Simplified Procedure for the Transformation of 22 into 24. **22** (100 mg, 0.44 mmol) in MeOH (3 mL) was hydrogenated (H_2, 1 atm) in the presence of 10% Pd/C (20 mg) at 20 °C (ca. 6 h). The mixture was filtered through Celite and then saturated with gaseous NH_3 at 0 °C (1 h). After 3 days at 20 °C (stopped flask), the solvent was evaporated and the residue purified by flash chromatography on silica gel (CH_2Cl_2/MeOH/ 30% aqueous NH_3 75:22:3), yielding 67 mg (94.5%) of yellowish oil.

Acknowledgment. We are grateful to Hoffmann-La Roche and Co., AG (Basel), the Fonds Herbette (Lausanne), and the Swiss National Science Foundation for financial support. We thank Miss D. Fontanella for her technical assistance.

Supplementary Material Available: UV, IR, ^{13}C NMR, and MS spectral data and elemental analyses of compounds **5**, **7**, and **9–24** (8 pages). Ordering information is given on any current masthead page.

Asymmetric Synthesis of (5*R*,6*S*)-6-Acetoxy-5-hexadecanolide, the Major Component of the Oviposition Attractant Pheromone of the Mosquito *Culex pipens fatigans*, and Two of Its Stereoisomers

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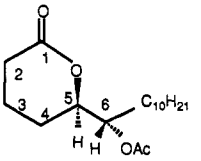
The benzyl derivatives of (*R*)- and (*S*)-2-hydroxydodecanal have been prepared by a previously described asymmetric synthesis based on a chiral 1,3-oxathiane and have been converted into (5*R*,6*S*)-6-acetoxy-5-hexadecanolide, a mosquito oviposition attractant pheromone, and its 5*R*,6*R* and 5*S*,6*R* stereoisomers in highly diastereoselective fashion. The steps involved are Grignard addition of 5-pentenylmagnesium bromide, Mitsunobu inversion for one of the erythro (5*R*,6*S*) isomers and oxidation–hydride reduction for the other, ozonization, oxidation, lactone formation, debenzylation, and acetylation, the overall yield in these steps being 30–42%.

In 1982, Laurence and Picket[2] isolated a substance from the apical droplets that form on the eggs of the mosquito *Culex pipens fatigans* (=*quinquefasciatus*) Wiedemann and identified it as *erythro*-6-acetoxy-5-hexadecanolide (1)

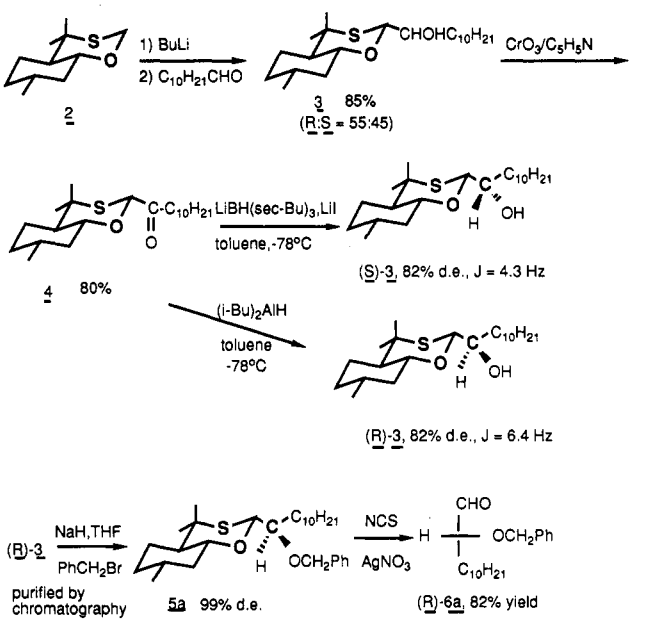


(5R,6S)-1

by mass spectral comparison with a synthetic, racemic sample. The substance acts as an oviposition attractant pheromone in that it attracts other gravid females of the same and some related mosquito species and induces them to oviposit in the same spot where the original eggs are found. Although the natural material is nonracemic, the amount available was too small to determine its optical rotation, and it was only later comparison of pheromonal activity of synthetic specimen of the (5*R*,6*S*)-**1** and (5*S*,6*R*)-**1** enantiomers which proved the former to be the natural substance.[3]

The first synthesis of the two enantiomeric erythro isomers of 1 was reported in 1982.[5] One of the two chiral centers (OH → OAc) was introduced in a chiral precursor (whose chiral center was later destroyed) in a synthesis of low diastereoselectivity (6:4) followed by chromatographic separation of the diastereomers; similarly low diastereoselectivity was encountered in the introduction of the second (lactone) chiral center and chromatography was again resorted to. Although the stereochemical efficiency

Scheme I



(1) From the Ph.D. Dissertation of K.-Y. Ko, University of North Carolina, 1985.

(2) Laurence, B. R.; Pickett, J. A. *J. Chem. Soc. Chem. Commun.* **1982**, 59.

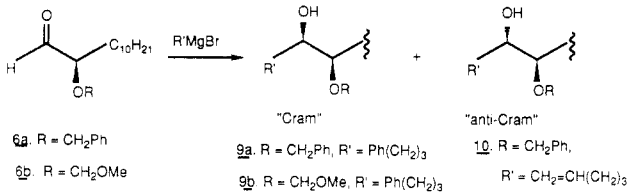
(3) Laurence, B. R.; Mori, K.; Otsuka, T.; Pickett, J. A.; Wadhams, L. J. *J. Chem. Ecol.* **1985**, *11*, 643.

(4) (a) Lin, G.-q.; Xu, H.-j.; Wu, B.-c.; Guo, G.-z.; Zhou, W.-s. *Tetrahedron Lett.* **1985**, 1233. (b) Machiya, K.; Ichimoto, I.; Kirihata, M.; Ueda, H. *Agric. Biol. Chem.* **1985**, *49*, 643.

