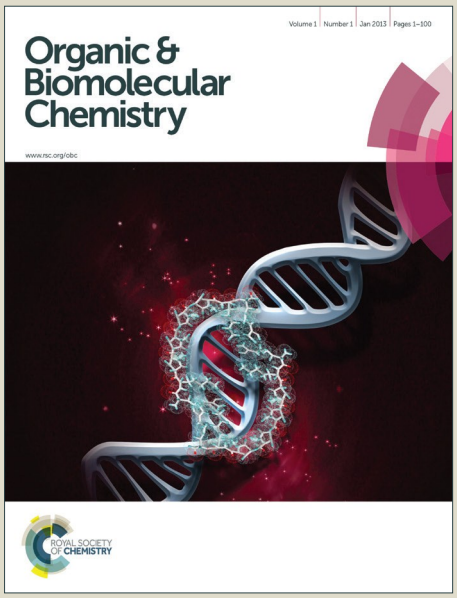
Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: Y. An, H. Xia and J. Wu, *Org. Biomol. Chem.*, 2015, DOI: 10.1039/C5OB02514A.



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

Organic & Biomolecular Chemistry

View Article Online
DOI: 10.1039/C5OB02514A

A palladium-catalyzed coupling reaction of aryl nonaflates, sulfur dioxide, and hydrazines

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

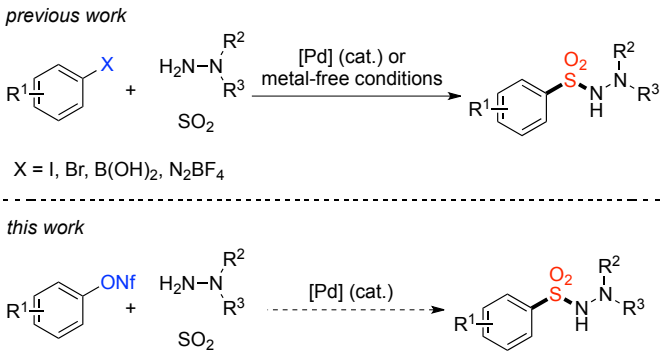
Yuanyuan An,[a] Hongguang Xia,[b,*] and Jie Wu[a,c,*]

A facile route to *N*-aminosulfonamides through a palladium-catalyzed coupling reaction of aryl nonaflates, sulfur dioxide, and hydrazines is reported. This transformation proceeds in the presence of $Pd(OAc)_2$/XantPhos, and TBAB in 1,4-dioxane at 80 °C, leading to the corresponding *N*-aminosulfonamides in moderate to good yields. The reaction scope has been demonstrated, and good functional tolerance is observed. A plausible mechanism is proposed through the insertion of sulfur dioxide.

Introduction

Palladium-catalyzed cross-coupling reactions are among the most highly powerful approaches for the efficient construction of carbon-carbon bonds and carbon-heteroatom bonds.[1] Among the electrophiles utilized in palladium-catalyzed cross-coupling reactions, "pseudohalides" are attractive since they can be readily prepared from aryl alcohols or ketones.[2] This development significantly expanded the range of compatible electrophiles in coupling reactions and further enhanced the synthetic utility of this approach. Recently, we have involved the cross-coupling reactions of sulfonates.[3] The easy availability of sulfonates prompted us to expand their further applications.

Currently, insertion of sulfur dioxide into small molecules have attracted growing interests in organic synthesis, [4-7] since the sulfonyl group can be found in many natural products, pharmaceuticals, agrochemical molecules, and materials.[8] For example, cafenstrole is known as the herbicide, and bicalutamide is employed for the treatment of prostate cancer.[8] Moreover, this functional group has been utilized broadly in organic synthesis due to its versatile reactivity.[9] Recently, we developed several efficient routes for the incorporation of sulfur dioxide into small molecules including transition metal catalyzed sulfonylation and radical process (Scheme 1).[6] For instance, aryl *N*-aminosulfonamides could be generated through a reaction of aryldiazonium tetrafluoroborates, sulfur dioxide, and hydrazines under metal-free conditions.[6c] An alternative route for the synthesis of aryl *N*-aminosulfonamides was developed as well via a palladium-catalyzed three-component reaction of aryl halides, sulfur dioxide, and hydrazines.[6b] Consistent with our continuing interest in the cross-coupling reactions of sulfonates and fixation of sulfur dioxide, we concieved that sulfonates could act as electrophiles as well in the palladium-catalyzed insertion of sulfur dioxide. Considering the reactivity and easy availability, aryl nonaflates were chosen as substrates for reaction development (Scheme 1).



