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

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Abstract: Chiral acetals derived from aldehydes and (-)-(2R,4R)-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 (-)-(2R,4R)-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.

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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^{(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, Br₂AlH, and Cl₂AlH) are practically needed for highly diastereoselective reductive cleavages of chiral acetals as well as the alkylative cleavages of chiral acetals.

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

Table I.	Alkylative	Cleavage	of Chiral	Acetals	Using	R ₃ Al ^a
1 8010 14	1 May Matter	Crea, aBe	or emilar	1.0000000	÷6	

$$1 (R1 = H) \rightarrow 3 (R1 = H; Nu = R)$$

entry	R ²	R	temp (°C)	yield (%)	ret:inv ^b
1	C ₆ H ₁₃	Me	52	90	70:30
2 ^c			40	76	77:23
34			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	$C_{6}H_{13}$	60	>99	97:3
8	$c-C_6H_{11}$	Me	52	87	78:22
9°			49	95	66:34
10		Et	50	85	94:6
11		Bu	60	>99	98:2
12	Ph	Me	25	ſ	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 reagents⁷ 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 2,6dihalo-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 Table II. Alkylative Cleavage of Chiral Acetals Using R2AlOAr^a

$$1 (R^1 = H) \rightarrow 3 (R^1 = H; Nu = R)$$

entry	R ²	R	ArOH ^b	yield (%)	ret:inv ^c
1	C ₆ H ₁₃	Me	Α	70	>99:1
2			В	59	97:3
3			С	87	89:11
4			D	86	87:13
5 ^d		Et	Α	70	93:7
6e			Α	40	96:4
7			В	59	98:2
8 ^d			С	87	89:11
9 ^d			D	86	88:12
10	$c-C_6H_{11}$	Me	Α	70	>99:1
11 ^d		Et	Α	87	>99:1
12	Ph	Me	Α	49	82:18
13 ^d		Et	Α	41	89:11
14	BuC=C	Me	Α	57	80:20
15 ^d		Et	Α	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 Et₂AlH was used in place of Et₃Al.

Table III. Alkylative Cleavage of Chiral Acetals^a

				R' Me	,OH
entry	R′	reagent	temp (°C)	yield (%)	ret:inv ^b
1	C ₆ H ₁₃	Me ₃ Al	51	62	86:14
2		Me ₂ AlOC ₆ F ₅	51	21	>99:1
3	Ph	Me ₃ Al	25	70	65:35
4		Me ₂ AlOC ₆ F ₅	25	70	82:18

^a Unless otherwise specified, Me₃Al (6 equiv) or Me₂AlOC₆F₅ (6 equiv) in toluene was used. ^b The ratio was determined by capillary GC.

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.

Next, we examined the reaction of acetals derived from (-)-(2R,3R)-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 (2SR,4RS)-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, 2,4,6trimethylphenol, 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.



^{*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 (2S,4S)-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 $= +1.23^{\circ}$ (c = 1.82, CHCl₃) (data for the natural (+)-(S)-6: lit.⁹

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







R=Me; 89% yield; inv : ret = 9 : 91

Scheme IV. Transition State of Oxetane Cleavage



 $[\alpha]^{22}_{D} = +1.06^{\circ} \pm 0.2 \ (c = 2.19, \text{CHCl}_3); \text{ lit.}^{10} \text{ mp } 78.5-79.5$ °C, $[\alpha]_{D} = +0.3^{\circ} \ (c = 19.5, \text{CHCl}_3); \text{ lit.}^{11} \text{ mp } 78-79 \text{ °C}, \ [\alpha]^{25}_{D} = +0.6^{\circ} \ (c = 3.3, \text{ MeOH})).$

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 (-)-(2R,4R)-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.





Table V. Reductive Cleavage of Chiral Acetals Using $Et_2AlF-C_6F_5OH^a$

 $1 \rightarrow 7$

entry	\mathbb{R}^1	R ²	solvent	yield (%)	ret:inv ^b $(S:R)^c$
1	Me	C ₅ H ₁₁	CH ₂ Cl 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 ₂ Cl ₂	71	97:3
			toluene	62	98:2
4	Me	Ph	CH ₂ Cl ₂	81	95:5
			toluene	68	>99:1
5	Et	Ph	CH ₂ Cl ₂	92	90:10
			toluene	84	93:7
6	Me	c-Hex	CH ₂ Cl ₂	94	96:4
			toluene	87	96:4
7	CH2 CH2		CH ₂ Cl 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 hydride³ (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 ($\mathbb{R}^1 = \mathbb{M}e$, $\mathbb{R}^2 = \mathbb{C}_5 \mathbb{H}_{11}$) derived from 2-heptanone and (-)-(2R,4R)-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 $\mathbb{R}_2AIOC_6F_5$ 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 $\mathbb{M}e_2AIOC_6F_5$ or $\mathbb{M}eAI(OC_6F_5)_2$ gave rather more reductively cleaved β -alkoxy ketones as main

Table VI. Reductive Cleavage of Chiral Acetal Using Me₃Al and $C_6F_5OH^a$

$$1 \xrightarrow{Me_{3-m}Al(OC_{6}F_{5})_{m}} 7 (R^{1} = Me, R^{2} = C_{5}H_{11})$$

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 ₆ F 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 $Al(OC_6F_5)_3$ Catalyst⁴

 $1 \rightarrow 7$

entry	\mathbb{R}^1	R ²	yield (%)	ret:inv ^b $(S:R)^c$
1	Me	C ₅ H 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.^{24,4 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 (R¹ = Me, R² = C₅H₁₁) 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 (-)-(2R,3R)-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 (-)-(2R,4R)-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 (-)-(2R,4R)-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. ¹H NMR spectra were measured on a Varian Gemini 200 (200 MHz) spectrometer. Chemical shifts of ¹H NMR are expressed in parts per million downfield relative to internal tetramethylsilane ($\delta = 0$) or chloroform ($\delta = 7.26$). 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 GF₂₅₄, 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 moisturesensitive 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. (-)-(2R,4R)-2,4-pentanediol, (-)-(2R,3R)-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.

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

(4R,6R)-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; ¹H NMR (CDCl₃) δ 0.92 (t, J = 7.1Hz, 3H, CH₃CH₂), 1.21 (d, J = 6.0 Hz, 3H, CH₃), 1.24-1.62 (m, 5H, Me(CH₂)₄ and OCHCHHCHO), 1.36 (d, J = 7.0 Hz, 3 H, CH₃), 1.84 (ddd, J = 6.0, 11.6, 13.2 Hz, 1H, OCHCHHCHO), 3.95 (dsextet, J =2.5, 6.0 Hz, 1H, OCHMe), 4.30 (quintet, J = 7.0 Hz, 1H, OCHMe), 4.86 (t, J = 5.1 Hz, 1H, O₂CH). Anal. Found: C, 68.29; H, 11.58. Calcd for C₉H₁₈O₂: C, 68.31; H, 11.46.

