Highly Diastereoselective Acetal Cleavages Using Novel Reagents Prepared from Organoaluminum and Pentafluorophenol

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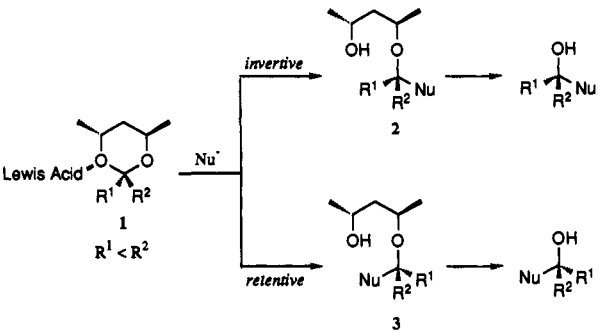
Abstract: Chiral acetals derived from aldehydes and (-)-(2*R*,4*R*)-2,4-pentanediol are cleaved selectively by organoaluminum reagents. The reaction proceeds *via* the retentive-alkylation process with >95% selectivities in most cases. Trialkylaluminum reagent is utilized for higher alkyl transfers, but for smaller alkyl transfers, a new reagent system, combining trialkylaluminum and the halophenols such as pentafluorophenol and 2,4,6-trichlorophenol, is employed. Chiral acetals derived from aldehydes and 1,3-butanediol are cleaved selectively by trialkylaluminum, even for smaller alkyl transfers. Oxetane is also exposed to these aluminum reagents, and the retentive-alkylation products are obtained stereoselectively. The reaction of acetals derived from (-)-(2*R*,4*R*)-2,4-pentanediol and ketones in the presence of a catalytic amount of aluminum pentafluorophenoxide produces reductively cleaved products with high diastereoselectivity. The reaction is a new means of diastereoselective cleavage of acetals: an intramolecular Meerwein-Ponndorf-Verley reductive and Oppenauer oxidative reaction on an acetal template.

Introduction

Controlling the stereochemistry of the addition of nucleophiles to acetals is an increasingly important problem in organic synthesis.[1] The great synthetic value of this approach comes from the relative asymmetric induction with chiral acetals derived from optically active alcohols (Scheme I). Preferential complexation of a Lewis acid with an oxygen of acetal and subsequent invertive substitution take place in the reaction of acetal using the Lewis acid-nucleophile system (**1** to **2**).[2] Our initial investigation of such a reaction, however, showed that when the nucleophile is aluminum hydride, reaction results in a retentive relationship between the incoming hydride and the departing oxygen atom.[3] This retentive substitution of acetal is exceptional and may be explained by the tight ion pair between the aluminum ate complex and the oxocarbenium ion.[3b,4] Similar retentive alkylation has not been reported, however, and the reaction of chiral acetals with trimethylaluminum, for example, is not stereoselective.[3b] It was then of interest to search for an appropriate reaction system that could deliver the *alkyl* group enantioselectively to the *re* face of an oxocarbenium ion (**1** to **3**, Nu = alkyl), both as a test of the mechanistic hypothesis and as a step toward development of a more general synthetic methodology. The results that follow verify this possibility and narrow the methodological gap.

Scheme I. Diastereoselective Acetal Cleavage Using Lewis Acid-Nucleophile Reagents



Results and Discussion

Alkylative Cleavage of Acetals.[5] It has been known for some time that reaction of chiral acetals with trimethylaluminum or triethylaluminum in nonpolar or less polar solvents such as hexane, toluene, or dichloromethane is not stereoselective.[3b] After further detailed investigation, however, an unexpectedly high selectivity was observed with homologous tripropylaluminum and even with

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(1) For a recent review, see: (a) Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 477. (b) Mash, A. E. In *Studies in Natural Product Synthesis*; Atta-Ur Rahman, Ed.; Elsevier: Amsterdam, 1988; Vol. 1, p 577. (c) Seebach, D.; Imwinkelried, R.; Weber, T. In *Modern Synthetic Methods*; Sheffold, R., Ed.; Springer-Verlag: Berlin, 1986; Vol. 4, p 125.

(2) Trialkylsilanes: (a) Mori, A.; Ishihara, K.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *27*, 987. (b) Mori, A.; Ishihara, K.; Arai, I.; Yamamoto, H. *Tetrahedron* **1987**, *43*, 755. Allylsilanes: (c) Johnson, W. S.; Crackett, P. H.; Elliott, J. D.; Jagodzinski, J. J.; Lindell, S. D.; Natarajan, S. *Tetrahedron Lett.* **1984**, *25*, 3591. Silyl enol ethers: (d) McNamara, J. M.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7371. (e) Sekizaki, H.; Jung, M.; McNamara, J. M.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7372. (f) Johnson, W. S.; Edington, C.; Elliott, J. D.; Silverman, I. R. *J. Am. Chem. Soc.* **1984**, *106*, 7588. (g) Silverman, I. R.; Edington, C.; Elliott, J. D.; Johnson, W. S. *J. Org. Chem.* **1987**, *52*, 180. Alkynylsilane: (h) Johnson, W. S.; Elliott, R.; Elliott, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2904. Silyl cyanide: (i) Elliott, J. D.; Choi, V. M. F.; Johnson, W. S. *J. Org. Chem.* **1983**, *48*, 2294. (j) Choi, V. M. F.; Johnson, W. S. *Tetrahedron Lett.* **1984**, *25*, 591. Ketene silyl acetal: (k) Elliott, J. D.; Steele, J.; Johnson, W. S. *Tetrahedron Lett.* **1985**, *26*, 2535. Alkylzinc, alkylmagnesium, or alkyllithium: (l) Lindell, S. D.; Elliott, J. D.; Johnson, W. S. *Tetrahedron Lett.* **1984**, *25*, 3947. (m) Mori, A.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1984**, *25*, 4421. Alkylcopper: (n) Ghribi, A.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1984**, *25*, 3083. (o) Normant, J. F.; Alexakis, A.; Ghribi, A.; Mangeney, P. *Tetrahedron* **1989**, *45*, 507.

(3) (a) Mori, A.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1983**, *24*, 4581. (b) Mori, A.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *J. Organomet. Chem.* **1985**, *285*, 83. (c) Ishihara, K.; Mori, A.; Arai, I.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *26*, 983. Six equivalents of aluminum hydride reagents (DIBAH, Br_2AlH, and Cl_2AlH) are practically needed for highly diastereoselective reductive cleavages of chiral acetals as well as the alkylative cleavages of chiral acetals.

(4) (a) Denmark, S. E.; Willson, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 3475. (b) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107. (c) Ishihara, K.; Mori, A.; Yamamoto, H. *Tetrahedron* **1990**, *46*, 4595. (d) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089. (e) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1991**, *56*, 6458. (f) Sammakia, T.; Smith, R. S. *J. Org. Chem.* **1992**, *57*, 2997. (g) Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 10998.

(5) For a preliminary report of part of this investigation, see: Ishihara, K.; Hanaki, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 7074.

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Table I. Alkylative Cleavage of Chiral Acetals Using R_3Al[a]

1 (R^1 = H) → 3 (R^1 = H; Nu = R)

entry	R^2	R	temp (°C)	yield (%)	ret:inv[b]
1	C_6H_{13}	Me	52	90	70:30
2[c]			40	76	77:23
3[d]			53	92	46:54
4		Et	52	99	87:13
5		Pr	60	>99	99:1
6[e]		*i*-Bu	65	60	95:5
7	Pr	C_6H_{13}	60	>99	97:3
8	c-C_6H_{11}	Me	52	87	78:22
9[c]			49	95	66:34
10		Et	50	85	94:6
11		Bu	60	>99	98:2
12	Ph	Me	25	*f*	60:40
13		Et	25	86	91:9
14		Pr	60	75	96:4
15	BuC≡C	Me	50	88	51:49
16		Et	50	60	82:18

[a] Unless otherwise specified, trialkylaluminum (6 equiv) in toluene was used. [b] The ratio was determined by capillary GC. [c] Dichloromethane was used as a solvent. [d] Hexane was used as a solvent. [e] Other product was also given by reductive cleavage of acetal. [f] In this case, the desired product could not be separated from byproducts by column chromatography.

higher alkylaluminums (Table I). The subtle difference between reactions of trimethylaluminum and tripropylaluminum might be the results, *inter alia*, of higher site selectivity in complexation of a bulkier reagent like tripropylaluminum with two different acetal oxygens and/or more nucleophilicity of alkyl groups, such as propyl, which accelerate the alkylation step.

To increase the selectivity of the reaction, we studied a variety of mono(aryloxy)aluminums, since the discriminating selectivity of a Lewis acid is significantly influenced by the size of the reagent.[6] Most of these reagents[7] gave exceedingly low yields of the alkylation products, which was not surprising because of the low nucleophilicity of the usual (aryloxy)aluminum reagents. We found, however, that the treatment of trialkylaluminum with 2,6-dihalo-substituted phenol derivatives produced a sufficiently reactive aluminum reagent, which was more reactive than the corresponding trialkylaluminum and effective in the clean and stereoselective cleavage of chiral acetals. Several examples of this transformation are given in Table II. Thus, trialkylaluminum and dialkylaluminum aryloxide methods are complementary to each other, and when an appropriate reagent system and reaction conditions are chosen, >95% selectivity can be achieved in most cases, except when R^2 is an aromatic or alkynyl group. In the reaction using pentafluorophenol and trialkylaluminum, the β-alkoxy ketone was given as a byproduct in low yield. In the case of aromatic acetal, in particular, the side reaction was increased, while, contrarily, the desirable coupling product was given in low yield. The byproduct was presumably produced by an intramolecular Meerwein–Ponndorf–Verley reductive cleavage.

The precise structure of the trialkylaluminum–pentafluorophenol complex is also not yet clear. However, it should be noted that, when trimethylaluminum and pentafluorophenol were premixed at 25 °C, 1 equiv of methane gas was generated in toluene, but was not generated in dichloromethane. Also, when triethylaluminum and pentafluorophenol were premixed at 25 °C in toluene, the evolving ethane gas was insufficient. On the other hand, when diethylaluminum hydride and pentafluorophenol were premixed at 25 °C, 1 equiv of hydrogen gas was generated in toluene, and diethylaluminum pentafluorophenoxide was produced. The reaction of acetal using the latter reagent (entry 6, Table II) gave higher diastereoselectivity and lower conversion than when the former reagent was used (entry 5, Table II). Further investigations to elucidate the present reaction are necessary.

Table II. Alkylative Cleavage of Chiral Acetals Using R_2AlOAr[a]

1 (R^1 = H) → 3 (R^1 = H; Nu = R)

entry	R^2	R	ArOH[b]	yield (%)	ret:inv[c]
1	C_6H_{13}	Me	A	70	>99:1
2			B	59	97:3
3			C	87	89:11
4			D	86	87:13
5[d]		Et	A	70	93:7
6[e]			A	40	96:4
7			B	59	98:2
8[d]			C	87	89:11
9[d]			D	86	88:12
10	c-C_6H_{11}	Me	A	70	>99:1
11[d]		Et	A	87	>99:1
12	Ph	Me	A	49	82:18
13[d]		Et	A	41	89:11
14	BuC≡C	Me	A	57	80:20
15[d]		Et	A	64	89:11

[a] Unless otherwise specified, trialkylaluminum (6 equiv) and phenol (6 equiv) in toluene was stirred at 25 °C for 1 h, followed by treatment of acetal for 3–12 h. [b] A, pentafluorophenol; B, 2,4,6-trichlorophenol; C, 2,4,6-tri-*tert*-butylphenol; D 2,6-di-*tert*-butyl-4-methylphenol. [c] The ratio was determined by capillary GC. [d] Insufficient gas evolution (50–60%) was observed during the preparation of the reagent. [e] Et_2AlH was used in place of Et_3Al.

Table III. Alkylative Cleavage of Chiral Acetals[a]

entry	R'	reagent	temp (°C)	yield (%)	ret:inv[b]
1	C_6H_{13}	Me_3Al	51	62	86:14
2		$Me_2AlOC_6F_5$	51	21	>99:1
3	Ph	Me_3Al	25	70	65:35
4		$Me_2AlOC_6F_5$	25	70	82:18

[a] Unless otherwise specified, Me_3Al (6 equiv) or $Me_2AlOC_6F_5$ (6 equiv) in toluene was used. [b] The ratio was determined by capillary GC.

Next, we examined the reaction of acetals derived from (–)-(2*R*,3*R*)-2,3-butanediol for the purpose of reducing the side reaction *via* an intramolecular hydride transfer. Some of our results are summarized in Table III. The use of 2,3-butanediol instead of 2,4-pentanediol clearly did depress the side reaction; however, alkylative cleavage of the acetal of dioxolane type was a slower process than that of the acetal of dioxane type. The stereoselectivity of the reaction was raised by the addition of pentafluorophenol in the same way as addition of acetal derived from 2,4-pentanediol.

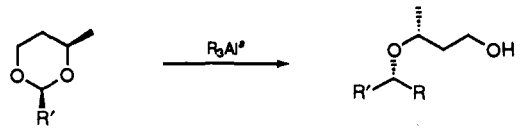
Finally, the reaction of acetals derived from 1,3-butanediol with trialkylaluminum or the trialkylaluminum–pentafluorophenol system was examined. This type of acetal represents an especially interesting situation, because the 2-position (derived from the aldehyde carbon) becomes chiral in the acetalization, and if the acetal can exist in the more stable diequatorial form of the (2*SR*,4*RS*)-cis compound, trialkylaluminum would be expected to have stereospecific coordination with the acetal oxygen which is less hindered;[8] hence, the stereoselectivity of this reaction should genuinely represent retentive or invertive directional selectivity on attack of the alkyl anion to the cleaved carbon–oxygen bond. The results are summarized in Table IV. Reactions

(6) Maruoka, K.; Nagahara, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 6115.

