Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 7667–7672

Cross-coupling of organoboronic acids and sulfinate salts using catalytic copper(II) acetate and 1,10-phenanthroline: synthesis of aryl and alkenylsulfones

Fang Huang and Robert A. Batey*

Department of Chemistry, 80 St. George Street, University of Toronto, Toronto, Ontario M5S 3H6, Canada

Received 27 October 2006; revised 5 May 2007; accepted 8 May 2007
Available online 13 May 2007

Abstract—A mild method for the preparation of aryl and alkenylsulfones from the cross-coupling reaction of organoboronic acids and sodium sulfinate salts is described. Optimized conditions utilize a catalytic amount of copper(II) acetate monohydrate with 1,10-phenanthroline as ligand in the presence of 4 Å molecular sieves. A co-solvent mixture of dichloromethane/DMSO was used, with reactions occurring at 40 °C under an atmosphere of oxygen. Reaction at room temperature also yields sulfone product, but in lower yields. The method tolerates a variety of substituents on the organoboronic acid, including amide, aldehyde, halide and nitro functionalities, as well as *ortho*-substituents. In general, the reaction is found to be less efficient using arylboronic acids bearing electron-withdrawing substituents, or using aryltrifluoroborate salts.

1. Introduction

Transition metal catalyzed cross-coupling reactions are now recognized as extremely powerful strategies for the formation of carbon–heteroatom bonds. Most commonly, nucleophiles such as amines, alcohols or thiols have been used in cross-coupling reactions with arylhalides to make substituted anilines, aryl ethers, and aryl thioethers respectively. The pioneering studies of Buchwald and Hartwig established palladium complexes as efficient catalysts for these reactions.[1] These studies provided the impetus to evaluate other transition metal catalysts, and have led to a renaissance in copper-based couplings.[2] Traditional Ullmann and Goldberg type couplings have been known for about a century. However, it is only relatively recently, with the advent of improved reaction conditions and ligands, that general and practical protocols, that are *catalytic* in copper, have become competitive with the more commonly used palladium catalysts for carbon–heteroatom bond forming cross-coupling reactions.[3]

Over the last few years a new copper catalyzed cross-coupling strategy for C–N, C–O, and C–S bond formations has emerged, using the coupling of organoboronic acids and organotrifluoroborate salts with various nucleophiles.[4–8] In addition, we have shown that potassium aryltrifluoroborate salts, which are air and water stable equivalents of arylboronic acids, can be utilized in copper catalyzed cross-coupling reactions, with aliphatic alcohols and amines undergoing cross-coupling in higher yields with potassium aryltrifluoroborate salts than their arylboronic acid counterparts.[9,10]

As an extension of these observations, we became interested in the possibility of using either organoboronic acids or potassium organotrifluoroborate salts in copper catalyzed cross-coupling reactions with sulfinic acids or their salts, as a method to synthesize sulfones. New synthetic methods for sulfone formation are desirable due to their importance as synthetic intermediates,[11,12] and their presence in biologically active compounds. For example, sulfones have been used as drugs for 80 years due to their strong in vitro and in vivo antibacterial and antifungicidal activity.[13] Diarylsulfones have been shown to inhibit the 3′ processing and strand transfer step in HIV replication.[14] The arylsulfone motif is also found in the COX-2 inhibitor rofecoxit (MK966, ViOXX).[15] The ability of α,β-unsaturated sulfones to act as acceptors in nucleophilic addition reactions has also been exploited in the design of biologically active molecules. For example, potent and selective inhibition of cysteine proteases by vinyl sulfones is believed to occur through conjugate addition of the cysteine thiol residue forming covalently linked enzyme-inhibitor derivatives.[16] Recently α,β-unsaturated sulfones were reported as inhibitors of inducible VCAM-1 expression.[17]

* Corresponding author. Tel./fax: +1 416 978 5059; e-mail: rbatey@chem.utoronto.ca

