Electronic Supplementary Information (ESI)

One-Pot Three-Steps Synthesis of 1,2,3-Triazoles by Copper-Catalyzed Cycloaddition of Azides with Alkynes formed by a Sonogashira Cross-Coupling and Desilylation

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General Methods.

All reactions were carried out in microwave pressure resistant vessels. Room temperature refers to ambient room temperature (20-22 °C). Reactions were monitored by Thin Layer Chromatography (TLC) using aluminium backed silica gel 60 (F254) plates, visualised using UV254nm and potassium permanganate and ninhydrin dips as appropriate. Flash chromatography was carried out routinely using silica gel G60 (SiliCycle, 60-200μm 60 Å) as the stationary phase unless otherwise stated. The NMR spectra were recorded on a Varian Mercury (300 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million (ppm) downfield from TMS. Coupling constants (*J*) are measured in Hertz (Hz) and are unadjusted; therefore, due to limits in resolution, in some cases there are small differences (<1 Hz) in the measured *J* value of the same coupling constant determined from different signals. Splitting patterns are designed as follows: s – singlet, d – doublet, t – triplet, dd – doublet of doublets, dt – doublet of triplets, td – triplet of doublets, ddd – doublet of doublet of doublets, tt – triplet of triplets, sp – septet, m – multiplet, br – broad. Various 2D techniques and DEPT experiments were used to establish the structures and to assign the signals. High-resolution mass spectra were obtained by using MALDI-ToF (Applied Biosystems 4700 Proteomics Analyzer) with 2,5-dihydroxybenzoic acid as an internal standard matrix. Microwave-assisted reactions were performed on a CEM microwave *Discover BenchMate*.

Materials.

All solvents were of reagent grade. All palladium catalysts, copper(I) iodide and TBAF as well as all starting TMS-protected alkynes, halides, and acyl chlorides were purchased from Sigma-Aldrich®. Benzyl azide and CuF_2 (99.5 % purity) were purchased from Alfa Aesar®. All benzyl chloride derivatives required for the synthesis of various substituted-benzyl azides were also purchased from Sigma-Aldrich®.

Experimental Procedures.

One-pot, Two-Steps TMS-Removal-Click Cycloaddition Procedures:

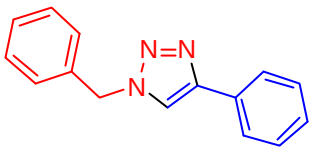
Method A. General Procedure for the Microwave-Assisted CuI/TBAF-Mediated TMS- Removal-Click Cycloaddition.

A solution of TBAF in THF (1.0M, 0.5 mL, 0.5 mmol, 1.0 equiv) was added to a solution of TMS-protected alkyne **1a-g** (0.5 mmol, 1.0 equiv), azide **2a-c** (0.5 mmol, 1.0 equiv), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and *N*,*N*-diisopropylethylamine (0.02 mL, 0.1 mmol, 20 mol%) in methanol (2.5 mL). The reaction mixture was stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel (8 g) using an appropriate mixture of hexane and ethyl acetate, affording pure 1,4-disubstituted triazoles **3a-i** (see table for respective yields).

Method B. General Procedure for the Microwave-Assisted CuF_2-Mediated TMS- Removal-Click Cycloaddition.

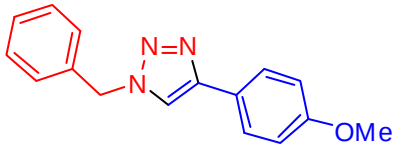
Azide **2a-c** (0.5 mmol, 1.0 equiv) was added to a solution of TMS-protected alkyne **1a-g** (0.5 mmol, 1.0 equiv) and copper(II) fluoride (101 mg, 1.0 mmol, 2.0 equiv) in methanol (3 mL). The reaction mixture was stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel (8 g) using an appropriate mixture of hexane and ethyl acetate, affording pure 1,4-disubstituted triazoles **3a-i** (see table for respective yields).

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole 3a.



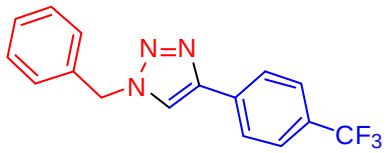
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (s, 2H, Ph-CH_2), 7.25-7.42 (m, 8H, aromH), 7.69 (s, 1H, 5-H), 7.80 (d, *J* = 7.2 Hz, 2H, aromH); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.09 (CH_2), 119.69 (CH-5), 125.65 (2×CHo), 127.98 (2×CHo), 128.11 (CHp), 128.68 (CHp), 128.78 (2×CHm), 129.07 (2×CHm), 130.56 (C), 134.74 (C), 148.09 (C-4); **HRMS** (MALDI) 236.1184 ($C_{15}H_{14}N_3$ (MH+) requires 236.1188).

1-Benzyl-4-(4'-methoxyphenyl)-1*H*-1,2,3-triazole 3b.



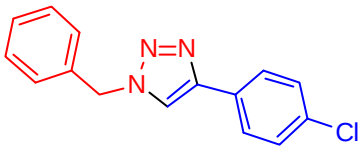
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 3H, OMe), 5.51 (s, 2H, Ph-CH_2), 6.91 (d, *J* = 8.9 Hz, 2H, 3'-H, 5'-H), 7.25-7.40 (m, 5H, aromH), 7.59 (s, 1H, 5-H), 7.71 (d, *J* = 8.9 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.13 (CH_2), 55.31 (CH_3), 114.22 (2×CH-3',5'), 118.85 (CH-5), 123.32 (C-1'), 127.01 (2×CH-2',6'), 128.02 (2×CH), 128.70 (CHp), 129.11 (2×CH), 134.86 (C), 148.04 (C-4), 159.60 (C-4'); **HRMS** (MALDI) 266.1205 ($C_{16}H_{16}N_3O$ (MH+) requires 266.1293).

1-Benzyl-4-[4'-(trifluoromethyl)phenyl]-1*H*-1,2,3-triazole 3c.



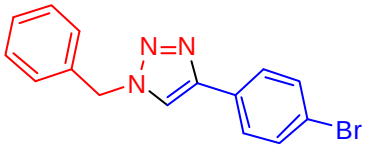
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.57 (s, 2H, Ph-CH_2), 7.29-7.44 (m, 5H, aromH), 7.62 (d, *J* = 8.2 Hz, 2H, 2'-H, 6'-H), 7.77 (s, 1H, 5-H), 7.90 (d, *J* = 8.2 Hz, 2H, 3'-H, 5'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.41 (CH_2), 120.47 (CH-5), 124.18 (q, *J* = 272.0 Hz, CF_3), 125.77-125.92 (m, 4×CH-2',3',5',6'), 128.18 (2×CHo), 128.99 (CHp), 129.29 (2×CHm), 129.99 (q, *J* = 32.7 Hz, C-4'), 134.09 (q, *J* = 1.3 Hz, C-1'), 134.50 (C), 146.86 (C-4); **HRMS** (MALDI) 304.1060 ($C_{16}H_{13}F_3N_3$ (MH+) requires 304.1062).

1-Benzyl-4-(4'-chlorophenyl)-1*H*-1,2,3-triazole 3d.



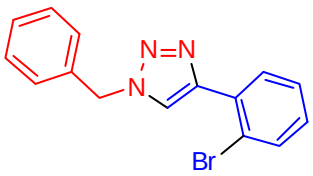
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (s, 2H, Ph-CH_2), 7.29-7.41 (m, 7H, aromH), 7.65 (s, 1H, 5-H), 7.71 (d, *J* = 8.6 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.37 (CH_2), 119.69 (CH-5), 127.02 (2×CH-2',6'), 128.18 (2×CHo), 128.94 (CHp), 129.08 (2×CHm), 129.17 (C-1'), 129.27 (2×CH-3',5'), 133.94 (C-4'), 134.62 (C), 147.23 (C-4); **HRMS** (MALDI) 270.0799 ($C_{15}H_{13}N_3{}^{35}Cl$ (MH+) requires 270.0798).

1-Benzyl-4-(4'-bromophenyl)-1*H*-1,2,3-triazole 3e.



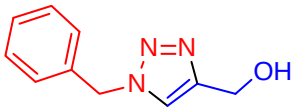
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (s, 2H, Ph-CH_2), 7.29-7.41 (m, 5H, aromH), 7.50 (d, *J* = 8.6 Hz, 2H, 3'-H, 5'-H), 7.65 (d, *J* = 8.6 Hz, 2H, 2'-H, 6'-H), 7.66 (s, 1H, 5-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.39 (CH_2), 119.70 (CH-5), 122.11 (C-4'), 127.31 (2×CH-2',6'), 128.19 (2×CHo), 128.96 (CHp), 129.29 (2×CHm), 129.61 (C-1'), 132.03 (2×CH-3',5'), 134.60 (C), 147.25 (C-4); **HRMS** (MALDI) 314.0294 ($C_{15}H_{13}N_3{}^{79}Br$ (MH+) requires 314.0293).

1-Benzyl-4-(2'-bromophenyl)-1*H*-1,2,3-triazole 3f.



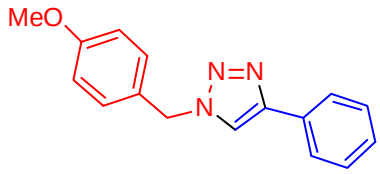
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (s, 2H, Ph-CH_2), 7.17 (td, *J* = 7.8, 1,7 Hz, 1H, 5'-H), 7.25-7.42 (m, 6H, aromH), 7.61 (dd, *J* = 7.8, 1.0 Hz, 1H, 6'-H), 8.11 (dd, *J* = 7.8, 1.7 Hz, 1H, 3'-H), 8.15 (s, 1H, 5-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.31 (CH_2), 121.25 (C-2'), 123.13 (CH-5), 127.76 (CH-4'), 128.01 (2×CHo), 128.81 (CHp), 129.22 (2×CHm), 129.42 (CH-5'), 130.68 (CH-3'), 131.36 (C), 133.58 (C-1'), 134.77 (CH-6'), 145.82 (C-4); **HRMS** (MALDI) 314.0297 ($C_{15}H_{13}N_3{}^{79}Br$ (MH+) requires 314.0293).

1-Benzyl-4-methanol-1*H*-1,2,3-triazole 3g.



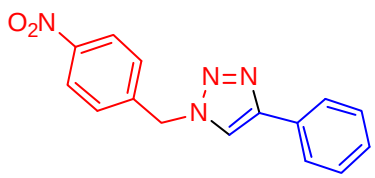
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.12 (br s, 1H, OH), 4.69 (s, 2H, CH_2OH), 5.44 (s, 2H, Ph-CH_2), 7.20-7.30 (m, 2H, aromH), 7.27-7.35 (m, 3H, aromH), 7.45 (s, 1H, 5-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.17 (CH_2Ph), 56.08 (CH_2OH), 121.93 (CH-5), 128.13 (2×CHo), 128.77 (CHp), 129.12 (2×CHm), 134.58 (C), 148.35 (C-4); **HRMS** (MALDI) 190.0985 ($C_{10}H_{12}N_3O$ (MH+) requires 190.0980).

1-(4'-Methoxybenzyl)-4-phenyl-1*H*-1,2,3-triazole 3h.



^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 3H, OMe), 5.48 (s, 2H, Ph-CH_2), 6.89 (d, J = 8.7 Hz, 2H, 2'-H, 6'-H), 7.25 (d, J = 8.7 Hz, 2H, 3'-H, 5'-H), 7.29 (t, J = 7.3 Hz, 1H, 4''-H), 7.38 (t, J = 7.3 Hz, 2H, 3''-H, 5''-H), 7.63 (s, 1H, 5-H), 7.78 (d, J = 7.3 Hz, 2H, 2''-H, 6''-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 53.82 (CH_2), 55.41 (OCH_3), 114.57 (2×CH-2',6'), 119.40 (CH-5), 125.74 (2×CHo), 126.73 (C-1'), 128.16 (CHp), 128.85 (2×CHm), 129.72 (2×CH-3',5'), 130.70 (C), 148.15 (C-4), 160.01 (C-4'); **HRMS** (MALDI) 266.1289 ($C_{16}H_{16}N_3O$ (MH+) requires 266.1293).

1-(4'-Nitrobenzyl)-4-phenyl-1*H*-1,2,3-triazole 3i.



^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69 (s, 2H, Ph-CH_2), 7.30-7.50 (m, 5H, aromH), 7.76 (s, 1H, 5-H), 7.81 (d, J = 8.5 Hz, 2H, 2'-H, 6'-H), 8.22 (d, J = 8.5 Hz, 2H, 3'-H, 5'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 53.28 (CH_2), 119.85 (CH-5), 124.44 (2×CH-2',6'), 125.85 (2×CHo), 128.60 (CHp), 128.66 (2×CHm), 129.03 (2×CH-3',5'), 130.23 (C-1'), 141.88 (C), 148.15 (C-4), 148.81 (C-4'); **HRMS** (MALDI) 281.1018 ($C_{15}H_{13}N_4O_2$ (MH+) requires 281.1039).

One-pot, Three-Steps Sonogashira Coupling-TMS-Removal-Click Reaction Procedure:

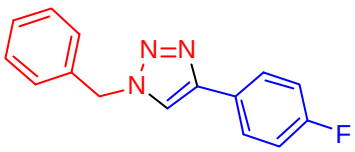
Method A. General Procedure for the Microwave-Assisted Sonogashira Coupling followed by CuI/TBAF-Mediated TMS-Removal-Click Cycloaddition.

Ethynyltrimethylsilane (0.09 mL, 0.65 mmol, 1.3 equiv) was added to a solution of aromatic halide **4a-i** (0.5 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol, 5 mol%), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and *N*,*N*-diisopropylethylamine (0.18 mL, 1.0 mmol, 2.0 equiv) in methanol (2 mL). The reaction mixture was stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, a solution of TBAF in THF (1.0M, 1 mL, 1.0 mmol, 2.0 equiv), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and azide **2a-c** (0.5 mmol, 1.0 equiv) were successively added to the latter methanolic solution. The reaction mixture was then stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel (8 g) using an appropriate mixture of hexane and ethyl acetate, affording pure 1,4-disubstituted triazoles **3a-c,h-m** (see table for respective yields).

Method B. General Procedure for the Microwave-Assisted Sonogashira Coupling followed by CuF_2-Mediated TMS-Removal-Click Cycloaddition.

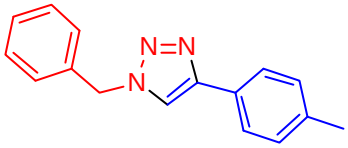
Ethynyltrimethylsilane (0.09 mL, 0.65 mmol, 1.3 equiv) was added to a solution of aromatic halide **4a-i** (0.5 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol, 5 mol%), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and *N*,*N*-diisopropylethylamine (0.18 mL, 1.0 mmol, 2.0 equiv) in methanol (3 mL). The reaction mixture was stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, copper(II) fluoride (101 mg, 1.0 mmol, 2.0 equiv) and azide **2a-c** (0.5 mmol, 1.0 equiv) were added successively to the latter methanolic solution. The reaction mixture was then stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel (8 g) using an appropriate mixture of hexane and ethyl acetate, affording pure 1,4-disubstituted triazoles **3a-c,h-m** (see table for respective yields).

1-Benzyl-4-(4'-fluorophenyl)-1*H*-1,2,3-triazole 3j.



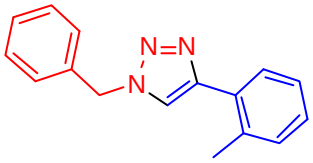
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (s, 2H, Ph-CH_2), 7.07 (t, *J* = 8.7 Hz, 2H, 3'-H, 5'H), 7.25-7.42 (m, 5H, aromH), 7.63 (s, 1H, 5-H), 7.76 (dd, *J* = 8.7, 5.3 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.32 (CH_2), 115.84 (d, *J* = 21.8 Hz, 2×CH-3',5'), 119.39 (CH-5), 126.88 (d, *J* = 3.3 Hz, C-1'), 127.50 (d, *J* = 8.1 Hz, 2×CH-2',6'), 128.14 (2×CHo), 128.89 (CHp), 129.24 (2×CHm), 134.70 (C), 147.41 (C-4), 162.71 (d, *J* = 247.2 Hz, C-4'); **HRMS** (MALDI) 254.1077 ($C_{15}H_{13}N_3F$ (MH+) requires 254.1094).

1-Benzyl-4-(4'-methylphenyl)-1*H*-1,2,3-triazole 3k.



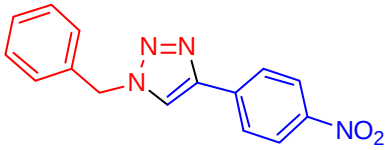
^{1}H NMR (300 MHz, $CDCl_3$) δ 2.36 (s, 3H, CH_3), 5.55 (s, 2H, Ph-CH_2), 7.20 (d, *J* = 7.9 Hz, 2H, 3'-H, 5'-H), 7.25-7.40 (m, 5H, aromH), 7.62 (s, 1H, 5-H), 7.69 (d, *J* = 7.9 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 21.37 (CH_3), 54.25 (CH_2), 119.27 (CH-5), 125.68 (2×CH-2',6'), 127.83 (C-1'), 128.13 (2×CHo), 128.81 (CHp), 129.20 (2×CHm), 129.56 (2×CH-3',5'), 134.86 (C), 138.06 (C-4'), 148.36 (C-4); **HRMS** (MALDI) 250.1338 ($C_{16}H_{16}N_3$ (MH+) requires 250.1344).

1-Benzyl-4-(2'-methylphenyl)-1*H*-1,2,3-triazole 3l.



^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (s, 3H, CH_3), 5.59 (s, 2H, Ph-CH_2), 7.20-7.25 (m, 3H, aromH), 7.27-7.32 (m, 2H, aromH), 7.23-7.40 (m, 3H, aromH), 7.57 (s, 1H, 5-H), 7.70-7.76 (m, 1H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 21.47 (CH_3), 54.22 (CH_2), 121.77 (CH-5), 126.14 (CH-5'), 128.05 (2×CHo), 128.23 (CH-6'), 128.81 (CH-3'), 128.97 (CHp), 129.22 (2×CHm), 129.98 (CH-4'), 130.94 (C), 134.93 (C-1'), 135.59 (C-2'), 147.65 (C-4); **HRMS** (MALDI) 250.1339 ($C_{16}H_{16}N_3$ (MH+) requires 250.1344).

1-Benzyl-4-(4'-nitrophenyl)-1*H*-1,2,3-triazole 3m.

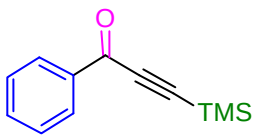


^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (s, 2H, Ph-CH_2), 7.30-7.45 (m, 5H, aromH), 7.82 (s, 1H, 5-H), 7.96 (d, *J* = 8.8 Hz, 2H, 2'-H, 6'-H), 8.24 (d, *J* = 8.8 Hz, 2H, 3'-H, 5'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.59 (CH_2), 121.11 (CH-5), 124.37 (2×CH-3',5'), 126.24 (2×CH-2',6'), 128.31 (2×CHo), 129.17 (CHp), 129.41 (2×CHm), 134.29 (C), 136.92 (C-1'), 146.15 (C-4'), 147.41 (C-4); **HRMS** (MALDI) 281.1018 ($C_{15}H_{13}N_4O_2$ (MH+) requires 281.1039).

General Procedure for the Microwave-Assisted Sonogashira Coupling between TMS-Acetylene and Acyl Chlorides.

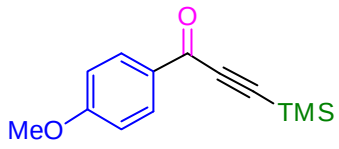
Ethynyltrimethylsilane (0.07 mL, 0.5 mmol, 1.0 equiv) was added to a solution of acyl chloride **6a-e** (0.5 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (17 mg, 0.025 mmol, 5 mol%), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and triethylamine (0.07 mL, 0.5 mmol, 1.0 equiv) in THF (2 mL). The reaction mixture was stirred at room temperature for 1 h. and concentrated under vacuum. The residue was then purified by flash chromatography on silica gel (8 g) using pure hexane, affording pure TMS-protected ynones **8a-e**.

1-Phenyl-3-(trimethylsilyl)-2-propyn-1-one 8a.



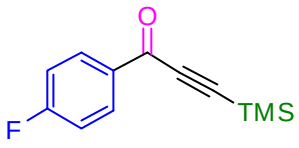
(45% yield): **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.32 (s, 9H, $Si(CH_3)_3$), 7.49 (t, *J* = 7.5 Hz, 2H, 3'-H, 5'-H), 7.61 (t, *J* = 7.5 Hz, 1H, 4'-H), 8.15 (d, *J* = 7.5 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ -0.55 (3×CH_3), 100.68 (C), 100.96 (C), 128.69 (2×CH-3',5'), 129.76 (2×CH-2',6'), 134.29 (CH-4'), 136.60 (C-1'), 177.80 (C=O).

1-(4'-Methoxyphenyl)-3-(trimethylsilyl)-2-propyn-1-one 8b.



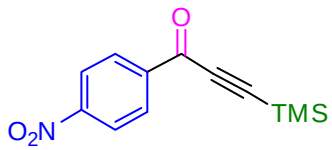
(98% yield): **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.28 (s, 9H, $Si(CH_3)_3$), 3.84 (s, 3H, OCH_3), 6.92 (d, *J* = 8.9 Hz, 2H, 3'-H, 5'-H), 8.08 (d, *J* = 8.9 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ -0.59 (3×CH_3), 55.61 (CH_3), 99.48 (C), 101.06 (C), 113.89 (2×CH-3',5'), 129.93 (C-1'), 132.06 (2×CH-2',6'), 164.58 (C-4'), 176.29 (C=O).

1-(4'-Fluorophenyl)-3-(trimethylsilyl)-2-propyn-1-one 8c.



(97% yield): **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.29 (s, 9H, $Si(CH_3)_3$), 7.12 (t, *J* = 8.6 Hz, 2H, 3'-H, 5'-H), 8.13 (dd, *J* = 8.8, 5.4 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ -0.66 (3×CH_3), 100.59 (C), 100.91 (C), 115.86 (d, *J* = 22.2 Hz, 2×CH-3',5'), 132.36 (d, *J* = 9.7 Hz, 2×CH-2',6'), 133.07 (d, *J* = 2.7 Hz, C-1'), 166.53 (d, *J* = 256.7 Hz, C-4'), 176.01 (C=O).

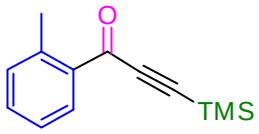
1-(4'-Nitrophenyl)-3-(trimethylsilyl)-2-propyn-1-one 8d.



(42% yield): **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.34 (s, 9H, $Si(CH_3)_3$), 8.29 (d, *J* = 8.9 Hz, 2H, 2'-H, 6'-H), 8.34 (d, *J* = 8.9 Hz, 2H, 3'-H, 5'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ -0.65 (3×CH_3), 100.25 (C), 103.62 (C), 123.94 (2×CH-

3',5'), 130.64 (2×CH-2',6'), 140.67 (C-1'), 151.05 (C-4'), 175.71 (C=O).

1-(2'-Methyphenyl)-3-(trimethylsilyl)-2-propyn-1-one 8e.



(96% yield): **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.30 (s, 9H, $Si(CH_3)_3$), 2.62 (s, 3H, CH_3), 7.23 (d, *J* = 7.5 Hz, 1H, 3'-H), 7.33 (t, *J* = 7.2 Hz, 1H, 5'-H), 7.44 (t, *J* = 7.4 Hz, 1H, 4'-H), 8.23 (d, *J* = 7.6 Hz, 1H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ -0.58 (3×CH_3), 22.00 (CH_3), 98.94 (C), 102.43 (C), 125.93 (CH-6'), 132.18 (CH-5'), 133.05 (CH-4'), 133.50 (CH-3'), 135.31 (C-1'), 140.63 (C-2'), 179.41 (C=O).

One-pot, Three-Steps Sonogashira Coupling-TMS-Removal-Click Reaction Procedure:

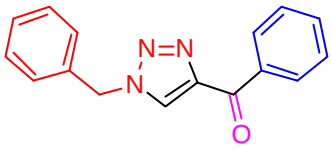
Method A. General Procedure for the Microwave-Assisted Sonogashira Coupling followed by CuI/TBAF-Mediated TMS-Removal-Click Cycloaddition.

Ethynyltrimethylsilane (0.07 mL, 0.5 mmol, 1.0 equiv) was added to a solution of acyl chloride **6a-e** (0.5 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (17 mg, 0.025 mmol, 5 mol%), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and triethylamine (0.07 mL, 0.5 mmol, 1.0 equiv) in THF (2 mL). The reaction mixture was stirred at room temperature for 1 h. A solution of TBAF in THF (1.0M, 1 mL, 1.0 mmol, 2.0 equiv), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%), benzyl azide **2a** (0.062 mL, 0.5 mmol, 1.0 equiv) and methanol (2.5 mL) were then successively added to the latter mixture. The reaction mixture was then stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel (8 g) using an appropriate mixture of hexane and ethyl acetate, affording pure 1-benzyl 4-acyl-1*H*-1,2,3-triazoles **7a-e** (see table for respective yields).

