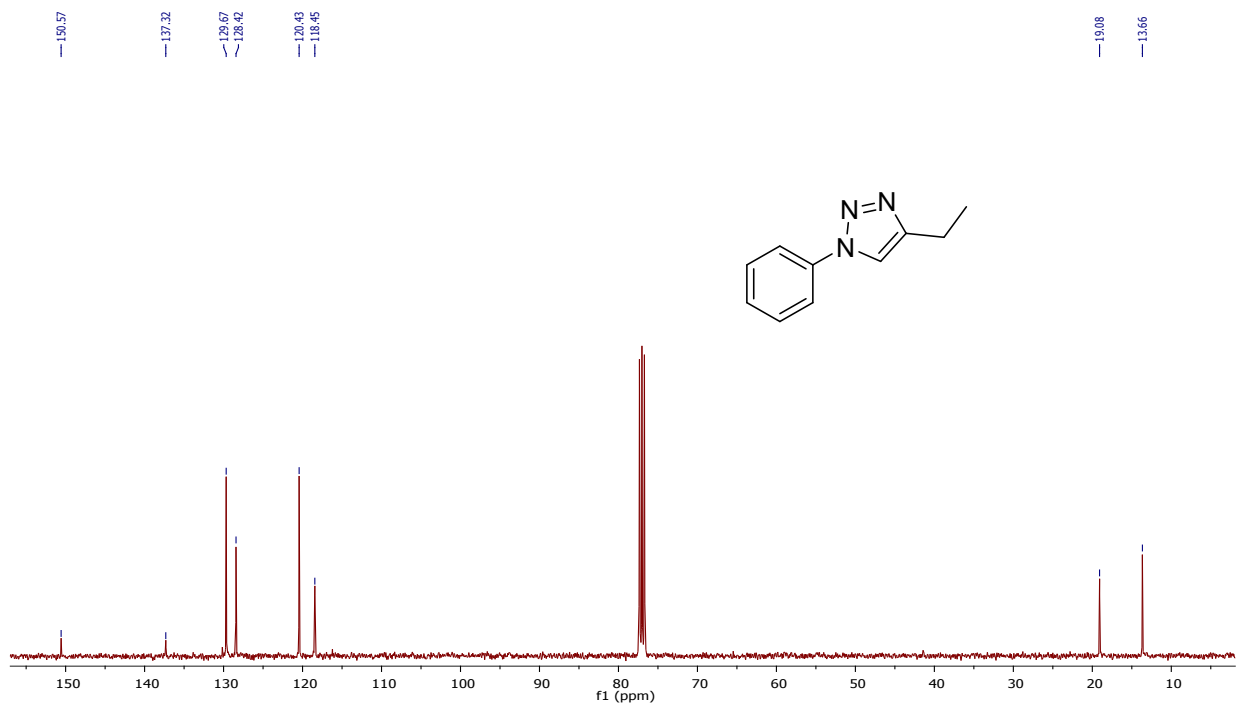
137.07
134.47
128.79
128.62
121.73
120.71



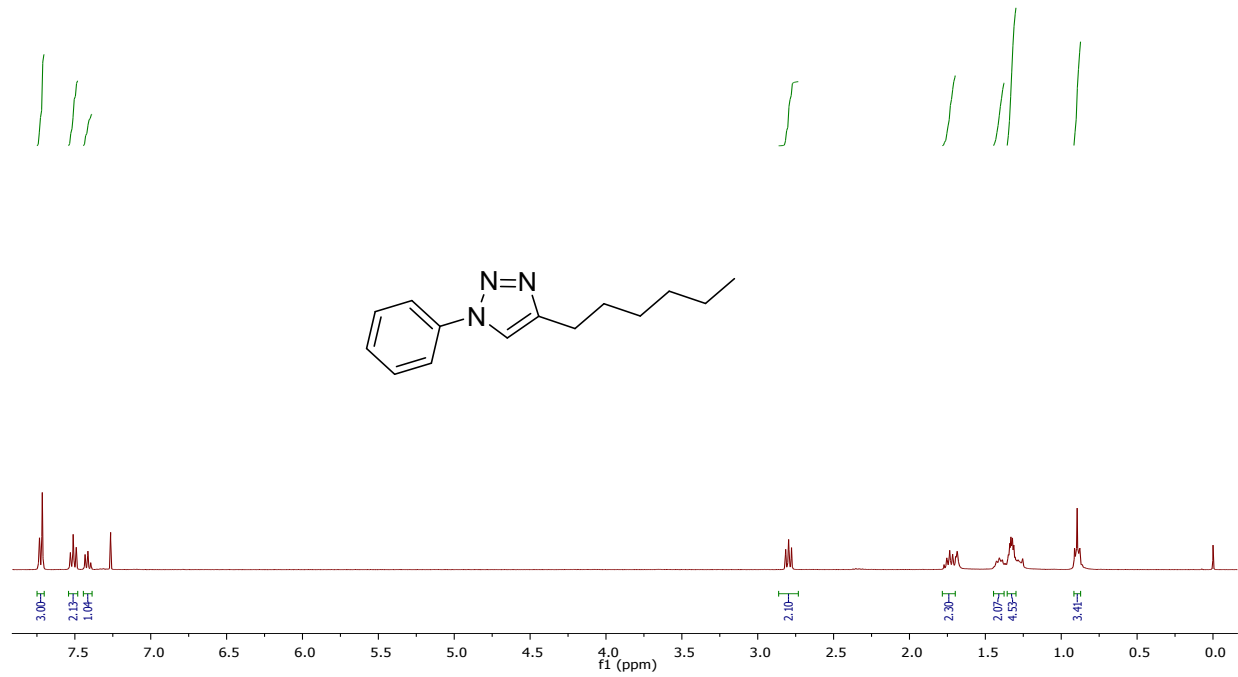
^{13}C NMR spectra at 100 MHz in CDCl_3 for compound (3p)



