Vinylic Organoboranes. 7. Stereoselective Synthesis of (*E*)-(1-Substituted-1-alkenyl)boronic Esters by the Nucleophilic Substitution of (*Z*)-(1-Bromo-1-alkenyl)boronic Esters with Organolithium or Grignard Reagents. Isolation and Oxidation to Ketones

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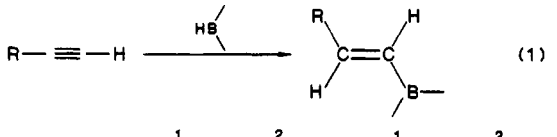
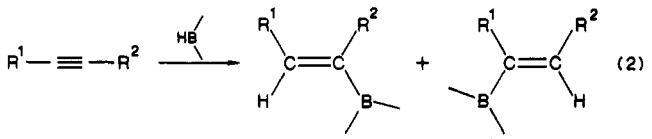
The title compounds, (*E*)-$R^1CH{=}CR^2B(OR)_2$ (**4a–g**), are prepared in a highly regio- and stereoselective manner by the reaction of (*Z*)-$R^1CH{=}CBrB(OR)_2$ (**3a–g**) with R^2Li or R^2MgX. The stereochemistry was established in two cases by isolating the *E* isomers **4** (R^1, R^2 = *n*-Bu; R^1 = *i*-Pr, R^2 = Me) in pure form and comparing the products with the corresponding *Z* isomers prepared by hydroboration of appropriate internal alkynes. Oxidation of **4** provides the corresponding ketones, $R^1CH_2COR^2$, in high yields, confirming the carbon structures of the intermediate. As established previously, protonolysis of these (*E*)-boronic esters provides a synthesis of the pure (*E*)-alkenes.

Alkenylboranes are readily available by hydroboration of alkynes and have been demonstrated to be valuable synthetic intermediates in organic synthesis.[2] In many cases, however, the applicability is limited by the limited availability of the desired structural types via these synthetic approaches. Hydroboration of 1-alkynes[2] provides (*E*)-1-alkenylboron species (eq 1) and internal alkynes[2] can give a mixture of (*Z*)-(1-substituted-1-alkenyl)boron derivatives (eq 2).

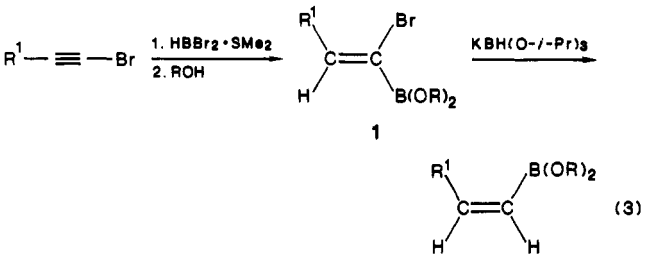


(1)



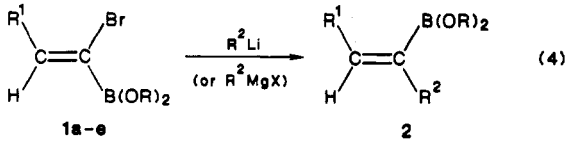
(2)

Recently we reported a stereoselective preparation of the (*Z*)-1-alkenylboronic esters via the α-bromoalkenyl boron intermediates (eq 3).[3]



(3)

In this study, we have developed a highly convenient, practical route for preparing (*E*)-(1-substituted-1-alkenyl)boronic esters in a regio- and stereoselective manner based on the intermediate **1** (eq 4). This route resembles



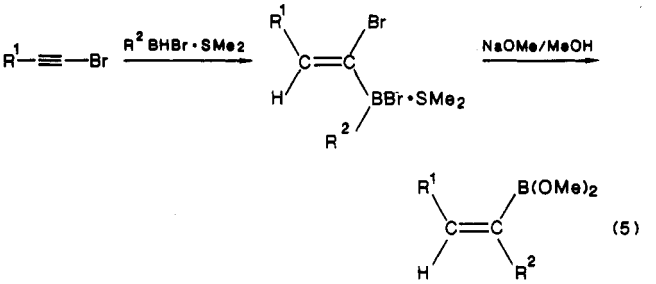
(4)

(1) (a) Postdoctoral research associate on National Science Foundation Grant CHE-79-18881. (b) Postdoctoral research associate on National Science Foundation Grant CHE-8414171.

(2) (a) Brown, H. C.; Campbell, J. B., Jr. *Aldrichimica Acta* **1981**, *14*, 3–10. (b) Negishi, E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: New York, 1983; Chapter 45.8, Vol. 7, pp 303–322.

(3) Brown, H. C.; Imai, T. *Organometallics* **1984**, *3*, 1392.

another closely related approach in which R^2 is introduced by hydroboration prior to the hydroboration of 1-bromo-1-alkynes (eq 5).[4] These two approaches nicely complement each other in permitting a wide variation in the structure of the R^2 groups.



(5)

Another entry to this type of alkenylboronic esters is dioxyborylation of the corresponding alkenyllithium or magnesium reagents.[5] This route, however, requires the starting alkenyl halides and does not always guarantee a high stereoselectivity.[5]

It should also be noted that (α-haloalkyl)boronic esters are well-known to undergo facile nucleophilic substitution by organolithium or Grignard reagents via ate complex formation and subsequent 1,2-migration.[6–8] However, the organometallic substitution of (α-haloalkenyl)boron derivatives (eq 4) has not been reported previously. Consequently, this investigation was undertaken to achieve the stereoselective synthesis of (*E*)-(1-substituted-1-alkenyl)-boronic esters via **1**. Indeed, we succeeded in isolating them in pure form and they were then compared with the corresponding *Z* isomers obtained by the hydroboration of appropriate internal alkynes. The carbon skeleton was proved by hydrogen peroxide deboronation to the corresponding ketones (eq 6).