Method B. General Procedure for the Microwave-Assisted Sonogashira Coupling followed by CuF_2-Mediated TMS-Removal-Click Cycloaddition.

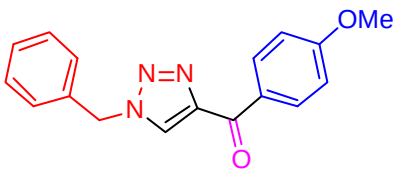
Ethynyltrimethylsilane (0.07 mL, 0.5 mmol, 1.0 equiv) was added to a solution of acyl chloride **6a-e** (0.5 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (17 mg, 0.025 mmol, 5 mol%), copper(I) iodide (10 mg, 0.05 mmol, 10 mol%) and triethylamine (0.07 mL, 0.5 mmol, 1.0 equiv) in THF (2 mL). The reaction mixture was stirred at room temperature for 1 h. Copper(II) fluoride (101 mg, 1.0 mmol, 2.0 equiv), benzyl azide **2a** (0.062 mL, 0.5 mmol, 1.0 equiv) and methanol (2.5 mL) were then added successively to the latter mixture. The reaction mixture was then stirred at 120 °C for 20 min. under microwave irradiation. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel (8 g) using an appropriate mixture of hexane and ethyl acetate, affording pure 1-benzyl 4-acyl-1*H*-1,2,3-triazoles **7a-e** (see table for respective yields).

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone 7a.



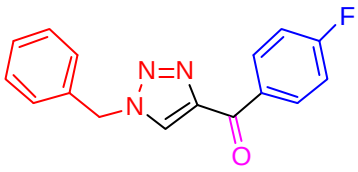
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.61 (s, 2H, Ph-CH_2), 7.30-7.45 (m, 5H, aromH), 7.51 (t, *J* = 7.4 Hz, 2H, 3'-H, 5'-H), 7.61 (t, *J* = 7.4 Hz, 1H, 4'-H), 8.17 (s, 1H, 5-H), 8.42 (d, *J* = 7.4 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.59 (CH_2), 128.37 (CHp), 128.49 (4×CHm), 129.29 (CH-5), 129.46 (2×CHo), 130.70 (2×CHo), 133.38 (CHp), 133.82 (C), 136.62 (C), 148.51 (C-4), 185.75 (C=O); **HRMS** (MALDI) 264.1168 ($C_{16}H_{14}N_3O$ (MH+) requires 264.1137).

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(4'-methoxyphenyl)methanone 7b.



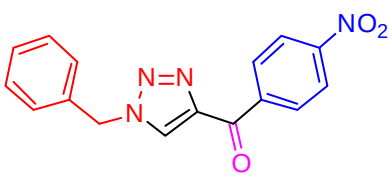
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H, OMe), 5.58 (s, 2H, Ph-CH_2), 6.98 (d, *J* = 9.0 Hz, 2H, 3'-H, 5'-H), 7.30-7.40 (m, 5H, aromH), 8.15 (s, 1H, 5-H), 8.50 (d, *J* = 9.0 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.47 (CH_2), 55.57 (CH_3), 113.74 (2×CH-3',5'), 128.23 (CH-5), 128.43 (2×CH), 129.17 (CHp), 129.37 (2×CH), 129.47 (C-1'), 133.17 (2×CH-2',6'), 133.90 (C), 148.86 (C-4), 163.88 (C-4'), 183.93 (C=O); **HRMS** (MALDI) 294.1283 ($C_{17}H_{16}N_3O_2$ (MH+) requires 294.1243).

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(4'-fluorophenyl)methanone 7c.



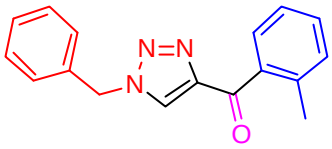
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (s, 2H, Ph-CH_2), 7.17 (t, *J* = 8.7 Hz, 2H, 3'-H, 5'H), 7.30-7.40 (m, 5H, aromH), 8.19 (s, 1H, 5-H), 8.53 (dd, *J* = 8.7, 5.5 Hz, 2H, 2'-H, 6'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.57 (CH_2), 115.60 (d, *J* = 21.8 Hz, 2×CH-3',5'), 128.47 (3×CH-5,Ho), 129.28 (CHp), 129.43 (2×CHm), 132.84 (d, *J* = 3.0 Hz, C-1'), 133.53 (d, *J* = 9.3 Hz, 2×CH-2',6'), 133.75 (C), 148.42 (C-4), 166.04 (d, *J* = 255.3 Hz, C-4'), 183.88 (C=O); **HRMS** (MALDI) 282.1081 ($C_{16}H_{13}N_3FO$ (MH+) requires 282.1043).

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(4'-nitrophenyl)methanone 7d.

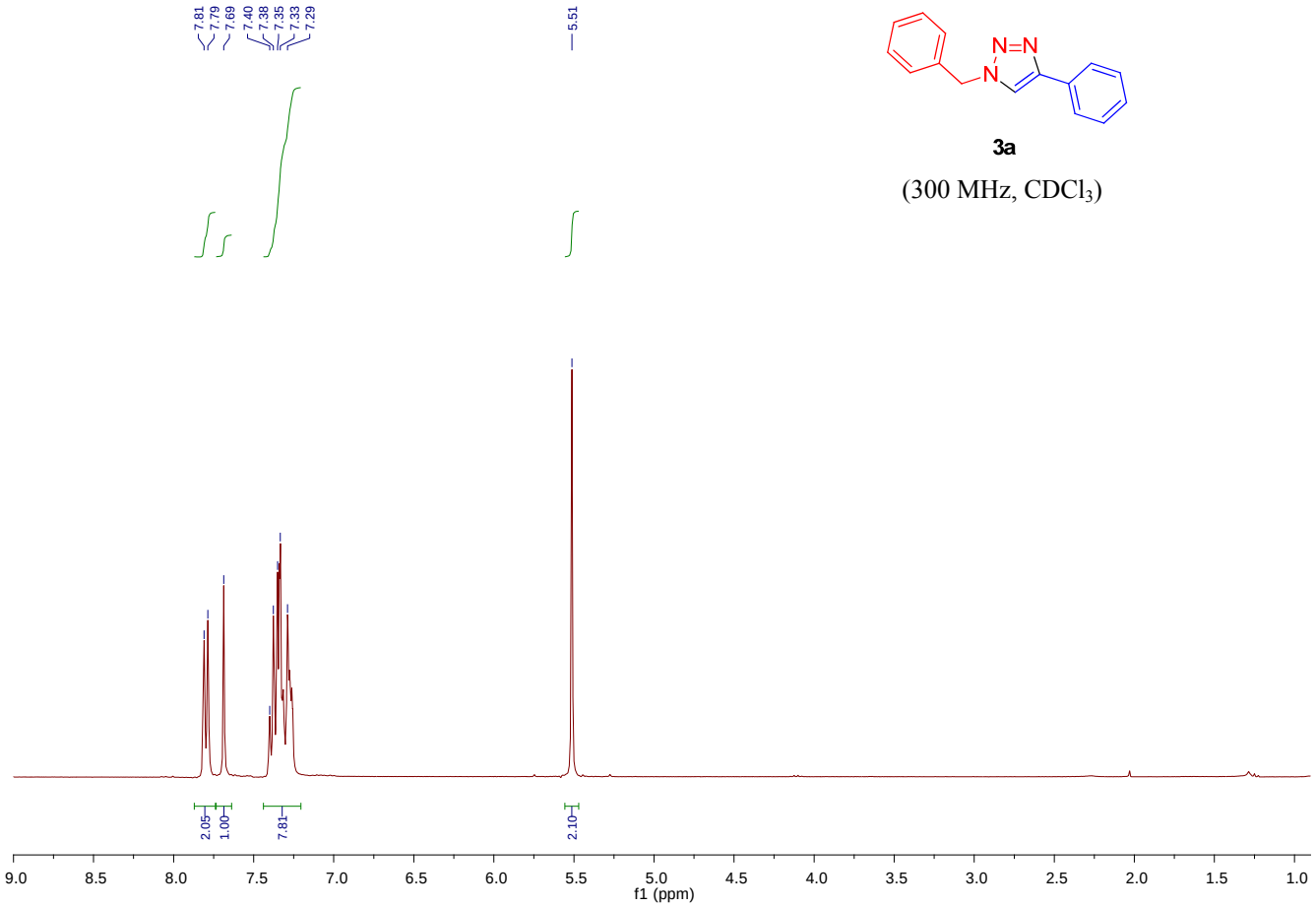


^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63 (s, 2H, Ph-CH_2), 7.30-7.50 (m, 5H, aromH), 8.23 (s, 1H, 5-H), 8.34 (d, *J* = 8.8 Hz, 2H, 2'-H, 6'-H), 8.61 (d, *J* = 8.8 Hz, 2H, 3'-H, 5'-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 54.80 (CH_2), 123.57 (2×CH-2',6'), 128.58 (2×CHo), 128.81 (CH-5), 129.50 (CHp), 129.58 (2×CHm), 131.80 (2×CH-3',5'), 133.51 (C), 141.20 (C-1'), 147.88 (C-4), 150.44 (C-4'), 183.90 (C=O); **HRMS** (MALDI) 309.0955 ($C_{16}H_{13}N_4O_3$ (MH+) requires 309.0988).

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(2'-methylphenyl)methanone 7e.

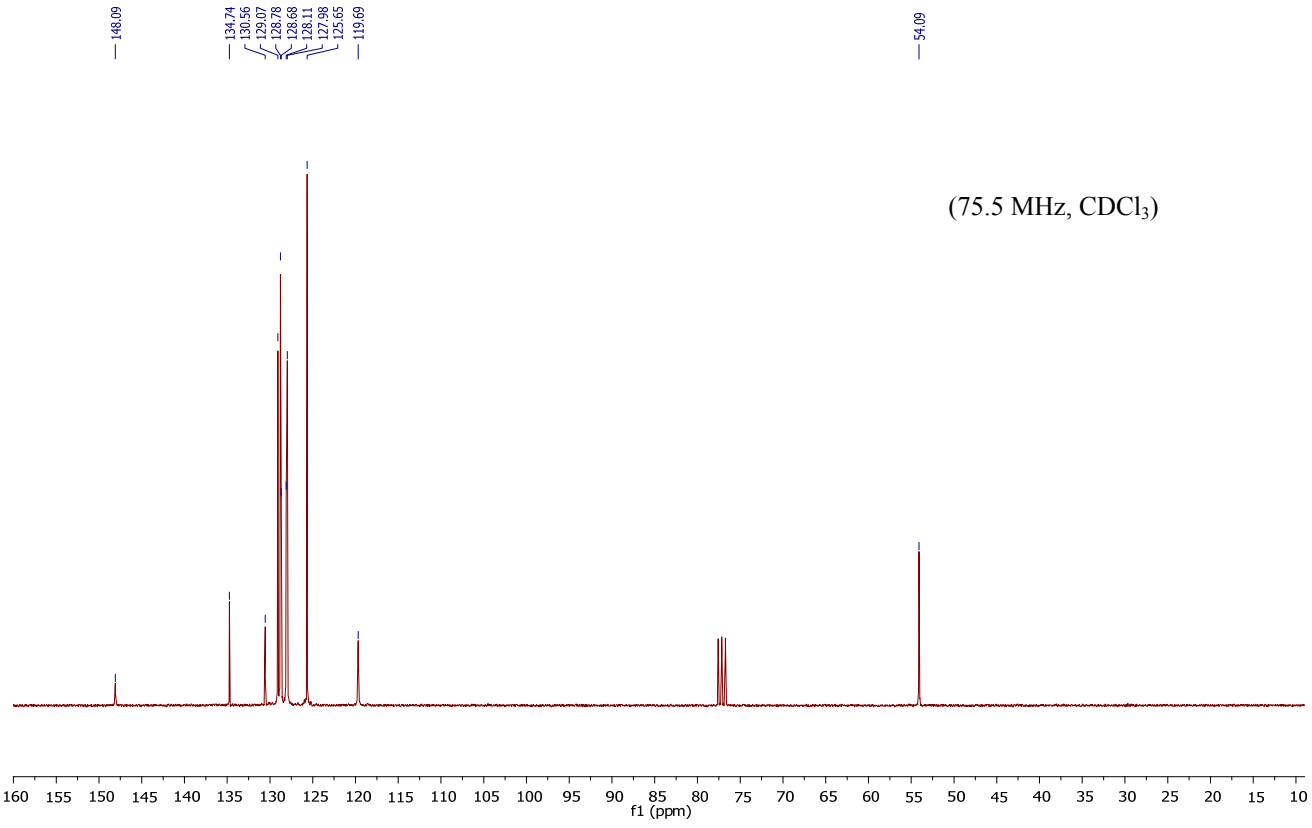


^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H, CH_3), 5.59 (s, 2H, Ph-CH_2), 7.25-7.45 (m, 8H, aromH), 7.78 (d, *J* = 8.6 Hz, 1H, 6'-H), 8.10 (s, 1H, 5-H); **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 20.44 (CH_3), 54.52 (CH_2), 125.36 (CH-5'), 127.81 (CH-5), 128.45 (2×CHo), 129.22 (CHp), 129.39 (2×CHm), 130.27 (CH-6'), 131.35 (CH-3'), 131.44 (CH-4'), 133.80 (C), 137.09 (C-1'), 138.05 (C-2'), 148.69 (C-4), 189.42 (C=O); **HRMS** (MALDI) 278.1222 ($C_{17}H_{16}N_3O$ (MH+) requires 278.1293).

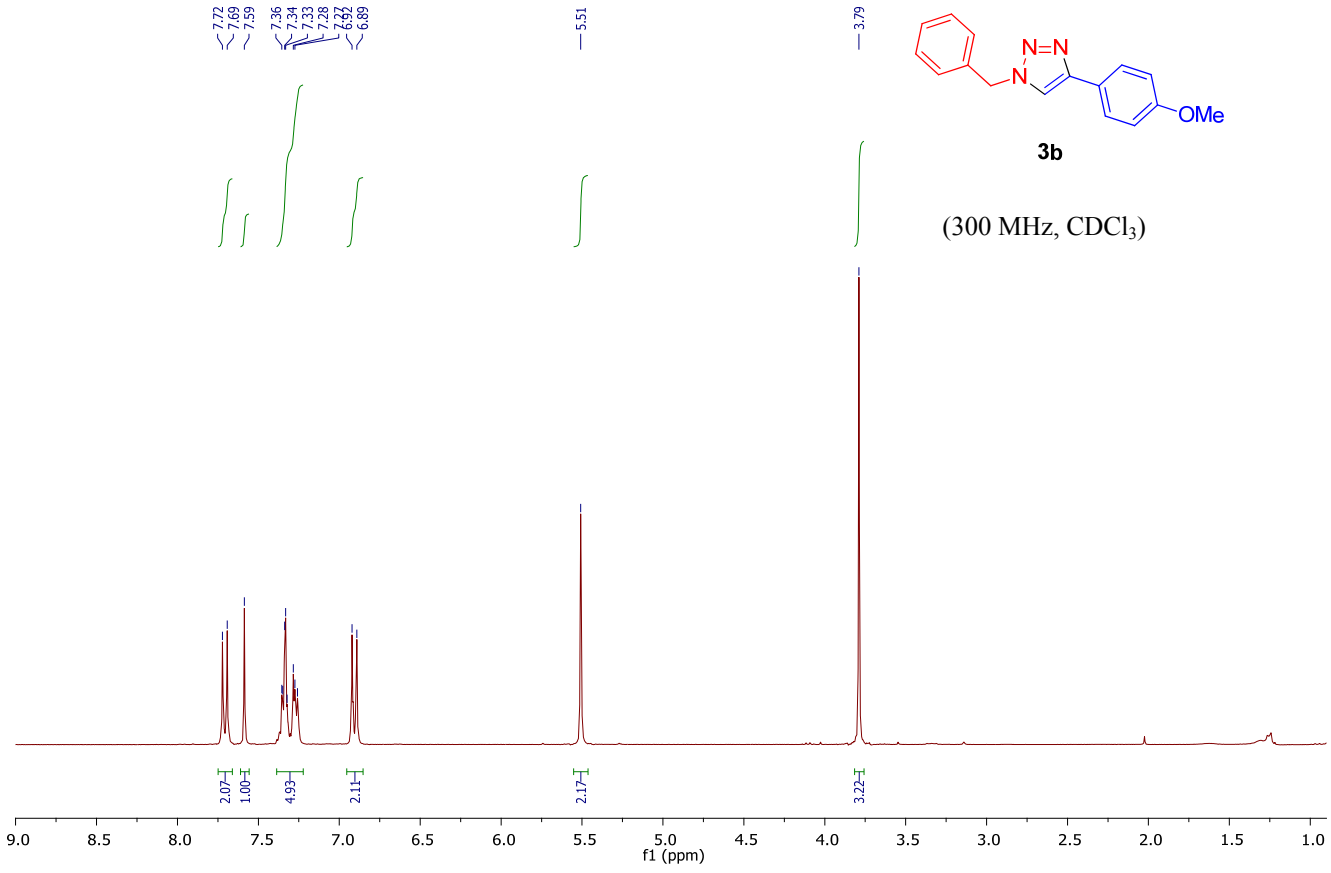


3a

(300 MHz, $CDCl_3$)

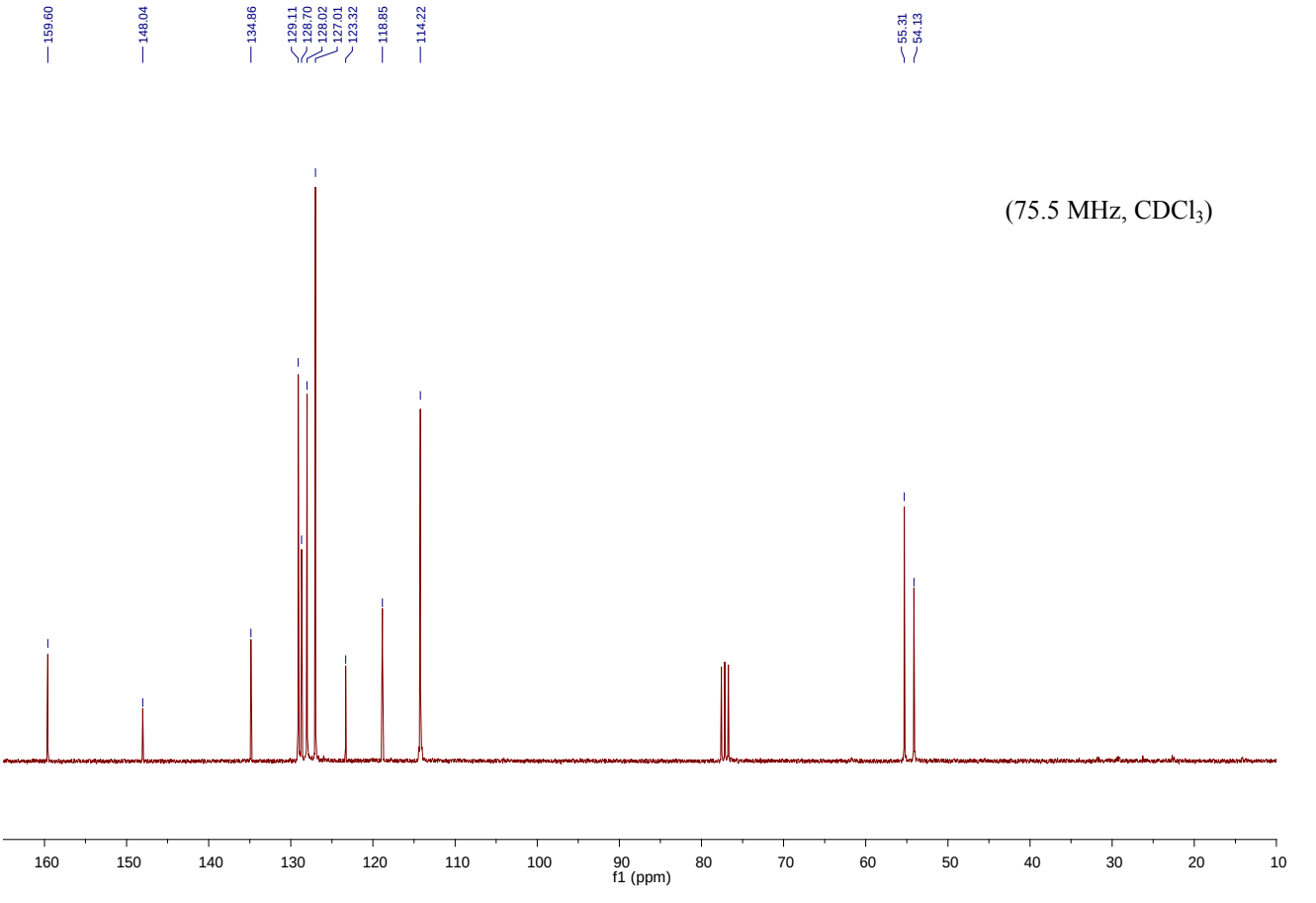


(75.5 MHz, $CDCl_3$)

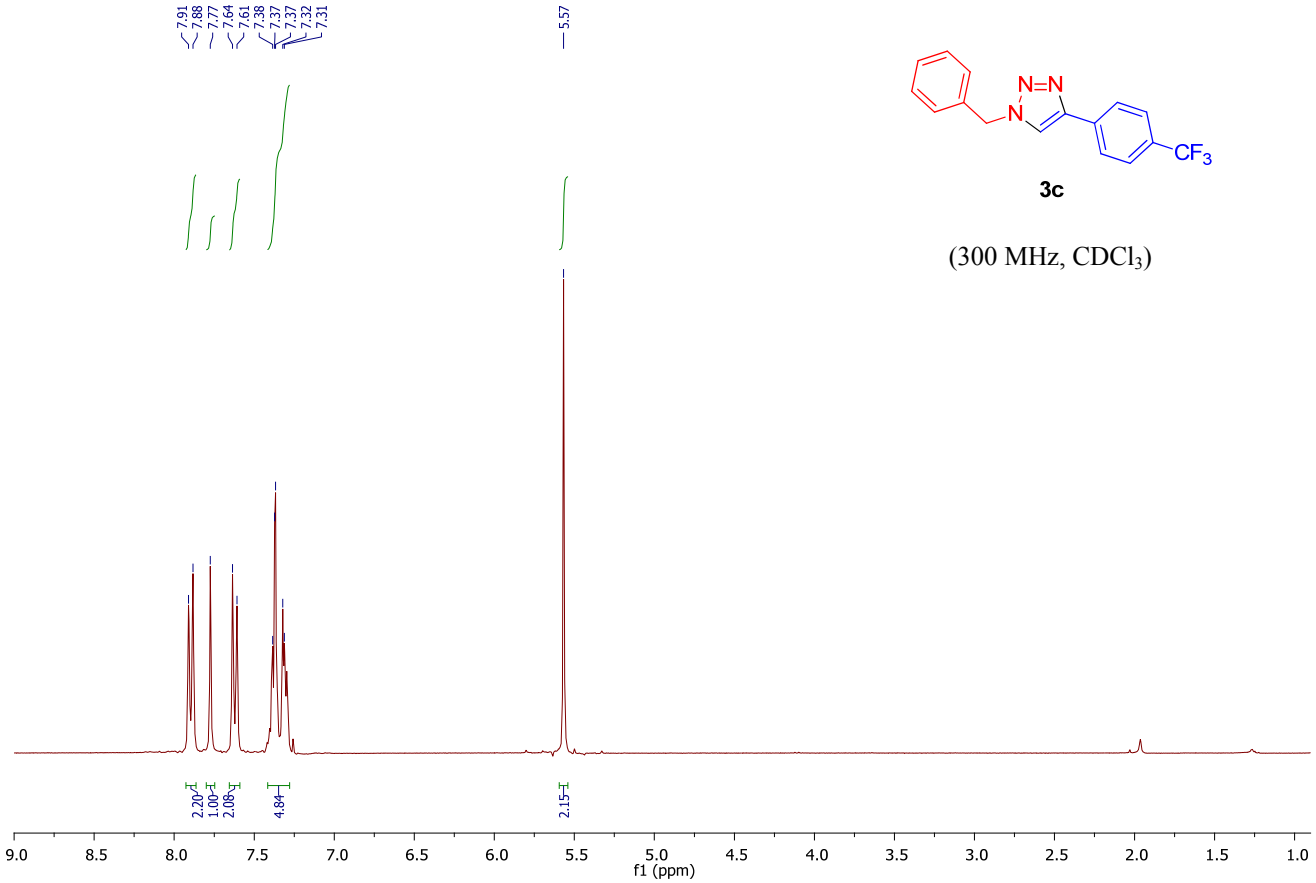


3b

(300 MHz, $CDCl_3$)

