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REDUCTIVE CLEAVAGES OF HOMOCHIRAL ACETALS: INVERSION OF THE STEREOSELECTIVITY

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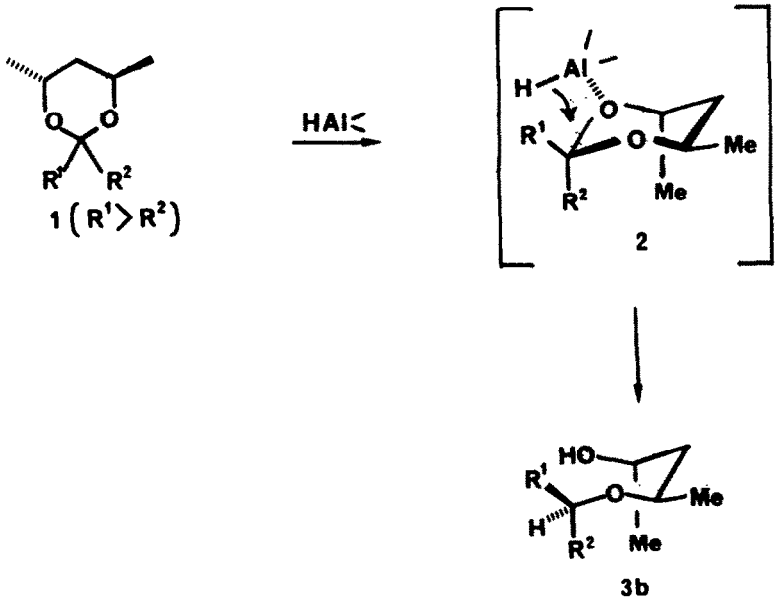
ABSTRACT - Reductive cleavages of homochiral acetals using Lewis acid-hydride systems and of alkynyl acetals using organoaluminum reagents are described. Stereochemical outcomes are found to be the opposite compared with our previous results on the aluminum hydride reduction of the acetal.

We have recently described the diastereoselective cleavage of homochiral acetals derived from the condensation of unsymmetrical ketones and (-)-(2R,4R)-2,4-pentanediol to give, after removal of chiral auxiliary, optically active alcohols with high enantiopurities. The observed high diastereoselectivity was ascribed to a stereospecific coordination of the organoaluminum reagent to one of the acetal oxygen followed by the hydride attack syn to the cleaved carbon-oxygen bond (Scheme 1).[1]

Scheme 1

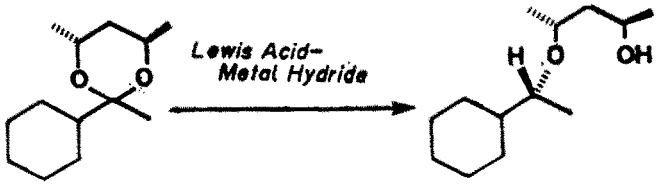


From the beginning of the studies of this work, we have been interested in the possibility to achieve the inversion of the stereochemical outcome of hydride attack to the acetal group, which, if successful, would provide a method to give both enantiomers from a single chiral starting acetal. Our approach to this enterprise was first focused on the Lewis acid catalyzed hydride attack anti to the departing oxygen atom. In fact, Johnson and his co-workers reported that the cleavage of the homochiral acetal with organosilicon reagents in the presence of Lewis acids such as titanium(IV) chloride was taken place via anti attack of the reagent.[2] Thus, the combination of Lewis acid and hydride reagent should also result the desired anti selectivity. Another indirect approach to this problem came from the consideration that homochiral acetal 1 would exist as conformer 2 where R' is sterically larger than R^2, whereas the employment of the sterically less hindered acetylenic group would result to occupy the axial position even R^1 is methyl. Furthermore, since the optically pure propargylic alcohols have been recognized as important synthetic intermediates for a variety of natural products, it is synthetically important to provide a general method for the preparation of this class of compounds.[3] Herein, we report the reductive cleavages of homochiral acetals by the combined use of Lewis acids and silyl hydride reagents and we also describe the selective cleavage of acetals of alkynyl ketones, a new method for the synthesis of optically pure propargylic alcohols after removal of chiral auxiliary.[4]

Reductive cleavages of homochiral acetal using Lewis acid-hydride systems: In 1962 the reagent combination of triethylsilane-zinc chloride was reported to reduce noncyclic acetals and ketals to ethers.[5] It was also reported that the reaction of the acetal with trimethylsilane in the presence of catalytic amount of trimethylsilyl trifluoromethanesulfonate gave a reduced ether by Noyori.[6] These papers encouraged us to explore the possibility on the selective cleavage of the homochiral acetal of 2,4-pentanediol by using Lewis acid-hydride system.