An interesting feature of the present reaction should be pointed out. It is well-known that alkenyl halides couple readily with organometallic reagents in the presence of transition-metal catalysts.[9] Such reactions generally

(4) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.* **1982**, *47*, 3808.

(5) Matteson, D. S.; Liedtke, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 1526.

(6) (a) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529 and references cited therein. (b) Tsai, D. J. S.; Jesthi, P. K.; Matteson, D. S. *Ibid.* **1983**, *2*, 1543.

(7) Brown, H. C.; De Lue, N. R.; Yamamoto, Y.; Maruyama, K.; Kasahara, T.; Murahashi, S.; Sonoda, A. *J. Org. Chem.* **1977**, *42*, 4088.

(8) Rathke, M. W.; Chao, E.; Wu, G. *J. Organomet. Chem.* **1976**, *122*, 145.

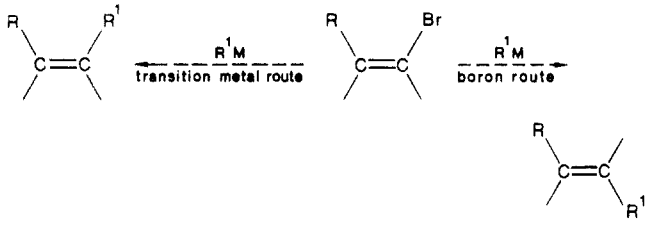
0022-3263/86/1951-5277$01.50/0

Table I. Formation of Ketones by the Reaction of RLi with (Z)-n-$C_4H_9CH{=}CBrB(OR^1)_2$ (I), Followed by Oxidation[a]

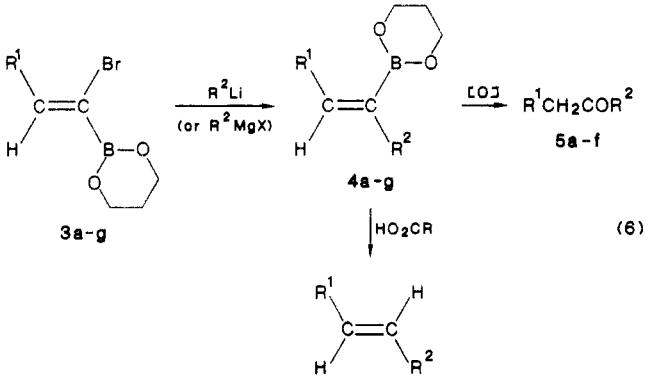
RLi	I	$(OR^1)_2$	solvent	additive	GC yield,[a] % n-$C_4H_9CH_2COR$	GC yield,[a] % n-C_4H_9OH
n-BuLi	a	$(OCH_3)_2$	ether	none	50	43
n-BuLi	b	$[OCH(CH_3)_2]_2$	ether	none	74	18
n-BuLi	c	$O(CH_2)_2O$	ether	none	58	34
n-BuLi	d	$O[C(CH_3)_2]_2O$	ether	none	11	82
n-BuLi	e	$O(CH_2)_3O$	THF	none	11	85
n-BuLi	e	$O(CH_2)_3O$	ether	none	79	11
n-BuLi	e	$O(CH_2)_3O$	ether	methanol[b]	93	6

[a] To a stirred solution of I (5 mmol) in a solvent (10 mL) was slowly added RLi (5 mmol) at −78 °C. The mixture was stirred overnight at room temperature and oxidized by transfer into a stirred mixture of 3 M NaOH (5 mmol) and 30% H_2O_2 (10 mmol) and stirring was continued for 1 h at room temperature. [b] Methanol (10 mL) was added before the removal of the cold bath. [c] n-Tetradecane was used as an internal standard.

proceed with retention of configuration. On the other hand, in the organoborane route described in this study, the halogen substituent is replaced by an organyl group with complete inversion of configuration at the vinylic center.



The boron intermediate has other capabilities. It can be protonolyzed to the *trans*-alkenes or oxidized to the ketones (eq 6).

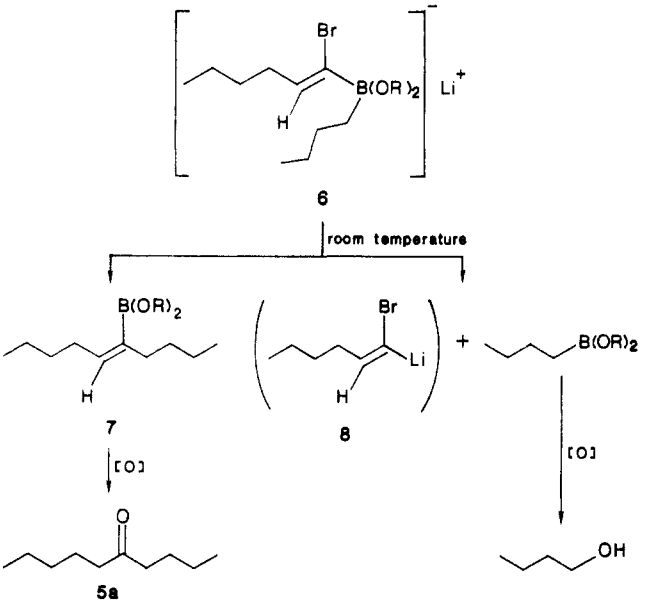


Results and Discussion

The reaction of n-butyllithium was studied in ether with five selected esters of (*Z*)-(1-bromo-1-hexenyl)boronic acid **1a–e**. The reagent was added to a stirred solution of the boronic esters in ether at −78 °C. The mixture was allowed to come to room temperature and monitored by ^{11}B NMR.