(4*R*,6*R*)-4,6-Dimethyl-2-(1'-hexynyl)-1,3-dioxane (1; $R^1 = H, R^2 = C_4H_9C=C$): 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; ¹H NMR (CDCl₃) δ 0.89 (t, J = 7.5 Hz, 3H, CH₃CH₂), 1.02-2.03 (m, 6H, CH₃CH₂CH₂ and CHCH₂CH), 1.26 (d, J = 6.2 Hz, 3H, CH₃), 1.39 (d, J = 7.2 Hz, 3H, CH₃), 2.24 (dt, J = 1.5, 7.2 Hz, 2H, CH₂C=C), 3.93–4.11 (m, 1H, CHMe), 4.38 (m, 1H, CHMe), 5.56 (t, J = 1.5 Hz, C, 73.43; H, 10.27.

(2SR,4RS)-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; ¹H NMR (CDCl₃) δ 0.89 (t, J = 6.5 Hz, 3H, CH₂CH₃), 1.20–1.78 (m, 12H, (CH₂)₅ and OCH₂CH₂CHO), 1.24 (d, J = 6.2 Hz, 3H, CHCH₃), 3.66–3.84 (m, 2H, OCHHCH₂CHO), 4.11 (ddd, J = 1.4, 5.0, 11.4 Hz, OCHH), 4.53 (t, J = 5.1 Hz, 1H, CHO₂). Anal. Found: C, 70.90; H, 12.10. Calcd for C₁₁H₂₂O₂: C, 70.92; H, 11.90.

(2RS,4RS)-2-Hexyl-4-methyl-1,3-dioxane ($R' = C_6H_{13}$): TLC, $R_f = 0.28$ (hexane-EtOAc, 10:1); ¹H NMR (CDCl₃) δ 0.88 (t, J = 6.4 Hz, 3H, Me), 1.20–1.70 (m, 11H, (CH₂)₅ and OCH₂CHHCHO), 1.36 (d, J = 7.0 Hz, 3H, Me), 2.12–2.22 (m, 1H, OCH₂CHHCHO), 3.92 (d, J = 2.6 Hz, 1H, OCHH), 3.94–4.00 (m, 1H, OCHH), 4.20–4.37 (m, 1H, OCHMe), 4.85 (t, J = 5.3 Hz, 1H, O₂CH).

(2SR,4RS)-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; ¹H NMR (CDCl₃) δ 0.89 (t, J = 6.1 Hz, 3H, CH₂CH₃), 1.20–1.60 (m, 16H, (CH₂)₇ and OCH₂CH₂CHO), 1.25 (d, J = 6.2 Hz, 3H, CHCH₃), 3.66–3.84 (m, 2H, CHHO and MeCHO), 4.11 (ddd, J = 1.4, 5.0, 11.4 Hz, 1H, CHHO), 4.53 (t, J = 5.0 Hz, 1H, CHO₂). Anal. Found: C, 72.81; H, 12.53. Calcd for C₁₃H₂₆O₂: C, 72.84; H, 12.23.

(2SR,4RS)-2-(2-Methylpropyl)-4-methyl-1,3-dioxane (R' = *i*-Bu): TLC, $R_f = 0.59$ (bexane-EtOAc, 5:2); IR (film) 2959, 2440, 1379, 1170, 1142, 1120 cm⁻¹; ¹H NMR (CDCl₃) δ 0.92 (d, J = 6.6 Hz, 3H, (CH₃)₂-CH), 1.23 (d, J = 6.2 Hz, 3H, CH₃CH), 1.37-1.92 (m, 5H, (CH₃)₂CHCH₂ and OCH₂CH₂CHO), 3.64-3.84 (m, 2H, OCH-HCH₂CHO), 4.10 (ddd, J = 1.4, 5.0, 11.4 Hz, 1H, OCHH), 4.58 (t, J = 5.5 Hz, 1H, CHO₂). Anal. Found: C, 68.41; H, 11.56. Calcd for C9H₁₈O₂: C, 68.31; H, 11.47.

(2SR,4RS)-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; ¹H NMR (CDCl₃) δ 0.80–1.85 (m, 13H, c-C₆ H_{11} and OC H_2 CH₃), 1.18 (d, J = 6.2 Hz, 3H, CH₃), 3.58–3.75 (m, 2H, OCHMe and OCHH), 4.05 (ddd, J = 1.4, 5.0, 11.4 Hz, 1H, OCHH), 4.19 (d, J = 5.4 Hz, 1H, OCHO). Anal. Found: C, 71.71; H, 11.22. Calcd for C₁₁H₂₀O₂: 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 \times 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 tetrachloridedialkylzinc 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.

(2R,1'R,3'R)-2-(3'-Hydroxy-1'-methylbutoxy)-3-octyne $(3, R^1 = H, R^2 = BuC = C, Nu = Me)$,^{2b} (2S,1'R,3'R)-2-(3'-Hydroxy-1'-methylbutoxy)-3-octyne $(2; R^1 = H, R^2 = BuC = C, Nu = Me)$,^{2b} (3R,1'R,3'R)-2-(3'-Hydroxy-1'-methylbutoxy)-4-nonyne $(3; R^1 = H, R^2 = BuC = C, Nu = Et)$,^{2b} (3S,1'R,3'R)-2-(3'-Hydroxy-1'-methylbutoxy)-4-nonyne $(2, R^1 = H, R^2 = BuC = C, Nu = Et)$,^{2b} (2S,1'R,2'R)-2-(2'-Hydroxy-1'-methylpropoxy)octane $(R' = C_6H_{13})$,^{2o} (2S,1'R,2'R)-2-(2'-Hydroxy-1'-methylpropoxy)-1-phenylheptane (R' = Ph),^{2o} (1S,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; ¹H NMR (CDCl₃) $\delta 0.89$ (t, J = 6.5 Hz, 3H, CH₃), 1.14 (d, J = 6.0 Hz, 3H, CH₃), 1.18 (d, J = 6.2 Hz, 3H, CH₃), 1.20 (d, J = 6.2 Hz, 3H, CH₃), 1.20–1.70 (m, 12H, CH₃(CH₂)₅ and CHCH₂CH), 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).

(2S,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).

(3R,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; ¹H NMR (CDCl₃) δ 0.89 (t, J = 7.4 Hz, 6H, 2CH₃), 1.19 (d, J = 6.4 Hz, 6H, 2CH₃), 1.22-1.75 (m, 14H, CH₃(CH₂)₅, CH₂CH₃ and CHCH₂CH), 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).

(3S,1'R,3'R)-3-(3'-Hydroxy-1'-methylbutoxy)nonane (2; R¹ = H, R² = C₆H₁₃, Nu = Et):^{3b} TLC, $R_f = 0.49$ (hexane-EtOAc, 5:2); GC (130 °C), $t_R = 10.3$ min (acetate form).