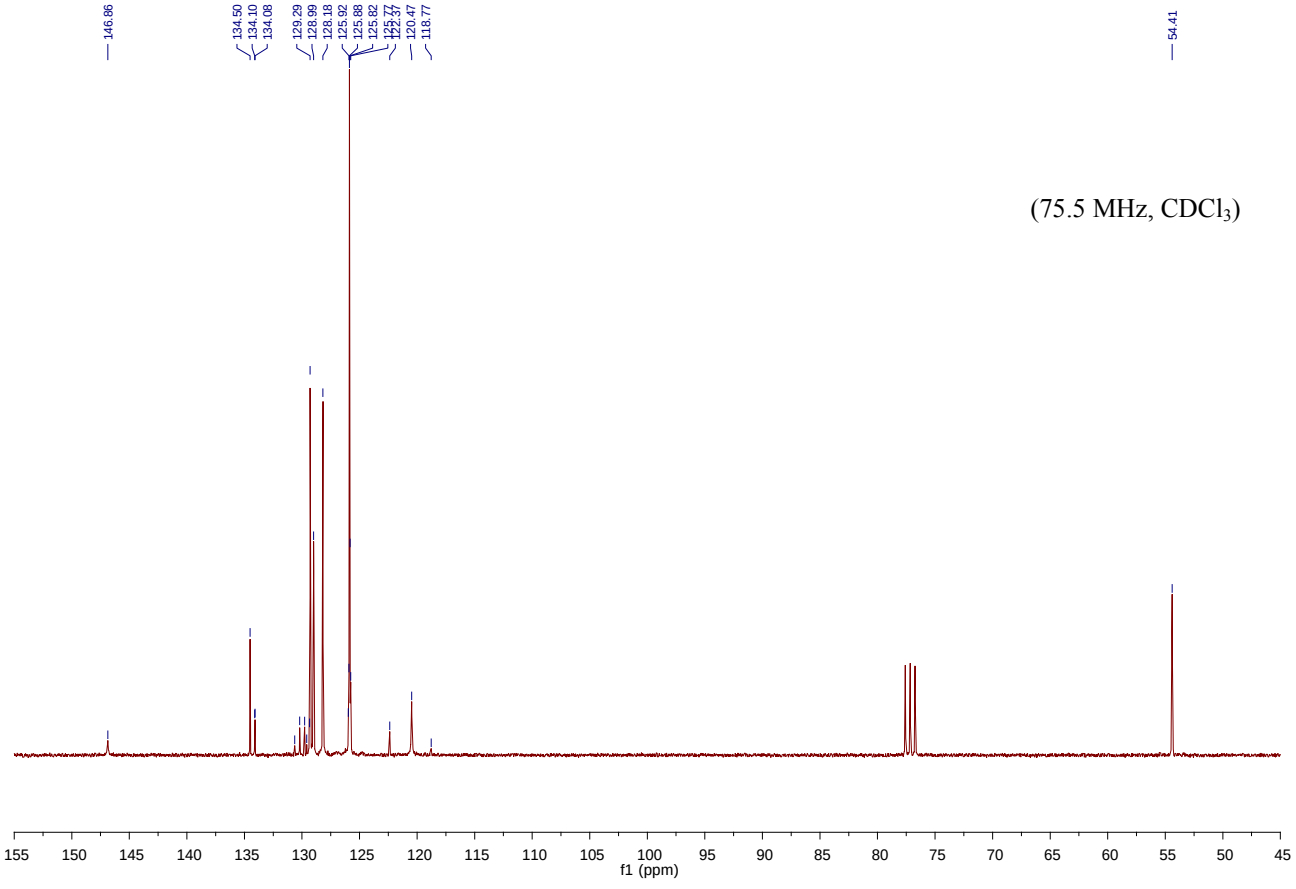


(75.5 MHz, $CDCl_3$)

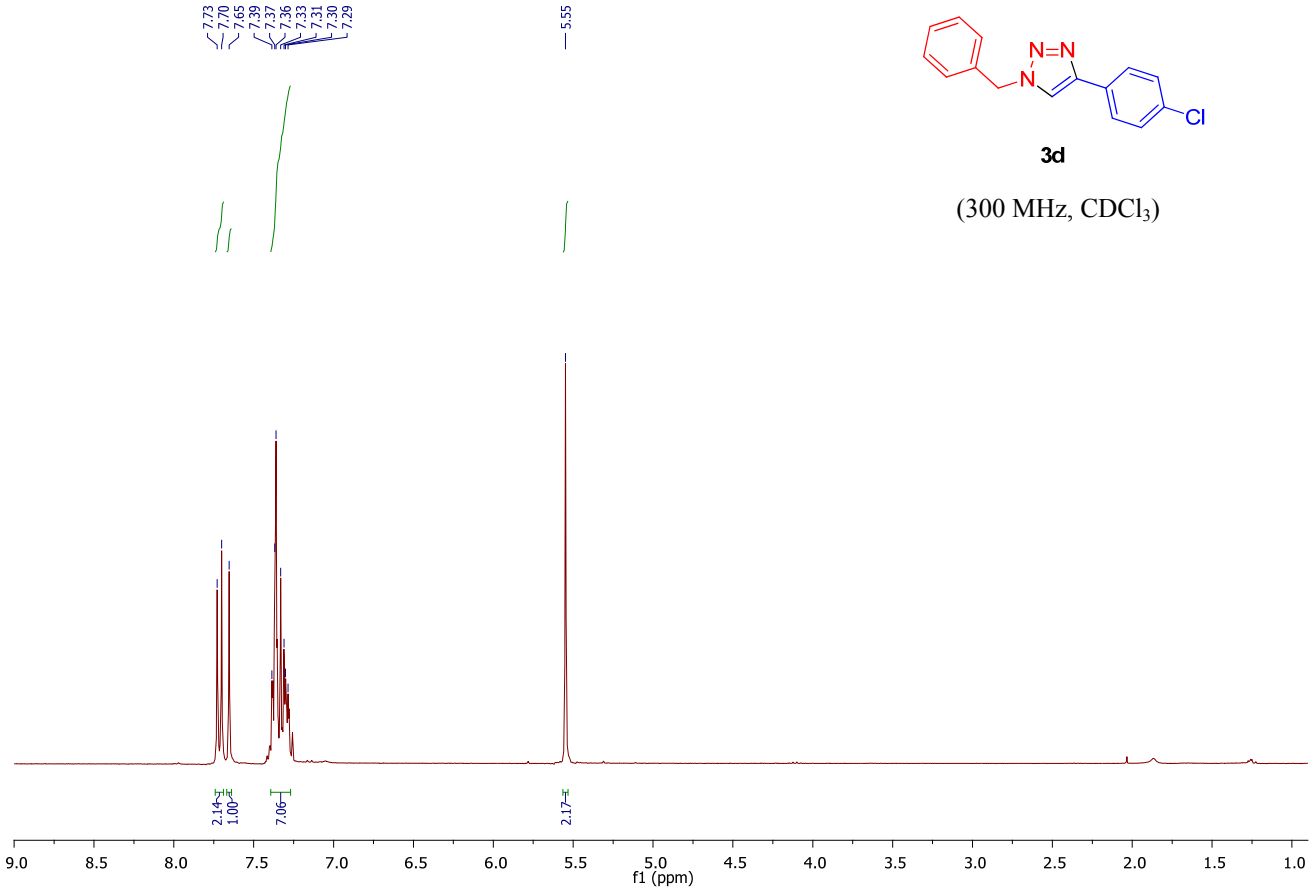


3c

(300 MHz, $CDCl_3$)

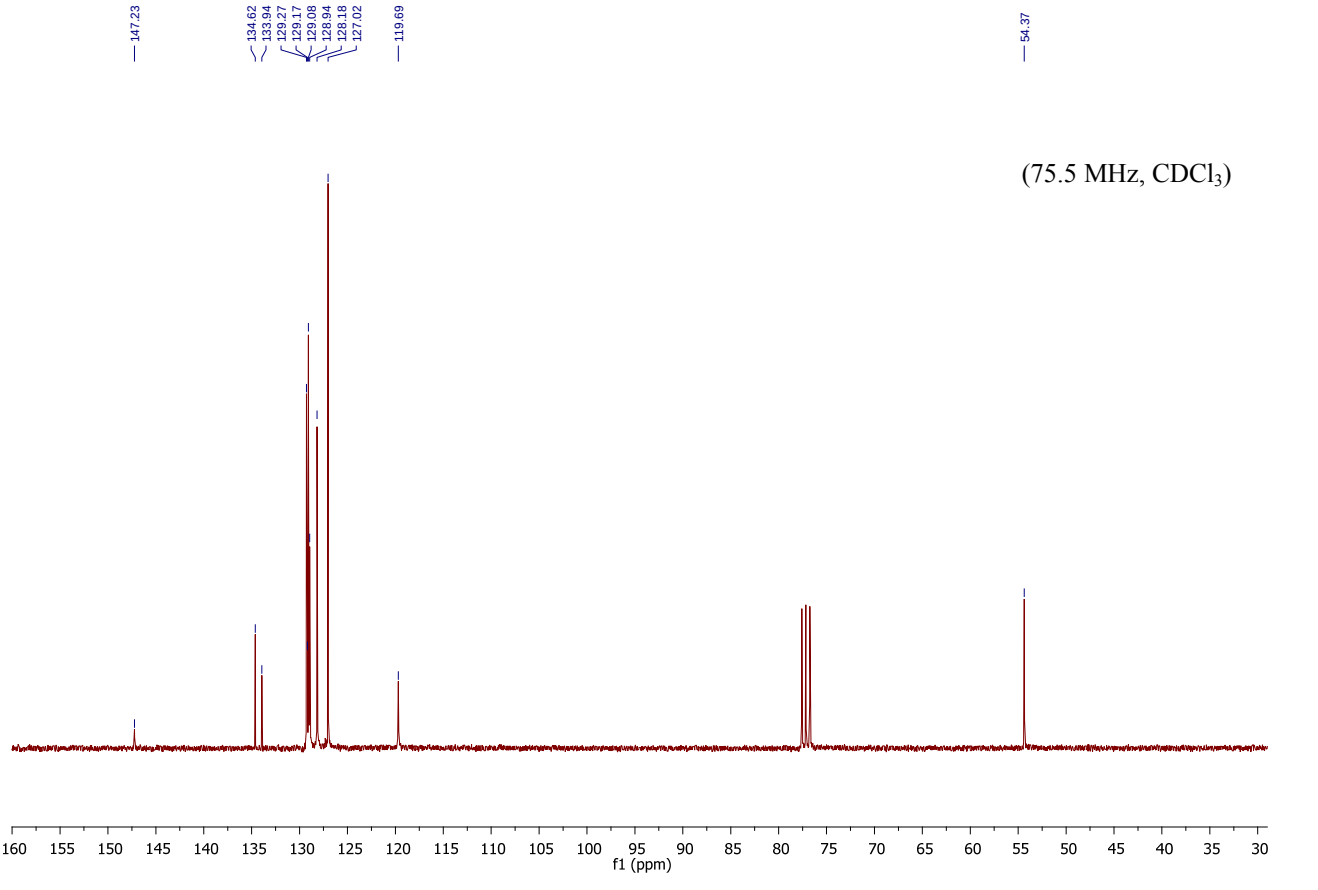


(75.5 MHz, $CDCl_3$)

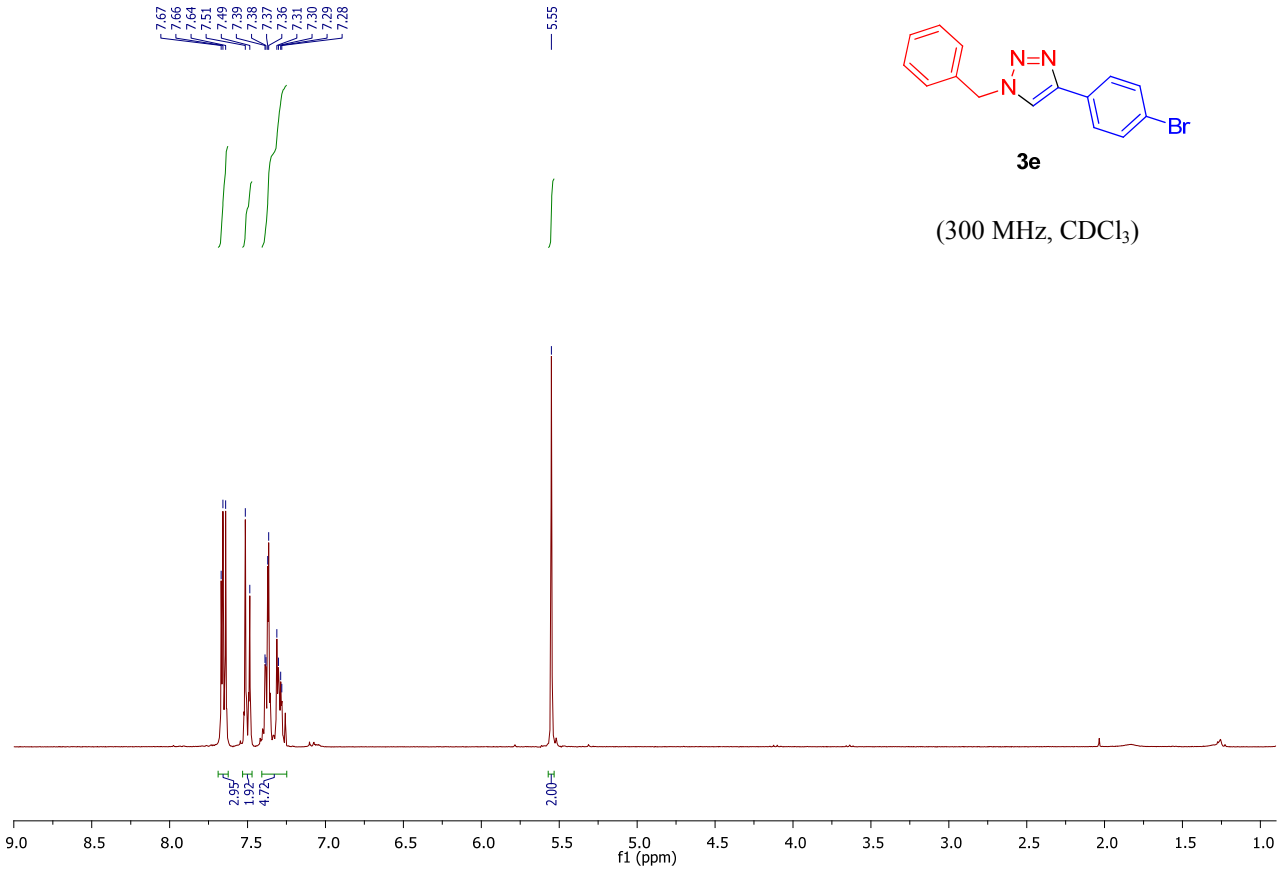


3d

(300 MHz, $CDCl_3$)

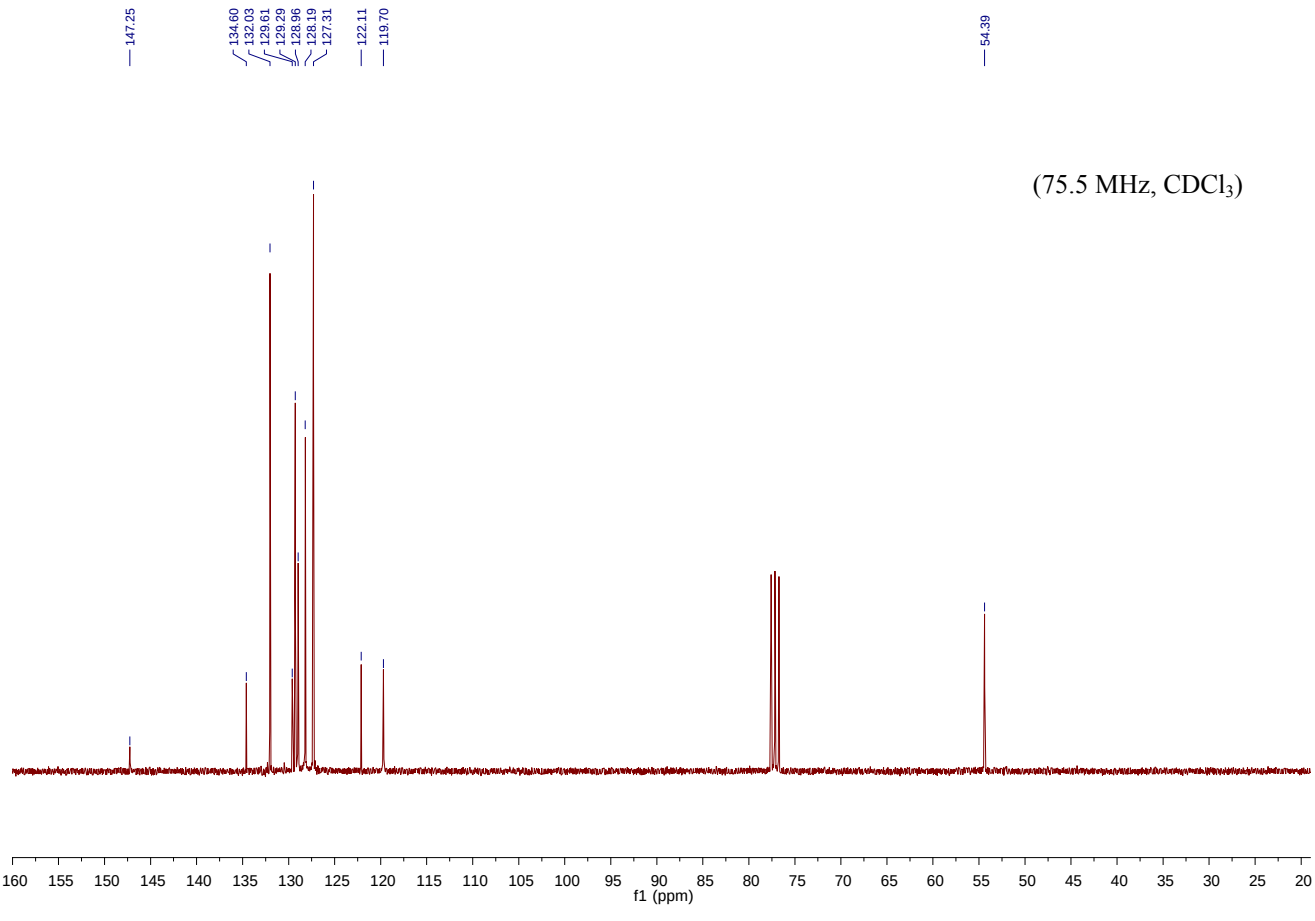


(75.5 MHz, $CDCl_3$)

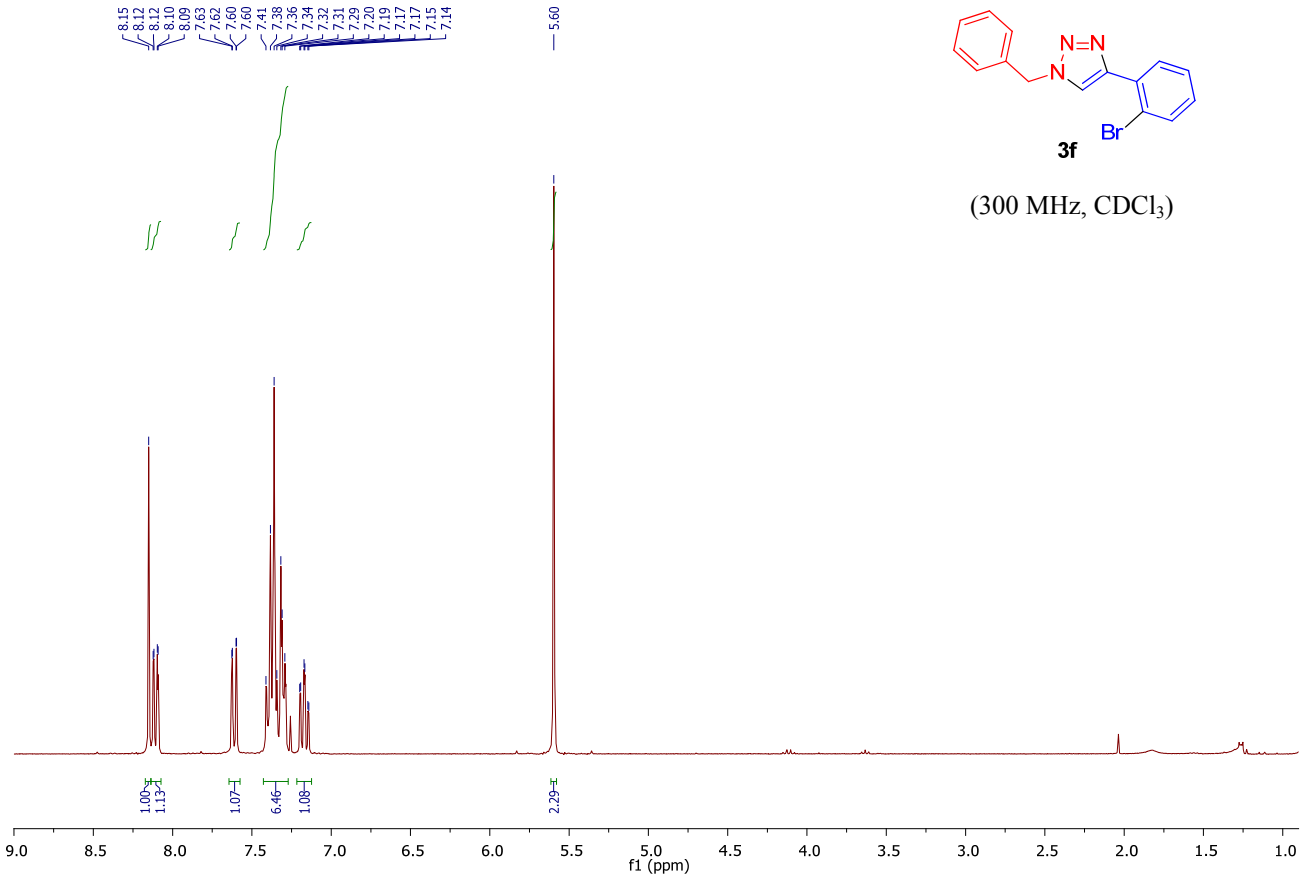


3e

(300 MHz, $CDCl_3$)

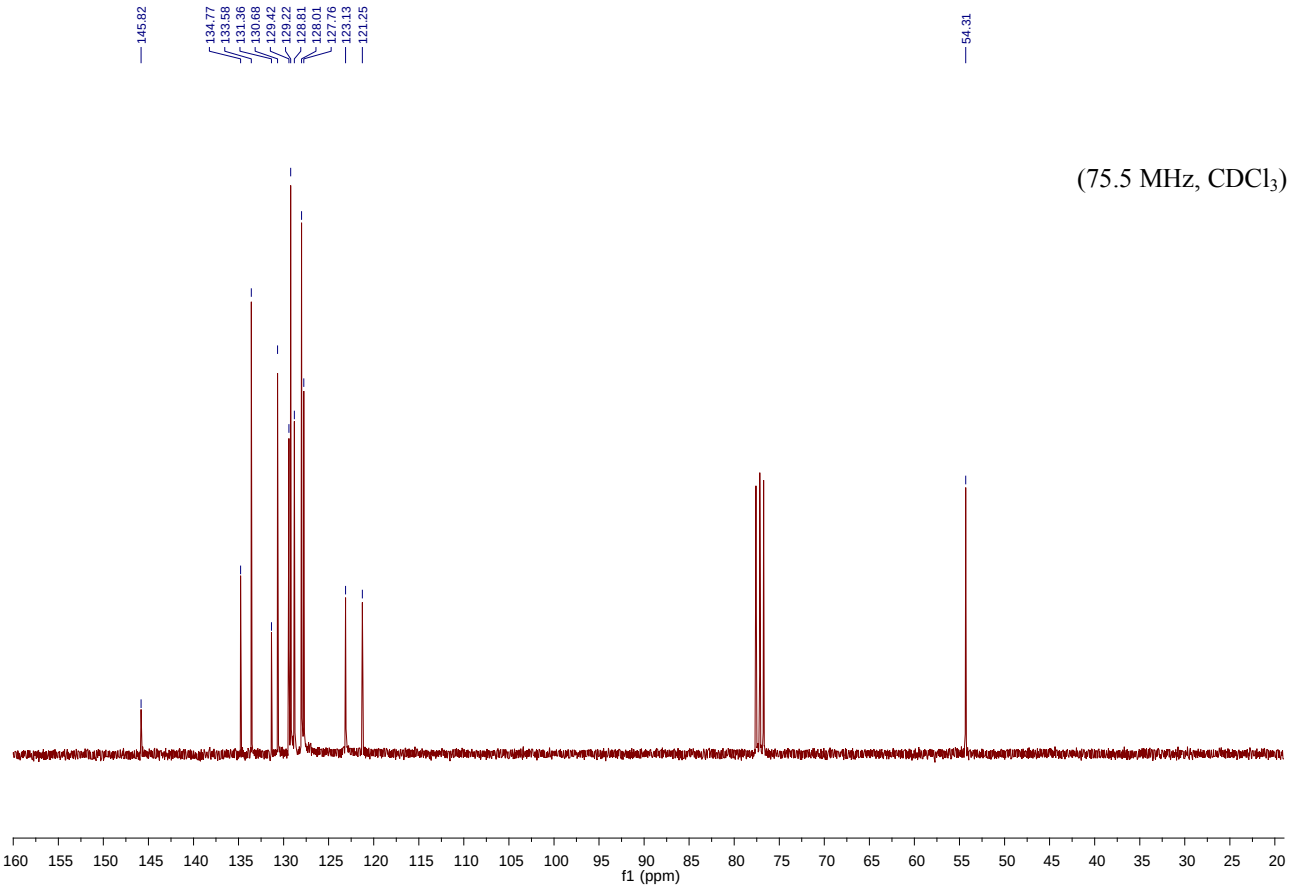


(75.5 MHz, $CDCl_3$)