For example, with the trimethylene ester **1e**, the formation of an "ate" complex intermediate was observed at δ 2.50. This peak disappeared almost completely with 2 h at room temperature, with concurrent increase of a boronic ester peak at δ 26.70. A similar spectral change was observed with the diisopropyl ester **1b** and the pinacol ester **1d**, although the transfer was significantly slower in the case of **1b** (complete transfer required overnight at room temperature). On the other hand, the reaction of n-butyllithium and the dimethyl ester **1a** resulted in the formation of a mixture of a trialkylborane (δ 86, very small amount), a borinic ester (δ 52), a boronic ester (δ 30), and an ate complex (δ 3.30). The ratio of the latter three was

Scheme I



1:1:2 after 1 day of stirring and no further change was observed. A similar mixture was formed in the reaction of the dimethylene ester **1c**. In these two cases, multialkylation might have taken place during the addition of n-butyllithium and the persistent ate complex would be the alkenyl(trialkoxy)borate formed by disproportionation.[10]

Such a multialkylation was negligible in the reactions with **1b**, **1d**, and **1e**. Nevertheless, even in these cases, subsequent oxidation gave a mixture of 1-butanol and 5-decanone (**5a**) in variable ratios (Table I). These products were identified by GC, isolation, and spectral comparison with authentic samples.

The ^{11}B NMR spectral observation and the formation of 1-butanol, as well as the ketone (**5a**), suggested two competitive paths for the fate of the ate complex intermediate, **6**, i.e., (i) 1,2-migration of the n-butyl group with displacement of bromine to give **7** and (ii) dissociation into n-butylboronic ester and (1-bromo-1-hexenyl)lithium (**8**) Scheme I).[11]

This undesirable dissociation was the major path for **1d**, while **1b** and **1e** gave reasonable yields of the substitution product **5a**. For further investigation, **1e** was chosen mainly because of the stability of the cyclic ester group.

(9) For a review of coupling reactions via transition metal complexes, see: Noyori, R. In *Transition Metal Organometallics in Organic Synthesis*; Alper, Ed.; Academic Press: New York, 1976; Vol. 1, Chapter 2.

(10) The results seem to be quite reasonable in light of our recent study on the reaction of organometallic reagents with trialkoxyboranes: Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316.

(11) Attempts to trap the bromoalkenyllithium with PhCHO and $PhCH_2Br$ failed. At room temperature the intermediate, if formed, might decompose very rapidly.

Table II. Formation of Ketones by the Reaction of RMgX and (*Z*)-*n*-$C_4H_9CH{=}CBrB(O_2C_3H_6)$ (1e) in Ether, Followed by Oxidation[a]

		GC yield,[a] %	
RMgX	additive[b]	*n*-C_4H_9CH-$_2COR$	ROH
n-BuMgCl	none	41	56
n-BuMgCl	MeOH	68	2
n-BuMgCl	NaOMe/MeOH (1 equiv)	81	4
n-BuMgCl	NaOMe/MeOH (2 equiv)	88	3
i-PrMgCl	NaOMe/MeOH (2 equiv)	97	
MeMgBr	NaOMe/MeOH (2 equiv)	69[d]	

[a] To a stirred solution of **1e** (5 mmol) in ether (10 mL) was slowly added RMgX (5 mmol) at −78 °C. Oxidation was done by transfer into a mixture of 3 M NaOH (5 mmol) and 30% H_2O_2 (10 mmol) and stirring was continued for 1 h at room temperature. [b] MeOH (10 mL) or 4.5 M NaOMe/MeOH (10 mmol, 2 equiv) was added before the removal of the cold bath. [c] *n*-Tetradecane was used as an internal standard. [d] The reaction mixture was refluxed for 1 day.

We could suppress the side reaction to 6% and improve the yield of **5a** to 93% simply by adding methanol before allowing the mixture to come to room temperature. This was hinted at by the closely related reaction[4] given in eq 5 in which methanolic sodium methoxide was used for promoting the migration.

The reaction of *n*-butylmagnesium chloride with the trimethylene ester **1e** was also studied in ether (Table II). In ether and in the absence of methanol, 1-butanol was the major oxidation product (58%). On the addition of methanol, this product became negligible (2%). At the same time, the yield of substitution product **5a** increased from 41% to 68%. The ^{11}B NMR spectrum clearly indicated the effect of methanol in the reaction medium. In the absence of methanol, the spectrum of the reaction mixture consisted of three peaks at δ 45 (a very broad borinate peak), δ 28 a boronate peak), and δ 5 (a very broad ate complex peak). Both the borinate and the ate complex peaks decreased and the boronate peak increased very slowly (incomplete, even after refluxing overnight). On the addition of methanol, the borinate peak vanished almost completely from the spectrum, leaving the other two peaks. The disappearance of the ate complex peak became faster and the change was achieved upon stirring overnight at room temperature, although a small ate complex peak, probably due to excess base, persisted.

The yield of the ketone **5a**, however, was still lower than that obtained with *n*-butyllithium. To further diminish the effect of $MgCl^+$, methanol was replaced with methanolic sodium methoxide in the hope that magnesium ion would be removed as magnesium methoxide. Indeed, when sodium methoxide was added, a white solid precipitated, and the yield of **5a** increased to 81% with 1 equiv and to 88% with 2 equiv of the base.

A variety of (*E*)-2-(1-substituted-1-alkenyl)-1,3,2-dioxaborinanes **4a–g** were easily isolated by quenching the reaction mixture with water (in the case of organolithiums) or with aqueous ammonium chloride (in the case of Grignard reagents), extracting with ether, reesterification,[12]

