Supplementary Information

for

Visible-light-initiated metal-free C_{sp3}–C_{sp3} to C_{sp3}–N conversion in homobenzylic sulfonamides with *N*-iodoimides

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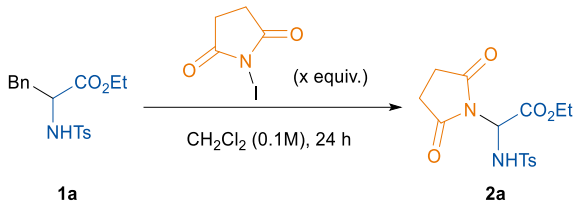
1. General information

All commercially available compounds were used as received. Reactions were carried out under nitrogen atmosphere with standard schlenck techniques. Solvents were purchased from commercial sources. Analytical thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merck 60 F254) and UV light as visualizing agent or phosphomolybdic acid solution as developing agent. Chromatography purifications were carried out using silica gel (40-63 μm, 60 Å). The irradiations were carried out with Kessil LED light A160WE Tuna Blue in a EvoluChem PhotoRedOx Box™ photoreactor.

NMR spectra were recorded at 298 K using either a Varian Mercury VX-300, Bruker Avance NEO 400, or Varian Unity 500 MHz spectrometer. Chemical shift values for ^{1}H and ^{13}C are reported as δ values (ppm) relative to the deuterated solvent ($CDCl_3$: 7.26 ppm, 77.16 ppm, CD_3OD: 3.31 ppm, 49.0 ppm, CD_3COCD_3: 2.05 ppm, 29.8 ppm) and coupling constants (*J*) in Hz. The following abbreviations are used in reporting NMR data: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; quin, quintuplet; m, multiplet. Optical rotations were obtained using a PerkinElmer 341 polarimeter and concentrations are given in g/100mL. Melting points were determined in open capillary tubes using a Stuart Scientific SMP3 melting point apparatus. High-resolution analysis (HRMS) were performed using an Agilent 6210 TOF LC/MS system by Centro de Instrumentación Científico-Técnica (CICT)- Servicios Centrales de Apoyo a la Investigación (SCAI)- Universidad de Jaén (UJA, MICINN, Junta de Andalucía, FEDER). Single crystal structure determination was performed using a Bruker D8 VENTURE Photon III area-detector diffractometer with CuKα radiation.

2. Optimization studies



1a **2a**

Table S1. Optimization of the reaction conditions under LED strips irradiation.

	LED strips (~30 W)	NIS (equiv)	Conversion[a] (%)
1	Violet LED	1,2	27
2	Blue LED	1,2	32
3	White LED	1,2	20
4	Bright blue LED [b]	1,2	64
5	Bright blue LED [b]	1,5	84
6	Bright blue LED [b]	0,75 x 2 [c]	74
7	Bright blue LED [b]	2	100

[a] Conversion measured by ^{1}H NMR, [b] Reaction temperature ~47 ºC, [c] Second addition after 8 hours.

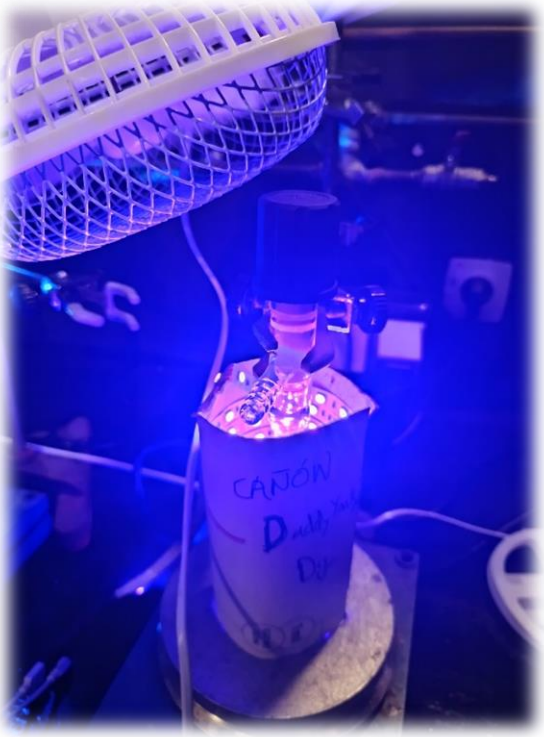


Figure S1. Reaction setup with LED strips. The reaction was exposed to LED strips positioned at 4 cm from the Schlenk tube. A fan was placed on top of the Schlenk tube to maintain the temperature constant.

Table S2. Optimization of the reaction conditions under Kessil LED irradiation.

	Kessil LED	Distance (cm)	NIS (equiv)	Conversion[a] (%)
1	370 nm (40 W) [b]	2	1,2	-
2	395 nm (40 W) [b]	2	1,2	-
3	405 nm (40 W) [b]	2	1,2	-
4	405 nm (40 W) [b]	5	1,2	-
5	440 nm (2x40 W) [c]	4	1,2	19
6	440 nm (2x40 W) [c]	2	1,2	25
7	525 nm (2x40 W) [b]	2	1,2	64
8	White Kessil (2x40 W) [c,d]	2	1,2	61
9	White Kessil (2x40 W) [c,d]	4	1,2	11
10	White Kessil (2x40 W) [c,d]	2	0,6 x 2 [e]	56
11	White Kessil (2x40 W) [c,d]	2	1,2 x 2 [e]	99
12	White Kessil (40 W) [c]	2	1,2	60

[a] Conversion measured by ^{1}H NMR, [b] Kessil LED PR160L, [c] Kessil LED A160WE Tuna Blue, [d] Reaction temperature ~65 ºC, [e] Second addition after 8 hours.

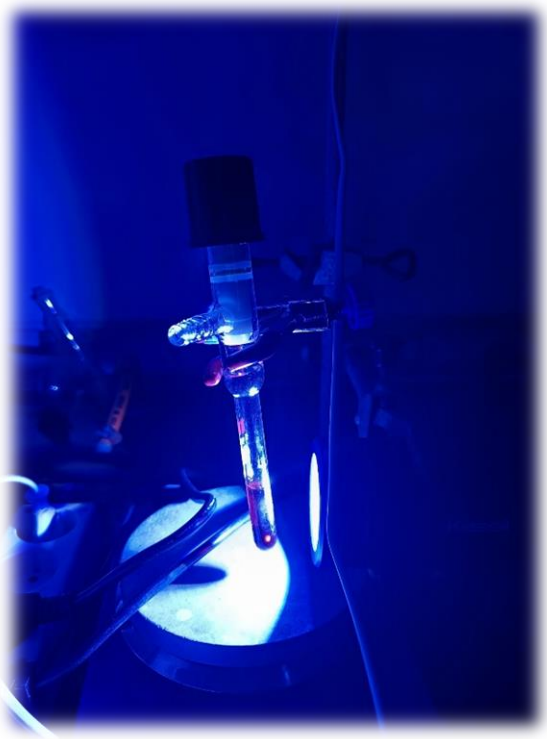


Figure S2. Reaction setup with Kessil LED. The reaction was exposed to Kessil LED lamp positioned at 2-5 cm from the Schlenk tube. A fan was placed on top of the Schlenk tube to maintain the temperature at 30 °C.

Table S3. Optimization of the reaction conditions under Kessil LED irradiation in EvoluChem PhotoRedOx Box™ photoreactor.

	Kessil LED 40 W (photoreactor)	Solvent	Conc.	NIS (equiv)	Conversion[a] (%)
1	395 nm [b]	CH_2Cl_2	0.1 M	1,2	10
2	405 nm [b]	CH_2Cl_2	0.1 M	1,2	32
3	440 nm [b]	CH_2Cl_2	0.1 M	2	78
4	525 nm [b]	CH_2Cl_2	0.1 M	2	84
5	White Kessil [c,d]	CH_2Cl_2	0.1 M	1,2	86
6	White Kessil [c,d]	CH_2Cl_2	0.1 M	1,5	78
7	White Kessil [c,d]	CH_2Cl_2	0.1 M	0,75 x 2 [e]	74
8	White Kessil [c,d]	CH_2Cl_2	0.1 M	2	100 (96) [f]
9	White Kessil [c,d]	CH_2Cl_2	0.05 M	2	85
10	White Kessil [c,d]	CH_2Cl_2	0,075 M	2	90
11	White Kessil [c,d]	CH_2Cl_2	0,125 M	2	80
12	White Kessil [c,d]	CH_3CN	0.1 M	2	30
13	White Kessil [c,d]	DMSO	0.1 M	2	-
14	White Kessil [c,d]	THF	0.1 M	2	-
15	White Kessil [c,d]	$MeNO_2$	0.1 M	2	82
16	White Kessil [c,d]	MeOH	0.1 M	2	-
17	White Kessil [c,d]	Toluene	0.1 M	2	8
18	No light (40 ºC)	DCM	0.1 M	2	-

[a] Conversion measured by ^{1}H NMR, [b] Kessil LED PR160L, [c] Kessil LED A160WE Tuna Blue, [d] Reaction temperature ~34 ºC, [f] Isolated yield, [e] Second addition after 8 hours.

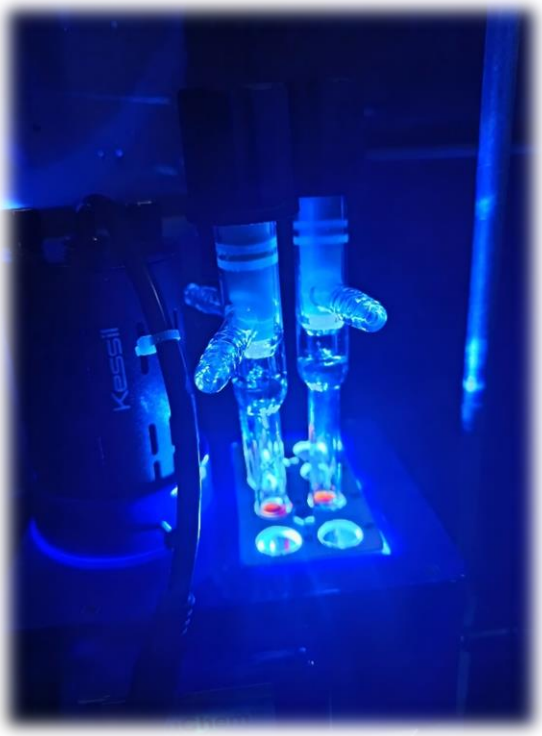
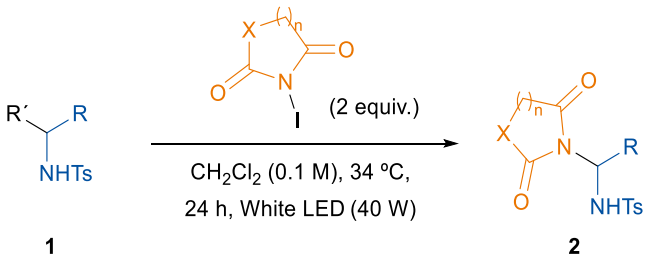


Figure S3. Reaction setup with Kessil LED in EvoluChem PhotoRedOx Box™ photoreactor.

3. General procedure



1 **2**

The corresponding sulfinamide **1** (0.20 mmol) and *N*-iodoimide (2 equiv., 0.40 mmol) were dissolved in CH_2Cl_2 (0.1 M) under inert atmosphere. The reaction mixture was stirred under irradiation with a white LED Kessil® (40 W) in a EvoluChem PhotoRedOx Box™ photoreactor for 24 h. The solvent was evaporated and the corresponding 1,1-diamine **2** was purified by column chromatography.

Unsuccessful substrates

The following scheme outlines the substrates that gave traces or no product under the optimised conditions:

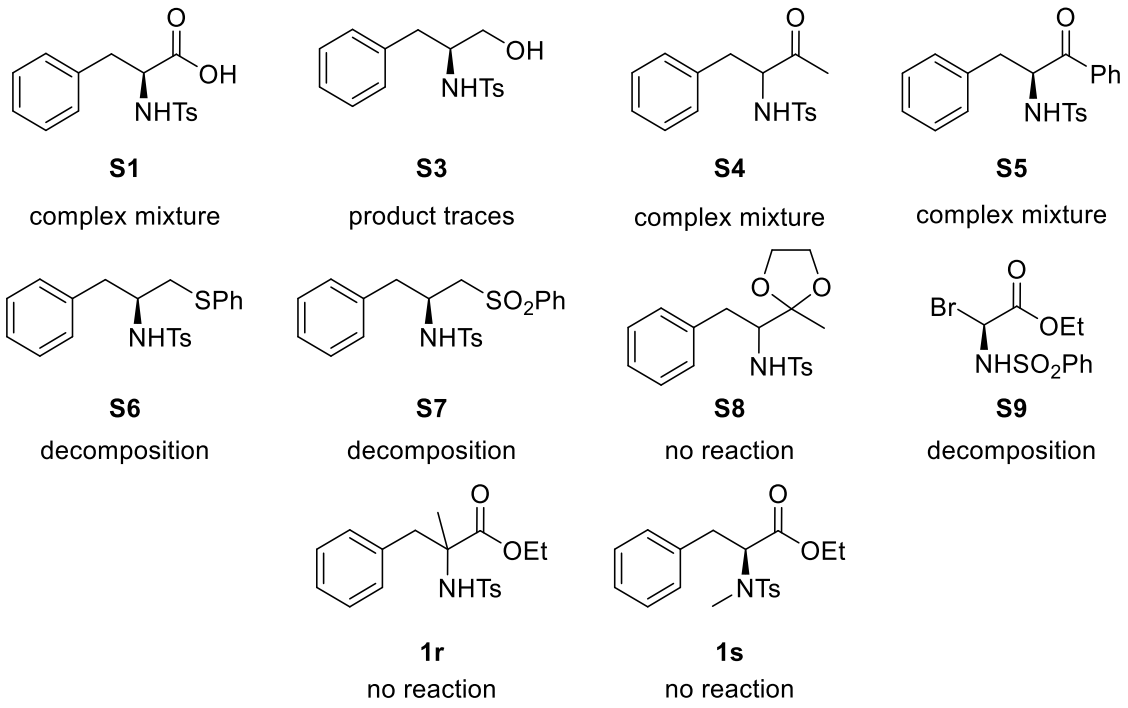
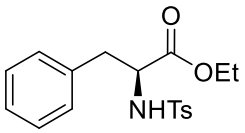


Figure S4. Unsuccessful substrates.

4. Characterization data

4.1 Substrates

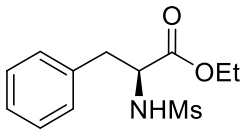
(*S*)-Ethyl 2-(4-methylphenylsulfonamido)-3-phenylpropanoate (1a)



L-Phenylalanine ethyl ester hydrochloride (2.00 g, 1.0 equiv., 8.71 mmol), DMAP (21 mg, 0.02 equiv., 0.17 mmol) and TsCl (1.83 g, 1.1 equiv., 9.58 mmol) were dissolved in DCM (20 mL) under inert atmosphere. TEA (2.4 mL, 2 equiv., 17.41 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous NH_4Cl saturated solution (4 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield compound **1a** as a white solid (2.95 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.27 – 7.21 (m, 5H), 7.08 (A_2X_2 part X, J_{XA} = 8.3 Hz, 2H), 5.03 (d, *J* = 9.1 Hz, 1H), 4.18 (dt, *J* = 9.1, 6.0 Hz, 1H), 3.91 and 3.90 (ABX_3 part AB, J_{AB} = 0.9 Hz, J_{AX} = J_{BX} = 7.2 Hz, 2H), 3.03 (d, *J* = 6.0 Hz, 2H), 2.40 (s, 3H), 1.05 (ABX_3 part X, J_{AX} = J_{BX} = 7.2 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.9, 143.7, 136.8, 135.1, 129.7, 129.6, 128.7, 127.4, 61.8, 56.8, 39.7, 21.6, 14.0 ppm.
NMR data were in agreement with those reported.[1]
Mp.: 70 – 72 ºC; **HRMS-ESI** m/z calculated for $C_{18}H_{21}NO_4S$ $[M+H]^+$ 348.1264, found 348.1266.
$[\alpha]_D^{25}$ = -11.6 (c = 0.99, $CHCl_3$).

(*S*)-Ethyl 2-(methylsulfonamido)-3-phenylpropanoate (1aMs)

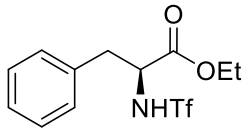


L-Phenylalanine ethyl ester hydrochloride (300 mg, 1.0 eq, 1.31 mmol), DMAP (3 mg, 0.02 eq, 26.12 µmol) and MsCl (0.1 ml, 1.1 eq, 1.44 mmol) were dissolved in DCM (8 ml) under inert atmosphere. TEA (0.4 ml, 2.1 eq, 2.74 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous HCl 3M (2 x 15 ml) and brine (2 x 15 ml) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (4:6) to yield compound **1aMs** as a white solid (328 mg, 93 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 6.96 (m, 5H), 5.34 (d, *J* = 9.3 Hz, 1H), 4.27 (ddd, *J* = 9.3, 7.9, 5.4 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.06 (dd, *J* = 13.8, 5.4 Hz, 1H), 2.91 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.55 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.5, 135.8, 129.5, 128.6, 127.2, 61.9, 57.3, 41.1, 39.2, 14.0 ppm.
Mp.: 63 – 66 ºC; **HRMS-ESI** m/z calculated for $C_{12}H_{17}NO_4S$ $[M+H]^+$ 272.0951, found 272.0951.
$[\alpha]_D^{25}$ = -5.8 (c = 1.00, $CHCl_3$).

[1] A. I. Almansour, N. Arumugam, R. Suresh Kumar, J. C. Menéndez, H. A. Ghabbour, H.-K. Fun and R. Ranjith Kumar, *Tetrahedron Lett.*, 2015, **56**, 6900.

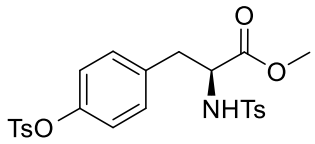
(*S*)-Ethyl 2-((trifluoromethyl)sulfonamido)-3-phenylpropanoate (1aTf)



L-Phenylalanine ethyl ester hydrochloride (300 mg, 1.0 eq, 1.31 mmol) was suspended in DCM (8 ml) under inert atmosphere. TEA (0.4 ml, 2.1 eq, 2.74 mmol) was added and the reaction was stirred at room temperature for 10 minutes. Then, at -78 ºC, trifluoromethanesulfonic anhydride (0.2 ml, 1.1 eq, 1.44 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with H_2O (2 x 15 ml) and brine (2 x 15 ml) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield compound **1aTf** as a white solid (362 mg, 85 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 3H), 7.20 – 7.01 (m, 2H), 5.50 (bs, 1H), 4.49 (t_{app}, *J* = 5.8 Hz, 1H), 4.22 (ABX_3, part AB, J_{AB} = 7.1 Hz, J_X = 2,1 Hz, 2H) 3.20 (dd, *J* = 14.0, 5.7 Hz, 1H), 3.12 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.9, 134.1, 129.6, 129.0, 127.9, 119.5 (q, *J* = 320.9 Hz), 62.6, 58.0, 39.8, 14.1 ppm.
^{19}F NMR (376 MHz, $CDCl_3$) δ -77.4 – -77.5 (m)
Mp.: 66 – 70 ºC; **HRMS-ESI** m/z calculated for $C_{12}H_{14}F_3NO_4S$ $[M+H]^+$ 326.0668, found 326.0670.
$[\alpha]_D^{25}$ = +20.4 (c = 1.00, $CHCl_3$).

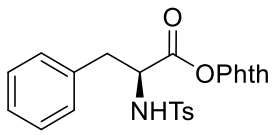
(*S*)-Methyl-2-(4-methylphenylsulfonamido)-3-(4-(tosyloxy)phenyl)propanoate (1b)



L-Tyrosine methyl ester hydrochloride (697 mg, 1.0 equiv., 3.01 mmol), DMAP (7 mg, 0.02 equiv., 0.06 mmol) and TsCl (1.26 g, 2.2 equiv., 6.62 mmol) were dissolved in DCM (17.5 mL) under inert atmosphere. TEA (1.3 mL, 3.2 equiv., 9.63 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous saturated NH_4Cl solution (4 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (6:4) to yield compound **1b** as a white solid (1.33 g, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (A_2X_2 system 1, part A, J_{AX} = 8.4 Hz, 2H), 7.63 (A_2X_2 system 2, part A, J_{AX} = 8.4 Hz, 2H), 7.31 (A_2X_2 system 1, part X, J_{XA} = 8.4 Hz, 2H), 7.25 (A_2X_2 system 2, part X, J_{XA} = 8.4 Hz, 2H), 7.01 (A_2X_2 system 3, part A, J_{AX} = 7.9 Hz, 2H), 6.85 (A_2X_2 system 3, part X, J_{XA} = 7.9 Hz, 2H), 5.00 (d, *J* = 8.9 Hz, 1H), 4.13 (dt, *J* = 8.9, 6.0 Hz, 1H), 3.48 (s, 3H), 3.03 (dd, *J* = 13.9, 5.8 Hz, 1H), 2.96 (dd, *J* = 13.9, 5.8 Hz, 1H), 2.45 (s, 3H), 2.41 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.1, 149.0, 145.6, 144.0, 136.6, 134.3, 132.4, 130.8, 129.9, 129.8, 128.7, 127.3, 122.6, 56.6, 52.6, 38.9, 21.9, 21.7 ppm.
Mp.: 111 – 114 ºC; **HRMS-ESI** m/z calculated for $C_{24}H_{25}NO_7S_2$ [M+H]+ 504.1145, found 504.1150.
$[\alpha]_D^{25}$ = +12.0 (c = 1.05, $CHCl_3$).

1,3-Dioxoisoindolin-2-yl-(2*S*)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanoate (1c)

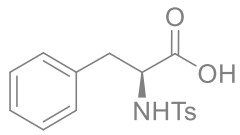


N-tosyl-L-Phenylalanine (900 mg, 1 equiv., 2.82 eq), DMAP (34 mg, 0,1 equiv., 0.28 eq), EDC hydrochloride (594 mg, 1,1 equiv., 3,10 mmol) and *N*-hydroxyphtalimide (552 mg, 1,2 equiv., 3.38 mmol) were dissolved in DCM (12 mL) under argon. Then, TEA (0.5 mL, 1.2 equiv., 3.38 mmol) was added dropwise and the reaction was stirred at room temperature for 3 h. The crude mixture was washed with aqueous HCl 1M (3 x 15 mL), aqueous $NaHCO_3$ 5% (3 x 15 mL), brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. Later, the solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (65:35) to yield the ester **1c** as a yellowish solid (702 mg, 54%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.80 (m, 2H), 7.79 – 7.73 (m, 2H), 7.63 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H) 7.30 – 7.16 (m, 7H), 5.00 (d, *J* = 9.8 Hz, 1H), 4.69 (dt, *J* = 9.8, 5.7 Hz, 1H), 3.30 (dd, *J* = 14.1, 5.8 Hz, 1H), 3.24 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.36 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.9, 161.2, 144.0, 136.5, 135.0, 133.6, 130.1, 130.0, 128.9, 128.8, 127.8, 127.1, 124.2, 54.7, 39.4, 21.7 ppm.
NMR data were in agreement with those reported.[2]
Mp.: 186 – 190 ºC; **HRMS-ESI** m/z calculated for $C_{24}H_{20}N_2O_6S$ $[M+NH_4]^+$ 482.1380, found 482.1382.
$[\alpha]_D^{25}$ = -4.6 (c = 1.00, $CHCl_3$).

(*S*)-*N*-Metoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (1d)

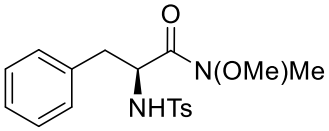
In a round bottom flask, L-Phenylalanine (2.00 g, 1 equiv., 12,1 mmol) and TsCl (2.30 g, 1 equiv., 12,1 mmol) were suspended in H_2O (36 mL). Then, NaOH (1.45 g, 3 equiv., 36.3 mmol) was added in portions and the reaction was stirred at 40 ºC during 24 h. The crude mixture was washed with EtOAc (3 x 30 mL) and acidified with aqueous HCl 3 M until pH = 2-3 was reached. Later, the aqueous layer was extracted with DCM (4 x 30 mL). The resulting organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to obtain the tosylamide **S1** as a white solid (2.01 g, 52 %).



S1

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.29 – 7.18 (m, 5H), 7.12 – 7.02 (m, 2H), 4.99 (d, *J* = 8.8 Hz, 1H), 4.22 (dt, *J* = 8.8, 5.9 Hz, 1H), 3.10 (dd, *J* = 13.9, 5.4 Hz, 1H), 3.00 (dd, *J* = 13.9, 6.4 Hz, 1H), 2,40 (s, 3H) ppm. ^{1}H NMR data were in agreement with those reported.[3]

Acid **S1** (590 mg, 1 equiv., 1.85 mmol) and *N*,*O*-dimethylhydroxylamine hydrochloride (198 mg, 1.1 equiv., 2.03 mmol) were suspended in DCM (6.2 mL) under inert atmosphere. Then, at 0 ºC, *N*- methylmorpholine (0.3 mL, 1.4 equiv., 2.59 mmol) and DCC (419 mg, 1.1 equiv., 2.03 mmol) were added consecutively. The reaction mixture was stirred at room temperature for 24 h. Upon the completion of the coupling step, the crude was filtered using a pad of Celite® eluting with DCM, washed with aqueous saturated $NaHCO_3$ (3 x 20 mL) and brine (2 x 20 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Finally, the residue wash purified by flash chromatography



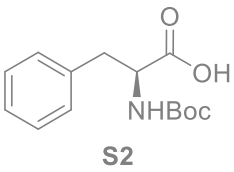
[2] D. Reich, A. Noble and V. K. Aggarwal, *Angew. Chem. Int. Ed.*, 2022, **61**, e202207063.
[3] D. Ghosh, D. Sahu, S. Saravanan, S. H. R. Abdi, B. Ganguly, N. H. Khan, R. I. Kureshy and H. C. Bajaj, *Org. Biomol. Chem.*, 2013, **11**, 3451.

eluting with Hex/EtOAc (1:1) to obtain the Weinreb amide **1d** as a white solid (425 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.9 Hz, 2H), 7.34 – 7.22 (m, 5H), 7.21 – 7.14 (m, 2H), 6.00 (d, *J* = 9.9 Hz, 1H), 4.61 (q, *J* = 7.7 Hz, 1H), 3.48 (s, 3H), 3.10 – 3.01 (m, 4H), 2.91 (dd, *J* = 13.6, 7.4 Hz, 1H), 2.43 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.0, 143.1, 137.0, 135.9, 129.4, 129.3, 128.3, 127.0, 126.7, 61.2, 54.0, 39.4, 31.9, 21.4 ppm.
NMR data were in agreement with those reported.[4]
Mp.: 92 – 96 ºC; **HRMS-ESI** m/z calculated for $C_{18}H_{22}N_2O_4S$ $[M+H]^+$ 363.1300, found 363.1372.
$[\alpha]_D^{25}$ = +43.6 (c = 1.00, $CHCl_3$).

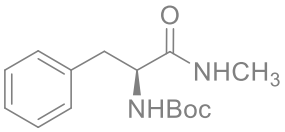
(*S*)-*N*-Methyl-2-(4-methylsulfonilamido)-3-phenylpropanamide (1e)

L-Phenylalanine (2.00 g, 1 equiv., 12.11 mmol), aqueous NaOH 1 M (20 mL) and 1,4-dioxane (10 mL) were added in a round bottom flask. Then, in an ice bath, di-*tert*-butyl-dicarbonate (3.17 g, 1.2 equiv., 14.53 mmol) was added and the reaction mixture was stirred at room temperature for 24 h. Dioxane was removed under reduced pressure and the aqueous phase was washed with Et_2O (3 x 15 mL). Later, aqueous HCl 3 M was added until pH = 2-3 was reached and the aqueous phase was extracted with EtOAc (3 x 20 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to obtain the carbamate **S2** as a colorless oil (3.21 g, quant.) that was used without further purification.



S2

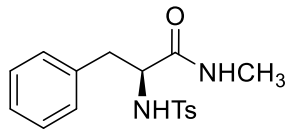
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.10 (m, 5H), 4.92, 4.60 (m, 1H, 2 conformers), 3.29 – 3.03 (m, 2H), 1.42 (s, 9H) ppm. ^{1}H NMR data were in agreement with those reported.[5]
Carbamate **S2** (1.50 g, 1.0 equiv., 5.65 mmol), methylamine hydrochloride (763 mg, 2 equiv., 11.31 mmol) and TBTU (2.00 g, 1.1 equiv., 6.22 mmol) were dissolved in ACN (60 mL) under inert atmosphere. DIPEA (5.0 mL, 5 equiv., 28.27 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. Then, the crude mixture was concentrated under reduced pressure, redissolved in EtOAc (20 mL) and washed with aqueous HCl 0.1 M (3 x 20 mL), aqueous $NaHCO_3$ 5% m/m (3 x 20 mL) and brine (2 x 20 mL). The resulting organic layer was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography eluting with Hex/EtOAc (3:7) to yield methyl amide derivative as a white solid (871 mg, 55 %).



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.04 (m, 5H), 5.00 (s, 1H), 4.69 (s, 1H), 3.52 – 2.87 (m, 3H), 2.07 (s, 3H), 1.48 (s, 9H) ppm. ^{1}H NMR data were in agreement with those reported.[6]
In a round bottom flask, amide derivative was dissolved in DCM (15 mL). Then, in an ice bath, TFA (15 mL) was added dropwise and the reaction mixture was stirred for 30 minutes. After that, the reaction was stirred at room temperature for 2.5 h. TFA and DCM were removed under reduced pressure to obtain the ammonium salt as an orange liquid (850 mg, 93 %) that was used

[4] T. Niu, K.-H. Wang, D. Huang, C. Xu, Y. Su, Y. Hu and Y. Fu, *Synthesis*, 2013, **46**, 320.
[5] A. Karmakar, M. Basha, G. T. Venkatesh Babu, M. Botlagunta, N. A. Malik, R. Rampulla, A. Mathur and A. K. Gupta, *Tetrahedron Lett.*, 2018, **59**, 4267.
[6] A. E. Sheshenev, E. V. Boltukhina, A. A. Grishina, I. Cisařova, I. M. Lyapkalo and K. K. (Mimi) Hii, *Chem. Eur. J.*, 2013, **19**, 8136.

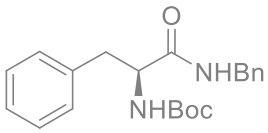
without further purification. Ammonium salt (850 mg, 1.0 equiv., 2.91 mmol), DMAP (7 mg, 0.02 equiv., 58.17 µmol) and TsCl (610 g, 1.1 equiv., 3.20 mmol) were dissolved in DCM (10 mL) under inert atmosphere. TEA (0.9 mL, 2.1 equiv., 6.11 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous NH_4Cl saturated solution (4 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (3:7) to yield compound **1e** as a white solid (249 mg, 26%).



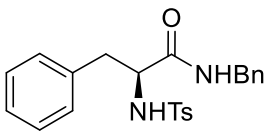
^{1}H NMR (400 MHz, CD_3OD) δ 7.56 (A_2X_2 part A, J_{AX} = 8.1 Hz, 2H), 7.24 (A_2X_2 part X, J_{XA} = 8.1, 2H), 7.20 – 7.12 (m, 3H), 7.09 – 7.02 (m, 2H), 3.88 (dd, *J* = 8.1, 6.7 Hz, 1H), 2.94 (dd, *J* = 13.6, 6.7 Hz, 1H), 2.72 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.48 (s, 3H), 2.41 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3OD) δ 173.6, 144.6, 138.7, 137.8, 130.5, 130.2, 129.4, 128.1, 127.7, 59.8, 40.0, 26.1, 21.4 ppm.
Mp.: 157 – 160 ºC; **HRMS-ESI** m/z calculated for $C_{17}H_{20}N_2O_3S$ [M+H]+ 333.1267, found 333.1269
$[\alpha]_D^{25}$ = +2.2 (c = 0.99, MeOH).

***(S)-N*-Bencyl-2-(4-methylphenyl)sulfonamido)-3-phenylpropanamide (1f)**

Carbamate **S1** (1.00 g, 1.0 equiv., 3.77 mmol), and TBTU (1.45 g, 1.2 equiv., 4.52 mmol) were dissolved in acetonitrile (40 mL) under inert atmosphere. DIPEA (3.3 mL, 5 equiv., 18.85 mmol) and benzylamine (0.8 mL, 2 equiv., 7.54 mmol) were added dropwise and the reaction mixture was stirred at room temperature for 24 h. Upon the completion of the reaction, the crude mixture was concentrated under reduced pressure, redissolved in EtOAc (20 mL) and washed with aqueous HCl 0.1 M (3 x 20 mL), aqueous $NaHCO_3$ 5% m/m (3 x 20 mL) and brine (2 x 20 mL). The resulting organic layer was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield benzyl amide as a white solid (591 mg, 44 %).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.14 (m, 8H), 7.13 – 7.03 (m, 2H), 6.64 (bs, 1H), 5.36 (d, *J* = 8.4 Hz, 1H), 4.60 – 4.19 (m, 3H), 3.05 (bs, 2H), 1.37 (s, 9H) ppm. ^{1}H NMR data were in agreement with those reported.[7]



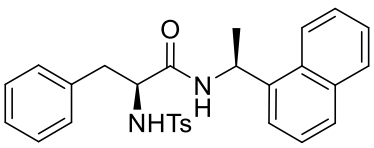
In a round bottom flask, benzyl amide was dissolved in DCM (10 mL). Then, in an ice bath, TFA (10 mL) was added dropwise, and the reaction mixture was stirred for 30 minutes. After that, the reaction was stirred at room temperature for 2.5 h. TFA and DCM were removed under reduced pressure to obtain the ammonium salt as an orange liquid (614 mg, quant) that was used without further purification. Ammonium salt (614 mg, 1.0 equiv., 1.67 mmol), DMAP (4 mg, 0.02 equiv., 33.34 µmol) and TsCl (350 mg, 1.1 equiv., 1.83 mmol) were dissolved in DCM (13 mL) under inert atmosphere. TEA (0.5 mL, 2.2 equiv., 3.67 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous NH_4Cl saturated solution (3 x 10 mL) and brine (2 x 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (6:4) to yield compound **1f** as a white solid (443 mg, 65%).



[7] Y. Saito, H. Ouchi and H. Takahata, *Tetrahedron*, 2008, **64**, 11129.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (A_2X_2, part A, J_{AX} = 8.4 Hz, 2H), 7.38 – 7.08 (m, 10H), 6.89 (A_2X_2, part X, J_{XA} = 8.4 Hz, 2H), 6.47 (t, *J* = 5.2 Hz, 1H), 4.83 (d, *J* = 6.9 Hz, 1H), 4.38 (dd, *J* = 14.8, 6.0 Hz, 1H), 4.30 (dd, $_A$ = 14.8, 5.6 Hz, 1H), 3.90 (q_{app}, *J* = 6.6 Hz, 1H), 3.04 (dd, *J* = 13.9, 6.6 Hz, 1H), 2.86 (dd, *J* = 13.9, 6.4 Hz, 1H), 2.44 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.0, 144.2, 137.5, 135.8, 135.2, 130.0, 129.3, 129.2, 128.8, 127.8, 127.7, 127.5, 127.3, 58.0, 43.8, 38.4, 21.8 ppm.
Mp.: 152 – 156 ºC; **HRMS-ESI** m/z calculated for $C_{23}H_{24}N_2O_3S$ $[M+H]^+$ 409.1580, found 409.1580.
$[\alpha]_D^{25}$ = -9.6 (c = 1.00, $CHCl_3$).
Characterization data were in agreement with those reported.[8]

(*S*)-2-((4-Methylphenyl)sulfonamido)-*N*-((*S*)-1-(naphthalen-1-yl)ethyl)-3-phenylpropanamide (1g)



N-Tosyl-Phenylalanine (300 mg, 1 equiv., 0.94 mmol) were dissolved in DCM (5.0 mL) and DMF (5.0 mL). Then, EDC·HCl (223 mg, 1.25 equiv., 1.17 mmol) and HOBt (159 mg, 1.25 equiv., 1.17 mmol) were added in portions and the reaction was stirred at room temperature for 5 minutes. Then, (*S*)-(-)-(1-naphthyl)ethylamine (0.2 mL, 1.3 equiv., 1.22 mmol) and DIPEA (0.6 mL, 4 equiv., 3.76 mmol) were added dropwise. The reaction was stirred at room temperature for 24 h. Upon completion of the reaction, the crude was washed with H_2O (8 x 15 mL), aqueous HCl 3 M (2 x 15 mL) and brine (2 x 15 mL). The organic layer was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield the amide **1g** as a white solid (120 mg, 27%)

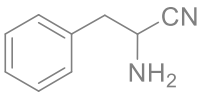
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.96 (m, 1H), 7.91 – 7.85 (m, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.46 (m, 4H), 7.39 (t_{app}, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.17 – 7.07 (m, 3H), 7.09 – 7.00 (m, 2H), 6.94 – 6.84 (m, 2H), 6.30 (d, *J* = 8.1 Hz, 1H), 5.78 ($quin_{app}$, *J* = 7.0 Hz, 1H), 5.04 (d, *J* = 7.6 Hz, 1H), 3.90 (q_{app}, *J* = 6.7 Hz, 1H), 3.08 (dd, *J* = 13.9, 6.1 Hz, 1H), 2.82 (dd, *J* = 13.9, 6.8 Hz, 1H), 2.38 (s, 3H), 1.47 (d, *J* = 6.8 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 144.0, 138.0, 136.1, 135.3, 134.0, 130.9, 129.9, 129.4, 129.0, 128.4, 127.3, 127.3, 126.6, 125.9, 125.5, 123.3, 122.6, 57.8, 45.2, 38.7, 21.7, 21.3 ppm.
Mp.: 195 – 198 º C; **HRMS-ESI** m/z calculated for $C_{28}H_{28}N_2O_3S$ $[M+H]^+$ 473.1893 found 473.1889.
$[\alpha]_D^{25}$ = -11.6 (c = 0.88, $CHCl_3$).
Characterization data were in agreement with those reported.[3]

***N*-(1-Cyano-2-phenylethyl)-4-methylbenzenesulfonamide (1h)**

2-((Diphenylmethylene)amino)acetonitrile (1.5 g, 1 equiv., 6.81 mmol) and TEBAC (155 mg, 0.1 equiv., 0.68 mmol) were dissolved in DCE (34 mL) under inert atmosphere. Later, benzyl bromide (0.9 mL, 1.1 equiv., 7.49 mmol) and aqueous NaOH 10 M (6.2 mL, 10 equiv., 68 mmol) were added dropwise to obtain an orange suspension. The reaction was stirred at room temperature for 24 h. Upon completion of the reaction, H_2O was added and the crude mixture was extracted with DCM (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to finally obtain the desired benzyl imine as an orange oil that was used in the next step without further

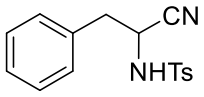
[8] S. Gou and Z. M. A. Judeh, *Chirality*, 2011, **23**, 105.

purification. Imine (2.11 g, 1 equiv., 6.80 eq) was suspended in THF (34 mL) and aqueous HCl 1M (20 mL) in a round bottom flask. The reaction was stirred at room temperature for 3 h, resulting in a bright yellow solution. Later, THF was removed under reduced pressure and the mixture was basified with aqueous NaOH 3 M until pH = 10 – 12 was obtained. Then, the crude was extracted with EtOAc (3 x 20 mL), dried over anhydrous $MgSO_4$ and concentrated to obtain de amine (714 mg, 72 % over 2 steps) as a yellow oil.



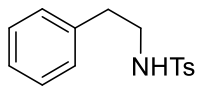
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.10 (m, 5H), 3.75 (t, *J* = 6.7 Hz, 1H), 2.98 – 2.76 (m, 2H), 1.59 (bs, 2H) ppm. ^{1}H NMR data were in agreement with those reported.[9] Synthesized according to the literature procedure.[10]

Amine (100 mg, 1 equiv., 0.68 mmol) and TsCl (130 mg, 1 equiv., 0.68 mmol) were dissolved in pyridine (1.6 mL) under inert atmosphere. The reaction was stirred at room temperature for 72 h. Then, DCM was added to the reaction and the mixture was washed with aqueous HCl 3 M (6 x 10 mL) and brine (2 x 15 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with Hex/EtOAc (65:35) to yield sulfonamide **1h** (149 mg, 73%) as a white solid.



^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.68 (d, *J* = 7.8 Hz, 2H), 7.46 (bs, 1H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.27 (s, 5H), 4.60 (t_{app}, *J* = 7.2 Hz, 1H), 3.22 – 3.01 (m, 2H), 2.40 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3COCD_3) δ 144.5, 138.3, 135.6, 130.5, 130.4, 129.3, 128.2, 127.8, 118.7, 46.6, 40.3, 21.4 ppm.
NMR data were in agreement with those reported.[11]
Mp.: 112 – 115 ºC; **HRMS-ESI** m/z calculated for $C_{16}H_{16}N_2O_2S$ $[M+H]^+$ 301.1005, found 301.1003

4-Methyl-*N*-phenylethylbencensulfonamide (1i)

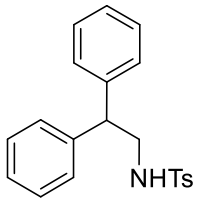


2-Phenylethylamine (0.10 mL, 1.0 equiv., 0.82 mmol), DMAP (2 mg, 0.02 equiv., 0.02 mmol) and TsCl (173 mg, 1.1 equiv., 0.91 mmol) were dissolved in DCM (5 mL) under inert atmosphere. TEA (0.2 mL, 2 equiv., 1.65 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous NH_4Cl saturated solution (4 x 5 mL) and brine (2 x 5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (6:4) to yield compound **1i** as a white solid (217 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.34 – 7.18 (m, 5H), 7.11 – 7.06 (m, 2H), 4.49 (t, *J* = 6.3 Hz, 1H), 3.22 (q_{app}, *J* = 6.8 Hz, 2H), 2.76 (t, *J* = 7.0 Hz, 2H), 2.43 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.5, 137.8, 137.0, 129.8, 128.9, 128.9, 127.2, 126.9, 44.3, 35.9, 21.6 ppm.
NMR data were in agreement with those reported.[12]
Mp.: 57 – 60 ºC; **HRMS-ESI** m/z calculated for $C_{15}H_{17}NO_2S$ $[M+H]^+$ 276.1053, found 276.1055.

[9] A. J. Wagner, D. Yu. Zubarev, A. Aspuru-Guzik and D. G. Blackmond, *ACS Cent. Sci.*, 2017, **3**, 322.
[10] G. Wu, Y. Deng, C. Wu, Y. Zhang and J. Wang, *Angew. Chem. Int. Ed.*, 2014, **53**, 10510.
[11] L. Zhou, S. Wei, Z. Lei, G. Zhu and Z. Zhang, *Chem. - Eur. J.*, 2021, **27**, 7103.
[12] R. Pothikumar, C. Sivaraj, K. Giridharan, M. K. Ravva and K. Namitharan, *Org. Lett.*, 2022, **24**, 4310.

***N*-(2,2-Diphenylethyl)-4-methylbenzenesulfonamide (1i´)**

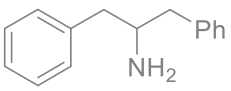


2,2-Diphenylethylamine (300 mg, 1.0 equiv., 1.52 mmol), DMAP (4 mg, 0.02 equiv., 30.41 µmol) and TsCl (319 mg, 1.1 equiv., 1.67 mmol) were dissolved in DCM (9.0 mL) under inert atmosphere. TEA (0.2 mL, 1.1 equiv., 1.67 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with aqueous HCl 1 M (3 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (8:2) to yield compound **1i´** as a white solid (501 mg, 94%).

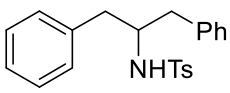
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.34 – 7.14 (m, 8H), 7.15 – 7.05 (m, 4H), 4.30 (t, *J* = 6.2 Hz, 1H), 4.07 (t, *J* = 7.9 Hz, 1H), 3.56 (dd, *J* = 7.9, 6.2 Hz, 2H), 2.45 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.7, 140.8, 136.9, 129.9, 129.0, 128.1, 127.3, 127.3, 50.7, 47.4, 21.7 ppm.
NMR data were in agreement with those reported.[13]
Mp.: 127 – 130 ºC; **HRMS-ESI** m/z calculated for $C_{21}H_{21}NO_2S$ $[M+H]^+$ 352.1366 found 352.1362.

***N*-(1,3-Diphenylpropan-2-yl)-4-methylbenzensulfonamide (1j)**

1,3-diphenylpropan-2-one (798 mg, 1 equiv., 3.80 mmol) was dissolved in MeOH (13 mL) under inert atmosphere. Then, NH_4OAc (2.64 g, 9 equiv., 34.24 mmol) and $NaBH_3CN$ (503 mg, 2 equiv., 7.61 mmol) were added in portions and the mixture was stirred at room temperature for 24 h. Later, the crude was acidified with aqueous HCl 4 M until pH = 2-3 was reached and washed with DCM (3 x 20 mL). Then, the aqueous layer was basified with aqueous NaOH 10 M until pH = 10-12 was reached and extracted with DCM (3 x 20 mL). This organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to obtain the amine as a colourless oil.



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.20 (m, 10H), 3.32 (tt, *J* = 8.9, 4.7, 1H), 2.88 (dd, *J* = 13.3, 4.7, 2H), 2.59 (dd, *J* = 13.3, 8.7 Hz, 2H), 1.40 (bs, 2H) ppm. ^{1}H NMR data were in agreement with those reported.[14] Synthesized according to the literature procedure.[15]
Amine (734 mg, 1 equiv., 3.47 mmol), DMAP (8 mg, 0.02 equiv., 69.49 µmol) and TsCl (795 mg, 1.2 equiv., 4.17 mmol) were dissolved with DCM (20 mL) under inert atmosphere. Then, TEA (0.6 mL, 1.2 equiv., 4.17 mL) was added dropwise and the reaction was stirred at room temperature for 24 h. Later, the crude was washed with aqueous HCl 0.4 M (3 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude was then purified by flash chromatography eluting with Hex/EtOAc (8:2) to obtain the sulfonamide **1j** as a white solid (452 mg, 36%)

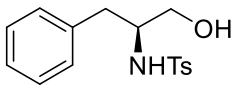


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (A_2X_2 part A, J_{AX} = 8.4 Hz, 2H), 7.08 – 6.99 (m, 6H), 6.94 – 6.86 (m, 6H), 4.92 (d, *J* = 7.4 Hz, 1H), 3.48 (h, *J* = 6.8 Hz, 1H), 2.70 – 2.54 (m, 4H), 2.19 (s, 3H) ppm.

[13] G. Yang, Y. Wang and Y. Qiu, *Chem. - Eur. J.*, 2023, **29**, e202300959.
[14] G. Blankson, A. K. Parhi, M. Kaul, D. S. Pilch and E. J. LaVoie, *Eur. J. Med. Chem.*, 2019, **178**, 30.
[15] J. Albarrán-Velo, V. Gotor-Fernández and I. Lavandera, *Adv. Synth. Catal.*, 2021, **363**, 4096.

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.6, 137.4, 137.0, 129.3, 129.3, 128.3, 126.6, 126.3, 56.7, 40.9, 21.3 ppm.
NMR data were in agreement with those reported.[16]
Mp.: 92 – 96 ºC; **HRMS-ESI** m/z calculated for $C_{22}H_{23}NO_2S$ $[M+H]^+$ 366.1522, found 366.1522.

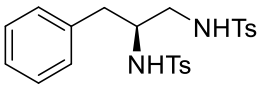
(*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (S3)



L-Phenylalaninol (1.3 g, 1 equiv., 8.60 mmol), DMAP (21 mg, 0.02 equiv., 0.17 mmol) and TsCl (1.64 g, 1 equiv., 8.60 mmol) were dissolved with DCM (50 mL) under inert atmosphere. Then, TEA (1.3 mL, 1.1 equiv., 9.46 mmol) was added dropwise and the reaction was stirred at room temperature for 24 h. Later, the crude was washed with aq. HCl 0.4 M (3 x 30 mL) and brine (2 x 30 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude was then purified by flash chromatography eluting with Hex/EtOAc (6:4) to obtain the sulfonamide **S3** as a white solid (2.1 g, 76%).

^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (A_2X_2 part A, J_{AX} = 8.0 Hz, 2H), 7.18 (A_2X_2 part X, J_{XA} = 8.0 Hz, 2H), 7.16 – 7.12 (m, 3H), 7.04 – 6.95 (m, 2H), 5.63 (d, *J* = 7.6 Hz, 1H), 3.65 (ddd, *J* = 11.1, 6.2, 3.7 Hz, 1H) , 3.58 – 3.42 (m, 2H), 3.09 (t, *J* = 5.8 Hz, 1H), 2.78 (dd, *J* = 13.8, 7.2 Hz, 1H), 2.66 (dd, *J* = 13.8, 7.0 Hz, 1H), 2.39 (s, 3H) ppm.
$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.3, 137.2, 137.1, 129.7, 129.2, 128.5, 127.0, 126.5, 63.9, 56.9, 37.7, 21.5 ppm.
NMR data were in agreement with those reported.[17]
Mp.: 76 – 79 ºC; **HRMS-ESI** m/z calculated for $C_{16}H_{19}NO_3S$ $[M+H]^+$ 306.1158, found 306.1158.
$[\alpha]_D^{25}$ = -23.1 (c = 1.00, $CHCl_3$).

(*S*)-*N*,*N´*-(3-Phenylpropane-1,2-diyl)bis(4-methylbenzensulfonamide) (1k)



Alcohol **S3** (420 mg, 1 equiv., 1.38) and PPh_3 (721 mg, 2 equiv., 2.75 mmol) and TsNHBoc (932 mg, 2.5 equiv., 3.44 mmol) were dissolved in THF (8.0 mL) under inert atmosphere. Then, at 0 ºC, DIAD (0.4 mL, 1.5 equiv., 2.06 mmol) were added dropwise. The reaction was stirred at 55 ºC for 24 h. The solvent was then removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (7:3) to obtain an impure fraction containing the protected sulfonamide (54 % purity), that was used in the next step without further purification.
The sulfonamide was dissolved in DCM (10 mL) and TFA (10 mL) was added dropwise at 0 ºC. The mixture was stirred at 0 ºC for 30 minutes and 2.5 h at room temperature. Upon completion of the reaction, the crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (9:1) to obtain the desired compound as a white solid (220 mg, 29%)

^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (A_2X_2 system 1, part A, J_{AX} = 8.3 Hz, 2H), 7.51 (A_2X_2 system 2, part A, J_{AX} = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.17 – 7.02 (m, 5H), 6.90 – 6.79 (m, 2H), 5.69 (t, *J* = 6.4 Hz, 1H), 5.47

[16] X.-F. Bai, Q.-C. Mu, Z. Xu, K.-F. Yang, L. Li, Z.-J. Zheng, C.-G. Xia and L.-W. Xu, *ACS Catal.*, 2019, **9**, 1431.
[17] P. M. Shukla, A. Pratap and B. Maji, *Org. Biomol. Chem.*, 2024, **22**, 501.

(d, *J* = 7.4 Hz, 1H), 3.43 – 3.32 (dtd, *J* = 12.2, 7.3, 4.9 Hz, 1H), 3.07 – 2.96 (m, 2H), 2.74 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.57 (dd, J_{BA} = 14.0, 7.5 Hz, 1H), 2.37 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.4, 143.3, 136.5, 136.5, 136.5, 129.7, 129.6, 129.1, 128.5, 127.1, 127.0, 126.5, 54.9, 46.4, 38.4, 21.5 ppm.

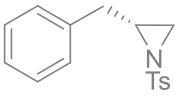
NMR data were in agreement with those reported.[18]

Mp.: 110 – 114 ºC; **HRMS-ESI** m/z calculated for $C_{23}H_{26}N_2O_4S_2$ $[M+H]^+$ 459.1407, found 459.1406.

$[\alpha]_D^{25}$ = -68.9 (c = 1.00, $CHCl_3$).

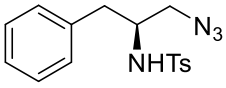
(*S*)-*N*-(1-Azido-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1l)

Alcohol **S3** (700 mg, 1 equiv., 2.29 mmol), DMAP (6 mg, 0.02 equiv., 45.84 µmol) and TsCl (481 mg, 1.1 equiv., 2.52 mmol) were dissolved in DCM (13 mL) under inert atmosphere. Then, TEA (0.4 mL, 1.1 equiv., 2.52 mmol) was added dropwise and the reaction was stirred at room temperature for 24 h. Later, the crude was washed with an aqueous HCl 0.4 M (3 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with Hex/EtOAc (8:2) to obtain the aziridine as a yellowish solid (535 mg, 81%).



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (A_2X_2 part A, J_{AX} = 8.2 Hz, 2H), 7.23 – 7.10 (m, 5H), 7.08 – 6.99 (m, 2H), 2.93 (tt, *J* = 7.0, 4.7 Hz, 1H), 2.87 – 2.75 (m, 1H), 2.73 – 2.58 (m, 2H), 2.40 (s, 3H), 2.15 (d, *J* =4.5 Hz, 1H) ppm. ^{1}H NMR data were in agreement with those reported.[19]

Aziridine (300 mg, 1 equiv., 1.04 mmol) and NaN_3 (102 mg, 1.5 equiv., 1.57 mmol) were suspended in acetonitrile (4.5 mL) and H_2O (0.5 mL). The reaction was stirred at reflux for 6 h. Then, acetonitrile was evaporated under reduced pressure and EtOAc (10 mL) and H_2O (10 mL) were added to the crude mixture. Layers were separated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure.



The residue was purified by flash chromatography eluting with Hex/EtOAc (8:2) to obtain the desired sulfonamide **1l** as a white solid (250 mg, 72%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.31 – 7.12 (m, 5H), 7.06 – 6.96 (m, 2H), 5.42 (d, *J* = 7.9 Hz, 1H), 3.55 (dtd, *J* = 12.1, 7.6, 4.6 Hz, 1H), 3.37 (dd, *J* = 12.4, 4.9 Hz, 1H) 3.31 (dd, *J* = 12.4, 4.3 Hz, 1H), 2.79 (dd, *J* = 13.8, 7.3 Hz, 1H), 2.70 (dd, *J* = 13.8, 7.1 Hz, 1H), 2.41 (s, 3H) ppm.

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.4, 137.1, 136.3, 129.6, 129.1, 128.6, 126.8, 126.7, 54.5, 53.8, 38.4, 21.4 ppm.

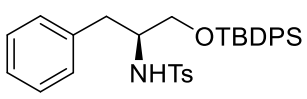
NMR data were in agreement with those reported.[20]

Mp.: 40 – 44 ºC; **HRMS-ESI** m/z calculated for $C_{16}H_{18}N_4O_2S$ $[M+H]^+$ 331.1223, found 331.1222.

$[\alpha]_D^{25}$ = -30.4 (c = 0.92, $CHCl_3$).

[18] T. D. Montgomery and V. H. Rawal, *Org. Lett.*, 2016, **18**, 740.
[19] T. Ankner and G. Hilmersson, *Org. Lett.*, 2009, **11**, 503.
[20] S. Matsukawa, K. Tsukamoto, S. Yasuda and T. Harada, *Synthesis*, 2013, **45**, 2959.

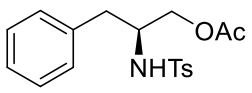
(*S*)-*N*-(-1-((*tert*-Butyldiphenylsilyl)oxy)-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1m)



Alcohol **S3** (200 mg, 1 equiv., 0.65 mmol) and imidazole (94 mg, 2.1 equiv., 1.38 mmol) were dissolved in DCM (1.5 mL) under inert atmosphere. Then, TBDPSCl (0.2 mL, 1.15 equiv., 0.75 mmol) was added dropwise and the reaction was stirred at room temperature for 24 h. The crude was washed with aqueous HCl 1 M (3 x 5 mL) and brine (2 x 5 mL). The organic layer was dried over $MgSO_4$ and purified by flash chromatography eluting with Hex/EtOAc (9:1) to obtain the protected alcohol **1m** as a colourless oil (300 mg, 84%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.56 (m, 6H), 7.53 – 7.45 (m, 2H), 7.44 – 7.38 (m, 4H), 7.26 – 7.13 (m, 5H), 7.11 – 7.00 (m, 2H), 5.02 (d, *J* = 7.3 Hz, 1H), 3.66 – 3.59 (m, 1H), 3.52 (m, 2H), 2.99 (dd, *J* = 13.7, 7.0 Hz, 1H), 2.92 (dd, *J* = 13.7, 5.9 Hz, 1H), 2.42 (s, 3H), 1.13 (s, 9H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.0, 137.6, 137.2, 135.6, 135.6, 132.9, 132.9, 129.9, 129.6, 129.4, 128.5, 127.8, 126.9, 126.5, 64.1, 56.2, 38.1, 27.0, 21.5, 19.3 ppm.
HRMS-ESI m/z calculated for $C_{32}H_{37}NO_3SSi$ $[M+H]^+$ 544.2336, found 544.2346.
$[\alpha]_D^{25}$ = -14.8 (c = 1.00, $CHCl_3$).

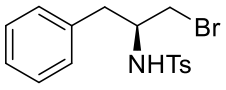
(*S*)-2-((4-Methylphenyl)sulfonamido)-3-phenylpropyl acetate (1n)



Alcohol **S3** (494 mg, 1 equiv., 1.62 mmol) and DMAP (4 mg, 0.02 equiv., 32.35 µmol) were dissolved in DCM (6.0 mL) under inert atmosphere. Then, acetyl chloride (0.1 mL, 1 equiv., 1.62 mmol) and TEA (0.4 mL, 2 equiv., 3.24 mmol) were added dropwise. The reaction was stirred at room temperature for 24 h. Upon completion of the reaction, the crude mixture was washed with H_2O (3 x 10 mL) and brine (2 x 10 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with Hex/EtOAc (7:3) to obtain the acetylated compound **1n** as a yellowish oil (430 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.24 – 7.08 (m, 5H), 7.13 – 6.91 (m, 2H), 5.05 (d, *J* = 8.1 Hz, 1H), 3.97 (dd, *J* = 11.5, 5.5 Hz, 1H), 3.93 (dd, *J* = 11.5, 4.6 Hz, 1H), 3.68 (dtdd, *J* = 8.1, 7.0, 5.5, 4.6 Hz, 1H), 2.78 (d, *J* = 7.0 Hz, 2H), 2.40 (s, 3H), 1.96 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.9, 143.4, 137.6, 136.4, 129.8, 129.3, 128.8, 127.0, 126.9, 65.0, 53.9, 38.7, 21.6, 20.8 ppm.
NMR data were in agreement with those reported.[21]
HRMS-ESI m/z calculated for $C_{18}H_{21}NO_4S$ $[M+H]^+$ 348.1264, found 348.1263.
$[\alpha]_D^{25}$ = -5.8 (c = 1.00, $CHCl_3$).

(*S*)-*N*-(1-Bromo-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1o)



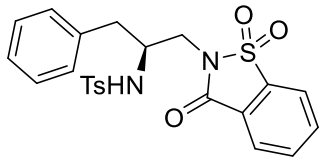
Alcohol **S3** (1 g, 1 equiv., 3.27 mmol) was dissolved in DCM (50 mL) under inert atmosphere. Then, at 0 ºC, CBr_4 (1.30 g, 1.2 equiv., 3.93 mmol) and PPh_3 (1.03 g, 1.2 equiv., 3.93 mmol) were added in portions. The reaction was stirred at room temperature for 24 h. Then, the reaction was concentrated under reduced pressure and purified by flash

[21] S. K. Manna and G. Panda, *RSC Adv.*, 2013, **3**, 18332.

chromatography eluting with Hex/EtOAc (7:3) to obtain the brominated compound **1o** as a white solid (1.04 g, 86%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (A_2X_2, part A, J_{AX} = 8.4 Hz, 2H), 7.27 – 7.15 (m, 5H), 7.09 – 7.02 (m, 2H), 4.93 (d, *J* = 8.4 Hz, 1H), 3.63 (tddd, *J* = 8.4, 6.4, 4.8, 3.4 Hz, 1H), 3.39 – 3.30 (m, 2H), 2.88 (dd, *J* = 13.7, 7.7 Hz, 1H), 2.77 (dd, *J* = 13.7, 6.4 Hz, 1H), 2.42 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.7, 137.3, 136.2, 129.9, 129.3, 128.9, 127.1, 127.1, 54.7, 39.3, 37.1, 21.7 ppm.
NMR data were in agreement with those reported.[21]
Mp.: 95 – 98 ºC; **HRMS-ESI** m/z calculated for $C_{16}H_{18}BrNO_2S$ $[M+H]^+$ 368.0314/370.0295, found 368.0313/370.0293.
$[\alpha]_D^{25}$ = -11.1 (c = 1.00, $CHCl_3$).

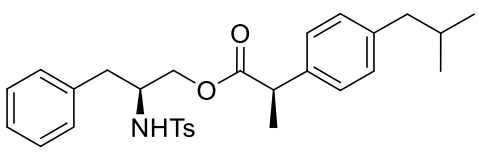
(*S*)-*N*-(1-(1,1-Dioxo-3-oxobenzo[*d*]isothiazol-2(3H)-yl)-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1p)



Alcohol **S3** (480 mg, 1 equiv., 1.57 mmol), PPh_3 (824 mg, 2 equiv., 3.14 mmol) and saccharine (576 mg, 2 equiv., 3.14 mmol) were dissolved in THF (8.0 mL) under inert atmosphere. Then, at 0 ºC, DIAD (0.5 mL, 1.6 equiv., 2.51 mmol) was added dropwise. The reaction was stirred at room temperature for 24 h. The crude was washed with H_2O (3 x 15 mL) and brine (2 x 15 mL). The organic layer was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography eluting with Hex/EtOAc (1:1) to obtain the compound **1p** as a white solid (140 mg, 19%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.77 (m, 4H), 7.54 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.32 – 7.22 (m, 3H), 7.19 – 7.11 (m, 2H), 6.87 (A_2X_2, part X, J_{XA} = 8.3 Hz, 2H), 4.96 (d, *J* = 7.6 Hz, 1H), 4.08 – 3.95 (m, 1H), 3.71 – 3.66 (m, 2H), 2.96 (d, *J* = 6.3 Hz, 2H), 2.13 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.3, 142.8, 137.3, 137.1, 135.7, 135.0, 134.4, 129.6, 129.3, 128.9, 127.2, 127.0, 125.3, 121.1, 53.6, 42.2, 40.5, 21.6 ppm.
Mp.: 117 – 121 ºC; **HRMS-ESI** m/z calculated for $C_{23}H_{22}N_2O_5S_2$ $[M+H]^+$ 471.1043, found 471.1037.
$[\alpha]_D^{25}$ = +16.8 (c = 0.98, $CHCl_3$).

(*S*)-2-((4-Methylphenyl)sulfonamido)-3-phenylpropyl (*S*)-2-(4-*iso*butylphenyl)propanoate (1q)

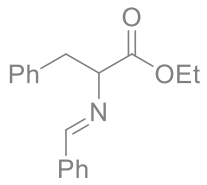


Alcohol **S3** (500 mg, 1 equiv., 1.64 mmol) and (*S*)-ibuprofen (372 mg, 1.1 equiv., 1.80 mmol) were dissolved in DCM (12 mL) under inert atmosphere. Then, at 0 ºC, DCC (372 mg, 1.1 equiv., 1.80 mmol) and DMAP (60 mg, 0.3 equiv., 0,49 mmol) were added in portions and the reaction was stirred at room temperature for 24 h. The crude was filtered off using a filter plate eluting with DCM (3 x 10 mL). The combined organic layers were washed with aqueous HCl 1 M (3 x 15 mL), aqueous $NaHCO_3$ 5% m/m (3 x 20 mL) and brine (2 x 20 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with Hex/EtOAc (8:2) to obtain the ester **1q** as a colourless oil (410 mg, 51%).

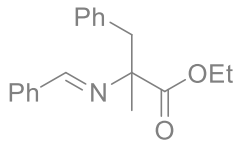
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (A_2X_2, part A, J_{AX} = 8.4 Hz, 2H), 7.25 – 7.17 (m, 4H), 7.15 – 7.07 (m, 5H), 6.82 – 6.66 (m, 2H), 5.11 (d, *J* = 8.4 Hz, 1H), 3.87 (d, *J* = 4.1 Hz, 2H), 3.68 (q, J = 7.1 Hz, 1H), 3.66 – 3.55 (m, 1H), 2.60 – 2.48 (m, 2H), 2.45 (d, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 1.92 – 1.76 (m, 1H), 1.47 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 2.3 Hz, 3H), 0.87 (d, *J* = 2.3 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.3, 143.4, 140.9, 137.7, 137.6, 136.4, 129.8, 129.5, 129.2, 128.6, 127.3, 127.0, 126.7, 64.6, 53.9, 45.1, 44.9, 38.1, 30.3, 22.5, 22.4, 21.6, 17.9 ppm.
HRMS-ESI m/z calculated for $C_{29}H_{35}NO_4S$ $[M+H]^+$ 494.2360, found 494.2355.
$[\alpha]_D^{25}$ = +29.7 (c = 0.95, $CHCl_3$).

Ethyl-2-methyl-2-(4-methylphenylsulfonamido)-3-phenylpropanoate (1r)

This compound was synthesized according to the literature procedure.[22]
L-Phenylalanine ethyl ester hydrochloride (2.00 g, 1.0 equiv., 8.71 mmol), was suspended in DCM (20 mL) under inert atmosphere. TEA (1.5 mL, 1.2 equiv., 10.45 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 30 minutes. Then, benzaldehyde (0.9 mL, 1 equiv., 8.71 mmol) and anhydrous $MgSO_4$ (1.05 g, 1 equiv., 8.71 mmol) were added consecutively and the reaction was stirred at room temperature for 24 h. The solvent was evaporated, and the crude was dissolved in EtOAc (15 mL) and filtered in a pad of Celite®. The resulting organic layer was washed with H_2O (2 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$ to obtain the desired imine as an orange liquid (2.45 g, quant) that was used without further purification.

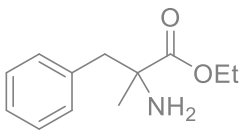


^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.81 – 7.71 (m, 2H), 7.53 – 7.41 (m, 3H), 7.35 – 7.21 (m, 5H), 4.33 – 4.17 (m, 3H), 3.42 (dd, *J* = 13.6, 3.4 Hz, 1H), 3.20 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm. ^{1}H NMR data were in agreement with those reported.[23]
A solution of NaHMDS (1 M) in THF (3.1 mL, 1.1 equiv., 3.09 mmol), and imine (791 mg, 1 equiv., 2.81 mmol) were added in THF (20 mL) under inert atmosphere at 0 ºC. The mixture was stirred for 45 minutes. Then, iodomethane (0.2 mL, 1.4 equiv., 3.94 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the crude was redissolved in EtOAc (15 mL), washed with H_2O (2 x15 mL), brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. Finally, the crude was concentrated under reduced pressure to obtain de desired α-methyl imine as a bright yellow liquid (831 mg, quant) that was used without further purification.



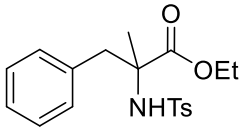
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.80 – 7.69 (m, 2H), 7.47 – 7.37 (m, 3H), 7.24 – 7.18 (m, 5H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.27 (s, 2H), 1.43 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm.
In a round bottom flask, α-methyl imine (798 mg, 1 equiv., 2.70 mmol) was dissolved in THF (2.5 mL). Then, aqueous HCl 3M (1.75 mL) was added and the reaction mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the aqueous phase was washed with EtOAc (3 x 2 mL). An aqueous solution NaOH 10 M was added until pH = 10 was reached. Then, this basified aqueous layer was extracted with DCM (3 x 5 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to obtain the amine as a yellowish oil (358 mg, 64%).

[22] R. Liu, Y. Wu, Q. Li, W. Liao, S.-H. Chen, G. Li, J. M. Betancort, D. T. Winn and D. A. Campbell, *Tetrahedron*, 2008, **64**, 4363.
[23] A. Calcagni, D. Rossi and G. Lucente, *Synthesis*, 1981, 445.



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.22 (m, 2H), 7.21 – 7.11 (m, 3H), 4.20 – 4.11 (m, 2H), 3.13 (d, *J* = 13.1 Hz, 1H), 2.80 (d, *J* = 13.1 Hz, 1H), 1.54 (s, 2H), 1.39 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H) ppm. ^{1}H NMR data were in agreement with those reported.[24]

Amine (358 mg, 1.0 equiv., 1.73 mmol), DMAP (4 mg, 0.02 equiv., 34.55 µmol) and TsCl (362 mg, 1.1 equiv., 1.90 mmol) were dissolved in DCM (9 mL) under inert atmosphere. TEA (0.3 mL, 1.2 equiv., 2.07 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous saturated NH_4Cl solution (4 x 10 mL) and brine (2 x 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude was purified by flash chromatography eluting with Hex/EtOAc (8:2) to yield compound **1r** as a white solid (534 mg, 86%).

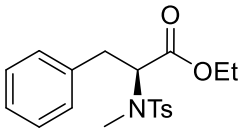


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.35 – 7.21 (m, 5H), 7.21 – 7.07 (m, 2H), 5.30 (s, 1H), 4.05 (ABX_3, part AB, J_{AB} = 7.2 Hz, J_{AX} = 3.4 Hz, 2H), 3.22 (d, *J* = 13.5 Hz, 1H), 3.02 (d, *J* = 13.5 Hz, 1H), 2.40 (s, 3H, CH_3Ar), 1.45 (s, 3H), 1.18 (ABX_3 part X, J_{AX} = J_{BX} = 7.2 Hz, 3H) ppm

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.8, 143.3, 140.0, 135.1, 130.4, 129.6, 128.5, 127.5, 127.1, 63.2, 62.1, 46.7, 22.0, 21.6, 14.1 ppm.

Mp.: 72 – 75 ºC; **HRMS-ESI** m/z calculated for $C_{19}H_{23}NO_4S$ $[M+H]^+$ 362.1421, found 362.1422.

(*S*)-Ethyl-2-(*N*,4-Dimethylphenylsulfonamido)-3-phenylpropanoate (1s)



Sulfonamide **1a** (300 mg, 1 equiv., 0.86 mmol) and K_2CO_3 (239 mg, 2 equiv., 1.73 mmol) were suspended in DMF (5.0 mL) under inert atmosphere. Iodomethane (64 µL, 1.2 equiv., 1.04 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 16 h. Then, aqueous HCl 0.2 M (10 mL) was added to the crude mixture and was extracted with Et_2O (4 x 10 mL). This organic layer was washed with H_2O (2 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude was purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield compound **1s** as a yellowish liquid (256 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (A_2X_2 part A, J_{AX} = 8.2 Hz, 2H), 7.32 – 7.21 (m, 3H), 7.22 – 7.15 (m, 4H), 4.93 (dd, *J* = 8.6, 7.1 Hz, 1H), 3.98 (AB de ABX_3, J_{AB} = 2.1 Hz, J_{AX} = J_{BX} = 7.2 Hz, 2H), 3.24 (dd, *J* = 14.0, 7.1 Hz, 1H), 2.88 (dd, *J* = 14.0, 8.6 Hz, 1H), 2.86 (s, 3H), 2.39 (s, 3H), 1.09 (X de ABX_3, J_{AX} = J_{BX} = 7.2 Hz, 3H) ppm.

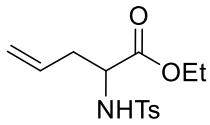
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.3, 143.3, 136.6, 136.3, 129.5, 129.3, 128.8, 127.6, 127.0, 61.3, 60.5, 36.0, 30.2, 21.6, 14.0 ppm.

HRMS-ESI m/z calculated for $C_{19}H_{23}NO_4S$ $[M+H]+$ 362.1421, found 362.1419.

$[\alpha]_D^{25}$ = -23.1 (c = 0.98, $CHCl_3$).

[24] K. Ishihara, H. Hamamoto, M. Matsugi and T. Shioiri, *Tetrahedron Lett.*, 2015, **56**, 3169.

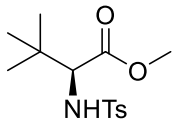
Ethyl-2-(4-methylsulfonamido)pent-4-enoate (1t)



Acetyl chloride (2.2 mL, 31.27 mmol) was added dropwise to a round bottom flask containing EtOH (50 mL) at 0 ºC. The mixture was stirred for 15 minutes. Then, 2-aminopentenoic acid (1.50 g, 13.03 mmol) was added and the reaction was stirred at reflux for 24 h. The solvent was removed under reduced pressure to yield the corresponding ester as an orange liquid (2.34 g, quant) that was used without further purification. The ethyl ester (2.00 g, 1.0 equiv., 11.13 mmol), DMAP (27 mg, 0.02 equiv., 0.22 mmol) and TsCl (2.33 g, 1.1 equiv., 12.25 mmol) were dissolved in DCM (33 mL) under inert atmosphere. TEA (3.1 mL, 2 equiv., 22.27 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous saturated NH_4Cl solution (3 x 20 mL) and brine (2 x 20 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield compound **1t** as a white solid (2.91 g, 88%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (A_2X_2 part A, J_{AX} = 8.1 Hz, 2H), 7.28 (A_2X_2 part A, J_{XA} = 8.1 Hz, 2H), 5.64 (ddt, *J* = 17.3, 10.3, 7.1 Hz, 1H), 5.18 – 5.02 (m, 3H), 4.05 – 3.90 (m, 3H), 2.47 (ddd, *J* = 7.1, 5.8, 1.2 Hz, 2H), 2.41 (s, 3H), 1.12 (t, *J* = 7.2 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.0, 143.8, 137.0, 131.4, 129.8, 127.4, 119.9, 61.9, 55.3, 37.8, 21.7, 14.1 ppm.
NMR data were in agreement with those reported.[25]
Mp.: 45 – 47ºC; **HRMS-ESI** m/z calculated for $C_{14}H_{19}NO_4S$ $[M+H]^+$ 298.1108, found 298.1109.

Methyl (*S*)-3,3-dimethyl-2-((4-methylphenyl)sulfonamido)butanoate (1u)

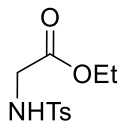


L-*tert*-Leucine methyl ester hydrochloride (500 mg, 1.0 equiv., 2.75 mmol), DMAP (7 mg, 0.02 equiv., 55.05 µmol) and TsCl (577 mg, 1.1 equiv., 3.03 mmol) were dissolved in DCM (16 mL) under inert atmosphere. TEA (0.8 mL, 2.1 equiv., 5.78 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous HCl 1M solution (3 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (8:2) to yield compound **1u** as a white solid (741 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.27 (A_2X_2, part X, J_{XA} = 8.3 Hz, 2H), 5.10 (d, *J* = 10.8 Hz, 1H), 3.56 (d, *J* = 10.8 Hz, 1H), 3.33 (s, 3H), 2.41 (s, 3H), 0.94 (s, 9H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.5, 143.7, 136.5, 129.6, 127.6, 64.3, 51.8, 34.7, 26.4, 21.6 ppm.
Mp.: 110 – 113 ºC; **HRMS-ESI** m/z calculated for $C_{14}H_{21}NO_4S$ $[M+H]^+$ 300.1264, found 300.1262.
$[\alpha]_D^{25}$ = +27.0 (c = 0.96, $CHCl_3$).

[25] T. Miura, T. Tanaka, T. Biyajima, A. Yada and M. Murakami, *Angew Chem Int Ed*, 2013, **52**, 3883.

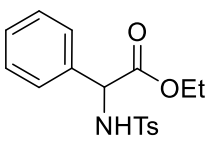
Ethyl-2-(4-methylsulfonilamide) acetate (1v)



Glycine ethyl ester hydrochloride (1.00 g, 1.0 equiv., 7.16 mmol), DMAP (18 mg, 0.02 equiv., 0.14 mmol) and TsCl (1.50 g, 1.1 equiv., 7.88 mmol) were dissolved in DCM (10 mL) under inert atmosphere. TEA (2.0 mL, 2 equiv., 14.33 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous NH_4Cl saturated solution (4 x 15 mL) and brine (2 x 15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (6:4) to yield compound **1v** as a white solid (1.20 g, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1, 2H), 5.05 (bs, 1H), 4.08 (dd, *J* = 7.2 Hz, 2H), 3.76 (s, 2H), 2.42 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 144.0, 136.3, 129.9, 127.4, 62.0, 44.3, 27.1, 14.1 ppm.
NMR data were in agreement with those reported.[26]
Mp.: 57 – 60 ºC; **HRMS-ESI** m/z calculated for $C_{11}H_{15}NO_4S$ [M+H]+ 258.0795, found 258.0796

Ethyl 2-((4-methylphenyl)sulfonamido)-2-phenylacetate (1w)



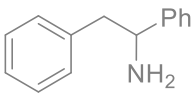
This compound was synthesized according to the literature procedure.[27]
Dichloro(*p*-cymene)ruthenium(ll)dimer (5 mg, 0.01 eq, 7.89 µmol) was dissolved in DCM (18 ml) under inert atmosphere. Then, ethyl 2-diazo-phenylacetate (150 mg, 1 eq, 0.79 mmol) and *p*-tosylamide (135 mg, 1 eq, 0.79 mmol) were added in portions. The reaction was stirred at room temperature for 30 min. The crude was concentrated under reduced pressure and the residue was purified by flash chromatography eluting with hexane/EtOAc (7:3) to obtain sulfonamide **1w** as a white solid (140 mg, 53 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, 2H), 7.20 – 7.15 (m, 5H), 7.13 (d, *J* = 8.2 Hz, 2H), 5.60 (bs, 1H), 4.97 (d, *J* = 8.1 Hz, 1H), 4.10 – 3.71 (m, 2H), 2.31 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.2, 143.6, 137.1, 135.5, 129.6, 128.9, 128.6, 127.3, 127.2, 62.4, 59.5, 21.6, 14.0 ppm.
NMR data were in agreement with those reported.[28]

***N*-(1,2-Diphenylethyl)-4-methylbenzensulfonamide (1x)**

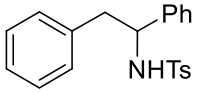
2-Phenylacetophenone (817 mg, 1 equiv., 4.08 mmol) was dissolved in MeOH (13 mL) under inert atmosphere. Then, NH_4OAc (2.83 g, 9 equiv., 36.72 mmol) and $NaBH_3CN$ (513 mg, 2 equiv., 8.16 mmol) were added in portions and the mixture was stirred at room temperature for 24 h. Later, the crude was acidified with aqueous HCl 4 M until pH = 2-3 was reached and washed with DCM (3 x 20 mL). Then, the aqueous layer was basified with aqueous NaOH 10 M until pH = 10-12 was reached and extracted with DCM (3 x 20 mL). This organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to obtain the amine as a colourless oil (282 mg, 35%).

[26] R. Takai, D. Shimbo, N. Tada and A. Itoh, *J. Org. Chem.*, 2021, **86**, 4699.
[27] Q.-H. Deng, H.-W. Xu, A. W.-H. Yuen, Z.-J. Xu and C.-M. Che, *Org. Lett.*, 2008, **10**, 1529.
[28] S. P. Fritz, J. F. Moya, M. G. Unthank, E. M. McGarrigle and V. K. Aggarwal, *Synthesis*, 2012, **44**, 1584.



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 6.99 (m, 10H), 4.15 – 4.03 (m, 1H), 2.92 (dd, *J* = 13.5, 4.4 Hz, 1H), 2.80 – 2.67 (m, 2H), 1.41 (bs, 2H) ppm. ^{1}H NMR data were in agreement with those reported.[29]

Amine (282 mg, 1 equiv., 1.43 mmol), DMAP (3 mg, 0.02 equiv., 28.59 µmol) and TsCl (327 mg, 1.2 equiv., 1.72 mmol) were dissolved with DCM (8 mL) under inert atmosphere. Then, TEA (0.2 mL, 1.2 equiv., 1.72 mmol) was added dropwise and the reaction was stirred at room temperature for 24 h. Later, the crude was washed with aqueous HCl 0.4 M (3 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude was then purified by flash chromatography eluting with Hex/EtOAc (8:2) to obtain sulfonamide **1x** as a white solid (147 mg, 29%).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.19 – 7.15 (m, 6H), 7.11 – 7.07 (m, 2H), 7.06 – 7.02 (m, 2H), 6.94 – 6.88 (m, 2H), 4.82 (d, *J* = 6.1 Hz, 1H), 4.51 (q_{app}, *J* = 6.8 Hz, 1H), 2.99 (ABX part AB, J_{AB} = 13.8, J_{AX} = 6.8, J_{BX} = 7.4 Hz 1H), 2.36 (s, 3H) ppm.

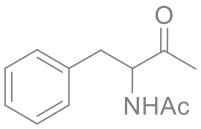
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.1, 140.5, 137.2, 136.4, 129.5, 128.7, 128.5, 127.6, 127.2, 127.0, 126.9, 59.3, 44.2, 21.6 ppm.

Mp.: 106 – 110 ºC; **HRMS-ESI** m/z calculated for $C_{21}H_{21}NO_2S$ $[M+H]^+$ 352.1366, found 352.1366.

4-Methyl-*N*-(3-oxo-1-phenylbutan-2-yl)benzensulfonamide (S4)

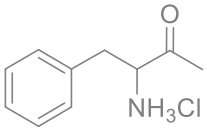
This compound was synthesized according to the literature procedure.[30]

L-Phe (1.5 g, 1 equiv., 9.08 mmol), anhydrous pyridine (7.3 mL, 10 equiv., 90.81 mmol) and acetic anhydride (3.0 mL, 3.5 equiv., 31.78 mmol) were added in a round bottom flask under inert atmosphere. The reaction was stirred at reflux for 24 h. Then, the crude was concentrated under reduced pressure, redissolved in DCM (15 mL) and washed with an aqueous saturated $NaHCO_3$ solution (3 x 15 mL) and brine (2 x 15 mL). The organic layer was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography eluting with Hex/EtOAc (4:6) to obtain the amide as a yellow solid (1.73 g, 73%).



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.21 (m, 3H), 7.15 – 7.09 (m, 2H), 6.07 (s, 1H), 4.87 (q, *J* = 6.6 Hz, 1H), 3.14 (dd, *J* = 14.0, 6.8 Hz, 1H), 3.06 (dd, *J* = 14.0, 5.7 Hz, 1H), 2.16 (s, 3H), 1.98 (s, 3H) ppm. ^{1}H NMR data were in agreement with those reported.[31]

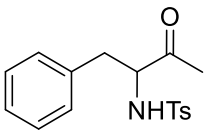
In a round bottom flask, amide (500 mg, 1 equiv., 2.44 mmol) was dissolved in EtOH (7.3 mL) and aqueous HCl 6 M (13.4 mL). The reaction was stirred at reflux for 24 h. Then, the reaction was concentrated under reduced pressure and redissolved in EtOH (3.5 mL). Later, Et_2O (40 mL) was poured and the precipitate was filtered off and washed with Et_2O to obtain the desired hydrochloride as a greenish solid (360 mg, 74%).



^{1}H NMR (300 MHz, CD_3OD) δ 7.48 – 7.18 (m, 5H), 4.44 (dd, J = 8.6, 5.9 Hz, 1H), 3.40 – 3.32 (m, 1H), 3.01 (dd, *J* = 14.5, 8.6 Hz, 1H), 2.23 (s, 3H) ppm.

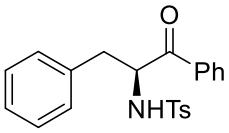
[29] Y. Yamashita, H. Suzuki, I. Sato, T. Hirata and S. Kobayashi, *Angew. Chem. Int. Ed.*, 2018, **57**, 6896.
[30] C. Yuan and D. Chen, *Synthesis*, 1992, 531.
[31] R. C. Wende, A. Seitz, D. Niedek, S. M. M. Schuler, C. Hofmann, J. Becker and P. R. Schreiner, *Angew. Chem. Int. Ed.*, 2016, **55**, 2719.

Hydrochloride (360 mg, 1 equiv., 1.80 mmol), DMAP (4 mg, 0.02 equiv., 36.06 μmol) and TsCl (412 mg, 1.2 equiv., 2.16 mmol) were dissolved with DCM (10 mL) under inert atmosphere. Then, TEA (0.5 mL, 2 equiv., 3.61 mmol) was added dropwise and the reaction was stirred at room temperature for 24 h. Later, the crude was washed with aqueous HCl 0.4 M (3 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude was then purified by flash chromatography eluting with Hex/EtOAc (7:3) to obtain sulfonamide **S4** as a white solid (286 mg, 50%).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.25 – 7.18 (m, 5H), 7.08 – 6.99 (m, 2H), 5.27 (d, *J* = 6.4 Hz, 1H), 4.10 (q, *J* = 6.4 Hz, 1H), 2.99 (dd, *J* = 14.1, 6.4 Hz, 1H), 2.92 (dd, *J* = 14.1, 6.5 Hz, 1H), 2.40 (s, 3H), 2.03 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.0, 143.8, 136.7, 135.1, 129.8, 129.4, 128.9, 127.4, 127.2, 62.8, 38.4, 27.7, 21.7 ppm.
NMR data were in agreement with those reported.[32]
Mp.: 100 – 104 ºC; **HRMS-ESI** m/z calculated for $C_{17}H_{19}NO_3S$ [M+H]$^+$ 318.1158, found 318.1160.

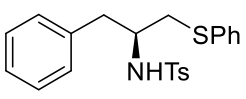
(*S*)-4-Methyl-*N*-(1-oxo-1,3-diphenylpropan-2-yl)benzensulfonamide (S5)



A solution of amide **1d** (250 mg, 1 equiv., 0.69 mmol) in THF (1.6 mL) was added dropwise to a solution of PhMgBr 3 M in Et_2O (0.8 mL, 3.4 equiv., 2.35 mmol) under inert atmosphere and at 0 ºC. The reaction was stirred at room temperature for 24 h. Then, the crude was quenched adding a saturated aqueous NH_4Cl solution (2 mL). After that, layers were separated, and the aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude was then purified by flash chromatography eluting with Hex/EtOAc (7:3) to obtain the ketone **S5** as a white solid (230 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.58 (m, 2H), 7.58 – 7.44 (m, 3H), 7.38 – 7.31 (m, 2H), 7.15 – 7.06 (m, 3H), 7.01 (A_2X_2 part X, J_{XA} = 8.1 Hz, 2H), 6.93 – 6.88 (m, 2H), 5.54 (bs, 1H), 5.06 (dt, *J* = 8.8, 5.7 Hz, 1H), 3.06 (dd, *J* = 13.9, 5.7 Hz, 1H), 2.88 (dd, *J* = 13.9, 5.7 Hz, 1H), 2.21 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 197.4, 143.6, 136.9, 135.0, 134.3, 134.1, 129.7, 129.7, 128.9, 128.5, 127.2, 127.2, 58.3, 40.3, 21.5 ppm.
NMR data were in agreement with those reported.[33]
Mp.: 108 – 111 ºC; **HRMS-ESI** m/z calculated for $C_{22}H_{21}NO_3S$ [M+H]$^+$ 380.1315, found 380.1313.
$[\alpha]_D^{25}$ = +78.0 (c = 1.00, $CHCl_3$).

(*S*)-4-Methyl-*N*-(1-phenyl-3-(phenylthio)propan-2-yl)benzensulfonamide (S6)



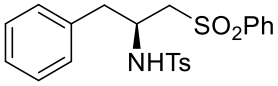
Alcohol **S3** (1 g, 1 equiv., 3.27 mmol) and PPh_3 (1.72 g, 2 equiv., 6.55 mmol) were dissolved in THF (20 mL) under inert atmosphere. Then, at 0 ºC, thiophenol (0.8 mL, 2.5 equiv., 8.19 mmol) and DIAD (1.0 mL, 1.6 equiv., 5.24 mmol) were added dropwise. The reaction was stirred at 55 ºC for 24 h. The crude was then removed under reduced

[32] S. Hata, D. Fukuda, I. Hachiya and M. Shimizu, *Chem. Asian J.*, 2010, **5**, 473.
[33] H. Qian, S. Sun, W. Zhao and J. Sun, *Chem. Commun.*, 2020, **56**, 11295.

pressure and the crude was purified by flash chromatography eluting with Hex/EtOAc (8:2) to obtain the thioether **S6** as a white solid (654 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.32 – 7.15 (m, 8H), 7.11 (d, *J* = 8.3 Hz, 2H), 7.02 – 6.94 (m, 2H), 5.07 (d, *J* = 7.1 Hz, 1H), 3.63 – 3.44 (m, 1H), 3.20 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.04 (dd, *J* = 13.9, 6.2 Hz, 1H), 2.89 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.79 (dd, *J* = 13.9, 7.0 Hz, 1H), 2.40 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.1, 136.7, 136.6, 135.1, 129.6, 129.5, 129.3, 129.1, 128.6, 127.0, 126.7, 126.4, 54.1, 39.5, 38.1, 21.5 ppm.
NMR data were in agreement with those reported.[34]
Mp.: 106 – 110 ºC; **HRMS-ESI** m/z calculated for $C_{22}H_{23}NO_2S_2$ $[M+H]^+$ 398.1243, found 398.1240.
$[\alpha]_D^{25}$ = -47.8 (c = 1.00, $CHCl_3$).

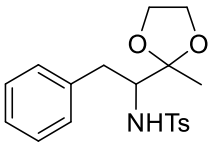
(*S*)-4-Methyl-*N*-(1-phenyl-3-(phenylsulfonyl)propan-2-yl)benzensulfonamide (S7)



In a round bottom flask, thioether **S6** (200 mg, 1 equiv., 0.50 mmol) was dissolved in DCM (7 mL). Then, *m*CPBA (217 mg, 2.5 equiv., 1.26 mmol) was added in portions. The reaction was stirred at room temperature for 24 h. After that, a solution of Na_2SO_3 (600 mg) in H_2O (6 mL) was added to the mixture and the reaction was stirred 3 h at room temperature. Then, layers were separated, and the organic phase was dried over $MgSO_4$ and purified by flash chromatography eluting with Hex/EtOAc (6:4) to obtain the sulfone **S7** as a white solid (182 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.64 (m, 2H), 7.64 – 7.52 (m, 1H), 7.50 – 7.38 (m, 2H), 7.26 (A_2X_2, part A, J_{AX} = 8.4 Hz, 2H), 7.11 – 6.95 (m, 5H), 6.90 – 6.72 (m, 2H), 5.26 (d, *J* = 6.5 Hz, 1H), 3.66 – 3.52 (m, 1H), 3.39 (dd, *J* = 14.4, 4.4 Hz, 1H), 3.16 (dd, *J* = 14.4, 7.4 Hz, 1H), 3.10 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.72 (dd, *J* = 14.1, 7.9 Hz, 1H), 2.29 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.5, 139.2, 135.9, 135.8, 134.0, 129.6, 129.4, 129.1, 128.7, 127.9, 127.1, 126.9, 59.0, 50.9, 40.0, 21.5 ppm.
Mp.: 115 – 118 ºC; **HRMS-ESI** m/z calculated for $C_{22}H_{23}NO_4S_2$ $[M+H]^+$ 430.1141, found 430.1135
$[\alpha]_D^{25}$ = -51.7 (c = 1.00, $CHCl_3$).

4-Methyl-*N*-(1-(2-methyl-1,3-dioxolan-2-yl)-2-phenylethyl)benzensulfonamide (S8)



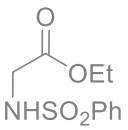
Ketone **S4** (300 mg, 1 equiv., 0.94 mmol), *p*-toluensulfonic acid monohydrate (3 mg, 0.02 equiv., 18.90 µmol), and Na_2SO_4 (269 mg, 2 equiv., 1.89 mmol) were suspended in toluene (6 mL) under inert atmosphere. Then, ethylene glycol (63 µL, 1.2 equiv., 1.13 mmol) was added dropwise and the reaction was stirred at reflux for 18 h. The mixture was diluted with Et_2O and washed with saturated aqueous $NaHCO_3$ (3 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with DCM to obtain the acetal **S8** as a white solid (98 mg, 29%).