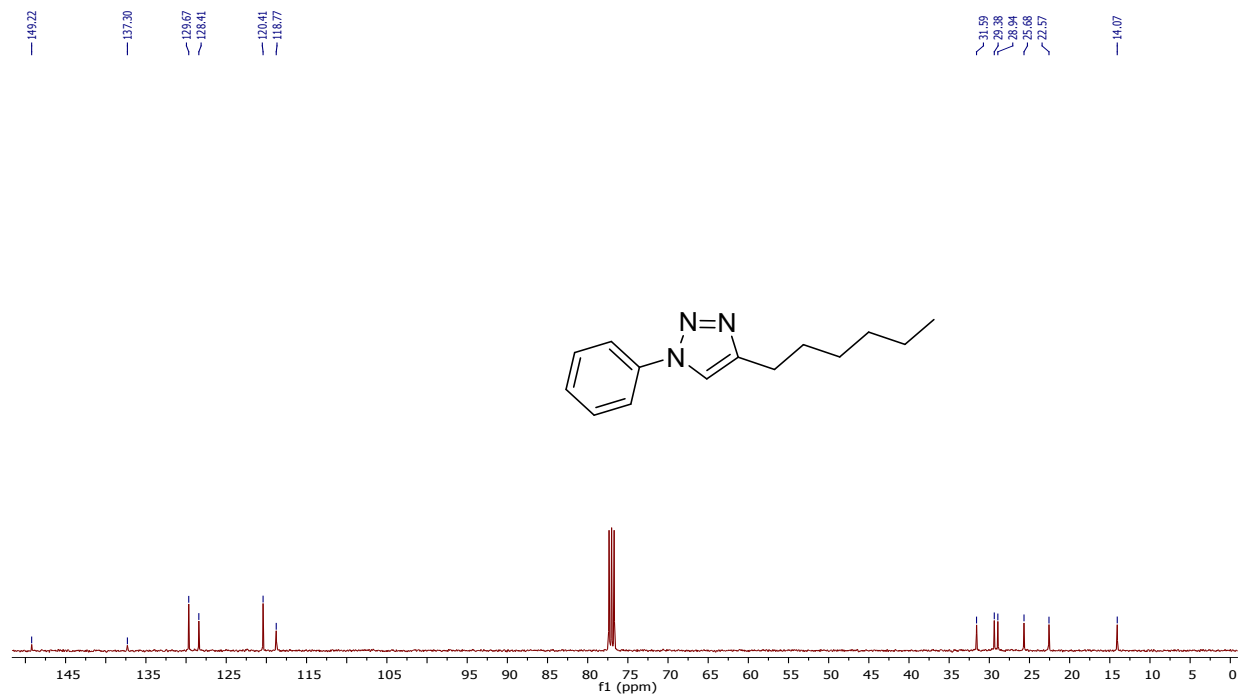
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3q)