(4R, 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; ¹H NMR (CDCl₃) δ 0.89 (t, J = 6.7 Hz, 3H, CH₃CH₂), 0.92 (t, J = 6.7 Hz, 3H, CH₃CH₂), 1.19 (d, J = 6.2 Hz, CH₃CH and CH₃CH), 1.12-1.76 (m, 16H, CH₃(CH₂)₅, CH(CH₂)₂, and

 $CHCH_2CH), 2.90-3.30 \ (br, 1H, OH), 3.26-3.42 \ (m, 1H, CHO), 3.76-3.94 \ (m, 1H, CHO), 4.04-4.22 \ (m, 1H, CHO). \ Anal. \ Found: \ C, 73.68; \\ H, 13.59. \ Calcol \ for \ C_{15}H_{32}O_2: \ C, \ 73.71; \ H, \ 13.20.$

(4S,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); ¹H NMR δ 0.83–0.96 (m, 6H, CH₃-(CH₂)₅ and CH₃(CH₂)₂), 1.18 (d, J = 6.2 Hz, 3H, CH₃CH), 1.19 (d, J = 6.2 Hz, 3H, CH₃CH), 1.19 (d, J = 6.2 Hz, 3H, CH₃CH), 1.18–1.76 (m, 16H, CH₃(CH₂)₅, CH₃(CH₂)₂), and CHCH₂CH), 3.26–3.50 (m, 2H, CHO and OH), 3.76–3.94 (m, 1H, CHO), 4.02–4.23 (m, 1H, CHO).

(4S,1'R,3'R)-4-(3'-Hydroxy-1'-methylbutoxy)-2-methyldecane (3; R¹ = H, R² = C₆H₁₃, 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; ¹H NMR (CDCl₃) δ 0.84–0.95 (m, 3H, CH₃CH₂), 0.89 (d, J = 6.6 Hz, 3H, CH₃CHCH₃), 0.90 (d, J = 6.6 Hz, 3H, CH₃CHCH₃), 1.19 (d, J = 6.4 Hz, 6H, CH₃CHCH₂CHCH₃), 1.22–1.82 (m, 15H, CH₃-(CH₂)₂, Me₂CHCH₂, and CH₃CHCH₂CHCH₃), 3.00–3.20 (br, 1H, OH), 3.33–3.48 (m, 1H, MeCHO), 3.80–3.97 (m, 1H, MeCHO), 4.06–4.23 (m, 1H, C₆H₁₃CHO). Anal. Found: C, 74.36; H, 13.65. Calcd for C₁₆H₃₄O₂: C, 74.36; H, 13.26.

(4R,1'R,3'R)-4-(3'-Hydroxy-1'-methylbutoxy)-2-methyldecane (2; R¹ = H, R² = C₆H₁₃, Nu =*i*-Bu): GC (120 °C) t_R = 23.5 min (alcohol form).

(1R, 1'R, 3'R)-1-Cyclohexyl-1-(3'-hydroxy-1'-methylbutoxy)ethane (3; R¹ = H, R² = c-C₆H₁₁, 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; ¹H NMR (CDCl₃) δ 0.80–1.80 (m, 13H, c-C₆H₁₁ and CHCH₂-CH), 1.06 (d, J = 6.2 Hz, 3H, CH₃), 1.13 (d, J = 6.2 Hz, 3H, CH₃), 1.16 (d, J = 6.2 Hz, 3H, CH₃), 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).

(15,1'R,3'R)-1-Cyclohexyl-1-(3'-hydroxy-1'-methylbutoxy)ethane (2; R¹ = H, R² = c-C₆H₁₁, Nu = Me):^{3b} TLC, R_f = 0.45 (hexane-EtOAc, 5:2); GC (130 °C), t_R = 12.9 min (acetate form); ¹H NMR (CDCl₃) δ 0.80–1.80 (m, 13H, c-C₆H₁₁ and CHCH₂CH), 1.05 (d, J = 6.4 Hz, 3H, CH₃), 1.15 (d, J = 6.2 Hz, 3H, CH₃), 1.17 (d, J = 6.2 Hz, 3H, CH₃), 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; ¹H NMR (CDCl₃) & 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, CH₃), 1.15 (d, J = 6.2 Hz, 3H, CH₃), 1.15 (d, J = 6.2 Hz, 3H, CH₃), 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 C₁₄H₂₈O₂: C, 73.63; H, 12.36.

(15,1'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); ¹H NMR (CDCl₃) δ 0.75-1.85 (m, 15H, $c-C_6H_{11}, CH_2CH_3$, and CHCH₂CH), 0.85 (t, J = 7.4 Hz, 3H, CH₃CH₂), 1.13 (d, J = 6.2 Hz, 3H, CH₃CH₂), 1.15 (d, J = 6.2 Hz, 3H, CH₃CH), 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).

(1R,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; ¹H NMR (CDCl₃) δ 0.93 (t, J = 6.7Hz, 3H, $CH_3(CH_2)_3$), 1.00-1.86 (m, 19H, c-C₆H₁₁, CH₃(CH₂)₃, and CHCH₂CH), 1.20 (d, J = 6.2 Hz, 3H, CH₃CH), 3.13 (q, J = 5.3 Hz, 1H, c-C₆H₁₁CHO), 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 Cl₁₆H₃₂O₂: C, 74.94; H, 12.58.

(15,1'R,3'R)-1-Cyclohexyl-1-(3'-hydroxy-1'-methylbutoxy)pentane (2; R¹ = H, R² = c-C₆H₁₁, Nu = Bu): TLC, R_f = 0.50 (hexane-EtOAc, 5:2); GC (130 °C) t_R = 33.4 min (alcohol form); ¹H NMR (CDCl₃) δ 0.90 (t, J = 6.2 Hz, 3H, CH₃(CH₂)₃), 0.96-1.86 (m, 19H, c-C₆H₁₁, CH₃(CH₂)₃, and CHCH₂CH), 1.17 (d, J = 6.2 Hz, 3H, CH₂CH₃), 1.19 (d, J = 6.2 Hz, 3H, CH₂CH₃), 3.05-3.18 (m, 1H, c-C₆H₁₁CHO), 3.42-3.55 (br, 1H, OH), 3.76-3.94 (m, 1H, CHO), 4.18-4.25 (m, 1H, CHO).

(1R, 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 (CDCl₃) δ 1.07 (d, J = 6.4 Hz, 3H, CH₃), 1.18 (d, J = 6.6 Hz, 3H, CH₃), 1.40 (d, J = 6.4 Hz, 3H, CH₃), 1.44–1.54 (m, 1H, CHCHHCH), 1.66–1.84 (m, 1H, CHCHHCH), 3.26 (br, 1H, OH), 3.68–3.84 (m, 1H, MeCH), 4.08–4.26 (m, 1H, MeCH), 4.57 (q, J = 6.4Hz, 1H, PhCH), 7.20–7.40 (m, 5H, Ph). Anal. Found: C, 73.71; H, 12.72. Calcd for C₁₃H₂₀O₂: C, 73.63; H, 12.36.

