

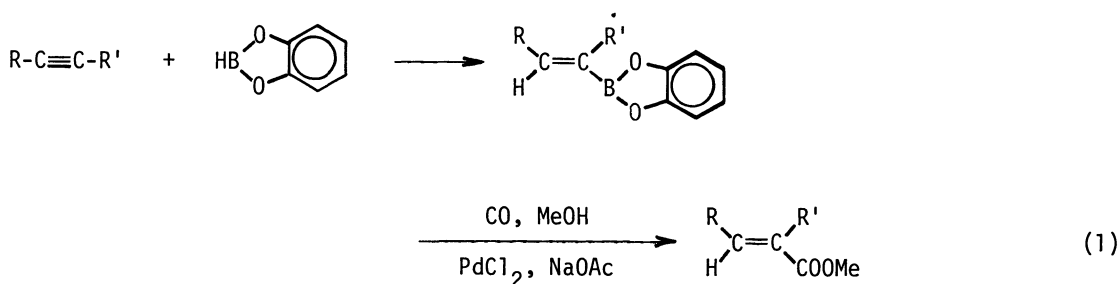
A CONVENIENT STEREOSPECIFIC SYNTHESIS OF α,β -UNSATURATED CARBOXYLIC ESTERS
VIA THE PALLADIUM-CATALYZED CARBONYLATION OF 1-ALKENYLBORANES

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1-Alkenylboranes readily prepared by the hydroboration of alkynes react smoothly with carbon monoxide in the presence of palladium chloride and sodium acetate in methanol to give the corresponding α,β -unsaturated carboxylic esters with retention of configuration with respect to alkenylboranes in good yields.

α,β -Unsaturated carboxylic ester synthesis from alkynes, carbon monoxide and alcohols with the aid of transition metal catalysts is important in industrial or laboratory applications. The alkynes are mainly hydrocarboxylated¹ in accordance with the Markownikoff rule. In our continuing studies on the organic synthesis using organoboranes, we have now discovered that 1-alkenylboranes readily react with carbon monoxide in the presence of palladium chloride and sodium acetate in methanol to give α,β -unsaturated carboxylic esters in good yields (eq. 1). The reaction provides a new regio- and stereoselective anti-Markownikoff hydrocarboxylation of alkynes via hydroboration.



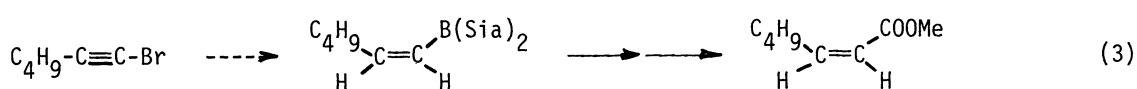
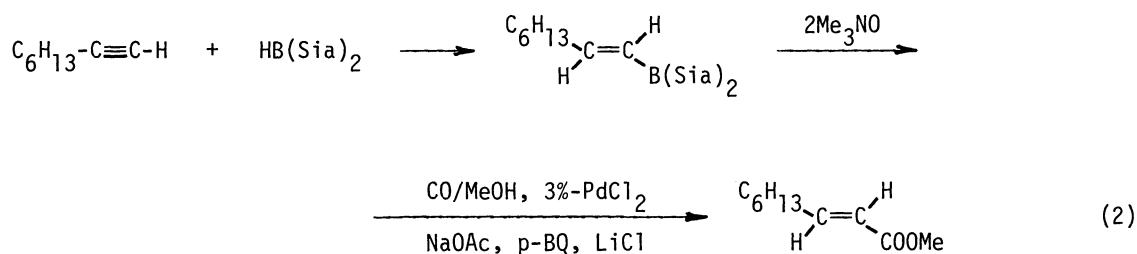
In 1975 Heck² reported that 1-hexenylboronic acid reacts smoothly with methyl acrylate in the presence of stoichiometric amounts of palladium acetate to give the corresponding methyl 2,4-nona-dienoate. Recently, we reported on the palladium-catalyzed cross-coupling reaction between 1-alkenylboranes and organic halides such as alkenyl,³ alkynyl,³ aryl,⁴ allylic,⁵ and benzylic⁵ halides. These reactions are believed to involve a stereospecific conversion of alkenylboranes to alkenyl-palladium compounds. Such alkenylpalladiums may be expected to react with carbon monoxide in alcoholic solution to produce α,β -unsaturated esters. Accordingly, (E)-1-hexenyl-1,3,2-benzodioxaborole prepared from 1-hexyne and catecholborane was treated with carbon monoxide under atmospheric pressure and an equimolar amount of palladium chloride at room temperature. Although the brown color of palladium chloride almost immediately changed to yellow, the formation of the desired methyl 2-heptenoate was not observed during the reaction over 5 h. Addition of sodium acetate to the above reaction mixture resulted in rapid precipitation of palladium black. When sodium acetate (1.5 equiv) was added, methyl (E)-2-heptenoate was obtained in a yield of 67% within 10 min at room

temperature.