(7) Other phenols that revealed no reactions are 2-fluorophenol, 2,4,6-trimethylphenol, and 2,6-diisopropylphenol. The complex of pentachlorophenol and trimethylaluminum was not soluble in toluene or dichloromethane.

(8) Kaino, M.; Naruse, Y.; Ishihara, K.; Yamamoto, H. *J. Org. Chem.* **1990**, *55*, 5814.

Table IV. Alkylative Cleavage of Chiral Acetals[a]



entry	R'	R	temp (°C)	yield (%)	ret:inv[b]
1	C_6H_{13}	Me	0	>99	97:3
2[c]			0	98	98:2
3		Pr	60	99	97:3
4[d]	C_8H_{17}	*i*-Bu	60	55	81:19
5	*i*-Bu	C_8H_{17}	60	>99	95:5
6	c-C_6H_{11}	Me	0	57	>99:1
7		Me(A)	0	69	>99:1
8		Et	25	>99	94:6
9		Et(A)	25	>99	>99:1
10	Ph	Me	0	91	96:4
11		Me(A)	0	81	83:17
12		Et	25	87	96:4
13		Et(A)	25	58	93:7

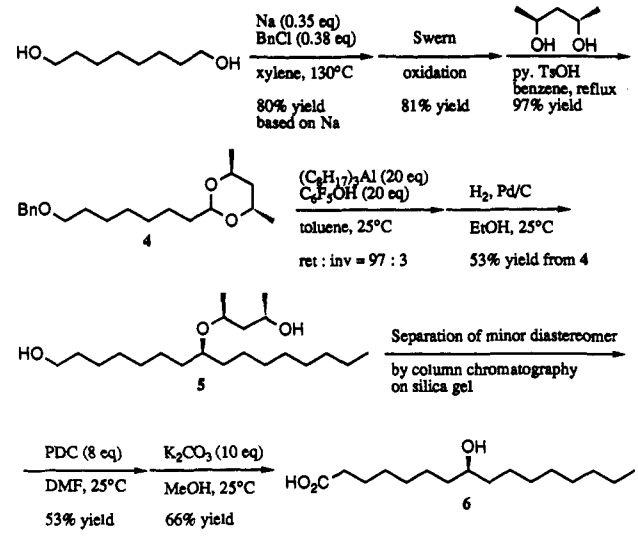
[a] Unless otherwise specified, trialkylaluminum (6 equiv) in toluene was used; A, pentafluorophenol (6 equiv) was added. [b] The ratio was determined by capillary GC. [c] Trans isomer of acetal was used. [d] Other product was also given by reductive cleavage of acetal.

of both cis and trans acetals gave the same stereoisomer (entries 1 and 2, Table IV). In most cases, the stereoselectivity of the reaction of acetals derived from 1,3-butanediol with trialkylaluminum is high enough, and in the case of aromatic acetal it is preferable to that with the trialkylaluminum–pentafluorophenol system. Trialkylaluminum completely discriminated the two different acetal oxygens and stabilized the cis oxocarbenium ion pair intermediate regardless of the stereochemistry of acetal. As a result, the relatively lower stereoselectivity of the reaction in the presence of pentafluorophenol can be understood in terms of a slightly extended oxocarbenium ion pair intermediate *via* the polarity of pentafluorophenol. The reaction did not produce β-alkoxy ketone as a byproduct.

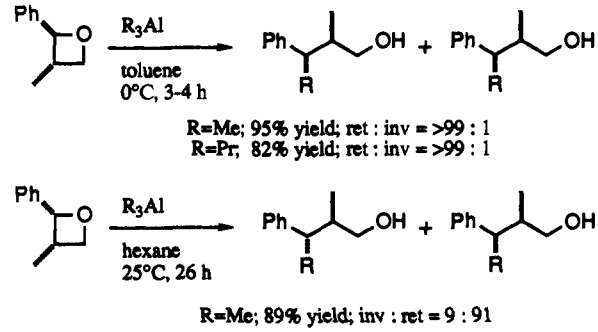
Synthesis of (+)-8-Hydroxypalmitic Acid (6). To demonstrate the general applicability of this retentive-alkylation methodology, we synthesized (+)-8-hydroxypalmitic acid (**6**),[9] and endogenous inhibitor of spore germination in *Lygodium japonicum*. The corresponding chiral acetal **4** was prepared by acetalization of 8-(benzyloxy)octanal, which was derived by monoprotection of 1,8-octanediol with benzyl chloride and subsequent Swern oxidation, with (2*S*,4*S*)-2,4-pentanediol (Scheme II). Diastereoselective cleavage of **4** using 6 equiv of trioctylaluminum in toluene gave the corresponding alcohols (diastereomeric ratio, ret:inv (retentive:invertive) 86:14).[3] The moderate diastereoselectivity of the reaction using trioctylaluminum was evident for not only **4** but also **1** (R^1 = H, R^2 = Pr; ret:inv = 89:11). The reason the selectivity of acetal cleavage using trioctylaluminum is low is not known; this reagent is specific as far as we know. Further investigation of the reaction conditions showed that the diastereoselectivity (up to 97%) of the reaction of **4** was increased when larger amounts and highly diluted trioctylaluminum and pentafluorophenol were used. The improved results may be attributed to the proper aggregation of the aluminum reagent. Diastereoselective cleavage of **4** using 20 equiv of trioctylaluminum and 20 equiv of pentafluorophenol in toluene gave the corresponding alcohols (diastereomeric ratio, ret:inv = 97:3). A minor diastereomer was easily removed by column chromatography on silica gel. Thus, hydrogenation (Pd/C) gave the corresponding diol **5**, which was oxidized with excess pyridinium dichromate (PDC) to give the keto acid in 53% yield. Treatment with potassium carbonate in methanol–water led to (+)-(*S*)-**6**, $[\alpha]^{24}_D$ = +1.23° (*c* = 1.82, $CHCl_3$) (data for the natural (+)-(*S*)-**6**: lit.[9]

(9) Masaoka, Y.; Sakakibara, M.; Mori, K. *Agric. Biol. Chem.* **1982**, *46*(9), 2319.

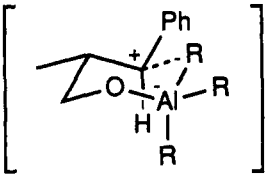
Scheme II. Synthesis of (+)-8-Hydroxypalmitic Acid



Scheme III. Diastereoselective Cleavage of Oxetanes



Scheme IV. Transition State of Oxetane Cleavage



$[\alpha]^{22}_D$ = +1.06° ± 0.2 (*c* = 2.19, $CHCl_3$); lit.[10] mp 78.5–79.5 °C, $[\alpha]_D$ = +0.3° (*c* = 19.5, $CHCl_3$); lit.[11] mp 78–79 °C, $[\alpha]^{25}_D$ = +0.6° (*c* = 3.3, MeOH)).

Alkylative Cleavage of Oxetanes. The retentive stereochemistry of the reaction using monoaryloxy aluminums may be due to the successful discrimination of the two acetal oxygens by these reagents. In fact, the treatment of oxetane with trialkylaluminums produced a ring-opening product with strict retentive stereoselectivity, as shown in Scheme III. In these cases, only one oxygen is present in the system and, particularly in the case of the trans isomer, an ideal six-membered transition state can be expected (Scheme IV). A slight decrease of selectivity and reactivity for the cis isomer may be caused by the axial methyl or phenyl group of the transition structure.

Reductive Cleavage of Acetals.[5,12] In the alkylative cleavage of chiral acetal derived from (−)-(2*R*,4*R*)-2,4-pentanediol, a small amount (~5%) of unexpected β-alkoxy ketone **7** was produced, which would be derived from a unique intramolecular Meerwein–Ponndorf–Verley–Oppenauer reaction. Our interests then focused on the exclusive preparation of β-alkoxy ketones from chiral

(10) Tulloch, A. P. *Can. J. Chem.* **1965**, *43*, 415.
(11) Yamane, H.; Sato, Y.; Takahashi, N.; Takano, K.; Furuya, M. *Agric. Biol. Chem.* **1980**, *44*, 1097.
(12) For a preliminary report of part of this investigation, see: Ishihara, K.; Hanaki, N.; Yamamoto, H. *Synlett* **1993**, 127.

Scheme V. Reductive Cleavages of Chiral Acetals

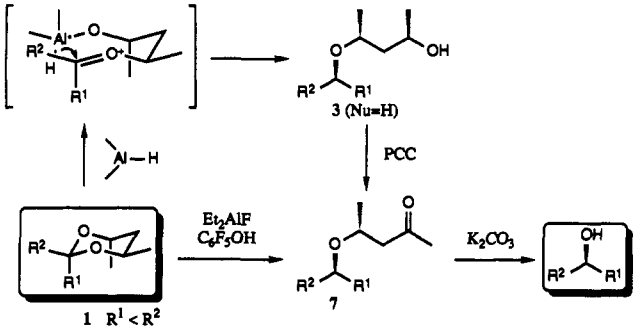


Table V. Reductive Cleavage of Chiral Acetals Using Et_2AlF–C_6F_5OH[a]

$1 \rightarrow 7$

entry	R^1	R^2	solvent	yield (%)	ret:inv[b] (S:R)[c]
1	Me	C_5H_{11}	CH_2Cl_2	91	81:19
			toluene	61	86:14
2	Me	*i*-Bu	CH_2Cl_2	81	72:28
			toluene	69	77:23
3	Me	*i*-Pr	CH_2Cl_2	71	97:3
			toluene	62	98:2
4	Me	Ph	CH_2Cl_2	81	95:5
			toluene	68	>99:1
5	Et	Ph	CH_2Cl_2	92	90:10
			toluene	84	93:7
6	Me	c-Hex	CH_2Cl_2	94	96:4
			toluene	87	96:4
7			CH_2Cl_2	99	80:20[d]
			toluene	99	84:16[d]

[a] A mixture of diethylaluminum fluoride (1.2 equiv) and pentafluorophenol (2.4 equiv) in toluene was stirred at 0 °C for 10 min, followed by treatment of acetal at 0 °C for 1 h. [b] The ratio was determined by capillary GC. [c] The absolute configuration at the reduced carbon of **7** was determined by comparison with authentic samples.[2a,4] [d] *trans*-β-Alkoxy ketone was obtained as a major diasteromer.

acetals, since the direct formation of the β-alkoxy ketone is practically quite useful at the point of removal of the chiral auxiliary, easily followed by base-catalyzed β-elimination of the β-alkoxy ketone to give the optically pure alcohol. It was soon realized that combined use of diethylaluminum fluoride (1.2 equiv) and pentafluorophenol (2.4 equiv) was most effective for a diastereoselective reductive cleavage reaction. The major isomer afforded a retentive product, and the observed high diastereoselectivity was similar to or better than that of reductive cleavage of acetals derived with aluminum hydride[3] (Scheme V). As shown in Table V, several chiral acetals derived from aliphatic or aromatic ketones are applicable in good yields and with high diastereoselectivities. In all cases, when toluene was used as a solvent instead of dichloromethane, diastereoselectivity was improved, but the yield was rather low.

Further investigation was done to develop a catalytic process for this new reductive cleavage. In preliminary studies,[5] the conversion of chiral acetal **1** (R^1 = Me, R^2 = C_5H_{11}) derived from 2-heptanone and (−)-(2*R*,4*R*)-2,4-pentanediol to a β-alkoxy ketone was initially chosen as a model, and the effect of pentafluorophenol was studied. The results of examinations of various reaction conditions using several aluminum reagents as Lewis acid are summarized in Table VI. Although we have already explained that $R_2AlOC_6F_5$ is a most effective reagent for chiral acetals derived from aldehydes and chiral diols to give alkylatively cleaved β-alkoxy alcohols, the treatment of chiral acetals derived from ketones with $Me_2AlOC_6F_5$ or $MeAl(OC_6F_5)_2$ gave rather more reductively cleaved β-alkoxy ketones as main

Table VI. Reductive Cleavage of Chiral Acetal Using Me_3Al and C_6F_5OH[a]

$1 \xrightarrow{Me_{3-n}Al(OC_6F_5)_n} 7$ (R^1 = Me, R^2 = C_5H_{11})

entry	Lewis acid[a] (equiv)	solvnt	temp (°C)	time (h)	yield (%)	ret:inv[b] (S:R)[c]
1	$Me_2AlOC_6F_5$ (6)	toluene	25	6	23[d]	85:15
2	$MeAl(OC_6F_5)_2$ (6)	toluene	25	3	34	76:24
3	$Al(OC_6F_5)_3$ (1.1)	toluene	0	2	>99	85:15
4	$Al(OC_6F_5)_3$ (0.05)	toluene	25	24	31	86:14
5	$Al(OC_6F_5)_3$ (0.05)	CH_2Cl_2	25	24	83	82:18

[a] A mixture of trimethylaluminum and pentafluorophenol was stirred at 25 °C for 1 h, followed by treatment of acetal. [b] The ratio was determined by capillary GC. [c] The absolute configuration at the reduced carbon of **7** was determined by comparison with authentic samples.[2a,4] [d] 2-Methyl-2-(1′-methyl-3′-oxobutyoxy)heptane was obtained in 11% yield.

