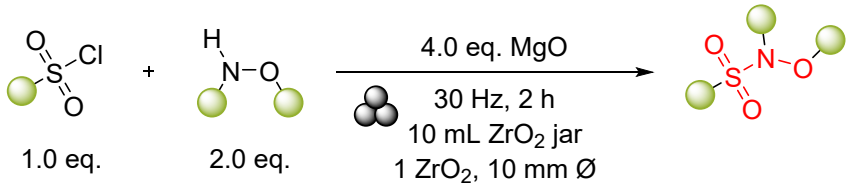
SUPPORTING INFORMATION

General Information

Commercially available reagents were purchased from Acros, Aldrich, Strem Chemicals, Alfa-Aesar, TCI Europe and used as received. All reactions were monitored by thin-layer chromatography (TLC) performed on glass-backed silica gel 60 F254, 0.2 mm plates (Merck), and compounds were visualized under UV light (254 nm). Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referred to the residual hydrogen in the solvent ($CDCl_3$, 7.260 ppm or DMSO-d_6 2.50 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, bs = broad singlet, and combination of thereof), coupling constant (*J*) in Hertz (Hz) and integration. Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$, δ 77.16 ppm or δ DMSO-d_6 δ 39.52 ppm). Deuterated NMR solvents were obtained from Aldrich. Chemical reactions were carried out using a Retsch MM500 Vario ball-milling instrument. The reagents were milled using a Zirconia grinding jar (10 mL) equipped with a Zirconia ball (10 mm Ø, weight of a single ball= 2.67 g).

Procedure A: Synthesis of *N*-Hydroxyarylsulfonamide derivatives



A 10 mL zirconia jar equipped with zirconia milling ball (10 mm diameter, 2.67 g) was filled with hydroxylamine hydrochloride derivates (2.00 mmol), Sulfonyl chloride (1.00 mmol), and MgO (4.00 mmol). The vessel was closed, and the mechanochemical reaction was conducted for 2 hours at 30 Hz. The reaction mixture was extracted with methanol at the end of the reaction. Then, the products were isolated by column chromatography.

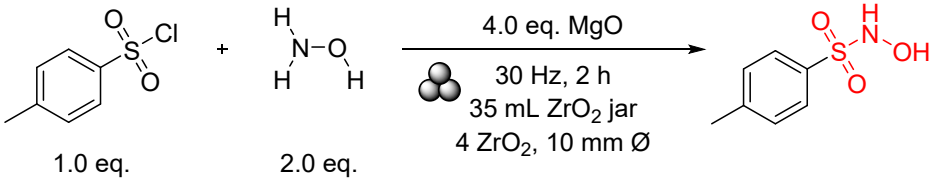
Gradient elution conditions

condition A: started with *n*-hexane and gradually changed to *n*-hexane/AcOEt = 7/3

condition B: started with *n*-hexane and gradually changed to *n*-hexane/AcOEt = 1/1

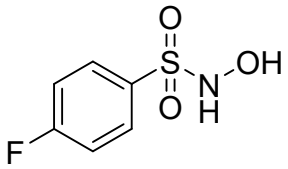
condition C: started with *n*-hexane and gradually changed to *n*-hexane/AcOEt /MeOH = 6/2/2

Procedure B: Gram scale of *N*-Hydroxy-4-Methylbenzenesulfonamide (2j)



A 35 mL zirconia jar equipped with 4 zirconia milling ball (10 mm diameter, 2.67 g) was filled with hydroxylamine hydrochloride (10.0 mmol), *p*-tosylchloride (5.0 mmol), and MgO (20.0 mmol). The vessel was closed, and the mechanochemical reaction was conducted for 2 hours at 30 Hz. The reaction mixture was extracted with methanol at the end of the reaction. Then, the conversion of the starting material was analysed through ^{1}H-NMR (60%).

4-Fluoro-N-Hydroxybenzenesulfonamide (2a)



The title compound was synthesized according to the general procedure **A**. Yield: 44% (83 mg).

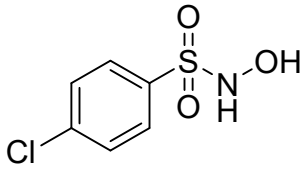
^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.62 (d, J = 8.9 Hz, 2H), 7.12 (t, J = 8.9 Hz, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 162.0 (d, *J* = 244.3 Hz), 144.78 (d), 127.88 (d, *J* = 8.4 Hz), 114.41 (d, *J* = 21.6 Hz).

^{19}F NMR (565 MHz, DMSO-*d*$_6$) δ -103.60.

The spectroscopic data closely match the ones previously reported in the literature.[1]

4-Chloro-N-Hydroxybenzenesulfonamide (2b)



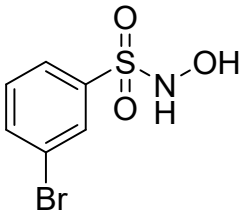
The title compound was synthesized according to the general procedure **A.** Yield: 75% (157 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 147.1, 133.9, 128.4, 128.1.

The spectroscopic data closely match the ones previously reported in the literature.[1]

3-Bromo-N-Hydroxybenzenesulfonamide (2c)



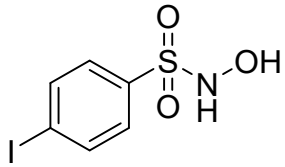
The title compound was synthesized according to the general procedure **A.** Yield: 43% (108 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.76 (d, J = 3.2 Hz, 1H), 9.74 (d, J = 3.2 Hz, 1H), 7.96 (d, J = 2.0 Hz, 1H), 7.92-7.90 (m, J = 8.0, 2.0 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.60 (t, J = 8.0 Hz, 1H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 139.5, 136.2, 131.4, 130.4, 127.4, 121.9.

The spectroscopic data closely match the ones previously reported in the literature.[2]

_N_-Hydroxy-4-Iodobenzenesulfonamide (2d)



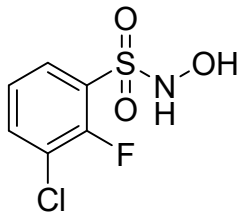
The title compound was synthesized according to the general procedure **A.** Yield: 18% (53 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.70 – 7.67 (m, 2H), 7.40 – 7.36 (m, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 147.4, 136.8, 127.9, 95.7.

The spectroscopic data closely match the ones previously reported in the literature.[3]

3-Chloro-2-Fluoro-*N*-Hydroxybenzenesulfonamide (2e)



The title compound was synthesized according to the general procedure **A.** Yield: 49% (103 mg).

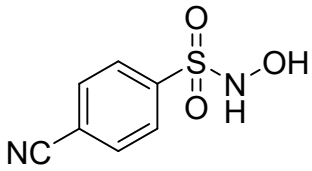
^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.61- 7.59 (m, 1H), 7.53-7.52 (m, 1H), 7.16-7.14 (m, 1H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 153.9 (d, *J* = 251.8 Hz), 136.8 (d, *J* = 16.8 Hz), 131.4 (d, *J* = 3.6 Hz), 127.8 (d, *J* = 2.4 Hz), 124.7, 120.4 (d, *J* = 18.6 Hz).

^{19}F NMR (565 MHz, DMSO-*d*$_6$) δ -114.37.

HRMS: calculated for $C_6H_6ClFNO_3S$: 225.9741 $[M+H]^+$; found: 225.9729.

4-Cyano-*N*-Hydroxybenzenesulfonamide (2f)



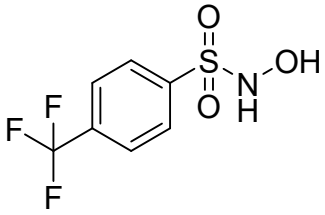
The title compound was synthesized according to the general procedure **A**. Yield: 18% (53 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.86 – 7.77 (m, 2H), 7.76 – 7.70 (m, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 152.3, 132.4, 126.6, 118.9, 111.5.

HRMS: calculated for $C_7H_7N_2O_3S$: 199.0177 $[M+H]^+$; found: 199.0165.

***N*-Hydroxy-4-(trifluoromethyl)benzenesulfonamide (2g)**



The title compound was synthesized according to the general procedure **A.** Yield: 48% (25 mg).

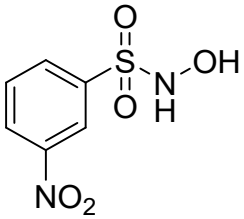
^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 8.06 – 8.00 (m, 2H), 7.97 (m, 2H), 7.61 (s, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 147.9, 131.7 (q, J = 32.1 Hz),

^{19}F NMR (565 MHz, DMSO-*d*$_6$) δ -61.51.

The spectroscopic data closely match the ones previously reported in the literature.[2]

***N*-Hydroxy-3-Nitrobenzenesulfonamide (2h)**



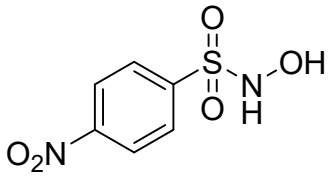
The title compound was synthesized according to the general procedure **A.** Yield: 44% (70 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.93 (s, *J* = 2.0 Hz, 1H), 9.89 (m, 1H), 8.57 (t, *J* = 2.0 Hz, 1H), 8.55 – 8.53 (m, 1H), 8.26 – 8.24 (m, 1H), 7.95 (m, 1H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 148.2, 139.3, 134.7, 131.6, 128.4, 123.2.

The spectroscopic data closely match the ones previously reported in the literature.[2]

***N*-Hydroxy-4-Nitrobenzenesulfonamide (2i)**



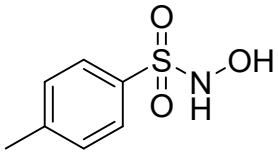
The title compound was synthesized according to the general procedure **A.** Yield: 20% (44 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.94 (d, J = 3.2 Hz, 1H), 9.86 (d, J = 3.2 Hz, 1H), 8.49 – 8.39 (m, 2H), 8.12 – 7.95 (m, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 150.4, 143.1, 129.9, 124.5.

The spectroscopic data closely match the ones previously reported in the literature.[2]

***N*-Hydroxy-4-Methylbenzenesulfonamide (2j)**



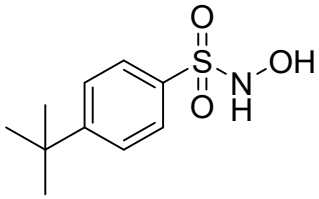
The title compound was synthesized according to the general procedure **A.** Yield: 48% (90 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.52 (S, 1H), 9.49 (s, 1H), 7.80 – 7.66 (m, 2H), 7.44 – 7.31 (m, 2H), 2.39 (s, 3H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 143.5, 134.4, 129.3, 128.0, 20.9.

The spectroscopic data closely match the ones previously reported in the literature.[4]

4-(tert-Butyl)-*N*-Hydroxybenzenesulfonamide (2k)

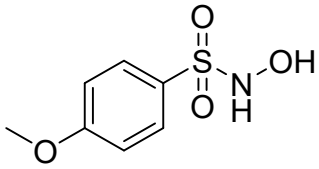


The title compound was synthesized according to the general procedure **A.** Yield: 38% (86 mg).

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 1.24 (s, 9H).**^{13}C NMR (151 MHz, DMSO-d_6)** δ 151.6, 145.6, 125.8, 124.8, 34.8, 31.6.

The spectroscopic data closely match the ones previously reported in the literature.[4]

***N*-Hydroxy-4-Methoxybenzenesulfonamide (2m)**



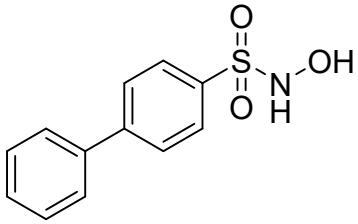
The title compound was synthesized according to the general procedure **A**. Yield: 40% (80 mg).

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.52 (d, J = 3.4 Hz, 1H), 9.41 (d, J = 3.4 Hz, 1H), 7.87 – 7.70 (m, 2H), 7.19 – 7.00 (m, 2H), 3.84 (s, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 162.8, 130.3, 128.8, 114.1, 55.6.

The spectroscopic data closely match the ones previously reported in the literature.[5]

***N*-Hydroxy-[1,1'-biphenyl]-4-sulfonamide (2n)**



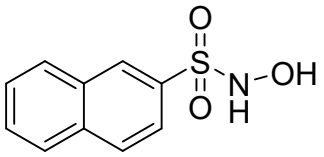
The title compound was synthesized according to the general procedure **A.** Yield: 63% (141 mg).

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.66 (m, 2H), 7.63 – 7.52 (m, 4H), 7.42 (, 2H), 7.31 (s, 1H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 146.9, 141.2, 140.0, 129.7, 128.4, 127.3, 126.8, 126.8.

HRMS: calculated for $C_{12}H_{10}NO_3S$: 248.0381[*M*-H]$^-$; found: 248.0373.

***N*-Hydroxynaphthalene-2-sulfonamide (2o)**



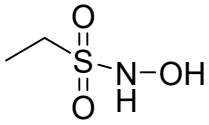
The title compound was synthesized according to the general procedure **A.** Yield: 63% (141 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 8.09 (d, *J* = 1.7 Hz, 1H), 7.90 (dd, *J* = 6.2, 3.4 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.66 (d, *J* = 1.7 Hz, 1H), 7.48 (d, 3.4 Hz, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 135.0, 134.9, 132.1, 130.0, 129.7, 129.5, 129.4, 128.3, 128.1, 123.8

The spectroscopic data closely match the ones previously reported in the literature.[3]

***N*-Hydroxyethanesulfonamide (2p)**



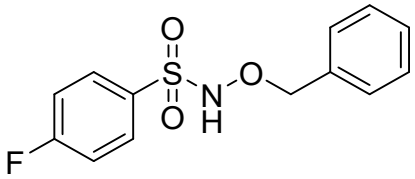
The title compound was synthesized according to the general procedure **A.** Yield: 58% (72 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.47 (s, 2H), 2.42 (q, J = 7.4 Hz, 2H), 1.06 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 45.6, 10.2.

HRMS: calculated for CH_6NO_4S: 146.9756 [(*M*-OH)+K]$^+$; found: 146.9735.

***N*-(Benzyloxy)-4-Fluorobenzenesulfonamide (2a')**



The title compound was synthesized according to the general procedure **A.** Yield: 68% (95 mg).

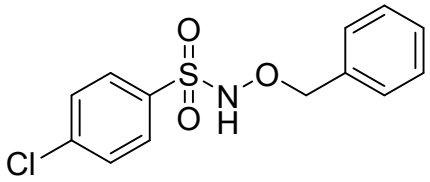
^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 10.52 (s, 1H), 7.96 – 7.90 (m, 2H), 7.51 – 7.44 (m, 2H), 7.39 – 7.30 (m, 5H), 4.90 (s, 2H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 164.9 (d, *J* = 252.5 Hz), 135.8, 133.6 (d, *J* = 3.1 Hz), 131.2 (d, *J* = 9.7 Hz), 128.9, 128.4, 128.3, 116.4 (d, *J* = 22.7 Hz), 78.2.

^{19}F NMR (565 MHz, DMSO-d_6) δ -105.09.

HRMS: calculated for $C_{13}H_{12}FNO_3SNa$: .304.0420 $[M+Na]^+$; found: 304.0402.

***N*-(Benzyloxy)-4-Chlorobenzenesulfonamide (2b')**



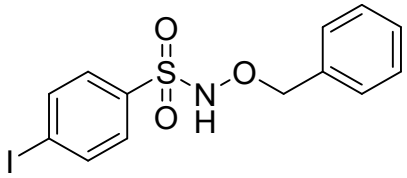
The title compound was synthesized according to the general procedure **A.** Yield: 73% (108 mg).

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.58 (s, 1H), 7.87 (d, J = 8.6 Hz, 2H), 7.73 (d, J = 8.6 Hz, 2H), 7.38 – 7.32 (m, 5H), 4.90 (s, 2H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 138.4, 135.9, 135.6, 129.8, 129.2, 128.7, 128.2, 128.2, 78.1.

HRMS: calculated for $C_{13}H_{13}ClNO_3S$: 298.0305 $[M+H]^+$; found: 298.0287.

***N*-(Benzyloxy)-4-Iodobenzenesulfonamide (2d')**



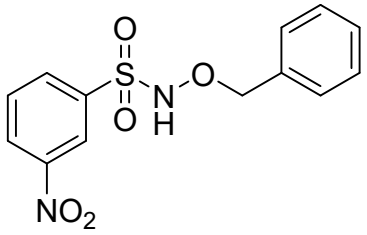
The title compound was synthesized according to the general procedure **A.** Yield: 76% (148 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.64 – 7.59 (m, 2H), 7.39 – 7.30 (m, 5H), 6.95 (s, 1H), 4.98 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.6, 136.4, 135.1, 129.9, 129.5, 128.9, 128.7, 101.9, 79.6.

HRMS: calculated for $C_{13}H_{13}INO_3S$: 389.9661 $[M+H]^+$; found: 389.9634.

***N*-(Benzyloxy)-3-Nitrobenzenesulfonamide (2h')**



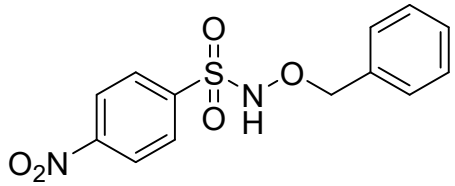
The title compound was synthesized according to the general procedure **A.** Yield: 55% (85 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 8.60 (m, 1H), 8.55-8.52 (m, 1H), 8.30-8.27 (m, 1H), 7.95 (m, 1H), 7.42 – 7.19 (m, 5H), 4.93 (s, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 147.4, 138.5, 135.1, 133.6, 130.8, 128.6, 128.0,127.9, 127.8, 122.3, 77.9.

HRMS: calculated for $C_{13}H_{13}N_2O_5S$: 309.0545 [*M*+H]$^+$; found: 309.0526.

***N*-(Benzyloxy)-4-Nitrobenzenesulfonamide (2i')**



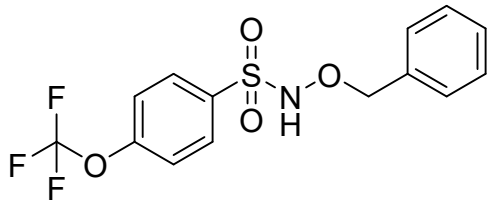
The title compound was synthesized according to the general procedure **A.** Yield: 81% (125 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 10.86 (s, 1H), 8.47 – 8.41 (m, 2H), 8.15 – 8.07 (m, 2H), 7.49 – 7.31 (m, 5H), 4.92 (s, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 150.1, 142.4, 135.3, 129.4, 128.7, 128.1, 128.1, 124.2, 78.2.

HRMS: calculated for $C_{13}H_{13}N_2O_5S$: 309.0545 [*M*+H]$^+$; found: 309.0541.

***N*-(Benzyloxy)-4-(trifluoromethoxy)benzenesulfonamide (2l')**



The title compound was synthesized according to the general procedure **A.** Yield: 65% (114 mg).

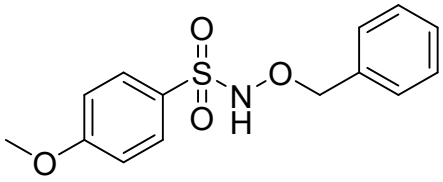
^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.99 (d, J = 8.9 Hz, 2H), 7.64 (d, J = 8.9 Hz, 2H), 7.40 – 7.30 (m, 5H), 4.90 (s, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 151.6 (q, *J* = 1.6 Hz), 136.2, 135.8, 130.7, 129.0, 128.4, 121.4, 119.8 (d, *J* = 258.2 Hz), 78.3.

^{19}F NMR (565 MHz, DMSO-*d*$_6$) δ -56.68.

HRMS: calculated for $C_{14}H_{13}F_3NO_4S$: 348.0517 [*M*+H]$^+$; found: 348.0485.

***N*-(Benzyloxy)-4-Methoxybenzenesulfonamide (2m')**



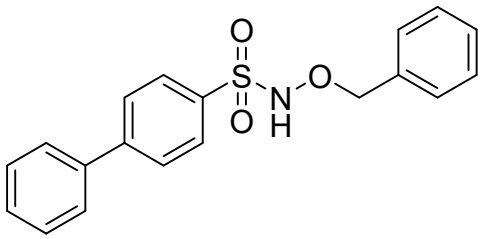
The title compound was synthesized according to the general procedure **A.** Yield: 57% (80 mg).

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 10.30 (s, 1H), 7.81 – 7.79 (m, 2H), 7.37 – 7.32 (m, 5H), 7.15 – 7.13 (m, 2H), 4.88 (s, 2H), 3.84 (s, 3H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 163.3, 136.2, 130.6, 129.1, 129.0, 128.6, 128.5, 114.6, 78.3, 56.0.

HRMS: calculated for $C_{14}H_{14}NO_4S$: 292.0644 [*M*-H]$^-$; found: 292.0637.

***N*-(Benzyloxy)-[1,1'-biphenyl]-4-sulfonamide (2n')**



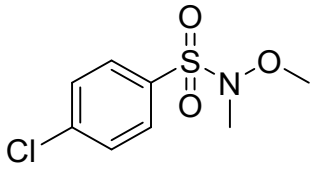
The title compound was synthesized according to the general procedure **A.** Yield: 54% (92 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (m, 2H), 7.75 – 7.72 (m, 2H), 7.61 – 7.58 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.38 – 7.34 (m, 5H), 6.96 (s, 1H), 5.02 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 146.8, 139.1, 135.1, 135.1, 129.3, 129.0, 128.7, 128.6, 128.5, 127.7, 127.3, 79.4.

HRMS: calculated for $C_{19}H_{16}NO_3S$: 338.0851 [*M*-H]$^-$; found: 338.0842.

4-Chloro-*N*-Methoxy-*N*-Methylbenzenesulfonamide (2b'')



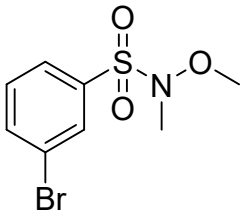
The title compound was synthesized according to the general procedure **A.** Yield: 64% (150 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, J = 8.6 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 3.81 (s, 3H), 2.78 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.8, 131.2, 130.9, 129.3, 63.9, 39.3.

HRMS: calculated for $C_8H_{11}ClNO_3S$: 236.0148 [*M*+H]$^+$; found: 236.0130.

3-Bromo-*N*-Methoxy-*N*-Methylbenzenesulfonamide (2c'')



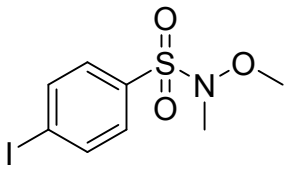
The title compound was synthesized according to the general procedure **A.** Yield: 71% (201 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01-7.90 (m, 1H), 7.86 – 7.69 (m, 2H), 7.50 – 7.33 (m, 1H), 3.88 – 3.75 (m, 3H), 2.80 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 136.8, 134.1, 132.3, 130.2, 128.1, 122.8, 63.8, 39.2.

HRMS: calculated for $C_8H_{11}BrNO_3S$: 279.9643, 281.9623 [*M*+H]$^+$; found: 279.9625, 281.9600.

4-Iodo-*N*-Methoxy-*N*-Methylbenzenesulfonamide (2d'')



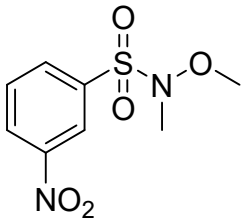
The title compound was synthesized according to the general procedure **A.** Yield: 68% (223 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 3.81 (s, 3H), 2.78 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.5, 132.3, 131.3, 102.2, 64.2, 39.6.

HRMS: calculated for $C_8H_{11}INO_3S$: 327.9504 $[M+H]^+$; found: 327.9481.

***N*-Methoxy-*N*-Methyl-3-Nitrobenzenesulfonamide (2h'')**



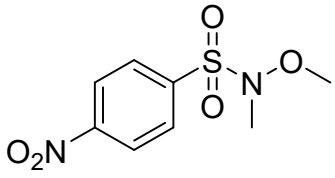
The title compound was synthesized according to the general procedure **A.** Yield: 65% (160 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (t, J = 2.0 Hz, 1H), 8.52-8.50 (m, 1H), 8.19-8.17 (m, J = 7.8, 1H), 7.80 (t, J = 7.8 Hz, 1H), 3.85 (s, 3H), 2.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 148.1, 135.0, 134.3, 130.1, 128.1, 124.7, 63.9, 39.2.

HRMS: calculated for $C_8H_{11}N_2O_5S$: 247.0389 $[M+H]^+$; found: 247.0373.

***N*-Methoxy-*N*-Methyl-4-Nitrobenzenesulfonamide (2i'')**



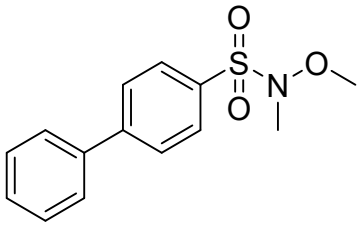
The title compound was synthesized according to the general procedure **A.** Yield: 69% (170 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 2.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 150.8, 138.0, 130.9, 123.9, 63.9, 39.2.

HRMS: calculated for $C_8H_{11}N_2O_5S$: 247.0389 $[M+H]^+$; found: 247.0377.

***N*-methoxy-*N*-methyl-[1,1'-biphenyl]-4-sulfonamide (2n'')**



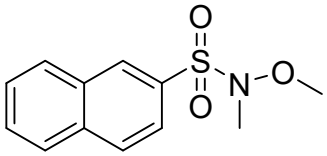
The title compound was synthesized according to the general procedure **A.** Yield: 56% (140 mg).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.78 – 7.75 (m, 2H), 7.64 – 7.61 (m, 2H), 7.57 – 7.48 (m, 2H), 7.46 – 7.40 (m, 1H), 3.85 (s, 3H), 2.84 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 146.7, 139.2, 130.8, 130.2, 129.1, 128.7, 127.4, 127.4, 63.8, 39.3.

HRMS: calculated for $C_{14}H_{16}NO_3S$: 278.0851 [*M*+H]$^+$; found: 278.0829.

***N*-Methoxy-*N*-Methylnaphthalene-2-sulfonamide (2o'')**



The title compound was synthesized according to the general procedure **A.** Yield: 63% (154 mg).

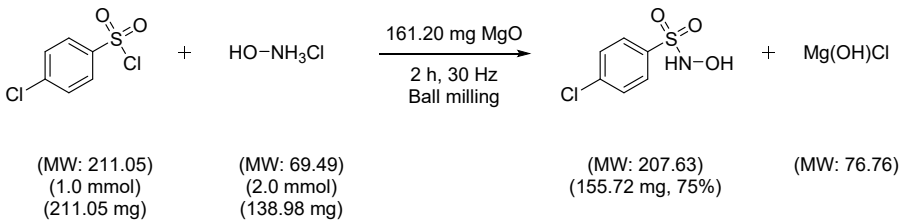
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 – 8.45 (m, 1H), 8.03 – 7.98 (m, 2H), 7.94 (dd, J = 8.6, 1.3 Hz, 1H), 7.88 (dd, J = 8.6, 1.3 Hz, 1H), 7.70 – 7.66 (m, 1H), 7.64 (dd, J = 8.6, 1.3 Hz, 1H), 3.85 (s, 3H), 2.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 135.6, 132.2, 131.6, 129.7, 129.6, 129.4, 128.9, 128.1, 127.7, 124.7, 63.9, 39.4.

HRMS: calculated for $C_{12}H_{14}NO_3S$: 252.0694 [*M*+H]$^+$; found: 252.0670.

