cooled to −20 °C again, and NaOMe (290 mmol, freshly prepared) in MeOH (150 mL) was added dropwise with vigorous stirring, maintaining the temperature below −15 °C. The mixture was allowed to warm to 20 °C, and water (100 mL) was added. The layers were separated, and the aqueous phase was extracted with methylene chloride (2 × 25 mL). The combined organic extracts were dried (Na_2SO_4), concentrated, and distilled. After a considerable low-boiling forerun, bromodecene **6a** (9.35 g, 71%), bp 56–57 °C (0.8 torr), was obtained, contaminated with 5% of two isomeric products: ^{1}H NMR ($CDCl_3$) δ 6.11 (dt, 1 H, J = 6.9, 1.3 Hz, H-1), 6.06 (dt, 1 H, J = 6.9, 6.9 Hz, H-2), 2.17 (tdd, 2 H, J = 6.9, 6.9, 1.3 Hz, H-3), 1.40 (m, 2 H, H-4), 1.32–1.20 (m, 10 H, H-5–H-9), 0.86 (t, 3 H, J = 6.8 Hz, H-10); IR (neat) λ_{max} 3090 (w), 2960 (m), 2930 (s), 2860 (s), 1625 (m), 1460 (m, br) cm^{-1}; MS, 218, 220 (M^+, 1.9), 162, 164 (1.8), 148, 150 (4.4), 135, 137 (2.3), 119, 121 (7.7), 97 (32), 83 (49), 69 (45), 57 (100), 55 (93), 43 (37). Yields and boiling points of **6b–e**: **6b** (77%), bp 45–50 °C (0.05 torr); **6c** (68%), bp 72–75 °C (0.1 torr); **6d** (90%), bp 86–88 °C (0.3 torr); **6e** (80%), bp 87–88 °C (0.07 torr). NMR and IR spectra of **6b–e** were analogous to those of **6a**. Mass spectra were characterized by pairs of molecular ion peaks (1–2%) and were otherwise similar to the mass spectrum of **6a**, with the exception of an additional fragment at m/z 111 (11–31%).

(3*Z*,9*Z*,6*S*,7*R*)-6,7-Epoxy-3,9-alkadienes ((6*S*,7*R*)-1a–e) and (6*R*,7*S*)-1a–e. The following procedure describes the synthesis of (6*S*,7*R*)-**1a**. The syntheses of (6*S*,7*R*)-**1b–e** were performed under identical conditions, using the appropriate (*Z*)-alkenyl bromides **6**. The syntheses of (6*R*,7*S*)-**1a–e** were carried out in similar fashion, using the other enantiomer of iodide **4**.

A solution of (*Z*)-1-decenylmagnesium bromide (**7a**) was prepared by slow addition of a THF solution (15 mL) of (*Z*)-1-bromo-1-decene (**6a**) (3.50 g, 16 mmol) to Mg turnings (1.556 g, 64 mmol) in THF, at 10–30 °C. The solution of alkenyl-Grignard was then added dropwise by syringe to a cooled (−23 °C) preformed solution of (2*R*,3*R*)-epoxy iodide **4** (2.016 g, 8 mmol), cuprous iodide (152 mg, 0.8 mmol), and HMPA (5.9 mL, 32 mmol) in THF (20 mL), maintaining the temperature below −20 °C. The resulting mixture was stirred 30 min at −23 °C and then quenched by addition of cold aqueous saturated ammonium chloride solution. The mixture was extracted with ether (1 × 50 mL, 2 × 25 mL), and the combined ether extracts were washed with water and brine (25 mL each), dried (Na_2SO_4), and concentrated. The crude product was then purified by flash chromatography on silica gel (4 cm i.d. × 20 cm, 1.5% ether in hexane), followed by flash chromatography on silica gel impregnated with silver nitrate (10% w/w; 3 cm i.d. × 20 cm, stepwise gradients of 10, 15, and 20% ether in hexane). Final purification was accomplished by Kugelruhr distillation (0.1 torr, oven temperature 150 °C), giving (6*S*,7*R*)-**1a** (1.05 g, 50%): $[\alpha]^{23}_{365}$ − 1.1 (*c* 6.47, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 5.52 (dtt, 2 H, J = 10.8, 7.2, 1.5 Hz, H-3, H-10), 5.40 (m, 2 H, H-4, H-9), 2.92 (m, 2 H, H-6, H-7), 2.38 (m, 2 H, H-5, H-8), 2.18 (m, 2 H, H-5, H-8), 2.03 (m, 4 H, H-2, H-11), 1.4–1.1 (m, 12 H, H-12–H-17), 0.95 (t, 3 H, J = 7.5 Hz, H-1), 0.84 (t, 3 H, J = 7.5 Hz, H-18); IR (neat) λ_{max} 3020 (w), 2970 (m), 2930 (s), 2860 (m) cm^{-1}; MS, 264 (M^+, 0.5), 235 (1.2), 195 (3.1), 181 (1.4), 177 (1.6), 165 (1.6), 151 (3.1), 137 (4.5), 121 (8.5), 111 (27.5), 109 (20.7), 95 (42.3), 83 (77.7), 67 (98.3), 55 (100), 43 (64.2).

