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Stereospecific Synthesis of Both (*E*)-and (*Z*)-1,3-Alkenynes Based on Stereodefined Alkenylboronate Esters

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The stereodefined synthesis of 1,3-alkenynes based on in situ generated stereodefined alkenylcopper reagents is presented. The hydroboration of alkynes with dibromoborane-methyl sulfide complex followed by treatment with trimethylene glycol provides stable (E)-1-alkenylboronate esters. These boronate esters readily undergo "ate" complexes with a hindered base such as potassium-tbutoxide. The transmetalation of the alkenyl group from boron to copper via the "ate" complexes retains the original stereochemistry defined from the starting alkenylboronate esters. The effect of representative bases on stereodefined alkenylboronate esters and subsequent reaction of these boronate esters in the transmetalation reaction with copper(I) bromide-methyl sulfide is investigated. The resulting stereodefined alkenylcopper species generated in situ readily couple with 1-bromo-1-alkynes to give the corresponding 1,3-alkenynes with retention of stereochemistry. Since (Z)-1-alkenylboronate esters are easily accessible, both cis and trans isomeric 1,3-alkenynes are synthesized.

KEYWORDS

Stereospecific synthesis, 1,3-Alkenynes, Alkenylboronate esters.

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INTRODUCTION

Many insect pheromones [1,2] contain a conjugated *cis*, *trans*-diene grouping. Because conjugated 1,3-enynes are readily converted to the corresponding conjugated *cis*, *trans*-dienes by a simple hydroboration-protonolysis sequence [3], the stereospecific synthesis of conjugated enynes is a highly desirable goal. Low yield procedures of several complexes have been described for the synthesis of conjugated enynes [4]. Some of these require the prior stereoselective synthesis of alkenyl halides [5]. Negishi and coworkers [6,7] developed a highly stereoselective synthesis of conjugated enynes and utilized the procedure for the synthesis of two insect pheromones. Suzuki and coworkers [8] synthesized the conjugated *trans*-enynes utilizing the palladium-catalyzed reaction of 1-alkenylboranes with 1-halo-1-alkynes.

Previously, the stereoselective syntheses of symmetrical conjugated dienes [9] and conjugated *trans*-enynes [10] from alkenyldialkylboranes *via* the reaction with sodium methoxide

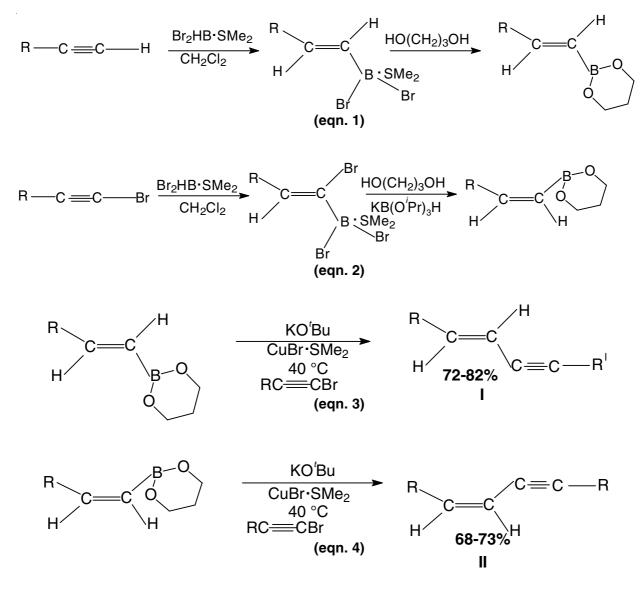
and copper(I) bromide-methyl sulfide complex have been reported. The reaction was demonstrated to probably proceed through formation of an alkenylcopper reagent at 0 °C, undergoes thermal decomposition stereospecifically to produce conjugated dienes [9]. *in situ* generated (*E*)-1-alkenylcopper reagent was reacted with 1-bromo-1-alkynes to produce the *trans*-conjugated enynes. Since the more stable stereodefined alkenylboronate esters [11,12] are readily available (eqns. 1 and 2), an investigation was undertaken to examine the reaction of 1-bromo-1-alkynes with the alkenylcopper intermediates generated from stereodefined alkenylboronate esters as a synthetic route to both (*E*)- and (*Z*)-1,3-alkenynes.

