

Radical Cyclization Studies of Alkenylboronates

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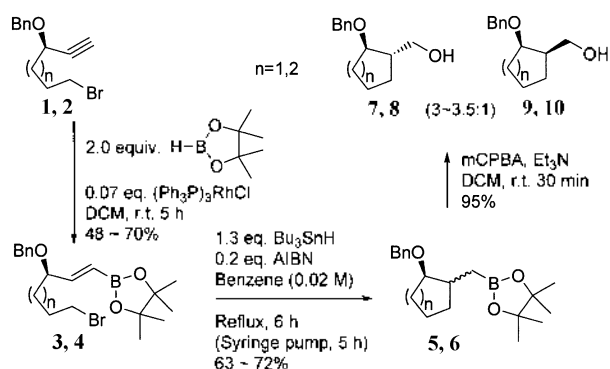
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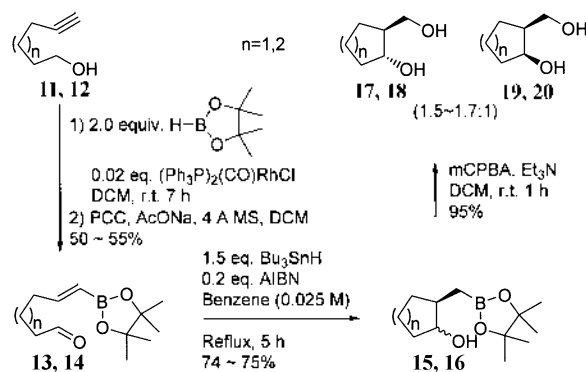
Alkenylboronates were shown to serve as effective inter- and intramolecular radical acceptors.¹ More recently, results on the boron-tethered radical cyclization reactions were reported.² In these reactions, the C-B bond oxidation eventually yields alcoholic products, the stereoselectivity being determined at the radical addition step.

In our continuing search for stereoselective radical cyclization reactions, we had occasion to examine further stereochemical characteristics of alkenylboronate radical cyclization reactions. First, the alkenylboronate **3** was prepared from 6-bromo-3-benzyloxy-1-hexyne (**1**) via Rh-catalyzed hydroboration with pinacolborane.³ Radical cyclization of **3** under the standard high dilution conditions led to the formation of the product mixture **5**, which yielded the benzyl ethers **7** and **9** of *trans*- and *cis*-2-(hydroxymethyl)cyclopentan-1-ol (**7** and **9**) in a 3 : 1 ratio upon oxidation with *m*-chloroperoxybenzoic acid (Scheme 1). Likewise, the alkenylboronate **4**, which was prepared from 7-bromo-3-benzyloxy-1-heptyne (**2**), was converted into the cyclohexanol products **6**, which eventually yielded the benzyl ethers **8** and **10** of *trans*- and *cis*-2-(hydroxymethyl)cyclohexan-1-ol (**8** and **10**) in a 3.5 : 1 ratio. It may be concluded that 5-exo and 6-exo radical cyclization reactions of the alkenylboronate substrates possessing allylic alkoxy substituents follow the general rule for 4-substituted 5-hexenyl radicals favoring production of the *trans* isomers.⁴

An alternative way of preparing compounds like **17/19** and **18/20** would be using ω -oxoalkenylboronate substrates; we were intrigued by the possibility of stereocontrol via intramolecular association involving the stannyloxyalkyl radical moiety, produced upon stannyl radical addition to the aldehyde group, and the resident boronate functionality. The substrate 6-oxohexenylboronate **13** was prepared from 5-hexyn-1-ol (**11**) via Rh-catalyzed hydroboration with pinacolborane and subsequent PCC oxidation. Reaction of



Scheme 1



Scheme 2

13 with tributylstannane proceeded smoothly producing a mixture of products **15**. Oxidation of the product mixture **15** led to the efficient formation of *trans*- and *cis*-2-(hydroxymethyl)cyclopentan-1-ol (**17** and **19**)⁵ in a 1.5 : 1 ratio (Scheme 2). Starting from 6-heptyn-1-ol (**12**), the 7-oxoheptenylboronate **14** was prepared analogously. When the radical cyclization product mixture **16** was subjected to the *m*CPBA oxidation, *trans*- and *cis*-2-(hydroxymethyl)cyclohexan-1-ol (**18** and **20**)⁶ were obtained in a 1.7 : 1 ratio.

In the present studies, modest levels of stereocontrol were ascertained in the radical cyclization reactions of ω -oxoalkenylboronates, negating the possible role of the boronate moiety in inducing high stereocontrol via intramolecular association. However, alkenylboronate radical cyclization strategy will probably serve as a viable alternative in the synthesis of complex 2-(hydroxymethyl)cycloalkan-1-ols.

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