Diaryl sulfones synthesis with aryltrifluoroborates and aryl sulfinic salts under mild conditions

Wei Zhang[a], Ke Li[c] and Baoli Zhao[b]*

[a]*Department of Chemistry and Chemical Engineering; Xinxiang University; Xinxiang 453003, P.R. China*

[b]*Institute of Applied Chemistry and Department of Chemistry, Shaoxing University, Shaoxing, Zhejiang Province 312000, P.R. China*

[c]*Jiaozuo City Environmental Protection Bureau, Jiaozuo, Henan Province, 453003, P.R. China*

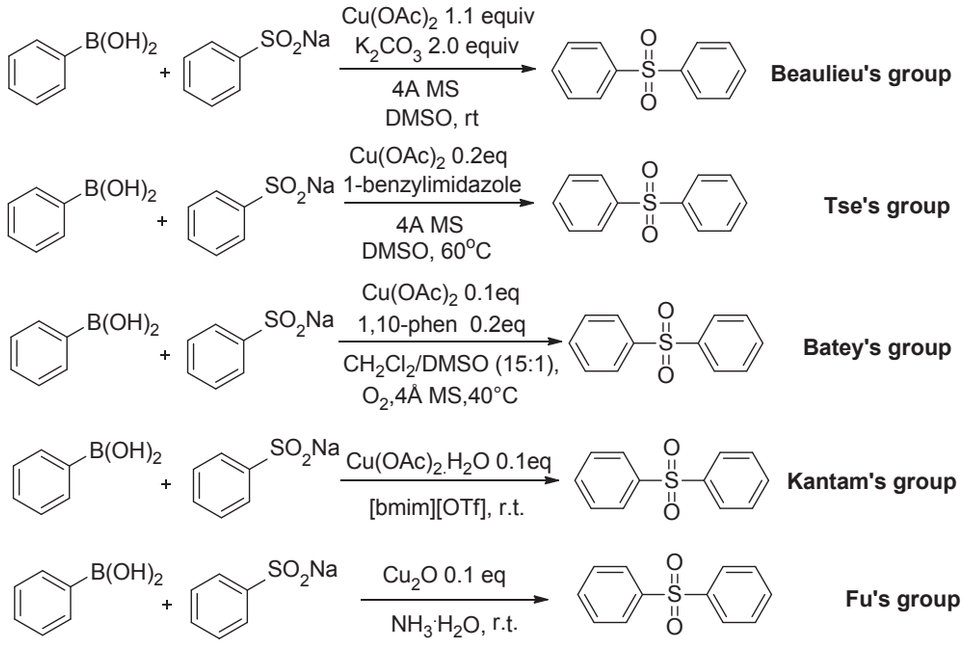
CuI-catalysed cross-coupling reactions of various aryltrifluoroborates with aryl sulfinic salts have been achieved in good yields. A new efficient method is described for the conversion of potassium aryltrifluoroborates into diaryl sulfones. The reported reactions are tolerant to common functional groups regardless of whether they are electron-rich or electron-deficient, making this transformation an attractive alternative to traditional approaches.

Keywords: aryltrifluoroborates, aryl sulfinic salts, cross-coupling, diaryl sulfone synthesis

The transition-metal-catalysed cross-coupling between aryl sulfinic salts and arylboronic acids is a versatile and widely utilised transformation in modern synthetic chemistry.[1–5] It is often the method of choice for the preparation of both symmetrical and unsymmetrical diaryl sulfones, which constitute the core skeleton of a number of pharmaceutical and pesticidal intermediates in organic synthesis.[6–9]

Over the last 10 years, copper catalysed cross-coupling strategy for diaryl sulfone synthesis has emerged, using the coupling of organoboronic acids with various aryl sulfinic salts. (Scheme 1) In 2004, Beaulieu *et al*.[1] reported a new efficient and mild preparation of sulfones from boronic acids and sulfinic salts mediated by 1.1 equiv. copper acetate with potassium carbonate. In 2007, Tse and co-workers[2] and Huang and Batey[3] respectively described a copper-catalysed method for the sulfonylation of arylboronic acids with sulfinate salts. The levels used for $Cu(OAc)_2$ have been reduced successfully with the assistance of nitrogen-containing ligands in the presence of molecular sieves (4 Å). The next year, Kantam *et al*.[4] reported copper acetate catalysed coupling reactions of arylboronic acids with sulfinic salts in ionic liquids (ILs) to afford aryl sulfones in good yields under ambient conditions. In 2011, Fu [5] *et al*. developed a simple and general Cu_2O-catalysed method for transformations of arylboronic acids and sulfinate salts in water at room temperature.