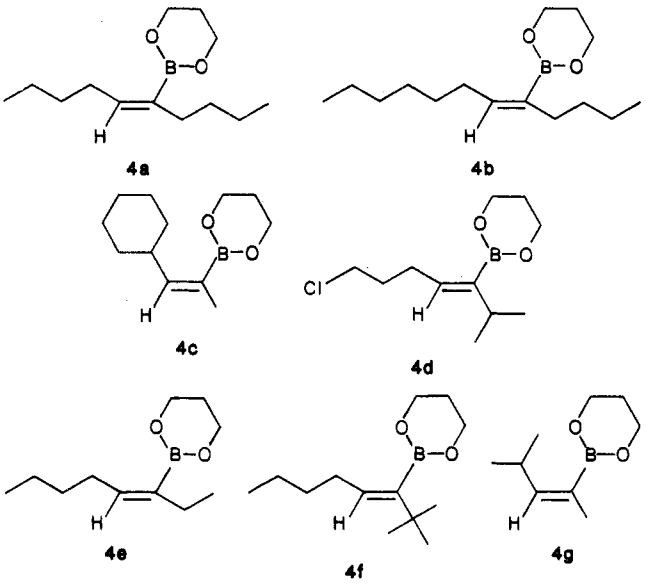
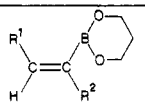


Table III. Preparation of (*E*)-$R^1CH{=}CR^2B(O_2C_3H_6)$ 4a–g by the Reaction of (*Z*)-$R^1CH{=}CBrB(O_2C_3H_6)$ 3a–g and R^2Li or R^2MgX[a]

R^1	R^2Li or R^2MgX		isolated yield, %	bp, °C/torr	n^{20}_D	^{11}B NMR[b] δ, ppm
n-Bu	*n*-BuLi	**4a**	87	74–76/0.10	1.4568	27.70
n-Hex	*n*-BuLi	**4b**	83	106–108/0.25	1.4580	27.96
Chx	MeLi	**4c**	77	82–84/0.25	1.4845	27.32
3-Cl-1-Pr	*i*-PrMgCl	**4d**	80	86–88/0.20	1.4743	28.00
n-Bu	EtMgBr	**4e**	79	64–66/0.20	1.4566	27.49
n-Bu	*t*-BuLi	**4f**	not isolated			27.56
i-Pr	MeLi	**4g**	74	100–102/22	1.4546	27.37

[a] All of the reactions were done on a 20-mmol scale. All of the compounds were characterized by spectral data. They showed ≥99% stereochemical purity by ^{13}C spectral data. [b] All ^{11}B NMR spectra were taken in $CDCl_3$ and the chemical shift values are relative to $BF_3{\cdot}OEt_2$.

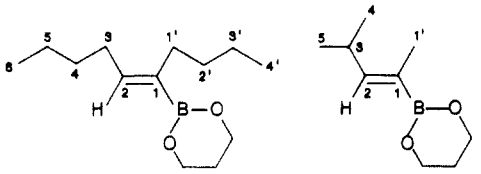
Table IV. Preparation of Ketones, $R^1CH_2COR^2$ 5a–f, by the Oxidation of (*E*)-$R^1CH{=}CR^2B(O_2C_3H_4)$ 4a–f

R^1	R^2	product (compd no.)	yield,[a] %	bp, °C/torr	n^{20}_D
n-Bu	*n*-Bu	5-decanone (**5a**)	(93)[b]		
n-Hex	*n*-Bu	5-dodecanone (**5b**)	87	66–68/0.25	1.4297
Chx	Me	1-cyclohexyl-2-propanone (**5c**)	86	48–50/1.10	1.4575
3-Cl-1-Pr	*i*-Pr	7-chloro-2-methyl-3-heptanone (**5d**)	86	58–60/0.60	1.4456
n-Bu	Et	3-octanone (**5e**)	87	52–54/3	1.4160
n-Bu	*t*-Bu	2,2-dimethyl-3-octanone (**5f**)	(59)[b]	75–77/15[c]	1.4188[c]

[a] All reactions were carried out on a 10-mmol scale. All yields are isolated yields based on pure distilled (*E*)-$R^1CH{=}CR^2B(O_2C_3H_6)$. All compounds showed ≥98% chemical purity by GC analysis. The compounds were characterized by spectral data. [b] Yields given in parentheses are GC yields using *n*-tetradecane. [c] Lit. bp 184–185 °C (745 torr; n^{20}_D 1.4208–1.4219: Whitmore, F. C.; Noll, C. I.; Meunier, V. C. *J. Am. Chem. Soc.* **1939**, *61*, 683.

and distillation. The results are summarized in Table III. These trimethylene esters **4a–f** were oxidized[13] to the corresponding ketones **5a–f** in excellent yields (Table IV).

In two cases (**4a** and **4g**), the corresponding *Z* isomers **9** and **10** were prepared by the hydroboration[14] or 5-decyne and 4-methyl-2-pentyne, respectively. In each pair, the *E* and *Z* isomers were nicely separated by GC with a SE-30 column, the *E* isomer exhibiting a shorter retention time than the *Z* isomer. Within the limit of detection (ca. 0.1%), no isomeric contamination was detected in each compound.



9 **10**

Although a significant difference in the C=C stretching vibration has been reported for a pair of (*E*)- and (*Z*)-(1-methyl-1-propenyl)boronic dibutyl esters (1650 cm^{-1} in the *E* isomer and 1630 cm^{-1} in the *Z* isomer),[5] both **4a** and **9** had the same frequency (1640 cm^{-1}) in this vibration mode. The ^1H NMR, as reported by Matteson,[5] the vinylic proton was more deshielded in the *Z* compound than in its *E* isomer: δ 6.20 in **9** vs. δ 5.87 in **4a**; δ 6.00 in **10** vs. δ 5.73 in **4g**. On the other hand, the allylic proton(s) on C(3) were more deshielded in an *E* compound than its *Z* isomer (the center of multiplets): δ 2.25 in **4a** vs. δ 2.10 in **9** (partially overlapping with the other allylic protons and the central methylene protons of the dioxaborinane ring); δ 2.90 in **4g** vs. δ 2.90 in **10**. These differences might be due to the deshielding effect by the dioxyboryl group located close to the protons, as discussed previously for pairs of isomeric 1-alkenylboronic esters.[3]

In the ^{13}C NMR spectra, the difference in the chemical shifts of C2 between the *E* and *Z* isomers ($\Delta\delta$ $C2_{E-Z}$) was 0.66 ppm in the **4a** and **9** pair and 1.76 ppm in the **4g** and **10** pair. The magnitude is very small and very close to the difference observed in pairs of simple (*E*)- and (*Z*)-1,2-disubstituted-alkenes.[15]

Conclusion

This reaction provides a new access to regio- and stereodefined (*E*)-(1-substituted-1-alkenyl)boronic esters, which can be easily isolated in a pure form. For this transformation, organolithium reagents appear to better tolerate various structural variations than the Grignard reagents, although the latter can be used equally well for the introduction of a primary or a secondary alkyl group. The present approach appears to be especially valuable for the introduction of bulky alkyl groups into the α-position, providing derivatives not available via hydroboration.