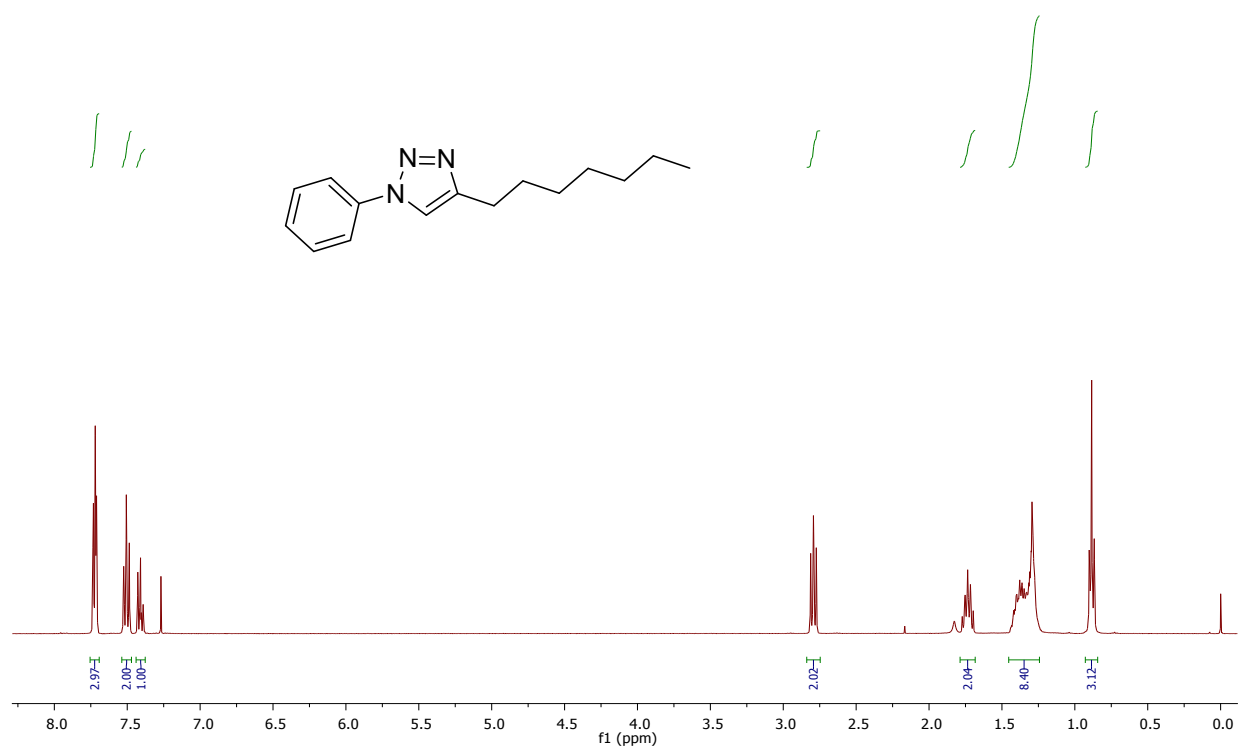
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3q)



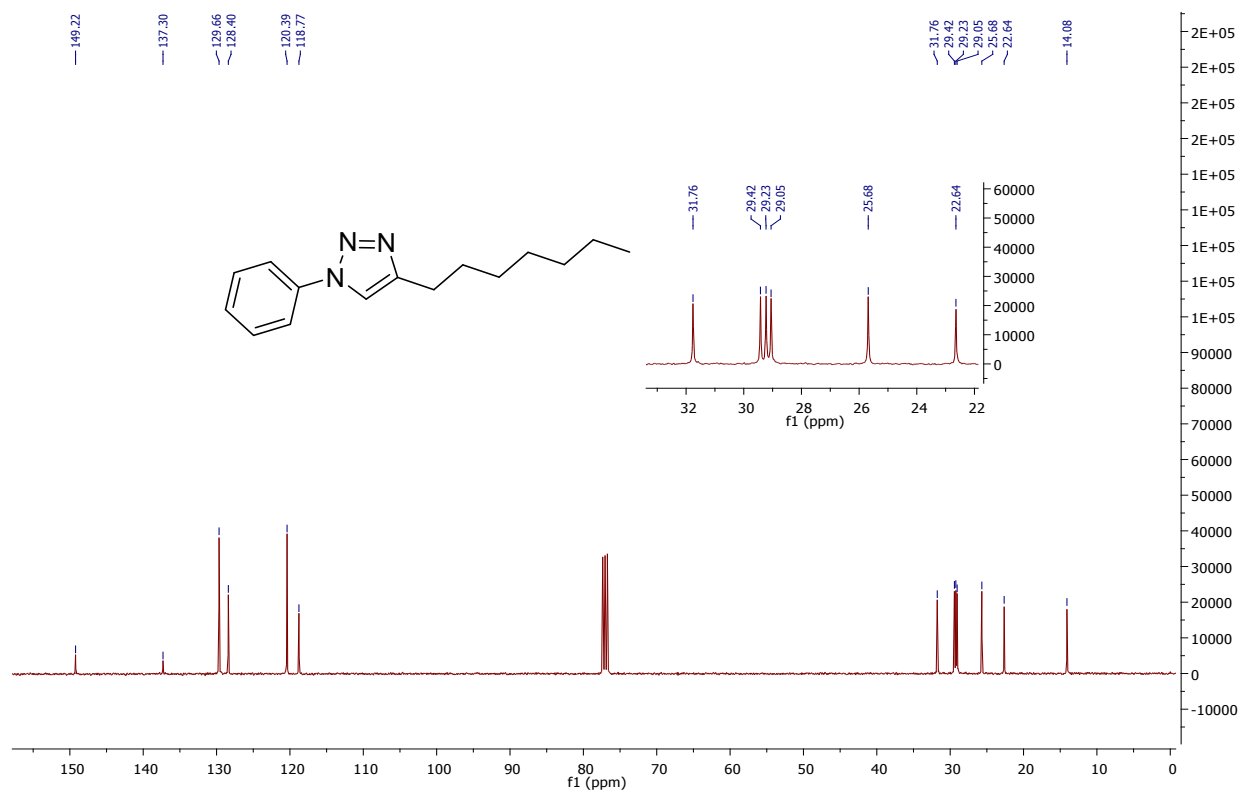
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3r)



