Supporting Information

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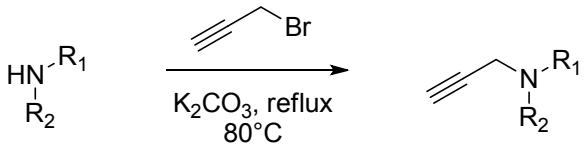
General Methods.

^{1}H-NMR spectra were recorded on Varian 200 (200 MHz) or Varian 400 (400 MHz) spectrometers. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuterochloroform: 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = duplet, t = triplet, q = quartet, sext = sextet, sept = septet, p = pseudo, b = broad, m = multiplet), coupling constants (Hz). ^{13}C-NMR spectra were recorded on a Varian 200 (50 MHz), Varian 400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard (deuterochloroform: 77.0 ppm). ^{31}P-NMR spectra were recorded on a Varian 400 (162 MHz), spectrometer with complete proton decoupling. Chemical shifts are reported in ppm using H_3PO_4 (85% H_2O solution, δ = 0 ppm) as an external standard. GC-MS spectra were taken by EI ionization at 70 eV on a Hewlett-Packard 5971 with GC injection. They are reported as: *m/z* (rel. intense). LC-electrospray ionization mass spectra were obtained with Agilent Technologies MSD1100 single-quadrupole mass spectrometer. ESI Q-TOF mass spectrometry was performed on a Xevo™ QTof (Waters MS Technologies, Manchester, UK), a quadrupole and orthogonal acceleration time-of-flight tandem mass spectrometer. IR spectra were performed as nujol mull or neat on a Bruker Alpha FT-IR Spectrometer. Chromatographic purification was done with 240-400 mesh silica gel. Anhydrous THF and DCM were distilled respectively from sodium-benzophenone and P_2O_5 prior to use. Elemental analyses were carried out by using a EACE 1110 CHNOS analyzer. Other anhydrous solvents were supplied by Fluka or Sigma Aldrich in Sureseal® bottles and used without any further purification. Commercially available chemicals were purchased from Sigma Aldrich, Stream and TCI and used without any further purification. Melting points were measured using open glass capillaries in a Bibby Stuart Scientific Melting Point Apparatus SMP 3 and are calibrated by comparison with literature values (Aldrich).

Synthesis of the propargyl amino derivative 2a-2e.



A solution of desired amine/sulfonylamide (2.5 mmol) in reagent grade acetone (8 mL) was treated with K_2CO_3 (2 eq) and propargyl bromide (80% in toluene, 2.2 eq). The mixture was refluxed for 8 h. The mixture was quenched with water, the aqueous phase was extracted three times with EtOAc, dried over Na_2SO_4 and the volatiles removed under reduce pressure.

(+/-)-**2a**: *c*Hex:AcOEt = 98:2, white solid, yield = 55% (not optimized), mp = 63-65 °C, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.43 (d, *J*(H,H) = 6.4 Hz, 3H), 2.23 (d, *J*(H,H) = 2.4 Hz, 1H), 3.17-3.22 (d, *J*(H,H) = 20.0 Hz, 1H), 3.42 (d, *J*(H,H) = 17.2 Hz, 1H), 3.52 (q, *J*(H,H) = 13.6 Hz, 2H), 3.82 (d, *J*(H,H) = 6.4 Hz, 1H), 7.20-7.36 (m, 8H), 7.46 (d, *J*(H,H) = 7.2 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 21.2, 38.4, 54.5, 60.9, 73.0, 78.9, 126.9, 127.0, 127.5(2C), 128.3(2C), 128.5(2C), 128.9(2C), 139.5, 145.4; LC/MS-ESI (m/z): 250 ($M+H^+$); IR (cm^{-1}, nujol mull): 2100 cm^{-1} (C≡C).

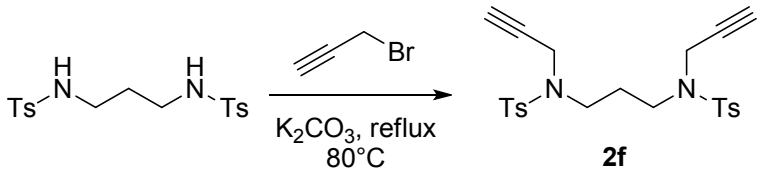
2b: *c*Hex:AcOEt = 7:3, white solid, yield = 75%, mp = 95-97 °C, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.09 (t, *J*(H,H) = 2 Hz, 1H), 2.44 (s, 3H), 2.83 (s, 3H), 4.02 (d, *J*(H,H) = 2.4 Hz, 2H), 7.31-7.33 (d, *J*(H,H) = 8.0 Hz, 2H), 7.72-7.70 (d, *J*(H,H) = 8.4 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 21.5, 34.3, 39.7, 74.0, 76.3, 127.9, 129.5, 134.1, 143.7; GC/MS(m/z): 223 (M+); IR (cm^{-1}, nujol mull): 2120 cm^{-1} (C≡C).

2c: *c*Hex:AcOEt = 8:2, white solid, yield = 85%, mp = 88-90 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.17 (s, 1H), 2.42 (s, 3H), 4.45 (s, 2H), 7.24-7.32 (m, 7H), 7.54-7.56 (d, *J*(H,H) = 6.4 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 21.5, 41.0, 73.8, 78.0, 128.0, 128.1, 128.4, 129.0, 129.2, 135.5, 139.3, 143.6; GC/MS(m/z): 285 (M+); IR (cm^{-1}, nujol mull): 2129 cm^{-1} (C≡C).

2d: *c*Hex:AcOEt = 7:3, dark yellow solid, yield = 60%, mp = 129-132 °C, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.07 (s, 1H), 2.91 (s, 3H), 4.14 (s, 2H), 8.02-8.05 (d, *J*(H,H) = 8.4 Hz, 2H), 8.36-8.38 (d, *J*(H,H) = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 34.3, 39.8, 74.7, 75.4, 124.1, 129.1, 143.4, 150.4; GC/MS (m/z): 254 (M+); IR (cm^{-1}, nujol mull): 2118 cm^{-1} (C≡C).

2e: *c*Hex:AcOEt = 7:3, light yellow solid, yield = 70%, mp = 55-57 °C, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.06 (t, *J*(H,H) = 2 Hz, 1H), 2.85 (s, 3H), 4.04-4.05 (d, *J*(H,H) = 2.8 Hz, 1H), 7.51-7.55 (m, 2H), 7.59-7.63 (m, 1H), 7.83-7.85 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 34.3, 39.7, 74.0, 76.1, 127.8, 128.9, 132.9, 137.3; LC/MS-ESI (m/z): 209(M+); IR (cm^{-1}, nujol mull): 2120 cm^{-1} (C≡C).

Synthesis of 2f.

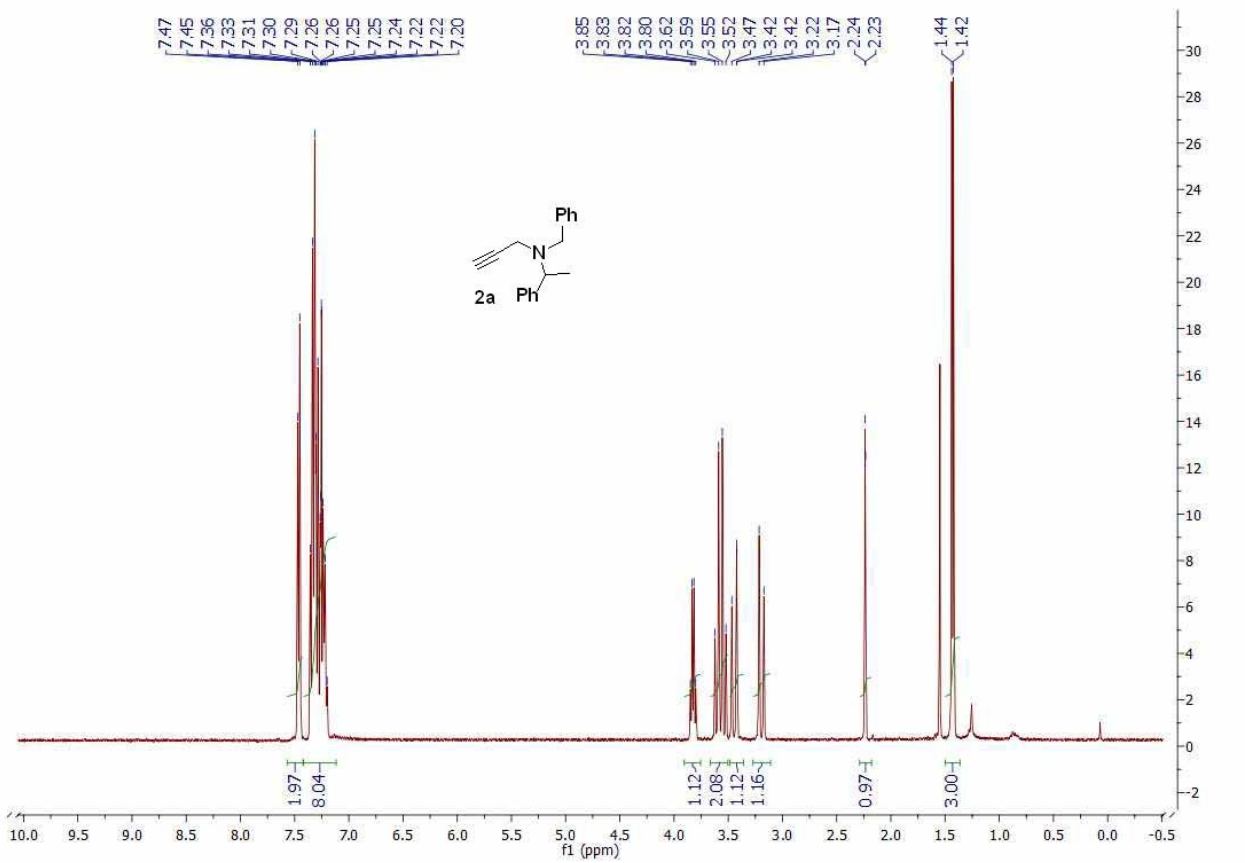


2f

A solution of *N,N′*-(propane-1,3-diyl)bis(4-methylbenzenesulfonamide) (1.12 mmol) in reagent grade acetone (7.5 mL) was treated with K_2CO_3 (2 eq) and propargyl bromide (80% in toluene, 4 eq). The mixture was refluxed for 8 h, when monitoring by TLC proved the complete consumption of the starting material. The mixture was quenched with water, the aqueous phase extracted three times with DCM, dried over Na_2SO_4 and the volatiles removed under reduce pressure.

2f: *c*Hex:AcOEt = 8:2, white solid, yield = 76%, mp = 110-112 °C, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.92 (qui, *J*(H,H)= 7.2 Hz, 2H), 2.02 (t, *J*(H,H)= 2.4, 2H), 2.41 (s, 6H), 3.24 (t, *J*(H,H)= 7.2 Hz, 4H), 4.12 (d, *J*(H,H)= 2.4 Hz, 4H), 7.28 (d, *J*(H,H)= 8.0 Hz, 4H), 7.69 (d, *J*(H,H)= 8.4 Hz, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 143.6, 135.4, 129.5, 127.7, 74.0, 44.1, 36.7, 26.1, 21.5; LC/MS-ESI (m/z): 459 ($M+H^+$), 939 ($2M+Na^+$); IR (cm^{-1}, nujol mull): 2114 cm^{-1} (C≡C).