[34] M. Wang, J. Wei, Q. Fan and X. Jiang, *Tetrahedron*, 2016, **72**, 2671.

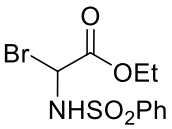
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.18 – 7.11 (m, 3H), 7.09 – 6.96 (m, 4H), 4.61 (d, *J* = 9.2 Hz, 1H), 4.01 – 3.72 (m, 5H), 3.05 (dd, *J* = 14.1, 4.3 Hz, 1H), 2.53 (dd , *J* = 14.1, 9.7 Hz, 1H), 2.35 (s, 3H), 1.35 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.4, 139.0, 138.1, 129.5, 129.3, 128.5, 126.8, 126.3, 110.1, 65.4, 65.1, 61.7, 37.2, 22.0, 21.5 ppm.
Mp.: 124 – 128 ºC; **HRMS-ESI** m/z calculated for $C_{19}H_{23}NO_4S$ $[M+H]^+$ 362.1421, found 362.1428

Ethyl 2-bromo-2(phenylsulfonamido)acetate (S9)

This compound was synthesized according to the literature procedure.[35]
Glycine ethyl ester hydrochloride (1.00 g, 1.0 eq, 7.16 mmol), DMAP (17 mg, 0.02 eq, 0.14 mmol) were suspended in DCM (41 ml) under inert atmosphere. TEA (2.1 ml, 2.1 eq, 15.05 mmol) and benzenesulfonyl chloride (1.01 ml, 1.1 eq, 7.88 mmol) were added dropwise at 0 ºC and the reaction mixture was stirred at room temperature for 24 h. The crude mixture was then washed with an aqueous HCl 1M (2 x 30 ml) and brine (2 x 30 ml) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography eluting with Hex/EtOAc (7:3) to yield phenyl sulfonamide as a white solid (1.32 g, 76 %).



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.73 (m, 2H), 7.63 – 7.35 (m, 3H), 5.66 (t, *J* = 5.8 Hz, 1H), 4.00 (q, *J* = 7.1 Hz, 2H), 3.74 (d, *J* = 5.8 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H) ppm.
Sulfonamide (300 mg, 1.0 eq, 1.23 mmol) was suspended in freshly distilled CCl_4 (2.4 ml) under inert atmosphere. Then, Br_2 (63 µl, 1.0 eq, 1.23 mmol) was added. The mixture was degassed bubbling Ar during 15 minutes and the reaction was stirred under 390 nm Kessil lamp irradiation for 6 h. Upon completion of the reaction, the crude was concentrated under reduced pressure and the residue was redissolved in DCM and precipitated with hexane to obtain the brominated compound **S9** as an orange wish solid (311 mg, 78 %), that decomposes in solid or in solution in a few hours.

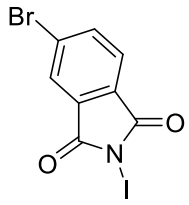


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.85 (m, 2H), 7.72 – 7.60 (m, 1H), 7.55 (m, 2H), 6.16 (d, *J* = 11.0 Hz, 1H), 6.06 (d, *J* = 11.0 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.6, 138.8, 134.0, 129.4, 128.0, 63.6, 53.9, 13.9 ppm.
NMR data were in agreement with those reported.[36]

[35] P. D. Clayman and T. K. Hyster, *J. Am. Chem. Soc.*, 2020, **142**, 15673.
[36] A. K. McFarlane, G. Thomas and A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2803.

***N*-iodoimides** have been prepared according to the literature procedure.[37]

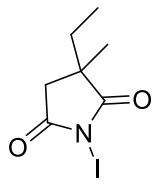
5-Bromo-2-iodoisoindoline-1,3-dione (S1ab)



5-bromoisoindoline-1,3-dione (500 mg, 1 equiv., 2.21 mmol), PIDA (427 mg, 0.6 equiv., 1.33 mmol) and I_2 (365 mg, 0.65 equiv., 1.44 mmol) were dissolved in MeCN (11 mL) under inert atmosphere. The mixture was stirred for 6 h and the solvent was removed under reduced pressure. The residue was redissolved in CCl_4 (11 mL) and stirred for 1 h at room temperature and 15 minutes at 0 ºC. Then, the precipitate was filtered with a filter plate and was washed with cold CCl_4 (4 x 10 mL), EtOAc (3 x 10 mL) and hexane (5 x 10 mL) to obtain pure **S1ab** as a white solid (560 mg, 72%).

^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.99 – 7.92 (m, 2H), 7.78 – 7.72 (m, 1H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3COCD_3) δ 169.8, 169.3, 137.4, 135.6, 132.7, 128.4, 126.8, 125.6 ppm.
Mp.: 236 – 240 ºC; **HRMS-ESI** m/z calculated for $C_8H_4NO_2$ $[M\text{-}I+H]^+$ 225.9498, found 225.9497.

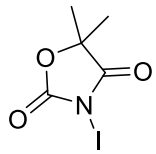
3-Ethyl-1-iodo-3-methylpyrrolidine-2,5-dione (*N*-iodoethosuxumide) (S1ac)



3-Ethyl-3-methylpyrrolidine-2,5-dione (565 mg, 1 equiv., 4.00 mmol), PIDA (773 mg, 0.6 equiv., 2.40 mmol) and I_2 (660 mg, 0.65 equiv., 2.60 mmol) were dissolved in MeCN (20 mL) under inertt atmosphere. The mixture was stirred for 6 h and the solvent was removed under reduced pressure. The residue was redissolved in CCl_4 (15 mL) and stirred for 1 h at room temperature and 15 minutes at 0 ºC. Then, the precipitate was filtered with a filter plate and was washed with cold CCl_4 (4 x 5 mL), EtOAc (1 x 5 mL) and hexane (5 x 10 mL) to obtain pure **S1ac** as a white solid (786 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88 (d, *J* = 18.0 Hz, 1H), 2.69 (d, *J* = 18.0 Hz), 1.75 (dd, *J* = 13.8, 7.5 Hz, 1H), 1.61 – 1.50 (m, 1H), 1.31 (s, 3H), 0.85 (t, *J* = 7.5 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, C) δ 183.8, 176.8, 47.2, 41.0, 32.0, 24.6, 8.8 ppm.
Mp.: 117 – 121 ºC.

3-Iodo-5,5-dimethyloxazolidine-2,4-dione (S1ad)



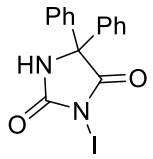
5,5-Dimethyloxazolidine-2,4-dione (520 mg, 1 equiv., 4.03 mmol), PIDA (778 mg, 0.6 equiv., 2.42 mmol) and I_2 (664 mg, 0.65 equiv., 2.62 mmol) were dissolved in MeCN (17 mL) under inertt atmosphere. The mixture was stirred for 6 h and the solvent was removed under reduced pressure. The residue was redissolved in CCl_4 (15 mL) and stirred for 1 h at room temperature and 15 minutes at 0 ºC. Then, the precipitate was filtered with a filter plate and was washed with cold CCl_4 (4 x 5 mL), EtOAc (1 x 3 mL) and hexane (5 x 10 mL) to obtain pure **S1ad** as a white solid (645 mg, 63%).

^{1}H NMR (400 MHz, CD_3COCD_3) δ 1.52 (s, 6H) ppm.

[37] A. Artaryan, A. Mardyukov, K. Kulbitski, I. Avigdori, G. A. Nisnevich, P. R. Schreiner and M. Gandelman, *J. Org. Chem.*, 2017, **82**, 7093.

$^{13}C\{^1H\}$ NMR (101 MHz, CD_3COCD_3) δ 179.7, 155.3, 85.9, 24.1 ppm.
Mp.: 190 – 194 ºC; **HRMS-ESI** m/z calculated for C_5H_7NO [M-I+H]$^+$ 130.0499, found 130.0496.

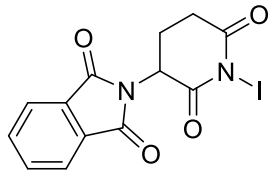
3-Iodo-5,5-diphenylimidazolidine-2,4-dione (S1af)



5,5-Diphenylimidazolidine-2,4-dione (520 mg, 1 equiv., 2.06 mmol), PIFA (492 mg, 0.6 equiv., 1.24 mmol) and I_2 (314 mg, 0.6 equiv., 1.24 mmol) were dissolved in MeCN (10 mL) under inert atmosphere. The mixture was stirred for 6 h and the solvent was removed under reduced pressure. The residue was redissolved in CCl_4 (8 mL) and stirred for 1 h at room temperature and 15 minutes at 0 ºC. Then, the precipitate was filtered with a filter plate and was washed with cold CCl_4 (4 x 10 mL) and hexane (5 x 10 mL). The solid was concentrated under reduced pressure to remove traces of TFA to obtain **S1af** as a reddish solid (585 mg, 75%).

^1H NMR (400 MHz, CD_3COCD_3) δ 7.48 – 7.42 (m, 5H), 7.42 – 7.34 (m, 3H), 7.33 – 7.25 (m, 3H) ppm.
$^{13}C\{^1H\}$ NMR (101 MHz, CD_3COCD_3) δ 176.0, 175.5, 156.2, 156.0, 138.7, 128.7, 128.5, 128.4, 128.2, 126.8, 78.5. ppm.
Mp.: 172 – 175 ºC; **HRMS-ESI** m/z calculated for $C_{15}H_{11}IN_2O_2$ [M+H]$^+$ 378.9938, found 378.9932.

***N*-iodothalidomide (S1ag)**

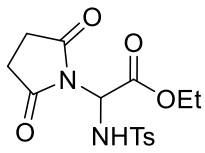


Thalidomide (500 mg, 1 equiv., 1.94 mmol), PIDA (374 mg, 0.6 equiv., 1.16 mmol) and I_2 (319 mg, 0.65 equiv., 1.26 mmol) were dissolved in MeCN (10 mL) under inert atmosphere. The mixture was stirred for 6 h and the solvent was removed under reduced pressure. The residue was redissolved in CCl_4 (11 mL) and stirred for 1 h at room temperature and 15 minutes at 0 ºC. Then, the precipitate was filtered with a filter plate and was washed with cold CCl_4 (4 x 10 mL), EtOAc (2 x 5 mL) and hexane (5 x 10 mL) to obtain pure **S1ag** as a white solid (423 mg, 57%).

^1H NMR (400 MHz, CD_3COCD_3) δ 7.91 (s, 4H), 5.32 (dd, *J* = 13.1, 5.4 Hz, 1H), 3.24 – 3.01 (m, 2H), 2.71 (qd, *J* = 13.1, 5.6 Hz, 1H), 2.11 (dtd, *J* = 13.1, 5.2, 2.8 Hz, 1H) ppm.
$^{13}C\{^1H\}$ NMR (101 MHz, CD_3COCOD_3) δ 173.8, 171.9, 167.9, 135.5, 132.8, 124.2, 49.9, 31.3, 23.2 ppm.
Mp: 230 – 232 ºC; **HRMS-ESI** m/z calculated for $C_{13}H_{10}N_2O_4$ [M-I+H]$^+$ 259.0713, found 259.0714.

4.2 *gem*-Diamines

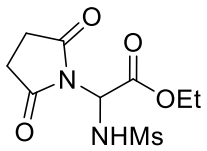
Ethyl-2-(2,5-dioxopyrrolidin-1-yl)-2-(4-methylphenylsulfonamide) acetate (2a)



Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was washed with an aqueous saturated $Na_2S_2O_3$ solution (3 x 5 mL), H_2O (2 x 5 mL) and brine (2 x 5 mL) to yield compound **2a** as a white solid (69 mg, 96%).
The general procedure was followed to scale-up the reaction to 1 mmol of Phe derivative **1a** to get 250 mg (70%, 82% conversion) after chromatography column (DCM/EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.31 (d, *J* = 8.7 Hz, 1H), 5.83 (d, *J* = 8.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 4H), 2.42 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.2, 165.0, 144.2, 136.7, 129.8, 127.5, 63.7, 58.5, 28.0, 21.7, 14.0 ppm.
Mp.: 177 – 180 ºC; **HRMS-ESI** m/z calculated for $C_{15}H_{18}N_2O_6S$ $[M+H]^+$ 355.0958, found 355.0962.

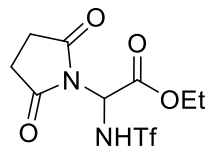
Ethyl 2-(2,5-dioxopyrrolidin-1-yl)-2-(methylsulfonamido)acetate (2aMs)



Compound **1aMs** (54 mg, 1.0 eq, 0.2 mmol) and NIS (90 mg, 2.0 eq, 0.4 mmol) were dissolved in DCM (2.0 ml) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (8:2) to yield compound **2aMs** as a yellowish solid (45 mg, 81 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (d, *J* = 9.1 Hz, 1H), 5.99 (d, *J* = 9.1 Hz, 1H), 4.28 (ABX_3, part AB, J_{AB} = 7.1 Hz, J_X = 1.4 Hz, 2H), 3.07 (s, 3H), 2.93 – 2.70 (m, 4H), 1.28 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.5, 165.8, 63.9, 58.6, 42.1, 28.3, 14.1 ppm.
Mp.: 144 – 149 ºC; **HRMS-ESI** m/z calculated for $C_9H_{14}N_2O_6S$ $[M+H]^+$ 279.0645, found 279.0647

Ethyl 2-(2,5-dioxopyrrolidin-1-yl)-2-((trifluoromethyl)sulfonamido)acetate (2aTf)

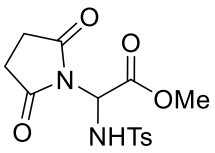


Compound **1aTf** (65 mg, 1.0 eq, 0.2 mmol) and NIS (90 mg, 2.0 eq, 0.4 mmol) were dissolved in DCM (2.0 ml) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (8:2) to yield compound **2aTf** as a yellowish solid (9 mg, 14 % [24% conversion]).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (s, 1H), 4.32 (ABX_3, part AB, J_{AB} = 7.1 Hz, J_X = 1.1 Hz, 2H), 2.84 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.0, 164.3, 119.34 (q, *J* = 323.9 Hz), 64.4, 58.7, 28.2, 14.1 ppm.

^{19}F NMR (376 MHz, $CDCl_3$) δ -77.5 (s) ppm.
Mp.: 122 – 126 ºC; **HRMS-ESI** m/z calculated for $C_9H_{11}F_3N_2O_6S$ $[M+H]^+$ 333.0363, found 333.0364.

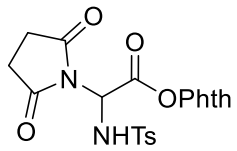
Methyl-2-(2,5-dioxopyrrolidin-1-yl)-2-(4-methylphenylsulfonamide) acetate (2b)



Compound **1b** (101 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (9:1) to yield compound **2b** as a white solid (61 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.20 (d, *J* = 8.7 Hz, 1H), 5.85 (d, *J* = 8.7 Hz, 1H), 3.75 (s, 3H), 2.50 (s, 4H), 2.43 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.1, 165.6, 144.4, 136.6, 129.9, 127.6, 58.4, 54.2, 28.1, 21.7 ppm.
Mp.: 194 – 196 ºC; **HRMS-ESI** m/z calculated for $C_{14}H_{16}N_2O_6S$ $[M+H]^+$ 341.0802, found 341.0808.

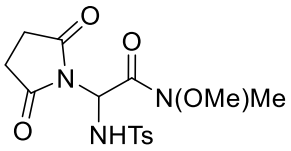
1,3-Dioxoisoindolin-2-yl 2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido) acetate (2c)



Compound **1c** (93 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (6:4). The fraction containing the product was concentrated, redissolved in EtOAc, extracted with H_2O (3 x 5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to obtain compound **2c** as a white solid (51 mg, 53%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.82 (m, 2H), 7.84 – 7.77 (m, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 1H), 6.44 (d, *J* = 10.4 Hz, 1H), 6.36 (d, *J* = 10.4 Hz, 1H), 2.57 (s, 4H), 2.44 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.7, 162.5, 160.9, 144.7, 135.3, 134.7, 130.1, 128.7, 127.5, 124.4, 123.8, 57.5, 28.1, 21.8 ppm.
Mp.: 188 – 192 ºC.

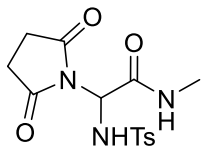
2-(2,5-Dioxopyrrolidin-1-il)-*N*-metoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido) acetamide (2d)



Compound **1d** (73 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (6:4). The fraction containing the product was concentrated, redissolved in EtOAc, extracted with H_2O (3 x 5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to obtain compound **2d** as a white solid (46 mg, 63%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (A_2X_2 part A, J_{AX} = 8.4 Hz, 2H), 7.30 (A_2X_2 part X, J_{XA} = 8.4 Hz, 2H), 6.65 (d, *J* = 9.1 Hz, 1H), 6.10 (d, *J* = 9.1 Hz), 3.67 (s, 3H), 3.17 (s, 3H), 2.42 (s, 3H), 2.36-2.32 (bs, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.3, 163.8, 144.2, 137.0, 129.8, 127.5, 62.0, 58.2, 33.0, 27.9, 21.7 ppm.
Mp.: 132 – 136 ºC; **HRMS-ESI** m/z calculated for $C_{15}H_{19}N_3O_6S$ $[M]^+$ 369.0995, found 369.0913.

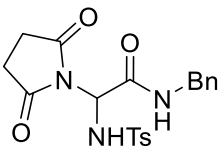
2-(2,5-Dioxopyrrolidin-1-yl)-2-(4-methylphenylsulfonamide)acetamide (2e)



Compound **1e** (30 mg, 1.0 equiv., 90 µmol) and NIS (41 mg, 2 equiv., 0.18 mmol) were dissolved in DCM (0.9 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (7:3). The fraction containing the product was concentrated, redissolved in EtOAc, extracted with H_2O (3 x 5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to obtain compound **2e** as a white solid (15 mg, 49%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.31 (A_2X_2 part X, J_{XA} = 8.3 Hz, 2H), 6.71 (bs), 6.46 (d, *J* = 11.3 Hz, 1H), 5.80 (d, *J* = 11.3 Hz, 1H), 2.86 (d, *J* = 4.9 Hz, 3H), 2.43 (s, 3H), 2.29 (bs, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.9, 164.2, 144.7, 136.1, 130.0, 127.5, 61.0, 28.0, 27.1, 21.7 (CH_3Ar) ppm.
Mp.: 175 – 178 ºC; **HRMS-ESI** m/z calculated for $C_{14}H_{17}N_3O_5S$ $[M+H]^+$ 340.0962, found 340.0960.

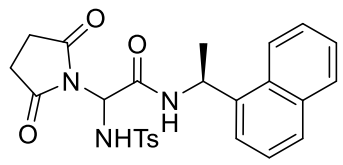
***N*-Bencyl-2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetamide (2f)**



Compound **1f** (82 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (8:2) to yield compound **2f** as a white solid (60 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.62 (A_2X_2 part A, J_{AX} = 8.4 Hz, 2H), 7.43 – 7.19 (m, 7H), 7.01 – 6.96 (m, 1H), 6.47 (d, *J* = 11.2 Hz, 1H), 5.86 (d, *J* = 11.2 Hz, 1H), 4.50 (dd, *J* = 14.8, 6.1 Hz, 1H), 4.40 (dd, *J* = 14.8, 5.7 Hz, 1H), 2.43 (s, 3H), 2.28 (s, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.9, 163.6, 144.7, 137.1, 136.1, 129.9, 129.0, 127.9, 127.5, 61.0 , 44.5, 28.0, 21.7 ppm.
Mp.: 188 – 192 ºC; **HRMS-ESI** m/z calculated for $C_{20}H_{21}N_3O_5S$ $[M]^+$ 415.1202, found 415.1229.

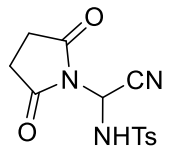
2-(2,5-Dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)-*N*-((*S*)-2-(naphthalen-1-yl)ethyl)acetamide (2g)



Compound **1g** (95 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (8:2) to obtain compound **2g** as a white solid (57 mg, 59% (69:31 *dr*))

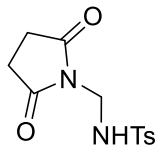
Major diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 – 7.92 (m, 1H), 7.90 – 7.85 (m, 1H), 7.85 – 7.77 (m, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.59 – 7.40 (m, 4H), 7.28 – 7.22 (m, 2H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.43 (d, *J* = 11.2 Hz, 1H), 5.84 ($quin_{app}$, *J* = 6.9 Hz, 1H), 5.77 (d, *J* = 11.2 Hz, 1H), 2.41 (s, 3H), 2.27 (bs, 4H), 1.68 (d, *J* = 6.9 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9, 162.6, 144.7, 137.2, 136.1, 134.1, 131.0, 129.9, 129.1, 128.8, 127.4, 126.9, 126.0, 125.4, 122.9, 122.8, 61.0, 46.1, 27.9, 21.7, 21.0 ppm.
Mp.: 129 – 133 ºC; **HRMS-ESI** m/z calculated for $C_{25}H_{25}N_3O_5S$ $[M+H]^+$ 480.1588 found 480.1589
$[\alpha]_D^{25}$ = -8.7 (c = 1.00, $CHCl_3$).

***N*-(Cyano(2,5-dioxopyrrolidin-1-yl)methyl)-4-methylbenzensulfonamide (2h)**



Compound **1h** (60 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (7:3). The fraction containing the product was concentrated, redissolved in EtOAc, extracted with H_2O (3 x 5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to obtain compound **2h** as a white solid (23 mg, 37% [49% brsm])

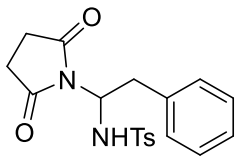
^{1}H NMR (400 MHz, CD_3COCD_3) δ 8.49 (d, *J* = 7.3 Hz, 1H), 7.75 (A_2X_2 part A, J_{AX} = 8.4 Hz, 2H), 7.46 (A_2X_2 part X, J_{XA} = 8.4 Hz, 2H), 6.40 (d, *J* = 7.3 Hz, 1H), 2.57 – 2.51 (m, 4H), 2.45 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3COCD_3) δ 175.2, 145.3, 138.5, 130.7, 127.8, 113.6, 48.6, 28.7, 21.5 ppm.
Mp.: 195 – 199 ºC; **HRMS-ESI** m/z calculated for $C_{13}H_{13}N_3O_4S$ $[M+Na]^+$ 330.0519, found 330.0505.
***N*-((2,5-Dioxopyrrolidin-1-yl)methyl)-2-(4-methylbencensulfonamide) (2i)**



Compound **1i** (55 mg, 1.0 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with White Kessil irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (98:2) to yield compound **2i** as a white solid (29 mg, 52 %). The same procedure was used for 0.2 mmol of compound **1ia** (45 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (A_2X_2 part A, J_{AX} = 8.4 Hz, 2H), 7.31 (A_2X_2 part X, J_{XA} = 8.3 Hz, 2H), 5.76 (t, *J* = 7.4 Hz, 1H), 4.81 (d, *J* = 7.4 Hz, 1H), 2.43 (s, 3H), 2.35 (s, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 176.1, 144.1, 137.4, 129.8, 127.4, 47.3, 28.1, 21.7 ppm.
Mp.: 186 – 188 ºC; **HRMS-ESI** m/z calculated for $C_{12}H_{14}N_2O_4S$ $[M+H]^+$ 283.0747, found 283.0745.

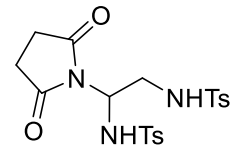
***N*-(1-(2,5-Dioxopyrrolidin-1-yl)-2-phenylethyl)-4-methylbenzensulfonamide (2j)**



Compound **1j** (73 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with DCM/EtOAc (95.5:0.5) to obtain compound **2j** as a white solid (30 mg, 40%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (A_2X_2 part A, J_{AX} = 8.3 Hz, 2H), 7.25 – 7.17 (m, 5H), 7.10 – 7.03 (m, 2H), 6.07 (d, *J* = 11.1 Hz, 1H), 5.59 (ddd, *J* = 11.1, 9.1, 6.9 Hz, 1H), 3.25 (dd, *J* = 13.8, 6.9 Hz, 1H), 3.11 (dd, *J* = 13.8, 9.1 Hz, 1H), 2.40 (s, 3H), 2.04 (bs, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.9, 137.0, 134.6, 129.7, 129.2, 128.8, 127.5, 127.4, 62.1, 39.4, 27.7, 21.7 ppm.
Mp.: 165 – 169 ºC; **HRMS-ESI** m/z calculated for $C_{19}H_{20}N_2O_4S$ $[M+NH_4]^+$ 390.1482, found 390.1478.

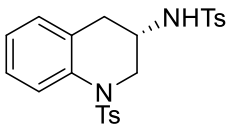
***N*-*N*` -(1-(2,5-Dioxopyrrolidin-1-yl)ethane-1,2-diyl)bis(4-methylbenzensulfonamide) (2k)**



Disulfonamide **1k** (92 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (8:2) to obtain compound **2k** as a white solid (18 mg, 19%).

^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.72 – 7.54 (m, 4H), 7.51 – 7.26 (m, 4H), 7.12 (d, *J* = 10.5 Hz, 1H), 6.78 (t, *J* = 6.9 Hz, 1H), 5.42 (ddd, *J* = 10.5, 9.0, 5.3 Hz, 1H), 3.46 (ddd, *J* = 13.9, 9.0, 6.9 Hz, 1H), 3.20 (ddd, *J* = 14.0, 6.9, 5.3 Hz, 1H), 2.44 (s, 3H), 2.42 (s, 3H), 2.19 (bs, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3COCD_3) δ 177.1, 144.7, 144.2, 138.8, 138.7, 130.7, 130.5, 127.7, 61.3, 44.2, 28.4, 21.4, 21.4 ppm.
Mp.: 160 – 164 ºC; **HRMS-ESI** m/z calculated for $C_{20}H_{23}N_3O_6S_2$ $[M+H]^+$ 466.1101, found 466.1074.

(*S*)-4-Methyl-*N*-(1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzensulfonamide (S8)

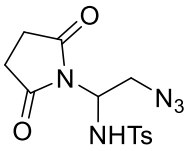


In the conditions described to obtain compound **2k**, tetrahydroquinoline **S8** was also isolated as a white solid (53 mg, 58 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 3H), 7.46 (A_2X_2, part A, J_{AX} = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.22 – 7.13 (m, 3H), 7.05 (td, *J* = 7.5, 1.2 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 4.85 (d,

J = 8.1 Hz, 1H), 4.09 (dd, *J* = 13.5, 4.5 Hz, 1H), 3.52 – 3.37 (m, 1H), 3.29 (dd, *J* = 13.5, 8.7 Hz, 1H), 2.59 (dd, *J* = 16.3, 5.8 Hz, 1H), 2.45 (s, 3H), 2.40 – 2.30 (m, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.0, 143.9, 137.6, 136.3, 136.0, 130.0, 129.9, 129.6, 127.4, 127.2, 127.2, 127.1, 125.5, 124.3, 50.8, 46.8, 34.2, 21.7, 21.7 ppm.
Mp.: 56 – 60 ºC; **HRMS-ESI** m/z calculated for $C_{23}H_{24}N_2O_4S_2$ $[M]^+$ 456.1172, found 456.1136.
$[\alpha]_D^{25}$ = -18.2 (c = 0.98, $CHCl_3$).

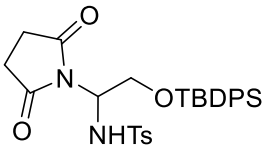
***N*-(2-Azido-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzensulfonamide (2l)**



Azide **1l** (66 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (9:1) to obtain compound **2l** as a white solid (37 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (A_2X_2, part A, J_{AX} = 8.2 Hz, 2H), 7.31 (A_2X_2, part A, J_{XA} = 8.2 Hz, 2H), 6.16 (d, *J* = 11.4 Hz, 1H), 5.51 (ddd, *J* = 11.4, 8.4, 6.2 Hz, 1H), 3.67 – 3.56 (m, 2H), 2.44 (s, 3H), 2.30 (s, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 176.1, 144.4, 136.8, 129.9, 127.4, 60.2, 51.4, 27.9, 21.7 ppm.
Mp.: 150 – 154 ºC; **HRMS-ESI** m/z calculated for $C_{13}H_{15}N_5O_4S$ $[M+Na]^+$ 360.0737, found 360.0737.

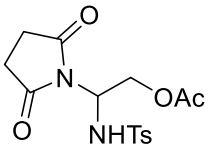
***N*-(2-((*tert*-Butyldiphenylsilyl)oxy)-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbencensulfonamide (2m)**



Compound **1m** (109 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (98:2) to obtain compound **2m** as a yellowish oil (23 mg, 21%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (A_2X_2, part A, J_{AX} = 8.1 Hz, 2H), 7.58 – 7.49 (m, 4H), 7.47 – 7.31 (m, 6H), 7.26 (d, *J* = 8.1 Hz, 1H), 6.03 (d, *J* = 11.4 Hz, 1H), 5.55 (ddd, *J* = 11.4, 8.4, 5.7 Hz, 1H), 4.12 – 3.57 (m, 2H), 2.41 (s, 3H), 2.14 (bs, 4H), 0.97 (s, 9H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 176.2, 143.9, 137.1, 135.6, 135.5, 132.7, 132.5, 130.2, 130.1, 129.7, 128.0, 127.9, 127.3, 62.6, 61.9, 27.8, 26.7, 21.6, 19.1 ppm.
HRMS-ESI m/z calculated for $C_{29}H_{34}N_2O_5SSi$ $[M+H]^+$ 551.2030, found 551.2031.

Ethyl-2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido) acetate (2n)

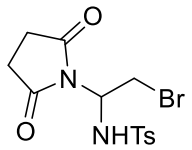


Compound **1n** (70 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and

purified by flash chromatography eluting with DCM/EtOAc (9:1) to obtain compound **2n** as a white solid (46 mg, 64%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.27 (d, *J* = 11.4 Hz, 1H), 5.58 (ddd, *J* = 11.4, 7.4, 5.5 Hz, 1H), 4.39 (dd, *J* = 11.4, 5.5 Hz, 1H), 4.22 (dd, *J* = 11.4, 7.4 Hz, 1H), 2.42 (s, 3H), 2.27 (s, 4H), 1.97 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 176.2, 170.5, 144.3, 137.0, 129.8, 127.4, 62.4, 60.0, 27.9, 21.7, 20.6 ppm.
Mp.: 183 – 186 ºC; **HRMS-ESI** m/z calculated for $C_{15}H_{18}N_2O_6S$ $[M+H]^+$ 355.0958, found 355.0953.

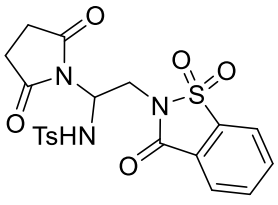
***N*-(2-Bromo-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzensulfonamide (2o)**



Brominated compound **1o** (74 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (9:1) to obtain compound **2o** as a white solid (47 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (A_2X_2, part A, J_{AX} = 8.2 Hz, 2H), 7.31 (A_2X_2, part A, J_{XA} = 8.2 Hz, 2H), 6.11 (d, *J* = 11.2 Hz, 1H), 5.59 (ddd, *J* = 11.2, 9.5, 5.6 Hz, 1H), 3.71 (dd, *J* = 10.7, 9.5 Hz, 1H), 3.62 (dd, *J* = 10.7, 5.6 Hz, 1H), 2.44 (s, 3H), 2.32 (s, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 175.9, 144.4, 136.6, 129.9, 127.5, 61.1, 29.6, 27.8, 21.7 ppm.
Mp.: 145 – 148 ºC; **HRMS-ESI** m/z calculated for $C_{13}H_{15}BrN_2O_4S$ $[M+Na]^+$ 396.9828/398.9808, found 396.9824/398.9802.

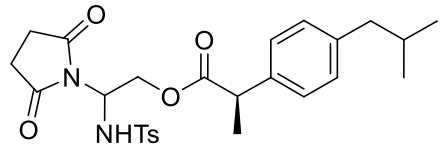
***N*-(2-(1,1-Dioxo-3-oxobenzo[*d*]isothiazol-2(3H)-yl)-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzensulfonamide (2p)**



Compound **1p** (95 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (95:5) to obtain compound **2p** as a white solid (42 mg, 44%).

^{1}H NMR (400 MHz, CD_3COCD_3) δ 8.20 – 7.95 (m, 4H), 7.68 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.45 – 7.36 (m, 3H), 5.86 (ddd, *J* = 10.6, 9.7, 4.7 Hz, 1H), 4.26 (dd, *J* = 14.9, 9.7 Hz, 1H), 4.05 (dd, *J* = 14.9, 4.7 Hz, 1H), 2.42 (s, 3H), 2.31 – 2.13 (m, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3COCD_3) δ 176.5, 158.9, 144.0, 137.8, 137.3, 135.9, 135.2, 129.6, 126.9, 126.3, 125.2, 121.3, 58.2, 39.7, 27.5, 20.5 ppm.
Mp.: 219 – 224 ºC; **HRMS-ESI** m/z calculated for $C_{20}H_{19}N_3O_7S_2$ $[M+H]^+$ 478.0737, found 478.0701.

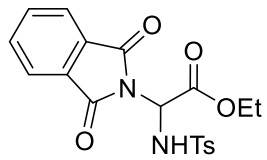
2-(2,5-Dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)ethyl (*2S*)-2-(4-*iso*butylphenyl)propanoate (2q)



Compound **1q** (100 mg, 1 equiv., 0.20 mmol) and NIS (90 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (95:5) to obtain compound **2q** as a white solid (73 mg, 71% (1:1 *dr*)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.54 (m, 4H, 2 diastereomers), 7.33 – 7.22 (m, 5H, 2 diastereomers), 7.15 – 6.97 (m, 8H, 2 diastereomers), 6.17 (d, *J* = 9.4 Hz, 1H), 6.14 (d, *J* = 9.3 Hz, 1H), 5.68 – 5.39 (m, 2H, 2 diastereomers), 4.42 – 4.30 (m, 2H), 4.29 – 4.17 (m, 2H), 3.70 – 3.44 (m, 2H, 2 diastereomers), 2.47 – 2.32 (m, 10H, 2 diastereomers), 2.09 (bs, 4H), 1.99 – 1.88 (m, 4H), 1.89 – 1.73 (m, 2H, 2 diastereomers), 1.42 (d, *J* = 6.2 Hz, 3H), 1.41 (d, *J* = 6.1 Hz, 3H), 0.92 – 0.84 (m, 12 H, 2 diastereomers) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 176.0, 174.0, 174.0, 144.2, 140.9, 137.5, 137.0, 137.0, 136.9, 129.8, 129.5, 129.5, 127.4, 127.3, 127.3, 62.3, 61.9, 59.6, 59.5, 45.1, 45.1, 44.9, 44.9 44.9, 30.3, 27.7, 27.6, 22.5, 22.5, 21.7, 21.7, 18.6, 18.1 ppm.
Mp.: 139 – 143 ºC; **HRMS-ESI** m/z calculated for $C_{26}H_{32}N_2O_6S$ $[M+H]^+$ 501.2054, found 501.2024.

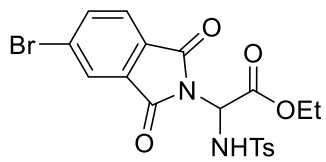
Ethyl 2-(1,3-dioxoisoindolin-2-yl)-2-((4methylphenyl)sulfonamido)acetate (2aa)



Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and *N*-Iodophtalimide (110 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography elutin with DCM/EtOAc (96:4) to obtain compound **2aa** as a white solid (58 mg, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.67 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.44 (d, *J* = 8.8 Hz, 1H), 6.02 (d, *J* = 8.8 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.11 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.2, 165.4, 143.8, 136.6, 134.5, 131.3, 129.6, 127.3, 123.8, 63.7, 58.1, 21.4, 14.0 ppm.
Mp.: 140 – 144 ºC; **HRMS-ESI** m/z calculated for $C_{19}H_{18}N_2O_6S$ $[M+H]^+$ 403.0958, found 403.0956.

Ethyl 2-(5-bromo-1,3-dioxoisoindolin-2-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ab)

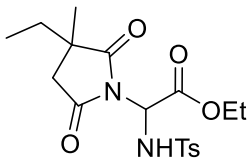


Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and 5-bromo-2-iodoisoindoline-1,3-dione (142 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure

and purified by flash chromatography eluting with DCM/EtOAc (98:2) to obtain compound **2ab** as a white solid (82 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.78 (m, 2H), 7.68 – 7.61 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.43 (d, *J* = 7.9 Hz, 1H), 5.99 (d, *J* = 7.9 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.4, 165.1, 164.8, 144.0, 137.6, 136.6, 132.9, 129.9, 129.7, 129.5, 127.4, 127.1, 125.2, 63.8, 58.2, 21.4, 14.0 ppm.
Mp.: 143 – 147 ºC; **HRMS-ESI** m/z calculated for $C_{19}H_{17}BrN_2O_6S$ $[M+H]^+$ 481.0063, found 481.0070.

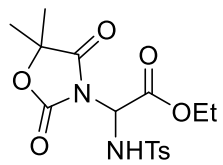
Ethyl 2-(3-ethyl-3-methyl-2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ac)



Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and 3-ethyl-1-iodo-3-methylpyrrolidine-2,5-dione (103 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (98:2) to obtain compound **2ac** as a white solid (61 mg, 78% (1:1 *d.r.*)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (A_2X_2, part A, J_{AX} = 8.2 Hz, 4H, 2 diastereomers), 7.30 (d, *J* = 8.2 Hz, 4H, 2 diastereomers), 6.19 (d, *J* = 8.0 Hz, 2H, 2 diastereomers), 5.79 (d, *J* = 8.0 Hz, 1H), 5.79 (d, *J* = 8.0 Hz, 1H), 4.31 – 4.07 (m, 4H, 2 diastereomers), 2.55 (d, *J* = 18.1 Hz, 1H), 2.47 (d, *J* = 18.3 Hz, 1H), 2.41 (s, 6H, 2 diastereomers), 2.28 (d, *J* = 18.3 Hz, 1H), 2.21 (d, *J* = 18.1 Hz, 1H), 1.67 – 1.55 (m, 2H, 2 diastereomers), 1.56 – 1.44 (m, 2H, 2 diastereomers), 1.25 – 1.16 (m, 6H, 2 diastereomers), 1.16 (s, 3H, CH_3), 1.11 (s, 3H), 0.88 – 0.64 (m, 6H, 2 diastereomers) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 181.1, 180.9, 174.4, 174.2, 165.2, 165.2, 144.3, 144.3, 136.8, 136.7, 129.9, 127.6, 63.7, 58.3, 58.3, 44.3, 44.2, 40.4, 40.3, 31.0, 30.7, 23.4, 23.4, 21.7, 14.0, 8.6 ppm.
Mp.: 131 – 135 ºC; **HRMS-ESI** m/z calculated for $C_{18}H_{24}N_2O_6S$ $[M+H]^+$ 397.1428, found 397.1424.

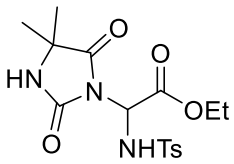
Ethyl 2-(5,5-dimethyl-2,4-dioxooxazolidin-3-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ad)



Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and 3-iodo-5,5-dimethyloxazolidine-2,4-dione (103 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (98:2) to obtain compound **2ad** as a white solid (61 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (A_2X_2, part A, J_{AX} = 8.4 Hz, 2H), 7.32 (A_2X_2, part X, J_{XA} = 8.4 Hz, 2H), 6.27 (d, *J* = 7.6 Hz, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 4.36 – 4.11 (m, 2H), 2.41 (s, 3H), 1.44 (s, 3H), 1.41 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.2, 164.3, 152.5, 144.1, 136.4, 130.1, 127.6, 84.5, 64.2, 59.5, 23.2, 23.0, 21.7, 14.0 ppm.
Mp.: 88 – 92 ºC; **HRMS-ESI** m/z calculated for $C_{16}H_{20}N_2O_7S$ $[M+Na]^+$ 407.0883, found 407.0879.

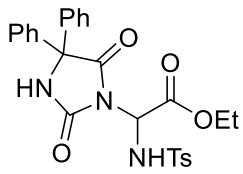
Ethyl 2-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ae)



Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and 1,3-Diiodo-5,5-dimethyl hydantoin (102 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (8:2). The fraction containing the product was concentrated, redissolved in EtOAc, extracted with H_2O (3 x 5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to obtain compound **2ae** as a white solid (60 mg, 78%).

^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.78 (A_2X_2, part A, J_{AX} = 8.1 Hz, 2H), 7.57 (d, J = 8.5 Hz), 7.37 (A_2X_2, part X, J_{XA} = 8.1 Hz, 2H), 7.29 (s, 1H), 5.89 (d, J = 8.7 Hz, 1H), 4.33 – 4.05 (m, 2H), 2.40 (s, 3H), 1.24 – 1.09 (m, 9H) ppm.
^{13}C{^{1}H} NMR (101 MHz, CD_3COCD_3) δ 176.4, 166.2, 154.4, 144.3, 139.5, 130.4, 127.9, 63.5, 59.5, 59.1, 24.6, 24.5, 21.4, 14.2 ppm.
Mp.: 154 – 158 ºC; **HRMS-ESI** m/z calculated for $C_{16}H_{21}N_3O_6S$ $[M+H]^+$ 384.1224, found 384.1221.

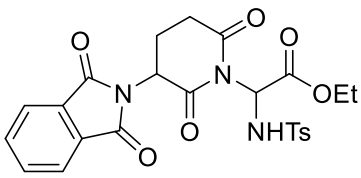
Ethyl 2-(2,5-dioxo-4,4-diphenylimidazolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2af)



Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and 3-Iodo-5,5-diphenylimidazolidine-2,4-dione (152 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (95:5) to obtain compound **2af** as a white solid (86 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (A_2X_2, part A, J_{AX} = 8.1 Hz, 2H), 7.37 – 7.27 (m, 8H), 7.25 – 7.19 (m, 2H), 7.02 (d, J = 8.1 Hz, 2H), 6.94 (s, 1H), 6.40 (d, J = 7.8 Hz, 1H), 5.92 (d, J = 7.8 Hz, 1H), 4.29 – 4.05 (m, 2H), 2.29 (s, 3H), 1.09 (t, J = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.0, 165.2, 154.6, 144.0, 138.6, 138.2, 136.7, 129.8, 128.9, 128.9, 128.9, 128.9, 127.2, 127.1, 127.0, 70.4, 63.8, 59.0, 21.7, 13.9 ppm.
Mp.: 153 – 157 ºC; **HRMS-ESI** m/z calculated for $C_{26}H_{25}N_3O_6S$ $[M+H]^+$ 508.1537, found 508.1536.

Ethyl 2-(3-(1,3-dioxoisoindolin-2-yl)-2,6-dioxopiperidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ag)

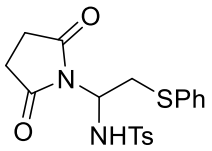


Compound **1a** (70 mg, 1 equiv., 0.20 mmol) and *N*-iodothalidomide (154 mg, 2 equiv., 0.40 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The crude was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (9:1) to obtain compound **2ag** as a white solid (93 mg, 93% (56:44 *d.r.*)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.84 (m, 4H, 2 diastereomers), 7.81 – 7.67 (m, 8H, 2 diastereomers), 7.39 – 7.31 (m, 4H, 2 diastereomers), 6.52 – 6.45 (m, 2H, 2 diastereomers), 6.22 (d, *J* = 9.6 Hz, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 4.69 (bs, 2H, 2 diastereomers), 4.28 – 4.00 (m, 4H, 2 diastereomers), 2.98 – 2.86 (m, 1H), 2.81 – 2.67 (m, 2H), 2.61 – 2.41 (m, 9H), 2.07 – 1.91 (m, 2H), 1.34 – 1.17 (m, 6H, 2 diastereomers) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.1 (bs), 167.1, 167.1, 165.7, 165.6, 144.2 (bs), 137.1, 137.1, 134.6, 134.6, 131.8, 130.0, 129.9, 127.7 (bs), 127.4, 123.9, 123.9, 63.5, 63.3, 59.9, 59.7, 49.8, 49.7, 31.8, 31.6, 21.7, 21.7 (bs), 21.5, 14.0, 13.9 ppm.
Mp.: 90 – 94 ºC; **HRMS-ESI** m/z calculated for $C_{24}H_{23}N_3O_8S$ $[M+H]^+$ 514.1279, found 514.1274.

4.3 Derivatization products

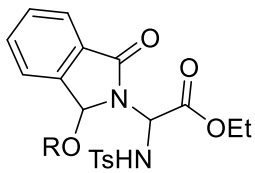
***N*-(1-(2,5-Dioxopyrrolidin-1-yl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (2ba)**



Brominated compound **1o** (50 mg, 1 equiv., 0.13 mmol) and imidazole (9 mg, 1 equiv., 0.13 mmol) were dissolved in DMF (0.8 mL) under inert atmosphere. Then, thiophenol (15 µL, 1.1 equiv., 0.15 mmol) was added to the mixture and the reaction was stirred at 60 ºC for 3 h. Crude mixture was concentrated under reduced pressure and purified by flash chromatography eluting with DCM/EtOAc (9:1). Fraction containing the product was concentrated under reduced pressure and crystallized with DCM/Hex to finally obtain the desired compound as a white solid (28 mg, 52 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.39 – 7.15 (m, 7H), 6.06 (d, *J* = 11.2 Hz, 1H), 5.50 (ddd, *J* = 11.2, 10.0, 4.6 Hz, 1H), 3.55 (dd, *J* = 14.6, 10.0 Hz, 1H), 3.22 (dd, *J* = 14.6, 4.6 Hz, 1H), 2.40 (s, 3H), 2.08 – 1.79 (m, 4H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.1, 136.9, 133.7, 131.1, 129.8, 129.3, 127.5, 127.4, 61.4, 36.3, 27.7, 21.7 ppm.
Mp.: 199 – 203 ºC; **HRMS-ESI** m/z calculated for $C_{19}H_{20}N_2O_4S_2$ $[M+H]^+$ 405.0937, found 405.0940.

Ethyl 2-(1-hydroxy-3-oxoisoindolin-2-yl)-2-((4-methylphenyl)sulfonamido)acetate (2bb) and ethyl 2-(1-acetoxy-3-oxoisoindolin-2-yl)-2-((4-methylphenyl)sulfonamido)acetate (2bc)



R = H, **2bb**
R = OAc, **2bc**

Conditions based on reported procedure.[38]
In a round bottom flask, compound **2aa** (45 mg, 1 equiv., 0.11 mmol) was dissolved in AcOH (1.2 mL). Then, Zn powder (56 mg, 7.6 equiv., 0.85 mmol) (previously activated with aqueous HCl 1 M during 5 min) and acetic anhydride (32 µL, 3 equiv., 0.36 mmol) were added and the reaction was stirred at reflux for 24 h. Then, the crude was filtered, washing with DCM (3 x 5 mL). The filtrates were concentrated under reduced pressure and the mixture was purified by flash chromatography eluting with DCM/EtOAc (98:2) to obtain alcohol **2bb** (18 mg,

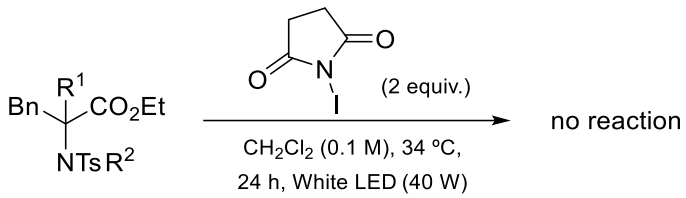
[38] C. Buchelt, J. Zuber and T. Bach, *Org. Lett.*, 2024, **26**, 7302.

40%) and acetate **2bc** (11 mg, 22%) as white solids. Alcohol **2bb** decomposes in solid or in solution in a few hours.

2bb: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 – 7.68 (m, 5H, 2 diastereomers), 7.63 – 7.47 (m, 7H, 2 diastereomers), 7.21 – 7.12 (m, 4H, 2 diastereomers), 6.42 (d, *J* = 8.7 Hz, NH), 6.34 (d, *J* = 5.5 Hz, NH), 5.93 – 5.84 (m, 3H), 5.57 (d, *J* = 8.7 Hz, 1H), 4.27 – 4.16 (m, 4H, 2 diastereomers), 2.87 – 2.68 (m, 2H, 2 diastereomers), 2.28 (s, 6H, 2 diastereomers), 1.25 – 1.16 (m, 6H, 2 diastereomers) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.9, 166.9, 167.0, 166.8, 144.1, 144.0, 143.9, 143.6, 137.0, 135.9, 133.2, 133.1, 130.4, 130.1, 130.1, 129.7, 129.6, 127.5, 127.0, 123.9, 123.7, 123.6, 123.4, 81.8, 80.0, 63.4, 61.2, 59.5, 21.5, 21.4, 14.0, 13.9 ppm.

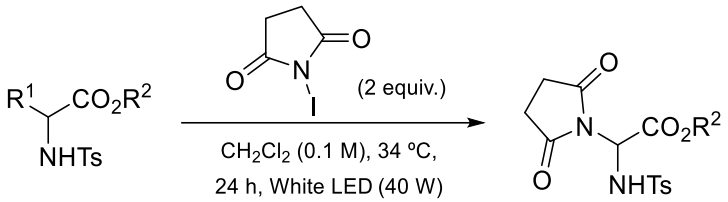
2bc: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 1H), 7.71 (A_2X_2, part A, J_{AX} = 8.3 Hz, 2H), 7.62 – 7.50 (m, 2H), 7.45 – 7.36 (m, 1H), 7.14 – 7.02 (A_2X_2, part X, J_{XA} = 8.3 Hz, 2H), 6.75 (s, 1H), 6.20 (d, *J* = 6.0 Hz, 1H), 6.09 (d, *J* = 6.0 Hz, 1H), 4.31 – 4.06 (m, 2H), 2.21 (s, 3H), 2.08 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.4, 167.5, 167.3, 144.0, 140.9, 136.5, 133.3, 130.6, 130.5, 129.7, 127.3, 124.3, 124.1, 78.5, 63.3, 60.2, 21.5, 20.9, 14.1 ppm.
Mp.: 108 – 112 ºC; **HRMS-ESI** m/z calculated for $C_{21}H_{22}N_2O_7S$ – C_2H_2O $[M+H]^+$ 405.1115, found 405.1112.

5. Mechanistic experiments



1r, $R^1 = CH_3$, $R^2 = H$
1s, $R^1 = H$, $R^2 = CH_3$

Sulfonamides **1r** and **1s** (50 mg, 1.0 equiv., 0.14 mmol) were treated with NIS (62 mg, 2.0 equiv., 0.28 mmol) in DCM (1.4 mL) following the general procedure, but no reaction was observed.

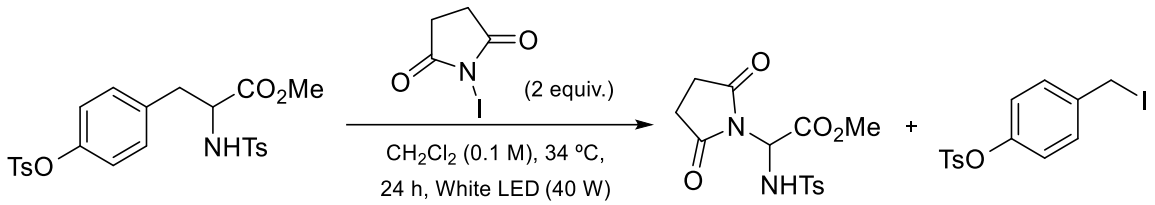


1t: R^1 = allyl, R^2 = Et — 62%, **2a**
1u: R^1 = *t*Bu, R^2 = Me — 29%, **2b**
1v: $R^1 = H$, R^2 = Et — 12% conv., **2a**

Sulfonamide **1t** (50 mg, 1.0 equiv., 0.17 mmol) was treated with NIS (76 mg, 2.0 equiv., 0.34 mmol) in DCM (1.7 mL) following the general procedure, to obtain **2a** as a white solid (37 mg, 62%).

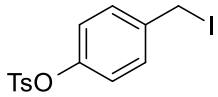
Sulfonamide **1u** (60 mg, 1.0 equiv., 0.2 mmol) was treated with NIS (90 mg, 2.0 equiv., 0.4 mmol) in DCM (2 mL) following the general procedure, to obtain **2b** as a white solid (20 mg, 29%).

Sulfonamide **1v** (50 mg, 1.0 equiv., 0.19 mmol) was treated with NIS (87 mg, 2.0 equiv., 0.39 mmol) in DCM (1.9 mL) following the general procedure. A 12% conversion rate to the product **2a** was measured by ^{1}H NMR.



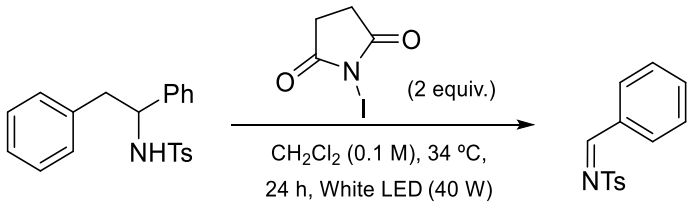
1b **2b** **3**

4-(Iodomethyl)phenyl-4-methylbenzensulfonate (3)



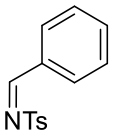
In the conditions described to obtain compound **2b**, benzyl iodide derivative **3** was also isolated as a white solid (49 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (A_2X_2 system 1, part A, J_{AX} = 8.0 Hz, 2H), 7.32 (A_2X_2 system 1, part X, J_{XA} = 8.0 Hz, 2H), 7.28 (A_2X_2 system 2, part A, J_{AX} = 8.6 Hz, 2H), 6.91 (A_2X_2 system 2, part X, J_{XA} = 8.6 Hz, 2H), 4.39 (s, 2H), 2.45 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.0, 145.6, 138.5, 132.5, 130.2, 129.9, 128.6, 122.9, 21.9, 3.9 ppm.
Mp.: 66-68 ºC; **HRMS-ESI** m/z calculated for $C_{14}H_{13}IO_3S$ $[M+H]^+$ 388.9703, found 388.9697.



1w **4**

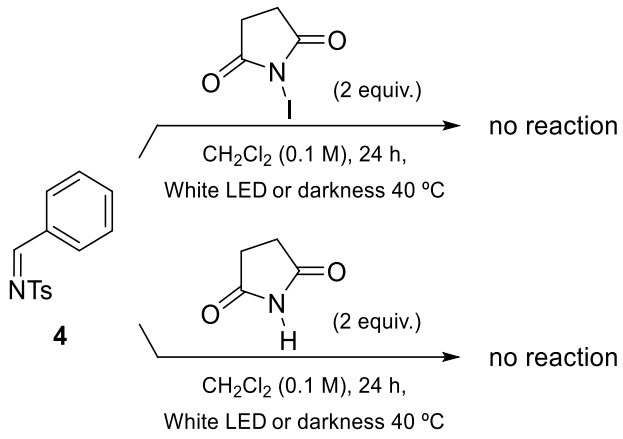
***N*-Benzylidene-4-methylphenylsulfonamide (4)**



Sulfonamide **1w** (70 mg, 1.0 equiv., 0.2 mmol) and NIS (90 mg, 2.0 equiv., 0.4 mmol) were dissolved in DCM (2.0 mL) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation for 24 h following the general procedure. The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography eluting with Hex/EtOAc (7:3) to obtain imine **4** as a white solid (36 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 7.95 – 7.91 (m, 2H), 7.89 (A_2X_2 part A, J_{AX} = 8.1 Hz, 2H), 7.65 – 7.58 (m, 1H), 7.52 – 7.46 (m, 2H), 7.35 (A_2X_2 part B, J_{BX} = 8.1 Hz, 2H), 2.44 (s, 3H) ppm.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.3, 144.8, 135.3, 135.1, 132.6, 131.5, 130.0, 129.3, 128.3, 21.8 ppm.
Mp.: 110 - 112 ºC.
Characterization data were in agreement with those reported.[39]

[39] M. Pinaud, E. Plantiveau, E. Huet, E. Le Gall and M. Presset, *Eur. J. Org. Chem.*, 2023, **26**, e202300572.



Imine **4** (52 mg, 1.0 eq, 0.2 mmol) and NIS (90 mg, 2.0 eq, 0.28 mmol) or succinimide (40 mg, 2.0 eq, 0.28 mmol) were dissolved in DCM (2 ml) under inert atmosphere. The reaction mixture was stirred at room temperature with white Kessil lamp irradiation following the general procedure or in darkness at 40 °C for 24 h. No conversion to the product was detected by ^{1}H NMR.

6. DFT studies

All the reported structures were optimized using Density Functional Theory as implemented in Gaussian 16.[40] The geometry optimizations were carried out with the B3LYP functional[41] and with a mixed basis set of LANL2DZ[42] for I and 6-311+G(d,p) basis set for all other atoms at 313.15 K. Solvent effects were considered in all calculations by applying the solvation model based on integral equation formalism polarizable continuum model (IEFPCM),[43] using dichloromethane as the solvent at 313.15 K. The reported energy values correspond to Gibbs Free (G) energies in kcal·mol^{-1}. All structures were optimized without geometrical constraints. Stationary points were characterized through frequency calculations (no negative frequency for minima and one negative frequency for transition states).

Several pathways have been calculated for the transformation under investigation. The complete reaction profiles with different species as hydrogen donors to reach the product are shown below. The transition state from the reaction of succinimide and ethyl (*Z*)-2-(tosylimino)acetate, as an alternative reaction pathway, could not be identified.

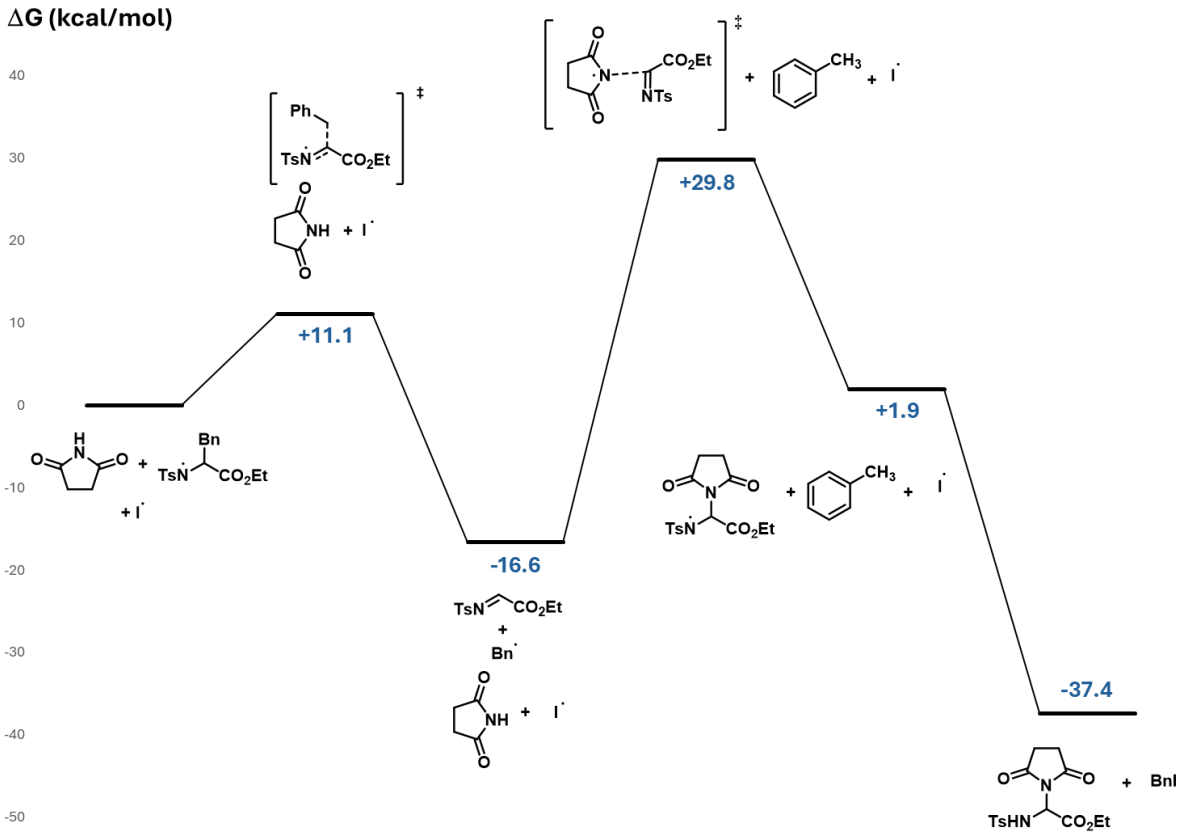


Figure S5. Energy profile considering toluene as hydrogen donor.

[40] Gaussian 16, Revision C.01; Frisch, M. J. *et al*. Gaussian, Inc., Wallingford CT, 2016

[41] a) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B*, 1998, **37**, 785-789; b) W. Kohn, A. D. Becke, R. G. Parr, *J. Phys. Chem.* 1996, **100**, 12974-12980; c) A. D. Becke, *Chem. Phys.* 1993, **98**, 5648.

[42] a) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* 1985, **82**, 270; b) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* 1985, **82**, 284; c) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* 1985, **82**, 299.

[43] a) B. Mennucci, R. Cammi, J. Tomasi, *J. Chem. Phys.* **1998**, *109*, 2798; b) E. Cancès, B. Mennucci, J. Tomasi, *J. Chem. Phys.* 1997, **107**, 3032.

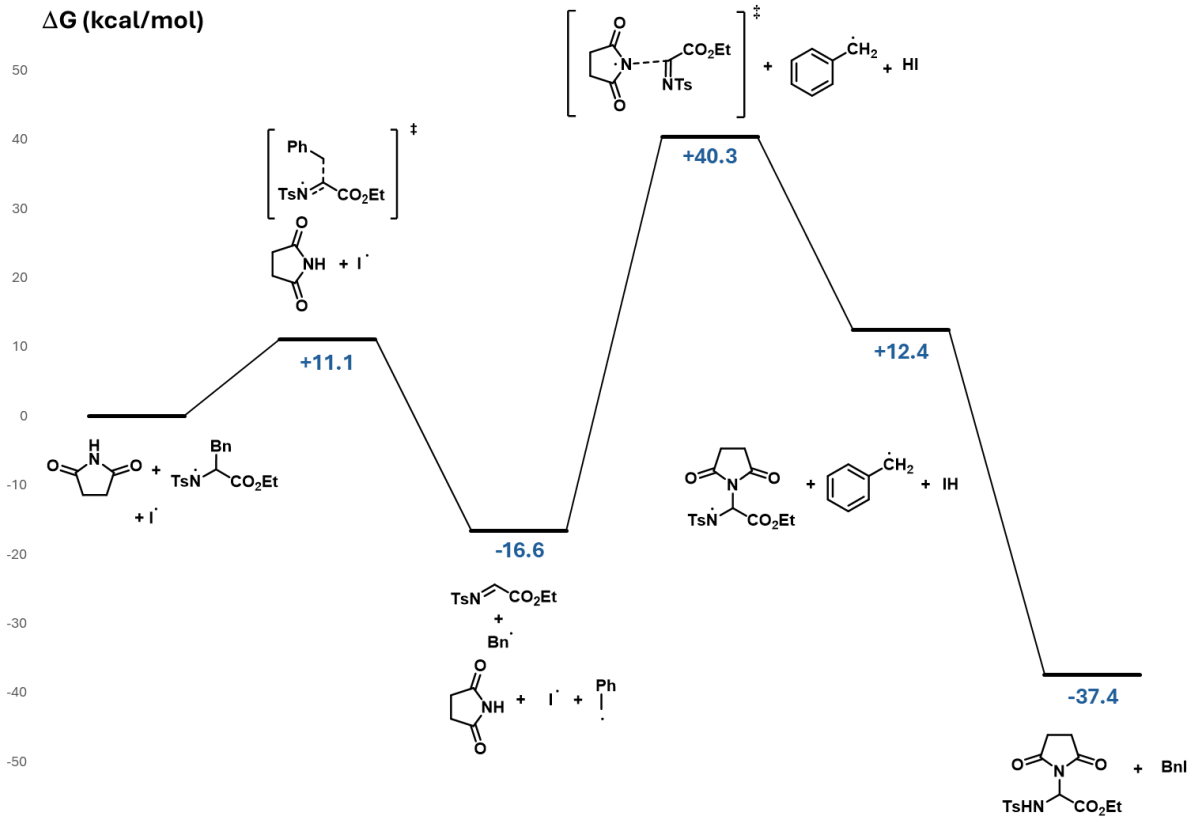
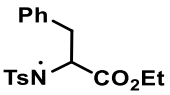


Figure S6. Energy profile considering HI as hydrogen donor.

CARTESIAN COORDINATES OF THE COMPUTED STRUCTURES



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O	-1.28718800	3.03015900	-0.31284000
C	-0.78149300	4.40007700	-0.41362400
H	-1.68142900	4.99799000	-0.54976000
H	-0.15828100	4.47129800	-1.30423400
C	-0.02782500	4.79616700	0.84171600
H	0.86708700	4.18646800	0.97554400
H	0.27864100	5.84250100	0.75863600
H	-0.66091300	4.69443000	1.72572700
N	-0.24954400	-0.42250200	-0.44798800
S	0.66375300	-0.39190800	1.00200000
O	0.66748900	0.92680600	1.65045100
O	0.15963200	-1.54582500	1.76181600
C	2.28881300	-0.75483500	0.37583500
C	3.17688500	0.29323300	0.13323100
C	2.64326500	-2.08306400	0.13003300
C	4.44477400	-0.00402900	-0.35274800
H	2.87740100	1.31613800	0.31781200
C	3.91456900	-2.35647700	-0.35782800
H	1.94106600	-2.88316800	0.32578100
C	4.83451800	-1.32654500	-0.60431000
H	5.14166200	0.80466900	-0.54216700
H	4.19820100	-3.38535500	-0.54913900
C	6.22091900	-1.63965400	-1.10271900
H	6.88916900	-1.85078500	-0.26079800
H	6.22183700	-2.51980900	-1.74879400
H	6.64444400	-0.79965700	-1.65609900
C	-2.42406300	0.56826400	0.29424400
H	-2.08033200	0.56842300	1.32962900
H	-2.98558200	1.49047700	0.14238600
C	-3.31289900	-0.62346500	0.01428400
C	-3.18928200	-1.81225200	0.74194600
C	-4.28989400	-0.54823200	-0.98632900
C	-4.01875400	-2.90051100	0.47227100
H	-2.43562300	-1.88846000	1.51764800
C	-5.11915400	-1.63518500	-1.25941000
H	-4.40883200	0.37060200	-1.55226500
C	-4.98510700	-2.81647700	-0.53001700
H	-3.91031100	-3.81376100	1.04682200
H	-5.87215900	-1.55702200	-2.03574800
H	-5.63068400	-3.66225600	-0.73820900
H	-1.56040600	0.51512500	-1.68341100

SCF Done: E(UB3LYP) = -1452.01233373
Zero-point correction= 0.348246 (Hartree/Particle)
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Thermal correction to Enthalpy= 0.375220
Thermal correction to Gibbs Free Energy= 0.285650
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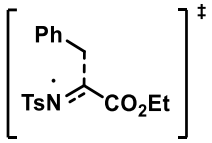

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O	-1.31060000	2.93143800	-0.18476800
C	-1.00130300	4.36109000	-0.26615300
H	-1.97161000	4.84001000	-0.14324500
H	-0.61539100	4.57185400	-1.26290000
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H	0.93442500	4.27645200	0.70269000
H	0.13229200	5.85574300	0.75850100
H	-0.42564800	4.54462900	1.81069400
N	-0.26705700	-0.37347100	-0.28000100
S	0.74658600	-0.09034300	1.04104200
O	0.83802900	1.34274400	1.37602700
O	0.31374500	-1.01933400	2.09492300
C	2.32580100	-0.64000000	0.40823400
C	3.15744800	0.27486400	-0.23661400
C	2.69427400	-1.97674700	0.55175300
C	4.37839400	-0.16388400	-0.73774300
H	2.85380200	1.30822200	-0.34509600
C	3.91941400	-2.39553700	0.04308500
H	2.03741600	-2.67242000	1.05789600
C	4.77977400	-1.50014600	-0.60601800
H	5.02917000	0.54366200	-1.23975500
H	4.21094300	-3.43430200	0.15323400
C	6.11893700	-1.95759800	-1.12486900
H	6.88576700	-1.85404300	-0.34958300
H	6.09286600	-3.00809200	-1.42115000
H	6.43786500	-1.36232400	-1.98263500
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H	-2.48788900	0.84672100	1.16417800
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C	-3.23815400	-1.74886600	0.86718500
C	-4.34092600	-0.90689700	-1.12732500
C	-3.82077500	-2.99053900	0.65911900
H	-2.57559900	-1.59136800	1.71050100
C	-4.92095600	-2.15100500	-1.32988300
H	-4.54425500	-0.09462300	-1.81703100
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H	-3.62079500	-3.80314000	1.34794600
H	-5.57553100	-2.31126900	-2.17879700
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SCF Done: E(UB3LYP) = -1451.99021702
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Thermal correction to Enthalpy= 0.372173
Thermal correction to Gibbs Free Energy= 0.281193
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Sum of electronic and thermal Enthalpies= -1451.618044
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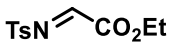

C	1.77946400	0.61944500	0.12780300
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H	-4.04821400	-0.89656200	-2.10833400
C	-5.07012000	-2.39300500	-0.07024900
H	-6.03425600	-1.87395400	-0.05289900
H	-5.03519300	-2.98250400	-0.98912400
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SCF Done: E(RB3LYP) = -1181.02192298
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Thermal correction to Enthalpy= 0.249139
Thermal correction to Gibbs Free Energy= 0.176066
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Sum of electronic and thermal Free Energies= -1180.845857

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C	1.13264700	-1.21124900	0.00000300
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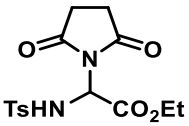
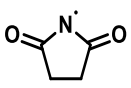
C	1.83808200	0.00000000	0.00000000
H	1.67498000	2.15042900	0.00002200
H	1.67498000	-2.15042900	0.00002100
H	2.92179100	0.00000000	0.00000700

SCF Done: E(UB3LYP) = -270.989881588
Zero-point correction= 0.114093 (Hartree/Particle)
Thermal correction to Energy= 0.120346
Thermal correction to Enthalpy= 0.121337
Thermal correction to Gibbs Free Energy= 0.082563
Sum of electronic and zero-point Energies= -270.875789
Sum of electronic and thermal Energies= -270.869536
Sum of electronic and thermal Enthalpies= -270.868544
Sum of electronic and thermal Free Energies= -270.907318



C	-1.34293100	-0.04268300	-1.13084700
C	-0.68361400	1.35552400	-1.11323700
O	0.48904500	1.55428400	-1.29324300
O	-1.63102100	2.28839000	-1.00470600
C	-1.22102500	3.69021300	-1.07522300
H	-2.09389500	4.19388400	-1.48823400
H	-0.39188600	3.76823500	-1.77778300
C	-0.85624300	4.23255900	0.29355100
H	0.01069400	3.71575500	0.70746800
H	-0.61169700	5.29430400	0.20007200
H	-1.69159200	4.13389500	0.98971000
N	-0.39536000	-1.12075400	-1.37037900
S	0.51510900	-1.97856200	-0.23096600
O	-0.20201200	-2.06971100	1.04340300
O	0.85644700	-3.20645000	-0.95758500
C	2.00834300	-1.03734700	0.04004900
C	2.15228100	-0.30311700	1.21221800
C	3.01967500	-1.08071700	-0.92044800
C	3.33588400	0.40147300	1.42145600
H	1.35380200	-0.27652000	1.94126500
C	4.18998000	-0.36946000	-0.69357800
H	2.89562800	-1.66208500	-1.82527800
C	4.36877200	0.38094600	0.47901500
H	3.45324700	0.97670200	2.33310900
H	4.97977600	-0.39904700	-1.43636900
C	5.65624300	1.12738400	0.71845900
H	6.46767000	0.43111200	0.95422100
H	5.95857600	1.68724000	-0.17017200
H	5.56291400	1.82618700	1.55116700
H	-0.69848000	-1.77858100	-2.07943300
C	-3.22975600	-0.25966200	2.13384100
C	-4.15187300	-1.01199100	1.16426000
H	-2.84846100	-0.88806000	2.94053100
H	-3.70145500	0.61161300	2.59146900
H	-4.29592200	-2.06082500	1.42974900
H	-5.14105900	-0.56072400	1.06859400
N	-2.26304100	-0.23424200	-0.01553100
C	-2.05578900	0.20557200	1.29636400
C	-3.45540500	-0.94539700	-0.17909900
O	-1.09879900	0.85431100	1.65032000
O	-3.82244100	-1.40677400	-1.23734400
H	-1.97780100	-0.04329900	-2.02069500

SCF Done: E(RB3LYP) = -1541.82118447
Zero-point correction= 0.324317 (Hartree/Particle)
Thermal correction to Energy= 0.350643
Thermal correction to Enthalpy= 0.351635
Thermal correction to Gibbs Free Energy= 0.262040
Sum of electronic and zero-point Energies= -1541.496867
Sum of electronic and thermal Energies= -1541.470542
Sum of electronic and thermal Enthalpies= -1541.469550
Sum of electronic and thermal Free Energies= -1541.559145

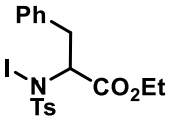


C	0.75217100	1.25577200	0.00039900
C	-0.75175200	1.25575500	-0.00046400
H	1.20416700	1.69794100	-0.88753600
H	1.20277400	1.69617000	0.88996800
H	-1.20367200	1.69752800	0.88770200
H	-1.20250300	1.69608400	-0.88996700
C	1.09399200	-0.26496700	-0.00031500
C	-1.09445500	-0.26531300	0.00025800
N	0.00026400	-1.07022200	-0.00030900
O	-2.23623200	-0.69876000	0.00026900
O	2.23593900	-0.69919700	0.00007300

SCF Done: E(UB3LYP) = -360.084732992
Zero-point correction= 0.074480 (Hartree/Particle)
Thermal correction to Energy= 0.081241
Thermal correction to Enthalpy= 0.082233
Thermal correction to Gibbs Free Energy= 0.041760
Sum of electronic and zero-point Energies= -360.010253
Sum of electronic and thermal Energies= -360.003492
Sum of electronic and thermal Enthalpies= -360.002500
Sum of electronic and thermal Free Energies= -360.042973

I·

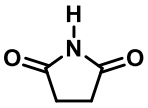
SCF Done: E(UB3LYP) = -11.3640767848
Zero-point correction= 0.000000 (Hartree/Particle)
Thermal correction to Energy= 0.001488
Thermal correction to Enthalpy= 0.002479
Thermal correction to Gibbs Free Energy= -0.018505
Sum of electronic and zero-point Energies= -11.364077
Sum of electronic and thermal Energies= -11.362589
Sum of electronic and thermal Enthalpies= -11.361598
Sum of electronic and thermal Free Energies= -11.382582



C	-1.15498800	1.14605500	-0.46666900
C	-0.41318000	2.47744800	-0.74215000
O	0.63881100	2.54097200	-1.33450800
O	-1.12245100	3.53342200	-0.34307000
C	-0.58770500	4.86380900	-0.62577000
H	-1.47598400	5.49006500	-0.69722900
H	-0.08437300	4.83520800	-1.59160100
C	0.33765000	5.32959400	0.48279500
H	1.22446500	4.69763100	0.55067400
H	0.66069100	6.35288900	0.27236900
H	-0.17527000	5.32435800	1.44695700
N	-0.15396800	0.08616900	-0.20997500
S	0.71624100	0.08256200	1.23794200
O	0.66940200	1.48517400	1.67704800
O	0.25454600	-0.95000100	2.17032600
C	2.37438300	-0.35128000	0.72103100
C	3.01471600	0.42560100	-0.24544200
C	3.01580600	-1.42267300	1.33557900
C	4.32356300	0.11428200	-0.59097300
H	2.48985600	1.24286300	-0.72523900
C	4.32918400	-1.71537000	0.97510700
H	2.49691100	-2.01675100	2.07618700
C	5.00298900	-0.95478600	0.01335000
H	4.82610300	0.70870100	-1.34630700
H	4.83287300	-2.55102400	1.44810700
C	6.43245300	-1.25934600	-0.35473300
H	7.11460600	-0.57296400	0.15806600
H	6.70964300	-2.27595400	-0.07098800
H	6.59923900	-1.14079400	-1.42780600
C	-2.32624700	1.23824800	0.53751300
H	-1.93042200	1.41193900	1.53882100
H	-2.90204900	2.12566300	0.27078700

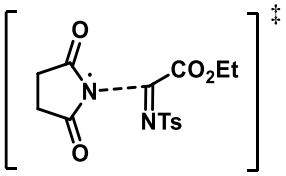
C	-3.24389700	0.03286500	0.52892500
C	-3.17665200	-0.93745800	1.53364600
C	-4.20133000	-0.11878300	-0.48293800
C	-4.03711400	-2.03592400	1.52440200
H	-2.43928700	-0.83940500	2.32218500
C	-5.06000200	-1.21598800	-0.49795700
H	-4.28210400	0.63228200	-1.26329000
C	-4.97966100	-2.18051300	0.50766700
H	-3.96959700	-2.77799100	2.31234800
H	-5.79591000	-1.31427100	-1.28844500
H	-5.64966100	-3.03296700	0.50060900
H	-1.57249100	0.89432800	-1.44598500
I	-0.34870900	-1.74734300	-1.20105900

SCF Done: E(RB3LYP) = -1463.42463665
Zero-point correction= 0.350609 (Hartree/Particle)
Thermal correction to Energy= 0.378443
Thermal correction to Enthalpy= 0.379435
Thermal correction to Gibbs Free Energy= 0.285185
Sum of electronic and zero-point Energies= -1463.074028
Sum of electronic and thermal Energies= -1463.046194
Sum of electronic and thermal Enthalpies= -1463.045202
Sum of electronic and thermal Free Energies= -1463.139451



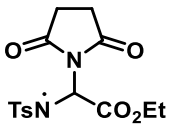
C	0.76856800	1.25686500	-0.00004400
C	-0.76857000	1.25686300	0.00004700
H	1.20113100	1.73727100	-0.87945900
H	1.20124400	1.73739900	0.87924300
H	-1.20112200	1.73727100	0.87946800
H	-1.20126100	1.73739400	-0.87923300
C	1.16872900	-0.21025200	0.00001800
C	-1.16872600	-0.21025500	0.00000800
N	0.00000000	-0.95866300	0.00009100
O	-2.28707000	-0.67663900	-0.00006900
O	2.28707100	-0.67663900	-0.00003300
H	0.00000000	-1.97179700	-0.00001400

SCF Done: E(RB3LYP) = -360.791207425
Zero-point correction= 0.091411 (Hartree/Particle)
Thermal correction to Energy= 0.097932
Thermal correction to Enthalpy= 0.098924
Thermal correction to Gibbs Free Energy= 0.058736
Sum of electronic and zero-point Energies= -360.699797
Sum of electronic and thermal Energies= -360.693276
Sum of electronic and thermal Enthalpies= -360.692284
Sum of electronic and thermal Free Energies= -360.732471



C	-0.75070100	0.35025700	-0.87111400
C	-1.44471400	1.66754400	-1.14752200
O	-1.93618600	1.88323000	-2.23235500
O	-1.41224600	2.50304500	-0.12387100
C	-2.03557000	3.81188600	-0.31740000
H	-3.08630000	3.65010300	-0.56416200
H	-1.54907400	4.29422000	-1.16663600
C	-1.86052600	4.59374700	0.96497600
H	-0.80311500	4.73481000	1.19782300
H	-2.32059000	5.57814600	0.84878900
H	-2.34140000	4.08643100	1.80362200
N	0.10190900	0.24572600	0.08741400
S	0.93783900	-1.27424100	0.19371100
O	0.62467500	-1.77812000	1.53181400
O	0.66237100	-2.11389200	-0.97759700
C	2.62294400	-0.70479100	0.13086500
C	3.19082200	-0.12978800	1.27004400
C	3.34121200	-0.83184800	-1.05752400
C	4.50404300	0.31627700	1.20839700
H	2.61928200	-0.04086600	2.18507700
C	4.65563900	-0.37936100	-1.09590000
H	2.88241100	-1.28093900	-1.92881000
C	5.25716300	0.19863100	0.02979800
H	4.95307300	0.76246900	2.08867600
H	5.22220500	-0.47835800	-2.01485100
C	6.68953600	0.66152600	-0.01190700
H	7.34891600	-0.10278800	0.41329900
H	7.01827700	0.85009300	-1.03511300
H	6.82880200	1.57287400	0.57353200
C	-4.33869200	-2.27778700	-0.03111000
C	-4.26832500	-1.59253800	1.34494200
H	-5.29127000	-2.13472400	-0.54320000
H	-4.14071800	-3.35070800	0.01013600
H	-5.13568800	-0.96722200	1.56241300
H	-4.11962000	-2.27762300	2.18013300
N	-2.65580700	-0.64387500	-0.04192100
C	-3.22495900	-1.62754000	-0.84781300
C	-3.03159800	-0.66258000	1.28645300
O	-2.89999700	-1.88901000	-1.98190600
O	-2.56206100	-0.06622200	2.22176600
H	-0.86341700	-0.39507100	-1.66245500

SCF Done: E(UB3LYP) = -1541.10453315
Zero-point correction= 0.305644 (Hartree/Particle)
Thermal correction to Energy= 0.332840
Thermal correction to Enthalpy= 0.333832
Thermal correction to Gibbs Free Energy= 0.239408
Sum of electronic and zero-point Energies= -1540.798889
Sum of electronic and thermal Energies= -1540.771693
Sum of electronic and thermal Enthalpies= -1540.770701
Sum of electronic and thermal Free Energies= -1540.865126
Frequency= -137.2587



C	-1.40973000	0.40931400	-0.42403700
C	-1.95862400	1.81057200	-0.06064600
O	-3.12007500	2.00700400	0.19942200
O	-1.01184500	2.72964900	-0.15259700
C	-1.40335500	4.11783200	0.09957800
H	-1.81618900	4.17076700	1.10786200
H	-2.18619600	4.38024200	-0.61363100
C	-0.16765500	4.97422200	-0.06098100
H	0.23690500	4.89573500	-1.07225100
H	-0.43038400	6.01894800	0.12269900
H	0.60636700	4.68489600	0.65273100
N	-0.07327700	0.22754000	0.10611700
S	0.67827300	-1.25711800	-0.31369600
O	0.29715000	-2.23167600	0.71441600
O	0.40988700	-1.54820500	-1.72684100

C	2.39430100	-0.82473900	-0.12081800
C	2.96891100	-0.86363800	1.14959900
C	3.12775400	-0.43938400	-1.24169600
C	4.30618700	-0.51319100	1.28865600
H	2.38540000	-1.16798500	2.00905200
C	4.46499400	-0.09256300	-1.07905000
H	2.66429800	-0.41705700	-2.21947100
C	5.07453800	-0.12402400	0.18168200
H	4.76055100	-0.54239500	2.27266400
H	5.04258200	0.20639500	-1.94650500
C	6.53152800	0.22351200	0.34315000
H	7.14724400	-0.68064300	0.28775200
H	6.86917700	0.90025500	-0.44373300
H	6.72356800	0.69045400	1.31122400
C	-4.06446900	-2.23325400	-0.19408700
C	-3.75527300	-1.97145100	1.28823500
H	-5.10170100	-2.02995400	-0.46427300
H	-3.83936400	-3.25548500	-0.50504800
H	-4.61027800	-1.57923900	1.84173500
H	-3.39740800	-2.85485500	1.81952500
N	-2.35043000	-0.62551700	-0.03927000
C	-3.16533600	-1.29003200	-0.96673700
C	-2.65917100	-0.92525300	1.29436700
O	-3.11910500	-1.10252500	-2.15982100
O	-2.11652000	-0.40873600	2.24193800
H	-1.36451500	0.36802000	-1.52455100

SCF Done: E(UB3LYP) = -1541.15602041
Zero-point correction= 0.310337 (Hartree/Particle)
Thermal correction to Energy= 0.336763
Thermal correction to Enthalpy= 0.337755
Thermal correction to Gibbs Free Energy= 0.246405
Sum of electronic and zero-point Energies= -1540.845684
Sum of electronic and thermal Energies= -1540.819257
Sum of electronic and thermal Enthalpies= -1540.818265
Sum of electronic and thermal Free Energies= -1540.909615

C	3.06018200	1.20728700	-0.26915400
C	1.79546900	1.20693700	0.31308600
C	1.14822100	-0.00006000	0.61174000
C	1.79553500	-1.20698600	0.31295900
C	3.06025200	-1.20720800	-0.26929000
C	3.69571100	0.00007100	-0.56311600
H	3.55107300	2.14809500	-0.49093100
H	1.30452300	2.14761800	0.53939800
H	1.30464000	-2.14772000	0.53916500
H	3.55119400	-2.14796600	-0.49116600
H	4.68075700	0.00012300	-1.01573800
C	-0.18408500	-0.00015100	1.26532500
H	-0.38425200	-0.89437100	1.84547600
I	-1.88398800	0.00001800	-0.21096600
H	-0.38428600	0.89392200	1.84569000

SCF Done: E(RB3LYP) = -282.423848642
Zero-point correction= 0.118200 (Hartree/Particle)
Thermal correction to Energy= 0.126096
Thermal correction to Enthalpy= 0.127088
Thermal correction to Gibbs Free Energy= 0.081627
Sum of electronic and zero-point Energies= -282.305648
Sum of electronic and thermal Energies= -282.297752
Sum of electronic and thermal Enthalpies= -282.296761
Sum of electronic and thermal Free Energies= -282.342222

HI

I	0.00000000	0.00000000	0.02976100
H	0.00000000	0.00000000	-1.57734700

SCF Done: E(RB3LYP) = -11.9889623886
Zero-point correction= 0.005256 (Hartree/Particle)
Thermal correction to Energy= 0.007736
Thermal correction to Enthalpy= 0.008728
Thermal correction to Gibbs Free Energy= -0.016051
Sum of electronic and zero-point Energies= -11.983706
Sum of electronic and thermal Energies= -11.981226
Sum of electronic and thermal Enthalpies= -11.980235
Sum of electronic and thermal Free Energies= -12.005013

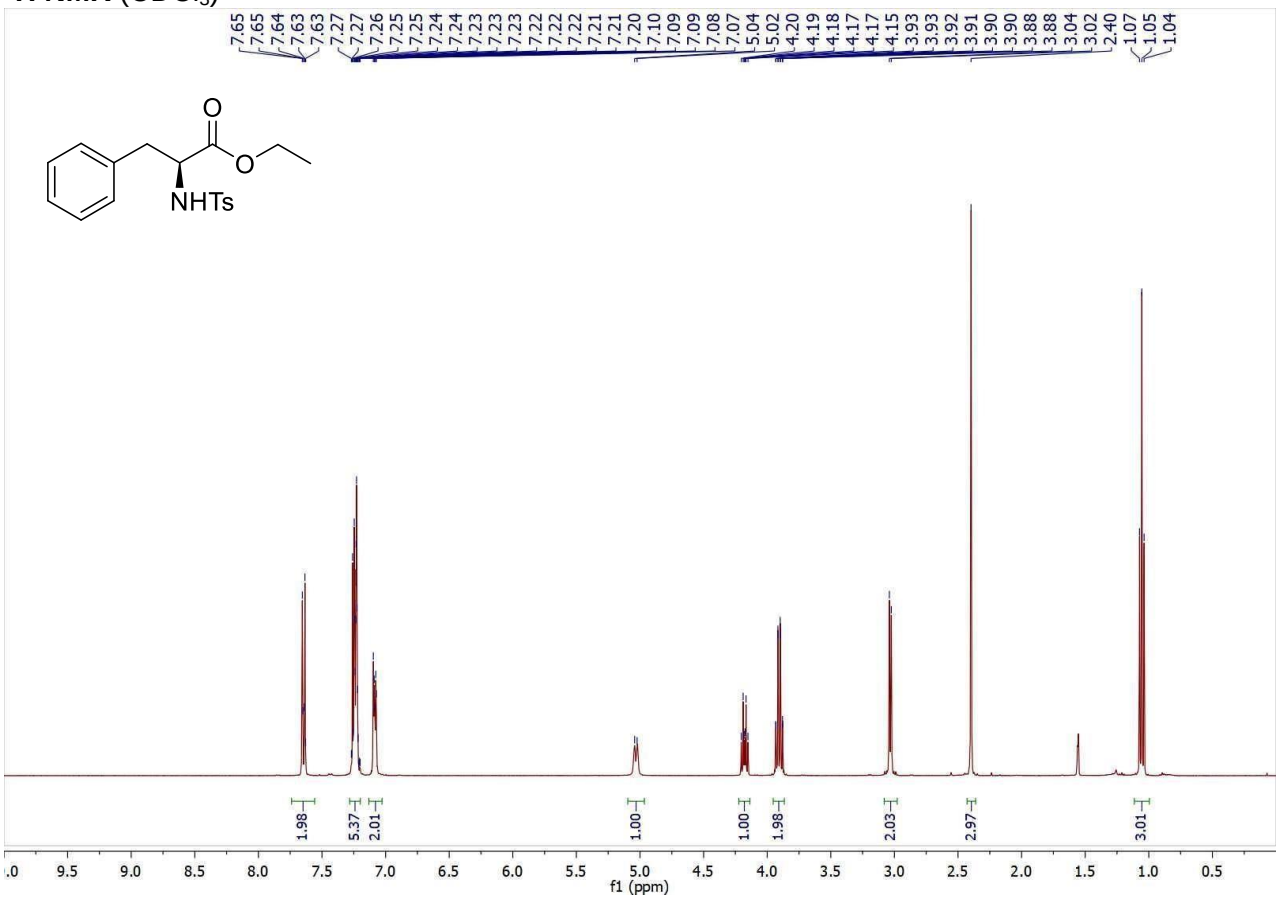
C	-1.20022500	1.20428900	0.00204100
C	0.19460400	1.20141700	-0.00875900
C	0.91409100	-0.00000100	-0.01115400
C	0.19460200	-1.20141800	-0.00875900
C	-1.20022700	-1.20428800	0.00204100
C	-1.90412300	0.00000100	0.00830800
H	-1.73649200	2.14705900	0.00175300
H	0.73209800	2.14451400	-0.01778700
H	0.73209400	-2.14451500	-0.01778700
H	-1.73649500	-2.14705700	0.00175300
H	-2.98831300	0.00000200	0.01363500
C	2.42433000	-0.00000100	0.00880300
H	2.82868500	-0.88546000	-0.48698200
H	2.82868600	0.88539300	-0.48710000
H	2.80141800	0.00006900	1.03738600

SCF Done: E(UB3LYP) = -271.641235309
Zero-point correction= 0.127205 (Hartree/Particle)
Thermal correction to Energy= 0.133997
Thermal correction to Enthalpy= 0.134989
Thermal correction to Gibbs Free Energy= 0.094719
Sum of electronic and zero-point Energies= -271.514031
Sum of electronic and thermal Energies= -271.507238
Sum of electronic and thermal Enthalpies= -271.506246
Sum of electronic and thermal Free Energies= -271.546516