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.05.029

Traditional methods for the preparation of sulfones include the oxidation of sulfides, sulfonylation of arenes, sulfinate–sulfone rearrangements, radical additions to sulfur dioxide, condensation of hydrocarbons with SO_2, and sulfolene reactions.[11] Drawbacks associated with these methods include the availability of precursors, chemoselectivity issues, and the use of harsh conditions or strong acid catalysts.[18,19] Alternative methods for the preparation of sulfones are therefore desirable. Cross-coupling strategies are one such approach to the synthesis of sulfones. The coupling of sulfinic acid salts with arylhalides to give sulfones has been demonstrated using both palladium and copper catalysis. An early study by Suzuki and Abe showed the use of 1.5 equiv of CuI for the coupling reaction of iodoarenes with sodium arenesulfinates.[20] More recently a catalytic version of the copper-mediated cross-coupling was reported by Baskin and Wang, using 5 mol % $Cu(OTf)_2 \cdot PhH$ and 10 mol % *N*,*N*′-dimethylethylenediamine in DMSO at 110 °C.[21] Zhu and Ma reported the couplings of aryl bromides with sodium arenesulfinates in the presence of 10 mol % CuI.[22] The major limitation of these reactions is the high reaction temperature (80–110 °C) that is required. Cacchi and co-workers have developed a somewhat milder palladium-mediated reaction, in which aryl and alkenyl bromides, iodides, and triflates undergo cross-coupling with sulfinic acid salts with 2.5 mol % $Pd_2(dba)_3$, 5 mol % xantphos, 1.5 equiv of Cs_2CO_3 and 1.2 equiv of Bu_4NCl in toluene, and reaction temperatures in the range of 80–120 °C.[23] Bandgar has recently reported a mild Pd catalyzed cross-coupling of arylboronic acids with arylsulfonyl chlorides, using K_2CO_3 in acetone/water.[24] Finally, during the course of our investigations, Beaulieu and Evans reported a stoichiometric copper catalyzed reaction of sodium methylsulfinate with various arylboronic acids.[25] This protocol employed 1.1 equiv of $Cu(OAc)_2$, 2.0 equiv of K_2CO_3, and 4 Å molecular sieves, using DMSO as solvent under air at room temperature or 60 °C. We now report a ligand-accelerated copper catalyzed protocol for the cross-coupling of organoboronic acids with sodium sulfinate salts, which occurs using catalytic quantities of Cu(II) salts and in the absence of an external base. This protocol provides a convenient alternative method for sulfone formation under relatively mild conditions, using both sodium arylsulfinate and methylsulfinate salts. In addition, it can also be employed using both aryl and alkenylboronic acid precursors.

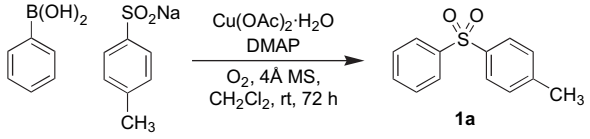
2. Results and discussion

The cross-coupling of sodium *p*-toluenesulfinate and phenylboronic acid to give phenyl *p*-tolyl sulfone **1a** was chosen as a model reaction for initial reaction evaluation and for subsequent optimization studies. DMAP was chosen as the ligand in the initial studies, since we had earlier established that it is the optimal ligand in cross-coupling reactions of alcohols with aryltrifluoroborate salts.[9] Reactions were conducted with stoichiometric quantities of copper salts and DMAP in CH_2Cl_2 at room temperature under oxygen (atmospheric pressure). A number of copper salts including copper(II) acetate, copper(II) sulfate, copper(I) iodide, copper(I) chloride, copper(II) acetate monohydrate, and copper(II) triflate were tested, giving yields ranging from 18 to 70%. Based on the yield and ease of handling, copper acetate monohydrate was chosen as the optimal copper source.

