A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

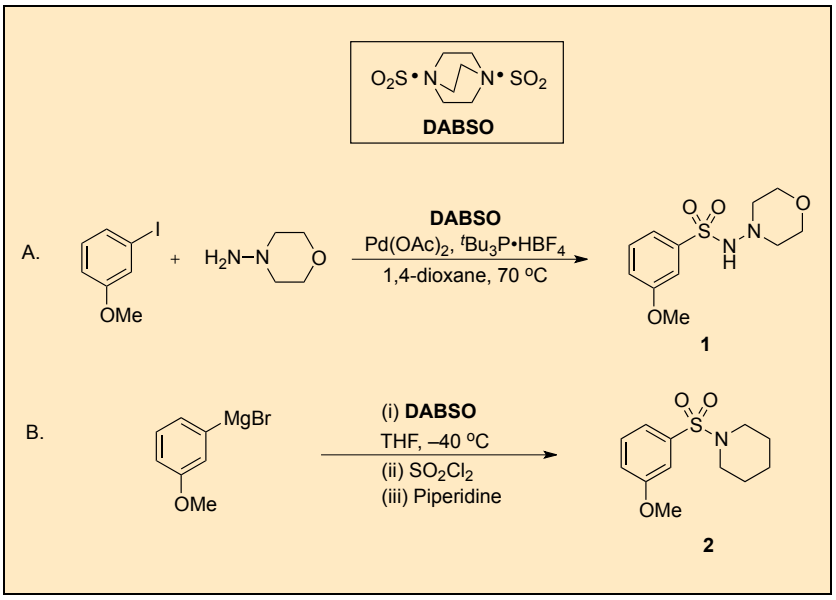
Organic Syntheses

DABCO-*bis*(sulfur dioxide), DABSO, as an easy-to-handle source of SO_2: Sulfonamide preparation

Edward J. Emmett and Michael C. Willis[1]*

University of Oxford, Chemistry Research Laboratory, 12 Mansfield Road, Oxford, OX1 3TA, United Kingdom

Checked by Changming Qin and Huw M. L. Davies



Procedure

*A. 3-Methoxy-N-morpholinobenzenesulfonamide (**1**).* An oven-dried (Note 1), two-necked 250 mL round-bottomed flask containing a dried magnetic stirrer bar (26 × 12 mm oval) is fitted with rubber septa and allowed to cool to room temperature under vacuum (0.3 mmHg). 1,4-Diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct (DABSO) (3.60 g, 15.0 mmol, 0.6 equiv) (Note 2), 1,4-diazabicyclo[2.2.2]octane (DABCO)

DOI: 10.15227/orgsyn.091.0125

(1.40 g, 12.5 mmol, 0.5 equiv), palladium(II) acetate (280 mg, 1.25 mmol, 5 mol%) and tri-*tert*-butylphosphonium tetrafluoroborate (510 mg, 1.75 mmol, 7 mol%) are weighed in air into a vial (Notes 3 and 4). The vacuum is switched to a positive argon pressure and the solids loaded into the flask. The flask is evacuated (0.3 mmHg) and filled with argon three times, being careful to avoid excessive dispersion of the solids. 3-Iodoanisole (3.0 mL, 5.85 g, 25.0 mmol, 1.0 equiv), 4-aminomorpholine (2.9 mL, 3.06 g, 30.0 mmol, 1.2 equiv) and 1,4-dioxane (140 mL) (Note 5) are added in this order *via* syringe through the septum. The flask, connected to the argon line, is clamped and placed in a pre-heated oil bath and stirred for 16 h at 70 °C (Note 6).

The reaction mixture, now a yellow solution with brown precipitate, is removed from the oil bath, allowed to cool to room temperature, diluted with DCM (50 mL) (Note 7), stirred for 5 min and filtered through a Celite® pad under low vacuum (Note 8). The reaction flask is rinsed clean (with sonication if required) with DCM (2 × 50 mL) and the Celite® pad washed with further DCM (100 mL). The filtrate is concentrated to dryness in a 500 mL round-bottomed flask on a rotary evaporator (40 °C, 40 mmHg) to give a partially solidified orange oil. The crude mixture is dissolved in DCM (approximately 100 mL) and silica gel (20 g) added. The DCM is removed on a rotary evaporator (40 °C, 40 mmHg) and the free-flowing silica with crude reaction mixture absorbed is dry-loaded onto a column of silica gel (Note 9). The column is run using a stepwise elution gradient from 50 – 100% Et_2O in hexane (Notes 7). The solvent is removed on a rotary evaporator (40 °C) and the solid dried under high-vacuum (room temperature, 0.1 mmHg, 4.0 h) to yield 3-methoxy-*N*-morpholinobenzenesulfonamide (**1**) as a white crystalline solid (5.14–5.45 g, 76–80 %) (Note 12).

*B. 1-((3-Methoxyphenyl)sulfonyl)piperidine (**2**).* An oven-dried (Note 1) three-necked 500 mL round-bottomed flask containing a dried magnetic stirrer bar (34 × 14 mm oval) is fitted with rubber septa and a thermometer and allowed to cool to room temperature under vacuum (0.3 mmHg). The vacuum is switched to a positive argon pressure and DABSO (8.4 g, 35.0 mmol, 1.25 equiv) (Note 2), weighed in air, is added to the flask. The flask is evacuated (0.3 mmHg) and filled with argon three times, being careful to avoid excessive dispersion of the solids. THF (160 mL) (Note 13) is added *via* syringe through the septum and the flask cooled to –45 °C (internal temperature, Note 14). 3-Methoxyphenylmagnesium bromide

solution (1M in THF, 28 mL, 28.0 mmol, 1.0 equiv) (Note 15) is added dropwise to the stirred white suspension *via* syringe pump (Note 16) and the reaction left stirring at the same temperature for 1.0 h. Sulfuryl chloride (2.3 mL, 3.78 g, 28.0 mmol, 1.0 equiv) (Note 15) is added dropwise *via* syringe pump (Note 17) and the resultant white suspension left stirring at the same temperature for 5 min. The cooling bath is removed, the suspension allowed to warm to room temperature (approximately 1 h) and left stirring for a further 30 min (Note 17). Piperidine (11.0 mL, 9.5 g, 112 mmol, 4.0 equiv) (Note 15) is added dropwise *via* syringe pump (Note 18) at room temperature and the reaction mixture left stirring overnight (16 h).