Some results of the reactions of the acetal derived from 1-cyclohexyl-ethanone and (-)-(2R,4R)-2,4-pentanediol with various Lewis acids and hydride reagents were shown in Table 1 (Scheme 2). In dramatic contrast to the

Scheme 2



1 (R^1=c-Hex, R^2=Me) *3a*

previous resluts with dibromoaluminum hydride reagent, the stereochemical outcome of the reaction was found to be the opposite: the reaction proceeds from the Si-face of the carbonyl. The diastereomeric ratio was determined by gc analysis of the cleaved ether which showed a clear base line separation of the two peaks. The minor peak was identical with the previously obtained (S)-

isomer from aluminum method. Among the various combination of Lewis acids and hydride reagents examined, the addition of triethylsilane to the mixture of the acetal and titanium (IV) chloride at low temperature found to be the most effective. The inverse addition (titanium (IV) chloride to the mixture of acetal and triethylsilane) also gives a similar diastereoselectivity, however, almost a 1:1 diastereomeric mixture was obtained from the reaction using the premixed reagent of trietylsilane and titanium (IV) chloride. Boron trifluoride etherate also showed the high diastereoselectivity with high chemical yield. The use of aluminum chloride or tin (IV) chloride as a Lewis acid gave the low selectivities. Interestingly, the reaction with t-butylmagnesium chloride in the presence of titanium (IV) chloride was also effective as a hydride source.[7]

Table 1. Reductive cleavage of the acetal 1 (R^1 = c-hex, R^2 = Me)

Lewis acid (equiv)	Hydride reagent (equiv)	Condition °C, h	3 Yield (%)	3 Ratio 3a:3b
$TiCl_4$ (1.2)	Et_3SiH (1.2)	-78, 0.5	85	98:2
$SnCl_4$ (1.0)	Et_3SiH (1.0)	-78, 0.5 -20, 2.0	93	65:35
$AlCl_3$ (1.2)	Et_3SiH (1.2)	-78, 8.0	69	66:34
BF_3OEt_2 (1.0)	Et_3SiH (1.0)	-78, 5.0 -20, 15.0	93	93:7
$TiCl_4$ (1.2)	^tBuMgCl (5.0)[a]	-78, 1.0	76	94:6

[a] A 0.82 M ether solution titrated prior to use.

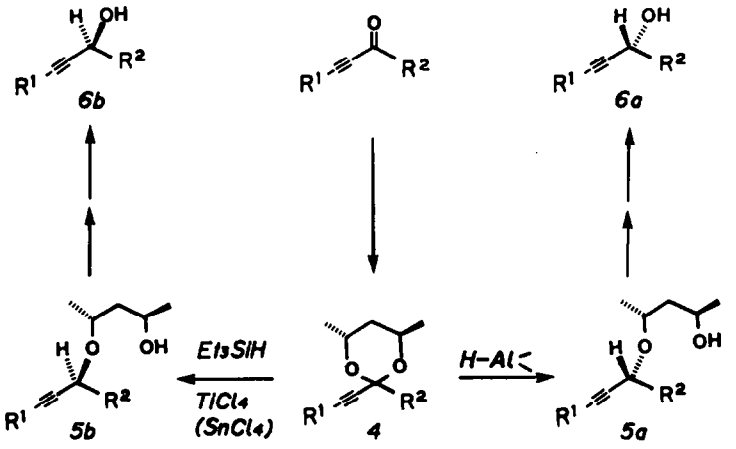
The reactions of the acetals of other ketones are summarized in Table 2. The selectivity was improved by lowering the reaction temperature. The reaction of aromatic acetal, however, afforded a complex mixture. The moderate selectivities were realized by the use of tin (IV) chloride as a Lewis acid. It should be noted that the reaction is highly chemoselective.[8] Thus, the acetal of ethyl levulinate which has acetal and ester groups in the molecule, gave the corresponding ether in good yield with high chemo- and diastereoselectivities.

