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Diastereoselective Synthesis of both Symmetrical (*E,E*)- and (*Z,Z*)-Conjugated Dienes Based on Stereodefined Alkenylboronate Esters

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ABSTRACT

2-([*E*]-1-Alkenyl)-1,3,2-dioxaborinanes prepared from the hydroboration of terminal alkynes with dibromoborane-methyl sulfide complex followed by treatment with 1,3-propane diol readily react with copper(I) bromide-methyl sulfide in the presence of a hindered base such as potassium-*t*-butoxide at 0 °C to afford (*E,E*)-symmetrical conjugated dienes. The dienes are formed with retention of configuration in a highly stereospecific manner predetermined from the alkenylboronate esters stereochemistry. Since the hydroboration of alkynes with dialkylboranes proceeds in a highly regio- and stereospecific manner under mild conditions, this then provides a direct route from acetylenes to the corresponding [*E,E*]-conjugated dienes. The recent accessibility of 2-([*Z*]-1-alkenyl)-1,3,2-dioxaborinanes also allows preparation of stereochemically pure [*Z,Z*]-conjugated dienes. The reaction is shown to probably proceed through an alkenylcopper (I) intermediate, which undergoes thermal dimerization to yield the corresponding stereodefined symmetrical dienes. The present procedures allow the preparation of either (*E,E*)- or (*Z,Z*)-symmetrical conjugated dienes in good yields and in high stereo-chemical purities (> 98 %).

KEYWORDS

Diastereoselective synthesis, Conjugated dienes, Alkenylboronate esters.

INTRODUCTION

Several investigators have recently reported the preparation of conjugated dienes, often in high stereochemical purity, employing a variety of organometallic intermediates [1]. However, reactive organometallic precursors, such as organolithium and Grignard reagents are frequently incompatible with many functional groups, hence, limiting the synthetic versatility. Also, stereodefined alkenyl halides, which are difficult to obtain in many cases are commonly used as starting materials.

A partial solution to these problems has involved the use of controlled hydrometallation of alkynes to obtain alkenyl-metalloidal derivatives. Several of these derivatives have found considerable utility in stereospecific conjugated diene synthesis. Both alkenylalanes [1a] and alkenyldicyclopentadienyl zirconium chlorides [1h] prepared by the hydroalumination and hydro-zirconation of alkynes respectively, undergo alkenyl coupling

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in the presence of copper(I) salts to form symmetrical dienes. However, the high cost of the requisite zirconium hydride complexes, precludes the adaptability of the alkenylzirconium compounds to large-scale reactions. The hydroalumination reaction requires diisobutylaluminum hydride, a powerful reducing agent of the many organic functional groups, hence, limiting the versatility. Dialkenylchloroboranes prepared by hydroboration of alkynes with monochloroborane etherate [2], undergo alkenyl coupling to give symmetrical dienes in the presence of three equivalents of methylcopper.

Although a variety of functional groups can be tolerated by reaction, there are still several difficulties. The dialkenylchloroboranes must be isolated by distillation and their instability necessitates immediate use. Finally, dialkenylchloroboranes derived from terminal alkynes require a 40 % excess of the alkyne to suppress significant competing dihydroboration [2].

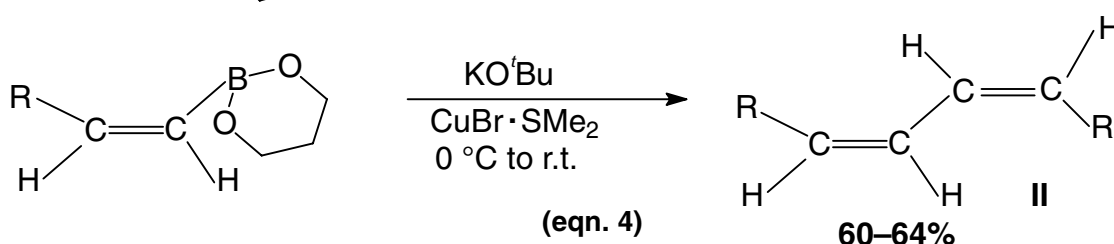
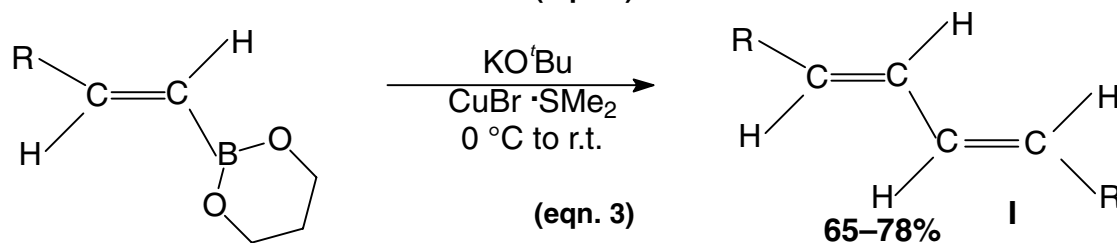
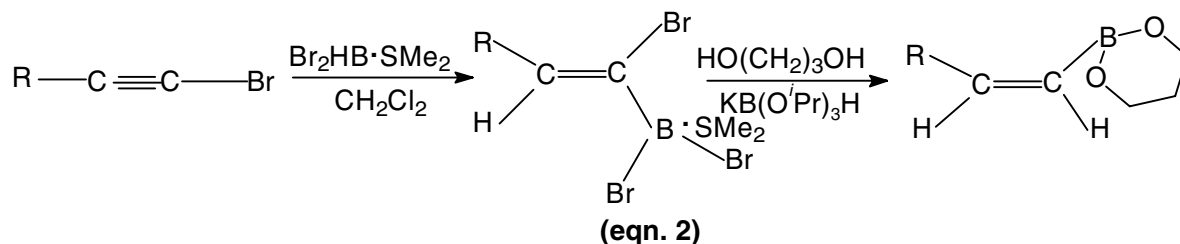
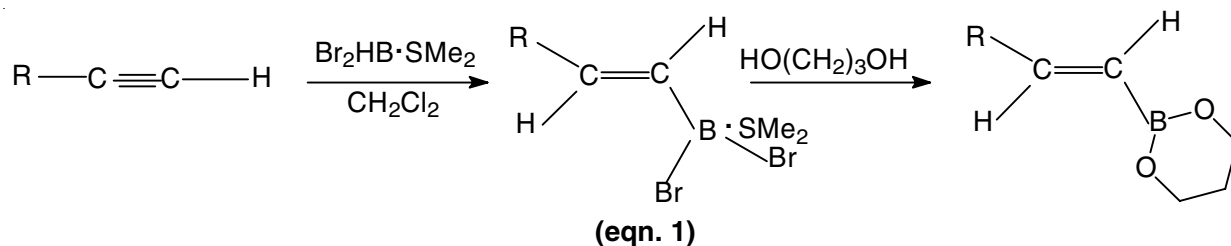
A previous report is available in literature which introduces a mild and versatile synthesis of symmetrical conjugated dienes that overcomes most of the difficulties associated with the existing methods. While related to the procedure using dialkenylchloroboranes, the method employed alkenyldialkylboranes readily obtained from the hydroboration of alkynes with dialkylboranes [3]. Like several of the reported methods based on hydrometallations, copper(I) salts are employed to effect the coupling; however, *via* sodium methoxide addition compounds of alkenyldialkylboranes. The reaction is believed to proceed