NMR spectra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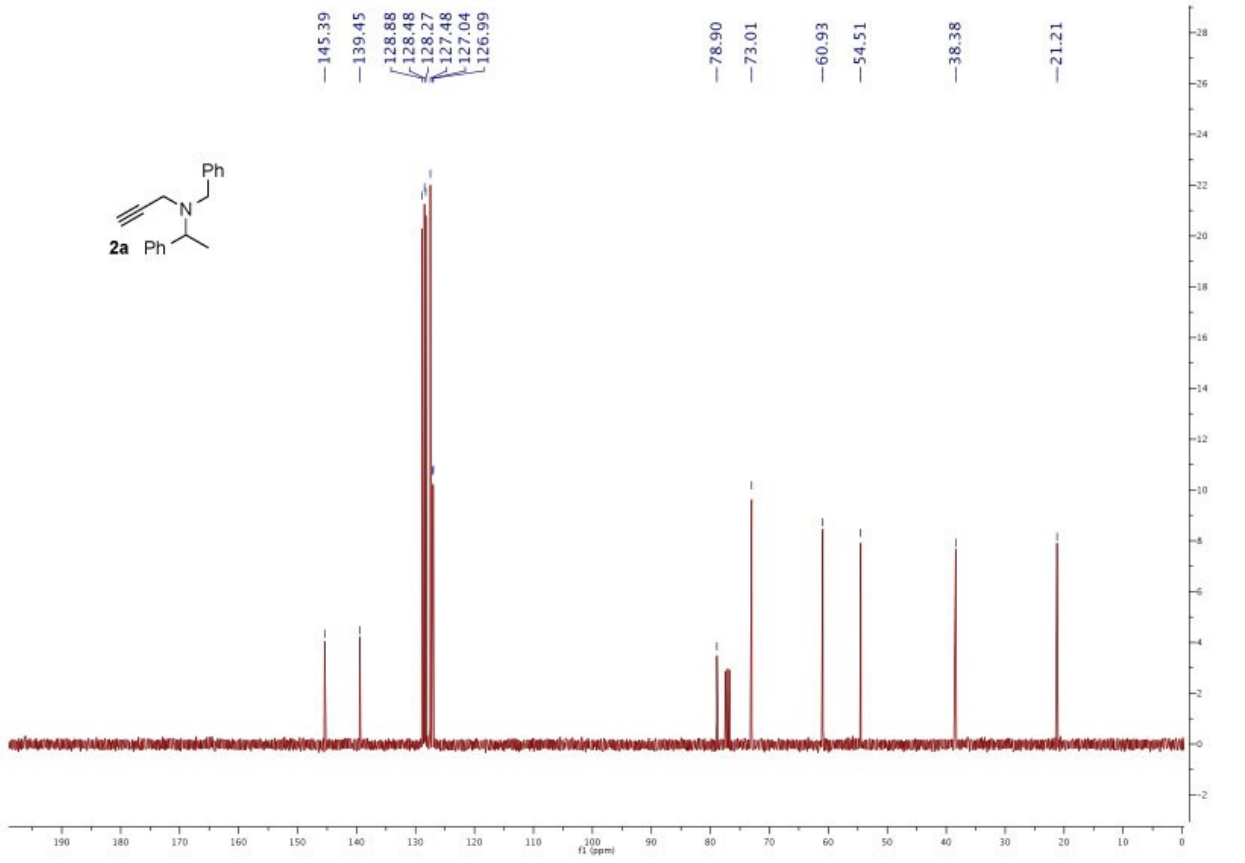
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Ph
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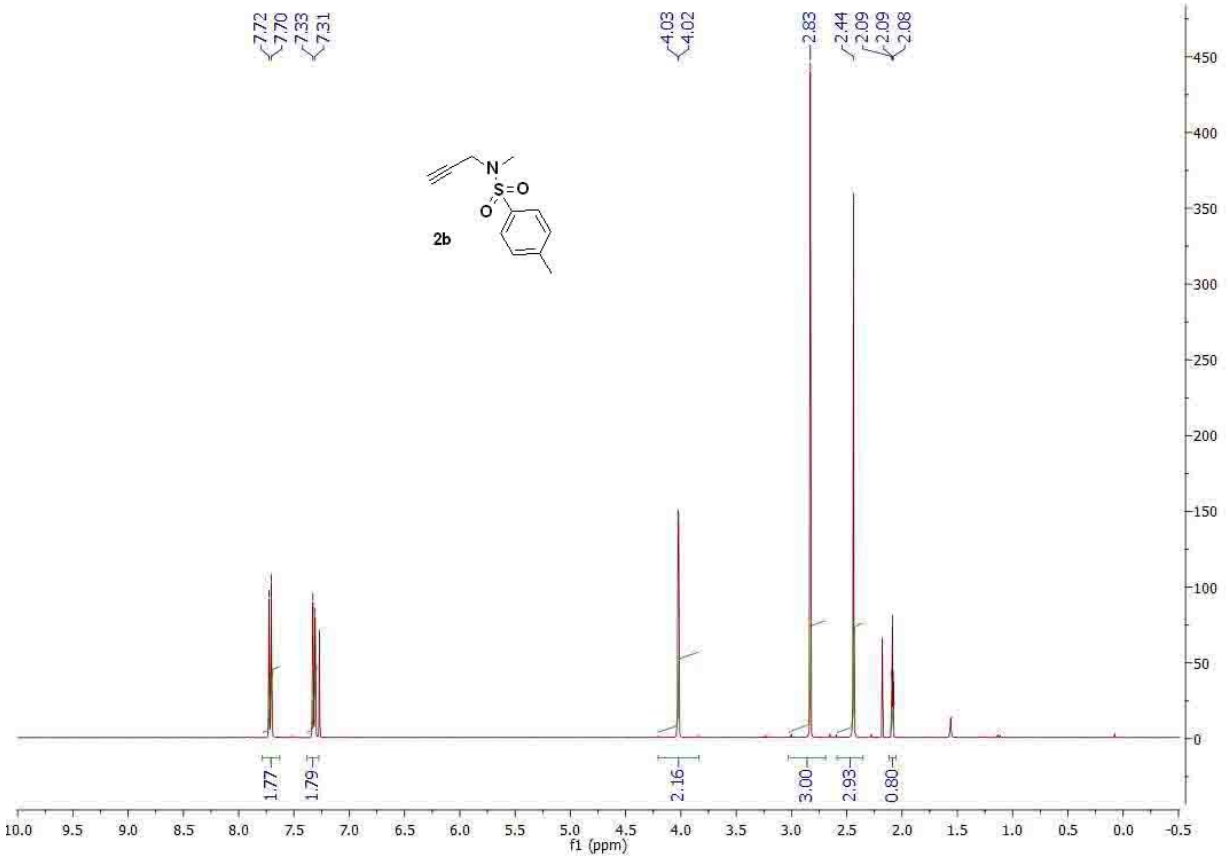
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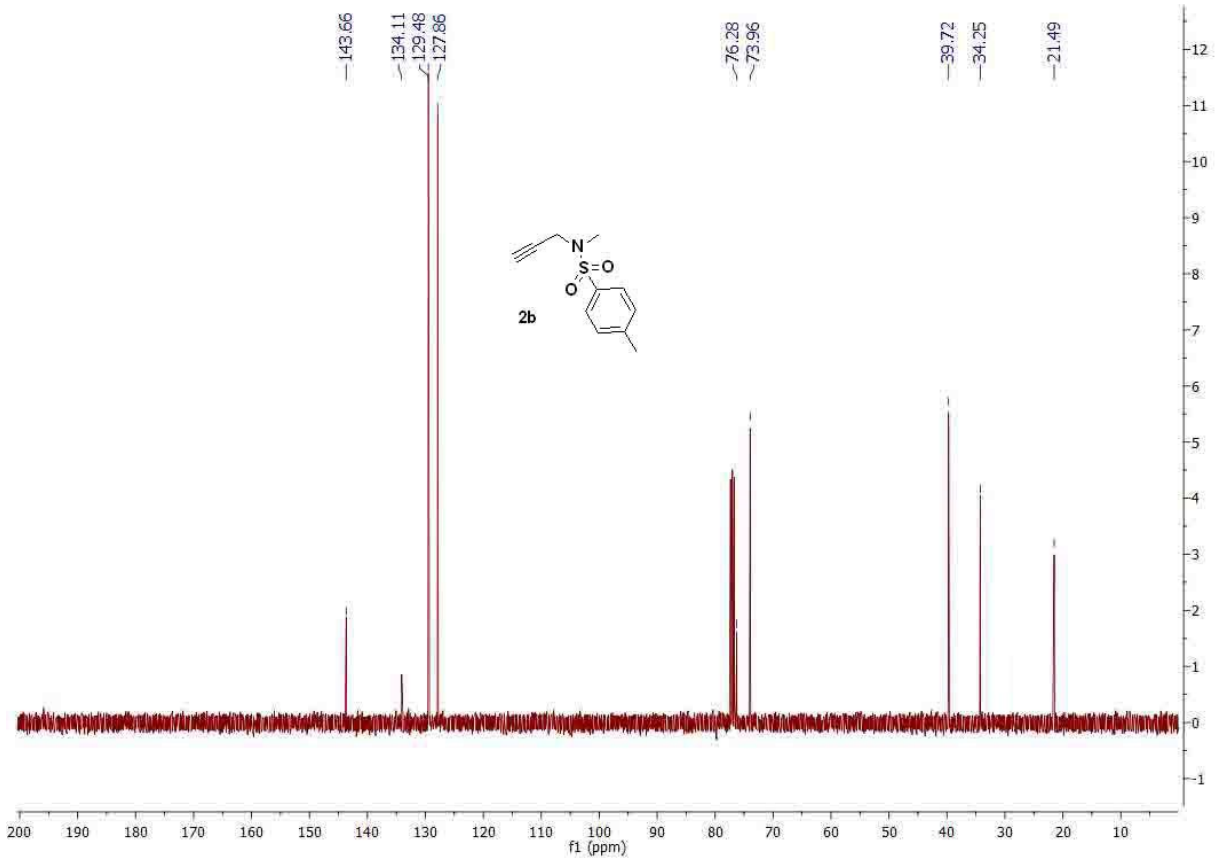
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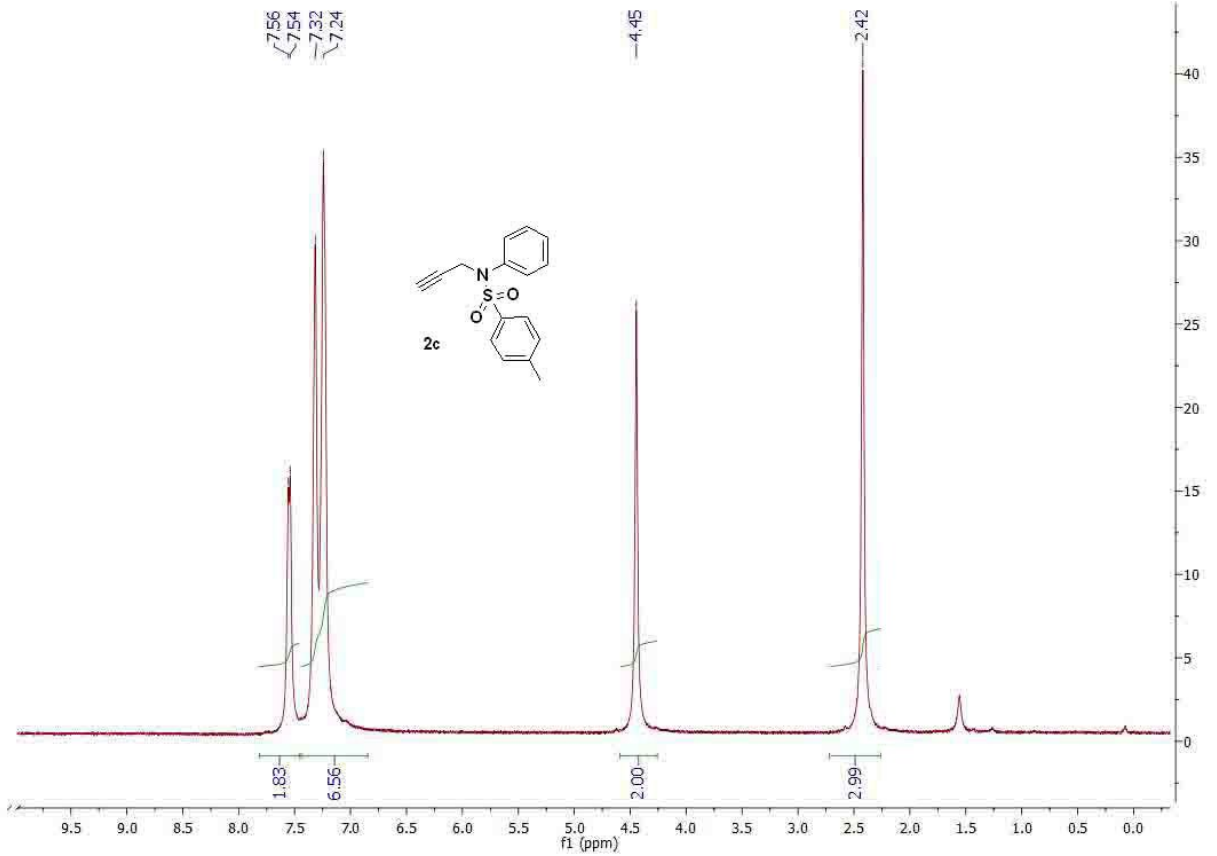
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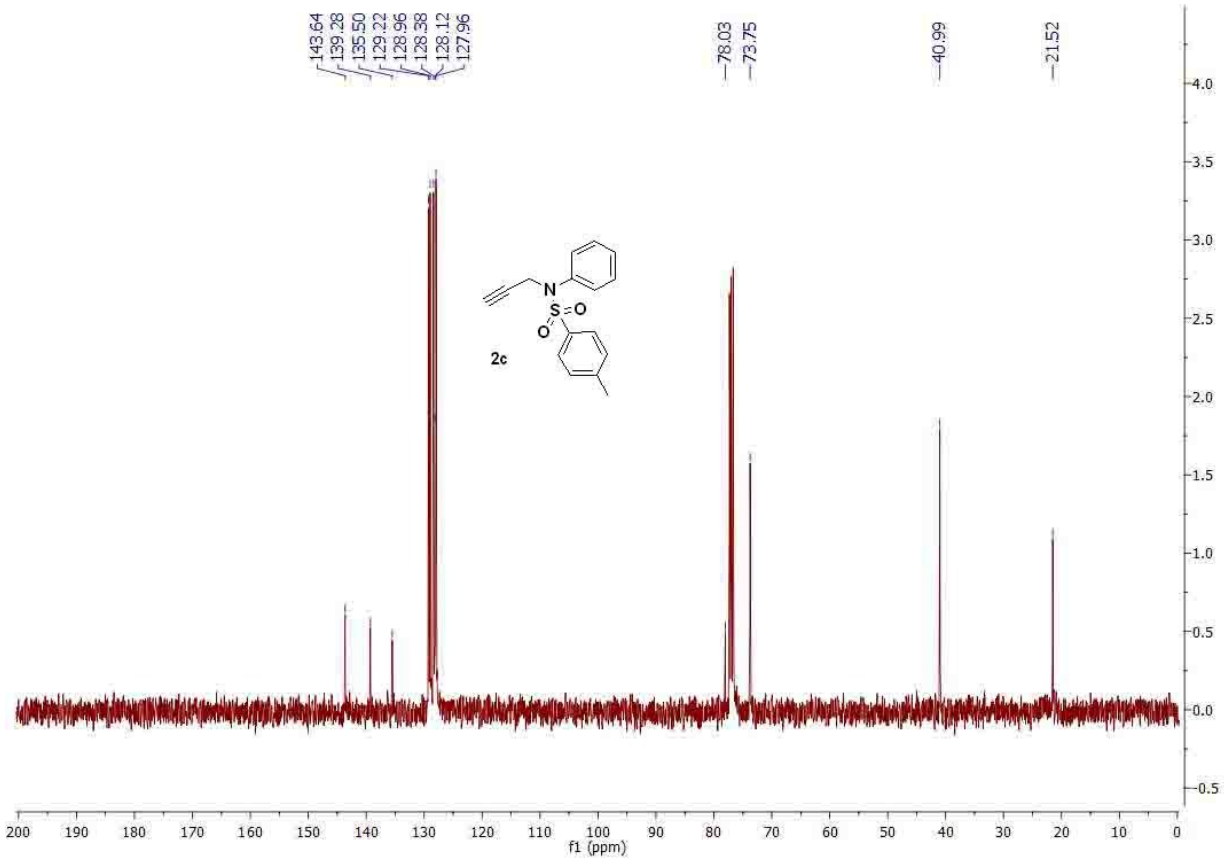
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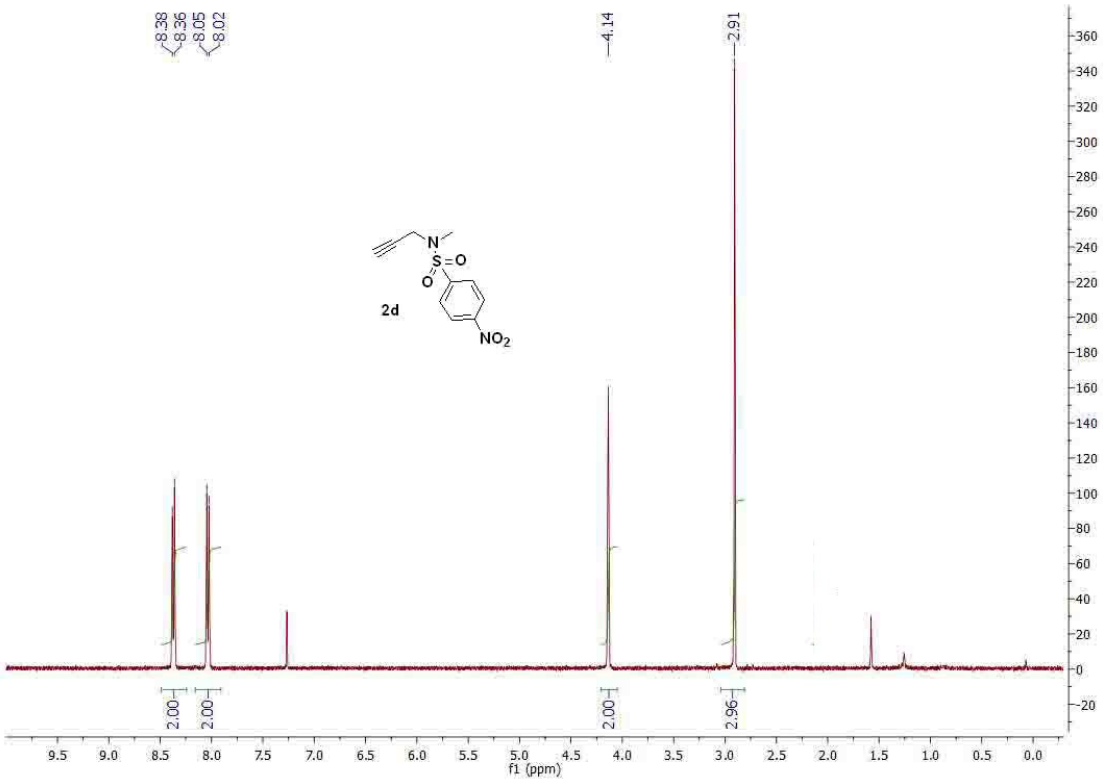
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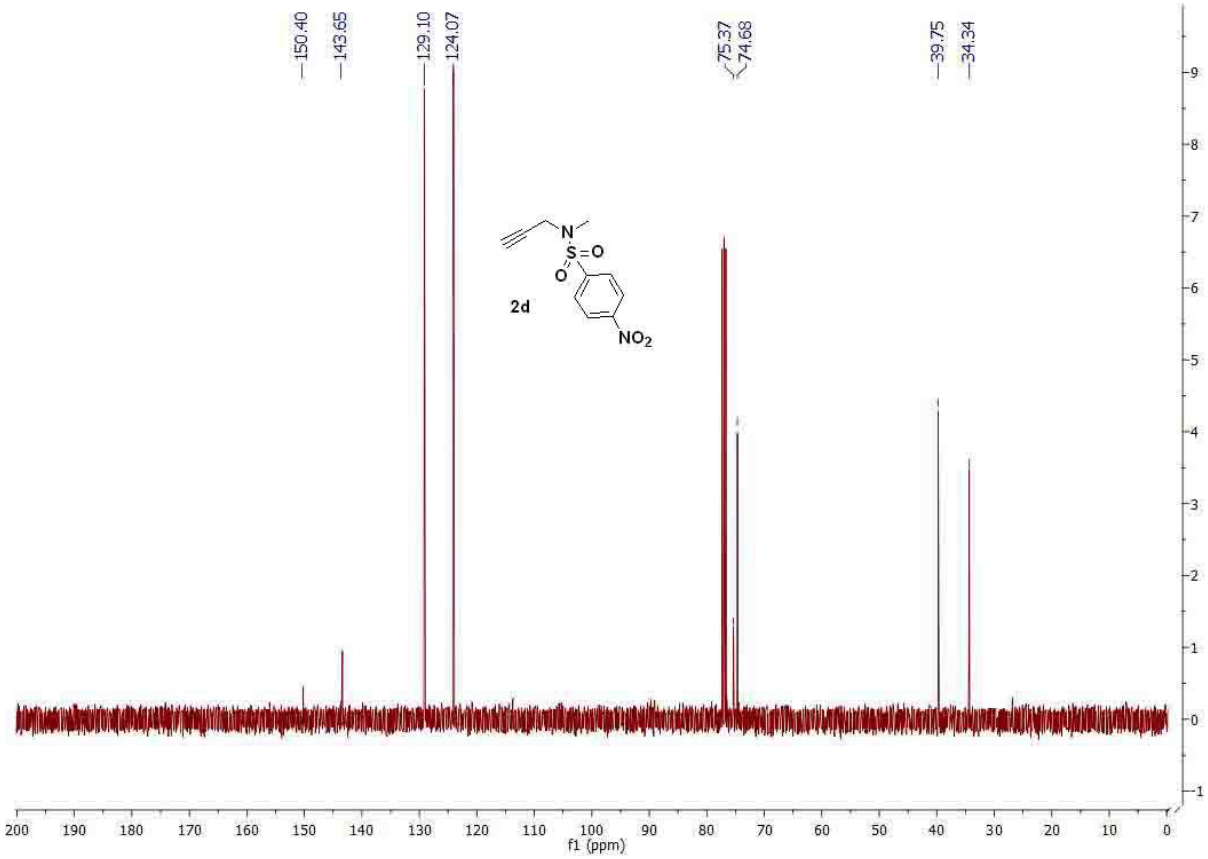
