From A^3/KA^2 to AYA/KYA Multicomponent Coupling Reactions with Terminal Ynamides as Alkyne Surrogates – A Direct, Green Route to γ-Amino-Ynamides

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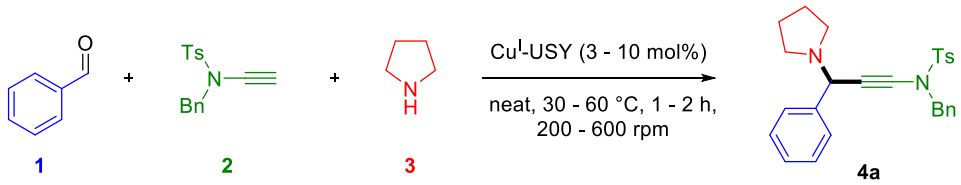
SUPPORTING INFORMATION

I. Optimisation of Reaction Conditions (Design of Experiment)

The solvent-free reaction between benzaldehyde (**1**), ynesulfonamide **2** and pyrrolidine (**3**) was used as a bench reaction to perform the optimisation studies *via* design of experiment (DoE).



Scheme S1. The bench reaction used to optimise the reaction conditions.

Six factors, namely temperature (**A**), catalyst loading (**B**), aldehyde equivalents (**C**), stirring rate (**D**), stirring bar type (**E**) and reaction time (**F**), were studied in a 2^{6-3} fractional factorial design giving a total number of eight experiments, which were run in parallel. **Table S1** shows the low and high levels for each factor.

Table S1. The investigated factors and their relative ranges.

Factor	Name	Units	Type	Min	Max	Mean	Std. Dev.
A	Temperature	°C	Numeric	30	60	45	16.04
B	Catalyst loading	mol%	Numeric	3	10	6.5	3.74
C	Aldehyde qty	eq	Numeric	1.0	1.5	1.25	0.2673
D	Stirring rate	rpm	Numeric	200	600	400	213.81
E	Stirring bar		Categoric	Small	Big	Levels:	2
F	Reaction time	min	Numeric	60	120	90	32.07

Table S2 shows the matrix of the design giving the standard run numbers, as well as the actual run number order together with the estimated yields (%) of formed γ-amino-ynamide **4a** (the recorded response) as determined *via* ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table S2. Design matrix.

		A	B	C	D	E	F	Resp.
Std	Run	Temperature (°C)	Catalyst loading (mol%)	Aldehyde qty (eq)	Stirring rate (rpm)	Stirring bar	Reaction time (min)	Yield **4a** (%)
1	1	30	3	1.0	600	Big	120	86
6	2	60	3	1.5	200	Big	60	59
4	3	60	10	1.0	600	Small	60	63
5	4	30	3	1.5	600	Small	60	86
2	5	60	3	1.0	200	Small	120	78
7	6	30	10	1.5	200	Small	120	84
3	7	30	10	1.0	200	Big	60	79
8	8	60	10	1.5	600	Big	120	83

The half-normal probability plot and PARETO chart were used for preliminary model selection. In this case, two models could be identified differing solely in the inclusion or exclusion of factor **D**, the stirring rate (**Figure S1**). Indeed, when included, factor **D** exceeds the t-value limit in the PARETO chart, however, significantly lays below the BONFERRONI limit (**Figure S1**, left). Consequently, stirring rate (**D**) was not included in the model. What can be deduced from both models is that temperature (**A**) was found to show the greatest impact on the ynamide yield, followed by the reaction time (**F**). In addition, the interaction term of both factors, **AF**, was found to significantly affect the ynamide yield. Considering this data set, the factors catalyst loading (**B**), aldehyde equivalents (**C**), and stirring bar type (**E**) do not significantly affect the ynamide yield within the investigated ranges. **Table S3** represents the ANOVA of the polynomial model including the factors temperature (**A**) and reaction time (**F**), as well as their interaction term AF. **Table S4** shows the corresponding Fit Statistics.

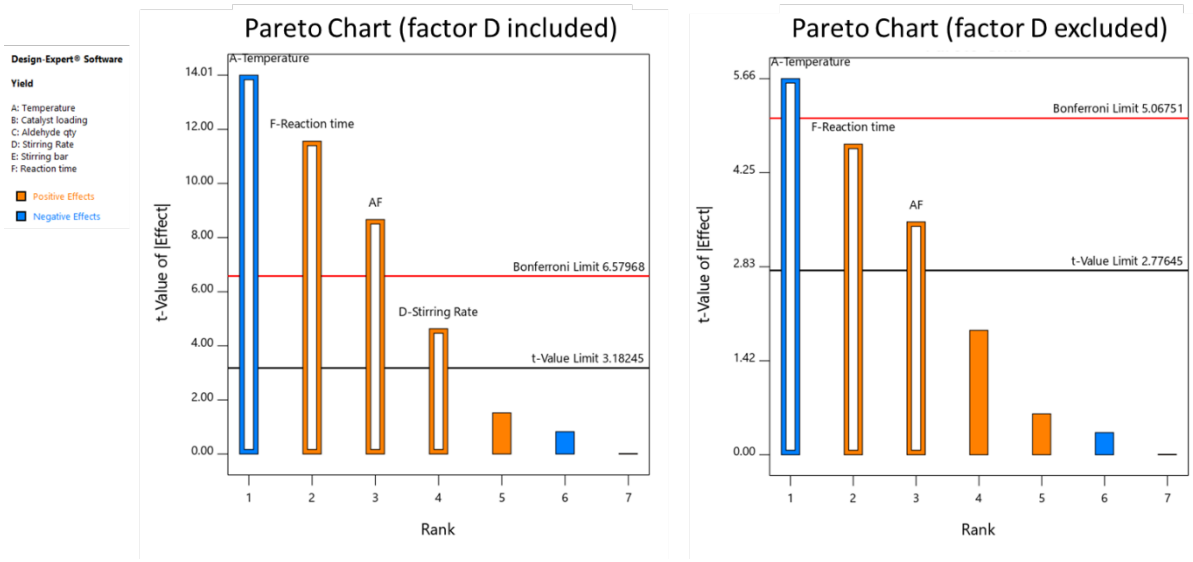


Figure S1. PARETO charts. Left: including factor D (stirring rate); right: excluding factor D.

Table S3. ANOVA for selected factorial model.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	739.48	3	246.49	22.08	0.0060	significant
A-Temperature	358.12	1	358.12	32.08	0.0048	
F-Reaction time	244.13	1	244.13	21.87	0.0095	
AF	137.24	1	137.24	12.29	0.0248	
Residual	44.65	4	11.16			
Cor Total	784.13	7				

Table S4. Fit Statistics.

Std. Dev.	3.34		**R^2**	0.9431
Mean	77.17		**Adjusted R^2**	0.9004
C.V. %	4.33		**Predicted R^2**	0.7722
			Adeq Precision	10.3408

The coded equation for the selected model is:

Yield = 77.1699 + (-6.69063 * **A**) + 5.52417 * **F** + 4.1418 * **AF**.

The actual equation for the selected model is:

Yield = 117.945 + (-1.2744 * **Temperature**) + (-0.230041 * **Reaction time**) + 0.009204 * **Temperature** * **Reaction time**

yielding the graphical representation shown in **Figure S2**.

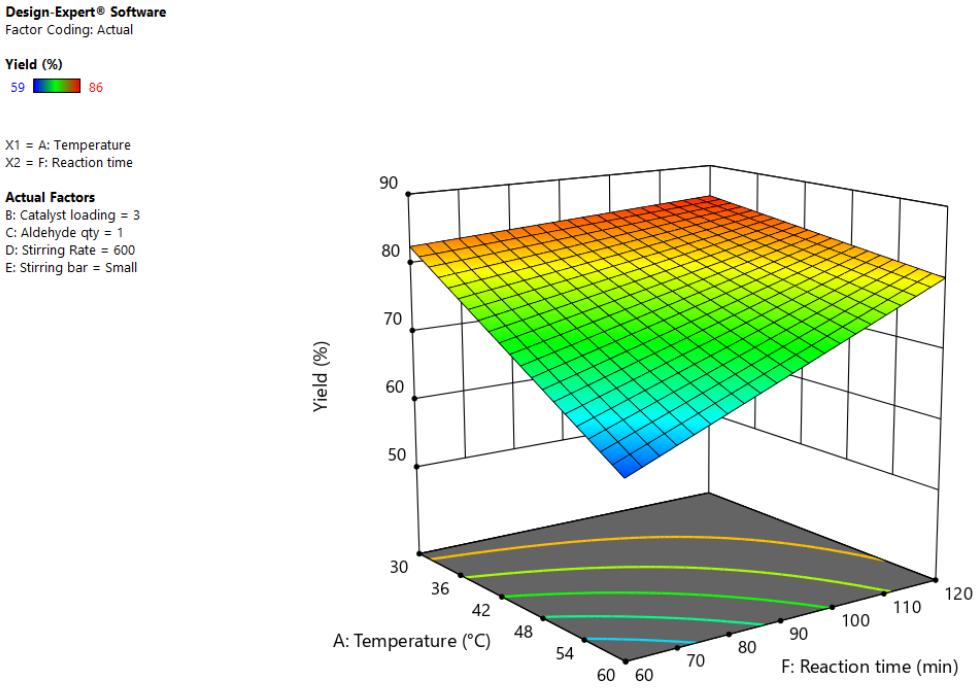


Figure S2. Response surface.

To conclude, temperature and reaction time were identified as the crucial factors to afford ynamide in high yield. This is in concordance with the preliminary results discussed above. As the optimal settings for those factors probably greatly depend on the substrate combination no further optimisation studies *via* DoE were performed. Nevertheless, the following conditions were set as the standard conditions for the scope based on the DoE results:

A: Temperature	B: Catalyst loading	C: Aldehyde qty	D: Stirring Rate	E: Stirring bar
30 °C	3 mol%	1.0 eq	600 rpm	Small

II. General Experimental Methods

All starting materials were purchased at the highest commercial quality and used as received unless otherwise stated. – Reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F254, Merck) using UV-light and/or $KMnO_4$ and/or vanillin dip for visualisation. Column chromatographies were performed on (deactivated) silica gel 60 (0.040-0.063 mm, Merck) using cyclohexane/EtOAc mixtures as eluents. – Evaporation of solvents was conducted under reduced pressure at temperatures equal to or less than 40 °C. – IR spectra were recorded neat on a Bruker Alpha ATR Diamant. Wave numbers are given in cm^{-1}. – ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance spectrometers at 300, 400 or 500 MHz for ^{1}H NMR experiments and 126 MHz for ^{13}C NMR experiments. Chemical shifts (δ) and coupling constants (J) are given in ppm and Hertz (Hz), respectively. The signal multiplicity is described according to the following abbreviations: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sextet (sext), septet (sept), and m (multiplet). Chemical shifts (δ) are reported relative to the residual solvent as an internal standard ($CDCl_3$: δ = 7.26 ppm for ^{1}H and δ = 77.16 ppm for ^{13}C). Carbon multiplicities were determined by DEPT135 experiments. – Electrospray Ionization (ESI) and Electrospray Ionization Time-Of- Flight (ESI-TOF) low/high-resolution mass spectra were obtained from the "Service de Spectroscopie de Masse" of the Fédération de Chimie "Le Bel" (FR2010).

III. General Procedures & Reusability Study

General Procedure for the Preparation of Cu^{I}-USY

Cu^{I}-USY was prepared according to a well-established solid/solid exchange procedure. Commercial NH_4-USY (ZEOLYST® CBV500) was first loaded in an oven and heated at 550°C for 4 h to give H-USY. A mixture of so-formed H-USY (1.0 g, 3.8 mmol acidic sites/g of zeolite) and CuCl (376 mg, 1.0 eq. related to the number of H-zeolite protons) were ground by mortar and pestle and then heated in a furnace under flowing nitrogen at 350°C for three days furnishing the expected Cu^{I}-USY.

General Procedure A: Synthesis of Sulfonamides

To an ice-cold solution of primary amine (1.0 eq.) and Et_3N (2.0 eq.) in dry CH_2Cl_2 (0.2 M) was added the corresponding sulfonyl chloride (1.1 eq.) in small portions and the mixture was stirred at room temperature until completion as indicated by thin layer chromatography. The reaction was then quenched with water (30 mL/10 mmol amine) and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. If necessary, the crude product was purified *via* column chromatography using silica gel.

General Procedure B: Synthesis of 1,2-Dichloroenamides

Amide (1.0 eq.) and powdered Cs_2CO_3 (1.5 eq.) were given into a flame-dried Schlenk flask equipped with a stirring bar. After three cycles of high vacuum evacuation and argon backfill of the flask, DMF (0.75 mL/mmol of amide substrate) was added and degassed for 5 minutes with argon. Next, the suspension was heated to 50 °C followed by a dropwise addition of trichloroethylene (1.1 eq.) over 5 to 10 minutes. The resulting mixture was stirred at 50 ºC until

completion, as analysed by TLC. Cooled to room temperature, the mixture was partitioned between ethyl acetate and water (ca. EtOAc/H_2O 2:1). Next, the organic layer was separated and further washed three times with water, and once with brine. The organic layer was then dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The crude mixtures were purified by column chromatography over silica gel (cyclohexane/ethyl acetate) if necessary.

General Procedure C: Synthesis of TIPS-protected Ynamides

To a solution of 1-bromo-2-(triisopropylsilyl)acetylene (1.1 eq.) in toluene (0.5 M) were successively added amide (1.0 eq.), K_2CO_3 or K_3PO_4 (2.0 eq), $CuSO_4 \cdot 5H_2O$ (10 mol%) (homogeneous)[1] or Cu^I-USY (8 mol%) (heterogeneous)[2] and 1,10-phenantroline (20 mol%). The vial was capped and placed into a pre-heated aluminium block (60-110 °C) and stirred at 600 rpm until completion of the reaction. Next, the reaction mixture was filtrated over celite, washed with ethyl acetate or dichloromethane and the solvent was removed under reduced pressure. The crude mixtures were purified by column chromatography over silica gel (cyclohexane/ethyl acetate).

General Procedure D: Synthesis of Terminal Ynamides from 1,2-Dichloroenamides

To a solution of 1,2-dichloroenamide (1.0 eq.) in freshly distilled THF (10 mL/mmol enamide) was added phenyllithium solution (1.9 M in Bu_2O, 2.2 eq.) dropwise over 2-10 min under vigorous magnetic stirring at – 78 °C. After completion (ca. 1 h at – 78 °C), the mixture was quenched with diethyl ether/water (1:1) at – 78 °C and let warm to room temperature. The two phases were separated, and the aqueous layer was extracted with diethyl ether (three times). The combined organic layers were washed once with saturated aqueous brine, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude mixtures were purified by column chromatography over silica gel (cyclohexane/ethyl acetate/triethylamine).

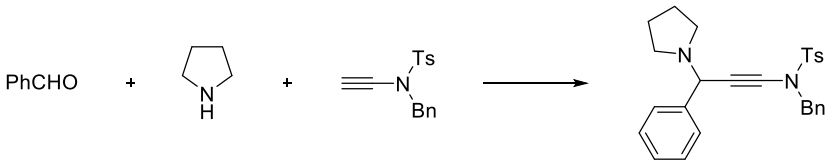
General Procedure E: Desilylation of TIPS-protected Ynamides

To a solution of silylated ynamide (1.0 eq.) in freshly distilled THF (1 M) was added TBAF (1 M in THF, 1.1 eq.) dropwise over 2-3 min under vigorous magnetic stirring at – 40 °C. After completion, the mixture was quenched with ethyl acetate/water (1:1) and let warm to room temperature. The two phases were separated, and the aqueous layer was extracted with ethyl acetate (three times). The combined organic layers were washed once with saturated aqueous brine, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude mixtures were purified by column chromatography over silica gel (cyclohexane/ethyl acetate/triethylamine).

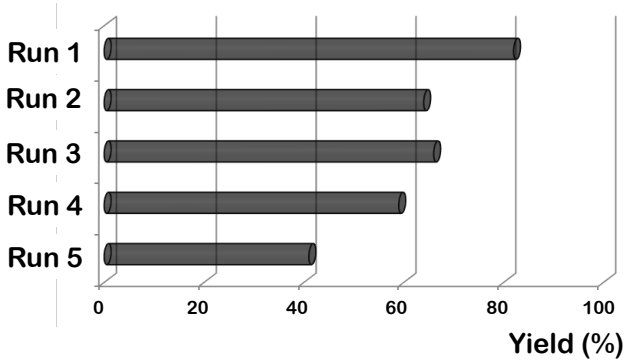
General Procedure F: Synthesis of γ-Amino-Ynamides

Aldehyde or ketone (1.0 eq.), amine (1.0 eq.), terminal ynamide (1.0 eq.), Cu^I-USY (3 mol%), and MS (4 Å, 75 mg/250 µmol if indicated) are added to a 10 mL screw cap tube. When needed, EtOAc (0.15 mL/250 µmol) is added and the tube is flushed with argon before sealing. The tube is placed into a pre-heated aluminium block at 30 °C and stirred until completion of starting material at 600 rpm. Next, the mixture was diluted with EtOAc (2 mL) and filtered over celite (wash with EtOAc). The crude product is purified by column chromatography over silica gel (cyclohexane/ethyl acetate/triethylamine).

Recyclability Study



A recyclability study was performed following the optimised procedure on a 250 µmol scale using benzaldehyde (26.5 mg), pyrrolidine (17.8 mg), TsBnN(CCH) (71.4 mg) and Cu^{I}-USY (9.0 mg, 10 mol% Cu) in dry EtOAc (0.15 mL, HPLC grade). 1,3,5-trimethoxybenze was added as internal standard for estimation of ^{1}H NMR yield. The reaction mixture was stirred for 15 min at 30 °C, then diluted with EtOAc (2 mL) and centrifuged (1000 rpm, 1 min). The supernatant was decanted, and centrifugation was repeated three times with EtOAc (2 mL) to wash the zeolite residue. The recovered zeolite was directly engaged in the next run.

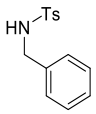


IV. Analytical Description of Products

Precursors of Terminal Ynamides

Sulfonamides

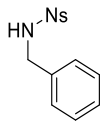
N-Benzyl-4-methylbenzenesulfonamide (CAS: 1576-37-0)[1]



Chemical Formula: $C_{14}H_{15}NO_2S$
Molecular Weight: 261,34

Following the **General Procedure A**, the title compound was obtained as an off-white solid (2.51 g, 9.60 mmol) and used without further purification. Yield 99%. – R_f = 0.13 (cyclohexane/EtOAc 9:1). – FTIR-ATR (neat) 3267, 3033, 2914, 1597, 1495, 1453, 1421, 1321, 1287, 1160, 1093, 1082, 1058, 1028, 874, 805, 740, 682 cm^{-1}. – ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.78 – 7.75 (m, 2H), 7.33 – 7.24 (m, 5H), 7.22 – 7.18 (m, 2H), 4.62 (t, *J* = 6.1 Hz, 1H), 4.13 (d, *J* = 6.1 Hz, 2H), 2.44 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 143.7, 136.9, 136.4, 129.9, 128.9, 128.1, 128.0, 127.3, 47.4, 21.7 ppm.

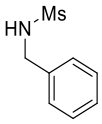
N-Benzyl-4-nitrobenzenesulfonamide (CAS: 52374-25-1)[2]



Chemical Formula: $C_{13}H_{12}N_2O_4S$
Molecular Weight: 292,3090

Following the **General Procedure A**, the title compound was obtained as a yellow solid (5.44 g, 18.61 mmol) and used without further purification. Yield 98%. – R_f = 0.28 (cyclohexane/EtOAc 8:2). – FTIR-ATR (neat) 3286, 3098, 3067, 2955, 2866, 2165, 1606, 1521, 1347, 1154, 1056, 856, 735 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.40 – 8.25 (m, 2H), 8.06 – 7.89 (m, 2H), 7.30 – 7.25 (m, 3H), 7.20 – 7.15 (m, 2H), 4.89 (t, *J* = 6.0 Hz, 1H), 4.24 (d, *J* = 6.1 Hz, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 150.1, 146.1, 135.5, 129.0, 128.4, 128.0, 124.5, 53.6, 47.6 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 315.04 (100) $[M+H]^+$.

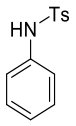
N-Benzylmethanesulfonamide (CAS: 3989-45-5)[2]



Chemical Formula: $C_8H_{11}NO_2S$
Molecular Weight: 185,2410

Following the **General Procedure A**, the title compound was obtained as a colourless solid (3.31 g, 11.32 mmol) and used without further purification. Yield 99%. – R_f = 0.21 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3224, 3062, 3034, 2016, 2934, 2864, 1605, 1493, 1455, 1293, 1160, 1081, 973, 874, 736 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.42 – 7.28 (m, 5H), 4.57 (br s, 1H), 4.33 (d, J = 6.1 Hz, 2H), 2.88 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 136.7, 129.1, 128.3, 128.0, 47.4, 41.3 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 208.04 (100) $[M+H]^+$.

4-Methyl-*N*-phenylbenzenesulfonamide (CAS: 68-34-8)[3]



Chemical Formula: $C_{13}H_{13}NO_2S$
Molecular Weight: 247,3120

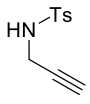
Following the **General Procedure A**, the title compound was obtained as an off-white solid (1.21 g, 4.90 mmol) and used without further purification. Yield 98%. – R_f = 0.50 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3234, 3103, 3028, 2970, 2897, 1597, 1481, 1414, 1335, 1153, 1090, 908, 817, 753, 693 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.67 – 7.61 (m, 2H), 7.27 – 7.19 (m, 4H), 7.15 – 7.08 (m, 1H), 7.07 – 7.03 (m, 2H), 6.42 (br s, 1H), 2.38 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.0, 136.5, 136.2, 129.8, 129.5, 127.4, 125.6, 121.9, 21.7 ppm.

N-Allyl-4-methylbenzenesulfonamide (CAS: 50487-71-3)[4]

Chemical Formula: $C_{10}H_{13}NO_2S$
Molecular Weight: 211,2790

Following the **General Procedure A**, the title compound was obtained as a colourless solid (2.07 g, 9.80 mmol). Yield 98%. – R_f = 0.43 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3245, 2927, 2853, 2105, 1747, 1648, 1595, 1493, 1422, 1373, 1318, 1157, 1092, 1062, 935, 810, 664 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.78 – 7.73 (m, 2H), 7.35 – 7.29 (m, 2H), 5.73 (ddt, J = 17.1, 10.2, 5.8 Hz, 1H), 5.17 (dq, J = 17.1, 1.5 Hz, 1H), 5.10 (dq, J = 10.2, 1.3 Hz, 1H), 4.39 (t, J = 5.9 Hz, 1H), 3.59 (tt, J = 6.0, 1.5 Hz, 2H), 2.43 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 143.7, 137.1, 133.1, 129.9, 127.3, 117.9, 45.9, 21.7 ppm.

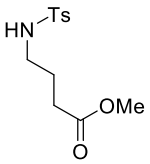
4-Methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (CAS: 55022-46-3)[5]



Chemical Formula: $C_{10}H_{11}NO_2S$
Molecular Weight: 209,2630

Following the **General Procedure A**, the title compound was isolated as a beige solid (2.69 g, 12.85 mmol) after recrystallisation in hot petrol ether and dichloromethane, followed by filtration of the residue over a silica plug washing with ethyl acetate. Yield 67%. – R_f = 0.37 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3265, 3023, 2935, 2860, 1596, 1493, 1436, 1291, 1157, 1062, 870, 696 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.97 – 7.59 (m, 2H), 7.44 – 7.16 (m, 2H), 4.60 (t, J = 5.9 Hz, 1H), 3.83 (dd, J = 6.1, 2.5 Hz, 2H), 2.43 (s, 3H), 2.11 (t, J = 2.5 Hz, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.0, 136.6, 129.9, 127.5, 78.0, 73.2, 33.0, 21.7 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 232.04 (100) $[M+Na]^+$.

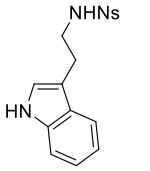
Methyl 4-((4-methylphenyl)sulfonamido)butanoate (CAS: 118429-43-9)[6]



Chemical Formula: $C_{12}H_{17}NO_4S$
Molecular Weight: 271,3310

N-Tosylpyrrolidin-2-one (19.8 g, 82.75 mmol, 1.0 eq.) was added portionwise to a stirred solution of NaOMe (5.37 g, 99.30 mmol, 1.2 eq.) in MeOH (160 mL) at room temperature. Next, the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc (250 mL). This organic phase was washed with H_2O (3 × 100 mL). The combined aqueous phases were back-extracted with EtOAc (100 mL) and the combined organic phases were washed with brine (150 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure to yield a colourless solid (19.45 g, 71.68 mmol). Yield 87%. – R_f = 0.30 (cyclohexane/EtOAc 6:4). – FTIR-ATR (neat) 3270, 2959, 2892, 2848, 1720, 1595, 1429, 1330, 1268, 1202, 1158, 1080, 1050, 977, 869, 819, 673 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.77 – 7.70 (m, 2H), 7.30 (d, J = 8.0 Hz, 2H), 4.68 (t, J = 6.3 Hz, 1H), 3.65 (s, 3H), 2.99 (q, J = 6.6 Hz, 2H), 2.42 (s, 3H), 2.35 (t, J = 7.1 Hz, 2H), 1.79 (quint, J = 6.9 Hz, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.7, 143.6, 136.9, 129.9, 127.2, 51.9, 42.7, 31.1, 24.8, 21.7 ppm.

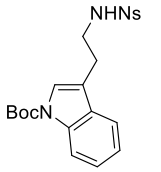
N-(2-(1*H*-Indol-3-yl)ethyl)-4-nitrobenzenesulfonamide (CAS: 33284-09-2)[7]



Chemical Formula: $C_{16}H_{15}N_3O_4S$
Molecular Weight: 345,3730

Following the **General Procedure A**, the title compound was obtained as a yellow solid (4.30 g, 12.45 mmol) and used without further purification. R_f = 0.75 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3410, 3242, 3109, 3086, 3071, 3049, 3039, 2986, 2958, 2909, 2895, 2856, 1610, 1529, 1436, 1346, 1305, 1149, 1069, 912, 854, 739 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.14 – 8.07 (m, 2H), 8.01 (br s, 1H), 7.80 – 7.73 (m, 2H), 7.35 – 7.29 (m, 2H), 7.21 – 7.13 (m, 1H), 7.06 – 6.96 (m, 2H), 4.45 (t, J = 5.8 Hz, 1H), 3.36 (q, J = 6.2 Hz, 2H), 2.97 (t, J = 6.3 Hz, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 149.8, 145.4, 136.5, 128.0, 126.6, 124.1, 122.7(8), 122.7(6), 119.9, 118.4, 111.5, 111.3, 43.1, 25.6 ppm.

tert-Butyl 3-(2-((4-nitrophenyl)sulfonamido)ethyl)-1*H*-indole-1-carboxylate (CAS: 1627199-33-0)[8]



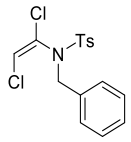
Chemical Formula: $C_{21}H_{23}N_3O_6S$
Molecular Weight: 445,4900

The title compound was prepared as described in the literature[8] and was isolated as a yellow foam (1.28 g, 2.87 mmol) after column chromatography (EtOAc/CH_2Cl_2/cyclohexane 1:1:8) on only a fraction of the crude mixture. R_f = 0.48 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3396, 3103, 3068, 3039, 2977, 2934, 2909, 2852, 1711, 1607, 1531, 1457, 1343, 1293, 1140, 1082, 1010, 912, 842, 736, 642 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.28 – 8.22 (m, 2H), 8.02 (br s, 1H), 7.99 – 7.94 (m, 2H), 7.69 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 7.13 (t, J = 7.4 Hz, 1H), 7.06 (d, J = 2.4 Hz, 1H), 4.17 – 4.09 (m, 2H), 3.27 – 3.19 (m, 2H), 1.32 (s, 9H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 150.7, 150.2, 145.7, 136.3, 129.4, 127.5, 123.9, 122.7, 122.5, 119.8, 118.9, 112.2, 111.3, 85.2, 48.2, 27.9, 26.2 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 484.09 (50) $[M+K]^+$.

1,2-Dichloroenamides

1,2-Dichloroenamides were prepared following a reported procedure.[9]

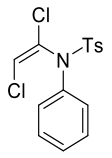
(*E*)-*N*-Benzyl-*N*-(1,2-dichlorovinyl)-4-methylbenzenesulfonamide (CAS: 1637778-11-0)



Chemical Formula: $C_{16}H_{15}Cl_2NO_2S$
Molecular Weight: 356,2610

Following the **General Procedure B**, the title compound was obtained as a colourless solid (6.52 g, 18.31 mmol) and used without further purification. Yield 94%. – R_f = 0.73 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3079, 3035, 2973, 2922, 2876, 1595, 1496, 1457, 1356, 1168, 1085, 1029, 952, 814, 693 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.91 – 7.81 (m, 2H), 7.41 – 7.27 (m, 7H), 6.27 (s, 1H), 4.40 (br s, 2H), 2.47 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.9, 135.2, 133.5, 129.9, 129.5(2), 129.5(0), 128.6(1), 128.6(0), 128.5, 121.9, 51.9, 21.9 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 393.98 (100) $[M+K]^+$.

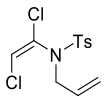
(*E*)-*N*-(1,2-dichlorovinyl)-4-methyl-*N*-phenylbenzenesulfonamide (CAS: 1198340-49-6)



Chemical Formula: $C_{15}H_{13}Cl_2NO_2S$
Molecular Weight: 342,2340

Following the **General Procedure B**, the title compound was isolated as a colourless solid (1.16 g, 3.38 mmol) after column chromatography over silica gel (cyclohexane/EtOAc). Yield 83%. – R_f = 0.42 (cyclohexane/EtOAc 9:1). – FTIR-ATR (neat) 3076, 3034, 2954, 2920, 2853, 1592, 1487, 1360, 1288, 1163, 1087, 944, 801, 698 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.68 – 7.61 (m, 2H), 7.40 – 7.29 (m, 5H), 7.27 – 7.21 (m, 2H), 6.46 (s, 1H), 2.43 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.7, 137.8, 135.6, 130.7, 129.5(4), 129.5(0), 129.2, 128.9, 128.7, 120.7, 21.8 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 379.96 (100) $[M+K]^+$.

(*E*)-*N*-Allyl-*N*-(1,2-dichlorovinyl)-4-methylbenzenesulfonamide



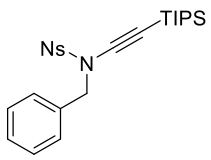
Chemical Formula: $C_{12}H_{13}Cl_2NO_2S$
Molecular Weight: 306,2010

Following the **General Procedure B**, the title compound was obtained as a light brown waxy solid (2.76 g, 9.01 mmol) and used without further purification. Yield 95%. – R_f = 0.65 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3088, 2983, 2923, 2870, 1597, 1495, 1446, 1358, 1291, 1163, 1088, 1041, 936, 804, 661 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.80 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 6.46 (s, 1H), 5.76 (ddt, J = 16.9, 10.1, 6.8 Hz, 1H), 5.31 – 5.15 (m, 2H), 3.87 (br s, 2H), 2.44 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.8, 135.2, 130.8, 129.8, 129.6, 128.5, 121.7, 120.8, 51.1, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{12}H_{13}Cl_2NNaO_2S$ 327.9936, found 327.9925 $[M+Na]^+$.

TIPS-protected ynamides

N-Benzyl-4-nitro-*N*-((triisopropylsilyl)ethynyl)benzenesulfonamide

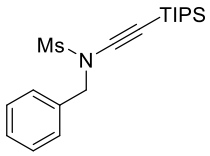
(CAS: 945536-25-4)[10]



Chemical Formula: $C_{24}H_{32}N_2O_4SSi$
Molecular Weight: 472,6750

Following the **General Procedure C** using K_2CO_3 and Cu^I-USY at 90 °C for two days, the title compound was isolated as a colourless solid (1.16 g, 2.45 mmol). Yield 80%. – R_f = 0.73 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3107, 2954, 2939, 2890, 2863, 2165, 1608, 1530, 1462, 1378, 1348, 1311, 1173, 1087, 1011, 941, 857, 781, 673 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.28 – 8.22 (m, 2H), 7.96 – 7.89 (m, 2H), 7.31 – 7.21 (m, 5H), 4.58 (br s, 2H), 0.96 (br s, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 150.5, 143.1, 133.8, 129.1, 129.0, 128.8, 128.7, 124.1, 95.5, 71.4, 56.3, 18.6, 11.3 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{24}H_{32}N_2NaO_4SSi$ 495.1744, found 495.1773 $[M+Na]^+$.

N-Benzyl-*N*-((triisopropylsilyl)ethynyl)methanesulfonamide (CAS: 1160723-59-0)[11]

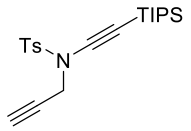


Chemical Formula: $C_{19}H_{31}NO_2SSi$
Molecular Weight: 365,6070

Following the **General Procedure C** using K_2CO_3 and Cu^I-USY at 60 °C for 18 h, the title compound was isolated as a yellow oil (1.72 g, 4.70 mmol). Yield 95%. – R_f = 0.80 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3091, 3066, 3034, 2942, 2891, 2864, 2726, 2162, 1459, 1360, 1162, 1016, 961, 882, 781, 675 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.47 – 7.42 (m, 2H), 7.39 – 7.34 (m, 3H), 4.61 (s, 2H), 2.87 (s, 3H), 1.02 (s, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 134.5, 129.2, 128.9, 128.8(6), 96.2, 71.0, 55.8, 38.6, 18.7, 11.4 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 405.15 (80) $[M+K]^+$.

4-Methyl-*N*-(prop-2-yn-1-yl)-*N*-((triisopropylsilyl)ethynyl)benzenesulfonamide

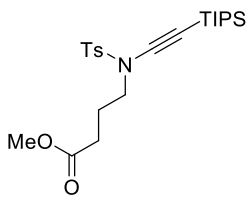
(CAS: 898827-45-7)[12]



Chemical Formula: $C_{21}H_{31}NO_2SSi$
Molecular Weight: 389,6290

Following the **General Procedure C** using K_2CO_3 and Cu^I-USY at 65 °C for 21 h, the title compound was isolated as an orange oil (636 mg, 1.63 mmol). Yield 80%. – R_f = 0.70 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3277, 2943, 2865, 2168, 1598, 1463, 1537, 1259, 1163, 1088, 1031, 881, 729, 663 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.26 (d, *J* = 2.6 Hz, 2H), 2.45 (s, 3H), 2.16 (t, *J* = 2.5 Hz, 1H), 1.03 (s, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.0, 134.1, 129.6, 128.4, 95.4, 75.9, 74.7, 70.5, 41.8, 21.8, 18.7, 11.4 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 412.17 (100) $[M+Na]^+$.

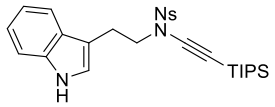
Methyl 4-((4-methyl-*N*-((triisopropylsilyl)ethynyl)phenyl)sulfonamido)butanoate



Chemical Formula: $C_{23}H_{37}NO_4SSi$
Molecular Weight: 451,6970

Following the **General Procedure C** using K_2CO_3 and $CuSO_4•5H_2O$ at 65 °C for 18 h, the title compound was isolated as a pale-yellow viscous oil (201 mg, 445 µmol). Yield 89%. – R_f = 0.44 (cyclohexane/EtOAc 8:2). – FTIR-ATR (neat) 2942, 2892, 2863, 2158, 1743, 1596, 1435, 1365, 1167, 1089, 1002, 945, 881, 816, 658 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.82 – 7.76 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.67 (s, 3H), 3.38 (t, *J* = 6.6 Hz, 2H), 2.44 (s, 3H), 2.41 (t, *J* = 7.3 Hz, 2H), 1.98 (quint, *J* = 7.0 Hz, 2H), 1.04 (s, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.2, 144.8, 134.5, 129.8, 127.8, 96.0, 69.8, 51.8, 50.6, 30.5, 23.1, 21.8, 18.7, 11.5 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{23}H_{37}NNaO_4SSi$ 474.2105, found 474.2112 $[M+Na]^+$.

N-(2-(1*H*-Indol-3-yl)ethyl)-4-nitro-*N*-((triisopropylsilyl)ethynyl)benzenesulfonamide

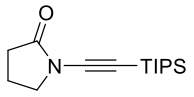


Chemical Formula: $C_{27}H_{35}N_3O_4SSi$
Molecular Weight: 525,7390

Following the **General Procedure C** using K_2CO_3 and $CuSO_4•5H_2O$ at 85 – 95 °C for 13 days, the title compound was isolated as a brown resin (118 mg, 225 µmol) from *tert*-butyl 3-(2-((4-nitrophenyl)sulfonamido)ethyl)-1*H*-indole-1-carboxylate.* Yield 45%. – R_f = 0.61 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3291, 3104, 2941, 2890, 2863, 2169, 1650, 1529, 1458, 1159, 919, 792, 735 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.14 – 8.09 (m, 2H), 7.82 – 7.77 (m, 2H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.15 – 7.10 (m, 1H), 7.00 (s, 1H), 4.67 (s, 1H), 3.37 (q, *J* = 5.6 Hz, 2H), 2.91 (t, *J* = 6.4 Hz, 2H), 1.21 – 1.15 (m, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 149.8, 145.4, 138.7, 128.0, 127.0, 126.6, 124.3, 124.1, 122.1, 118.8, 114.0, 111.8, 93.9, 69.5, 42.8, 25.6, 18.9, 11.5 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{35}KN_3O_4SSi$ 564.1749, found 564.1733 $[M+K]^+$.

*N.B.: Boc-deprotection occurred under the above stated reaction conditions and was not performed as an additional step.

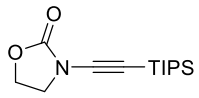
1-((Triisopropylsilyl)ethynyl)pyrrolidin-2-one (CAS: 1007597-70-7)[13]



Chemical Formula: $C_{15}H_{27}NOSi$
Molecular Weight: 265,4720

Following the **General Procedure C** using K_2CO_3 and Cu^I-USY at 105 °C, the title compound was isolated as a colourless solid (138 mg, 520 µmol). Yield 43%. – R_f = 0.43 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 2940, 2892, 2863, 2725, 2168, 1719, 1460, 1381, 1460, 1381, 1191, 882, 672, 501 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 3.75 – 3.66 (m, 2H), 2.46 – 2.38 (m, 2H), 2.18 – 2.05 (m, 2H), 1.12 – 1.06 (m, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 175.8, 94.7, 70.8, 50.1, 29.7, 18.8, 18.6, 11.3 ppm – MS (ESI-TOF, positive mode) m/z (rel intensity) 288.18 (100) $[M+Na]^+$.

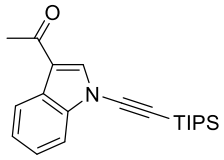
3-((Triisopropylsilyl)ethynyl)oxazolidin-2-one (CAS: 1007597-70-7)[13]



Chemical Formula: $C_{14}H_{25}NO_2Si$
Molecular Weight: 267,4440

Following the **General Procedure C** using K_2CO_3 and Cu^I-USY at 110 °C for 21 h, the title compound was isolated as a colourless solid (110 mg, 411 µmol). Yield 82%. – R_f = 0.43 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 2960, 2942, 2889, 2864, 2177, 1758, 1478, 1463, 1397, 1296, 1197, 1104, 1034, 992, 881, 809, 751, 707 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 4.47 – 4.39 (m, 2H), 3.98 – 3.90 (m, 2H), 1.08 (s, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 155.9, 93.1, 70.2, 62.9, 47.1, 18.7, 11.3 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 290.15 (60) $[M+Na]^+$.

1-(1-((Triisopropylsilyl)ethynyl)-1*H*-indol-3-yl)ethan-1-one (CAS: 1007597-74-1)[13]

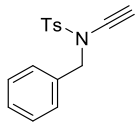


Chemical Formula: $C_{21}H_{29}NOSi$
Molecular Weight: 339,5540

Following the **General Procedure C** using K_2CO_3 and Cu^I-USY at 90 °C for two days, the title compound was isolated as an orange solid (932 mg, 2.75 mmol). Yield 87%. – R_f = 0.53 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3116, 3055, 2942, 2891, 2864, 2379, 2177, 1738, 1633, 1613, 1533, 1456, 1205, 882, 670 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.36 (d, *J* = 7.7 Hz, 1H), 7.87 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.34 (m, 2H), 2.56 (s, 3H), 1.20 – 1.14 (m, 21H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 193.1, 138.8, 135.5, 125.2, 125.1, 124.4, 123.1, 119.6, 111.5, 92.8, 71.2, 27.9, 18.8, 11.4 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 362.19 (100) $[M+Na]^+$.

Terminal Ynamides

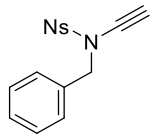
N-Benzyl-*N*-ethynyl-4-methylbenzenesulfonamide (CAS: 205885-39-8)[14]



Chemical Formula: $C_{16}H_{15}NO_2S$
Molecular Weight: 285,3610

Following the **General Procedure D**, the title compound **3** was isolated as a colourless solid (4.0 g, 14.02 mmol). Yield 93%. – R_f = 0.55 (cyclohexane/EtOAc 9:1). – FTIR-ATR (neat) 3275, 3062, 2963, 2929, 2132, 1596, 1495, 1431, 1356, 1164, 1087, 1026, 930, 798, 689 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$) δ = 7.78 – 7.74 (m, 2H), 7.34 – 7.27 (m, 7H), 4.50 (s, 2H), 2.67 (s, 1H), 2.45 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.9, 134.8, 134.4, 129.9, 128.8, 128.7, 128.5, 127.9, 76.4, 59.8, 55.4, 21.8 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 324.05 (100) $[M+K]^+$, 155.02 (25) $[C_7H_7O_2S]^+$.

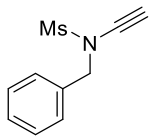
N-Benzyl-*N*-ethynyl-4-nitrobenzenesulfonamide (CAS: 329354-15-6)[10]



Chemical Formula: $C_{15}H_{12}N_2O_4S$
Molecular Weight: 316,3310

Following the **General Procedure E**, the title compound was isolated as an off-white solid (49 mg, 155 µmol). Yield 84%. – R_f = 0.90 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3279, 3126, 3106, 3068, 3031, 2998, 2956, 2923, 2854, 2133, 1524, 1344, 1303, 1175, 1087, 1024, 852, 686 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.32 – 8.26 (m, 2H), 7.98 – 7.91 (m, 2H), 7.34 – 7.27 (m, 5H), 4.60 (s, 2H), 2.78 (s, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 150.6, 143.1, 133.7, 129.0, 128.9(6), 128.9(0), 128.8, 124.3, 75.6, 60.5, 56.1 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 317.06 (30) $[M+H]^+$.

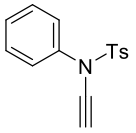
N-Benzyl-*N*-ethynylmethanesulfonamide (CAS: 737004-80-7)[15]



Chemical Formula: $C_{10}H_{11}NO_2S$
Molecular Weight: 209,2630

Following the **General Procedure E**, the title compound was isolated as an off-white solid (85 mg, 406 µmol). Yield 81%. – R_f = 0.44 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3273, 3065, 3033, 3015, 2930, 2852, 2494, 2293, 2133, 2063, 1496, 1456, 1341, 1154, 1020, 924, 784, 698 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.47 – 7.43 (m, 2H), 7.42 – 7.34 (m, 3H), 4.63 (s, 2H), 2.89 (s, 3H), 2.84 (s, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 134.4, 129.0, 128.9(9), 128.9(6), 76.0, 60.3, 55.5, 39.0 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 232.04 (100) $[M+Na]^+$.

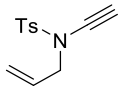
N-Ethynyl-4-methyl-*N*-phenylbenzenesulfonamide (CAS: 312329-87-6)[9]



Chemical Formula: $C_{15}H_{13}NO_2S$
Molecular Weight: 271,3340

Following the **General Procedure D**, the title compound was isolated as a colourless solid (554 mg, 2.04 mmol) after recrystallization in refluxed Et_2O. Yield 68%. – R_f = 0.54 (cyclohexane/EtOAc 8:2). – FTIR-ATR (neat) 3293, 3065, 3042, 2955, 2924, 2130, 1697, 1595, 1556, 1488, 1371, 1293, 1173, 1089, 925, 813, 761, 673 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.62 – 7.57 (m, 2H), 7.37 – 7.24 (m, 7H), 2.85 (s, 1H), 2.46 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.2, 138.4, 133.0, 129.7, 129.3, 128.6, 128.4, 126.4, 76.7, 59.0, 21.9 ppm.

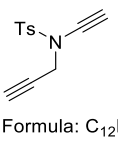
N-Allyl-*N*-ethynyl-4-methylbenzenesulfonamide (CAS: 312329-85-4)[10]



Chemical Formula: $C_{12}H_{13}NO_2S$
Molecular Weight: 235,3010

Following the **General Procedure D**, the title compound was isolated as pale-yellow solid (167 mg, 710 µmol). Yield 71%. – R_f = 0.60 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3270, 2925, 2137, 1647, 1594, 1490, 1429, 1352, 1294, 1159, 1118, 1086, 1032, 991, 921, 899, 814, 739, 709, 659 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.84 – 7.78 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.72 (ddt, *J* = 16.6, 10.1, 6.3 Hz, 1H), 5.29 – 5.19 (m, 2H), 3.96 (dt, *J* = 6.4, 1.3 Hz, 2H), 2.73 (s, 1H), 2.46 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.0, 134.8, 130.7, 129.9, 127.9, 120.3, 76.0, 59.4, 54.1, 21.8 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 258.05 (20) $[M+Na]^+$.

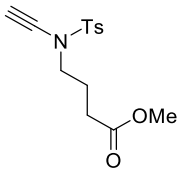
N-Ethynyl-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (CAS: 2445280-24-8)[16]



Chemical Formula: $C_{12}H_{11}NO_2S$
Molecular Weight: 233,2850

Following the **General Procedure E**, the title compound was isolated as yellow oil (93 mg, 399 µmol). Yield 52%. – R_f = 0.70 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3286, 2985, 2921, 2853, 2168, 1594, 1426, 1534, 1160, 1045, 599, 812, 705, 654 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.87 – 7.83 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.27 (d, *J* = 2.5 Hz, 2H), 2.80 (s, 1H), 2.46 (s, 3H), 2.20 (t, *J* = 2.5 Hz, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.3, 134.1, 129.8, 128.3, 75.6, 75.3, 74.8, 60.0, 41.5, 21.9 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{12}H_{11}NO_2SNa$ 256.0403, found 256.0411 $[M+Na]^+$.

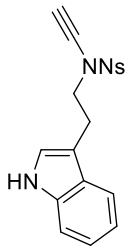
Methyl 4-((*N*-ethynyl-4-methylphenyl)sulfonamido)butanoate



Chemical Formula: $C_{14}H_{17}NO_4S$
Molecular Weight: 295,3530

Following the **General Procedure E**, the title compound was isolated as an off-white solid (119 mg, 263 µmol). Yield 62%. – R_f = 0.43 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3264, 3054, 3000, 2955, 2925, 2852, 2135, 1738, 1598, 1438, 1355, 1167, 1099, 968, 808, 708, 652 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.83 – 7.75 (m, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 3.68 (s, 3H), 3.37 (t, *J* = 6.8 Hz, 2H), 2.74 (s, 1H), 2.45 (s, 3H), 2.40 (t, *J* = 7.3 Hz, 2H), 1.98 (quint, *J* = 7.0 Hz, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.2, 145.0, 134.5, 130.0, 127.8, 75.8, 59.5, 51.9, 50.5, 30.4, 23.0, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{14}H_{17}NNaO_4S$ 318.0770, found 318.0783 $[M+Na]^+$.

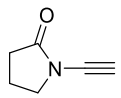
N-(2-(1*H*-Indol-3-yl)ethyl)-*N*-ethynyl-4-nitrobenzenesulfonamide



Chemical Formula: $C_{18}H_{15}N_3O_4S$
Molecular Weight: 369,40

Following the **General Procedure E**, the title compound was isolated as an orange sticky solid (58 mg, 157 µmol). Yield 87%. – R_f = 0.38 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3273, 3104, 2937, 2890, 2855, 2147, 1607, 1523, 1457, 1346, 1311, 1226, 1152, 1090, 1011, 914, 851, 735, 682 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.11 – 8.04 (m, 2H), 7.76 – 7.69 (m, 2H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.90 (s, 1H), 4.94 – 4.35 (m, 1H), 3.38 (t, *J* = 6.3 Hz, 2H), 3.12 (s, 1H), 2.88 (t, *J* = 6.3 Hz, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 149.8, 145.5, 138.6, 127.9, 126.8, 126.7, 124.4, 124.1, 122.2, 118.9, 114.5, 111.7, 73.7, 59.5, 42.9, 25.5 ppm.

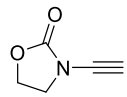
1-Ethynylpyrrolidin-2-one (CAS: 1312921-13-3)[17]



Chemical Formula: C_6H_7NO
Molecular Weight: 109,1280

Following the **General Procedure E**, the title compound was isolated as a colourless solid (36 mg, 330 µmol). Yield 27%. – R_f = 0.19 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3399, 3216, 2962, 2924, 2901, 2854, 2771, 2136, 1704, 1456, 1261, 1193, 1022, 929, 802, 635 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.71 (t, *J* = 7.2 Hz, 2H), 2.92 (s, 1H), 2.45 (t, *J* = 8.1 Hz, 2H), 2.19 – 2.10 (m, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 176.7, 74.0, 61.0, 49.6, 29.6, 19.0 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 132.04 (50) $[M+Na]^+$.

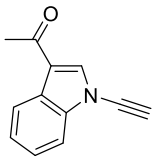
3-Ethynyloxazolidin-2-one (CAS: 660866-29-5)[18]



Chemical Formula: $C_5H_5NO_2$
Molecular Weight: 111,1000

Following the **General Procedure E**, the title compound was isolated as an orange solid (37 mg, 333 µmol). Yield 88%. – R_f = 0.15 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3281, 2989, 2920, 2865, 2152, 1755, 1478, 1401, 1272, 1089, 1028, 970, 748, 688, 632 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.49 – 4.42 (m, 2H), 3.98 – 3.90 (m, 2H), 2.86 (s, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 156.3, 72.7, 63.2 (CH_2), 60.0 (CH), 46.6 ppm. – MS (ESI-TOF, positive mode) *m/z* (rel intensity) 134.02 (100) $[M+Na]^+$.

1-(1-Ethynyl-1*H*-indol-3-yl)ethan-1-one (CAS: 1574275-58-3)



Chemical Formula: $C_{12}H_9NO$
Molecular Weight: 183,2100

Following the **General Procedure E**, the title compound was isolated as an off-white solid (110 mg, 600 µmol). Yield 60%. – R_f = 0.48 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3308, 3105, 3049, 2924, 2853, 2470, 1735, 1642, 1453, 1218, 930, 738 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.37 (d, *J* = 7.7 Hz, 1H), 7.85 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.33 (m, 2H), 3.20 (s, 1H), 2.54 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 193.0, 138.6, 135.2, 125.2, 125.0, 124.5, 123.1, 120.0, 111.3, 72.8, 60.5, 27.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{12}H_{10}NO$ 184.0757, found 184.0776 $[M+H]^+$.

γ-Amino-Ynamides

N-Benzyl-4-methyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**4a**)

Following the **General Procedure F**, the title compound **4a** was isolated as a colourless resin (196 mg, 441 µmol). Yield 88%. – R_f = 0.30 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3062, 3031, 2965, 2930, 2873, 2816, 2239, 1597, 1494, 1366, 1169, 1090, 1027, 877, 814, 719, 700 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.4 Hz, 2H), 7.27 – 7.15 (m, 12H), 4.67 (s, 1H), 4.52 (d, *J* = 13.7 Hz, 1H), 4.46 (d, *J* = 13.7 Hz, 1H), 2.39 (s, 3H), 2.38 – 2.22 (m, 4H), 1.62 – 1.54 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.7, 139.5, 134.6(1), 134.6(0), 129.8, 129.0, 128.6, 128.4, 128.2, 128.1, 127.9, 127.4, 79.9, 68.0, 58.4, 55.6, 49.6, 23.4, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{29}N_2O_2S$ 445.1944, found 445.1929 $[M+H]^+$.

N-Benzyl-*N*-(3-(4-chlorophenyl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4b**)

Following the **General Procedure F**, the title compound **4b** was isolated as a pale-yellow viscous oil (206 mg, 430 µmol). Yield 86%. – R_f = 0.48 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 2964, 2911, 2874, 2821, 2241, 1597, 1485, 1443, 1368, 1184, 1168, 1086, 1016, 893, 811, 735, 693 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.4 Hz, 2H), 7.35 – 7.26 (m, 7H), 7.19 (s, 4H), 4.69 (s, 1H), 4.56 (d, *J* = 13.7 Hz, 1H), 4.49 (d, *J* = 13.6 Hz, 1H), 2.45 (s, 3H), 2.40 – 2.23 (m, 4H), 1.68 – 1.56 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.8, 138.2, 134.6, 134.5, 133.1, 129.9, 129.5, 129.1, 128.7, 128.5, 128.2, 127.9, 80.2, 67.6, 57.7, 55.5, 49.5, 23.5, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{28}ClN_2O_2S$ 479.1555, found 479.1562 $[M+H]^+$.

N-Benzyl-*N*-(3-(4-methoxyphenyl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4c**)

Following the **General Procedure F**, the title compound **4c** was isolated as an orange viscous oil (209 mg, 440 µmol). Yield 88%. – R_f = 0.19 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3063, 3032, 2960, 2930, 2873, 2833, 2814, 2237, 1610, 1509, 1456, 1362, 1302, 1244, 1166, 1089, 1029, 874, 837, 812, 717, 695 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.79 – 7.73 (m, 2H), 7.33 – 7.27 (m, 7H), 7.22 – 7.16 (m, 2H), 6.80 – 6.74 (m, 2H), 4.65 (s, 1H), 4.55 (d, *J* = 13.7 Hz, 1H), 4.49 (d, *J* = 13.7 Hz, 1H), 3.79 (s, 3H), 2.44 (s, 3H), 2.41 – 2.25 (m, 4H), 1.67 – 1.55 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 158.9, 144.7, 134.7(3), 134.7(0), 131.9, 129.8, 129.3, 129.1, 128.7, 128.4, 128.0, 113.5, 79.7, 68.4, 57.8, 55.6, 55.4, 49.6, 23.5,

21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{28}H_{31}N_2O_3S$ 475.2050, found 475.2072 $[M+H]^+$.

N-Benzyl-*N*-(3-(2-hydroxyphenyl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4d**)

Following the **General Procedure F**, the title compound **4d** was isolated as a highly viscous red oil (195 mg, 423 µmol). Yield 85%. – R_f = 0.35 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3063, 3032, 2962, 2929, 2875, 2849, 2243, 1591, 1457, 1364, 1246, 1166, 1090, 1025, 881, 812, 755, 695 cm^{-1}. – ^1H NMR (500 MHz, CD_3CN) δ = 7.84 – 7.80 (m, 2H), 7.46 – 7.42 (m, 2H), 7.38 – 7.30 (m, 5H), 7.14 (tdd, *J* = 8.2, 1.7, 0.7 Hz, 1H), 6.99 – 6.93 (m, 1H), 6.71 – 6.66 (m, 2H), 5.02 (s, 1H), 4.63 (d, *J* = 13.9 Hz, 1H), 4.55 (d, *J* = 13.8 Hz, 1H), 2.50 – 2.44 (m, 5H), 2.35 – 2.28 (m, 2H), 1.69 – 1.59 (m, 4H) ppm. – ^{13}C NMR (126 MHz, CD_3CN) δ = 158.5, 146.6, 135.7, 135.1, 131.0, 130.1, 130.0, 129.6, 129.4, 128.7, 128.6, 123.3, 119.6, 116.7, 82.3, 66.3, 57.2, 56.2, 49.3, 24.3, 21.6 ppm. – HRMS (ESI-TOF, positive mode): m/z: calcd for $C_{27}H_{28}N_2NaO_3S$ 483.1713, found 483.1710 $[M+Na]^+$.

N-Benzyl-4-methyl-*N*-(3-(pyridin-3-yl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**4f**)

Following the **General Procedure F**, the title compound **4f** was isolated as a pale-red solid (186 mg, 417 µmol). Yield 83%. – R_f = 0.20 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3063, 3051, 3031, 2962, 2928, 2874, 2810, 2239, 1595, 1577, 1495, 1421, 1362, 1292, 1166, 1088, 979, 812, 766, 698 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 2.3 Hz, 1H), 8.48 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.80 – 7.75 (m, 2H), 7.57 (dt, *J* = 8.0, 2.1 Hz, 1H), 7.34 – 7.29 (m, 7H), 7.17 (ddd, *J* = 7.8, 4.8, 0.9 Hz, 1H), 4.77 (s, 1H), 4.56 (d, *J* = 13.7 Hz, 1H), 4.51 (d, *J* = 13.6 Hz, 1H), 2.46 (s, 3H), 2.43 – 2.24 (m, 4H), 1.68 – 1.57 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 149.8, 148.7, 144.9, 135.6, 135.2, 134.6, 134.4, 129.9, 129.0, 128.7, 128.5, 127.8, 123.1, 80.5, 66.9, 56.2, 55.5, 49.5, 23.5, 21.7 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{26}H_{28}N_3O_2S$ 446.1897, found 446.1897 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(3-(pyrrolidin-1-yl)-3-(thiophen-2-yl)prop-1-yn-1-yl)benzenesulfonamide (**4g**)

Following the **General Procedure F**, the title compound **4g** was isolated as a pale-red solid (218 mg, 484 µmol). Yield 97%. – R_f = 0.43 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 2961, 2923, 2874, 2856, 2810, 2237, 1596, 1494, 1455, 1360, 1286, 1260, 1230, 1168, 1128, 1087, 1041, 978, 877, 754, 655 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.77 – 7.71 (m, 2H), 7.29 – 7.24 (m, 7H), 7.15 (dd, *J* = 4.9, 1.3 Hz, 1H), 6.84 – 6.76 (m, 2H), 4.94 (d, *J* = 1.2 Hz, 1H), 4.52 (d, *J* = 13.7 Hz, 1H), 4.46 (d, *J* = 13.7 Hz, 1H), 2.41 (s, 3H), 2.40 – 2.31 (m, 4H), 1.64 – 1.53 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.8, 144.6, 134.8, 134.6, 129.9, 129.1, 128.7, 128.4, 128.0, 126.2, 125.4, 125.2, 79.4, 67.5, 55.6, 54.0, 49.3, 23.6, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{25}H_{27}N_2O_2S_2$ 451.1508, found 451.1507 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(3-ferrocenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**4h**)

Following the **General Procedure F**, the title compound **4h** was isolated as an orange solid (116 mg, 210µmol). Yield 84%. – R_f = 0.14 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3104, 3062, 3038, 2965, 2925, 2869, 2814, 2251, 1596, 1496, 1455, 1356, 1267, 1162, 1091, 928, 810, 756, 694 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.90 – 7.83 (m, 2H), 7.40 – 7.28 (m, 7H), 4.59 (s, 2H), 4.56 (s, 1H), 4.17 (dt, *J* = 2.6, 1.4 Hz, 1H), 4.07 (dt, *J* = 2.6, 1.4 Hz, 1H), 4.05 –

4.01 (m, 2H), 3.99 (s, 5H), 2.46 (s, 3H), 2.37 – 2.23 (m, 4H), 1.60 – 1.53 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.8, 135.1, 134.9, 129.9, 128.8(0), 128.7(7), 128.5, 127.9, 86.8, 78.0, 69.1, 68.7, 68.4, 68.2, 68.1, 67.5, 55.7, 54.4, 49.2, 23.3, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{31}H_{32}FeN_2O_2S$ 552.1529, found 552.1508 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(3-(pyrrolidin-1-yl)non-1-yn-1-yl)benzenesulfonamide (**4i**)

Following the **General Procedure F**, the title compound **4i** was isolated as a yellow viscous oil (90 mg, 199µmol). Yield 80%. – R_f = 0.10 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3064, 3032, 2954, 2926, 2857, 2816, 2240, 1597, 1495, 1366, 1292, 1167, 1090, 1025, 812, 697 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.79 – 7.73 (m, 2H), 7.34 – 7.27 (m, 7H), 4.52 (d, *J* = 13.7 Hz, 1H), 4.43 (d, *J* = 13.6 Hz, 1H), 3.46 (dd, *J* = 9.9, 5.0 Hz, 1H), 2.45 (s, 3H), 2.41 – 2.33 (m, 4H), 1.65 – 1.58 (m, 4H), 1.57 – 1.35 (m, 2H), 1.29 – 1.19 (m, 8H), 0.88 (t, *J* = 7.1 Hz, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.6, 134.7, 129.7, 129.0, 128.5, 128.3, 127.9, 78.0, 69.5, 55.6, 54.6, 49.3, 35.3, 31.9, 29.2, 26.7, 23.4, 22.8, 21.8, 14.3 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{37}N_2O_2S$ 453.2570, found 453.2572 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(4-methyl-3-(pyrrolidin-1-yl)pent-1-yn-1-yl)benzenesulfonamide (**4j**)

Following the **General Procedure F**, the title compound **4j** was isolated as a colourless solid (83 mg, 202 µmol). Yield 81%. – R_f = 0.20 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3061, 3032, 2962, 2930, 2905, 2870, 2835, 2796, 2241, 1596, 1495, 1358, 1293, 1211, 1166, 1044, 996, 861, 728, 694 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.79 – 7.74 (m, 2H), 7.30 (m, 7H), 4.52 (d, *J* = 13.6 Hz, 1H), 4.43 (d, *J* = 13.7 Hz, 1H), 3.03 (d, *J* = 8.4 Hz, 1H), 2.45 (s, 3H), 2.39 – 2.26 (m, 4H), 1.68 – 1.55 (m, 5H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.6, 134.7(6), 134.7(5), 129.7, 129.0, 128.5, 128.3, 127.9, 78.0, 69.0, 61.9, 55.6, 49.8, 32.1, 23.5, 21.8, 20.2, 19.7 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{24}H_{31}N_2O_2S$ 411.2101, found 411.2102 $[M+H]^+$.

N-Benzyl-*N*-(4,4-dimethyl-3-(pyrrolidin-1-yl)pent-1-yn-1-yl)-4-methylbenzenesulfonamide (**4k**)

Following the **General Procedure F**, the title compound **4k** was isolated as a pale-yellow solid (85 mg, 200 µmol). Yield 80%. – R_f = 0.50 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3085, 3064, 2958, 2872, 2812, 2239, 1599, 1495, 1455, 1356, 1292, 1168, 1091, 1045, 914, 812, 692 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.80 – 7.75 (m, 2H), 7.33 – 7.27 (m, 7H), 4.53 (d, *J* = 13.7 Hz, 1H), 4.45 (d, *J* = 13.7 Hz, 1H), 3.23 (s, 1H), 2.45 (s, 3H), 2.43 – 2.37 (m, 4H), 1.58 – 1.48 (m, 4H), 0.83 (s, 9H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.5, 134.8(0), 134.7(9), 129.7, 129.0, 128.6, 128.3, 127.9, 79.2, 68.0, 64.8, 55.7, 51.3, 36.0, 27.8, 24.1, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{25}H_{33}N_2O_2S$ 425.2257, found 425.2256 $[M+H]^+$.