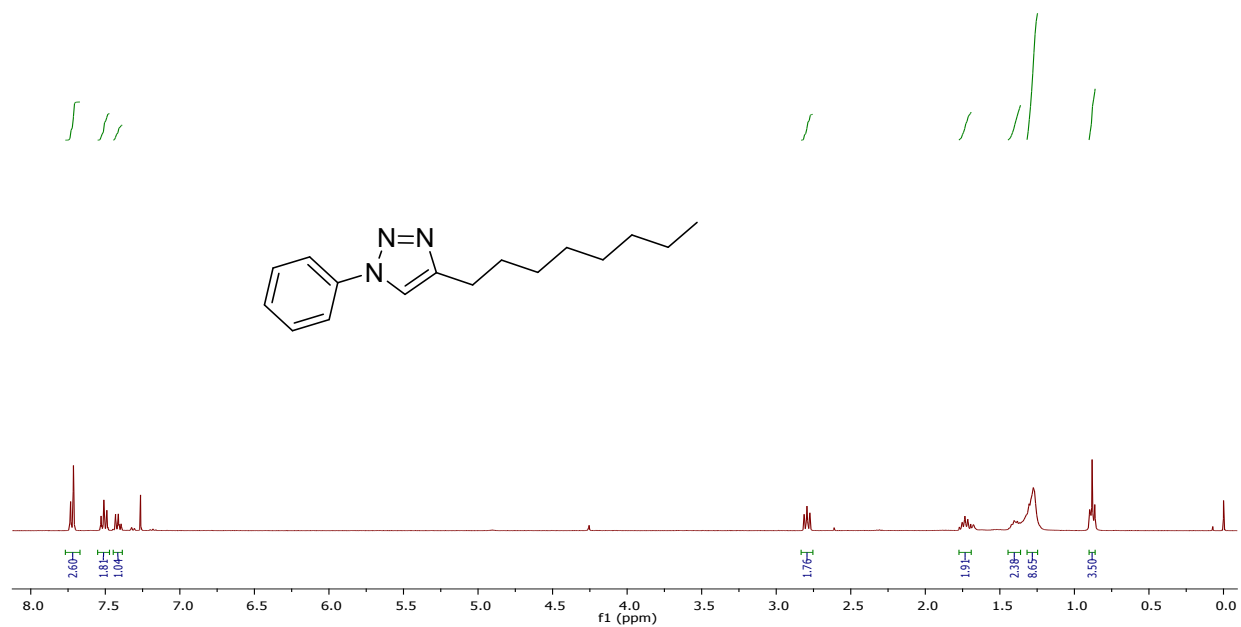
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3r)



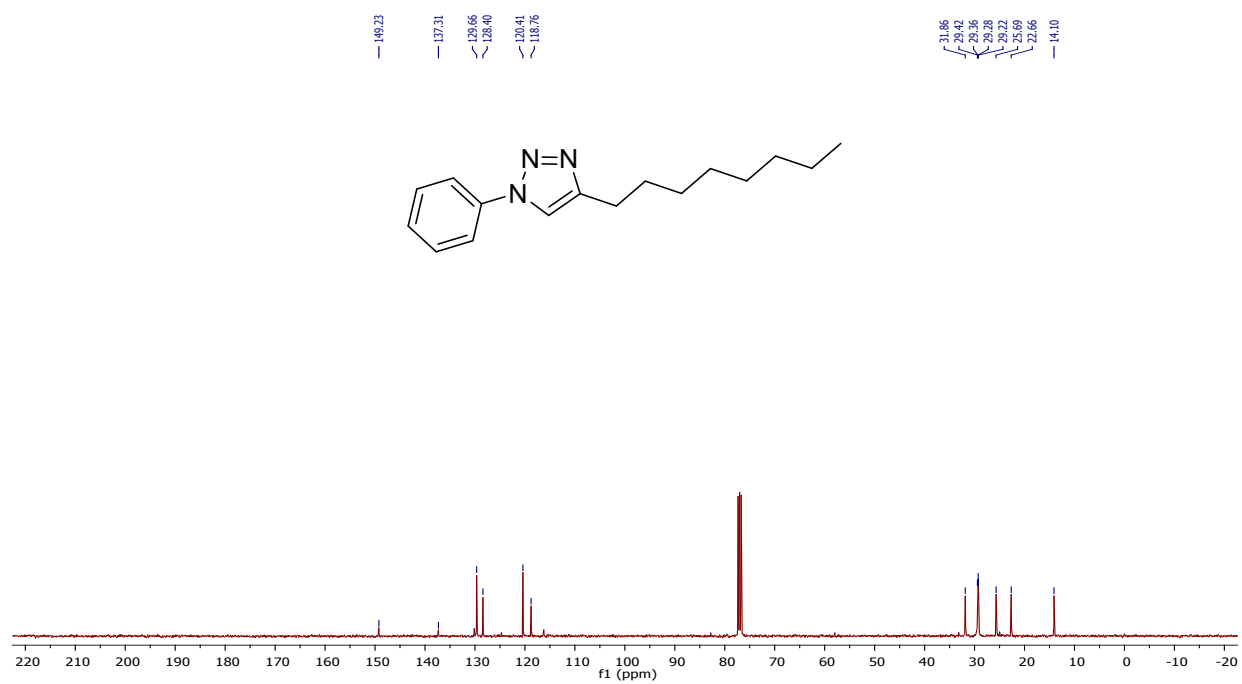
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3s)



