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THE REACTION OF TRIALKYLBORANES WITH LITHIUM ACETYLIDES PREPARED FROM TRIETHYL ORTHOPROPIOLATE AND PROPIOLALDEHYDE DIETHYL ACETAL

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Lithium acetylides with functional groups such as orthoester or acetal group in the molecule react with trialkylboranes with the migration of alkyl groups. The oxidation of the intermediates obtained from triethyl orthopropiolate gives a mixture of β-hydroxy- and α,β-unsaturated esters, and the oxidation of those from propiolaldehyde diethyl acetal gives (E)-1-ethoxy-1-alken-3-ones respectively.

In spite of the potential significance of alkynyltrialkylborates,[1] their synthetic usefulness is limited because of their low reactivity to weak electrophiles.[2] Recently, we found that the alkynyltrialkylborates can react with weak electrophiles such as methyl vinyl ketone[3] and orthoesters[4] by the activation with titanium tetrachloride. This method has spread the applicability of alkynylborates. In this paper, we wish to report the reaction of alkynyltrialkylborates prepared from triethyl orthopropiolate[5] or propiolaldehyde diethyl acetal[6] which has orthoester or acetal group in the molecule.

In the case of intermolecular reactions, orthoesters and acetals are inert to alkynylborates unless Lewis acids are present. However, in the reaction of an alkynylborate (1), two alkyl groups migrate from boron to the adjacent carbon simply by refluxing in ether or THF solvent, and the usual hydrogen peroxide oxidation gives a mixture of β-hydroxy ester (2) and α,β-unsaturated ester (3) (Eq. 1).

$$R_3\overset{-}{B}C{\equiv}CC(OEt)_3 \xrightarrow[2.\ [O]]{1.\ \Delta} R_2CCH_2COOEt \;(OH) + R_2C{=}CHCOOEt \qquad (1)$$

1 2 3

In order to improve the yield and selectivity of products, we explored the oxidation step under different conditions. Finally, it was found that the hydrogen peroxide oxidation carried out in a medium buffered at pH 5.10 gives the maximum yield for preferential formation of the β-hydroxy ester (Method A), whereas trimethylamine N-oxide is a selective oxidation reagent to the α,β-unsaturated ester (Method B), as revealed in Table 1. A typical procedure of Method A is as follows. To a stirring solution of triethyl orthopropiolate (413 mg, 2.4 mmol) in 3 mL of dry ether was added butyllithium in ether (1.1 mL of a 2 M solution, 2.2 mmol) at 0 °C. After stirring for 30 min at the temperature, tributylborane in THF (2 mL of a 1 M solution, 2 mmol) was added. The reaction mixture was stirred for 30 min at room temperature to complete the formation of the alkynylborate

and then refluxed with stirring for 2 h, followed by cooling to 0 °C. The buffer solution (pH 5.10, 2 mL) was added and the resulting mixture was stirred for 30 min at 0 °C, then oxidized with 2 mL of 30% hydrogen peroxide with stirring for 1 h at room temperature. Finally, 5 mL of 3M HCl was added and the mixture was stirred at room temperature overnight. Analysis of the products by glpc showed that ethyl 3-butyl-3-hydroxyheptanoate (1.6 mmol, 80%) and ethyl 3-butyl-2-heptenoate (0.4 mmol, 20%) was formed. For the selective formation of unsaturated esters (3), the following procedure is representative (Method B). The alkynylborate (4) was prepared by the procedure described in Method A, by using a THF solution of the orthopropiolate.[7] Solid trimethylamine N-oxide dihydrate (1.1 g, 10 mmol) was added, and the mixture was stirred under refluxing for 2 h and then at room temperature overnight. After addition of 6 mL of 3 M HCl, the solution was stirred for 2 h at room temperature. Glpc analysis indicated the formation of 1.26 mmol (63%) of ethyl 3-butyl-2-heptenoate (6) with a trace amount of the hydroxy ester (5). When triisobutylborane was used, the oxidation with trimethylamine N-oxide (Method B) was slow. Consequently, a large excess of the reagent and longer reaction time were required. Thus 10 equivalents of trimethylamine N-oxide was used, and the reaction was carried out at 66 °C for 14 h (Method C). For sterically hindered tri-sec-butylborane, anhydrous zinc iodide (1.1 equiv.) was added to accelerate the reaction with orthopropiolate, and the mixture was refluxed in THF for 2 h (Method A'). In this case, the α,β-unsaturated ester was selectively obtained.[8] The representative results are summarized in Table 2.