RESULTS AND DISCUSSION

To investigate this as a synthetic preparation of (E)-1,3alkenynes, B-(E)-1-hexenylboronate ester and 1-bromohexyne were selected as representative substrates. Isolated B-(E)-1-hexenylboronate ester prepared by the hydroboration of 1-hexyne with dibromoborane-methyl sulfide complex followed by treatment with trimethylene glycol was employed. Accordingly, the sodium methoxide addition compound of B-(E)-1-hexenylboronate ester was prepared followed by addition of CuBr.SMe₂ in diethyl ether at - 40 °C. 1-Bromo-1hexyne was then added followed by immediate removal of the cooling bath with the reaction mixture warming slowly to room temperature.

Gas chromatographic analysis revealed an 53 % yield of (*E*)-5-dodecen-7-yne. By permitting the reaction to stir for 1 h at - 15 °C before warming increased the yield of (*E*)-5-dodecen-7-yne to 58 %. The pure conjugated enyne isolated proved to be exclusively the *trans* isomer, indicating the coupling to occur with strict retention of configuration.

B-(*E*)-1-hexenylboronate ester was then transmetalated with CuBr.SMe₂ in the presence of bases such as potassium methoxide, sodium isopropoxide and potassium *tert*-butoxide followed by treatment with 1-bromo-1-hexyne in diethyl ether to afford the corresponding (*E*)-5-dodecen-7-yne in 64, 72, and 92 % yields, respectively. Consequently, we settled on the use of potassium *tert*-butoxide as a base during transmetalation step. It was quite obvious by increasing the steric bulk of the "ate" complex during transmetalation step followed by coupling reaction with 1-bromo-1-hexyne dramatically increased the yield of (*E*)-5-dodecen-7-yne. Using this procedure, representative (*E*)-1,3-alkenynes (eqn. 3) were prepared (Table-1). Also the direct accessibility of the corresponding (*Z*)-1-alkenylboronate esters permitted the preparation of isomeric (*Z*)-1,3-alkenynes



(eqn. 4). Using the above procedure, the representative (*Z*)-1,3-alkenynes were prepared (Table-1).

(Z)-1,3-ALKE	TABLE-1 STEREOSPECIFIC SYNTHESIS OF BOTH (<i>E</i>)- AND (<i>Z</i>)-1,3-ALKENYNES BASED ON STEREODEFINED ALKENYLBORONATE ESTERS				
No.	R and R' =	Yield (%) ^a			
1	I, <i>n</i> -C ₄ H ₉	82			
2	I, $-C(CH_3)_3$	78			

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	3	I, (CH ₂) ₃ Cl	72	
	4	II, n -C ₄ H ₉	68	
	5	II, -C(CH ₃) ₃	72	
	6	II, -(CH ₂) ₃ Cl	73	
^a All of the reactions were corried out on a 10 mmol scale and the vial				

"All of the reactions were carried out on a 10 mmol scale and the yields are isolated yields.

Conclusion

The stereodefined alkenylcopper intermediates generated *in situ* from (*E*)- and (*Z*)-1- alkenylboronate esters *via* transmetalation with copper(I) bromide-methyl sulfide complex in the presence of a hindered base such as potassium-*t*-butoxide readily undergo a coupling reaction with 1-bromo-1-alkynes to provide stereodefined 1,3-alkenynes. Using the present procedure, both (*E*)- and (*Z*)-1,3-alkenynes are prepared in high stereochemical purities. Since the both (*E*)- and (*Z*)-1-alkenyl-boronate esters are readily prepared and stored at 0 °C under nitrogen atmosphere for considerable length of time, the present procedure is useful in preparing stereodefined 1,3-alkenynes in high stereochemical purities.

A C K N O W L E D G E M E N T S

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