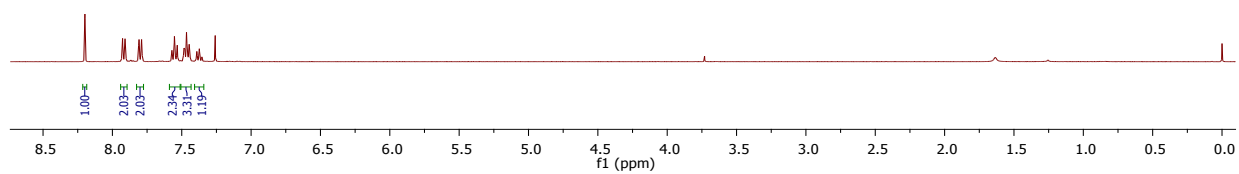
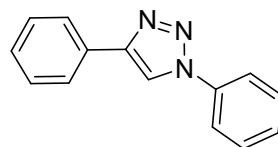
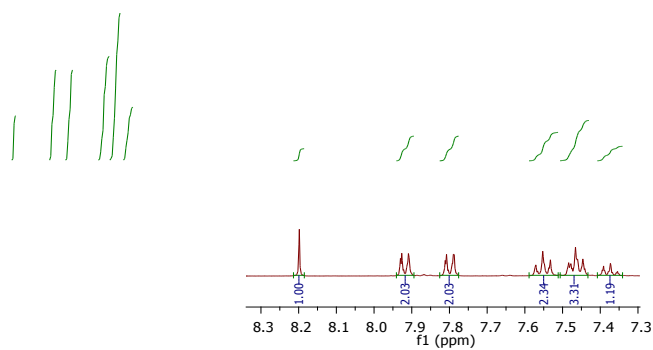
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3s)



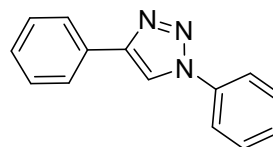
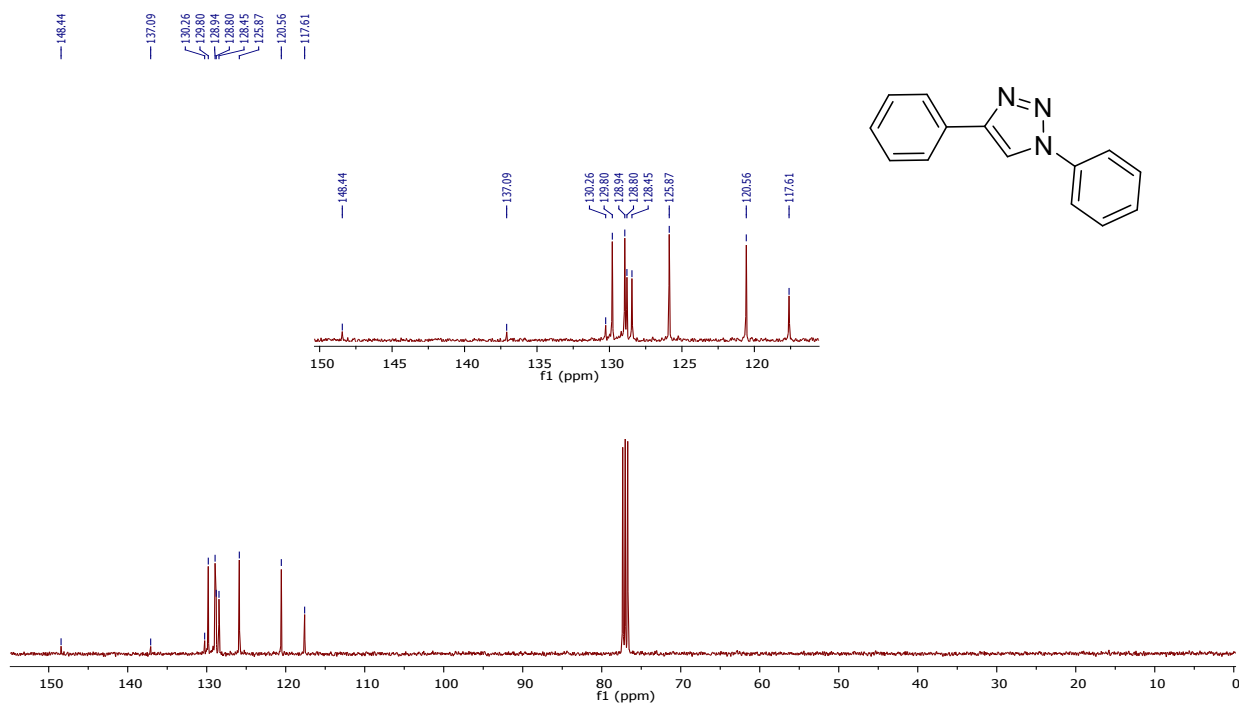
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3t)