The compounds (6*S*,7*R*)-**1b–e** and the enantiomeric series (6*R*,7*S*)-**1a–e** were synthesized by the same procedure and on the same scale, using the appropriate iodide enantiomers and the appropriate alkenylmagnesium bromides. 6*S*,7*R* series: **1b** (63%), $[\alpha]^{23}_{365}$ −1.0° (*c* 8.20, CH_2Cl_2); **1c** (49%), $[\alpha]^{21}_{365}$ − 1.1° (*c* 7.26, CH_2Cl_2); **1d** (42%), $[\alpha]^{24}_{365}$ − 1.0° (*c* 7.40, CH_2Cl_2); **1e** (59%) $[\alpha]^{24}_{365}$ −1.1° (*c* 6.22, CH_2Cl_2). 6*R*,7*S* series: **1a** (53%), $[\alpha]^{23}_{365}$ +1.1° (*c* 5.69, CH_2Cl_2); **1b** (51%), $[\alpha]^{23}_{365}$ +1.2° (*c* 5.68, CH_2Cl_2); **1c** (54%), $[\alpha]^{21}_{365}$ +1.1 (*c* 5.33, CH_2Cl_2); **1d** (40%), $[\alpha]^{24}_{365}$ +1.0° (*c* 5.11, CH_2Cl_2); **1e** (59%), $[\alpha]^{23}_{365}$ +1.2° (*c* 6.10, CH_2Cl_2).

The NMR and IR spectra of (6*S*,7*R*)-**1b–e** and (6*R*,7*S*)-**1a–e** were entirely analogous to those of (6*S*,7*R*)-**1a** reported above. The mass spectra of the series were characterized by ions corresponding to M, M − 29, M − 69, M − 83, M − 87, m/z 111, and clusters of peaks centered at m/z 165, 151, 137, 121, 109, 95, 83, 67, 55, and 43, at intensities similar to those of the corresponding ions in the spectrum of (6*S*,7*R*)-**1a**.

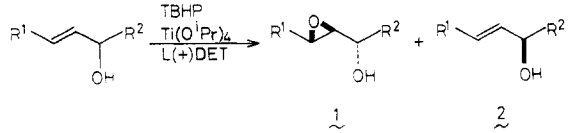
Anal. Calcd for (6*R*,7*S*)-**1e**, $C_{22}H_{40}O$: C, 82.43; H, 12.58. Found: C, 82.52; H, 12.65.

Communications

Synthesis of Optically Active β,γ-Epoxy Alcohols and Secondary Allylic Alcohols via Diastereoselective Addition of α-Trimethylsilyl-α,β-epoxy Aldehydes with Organometallic Compounds

Summary: Optically active α-trimethylsilyl-α,β-epoxy aldehydes **3** react with various Grignard reagents or organolithium compounds highly stereoselectively to give erythro adducts **4**, which can be readily converted into β,γ-epoxy secondary alcohols **1** or secondary allylic alcohols **2**.

Sir: Kinetic resolution of racemic allylic alcohols by the Sharpless process used to prepare optically active β,γ-epoxy alcohols **1** or secondary allylic alcohols **2** is highly effective and reliable (eq 1).[1,2]

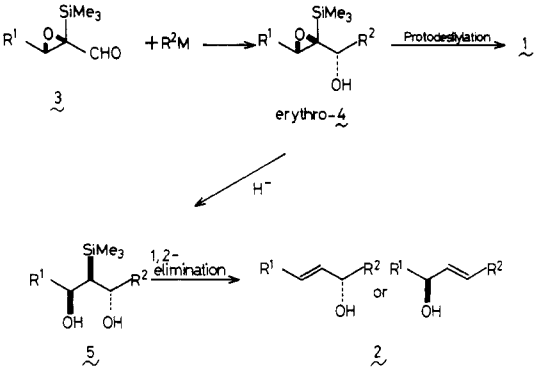


(1)