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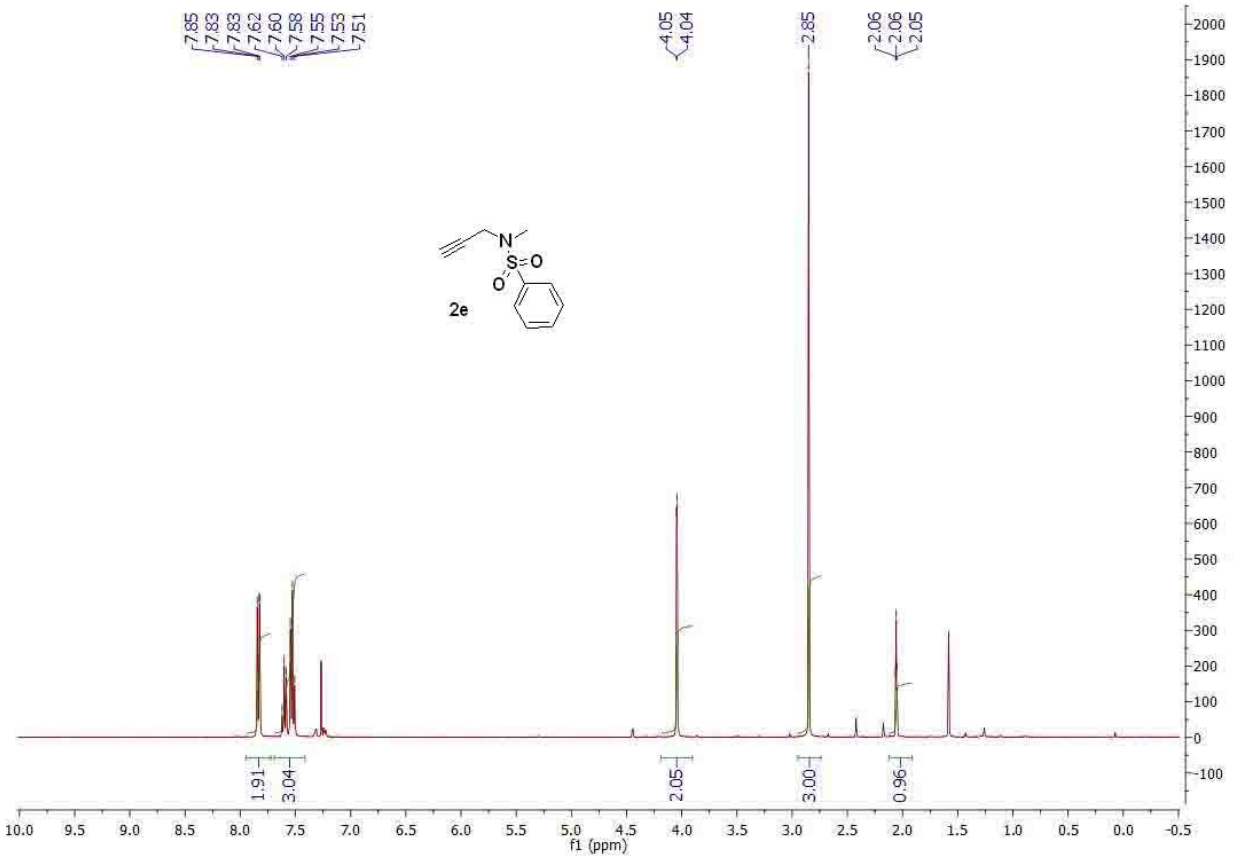
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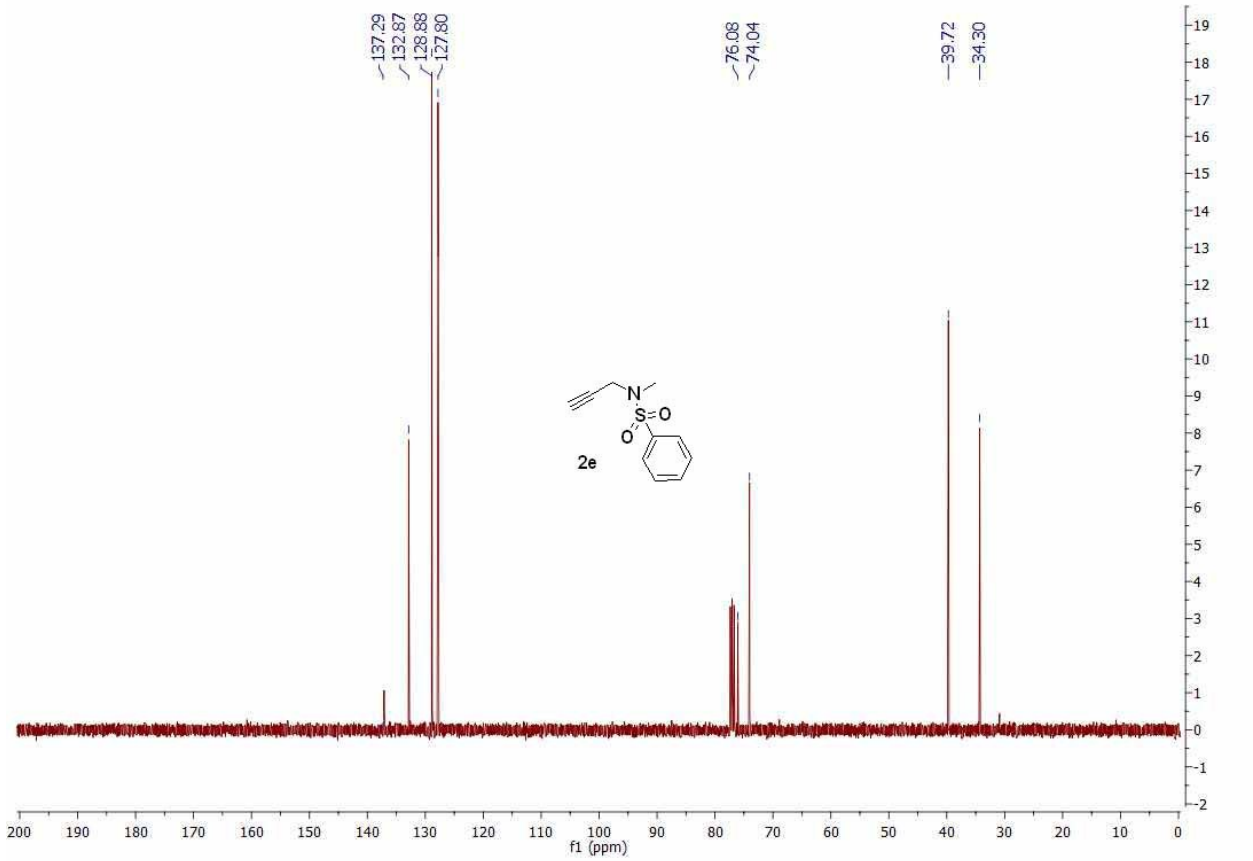
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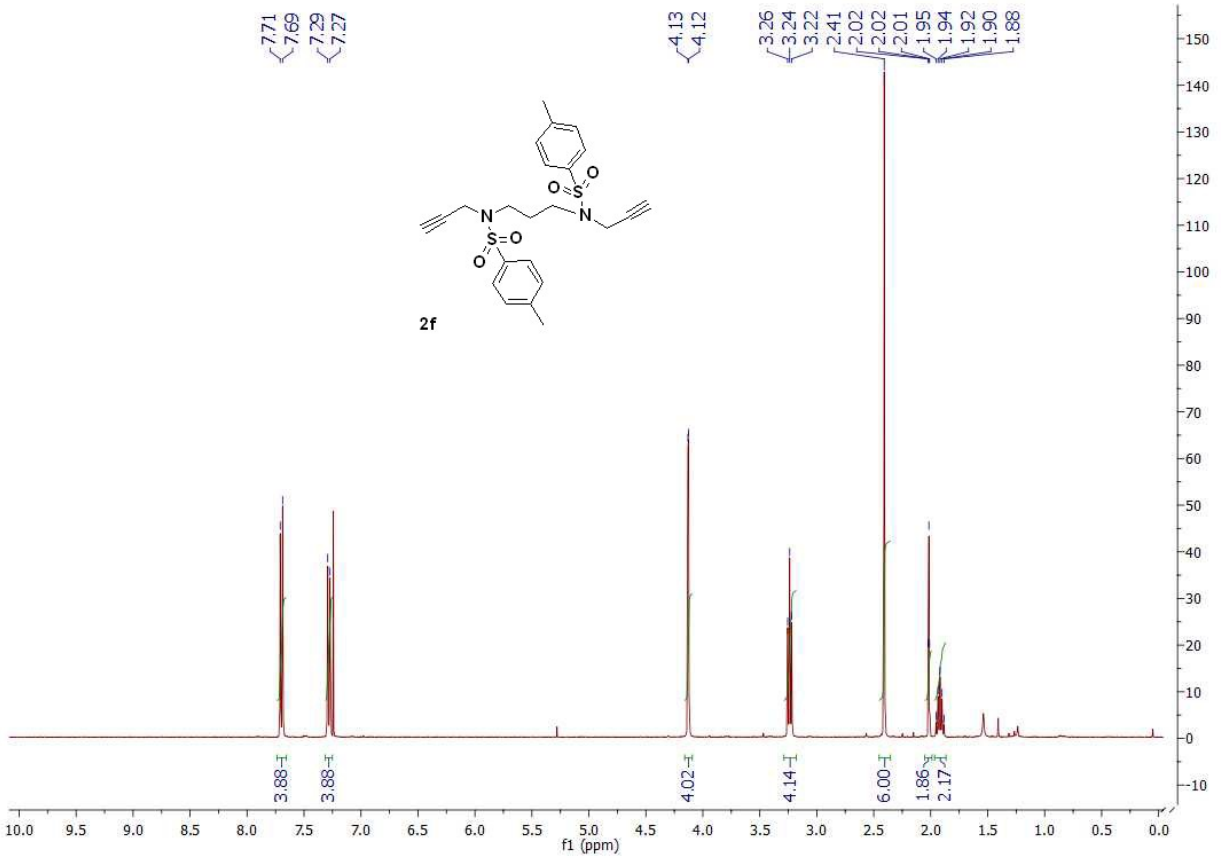
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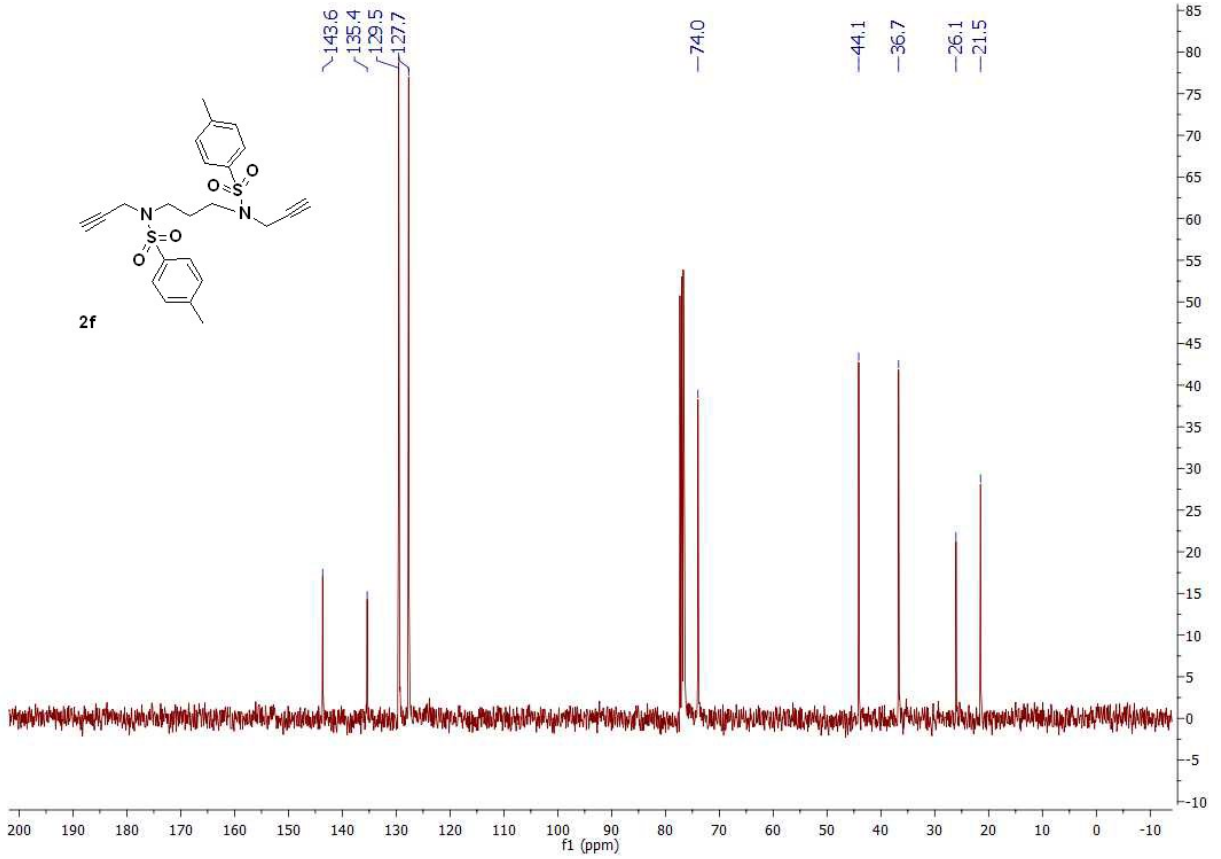
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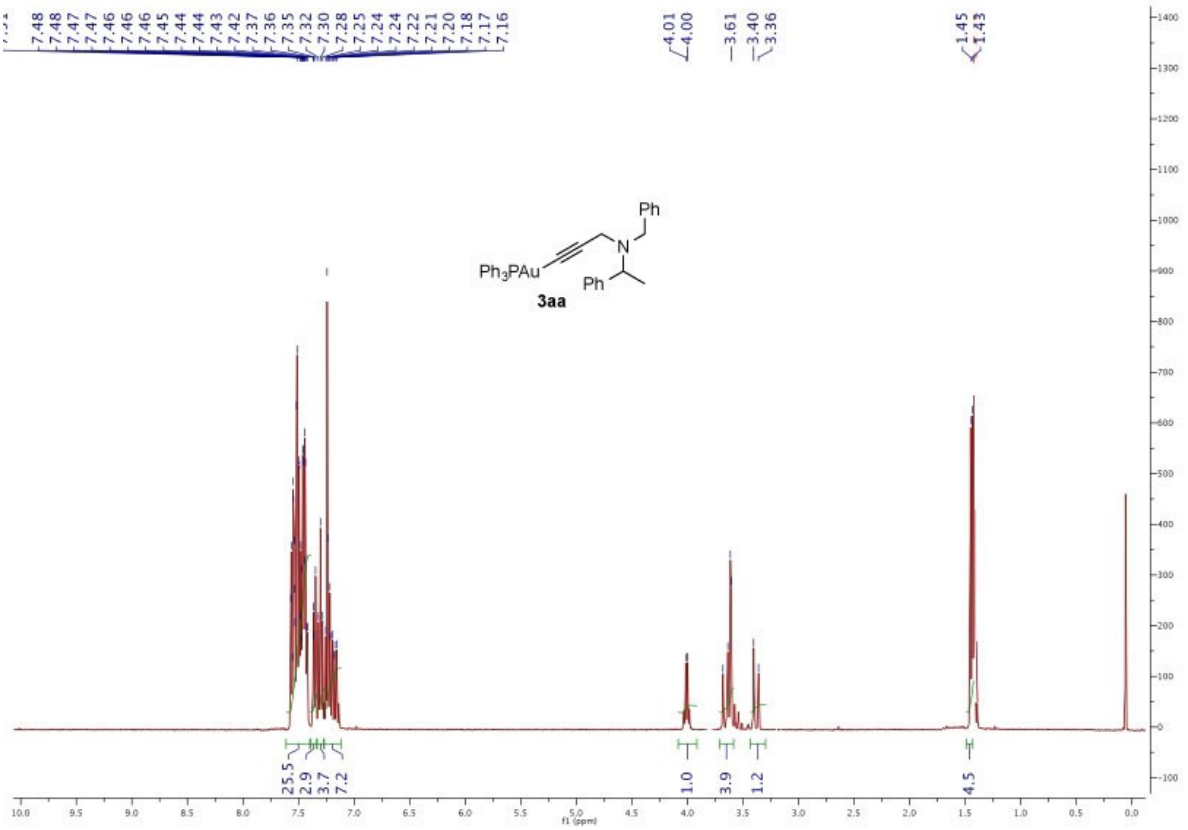
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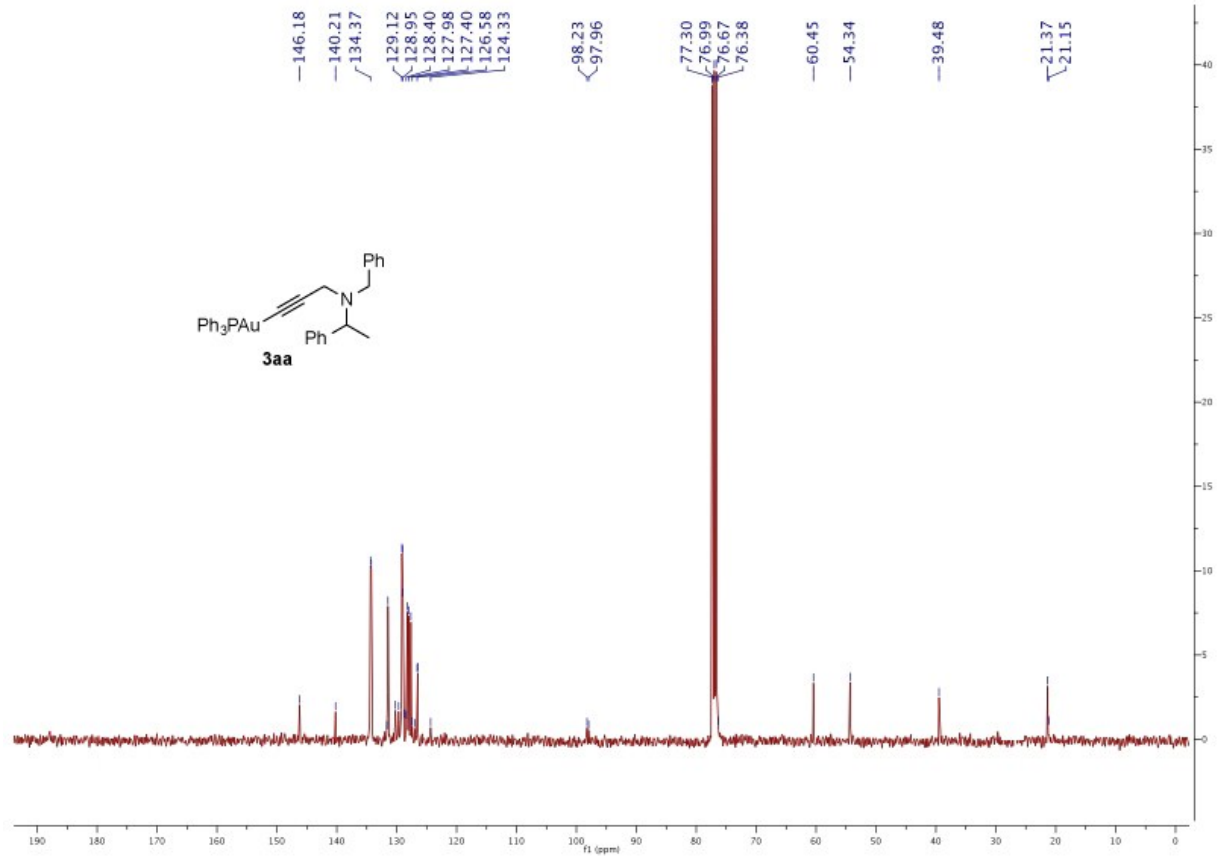
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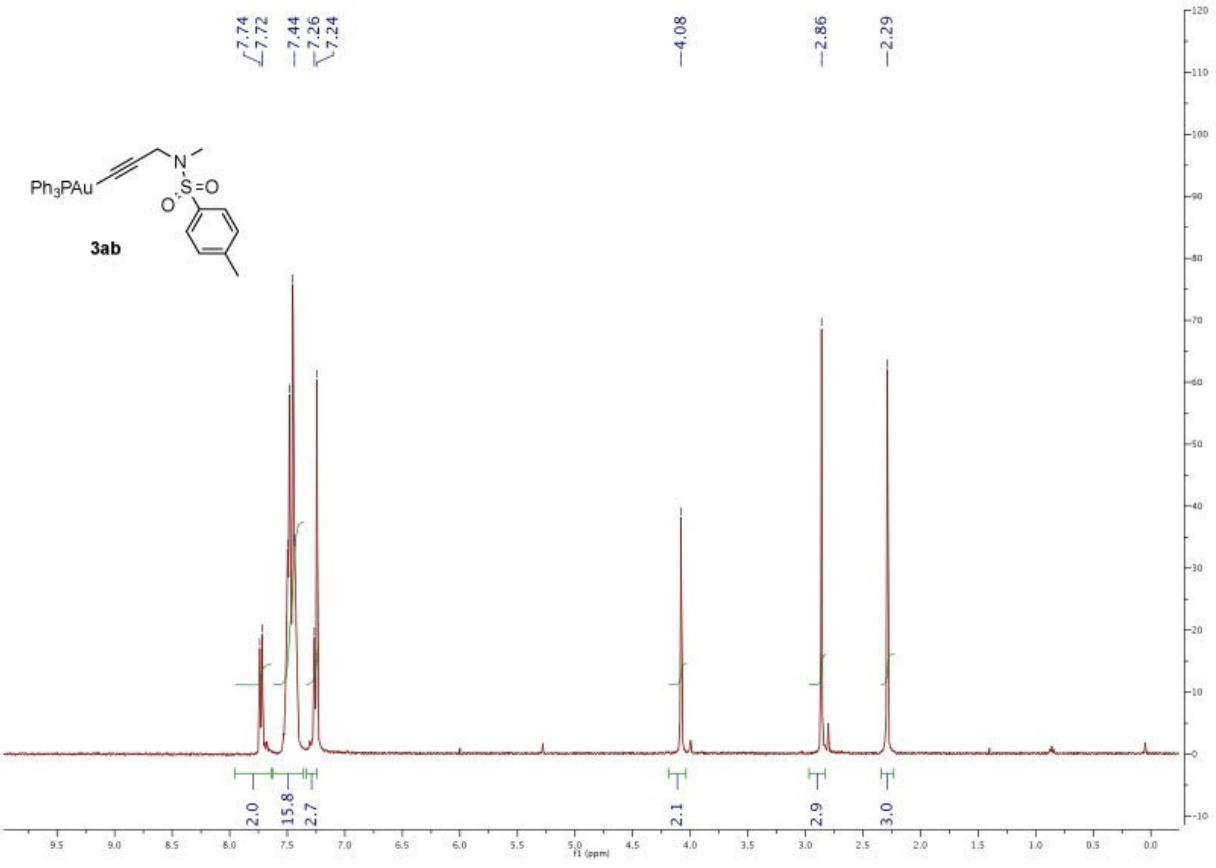
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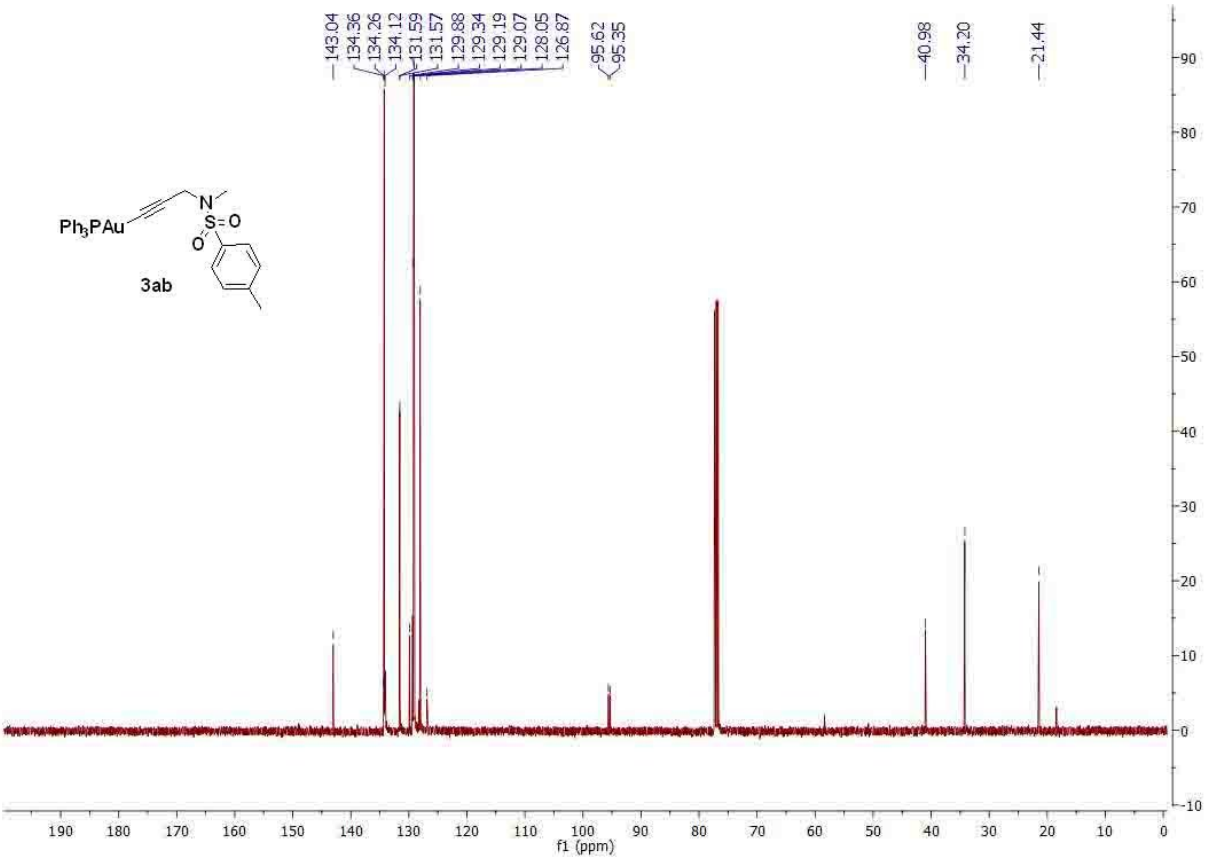