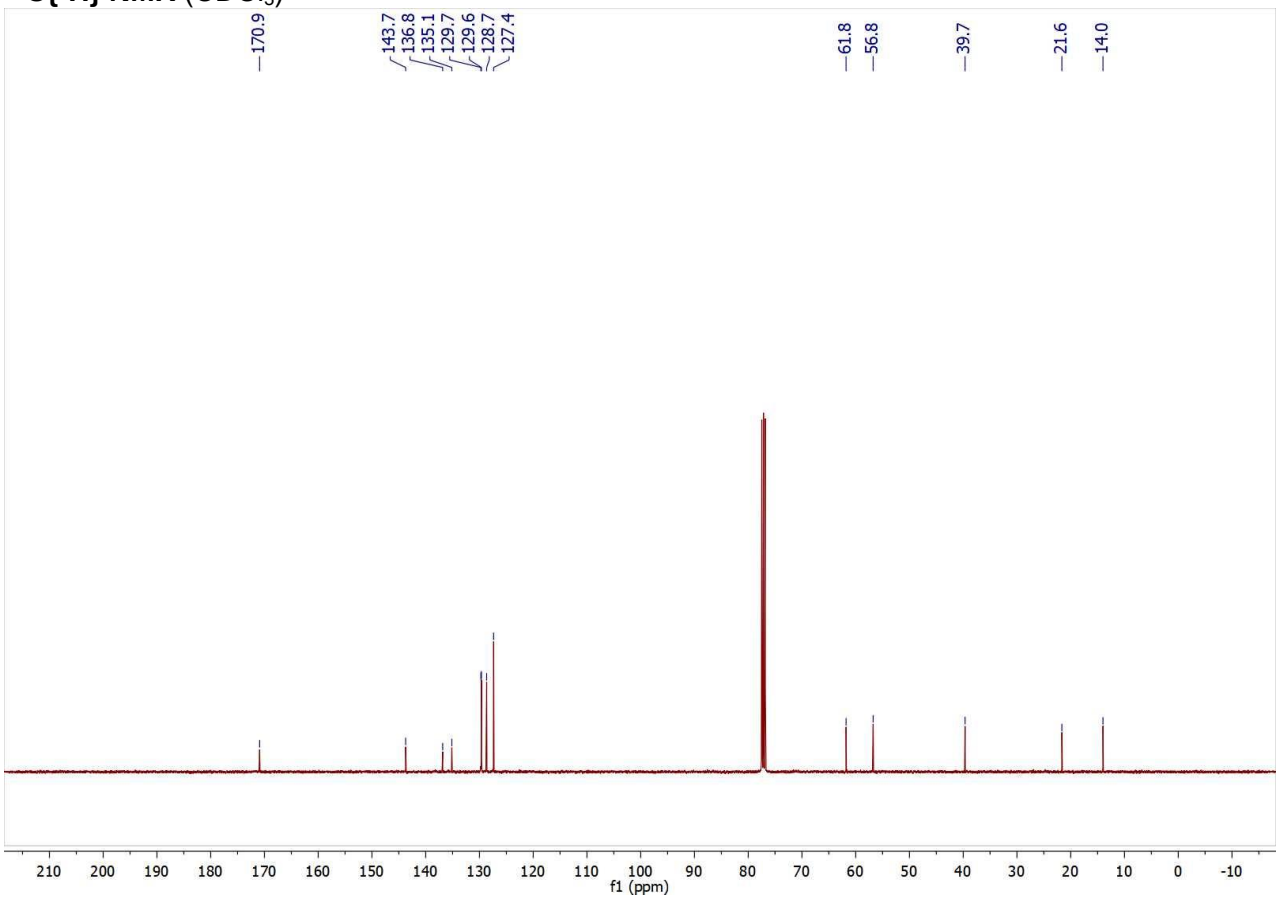
7. NMR Spectra

(*S*)-Ethyl-2-(4-methylphenylsulfonamido)-3-phenylpropanoate (1a)

^{1}H NMR ($CDCl_3$)

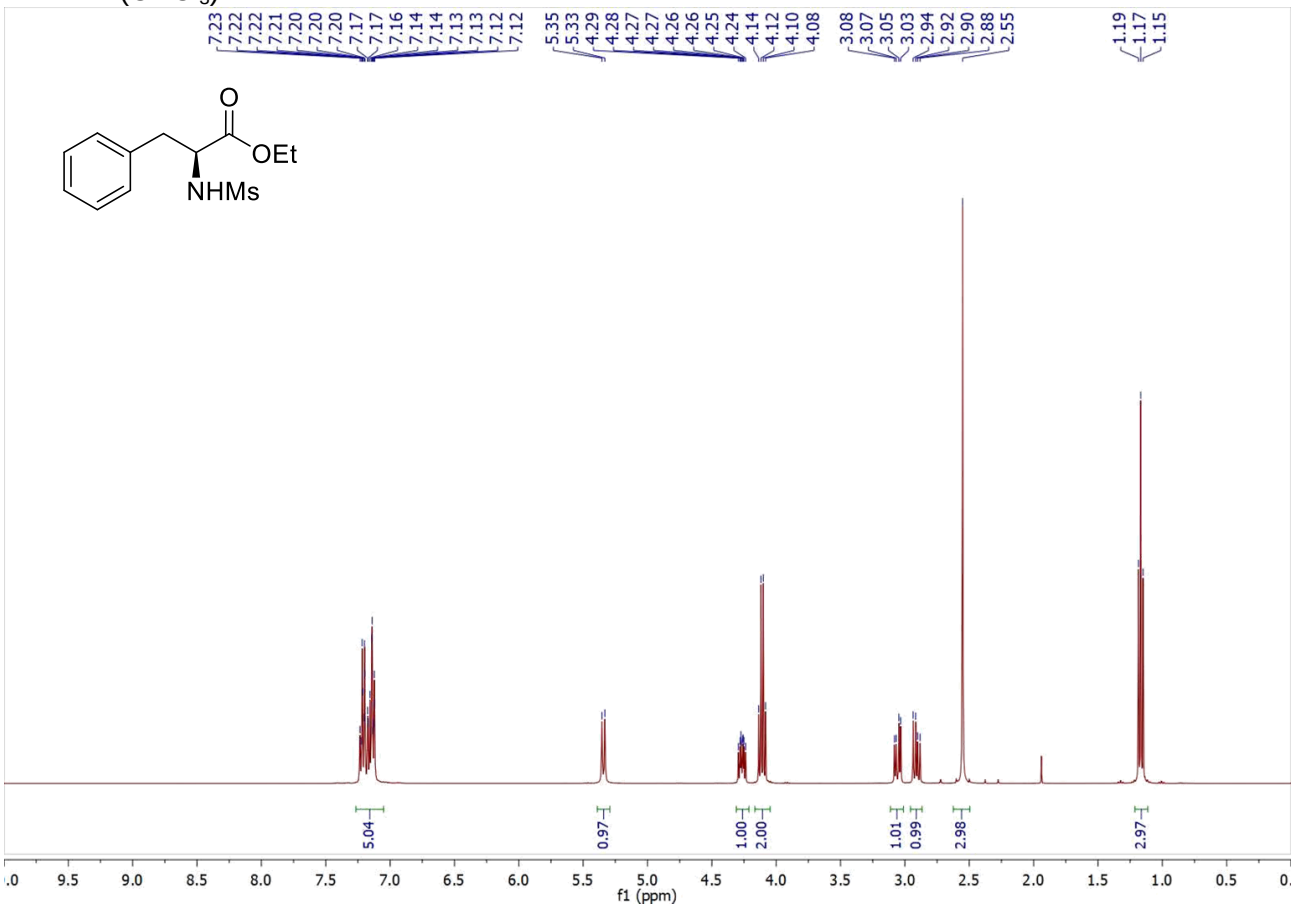


^{13}C{^{1}H} NMR ($CDCl_3$)

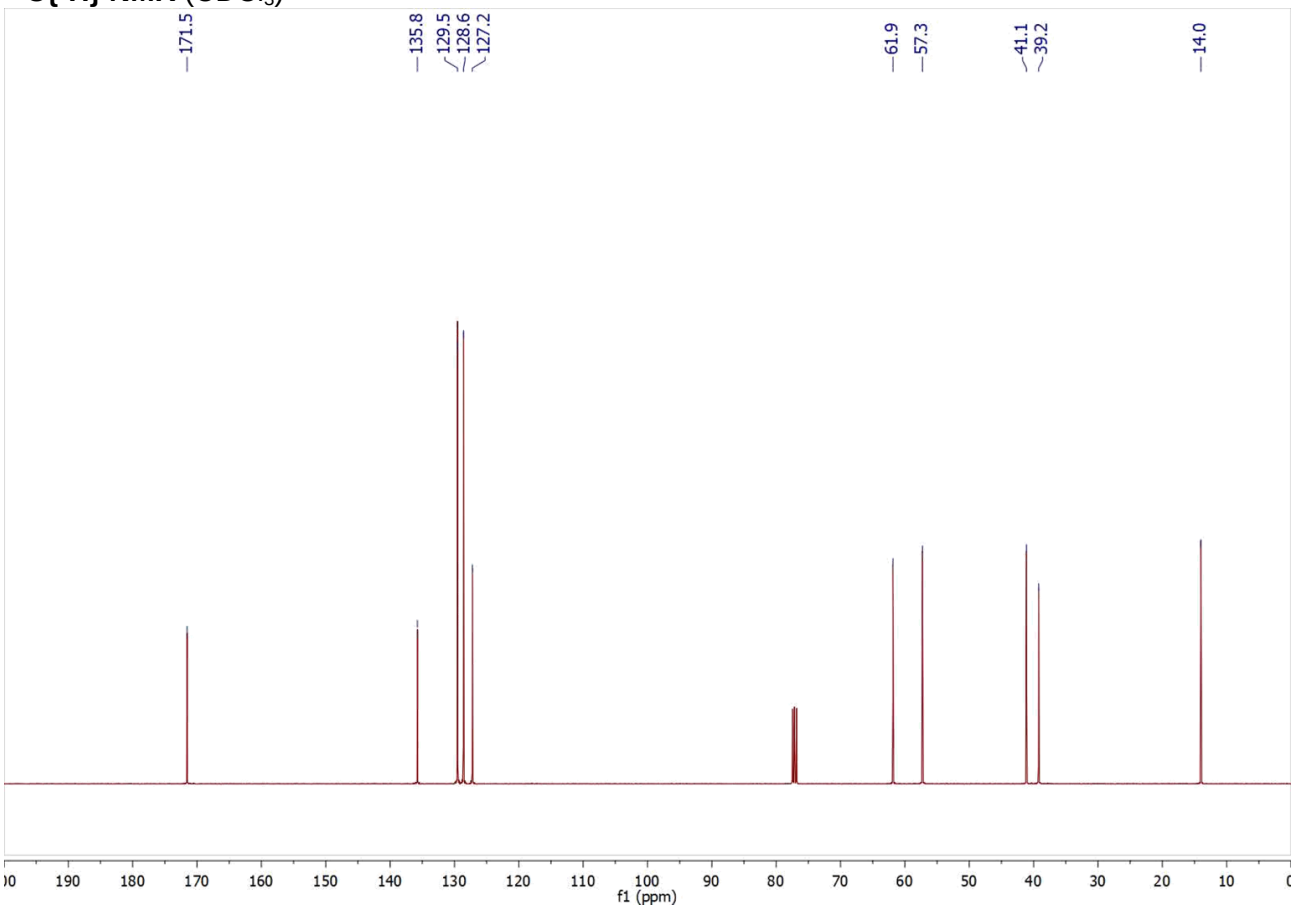


Ethyl 2(*S*)-3-phenyl-2-(methylsulfonamido)propanoate (1aMs)

^{1}H NMR ($CDCl_3$)

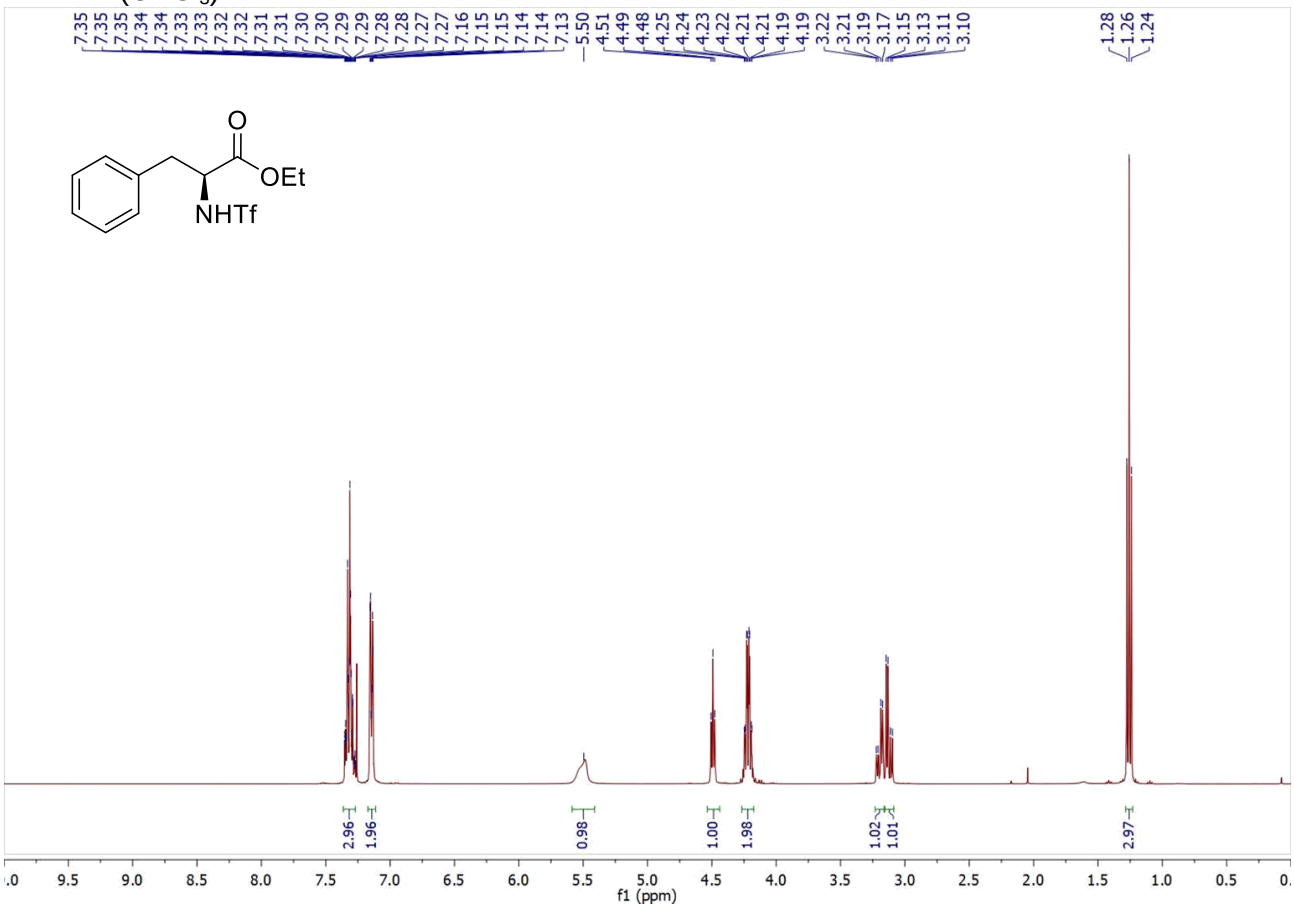


^{13}C{^{1}H} NMR ($CDCl_3$)

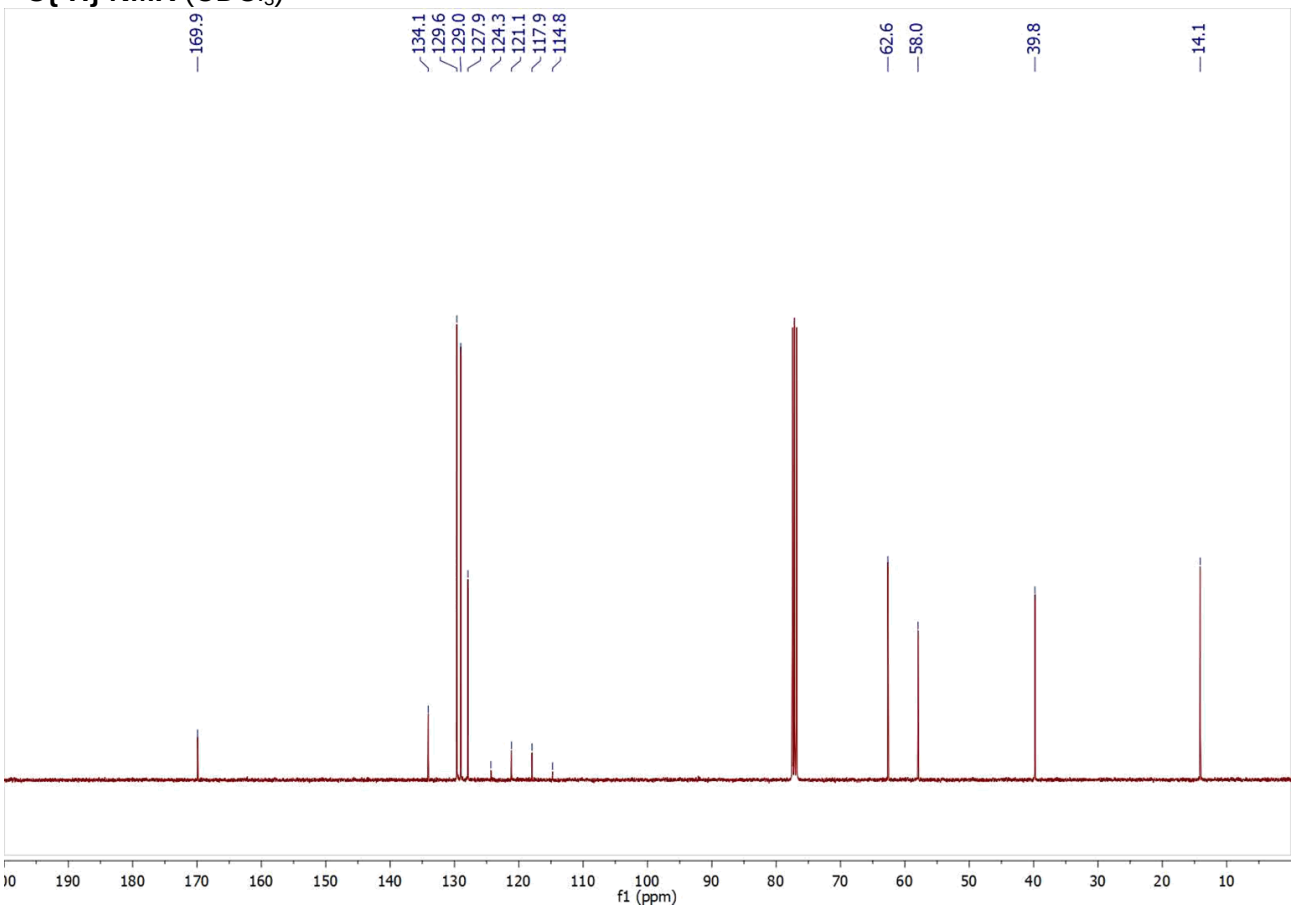


(S)-Ethyl 2-((trifluoromethyl)sulfonamido)-3-phenylpropanoate (1aTf)

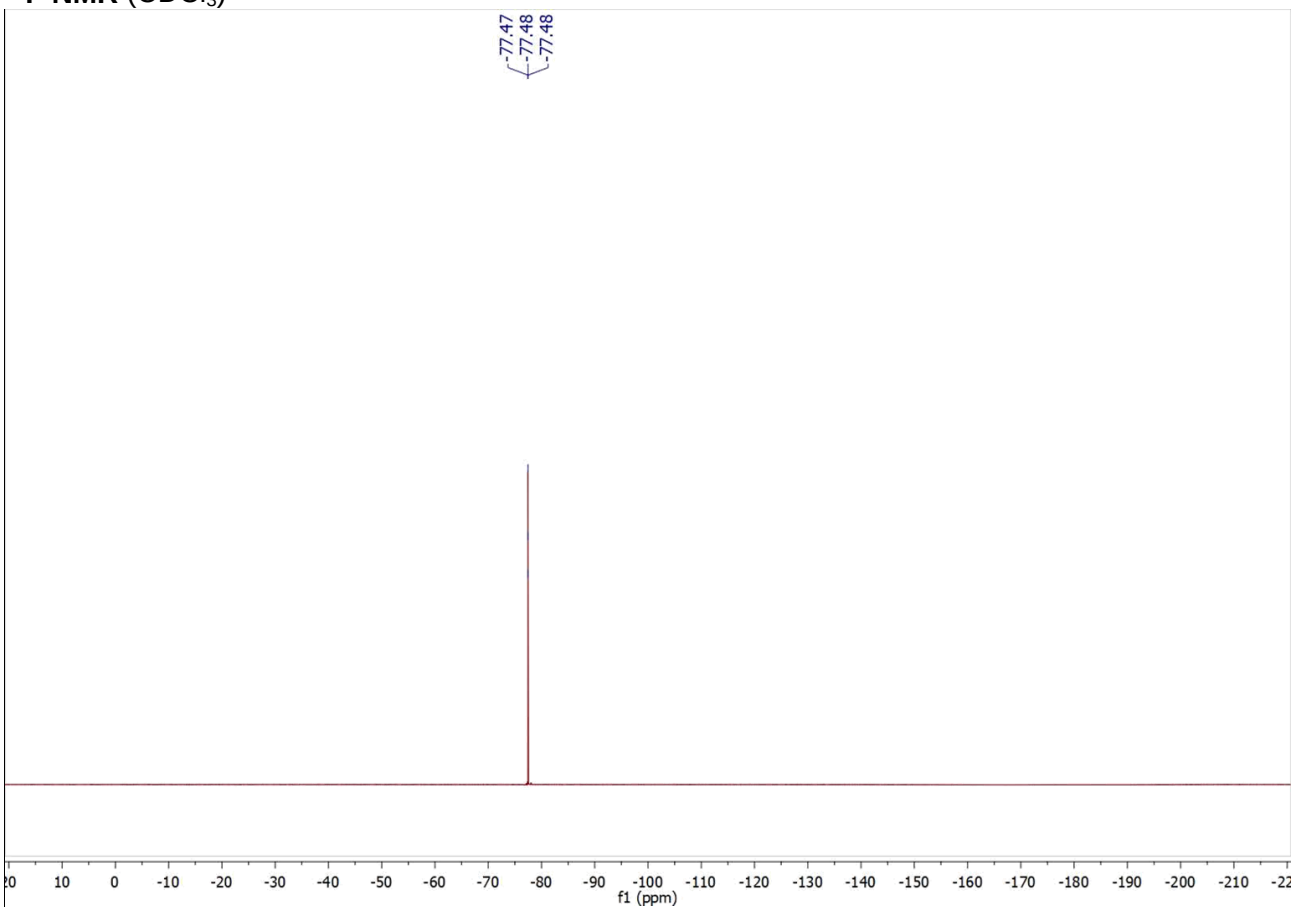
^{1}H NMR ($CDCl_3$)



^{13}C{^{1}H} NMR ($CDCl_3$)

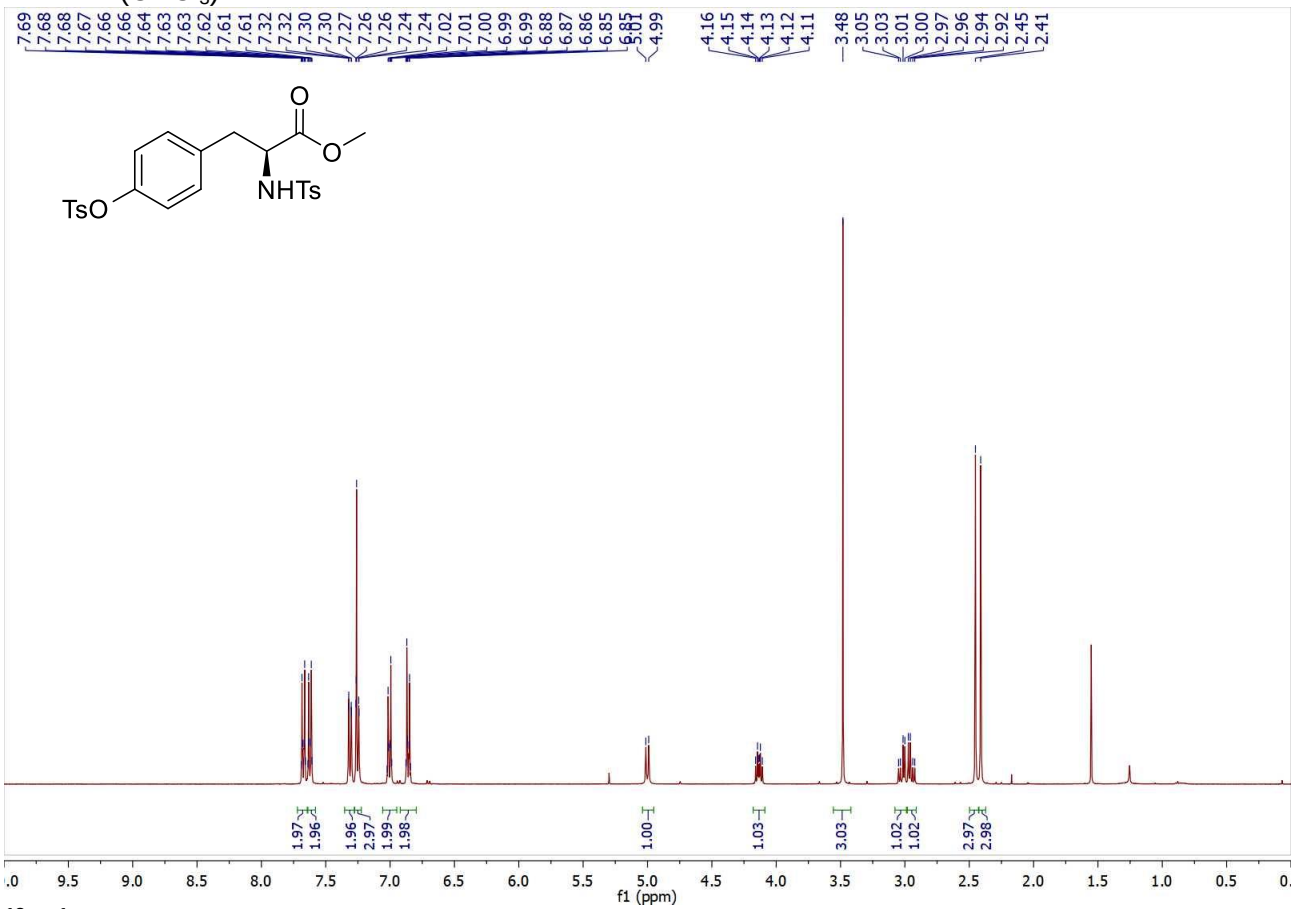


^{19}F NMR ($CDCl_3$)

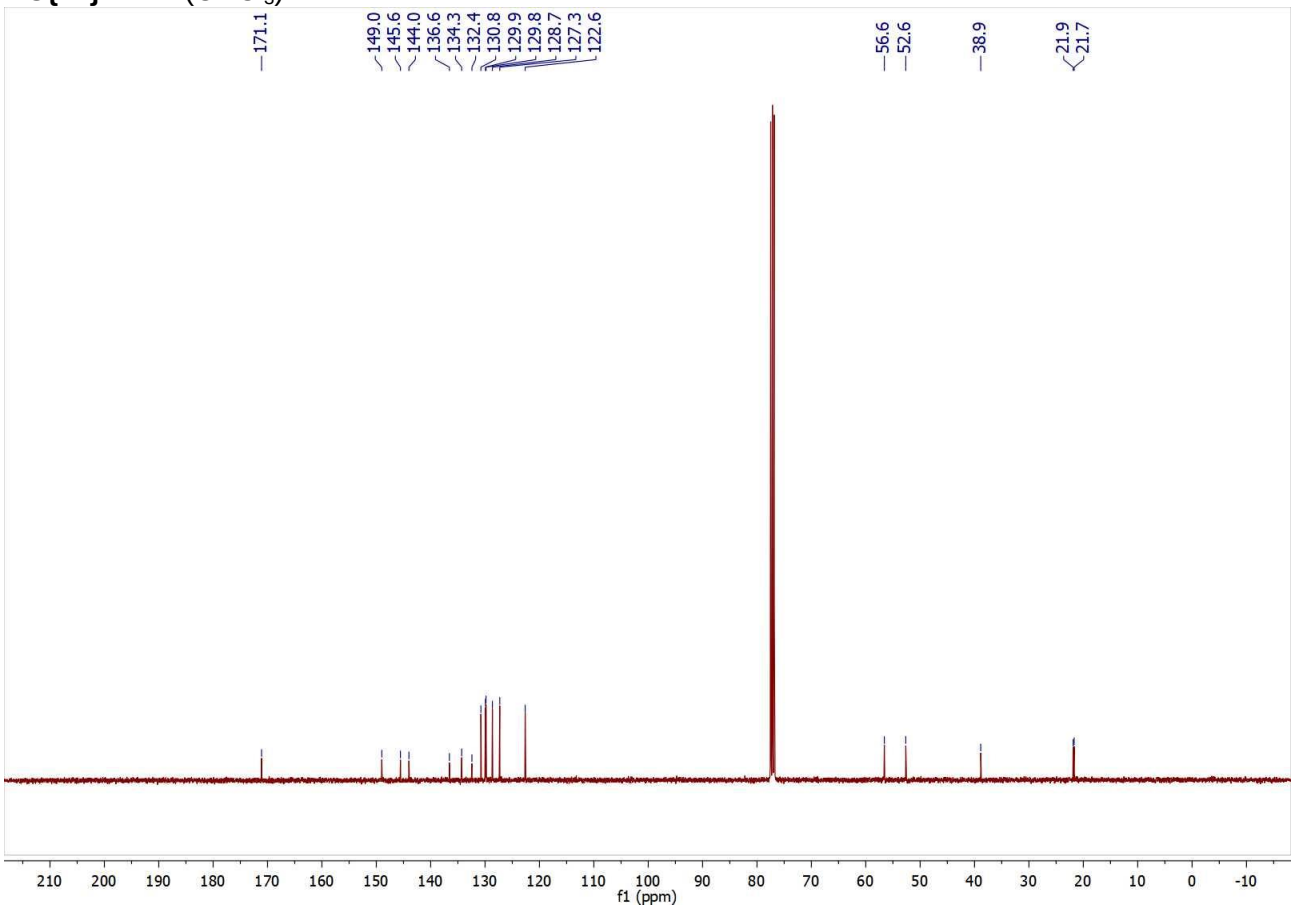


(*S*)-Methyl-2-(4-methylphenylsulfonamido)-3-(4-(tosyloxy)phenyl)propanoate (1b)

^{1}H NMR ($CDCl_3$)

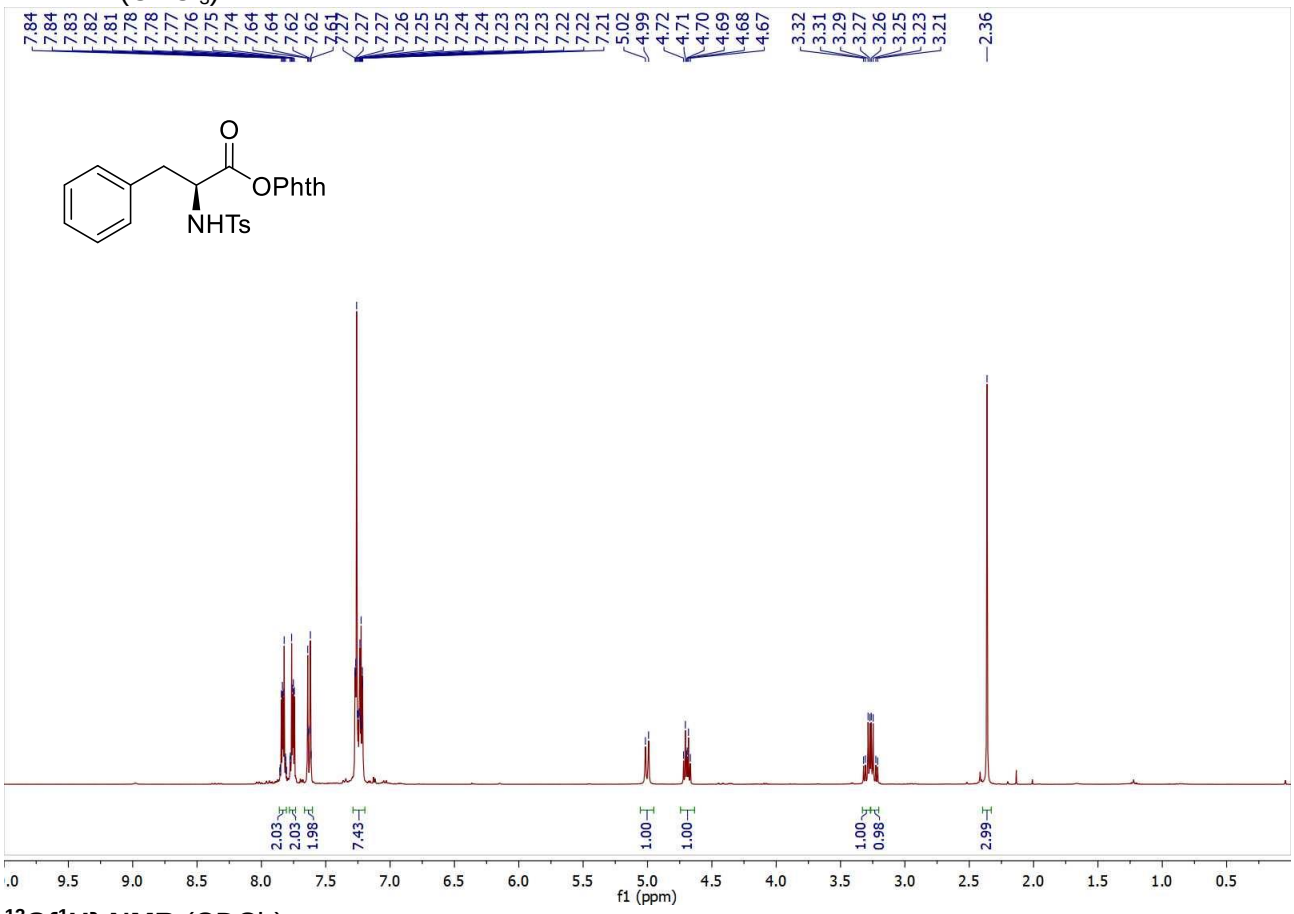


^{13}C{^{1}H} NMR ($CDCl_3$)

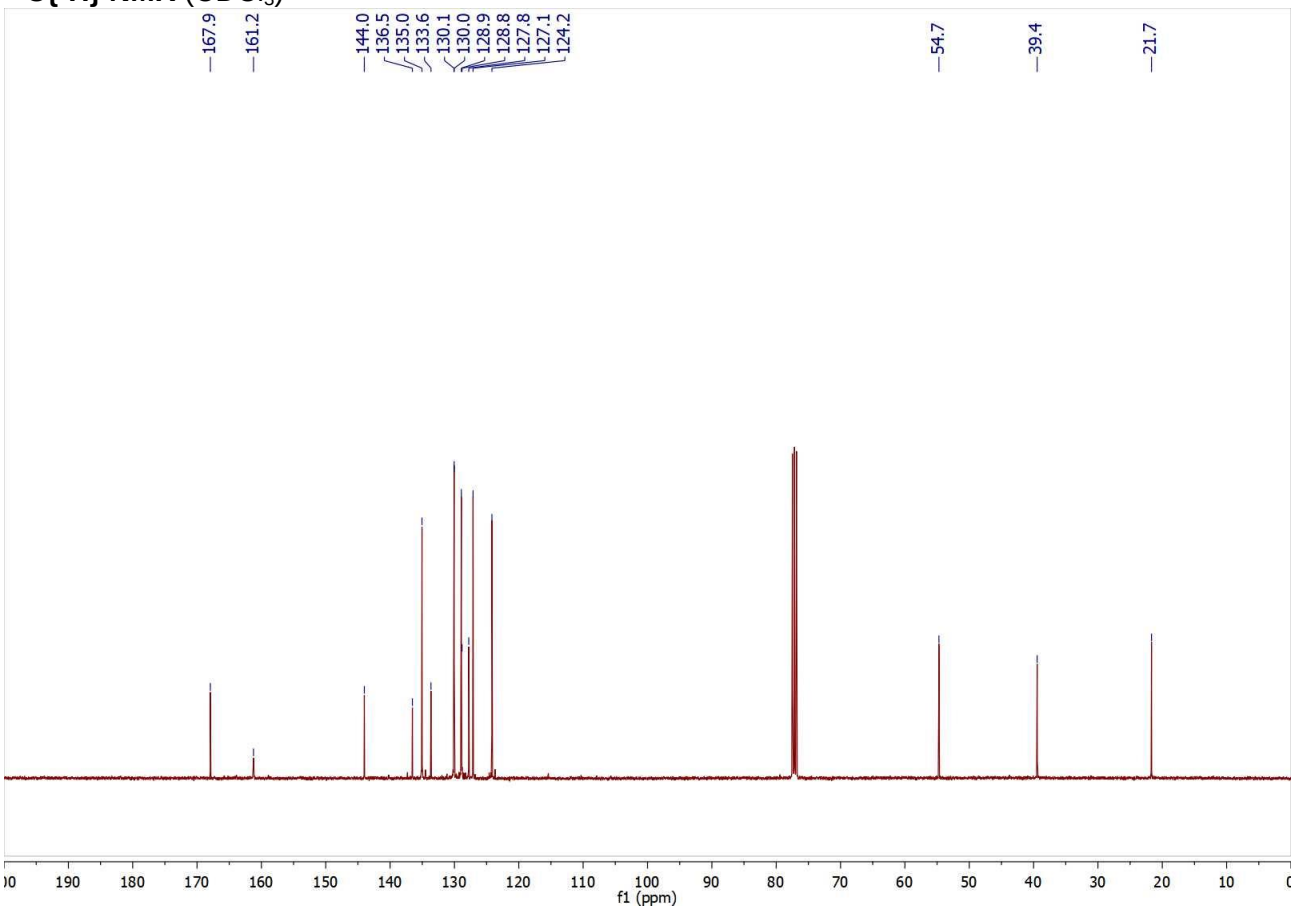


1,3-Dioxoisoindolin-2-yl-(2*S*)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanoate (1c)

^{1}H NMR ($CDCl_3$)

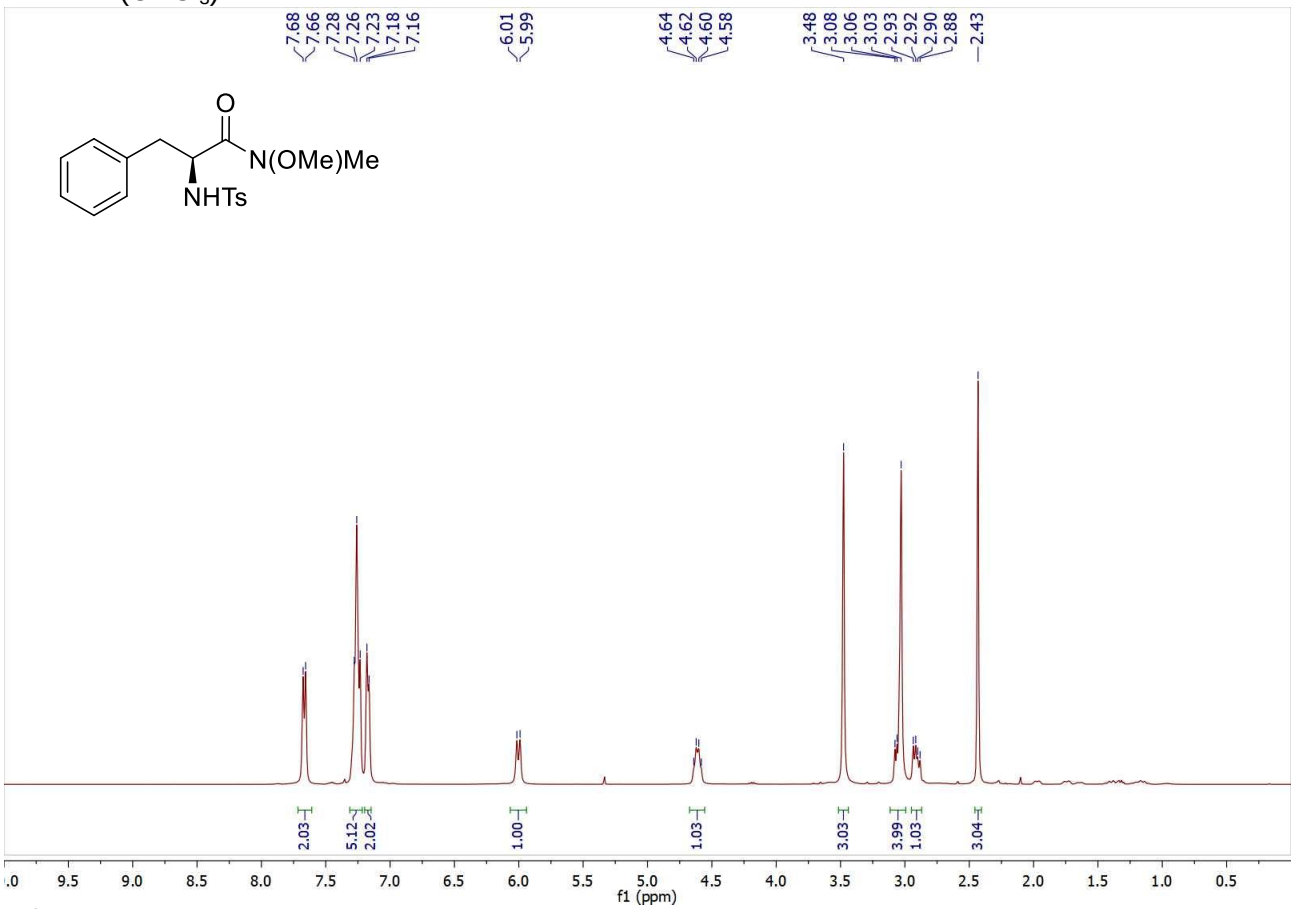


^{13}C{^{1}H} NMR ($CDCl_3$)

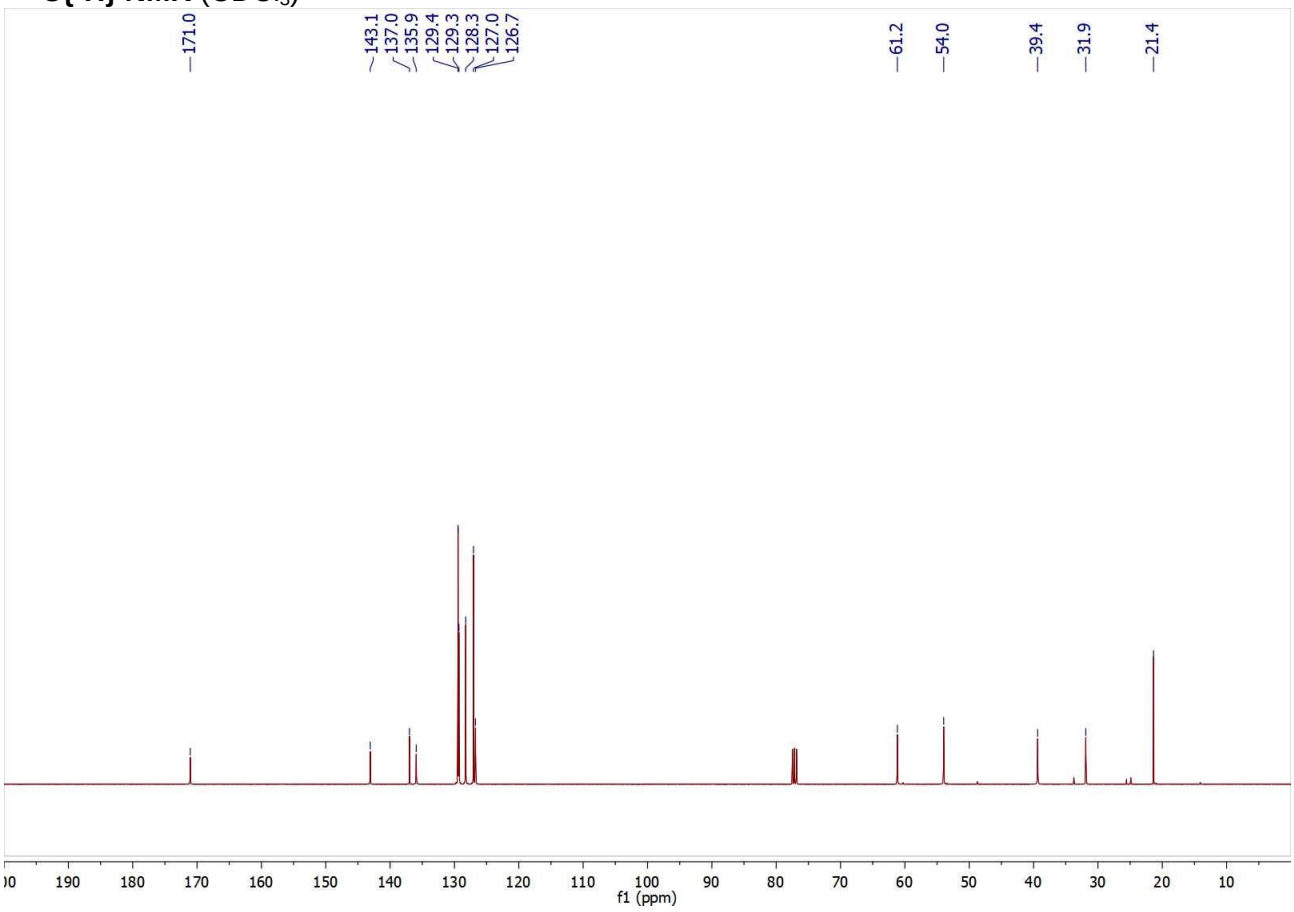


(*S*)-*N*-metoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (1d)

^{1}H NMR ($CDCl_3$)

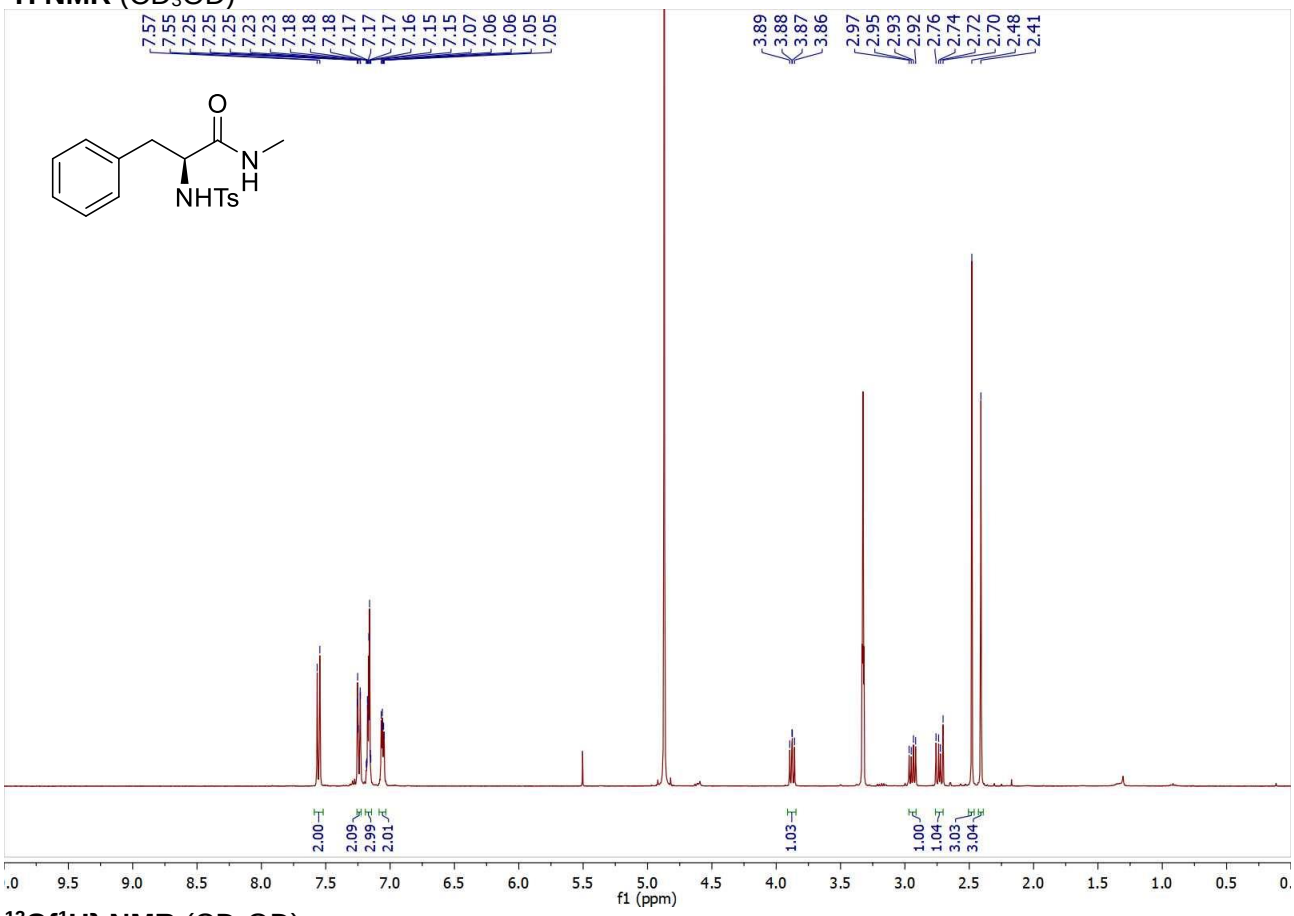


^{13}C{^{1}H} NMR ($CDCl_3$)

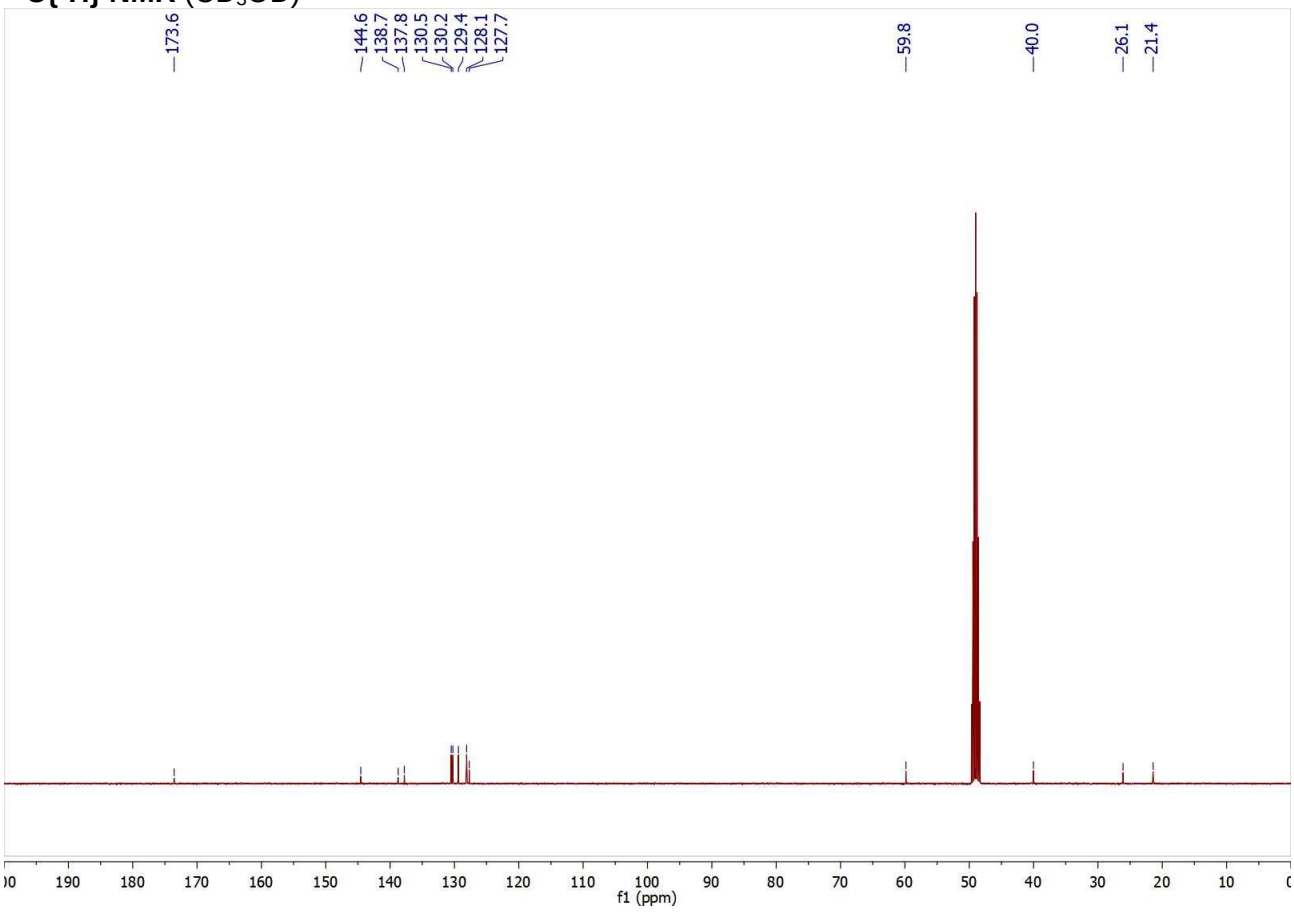


(S)-N-Methyl-2-(4-methylsulfonilamido)-3-phenylpropanamide (1e)

^{1}H NMR (CD_3OD)

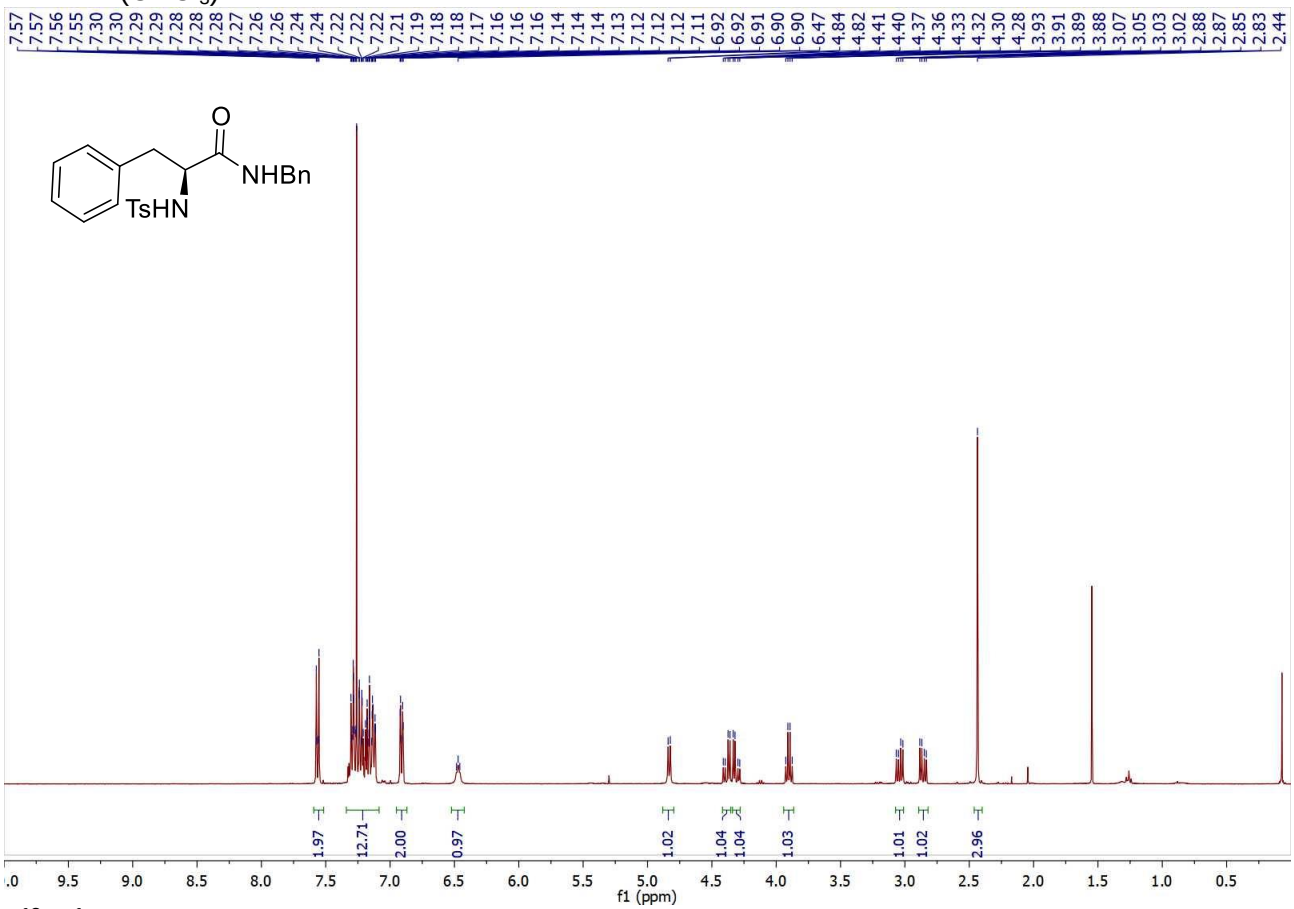


^{13}C{^{1}H} NMR (CD_3OD)

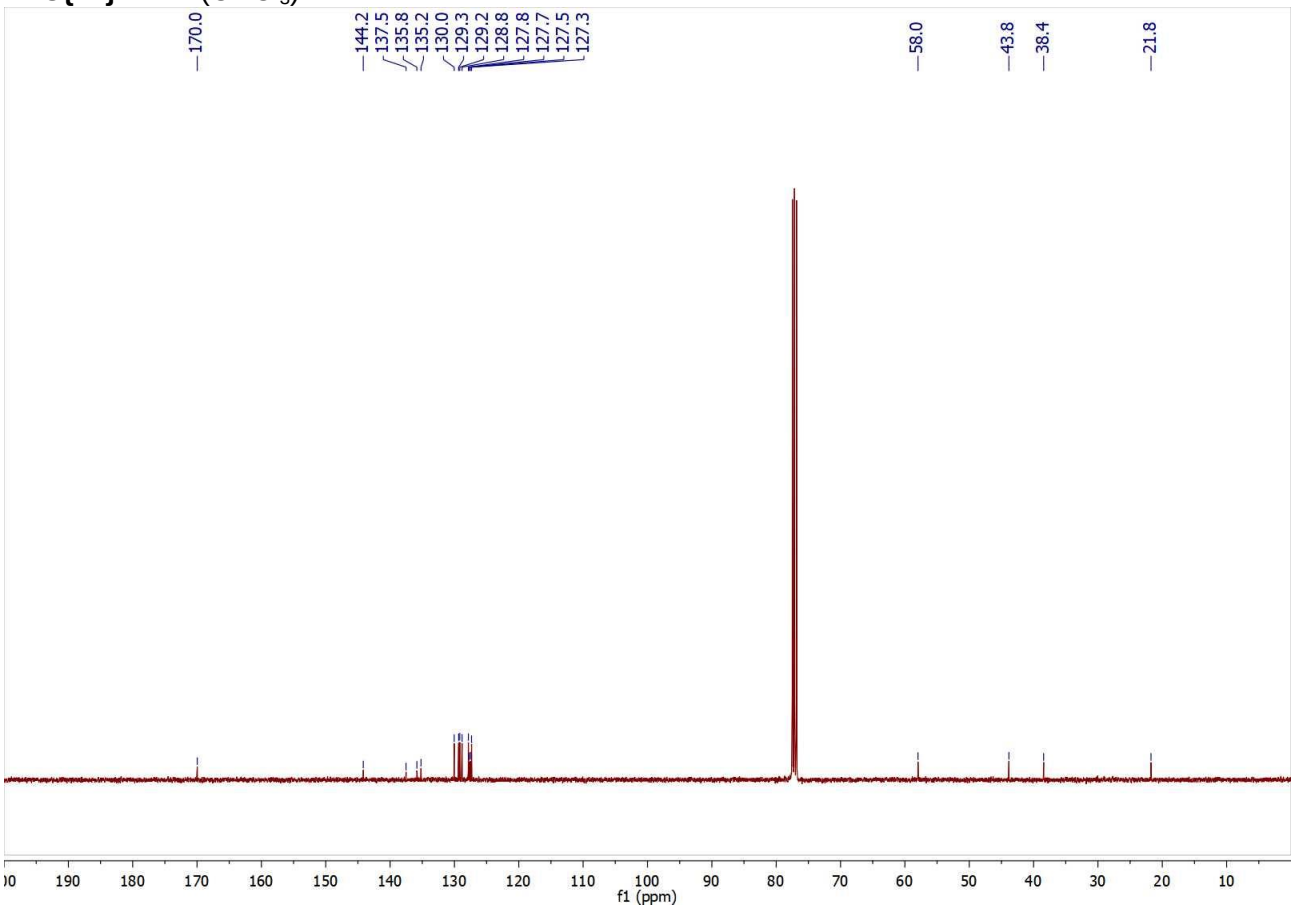


***(S)-N*-Bencyl-2-(4-methylphenyl)sulfonamido)-3-phenylpropanamide (1f)**

^{1}H NMR ($CDCl_3$)

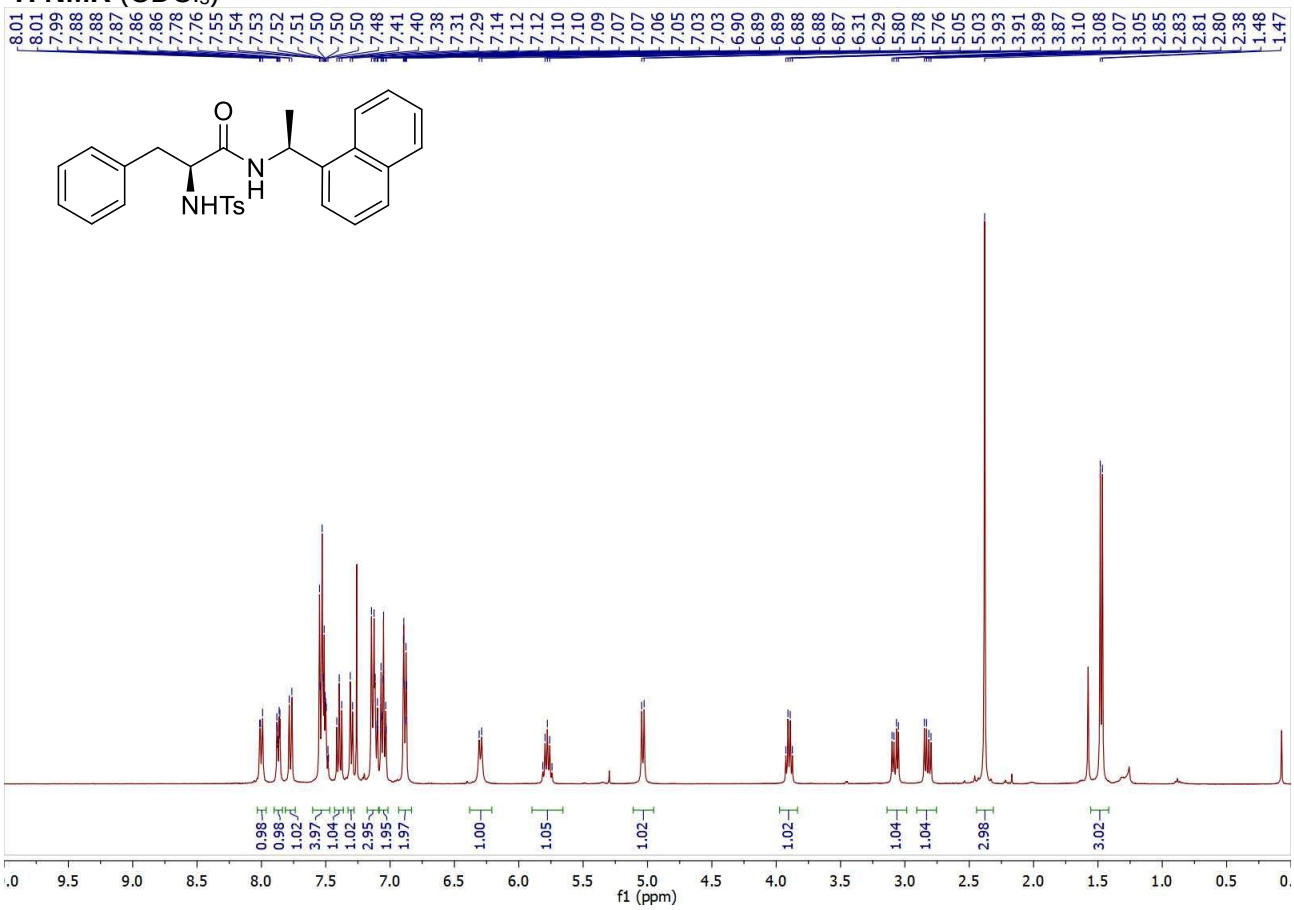


^{13}C{^{1}H} NMR ($CDCl_3$)

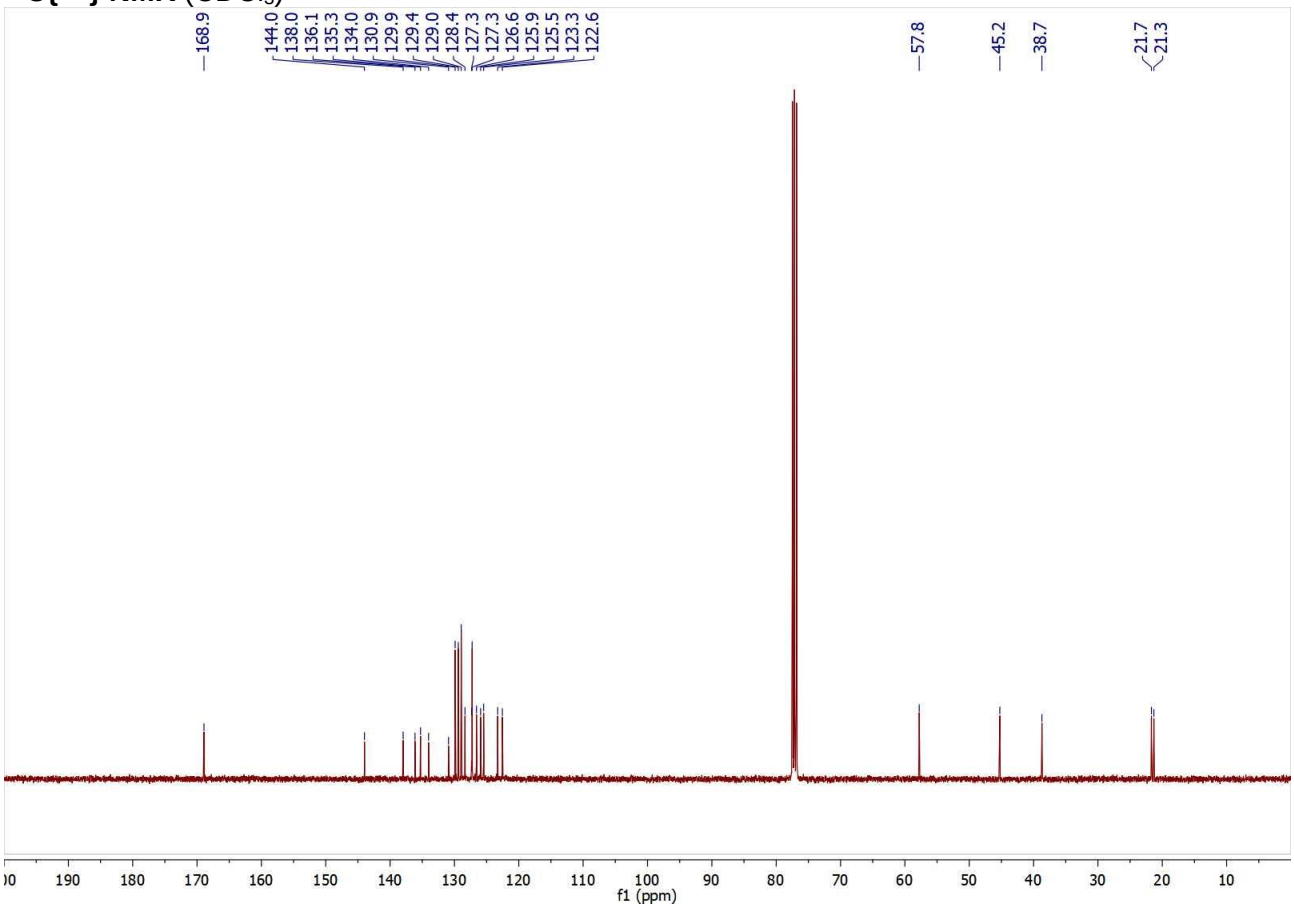


(*S*)-2-((4-Methylphenyl)sulfonamido)-*N*-((*S*)-1-(naphthalen-1-yl)ethyl)-3-phenylpropanamide (1g)

^{1}H NMR ($CDCl_3$)

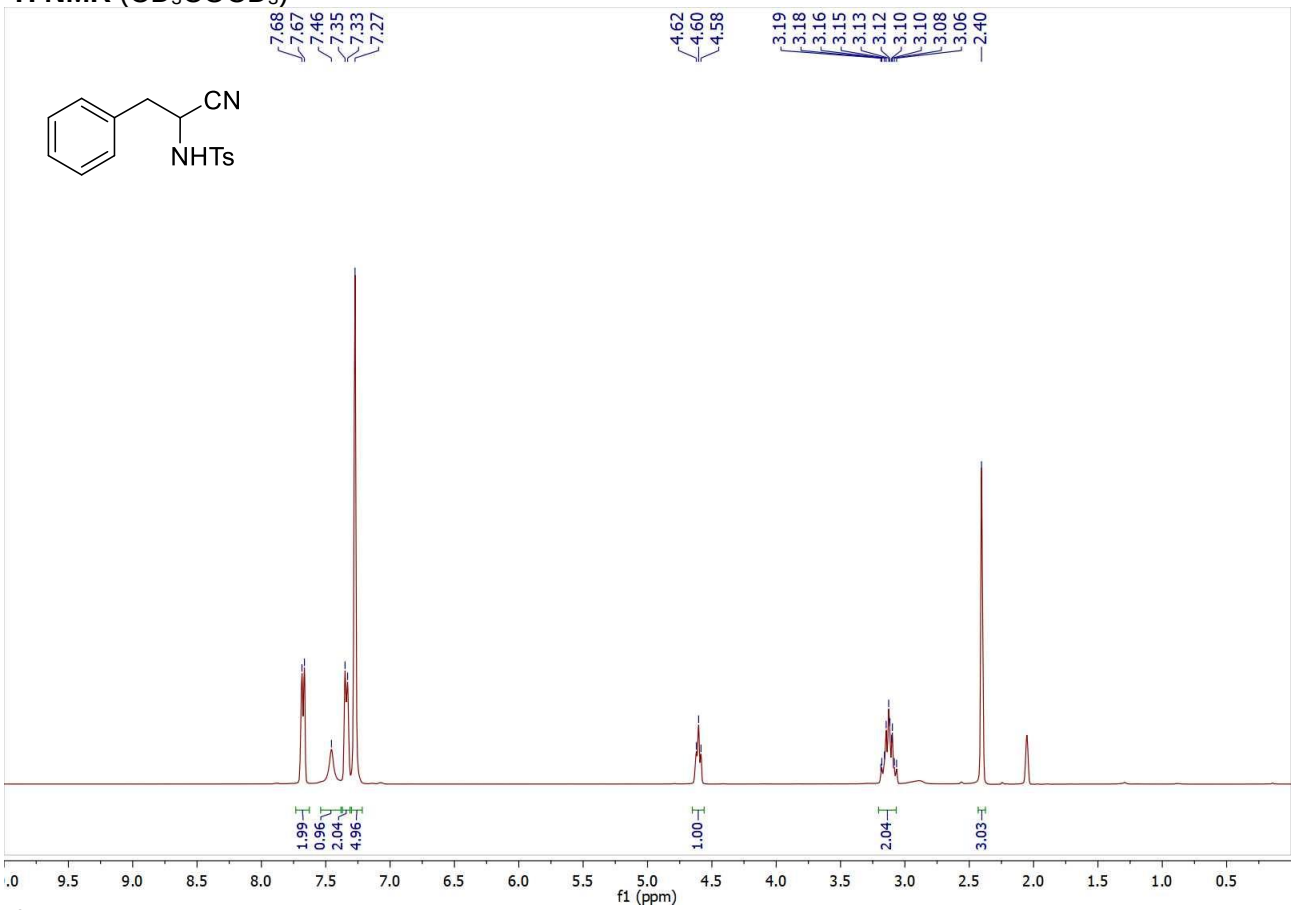


^{13}C{^{1}H} NMR ($CDCl_3$)

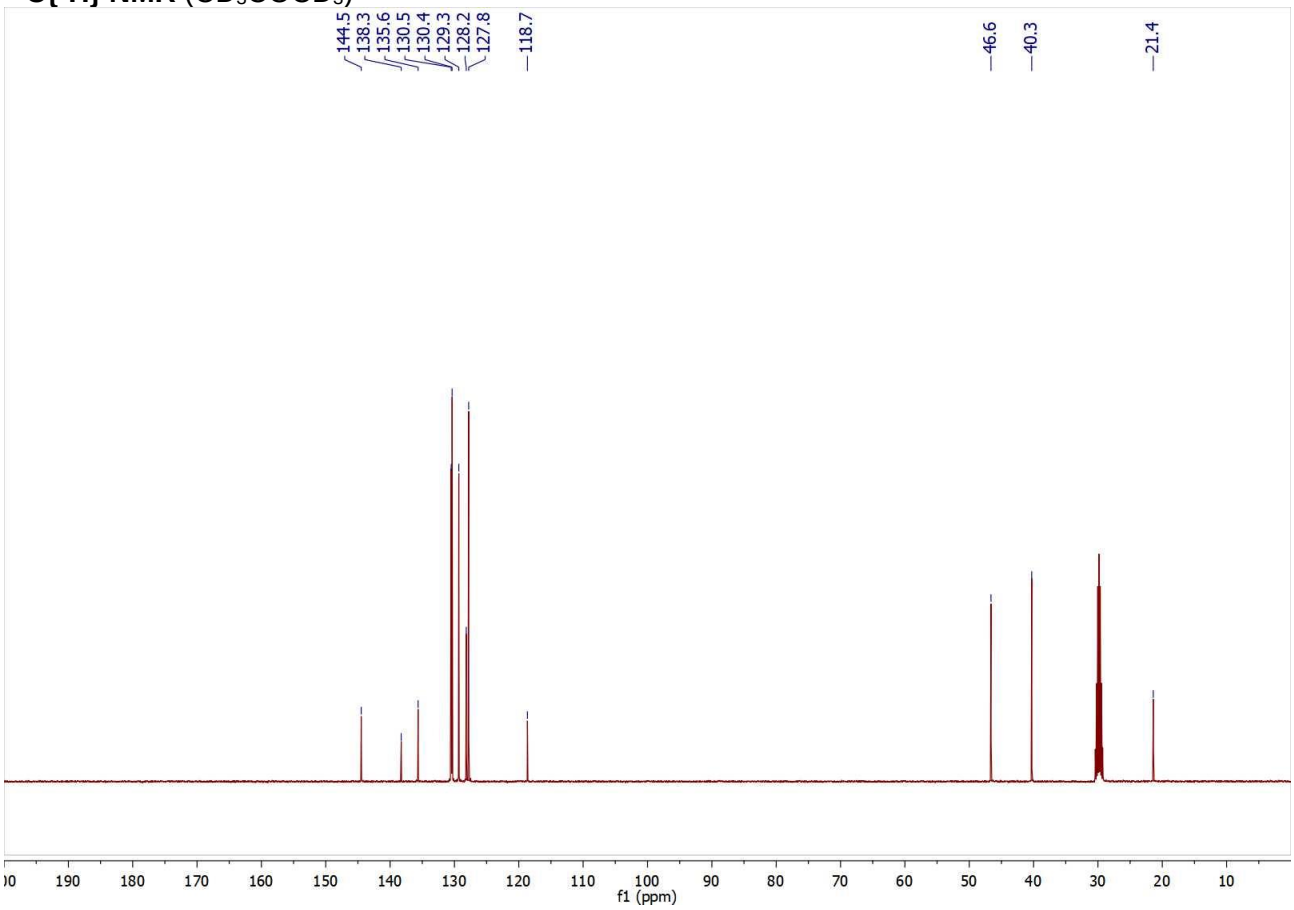


***N*-(1-Cyano-2-phenylethyl)-4-methylbenzenesulfonamide (1h)**

^{1}H NMR (CD_3COCD_3)

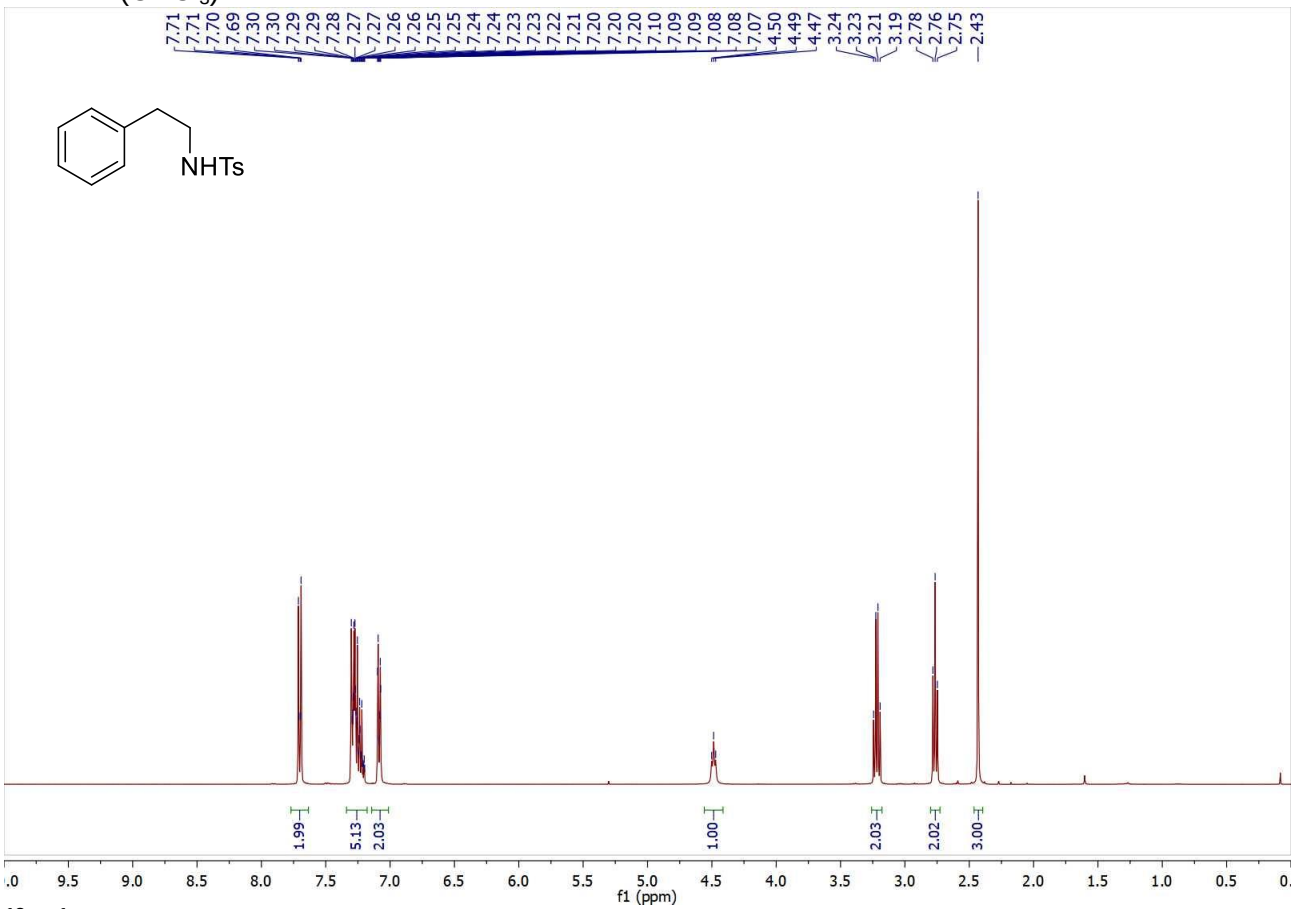


^{13}C{^{1}H} NMR (CD_3COCD_3)

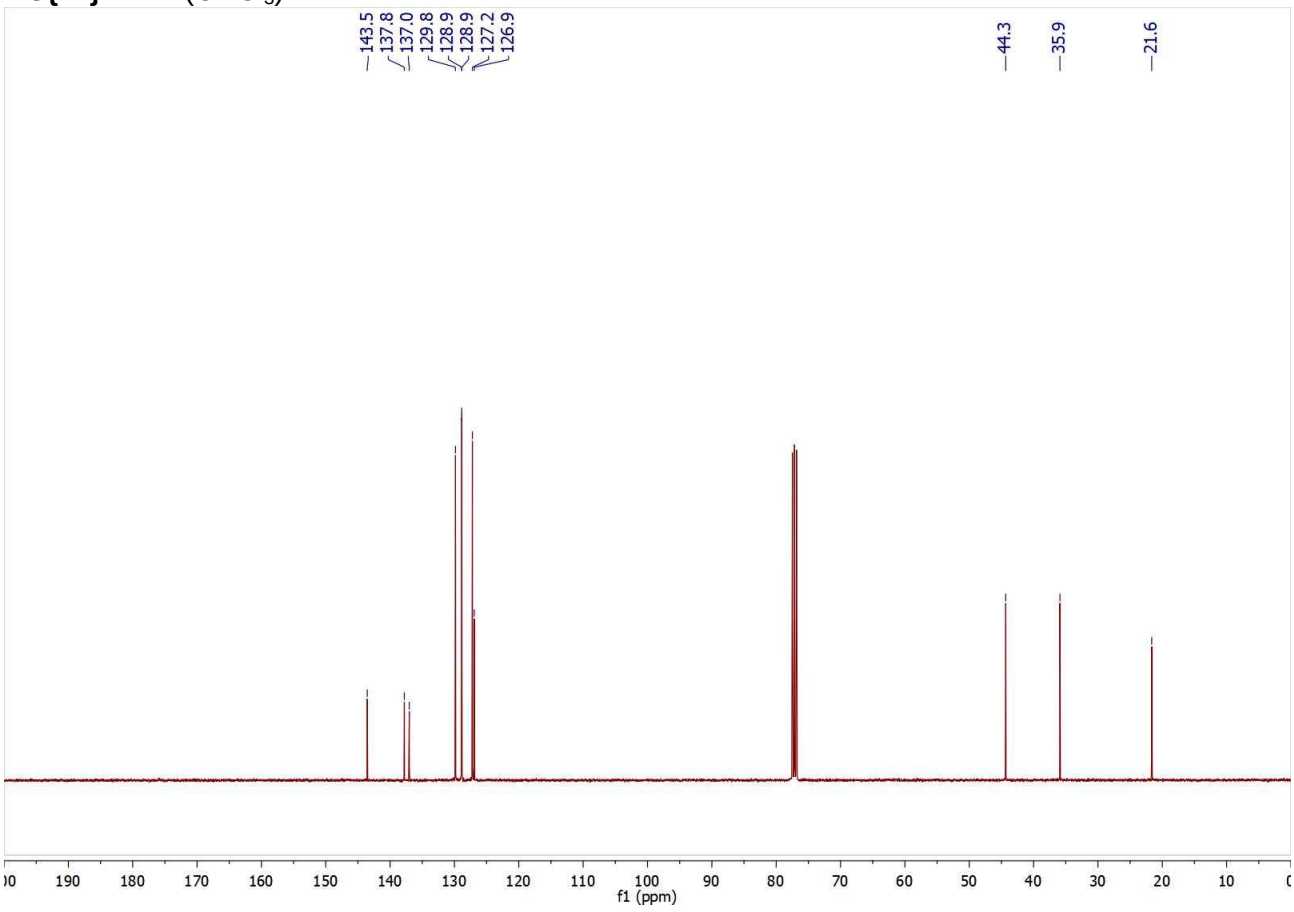


4-Methyl-*N*-phenylethylbencensulfonamide (1i)

^{1}H NMR ($CDCl_3$)

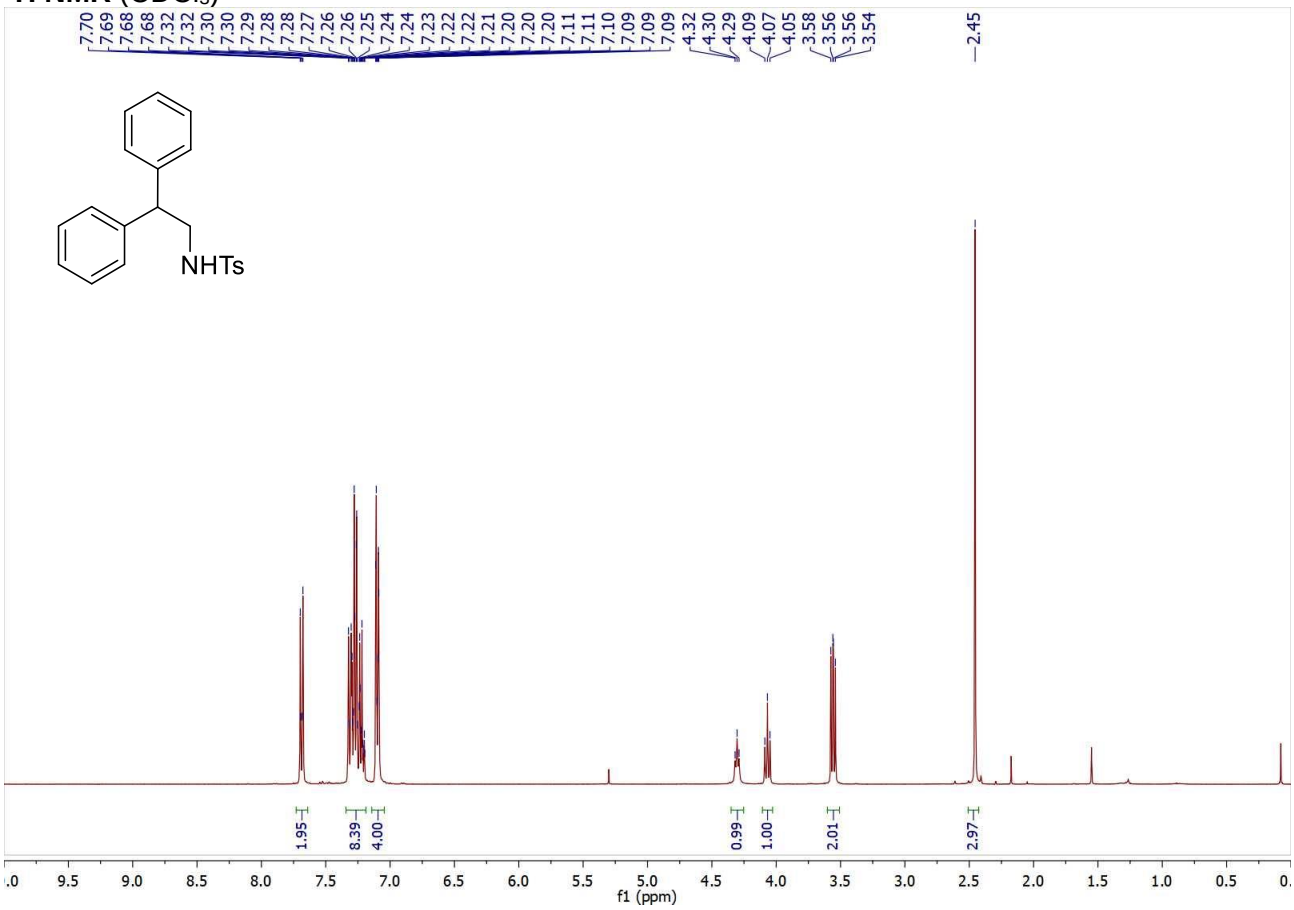


^{13}C{^{1}H} NMR ($CDCl_3$)

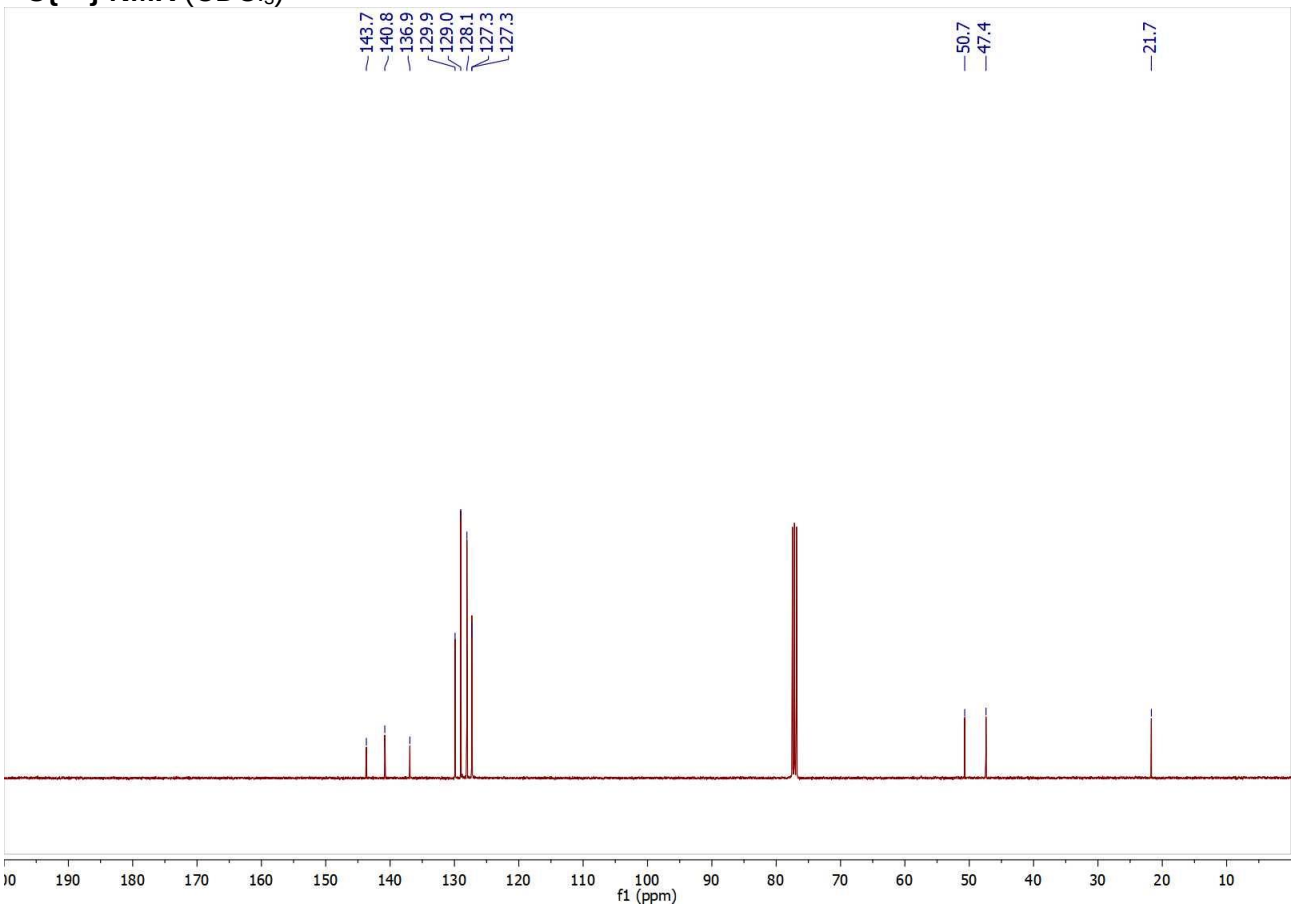


***N*-(2,2-Diphenylethyl)-4-methylbenzenesulfonamide (1i`)**

^{1}H NMR ($CDCl_3$)

