SUPPORTING INFORMATION

Palladium-Catalyzed α-Arylation of Methyl Sulfonamides with Aryl Chlorides

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TABLE OF CONTENTS

1. General Information

All reactions were carried out under an atmosphere of dry nitrogen. Anhydrous dioxane, CPME, and toluene were purchased from Sigma-Aldrich and used without further purification. THF was dried through activated alumina columns. Unless otherwise stated, all reagents were commercially available and used without further purification. Flash chromatography was performed with silica gel (300–400 mesh). The NMR spectra were obtained using a Brüker 500 MHz Fourier-transform NMR spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using chemical ionization (CI) or electrospray ionization (ESI) in positive or negative mode, depending on the analyte.

2. Preparation of Sulfonamides

Methyl sulfonamides were prepared according to literatures.[1]

3. High-throughput Experimentation Screening for Palladium-Catalyzed α-Arylation of Methyl Sulfonamides with Aryl Chlorides:

(1) Screening of ligands:

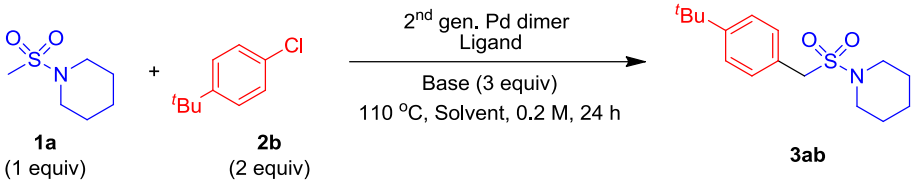
Set up:

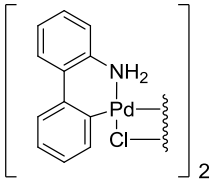
Two 24-Well Plate:

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with Buchwald-type 2nd generation palladium dimer (0.5 μmol) and the phosphine ligands (2 μmol for monodentate ligands and 1 μmol for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and LiO^{t}Bu (30 μmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. 1-(Methylsulfonyl)piperidine **1a** (10 μmol/reaction) and 1-(*tert*-butyl)-4-chlorobenzene **2b** (20 μmol) were then dosed together into each reaction vial as a solution in toluene (50 μL, 0.2 M). The 24-well plate was then sealed and stirred for 24 h at 110 ^{o}C.

Work up:

Upon opening the plate to air, 500 μL of a solution of biphenyl (used as internal standard to measure HPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min to ensure good homogenization. Into a separate 96-well LC block was added 700 μL of acetonitrile, followed by 25 μL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated HPLC instrument for analysis.





2nd gen. Pd dimer

Ligands	Pdt/IS
1–[2–[Bis(*t*–butyl)phosphino]phenyl]–3,5–diphenyl–1H–pyrazole (Trippyphos)	1.10
P(*o*-tol)$_3$	0.35
1,2,3,4,5–Pentaphenyl–1'–(di–*t*–butylphosphino)ferrocene (QPhos)	1.03
2–Dicyclohexylphosphino–2'–(*N*,*N*–dimethylamino)biphenyl (DavePhos)	1.36
Bis[(2–diphenylphosphino)phenyl] ether (DCEPhos)	0.51
1,3-Bis(diphenylphosphino)propane (Dppp)	0.00
2–Dicyclohexylphosphino–2',6'–dimethoxy–1,1'–biphenyl (SPhos)	1.40
N-(dicyclohexylphosphino)-2-(2'-methylphenyl)-1H-indole	**2.05**
5–(Di–*t*–butylphosphino)–1', 3', 5'–triphenyl–1'H–[1,4']bipyrazole (BippyPhos)	1.17
1,1'–Bis(diisopropylphosphino)ferrocene (Dippf)	1.35
2–Di–*tert*-butylphosphino-3,4,5,6-tetramethyl-2′,4′,6′-triisopropyl-1,1′-biphenyl (Me-4–*t*–Bu XPhos)	1.50
Bis[(2–diphenylphosphino)phenyl] ether (DPEPhos)	0.00
N–phenyl–2–(dicyclohexylphosphino)pyrrole (CataCXium PCy)	1.13
(2–Biphenyl)dicyclohexylphosphine (Cy-JohnPhos)	0.71
Tri(furan-2-yl)phosphine	0.00
2-Di-*tert*-butylphosphino-1,1'-binaphthyl (TrixiePhos)	1.32
1,1'–Bis(diphenylphosphino)ferrocene (Dppf)	0.12
2-Dicyclohexylphosphino-2'-methylbiphenyl (MePhos)	1.33
2,2'-Bis(diphenylphosphino)-1,1'-biphenyl (BIPHEP)	0.00
2-(Dicyclohexylphosphino)-1-phenylindole (CataCXium PInCy)	0.97
Di(1-adamantyl)-2-dimethylaminophenylphosphine (MeDal Phos)	0.00
2–Di–tert–butylphosphino–3–Methoxy–6–Methyl–2'–4'–6'–triisopropylbiphenyl (RockPhos)	0.33
1,1′-Bis(dicyclohexylphosphino)ferrocene	1.33
Tricyclohexylphosphine tetrafluoroborate (PCy$_3$ HBF4)	1.01
1,2-Bis(diphenylphosphino)ethane (Dppe)	0.00
Benzyldi–1–adamantylphosphine (cataCXium ABn)	**1.83**
Dicyclohexyl–[3,6–dimethoxy–2–(2,4,6–triisopropylphenyl)phenyl]phosphane(Brettphos)	0.84
2-Di-tert-butylphosphino-2'-methylbiphenyl (^{t}Bu-MePhos)	0.94
(2R)-1-[(1R)-1-[Bis(1,1-dimethylethyl)phosphino]ethyl]-2-(dicyclohexylphosphino)ferrocene (Josiphos SL-J009-1)	**1.75**
Tri-tert-butylphosphonium tetrafluoroborate (P^{t}Bu$_3$ HBF$_4$)	1.42
9,9–Dimethyl–4,5–bis(diphenylphosphino)xanthene (Xantphos)	1.03
N–phenyl–2–(di–*t*–butylphosphino)pyrrole (CataXCium PtB)	0.00
Tris(2,4,6-trimethylphenyl)phosphine (PXy$_3$)	0.00
1,1'–Bis(di–*t*–butylphosphino)ferrocene (Dtbpf)	1.14
2–(Di–*t*–butylphosphino)biphenyl (JohnPhos)	0.96

4,6–Bis(diphenylphosphino)phenoxazine (NIXANTPHOS)	0.00
Di–*t*–butyl–(1–phenylindol–2–yl)phosphane (CataCXium PIntB)	1.23

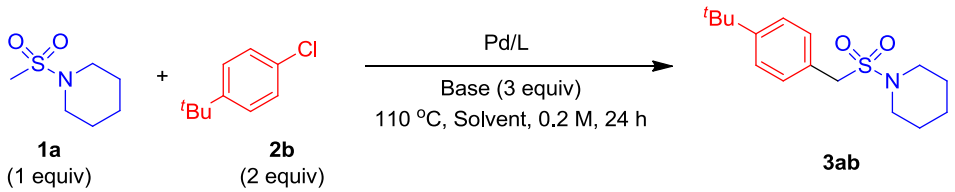
(2) Screening of Pd Source, base and solvent:

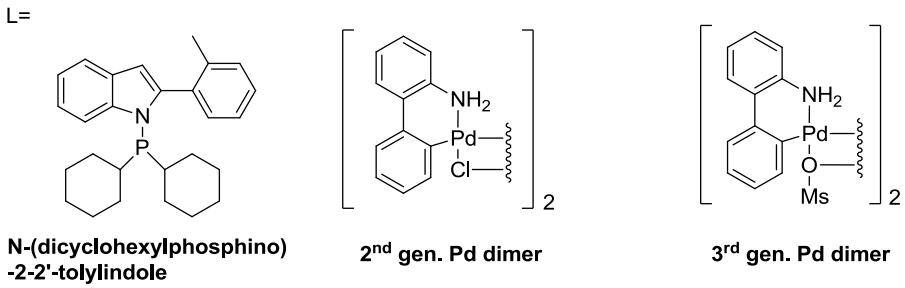
Set up:

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with 2nd gen. Pd dimer (0.5 µmol) and the N-(dicyclohexylphosphino)-2-2'-tolylindole (2 µmol) in THF. The solvent was removed to dryness using a GeneVac and 6 different bases (LiO^{t}Bu, NaO^{t}Bu, KO^{t}Bu, LiN(SiMe$_3$)$_2$, NaN(SiMe$_3$)$_2$, KN(SiMe$_3$)$_2$ 30 µmol) in THF were added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. 1-(Methylsulfonyl)piperidine **1a** (10 µmol/reaction) and 4-*tert*-butyl chlorobenzene **2b** (20 µmol/reaction) were then dosed together into each reaction vial as a solution in 4 different solvents (CPME, THF, DME, toluene, 50 µL, 0.2 M). The 24-well plate was then sealed and stirred for 24 h at 110 ℃ then cooled to room temperature.

Work up:

Upon opening the plate to air, 500 µL of a solution of biphenyl (used as internal standard to measure HPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated HPLC instrument for analysis.





Screening of 4 solvent and 6 base with 2ndgen. Pd dimer:

Solvent	Base	Prod/IS
CPME	LiO^{t}Bu	**11.84**
CPME	NaO^{t}Bu	3.22
CPME	KO^{t}Bu	0.00
CPME	LiN(SiMe$_3$)$_2$	4.55
CPME	NaN(SiMe$_3$)$_2$	0.00
CPME	KN(SiMe$_3$)$_2$	0.00
THF	LiO^{t}Bu	9.63

THF	NaO^{t}Bu	0.00
THF	KO^{t}Bu	0.00
THF	LiN(SiMe$_3$)$_2$	1.57
THF	NaN(SiMe$_3$)$_2$	1.81
THF	KN(SiMe$_3$)$_2$	1.27
DME	LiO^{t}Bu	9.37
DME	NaO^{t}Bu	1.55
DME	KO^{t}Bu	0.00
DME	LiN(SiMe$_3$)$_2$	3.15
DME	NaN(SiMe$_3$)$_2$	0.67
DME	KN(SiMe$_3$)$_2$	0.00
Toluene	LiO^{t}Bu	**12.61**
Toluene	NaO^{t}Bu	1.24
Toluene	KO^{t}Bu	0.00
Toluene	LiN(SiMe$_3$)$_2$	1.71
Toluene	NaN(SiMe$_3$)$_2$	1.30
Toluene	KN(SiMe$_3$)$_2$	0.00

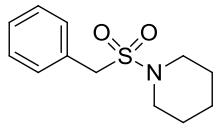
Screening of 4 solvent and 6 base with 3rd gen. Pd dimer:

Solvent	Base	Prod/IS
CPME	LiO^{t}Bu	**11.65**
CPME	NaO^{t}Bu	0.00
CPME	KO^{t}Bu	0.00
CPME	LiN(SiMe$_3$)$_2$	0.74
CPME	NaN(SiMe$_3$)$_2$	0.00
CPME	KN(SiMe$_3$)$_2$	0.00
THF	LiO^{t}Bu	7.95
THF	NaO^{t}Bu	0.00
THF	KO^{t}Bu	0.00
THF	LiN(SiMe$_3$)$_2$	1.38
THF	NaN(SiMe$_3$)$_2$	0.00
THF	KN(SiMe$_3$)$_2$	0.00
DME	LiO^{t}Bu	6.45
DME	NaO^{t}Bu	0.38
DME	KO^{t}Bu	0.00
DME	LiN(SiMe$_3$)$_2$	1.75
DME	NaN(SiMe$_3$)$_2$	2.43
DME	KN(SiMe$_3$)$_2$	1.75
Toluene	LiO^{t}Bu	**12.26**
Toluene	NaO^{t}Bu	0.00
Toluene	KO^{t}Bu	0.00
Toluene	LiN(SiMe$_3$)$_2$	0.00
Toluene	NaN(SiMe$_3$)$_2$	0.00
Toluene	KN(SiMe$_3$)$_2$	0.00

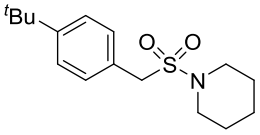
4. Procedure and Characterization for the Pd-Catalyzed Arylation of Sulfonamides.

General Procedure: An oven-dried microwave vial equipped with a stir bar was charged with 2nd generation Pd dimer (7.2 mg, 0.010 mmol) and ligand **L** (16.2 mg, 0.040 mmol) under a nitrogen atmosphere, followed by 1 mL

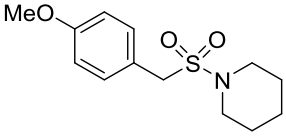
dry toluene via syringe. After the catalyst solution stirred for 120 min at 25 ℃, LiO^tBu (48.3 mg, 0.60 mmol, 3.0 equiv) was added to the reaction vial and 1-(methylsulfonyl) piperidine (32.6 mg, 0.20 mmol, 1.0 equiv) was added dropwise. The microwave vial was sealed and chlorobenzene (40.6 μL, 0.40 mmol, 2.0 equiv) was added by syringe while under a nitrogen atmosphere. The reaction was stirred at 110 ^oC for the specified time then allowed to cool to room temperature. The reaction mixture was quenched with H_2O (0.2 mL) and passed through a short pad of silica gel and eluted with ethyl acetate. The combined organics were dried over Na_2SO_4 and concentrated in vacuo. The crude residue was purified by flash column chromatography to yield the monoarylated sulfonamides derivatives **3**.



1-(Benzylsulfonyl)piperidine (3aa): The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc : hexanes = 1:10) to give the product (38.3 mg, 80% yield) as a white solid. The ^1H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data.[1]

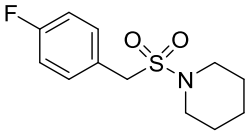


1-((4-(*tert*-Butyl)benzyl)sulfonyl)piperidine (3ab): The reaction was performed following the General Procedure with **2b** (66.6 μL, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (50.2 mg, 85% yield) as a white solid. R_f = 0.48 (hexanes:EtOAc = 5:1); ^1H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 4.14 (s, 2H), 3.40 (d, *J* = 5.0 Hz, 4H), 1.53-1.51 (m, 6H), 1.32 (s, 9H), ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 151.9, 130.6, 126.2, 125.8, 56.2, 47.1, 34.8, 31.5, 25.9, 23.9 ppm; HRMS calc'd for $C_{16}H_{25}NNaO_2S^+$ 318.1504, found 318.1512 $[M+Na]^+$.

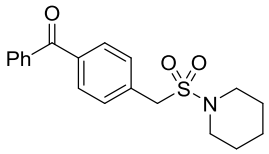


1-((4-Methoxybenzyl)sulfonyl)piperidine (3ac): The reaction was performed following the General Procedure with **2c** (49.0 μL, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (42.6 mg, 79% yield) as a white solid. R_f = 0.23 (hexanes:EtOAc = 5:1); ^1H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 4.12 (s, 2H), 3.82 (s, 3H), 3.08 (t, *J* = 5.0 Hz, 4H), 154-1.51 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.1,

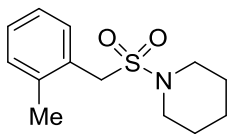
132.1, 121.3, 114.3, 56.2, 55.5, 47.2, 26.1, 24.0 ppm; HRMS calc'd for $C_{13}H_{19}NNaO_3S^+$ 292.0983, found 292.0990 $[M+Na]^+$.