Next, we tried an examination to see whether the reaction could be carried out in the presence of a catalytic amount of palladium(II) salts and reoxidants. It was found that the reaction proceeds smoothly by employing palladium chloride as a catalyst and *p*-benzoquinone⁶ as a reoxidant.

Simplicity and efficiency of the present reaction are demonstrated by the following typical procedure: A dry 100 ml-flask was charged with PdCl₂ (8.86 mg, 0.05 mmol), sodium acetate (0.615 g, 7.5 mmol), *p*-benzoquinone (0.81 g, 7.5 mmol), and lithium chloride (2.1 g, 50 mmol). Then the flask was flushed with carbon monoxide. To the mixture were added anhydrous methanol (25 ml) and (E)-1-hexenyl-1,3,2-benzodioxaborole⁷ (1.01 g, 5 mmol), and then the solution was stirred for 2 h at room temperature under atmospheric pressure of carbon monoxide. After the reaction was completed, the mixture was poured into 200 ml of water, extracted with ether, washed with a 10% Na₂CO₃ aqueous solution, and finally dried over magnesium sulfate. The organic layer thus obtained was analyzed by glpc (15% SE-30 on Uniport B), revealing the formation of methyl (E)-2-heptenoate (4.6 mmol, 92%): n_D^{24} 1.4372 (lit.⁸ n_D^{23} 1.4393); ¹H NMR (90 MHz, CCl₄, TMS), δ, 0.93 (t, 3H), 1.2-1.6 (m, 4H), 2.0-2.4 (m, 2H), 3.69 (s, 3H), 2.76 (d, 1H, J=16 Hz), and 6.90 (dt, 1H, J=7 and 16 Hz); IR (neat), 1730 and 1665 cm.⁻¹


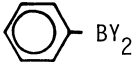
Instead of 1-alkenyl-1,3,2-benzodioxaboroles,⁷ when 1-alkenyl-disiamylboranes⁷ formed by the hydroboration of alkynes with disiamylborane were used, the reaction failed to afford the expected esters under the same conditions described above. However, it was found that this difficulty was overcome by the oxidation of two siamyl groups with trimethylamine oxide⁹ before the carbomethoxylation. Thus, the hydroboration of 1-octyne with disiamylborane, oxidation with two equivalents of trimethylamine oxide at 50 °C for 1 h followed by carbonylation in methanol gave a 73% yield of methyl (E)-2-nonenoate (eq. 2). Similarly, by applying the same sequence of reaction to (Z)-1-hexenyl-disiamylborane,¹⁰ methyl (Z)-2-heptenoate was obtained stereoselectively in a yield of 42% (eq. 3).



The representative results are summarized in Table 1. The present reaction provides a fairly general synthetic method of α,β-unsaturated esters. One of the most remarkable features is the high stereoselectivity of the carbonylation step. Although the reaction mechanism has not been clarified, the reaction may proceed most probably via transmetalation from alkenylboranes to alkenylpalladium salts followed by insertion of carbon monoxide into alkenyl-palladium bond. The results indicate that the transmetalation from boron to palladium salts occurs with retention of configuration with respect to alkenylboranes.

There have been some published procedures on similar conversions by means of alkenyl-mercurials¹¹ and silicates.¹² The hydroboration reaction has made the organoboranes readily available. Such organoboranes are truly remarkable reagents, possibly the most versatile for organic syntheses. The present reaction provides a new transformation of organoboranes involving the conversion of boron-carbon bonds to carbon-carbon bonds. In addition to the usual preparation of alkenylboranes by hydroboration of alkynes, alkenylboranes have been recently produced by other methods including the base induced transfer reaction of alkyl group from α -halovinylboranes¹³ and the reaction of lithium 1-alkynylorganoborates with electrophiles.¹³ Currently we are exploring the scope of the reaction with such a wide variety of alkenylboranes.