Table 1. The Effect of the Oxidation Conditions on the Yield and Selectivity of the Products in the Following Reaction

$$Bu_3\overset{-}{B}C{\equiv}CC(OEt)_3 \xrightarrow[2.\ [O]]{1.\ \Delta} Bu_2CCH_2COOEt + Bu_2C{=}CHCOOEt$$
$$\qquad\qquad\qquad\qquad\qquad\quad OH$$

4 5 6

Oxidation Conditions	Solvent	5,[a] (%)	6 ,[a] (%)	Total Yield,[a] (%)
4.2 M MeONa-30% H_2O_2	Ether	39	42	81
3 M NaOH-30% H_2O_2	"	66	19	85
Buffer at pH 5.10[b]-30% H_2O_2	"	80	20	100
Buffer at pH 3.25[b]-30% H_2O_2	"	68	8	76
3 MHCl-30% H_2O_2	"	27	8	35
5equiv. of Me_3NO, $2H_2O$	THF	trace	63	63

a) GLPC yield based on the organoborane used.

b) Sodium citrate buffer solutions purchased from Wako Pure Chemical Industries, Ltd. were used.

The reaction may proceed through the following reaction pathways. The heating of I causes the migration of an alkyl group to give the allenylic borane (7). The second migration of alkyl group occurs to yield propargylic borane derivative (8a) which exists in equilibrium with 8b. Oxidation of 8a followed by protonolysis of the alkynyl ether (9) produces the hydroxy ester (2). On the other hand, oxidation of VIIIb affords the unsaturated ester (3).[9]