Water (75 mL) (Note 19) and EtOAc (200 mL) (Note 7) are added in one portion to the flask at room temperature and the resultant mixture stirred for 5 min. The reaction mixture is transferred to a 1.0 L separating funnel and water (200 mL) added. The funnel is gently shaken, the layers separated and the aqueous layer extracted with further EtOAc (3 × 100 mL). The combined organic layers are washed with saturated brine (200 mL), dried ($MgSO_4$, 15.0 g), filtered through a medium porosity sinter funnel under low vacuum and concentrated on a rotary evaporator (40 °C, 40 mmHg) to give an off-white solid.

The solid is dissolved in DCM (approximately 100 mL) (Note 7) and transferred to a 250 mL round-bottomed flask and silica gel (16 g) added. The DCM is removed on a rotary evaporator (40 °C, 40 mmHg) and the free-flowing silica with crude product absorbed is dry-loaded onto a column of silica gel (Note 20). The column is run using a stepwise elution gradient from 10 – 45% Et_2O in hexane (Notes 7 and 21) The solvent is removed on a rotary evaporator (40 °C, 40 mmHg) and dried under high-vacuum (room temperature, 0.1 mmHg, 4.0 h) to yield 1-((3-methoxyphenyl)sulfonyl)piperidine (**2**) as a crystalline white solid (6.28–6.42 g, 88–90%) (Note 23).

Notes

1. "Oven-dried" (and "dried" thereafter) refers to equipment kept for at least 24 h in an >200 °C oven.
2. DABSO was prepared by the *Organic Syntheses* procedure "Preparation of DABSO from Karl-Fischer Reagent" *Org. Synth.* **2013**, *90*, 301. The

submitter purchased DABSO from Sigma-Aldrich (≥95%). The lumps were broken-up and the material weighed out as a fine powder.

3. DABCO was bought from Alfa-Aesar (98%) and sublimed (50 °C, 0.3 mmHg) prior to use. Following sublimation it was ground to give a fine white powder. Due to DABCO's hygroscopicity, care should be taken, where possible, to minimize contact with the air. Purified DABCO was stored under a nitrogen atmosphere.
4. Palladium(II) acetate (Pd 45.9-48.2%) and tri-*tert*-butylphosphonium tetrafluoroborate (97%) were purchased from Alfa Aesar and used as received.
5. 3-Iodoanisole was purchased from Sigma Aldrich (99%) and 4-aminomorpholine from Alfa Aesar (98%) and both reagents were used as received. 1,4-Dioxane (anhydrous, 99.8%) was bought from Sigma Aldrich and was degassed with dry argon bubbling for 30 min prior to use. The submitter reported that 4-aminomorpholine decomposes over time to morpholine, therefore purity was confirmed to be 95% by ^{1}H NMR spectroscopy before use.
6. The initial orange-beige suspension changed to a dark brown solution in ca. 30 min. A precipitate begins to form after ca. 1 h. The submitter reported that the reaction can be monitored *via* TLC - product R_f = 0.2, 3-iodoanisole R_f = 0.75 (eluent 75% Et_2O in petroleum ether) - although starting material is not fully consumed before catalyst deactivation occurs.
7. Dichloromethane (DCM; HPLC grade) was purchased from Sigma-Aldrich; Hexanes (Certified ACS), Et_2O (Certified ACS) and EtOAc (Certified ACS) were purchased from Fisher Chemical and used without further purification.
8. A Celite® 545 pad (30 g) was packed with DCM in a 7 cm diameter medium porosity sintered glass funnel under low vacuum.
9. Flash column chromatography was performed with Silicycle Silica Flash® Si P60 silica gel (40 – 63 μm) (125 g slurried in hexane) in an 8.0 cm diameter column with a thin band of sand protecting the top of the silica under a slightly positive pressure.
10. Stepwise elution gradient as follows: 700 mL 50%, 500 mL 60%, 500 mL 70%, 500 mL 80%, 100% Et_2O in hexanes until no further product was detected by TLC.
11. The desired product has an R_f = 0.13 when a TLC is run in 75% EtOAc in hexanes as the eluent (3-iodoaniosle R_f = 0.84). The product is

visualized using a UV lamp and staining in phosphomolybdic acid (giving a dark-blue spot).