(5) Fuganti, C.; Grasselli, P.; Servi, S. *J. Chem. Soc., Chem. Commun.* **1982**, 1285.

0022-3263/86/1951-5353$01.50/0

Table I. Stereoselectivity in the Reaction of 2-Alkoxy Aldehydes with Grignard Reagents



6a. R = CH_2Ph
6b. R = CH_2OMe

9a. R = CH_2Ph, R' = $Ph(CH_2)_3$
9b. R = CH_2OMe, R' = $Ph(CH_2)_3$

10. R = CH_2Ph, R' = $CH_2{=}CH(CH_2)_3$

R	R'	solvent	temp, °C	% product: Cram	% product: anti-Cram	de %[a]
Bz	$Ph(CH_2)_3$	THF	−78	60	40	20
		THF	RT[b]	63	37	26
		ether	−78	94	6	88
		ether	RT	90	10	80
MOM	$Ph(CH_2)_3$	THF	−78	55	45	10
		THF	RT	70	30	40
		ether	−78	94	6	88
		ether	RT	90	10	80
Bz	$CH_2{=}CH(CH_2)_3$	ether	−78	95	5	90
		ether	RT	91	9	82

[a] Determined by ^{13}C NMR. [b] Room temperature.

of the synthesis is thus low, our own chemical approach to **1** (see Scheme I) involves some of the same intermediates used by Fuganti et al.[5] Two subsequent asymmetric syntheses[4,6] employed the Sharpless oxidation[7] to introduce asymmetry with overall yields of 30% in seven steps[6] or 15–20% in eight steps,[4] respectively. Additional syntheses from 2-cyclohexenol (obtained by asymmetric reduction of 2-cyclohexenone[8] (seven steps, 10% overall yield) and from optically active diethyl tartrate (twelve steps, 8% overall))[9] have been reported.

It appeared that a convenient asymmetric synthesis of α-hydroxy aldehydes earlier developed by us[10,11] might provide an efficient route to the Fuganti intermediate **6a** (Scheme I). The approach proved successful: (*R*)-**6a** was obtained from **2**[12] in 99% enantiomeric excess as shown in Scheme I.[13]

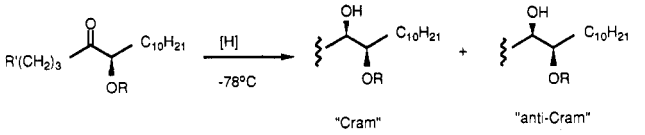
Treatment of oxathiane **2**[12] with butyllithium and undecanal followed by oxidation with chromium trioxide–pyridine[14] yielded the ketone **4** which was reduced either to carbinol (*S*)-**3** by lithium tri-*sec*-butylborohydride (L-Selectride (Aldrich))–lithium iodide (82% de) or to (*R*)-**3** by diisobutylaluminum hydride (DIBAL) (82% de). In accord with earlier experience[10] L-Selectride gives mainly (*S*)-carbinol, DIBAL mainly (*R*)-carbinol, the former reduction but not the latter proceeding in accord with Cram's chelate rule.[15] This was proved in the present case by cleavage and sodium chlorite oxidation[16] of (*R*)-**6a** to methyl (*R*)-(+)-2-(benzyloxy)dodecanoate (**7**) followed by lithium aluminum hydride reduction to (*R*)-(−)-(benzyloxy)-1-dodecanol (**8a**) whose configuration [the *S* isomer is dextrorotatory in chloroform] has been established in the literature.[17] It has been found[1] that the coupling constant between the carbinol hydrogen and C(2) in the oxathiane is larger in the *R* than in the *S* isomer since, in the intramolecularly hydrogen-bonded conformation, the two hydrogens are closer to anti in the *R* and closer to gauche in the *S* isomer; this difference (Scheme I) is in accord with the configurations assigned. Although the reductions are not completely stereoselective, the two diastereomers are easily separated and hence purified by flash chromatography or HPLC on silica gel, presumably because intramolecular hydrogen bonding is more favorable, sterically, in one diastereomer than in the other. Benzylation of purified (*R*)-**3** to ether **5a** followed by NCS–$AgNO_3$ cleavage[18] gave aldehyde **6a**. That there is little loss of enantiomeric purity during the aldehyde formation was ascertained in one case by the comparison of the ee (96%, ^1H NMR, $Eu(hfc)_3$) of the 2-methoxymethoxy alcohol **8b** derived from $LiAlH_4$ reduction of the aldehyde **6b** (prepared by methoxymethylation of (*S*)-**3** followed by cleavage) with the de (97%) of the starting **3**.

Although it was recognized from the beginning that treatment of (*R*)-**6a** with a Grignard reagent would, following Cram's rule, lead to the undesired threo product[5,19,20] we decided to synthesize this stereoisomer in order to evaluate the subsequent steps in the synthesis of **1**. This seemed of interest also because there have been conflicting reports on the stereoselectivity[19,20] of the Grignard addition; there was also the danger that the aldehyde (*R*)-**6a** might be partially racemized during the Grignard addition. In the event (see below) it was found that the Grignard addition, if effected in ether rather than tetrahydrofuran, was quite selective (Table I) and that no appreciable racemization occurred.

As a synthon for the carboxyl function of the lactone **1**, we selected initially either a phenyl or a vinyl group. The Grignard additions thus studied were those of (3-phenylpropyl)magnesium bromide, $Ph(CH_2)_3MgBr$, and of 4-pentenylmagnesium bromide, $CH_2{=}CH(CH_2)_3MgBr$; in addition to the benzyl ether (*R*)-**6a** the corresponding MOM ether (*R*)-**6b** [prepared by methoxymethylating instead of benzylating (*R*)-**3**, Scheme I, followed by cleavage] was studied. The results are shown in Table I.

