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Convenient synthesis of α,β-unsaturated sulfones via a Mizoroki–Heck reaction of arylboronic acids with phenyl vinyl sulfones

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Abstract—Palladium acetate catalyzed Mizoroki–Heck reaction of arylboronic acids with phenyl vinyl sulfones afford α,β-unsaturated sulfones in good yields.

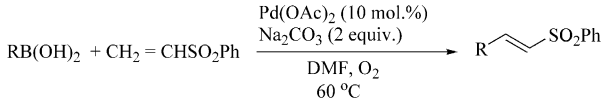
Vinyl sulfones are extensively used as intermediates in organic synthesis[1–6] due to the chemical versatility of the sulfone moiety. Vinyl sulfones are also excellent acceptors in Michael additions [7] and 2π partners in cycloaddition reactions.[8] Several biologically active sulfone molecules, prepared from alkenyl sulfones,[9–12] and α,β-unsaturated sulfones, have been found to have anticancer[13,14] and carcinogenesis-suppressing activity.[15,16]

Numerous methods have been developed for the synthesis of alkenyl sulfones. Recent examples include hydrozirconation of 1-alkenyl sulfones,[17] hydrozirconation of terminal alkynes followed by reaction with sulfonyl chlorides,[18] hydrotelluration of 1-alkenyl sulfones,[19] cerium(IV) ammonium nitrate mediated oxidative addition of sulfinate and iodine to alkenes,[20] boron trifluoride, or AIBN catalyzed addition of polystyrene-supported selenosulfonates to alkenes,[21] Heck reactions of polystyrene–resin supported aryl iodides with vinyl sulfones,[22] and the reaction of alkenyltriphenylbismuthonium tetrafluoroborates with arylsulfinate salt.[23] These methods are sometimes complex, do not tolerate sensitive functional groups, and the reagents and starting materials are not always readily available.

Organoboronic acids comprise a family of organometallic reagents that tolerate a wide range of functional groups. They are widely available, generally eco-friendly, relatively inert to air and water, and thermally stable and readily handled without special precautions. As a part of an ongoing research program focused on the use of boronic acids in organic synthesis,[24–29] we investigated their use in the synthesis of alkenyl sulfones. We wish to report the results of this study.

Heating phenyl vinyl sulfone with *p*-tolylboronic acid in the presence of palladium acetate and sodium carbonate in *N*,*N*-dimethylformamide at 60 °C under a nitrogen atmosphere afforded β-*p*-tolylvinyl phenyl sulfone in poor yield. However, carrying out the reaction in the presence of oxygen markedly improved the yield. Optimal reaction yields were obtained when sulfone (1.0 mmol), organoboronic acid (1.2 mmol), sodium carbonate (2.0 mmol), and palladium acetate (10 mol %) were allowed to react in an oxygen atmosphere at 60 °C. *N*,*N*-Dimethylformamide was found to be a more effective solvent than DMSO, MeCN, EtOH, PEG-400, or toluene. Palladium powder and nickel chloride were completely ineffective catalysts in the reaction (Scheme 1).

A variety of arylboronic acids readily underwent reaction with phenyl vinyl sulfone to produce the corresponding β-arylvinyl phenyl sulfones in good to high yields (Table 1). Aliphatic vinylboronic acids produced modest yields (<20%) but alkylboronic acids were unreactive. Functional groups such as methoxy, nitro, acetyl, chloro, bromo were unaffected by the reaction. It



Scheme 1.

Keywords: Vinyl sulfones; Arylboronic acids; Palladium catalysis.
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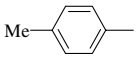
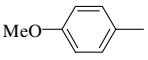
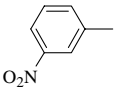
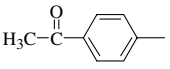
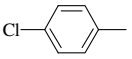
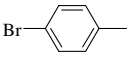
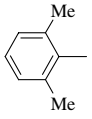
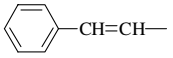
Table 1. Reactions of arylboronic acids with phenyl vinyl sulfones (Scheme 1)[30]

Entry	R	Time (h)	Yield (%)[a,b]
1		15	84[17]
2		15	81[17]
3		15	76[31]
4		15	70[32]
5		18	79[17,31]
6		18	74[17]
7		18	74[33]
8		18	70[34]

[a] Isolated yields based on vinyl sulfone.
[b] All compounds characterized by elemental analysis and NMR spectroscopy.

is noteworthy that the reaction is insensitive to the electronic nature of the functional groups present in the arylboronic acids. In addition, sterically hindered, 2,6-dimethylphenylboronic acid (entry 7) readily participates in the reaction.

In conclusion, we have developed a novel synthesis of β-arylvinyl phenyl sulfones via a Mizoroki–Heck type reaction of boronic acids with phenyl vinyl sulfones. The method tolerates a wide variety of functional groups, is straightforward, and provides good yields of products from readily accessible starting materials.

Acknowledgement

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30. Phenyl vinyl sulfone (1 mmol) was placed in an oven-dried, round bottomed flask under a nitrogen atmosphere. Dry dimethylformamide (2.5 mL) was added and the resultant solution stirred. Arylboronic acid (1.2 mmol), Na_2CO_3 (2.0 mmol) and $Pd(OAc)_2$ (10.0 mmol%) were then added. A balloon filled with oxygen was attached to the flask and the mixture was stirred at 60 °C for the indicated time. The resultant mixture was diluted with ethyl acetate (50 mL) and washed with water (3×10 mL). The organic layer was separated, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure and the product purified by silica gel chromatography (ethyl acetate–hexane). ^1H and ^{13}H NMR spectra were carried out in $CDCl_3$.
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32. White solid, mp 150 °C, ^1H NMR (250 MHz, $CDCl_3$): δ 2.60 (3H), 7.02 (d, $J = 15.5$ Hz, 1H), 7.53–7.64 (m, 5H), 7.71 (d, $J = 15.5$ Hz, 1H), 7.97 (d, $J = 7.8$ Hz, 4H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 26.6, 127.6, 128.6, 128.8, 129.3, 129.7, 133.5, 136.4, 138.5, 140.0, 140.6, 197.0. Anal. Calcd for $C_{16}H_{14}O_3S$: C, 67.11; H, 4.93. Found: C, 67.05; H, 5.01.
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