Scheme 1 Generation of aryl *N*-aminosulfonamides via insertion of sulfur dioxide

Due to the disadvantages of gaseous state of sulfur dioxide, the source of sulfur dioxide includes $DABCO\cdot(SO_2)_2$ (named: DABSO)[4] and inorganic metal sulfites was considered. Since the palladium-catalyzed coupling reaction usually proceeded under base conditions and the release of sulfur dioxide from inorganic metal sulfites should be performed in the presence of an acid, we therefore selected $DABCO\cdot(SO_2)_2$ as the source of sulfur dioxide during the transformation. This reagent developed by Willis,[5a] has been utilized widely due to its stability at bench and easy availability. Encouraged by these results, we thus started to explore

[a] *Department of Chemistry, Fudan University, 220 Handan Road, Shanghai 200433, China. E-mail: jie_wu@fudan.edu.cn*
[b] *Department of Biochemistry and Molecular Biology, Zhejiang University School of Medicine, Hangzhou 310058, China. Email: hongguangxia@zju.edu.cn*
[c] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China*

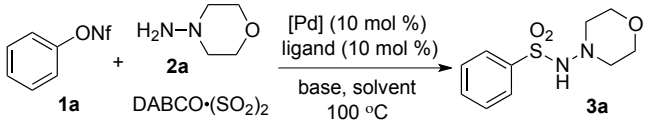
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

the palladium-catalyzed coupling reaction of aryl nonaflates, sulfur dioxide, and hydrazines.

Results and discussion

A model reaction of phenyl nonaflate **1a**, sulfur dioxide, and morpholin-4-amine **2a** was initially investigated (Table 1). At the outset, the reaction was performed in the presence of palladium chloride (10 mol %), XPhos (10 mol %) and TBAB (2.0 equiv.) in 1,4-dioxane at 100 °C (Table 1, entry 1). However, the result was not promising and only a trace amount of product was detected. A similar result was observed when the ligand was changed to tricyclohexylphosphine (Table 1, entry 2). To our delight, the reaction proceeded smoothly when XantPhos was employed as the ligand, leading to the desired *N*-aminosulfonamide **3a** in 45% yield (Table 1, entry 3). Further exploration of bases revealed that the yield was lower when TBAB was replaced by TBAC, TBAI, TEAB, or sodium carbonate (Table 1, entries 4-7). Gratifyingly, the result was dramatically improved when palladium acetate was used as the catalyst (Table 1, entry 8). No better yields were obtained when other palladium catalysts were screened (Table 1, entries 9 and 10). Next, we examined other solvents in the reaction (Table 1, entries 11 and 12). However, 1,4-dioxane was demonstrated as the best choice. Interestingly, the yield was increased to 70% when the reaction was occurred at 80 °C (Table 1, entry 13). However, the reaction was inert when the temperature was changed to 60 °C (Table 1, entry 14).

Table 1. Initial studies for the palladium-catalyzed coupling reaction of phenyl nonaflate **1a**, sulfur dioxide, and morpholin-4-amine **2a**.