The substitution products can be cleanly oxidized to ketones without isolation. Other important synthetic applications may be found in their protonolysis to (*E*)-alkenes,[4] their conversion to stereodefined trisubstituted alkenes,[16,17] their homologation to allylic derivatives,[18,19] and the palladium-catalyzed coupling reactions.[20]

The effect of ester groups revealed in this study might be generally applicable to other boron-assisted nucleophilic subsitution reactions such as organometallic substitution of dichloromethylboronic esters, in which the reported yields of the substitution products are not always satisfactory.[8,21] It is also interesting to note that the addition of methanol quenches any excess of an organometallic reagent remaining in the reaction mixture and thus makes the reaction cleaner. It should be particularly valuable in cases where multialkylation is undesirable.

Summary

1. G. Zweifel introduced an elegant method for the synthesis of (*E*)-alkenes[22] involving hydroboration of 1-bromo-1-alkynes and R_2BH, base-induced migration, and protonolysis. The procedure suffered from the lack of a general procedure for the synthesis of diorganylborane and the loss of one of these groups.

2. The synthesis of R_2BBr by hydroboration, followed by conversion to R_2BH,[23] solved one of these problems; the need for a general synthesis of R_2BH.

3. The use of thexylborane[24] permitted the synthesis of thexylmonoalkylborane for all alkenes other than simple terminal alkenes. This avoided the loss of one of the alkyl groups.

4. The use of thexylmonochloroborane[25] made it possible to synthesize thexylmonoalkylboranes utilizing even the unhindered terminal alkenes.

5. Use of $RBBr_2 \rightarrow RBBrH$[4] avoided the use and then loss of the thexyl group.

6. Finally, the present study utilizes RLi or RMgX to introduce organyl groups that may not be available via hydroboration.

Consequently, our program has achieved making the Zweifel synthesis of *trans*-alkenes general, with complete utilization of the reagents. As mentioned earlier, the intermediate boronic esters produced can be protonolyzed to the *trans*-alkenes,[4] oxidized to ketones,[4] converted into stereodefined trisubstituted olefins,[17] converted into allylic derivatives[18,19] by homologation, and utilized in palladium-catalyzed coupling reactions.[20]

Experimental Section

General Procedures. All of the boiling points are uncorrected. The spectroscopic studies [^1H, ^{13}C, and ^{11}B NMR (all in $CDCl_3$) and IR (all in neat liquid)] were performed with the same instruments described previously.[3] For GC analyses, SE-30 (5%

(12) Brown, H. C.; Bhat, N. G.; Somayaji, V. *Organometallics* **1983**, *2*, 1311.
(13) Brown, H. C.; Scouten, C. G.; Liotta, R. J. *J. Am. Chem. Soc.* **1979**, *101*, 96.
(14) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 389.
(15) Dorman, D. E.; Jautelat, M.; Roberts, J. D. *J. Org. Chem.* **1971**, *36*, 2757.
(16) Brown, H. C.; Bhat, N. G., research in progress.
(17) Personal communication from A. Suzuki.
(18) (a) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529. (b) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. S. *Ibid.* **1983**, *2*, 1536 and references cited therein.
(19) The homologation of boronic esters to α-methoxy derivatives by successive treatment with LiCH(OMe)SPh and $HgCl_2$ [Brown, H. C.; Imai, T. *J. Am. Chem. Soc.* **1983**, *105*, 6285] at present has not been successful with these alkenylboronic esters. The mercury(II) ion seems to attack the double bond of the ate complex intermediate rather than the sulfur (unpublished results).
(20) Suzuki, A. *Acc. Chem. Res.* **1982**, *15*, 178.
(21) Recently, it was reported that such nucleophilic substitution reactions are catalyzed by $ZnCl_2$ and successfully applied for the asymmetric reaction of (+)-pinane dioldichloromethylboronate: Tsai, D. J. S.; Jesthi, P. K.; Matteson, D. S. *Organometallics* **1983**, *2*, 1643.
(22) (a) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086. (b) Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *Ibid.* **1971**, *93*, 6309.
(23) Brown, H. C.; Basavaiah, D. *J. Org. Chem.* **1982**, *47*, 754.
(24) Negishi, E.; Katz, J.-J.; Brown, H. C. *Synthesis* **1972**, 555.
(25) Brown, H. C.; Lee, H. D.; Kulkarni, S. U. *Synthesis* **1982**, 195.

on Chromosorb W, 9 ft × 0.25 in.) was used for boronic esters. The GC analyses of ketones were carried out either on a Varian 1400 gas chromatograph (column 12 ft × $^1/_8$ in. packed with 10% SE-30 on Chromosorb W AW DMCS) or on columns DEGS (20% on Chromosorb W, 8 ft × 0.25 in.) and FFAP (20% on Chromosorb W, 6 ft × 0.25 in.).