N-Benzyl-*N*-(3-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4l**)

Following the **General Procedure F**, the title compound **4l** was isolated as a colourless oil (84 mg, 179 µmol) in a diastereomeric ratio of 9:1. Yield 70% (both diastereoisomers combined). – R_f = 0.10 (cyclohexane/EtOAc 8:2). – FTIR-ATR (neat) 3409, 3239, 3066, 3033, 2981, 2962, 2932, 2875, 2814, 2238, 1597, 1544, 1496, 1456, 1366, 1186, 1069, 844, 656 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) (major diastereomer) δ = 7.76 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.28 (m, 5H), 7.26 – 7.22 (m, 2H), 4.49 (d, *J* = 13.6 Hz, 1H), 4.44 (d, *J* = 13.6 Hz, 1H), 3.96 (ddd, *J*

= 8.6, 7.5, 6.1 Hz, 1H), 3.73 (dd, *J* = 8.5, 6.2 Hz, 1H), 3.65 (d, *J* = 8.6 Hz, 1H), 3.50 (dd, *J* = 8.4, 7.5 Hz, 1H), 2.46 (s, 3H), 2.46 – 2.38 (m, 4H), 1.68 – 1.60 (m, 4H), 1.36 (s, 3H), 1.32 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.9, 134.6, 134.4, 129.9, 129.0, 128.7, 128.6, 127.8, 110.2, 79.5, 76.6, 67.9, 65.7, 58.3, 55.4, 49.4, 25.8, 23.5, 21.8, 1.2 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{26}H_{33}N_2O_4S$ 469.2156, found 469.2131 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**4m**)

Following the **General Procedure F**, the title compound **4m** was isolated as an off-white solid (87 mg, 199 µmol). Yield 80%. – R_f = 0.26 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3029, 2955, 2929, 2854, 2825, 2233, 1597, 1495, 1447, 1361, 1258, 1122, 1045, 971, 809, 735, 694 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.80 – 7.75 (m, 2H), 7.35 – 7.26 (m, 7H), 4.48 (s, 2H), 2.46 (s, 3H), 2.45 – 2.38 (m, 4H), 1.78 – 1.71 (m, 2H), 1.64 – 1.55 (m, 4H), 1.55 – 1.43 (m, 2H), 1.38 – 1.18 (m, 5H), 1.13 – 1.01 (m, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.6, 134.7(0), 134.6(5), 129.7, 129.1, 128.5, 128.3, 127.9, 78.8, 71.3, 59.3, 55.6, 46.9, 38.0, 25.6, 23.3, 22.9, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{26}H_{33}N_2O_2S$ 437.2257, found 437.2250 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cyclopentyl)ethynyl)benzenesulfonamide (**4n**)

Following the **General Procedure F**, the title compound **4n** was isolated as a yellow solid (150 mg, 355 µmol). Yield 71%. – R_f = 0.37 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3268, 3060, 3031, 2961, 2929, 2869, 2808, 2232, 1597, 1495, 1454, 1423, 1365, 1323, 1309, 1292, 1188, 1165, 1090, 1059, 1012, 940, 912, 875, 816, 801, 781, 741, 700, 662 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.26 (m, 7H), 4.47 (s, 2H), 2.46 (s, 3H), 2.42 – 2.37 (m, 4H), 1.77 – 1.71 (m, 2H), 1.70 – 1.47 (m, 9H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.7, 134.8, 129.8, 129.3, 128.6, 128.4, 128.0, 127.5, 78.1, 72.4, 65.6, 55.7, 49.2, 40.7, 23.7, 23.4, 21.9 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{25}H_{31}N_2O_2S$ 423.2101, found 423.2112 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cycloheptyl)ethynyl)benzenesulfonamide (**4o**)

Following the **General Procedure F**, the title compound **4o** was isolated as a yellow solid (189 mg, 419 µmol). Yield 84%. – R_f = 0.54 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3104, 3062, 3038, 2965, 2925, 2869, 2814, 2251, 1596, 1496, 1455, 1356, 1267, 1162, 1129, 1091, 1025, 928, 905, 881, 756, 694 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.26 (m, 4H), 4.47 (s, 2H), 2.45 (s, 3H), 2.44 – 2.38 (m, 4H), 1.78 – 1.69 (m, 2H), 1.65 – 1.44 (m, 12H), 1.42 – 1.31 (m, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.5, 134.7(9), 134.7(6), 129.7, 129.1, 128.5, 128.3, 128.0, 77.6, 73.1, 62.5, 55.7, 47.6, 40.3, 28.1, 23.6, 22.0, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{35}N_2O_2S$ 451.2414, found 451.2431 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-((2-methyl-1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**4p**)

Following the **General Procedure F**, the title compound **4p** was isolated as a colourless viscous oil (30 mg, 68 µmol) as a mixture of both diastereoisomers in a 1:1 ratio. Yield 27%. – R_f = 0.10 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3065, 3032, 2928, 2859, 2816, 2234, 1598, 1496, 2455, 1364, 1090, 812, 657 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) (both diastereoisomers, proportion 1:1) δ = 7.78 – 7.70 (m, 4H), 7.32 – 7.22 (m, 14H), 4.49 – 4.39

(m, 4H), 2.46 – 2.37 (m, 10H), 2.36 – 2.27 (m, 4H), 1.80 – 1.33 (m, 19H), 1.30 – 1.12 (m, 7H), 1.11 – 1.02 (m, 1H), 0.86 (d, *J* = 11.7 Hz, 3H), 0.84 (d, *J* = 11.6 Hz, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.5, 144.4, 134.8(2), 134.8(0), 134.7, 129.7(1), 129.7(0), 129.0, 128.5(2), 128.5(0), 128.3, 128.2, 127.9(3), 127.9(1), 78.5, 77.9, 72.6, 72.4, 62.0, 61.3, 55.7, 55.6(6), 46.4, 46.0, 36.5, 31.5, 29.6, 23.9, 23.3, 23.1, 21.8(3), 21.8(0), 21.7(6), 19.5, 16.6, 13.0 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{35}N_2O_2S$ 451.2414, found 451.2407 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(3-methyl-3-(pyrrolidin-1-yl)hept-1-yn-1-yl)benzenesulfonamide (**4r**)

Following the **General Procedure F**, the title compound **4s** was isolated as a colourless solid (68 mg, 203 µmol). Yield 79%. – R_f = 0.12 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3065, 3032, 2955, 2935, 2870, 2816, 2235, 1597, 1495, 1455, 1364, 1306, 1166, 1089, 960, 898, 776, 697 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76 – 7.70 (m, 2H), 7.31 – 7.21 (m, 6H), 4.46 (d, *J* = 13.6 Hz, 1H), 4.42 (d, *J* = 13.5 Hz, 1H), 2.43 (s, 3H), 2.41 – 2.37 (m, 4H), 1.61 – 1.54 (m, 4H), 1.50 – 1.35 (m, 2H), 1.25 – 1.10 (m, 7H), 0.85 – 0.80 (m, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.5, 134.7, 134.6, 129.7, 129.1, 128.5, 128.3, 128.0, 72.4, 58.0, 55.6, 47.6, 41.4, 31.1, 26.6, 26.0, 23.5, 23.2, 21.8, 14.2 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{26}H_{35}N_2O_2S$ 439.2414, found 439.2436 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(3-phenyl-3-(piperidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**5a**)

Following the **General Procedure F**, the title compound **5a** was isolated as a yellow solid (214 mg, 467 µmol). Yield 93%. – R_f = 0.43 (cyclohexane/EtOAc 8:2). – FTIR-ATR (neat) 3056, 3029, 2938, 2917, 2856, 2800, 2753, 2238, 1596, 1491, 1452, 1357, 1300, 1167, 1087, 986, 811, 768, 698 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83 – 7.75 (m, 2H), 7.35 – 7.27 (m, 8H), 7.25 – 7.19 (m, 2H), 4.59 (d, J = 13.7 Hz, 1H), 4.55 (s, 1H), 4.51 (d, J = 13.7 Hz, 1H), 2.45 (s, 3H), 2.22 – 2.12 (m, 4H), 1.51 – 1.38 (m, 3H), 1.35 – 1.24 (m, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.7, 138.8, 134.7, 134.7, 129.8, 129.1, 128.7, 128.5, 128.4, 128.0, 128.0, 127.3, 80.6, 67.5, 61.9, 55.7, 31.1, 26.2, 24.4, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{28}H_{31}N_2O_2S$ 459.2101, found 459.2095 $[M+H]^+$.

N-Benzyl-4-methyl-*N*-(3-morpholino-3-phenylprop-1-yn-1-yl)benzenesulfonamide (**5b**)

Following the **General Procedure F**, the title compound **5b** was isolated as a colourless solid (98 mg, 213 µmol). Yield 85%. – R_f = 0.20 (Cy/EtOAc 7:3). – FTIR-ATR (neat) 3268, 3064, 3048, 3029, 2965, 2925, 2860, 2834, 2247, 1596, 1493, 1449, 1371, 1321, 1249, 1167, 1111, 1002, 892, 804, 740, 695 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83 – 7.73 (m, 2H), 7.34 – 7.26 (m, 9H), 7.26 – 7.22 (m, 3H), 4.59 (d, *J* = 13.7 Hz, 1H), 4.54 – 4.47 (m, 2H), 3.64 – 3.50 (m, 4H), 2.45 (s, 3H), 2.28 – 2.20 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.9, 137.9, 134.6, 134.5, 129.9, 129.1, 128.7, 128.6, 128.5, 128.2, 128.0, 127.7, 81.1, 67.1, 66.9, 61.6, 55.6, 49.4, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{28}N_2NaO_3S$ 483.1713, found 483.1705 $[M+Na]^+$.

N-Benzyl-*N*-(3-(3,4-dihydroisoquinolin-2(1*H*)-yl)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5c**)

Following the **General Procedure F**, the title compound **5c** was isolated as a yellow resin (107 mg, 211 µmol). Yield 84%. – R_f = 0.57 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3062, 3028, 2923, 2892, 2830, 2785, 2244, 1736, 1637, 1597, 1494, 1453, 1255, 1088, 1039, 985, 886, 816, 722, 656 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 8.0 Hz, 2H), 7.41

– 7.36 (m, 2H), 7.34 – 7.21 (m, 10H), 7.14 – 7.05 (m, 3H), 6.94 – 6.89 (m, 1H), 4.82 (s, 1H), 4.60 (d, *J* = 13.5 Hz, 1H), 4.52 (d, *J* = 13.4 Hz, 1H), 3.48 (d, *J* = 14.9 Hz, 1H), 3.41 (d, *J* = 14.8 Hz, 1H), 2.76 (qt, *J* = 16.0, 5.8 Hz, 2H), 2.50 – 2.40 (m, 3H), 2.39 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.8, 138.3, 135.3, 134.5, 134.4(1), 134.4(0), 129.8, 129.1, 128.6(8), 128.6(7), 128.5, 128.4, 128.1, 127.9, 127.6, 126.8, 125.9, 125.5, 81.1, 66.8, 61.2, 55.6, 51.8, 46.7, 29.6, 21.7 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{32}H_{31}N_2O_2S$ 507.2101, found 507.2076 $[M+H]^+$.

N-Benzyl-*N*-((*R*)-3-((*R*)-2-(hydroxymethyl)pyrrolidin-1-yl)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5d**)

Following the **General Procedure F**, the title compound **5d** was isolated as a pale-yellow solid (105 mg, 221 µmol) in a diastereomeric ratio of 92:8. Yield 88%. – R_f = 0.13 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3476, 3059, 3031, 2961, 2923, 2874, 2820, 2243, 1595, 1493, 1448, 1402, 1354, 1249, 1166, 1085, 1001, 882, 814, 768, 695 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) (major diastereomer) δ = 7.84 – 7.78 (m, 2H), 7.37 – 7.30 (m, 8H), 7.27 – 7.23 (m, 5H), 4.86 (s, 1H), 4.61 (d, *J* = 13.5 Hz, 1H), 4.52 (d, *J* = 13.6 Hz, 1H), 3.65 (dd, *J* = 10.9, 3.4 Hz, 1H), 3.39 (dd, *J* = 11.0, 2.3 Hz, 1H), 2.77 – 2.70 (m, 1H), 2.61 – 2.51 (m, 1H), 2.47 (s, 3H), 2.36 – 2.28 (m, 2H), 1.75 – 1.62 (m, 2H), 1.55 – 1.46 (m, 2H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.9, 139.1, 134.6, 134.5, 129.9, 129.1, 128.7, 128.5, 128.3, 128.1, 127.9, 127.5, 80.3, 67.2, 61.7, 61.5, 55.8, 55.5, 47.5, 27.8, 23.4, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{28}H_{31}N_2O_3S$ 475.2050, found 475.2067 $[M+H]^+$.

N-(3-(Allyl(4-methoxybenzyl)amino)-3-phenylprop-1-yn-1-yl)-*N*-benzyl-4-methylbenzenesulfonamide (**5f**)

Following the **General Procedure F**, the title compound **5f** was isolated as a colourless resin (100 mg, 182 µmol). Yield 67%. – R_f = 0.57 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3062, 3031, 3001, 2929, 2833, 2240, 1611, 1511, 1450, 1365, 1301, 1247, 1167, 1090, 1034, 919, 870, 831, 740, 697 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.23 (m, 9H), 7.19 – 7.09 (m, 3H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.77 – 6.68 (m, 2H), 5.63 (dddd, *J* = 16.9, 9.9, 8.5, 3.9 Hz, 1H), 5.03 (dt, *J* = 17.1, 2.2 Hz, 1H), 4.97 (dt, *J* = 10.1, 2.0 Hz, 1H), 4.63 (s, 1H), 4.55 (d, *J* = 13.6 Hz, 1H), 4.51 (d, *J* = 13.7 Hz, 1H), 3.69 (s, 3H), 3.41 (d, *J* = 13.3 Hz, 1H), 2.88 – 2.80 (m, 2H), 2.48 (dd, *J* = 14.1, 8.6 Hz, 1H), 2.37 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 158.7, 144.8, 139.4, 136.8, 134.6, 131.6, 130.0, 129.9, 129.1, 128.8, 128.5, 128.2, 128.0(1), 128.0(0), 127.3, 117.2, 113.6, 80.7, 66.8, 55.8, 55.6, 55.4, 53.8, 53.1, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{34}H_{34}N_2NaO_3S$ 573.2182, found 573.2183 $[M+Na]^+$.

N-Benzyl-*N*-(3-(diethylamino)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5g**)

Following the **General Procedure F**, the title compound **5g** was isolated as a colourless oil (59 mg, 133 µmol). Yield 53% (69% based on recovered starting material). – R_f = 0.31 (cyclohexane/EtOAc 8:2). – FTIR-ATR (neat) 3087, 3062, 3030, 2968, 2931, 2872, 2820, 2237, 1597, 1493, 1449, 1364, 1166, 1089, 1026, 868, 812, 717, 695 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.77 – 7.71 (m, 2H), 7.30 – 7.23 (m, 7H), 7.22 – 7.14 (m, 5H), 4.73 (s, 1H), 4.51 (d, *J* = 13.6 Hz, 1H), 4.46 (d, *J* = 13.6 Hz, 1H), 2.40 (s, 3H), 2.29 (dq, *J* = 12.7, 7.4 Hz, 2H), 2.03 (dq, *J* = 13.6, 6.9 Hz, 2H), 0.85 (t, *J* = 7.1 Hz, 6H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.7, 140.0, 134.7, 134.6, 129.8, 129.1, 128.7, 128.4(3), 128.4(0), 128.0, 127.9(6), 127.1, 80.0, 67.5, 56.6, 55.6, 44.4, 21.8, 13.6 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{27}H_{31}N_2O_2S$ 447.2101, found 447.2133 $[M+H]^+$.

N-Benzyl-*N*-(3-(benzylamino)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5k**)

$Ti(OEt)_4$ (20.0 µL, 64 µmol, 1.0 eq.) was added to a suspension of *N*-benzylbenzaldimine (25.0 mg, 128 µmol, 2.0 eq.), **3** (18.5 mg, 64 µmol, 1.0 eq.) and Cu^I-USY (2.9 mg, 8 mol%) in EtOAc (1 mL) at room temperature. The vial was flushed with argon and capped. The mixture was stirred at 30 °C for six days. Then, the mixture was dissolved in EtOAc, filtered over celite and concentrated. The crude was purified by column chromatography on silica gel (cyclohexane/EtOAc/Et_3N 99:0:1 to 89:10:1). The title compound **5k** was isolated as a yellow oil (5.3 mg, 11 µmol). Yield 17%. – R_f = 0.45 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3320, 3086, 3061, 3029, 2922, 2852, 2241, 1597, 1494, 1360, 1166, 1089, 813, 695 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.77 – 7.73 (m, 2H), 7.35 – 7.21 (m, 17H), 4.56 (d, *J* = 13.7 Hz, 1H), 4.55 (s, 1H), 4.51 (d, *J* = 13.7 Hz, 1H), 3.72 (d, *J* = 13.0 Hz, 1H), 3.65 (d, *J* = 13.0 Hz, 1H), 2.42 (s, 3H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.8, 140.3, 139.9, 134.6(1), 134.6(0), 129.9, 129.1, 128.7, 128.5(3), 128.5(1), 128.4, 128.4, 127.9, 127.7, 127.6, 127.1, 78.9, 71.1, 55.6, 53.1, 50.9, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{30}H_{28}N_2NaO_2S$ 503.1764, found 503.1727 $[M+Na]^+$.

N-Benzyl-4-nitro-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**6a**)

Following the **General Procedure F**, the title compound **6a** was isolated as an orange solid (83 mg, 175 µmol). Yield 70%. – R_f = 0.36 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3104, 3063, 3026, 2959, 2925, 2870, 2848, 2241, 1604, 1529, 1450, 1368, 1307, 1171, 1088, 1006, 898, 854, 740, 700 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.26 – 8.22 (m, 2H), 7.96 – 7.90 (m, 2H), 7.35 – 7.27 (m, 10H), 4.67 (s, 1H), 4.62 (d, *J* = 13.9 Hz, 1H), 4.58 (d, *J* = 13.9 Hz, 1H), 2.46 – 2.30 (m, 4H), 1.73 – 1.57 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 150.5, 143.0, 139.3, 133.9, 129.1, 128.9, 128.8, 128.4, 128.1, 127.8, 124.3, 78.8, 69.4, 58.7, 56.2, 50.1, 23.5 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{26}H_{26}N_3O_4S$ 476.1639, found 476.1630 $[M+H]^+$.

N-Benzyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)methanesulfonamide (**6b**)

Following the **General Procedure F**, the title compound **6b** was isolated as a pale-yellow oil (66 mg, 179 µmol). Yield 71%. – R_f = 0.53 (cyclohexane/EtOAc 1:1). – FTIR-ATR (neat) 3086, 3060, 3030, 3012, 2959, 2931, 2873, 2814, 2240, 1624, 1602, 1587, 1493, 1450, 1346, 1154, 959, 906, 780, 698 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.46 – 7.42 (m, 2H), 7.41 – 7.35 (m, 5H), 7.33 – 7.22 (m, 3H), 4.79 (s, 1H), 4.66 (d, *J* = 14.2 Hz, 1H), 4.62 (d, *J* = 14.2 Hz, 1H), 2.94 (s, 3H), 2.54 – 2.40 (m, 4H), 1.76 – 1.64 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 139.5, 134.6, 129.2, 128.9, 128.8, 128.3, 128.2, 127.6, 79.5, 68.8, 58.6, 55.7, 50.0, 38.7, 23.5 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{21}H_{25}N_2O_2S$ 369.1631, found 369.1648 $[M+H]^+$.

N-Benzyl-4-nitro-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**6c**)

Following the **General Procedure F**, the title compound **6c** was isolated as a pale-yellow solid (96 mg, 205 µmol). Yield 82%. – R_f = 0.60 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3100, 3072, 3032, 2928, 2855, 2822, 2230, 1604, 1527, 1454, 1376, 1346, 1251, 1172, 1123, 1086, 1018, 903, 785, 740, 684 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 8.36 – 8.29 (m, 2H), 8.03 – 7.96 (m, 2H), 7.34 – 7.27 (m, 5H), 4.57 (s, 2H), 2.53 – 2.40 (m, 4H), 1.80 – 1.74 (m, 2H), 1.67 – 1.59 (m, 4H), 1.58 – 1.46 (m, 3H), 1.37 (td, *J* = 12.3, 3.3 Hz, 2H), 1.31 – 1.21 (m, 3H), 1.17 – 1.07 (m, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 150.5, 143.2, 134.0, 129.0(5), 129.0(3), 128.8,

128.7, 124.2, 77.9, 72.4, 59.3, 56.3, 47.0, 37.9, 25.6, 23.4, 22.9 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{25}H_{29}N_3NaO_4S$ 490.1771, found 490.1753 $[M+Na]^+$.

N-Benzyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)methanesulfonamide (**6d**)

Following the **General Procedure F**, the title compound **6d** was isolated as a colourless solid (49 mg, 136 µmol). Yield 54%. – R_f = 0.42 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3069, 3025, 2950, 2930, 2858, 2812, 2232, 1495, 1354, 1161, 956, 787, 695 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.44 – 7.31 (m, 5H), 4.58 (s, 2H), 2.92 (s, 3H), 2.61 – 2.48 (m, 4H), 1.89 – 1.80 (m, 2H), 1.71 – 1.64 (m, 4H), 1.64 – 1.49 (m, 3H), 1.45 – 1.34 (m, 4H), 1.18 – 1.08 (m, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 134.6, 129.2, 128.7(4), 128.7(0), 78.5, 72.0, 59.3, 55.7, 47.0, 38.2, 38.0, 25.6, 23.4, 23.1 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{20}H_{29}N_2O_2S$ 361.1944, found 361.1929 $[M+H]^+$.

1-(3-Phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)pyrrolidin-2-one (**6e**)

Following the **General Procedure F**, the title compound **6e** was isolated as a pale-orange solid (18 mg, 68 µmol). Yield 27%. – R_f = 0.42 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3084, 3060, 3028, 2962, 2932, 2875, 2807, 2704, 2246, 1716, 1627, 1602, 1392, 1262, 1194, 1028, 700 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.51 – 7.43 (m, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.22 – 7.17 (m, 1H), 4.77 (s, 1H), 3.68 – 3.62 (m, 2H), 2.59 – 2.48 (m, 4H), 2.38 (t, *J* = 8.1 Hz, 2H), 2.07 (quint, *J* = 7.6 Hz, 2H), 1.75 – 1.63 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 176.2, 139.6, 128.3, 128.3, 127.6, 77.9, 69.4, 58.8, 50.3, 50.2, 29.8, 23.5, 18.9 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{17}H_{21}N_2O$ 269.1648, found 269.1639 $[M+H]^+$.

3-(3-Phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)oxazolidin-2-one (**6f**)

Following the **General Procedure F**, the title compound **6f** was isolated as a pale-red solid (77 mg, 285 µmol). Yield 90%. – R_f = 0.52 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3058, 3032, 2964, 2915, 2873, 2805, 2246, 1752, 1475, 1418, 1218, 1199, 1110, 1028, 865, 748, 702 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.56 – 7.49 (m, 2H), 7.37 – 7.31 (m, 2H), 7.30 – 7.26 (m, 1H), 4.80 (s, 1H), 4.49 – 4.40 (m, 2H), 3.98 – 3.89 (m, 2H), 2.60 (m, 4H), 1.77 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 156.4, 139.4, 128.4, 128.3, 127.7, 76.5, 68.3, 63.0, 58.8, 50.4, 47.1, 23.5 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{16}H_{18}N_2NaO_2$ 293.1260, found 293.1251 $[M+H]^+$.

4-Methyl-*N*-phenyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**6h**)

Following the **General Procedure F**, the title compound **6h** was isolated as a yellow solid (181 mg, 420 µmol). Yield 84%. – R_f = 0.39 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3059, 3028, 2958, 2924, 2874, 2853, 2814, 2244, 1685, 1595, 1542, 1489, 1446, 1370, 1257, 1156, 1088, 1028, 922, 888, 812, 755, 691 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.56 – 7.52 (m, 2H), 7.53 – 7.47 (m, 2H), 7.36 – 7.27 (m, 8H), 7.22 (d, *J* = 8.1 Hz, 2H), 4.84 (s, 1H), 2.65 – 2.52 (m, 4H), 2.42 (s, 3H), 1.80 – 1.71 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.0, 139.7, 139.2, 133.1, 129.5, 129.2, 128.4, 128.3(1), 128.3(0), 128.2, 127.6, 126.2, 80.4, 67.6, 58.7, 50.1, 23.6, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{26}H_{26}N_2NaO_2S$ 453.1607, found 453.1592 $[M+Na]^+$.

4-Methyl-*N*-phenyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**6i**)

Following the **General Procedure F**, the title compound **6i** was isolated as an orange solid (165 mg, 390 µmol). Yield 78%. – R_f = 0.45 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3061,

2955, 2934, 2856, 2818, 2226, 1592, 1487, 1365, 1242, 1165, 1087, 926, 812, 768, 690 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$) δ = 7.59 – 7.50 (m, 2H), 7.40 – 7.20 (m, 7H), 2.74 – 2.60 (m, 4H), 2.43 (s, 3H), 1.98 – 1.88 (m, 2H), 1.79 – 1.68 (m, 4H), 1.68 – 1.38 (m, 7H), 1.24 – 1.10 (m, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.9, 139.6, 132.9, 129.4, 129.1, 128.4, 128.0, 126.1, 79.5, 71.0, 59.4, 47.2, 38.1, 25.7, 23.5, 23.1, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{25}H_{31}N_2O_2S$ 423.2101, found 423.2128 $[M+H]^+$.

N-Allyl-4-methyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**6j**)

Following the **General Procedure F**, the title compound **6j** was isolated as an off-white viscous oil (77 mg, 195 µmol). Yield 80%. – R_f = 0.20 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3084, 3061, 3028, 2963, 2928, 2874, 2810, 2237, 1646, 1597, 1493, 1449, 1363, 1291, 1166, 1089, 1028, 928, 862, 758, 660 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.79 – 7.75 (m, 2H), 7.46 (dd, *J* = 7.1, 1.8 Hz, 2H), 7.34 – 7.27 (m, 5H), 5.77 (ddt, *J* = 16.6, 10.1, 6.3 Hz, 1H), 5.26 (dd, *J* = 17.1, 1.4 Hz, 1H), 5.22 (dd, *J* = 10.2, 1.2 Hz, 1H), 4.79 (s, 1H), 4.01 (dq, *J* = 6.4, 1.4 Hz, 2H), 2.58 – 2.46 (m, 4H), 2.44 (s, 3H), 1.75 – 1.69 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.7, 139.7, 134.7, 131.2, 129.8, 128.3, 128.2, 128.0, 127.6, 120.2, 79.7, 67.5, 58.6, 54.4, 50.0, 23.5, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{23}H_{27}N_2O_2S$ 395.1788, found 395.1784 $[M+H]^+$.

N-Allyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**6k**)

Following the **General Procedure F**, the title compound **6k** was isolated as an off-white viscous oil (76 mg, 197 µmol). Yield 79%. – R_f = 0.36 (CH_2Cl_2/MeOH 9:1). – FTIR-ATR (neat) 3070, 2929, 2854, 2812, 2232, 1645, 1597, 1494, 1364, 1167, 1123, 1090, 1034, 925, 812, 760, 660 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.81 – 7.77 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 5.73 (ddt, *J* = 16.6, 10.1, 6.3 Hz, 1H), 5.26 – 5.18 (m, 2H), 3.97 (dt, *J* = 6.3, 1.3 Hz, 2H), 2.65 – 2.57 (m, 4H), 2.45 (s, 3H), 1.90 – 1.83 (m, 2H), 1.73 – 1.68 (m, 4H), 1.62 – 1.52 (m, 3H), 1.50 – 1.36 (m, 4H), 1.19 – 1.09 (m, 1H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.6, 134.7, 131.3, 129.7, 128.0, 120.0, 78.7, 70.7, 59.4, 54.6, 47.1, 38.1, 25.7, 23.5, 23.1, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{22}H_{31}N_2O_2S$ 387.2101, found 387.2127 $[M+H]^+$.

Methyl 4-((4-methyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)phenyl)sulfonamido)-butanoate (**6n**)

Following the **General Procedure F**, the title compound **6n** was isolated as a yellow viscous oil (110 mg, 242 µmol). Yield 97%. – R_f = 0.15 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3062, 3029, 2954, 2875, 2807, 2236, 1735, 1627, 1597, 1493, 1448, 1363, 1166, 1090, 1029, 900, 814, 701, 668 cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$) δ = 7.78 – 7.73 (m, 2H), 7.49 – 7.44 (m, 2H), 7.35 – 7.26 (m, 5H), 4.78 (s, 1H), 3.67 (s, 3H), 3.47 – 3.35 (m, 2H), 2.58 – 2.48 (m, 4H), 2.45 – 2.40 (m, 5H), 2.00 (quint, *J* = 7.0 Hz, 2H), 1.78 – 1.68 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.2, 144.7, 139.7, 134.5, 129.9, 128.3(2), 128.3(0), 127.8, 127.6, 79.4, 67.7, 58.7, 51.8, 50.7, 50.1, 30.5, 23.6, 23.2, 21.8 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{25}H_{30}N_2NaO_4S$ 477.1818, found 477.1835 $[M+Na]^+$.

N-(2-(1*H*-Indol-3-yl)ethyl)-4-nitro-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**6o**)

Following the **General Procedure F**, the title compound **6o** was isolated as an orange foam (55 mg, 104 µmol). Yield 77%. – R_f = 0.14 (cyclohexane/EtOAc 7:3). – FTIR-ATR (neat) 3285, 3102, 3060, 3033, 2961, 2929, 2873, 2808, 2249, 1607, 1527, 1461, 1346, 1308, 1230, 1158,

1093, 925, 853, 735, 606 cm^{-1}. – ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.12 – 8.05 (m, 2H), 7.82 – 7.76 (m, 2H), 7.67 – 7.60 (m, 2H), 7.45 – 7.26 (m, 6H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.99 (s, 1H), 4.98 (s, 1H), 3.38 (t, *J* = 6.4 Hz, 2H), 2.91 (t, *J* = 6.4 Hz, 2H), 2.77 – 2.66 (m, 4H), 1.87 – 1.78 (m, 4H) ppm. – ^{13}C NMR (126 MHz, $CDCl_3$) δ = 149.7, 145.4, 139.6, 138.7, 128.5, 128.0, 127.9, 127.1, 126.7, 124.2, 124.1, 121.9, 118.9, 114.0, 111.7, 77.5, 67.8, 59.0, 50.5, 42.9, 25.5, 23.6 ppm. – HRMS (ESI-TOF, positive mode): *m/z*: calcd for $C_{29}H_{29}N_4O_4S$ 529.1904, found 529.1905 $[M+H]^+$.

V. References

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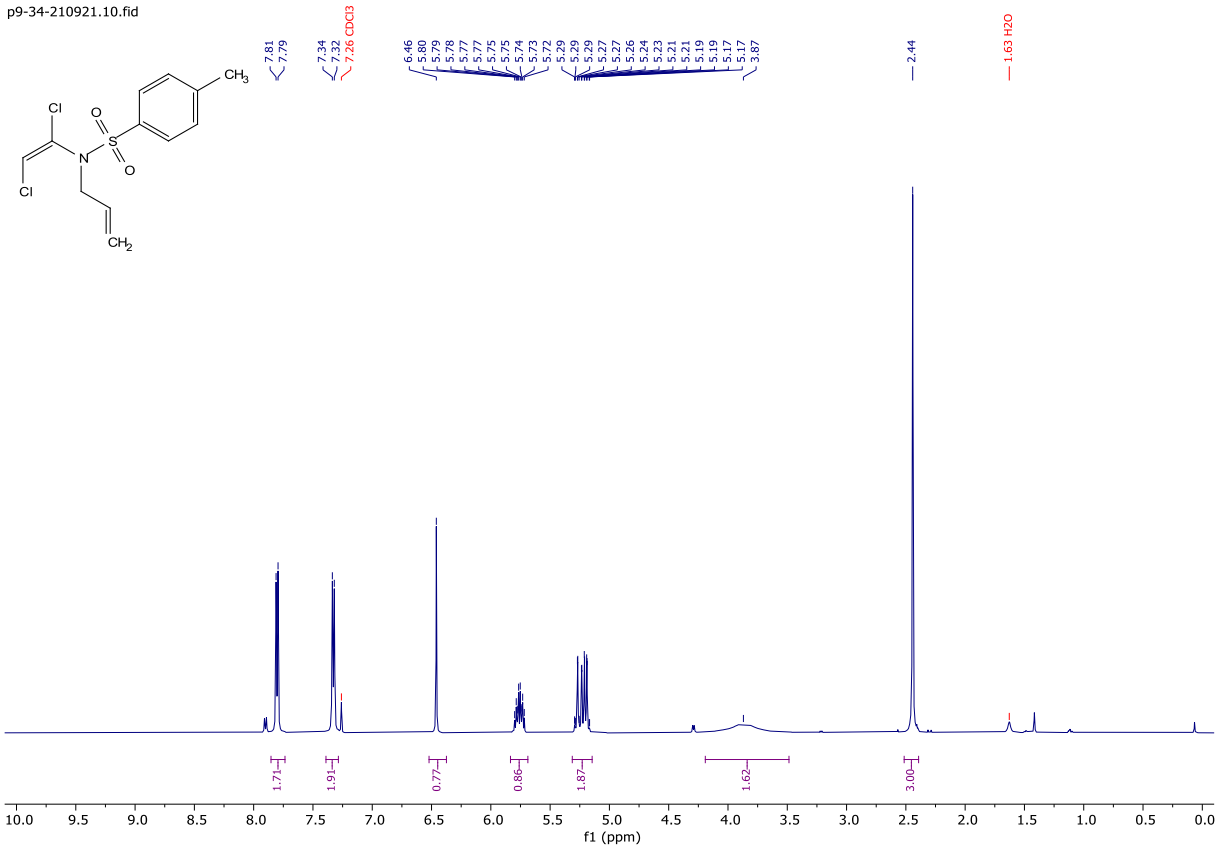
VI. NMR Spectra of Previously Unreported Products

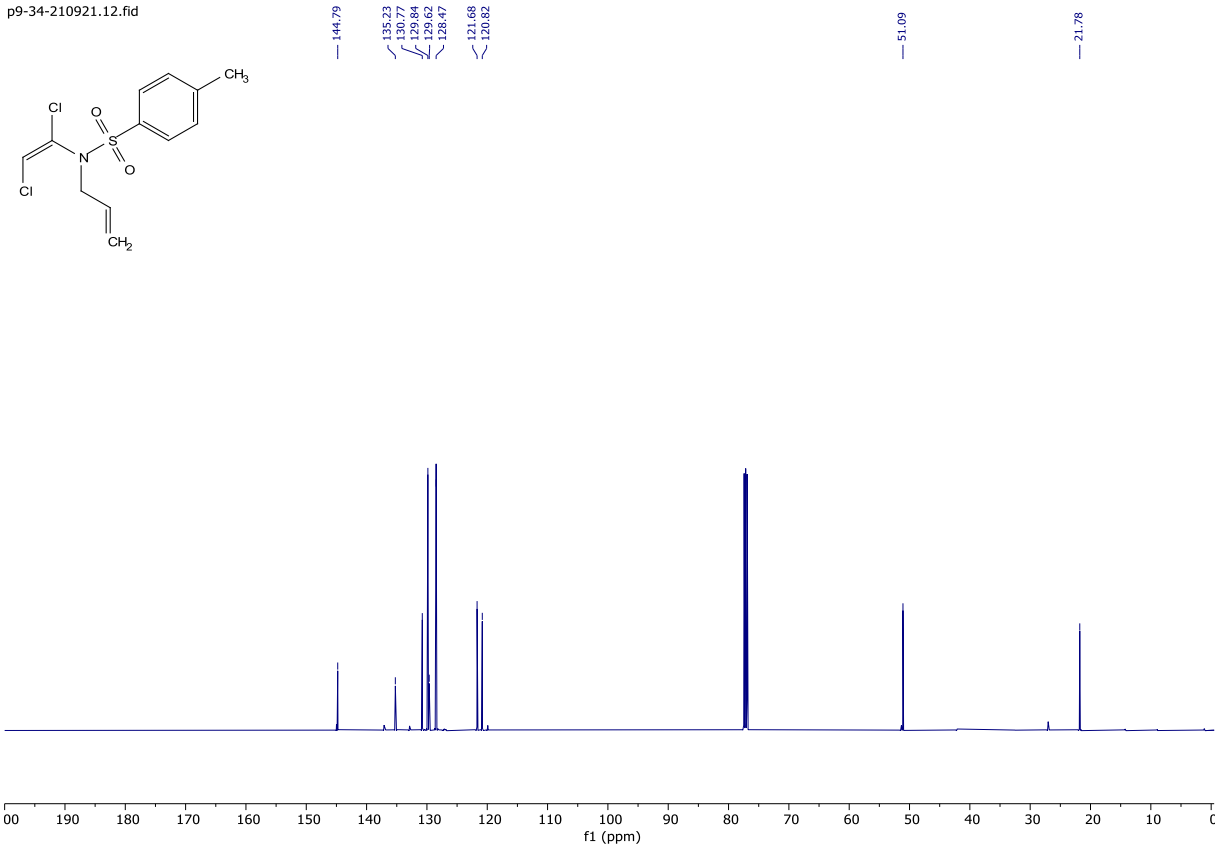
Precursors of Terminal Ynamides

(*E*)-*N*-Allyl-*N*-(1,2-dichlorovinyl)-4-methylbenzenesulfonamide

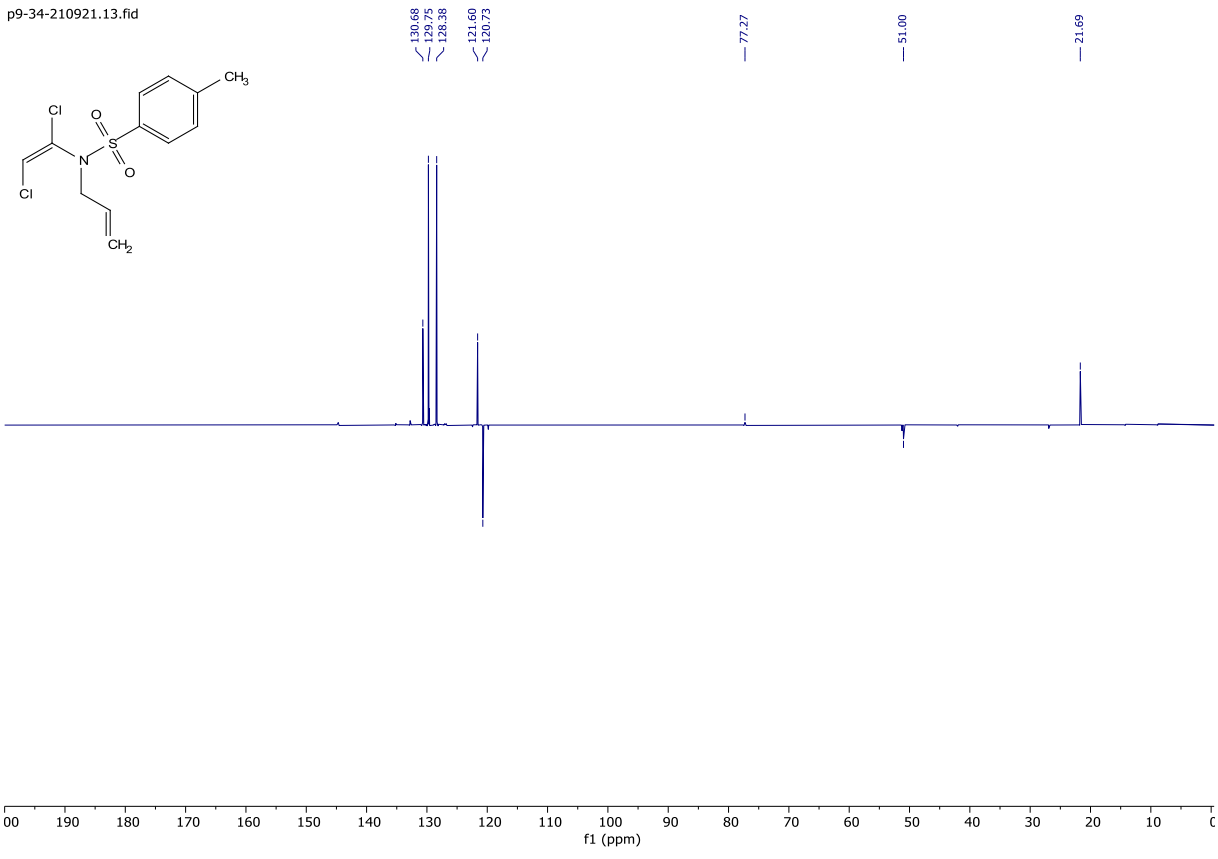
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$



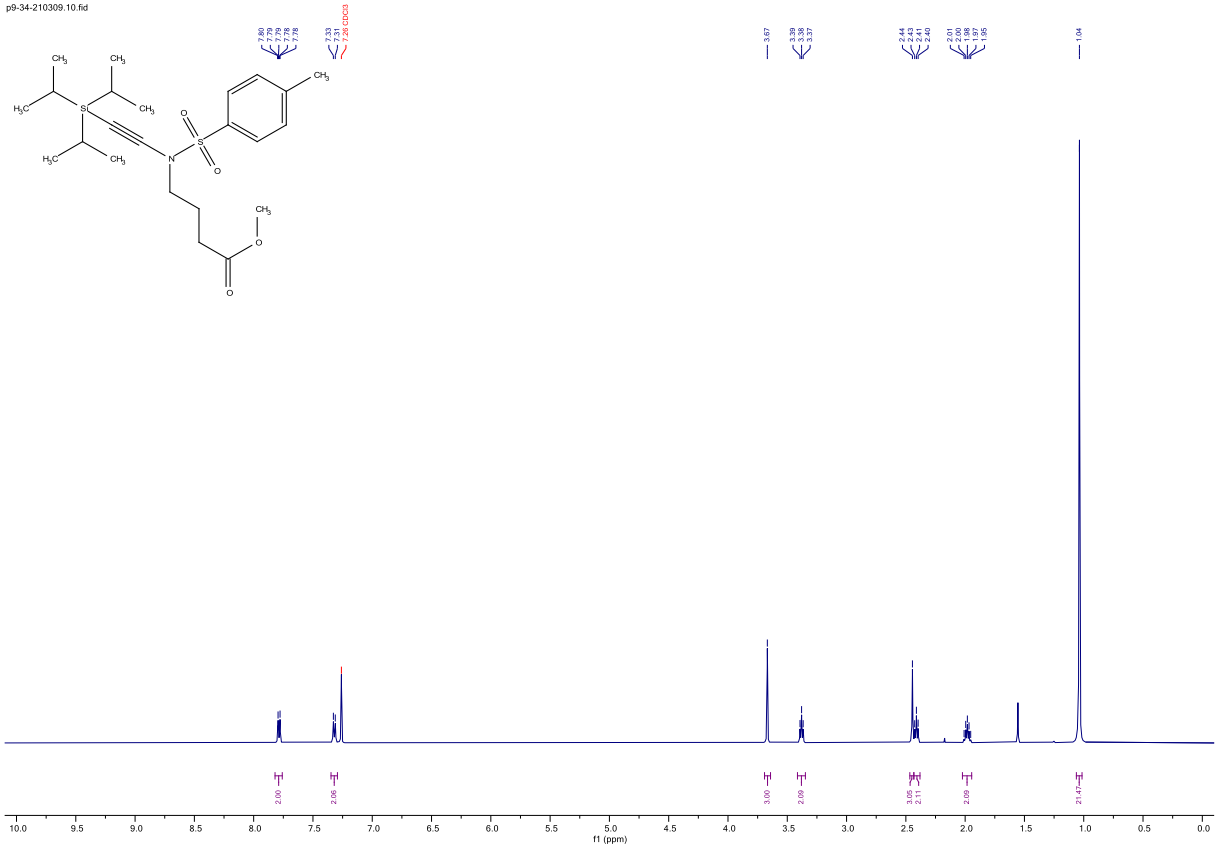
DEPT135 NMR (126 MHz) in $CDCl_3$



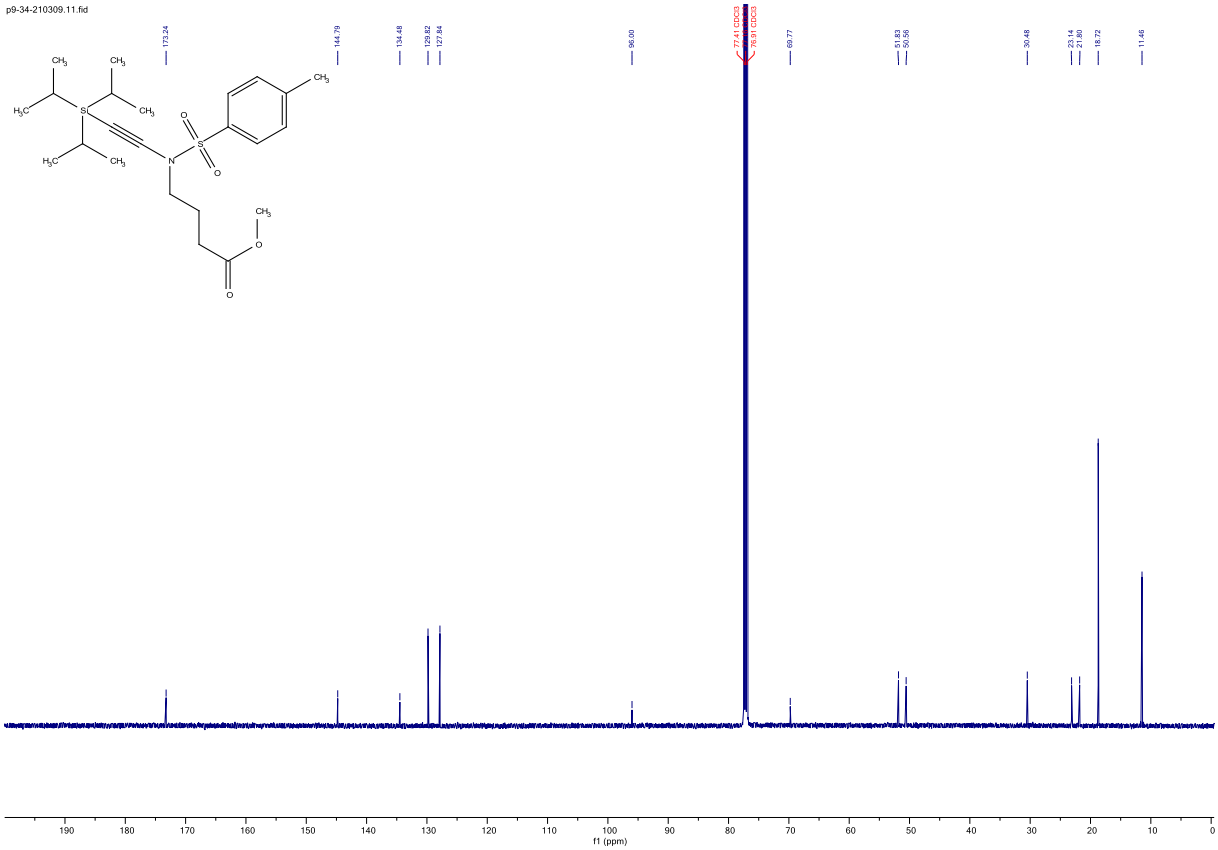
TIPS-protected ynamides

Methyl 4-((4-methyl-*N*-((triisopropylsilyl)ethynyl)phenyl)sulfonamido)butanoate

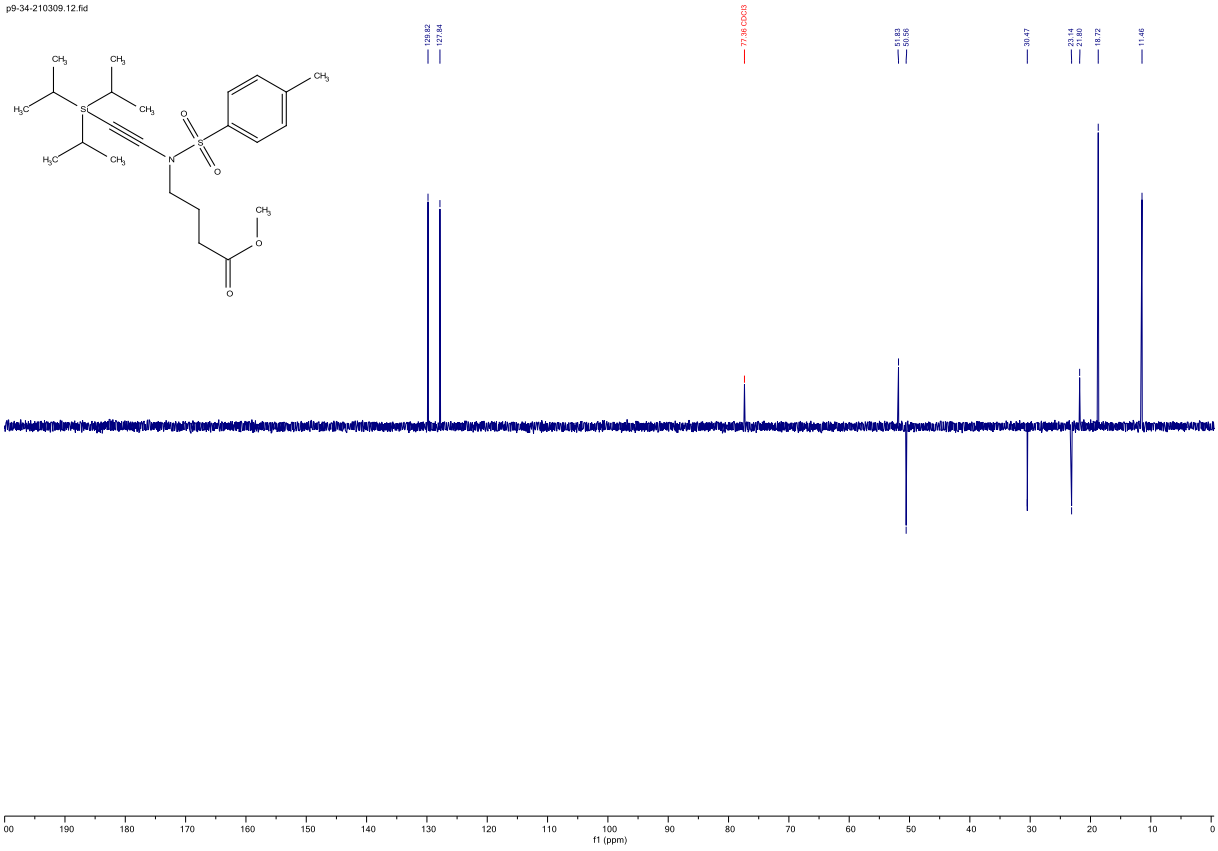
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

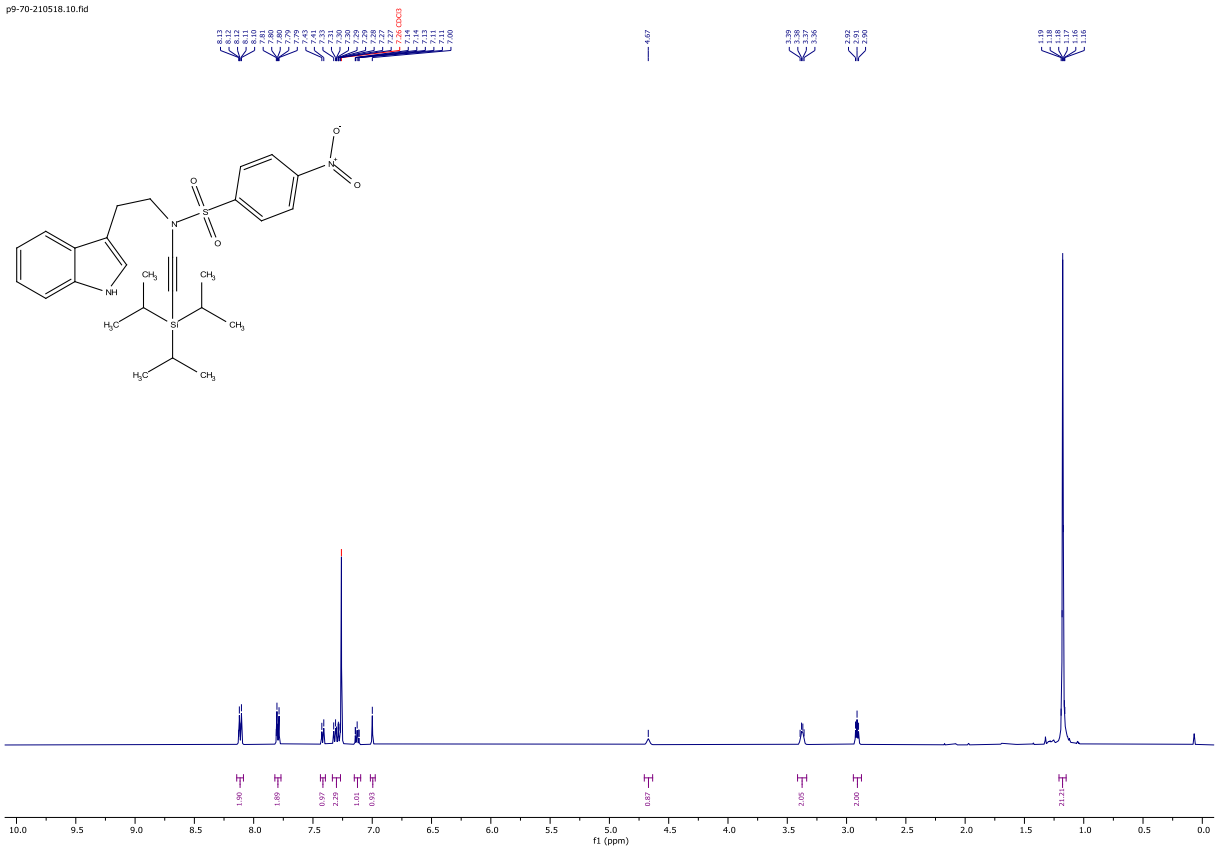


DEPT135 NMR (126 MHz) in $CDCl_3$

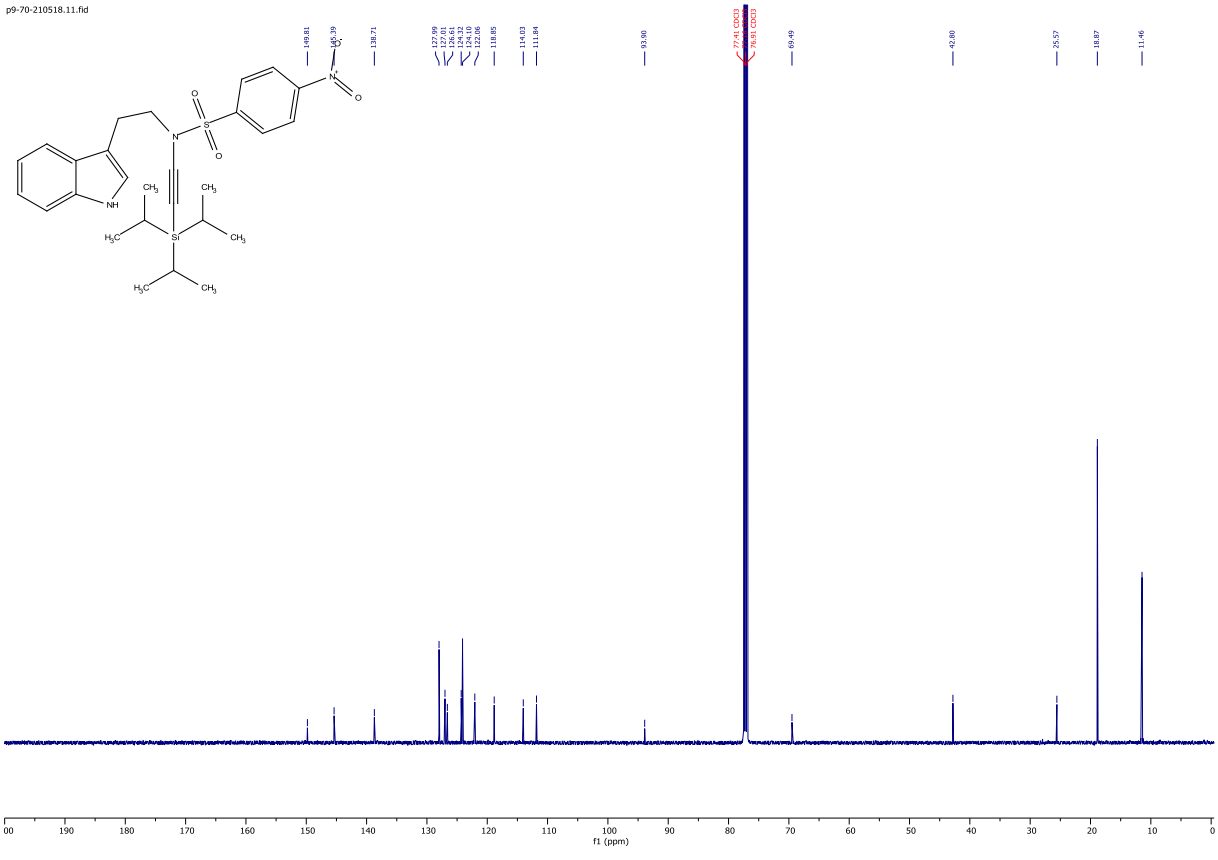


N-(2-(1*H*-Indol-3-yl)ethyl)-4-nitro-*N*-((triisopropylsilyl)ethynyl)benzenesulfonamide

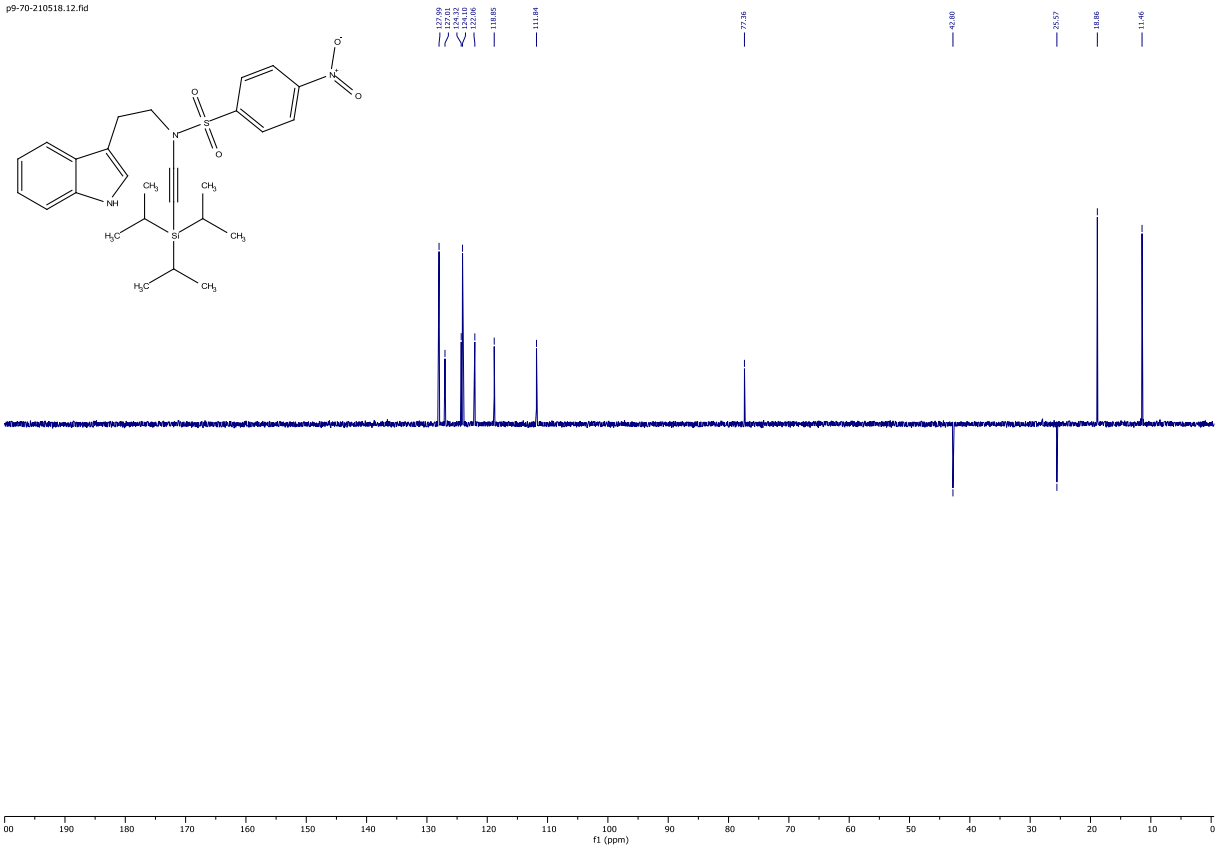
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$



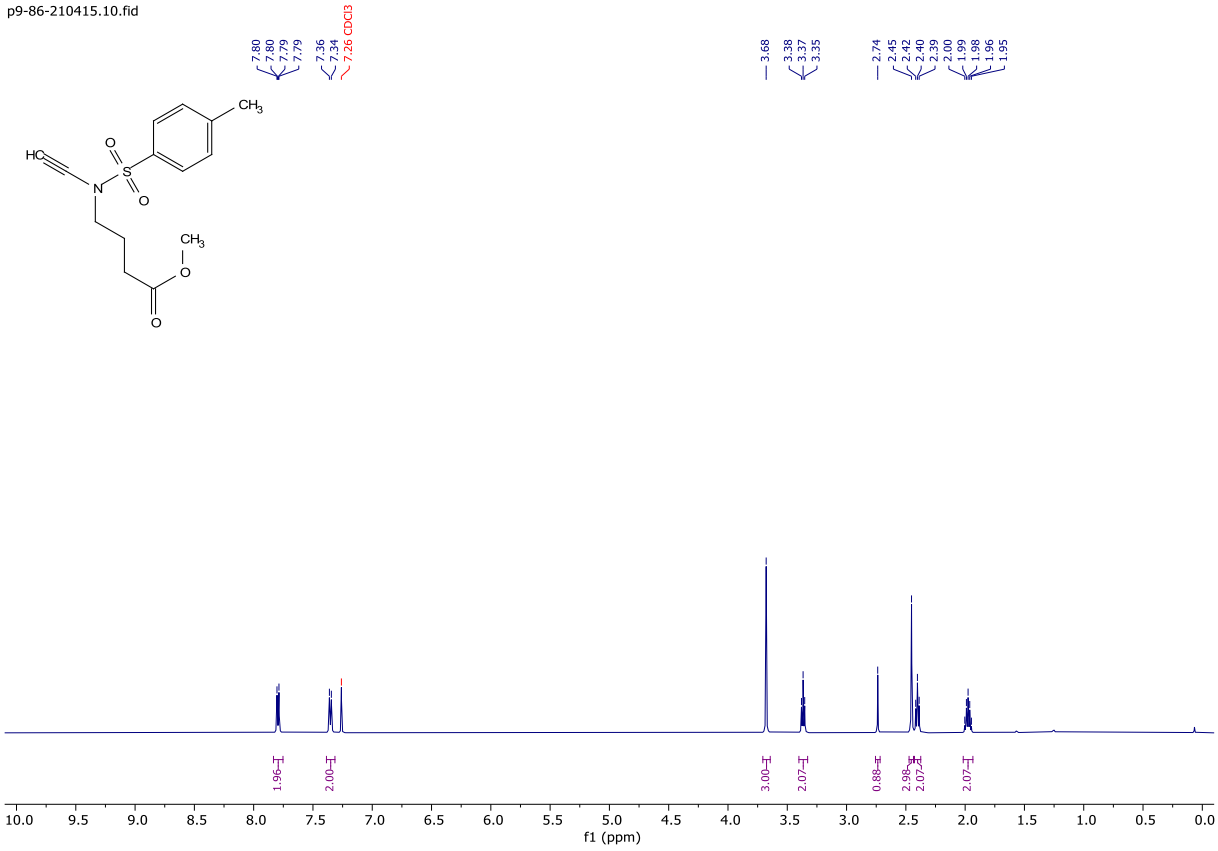
DEPT135 NMR (126 MHz) in $CDCl_3$



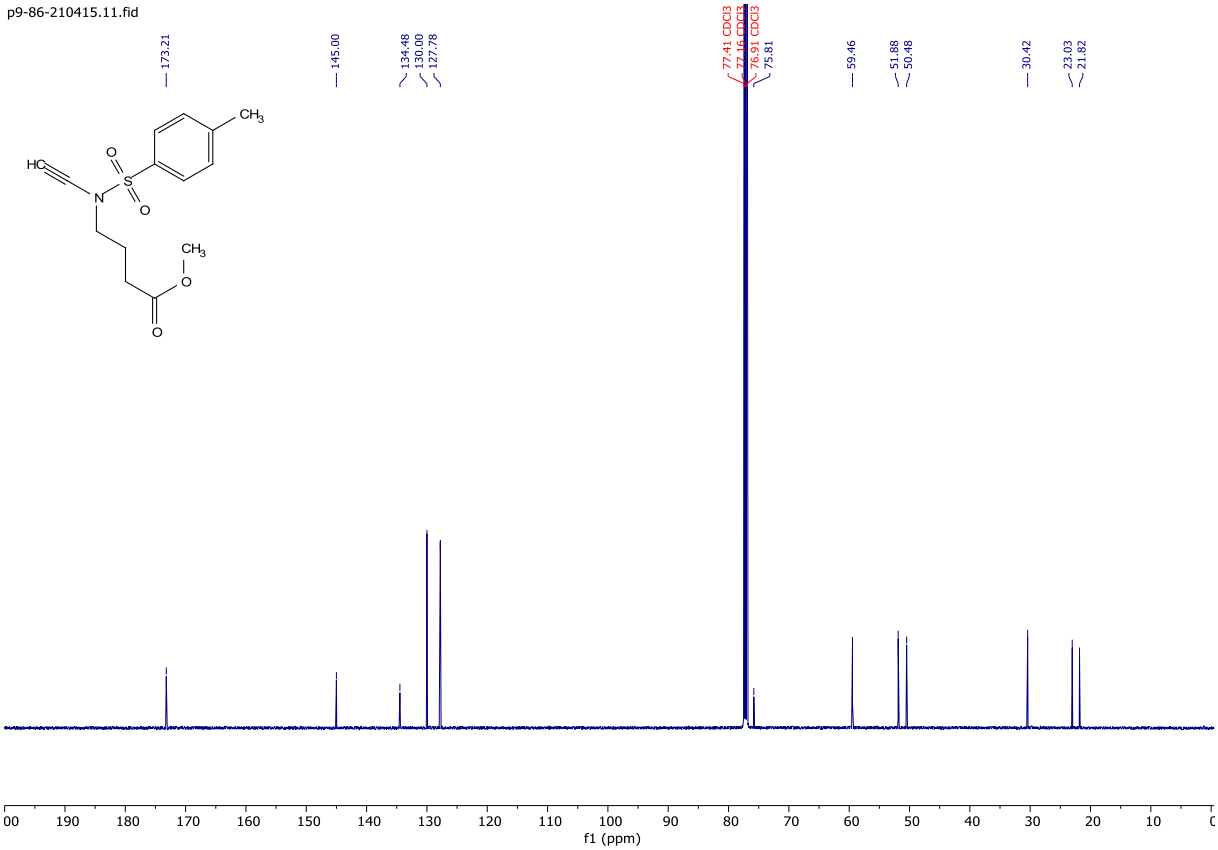
Terminal Ynamides

Methyl 4-((*N*-ethynyl-4-methylphenyl)sulfonamido)butanoate

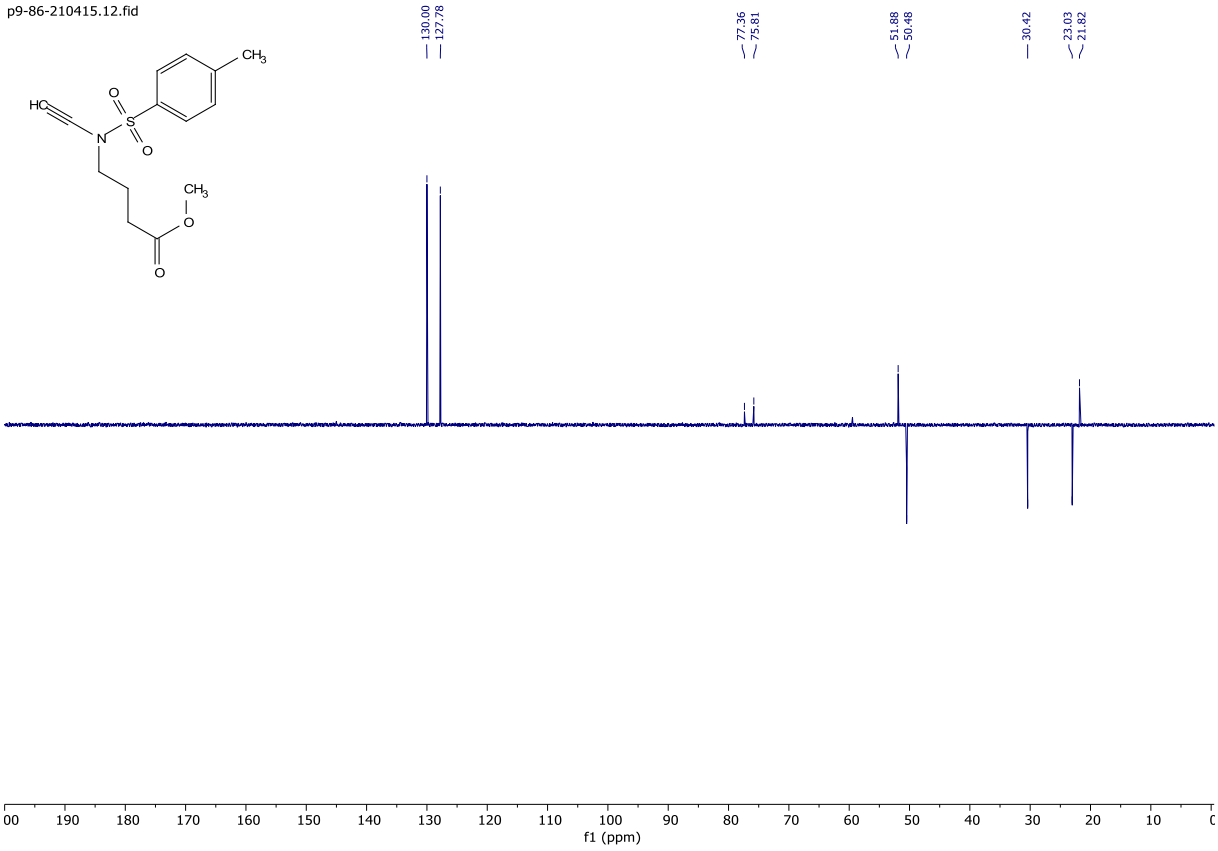
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

