of other ketones revealed a trend of decreasing asymmetric induction with increasing size of the alkyl group. These results as well as results for other ketones are presented in Table I.

The reduction products were generally isolated in 70–80% yield. In most cases the *S* alcohol was obtained. Thus the reduction occurs as depicted in eq 2 with the sterically larger group occupying the phenyl position. In the case of α,α,α-trifluoroacetophenone and 4-heptyn-3-one the *R* enantiomer is produced since the priorities of the sterically small and large groups are reversed. (However, with 4-phenyl-3-butyn-2-one the reduction does occur in the opposite steric sense.) The hydride thus gives the opposite configuration of that obtained with the corresponding borane. Thus the NB-Enantride gives (*S*)-phenylethanol while the Alpine-borane prepared from (−)-α-pinene would give the *R* enantiomer.[12]

The following procedure is typical. An oven-dried, 50-mL, round-bottomed flask equipped with a septum-capped side arm, magnetic stirring bar, reflux condenser, and stopcock adaptor connected to a mercury bubbler was assembled while hot and flushed with a stream of nitrogen. Then 10.64 mL (5 mmol) of a 0.47 M THF solution of 9-BBN was added by a syringe followed by a solution of 1.408 g (5.5 mmol) of nopol benzyl ether in 5 mL of THF. The solution was refluxed overnight and cooled to a room temperature, and 5 mL of dry diethyl ether and 5 mL of dry pentane were added. The mixture was cooled to −78 °C (dry ice–acetone bath), and 3.95 mL (5 mmol) of a 1.27 M pentane solution of *tert*-butyllithium was introduced dropwise. The resulting slightly yellow solution was stirred for 0.5 h at −78 °C, and then it was added dropwise by using a double-ended needle.[13] to a solution of 0.577 g (4.5 mmol) of 2-octanone in 40 mL of a THF/Et_2O/pentane (4:1:1) mixture in a 100 mL reaction flask cooled to −100 °C [petroleum ether (30–60 °C)/isopropyl alcohol/acetone (4:1:1)/liquid N_2 bath].[14] After the addition, the reaction mixture was stirred at −100 °C for 3 h. The excess of hydride was then destroyed by an addition of 1-mL of ethanol, and the solution was brought to the room temperature. The organoborane was oxidized (1.7 mL of 3 M sodium hydroxide, 1.2 mL of 30% hydrogen peroxide, 1 h at 40–50 °C) and the mixture saturated with anhydrous potassium carbonate. The organic phase was separated, the aqueous phase was extracted with ether, and the combined extracts were dried over anhydrous potassium carbonate. After evaporation of the solvents, the crude mixture was partially purified by Kugelrohr distillation (pot temperature 140 °C, 2.5 mm) and finally by column chromatography[15] over silica gel (70–200 mesh) with hexane/ether (5:1). Thus 0.446 g (76% yield) of 2-octanol [bp 80 °C (27 mm, Kugelrohr distillation); $[\alpha]^{25}_D$ +7.33° (neat, d = 0.838) [lit.[16] $[\alpha]^{25}_D$ +9.57° (neat)]] was obtained. Examination of the NMR specturm in the presence of tris(dicampholylmethanato)europium(III) [Eu(dcm)$_3$][17] indicated an enantiomeric mixture of 89.5% *S* and 10.5% *R* (79% ee).[18]

In conclusion, NB-Enantride is a new and very attractive reducing agent for the asymmetric reductions of ketones. Its high efficiency in the case of straight-chain aliphatic ketone reductions is noteworthy. The cause of this remarkable selectivity remains to be explored.

Editor's Note: This paper was originally scheduled to appear in the April 9, 1982 issue along with the communication by Brown and Pai (ref 12). Due to an error in our office, this did not occur. We apologize for the delay in publication.

Acknowledgment. We thank the National Institutes of Health (Grant No. GM-24517) for support of this work. We thank Professor R. Noyori for data on the absolute configuration of β-ionol and Professors J. D. Morrison and H. S. Mosher for calling our attention to the structure of nopol. NB-Enantrane, NB-Enantride, Alpine-borane, Alpine-hydride, and L-Selectride are trademarks of Aldrich Chemical Company.

