comparison of the spectroscopic data of both ketals that **10** differs from **8** only in the position of the diene system. When **10** was treated with 1.5 equiv of *p*-toluenesulfonic acid in methanol for 3 h, cyclization did not occur; instead, the acrylate ester group was lost, giving **9**, isolated as the known fumarate (40%).

When thebaine and DMAD were allowed to react for 15 min in MeOH, the ketal **11** was obtained in 35% yield: mp 172–174 °C: $[\alpha]_D$ −109°C ($CHCl_3$); UV(EtOH) λ_{max} 284 nm (log ϵ 4.09); IR (KBr) 1740, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88 (t, 2 H, H-15), 2.74 (s, 3 H, NCH_3), 2.92 (s, 3 H, OCH_3), 3.05–3.45 (m, 4 H, H-10, H-16), 3.55 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.90 (s, 3H, OCH_3), 4.51 (s, 1 H, H-19), 4.75 (s, 1 H, H-5), 5.62 (d, 1 H, H-7, J = 10 Hz), 5.94 (dd, 1 H, H-9), 6.59 (d, 1 H, H-8, J = 10 Hz), 6.67 (s, 2 H, H-1, H-2). The NMR spectrum of **11** was similar to that of **8** except for the presence of additional OCH_3 protons and the absence of an H- 18 proton signal. Accordingly, the signal for the H-19 proton appeared as a singlet at δ 4.51, characteristic of a dialkyl aminomaleate.[6] Hydrolysis of **11** with NaOH over a period of several days afforded **9**, the fumarate of which was identical with that obtained previously.

Preliminary experiments with EP and thebaine in MeOH suggested that a ketal corresponding to **8** was obtained. Thus, the condensation of acetylenic dienophiles with thebaine in methanol to produce ketals such as **8** and **11** seems to be general.

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Registry No. 1, 115-37-7; 5, 78923-43-0; 7, 78914-30-4; 8, 80410-25-9; 9, 80410-26-0; 9 fumarate, 80446-41-9; 10, 80410-27-1; 11, 80410-28-2; methyl propiolate, 922-67-8; dimethyl acetylenedicarboxylate, 762-42-5.

Supplementary Material Available: Tables I–III, listing fractional coordinates and temperature factors for **2** and bond distances and angles for **7** (4 pages). Ordering information is given on any current masthead page.

Amrik Singh, Sydney Archer*
Cogswell Laboratory
Department of Chemistry
Rensselaer Polytechnic Institute
Troy, New York 12181

Karst Hoogsteen, Jordan Hirshfield
Merck Institute for Therapeutic Research
Rahway, New Jersey 07065

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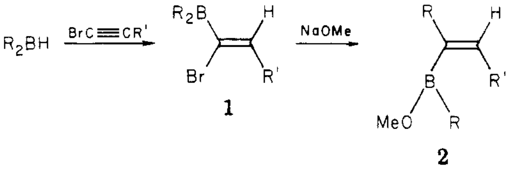
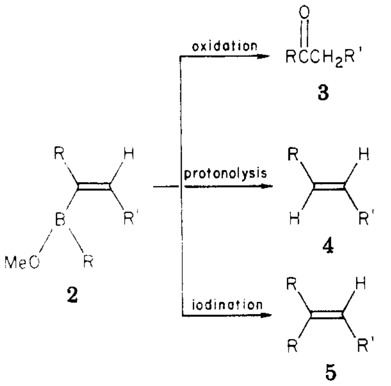
A General Synthesis of *B*-(*cis*-1-Bromo-1-alkenyl)dialkylboranes. Valuable Intermediates for the Synthesis of Ketones, Trans Alkenes, and Trisubstituted Alkenes

Summary: Dialkylboranes, generated in situ via hydridation of dialkylhaloboranes, hydroborate 1-bromo-1-alkynes to provide cleanly *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes. Treatment of these intermediates with sodium methoxide results in the migration of one of the alkyl groups on boron to the adjacent carbon, displacing the bromine, providing *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters. These intermediates provide ketones on oxidation, stereospecific trans alkenes on protonolysis, and trisubstituted alkenes on iodination, all in high yields.