(15,1'R,3'R)-1-(3'-Hydroxy-1'-methylbutoxy)-1-phenylethane (2; R¹ = H, R² = 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 (CDCl₃) δ 1.07 (d, J = 6.2 Hz, 3H, CH₃), 1.18 (d, J = 6.2 Hz, 3H, CH₃), 1.42 (d, J = 6.2 Hz, 3H, CH₃), 1.49 (t, J = 5.7 Hz, 2H, CHCH₂CH), 2.65 (d, J = 3.0 Hz, 1H, OH), 3.48-3.64 (m, 1H, MeCHO), 3.94-4.13 (m, 1H, MeCHOH), 4.52 (q, J = 6.2 Hz, 1H, PhCH), 7.20-7.40 (m, 5H, Ph).

(1R, 1'R, 3'R)-1-(3'-Hydroxy-1'-methylbutoxy)-1-phenylpropane $(3; \mathbb{R}^1 = H, \mathbb{R}^2 = Ph, \mathbb{N}u = Et)$: TLC, $R_f = 0.39$ (hexane-EtOAc, 5:2); GC (170 °C), $t_{\mathbb{R}} = 8.6$ 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 (CDCl₃) $\delta 0.81$ (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), 1.02 (d, J = 6.4 Hz, 3H, CH_2), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.40–1.90 (m, 4H, CH₃CH₂ and CHCH₂CH), 3.25 (d, J = 2.2 Hz, 1H, OH), 3.65–3.80 (m, 1H, CH₃CHO), 4.05–4.25 (m, 1H, CH₃CHOH), 4.28 (t, J = 6.6 Hz, 1H, PhCH), 7.20–7.40 (m, SH, Ph). Anal. Found: C, 75.67; H, 9.67. Calcd for C₁₄H₂₂O₂: C, 75.63; H, 9.97.

(15,1'R,3'R)-1-(3'-Hydroxy-1'-methylbutoxy)-1-phenylpropane (2; \mathbb{R}^1 = H, \mathbb{R}^2 = Ph, Nu = Et): TLC, $R_f = 0.39$ (hexane-EtOAc, 5:2); GC (170 °C), $t_{\mathbb{R}} = 7.0$ min (alcohol form); ¹H NMR (CDCl₃) δ 0.86 (t, J = 7.3 Hz, 3H, CH₃), 1.06 (d, J = 6.4 Hz, 3H, CH₃), 1.18 (d, J = 6.0 Hz, 3H, CH₃), 1.44-1.90 (m, 4H, CH₃CH₂ and CHCH₂CH), 2.76 (d, J = 3.2 Hz, 1H, OH), 3.50-3.65 (m, 1H, CH₃CHO), 3.95-4.14 (m, 1H, CH₃CHOH), 4.22 (dd, J = 6.0, 7.4 Hz, 1H, PhCH), 7.20-7.40 (m, 5H, Ph).

(1R,1'R,3'R)-1-(3'-Hydroxy-1'-methylbutoxy)-1-phenylbutane (3; R¹ = H, R² = Ph, Nu = Pr): GC (140 °C), t_R = 29.4 min (alcohol form).

(1.5,1'R,3'R)-1-(3'-Hydroxy-1'-methylbutoxy)-1-phenylbutane (2; R¹ = H, R² = Ph, Nu = Pr): GC (140 °C), t_R = 23.1 min (alcohol form). Physical properties were identical with those reported.^{3b}

(2RS,1'RS)-2-(3'-Hydroxy-1'-methylpropoxy)octane ($\mathbf{R}' = C_6H_{13}$, $\mathbf{R} = \mathbf{M}e$): TLC, $R_f = 0.27$ (hexane–EtOAc, 5:2); GC (110 °C), $t_{\mathbf{R}} = 25.9$ min (acetate form); IR (film) 3600–3000, 2964, 2930, 2858, 1458, 1375, 1057 cm⁻¹; ¹H NMR (CDCl₃) δ 0.89 (t, J = 6.5 Hz, 3H, CH_3 CH₂), 1.14 (d, J = 6.2 Hz, 3H, CH_3 CH), 1.15 (d, J = 6.0 Hz, 3H, CH_3 CH), 1.20–1.58 (m, 10H, CH₃(CH₂)₅), 1.66–1.80 (m, 2H, CH₂OH), 3.04–3.18 (br, 1H, OH), 3.40–3.58 (m, 1H, CHO), 3.68–3.88 (m, 3H, CHO and CH₂-OH). Anal. Found: C, 71.22; H, 13.31. Calcd for C₁₂H₂₆O₂: C, 71.23; H, 12.95.

(2SR,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 (CDCl₃) δ 0.89 (t, J = 6.5 Hz, 3H, CH₃-CH₂), 1.13 (d, J = 6.2 Hz, 3H, CH₃CH), 1.18 (d, J = 6.4 Hz, 3H, CH₃CH), 1.20–1.90 (m, 12H, CH₃(CH₂)₅ and CH₂CH₂OH), 2.88–3.02 (br, 1H, OH), 3.38–3.60 (m, 1H, CHO), 3.67–3.87 (m, 3H, CHO and CH₂OH).

(2RS,1'RS)-4-(3'-Hydroxy-1'-methylpropoxy)decane (R' = C₆H₁₃, 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 (CDCl₃) δ 0.89 (t, J = 6.4 Hz, 3H, CH₃CH₂), 0.93 (t, J = 6.8 Hz, 3H, CH₃CH₂), 1.16 (d, J = 6.2 Hz, 3H, CH₃CH), 1.19-1.56 (m, 14H, CH₃(CH₂)₅ and CH₃(CH₂)₂), 1.66-1.78 (m, 2H, CH₂CH₂-OH), 2.70-3.20 (br, 1H, OH), 3.26-3.40 (m, 1H, CHO), 3.68-3.88 (m, 3H, CH₂OH and CHO). Anal. Found: C, 72.89; H, 13.51. Calcd for C₁₄H₃₀O₂: C, 72.99; H, 13.13.

(2SR,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 (CDCl₃) δ 0.81-0.98 (m, 6H, CH₃(CH₂)₅ and CH₃(CH₂)₂), 1.16 (d, J = 6.2 Hz, 3H, CH₃CH), 1.20-1.60 (m, 14H, CH₃(CH₂)₅ and CH₃(CH₂)₂), 2.90-3.17 (br, 1H, OH), 3.24-3.40 (m, 1H, CHO), 3.68-3.88 (m, 3H, CH₂OH and CHO).

(4RS,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 (CDCl₃) δ 0.82–0.96 (m, 9H, CH₃CH₂ and (CH₃)₂CH), 1.15 (d, J = 6.0 Hz, 3H, CH₃CH), 1.19–1.82 (m, 19H, Me₂CHCH₂, CH₃(CH₂)₇, and CH₂CH₂OH), 2.13–2.67 (br, 1H, OH), 3.32–3.48 (m, 1H, CHO), 2.70–2.89 (m, 3H, CHO and CH₂OH).