(6) Mori, K.; Otsuka, T. *Tetrahedron* **1983**, *39*, 3267.
(7) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(8) Sato, T.; Watanabe, M.; Honda, N.; Fujisawa, T. *Chem. Lett.* **1984**, 1175.
(9) Masaki, Y.; Nagata, K.; Kaji, K. *Chem. Lett.* **1983**, 1835.
(10) Ko, K.-Y.; Frazee, W. J.; Eliel, E. L. *Tetrahedron* **1984**, *40*, 1333.
(11) For a review, see Eliel, E. L. *Phosphorus Sulfur* **1985**, *24*, 73.
(12) Eliel, E. L.; Lynch, J. E.; Kume, F.; Frye, S. V. *Org. Synth.*, in press.
(13) At the time this experiment was first carried out, we did not know the absolute configuration of pheromone 1.
(14) Poos, G. I.; Arth, G. E.; Beyler, R. E.; Sarett, L. H. *J. Am. Chem. Soc.* **1953**, *75*, 422.
(15) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748.
(16) Kraus, G. A.; Roth, B. *J. Org. Chem.* **1980**, *45*, 4825.
(17) Helmchen, G.; Wierzchowski, R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 60.
(18) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553.
(19) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, 1035.
(20) Eliel, E. L. in *Asymmetric Synthesis*, Morrison, J. D., Ed., Academic: New York, 1984; Vol. 2, p 125.
(21) Reference 20, p 129.

Table II. Stereoselectivity of Reduction of 2-Alkoxy Ketones at −78 °C



(R)-14. R' = CH_2=CH, R = CH_2Ph

(R)-15a. R' = Ph, R' = CH_2Ph

(R)-15b. R' = Ph, R = CH_2OMe

entry	R'	R	[H]	solvent	% product: Cram	% product: anti-Cram	de %[a]
1	Ph	Bz	L-Selectride	hexanes	45	55	−10
2				ether	48	52	−4
3				THF	9	91	−82
4			$LiAlH_4$	ether	76	24	52
5				THF	33	67	−34
6			Dibal	hexanes	20	80	−60
7			*t*-BuMgCl	ether	60	40	20
8	Ph	MOM	L-Selectride	hexanes	66	34	32
9				ether	82	18	64
10				THF	22	78	−56
11			$LiAlH_4$	ether	68	32	36
12				THF	33	67	−34
13			$NaBH_4$	2-PrOH	62	38	24
14	CH_2=CH	Bz	$LiAlH_4$	ether	80	20	60

[a] Determined by ^{13}C NMR; a minus sign indicates that the product predicted by Cram's chelate model is the minor one.

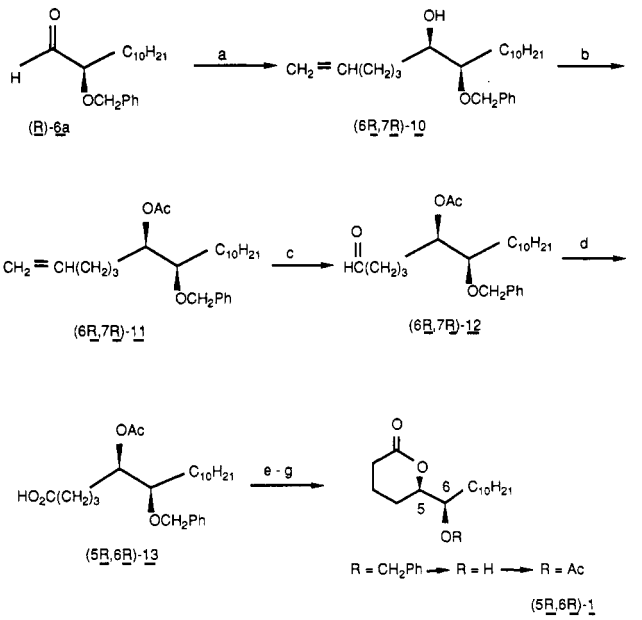
It is clear that all three Grignard additions proceeded with diastereoselectivities exceeding 80%, provided the reactions were carried out in ether. However, while the two benzyl ethers (**9a** and **10**) could be further purified to essentially complete diasteromeric purity by chromatography (as already reported for **10** by Fuganti et al.[5]), we were unable to purify **9b**. This precluded the use of **9b**, and there was concern that the contemplated subsequent ruthenium tetroxide oxidation of the benzyl ether **9a** might not be feasible with another phenyl moiety (that of the benzyl protective group) present. Therefore **9a** was debenzylated by catalytic hydrogenolysis and converted to either the diacetate or the acetonide. In neither of these compounds, however, was clean RuO_4 oxidation of the phenyl group successful in our hands.

We therefore proceeded with compound **10** as shown in Scheme II. (6*R*,7*R*)-**10** was acetylated with acetic anhydride/4-(dimethylamino)pyridine, ozonized, and then oxidized with sodium chlorite.[16] Saponification of the acetate followed by acidification and stirring in benzene in the presence of *p*-TsOH led to lactonization; finally the lactone was debenzylated and acetylated to give (5*R*,6*R*)-**1** whose rotation, $[\alpha]^{20}_D$ +14.4° ($CHCl_3$), agreed well with literature values (+14.6°,[4] +14.5°[5]), thus proving that no racemization occurs in the synthesis from (*R*)-**6a**. The yield of (5*R*,6*R*)-**1** from (*R*)-**6a** was 42% in seven steps.

