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Stereoselective Synthesis of *cis*- and *trans*- β,γ -Unsaturated Carboxylic Esters *via* Reaction of
Alkenyldichloroboranes with Ethyl Diazoacetate

by

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Prepared for Publication

in the

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Stereoselective Synthesis of *cis*- and *trans*- β,γ -Unsaturated Carboxylic Esters via Reaction of Alkenyldichloroboranes with Ethyl Diazoacetate

Herbert C. Brown*, Ashok M. Salunkhe

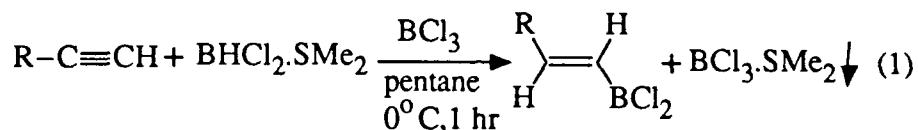
H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907

Abstract: *trans*-Alkenyldichloroboranes, easily prepared by the reaction of dichloroborane-dimethyl sulfide complex with various alkynes in the presence of boron trichloride, react smoothly with ethyl diazoacetate at -65°C with the liberation of nitrogen. Treatment of the intermediates with methanol-water produces *trans*- β,γ -unsaturated carboxylic esters stereoselectively in good yields. Similar treatment of *cis*-alkenyldichloroboranes provides the corresponding *cis*- β,γ -unsaturated esters.

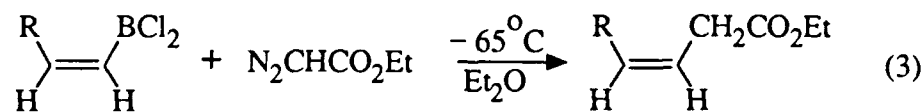
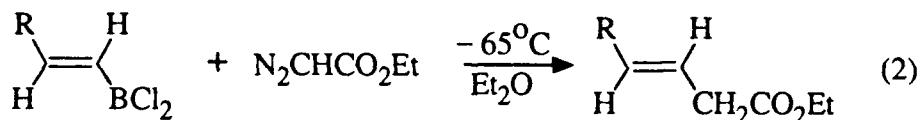
Alkylation α to a carbonyl group is an important reaction for organic synthesis. Numerous studies have shown that trialkylboranes are valuable intermediates for the alkylation of ylides,¹ carbanions,² and diazo compounds.³ In all of these reactions, only one of the three groups of trialkylborane is constructively utilized. This undesirable feature was circumvented by using B-alkyl-9-BBN derivatives for the synthesis of esters,⁴ ketones,⁵ and nitriles.⁶

The introduction of alkenyl groups α to a carbonyl group has received much attention in recent years, owing to the active study of routes to biologically important compounds, with the concurrent search for new synthetic methods. There have been however, only two reports of the direct introduction of alkenyl groups using boron. These involve the reaction of B-alkenyl-9-BBN with ethyl diazoacetate⁷ or the reaction of B-alkenyl-9-BBN with the carbanion generated from ethyl bromoacetate, phenacyl bromide and chloroacetonitrile.⁸ However, in the former case the yields are lowered by the concurrent migration of the B-cyclooctyl bond and in the latter case the maximum isomeric purity achieved is $\geq 95\%$.

The success achieved in the reaction of alkyl and aryl-dichloroboranes with ethyl diazoacetate⁹ to give the corresponding homologated esters, led us to consider the possibility of extending the reaction to achieve comparable alkenylation. The emphasis was directed towards the development of a practical synthetic route for the synthesis of stereodefined β,γ -unsaturated esters in high isomeric purity using alkenyldichloroboranes and ethyl diazoacetate. The *trans*-alkenyldichloroboranes¹⁰ were easily prepared, in high yields and in excellent isomeric purity, by the hydroboration of various alkynes with dichloroborane-dimethyl sulfide complex in the presence of one equivalent of boron trichloride in pentane (eqn. 1). The corresponding *cis*-alkenyldichloroboranes were prepared¹¹ from the *cis*-boronate esters.¹²



The alkenyldichloroboranes react with ethyl diazoacetate under mild conditions to give β,γ -unsaturated esters of excellent isomeric purity and in good yields (60-65%) (eqns. 2 and 3).