(4SR,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 (CDCl₃) δ 0.91 (t, J = 6.1 Hz, 3H, CH_3CH_2), 0.83-0.96 (m, 6H, (CH₃)₂CH), 1.16 (d, J = 6.2 Hz, 3H, CH₃CH₂), 1.18 (m, 19H, Me₂CHCH₂, CH₃(CH₂)7, and CH₂CH₂-OH), 2.74-3.08 (br, 1H, OH), 3.27-3.48 (m, 1H, CHO), 3.67-3.89 (m, 3H, CHO and CH₂OH). Anal. Found: C, 74.93; H, 13.70. Calcd for C₁₇H₃₆O₂: C, 74.94; H, 13.32.

(1RS,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 (CDCl₃) δ 1.07 (d, J = 6.0 Hz, 3H, CH₃), 1.10 (d, J = 6.2 Hz, 3H, CH₃), 0.75-1.90 (m, 13H, $c-C_6H_{11}$ and CH(CH₃)CH₂CH₂OH), 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, OCHCH₃ and CH₂OH). Anal. Found: C, 71.91; H, 12.12. Calcd for C₁₂H₂₄O₂: C, 71.95; H, 12.08.

(1SR,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 (CDCl₃) δ 0.50–1.95 (m, 13H, $c-C_6H_{11}$ and CH_2CH_2OH), 1.05 (d, J = 6.4 Hz, 3H, CH₃), 1.15 (d, J = 6.0 Hz, 3H, CH₃), 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, OCHCH₃ and CH₂OH).

(1RS,1'RS)-1-Cyclohexyl-1-(3'-hydroxy-1'-methylpropoxy)propane (R' = c-C₆H₁₁, 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 (CDCl₃) δ 0.60-1.85 (m, 15H, c-C₆H₁₁, CH₃CH₂, and CH₂CH₂OH), 0.84 (t, J = 7.4 Hz, 3H, CH₃-CH₂CH), 1.09 (d, J = 6.2 Hz, 3H, CH₃), 2.55-3.30 (br, 1H, OH), 3.40 (q, J = 5.4 Hz, 1H, c-C₆H₁₁CH), 3.60-3.90 (m, 3H, OCHCH₃ and CH₂OH). Anal. Found: C, 72.92; H, 12.09. Calcd for C₁₃H₂₆O₂: C, 72.85; H, 12.23.

(1SR,1'RS)-1-Cyclohexyl-1-(3'-hydroxy-1'-methylpropoxy)propane (R' = c-C₆H₁₁, R = Et): TLC, $R_f = 0.44$ (hexane-EtOAc, 5:2); GC (130 °C), $t_R = 21.9$ min (acetate form); ¹H NMR (CDCl₃) $\delta 0.87$ (t, J = 7.4 Hz, 3H, CH₃CH₂CH), 1.13 (d, J = 6.2 Hz, 3H, CH₃). Other resonances could not be discerned for this minor isomer.

(1RS,1'RS)-1-(3'-Hydroxy-1'-methylpropoxy)-1-phenylethane (R' = Ph, R = Me): TLC, $R_f = 0.16$ (hexanc-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 (CDCl₃) δ 1.04 (d, J = 6.4 Hz, 3H, CH₃), 1.42 (d, J = 6.6 Hz, 3H, CH₃), 1.55-1.95 (m, 2H, CH₂CH₂OH), 2.60 (t, J = 5.3 Hz, OH), 3.65-3.95 (m, 3H, OCHCH₃ and CH₂OH), 4.55 (q, J = 6.4 Hz, 1H, PhCHCH₃), 7.15-7.40 (m, 5H, Ph). Anal. Found: C, 74.19; H, 9.34. Calcd for C₁₂H₁₈O₂: C, 74.19; H, 9.34.

(1SR,1'RS)-1-(3'-Hydroxy-1'-methylpropoxy)-1-phenylethane (R' = Ph, R = Me):²⁰ TLC, $R_f = 0.16$ (hexane-EtOAc, 5:2); GC (170 °C), $t_R = 8.4$ min (alcohol form); ¹H NMR (CDCl₃) δ 1.16 (d, J = 6.2 Hz, 3H, CH₃), 1.42 (d, J = 6.6 Hz, 3H, CH₃). 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 (CDCl₃) δ 0.83 (t, J = 7.4 Hz, 3H, CH₂CH₃), 0.98 (d, J = 6.4 Hz, 3H, CH₃), 1.45–1.90 (m, 4H, CH₂CH₂OH and CH₃CH₂), 2.55–3.10 (br, 1H, OH), 3.40–3.95 (m, 3H, OCHCH₃ and CH₂OH), 4.25 (t, J = 6.6 Hz, 1H, PhCHO), 7.10–7.45 (m, 5H, Ph). Anal. Found: C, 74.91; H, 9.64. Calcd for C₁₃H₂₀O₂: C, 74.96; H, 9.68.

(1SR,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 (CDCl₃) δ 1.32 (d, J = 6.4 Hz, 3H, CH₃), 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; ¹H NMR (CDCl₃) δ 1.15-1.80 (m, 11H, (CH₂)₅ and OH), 3.47 (t, J = 6.6 Hz, 2H, BnOCH₂), 3.63 (t, J = 6.6 Hz, 2H, HOCH₂), 4.50 (s, 2H, PhCH₂O), 7.15-7.50 (m, 5H, Ph). Anal. Found: C, 76.19; H, 10.36. Calcd for C₁₅H₂₄O₂: 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; ¹H NMR (CDCl₃) δ 1.25–1.75 (m, 10H, (CH₂)₅), 2.41 (dt, J = 1.8, 7.4 Hz, 2H, CH₂CHO), 3.46 (t, J = 6.6 Hz, 2H, BnOCH₂), 4.50 (s, 2H, PhCH₂O), 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 C15H22O2: C, 76.88; H, 9.46.

(4S,6S)-2-(7-(Benzyloxy)heptyl)-4,6-dimethyl-1,3-dioxane (4). A mixture of 8-(benzyloxy)octanal (1.1752 g, 5 mmol), (+)-(2S,4S)-2,4pentanediol (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; ¹H NMR (CDCl₃) δ 1.20 (d, J = 6.2Hz, 3H, CH₃CHO), 1.34 (d, J = 7.0 Hz, 3H, CH₃CHO), 1.15-1.90 (m, 14H, $(CH_2)_6$ and OCHCH₂CHO), 3.46 (t, J = 6.6 Hz, 2H, BnOCH₂), 3.93 (dsextet J = 2.4, 6.0 Hz, 1H, OCHMe), 4.26 (quintet J = 6.8 Hz, 1H, OCHMe), 4.50 (s, 2H, PhCH₂O), 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 C₂₀H₃₂O₃: C, 74.96; H, 10.07.