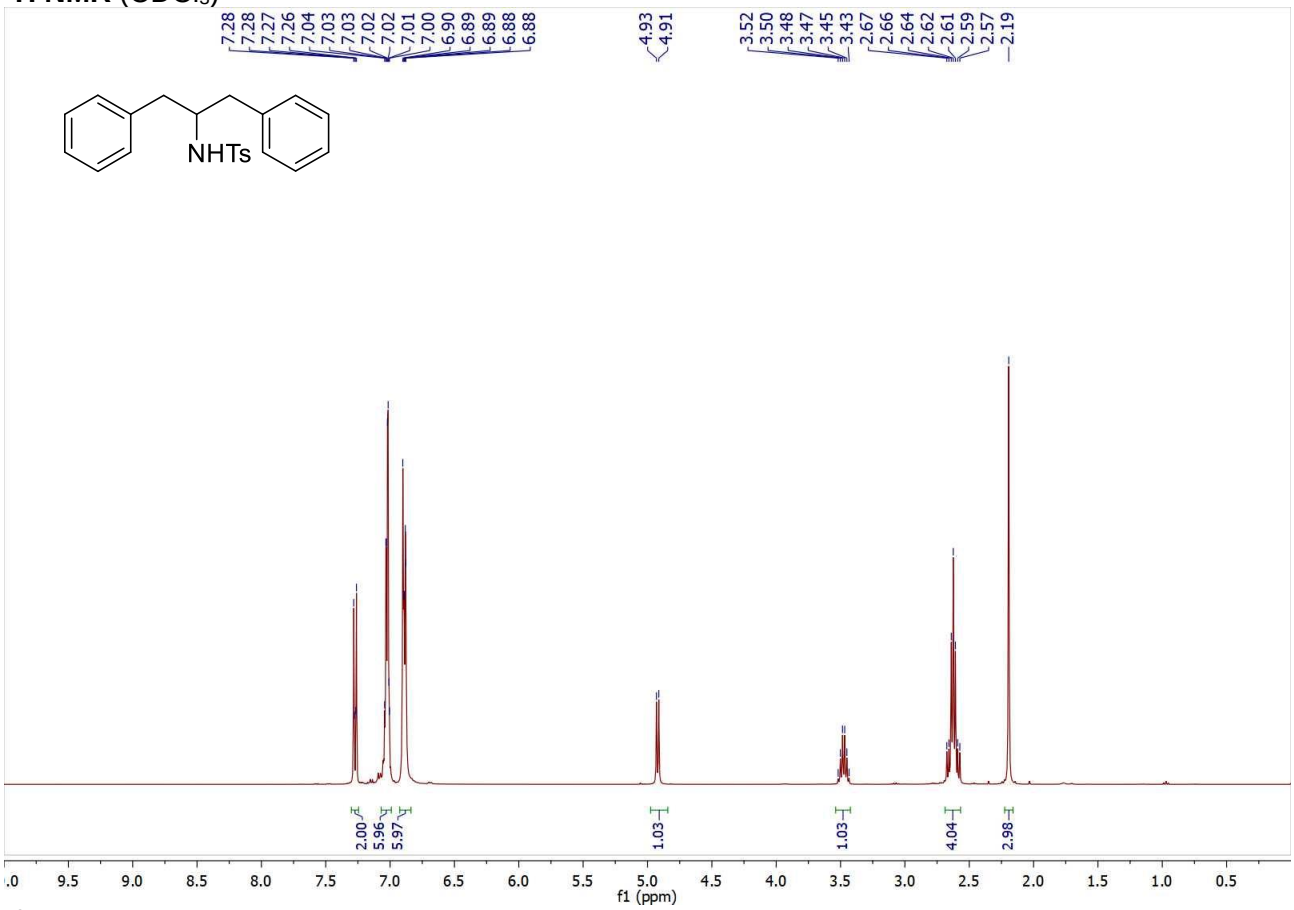


^{13}C{^{1}H} NMR ($CDCl_3$)

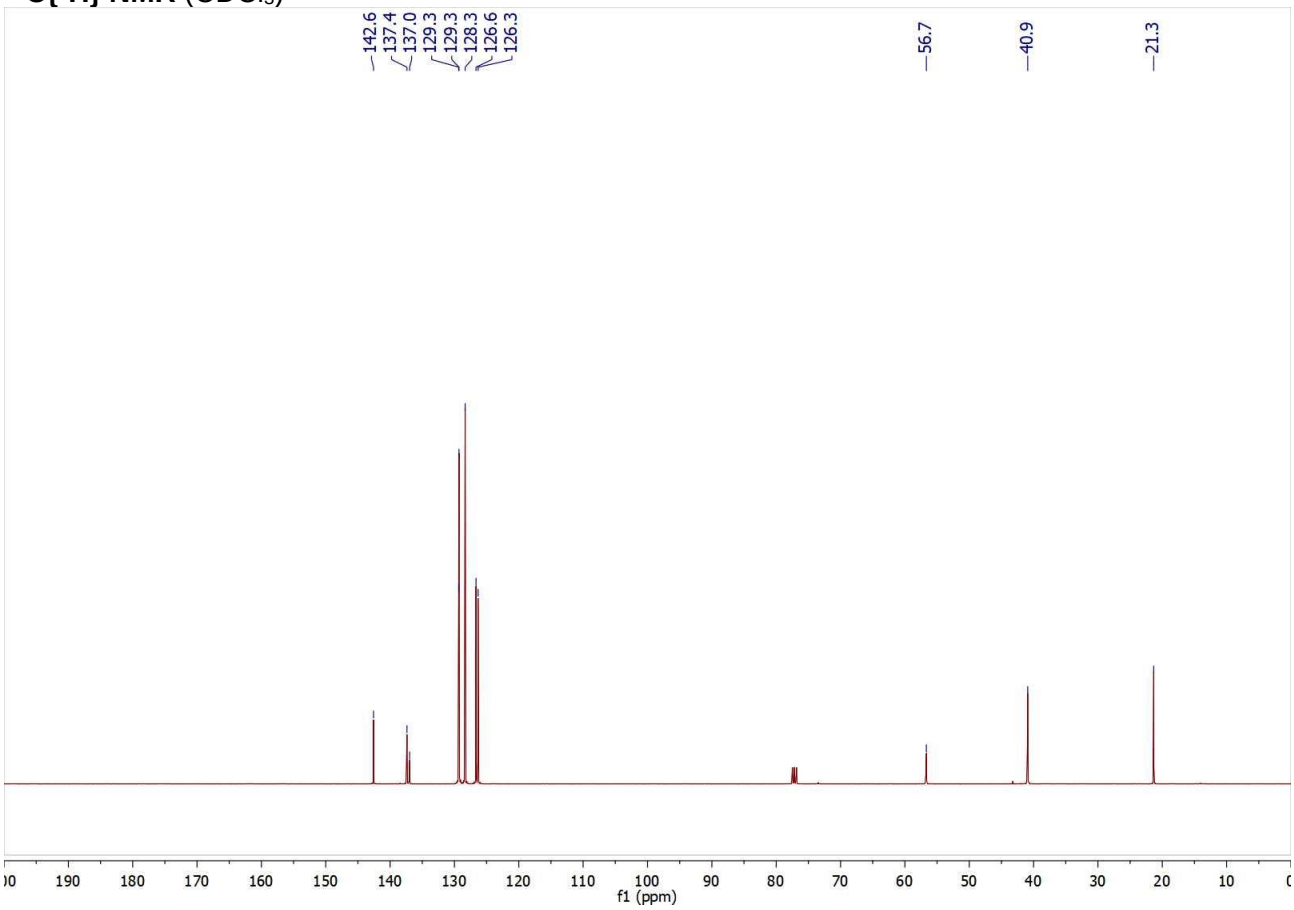


***N*-(1,3-Diphenylpropan-2-yl)-4-methylbenzensulfonamide (1j)**

^{1}H NMR ($CDCl_3$)

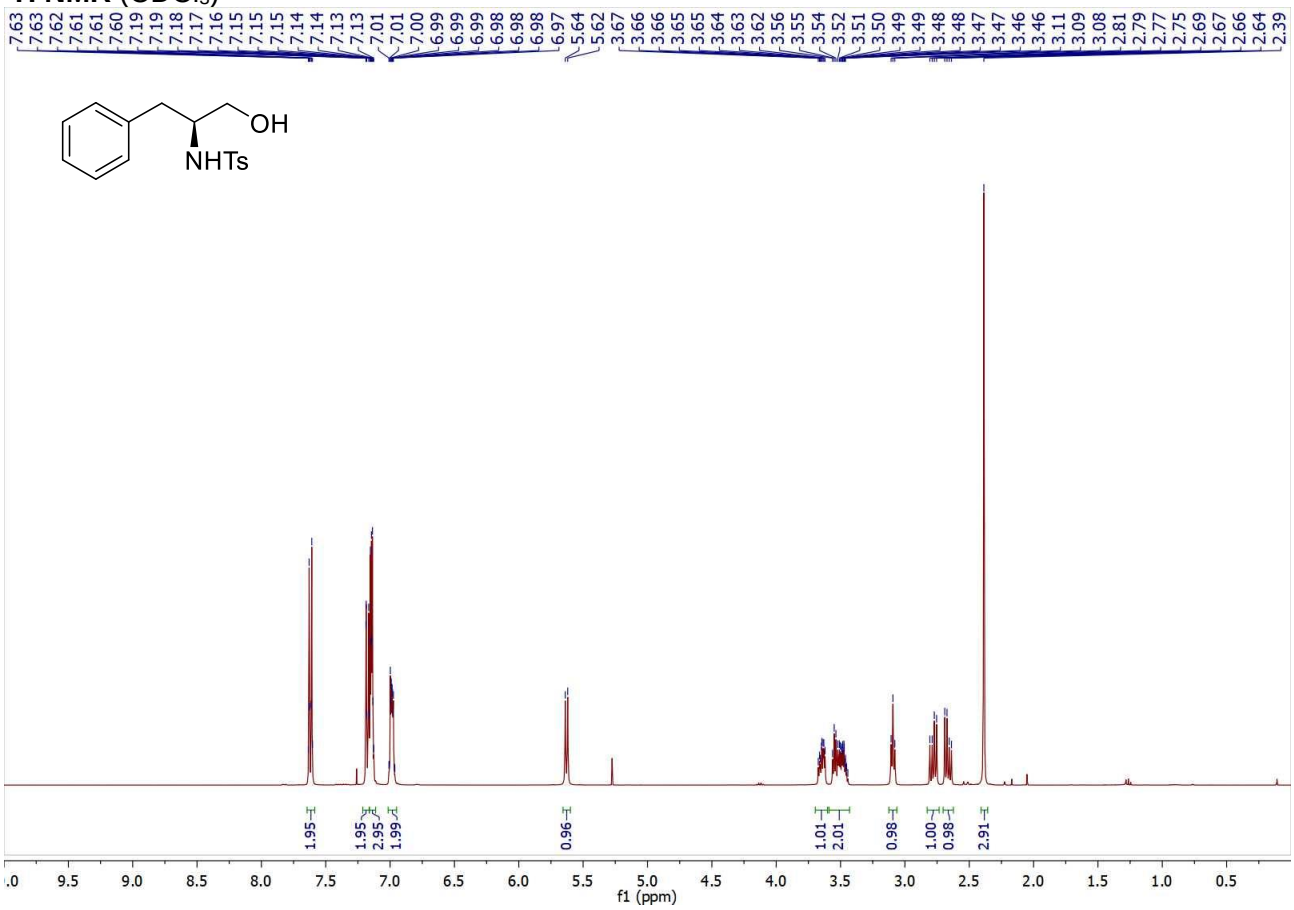


^{13}C{^{1}H} NMR ($CDCl_3$)

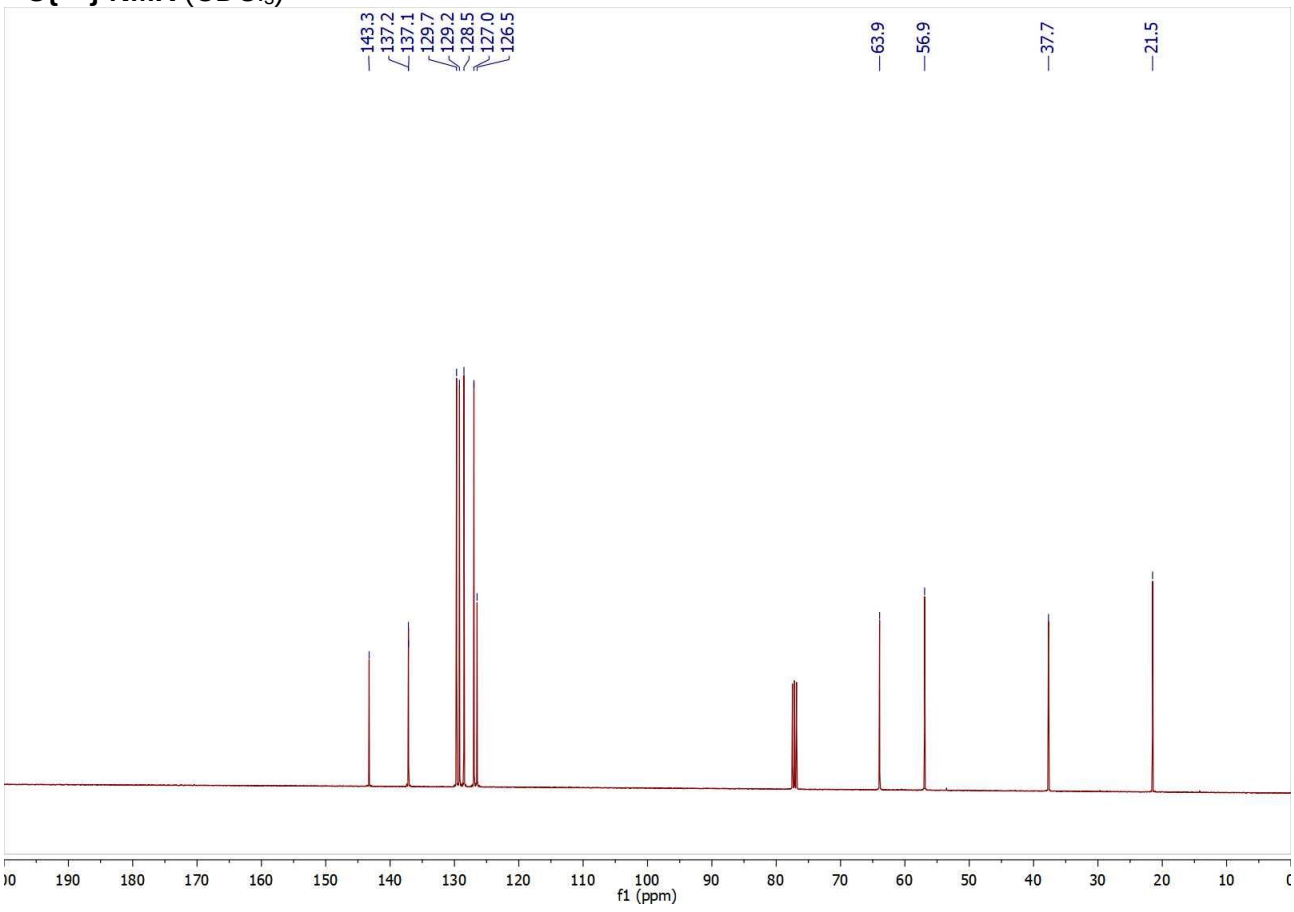


(*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (S3)

^{1}H NMR ($CDCl_3$)

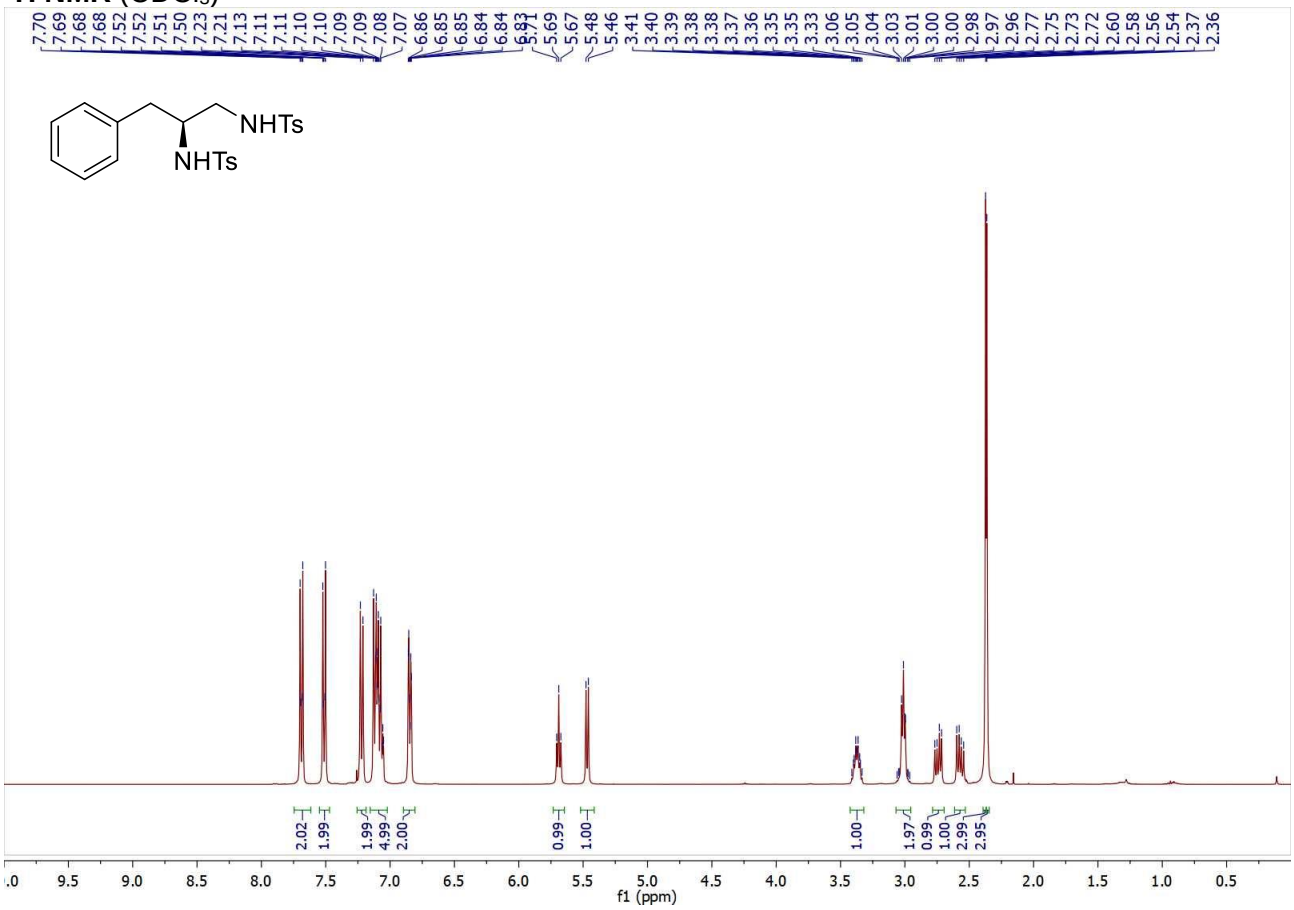


^{13}C{^{1}H} NMR ($CDCl_3$)

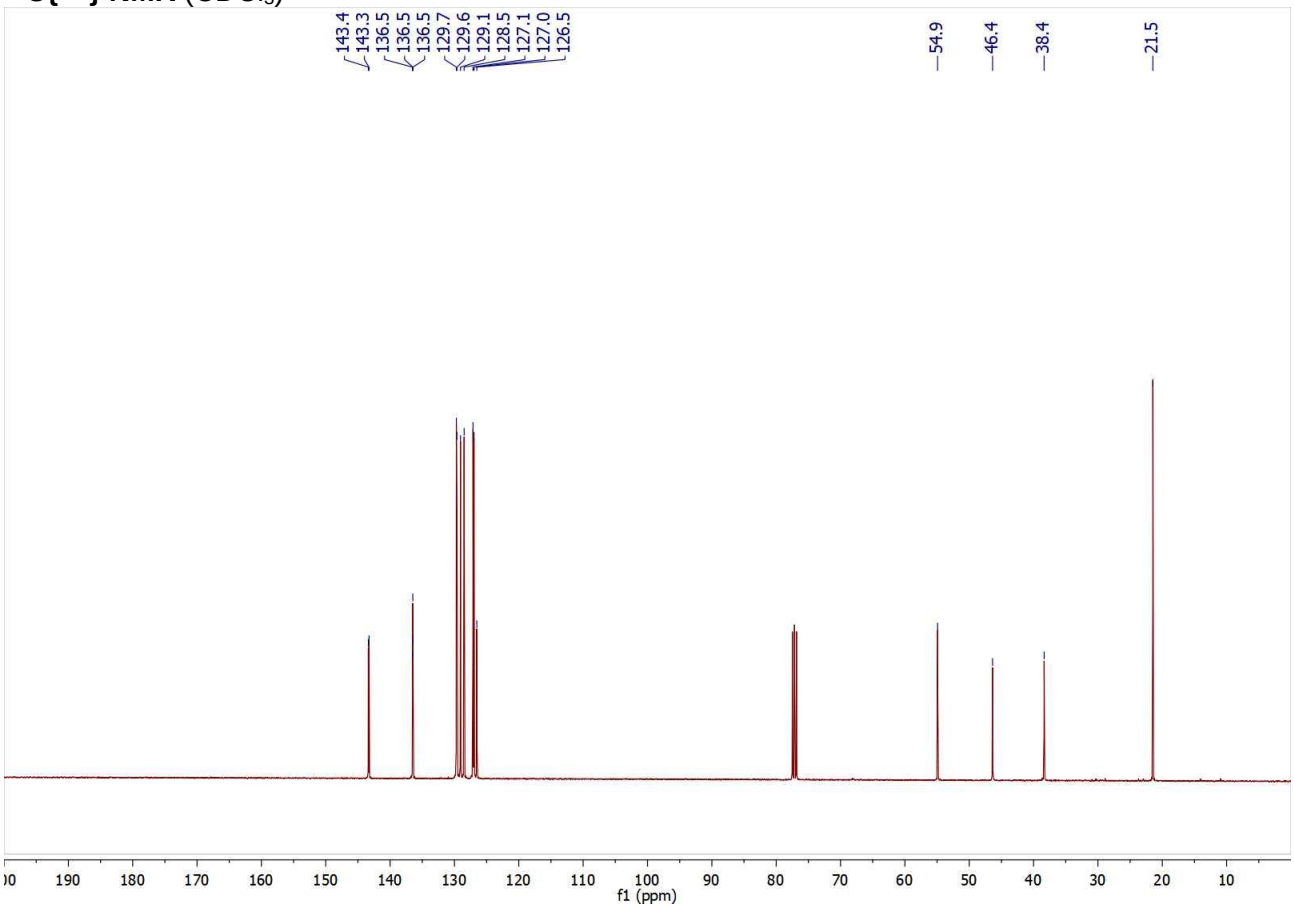


(*S*)-*N*,*N*´-(3-Phenylpropane-1,2-diyl)bis(4-methylbenzensulfonamide) (1k)

^{1}H NMR ($CDCl_3$)

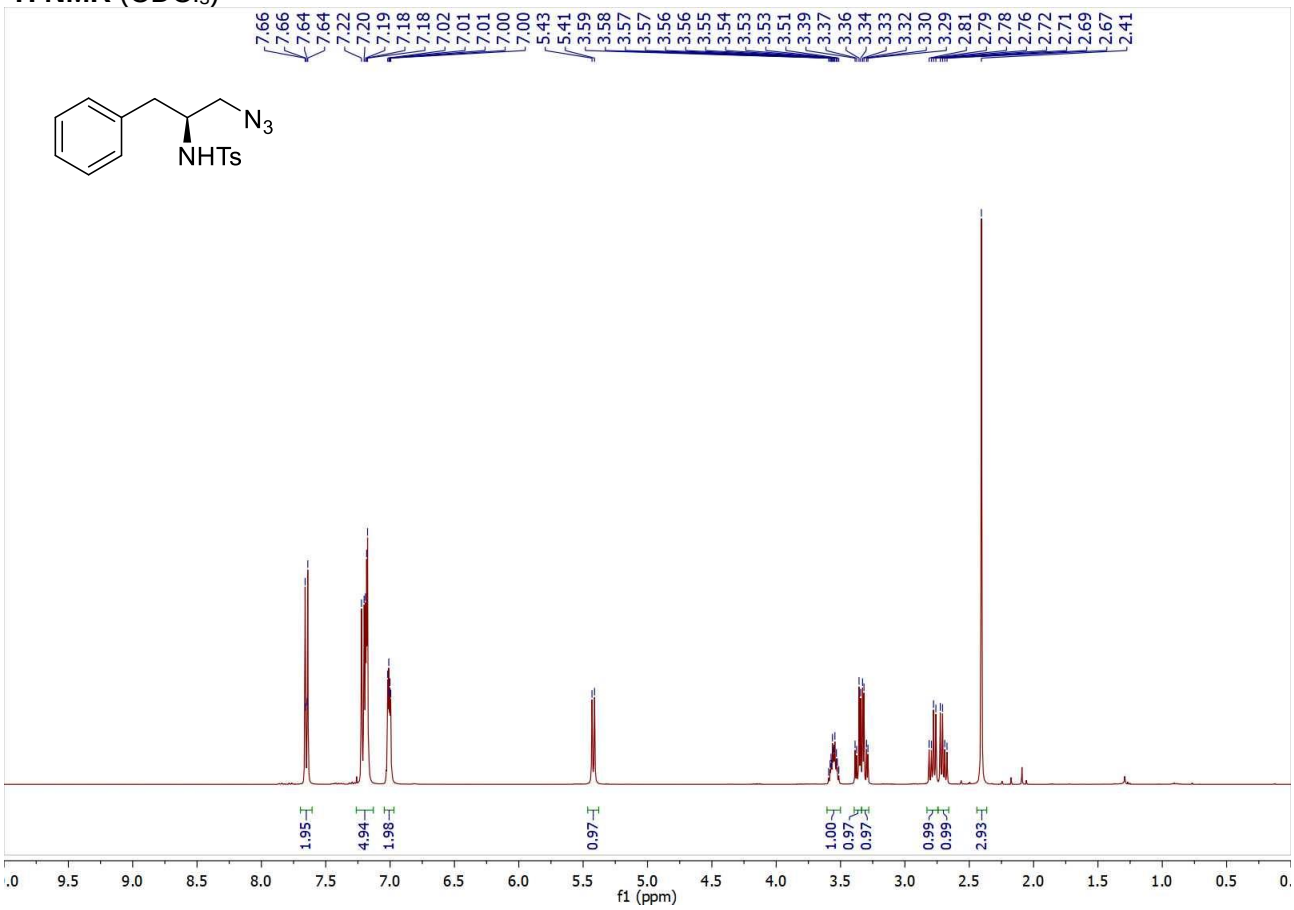


^{13}C{^{1}H} NMR ($CDCl_3$)

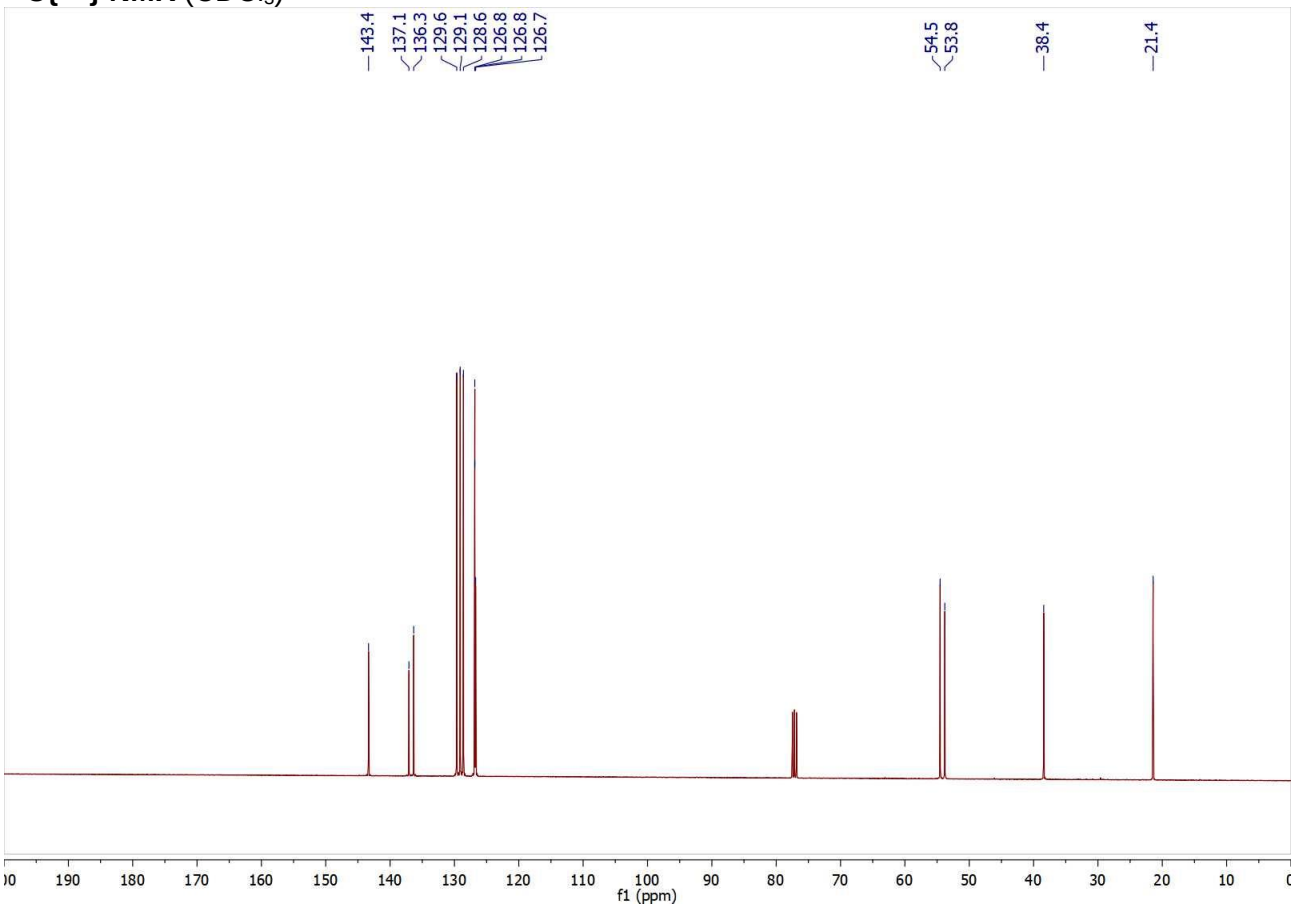


(*S*)-*N*-(1-Azido-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1l)

^{1}H NMR ($CDCl_3$)

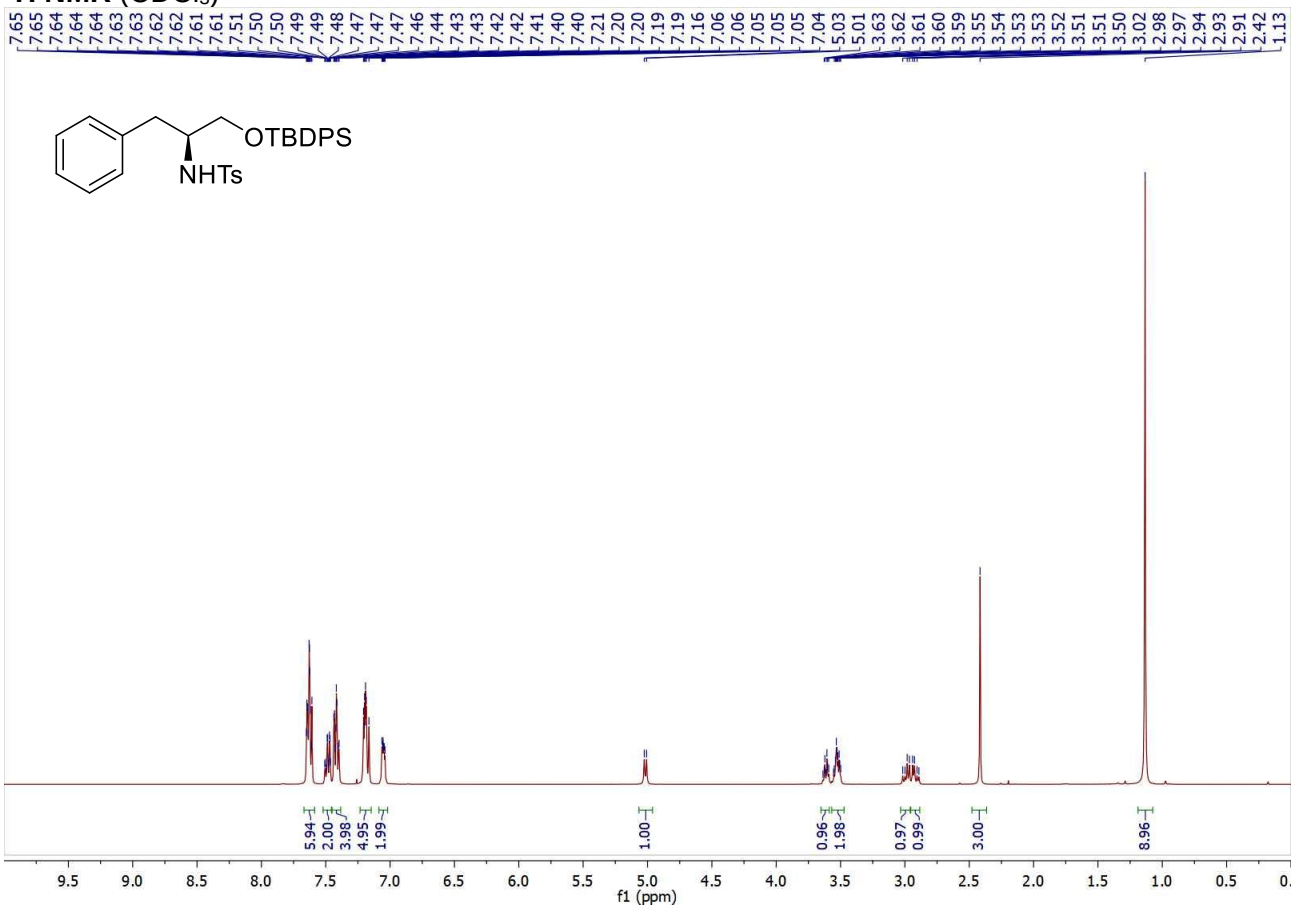


^{13}C{^{1}H} NMR ($CDCl_3$)

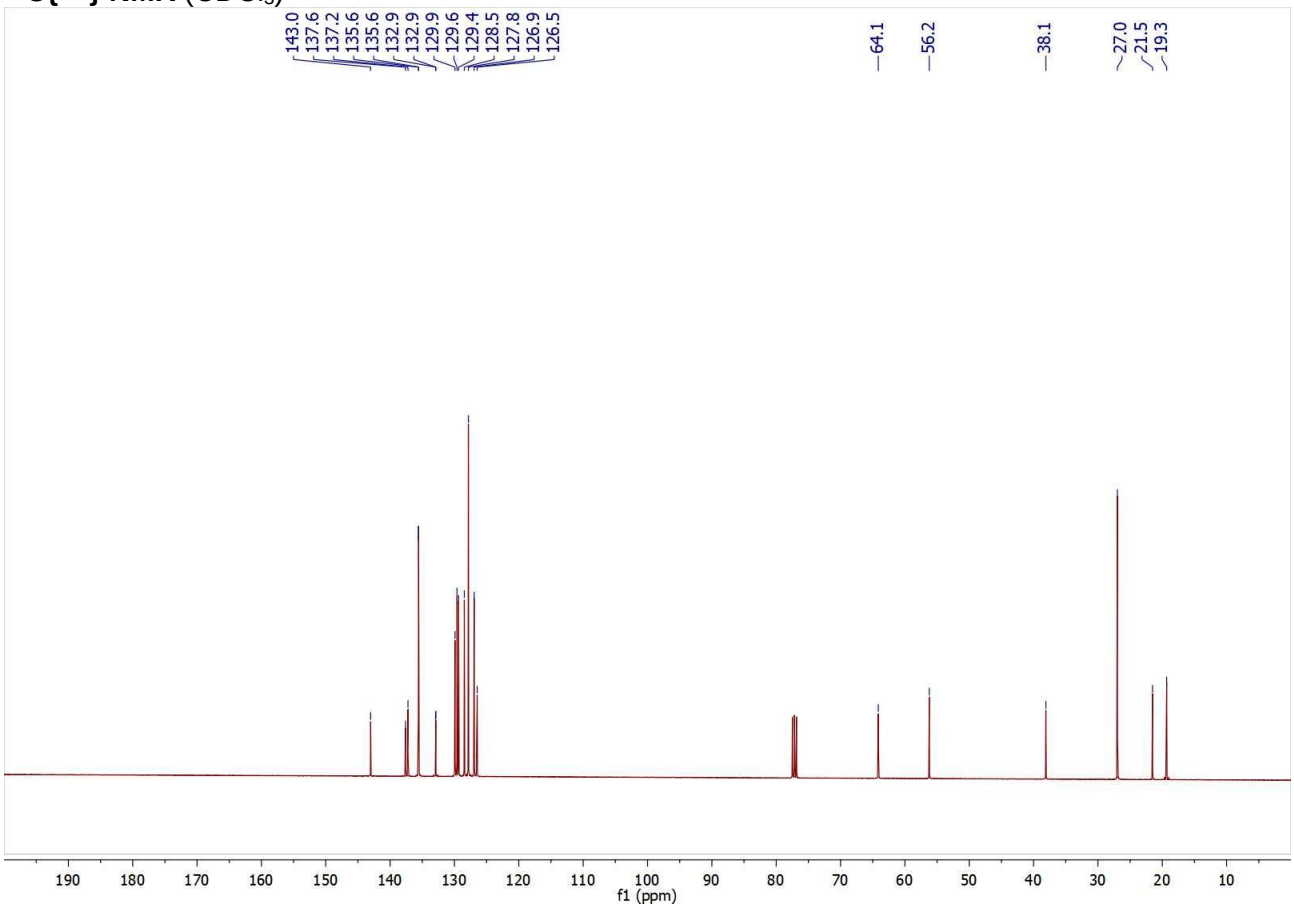


(*S*)-*N*-(-1-((*tert*-Butyldiphenylsilyl)oxy)-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1m)

^{1}H NMR ($CDCl_3$)

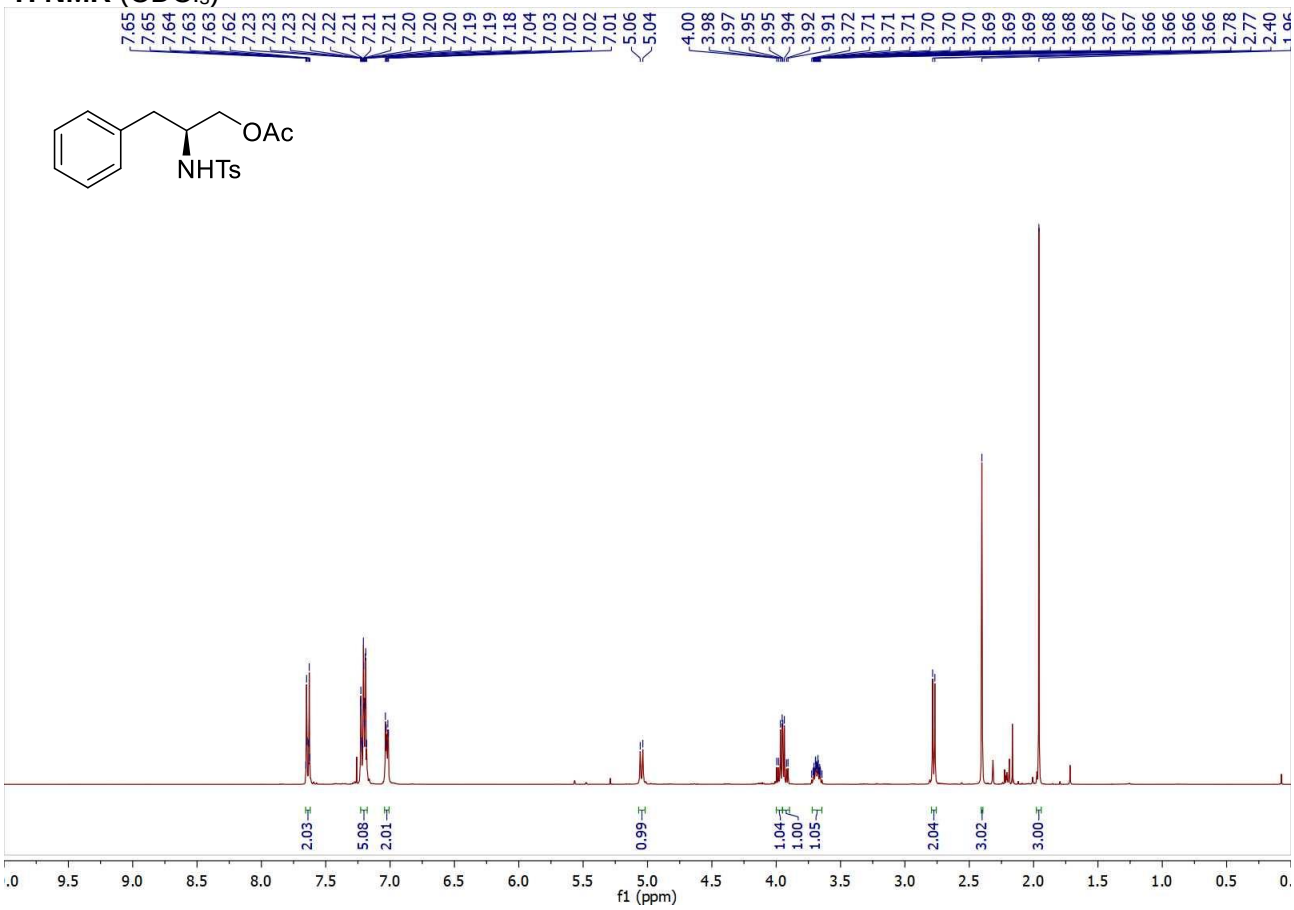


^{13}C{^{1}H} NMR ($CDCl_3$)

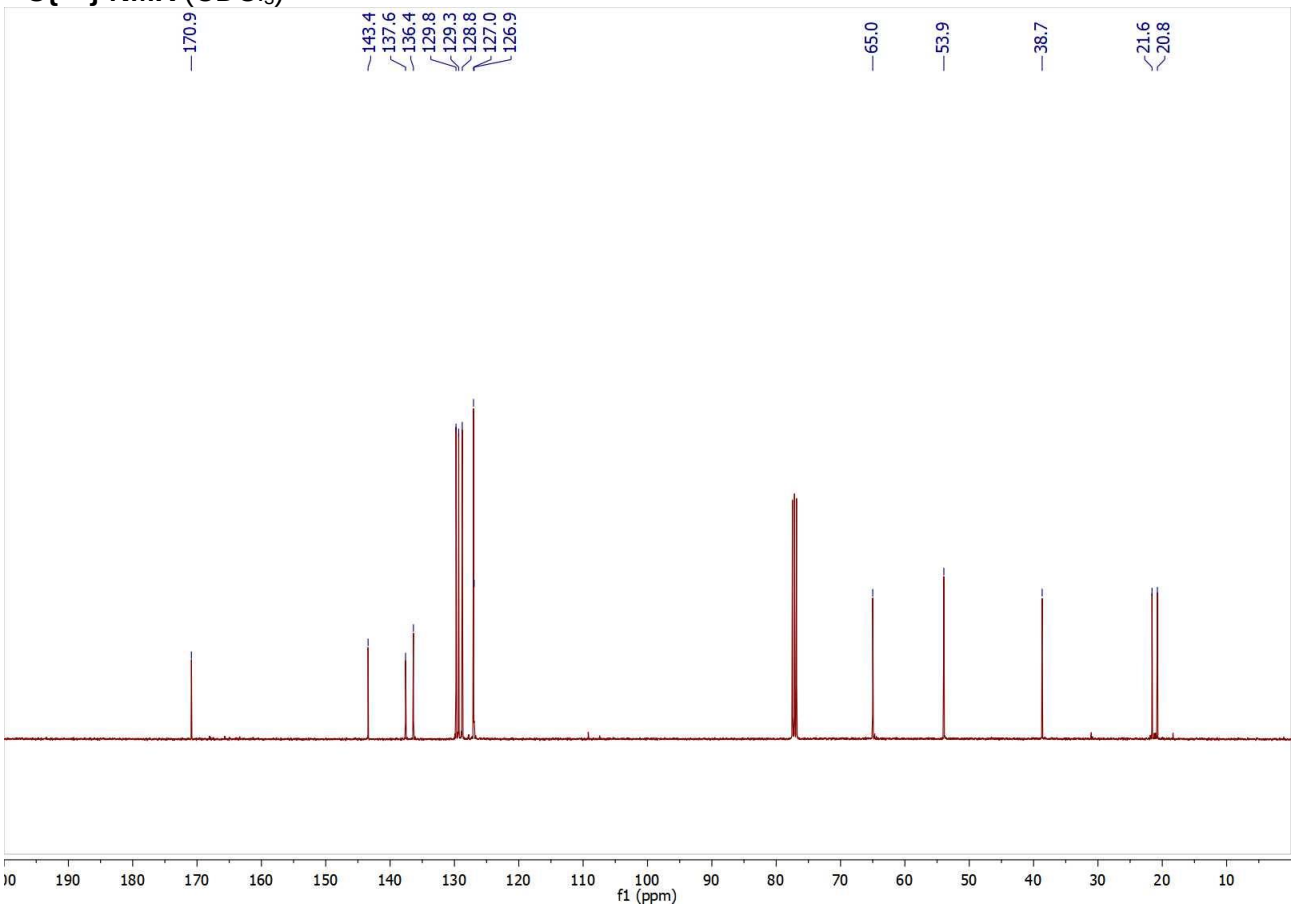


(*S*)-2-((4-Methylphenyl)sulfonamido)-3-phenylpropyl acetate (1n)

^{1}H NMR ($CDCl_3$)

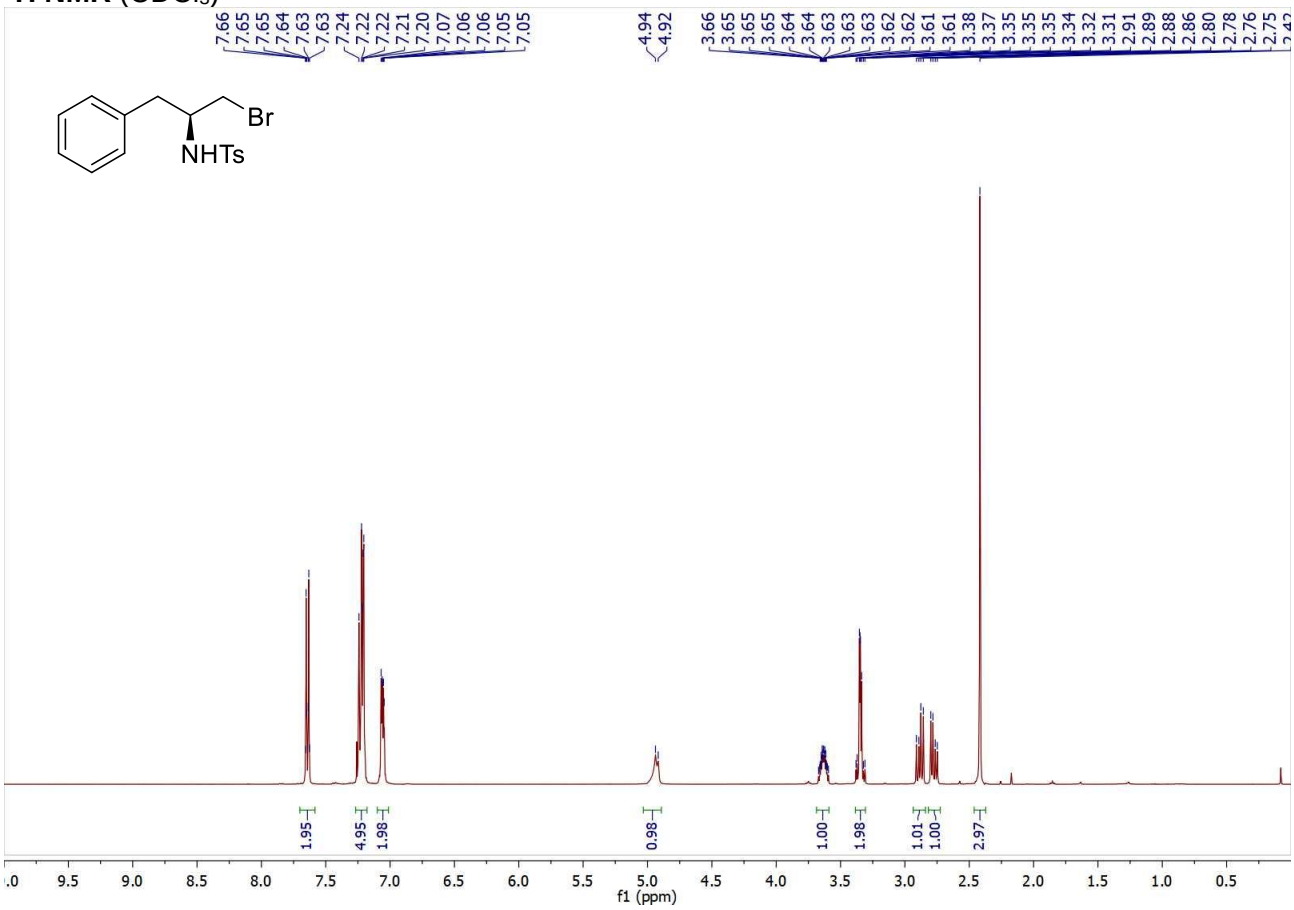


^{13}C{^{1}H} NMR ($CDCl_3$)

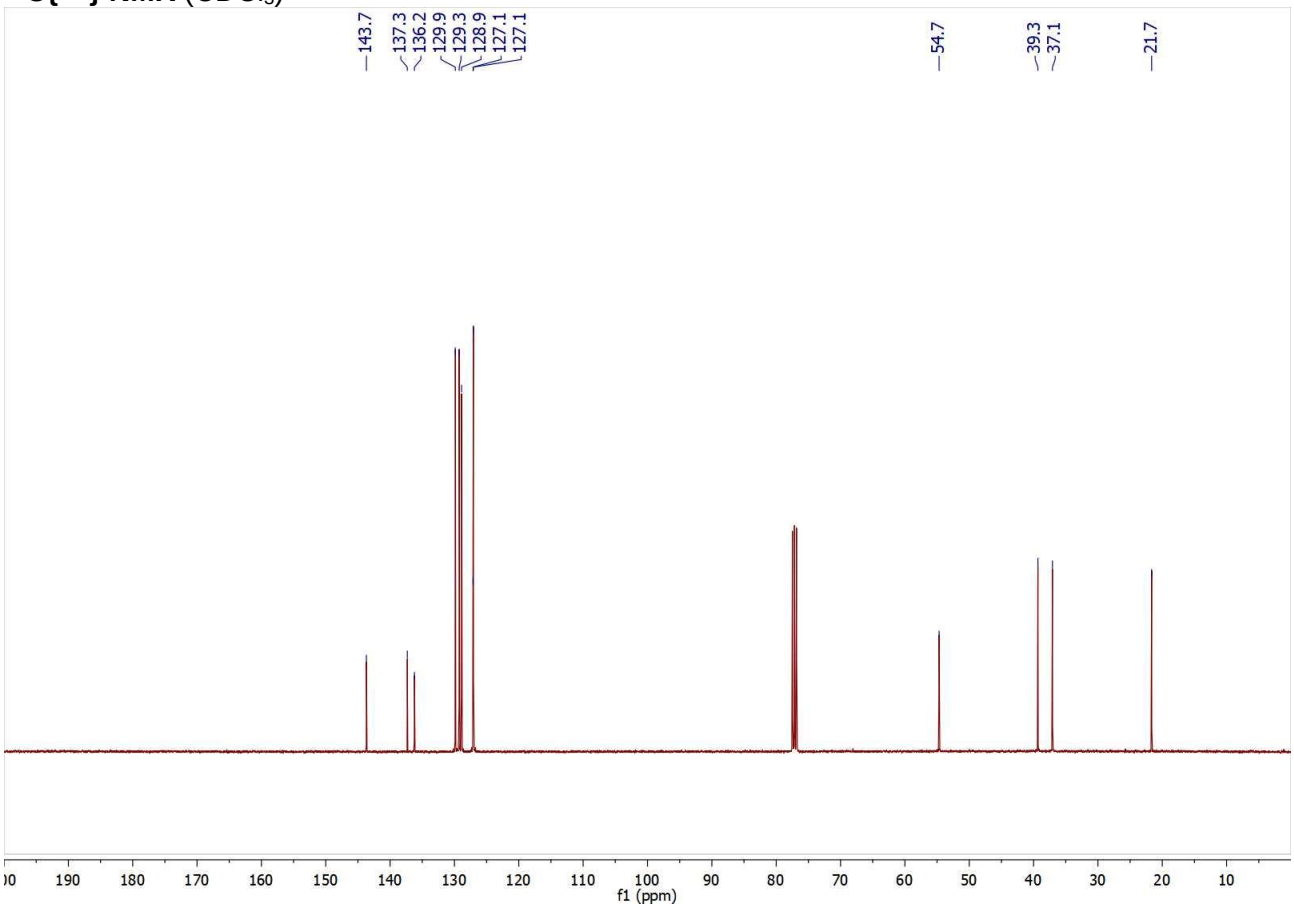


(*S*)-*N*-(1-Bromo-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1o)

^{1}H NMR ($CDCl_3$)

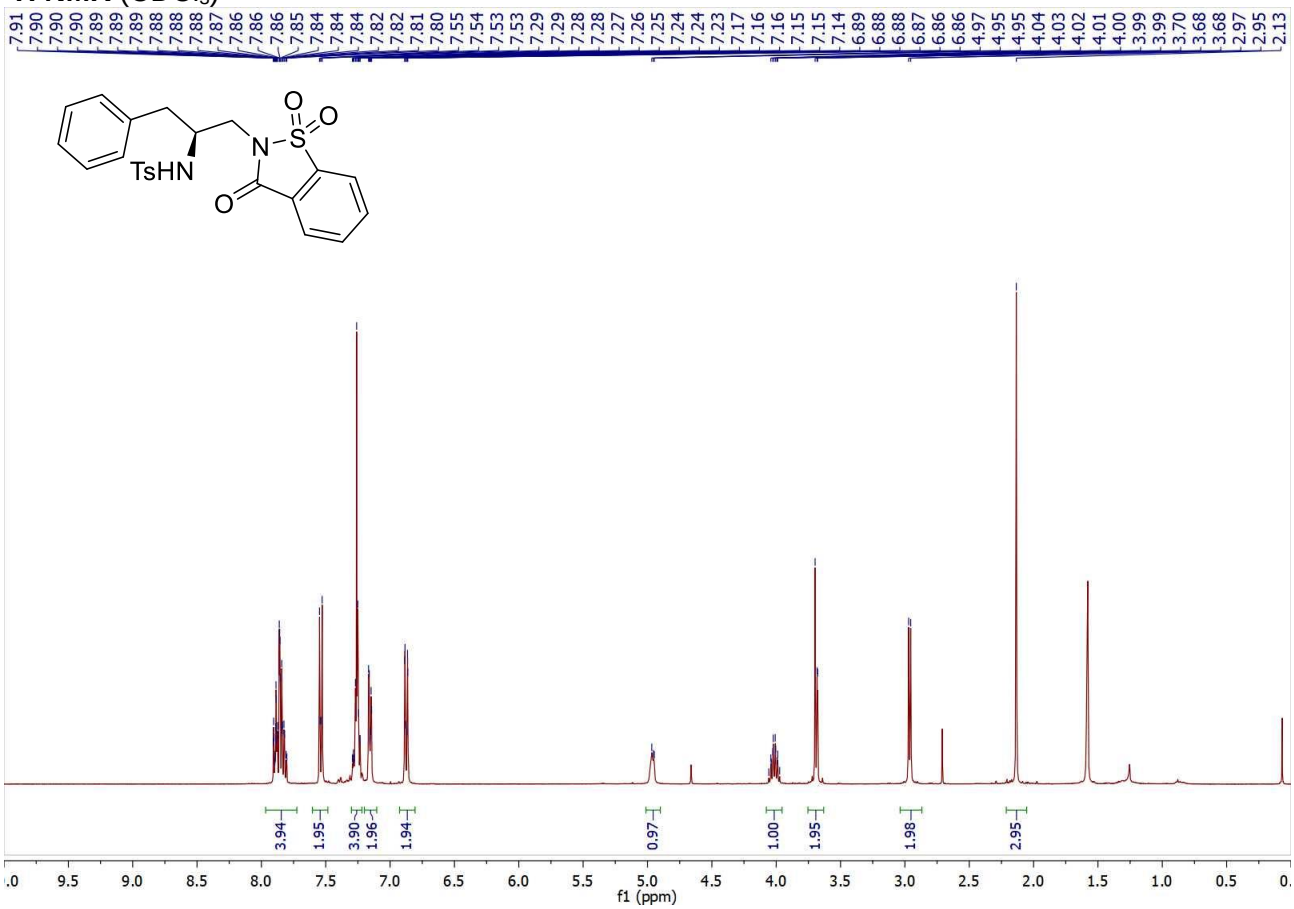


^{13}C{^{1}H} NMR ($CDCl_3$)

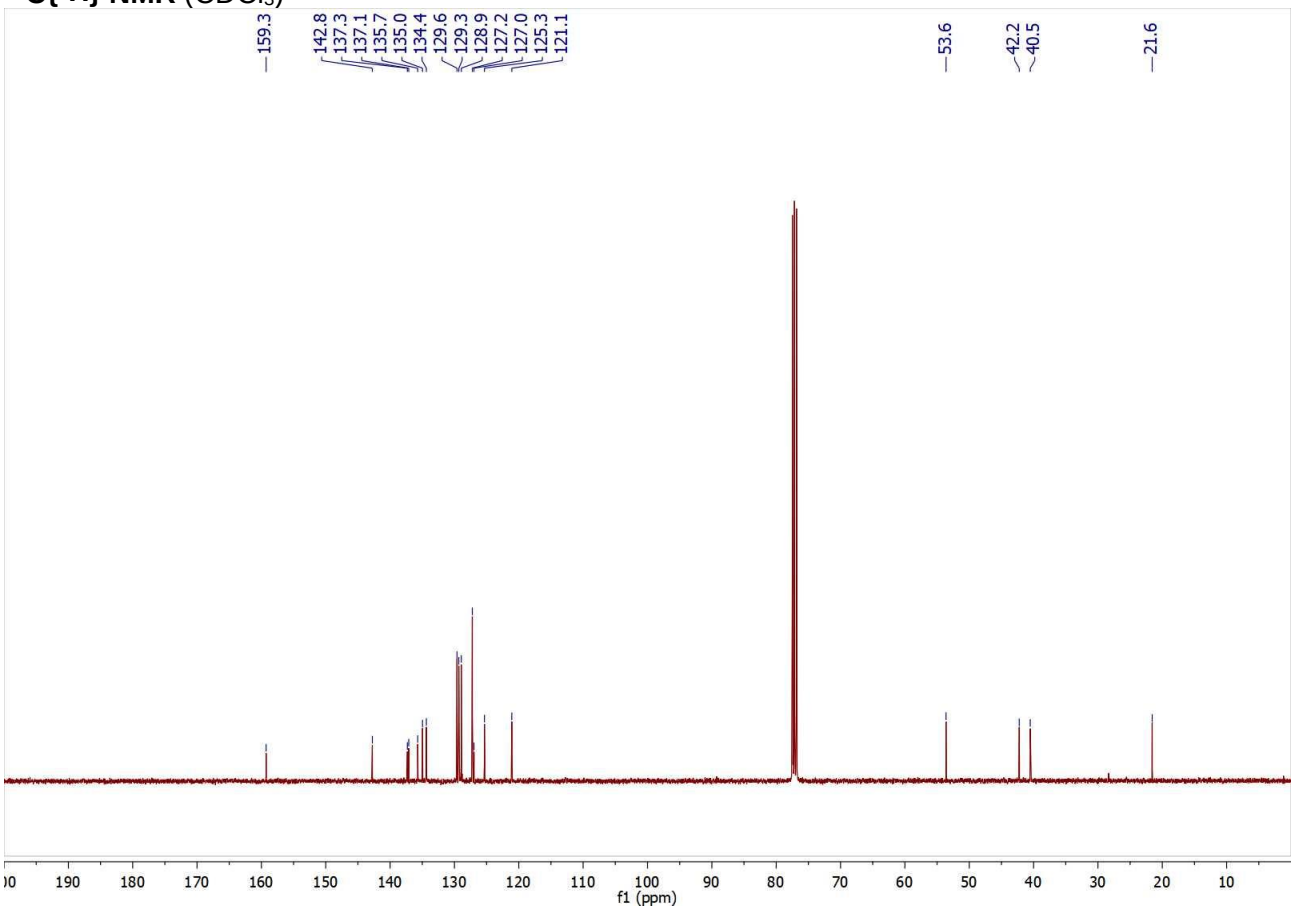


(*S*)-*N*-(1-(1,1-Dioxo-3-oxobenzo[*d*]isothiazol-2(3H)-yl)-3-phenylpropan-2-yl)-4-methylbenzensulfonamide (1p)

^{1}H NMR ($CDCl_3$)

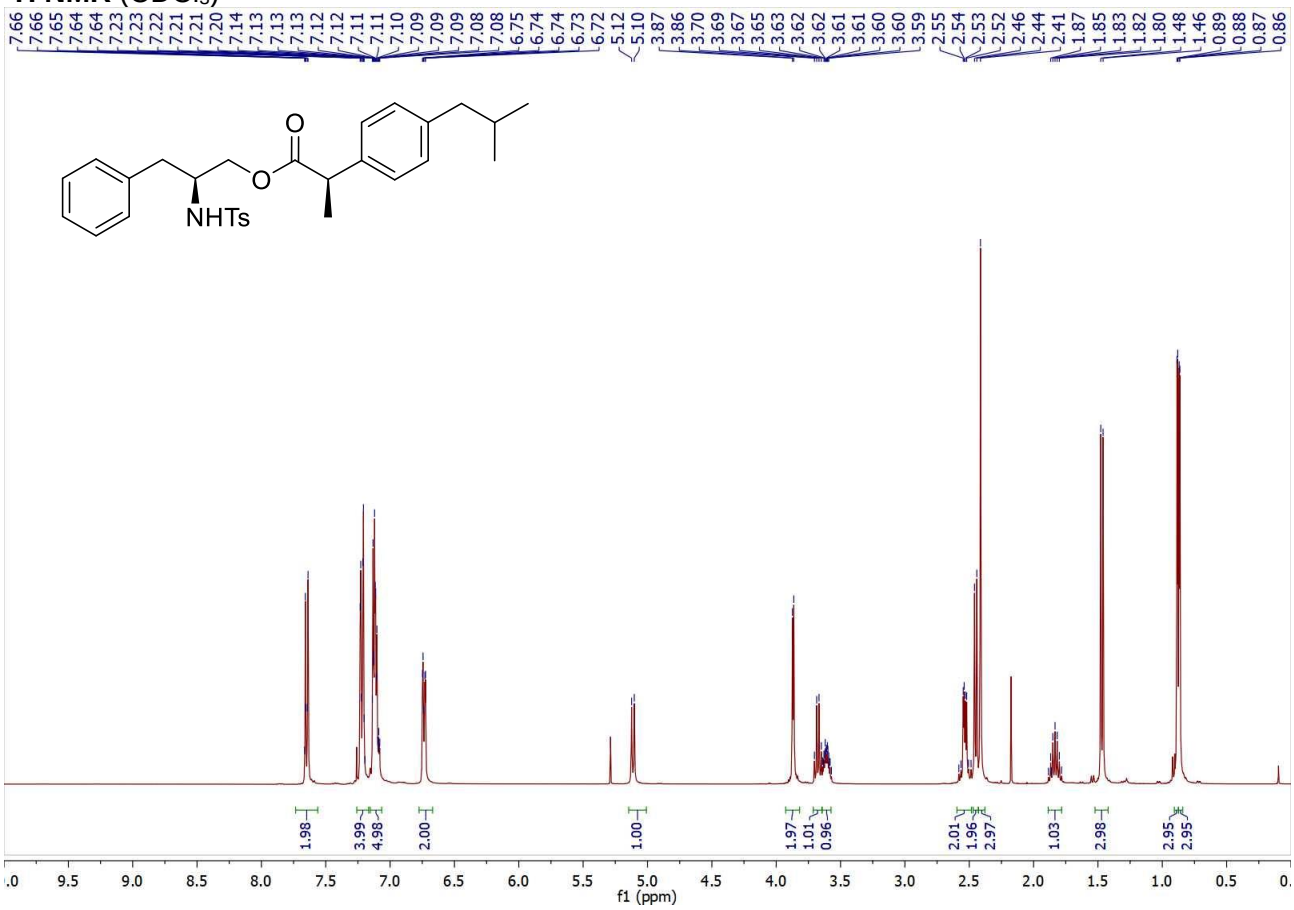


^{13}C{^{1}H} NMR ($CDCl_3$)

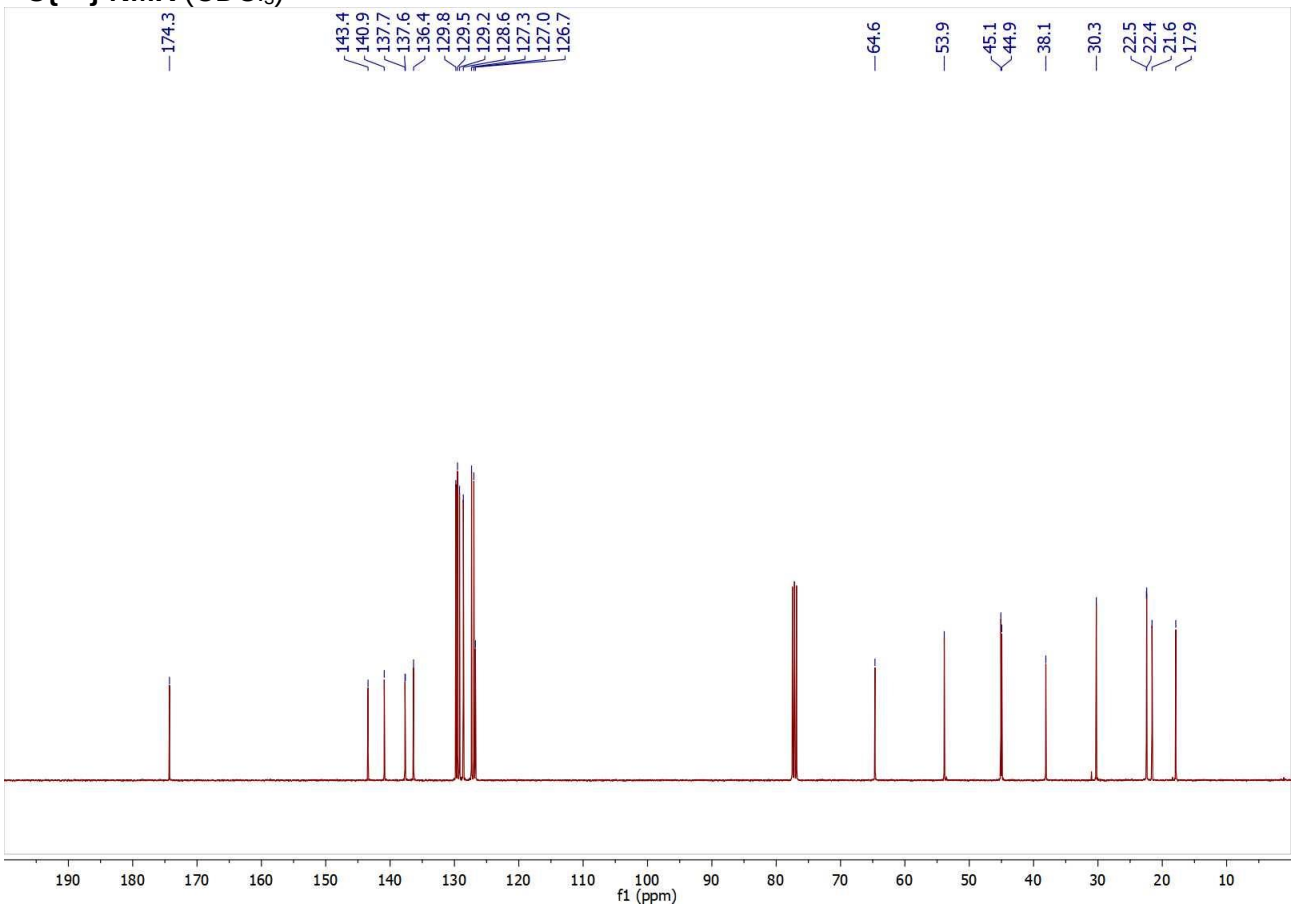


(*S*)-2-((4-Methylphenyl)sulfonamido)-3-phenylpropyl (*S*)-2-(4-isobutylphenyl)propanoate (1q)

^{1}H NMR ($CDCl_3$)

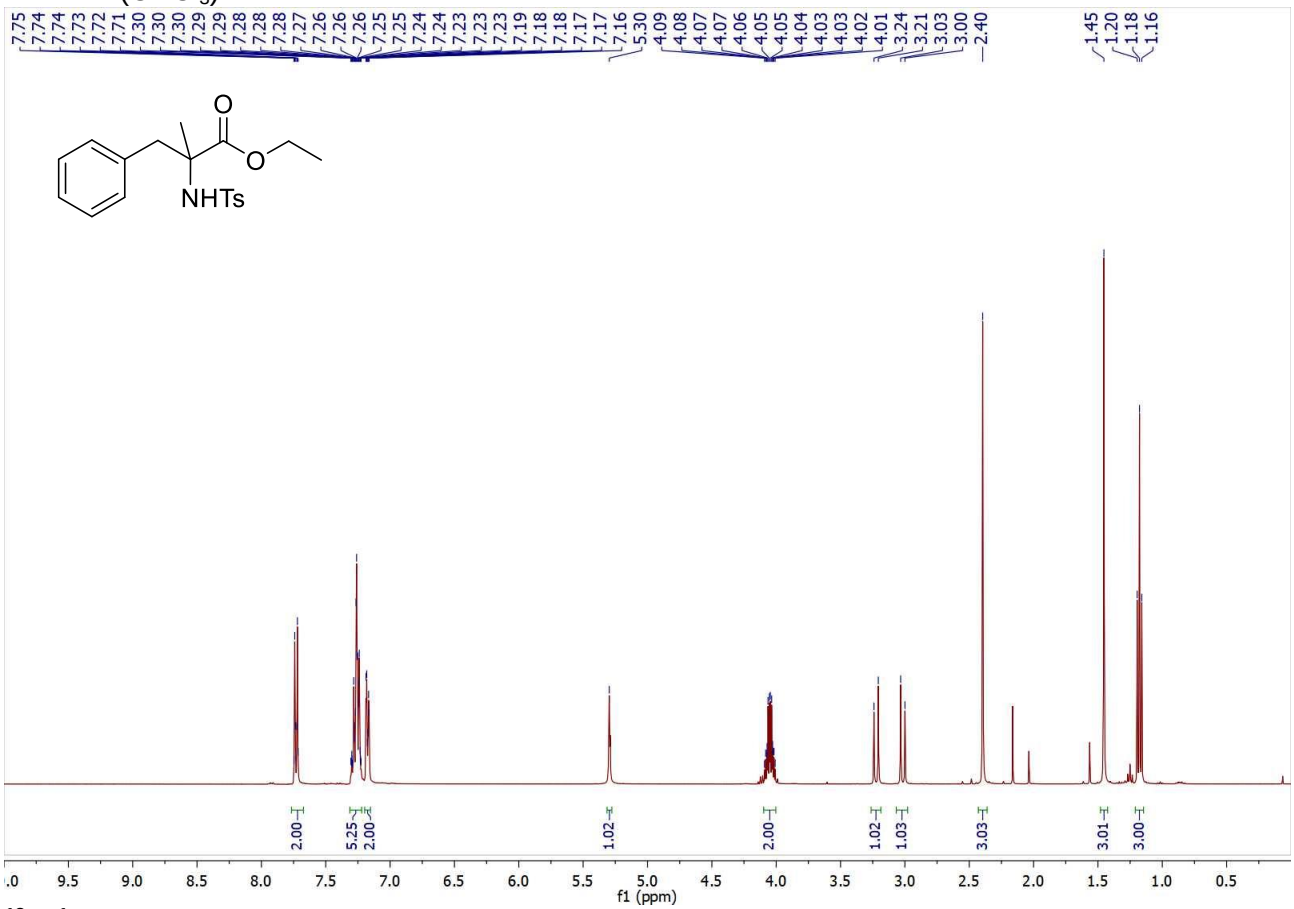


^{13}C{^{1}H} NMR ($CDCl_3$)

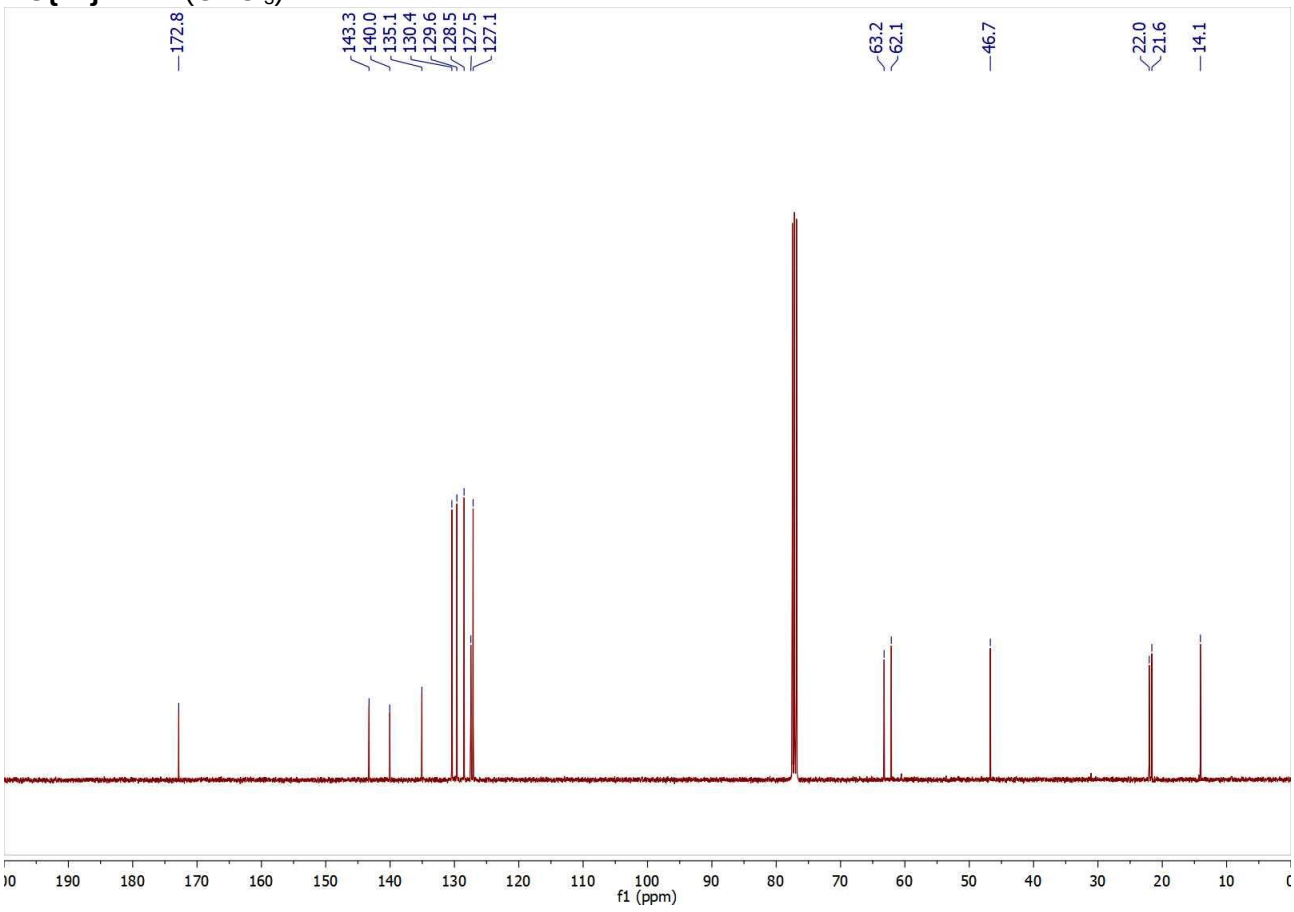


Ethyl 2-methyl-2-(4-methylphenylsulfonamido)-3-phenylpropanoate (1r)

^{1}H NMR ($CDCl_3$)

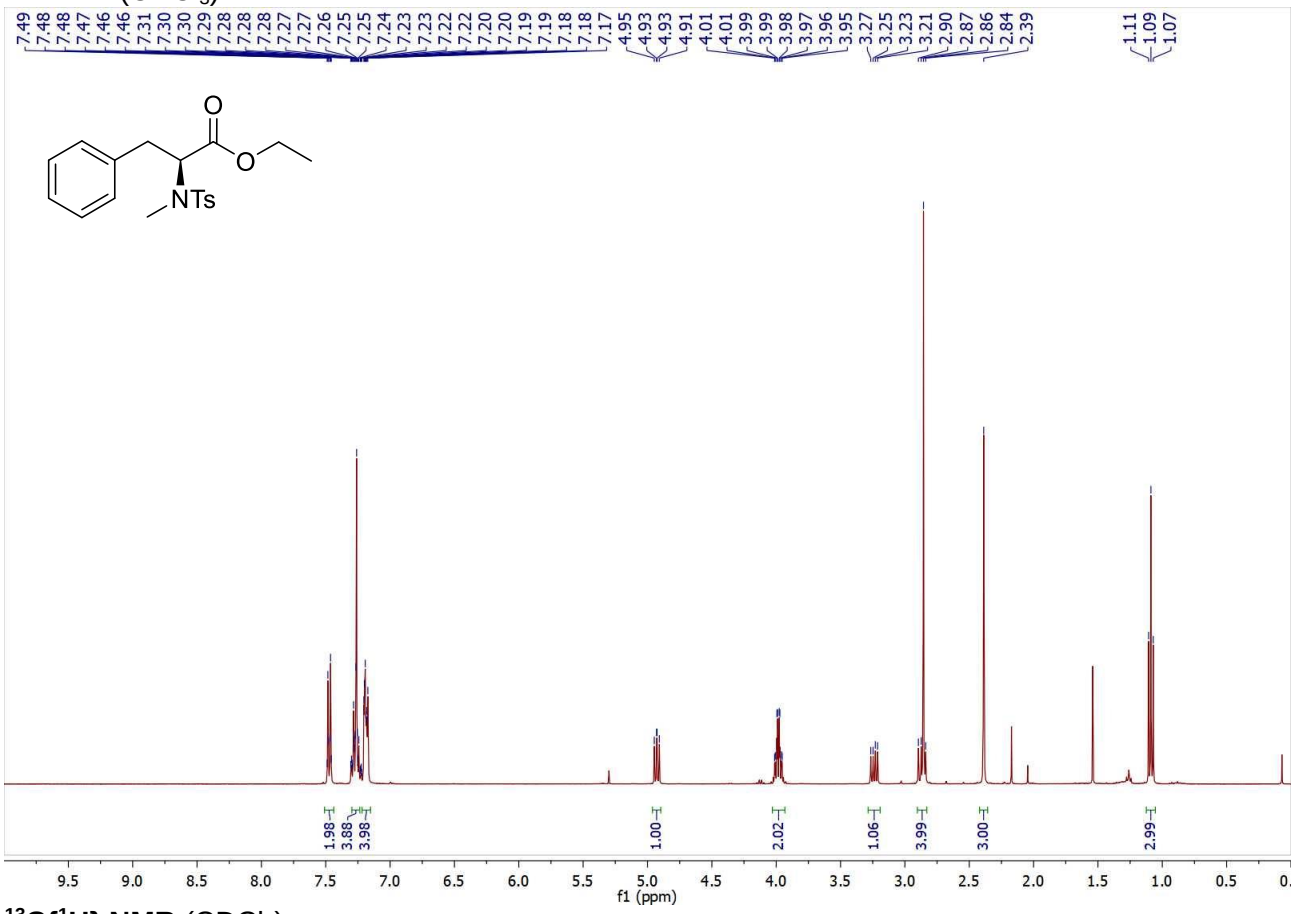


^{13}C{^{1}H} NMR ($CDCl_3$)

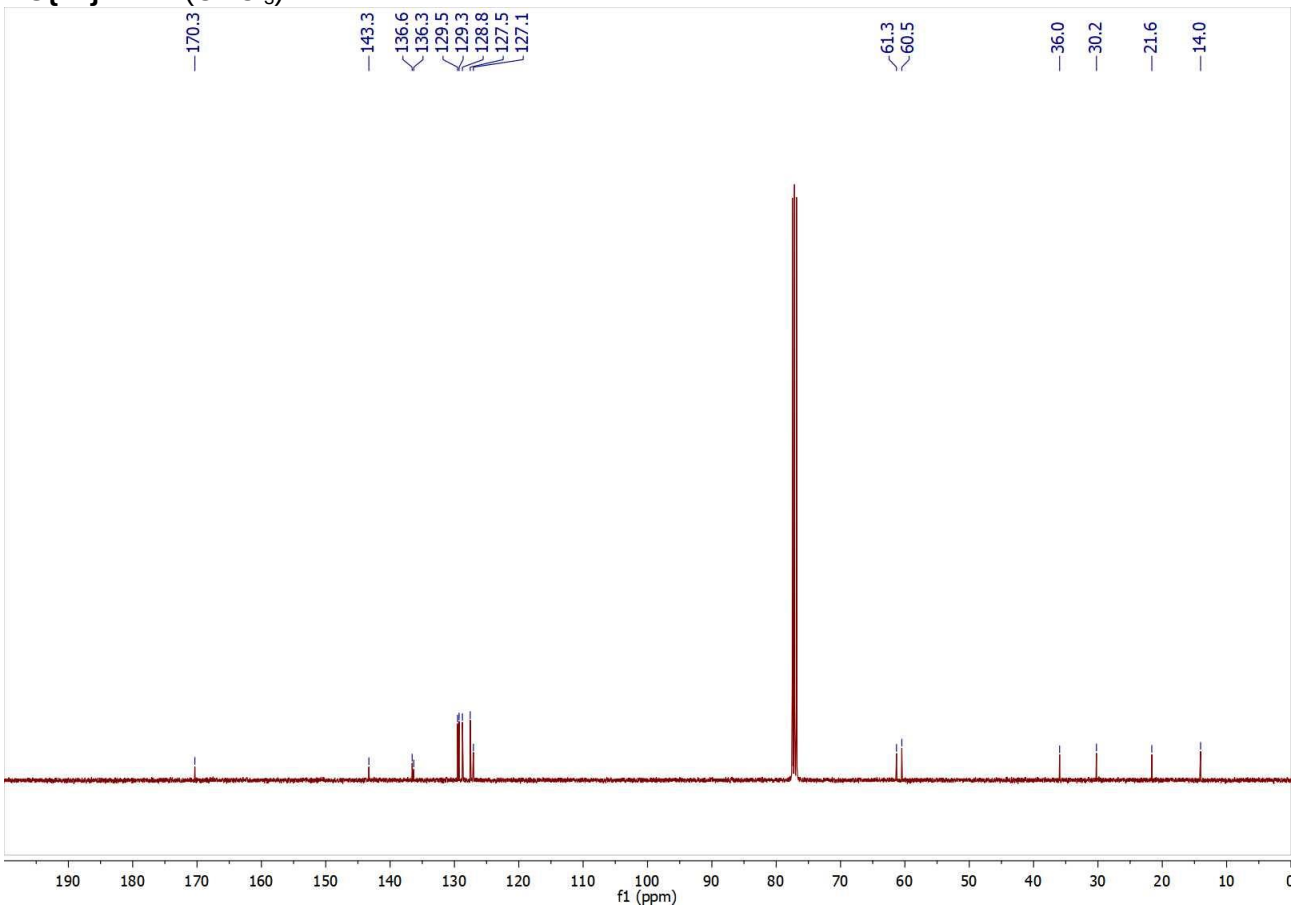


(*S*)-Ethyl-2-(*N*,4-Dimethylphenylsulfonamido)-3-phenylpropanoate (1s)

^{1}H NMR ($CDCl_3$)

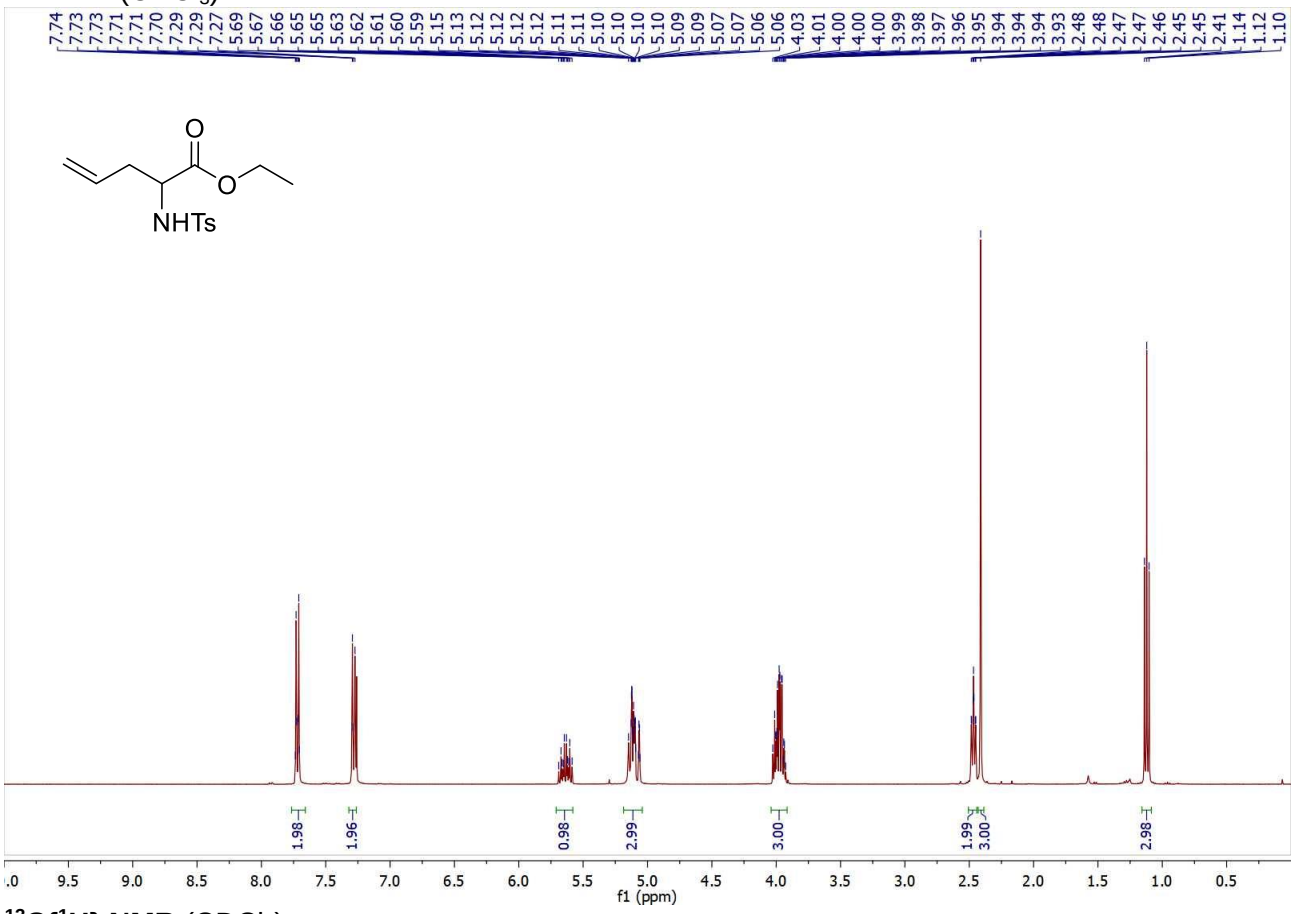


^{13}C{^{1}H} NMR ($CDCl_3$)

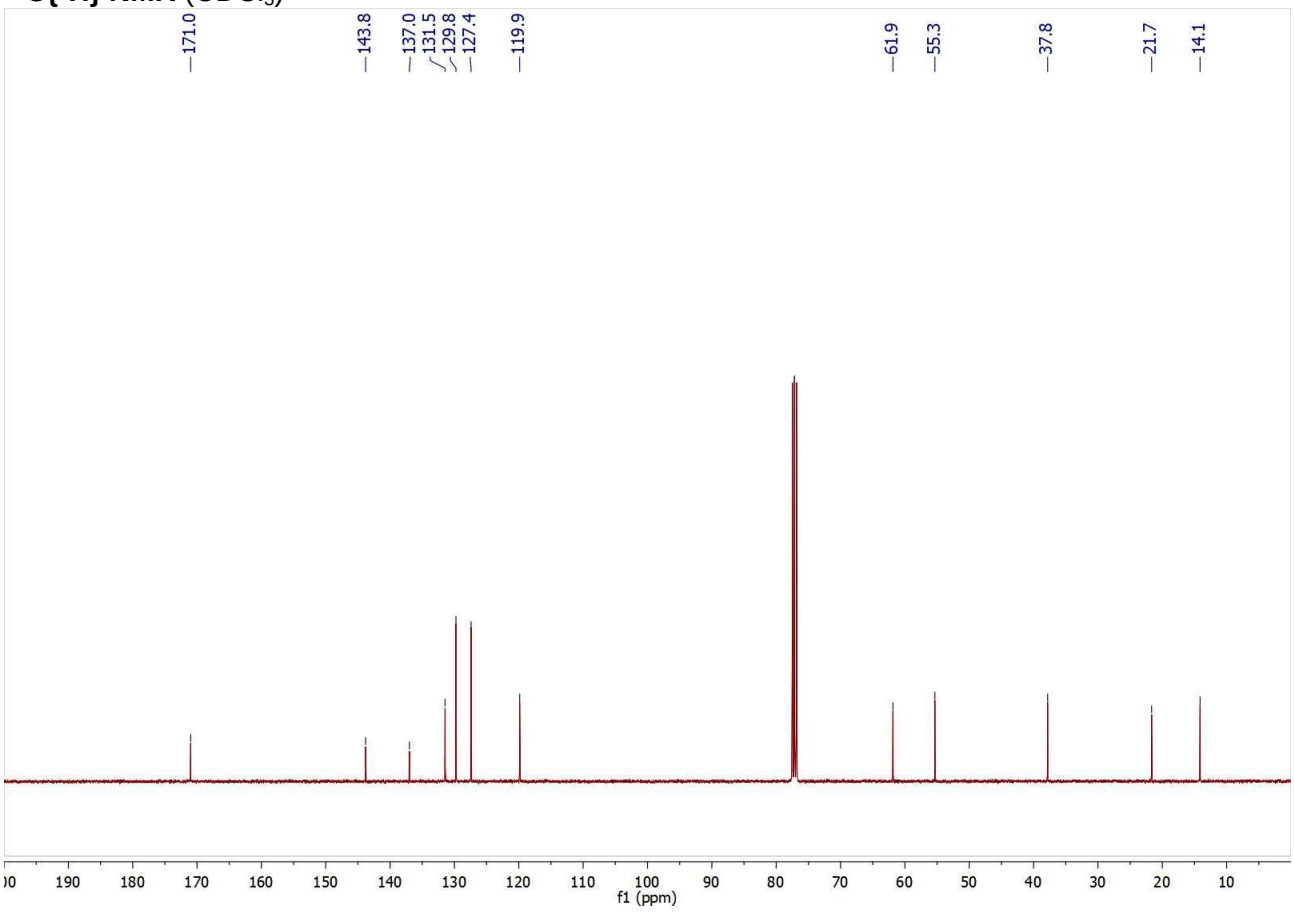


Ethyl 2-(4-methylsulfonamido)pent-4-enoate (1t)