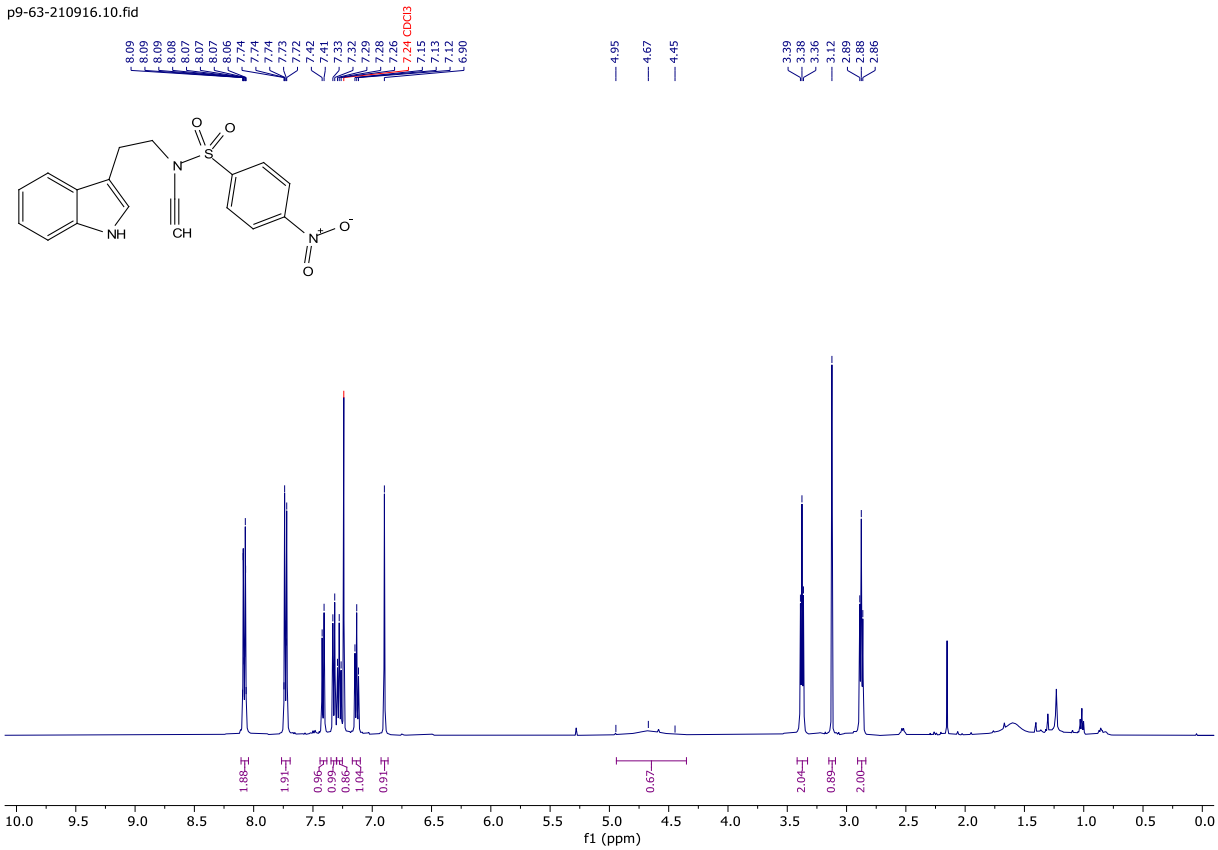


DEPT135 NMR (126 MHz) in $CDCl_3$

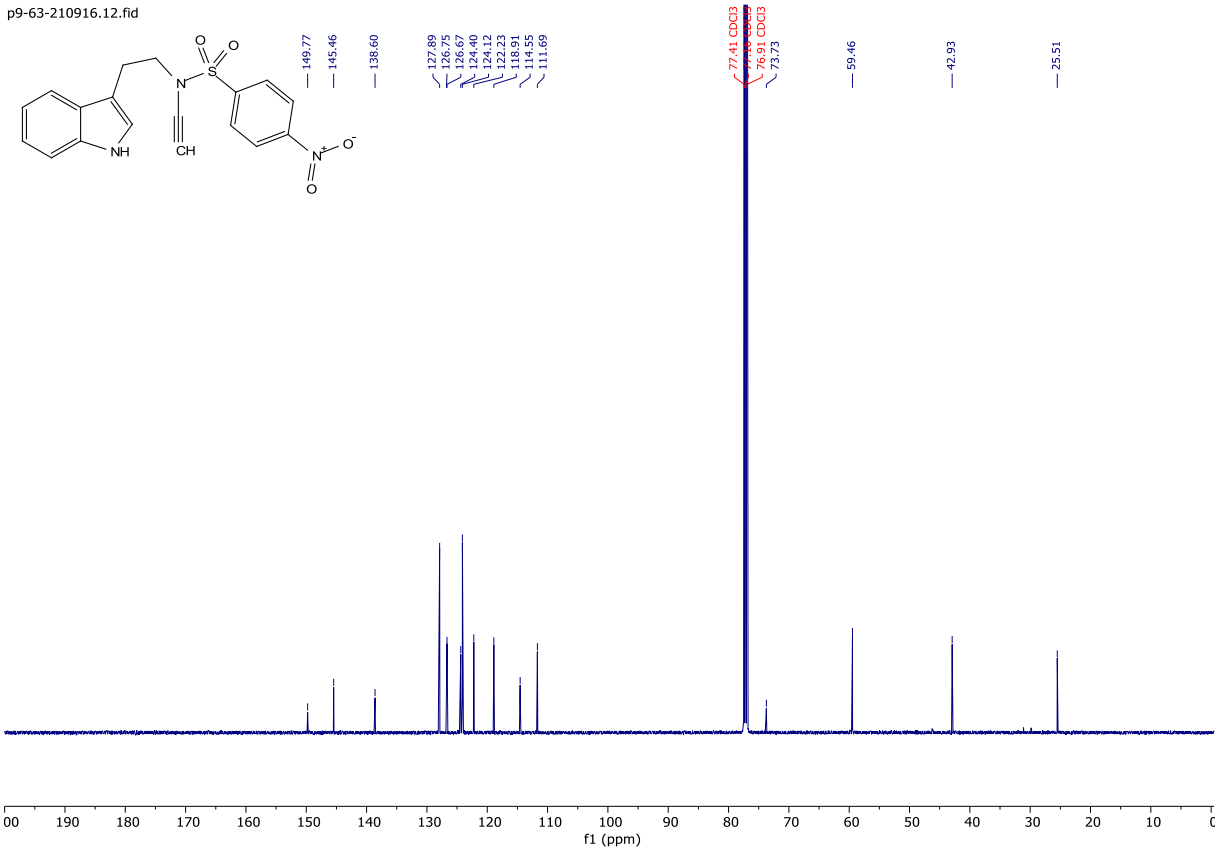


N-(2-(1*H*-Indol-3-yl)ethyl)-*N*-ethynyl-4-nitrobenzenesulfonamide

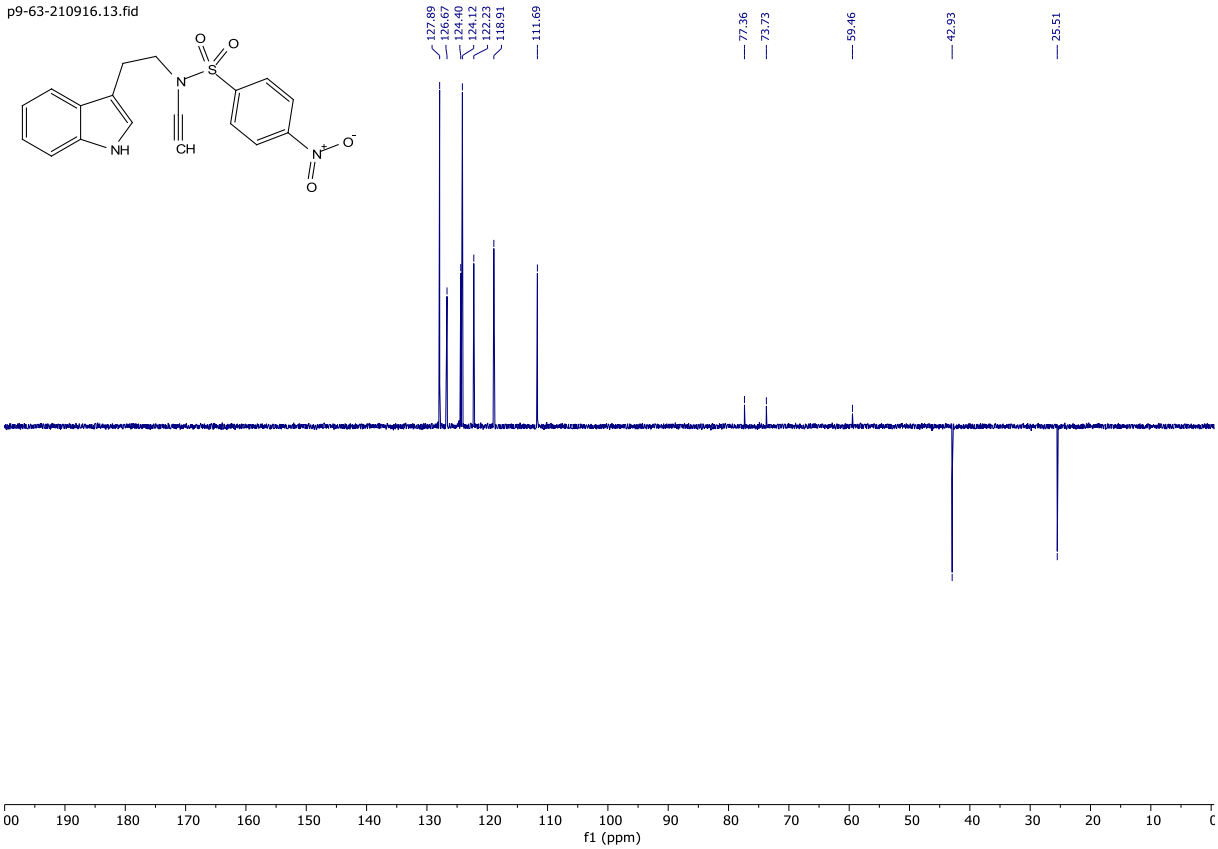
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$



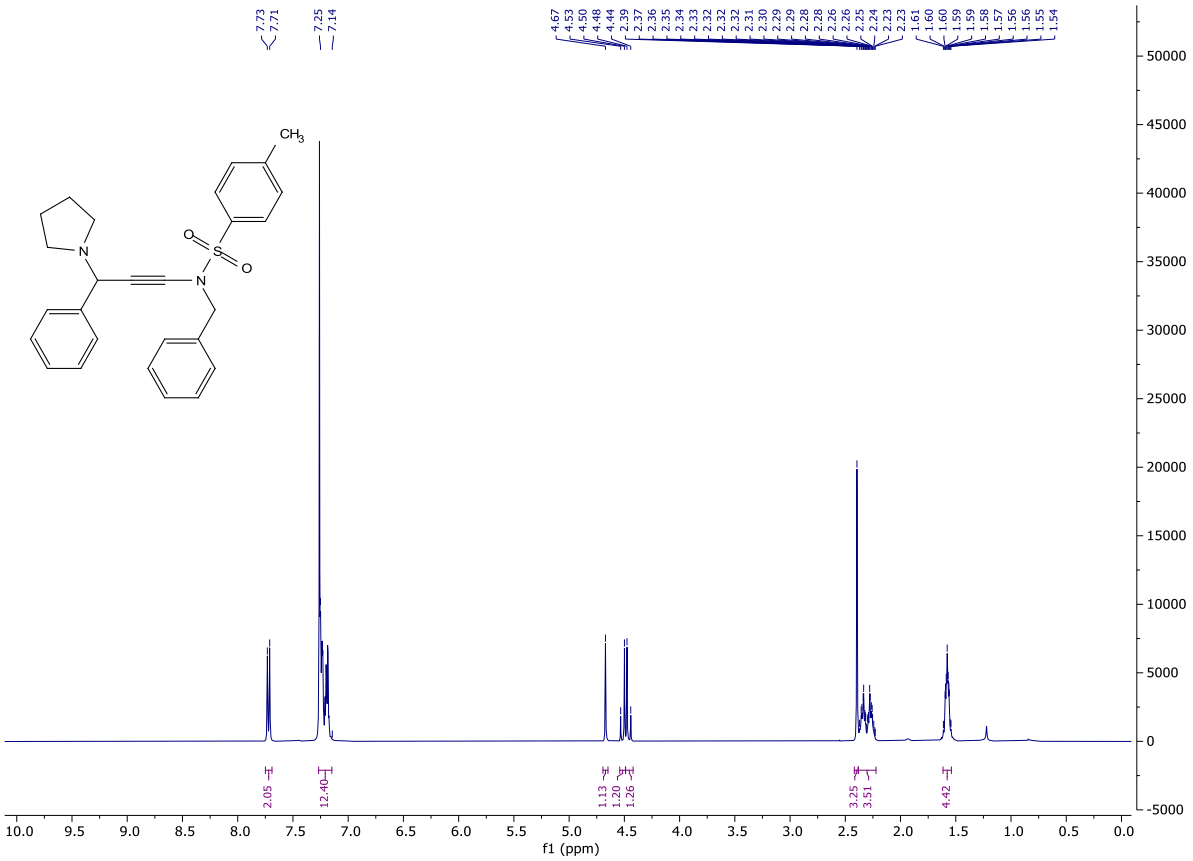
DEPT135 NMR (126 MHz) in $CDCl_3$



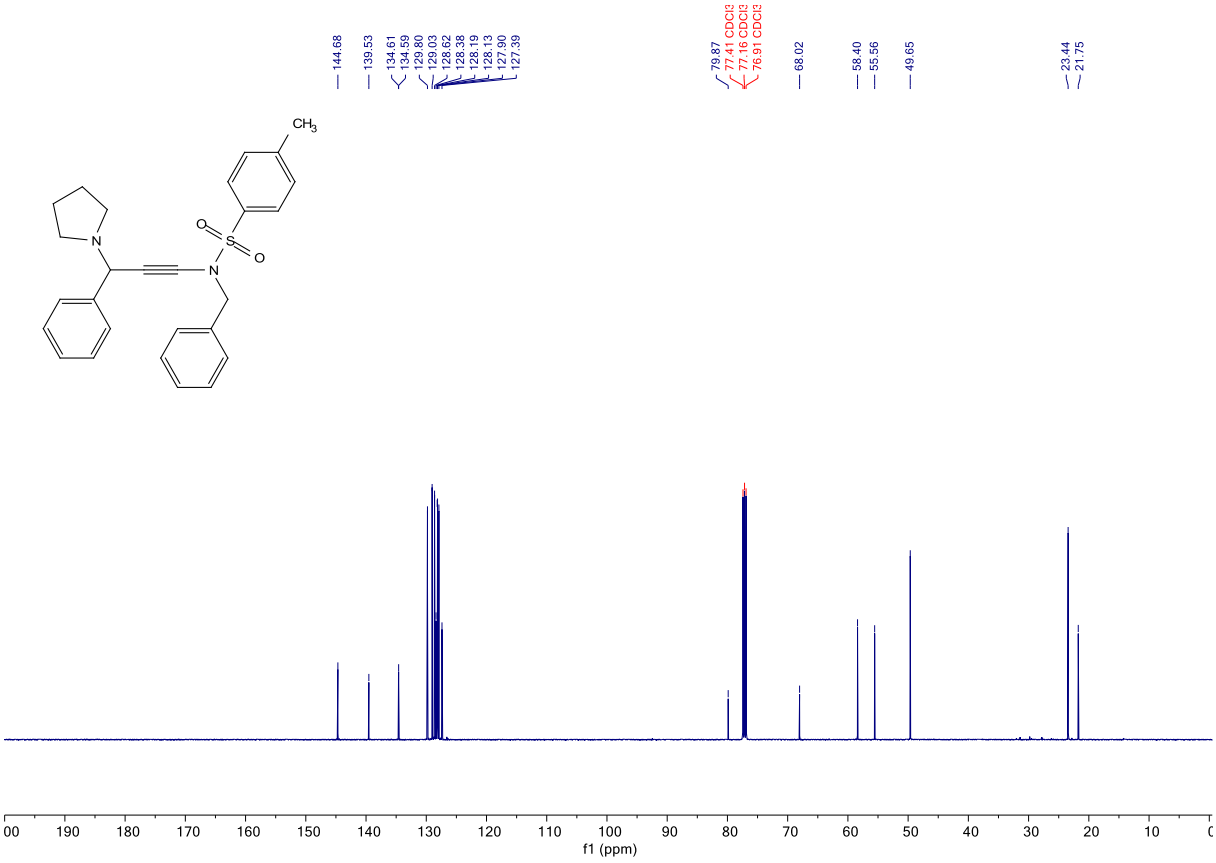
γ-Amino-Ynamides

N-Benzyl-4-methyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**4a**)

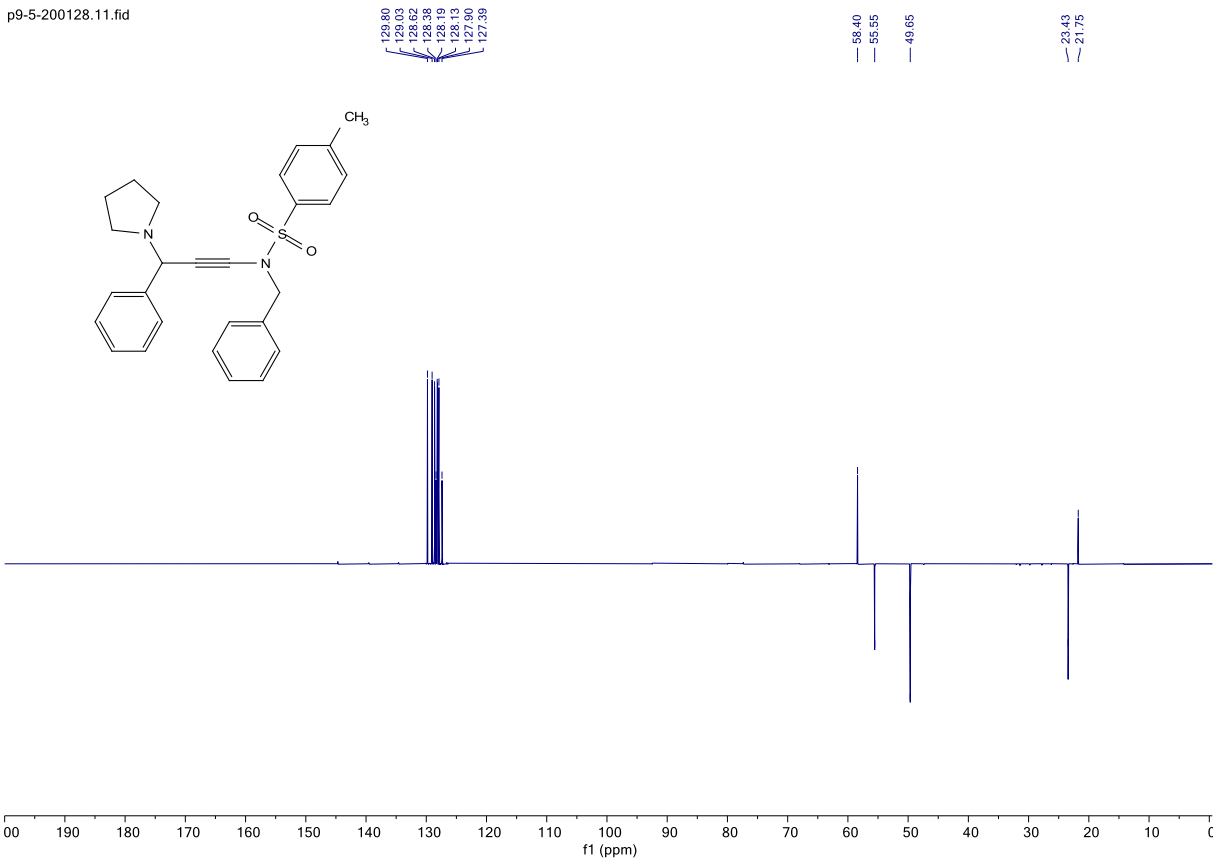
^{1}H NMR (400 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

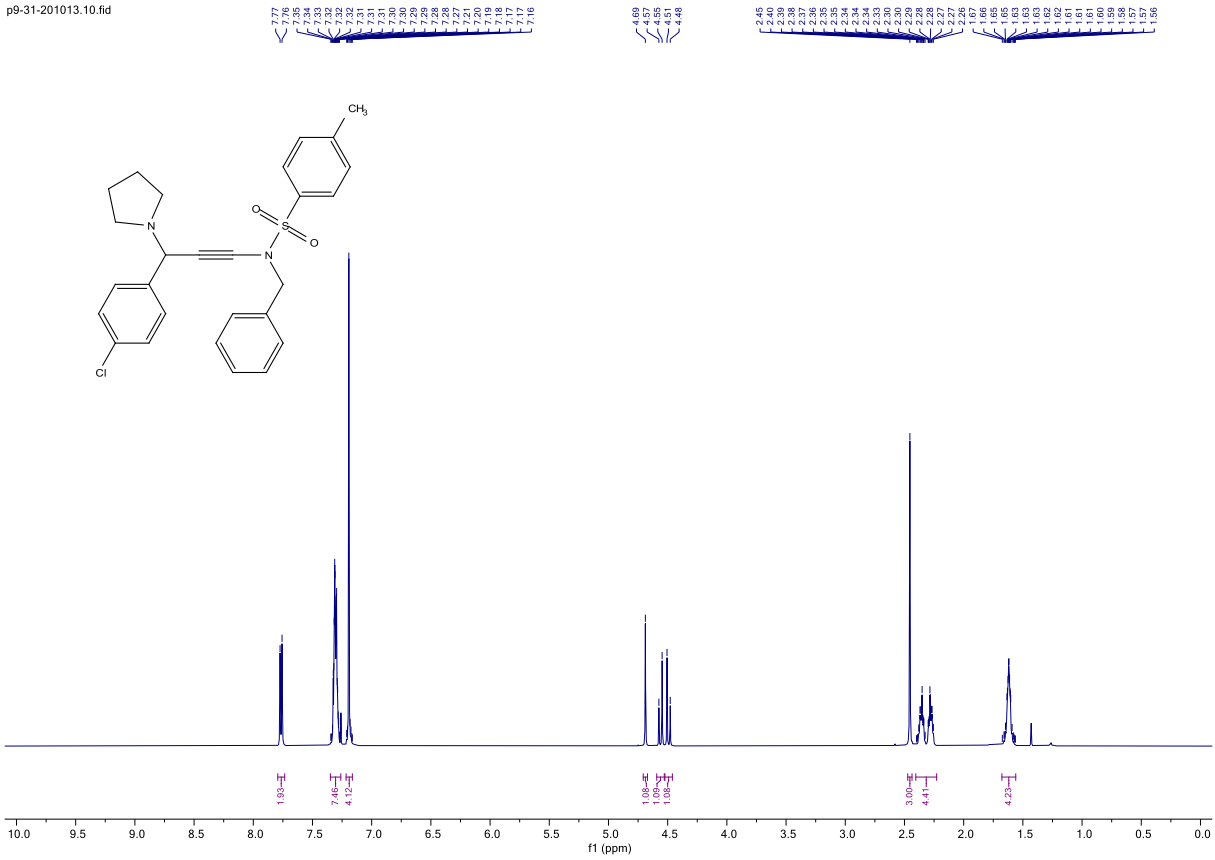


DEPT135 NMR (126 MHz) in $CDCl_3$

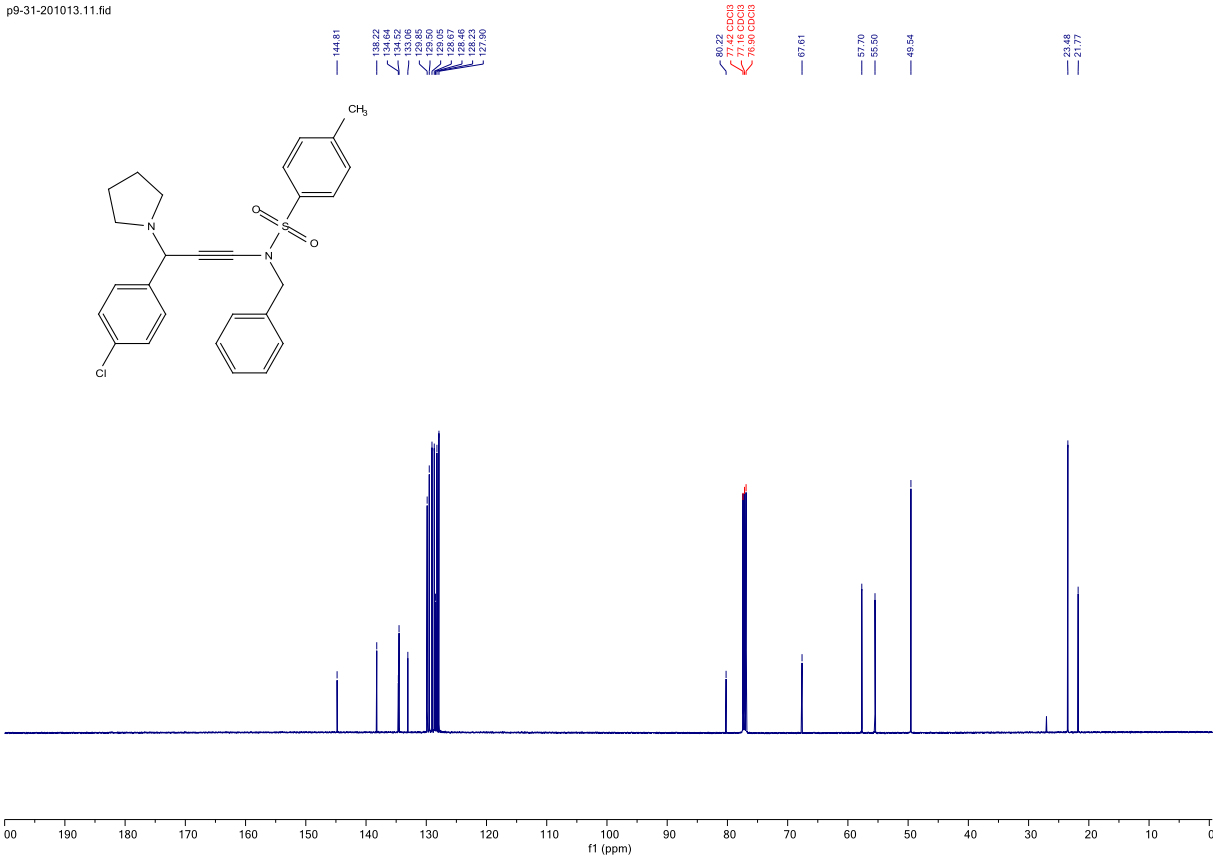


N-Benzyl-*N*-(3-(4-chlorophenyl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4b**)

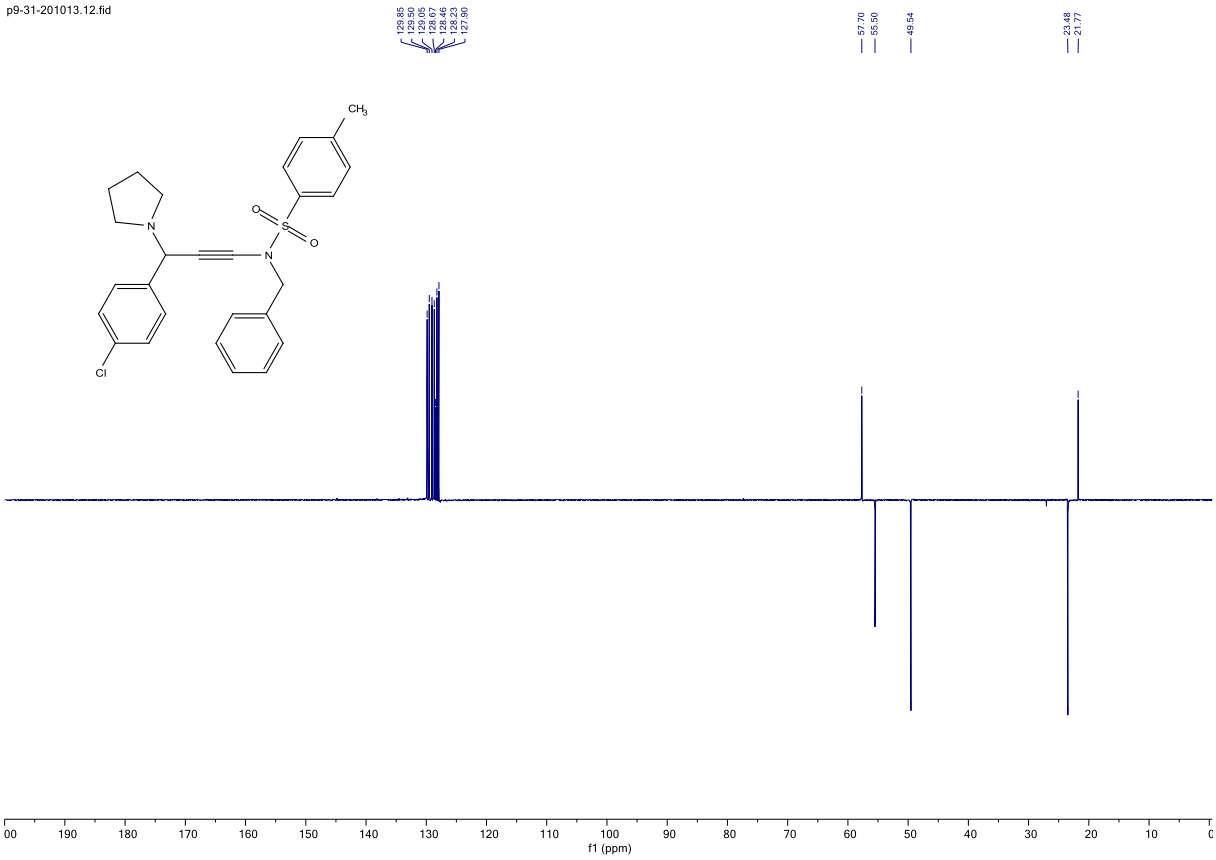
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

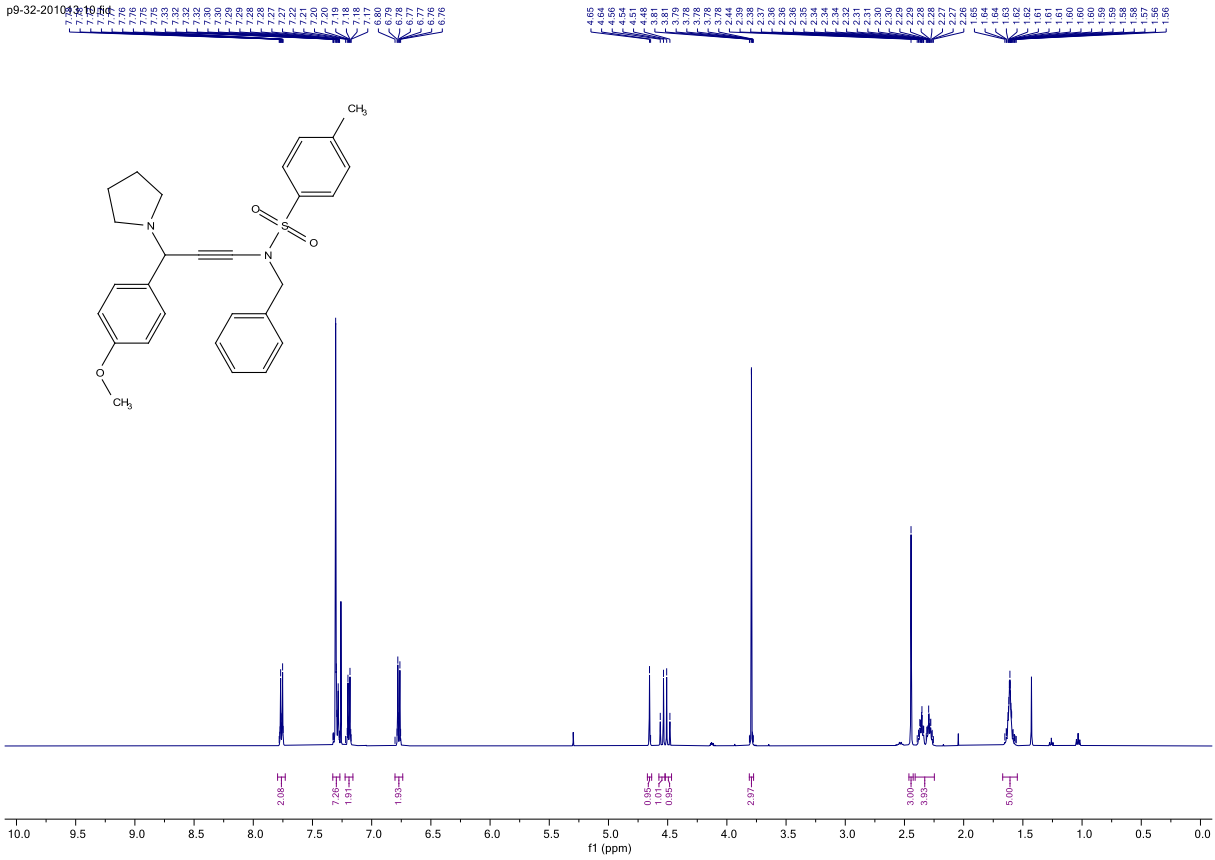


DEPT135 NMR (126 MHz) in $CDCl_3$

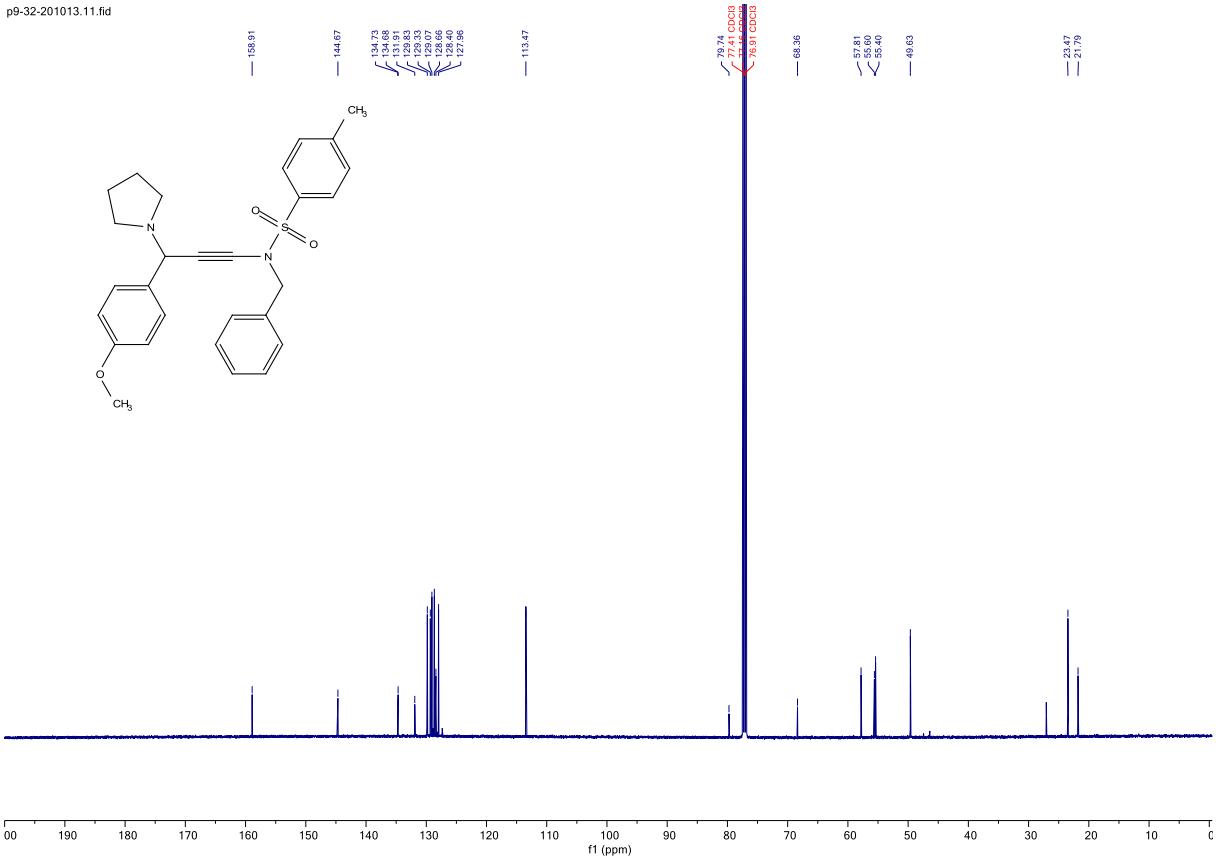


N-Benzyl-*N*-(3-(4-methoxyphenyl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4c**)

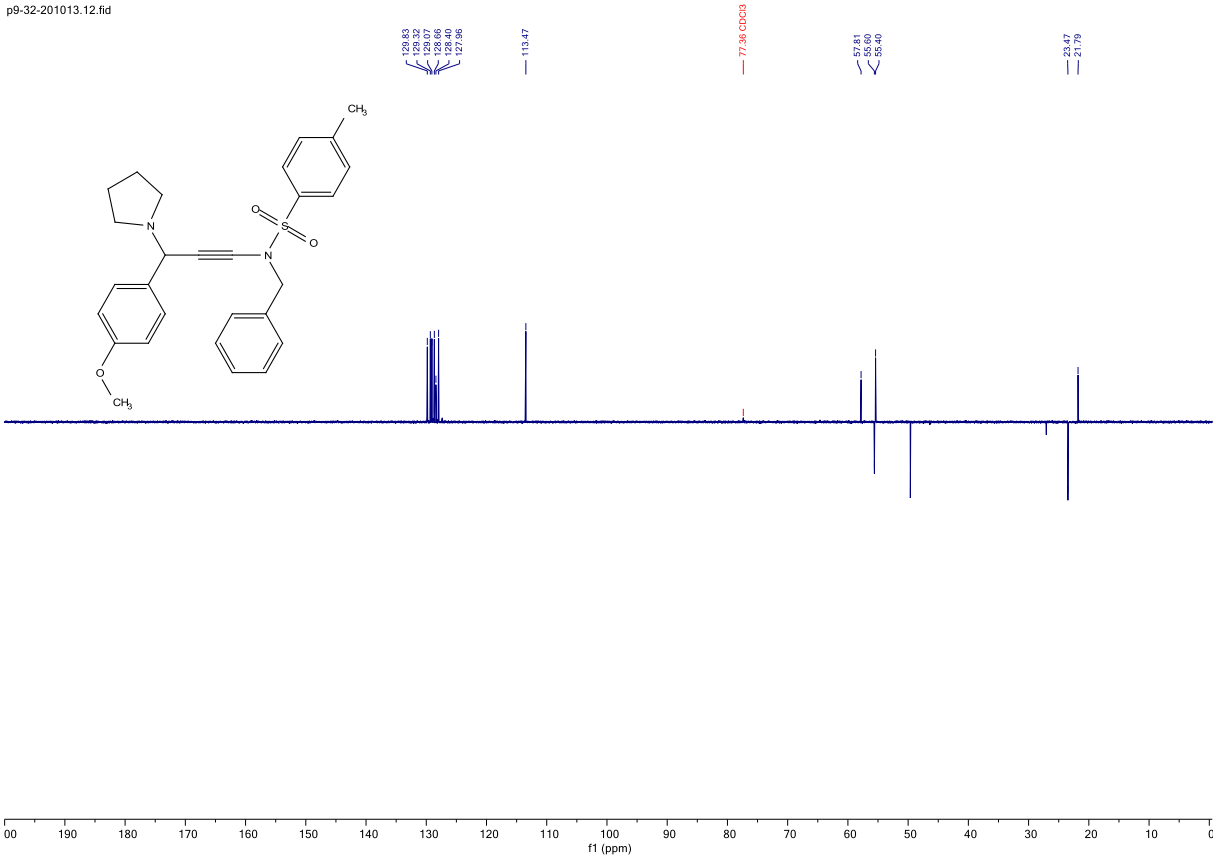
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

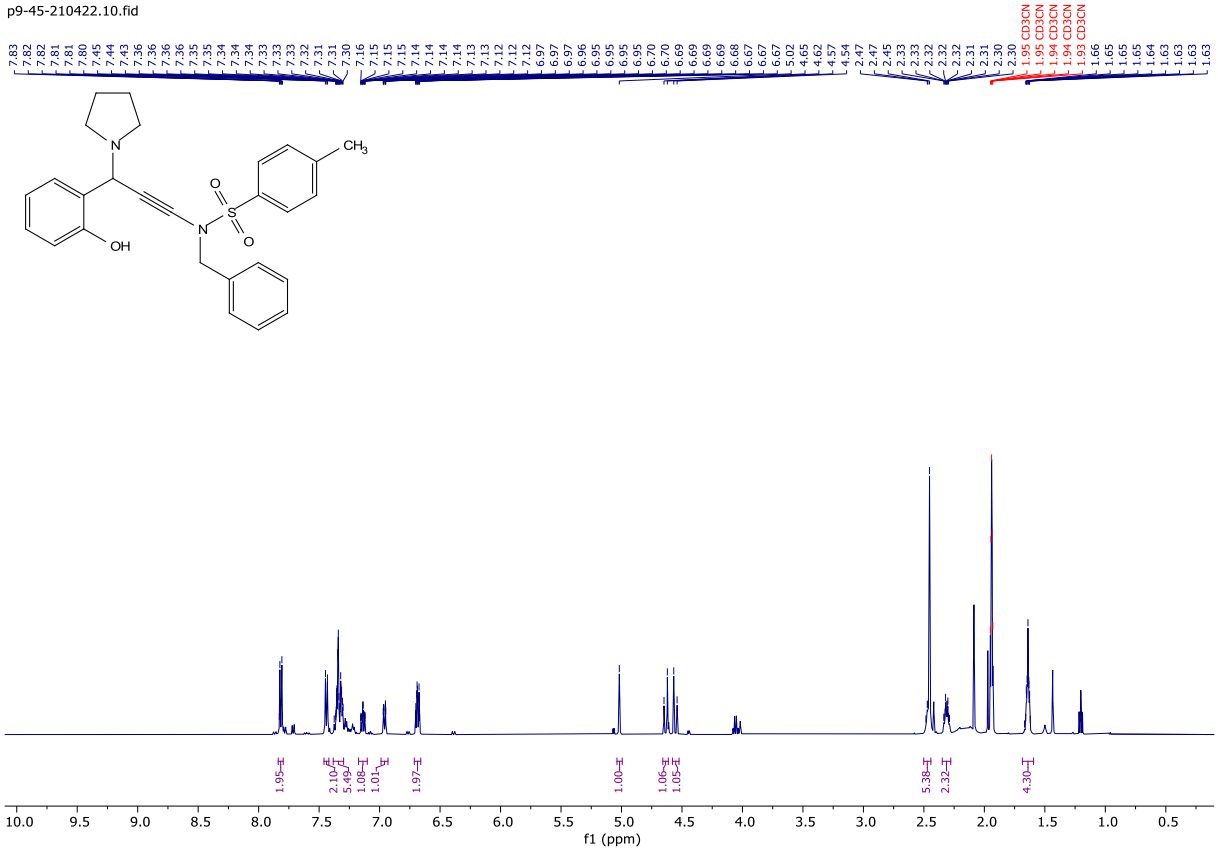


DEPT135 NMR (126 MHz) in $CDCl_3$

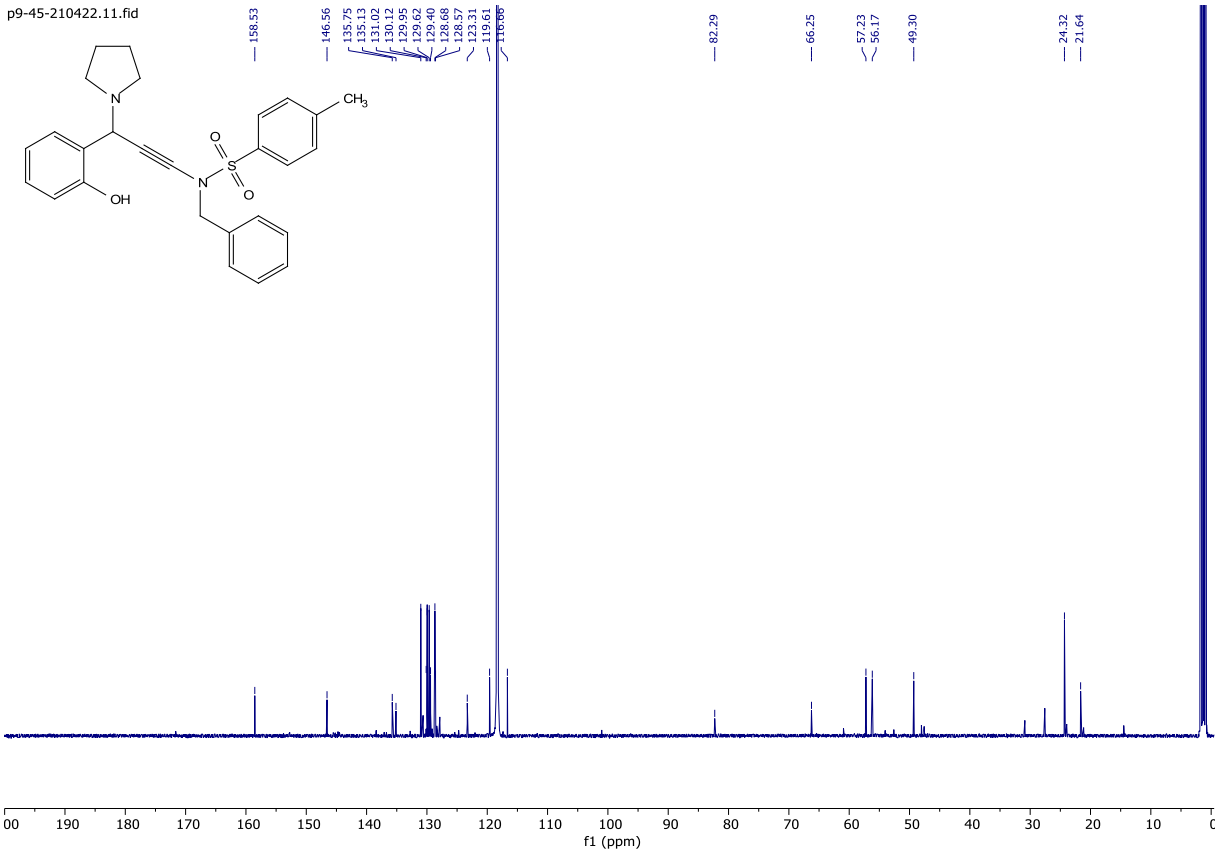


N-Benzyl-*N*-(3-(2-hydroxyphenyl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4d**)

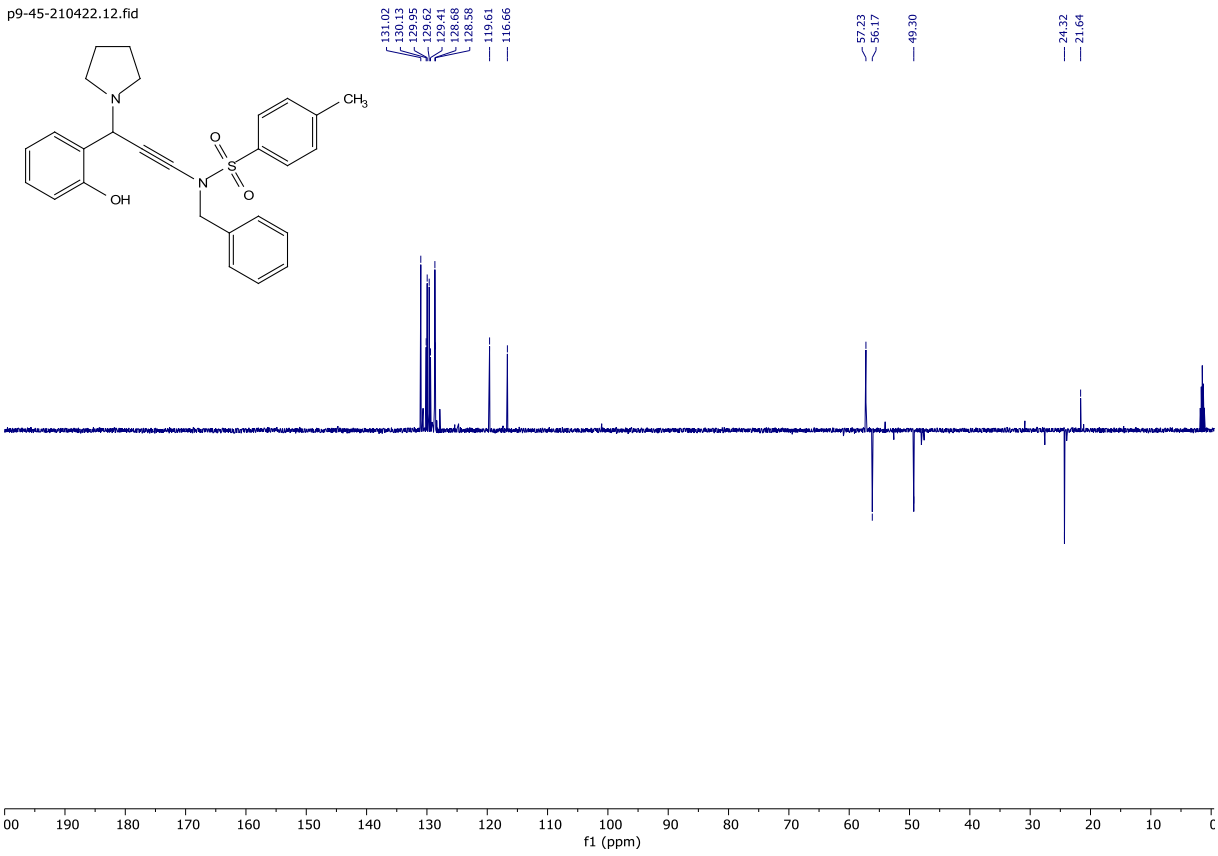
^{1}H NMR (500 MHz) in CD_3CN



^{13}C NMR (126 MHz) in CD_3CN

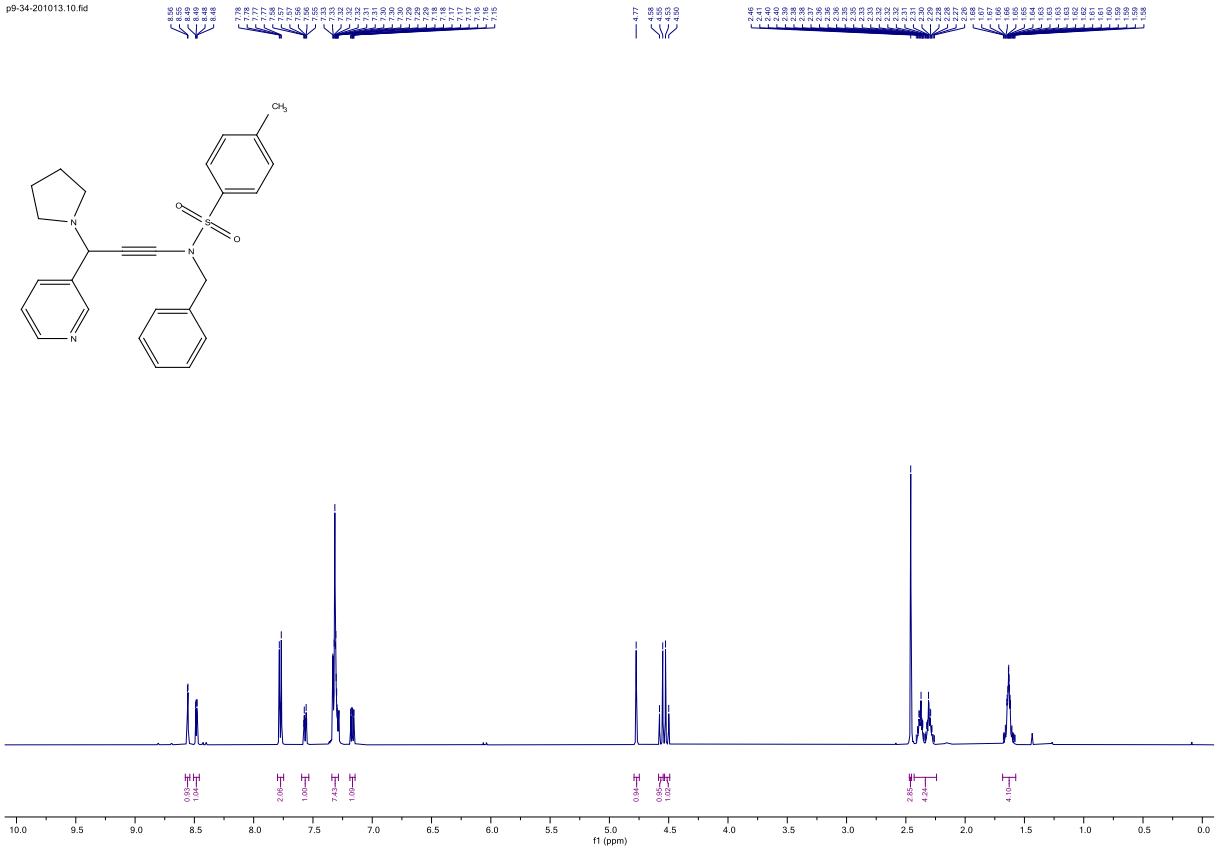


DEPT135 NMR (126 MHz) in CD_3CN

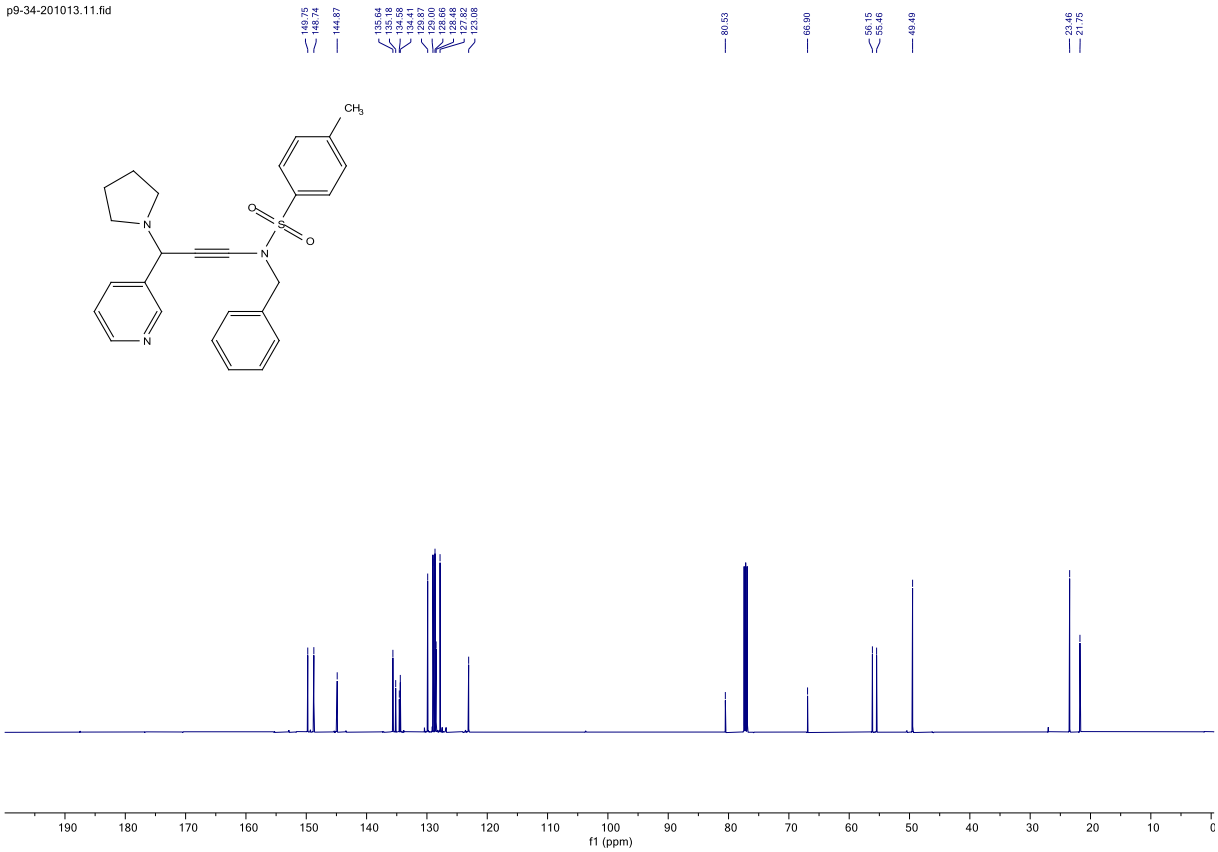


N-Benzyl-4-methyl-*N*-(3-(pyridin-3-yl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**4f**)

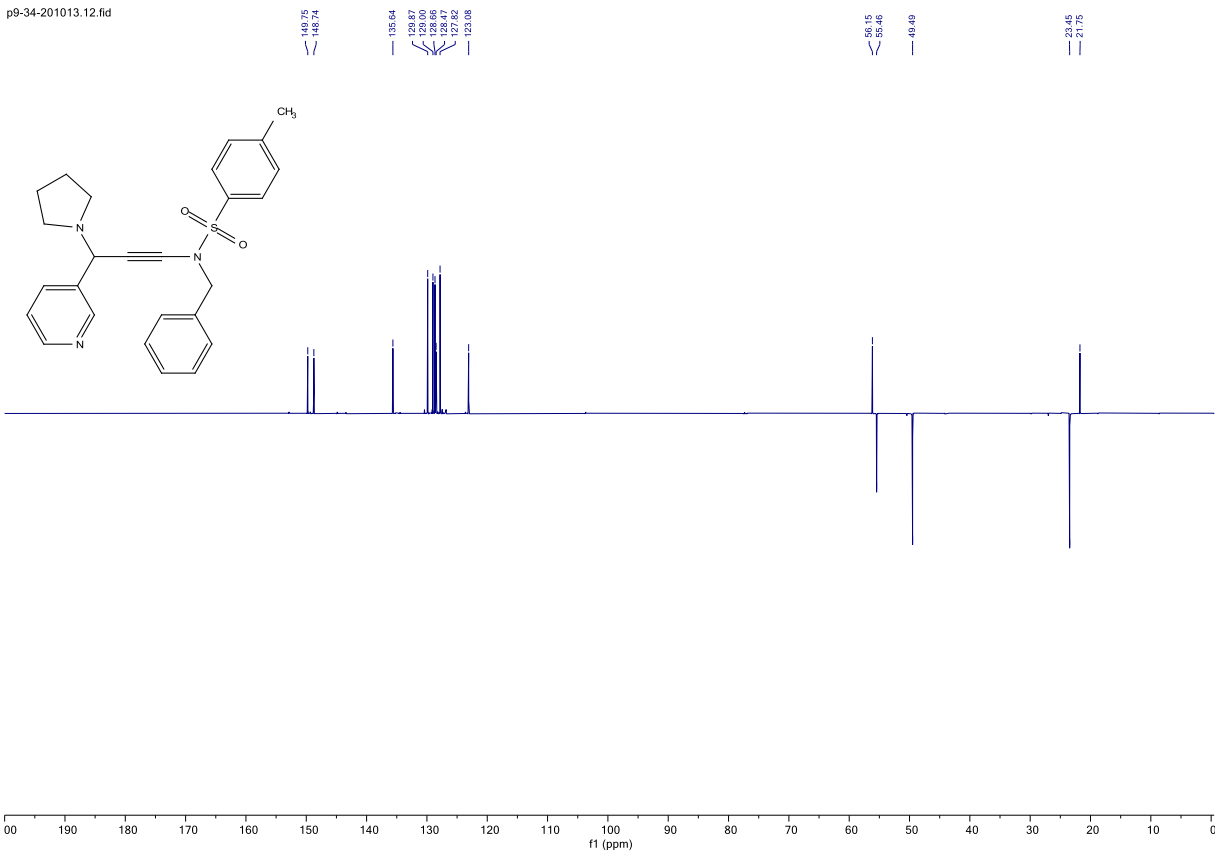
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