Another research area in Suzuki–Miyaura-type reactions which remains underdeveloped is in the search for alternatives to organoboron cross-coupling partners. Among the most promising alternatives to arylboronic reagents are potassium aryltrifluoroborates, which are easily prepared by treatment of commercially available arylboronic acids or esters with aqueous KHF_2.[10–14] Compared to most common organoboron compounds, aryltrifluoroborates are completely air- and moisture-stable, and can be prepared simply and in large quantities. That they are monomeric species makes their stoichiometric determination highly reliable. However, the cross-coupling of potassium aryltrifluoroborates with aryl sulfinic salts is still underdeveloped. In the report of Huang



Scheme 1 Copper-catalysed cross-coupling between aryl sulfinic salts and arylboronic acids.

* Correspondent. E-mail: babygarfield@126.com

and Batey,[3] the use of potassium trifluorophenyl borate as the reaction partner led to a disappointing yield (28%) of diphenyl sulfone. There is still an urgency to develop a new efficient method for the conversion of potassium trifluorophenyl borates into diaryl sulfone. We report here a practical synthetic method to prepare diaryl sulfones using potassium aryltrifluoroborates in efficient couplings with aryl sulfinic salts catalysed by Cu salts.

Results and discussion

We optimised the reaction conditions with the potassium phenyl fluoborate and sodium phenylsulfinate as template substrates in the presence of 10 mol% $Cu(OAc)_2$ in DCE (1,2-dichloroethane). However, only a 33% yield of diphenyl sulfone was formed. BF_3 along with BF_2OH and HF were formed during the transformation. So we considered that the addition of base to neutralise the acid and promote the reaction. When NaF was added to the solution, diphenyl sulfone was formed 55% yield. We speculate that base may play the role of accelerator to this copper catalysed process.

CAUTION: These experiments should be carried out taking due precautions because of the formation of toxic hydrogen fluoride (HF).

We screened many bases to promote the reaction and the results are summarised in Table 1. The bases with sodium and potassium cations were selected as candidates, and the influence on the reaction of different anions has been studied. The activity of sodium (entries 1–6) and potassium (entries 7–12) salts with the same anion is relatively similar and with no obvious pattern. The comparison between different anions has also been studied. Carbonate and hydroxide ions promote the reaction slightly (entries 1–2, 7–8), and *tert*-butoxy ion, phosphate ion and bicarbonate ion obviously facilitate the transformation with yields of 71–79% (entries 3–5, 9–11), Sodium acetate and potassium acetate were the best with 86% and 83% yields, respectively (entries 6, 12), so we choose sodium acetate as the optimal base.

Subsequently, to improve this process further, we investigated the effect of the catalyst and the solvent on the yield. (Table 2). The cross-coupling reactions of potassium phenyl trifluoborate with sodium phenylsulfinate were investigated carefully in order to determine the optimum reaction conditions. The study of the reaction with several catalysts in DCE showed that the use of copper salts is necessary to achieve acceptable yields (entries 1–8). Specifically, Cu(I) salts lead to higher yields compared to Cu(II) salts (entries 1–4 and 5–7). The cross-coupling reaction proceeds in a higher yield in the presence of CuI compared to CuOTf, CuCl and CuBr (entries 1–4). Reactions conducted in various organic solvents occurred with high yield within 3 h under mild conditions, despite the low solubility of sodium benzenesulfinate in organic solvents (entries 9–16). Specifically, chlorinated solvents lead to a higher yields than other solvents (entries 14–16).