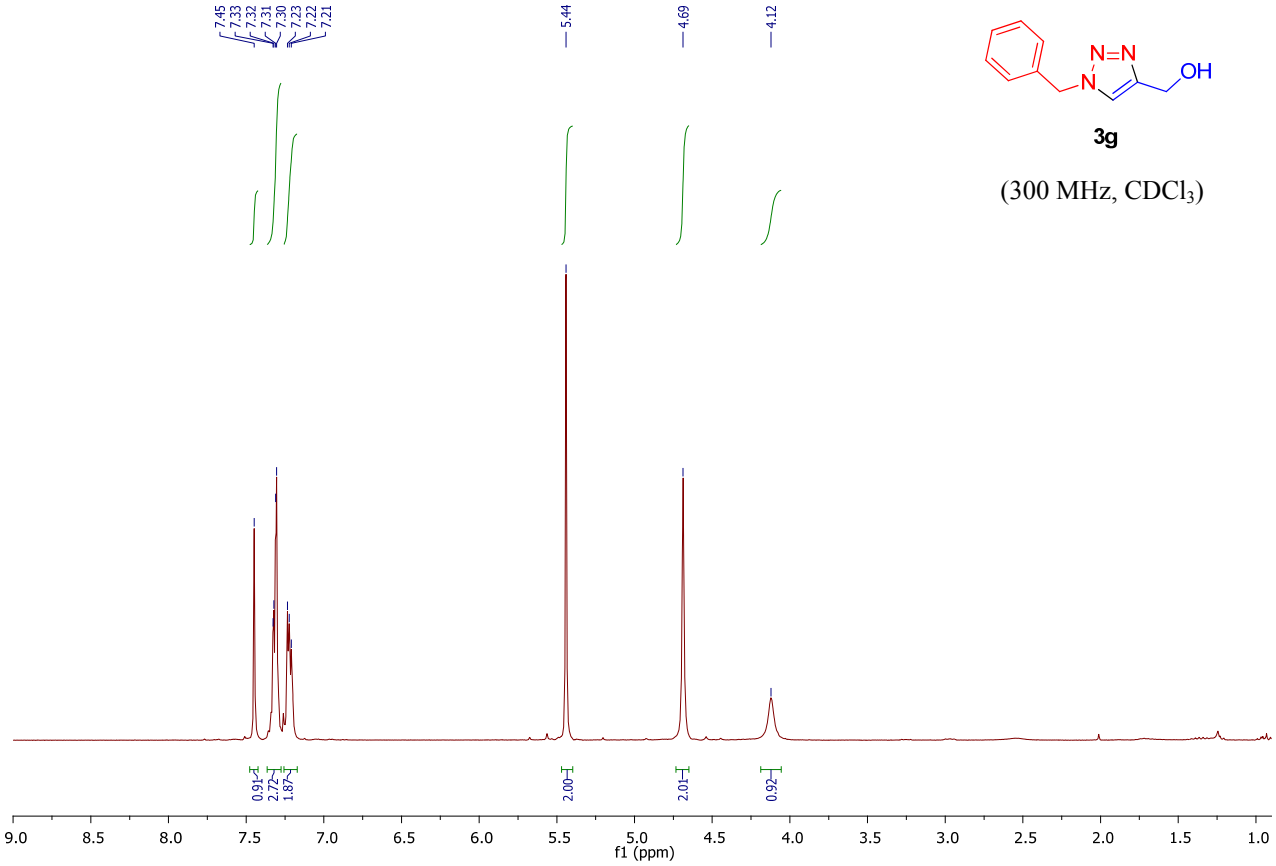


3f

(300 MHz, $CDCl_3$)

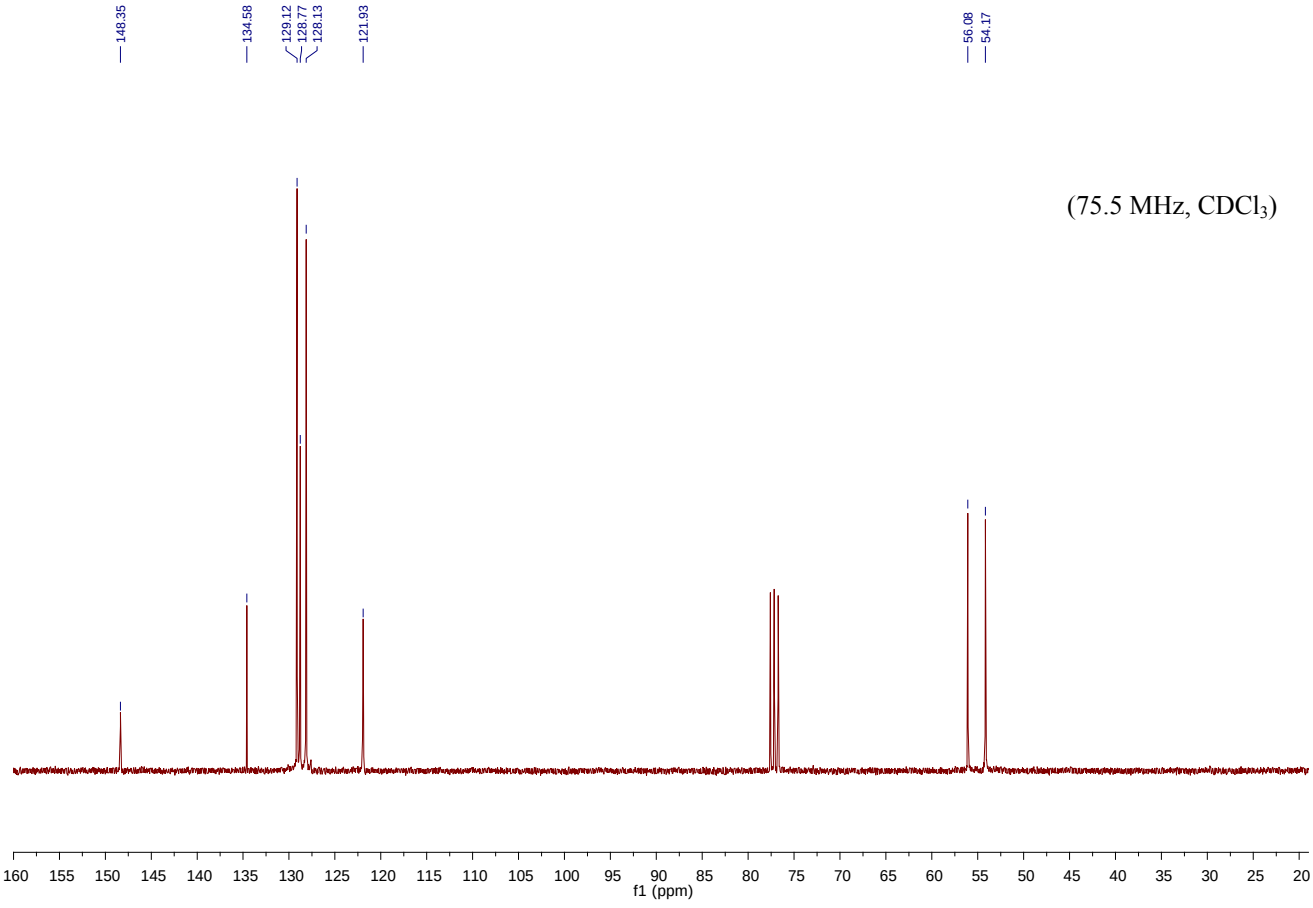


(75.5 MHz, $CDCl_3$)

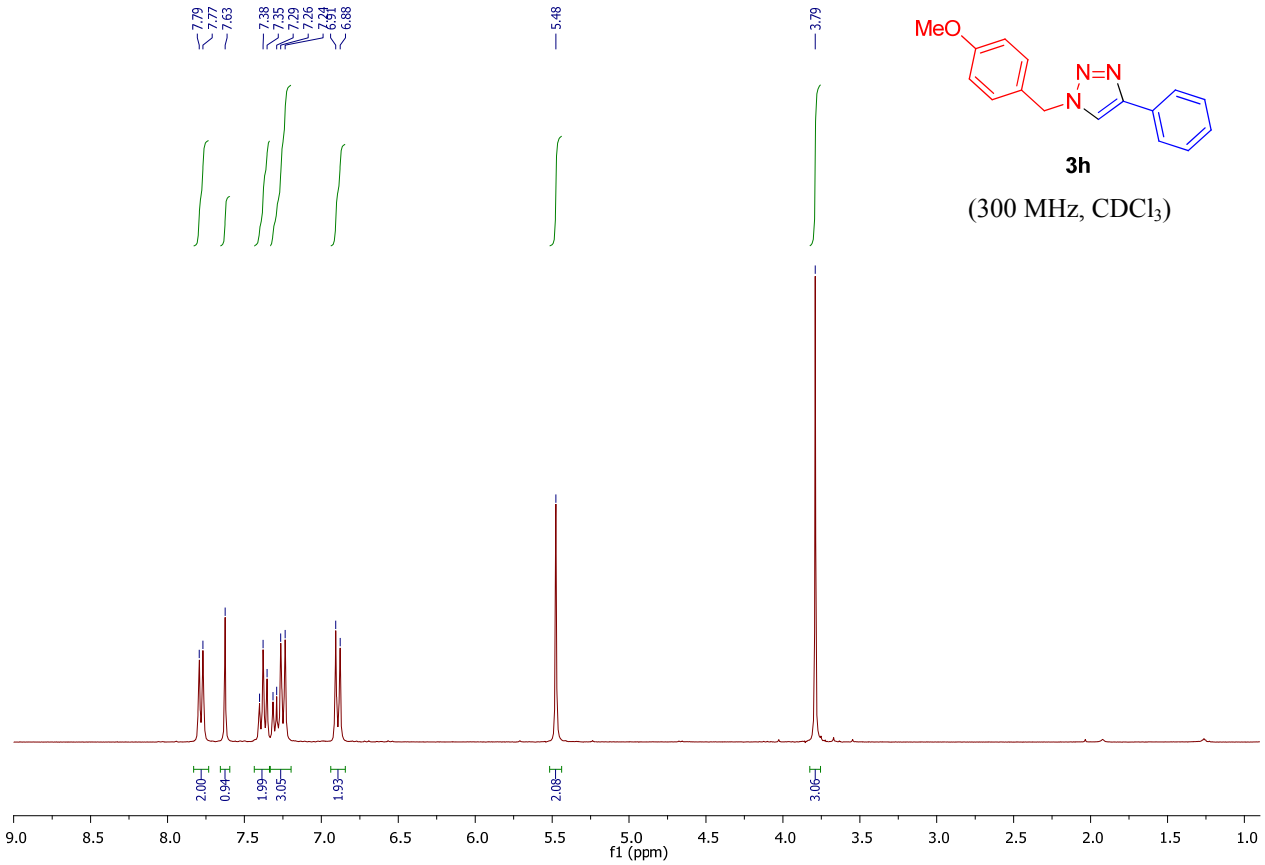


3g

(300 MHz, $CDCl_3$)

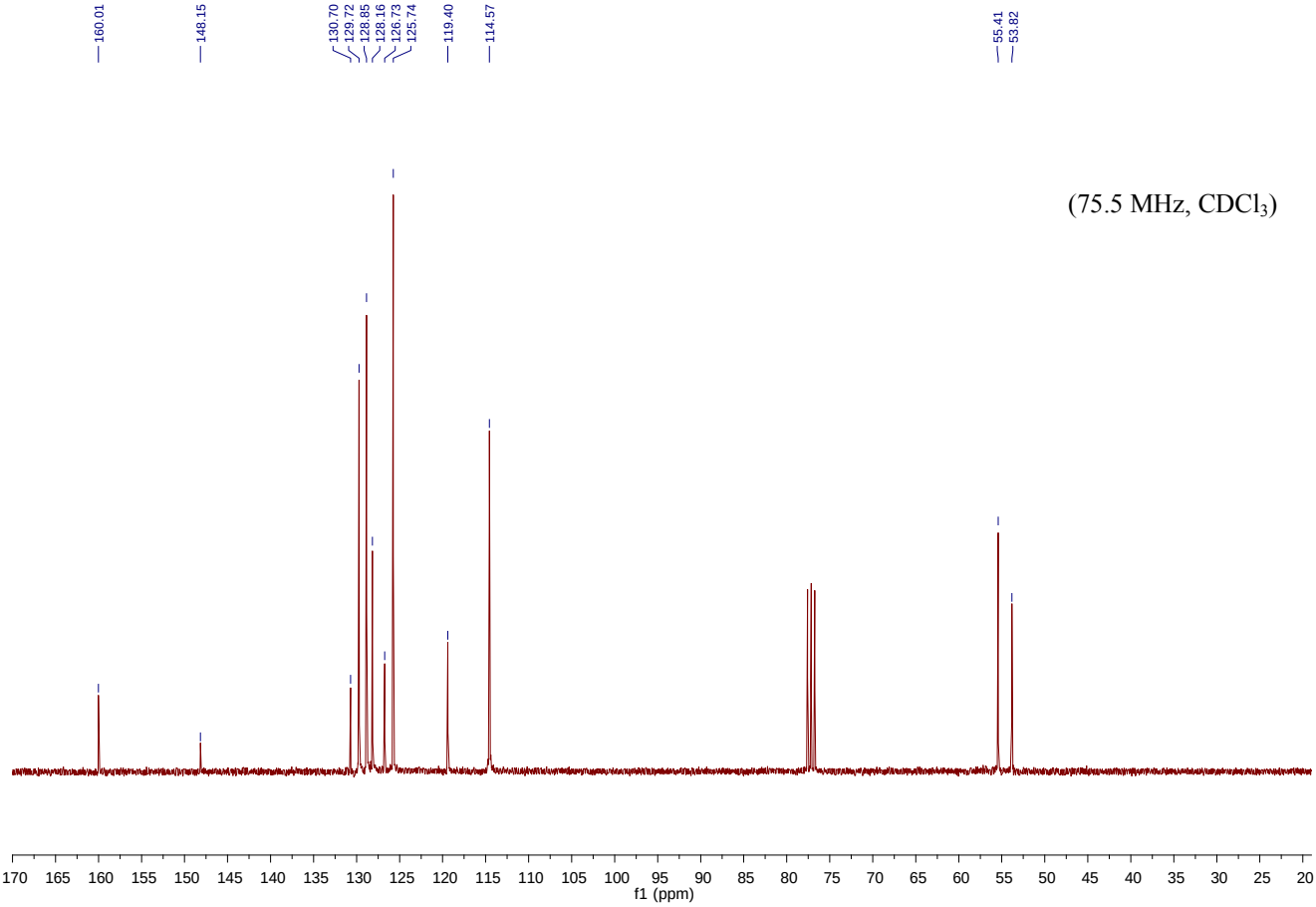


(75.5 MHz, $CDCl_3$)

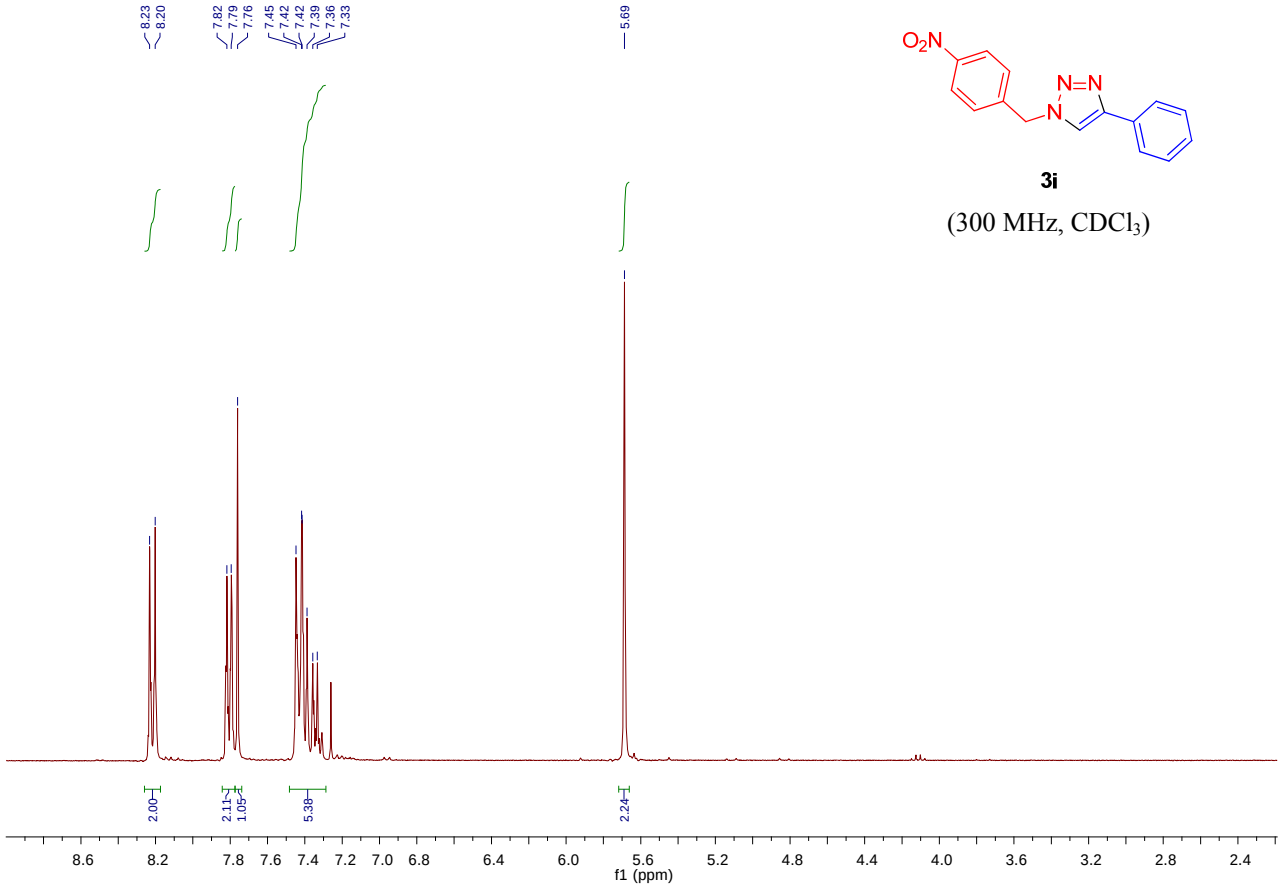


3h

(300 MHz, $CDCl_3$)

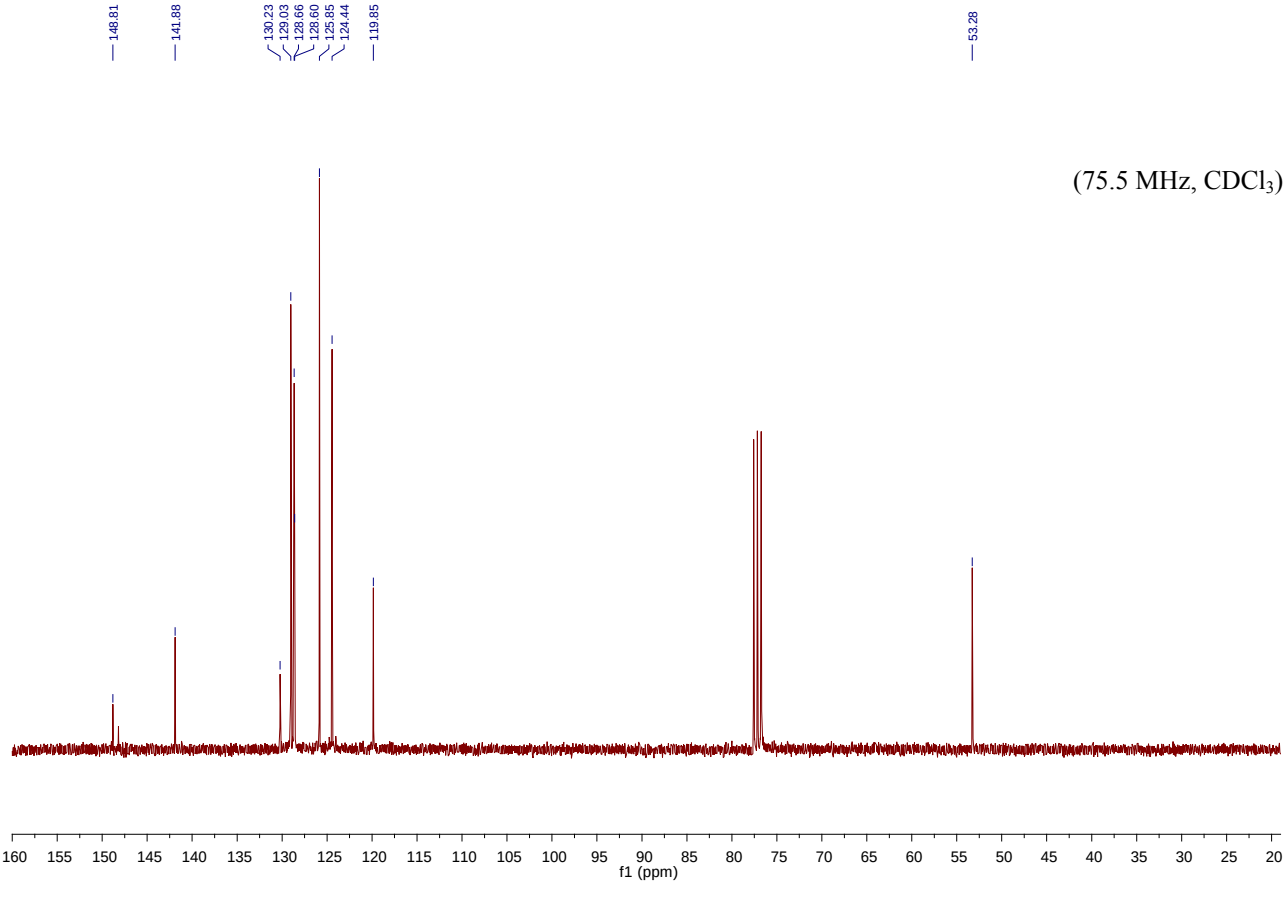


(75.5 MHz, $CDCl_3$)

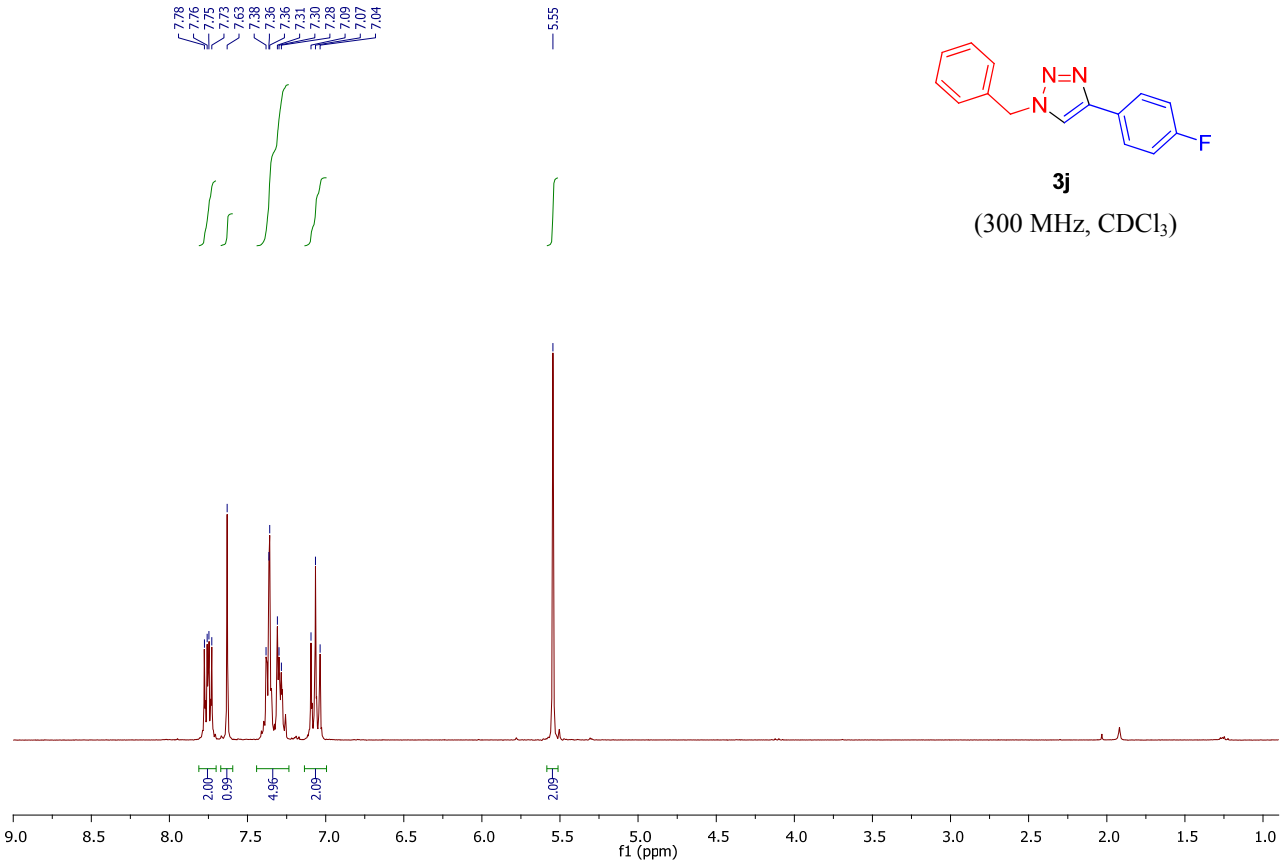


3i

(300 MHz, $CDCl_3$)