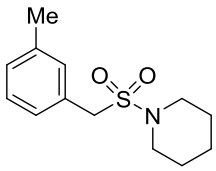
1-((4-Fluorobenzyl)sulfonyl)piperidine (3ad): The reaction was performed following the General Procedure with **2d** (42.0 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (35.5 mg, 69% yield) as a white solid. R_f = 0.28 (hexanes:EtOAc = 5:1);; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (dd, J = 8.5 Hz, 5.2 Hz, 2H), 7.07 (t, J = 8.5 Hz, 2H), 4.14 (s, 2H), 3.09 (d, J = 5.0 Hz, 4H), 1.53 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 164.1, 162.1, 132.6 (d, $J_{C\text{-}F}$ = 7.5Hz), 125.3 (d, $J_{C\text{-}F}$ = 2.5Hz), 116.0 (d, $J_{C\text{-}F}$ = 22.5Hz), 55.9, 47.1, 25.9, 23.9 ppm; HRMS calc'd for $C_{12}H_{16}FNNaO_2S^+$ 280.0783, found 280.0800 $[M+Na]^+$.



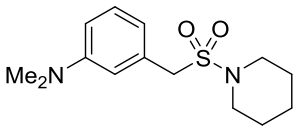
Phenyl(4-((piperidin-1-ylsulfonyl)methyl)phenyl)methanone (3ae): The reaction was performed following the General Procedure with **2j** (86.7 mg, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:3) to give the product (39.2 mg, 57% yield) as a white solid; R_f = 0.60 (DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (t, J = 8.0 Hz, 4H), 7.61-7.45 (m, 5H), 4.23 (s, 2H), 3.13 (d, J = 5.0 Hz, 4H), 1.53 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 195.8, 137.4, 137.1, 133.5, 132.4, 130.5, 130.1, 129.8, 128.2, 55.9, 46.8, 25.6, 23.5 ppm; HRMS calc'd for $C_{19}H_{21}NNaO_3S^+$ 366.1140, found 366.1141 $[M+Na]^+$.



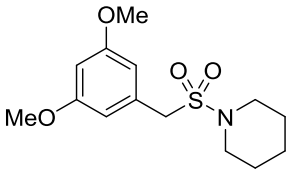
1-((2-Methylbenzyl)sulfonyl)piperidine (3af): The reaction was performed following the General Procedure with **2f** (46.9 mg, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (35.5 mg, 70% yield) as a white solid. R_f = 0.43 (hexanes:EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19-7.11 (m, 4H), 4.06 (s, 2H), 3.02 (s, 4H), 2.29 (s, 3H), 1.44 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 138.4, 132.0, 131.1, 128.9, 127.8, 126.3, 54.1, 47.2, 26.1, 24.1, 19.9 ppm; HRMS calc'd for $C_{13}H_{19}NNaO_2S^+$ 276.1034, found 276.1043 $[M+Na]^+$.



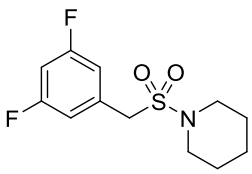
1-((3-Methylbenzyl)sulfonyl)piperidine (3ag): The reaction was performed following the General Procedure with **2g** (47.2 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (38.0 mg, 75% yield) as a white solid. R_f = 0.42(hexanes:EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ7.32 (d, *J* = 7.4 Hz, 1H), 7.26-7.18 (m, 3H), 4.22 (s, 2H), 3.16 (t, *J* = 5.0 Hz, 4H), 2.46 (s, 3H), 1.59-1.54 (m, 6H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 138.1, 131.1, 129.0, 128.7, 128.2, 127.5, 56.3, 46.7, 25.5, 23.5, 21.0 ppm; HRMS calc'd for $C_{13}H_{19}NNaO_2S^+$ 276.1034, found 276.1039 $[M+Na]^+$.



***N,N*-Dimethyl-3-((piperidin-1-ylsulfonyl)methyl)aniline (3ah):** The reaction was performed following the General Procedure with **2h** (62.4 mg, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:3) to give the product (44.0 mg, 78% yield) as a light yellow solid. R_f = 0.34 (DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.18 (m, 1H), 6.75 (d, *J* = 2.6 Hz, 1H), 6.72 (d, *J* = 4.8 Hz, 1H), 6.69 (d, *J* = 4.4 Hz, 1H), 4.15 (s, 2H), 3.10 (t, *J* = 5.0 Hz, 4H), 2.96 (s, 6H), 1.54-1.50 (m, 6H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.5, 129.5, 129.0, 118.6, 114.5, 112.5, 57.0, 46.8, 40.3, 25.7, 23.7 ppm; HRMS calc'd for $C_{14}H_{22}N_2NaO_2S^+$ 305.1300, found 305.1315 $[M+Na]^+$.

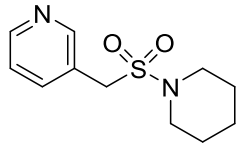


1-((3,5-Dimethoxybenzyl)sulfonyl)piperidine (3ai): The reaction was performed following the General Procedure with **2i** (69.0 mg, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol).The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (47.3 mg, 79% yield) as a white solid. R_f = 0.64 (DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.54 (d, *J* = 2.1 Hz, 2H), 6.44 (d, *J* = 2.1 Hz, 1H), 4.10 (s, 2H), 3.79 (s, 6H), 3.10 (d, *J* = 5.0 Hz, 4H), 1.52 (s, 6H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.7, 130.9, 108.6, 100.4, 56.6, 55.2, 46.8, 25.6, 23.6 ppm; HRMS calc'd for $C_{14}H_{21}NNaO_4S^+$ 322.1089, found 322.1096 $[M+Na]^+$.

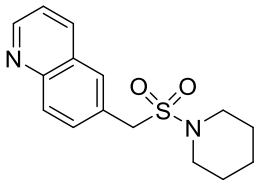


1-((3,5-Difluorobenzyl)sulfonyl)piperidine (3aj): The reaction was performed following the General Procedure with **2j** (43.9 mg, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and

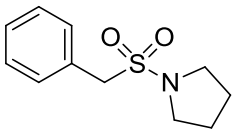
1a (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (33.0 mg, 60% yield) as a white solid. R_f = 0.47 (hexanes:EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (d, *J* = 5.8 Hz, 2H), 6.86–6.79 (m, 1H), 4.11 (s, 2H), 3.14 (q, *J* = 5.0 Hz, 4H), 1.56 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 164.4 (d, $J_{C\text{-}F}$ = 21.2Hz), 161.1(d, $J_{C\text{-}F}$ = 21.2Hz), 132.5(d, $J_{C\text{-}F}$ = 16.2Hz), 129.1, 128.3, 113.6 (dd, $J_{C\text{-}F}$ = 13.8, 28.8Hz), 104.0 (t, $J_{C\text{-}F}$ = 41.2Hz), 55.6, 46.8, 25.6, 23.5 ppm; HRMS calc'd for $C_{12}H_{15}F_2NNaO_2S^+$ 298.0689, found 298.0690 $[M+Na]^+$.



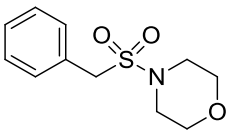
3-((Piperidin-1-ylsulfonyl)methyl)pyridine (3ak): The reaction was performed following the General Procedure with **2k** (38.0 mg, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (34.6 mg, 72% yield) as a white solid. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data. [1]



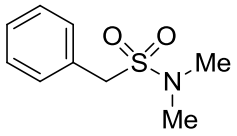
6-((Piperidin-1-ylsulfonyl)methyl)quinoline (3al): The reaction was performed following the General Procedure with **2l** (65.4 mg, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1a** (32.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:1) to give the product (36.6 mg, 63% yield) as a light yellow solid. R_f = 0.62 (DCM:EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.16-8.09 (m, 2H), 7.86 (d, *J* = 1.4 Hz, 1H), 7.74 (d, *J* = 1.9 Hz, 1H), 7.42 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.34 (s, 2H), 3.09 (d, *J* = 5.2 Hz, 4H), 1.50 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 150.9, 147.8, 135.8, 131.4, 129.8, 129.7, 127.9, 127.4, 121.5, 56.2, 46.8, 25.6, 23.5 ppm; HRMS calc'd for $C_{15}H_{18}N_2NaO_2S^+$ 313.0987, found 313.0988 $[M+Na]^+$.



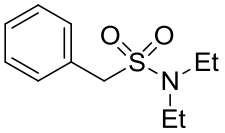
1-(Benzylsulfonyl)pyrrolidine (3ba): The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1b** (29.8 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:20) to give the product (33.9 mg, 75% yield) as a white solid. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data.[1]



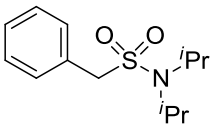
4-(Benzylsulfonyl)morpholine (3ca): The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1c** (33.0 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:20) to give the product (33.3 mg, 69% yield) as a white solid. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [1]



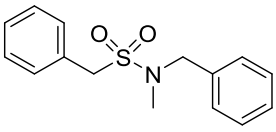
***N,N*-Dimethyl-1-phenylmethanesulfonamide (3da)**: The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1d** (24.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (31.1 mg, 78% yield) as a white solid; The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [1]



***N,N*-Diethyl-1-phenylmethanesulfonamide (3ea)**: The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1e** (30.2 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (34.9 mg, 63% yield) as a white solid; The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[2]

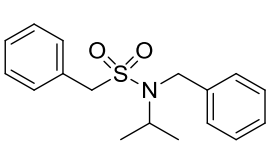


***N,N*-Diisopropyl-1-phenylmethanesulfonamide (3fa)**: The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1f** (35.8 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (40.9 mg, 80% yield) as a white solid. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [1]

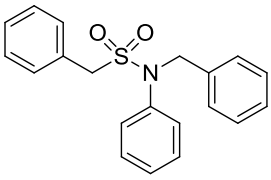


***N*-Benzyl-*N*-methyl-1-phenylmethanesulfonamide (3ga)**: The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^{t}Bu (48.3 mg, 0.60 mmol) and **1g** (40.0 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (45.7 mg, 83% yield) a white solid; R_f = 0.44 (hexanes:EtOAc = 5:1); ^{1}H NMR (500 MHz, CDCl3): δ 7.40 (s, 5H), 7.31-7.29 (m, 5H), 4.30

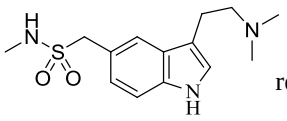
(s, 2H), 4.09 (s, 2H), 2.62 (s, 3H) ppm; $^{13C}\{^{1}H\}$ NMR (125 MHz, CDCl3): δ 136.0, 130.7, 129.2, 128.8, 128.7, 128.6, 128.3, 127.9, 57.3, 54.2, 34.6 ppm; HRMS calc'd for $C_{15}H_{17}NNaO_2S^+$ 298.0878, found 298.0897 $[M+Na]^+$.



***N*-Benzyl-*N*-isopropyl-1-phenylmethanesulfonamide (3ha)**: The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1h** (45.4 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (42.5 mg, 70% yield) as a white solid. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data. [1]



***N*-Benzyl-*N*,1-diphenylmethanesulfonamide (3ia)**: The reaction was performed following the General Procedure with **2a** (40.6 μL, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1i** (52.2 mg, 0.20 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:10) to give the product (47.2 mg, 70% yield) as a white solid. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data. [1]



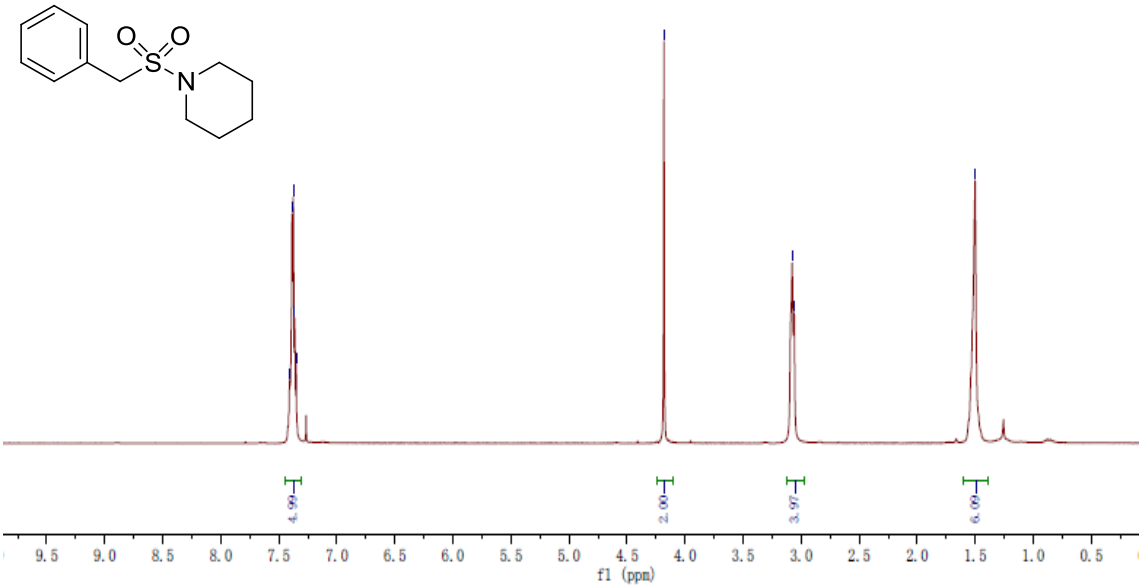
1-(3-(2-(Dimethylamino)ethyl)-1H-indol-5-yl)-N-methylmethanesulfonamide (3ja): The reaction was performed following General Procedure with **2m** (128.9mg, 0.40 mmol), LiO^tBu (48.3 mg, 0.60 mmol) and **1g** (39.8 mg, 0.20 mmol). Then the crude material was reacted in CF_3COOH at 12h, which was purified by flash chromatography on silica gel (eluted with MeOH:CH_2Cl_2 = 2:1) to give the product **3ja** (44.2 mg, 75% yield) as a white solid. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data. [3]

5. References.

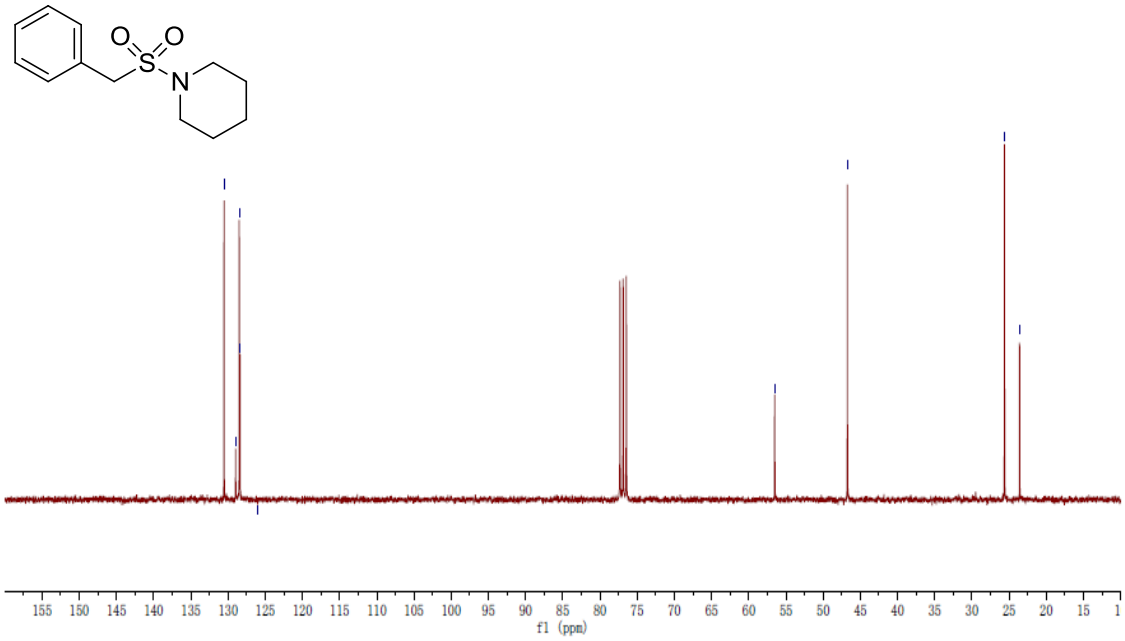
1. G. Zhou, P. Ting, R. Aslanian, J. J. Piwinski. *Org. Lett.* 2008**, 10**, 2517.
2. H. Woolven, C. Gonzalez-Rodriguez, I. Marco, A. L. Thompson, M. C. Willis. *Org. Lett.* 2011**, 13**, 4876.
3. T. Xie, J. Cai, J. Yu. *Huaxue Shiji* 2012, **34**, 190-192.