Sir: Hydroboration of 1-halo-1-alkynes with dialkylboranes results in the formation of *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes (**1**).[1-3] As demonstrated by Zweifel and coworkers,[1-3] these vinylboranes are valuable synthetic intermediates. Thus, treatment with base induces migration of one of the alkyl groups from boron to the attached carbon, providing vinylboron intermediates (**2**) not available by direct hydroboration (eq 1). These intermediates (**2**) can be readily transformed into ketones (**3**)[1] via oxidation, into trans alkenes (**4**)[1,3] via protonolysis, and into trisubstituted alkenes (**5**)[2] via iodination (eq 2).



(1)



(2)

However, the applicability of this reaction sequence is presently restricted by the availablility of stable dialkylboranes. Only in the case of relatively hindered alkenes, such as cyclohexene, α-pinene, etc., does direct hydroboration lead cleanly to the formation of dialkylboranes. Consequently, this route has had limited application in organic synthesis.

Recently a convenient general method for the preparation of dialkylboranes via hydridation of dialkylhaloboranes has been developed in this laboratory.[4] We reported that these dialkylboranes hydroborate terminal and internal alkynes to provide the corresponding dialkylvinylboranes[5] which serve as valuable intermediates for the synthesis of cis alkenes[6] and trisubstituted alkenes,[7] greatly extending the generality of the Zweifel syntheses. We now report the utility of such dialkylboranes for a general synthesis of *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes and their transformations into ketones, trans alkenes, and trisubstituted alkenes.

Dialkylboranes, generated in situ via the hydridation of dialkylhaloboranes, hydroborate 1-bromo-1-alkynes cleanly to provide the corresponding *B*-(*cis*-1-bromo-1-alkenyl)-

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(1) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.

(2) Zweifel, G.; Fisher, R. P. *Synthesis* **1972**, 557.

(3) Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1971**, *93*, 6309.

(4) Brown, H. C.; Kulkarni, S. U. *J. Organometal. Chem.* **1981**, *218*, 309.

(5) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Organometal. Chem.*, in press.

(6) Kulkarni, S. U.; Basavaiah, D.; Brown, H. C. *J. Organometal. Chem.*, in press.

(7) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.* **1982**, *47*, 171.

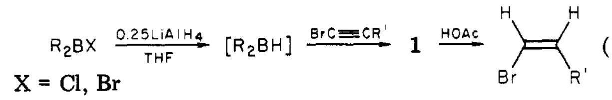
0022-3263/82/1947-0754$01.25/0

Table I. Synthesis of Ketones, Trans Alkenes, and Trisubstituted Alkenes from Dialkylhaloborane and 1-Bromo-1-alkyne[a]

alkene for R_2BX	X	1-bromo-1-alkyne	product[b]	% yield[c]	bp, °C/mm	$n^{20}D$
cyclopentene	Br	1-bromo-1-hexyne	3A	81	77-79/0.9	1.4516
			4A[d]	73	66-67/3	1.4526
cyclopentene	Br	1-bromo-1-octyne	3B	80	100-102/0.8	1.4542
			4B[d]	70	73-74/0.6	1.4562
2-methylpentene[e]	Cl	1-bromo-1-octyne	3C	83	114-116/1 (136.5/10[15])	1.4357 (1.4358[15])
			4C[d]	77	88-90/1	1.4365
1-hexene[e]	Cl	1-bromo-1-hexyne	3D	84	67-69/0.7 (125/12[16])	1.4300 (1.4339[16])
			4D[d]	79	85-87/6 (213.5/760[17])	1.4304
1-hexene[e]	Cl	1-bromo-1-octyne	5A	69	127-128/0.2	1.4482

[a] All reactions were carried out in a 30-mmol scale. [b] Chemical purities of all compounds (**3A-D**, **4A-D**) are >99% by GC analysis on a 6-ft SE-30 column; the chemical purity of **5A** is >95%. [c] Yields of pure products isolated by distillation based on R_2BX or 1-bromo-1-alkyne. [d] Isomeric purities are >99% determined by ^{13}C NMR analysis.[18] [e] Distilled R_2BX was utilized.