Table 2. Cleavage of various acetals with triethylsilane

1		Lewis acid	Condition	3	
R^1	R^2	(equiv)	°C , h	Yield (%)	Ratio 3a:3b
Hex	Me	$TiCl_4$ (1.2)	-78 , 1.5	97	88:12
		$TiCl_4$ (1.2)	-90 , 0.5	76	93:7
Ph	Me	$SnCl_4$ (1.2)	-78 , 0.5 -40 , 1.5	24	81:19
$(CH_2)_2$-COOEt	Me	$TiCl_4$ (1.2)	-78 , 1.0	85	94:6

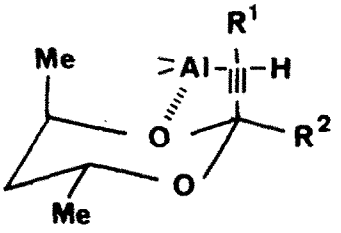
Reductive cleavage of α,β-alkynyl acetal: The sequence of the reaction was summarized in Scheme 3. Reduction of the acetal was carried out with

Scheme 3



excess organoaluminum reagents such as diisobutylaluminum hydride (DIBAH) and dibromoaluminum hydride (Br_2AlH). The diastereomeric ratio of the cleaved ether 5 was determined by gc analysis, which showed a baseline separation of two isomers. Especially noteworthy is the easy separation of isomers by simple column chromatography on silica gel. Thus, the optically pure propargylic alcohol was obtained after removal of chiral auxiliary by the previously reported manner (oxidation followed by the base treatment). The optical purity of the obtained propargylic alcohols was confirmed to be pure by the measurement of specific rotation and gc analysis of the corresponding (+)-MTPA esters.[9]

Table 3 shows the results of the cleavage of some alkynyl acetals. Both DIBAH and Br_2AlH were equally effective for the cleavage reaction. It should be noted that the carbinol **6a** shows (R)-configuration. Thus, sterically less hindered alkynyl group should occupy the axial position in the six-membered transition state **7** as shown below. As the steric bulkiness of R^2 group is getting larger, diastereoselectivity of the cleavage reaction was improved.



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The reaction of the acetal **4** with triethylsilane in the presence of Lewis acid ($TiCl_4$ or $SnCl_4$) could also inverse the stereoselectivity compared with the case using aluminum hydrides to afford the corresponding ether **5b** with the ratio of 96:4.

Table 3. Reduction of the alkynyl acetals **4**

4		Reagent	Conditions	5	
R^1	R^2	(equiv)	°C , h	Yield (%)	Ratio **5a:5b**
Bu	Me	DIBAH (2)	0 , 6	68	85:15
		DIBAH (4)	0 , 1	80	93:7
		DIBAH (6)	0 , 1	90	96:4
		Br_2AlH (2)	-20 , 5	53	50:50
		Br_2AlH (4)	-20 , 3	99	68:32
		Br_2AlH (6)	-20 , 3	100	93:7
Bu	Et	DIBAH (4)	0 , 1	93	97:3
		Br_2AlH (6)	-20 , 5	98	98:2
Me	^{i}Bu	Br_2AlH (6)	-20 , 4	99	98:2
Ph	Me	DIBAH (6)	0 , 2	86	90:10
		Br_2AlH (6)	-20 , 2	92	90:10
Ph	Et	Br_2AlH (6)	-20 , 2	99	95:5
Me	^{c}Hex	Br_2AlH (6)	-20 , 1	98	99:1

In conclusion, two independent methods were now established to achieve the stereoselective route to the (R)-alcohol. The method described herein provides methodology for the synthesis of optically active alcohols which have never been synthesized by the previous procedure. Taken together with the previous procedure, we could synthesized either (R)- or (S)-alcohols selectively from the same acetal. Furthermore, a new method is established for the stereocontrolled sythesis of optically active propargylic alcohols and the resulting (R)-alcohol 6 may be converted to the corresponding saturated alcohol after hydrogenation of triple bond.