Registry No. 1, 74851-17-5; 3, 81572-37-4; (*S*)-1-phenylethanol, 1445-91-6; (*R*)-α-(trifluoromethyl)benzyl alcohol, 10531-50-7; (*S*)-1-phenyl-1-butanol, 22135-49-5; (*S*)-β-ionol, 81600-95-5; (*R*)-4-heptyn-3-ol, 81555-85-3; (*S*)-4-phenyl-3-butyn-2-ol, 81555-86-4; (*S*)-3,3-dimethyl-2-butanol, 1517-67-5; (*S*)-4-methyl-2-pentanol, 14898-80-7; (*S*)-3-methyl-2-butanol, 1517-66-4; (*S*)-2-butanol, 4221-99-2; (*S*)-2-octanol, 6169-06-8; acetophenone, 98-86-2; α,α,α-trifluoroacetophenone, 434-45-7; butyrophenone, 495-40-9; β-ionone, 14901-07-6; 4-heptyn-3-one, 32398-68-8; 4-phenyl-3-butyn-2-one, 1817-57-8; 3,3-dimethyl-2-butanone, 75-97-8; 7-methyl-2-pentanone, 108-10-1; 3-methyl-2-butanone, 563-80-4; 2-butanone, 78-93-3; 2-octanone, 111-13-7; nopol, 35836-73-8; nopol phthalate, 81555-87-5; nopol phthalate (−)-α-methylbenzylamine, 81601-67-4; 9-BBN, 280-64-8.

(12) Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1982**, *47*, 1606. We thank Professor Brown for informing us of his results prior to publication.
(13) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Organoboranes"; Wiley: New York, 1975; Chapter 9.
(14) Köbrich, G.; Trapp, H. *Chem. Ber.* **1966**, *99*, 680.
(15) In the case of low-boiling alcohols, distillation under atmospheric pressure was used. The alcohol was then purified by preparative gas chromatography.
(16) Cristol, S. J.; Franzus, B.; Shadan, A. *J. Am. Chem. Soc.* **1955**, *77*, 2512.
(17) McCreary, M. D.; Lewis, D. W.; Wernick, D. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 1038.
(18) When unpurified nopol was used, material of 66% ee was obtained.
(19) Alfred P. Sloan Foundation Fellow, 1978–1982.

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Reaction of 2-Methoxyethyl Hemiacetals with Allylsilanes in the Presence of Titanium Tetrachloride: Regioselective C–O Bond Cleavage of the Unsymmetrical Acetals

Summary: Reaction of 2-methoxyethyl hemiacetals with allylsilanes in the presence of titanium tetrachloride gave the corresponding homoallyl ethers in good yields by the regioselective C–O bond cleavage of the hemiacetals. A new carbon-homologative cyclization was described as an application of this selective reaction. Furthermore, the information obtained from this study made clear the exact mode of the cleavage of (2-methoxyethoxy)methyl (MEM) ether; titanium tetrachloride should facilitate the elimination of the methoxyethoxy group from the MEM ether by an effective bidentate chelation.

Sir: It has been elaborated considerably that symmetrical acetals react with allylsilanes in the presence of Lewis acids to give homoallyl ethers.[1] We report here the regiose-

(1) (a) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941. (b) Hosomi, A.; Endo, M.; Sakurai, H. *Ibid.* **1978**, 499. (c) Ojima, I.; Kumagai, M. *Ibid.* **1978**, 575. (d) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, 71.

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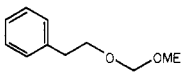
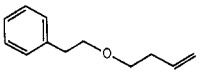
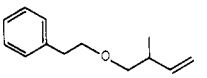
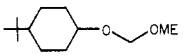
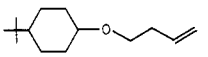
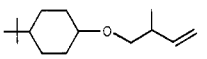
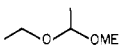
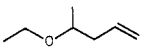
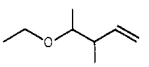
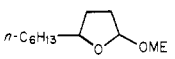
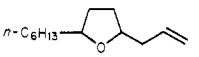
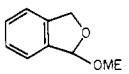
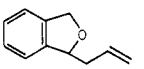
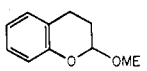
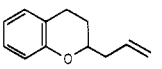
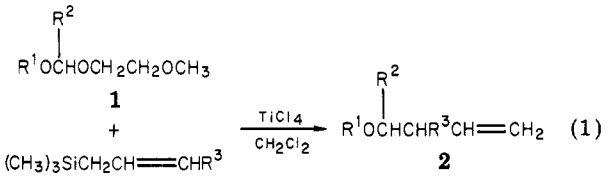
Table I. Reaction of 2-Methoxyethyl Hemiacetals with Allylsilanes in the Presence of Titanium Tetrachloride

acetal[a,f]	allylsilane[b] type	allylsilane[b] equiv[c]	$TiCl_4$, equiv[c]	product	% yield[d]
 1a	A	1.3	1.2		93
	B	1.3	1.2		94
 1b (*Z* and *E*)	A	1.3	1.2		95
	B	1.3	1.2		96
 1c	A	1.5	1.3		86[e]
	B	1.5	1.3		90[e]
 1d	A	1.3	1.2		96
 1e	A	1.5	1.3		90
 1f	A	1.5	1.3		90

[a] 0.5 mmol. [b] A = $(CH_3)_3SiCH_2CH{=}CH_2$, B = $(CH_3)_3SiCH_2CH{=}CHCH_3$. [c] Equimolar amount of the acetal. [d] Isolated yield. [e] Determined by ^1H NMR. [f] ME = $CH_3OCH_2CH_2$.

lective cleavage of unsymmetrical acetals in the reaction of 2-methoxyethyl hemiacetals with allylsilanes promoted by titanium tetrachloride. Application of the selective cleavage for a new carbon-homologative etherification or cyclization was also described and the exact mode of the cleavage of (*2-methoxyethoxy*)*methyl* (MEM) ether[2] as a protecting group of alcohols are here clarified.