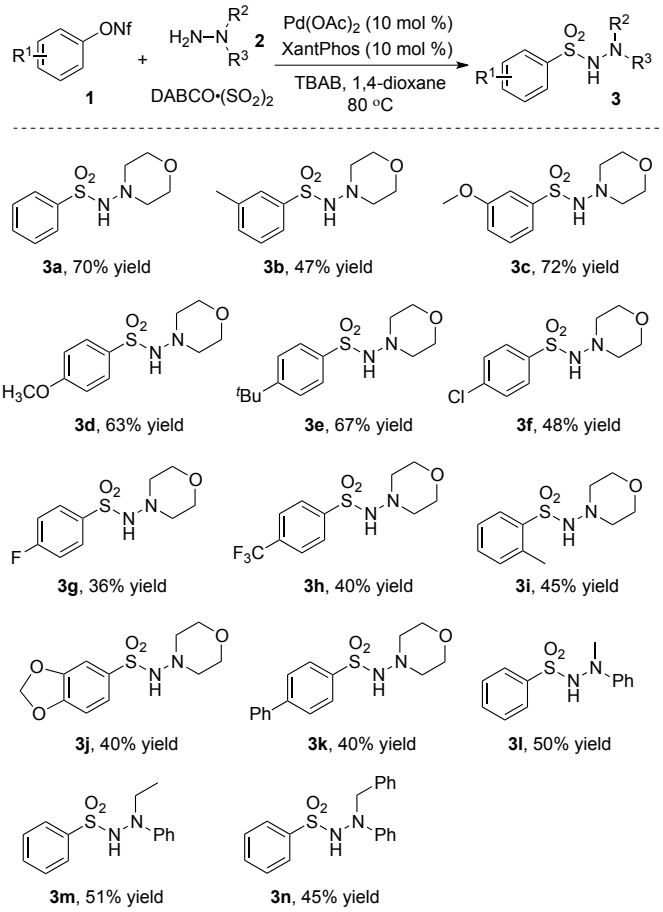


Entry	[Pd]	Ligand	Base	Solvent	Yield (%)[a]
1	$PdCl_2$	XPhos	TBAB	1,4-dioxane	trace
2	$PdCl_2$	PCy_3	TBAB	1,4-dioxane	trace
3	$PdCl_2$	XantPhos	TBAB	1,4-dioxane	45
4	$PdCl_2$	XantPhos	TBAC	1,4-dioxane	33
5	$PdCl_2$	XantPhos	TBAI	1,4-dioxane	33
6	$PdCl_2$	XantPhos	TEAB	1,4-dioxane	26
7	$PdCl_2$	XantPhos	Na_2CO_3	1,4-dioxane	trace
8	$Pd(OAc)_2$	XantPhos	TBAB	1,4-dioxane	59
9	$Pd(PPh_3)_4$	XantPhos	TBAB	1,4-dioxane	28
10	$Pd(CO_2CF_3)_2$	XantPhos	TBAB	1,4-dioxane	41
11	$Pd(OAc)_2$	XantPhos	TBAB	NMP	57
12	$Pd(OAc)_2$	XantPhos	TBAB	DMF	40
13[b]	$Pd(OAc)_2$	XantPhos	TBAB	1,4-dioxane	70
14[c]	$Pd(OAc)_2$	XantPhos	TBAB	1,4-dioxane	trace

[a] Isolated yield based on phenyl nonaflate **1a**. [b] The reaction was performed at 80 °C. [c] The reaction occurred at 60 °C.

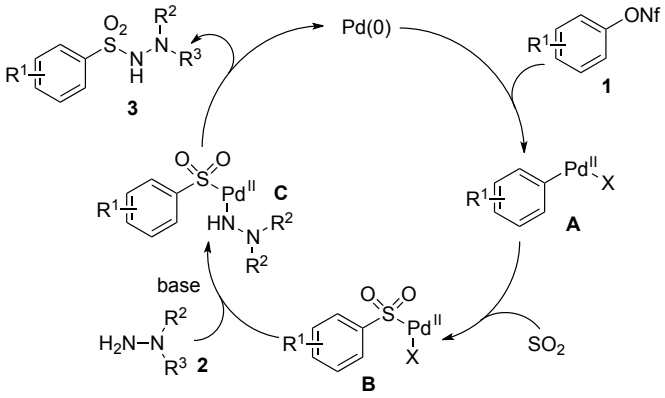
With the optimized conditions in hand, we next explored the scope of this palladium-catalyzed coupling reaction of aryl nonaflates **1**, sulfur dioxide, and hydrazines **2**. The corresponding results are presented in Table 2. It was found that all reactions worked smoothly to produce the desired products in moderate to good yields. Aryl nonaflates **1** participated successfully in the transformation, including the substrates substituted by electron-donating and electron-withdrawing groups. Different functional groups including methyl, methoxy, fluoro, chloro, and trifluoromethyl groups attached on the aromatic ring of aryl nonaflates **1** were tolerated under the standard conditions. For example, 4-chlorophenyl nonaflate reacted with sulfur dioxide and morpholin-4-amine **2a** gave rise to the corresponding product **3g** in 48% yield. During the transformation, the chloro group was remained, which was not involved in the reaction. The reaction was also workable when sterically hindered 2-methylphenyl nonaflate was employed as the substrate, affording the expected product **3i** in 45% yield. Other hydrazines were employed in the palladium-catalyzed coupling reaction of aryl nonaflate **1** and sulfur dioxide in the meantime. As expected, all reactions proceeded well to afford the corresponding products. For instance, the coupling reaction of phenyl nonaflate **1a**, sulfur dioxide, and 1-ethyl-1-phenylhydrazine generated the desired *N*'-ethyl-*N*'-phenylbenzenesulfonohydrazide **3m** in 51% yield.