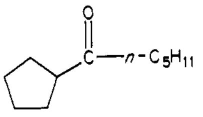
dialkylboranes (**1**), as evidenced by their conversion into the *cis*-1-bromo-1-alkenes on protonolysis with acetic acid (eq 3).



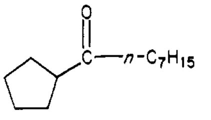
(3)

Treatment of **1** with sodium methoxide results in the displacement of bromine by one of the alkyl groups on boron to afford *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters (**2**). The synthetic utility of such derivatives was demonstrated by converting them into ketones, trans alkenes, and trisubstituted alkenes (eq 2).

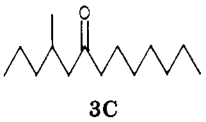
Treatment of **2** with alkaline hydrogen peroxide affords the corresponding ketones in excellent yields. A representative group of ketones (**3A-D**) was prepared from 1-bromo-1-alkynes and alkenes (Table I).



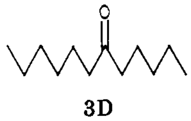
3A



3B

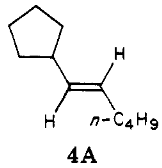


3C

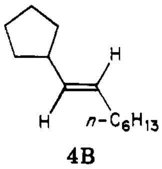


3D

The intermediates **2** were also treated with acetic acid at reflux temperature for 3 h, providing trans alkenes stereospecifically, which represents a general, one-pot and stereospecific synthesis of such trans alkenes. A variety of pure trans disubstituted alkenes (**4A-D**) were prepared from representative alkenes and 1-bromo-1-alkynes (Table I).



4A

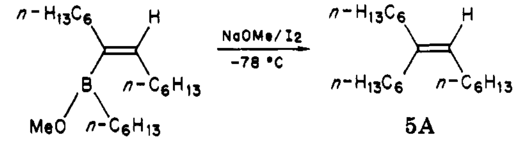


4B

4C

4D

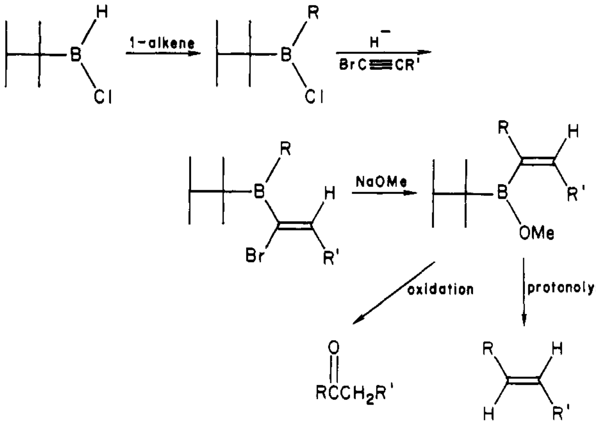
Iodination[5,8] of vinylboranes, obtained via hydroboration of 1-alkynes with dialkylboranes, affords cis alkenes stereospecifically. We carried out the iodination of *B*-(*trans*-1-*n*-hexyl-1-octenyl)-*n*-hexylborinate at −78 °C to produce 7-*n*-hexyl-7-tetradecene (**5A**) in 69% isolated yield[9] (eq 4).



5A

(4)

A disadvantage of the present procedure is the loss of one of the two alkyl groups on boron. In cases where R is a valuable group whose loss must be avoided, it is possible to use thexylborane[10] (for secondary and 2-substituted primary groups) or thexylchloroborane[11,12] (for both secondary and primary groups) for the synthesis of ketones and trans alkenes (eq 5). However, the present procedure is more convenient and is preferable for the synthesis of ketones and trans alkenes in cases where the R group is a readily available intermediate. It is also applicable for the synthesis of trisubstituted alkenes.