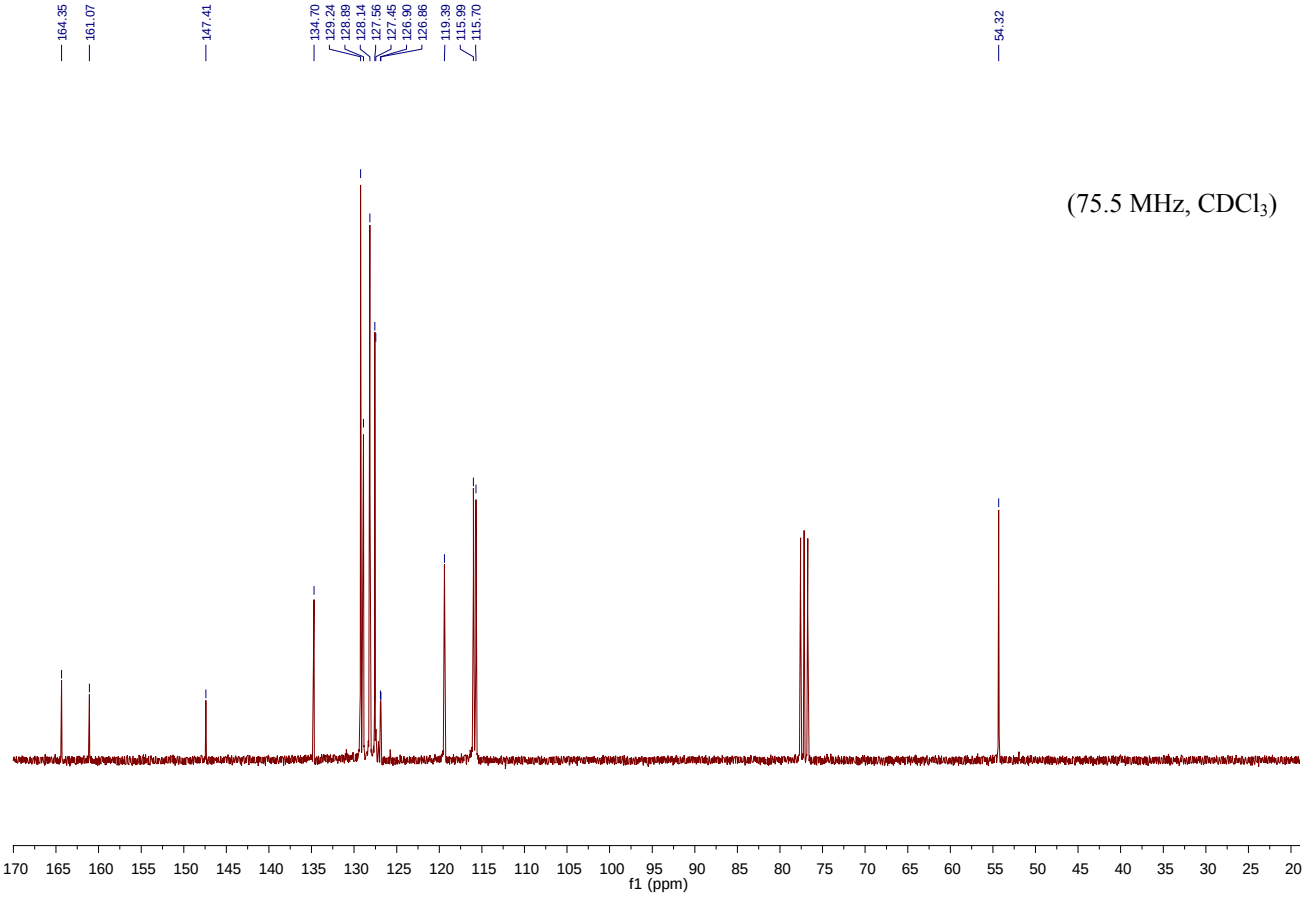


(75.5 MHz, $CDCl_3$)

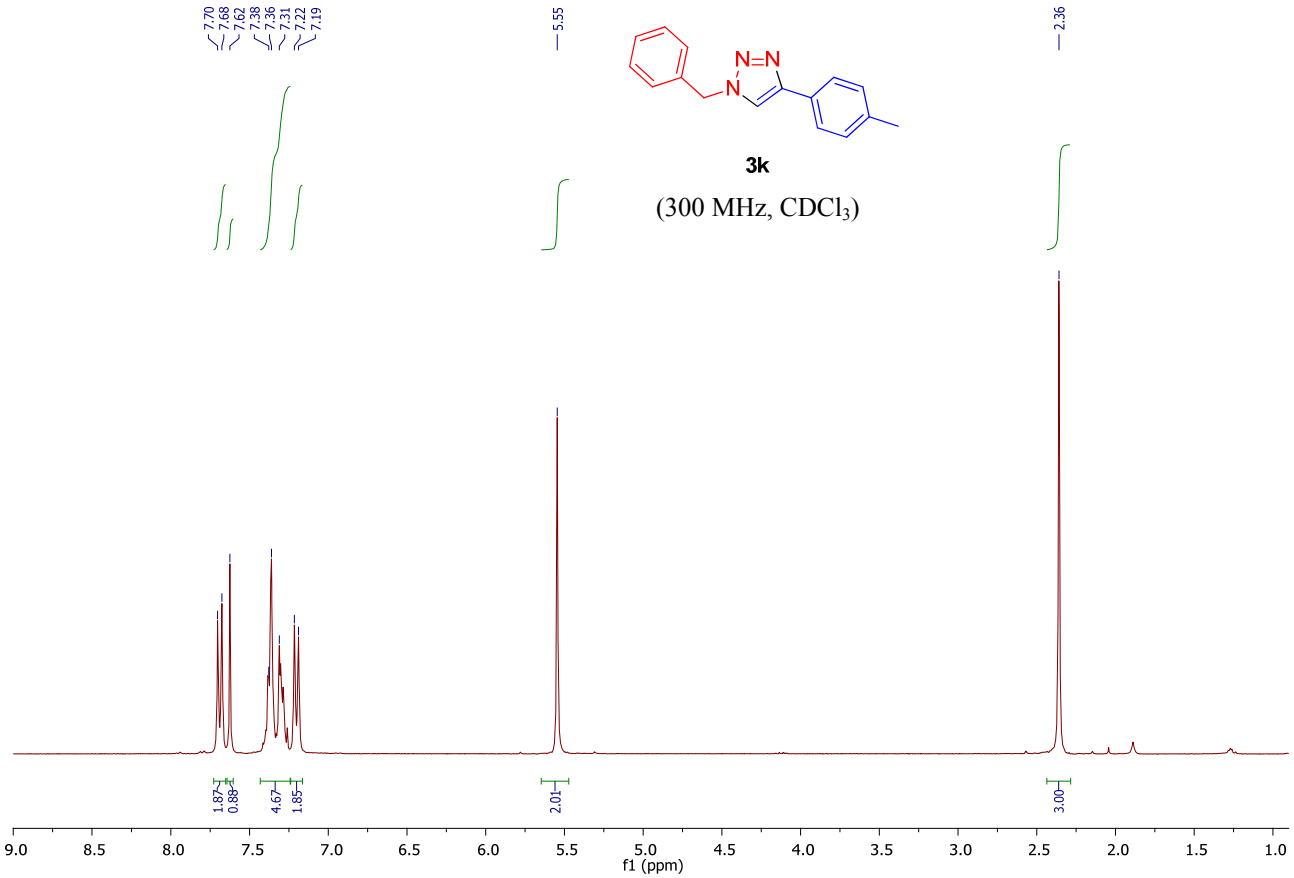


3j

(300 MHz, $CDCl_3$)

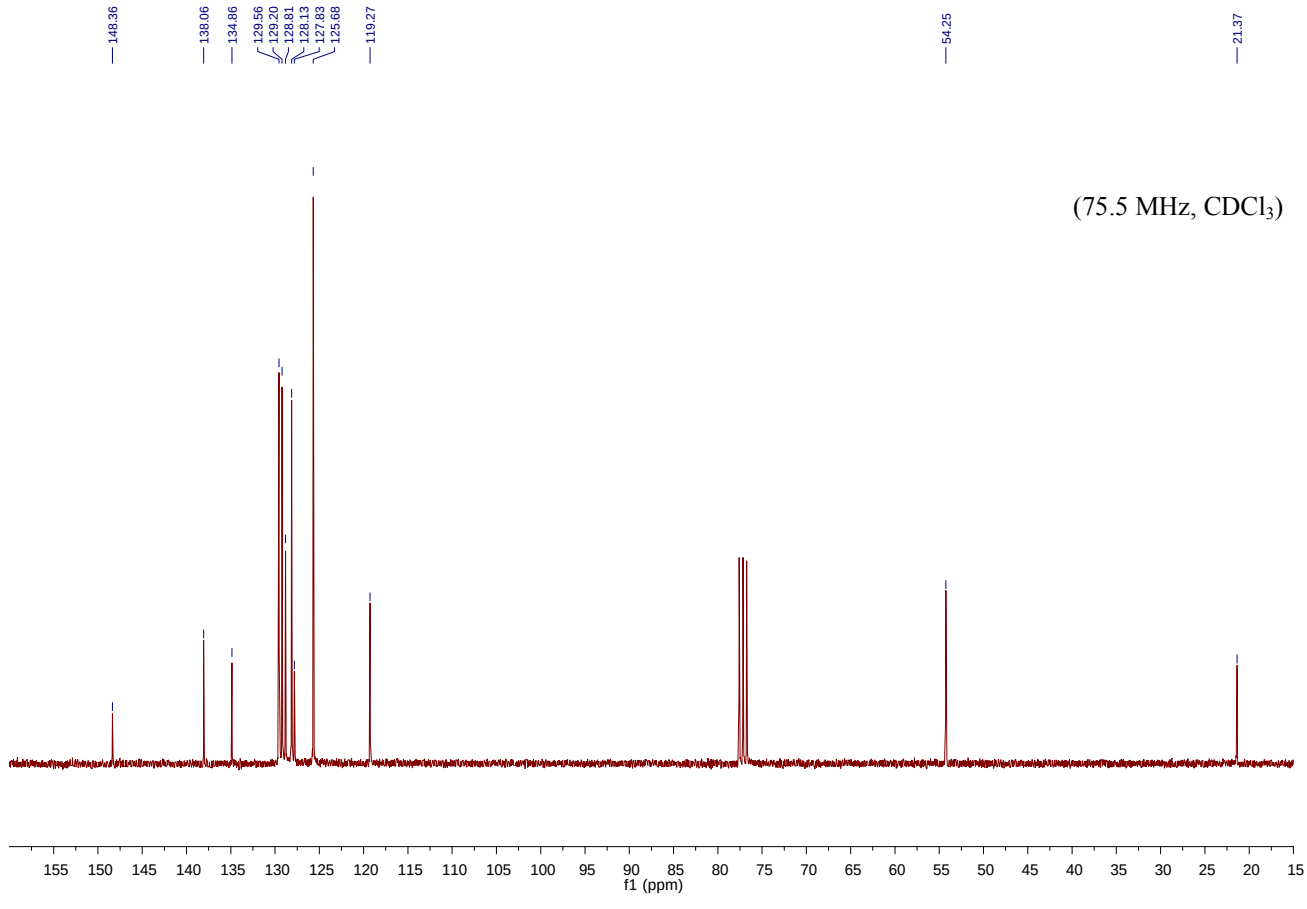


(75.5 MHz, $CDCl_3$)

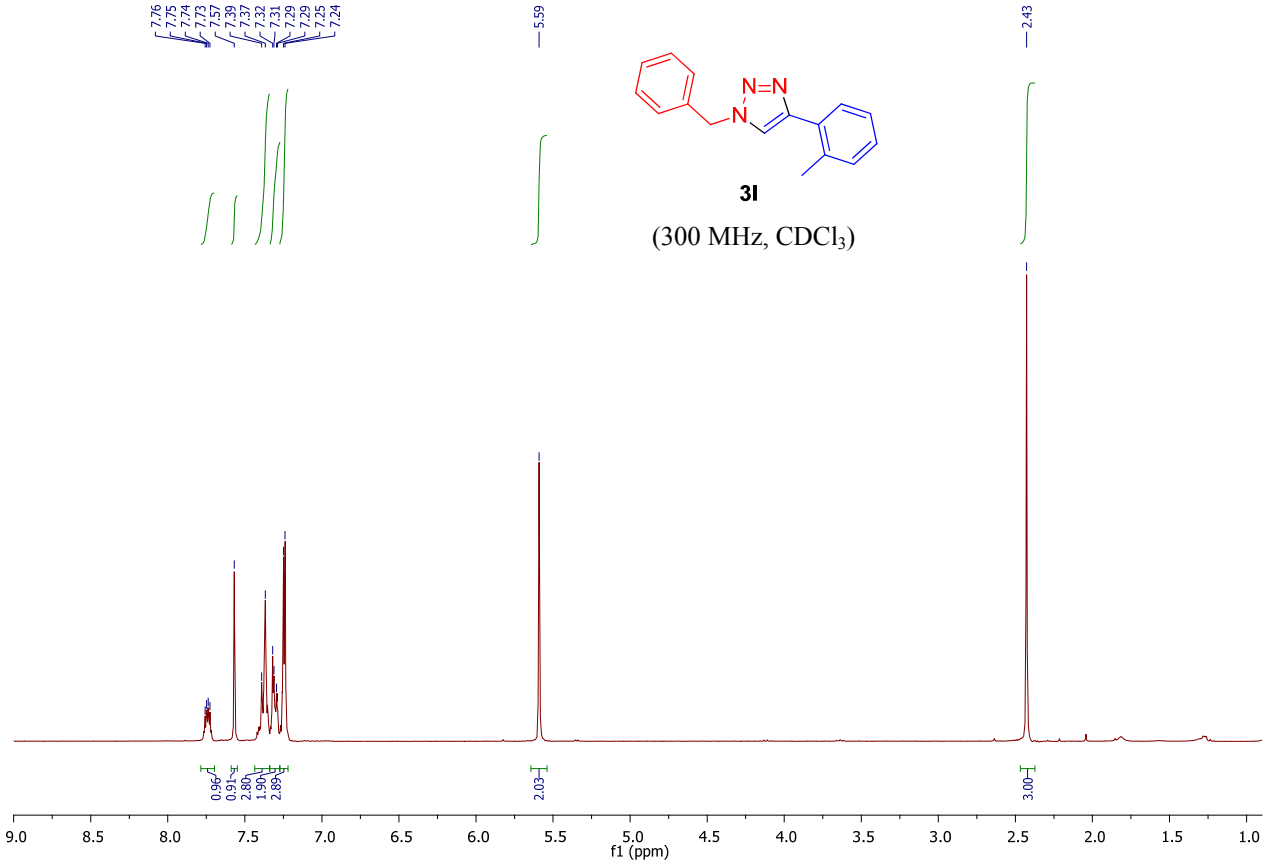


3k

(300 MHz, $CDCl_3$)

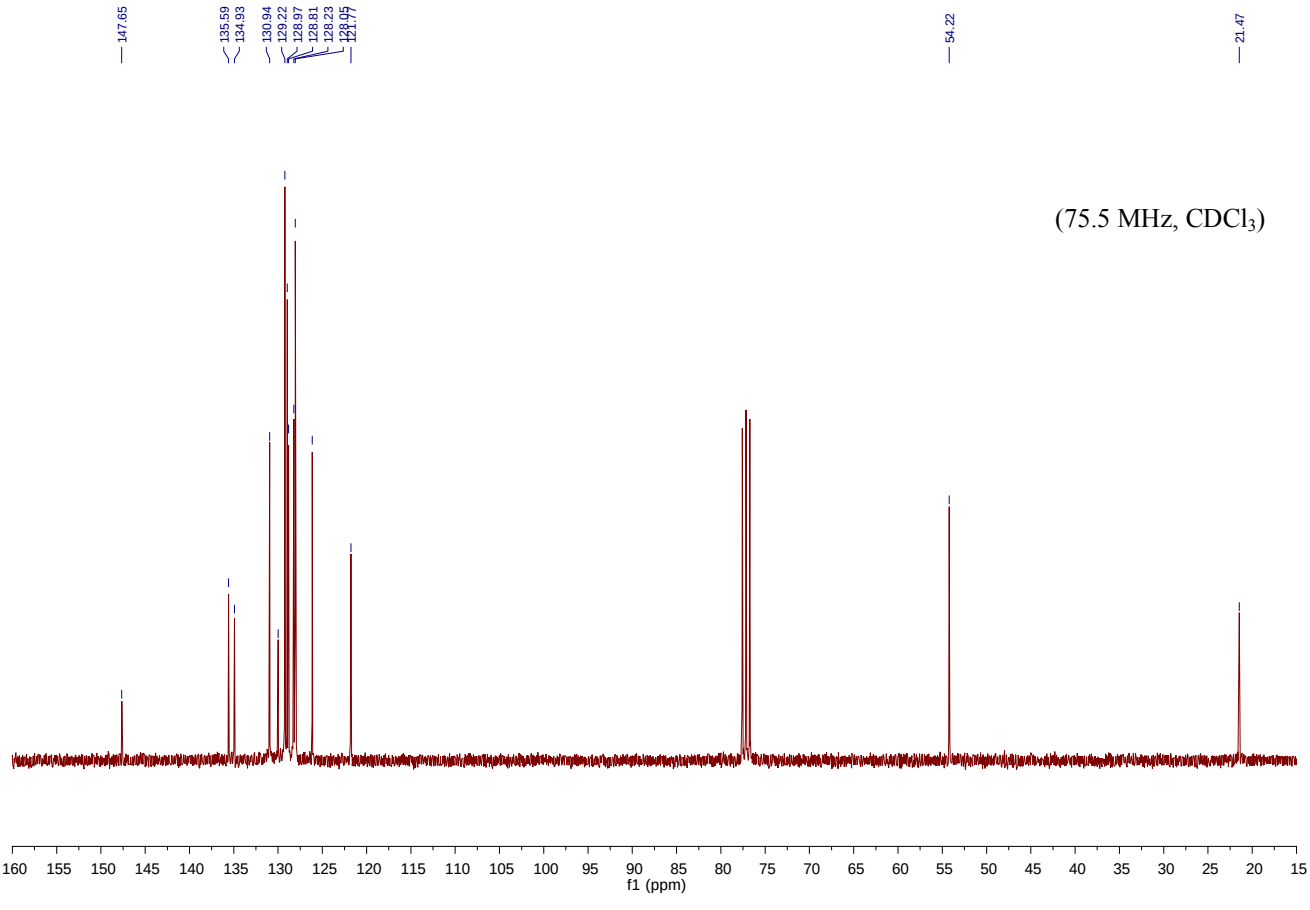


(75.5 MHz, $CDCl_3$)

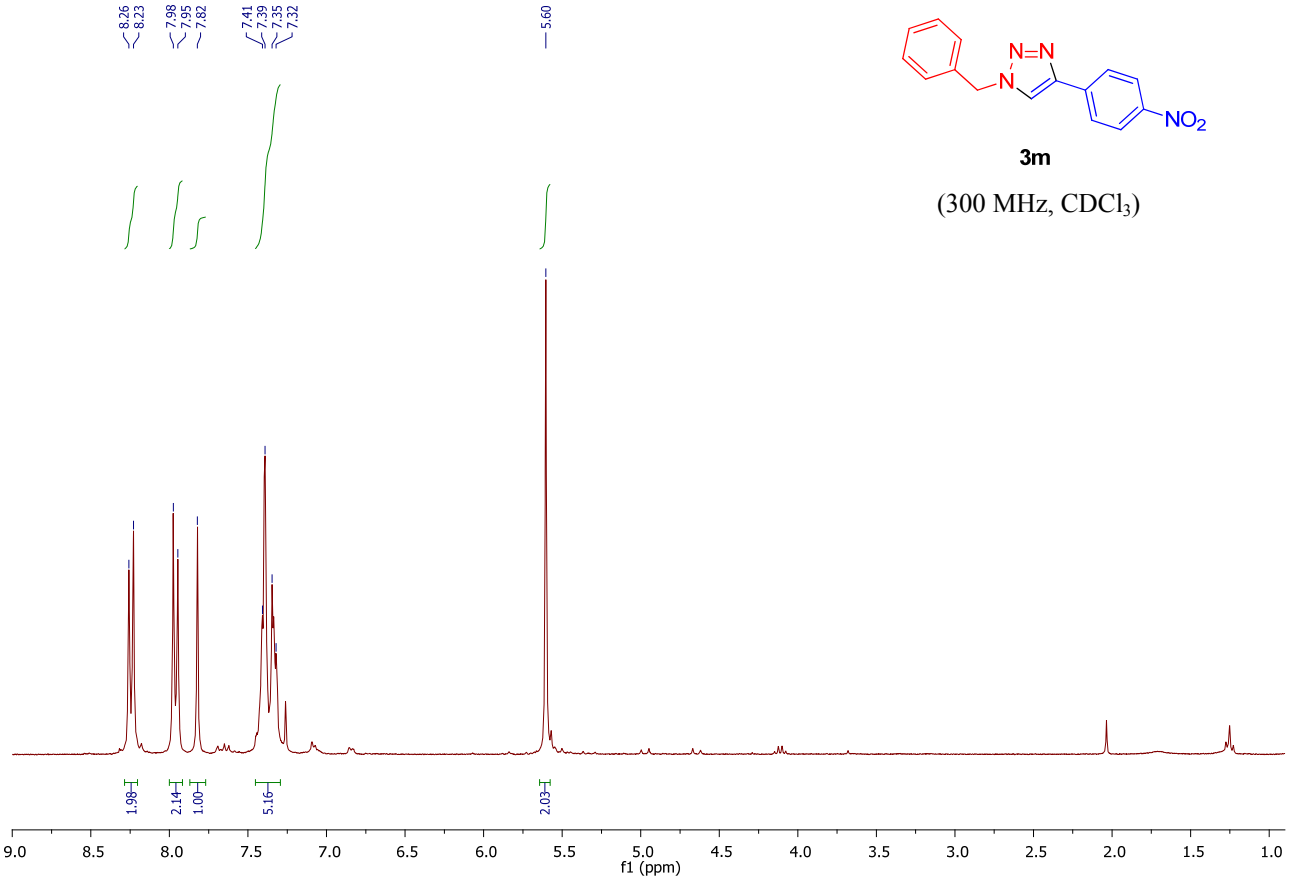


3l

(300 MHz, $CDCl_3$)