1 **2**

(1) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

Scheme I



3 **5**

However, kinetic resolution suffers from the disadvantage that at least half of the starting material is lost. We wish to report a new method for preparation of **1** and **2**

(2) Recent other method for preparation of optically active secondary allylic alcohols: (a) Noyori, R. *Pure Appl. Chem.* **1981**, *53*, 2315. (b) Yamamoto, H.; Fujiwara, J.; Fukutani, Y.; Hasegawa, M.; Maruoka, K. *J. Am. Chem. Soc.* **1981**, *53*, 2315. (c) For related work, see: Kitano, Y.; Matsumoto, T.; Sato, F. *J. Chem. Soc., Chem. Commun.*, in press.

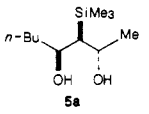
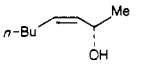
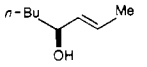
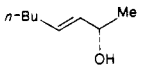
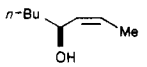
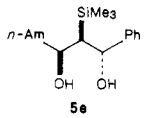
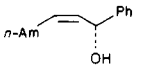
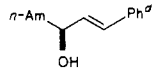
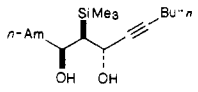
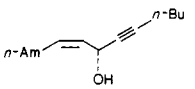
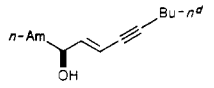
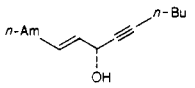
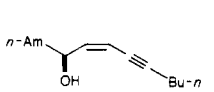
0022-3263/86/1951-4728$01.50/0

Table I. Reactions of 3 with Organometallic Compounds (R^2M)[a]

aldehyde 3, R	R^2M	product ratio, erythro:threo[b,c]	total yield, %[d]	$[\alpha]^{25}_D$ of *erythro*-4[e]
n-Bu	MeMgBr	7:1	89	**4a** −5.6° (*c* 1.07, $CHCl_3$)
n-Bu	MeLi	5.4:1	89	
n-Am	EtMgBr	26:1[f]	86	**4b** −18.3° (*c* 0.808, $CHCl_3$)
n-Am	*i*-PrMgBr	23:1	81	**4c** −8.8° (*c* 0.640, $CHCl_3$)
n-Bu	CH_2=$CHCH_2MgBr$	5.6:1	90	**4d** −23.0° (*c* 0.556, $CHCl_3$)
n-Am	PhMgBr	7.9:1	97	**4e** +65.6° (*c* 1.00, $CHCl_3$)
n-Am	*n*-BuC≡CLi	9.8:1[g]	93	**4f** +20.0° (*c* 0.918, $CHCl_3$)

[a] The reactions were carried out at −78~0 °C (1–2 h) in ether. [b] Determined by HPLC analysis. [c] Erythro isomers were assigned by spectroscopic methods and by comparison with the authentic materials. [d] Isolated yields. [e] Purified by column chromatography on silica gel. [f] The ratio was lowered to 2.8:1 by using THF as solvent. [g] The ratio was lowered to 2.6:1 in THF.

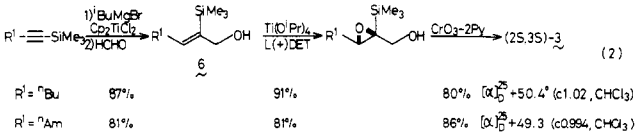
Table II. Peterson Olefination Reactions of 5

diol 5	reagent/solvent (reaction conditions)	products ratio[a]		total yield, %[b]
 **5a**	H_2SO_4/MeOH (−10~0 °C, 0.5 h)		 1:1	*c*
5a	*n*-BuLi/HMPA (−10 °C, 1 h)		 4:1	*c*
 **5e**	H_2SO_4/MeOH (−10 °C, 1 h)		 1:99	91
 **5f**	H_2SO_4/MeOH (0~20 °C, 2 h)		 1:99	79
5f	NaH/THF (0 °C, 0.5 h)		 1:1	*c*

[a] Determined by ^1H NMR. [b] Isolated yield. [c] Not determined. [d] Enantiomeric purity was confirmed by transformation to (*S*)-(−)-2-acetoxyheptanal via ozonolysis after acetylation. $[\alpha]^{20}_D$ −38.0° and −37.4° (*c* 0.50, $CHCl_3$) [lit.[16] $[\alpha]^{20}_D$ −37.8° (*c* 0.5, $CHCl_3$)].