Table 2. Scope exploration of palladium-catalyzed coupling reaction of aryl nonaflates **1**, sulfur dioxide, and hydrazines **2** [a]



[a] Isolated yield based on aryl nonaflate **1**.

A possible mechanism of this palladium-catalyzed coupling reaction of aryl nonaflates **1**, sulfur dioxide, and hydrazines **2** is provided in Scheme 2. We reasoned that an oxidative addition of palladium(0) to aryl nonaflate **1** would occur firstly to generate Pd(II) species **A**. Subsequently, the insertion of sulfur dioxide to Pd(II) **A** would happen to produce intermediate **B**. In the presence of a base, the nucleophilic attack of hydrazine **2** to Pd(II) **B** would afford the corresponding aryl *N*-aminosulfonamide **3** with the release of Pd(0), which would then re-enter the catalytic cycle.



Scheme 2. A plausible mechanism for the palladium-catalyzed coupling reaction of aryl nonaflates **1**, sulfur dioxide, and hydrazines **2**.

View Article Online
DOI: 10.1039/C5OB02514A

Conclusions

In conclusion, we have developed a convenient route to *N*-aminosulfonamides through a palladium-catalyzed coupling reaction of aryl nonaflates, sulfur dioxide, and hydrazines. This transformation proceeds in the presence of $Pd(OAc)_2$/XantPhos (10 mol %), and TBAB in 1,4-dioxane at 80 °C, leading to the corresponding *N*-aminosulfonamides in moderate to good yields. The reaction scope has been demonstrated, and good functional tolerance is observed. The easy availability of substrates and mild reaction conditions of this approach would enable this protocol to be attractive for further applications.

Experimental Section

General experimental methods

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63μm, standard grade). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

*General experimental procedure for the palladium-catalyzed coupling reaction of aryl nonaflates **1**, sulfur dioxide, and hydrazines **2***

Aryl nonaflate **1** (0.3 mmol) and hydrazine **2** (0.6 mmol, 2 equiv.) was added to a solution of DABCO•$(SO_2)_2$ (0.3 mmol, 1 equiv.), $Pd(OAc)_2$ (0.03 mmol, 10 mol %), XantPhos (0.03 mmol, 10 mol %), and TBAB (0.6 mmol, 2 equiv.) in 1,4-dioxane (2.5 mL) under N_2 atmosphere. The mixture was stirred at 80 °C for 8-10 hours. After completion of the reaction as indicated by TLC, the solvent was evaporated and the residue was purified directly by flash column chromatograph (EaOAc/*n*-hexane, 1: 2) to give the desired *N*-aminosulfonamide **3**.

N-Morpholinobenzenesulfonamide (**3a**).[6c] Yield: 70%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (t, *J* = 4.6 Hz, 4H), 3.60 (t, *J* = 4.6 Hz, 4H), 3.84 (s, 1H), 7.53 (t, *J* = 7.5 Hz), 7.61 (t, *J* =

7.4 Hz), 7.99 (d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.6, 66.6, 128.1, 128.8, 133.1, 138.6.

3-Methyl-*N*-morpholinobenzenesulfonamide (**3b**).[6c] Yield: 47%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.62 (t, *J* = 4.4 Hz, 4H), 3.61 (t, *J* = 4.4 Hz, 4H), 5.58 (s, 1H), 7.41(d, *J* = 4.8 Hz, 2H), 7.77-7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 56.7, 66.6, 125.2, 128.4, 128.7, 133.9, 138.4, 139.0; HRMS (ESI) calcd for $C_{11}H_{16}N_2O_3S$: 279.0774 (M + Na^+), found: 279.0775.