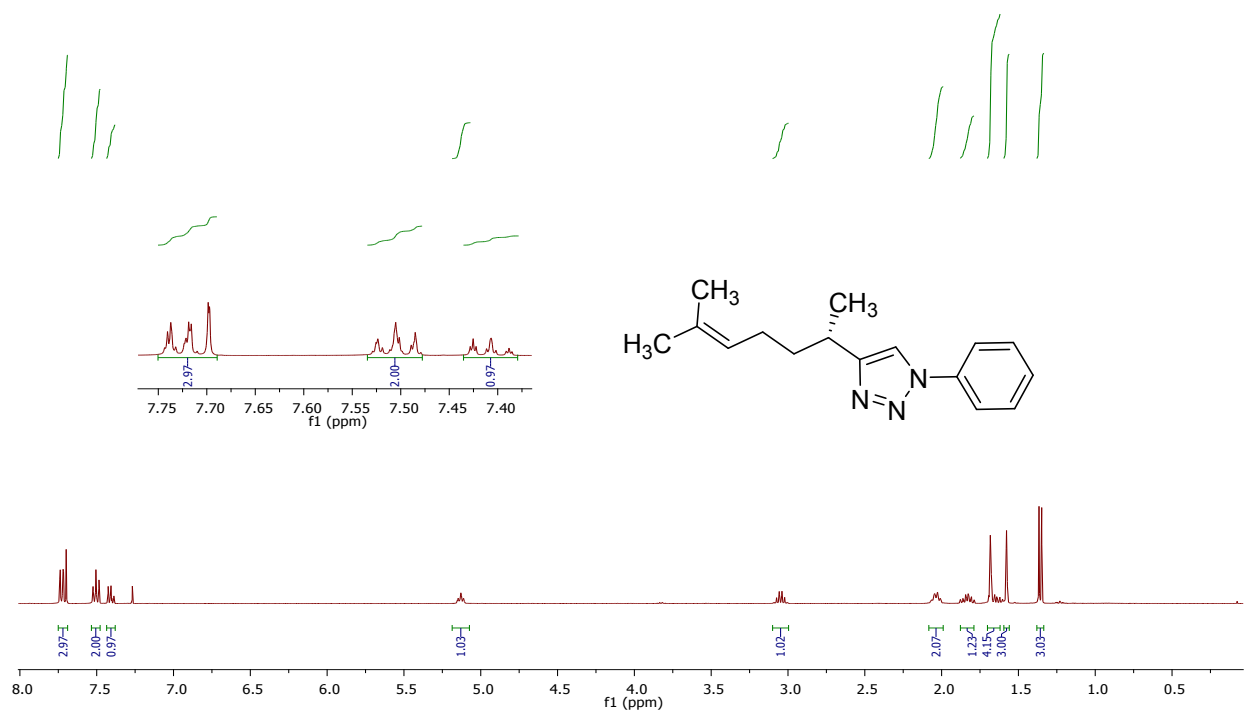
¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3t)



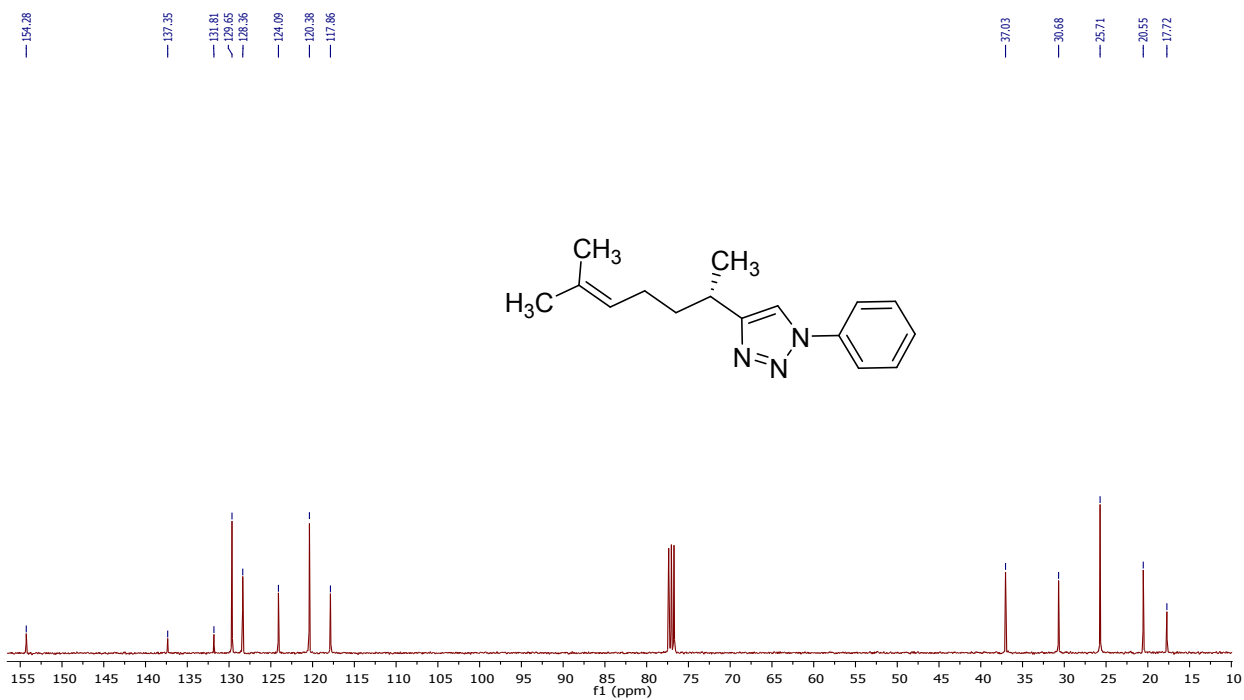
¹H NMR spectra at 400 MHz in CDCl₃ for compound (3u)