Initial attempts to render the reaction catalytic using copper(II) acetate monohydrate and DMAP at room temperature were unsuccessful (Table 1). The yields of the desired sulfone product **1a** decreased with catalyst loading and were lower than the amount of copper used. Moreover, there were significant amounts of biphenyl and biphenyl ether by-products that were isolated. Although not always reported, these side products often complicate copper-based cross-couplings of boron compounds.

The formation of the sulfone product presumably occurs through a $PhCu(SO_2Ar)X_nL_m$ species, either in the Cu(II) or Cu(III) oxidation state. Reductive elimination from this species would then release the sulfone and a Cu(0) or Cu(I) species, respectively. The $PhCu(SO_2Ar)X_nL_m$ species would be formed by transmetallation of the boronic acid to copper, but neither the timing of the transmetallation step nor the oxidation state of the copper species that undergoes transmetallation is known. In addition, the intermediacy of dinuclear copper species may occur. The requirement for oxygen in the reaction is presumably necessary to regenerate

Table 1. Effect of variation of catalyst and ligand stoichiometry on the copper catalyzed cross-coupling of phenylboronic acid with sodium *p*-toluenesulfinate[a]



Entry	$Cu(OAc)_2 \cdot H_2O$	DMAP	$PhSO_2Tol$[b,c] (%)	Ph–Ph[b,d] (%)	Ph–O–Ph[b,d] (%)	PhOH[b,d] (%)	$PhB(OH)_2$[b,d] (%)
1	1.0 equiv	2.0 equiv	55	0	39	0	0
2	50 mol %	1.0 equiv	34	2	39	0	0
3	25 mol %	50 mol %	22	21	23	0	0
4	15 mol %	30 mol %	8	29	22	0	0
5	10 mol %	20 mol %	9	31	1	0	Traces
6	5 mol %	10 mol %	3	18	Traces	0	—

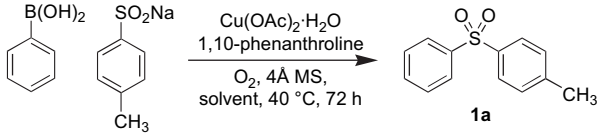
[a] Reaction conditions employ 1 equiv of sodium *p*-toluenesulfinate with 2 equiv of $PhB(OH)_2$, $Cu(OAc)_2 \cdot H_2O$, DMAP, and 4 Å molecular sieves in CH_2Cl_2 at rt under an atmosphere of O_2 for 72 h.
[b] Isolated yield.
[c] Yield calculated based on limiting sulfinate reagent.
[d] Yield was calculated based on $PhB(OH)_2$.

the catalytically active species (i.e., by reoxidation of the Cu(0) or Cu(I) species that form from the reductive elimination step). The presence of oxygen is also consistent with the involvement of Cu(III) intermediates. The biphenyl side products presumably arise through transmetallation of 2 equiv of phenylboronic acid to give a $Ph_2CuX_nL_m$ species, which can then yield Ph–Ph on reductive elimination.[25,26] This process is analogous to the Glaser or Cadiot–Chodkiewicz coupling of alkynes to give symmetrical 1,3-diynes. Phenol formation has been shown by Lam and co-workers to occur through a copper catalyzed cross-coupling reaction of water with phenylboronic acid.[27] The presence of powdered 4 Å molecular sieves to remove water is helpful in minimizing this process. The biphenyl ether side product is presumably formed via copper catalyzed cross-coupling of the phenol with a second equivalent of phenylboronic acid. It is also possible that initial cross-coupling with water directly gives a $PhOCuX_nL_m$ species and that subsequent transmetallation from phenylboronic acid is more rapid than release of free phenol. Reductive elimination from the resultant $Ph(PhO)CuX_nL_m$ species would give the Ph–O–Ph side product.