^{1}H NMR ($CDCl_3$)

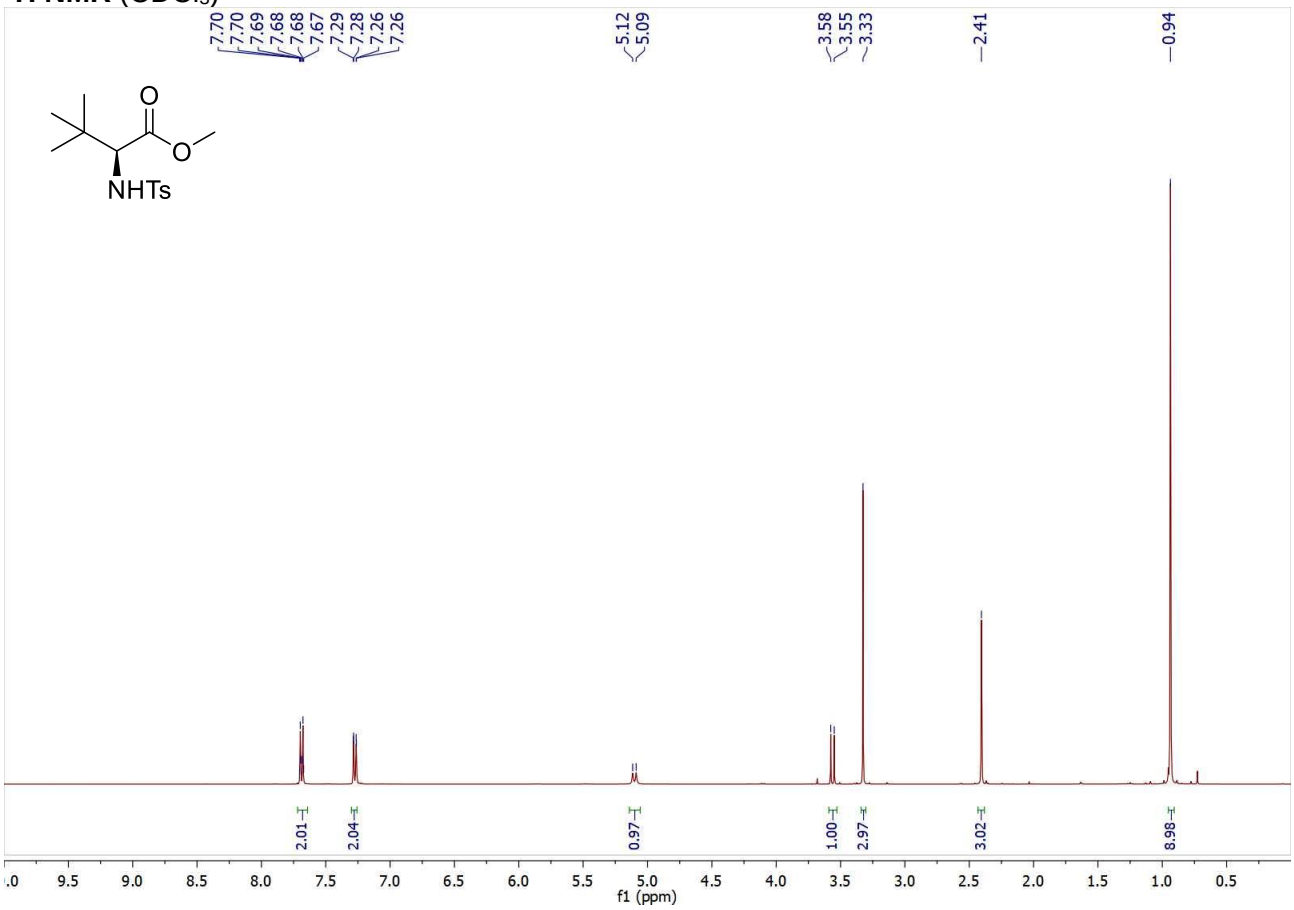


^{13}C{^{1}H} NMR ($CDCl_3$)

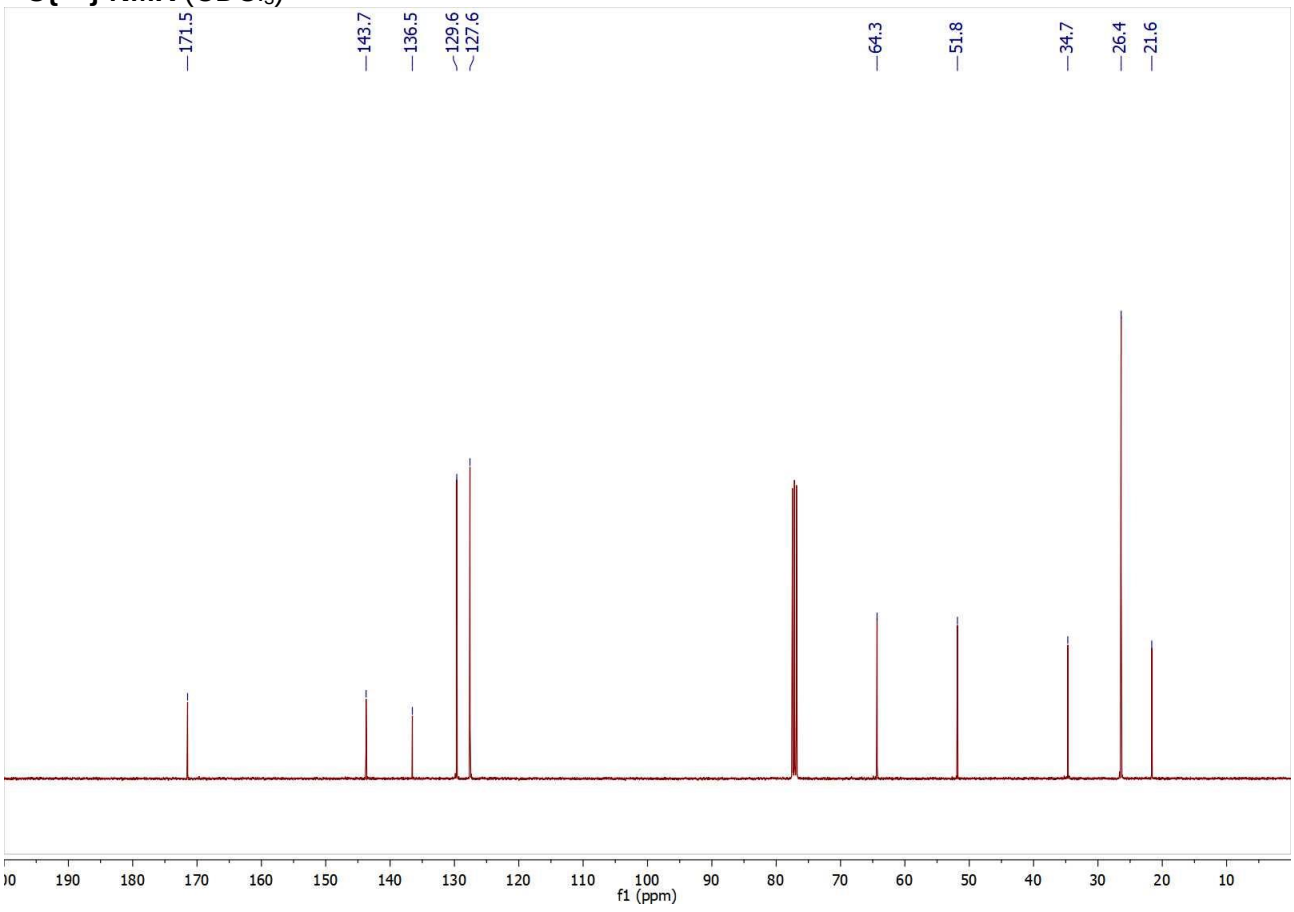


Methyl (*S*)-3,3-dimethyl-2-((4-methylphenyl)sulfonamido)butanoate (1u)

^{1}H NMR ($CDCl_3$)

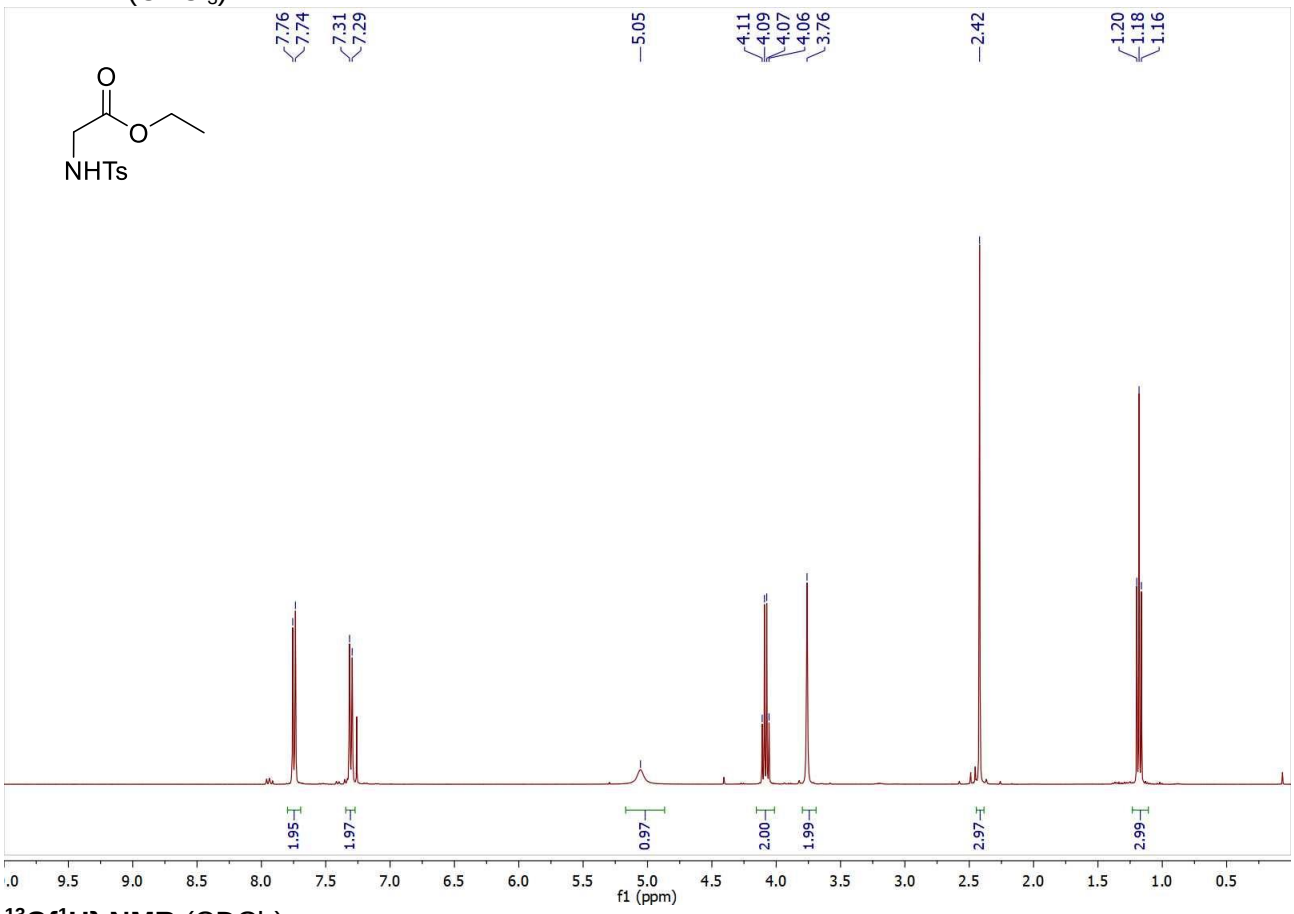


^{13}C{^{1}H} NMR ($CDCl_3$)

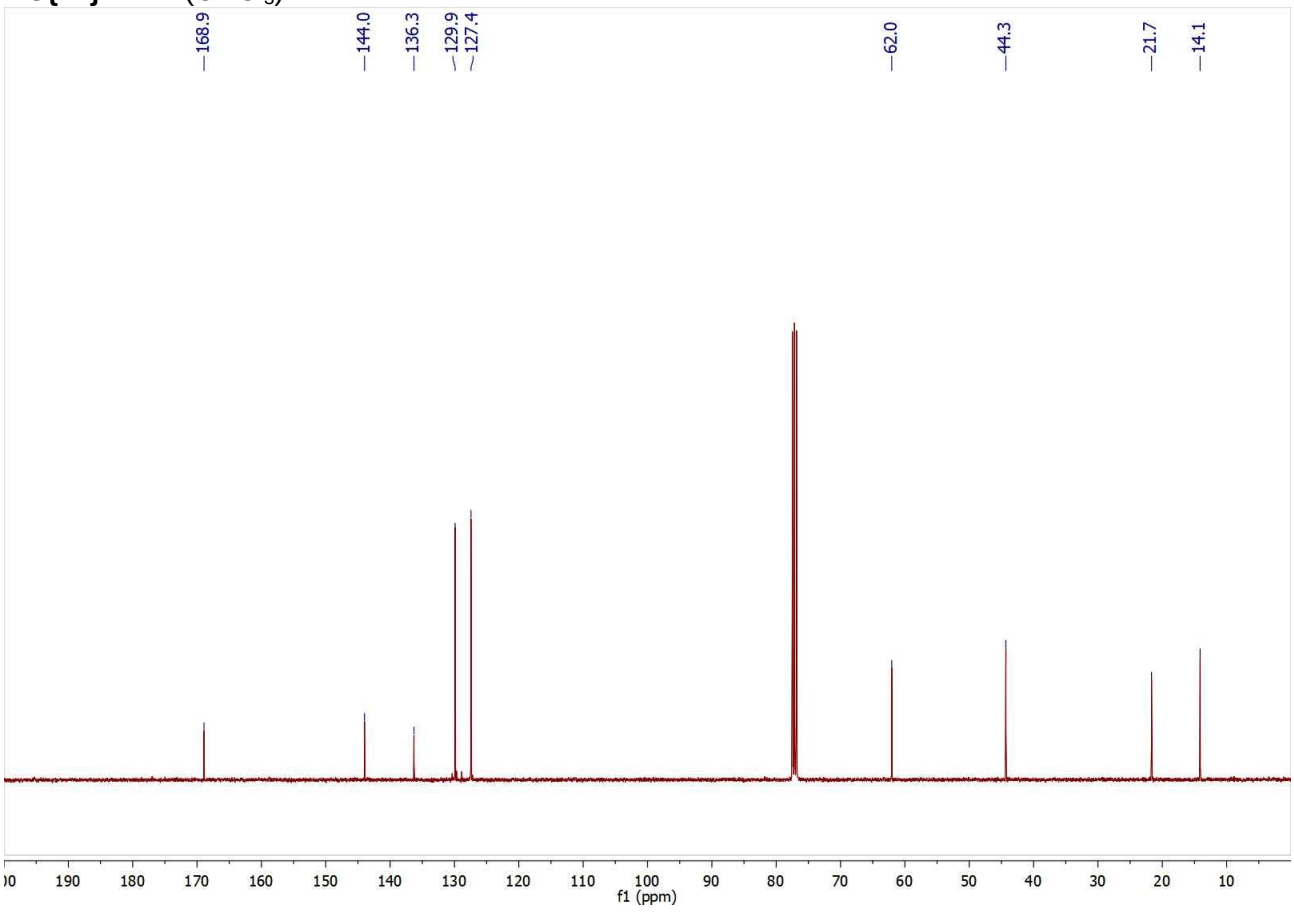


Ethyl 2-(4-methylsulfonilamide) acetate (1v)

^{1}H NMR ($CDCl_3$)

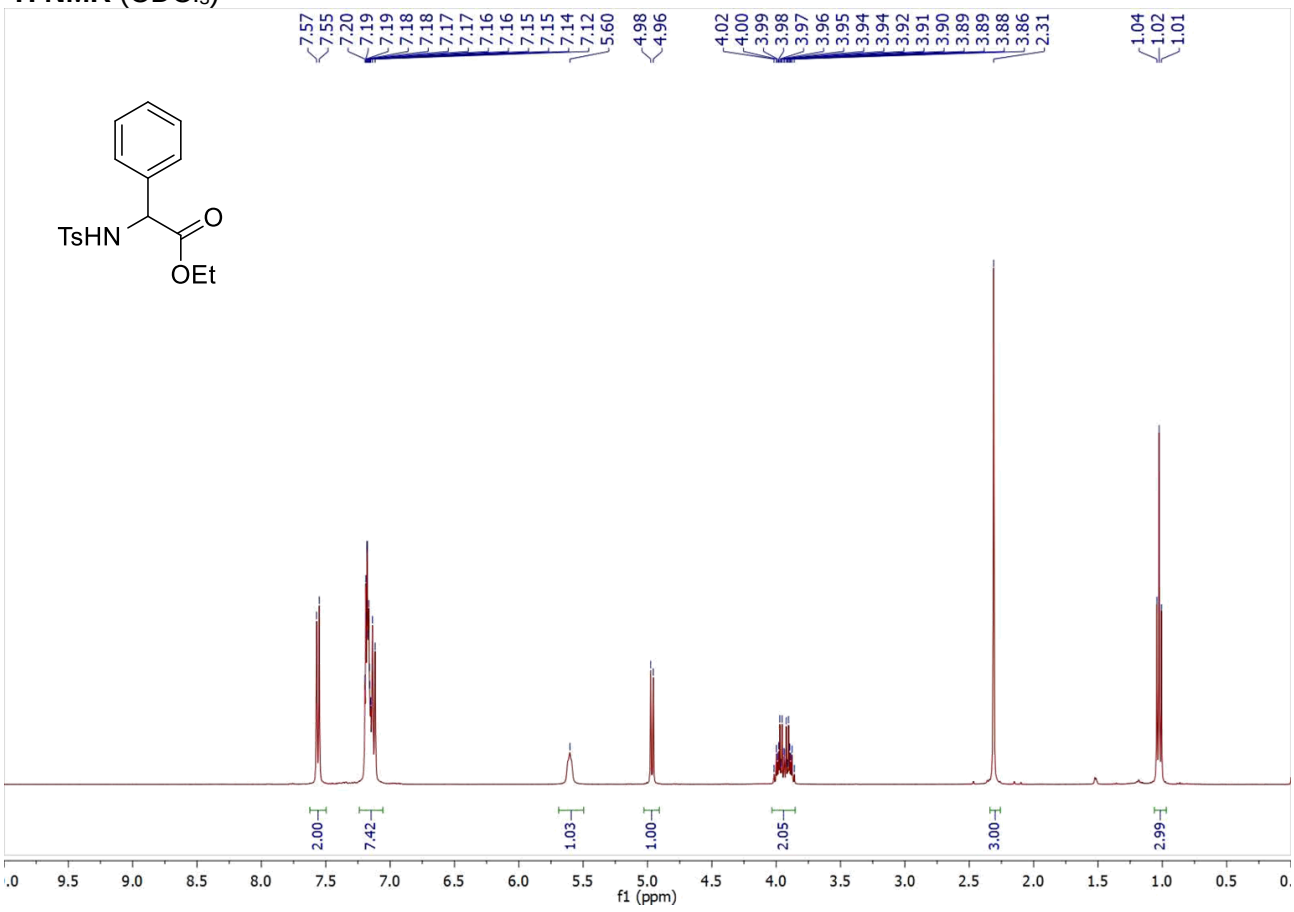


^{13}C{^{1}H} NMR ($CDCl_3$)

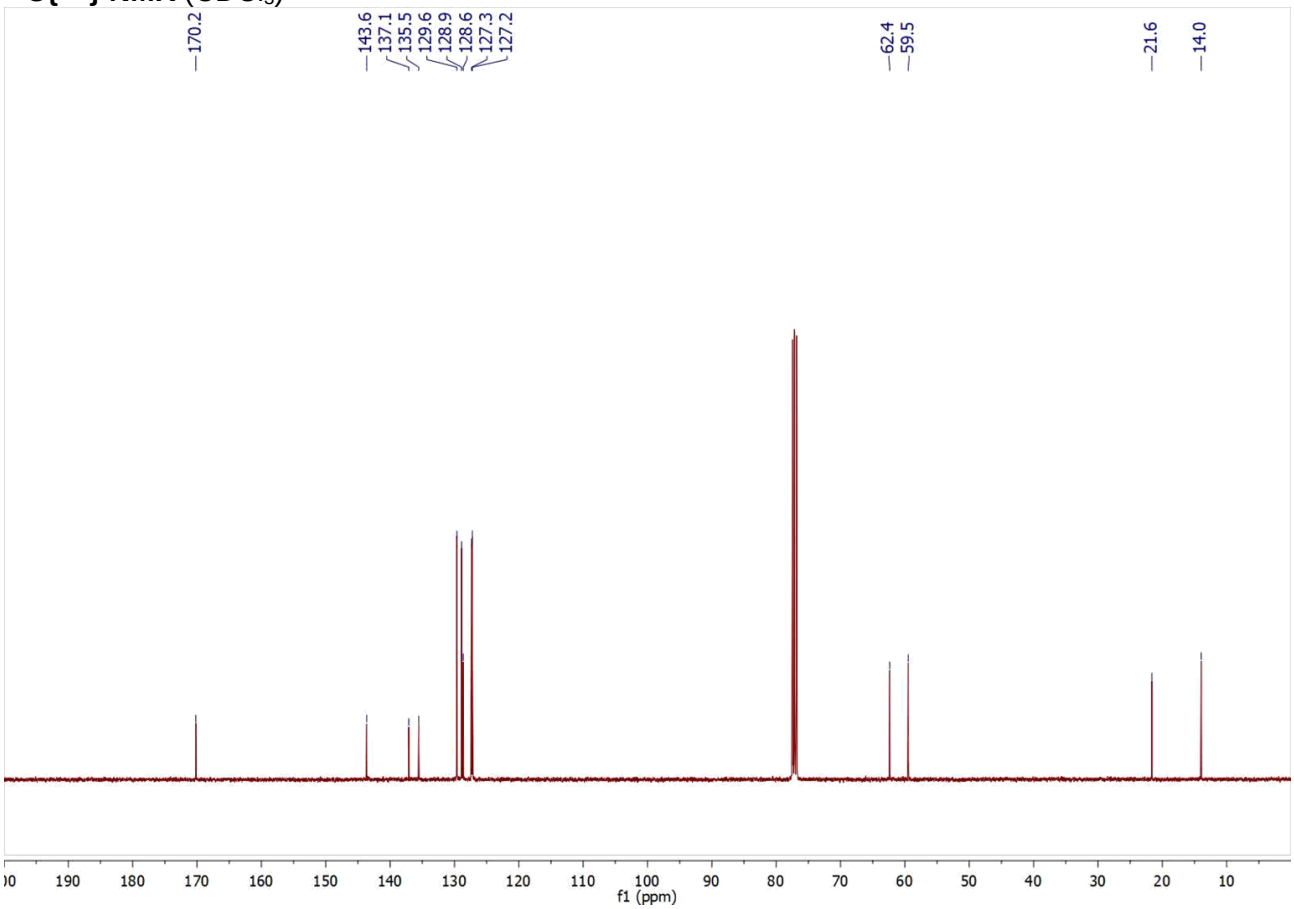


Ethyl 2-((4-methylphenyl)sulfonamido)-2-phenylacetate (1w)

^{1}H NMR ($CDCl_3$)

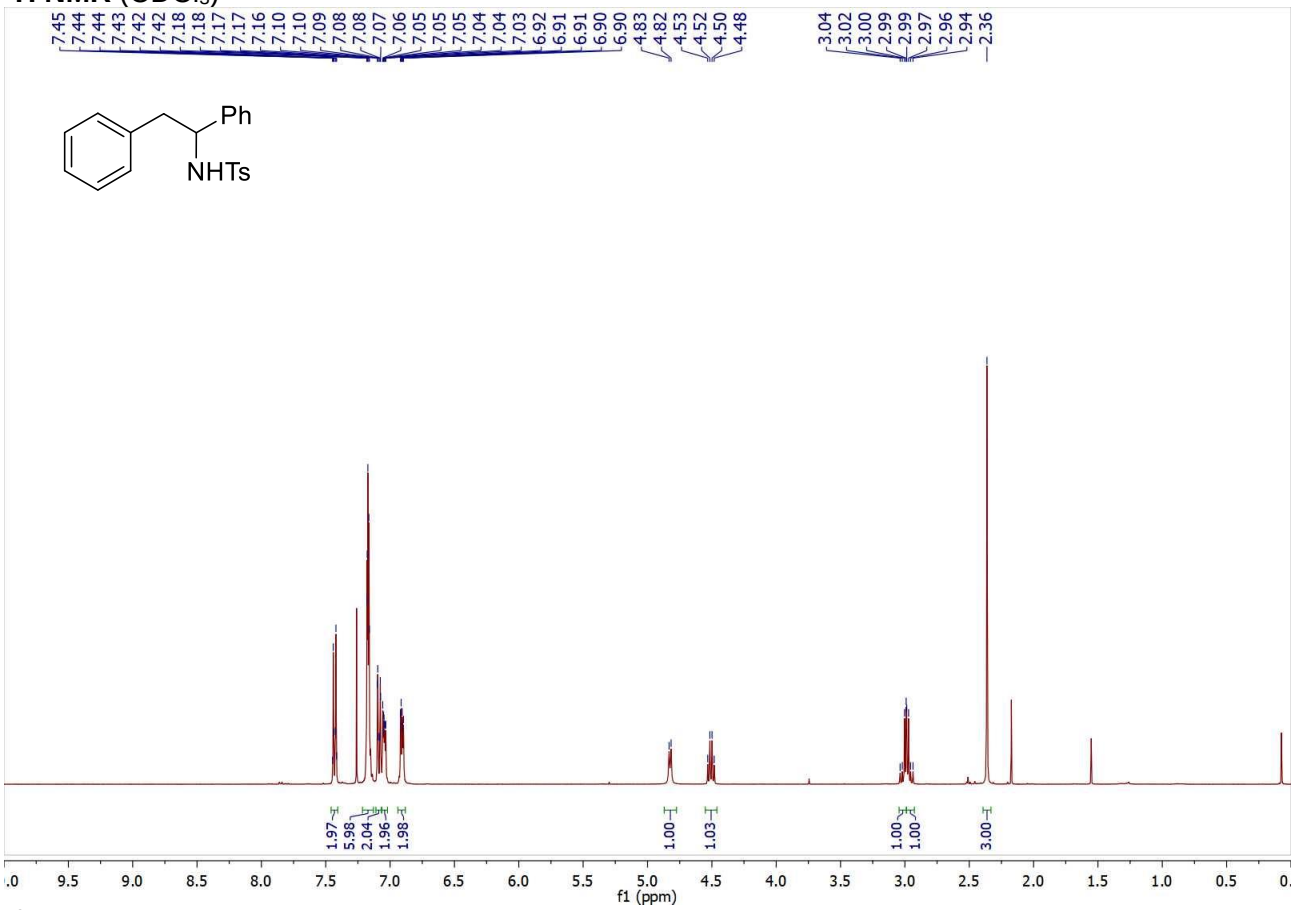


^{13}C{^{1}H} NMR ($CDCl_3$)

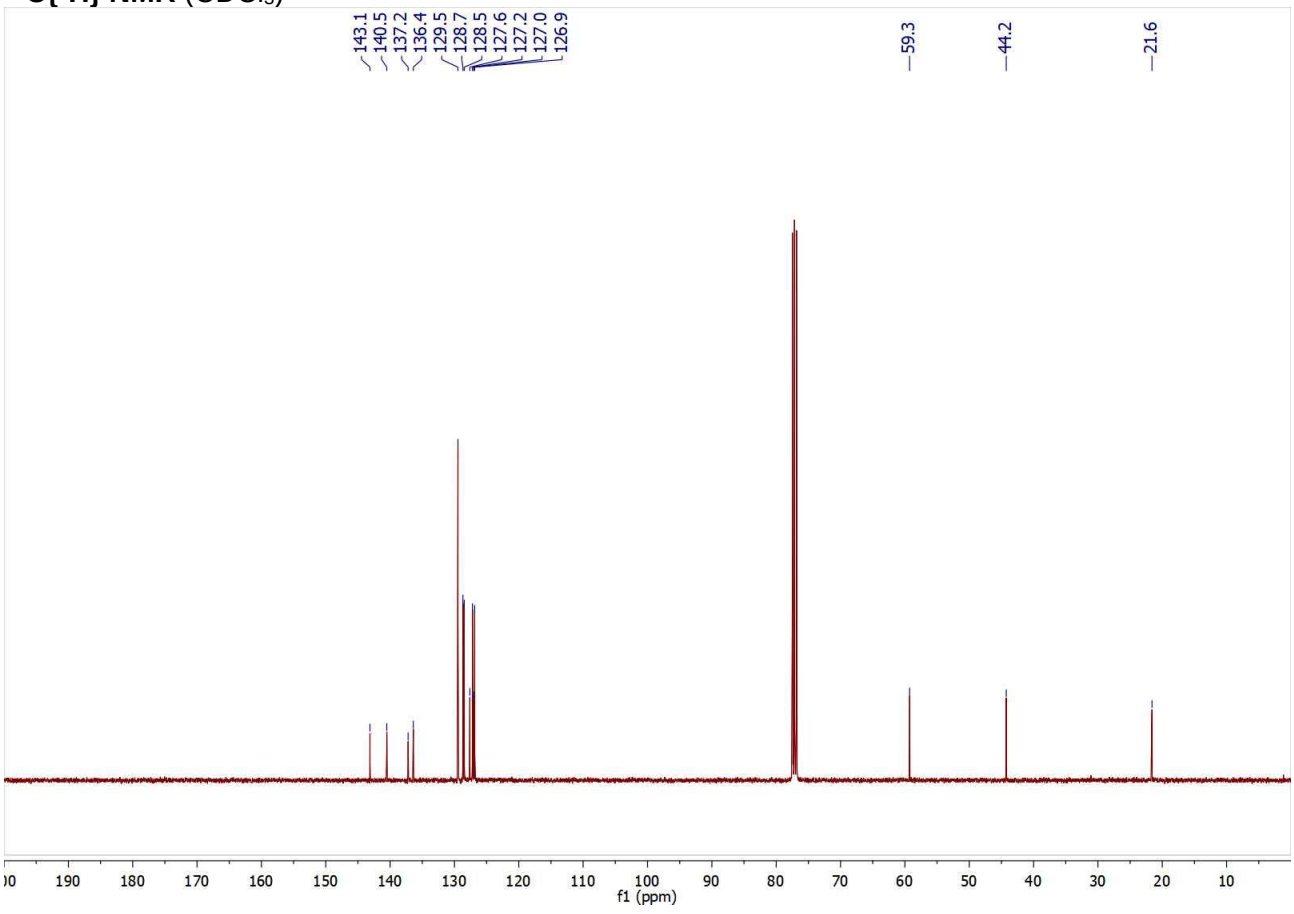


N-(1,2-Diphenylethyl)-4-methylbenzensulfonamide (1x)

^{1}H NMR ($CDCl_3$)

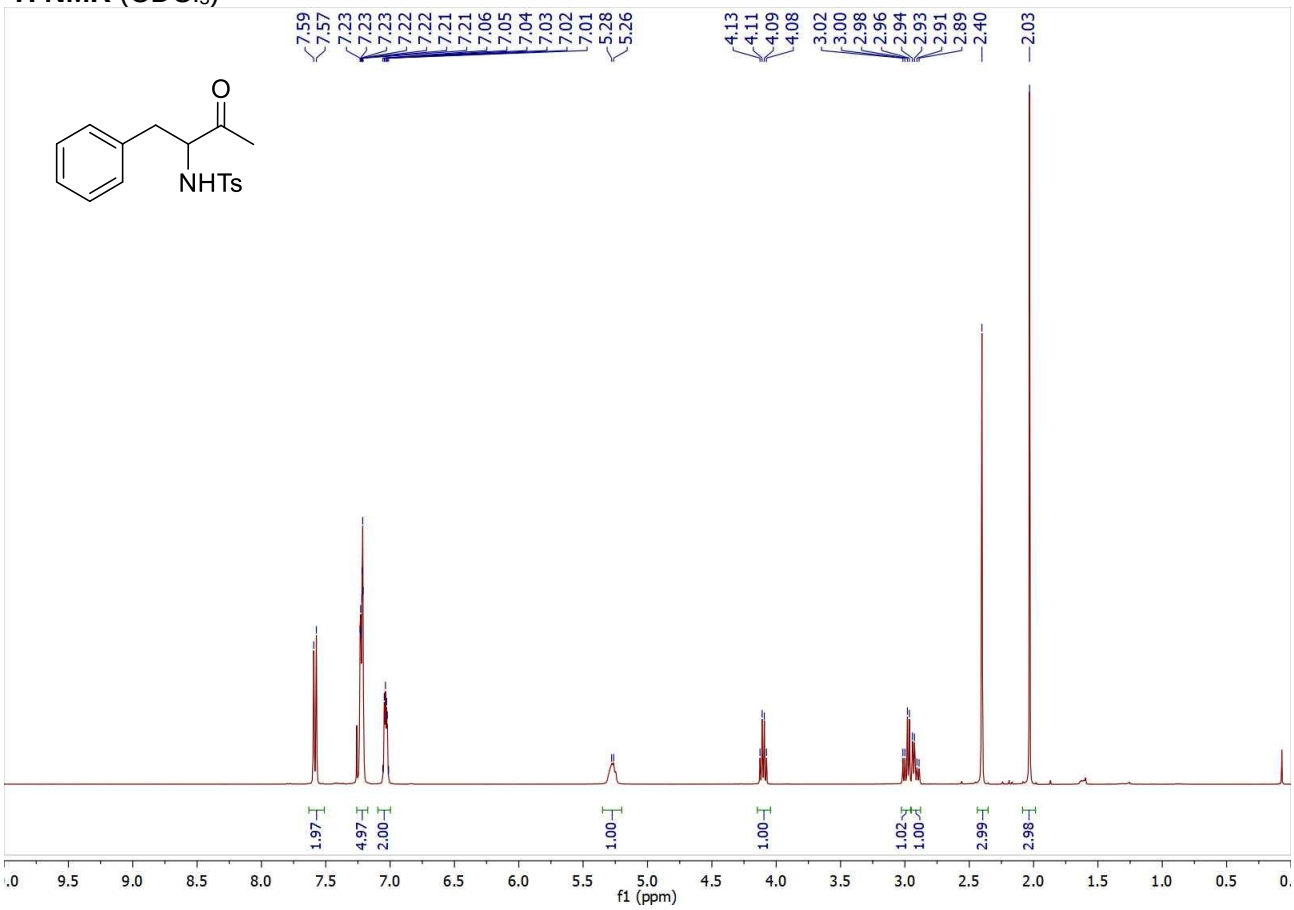


^{13}C{^{1}H} NMR ($CDCl_3$)

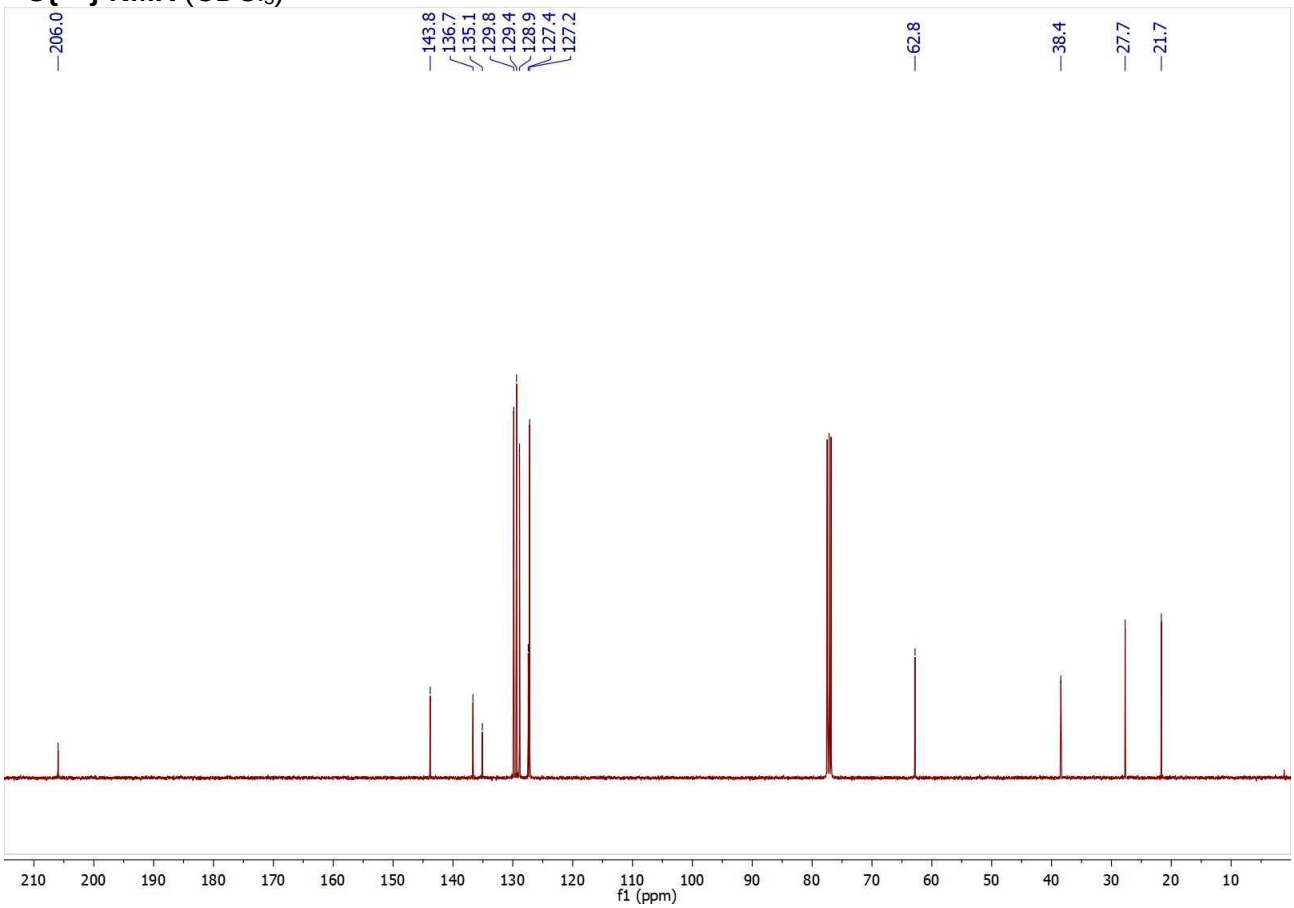


4-Methyl-*N*-(3-oxo-1-phenylbutan-2-yl)benzensulfonamide (S4)

^{1}H NMR ($CDCl_3$)

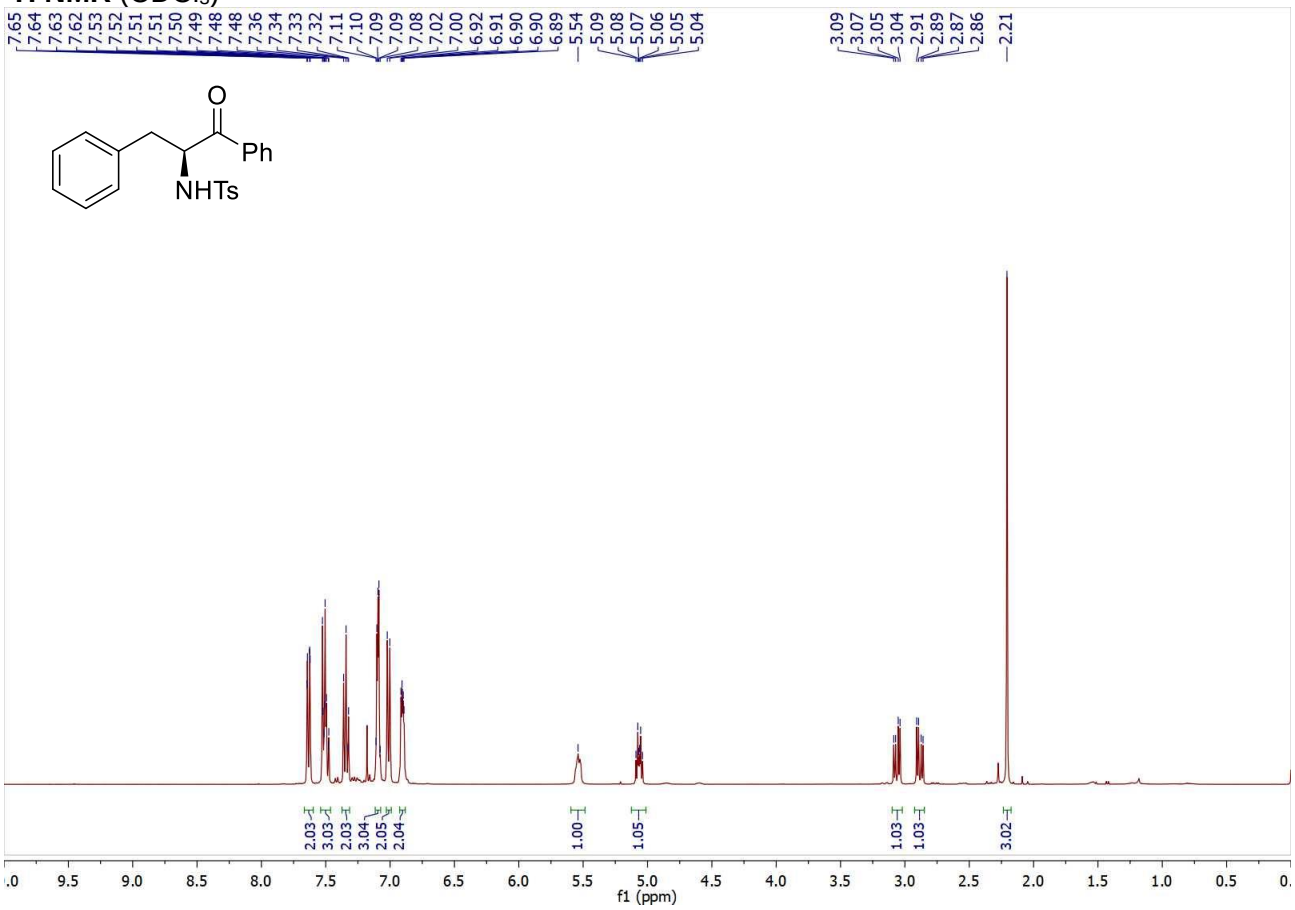


^{13}C{^{1}H} NMR ($CDCl_3$)

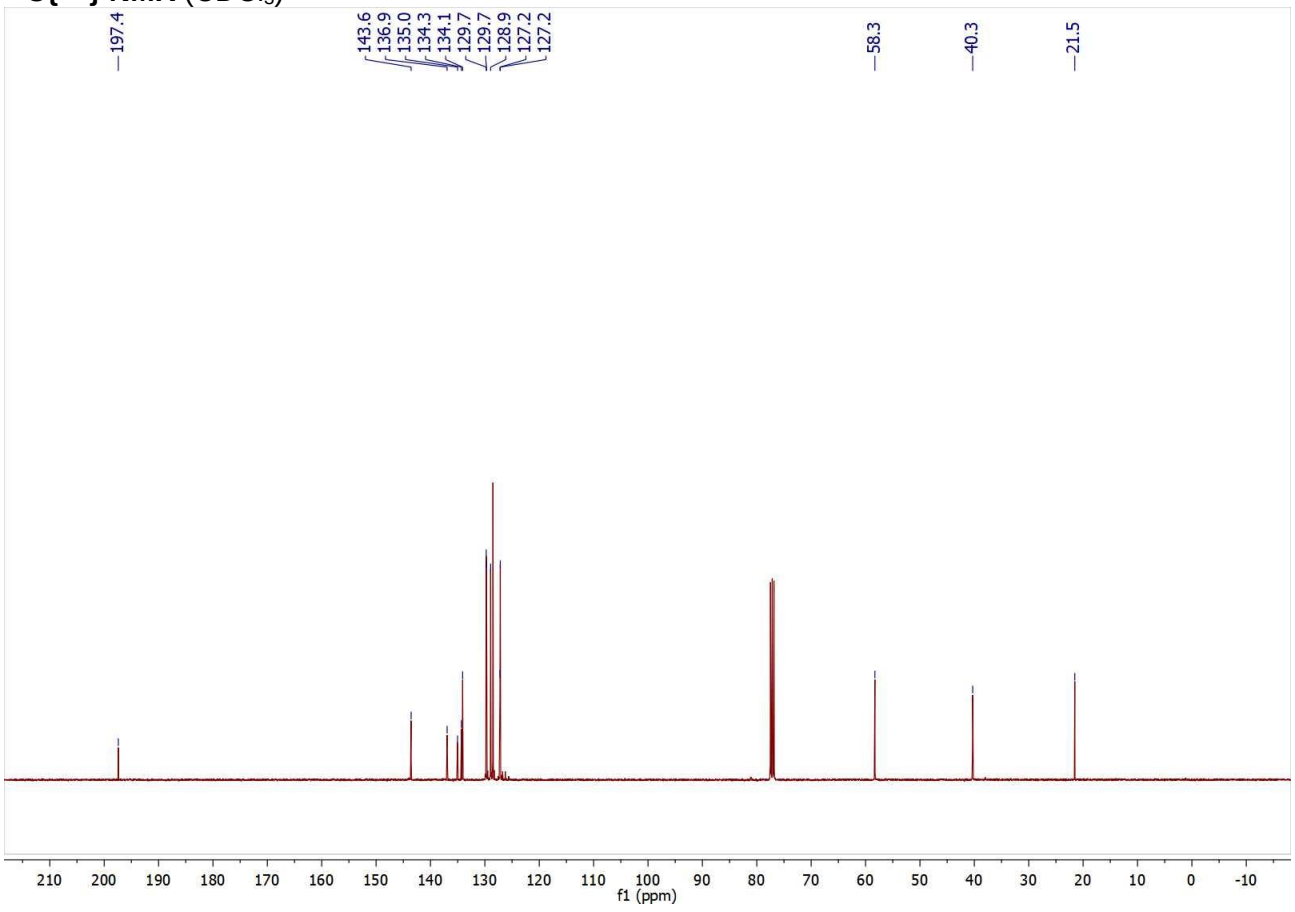


(*S*)-4-Methyl-*N*-(1-oxo-1,3-diphenylpropan-2-yl)benzensulfonamide (S5)

^{1}H NMR ($CDCl_3$)

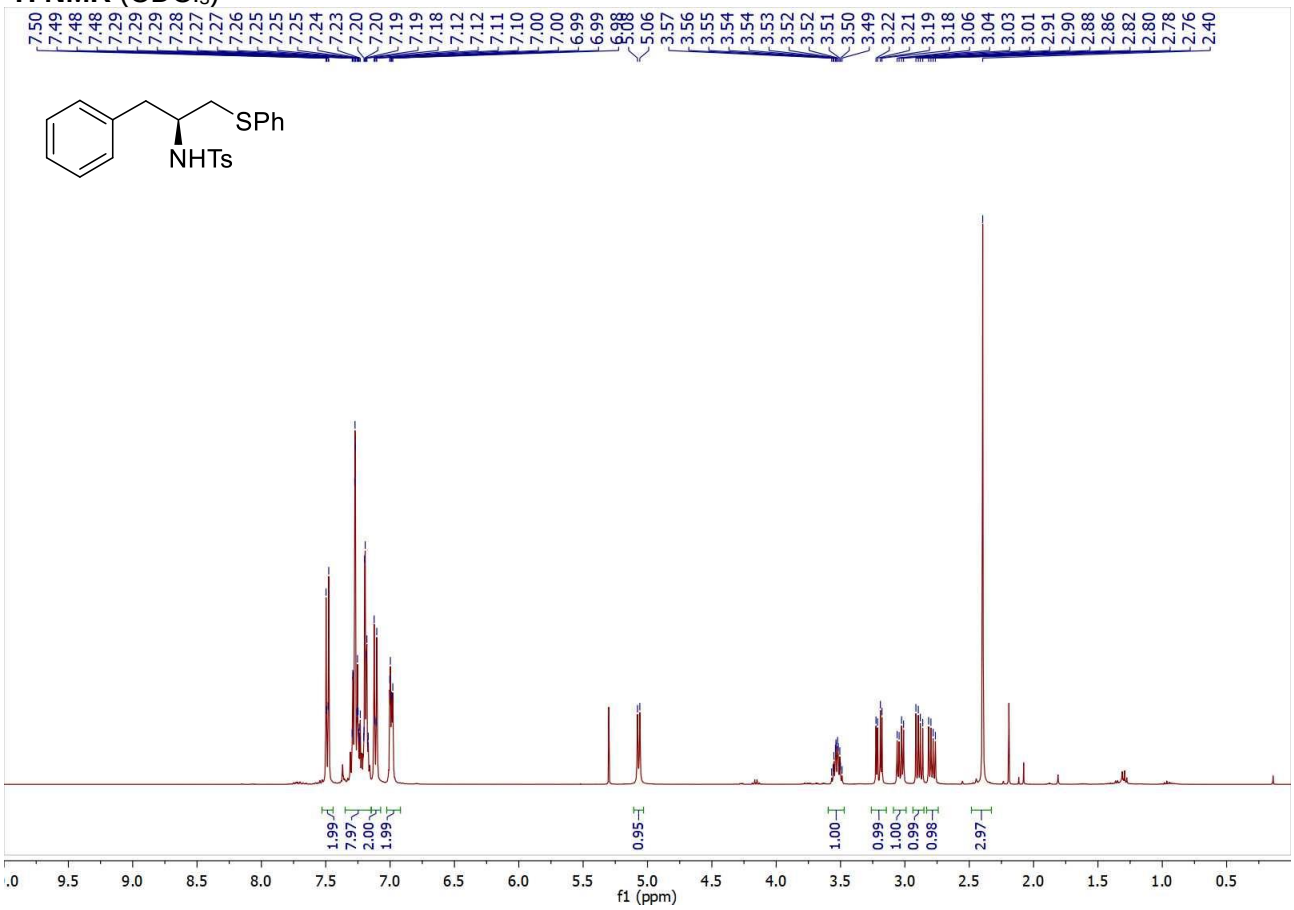


^{13}C{^{1}H} NMR ($CDCl_3$)

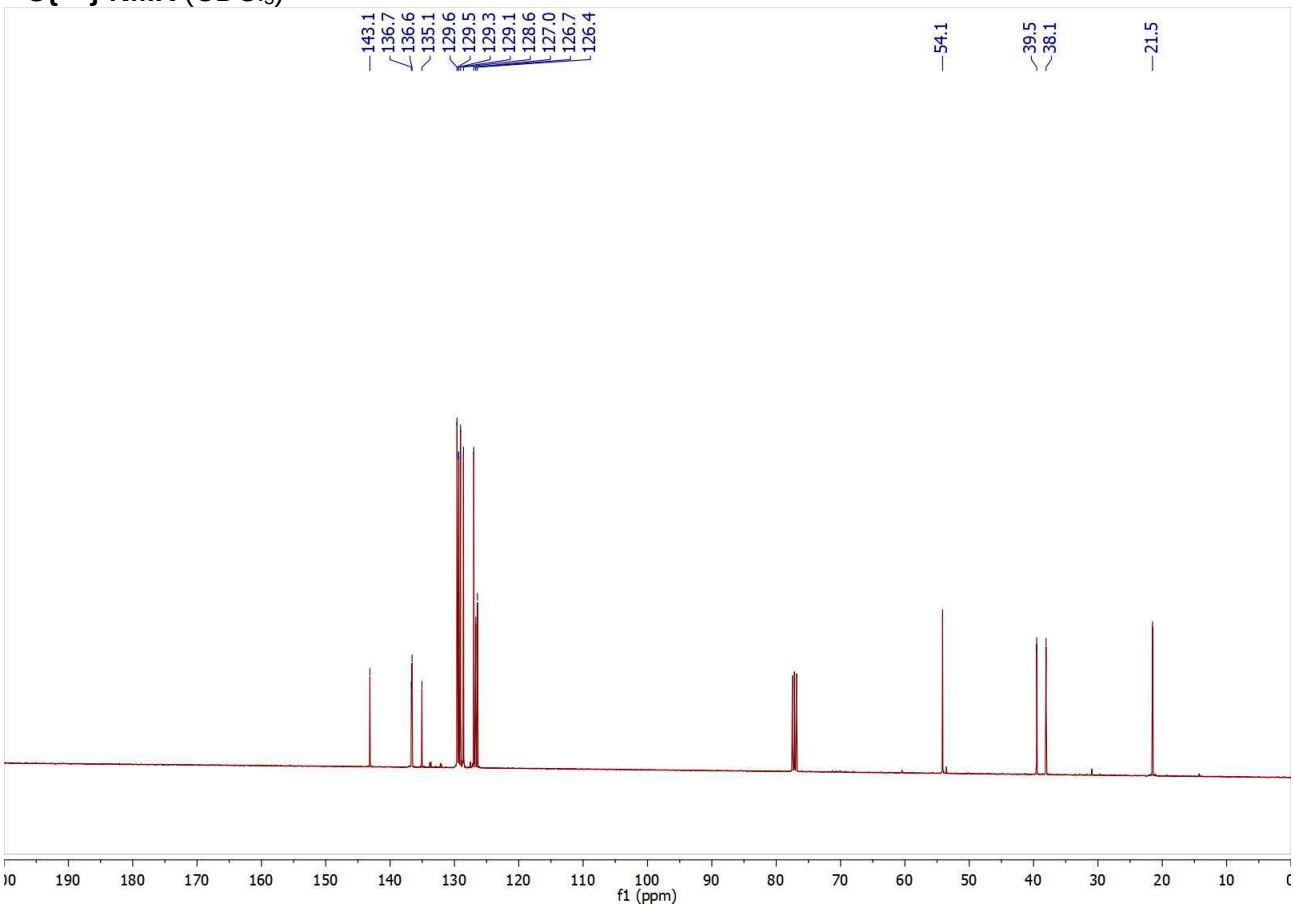


(*S*)-4-Methyl-*N*-(1-phenyl-3-(phenylthio)propan-2-yl)benzensulfonamide (S6)

^{1}H NMR ($CDCl_3$)

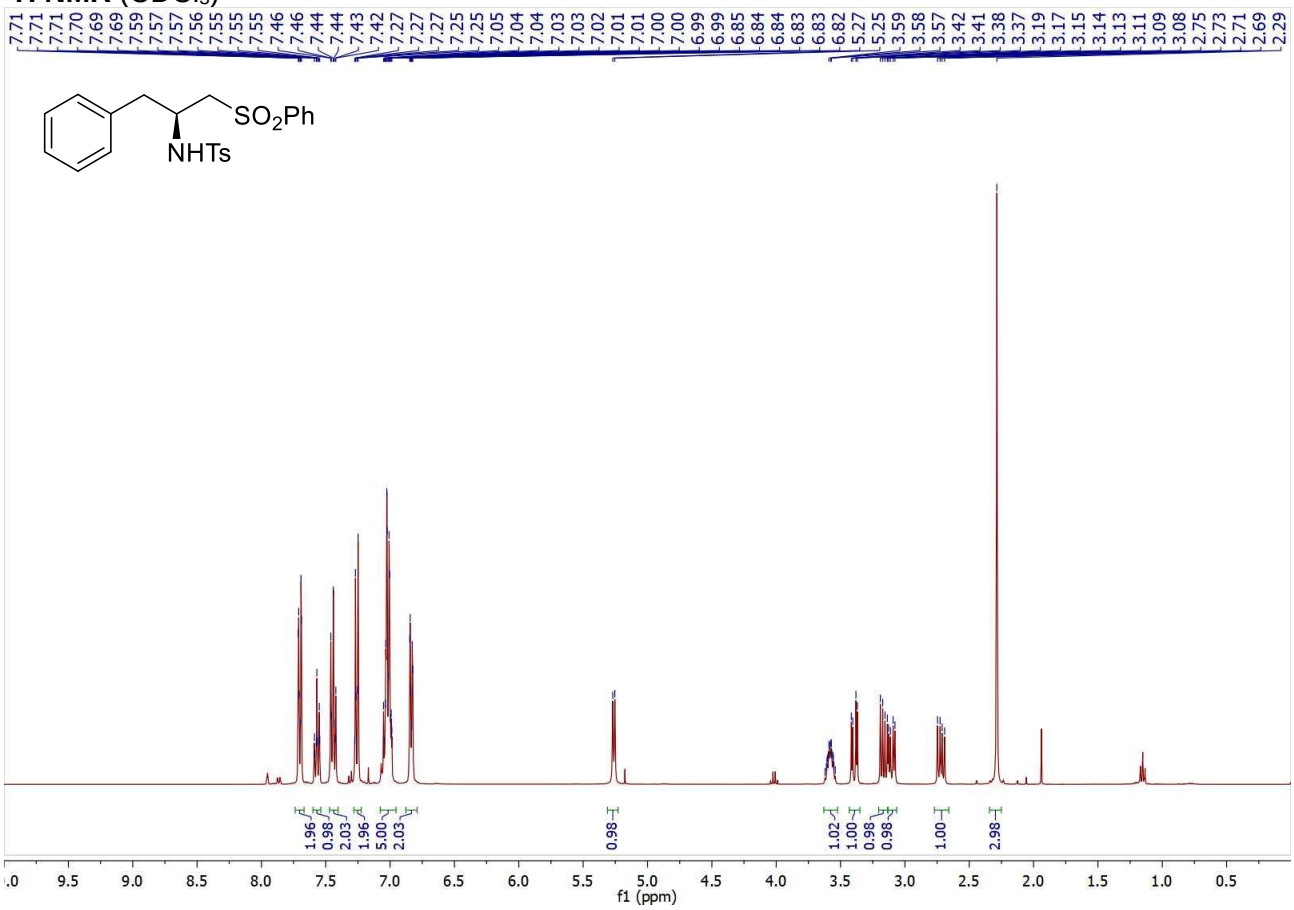


^{13}C{^{1}H} NMR ($CDCl_3$)

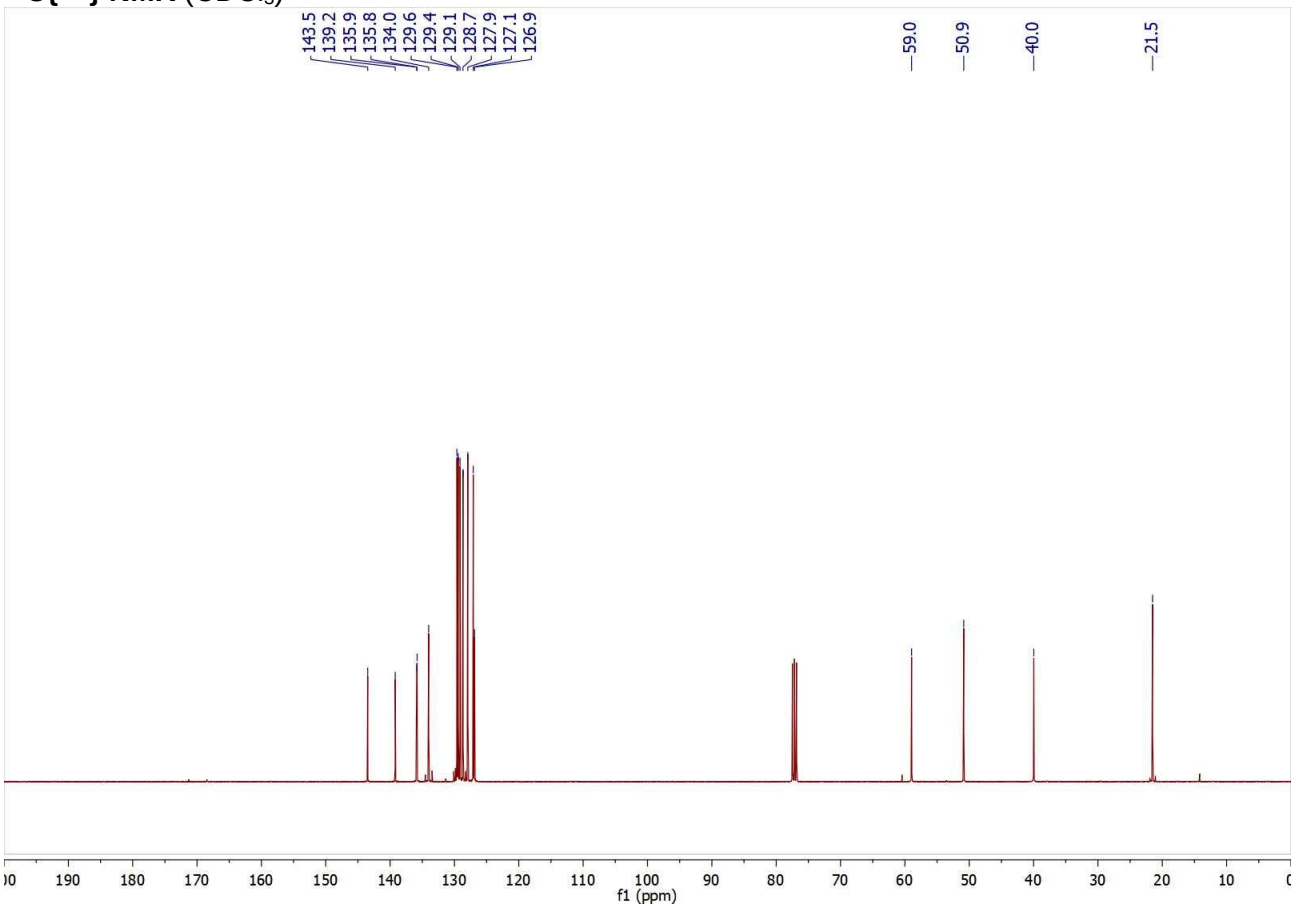


***(S)*-4-Methyl-*N*-(1-phenyl-3-(phenylsulfonyl)propan-2-yl)benzensulfonamide (S7)**

^{1}H NMR ($CDCl_3$)

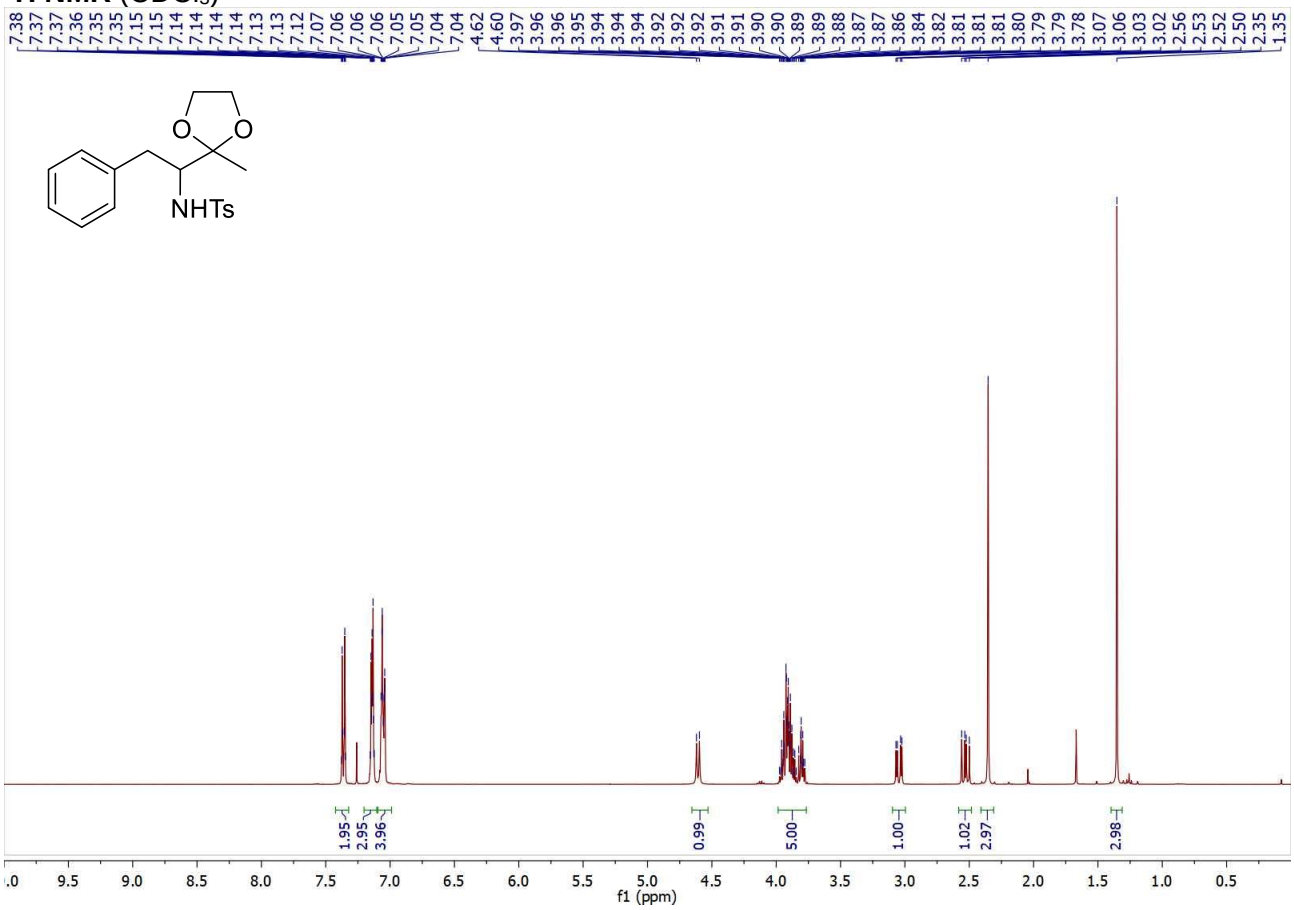


^{13}C{^{1}H} NMR ($CDCl_3$)

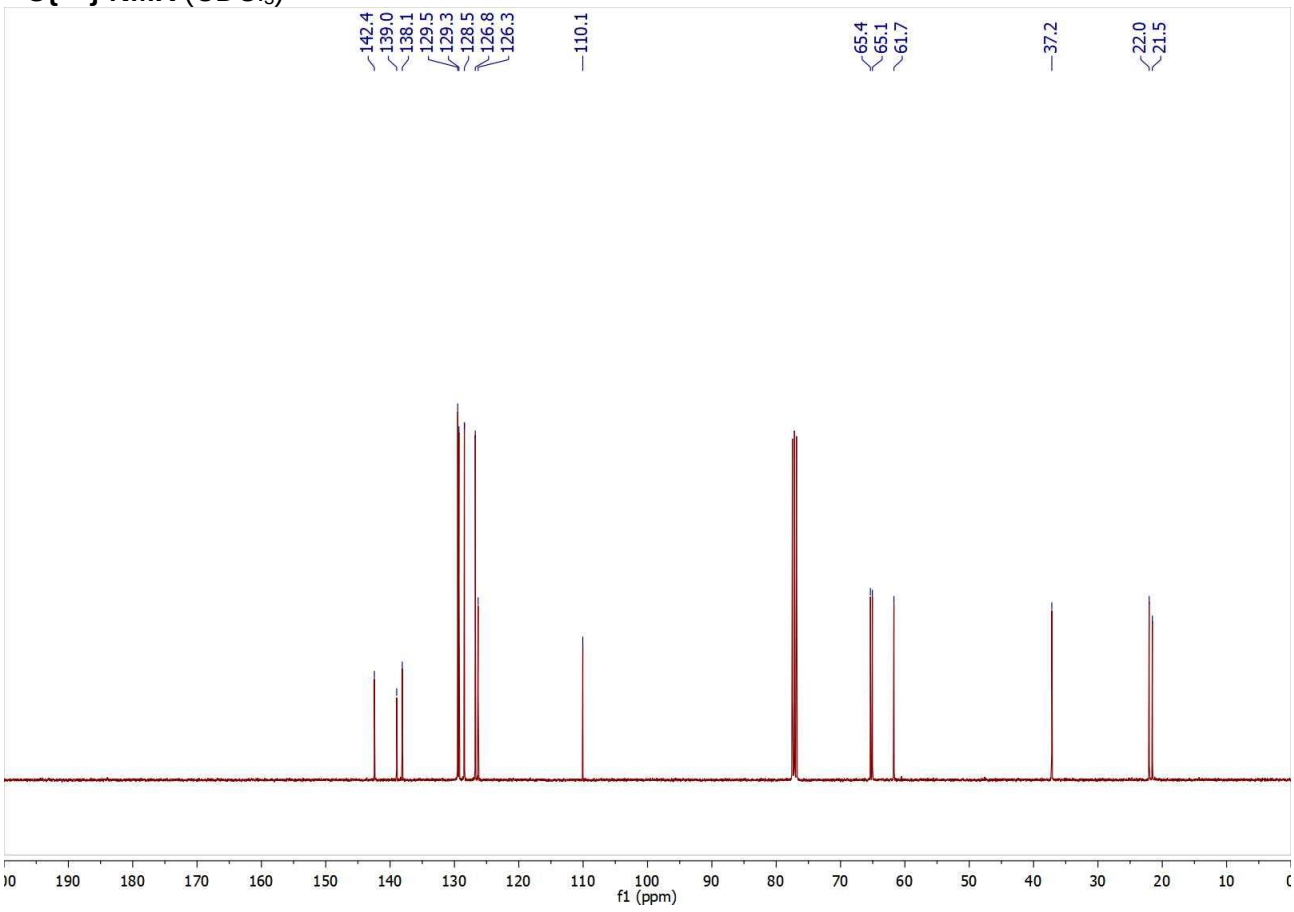


4-Methyl-*N*-(1-(2-methyl-1,3-dioxolan-2-yl)-2-phenylethyl)benzensulfonamide (S8)

^{1}H NMR ($CDCl_3$)

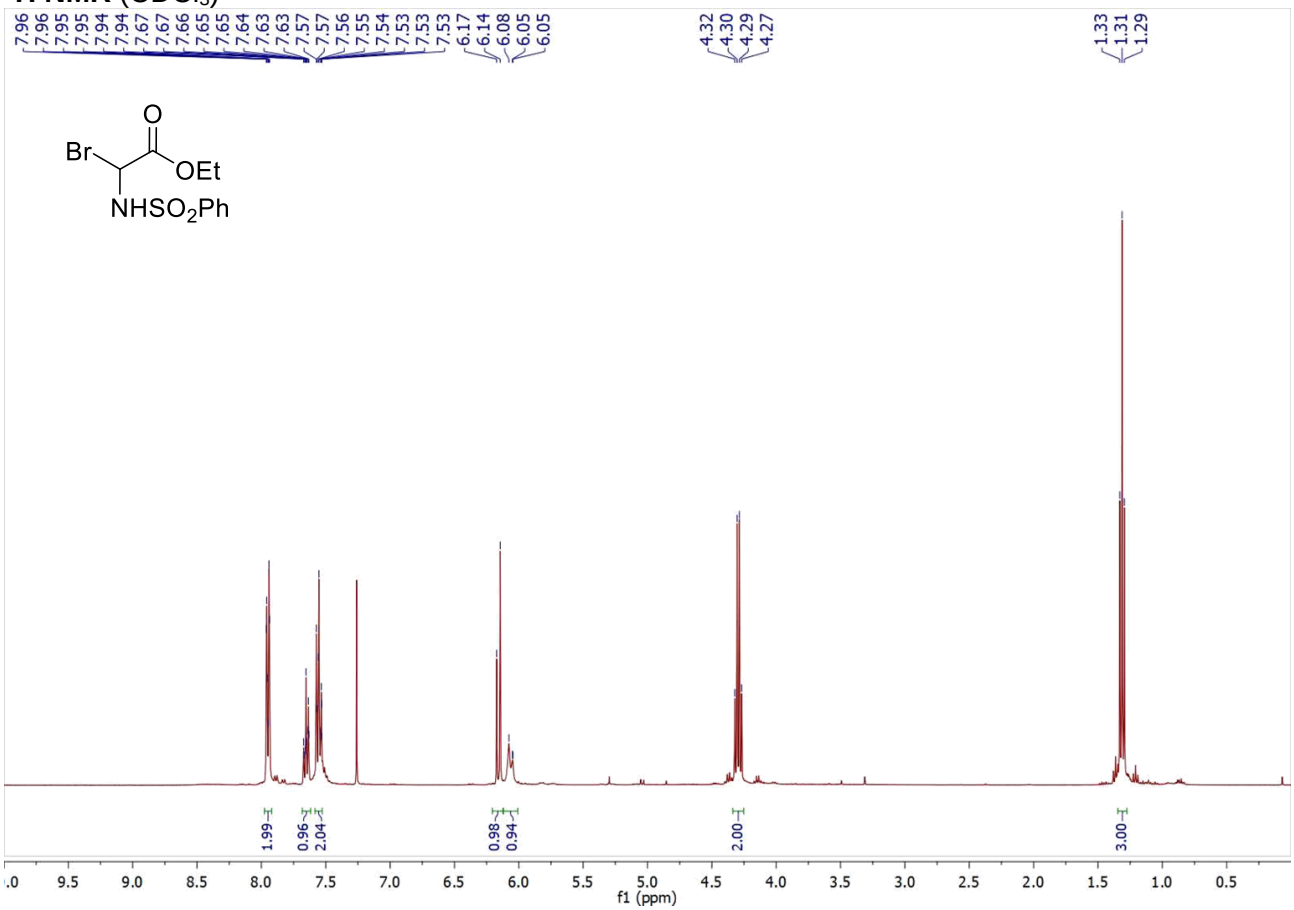


^{13}C{^{1}H} NMR ($CDCl_3$)

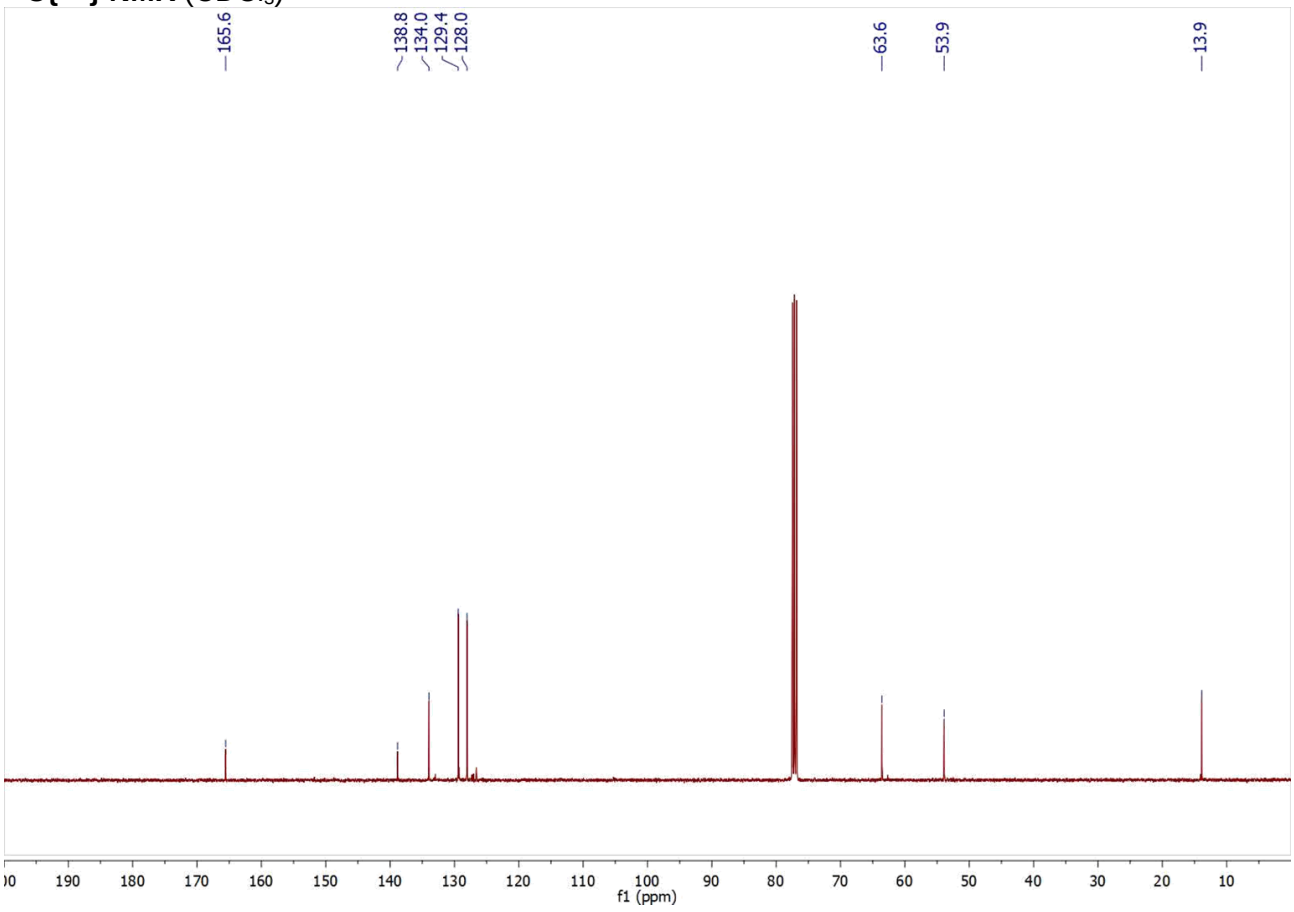


Ethyl 2-bromo-2(phenylsulfonamido)acetate (S9)

^{1}H NMR ($CDCl_3$)

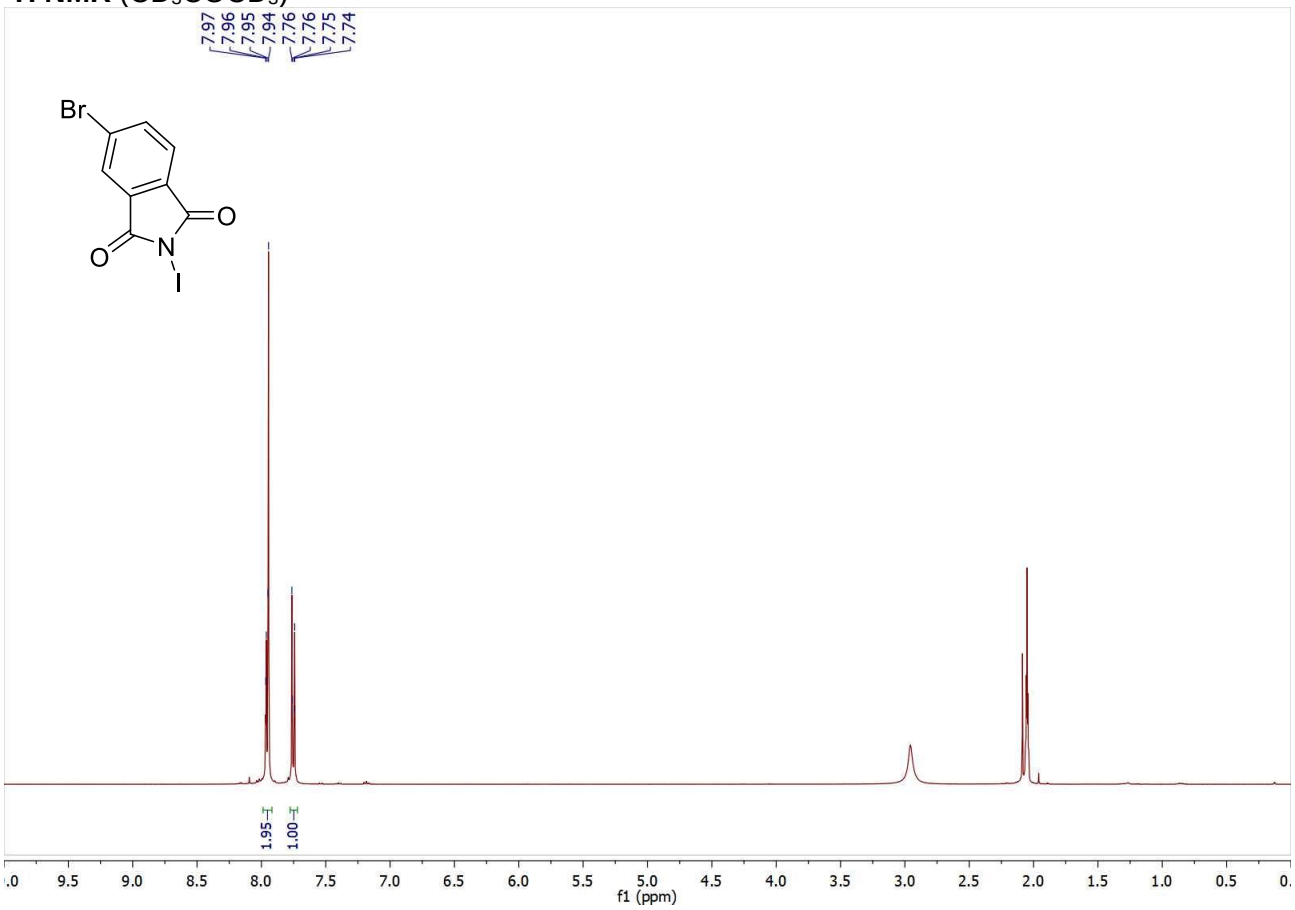


^{13}C{^{1}H} NMR ($CDCl_3$)

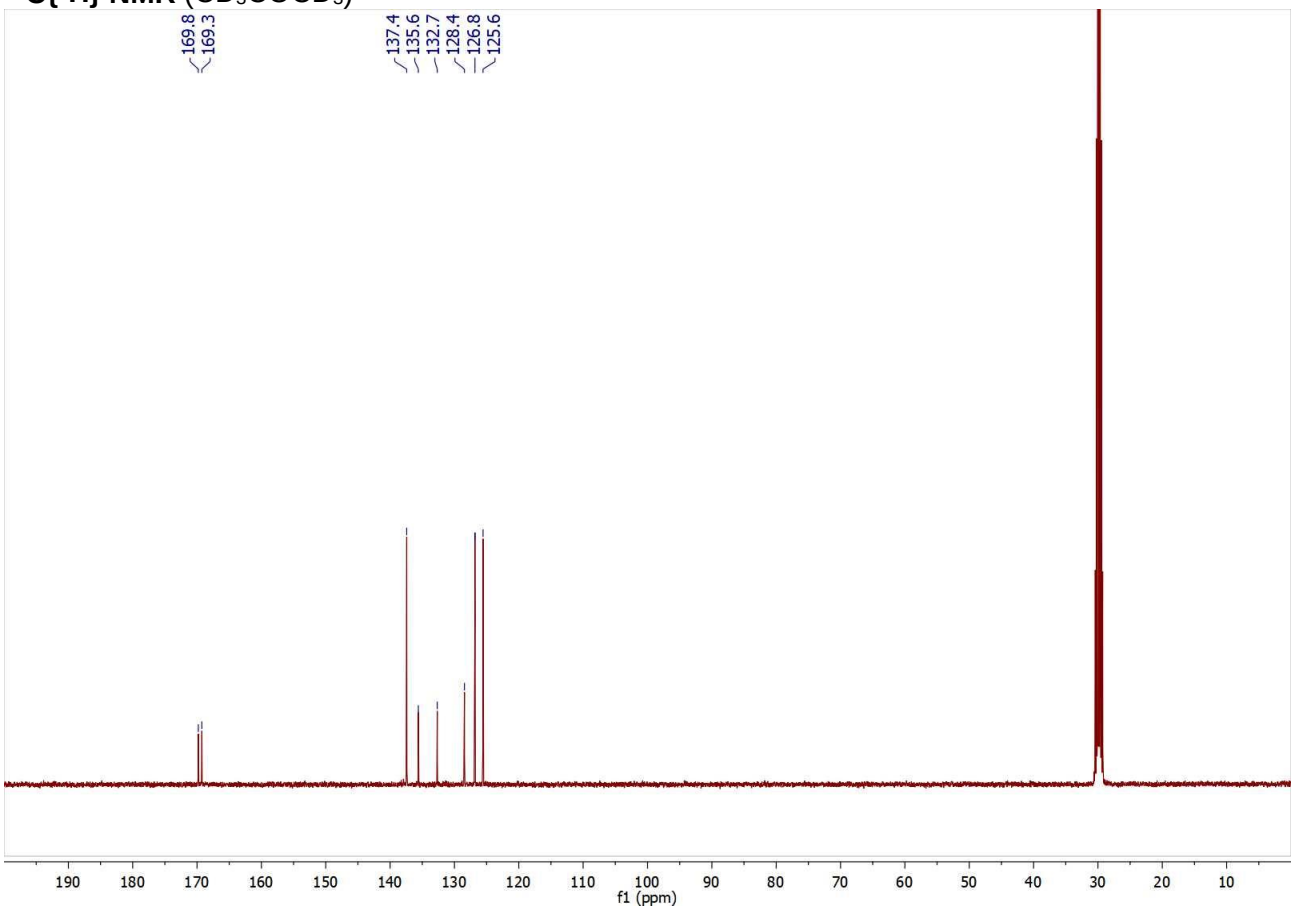


5-Bromo-2-iodoisoindoline-1,3-dione (S1ab)

^{1}H NMR (CD_3COCD_3)

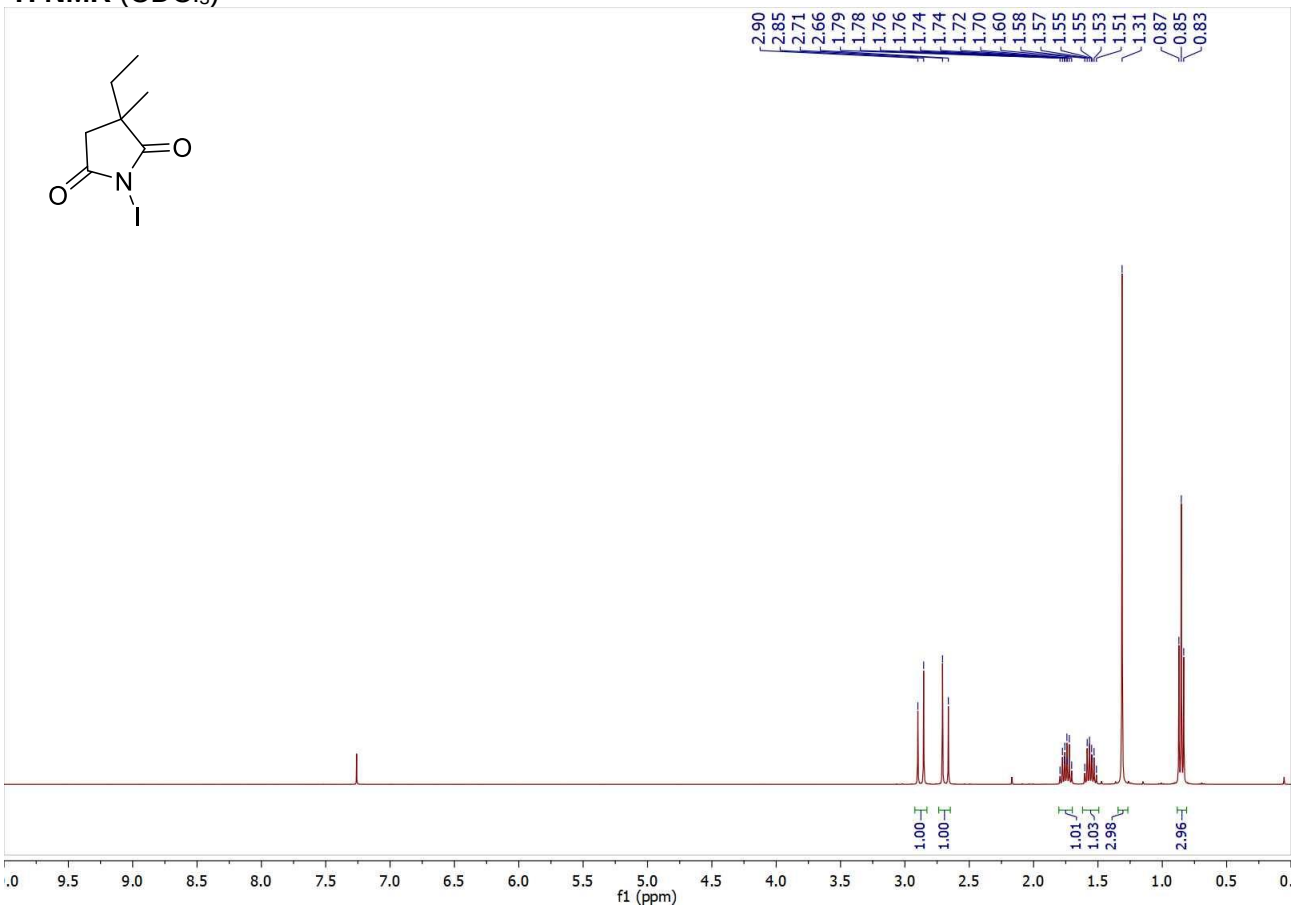


^{13}C{^{1}H} NMR (CD_3COCD_3)

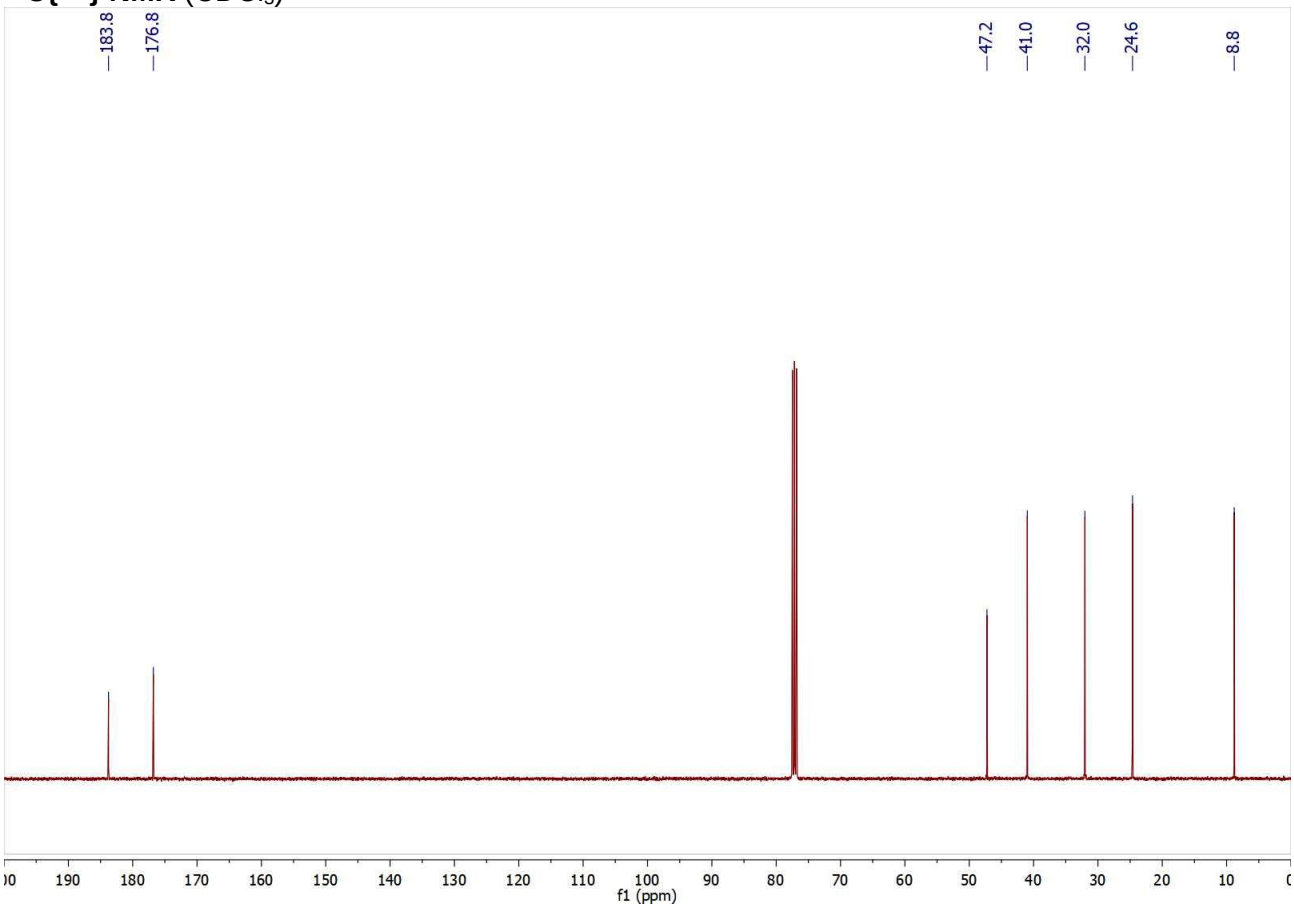


3-Ethyl-1-iodo-3-methylpyrrolidine-2,5-dione (*N*-iodoethosuxumide) (S1ac)