A brief survey indicated that reaction efficiencies are highest when NaOAc is used as base, DCE is used as solvent and CuI is used as catalyst. Table 3 summarises the scope of the reactions conducted under the optimised conditions. The reactions of the more electron-deficient of the aromatic trifluoroborates occurred in higher yield than those of the electron-rich aryltrifluoroborates (entries 1–6). More strikingly, the reaction of aryltrifluoroborates with substitutions of halogen occurred with high selectivity (entries 7–10). No by-product was detected

Table 1 Base effects on the reaction[a]

Entry	Base	Yield/%[b]	Entry	Base	Yield/%[b]
1	None	33	7	$NaHCO_3$	43
2	Na_2CO_3	56	8	K_2CO_3	52
3	NaOH	79	9	KOH	78
4	t-BuONa	77	10	t-BuOK	73
5	Na_3PO_4	71	11	K_3PO_4	76
6	NaOAc	86	12	KOAc	83

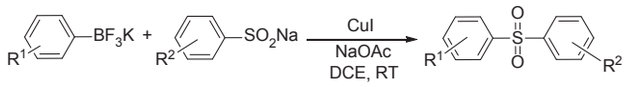
[a]Reaction conditions: $PhBF_3K$ (1.0 mmol), $PhSO_2Na$ (1.0 mmol), CuI (0.1 mmol), base (1.2 mmol), DCE (2 mL), 25 °C, 3 h. See the safety caution.
[b]Isolated yield.

Table 2 Catalyst and solvent selection on the reaction[a]

Entry	Catalyst	Yield/%[b]	Entry	Solvent	Yield/%[c]
1	CuOTf	77	9	DMSO	51
2	CuCl	82	10	DMF	46
3	CuBr	81	11	CH_3CN	50
4	CuI	86	12	toluene	39
5	$Cu(OAc)_2$	55	13	THF	45
6	$CuCl_2$	59	14	CCl_4	77
7	$Cu(OTf)_2$	47	15	CH_2Cl_2	80
8	None	0	16	$CHCl_3$	71

[a]Reaction conditions: $PhBF_3K$ (1.0 mmol), $PhSO_2Na$ (1.0 mmol), catalyst (0.1 mmol), NaOAc (1.2 mmol), solvent (2 mL), 25 °C, 3 h. See safety caution.
[b]Isolated yield using DCE as solvent.
[c]Isolated yield using CuI as catalyst.

Table 3 The scope of the reactions[a]



Entry	R_1	R_2	Yield/%[b]
1	4-OCH_3	H	82
2	4-CH_3	H	87
3	4-*t*-Bu	H	83
4	4-$COCH_3$	H	90
5	4-NO_2	H	93
6	4-CF_3	H	91
7	4-F	H	89
8	4-Cl	H	85
9	4-Br	H	86
10	3-Cl	H	83
11	2-F	H	87
12	2-Naphthyl[c]	H	91
13	H	4-OCH_3	88
14	H	4-CH_3	93
15	H	4-*t*-Bu	83
16	H	4-$COCH_3$	87
17	H	4-NO_2	81
18	H	4-CF_3	84
19	H	4-F	89
20	H	4-Cl	87
21	H	4-Br	91
22	H	3-Cl	90
23	H	2-F	87
24	H	2-Naphthyl[d]	93

[a]Reaction conditions: $ArBF_3K$ (1.0 mmol), $ArSO_2Na$ (1.0 mmol), CuI (0.1 mmol), NaOAc (1.2 mmol), DCE (2 mL), 25 °C, 3 h. See safety caution.
[b]Isolated yield.
[c]2-Naphthyltrifluoroborate was used.
[d]Sodium 2-naphthyl sulfinic acid was used.

in CuI-catalysed dehalogenation with sulfinate salts. More bulky substrates also reacted efficiently with sulfinate salts and gave the product in a comparable yield (entry 11). As shown in entry 12, we were able to extend the methodology to fused ring trifluoroborates to afford the desired sulfone in 91% yield under our standard conditions. Then we chose the same substituents on sodium aryl sulfinate salts to investigate the scope of the coupling with respect to other sulfinate salts (Table 3, entries 13–24). The transformation worked equally as well with aryltrifluoroborates with a diverse range of substituents, to afford the products in good to excellent yields.

Conclusions

In conclusion, we have shown that aryltrifluoroborate salts, which are water and air stable equivalents of arylboronic acids, can be utilised in copper-catalysed cross-coupling reactions with aryl sulfinate salts. Diaryl sulfones derivatives were easily synthesised in high yields with the assistance of base. Investigation of the mechanism of these reactions is ongoing in our laboratory.