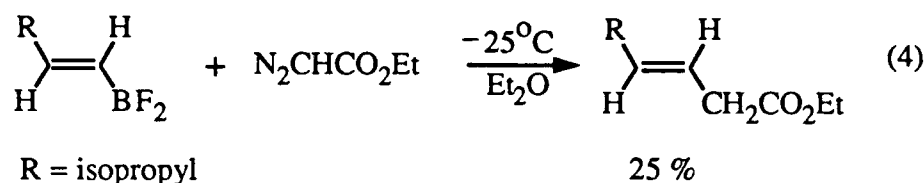


R = n-butyl, isopropyl, cyclopentyl, phenyl

The reaction of alkenyldichloroboranes with ethyl diazoacetate proceeds smoothly in ethyl ether (Et₂O) at -65°C . Hydrolysis of the intermediate with methanol-water (1:1) mixture at -30°C provides the desired *cis*- and *trans*- β,γ -unsaturated esters (see Table I and Table II). The isomeric purity of the alkenyl group is retained completely.¹³

This reaction provides a simple route to stereodefined synthesis of β,γ -unsaturated esters. With the intention of improving the yields,

the reaction of *trans*-alkenyldifluoroboranes with ethyl diazoacetate was carried out, but only poor yields were realized (eqn. 4).



The following procedure for the preparation of ethyl (*E*)-3-octenoate is representative. In a 50 ml round bottom flask equipped with rubber septum and magnetic stirring bar was placed pure 1-hexenyldichloroborane (0.825 gm, 5 mmol) in anhydrous Et₂O (5 ml) and the solution was cooled to -65°C using chloroform-dry ice bath. Ethyl diazoacetate was slowly added while the evolved nitrogen was measured (~1 hr). After the addition was over, the reaction mixture was allowed to warm to -30°C to ensure the completion of the reaction. At this temperature, methanol-water (1:1, 5 ml) was added and the cooling bath was removed. The reaction mixture was then poured into saturated aqueous sodium carbonate (25 ml) and extracted with ethyl ether (3 x 20 ml). The combined extracts were dried over anhydrous MgSO₄, concentrated and the residue was distilled to afford 0.550 gm (65 %) of ethyl (*E*)-3-octenoate, bp 120°C (25 mm of Hg). GC analysis of the ester indicated it to be ≥99% isomerically pure.

IR (neat): 1735 (ester carbonyl), 970 (C=C) cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ 0.85 (t, 3H); 1.3 (m, 7H); 2.0 (m, 2H); 3.0 (d, *J*=4Hz, 2H); 4.1 (q, 2H); 5.5 (m, 2H).

¹³C NMR (50.3 MHz, CDCl₃): δ 135.3, 122.0, 60.7, 38.4, 32.3, 31.5, 22.3, 14.3, 14.0.

mass spectrum: 170 (M⁺)

The same procedure was adopted for the reaction of *trans*-alkenyldifluoroboranes and *cis*-alkenyldichloroboranes with ethyl diazoacetate.

Acknowledgement. We express our deep appreciation to the Office of Naval Research for the support which made this research possible.

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- (13) Stereochemistry of the double bond was established by analyzing the samples on capillary GC fitted with a 15 m SPB-5, column.

Table 1. β,γ -Unsaturated esters from *trans*-alkenyldichloroboranes and ethyl diazoacetate.

<i>trans</i> -alkenyldichloroboranes	β,γ -unsaturated esters ^a	yield ^b (%)	bp (⁰ C)/ Torr	isomeric purity ^c (%)
1-hexenyldichloroborane	ethyl (<i>E</i>)-3-octenoate	65	120/25	≥99
3-methyl-1-butenyldichloroborane	ethyl (<i>E</i>)-5-methyl -3-hexenoate	66	60/20	≥99
2-cyclopentyl-1-ethenyldichloro- borane	ethyl (<i>E</i>)-4-cyclo- -pentyl-3-butenoaie	68	85/2	≥99
2-phenyl-1-ethenyldichloroborane	ethyl (<i>E</i>)-4-phenyl -3-butenoaie	63	100/2	≥99

(a) Structures confirmed by IR, ¹H NMR, ¹³C NMR and mass spectral data.

(b) Yields of pure product isolated by distillation.

(c) The isomeric ratios were determined by analyzing samples on 5890 A capillary GC.

Table II. β,γ -Unsaturated esters from *cis*-alkenyldichloroboranes and ethyl diazoacetate.

<i>cis</i> -alkenyldichloroboranes	β,γ -unsaturated esters ^a	yield ^b (%)	bp (°C)/ Torr	isomeric purity ^c (%)
1-hexenyldichloroborane	ethyl (Z)-3-octenoate	60	105/15	≥99
3-methyl-1-butenyldichloroborane	ethyl (Z)-5-methyl -3-hexenoate	58	50/20	≥99
2-cyclopentyl-1-ethenyldichloro- borane	ethyl (Z)-4-cyclo- pentyl-3-butenate	63	70/2	≥99
2-phenyl-1-ethenyldichloroborane	ethyl (Z)-4-phenyl -3-butenate	53	100/1.5	≥99

(a) Structures confirmed by IR, ¹H NMR, ¹³C NMR and mass spectral data.

(b) Yields of pure product isolated by distillation.

(c) The isomeric ratios were determined by analyzing samples on 5890 A capillary GC.

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