While this route was being pursued, we sought reversal of the stereochemistry of organometal addition to (*R*)-**6a** by using the titanium reagents developed by Reetz.[22] Indeed, the addition of $CH_3Ti(O\text{-}iPr)_3$ to (*R*)-**6a** gave the Cram and anti-Cram addition product in a ratio of 18:82, in contrast to CH_3MgBr, which gave predominantly the Cram product (87:13). However, while the corresponding titanium complex $C_6H_5(CH_2)_3Ti(O\text{-}iPr)_3$ added normally to heptanal, we were unable to add the same reagent to (*R*)-**6a**. Discouraged by this finding, we sought an alternative route to the (5*S*,6*R*) isomer of **1**.

It would appear that reduction of the ketone corresponding to carbinol **10** by appropriate hydride reagents should proceed by Cram's rule and thereby yield the diastereomer of the Grignard addition product shown in Table I and Scheme II, namely (6*S*,7*R*)-**10**. To our disappointment, the steroselectivity in this reduction was only 60% (Table II). Even so, it was among the highest of all the reductions studied in this series; as shown in Table II, reductions leading to carbinols **9a** and **9b** generally proceeded with even poorer stereoselectivity, with none at all, or in a number of instances even contrary to Cram's chelate rule! These results are difficult to rationalize, especially in the absence of control experiments to demonstrate that the outcome was indeed in all cases kinetically controlled and not the result of a partial or complete Meerwein–Ponndorf–Oppenauer equilibration of the product alu-

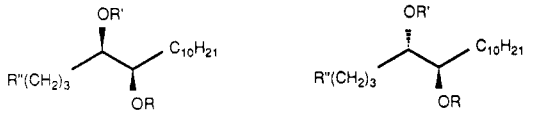
Scheme II[a]



[a] (a) CH_2=$CH(CH_2)_3MgBr$, ether, −78 °C/separation, 84%; (b) acetic anhydride, DMAP, 93%; (c) O_3, CH_2Cl_2, −78 °C/Me_2S, 80%; (d) $NaClO_2$, 96%; (e) KOH, EtOH, H_2O/*p*-TsOH, benzene, 86%; (f) H_2, Pd/C, 93%; (g) Ac_2O, DMAP, 87%.

(22) Reetz, M. T. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 556.

Table III. Optical Rotations ($[\alpha]^{20}_D$, deg) of 1,2-Diols and Their Derivatives



				syn		anti	
compd	R″	R	R′	MeOH	$CHCl_3$	MeOH	$CHCl_3$
9a	Ph	Bz	H	+17.0	−9.1	+6.7	+4.2
19		H	H	+22.3	+19.1		
20		Ac	Ac		+21.3		
21		acetonide		+29.7	+21.0		
10	CH_2=CH	Bz	H	+17.6	−10.5	+9.3	+4.3
11		Bz	Ac	+21.7	+14.5		+6.1

Tiable IV. Optical Rotation ($[\alpha]^{20}_D$, deg) of 2-Alkoxy Alcohols RCH(OR′)CH_2OH and Their Methyl Ethers RCH(OR′)CH_2OMe

			de	2-alkoxy alcohol		methyl ether	
R	R′[a]	config	%	MeOH	$CHCl_3$	MeOH	$CHCl_3$
hexyl	Bz	*R*	98	+18.7	−18.5	+17.7	+15.2
	MOM	*S*	86	−13.0	+40.8	−14.3	−8.8
	Me	*R*	98	−1.5	−26.8		
decyl	MOM	*S*	97	−10.9	+37.9		
isopropyl	Bz		96	+19.3	−10.8	+17.3	+23.6
cyclohexyl	Bz	*R*	98	+14.8	−12.4	+12.9	+15.4
tert-butyl	Bz	*R*	100	+5.4	−9.7	+8.7	+17.5
Ph	Bz	*S*	100	+93.7	+104		
Ph	MOM	*S*	100	+189	+196		

[a] Bz = benzyl; MOM = methoxymethyl; Me = methyl.

minates. However, they mirror similar results reported elsewhere.[23,24]

LAH reduction of the ketone (7*R*)-**14** obtained by Collins oxidation of a diastereomer mixture of (6*RS*,7*R*)-**10**, followed by chromatographic separation gave (6*S*,7*R*)-**10** in 55% recovery from the stereochemically heterogeneous starting material. Further conversion to (5*S*,6*R*)-**1** in analogy with Scheme II proceeded in 54% overall yield to give material $[\alpha]^{20}_D$ +37.2° ($CHCl_3$) which is in reasonable agreement with literature values (+38.8°,[6] +37.2°,[4] +39.1°,[8] +42.0°,[9] +38.0° [5]).

At this stage in the synthesis we learned that the natural pheromone has the 5*R*,6*S* configuration,[3] i.e., is enantiomeric to the materail we had prepared. To obtain the natural product, it was therefore necessary to start from (*S*)-**3**, obtained by L-Selectride–lithium iodide reduction of ketone **4** (Scheme I). The stereoisomerically impure product was readily purified by chromatography. The subsequent stepts of the synthesis followed those shown in Scheme I to obtain (*S*)-**6a**. However, rather than converting (6*S*,7*S*)-**10** (prepared analogously as its enantiomer; cf. Scheme II) into the corresponding 6*R*,7*S* isomer by oxidation followed by hydride reduction (cf. Table II) we chose to effect inversion at C(6) by a Mitsunobu reaction.[25] Treatment of (6*S*,7*S*)-**10** with DEAD (diethyl azodicarboxylate), triphenylphosphine, and benzoic acid yielded the benzoate of (6*R*,7*S*)-**10** in 78% isolated yield, along with some elimination product, but free, according to proton NMR, of any benzoate of the starting (6*S*,7*S*)-**10**. The remainder of the synthesis proceeded as shown in Scheme II, but with benzoate in place of acetate. The final product, (5*R*,6*S*)-**1**, was obtained from (*S*)-**6a** in 36% overall yield (in 7 steps) and had $[\alpha]^{20}_D$ −37.2° ($CHCl_3$) (lit. −36.2°,[6] −37.4°,[4] −37.6°,[5] −39.2° [8]).