Experimental Section

General. Infrared (IR) spectra were recorded on a Hitachi 260-10 spectrometer. ^{1}H NMR spectra were measured on a JNM-PMX 60 spectrometer. The chemical shifts are expressed in parts per million downfield from internal tetramethylsilane (δ=0). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Optical rotations were measured on a JASCO DIP-140 digital polarimeter. Gas liquid phase chromatographic (GC) analyses were performed on Hitachi 164 instruments equipped with 25-m PEG-HT capillary column and a flame ionization detector, using nitrogen as a carrier gas. All experiments were carried out under an atmosphere of dry argon. For thin layer chromatographic (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel E, Merck Art 9385. Microanalyses were accomplished at the Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University. In experiments requiring dry solvents, ether and tetrahydrofuran (THF) were distilled from sodium-benzophenone. Benzene, hexane, and toluene were dried over sodium metal. Dichloromethane was distilled from phosphorous pentoxide and stored over 4A molecular sieves. (-)-(2R,4R)-2,4-pentanediol was purchased and used after recrystallization from dry ether[10]; $[\alpha]^{24}_D$ -41.2° (c 9.99, $CHCl_3$). Other chemicals were purchased and used as such.

Preparation of the chiral acetal 1: The acetals 1 were synthesized in the manner described previously.[1] The physical property and analytical data of the acetal 1 (R^1 = $(CH_2)_2COOEt$, R^2 = Me) is as follows: $[\alpha]^{23}_D$-36.73° (c 1.05, $CHCl_3$); IR (neat) 2960, 2930, 1730, 1435, 1050, 905 cm^{-1}; ^{1}H NMR (CCl_4) δ 3.73 (q, J = 6.8 Hz, 2 H), 0.90 (s, 3 H), 0.83 (t, J = 6.8 Hz, 3 H); Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.58; H, 9.63.

General procedure for the reductive cleavage of the acetal 1 with Et_3SiH-$TiCl_4$: To a solution of the acetal 1 (0.5 mmol, 0.099 g) in 3 mL of dichloromethane was added titanium (IV) chloride (0.6 mmol, 0.6 mL of 1 M dichloromethane solution) at -78°C. After stirring there for 10 min, triethylsilane (0.6 mmol, 0.096 mL) was added and stirring was continued for 30 min. The product was poured into 2 N hydrochloric acid and extracted with ether twice. The combined organic layers were dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* afforded the crude product which was

treated with potassium fluoride (0.2 g) in 3 mL of methanol for 2 h to remove the silyl group of the product. The resulting mixture was poured into water and the product was extracted with ether. The organic layers were dried over anhydrous sodium sulfate, concentrated in vacuo and purified by column chromatography on silica gel (hexane-ether, 5:1) to give 3 in 85% yield as a colorless oil. Gc analysis (130°C) showed two peaks with the ratio of 98:2, and the minor peak was identical with previously obtained (S)-isomer: t_R = 15.0 (minor) and 15.8 (major) min. The reactions of the acetal 1 with other Lewis acids were carried out in the similar manner described above. The results of gc analyses of acetals 3 were listed below: 3 (R^1 = n-hexyl, R^2 = Me; 115°C); t_R = 11.4 (minor) and 12.3 (major) min. 3 (R^1 = Ph, R^2 = Me; 150°C); t_R = 10.9 (minor) and 14.0 (major) min. The physical property and analytical data of 3 (R^1 = $(CH_2)_2COOEt$, R^2 = Me) is as follows; Gc (180°C) t_R = 9.4 (minor) and 10.2 (major) min; IR (neat) 3760-3000 (br), 2960, 2920, 1720, 1470, 975 cm^{-1}; ^1H NMR (CCl_4) δ 4.03 (q, J = 6.8 Hz, 2 H), 1.20 (t, J = 6.8 Hz, 3 H), 1.12 (d, J = 6.0 Hz, 3 H); Anal. Calcd for $C_{12}H_{24}O_4$: C, 62.04; H, 10.04. Found: C, 62.26; H, 10.19.

Preparation of α,β-alkynyl acetal 4: Acetals 4 were prepared from α,β-alkynyl ketones[3] and (-)-(2R,4R)-2,4-pentanediol in the presence of catalytic amount of pyridinium tosylate.[1] The physical properties and analytical data of the acetal 4 were listed below.