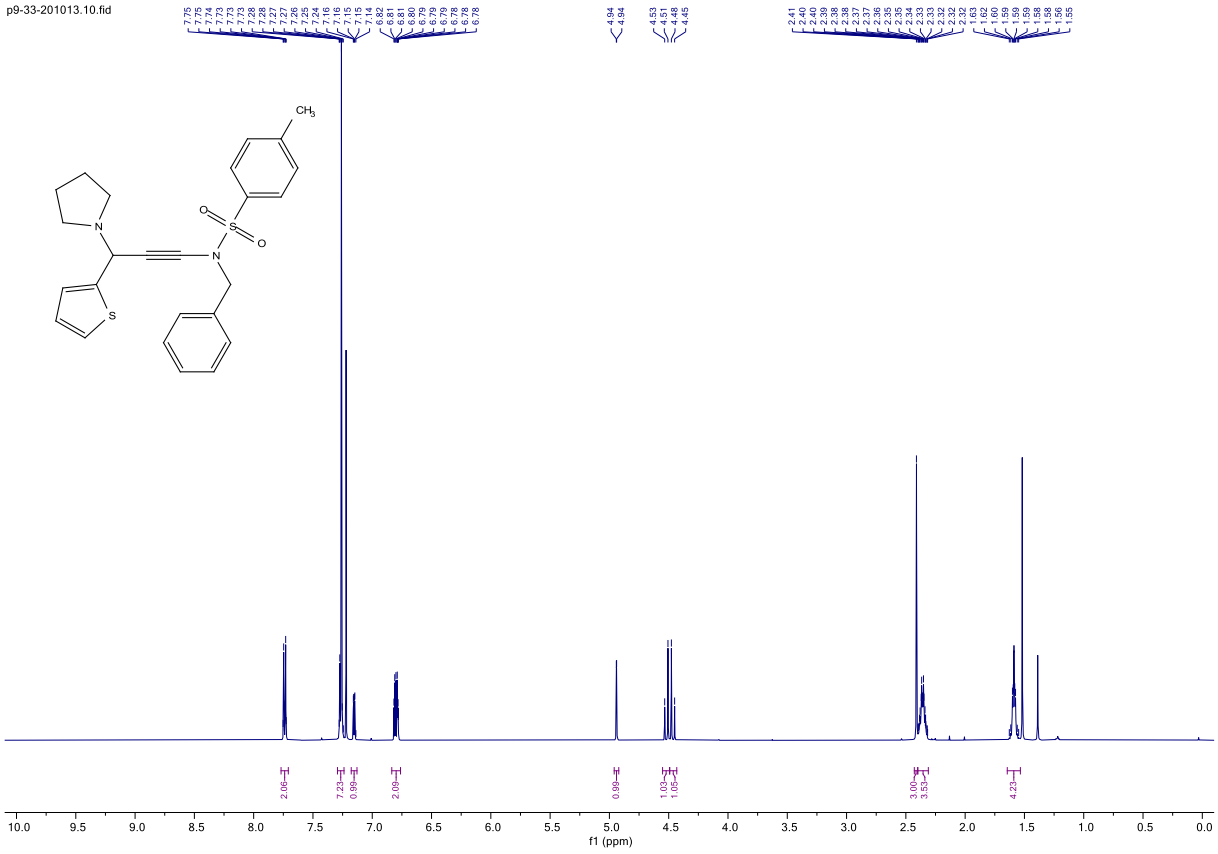


DEPT135 NMR (126 MHz) in $CDCl_3$

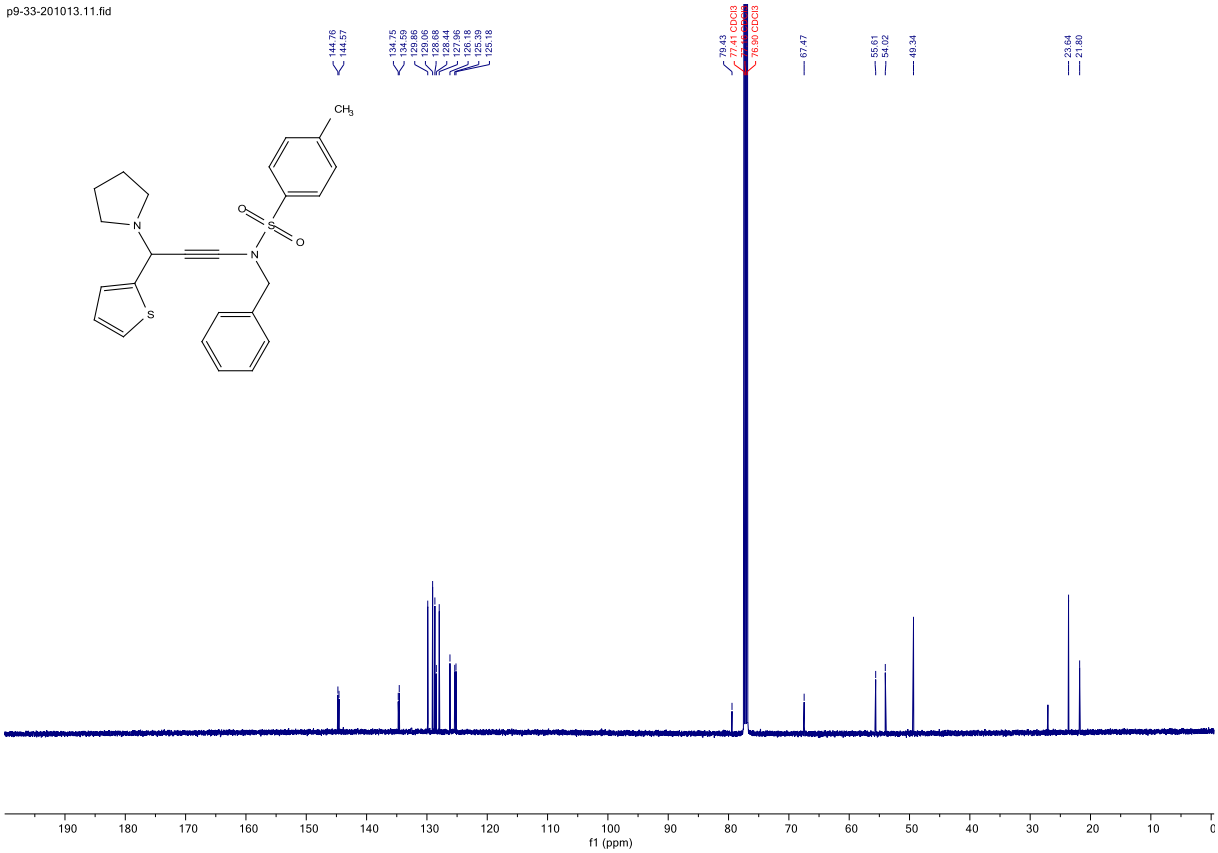


N-Benzyl-4-methyl-*N*-(3-(pyrrolidin-1-yl)-3-(thiophen-2-yl)prop-1-yn-1-yl)benzenesulfonamide (**4g**)

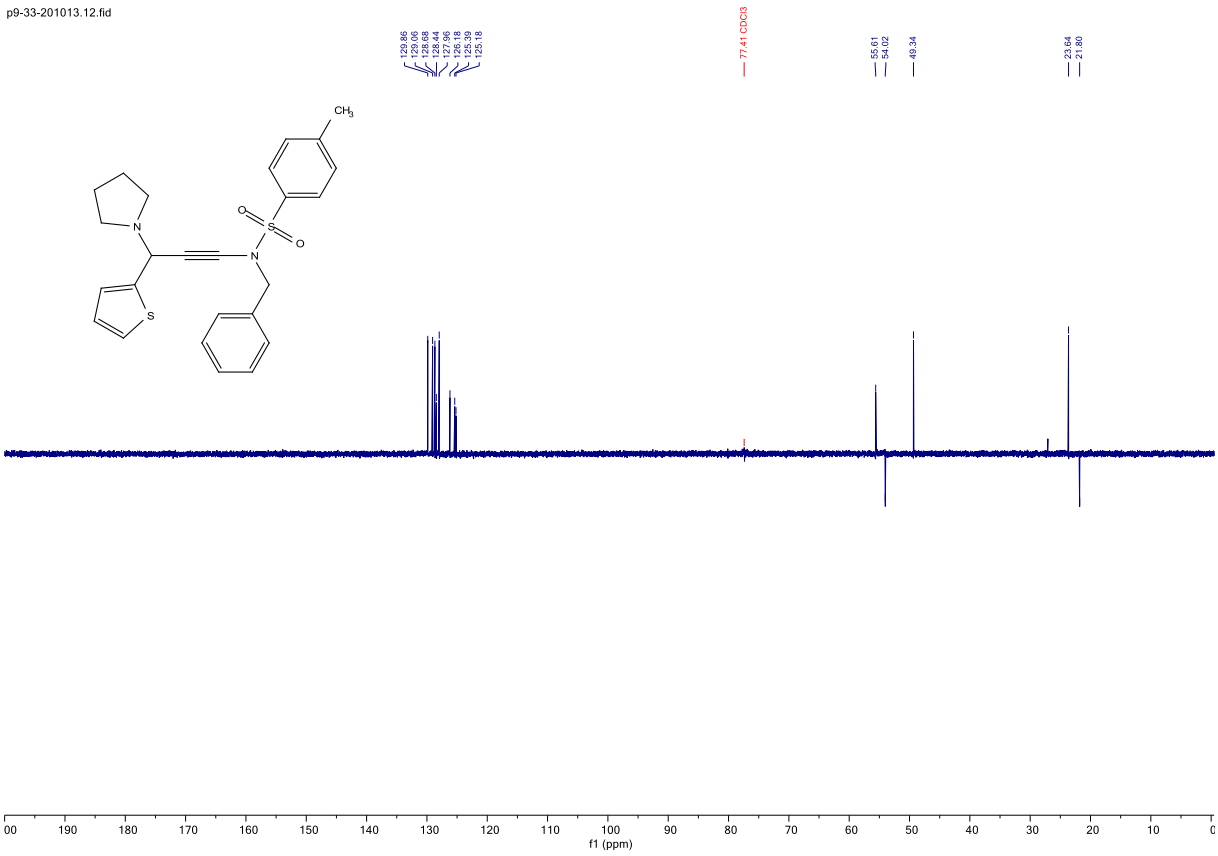
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

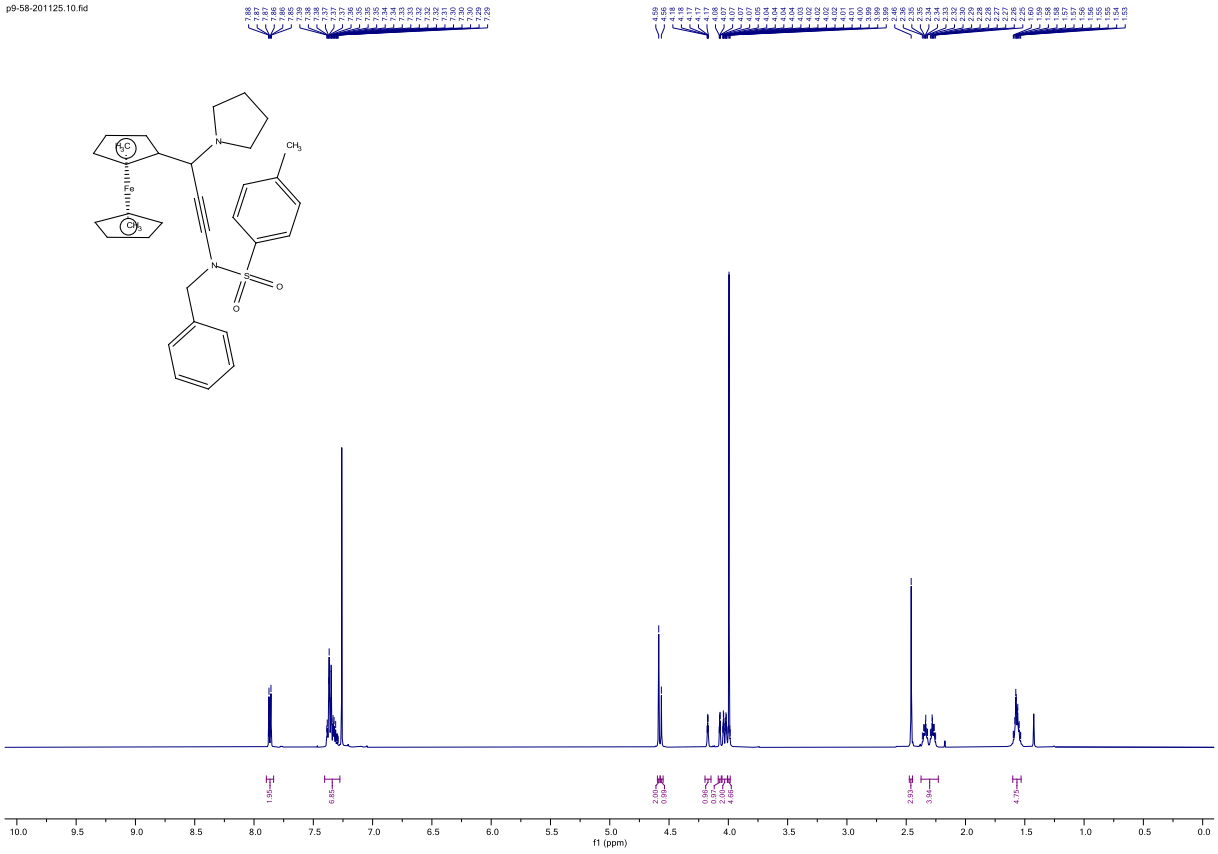


DEPT135 NMR (126 MHz) in $CDCl_3$

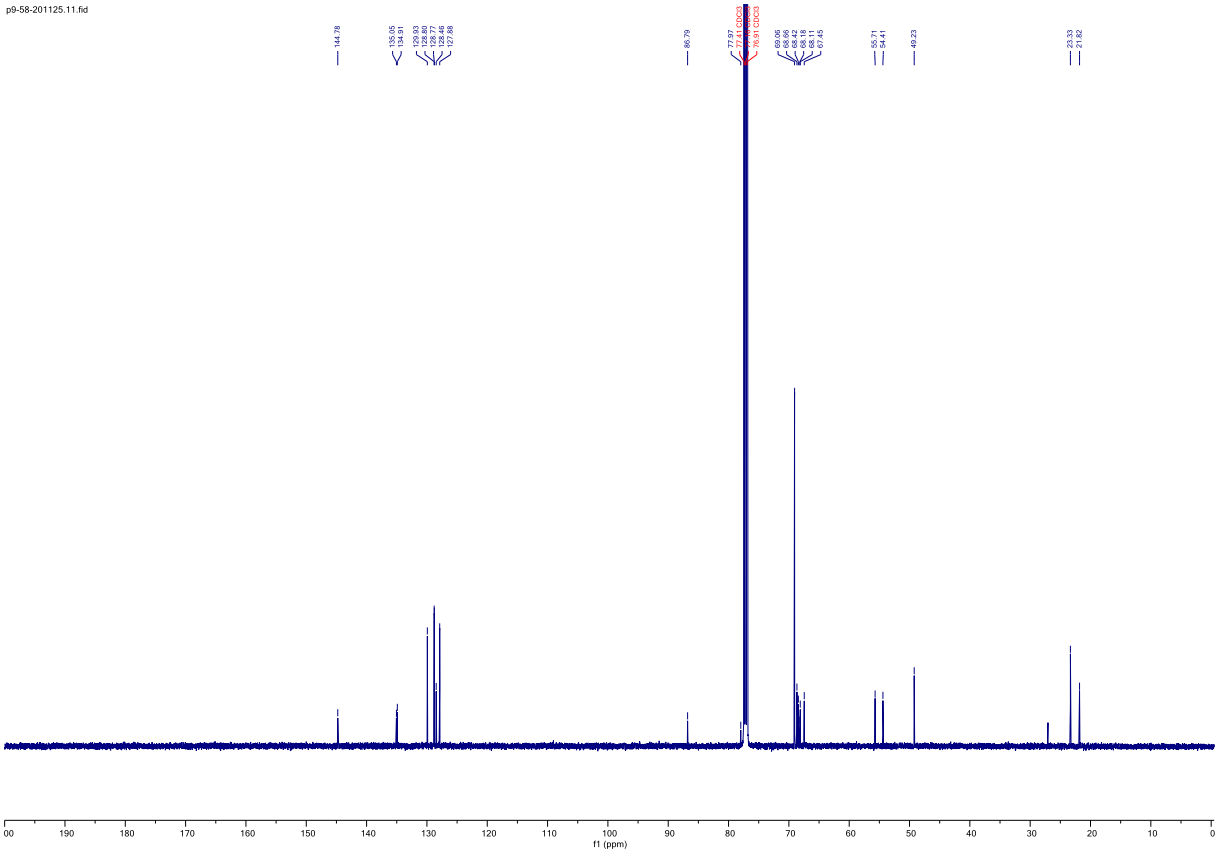


N-Benzyl-4-methyl-*N*-(3-ferrocenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**4h**)

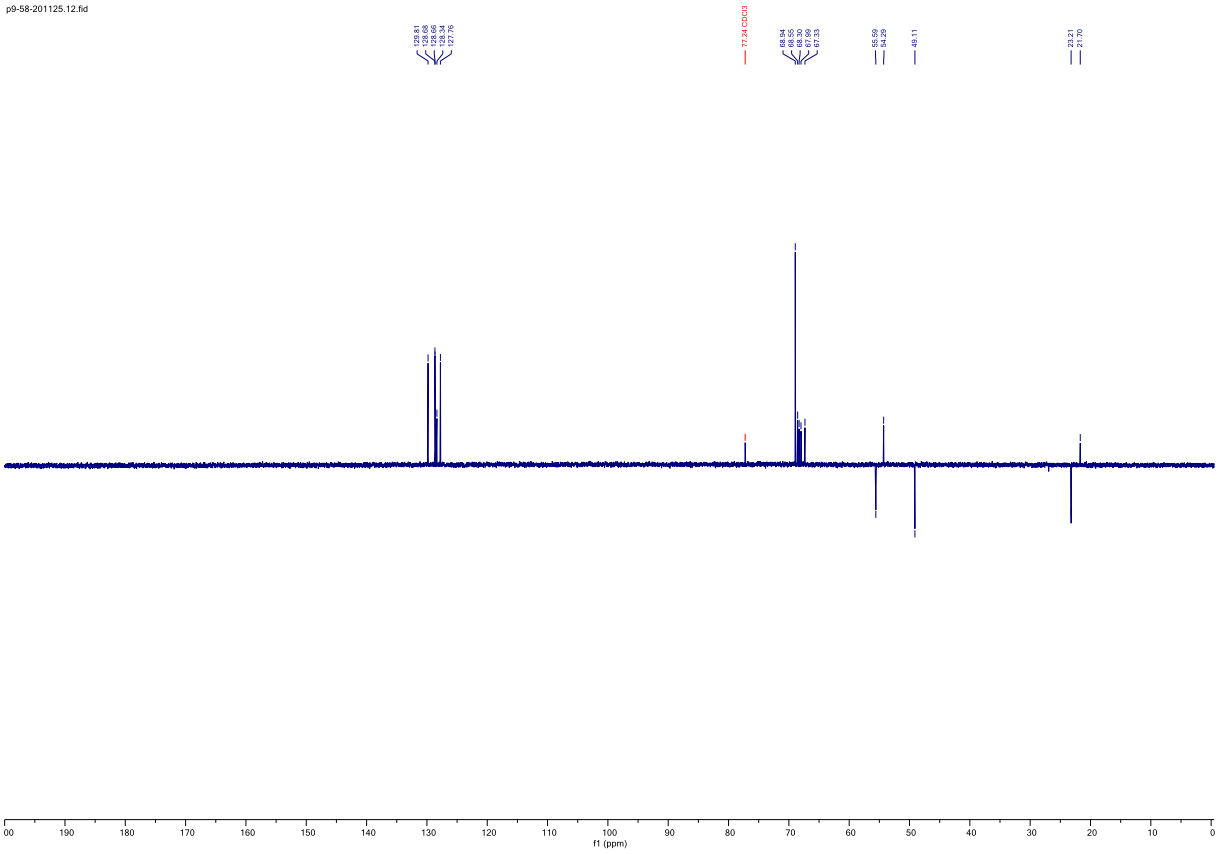
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

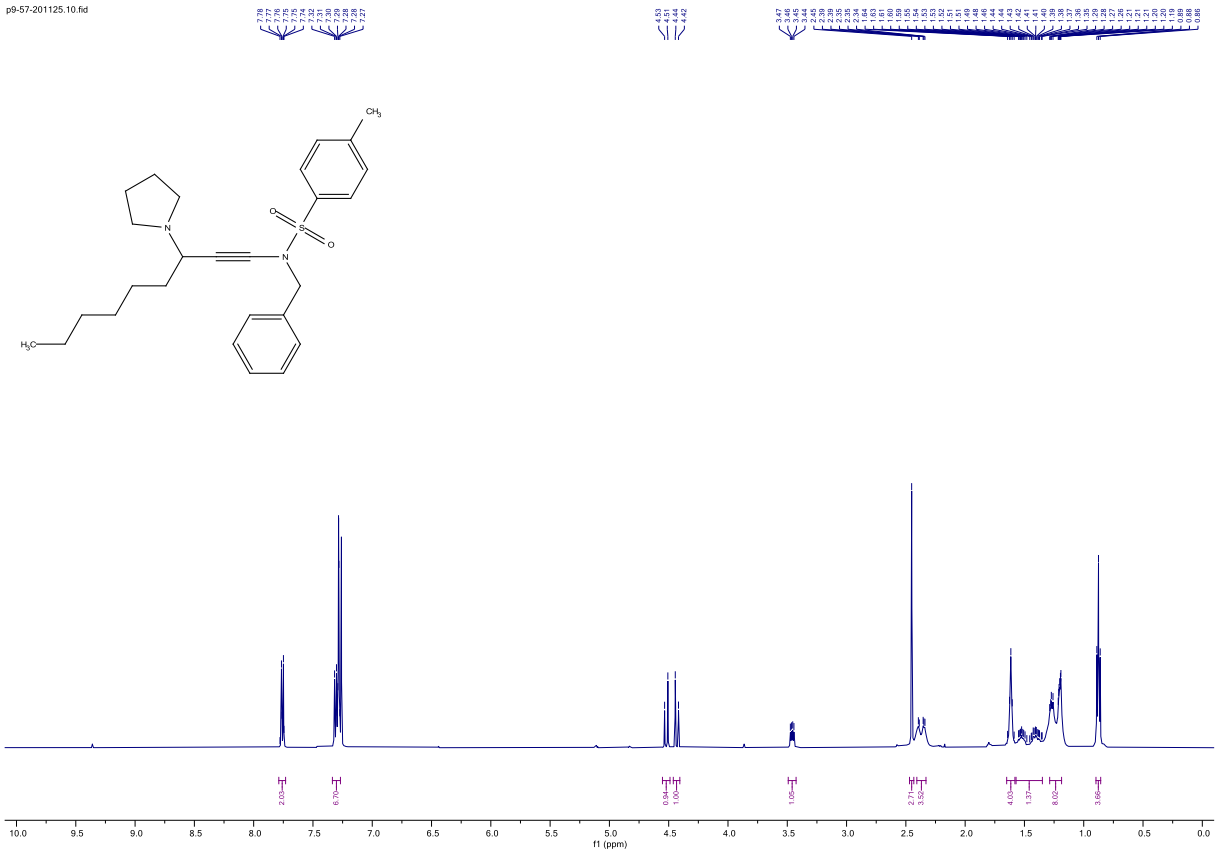


DEPT135 NMR (126 MHz) in $CDCl_3$

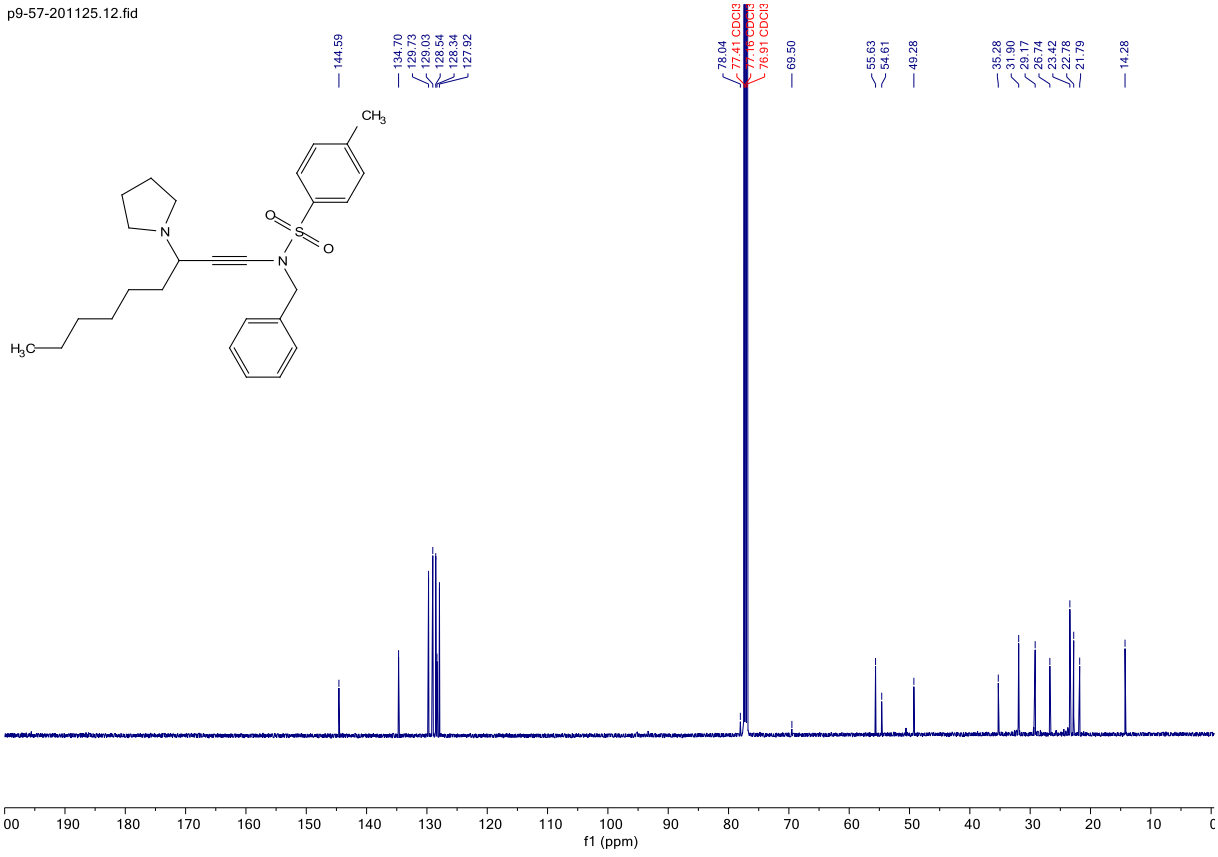


N-Benzyl-4-methyl-*N*-(3-(pyrrolidin-1-yl)non-1-yn-1-yl)benzenesulfonamide (**4i**)

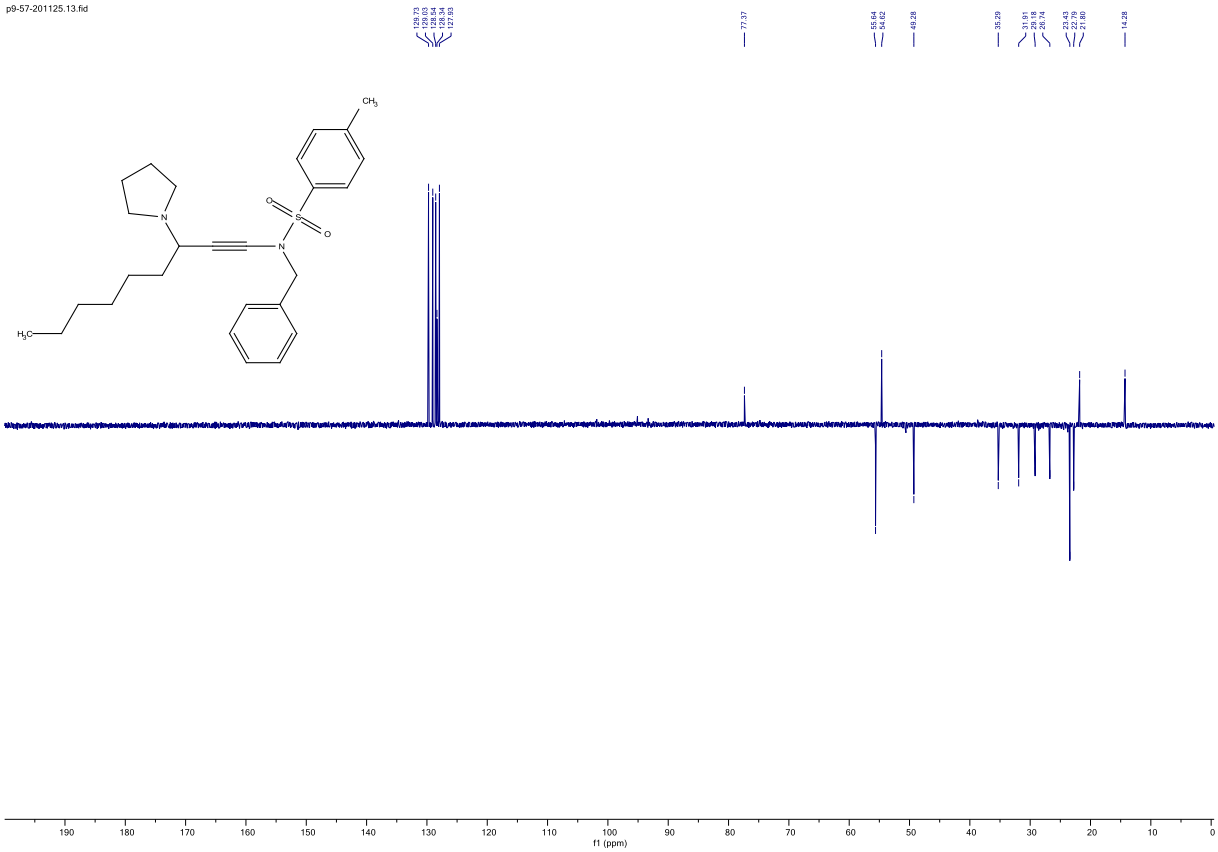
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

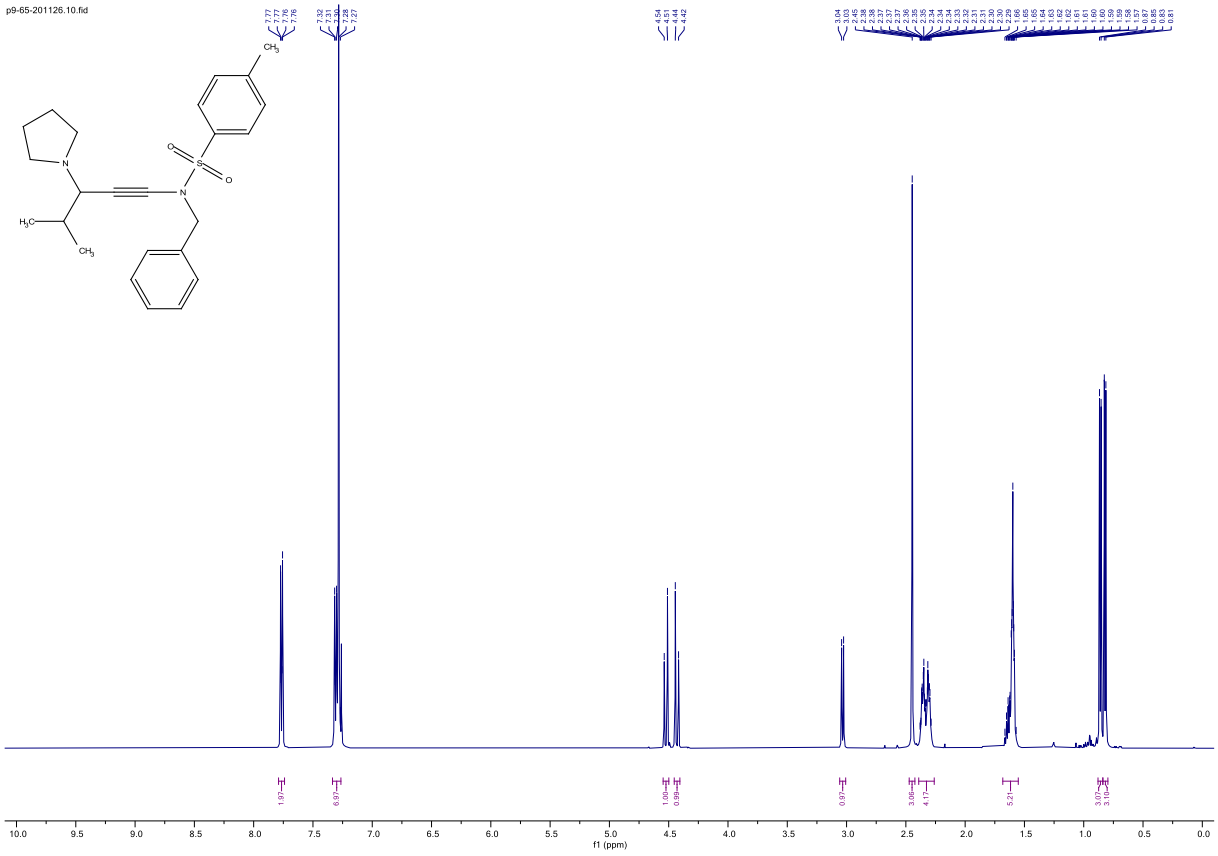


DEPT135 NMR (126 MHz) in $CDCl_3$

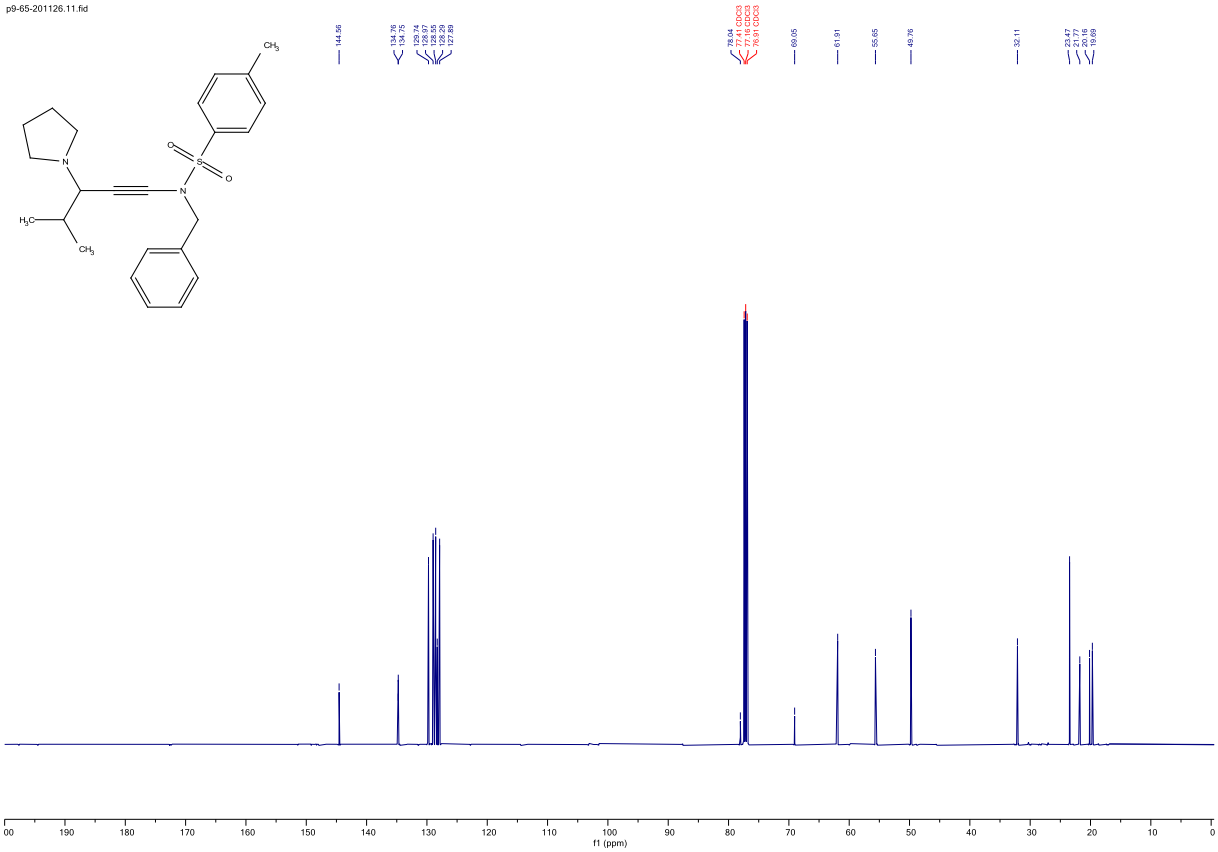


N-Benzyl-4-methyl-*N*-(4-methyl-3-(pyrrolidin-1-yl)pent-1-yn-1-yl)benzenesulfonamide (**4j**)

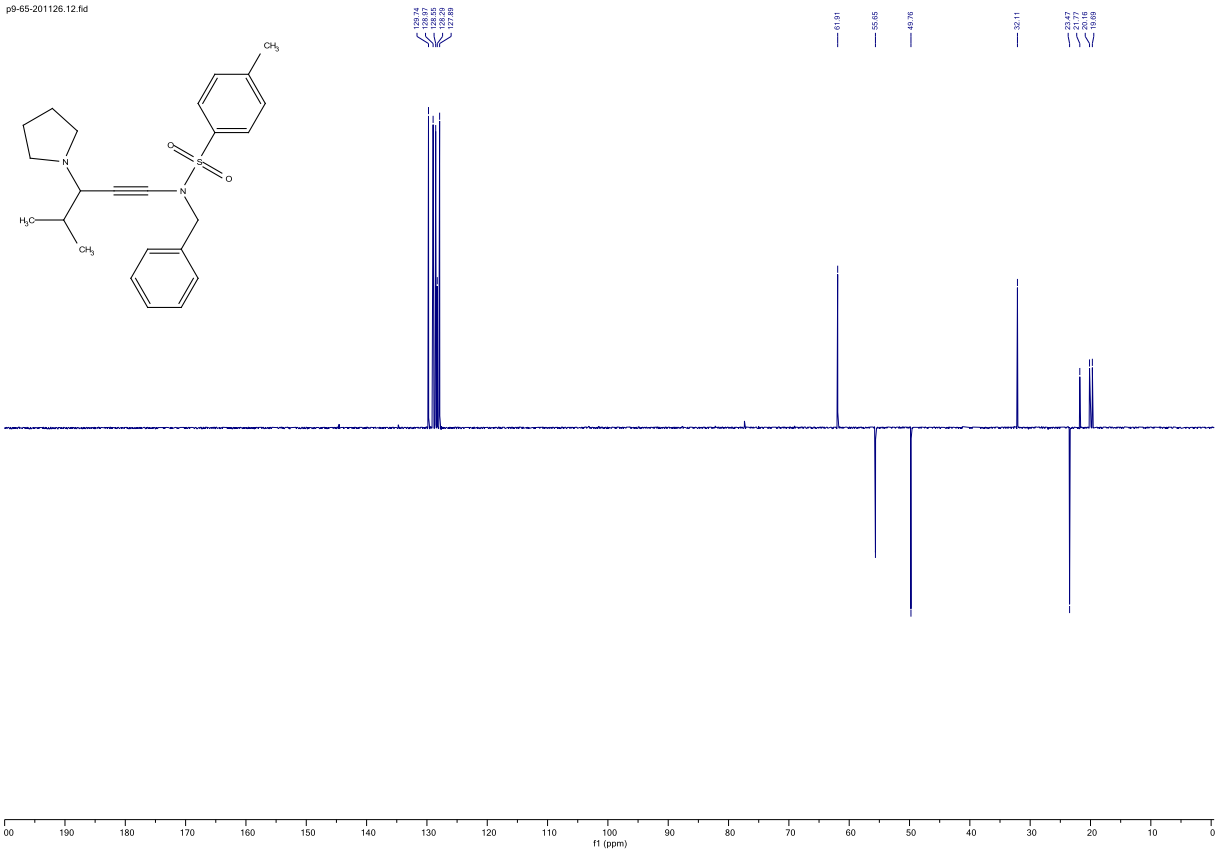
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

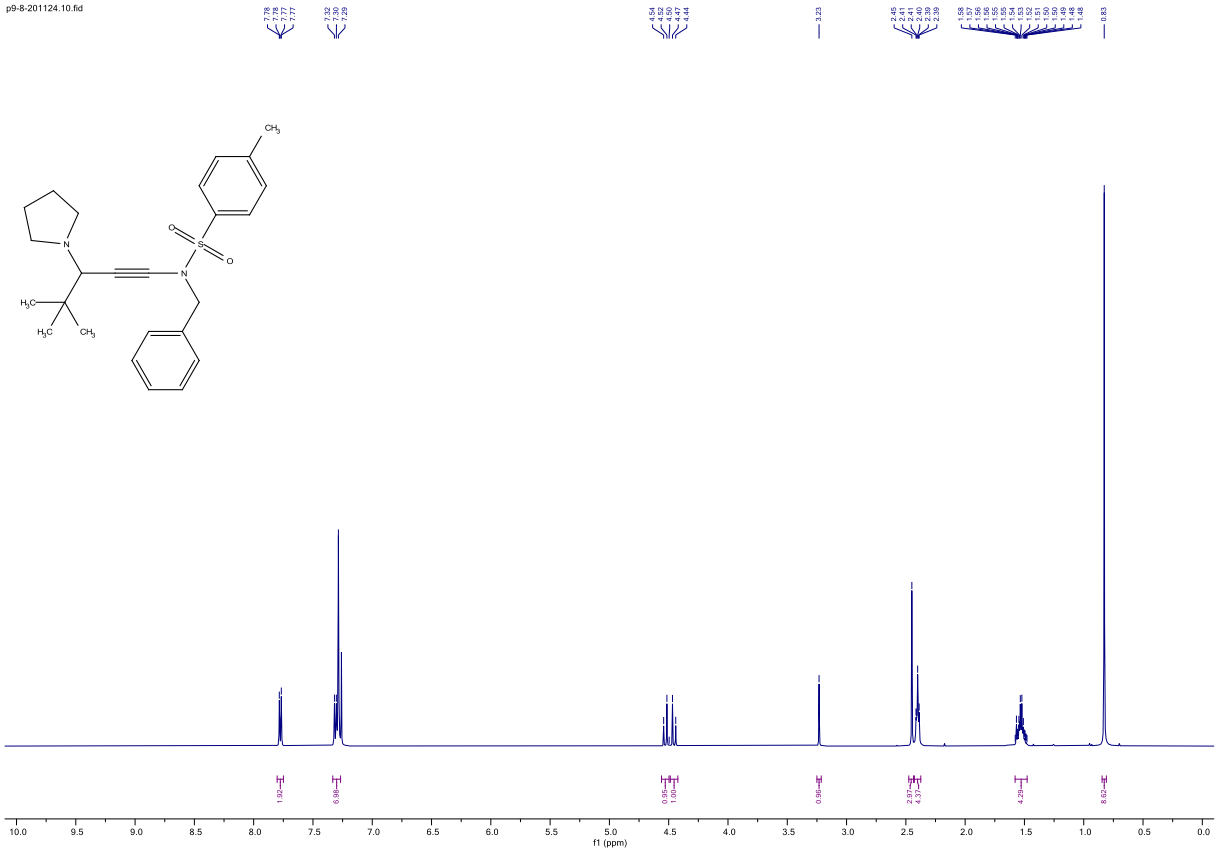


DEPT135 NMR (126 MHz) in $CDCl_3$

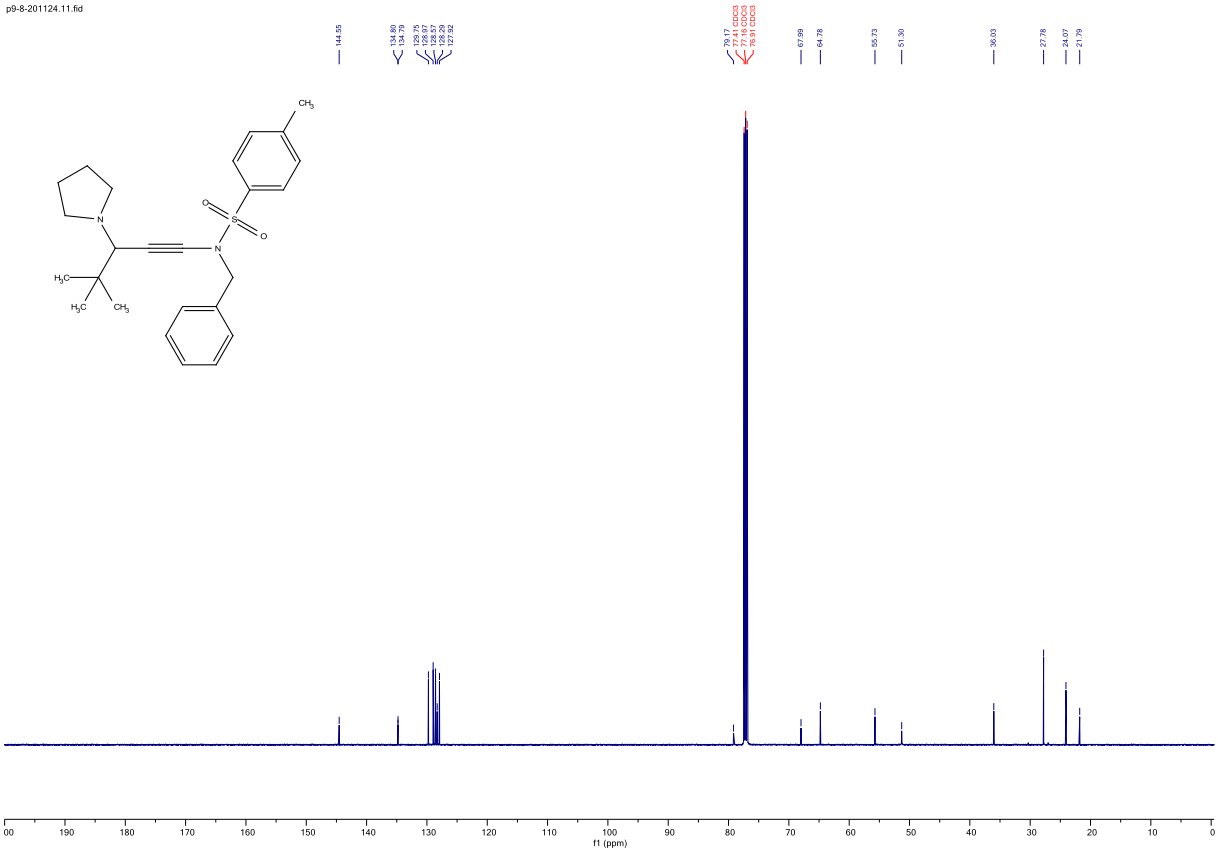


N-Benzyl-*N*-(4,4-dimethyl-3-(pyrrolidin-1-yl)pent-1-yn-1-yl)-4-methylbenzenesulfonamide (**4k**)

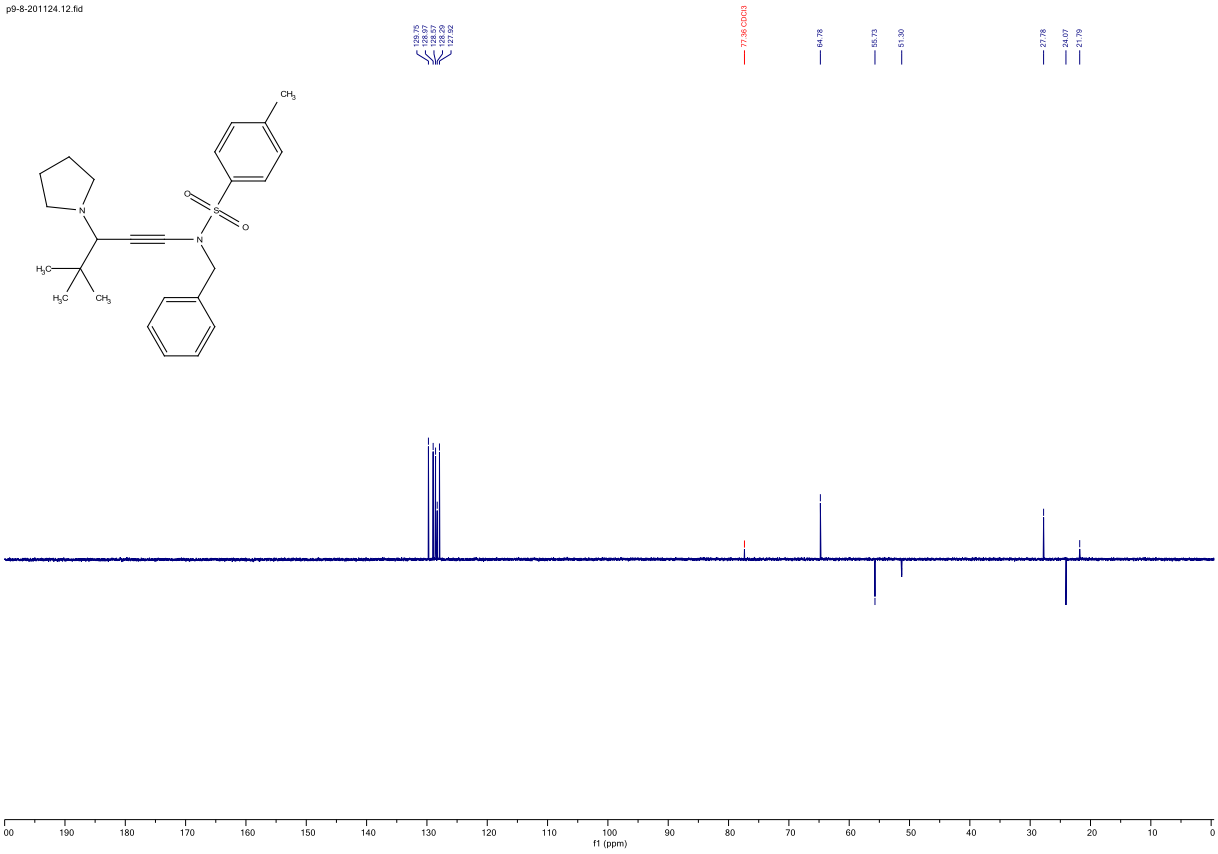
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

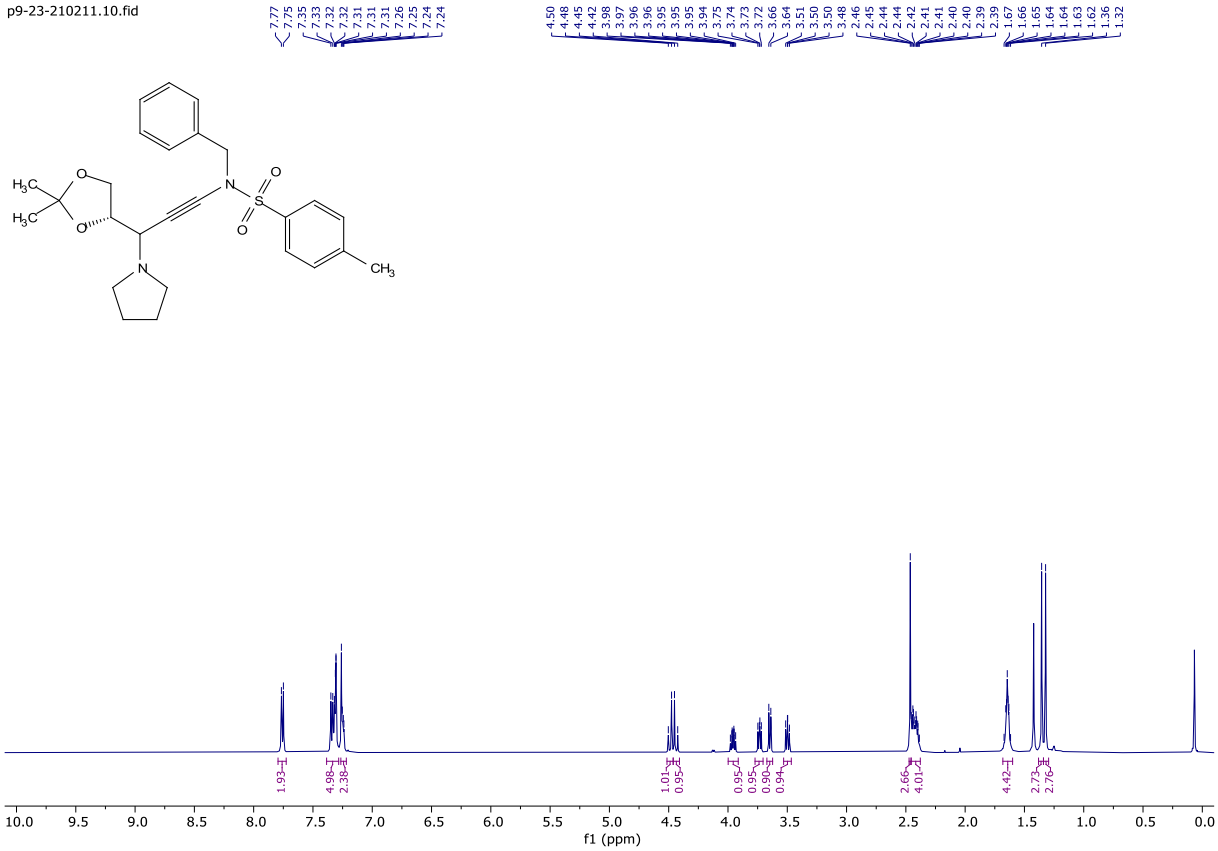


DEPT135 NMR (126 MHz) in $CDCl_3$



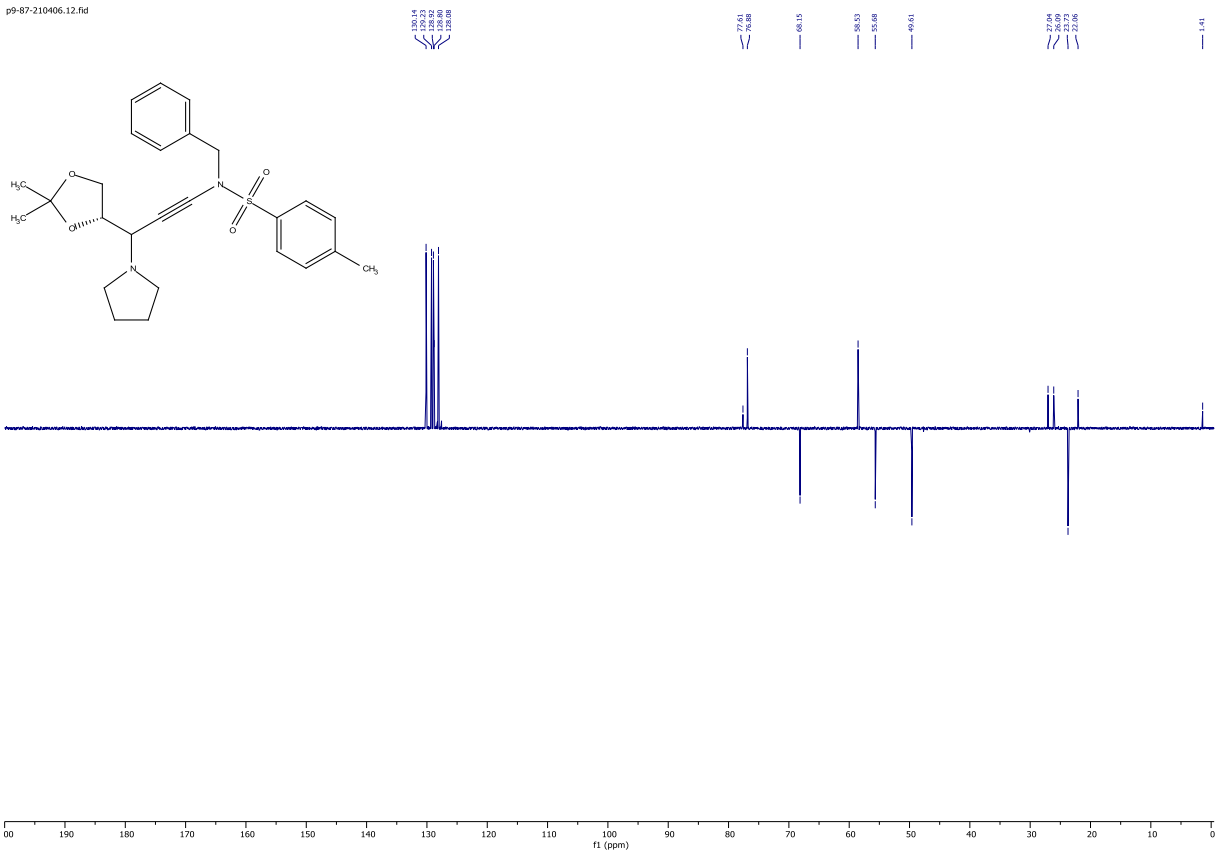
N-Benzyl-*N*-(3-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)-4-methylbenzenesulfonamide (**4l**)

^{1}H NMR (500 MHz) in $CDCl_3$



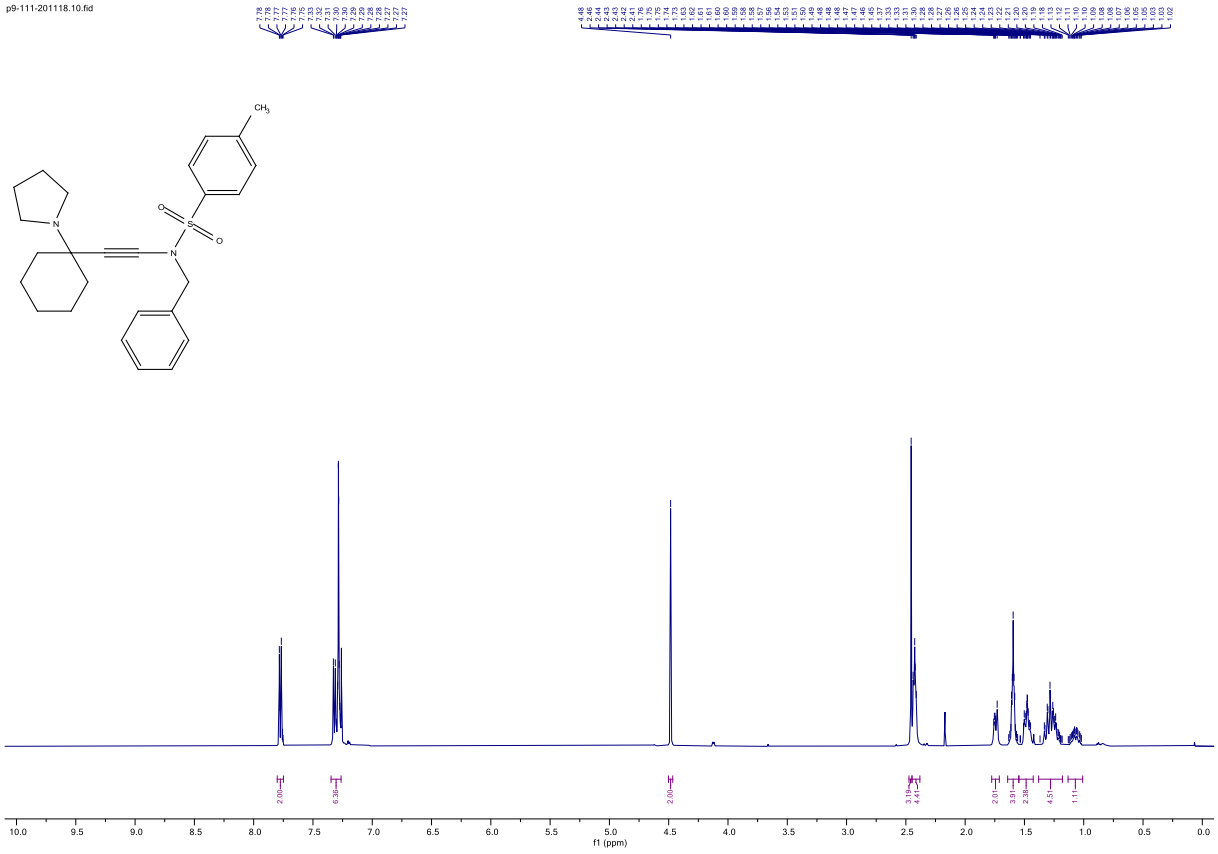
^{13}C NMR (126 MHz) in $CDCl_3$

DEPT135 NMR (126 MHz) in $CDCl_3$

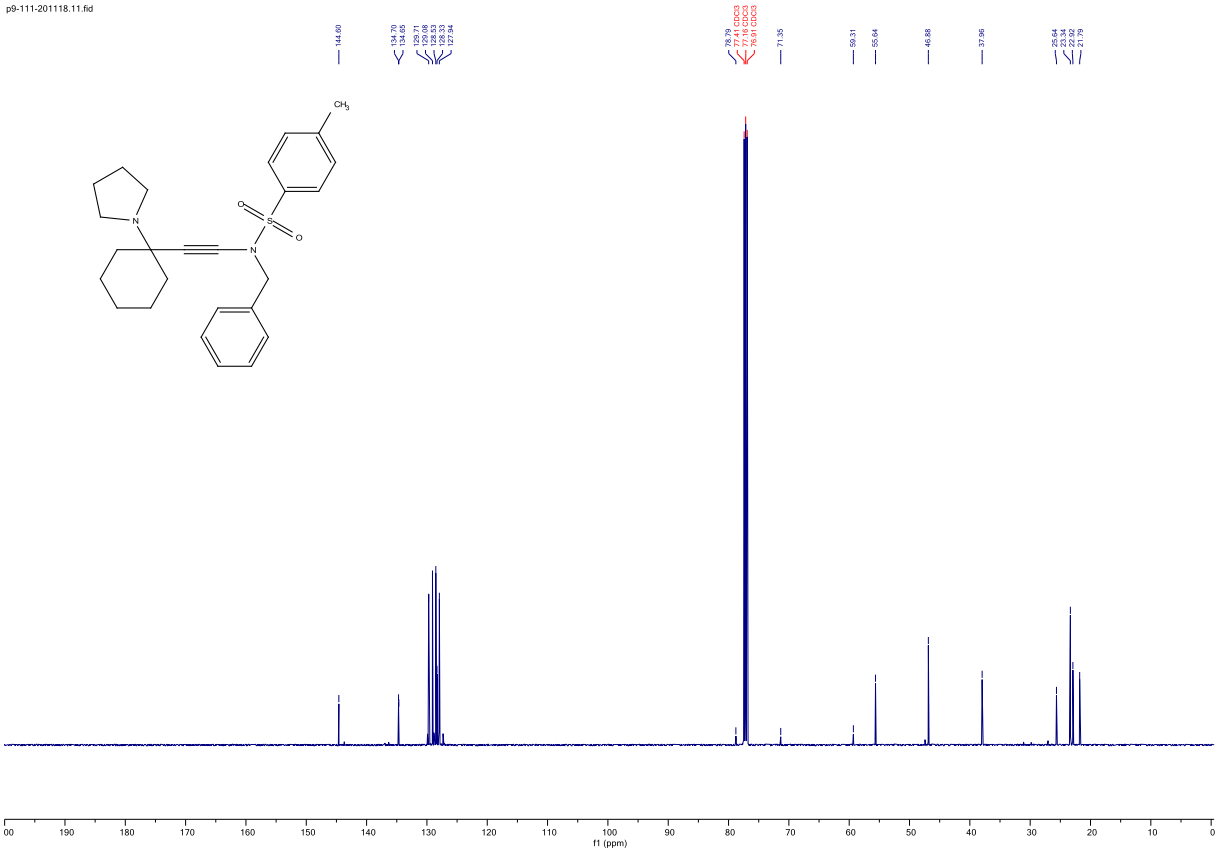


N-Benzyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**4m**)

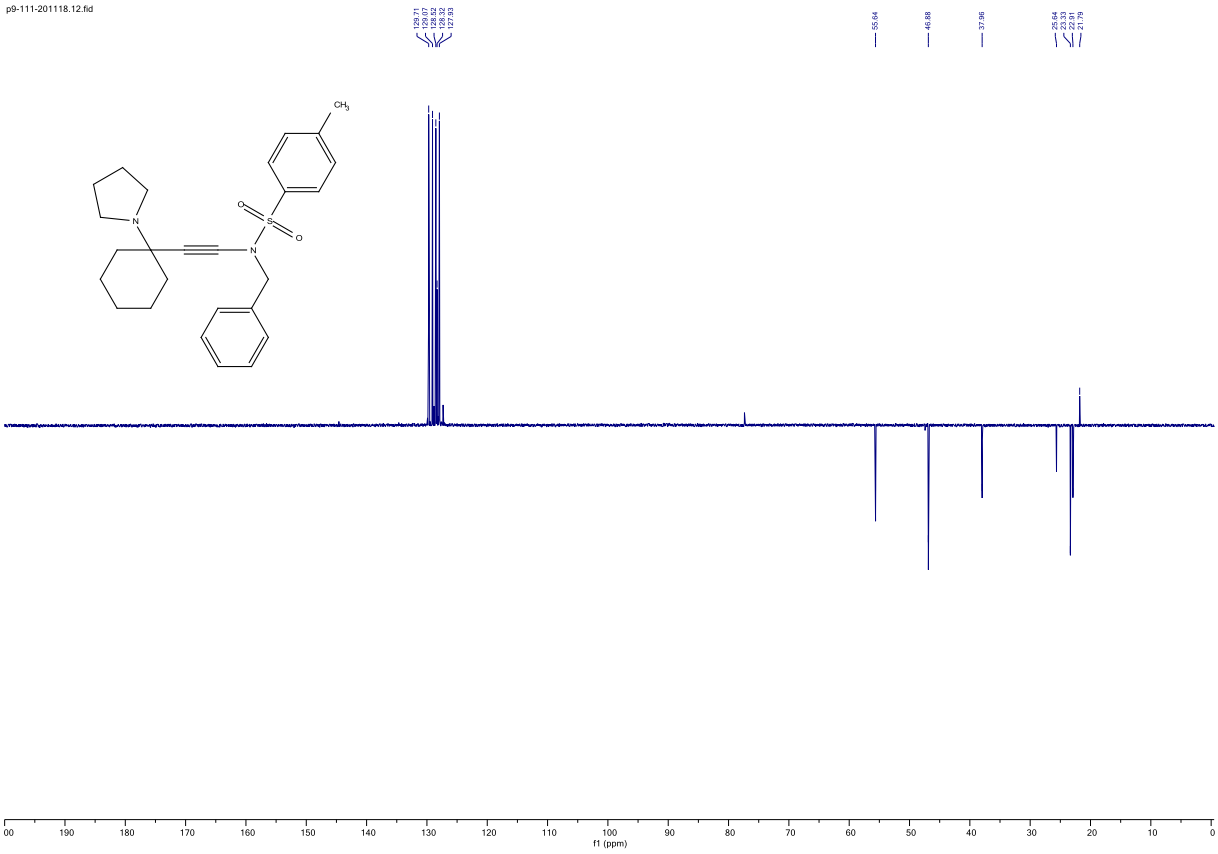
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