3-Methoxy-*N*-morpholinobenzenesulfonamide (**3c**).[6c] Yield: 72%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (t, *J* = 4.6 Hz, 4H), 3.62 (t, *J* = 4.6 Hz, 4H), 3.87 (s, 3H), 5.86 (s, 1H), 7.12-7.15(m, 1H), 7.43 (t, *J* = 8.0 Hz， 1H), 7.49 (t, *J* = 2.0 Hz， 1H) ， 7.56 (d, *J*= 7.8 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 55.7, 56.6, 66.6, 112.6, 119.6, 120.2, 129.9, 139.8, 159.7.

4-Methoxy-*N*-morpholinobenzenesulfonamide (**3d**).[6c] Yield: 63%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (t, *J* = 4.4 Hz, 4H), 3.62 (t, *J* = 4.3 Hz, 4H), 3.89 (s, 3H), 5.56 (s, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 7.90 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 56.7, 114.0, 128.8, 130.3, 163.2.

4-(*tert*-Butyl)-*N*-morpholinobenzenesulfonamide (**3e**).[6c] Yield: 67%, brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 9H), 2.64 (t, *J* = 4.6 Hz, 4H), 3.61 (t, *J* = 4.6 Hz, 4H), 5.75 (s, 1H), 7.53 (d, *J* = 8.6 Hz), 7.89 (d, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.0, 35.2, 56.7, 66.6, 125.8, 128.0, 135.6, 157.0.

4-Chloro-*N*-morpholinobenzenesulfonamide (**3f**).[6c] Yield: 48%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65 (t, *J* = 4.5 Hz, 4H), 3.62 (t, *J* = 4.6 Hz, 4H), 5.53 (s, 1H), 7.50(d, *J* = 8.6 Hz, 2H), 7.91 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.7, 66.6, 125.8, 127.9, 129.1, 129.6.

4-Fluoro-*N*-morpholinobenzenesulfonamide (**3g**).[6c] Yield: 36%, brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (t, *J* = 4.5 Hz, 4H), 3.62 (t, *J* = 4.4 Hz, 4H), 5.52 (s, 1H), 7.21(t, *J* = 8.5 Hz, 2H), 7.98-8.01 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) *δ* 56.3, 66.4, 116.7 (d, J_F = 22.9 Hz), 131.1 (d, J_F = 9.5 Hz), 136.1, 164.9 (d, J_F = 250.7 Hz).

N-Morpholino-4-(trifluoromethyl)benzenesulfonamide (**3h**).[6c] Yield: 40%, brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (t, *J* = 4.5 Hz, 4H), 3.63 (t, *J* = 4.5 Hz, 4H), 5.61 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 142.3, 134.9 (q, *J* = 33.4 Hz), 128.6, 126.0 (d, *J* = 3.1 Hz), 124.5, 66.5, 56.8.

2-Methyl-*N*-morpholinobenzenesulfonamide (**3i**).[6c] Yield: 45%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (t, *J* = 4.6 Hz, 4H), 2.70 (s, 3H), 3.58 (t, *J* = 4.5 Hz, 4H), 5.52 (s, 1H), 7.30-7.36 (m, 2H), 7.47-7.50 (m, 1H), 8.07 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 56.7, 66.5, 126.1, 131.0, 132.3, 133.2, 136.4, 138.0.

N-Morpholinobenzo[d][1,3]dioxole-5-sulfonamide (**3j**). Yield: 40%, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (t, *J* = 4.6 Hz, 4H), 3.64 (t, *J* = 4.6 Hz, 4H), 5.42 (s, 1H), 6.10 (s, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 7.38 (d, *J* = 1.6 Hz, 1H), 7.54 (dd, J_1 = 1.7 Hz, J_2 = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.8, 66.6, 102.3, 108.1, 108.3, 116.2, 124.0, 156.0, 156.6; HRMS (ESI) calcd for $C_{11}H_{14}N_2O_5S$: 287.0696 (M + H^+), found: 287.0694.