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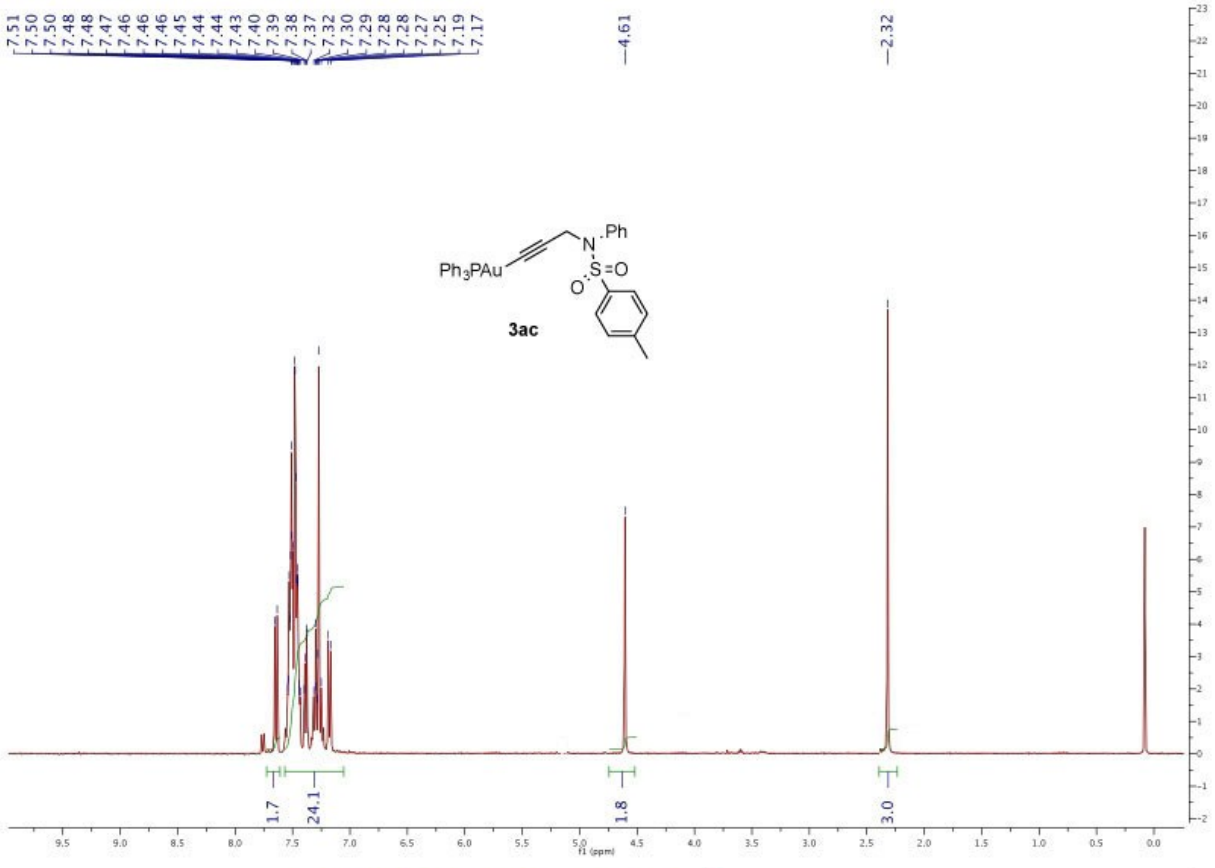
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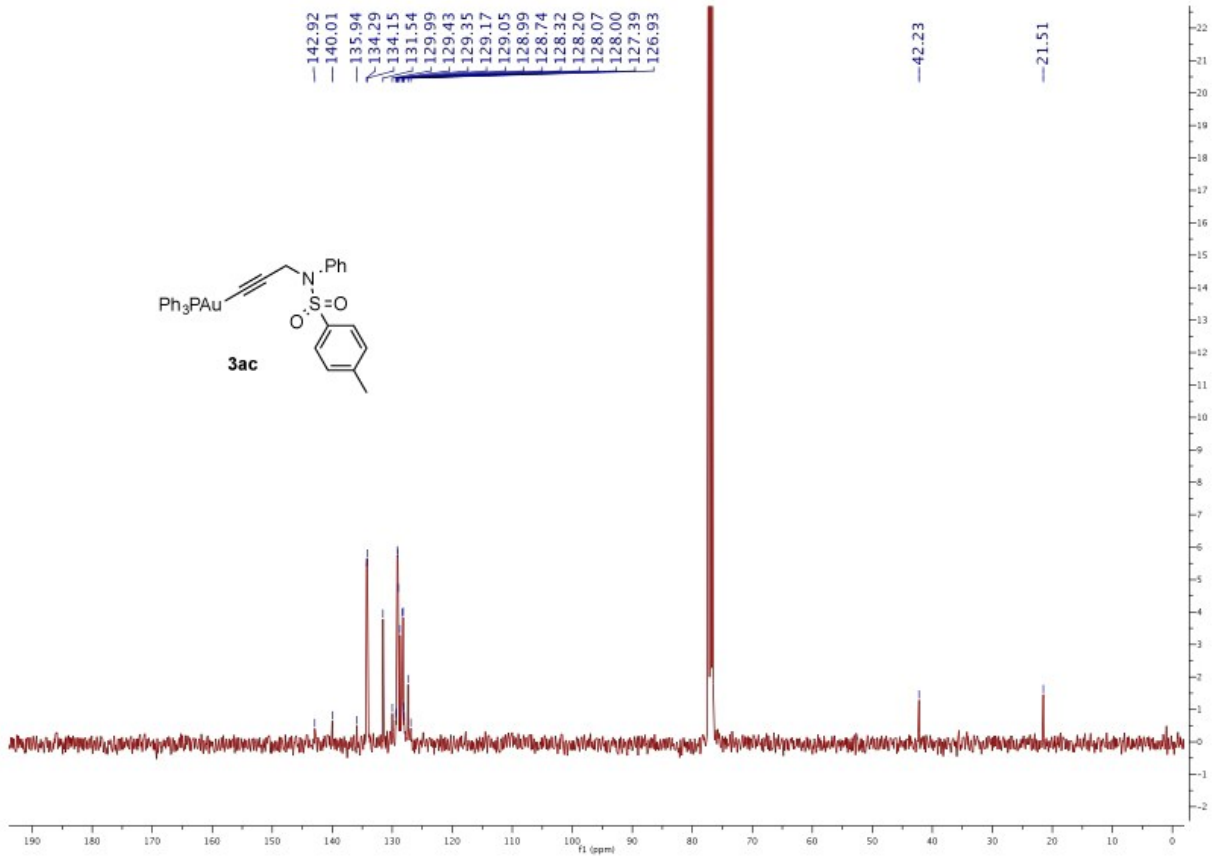
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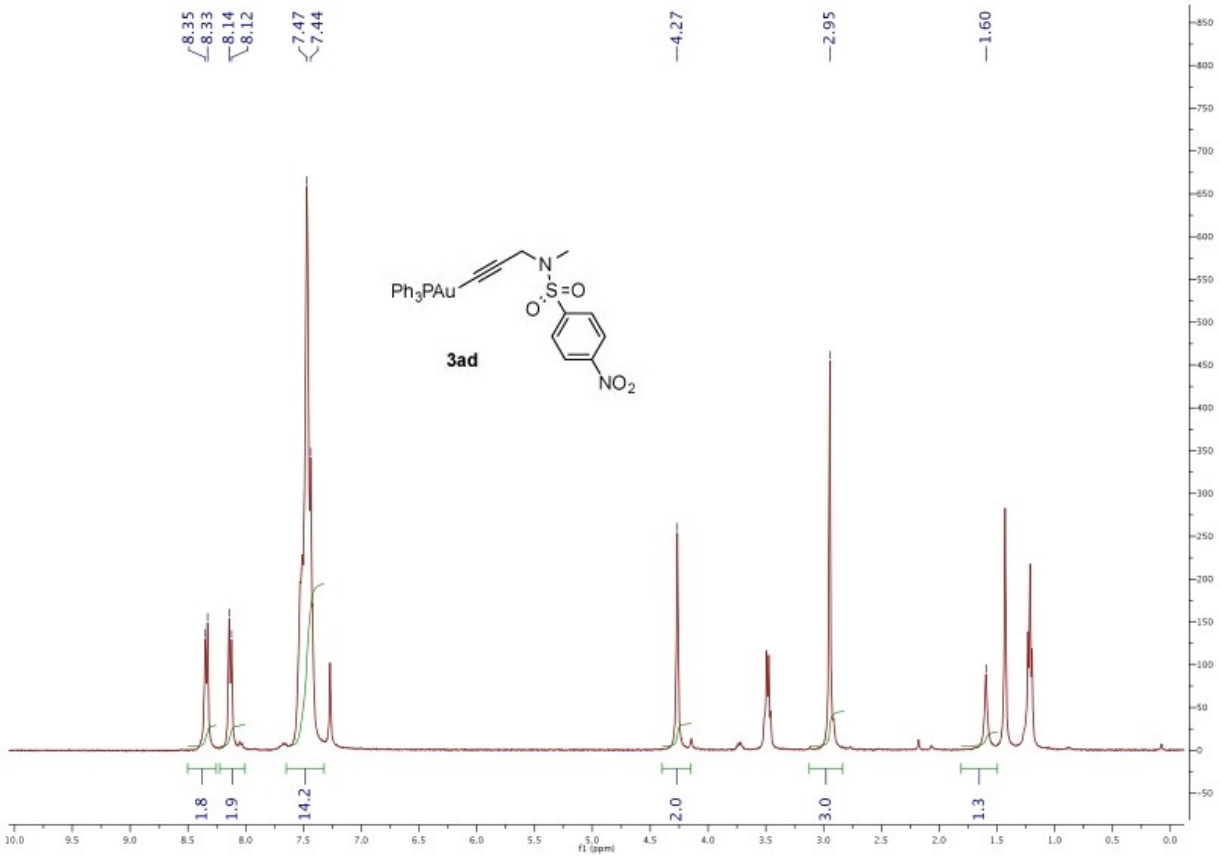
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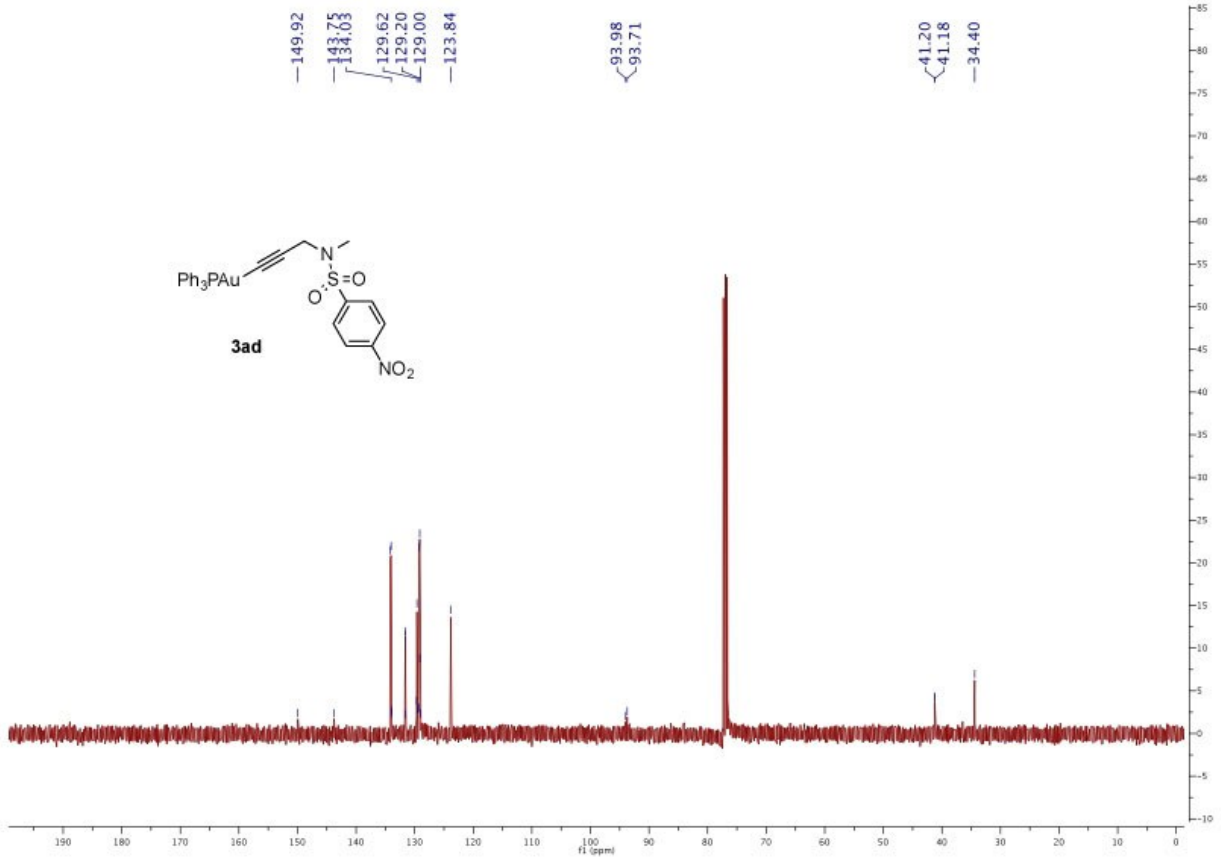
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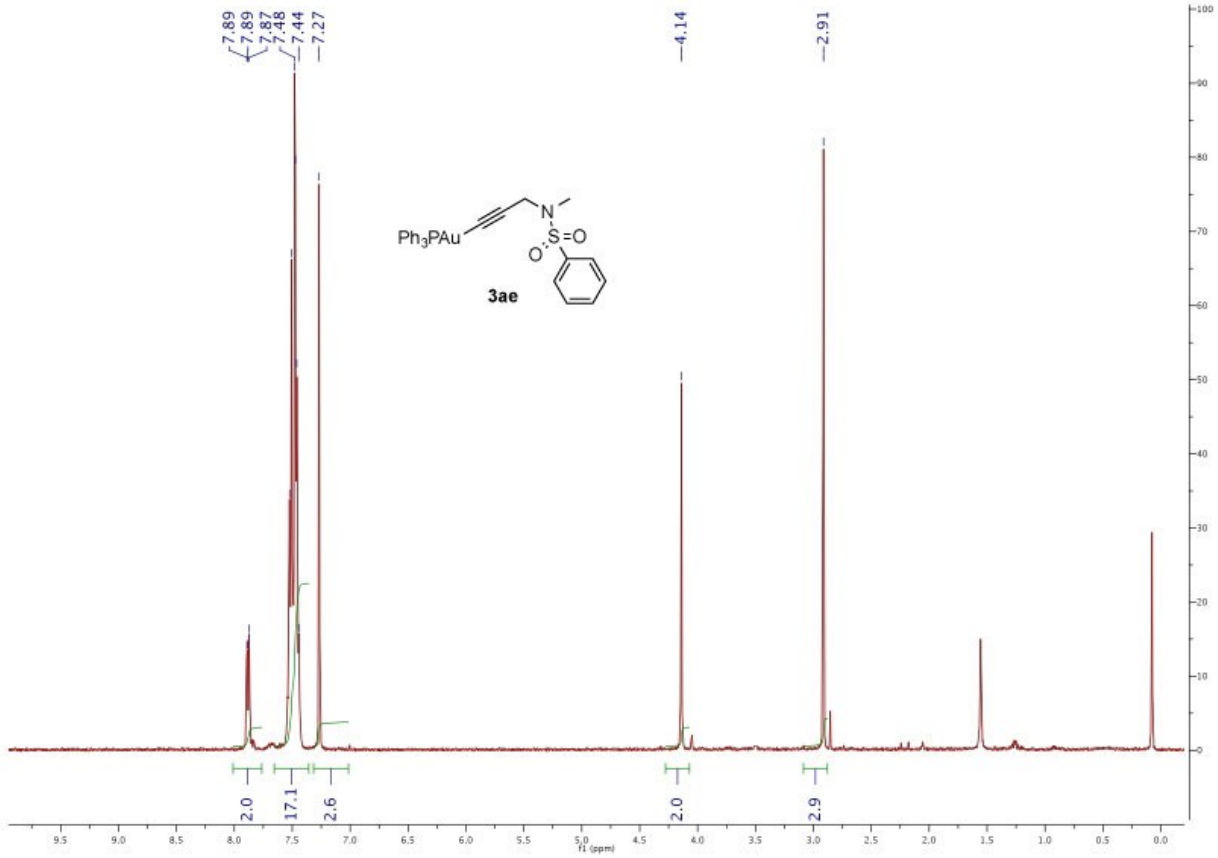
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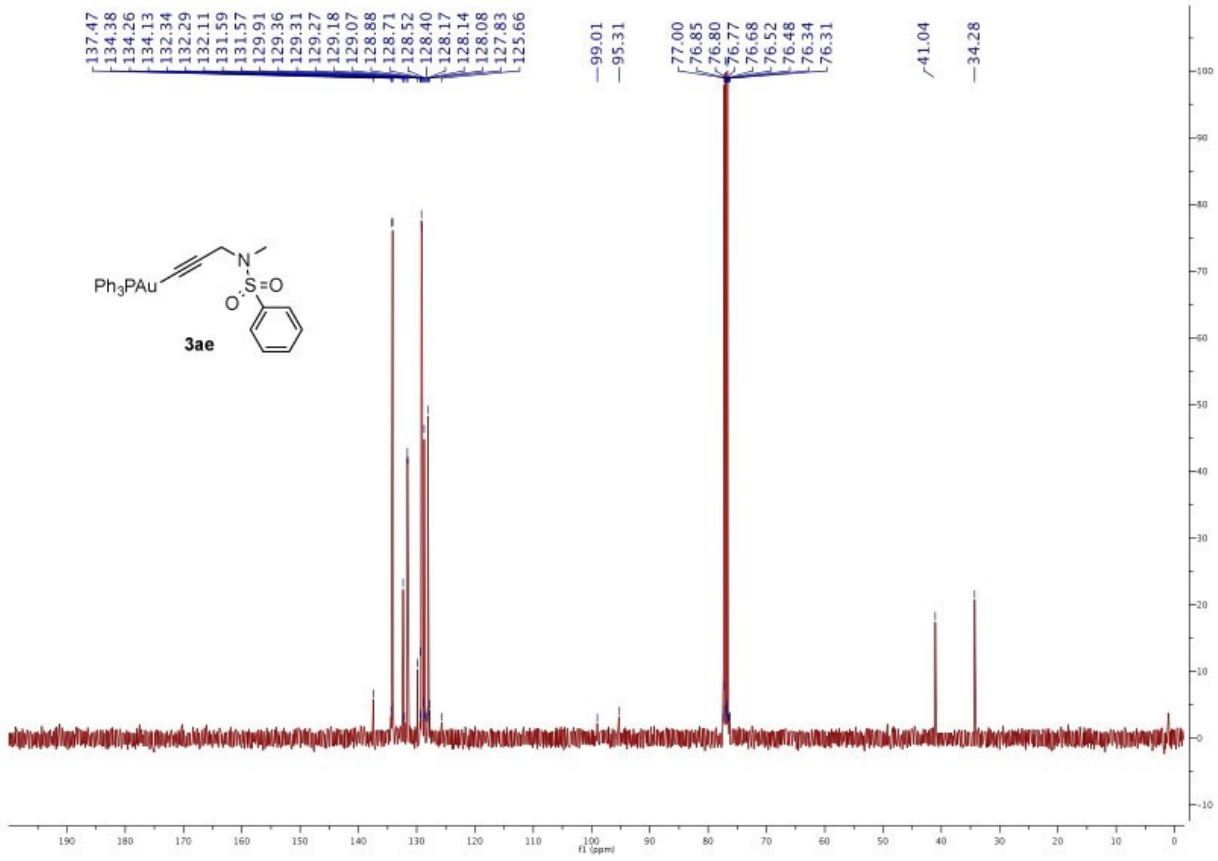
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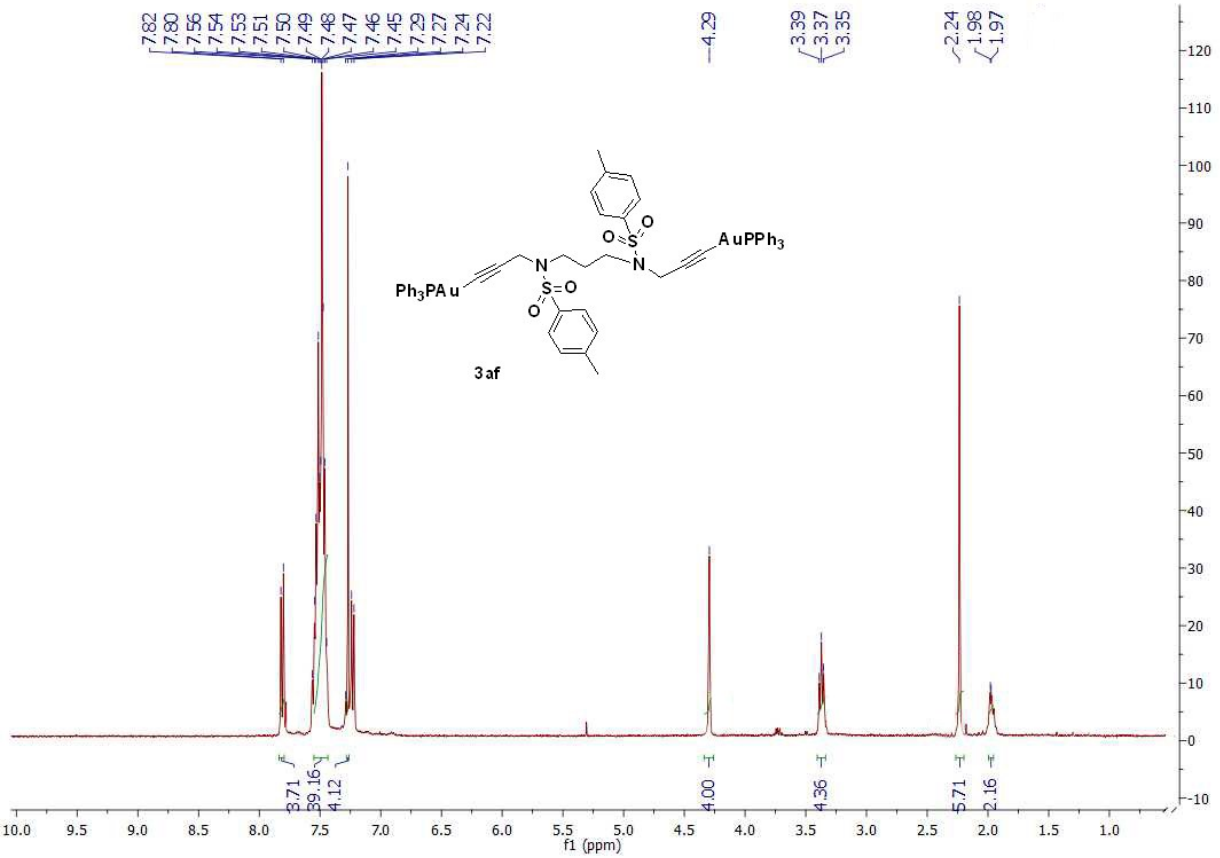
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2.24
1.98
1.97
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Ph3PAu