6. NMR Spectra

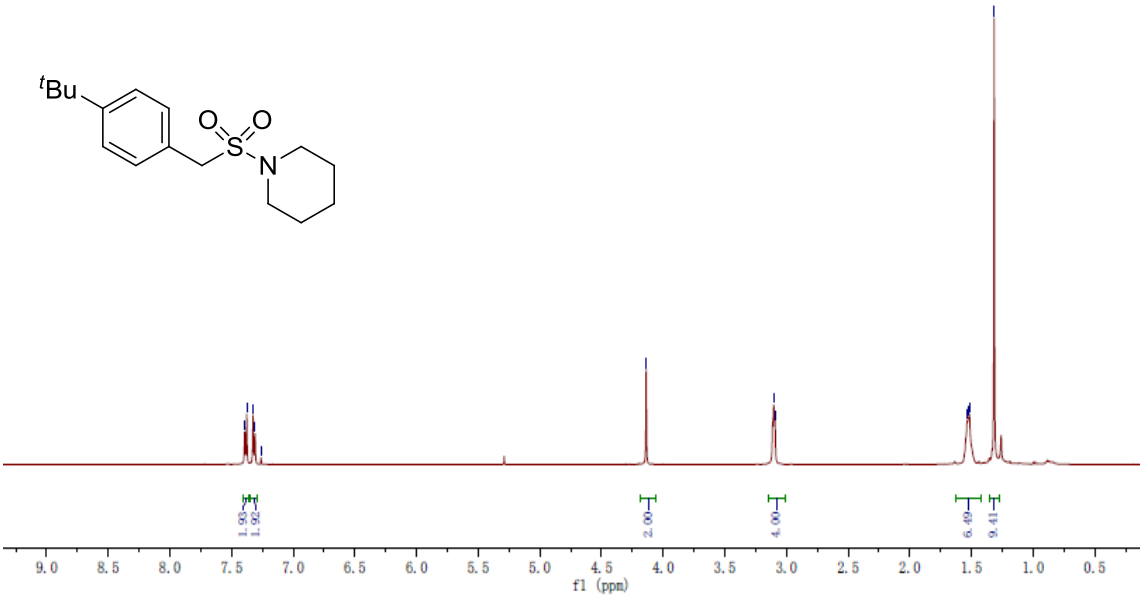
^{1}H spectra (500 MHz) of 1-(Benzylsulfonyl)piperidine (3aa)



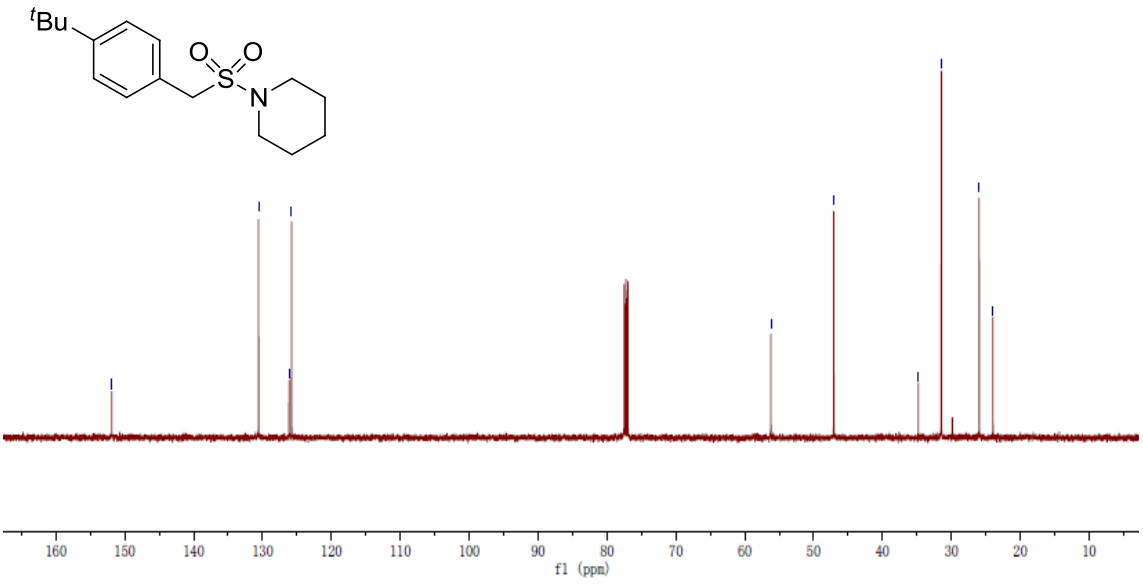
^{13}C (^{1}H) spectra (125 MHz) of 1-(Benzylsulfonyl)piperidine (3aa)



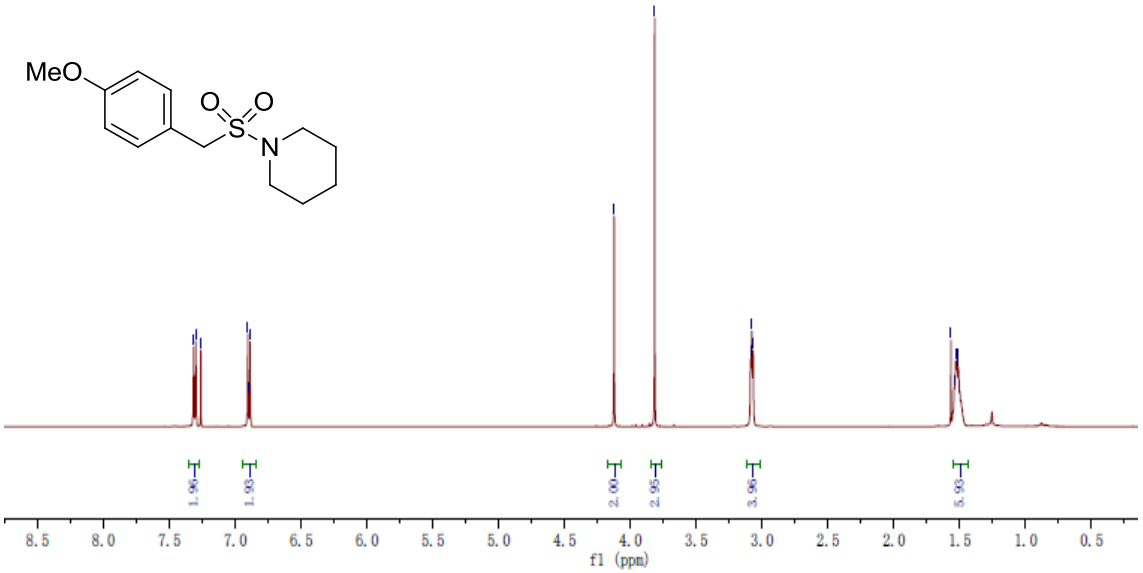
^{1}H spectra (500 MHz) of 1-((4-(*tert*-Butyl)benzyl)sulfonyl)piperidine (3ab)



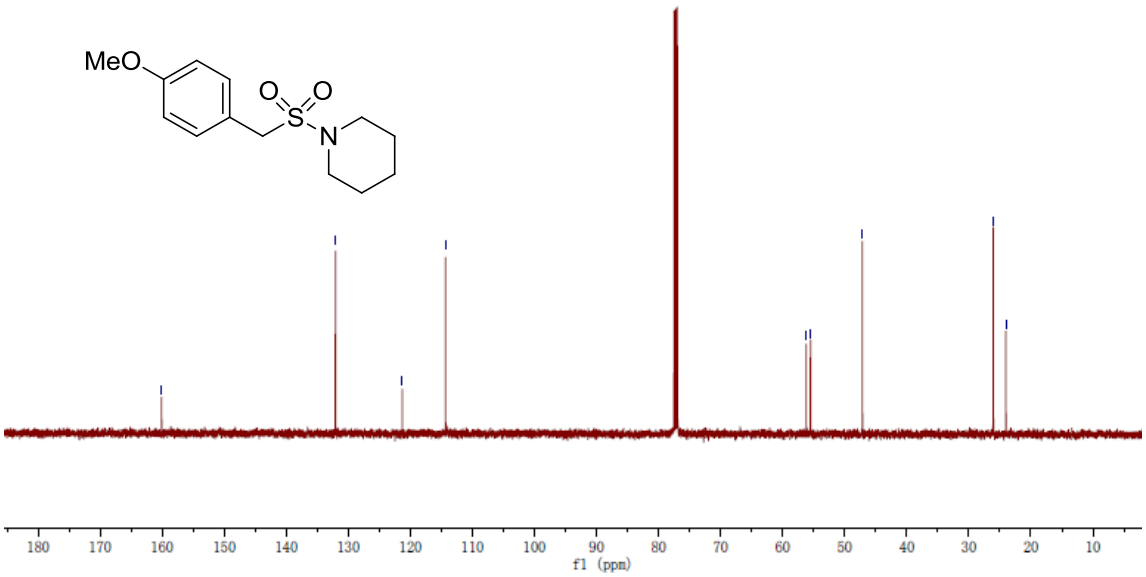
^{13}C (^{1}H) spectra (125 MHz) of 1-((4-(*tert*-Butyl)benzyl)sulfonyl)piperidine (3ab)



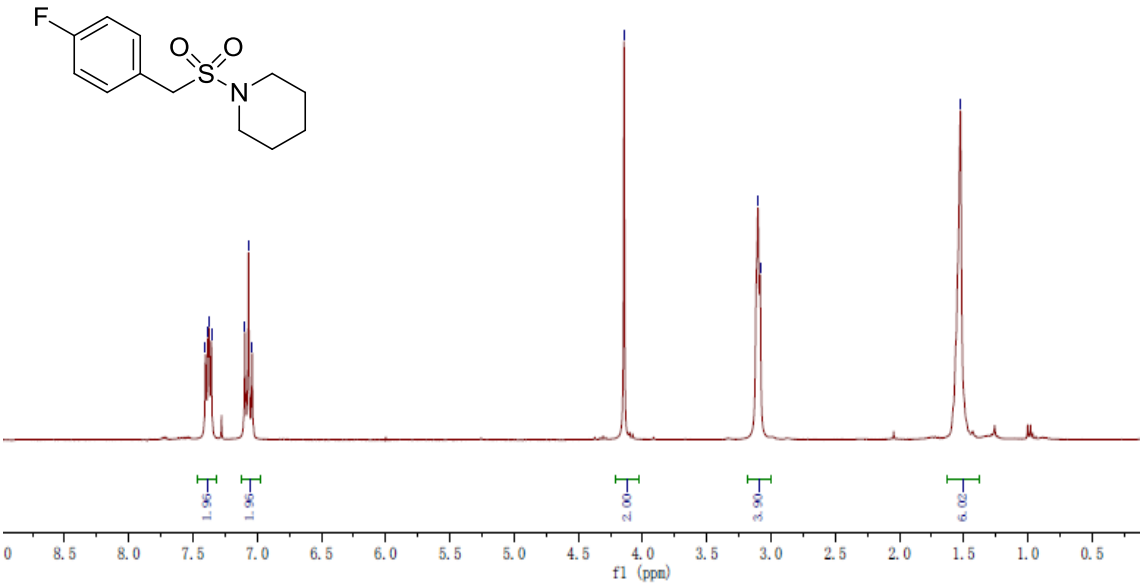
^{1}H spectra (500 MHz) of 1-((4-Methoxybenzyl)sulfonyl)piperidine (3ac)



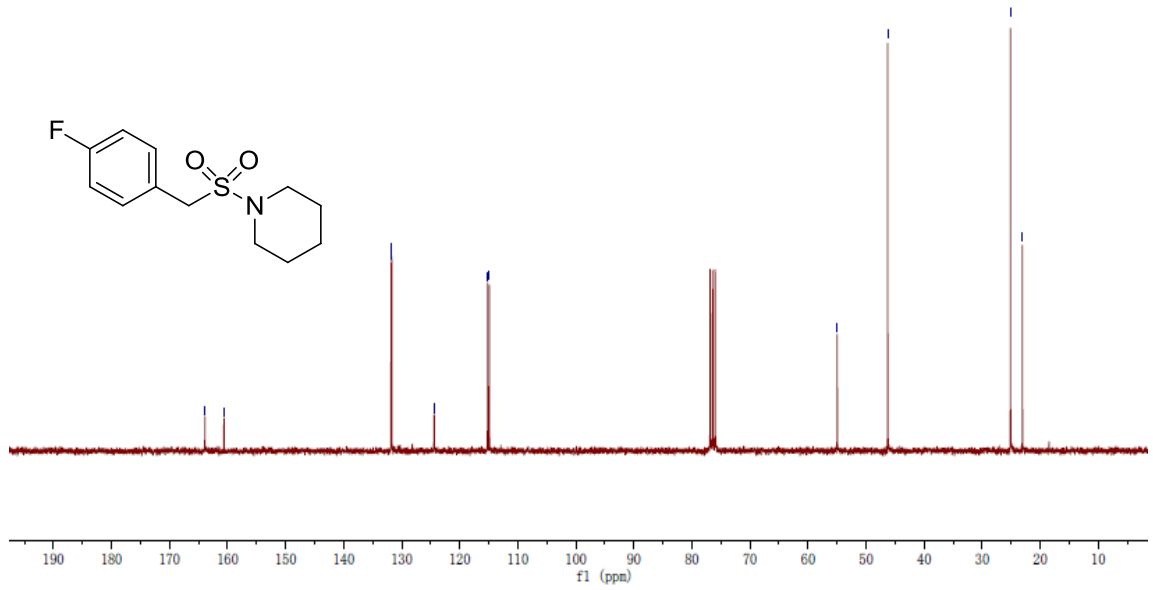
^{13}C (^{1}H) spectra (125 MHz) of 1-((4-Methoxybenzyl)sulfonyl)piperidine (3ac)