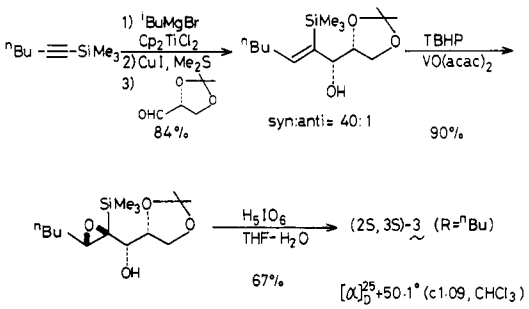
which is based on a highly diastereoselective addition reaction of optically active α-trimethylsilyl-α,β-epoxy aldehydes **3** with organometallic compounds and the reactivities of the epoxysilyl moiety[3] of the products **4** thus obtained. Our procedure is summarized in Scheme I.

The preparation of the starting aldehyde **3** was carried out by two procedures. The procedure shown in eq 2 which gives (2*S*,3*S*)-**3** includes the Katsuki and Sharpless asymmetric epoxidation of the prochiral allylic alcohols **6** as the key step.[4] The alcohols **6** were readily prepared by hydromagnesiation of 1-(trimethylsilyl)-1-alkyne followed by treatment with formaldehyde.[5] The key feature of another approach is based on the highly diastereoselective addition reactions of glyceraldehyde acetonide with 1-(trimethylsilyl)vinylcopper compounds[6] and V^{5+}-catalyzed epoxidation of the resulting adducts with TBHP, which proceeds with almost 100% diastereoselectivity (eq 3).[7]



(2)

R^1 = ^{n}Bu	87%	91%	80%	$[\alpha]^{25}_D$ +50.4° (c1.02, $CHCl_3$)
R^1 = ^{n}Am	81%	81%	86%	$[\alpha]^{25}_D$ +49.3 (c0.994, $CHCl_3$)



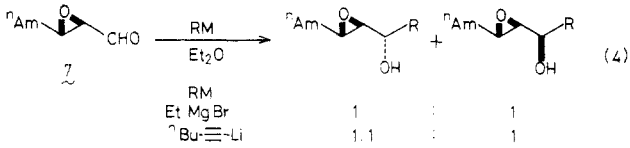
(3)

It should be noted that (2*R*,3*R*)-**3** can be obtained by using (−)-instead of (+)-diisopropyl tartrate at the epoxidation step in the procedure shown in eq 2 or by

(3) (a) Colvin, E. W. In *Silicon in Organic Synthesis*; Butterworths: London, 1981. (b) Weber, W. P. In *Silicon Reagents for Organic* Synthesis; Springer Verlag: New York, 1983.
(4) Katsuki, T.; Sharpress, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(5) (a) Sato, F.; Ishikawa, H.; Sato, M. *Tetrahedron Lett.* **1981**, *22*, 85. (b) Sato, F. *J. Organomet. Chem.* **1985**, *285*, 53.
(6) Sato, F.; Kobayashi, Y.; Takahashi, O.; Chiba, T.; Takeda, Y.; Kusakabe, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1636.
(7) (a) Tomioka, H.; Suzuki, T.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 3387. (b) Narura, A. S. *Ibid.* **1982**, *23*, 5579.

starting with (*S*)- in place of (*R*)-glyceraldehyde acetonide in the case of eq 3.

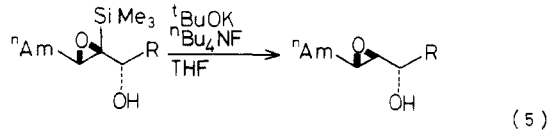
The results of the reaction of **3** with various Grignard reagents or organolithium compounds are summarized in Table I. It can be seen from Table I that the reaction proceeds with synthetically useful high diastereoselectivity to afford erythro isomers predominantly.[8] Especially noteworthy is the very high diastereoselectivity of more than 23:1 observed in the reaction with an alkyl Grignard reagent except for methyl Grignard reagent. Noteworthy also is the fact that the degree of the diastereoselectivity is highly dependent on the solvent used and it decreases significantly by using THF instead of ether. The stereochemistry of nucleophilic addition to the α,β-epoxy aldehyde had never been investigated,[9] and it must await further study to explain the mechanism to afford erythro products predominantly in the present reaction. However it should be noted that the presence of $SiMe_3$ is indispensable to get high diastereoselectivity, since the reaction of the epoxy aldehyde **7** which does not contain $SiMe_3$ group with EtMgBr provided an almost equal amount of erythro and threo products (eq 4).