Green Metrics

Calculation of the Green Chemistry Metrics for the Preparation of **2b**:



Excess Reagents Waste	$HO-NH_3Cl$	MgO	
	69.49 mg	80.60 mg	
Reaction Waste	Mg(OH)Cl		
	153.52 mg		
Purification Step Waste	MeOH for recovery	Hexane for Chromatography	EtOAc for Chromatography
	2370.00 mg	23121.00 mg	13509.00 mg

Scheme S1. Preparation of **2b**. For the purification step, the eluent volume (Hexane/Ethyl Acetate 7:3) is 50 mL.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Total molecular weight of desired product}}{\text{Total molecular weight of all reactants}} \times 100$$

$$= \frac{207.63}{211.05 + 69.49 + 80.60} \times 100 = 58\%$$

Process Mass Intensity (PMI)

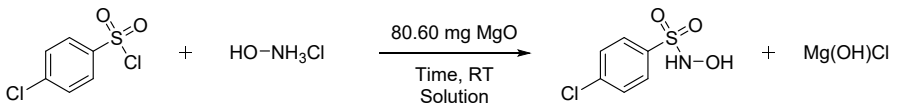
$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{69.49 + 80.60 + 153.52 + 2370.00 + 23121.00 + 13509.00}{155.72}$$

$$= 252.40$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{155.72}{211.05 + 138.98 + 161.20} \times 100 = 30.5\%$$

Calculation of the Green Chemistry Metrics for the Preparation of **2b** using a solution approach reported in the literature:[6]



(MW: 211.05) (1.0 mmol) (211.05 mg) | (MW: 69.49) (2.3 mmol) (161.60 mg) | (MW: 207.63) (186.87 mg, 90%) | (MW: 76.76)

Excess Reagents Waste	$HO-NH_3Cl$			
	92.11 mg			
Reaction Waste	Mg(OH)Cl	THF	MeOH	H_2O
	153.52 mg	6195.35 mg	552.50 mg	462.3 mg
Purification Step Waste	Celite for filtration	$MgSO_4$ for drying	Hexane for Chromatography	EtOAc for Chromatography
	5000.00 mg	441.63 mg	5601.50 mg	37374.90 mg

Scheme S2. Preparation of **2b** in solution.[6] The calculations were made by considering the process reported on a 1.0 mmol scale for a better comparison with the mechanochemical process. For the purification step, the amount of celite and the eluent volume (Ethyl Acetate/Hexane 83:17) were not reported; therefore, a value of 5 grams and 50 mL were assumed for the calculations, respectively. The amount of $MgSO_4$ to be used was calculated by taking into account the amount of water present in the reaction mixture which was complexed at least by 3.67 mmol of the drying agent (ratio 1:7). The time for the reaction was not reported. The amount of solvents used for the filtration and drying step were not reported.

Calculation of Green Chemistry Metrics

Atom Economy (AE)

$$\frac{\text{Total molecular weight of desired product}}{\text{Total molecular weight of all reactants}} \times 100$$

$$= \frac{207.63}{211.05 + 69.49 + 80.60} \times 100 = 58\%$$

Process Mass Intensity (PMI)

$$\frac{\text{Mass of total waste}}{\text{Mass of desired product}}$$

$$= \frac{92.11 + 153.52 + 6195.35 + 552.50 + 462.3 + 5000.00 + 441.63 + 5}{186.87}$$

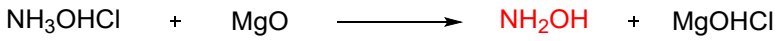
$$= 299.0$$

Reaction Mass Efficiency (RME)

$$\frac{\text{Actual mass of desired product}}{\text{Mass of reactants}} \times 100 = \frac{186.87}{211.05 + 161.60 + 80.60} \times 100 = 41.2\%$$

Analysis of hydroxylamine release during the milling process

The deprotonation of hydroxylamine hydrochloride was investigated to understand whether the formation of free hydroxylamine would be associated with either any release of gas or decomposition pathway which will cause an increase of pressure. The decomposition pathways that may take place imply the release of ammonia, nitrogen or nitrogen oxides as by-products. For this kind of analysis, it was analysed the mass loss after milling hydroxylamine hydrochloride (4 mmol) and magnesium oxide (8 mmol) by taring the grinding vessels used. The quantities measured through a duplicate analysis showed a negligible loss of mass with values of 2.8 mg and 9.5 mg, respectively.



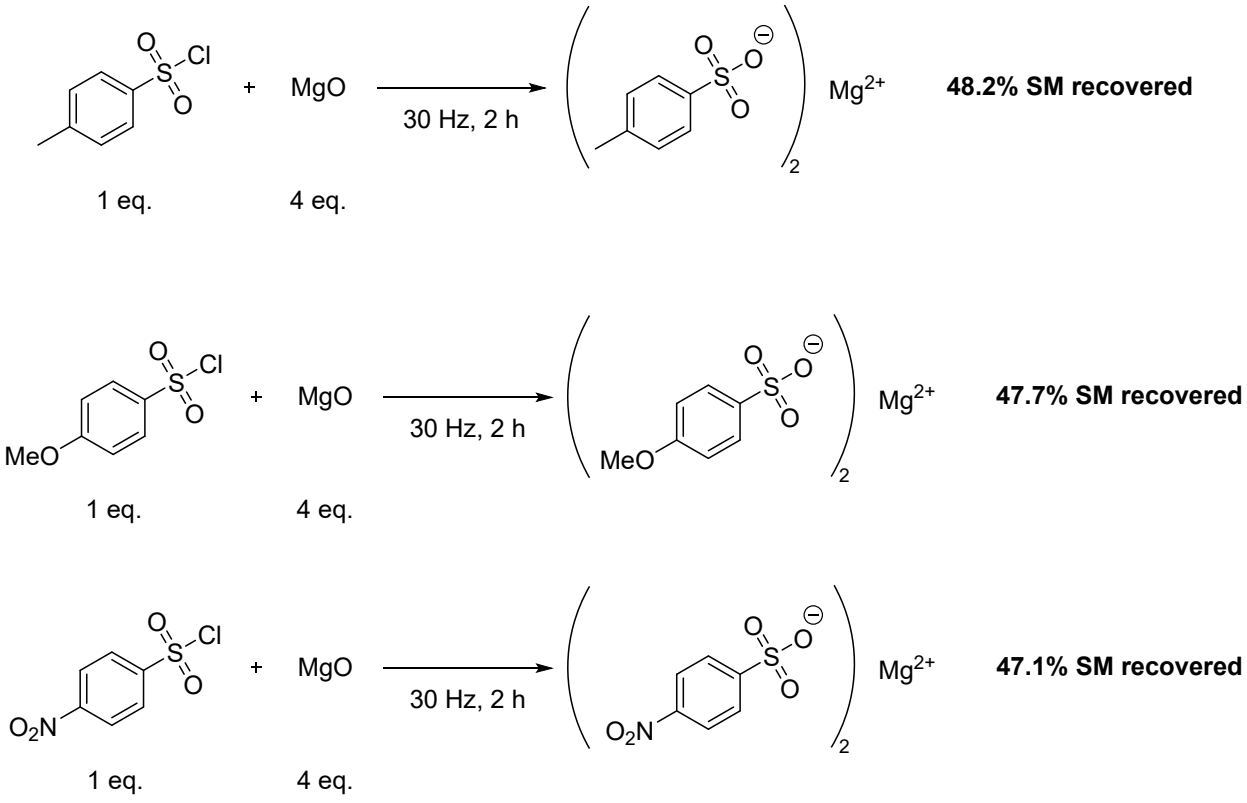
Reagents				Products		
Formula	ClH_4NO	MgO		**Formula**	H_3NO	ClHMgO
MW	69.49	40.3			33.03	76.76
Equivalents	1.00	2.00			1.00	1.00
Sample Mass	279.9 mg	322.8 mg		**Expected Mass**	133.05 mg	309.20 mg
Reactant mass total	602.7 mg			**Mass detected after milling**	599.9 mg	
Hypothesised mass of gas released	2.8 mg			**% of possible gas release**	2.10%	

Reagents				Products		
Formula	ClH_4NO	MgO		**Formula**	H_3NO	ClHMgO
MW	69.49	40.3			33.03	76.76
Equivalents	1.00	2.00			1.00	1.00
Sample Mass	281.1 mg	323.0 mg		**Expected Mass**	133.62 mg	310.53 mg
Reactant mass total	610.1 mg			**Mass detected after milling**	600.6 mg	
Hypothesised mass of gas released	9.5 mg			**% of possible gas release**	7.11%	

As shown in the tables, the mass loss observed over 2 h is minimal, making the release of gaseous hydroxylamine or its decomposition under the optimized reaction conditions highly unlikely. Moreover, the persistently solid appearance of the mixture might rule out also any melting or liquefaction event associated with hydroxylamine generated *in-situ* after deprotonation.

Degradation of sulfonyl chlorides in the presence of magnesium oxide

The hydrolysis of 3 different sulfonyl chlorides has been evaluated by grinding the starting material with MgO (ratio 1 sulfonyl chloride : 4 MgO) showing a consistent partial hydrolysis in all cases tested.



The reactions were conducted on a 0.5 mmol scale. The crude mixtures were washed and filtered with dry diethyl ether to selectively recover unreacted starting material. After solvent evaporation, the recovered mass indicated a general trend in which approximately half of the starting material had degraded to the corresponding sulfonate derivative. The purity of the recovered sulfonyl chloride was then checked through ^{1}H-NMR analysis showing an excellent purity of the recovered organic derivatives.

However, we believe this degradation pathway is less relevant under our reaction conditions, due to the faster acid–base reaction between MgO and hydroxylamine hydrochloride, which preserves the integrity of the starting material. The low isolated yields, particularly for the free sulfohydroxamic acids, are primarily attributable to the high intrinsic reactivity of these derivatives and the difficulties encountered during purification.

Spectra

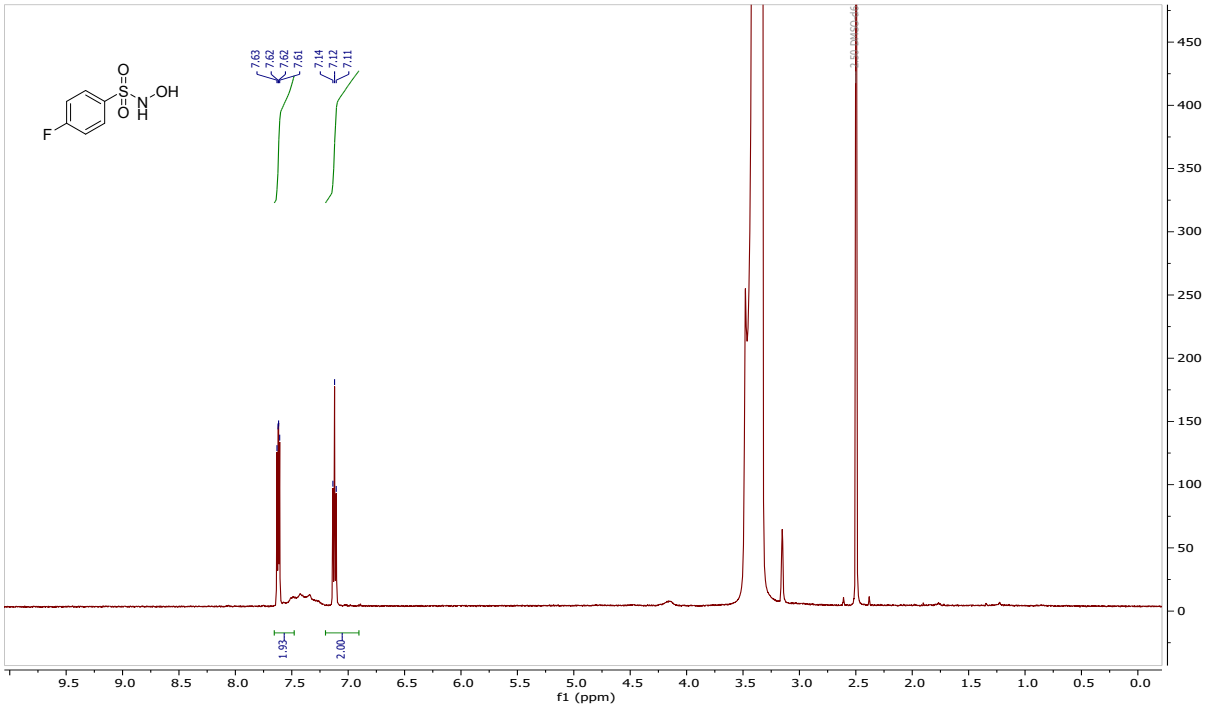


Figure S1. ^{1}H NMR spectrum of 4-Fluoro-N-Hydroxybenzenesulfonamide (2a)

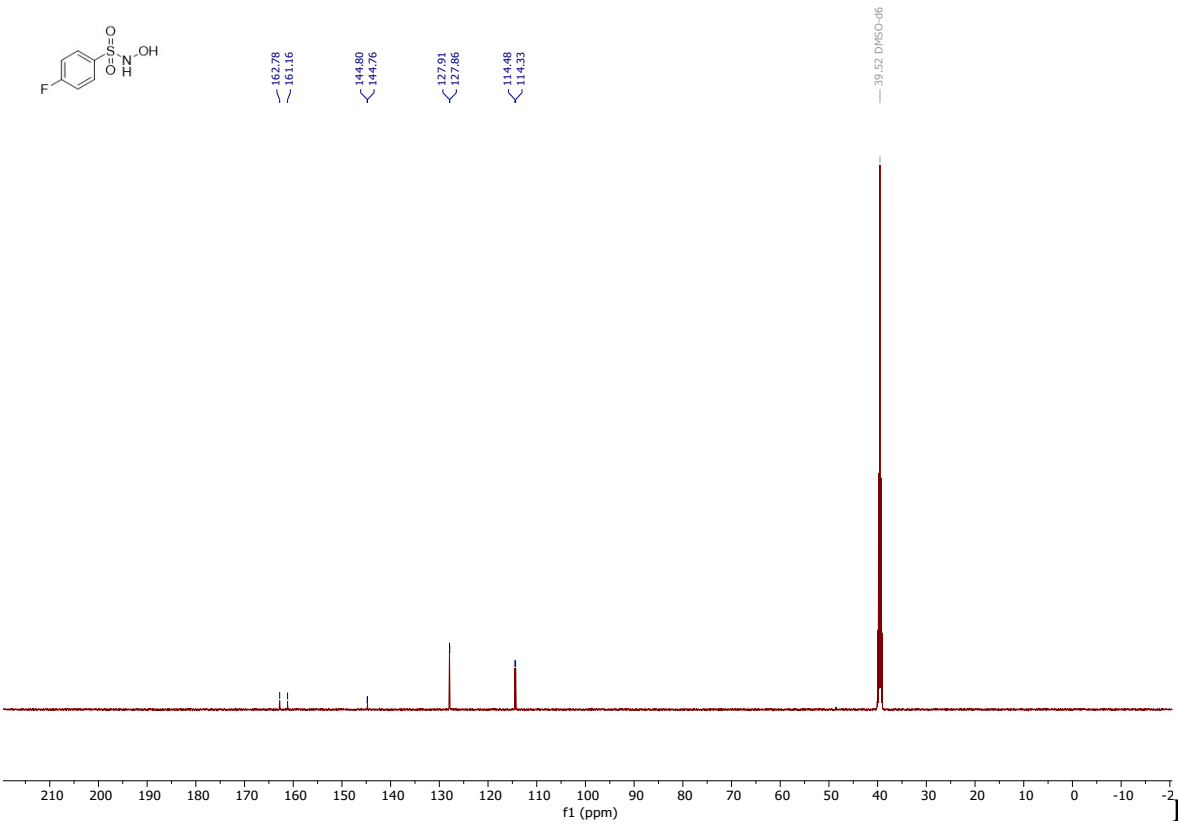


Figure S2. ^{13}C NMR spectrum of 4-Fluoro-N-Hydroxybenzenesulfonamide (2a)

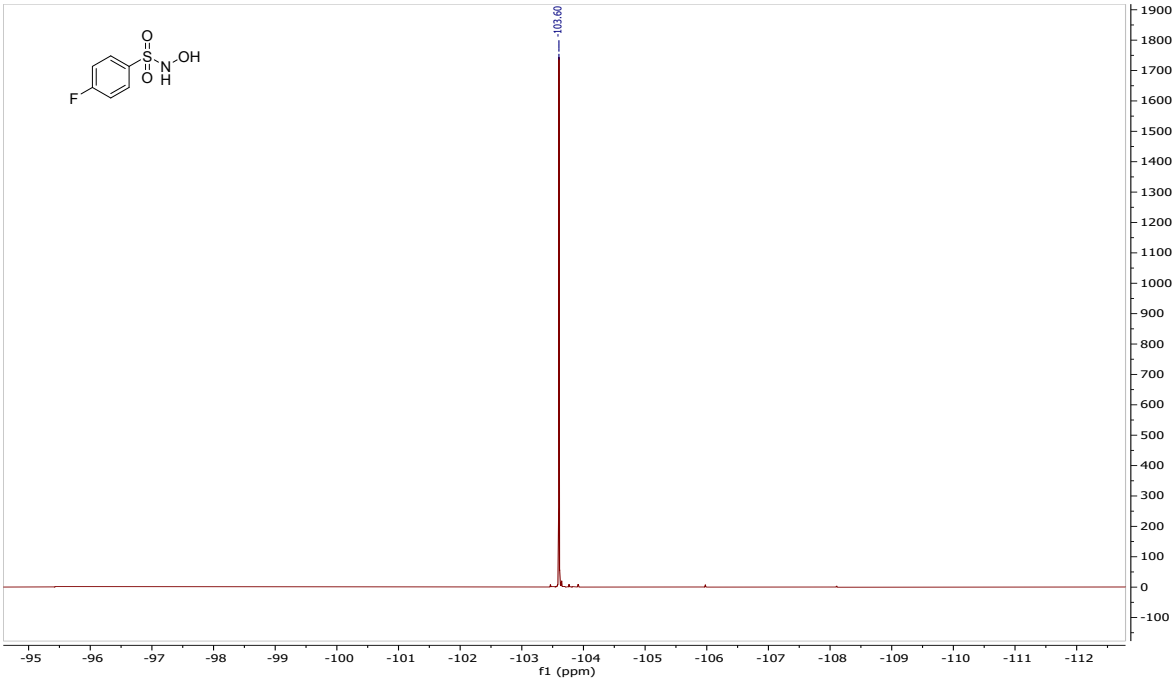


Figure S3. ^{19}F NMR spectrum of N-Hydroxy-4-(trifluoromethyl)benzenesulfonamide (2a)

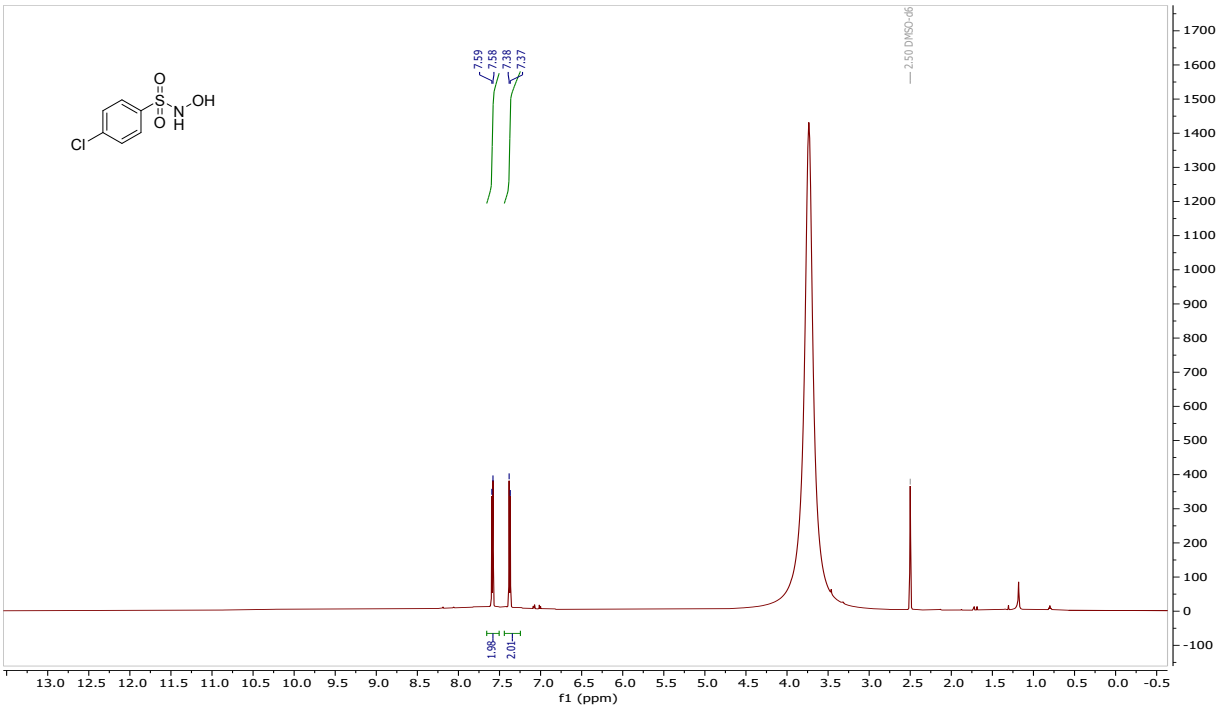


Figure S4. ^{1}H NMR spectrum of 4-Chloro-N-Hydroxybenzenesulfonamide (2b)

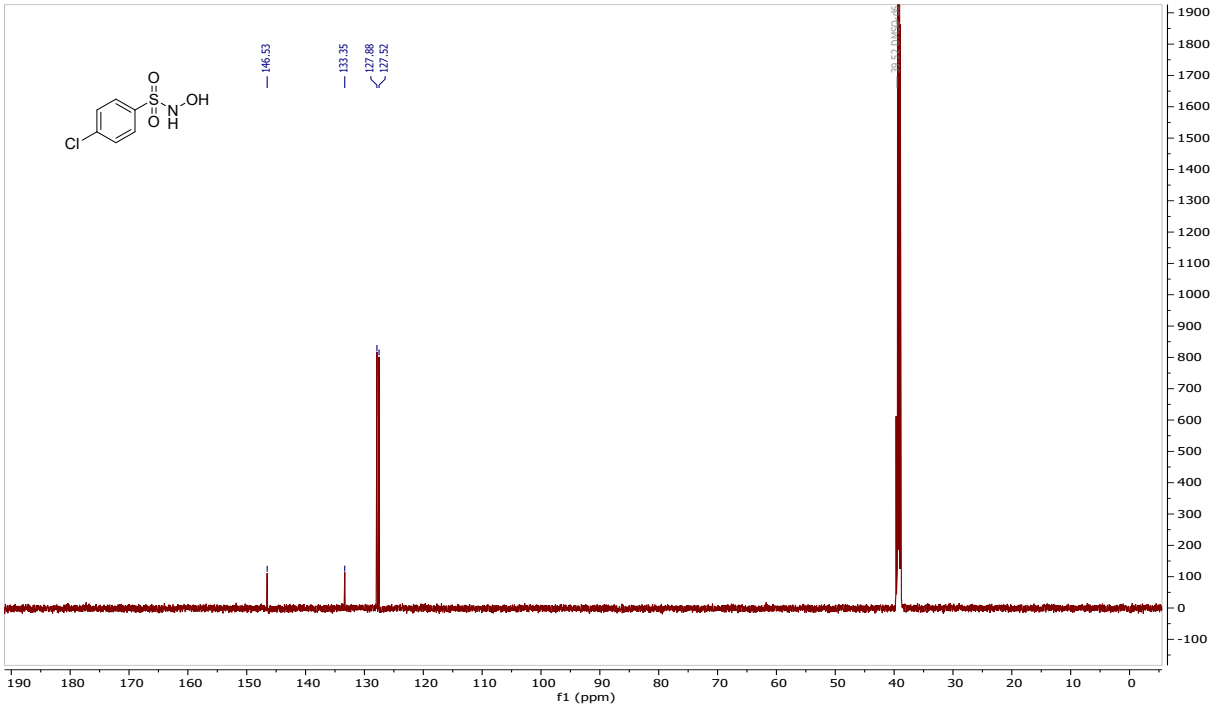


Figure S5. ^{13}CNMR spectrum of 4-Chloro-N-Hydroxybenzenesulfonamide (2b)

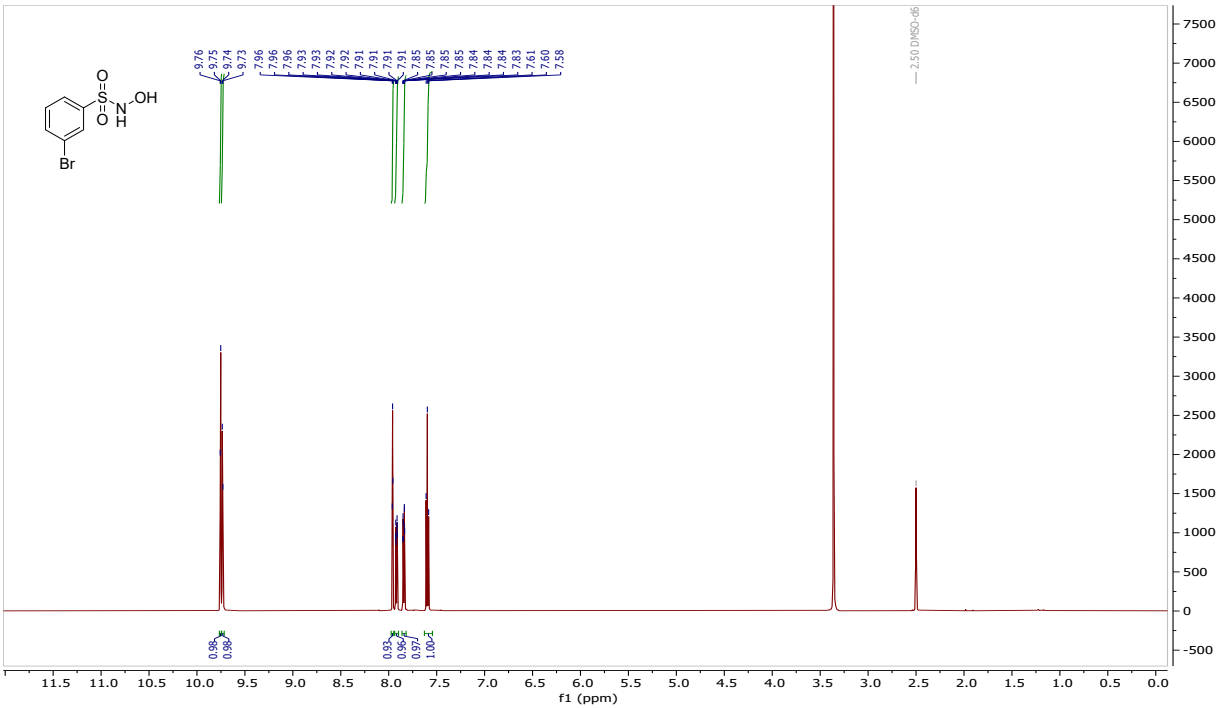


Figure S6. [1]H NMR spectrum of 3-Bromo-N-Hydroxybenzenesulfonamide (2c)

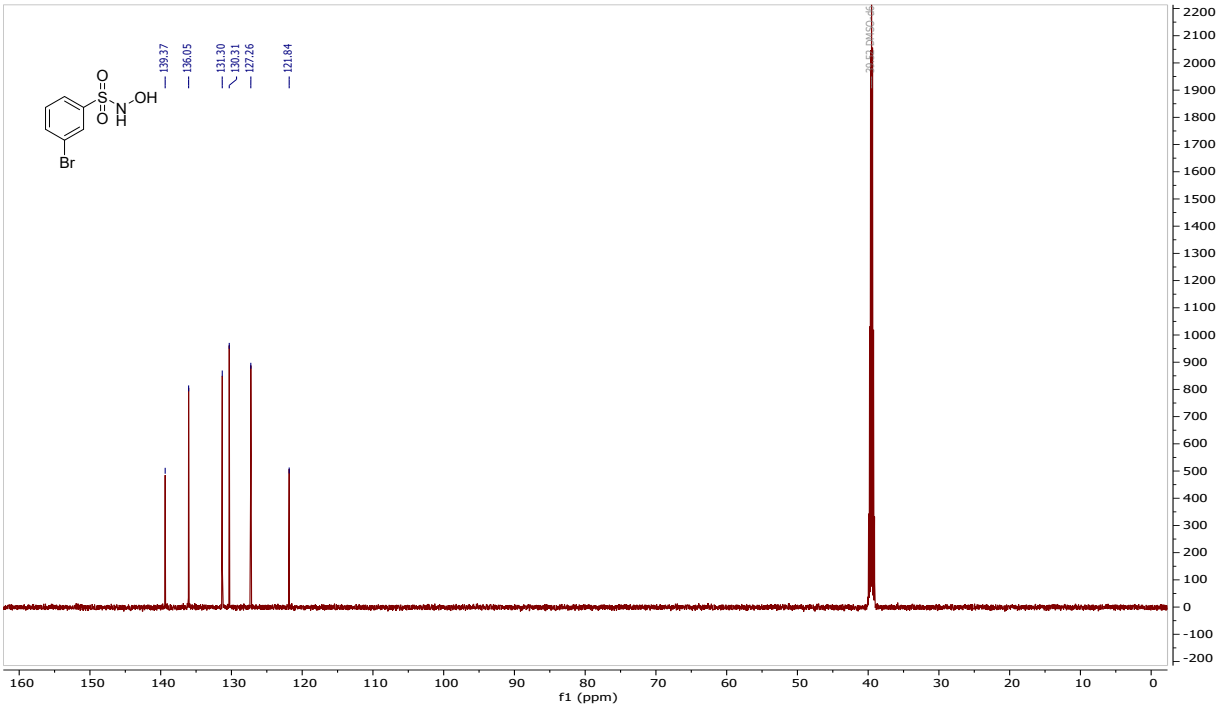


Figure S7. [13]C NMR spectrum of 3-Bromo-N-Hydroxybenzenesulfonamide (2c)