(23) Larchevêque, M.; Lalande, J. *J. Chem. Soc. Commun.* **1985**, 83.
(24) Shimagaki, M.; Maeda, T.; Matsuzaki, Y.; Hori, I.; Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1984**, 4775.
(25) Mitsunobu, O. *Synthesis* **1981**, 1.

Solvent Dependence of Optical Rotation of 1,2-Diols and Their Derivatives

In the course of determining the optical rotation of **9**, **10**, and a number of their derivatives (Table III) we found a remarkable dependence in sign on solvent for the syn (threo) derivatives which was not seen in the anti (erythro) isomers. In the case of the monoethers of the diols (but not for the diols themselves, or their acetonides, or their benzyl ether acetates) there is a reversal of the sign of rotation as one passes from solvent methanol to solvent chloroform. In methanol, the *R*,*R* (syn or threo) compounds are dextrorotatory, as are the free glycols and their disubstitution products. In chloroform, however, the monoethers (but not the diols or their disubstitution products) are levorotatory. We tentatively ascribe this difference to intramolecular hydrogen bonding of the monoethers in chlorform which leads to a OH/OR gauche conformation, whereas in methanol, where the hydrogen bonds are broken by bonding to the solvent, OH and OR are anti. No intramolecular hydrogen bonding can evidently take place in the disubsituted syn glycols. In the free glycols, on the other hand, it appears, according to calculations,[26] that the gauche form is preferred regardless of solvent. As mentioned earlier in the context of chromatographic separation, intramolecular hydrogen bonding is less facile in the anti (erythro) isomers because in the predominant conformation, in which the chain forms a zig-zag (all-anti), the OH and OR functionalities are too far away from each other to allow formation of an intramolecular hydrogen bond.

Similar phenomena are seen in 2-alkoxy alcohols, RCH(OR′)CH_2OH,[10] and their methyl ethers, RCH(OR′)CH_2OCH_3 (for preparation, see Experimental Section), as shown in Table IV. The free alkoxy alcohols (except when R = Ph) show reversal in sign of optical

(26) van Duin, M.; Baas, J. M. A.; van de Graaf, B. *J. Org. Chem.* **1986**, *51*, 1298.

rotation (or at least a large shift toward levorotation) as the solvent is changed from methanol to chloroform; the diethers, on the other hand, fail to show this reversal. Moreover, in all cases the rotation of the diether corresponds to that of the alkoxy alcohol in solvent methanol where, presumably, no intramolecular hydrogen bonding occurs.

Even the free diol, (S)-1,2-dodecanediol (ee 89%) displays reversal in sign of optical rotation in ethanol ($[\alpha]^{20}_D$ −10.1°) vs. chloroform ($[\alpha]^{20}_D$ +0.9°). The corresponding methylene acetal was dextrorotatory in both methanol ($[\alpha]^{20}_D$ +7.6°) and chloroform ($[\alpha]^{20}_D$ +14.4°), suggesting that the intramolecularly hydrogen-bonded species of the diol (conformationally analogous to the methylene acetal) is responsible for the small dextrorotation in chloroform.

The preparation of the ethers shown in Table IV, which, except for the above-mentioned dodecyl compound **8b**, are derivatives of the previously prepared[10] glycols, is described in the Experimental Section.

Experimental Section

Melting points were measured in capillary tubes on an Electrothermal melting point apparatus and are uncorrected. Boiling points reported in Kugelrohr distillations indicate temperature of the air bath during distillation. Infrared (IR) spectra were recorded in carbon tetrachloride on a Beckman Model 4250 spectrophotometer. The following symbols are used to indicate approximate intensities of the IR absorption signals: w = weak, m = medium, s = strong, vs = very strong. Proton NMR spectra were recorded on a Perkin-Elmer R24B (60 MHz), a varian XL-100 (100 MHz), or a Bruker WM-250 (250 MHz) spectrometer using tetramethylsilane as an internal standard. The following abbreviations are used to designate the multiplicity of individual signals: s = singlet, bs = broad singlet, d = doublet, t = triplet, dd = double doublet, dt = double triplet, m = multiplet. Carbon-13 NMR spectra were recorded on a Varian XL-100 (25.16 MHz) or a Bruker WM-250 (62.89 MHz) spectrometer using tetramethylsilane as an internal standard. All NMR spectra were recorded in deuteriochloroform unless otherwise noted and are expressed in parts per million downfield from tetramethylsilane; couplings are in hertz. Mass spectra (electron impact, 70 ev) were obtained with a VG-Micromass Model 7070F double focusing mass spectrometer equipped with a VG-Data System 2035 computer. Optical rotations were measured on a Perkin-Elmer Model 141 Polarimeter equipped with Na and Hg light sources using a 10-cm thermostated cell at 20 °C. Thin layer chromatography (TLC) was performed by using aluminum backed silica gel plates (E. Merck 60 F-254, 0.2 mm). Developed plates were visualized by staining with a 10% solution of phosphomolybdic acid in ethanol or by UV light. Flash chromatography was performed with EM Reagent Kieselgel 60 (230–400 mesh ASTM). Preparative high-pressure liquid chromatography was performed on a Waters LS 500A instrument equipped with a refractive index detector by using one or two columns [2.0 in (i.d.) × 11.25 in. packed with silica (Water Prepak-500)]. Elemental analyses were performed by M-H-W Laboratories at Phoenix, AZ.

