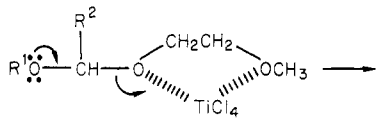
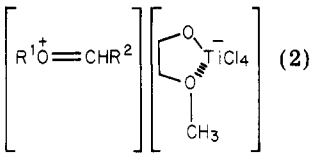
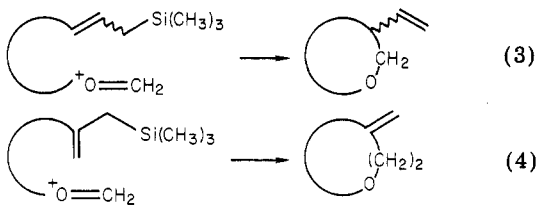


i



(2)

ii



(3)

(4)

Hydroxyallylsilanes (**3**, **6**, and **9**)[5] were converted to MEM-substituted allylsilanes (**4**, **7**, and **10**, respectively) by reaction of the corresponding lithio derivatives[6] of the hydroxy allylsilanes with (2-methoxyethoxy)methyl chloride in tetrahydrofuran (at ambient temperature for 5 h for **3** and **9** and at 0 °C for 1 h for **6**). The MEM-substituted allylsilanes were treated with 1.1 equiv of titanium tetrachloride in dichloromethane at −50 to −78 °C[7] for 30 min to give the tetrahydrofuran derivative **5** or the tetrahydropyran derivatives **8** and **11** in good yields, respectively.[8]

Registry No. 1a, 81616-92-4; (*E*)-**1b**, 81616-93-5; (*Z*)-**1b**, 81616-94-6; **1c**, 81616-95-7; **1d**, 81616-96-8; **1e**, 81616-97-9; **1f**, 81616-98-0; **3**, 81616-99-1; **4**, 81617-00-7; **5**, 81617-01-8; **6**, 81617-02-9; **7**, 81617-03-0; **8**, 81617-04-1; **9**, 81617-05-2; **10**, 81617-06-3; **11**, 81617-07-4; **12**, 81617-08-5; $TiCl_4$, 7550-45-0; trimethyl-2-propenylsilane, 762-72-1; trimethyl-2-butenylsilane, 18292-28-9; [2-(3-butenyloxy)ethyl]-benzene, 81617-09-6; [2-(2-methyl-3-butenyloxy)ethyl]benzene, 81617-10-9; 1-(3-butenyloxy)-4-(1,1-dimethylethyl)cyclohexane, 81617-11-0; 1-(2-methyl-3-butenyloxy)-4-(1,1-dimethylethyl)cyclohexane, 81617-12-1; 4-ethoxy-1-pentene, 81617-13-2; 4-ethoxy-3-methyl-1-pentene, 81617-14-3; 2-(2-propenyl)-5-hexyltetrahydrofuran, 81617-15-4; 1-(2-propenyl)-1,3-dihydroisobenzofuran, 81617-16-5; 2-(2-propenyl)-2,3-dihydro-4*H*-1-benzopyran, 81617-17-6.

(4) For cyclization using alkenylsilanes or alkynylsilanes see the following. Cation induced: Fleming, I.; Pearce, A.; Snowden, R. L. *J. Chem. Soc., Chem. Commun.* **1976**, 182. Sarkar, T. K.; Anderson, A. *Tetrahedron Lett.* **1978**, 3513. Uchimoto, K.; Tanaka, M.; Kitani, M.; Nozaki, H. *Ibid.* **1978**, 2301. Johnson, W. S.; Yarnell, T. M.; Myers, R. F.; Morton, D. R. *Ibid.* **1978**, 2549. Kuwajima, I.; Tanaka, T.; Atsumi, K. *Chem. Lett.* **1979**, 779. Itoh, A.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1979**, 1783. Hughes, L. R.; Schmid, R.; Johnson, W. S. *Bioorg. Chem.* **1979**, *8*, 513. Overman, L. E.; Bell, K. L. *J. Am. Chem. Soc.* **1981**, *103*, 1851. Brinkmeyer, R. S. *Tetrahedron Lett.* **1979**, 207. Trost, B. M.; Murayama, E. *J. Am. Chem. Soc.* **1981**, *103*, 6529. Fluoride anion induced: Ito, Y.; Nakatsuka, M.; Saegusa, T. *Ibid.* **1980**, *102*, 863. Trost, B. M.; Vincent, J. E. *Ibid.* **1980**, *102*, 5680. Djuric, S.; Sarkar, T.; Magnus, P. *Ibid.* **1980**, *102*, 6885. Ito, Y.; Nakatsuka, M.; Saegusa, T. *Ibid.* **1981**, *103*, 476.