¹³C NMR spectra at 100 MHz in CDCl₃ for compound (3u)

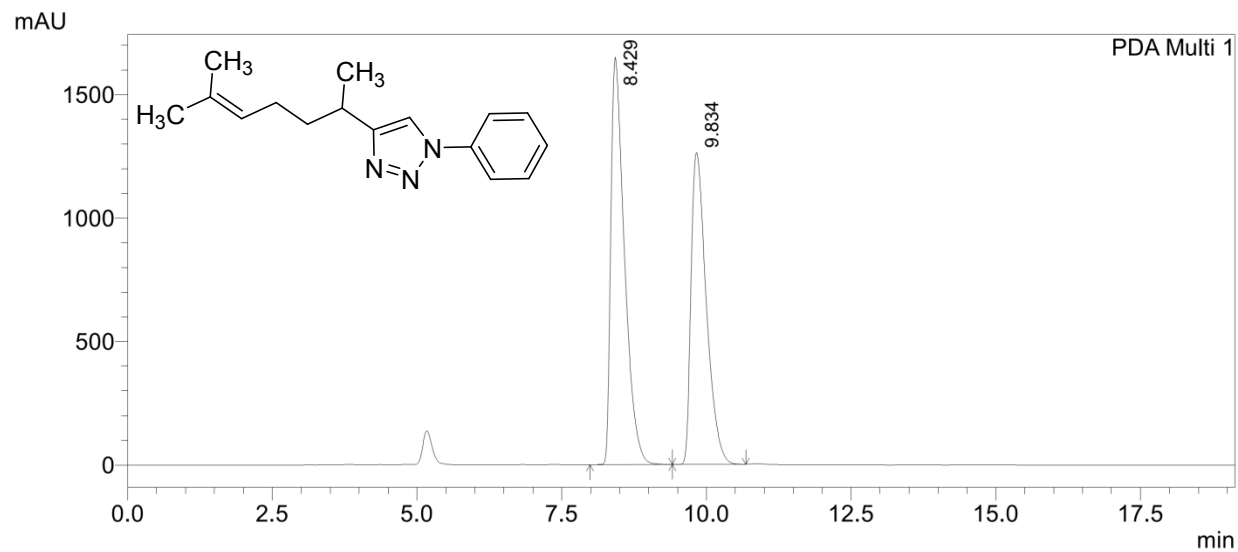


¹H NMR spectra at 400 MHz in CDCl₃ for compound (3v)



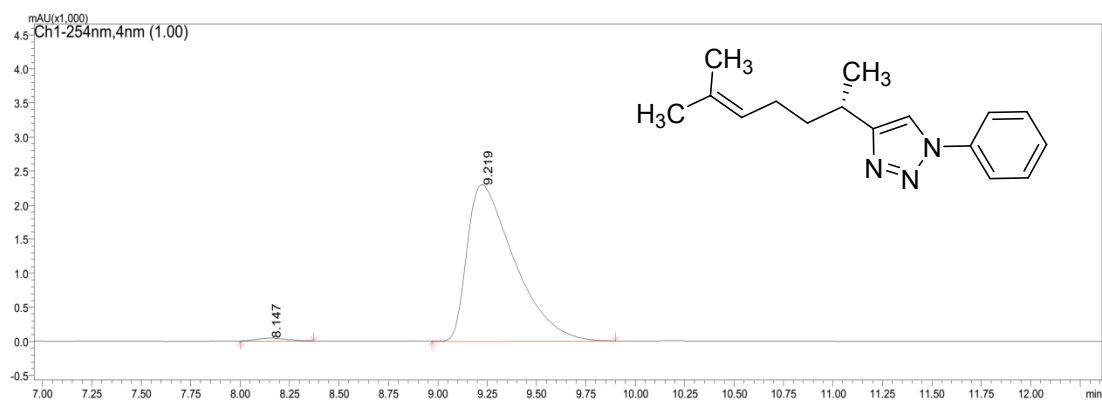
¹³CNMR spectra at 100 MHz in CDCl₃ for compound (3v)