Materials. The preparation and characterization of all of the (*Z*)-(1-bromo-1-alkenyl)boronic esters **1a–e** have been described previously.[3] The structures of all **3a–g** have been confirmed by spectral data. All of the organolithiums were purchased and titrated with 1,3-diphenyl-2-propanone (*p*-toluene sulfonyl)-hydrazone.[26] All of the Grignard reagents were purchased from Aldrich. Ether (Mallinckrodt, anhydrous) and *n*-pentane (Phillips) were further dried over molecular sieves (4 Å). Tetrahydrofuran was freshly distilled from benzophenone ketyl solution. All manipulations of the boron compounds were done under nitrogen by using standard procedures.[27]

Isolation of (*E*)-2-(1-Substituted-1-alkenyl)-1,3,2-dioxaborinanes. The following compounds were prepared, all in 20-mmol scale reactions. The procedure described for preparing **4a** is representative. The yields, bp, n^{20}_D, and ^{11}B NMR data are summarized in Table III.

(*E*)-2-(1-Butyl-1-hexenyl)-1,3,2-dioxoaborinane (4a). In a dry, nitrogen-flushed, 250-mL flask equipped with a magnetic stirring bar, a septum inlet was placed a solution of **3a** (20 mmol, 4.94 g) in ether (40 mL), and it was cooled to −78 °C. With stirring, *n*-butyllithium (21 mmol, 9.13 mL) was added slowly through the cold inner surface of the flask in a period of ca. 15 min. After 15 min of stirring, methanol (40 mL) was added over a period of ca. 5 min. Then the cold bath was removed and the mixture was allowed to come to room temperature. The stirring was continued overnight. The solvents are then pumped off and a solution of brine (50 mL) was added. Stirring was continued for half an hour at room temperature. The resulting boronic acid was extracted with ether (3 × 25 mL). The ether extracts were combined, washed, with brine (50 mL), and dried over magnesium sulfate. The ether was removed and the boronic acid was reesterified with 1,3-propanediol (20 mmol, 1.45 mL) in *n*-pentane (50 mL). It was then stirred for an hour at room temperature. The water layer was removed and the pentane layer was dried over magnesium sulfate. Pentane was removed and vacuum distillation furnished **4a** (isomeric purity >99.9%, chemical purity >97% by GC). IR (neat): ν 1400, 1385, 1240, and 700 cm^{-1} (characteristic of the *E* isomer). ^{1}H NMR ($CDCl_3$): δ 0.70–1.05 (m, 6 H, 2 × CH_3), 1.05–1.55 (m, 8 H, 4 × CH_2), 1.75–2.50 (m, 6 H, 2 × allylic CH_2 and dioxaborinane CH_2), 4.00 (t, J = 5.80 Hz, 4 H, 2 × OCH_2), and 5.87 (br t, J = 7.10 Hz, 1 H, vinylic C*H*). ^{13}C NMR ($CDCl_3$): δ 143.50, 61.30, 36.50, 32.80, 32.30, 30.40, 27.50, 22.30, 22.10, 13.80, and 13.70. Mass spectrum: m/e M$^+$ 224.

(*E*)-2-(1-Butyl-1-octenyl)-1,3,2-dioxaborinane (4b). This compound was prepared by the procedure described above from **3b** and *n*-butyllithium. IR (neat): ν 1627, 1206, and 701 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.90 (closed t, 6 H, 2 × CH_3), 1.10–1.50 (m, 12 H, 6 × CH_2), 1.80–2.36 (m, 6 H, 2 × allylic CH_2 and dioxaborinane CH_2), 4.03 (t, J = 5 Hz, 4 H, 2 × OCH_2) and 5.86 (br t, J = 6.20 Hz, 1 H, vinylic C*H*). ^{13}C NMR ($CDCl_3$): δ 143.57, 61.37, 36.51, 32.84, 31.74, 30.76, 30.10, 28.82, 27.53, 22.56, 22.40, and 13.90. Mass spectrum: m/e M$^+$ 252.

(*E*)-2-(1-Methyl-2-cyclohexyl-1-ethenyl)-1,3,2-dioxaborinane (4c) from 3c and Methyllithium. IR (neat): ν 1630, 1225, and 707 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.96–1.76 (m, 13 H, 5 × cyclohexyl CH_2 + CH_3), 1.83–2.20 (m, 2 H, dioxaborinane CH_2), 2.40 (m, 1 H, cyclohexyl CH), 4.01 (t, J = 5 Hz, 4 H, 2 × OCH_2), and 5.73 (d, J = 9 Hz, 1 H, vinylic C*H*). ^{13}C NMR ($CDCl_3$): δ 150.78, 61.49, 39.13, 33.47, 27.48, 26.19, 26.01, and 22.47. Mass spectrum: m/e M$^+$ 208.

(*E*)-2-(5-Chloro-1-isopropyl-1-pentenyl)-1,3,2-dioxaborinane (4d) from 3d and Isopropylmagnesium Chloride. In this case, water was replaced by 2 M aqueous ammonium chloride (50 mL). Other procedures were the same. IR (neat): ν 1628, 1221, and 704 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.00 (d, J = 6.20 Hz, 6 H, 2 × CH_3), 1.63–2.60 (m, 7 H, 2 × CH_2 + allylic CH + dioxaborinane CH_2), 3.51 (t, J = 7 Hz, 2 H, 1 × CH_2-Cl), 4.06 (t, J = 6 Hz, 4 H, 2 × OCH_2), and 5.73 (t, J = 8 Hz, 1 H, vinylic C*H*). ^{13}C NMR ($CDCl_3$): 135.62, 61.59, 44.67, 33.69, 33.14, 28.44, 27.58, and 22.83.

(*E*)-2-(1-Ethyl-1-hexenyl)-1,3,2-dioxaborinane (4e) from 3e and Ethylmagnesium Bromide. The procedure for preparing **4d** is also followed here. IR (neat): ν 1625, 1239, and 703 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.76–1.53 (m, 10 H, 2 × CH_2 + 2 × CH_3), 1.73–2.36 (m, 6 H, 2 × allylic CH_2 and dioxaborinane CH_2), 4.00 (t, J = 6 Hz, 4 H, 2 × OCH_2), and 5.68 (br t, J = 7 Hz, 1 H, vinylic C*H*); ^{13}C NMR ($CDCl_3$): δ 142.74, 61.30, 32.32, 30.33, 29.58, 27.47, 22.11, 14.95, and 13.73. Mass spectrum: m/e M$^+$ 196.