3af
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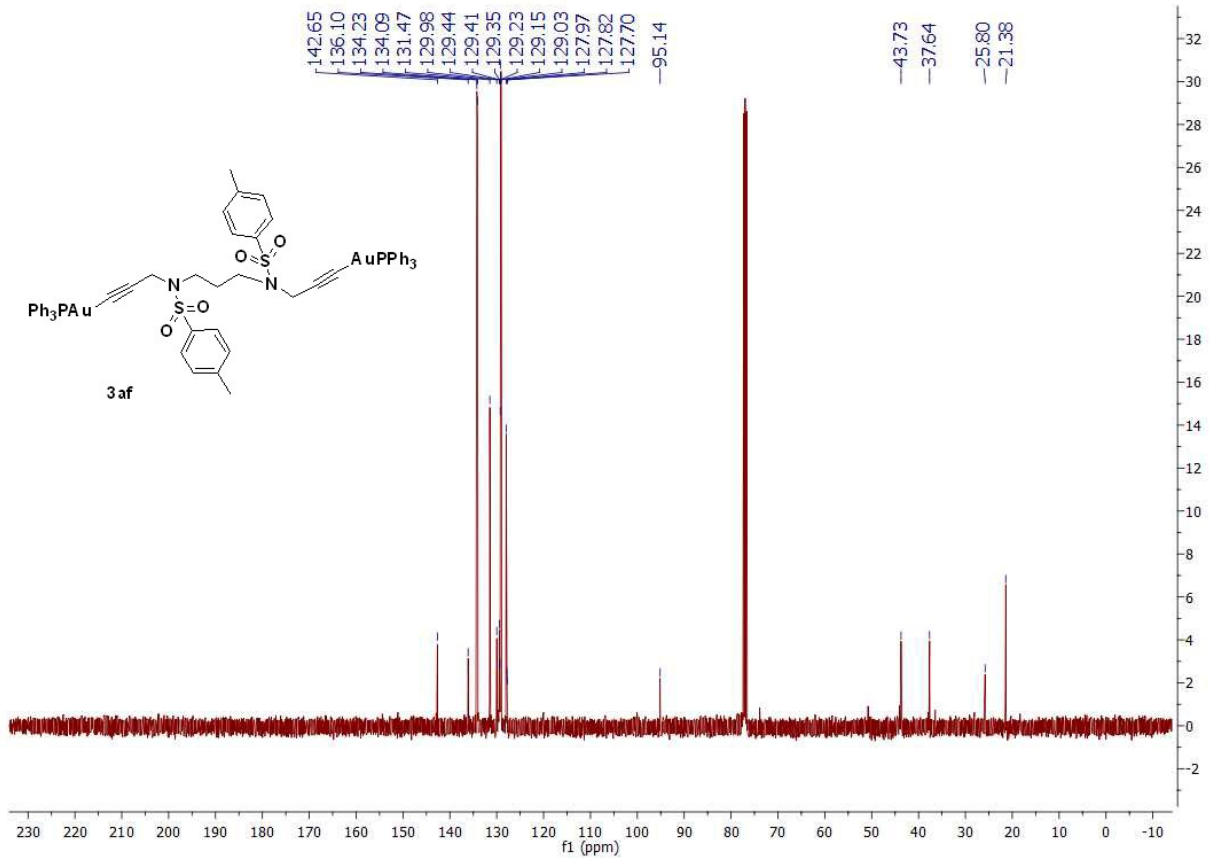
39.16
4.12
4.00
4.36
5.71
2.16
f1 (ppm)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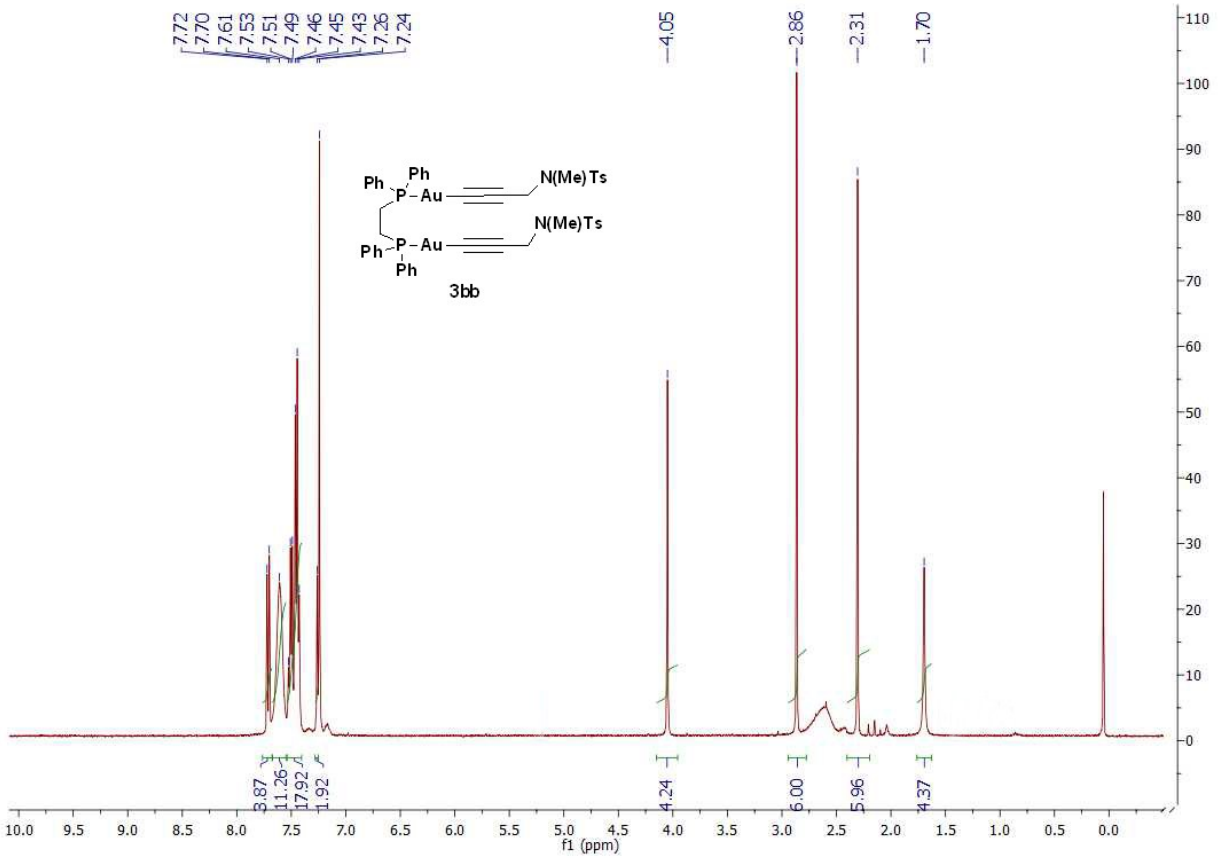
f1 (ppm)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2.31
1.70
Ph
Ph
P–Au
N(Me)Ts
Ph
P–Au
N(Me)Ts
Ph
Ph
3bb
3.87
11.26
17.92
1.92
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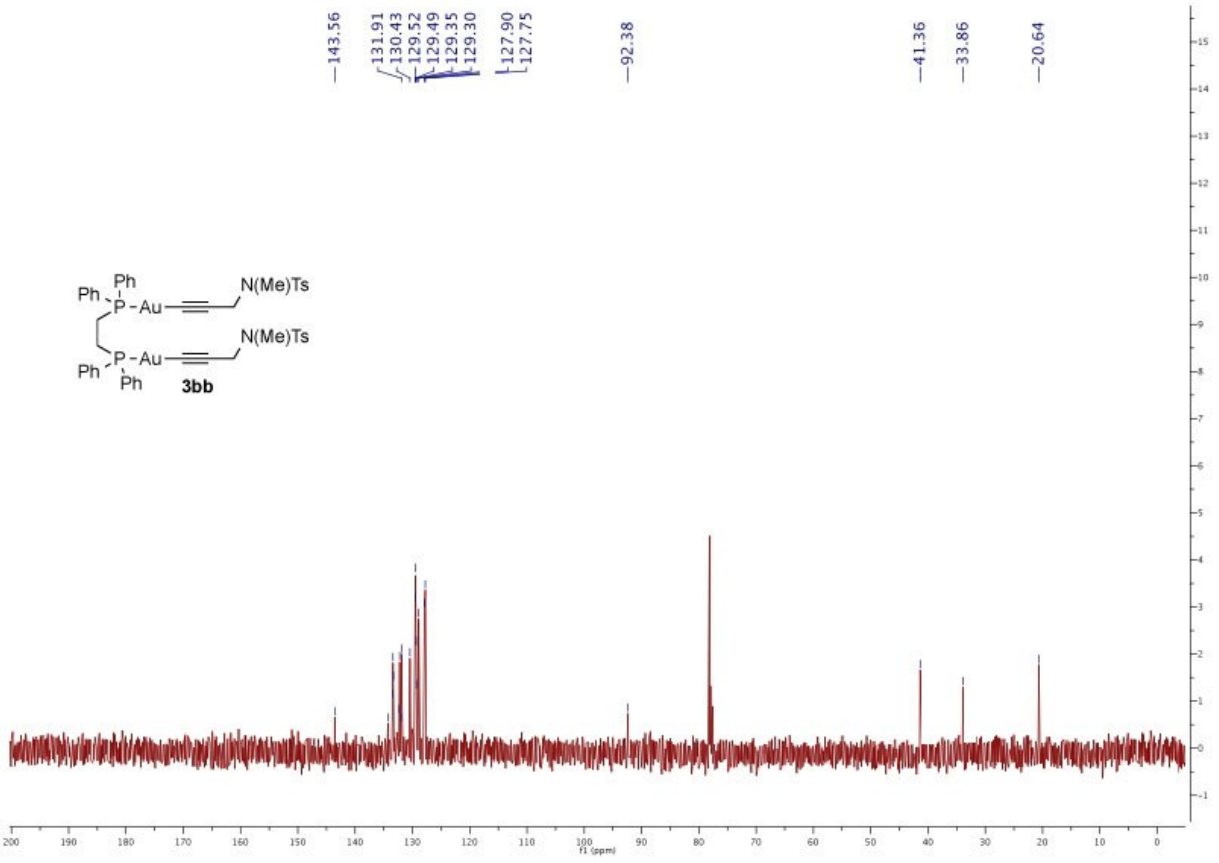
f1 (ppm)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129.52
129.49
129.35
129.30
127.90
127.75
92.38
41.36
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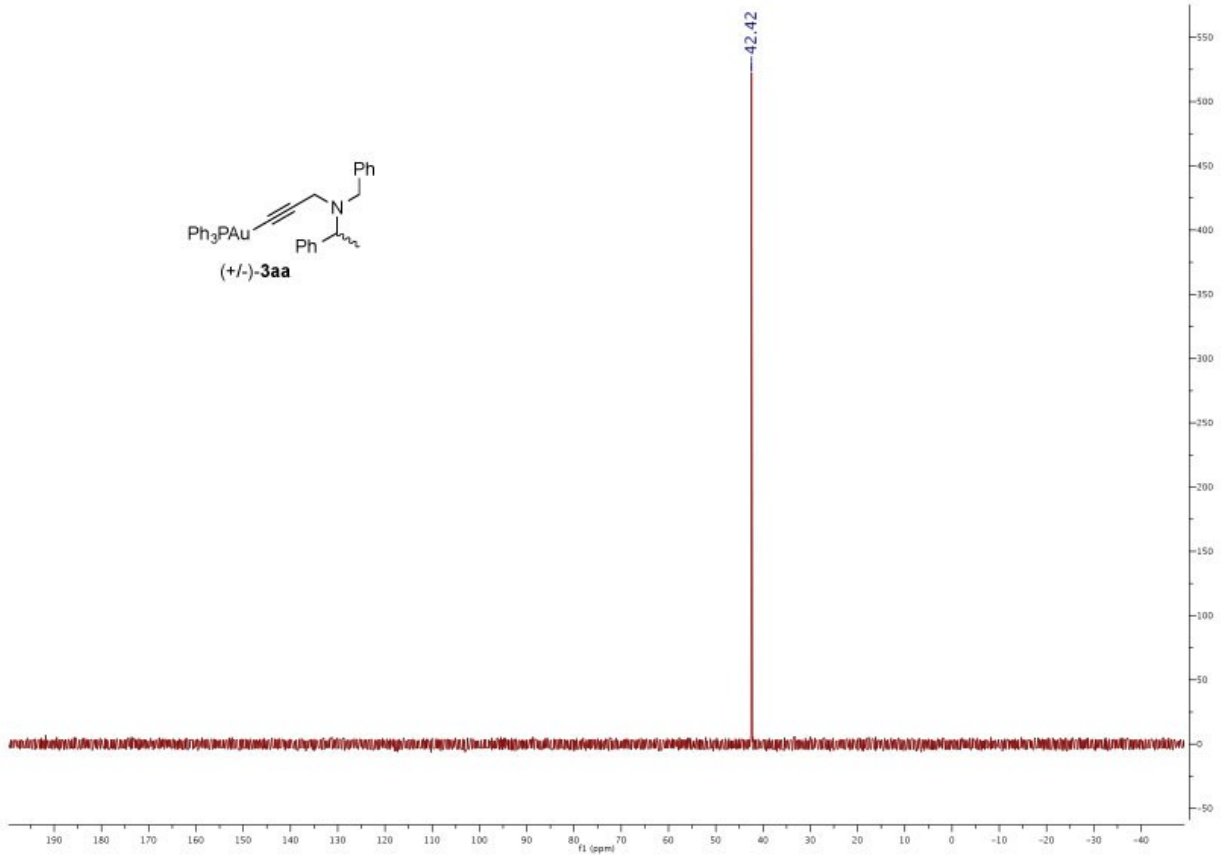
Ph
P–Au
N(Me)Ts
Ph
Ph
3bb