2-(1(*R*)-Hydroxyundecyl)-2 and 2-(1(*S*)-Hydroxyundecyl)-2 (3). To a stirred, cooled (−78 °C) solution of 10.0 g (50.0 mmol) of 1,3-oxathiane **2**, prepared as described,[12] and 6.40 g (55.2 mmol) of *N,N,N′,N′*-tetramethylethylenediamine in 250 mL of dry THF was added dropwise 32.8 mL (55.6 mmol) of 1.69 M butyllithium in hexanes over 5 min under nitrogen. The solution was stirred for an additional 10 h at −78 °C and then was treated with a solution of 9.40 g (55.2 mmol) of undecylic aldehyde in 50 mL of dry THF over 10 min. After stirring for 10 min at −78 °C, 20 mL of saturated ammonium chloride was added followed by 50 mL of water. The organic layer was separated, and the aqueous phase was extracted with ether (3 × 30 mL). The combined organic phase was washed with dilute HCl, dried ($MgSO_4$), and concentrated to give 18.16 g (98% crude yield) of pale yellow oil. TLC showed presence of a small amount of starting material **2** as well as 5-pentadecanol (addition product of butyllithium to undecylic aldehyde) in addition to oxathianecarbinols **3**. The proton NMR spectrum of the crude product indicated a proportion of 55% 2-(1(*R*)-hydroxyundecyl)-**2** and 45% 2-(1(*S*)-hydroxyundecyl)-**2**. Purification by flash chromatography [hexanes–ethyl acetate (20:1)] gave 15.72 g (85%) of mixed **3** as a colorless oil.

R isomer: ^{1}H NMR (250 MHz) δ 4.75 (d, 1 H, *J* = 6.8 Hz), 3.68–3.54 (m, 1 H), 3.40 (dt, 1 H, *J* = 10.5, 4.3 Hz), 2.70 (bs, 1 H) and others; ^{13}C NMR (62.89 MHz) δ 82.2, 77.0, 73.1, 50.8, 42.9, 41.6, 34.7, 32.6, 31.9, 31.4, 29.6, 29.4, 25.2, 24.4, 22.9, 22.7, 22.1, 14.1; IR (cm^{-1}) 3600 m, 2920 vs, 2860 a, 1370 m, 1210 s, 1150 s, 1090 s, 1060 vs, and others.

S isomer: ^{1}H NMR (250 MHz) δ 4.94 (d, 1 H, *J* = 3.6 Hz), 3.81–3.71 (m, 1 H), 3.43 (dt, 1 H, *J* = 10.4, 4.3 Hz), 2.21 (bs, 1 H) and others; ^{13}C NMR (62.89 MHz) δ 82.8, 77.4, 73.3, 51.0, 42.6, 41.8, 34.7, 32.4, 31.9, 31.4, 29.7, 29.6, 29.3, 25.7, 24.4, 22.8, 22.7, 22.1, 14.1; IR (cm^{-1}) 3600 m, 2920 vs, 2860 s, 1370 m, 1210 s, 1150 s, 1090 s, 1060 s, and others.

Separation. Small amounts (1–2 g) of **3** were separated by flash column chromatography, using hexanes–ethyl acetate (30:1) as the eluent. Larger amounts (6–7 g) were conveniently separated with a Waters LS 500A preparative liquid chromatography instrument using the same solvent mixture. The *R* isomer was the less polar one.

2-Undecanoyl-2 (4). To a suspension of chromium trioxide–pyridine complex in dichloromethane, generated in situ by adding 21.4 g (214 mmol) of dry chromium trioxide to a solution of 33.8 g (428 mmol) of pyridine in 250 mL of dry dichloromethane was added a solution of 13.22 g (35.7 mmol) of **3** in 30 mL of dry dichloromethane all at once. The mixture was stirred at room temperature for 1 h and then passed through a short column of Florisil to remove the chromium salt. The eluent was washed with dilute HCl solution, dried with sodium sulfate, and concentrated. Purification of the resulting residue by flash column chromatography [hexanes–ethyl acetate (40:1)] gave 10.52 g of **4** (80%) as a pale yellow oil: ^{1}H NMR (250 MHz) δ 5.44 (s, 1 H), 3.43 (dt, 1 H, *J* = 10.5, 4.3 Hz), 2.63 (t, 2 H, *J* = 7.4 Hz), 1.46 (s, 3 H), 1.28 (s, 3 H) and others; ^{13}C NMR (62.89 MHz) δ 205.0, 82.5, 76.7, 50.2, 43.5, 41.4, 37.6, 34.4, 31.7, 31.1, 29.3, 29.2, 29.1, 28.9, 24.1, 23.0, 22.4, 22.3, 21.8, 13.8; IR (cm^{-1}) 2920 vs, 2860 s, 1730 s, 1470 m, 1460 m, 1375 m, 1310 w, 1210 m, 1190 m, 1150 s, 1090 s, 1070 vs, and others.

Reduction of 4. (a) With Lithium Tri-*sec*-butylborohydride (L-Selectride). A mixture of 1.40 g (3.80 mmol) of **4** and 1.02 g (7.62 mmol) of anhydrous LiI in 100 mL of dry toluene was treated with 7.6 mL of 1 M solution of L-Selectride in THF at −78 °C over 2 min. After stirring for 4 h the excess reducing agent was quenched with 5 mL of saturated ammonium chloride at −78 °C. The toluene layer was separated and concentrated. The resulting oil was refluxed with 50 mL of 0.2 M NaOH in methanol for several hours. Then, methanol was removed in vacuo, and the resulting residue was treated with 50 mL of water. Extraction of the organic product with ether (3 × 50 mL) followed by concentration gave 1.34 g (95%) of (*S*)-**3** and (*R*)-**3** in a ratio of 91:9 (^{1}H NMR).