^{1}H NMR ($CDCl_3$)

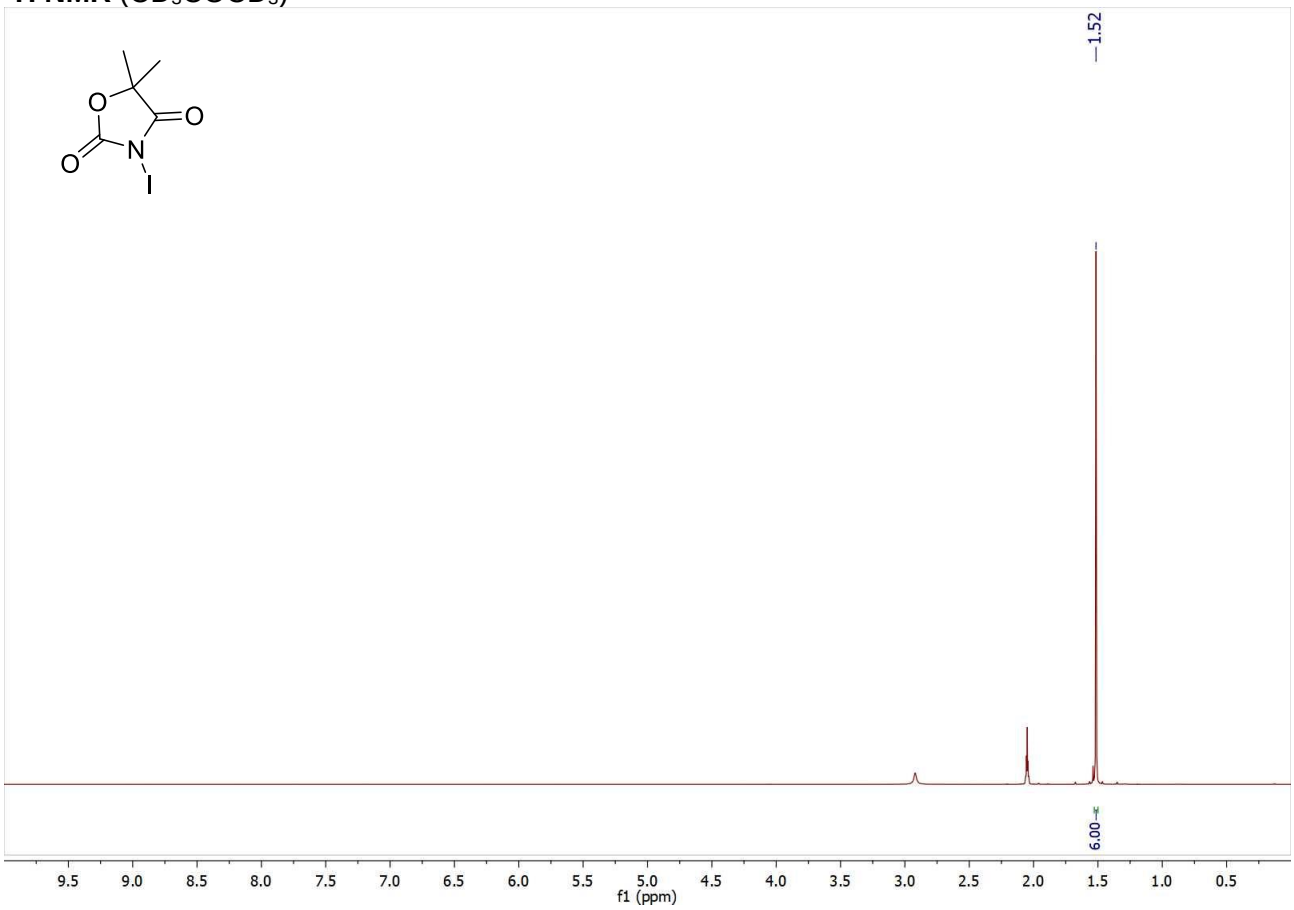


^{13}C{^{1}H} NMR ($CDCl_3$)

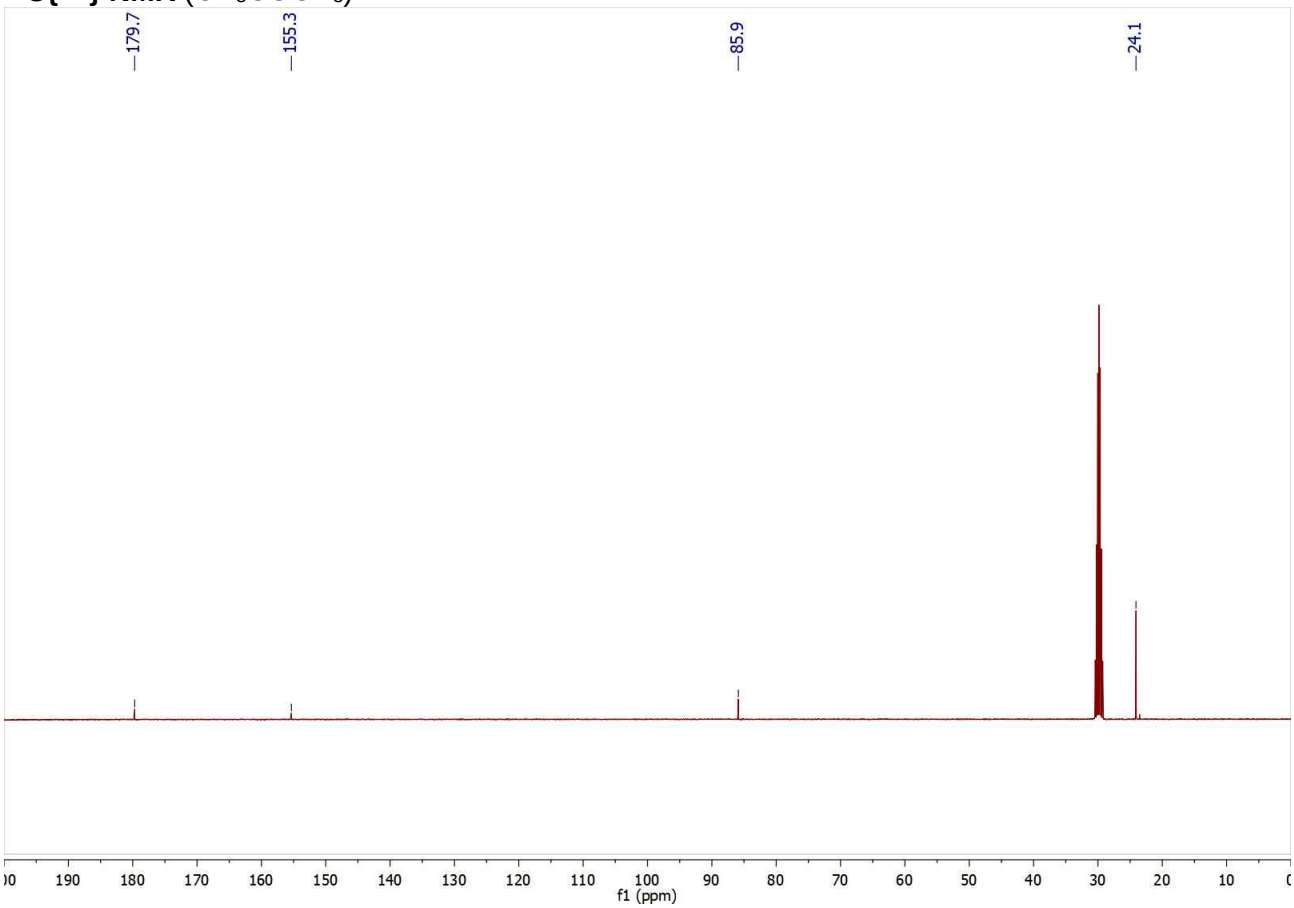


3-Iodo-5,5-dimethyloxazolidine-2,4-dione (S1ad)

^{1}H NMR (CD_3COCD_3)

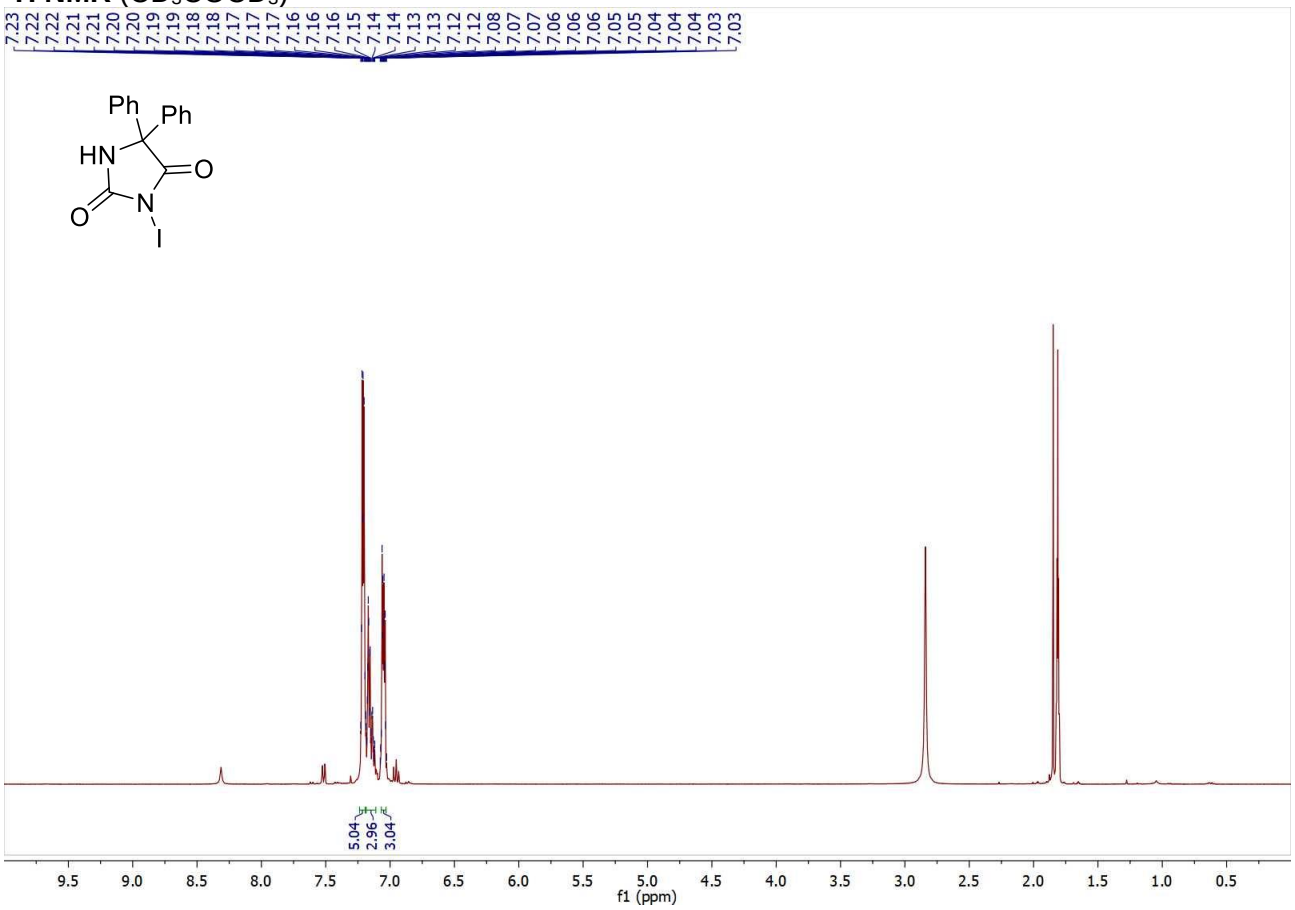


^{13}C{^{1}H} NMR (CD_3COCD_3)

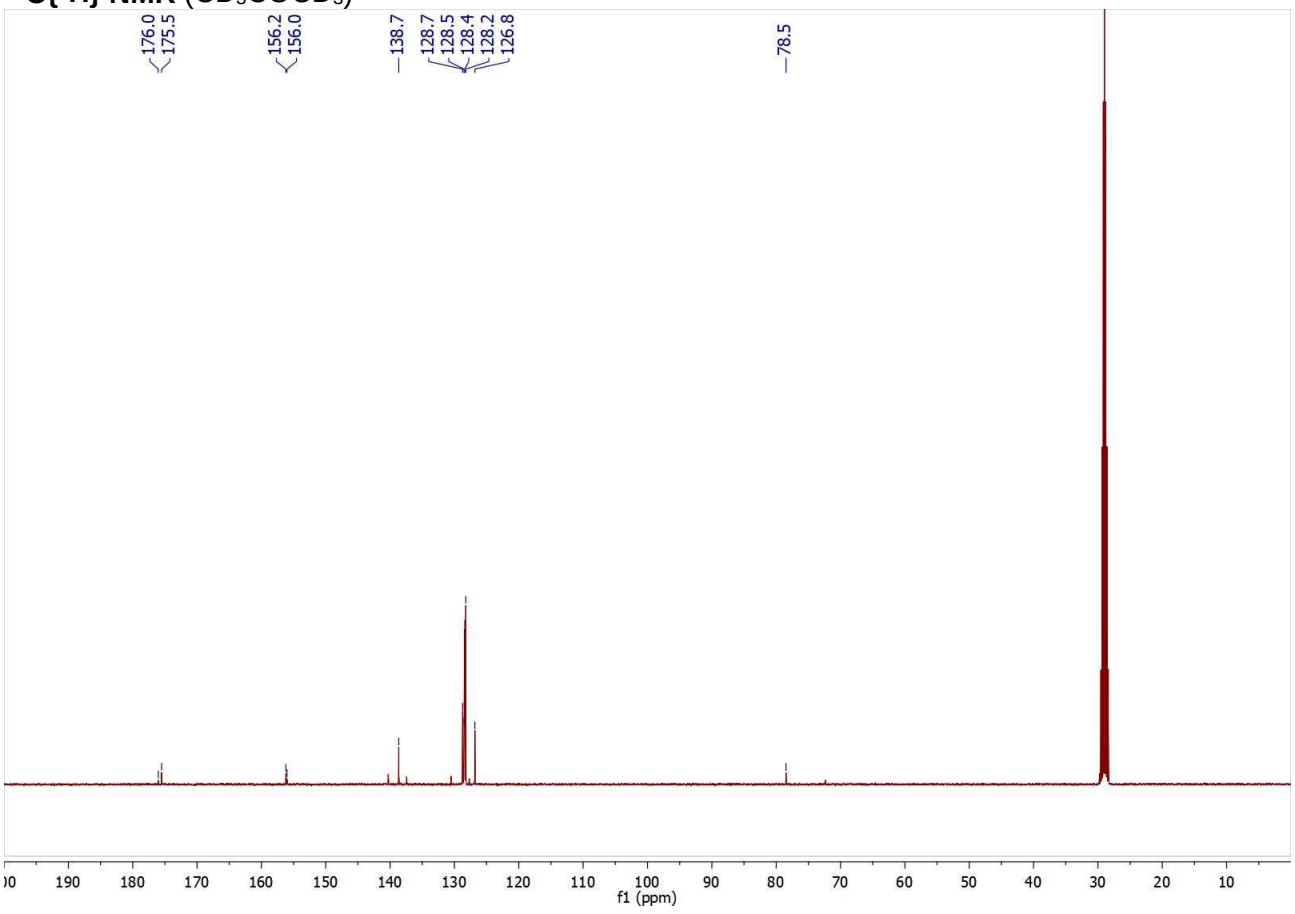


3-Iodo-5,5-diphenylimidazolidine-2,4-dione (S1af)

^{1}H NMR (CD_3COCD_3)

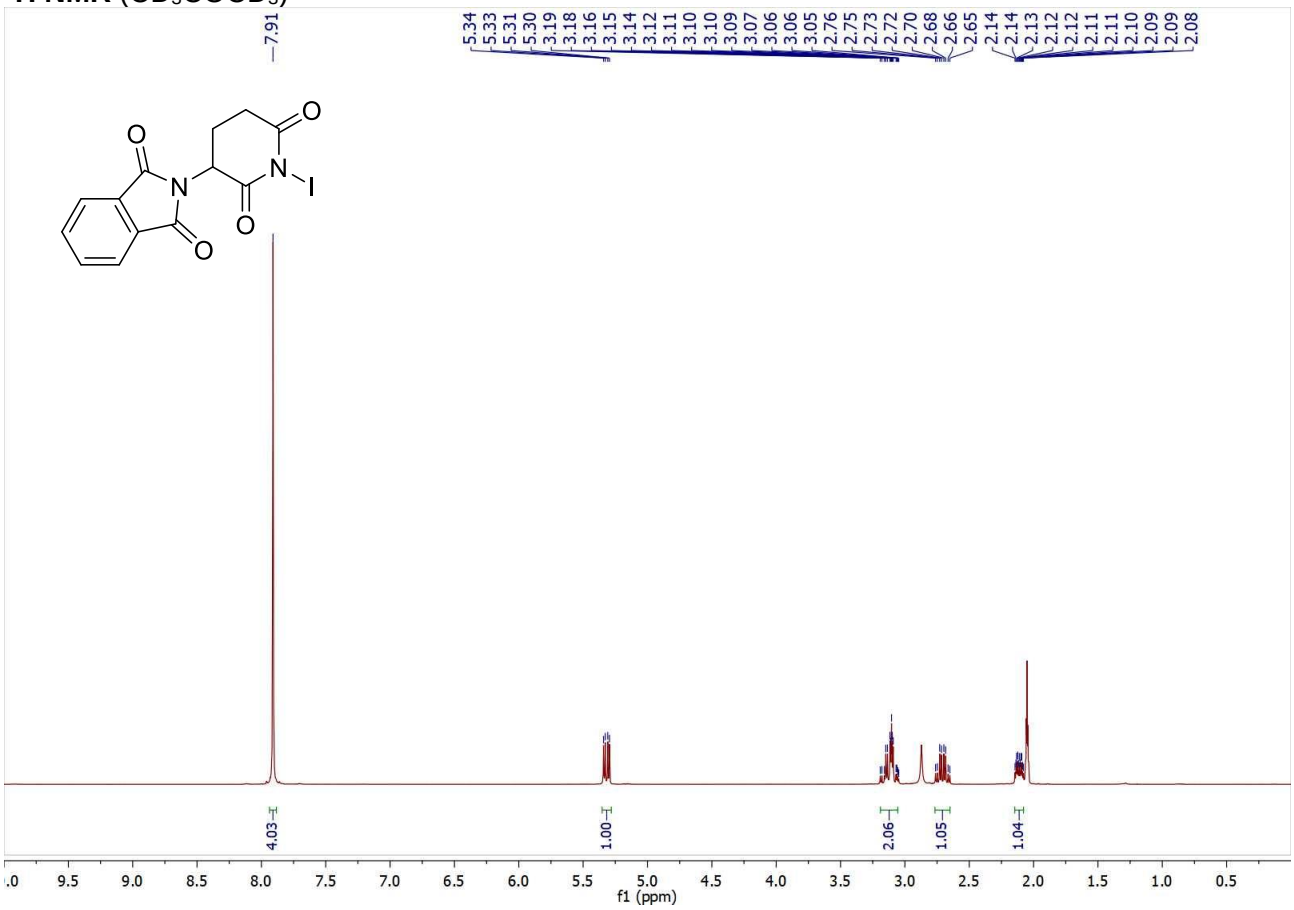


^{13}C{^{1}H} NMR (CD_3COCD_3)

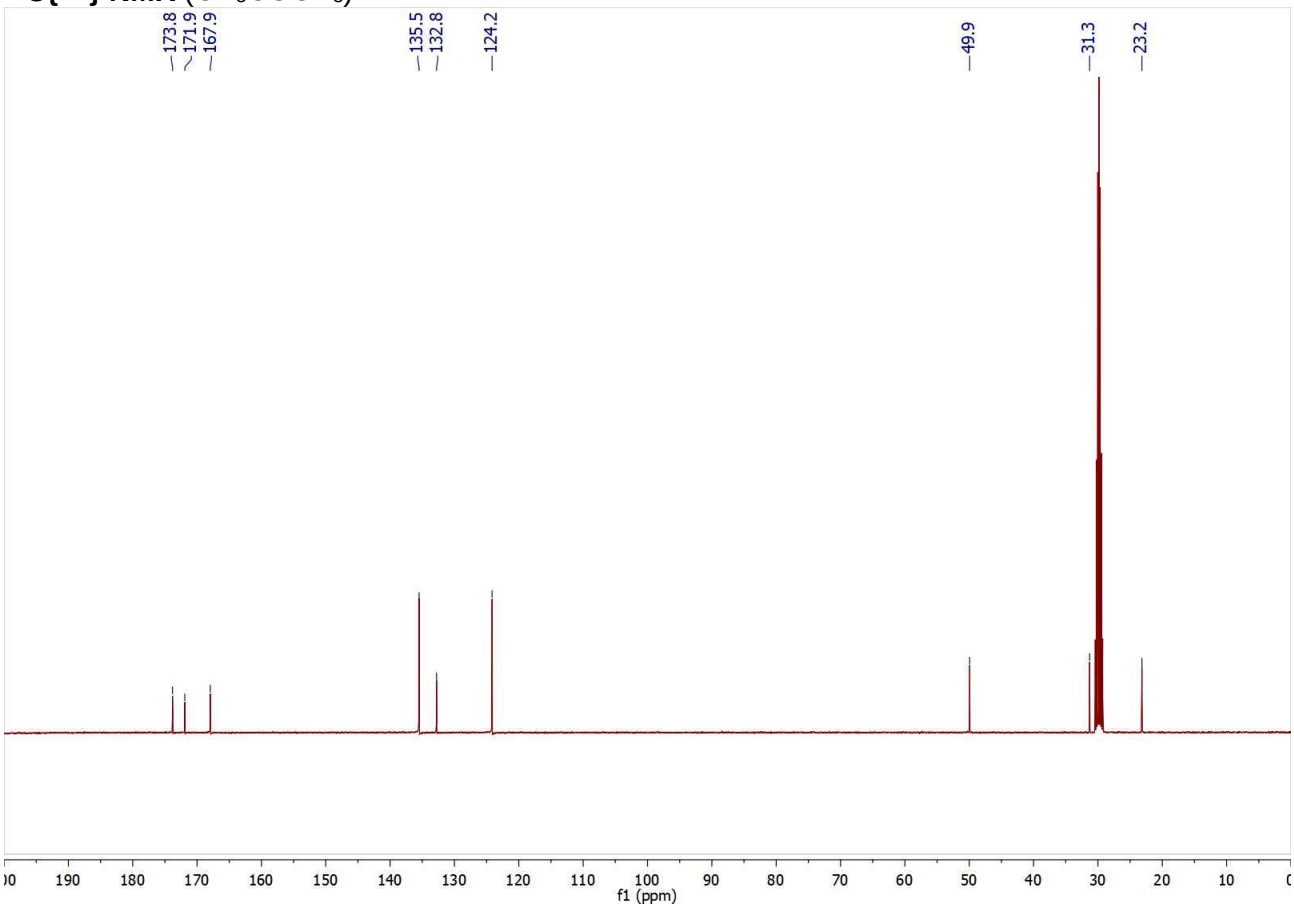


***N*-iodothalidomide (S1ag)**

^{1}H NMR (CD_3COCD_3)

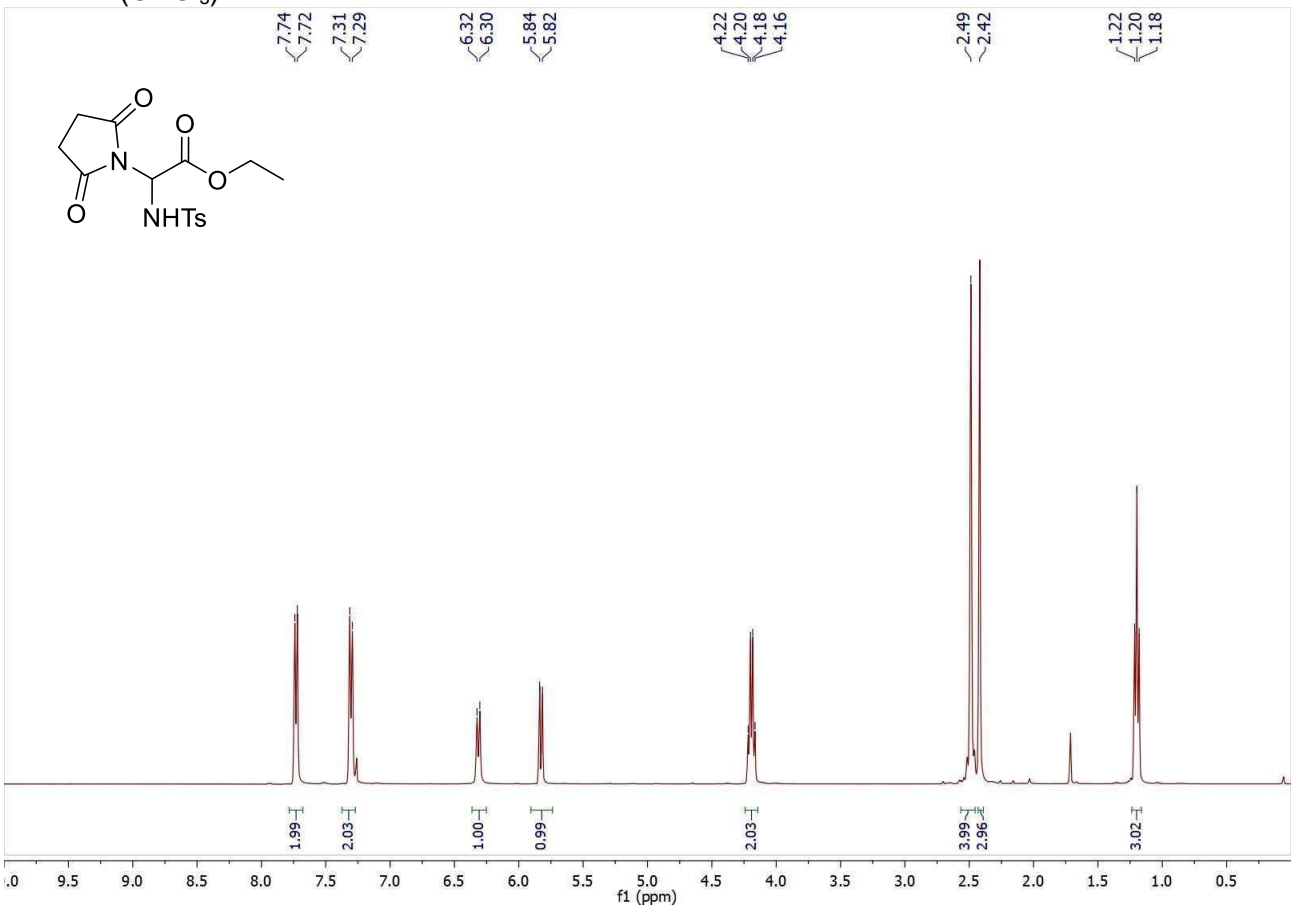


^{13}C{^{1}H} NMR (CD_3COCD_3)

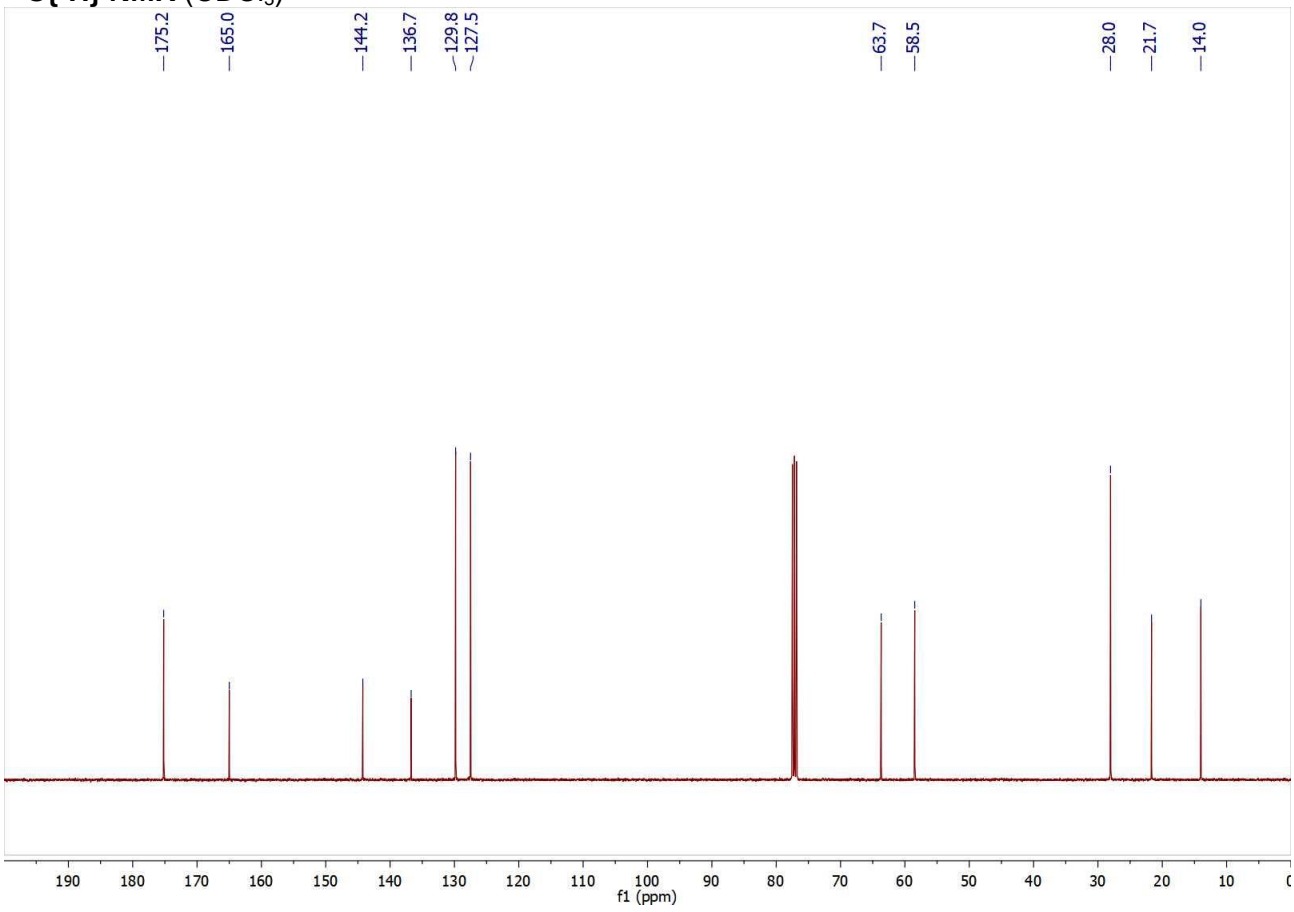


Ethyl 2-(2,5-dioxopyrrolidin-1-yl)-2-(4-metilfenilsulfonamide)acetate (2a)

^{1}H NMR ($CDCl_3$)

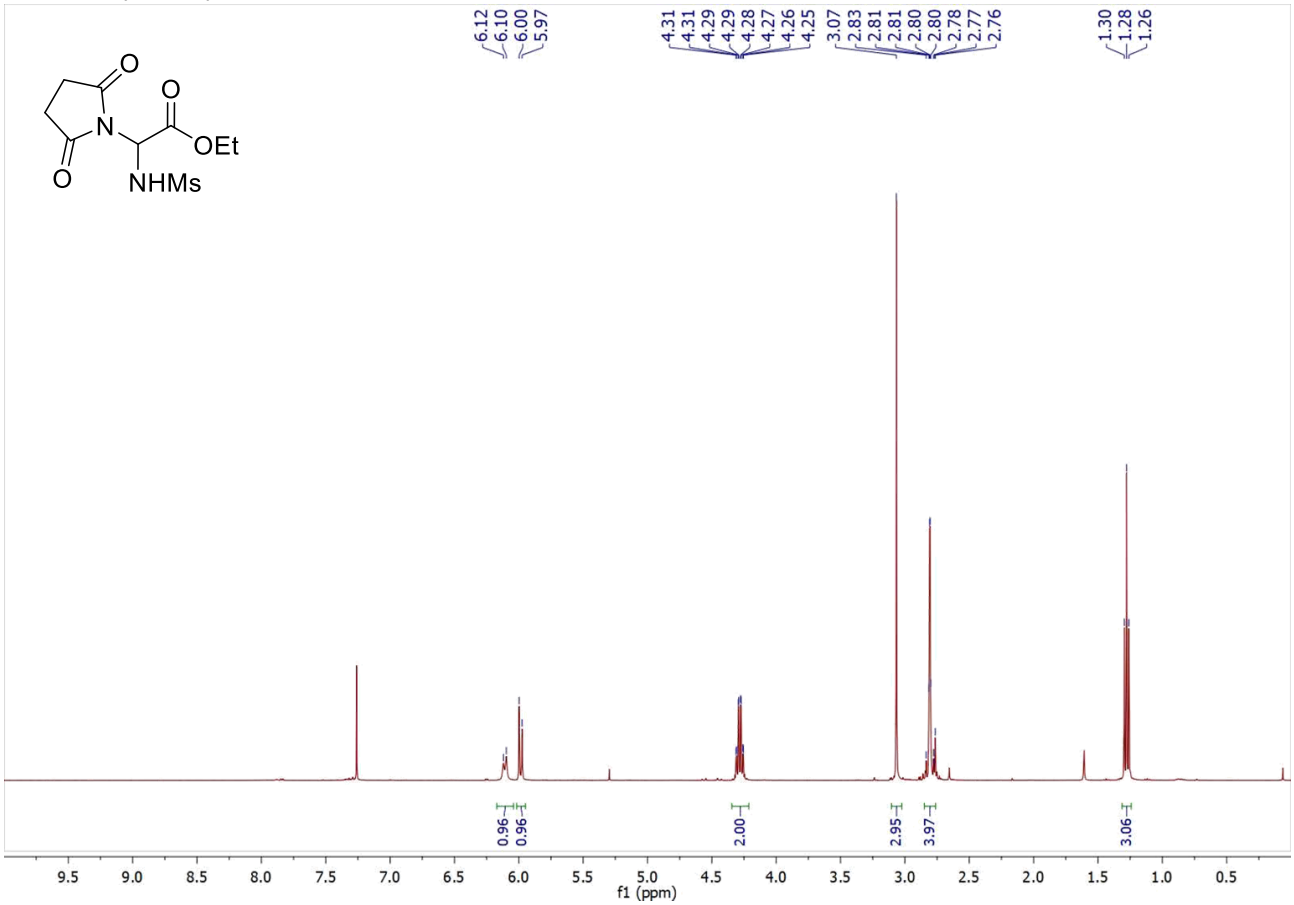


^{13}C{^{1}H} NMR ($CDCl_3$)

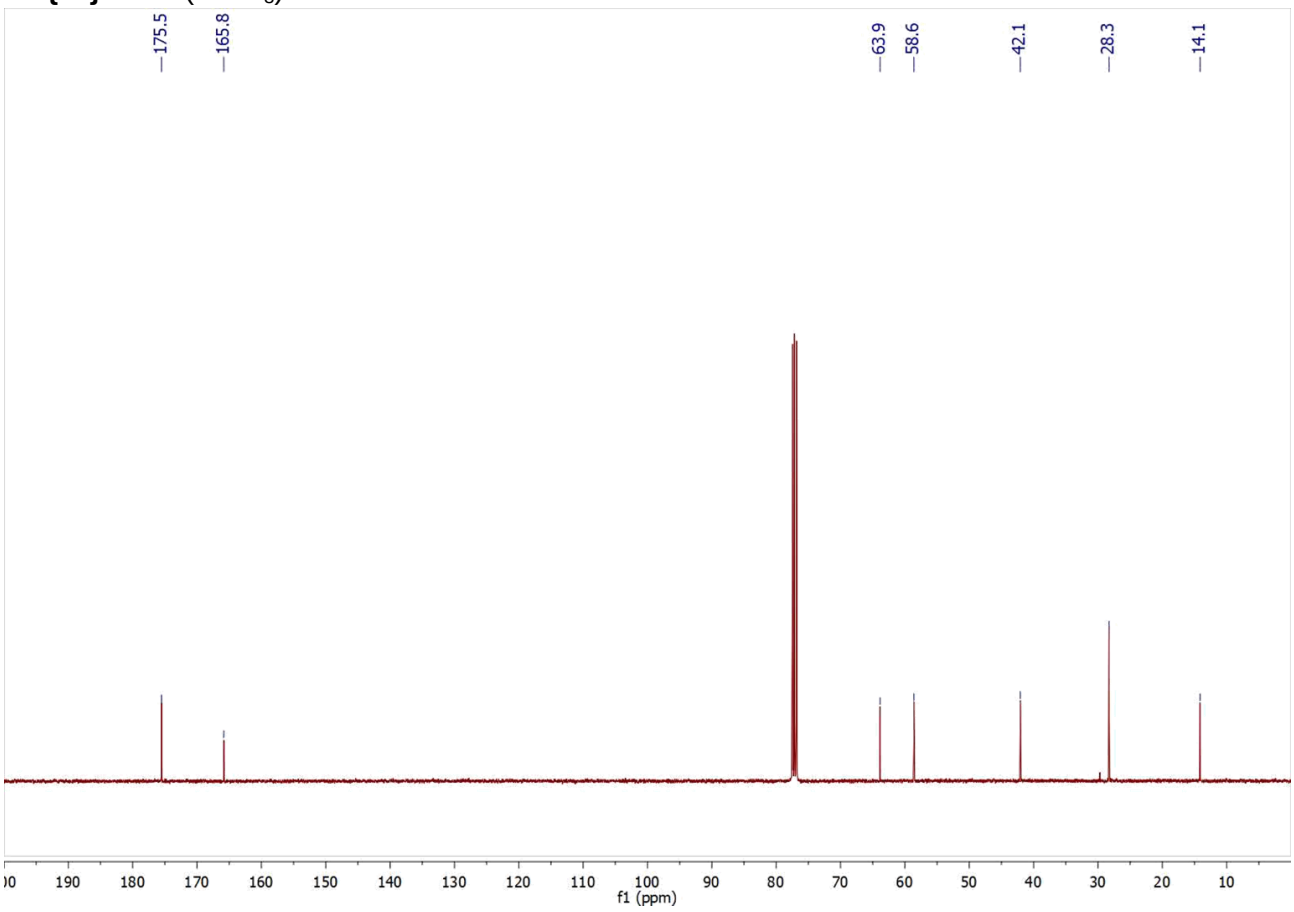


Ethyl 2-(2,5-dioxopyrrolidin-1-yl)-2-(methylsulfonamido)acetate (2aMs)

^{1}H NMR ($CDCl_3$)

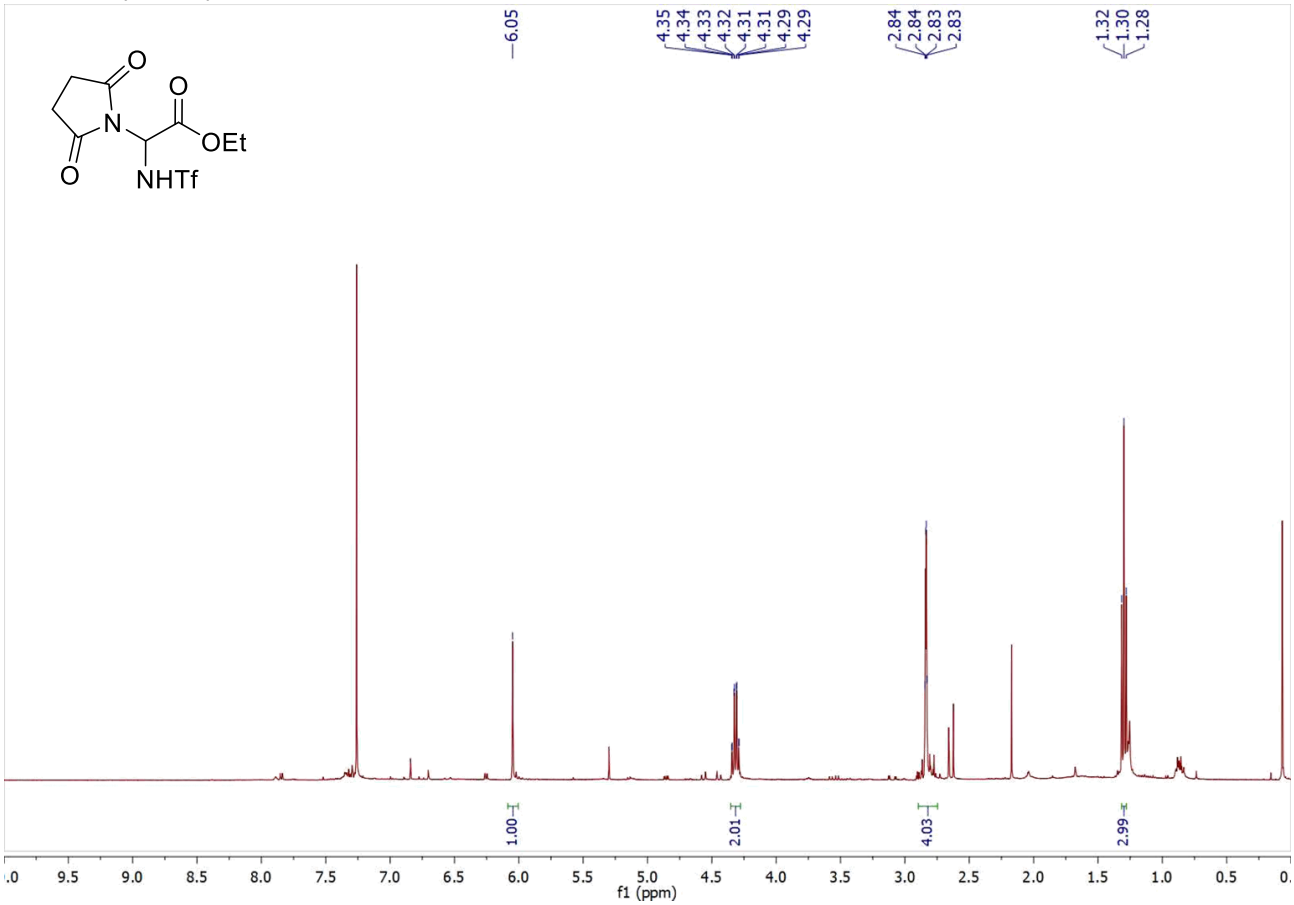


^{13}C{^{1}H} NMR ($CDCl_3$)

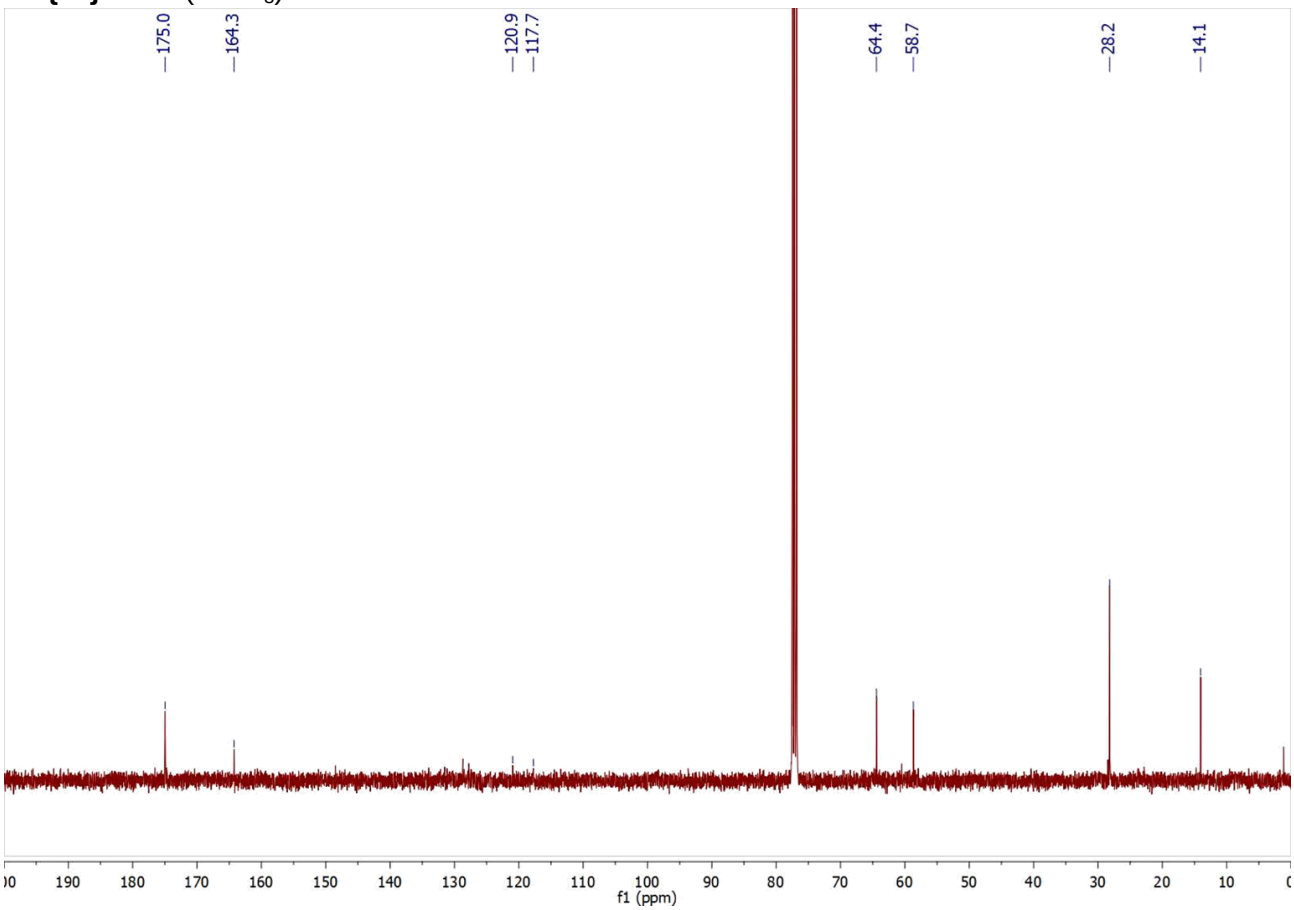


Ethyl 2-(2,5-dioxopyrrolidin-1-yl)-2-((trifluoromethyl)sulfonamido)acetate (2aTf)

^{1}H NMR ($CDCl_3$)

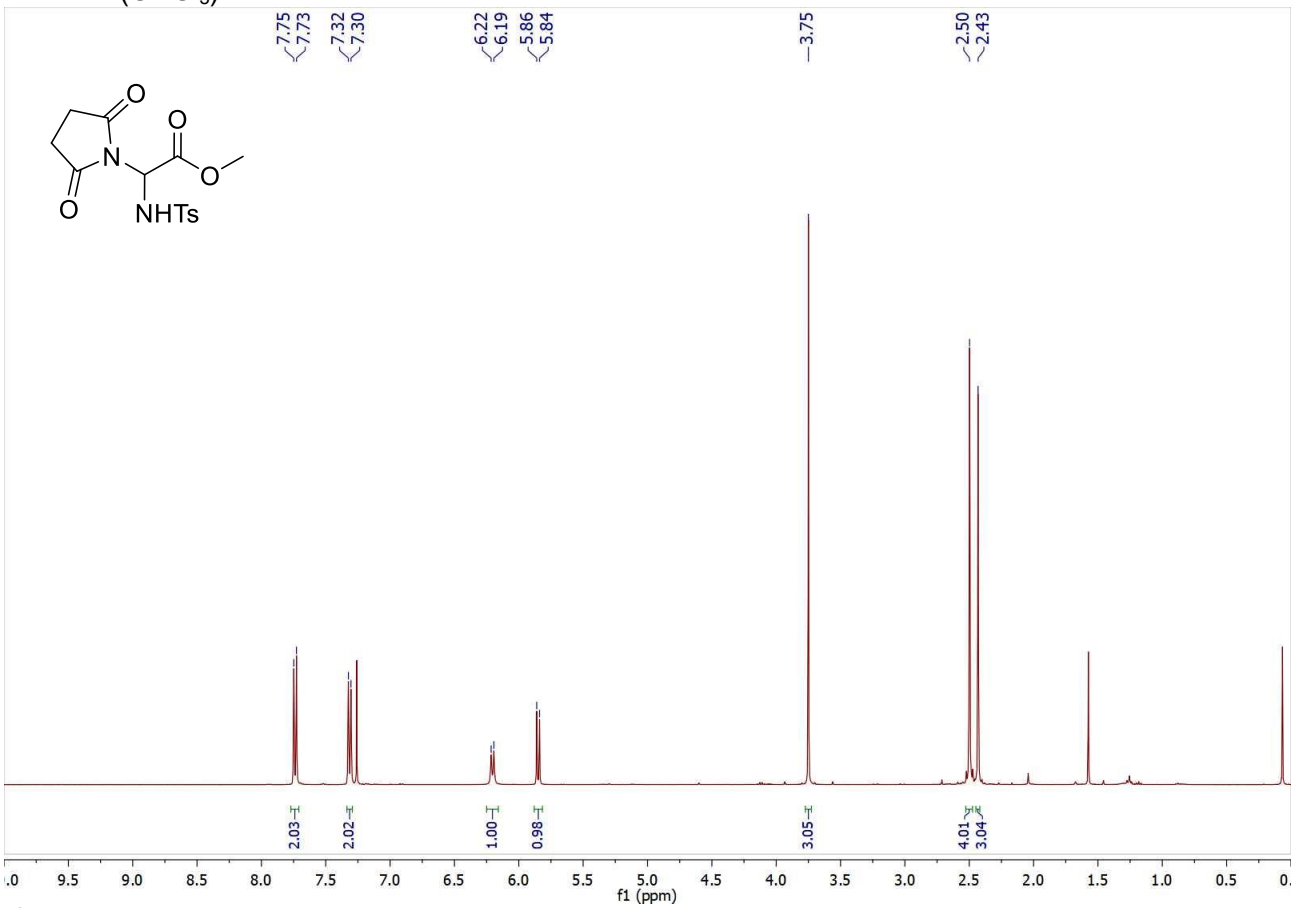


^{13}C{^{1}H} NMR ($CDCl_3$)

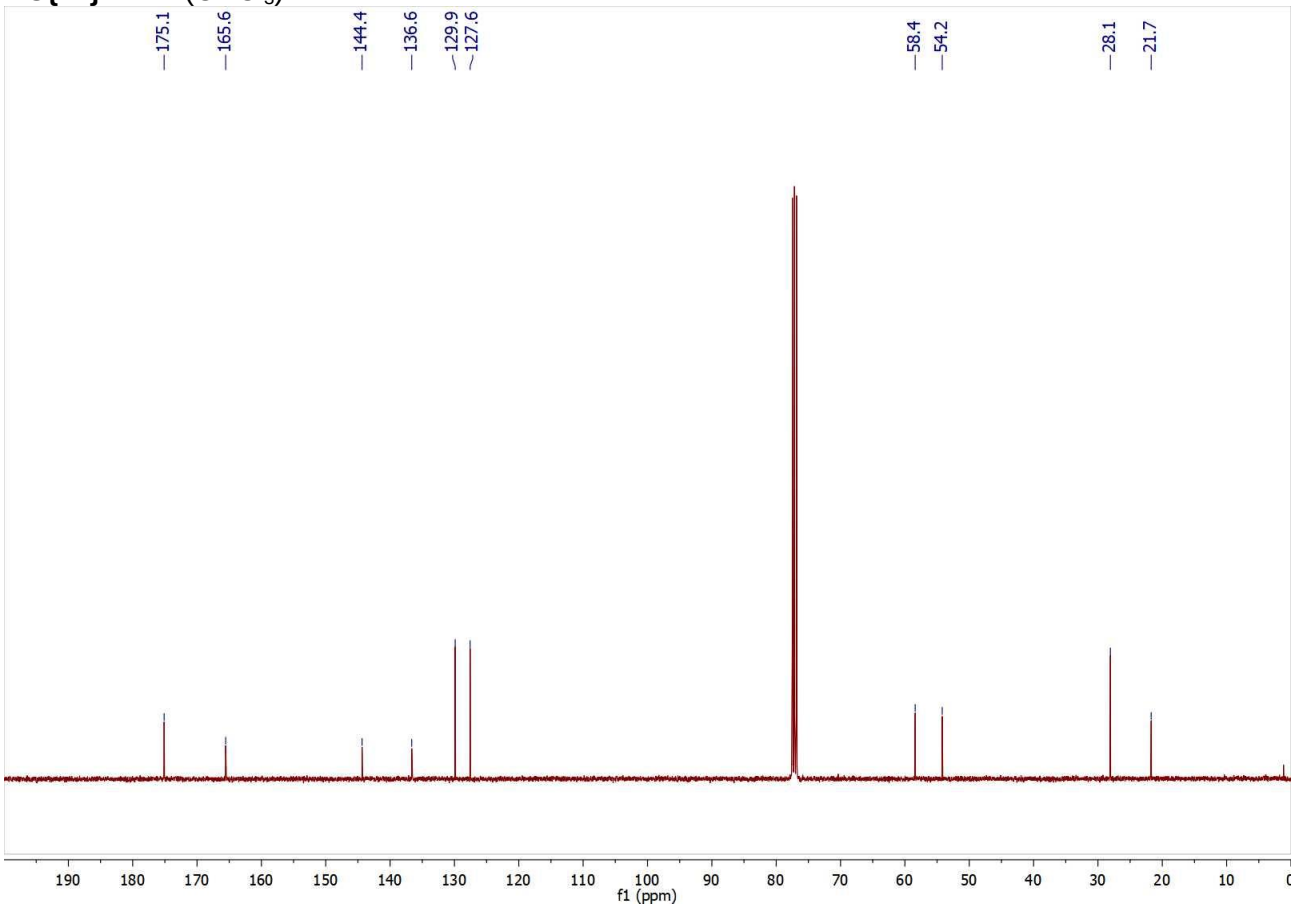


Methyl-2-(2,5-dioxopyrrolidin-1-yl)-2-(4-methylphenylsulfonamide) acetate (2b)

^{1}H NMR ($CDCl_3$)

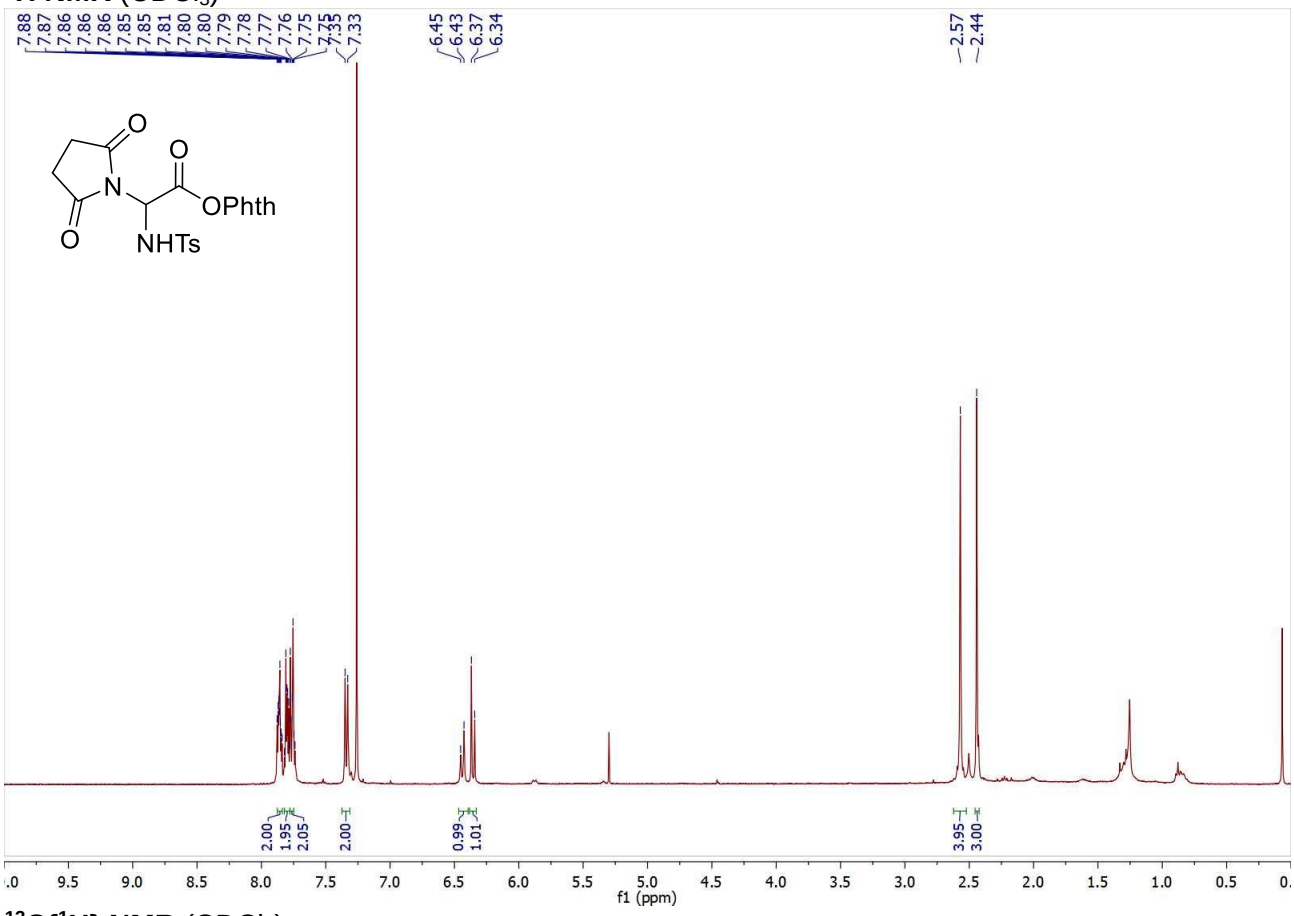


^{13}C{^{1}H} NMR ($CDCl_3$)

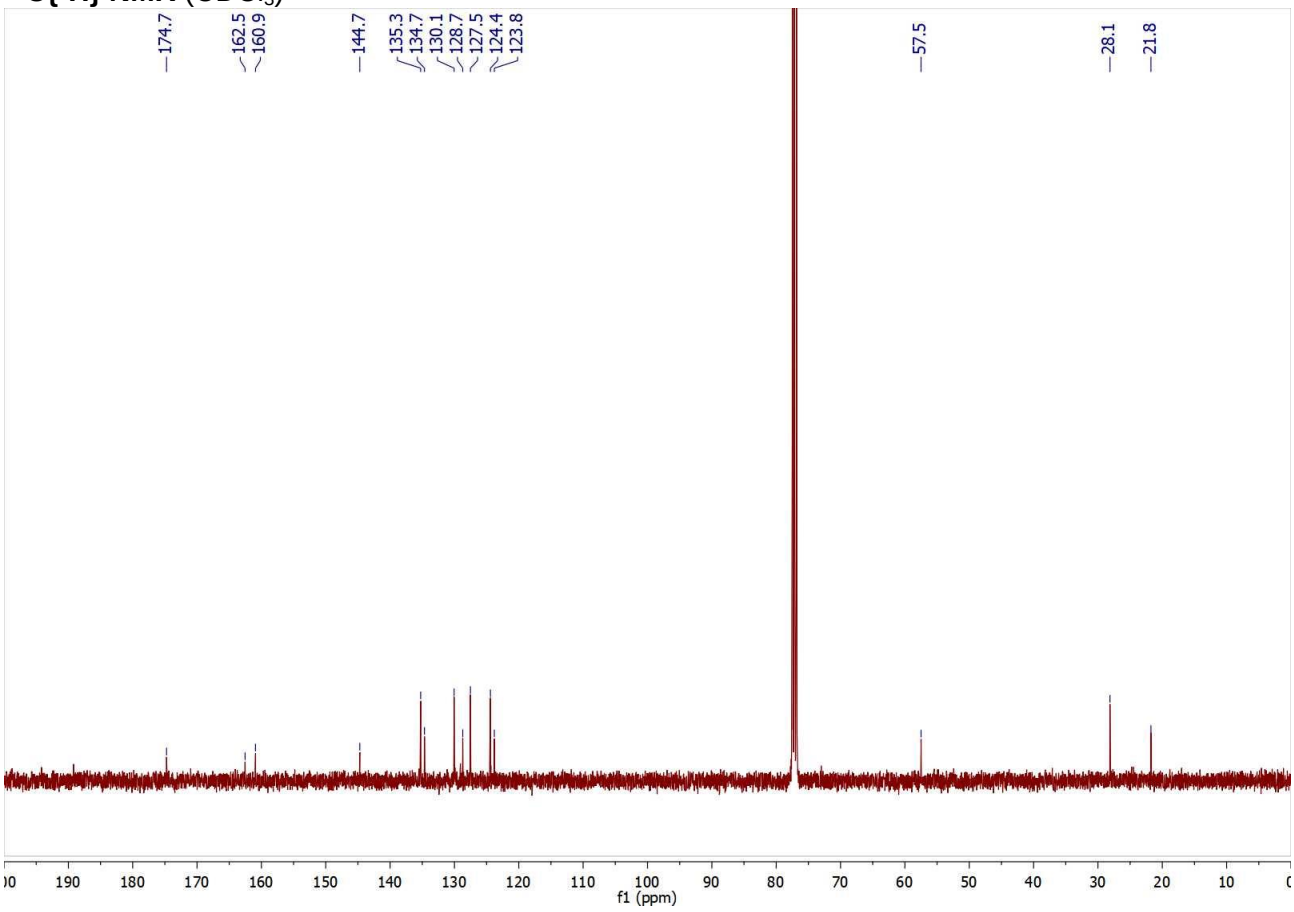


1,3-Dioxoisoindolin-2-yl 2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido) acetate (2c)

^{1}H NMR ($CDCl_3$)

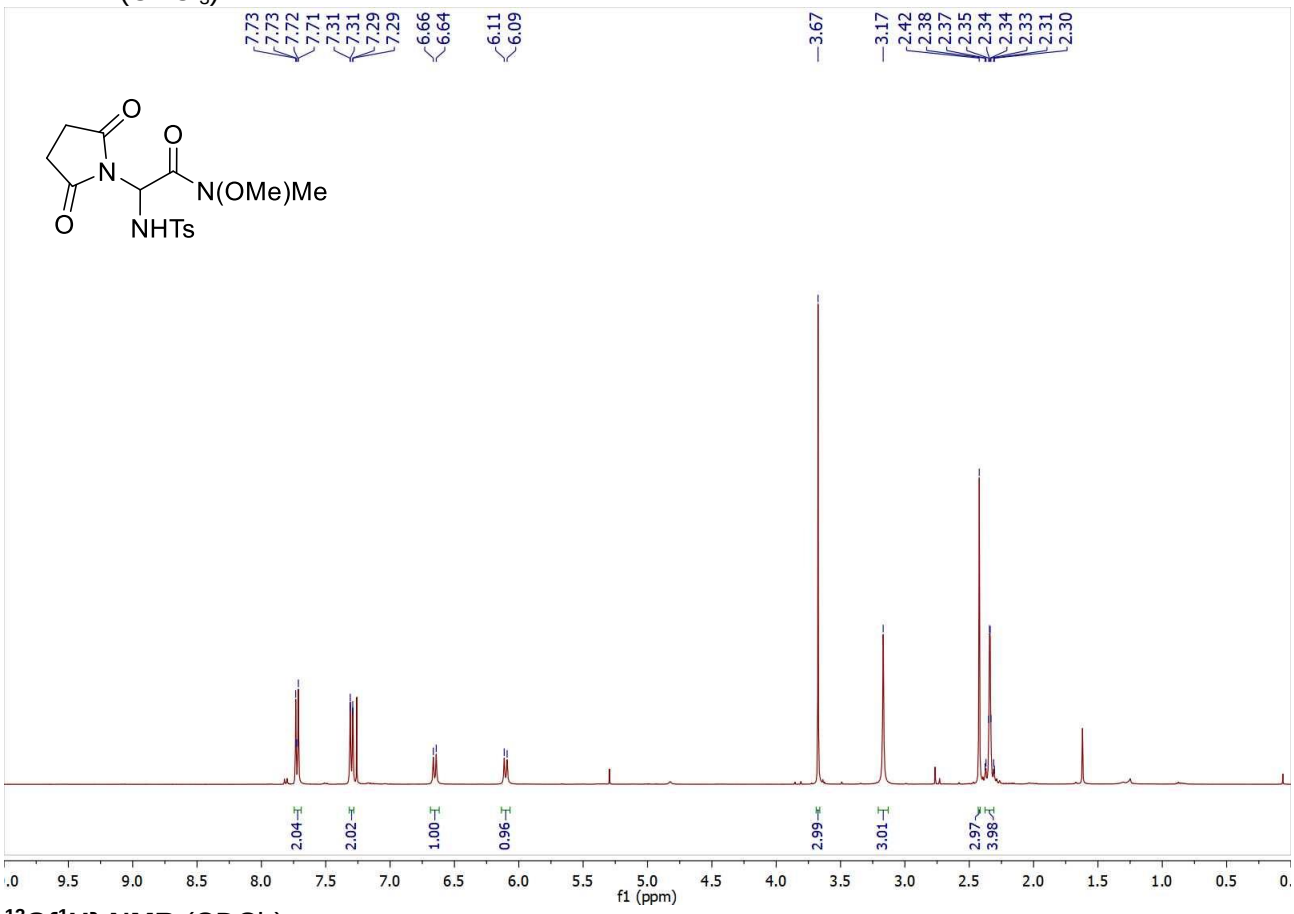


^{13}C{^{1}H} NMR ($CDCl_3$)

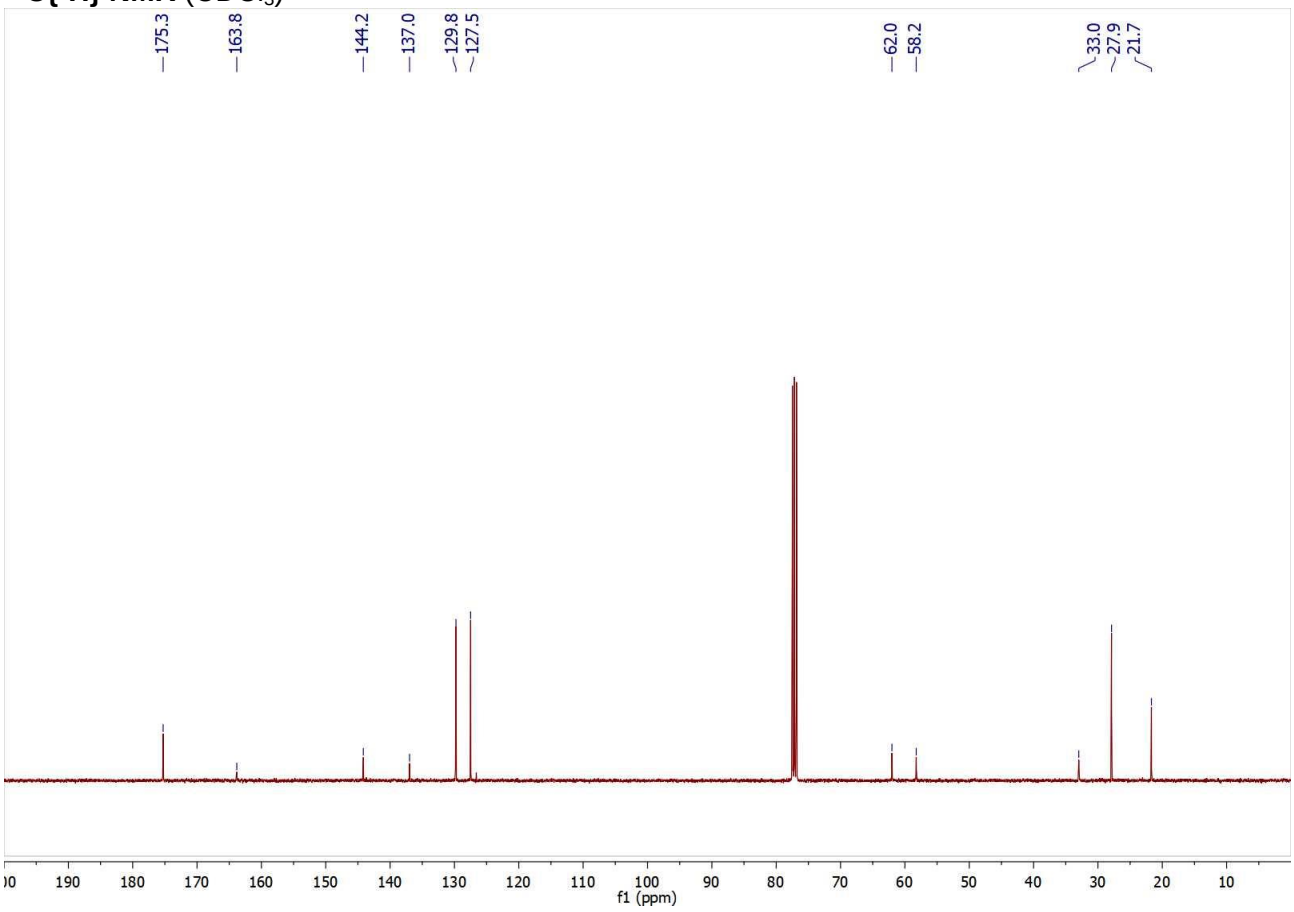


2-(2,5-Dioxopyrrolidin-1-il)-*N*-metoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido) acetamide (2d)

^{1}H NMR ($CDCl_3$)

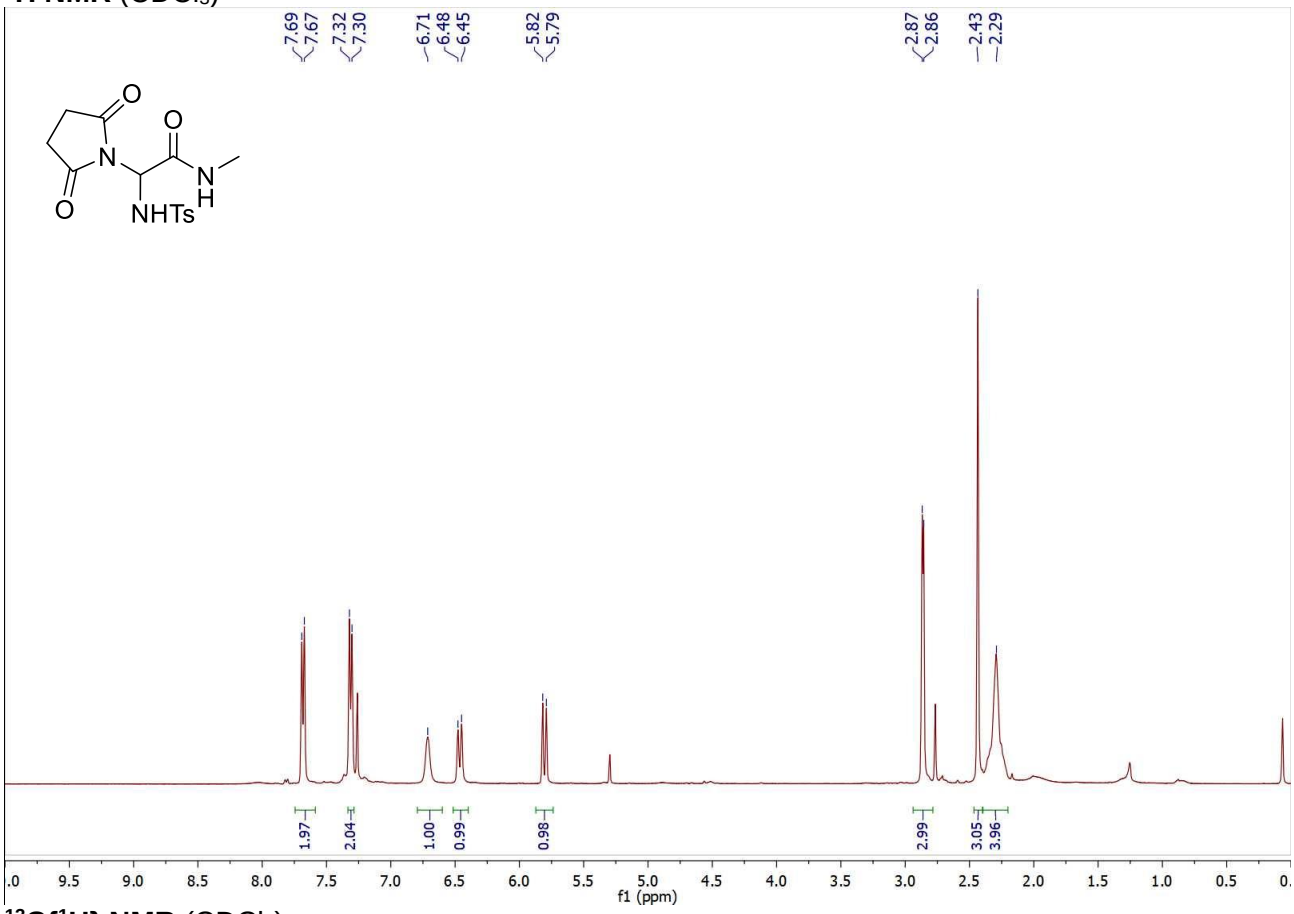


^{13}C{^{1}H} NMR ($CDCl_3$)

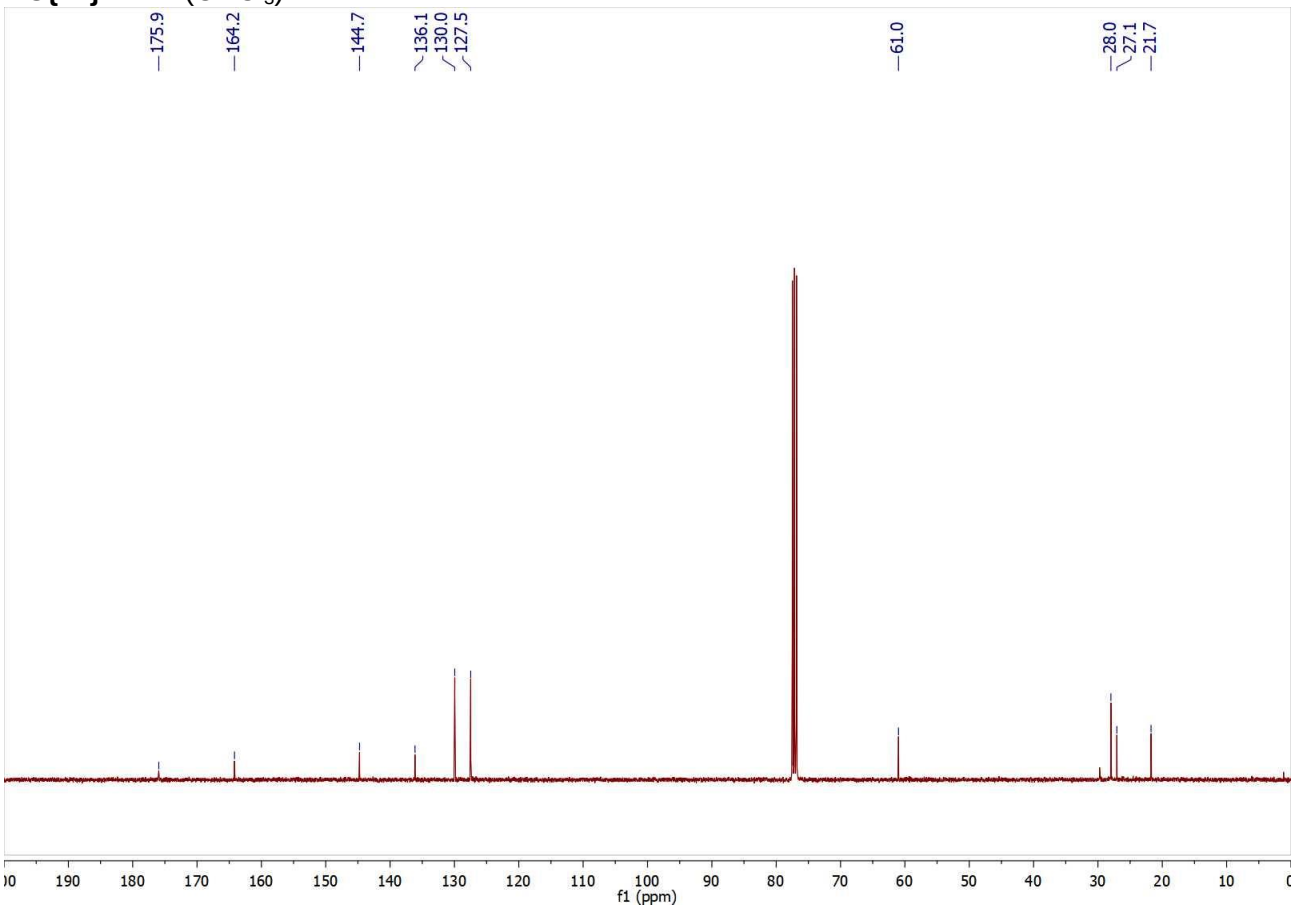


2-(2,5-Dioxopyrrolidin-1-yl)-2-(4-methylphenylsulfonamide)acetamide (2e)

^{1}H NMR ($CDCl_3$)

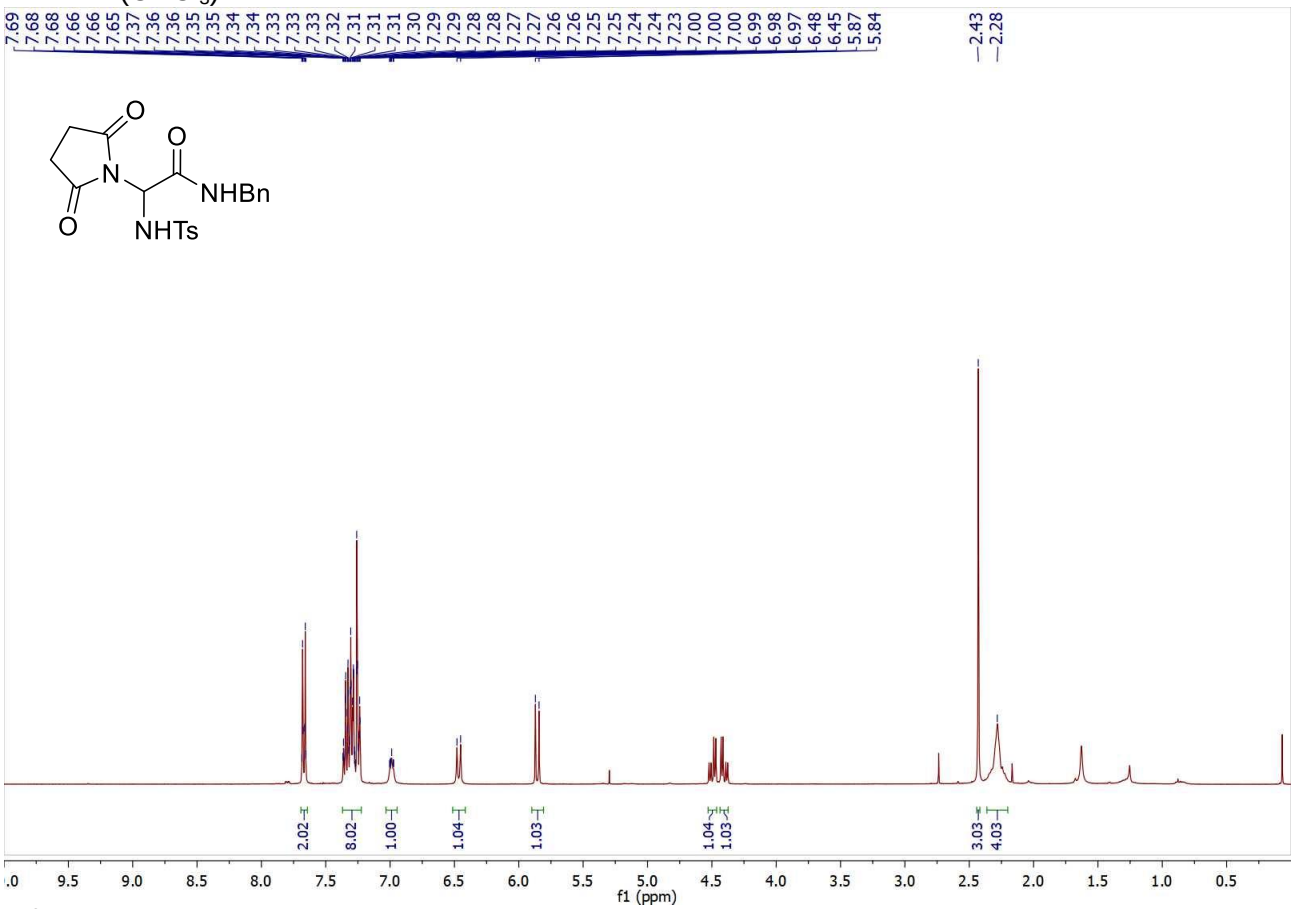


^{13}C{^{1}H} NMR ($CDCl_3$)

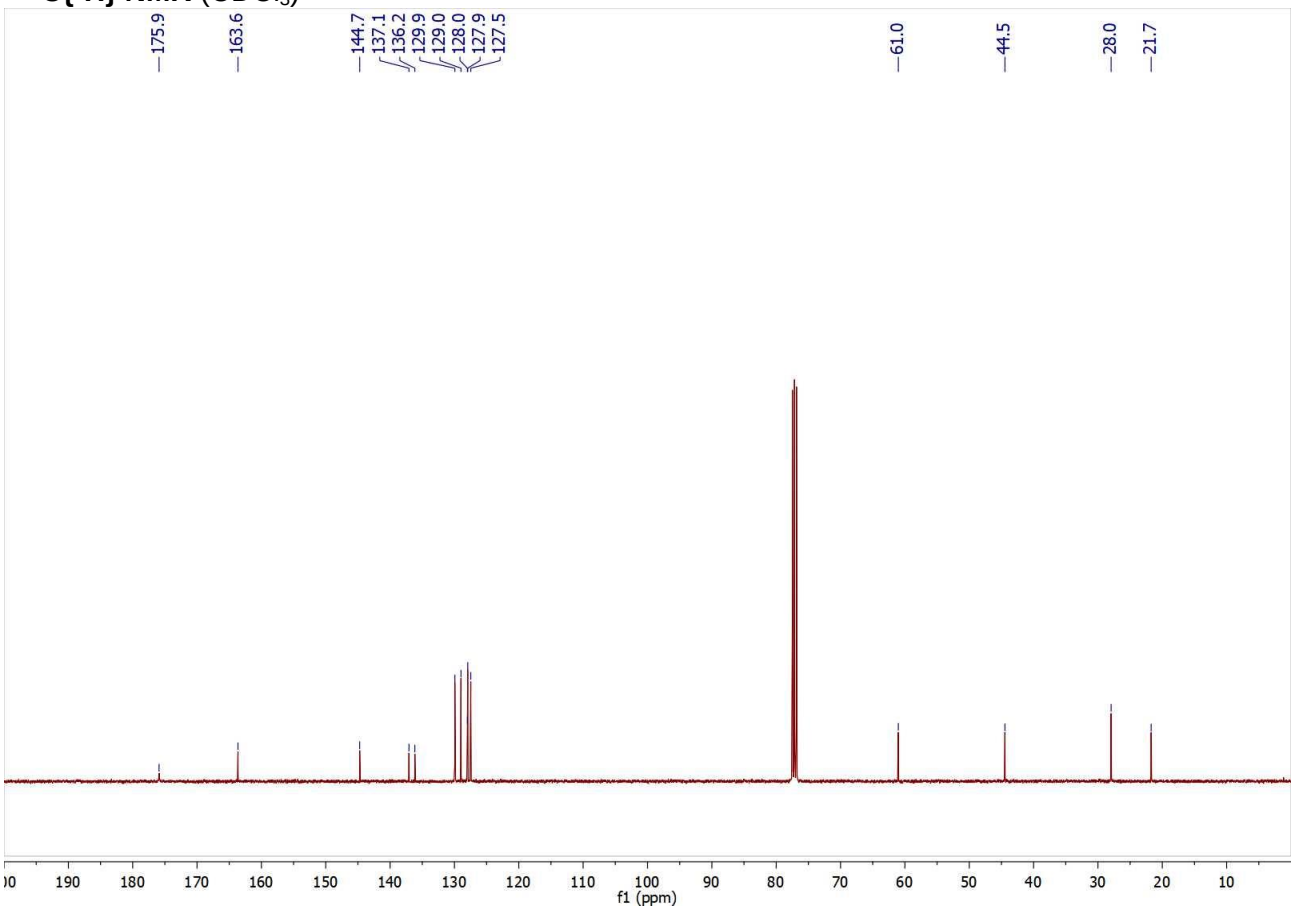


***N*-Bencyl-2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetamide (2f)**

^{1}H NMR ($CDCl_3$)

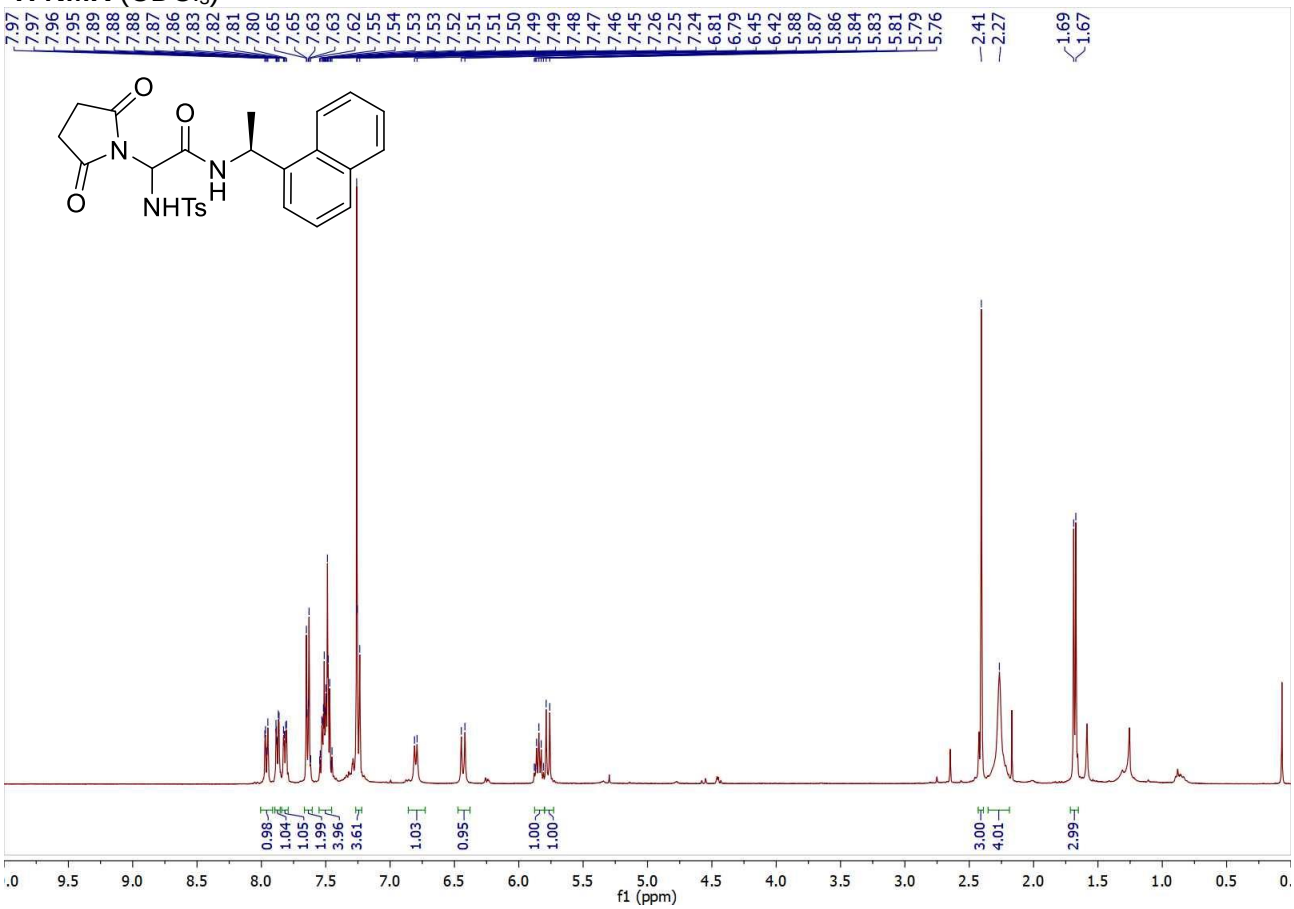


^{13}C{^{1}H} NMR ($CDCl_3$)

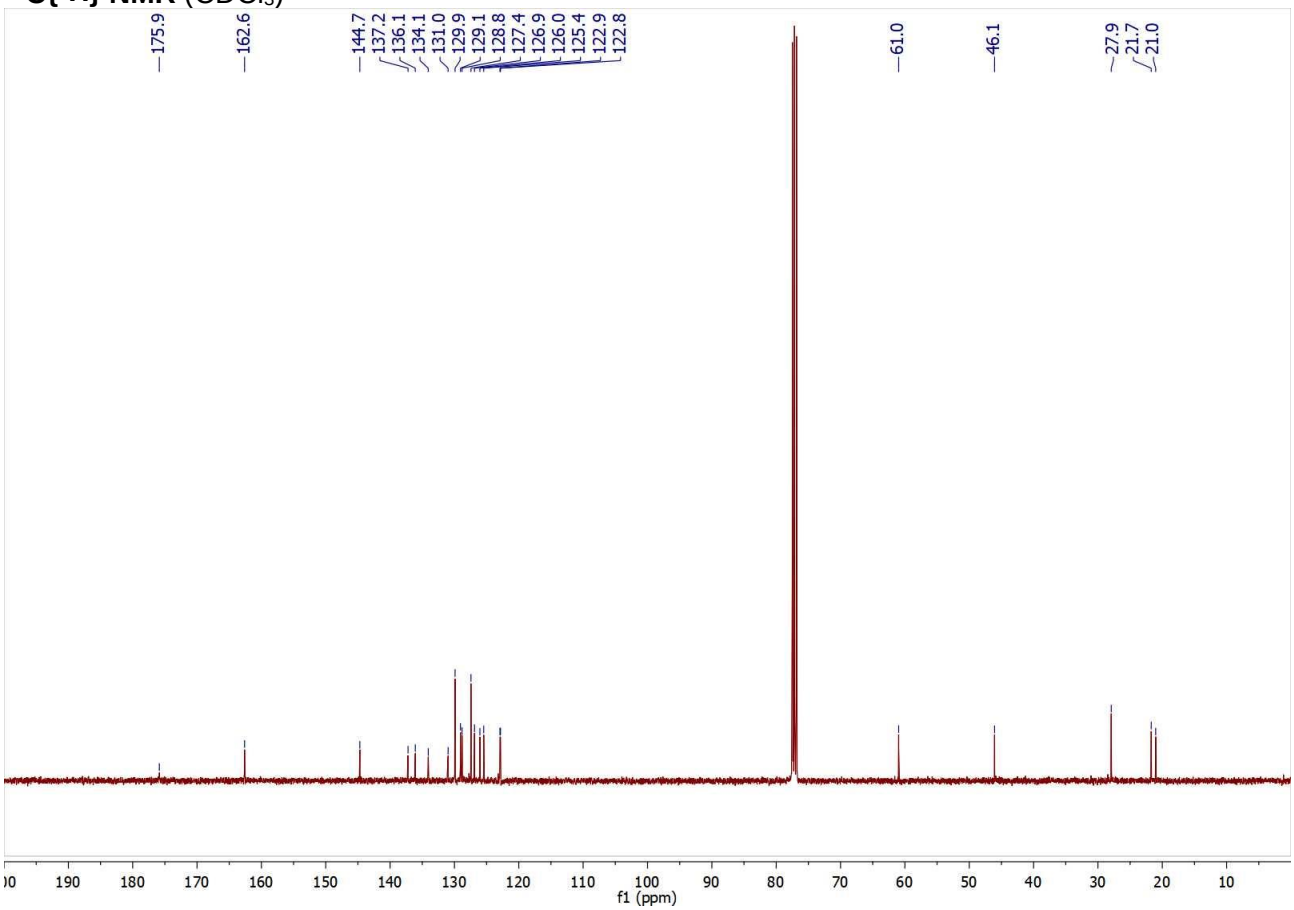


2-(2,5-Dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)-*N*-((*S*)-2-(naphthalen-1-yl)ethyl)acetamide (2g) (Major diastereomer)

