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Hydroboration of Unsaturated Phosphonic Esters: Synthesis of Boronophosphonates and Trisubstituted Vinylphosphonates

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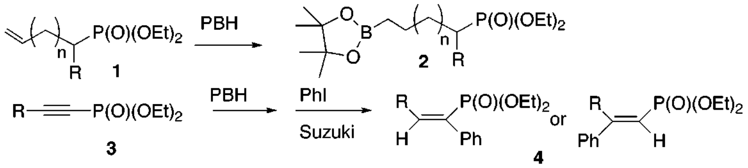
ABSTRACT



Hydroboration of vinyl phosphonates with pinacolborane (PBH) proceeds to give phosphonoboronates, 2. Surprisingly, such compounds have not been reported before. The reaction works well with terminal alkenylphosphonates. Internal alkenylphosphonates give complex mixtures. Hydroboration/Suzuki coupling of alkynylphosphonates, with PBH, in a one-pot procedure gives trisubstituted vinylphosphonates in good overall yields and provides a new synthesis of these compounds.

Of the various methods available for preparing phosphorus−boron compounds, hydroboration of alkenyl phosphines has been used extensively for the synthesis of phosphineboranes.[1] Phosphonoboronates, on the other hand, surprisingly have not been prepared by hydroboration. Only isolated examples of hydroboration of alkenylphosphonates by borane have been reported.[2] No examples of hydroboration of alkynylphosphonates appear in the literature. Phosphonoboronates are potentially interesting reagents and may possess some biological activity.[3] In this report we present our results for the hydroboration of various unsaturated alkenyl- and alkynylphosphonates with pinacolborane (PBH). The intermediate vinylphosphonoboronates readily undergo Suzuki coupling to give trisubstituted vinylphosphonates. The latter are important synthetic compounds.[4]

Hydroboration of Alkenylphosphonates with Pinacolborane (PBH). Preparation of Boronophosphonates 2. Compound **1a** was prepared by esterification of commercially available vinyl phosphonic acid.[5] Compounds **1b**−**d** were prepared in high yields by Michaelis Becker reaction of bromoalkenes and sodium diethyl phosphite.[6] Phosphonate **1e** was obtained from 1-chloromethylphosphonate as described in the literature.[7] Compounds **1f** and **1g** were prepared by acetylation and silylation of 1-hydroxyallylphosphonate, which was formed from acrolein, diethyl phosphite, and basic Al$_2$O$_3$.[8] Initially, the effect of the ester groups on hydroboration was explored (Scheme 1).

Several esters were prepared and hydroborated with PBH

Scheme 1

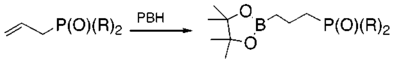


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Table 1. Hydroboration of Allylphosphonic Esters $CH_2{=}CH{-}CH_2P(O)(R)_2$ with PBH[a]

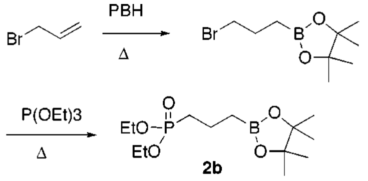
allylphosphonic ester, R	phosphonoboronate, % yield[b]
OMe	~100
OEt	~95
i-OPr	60
OPh	20
Cl	polymeric products

[a] Neat, 1 h, 80 °C. [b] By GCMS. Isolated yields were in the 20−30% range as a result of polymerization of the starting compounds.

(Table 1). Methyl and ethyl allylphosphonates gave comparable results; the isopropyl ester was less effective. Reaction with the phenol esters proceeded sluggishly and conversion of only 20% was observed, while the dichlorophosphonate gave only polymeric products. As a result of the greater availability of the ethyl derivatives, they were selected for subsequent studies. Hydroboration of **1** with neat PBH gave best conversions and yields. The reaction takes place readily without solvent or catalyst in the temperature range 70−110 °C. Reactions were monitored by GC−MS spectroscopy. Hydroboration with catecholborane under the same conditions provided only about 20−30% conversion, and the resulting compounds were difficult to purify. Use of $HBBr_2$-SMe_2 gave a mixture of products and also cleaved the ester groups.