f1 (ppm)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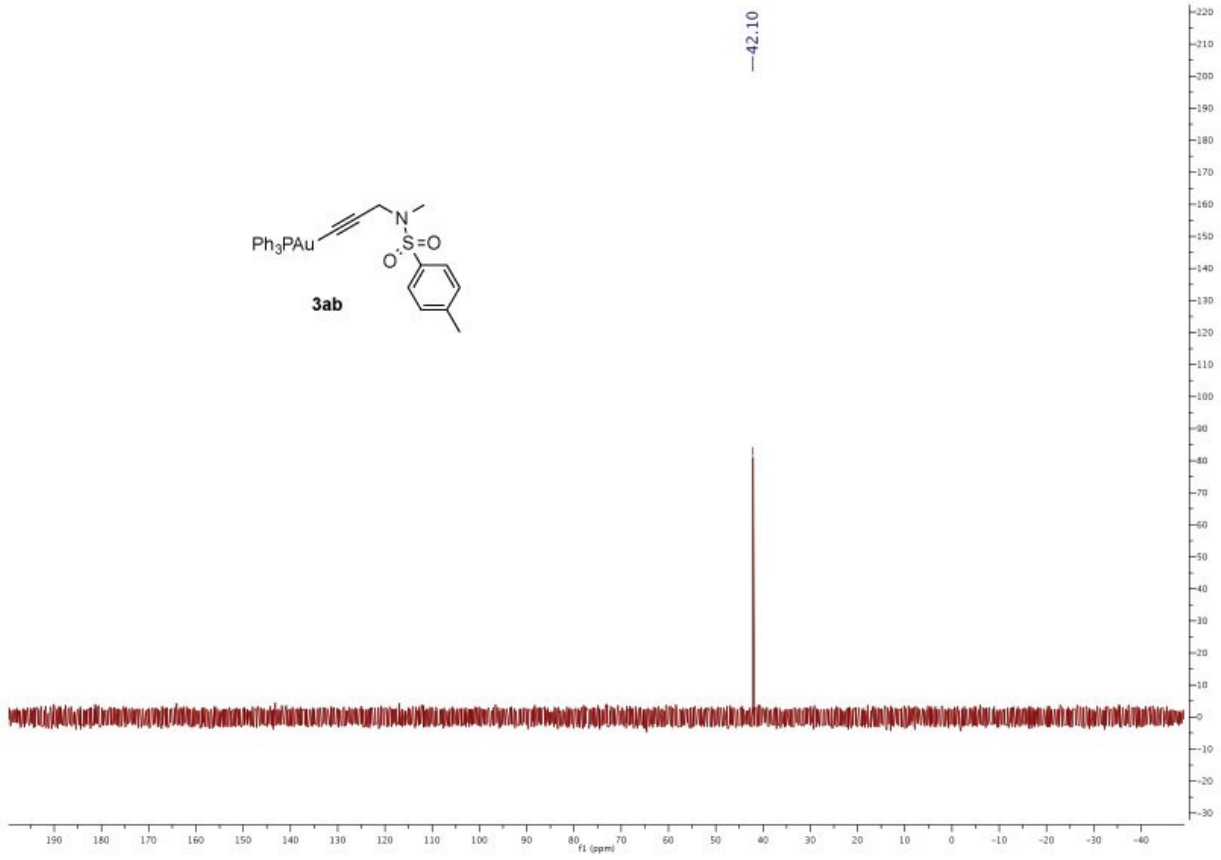
N
Ph
Ph3PAu
(+/-)-3aa
f1 (ppm)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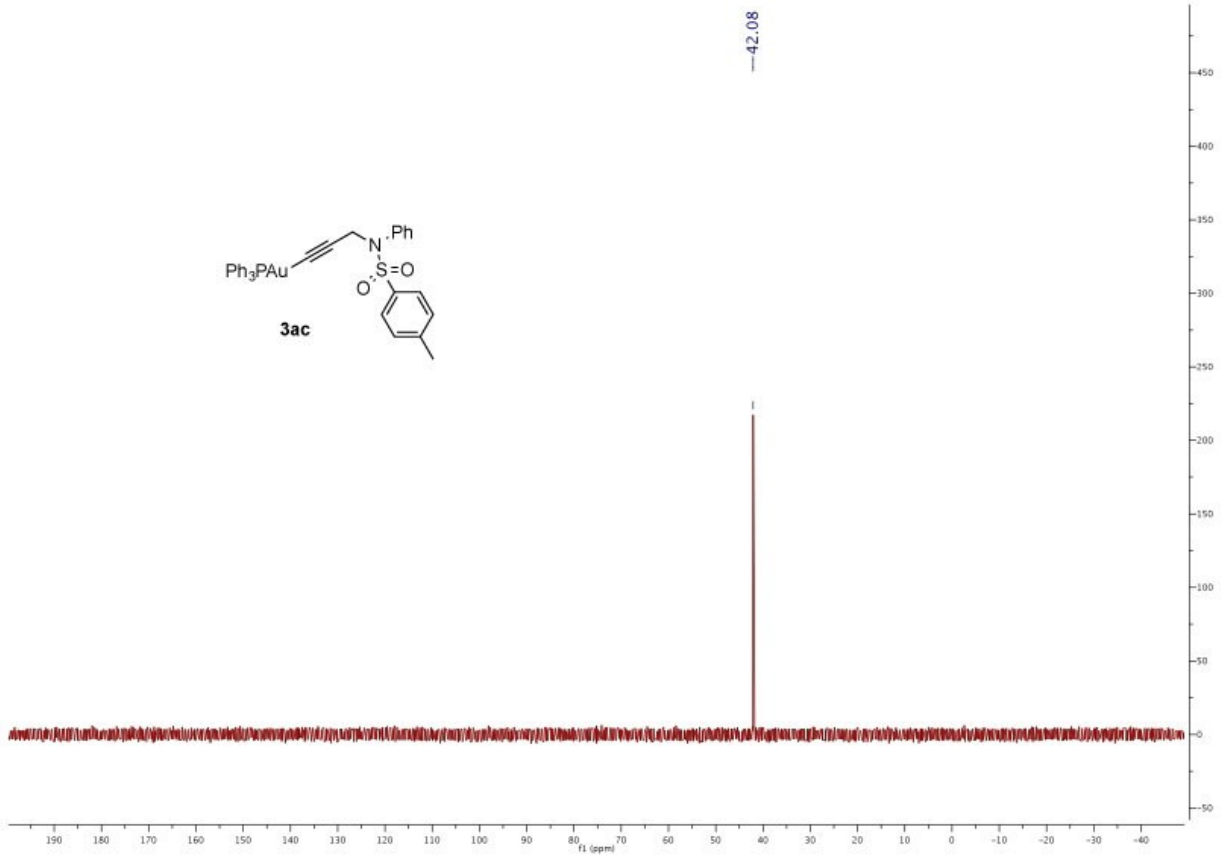
N
S=O
O
Ph3PAu
3ab
f1 (ppm)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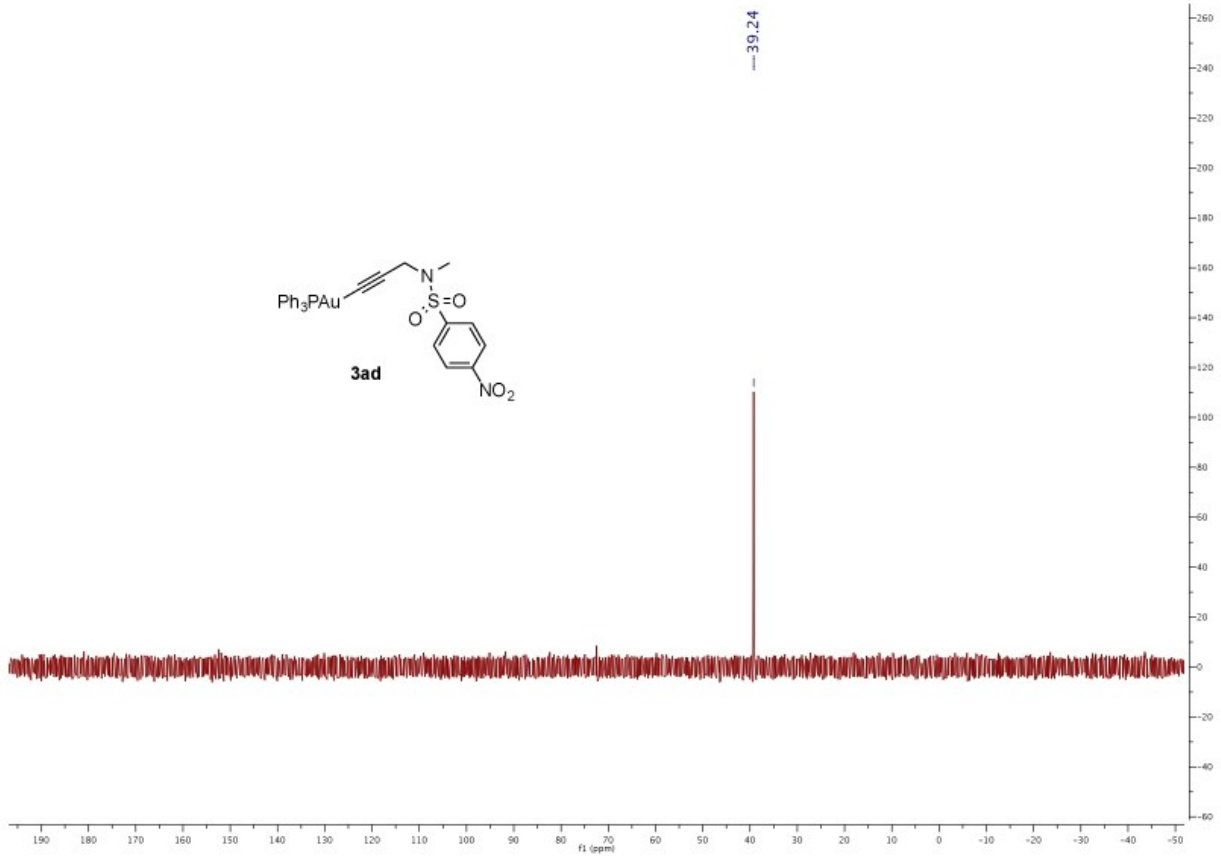
N
Ph3PAu
S=O
O
3ac
f1 (ppm)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N
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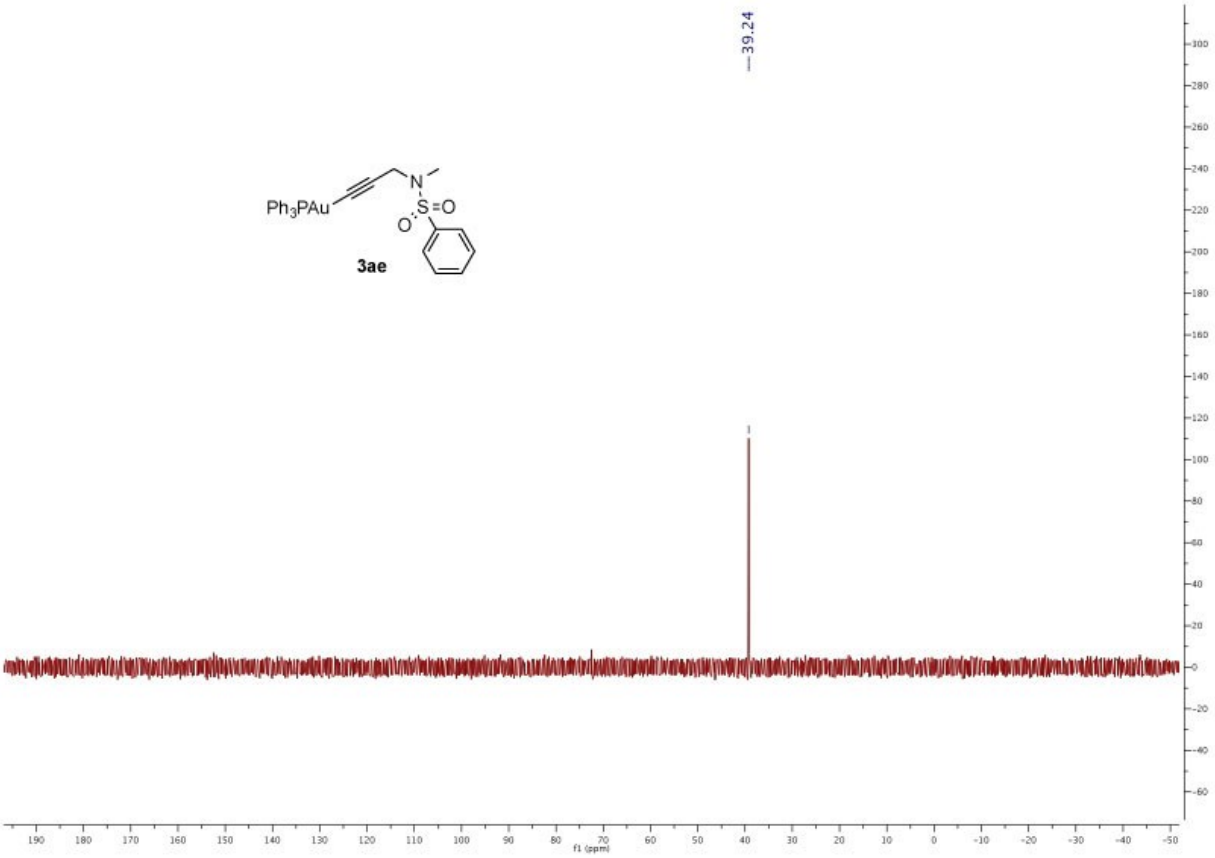
O
3ad
NO2
f1 (ppm)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N
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O
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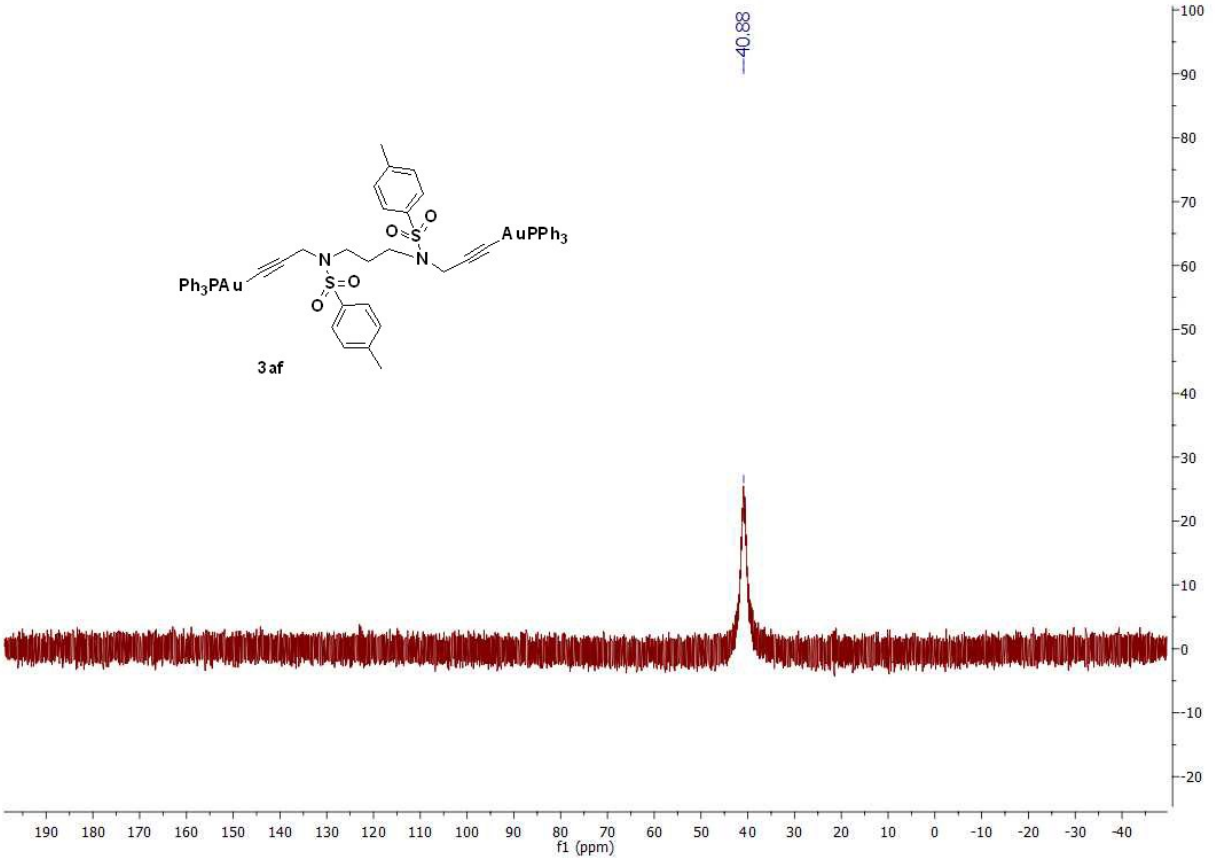
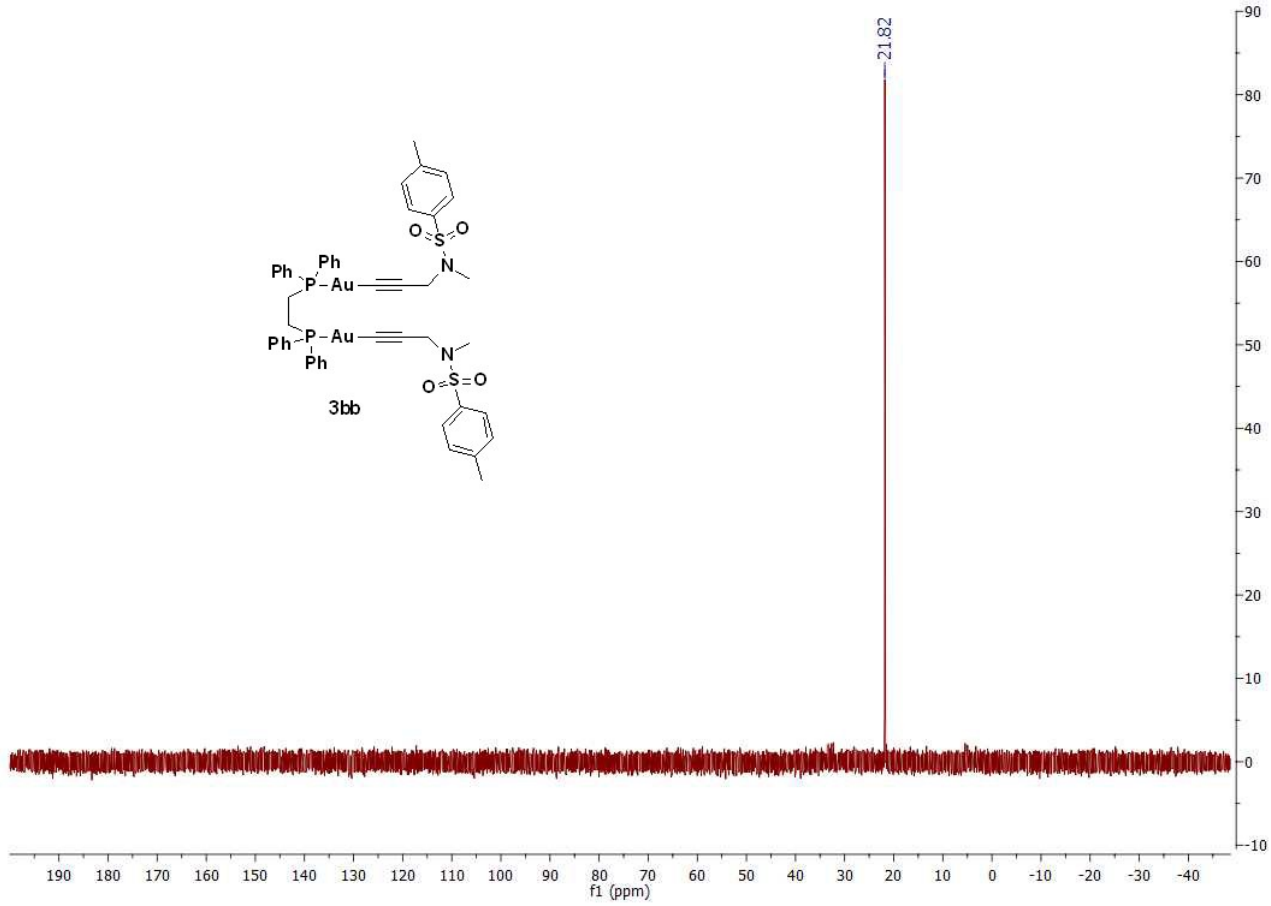
f1 (ppm)