Table VII. Reductive Cleavage of Chiral Acetals Using $Al(OC_6F_5)_3$ Catalyst[a]

$1 \rightarrow 7$

entry	R^1	R^2	yield (%)	ret:inv[b] (S:R)[c]
1	Me	C_5H_{11}	83	82:18
2	Me	*i*-Bu	61	73:27
3	Me	*i*-Pr	90	94:6
4	Me	Ph	71	>99:1
5	Et	Ph	78	92:8
6	Me	c-Hex	89	95:5
7			67	81:19[d]

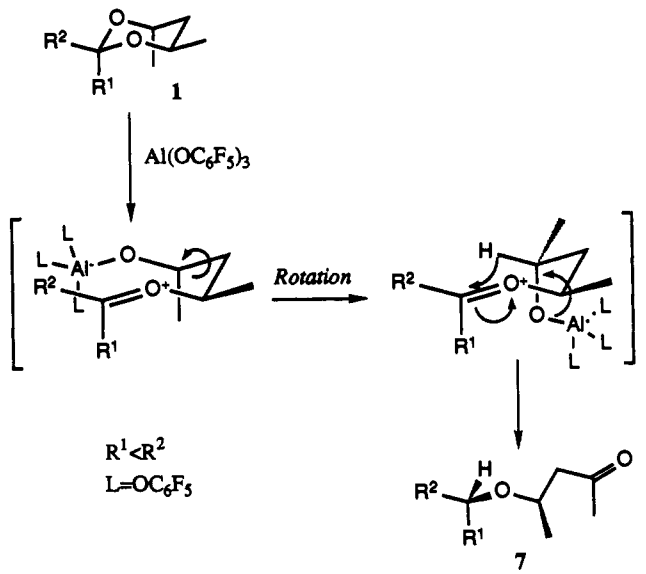
[a] A mixture of trimethylaluminum (0.05 equiv) and pentafluorophenol (0.15 equiv) in toluene was stirred at 25 °C for 1 h, followed by treatment of acetal at 25 °C for 1 day. [b] The ratio was determined by capillary GC. [c] The absolute configuration at the reduced carbon of β-alkoxy ketone **7** was determined by comparison with authentic samples.[2a,4] [d] *trans*-β-Alkoxy ketone was obtained as a major diasteromer.

products than alkylatively cleaved β-alkoxy alcohols (entries 1 and 2, Table VI). We found that aluminum pentafluorophenoxide (1.1 equiv) was an excellent reagent for the diastereoselective cleavage (entry 4, Table VI). When the reaction medium was changed from toluene to dichloromethane, the chemical yield was increased from 31% to 83%, even when using 5 molar % of aluminum pentafluorophenoxide, but the diastereomeric ratio of **7** (R^1 = Me, R^2 = C_5H_{11}) was reduced from 86:14 to 82:18 (entry 4 vs entry 5, Table VI). The major isomer afforded retentively reduced products, and the observed high diastereoselectivity was similar to that of reductive cleavages of acetals with organoaluminum hydride reagents.[3] It was also noted that, in the presence of a catalytic amount of diethylaluminum fluoride (10 molar %) and pentafluorophenol (20 molar %), the reaction did not proceed, even when heated to 80 °C.

Several examples of the present reaction are demonstrated in Table VII. Chiral acetals derived from both aliphatic and aromatic ketones were cleaved in good yields and with high diastereoselectivities. These diastereoselectivities tended to be similar to those in the reductive cleavage using aluminum hydride.[3]

Acetals derived from several different alcohols were next examined for this transformation. Acetals of 2-heptanone derived from 1,3-propanediol and (−)-(2*R*,3*R*)-butanediol were not converted, even at room temperature. The acyclic acetal derived from 2-heptanone and 2-propanol was converted to isopropoxy ether in low yield. Therefore, the structure of acetal derived from (−)-(2*R*,4*R*)-2,4-pentanediol was found to be a suitable substrate in the present intramolecular hydride-transfer reaction

Scheme VI. Reductive and Oxidative Cleavage of Chiral Acetals



(Scheme VI). Although the detailed mechanism is not yet clear, it is assumed that an energetically stable tight ion-paired intermediate is generated by stereoselective coordination of Al-$(OC_6F_5)_3$ to one of the oxygens of the acetal: the hydrogen atom of the alkoxide is then transferred as a hydride from the retentive direction to this departing oxygen, which leads to the *S* configuration at the resulting ether carbon, as observed (Scheme VI).

Aluminum pentafluorophenoxide is the first aluminum Lewis acid catalyst for cationic reduction of acetals. It is particularly noteworthy that our developed intramolecular Meerwein–Ponndorf–Verley reductive and Oppenauer oxidative cleavage reaction is chemoselective: the present reaction proceeds only for chiral acetals derived from (–)-(2*R*,4*R*)-2,4-pentanediol and does not proceed for aldehyde, ketone, or other cyclic acetals. We also found that pentafluorophenol is an effective accelerator for Meerwein–Ponndorf–Verley reduction of 4-*tert*-butylcyclohexanone with aluminum isopropoxide (3 equiv) in dichloromethane; for example, the reduction was very slow at 0 °C (<5% for 5 h), but in the presence of pentafluorophenol (1 equiv), it was cleanly completed within 4 h at 0 °C.

Conclusions

In summary, this paper describes two new methodologies for cationic retentive alkylation and reduction of acetals. The results reflect the unusual effect of a halophenol ligand on the reactivity of organoaluminum reagents. The question of why these reagents retain sufficient nucleophilicity is still open. It is possible that the *o*-halo substituents of a phenoxide ligand may coordinate with the aluminum atom, thus increasing the nucleophilicity of the reagent. Whatever the reason, the coordination of halophenol and organoaluminum reagent offers unique opportunities in organometallic reactions.

Experimental Section

General. Infrared (IR) spectra were recorded on Hitachi 260-10 or Shimadzu FTIR-8100 spectrometers. ^{1}H NMR spectra were measured on a Varian Gemini 200 (200 MHz) spectrometer. Chemical shifts of ^{1}H NMR are expressed in parts per million downfield relative to internal tetramethylsilane (δ = 0) or chloroform (δ = 7.26). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; br, broad peak. Analytical gas–liquid phase chromatography (GC) was performed on a Shimadzu Model 8A instrument with a flame-ionization detector and a capillary column of PEG-20M Bonded (25 m) using nitrogen as carrier gas. High-performance liquid chromatography (HPLC) was done with a Shimadzu 9A instrument using a 4.6 mm × 25 cm JASCO Finepak Sil column. 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 60 E. Merck Art. No. 9385. Microanalyses were accomplished at the Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University. Reactions involving air- or moisture-sensitive compounds were conducted in appropriate round-bottomed flasks with magnetic stirring bars under an atmosphere of dry argon.

In experiments requiring dry solvents, benzene and toluene were dried over sodium metal. Dichloromethane was distilled from phosphorus pentoxide and over 4A molecular sieves. Unless otherwise noted, materials were obtained from commerical suppliers and were used without further purification.

Alkylative Cleavage of Acetals. Preparation of Acetals.[3b,4c] Acetals were prepared in excellent yield from the corresponding aldehydes and chiral diols, e.g. (–)-(2*R*,4*R*)-2,4-pentanediol, (–)-(2*R*,3*R*)-2,3-butanediol, 1,3-butanediol, in the presence of a catalytic quantity of *p*-toluenesulfonic acid or pyridinium *p*-toluenesulfonate.

The physical properties and analytical data of the acetals thus obtained are listed below.

(4*R*,6*R*)-4,6-Dimethyl-2-hexyl-1,3-dioxane (**1**; R^1 = H, R^2 = C_6H_{13}),[3b] **(4*R*,6*R*)-2-Cyclohexyl-4,6-dimethyl-1,3-dioxane** (**1**; R^1 = H, R^2 = c-C_6H_{11}),[3b] **(4*R*,6*R*)-4,6-dimethyl-2-phenyl-1,3-dioxane** (**1**; R^1 = H, R^2 = Ph),[2o] **(4*R*,5*R*)-4,5-Dimethyl-2-hexyl-1,3-dioxolane** (R′ = C_6H_{13}),[3b] **(4*R*,5*R*)-4,5-Dimethyl-2-phenyl-1,3-dioxolane** (R′ = Ph),[3b] **(2*SR*,4*RS*)-4-methyl-2-phenyl-1,3-dioxane** (R′ = Ph).[2o] Physical properties were identical with those reported.

(4*R*,6*R*)-4,6-Dimethyl-2-propyl-1,3-dioxane (**1**; R^1 = H, R^2 = C_3H_7): TLC, R_f = 0.57 (hexane–EtOAc, 5:2); IR (film) 2990, 2950, 2900, 1380, 1170, 1155, 1120, 1010, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, *J* = 7.1 Hz, 3H, C*H*$_3$CH$_2$), 1.21 (d, *J* = 6.0 Hz, 3H, CH$_3$), 1.24-1.62 (m, 5H, Me(CH$_2$)$_4$ and OCHC*H*HCHO), 1.36 (d, *J* = 7.0 Hz, 3 H, CH$_3$), 1.84 (ddd, *J* = 6.0, 11.6, 13.2 Hz, 1H, OCHCH*H*CHO), 3.95 (dsextet, *J* = 2.5, 6.0 Hz, 1H, OC*H*Me), 4.30 (quintet, *J* = 7.0 Hz, 1H, OC*H*Me), 4.86 (t, *J* = 5.1 Hz, 1H, O$_2$CH). Anal. Found: C, 68.29; H, 11.58. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46.

(4*R*,6*R*)-4,6-Dimethyl-2-(1′-hexynyl)-1,3-dioxane (**1**; R^1 = H, R^2 = $C_4H_9C{\equiv}C$): TLC, R_f = 0.56 (hexane–EtOAc, 5:2); IR (film) 2980, 2950, 2880, 2270, 1400, 1380, 1180, 1155, 1140, 1110, 1035, 1000, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.02-2.03 (m, 6H, CH$_3$C*H*$_2$C*H*$_2$ and CHC*H*$_2$CH), 1.26 (d, *J* = 6.2 Hz, 3H, CH$_3$), 1.39 (d, *J* = 7.2 Hz, 3H, CH$_3$), 2.24 (dt, *J* = 1.5, 7.2 Hz, 2H, CH$_2$C≡C), 3.93–4.11 (m, 1H, C*H*Me), 4.38 (m, 1H, C*H*Me), 5.56 (t, *J* = 1.5 Hz, 1H, CHC≡C). Anal. Found: C, 73.42; H, 10.47. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27.

(2*SR*,4*RS*)-2-Hexyl-4-methyl-1,3-dioxane (R′ = C_6H_{13}): TLC, R_f = 0.36 (hexane–EtOAc, 10:1); IR (film) 2955, 2855, 2379, 2269, 2238, 2228 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 6.5 Hz, 3H, CH$_2$C*H*$_3$), 1.20–1.78 (m, 12H, (C*H*$_2$)$_5$ and OCH$_2$C*H*$_2$CHO), 1.24 (d, *J* = 6.2 Hz, 3H, CHC*H*$_3$), 3.66–3.84 (m, 2H, OC*H*HCH$_2$C*H*O), 4.11 (ddd, *J* = 1.4, 5.0, 11.4 Hz, OCH*H*), 4.53 (t, *J* = 5.1 Hz, 1H, CHO$_2$). Anal. Found: C, 70.90; H, 12.10. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90.

(2*RS*,4*RS*)-2-Hexyl-4-methyl-1,3-dioxane (R′ = C_6H_{13}): TLC, R_f = 0.28 (hexane–EtOAc, 10:1); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.4 Hz, 3H, Me), 1.20–1.70 (m, 11H, (C*H*$_2$)$_5$ and OCH$_2$C*H*HCHO), 1.36 (d, *J* = 7.0 Hz, 3H, Me), 2.12–2.22 (m, 1H, OCH$_2$CH*H*CHO), 3.92 (d, *J* = 2.6 Hz, 1H, OC*H*H), 3.94–4.00 (m, 1H, OCH*H*), 4.20–4.37 (m, 1H, OC*H*Me), 4.85 (t, *J* = 5.3 Hz, 1H, O$_2$CH).

(2*SR*,4*RS*)-4-Methyl-2-octyl-1,3-dioxane (R′ = C_8H_{17}): TLC, R_f = 0.61, (hexane–EtOAc, 5:2); IR (film) 2926, 2855, 1379, 1169, 1138, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 6.1 Hz, 3H, CH$_2$C*H*$_3$), 1.20–1.60 (m, 16H, (C*H*$_2$)$_7$ and OCH$_2$C*H*$_2$CHO), 1.25 (d, *J* = 6.2 Hz, 3H, CHC*H*$_3$), 3.66–3.84 (m, 2H, C*H*HO and MeC*H*O), 4.11 (ddd, *J* = 1.4, 5.0, 11.4 Hz, 1H, CH*H*O), 4.53 (t, *J* = 5.0 Hz, 1H, CHO$_2$). Anal. Found: C, 72.81; H, 12.53. Calcd for $C_{13}H_{26}O_2$: C, 72.84; H, 12.23.

(2*SR*,4*RS*)-2-(2-Methylpropyl)-4-methyl-1,3-dioxane (R′ = *i*-Bu): TLC, R_f = 0.59 (hexane–EtOAc, 5:2); IR (film) 2959, 2440, 1379, 1170, 1142, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, *J* = 6.6 Hz, 3H, (C*H*$_3$)$_2$-CH), 1.23 (d, *J* = 6.2 Hz, 3H, C*H*$_3$CH), 1.37–1.92 (m, 5H, (CH$_3$)$_2$C*H*CH$_2$ and OCH$_2$C*H*$_2$CHO), 3.64–3.84 (m, 2H, OC*H*-HCH$_2$C*H*O), 4.10 (ddd, *J* = 1.4, 5.0, 11.4 Hz, 1H, OCH*H*), 4.58 (t, *J* = 5.5 Hz, 1H, CHO$_2$). Anal. Found: C, 68.41; H, 11.56. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47.