(4)

RM		
EtMgBr	1	1
^{n}Bu-≡-Li	1.1	1

The addition products **4** thus prepared can be readily protodesilylated to **1** in excellent yields by treatment with KO-*t*-Bu and Bu_4NF in THF as is exemplified by eq 5.[10]

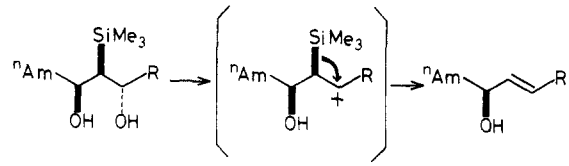


(5)

4b, R = Et — **1b**, 93%

4f, R = -≡-^{n}Bu — **1f**, 89%

Reaction of **4a**, **4e**, and **4f** with AlH_3 in ether resulted regiospecific epoxide ring opening to afford the corresponding diols **5** in the yields of 85%, 80%, and 86%, respectively.[11] On treatment with either basic or acidic reagents, the compounds **5** were converted into the allylic alcohols[3] (Table II). It can be seen from Table II that the regiochemistry of 1,2-elimination reaction was strongly dependent on both the reaction conditions and the substituents R^1 and R^2 in **5**. Under the basic conditions.[12] the regioselectivity was low to moderate to form the mixtures of allylic alcohols. Very low regioselectivity was also observed in the reaction of **5a** under the acidic conditions;[12,13] however, almost 100% of regioselectivity was attained in the case of **5e** and **5f** thus making the reaction useful for the preparation of allylic alcohols bearing alkynyl or phenyl substituents at γ-position. The specific production of these alcohols can be explained by the intermediacy of more stable propargyl or benzyl cation, respectively (eq 6).

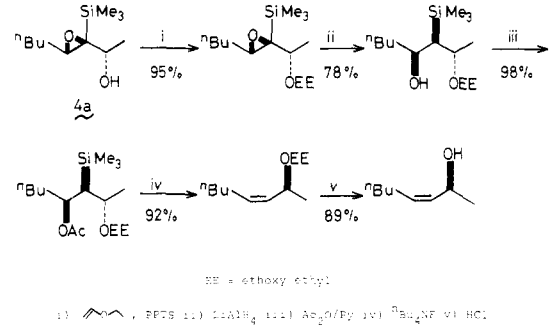


(6)

5e, R = Ph

5f, R = -≡-^{n}Bu

Direct 1,2-elimination reaction of **5** in which both R^1 and R^2 are alkyl groups such as **5a** did not proceed with synthetically useful regioselectivity. However, specific conversion of **4** to **2** can be readily realized by protection of the hydroxyl group of **4** before epoxide ring opening with hydride anion. Thus, (*Z*)-3-octen-2-ol was obtained from **4a** via a five-step sequence as shown in eq 7: (i) protection



(7)

EE = ethoxy ethyl

i) , PPTS ii) $LiAlH_4$ iii) Ac_2O/Py iv) ^{n}Bu_4NF v) HCl

(ethyl vinyl ether; PPTS); (ii) specific epoxide ring opening with $LiAlH_4$[11c]; (iii) acetylation; (iv) 1,2-elimination with *n*-Bu_4NF;[14] (v) deprotection. Enantiometric purity of the alcohol thus obtained was confirmed by transformation to (*S*)-(+)-2-octanol by hydrogenation ($[\alpha]^{21}_D$ +9.90° (*c* 2.06, EtOH), lit.[15] $[\alpha]^{21}_D$ +10.1° (*c* 5.57, EtOH)).