through the formation of an alkenyl-copper(I) intermediate. However, the above procedure suffers from some disadvantages. First of all, one has to separate the by-product and also the stereodefined alkenyldialkylboranes could not be stored for a long time and therefore will have to be prepared freshly. We have surmounted these difficulties by using stereodefined alkenylboronate esters as starting materials. They could be stored under nitrogen at 0 °C for a long time without isomerization. Since both (*E*)- and (*Z*)-1 alkenylboronate esters [4,5] (eqns. 1 and 2) are easily available, we undertook the synthesis of both symmetrical (*E,E*)- and (*Z,Z*)-conjugated dienes based on (*E*)- and (*Z*)-1-alkenylboronate esters in high stereochemical purities.

RESULTS AND DISCUSSION

In a typical experiment, 2-(*E*)-1-hexenyl-1,3,2-dioxaborinane prepared from the hydroboration of 1-hexyne with dibromoborane-methyl sulfide complex followed by treatment with 1,3-propane diol was chosen. It was reacted with potassium-*t*-butoxide in tetrahydrofuran at 0 °C for 1 h. The resulting "ate" complex was transferred to a flask containing copper(I) bromide-methyl sulfide complex at 0 °C with stirring and the stirring continued at 0 °C for 1 h followed by 2 h at room temperature.

After workup, the desired diene, (*5E,7E*)-dodecadiene was isolated in 72 % yield and in high stereochemical purity



(> 98 % as evidenced by GC analysis). Representative selection of symmetrical (*E,E*)-conjugated dienes (eqn. 3) was prepared using the present procedure (Table-1). In the similar manner, using 2-(*E*)-1-hexenyl-1,3,2-dioxaborinanes the synthesis of the opposite diastereomers, (*Z,Z*)-symmetrical conjugated dienes were prepared in high stereochemical purities (98 % as indicated by GC analysis). Representative symmetrical (*Z,Z*)-conjugated dienes were prepared using the above procedure (eqn. 4) as shown in Table-1. In both of these procedures, the reactions must have been proceeded *via in situ* generation of stereodefined alkenylcopper species followed by thermal dimerization to provide stereospecific conjugated dienes. The results are summarized in Table-1.

TABLE-1
DIASTEREOSELECTIVE SYNTHESIS OF BOTH
SYMMETRICAL (*E,E*)- AND (*Z,Z*)-CONJUGADIENES BASED
ON STEREODEFINED ALKENYL BORONATE ESTERS

No.	R =	Yield (%) ^a
1	I, <i>n</i> -C ₄ H ₉	78
2	I, -C(CH ₃) ₃	69
3	I, (CH ₂) ₃ Cl	65
4	II, <i>n</i> -C ₄ H ₉	62
5	II, -C(CH ₃) ₃	64
6	II, -(CH ₂) ₃ Cl	60

^aAll 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 an hindered base such as potassium-*t*-butoxide readily undergo thermal dimerization to provide stereospecific symmetrical conjugated dienes. Using the present procedure, both (*E,E*)- and (*Z,Z*)-symmetrical conjugated dienes are prepared in high stereochemical purities. Since, both (*E*)- and (*Z*)-1-alkenylboronate 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 symmetrical conjugated dienes.

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