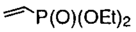
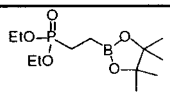
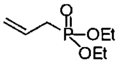
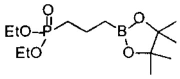
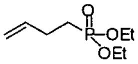
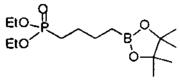
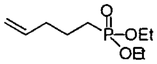
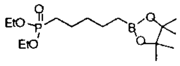
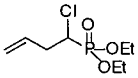
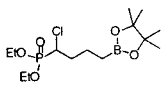
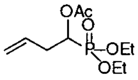
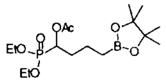
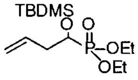
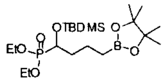
Hydroboration of **1** was followed by ^{31}P NMR. For instance, compound **1b** absorbs at 26.47 ppm. After the addition of 1.2 equiv of PBH at room temperature, a peak was observed at 30.45 ppm, which we attribute to **2b**, After 1 h of heating at 70 °C, the signal of starting material disappeared. No additional signals were observed, indicating the absence of any coordination between boron and phosphorus. In contrast to **1b**, **1f** and **1g** required heating before products could be detected by ^{31}P NMR (**2f** (30.86 ppm) and **2g** (24.02 ppm)). Additional heating of **1f** and **1g** gave rise to phosphorus signals in the 19−23 ppm region. This can be explained as a result of isomerizations at phosphorus for both starting materials and products during the reaction. Cleavage of the acetyl groups or TBDMS groups result in transesterification of the hydroxy group with nearby alkoxy groups bonded to phosphorus and lead to cyclization products.[9] We checked the importance of the order of insertion. Thus, **2b** was also obtained by hydroboration of allylbromide with PBH followed by Arbuzov reaction with triethyl phosphite (Scheme 2). Despite the comparable yields of the two methods, the synthetic protocol of Scheme 1 has several advantages: (1) vinyl phosphonates **1a**−**h** are much more stable than boronic alkyl bromides; and (2) substituted vinyl phosphonates are more readily available and they can contain other functional groups useful for further reactions.

Scheme 2



For compounds **1a**−**e** maximum yields were obtained by heating with PBH at 70 °C for 1 h. Higher temperatures resulted in polymerization and elimination products. Hydroboration of **1f** and **1g** required higher temperatures (110 °C) and longer reaction times (3−5 h, see Table 2).

Table 2. Hydroboration of Alkenylphosphonates with PBH

Entry	Alkenyl Phosphonate,1	Phosphonoboronate, 2	% Yield[a]
a			98, A[b]
b			99, A
c			99. A
d			98, A
e			97, A
f[a]			75, B[c]
g			70, B

[a] As determined by GCMS. Isolated yields were in the range, 20−30% after chromatography. [b] Method A: 1.2 equiv PBH, 70 °C, 1 h. [c] Method B: 2 eqiov PBH, 110 °C, 5 h.

The optimum phosphonate/PBH molecular ratio was investigated. For compounds **1a**−**e** the ratio was 1:1.2. Higher amounts of PBH gave lower yields. Compound **2f,** which contains an acetyl, group required 2 equiv of PBH. More than 2 equiv of PBH resulted in the removal of the acetyl group. Compounds **2a**−**g** were purified by chromatography. The isolated yields were in the range 20−30%. This apparently is due to competing polymerization of the alkenylphosphonates by PBH. Internal alkenes gave complex reaction mixtures from which no products could be isolated. The structures of all new products **2a**−**g** were confirmed by