(*E*)-2-(1,3-Dimethyl-1-butenyl)-1,3,2-dioxaborinane (4g) from 3g and Methyllithium. IR (neat): δ 1631, 1222, and 709 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.90 (d, J = 6 Hz, 6 H, 2 × CH_3), 1.68 (s, 3 H, vinylic CH_3), 1.73–2.10 (m, 2 H, dioxaborinane CH_2), 2.90 (m, 1 H, allylic CH_2), 4.03 (t, J = 5 Hz, 4 H, 2 × OCH_2), and 5.73 (d, J = 10 Hz, 1 H, vinylic C*H*). ^{13}C NMR ($CDCl_3$): δ 152.11, 61.44, 29.28, 27.42, 23.39, and 22.32. Mass spectrum: m/e M$^+$ 156.

(*Z*)-2-(1-Butyl-1-hexenyl)-1,3,2-dioxaborinane (9). By the same procedure described previously,[3,11,13] **9** was prepared from 5-decyne (20 mmol) by hydroboration with dibromoborane–dimethyl sulfide (20 mmol) hydrolysis to the boronic acid and esterification with 1,3-propanediol: yield, 85%; bp 88–90 °C (0.20 mm); n^{20}_D 1.4593; isomeric purity > 98% by GC. (The compound isomerizes on long-standing at room temperature.) IR (neat): ν 1640, 1325, and 685 cm^{-1} (characteristic of the *Z* isomer). ^{11}B NMR ($CDCl_3$): δ 27.40. ^{1}H NMR ($CDCl_3$): δ 0.70–1.05 (m, 6 H, 2 × CH_3), 1.05–1.55 (m, 8 H, 4 × CH_2), 1.70–2.3 (m, 6 H, 2 × allylic CH_2 and dioxaborinane CH_2), 3.97 (t, J = 5.7 Hz, 4 H, 2 × OCH_2), 6.20 (t, J = 7.0 Hz, 1 H, vinylic C*H*).

(*Z*)-2-(1,3-Dimethyl-1-butenyl)-1,3,2-dioxaborinane (10). This was prepared by using the literature procedure.[11,13] Yield: 82%; bp 112–114 °C (24 mm); n^{20}_D 1.4616; isomeric purity > 98%; regioisomeric purity 5%. IR (neat): <<v 1628, 1319, and 688 cm^{-1}. ^{11}B NMR ($CDCl_3$): δ 27.47. ^{1}H NMR ($CDCl_3$): δ 0.93 (d, J = 6.5 Hz, 6 H, 2 × CH_3), 1.5–2.10 (m, 5 H, vinylic CH_3 and dioxaborinane CH_2), 2.60 (m, 1 H, allylic C*H*), 4.00 (t, J = 5 Hz, 4 H, 2 × OCH_2), and 6.00 (d, J = 9 Hz, 1 H, vinylic C*H*).

Preparation and Isolation of Ketones 5a–f. The following ketones were prepared all in 10-mmol scale and the yields, bp, and n^{20}_D are summarized in Table IV.

Preparation of 5-Dodecanone (5b) from 4b is Representative. In a dry 100-mL flask were placed 10 mL of tetrahydrofuran and **4b** (10 mmol, 2.50 mL). Then, 3 M sodium hydroxide (10 mmol, 3.30 mL) was introduced into the flask and 30% hydrogen peroxide (10 mmol, 1 mL) was slowly added with vigorous stirring. During the addition, the exothermic reaction was controlled by the rate of addition and water bath cooling. Stirring was continued vigorously for 2 h at room temperature. It was then diluted with water (50 mL) and extracted with ether (3 × 25 mL). The ether extracts were combined, washed with brine (1 × 50 mL), and dried over magnesium sulfate. Filtration, solvent removal at ordinary pressure, and vacuum distillation gave the ketone **5b**; >98% chemical purity by GC. IR (neat): ν 1712 cm^{-1}, (–C(O)–). ^{1}H NMR ($CDCl_3$): δ 0.90 (distorted t, 6 H, 2 × CH_3), 1.10–1.80 (m, 12 H, 2 × CH_2), and 2.40 (distorted t, J = 6 Hz, 4 H, $CH_2C(O)CH_2$). ^{13}C NMR ($CDCl_3$): δ 201.31, 42.69, 42.38, 31.63, 29.19, 29.02, 25.96, 23.85, 22.53, 22.30, 13.87, and 13.68. Mass spectrum: m/e M$^+$ 184.

1-Cyclohexyl-2-propanone (5c). IR (neat): δ 1712 cm^{-1} (–C(O)–). ^{1}H NMR ($CDCl_3$): δ 1.03–1.93 (m, 11 H, cyclohexyl ring protons), 2.10 (s, 3 H, –C(O)C*H*$_3$), and 2.30 (d, J = 5 Hz, 2 H –C(O)C*H*$_2$C$_6$H$_{11}$). ^{13}C NMR ($CDCl_3$): δ 204.14, 51.35, 33.90, 33.19, 30.27, 26.19, 26.06, and 25.55. Mass spectrum: m/e M$^+$ 140.

7-Chloro-2-methyl-3-heptanone (5d). IR (neat): ν 1708 cm^{-1} (–C(O)–). ^{1}H NMR ($CDCl_3$): δ 1.10 (d, J = 6.50 Hz, 6 H, 2 × CH_3), 1.60–1.96 (m, 4 H, 2 × CH_2), 2.33–2.83 (m, 3 H, $CH_2C(O)$– and >CH), and 3.53 (distorted t, 2 H, 1 × CH_2Cl). ^{13}C NMR C(O)–($CDCl_3$): δ 198.79, 44.62, 40.72, 39.19, 32.11, 21.11, and 18.18.