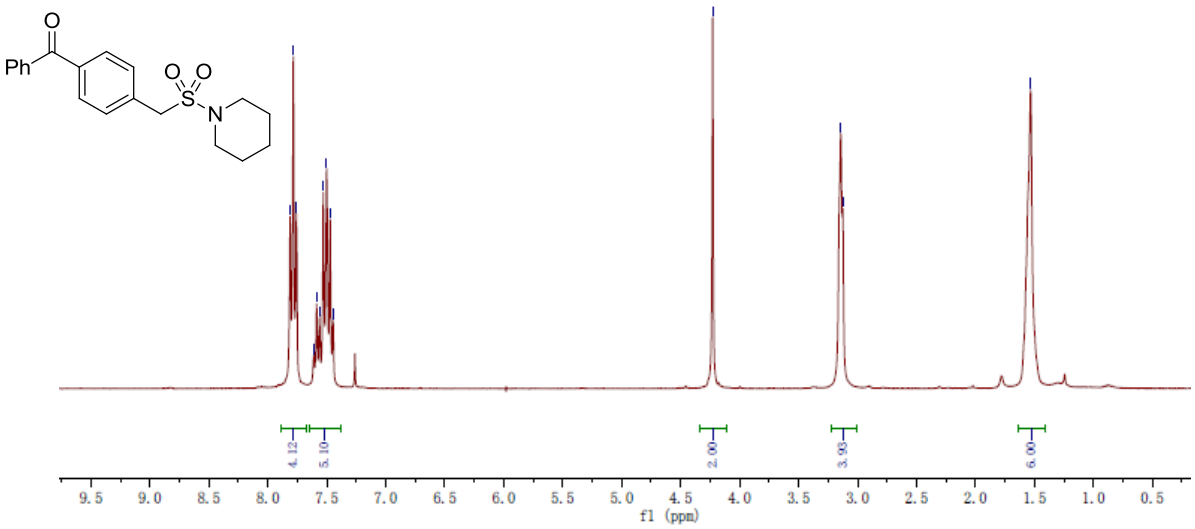
^{1}H spectra (500 MHz) of 1-((4-Fluorobenzyl)sulfonyl)piperidine (3ad)



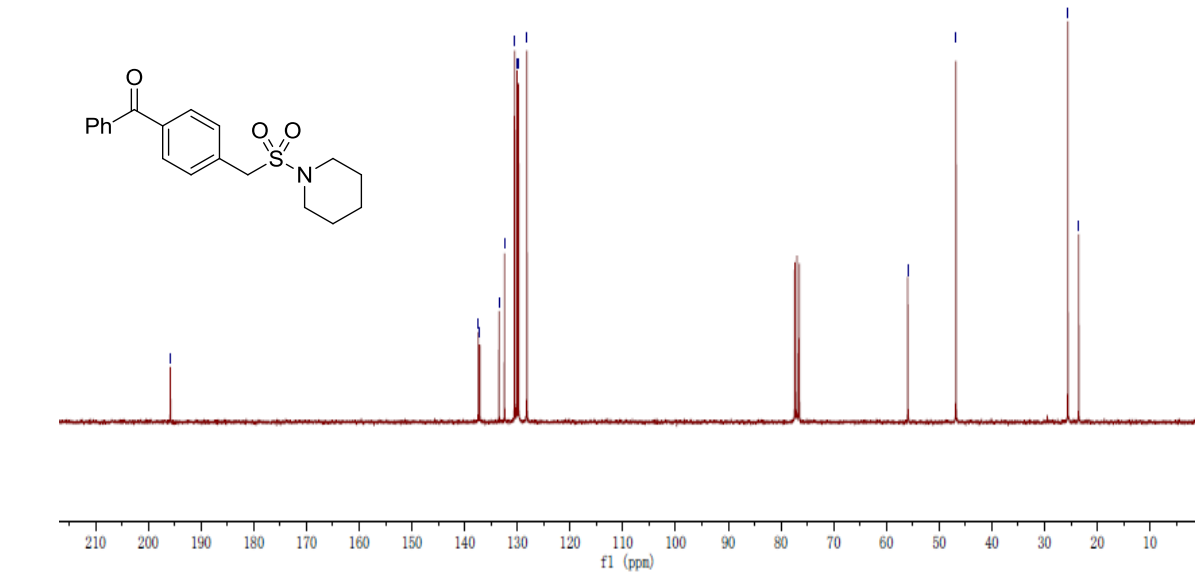
^{13}C (^{1}H) spectra (125 MHz) of 1-((4-Fluorobenzyl)sulfonyl)piperidine (3ad)



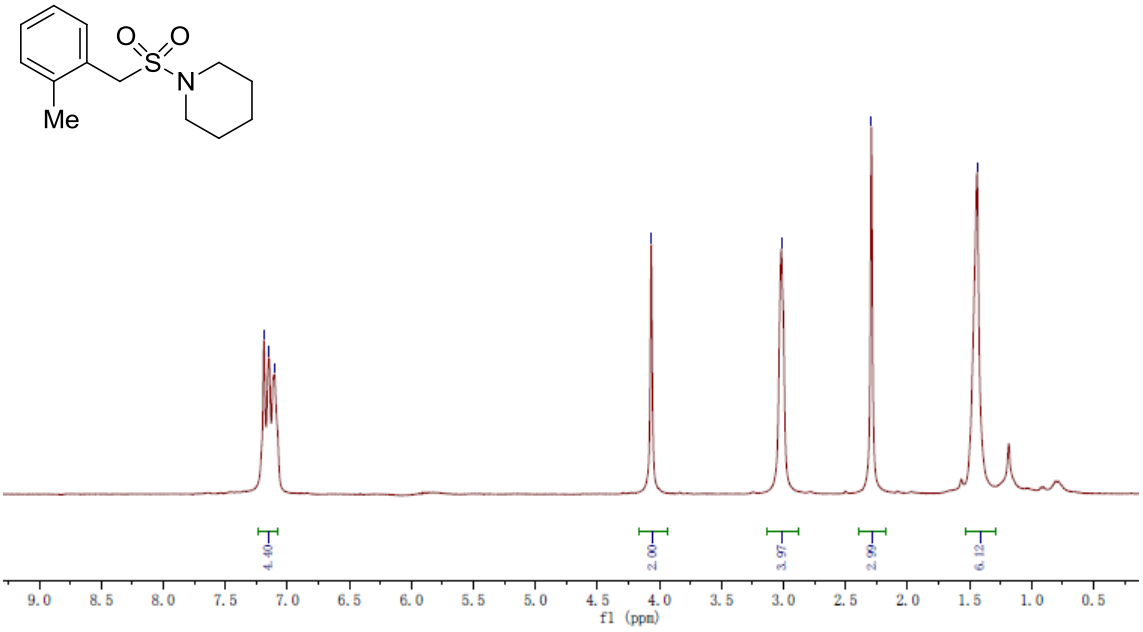
^{1}H spectra (500 MHz) of Phenyl(4-((piperidin-1-ylsulfonyl)methyl)phenyl)methanone (3ae)



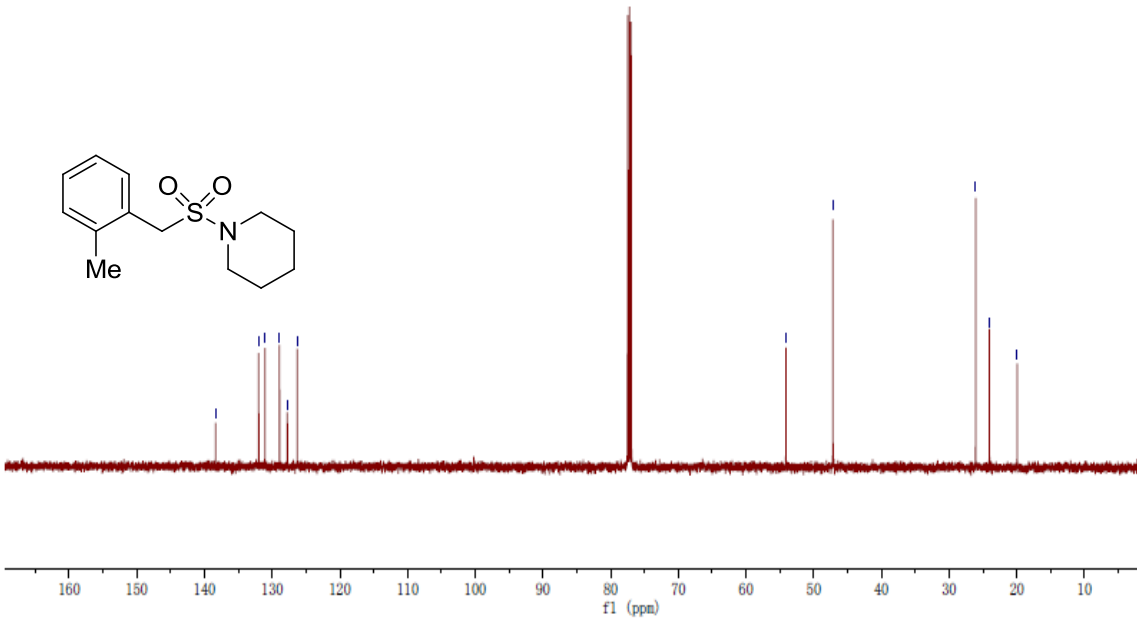
^{13}C (^{1}H) spectra (125 MHz) of Phenyl(4-((piperidin-1-ylsulfonyl)methyl)phenyl)methanone (3ae)



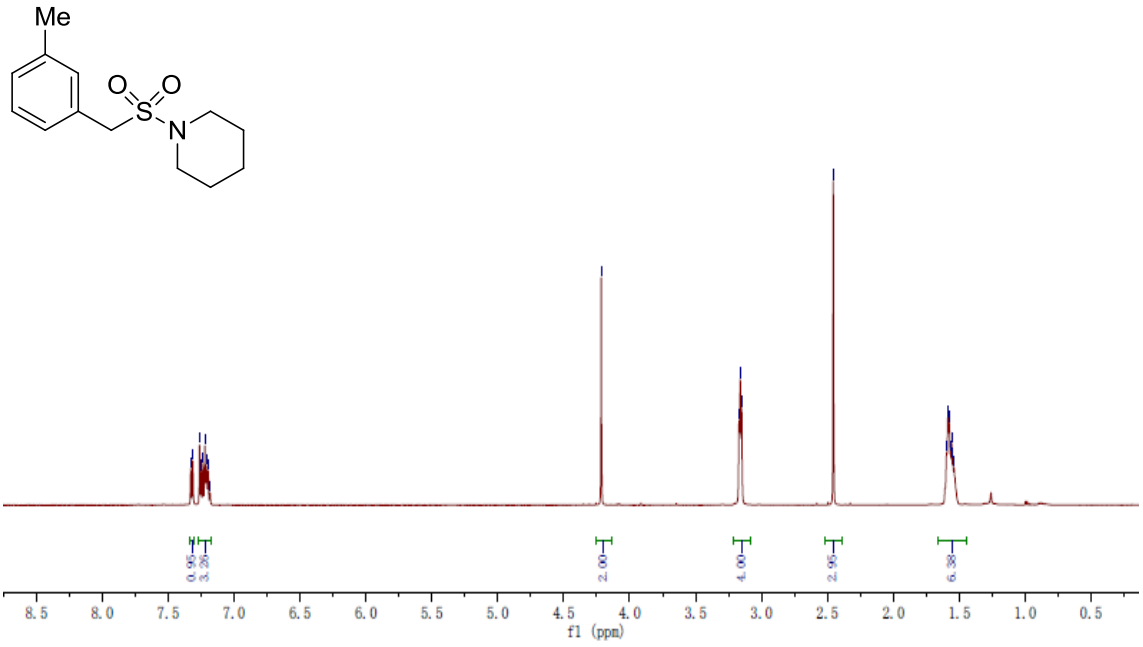
^{1}H spectra (500 MHz) of 1-((2-Methylbenzyl)sulfonyl)piperidine (3af)



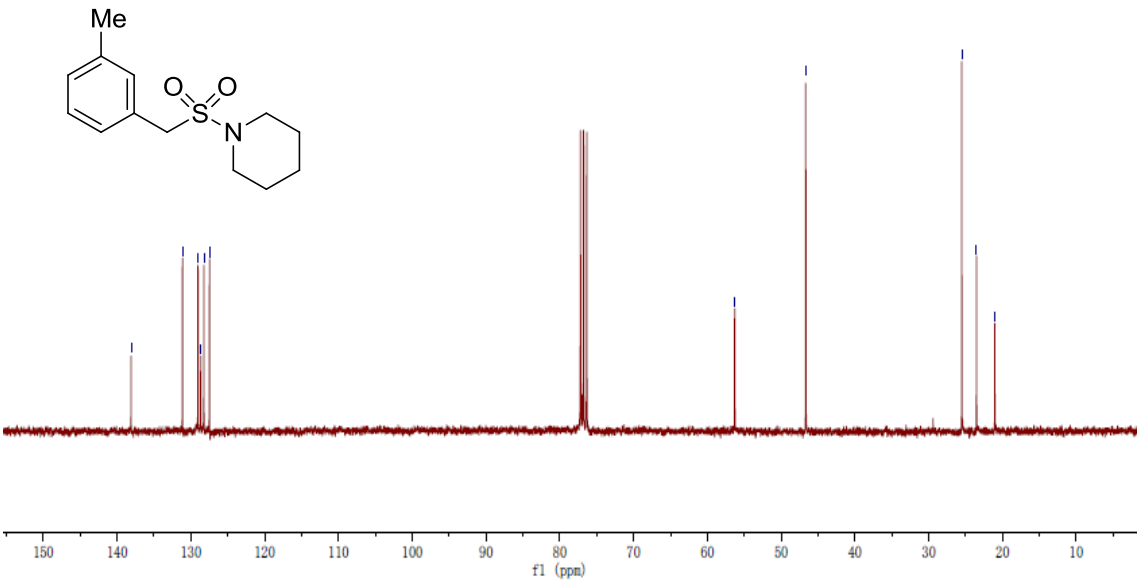
^{13}C (^{1}H) spectra (125 MHz) of 1-((2-Methylbenzyl)sulfonyl)piperidine (3af)