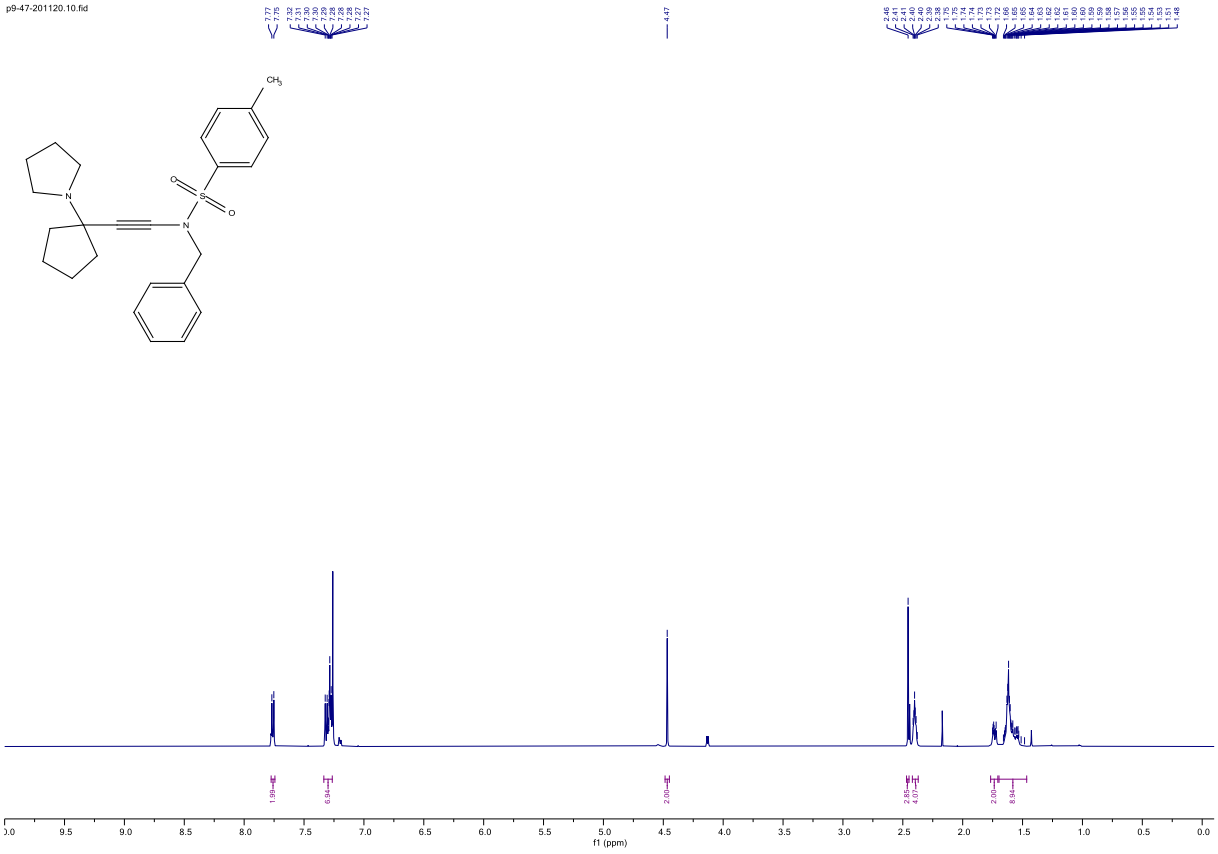


DEPT135 NMR (126 MHz) in $CDCl_3$

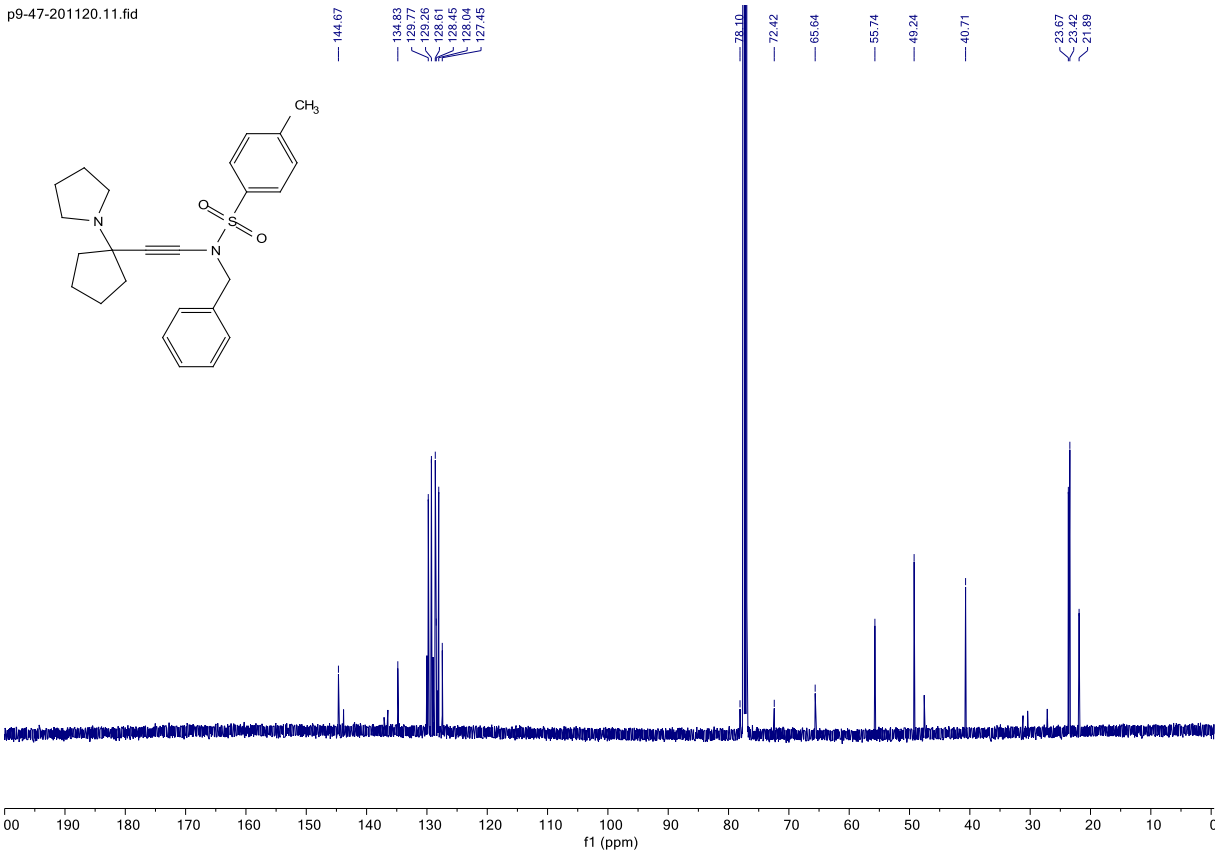


N-Benzyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cyclopentyl)ethynyl)benzenesulfonamide (**4n**)

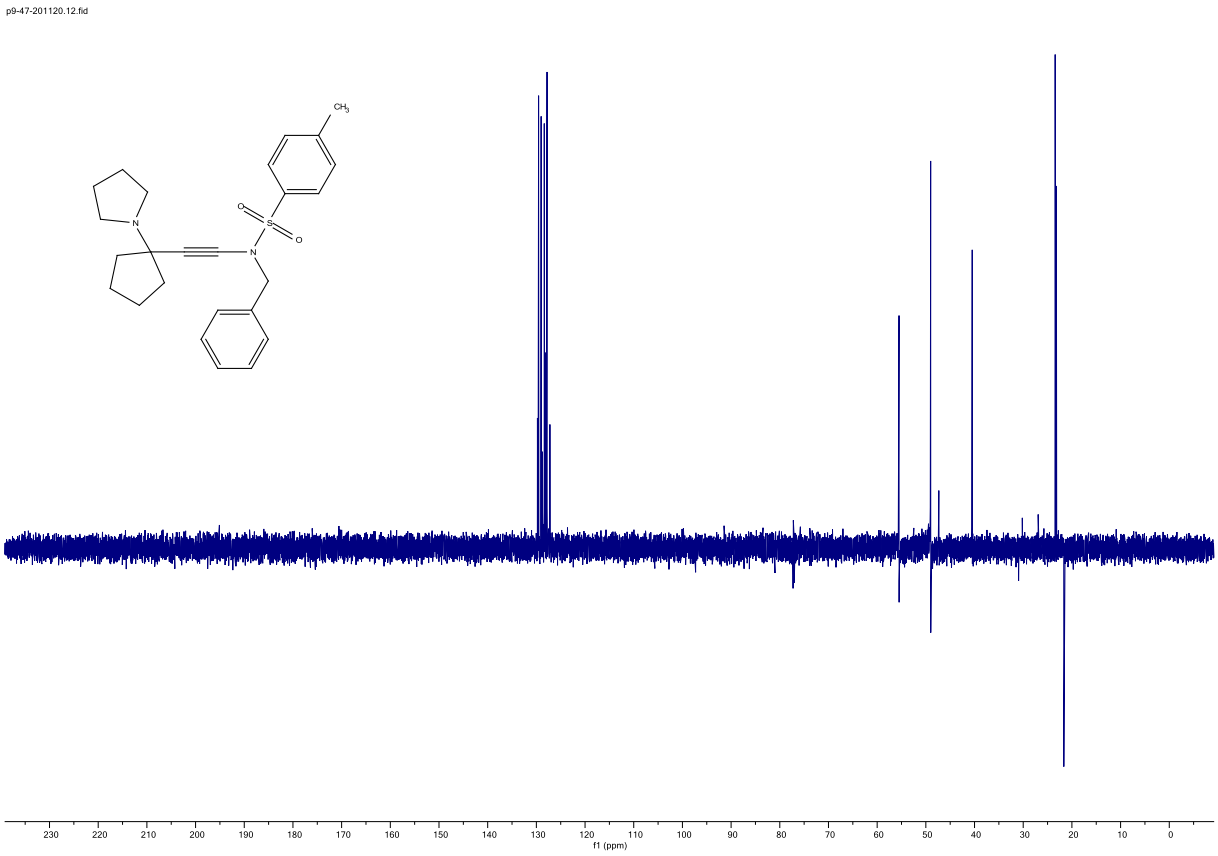
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

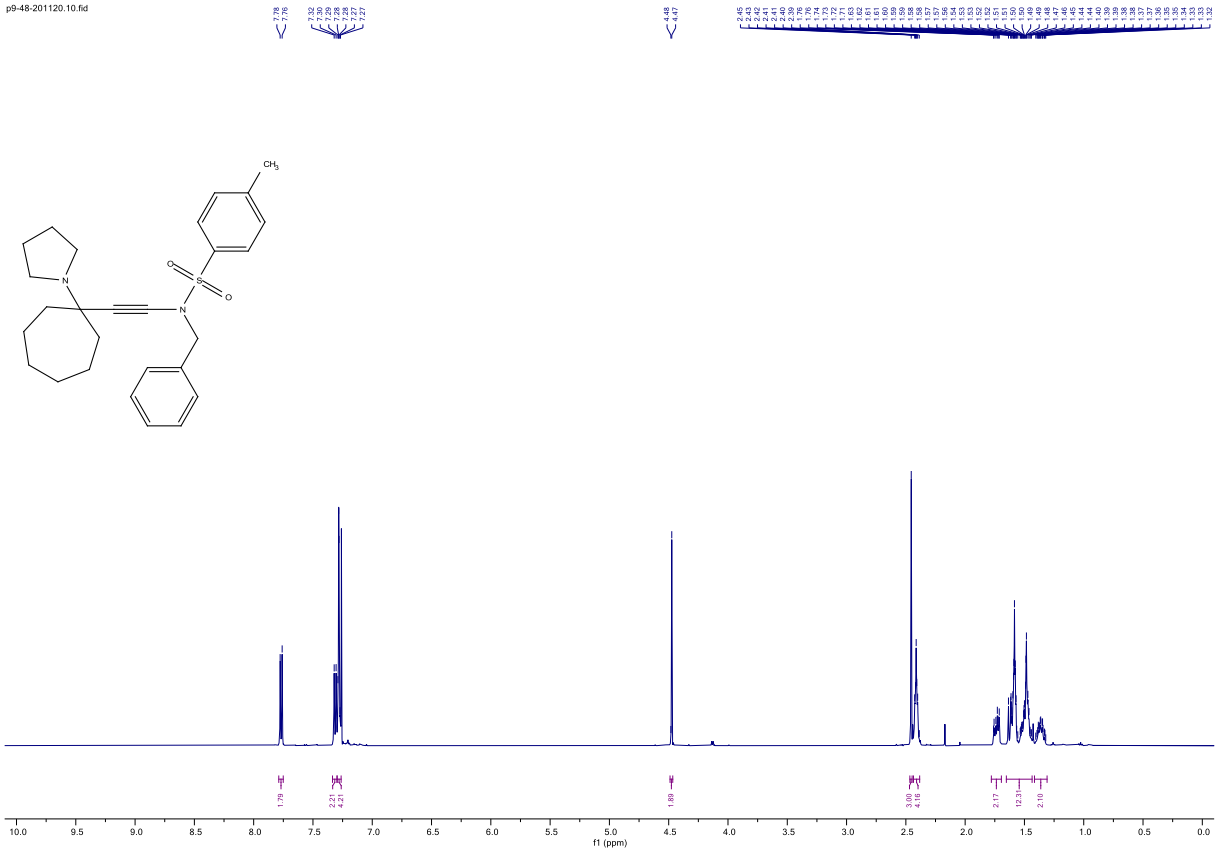


DEPT135 NMR (126 MHz) in $CDCl_3$

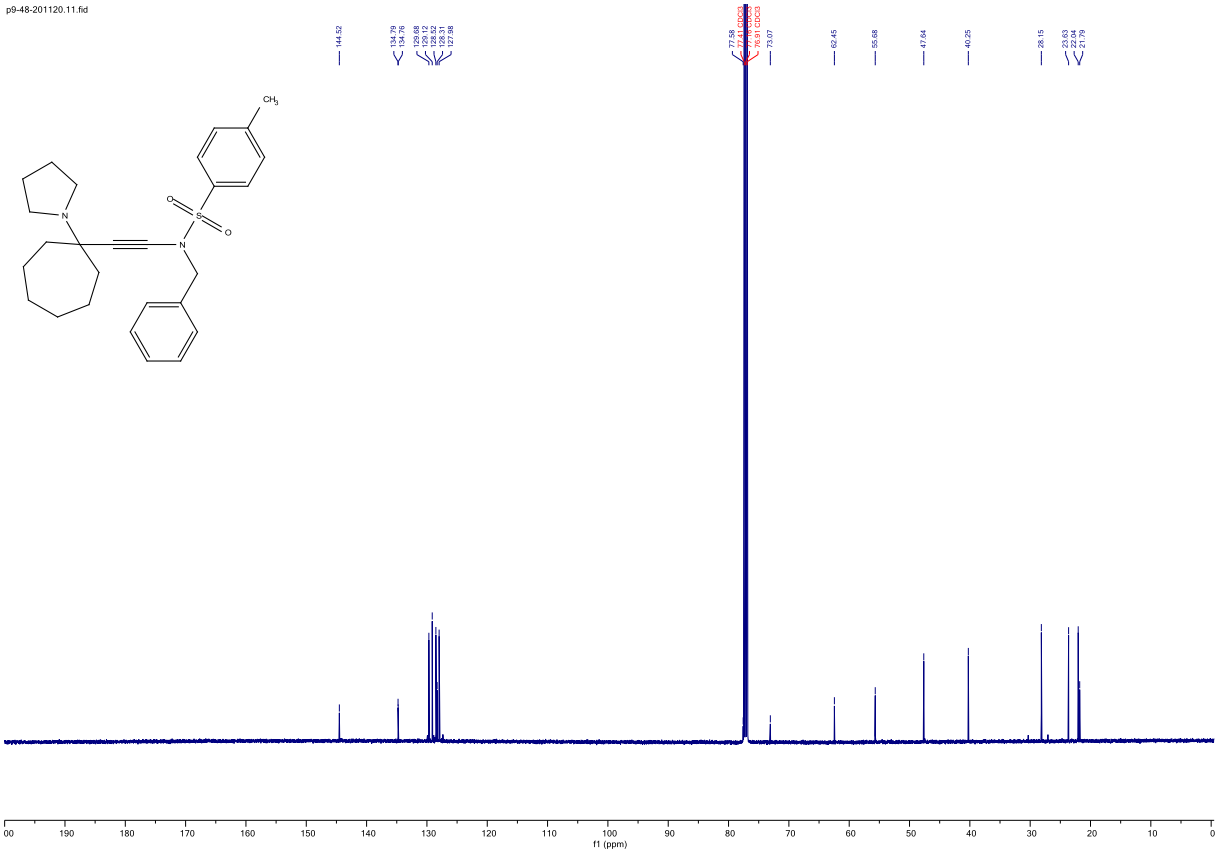


N-Benzyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cycloheptyl)ethynyl)benzenesulfonamide (**4o**)

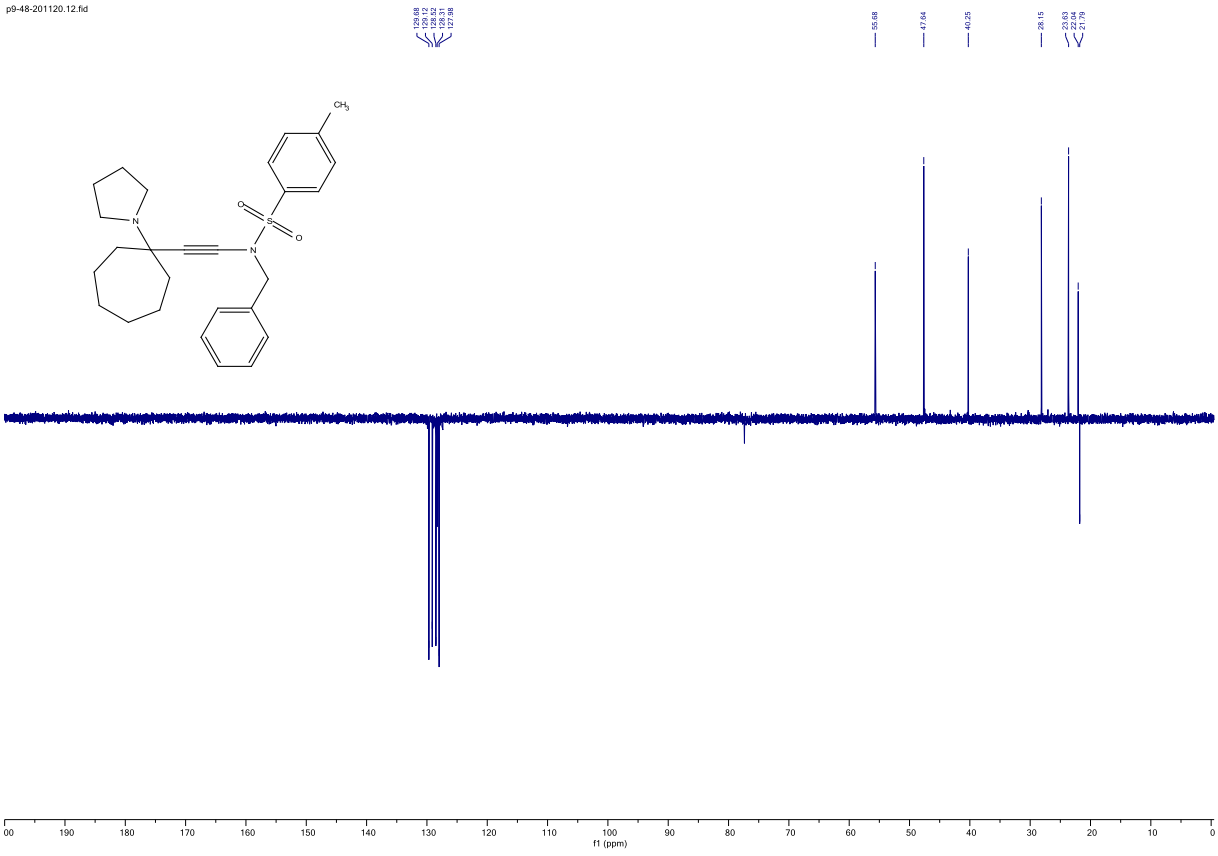
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

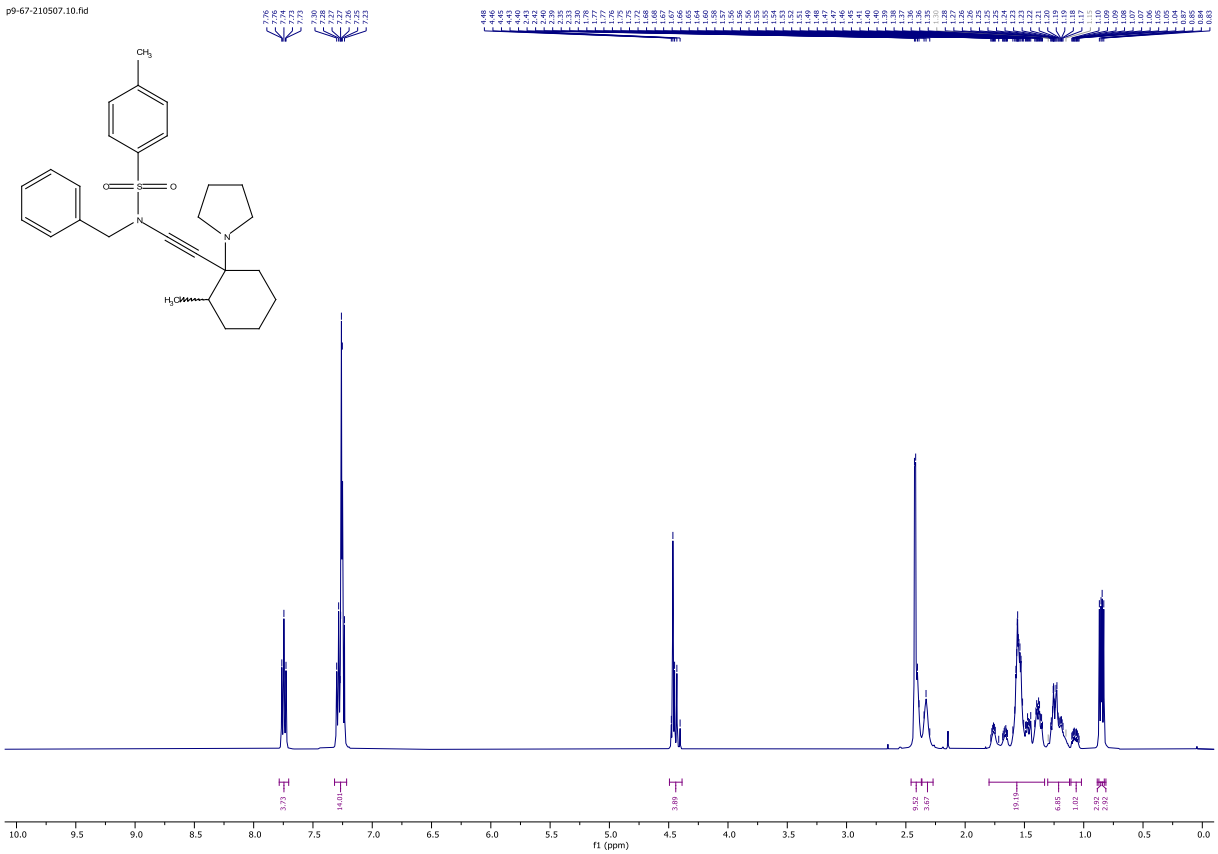


DEPT135 NMR (126 MHz) in $CDCl_3$

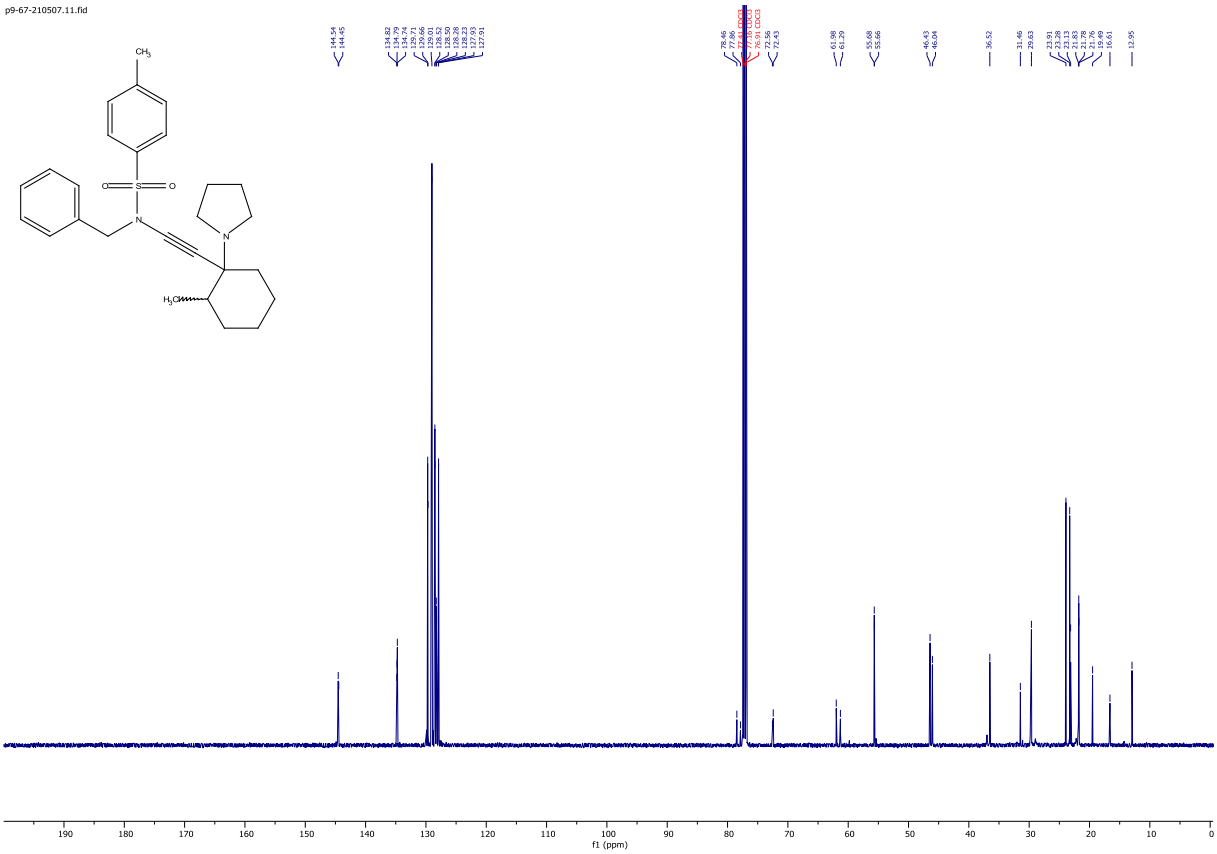


N-Benzyl-4-methyl-*N*-((2-methyl-1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**4p**)

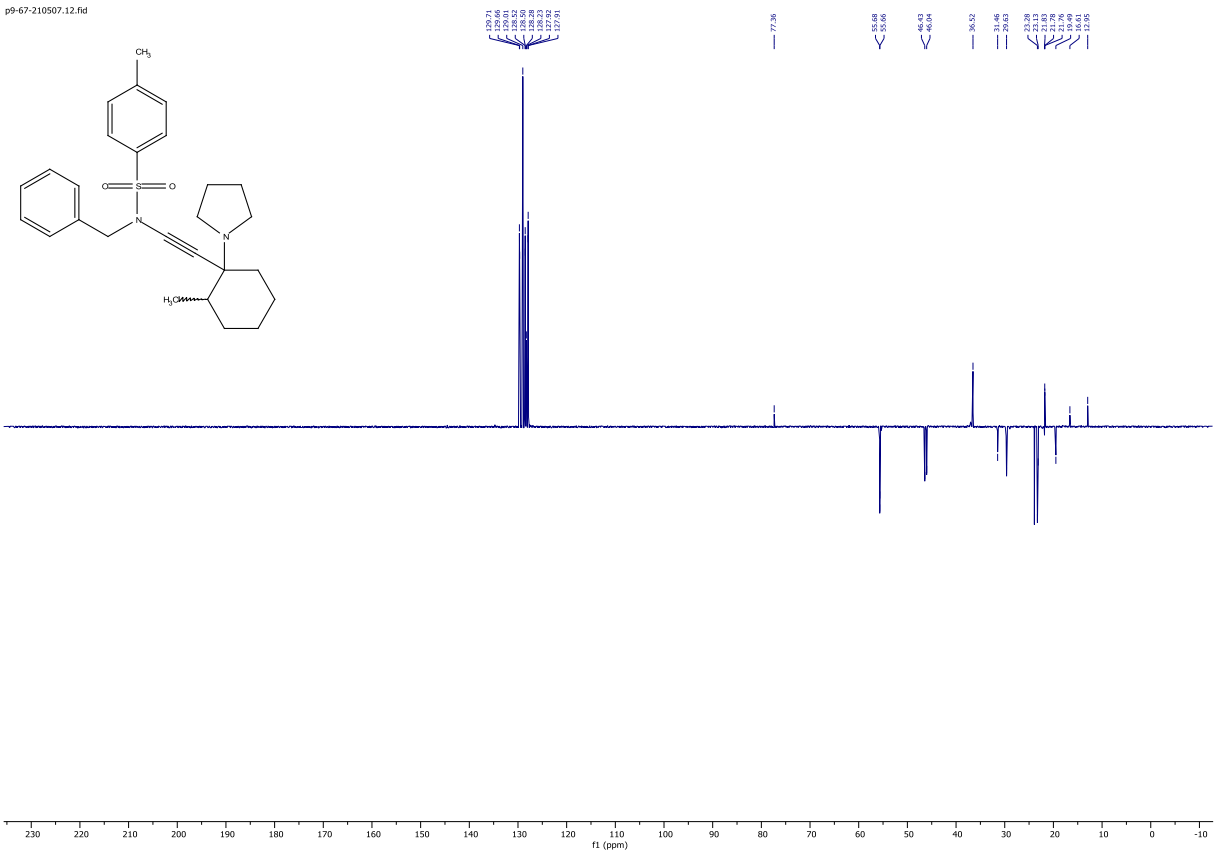
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

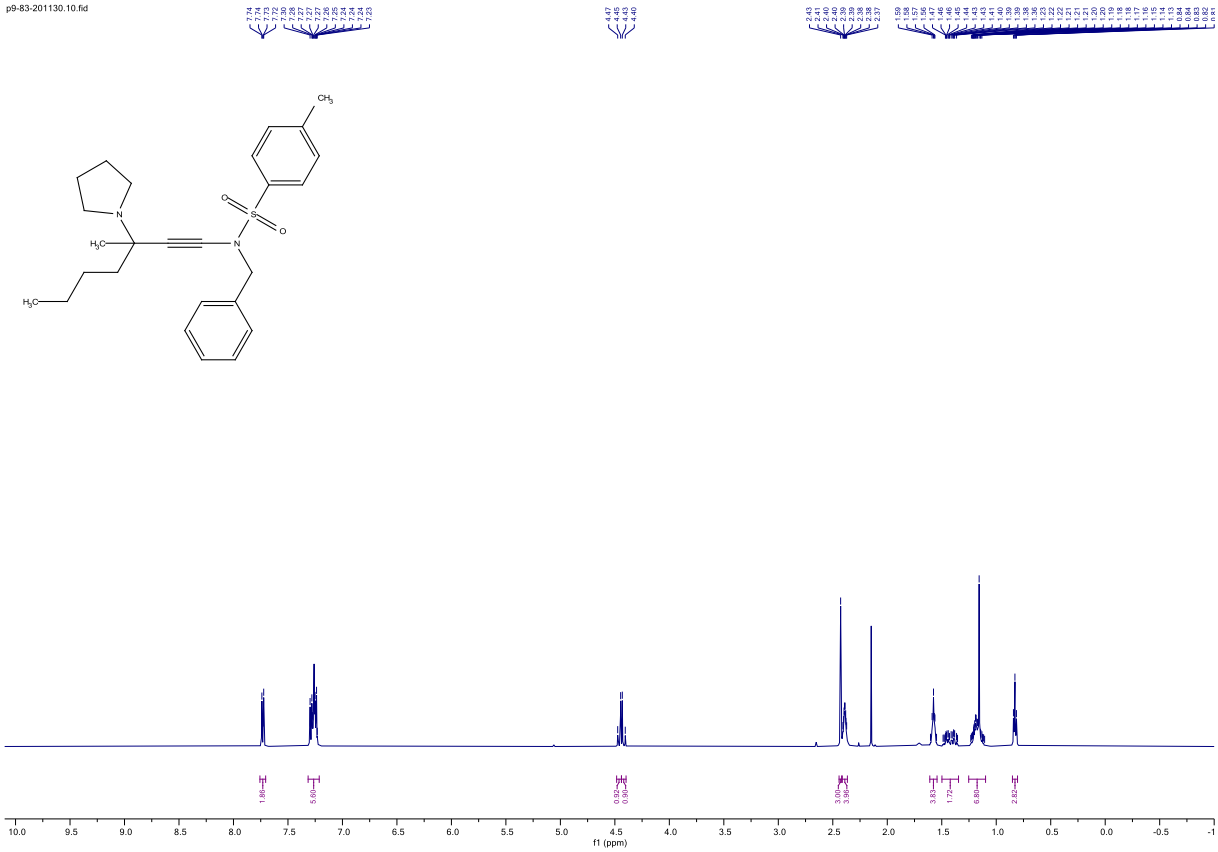


DEPT135 NMR (126 MHz) in $CDCl_3$

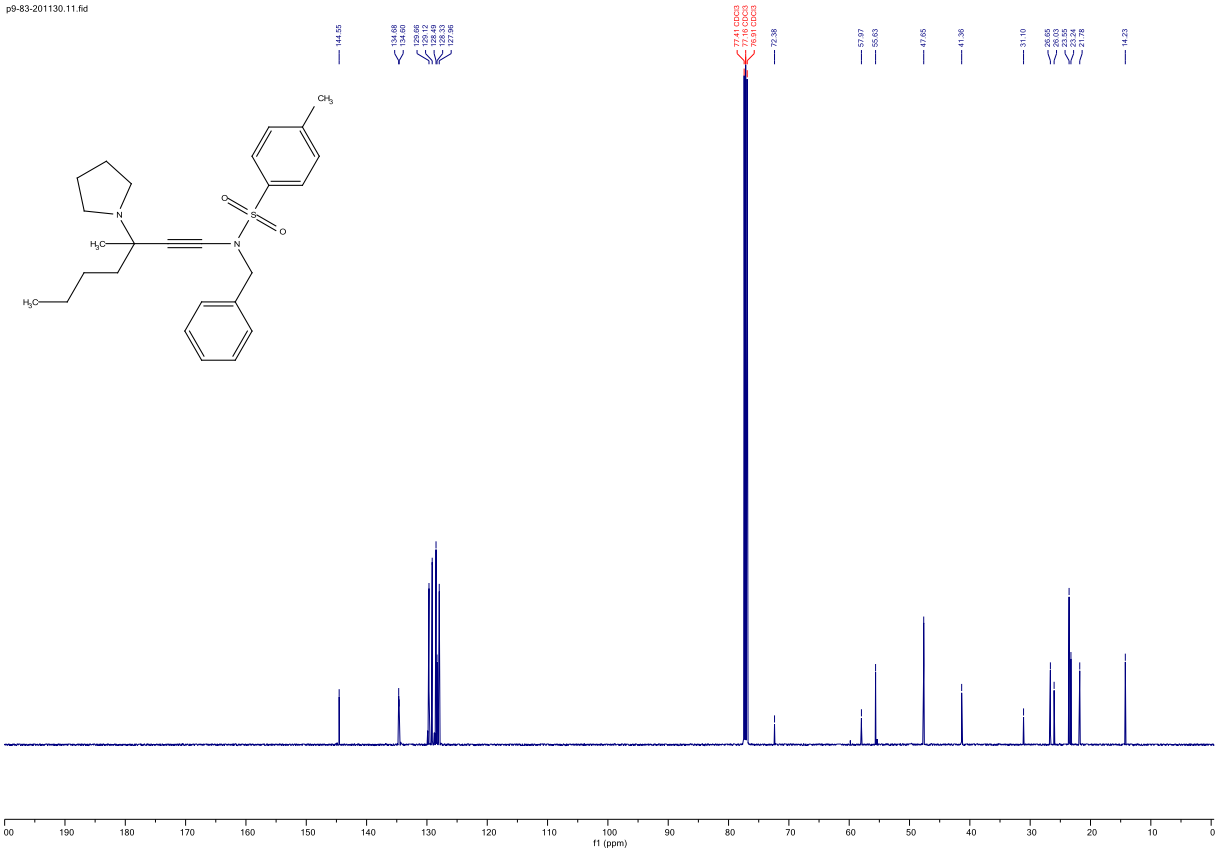


N-Benzyl-4-methyl-*N*-(3-methyl-3-(pyrrolidin-1-yl)hept-1-yn-1-yl)benzenesulfonamide (**4r**)

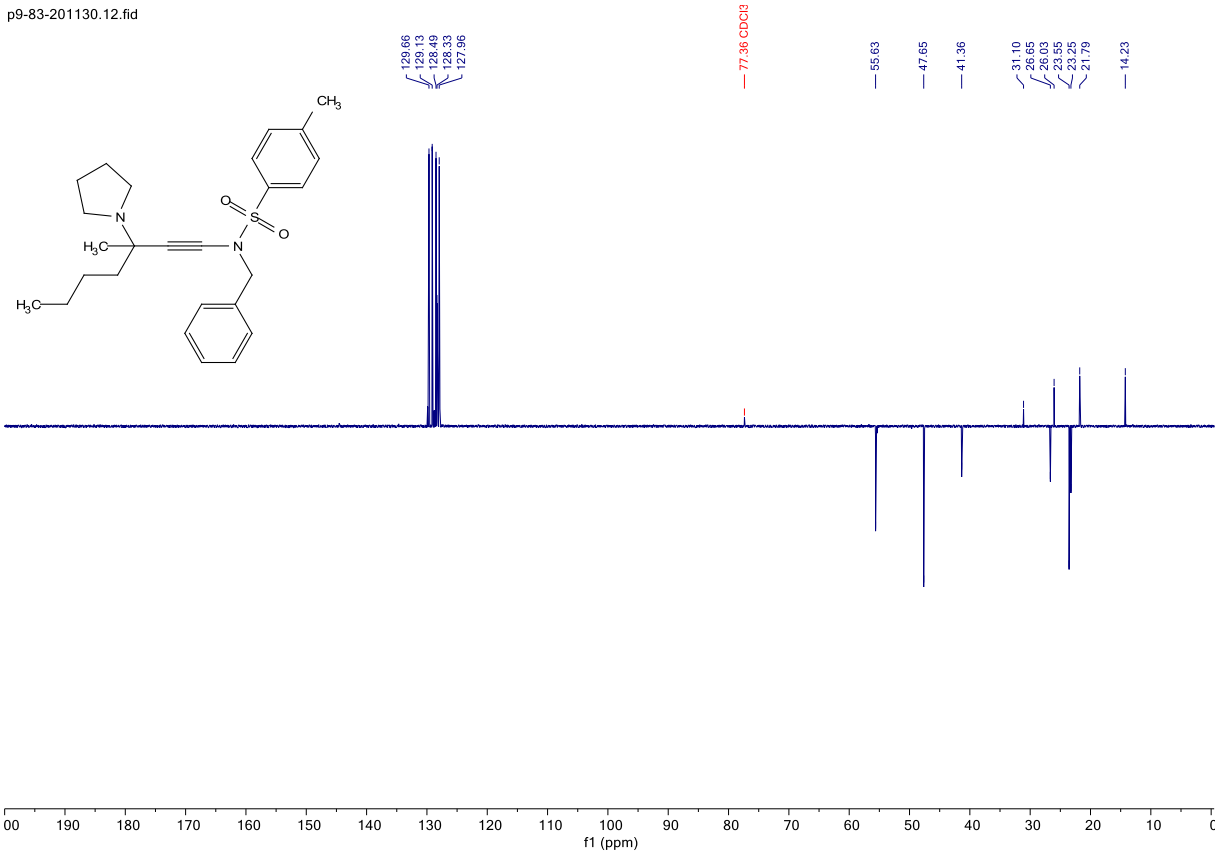
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

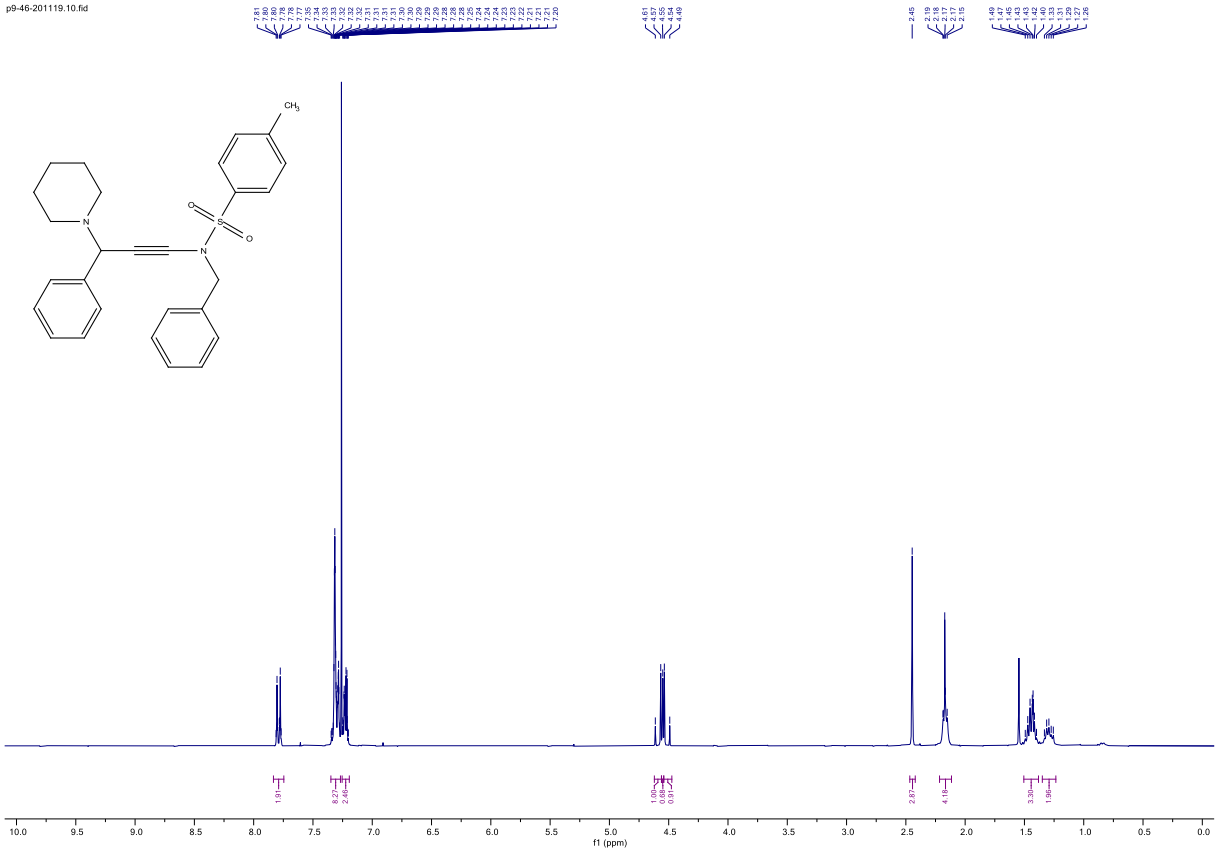


DEPT135 NMR (126 MHz) in $CDCl_3$

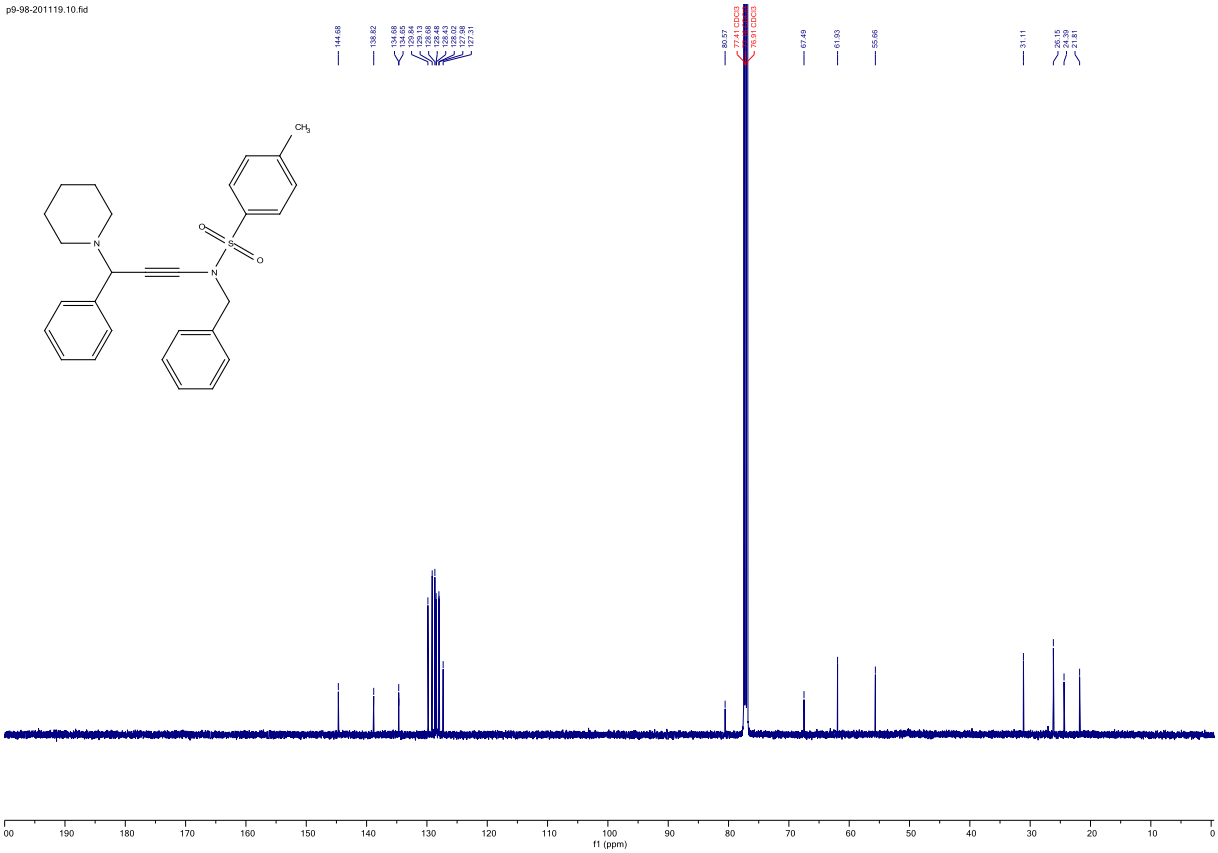


N-Benzyl-4-methyl-*N*-(3-phenyl-3-(piperidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**5a**)

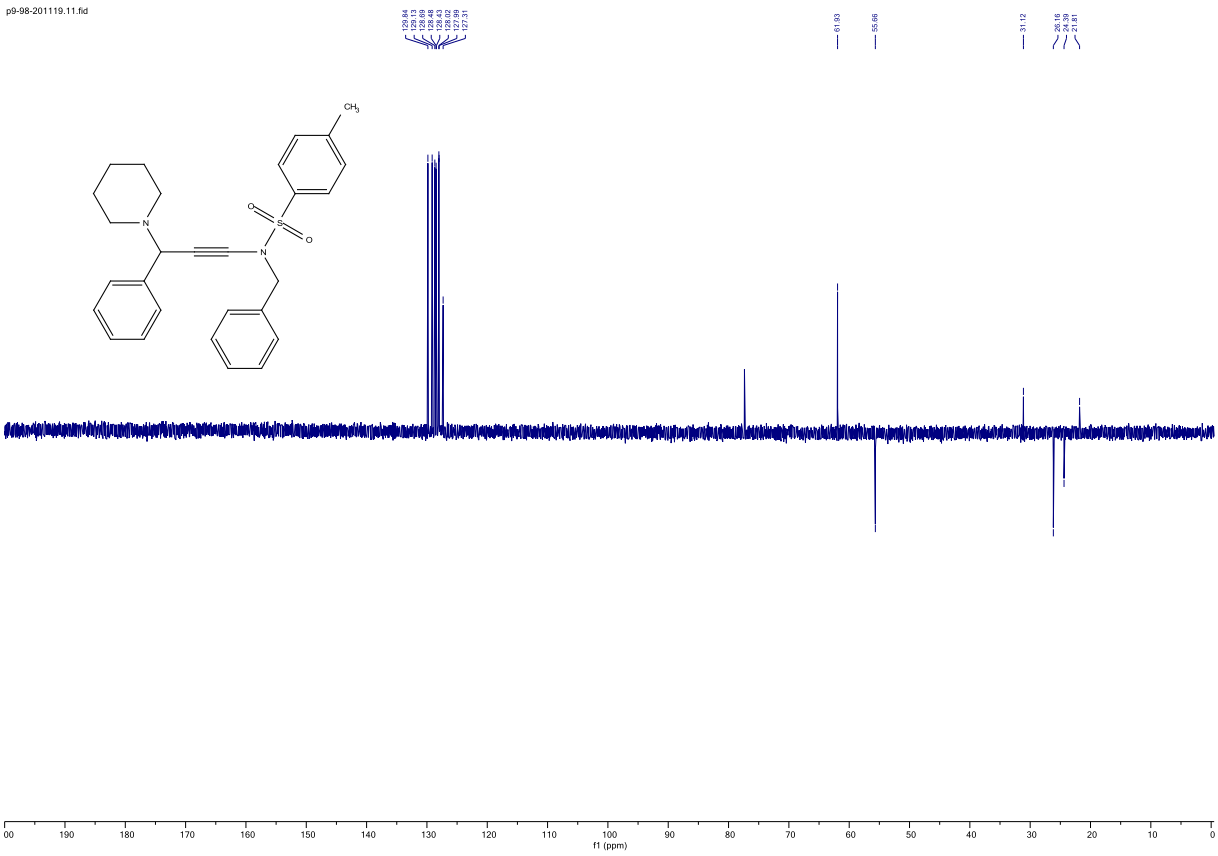
^{1}H NMR (300 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

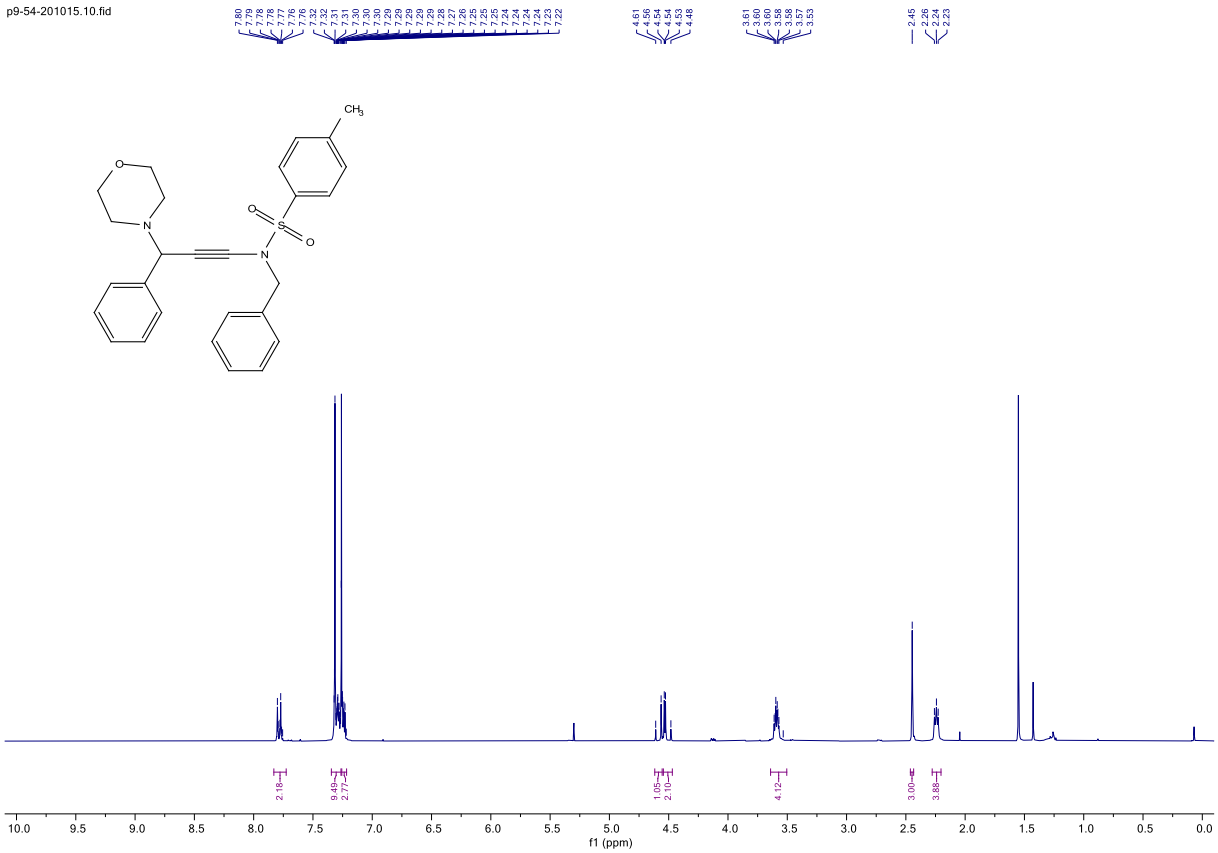


DEPT135 NMR (126 MHz) in $CDCl_3$

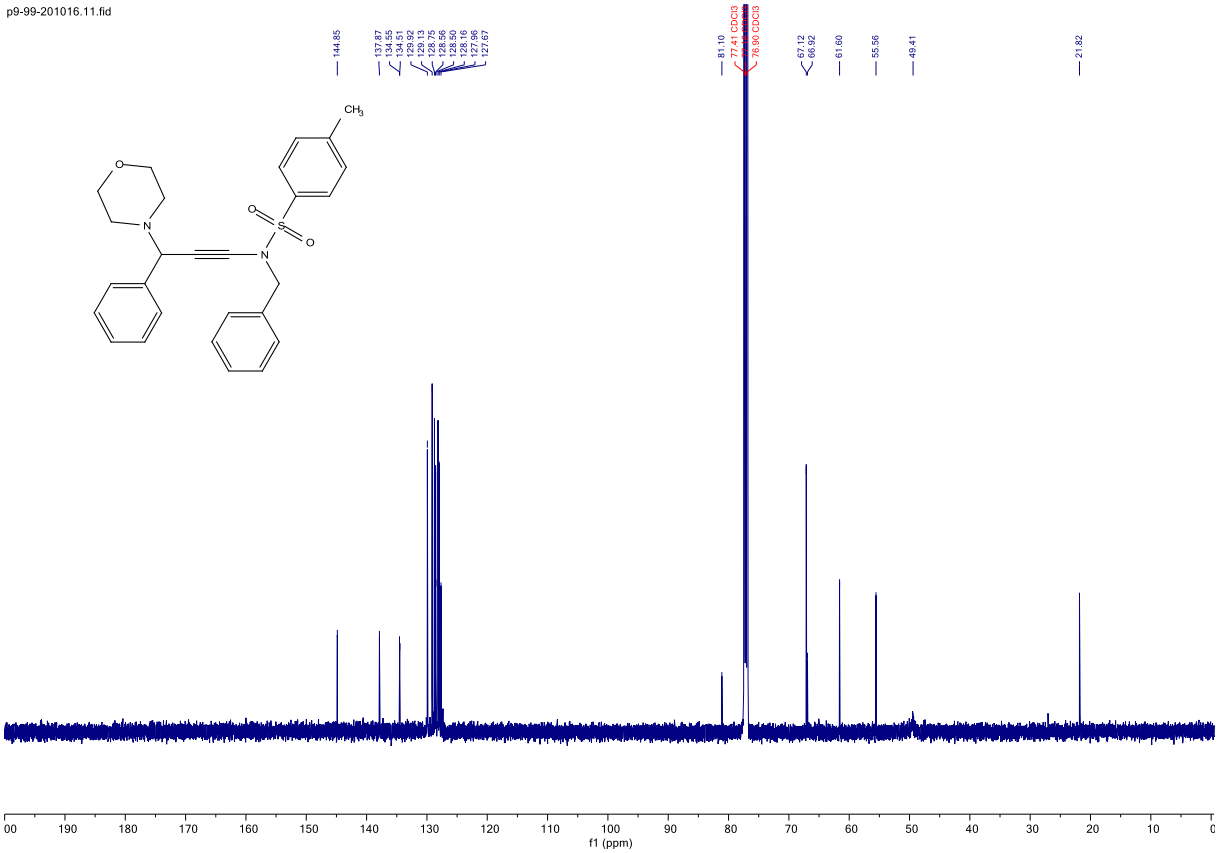


N-Benzyl-4-methyl-*N*-(3-morpholino-3-phenylprop-1-yn-1-yl)benzenesulfonamide (**5b**)

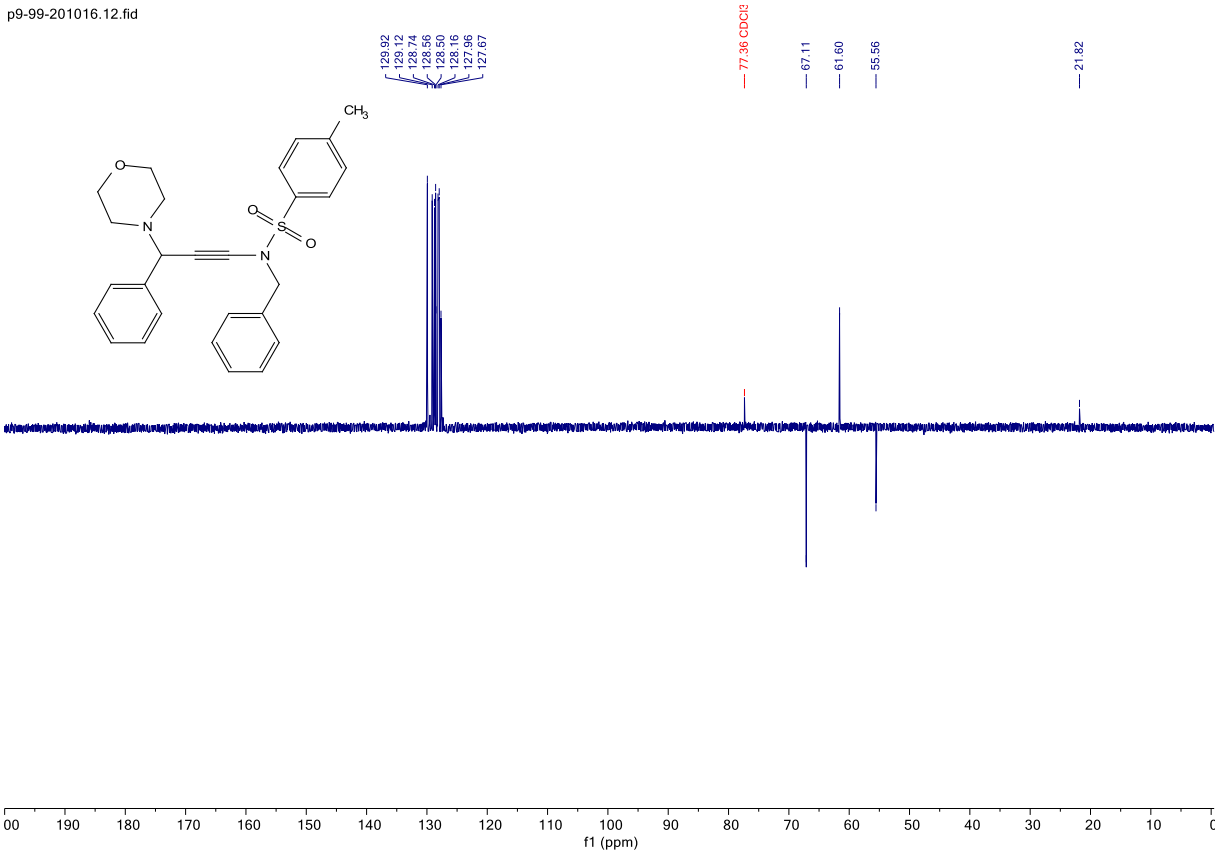
^{1}H NMR (300 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

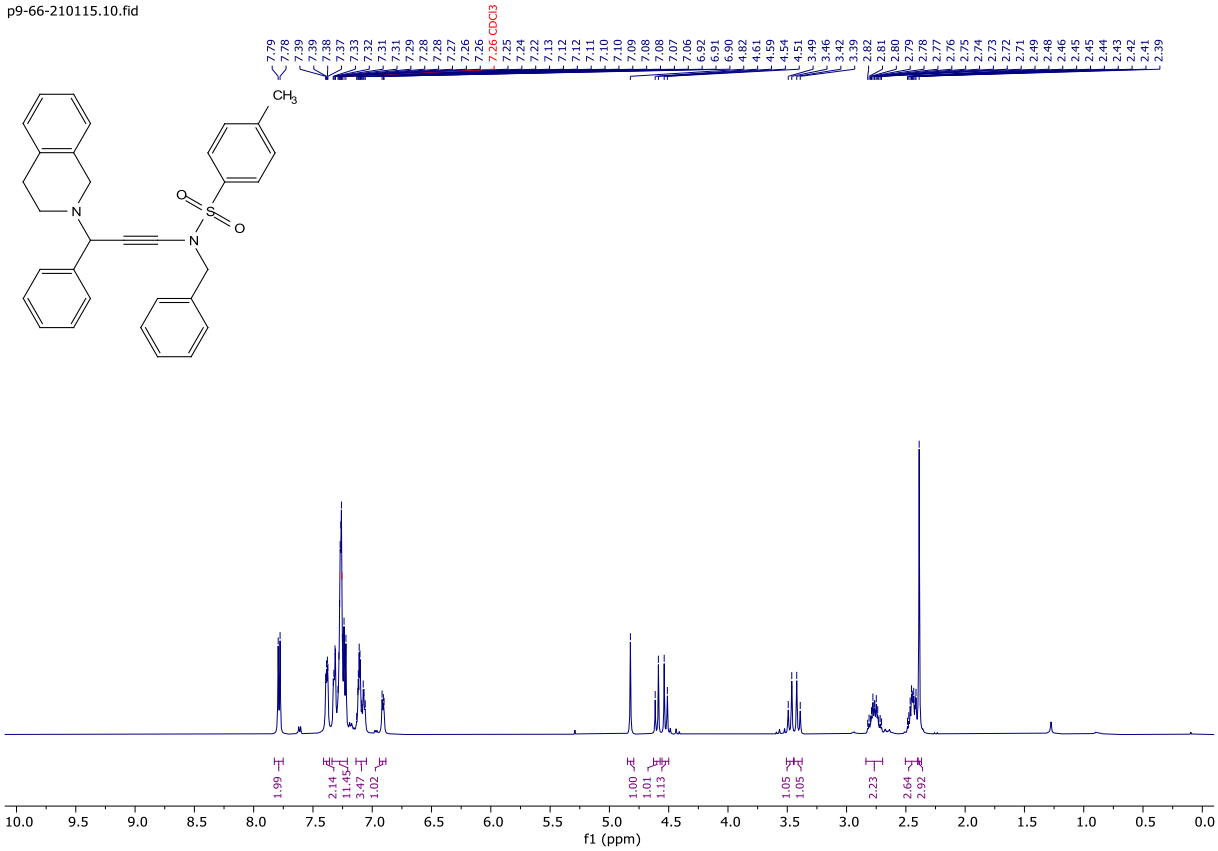


DEPT135 NMR (126 MHz) in $CDCl_3$

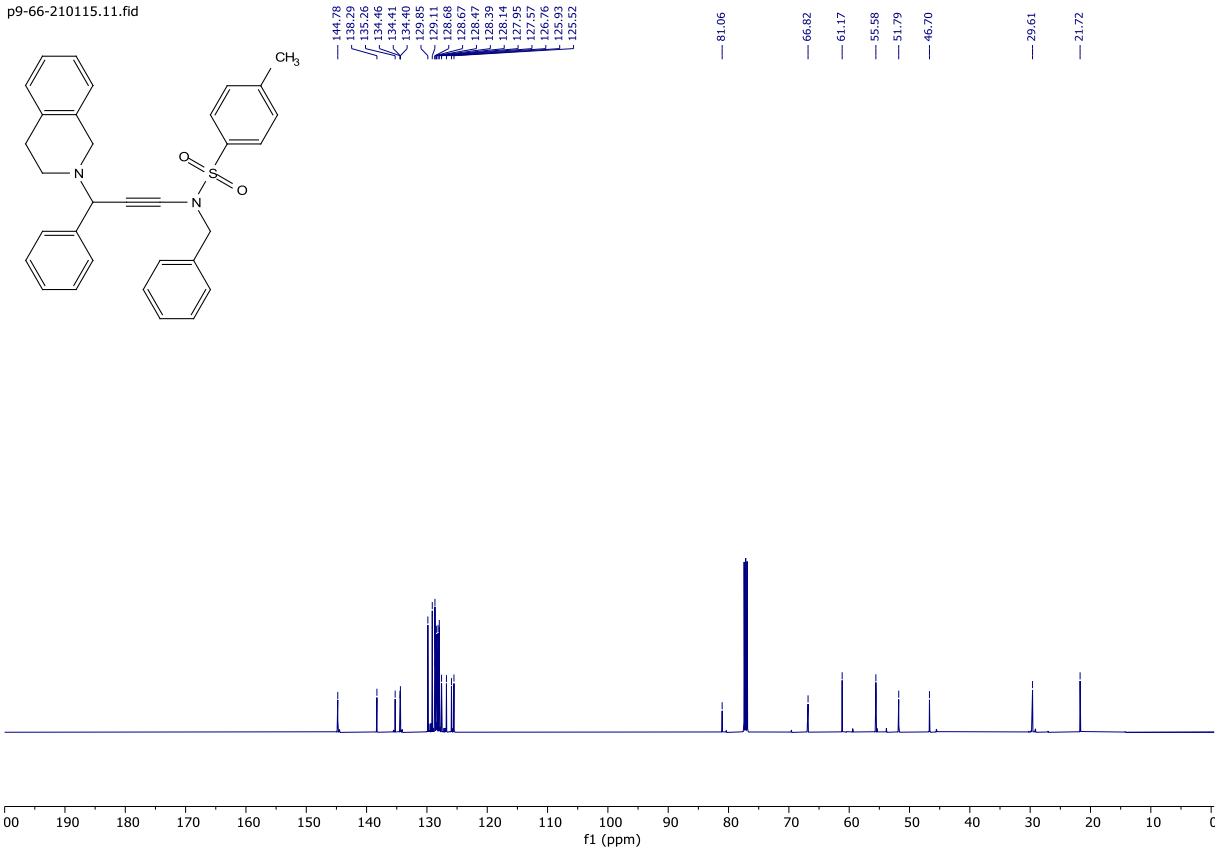


N-Benzyl-*N*-(3-(3,4-dihydroisoquinolin-2(1*H*)-yl)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5c**)