Registry No. **1b** (isomer 1), 104995-75-7; **1b** (isomer 2), 105087-02-3; **1f** (isomer 1), 104995-76-8; **1f** (isomer 2), 105087-03-4; (*S*)-**2**-(*Z*) (R^1 = *n*-butyl, R^2 = Me), 105087-04-5; (*S*)-**2**-(*Z*) (R^1 = *n*-butyl, R^2 = Me)(ethoxyethyl ether), 104995-89-3; (*S*)-**2**-(*E*) (R^1 = *n*-butyl, R^2 = Me), 105087-06-7; (*S*)-**2**-(*Z*) (R^1 = Me, R^2 = *n*-butyl), 105087-07-8; (*S*)-**2**-(*E*) (R^1 = Me, R^2 = *n*-butyl), 105087-05-6; (*R*)-**2**-(*Z*) (R^1 = *n*-pentyl, R^2 = Ph), 104995-80-4; (*S*)-**2**-(*E*) (R^1 = Ph, R^2 = *n*-pentyl), 104995-81-5; (*R*)-**2**-(*Z*) (R^1 = *n*-pentyl, R^2 = 1-hexynyl), 104995-82-6; (*S*)-**2**-(*E*) (R^1 = 1-hexynyl, R^2 = *n*-pentyl), 104995-83-7; (*R*)-**2**-(*E*) (R^1 = *n*-pentyl, R^2 = 1-hexynyl), 104995-84-8; (*S*)-**2**-(*Z*) (R^1 = 1-hexynyl, R^2 = *n*-pentyl), 104995-85-9; (2*S*,3*S*)-**3** (R^1 = *n*-butyl), 104995-67-7; (2*S*,3*S*)-**3** (R^1 = *n*-pentyl), 104995-68-8; **4** (R^1 = *O*-butyl, R^2 = 2,2-dimethyl-1,3-dioxolan-4-yl) stereoisomer, 104995-69-9; **4a**, 105087-01-2; **4a** (ethoxy ethyl ether), 104995-86-0; **4b**, 104995-70-2; **4c**, 104995-71-3; **4d**, 104995-72-4; **4e**, 104995-73-5; **4f**, 104995-74-6; **5a**, 104995-77-9; **5a** (2-(ethoxy ethyl ether)), 104995-87-1; **5a** (2-(ethoxy ethyl ether), 4-(acetoxy)), 104995-88-2; **5e**, 104995-78-0; **5f**, 104995-79-1; **6** (R^1 = *n*-butyl), 104995-66-6; **6** (R^1 = *n*-pentyl), 87922-58-5; **7**, 89461-52-9; L-(+)DET, 87-91-2; $CH_3(CH_2)_3C{\equiv}CSi(Me)_3$, 3844-94-8; $CH_3(CH_2)_4C{\equiv}CSi(Me)_3$, 15719-56-9; $(C_4H_9)_2CHCH_2MgBr$, 926-62-5; Cp_2TiCl_2, 1271-19-8; H_2CO, 50-00-0; $Ti(OPr\text{-}i)_4$, 546-68-9; CH_3Br, 74-83-9; CH_3Li, 917-54-4; CH_3CH_2Br, 74-96-4; $(CH_3)_2CHBr$, 75-26-3; $CH_2{=}CHCH_2Br$, 106-95-6; PhBr, 108-86-1; $CH_3(CH_2)_3C{\equiv}CLi$, 17689-03-1; $CH_2{=}CHOEt$, 109-92-2;

(8) The high stereoselectivity was observed in the reaction of α-silyl aldehydes with Grignard reagents: Hudrlik, P. F.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1981**, *103*, 6251.

(9) For the stereochemical features of metal hydride reduction of α,β-epoxy ketones: (a) Chautemps, P.; Pierre, J. L. *Tetrahedron* **1976**, *32*, 549. (b) Oishi, T.; Nakata, T.; Tanaka, T. *Tetrahedron Lett.* **1981**, *22*, 4723.

(10) (a) Sato, F.; Uchiyama, H.; Kobayashi, Y. *Chem. Lett.* **1985**, 467. (b) Yamamoto, K.; Kimura, T.; Tomo, Y. *Tetrahedron Lett.* **1985**, *26*, 4505.

(11) (a) Yamamoto, K.; Kimura, T.; Tomo, Y. *Tetrahedron Lett.* **1984**, *25*, 2155. (b) Paquette, L. A.; Fristad, W. E.; Bailey, T. *J. Organomet. Chem.* **1978**, *433*, 1620. (c) Eisch, J. J.; Trainor, J. T. *J. Organomet. Chem.* **1963**, *28*, 2870.

(12) (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. (b) Hudrlik, P. F.; Peterson, D. *J. Am. Chem. Soc.* **1975**, *97*, 1464. (c) Hudrlik P. F.; Peterson, D.; Rona, R. J. *J. Org. Chem.* **1975**, *40*, 2263.

(13) Whitmore, F. C.; Sommer, L. H.; Gold, J.; Strien, R. E. V. *J. Am. Chem. Soc.* **1947**, *69*, 1551.

(14) (a) Cunico, R. F.; Dexheimer, E. M. *J. Am. Chem. Soc.* **1972**, *94*, 2868. (b) Chan, T. H. *Acc. Chem. Res.* **1977**, *10*, 442.

(15) Hill, R. K. *J. Am. Chem. Soc.* **1958**, *80*, 1611.

(16) Noyori, R.; Tomino, I.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.