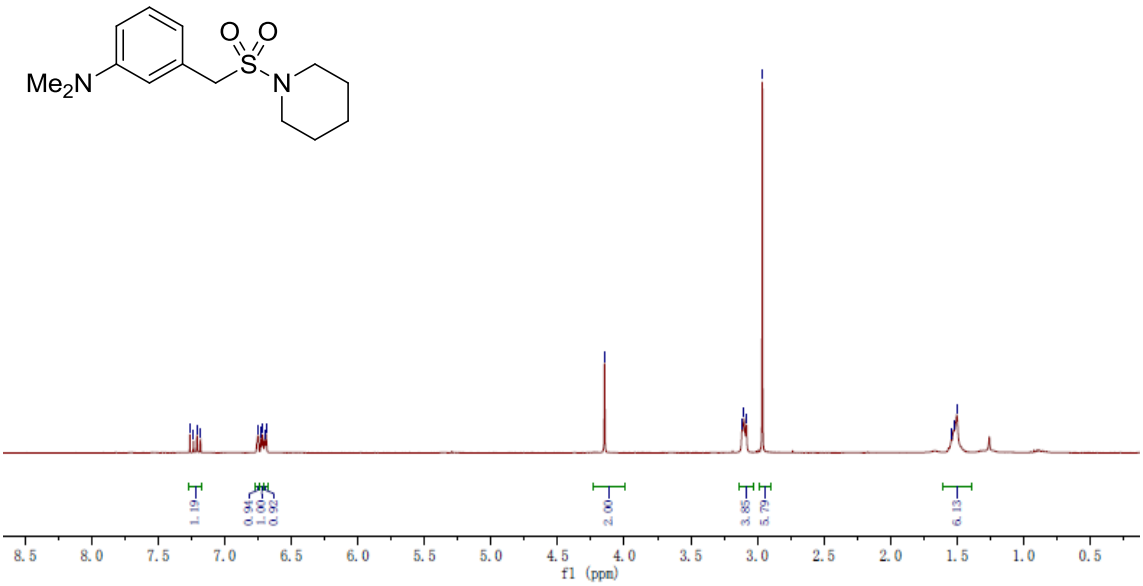
^{1}H spectra (500 MHz) of 1 -((3-Methylbenzyl)sulfonyl)piperidine (3ag)



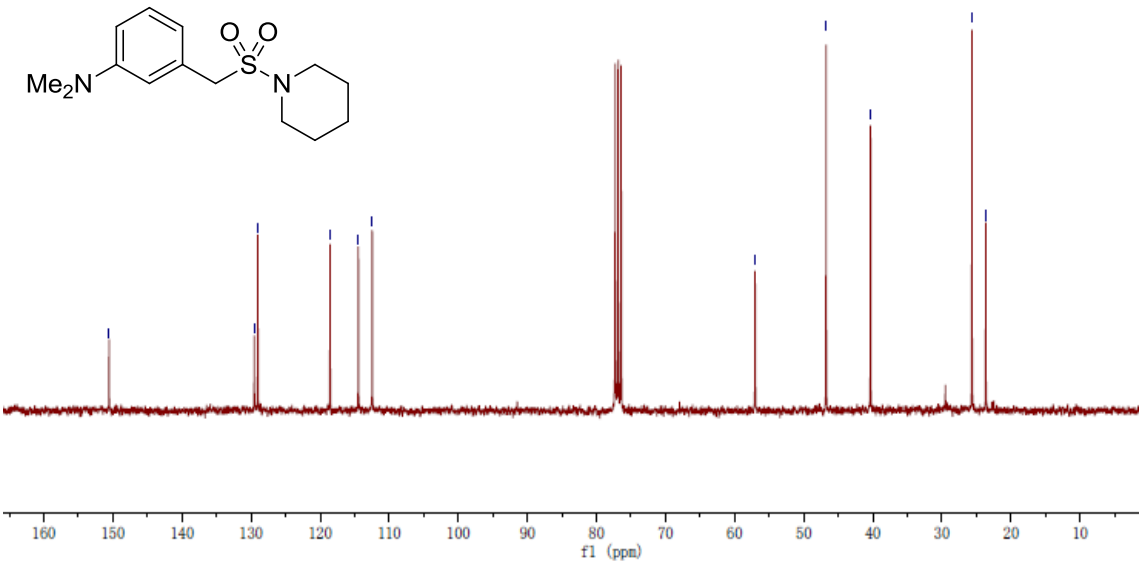
^{13}C (^{1}H) spectra (125 MHz) of 1-((3-Methylbenzyl)sulfonyl)piperidine (3ag)



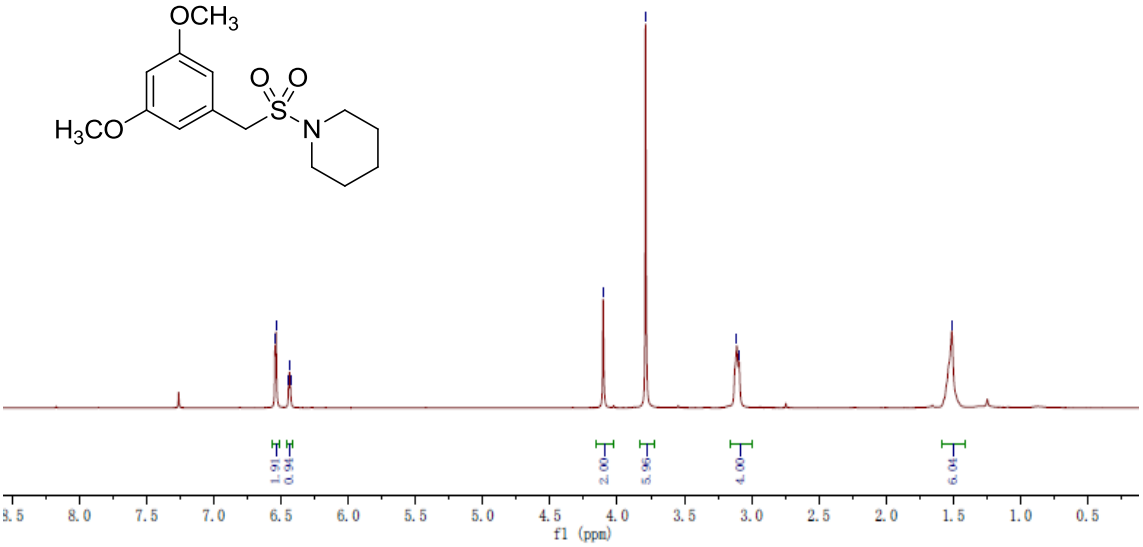
^{1}H spectra (500 MHz) of *N, N*-Dimethyl-3-((piperidin-1-ylsulfonyl)methyl)anilin (3ah)



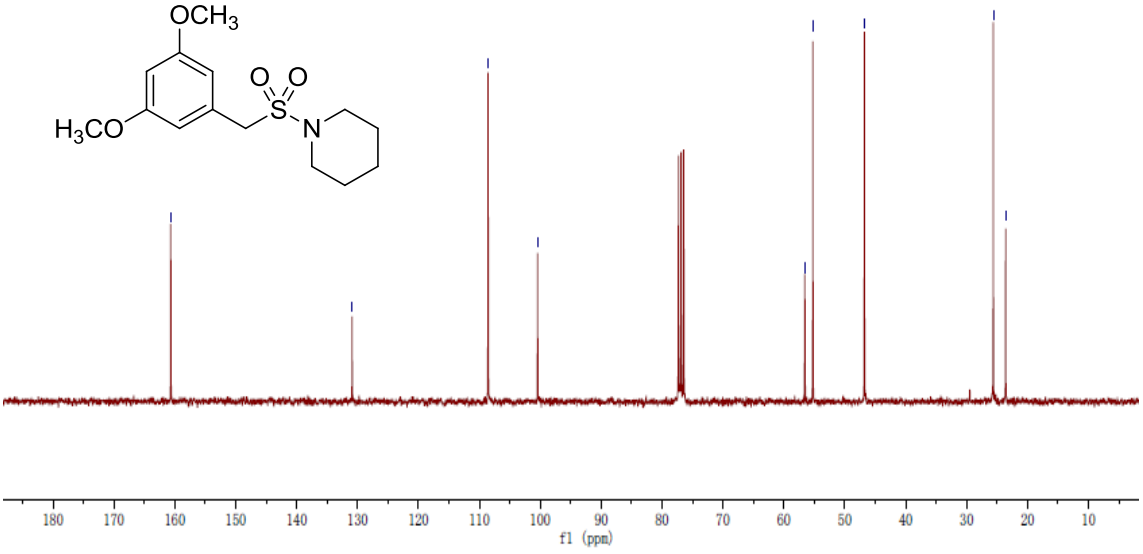
^{13}C (^{1}H) spectra (125 MHz) of *N, N*-Dimethyl-3-((piperidin-1-ylsulfonyl)methyl)anilin (3ah)



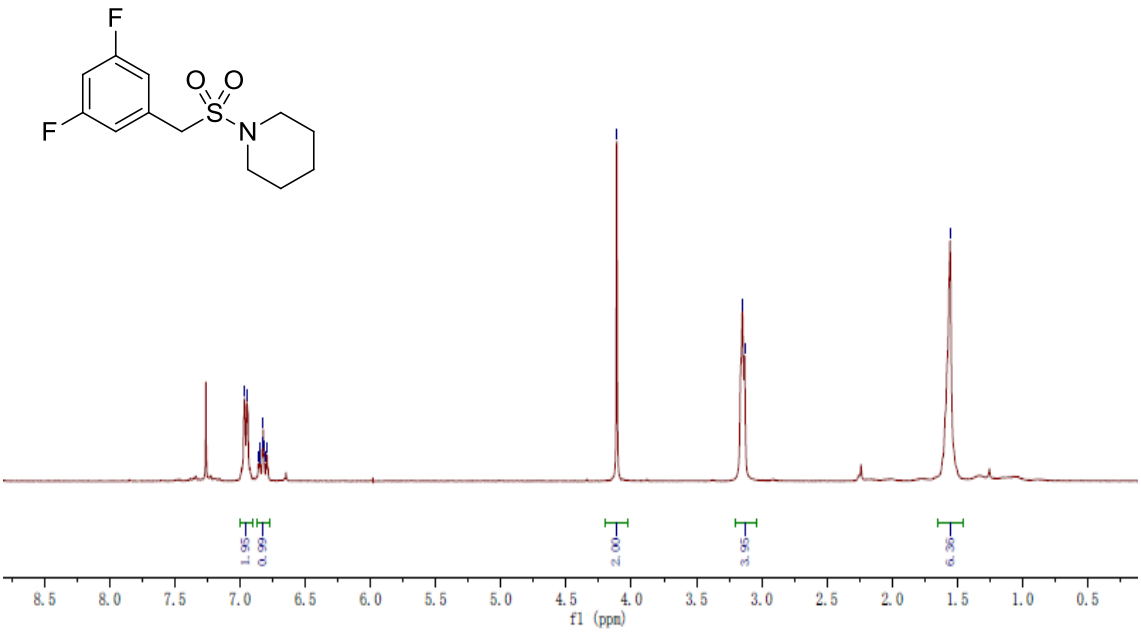
^{1}H spectra (500 MHz) of 1-((3,5-Dimethoxybenzyl)sulfonyl)piperidine (3ai)



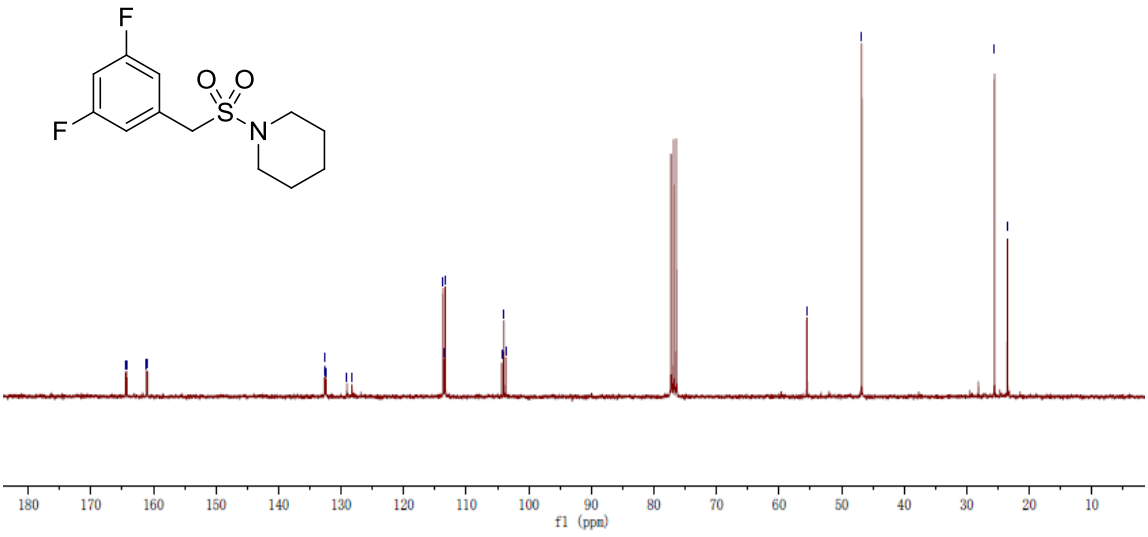
^{13}C (^{1}H) spectra (125 MHz) of 1-((3,5-Dimethoxybenzyl)sulfonyl)piperidine (3ai)



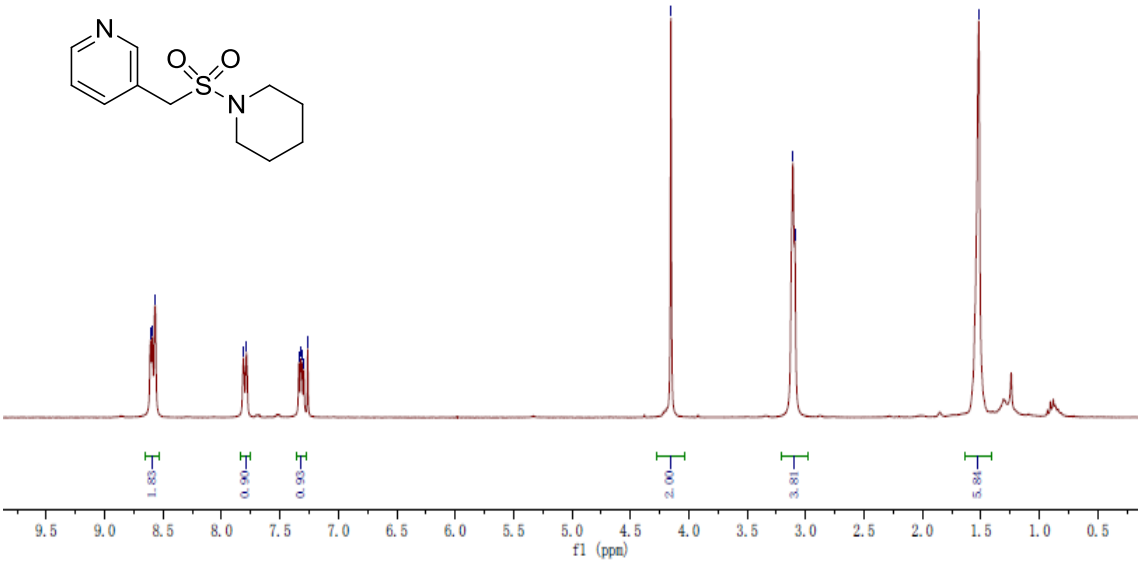
^{1}H spectra (500 MHz) of 1-((3,5-Difluorobenzyl)sulfonyl)piperidine (3aj)