3-Octanone (5e). IR (neat): ν 1714 cm^{-1} (–C(O)–). ^{1} HNR ($CDCl_3$): δ 0.90–1.80 (m, 12 H, 2 × CH_3 + 3 × CH_2) and 2.20–2.60

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(m, 4 H, $CH_2C(O)CH_2$). ^{13}C NMR ($CDCl_3$): δ 210.57, 42.38, 35.79, 31.46, 23.64, 22.42, 13.81, and 7.80. Mass spectrum: *m/e* M^+ 128.

2,2-Dimethyl-3-octanone (5f). IR (neat): δ 1705 cm^{-1} (–C(O)–). ^1H NMR ($CDCl_3$): δ 0.90 (distorted t, 3 H, 1 × CH), 1.16 (s, 9 H, 1 × $C(CH_3)_3$, 1.23–2.00 (m, 6 H, 3 × CH_2), and 2.46 (t, J = 7 Hz, 2 H, $CH_2C(O)$–). ^{13}C NMR ($CDCl_3$): δ 196.57, 44.01, 36.36, 31.54, 26.37, 23.61, 22.51, and 13.84. Mass spectrum: *m/e* M^+ 156.

Pheromones via Organoboranes. 2. Vinylic Organoboranes. 8. Applications of the General Stereoselective Synthesis of (*E*)-Disubstituted Alkenes via Thexylchloroborane–Dimethyl Sulfide to the Synthesis of Pheromones Containing an (*E*)-Alkene Moiety

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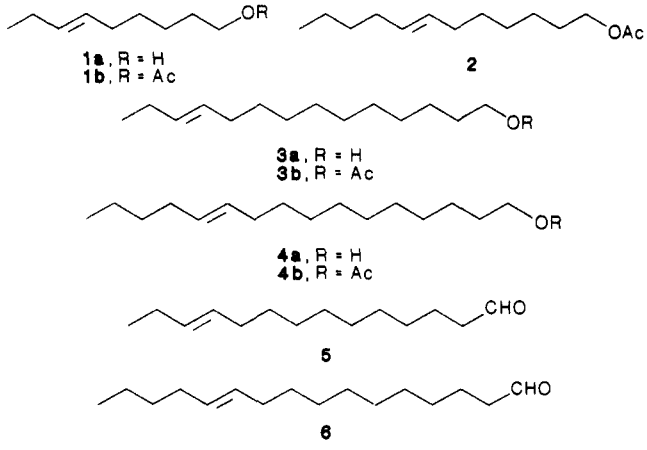
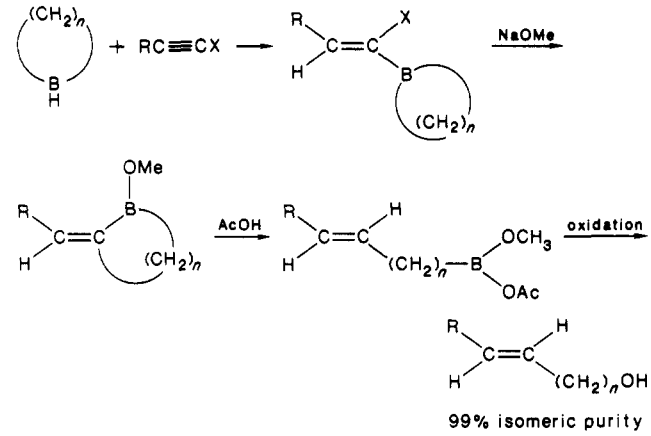
Various (*E*)-pheromones of the general structures (*E*)-X-alken-1-yl acetates, (*E*)-X-alken-1-ols, and (*E*)-X-alken-1-als have been prepared via thexylchloroborane–dimethyl sulfide (ThxBHCl·SMe_2). Hydroboration of acetate-functionalized alkenes with ThxBHCl·SMe_2 gives cleanly the corresponding thexylalkylchloroboranes (ThxBRCl, B). Hydridation of B with potassium triisopropoxyborohydride (KIPBH) at –78 °C gives cleanly the corresponding thexylalkylboranes (ThxBRH, C). These are quenched immediately with 1-halo-1-alkynes to give *B*-(*cis*-1-halo-1-alkenyl)thexylalkylboranes (D). Treatment of D with sodium methoxide results in the displacement of bromine by the alkyl group on boron to produce *B*-(*trans*-1-alkyl-1-alkenyl)thexylborinates (E). Protonolysis of E with acetic acid provides (*E*)-X-alken-1-yl acetates in high yields and in >99% isomeric purities. Treatment of (*E*)-X-alken-1-yl acetates with base affords the corresponding (*E*)-X-alken-1-ols. Oxidation of (*E*)-X-alken-1-ols with dimethyl sulfoxide activated by oxalyl chloride or the complex of dimethyl sulfide and chlorine produces (*E*)-X-alken-1-als quantitatively. By properly choosing the starting functionalized alkenes and 1-halo-1-alkynes, various (*E*)-pheromones can be prepared easily. The present procedure appears to be general. There does not appear to be any limitation on the length of the carbon chain or the position of the double bond in the target molecules.

Many sex pheromones produced by moth and butterfly species (Lepidoptera) are straight-chain functionalized (*E*)-alkenes[2] of the general structures (*E*)-X-alken-1-ols, (*E*)-X-alken-1-yl acetates, or (*E*)-X-alken-1-als. Examples are (*E*)-6-nonen-1-ol (**1a**) from the male Mediterranean fruitfly (*Ceratitis capitata*),[3a] (*E*)-6-nonen-1-yl acetate (**1b**),



Scheme I



the attractant for the female melonfly (*Daucus cucurbitae*),[3b] (*E*)-7-dodecen-1-yl acetate (**2**) from the female false coddling moth (*Cryptophlebia leucotreta*),[3c] (*E*)-11-tetradecen-1-ol (**3a**) and its corresponding acetate (**3b**) from

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