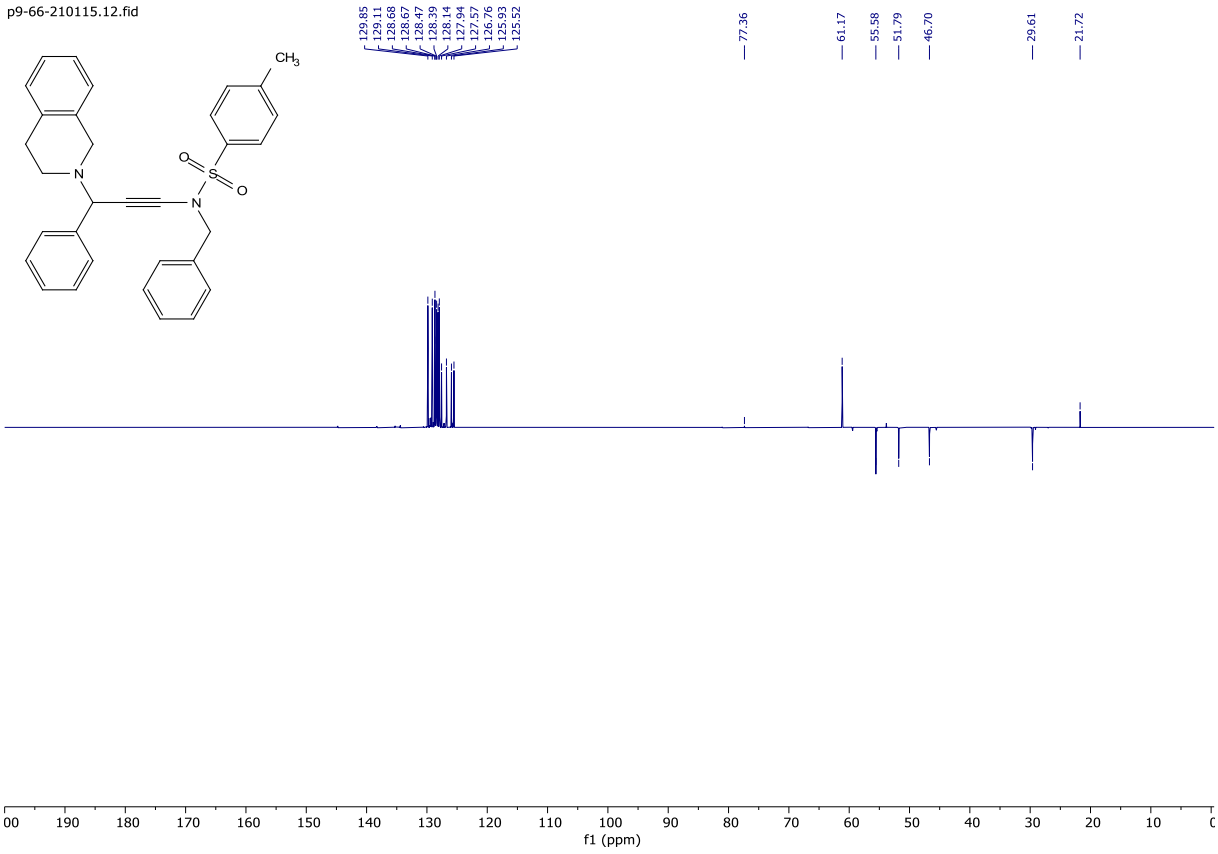
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

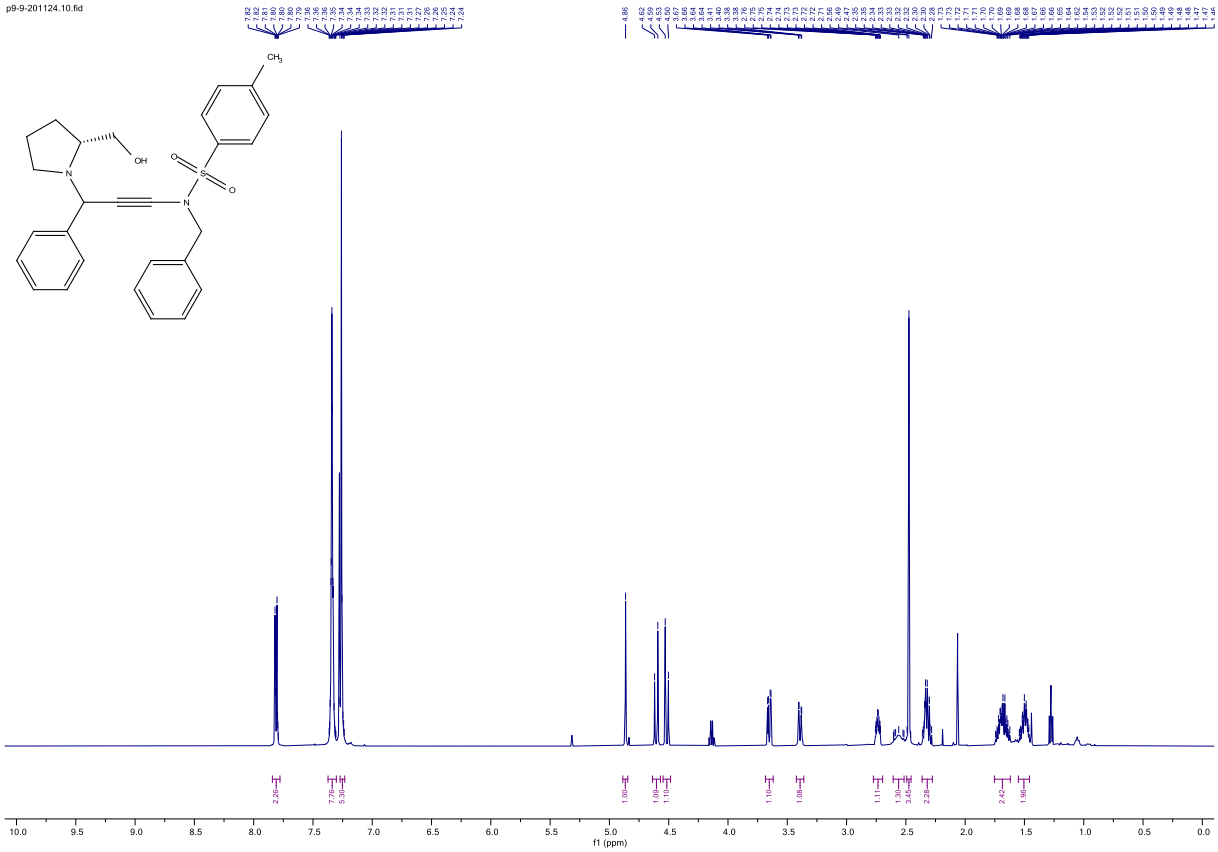


DEPT135 NMR (126 MHz) in $CDCl_3$

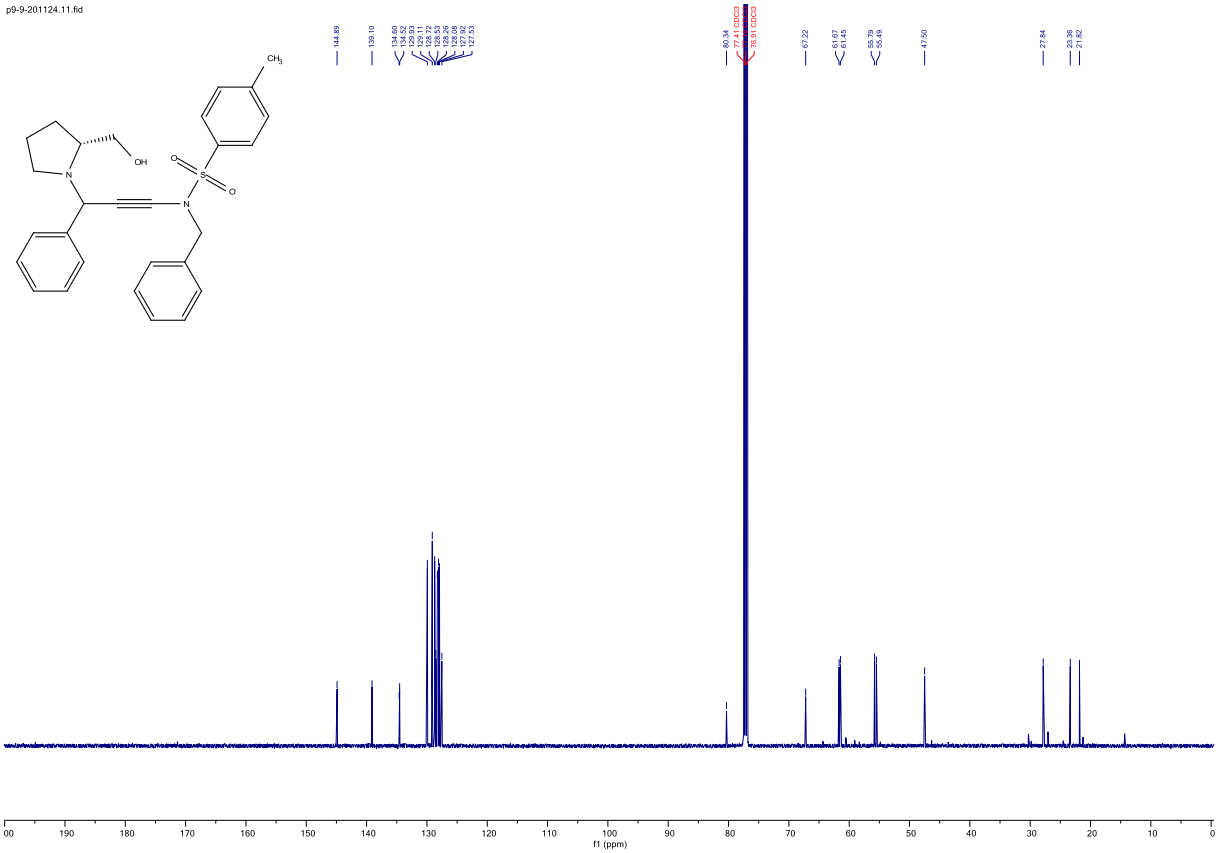


N-Benzyl-*N*-((*R*)-3-((*R*)-2-(hydroxymethyl)pyrrolidin-1-yl)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5d**)

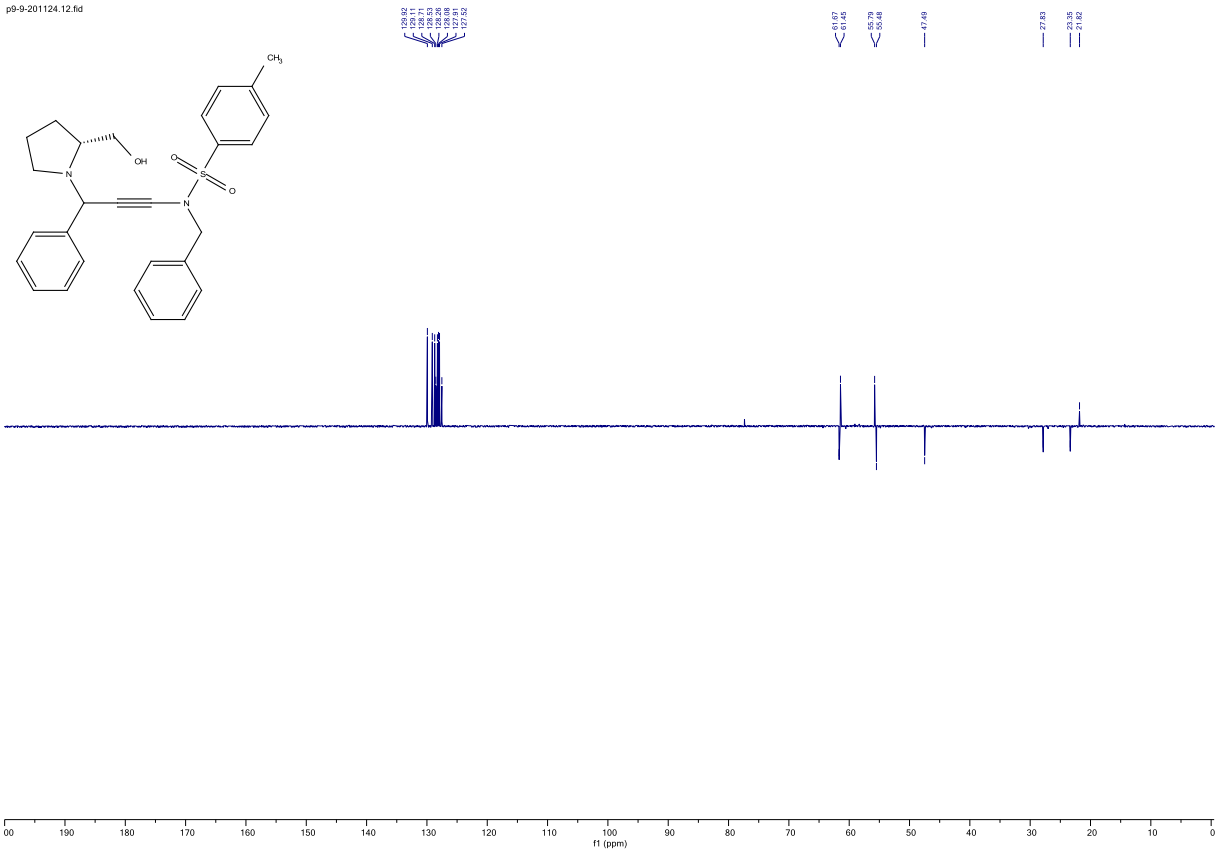
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

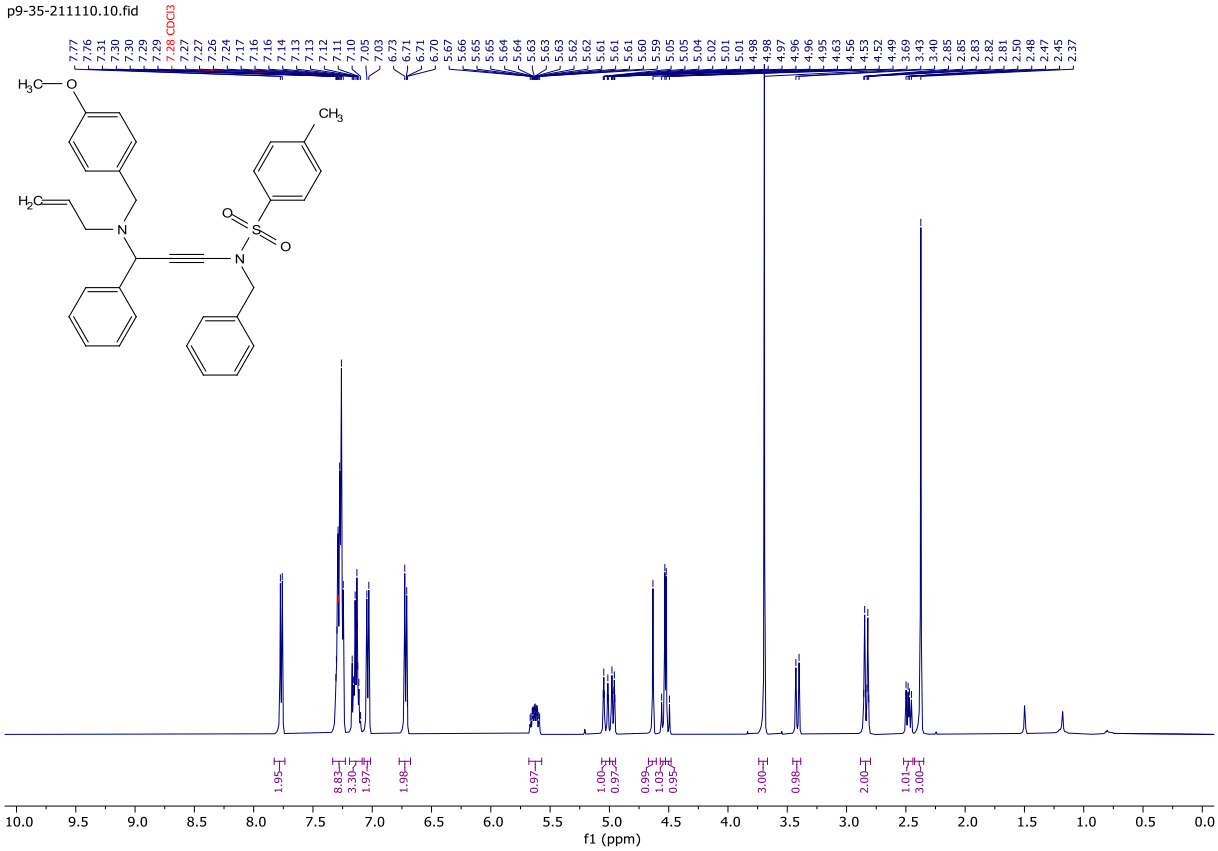


DEPT135 NMR (126 MHz) in $CDCl_3$

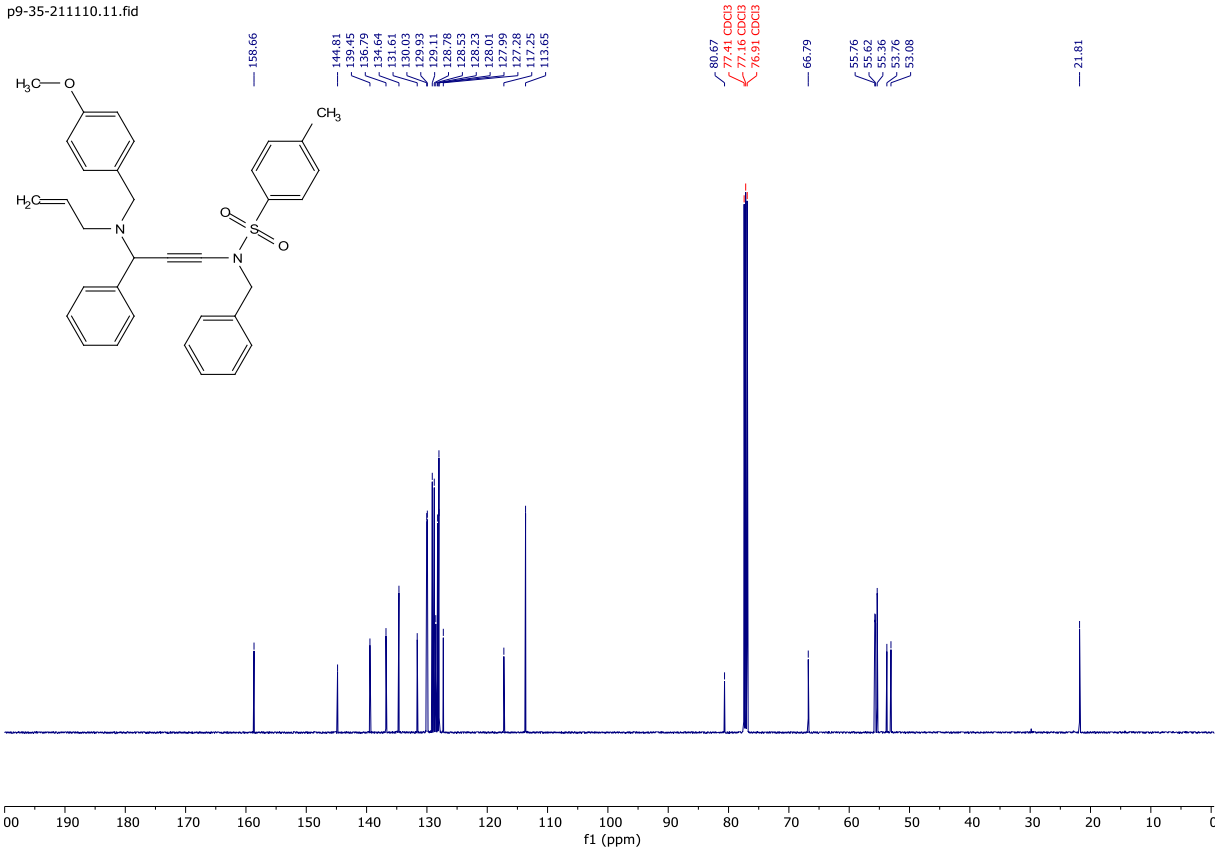


N-(3-(Allyl(4-methoxybenzyl)amino)-3-phenylprop-1-yn-1-yl)-*N*-benzyl-4-methylbenzenesulfonamide (**5f**)

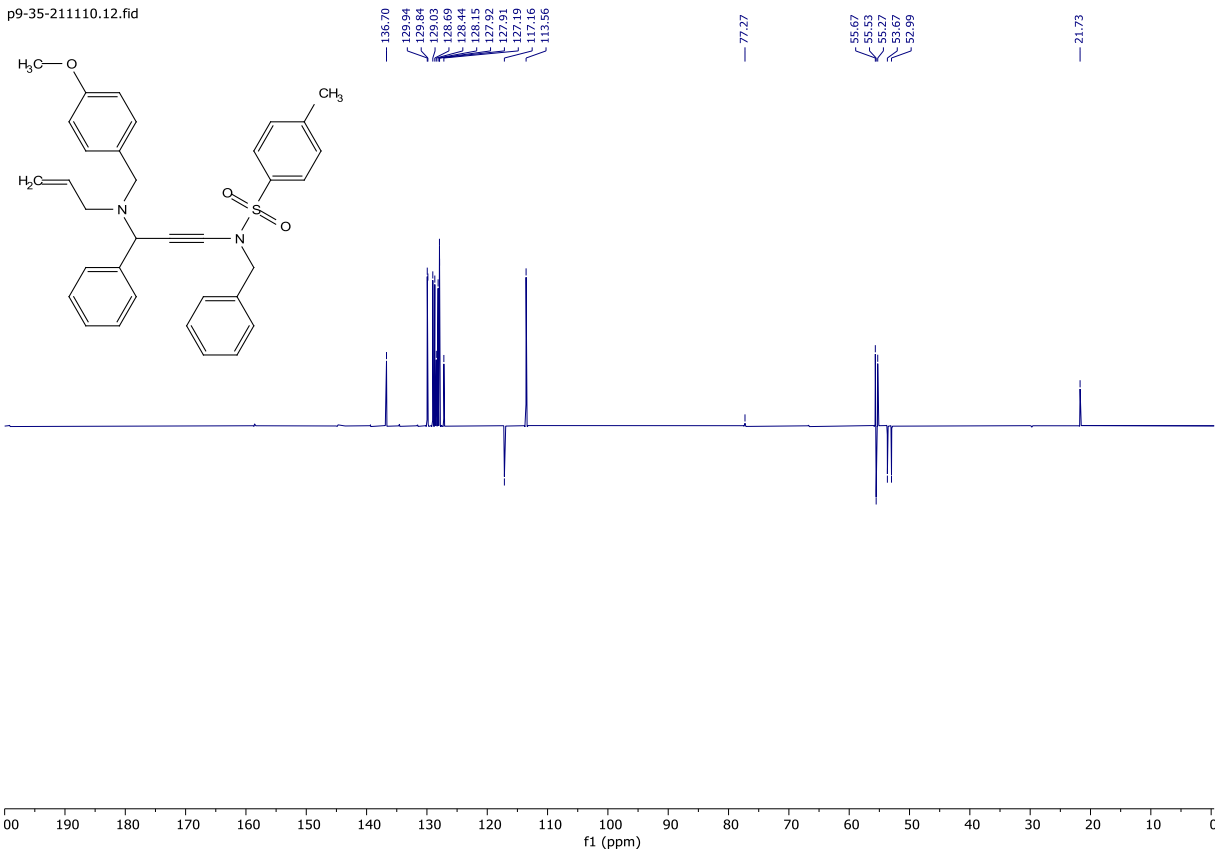
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

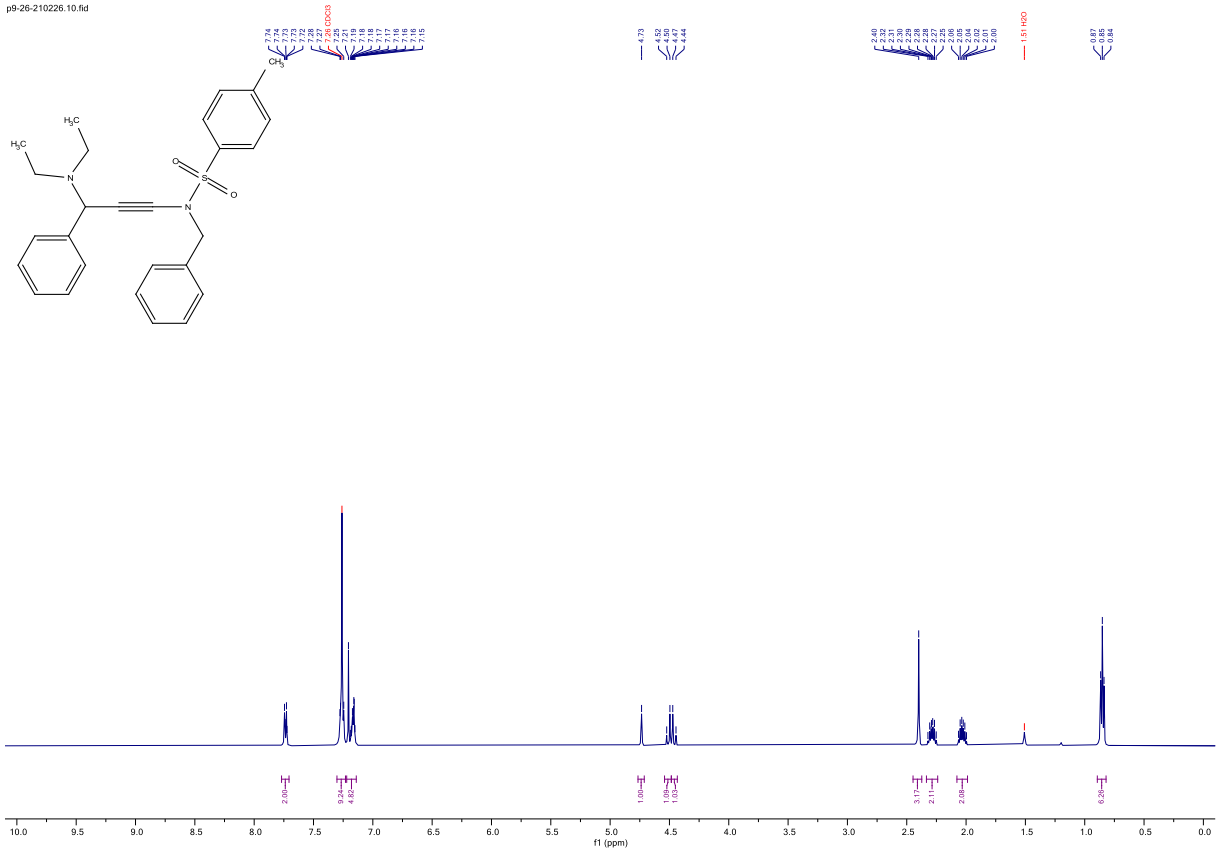


DEPT135 NMR (126 MHz) in $CDCl_3$

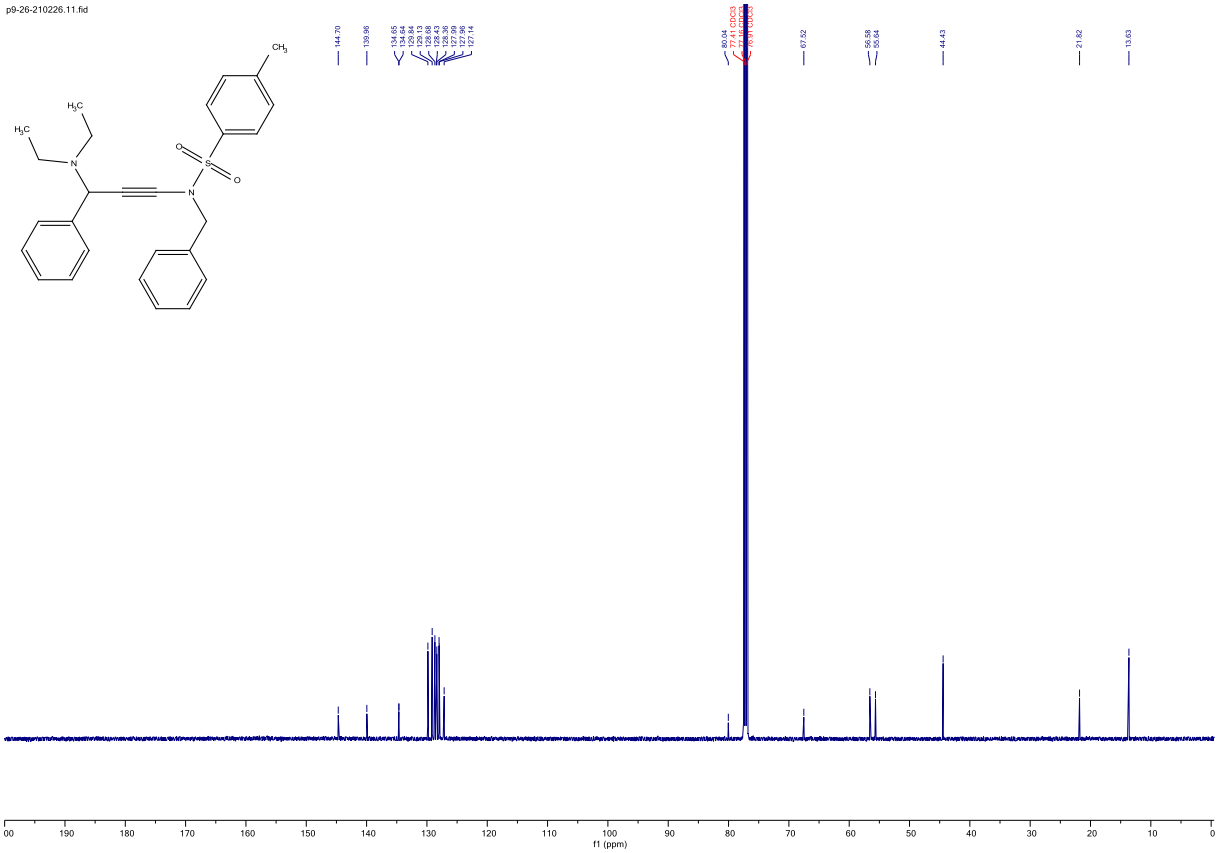


N-Benzyl-*N*-(3-(diethylamino)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5q**)

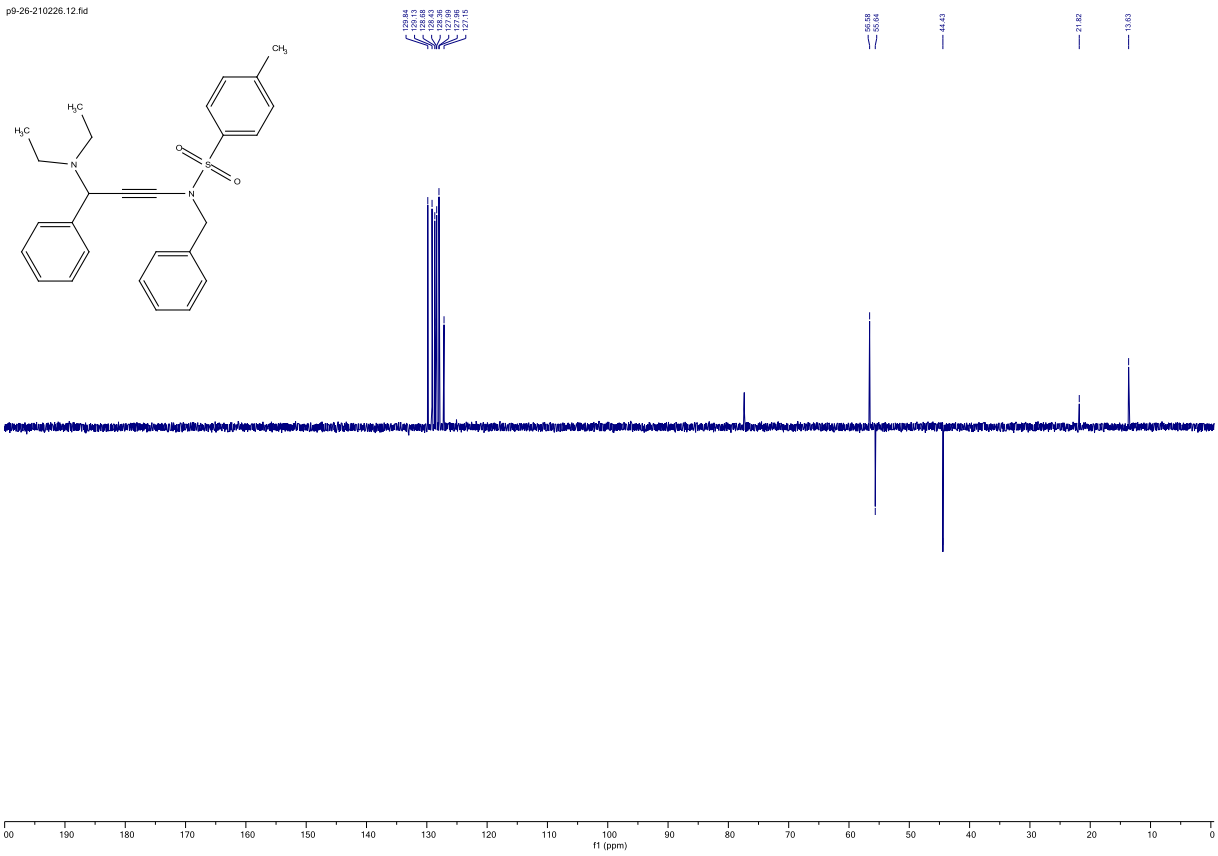
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

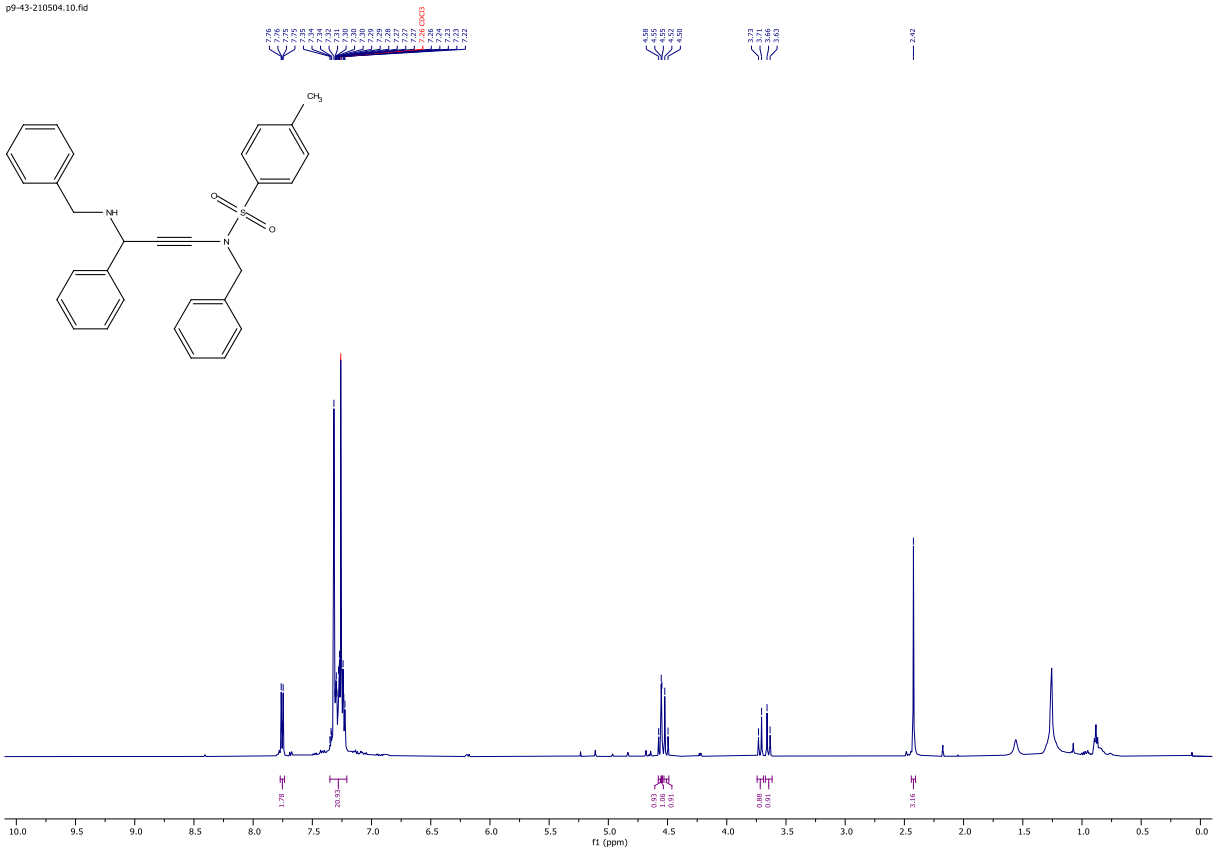


DEPT135 NMR (126 MHz) in $CDCl_3$

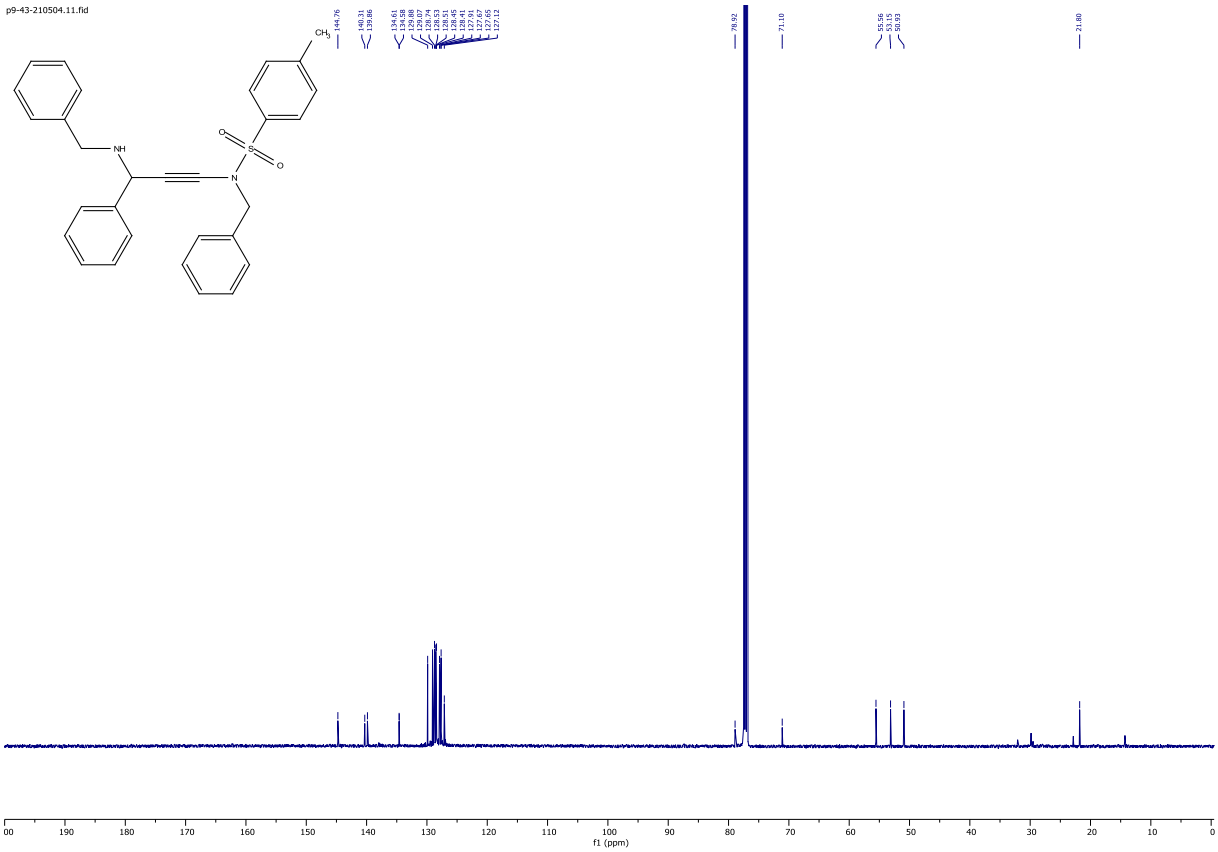


N-Benzyl-*N*-(3-(benzylamino)-3-phenylprop-1-yn-1-yl)-4-methylbenzenesulfonamide (**5k**)

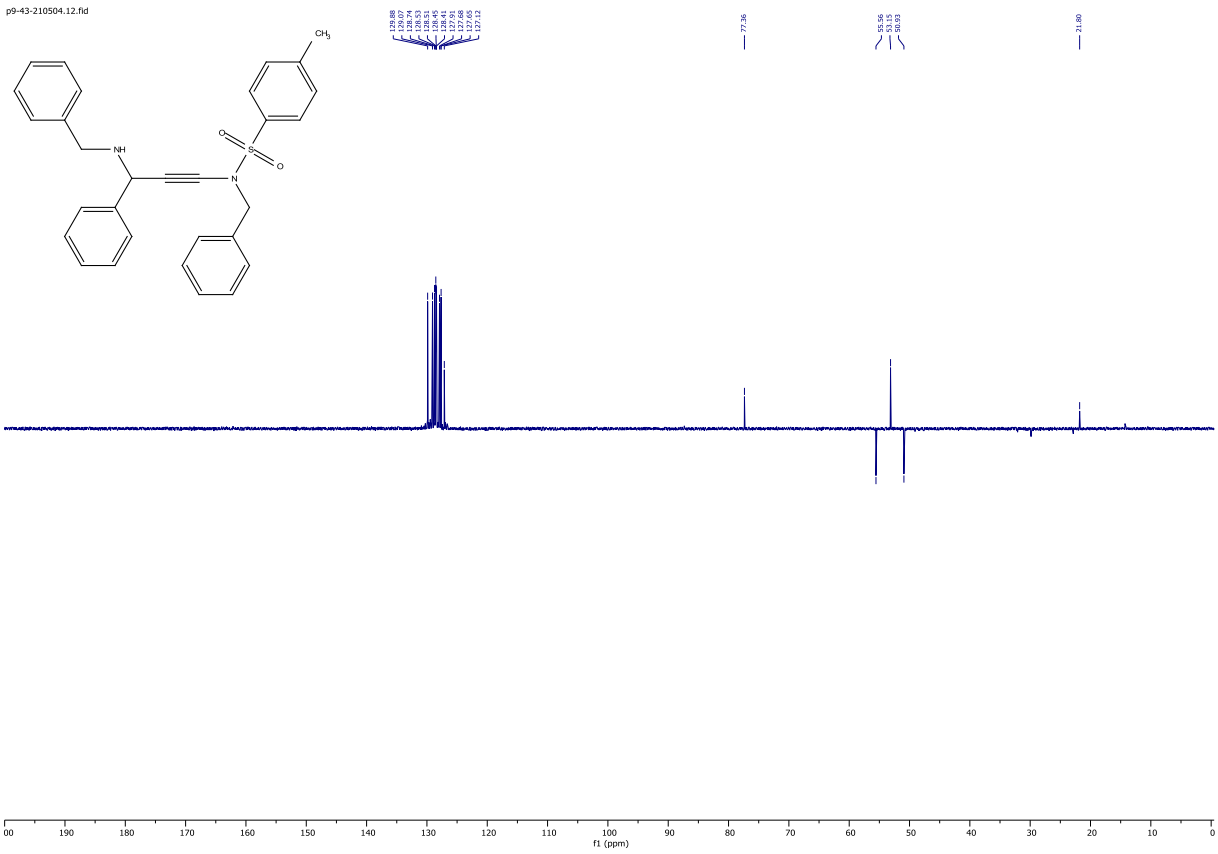
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

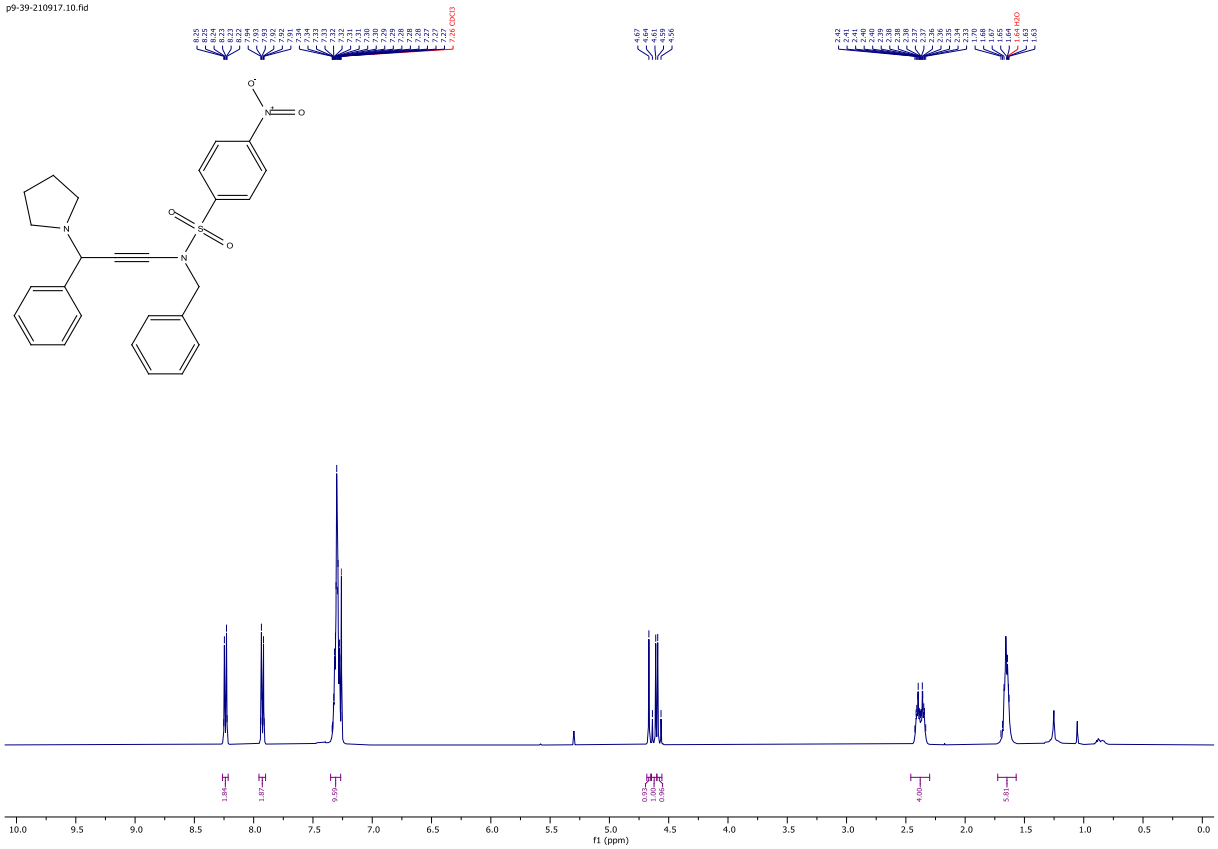


DEPT135 NMR (126 MHz) in $CDCl_3$

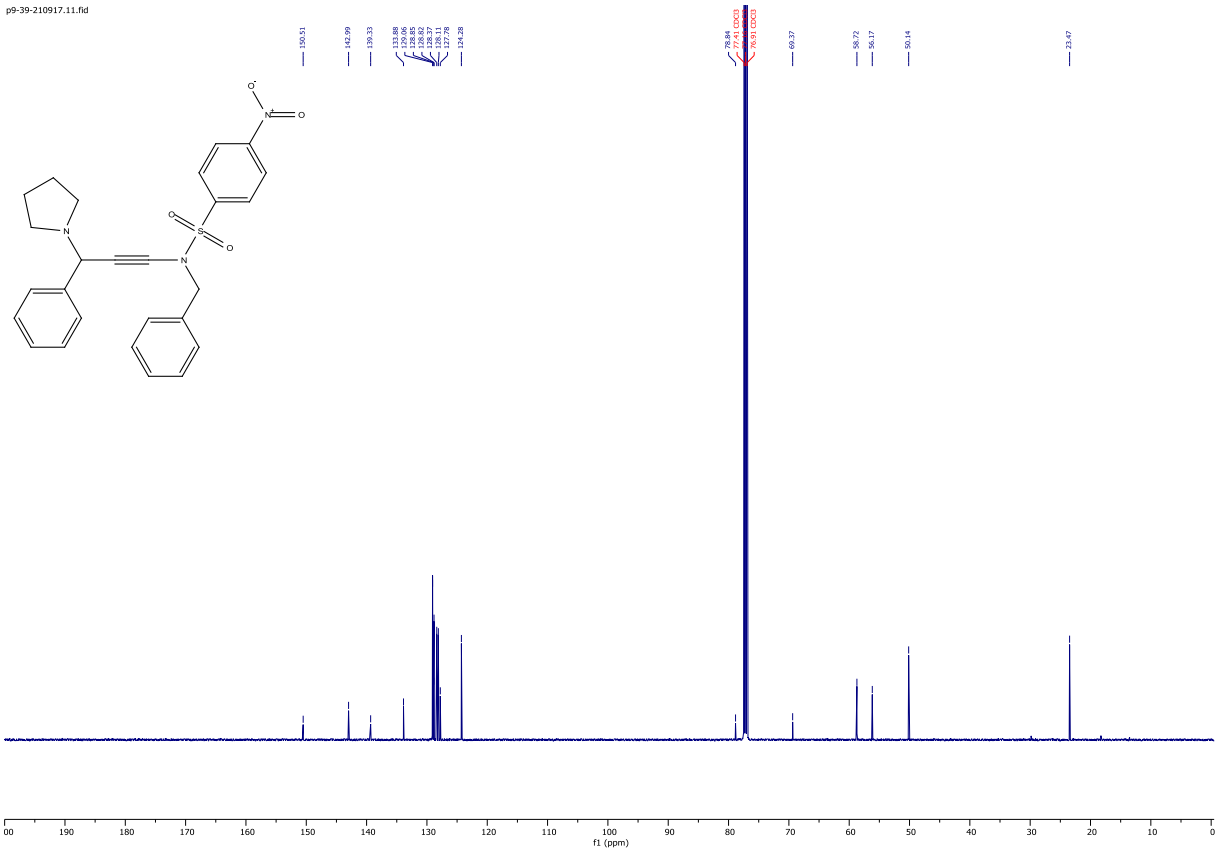


N-Benzyl-4-nitro-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**6a**)

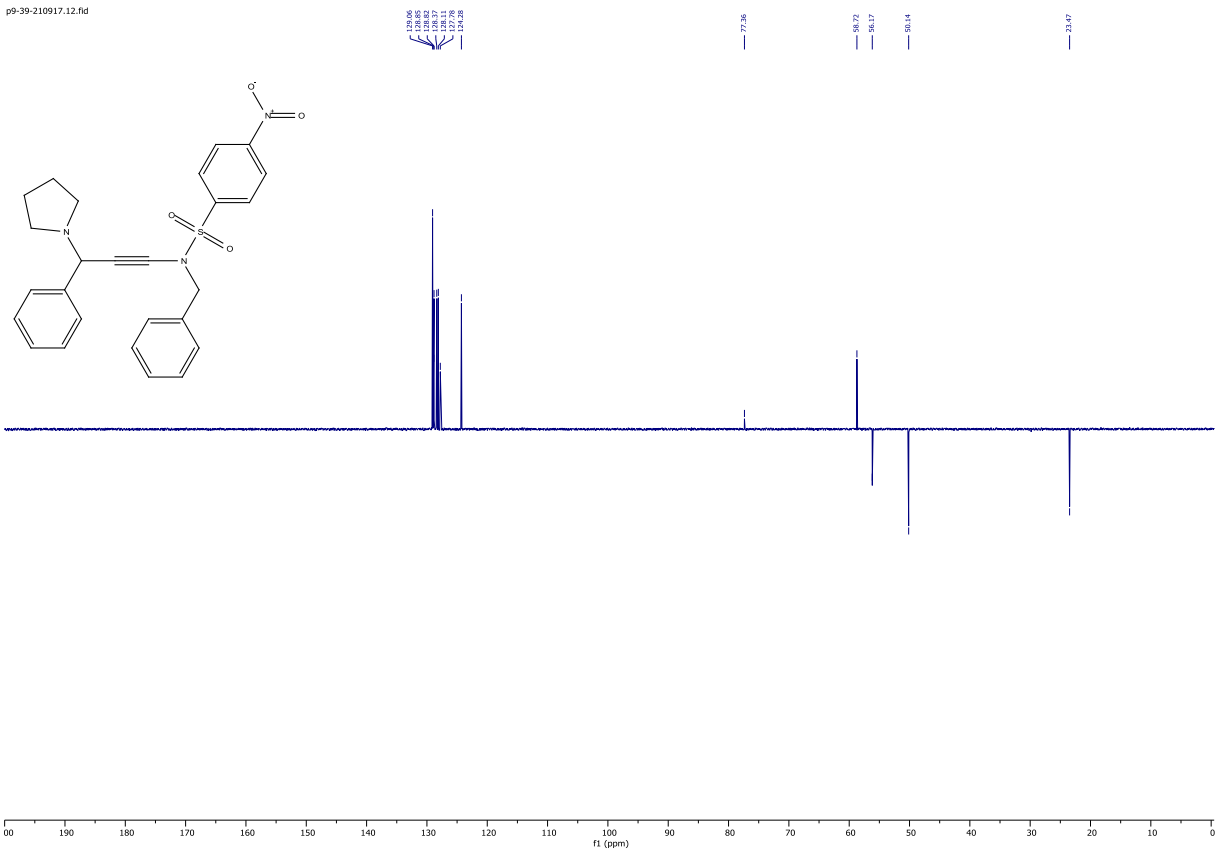
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

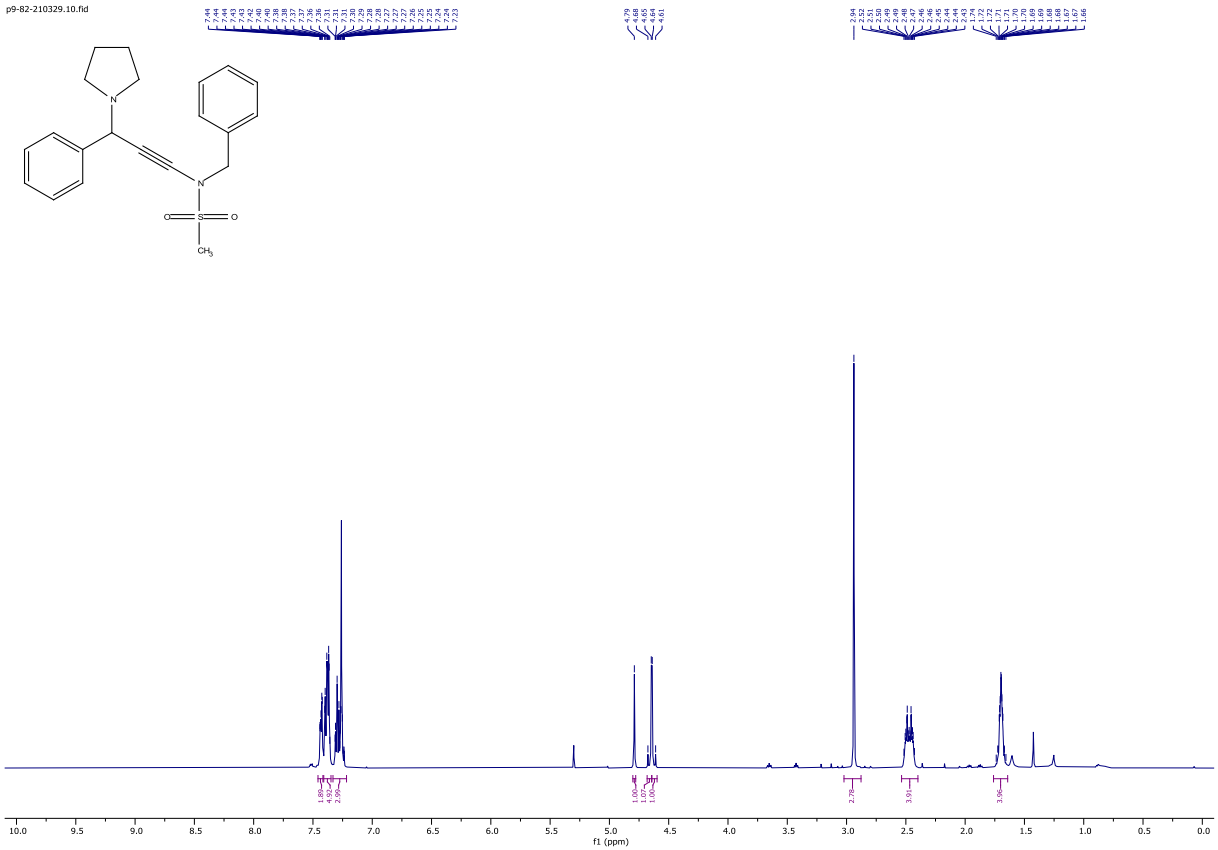


DEPT135 NMR (126 MHz) in $CDCl_3$

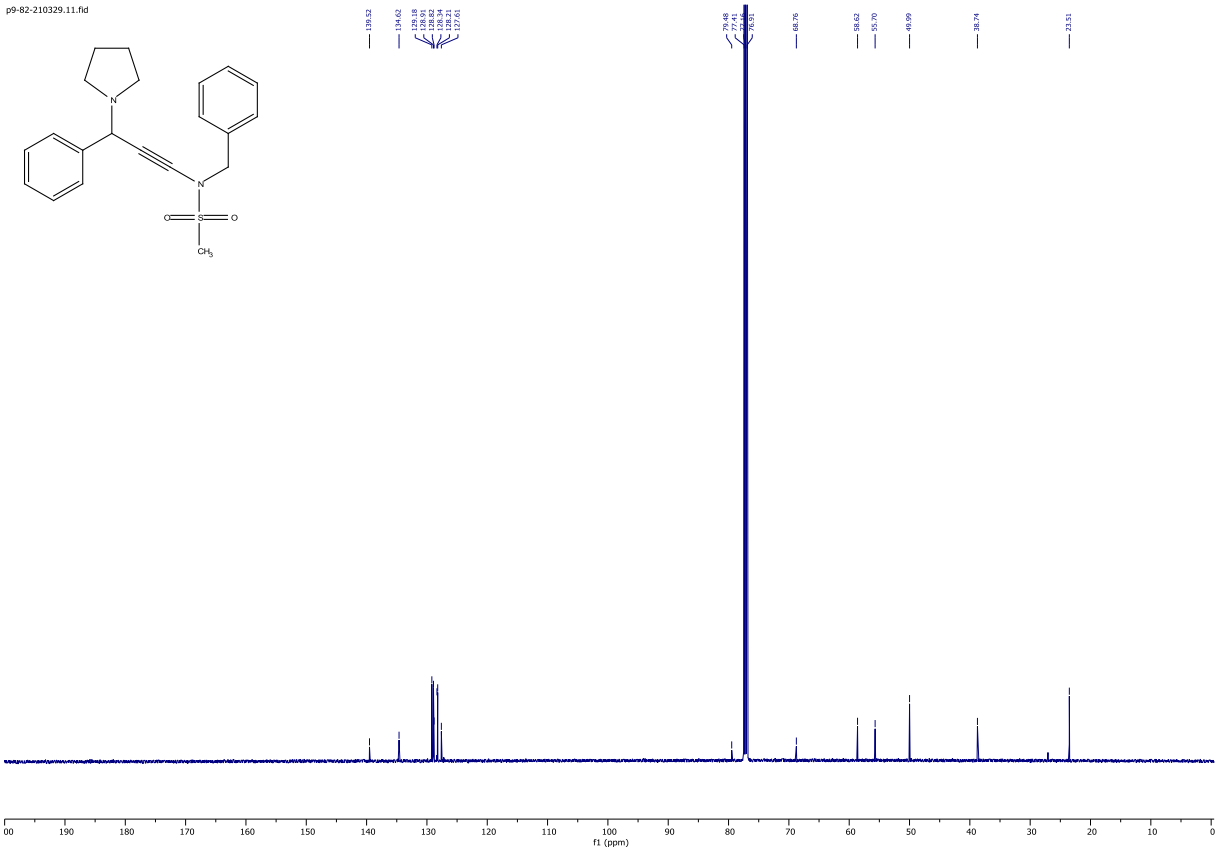


N-Benzyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)methanesulfonamide (**6b**)

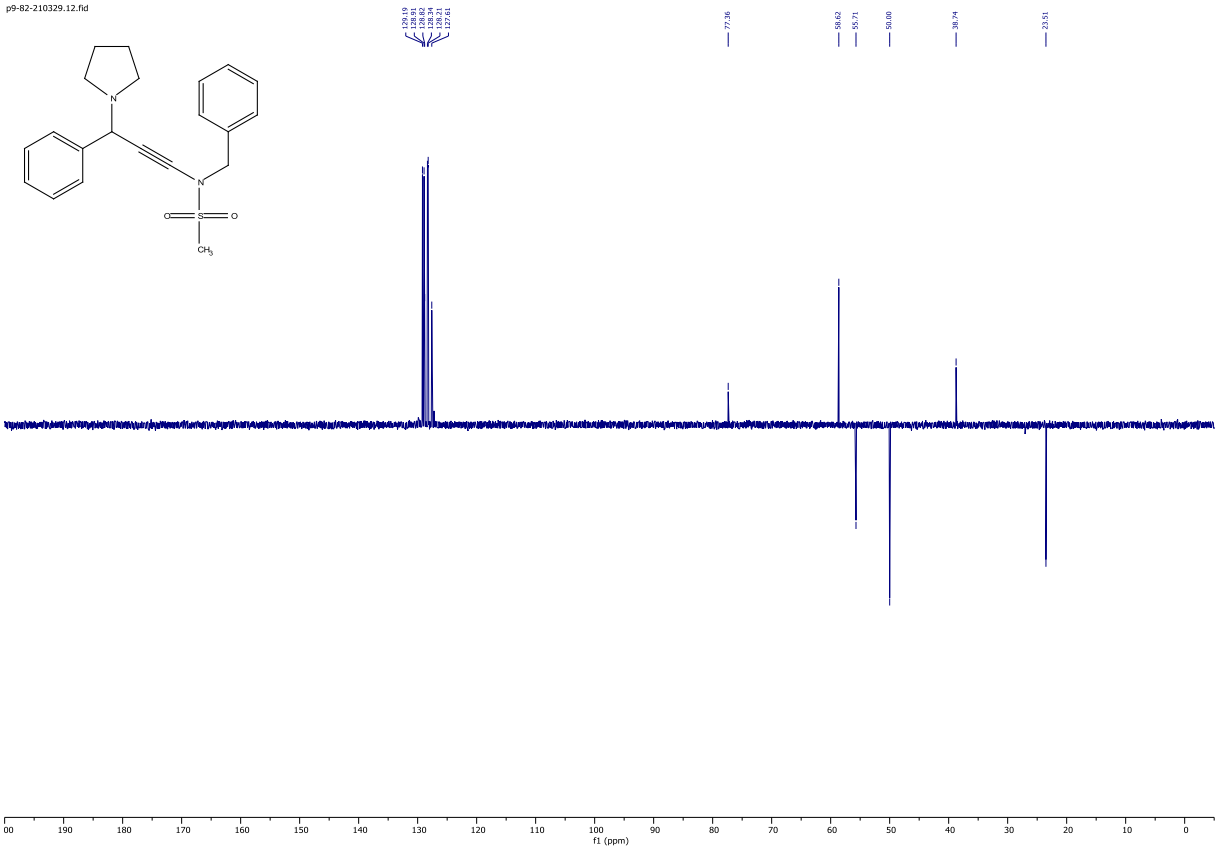
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