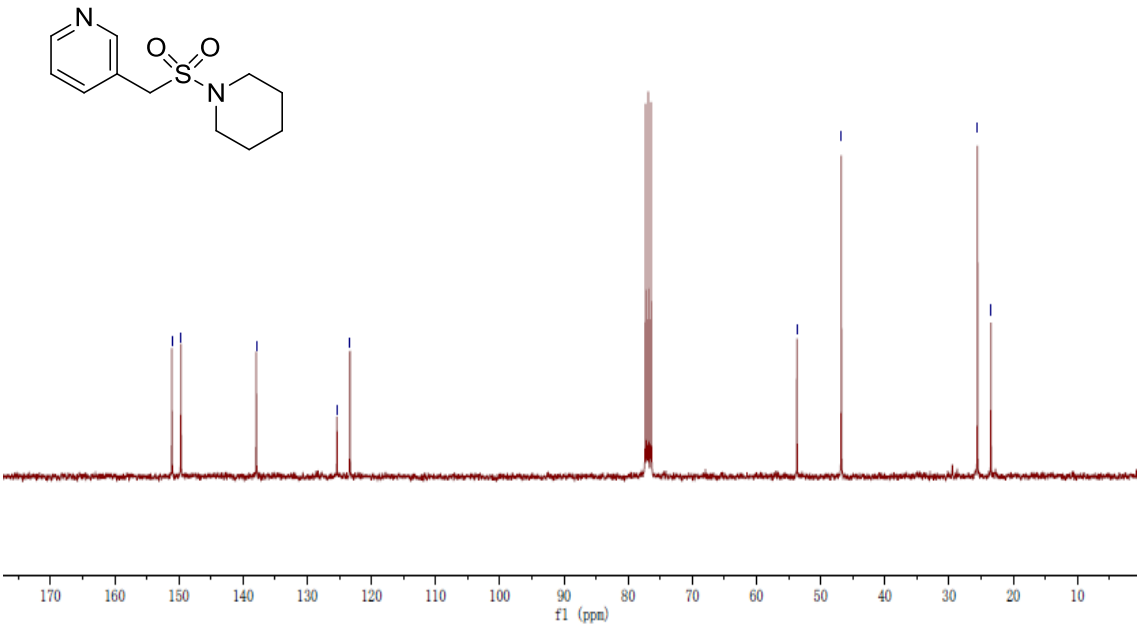
^{13}C (^{1}H) spectra (125 MHz) of 1-((3,5-Difluorobenzyl)sulfonyl)piperidine (3aj)



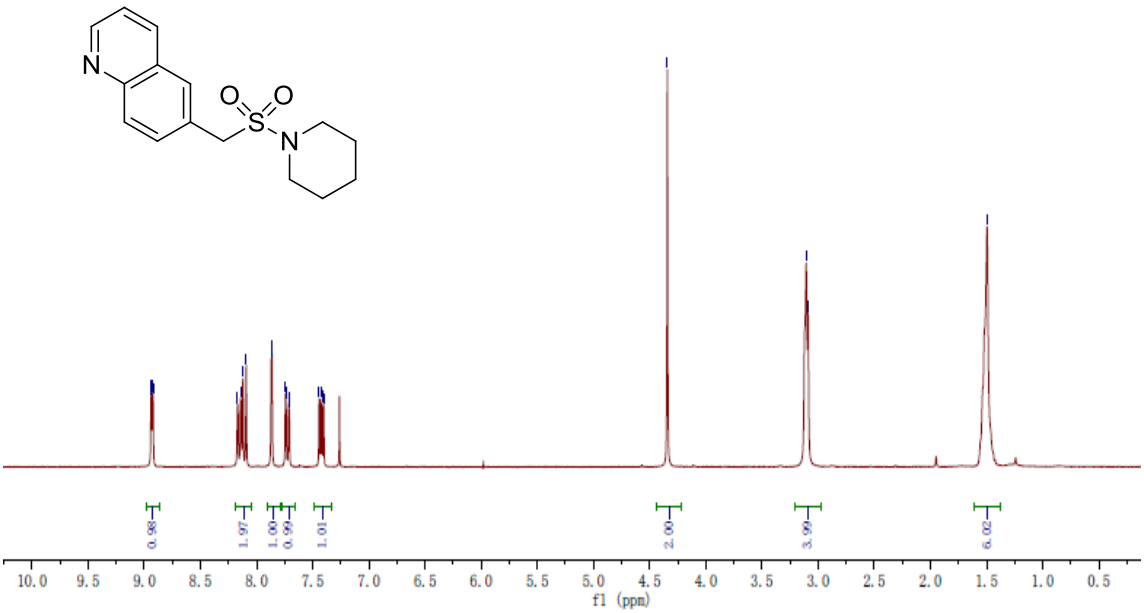
^{1}H spectra (500 MHz) of 3-((Piperidin-1-ylsulfonyl)methyl)pyridine (3ak)



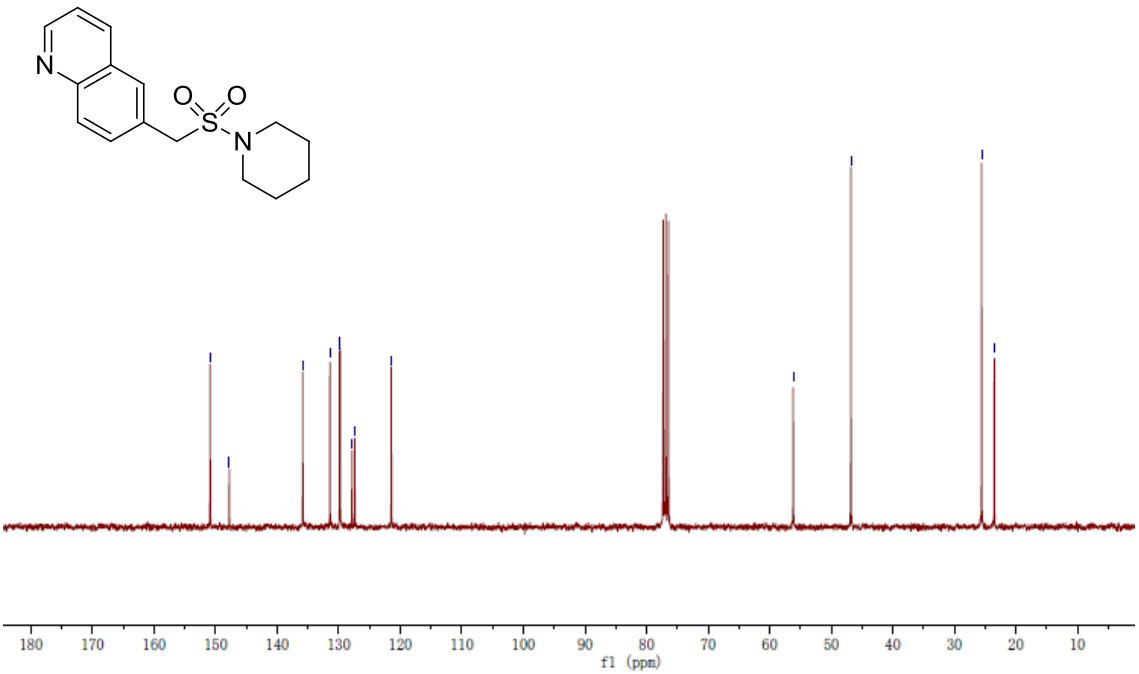
^{13}C (^{1}H) spectra (125 MHz) of 3-((Piperidin-1-ylsulfonyl)methyl)pyridine (3ak)



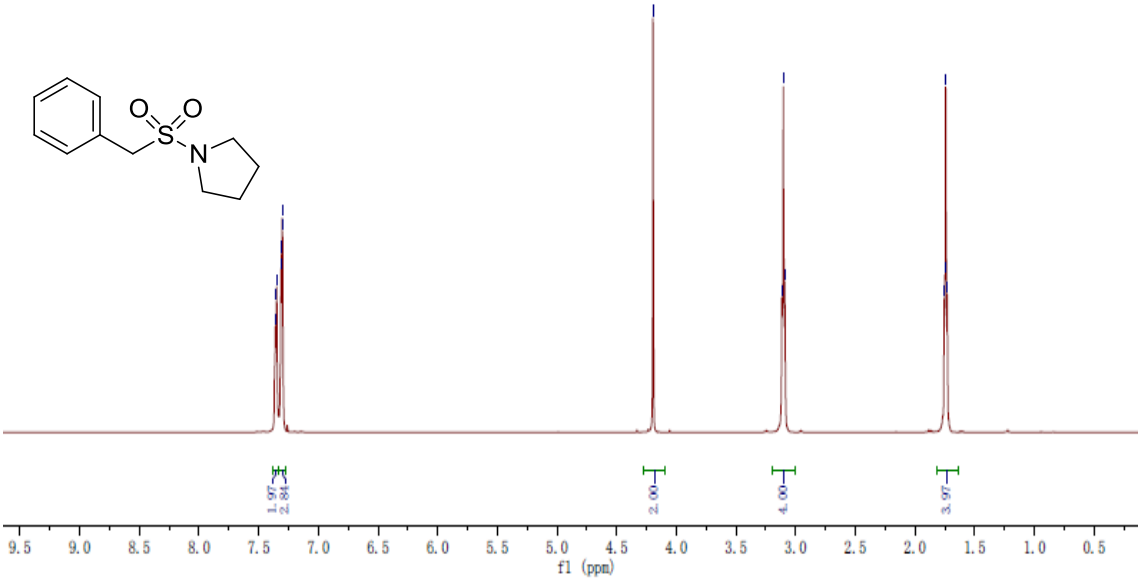
^{1}H spectra (500 MHz) of 6-((Piperidin-1-ylsulfonyl)methyl)quinoline (3al)



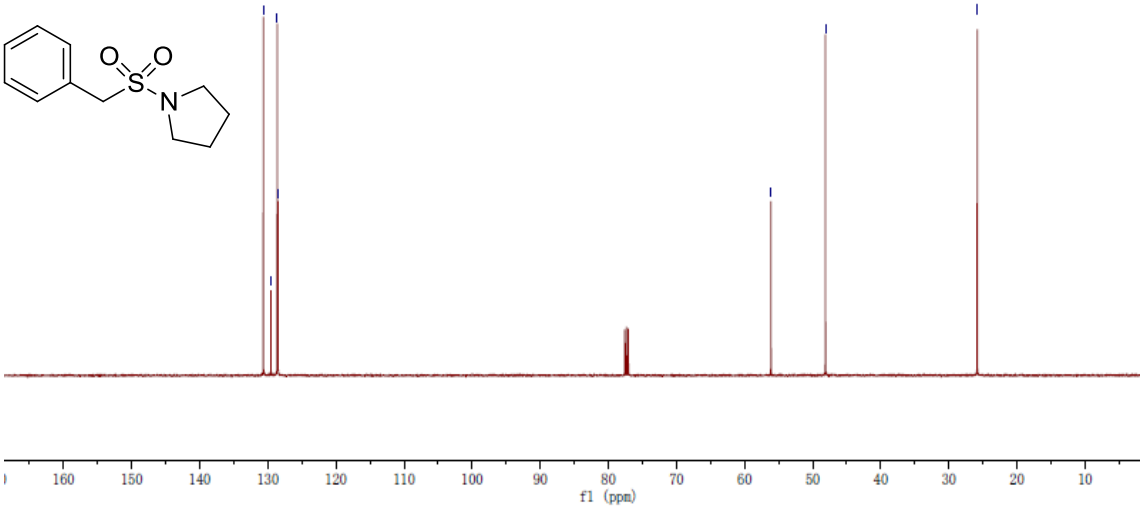
^{13}C (^{1}H) spectra (125 MHz) of 6-((Piperidin-1-ylsulfonyl)methyl)quinoline (3al)



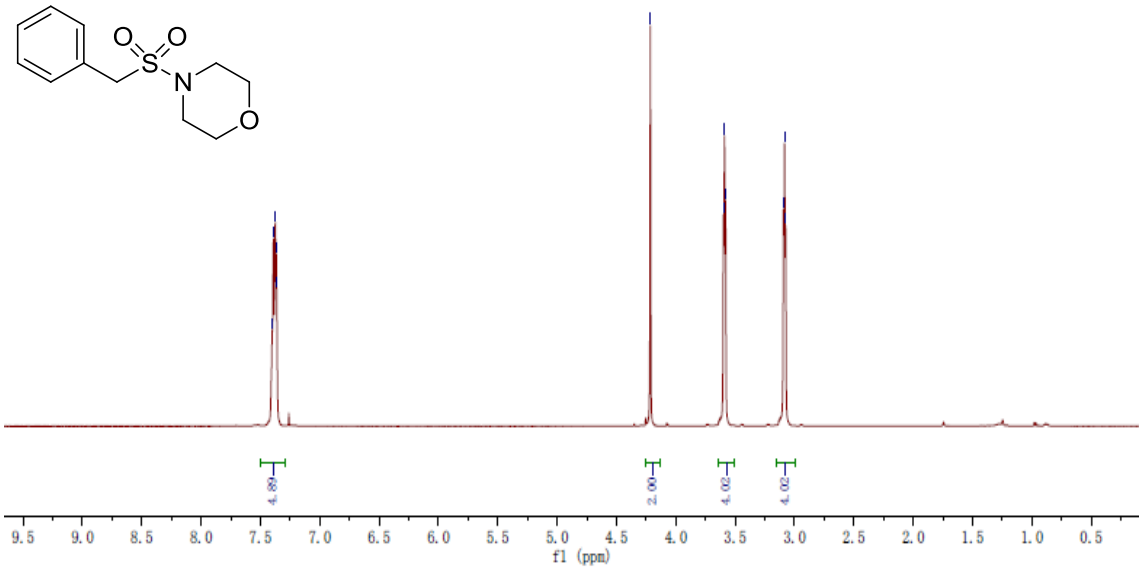
^{1}H spectra (500 MHz) of 1-(Benzylsulfonyl)pyrrolidine (3ba)



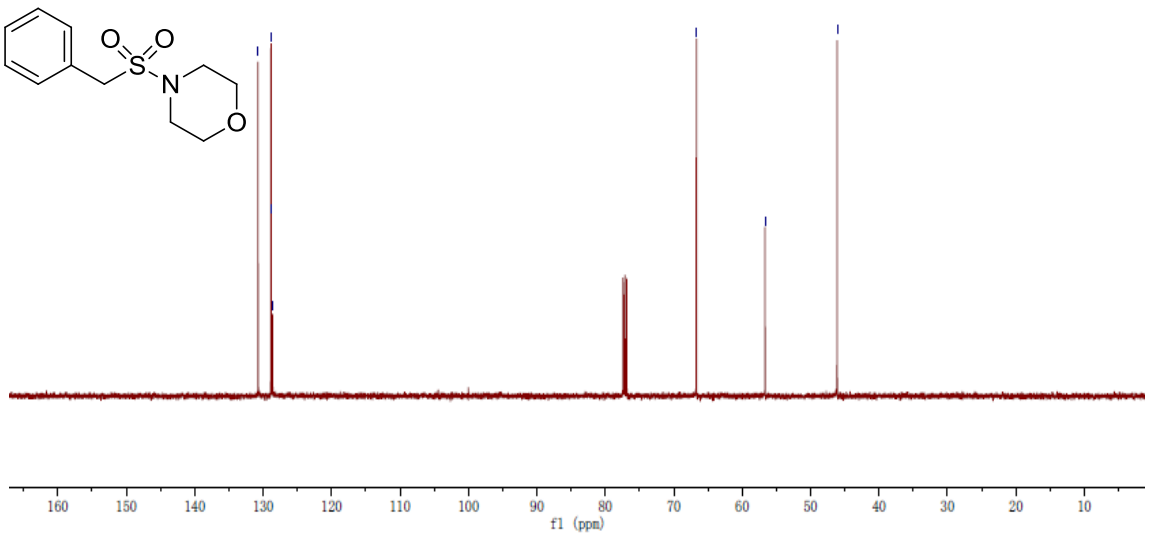
^{13}C (^{1}H) spectra (125 MHz) of 1-(Benzylsulfonyl)pyrrolidine (3ba)



