

Use of *gem*-Borazirconocene Alkanes in the Regioselective Synthesis of α -Allenic Boronic Esters and Conversion of the Latter to Dienes and Trienes

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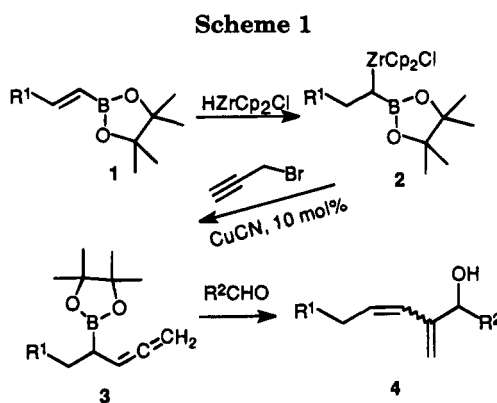
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1,1-Mixed bimetallics that undergo sequential and selective reactions at each of the carbon–metal bonds have attracted much attention lately in that they potentially offer a high degree of control in carbon–carbon bond-forming reactions.¹ Thus Knochel has prepared a series of zinc–boron and copper–boron 1,1-bimetallics that take advantage of the different reactivities to synthesize various polyfunctionalized ketones.² Lipshutz is developing reagents based on tin and zirconium.³ Other mixed 1,1-bimetallics based on zirconocene have been reported.⁴ They react like Tebbe's reagent, but with greater selectivity in some instances. Pelter has been exploring the chemistry of 1-lithio boranes.⁵

Our approach to the synthesis of mixed 1,1-bimetallics is based on boron and zirconium. Prior to our studies, the chemistry of these compounds have not been previously explored.⁶ The different reactivities of the carbon–boron and carbon–zirconium bonds toward electrophiles are perhaps a consequence of the different bond polarities and different electronegativities of boron and zirconium. Also, zirconium is a transition metal while boron has intriguing transition metallike chemistry.⁷ It is thus reasonable to presume that a union of boron–zirconium organic chemistry should be synergistic, affording products and chemistry not attainable by each reagent itself. In this communication we provide the first evidence of the utility of borazirconocene 1,1-alkanes in carbon–carbon bond-forming reactions. The synthetic route is outlined in Scheme 1.

The alkenylboronic esters **1** were synthesized according to the literature.⁸ Hydrozirconation of alkenylboronic esters **1** with zirconocene hydrochloride, $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$, prepared by Buchwald's procedure,⁹ took place smoothly in CH_2Cl_2 , providing in each case the corresponding



borazirconocene 1,1-alkanes **2**.^{6c} Addition of propargyl bromide and a catalytic amount of copper(I) cyanide was accompanied by the disappearance of the yellow color associated with these compounds and by carbon–carbon bond formation with exclusive cleavage of the C–Zr bond. α -Allenic boronic esters **3** were isolated in good yields.¹⁰ The assignment of the allenic structure is in complete agreement with ¹H-NMR and ¹³C-NMR chemical shifts reported in the literature.¹¹ The reaction works well for both hindered and nonhindered borazirconocene 1,1-alkanes.

α -Allenic boronic esters **3** are also allylboranes. Addition of an aldehyde to the boryl allenes afforded the corresponding 1,3-dienyl allylic alcohols **4**.¹² The results are summarized in Table 1. Allylboration with **3** works exceedingly well for aromatic aldehydes, except for the reaction with *m*-hydroxybenzaldehyde (entry 8). The low yield in the latter case may be due to the known sensitivity of allylboranes to protic sources.¹³ The reaction is both slower for aliphatic aldehydes, and the yields are somewhat lower too. The predominant isomer of the newly formed double bond in all cases is the *Z*-isomer.

Addition of an α,β -unsaturated aldehyde to **3** lead to trienes **5** or **6** depending on the reaction conditions (Scheme 2). Results are summarized in Table 2.

The geometry of the newly formed double bond (C5–C6) in both **5** and **6** was predominantly *Z*. Two types of trienes were obtained, depending on the reaction conditions. Method A involves the reaction of isolated α -allenic

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(12) A one-pot procedure for preparation of **4a** is as follows: A suspension of $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$ (193 mg, 0.75 mmol) in dry CH_2Cl_2 (1.5 mL) was stirred at ambient temperature under an atmosphere of argon. A solution of **1a** (1.2 mL, 0.5 M) in CH_2Cl_2 was added. After being stirred for 20 min, a solution of propargyl bromide (78 mg, 0.66 mmol, in 80% toluene) was injected and followed by a solution of CuCN (6 mg, 10 mol %) and CH_2Cl_2 (0.5 mL). The reaction mixture was stirred overnight and resulted in the discharge of the color of solution and the formation of pale precipitate. Distilled benzaldehyde (65 mg, 0.6 mmol) was then added in situ. The next day a solution of saturated aqueous NaCl (2 mL) was added in the reaction mixture in one portion, and the reaction mixture was extracted with ethyl acetate (3×8 mL). Drying of the organic layer over Na_2SO_4 , filtration through a silica pad, and removal of solvent provided an oily residue which was subjected to column chromatography on silica gel (hexanes/ ether) to yield 118 mg (86%) of a 94:6 mix of *cis:trans* **4a**.