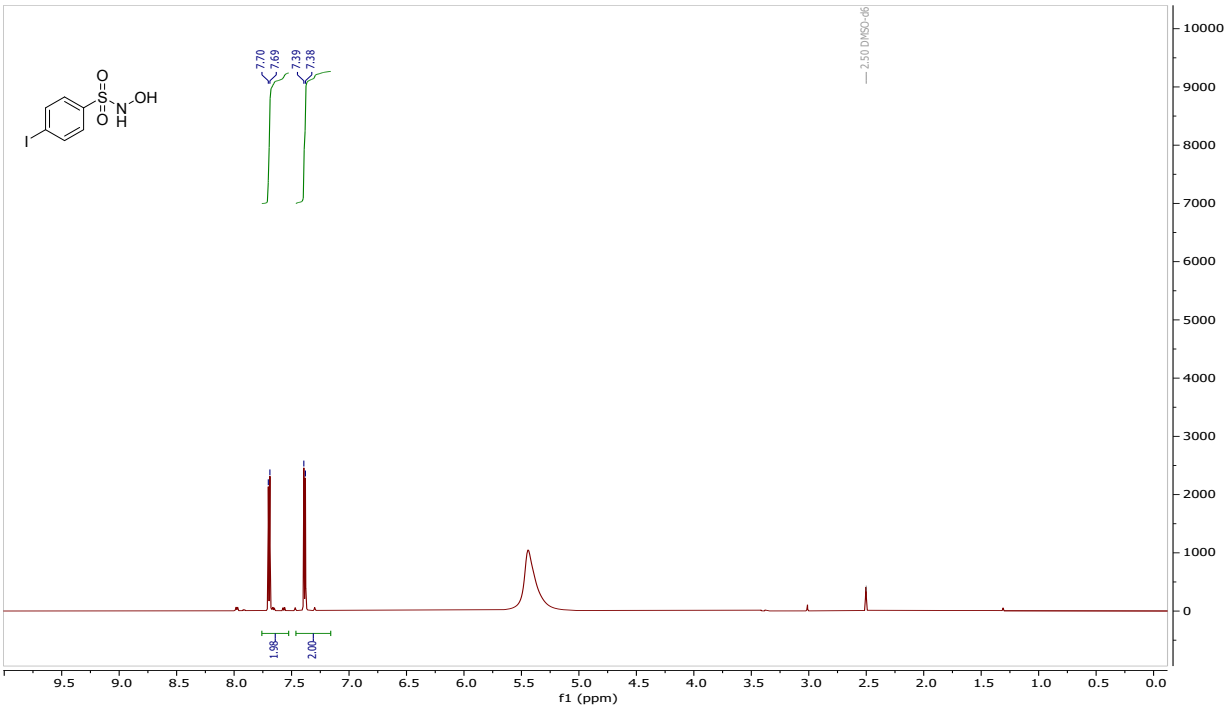


Figure S8. [1]H NMR spectrum of N-Hydroxy-4-Iodobenzenesulfonamide (2d)

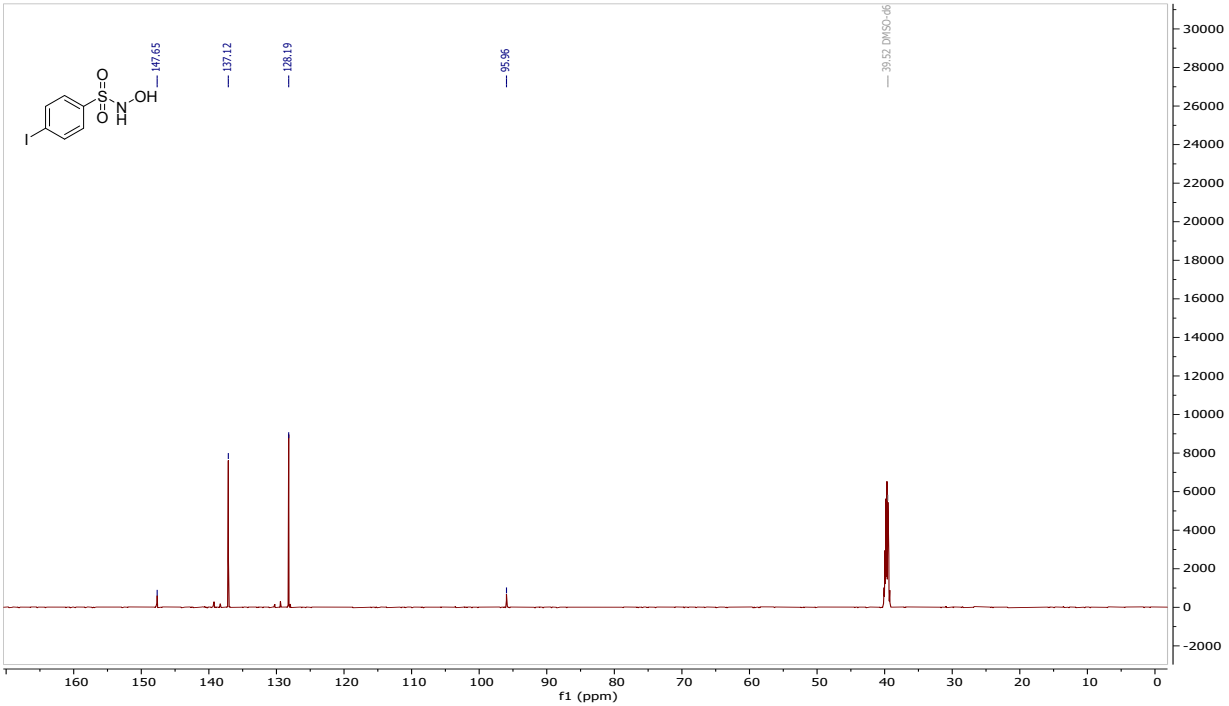


Figure S9. [13] CNMR spectrum of N-Hydroxy-4-Iodobenzenesulfonamide (2d)

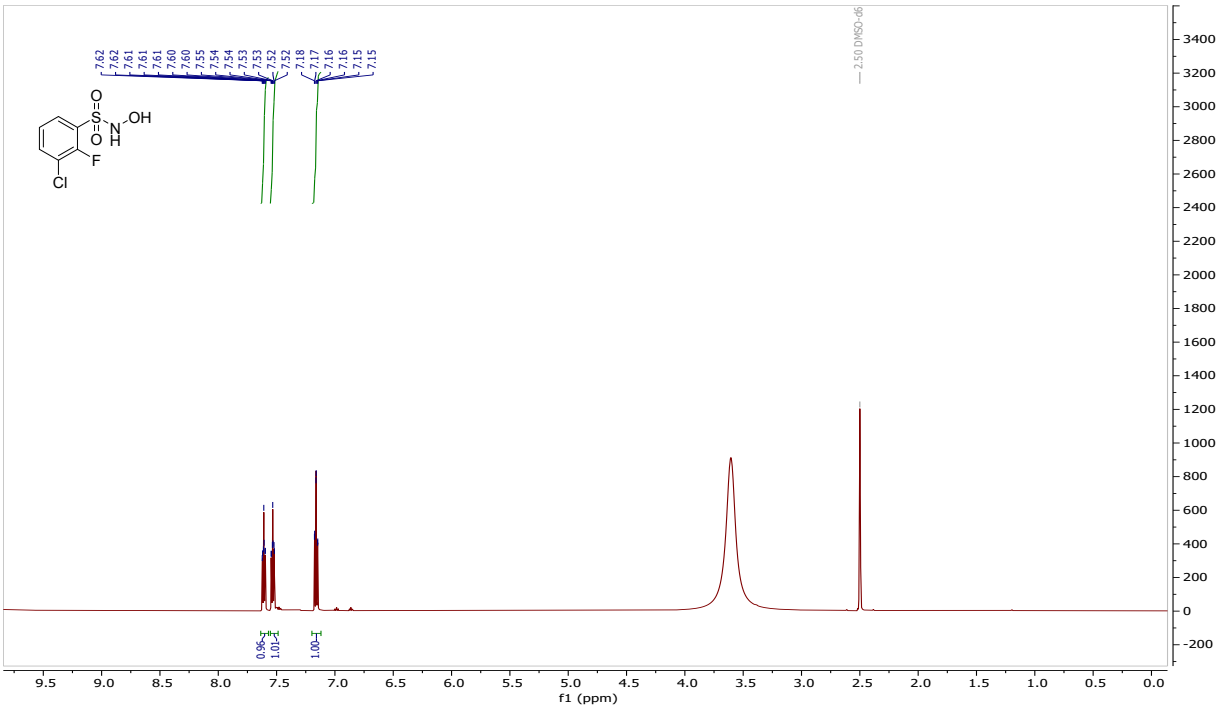


Figure S10. [1]H NMR spectrum of 3-Chloro-2-Fluoro-N-Hydroxybenzenesulfonamide (2e)

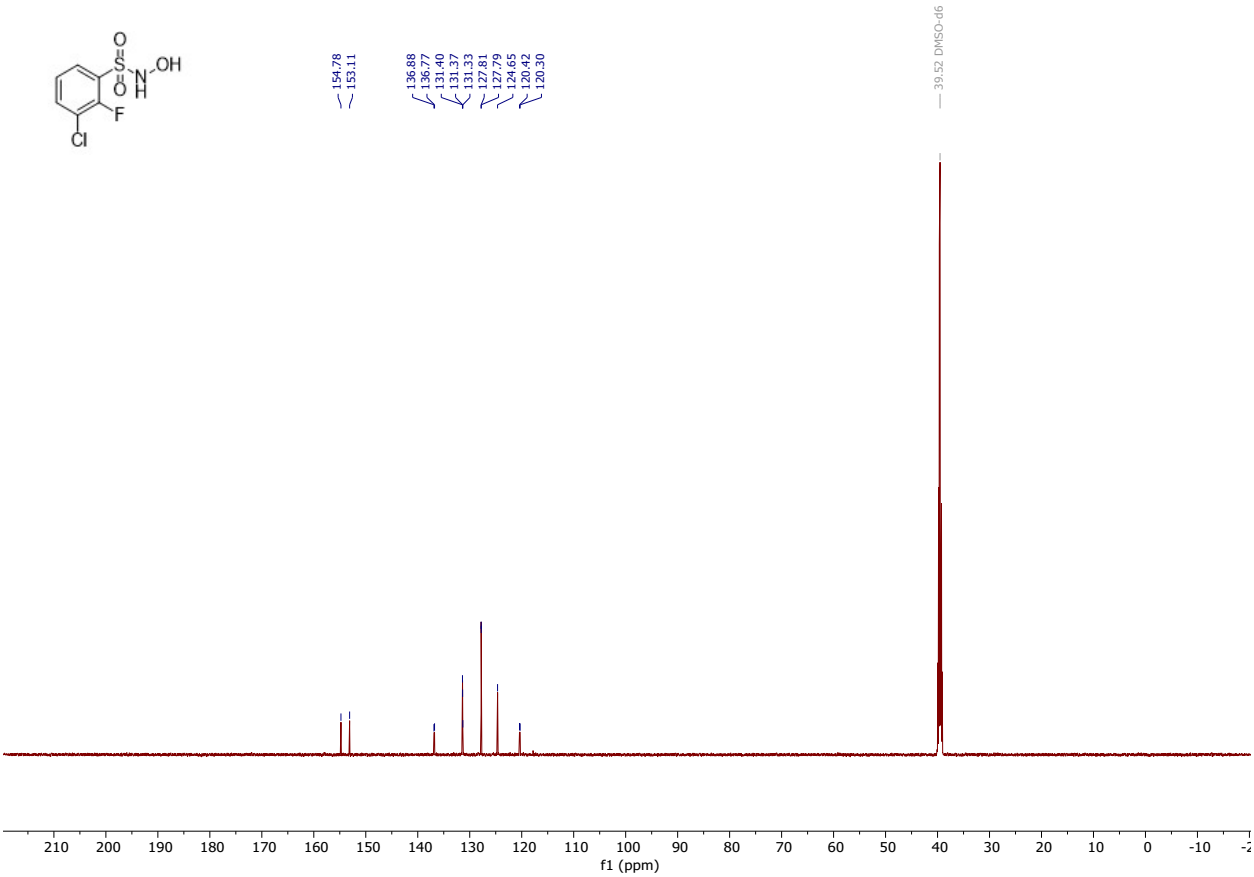


Figure S11. [13]C NMR spectrum spectrum of 3-Chloro-2-Fluoro-N-Hydroxybenzenesulfonamide (2e)

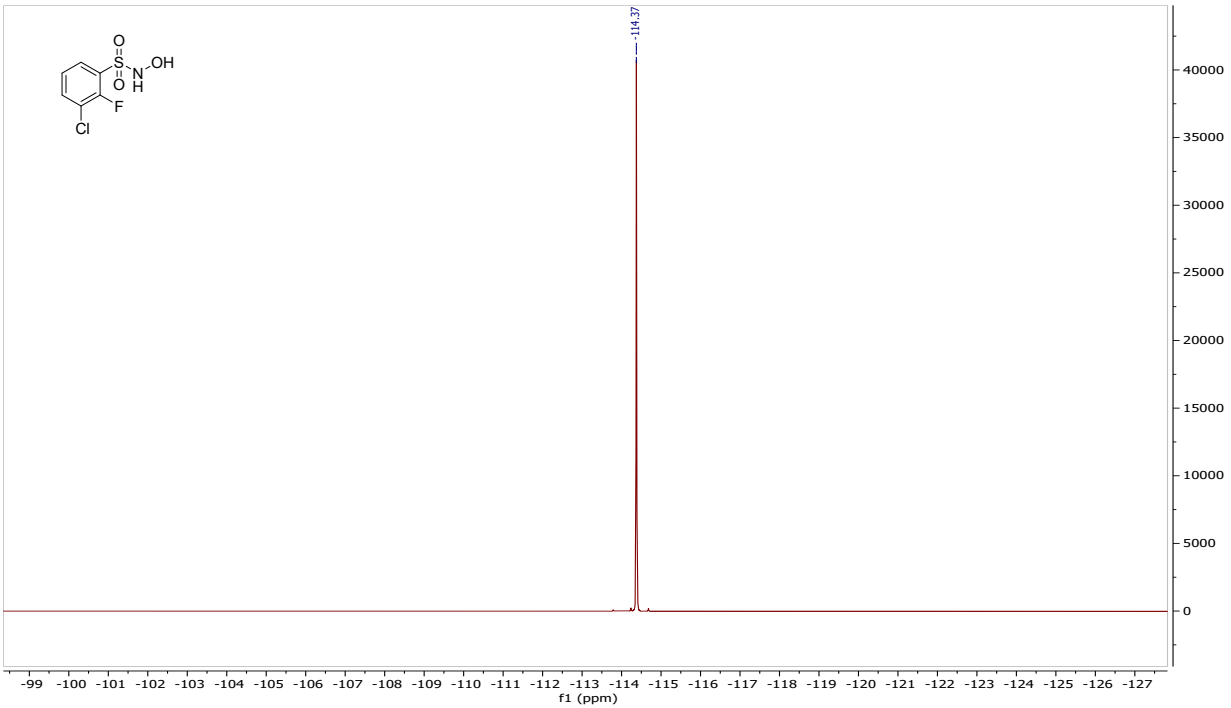


Figure S12. ^{19}F NMR spectrum of 3-Chloro-2-Fluoro-N-Hydroxybenzenesulfonamide (2e)

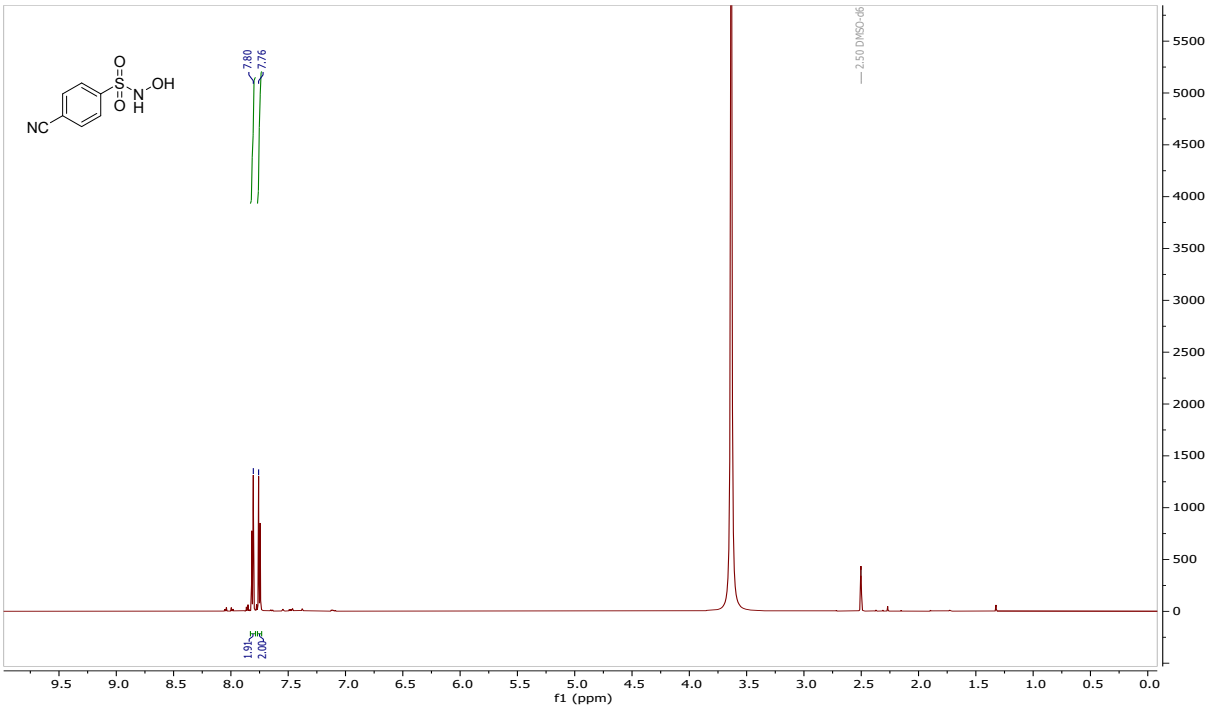


Figure S13. ^{1}H NMR spectrum of 4-Cyano-N-Hydroxybenzenesulfonamide (2f)

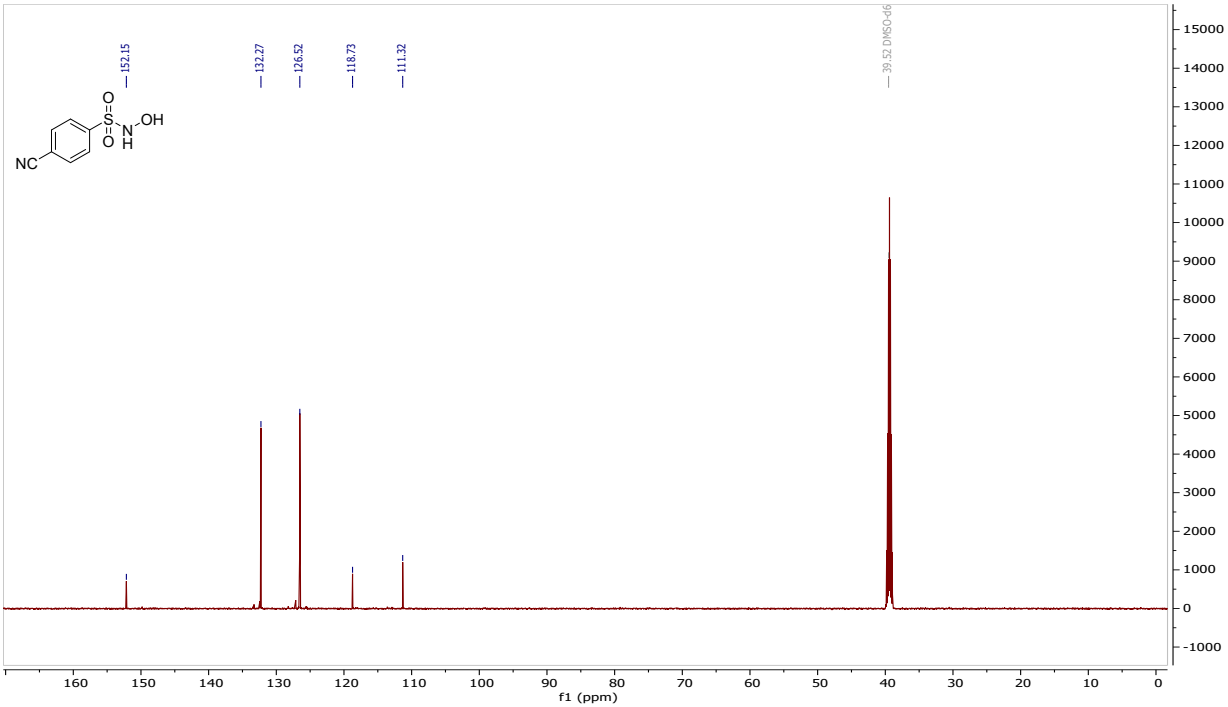


Figure S14. ^{13}CNMR spectrum of 4-Cyano-N-Hydroxybenzenesulfonamide (2f)

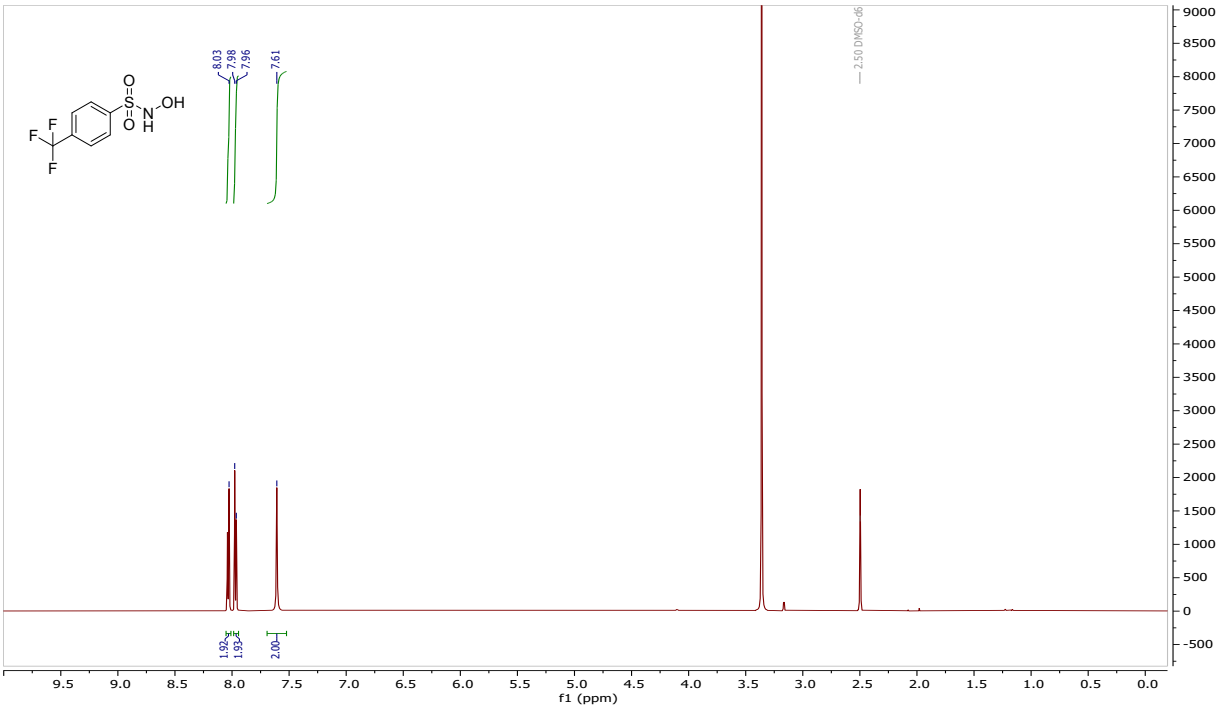


Figure S15. ^{1}H NMR spectrum of N-Hydroxy-4-(trifluoromethyl)benzenesulfonamide (2g)

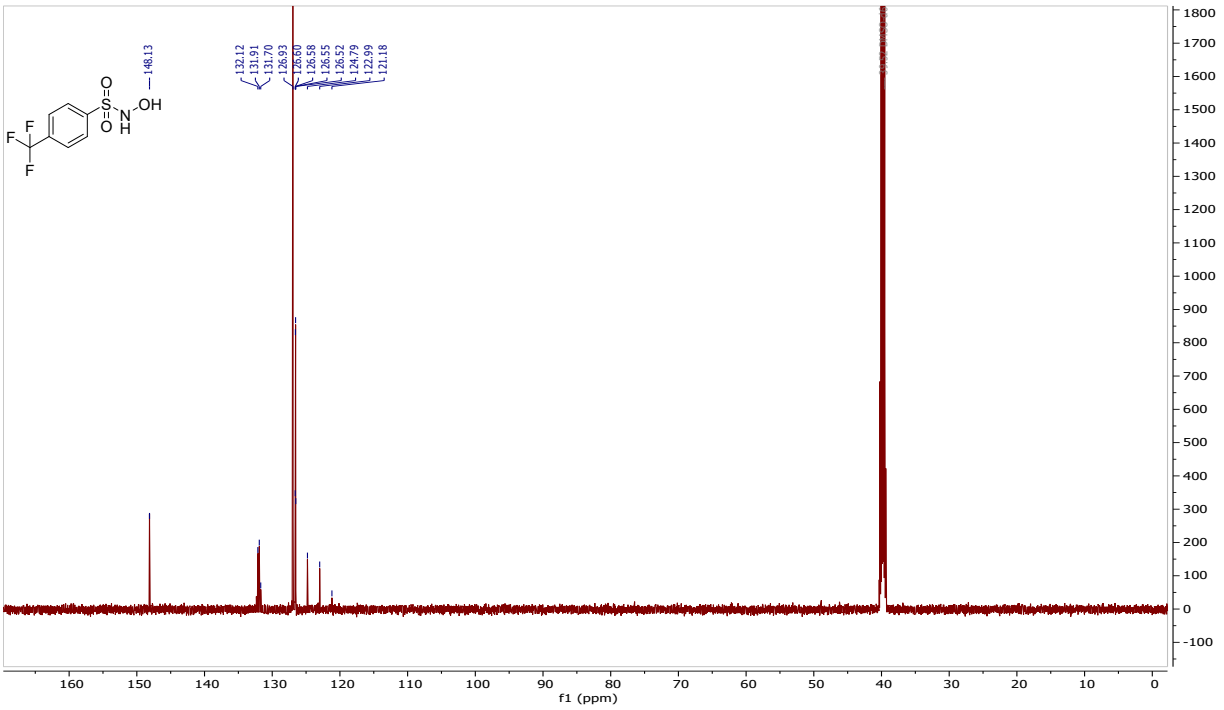


Figure S16. ^{13}C NMR spectrum of N-Hydroxy-4-(trifluoromethyl)benzenesulfonamide (2g)