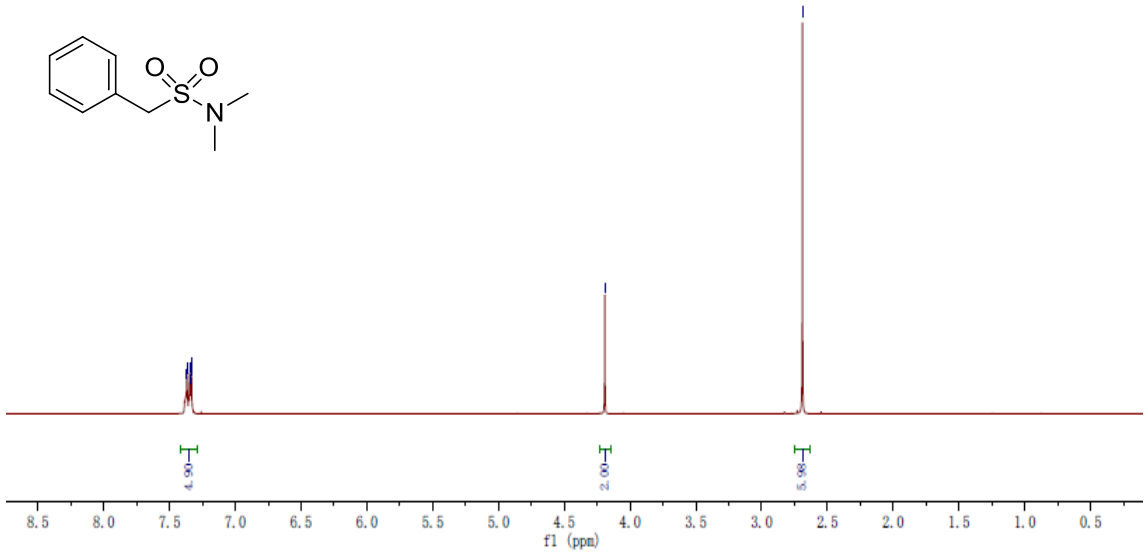
^{1}H spectra (500 MHz) of 4-(Benzylsulfonyl)morpholine (3ca)



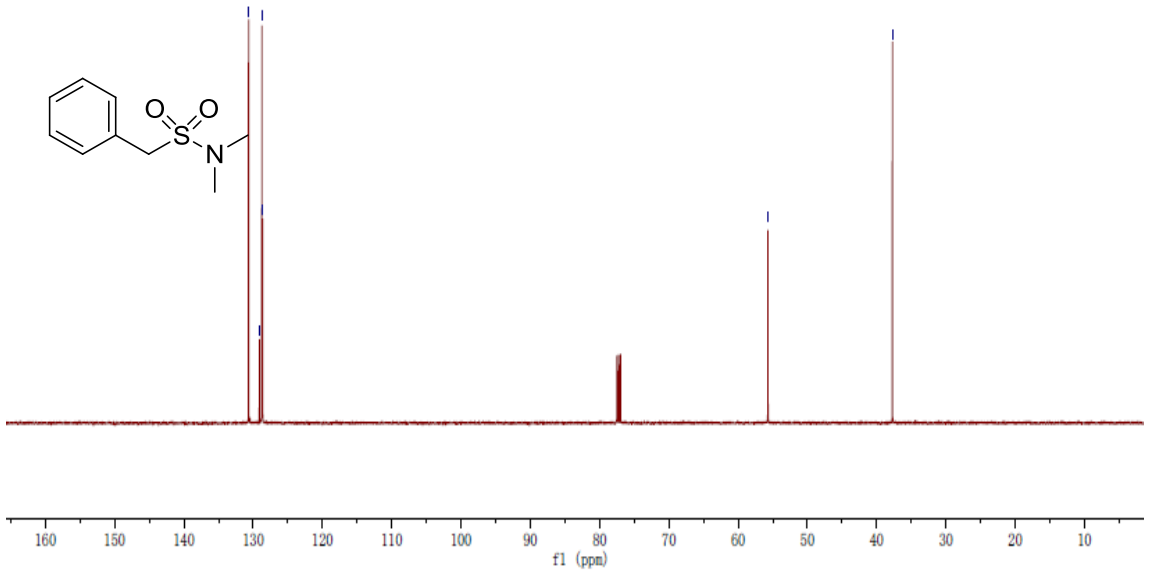
^{13}C (^{1}H) spectra (125 MHz) of 4-(Benzylsulfonyl)morpholine (3ca)



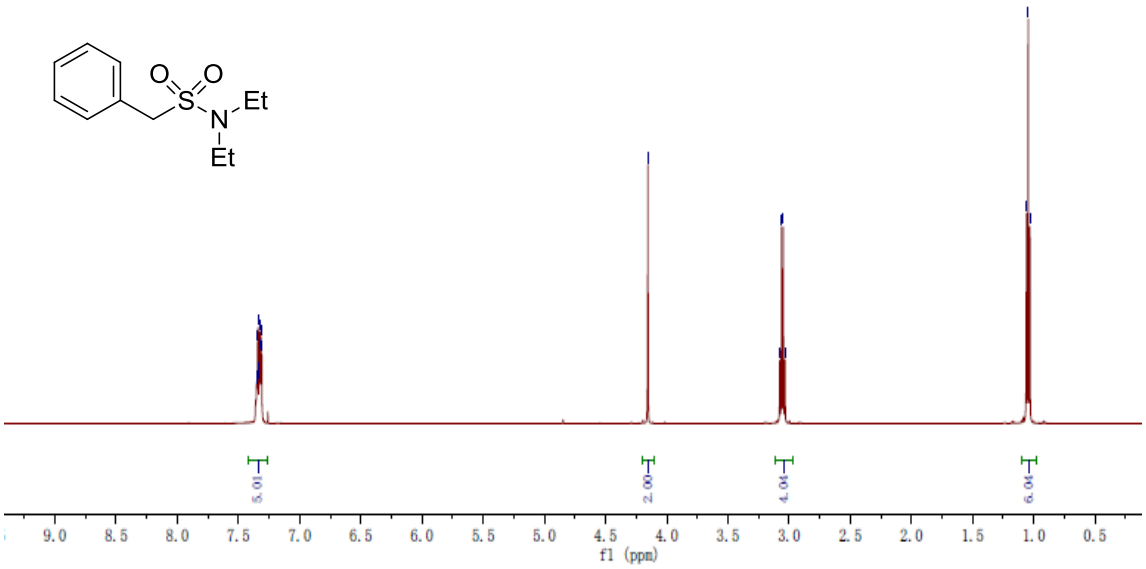
^{1}H spectra (500 MHz) of *N, N*-Dimethyl-1-phenylmethanesulfonamide (3da)



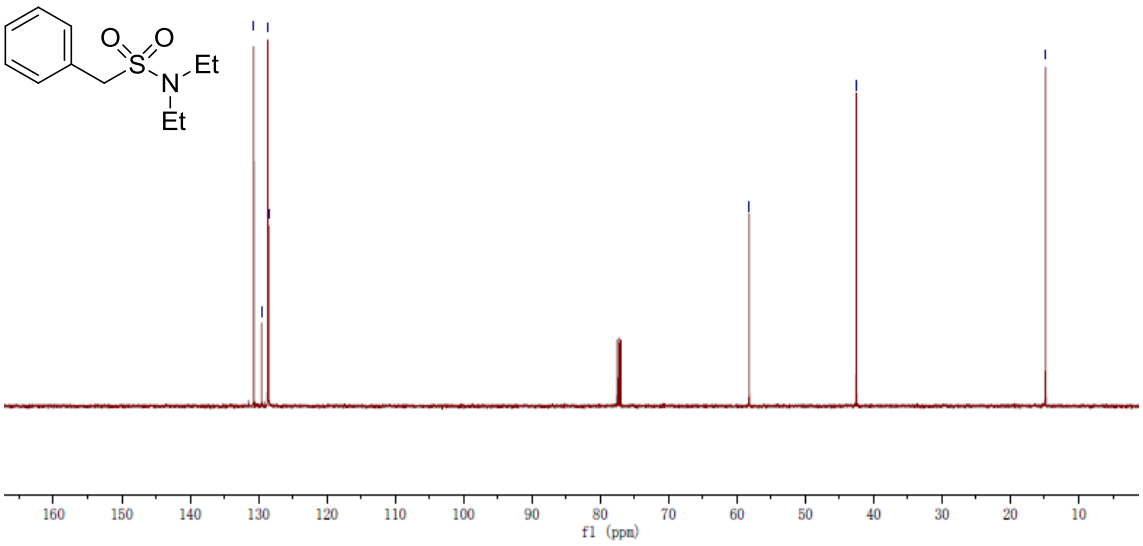
^{13}C (^{1}H) spectra (125 MHz) of *N, N*-Dimethyl -1-phenylmethanesulfonamide (3da)



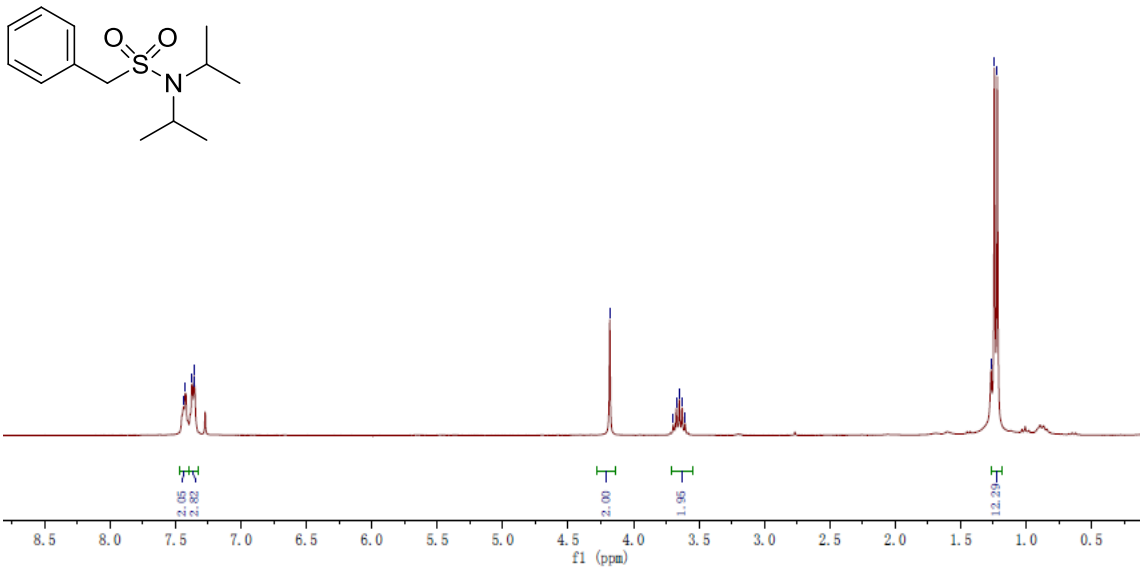
^{1}H spectra (500 MHz) of *N, N*-Diethyl-1-phenylmethanesulfonamide (3ea)



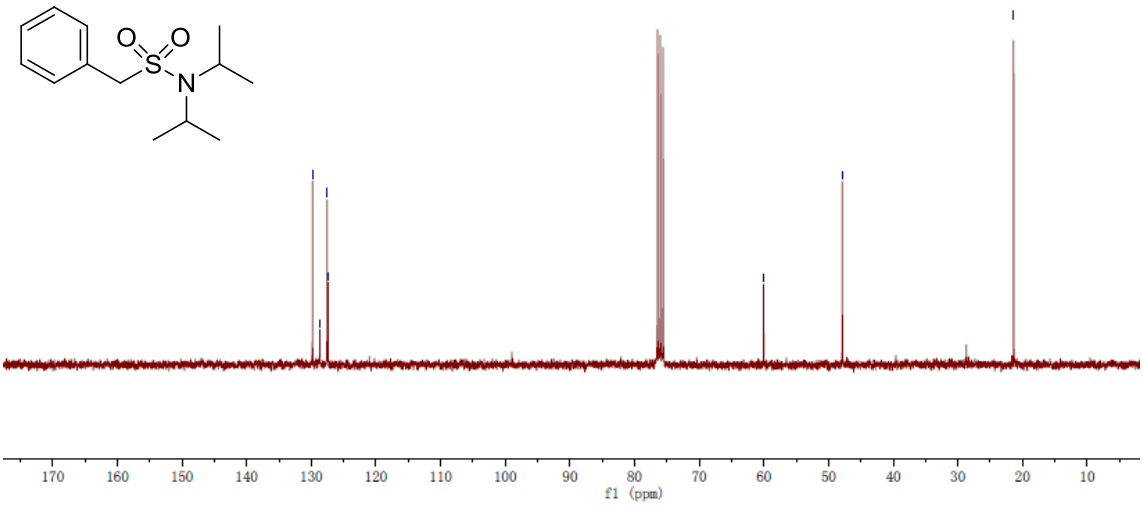
^{13}C (^{1}H) spectra (125 MHz) of *N, N*-Diethyl -1-phenylmethanesulfonamide (3ea)



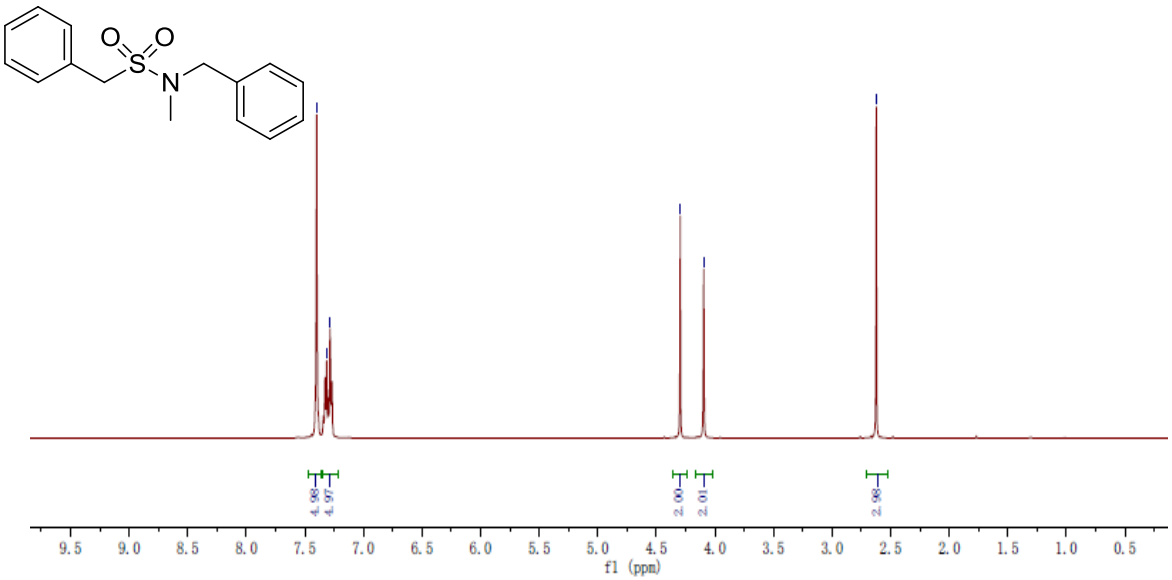
^{1}H spectra (500 MHz) of *N, N*-Diisopropyl-1-phenylmethanesulfonamide (3fa)



