

Convenient synthesis of α,β -unsaturated phosphonates via a Mizoroki–Heck reaction of arylboronic acids with diethyl vinylphosphonate

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Abstract—Palladium acetate catalyzed Mizoroki–Heck reactions of arylboronic acids with diethyl vinylphosphonates afford α,β -unsaturated phosphonates in good yields.
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Alkenylphosphonates are routinely used to prepare biologically active molecules,^{1–4} flame-retardants,⁵ polymer additives,⁶ and have been evaluated for their pharmacological activity.^{7,8} They are important intermediates⁹ in the synthesis of stereoisomeric trisubstituted olefins,^{10–12} carbo- and heterocyclic compounds,^{9,13,14} and they are used in transformations such as Michael additions,¹⁵ cycloadditions,^{16,17} aminohydroxylations,¹⁸ dihydroxylations,¹⁹ aziridinations,²⁰ epoxidations,²¹ C-glycosylations,²² and hydrogenations.²³

Numerous methods have been developed for the synthesis of alkenylphosphonates. Recent examples include the formation of titanacycles from 1-alkynylphosphonates,²⁴ hydrotelluration of 1-alkynylphosphonates,²⁵ hydrozirconation of terminal alkynes followed by reaction with dialkyl chlorophosphates,²⁶ olefin metathesis,²⁷ resin supported palladium catalyzed Heck reactions,²⁸ Heck reactions of aryldiazonium salts,²⁹ and reactions between vinyl bromides and dialkylphosphonates.³⁰ These methods are sometimes complex, often intolerant of sensitive functional groups, and the reagents are not always readily accessible. Very recently,

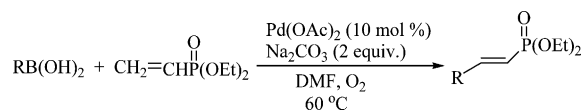
we reported a stereoselective synthesis of alkenylphosphonates using vinylboronates.³¹

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. Boronic acids are readily handled without special precautions. They are thus increasingly important in organic synthesis. As part of an ongoing research program focused on the use of boronic acids in organic synthesis,^{31–36} we examined the synthesis of α,β -unsaturated phosphonates using boronic acids. We wish to report the results of this study (Scheme 1).

Heating diethyl vinylphosphonate 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 diethyl β -*p*-tolylvinylphosphonate in poor yield. Running the reaction in an oxygen^{31,32} atmosphere markedly improved the yield. Optimal reaction conditions were obtained utilizing vinylphosphonate (1.0 mmol), boronic acid (1.2 mmol), sodium carbonate (2.0 mmol), and palladium acetate

Keywords: Vinyl phosphonates; Arylboronic acids; Mizoroki–Heck reaction.

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Scheme 1.

(10 mol%) 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.


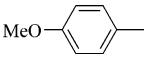
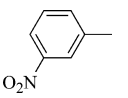
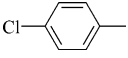
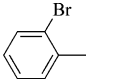
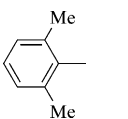
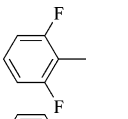
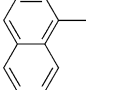
A variety of arylboronic acids readily reacted with diethyl vinylphosphonates to produce the corresponding diethyl β -arylvinylphosphonates in good to high yields (Table 1).

Alkylboronic acids were found to be unreactive, whereas, alkenylboronic acids such as 2-phenylvinylboronic acid produced the expected product in modest yield.

Functional groups such as methoxy, nitro, chloro, and bromo were unaffected. It is noteworthy that the reaction is insensitive to the electronic nature of the functional groups present in the arylboronic acids. Sterically hindered, di-*ortho* substituted boronic acid (entries 6 and 7) readily participate in the reaction.

In conclusion, we have developed a novel oxidative Heck reaction utilizing boronic acids and vinylphosphonate for the synthesis of dialkyl 2-arylvinylphosphonates. The method has the advantages in that it tolerates a wide variety of functional groups, is straightforward, and provides good yields of products from readily accessible starting materials.

Table 1. Reactions of arylboronic acids with diethyl vinylphosphonates (Scheme 1)³⁷

Entry	R	Time (h)	Yield (%) ^{a,b}
1		18	82
2		20	85
3		15	83
4		18	73
5		18	62
6		20	86
7		18	34
8		15	66

^a Isolated yields based on diethyl vinylphosphonates.

^b All compounds exhibited physical and spectral properties in accord with literature values.

Acknowledgements

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37. Diethyl vinylphosphonate (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), Na₂CO₃ (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 and washed with water (3×10 mL). The organic layer was dried over anhydrous MgSO₄, filtered, and the solvent removed under reduced pressure. The product was purified by silica gel chromatography (ethyl acetate–hexane). ¹H and ¹³C NMR spectra were carried out in CDCl₃.