4 (R^1 = Me, R^2 = n-Bu): 78% yield. $[\alpha]^{25}_D$ +8.86° (c 1.10, $CHCl_3$) TLC, R_f = 0.55 (hexane-EtOAc, 5:1); IR (neat) 2930, 2860, 2230, 1363 cm^{-1}; ^1H NMR (CCl_4) δ 3.80-4.58 (m, 2 H), 2.03-2.60 (m, 2 H), 1.43 (s, 3 H); Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.00; H, 10.78.

4 (R^1 = n-Bu, R^2 = Et): 81% yield; $[\alpha]^{25}_D$ +10.1° (c 1.01, $CHCl_3$); TLC, R_f = 0.56 (hexane-EtOAc, 5:1) ; IR (neat) 2970, 2930, 2870, 2210 cm^{-1}; ^1H NMR (CCl_4) δ 3.73-4.57 (m, 2 H), 2.00-2.67 (m, 2 H); Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.76; H, 10.97.

4 (R^1 = Ph, R^2 = Me): 91% yield; $[\alpha]^{24}_D$ +10.3° (c 1.14, $CHCl_3$); TLC, R_f = 0.53 (hexane-EtOAc, 5:1) IR (neat) 2980, 2940, 2230, 1140 cm^{-1}; ^1H NMR (CCl_4) δ 7.07-7.64 (m, 5 H, ArH), 3.87-4.67 (m, 2 H), 1.57 (s, 3 H); Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.19; H, 7.92.

4 (R^1 = Ph, R^2 = Et): 92% yield; $[\alpha]^{25}_D$ +9.41° (c 1.06, $CHCl_3$); TLC, R_f = 0.65 (hexane-EtOAc, 5:1); IR (neat) 2980, 2930, 2880, 2230 cm^{-1}; ^1H NMR (CCl_4) δ 7.07-7.57 (m, 5 H, ArH), 3.87-4.64 (m, 2 H); Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.57; H, 8.33.

4 (R^1 = Me, R^2 = i-Bu): 38% yield; $[\alpha]^{25}_D$ +2.41° (c 1.02, $CHCl_3$); TLC, R_f = 0.63 (hexane-EtOAc, 5:1); IR (neat) 2950, 2890, 2270, 1380 cm^{-1}; ^1H NMR (CCl_4) δ 3.70-4.54 (m, 2 H), 1.84 (s, 3 H); Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.04; H, 10.74.

4 (R^1 = Me, R^2 = cyclohexyl): 63% yield; $[\alpha]^{25}_D$ +7.07° (c 1.03, $CHCl_3$); TLC, R_f = 0.57 (hexane-EtOAc, 5:1); IR (neat) 2930, 2860, 2250, 1140 cm^{-1}; ^1H NMR (CCl_4) δ 3.67-4.57 (m, 2 H), 1.83 (s, 3 H); Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.23. Found: C, 76.15; H, 10.31.

General procedure for the reduction of chiral acetal 4 (R^1 = n-Bu, R^2 = Me) using DIBAH. To a solution of the acetal 4 (105.2 mg, 0.5 mmol; R^1 = n-Bu, R^2 = Me) in dry dichloromethane (3 mL) was added diisobutylaluminium

hydride (DIBAH, 3 mL of an 1 M hexane solution) at 0°C. After being stirred for 1 h, the mixture was poured into ice cold dilute hydrochloric acid and the product was extracted with ether. Removal of the dried solvent left a crude oil which was purified by column chromatography on silica gel (hexane-EtOAc, 8:1) to afford the alcohol 5 (R^1 = n-Bu, R^2 = Me) as an oil (yield 90%). The diastereomeric ratio was determined by Gc (5a/5b = 96/4); t_R = 9.4 (5b), 13.7 (5a) min (150°C); TLC, R_f(5b) = 0.22, R_f(5a) = 0.30 (hexane-EtOAc, 5:1); IR (neat) 3410 (br), 2960, 2940, 2870, 2250, 1450, 1370, 1330, 1080 cm^{-1}; ^1H NMR (CCl_4) δ 3.60-4.43 (m, 3 H), 1.97-2.63 (m, 3 H); Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.59; H, 11.34.