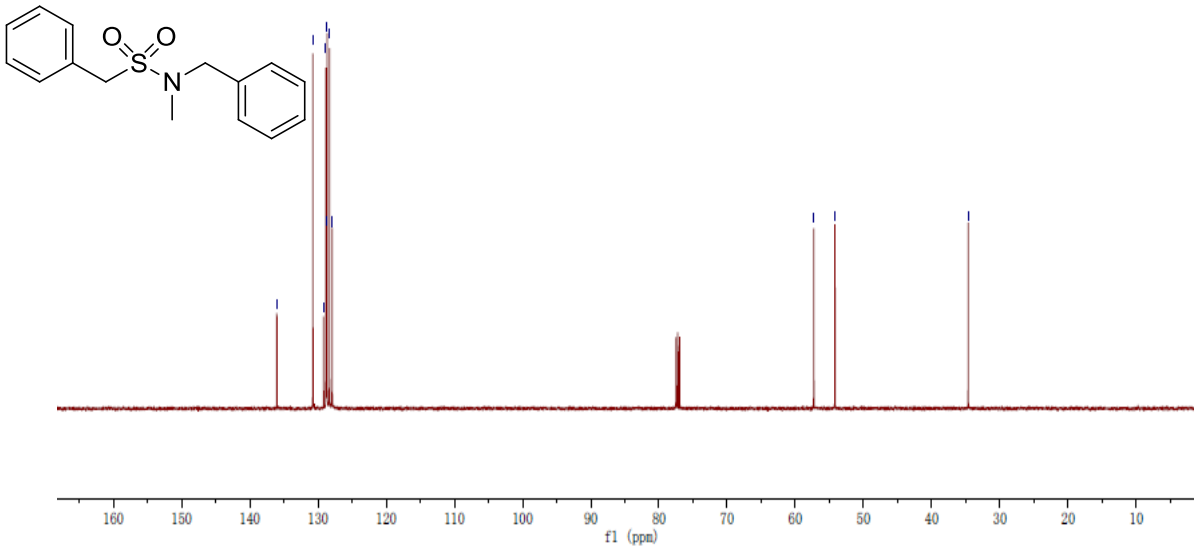
^{13}C (^{1}H) spectra (125 MHz) of *N, N*-Diisopropyl -1-phenylmethanesulfonamide (3fa)



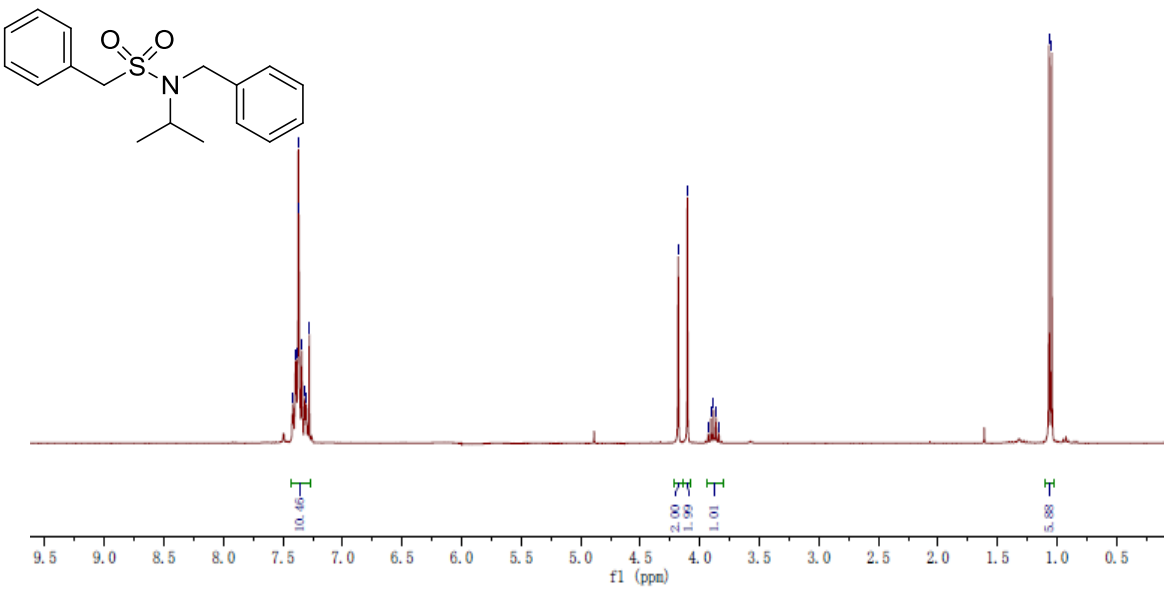
^{1}H spectra (500 MHz) of *N*-Benzyl-*N*-methyl-1-phenylmethanesulfonamide (3ga)



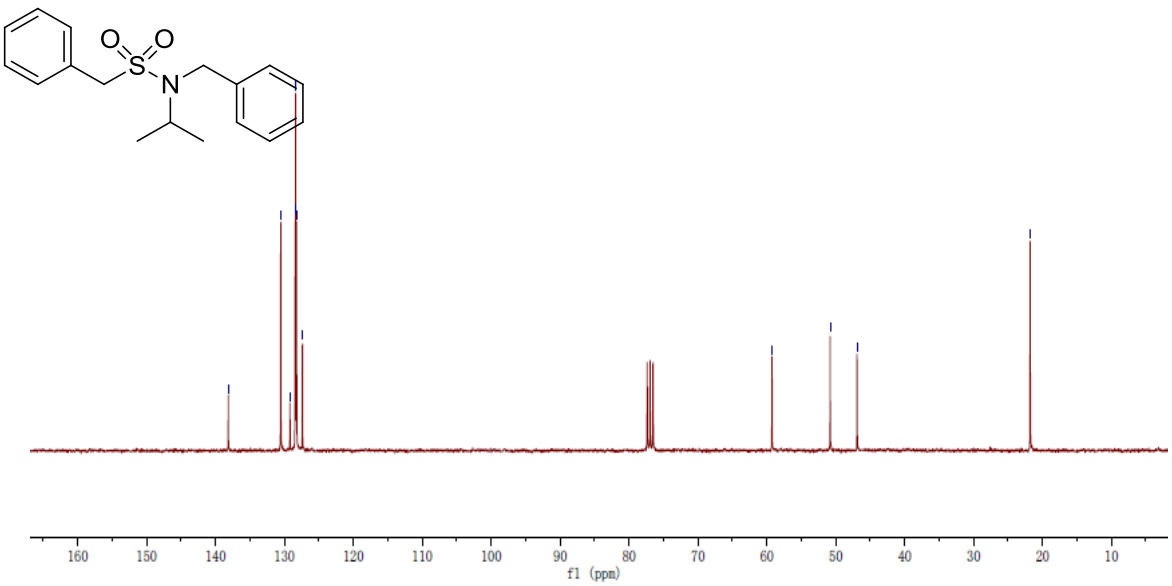
^{13}C (^{1}H) spectra (125 MHz) of *N*-Benzyl-*N*-methyl-1-phenylmethanesulfonamide (3ga)



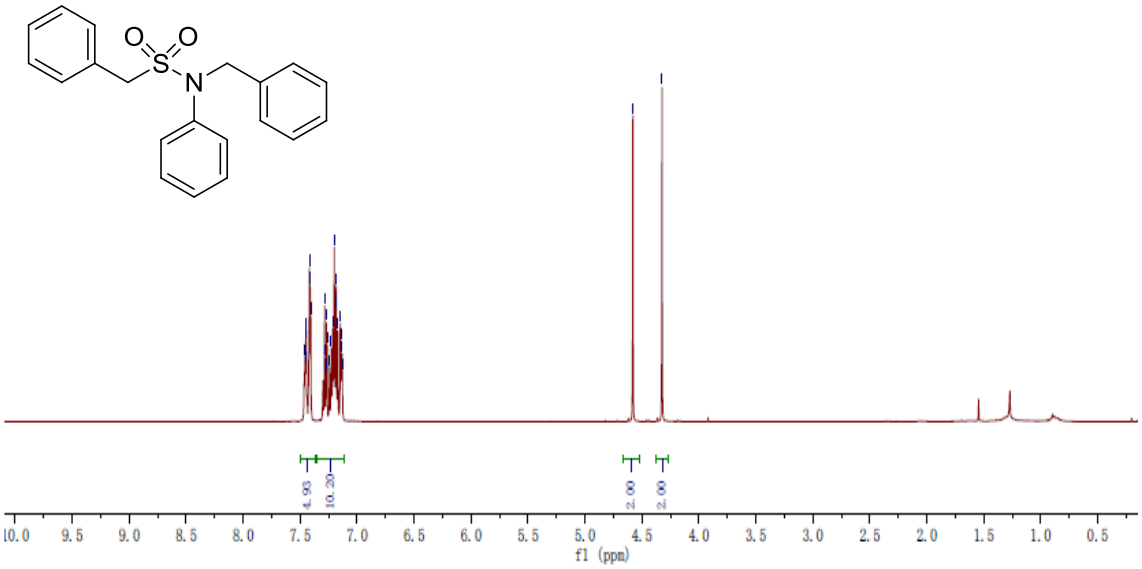
^{1}H spectra (500 MHz) of *N*-Benzyl-*N*-isopropyl-1-phenylmethanesulfonamide (3ha)



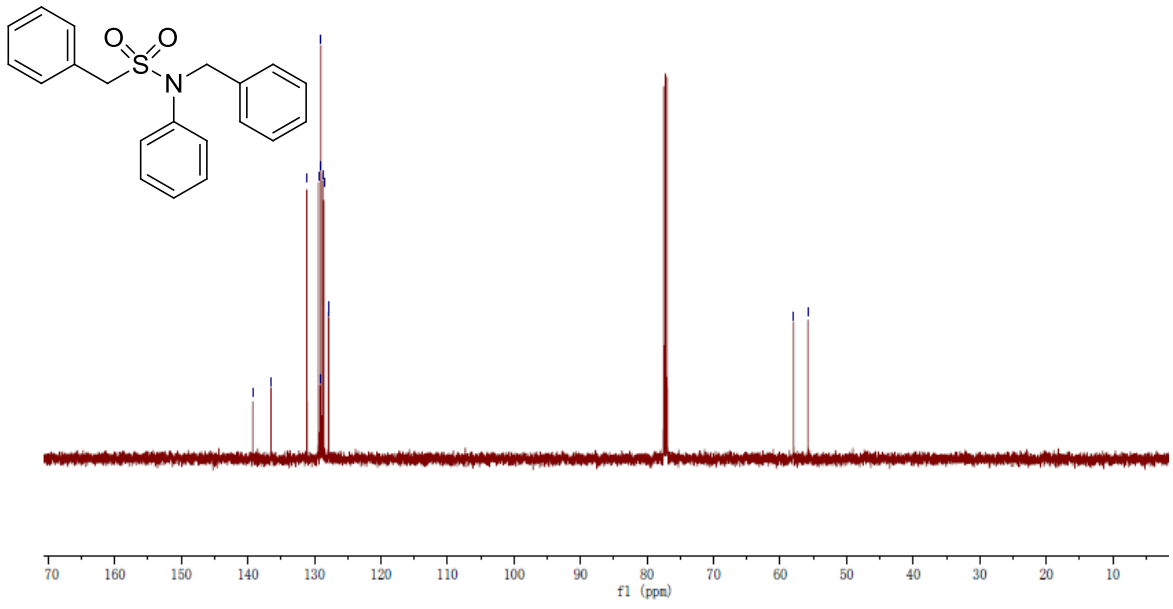
^{13}C (^{1}H) spectra (125 MHz) of *N*-Benzyl-*N*-isopropyl-1-phenylmethanesulfonamide (3ha)



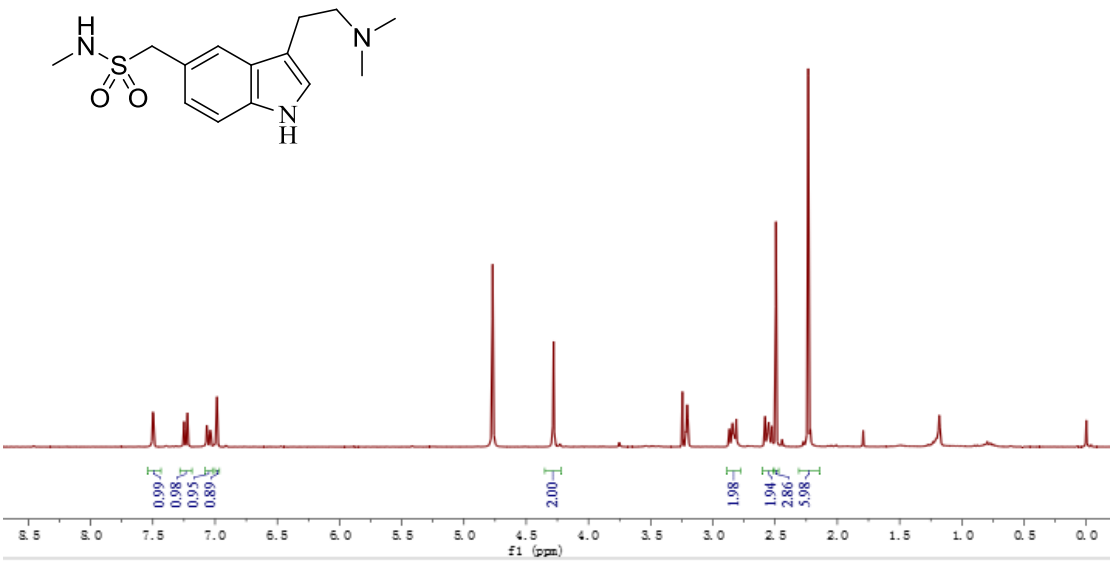
^{1}H spectra (500 MHz) of *N*-Benzyl-*N*,1-diphenylmethanesulfonamide (3ia)



^{13}C (^{1}H) spectra (125 MHz) of *N*-Benzyl-*N*,1-diphenylmethanesulfonamide (3ia)



^{1}H spectra (500 MHz) of 1-(3-(2-(Dimethylamino)ethyl)-1H-indol-5-yl)-N-methylmethanesulfonamide (3ja)



^{13}C (^{1}H) spectra (125 MHz) of 1-(3-(2-(Dimethylamino)ethyl)-1H-indol-5-yl)-N-methylmethanesulfonamide (3ja)