(2*SR*,4*RS*)-2-Cyclohexyl-4-methyl-1,3-dioxane (R′ = c-Hex): TLC, R_f = 0.68 (hexane–EtOAc, 5:2); IR (film) 2980, 2930, 2870, 1460, 1380, 1330, 1175, 1135, 1115, 1040, 1010, 985 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ

0.80–1.85 (m, 13H, c-C_6H_{11} and OCH_2CH_3), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 3.58–3.75 (m, 2H, OC*H*Me and OC*H*H), 4.05 (ddd, J = 1.4, 5.0, 11.4 Hz, 1H, OCH*H*), 4.19 (d, J = 5.4 Hz, 1H, OCHO). Anal. Found: C, 71.71; H, 11.22. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94.

General Procedure for Alkylative Cleavage of Acetals with Trialkylaluminum. To a solution of acetal (0.5 mmol) in toluene (10 mL) was added dropwise trialkylaluminum (1.5 mL of 2.0 M in hexane, 3.0 mmol) at 0 °C. The reaction mixture was stirred at a suitable temperature. After complete conversion, the resulting mixture was poured into 2 N aqueous sodium hydroxide (20 mL) and extracted with hexane three times (20 mL × 3). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluant: hexane–EtOAc) to give a diastereomeric mixture of alkylation products as a colorless oil.

General Procedure for Alkylative Cleavage of Acetals with the Combined Use of Trialkylaluminum and Pentafluorophenol. To a solution of trialkylaluminum (1.5 mL of a 2.0 M solution in hexane, 3.0 mmol) in toluene (10 mL) was added pentafluorophenol (1.5 mL of a 2.0 M solution in toluene, 3.0 mmol) at 25 °C under argon. The reaction mixture was stirred for 1 h at that temperature, during which period the evolution of alkane gas ceased. To this was introduced acetal (0.5 mmol) in toluene (1 mL) at 25 °C. After being stirred for 3–12 h, the solution was poured into 2 N aqueous sodium hydroxide (20 mL), and the product was extracted with hexane three times (20 mL × 3). The combined organic layers were dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by column chromatography on silica gel (eluant: hexane–EtOAc) to give a diastereomeric mixture of alkylation products as a colorless oil.

The diastereomeric ratios were determined by GC analysis by comparison with the authentic samples, which were prepared by alkylative cleavage of the corresponding acetals using a titanium tetrachloride–dialkylzinc system[1m,3b] or a titanium tetrachloride–dialkylcopper lithium system.[1n,o] In the case of some adducts, it was necessary to prepare the corresponding acetates in order to obtain a base-line separation of the two peaks.

The physical properties and analytical data of the alcohols thus obtained are listed below.

(2*R*,1′*R*,3′*R*)-2-(3′-Hydroxy-1′-methylbutoxy)-3-octyne (3, R^1 = H, R^2 = BuC≡C, Nu = Me),[2b] **(2*S*,1′*R*,3′*R*)-2-(3′-Hydroxy-1′-methylbutoxy-3-octyne** (2; R^1 = H, R^2 = BuC≡C, Nu = Me),[2b] **(3*R*,1′*R*,3′*R*)-2-(3′-Hydroxy-1′-methylbutoxy)-4-nonyne** (3; R^1 = H, R^2 = BuC≡C, Nu = Et),[2b] **(3*S*,1′*R*,3′*R*)-2-(3′-Hydroxy-1′-methylbutoxy)-4-nonyne** (2, R^1 = H, R^2 = BuC≡C, Nu = Et),[2b] **(2*R*,1′*R*,2′*R*)-2-(2′-Hydroxy-1′-methylpropoxy)octane** (R′ = C_6H_{13}),[2o] **(2*S*,1′*R*,2′*R*)-2-(2′-Hydroxy-1′-methylpropoxy)octane** (R′ = C_6H_{13}),[2o] **(1*R*,1′*R*,2′*R*)-1-(2′-Hydroxy-1′-methylpropoxy)-1-phenylheptane** (R′ = Ph),[2o] **(1*S*,1′*R*,2′*R*)-1-(2′-Hydroxy-1′-methylpropoxy)-1-phenylheptane** (R′ = Ph).[2o] Physical properties were identical with those reported.

(2*R*,1′*R*,3′*R*)-2-(3′-Hydroxy-1′-methylbutoxy)octane (3; R^1 = H, R^2 = C_6H_{13}, Nu = Me):[2b] TLC, R_f = 0.39 (hexane–EtOAc, 5:2); GC (110 °C), t_R = 18.3 min (alcohol form); IR (film) 3750–3100, 2970, 2930, 2870, 1465, 1380, 1340, 1160, 1120, 1080, 1060, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.5 Hz, 3H, CH_3), 1.14 (d, J = 6.0 Hz, 3H, CH_3), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.20 (d, J = 6.2 Hz, 3H, CH_3), 1.20–1.70 (m, 12H, $CH_3(CH_2)_5$ and $CHCH_2CH$), 3.36 (br, 1H, OH), 3.42–3.60 (m, 1H, CHO), 3.80–3.98 (m, 1H, CHO), 4.04–4.23 (m, 1H, CHO).

(2*S*,1′*R*,3′*R*)-2-(3′-Hydroxy-1′-methylbutoxy)octane (2; R^1 = H, R_2 = C_6H_{13}, Nu = Me):[3b] TLC, R_f = 0.39 (hexane–EtOAc, 5:2); GC (110 °C), t_R = 16.9 min (alcohol form).

(3*R*,1′*R*,3′*R*)-3-(3′-Hydroxy-1′-methylbutoxy)nonane (3; R^1 = H, R^2 = C_6H_{13}, Nu = Et): TLC, R_f = 0.44 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 12.2 min (acetate form); IR (film) 3750–3100, 2970, 2930, 2870, 1465, 1380, 1340, 1160, 1120, 1080, 1060, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7.4 Hz, 6H, $2CH_3$), 1.19 (d, J = 6.4 Hz, 6H, $2CH_3$), 1.22–1.75 (m, 14H, $CH_3(CH_2)_5$, CH_2CH_3 and $CHCH_2CH$), 3.20–3.44 (m, 2H, OH and OCH), 3.77–3.93 (dquintet, J = 4.1, 6.2 Hz, 1H, OCH), 4.05–4.23 (m, 1H, OCH).

(3*S*,1′*R*,3′*R*)-3-(3′-Hydroxy-1′-methylbutoxy)nonane (2; R^1 = H, R^2 = C_6H_{13}, Nu = Et):[3b] TLC, R_f = 0.49 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 10.3 min (acetate form).

(4*R*,1′*R*,3′*R*)-4-(3′-Hydroxy-1′-methylbutoxy)decane (3; R^1 = H, R^2 = C_6H_{13}, Nu = Pr): TLC, R_f = 0.47 (hexane–EtOAc, 5:2); GC (110 °C); t_R = 35.8 min (alcohol form); IR (film) 3770–3100, 2980, 2950, 2900, 1460, 1380, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3H, CH_3CH_2), 0.92 (t, J = 6.7 Hz, 3H, CH_3CH_2), 1.19 (d, J = 6.2 Hz, CH_3CH and CH_3CH), 1.12–1.76 (m, 16H, $CH_3(CH_2)_5$, $CH(CH_2)_2$, and $CHCH_2CH$), 2.90–3.30 (br, 1H, OH), 3.26–3.42 (m, 1H, CHO), 3.76–3.94 (m, 1H, CHO), 4.04–4.22 (m, 1H, CHO). Anal. Found: C, 73.68; H, 13.59. Calcd for $C_{15}H_{32}O_2$: C, 73.71; H, 13.20.

(4*S*,1′*R*,3′*R*)-4-(3′-Hydroxy-1′-methylbutoxy)decane (2; R^1 = H, R^2 = C_6H_{13}, Nu = Pr): TLC, R_f = 0.47 (hexane–EtOAc, 5:2); GC (110 °C), t_R = 34.5 min (alcohol form); ^{1}H NMR δ 0.83–0.96 (m, 6H, $CH_3(CH_2)_5$ and $CH_3(CH_2)_2$), 1.18 (d, J = 6.2 Hz, 3H, CH_3CH), 1.19 (d, J = 6.2 Hz, 3H, CH_3CH), 1.18–1.76 (m, 16H, $CH_3(CH_2)_5$, $CH_3(CH_2)_2$, and $CHCH_2CH$), 3.26–3.50 (m, 2H, CHO and OH), 3.76–3.94 (m, 1H, CHO), 4.02–4.23 (m, 1H, CHO).

(4*S*,1′*R*,3′*R*)-4-(3′-Hydroxy-1′-methylbutoxy)-2-methyldecane (3; R^1 = H, R^2 = C_6H_{13}, Nu = *i*-Bu): GC (120 °C) t_R = 24.6 min (alcohol form); IR (film) 3700–3100, 2975, 2950, 2900, 1470, 1375, 1130, 1065 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84–0.95 (m, 3H, CH_3CH_2), 0.89 (d, J = 6.6 Hz, 3H, CH_3CHCH_3), 0.90 (d, J = 6.6 Hz, 3H, CH_3CHCH_3), 1.19 (d, J = 6.4 Hz, 6H, $CH_3CHCH_2CHCH_3$), 1.22–1.82 (m, 15H, $CH_3(CH_2)_5$, Me_2CHCH_2, and $CH_3CHCH_2CHCH_3$), 3.00–3.20 (br, 1H, OH), 3.33–3.48 (m, 1H, MeC*H*O), 3.80–3.97 (m, 1H, MeC*H*O), 4.06–4.23 (m, 1H, $C_6H_{13}CHO$). Anal. Found: C, 74.36; H, 13.65. Calcd for $C_{16}H_{34}O_2$: C, 74.36; H, 13.26.

(4*R*,1′*R*,3′*R*)-4-(3′-Hydroxy-1′-methylbutoxy)-2-methyldecane (2; R^1 = H, R^2 = C_6H_{13}, Nu = *i*-Bu): GC (120 °C) t_R = 23.5 min (alcohol form).

(1*R*,1′*R*,3′*R*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylbutoxy)ethane (3; R^1 = H, R^2 = c-C_6H_{11}, Nu = Me):[2b] TLC, R_f = 0.45 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 15.4 min (acetate form); IR (film) 3750–3100, 2980, 2930, 2860, 1460, 1380, 1345, 1335, 1160, 1130, 1100, 1080, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.80 (m, 13H, c-C_6H_{11} and $CHCH_2CH$), 1.06 (d, J = 6.2 Hz, 3H, CH_3), 1.13 (d, J = 6.2 Hz, 3H, CH_3), 1.16 (d, J = 6.2 Hz, 3H, CH_3), 3.23 (quintet, J = 6.2 Hz, 1H, CHO), 3.48 (d, J = 3.0 Hz, 1H, OH), 3.72–3.92 (m, 1H, CHO), 4.01–4.18 (m, 1H, CHO).

(1*S*,1′*R*,3′*R*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylbutoxy)ethane (2; R^1 = H, R^2 = c-C_6H_{11}, Nu = Me):[3b] TLC, R_f = 0.45 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 12.9 min (acetate form); ^{1}H NMR ($CDCl_3$) δ 0.80–1.80 (m, 13H, c-C_6H_{11} and $CHCH_2CH$), 1.05 (d, J = 6.4 Hz, 3H, CH_3), 1.15 (d, J = 6.2 Hz, 3H, CH_3), 1.17 (d, J = 6.2 Hz, 3H, CH_3), 3.18–3.33 (m, 2H, OH and CHO), 3.70–3.86 (m, 1H, CHO), 4.02–4.21 (m, 1H, CHO).

(1*R*,1′*R*,3′*R*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylbutoxy)propane (3; R^1 = H, R^2 = c-C_6H_{11}, Nu = Et): TLC, R_f = 0.49 (hexane–EtOAc, 5:2); GC (140 °C), t_R = 13.8 min (alcohol form); IR (film) 3750–3100, 2980, 2940, 2870, 1460, 1430, 1380, 1345, 1315, 1280, 1165, 1125, 1105, 1080, 1065, 1025, 1000, 970 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.85 (m, 15H, c-C_6H_{11}, CH_2CH_3, and $CHCH_2CH$), 0.85 (t, J = 7.4 Hz, 3H, CH_2CH_3), 1.13 (d, J = 6.2 Hz, 3H, CH_3), 1.15 (d, J = 6.2 Hz, 3H, CH_3), 1.15 (d, J = 6.2 Hz, 3H, CH_3), 3.03 (q, J = 5.4 Hz, 1H, *c*-$C_6H_{11}CHO$), 3.56 (d, J = 2.8 Hz, 1H, OH), 3.73–3.89 (m, 1H, CHO), 4.03–4.21 (m, 1H, CHO). Anal. Found: C, 73.63; H, 12.37. Calcd for $C_{14}H_{28}O_2$: C, 73.63; H, 12.36.

(1*S*,1′*R*,3′*R*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylbutoxy)propane (2; R^1 = H, R^2 = c-C_6H_{11}, Nu = Et): TLC, R_f = 0.49 (hexane–EtOAc, 5:2); GC (140 °C), t_R = 12.9 min (alcohol form); ^{1}H NMR ($CDCl_3$) δ 0.75–1.85 (m, 15H, c-C_6H_{11}, CH_2CH_3, and $CHCH_2CH$), 0.85 (t, J = 7.4 Hz, 3H, CH_3CH_2), 1.13 (d, J = 6.2 Hz, 3H, CH_3CH_2), 1.15 (d, J = 6.2 Hz, 3H, CH_3CH), 3.03 (q, J = 5.4 Hz, 1H, *c*-$C_6H_{11}CHO$), 3.73–3.89 (m, 1H, CHO), 4.03–4.21 (m, 1H, CHO).