HPLC: Chiracel OD-H column (n-hexane/*i*-PrOH 95:05, 25°C) at 1 mL/min



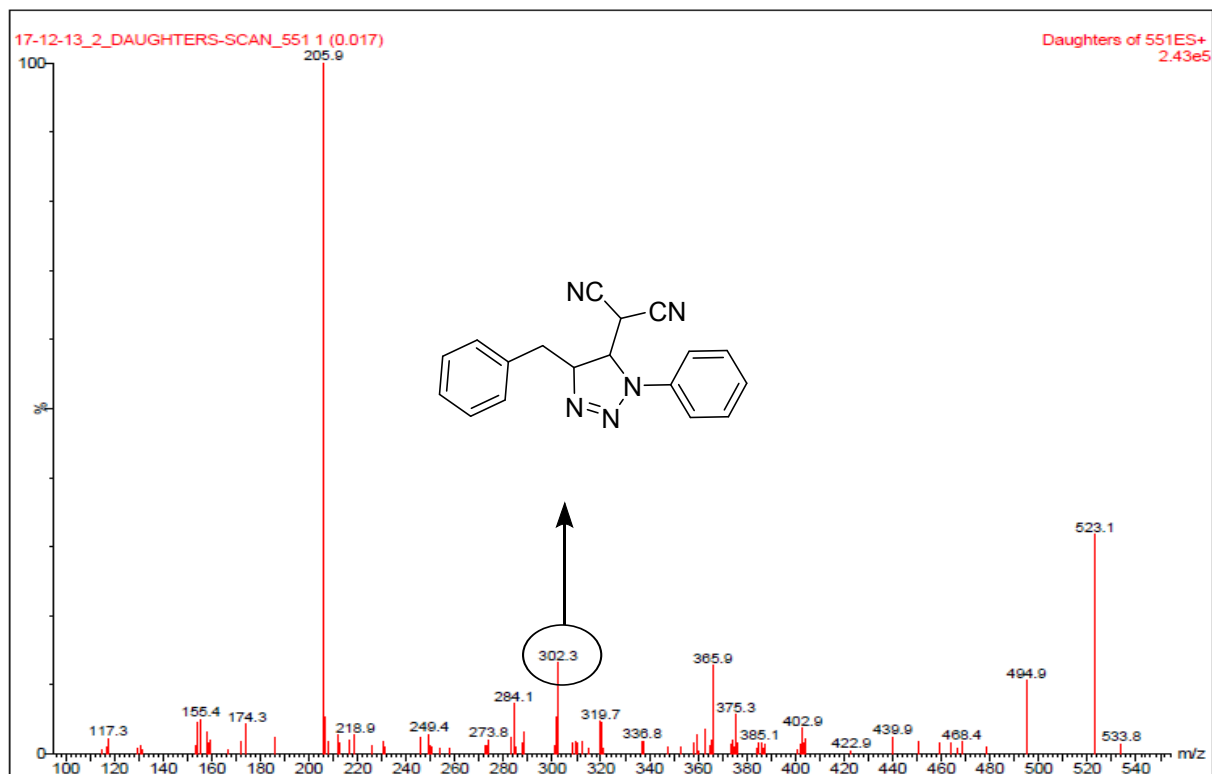
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.429	27164017	1564176	54.012	55.783
2	9.834	23128221	1239877	45.988	44.217
Total		50292239	2804052	100.000	100.000

HPLC result of racemic 4-(6-methylhept-5-en-2-yl)-1-phenyl-1*H*-1,2,3-triazole (3v)



Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.147	412107	39452	1.065	1.689
2	9.219	38277665	2296772	98.935	98.311
Total		38689772	2336223	100.000	100.000

HPLC result of racemic (*S*)-4-(6-methylhept-5-en-2-yl)-1-phenyl-1*H*-1,2,3-triazole (3v)



Mass spectrum obtained from the crude reaction mixture of the model reaction.

References;

- 1 H. Cheng, J. Wan, M. -I Lin, Y. Liu, X. Lu, J. Liu, Y. Xu, J. Chen, Z. Tu, Y. -S., E. Cheng and K. Ding, *J. Med. Chem.* 2012, **55**, 2144–2153.
- 2 F. Bigi, M. L. Conforti, R. Maggi, A. Piccinno and G. Sartori, *Green Chem.*, 2000, **2**, 101-103.
- 3 J. E. Macdonald, J. A. Kelly and J. G. C. Veinot, *Langmuir* 2007, **23**, 9543-9545.
- 4 A. Kolarovic, M. Schnurch and M. D. Mihovilovic, *J. Org Chem.* 2011, **76**, 2613-1618.
- 5 B. Kaboudin, R. Mostafalua and T. Yokomatsub, *Green Chem.*, 2013, **15**, 2266–2274.
- 6 J. Yan and L. Wang, *Synthesis* 2010, **3**, 447–452.
- 7 Jee. Kim, J. C. Park, H. Kang, H. Song, K. H. Park., *Chem. Commun.*, 2010, **46**, 439.