(5) The hydroxyallylsilanes (**3**, **6**, and **9**) were readily prepared by reaction of the corresponding Grignard reagents derived from (2- or 3-bromoallyl)trimethylsilanes and 1-octene oxide, styrene oxide, and cyclohexene oxide in the presence of cuprous iodide, respectively. See: Nishiyama, H.; Narimatsu, S.; Itoh, K. *Tetrahedron Lett.* **1981**, 5289. Nishiyama, H.; Yokoyama, H.; Narimatsu, S.; Itoh, K. *Ibid.* **1982**, 1267.

(6) The lithio derivatives were prepared in situ by treatment of the hydroxyallylsilanes with *n*-butyllithium (1.5 N in hexane) in tetrahydrofuran at −50 °C.

(7) Treatment of **10** with titanium tetrachloride at −20 °C gave double bond isomeric product **12** in 86% yield.

12

(8) All compounds reported showed ^1H NMR, IR, and mass spectra consistent with the assigned structure. Characterization data for **5**, **8**, and **11** are as follows. **5**: ^1H NMR (60 MHz, $CDCl_3$) δ 0.92 (t, 3 H), 1.2–1.6 (m, 12 H), 2.8 (m, 1 H), 3.3–4.0 (m, 3 H), 4.8–6.1 (m, 3 H, vinylic); IR (film) 1640 cm^{-1}; MS *m/e* 183 (M + 1), 126, 98, 30 (base peak). **8**: ^1H NMR (60 MHz, $CDCl_3$) δ 2.37 (t, 2 H), 3.6–4.2 (m, 5 H), 4.43 (s, 1 H, olefinic), 4.80 (s, 1 H, olefinic), 7.2 (5 H); IR (film) 1656 cm^{-1}; MS *m/e* (175 (M + 1), 130 (base peak). **11**: ^1H NMR (60 MHz, $CDCl_3$) δ 1.2–2.9 (m, 11 H), 3.5 (dt, 2 H), 4.1 (m, 1 H), 4.57 (s, 1 H, olefinic), 4.70 (s, 1 H, olefinic); Ir (film) 1650 cm^{-1}; MS *m/e* 153 (M + 1), 74 (base peak).

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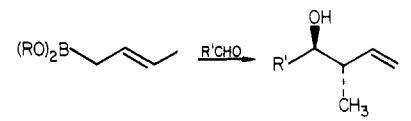
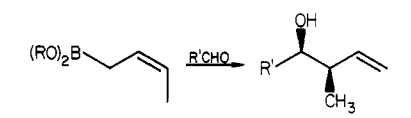
(γ-Alkoxyallyl)boronates as Useful Reagents for Preparation of Differentially Protected Diol Derivatives

Summary: The preparation of (γ-alkoxyallyl)boronates and their reactions with aldehydes to form mono protected threo 1,2-diol derivatives is described.

Sir: Aldol[1] and related condensation reactions[2] which proceed with a high degree of diastereoselection are of fundamental importance in the synthesis of macrolide[3] and ionophore[4] antibiotics. Among such condensation reactions are stereoselective allylboronate condensations with aldehydes which afford homoallylic alcohols (eq 1).[2] Re-



(1a)



(1b)

actions of this type have an advantage over aldol condensations in that the newly formed alkenes may more readily be transformed to aldehydes and that the alkenes may be selectively epoxidized, thus readily introducing a third chiral center.