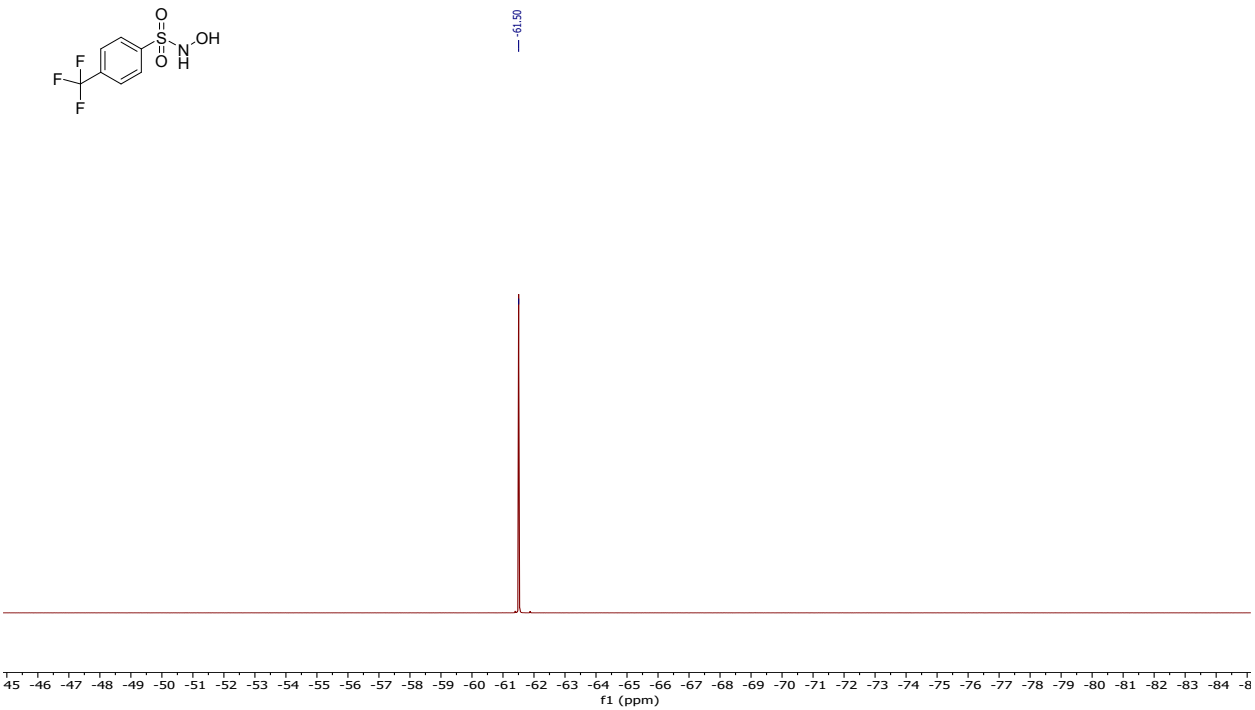


Figure S17. ^{19}F NMR spectrum of N-Hydroxy-4-(trifluoromethyl)benzenesulfonamide (2g)

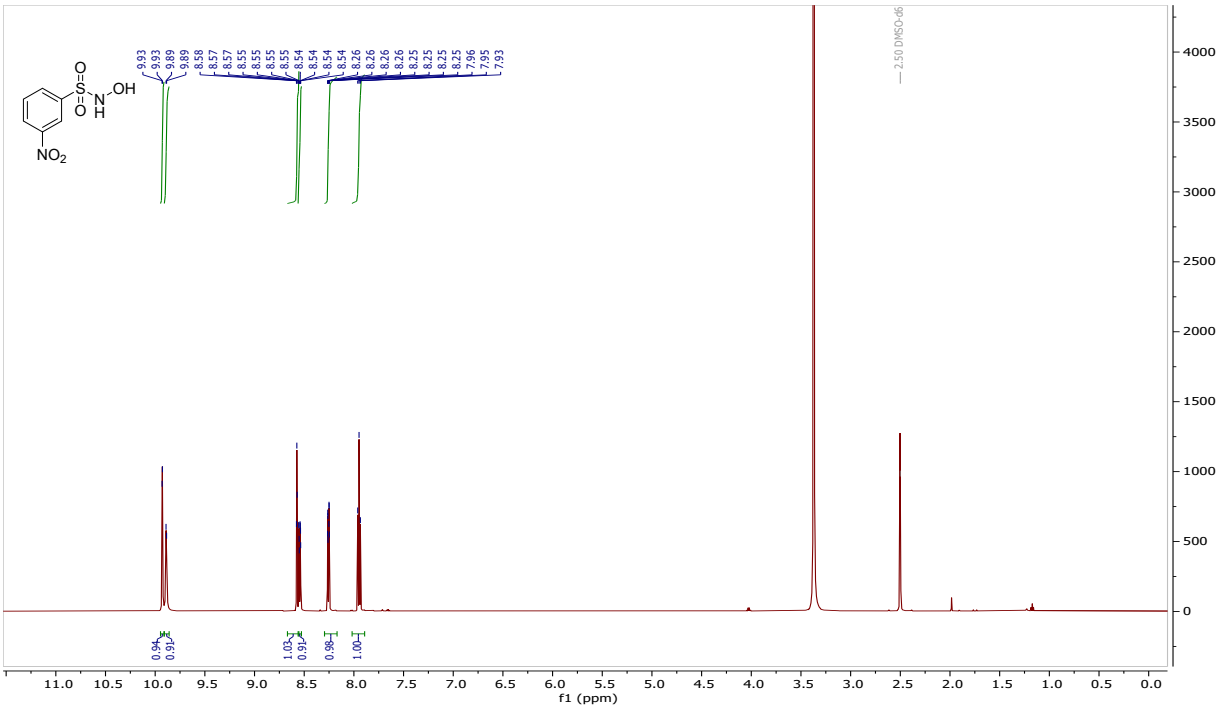


Figure S18. [1]H NMR spectrum of N-Hydroxy-3-Nitrobenzenesulfonamide (2h)

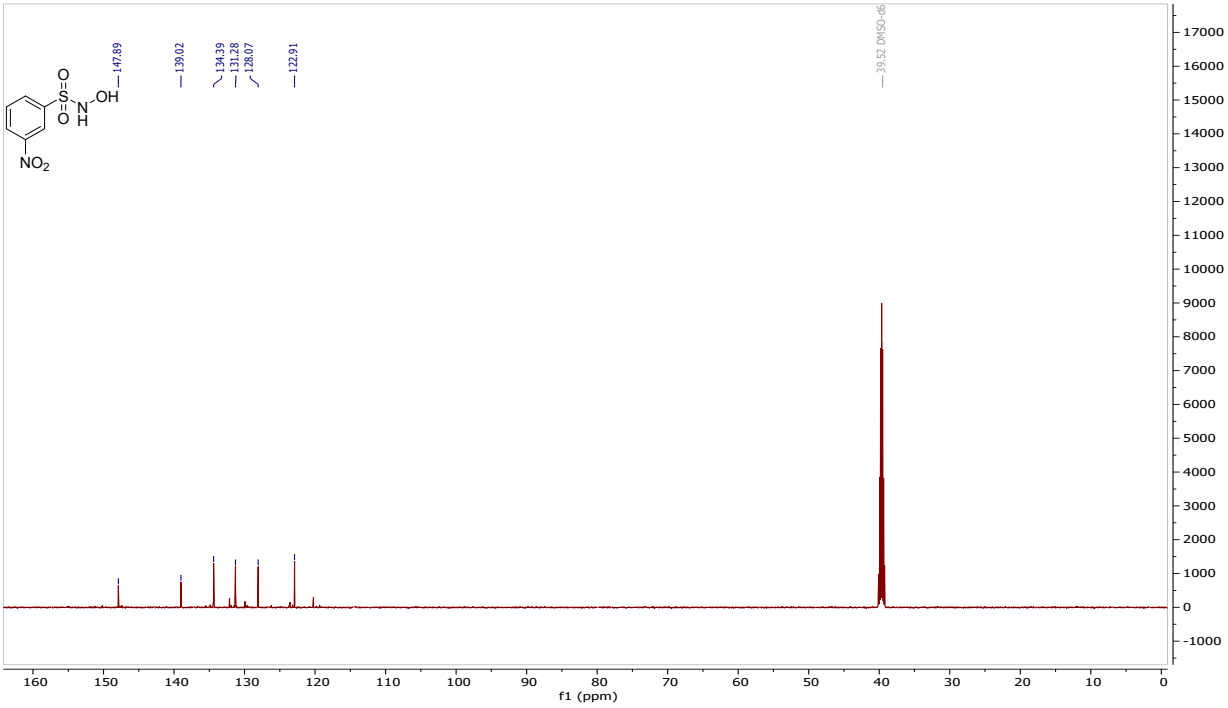


Figure S19. [13]C NMR spectrum of N-Hydroxy-3-Nitrobenzenesulfonamide (2h)

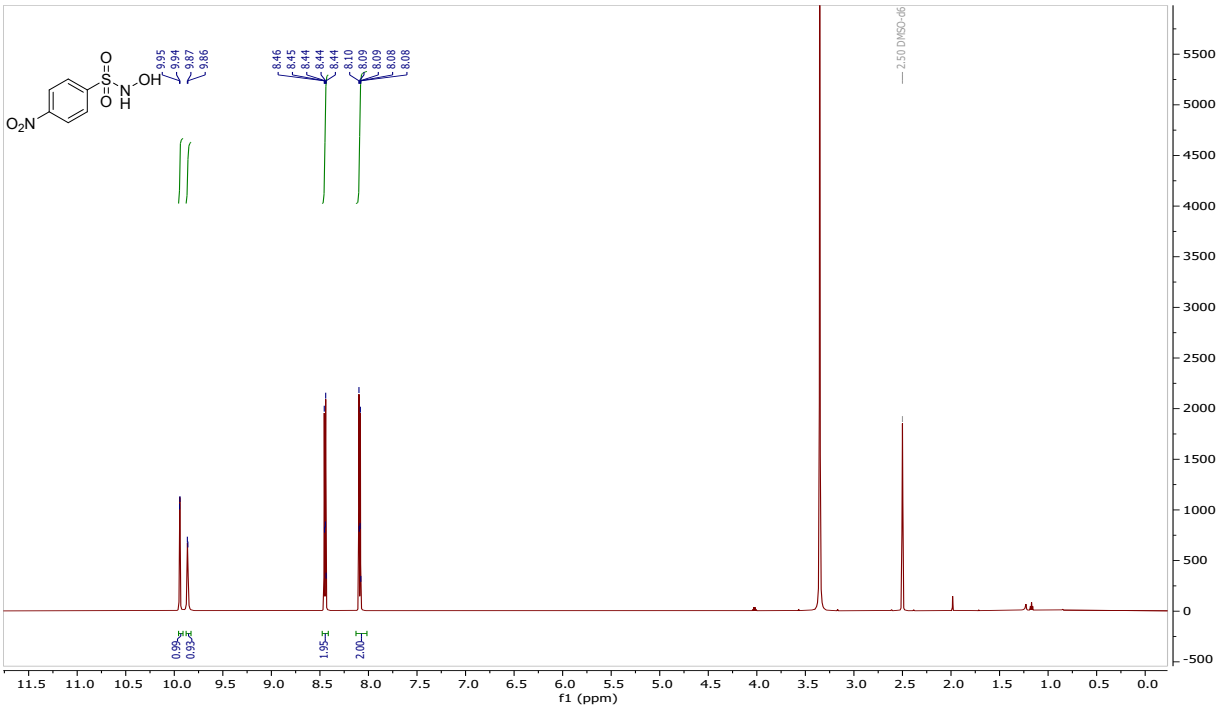


Figure S20. ^{1}H NMR spectrum of N-Hydroxy-4-Nitrobenzenesulfonamide (2i)

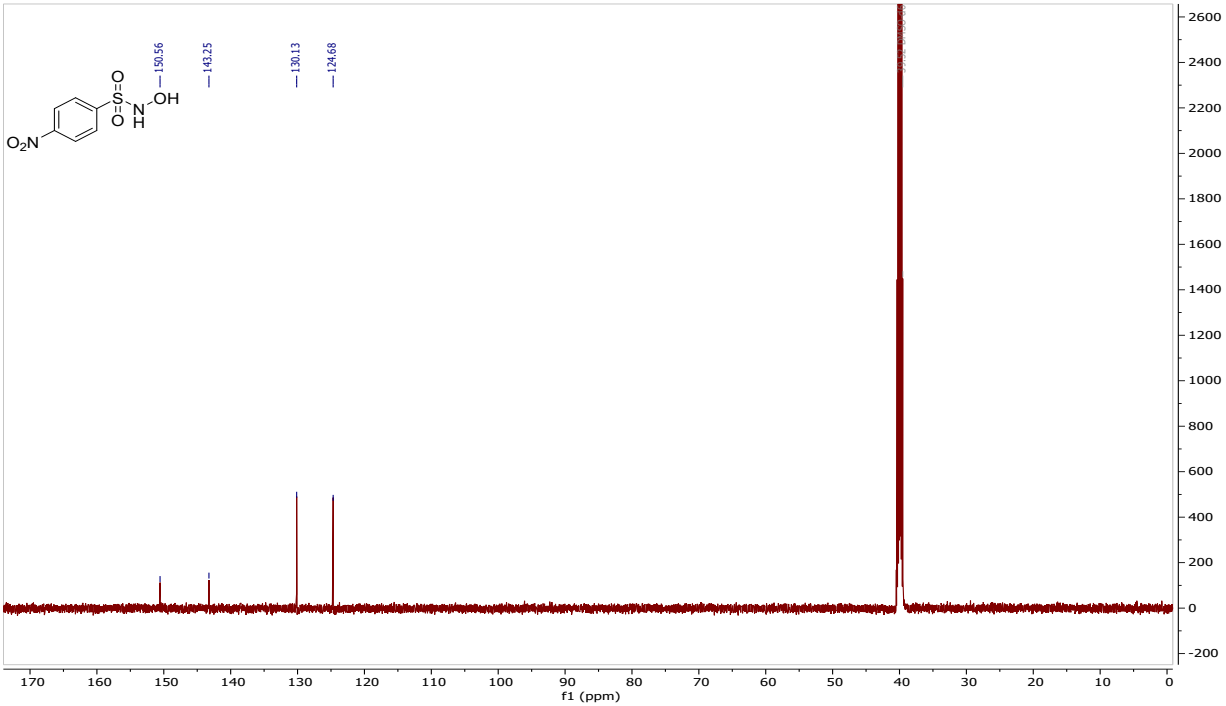


Figure S21. ^{13}C NMR spectrum of N-Hydroxy-4-Nitrobenzenesulfonamide (2i)

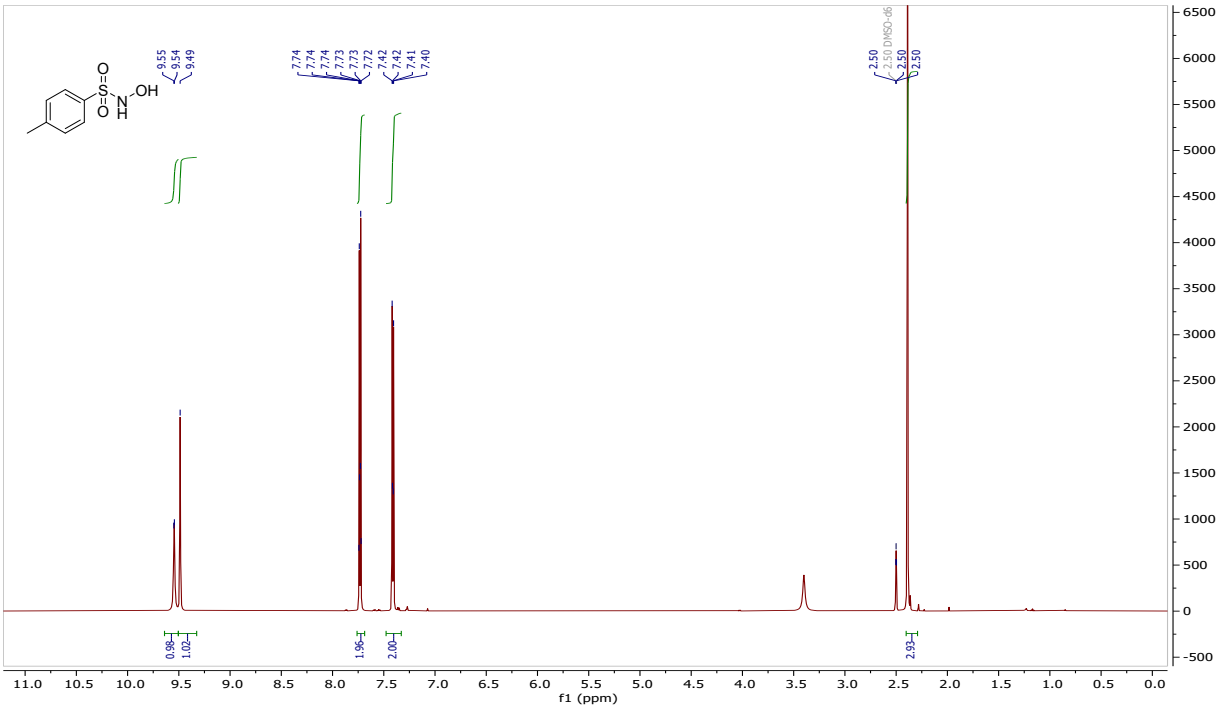


Figure S22. ^{1}H NMR spectrum of N-Hydroxy-4-Methylbenzenesulfonamide (2j)

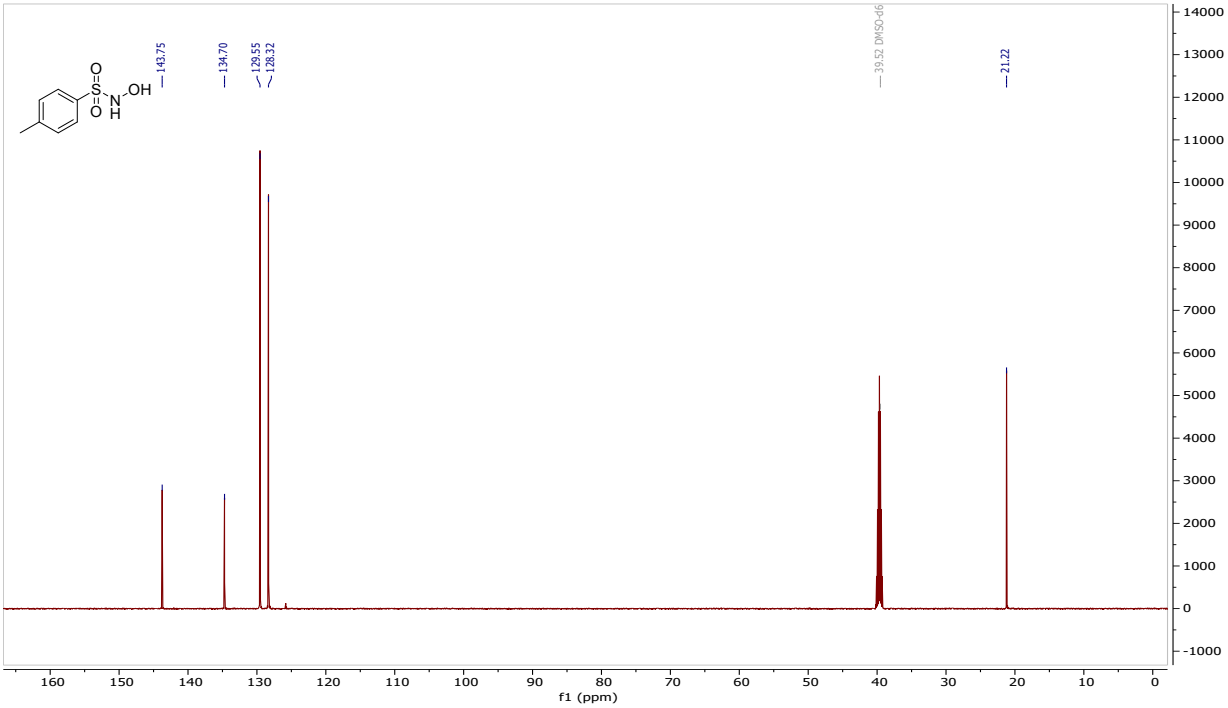


Figure S23. ^{13}C NMR spectrum of N-Hydroxy-4-Methylbenzenesulfonamide (2j)

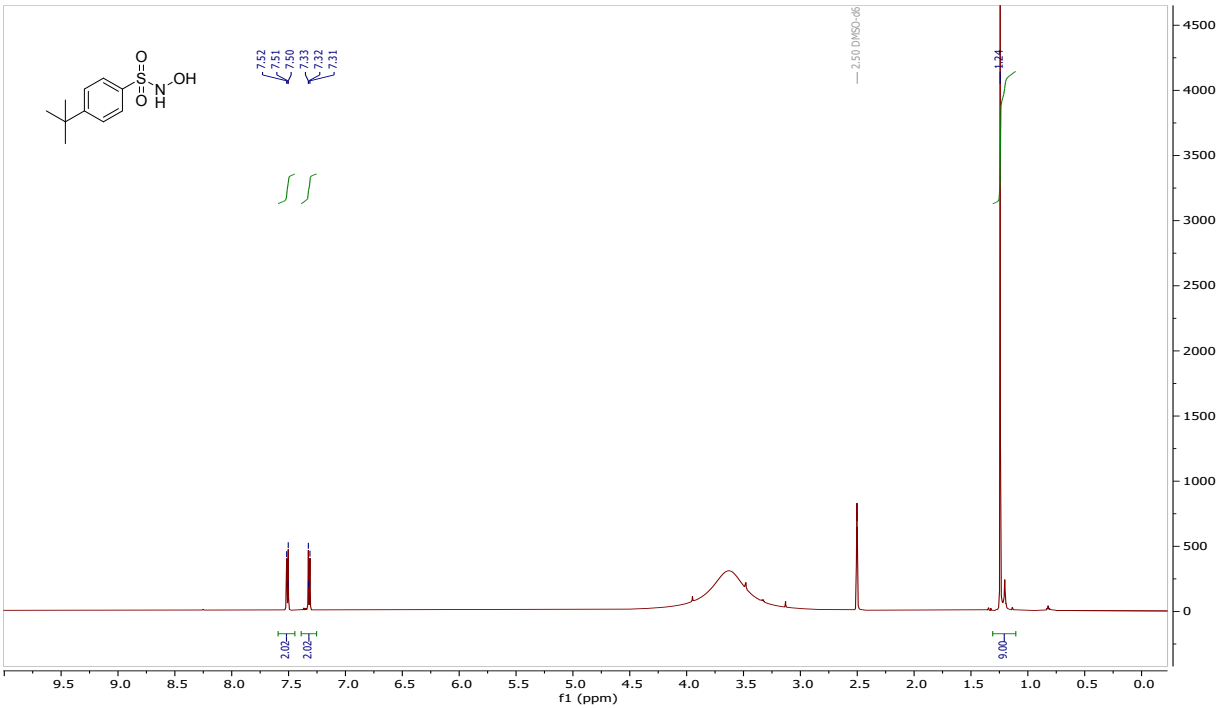


Figure S24. ^{1}H NMR spectrum of 4-(tert-Butyl)-N-Hydroxybenzenesulfonamide (2k)

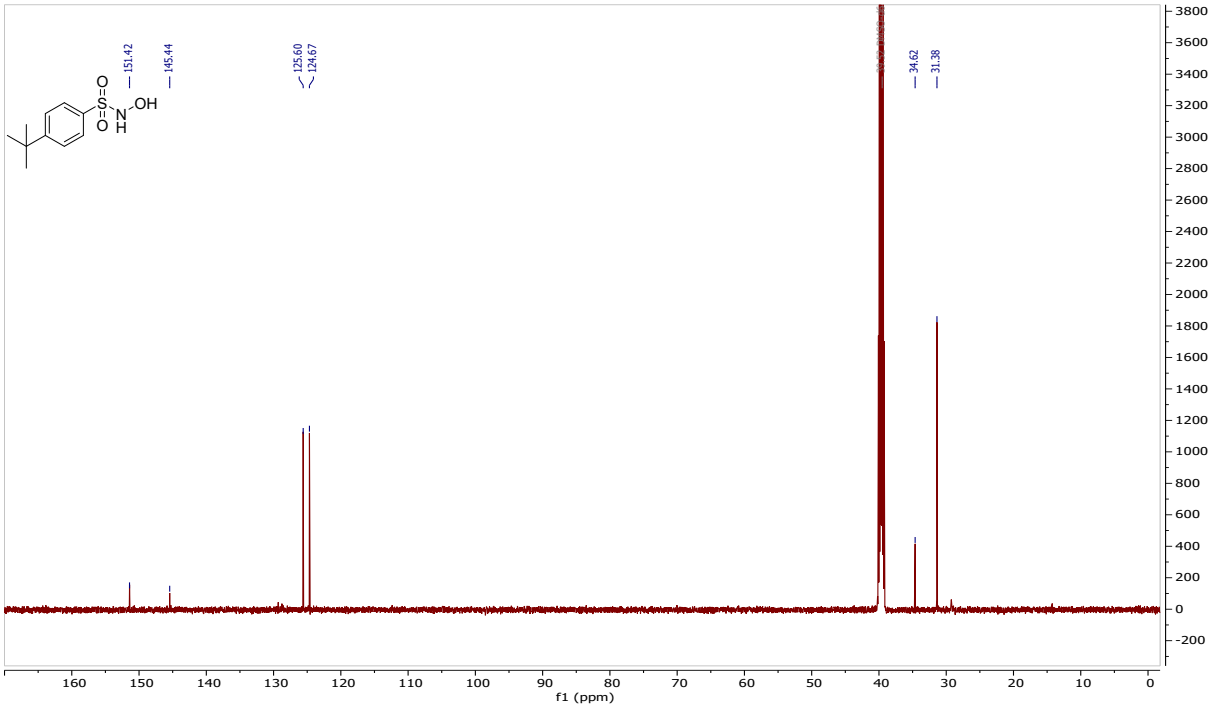


Figure S25. ^{13}C NMR spectrum of 4-(tert-Butyl)-N-Hydroxybenzenesulfonamide (2k)

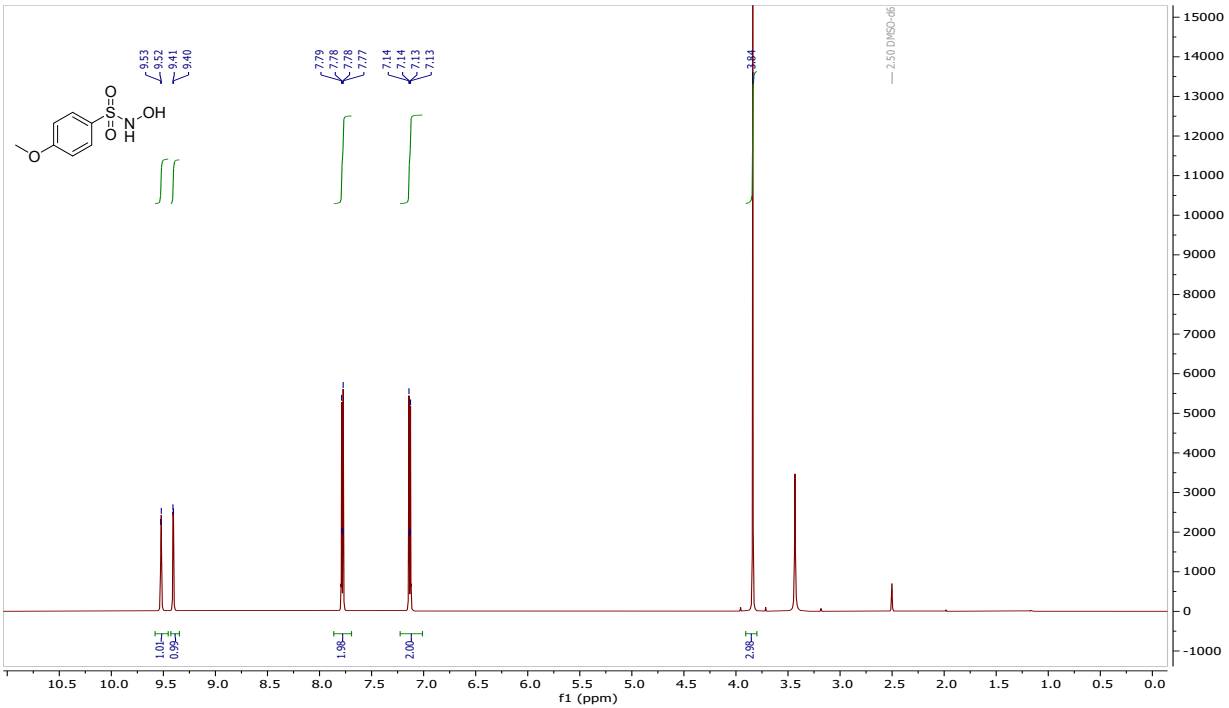


Figure S26. [1]H NMR spectrum of N-Hydroxy-4-Methoxybenzenesulfonamide (2m)