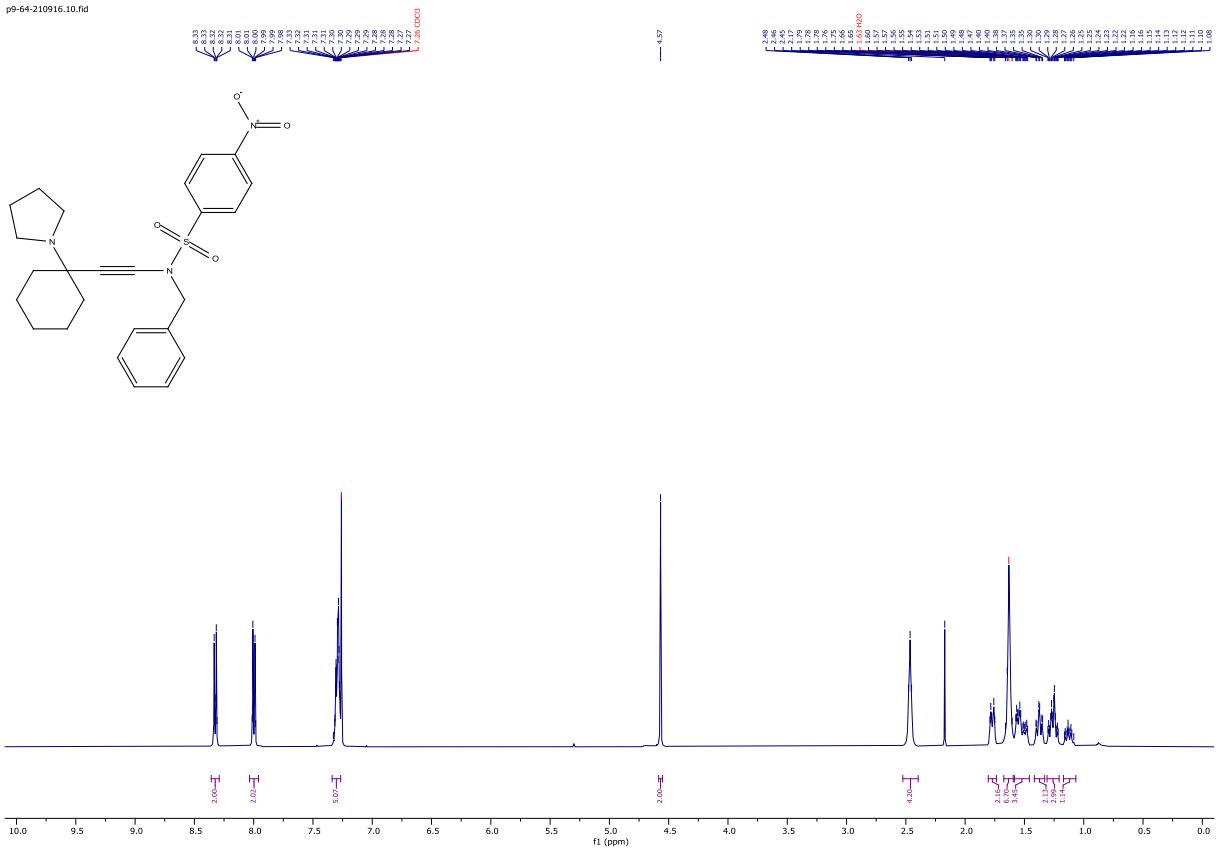


DEPT135 NMR (126 MHz) in $CDCl_3$

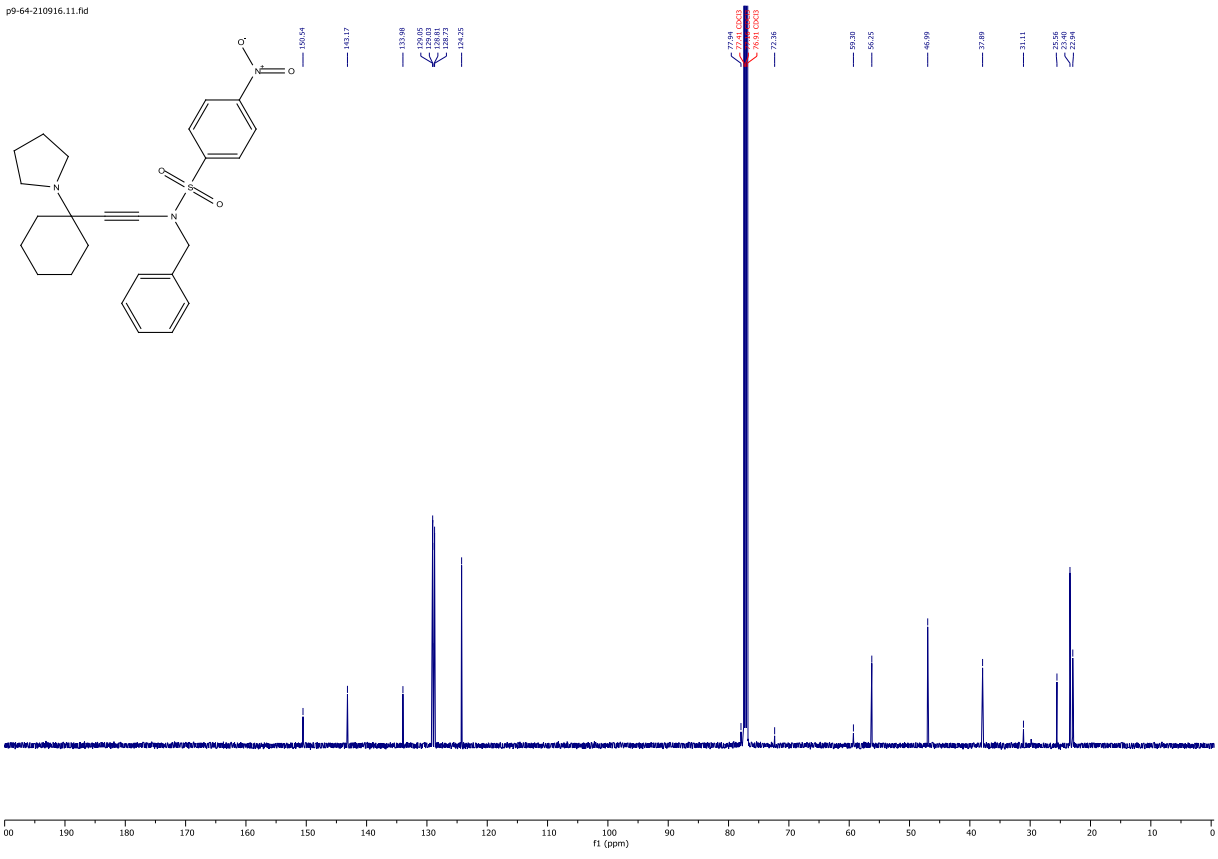


N-Benzyl-4-nitro-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**6c**)

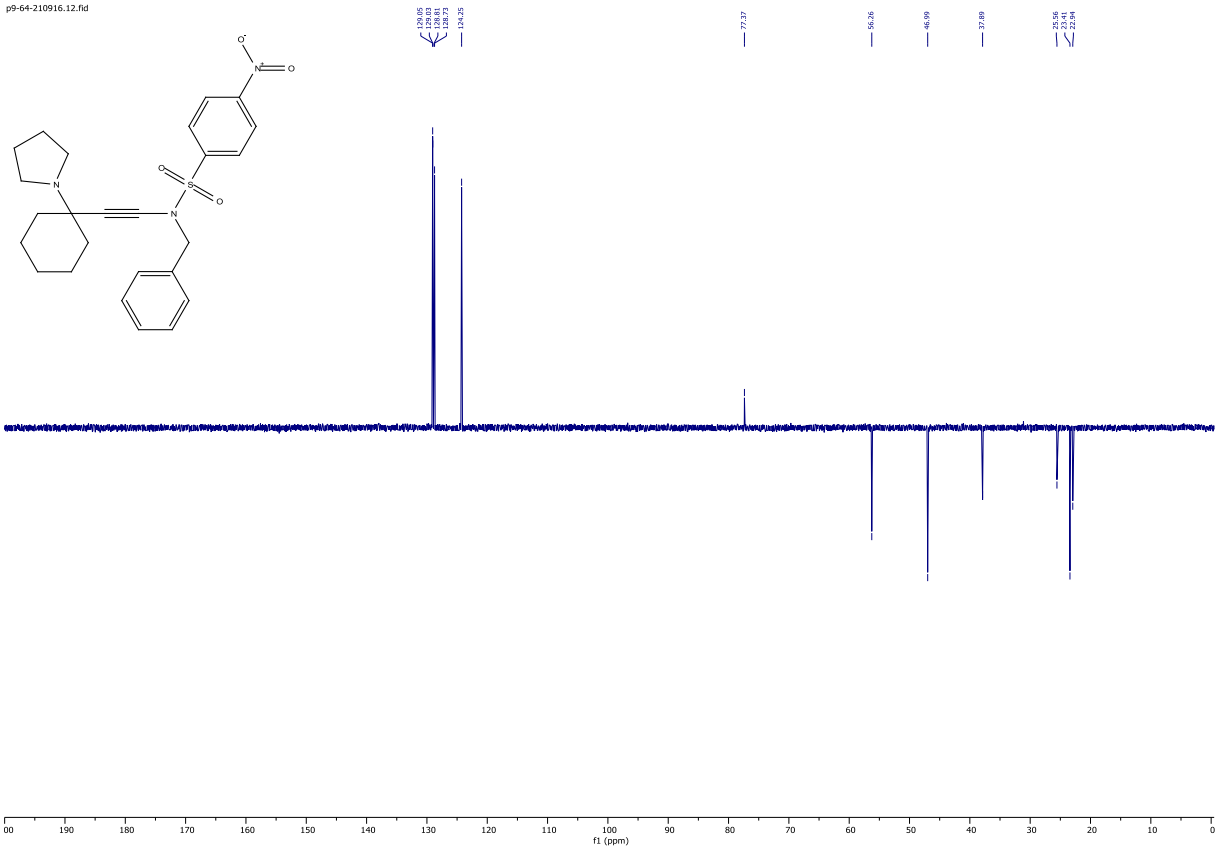
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

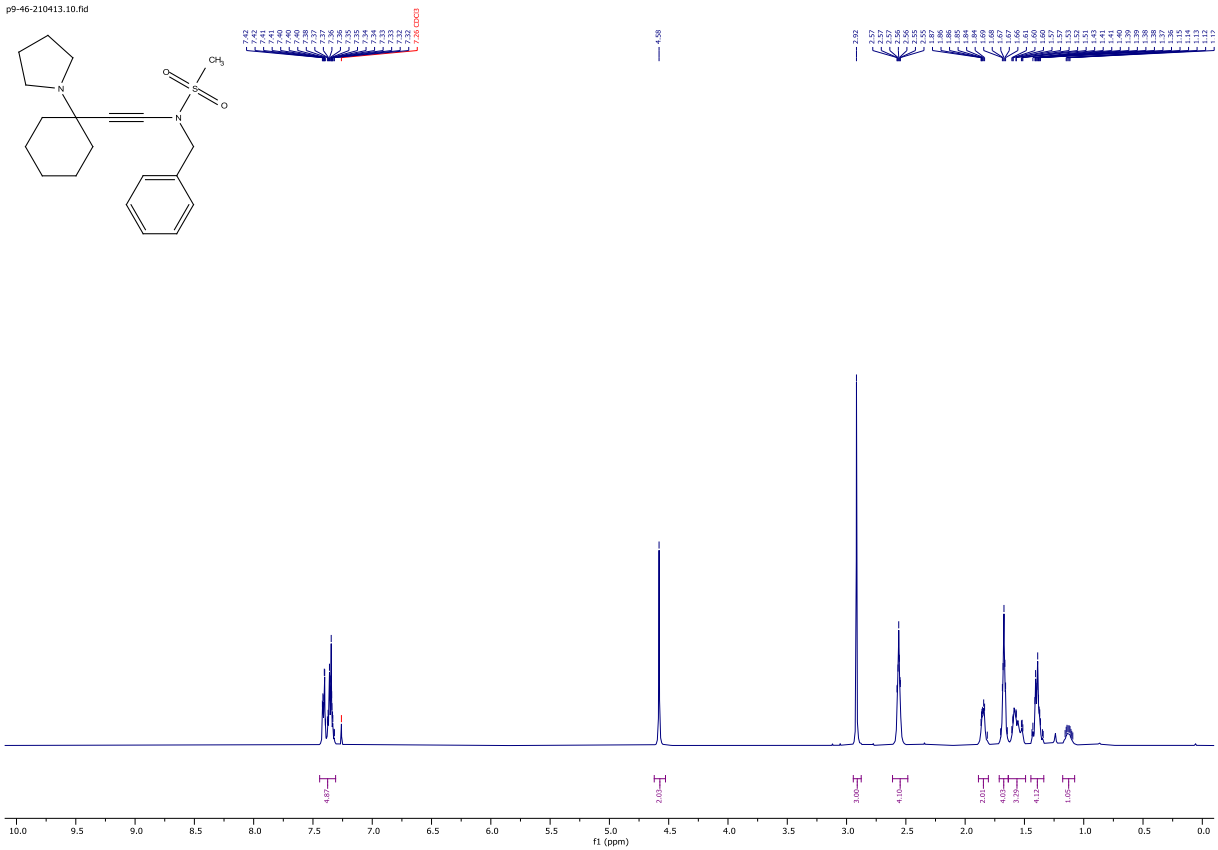


DEPT135 NMR (126 MHz) in $CDCl_3$

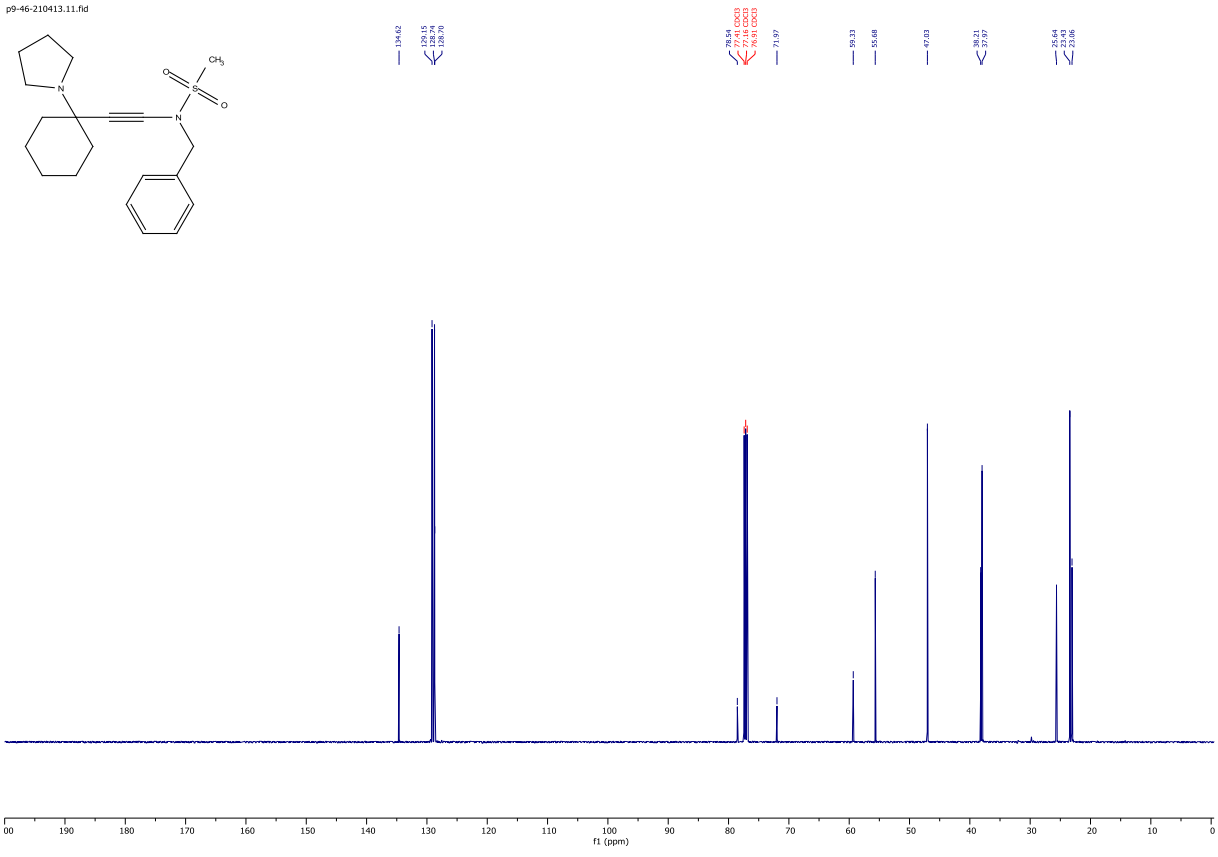


N-Benzyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)methanesulfonamide (**6d**)

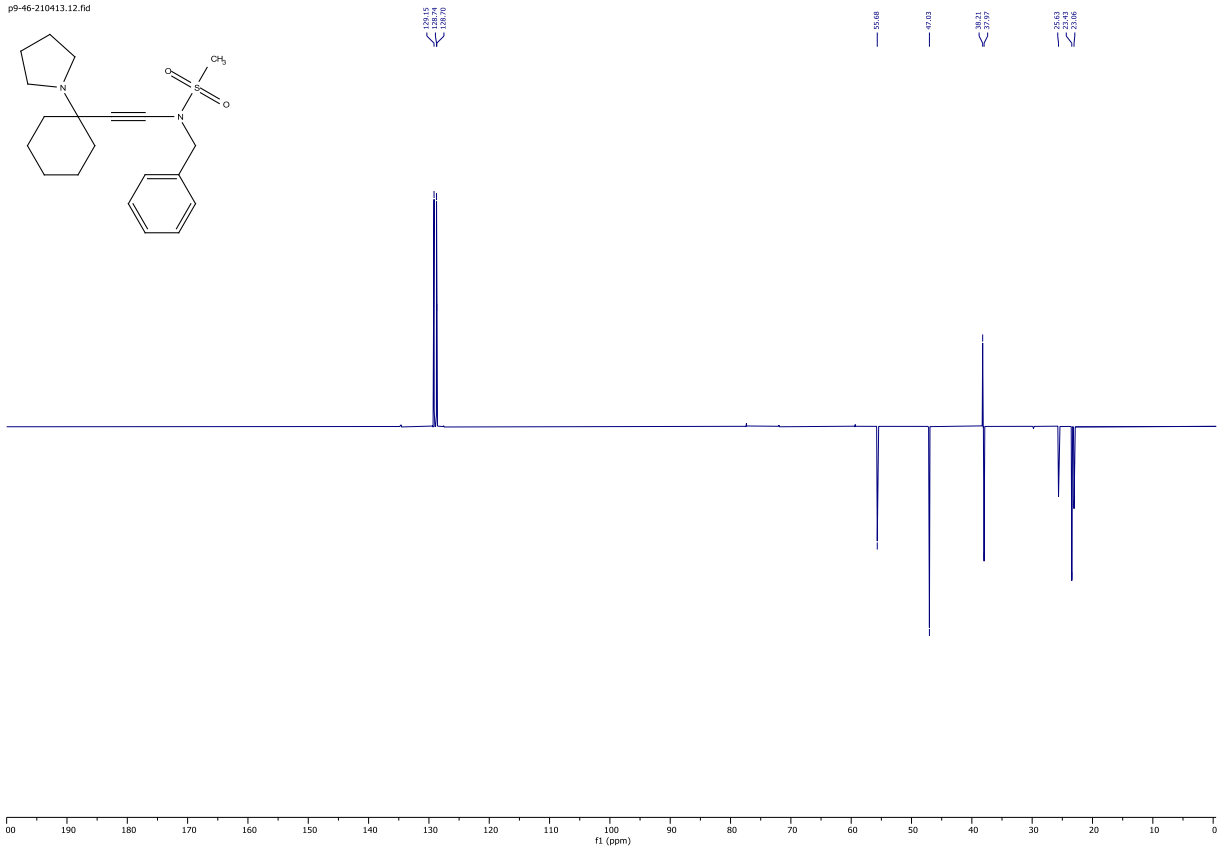
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

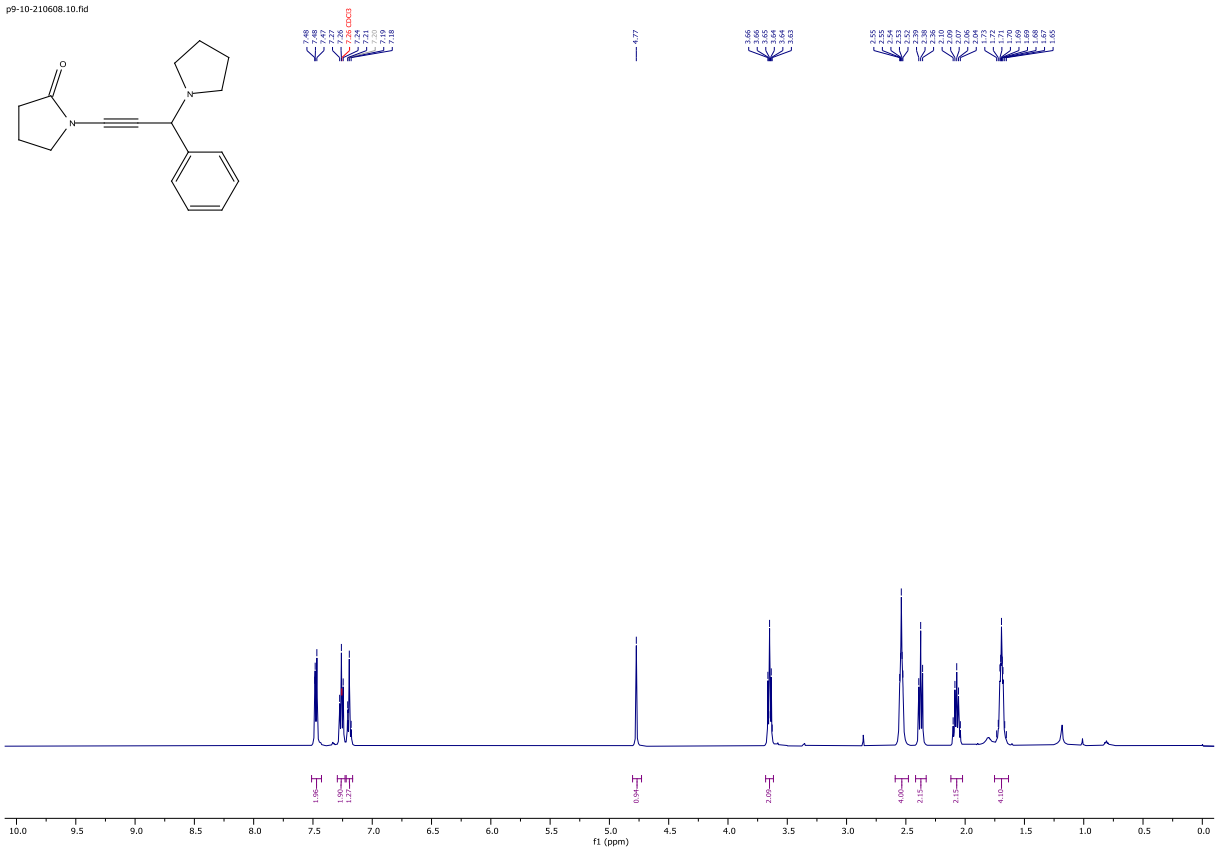


DEPT135 NMR (126 MHz) in $CDCl_3$

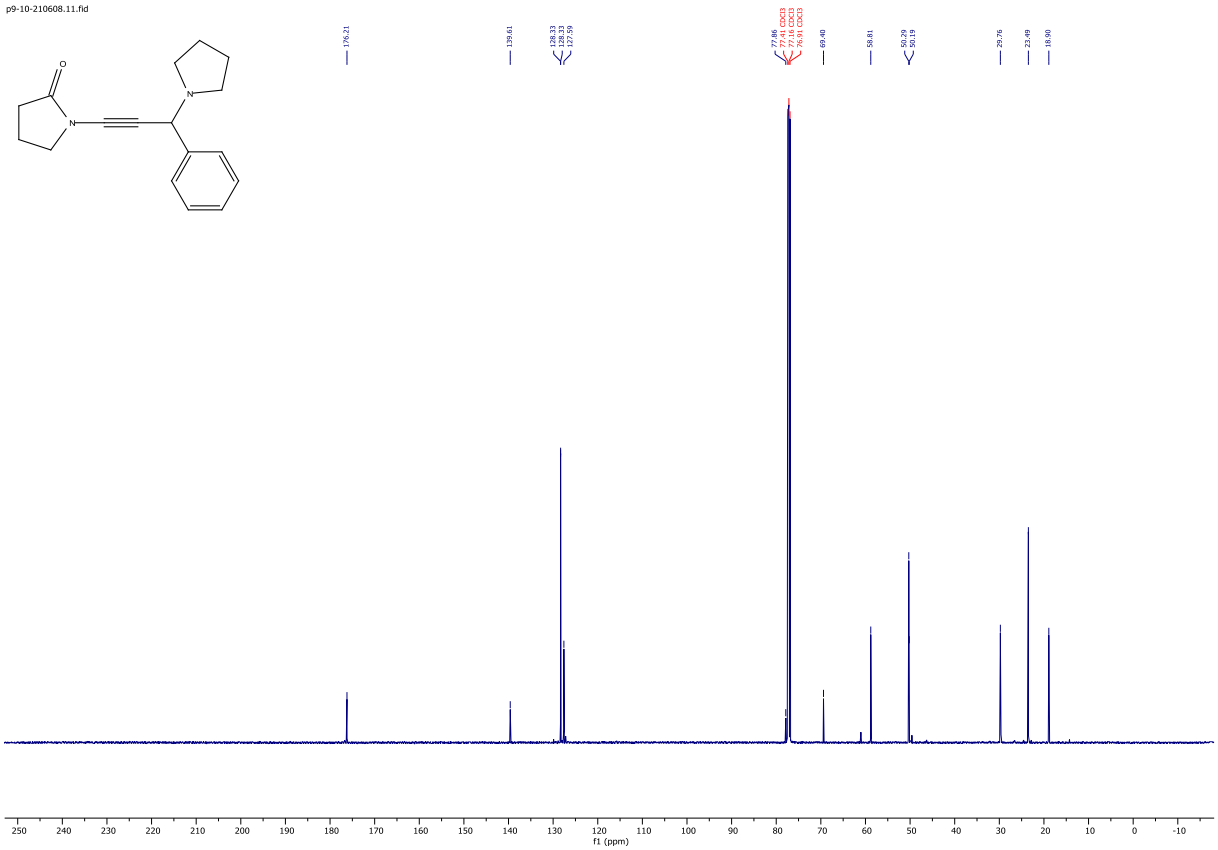


1-(3-Phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)pyrrolidin-2-one (**6e**)

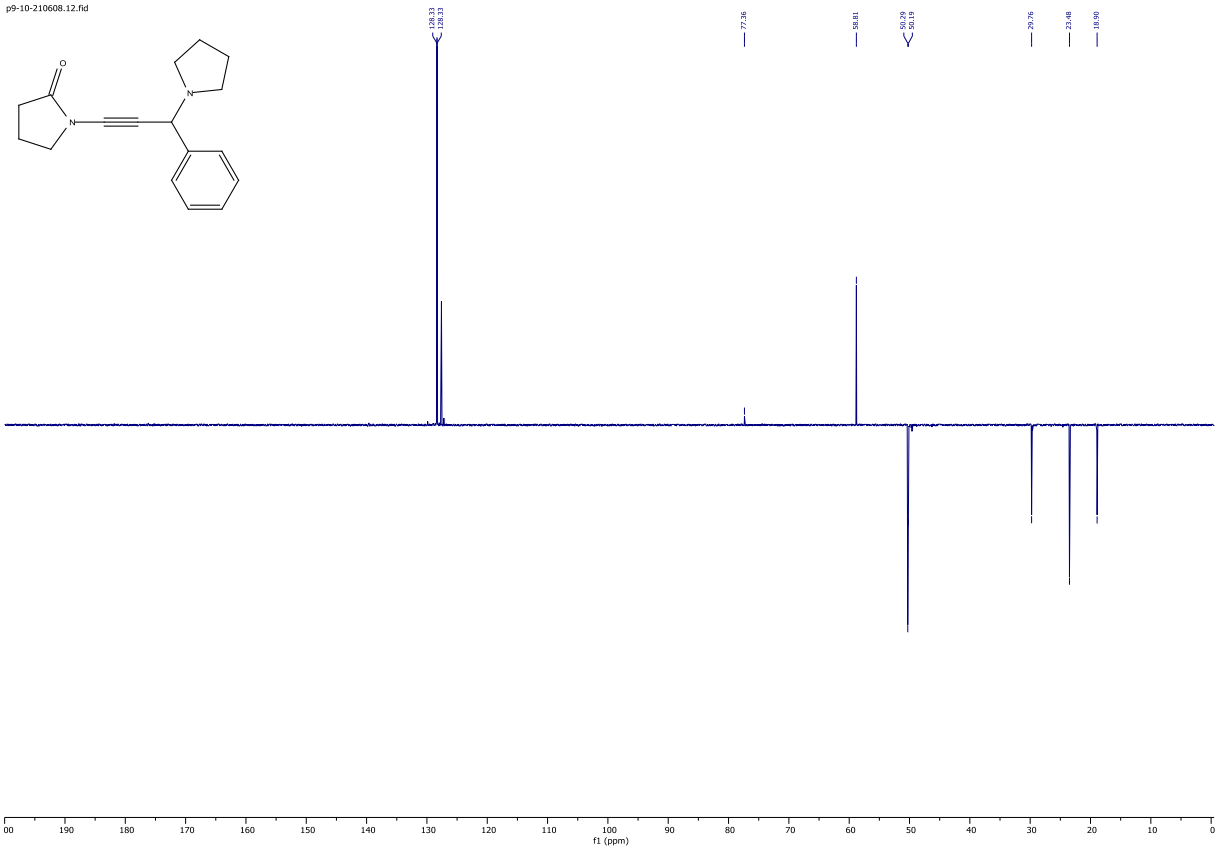
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

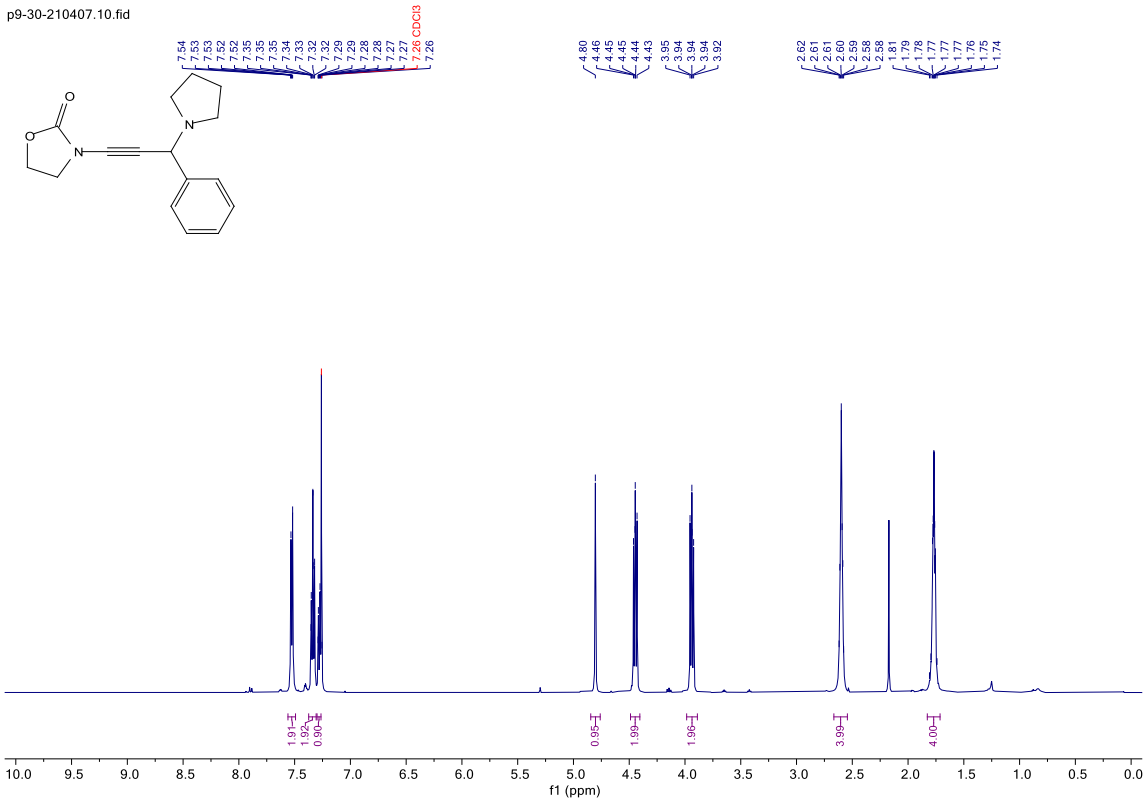


DEPT135 NMR (126 MHz) in $CDCl_3$

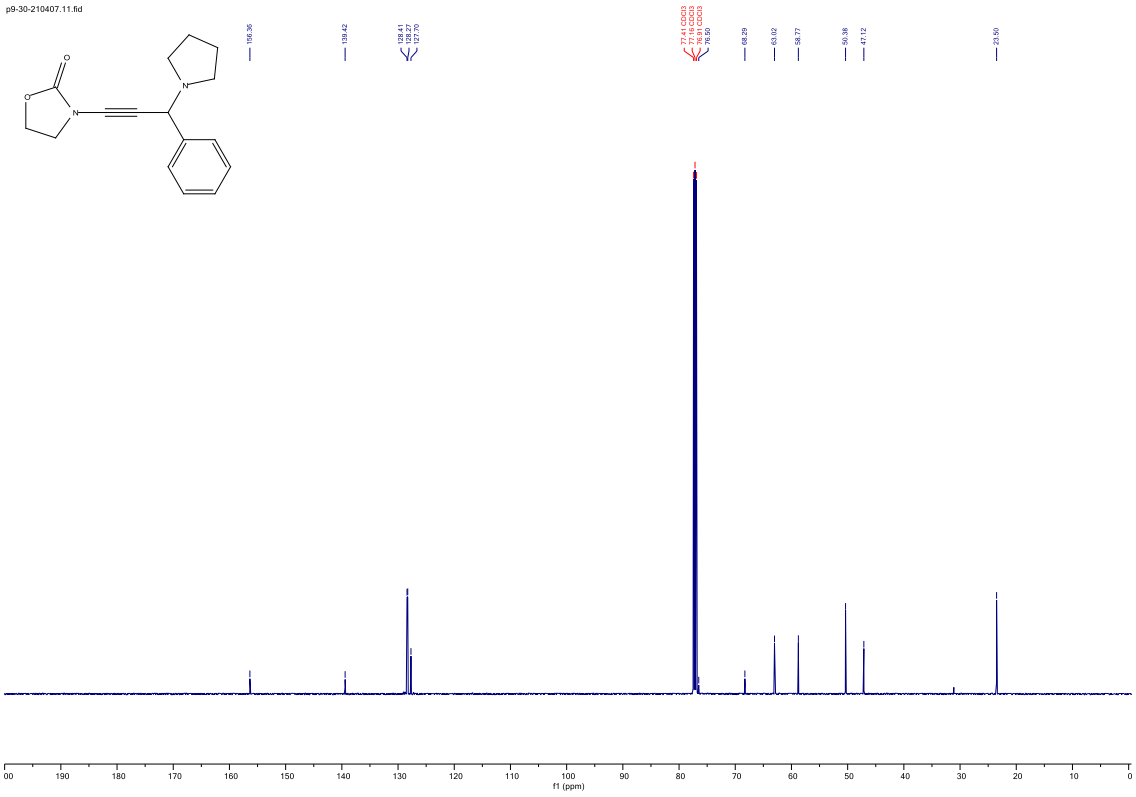


3-(3-Phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)oxazolidin-2-one (**6f**)

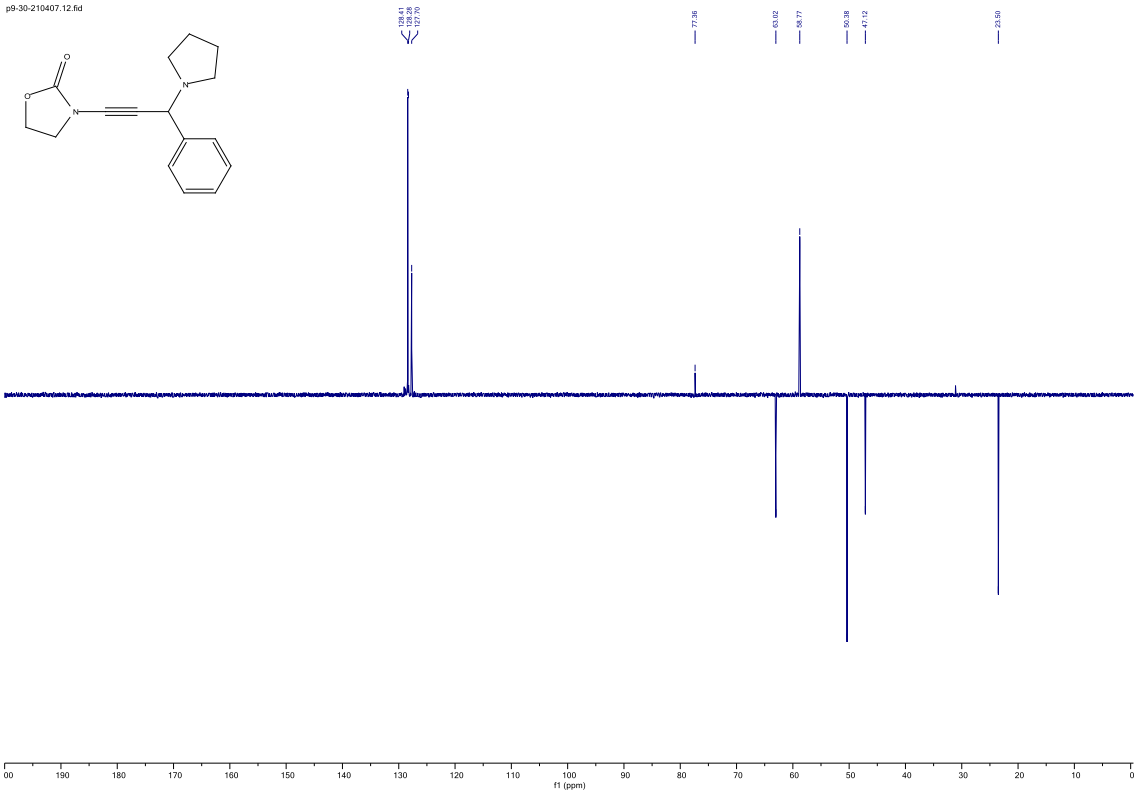
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$



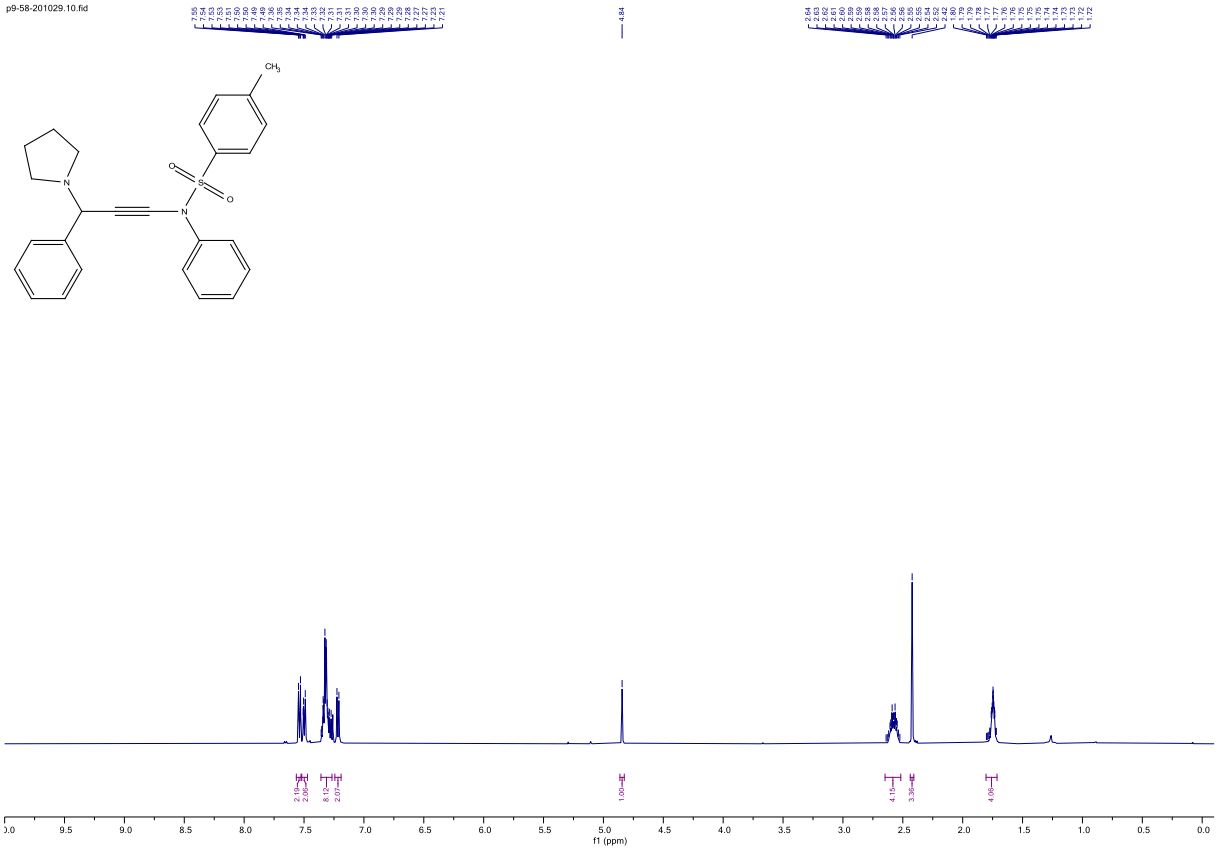
DEPT135 NMR (126 MHz) in $CDCl_3$



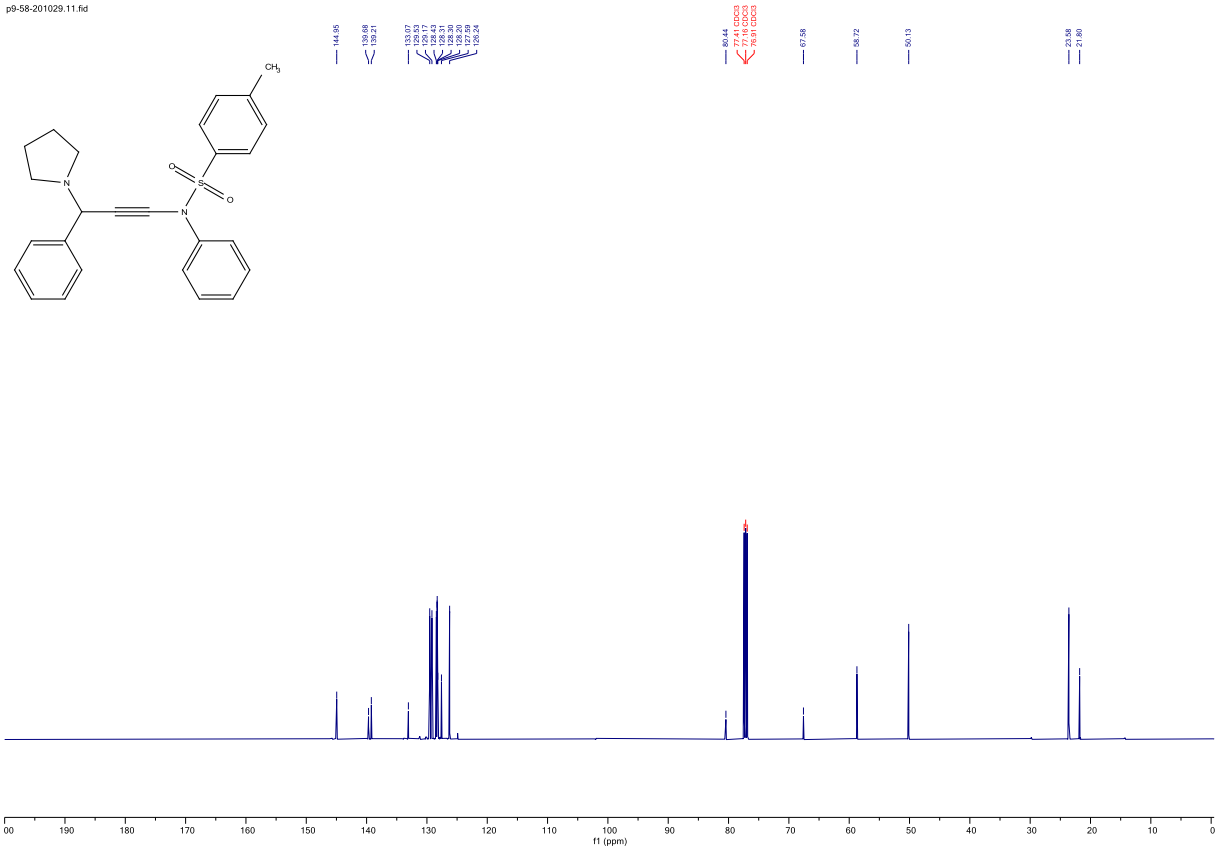
4-Methyl-*N*-phenyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide

(**6h**)

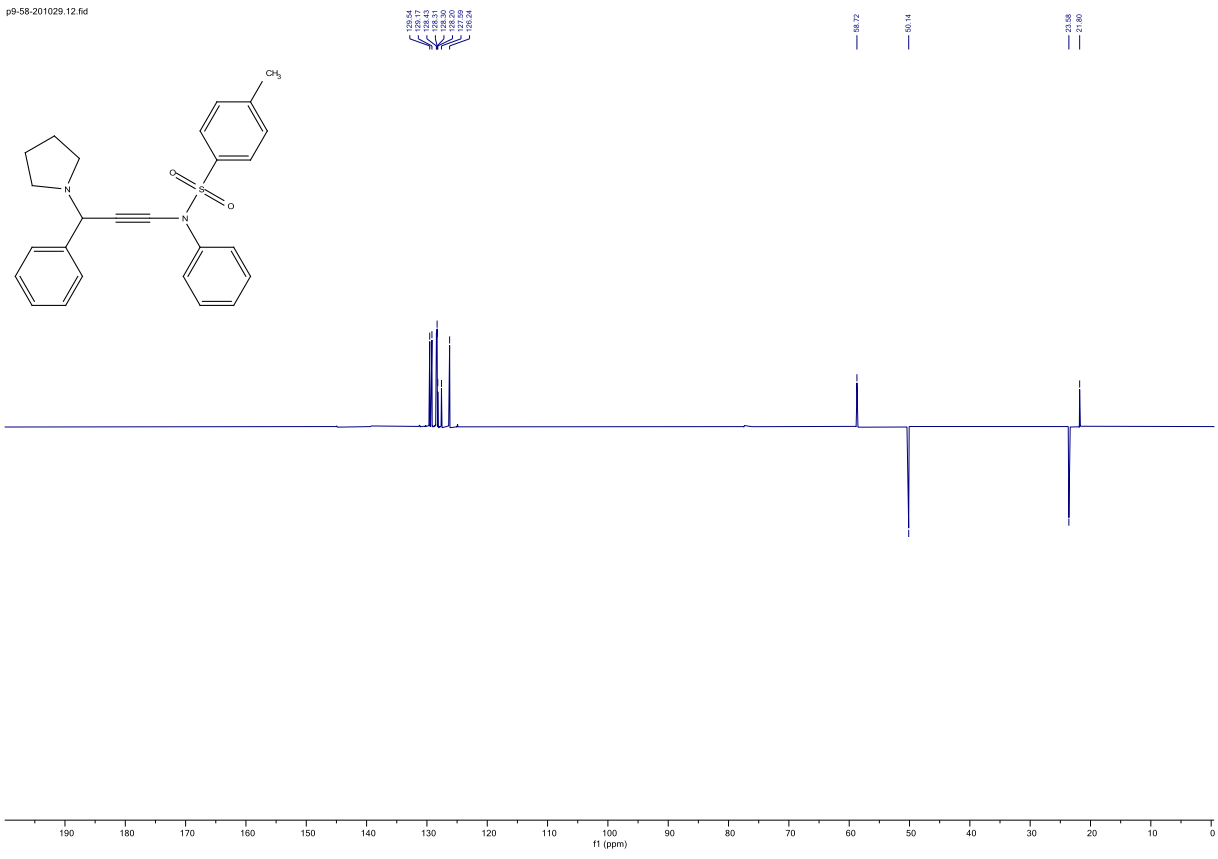
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

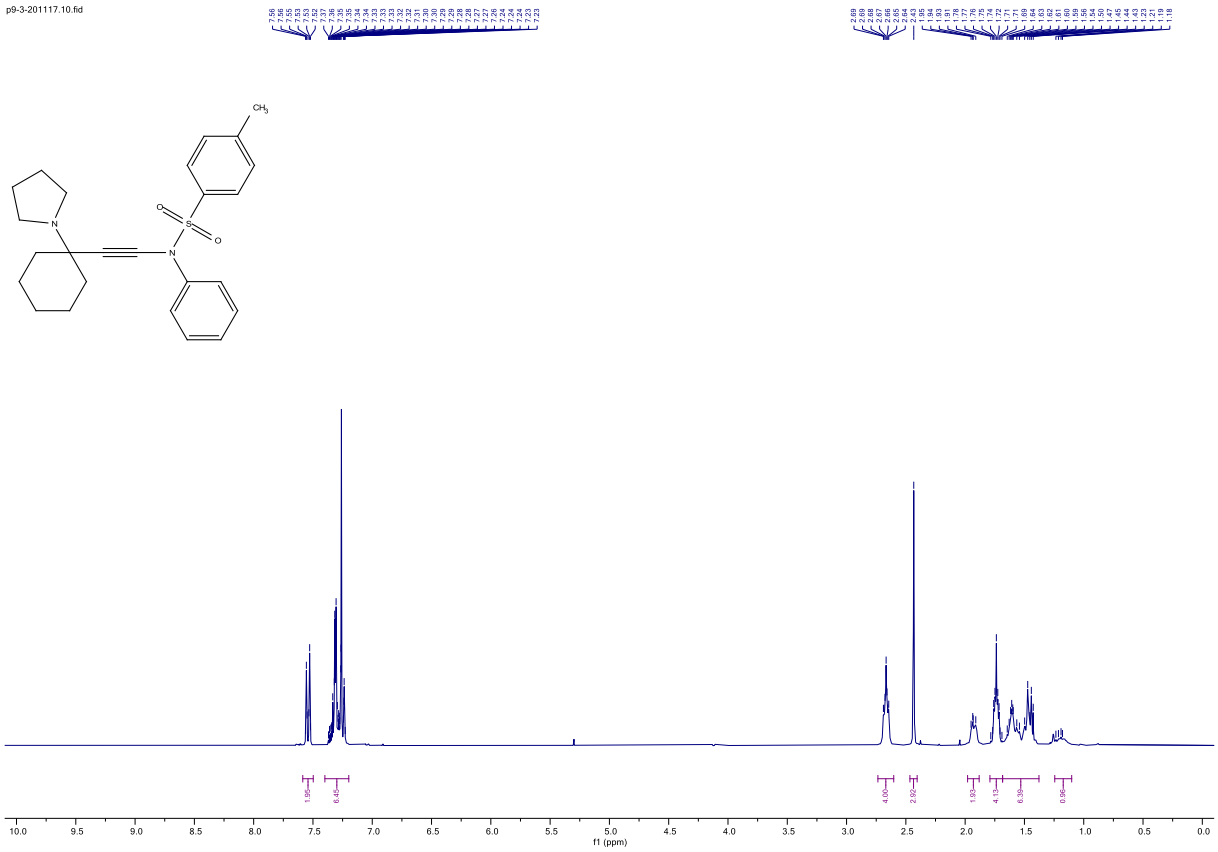


DEPT135 NMR (126 MHz) in $CDCl_3$

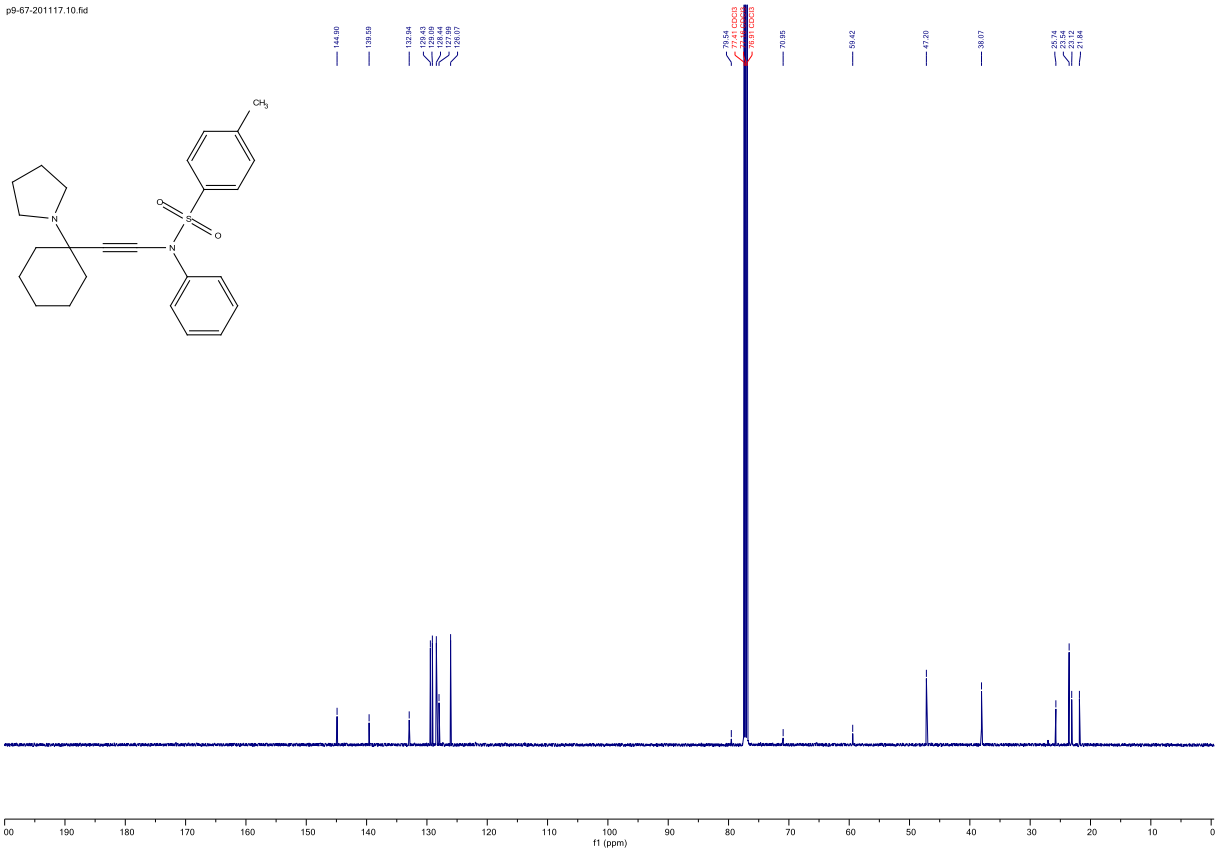


4-Methyl-*N*-phenyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**6i**)

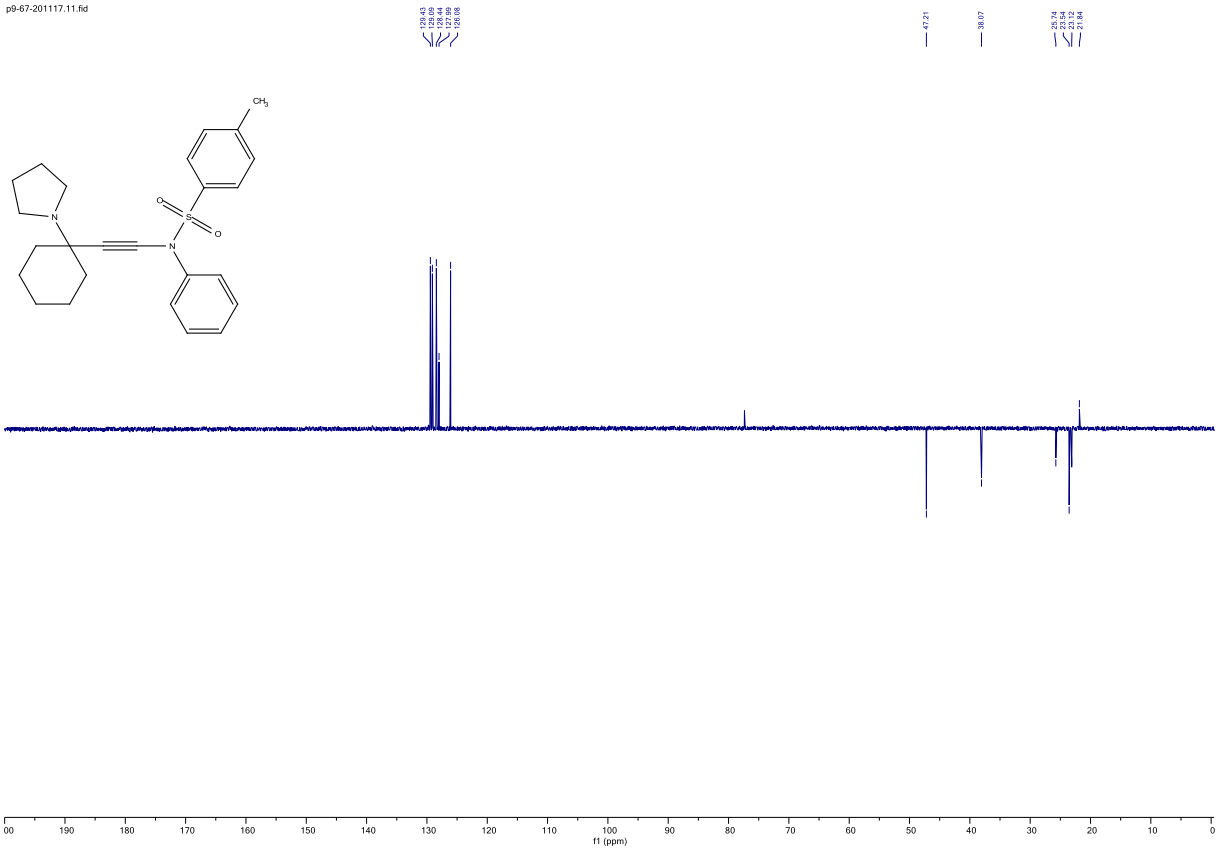
^{1}H NMR (300 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$



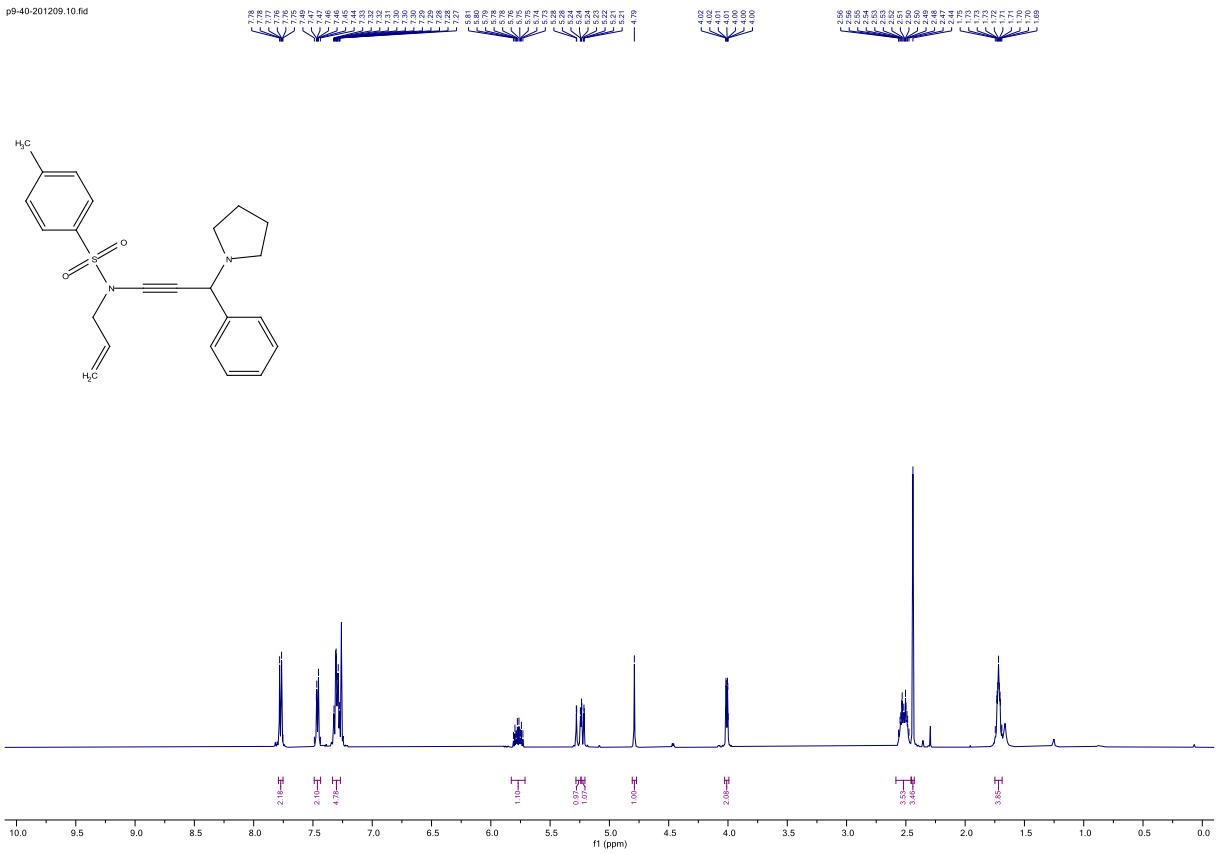
DEPT135 NMR (126 MHz) in $CDCl_3$



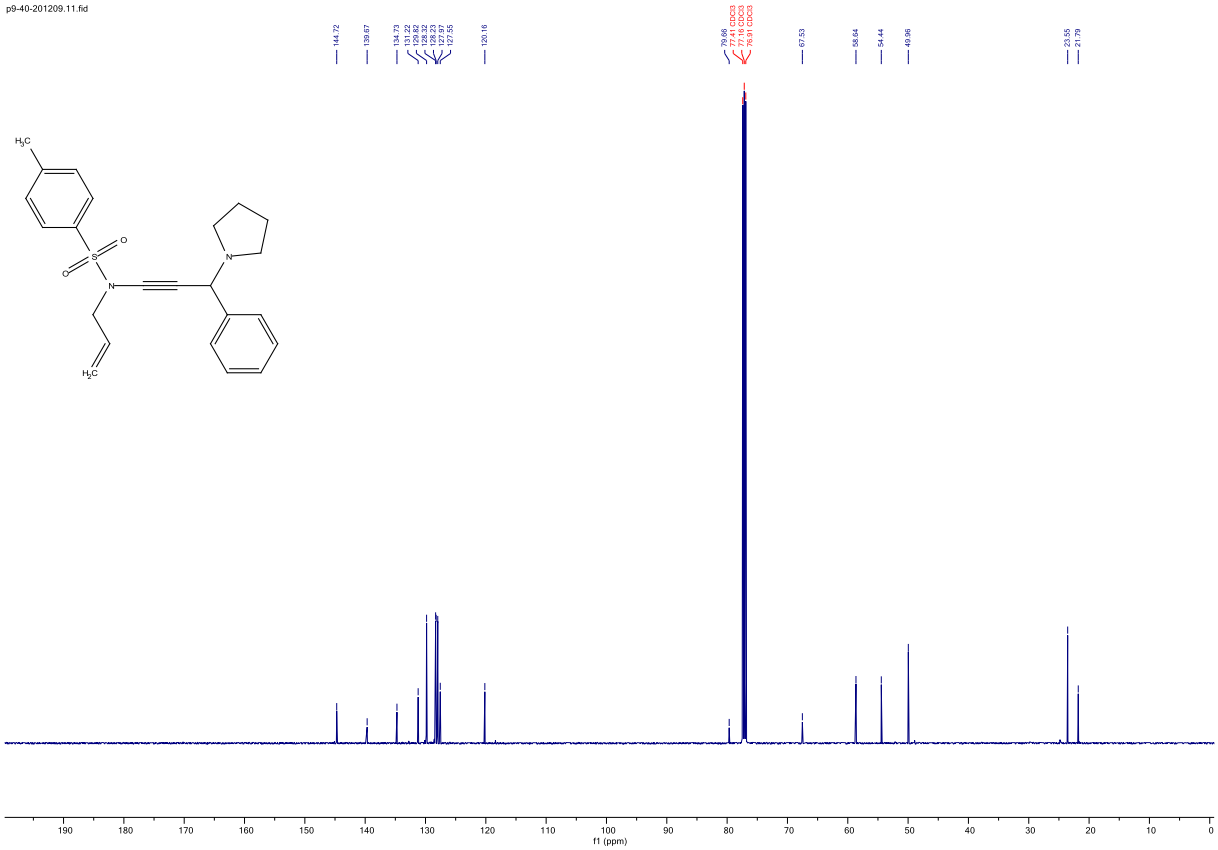
N-Allyl-4-methyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide

(6j)

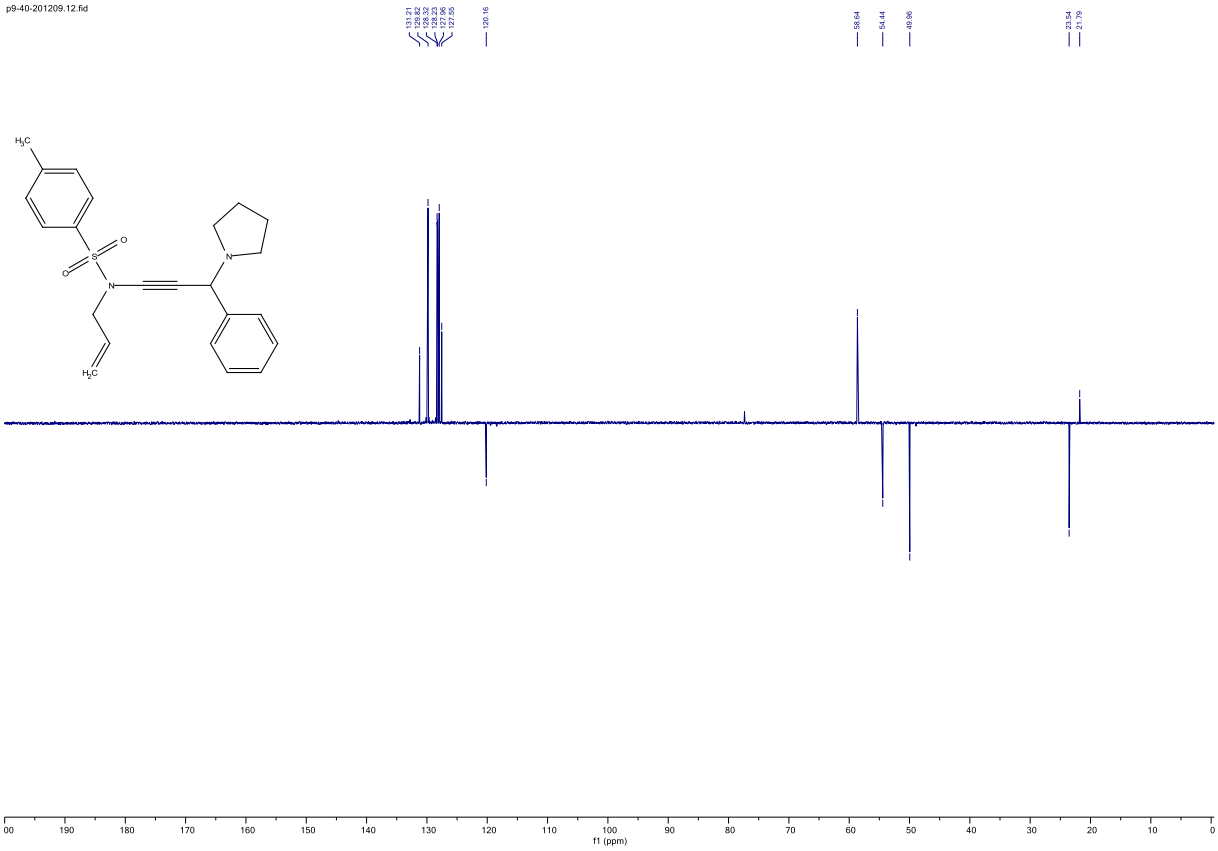
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