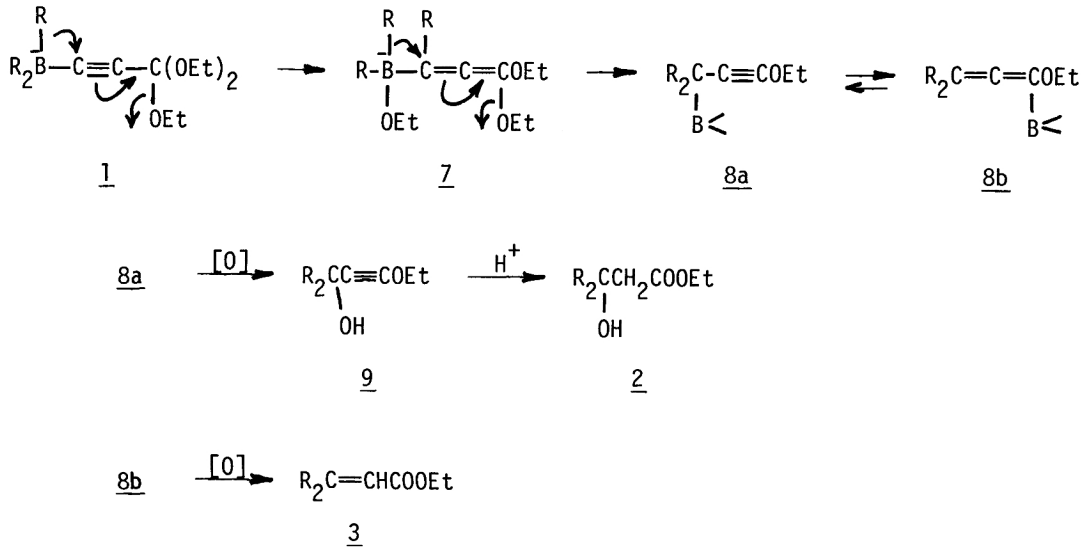


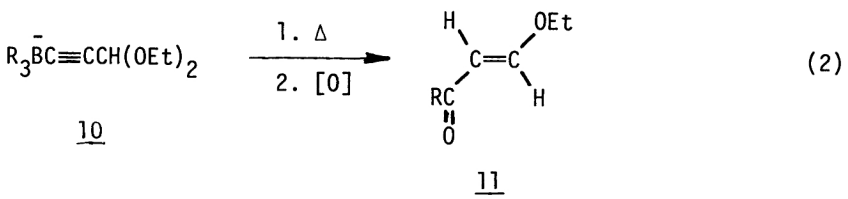
Table 2. The Synthesis of β-Hydroxy Esters (2) and α,β-Unsaturated Esters (3)

R, R_3B	Oxidation Method[a]	Solvent	2,[b] (%)	3,[b] (%)	Total Yield,[b] (%)
Butyl	A	Ether	80	20	100
"	B	THF	trace	63	63
Propyl	A	Ether	76	14	90
"	B	THF	trace	75	75
Isobutyl	A	Ether	58	26	84
"	C	THF	0	47	47
s-Butyl	A'	THF	0	70	70
Pentyl	A	Ether	69	11	80
"	B	THF	trace	61	61

a) Indicated in the text.

b) GLPC yield based on the organoborane used. The structures were determined by NMR, IR, and MS spectra.

In the reaction of alkynylborates (10) prepared from propiolaldehyde diethyl acetal, the alkyl group migration also occurred by refluxing in THF. Oxidation of the intermediates with hydrogen peroxide in a medium buffered at pH 5.10 gave (E)-1-ethoxy-1-alken-3-ones (11)[10] selectively in resonable yields (Eq. 2).



(2)

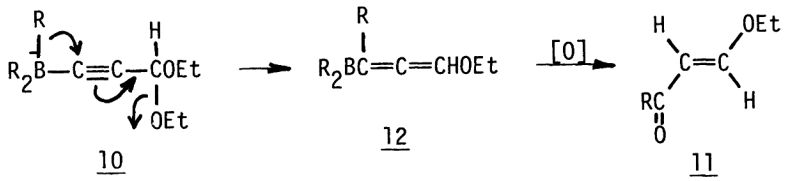
The following procedure for the preparation of (E)-1-ethoxy-1-hepten-3-one is representative. To a stirring solution of propiolaldehyde diethyl acetal (384 mg, 3 mmol) in 3 mL of dry THF was added butyllithium in ether (1.73 mL of a 1.5 M solution, 2.6 mmol) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and followed by the addition of tributylborane in THF (0.9 mL of a 2.2 M solution, 2 mmol). After stirring for 15 min at room temperature, the solution was refluxed with stirring for 2 h, and then cooled to 0 °C. Finally the reaction mixture was oxidized with 2 mL of pH 5.10 buffer and 2 mL of 30 % hydrogen peroxide. Analysis of the products by GLPC showed that (E)-1-ethoxy-1-hepten-3-one was produced in a 63% yield. The representative results are shown in Table 3.

Table 3. The Synthesis of (E)-1-Ethoxy-1-alken-3-ones

R, R_3B	Reaction time, h	Product yield,[a] (%)
Propyl	2	61
Butyl	2	63
Isobutyl	2	62
sec-Butyl	2	59
Hexyl	8	67

a) GLPC yield based on the organoborane used. The structures of products were determined by NMR, IR, and MS spectra.

The reaction seems to be understood through the alkyl group migration from boron to the adjacent carbon with leaving of ethoxy group to give allenylic borane (12). In this case, the second migration does not occur and the oxidation of XII provides the product (11).



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7) In Method A, a solution of orthopropiolate in ether was used.
8) In other cases, this method is not effective for the selective synthisis of α,β-unsaturated esters.
9) The dehydration of the hydrxy ester (II) also appears to give the α,β-unsaturated ester (III), but under such oxidation and protonation conditions, II does not change to III at all. Therefore the α,β-unsaturated ester (III) is not considered to be derived from II.
10) Coupling constants of the vinlyic protons (J=12-14 Hz) showed the stereochemistry of the products to be E-structures.

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