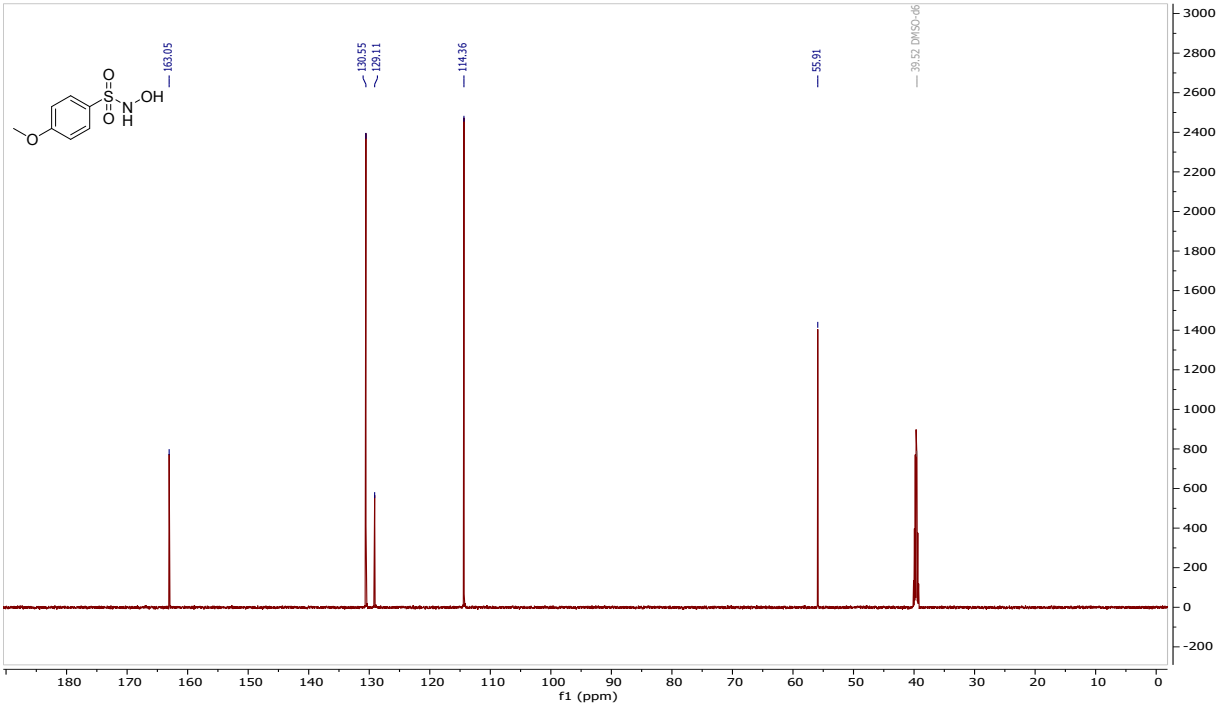


Figure S27. [13]C NMR spectrum of N-Hydroxy-4-Methoxybenzenesulfonamide (2m)

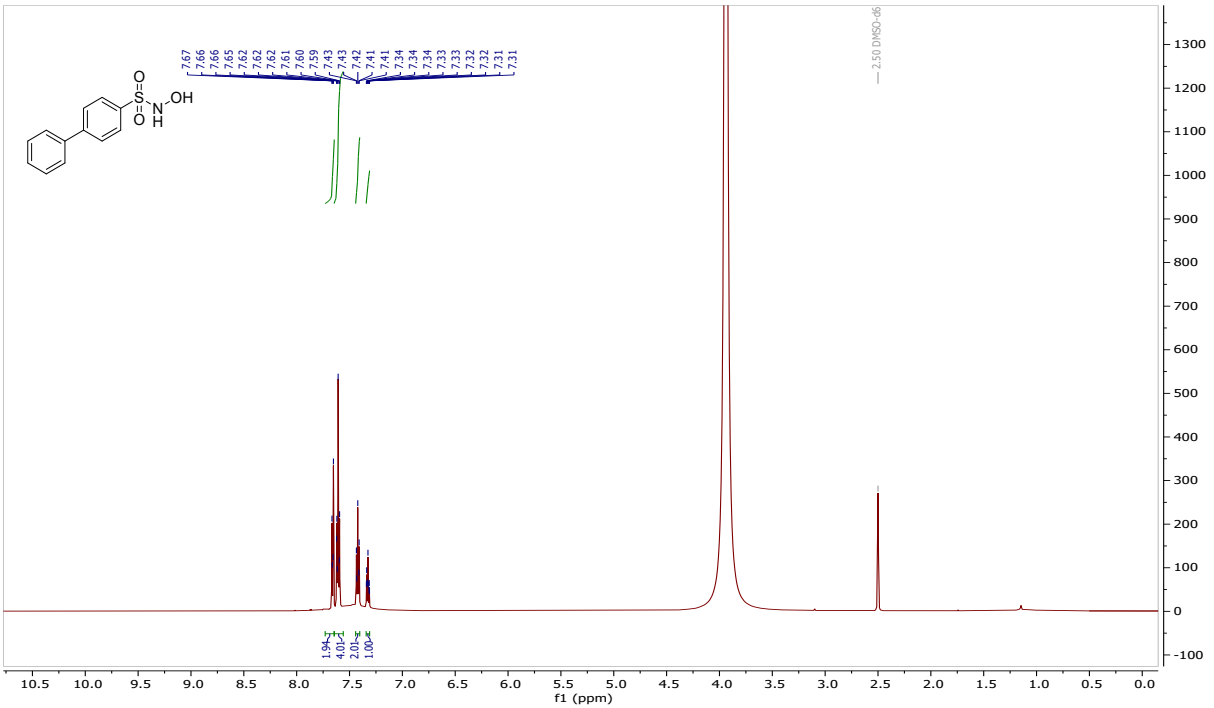


Figure S28. [1]H NMR spectrum of N-Hydroxy-[1,1'-biphenyl]-4-sulfonamide (2n)

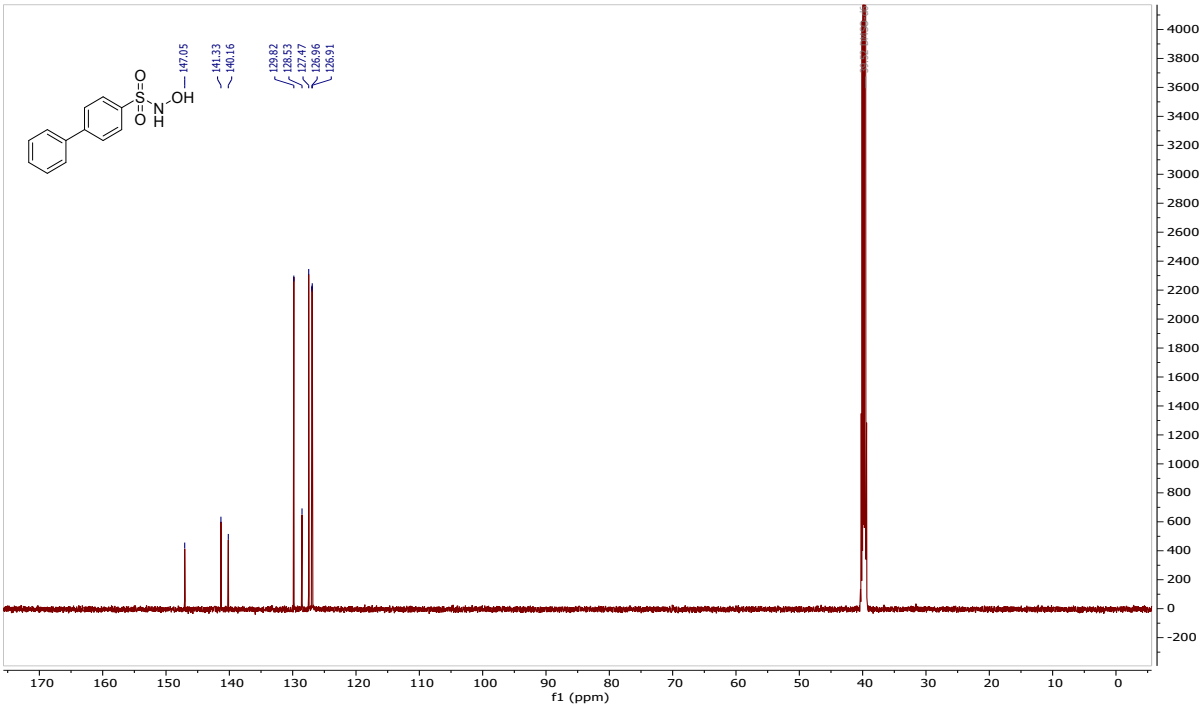


Figure S29. [13]C NMR spectrum of N-Hydroxy-[1,1'-biphenyl]-4-sulfonamide (2n)

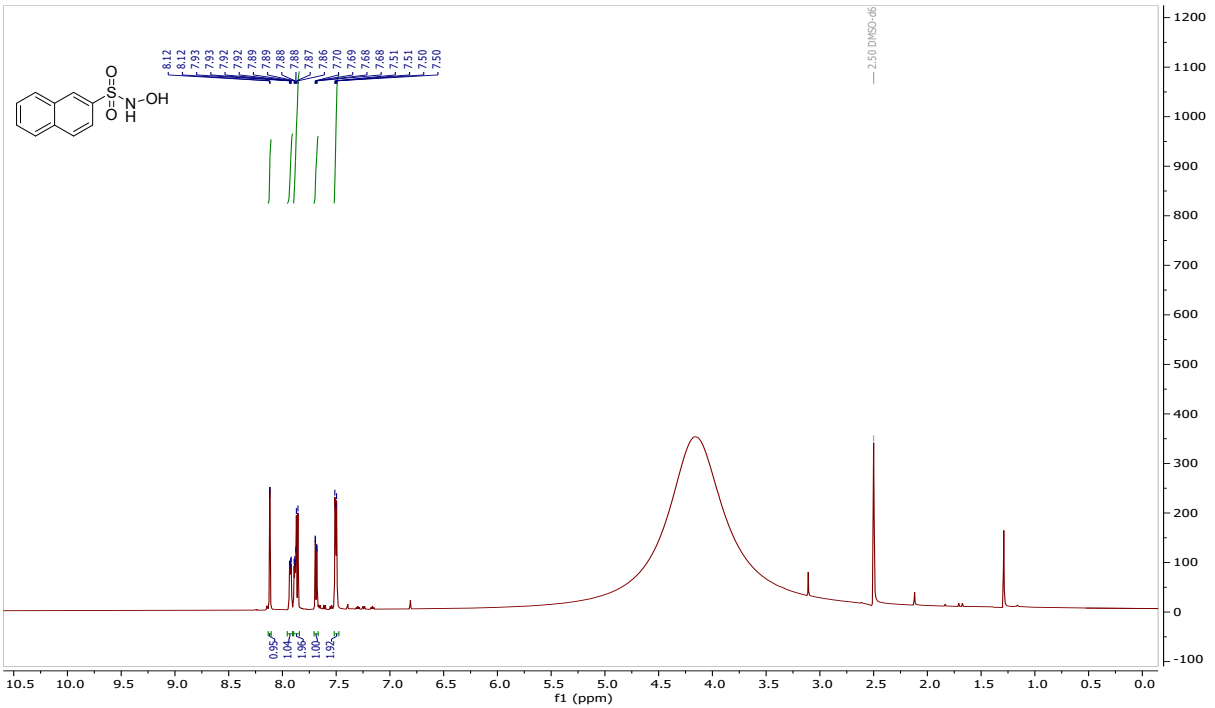


Figure S30. ^{1}H NMR spectrum of N-Hydroxynaphthalene-2-sulfonamide (2o)

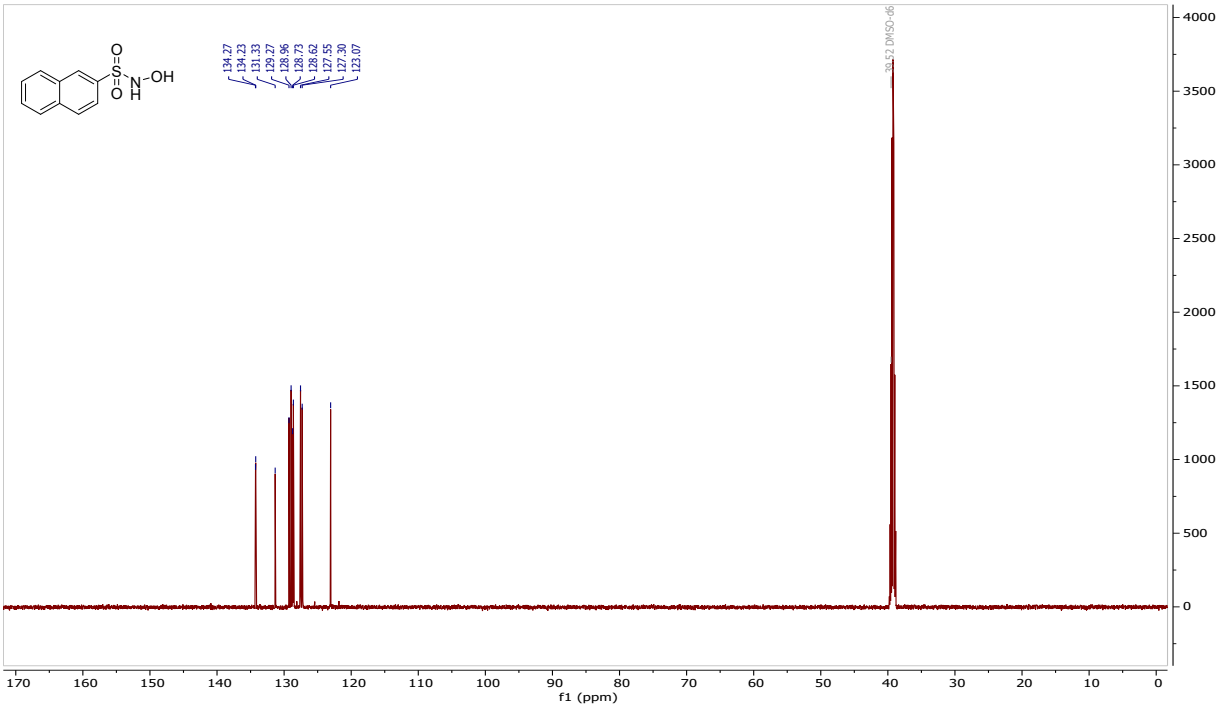


Figure S31. ^{13}C NMR spectrum of N-Hydroxynaphthalene-2-sulfonamide (2o)

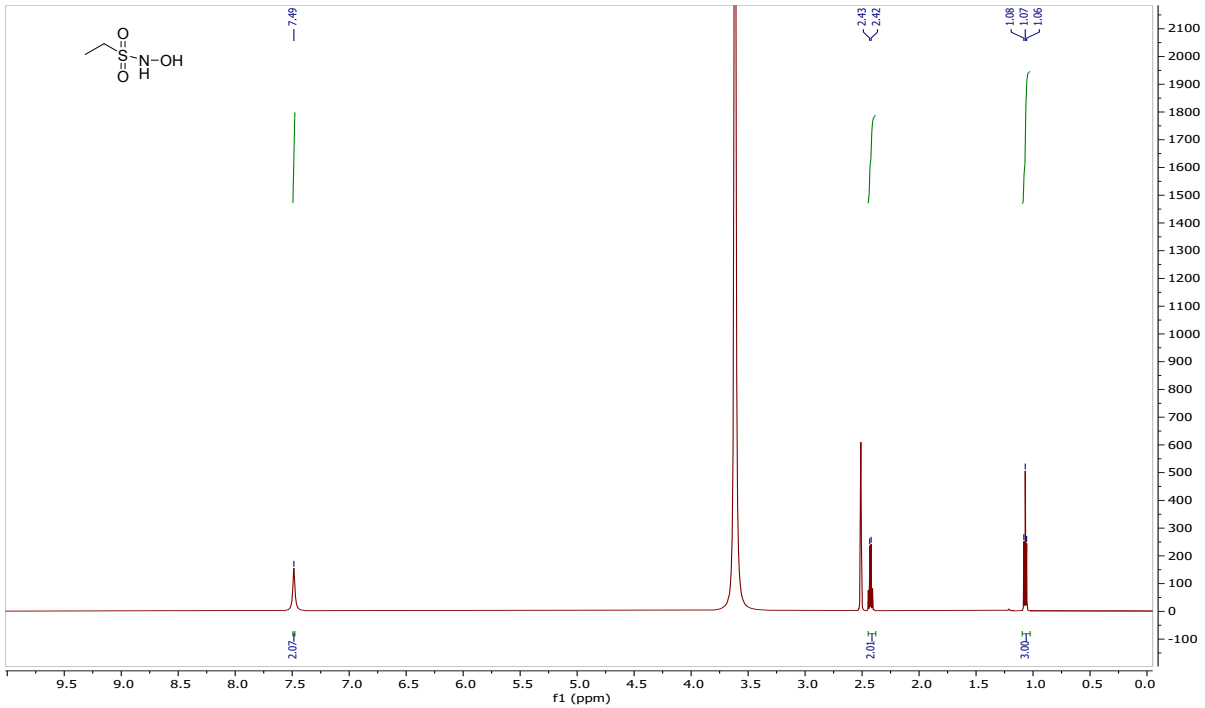


Figure S32. ^{1}H NMR spectrum of N-Hydroxyethanesulfonamide (2p)

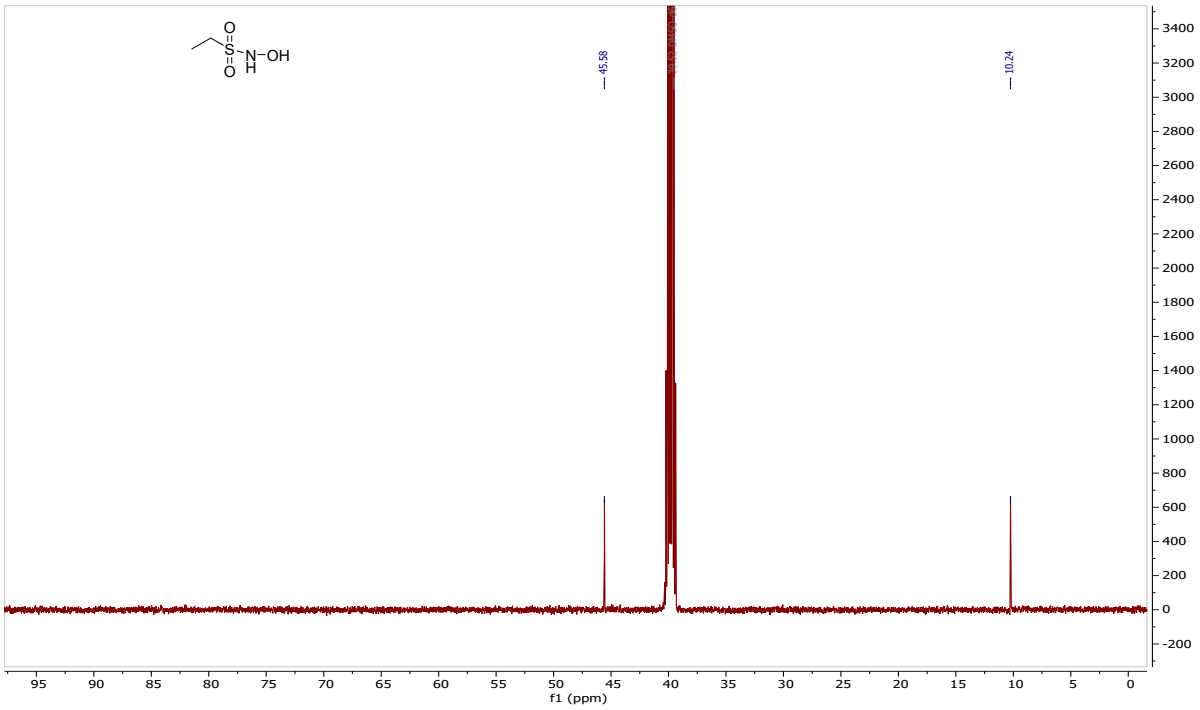


Figure S33. ^{13}C NMR spectrum of N-Hydroxyethanesulfonamide (2p)

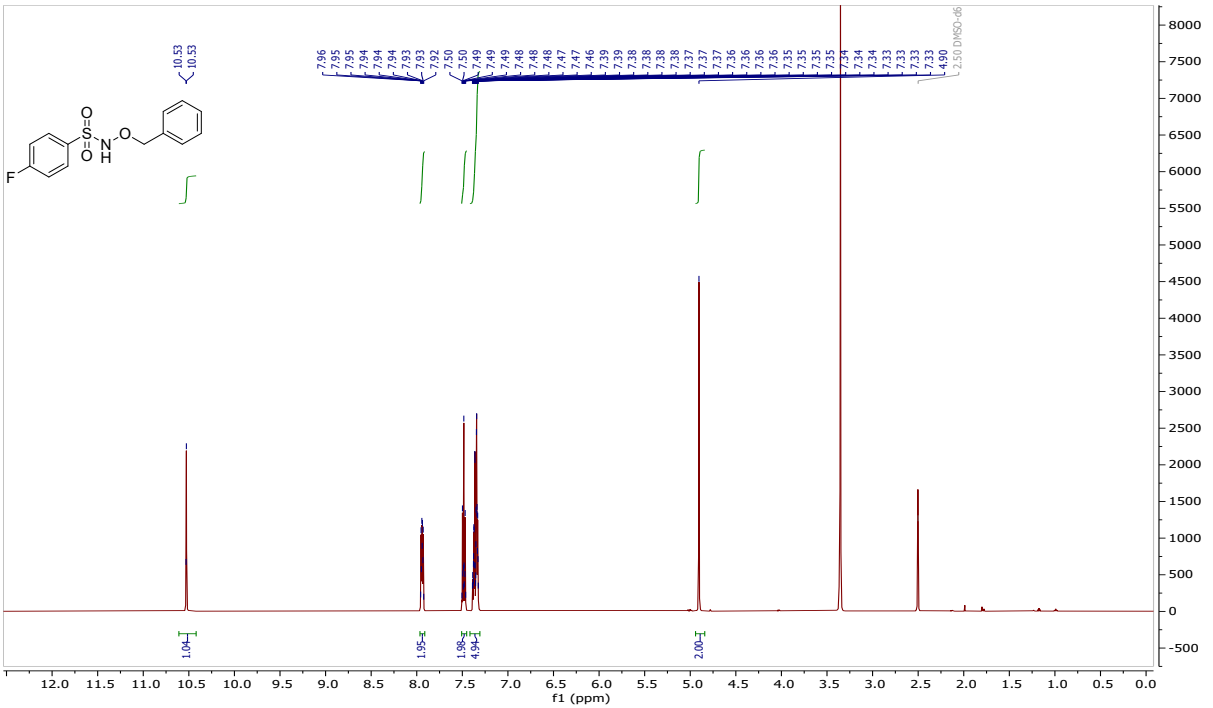


Figure S34. ^{1}H NMR spectrum of N-(Benzyloxy)-4-Fluorobenzenesulfonamide (2a')

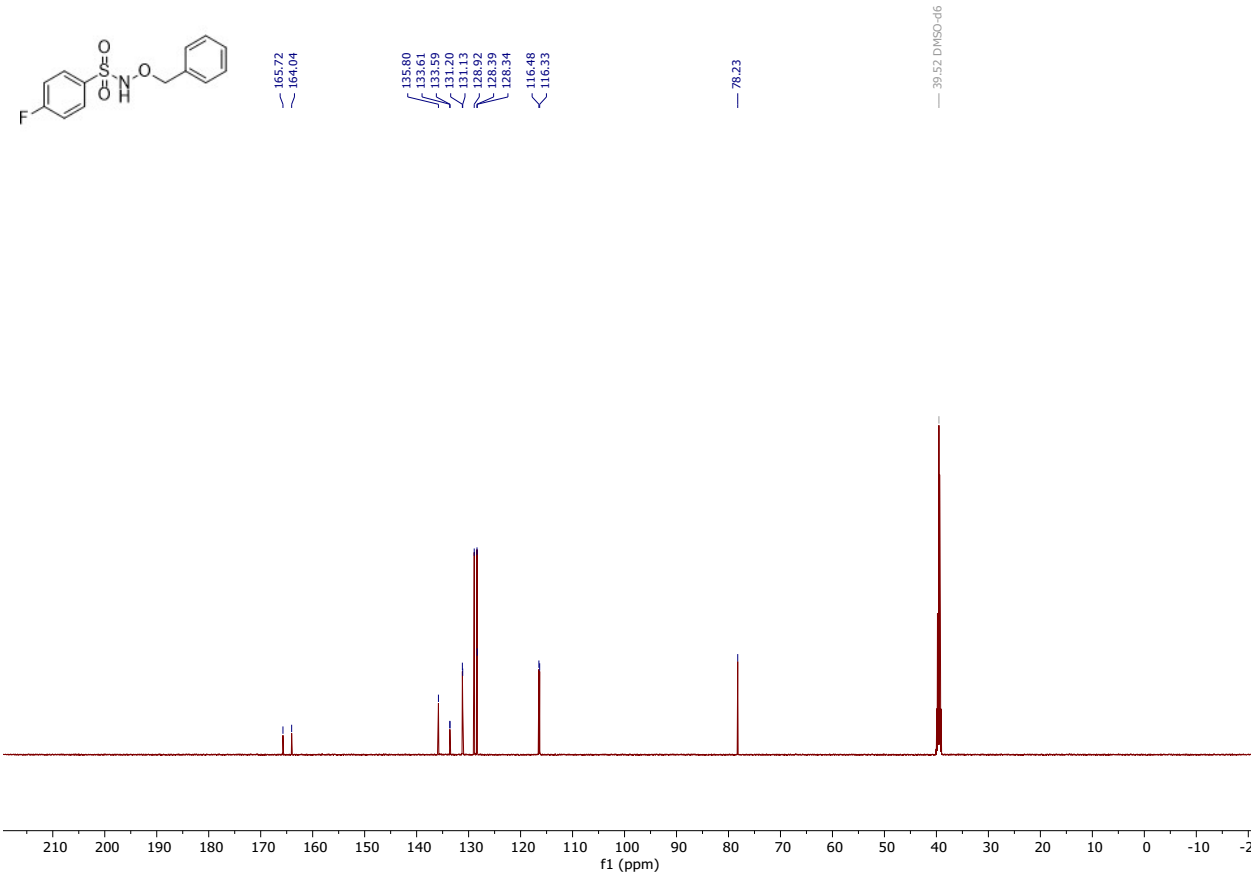


Figure S35. ^{13}C NMR spectrum of N-(Benzyloxy)-4-Fluorobenzenesulfonamide (2a')

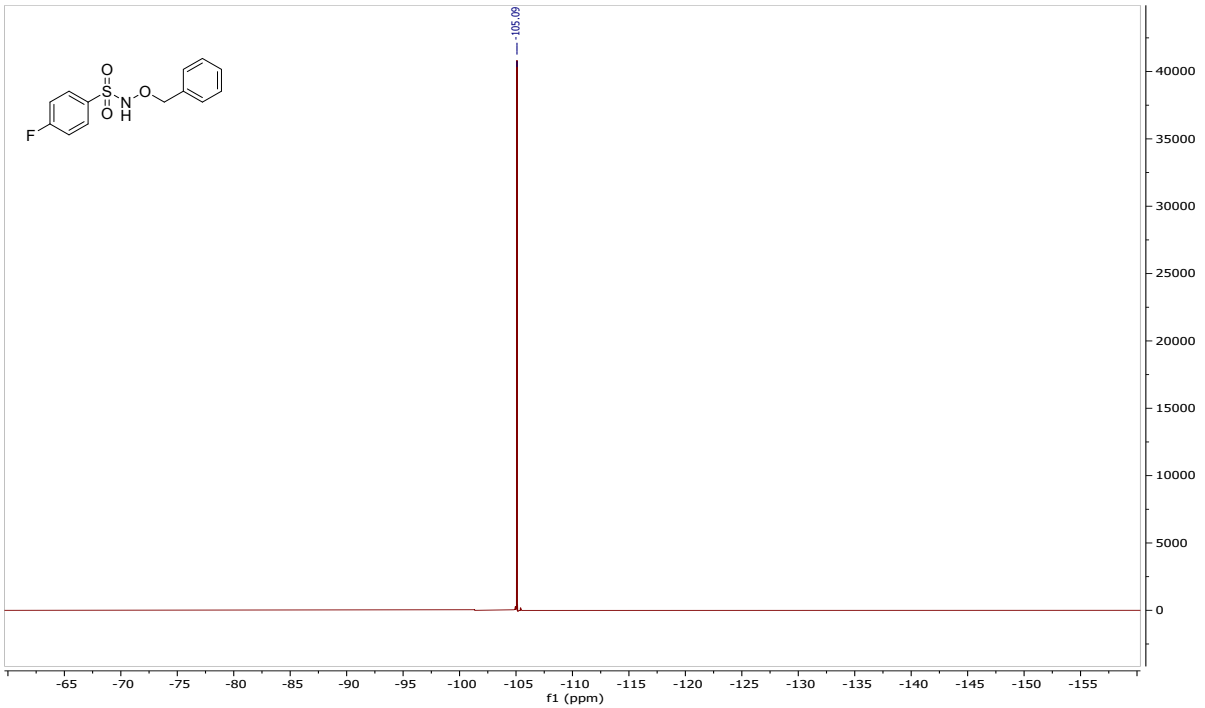


Figure S36. ^{19}F NMR spectrum of N-(Benzyloxy)-4-Fluorobenzenesulfonamide (2a')