(8S,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 H₂ 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; ¹H NMR (CDCl₃) $\delta 0.88 (t, J = 6.5 Hz, 3H, CH_3CH_2), 1.17 (d, J = 6.5 Hz, 3H, CH_3CHO),$ 1.18 (d, J = 6.0 Hz, 3H, CH₃CHO), 1.10–1.75 (m, 30H, Me(CH₂)₇-CHO, HOCH₂(CH₂)₆CHO, CHCH₂CH, and 2OH), 3.25-3.40 (m, 1H, CHO), 3.64 (t, J = 6.5 Hz, 2H, HOCH₂), 3.78–3.94 (m, 1H, CHO), 4.05-4.25 (m, 1H, CHO). Anal. Found: C, 73.02; H, 13.09. Calcd for C₂₁H₄₄O₃: C, 73.20; H, 12.87.

(8S,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; ¹H NMR (CDCl₃) δ 0.88 (t, J = 6.4 Hz, 3H, CH₃CH₂), 1.14 (d, J = 6.2 Hz, 3H, CH₃CHO), 1.10-1.75 (m, 24H, Me(CH₂)₇CHO and (CH₂)₅CH₂-COOH), 2.17 (s, 3H, CH₃CO), 2.30-2.50 (complex of t and dd, 3H, CH₂COOH and CHHCO), 2.72 (dd, J = 6.6, 15.4 Hz, 1H, CHHCO), 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 C₂₁H₄₀O₄: C, 70.74; H, 11.31.

(S)-(+)-8-Hydroxyhexadecanoic Acid (6). A mixture of (8S,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 $1:3 \sim 0:1$) 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 (CHCl₃) 3700–2400, 2932, 2859, 1709, 1412, 1377, 1288, 1138 cm⁻¹; ¹H NMR (CDCl₃) δ 0.88 (t, J = 6.6 Hz, 3H, CH₃CH₂), 1.10-1.75 (m, 24H, Me(CH₂)₇ and (CH₂)₅CH₂-COOH), 3.52–3.67 (m, 1H, CHOH), 3.20–4.70 (br, 2H, OH and COOH). Anal. Found: C, 70.50; H, 11.86. Calcd for C₁₆H₃₂O₃: C, 70.54; H, 11.84. $[\alpha]^{24}_{D} = +1.23^{\circ} (c = 1.82, CHCl_3) (lit.⁹ [<math>\alpha$]²²_D = +1.06 ± 0.2° $(c = 2.09, CHCl_3)).$

Alkylative Cleavage of Oxetanes. Preparation of 1-Phenyl-2-methy-loxetanes.¹⁴

trans-2-Phenyl-3-methyloxetane: TLC, $R_f = 0.49$ (hexane-EtOAc, 5:2); ¹H NMR (CDCl₃) δ 1.33 (d, J = 6.8 Hz, 3H, CH₃), 2.85-3.10 (m, 1H, CH₃OH), 4.43 (dd, J = 5.8, 7.2 Hz, 1H, OCHH), 4.74 (dd, J = 5.8, 8.4 Hz, 1H, OCHH), 5.35 (d, J = 6.6 Hz, 1H, PhCH), 7.25-7.50 (m, 5H, Ph).

cis-2-Phenyl-3-methyloxetane: TLC, $R_f = 0.49$ (hexane-EtOAc, 5:2); ¹H NMR (CDCl₃) δ 1.33 (d, J = 6.8 Hz, 3H, CH₃), 2.85-3.10 (m, 1H, PhCH), 4.43 (dd, J = 5.8, 7.2 Hz, 1H, OCHH), 4.74 (dd, J = 5.8, 8.4 Hz, 1H, OCHH), 5.35 (d, J = 6.6 Hz, 1H, PhCH), 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 \times 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.

(2SR,3RS)-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; ¹H NMR (CDCl₃) δ 0.98 (d, J = 6.8 Hz, 3H, CH₃CHCH₂), 1.24 (d, J = 7.2 Hz, 3H, CH₃CHPh), 1.40–1.54 (br, 1H, OH), 1.70–1.92 (m, 1H, CHCH₂OH), 2.68 (quintet, J = 7.2 Hz, 1H, PhCH), 3.27 (dd, J = 6.4, 6.4 Hz, 1H, CHHOH), 3.42 (dd, J = 6.4, 6.4 Hz, 1H, CHHOH), 7.10–7.40 (m, 5H, Ph). Anal. Found: C, 80.42; H, 9.83. Calcd for C₁₁H₁₆O: C, 80.44; H, 9.82.

(2SR,3SR)-2-Methyl-3-phenylbutanol: TLC, $R_f = 0.28$ (hexane-EtOAc, 5:2); GC (140 °C), $t_R = 19.5$ min; ¹H NMR (CDCl₃) δ 0.79 (d, J = 6.8 Hz, 3H, CH₃CHCH₂OH), 1.29 (d, J = 7.2 Hz, 3H, CH₃CHPh), 1.40–1.60 (br, 1H, OH), 1.73–1.94 (m, 1H, CHCH₂OH), 2.79 (quintet, J = 7.2 Hz, 1H, PhCH), 3.46–3.67 (m, 2H, CH₂OH), 7.10–7.35 (m, 5H, Ph).

(2SR,3RS)-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; ¹H NMR (CDCl₃) δ 0.82 (t, J = 6.8 Hz, 3H, CH₃CH₂), 1.05 (d, J = 6.8 Hz, 3H, CH₃CH), 0.60–1.40 (m, 3H, CH₃CH₂ and OH), 1.45–1.95 (m, 3H, CH₃CH₂CH₂ and CH₃CH),

(14) Balsamo, A.; Ceccarelli, G.; Crooti, P.; Macchia, F. J. Org. Chem. 1975, 40, 473. 2.39-2.45 (m, 1H, PhCH), 3.15-3.45 (m, 2H, CH2OH), 7.10-7.35 (m, 5H, Ph). Anal. Found: C, 81.10; H, 10.48. Calcd for C₁₃H₂₀O: C, 81.20; H, 10.48.

(2SR, 3SR)-2-Methyl-3-phenylhexanol: TLC, $R_f = 0.33$ (hexane-EtOAc, 5:2); GC (150 °C), $t_{\rm R} = 20.4$ min; ¹H NMR (CDCl₃) δ 0.76 (t, J = 6.8 Hz, 3H, CH₃CH), 0.84 (d, J = 7.0 Hz, 3H, CH₃CH₂), 1.00–1.22 (m, 2H, CH₃CH₂), 1.40-1.50 (br, 1H, OH), 1.65-1.74 (m, 2H, CH₃- CH_2CH_2 , 1.78–1.98 (m, 1H, CH_3CH), 2.69 (q, J = 7.2 Hz, 1H, PhCH), 3.46 (dd, J = 6.0, 10.6 Hz, 1H, CHHOH), 3.55 (dd, J = 6.0, 10.6 Hz,1H, CHHOH), 7.20-7.35 (m, 5H, Ph).

Authentic Sample of (2SR, 3SR)-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 (LiAlH₄)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-2methyl-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 H₂ at room temperature for 21 h. Filtration and concentration provided a diastereomeric mixture of 2-methyl-3-phenylbutanols as an 80:20 ratio of (2SR,3SR):(2SR,3RS) in good yield.

Stereochemistry of (2SR,3SR)- or (2SR,3RS)-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 (-)-(2R,4R)-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.