12. Melting point was measured by the dry sample, mp 116–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 7.27 ppm) δ: 2.64 (t, *J* = 4.8 Hz, 4 H $(NCH_2CH_2O)_2$), 3.62 (t, *J* = 4.8 Hz, 4 H, $(NCH_2CH_2O)_2$), 3.87 (s, 3 H, OMe), 5.60 (s, 1 H, NH), 7.14 (dd, *J* = 8.0, 2.0 Hz, 1 H, Ar-H), 7.43 (t, *J* = 8.0 Hz, 1 H, Ar-H), 7.49 (t, *J* = 2.0 Hz, 1 H, Ar-H), 7.57 (d, *J* = 8.0 Hz, 1 H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, 77.0 ppm) δ: 55.6, 56.4, 66.5, 112.5, 119.4, 120.1, 129.8, 139.7, 159.6; IR ν_{max} (film)/cm^{-1} 3212, 2963, 2856, 1597, 1478, 1433, 1361, 1317, 1287, 1242, 1157, 1109, 1034, 864, 685 (principal peaks); HRMS (FTMS+ p-NSI) found *m*/*z* 295.0721 $[M+Na]^+$, $C_{11}H_{16}N_2O_4SNa$ requires *m*/*z* 295.0723. Reverse phase HPLC analysis reveals purity >99% (run on an Agilent Zorbax SB-C18, 5 μm, 4.6 × 150 mm column (23 °C) at a flow rate of 1.5 mL/min of 70:30 MeCN:H_2O observed at 210 nm giving a retention time of 1.32 min, 1.0 mg/mL in CH_3CN).
13. THF (HPLC) was used as dried by an in-house solvent purification system (SG Water USA LLC) having passed through anhydrous alumina columns. It was degassed by bubbling argon for 30 min before use. The submitter determined the water content in THF was <10 ppm by regular Karl Fischer titrations.
14. Cooling was achieved using a dry-ice-acetone bath in a Dewar flask and maintained within ±5 °C of the specified temperature by addition of dry ice as necessary.
15. 3-Methoxyphenylmagnesium bromide solution and piperidine (99%) were purchased from Sigma Aldrich and used as received. Sulfuryl chloride (97%) was purchased from Sigma Aldrich and fractionally distilled (with a Vigreux column) under argon to give a colorless fraction (oil bath temperature, 85 °C, 1 atm) on the day of use. Piperidine was used in significant excess because it was used as both a base and a nucleophile. In addition, residual SO_2 (from DABSO and the oxidative chlorination) can complex to piperidine, thereby removing it from availability for sulfonylation. A reduction in loading leads to a reduction in sulfonamide yield. The submitter determined the molarity of Grignard reagent to be at least 1M by titration with salicylaldehyde phenylhydrazone.[17]
16. Added at a rate of 0.4 mL/min. The internal temperature was maintained between –40 and –50 °C. The white suspension thinned as

the Grignard reagent was added before re-thickening to form another white suspension.

17. Added at a rate of 0.15 mL/min. The internal temperature was maintained between –40 and –50 °C. Upon warming to room temperature the white suspension turned to a yellow suspension.
18. Added at a rate of 0.3 mL/min. Although a slight exotherm was observed, the internal temperature did not exceed 40 °C at this addition rate. The yellow suspension became white by the end of the addition.
19. ASTM type II water, produced by RO/DI (HARLECO) was used as received.
20. Flash column chromatography was performed with Silicycle Silica Flash® Si P60 silica gel (40 – 63 μm) (200 g slurried in hexane) in an 8.0 cm diameter column with a thin band of sand protecting the top of the silica under slightly positive pressure.
21. Stepwise elution gradient as follows: 500 mL 10%, 500 mL 15%, 500 mL 20%, 1.5 L 25%, 1.5 L 35%, 45% Et_2O in hexanes until no product was detected by TLC.
22. The product has an R_f = 0.44 when a TLC is run in 75 % EtOAc in hexane as the eluent. The product is visualized using a UV lamp.
23. Melting point was measured by the dry sample, mp 115–116 °C; ^{1}H NMR (400 MHz, DMSO-d_6, 2.50 ppm) δ: 1.30–1.35 (m, 2 H, $N(CH_2CH_2)_2CH_2$), 1.47–1.52 (m, 4 H, $N(CH_2CH_2)_2CH_2$), 2.85 (t, J = 5.2 Hz, 4 H, $N(CH_2CH_2)_2CH_2$), 3.83 (s, 3 H, O*Me*), 7.16 (t, J = 2.1 Hz, 1 H, Ar-*H*), 7.25–7.30 (m, 2 H, Ar-*H*), 7.55 (t, J = 8.0 Hz, 1 H, Ar-*H*); ^{13}C NMR (100 MHz, DMSO-d_6, 39.5 ppm) δ: 22.8, 24.7, 46.6, 55.6, 112.3, 118.7, 119.5, 130.5, 136.7, 159.5; IR ν_{max} (film)/cm^{-1} 2940, 2851, 1597, 1478, 1359, 1340, 1318, 1287, 1241, 1167, 1098, 1040, 931, 856, 724, 688; (principal peaks); HRMS (FTMS+p-NSF) found m/z 256.1002 $[M+H]^+$, $C_{12}H_{18}NO_3S$ requires m/z 256.1002. Reverse phase HPLC analysis reveals purity >99% (run on an Agilent Zorbax SB-C18, 5 μm, 4.6 × 150 mm column (23 °C) at a flow rate of 1.5 mL/min of 75:25 MeCN:H_2O observed at 210 nm giving a retention time of 1.95 min, 1.0 mg/mL in MeCN).