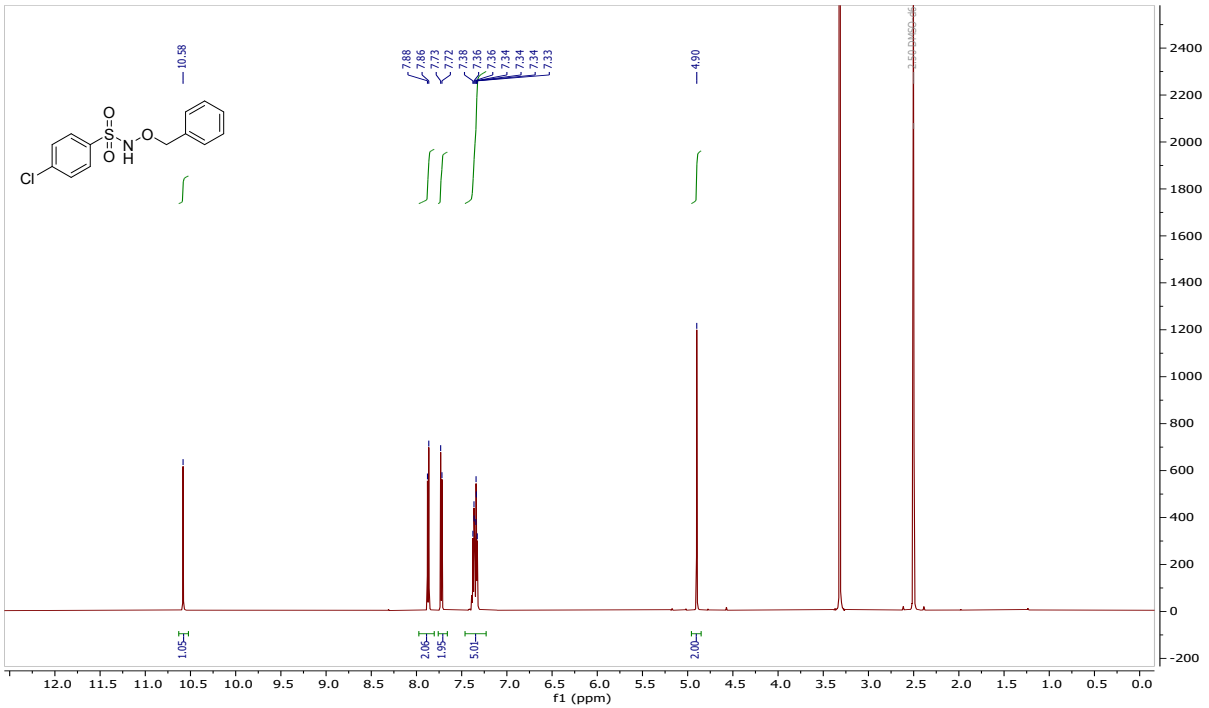


Figure S37. ^{1}H NMR spectrum of N-(Benzyloxy)-4-Chlorobenzenesulfonamide (2b')

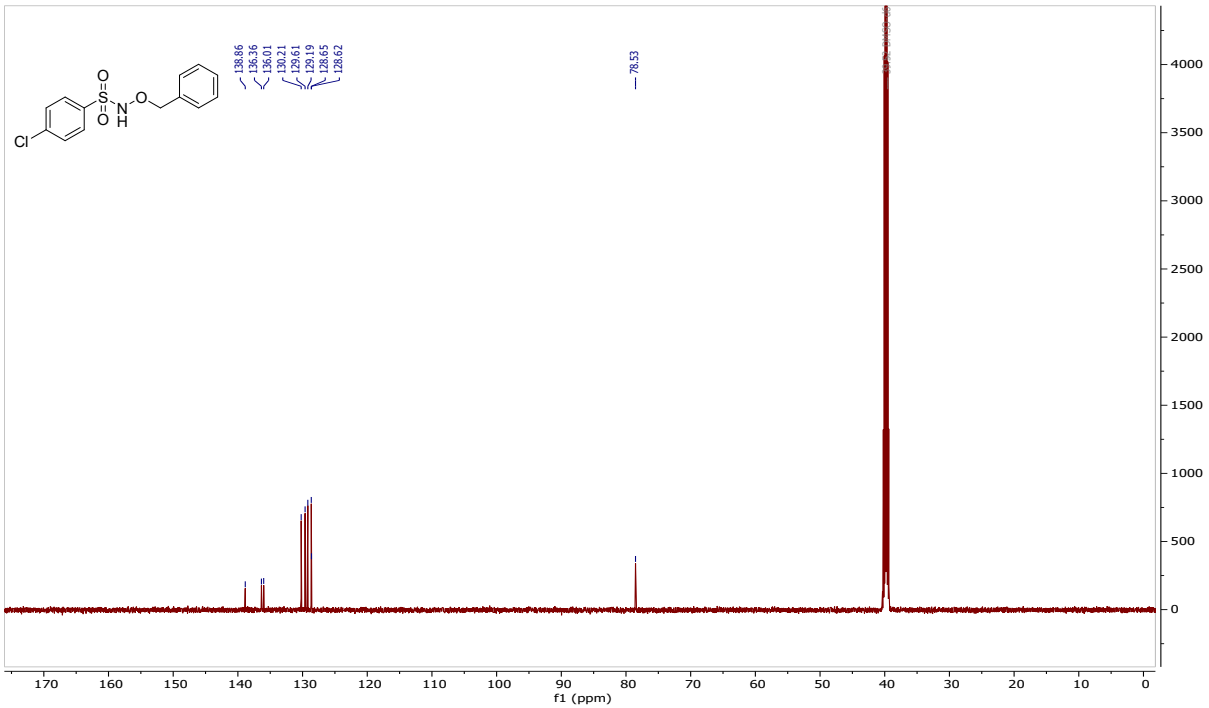


Figure S38. ^{13}C NMR spectrum of N-(Benzyloxy)-4-Chlorobenzenesulfonamide (2b')

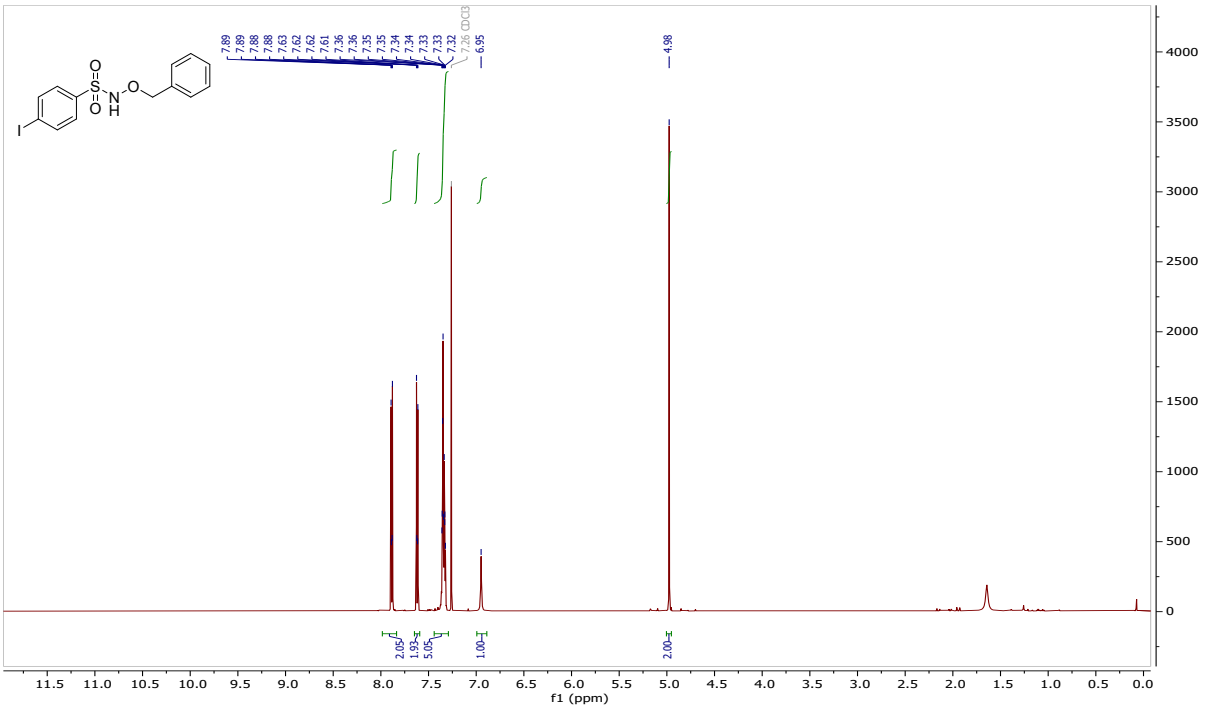


Figure S39. ^{1}H NMR spectrum of N-(Benzyloxy)-4-Iodobenzenesulfonamide (2d')

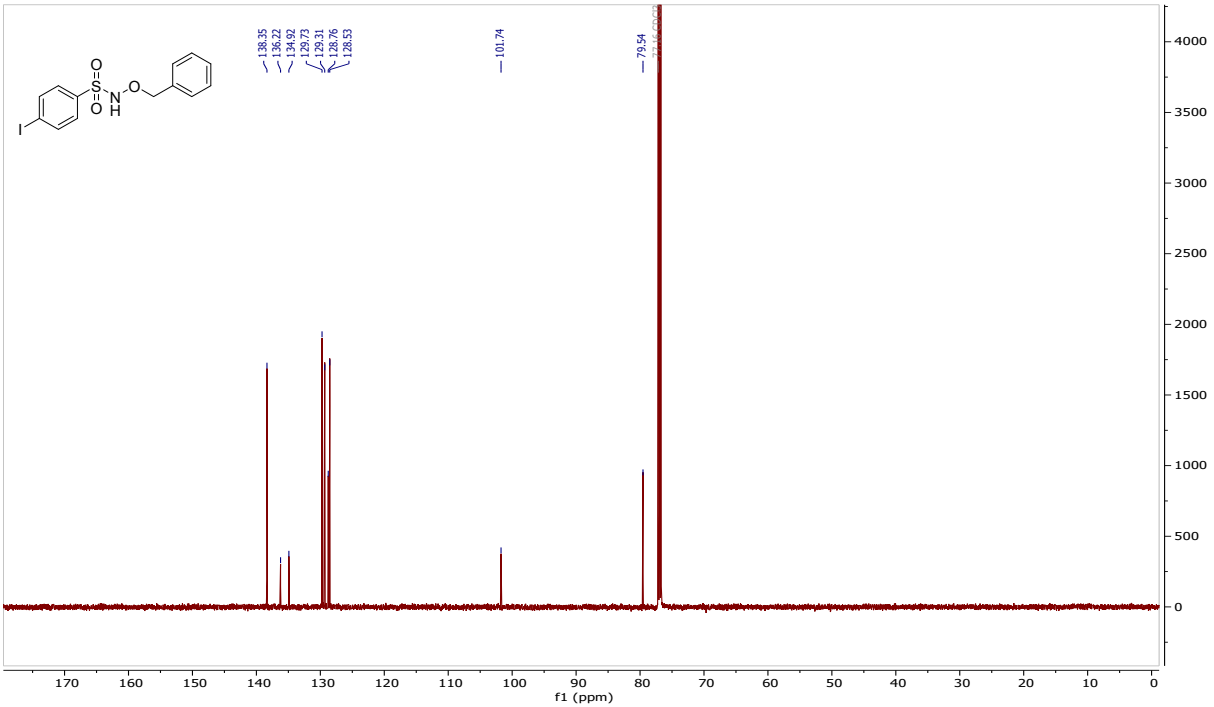


Figure S40. ^{13}C NMR spectrum of N-(Benzyloxy)-4-Iodobenzenesulfonamide (2d')

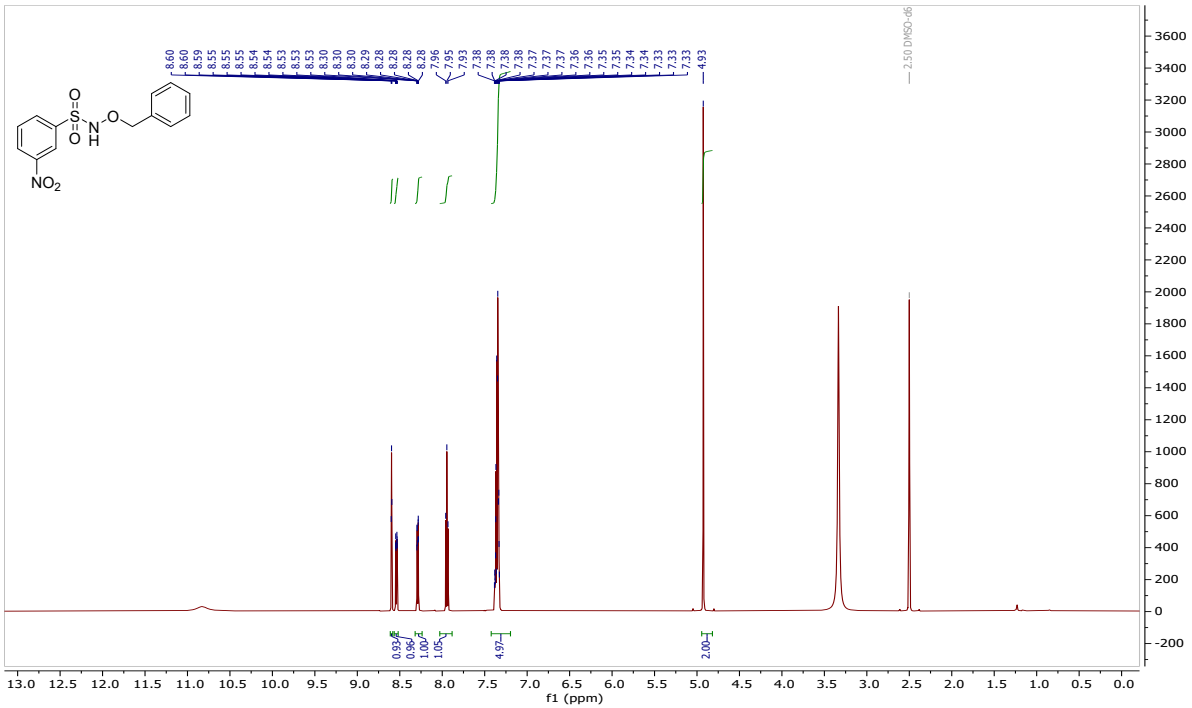


Figure S41. ^{1}H NMR spectrum of N-(Benzyloxy)-3-Nitrobenzenesulfonamide (2h')

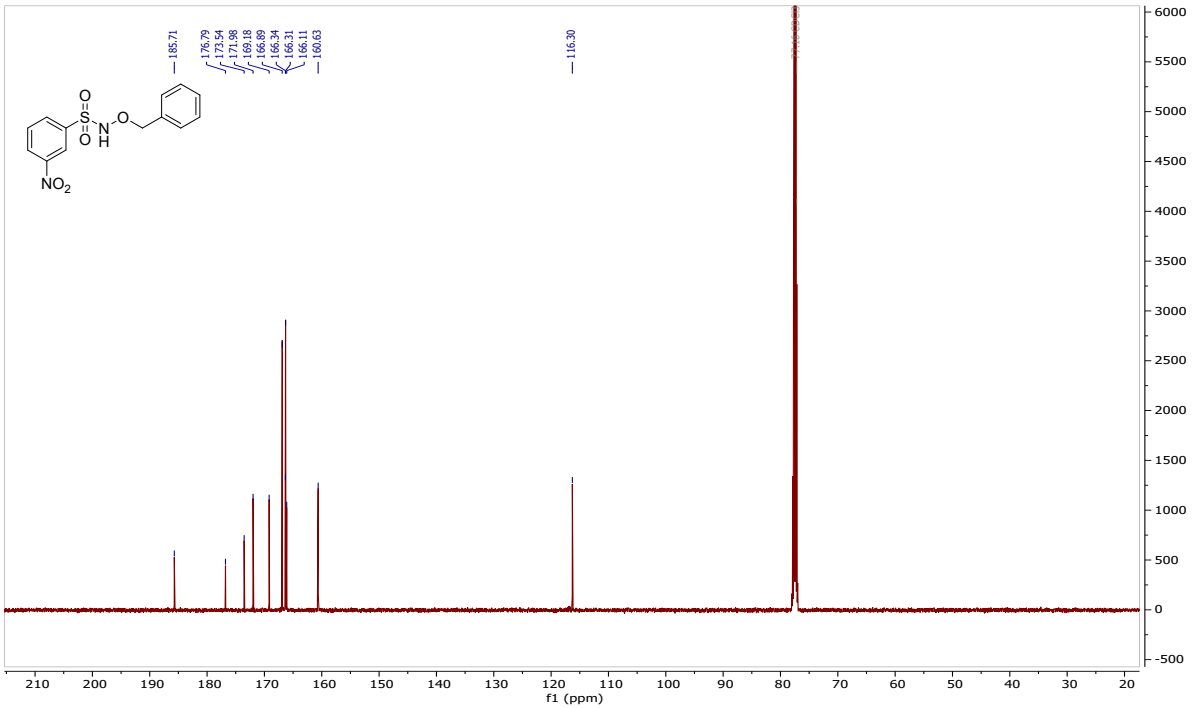


Figure S42. ^{13}C NMR spectrum of N-(Benzyloxy)-3-Nitrobenzenesulfonamide (2h')

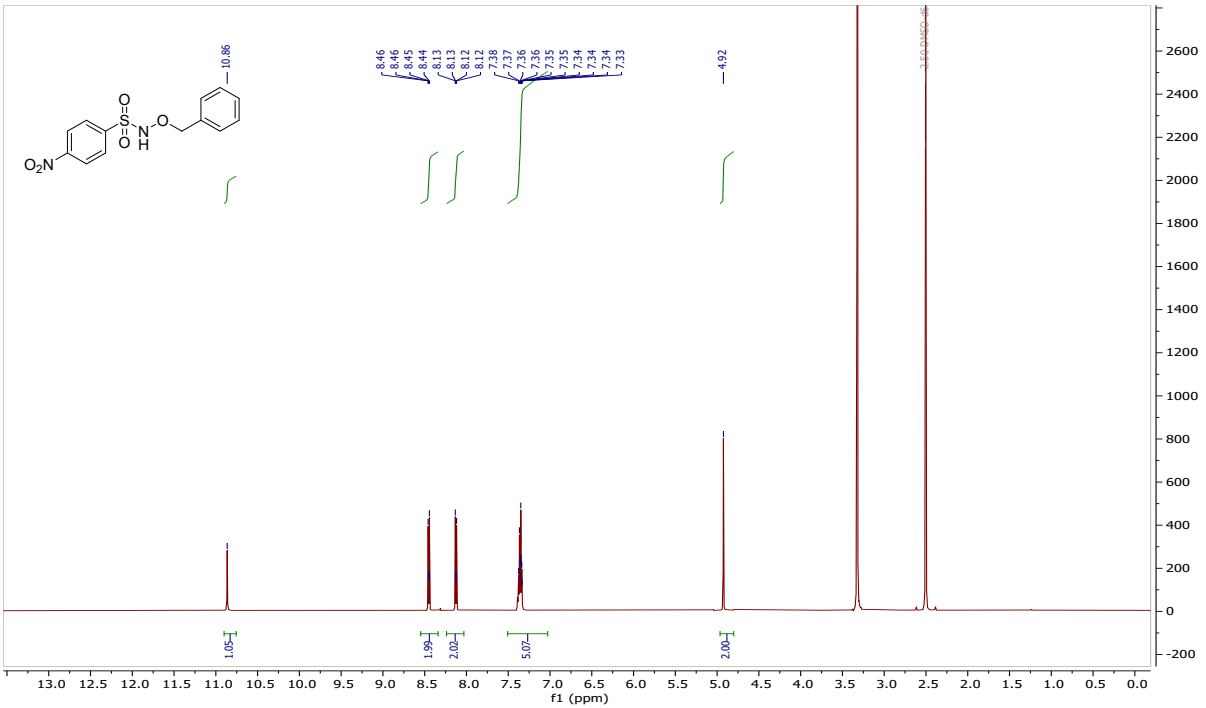


Figure S43. ^{1}H NMR spectrum of N-(Benzyloxy)-4-Nitrobenzenesulfonamide (2i')

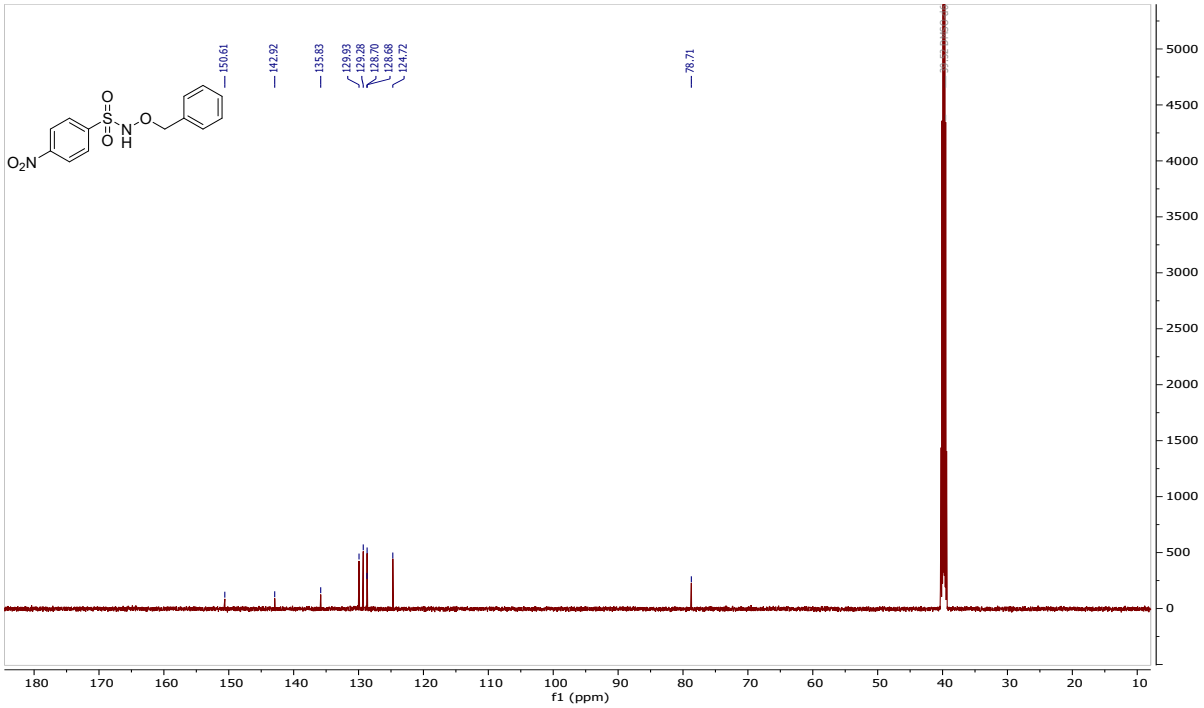


Figure S44. ^{13}C NMR spectrum of N-(Benzyloxy)-4-Nitrobenzenesulfonamide (2i')

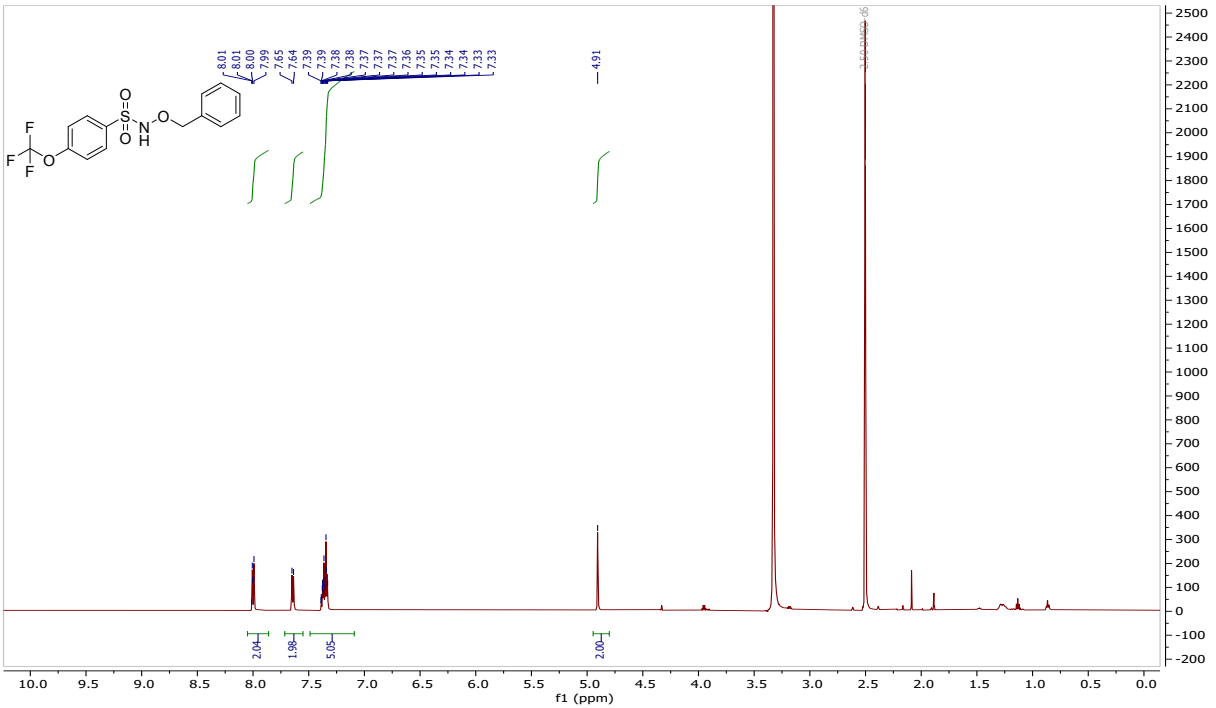


Figure S45. ^{1}H NMR spectrum of N-(Benzyloxy)-4-(trifluoromethoxy)benzenesulfonamide (2l')

