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A diastereoselective synthesis 1-trimethylsilyl-(*E*)-1,3-alkenynes and a simple synthesis of alkyl trimethylsilylethynyl ketones via organoboranes

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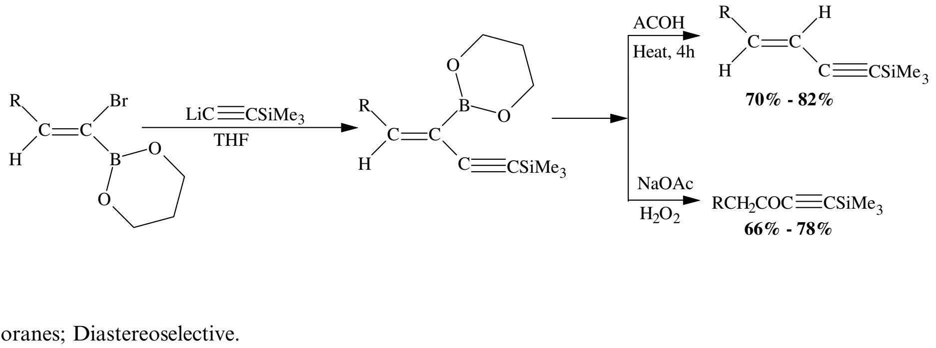
Abstract—A convenient, novel diastereoselective synthesis of 1-trimethylsilyl-(*E*)-1,3-alkenynes and a convenient synthesis of alkyl trimethylsilylethynyl ketones based on *Z*-1-bromo-1-alkenylboronate esters are developed. α-Bromo-(*Z*)-1-alkenylboronate esters readily available using literature procedures smoothly undergo a reaction with trimethylsilylethynyllithium (derived from the deprotonation of trimethylsilylethyne with *n*-butyllithium) in tetrahydrofuran to provide the corresponding 'ate' complexes. These 'ate' complexes undergo intramolecular nucleophilic substitution reactions to afford the corresponding (*E*)-1-alkenylboronate esters containing trimethylsilylethynyl moiety which upon protonolysis with acetic acid provide the corresponding 1-trimethylsilyl-(*E*)-1,3-alkenynes in good yields (70–82%) and in high stereochemical purities (>98%). These intermediates upon oxidation with hydrogen peroxide and sodium acetate afford the corresponding alkyl trimethylsilylethynyl ketones in good yields (66–78%).

1. Introduction

1-Trimethylsilyl-(*E*)-1,3-alkenynes[1] and alkyl trimethylsilylethynyl ketones[2] are important intermediates in organic synthesis. The alkyl trimethylsilylethynyl ketones are potential prochiral ketones for asymmetric reduction reactions. In view of the synthetic importance of 1-trimethylsilyl-(*E*)-1,3-alkenynes and alkyl trimethylsilylethynyl ketones, it was desirable to have a general, convenient methodology to their synthesis especially from readily available organoborane reagents.

In a previous study, a stereoselective preparation of the (*Z*)-1-bromo-1-alkenylboronate esters via the hydroboration of 1-bromo-1-alkynes followed by treatment with 1,3-propane diol has been reported.[3] It should be noted that these α-halo-(*Z*)-1-alkyenylboronate esters are known to undergo intramolecular nucleophilic substitution reactions[4–7] with nucleophiles such as hydrides,[8] Grignard reagents,[9] organolithium reagents,[9] allylmagnesium bromide,[10] trimethylsilylmethyllithium,[11] and trimethylsilyllithium.[12]



(1)

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In this letter, we reacted 1-bromo-(*Z*)-1-hexenylboronate esters with a nucleophilic reagent such as trimethylsilylethynyllithium (Eq. 1). Consequently, we describe a facile synthesis of 1-trimethylsilyl-(*E*)-1,3-alkenynes and alkyl trimethylsilylethynyl ketones based on versatile intermediates such as α-bromo-(*Z*)-1-alkenylboronate esters.

2. Results and discussion

The required starting materials such as 1-bromo-1-alkynes and α-bromo-(*Z*)-1-alkenylboronate esters were prepared using the literature procedures.[3] In a typical experiment, α-bromo-(*Z*)-1-hexenyl boronate ester was reacted with trimethylsilylethynyllithium generated from trimethylsilylethyne by reacting with *n*-butyllithium at −78 °C in tetrahydrofuran under an inert atmosphere and the reaction mixture was stirred at −78 °C for 2 h followed by stirring overnight at room temperature. The solvents were then pumped off and the resulting product was subjected to protonolysis using a large excess of acetic acid under reflux for 4 h. After workup, the reaction provided 1-trimethylsilyl-(*E*)-1,3-octenyne (Table 1, entry 1) in 70% yield.