40.88
O=S=O
AuPPh3
Ph3PAu
N
S=O
O
3af
f1 (ppm)


21.82
3bb
f1 (ppm)

Crystallographic Data Collection and Structure Determination for 3ab and **3ac.**

The X-ray intensity data were measured on a Bruker SMART Apex II CCD area detector diffractometer. Cell dimensions and the orientation matrix were initially determined from a least-squares refinement on reflections measured in three sets of 20 exposures, collected in three different ω regions, and eventually refined against all data. A full sphere of reciprocal space was scanned by 0.3° ω steps. The software SMART[1] was used for collecting frames of data, indexing reflections, and determination of lattice parameters. The collected frames were then processed for integration by the SAINT program[2] and an empirical absorption correction was applied using SADABS.[2] The structures were solved by direct methods (SIR 2004)[3] and subsequent Fourier syntheses and refined by full-matrix least-squares on F^2 (SHELXTL)[4], using anisotropic thermal parameters for all non-hydrogen atoms. All hydrogen atoms were added in calculated positions, included in the final stage of refinement with isotropic thermal parameters, U(H) = 1.2 U_{eq}(C) [U(H) = 1.5 U_{eq}(C-Me)], and allowed to ride on their carrier carbons. Crystal data and details of the data collection for **3ab** and **3ac** are reported in Table S1.

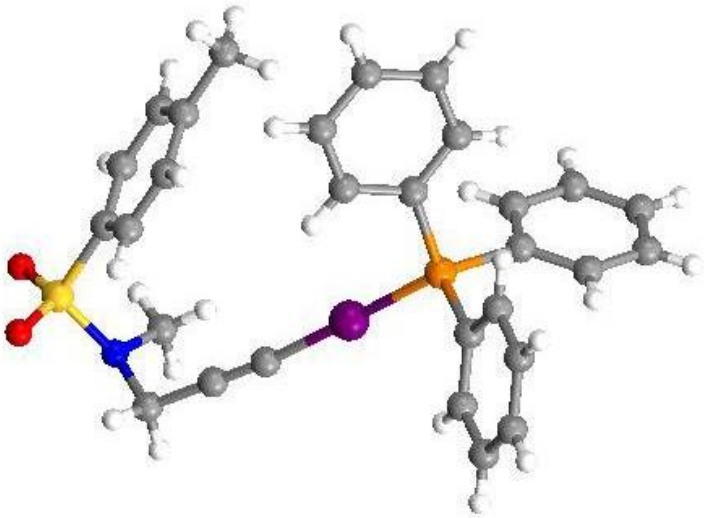
X-ray crystal structure of 3ab.

[1] *SMART & SAINT Software Reference Manuals*, version 5.051 (Windows NT Version), Bruker Analytical X-ray Instruments Inc.: Madison, WI, **1998**.