The poor results obtained using catalytic quantities of copper(II) acetate monohydrate/DMAP at room temperature, led us to investigate the nature of the ligand, solvent, and temperature on the efficiency of cross-coupling. The reaction temperature was therefore raised to 40 °C, and a variety of ligands (DMAP, pyridine, imidazole, triethylamine, 1,10-phenanthroline, ethylenediamine, DMEDA, and TMEDA) were screened using 10 mol % of copper(II) acetate monohydrate and DMSO as solvent. Product yields were typically improved at higher temperatures, but the distribution of biphenyl, biphenyl ether, and phenol side products was found to be quite sensitive to the choice of ligand. Product formation was also quite sensitive to the stirring efficiency, the choice of ligand, and the copper/ligand stoichiometry. Further investigation of the above ligands in a variety of solvents led to the optimal use of 1,10-phenanthroline as ligand (2:1 ligand/copper stoichiometry) and a CH_2Cl_2/DMSO (15:1) co-solvent mixture (Table 2). It is interesting to note that the use of DMSO as solvent, as employed by Beaulieu and Evans,[25] led to lower yields of the product. Attempts to optimize the reaction by varying the oxidant (e.g., NMO and TEMPO) gave the products in lower yields. Finally, modification of the 1:2 stoichiometry of the sulfinate salt to the boronic acid did not increase the isolated yields of the sulfone product. The product yields did not increase by using more than 2 equiv of the boronic acid, whereas modest reductions in yield occurred when less than 2 equiv of the boronic acid was used. Also, the use of the boronic acid as the limiting reagent led to decreased product yields. Therefore, optimized conditions were chosen using 1 equiv of sulfinate with 2 equiv of organoboronic acid, $Cu(OAc)_2 \cdot H_2O$ (10 mol %), 1,10-phenathroline (20 mol %), and 4 Å molecular sieves in CH_2Cl_2/DMSO (15:1) at 40 °C under an atmosphere of O_2 for 72 h. Compared to the stoichiometric conditions employed by Beaulieu and Evans, these conditions avoid the use of external base and are of course catalytic in the copper salt.

With an optimized protocol established, we next evaluated the scope and limitations of the reaction for the formation of sulfones **1**–**3** (Tables 3–5). The individual reactions were not further optimized for reaction conditions (e.g., catalyst, ligand, and solvent) or reaction time/temperature. It is therefore likely that further improvement in individual reaction yields for **1**–**3** are possible, given the heterogenous nature of the reactions and the sensitivity of product distribution to variation in reaction parameters. The cross-coupling protocol works well with a variety of arylboronic acid partners to form arylsulfones **1** (Table 3). In general, the diarylsulfone product yields were highest with the arylboronic acids bearing electron-donating substituents. The use of arylboronic acids bearing electron-withdrawing substituents led to the products in modest isolated yields (Table 3, entries 5, 6, 7, and 10). The reaction also tolerates the presence of an *ortho*-substituent on the arylboronic acid (Table 3, entry 8), but the presence of two *ortho*-substituents leads to a sharp decrease in reaction efficiency (Table 3, entry 9). The presence of an amino group, as with 4-dimethylaminophenylboronic acid, was not tolerated and product formation was not observed, perhaps due to coordination of the amino group to copper.

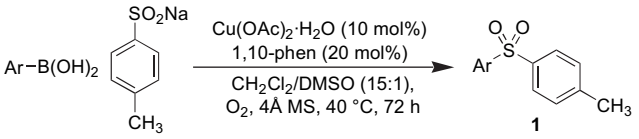
Table 2. Effect of ligand and solvent on the copper catalyzed cross-coupling of phenylboronic acid with sodium *p*-toluenesulfinate[a]

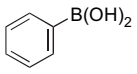
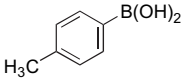
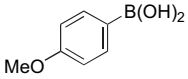
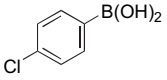
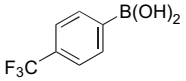
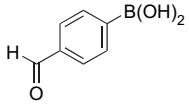
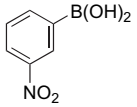
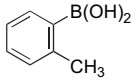
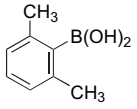
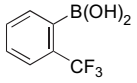
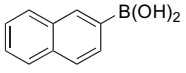