Handling and Disposal of Hazardous Chemicals

The procedures in this article are intended for use only by persons with prior training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011 www.nap.edu). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

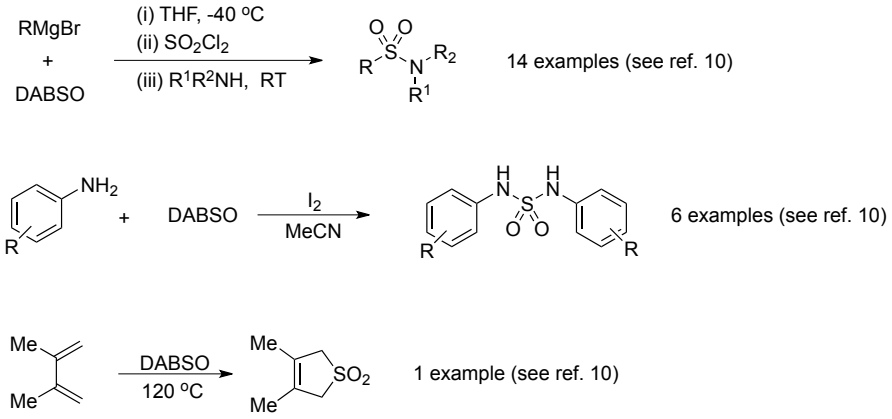
These procedures must be conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

Discussion

Despite its established utility in organic synthesis,[2] sulfur dioxide remains an underexploited reagent. The reasons for this are arguably the issues associated with both its toxicity and the specialist equipment required to handle gaseous reagents safely. A bench-stable, easy-to-use solid equivalent of sulfur dioxide would therefore be of considerable value to practicing synthetic chemists. We proposed that amine-sulfur dioxide complexes, many of which are solid, could provide such an equivalent.

Amine-sulfur dioxide charge transfer complexes of the form $R_3N{\rightarrow}SO_2$ (R = C or H), have been reported in the literature as early as 1900.[3] Although they have been studied widely, both theoretically[4] and spectroscopically,[5] to investigate the nature of the dative bonding, they appear to have found only a few practical uses. Olah used trimethyl(ethyl)amine complexes as reducing agents,[6] for example deoxygenating *N*-oxides to amines, nitro groups to nitriles and sulfoxides to sulfides; whilst Rudkevich developed a metalloporphyrin assay for sulfur dioxide concentration based on this Lewis acid-base chemistry.[7] However, they occur most extensively in industrial settings where amine solutions have been patented as sulfur dioxide gas effluent scrubbers.[8] We found that the complex formed from sulfur dioxide and 1,4-diazabicyclo[2.2.2]octane (DABCO), DABCO-

bis(sulfur dioxide), which we have abbreviated to DABSO, proved to be an excellent choice as it was an air-stable microcrystalline white powder which underwent a range of desired transformations functioning as a sulfur dioxide equivalent. This complex was first synthesized by Santos and Mello for spectroscopic investigation, but the compound, to the best of our knowledge, has not been reported on since.[9]

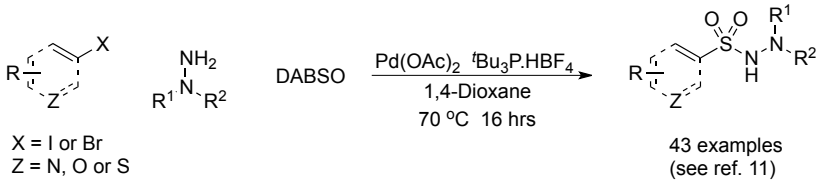


Scheme 1. Replacement of SO_2 gas with DABSO in known transformations

We successfully used DABSO in place of sulfur dioxide gas in a range of known transformations (Scheme 1);[10] sulfonamides, sulfamides and sulfolenes were synthesized by adapting procedures originally developed for the gaseous reagent.

In addition to this, we have developed the first palladium-catalyzed aryl halide cross coupling to incorporate sulfur dioxide.[11] Inspired by the prevalence of palladium-catalyzed carbonylations,[12] we noted several similarities between CO and SO_2. These included frontier molecular orbital symmetry,[13] their behaviors as ligands for transition metals[14] and their ability to insert into metal-alkyl bonds.[15] By using aryl, heterocyclic or alkenyl iodides in tandem with *N*,*N*-disubstituted hydrazines and DABSO with a $Pd(OAc)_2$/^{t}Bu$_3$P catalytic system, *N*-aminosulfonamides were delivered in good to excellent yields (Scheme 2).[11] This amino*sulfonylation* is a sulfonylative analogue of the well precedented amino*carbonylation*, where aryl halide, carbon monoxide and amine combine under palladium catalysis to furnish amides.[12] It is also noted that the controlled loading of sulfur

dioxide in only slight excess that DABSO allows, is key to this reactivity. Saturation with SO_2 gas in place of DABSO leads only to a very poor yield.



Scheme 2. Our novel palladium-catalyzed aminosulfonylation

In this *Organic Syntheses* publication, we demonstrate the utility of DABSO in two methods of sulfonamide formation; one *via* our novel palladium-catalyzed aminosulfonylation and the other using a Grignard reagent (Scheme 1). The sulfonamide functional group is particularly relevant to the pharmaceutical industry, present in 10% of the top 50 grossing pharmaceutical products of 2009.[16] Our methods of sulfonamide formation allow the $–SO_2N–$ moiety to be introduced into a wide variety of positions in the molecule, demonstrating the potential for a diverse library synthesis. Current methods of sulfonamide formation (such as traditional electrophilic aromatic sulfonylation chemistry) would not provide such diversity without resorting to sulfur dioxide gas – a problem which is now eliminated by the use of DABSO.

References

1. University of Oxford, Chemistry Research Laboratory, 12 Mansfield Road, Oxford, OX1 3TA, United Kingdom. E-mail: michael.willis@chem.ox.ac.uk
2. For a review see: Florjanczyk, Z.; Raducha, D. *Pol. J. Chem.* **1995**, *69*, 481–508. For recent advancements see: Vogel, P.; Turks, M.; Bouchez, L.; Markovic, D.; Varela-Alvarez, A.; Sordo, J. A. *Acc. Chem. Res.* **2007**, *40*, 931–942.
3. Divers, E.; Ogawa, M. *J. Chem. Soc., Trans.* **1900**, *77*, 327–335.
4. Wong, M. W.; Wiberg, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7527–7535.