(4R,6R)-2-Phenyl-2,4,6-trimethyl-1,3-dioxane (1; R¹ = Me, R² = Ph),^{3b} (4R,6R)-2-Cyclohexyl-2,4,6-trimethyl-1,3-dioxane (1; $R^1 = Me$, $R^2 =$ c-Hex),^{3b} (2R,4R)-2,4-Dimethyl-9-(1,1-dimethylethyl)-1,5-dioxaspiro-[5.5]undecane.¹⁷ Physical properties were identical with those reported.

(4R,6R)-2-Pentyl-2,4,6-trimethyl-1,3-dioxane (1; R¹ = Me, R² = 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; ¹H NMR (CDCl₃) δ 0.90 (t, J = 6.5 Hz, 3H, CH₃), 1.19 (d, J = 6.2 Hz, 6H, 2CH₃), 1.31 (s, 3H, CH₃), 1.24-1.80 (m, 10H, (CH₂)₄ and C(5)H₂), 3.85-4.10 (m, 2H, 2CHO). Anal. Found: C, 71.98; H, 12.48. Calcd for C₁₂H₂₄O₂: C, 71.95; H, 12.08.

(4R,6R)-2-(2'-Methylpropyl)-2,4,6-trimethyl-1,3-dioxane(1; R¹ = Me, $R^2 = i-Bu$): IR (film) 2934, 1379, 1184, 1149 cm⁻¹; ¹H NMR (CDCl₃) δ 0.94 (d, J = 6.4 Hz, 3H, CH₃), 0.95 (d, J = 6.4 Hz, 3H, CH₃), 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 Me₂CHCH₂), 3.83-4.07 (m, 2H, 2OCH). Anal. Found: C, 70.89; H, 11.96. Calcd for C₁₁H₂₂O₂: C, 70.92; H, 11.90.

(4R,6R)-2-(2'-Methylethyl)-2,4,6-trimethyl-1,3-dioxane (1; R¹ = 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; ¹H NMR $(CDCl_3) \delta 0.90 (d, J = 7.0 Hz, 3H, CH_3), 0.94 (d, J = 6.6 Hz, 3H, CH_3),$ 1.13-1.21 (complex of d and s, 9H, 3CH₃), 1.52-1.62 (m, 2H, C(15)H₂), 2.04 (septet, J = 7.0 Hz, 1H, Me₂CH), 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.

(4R,6R)-4,6-Dimethyl-2-ethyl-2-phenyl-1,3-dioxane (1; R¹ = Et, R²) = 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; ¹H NMR (CDCl₃) δ 0.73 (t, J = 7.4 Hz, 3H, CH₃), 1.19 (d, J = 6.4 Hz, 3H, CH₃), 1.21 (d, J = 6.4 Hz, 3H, CH₃), 1.40–2.00 (m, 4H, C(5) H_2 and CH2CH3), 3.59-3.78 (m, 1H, CHO), 4.07-4.25 (m, 1H, CHO). Anal. Found: C, 76.32; H, 9.18. Calcd for C14H20O2: C, 76.33; H,

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 \times 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 diastereometic 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 $(10 \text{ mL} \times 3)$. 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 diastereometic 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.

(2R,1'R)-2-(1'-Methyl-3'-oxobutoxy)heptane: TLC, $R_f = 0.53$ (hexane–EtOAc, 5:2); GC (100 °C), $t_{\rm R} = 11.8 \text{ min}$; ¹H NMR (CDCl₃) $\delta 0.88$ $(t, J = 6.5 Hz, 3H, CH_3), 1.06 (d, J = 6.0 Hz, 3H, CH_3), 1.13 (d, J =$ 6.0 Hz, 3H, CH₃), 1.20-1.49 (m, 8H, (CH₂)₄), 2.17 (s, 3H, CH₃), 2.40 (dd, J = 5.4, 15.4 Hz, 1H, CHHC=0), 2.70 (dd, J = 7.4, 15.4 Hz, 1H, 1H)CHHC=O), 3.32-3.53 (m, 1H, CHO), 3.94 (sextet, J = 6.0 Hz, 1H, CHO).

(2S,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), $t_{\rm R} = 10.8$ min; ¹H NMR (CDCl₃) δ 0.88 (t, J = 6.3 Hz, 3H, CH₃), 1.11 (d, J = 6.2 Hz, 3H, CH₃), 1.16 (d, J = 6.2 Hz, 3H, CH₃), 1.20–1.50 (m, 8H, $(CH_2)_4$, 2.17 (s, 3H, CH₃), 2.40 (dd, J = 5.8, 15.8 Hz, 1H, CHHC=O), 2.72 (dd, J = 6.9, 15.8 Hz, 1H, CHHC=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 C₁₂H₂₄O₂: C, 71.95; H, 12.08.

(2R,1'R)-4-Methyl-2-(1'-methyl-3'-oxobutoxy)pentane: TLC, $R_f =$ 0.48 (hexane-EtOAc, 5:2); GC (90 °C), $t_{\rm R}$ = 8.0 min; ¹H NMR (CDCl₃) $\delta 0.887$ (d, J = 6.6 Hz, 3H, CH₃), 0.895 (d, J = 6.6 Hz, 3H, CH₃), 1.06 $(d, J = 6.2 \text{ Hz}, 3\text{H}, \text{CH}_3), 1.09-1.22 \text{ (m, 1H, Me}_2\text{CHCHH}), 1.15 \text{ (d,}$ J = 6.0 Hz, 3H, CH₃), 1.41 (ddd, J = 6.0, 7.6, 13.8 Hz, 1H, Me₂-CHCHH), 1.58-1.82 (m, 1H, Me₂CH), 2.18 (s, 3H, CH₃), 2.41 (dd, J = 5.4, 15.4 Hz, CHHC==O), 2.70 (dd, J = 7.3, 15.4 Hz, CHHC=O), 3.53 (dquintet, J = 7.6, 6.0 Hz, 1H, CHO), 3.88-4.05 (m, 1H, CHO).

(2S,1'R)-4-Methyl-2-(1'-methyl-3'-oxobutoxy)pentane (7; R¹ = 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; ¹H NMR (CDCl₃) δ 0.88 (d, J = 6.6 Hz, 3H, CH₃), 0.89 (d, J = 6.6 Hz, 3H, CH₃), 1.12 (d, J = 6.0 Hz, 3H, CH₃), 1.10–1.22 (m, 1H, Me₂-CHCHH), 1.18 (d, J = 6.2 Hz, 3H, CH₃), 1.33-1.80 (m, 2H, Me_2CHCHH , 2.18 (s, 3H, CH₃), 2.42 (dd, J = 5.8, 15.8 Hz, 1H, CHHC=O), 2.73 (dd, J = 6.6, 15.8 Hz, 1H, CHHC=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 C11H22O2: C, 70.92; H, 11.90.