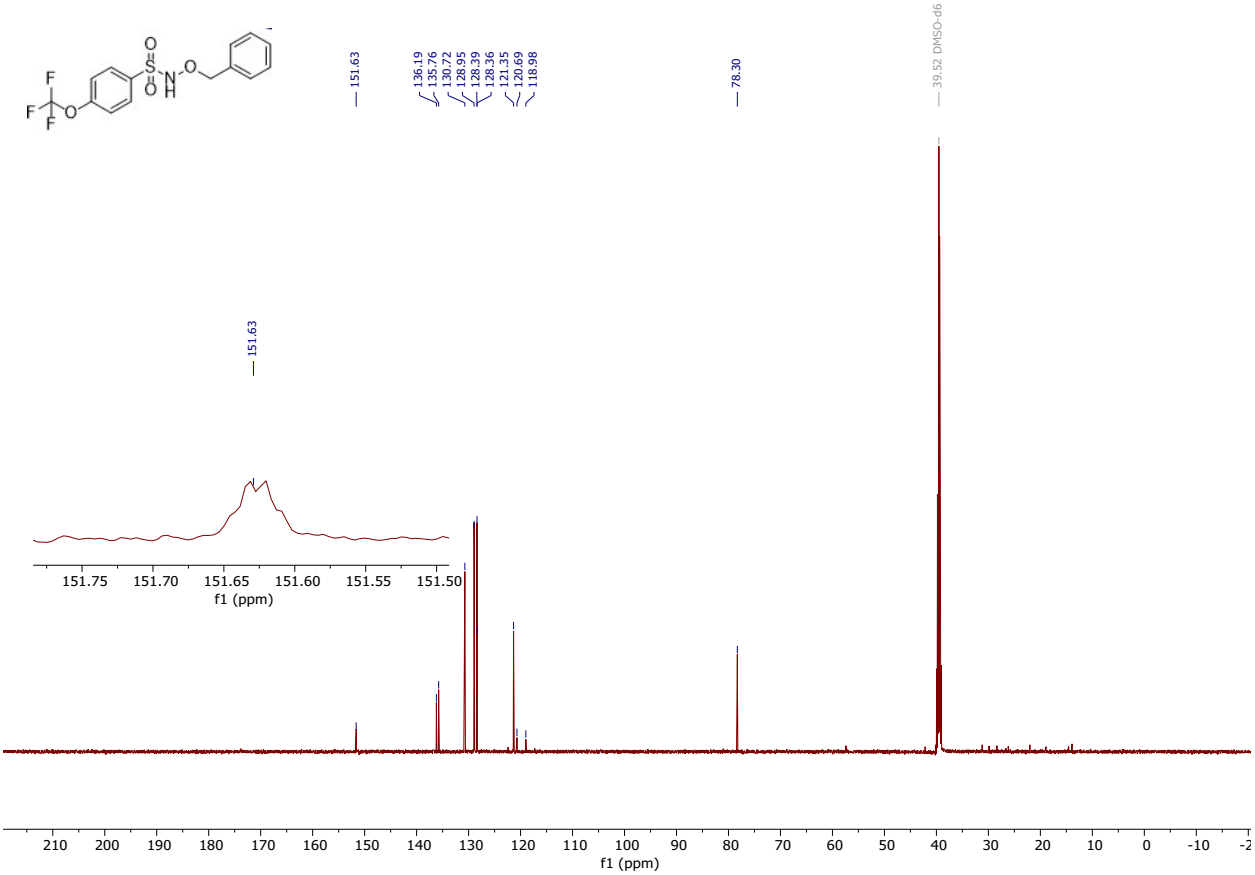


Figure S46. ^{13}C NMR spectrum of N-(Benzyloxy)-4-(trifluoromethoxy)benzenesulfonamide (2l')

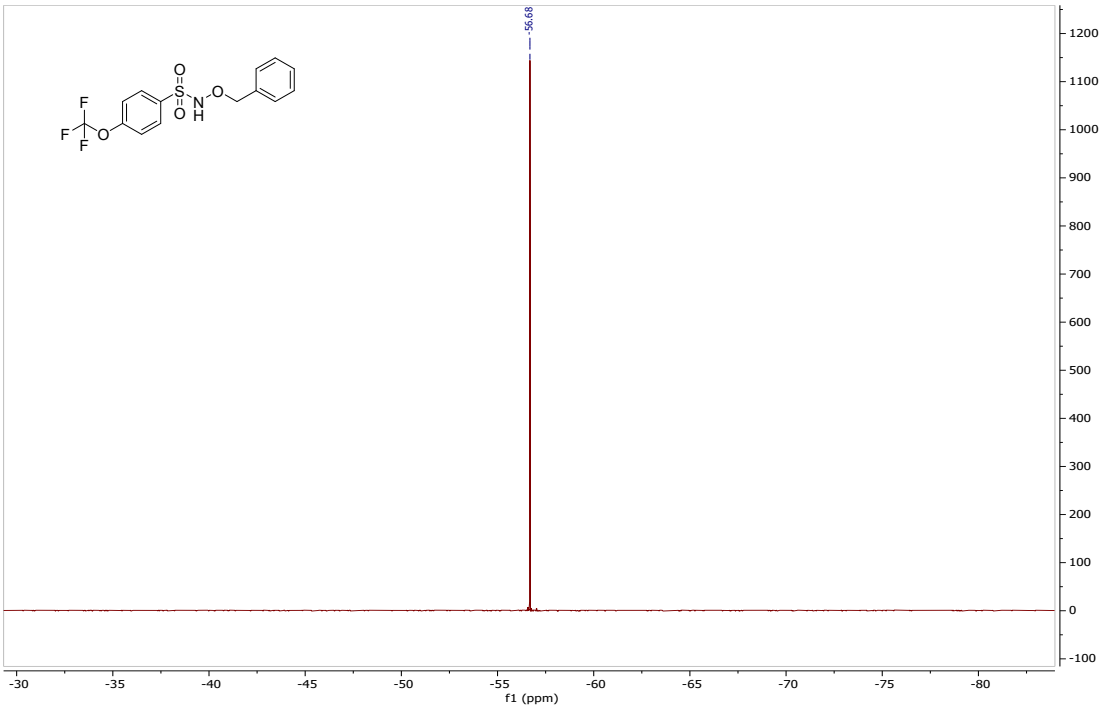


Figure S47. ^{19}F NMR spectrum of N-(Benzyloxy)-4-(trifluoromethoxy)benzenesulfonamide (2l')

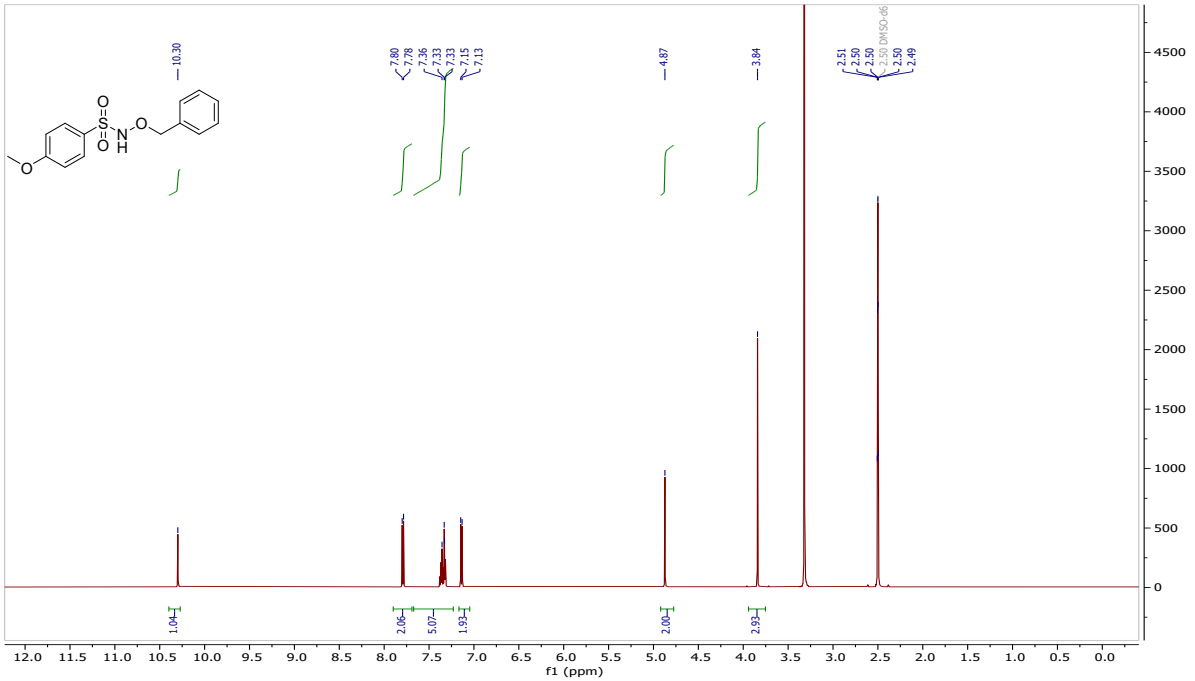


Figure S48. ^{1}H NMR spectrum of N-(Benzyloxy)-4-Methoxybenzenesulfonamide (2m')

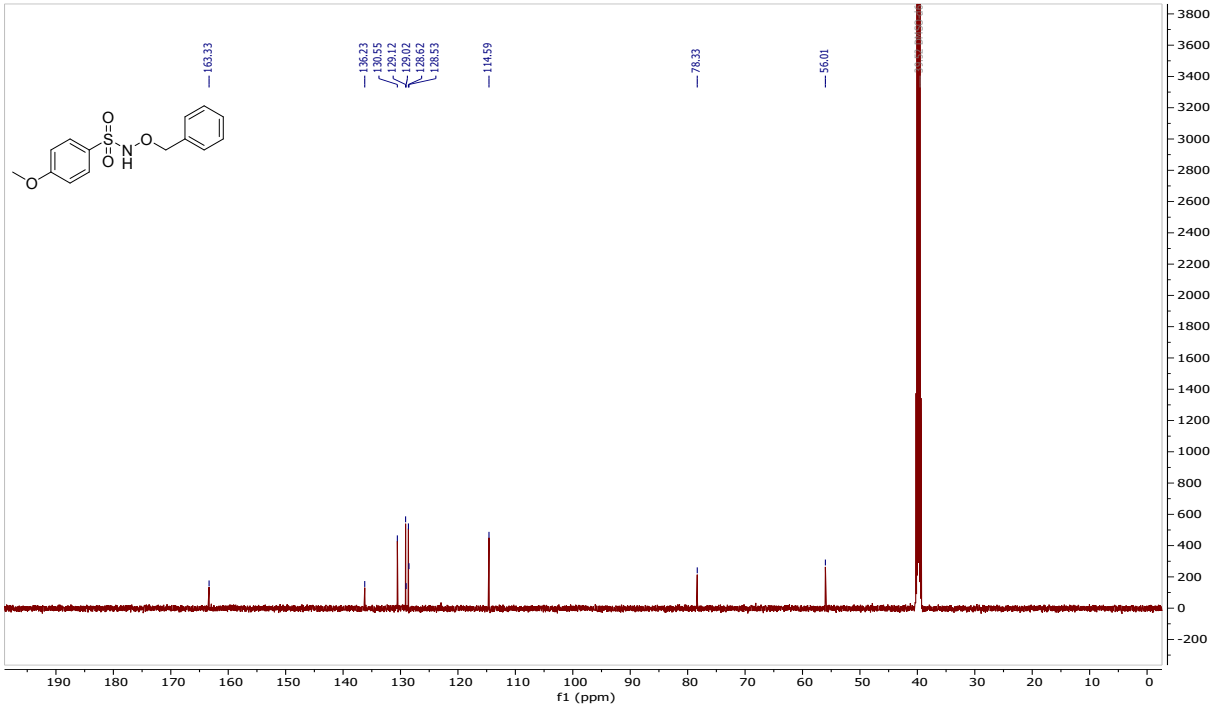


Figure S49. ^{13}C NMR spectrum of N-(Benzyloxy)-4-Methoxybenzenesulfonamide (2m')

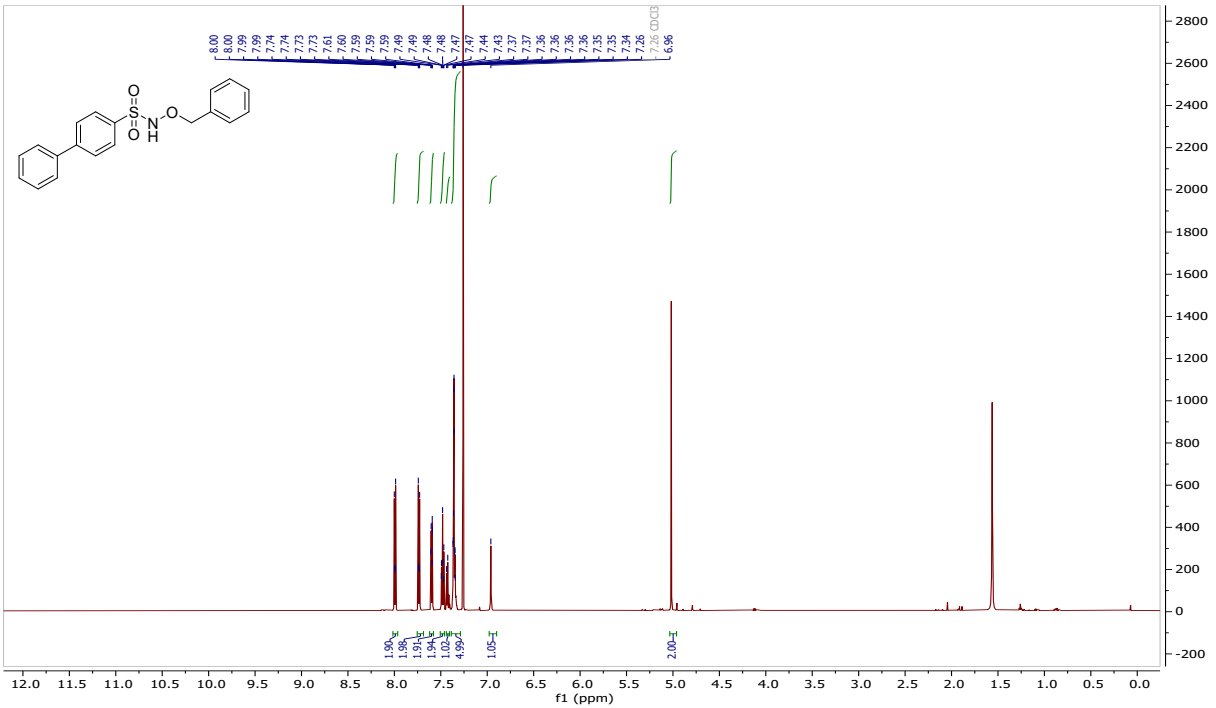


Figure S50. ^{1}H NMR spectrum of N-(Benzyloxy)-[1,1'-biphenyl]-4-sulfonamide (2n')

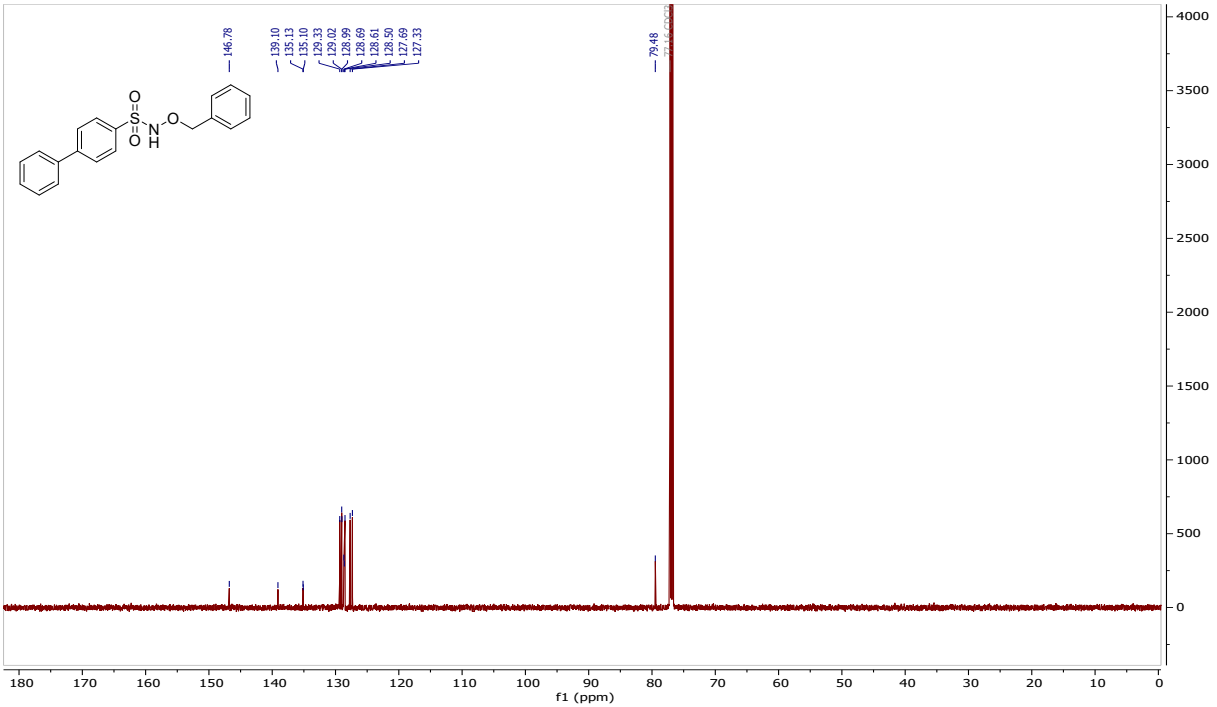


Figure S51. ^{13}C NMR spectrum of N-(Benzyloxy)-[1,1'-biphenyl]-4-sulfonamide (2n')

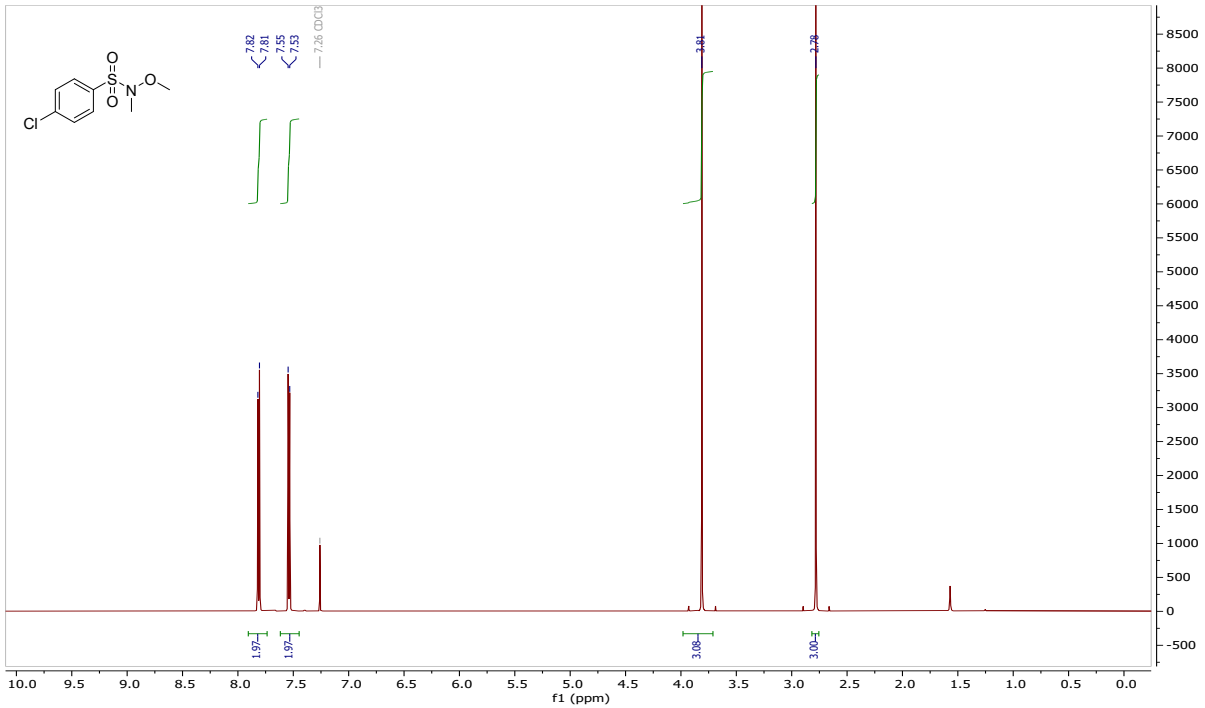


Figure S52. ^{1}H NMR spectrum of 4-Chloro-N-Methoxy-N-Methylbenzenesulfonamide (2b'')

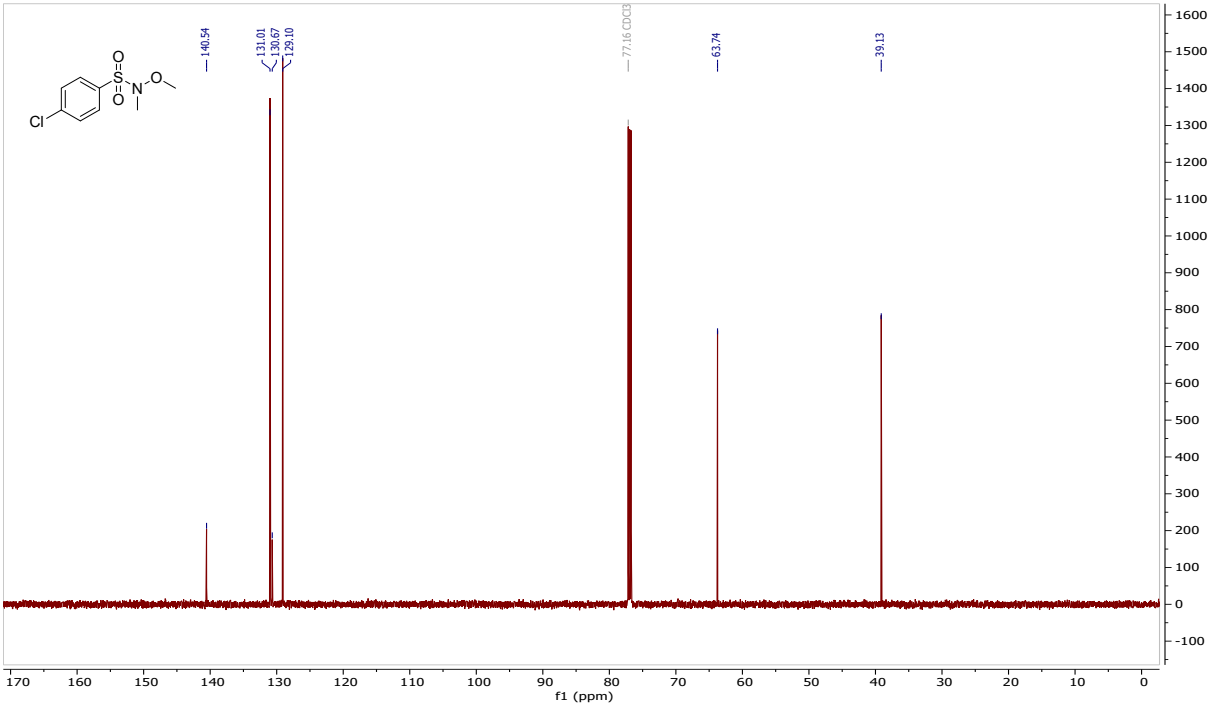


Figure S53. ^{13}C NMR spectrum of 4-Chloro-N-Methoxy-N-Methylbenzenesulfonamide (2b'')

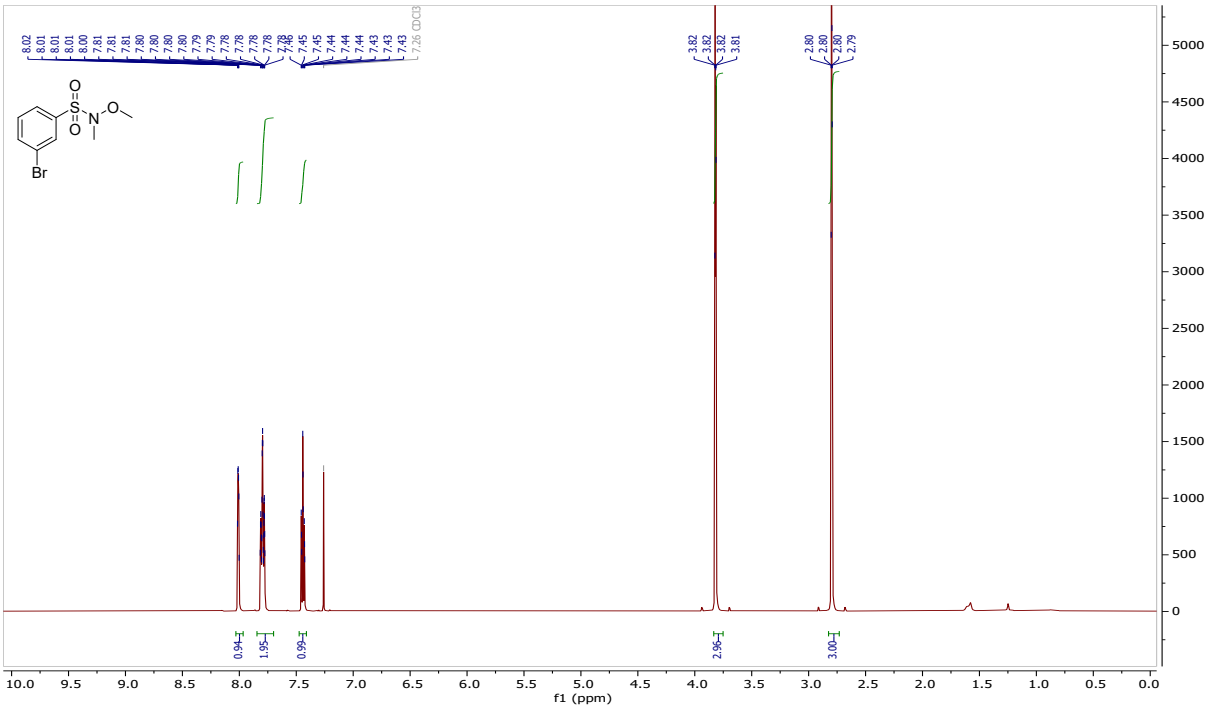


Figure S54. [1]H NMR spectrum of 3-Bromo-N-Methoxy-N-Methylbenzenesulfonamide (2c")

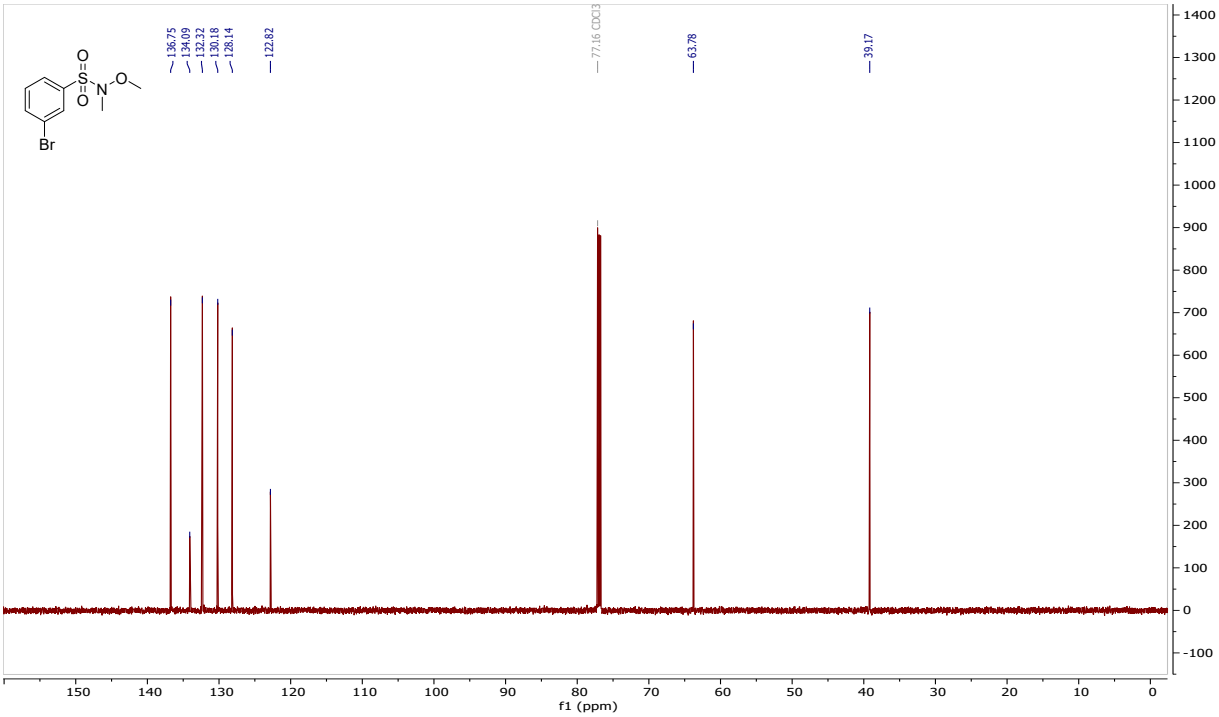


Figure S55. [13]C NMR spectrum of 3-Bromo-N-Methoxy-N-Methylbenzenesulfonamide (2c")