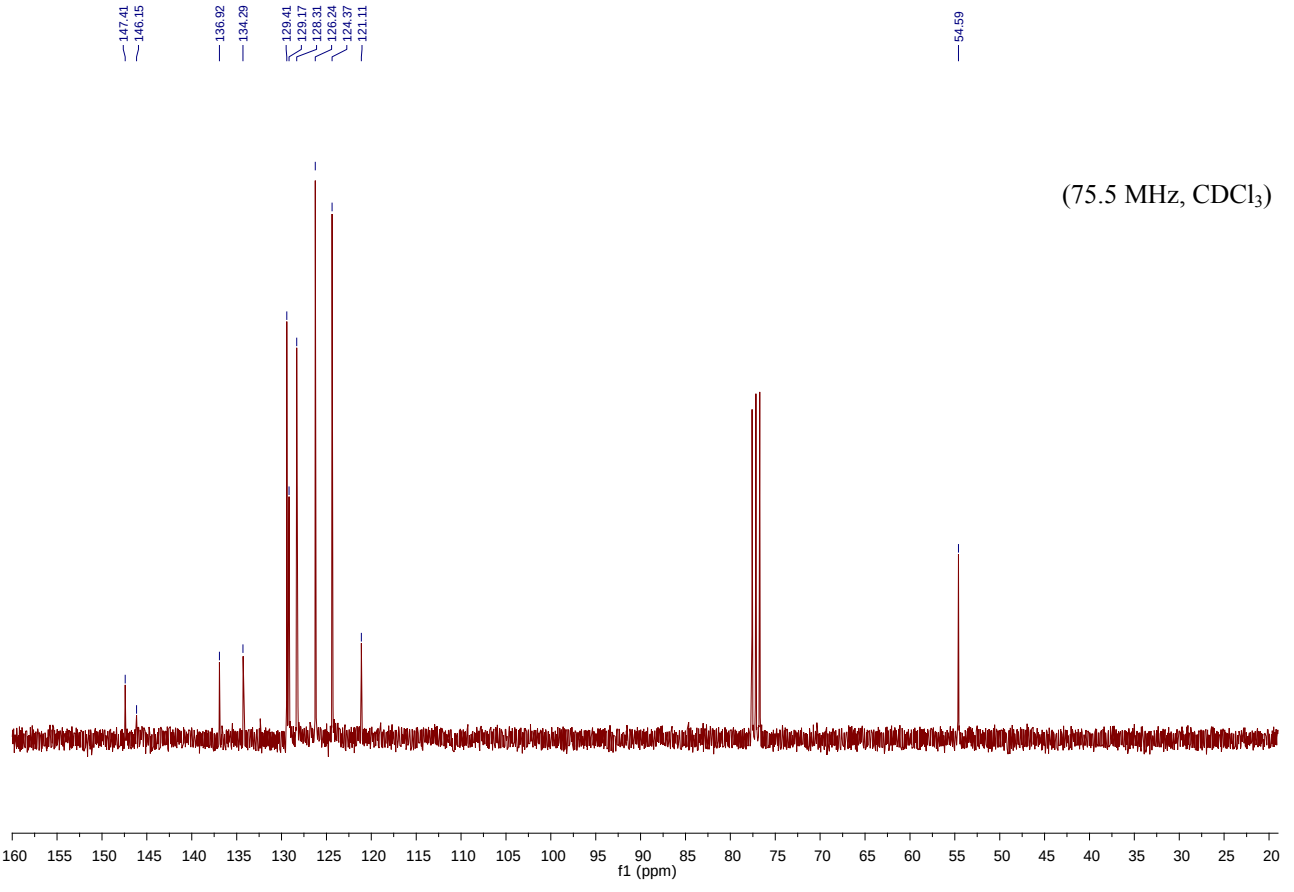


(75.5 MHz, $CDCl_3$)

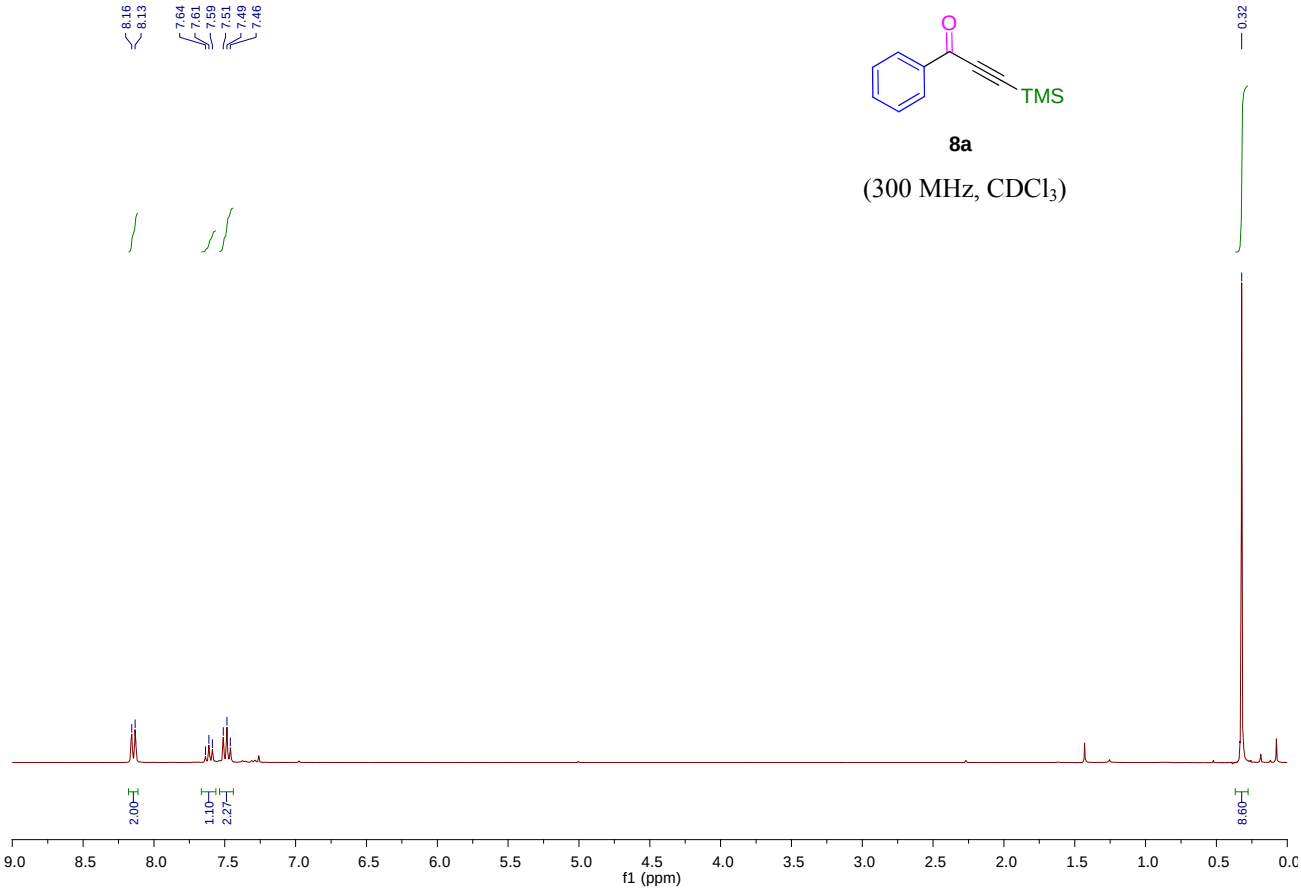


3m

(300 MHz, $CDCl_3$)

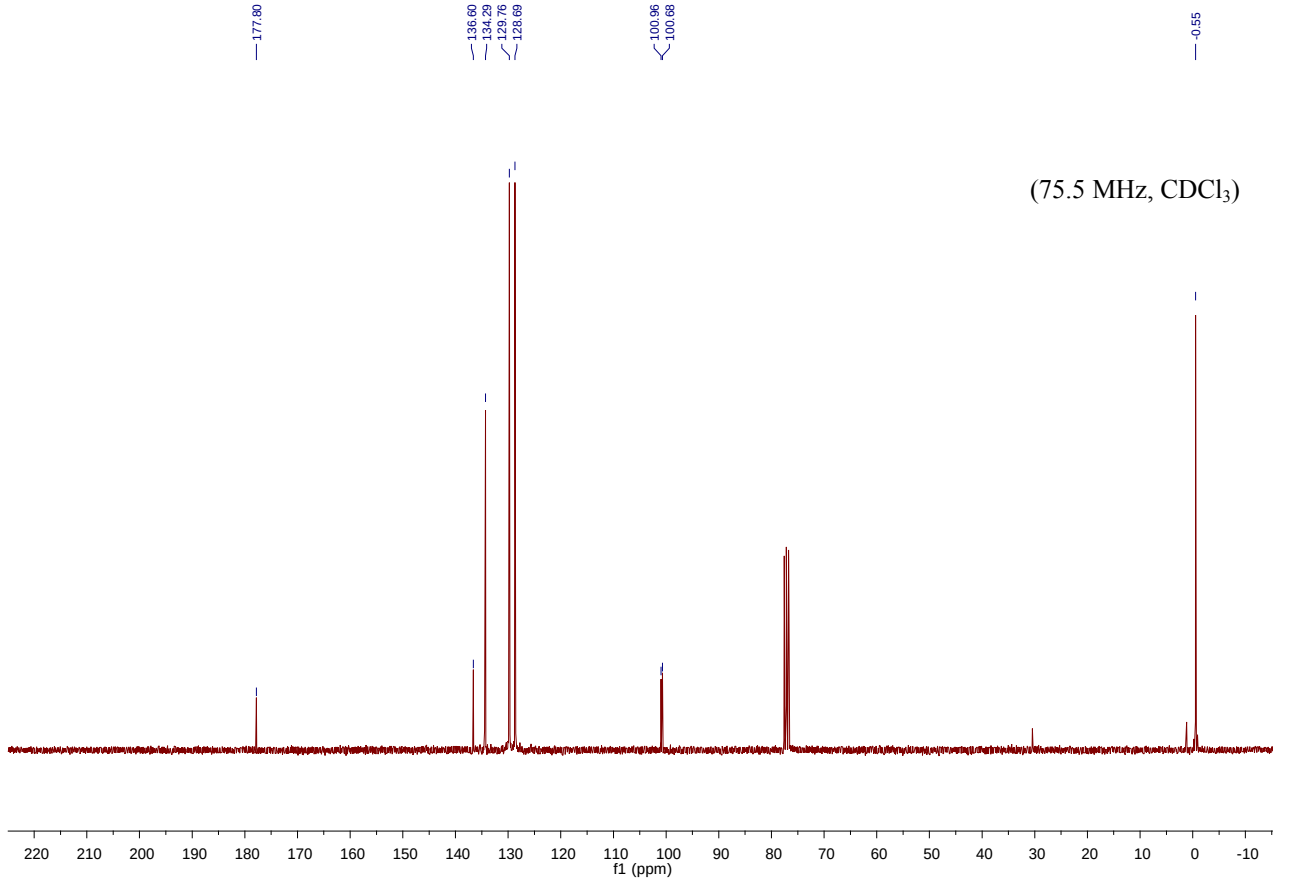


(75.5 MHz, $CDCl_3$)

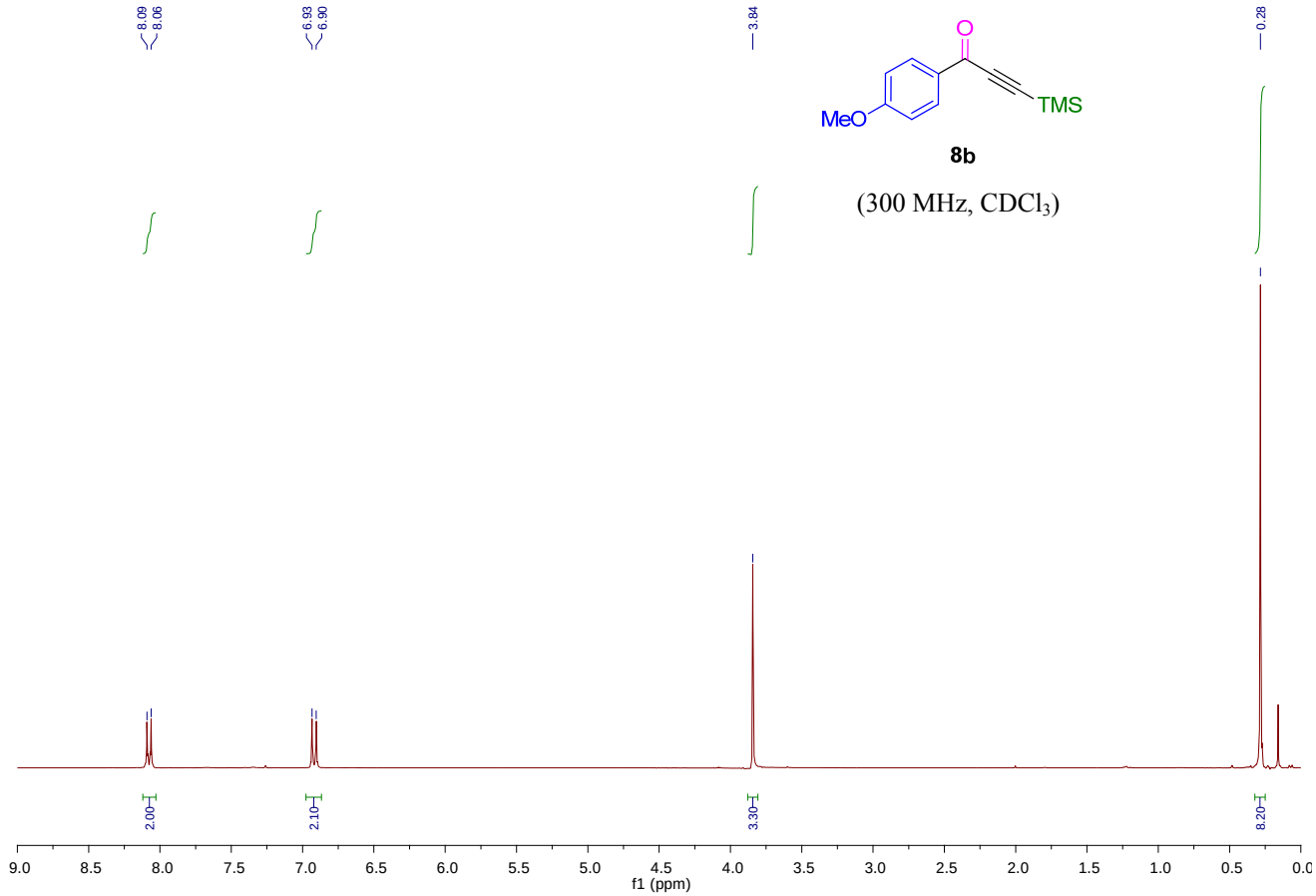


8a

(300 MHz, $CDCl_3$)

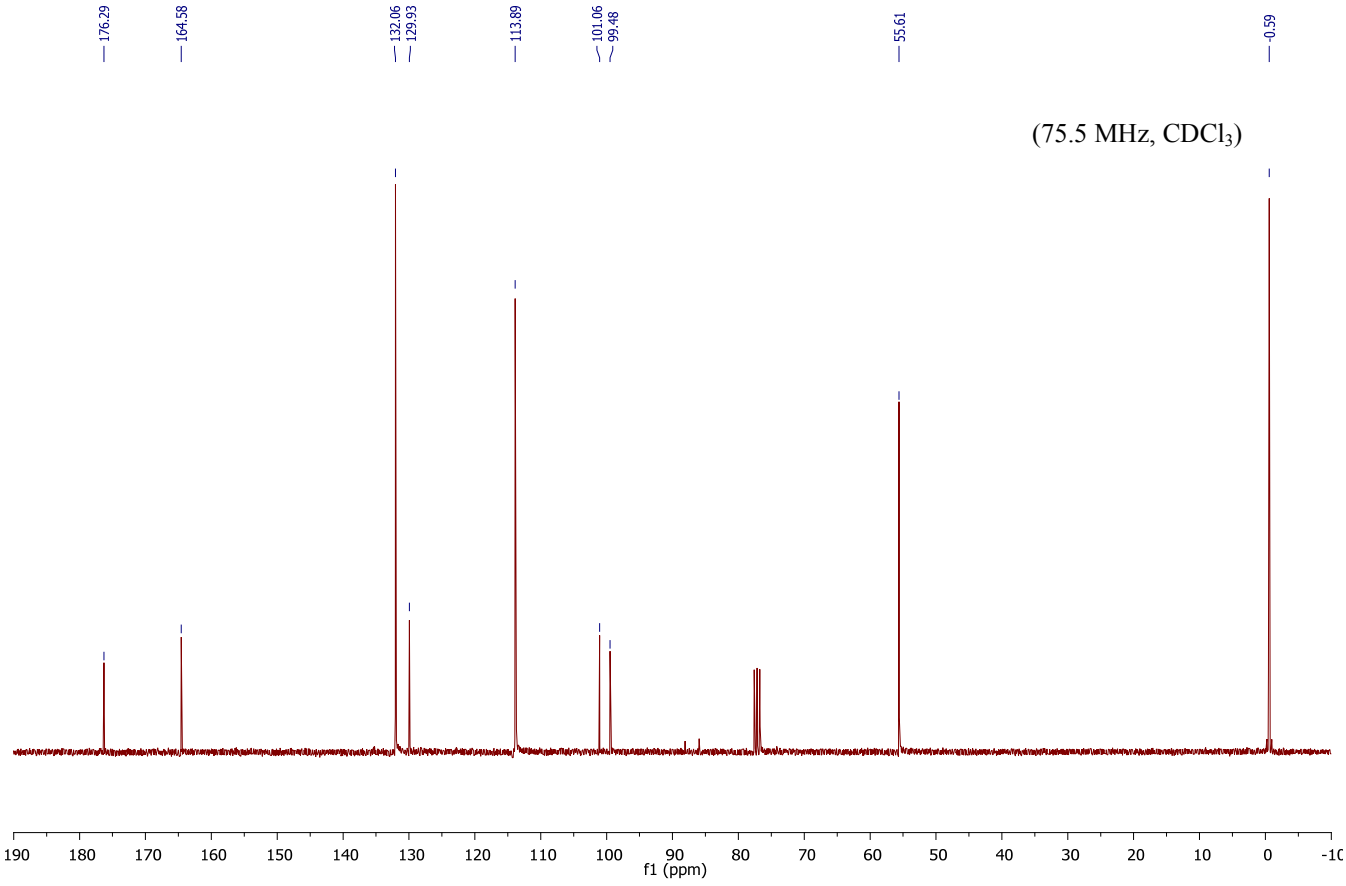


(75.5 MHz, $CDCl_3$)

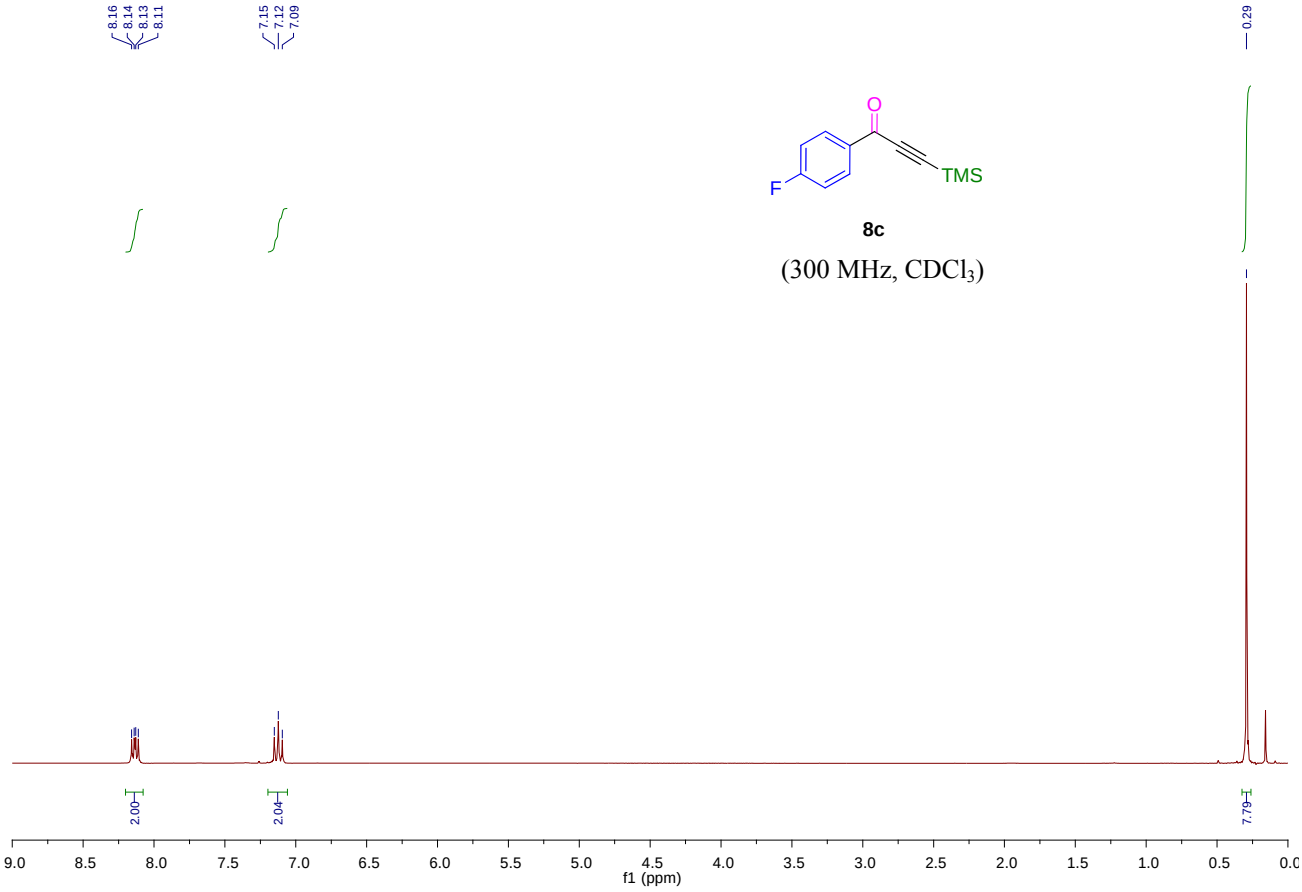


8b

(300 MHz, $CDCl_3$)

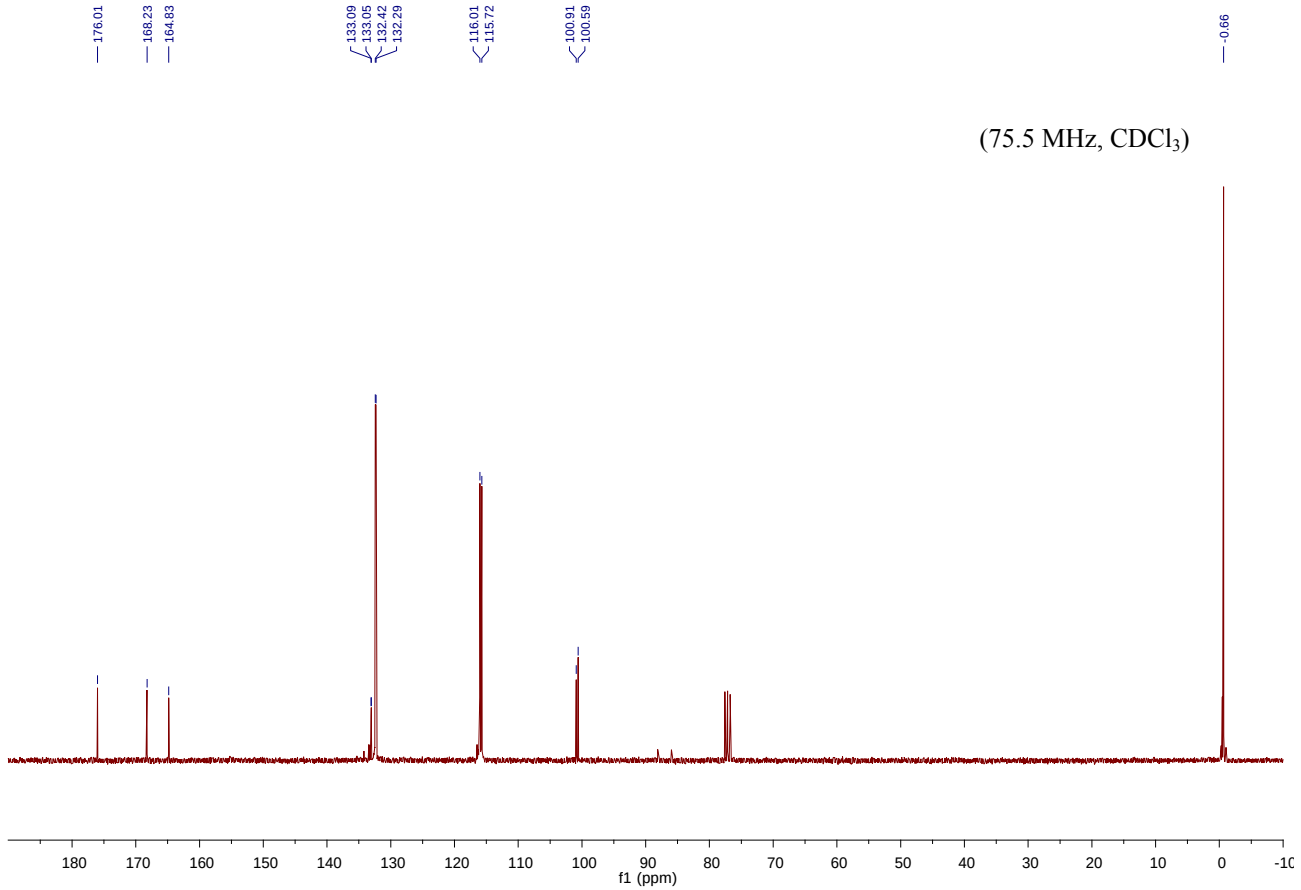


(75.5 MHz, $CDCl_3$)