(1*R*,1′*R*,3′*R*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylbutoxy)pentane (3; R^1 = H, R^2 = c-C_6H_{11}, Nu = Bu): TLC, R_f = 0.50 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 32.6 min (alcohol form); IR (film) 3650–3050, 2960, 2930, 2860, 1455, 1125 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 6.7 Hz, 3H, $CH_3(CH_2)_3$), 1.00–1.86 (m, 19H, c-C_6H_{11}, $CH_3(CH_2)_3$, and $CHCH_2CH$), 1.20 (d, J = 6.2 Hz, 3H, CH_3CH), 3.13 (q, J = 5.3 Hz, 1H, *c*-$C_6H_{11}CHO$), 3.20–3.76 (br, 1H, OH), 3.78–3.86 (m, 1H, CHO), 4.08–4.26 (m, 1H, CHO). Anal. Found: C, 72.63; H, 12.49. Calcd for $C_{16}H_{32}O_2$: C, 74.94; H, 12.58.

(1*S*,1′*R*,3′*R*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylbutoxy)pentane (2; R^1 = H, R^2 = c-C_6H_{11}, Nu = Bu): TLC, R_f = 0.50 (hexane–EtOAc, 5:2); GC (130 °C) t_R = 33.4 min (alcohol form); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6.2 Hz, 3H, $CH_3(CH_2)_3$), 0.96–1.86 (m, 19H, c-C_6H_{11}, $CH_3(CH_2)_3$, and $CHCH_2CH$), 1.17 (d, J = 6.2 Hz, 3H, CH_2CH_3), 1.19 (d, J = 6.2 Hz, 3H, CH_2CH_3), 3.05–3.18 (m, 1H, c-$C_6H_{11}CHO$), 3.42–3.55 (br, 1H, OH), 3.76–3.94 (m, 1H, CHO), 4.18–4.25 (m, 1H, CHO).

(1*R*,1′*R*,3′*R*)-1-(3′-Hydroxy-1′-methylbutoxy)-1-phenylethane (3; R^1 = H, R^2 = Ph, Nu = Me):[2b] TLC, R_f = 0.35 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 7.8 min (alcohol form); IR (film) 3750–3150, 2980, 2950,

1460, 1380, 1165, 1125, 1095, 1060, 1040, 1030, 765, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, J = 6.4 Hz, 3H, CH_3), 1.18 (d, J = 6.6 Hz, 3H, CH_3), 1.40 (d, J = 6.4 Hz, 3H, CH_3), 1.44–1.54 (m, 1H, CHC*H*HCH), 1.66–1.84 (m, 1H, CHCH*H*CH), 3.26 (br, 1H, OH), 3.68–3.84 (m, 1H, MeC*H*), 4.08–4.26 (m, 1H, MeC*H*), 4.57 (q, J = 6.4 Hz, 1H, PhC*H*), 7.20–7.40 (m, 5H, Ph). Anal. Found: C, 73.71; H, 12.72. Calcd for $C_{13}H_{20}O_2$: C, 73.63; H, 12.36.

(1*S*,1′*R*,3′*R*)-1-(3′-Hydroxy-1′-methylbutoxy)-1-phenylethane (**2**; R^1 = H, R^2 = Ph, Nu = Me):[3b] TLC, R_f = 0.35 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 6.5 min (alcohol form); ^1H NMR ($CDCl_3$) δ 1.07 (d, J = 6.2 Hz, 3H, CH_3), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.42 (d, J = 6.2 Hz, 3H, CH_3), 1.49 (t, J = 5.7 Hz, 2H, CHCH_2CH), 2.65 (d, J = 3.0 Hz, 1H, OH), 3.48–3.64 (m, 1H, MeC*H*O), 3.94–4.13 (m, 1H, MeC*H*OH), 4.52 (q, J = 6.2 Hz, 1H, PhC*H*), 7.20–7.40 (m, 5H, Ph).

(1*R*,1′*R*,3′*R*)-1-(3′-Hydroxy-1′-methylbutoxy)-1-phenylpropane (**3**; R^1 = H, R^2 = Ph, Nu = Et): TLC, R_f = 0.39 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 8.6 min (alcohol form); IR (film) 3750–3150, 2980, 2940, 2890, 1470, 1460, 1380, 1160, 1125, 1110, 1090, 1060, 1020, 760, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (t, J = 7.4 Hz, 3H, CH_3), 1.02 (d, J = 6.4 Hz, 3H, CH_3), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.40–1.90 (m, 4H, CH_3CH_2 and $CHCH_2CH$), 3.25 (d, J = 2.2 Hz, 1H, O*H*), 3.65–3.80 (m, 1H, CH_3CHO), 4.05–4.25 (m, 1H, CH_3CHOH), 4.28 (t, J = 6.6 Hz, 1H, PhC*H*), 7.20–7.40 (m, 5H, Ph). Anal. Found: C, 75.67; H, 9.67. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97.

(1*S*,1′*R*,3′*R*)-1-(3′-Hydroxy-1′-methylbutoxy)-1-phenylpropane (**2**; R^1 = H, R^2 = Ph, Nu = Et): TLC, R_f = 0.39 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 7.0 min (alcohol form); ^1H NMR ($CDCl_3$) δ 0.86 (t, J = 7.3 Hz, 3H, CH_3), 1.06 (d, J = 6.4 Hz, 3H, CH_3), 1.18 (d, J = 6.0 Hz, 3H, CH_3), 1.44–1.90 (m, 4H, CH_3CH_2 and $CHCH_2CH$), 2.76 (d, J = 3.2 Hz, 1H, O*H*), 3.50–3.65 (m, 1H, CH_3CHO), 3.95–4.14 (m, 1H, CH_3CHOH), 4.22 (dd, J = 6.0, 7.4 Hz, 1H, PhC*H*), 7.20–7.40 (m, 5H, Ph).

(1*R*,1′*R*,3′*R*)-1-(3′-Hydroxy-1′-methylbutoxy)-1-phenylbutane (**3**; R^1 = H, R^2 = Ph, Nu = Pr): GC (140 °C), t_R = 29.4 min (alcohol form).

(1*S*,1′*R*,3′*R*)-1-(3′-Hydroxy-1′-methylbutoxy)-1-phenylbutane (**2**; R^1 = H, R^2 = Ph, Nu = Pr): GC (140 °C), t_R = 23.1 min (alcohol form). Physical properties were identical with those reported.[3b]

(2*RS*,1′*RS*)-2-(3′-Hydroxy-1′-methylpropoxy)octane (R′ = C_6H_{13}, R = Me): TLC, R_f = 0.27 (hexane–EtOAc, 5:2); GC (110 °C), t_R = 25.9 min (acetate form); IR (film) 3600–3000, 2964, 2930, 2858, 1458, 1375, 1057 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.5 Hz, 3H, CH_3CH_2), 1.14 (d, J = 6.2 Hz, 3H, CH_3CH), 1.15 (d, J = 6.0 Hz, 3H, CH_3CH), 1.20–1.58 (m, 10H, $CH_3(CH_2)_5$), 1.66–1.80 (m, 2H, CH_2OH), 3.04–3.18 (br, 1H, OH), 3.40–3.58 (m, 1H, CHO), 3.68–3.88 (m, 3H, C*H*O and CH_2OH). Anal. Found: C, 71.22; H, 13.31. Calcd for $C_{12}H_{26}O_2$: C, 71.23; H, 12.95.

(2*SR*,1′*RS*)-2-(3′-Hydroxy-1′-methylpropoxy)octane (R′ = C_6H_{13}, R = Me): TLC, R_f = 0.27 (hexane–EtOAc, 5:2); GC (110 °C), t_R = 21.9 min (acetate form); ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.5 Hz, 3H, CH_3CH_2), 1.13 (d, J = 6.2 Hz, 3H, CH_3CH), 1.18 (d, J = 6.4 Hz, 3H, CH_3CH), 1.20–1.90 (m, 12H, $CH_3(CH_2)_5$ and CH_2CH_2OH), 2.88–3.02 (br, 1H, OH), 3.38–3.60 (m, 1H, CHO), 3.67–3.87 (m, 3H, C*H*O and CH_2OH).

(2*RS*,1′*RS*)-4-(3′-Hydroxy-1′-methylpropoxy)decane (R′ = C_6H_{13}, R = Pr): TLC, R_f = 0.36 (hexane–EtOAc, 5:2); GC (120 °C), t_R = 28.4 min (acetate form); IR (film) 3600–3000, 2959, 2930, 1466, 1374, 1057 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.4 Hz, 3H, CH_3CH_2), 0.93 (t, J = 6.8 Hz, 3H, CH_3CH_2), 1.16 (d, J = 6.2 Hz, 3H, CH_3CH), 1.19–1.56 (m, 14H, $CH_3(CH_2)_5$ and $CH_3(CH_2)_2$), 1.66–1.78 (m, 2H, CH_2CH_2OH), 2.70–3.20 (br, 1H, OH), 3.26–3.40 (m, 1H, CHO), 3.68–3.88 (m, 3H, CH_2OH and C*H*O). Anal. Found: C, 72.89; H, 13.51. Calcd for $C_{14}H_{30}O_2$: C, 72.99; H, 13.13.

(2*SR*,1′*RS*)-4-(3′-Hydroxy-1′-methylpropoxy)decane (R′ = C_6H_{13}, R = Pr): TLC, R_f = 0.36 (hexane–EtOAc, 5:2); GC (120 °C), t_R = 25.6 min (acetate form); ^1H NMR ($CDCl_3$) δ 0.81–0.98 (m, 6H, $CH_3(CH_2)_5$ and $CH_3(CH_2)_2$), 1.16 (d, J = 6.2 Hz, 3H, CH_3CH), 1.20–1.60 (m, 14H, $CH_3(CH_2)_5$ and $CH_3(CH_2)_2$), 2.90–3.17 (br, 1H, OH), 3.24–3.40 (m, 1H, CHO), 3.68–3.88 (m, 3H, CH_2OH and C*H*O).

(4*RS*,1′*RS*)-4-(3′-Hydroxy-1′-methylpropoxy)-2-methyldodecane (R′ = C_8H_{17}, R = *i*-Bu): TLC, R_f = 0.39 (hexane–EtOAc, 5:2); TC (140 °C), t_R = 27.3 min (acetate form); ^1H NMR ($CDCl_3$) δ 0.82–0.96 (m, 9H, CH_3CH_2 and $(CH_3)_2CH$), 1.15 (d, J = 6.0 Hz, 3H, CH_3CH), 1.19–1.82 (m, 19H, Me_2CHCH_2, $CH_3(CH_2)_7$, and CH_2CH_2OH), 2.13–2.67 (br, 1H, OH), 3.32–3.48 (m, 1H, CHO), 2.70–2.89 (m, 3H, C*H*O and CH_2OH).

(4*SR*,1′*RS*)-4-(3′-Hydroxy-1′-methylpropoxy)-2-methyldodecane (R′ = C_8H_{17}, R = *i*-Bu): TLC, R_f = 0.39 (hexane–EtOAc, 5:2); GC (140 °C), t_R = 29.8 min (acetate form); IR (film) 3600–3000, 2957, 2926, 2856, 1461, 1375, 1057 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, J = 6.1 Hz, 3H, CH_3CH_2), 0.83–0.96 (m, 6H, $(CH_3)_2CH$), 1.16 (d, J = 6.2 Hz, 3H, CH_3CH), 1.18–1.78 (m, 19H, Me_2CHCH_2, $CH_3(CH_2)_7$, and CH_2CH_2-OH), 2.74–3.08 (br, 1H, OH), 3.27–3.48 (m, 1H, CHO), 3.67–3.89 (m, 3H, C*H*O and CH_2OH). Anal. Found: C, 74.93; H, 13.70. Calcd for $C_{17}H_{36}O_2$: C, 74.94; H, 13.32.

(1*RS*,1′*RS*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylpropoxy)ethane (R′ = c-C_6H_{11}, R = Me): TLC, R_f = 0.28 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 17.8 min (acetate form); IR (film) 3700–2950, 2980, 2950, 2870, 1455, 1380, 1090, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, J = 6.0 Hz, 3H, CH_3), 1.10 (d, J = 6.2 Hz, 3H, CH_3), 0.75–1.90 (m, 13H, *c*-C_6H_{11} and $CH(CH_3)CH_2CH_2OH$), 2.20–2.85 (br, 1H, OH), 3.22 (quintet, J = 6.2 Hz, 1H, *c*-$C_6H_{11}CH$), 3.57– 3.90 (m, 3H, OC*H*CH_3 and CH_2OH). Anal. Found: C, 71.91; H, 12.12. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08.

(1*SR*,1′*RS*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylpropoxy)ethane (R′ = c-C_6H_{11}, R = Me): TLC, R_f = 0.28 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 16.3 min (acetate form); ^1H NMR ($CDCl_3$) δ 0.50–1.95 (m, 13H, c-C_6H_{11} and CH_2CH_2OH), 1.05 (d, J = 6.4 Hz, 3H, CH_3), 1.15 (d, J = 6.0 Hz, 3H, CH_3), 1.95–2.65 (br, 1H, OH), 3.12 (quintet, J = 6.0 Hz, 1H, *c*-$C_6H_{11}CH$), 3.43–3.86 (m, 3H, OC*H*CH_3 and CH_2OH).