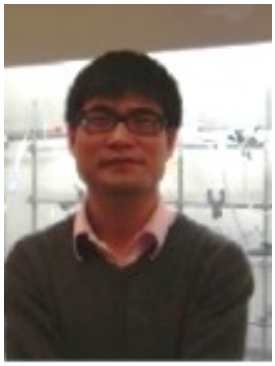
5. For selected examples see: (a) Faria, D. L. A.; Santos, P. S. *J. Raman Spectrosc.* **1988**, *19*, 471–478; (b) Hata, T.; Kinumaki, S. *Nature* **1964**, *203*, 1378–1379; (c) Oh, J. J.; LaBarge, M. S.; Matos, J.; Kampf, J. W.; Hillig, K. W.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1991**, *113*, 4732–4738; (d) Byrd, W. E. *Inorg. Chem.* **1962**, *1*, 762–768.
6. (a) Olah, G. A.; Arvanaghi, M.; Vankar, Y. D. *Synthesis* **1980**, 660–661; (b) Olah, G. A.; Vankar, Y. D.; Gupta, B. G. B. *Synthesis* **1979**, 36–37; (c) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M. *Synthesis* **1979**, 984–985.
7. Leontiev, A. V.; Rudkevich, D. M. *J. Am. Chem. Soc.* **2005**, *127*, 14126–14127.
8. Klass, D. L.; Conrad J. R. Removal of Sulfur Dioxide from Waste Gases. U.S. Patent 4,208,387, Jun 17, 1980.
9. Santos, P. S.; Mello, M. T. S. *J. Mol. Struct.* **1988**, *178*, 121–133.
10. Woolven, H.; Gonzalez-Rodriguez, C.; Marco, I.; Thompson, A. L.; Willis, M. C. *Org. Lett.* **2011**, *13*, 4876–4878.
11. (a) Nguyen, B.; Emmett, E. J.; Willis, M. C. *J. Am. Chem. Soc.* **2010**, *132*, 16372–16373; (b) Emmett, E. J.; Richards-Taylor, C. S.; Nguyen, B.; Garcia-Rubia, A.; Hayter, B. R.; Willis, M. C. *Org. Biomol. Chem.* **2012**, *10*, 4007–4014.
12. For a review see: Brennfuhrer, A.; Neumann, H.; Beller, M. *Angew. Chem.Int. Edit.* **2009**, *48*, 4114–4133.
13. Lloyd, D. R.; Roberts, P. *J. Mol. Phys.* **1973**, *26*, 225–230.
14. For selected examples see: (a) Schenk, W. A. *Agnew. Chem. Int. Edit.* **1987**, *26*, 98–109; (b) D. L. Lichtenberger, A. Rai-Chaudhuri, and R. H. Hogan, in *Inorganometallic Chemistry*, Ed. T. P. Fehlner, Plenum Press, New York-London, 1992, Ch. 5, 223; (c) Kubas, G. J. *Acc. Chem. Res.* **1994**, *27*, 183–190.
15. For a selected examples see: (a) Wojcicki, A. *Acc. Chem. Res.* **1971**, *4*, 344–352; (b) Lefort, L.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **1998**, *17*, 1420–1425.
16. Njardarson group: http://cbc.arizona.edu/njardarson/group/sites/default/files/Top200PharmaceuticalProductsByWorldwideSalesin2009.pdf
17. Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755-3756.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