An interest in highly oxygenated natural products such as the macrolides and ionophores led us to explore (γ-

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(2) Mikhailov, B. M. *Organomet. Chem. Rev., Sect. A* **1965**, *8*, 1. Hoffmann, R. W.; Zeiss, H. J. *Angew Chem.* **1979**, *91*, 329. Hoffmann, R. W.; Zeiss, U. J. *J. Org. Chem.* **1981**, *46*, 1309. Brown, H. C.; De Leu, N. R. *Ibid.* **1977**, *42*, 4088. Blais, J.; L'Honore, A.; Soulie, J.; Cadiot, P. *J. Organomet. Chem.* **1974**, *78*, 323. Herald, T.; Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 768. Hoffmann, R. W.; Feussner, C.; Zeiss, M. J.; Schultz, S. *J. Organomet. Chem.* **1980**, *187*, 321. Buse, C. T.; Heathcock, C. H. *Tetrahedron Lett.* **1978**, 1685. Okude, Y.; Hirano, S.; Hiyama, T.; Nazaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179. Sato, F.; Ijima, S.; Sato, M. *Tetrahedron Lett.* **1981**, 243.

(3) Masamune, S.; Choy, W.; Kevdesky, F. A. J.; Imperiali, B. *J. Am. Chem. Soc.* **1981**, *103*, 1566.

(4) Van Horn, D. E.; Masamune, S. *Tetrahedron Lett.* **1979**, 2229.

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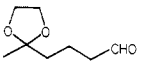
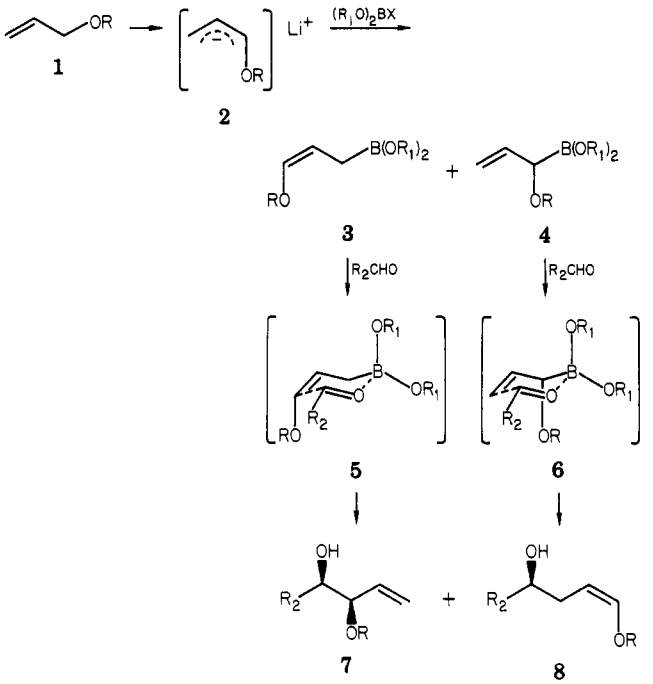
Table I. Reactions of (γ-Alkoxyallyl)boronates

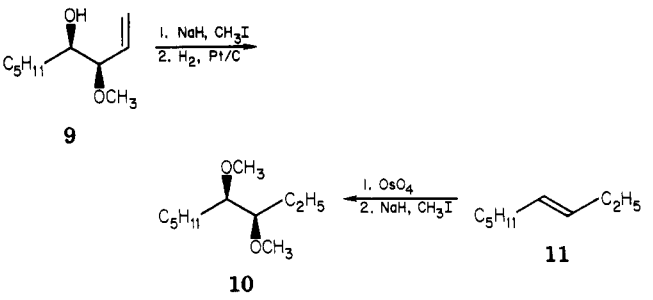
entry	R	R_1	X	R_2	% yield[a] 7	% yield[a] 8	ratio of 7/8
1	CH_3	$(CH_2)_3$	Cl	Ph	95	0	
2	CH_3	C_4H_9	F	n-C_5H_{11}	65	0	
3	CH_3	C_4H_9	F	$AcOCH_2CH_2$	59	0	
4	MEM	$CH_2C(CH_3)_2CH_2$	Cl	Ph	59	0	
5	THP	$(CH_2)_3$	Cl	Ph(E)-PhCH=CH	76	13	5.9:1
6	Ph	CH_3	F	t-BuCH=CH	73	10	7.3:1
7	Ph	CH_3	F	$(CH_3)_2CH$	72	24	3:1
8	Ph	$(CH_2)_3$	Cl	Ph	69	21	3.3:1
9	Ph	C_4H_9	F		50	27	1.85:1
10	Ph	$CH_2C(CH_3)_2CH_2$	Cl	Ph	80	17	4.7:1
11	Ph	C_4H_9	F	n-C_5H_{11}	61	17	3.5:1