(b) With Diisobutylaluminum Hydride (DIBAL). A solution of 1.50 g (4.07 mmol) of **4** in 50 mL of dry toluene was treated with 8.1 mL of 1 M DIBAL in hexanes at −78 °C over 1 min. After the reaction had been stirred for 2 h, the excess reducing agent was destroyed with 5 mL of saturated ammonium chloride at −78 °C. The mixture was allowed to warm to room temperature, and the product was extracted with ether (3 × 50 mL). Drying and concentration gave 1.48 g (98%) of (*R*)-**3** and (*S*)-**3** in a ratio of 91:1 (^{1}H NMR).

2-(1(*R*)-(Benzyloxy)undecyl)-2 (5a, R = Benzyl). To a solution of 3.04 g (8.20 mmol) of (*R*)-**3** in 100 mL of dry THF was added 0.79 g (32.8 mmol) of sodium hydride, followed by 1.60 g (9.36 mmol) of benzyl bromide. The mixture was refluxed for 10 h and then cooled to 0 °C, and the excess sodium hydride was quenched by dropwise addition of water (20 mL). The organic layer was separated, dried ($MgSO_4$), and concentrated to give 3.47 g (92%) of the benzyl ether as an oil after purification by flash column chromatography [hexanes–ethyl acetate (40:1)]. The *S* isomer was prepared similarly from the alcohol (*S*)-**3**.

R isomer: ^{1}H NMR (250 MHz) δ 7.38–7.20 (m, 5 H), 5.02 (d, 1 H, *J* = 6.5 Hz), 4.84, 4.59 (AB q, 2 H, *J* = 11.5 Hz), 3.60–3.50 (m, 1 H), 3.39 (dt, 1 H, *J* = 10.3, 4.1 Hz) and others; ^{13}C NMR (62.89 MHz) δ 139.1, 128.2, 128.0, 127.4, 82.8, 81.1, 77.3, 73.8, 50.8,

43.0, 41.8, 34.8, 31.9, 31.5, 31.2, 29.7, 29.62, 29.55, 29.4, 25.4, 24.4, 22.9, 22.7, 22.1, 14.1.

S isomer: ^{1}H NMR (250 MHz) δ 7.40–7.24 (m, 5 H), 5.00 (d, 1 H, *J* = 4.3 Hz), 4.75, 4.58 (AB q, 2 H, *J* = 11.7 Hz), 3.54–3.47 (m, 1 H), 3.33 (dt, 1 H, *J* = 10.4, 4.2 Hz) and others; ^{13}C NMR (62.89 MHz) δ 138.8, 128.1, 128.0, 127.3, 82.2, 80.8, 77.3, 72.6, 51.0, 42.5, 41.8, 34.8, 31.9, 31.4, 31.3, 29.8, 29.6, 29.3, 25.4, 24.4, 22.8, 22.7, 22.1, 14.1.

2-(1(*R*)-(Methoxymethoxy)undecyl)-2 (5b, R = Methoxymethyl). To a solution of 5.00 g (13.5 mmol) of (*R*)-**3** in 100 mL of dry dichloromethane was added 40 mL of dimethoxymethane, followed by 10 g of P_2O_5. The mixture was stirred at room temperature until TLC showed the absence of the starting alcohol (R_f 0.48, hexanes–ethyl acetate (5:1); for **5b**, R_f 0.59); then the solution was poured into 50 mL of 5% sodium carbonate solution. The lower phase was separated, dried ($MgSO_4$), and concentrated to give 5.26 g [94% purified yield, flash chromatography, hexanes–ethyl acetate (30:1)] of **5b** as a colorless oil. The *S* isomer was similarly prepared from (*S*)-**3**.

R isomer: ^{1}H NMR (250 MHz) δ 5.02 (d, 1 H, *J* = 5.3 Hz), 4.77, 4.70 (AB q, 2 H, *J* = 6.7 Hz), 3.67–3.64 (m, 1 H), 3.40 (s, 3 H), 3.39 (dt, 1 H, *J* = 10.5, 4.3 Hz), and others; ^{13}C NMR (62.89 MHz) δ 97.2, 82.0, 79.4, 77.4, 55.8, 50.8, 42.8, 41.8, 34.8, 31.9, 31.5, 30.9, 29.7, 29.6, 29.4, 25.3, 24.4, 22.8, 22.7, 22.1, 14.1.

S isomer: ^{1}H NMR (250 MHz) δ 5.02 (d, 1 H, *J* = 4.0 Hz), 4.81, 4.67 (AB q, 2 H, *J* = 6.8 Hz), 3.72–3.65 (m, 1 H), 3.40 (s, 3 H), 3.36 (dt, 1 H, *J* = 10.5, 4.3 Hz), and others; ^{13}C NMR (62.89 MHz) δ 96.3, 81.8, 79.0, 77.4, 55.6, 50.9, 42.6, 41.8, 34.8, 31.9, 31.5, 31.1, 29.7, 29.6, 29.4, 25.4, 24.4, 22.8, 22.7, 22.1, 14.1.