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Table 1. Preparation of α -Allenic Boronic Esters **3** and 1,3-Dienyl Allylic Alcohols **4**

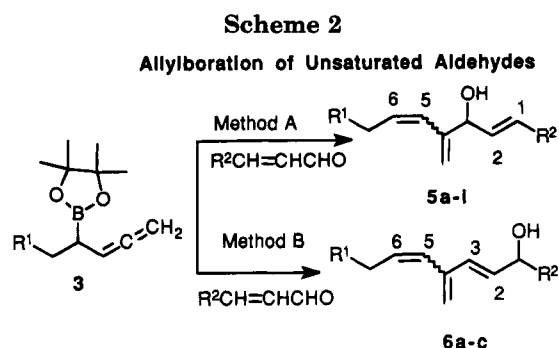
entry	R ¹ in Scheme 1	α -allenyl boronic esters 3 , ^a Yield, % ^b	aldehydes	1,3-dienyl allylic alcohols 4	
				yield, % ^e	cis:trans ^f
1	<i>n</i> -Butyl	3a , 89	benzaldehyde ^c	4a , 86	94:6
2	3-chloropropyl	3b , 85	benzaldehyde ^c	4b , 82	95:5
3	1-methylpropyl	3c , 77	benzaldehyde ^c	4c , 72 ^g	94:6
4	cyclopentyl	3d , 82	benzaldehyde ^c	4d , 77	95:5
5	<i>tert</i> -butyl	3e , 71	benzaldehyde ^c	4e , 65	95:5
6	3-phenylpropyl	3f , 90	benzaldehyde ^c	4f , 88	96:4
7	<i>n</i> -butyl	—	<i>m</i> -methylbenzaldehyde ^c	4g , 87	95:5
8	<i>n</i> -butyl	—	<i>m</i> -hydroxybenzaldehyde ^c	4h , 35	90:10
9	<i>n</i> -butyl	—	3-phenylpropionaldehyde ^d	4i , 75	95:5
10	<i>n</i> -butyl	—	propionaldehyde ^d	4j , 51	90:10

^a Coupling reactions were carried out in situ at rt overnight. ^b Isolated yields, based on alkenylboronic esters **1**. ^c Reactions were carried out overnight. ^d Reactions were run for 48 h. ^e Isolated yields, based on alkenylboronic esters **1** in one-pot reactions. ^f Determined by ¹H NMR analysis of crude products. ^g As an undetermined mixture of diastereomers.

Table 2. Preparation of Trienyl Alcohols **5** and **6**

entry	R ¹ in Scheme 2	aldehydes	method ^a	trienyl alcohols	
				yield, ^b %	cis:trans ^c
1	<i>n</i> -butyl	crotonaldehyde	A	5a , 82	90:10
2	3-chloropropyl	crotonaldehyde	A	5b , 80	91:9
3	1-methylpropyl	crotonaldehyde	A	5c , 75 ^d	89:11
4	cyclopentyl	crotonaldehyde	A	5d , 79	88:12
5	<i>tert</i> -butyl	crotonaldehyde	A	5e , 62	88:12
6	3-phenylpropyl	crotonaldehyde	A	5f , 83	90:10
7	<i>n</i> -butyl	cinnamaldehyde	A	5g , 77	91:9
8	<i>n</i> -butyl	<i>trans</i> -2-nonenal	A	5h , 85	90:10
9	<i>n</i> -butyl	<i>trans</i> -3-(pentylthio)-2-propenal	A	5i , 64	90:10
10	<i>n</i> -butyl	crotonaldehyde	B	6a , 33	85:15
11	<i>n</i> -butyl	<i>trans</i> -2-nonenal	B	6b , 35	85:15
12	cyclopentyl	crotonaldehyde	B	6c , 34	82:18

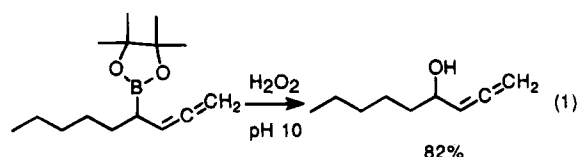
^a For the conditions, see text. ^b Isolated yields of purified trienyl alcohols, based on alkenylboronates. ^c Determined by ¹H NMR analysis of crude reaction mixtures. ^d As an undetermined mixture of diastereomers.



boronates **2** with aldehydes under salt-free conditions and provided trienes **5**. In method B, the α -allenic boronates were not isolated but prepared *in-situ* and allowed to react with aldehydes to give the rearranged trienes **6**. Results are summarized in Table 2. The yields in method A were much better than those of method B. The assignment of structure **5** is consistent with the postulated mechanism of the allylboration reaction.¹⁴ The geometry of the newly formed double bond in **5** (C5–C6) was readily apparent from the ¹H NMR spectra. Since both the *cis* and *trans* diastereomers were detected in the reaction mixture, the vicinal coupling constants for each isomer could be determined after appropriate decoupling experiments. The *5-cis* isomer was assigned on the basis of its smaller coupling constant.¹⁵ The C5–C6 double bond in **6** was assigned in an analogous man-

ner. The *trans* geometry of the double bond of unsaturated aldehydes used in the allylboration was retained in the products **5** (C1–C2) and **6** (C2–C3). These type of trienes are possible precursors for the synthesis of lipoxygenase inhibitors.¹⁶

We postulate that compounds **6** are obtained by allylic rearrangement of **5** facilitated by the presence of the various salts acting as Lewis acids. When compounds **5** were treated with Lewis acids, i.e. ZnCl₂, complex reaction mixtures were observed, including **6**. α -Allenic boronic esters **3** can also be easily converted to α -allenic alcohols (useful intermediates in organic transformations,^{17a} and constituents of numerous natural products^{17b} and biologically active molecules^{17c}) by controlled alkaline oxidation (eq 1).



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Supplementary Material Available: General experimental procedures, and ¹H NMR and ¹³C NMR spectra for compounds in Tables 1 and 2 (66 pages).

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