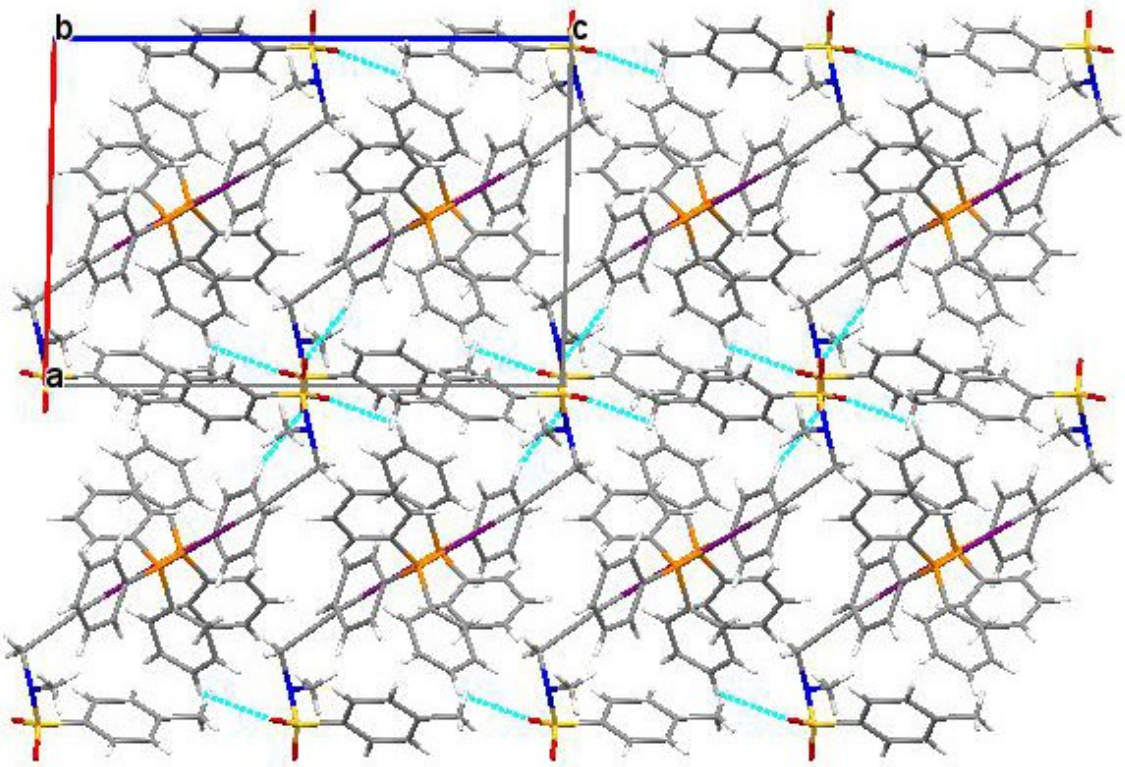
[2] G. M. Sheldrick, *SADABS, program for empirical absorption correction*, University of Göttingen, Germany, **1996**.

[3] M. C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, Cascarano, G. L. De Caro, C. Giacovazzo, G. Polidori, R. Spagna, *J. Appl. Crystallogr.* **2005**, *38*, 381-388.

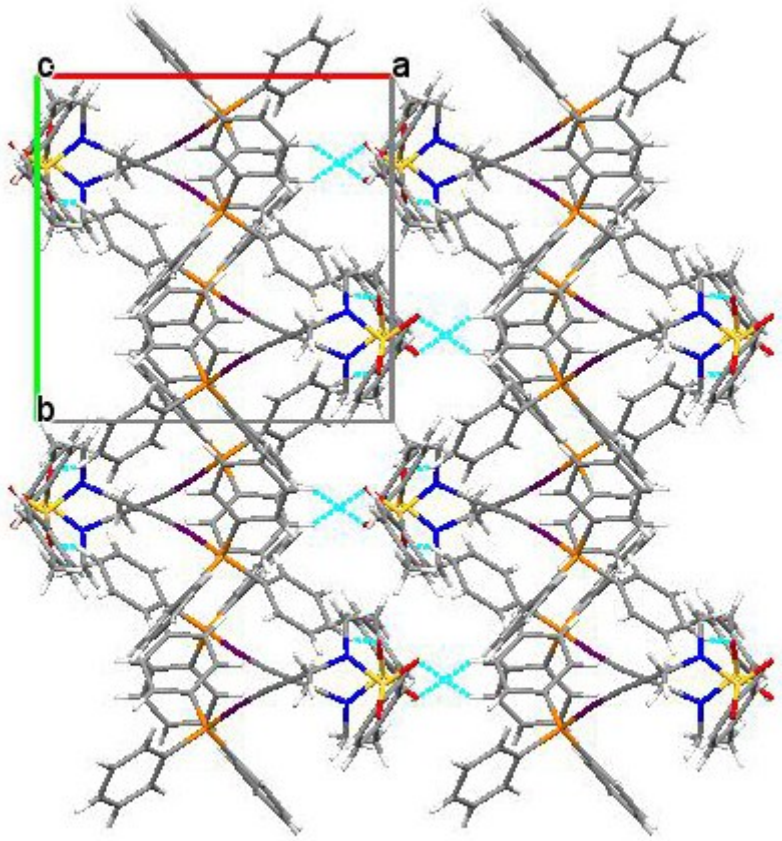
[4] G. M. Sheldrick, SHELXTL*plus (Windows NT Version) Structure Determination Package,* Version 5.1. Bruker Analytical X-ray Instruments Inc.: Madison, WI, USA, 1998.



a)



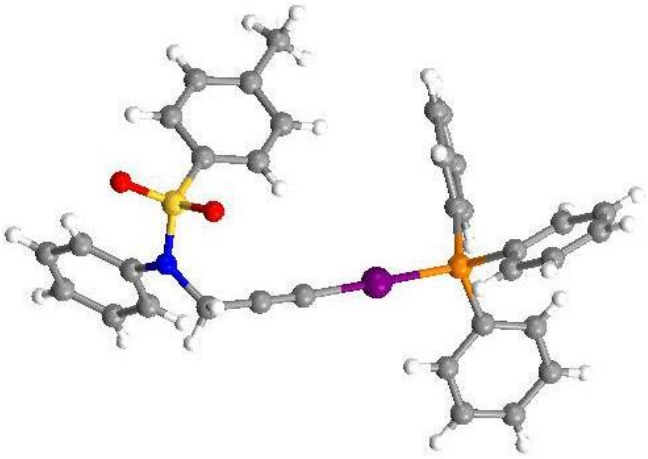
b)



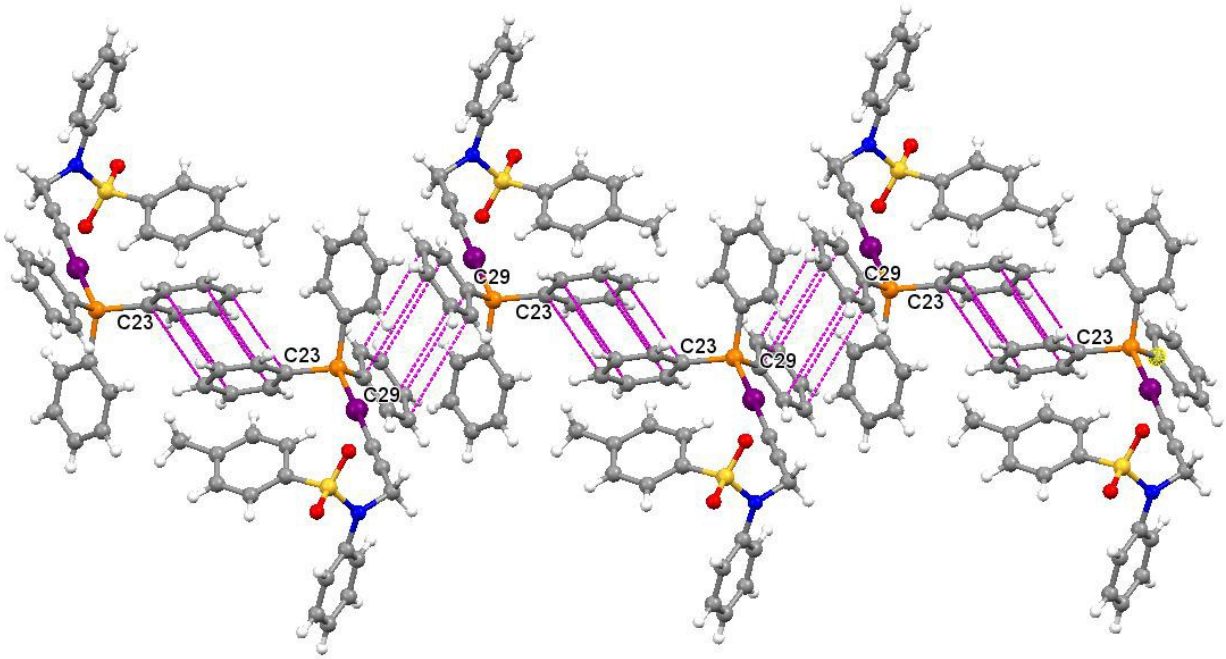
c)

Figure S1. a) Molecular structure of 3ab; b) View along the b axis of the crystal packing of 3ab (pale blue dotted lines show non classical intermolecular C-H…O hydrogen bonds); c) View along the c axis of the crystal packing of 3ab.

X-ray crystal structure of 3ac.



a)



b)

Figure S2 a) Molecular structure of **3ac**; b) View down the *b* axis of the crystal packing of **3ac**. π-π interactions involving two symmetry equivalent phosphine phenyl rings in each molecule generate infinite zig-zag chains running along the *c* axis.

Table S1. Crystal data and structure refinement for **3ab** and **3ac**.

	3ab	**3ac**
Formula	$C_{29}H_{27}AuNO_2PS$	C34H29AuNO2PS
Fw	681.51	743.58
T, K	296 (2)	296 (2)
Crystal symmetry	monoclinic	triclinic
Space group	*P* $2_1/c$	*P -1*
a, Å	12.285(5)	8.943(5)
b, Å	11.956(5)	12.762(7)
c, Å	18.281(8)	13.472(7)
α, °	90	90.434(5)
β, °	91.473	103.985(5)
γ, °	90	90.154(5)
Cell volume, $Å^3$	2684(2)	1491.9(14)
Z	4	2
D_c, Mg m^{-3}	1.686	1.655
μ(Mo-K_α), mm^{-1}	5.644	5.086
F(000)	1336	732
Crystal size mm	0.15 × 0.20 × 0.25	0.20 x 0.20 x 0.25
θ limits, °	1.66-26.00	1.56-27.03
Refl. collected, unique (R_{int})	23071, 5253 (0.0715)	14559, 6424 (0.0500)
Goodness-of-fit-on F^2	0.984	0.973
$R_1(F)$[a], wR_2 (F^2) [$I > 2\sigma(I)$][b]	0.0395, 0.0533	0.0376, 0.0653
Largest diff. peak and hole, e. $Å^{-3}$	0.545, -0.557	0.838, -1.252

[a] $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$. [b] $wR_2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$ where $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ where $P = (F_o^2 + F_c^2)/3$.

Liquid chromatography and mass spectrometry analysis.

TrxR alone or in combination with **3ab** or **3bb** was analysed by liquid chromatography tandem mass spectrometry (LC-MS) in order to evaluate the possible covalent interaction between the enzyme and the two moieties.

In details, the analyses were performed using a Jasco PU-1585 liquid chromatograph (Jasco Corporation, Tokio, Japan) equipped with a Reodyne 7281 injection valve (20 µL sample loop). The chromatographic separation was achieved using a monolithic column CIMac C4 Analytical (5.3 mm I.D. X 5 mm), a not commercial prototype provided by BIA Separations (Ljubljana, Slovenia). Mobile phases A [water:acetonitrile:formic acid (99/1/0.1) (v/v/v),] and B [acetonitrile:water:formic acid (98/2/0.1) (v/v/v)] were used to develop a gradient. The optimized mobile phase B gradient program was 0–80 % in 5 min and 80 % of B for 5 min. The column was equilibrated with the mobile phase composition of the starting conditions for 3 min before the next injection. The flow rate was set at 0.5 mL/min. The injection volume was 20 µL.

Mass spectrometry analysis was carried out on a Quadrupole-Time of Flight hybrid analyser (Q-ToF Micro, Micromass, Manchester, UK) with Z-spray electrospray ion source (ESI). The ESI-Q-ToF source temperature was set at 120°C, the capillary voltage at 3.2 kV and the cone voltage at 30 V. The scan time was set at 2.0 s and the inter scan time at 0.1 s. The cone gas flow was set at 120 L/h and the desolvatation gas at 500 L/h. The mass chromatograms were recorded in total ion current (TIC), within 500 m/z and 2000 m/z. The HSA baseline-subtracted spectrum (m/z 1000–1600) was deconvoluted onto a true mass scale using the maximum entropy (MaxEnt1)-based software supplied with MassLynx 4.1 software. Output parameters were as follows: mass range 20000–70000 Da and resolution 5 Da/channel. The uniform Gaussian model was used, with 0.5 Da width at half height.

Result and discussion.

- Naldi M, Giannone F a, Baldassarre M, Domenicali M, Caraceni P, Bernardi M, et al. Eur J Mass Spectrom (Chichester, Eng). **2013**;19(6):491–6.

The mass spectrometric analysis of protein allows the identification of the covalent modification affecting its structure and hence its molecular weight [5]. In order to evaluate the possible covalent interaction between TrxR and **3ab** and **3bb**, the LC-MS analyses were performed (Fig. S3). TrxR was previously analysed independently and its multicharged mass spectrum was acquired on its chromatographic peak (5 min retention time). From this spectrum the deconvoluted-ESI mass spectrum was obtained; it reports the molecular weight of the enzyme (Fig. S4). Being TrxR a mixture of isoforms we obtained three different principal molecular weights (54342, 58856 and 60885 Da). Analysing the mixtures of the enzyme with **3ab** and **3bb** a second peak appeared in the chromatogram indicating that these moieties have a different chromatographic behaviour compared to that of the enzyme. This peak could derived from the molar excess of **3ab** and **3bb**. Concerning the mass spectrometric analysis however no significant changes were detected analysing the enzyme peak. In the presence of a covalent bound the signal corresponding to the adduct would have appeared but no new signal was detected thus we can conclude that no covalent bound exists between TrxR and **3ab** or **3bb**.

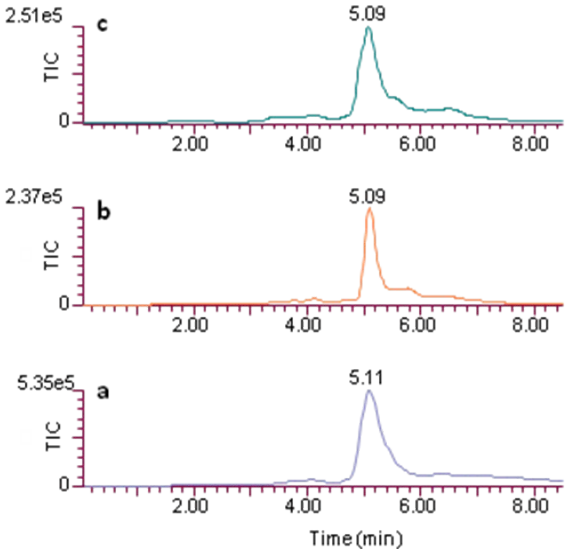


Figure S3**.** LC-ESI-MS analysis of TrxR alone and in combination with 3ab and 3bb

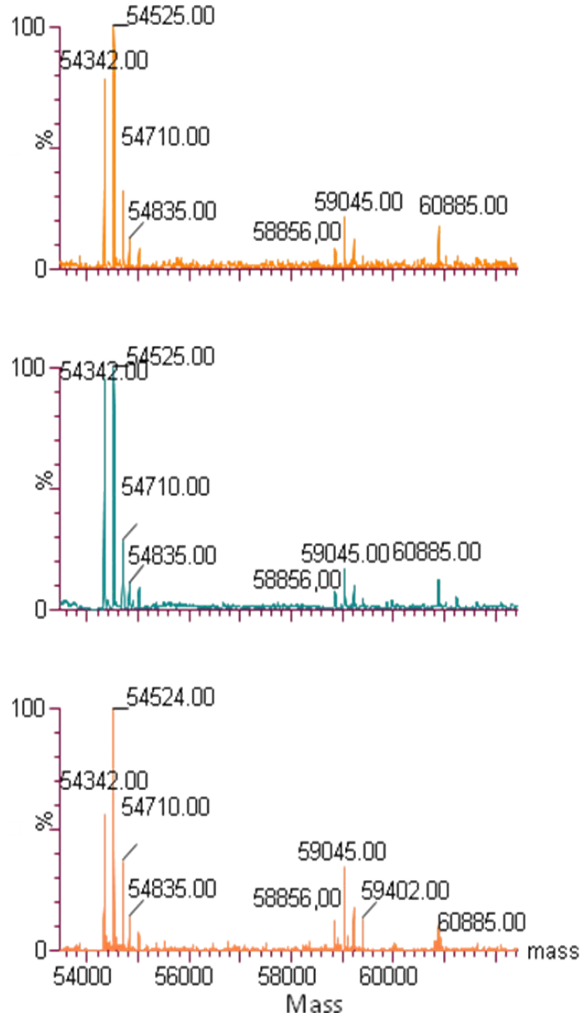


Figure S4. Deconvoluted ESI mass spectra of TrxR alone or after the combination with 3ab and 3bb.