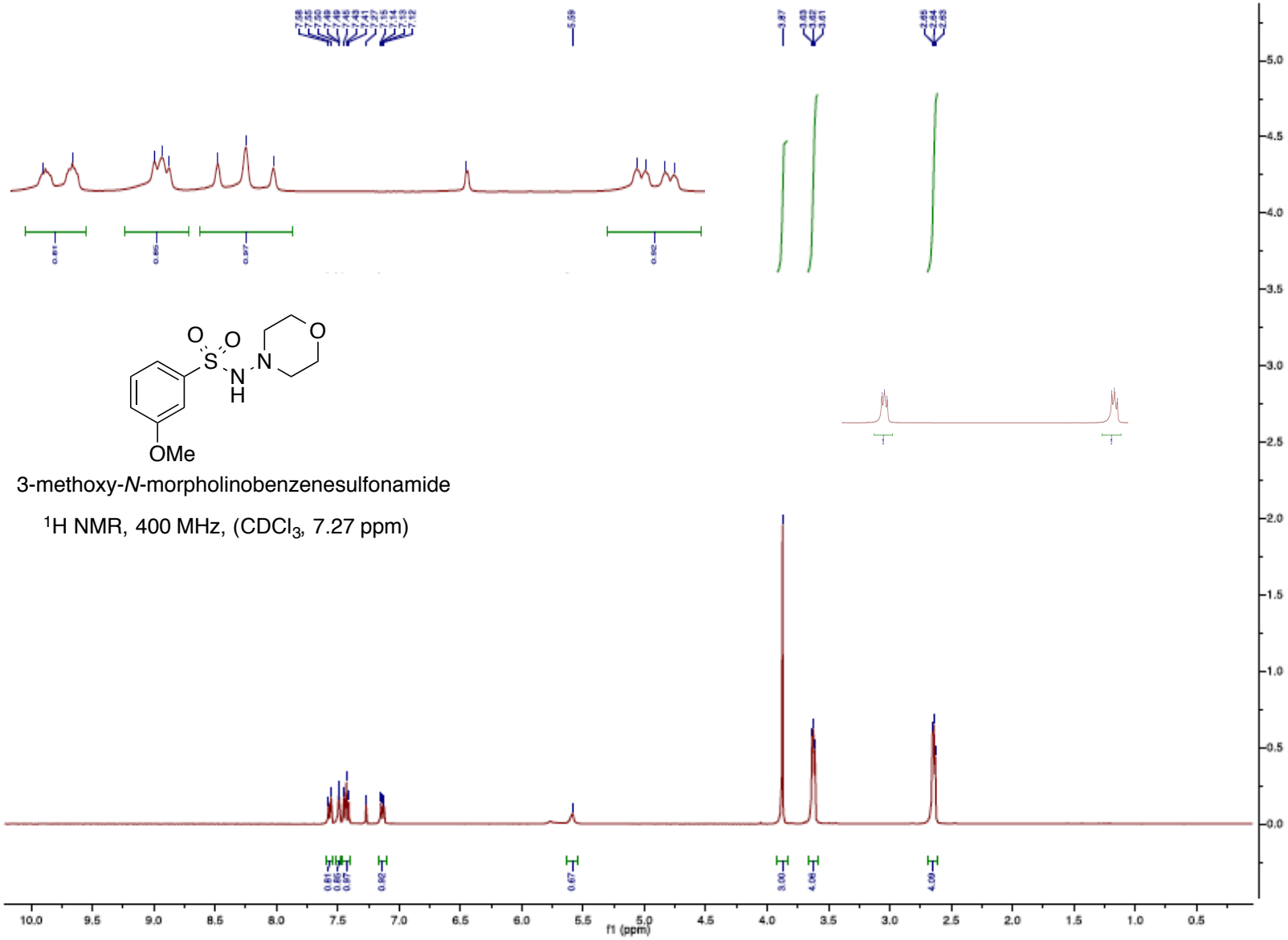
DABCO: 1,4-Diazabicyclo[2.2.2]octane; (280-57-9)
SO_2: Sulfur dioxide; (7446-09-5)
DABSO, DABCO-*bis*(sulfur dioxide): 1,4-Diazoniabicyclo[2.2.2]octane, 1,4-disulfino-, bis(inner salt); (119752-83-9)
Palladium(II) acetate: Acetic acid, palladium(2+) salt (2:1); (3375-31-3)
Tri-*tert*-butylphosphonium tetrafluoroborate: Phosphine, tris(1,1-dimethylethyl)-, tetrafluoroborate(1-) (1:1); (131274-22-1)
3-Iodoanisole: Benzene, 1-iodo-3-methoxy-; (766-85-8)
4-Aminomorpholine: 4-Morpholinamine; (4319-49-7)
3-Methoxy-*N*-morpholinobenzenesulfonamide: Benzenesulfonamide, 3-methoxy-*N*-4-morpholinyl-; (1255365-27-5)
3-Methoxyphenylmagneisum bromide: Magnesium, bromo(3-methoxyphenyl)-; (36282-40-3)
1-((3-Methoxyphenyl)sulfonyl)piperidine: Piperidine, 1-[(3-methoxyphenyl)sulfonyl]-; (173681-65-7)

Michael Willis received his undergraduate education at Imperial College London, and his PhD from the University of Cambridge working with Prof. Steven V. Ley. After a postdoctoral stay with Prof. David A. Evans at Harvard University, as a NATO/Royal Society Research Fellow, he was appointed to a lectureship at the University of Bath in November 1997. In January 2007 he moved to the University of Oxford, where he is now a Professor of Chemistry and a Fellow of Lincoln College. His group's research interests are based on the development and application of new catalytic processes for organic synthesis.

Edward Emmett is originally from London and received his MChem from the University of Oxford in 2010. He joined Prof. Michael Willis's research group as an undergraduate student and remained to study for his DPhil in Organic Chemistry. His research focuses on the development of amine-sulfur dioxide complexes as SO_2 surrogates in both catalytic and non-catalytic methodologies.