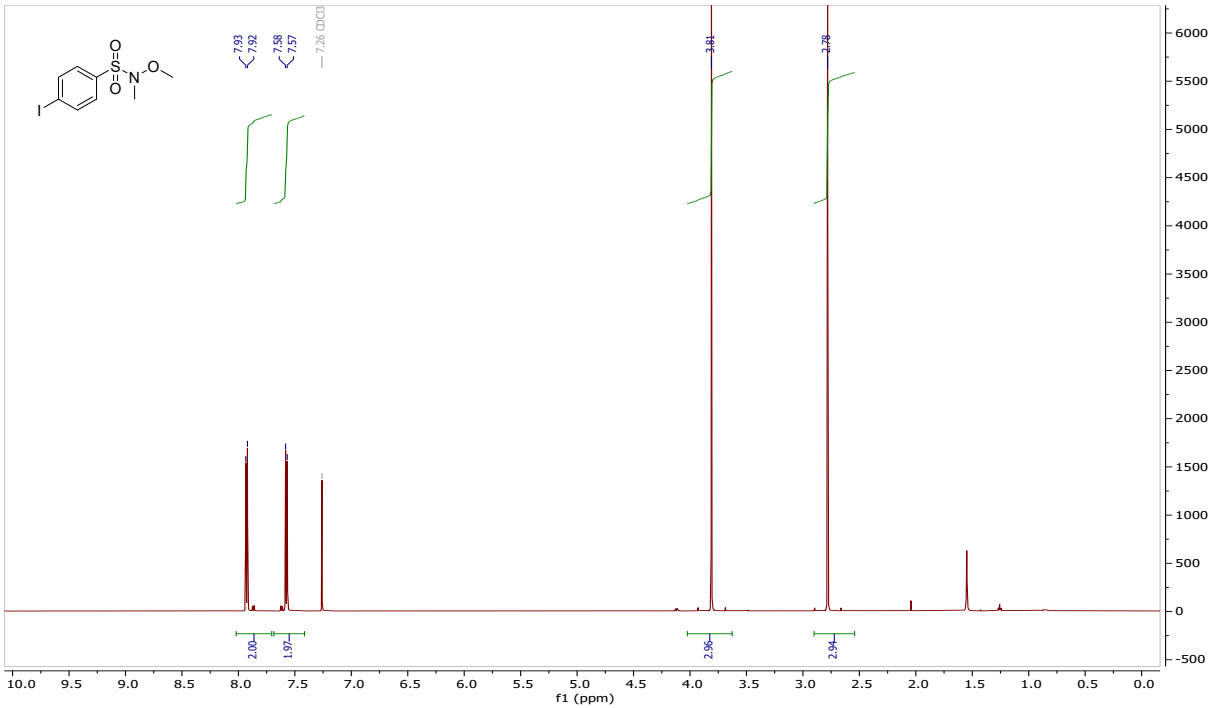


Figure S56. ^{1}H NMR spectrum of 4-Iodo-N-Methoxy-N-Methylbenzenesulfonamide (2d")

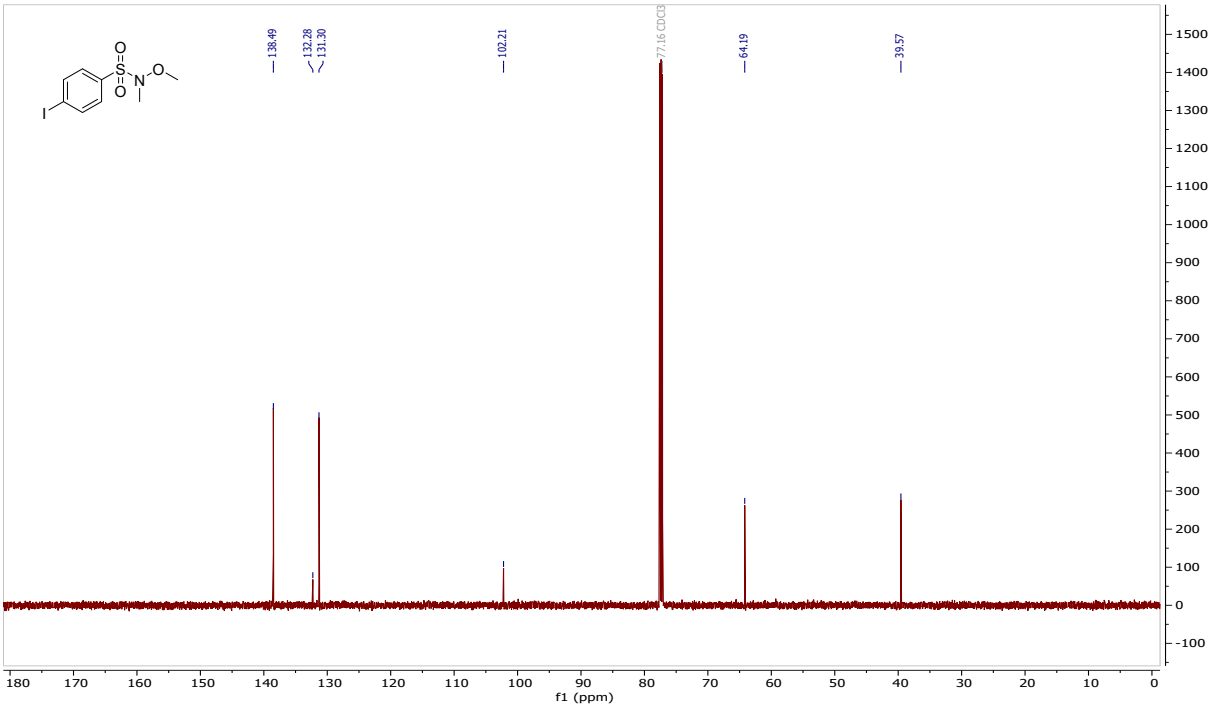


Figure S57. ^{13}C NMR spectrum of 4-Iodo-N-Methoxy-N-Methylbenzenesulfonamide (2d")

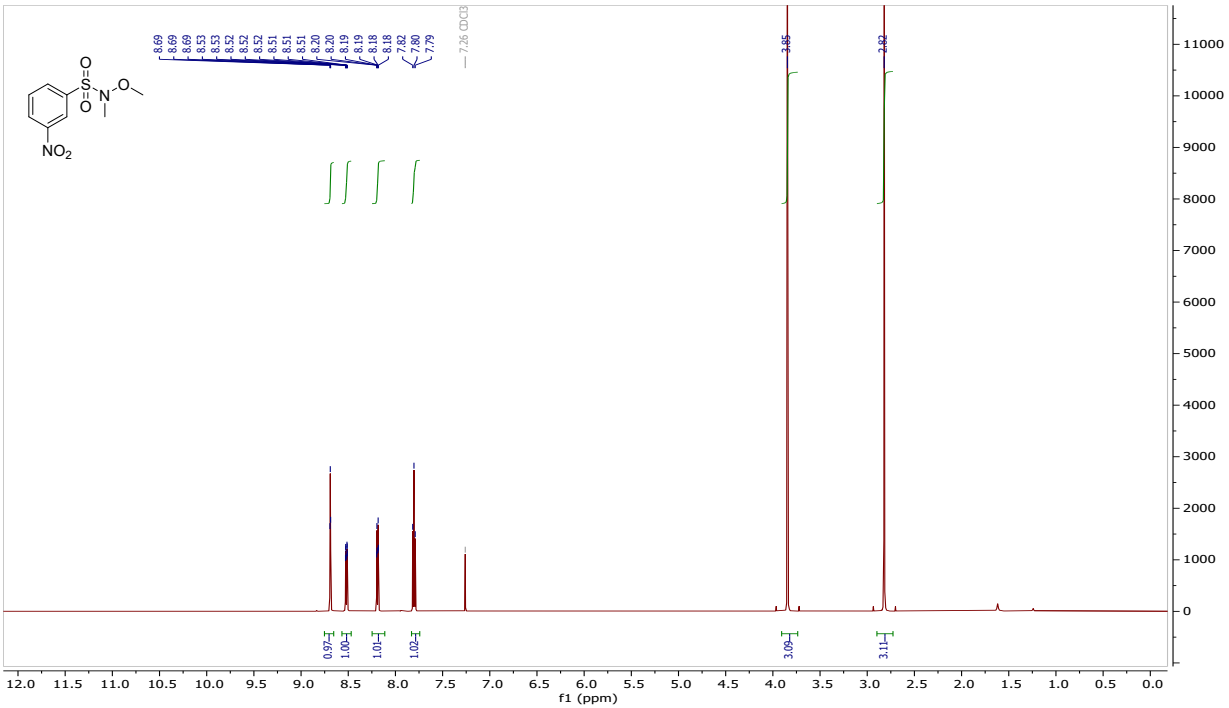


Figure S58. ^{1}H NMR spectrum of N-Methoxy-N-Methyl-3-Nitrobenzenesulfonamide (2h'')

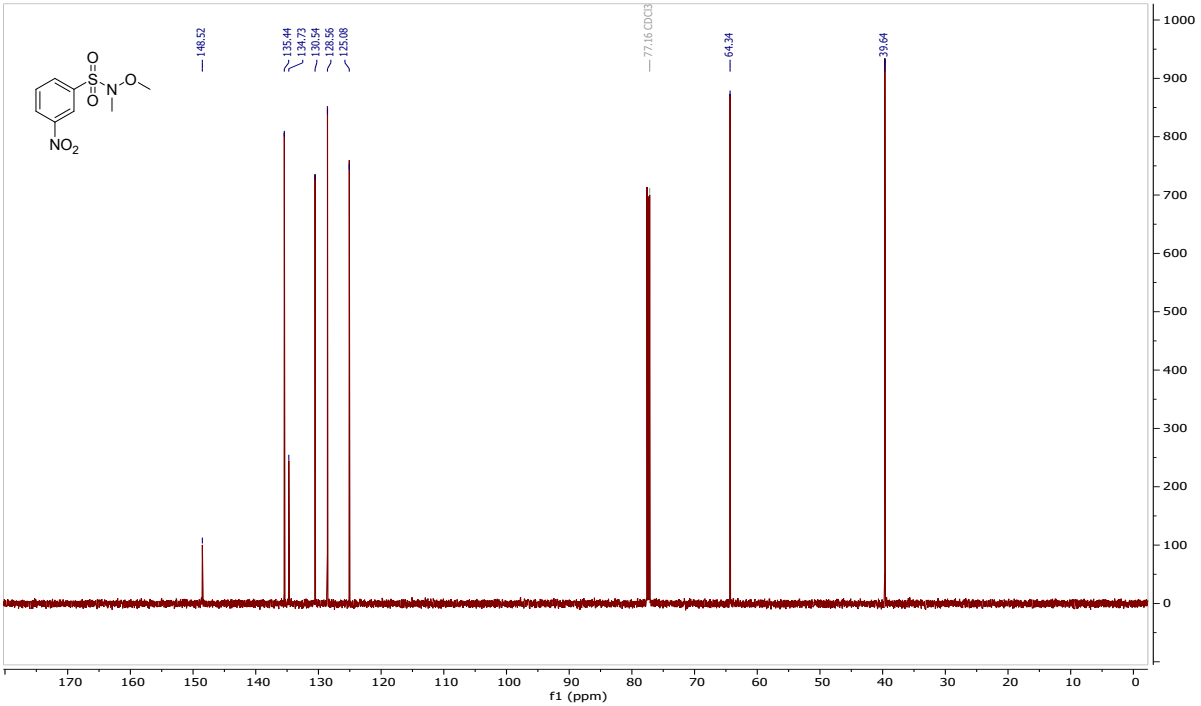


Figure S59. ^{13}C NMR spectrum of N-Methoxy-N-Methyl-3-Nitrobenzenesulfonamide (2h'')

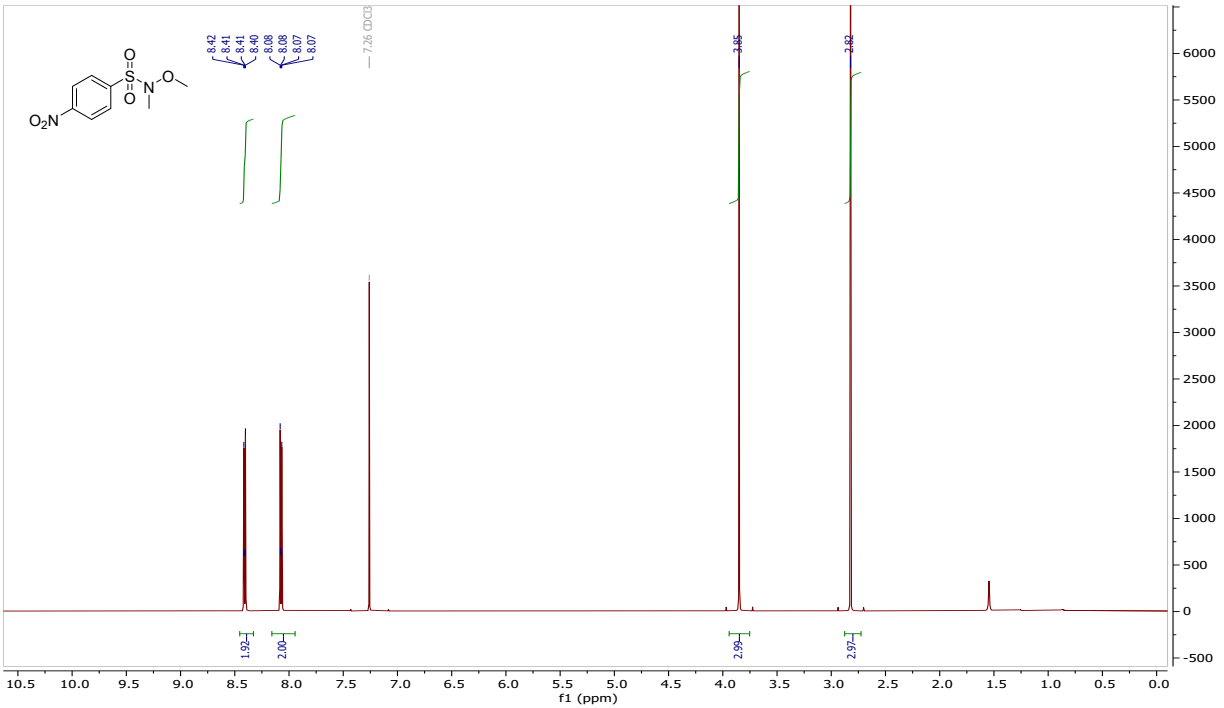


Figure S60. ^{1}H NMR spectrum of N-Methoxy-N-Methyl-4-Nitrobenzenesulfonamide (2i")

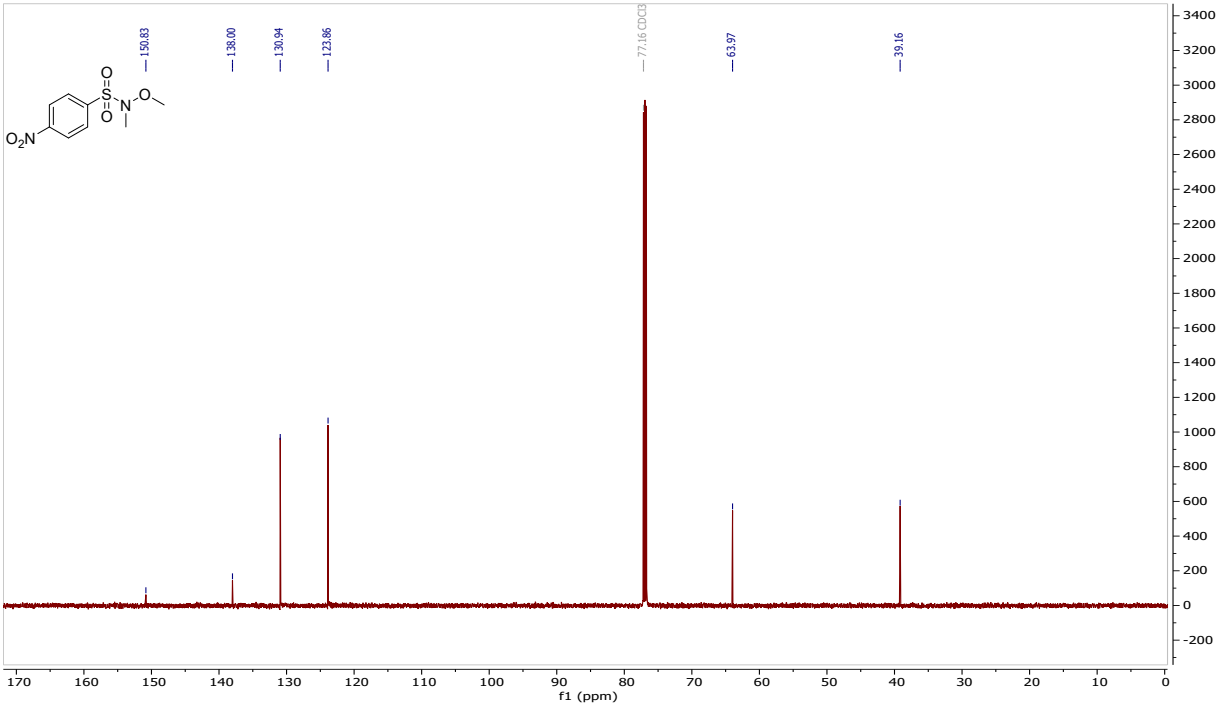


Figure S61. ^{13}C NMR spectrum of N-Methoxy-N-Methyl-4-Nitrobenzenesulfonamide (2i")

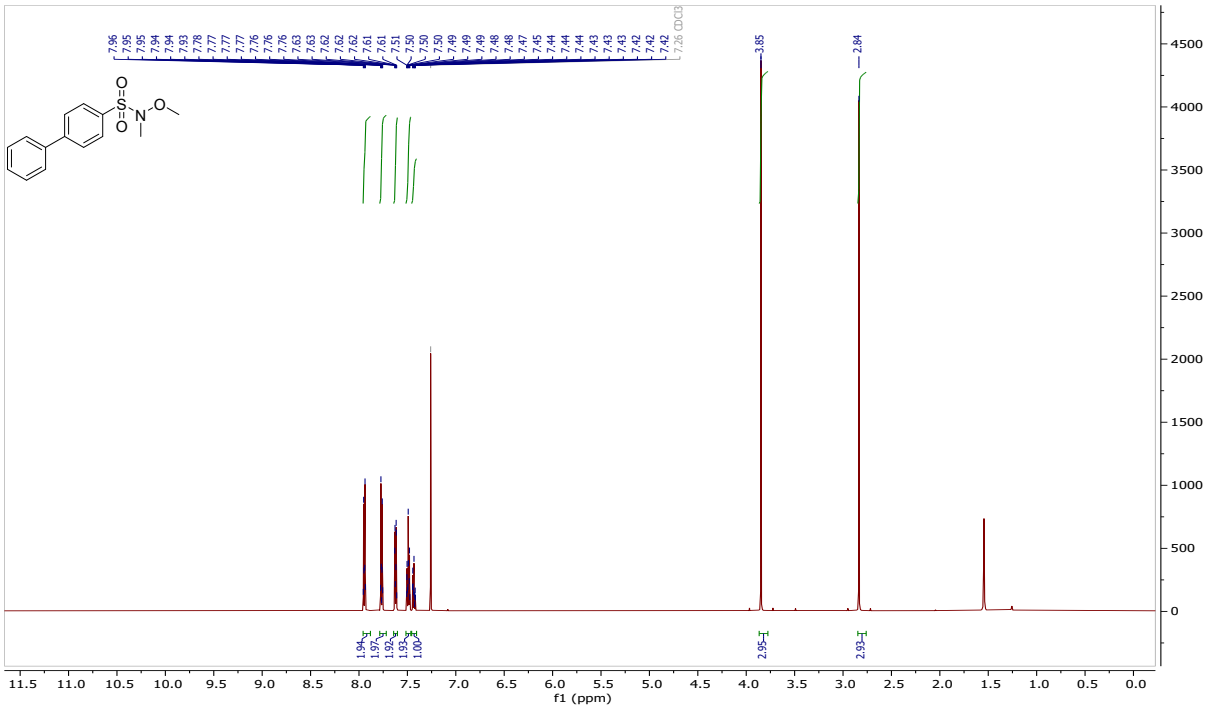


Figure S62. ^{1}H NMR spectrum of N-methoxy-N-methyl-[1,1'-biphenyl]-4-sulfonamide (2n")

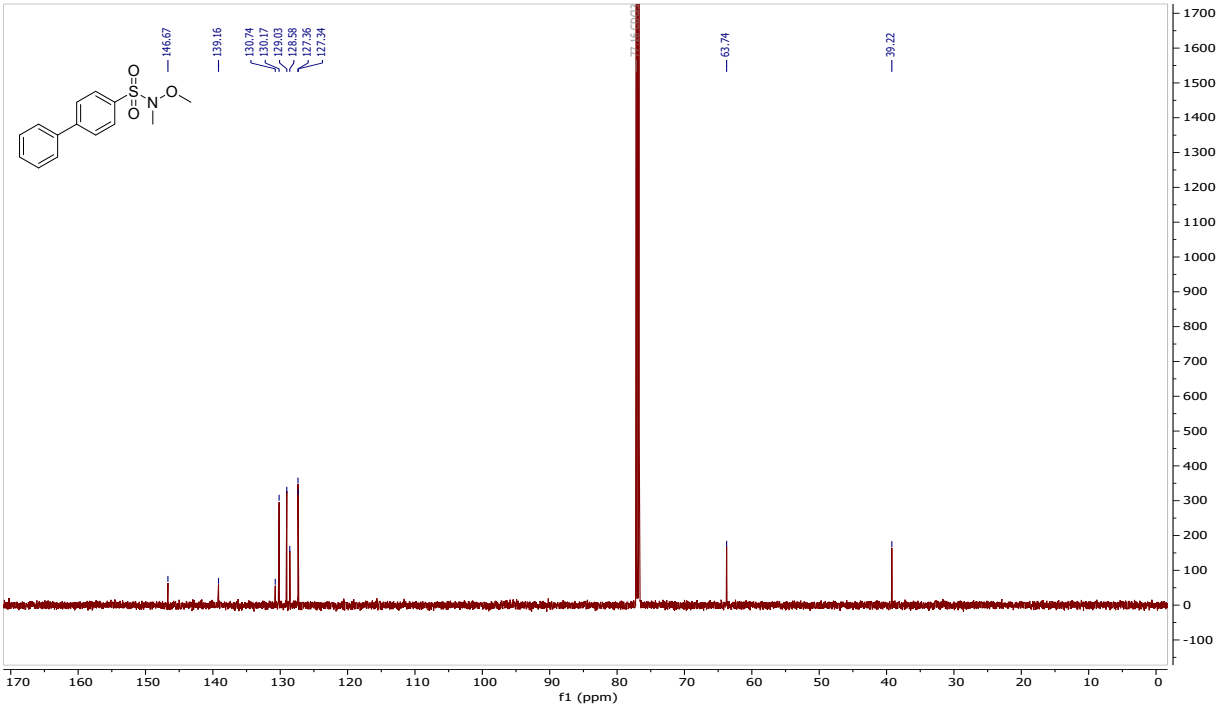


Figure S63. ^{13}C NMR spectrum of N-methoxy-N-methyl-[1,1'-biphenyl]-4-sulfonamide (2n")

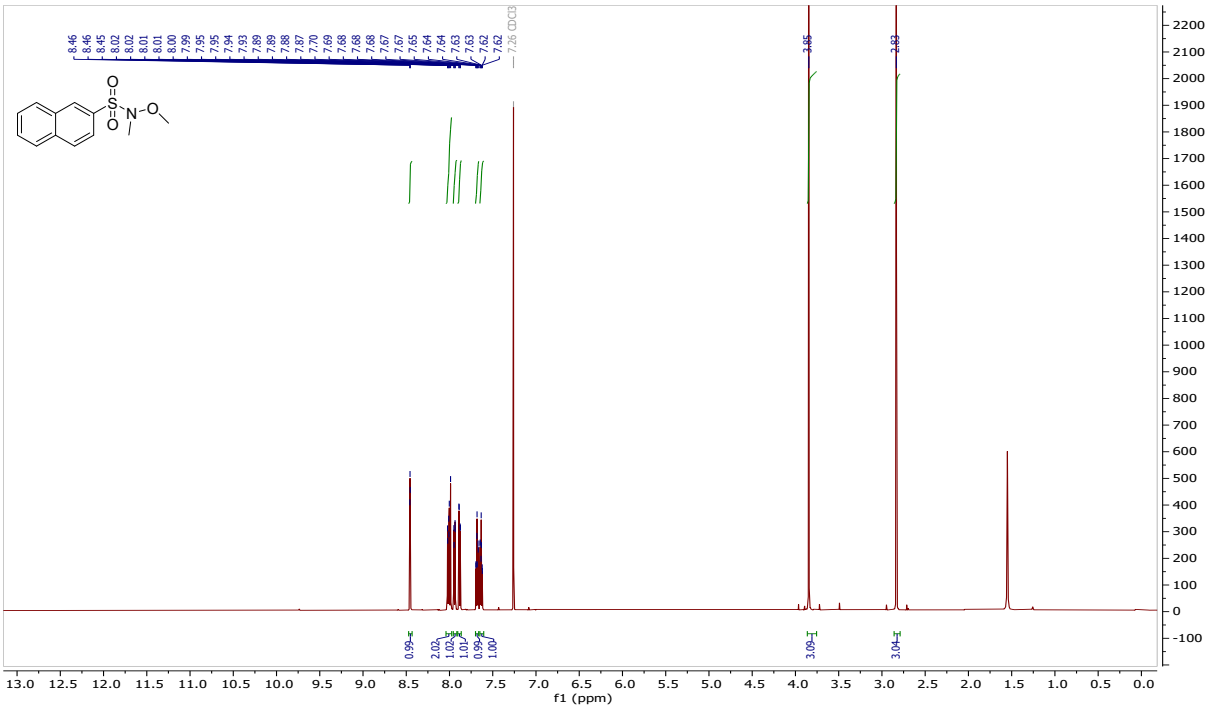


Figure S64. ^{1}H NMR spectrum of N-Methoxy-N-Methylnaphthalene-2-sulfonamide (2o")

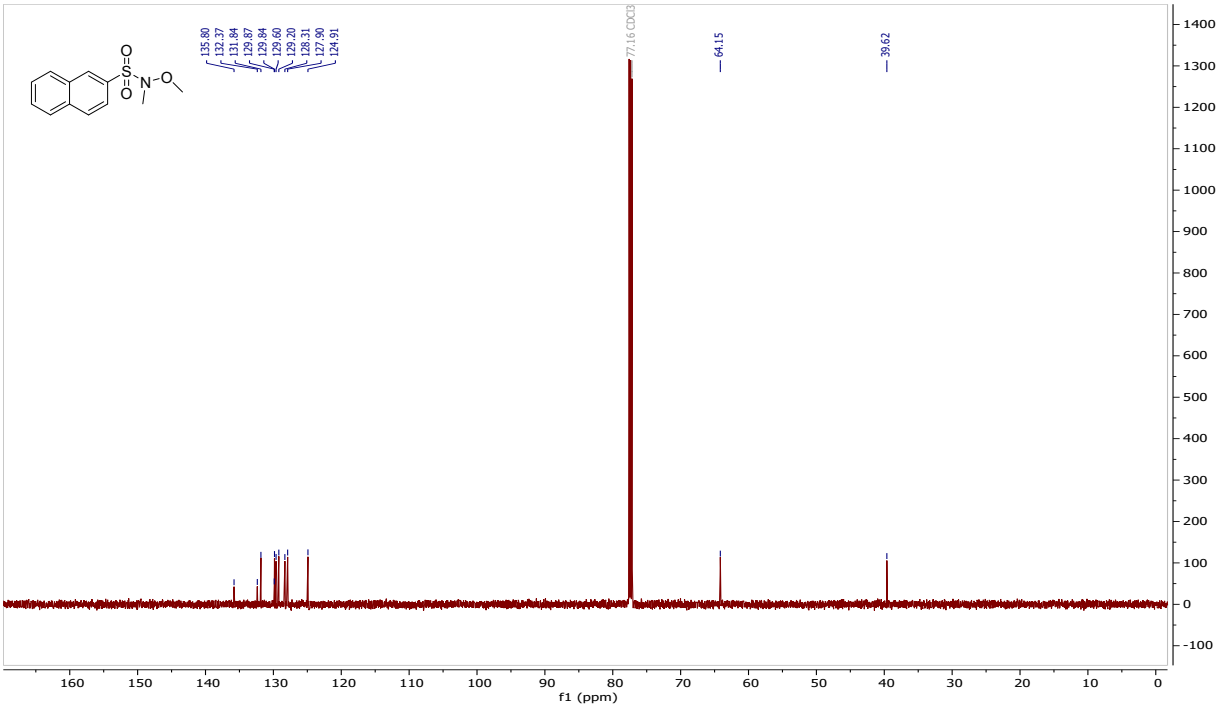


Figure S65. ^{13}C NMR spectrum of N-Methoxy-N-Methylnaphthalene-2-sulfonamide (2o")

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