N-Morpholino-[1,1'-biphenyl]-4-sulfonamide (**3k**).[6c] Yield: 40%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (t, *J* = 4.6 Hz, 4H), 3.63 (t, *J* = 4.6 Hz, 4H), 5.70 (s, 1H), 7.41-7.45 (m, 1H), 7.47-7.51 (m, 2H), 7.62-7.64 (m, 2H), 7.74 (d, *J* = 8.6 Hz, 2H), 8.04 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.8, 66.6, 127.3, 127.4, 128.6, 128.6, 129.1, 137.2, 139.1, 146.0.

N'-Methyl-*N'*-phenylbenzenesulfonohydrazide (**3l**).[6c] Yield: 50%, brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.94 (s, 3H), 6.36 (s, 1H), 6.84 (dd, J_1 = 8.0 Hz, J_2 = 11.0 Hz, 3H), 7.15 (t, *J* = 8.3 Hz, 2H) 7.48 (t, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.95 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7, 114.4, 120.9, 128.1, 128.9, 129.1, 133.3, 138.5, 149.6.

N'-Ethyl-*N'*-phenylbenzenesulfonohydrazide (**3m**).[6c] Yield: 51%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (t, *J* = 7.1 Hz, 3H), 3.41-3.49 (m, 2H), 6.67 (s, 1H), 6.80 (dd, J_1 = 7.6 Hz, J_2 = 12.6 Hz, 3H), 7.12 (t, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.92 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.5, 49.2, 113.6, 115.1, 120.8, 128.1, 128.9, 133.2, 138.7, 147.6.

N'-Benzyl-*N'*-phenylbenzenesulfonohydrazide (**3n**).[6c] Yield: 45%, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (s, 2H), 6.36 (s, 1H), 6.85-6.93 (m, 3H), 7.04-7.06 (m, 2H), 7.16 (t, *J* = 8.3 Hz, 2H), 7.27 (t, *J* = 3.3 Hz, 3H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.1, 115.3, 121.0, 128.0, 128.0, 128.3, 128.6, 128.8, 129.0, 133.3, 134.4, 138.8, 148.6.

Acknowledgements

Financial support from National Natural Science Foundation of China (Nos. 21372046 and 21532001) and the Science & Technology Commission of Shanghai Municipality (No. 12JC1403800) is gratefully acknowledged.

Notes and references

1 For selected reviews, see: a) J. C. Seechurn, M. O. Kitching, T. J. Colacot and V. Snieckus, *Angew. Chem. Int. Ed.* 2012, **51**, 5062; b) X.-F. Wu, P. Anbarasan, H. Neumann and M. Beller, *Angew. Chem. Int. Ed.* 2010, **49**, 9047; c) A. Roglans, A. Pla-Quintana and M. Moreno-Manas, *Chem. Rev.* 2006, **106**, 4622; d) N. Miyaura and A. Suzukint, *Chem. Rev.* 1995, **95**, 2457; e) L.-X. Yin and J. Liebscher, *Chem. Rev.* 2007, **107**, 133; f) *Transition Metal Reagents and Catalysts*, Edited by J. Tsuji, John Wiley & Sons, Ltd, 2000.

2 For selected reviews, see: a) J. Högermeier and H.-U. Reissig, *Adv. Synth. Catal.* 2009, **351**, 2747; b) P. J. Stang, M. Hanack and L. R. Subrmanian, *Synthesis* 1982, 85; c) K. Ritter, *Synthesis* 1993, 735.

3 For selected examples, see: a) L. Zhang and J. Wu, *J. Am. Chem. Soc.* 2008, **130**, 12250; b) Y. Luo and J. Wu, *Organometallics* 2009, **28**, 6823; c) L. Zhang, J. Qing, P. Yang and J. Wu, *Org. Lett.* 2008, **10**, 4971; d) L. Zhang and J. Wu, *Adv. Synth. Catal.* 2008, **350**, 2409.