(S)-(+)-$CH_3CH(OH)(CH_2)_5CH_3$, 6169-06-8; (R)-glyceraldehyde acetonide, 15186-48-8; 4(R)-(1(S)-hydroxy-2-(trimethylsilyl)-hept-2(Z)-en-1-yl)-2,2-dimethyl-1,3-dioxolane, 102357-26-6; (S)-(-)-2-acetoxyheptanol, 75584-25-7.

Supplementary Material Available: Spectral data [IR, ^1H and ^{13}C NMR, and $[\alpha]_D$] for **2-5** and their derivatives (3 pages). Ordering information is given on any current masthead page.

Yoshiyuki Takeda, Takashi Matsumoto, Fumie Sato*

Department of Chemical Engineering
Tokyo Institute of Technology, Meguro
Tokyo 152, Japan

Received September 2, 1986

Calcium in Liquid Ammonia for the Reduction of Benzyl Ethers. Mechanistic Clues Derived from Chemoselectivity Studies

Summary: Extremely high selectivity was provided by calcium in liquid ammonia in the cleavage of the benzylic carbon–oxygen bond in benzyl ethers containing various other functionalities. Results of controlled experiments indicate that the selectivities offered by the $Ca \rightarrow Ca^+ + e^-$ and the $Ca^+ \rightarrow Ca^{2+} + e^-$ processes are 4.6 and 47 times greater, respectively, than that afforded by the $Li \rightarrow Li^+ + e^-$ process.

Sir: Dissolving metals in liquid ammonia have been used extensively to perform reductions for decades.[2a,b,c] The most notable systems are the Birch reduction with sodium, ammonia, and alcohol and the Benkeser reduction with lithium in alkylamines.[3] Calcium metal has also been utilized occasionally.[4] However, studies on its chemoselectivity in reduction have not been carried out.

In general, calcium is considered to be less reactive than the alkali metals.[2d] Its lower oxidation potential in ammonia than that of lithium, sodium, or potassium[5] makes it a more likely candidate for selective reduction of substrates with multiple functional groups. Calcium has two different oxidation potentials in aqueous solution[6] based on the processes $Ca \rightarrow Ca^+ + e^-$ and $Ca^+ \rightarrow Ca^{2+} + e^-$. If similar differences exist in solutions of calcium in liquid ammonia, we deemed it possible to obtain a selective reduction of organic compounds having multiple reduction sites.

The benzyl group is commonly used for protecting the hydroxyl moiety. The resulting benzyl ethers are stable to most acidic, basic, and oxidative conditions.[7] It is also known that the benzyl ether moiety can be readily cleaved by dissolving metals.[7a] Consequently, we chose substrates containing a benzyloxy group in conjunction with other functionalities for the study of chemoselective reduction with calcium metal in liquid ammonia. The results are listed in Table I.

A typical procedure includes the addition of a substrate in a small amount of anhydrous ether or tetrahydrofuran to a blue solution of calcium metal in liquid ammonia. The concentration of the substrate to ammonia was 0.05–0.10 M. After 2 h of being stirred at refluxing ammonia temperature, the reaction was quenched with saturated aqueous ammonium chloride solution followed by a normal workup procedure. The products were analyzed by capillary GLC and purified by column chromatography. We have tried various conditions for the reductions and found that optimal selectivity was obtained when 2.0–2.2 equiv of calcium metal were employed.[8] Use of larger quantities of calcium resulted in lowered selectivity. With shorter reaction times, debenzylation was not always complete.

The benzyloxy alkyne **1a** contains two functional groups, a benzyl ether moiety and a nonterminal carbon–carbon triple bond,[9a,b] that can be reduced under dissolving metal conditions. We found that calcium preferentially reduced the benzyl ether moeity, providing the hydroxy alkyne **1b** in 90% yield. Under similar conditions, aromatic rings such as a phenyl group,[9c] directly attached to an alkyl chain, or a furan nucleus[9d] are resistant to reduction, as evidenced in the conversion of **2a** to **2b** in quantitative yield and **3a** to **3b** in 69% yield. The lower yield of **3b** was due primarily to the instability of the furan ring toward the workup conditions.[10] In the cases where the benzyl ether shares a common oxygen with a 2-furfuryl[9e] or allylic ether,[9f] as in **3a** and **4a**, the only reduction products detected came from cleavage of the benzylic carbon–oxygen bond. In the conversion of **4a** to **4b** and **5a** to **5b**, the carbon–carbon bonds in the cyclobutyl ring and the cyclopropyl ring and the carbon–oxygen bond in the 1-cyclopropylalkoxyl moiety are not cleaved. The reduction of **6a** to **6b** in 93% yield indicates that the oxygen–silicon bond in the *tert*-butyldimethylsilyl ether moiety is resistant to the reduction and workup conditions.