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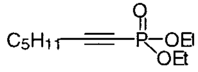
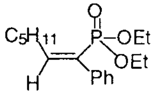
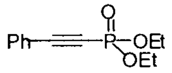
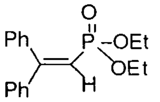
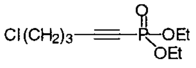
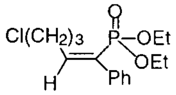
NMR spectroscopy. The NMR spectra of products are complex because of heteronuclear coupling. Despite such complications, structures **2a−g** were deduced from their ^1H and ^{13}C spectra. Thus, the triplet in the ^1H spectra in the region 0.75−0.85 ppm was assigned to the -CH_2-B- group. It corresponded to a broad signal in the region of 9−12 ppm in the ^{13}C spectra. The proton signals in the aliphatic chain in **2c−g** are overlapped and the multiplicity is not clear. Also the corresponding carbons gave overlapping signals at 24.5−24.7 ppm in the region of the pinacol groups. COSY and HETCOR experiments established the connectivity between protons and the corresponding carbons. In the ^{13}C spectra of **2e−g**, the doublets in the region 68−72 ppm (J_{CP} = ∼200 Hz) are characteristic for -O-$\underline{CH}$-P(O)(OR)$_2$ or -Hal-$\underline{CH}$-P(O)(OR)$_2$.[10] In the ^{31}P NMR spectra of **2** higher shielding of the phosphonates was observed (∼30 ppm) relative to the starting materials **1** (∼17−25 ppm).

Hydroboration of Alkynylphosphonates. Starting materials **3** were prepared by lithiation of the alkynes and treatment with diethylchlorophosphonate. Hydroboration of **3** with PBH gave products, which were difficult to isolate by chromatography and to characterize.[11] Instead, they were immediately Suzuki coupled[12] with phenyl iodide to give trisubstituted alkenylphosphonates (Table 3).[13] This represents a new one-pot synthesis of trisubstituted vinylphosphonates. The stereochemistry of the double bond was determined by J_{PH} coupling constants. Thus a trans configuration of the phosphorus and hydrogen atoms has a coupling constant of around 50 Hz, while a coupling constant of ∼20 Hz is consistent with hydrogen and phosphorus on the same carbon.[14] Compounds **4a** and **4c** are therefore assigned *Z*, while **4b** has the vinylic hydrogen and phosphorus on the same carbon. Thus hydroboration of **3b** places boron on C2, on the same carbon as the phenyl group. Similar directive effects are known in the hydroboration of styrene by borane-type reagents[15] and in metal-catalyzed hydroborations.[16]

Table 3. Hydroboration/Suzuki Coupling of Alkynylphosphonate

Entry	Alkynyl Phosphonate,3	Vinylphosphonoboronate, 4	(PH) Hz, % Yield[a]
a			48, 40
b			17, 35
c			47, 38

[a] Overall isolated yields from **3.** GC−MS yields were in the 70−90% range.

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Supporting Information Available: Detailed descriptions of experimental procedures for compounds **1−4**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL006836O

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(10) Teulade, M.-P.; Savignac, P. *J. Organomet. Chem.* **1988**, *338*, 295.

(11) The vinylic protons of the intermediate alkenyl boronophosphonates could not be resolved. However, the carbon not bearing the boron atom was detectable in the ^{13}C spectra. In addition, the intermediate alkenyl boronophosphonates had significantly different chemical shifts in the ^{31}P NMR. Thus, in the series **3a**, intermediate, **4a**, the ^{31}P shifts were −7.58, 31.16, and 15.33 ppm, respectively, and are consistent with our assignments.

(12) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(13) For the synthesis of vinylphosphonates by addition of copper reagents to alkynylphosphonates, see: (a) Cristau, H.-J.; Mbianda, X. Y.; Beziat, Y.; Gasc M.-B. *J. Organomet. Chem.* **1997**, *529*, 301. (b) Gil, J. M.; Oh, D. Y. *J. Org. Chem.* **1999**, *64*, 2950. For biological activity, see: (c) Breaker, R. R.; Gough, G. R.; Gilham, P. T. *Biochemistry* **1993**, *32*, 9125. (d) Harnden, M. R.; Parkin, A.; Paratt, M. J.; Perkins, R. M. *J. Med. Chem.* **1993**, *36*, 1345.

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