Entry	Solvent	$PhSO_2Tol$[b,c] (%)	Ph–Ph[b,d] (%)	Ph–O–Ph[b,d] (%)	PhOH[b,d] (%)	$PhB(OH)_2$[b,d] (%)
1	CH_2Cl_2	23	Traces	Traces	Traces	0
2	EtOAc	13	12	9	6	0
3	DMSO	9	Traces	Traces	Traces	66
4	CH_2Cl_2/DMSO (3:1)	46	20	0	Traces	0
5	CH_2Cl_2/DMSO (7:1)	52	10	0	Traces	0
6	CH_2Cl_2/DMSO (15:1)	70	22	0	Traces	0

[a] Reaction conditions employ 1 equiv of sodium *p*-toluenesulfinate with 2 equiv of $PhB(OH)_2$, $Cu(OAc)_2 \cdot H_2O$ (10 mol %), 1,10-phenanthroline (20 mol %), and 4 Å molecular sieves at 40 °C under an atmosphere of O_2 for 72 h.
[b] Isolated yield.
[c] Yield calculated based on limiting sulfinate reagent.
[d] Yield was calculated based on $PhB(OH)_2$.

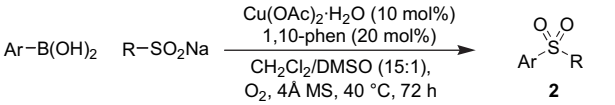
Table 3. Copper catalyzed cross-coupling of various arylboronic acids with sodium *p*-toluenesulfinate

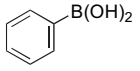
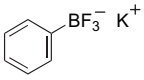
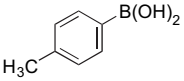
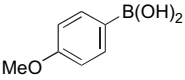
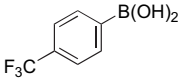
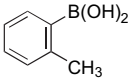
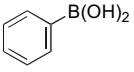
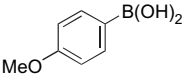
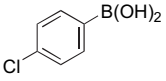
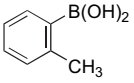
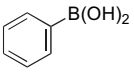
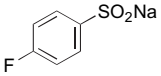
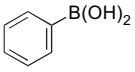
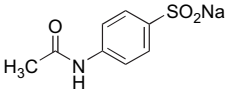


Entry	Arylboronic acid	Sulfone product	Yield[a] (%)
1		**1a**	70
2		**1b**	73
3		**1c**	76
4		**1d**	90
5		**1e**	47
6		**1f**	34
7		**1g**	35
8		**1h**	80
9		**1i**	13
10		**1j**	40
11		**1k**	98

[a] Isolated yield.

Table 4. Copper catalyzed cross-coupling of various arylboronic acids with sulfinate salts



Entry	Arylboron compound	Sulfinate salt	Sulfone product	Yield[a] (%)
1		$PhSO_2Na$	**2a**	70
2		$PhSO_2Na$	**2a**	28
3		$PhSO_2Na$	**1a**	53
4		$PhSO_2Na$	**2b**	48
5		$PhSO_2Na$	**2c**	51
6		$PhSO_2Na$	**2d**	79
7		$MeSO_2Na$	**2e**	90
8		$MeSO_2Na$	**2f**	60
9		$MeSO_2Na$	**2g**	67
10		$MeSO_2Na$	**2h**	62
11	 		**2i**	66
12	 		**2j**	64

[a] Isolated yield.