(1*RS*,1′*RS*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylpropoxy)propane (R′ = c-C_6H_{11}, R = Et): TLC, R_f = 0.44 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 24.2 min (acetate form); IR (film) 3700–3000, 2980, 2950, 2880, 1455, 1100, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.60–1.85 (m, 15H, c-C_6H_{11}, CH_3CH_2, and CH_2CH_2OH), 0.84 (t, J = 7.4 Hz, 3H, CH_3-CH_2CH), 1.09 (d, J = 6.2 Hz, 3H, CH_3), 2.55–3.30 (br, 1H, OH), 3.40 (q, J = 5.4 Hz, 1H, *c*-$C_6H_{11}CH$), 3.60–3.90 (m, 3H, OC*H*CH_3 and CH_2OH). Anal. Found: C, 72.92; H, 12.09. Calcd for $C_{13}H_{26}O_2$: C, 72.85; H, 12.23.

(1*SR*,1′*RS*)-1-Cyclohexyl-1-(3′-hydroxy-1′-methylpropoxy)propane (R′ = c-C_6H_{11}, R = Et): TLC, R_f = 0.44 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 21.9 min (acetate form); ^1H NMR ($CDCl_3$) δ 0.87 (t, J = 7.4 Hz, 3H, CH_3CH_2CH), 1.13 (d, J = 6.2 Hz, 3H, CH_3). Other resonances could not be discerned for this minor isomer.

(1*RS*,1′*RS*)-1-(3′-Hydroxy-1′-methylpropoxy)-1-phenylethane (R′ = Ph, R = Me): TLC, R_f = 0.16 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 10.0 min (alcohol form); IR (film) 3750–3050, 3110, 3080, 3060, 3000, 2950, 2900, 1500, 1460, 1380, 1360, 1335, 1315, 1290, 1220, 1150, 1100, 1075, 1060, 1040, 1025, 1010, 760, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (d, J = 6.4 Hz, 3H, CH_3), 1.42 (d, J = 6.6 Hz, 3H, CH_3), 1.55–1.95 (m, 2H, CH_2CH_2OH), 2.60 (t, J = 5.3 Hz, OH), 3.65–3.95 (m, 3H, OC*H*CH_3 and CH_2OH), 4.55 (q, J = 6.4 Hz, 1H, PhC*H*CH_3), 7.15–7.40 (m, 5H, Ph). Anal. Found: C, 74.19; H, 9.34. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34.

(1*SR*,1′*RS*)-1-(3′-Hydroxy-1′-methylpropoxy)-1-phenylethane (R′ = Ph, R = Me):[2o] TLC, R_f = 0.16 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 8.4 min (alcohol form); ^1H NMR ($CDCl_3$) δ 1.16 (d, J = 6.2 Hz, 3H, CH_3), 1.42 (d, J = 6.6 Hz, 3H, CH_3). Other resonances could not be discerned for this minor isomer.

(1*RS*,1′*RS*)-1-(3′-Hydroxy-1′-methylpropoxy)-1-phenylpropane (R′ = Ph, R = Et): TLC, R_f = 0.27 (hexane–EtOAc, 5:2); GC (170 °C), t_R = 11.5 min (alcohol form); IR (film) 3770–3050, 3100, 3075, 3050, 2975, 2950, 2890, 1500, 1460, 1390, 1345, 1140, 1095, 1060, 1020, 760, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (t, J = 7.4 Hz, 3H, CH_2CH_3), 0.98 (d, J = 6.4 Hz, 3H, CH_3), 1.45–1.90 (m, 4H, CH_2CH_2OH and CH_3CH_2), 2.55–3.10 (br, 1H, OH), 3.40–3.95 (m, 3H, OC*H*CH_3 and CH_2OH), 4.25 (t, J = 6.6 Hz, 1H, PhC*H*O), 7.10–7.45 (m, 5H, Ph). Anal. Found: C, 74.91; H, 9.64. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68.

(1*SR*,1′*RS*)-1-(3′-Hydroxy-1′-methylpropoxy)-1-phenylpropane (R′ = Ph, R = Et): TLC, R_f = 0.27 (hexane-EtOAc, 5:2); GC (170 °C), t_R = 9.3 min (alcohol form); ^1H NMR ($CDCl_3$) δ 1.32 (d, J = 6.4 Hz, 3H, CH_3), 4.10 (t, J = 6.6 Hz, 1H, PhCHO). Other resonances could not be discerned for this minor isomer.

Synthesis of (+)-8-Hydroxyhexadecanoic Acid (6). 8-(Benzyloxy)-octanol.[13] To 1,8-octanediol (5.758 g, 39.4 mmol), covered, with dry xylene (2.5 mL) and heated to 130 °C, was cautiously added sodium (316 mg, 13.75 mmol) in small pieces. The reaction was easily controlled and soon complete. To the mixture cooled to 120 °C was added benzyl chloride (1.73 mL, 15 mmol) in small portions, and the reaction was completed by boiling the whole mixture for 15 min. After addition of benzene

(13) Bennett, G. M.; Hock, A. L. *J. Chem. Soc.* **1927**, 472.

to increase the precipitation of the sodium chloride, the solution was filtrated, and the solvents were evaporated. The residue was purified by column chromatography on silica gel (eluant: hexane–EtOAc 5:1) to give the monobenzyl ether as a colorless oil (2.6 g, 11 mmol, 80% yield based on sodium): TLC, R_f = 0.24 (hexane–EtOAc, 5:2); IR (film) 3500–3050, 2932, 2857, 1455, 1364, 1100, 735, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15–1.80 (m, 11H, $(CH_2)_5$ and OH), 3.47 (t, J = 6.6 Hz, 2H, BnOCH_2), 3.63 (t, J = 6.6 Hz, 2H, HOCH_2), 4.50 (s, 2H, PhCH_2O), 7.15–7.50 (m, 5H, Ph). Anal. Found: C, 76.19; H, 10.36. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24.

8-(Benzyloxy)octanal. To a solution of oxalyl chloride (1.0 mL, 11.4 mmol) in dichloromethane (25 mL) was added dimethyl sulfoxide (DMSO) (1.7 mL, 22.8 mmol) in dichloromethane (5 mL) at −78 °C under argon, and the solution was stirred at that temperature for 10 min. To the solution was added 8-(benzyloxy)octanol (2.4503 g, 10.4 mmol) in dichloromethane (10 mL) at −78 °C, and the suspension was stirred at that temperature. After stirring for 1.5 h, triethylamine (7.2 mL, 52 mmol) was added dropwise to the suspension at −78 °C, and then the mixture was warmed to room temperature for 1 h. The resulting mixture was quenched with aqueous ammonium chloride and extracted with ether. The organic layer was dried over magnesium sulfate, concentrated *in vacuo*, and purified by column chromatography on silica gel (eluant: hexane–EtOAc 20:1) to give the aldehyde as a colorless oil (1.973 g, 8.4 mmol, 81% yield): TLC, R_f = 0.51 (hexane–EtOAc, 5:2); IR (film) 2934, 2857, 1725, 1455, 1364, 1102, 737, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25–1.75 (m, 10H, $(CH_2)_5$), 2.41 (dt, J = 1.8, 7.4 Hz, 2H, CH_2CHO), 3.46 (t, J = 6.6 Hz, 2H, BnOCH_2), 4.50 (s, 2H, PhCH_2O), 7.25–7.40 (m, 5H, Ph), 9.76 (t, J = 1.8 Hz, 1H, CHO). Anal. Found: C, 76.84; H, 9.60. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46.

(4*S*,6*S*)-2-(7-(Benzyloxy)heptyl)-4,6-dimethyl-1,3-dioxane (4). A mixture of 8-(benzyloxy)octanal (1.1752 g, 5 mmol), (+)-(2*S*,4*S*)-2,4-pentanediol (0.63 g, 6 mmol), and a small amount of pyridinium *p*-toluenesulfonate in benzene (10 mL) was refluxed with continuous azeotropic removal of water for 2 h. After cooling, the resulting mixture was poured into aqueous sodium bicarbonate, and the product was extracted with hexane. The organic layer was dried over magnesium sulfate and concentrated *in vacuo*. Purification of the crude oil by column chromatography on silica gel (eluant: hexane–EtOAc 15:1) gave the acetal **4** as a colorless oil (1.5402 g, 4.8 mmol, 97% yield): TLC, R_f = 0.53 (hexane–EtOAc, 5:2); IR (film) 2932, 2857, 1455, 1375, 1157, 1142, 1103, 997, 735, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.34 (d, J = 7.0 Hz, 3H, CH_3CHO), 1.15–1.90 (m, 14H, $(CH_2)_6$ and OCHCH_2CHO), 3.46 (t, J = 6.6 Hz, 2H, BnOCH_2), 3.93 (dsextet J = 2.4, 6.0 Hz, 1H, OC*H*Me), 4.26 (quintet J = 6.8 Hz, 1H, OC*H*Me), 4.50 (s, 2H, PhCH_2O), 4.82 (t, J = 5.0 Hz, 1H, OCHO), 7.20–7.40 (m, 5H, Ph). Anal. Found: C, 74.96; H, 10.39. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.07.

(8*S*,1′*S*,2′*S*)-8-(3′-Hydroxy-1′-methylbutoxy)hexadecanol (5). To a solution of pentafluorophenol (2.0 M in toluene, 3 mL, 6.0 mmol) in toluene (25 mL) was added dropwise trioctylaluminum (1.0 M in hexane, 6 mL, 6.0 mmol) at 0 °C. The solution was heated at reflux for 1 h. Then, a solution of acetal **4** (0.0948 g, 0.3 mmol) in toluene (5 mL) was added dropwise to the solution at 0 °C. The reaction solution was stirred at room temperature for 22 h. The resulting solution was poured into cooled 2 N aqueous sodium hydroxide (30 mL) and extracted with ether. The combined organic layer was dried over magnesium sulfate and concentrated *in vacuo*. The diastereomeric ratio was determined by HPLC analyis (97:3). A mixture of the residue and 10% Pd/C (20 mg) in ethanol (10 mL) was stirred at room temperature for 20 h under H_2 gas. The reaction mixture was filtrated, and the catalyst was washed with EtOAc. The organic layer was concentrated *in vacuo*. The crude oil was purified and separated from the diastereomeric isomer by column chromatography on silica gel (eluant: hexane–EtOAc 2:1) to give diastereomeric pure alcohol **5** as a colorless oil (0.0543 g, 0.16 mmol, 53% yield (the whole of the alcohols)): TLC, R_f = 0.14 (hexane–EtOAc, 5:2); IR (film) 3550–3200, 2928, 2857, 1374, 1057 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.5 Hz, 3H, CH_3CH$_2$), 1.17 (d, J = 6.5 Hz, 3H, CH_3CHO), 1.18 (d, J = 6.0 Hz, 3H, CH_3CHO), 1.10–1.75 (m, 30H, Me(CH_2)$_7$-CHO, HOCH$_2$(CH_2)$_6$CHO, CHCH_2CH, and 2OH), 3.25–3.40 (m, 1H, CHO), 3.64 (t, J = 6.5 Hz, 2H, HOCH_2), 3.78–3.94 (m, 1H, CHO), 4.05–4.25 (m, 1H, CHO). Anal. Found: C, 73.02; H, 13.09. Calcd for $C_{21}H_{44}O_3$: C, 73.20; H, 12.87.

(8*S*,1′*S*)-8-(1′-Methyl-3′-oxobutoxy)hexadecanoic Acid. A mixture of the alcohol **5** (0.2492 g, 0.72 mmol) and pyridinium dichromate (PDC) (2.18 g, 5.8 mmol) in *N*,*N*-dimethylformamide (DMF) (10 mL) was stirred at room temperature for 40 h. The resulting mixture was poured into aqueous sodium bisulfite, and the product was extracted with ether. The organic layer was dried over magnesium sulfate and concentrated *in vacuo*. The crude oil was purified by chromatography on silica gel (eluant: hexane–EtOAc 2:1 ~ 1:2) to give the carboxylic acid as a colorless oil (0.1363 g, 0.38 mmol, 53% yield): TLC, R_f = 0.53 (EtOAc); IR (film) 3400–2300, 2930, 2857, 1713, 1460, 1372, 1084 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3H, CH_3CH$_2$), 1.14 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.10–1.75 (m, 24H, Me(CH_2)$_7$CHO and (CH_2)$_5$CH$_2$-COOH), 2.17 (s, 3H, CH_3CO), 2.30–2.50 (complex of t and dd, 3H, CH_2COOH and C*H*HCO), 2.72 (dd, J = 6.6, 15.4 Hz, 1H, CH*H*CO), 3.20–3.36 (m, 1H, CHO), 3.93 (sextet, J = 6.2 Hz, 1H, CHO), 7.50–12.80 (br, 1H, COOH). Anal. Found: C, 70.71; H, 11.70. Calcd for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31.

(*S*)-(+)-8-Hydroxyhexadecanoic Acid (6). A mixture of (8*S*,1′*S*)-8-(1′-methyl-3′-oxobutoxy)hexadecanoic acid (0.1061 g, 0.3 mmol) and potassium carbonate (0.5146 g, 3 mmol) in methanol (5 mL) was stirred at room temperature for 15 h. The resulting mixture was poured into cooled 1 N aqueous hydrogen chloride, and the product was extracted with ether. The organic layer was dried over magnesium sulfate and concentrated *in vacuo*. The crude oil was purified by column chromatography on silica gel (eluant: hexane–EtOAc 1:3 ~ 0:1) and recrystallized from acetone to give **6** as a white powder (0.0538 g, 0.20 mmol, 66% yield): TLC, R_f = 0.34 (EtOAc); IR ($CHCl_3$) 3700–2400, 2932, 2859, 1709, 1412, 1377, 1288, 1138 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.6 Hz, 3H, CH_3CH$_2$), 1.10–1.75 (m, 24H, Me(CH_2)$_7$ and (CH_2)$_5$CH$_2$-COOH), 3.52–3.67 (m, 1H, C*H*OH), 3.20–4.70 (br, 2H, OH and COOH). Anal. Found: C, 70.50; H, 11.86. Calcd for $C_{16}H_{32}O_3$: C, 70.54; H, 11.84. $[\alpha]^{24}_D$ = +1.23° (c = 1.82, $CHCl_3$) (lit.[9] $[\alpha]^{22}_D$ = +1.06 ± 0.2° (c = 2.09, $CHCl_3$)).