^{1}H NMR ($CDCl_3$)

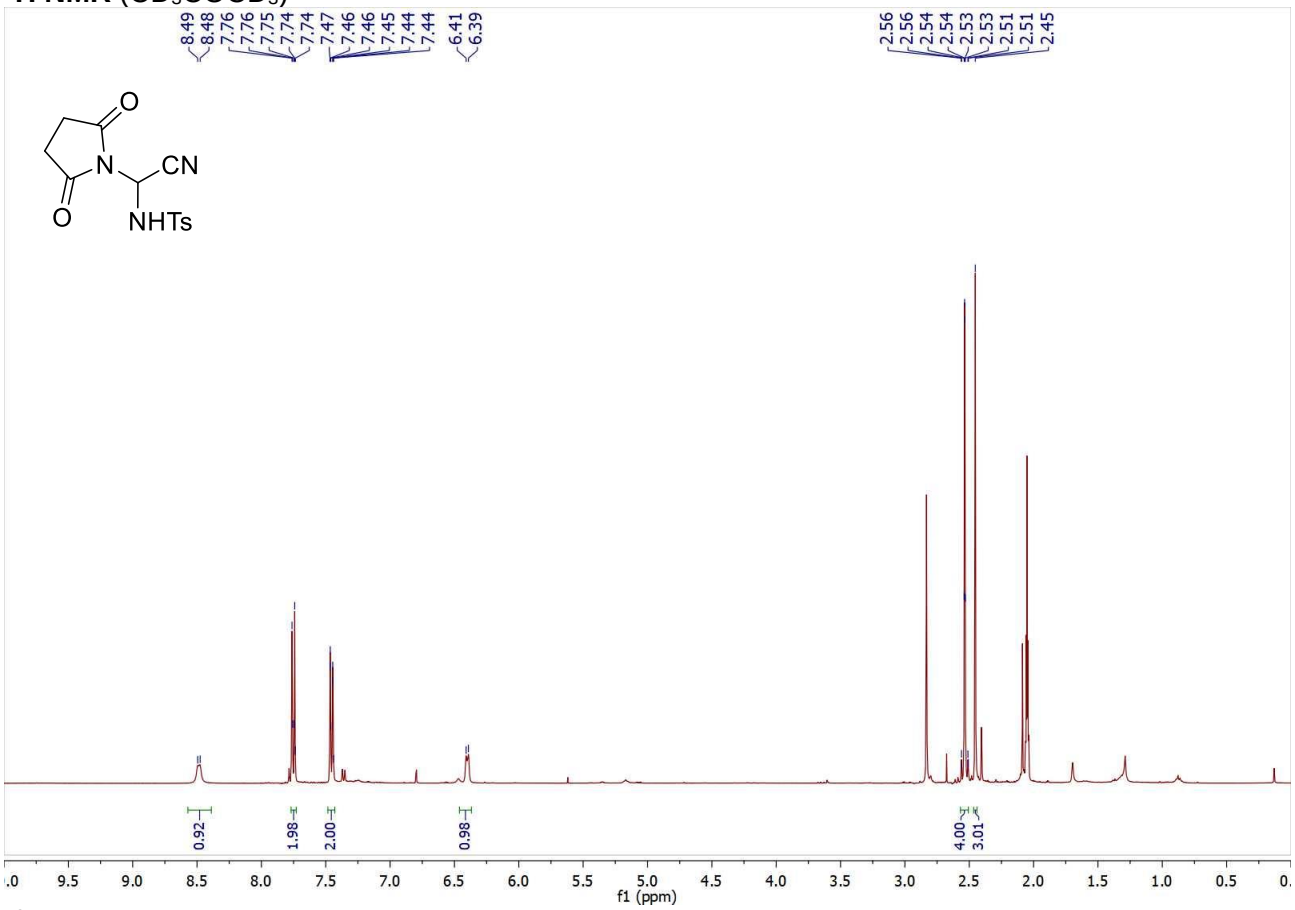


^{13}C{^{1}H} NMR ($CDCl_3$)

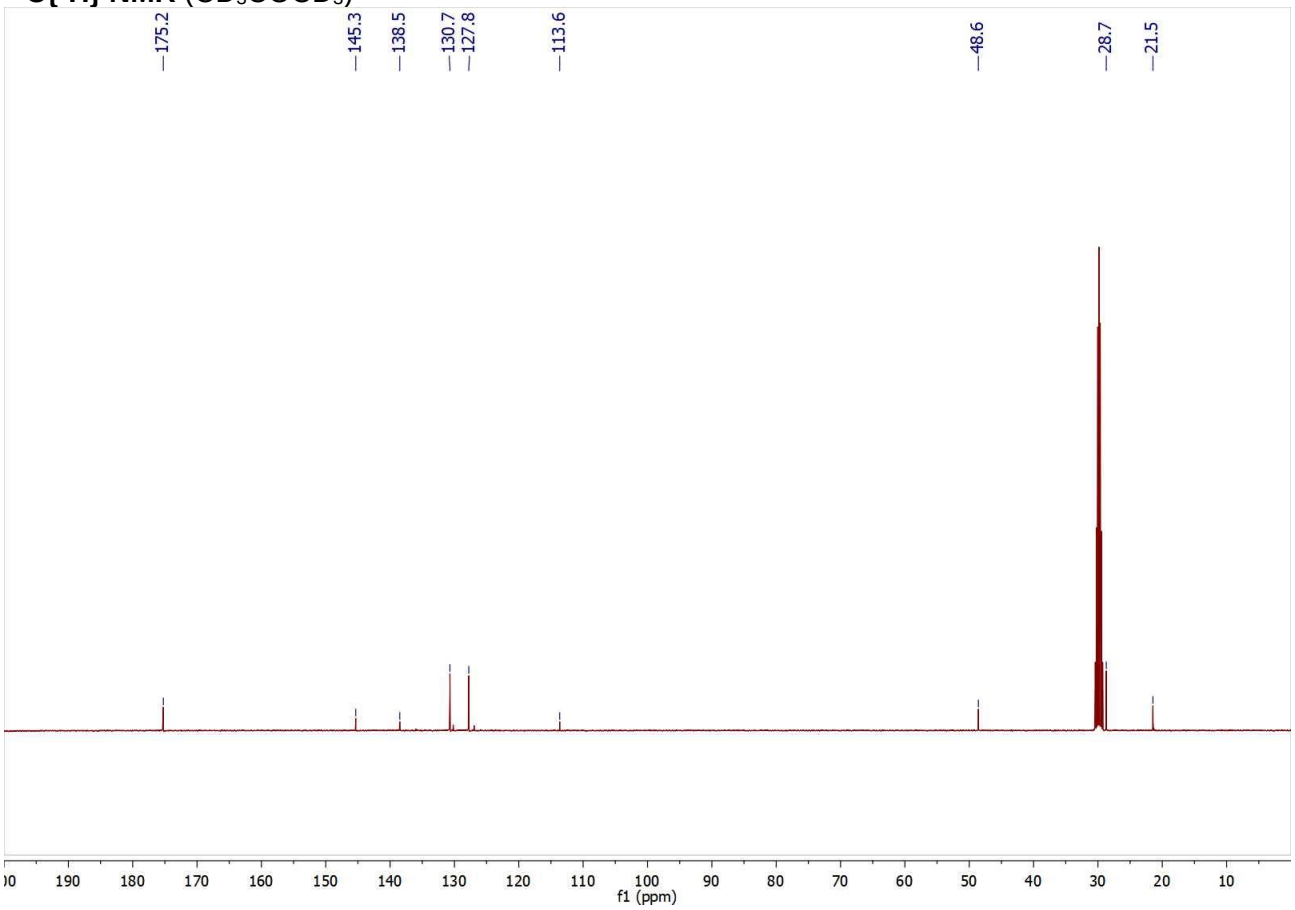


***N*-(Cyano(2,5-dioxopyrrolidin-1-yl)methyl)-4-methylbenzensulfonamide (2h)**

^{1}H NMR (CD_3COCD_3)

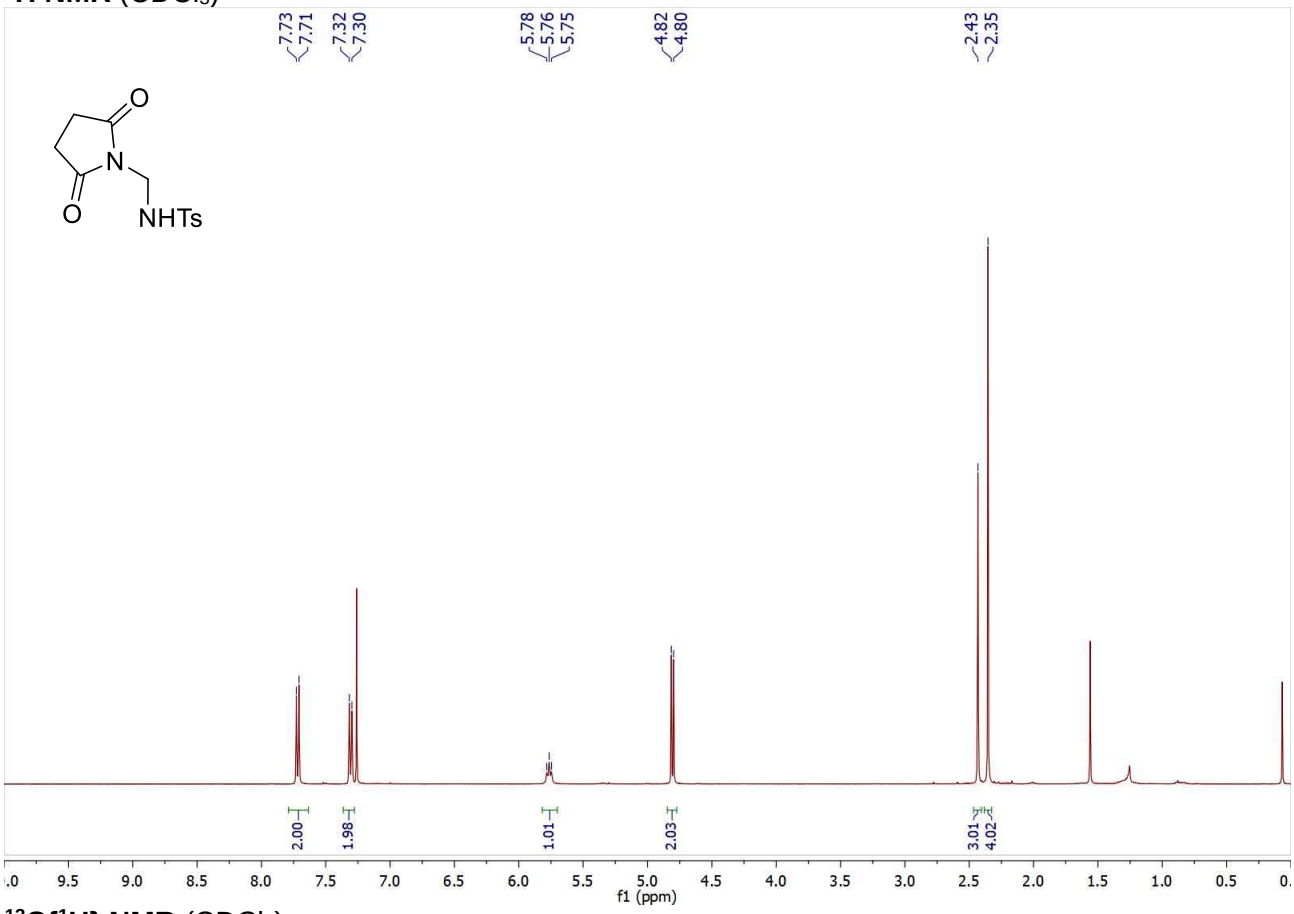


^{13}C{^{1}H} NMR (CD_3COCD_3)

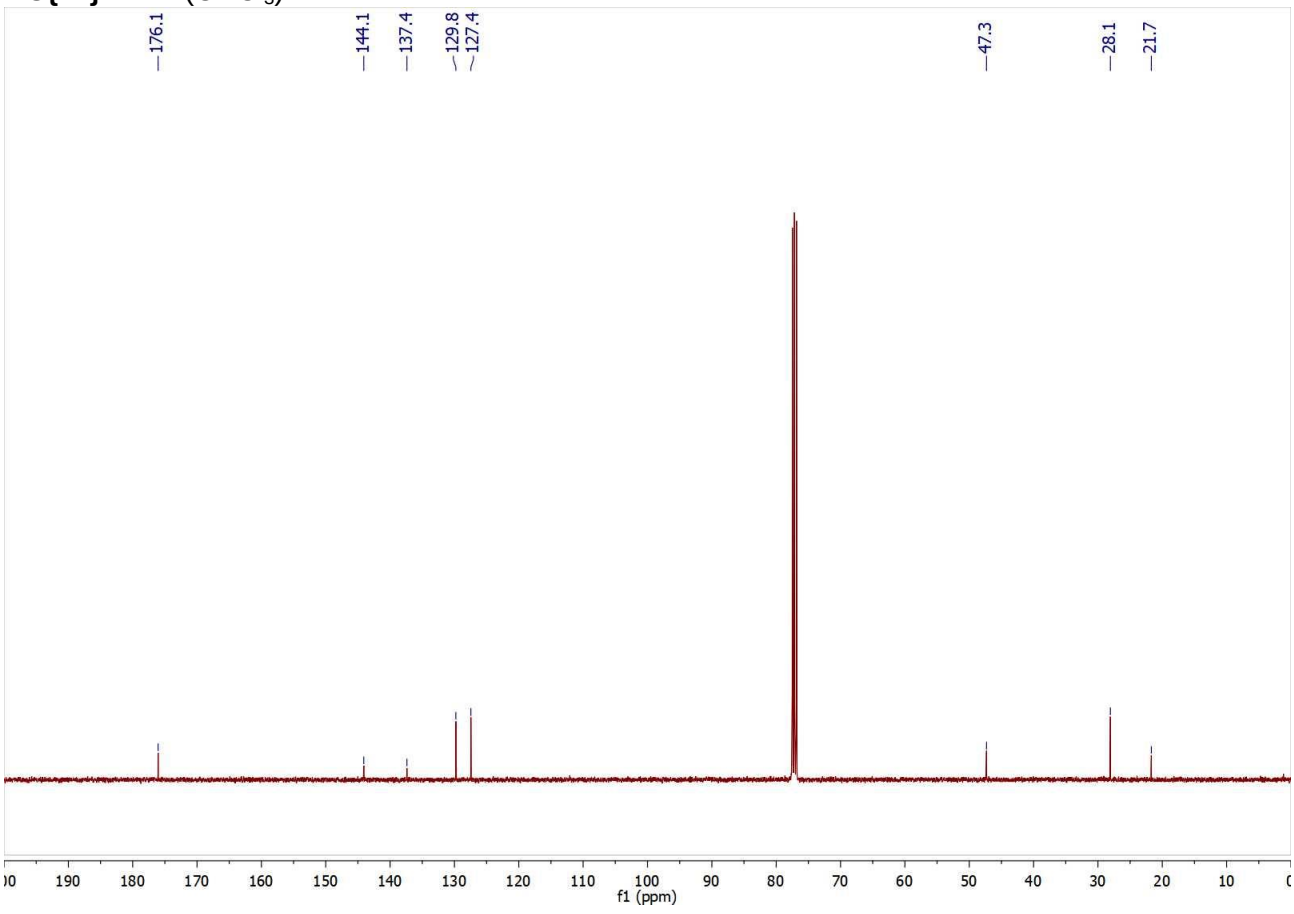


***N*-((2,5-Dioxopyrrolidin-1-yl)methyl)-2-(4-methylbencensulfonamide) (2i)**

^{1}H NMR ($CDCl_3$)

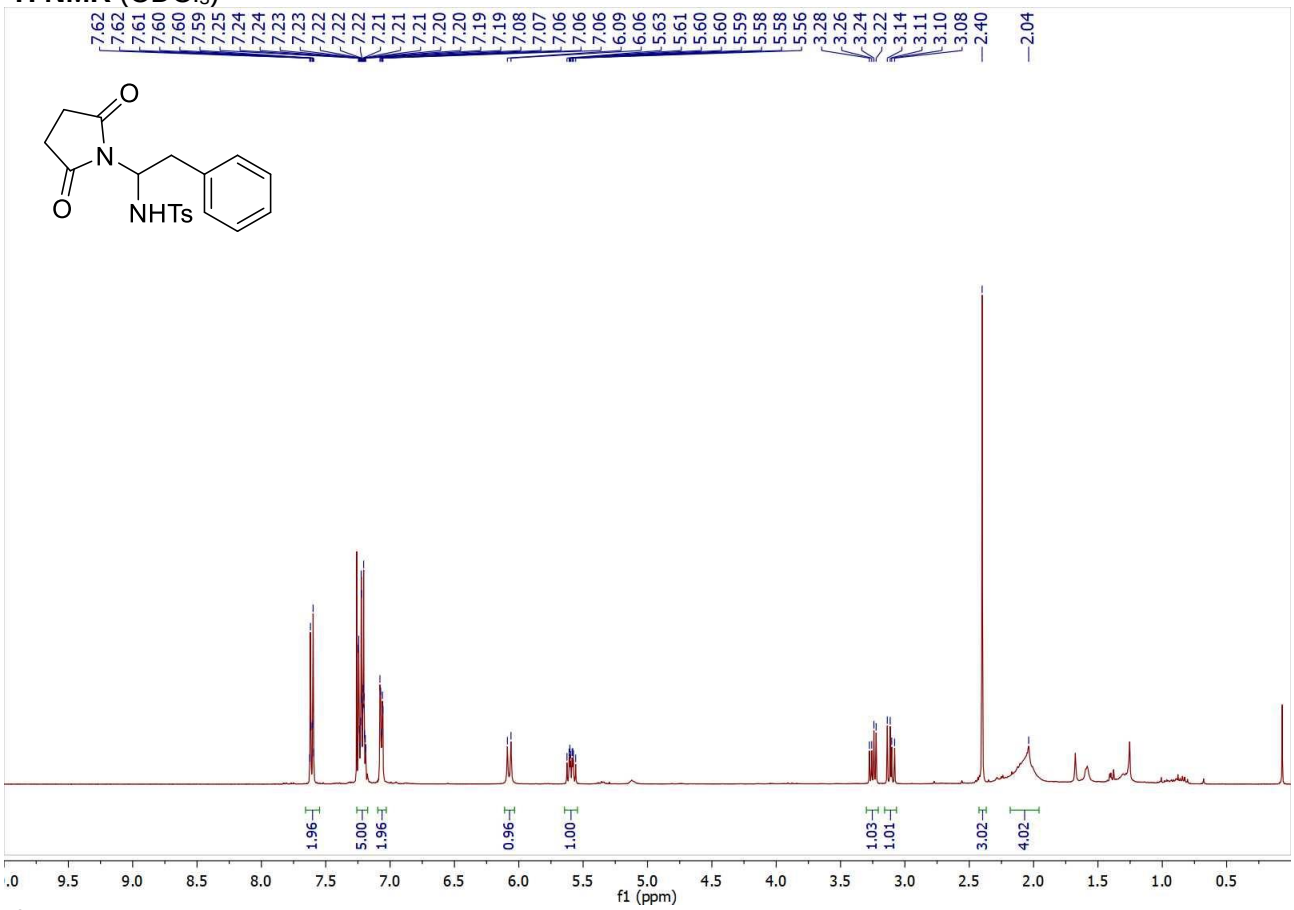


^{13}C{^{1}H} NMR ($CDCl_3$)

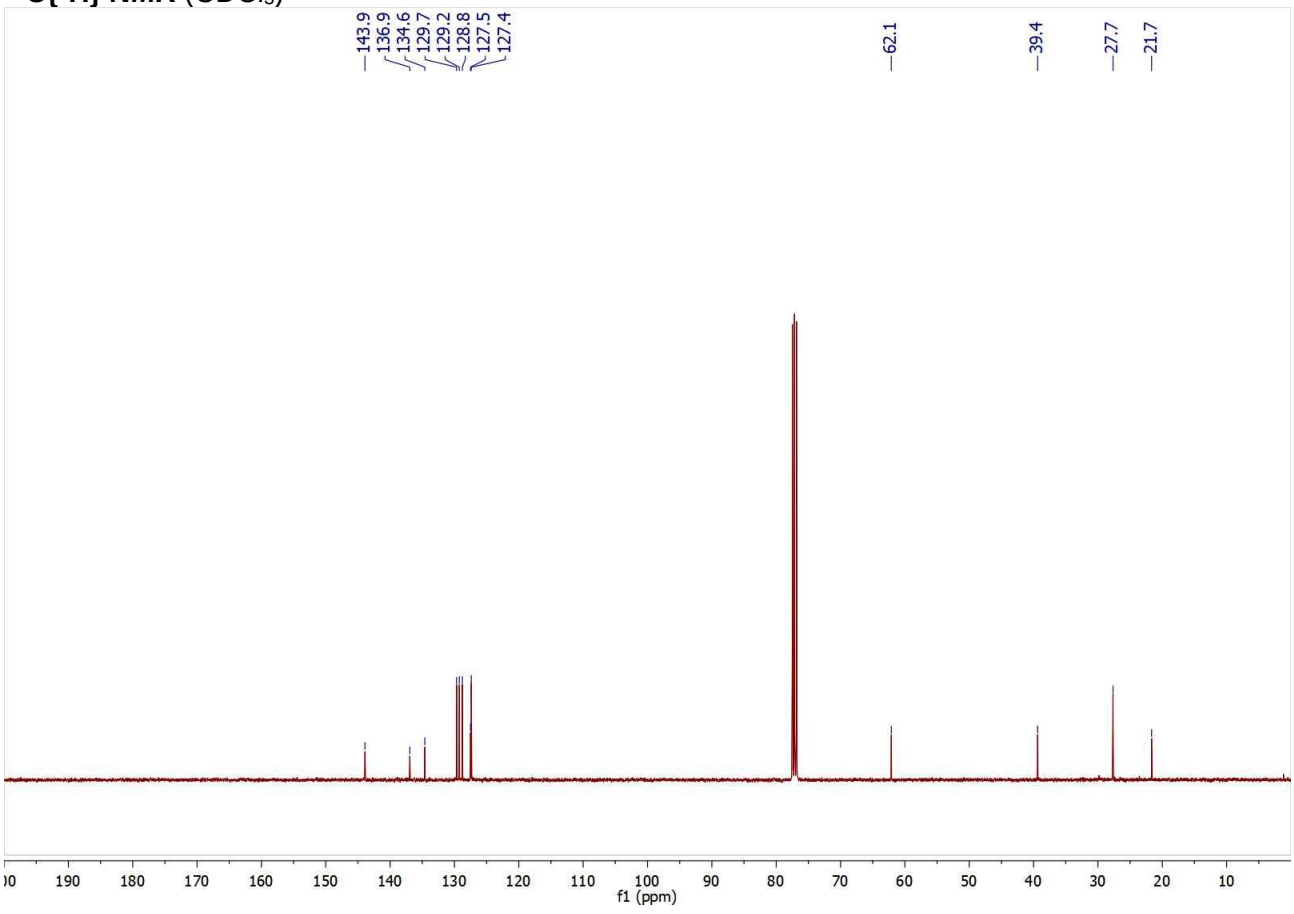


***N*-(1-(2,5-Dioxopyrrolidin-1-yl)-2-phenylethyl)-4-methylbenzensulfonamide (2j)**

^{1}H NMR ($CDCl_3$)

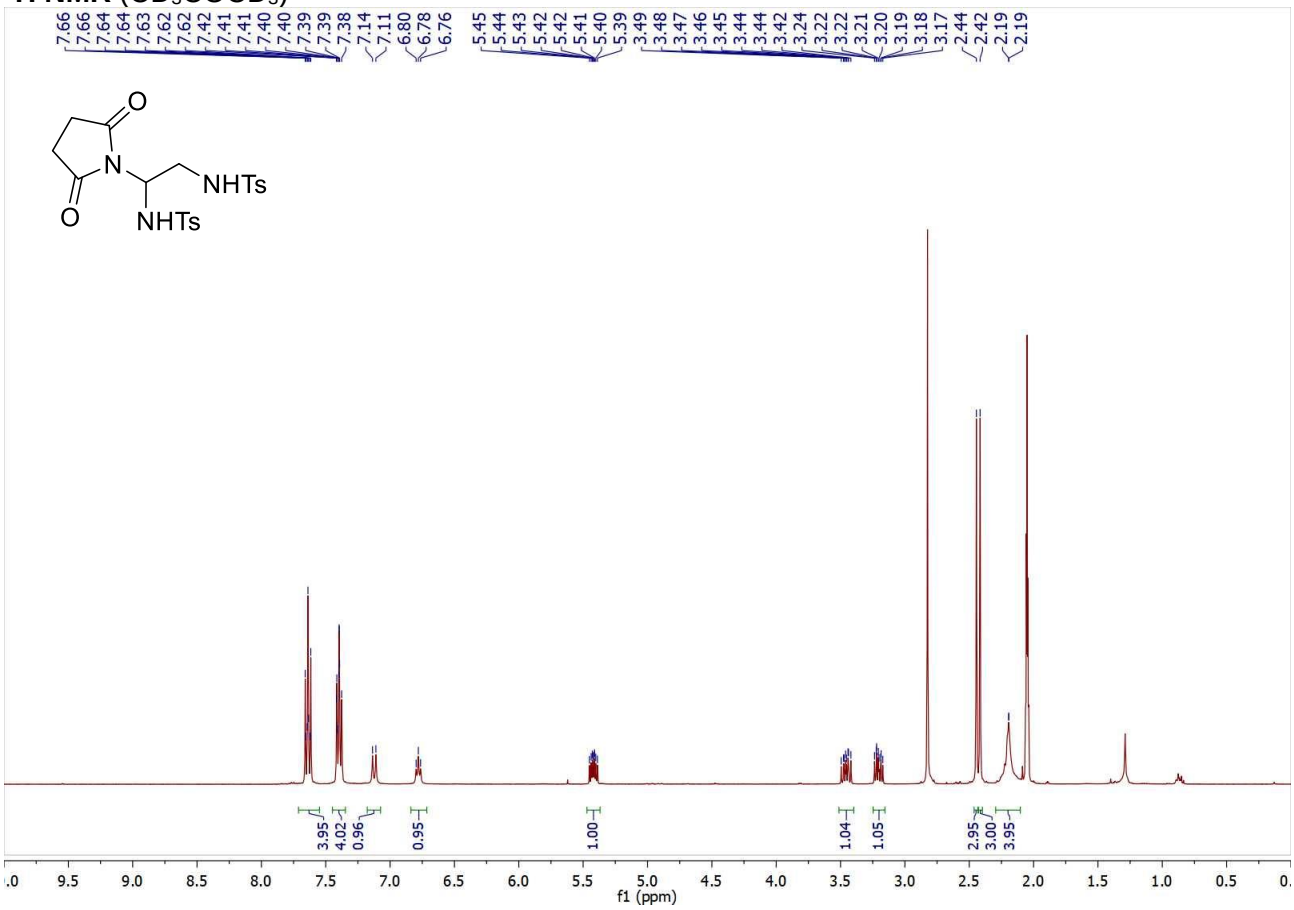


^{13}C{^{1}H} NMR ($CDCl_3$)

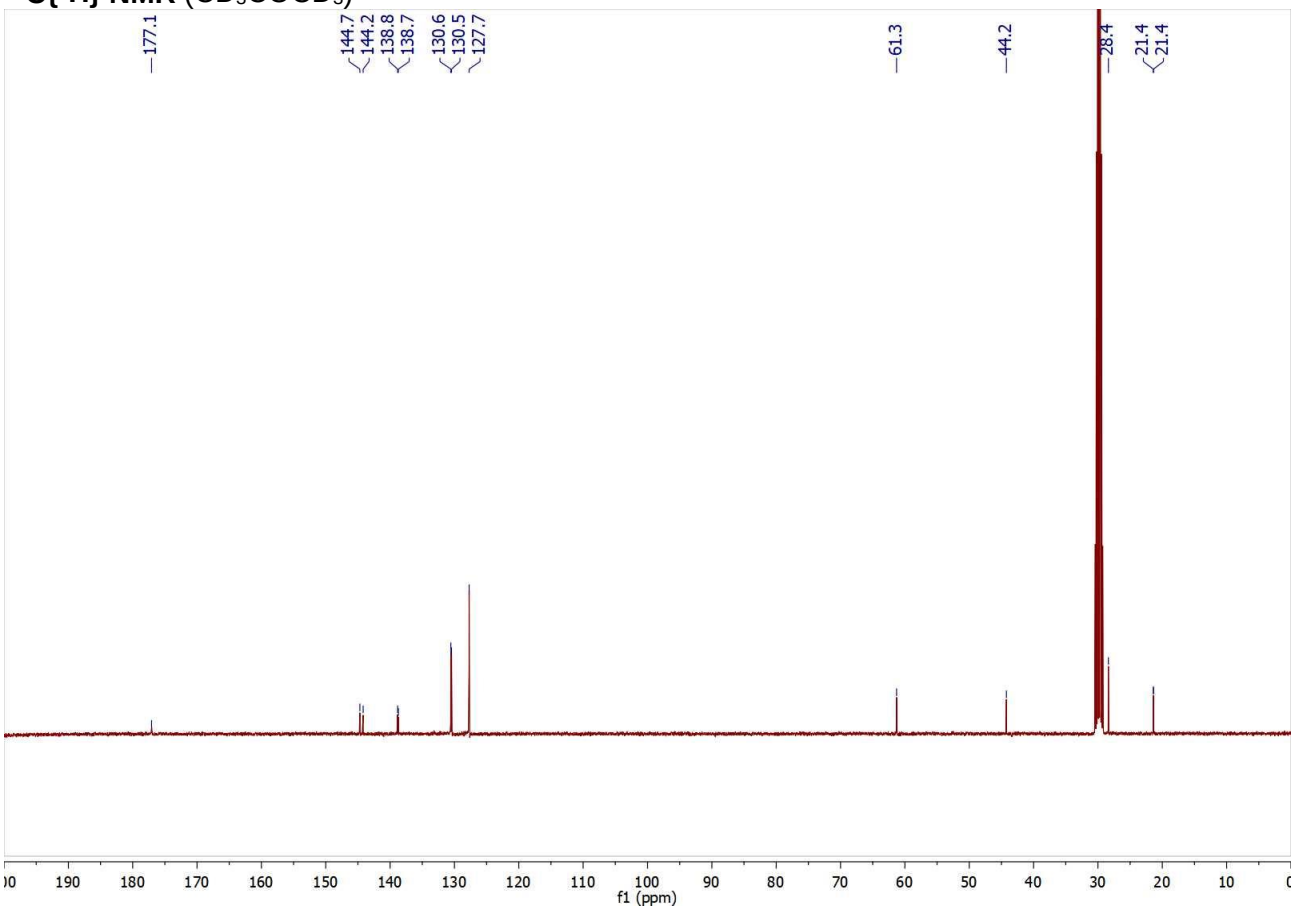


***N-N`*-(1-(2,5-Dioxopyrrolidin-1-yl)ethane-1,2-diyl)bis(4-methylbenzensulfonamide) (2k)**

^{1}H NMR (CD_3COCD_3)

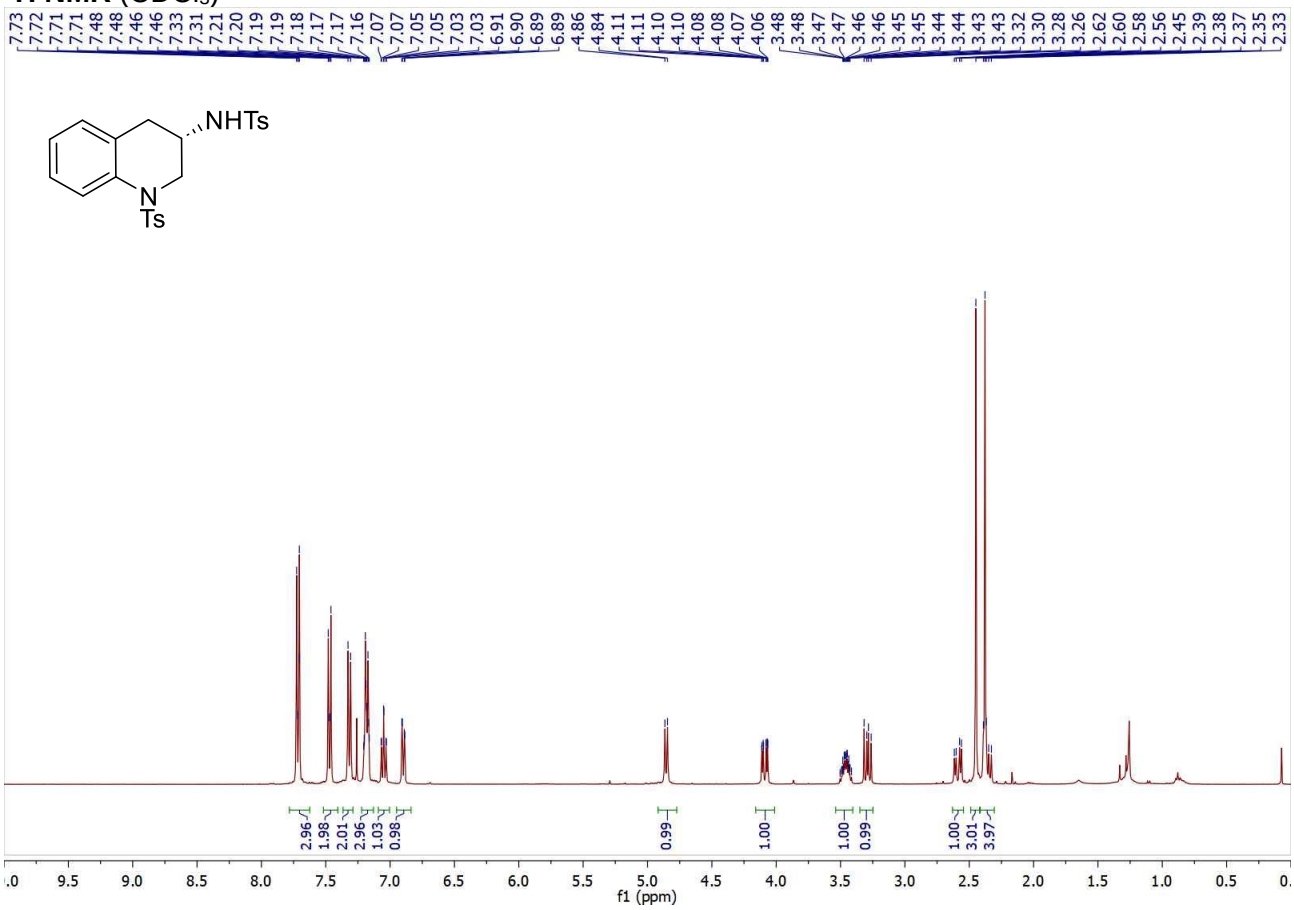


^{13}C{^{1}H} NMR (CD_3COCD_3)

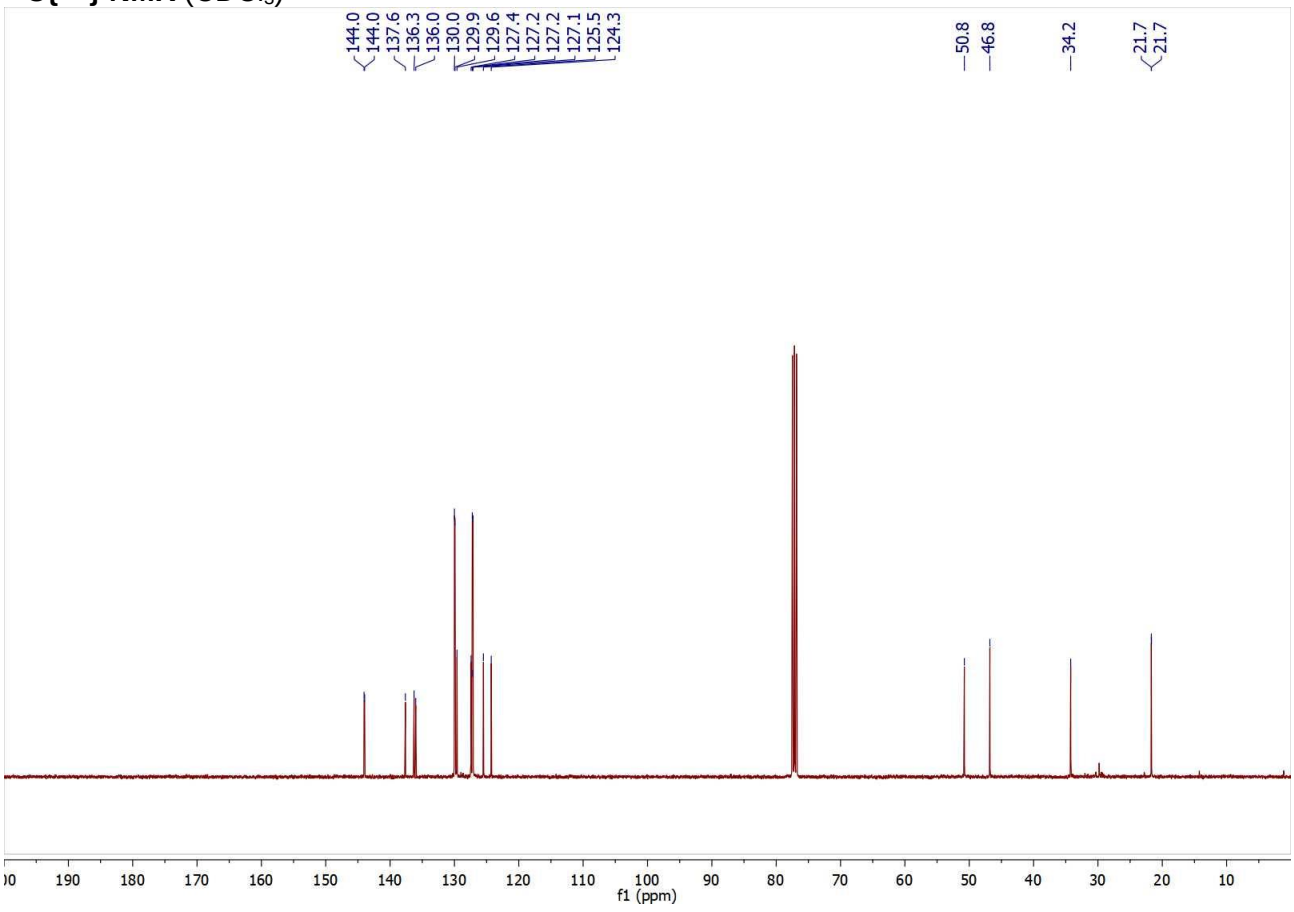


(*S*)-4-Methyl-*N*-(1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzensulfonamide (S8)

^{1}H NMR ($CDCl_3$)

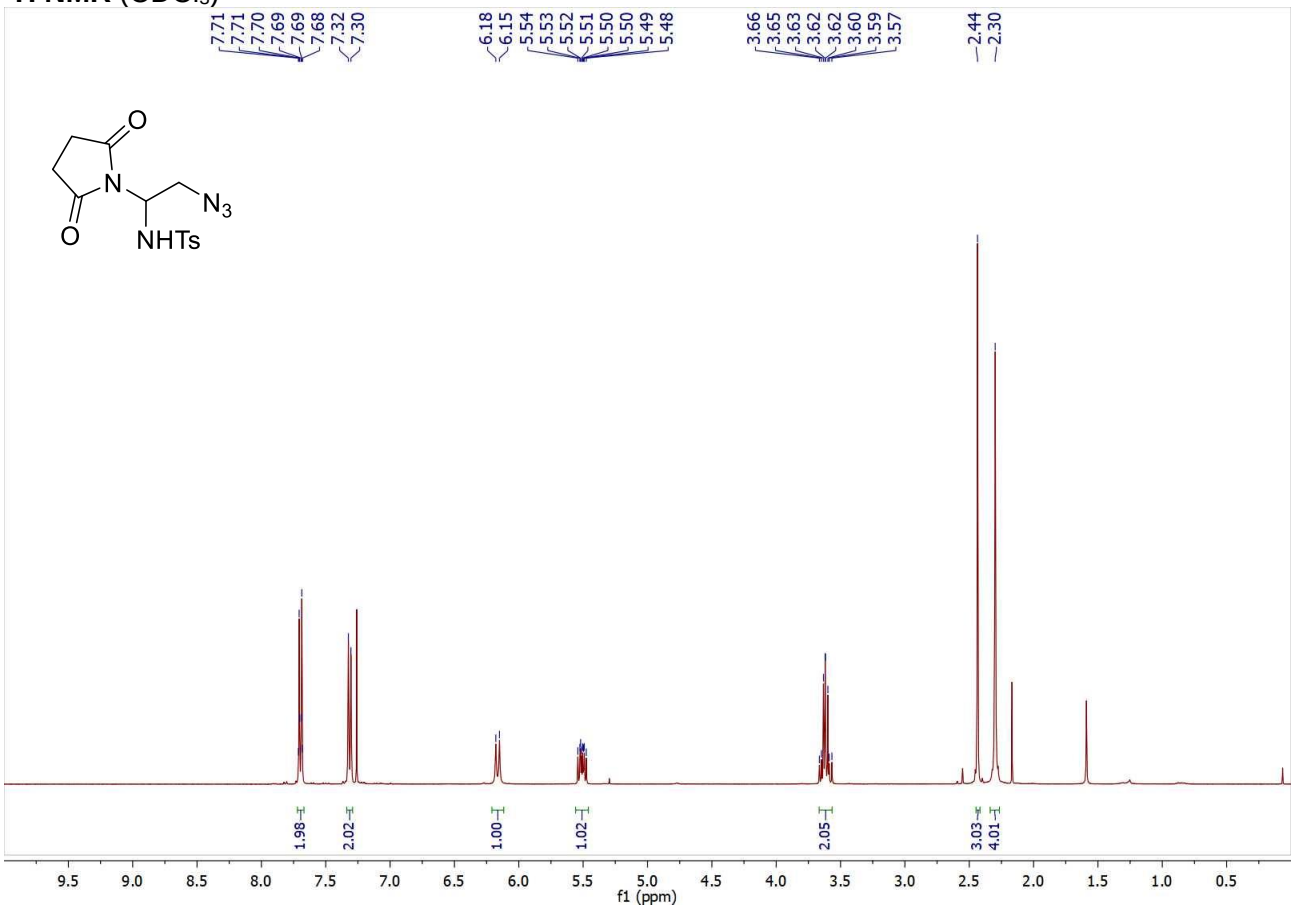


^{13}C{^{1}H} NMR ($CDCl_3$)

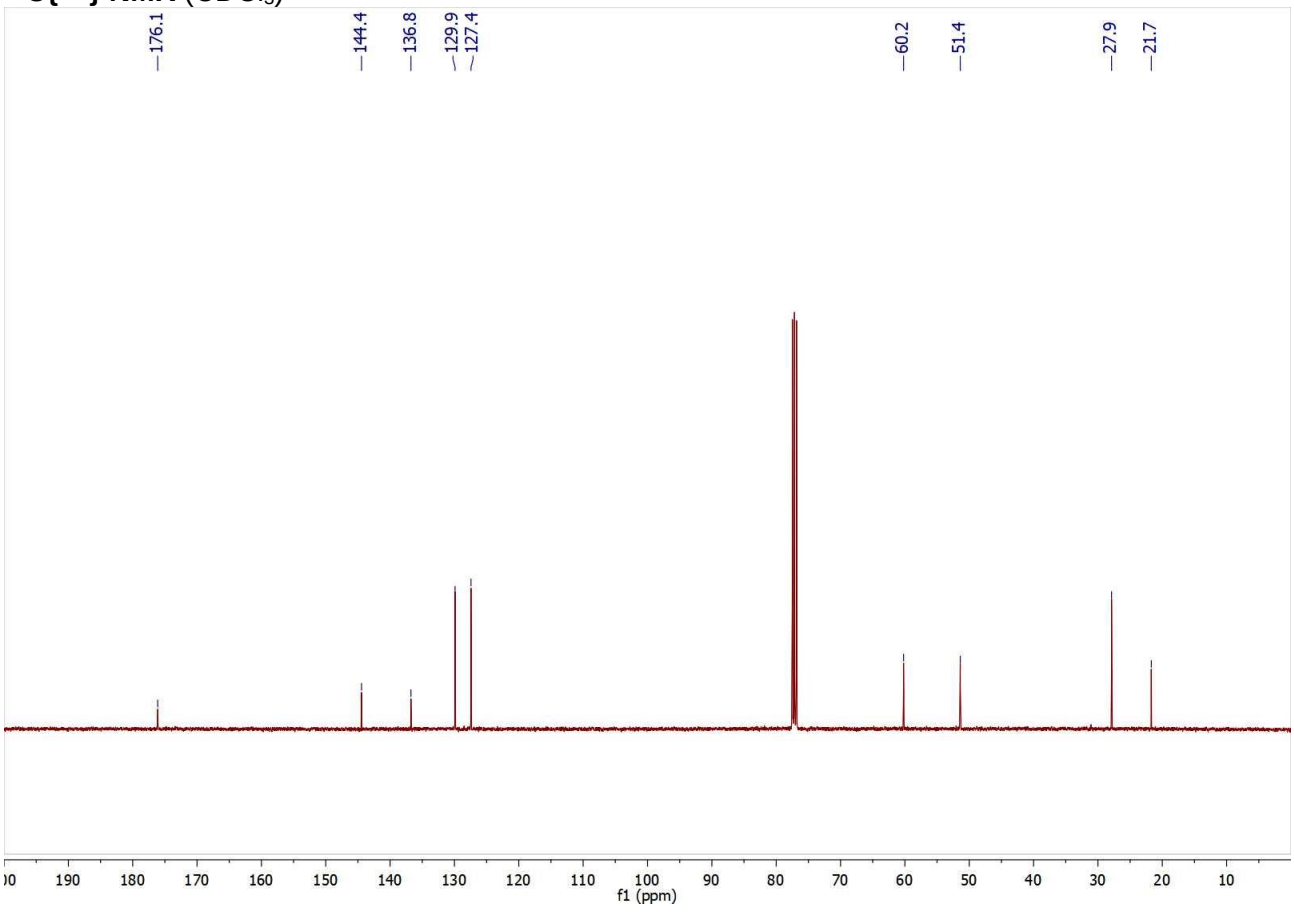


***N*-(2-Azido-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzensulfonamide (2l)**

^{1}H NMR ($CDCl_3$)

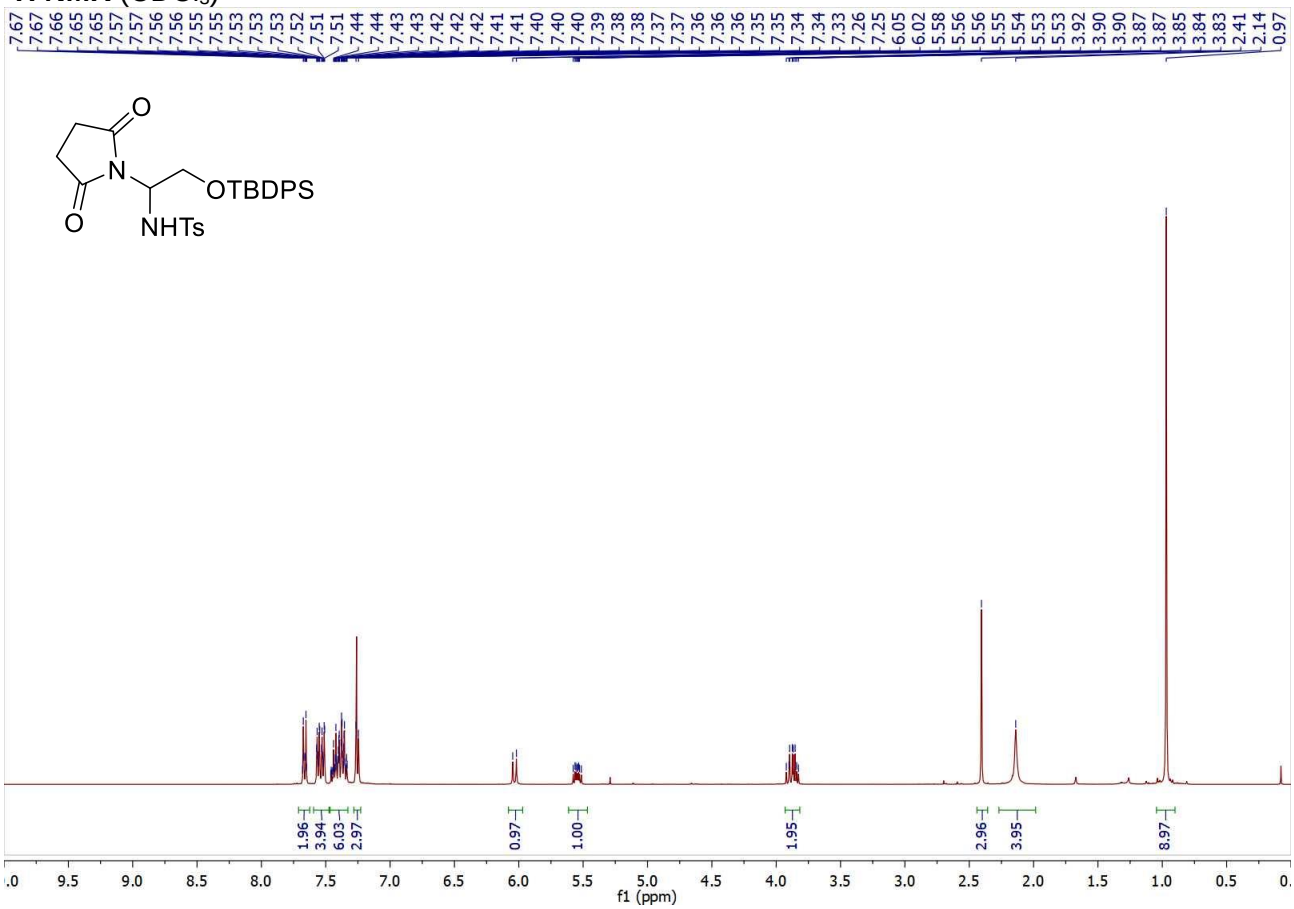


^{13}C{^{1}H} NMR ($CDCl_3$)

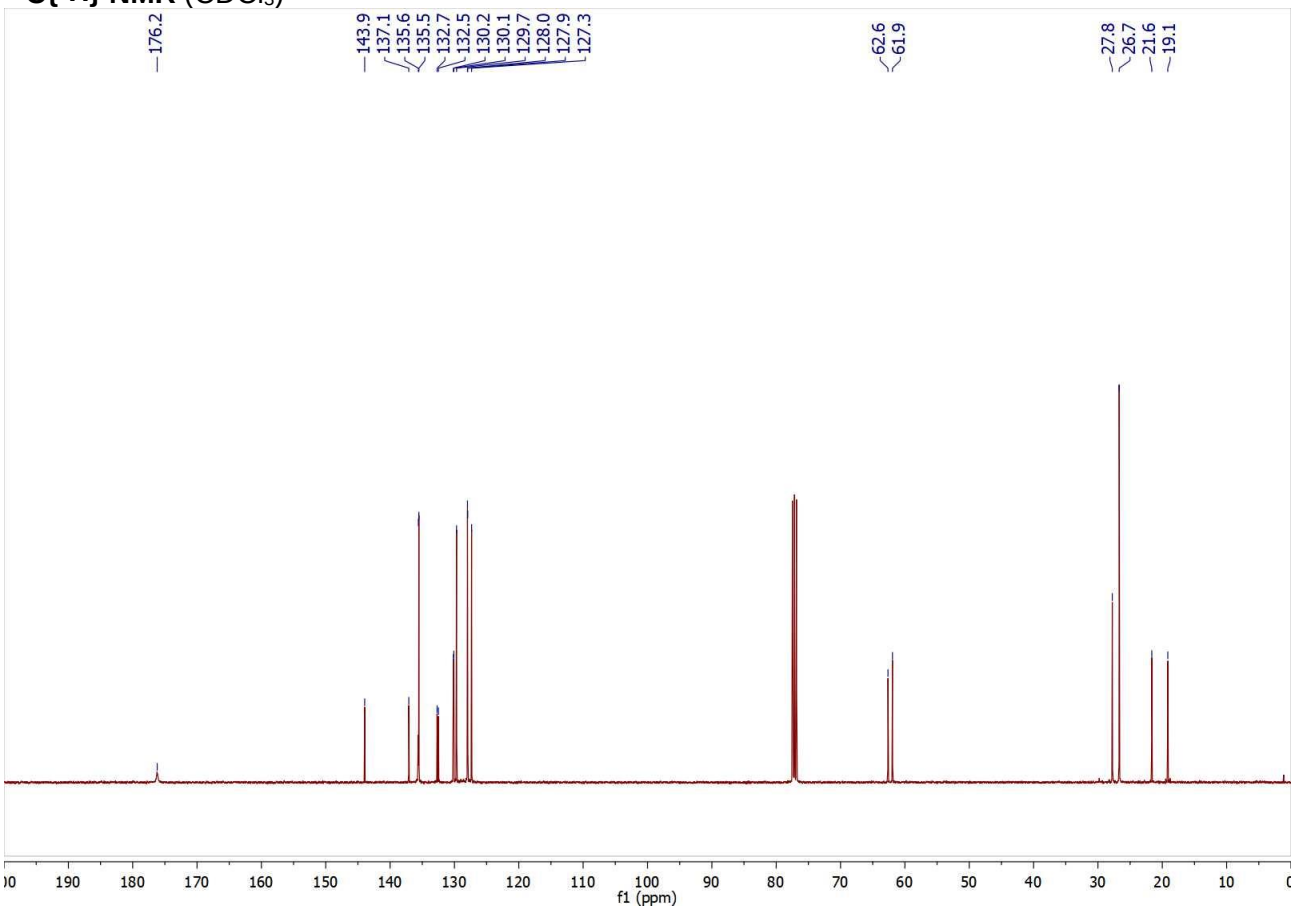


***N*-(2-((*tert*-Butyldiphenylsilyl)oxy)-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbencensulfonamide (2m)**

^{1}H NMR ($CDCl_3$)

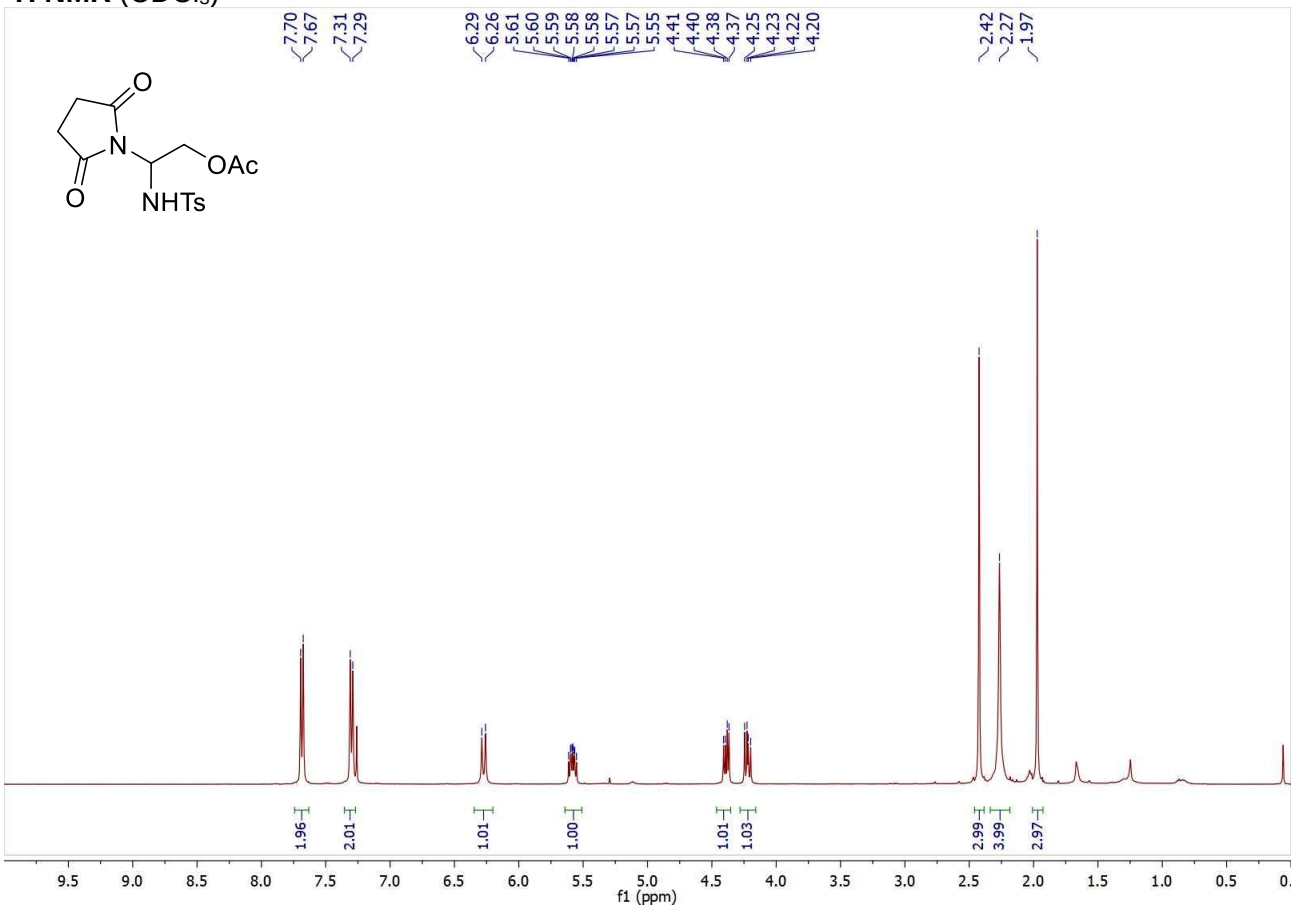


^{13}C{^{1}H} NMR ($CDCl_3$)

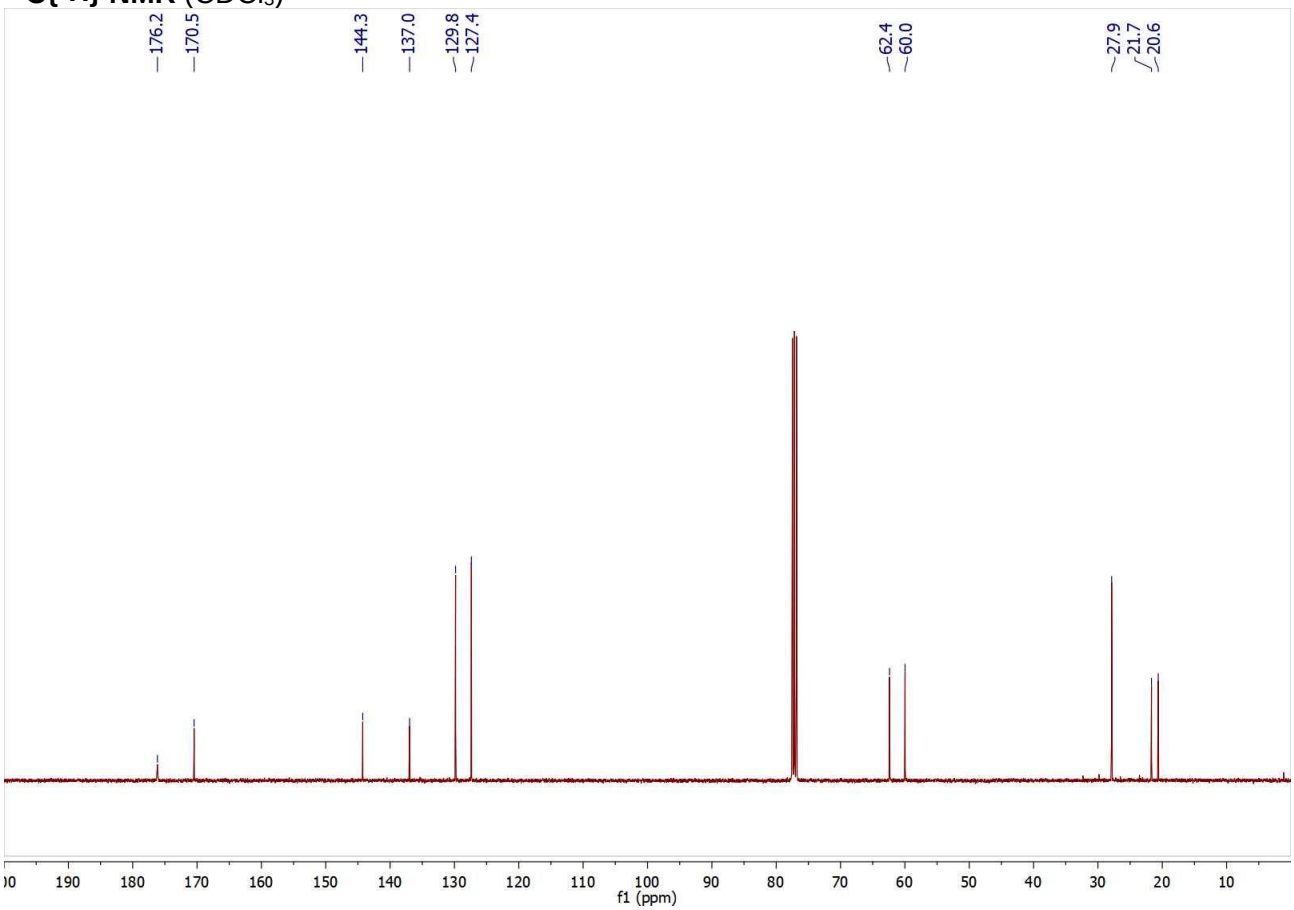


Ethyl 2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido) acetate (2n)

^{1}H NMR ($CDCl_3$)

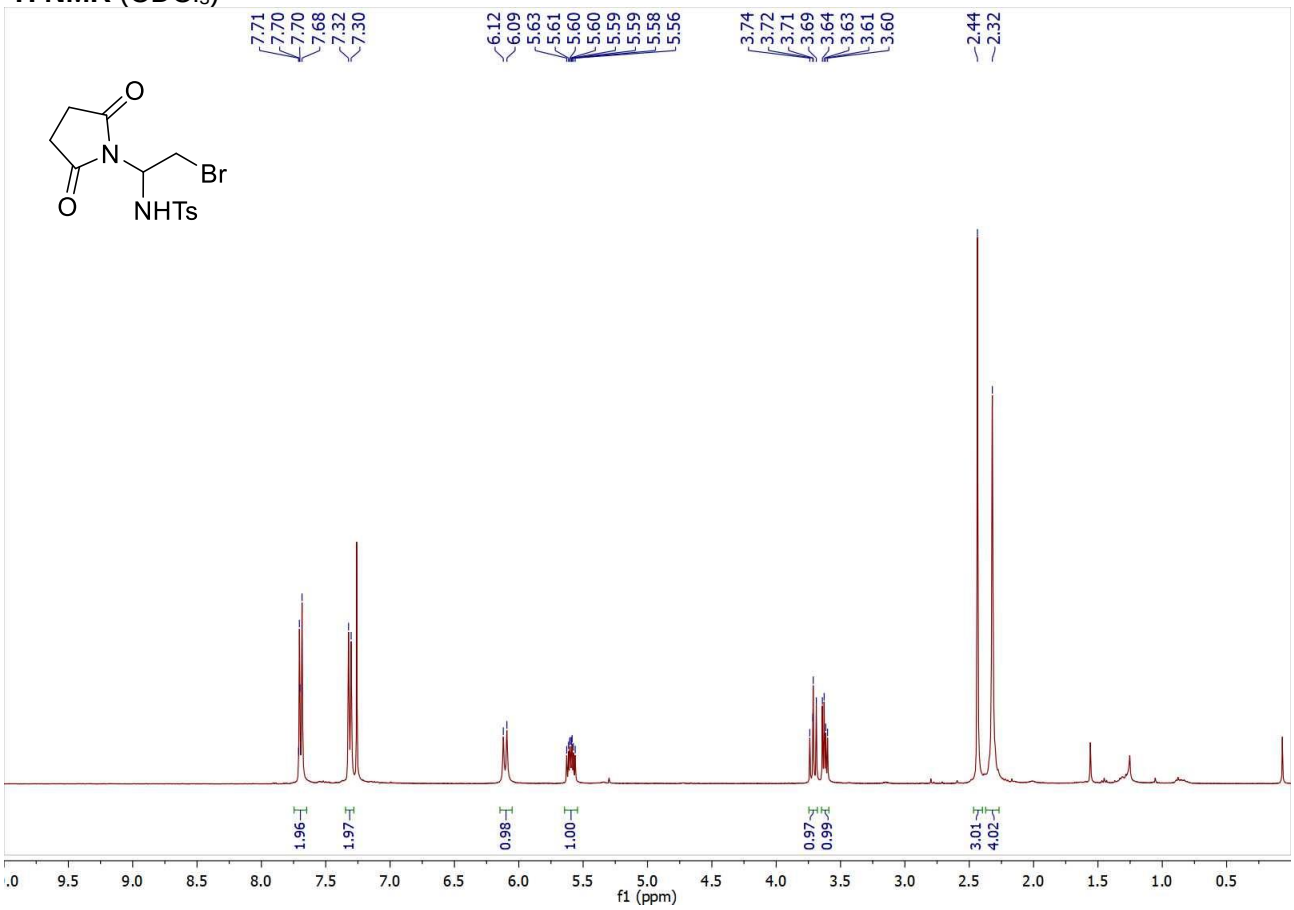


^{13}C{^{1}H} NMR ($CDCl_3$)

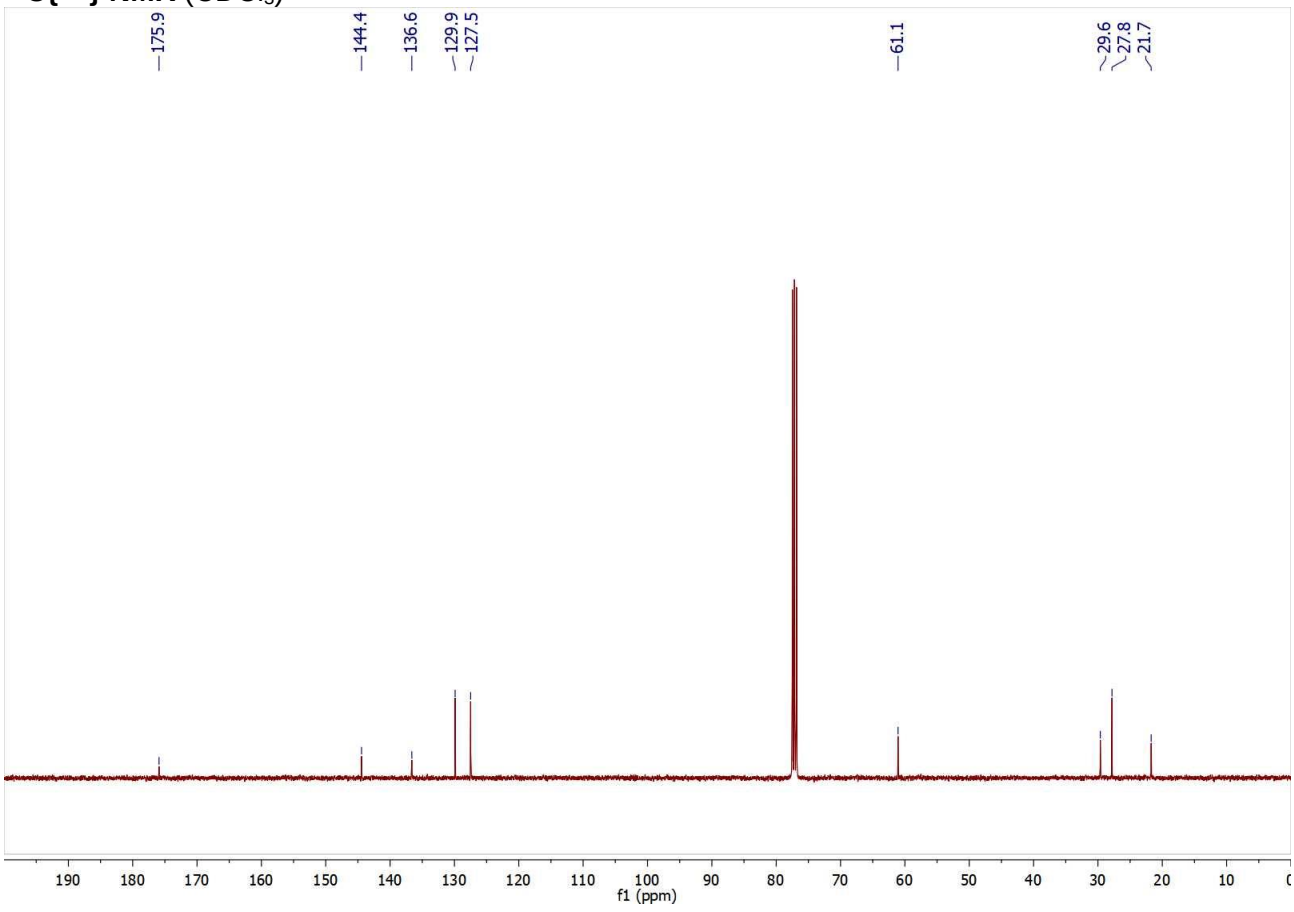


***N*-(2-Bromo-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzensulfonamide (2o)**

^{1}H NMR ($CDCl_3$)

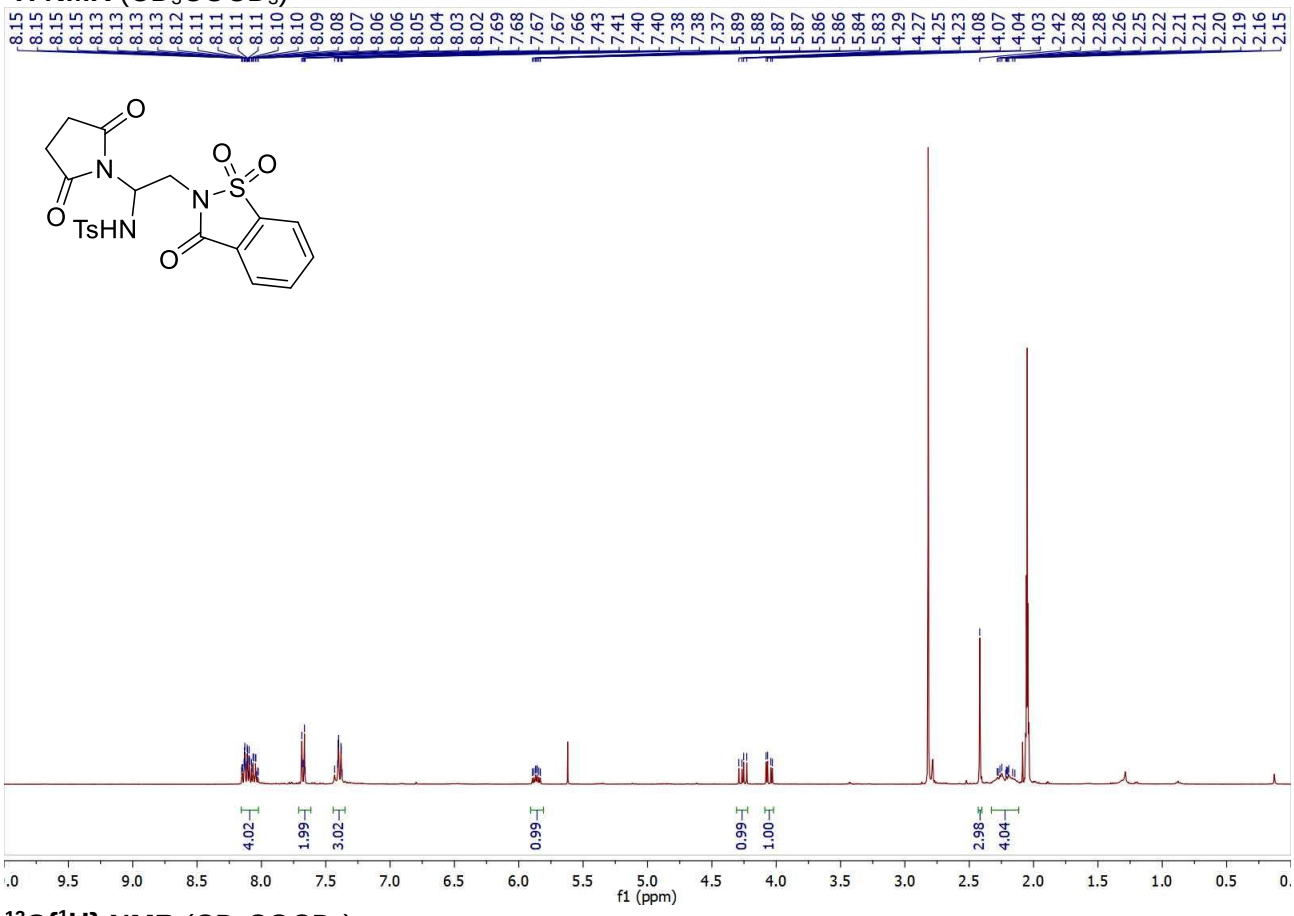


^{13}C{^{1}H} NMR ($CDCl_3$)

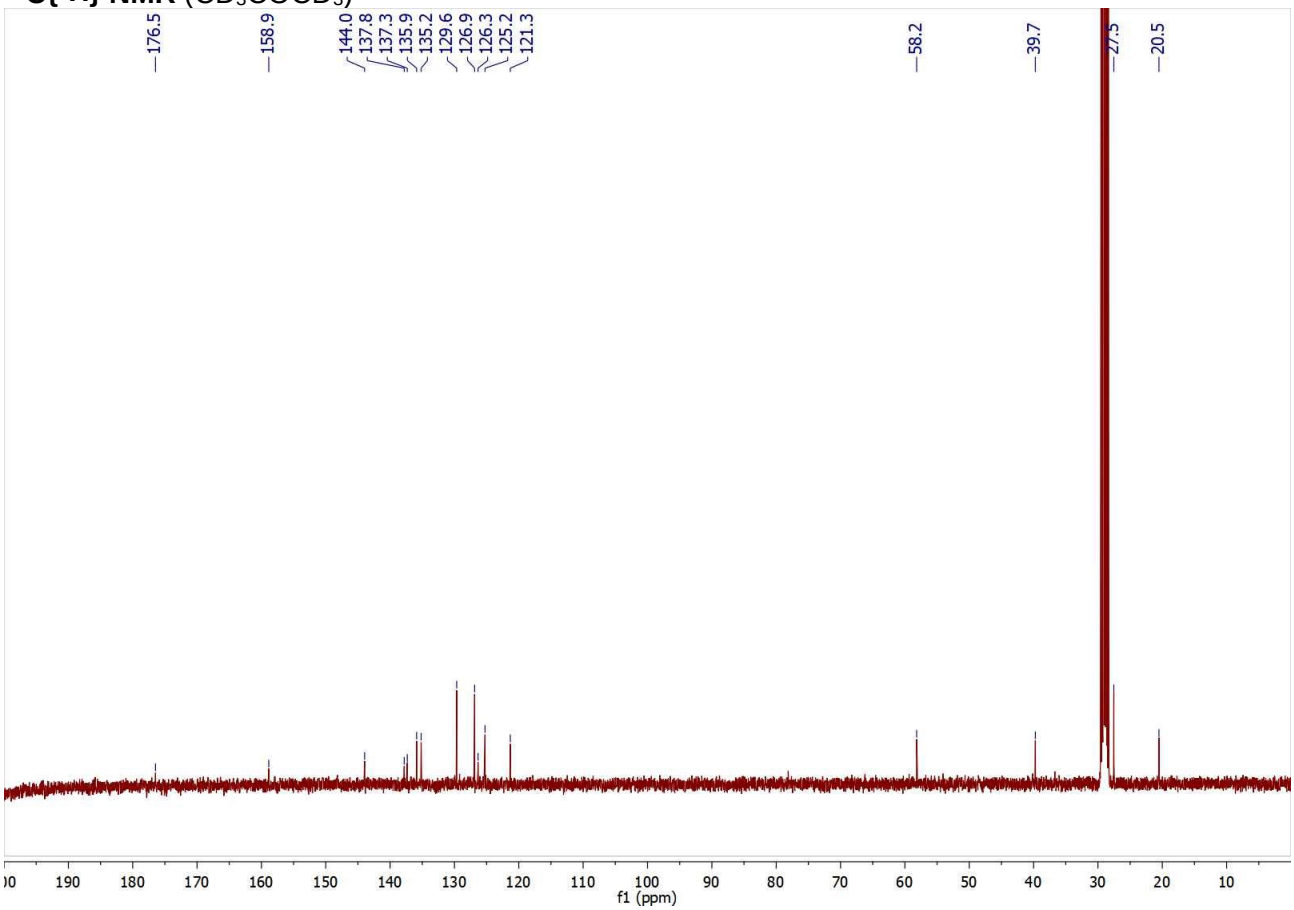


***N*-(2-(1,1-Dioxo-3-oxobenzo[*d*]isothiazol-2(3H)-yl)-1-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzensulfonamide (2p)**

^{1}H NMR (CD_3COCD_3)

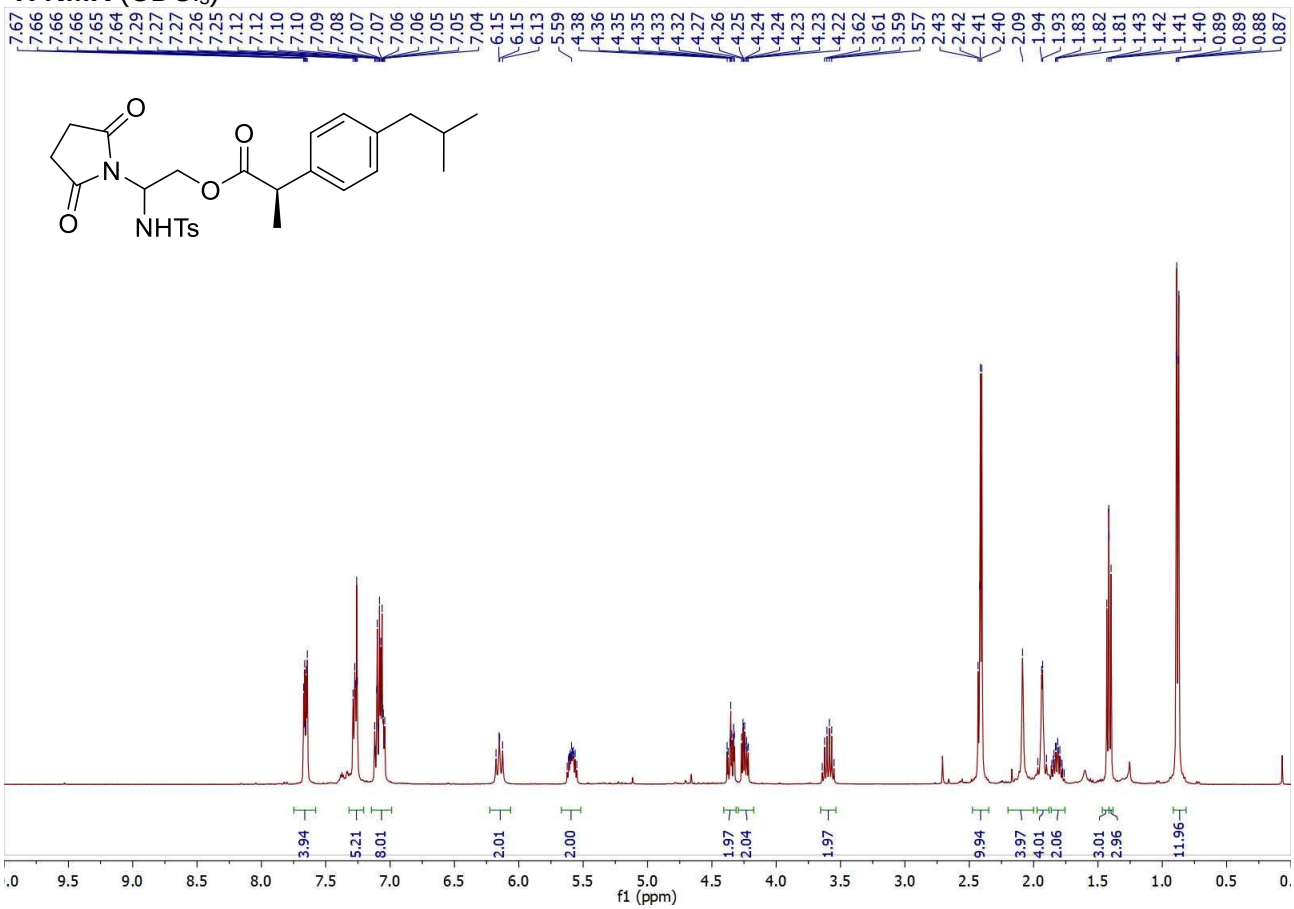


^{13}C{^{1}H} NMR (CD_3COCD_3)

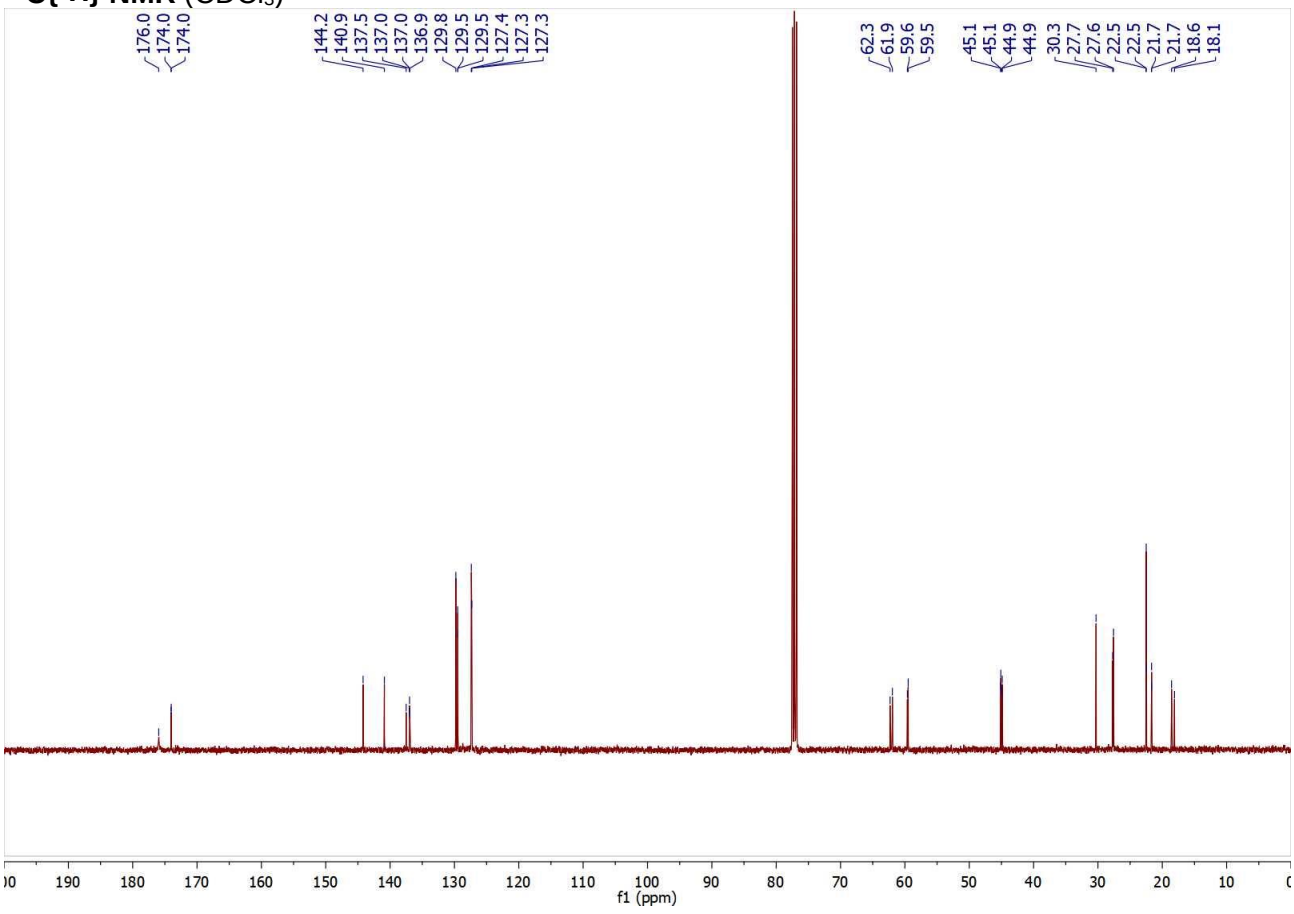


2-(2,5-Dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)ethyl (*2S*)-2-(4-isobutylphenyl)propanoate (2q)

^{1}H NMR ($CDCl_3$)

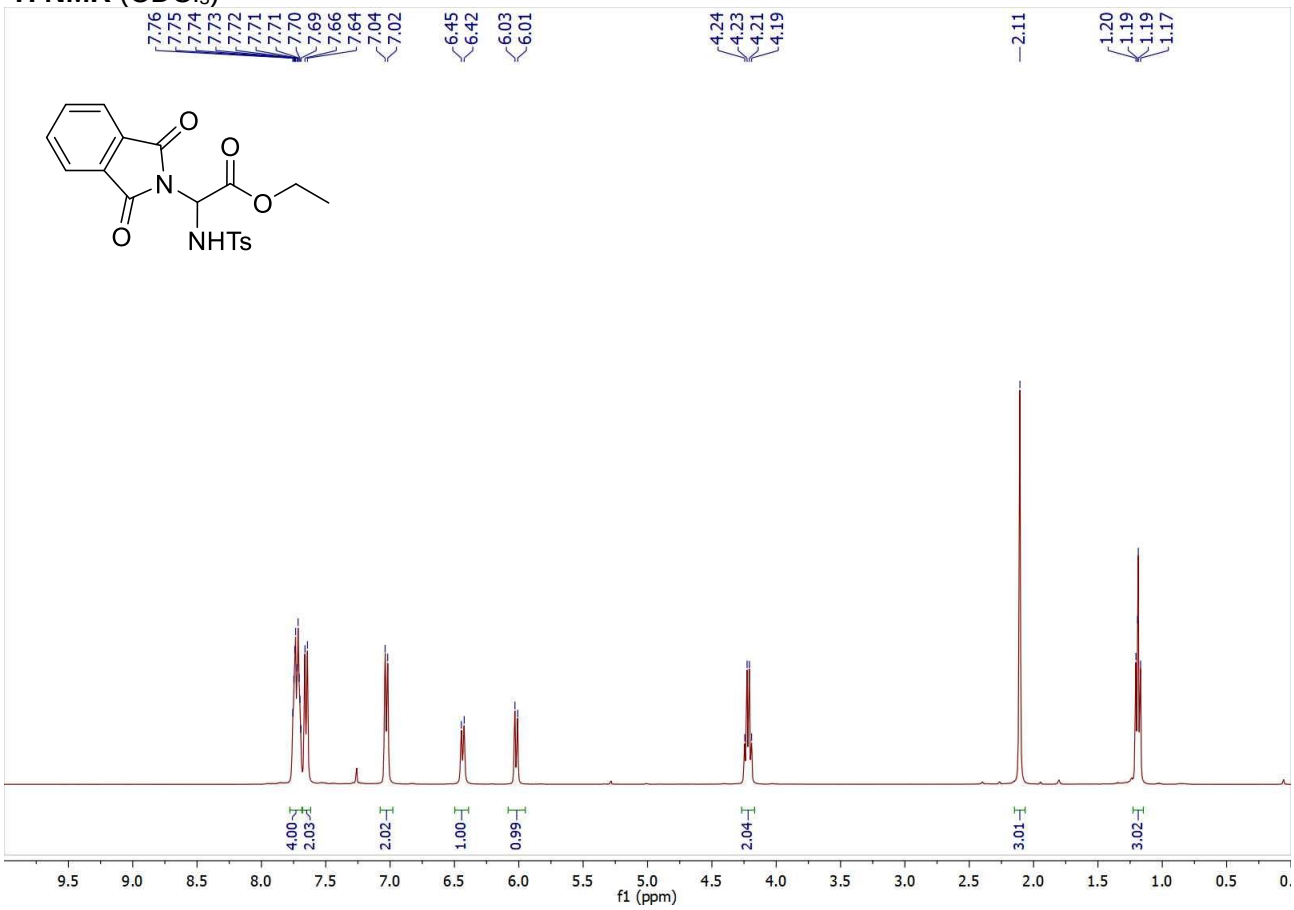


^{13}C{^{1}H} NMR ($CDCl_3$)

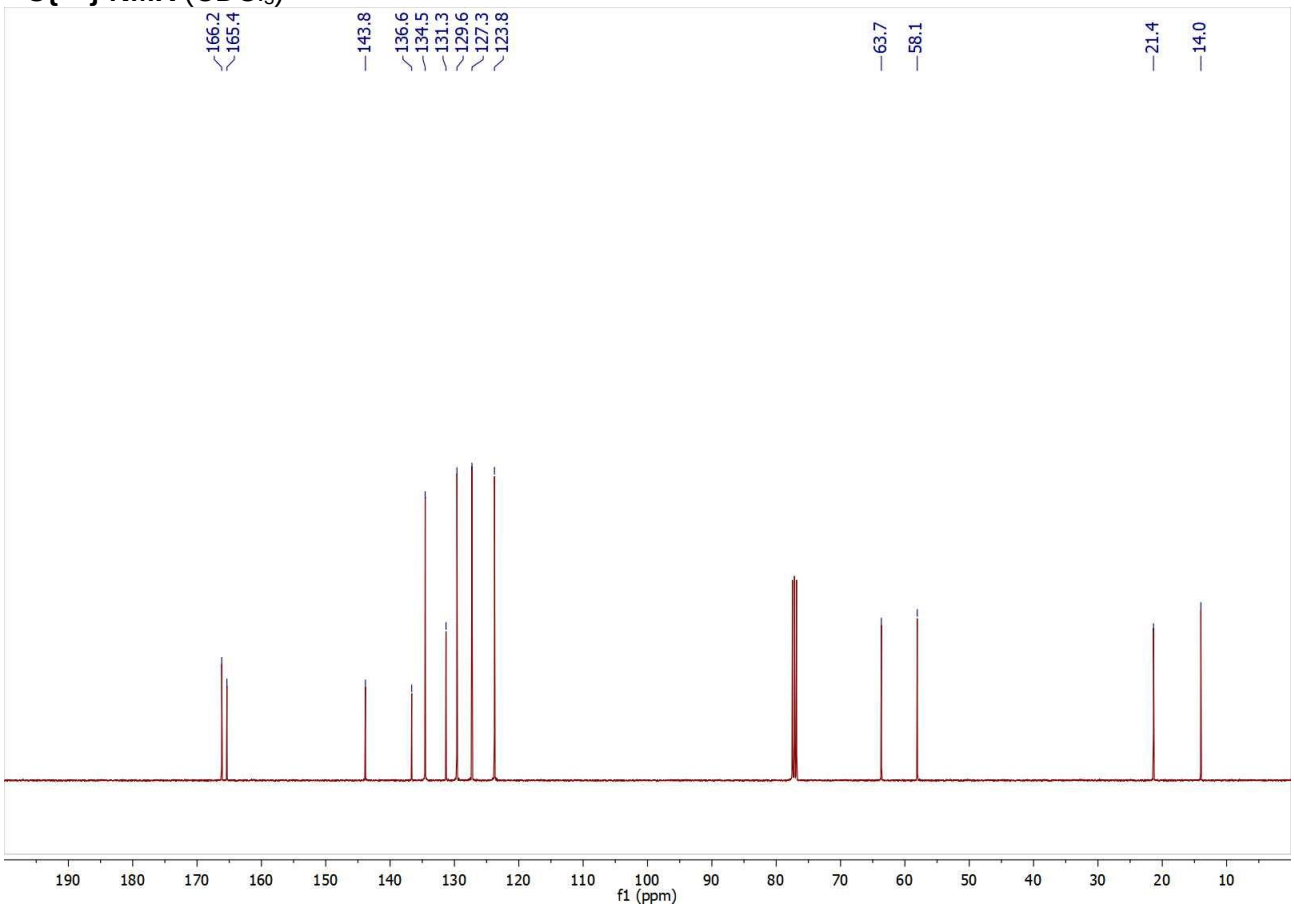


Ethyl 2-(1,3-dioxoisoindolin-2-yl)-2-((4methylphenyl)sulfonamido)acetate (2aa)