Experimental

All solvents were purified and dried according to standard methods prior to use. Proton NMR spectra were recorded in $CDCl_3$ on a Bruker Avance III 400 M Hz spectrometer. Proton chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS) with the residual solvent peak as the internal reference. Multiplicities are reported as: singlet (s), doublet (d), triplet (t) and multiplet (m). ^{13}C NMR spectra were recorded at 100 MHz with TMS as an internal reference. HRMS (EI) data were collected on high resolution mass spectrometer (MAT 900 XL, Thermo Finnigan, USA). All materials were purchased from common commercial sources and used without additional purification.

Synthesis; typical procedure

A mixture of potassium arylfluoborate (1 mmol), sodium aryl sulfinate (1 mmol), CuI (0.1 mmol), sodium acetate (1.2 mmol) and DCE (2 mL) was stirred at 25 °C under air for 3 h. After filtration, the organic phases were evaporated under reduced pressure, and the residue was subjected to flash column chromatography [silica gel, ethyl acetate/petroleum ether (60–90 °C) = 1/8] to obtain the desired product.

Diphenyl sulfone: White solid, m.p. 126–127 °C (lit.[15] 125–126 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.6 Hz, 4H), 7.55 (t, J = 7.6 Hz, 2H), 7.50 (t, J = 7.6 Hz, 4H). HRMS calcd for $C_{12}H_{10}O_2S$: 218.0402, found: 218.0405.

4-Methoxyphenyl phenyl sulfone: Yellow solid, m.p. 90–92 °C (lit.[16] 88–90 °C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (m, 4H), 7.51 (m, 3H), 6.96 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 144.6, 138.7, 133.0, 129.7, 129.0, 127.4, 127.1, 56.1; HRMS calcd for $C_{13}H_{12}O_3S$: 248.0507, found: 248.0509.

4-Methylphenyl phenyl sulfone: White solid, m.p. 125–127 °C (lit.[15] 126–127 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 2.37 (s, 3H). HRMS calcd for $C_{13}H_{12}O_2S$: 232.0558, found: 232.0557.

4-tert-*Butylphenyl phenyl sulfone*: White solid, m.p. 129–131 °C (lit.[17] 127–128 °C); ^1H NMR (400 MHz, $CDCl_3$): δ7.94–7.98 (m, 2H), 7.83–7.88 (m, 2H), 7.47–7.57 (m, 5H), 1.35 (s, 9H). HRMS calcd for $C_{16}H_{18}O_2S$: 274.1028, found: 274.1031.

4-Acetylphenyl phenyl sulfone: Yellow solid, m.p. 132–133 °C (lit.[16] 132–134 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.94–8.04 (m, 6H), 7.50–7.61 (m, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ196.4, 142.9, 140.7, 140.1, 133.7, 130.1, 129.2, 128.8, 127.3, 27.6; mHRMS calcd for $C_{14}H_{12}O_3S$: 260.0507, found: 260.0510.

4-Nitrophenyl phenyl sulfone: Yellow solid, m.p. 145–149 °C (lit.[17] 143–145 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 8.27–8.38 (m, 2H), 8.07–8.15 (m, 2H), 7.92–8.00 (m, 2H), 7.58–7.66 (m, 1H), 7.51–7.61 (m, 2H). HRMS calcd for $C_{12}H_9NO_4S$: 263.0252, found: 263.0250.

4-Trifluoromethylphenyl phenyl sulfone: Colourless solid, m.p. 89–90 °C (lit.[17] 90–91 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.0 Hz, 2H), 7.90–8.03 (m, 2H), 7.80 (d, J = 8.8 Hz, 2H), 7.50–7.65(m, 3H). HRMS calcd for $C_{13}H_9F_3O_2S$: 286.0275, found: 286.0276.

4-Fluorophenyl phenyl sulfone: White solid, m.p. 103–104 °C (lit.[15] 105–107 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (m, 4H), 7.57 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.18 (m, 2H). HRMS calcd for $C_{12}H_9FO_2S$: 236.0307, found: 236.0305.

4-Chlorophenyl phenyl sulfone: White solid, m.p. 90–91 °C (lit.[17] 92–93 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.80–8.01 (m, 4H), 7.44–7.64 (m, 5H). HRMS calcd for $C_{12}H_9{}^{35}ClO_2S$: 252.0012, found: 252.0017.