Reduction of chiral acetal 4 (R^1 = n-Bu, R^2 = Me) using Br_2AlH: Lithium aluminium hydride (29 mg, 0.75 mmol) was added to a solution of aluminium bromide (0.60 g, 2.25 mmol) in dry ether (3 mL) at 0°C. After stirring the resulting suspension for 10 min, was added dropwise at -20°C the acetal 4 (0.5 mmol) in dry ether (3 mL). After being stirred for 3 h, the mixture was poured into ice cold dilute hydrochloric acid and the product was extracted with ether. Removal of the dried solvent left a crude oil which was purified by column chromatography on silica gel (hexane-EtOAc, 8:1) to afford the alcohol 5 (R^1 = n-Bu, R^2 = Me) as an oil (yield >99%). The diastereomeric ratio of the product was determined by Gc (93:7). Reductive cleavages of other acetals were carried out in the similar manner. The physical properties and analytical data of the alcohols thus obtained are listed below.

5 (R^1 = n-Bu, R^2 = Et): Gc (150°C) t_R = 12.1 (5b), 18.4 (5a) min; TLC, R_f(5b) = 0.27, R_f(5a) = 0.22 (hexane-EtOAc, 5:1); IR (neat) 3450 (br), 2970, 2940, 2250, 1460, 1380, 1330, 1130 cm^{-1}; ^1H NMR (CCl_4) δ 3.64-4.30 (m, 3 H), 2.30-2.40 (m, 3 H); Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.02; H, 11.85.

5 (R^1 = Ph, R^2 = Me): Gc (200°C) t_R = 11.8 (5b), 15.7 (5a) min; TLC, R_f(5b) = 0.27, R_f(5a) = 0.19 (hexane-EtOAc, 5:1); IR (neat) 3430 (br), 2980, 2940, 1610, 1100, 760 cm^{-1}; ^1H NMR (CCl_4) δ 7.03-7.53 (m, 5 H, ArH), 3.73-4.67 (m, 3 H), 1.97 (s, 1 H, OH); Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.56; H, 8.67.

5 (R^1 = Ph, R^2 = Et): Gc (200°C) t_R = 15.3 (5b), 20.7 (5a) min; TLC, R_f(5b) = 0.19, R_f(5a) = 0.11 (hexane-EtOAc, 5:1); IR (neat) 3450 (br), 2980, 2950, 1610, 1100, 1070, 760 cm^{-1}; ^1H NMR (CCl_4) δ 7.00-7.57 (m, 5 H, ArH), 3.67-4.43 (m, 3 H), 2.37 (s, 1 H, OH); Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.00; H, 9.00. Found: C, 78.00; H, 9.00.

5 (R^1 = Me, R^2 = i-Bu): Gc (150°C) t_R = 7.1 (5b), 9.4 (5a) min; TLC, R_f(5b) = 0.36, R_f(5a) = 0.22 (hexane-EtOAc, 5:1); IR (neat) 3400 (br), 2950, 2100, 1640 cm^{-1}; ^1H NMR (CCl_4) δ 3.50-4.40 (m, 3 H), 2.60 (s, 1 H, OH), 1.80 (d, J=1.9 Hz, 3 H); Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.49; H, 11.44.

5 (R^1 = Me, R^2 = cyclohexyl): Gc (180°C) t_R = 7.1 (5b), 9.0 (5a) min; TLC, R_f(5b) = 0.26, R_f(5a) = 0.21 (hexane-EtOAc, 5:1); IR (neat) 3430 (br), 2930, 2860, 1450, 1380, 1330, 1060 cm^{-1}; ^1H NMR (CCl_4) δ 3.60-4.30 (m, 3 H), 2.60 (s, 1 H, OH), 1.83 (d, J=2.0 Hz, 3 H); Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10,99. Found: C, 75.53; H, 11.04.

Reductive cleavage of the acetal 4 with Et_3SiH in the presence of $TiCl_4$: To a solution of the acetal **4** (0.105 g, 0.5 mmol) and triethylsilane (0.080 mL, 0.5 mmol) in 3 mL of dichloromethane was added $TiCl_4$ (0.5 mL of 1 M dichloromethane solution, 0.5 mmol) at -78°C. The mixture was stirred there for 2 h. 0.5 mL of methanol was added and the resulting mixture was raised to room temperature and the product was poured into 2 N hydrochloric acid. Extraction of the product with ether twice followed by the removal of dried solvent to give a crude oil which was treated with KF-MeOH in a similar manner as carried out in the reduction of the acetal **1** to give a 61.2 mg of **5b** (58%). Gc analysis showed the ratio of 94:6; t_R = 9.4 (major) and 13.7 (minor) min (150°C) which was identical with those of the product of aluminum hydride reduction. The reaction of **4** with $SnCl_4$ was also carried out similarly to afford **5b** in 67% yield with the ratio of 95:5.