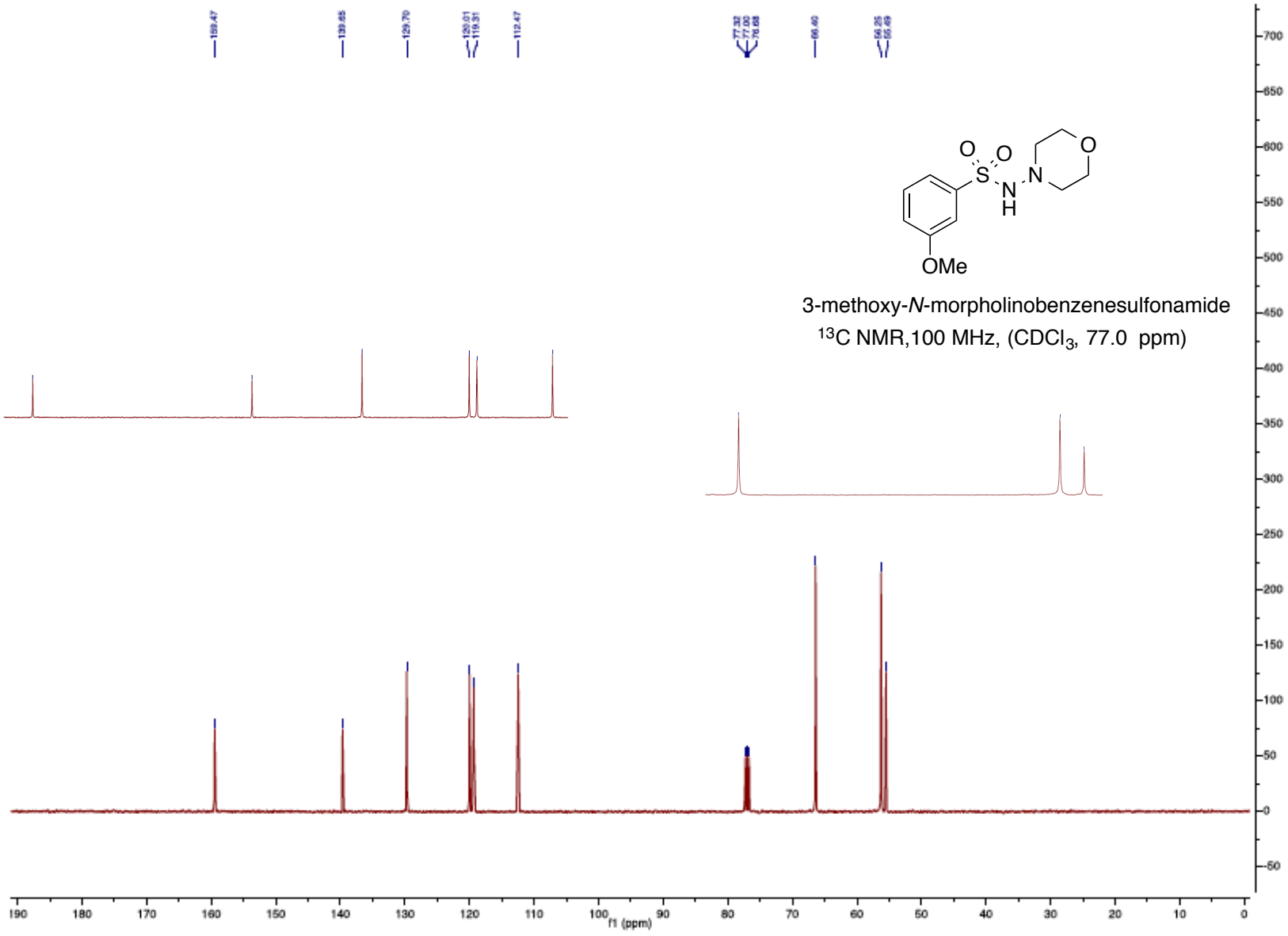


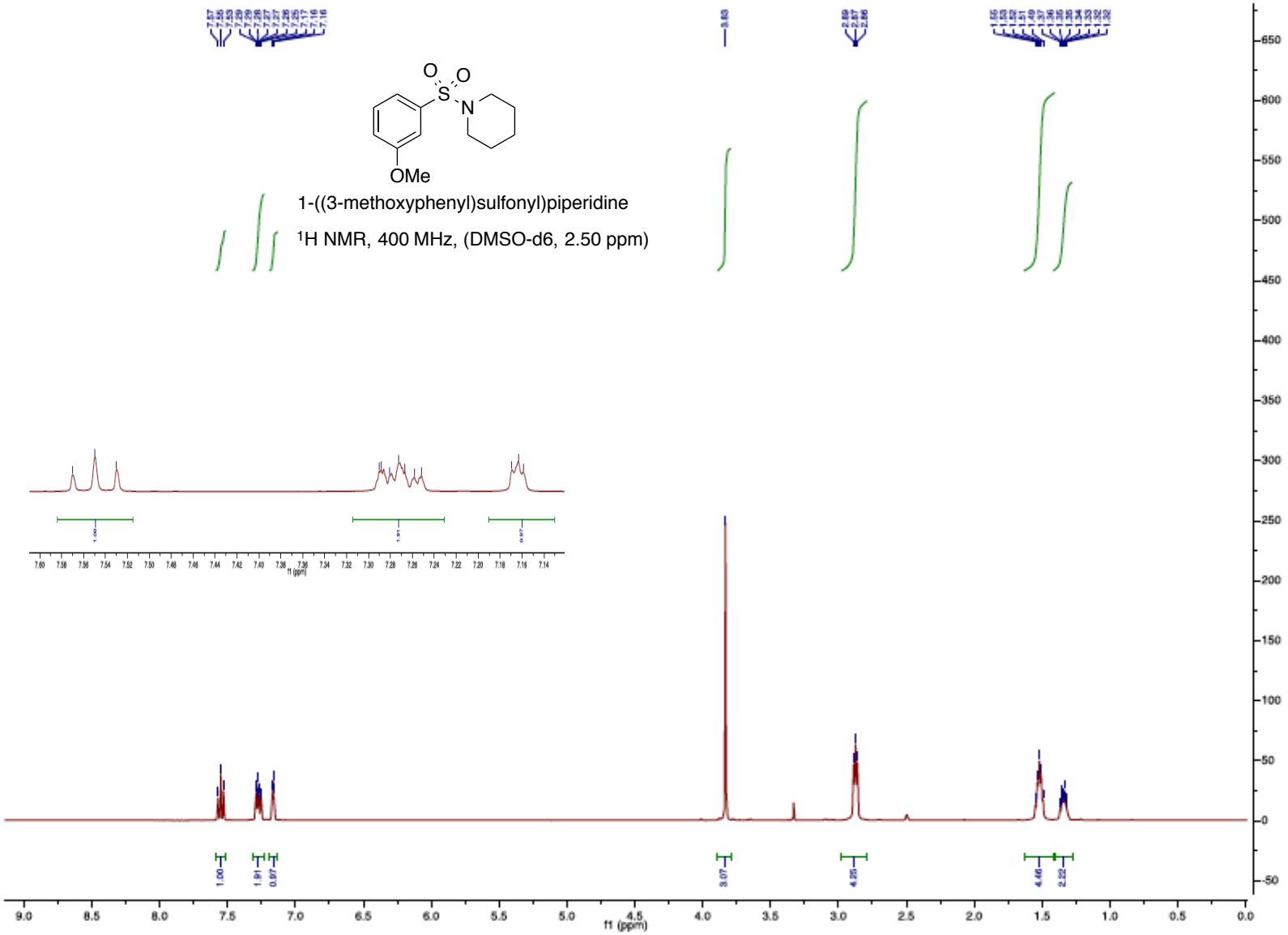
Changming Qin was born in Shandong, China, in 1982. He did his undergraduate work at Ludong University on preparation polymer nanocomposites under the guidance of Prof. Yucai Hu. He obtained his Masters degree in organic chemistry in 2008 at Wenzhou University under the supervision of Prof. Huayue Wu while working on palladium-catalyzed transformations of aryl boronic acids. After graduation, he went to the University of Hong Kong to work with Prof. Chi-Ming Che in 2008-2009, and then joined Prof. Huw Davies' group at Emory University in 2010. His current research is focused on design and synthesis of chiral dirhodium catalysts and their application in novel asymmetric carbenoid transformations.