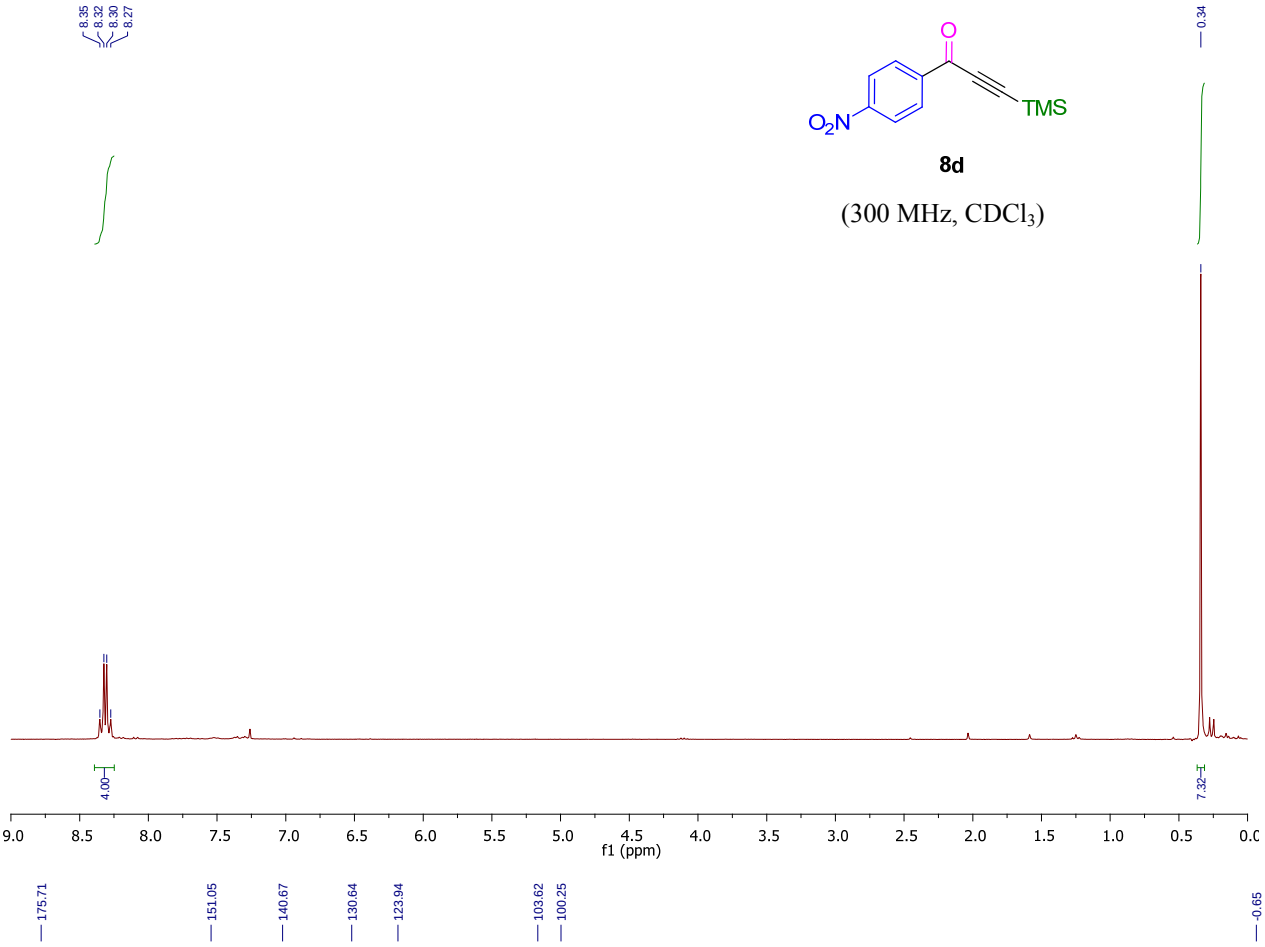


8c

(300 MHz, $CDCl_3$)



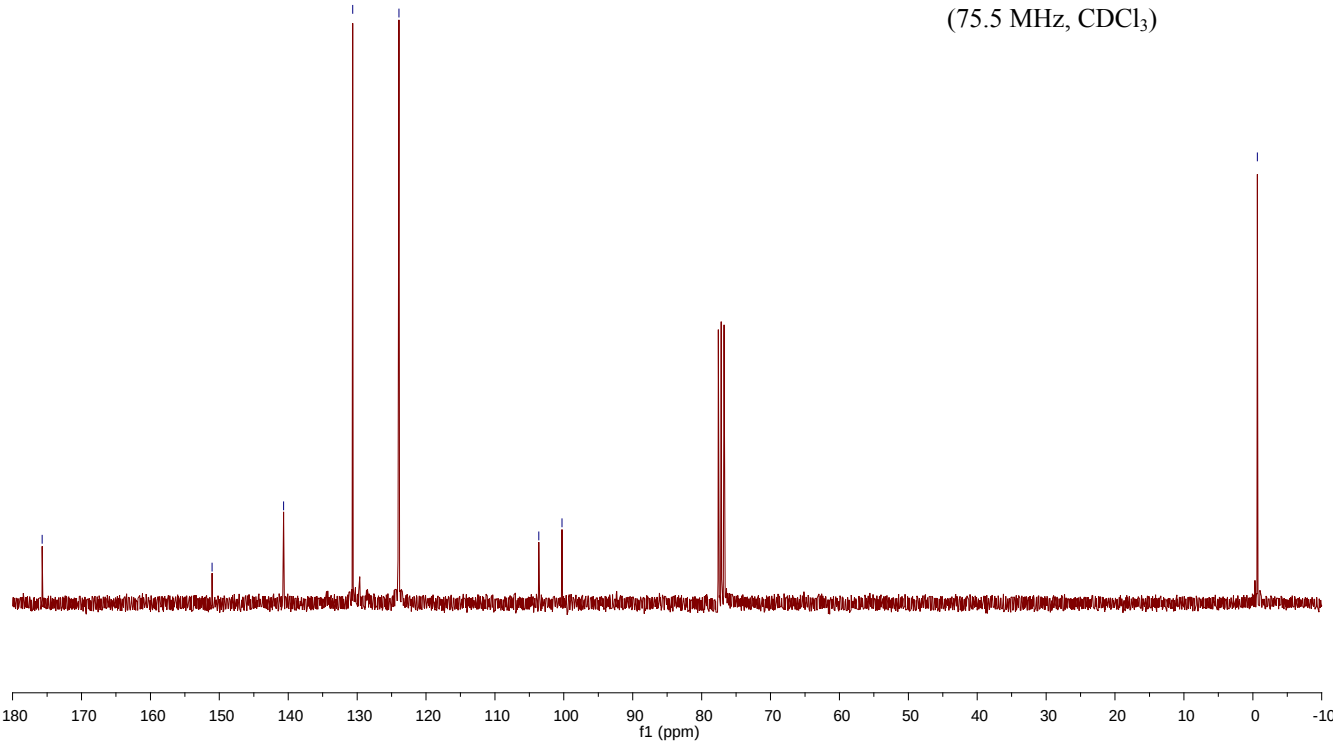
(75.5 MHz, $CDCl_3$)

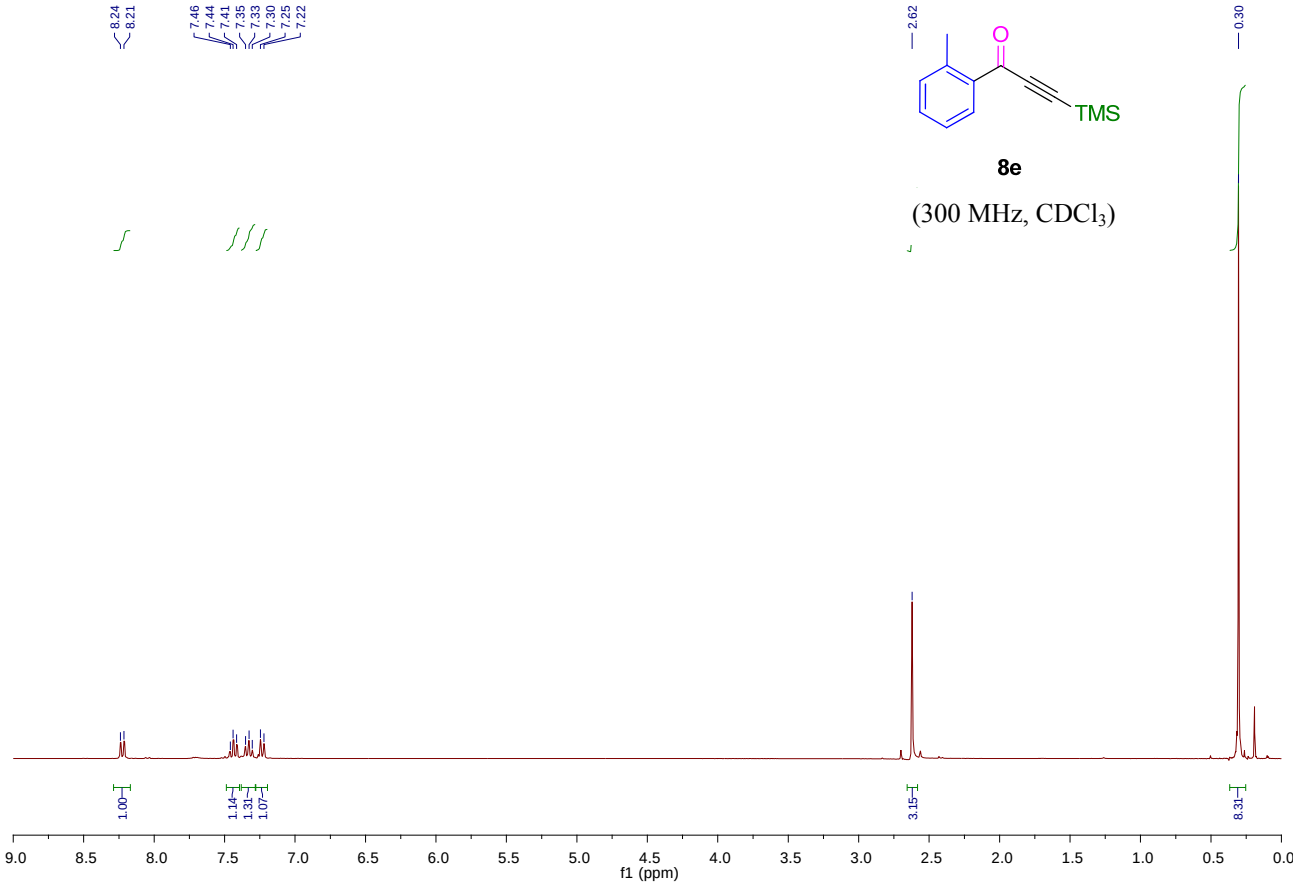


8d

(300 MHz, $CDCl_3$)

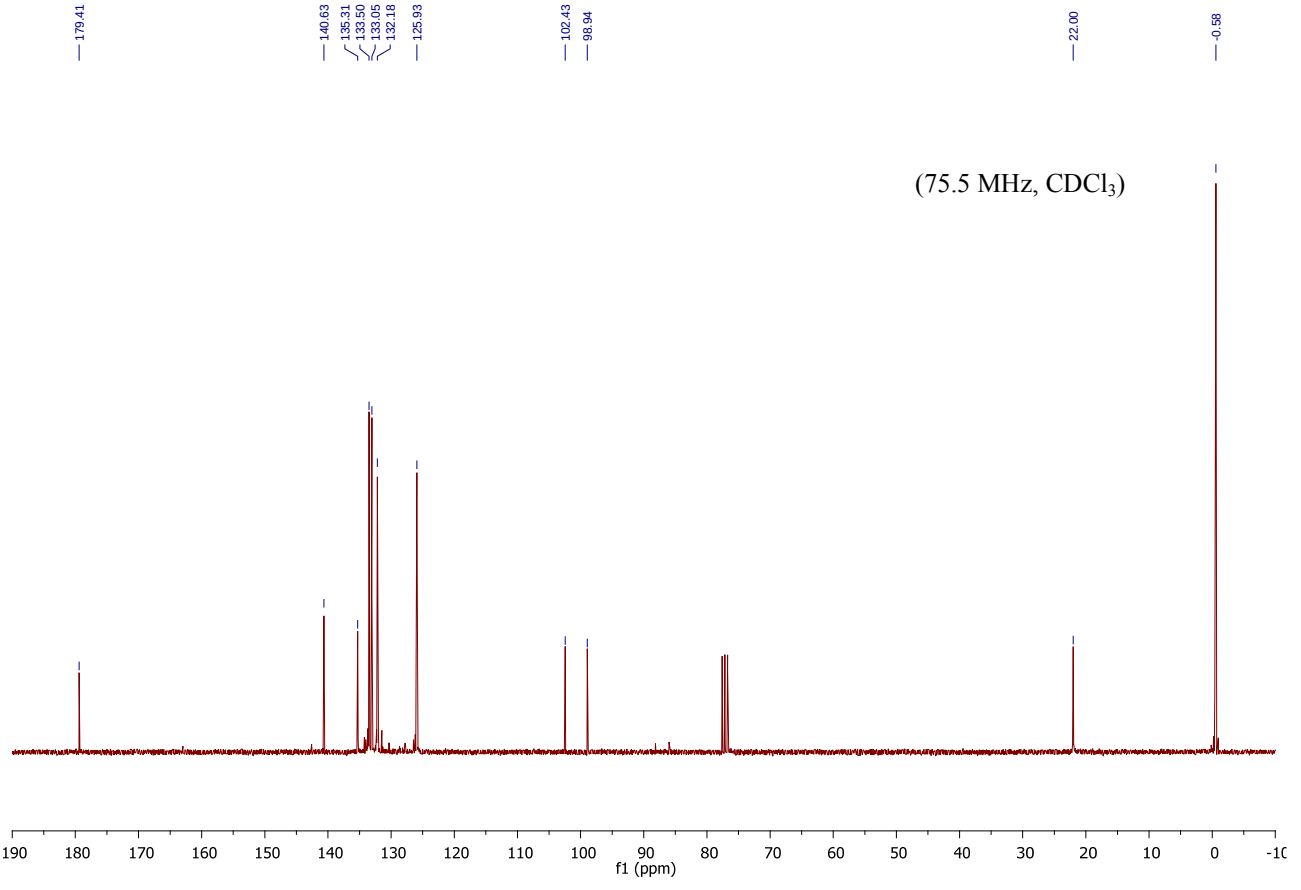
(75.5 MHz, $CDCl_3$)



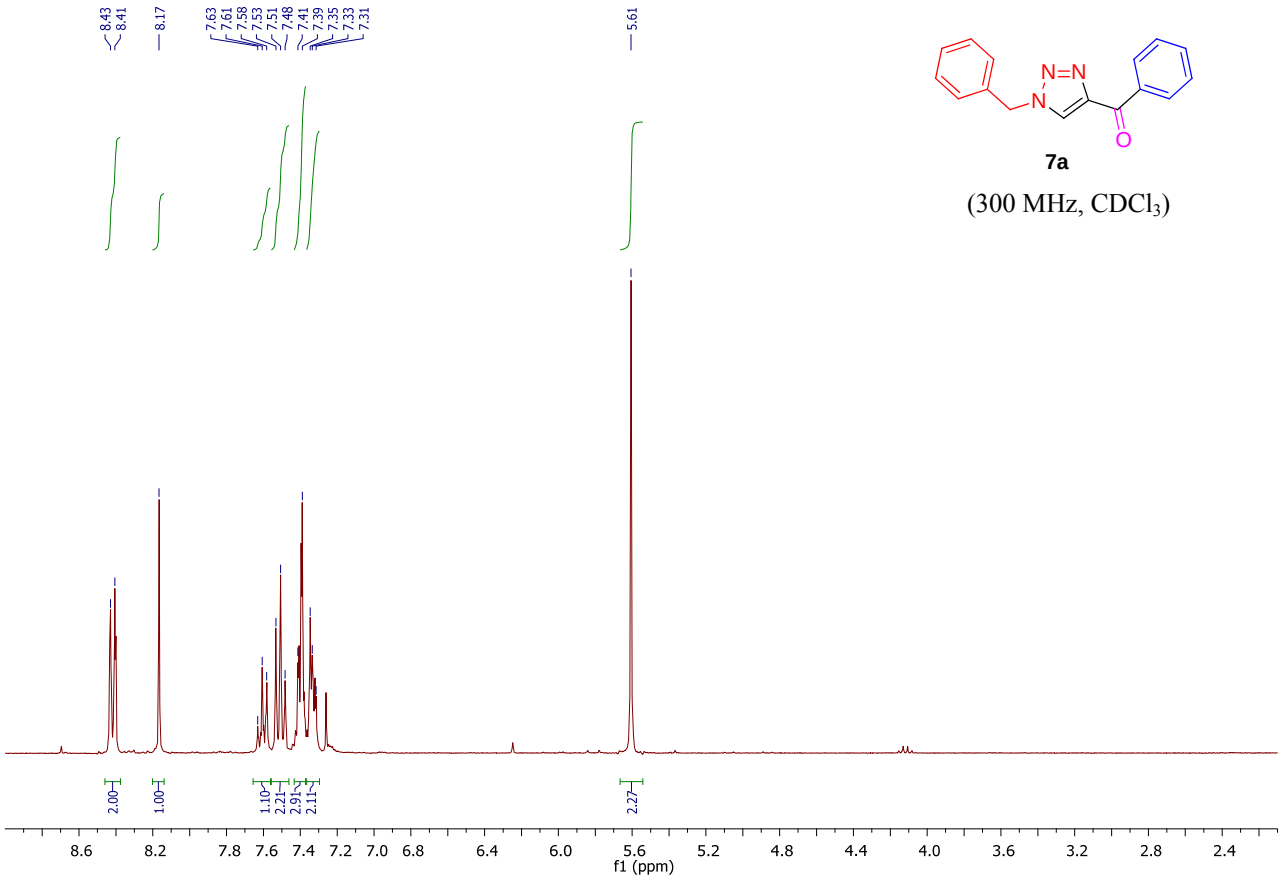


8e

(300 MHz, $CDCl_3$)

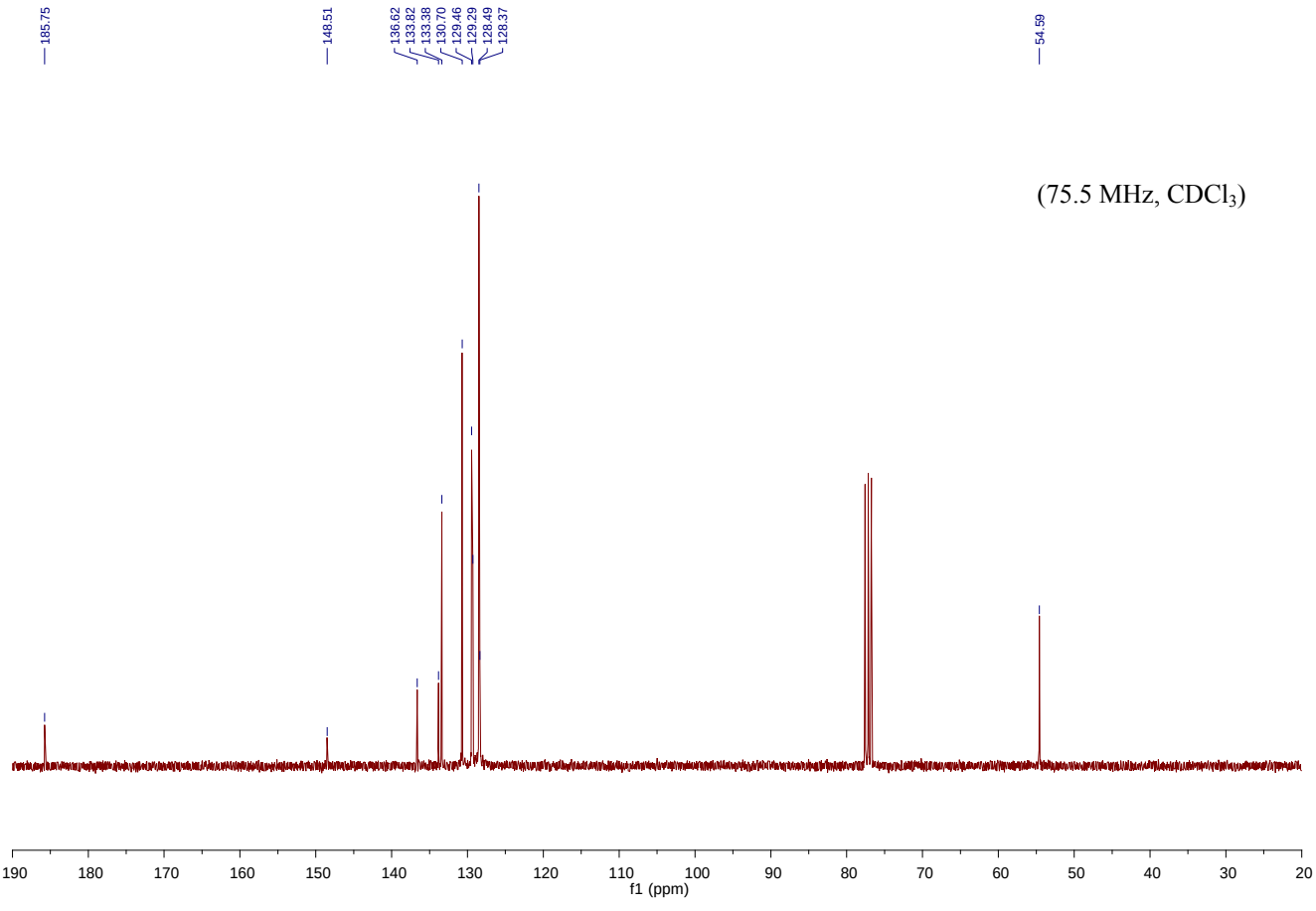


(75.5 MHz, $CDCl_3$)

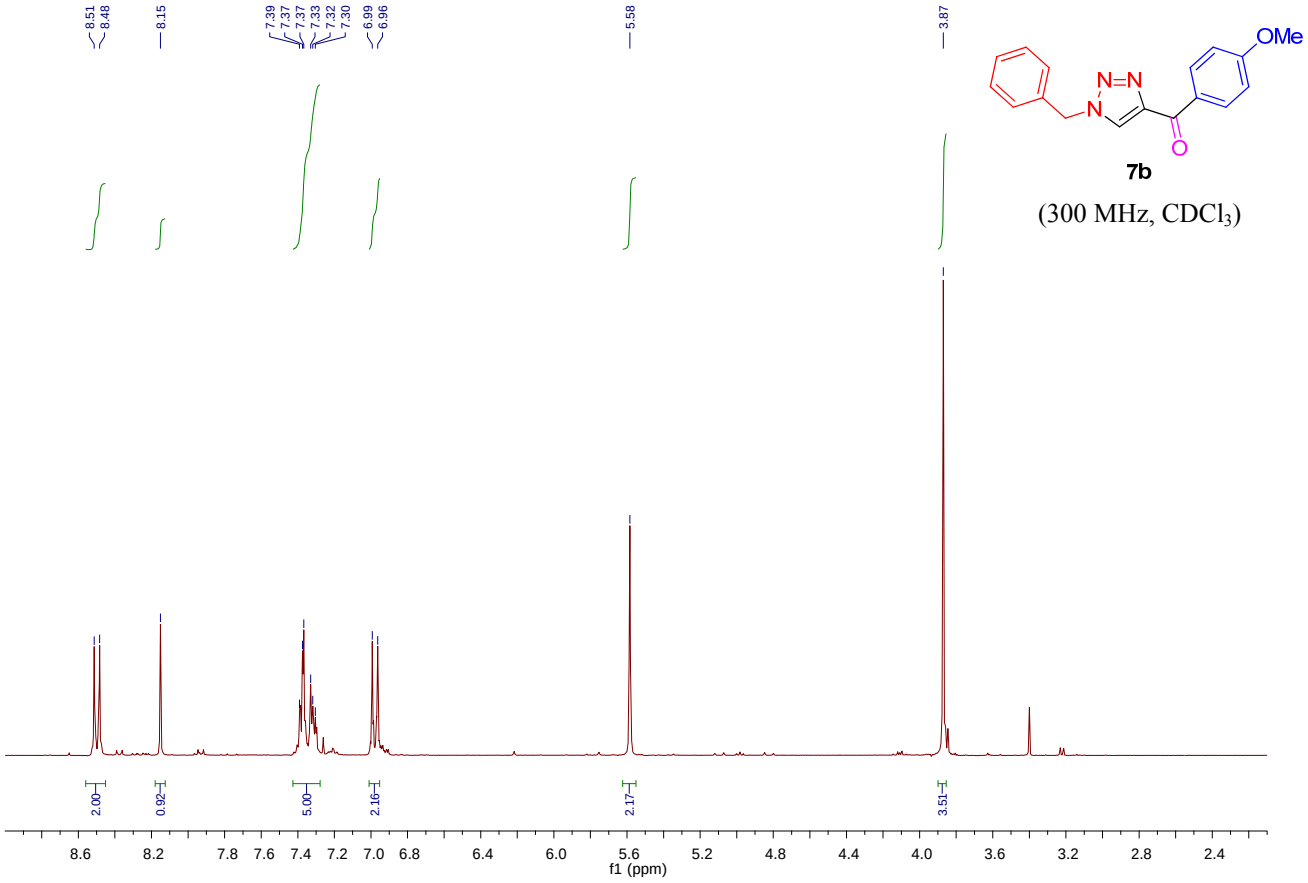


7a

(300 MHz, $CDCl_3$)