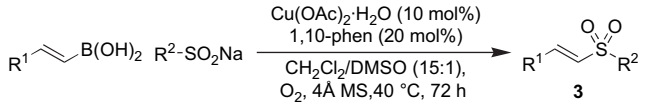
Reaction using sodium phenylsulfinate or sodium methylsulfinate as the reaction partners with various arylboronic acid partners also led to similar results forming arylsulfones **2** (Table 4). The use of potassium trifluorophenyl borate, rather than phenylboronic acid, as the reaction partner led to a disappointing yield (28%) of sulfone **2a** (Table 4, entry 2). This observation is noteworthy, because in other copper catalyzed cross-coupling reactions, we have shown that organotrifluoroborate salts lead to comparable or improved yields of products.[9,10] The use of other substituted sulfinate salts, such as sodium 4-fluorobenzene sulfinate and sodium 4-acetamidobenzene sulfinate was also tolerated (Table 4, entries 11–12).

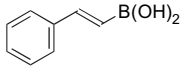
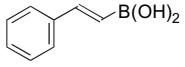
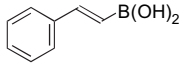
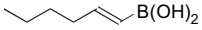
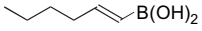
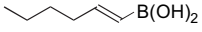
Extension of the procedure to the cross-coupling of alkenylboronic acids with sulfinate salts to prepare various alkenylsulfones **3** was also successful (Table 5). Thus, the use of hexenylboronic acid and (*E*)-styrylboronic acid led to generally good yields of the alkenylsulfone products. The use of alkylboronic acids did not result in the formation of sulfone products under these conditions.

3. Conclusions

In conclusion, a mild copper-based protocol for the synthesis of aryl and vinyl sulfones has been developed, via the cross-coupling of aryl and vinyl boronic acid with sodium sulfinate salts. The reaction protocol utilizes catalytic amounts of copper(II) salts in the presence of 4 Å molecular sieves, and with 1,10-phenanthroline as ligand. In the case of arylboronic acids, the major side products in the reactions were

Table 5. Copper catalyzed cross-coupling of alkenyboronic acids with sodium sulfinate salts



Entry	Alkenylboronic acid	Sulfinate salt	Sulfone product	Yield[a] (%)
1		$PhSO_2Na$	**3a**	84
2		$TolSO_2Na$	**3b**	84
3		$MeSO_2Na$	**3c**	76
4		$PhSO_2Na$	**3d**	52
5		$TolSO_2Na$	**3e**	68
6		$MeSO_2Na$	**3f**	47

[a] Isolated yield.

symmetric copper-based cross-couplings to biaryls, and oxidative coupling to phenols and biaryl ethers.

4. Experimental section

4.1. General

CH_2Cl_2 was distilled from CaH_2 under nitrogen. All other commercial reagents were used as received (Aldrich, Fischer Scientific Ltd. or BDH). All glassware was flame-dried. Melting points are uncorrected. ^1H and ^{13}C NMR were recorded at 400 and 300 MHz, respectively, on a Varian Unity 400 spectrometer, Mercury 300 MHz spectrometer, and Gemini 300 MHz spectrometer. Proton chemical shifts were internally referenced to the residual proton resonance in $CDCl_3$ (δ 7.26). Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.23). FTIR spectra were recorded on a Perkin–Elmer Spectrum 1000, with samples loaded as neat films on NaCl plates. Low resolution mass spectra were recorded on a Bell and Howell 21-490 spectrometer, and high resolution spectra were recorded on an AEI MS3074 spectrometer. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel plates (Silicycle Inc.), visualized with a UV254 lamp (Spectroline, Longlife Filter) and stained with 20% phosphomolybdic acid in ethanol. Full spectral data are provided for new compound **1e** and ^1H and ^{13}C NMR are provided for the known compounds **1j**, **2f**, and **3f**, which lack full characterization in the literature.