^{1}H NMR ($CDCl_3$)

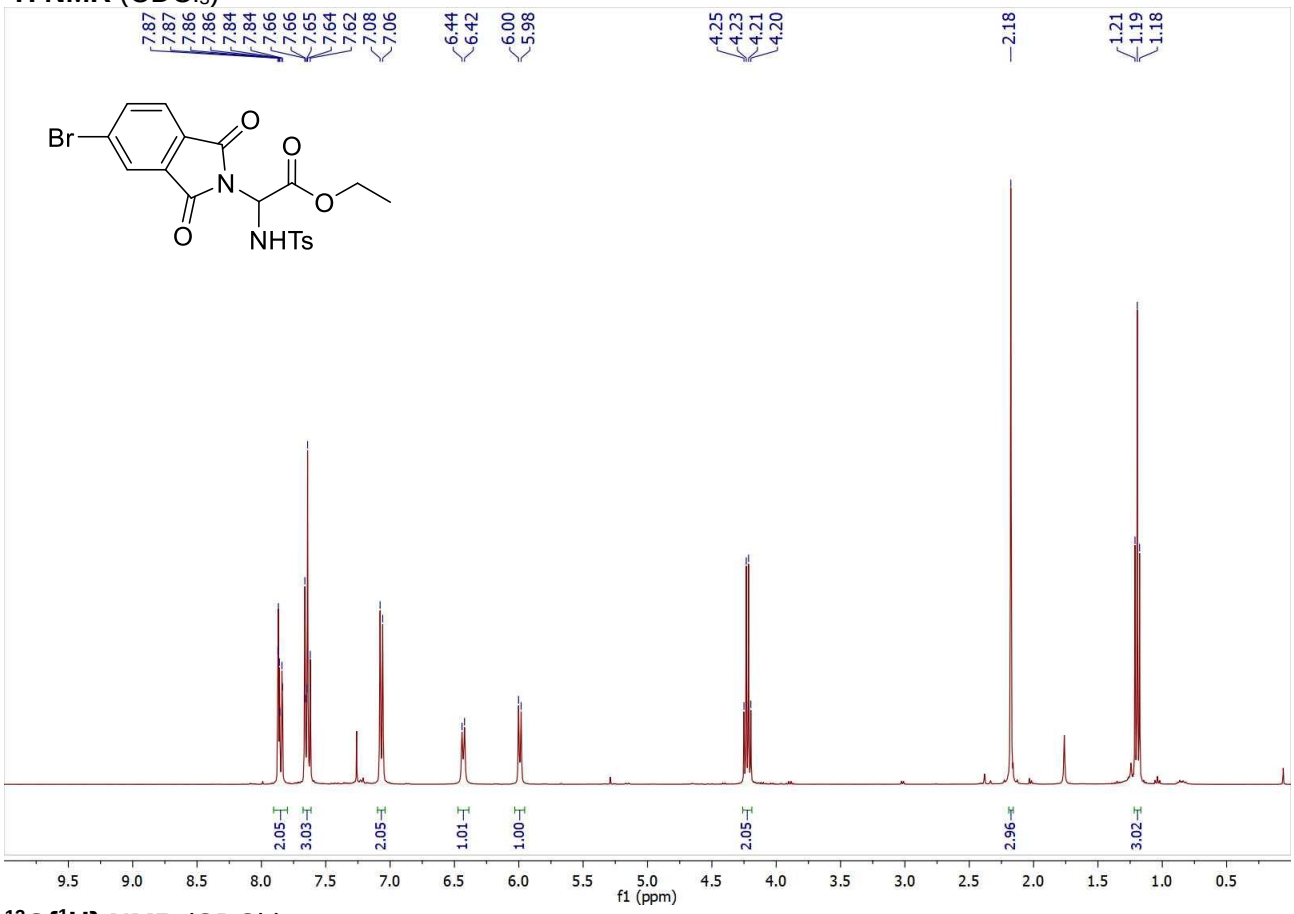


^{13}C{^{1}H} NMR ($CDCl_3$)

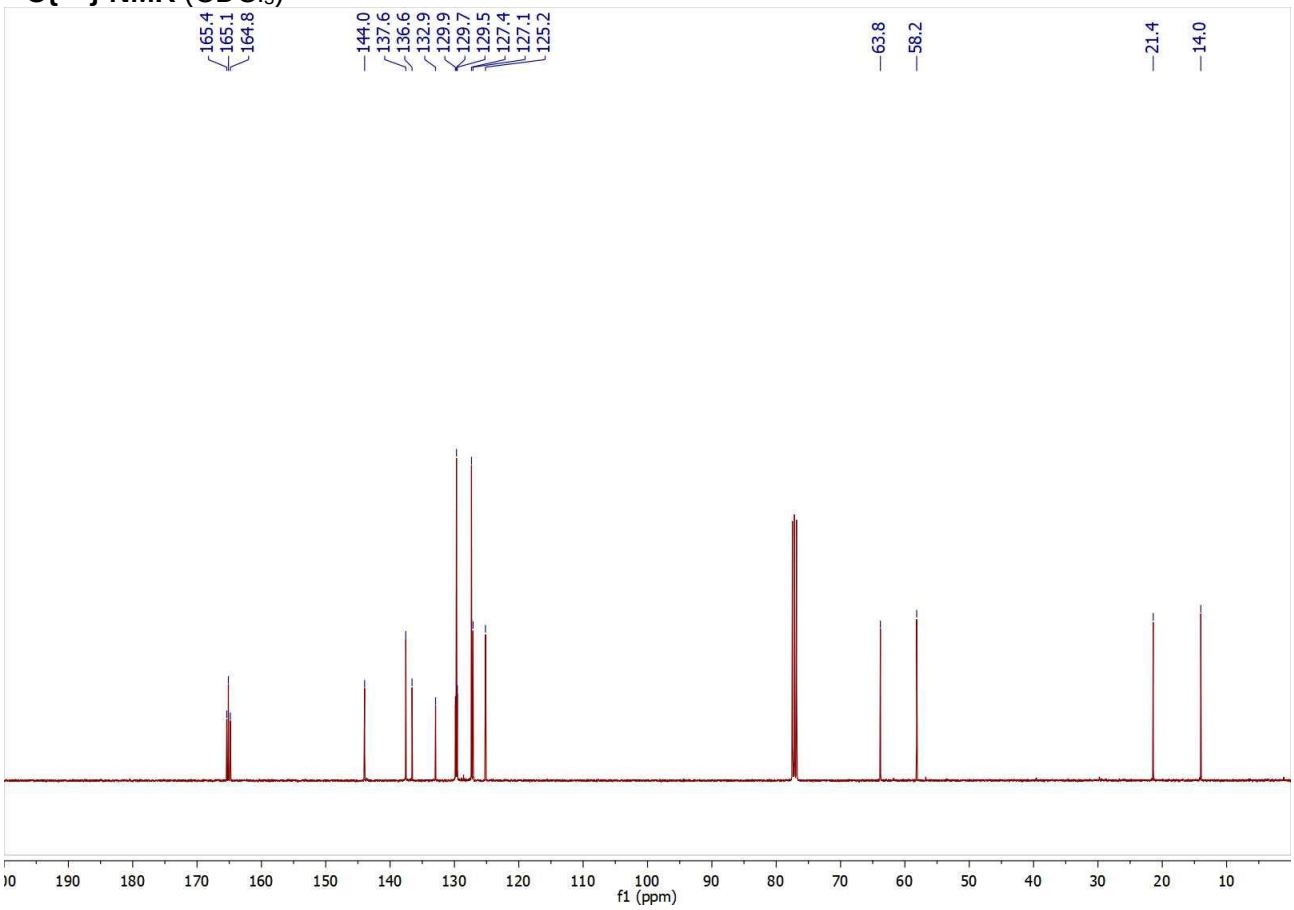


Ethyl 2-(5-bromo-1,3-dioxoisoindolin-2-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ab)

^{1}H NMR ($CDCl_3$)

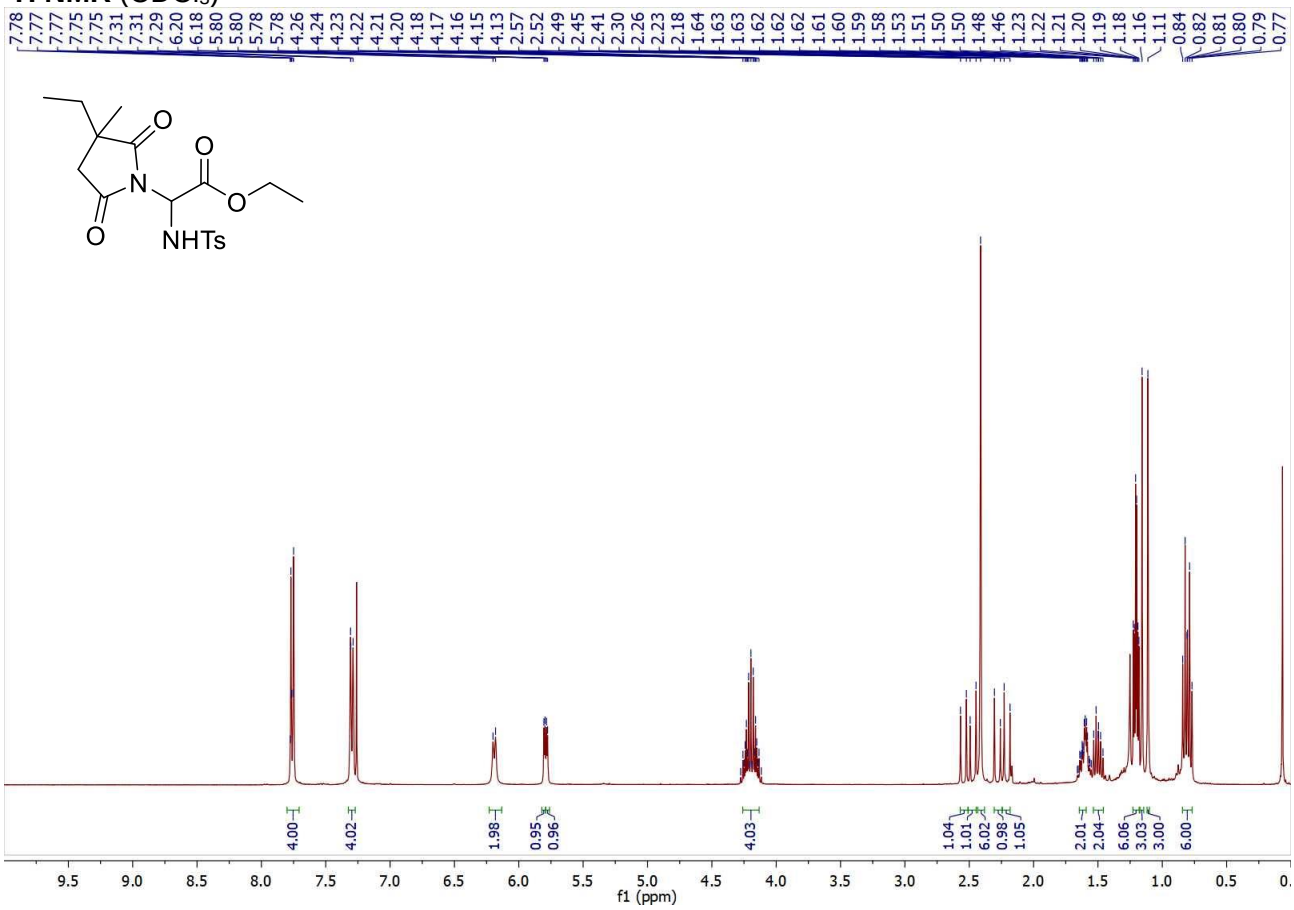


^{13}C{^{1}H} NMR ($CDCl_3$)

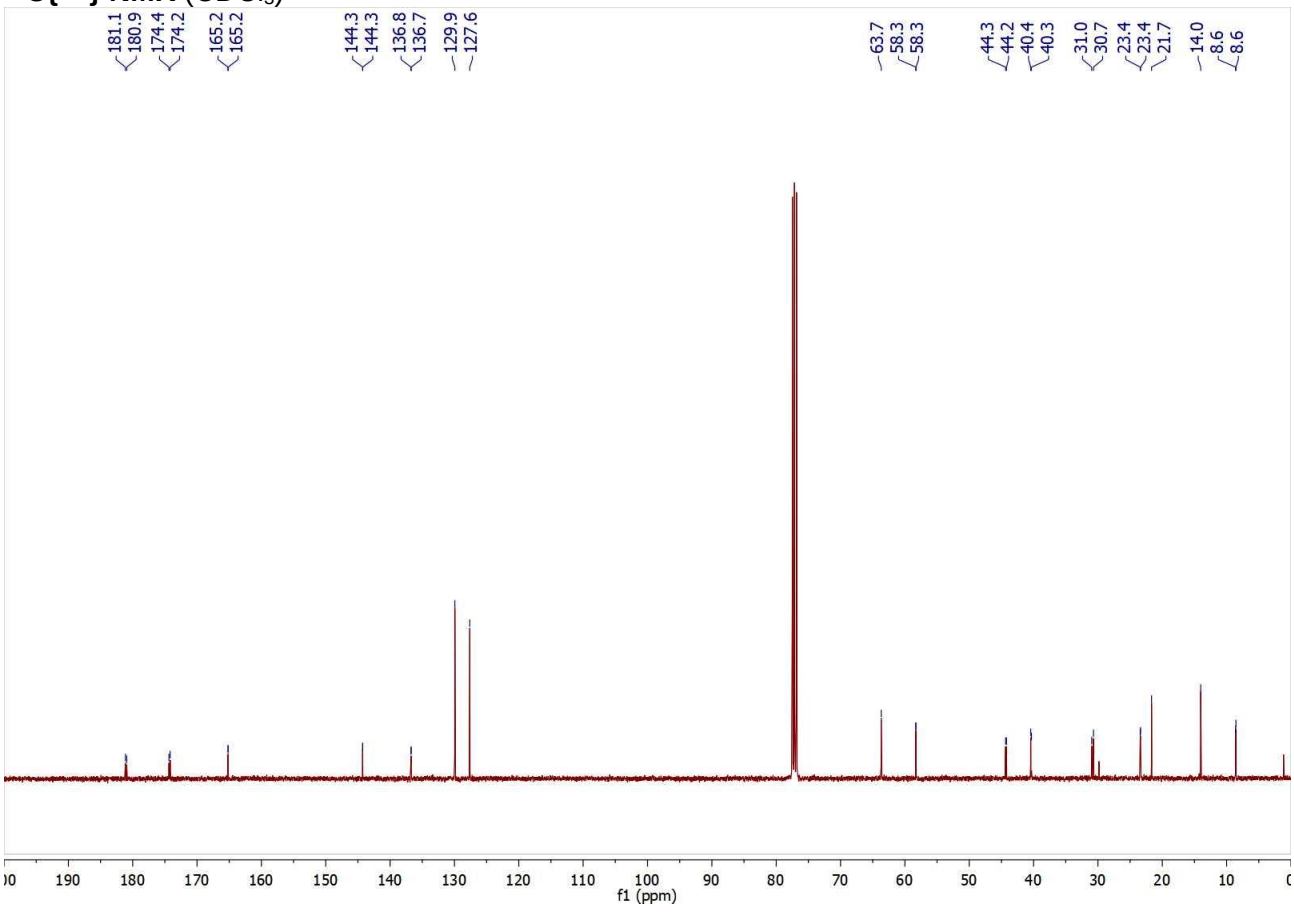


Ethyl 2-(3-ethyl-3-methyl-2,5-dioxopyrrolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ac)

^{1}H NMR ($CDCl_3$)

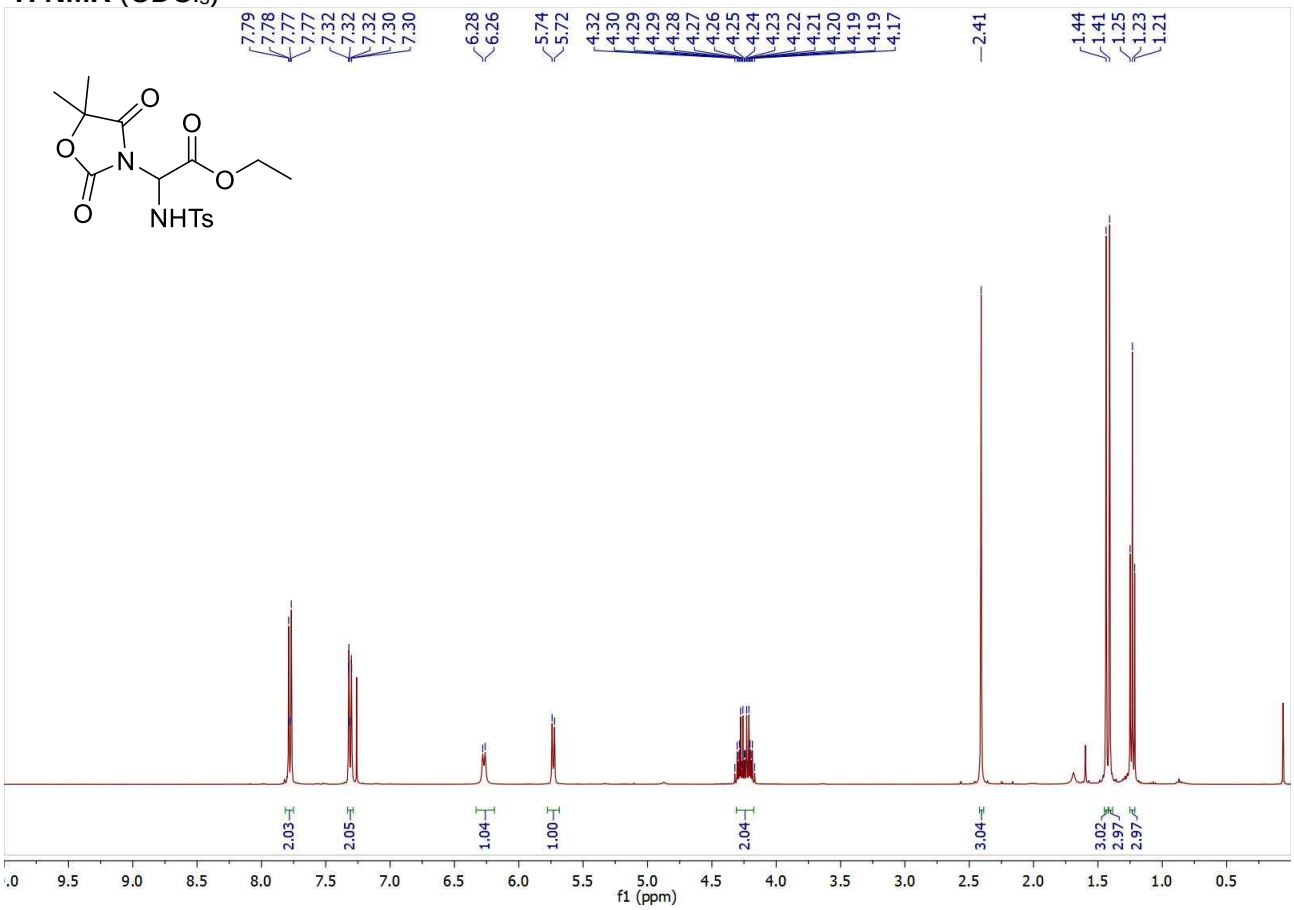


^{13}C{^{1}H} NMR ($CDCl_3$)

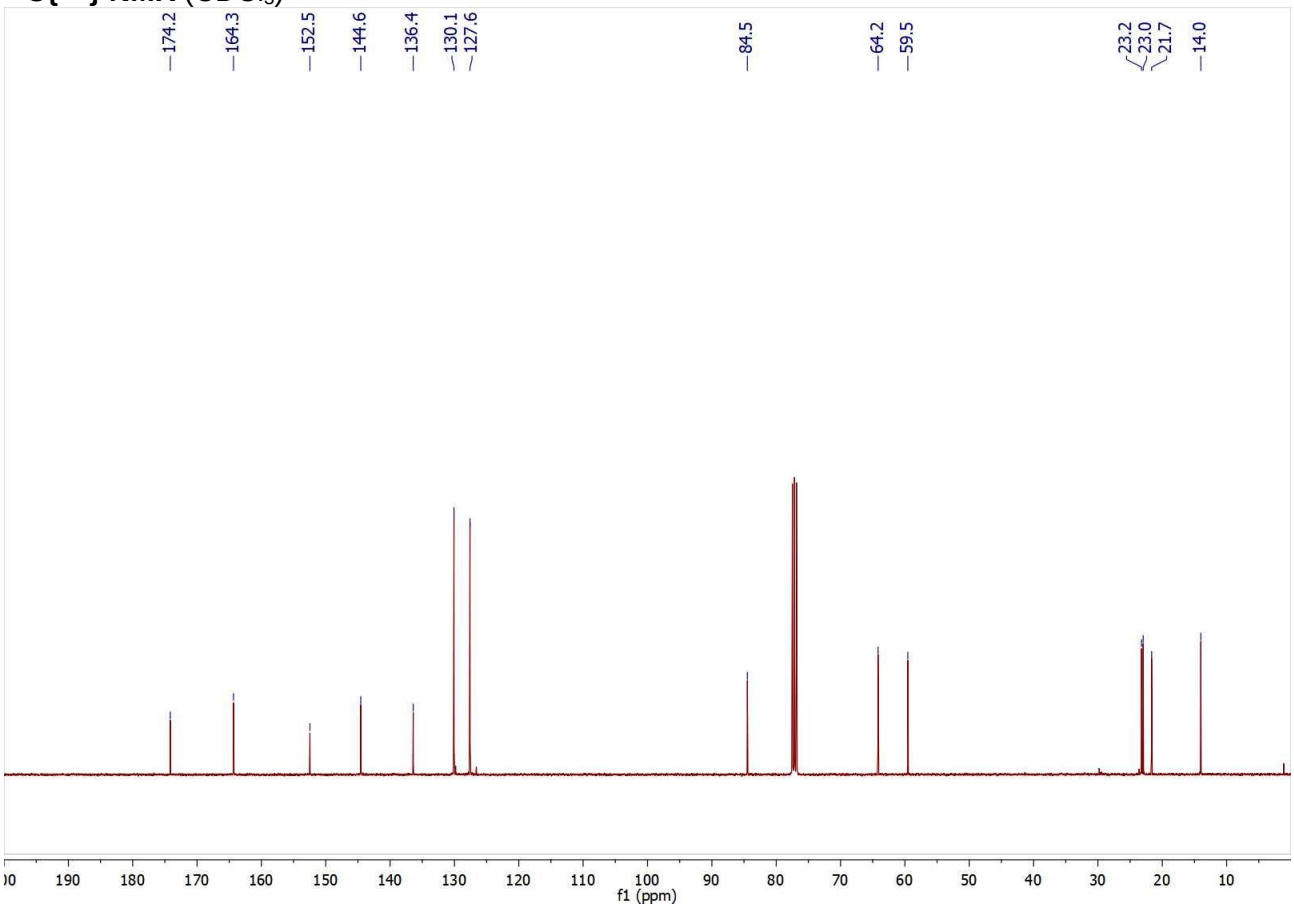


Ethyl 2-(5,5-dimethyl-2,4-dioxooxazolidin-3-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ad)

^{1}H NMR ($CDCl_3$)

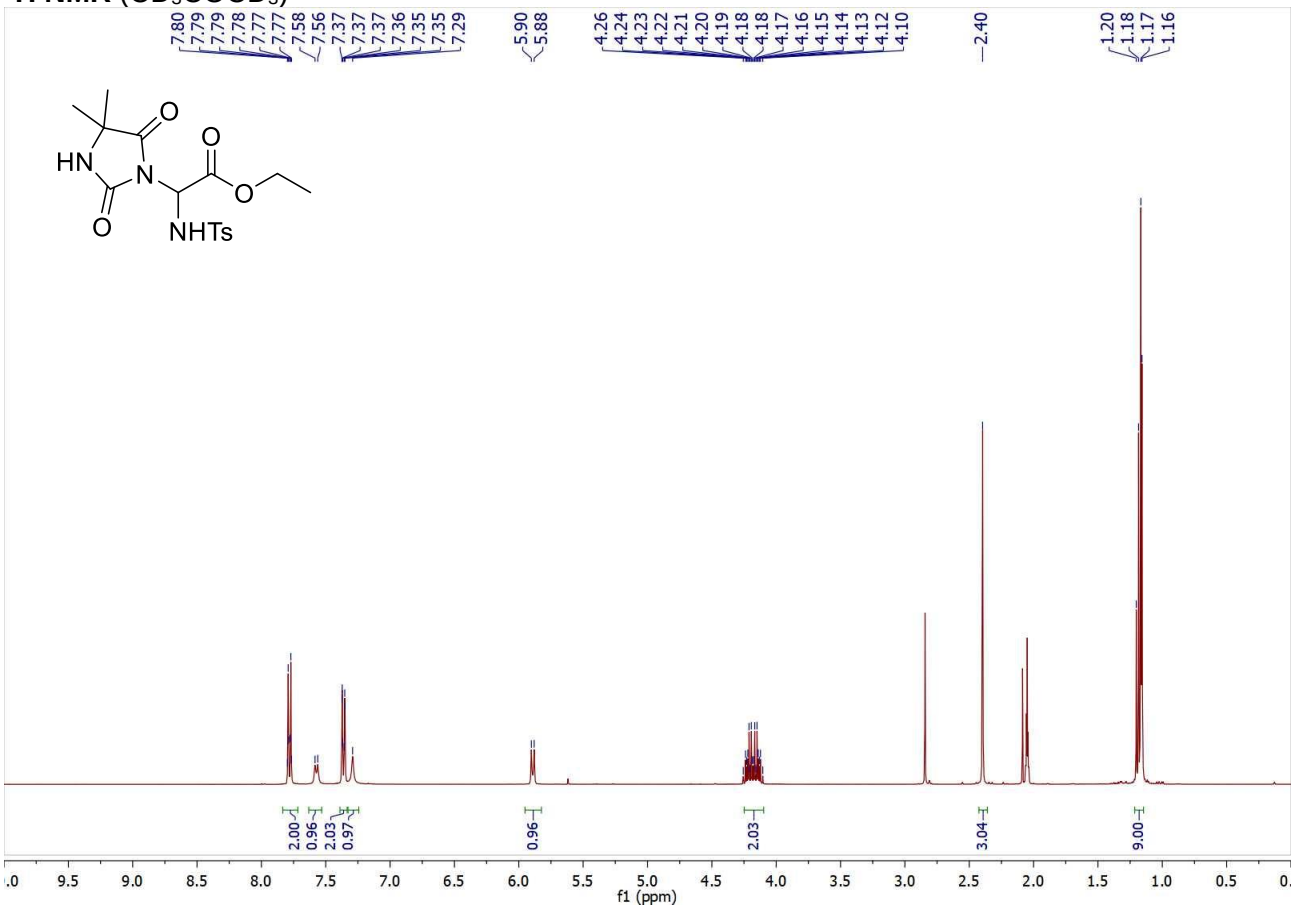


^{13}C{^{1}H} NMR ($CDCl_3$)

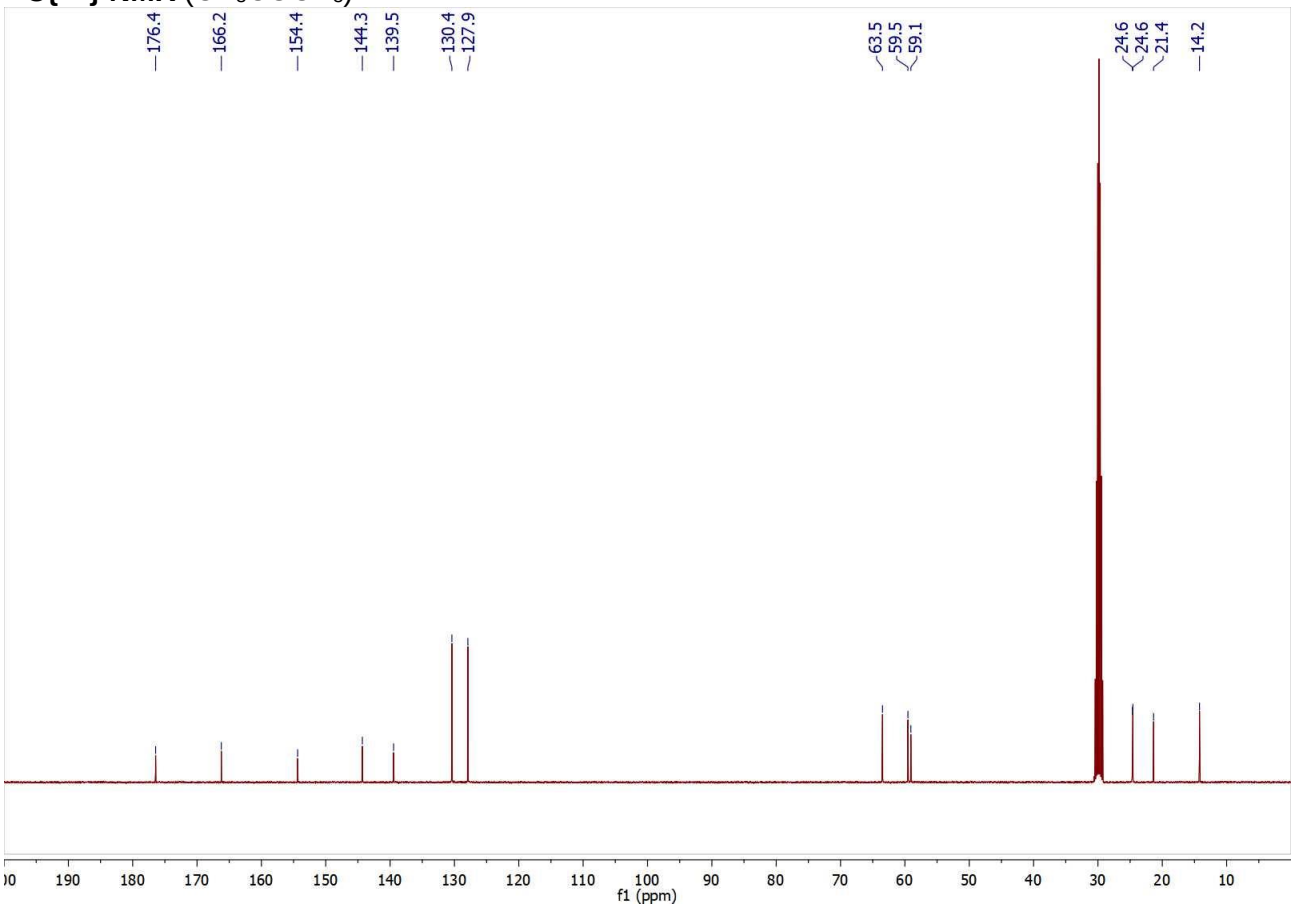


Ethyl 2-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ae)

^{1}H NMR (CD_3COCD_3)

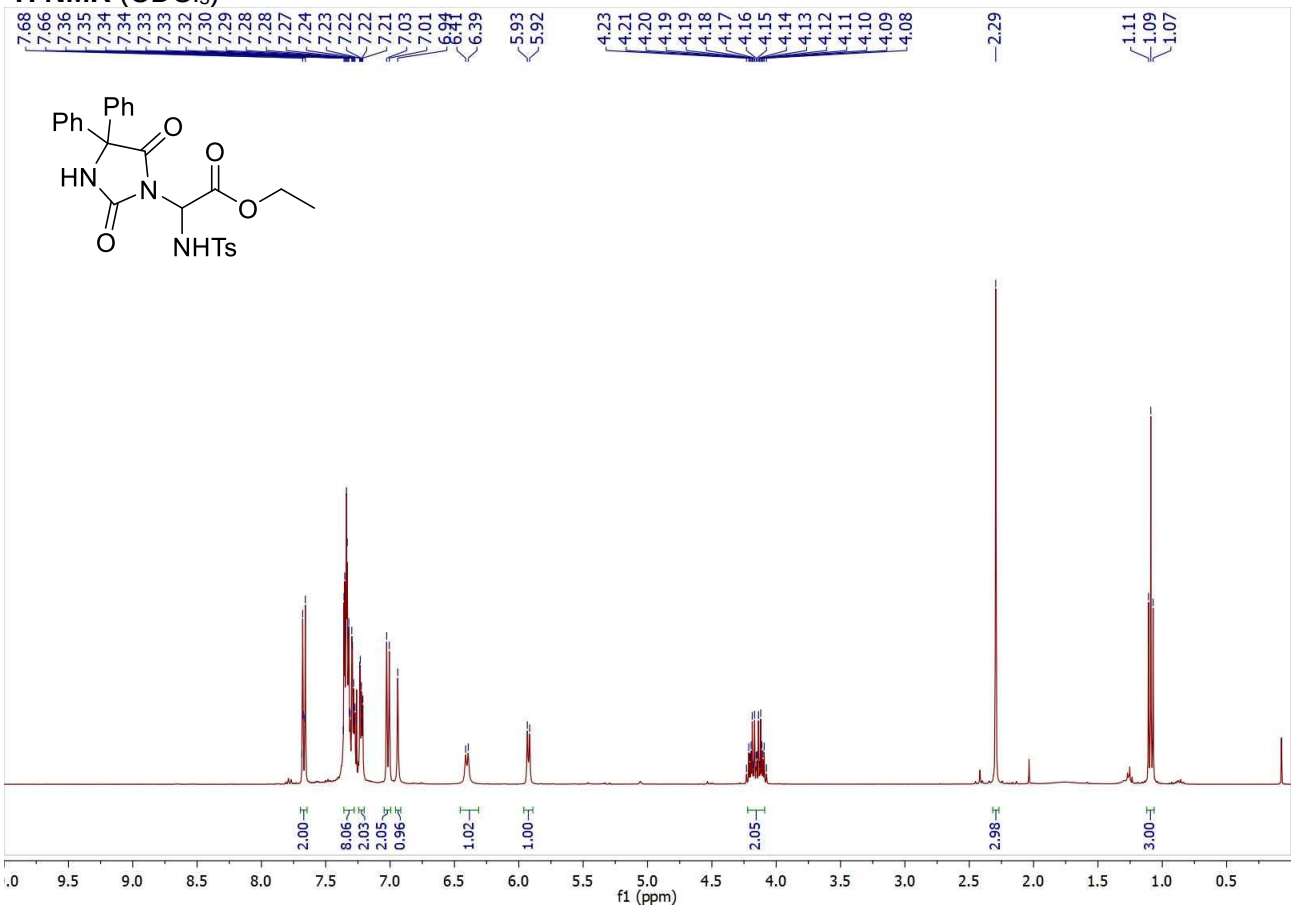


^{13}C{^{1}H} NMR (CD_3COCD_3)

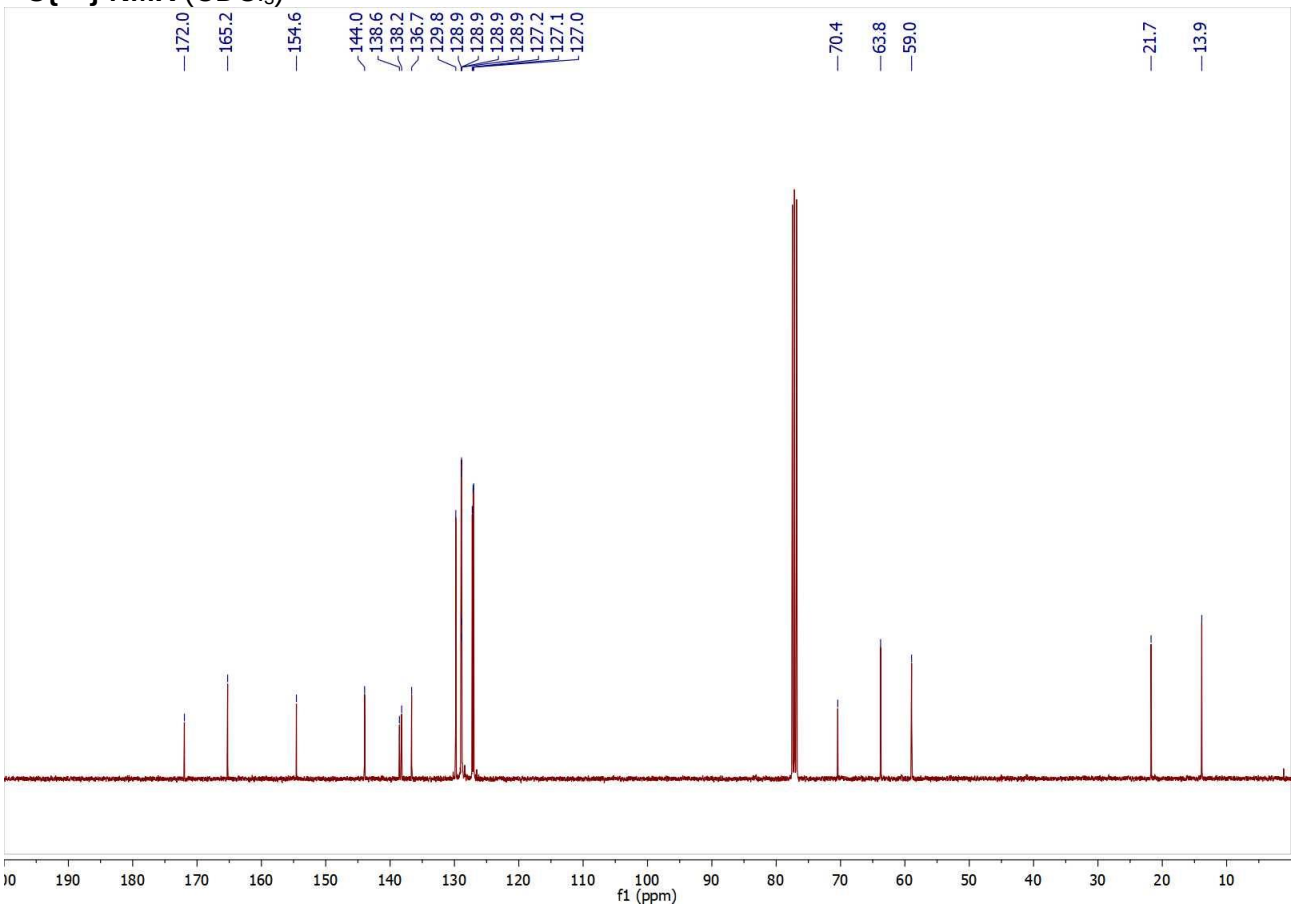


Ethyl 2-(2,5-dioxo-4,4-diphenylimidazolidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2af)

^{1}H NMR ($CDCl_3$)

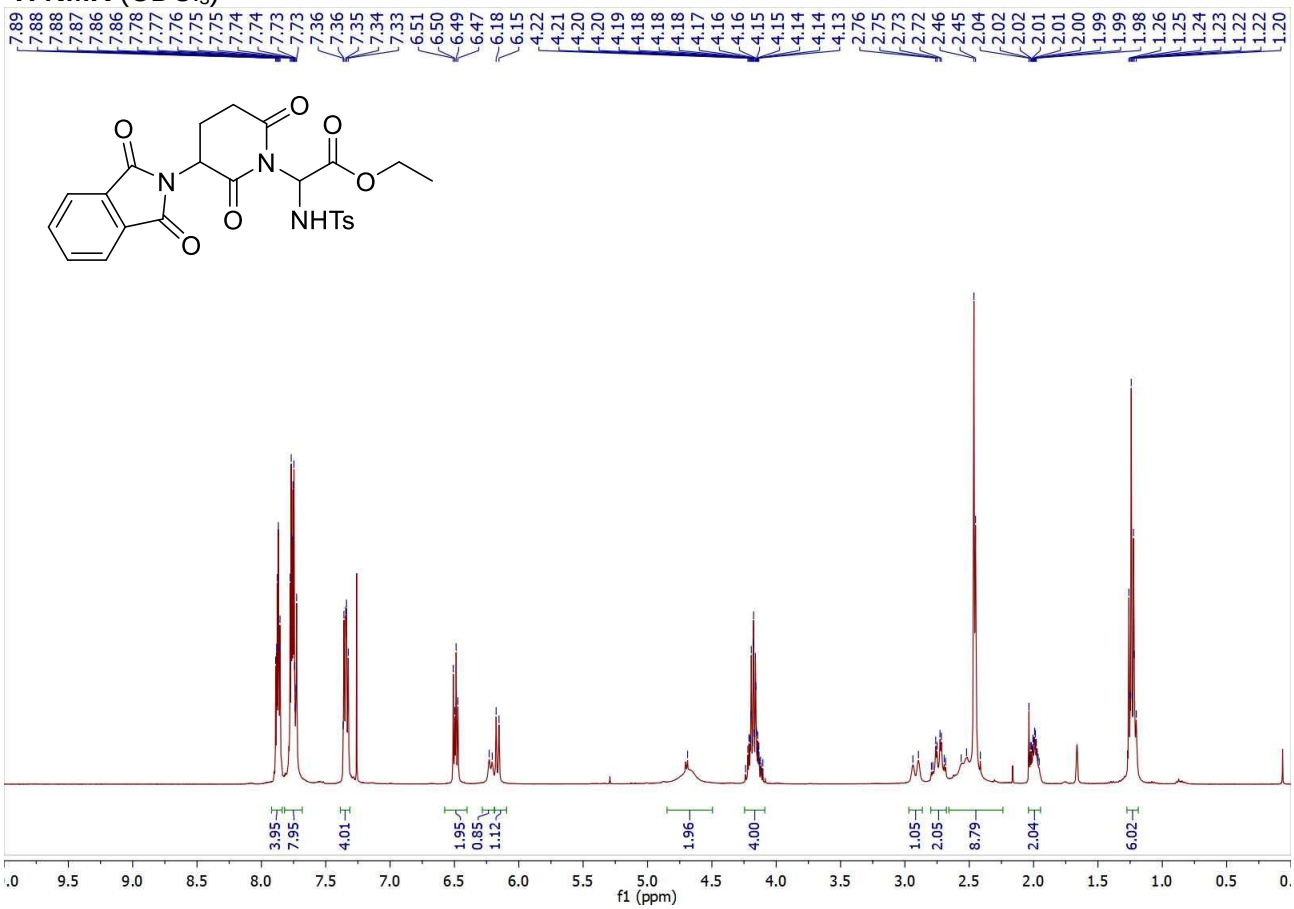


^{13}C{^{1}H} NMR ($CDCl_3$)

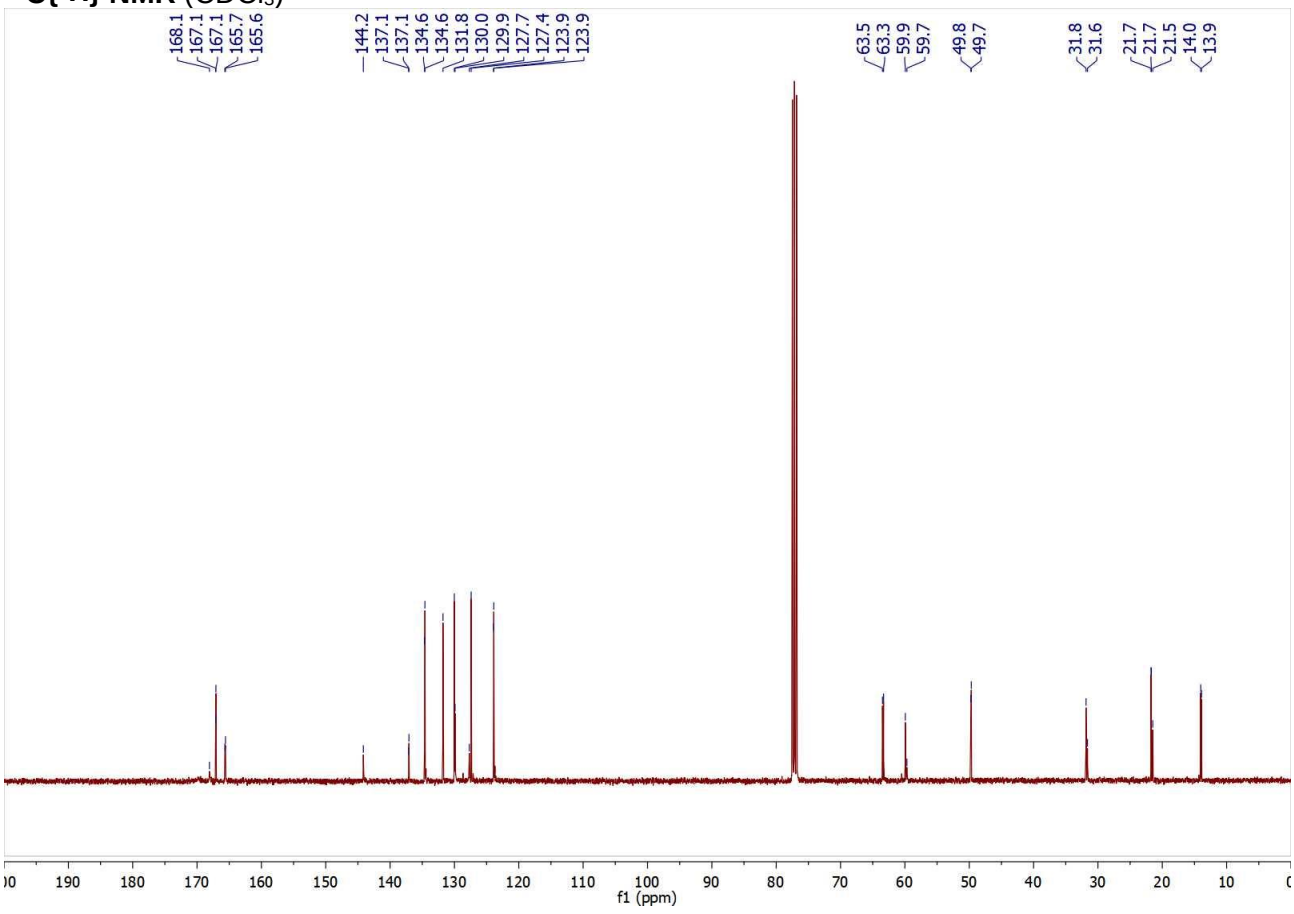


Ethyl 2-(3-(1,3-dioxoisoindolin-2-yl)-2,6-dioxopiperidin-1-yl)-2-((4-methylphenyl)sulfonamido)acetate (2ag)

^{1}H NMR ($CDCl_3$)

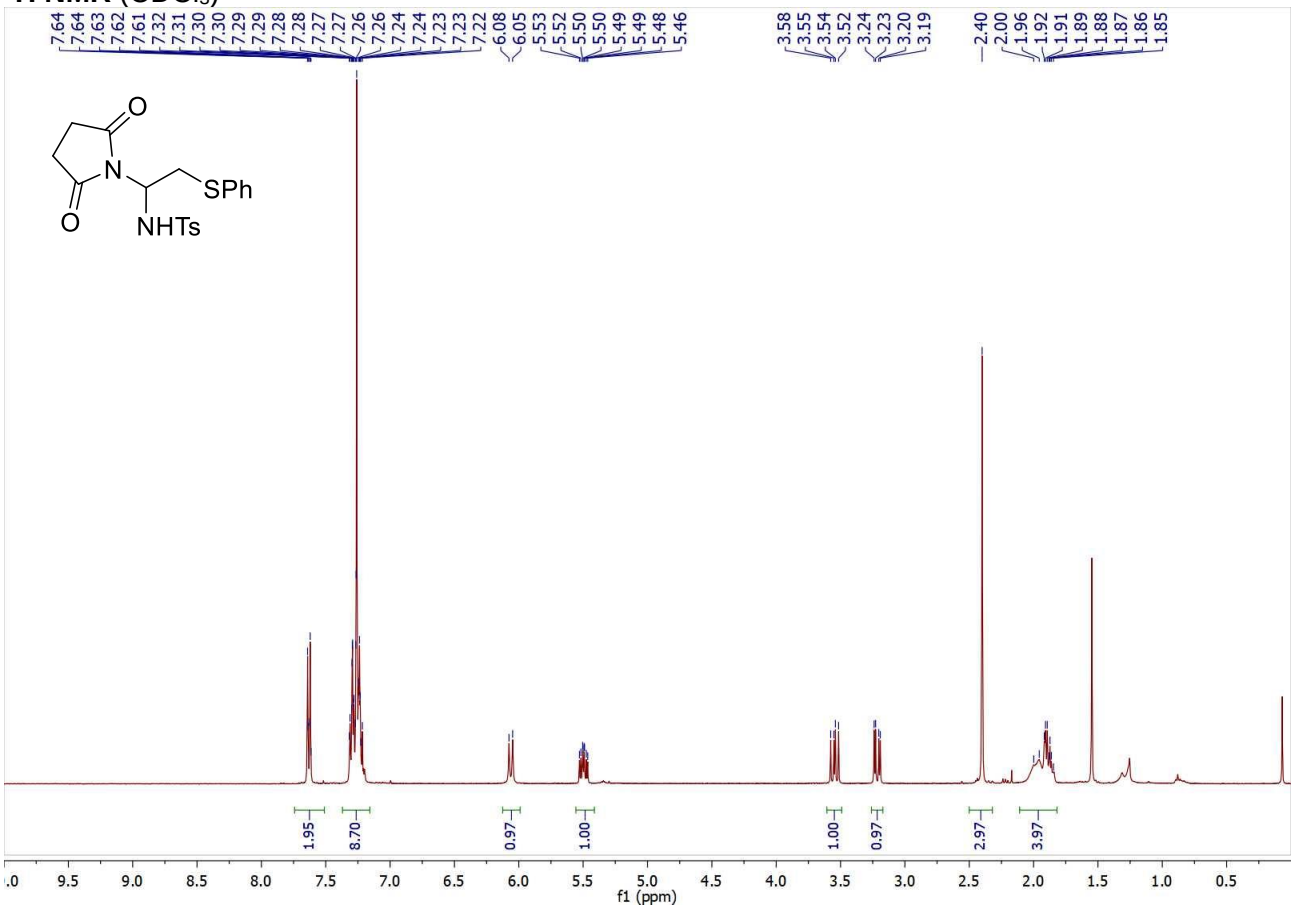


^{13}C{^{1}H} NMR ($CDCl_3$)

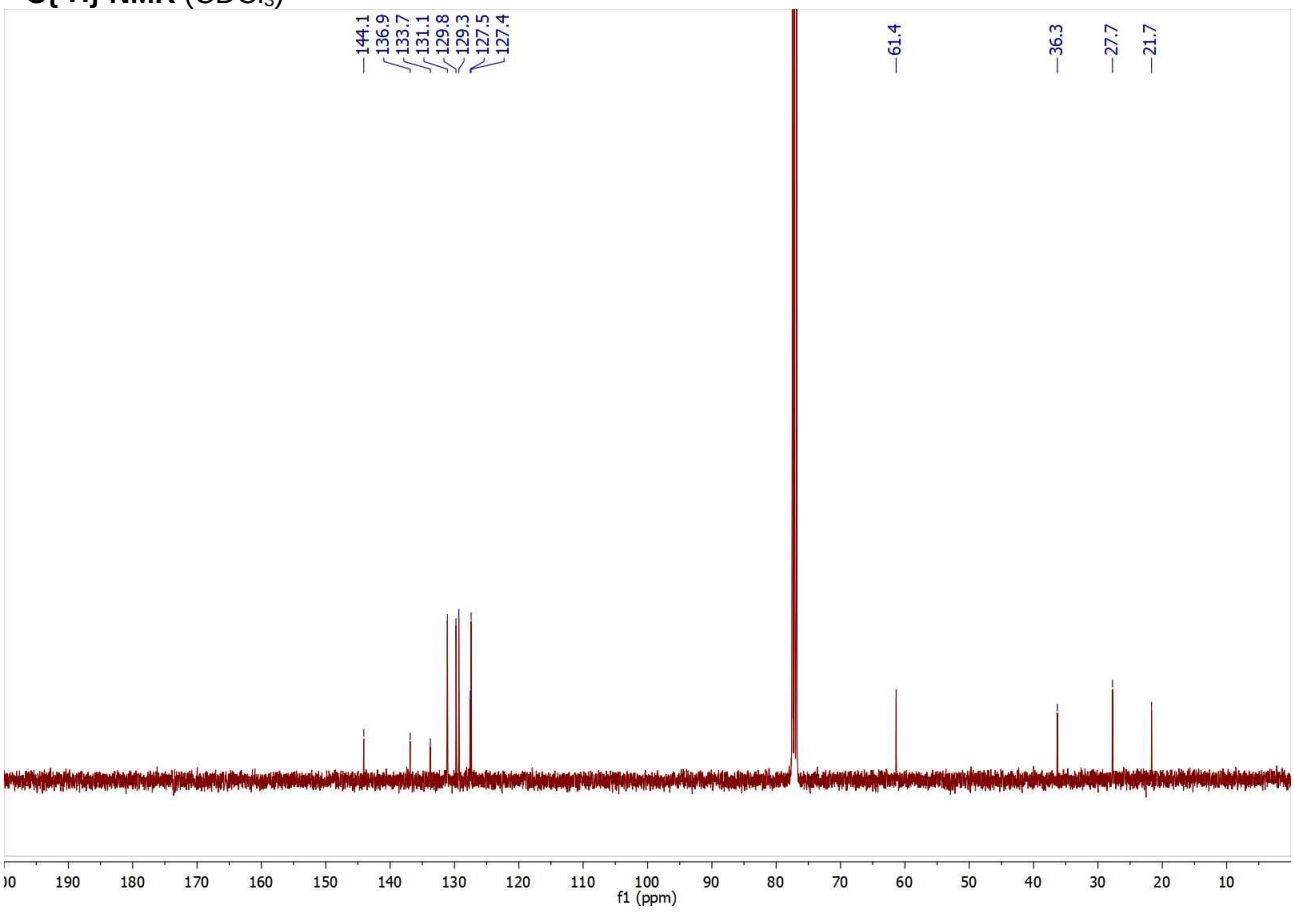


***N*-(1-(2,5-Dioxopyrrolidin-1-yl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (2ba)**

^{1}H NMR ($CDCl_3$)

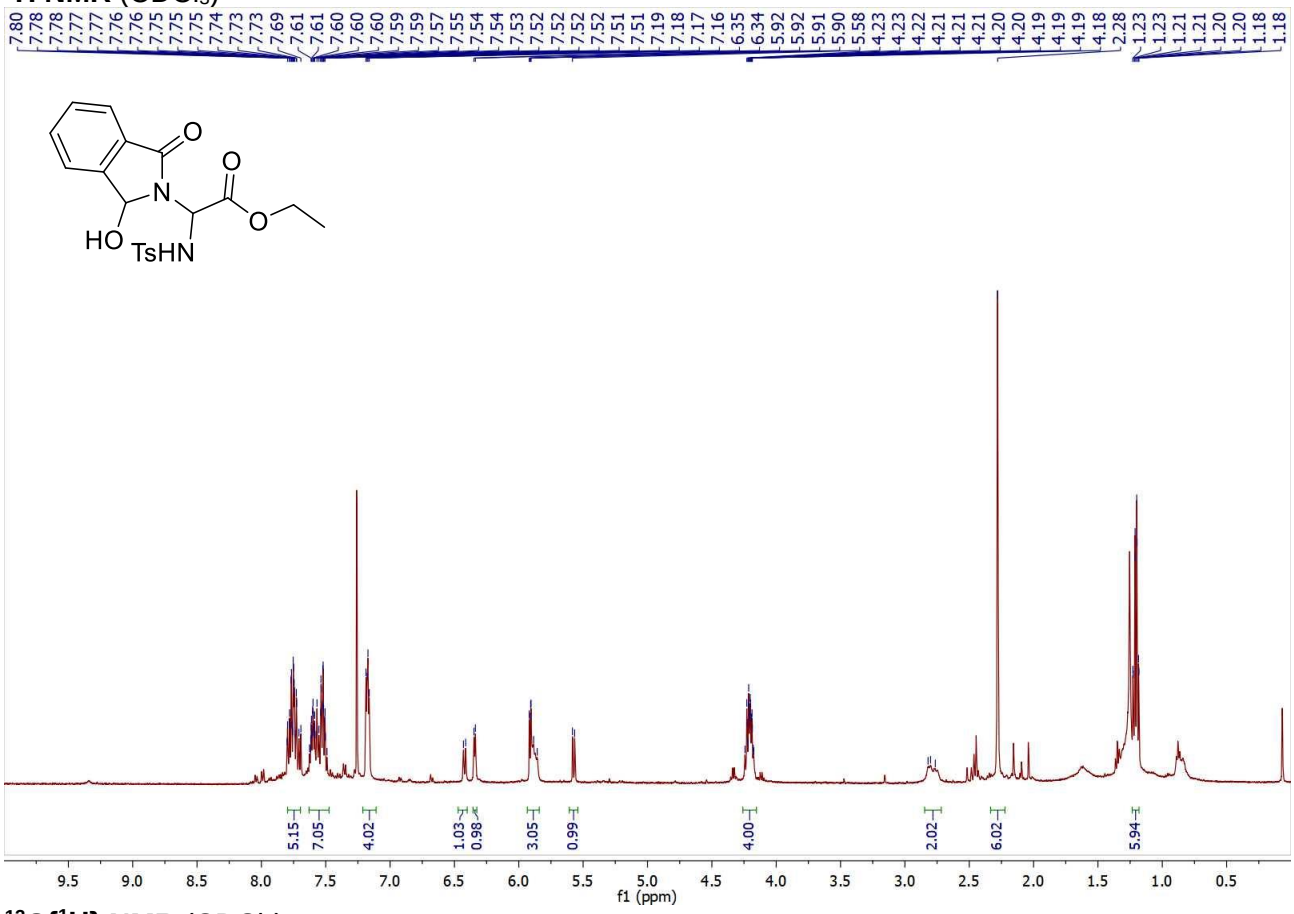


^{13}C{^{1}H} NMR ($CDCl_3$)

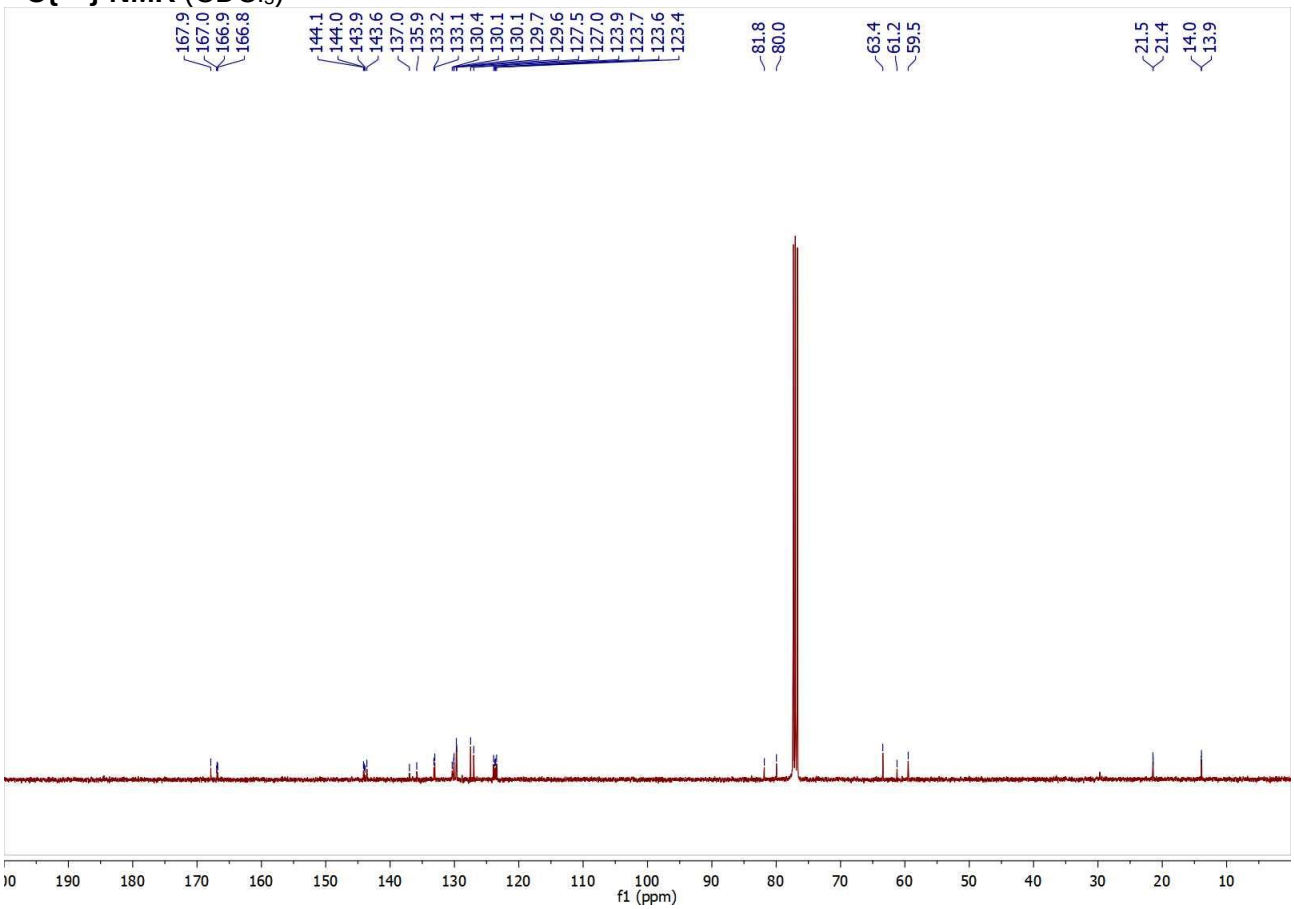


Ethyl 2-(1-hydroxy-3-oxoisoindolin-2-yl)-2-((4-methylphenyl)sulfonamido)acetate (2bb)

^{1}H NMR ($CDCl_3$)

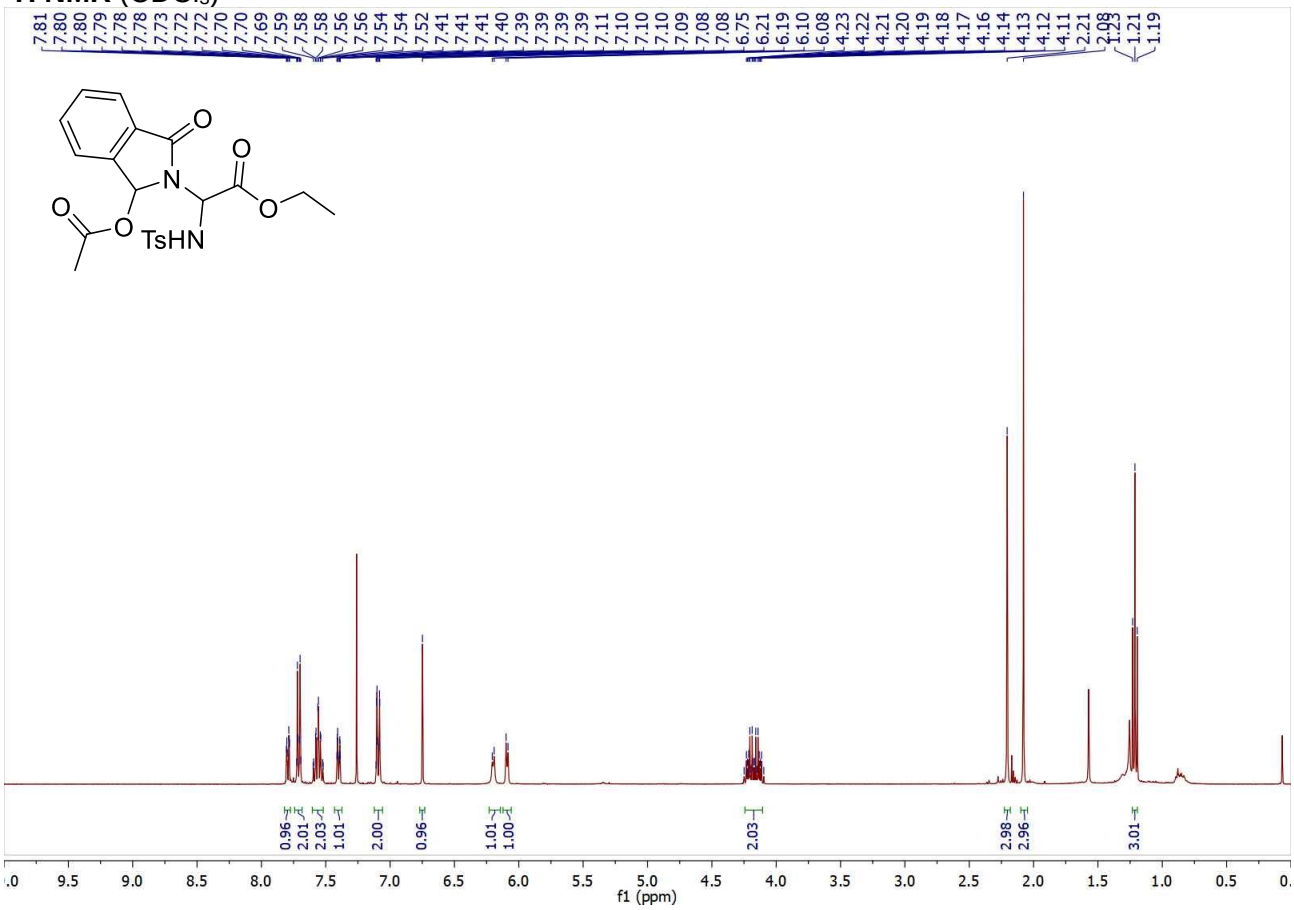


^{13}C{^{1}H} NMR ($CDCl_3$)

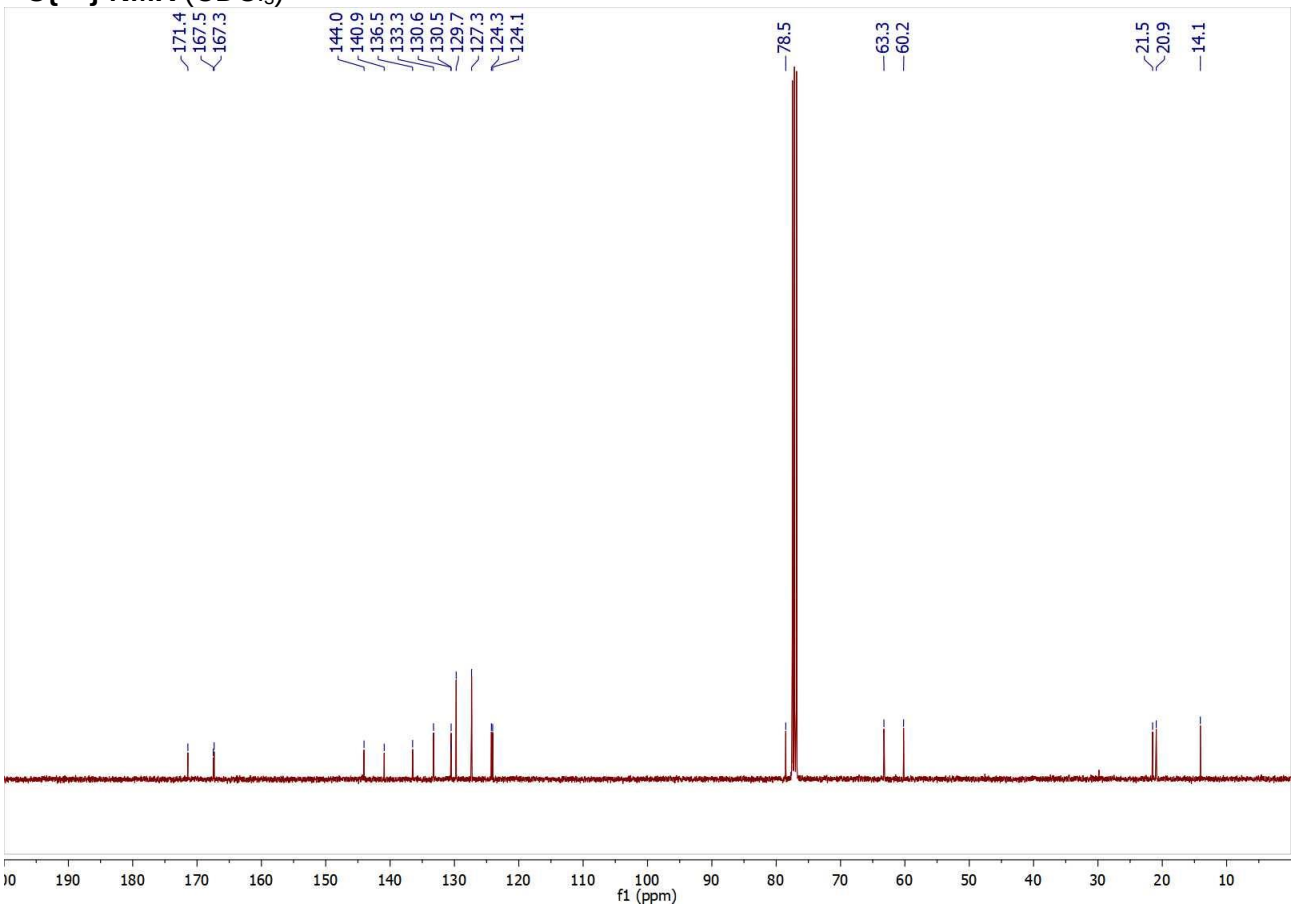


Ethyl 2-(1-acetoxy-3-oxoisoindolin-2-yl)-2-((4-methylphenyl)sulfonamido)acetate (2bc)

^{1}H NMR ($CDCl_3$)

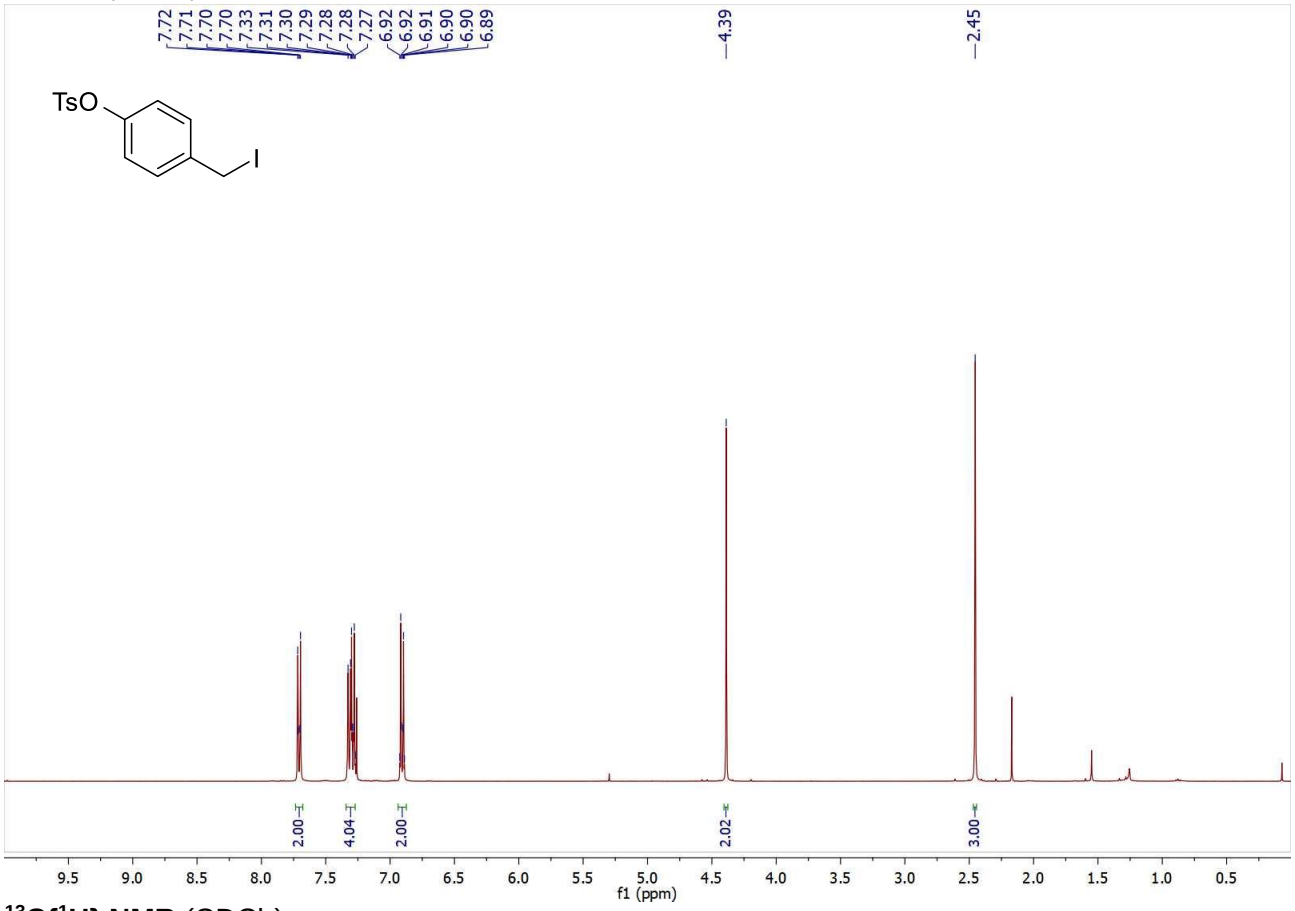


^{13}C{^{1}H} NMR ($CDCl_3$)

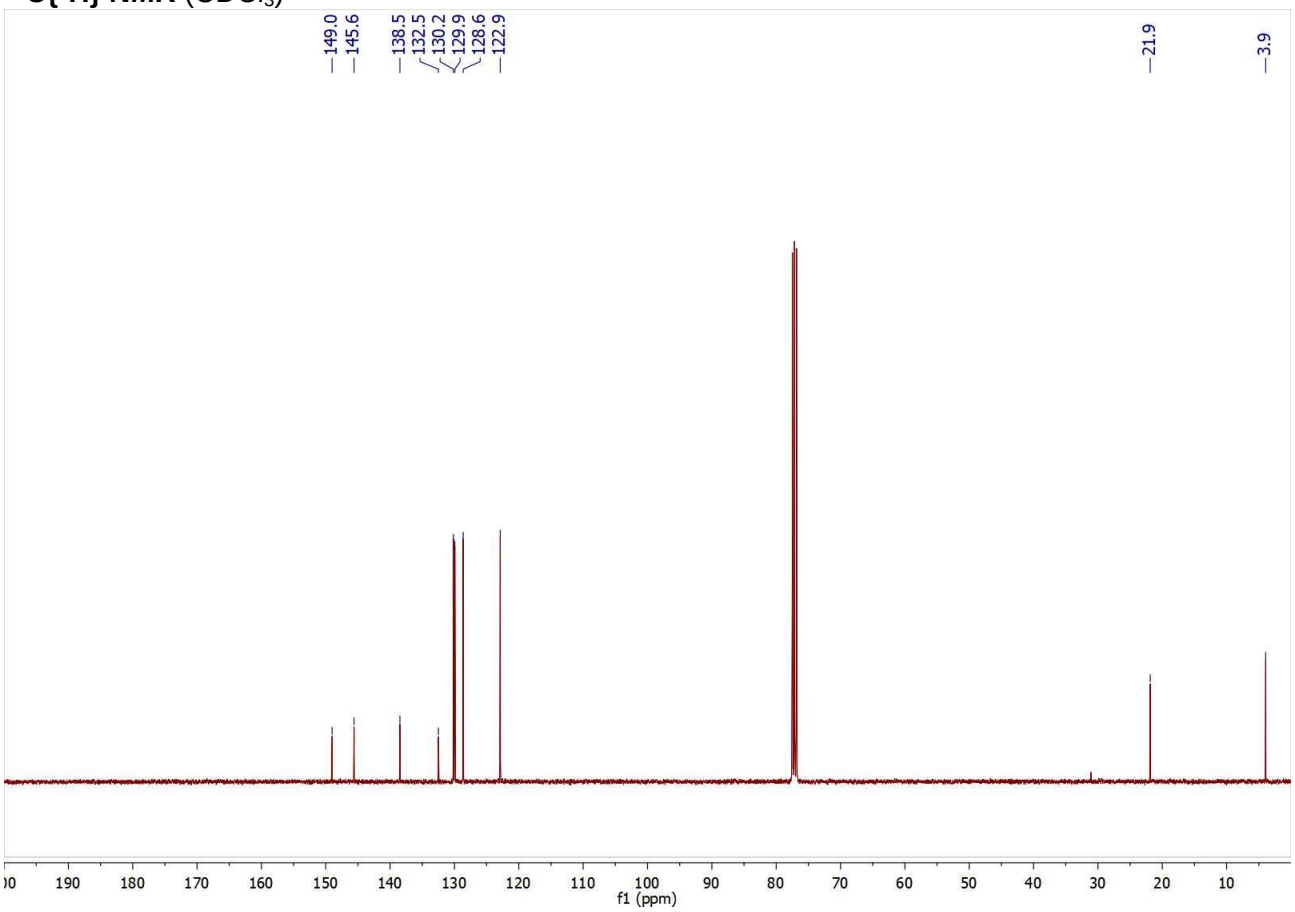


4-(Iodomethyl)phenyl-4-methylbenzensulfonate (3)

^{1}H NMR ($CDCl_3$)

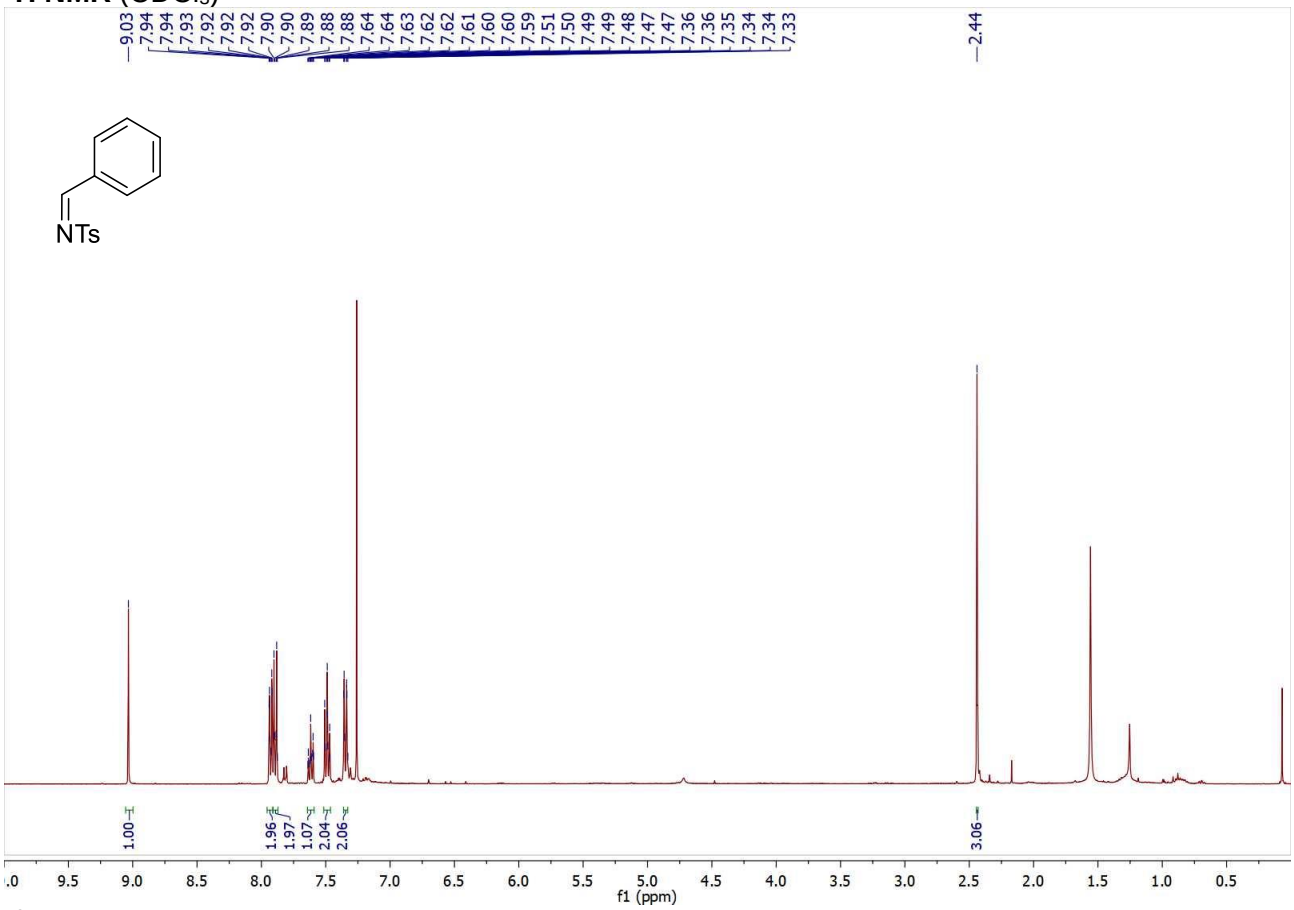


^{13}C{^{1}H} NMR ($CDCl_3$)

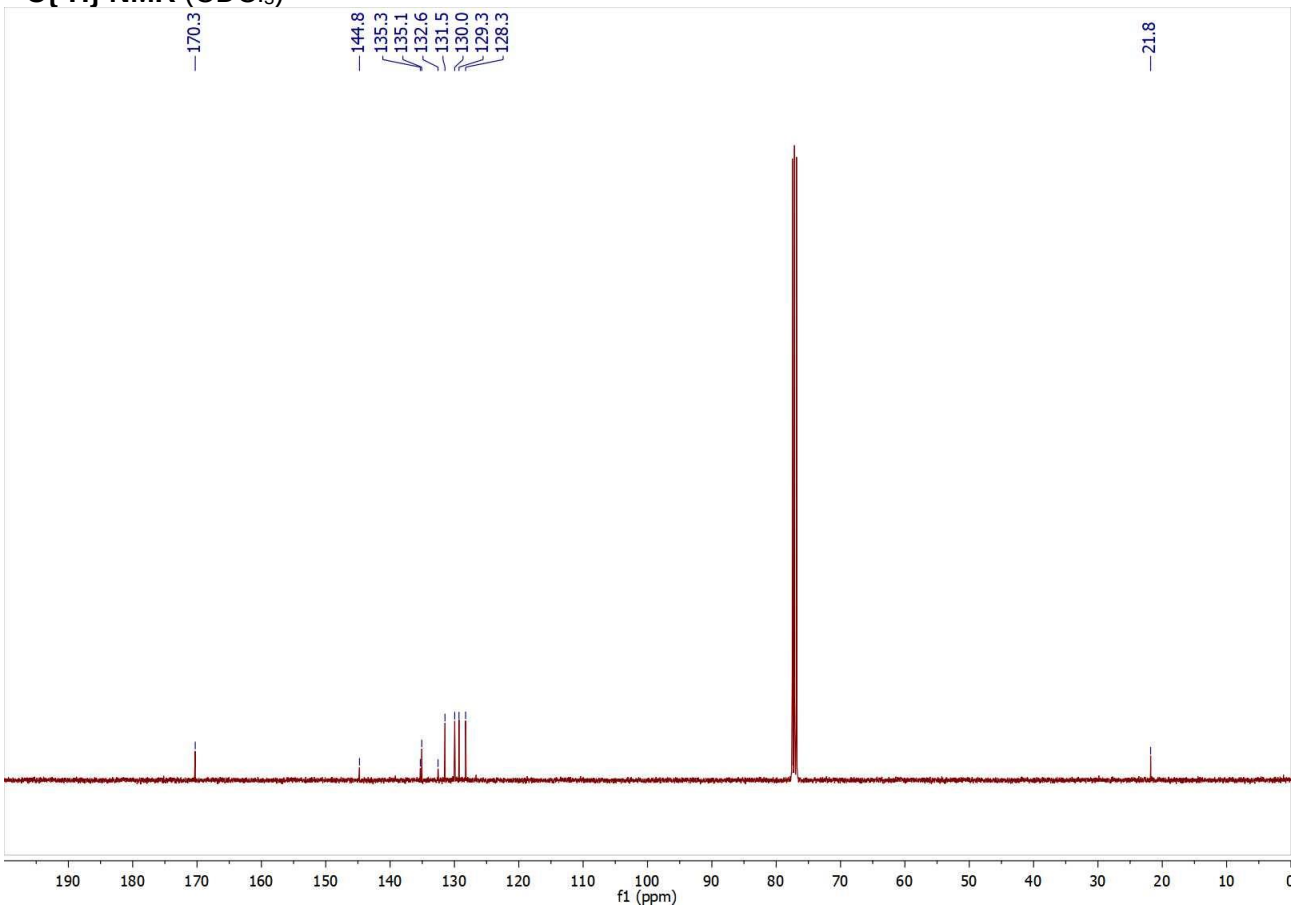


N-Benzylidene-4-methylphenylsulfonamide (4)

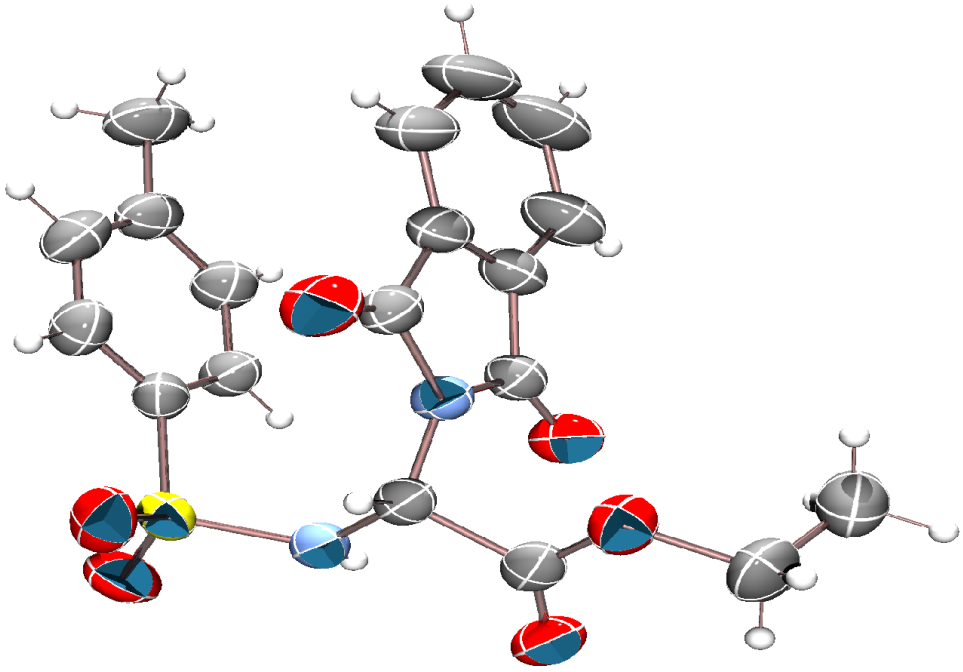
^{1}H NMR ($CDCl_3$)



^{13}C{^{1}H} NMR ($CDCl_3$)



8. X-ray diffraction data of 2aa



Thermal ellipsoids are drawn at the 50% probability level.

Table S4. Crystal data and structure refinement for **2aa**.

CCDC number	2431275	Crystal colour	colourless
Empirical formula	$C_{19}H_{18}N_2O_6S$	Crystal shape	prism
Formula weight	402.41	Radiation	CuKα (λ = 1.54178)
Temperature [K]	300.0	2Θ range [°]	12.824 to 144.858
Crystal system	triclinic	Index ranges	-10 ≤ h ≤ 9 -13 ≤ k ≤ 13 -15 ≤ l ≤ 15
Space group (number)	P-1		
a [Å]	8.2636(3)	Reflections collected	25306
b [Å]	10.5834(4)	Independent reflections	3656 R_{int} = 0.0549 R_{sigma} = 0.0322
c [Å]	12.5316(4)		
α [°]	72.0730(10)	Data / Restraints / Parameters	3656/0/259
β [°]	74.0080(10)		
γ [°]	67.2850(10)	Goodness-of-fit on F^2	1.061
Volume [Å^3]	946.44(6)	Final *R* indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0458 wR_2 = 0.1184
Z	2		
ρ_{calc} [gcm^{-3}]	1.412	Final *R* indexes [all data]	R_1 = 0.0533 wR_2 = 0.1286
μ [mm^{-1}]	1.872		
F(000)	420.0	Largest peak/hole [eÅ^{-3}]	0.36/-0.37
Crystal size [mm^3]	0.15 × 0.1 × 0.04		

Single crystals of **2aa** were obtained from CH_2Cl_2/hexane mixture by slow evaporation. A colorless prism-like specimen, approximate dimensions 0.040 mm x 0.100 mm x 0.150 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54184 Å). A total of 1908 frames were collected. The total exposure time was 5.30 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm.[44] The integration of the data using a triclinic unit cell yielded a total of 26325 reflections to a maximum θ angle of 72.38° (0.81 Å resolution). The final cell constants of a = 8.2636(3) Å, b = 10.5834(4) Å, c = 12.5316(4) Å, α = 72.0734(12)°, β = 74.0080(11)°, γ = 67.2846(11)°, volume = 946.44(6) Å3, are based upon the refinement of the XYZ-centroids of 9917 reflections above 20 σ(I) with 12.82° < 2θ < 144.3°. Data were corrected for absorption effects using the Multi-Scan method (SADABS).[45] The ratio of minimum to maximum apparent transmission was 0.699. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements. The structure was solved by ShelXT structure solution program using Intrinsic Phasing and refined with the XL refinement package using Least Squares minimisation.[46] All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints and all other hydrogen atoms were constrained to ideal geometries and refined with fixed isotropic displacement parameters. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre.[47] CCDC 2431275 contain the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

[44] a) SAINT integration software, SAINT V8.38A (Bruker AXS Inc., 2017); b) G.M. Sheldrick, *Acta Cryst.* 2015, **A71**, 3; APEX3 Version 2016.7 (Bruker AXS Inc.) Bruker Instrument Service vV6.2.10.

[45] SADABS-2016/2 - Bruker AXS area detector scaling and absorption correction (Sheldrick, Bruker AXS Inc.).

[46] *SHELXTL program system version 6.1;* XPREP Version 2013/3 (Sheldrick, Bruker AXS Inc.) XS Version 2013/1 (G. M. Sheldrick, *Acta Cryst.* 2008, **A64**, 112).

[47] C. R. Groom, I. J. Bruno, M. P. Lightfoot, S. C. Ward, *Acta Cryst.* 2016, **B72**, 171.