Alkylative Cleavage of Oxetanes. Preparation of 1-Phenyl-2-methyloxetanes.[14]

***trans*-2-Phenyl-3-methyloxetane**: TLC, R_f = 0.49 (hexane–EtOAc, 5:2); ^{1}H NMR ($CDCl_3$) δ 1.33 (d, J = 6.8 Hz, 3H, CH_3), 2.85–3.10 (m, 1H, CH$_3$O*H*), 4.43 (dd, J = 5.8, 7.2 Hz, 1H, OC*H*H), 4.74 (dd, J = 5.8, 8.4 Hz, 1H, OCH*H*), 5.35 (d, J = 6.6 Hz, 1H, PhC*H*), 7.25–7.50 (m, 5H, Ph).

***cis*-2-Phenyl-3-methyloxetane**: TLC, R_f = 0.49 (hexane–EtOAc, 5:2); ^{1}H NMR ($CDCl_3$) δ 1.33 (d, J = 6.8 Hz, 3H, CH_3), 2.85–3.10 (m, 1H, PhC*H*), 4.43 (dd, J = 5.8, 7.2 Hz, 1H, OC*H*H), 4.74 (dd, J = 5.8, 8.4 Hz, 1H, OCH*H*), 5.35 (d, J = 6.6 Hz, 1H, PhC*H*), 7.25–7.50 (m, 5H, Ph).

General Procedure for Alkylative Cleavage of Oxetanes with Trialkylaluminum. To a solution of trialkylaluminum (2.0 M in hexane, 1.5 mL, 3.0 mmol) in solvent (15 mL) was added dropwise oxetane (0.5 mmol) at 0 °C. The reaction solution was stirred at a suitable temperature. After complete conversion, the resulting solution was poured into cooled 2 N aqueous sodium hydroxide (20 mL) and extracted with hexane three times (20 mL × 3). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluant: hexane–EtOAc) to give the diastereomeric mixture of the corresponding alcohols as a colorless oil.

The physical properties and analytical data of alcohol thus obtained are listed below.

(2*SR*,3*RS*)-2-Methyl-3-phenylbutanol: TLC, R_f = 0.28 (hexane–EtOAc, 5:2); GC (140 °C), t_R = 18.5 min; IR (film) 3800–3000, 2970, 2950, 2900, 1500, 1460, 1050, 1035, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.98 (d, J = 6.8 Hz, 3H, CH_3CHCH$_2$), 1.24 (d, J = 7.2 Hz, 3H, CH_3CHPh), 1.40–1.54 (br, 1H, OH), 1.70–1.92 (m, 1H, C*H*CH$_2$OH), 2.68 (quintet, J = 7.2 Hz, 1H, PhC*H*), 3.27 (dd, J = 6.4, 6.4 Hz, 1H, C*H*HOH), 3.42 (dd, J = 6.4, 6.4 Hz, 1H, C*H*HOH), 7.10–7.40 (m, 5H, Ph). Anal. Found: C, 80.42; H, 9.83. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82.

(2*SR*,3*SR*)-2-Methyl-3-phenylbutanol: TLC, R_f = 0.28 (hexane–EtOAc, 5:2); GC (140 °C), t_R = 19.5 min; ^{1}H NMR ($CDCl_3$) δ 0.79 (d, J = 6.8 Hz, 3H, CH_3CHCH$_2$OH), 1.29 (d, J = 7.2 Hz, 3H, CH_3CHPh), 1.40–1.60 (br, 1H, OH), 1.73–1.94 (m, 1H, C*H*CH$_2$OH), 2.79 (quintet, J = 7.2 Hz, 1H, PhC*H*), 3.46–3.67 (m, 2H, CH_2OH), 7.10–7.35 (m, 5H, Ph).

(2*SR*,3*RS*)-2-Methyl-3-phenylhexanol: TLC, R_f = 0.33 (hexane–EtOAc, 5:2); GC (150 °C), t_R = 18.3 min; IR (film) 3700–3000, 2970, 2950, 2880, 1455, 1035, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (t, J = 6.8 Hz, 3H, CH_3CH$_2$), 1.05 (d, J = 6.8 Hz, 3H, CH_3CH), 0.60–1.40 (m, 3H, CH$_3$CH_2 and O*H*), 1.45–1.95 (m, 3H, CH$_3$CH$_2$CH_2 and CH$_3$C*H*),

(14) Balsamo, A.; Ceccarelli, G.; Crooti, P.; Macchia, F. *J. Org. Chem.* **1975**, *40*, 473.

2.39–2.45 (m, 1H, PhC*H*), 3.15–3.45 (m, 2H, CH_2OH), 7.10–7.35 (m, 5H, Ph). Anal. Found: C, 81.10; H, 10.48. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48.

(2*SR*,3*SR*)-2-Methyl-3-phenylhexanol: TLC, R_f = 0.33 (hexane–EtOAc, 5:2); GC (150 °C), t_R = 20.4 min; ^{1}H NMR ($CDCl_3$) δ 0.76 (t, J = 6.8 Hz, 3H, CH_3CH), 0.84 (d, J = 7.0 Hz, 3H, CH_3CH$_2$), 1.00–1.22 (m, 2H, CH$_3$CH_2), 1.40–1.50 (br, 1H, OH), 1.65–1.74 (m, 2H, CH$_3$-CH$_2$CH_2), 1.78–1.98 (m, 1H, CH$_3$C*H*), 2.69 (q, J = 7.2 Hz, 1H, PhC*H*), 3.46 (dd, J = 6.0, 10.6 Hz, 1H, C*H*HOH), 3.55 (dd, J = 6.0, 10.6 Hz, 1H, CH*H*OH), 7.20–7.35 (m, 5H, Ph).

Authentic Sample of (2*SR*,3*SR*)-2-Methyl-3-phenylbutanol. A mixture (81 mg, 0.5 mmol, 81:19) of *cis*-2-methyl-3-phenyl-2-butenol and 2-(1′-phenylethyl)-2-propenol (byproduct), which was prepared by reduction ($LiAlH_4$)[15] of a mixture of *cis*-2-methyl-3-phenyl-2-butenoic acid and 2-methyl-3-butenoic acid (byproduct) derived from ethyl 3-hydroxy-2-methyl-3-phenylbutyrate according to the procedure of Jackman and Lown,[16] was reduced in the presence of 10% Pd/C (10 mg) in 2 mL of ethanol under 1 atm of H_2 at room temperature for 21 h. Filtration and concentration provided a diastereomeric mixture of 2-methyl-3-phenylbutanols as an 80:20 ratio of (2*SR*,3*SR*):(2*SR*,3*RS*) in good yield.

Stereochemistry of (2*SR*,3*SR*)- or (2*SR*,3*RS*)-2-methyl-3-phenylhexanol was assigned by analogy with 2-methyl-3-phenylbutanol.

Reductive Cleavage of Acetals. Preparation of Acetals.[3b,4c] Acetals were prepared in excellent yield from the corresponding ketone and (–)-(2*R*,4*R*)-2,4-pentanediol in the presence of a catalytic quantity of *p*-toluenesulfonic acid.

The physical properties and analytical data of the acetals thus obtained are listed below.

(4*R*,6*R*)-2-Phenyl-2,4,6-trimethyl-1,3-dioxane (**1**; R^1 = Me, R^2 = Ph),[3b] **(4*R*,6*R*)-2-Cyclohexyl-2,4,6-trimethyl-1,3-dioxane** (**1**; R^1 = Me, R^2 = c-Hex),[3b] **(2*R*,4*R*)-2,4-Dimethyl-9-(1,1-dimethylethyl)-1,5-dioxaspiro-[5.5]undecane.**[17] Physical properties were identical with those reported.

(4*R*,6*R*)-2-Pentyl-2,4,6-trimethyl-1,3-dioxane (**1**; R^1 = Me, R^2 = C_5H_{11}): TLC, R_f = 0.68 (hexane–EtOAc, 5:2); IR (film) 2990, 2950, 2880, 1380, 1260, 1180, 1165, 1130, 1060, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6.5 Hz, 3H, CH$_3$), 1.19 (d, J = 6.2 Hz, 6H, 2CH$_3$), 1.31 (s, 3H, CH$_3$), 1.24–1.80 (m, 10H, (CH$_2$)$_4$ and C(5)H$_2$), 3.85–4.10 (m, 2H, 2CHO). Anal. Found: C, 71.98; H, 12.48. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08.

(4*R*,6*R*)-2-(2′-Methylpropyl)-2,4,6-trimethyl-1,3-dioxane (**1**; R^1 = Me, R^2 = *i*-Bu): IR (film) 2934, 1379, 1184, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (d, J = 6.4 Hz, 3H, CH$_3$), 0.95 (d, J = 6.4 Hz, 3H, CH$_3$), 1.17 (d, J = 6.2 Hz, 6H, 2CH$_3$), 1.33 (s, 3H, CH$_3$), 1.40–1.86 (m, 5H, C(5)H_2 and Me$_2$C*H*CH_2), 3.83–4.07 (m, 2H, 2OCH). Anal. Found: C, 70.89; H, 11.96. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90.

(4*R*,6*R*)-2-(2′-Methylethyl)-2,4,6-trimethyl-1,3-dioxane (**1**; R^1 = Me, R^2 = *i*-Pr): TLC, R_f = 0.65 (hexane–EtOAc, 5:2); IR (film) 2990, 2950, 2910, 2880, 1380, 1250, 1180, 1130, 1090, 1050, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (d, J = 7.0 Hz, 3H, CH$_3$), 0.94 (d, J = 6.6 Hz, 3H, CH$_3$), 1.13–1.21 (complex of d and s, 9H, 3CH$_3$), 1.52–1.62 (m, 2H, C(15)H$_2$), 2.04 (septet, J = 7.0 Hz, 1H, Me$_2$C*H*), 3.86–4.09 (m, 2H, 2CHO). Anal. Found: C, 69.70; H, 11.86. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70.

(4*R*,6*R*)-4,6-Dimethyl-2-ethyl-2-phenyl-1,3-dioxane (**1**; R^1 = Et, R^2 = Ph): TLC, R_f = 0.67 (hexane–EtOAc, 5:2); IR (film) 3900–3000, 3000, 2950, 1390, 1180, 1140, 1125, 1030, 1000, 760, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.73 (t, J = 7.4 Hz, 3H, CH$_3$), 1.19 (d, J = 6.4 Hz, 3H, CH$_3$), 1.21 (d, J = 6.4 Hz, 3H, CH$_3$), 1.40–2.00 (m, 4H, C(5)H_2 and CH_2CH$_3$), 3.59–3.78 (m, 1H, CHO), 4.07–4.25 (m, 1H, CHO). Anal. Found: C, 76.32; H, 9.18. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15.

General Procedure for Reductive Cleavage of Acetals with the Combined Use of Diethylaluminum Fluoride–Pentafluorophenol. To a solution of pentafluorophenol (2.0 M in toluene or dichloromethane, 0.6 mL, 1.2 mmol) in toluene (9 mL) or dichloromethane (9 mL) was added dropwise diethylaluminum fluoride (1.0 M in hexane, 0.6 mL, 0.6 mmol) at 0 °C, and the solution was stirred at that temperature for 10 min. Then, a solution of acetal **1** (0.5 mmol) in toluene (1 mL) or dichloromethane (1 mL) was added dropwise to the solution at 0 °C. After stirring for 1 h, the resulting mixture was poured into 2 N aqueous sodium hydroxide (20 mL) and extracted with hexane three times (20 mL × 3). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluant: hexane–EtOAc) to give a diastereomeric mixture of the corresponding β-alkoxy ketones **7** as a colorless oil. The diastereomeric ratio was determined by capillary GC analysis by comparison with the authentic samples, which were prepared by reductive cleavages of the corresponding acetals using a titanium tetrachloride–triethylsilane system[2a,b] or using diisobutylaluminum hydride[2b,3] and subsequent oxidation with pyridinium chlorochromate.

General Procedure for Reductive Cleavage of Acetals Under Catalysis by Aluminum Pentafluorophenoxide. To a solution of aluminum pentafluorophenoxide (0.08 M in toluene, 0.25 mL, 0.02 mmol; prepared in another flask from trimethylaluminum (1.0 M in hexane, 0.3 mL, 0.3 mmol) and pentafluorophenol (2.0 M in toluene, 0.45 mL, 0.9 mmol) in toluene (3.0 mL) at room temperature for 1 h) in dichloromethane (2 mL) was added dropwise a solution of acetal **1** (0.4 mmol) in dichloromethane (0.5 mL) at 0 °C under argon. The reaction solution was stirred at room temperature. After stirring for 24 h, the resulting solution was poured into cooled 2 N aqueous sodium hydroxide (10 mL) and extracted with ether three times (10 mL × 3). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluant: hexane–EtOAc) to give a diastereomeric mixture of the corresponding β-alkoxy ketones **7** as a colorless oil. The diastereomeric ratio was determined by capillary GC analysis by comparison with the authentic samples, which were prepared by reductive cleavages of the corresponding acetals using a titanium tetrachloride–triethylsilane system[2a,b] or using diisobutylaluminum hydride[2b,3] and subsequent oxidation with pyridinium chlorochromate.

The physical properties and analytical data of the β-alkoxy ketones thus obtained are listed below.