4.2. General procedure for the preparation of sulfones 1–3

To a mixture of the organoboronic acid (2.00 mmol), copper acetate monohydrate (20.0 mg, 0.100 mmol), 1,10-phenanthroline (36.0 mg, 0.200 mmol), powdered 4 Å molecular sieves (0.75 g), and sodium sulfinate salt (1.00 mmol) under an atmosphere of oxygen (reaction vessels are attached to an oxygen manifold at atmospheric pressure) were added dichloromethane (7.5 ml) and DMSO (0.5 ml). The mixture was stirred for 72 h at 40 °C. After cooling, the reaction mixture was filtered through Celite and the filter cake was washed with ethyl acetate. The filtrate was concentrated in vacuo and purified by flash column chromatography (silica gel) to give the sulfone products.

4.2.1. 1-Trifluoromethyl-4-(toluene-4-sulfonyl)benzene (1e). White solid; mp=112–113 °C; R_f=0.48 (EtOAc/hexanes, 4:1); IR (Thin Film) (NaCl) 3153, 3023, 1594, 1404, 1323, 1155, 1106, 1072, 1060, 717, 660 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (2H, d, J=8.0 Hz), 7.86–7.83 (2H, m), 7.76 (2H, d, J=8.5 Hz), 7.33 (2H, d, J=8.0 Hz), 2.41 (3H, s); ^{13}C NMR (300 MHz, $CDCl_3$) δ 145.8, 145.2, 137.8, 134.8 (q, J=33.0 Hz), 130.4, 128.2, 128.1, 126.6 (q, J=4.0 Hz), 123.3 (q, J=273.0 Hz), 21.8; MS (EI) *m/e* (rel intensity) 91 (31), 107 (50), 139 (35), 300 (100); HRMS (EI) *m/e* calcd (M^+) 300.0432, found 300.0434.

4.2.2. 1-Trifluoromethyl-2-(toluene-4-sulfonyl)benzene (1j). White solid; R_f=0.24 (EtOAc/hexanes, 4:1); ^1H NMR (300 MHz, $CDCl_3$) δ 8.43 (1H, d, J=6.5 Hz), 7.85–7.71 (5H, m), 7.30 (2H, d, J=8.0 Hz), 2.41 (3H, s); ^{13}C NMR (300 MHz, $CDCl_3$) δ 144.6, 140.4, 138.4, 133.5, 132.7, 132.5, 129.8, 128.9 (q, J=33.0 Hz), 128.6 (q, J=6.5 Hz), 128.1, 122.7 (q, J=274.5 Hz), 21.8.

4.2.3. 1-Benzenesulfonyl-4-methoxybenzene (2f). White solid; R_f=0.10 (EtOAc/hexanes, 4:1); ^1H NMR (300 MHz, $CDCl_3$) δ 7.90–7.85 (2H, m), 7.27–7.70 (2H, m), 3.89 (3H, s), 3.04 (3H, s); ^{13}C NMR (300 MHz, $CDCl_3$) δ 163.9, 132.4, 129.7, 114.7, 55.9, 45.0.

4.2.4. (*E*)-Methanesulfonyl-hex-1-ene (3f). Light yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 6.96 (1H, dt, J=15.0, 7.0 Hz), 6.37 (1H, dt, J=15.5, 1.5 Hz), 2.93 (3H, s), 2.32–2.25 (2H, m), 1.53–1.26 (4H, m), 0.93 (3H, t, J=7.5 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 149.0, 129.5, 43.1, 31.3, 29.8, 22.3, 13.9.

Acknowledgements

This work was supported by the Natural Science and Engineering Research Council (NSERC) of Canada. We thank Dr. A. B. Young for mass spectrometric analysis.