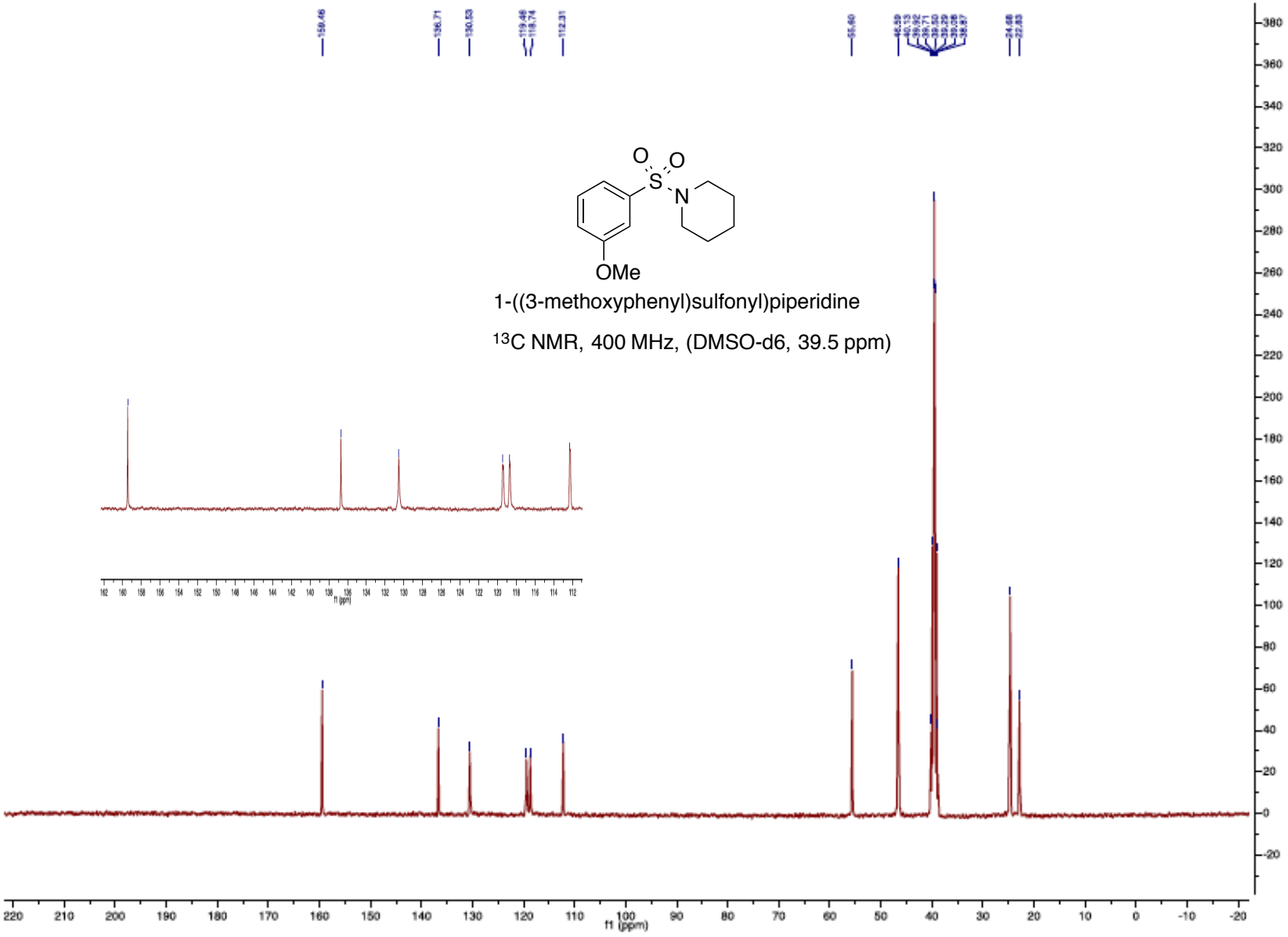


3-methoxy-*N*-morpholinobenzenesulfonamide

^{1}H NMR, 400 MHz, ($CDCl_3$, 7.27 ppm)


159.47
139.65
129.70
120.01
119.51
112.47
77.32
77.00
76.68
66.40
56.25
55.49
O
O
S
N
H
N
O
OMe
3-methoxy-*N*-morpholinobenzenesulfonamide
^{13}C NMR,100 MHz, ($CDCl_3$, 77.0 ppm)
f1 (ppm)


OMe
1-((3-methoxyphenyl)sulfonyl)piperidine
1H NMR, 400 MHz, (DMSO-d6, 2.50 ppm)
f1 (ppm)


159.46
136.71
130.53
119.46
118.74
112.31
55.60
45.59
40.13
39.92
39.71
39.50
39.29
39.08
36.87
24.48
22.83
O
O
S
N
OMe
1-((3-methoxyphenyl)sulfonyl)piperidine
13C NMR, 400 MHz, (DMSO-d6, 39.5 ppm)
f1 (ppm)