4 For reviews: a) G. Liu, C. Fan and J. Wu, *Org. Biomol. Chem.* 2015, **13**,1592; b) P. Bisseret and N. Blanchard, *Org. Biomol. Chem.* 2013, **11**, 5393; c) A. S. Deeming, E. J. Emmett, C. S. Richards-Taylor and M. C. Willis, *Synthesis* 2014, **46**, 2701.

View Article Online
DOI: 10.1039/C5OB02514A

5 a) B. Nguyen, E. J. Emmet, M. C. Willis, *J. Am. Chem. Soc.* 2010, **132**, 16372; b) E. J. Emmet, C. S. Garcia-Rubia, B. Nguyen, A. B. Garcia-Rubia, R. Hayter and M. C. Willis, *Org. Biomol. Chem.* 2012, **10**, 4007; c) L. Martial, *Synlett* 2013, **24**, 1595; d) W. Li, H. Li, P. Langer, M. Beller and X.-F. Wu, *Eur. J. Org. Chem.* 2014, 3101; e) W. Li, M. Beller and X.-F. Wu, *Chem. Commun.* 2014, **50**, 9513; f) X. Wang, L. Xue and Z. Wang, *Org. Lett.* 2014, **16**, 4056; g) A. S. Deeming, C. J. Russell and M. C. Willis, *Angew. Chem. Int. Ed.* 2015, **54**, 1168.

6 a) S. Ye and J. Wu, *Chem. Commun.* 2012, **48**, 7753; b) S. Ye and Wu, J. *Chem. Commun.* 2012, **48**, 10037; c) D. Zheng, Y. An, Z. Li and J. Wu, *Angew. Chem. Int. Ed.* 2014, **53**, 2451; d) S. Ye, H. Wang, Q. Xiao, Q. Ding and J. Wu, *Adv. Synth. Catal.* 2014, **356**, 3225; e) Y. An, D. Zheng and J. Wu, *Chem. Commun.* 2014, **50**, 11746; f) Y. Luo, X. Pan, C. Chen, L. Yao and J. Wu, *Chem. Commun.* 2015, **51**, 180; g) D. Zheng, Y. Li, Y. An and J. Wu, *Chem. Commun.* 2014, **50**, 8886.

7 a) C. C. Chen and J. Waser, *Org. Lett.* 2015, **17**, 736; b) A. S. Deeming, C. J. Rusell, A. J. Hennessy and M. C. Willis, *Org. Lett*. 2014, **16**, 150; c) B. N. Rocke, K. B. Bahnck, M. Herr, S. Lavergne, V. Mascitti, C. Perreault, J. Polivkova and A. Shavnya, *Org. Lett.* 2014, **16**, 154; d) E. J. Emmett, B. R. Hayter and M. C. Willis, *Angew. Chem. Int. Ed.* 2013, **52**, 12679; e) E. J. Emmett, B. R. Hayter and M. C. Willis, *Angew. Chem . Int. Ed.* 2014, **38**, 10204; f) A. Shavnya, S. B. Coffey, A. C. Smith and V. Mascitti, *Org. Lett.* 2013, **15**, 6226; g) M. W. Johnson, S. W. Bagley, N. P. Mankad, R. G. Bergman, V. Mascitti and F. D. Toste, *Angew. Chem. Int. Ed.* 2014, **53**, 4404; h) A. Shavnya, K. D. Hesp, V. Mascitti and A. C. Smith, *Angew. Chem. Int. Ed.* 2015, **54**, 13571; i) A. S. Deeming, C. J. Russell and M. C. Willis, *Angew. Chem. Int. Ed.* 2015, DOI: 10.1002/anie.201508370.

8 a) P. Tfelt-Hansen, P. De Vries and P. R. Saxena, *Drugs* 2000, **60**, 1259; b) P. F. Schnellhammer, *Expert Opin. Pharmacother.* 2002, **3**, 1313; c) G. Mitchell, D. W. Bartlett, T. E. M. Fraser, T. R. Hawkes, D. C. Holt, J. K. Townson and R. A. Wichert, *Pest Manage. Sci.* 2001, **57**, 120; d) P. Boger, *J. Pestic. Sci.* 2003, **28**, 324.

9 N. S. Simpkins, *Sulfones in Organic Synthesis*, Pergamon Press, Oxford, 1993.