For substrates containing a benzyloxy function and another readily reducible moiety, we determined the susceptibilities of the respective functional groups to cleavage from the ratio of the reduced products. Reduction of the epoxybenzyl ether **7a** resulted in complete cleavage of the benzylic carbon–oxygen bond and partial scission of the oxirane ring[9g,h] at the less substituted carbon–oxygen bond. The alcohols **7b** and **7c** were obtained in 1:1 ratio, indicating that the reduction selectivity for the benzyl ether to the oxirane was on the order of 2:1. Poor selectivity between phenylsulfonyl[9i] and benzyloxy moieties was also found in the reduction of **8a**. Benzene and toluene were detected in the ratio 1:1.6. Even though calcium is a mild reducing agent, we did not find any selectivity between benzyl ether and thiophenyl[9i] or ketone[9j] moieties. The

(1) Research Fellow of the Alfred P. Sloan Foundation, 1986–1988.
(2) (a) Johnstone, R. A. W.; Wilby, A. H.; Entwhistle, I. D. *Chem. Rev.* **1985**, *85*, 129. (b) Smith, M. In *Reduction: Techniques and Applications in Organic Synthesis*; Augustine, R. L., Ed.; Marcel Dekker: New York, 1968; Chapter 2. (c) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Menlo Park, CA, 1972; Chapter 3. (d) See ref 2c, p 191.
(3) Kaiser, E. M. *Synthesis* **1972**, 391.
(4) (a) Benkeser, R. A.; Belmonte, F. G. *J. Org. Chem.* **1984**, *49*, 1662. (b) Benkeser, R. A.; Belmonte, F. G.; Kang, J. *J. Org. Chem.* **1983**, *48*, 2796. (c) Benkeser, R. A.; Kang, J. *J. Org. Chem.* **1979**, *44*, 3737.
(5) (a) Pleskov, V. A.; Monossohn, A. M. *Acta Physicochim. URSS* **1935**, *2*, 615. (b) Pleskov, V. A. *Zh. Fiz. Khim.* **1937**, *9*, 12; *Acta Physicochim. URSS* **1937**, *6*, 1. (c) Lagowski, J. J.; Moczygemba, G. A. In *The Chemistry of Nonaqueous Solvents*; Lagowski, J. J., Ed.; Academic: New York, 1967; Vol. 2, p 341.
(6) (a) *CRC Handbook of Chemistry and Physics*, 67th ed.; Weast, R. C., Ed.; CRC: Boca Raton, FL; 1986–1987, p D-152. (b) Antelman, M. S.; Harris, F. J. Jr. *The Encyclopedia of Chemical Electrode Potentials*; Plenum: New York, 1982; pp 102, 103.
(7) (a) Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981; pp 29–31 and references therein. (b) Reese, C. B. In *Protective Groups in Organic Chemistry*; McOmie, J. F. W., Ed.; Plenum: New York, 1973; pp 98–100.
(8) For example, 2.0–2.2 mmol of calcium was used for the reduction of 1.0 mmol of substrate with two reducible functional groups.
(9) For the reduction of this moiety under dissolving metal conditions, see: (a) House, H. O.; Kinloch, E. F. *J. Org. Chem.* **1974**, *39*, 747. (b) see ref 4a. (c) see ref 3 and 4b. (d) Bedenbaugh, A. O.; Bedenbaugh, J. H.; Adkins, J. D.; Bergin, W. A. *J. Org. Chem.* **1970**, *35*, 543. (e) Yamakawa, K.; Satoh, T. *Chem. Pharm. Bull.* **1978**, *26*, 3704. (f) Hallsworth, A. S.; Henbest, H. B.; Wrigley, T. I. *J. Chem. Soc.* **1957**, 1969. (g) Hallsworth, A. S.; Henbest, H. B. *J. Chem. Soc.* **1957**, 4604. (h) Brown, H. C.; Ikegami, S.; Kawakami, J. H. *J. Org. Chem.* **1970**, *35*, 3243. (i) Truce, W. E.; Tate, D. P.; Burdge, D. N. *J. Org. Chem.* **1960**, *25*, 2872. (j) Sondheimer, F.; Mancera, O.; Rosenkranz, G.; Djerassi, C. *J. Am. Chem. Soc.* **1953**, *75*, 1282.
(10) Acheson, R. M. *An Introduction to the Chemistry of Heterocyclic Compounds*; Wiley: New York, 1976; p 126.

0022-3263/86/1951-4731$01.50/0