[a] Yields refer to isolated chromatographically pure material.[12]

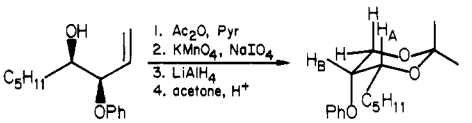
Scheme I



Scheme II



Scheme III. Stereochemical Proof



alkoxyallyl)boronates **3** as possible intermediates for stereoselective formation of 1,2-diol derivatives **7**.[5] The proclivity of allyl ether anions to react predominantly at the γ-position with exclusive formation of (*Z*)-vinyl ethers upon reaction with various electrophiles[6] led to their application in the synthesis of the requisite stereodefined (γ-alkoxyallyl)boronates **3**. Thus, alkylation of allyl ether anions **2** with haloboronate esters[7] gave the desired allylboronates **3** (Scheme I). Unfortunately, phenyl and tetrahydropyranyl ethers also gave regioisomeric (α-alkoxyallyl)boronates **4** (Table I, entries 5–10) which is in keeping with the observations of Evans that the site of alkylation is partially dependent upon the nature of the ether function.[6] Attempts to improve the diol to vinyl ether ratios by thermal isomerization of the (α- and γ-alkoxyallyl)boronate mixture were unsuccessful due to decomposition. The Z stereochemistry was firmly established by examination of the NMR spectrum of boronate **3** (R = CH_3, R_1 = $CH_2C(CH_3)_2CH_2$) which exhibited a cis coupling constant of 6 Hz. In general, allylboronates were not isolated but treated directly with aldehydes to give diol derivative **7** and vinyl ether **8** which were readily separated by flash chromatography.

From Table I it is clear that the reaction is compatible with a variety of functional groups and a variety of allyl ethers. Silyl and benzyl ethers, however, fail due to Brook[8] and Wittig[9] rearrangements of their respective anions.

With regard to the stereochemistry of the diols and vinyl ether derivatives, both may be produced by the pericyclic transition states **5** and **6** illustrated in Scheme I. The threo relationship of diols was established by transformation of methoxy alcohol **9** (Table I, entry 2) to diether **10** with NaH, CH_3I followed by hydrogenation (Scheme II). Comparison of the carbon-13 and proton NMR and IR spectra of this material with those of an authentic sample prepared from (*Z*)-3-nonene (**11**) by OsO_4 oxidation and ether formation clearly indicated the threo stereochemistry.

The threo relationship was alternatively established by conversion of alcohol **12** (Table I, entry 11) to acetonide **13** by the indicated transformations (Scheme III). Careful examination of a series of decoupled 360-MHz NMR

(5) For an independent and related study see: Hoffmann, R. W.; Kemper, B. *Tetrahedron Lett.* **1980**, 4883.

(6) Still, W. C.; McDonald, T. C. *J. Am. Chem. Soc.* **1974**, *96*, 5563. Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560.

(7) Chloroboronate ester preparation: Balu, J. A.; Gerrard, W.; Luppert, M. F. *J. Chem. Soc.* **1957**, 4116. Fluoroboronates were prepared by a redistribution reaction of the ester and BF_3-Et_2O: Cook, H. C.; Ilatt, J. O.; Saunders, B. C.; Starey, G. J. *Ibid.* **1950**, 3125.

(8) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77.

(9) Wittig, G.; Lõhmann, L. *Justus Liebigs Ann. Chem.* **1942**, *550*, 260.

spectra resulted in a 5.6-Hz coupling constant for J_{ab} which is in accord with the threo stereochemistry. Diastereoface selection was >95% in every case as determined by 360-MHz NMR.