(5)

The following procedure for the synthesis of 4-methyl-6-tridecene (**4C**) is representative. To 30 mmol of bis(2-methyl-1-pentyl)chloroborane[13] (6.48 g) in THF at 0 °C was added slowly 7.5 mmol of $LiAlH_4$ in THF with stirring under nitrogen.[14] After 1 h at 0 °C, the resulting di-

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[8] Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652.

[9] Under these conditions, the formation of vinyl iodide [(R)IC=CH(R')] was minimized.

[10] Negishi, E.; Katz, J.-J.; Brown, H. C. *Synthesis* **1972**, 555.

[11] Kulkarni, S. U.; Lee, H. D.; Brown, H. C. *Synthesis*, in press. Brown, H. C.; Lee, H. D.; Kulkarni, S. U. *Ibid.* in press.

[12] Kulkarni, S. U.; Lee, H. D.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 4542.

[13] Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1979**, *44*, 2417.

[14] For detailed experimental techniques in handling air-sensitive materials, see Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.

alkylborane was slowly transferred to the solution of 1-bromo-1-octyne (30 mmol) in THF at −78 °C. The reaction mixture was allowed to warm to 0 °C and the stirring was continued for an additional 3 h at 0 °C. Sodium methoxide (75 mmol) in methanol was added at 0 °C and the mixture was stirred at room temperature for 1 h. Acetic acid (3 mL) was added slowly to neutralize any excess sodium methoxide. Solvents and volatile materials were removed under vacuum. Acetic acid (40 mL) was added and the mixture heated under reflux for 3 h. The reaction mixture was cooled and the usual workup[14] afforded 4-methyl-6-tridecene (**4C**; 4.52 g, 77%): bp 88–90 °C (1 mm): $n^{20}D$ 1.4365. GC analysis indicated 100% chemical purity and ^{13}C NMR showed 99% isomeric purity.

To the reaction mixture containing 30 mmol of **1** (R = 2-methyl-1-pentyl), was slowly added 25 mL of 3 N sodium hydroxide at 0 °C and the mixture was stirred at room temperature for 1 h. The usual oxidation[14] furnished 4-methyl-6-tridecanone (**3C**; 5.27 g, 83%): bp 114–116 °C (1 mm); $n^{20}D$ 1.4357 [lit.[15] bp 136.5 °C (10 mm); $n^{20}D$ 1.4358]. GC analysis indicated 100% chemical purity and ^{1}H NMR spectrum is consistent with the structure.

The iodination of the reaction mixture containing 30 mmol of *B*-(*trans*-1-*n*-hexyl-1-octeny)-*n*-hexylborinate was carried out at −78 °C as described elsewhere.[6] The usual workup provided 7-*n*-hexyl-7-tetradecene (5.77 g, 69%): bp 127–128 °C (0.2 mm); $n^{20}D$ 1.4482. GC analysis showed >95% chemical purity and ^{1}H NMR is in agreement with the structure.

Consequently, the present modification greatly extends the range of applicability of Zweifel's (α-halovinyl)boranes, providing simple, general, and one-pot synthesis of ketones, trans alkenes, and trisubstituted alkenes.

Herbert C. Brown,* D. Basavaiah[19]
Richard B. Wetherill Laboratory
Purdue University
West Lafayette, Indiana 47907

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[15] Schlenk, W., Jr. *Justus Liebigs Ann. Chem.* **1973**, 1195.

[16] Rabilloud, G. *Bull. Soc. Chim. Fr.* **1966**, 634.

[17] Soják, L.; Hrivnák, J. *J. Chromatogr. Sci.* **1972**, *10*, 701.

[18] In a mixture of isomers, the vinylic carbons of trans alkenes can be distinguished from the corresponding carbons of the cis isomers: Dorman, D. E.; Jautelat, M.; Roberts, J. D. *J. Org. Chem.* **1971**, *36*, 2757.

[19] Postdoctoral research associate on Grant GM-10937 from the National Institutes of Health.