4-Bromophenyl phenyl sulfone: Yellow solid, m.p. 100–101 °C (lit.[17] 98–99 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.88–7.99 (m, 2H), 7.76–7.86 (m, 2H), 7.61–7.69 (m, 2H), 7.55–7.61 (m, 1H),7.46–7.52 (m, 2H). HRMS calcd for $C_{12}H_9{}^{79}BrO_2S$: 295.9507, found: 295.9508.

3-Chlorophenyl phenyl sulfone: Yellow solid, m.p. 99–100 °C (lit.[15] 100–101 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (m, 3H), 7.82 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.52 (m, 3H), 7.45 (t, J = 8.4 Hz, 1H). HRMS calcd for $C_{12}H_9ClO_2S$: 252.0012, found: 252.0017.

2-Fluorophenyl phenyl sulfone: White solid, m.p. 93–96 °C (lit.[17] 92–94 °C);

^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.51 (m, 5 H), 7.09–7.20 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9; 141.4, 136.7; 133.1; 130.2, 129.3, 127.5,127.1, 125.8, 117.8; HRMS calcd for $C_{12}H_9FO_2S$: 236.0307, found: 236.0309.

2-Napthyl phenyl sulfone: Colourless solid, m.p. 119–120 °C (lit.[17] 119–121 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.95–8.06 (m, 3H), 7.93 (d, J = 8.8 Hz, 1H), 7.82–7.89 (m, 2H),7.48–7.66 (m, 5H). HRMS calcd for $C_{16}H_{12}O_2S$: 268.0558, found: 268.0556.

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References

1 C. Beaulieu, D. Guay, Z. Wang and D.A. Evans. *Tetrahedron Lett*., 2004, **45**, 3233.
2 A. Kar, I.A. Sayyed, W.F. Lo, H.M. Kaiser, M. Beller and M.K. Tse. *Org. Lett*., 2007, **9**, 3405.
3 F. Huang and R.A. Batey *Tetrahedron,* 2007, **63**, 7667.
4 M.L. Kantam, B. Neelima, B. Sreedhar and R. Chakravarti. *Synlett*, 2008, **10**, 1455.
5 H. Yang, Y. Li, M. Jiang, J. Wang and H. Fu. *Chem. Eur. J*., 2011, **17**, 5652.
6 I.C. Richards and P.S. Thomas, *Pestic. Sci.,* 1990, **30**, 275.
7 W.M. Wolf, *J. Mol. Struct.,* 1999, **474**, 113.
8 T. Otzen, E.G. Wempe, B. Kunz, R. Bartels, G.L. Yvetot, W. Hansel, K.-J. Schaper and J.K. Seydel, *J. Med. Chem.,* 2004, **47**, 240.
9 A.-M. Faucher, P.W. White, C. Brochu, C.G. Maitre, J. Rancourt and G. Fazal, *J. Med. Chem.,* 2004, **47**, 18.
10 J. Masllorens, I. González and A. Roglans, *Eur. J. Org. Chem*., 2007, 158.
11 L.S. Varnedoe, B.D. Angel, J.L. McClellan and J.M. Hanna Jr, *Lett. Org. Chem*., 2010, **7**, 1.
12 N. Taccardi, R. Paolillo, V. Gallo, P. Mastrorilli, C.F. Nobile, M. Räisänen and T. Repo, *Eur. J. Inorg. Chem*., 2007, 4645.
13 B. Schmidt and F. Hölter, *Org. Biomol. Chem*., 2011, **9**, 4914.
14 S. Cacchi, E. Caponetti, M.A. Casadei, A.D. Giulio, G. Fabrisi, G. Forte, A. Goggiamani, S. Moreno, P. Paolicelli, F. Petrucci, A. Prastaro and M.L. Saladino, *Green Chem*., 2012, **14**, 317.
15 H. Yang, Y. Li, M. Jiang, J. Wang and H. Fu, *Chem. Eur. J*., 2011, **17**, 5652.
16 W. Zhu and D. Ma, *J. Org. Chem*., 2005, **70**, 2696.
17 B.P. Bandgar, S.V. Bettigeri and J. Phopase, *Org. Lett*., 2004, **6**, 2105.