Removal of chiral auxiliary. Preparation of 3-octyn-2-ol (R^1 = n-Bu, R^2 = Me). Oxidation of **5a** (R^1 = n-Bu, R^2 = Me), was carried out with pyridinium chlorochromate (215.6 mg, 1.0 mmol) in dichloromethane (3 mL) at room temperature for 14 h. A saturated aqueous sodium bisulfite (10 mL) was poured into the resulting suspension and the separated organic layers were concentrated in vacuo to give the crude oil which was subsequently treated with potassium carbonate (0.7 g) in methanol (5 mL) at room temperature for 2 h. The mixture was diluted with water and the product was extracted with hexane twice, concentration in vacuo and chromatography on silica gel (hexane-ether, 10 : 1) furnished the optically pure (R)-3-octyn-2-ol (**6a**, R^1 = Bu, R^2 = Me) in 71 % yield from **5a** as a colorless liquid. TLC, R_f = 0.22 (hexane-EtOAc, 5:1); IR (neat) 3350 (br), 2950, 2930, 2860, 2250, 1150, 1080 cm^{-1}; ^1H NMR (CCl_4) δ 4.37 (q, J = 7.0 Hz, 1 H), 2.63 (s, 1 H, OH), 1.93-2.50 (m, 2 H), 1.33 (d, J = 7.0 Hz, 3 H); $[\alpha]^{24}_D$ +39.11° (c 1.63, ether); lit. $[\alpha]^{23}_D$ +33.0 (c 1.62, ether).[3a]

4-Nonyn-3-ol (6a, R^1 = n-Bu, R^2 = Et): TLC, R_f = 0.41 (hexane-EtOAc, 5:1); IR (neat) 3350 (br), 2970, 2950, 2890, 2270, 1460 cm^{-1}; ^1H NMR (CCl_4) δ 4.00-4.44 (m, 1 H), 1.90-2.47 (m, 3 H); $[\alpha]^{26}_D$ +21.60° (c 1.03, ether).

4-Phenyl-3-butyn-2-ol (6a, R^1 = Ph, R^2 = Me): TLC, R_f = 0.10 (hexane- EtOAc, 5:1); IR (neat) 3330 (br), 2990, 2250, 1610, 1100, 750 cm^{-1}; ^1H NMR (CCl_4) δ 6.93-7.87 (m, 5 H, ArH), 4.67 (q, J = 6.0 Hz, 1 H), 3.23 (s, 1 H, OH), 1.50 (d, J = 6.0 Hz, 3 H); $[\alpha]^{21}_D$ +36.68° (c 0.81, $CHCl_3$); lit. $[\alpha]^{25}_D$ +51.8° (neat).[3e]

1-Phenyl-1-pentyn-3-ol (6a, R^1 = Ph, R^2 = Et): TLC, R_f = 0.16 (hexane-EtOAc, 5:1); IR (neat) 3330 (br), 2970, 2940, 2880, 2240, 1660, 1490, 1440, 760, 690 cm^{-1}; ^1H NMR (CCl_4) δ 6.97-7.50 (m, 5 H, ArH), 4.43 (t, J = 6.0 Hz, 1 H), 2.67 (s, 1 H, OH), 1.50-2.10 (m, 2 H), 1.03 (t, J = 6.0 Hz, 3 H); $[\alpha]^{21}_D$ +21.97° (c 1.27, ether).

6-Methyl-2-heptyn-4-ol (6a, R^1 = Me, R^2 = i-Bu): TLC, R_f = 0.21, (hexane-EtOAc, 5:1); IR (neat) 3350 (br), 2960, 2940, 2880, 2250, 1460, 1030 cm^{-1}; ^1H NMR (CCl_4) δ 4.00-4.44 (m, 1 H), 2.27 (s, 1 H, OH), 1.80 (d, J = 1.8 Hz, 3 H), 0.90 (d, J = 6.0 Hz, 6 H); $[\alpha]^{24}_D$ +15.10° (c 2.47, $CHCl_3$); lit. $[\alpha]^{25}_D$ +13.48° (c 4.9, $CHCl_3$).[3d]

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