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Synthesis of (*E*)- and (*Z*)-Alkenylphosphonates Using Vinylboronates

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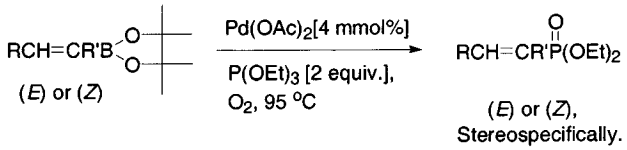
ABSTRACT



(*E*)- and (*Z*)-alkenylphosphonates have been prepared stereospecifically via the reaction of vinylboronate esters with triethyl phosphite in the presence of palladium acetate.

Alkenylphosphonates are routinely used to prepare biologically active molecules,[1] flame retardants,[2] polymer additives,[3] and other transformations[4] such as Michael additions,[4a] aminohydroxylations,[4b,] dihydroxylations,[4c] aziridinations,[4d,e] epoxidations,[4e] C-glycosylations,[4f] Horner−Wadsworth−Emmons reactions,[4g] and hydrogenations.[4h] (*E*)- and (*Z*)-alkenylphosphonates exhibit different biological activities in nucleotide derivatives[1c,e] and produce stereoisomeric intermediates in asymmetric reactions.[4a−e] Thus, the development of stereoselective methods to prepare (*E*)- and (*Z*)-alkenylphosphonates has become important in organic synthesis. A survey of the literature[5] reveals that most synthetic methods produce either (*E*)- or a mixture of (*E*)- and (*Z*)-vinylphosphonates. Coupling of dialkyl phosphites with vinyl bromides does produce (*E*)- and (*Z*)-vinylphosphonates stereoselectively,[6,7] but it is difficult to prepare stereochemically pure vinyl bromides. Recently, Srebnik reported a method for the synthesis of (*Z*)-vinylphosphonates.[8]

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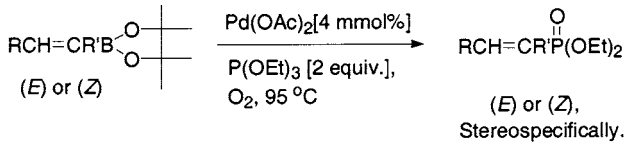
Table 1. Survey of Catalysts Used in the Reaction of Pinacolato (*E*)-1-Octenylboronate with $P(OEt)_3$[a]

catalyst	reaction time (h)	yield[b] (%)
$Pd(OAc)_2$	8	84
$PdCl_2$	8	75
$NiCl_2$ (anhy)[c]	25	43
$Pd(OAc)_2$, PPh_3[d]	12	55
$Pd(dppf)Cl_2$	40	incomplete reaction

[a] Reaction conditions: pinacolato (*E*)-1-octenylboronate (1 mmol), $P(OEt)_3$ (2 mmol), catalyst (4 mol %), 95 °C under O_2. [b] Isolated yields.[c] 6 mol %. [d] PPh_3 (4 equiv) was added.

Since (*E*)- and (*Z*)-vinylboronates[9,10] can be prepared stereospecifically, they are ideal precursors for the stereospecific formation of (*E*)- and (*Z*)-alkenylphosphonates. We decided to explore the preparation of (*E*)- and (*Z*)-alkenylphosphonates from vinylboronates as a part of an ongoing research program focused on reactions of boronic acids and their esters.[11] Herein, we wish to report the results of this study (Scheme 1).

Scheme 1



We first examined the reaction of pinacolato (*E*)-1-octenylboronate with $P(OEt)_3$ in the presence of $Pd(OAc)_2$ in refluxing EtOH. Diethyl (*E*)-1-octenylphosphonate was formed in 54% yield in 35 h. Acetonitrile, tetrahydrofuran, and toluene were ineffective as solvents. We then examined the reaction in the absence of solvents. When pinacolato (*E*)-1-octenylboronate was heated with triethyl phosphite and palladium acetate at 95 °C under nitrogen, diethyl (*E*)-1-octenylphosphonate was formed in 60% yield. Carrying out the reaction in the presence of oxygen improved the yield to 85%.[12]

A survey of various catalysts (Table 1) revealed that palladium acetate was the most effective. Addition of Ph_3P to the $Pd(OAc)_2$ (or the use of $Pd(dppf)Cl_2$) did not improve the yield. In general, an excess of $P(OEt)_3$ was required to attain the highest yields.

We then examined the reactions of various (*E*)- and (*Z*)-vinylboronates (Table 2). The $Pd(OAc)_2$-catalyzed reaction of vinylboronates with $P(OEt)_3$ at 95 °C under an oxygen atmosphere furnished vinylphosphonates in good to high yield.[13] Significantly, (*E*)- and (*Z*)-vinylboronates (entries 1−6) were stereospecifically converted to corresponding (*E*)- and (*Z*)-alkenylphosphonates, respectively. The method is suitable for both aryl- and alkyl-substituted vinylboronates. Halogen functionalities (entries 3, 4, and 7) were unaffected under the reaction conditions. An α-substituted vinylboronate also underwent the reaction to afford a moderate yield of expected product, although the reaction was slow (entry 8). The reaction does not appear to require a boronate ester since boronic acids also react, although an excess of $P(OEt)_3$ is required to solubilize the boronic acid. The use of $P(OMe)_3$ required a longer reaction time but produced the desired product.

In conclusion, we have developed an improved method for preparing (*E*)- and (*Z*)-alkenylphosphonates stereospecifically from vinylboronates. To the best of our knowledge, this is the first report of the conversion of vinylboronic esters and their acids to 1-alkenylphosphonates. The new method has the advantage that (*E*)- and (*Z*)-vinylphosphonates can be prepared stereospecifically in good yields using readily accessible starting materials. Further investigations are in progress.

Table 2. $Pd(OAc)_2$-Catalyzed Conversion of Vinylboronates to Alkenylphosphonates,[a] Scheme 1

entry	R	R′	stereochemistry	time (h)	product	yield[b] (%)	ref[c]
1	Ph	H	*E*	9	$PhCH{=}CHP(O)(OEt)_2$ *E*	78	5i, 6
2	Ph	H	*Z*	7	$PhCH{=}CHP(O)(OEt)_2$ *Z*	75	5e,i, 6, 8
3	*p*-Cl-C_6H_4	H	*E*	9	*p*-Cl−$C_6H_4CH{=}CHP(O)(OEt)_2$ *E*	79	5i
4	*p*-Cl-C_6H_4	H	*Z*	6	*p*-Cl−$C_6H_4CH{=}CHP(O)(OEt)_2$ *Z*	60	5i
5	*n*-C_6H_{13}	H	*E*	8	*n*-$C_6H_{13}CH{=}CHP(O)(OEt)_2$ *E*	84	5b
6	*n*-C_6H_{13}	H	*Z*	6	*n*-$C_6H_{13}CH{=}CHP(O)(OEt)_2$ *Z*	63	13a
7	*p*-F-C_6H_4	H	*E*	9	*p*-F−$C_6H_4CH{=}CHP(O)(OEt)_2$ *E*	81	13b
8	Ph	CH_3	*E*	120	$PhCH{=}C(CH_3)P(O)(OEt)_2$ *E*	55	13c

[a] Reaction conditions: vinylboronate (1 mmol), $P(OEt)_3$ (2 mmol), and $Pd(OAc)_2$ (4 mmol %), 95 °C, O_2. [b] Isolated yields. [c] Literature reference.

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Supporting Information Available: General experimental procedure and ^{1}H, ^{13}C, and ^{31}P NMR spectroscopic data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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