References and notes

1. For reviews on Pd catalyzed Buchwald–Hartwig C–N and C–O bond formation reactions, see: (a) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131–209; (b) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046–2067.
2. For an excellent general review of the early literature, see: Lindley, J. *Tetrahedron* **1984**, *40*, 1433–1456.
3. For more reviews on more recent developments in Cu catalyzed C–C, C–N, and C–O bond formation reactions, see: (a) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337–2364; (b) Nelson, T. D.; Crouch, R. D. *Org. React.* **2004**, *63*, 265–555; (c) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428–2439; (d) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*,

1359–1469; (e) Finet, J.-P.; Fedorov, A. Y.; Combes, S.; Boyer, G. *Curr. Org. Chem.* **2002**, *6*, 597–626.
4. For a review of copper-based couplings of boronic acids, see: Chan, D. M. T.; Lam, P. Y. S. *Boronic Acids*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2005; pp 205–240.
5. Thomas, A. W.; Ley, S. V. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400–5449.
6. Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000**, *2*, 2019–2022.
7. Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937–2940.
8. Chan, D. M. T.; Monaco, K. L.; Wang, R.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933–2936.
9. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 1381–1384.
10. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397–4400.
11. Simpkins, N. S. *Sulphones in Organic Synthesis*; Baldwin, J. E., Magnus, P. D., Eds.; Tetrahedron Organic Chemistry Series; Pergamon: Oxford, 1993; Vol. 10, Chapter 2.
12. Schank, K. *The Syntheses of Sulfones, Sulfoxide and Cyclic Sulphides*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, NY, 1994; Chapter 1.
13. Wolf, W. M. *J. Mol. Struct.* **1999**, *474*, 113–124.
14. Neamati, N.; Mazumder, A.; Zhao, H.; Sunder, S.; Burke, T. R., Jr.; Schultz, R. J.; Pommier, Y. *Antimicrob. Agents Chemother.* **1997**, *41*, 385–393.
15. Prasit, P.; Wang, Z.; Brideau, C.; Chan, C.-C.; Charleson, S.; Cromlish, W.; Ethier, D.; Evans, J. F.; Ford-Hutchinson, A. W.; Gauthier, J. Y.; Gordon, R.; Guay, J.; Gresser, M.; Kargman, S.; Kennedy, B.; Leblanc, Y.; Léger, S.; Mancini, J.; O'Neil, G. P.; Duellet, M.; Dercival, M. D.; Perrier, H,; Riendeau, D.; Rodger, I.; Tagari, D.; Thérien, M.; Vichers, P.; Wong, E.; Xu, L.-J.; Young, R. N.; Zamboni, R. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1773–1778.
16. Forristal, I. *J. Sulfur Chem.* **2005**, *26*, 163–195.
17. Ni, L.; Zheng, X. S.; Somers, P. K.; Hoong, L. K.; Hill, R. R.; Marino, E. M.; Suen, K.-L.; Saxena, U.; Meng, C. Q. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 745–748.
18. Graybill, B. M. *J. Org. Chem.* **1967**, *32*, 2931–2933.
19. Gilman, H.; Beaver, N. J.; Meyer, C. H. *J. Am. Chem. Soc.* **1925**, *47*, 2047–2052.
20. Suzuki, H.; Abe, H. *Tetrahedron Lett.* **1995**, *3*, 6239–6242.
21. Baskin, J. M.; Wang, Z. *Org. Lett.* **2002**, *4*, 4424–4425.
22. Zhu, W.; Ma, D. *J. Org. Chem.* **2005**, *70*, 2696–2700.
23. Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Parisi, L. M.; Bernini, R. *J. Org. Chem.* **2004**, *69*, 5608–5614.
24. Bandgar, B. P.; Bettigeri, S. V.; Phopase, J. *Org. Lett.* **2004**, *6*, 2105–2108.
25. Beaulieu, C.; Guay, D.; Wang, Z.; Evans, D. A. *Tetrahedron Lett.* **2004**, *45*, 3233–3236.
26. Demir, A. S.; Reis, Ö.; Emrullahoglu, M. *J. Org. Chem.* **2003**, *68*, 10130–10134.
27. Lam, P. Y. S.; Bonne, D.; Vincent, G.; Clark, C. G.; Combs, A. P. *Tetrahedron Lett.* **2003**, *44*, 1691–1694.