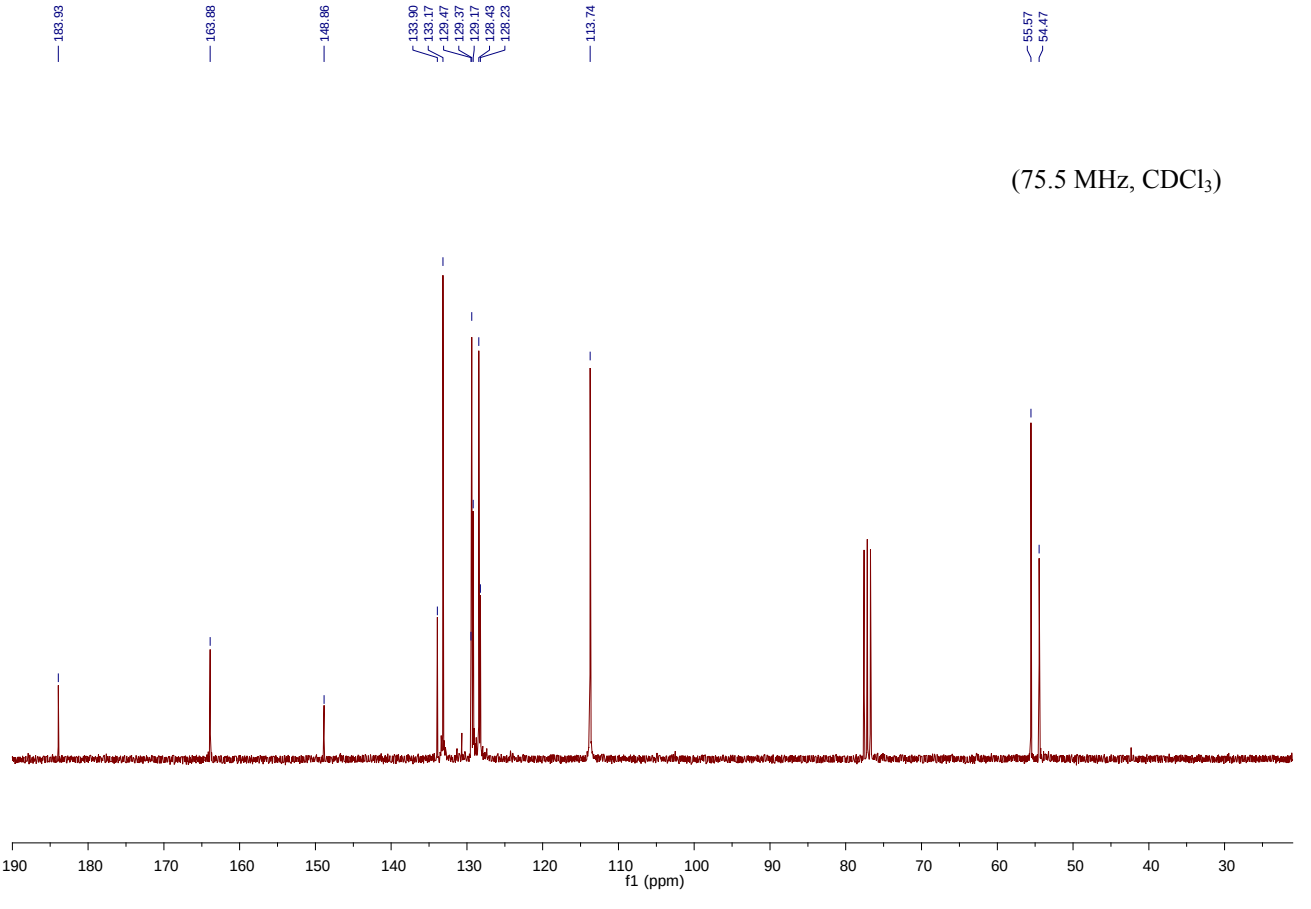


(75.5 MHz, $CDCl_3$)

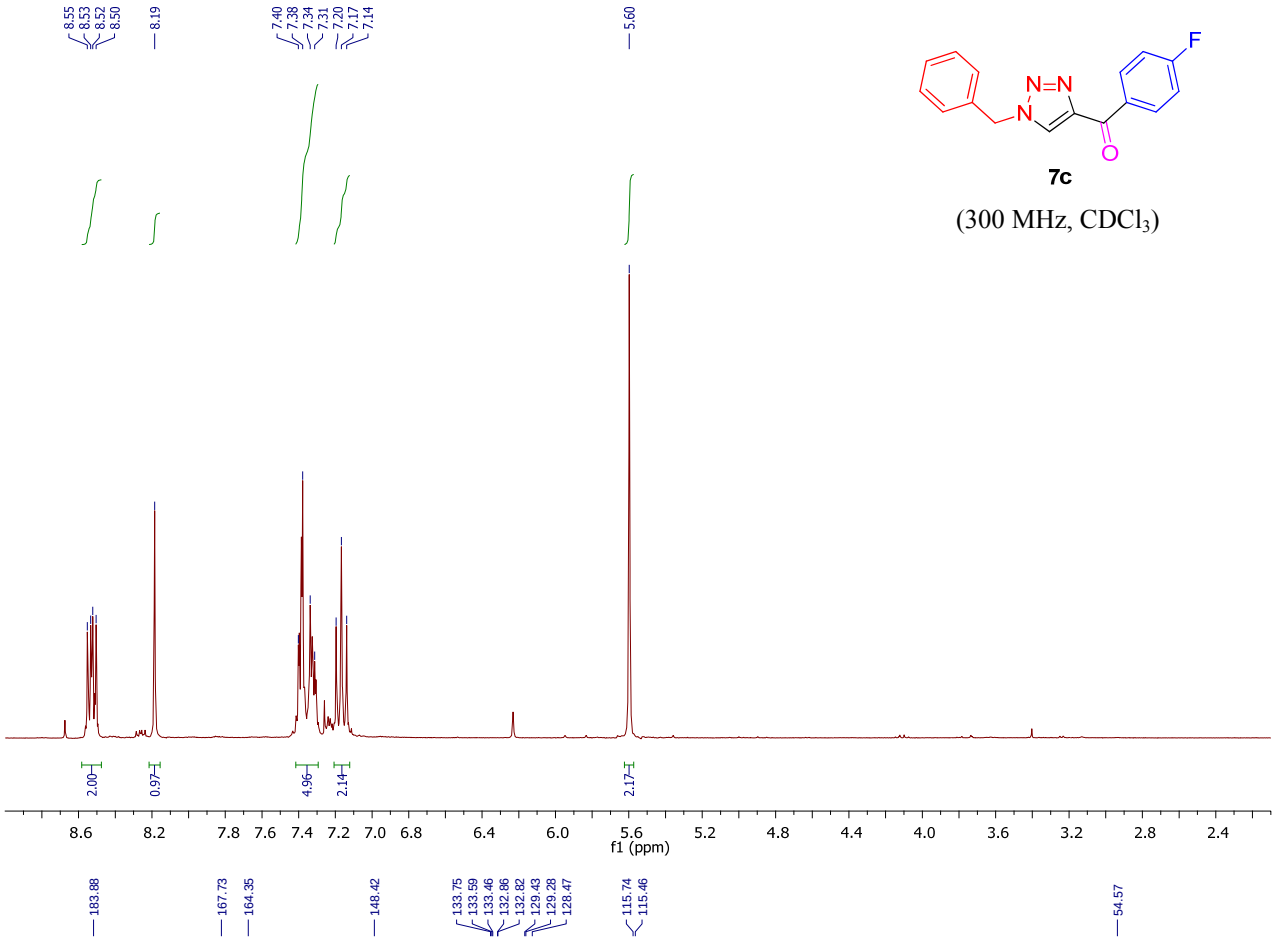


7b

(300 MHz, $CDCl_3$)

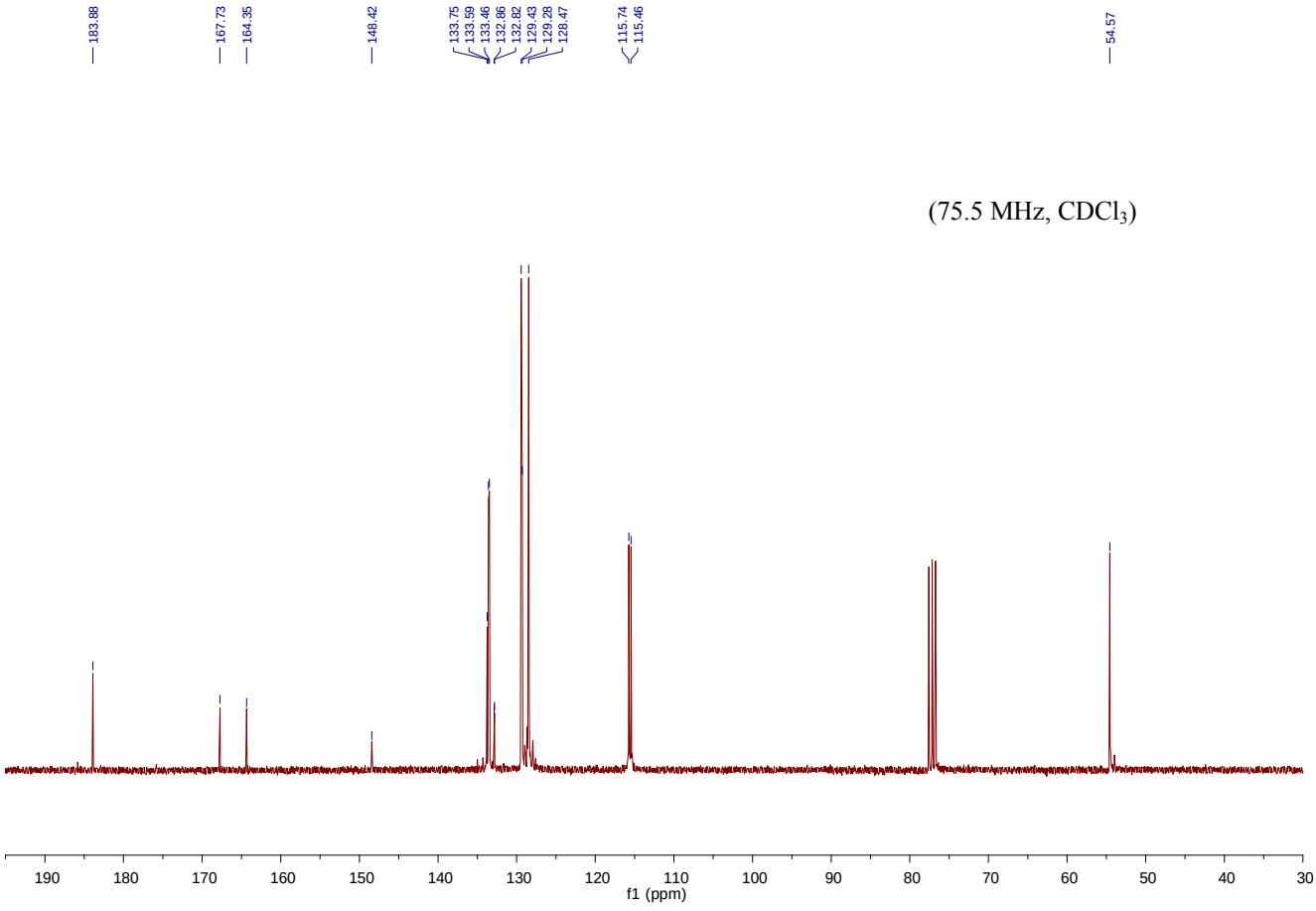


(75.5 MHz, $CDCl_3$)

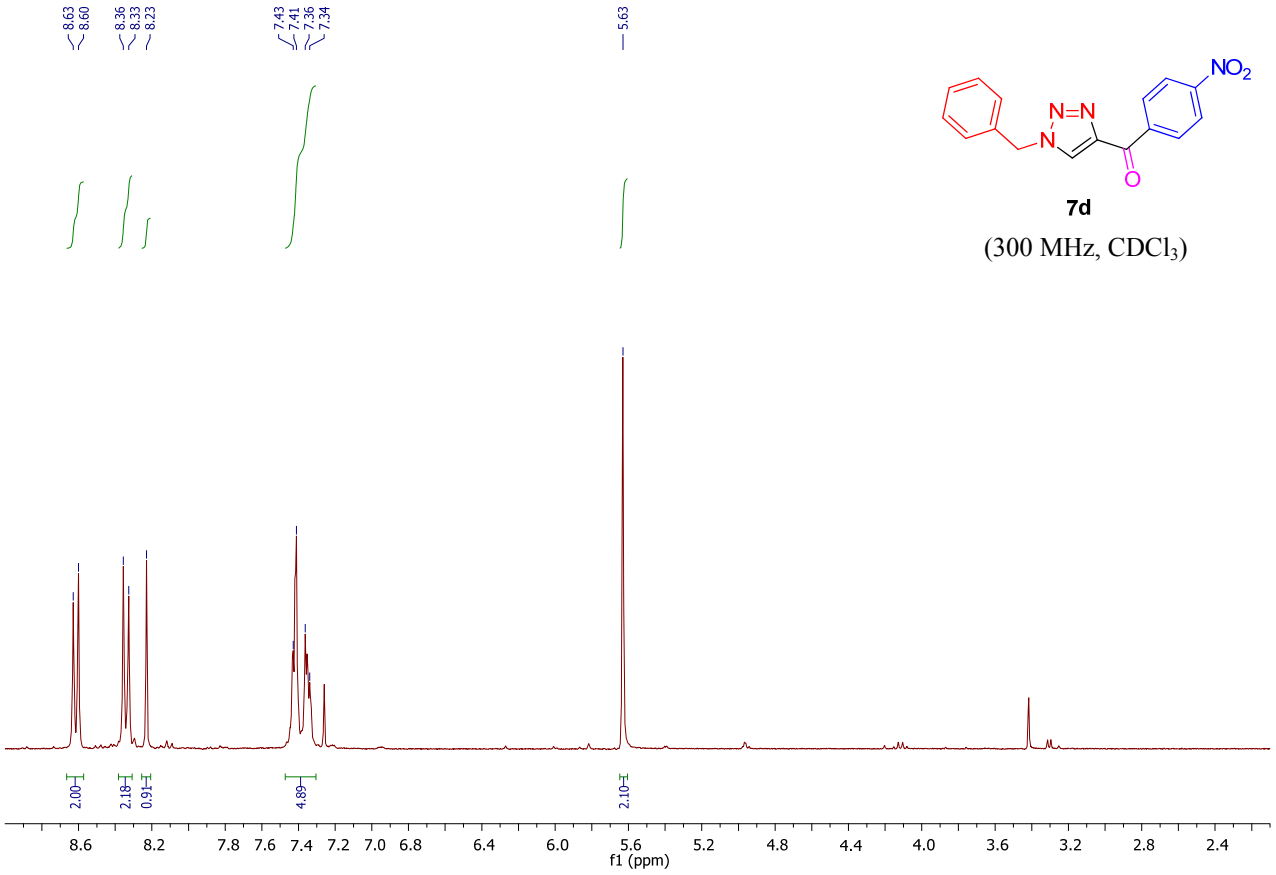


7c

(300 MHz, $CDCl_3$)



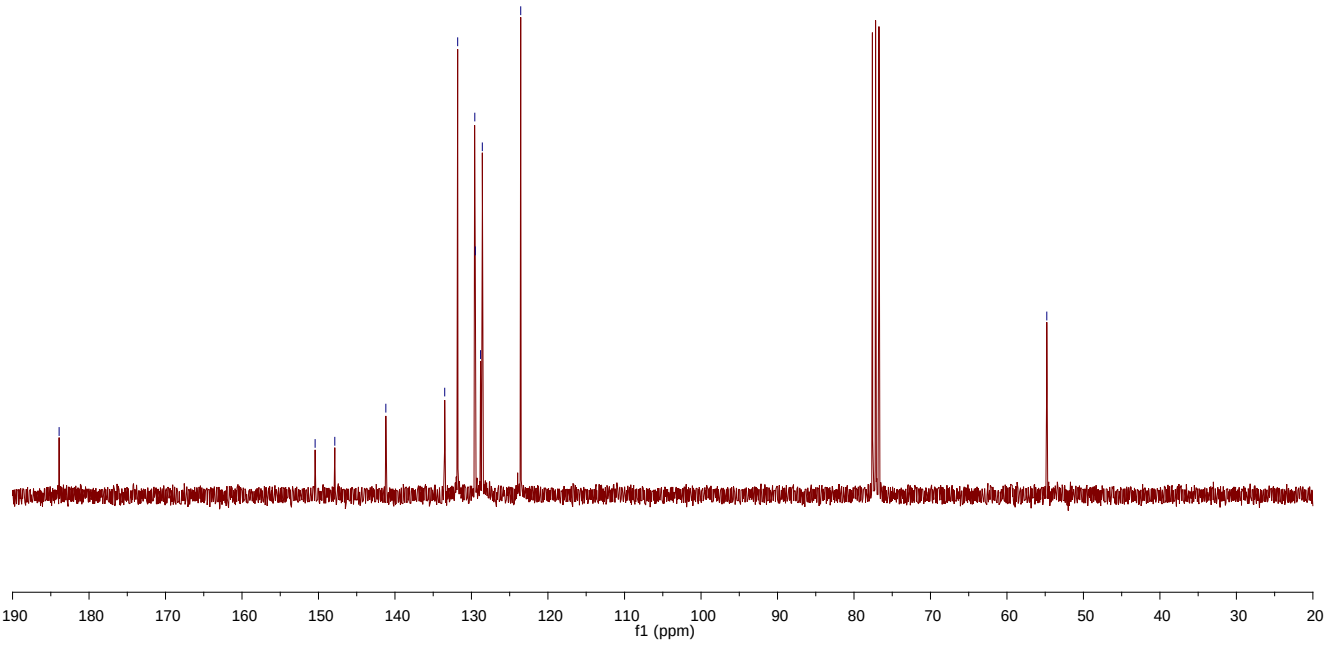
(75.5 MHz, $CDCl_3$)

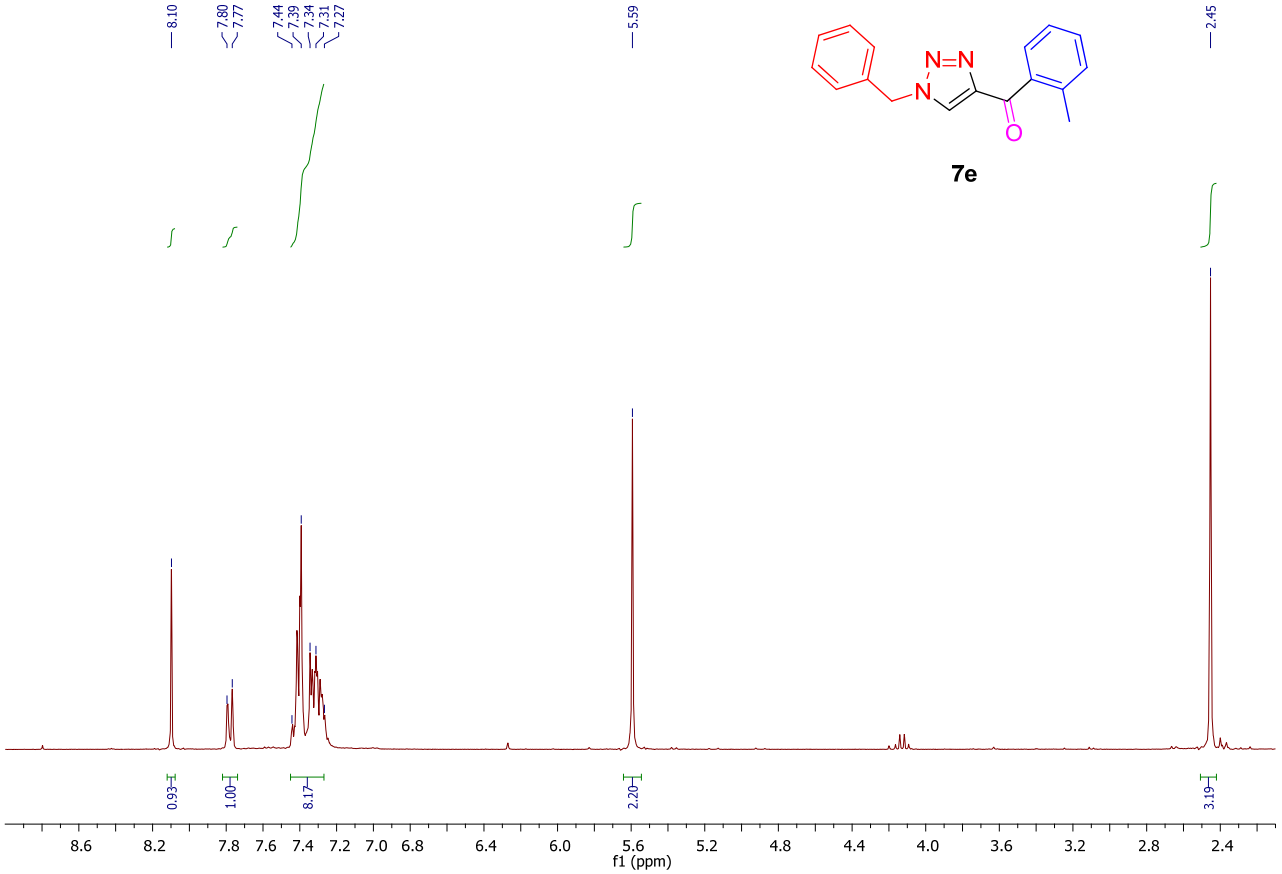


7d

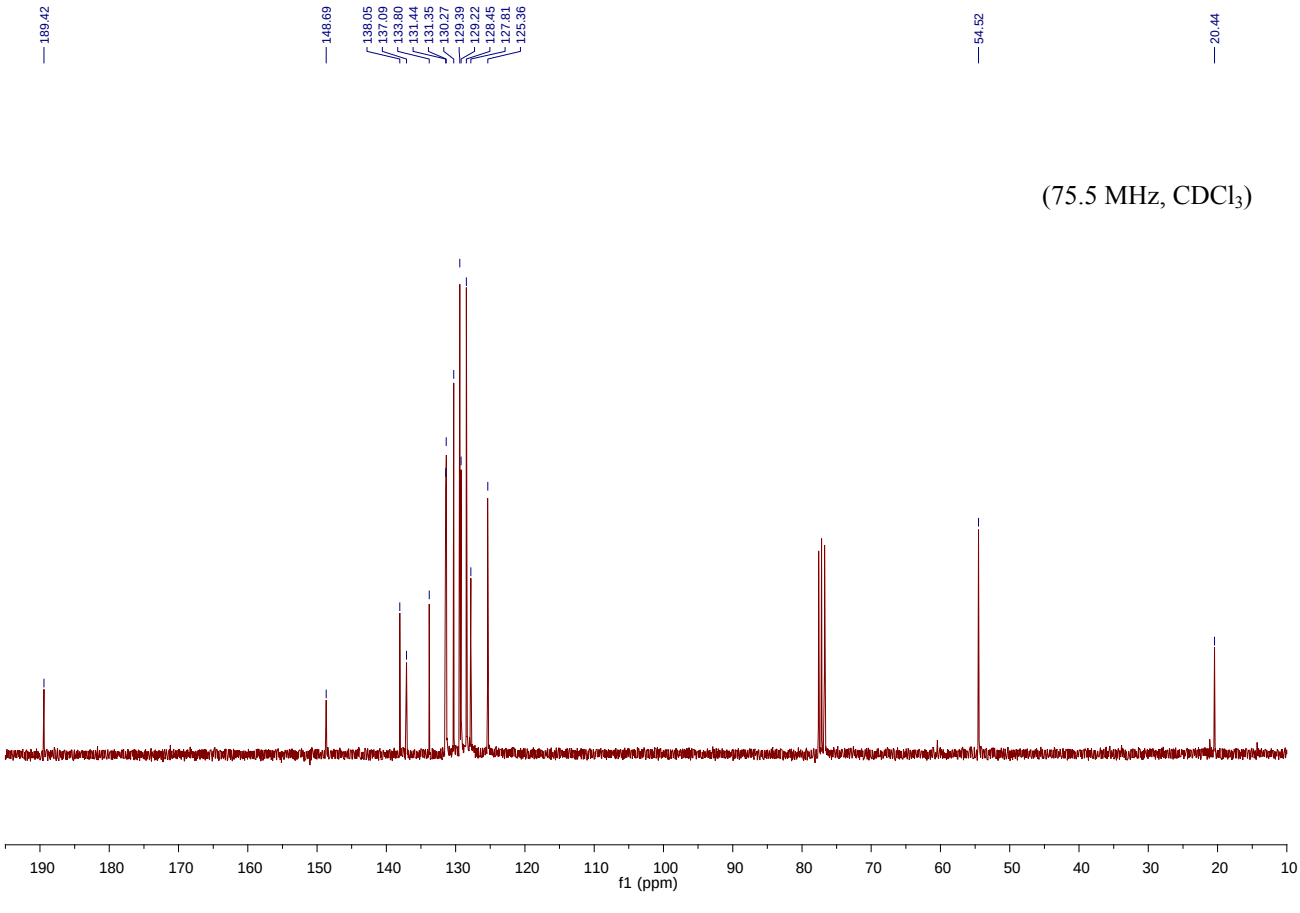
(300 MHz, $CDCl_3$)

(75.5 MHz, $CDCl_3$)





7e



(75.5 MHz, $CDCl_3$)