The *Z* stereochemistry of vinyl ethers **8** was established by the 5–6-Hz coupling constants for their vinyl protons.[10] The rather unexpected *Z* stereochemistry implies as axial OR group in transition-state **6**. The axial orientation is attributed to a reduced gauche interaction between OR and OR_1 in the transition state with an axial substituent as opposed to its equatorial counterpart.[11]

In conclusion, we have developed a stereospecific diol synthesis with concomitant C–C bond formation. Efforts are now underway to apply this methodology in macrolide synthesis and carbohydrate synthesis.

Acknowledgment. We express our appreciation to the University of Michigan, The Rackman School of Graduate Studies, the National Institutes of Health, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. The 360-MHz NMR instrument was purchased with the aid of a National Science Foundation Instrumentation Grant.

(10) Jackman, L. M.; Sternhall, S. "Applications of Nuclear Magnetic Resonance Spectroscopy"; Pergamon Press: New York, 1969.
(11) Hoffmann, R. W.; Weidmann, U. *J. Organomet. Chem.* **1980**, *195*, 137.
(12) All new compounds gave satisfactory analytical data (±0.4%) and infrared and NMR spectra.

Registry No. **7** (R = CH_3; R_2 = Ph), 81656-05-5; **7** (R = CH_3; R_2 = $AcOCH_2CH_2$), 81656-06-6; **7** (R = $CH_2OCH_2CH_2OMe$; R_2 = Ph), 81656-07-7; **7** (R = THP; R_2 = Ph), 81656-08-8; **7** (R = Ph; R_2 = PhCH=CH), 81656-09-9; **7** (R = Ph; R_2 = $(CH_3)_2CH$), 81656-10-2; **7** (R = R_2 = Ph), 81656-11-3; **7** (R = Ph; R_2 = $\overline{OCH_2CH_2OC}(Me)(CH_2)_3$), 81656-12-4; **8** (R = THP; R_2 = Ph), 81656-13-5; **8** (R = Ph; R_2 = PhCH=CH), 81671-25-2; **8** (R = Ph; R_2 = $(CH_3)_2CH$), 81656-14-6; **8** (R = R_2 = Ph), 81656-15-7; **8** (R = Ph; R_2 = $\overline{OCH_2CH_2OC}(Me)(CH_2)_3$), 81656-16-8; **8** (R = Ph; R_2 = C_5H_{11}, 81671-26-3; **9**, 81656-17-9; **10**, 81656-18-0; **11**, 20237-46-1; **12**, 81656-19-1; **13**, 81656-20-4; 2-chloro-1,3-dioxa-2-boracyclohexane, 1003-43-6; benzaldehyde, 100-52-7; allyl methyl ether, 627-40-7; hexanal, 66-25-1; 3-acetoxypropanal, 18545-28-3; MEM allyl ether, 77120-79-7; 5,5-dimethyl-1,3-dioxa-2-chloroboracyclohexane, 81656-21-5; tetrahydropyranyl allyl ether, 4203-49-0; phenyl allyl ether, 1746-13-0; *trans*-cinnamaldehyde, 14371-10-9; isobutyraldehyde, 78-84-2; 2-bora-5,5-dimethyl-2-fluoro-1,3-dioxane, 81656-22-6; 2-methyl-2-(3-formylpropyl)-1,3-dioxacyclopentane, 42991-09-3; (3*R**,4*R**)-3,4-dihydroxynonane, 81656-23-7; (*E*)-3-nonene, 20063-92-7; (3*R**,4*R**)-3,4-dimethoxynonane, 81656-18-0; (3*R**,4*R**)-3,4-dimethoxynon-1-ene, 81656-24-8; (5*R**,6*R**)-2,2-dimethyl-6-pentyl-5-phenoxy-1,3-dioxacyclohexane, 81656-20-4; $(n\text{-BuO})_2BF$, 462-19-1; $(CH_3O)_2BF$, 367-46-4.

Supplementary Material Available: Full experimental details for all new compounds (12 pages). Ordering information is given on any current masthead page.

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