To a solution of 2-methoxyethyl (ME) hemiacetal 1[3] (0.5 mmol) and allylsilane (0.75 mmol) in anhydrous dichloromethane (3 mL) was added dropwise titanium tetrachloride (0.6 mmol) at −20 °C (eq 1). The mixture was



(1)

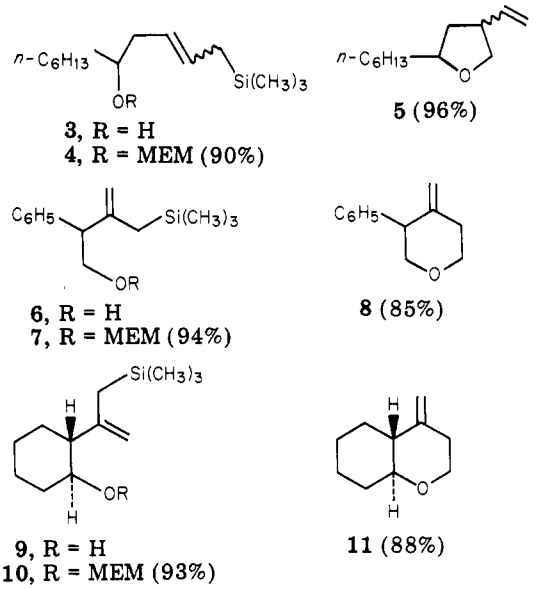
stirred for 30 min, was treated with aqueous sodium bicarbonate, and was extracted with ether (30 mL). The extract was concentrated, and the residual oil was purified by silica gel column chromatography to give the corresponding homoallyl ether 2 in high yield (Table I).

The selective elimination of the 2-methoxyethoxy group was nicely accounted for the effective bidentate coordination of the 2-methoxyethoxy group to the titanium atom to form the oxonium species ii (eq 2), which spontaneously caused electrophilic attack on the allylsilanes.

Thus, we have found a regioselective C–O bond cleavage reaction of the unsymmetric acetals having a 2-methoxyethyl group as a leaving group. This reaction with allylsilanes will serve as a new synthetic method for *carbon-homologative etherification* of alcohols.

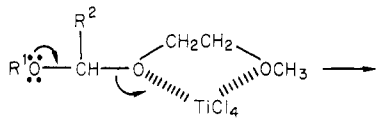
As an application of this reaction, a new method of oxonium ion–allylsilane cyclization for forming an oxacyclic ring was demonstrated[4] (eq 3 and 4).

Chart I

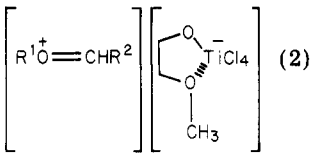


(2) Corey, E. J.; Gras, J.-L.; Ulrich, P. *Tetrahedron Lett.* **1976**, 809.

(3) The 2-methoxyethyl hemiacetals were prepared by Corey's method for **1a** and **1b**, by reaction of ethyl vinyl ether and 2-methoxyethyl alcohol in the presence of *p*-toluenesulfonic acid for **1c**, and by reaction of the corresponding hemiacetals and 2-methoxyethyl alcohol in the presence of boron trifluoride etherate for **1d–f**; see: Corey, E. J.; Noyori, R. *Tetrahedron Lett.* **1970**, 331. Sandler, S. R.; Karo, W. "Organic Functional Group Preparations" Academic Press: New York, 1972; Vol. III, pp 1–75.

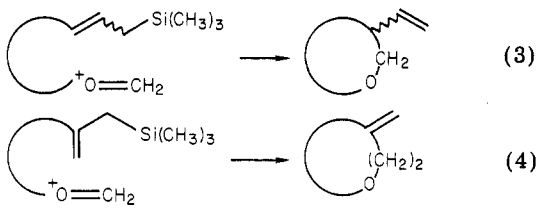


i



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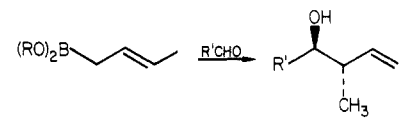
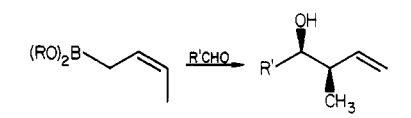
(γ-Alkoxyallyl)boronates as Useful Reagents for Preparation of Differentially Protected Diol Derivatives

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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