(2R, 1'R)-3-Methyl-2-(1'-methyl-3'-oxobutoxy)butane: TLC, $R_f = 0.43$ (hexane-EtOAc, 5:2); GC (40 °C), $t_{R} = 32.9 \text{ min}; {}^{1}\text{H NMR}$ (CDCl₃) δ 0.86 (d, J = 6.8 Hz, 3H, CH₃), 0.88 (d, J = 6.8 Hz, 3H, CH₃), 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, Me₂CH), 2.18 (s, 3H, CH₃), 2.40 (dd, J = 5.4, 15.0 Hz, 1H, CHHC=O), 2.70 (dd, J = 7.3, 15.0 Hz, 1H, CHHC=O), 3.14-3.29 (m, 1H, CHO), 3.84-4.02 (m, 1H, CHO).

(2S,1'R)-3-Methyl-2-(1'-methyl-3'-oxobutoxy)butane (7; R¹ = 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; ¹H NMR (CDCl₃) δ 0.82 (d, J = 6.0 Hz, 3H, CH₃), 0.85 (d, J =6.8 Hz, 3H, CH₃), 1.05 (d, J = 6.4 Hz, 3H, CH₃), 1.16 (d, J = 6.0 Hz, 3H, CH₃), 1.55-1.77 (m, 1H, Me₂CH), 2.18 (s, 3H, CH₃), 2.40 (dd, J

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= 5.8, 15.8 Hz, 1H, CHHC=O), 2.74 (dd, J = 6.9, 15.8 Hz, 1H, CHHC=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 C₁₀H₂₀O₂: 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; ¹H NMR (CDCl₃) δ 1.06 (d, J = 6.2 Hz, 3H, CH₃), 2.21 (s, 3H, CH₃). Other resonances could not be discerned for this minor isomer.

(15,1'R)-1-(1'-Methyl-3'-oxobutoxy)-1-phenylethane (7; R¹ = Me, R² = 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; ¹H NMR (CDCl₃) δ 1.21 (d, J = 6.2 Hz, 3H, CH₃), 1.42 (d, J = 6.4 Hz, 3H, CH₃), 2.04 (s, 3H, CH₃), 2.41 (dd, J = 6.1, 15.4 Hz, 1H, CHHC=O), 2.66 (dd, J = 7.0, 15.4 Hz, 1H, CHHC=O), 3.74–3.92 (m, 1H, CHO), 4.55 (q, J = 6.4 Hz, 1H, CHO).

(1R,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; ¹H NMR (CDCl₃) δ 1.01 (d, J = 6.2 Hz, 3H, CH₃), 2.20 (s, 3H, CH₃), 2.47 (dd, J = 6.0, 15.6 Hz, 1H, CHHC=O), 2.82 (dd, J = 6.4, 15.6 Hz, 1H, CHHC=O), 3.91 (sextet, J = 6.2 Hz, 1H, OCHMe). Other resonances could not be discerned for this minor isomer.

(15,1'R)-1-(1'-Methyl-3'-oxobutoxy)-1-phenylpropane (7; R¹ = Et, R² = Ph): TLC, $R_f = 0.47$ (hexanc-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; ¹H NMR (CDCl₃) δ 0.88 (t, J = 7.4 Hz, 3H, CH₃), 1.20 (d, J = 6.2 Hz, 3H, CH₃), 1.50-1.90 (m, 2H, CH₂CH₃), 2.02 (s, 3H, CH₃), 2.40 (dd, J = 6.0, 15.3 Hz, 1H, CHHC=O), 2.63 (dd, J = 6.8, 15.3 Hz, 1H, CHHC=O), 3.81 (sextet, J = 6.2 Hz, 1H, OCHMe), 4.24 (dd, J = 6.2, 7.2 Hz, 1H, PhCH), 7.20-7.40 (m, 5H, Ph). Anal. Found: C, 76.20; H, 9.55. Calcd for C₁₄H₂₀O₂: C, 76.33; H, 9.15.

(1R,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; ¹H NMR (CDCl₃) δ 1.01 (d, J = 6.4 Hz, 3H, CH₃), 1.12 (d, J = 6.0 Hz, 3H, CH₃), 0.80-1.90 (m, 11H, c-C₆H₁), 2.17 (s, 3H, CH₃CO), 2.39 (dd, J = 5.4, 15.0 Hz, 1H, CHHC=-0), 2.70 (dd, J = 7.6, 15.0 Hz, 1H, CHHC=-0), 3.18 (quintet, J = 6.0 Hz, 1H, MeCH-c-Hex), 3.83-4.00 (m, 1H, MeCHO).

(15,1'*R*)-1-Cyclohexyl-1-(1'-methyl-3'-oxobutoxy)ethane (7; R¹ = Me, R² = c-Hex):³⁵ TLC, $R_f = 0.47$ (hexane-EtOAc, 5:2); IR (film) 2972, 2855, 1716, 1450, 1370, 1080 cm⁻¹; GC (110 °C), $r_R = 29.1$ min; ¹H NMR (CDCl₃) δ 1.07 (d, J = 6.2 Hz, 3H, CH₃), 1.15 (d, J = 6.2 Hz, 3H, CH₃), 0.80-1.85 (m, 11H, c-C₆H₁₁), 2.08 (s, 3H, CH₃CO), 2.41 (dd, J = 6.2, 15.8 Hz, 1H, CHHC=O), 2.74 (dd, J = 6.4, 15.8 Hz, 1H, CHHC=O), 3.19 (quintet, J = 6.2 Hz, 1H, MeCH-c-Hex), 3.93 (sextet, J = 6.2 Hz, 1H, MeCHO). Anal. Found: C, 73.49; H, 11.78. Calcd for C₁₃H₂₄O₂: 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; ¹H NMR (CDCl₃) $\delta 0.84$ (s, 9H, t-Bu), 1.16 (d, J = 6.2 Hz, 3H, CH₃), 0.85–1.30 (m, 5H, c-C₆H₅H₅), 1.68–1.83 (m, 2H, c-C₆H₂H₈), 1.90–2.08 (m, 2H, c-C₆H₂H₈), 2.17 (s, 3H, CH₃), 2.40 (dd, J = 5.4, 15.4 Hz, 1H, CHHC=O), 2.72 (dd, J = 7.4, 15.4 Hz, 1H, CHHC=O), 3.20 (m, 1H, CHO), 3.95–4.10 (m, 1H, CHO). Anal. Found: C, 74.81; H, 12.14. Calcd for C₁₅H₂₈O₂: 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; ¹H NMR (CDCl₃) δ 0.84 (s, 9H, t-Bu), 1.16 (d, J = 6.0 Hz, 3H, CH₃), 0.80-1.65 (m, 7H, c-C₆H₇H₃), 1.78-1.97 (m, 2H, c-C₆H₂H₈), 2.21 (s, 3H, CH₃), 2.38 (dd, J = 5.0, 14.8 Hz, 1H, CHHC=0), 2.73 (dd, J =7.8, 14.6 Hz, 1H, CHHC=0), 3.57-3.67 (br, 1H, CHO), 3.78-4.05 (m, 1H, CHO).

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