Using the above procedure, the representative 1-trimethylsilyl-(*E*)-1,3-alkenynes were prepared (see Table 1). The boron intermediate was also subjected to oxidation using hydrogen peroxide and sodium acetate in tetrahydrofuran at room temperature for 4 h. After workup, the reaction provided *n*-pentyl trimethylsilylethynyl ketone (Table 2, entry 1) in 76% isolated yield. Using the above procedure, the representative alkyl trimethylsilylethynyl ketones were prepared (see Table 2).

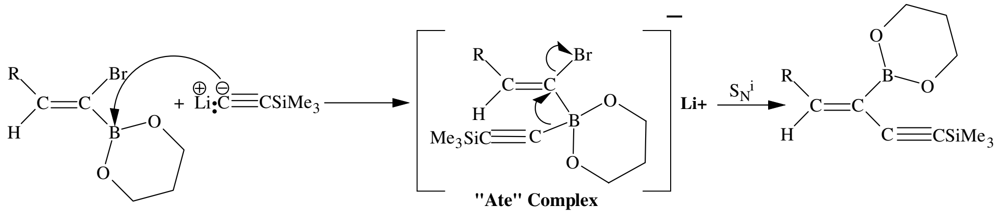
Table 2. Synthesis of alkyl trimethylsilylethynyl ketones via organoboranes (Eq. 2)

Entry	R =	Isolated yield[a,b] (%)
1	*n*-C_4H_9	76
2	*n*-C_5H_{11}	74
3	*n*-C_6H_{13}	78
4	*n*-$Cl(CH_2)_3$	70
5	$-C(CH_3)_3$	68
6	$-CH_2CH_2CH(CH_3)_2$	66

[a] All of the reactions were carried out on a 10 mmol scale. The yields were based on the corresponding α-bromo-(*Z*)-1-alkenylboronate esters.

[b] All of the compounds were isolated by column chromatography over alumina and were characterized by IR and NMR spectral data.

Presumably, the starting α-bromo-(*Z*)-1-alkenylboronate ester could form an 'ate' complex as a result of a reaction with trimethylsilylethynyllithium. This would further undergo an anionotropic rearrangement involving the migration of the trimethylsilylethynyl group from boron to the adjacent alkenyl carbon with inversion of configuration to provide (*E*)-trisubstituted boron intermediate containing trimethylsilylethynyl moiety, the oxidation of which would provide alkyl trimethylsilylethynyl ketones. These intermediates were previously shown to undergo protonolysis with acetic acid to give the corresponding 1-trimethylsilyl-(*E*)-1,3-alkenynes. The mechanism of the reaction of α-bromo-(*Z*)-1-alkenylboronate ester with trimethylsilylethynyllithium is shown below (Eq. 2).



(2)

Table 1. Synthesis of 1-trimethylsilyl-(*E*)-1,3-alkenynes via organoboranes (Eq. 2)

Entry	R =	Isolated yield[a,b] (%)
1	*n*-C_4H_9	70
2	*n*-C_5H_{11}	74
3	*n*-C_6H_{13}	75
4	*n*-$Cl(CH_2)_3$	71
5	$-C(CH_3)_3$	68
6	$-CH_2CH_2CH(CH_3)_2$	65

[a] All of the reactions were carried out on a 10 mmol scale. The yields were based on the corresponding α-bromo-(*Z*)-1-alkenylboronate esters.

[b] All of the compounds were isolated by column chromatography over alumina and were characterized by IR and NMR spectral data. The stereochemical purities[13] (>98%) were confirmed by NMR spectral data.

3. Conclusions

In summation, we have developed a novel synthetic route for the preparation of 1-trimethylsilyl (*E*)-1,3-alkenynes based on the reactions of trimethylsilylethynyllithium with α-bromo-(*Z*)-1-alkenylboronate esters followed by protonolysis and oxidation, respectively. We are presently isolating the potential organoborane intermediate precursors to 1-trimethylsilyl-(*E*)-1,3-alkenynes and alkyl trimethylsilylethynyl ketones and confirming their structures by NMR spectral data. The representative synthetic applications of these (*E*)-trisubstituted organoborane intermediates containing trimethylsilylethynyl moiety are also currently underway.

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