Table 1. Carbomethoxylation of Alkenylboranes^{a)}

Alkenylborane, $\begin{matrix} R^1 & & R^3 \\ & \diagdown & / \\ & C=C & \\ & / & \diagdown \\ R^2 & & BY_2 \end{matrix}$				PdCl ₂	Temp.	Time	Yield of $\begin{matrix} R^1 & & R^3 \\ & \diagdown & / \\ & C=C & \\ & / & \diagdown \\ R^2 & & COOMe \end{matrix}$
R ¹	R ²	R ³	Y ₂ ^{b)}	(mole %)	(° C)	(h)	(%) ^{e)}
Butyl	H	H	BDOB	1	r.t.	2	92
H	Butyl	H	(Sia) ₂	3	0	2	42 ^{c)}
Hexyl	H	H	BDOB	1	50	2	93
Hexyl	H	H	(Sia) ₂	3	r.t.	2	73 ^{c)}
Ethyl	H	Ethyl	BDOB	1	50	2	95
Butyl	H	Me ₃ Si-	BDOB	1	50	2	87
HC≡C-(CH ₂) ₄ -	H	H	BDOB	1	r.t.	2	66
Phenyl	H	H	BDOB	1	50	2	70
			BDOB	3	r.t.	4	84 ^{d)f)}
			(OH) ₂	1	r.t.	2	41

a) The reaction was carried out in methanol using NaOAc (7.5 mmol), *p*-benzoquinone (7.5 mmol), and LiCl (50 mmol). b) Sia=SiamyI and BDOB=1,3,2-benzodioxaborole. c) Two siamyI groups were oxidized with two equivalents of trimethylamine oxide at 50° C for 1 h before the carbomethoxylation. d) The yield of diester. e) By glcp based on the alkenylborane used. The stereoisomeric purity in each case was determined by glcp, ¹H NMR (J_{trans} = 16 Hz) and IR, indicating \geq 99%. f) Dimethyl 1,7-octadiene-1,8-dicarboxylate.

References and Notes

1. (a) P. M. Maitlis, "The Organic Chemistry of Palladium," Vols. 1 and 2, Academic Press, New York, 1971; (b) I. Wender and P. Pino, "Organic Synthesis via Metal Carbonyls," Vol. 2, John Wiley & Sons, New York, 1977.
2. H. A. Dieck and D. F. Heck, *J. Org. Chem.*, **40**, 1083 (1975).
3. (a) N. Miyaura, K. Yamada, and A. Suzuki, *Tetrahedron Lett.*, 3437 (1979); (b) N. Miyaura, H. Suginome, and A. Suzuki, *Tetrahedron Lett.*, 127 (1981).
4. N. Miyaura and A. Suzuki, *J. C. S. Chem. Commun.*, 866 (1979).
5. N. Miyaura, T. Yano, and A. Suzuki, *Tetrahedron Lett.*, 2865 (1980).
6. L. S. Hegedus, G. F. Allen, J. J. Bozell, and E. L. Waterman, *J. Amer. Chem. Soc.*, **100**, 5800 (1978).
7. For the preparation of alkenylbenzodioxaboroles and alkenyldisiamylboranes, see H. C. Brown, "Organic Syntheses via Boranes," John Wiley & Sons, New York, 1975.
8. K. Yamada, N. Miyaura, M. Itoh, and A. Suzuki, *Bull. Chem. Soc. Japan*, **50**, 3431 (1977).
9. (a) A. F. Kluge, K. G. Untch, and J. F. Fried, *J. Amer. Chem. Soc.*, **94**, 7827 (1972); (b) G. Zweifel, N. L. Polston, and C. C. Whitney, *J. Amer. Chem. Soc.*, **90**, 6243 (1978).
10. J. R. Campbell and G. A. Molander, *J. Organometal. Chem.*, **156**, 71 (1978).
11. R. C. Larock, *J. Org. Chem.*, **40**, 3237 (1975).
12. K. Tamao, T. Kakui, and M. Kumada, *Tetrahedron Lett.*, 619 (1979).
13. For such a review, see E. Negishi, "New Applications of Organometallic Reagents in Organic Synthesis," Edited by D. Seyferth, Elsevier, Amsterdam, 1976, p. 93.

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