(2*R*,1′*R*)-2-(1′-Methyl-3′-oxobutoxy)heptane: TLC, R_f = 0.53 (hexane–EtOAc, 5:2); GC (100 °C), t_R = 11.8 min; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.5 Hz, 3H, CH$_3$), 1.06 (d, J = 6.0 Hz, 3H, CH$_3$), 1.13 (d, J = 6.0 Hz, 3H, CH$_3$), 1.20–1.49 (m, 8H, (CH$_2$)$_4$), 2.17 (s, 3H, CH$_3$), 2.40 (dd, J = 5.4, 15.4 Hz, 1H, C*H*HC=O), 2.70 (dd, J = 7.4, 15.4 Hz, 1H, CH*H*C=O), 3.32–3.53 (m, 1H, CHO), 3.94 (sextet, J = 6.0 Hz, 1H, CHO).

(2*S*,1′*R*)-2-(1′-Methyl-3′-oxobutoxy)heptane (**7**; R^1 = Me, R^2 = C_5H_{11}): TLC, R_f = 0.53 (hexane–EtOAc, 5:2); IR (film) 2980, 2950, 2890, 1730, 1380, 1365, 1140, 1125, 1095 cm^{-1}; GC (100 °C), t_R = 10.8 min; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.3 Hz, 3H, CH$_3$), 1.11 (d, J = 6.2 Hz, 3H, CH$_3$), 1.16 (d, J = 6.2 Hz, 3H, CH$_3$), 1.20–1.50 (m, 8H, (CH$_2$)$_4$), 2.17 (s, 3H, CH$_3$), 2.40 (dd, J = 5.8, 15.8 Hz, 1H, C*H*HC=O), 2.72 (dd, J = 6.9, 15.8 Hz, 1H, CH*H*C=O), 3.34–3.52 (m, 1H, CHO), 3.95 (sextet, J = 6.2 Hz, 1H, CHO). Anal. Found: C, 71.96; H, 12.44. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08.

(2*R*,1′*R*)-4-Methyl-2-(1′-methyl-3′-oxobutoxy)pentane: TLC, R_f = 0.48 (hexane–EtOAc, 5:2); GC (90 °C), t_R = 8.0 min; ^{1}H NMR ($CDCl_3$) δ 0.887 (d, J = 6.6 Hz, 3H, CH$_3$), 0.895 (d, J = 6.6 Hz, 3H, CH$_3$), 1.06 (d, J = 6.2 Hz, 3H, CH$_3$), 1.09–1.22 (m, 1H, Me$_2$CHC*H*H), 1.15 (d, J = 6.0 Hz, 3H, CH$_3$), 1.41 (ddd, J = 6.0, 7.6, 13.8 Hz, 1H, Me$_2$-CHCH*H*), 1.58–1.82 (m, 1H, Me$_2$C*H*), 2.18 (s, 3H, CH$_3$), 2.41 (dd, J = 5.4, 15.4 Hz, C*H*HC=O), 2.70 (dd, J = 7.3, 15.4 Hz, CH*H*C=O), 3.53 (dquintet, J = 7.6, 6.0 Hz, 1H, CHO), 3.88–4.05 (m, 1H, CHO).

(2*S*,1′*R*)-4-Methyl-2-(1′-methyl-3′-oxobutoxy)pentane (**7**; R^1 = Me, R^2 = *i*-Bu): TLC, R_f = 0.48 (hexane–EtOAc, 5:2); GC (90 °C), t_R = 7.5 min; IR (film) 2961, 2932, 2872, 1730, 1371, 1122, 1086 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (d, J = 6.6 Hz, 3H, CH$_3$), 0.89 (d, J = 6.6 Hz, 3H, CH$_3$), 1.12 (d, J = 6.0 Hz, 3H, CH$_3$), 1.10–1.22 (m, 1H, Me$_2$-CHC*H*H), 1.18 (d, J = 6.2 Hz, 3H, CH$_3$), 1.33–1.80 (m, 2H, Me$_2$C*H*CH*H*), 2.18 (s, 3H, CH$_3$), 2.42 (dd, J = 5.8, 15.8 Hz, 1H, C*H*HC=O), 2.73 (dd, J = 6.6, 15.8 Hz, 1H, CH*H*C=O), 3.43–3.61 (m, 1H, CHO), 3.87–4.05 (m, 1H, CHO). Anal. Found: C, 70.97; H, 12.30. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90.

(2*R*,1′*R*)-3-Methyl-2-(1′-methyl-3′-oxobutoxy)butane: TLC, R_f = 0.43 (hexane–EtOAc, 5:2); GC (40 °C), t_R = 32.9 min; ^{1}H NMR ($CDCl_3$) δ 0.86 (d, J = 6.8 Hz, 3H, CH$_3$), 0.88 (d, J = 6.8 Hz, 3H, CH$_3$), 1.01 (d, J = 6.4 Hz, 3H, CH$_3$), 1.13 (d, J = 6.2 Hz, 3H, CH$_3$), 1.65 (septet, J = 6.8 Hz, 1H, Me$_2$C*H*), 2.18 (s, 3H, CH$_3$), 2.40 (dd, J = 5.4, 15.0 Hz, 1H, C*H*HC=O), 2.70 (dd, J = 7.3, 15.0 Hz, 1H, CH*H*C=O), 3.14–3.29 (m, 1H, CHO), 3.84–4.02 (m, 1H, CHO).

(2*S*,1′*R*)-3-Methyl-2-(1′-methyl-3′-oxobutoxy)butane (**7**; R^1 = Me, R^2 = *i*-Pr): TLC, R_f = 0.43 (hexane–EtOAc, 5:2); IR (film) 2990, 2950, 2900, 1730, 1385, 1140, 1120, 1100, 1050 cm^{-1}; GC (40 °C), t_R = 33.8 min; ^{1}H NMR ($CDCl_3$) δ 0.82 (d, J = 6.0 Hz, 3H, CH$_3$), 0.85 (d, J = 6.8 Hz, 3H, CH$_3$), 1.05 (d, J = 6.4 Hz, 3H, CH$_3$), 1.16 (d, J = 6.0 Hz, 3H, CH$_3$), 1.55–1.77 (m, 1H, Me$_2$C*H*), 2.18 (s, 3H, CH$_3$), 2.40 (dd, J

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= 5.8, 15.8 Hz, 1H, C*H*HC=O), 2.74 (dd, *J* = 6.9, 15.8 Hz, 1H, CH*H*C=O), 3.22 (quintet, *J* = 6.0 Hz, 1H, CHO), 3.85–4.03 (m, 1H, CHO). Anal. Found: C, 69.74; H, 12.03. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70.

(1*R*,1′*R*)-1-(1′-Methyl-3′-butoxy)-1-phenylethane:[2b] TLC, R_f = 0.43 (hexane–EtOAc, 5:2); GC (120 °C), t_R = 29.7 min; ^{1}H NMR ($CDCl_3$) δ 1.06 (d, *J* = 6.2 Hz, 3H, CH_3), 2.21 (s, 3H, CH_3). Other resonances could not be discerned for this minor isomer.

(1*S*,1′*R*)-1-(1′-Methyl-3′-oxobutoxy)-1-phenylethane (7; R^1 = Me, R^2 = Ph):[3b] TLC, R_f = 0.43 (hexane–EtOAc, 5:2); IR (film) 3000, 2960, 2910, 1740, 1725, 1460, 1380, 1365, 1100, 1040, 1030, 770, 710 cm^{-1}; GC (120 °C), t_R = 26.6 min; ^{1}H NMR ($CDCl_3$) δ 1.21 (d, *J* = 6.2 Hz, 3H, CH_3), 1.42 (d, *J* = 6.4 Hz, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.41 (dd, *J* = 6.1, 15.4 Hz, 1H, C*H*HC=O), 2.66 (dd, *J* = 7.0, 15.4 Hz, 1H, CH*H*C=O), 3.74–3.92 (m, 1H, CHO), 4.55 (q, *J* = 6.4 Hz, 1H, CHO).

(1*R*,1′*R*)-1-(1′-Methyl-3′-oxobutoxy)-1-phenylpropane: TLC, R_f = 0.47 (hexane–EtOAc, 5:2); GC (130 °C), t_R = 23.7 min; ^{1}H NMR ($CDCl_3$) δ 1.01 (d, *J* = 6.2 Hz, 3H, CH_3), 2.20 (s, 3H, CH_3), 2.47 (dd, *J* = 6.0, 15.6 Hz, 1H, C*H*HC=O), 2.82 (dd, *J* = 6.4, 15.6 Hz, 1H, CH*H*C=O), 3.91 (sextet, *J* = 6.2 Hz, 1H, OC*H*Me). Other resonances could not be discerned for this minor isomer.

(1*S*,1′*R*)-1-(1′-Methyl-3′-oxobutoxy)-1-phenylpropane (7; R^1 = Et, R^2 = Ph): TLC, R_f = 0.47 (hexane–EtOAc, 5:2); IR (film) 3000, 2950, 2900, 1735, 1725, 1460, 1380, 1370, 1100, 1060, 1025, 770, 710 cm^{-1}; GC (130 °C), t_R = 22.1 min; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H, CH_3), 1.20 (d, *J* = 6.2 Hz, 3H, CH_3), 1.50–1.90 (m, 2H, CH_2CH$_3$), 2.02 (s, 3H, CH_3), 2.40 (dd, *J* = 6.0, 15.3 Hz, 1H, C*H*HC=O), 2.63 (dd, *J* = 6.8, 15.3 Hz, 1H, CH*H*C=O), 3.81 (sextet, *J* = 6.2 Hz, 1H, OC*H*Me), 4.24 (dd, *J* = 6.2, 7.2 Hz, 1H, PhC*H*), 7.20–7.40 (m, 5H, Ph). Anal. Found: C, 76.20; H, 9.55. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15.

(1*R*,1′*R*)-1-Cyclohexyl-1-(1′-methyl-3′-oxobutoxy)ethane:[2b] TLC, R_f = 0.47 (hexane–EtOAc, 5:2); GC (110 °C), t_R = 31.5 min; ^{1}H NMR ($CDCl_3$) δ 1.01 (d, *J* = 6.4 Hz, 3H, CH_3), 1.12 (d, *J* = 6.0 Hz, 3H, CH_3), 0.80–1.90 (m, 11H, c-C_6H_{11}), 2.17 (s, 3H, CH_3CO), 2.39 (dd, *J* = 5.4, 15.0 Hz, 1H, C*H*HC=O), 2.70 (dd, *J* = 7.6, 15.0 Hz, 1H, CH*H*C=O), 3.18 (quintet, *J* = 6.0 Hz, 1H, MeC*H*-c-Hex), 3.83–4.00 (m, 1H, MeC*H*O).

(1*S*,1′*R*)-1-Cyclohexyl-1-(1′-methyl-3′-oxobutoxy)ethane (7; R^1 = Me, R^2 = c-Hex):[3b] TLC, R_f = 0.47 (hexane–EtOAc, 5:2); IR (film) 2972, 2855, 1716, 1450, 1370, 1080 cm^{-1}; GC (110 °C), t_R = 29.1 min; ^{1}H NMR ($CDCl_3$) δ 1.07 (d, *J* = 6.2 Hz, 3H, CH_3), 1.15 (d, *J* = 6.2 Hz, 3H, CH_3), 0.80–1.85 (m, 11H, c-C_6H_{11}), 2.08 (s, 3H, CH_3CO), 2.41 (dd, *J* = 6.2, 15.8 Hz, 1H, C*H*HC=O), 2.74 (dd, *J* = 6.4, 15.8 Hz, 1H, CH*H*C=O), 3.19 (quintet, *J* = 6.2 Hz, 1H, MeC*H*-c-Hex), 3.93 (sextet, *J* = 6.2 Hz, 1H, MeC*H*O). Anal. Found: C, 73.49; H, 11.78. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39.

(1′*R*)-*trans*-4-(1′,1′-Dimethylethyl)-1-(1′-methyl-3′-oxobutoxy)cyclohexane: TLC, R_f = 0.42 (hexane–EtOAc, 5:2); GC (150 °C), t_R = 15.9 min; IR (film) 2950, 2863, 1730, 1367, 1132, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84 (s, 9H, *t*-Bu), 1.16 (d, *J* = 6.2 Hz, 3H, CH_3), 0.85–1.30 (m, 5H, c-$C_6H_5H_5$), 1.68–1.83 (m, 2H, c-$C_6H_2H_8$), 1.90–2.08 (m, 2H, c-$C_6H_2H_8$), 2.17 (s, 3H, CH_3), 2.40 (dd, *J* = 5.4, 15.4 Hz, 1H, C*H*HC=O), 2.72 (dd, *J* = 7.4, 15.4 Hz, 1H, CH*H*C=O), 3.20 (m, 1H, CHO), 3.95–4.10 (m, 1H, CHO). Anal. Found: C, 74.81; H, 12.14. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74.

(1′*R*)-*cis*-4-(1′,1′-Dimethylethyl)-1-(1′-methyl-3′-oxobutoxy)cyclohexane: TLC, R_f = 0.48 (hexane–EtOAc, 5:2); GC (150 °C), t_R = 11.0 min; ^{1}H NMR ($CDCl_3$) δ 0.84 (s, 9H, *t*-Bu), 1.16 (d, *J* = 6.0 Hz, 3H, CH_3), 0.80–1.65 (m, 7H, c-$C_6H_7H_3$), 1.78–1.97 (m, 2H, c-$C_6H_2H_8$), 2.21 (s, 3H, CH_3), 2.38 (dd, *J* = 5.0, 14.8 Hz, 1H, C*H*HC=O), 2.73 (dd, *J* = 7.8, 14.6 Hz, 1H, CH*H*C=O), 3.57–3.67 (br, 1H, CHO), 3.78–4.05 (m, 1H, CHO).

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