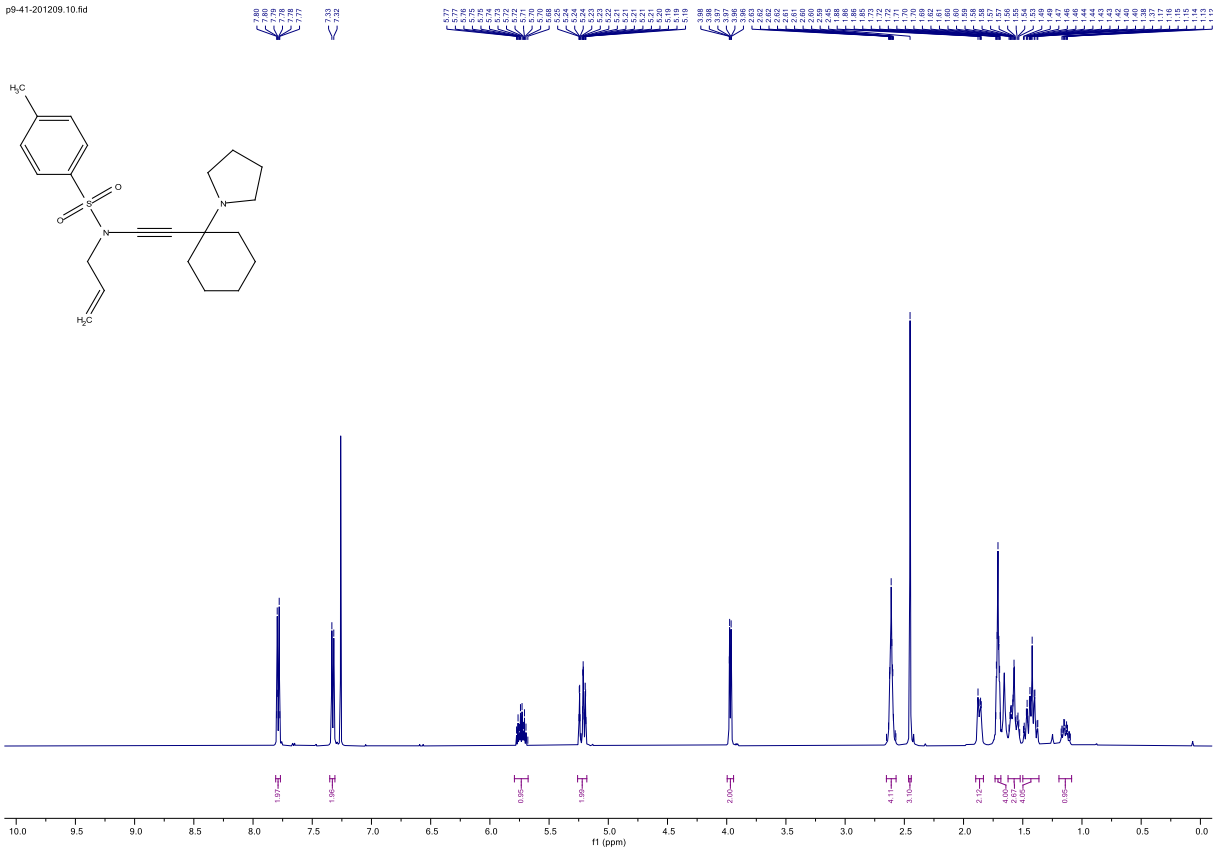


DEPT135 NMR (126 MHz) in $CDCl_3$

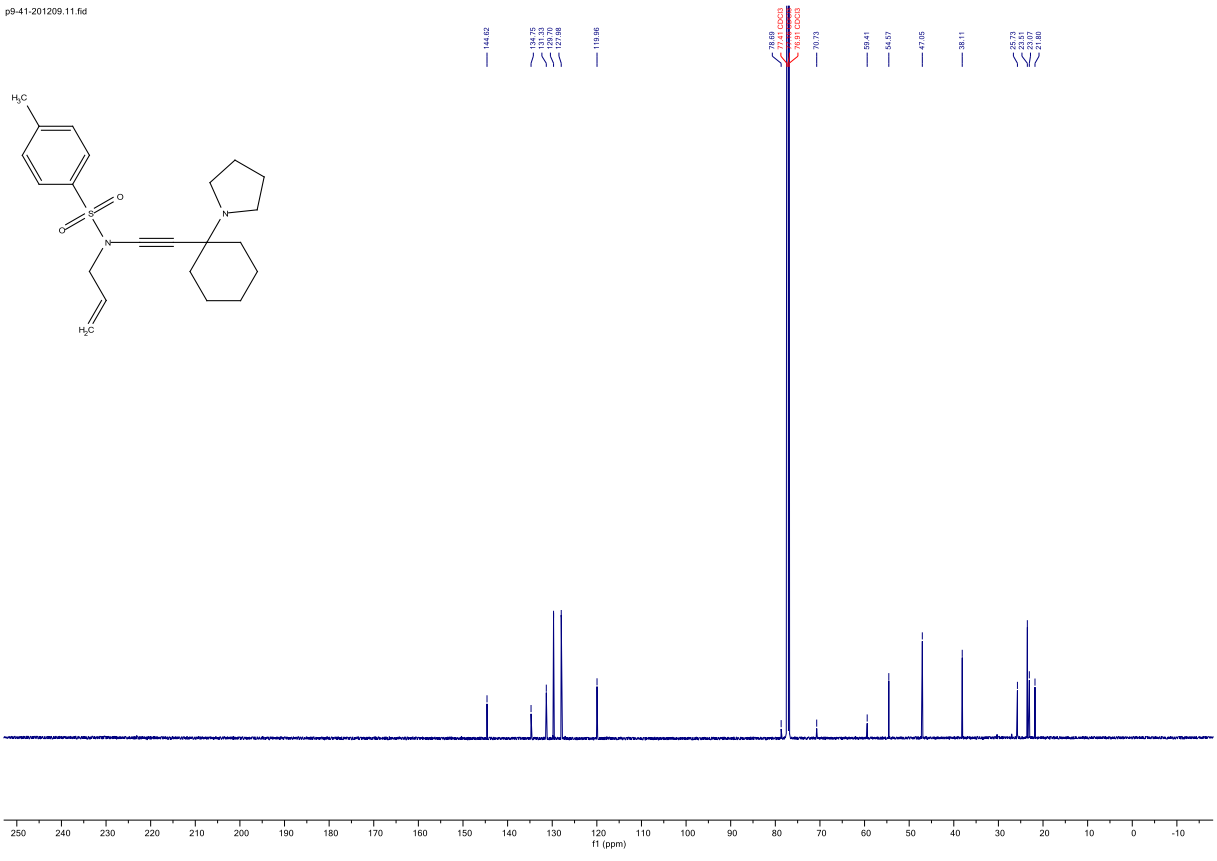


N-Allyl-4-methyl-*N*-((1-(pyrrolidin-1-yl)cyclohexyl)ethynyl)benzenesulfonamide (**6k**)

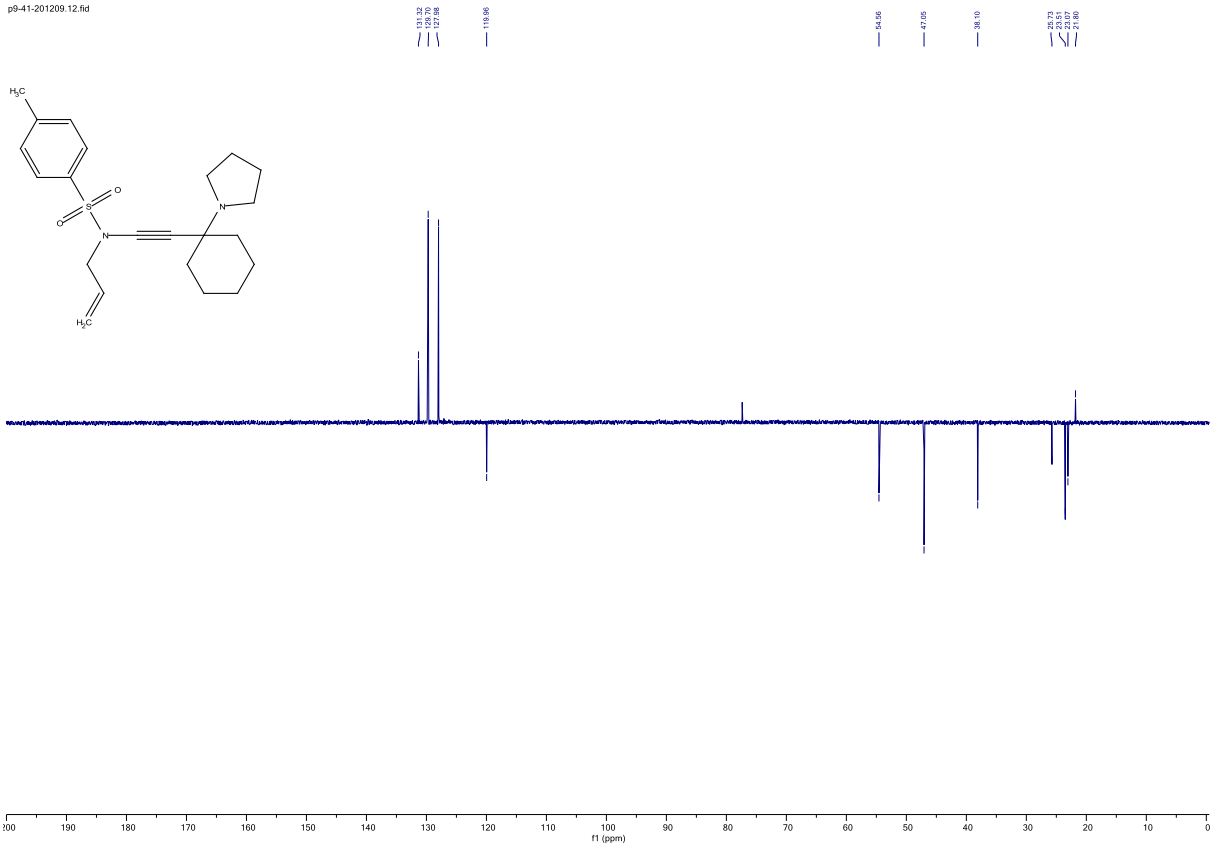
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

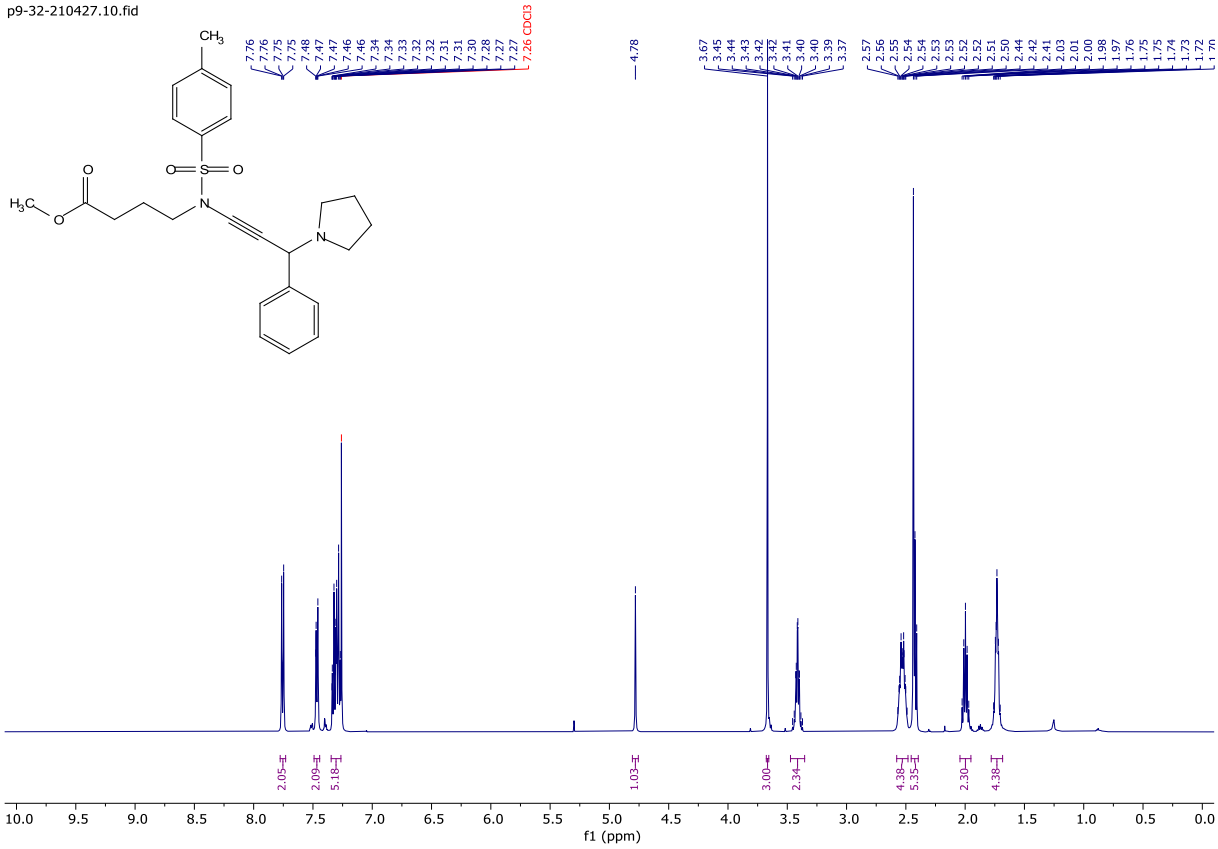


DEPT135 NMR (126 MHz) in $CDCl_3$

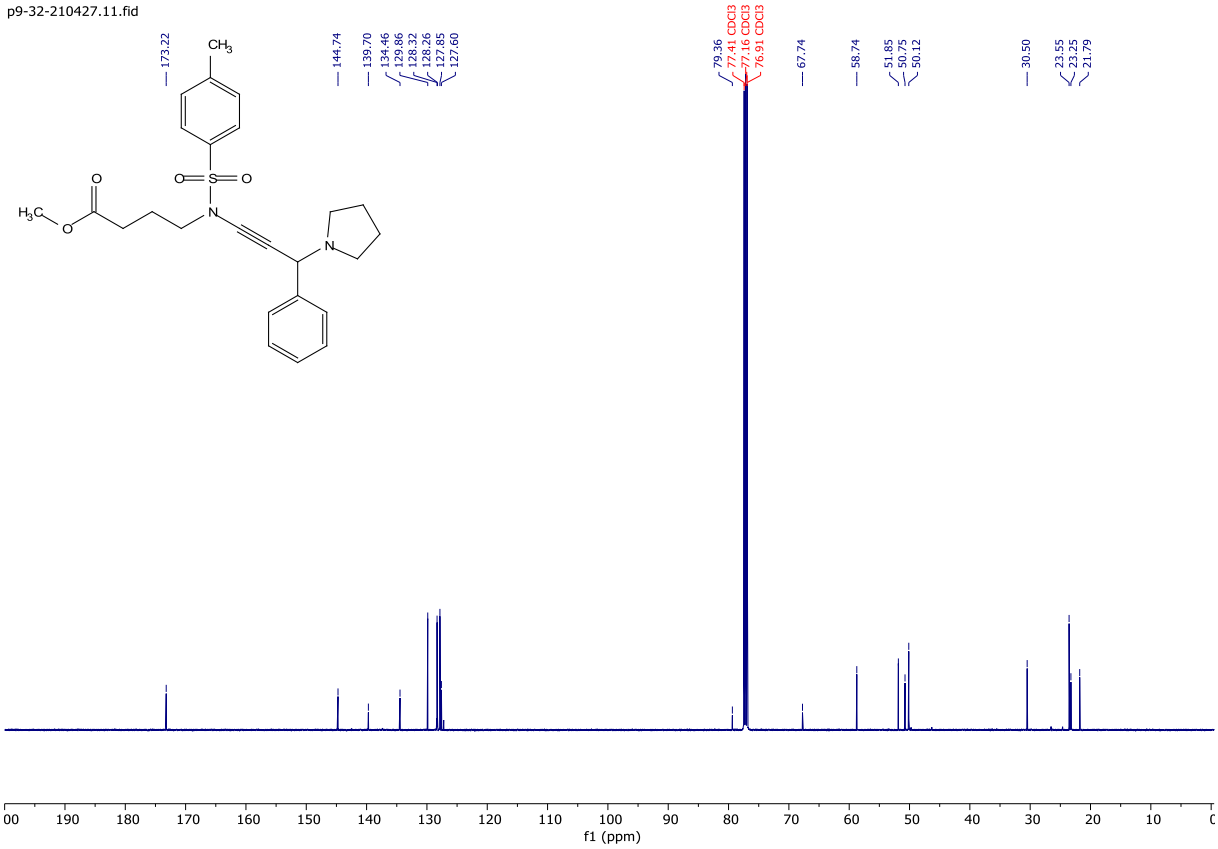


Methyl 4-((4-methyl-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)phenyl)sulfonamido)-butanoate (**6n**)

^{1}H NMR (500 MHz) in $CDCl_3$



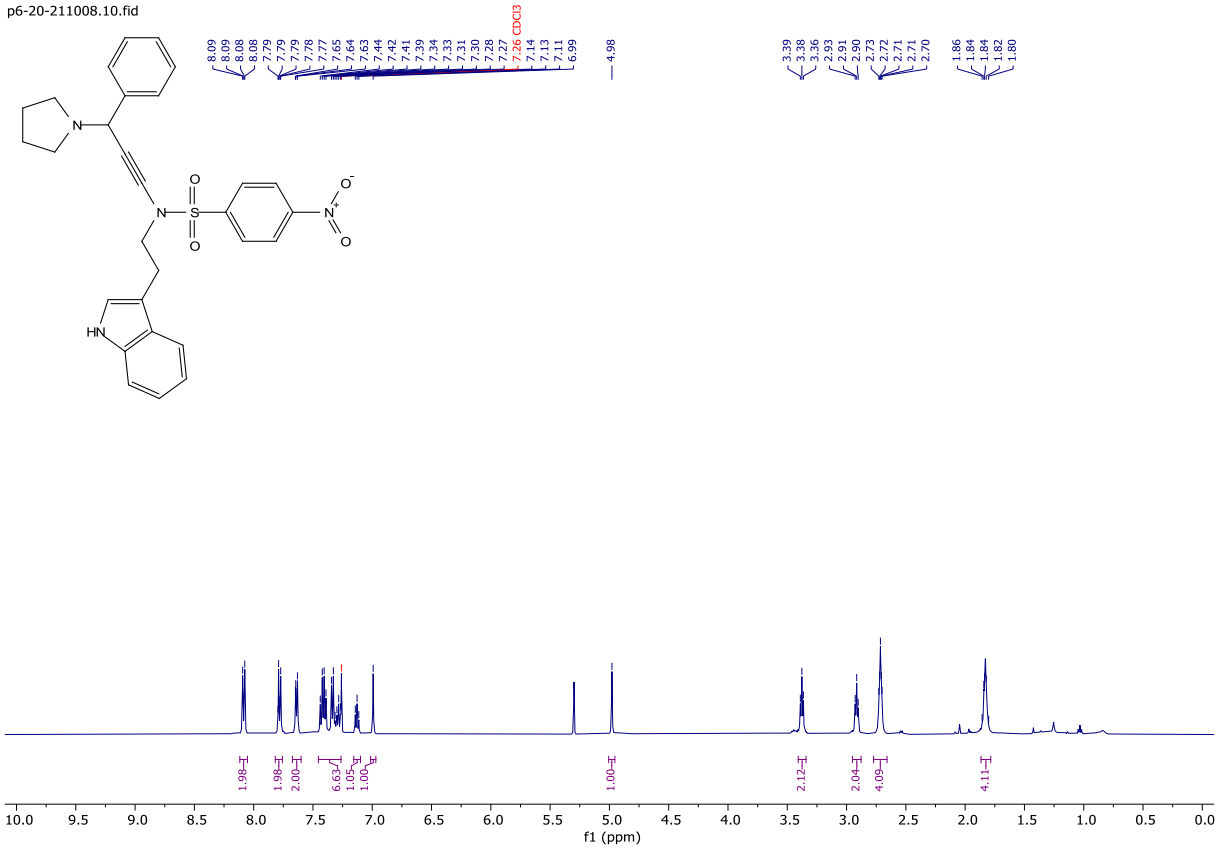
^{13}C NMR (126 MHz) in $CDCl_3$



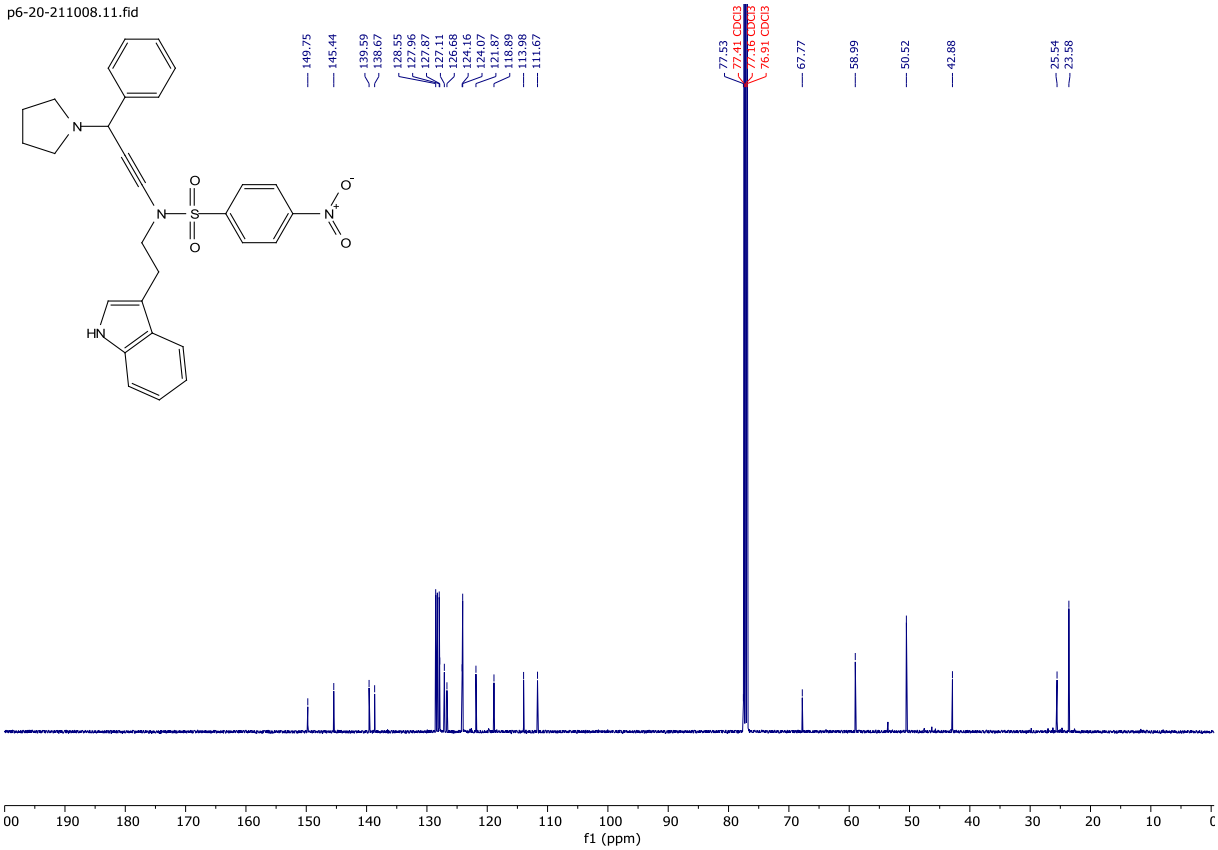
DEPT135 NMR (126 MHz) in $CDCl_3$

N-(2-(1*H*-Indol-3-yl)ethyl)-4-nitro-*N*-(3-phenyl-3-(pyrrolidin-1-yl)prop-1-yn-1-yl)benzenesulfonamide (**6o**)

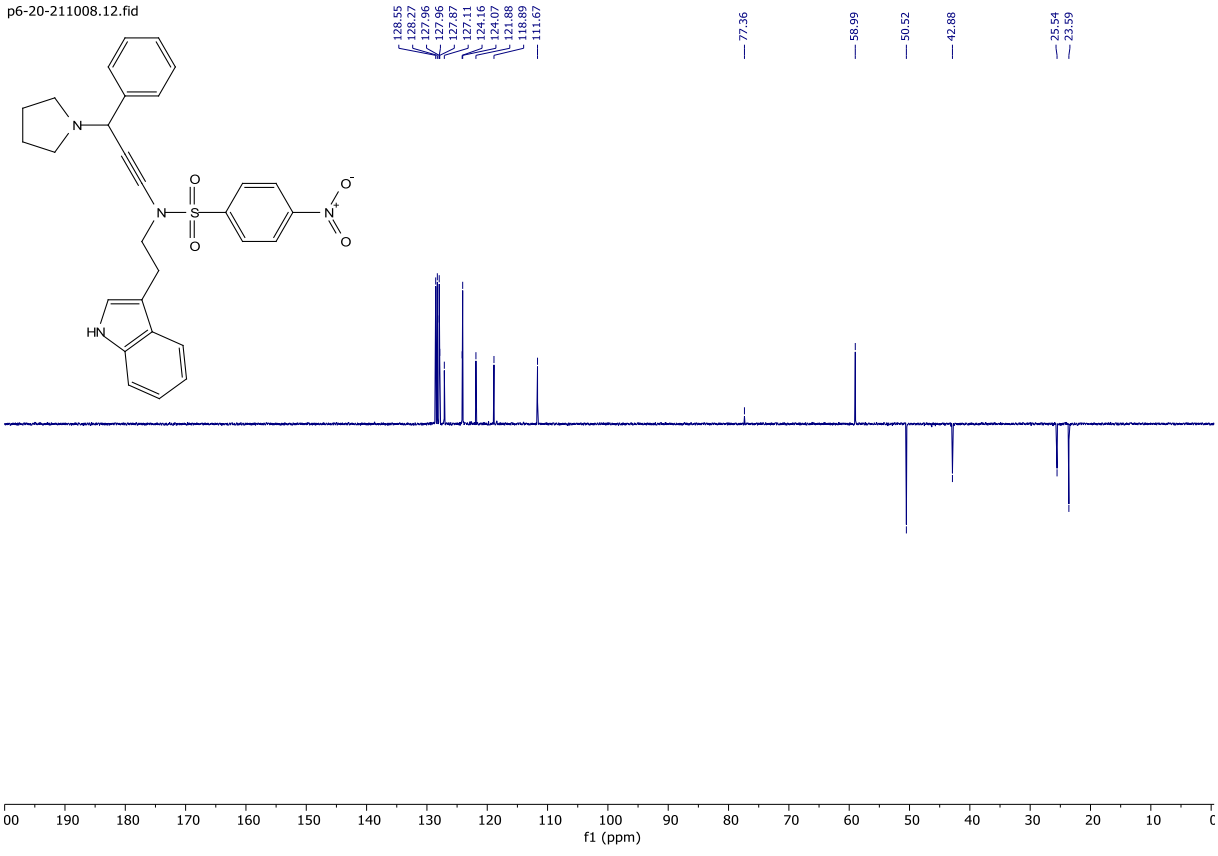
^{1}H NMR (500 MHz) in $CDCl_3$



^{13}C NMR (126 MHz) in $CDCl_3$

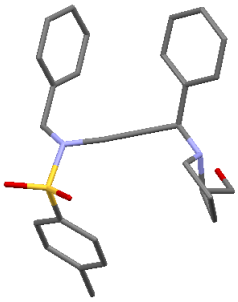


DEPT135 NMR (126 MHz) in $CDCl_3$



VII. X-Ray Crystallographic Data for Compound 5d

Crystal Structure Report for Compound 5d



A specimen of $C_{28}H_{30}N_2O_3S$, approximate dimensions 0.100 mm x 0.200 mm x 0.200 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å).

The integration of the data using an orthorhombic unit cell yielded a total of 52110 reflections to a maximum θ angle of 66.56° (0.84 Å resolution), of which 8605 were independent (average redundancy 6.056, completeness = 99.8%, R_{int} = 4.96%, R_{sig} = 2.89%) and 8115 (94.31%) were greater than $2\sigma(F^2)$. The final cell constants of a = 10.6469(3) Å, b = 15.8266(4) Å, c = 28.9384(7) Å, volume = 4876.2(2) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6327 and 0.7528.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21 21 21, with Z = 8 for the formula unit, $C_{28}H_{30}N_2O_3S$. The final anisotropic full-matrix least-squares refinement on F^2 with617 variables converged at R1 = 3.27%, for the observed data and wR2 = 9.07% for all data. The goodness-of-fit was 1.043. The largest peak in the final difference electron density synthesis was 0.298 $e^-/Å^3$ and the largest hole was-0.306 $e^-/Å^3$ with an RMS deviation of 0.039 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.293 g/cm^3 and F(000), 2016 e^-.

Table 1. Sample and crystal data for Compound 5d.

Identification code	PPFS210322	
Chemical formula	$C_{28}H_{30}N_2O_3S$	
Formula weight	474.60 g/mol	
Temperature	120(2) K	
Wavelength	1.54178 Å	
Crystal size	0.100 x 0.200 x 0.200 mm	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 10.6469(3) Å	α = 90°
	b = 15.8266(4) Å	β = 90°
	c = 28.9384(7) Å	γ = 90°
Volume	4876.2(2) $Å^3$	
Z	8	

Density (calculated)	1.293 g/cm^3
Absorption coefficient	1.438 mm^{-1}
F(000)	2016

Table 2. Data collection and structure refinement for Compound 5d.

Theta range for data collection	3.05 to 66.56°
Index ranges	-12<=h<=12, -18<=k<=18, -34<=l<=34
Reflections collected	52110
Independent reflections	8605 [R(int) = 0.0496]
Max. and min. transmission	0.7528 and 0.6327
Structure solution technique	direct methods
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	8605 / 0 / 617
Goodness-of-fit on F^2	1.043
Δ/σ_{max}	0.001
Final R indices	8115 data; I>2σ(I) R1 = 0.0327, wR2 = 0.0886
	all data R1 = 0.0356, wR2 = 0.0907
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0504P)^2+1.3595P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.009(6)
Largest diff. peak and hole	0.298 and -0.306 eÅ^{-3}
R.M.S. deviation from mean	0.039 eÅ^{-3}

Table 3. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for Compound 5d.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
N1	0.0721(2)	0.95467(14)	0.33391(7)	0.0209(5)
C1	0.1048(3)	0.88946(16)	0.36238(9)	0.0220(6)
C2	0.1392(2)	0.83507(16)	0.38791(9)	0.0232(5)
C3	0.1843(2)	0.76751(16)	0.41872(9)	0.0227(5)
N2	0.1324(2)	0.68344(14)	0.40711(8)	0.0267(5)
C4	0.1700(4)	0.6509(2)	0.36127(11)	0.0480(10)
C5	0.0610(5)	0.5913(3)	0.34782(14)	0.0694(14)
C6	0.9654(4)	0.5959(2)	0.38704(14)	0.0567(11)
C7	0.9942(3)	0.67955(19)	0.40926(11)	0.0351(7)
C8	0.2956(5)	0.6075(3)	0.36658(12)	0.0581(12)
O1	0.2929(3)	0.54916(16)	0.40389(8)	0.0580(7)
C9	0.1589(2)	0.78579(17)	0.46964(9)	0.0220(5)
C10	0.2258(3)	0.74001(19)	0.50245(10)	0.0274(6)
C11	0.2076(3)	0.7546(2)	0.54911(10)	0.0332(7)
C12	0.1224(3)	0.8148(2)	0.56376(10)	0.0341(7)
C13	0.0551(3)	0.8609(2)	0.53133(10)	0.0317(7)
C14	0.0734(3)	0.84650(18)	0.48440(10)	0.0263(6)
S1	0.12313(6)	0.94671(4)	0.27921(2)	0.01998(14)
O2	0.24419(17)	0.90861(12)	0.28136(6)	0.0266(4)
O3	0.10789(19)	0.02931(12)	0.25993(6)	0.0267(4)
C15	0.0190(2)	0.87758(16)	0.25083(9)	0.0184(5)
C16	0.0480(3)	0.79173(17)	0.24813(9)	0.0237(6)
C17	0.9662(3)	0.73877(17)	0.22473(10)	0.0250(6)
C18	0.8568(3)	0.76971(17)	0.20447(9)	0.0238(6)
C19	0.8289(3)	0.85533(17)	0.20835(9)	0.0222(5)
C20	0.9095(2)	0.90964(16)	0.23175(8)	0.0209(5)
C21	0.7703(3)	0.71155(19)	0.17802(10)	0.0307(7)
C22	0.9452(3)	0.99383(18)	0.34020(10)	0.0254(6)
C23	0.9210(3)	0.01563(17)	0.38995(10)	0.0235(6)
C24	0.9841(3)	0.0806(2)	0.41166(12)	0.0358(7)
C25	0.9586(3)	0.1005(2)	0.45730(12)	0.0446(9)
C26	0.8673(3)	0.0569(2)	0.48155(10)	0.0374(7)
C27	0.8014(3)	0.9939(2)	0.45968(12)	0.0383(8)
C28	0.8280(3)	0.97301(19)	0.41445(11)	0.0316(6)
N3	0.5702(2)	0.05202(15)	0.33543(8)	0.0239(5)
C29	0.5798(3)	0.12326(17)	0.36258(10)	0.0267(6)
C30	0.5819(3)	0.18249(17)	0.38830(10)	0.0281(6)
C31	0.5929(3)	0.25553(17)	0.42049(9)	0.0252(5)
N4	0.6806(2)	0.32020(14)	0.40313(8)	0.0236(5)

	x/a	y/b	z/c	U(eq)
C32	0.6318(3)	0.36880(18)	0.36375(10)	0.0292(6)
C33	0.7501(3)	0.4096(2)	0.34297(12)	0.0448(8)
C34	0.8604(3)	0.3681(2)	0.36825(10)	0.0341(7)
C35	0.8040(3)	0.28963(18)	0.38937(10)	0.0300(6)
C36	0.5360(3)	0.4352(2)	0.37666(12)	0.0377(7)
O4	0.4161(2)	0.39726(15)	0.38694(10)	0.0478(6)
C37	0.6264(3)	0.22544(17)	0.46931(9)	0.0260(6)
C38	0.5639(3)	0.15599(18)	0.48702(10)	0.0295(6)
C39	0.5806(3)	0.1320(2)	0.53262(11)	0.0348(7)
C40	0.6637(3)	0.1757(2)	0.56061(10)	0.0349(7)
C41	0.7291(3)	0.24352(19)	0.54268(10)	0.0294(6)
C42	0.7116(3)	0.26815(18)	0.49730(10)	0.0284(6)
S2	0.62823(6)	0.06031(4)	0.28192(2)	0.02555(16)
O5	0.74705(19)	0.10139(14)	0.28617(8)	0.0360(5)
O6	0.6192(2)	0.97740(13)	0.26254(8)	0.0353(5)
C43	0.5268(3)	0.12766(17)	0.25141(9)	0.0212(5)
C44	0.5532(3)	0.21344(17)	0.24919(9)	0.0248(6)
C45	0.4707(3)	0.26630(17)	0.22606(10)	0.0268(6)
C46	0.3627(3)	0.23492(17)	0.20532(9)	0.0229(5)
C47	0.3377(3)	0.14865(17)	0.20844(9)	0.0249(6)
C48	0.4188(3)	0.09470(17)	0.23132(9)	0.0235(6)
C49	0.2735(3)	0.29289(19)	0.18036(9)	0.0301(7)
C50	0.4480(3)	0.00569(17)	0.33991(10)	0.0266(6)
C51	0.4201(3)	0.98539(17)	0.38989(10)	0.0247(6)
C52	0.3268(3)	0.02885(18)	0.41298(11)	0.0307(6)
C53	0.2974(3)	0.00987(19)	0.45869(12)	0.0326(7)
C54	0.3631(3)	0.9468(2)	0.48145(11)	0.0345(7)
C55	0.4548(3)	0.9023(2)	0.45804(12)	0.0408(8)
C56	0.4833(3)	0.9214(2)	0.41267(11)	0.0352(7)

Table 4. Bond lengths (Å) for Compound 5d.

N1-C1	1.366(3)	N1-C22	1.498(3)
N1-S1	1.678(2)	C1-C2	1.192(4)
C2-C3	1.473(3)	C3-N2	1.479(3)
C3-C9	1.526(3)	C3-H3	1.0
N2-C7	1.473(4)	N2-C4	1.478(4)
C4-C8	1.511(5)	C4-C5	1.546(6)
C4-H4	1.0	C5-C6	1.527(7)

C5-H5A	0.99	C5-H5B	0.99
C6-C7	1.503(4)	C6-H6A	0.99
C6-H6B	0.99	C7-H7A	0.99
C7-H7B	0.99	C8-O1	1.421(4)
C8-H8A	0.99	C8-H8B	0.99
O1-H1A	0.84	C9-C10	1.390(4)
C9-C14	1.391(4)	C10-C11	1.384(4)
C10-H10	0.95	C11-C12	1.382(5)
C11-H11	0.95	C12-C13	1.388(4)
C12-H12	0.95	C13-C14	1.391(4)
C13-H13	0.95	C14-H14	0.95
S1-O2	1.424(2)	S1-O3	1.431(2)
S1-C15	1.761(3)	C15-C20	1.386(4)
C15-C16	1.396(4)	C16-C17	1.385(4)
C16-H16	0.95	C17-C18	1.394(4)
C17-H17	0.95	C18-C19	1.392(4)
C18-C21	1.510(4)	C19-C20	1.391(4)
C19-H19	0.95	C20-H20	0.95
C21-H21A	0.98	C21-H21B	0.98
C21-H21C	0.98	C22-C23	1.503(4)
C22-H22A	0.99	C22-H22B	0.99
C23-C24	1.379(4)	C23-C28	1.392(4)
C24-C25	1.385(5)	C24-H24	0.95
C25-C26	1.383(5)	C25-H25	0.95
C26-C27	1.375(5)	C26-H26	0.95
C27-C28	1.379(4)	C27-H27	0.95
C28-H28	0.95	N3-C29	1.378(4)
N3-C50	1.499(4)	N3-S2	1.672(2)
C29-C30	1.197(4)	C30-C31	1.489(4)
C31-N4	1.473(3)	C31-C37	1.533(4)
C31-H31	1.0	N4-C35	1.455(4)
N4-C32	1.470(4)	C32-C36	1.512(4)
C32-C33	1.537(4)	C32-H32	1.0
C33-C34	1.531(5)	C33-H33A	0.99
C33-H33B	0.99	C34-C35	1.509(4)
C34-H34A	0.99	C34-H34B	0.99
C35-H35A	0.99	C35-H35B	0.99
C36-O4	1.442(4)	C36-H36A	0.99
C36-H36B	0.99	O4-H4A	0.84
C37-C38	1.383(4)	C37-C42	1.392(4)

C38-C39	1.385(4)	C38-H38	0.95
C39-C40	1.385(5)	C39-H39	0.95
C40-C41	1.381(4)	C40-H40	0.95
C41-C42	1.383(4)	C41-H41	0.95
C42-H42	0.95	S2-O5	1.428(2)
S2-O6	1.430(2)	S2-C43	1.755(3)
C43-C44	1.388(4)	C43-C48	1.390(4)
C44-C45	1.386(4)	C44-H44	0.95
C45-C46	1.389(4)	C45-H45	0.95
C46-C47	1.394(4)	C46-C49	1.506(4)
C47-C48	1.383(4)	C47-H47	0.95
C48-H48	0.95	C49-H49A	0.98
C49-H49B	0.98	C49-H49C	0.98
C50-C51	1.511(4)	C50-H50A	0.99
C50-H50B	0.99	C51-C52	1.381(4)
C51-C56	1.382(4)	C52-C53	1.392(5)
C52-H52	0.95	C53-C54	1.386(4)
C53-H53	0.95	C54-C55	1.382(5)
C54-H54	0.95	C55-C56	1.381(5)
C55-H55	0.95	C56-H56	0.95

Table 5. Bond angles (°) for Compound 5d.

C1-N1-C22	118.0(2)	C1-N1-S1	115.46(18)
C22-N1-S1	115.95(17)	C2-C1-N1	176.3(3)
C1-C2-C3	178.6(3)	C2-C3-N2	113.2(2)
C2-C3-C9	112.9(2)	N2-C3-C9	108.9(2)
C2-C3-H3	107.2	N2-C3-H3	107.2
C9-C3-H3	107.2	C7-N2-C4	107.1(3)
C7-N2-C3	113.6(2)	C4-N2-C3	114.5(2)
N2-C4-C8	107.9(3)	N2-C4-C5	103.6(3)
C8-C4-C5	114.3(3)	N2-C4-H4	110.3
C8-C4-H4	110.3	C5-C4-H4	110.3
C6-C5-C4	106.5(3)	C6-C5-H5A	110.4
C4-C5-H5A	110.4	C6-C5-H5B	110.4
C4-C5-H5B	110.4	H5A-C5-H5B	108.6
C7-C6-C5	102.9(3)	C7-C6-H6A	111.2
C5-C6-H6A	111.2	C7-C6-H6B	111.2
C5-C6-H6B	111.2	H6A-C6-H6B	109.1
N2-C7-C6	102.9(3)	N2-C7-H7A	111.2

C6-C7-H7A	111.2	N2-C7-H7B	111.2
C6-C7-H7B	111.2	H7A-C7-H7B	109.1
O1-C8-C4	110.8(3)	O1-C8-H8A	109.5
C4-C8-H8A	109.5	O1-C8-H8B	109.5
C4-C8-H8B	109.5	H8A-C8-H8B	108.1
C8-O1-H1A	109.5	C10-C9-C14	119.1(3)
C10-C9-C3	118.0(2)	C14-C9-C3	122.9(2)
C11-C10-C9	120.5(3)	C11-C10-H10	119.7
C9-C10-H10	119.7	C12-C11-C10	120.4(3)
C12-C11-H11	119.8	C10-C11-H11	119.8
C11-C12-C13	119.6(3)	C11-C12-H12	120.2
C13-C12-H12	120.2	C12-C13-C14	120.1(3)
C12-C13-H13	119.9	C14-C13-H13	119.9
C13-C14-C9	120.3(3)	C13-C14-H14	119.9
C9-C14-H14	119.9	O2-S1-O3	120.43(12)
O2-S1-N1	106.46(11)	O3-S1-N1	105.23(11)
O2-S1-C15	109.08(12)	O3-S1-C15	108.33(12)
N1-S1-C15	106.44(12)	C20-C15-C16	121.3(2)
C20-C15-S1	119.19(19)	C16-C15-S1	119.5(2)
C17-C16-C15	118.5(3)	C17-C16-H16	120.7
C15-C16-H16	120.7	C16-C17-C18	121.2(3)
C16-C17-H17	119.4	C18-C17-H17	119.4
C19-C18-C17	119.1(2)	C19-C18-C21	120.3(3)
C17-C18-C21	120.6(3)	C20-C19-C18	120.6(3)
C20-C19-H19	119.7	C18-C19-H19	119.7
C15-C20-C19	119.1(2)	C15-C20-H20	120.4
C19-C20-H20	120.4	C18-C21-H21A	109.5
C18-C21-H21B	109.5	H21A-C21-H21B	109.5
C18-C21-H21C	109.5	H21A-C21-H21C	109.5
H21B-C21-H21C	109.5	N1-C22-C23	111.5(2)
N1-C22-H22A	109.3	C23-C22-H22A	109.3
N1-C22-H22B	109.3	C23-C22-H22B	109.3
H22A-C22-H22B	108.0	C24-C23-C28	118.4(3)
C24-C23-C22	121.6(3)	C28-C23-C22	119.9(3)
C23-C24-C25	120.6(3)	C23-C24-H24	119.7
C25-C24-H24	119.7	C26-C25-C24	120.6(3)
C26-C25-H25	119.7	C24-C25-H25	119.7
C27-C26-C25	119.2(3)	C27-C26-H26	120.4
C25-C26-H26	120.4	C26-C27-C28	120.4(3)
C26-C27-H27	119.8	C28-C27-H27	119.8

C27-C28-C23	120.9(3)	C27-C28-H28	119.6
C23-C28-H28	119.6	C29-N3-C50	114.6(2)
C29-N3-S2	115.85(19)	C50-N3-S2	116.05(18)
C30-C29-N3	175.2(3)	C29-C30-C31	176.5(3)
N4-C31-C30	112.1(2)	N4-C31-C37	112.5(2)
C30-C31-C37	110.7(2)	N4-C31-H31	107.1
C30-C31-H31	107.1	C37-C31-H31	107.1
C35-N4-C32	106.3(2)	C35-N4-C31	115.7(2)
C32-N4-C31	113.8(2)	N4-C32-C36	114.2(2)
N4-C32-C33	103.5(2)	C36-C32-C33	111.0(3)
N4-C32-H32	109.3	C36-C32-H32	109.3
C33-C32-H32	109.3	C34-C33-C32	105.1(2)
C34-C33-H33A	110.7	C32-C33-H33A	110.7
C34-C33-H33B	110.7	C32-C33-H33B	110.7
H33A-C33-H33B	108.8	C35-C34-C33	104.0(3)
C35-C34-H34A	111.0	C33-C34-H34A	111.0
C35-C34-H34B	111.0	C33-C34-H34B	111.0
H34A-C34-H34B	109.0	N4-C35-C34	101.3(2)
N4-C35-H35A	111.5	C34-C35-H35A	111.5
N4-C35-H35B	111.5	C34-C35-H35B	111.5
H35A-C35-H35B	109.3	O4-C36-C32	111.0(3)
O4-C36-H36A	109.4	C32-C36-H36A	109.4
O4-C36-H36B	109.4	C32-C36-H36B	109.4
H36A-C36-H36B	108.0	C36-O4-H4A	109.5
C38-C37-C42	118.9(3)	C38-C37-C31	118.5(3)
C42-C37-C31	122.5(2)	C37-C38-C39	120.6(3)
C37-C38-H38	119.7	C39-C38-H38	119.7
C38-C39-C40	120.1(3)	C38-C39-H39	119.9
C40-C39-H39	119.9	C41-C40-C39	119.4(3)
C41-C40-H40	120.3	C39-C40-H40	120.3
C40-C41-C42	120.5(3)	C40-C41-H41	119.7
C42-C41-H41	119.7	C41-C42-C37	120.3(3)
C41-C42-H42	119.9	C37-C42-H42	119.9
O5-S2-O6	120.76(13)	O5-S2-N3	106.46(13)
O6-S2-N3	105.43(13)	O5-S2-C43	108.17(13)
O6-S2-C43	108.56(13)	N3-S2-C43	106.63(12)
C44-C43-C48	121.0(2)	C44-C43-S2	119.5(2)
C48-C43-S2	119.4(2)	C45-C44-C43	119.0(3)
C45-C44-H44	120.5	C43-C44-H44	120.5
C44-C45-C46	121.2(3)	C44-C45-H45	119.4

C46-C45-H45	119.4	C45-C46-C47	118.7(3)
C45-C46-C49	120.8(2)	C47-C46-C49	120.5(3)
C48-C47-C46	121.1(3)	C48-C47-H47	119.5
C46-C47-H47	119.5	C47-C48-C43	119.0(2)
C47-C48-H48	120.5	C43-C48-H48	120.5
C46-C49-H49A	109.5	C46-C49-H49B	109.5
H49A-C49-H49B	109.5	C46-C49-H49C	109.5
H49A-C49-H49C	109.5	H49B-C49-H49C	109.5
N3-C50-C51	110.9(2)	N3-C50-H50A	109.5
C51-C50-H50A	109.5	N3-C50-H50B	109.5
C51-C50-H50B	109.5	H50A-C50-H50B	108.0
C52-C51-C56	118.9(3)	C52-C51-C50	119.9(3)
C56-C51-C50	121.1(3)	C51-C52-C53	120.9(3)
C51-C52-H52	119.5	C53-C52-H52	119.5
C54-C53-C52	119.6(3)	C54-C53-H53	120.2
C52-C53-H53	120.2	C55-C54-C53	119.4(3)
C55-C54-H54	120.3	C53-C54-H54	120.3
C56-C55-C54	120.6(3)	C56-C55-H55	119.7
C54-C55-H55	119.7	C55-C56-C51	120.5(3)
C55-C56-H56	119.8	C51-C56-H56	119.8

Table 6. Torsion angles (°) for Compound 5d.

C2-C3-N2-C7	-59.5(3)	C9-C3-N2-C7	67.0(3)
C2-C3-N2-C4	64.1(3)	C9-C3-N2-C4	-169.5(2)
C7-N2-C4-C8	-147.8(3)	C3-N2-C4-C8	85.2(3)
C7-N2-C4-C5	-26.2(3)	C3-N2-C4-C5	-153.2(3)
N2-C4-C5-C6	1.5(4)	C8-C4-C5-C6	118.7(3)
C4-C5-C6-C7	22.6(4)	C4-N2-C7-C6	41.3(3)
C3-N2-C7-C6	168.8(2)	C5-C6-C7-N2	-38.3(3)
N2-C4-C8-O1	50.1(4)	C5-C4-C8-O1	-64.5(4)
C2-C3-C9-C10	-162.6(2)	N2-C3-C9-C10	70.8(3)
C2-C3-C9-C14	16.7(4)	N2-C3-C9-C14	-109.9(3)
C14-C9-C10-C11	0.0(4)	C3-C9-C10-C11	179.3(3)
C9-C10-C11-C12	0.2(5)	C10-C11-C12-C13	-0.3(5)
C11-C12-C13-C14	0.1(5)	C12-C13-C14-C9	0.1(5)
C10-C9-C14-C13	-0.1(4)	C3-C9-C14-C13	-179.4(3)
C1-N1-S1-O2	-36.2(2)	C22-N1-S1-O2	179.73(19)
C1-N1-S1-O3	-165.10(19)	C22-N1-S1-O3	50.8(2)

C1-N1-S1-C15	80.1(2)	C22-N1-S1-C15	-64.0(2)
O2-S1-C15-C20	-159.7(2)	O3-S1-C15-C20	-27.0(2)
N1-S1-C15-C20	85.8(2)	O2-S1-C15-C16	20.5(2)
O3-S1-C15-C16	153.3(2)	N1-S1-C15-C16	-94.0(2)
C20-C15-C16-C17	1.7(4)	S1-C15-C16-C17	-178.5(2)
C15-C16-C17-C18	-0.4(4)	C16-C17-C18-C19	-0.7(4)
C16-C17-C18-C21	178.4(3)	C17-C18-C19-C20	0.6(4)
C21-C18-C19-C20	-178.5(2)	C16-C15-C20-C19	-1.8(4)
S1-C15-C20-C19	178.4(2)	C18-C19-C20-C15	0.7(4)
C1-N1-C22-C23	49.6(3)	S1-N1-C22-C23	-167.27(19)
N1-C22-C23-C24	70.3(3)	N1-C22-C23-C28	-113.4(3)
C28-C23-C24-C25	2.5(5)	C22-C23-C24-C25	178.8(3)
C23-C24-C25-C26	-1.6(5)	C24-C25-C26-C27	-0.4(5)
C25-C26-C27-C28	1.5(5)	C26-C27-C28-C23	-0.5(5)
C24-C23-C28-C27	-1.4(5)	C22-C23-C28-C27	-177.9(3)
C30-C31-N4-C35	-51.4(3)	C37-C31-N4-C35	74.2(3)
C30-C31-N4-C32	72.2(3)	C37-C31-N4-C32	-162.2(2)
C35-N4-C32-C36	-154.9(2)	C31-N4-C32-C36	76.5(3)
C35-N4-C32-C33	-34.1(3)	C31-N4-C32-C33	-162.7(2)
N4-C32-C33-C34	9.1(3)	C36-C32-C33-C34	132.1(3)
C32-C33-C34-C35	17.6(3)	C32-N4-C35-C34	45.5(3)
C31-N4-C35-C34	173.0(2)	C33-C34-C35-N4	-37.9(3)
N4-C32-C36-O4	-75.5(3)	C33-C32-C36-O4	167.9(3)
N4-C31-C37-C38	-170.3(2)	C30-C31-C37-C38	-44.0(3)
N4-C31-C37-C42	13.5(4)	C30-C31-C37-C42	139.8(3)
C42-C37-C38-C39	3.5(4)	C31-C37-C38-C39	-172.9(3)
C37-C38-C39-C40	-2.3(5)	C38-C39-C40-C41	0.3(5)
C39-C40-C41-C42	0.4(4)	C40-C41-C42-C37	0.9(4)
C38-C37-C42-C41	-2.8(4)	C31-C37-C42-C41	173.4(3)
C29-N3-S2-O5	44.9(2)	C50-N3-S2-O5	-176.43(19)

C29-N3-S2-O6	174.3(2)	C50-N3-S2-O6	-47.0(2)
C29-N3-S2-C43	-70.4(2)	C50-N3-S2-C43	68.3(2)
O5-S2-C43-C44	-20.5(3)	O6-S2-C43-C44	-153.2(2)
N3-S2-C43-C44	93.7(2)	O5-S2-C43-C48	161.9(2)
O6-S2-C43-C48	29.2(3)	N3-S2-C43-C48	-83.9(2)
C48-C43-C44-C45	-0.8(4)	S2-C43-C44-C45	-178.3(2)
C43-C44-C45-C46	0.1(4)	C44-C45-C46-C47	0.5(4)
C44-C45-C46-C49	179.8(3)	C45-C46-C47-C48	-0.6(4)
C49-C46-C47-C48	-179.9(3)	C46-C47-C48-C43	0.0(4)
C44-C43-C48-C47	0.7(4)	S2-C43-C48-C47	178.2(2)
C29-N3-C50-C51	-53.5(3)	S2-N3-C50-C51	167.32(19)
N3-C50-C51-C52	107.6(3)	N3-C50-C51-C56	-75.0(3)
C56-C51-C52-C53	1.0(4)	C50-C51-C52-C53	178.4(3)
C51-C52-C53-C54	0.3(5)	C52-C53-C54-C55	-1.5(5)
C53-C54-C55-C56	1.4(5)	C54-C55-C56-C51	-0.1(5)
C52-C51-C56-C55	-1.1(5)	C50-C51-C56-C55	-178.5(3)

Table 7. Anisotropic atomic displacement parameters (Å^2) for Compound 5d.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N1	0.0250(11)	0.0185(11)	0.0192(10)	-0.0003(9)	-0.0037(9)	0.0021(9)
C1	0.0272(14)	0.0193(12)	0.0194(12)	-0.0021(10)	-0.0024(10)	-0.0012(11)
C2	0.0249(14)	0.0230(13)	0.0218(12)	-0.0007(11)	-0.0006(11)	0.0001(10)
C3	0.0237(13)	0.0222(12)	0.0223(12)	0.0004(10)	-0.0019(10)	0.0020(10)
N2	0.0376(13)	0.0191(11)	0.0235(11)	-0.0018(9)	-0.0040(10)	0.0083(10)
C4	0.091(3)	0.0315(17)	0.0212(14)	-0.0029(13)	-0.0046(16)	0.0236(18)
C5	0.118(4)	0.041(2)	0.049(2)	-0.0200(18)	-0.039(3)	0.012(2)
C6	0.084(3)	0.0327(18)	0.054(2)	-0.0015(17)	-0.030(2)	-0.0099(19)
C7	0.0379(17)	0.0262(15)	0.0411(16)	0.0040(13)	-0.0124(14)	-0.0060(12)
C8	0.088(3)	0.049(2)	0.0374(18)	0.0047(16)	0.022(2)	0.038(2)
O1	0.083(2)	0.0495(15)	0.0410(12)	0.0078(11)	0.0141(13)	0.0401(14)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C9	0.0234(13)	0.0204(12)	0.0224(12)	0.0011(10)	-0.0037(10)	-0.0038(10)
C10	0.0278(15)	0.0271(14)	0.0273(13)	0.0045(12)	-0.0040(11)	0.0010(12)
C11	0.0364(16)	0.0379(17)	0.0252(13)	0.0069(13)	-0.0082(12)	-0.0051(13)
C12	0.0400(16)	0.0404(16)	0.0219(13)	-0.0026(12)	-0.0002(13)	-0.0081(14)
C13	0.0307(16)	0.0325(16)	0.0319(15)	-0.0064(13)	0.0006(12)	0.0002(12)
C14	0.0266(14)	0.0263(14)	0.0259(13)	-0.0011(11)	-0.0047(11)	0.0017(11)
S1	0.0218(3)	0.0194(3)	0.0188(3)	-0.0005(2)	-0.0014(2)	-0.0042(2)
O2	0.0206(9)	0.0334(10)	0.0259(9)	-0.0039(8)	-0.0016(8)	-0.0030(8)
O3	0.0368(11)	0.0195(9)	0.0239(9)	0.0022(8)	-0.0029(8)	-0.0092(8)
C15	0.0223(13)	0.0167(12)	0.0162(12)	-0.0008(10)	-0.0007(10)	-0.0046(10)
C16	0.0268(14)	0.0212(13)	0.0230(13)	0.0017(11)	-0.0035(11)	0.0007(11)
C17	0.0324(14)	0.0165(12)	0.0261(13)	-0.0002(11)	0.0009(11)	-0.0012(11)
C18	0.0286(14)	0.0258(13)	0.0169(12)	-0.0016(10)	0.0021(10)	-0.0085(11)
C19	0.0213(13)	0.0270(14)	0.0183(12)	0.0006(11)	-0.0013(10)	-0.0014(11)
C20	0.0248(14)	0.0192(12)	0.0188(12)	0.0003(10)	0.0008(10)	0.0002(10)
C21	0.0362(16)	0.0322(16)	0.0237(13)	-0.0053(12)	-0.0013(12)	-0.0123(13)
C22	0.0223(15)	0.0276(15)	0.0262(15)	0.0015(11)	-0.0039(11)	0.0047(11)
C23	0.0202(13)	0.0219(13)	0.0285(14)	-0.0018(12)	-0.0020(11)	0.0053(11)
C24	0.0249(15)	0.0374(17)	0.0451(18)	-0.0136(15)	0.0046(13)	-0.0069(13)
C25	0.0288(16)	0.057(2)	0.0476(19)	-0.0287(18)	-0.0041(15)	-0.0007(16)
C26	0.0333(16)	0.0506(19)	0.0282(15)	-0.0106(14)	-0.0015(13)	0.0169(16)
C27	0.0428(19)	0.0362(18)	0.0360(17)	0.0023(14)	0.0136(15)	0.0021(15)
C28	0.0326(16)	0.0257(14)	0.0365(16)	-0.0011(13)	0.0016(13)	-0.0062(12)
N3	0.0250(12)	0.0191(11)	0.0276(12)	0.0000(9)	-0.0066(9)	0.0001(10)
C29	0.0328(15)	0.0201(13)	0.0272(14)	0.0042(11)	-0.0077(11)	-0.0047(11)
C30	0.0315(14)	0.0248(14)	0.0279(13)	0.0057(12)	-0.0022(12)	-0.0040(12)
C31	0.0249(13)	0.0226(13)	0.0280(13)	0.0000(11)	0.0005(11)	-0.0004(11)
N4	0.0237(11)	0.0202(10)	0.0271(11)	0.0003(9)	-0.0003(9)	-0.0024(9)
C32	0.0306(15)	0.0293(14)	0.0277(14)	-0.0001(11)	0.0002(12)	0.0015(12)
C33	0.0346(17)	0.058(2)	0.0415(17)	0.0204(17)	0.0049(14)	-0.0021(16)
C34	0.0315(16)	0.0389(16)	0.0320(15)	0.0029(13)	0.0055(12)	-0.0012(13)
C35	0.0275(14)	0.0307(14)	0.0319(14)	-0.0036(12)	0.0023(12)	-0.0001(12)
C36	0.0400(17)	0.0272(15)	0.0459(18)	0.0081(13)	0.0050(14)	0.0042(13)
O4	0.0434(14)	0.0339(12)	0.0659(16)	0.0119(12)	0.0187(12)	0.0142(10)
C37	0.0305(14)	0.0217(12)	0.0258(13)	-0.0008(11)	0.0014(11)	0.0023(12)
C38	0.0274(15)	0.0260(15)	0.0350(15)	-0.0017(12)	-0.0009(13)	-0.0008(12)
C39	0.0396(17)	0.0326(16)	0.0321(15)	0.0019(13)	0.0112(13)	-0.0030(13)
C40	0.0451(18)	0.0390(17)	0.0205(13)	-0.0014(12)	0.0065(12)	0.0047(14)
C41	0.0293(15)	0.0320(15)	0.0269(14)	-0.0058(12)	-0.0021(11)	0.0011(12)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C42	0.0334(15)	0.0263(15)	0.0255(13)	-0.0020(12)	0.0026(11)	-0.0020(12)
S2	0.0231(3)	0.0225(3)	0.0311(3)	0.0016(3)	-0.0019(3)	0.0067(3)
O5	0.0209(10)	0.0399(12)	0.0470(13)	0.0075(10)	-0.0015(9)	0.0040(9)
O6	0.0410(12)	0.0261(10)	0.0388(11)	-0.0043(9)	0.0025(10)	0.0137(9)
C43	0.0216(13)	0.0215(13)	0.0205(13)	-0.0012(10)	0.0006(10)	0.0039(10)
C44	0.0241(14)	0.0230(13)	0.0274(14)	0.0009(11)	-0.0012(11)	-0.0023(11)
C45	0.0338(15)	0.0190(13)	0.0275(14)	0.0035(11)	-0.0032(12)	-0.0010(11)
C46	0.0281(14)	0.0240(13)	0.0164(11)	0.0007(10)	0.0016(10)	0.0038(11)
C47	0.0273(14)	0.0262(14)	0.0211(12)	-0.0040(11)	-0.0031(10)	-0.0013(11)
C48	0.0279(14)	0.0186(12)	0.0239(13)	-0.0023(11)	0.0008(11)	-0.0003(11)
C49	0.0360(17)	0.0325(16)	0.0219(13)	0.0005(12)	-0.0038(12)	0.0075(13)
C50	0.0275(15)	0.0226(14)	0.0298(16)	-0.0018(11)	-0.0062(12)	-0.0037(12)
C51	0.0238(14)	0.0181(12)	0.0321(15)	-0.0007(12)	-0.0049(12)	-0.0038(11)
C52	0.0345(16)	0.0202(13)	0.0373(16)	0.0018(13)	-0.0059(13)	0.0019(12)
C53	0.0310(16)	0.0250(15)	0.0418(18)	-0.0043(13)	0.0014(14)	-0.0006(13)
C54	0.0310(16)	0.0337(16)	0.0389(16)	0.0083(13)	0.0003(13)	-0.0064(14)
C55	0.0292(16)	0.0412(18)	0.052(2)	0.0209(16)	0.0020(14)	0.0064(14)
C56	0.0259(15)	0.0334(17)	0.0464(18)	0.0086(15)	0.0049(14)	0.0063(13)

Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for Compound 5d.

	x/a	y/b	z/c	U(eq)
H3	0.2774	0.7640	0.4148	0.027
H4	0.1767	0.6984	0.3386	0.058
H5A	0.0224	0.6098	0.3184	0.083
H5B	0.0920	0.5328	0.3440	0.083
H6A	-0.1216	0.5946	0.3750	0.068
H6B	-0.0231	0.5488	0.4091	0.068
H7A	-0.0444	0.7267	0.3919	0.042
H7B	-0.0358	0.6812	0.4416	0.042
H8A	0.3166	0.5773	0.3376	0.07
H8B	0.3616	0.6503	0.3722	0.07
H1A	0.2451	0.5675	0.4247	0.087
H10	0.2844	0.6984	0.4927	0.033
H11	0.2541	0.7231	0.5712	0.04
H12	0.1099	0.8245	0.5958	0.041
H13	-0.0035	0.9024	0.5412	0.038
H14	0.0272	0.8783	0.4623	0.032

	x/a	y/b	z/c	U(eq)
H16	0.1221	0.7701	0.2620	0.028
H17	-0.0149	0.6803	0.2224	0.03
H19	-0.2459	0.8769	0.1949	0.027
H20	-0.1102	0.9679	0.2346	0.025
H21A	-0.1990	0.7053	0.1463	0.046
H21B	-0.3145	0.7355	0.1775	0.046
H21C	-0.2317	0.6561	0.1931	0.046
H22A	-0.1201	0.9540	0.3293	0.03
H22B	-0.0605	1.0457	0.3212	0.03
H24	0.0456	1.1119	0.3952	0.043
H25	0.0043	1.1444	0.4721	0.053
H26	-0.1496	1.0704	0.5129	0.045
H27	-0.2629	0.9645	0.4758	0.046
H28	-0.2178	0.9290	0.3998	0.038
H31	0.5082	0.2825	0.4223	0.03
H32	0.5942	0.3291	0.3407	0.035
H33A	0.7550	0.3985	0.3093	0.054
H33B	0.7499	0.4714	0.3481	0.054
H34A	0.9286	0.3534	0.3464	0.041
H34B	0.8943	0.4060	0.3924	0.041
H35A	0.7975	0.2433	0.3665	0.036
H35B	0.8532	0.2700	0.4163	0.036
H36A	0.5660	0.4670	0.4040	0.045
H36B	0.5263	0.4756	0.3508	0.045
H4A	0.3648	0.4351	0.3945	0.072
H38	0.5091	0.1244	0.4677	0.035
H39	0.5349	0.0854	0.5447	0.042
H40	0.6756	0.1592	0.5919	0.042
H41	0.7867	0.2735	0.5617	0.035
H42	0.7580	0.3144	0.4852	0.034
H44	0.6267	0.2356	0.2633	0.03
H45	0.4883	0.3251	0.2244	0.032
H47	0.2637	0.1265	0.1946	0.03
H48	0.4010	0.0360	0.2333	0.028
H49A	0.2963	0.3518	0.1867	0.045
H49B	0.1876	0.2824	0.1911	0.045
H49C	0.2784	0.2823	0.1470	0.045
H50A	0.4519	-0.0474	0.3219	0.032
H50B	0.3794	0.0408	0.3271	0.032

	x/a	y/b	z/c	U(eq)
H52	0.2820	0.0723	0.3975	0.037
H53	0.2327	0.0400	0.4742	0.039
H54	0.3452	-0.0658	0.5129	0.041
H55	0.4988	-0.1419	0.4733	0.049
H56	0.5467	-0.1096	0.3970	0.042