(*R*)-2-(Benzyloxy)dodecanal (6a). To a stirred mixture of 1.94 g (14.52 mmol) of *N*-chlorosuccinimide, 2.06 g (12.1 mmol) of silver nitrate, and 1.22 g (14.52 mmol) of sodium bicarbonate in 200 mL of 80% acetone in water was added all at once a solution of 2.23 g (4.84 mmol) of (*R*)-benzyl ether **5a** (precursor de 99%) in 20 mL of acetone at room temperature. The mixture was stirred for 10 min and then treated with 2 mL of saturated sodium sulfite, followed by 20 mL of saturated NaCl. Silver chloride was filtered, and the filtrate was transferred to a separatory funnel. The upper organic phase was separated, and the aqueous phase was extracted with ether (3 × 20 mL). The combined organic solution was concentrated under reduced pressure. Flash chromatography of the residue using hexanes–ethyl acetate (10:1) as the eluent provided 1.15 g (82%) of the aldehyde as an oil: R_f 0.55 [hexanes–ethyl acetate (5:1)] (for sultines[10] R_f 0.24), $[\alpha]^{20}_D$ +53.8° (*c* 2.09, $CHCl_3$), also $[\alpha]^{20}_{578}$ + 56.6°, $[\alpha]^{20}_{546}$ +65.8°, $[\alpha]^{20}_{436}$ +136°, $[\alpha]^{20}_{365}$ +351°; ^{1}H NMR (250 MHz) δ 9.62 (d, 1 H, *J* = 2.1 Hz), 4.65, 4.51 (AB q, 2 H, *J* = 11.8 Hz), 3.73 (dt, 1 H, *J* = 6.4, 2.1 Hz), and others; ^{13}C NMR (62.89 MHz) δ 203.7, 137.4, 128.5, 128.3, 128.0, 83.5, 72.5, 31.9, 30.1, 29.6, 29.5, 29.4, 29.3, 24.8, 22.7, 14.1; IR (cm^{-1}) 3100 w, 3080 m, 3040 m, 2910 vs, 2860 s, 1730 vs, 1460 s, 1380 m, 1200 m, 1150 m, 1100 vs, and others.

(*S*)-2-(Methoxymethoxy)dodecanal (6b) was similarly prepared in 70% isolated yield from (*S*)-methoxymethyl ether **5b** (precursor de 97%): $[\alpha]^{20}_D$ −15.1° (*c* 1.95, $CHCl_3$) also $[\alpha]^{20}_{578}$ −16.3°, $[\alpha]^{20}_{546}$ −19.1°, $[\alpha]^{20}_{436}$ −41.8°, $[\alpha]^{20}_{365}$ −115°; ^{1}H NMR (250 MHz) δ 9.61 (d, 1 H, *J* = 2.1 Hz), 4.73, 4.70 (AB q, 2 H, *J* = 6.9 Hz), 3.89 (dt, 1 H, *J* = 6.5, 2.1 Hz), 3.41 (s, 3 H), 1.72–1.63 (m, 2 H), 1.46–1.20 (m, 16 H), 0.88 (t, 3 H, *J* = 6.6 Hz); ^{13}C NMR (62.89 MHz) δ 202.3, 96.5, 82.2, 55.6, 31.8, 29.9, 29.4, 29.3, 29.2, 24.7, 22.5, 13.9; IR cm^{-1} 2920 vs, 2860 s, 1730 s, 1465 s, 1455 s, 1450 s, 1380 s, 1150 vs, 1100 vs, 1040 vs, and others.

(*S*)-2-(Methoxymethoxy)-1-dodecanol (8b). To a suspension of 20 mg (0.53 mmol) of lithium aluminum hydride in 50 mL of dry ether was added a solution of 200 mg (0.82 mmol) of the aldehyde **6b** (oxathiane precursor de 97%) in 10 mL of dry ether over 5 min at room temperature. After 10 min of stirring the excess reducing agent was quenched with sodium sulfate hydrate. Filtration, concentration, and Kugelrohr distillation (130–140 °C, 0.1 mmHg) gave 190 mg (95%) of the alcohol **8b** as an oil: $[\alpha]^{20}_D$ +37.9° (*c* 3.09, $CHCl_3$), also $[\alpha]^{20}_{578}$ +39.4°, $[\alpha]^{20}_{546}$ +44.5°, $[\alpha]^{20}_{436}$ +73.5°, $[\alpha]^{20}_{365}$ +111°; $[\alpha]^{20}_D$ −10.9° (*c* 1.90 MeOH), also $[\alpha]^{20}_{578}$ −11.4°, $[\alpha]^{20}_{546}$ −12.8°, $[\alpha]^{20}_{436}$ −20.8°, $[\alpha]^{20}_{365}$ −30.8°. Examination of the proton NMR spectrum (250 MHz, $CDCl_3$) of **8b** doped with Eu(hfc)$_3$ indicated an ee of 96%: ^{1}H NMR (250 MHz) δ 4.74, 4.69 (AB q, 2 H, *J* = 6.9 Hz), 3.62–3.48 (m, 3 H), 3.43 (s, 3 H) and others; ^{13}C NMR (62.89 MHz) δ 96.9, 81.8, 65.6, 55.6, 32.0, 31.8, 29.74, 29.66, 29.6, 29.4, 25.6, 22.7, 14.1.

Methyl (*R*)-2-(Benzyloxy)dodecanoate (7). A solution of 2.00 g (4.34 mmol) of (*R*)-benzyl ether **5a** (precursor de 98%) in 10 mL of acetone was added all at once to a stirred mixture of 1.74 g (13.0 mmol) of *N*-chlorosuccinimide, 1.84 g (10.8 mmol) of silver nitrate, and 1.46 g (17.4 mmol) of sodium bicarbonate in 150 mL of 80% acetone in water at room temperature. A white precipitate formed immediately. The mixture was stirred for 10 min, then treated with 1 mL of saturated sodium sulfite, followed by 10 mL of saturated sodium chloride. Silver chloride was filtered off and the filtrate treated with 10 mL of 2-methyl-2-butene (chlorine scavenger), followed by a solution of 3.50 g (purity 80%, 31.5 mmol) of sodium chlorite and 3.90 g of potassium dihydrogen phosphate (KH_2PO_4) in 50 mL of water over 5 min at room temperature. Stirring was continued for an additional 30 min, the organic solvent was removed under reduced pressure, and the resulting aqueous solution was extracted with 3 × 50 mL of ether. The combined ethereal solution was dried and treated with excess ethereal diazomethane. After removal of ether, flash chromatography of the residue using hexanes–ethyl acetate (10:1) as the eluent provided 1.11 g (80%) of the ester **7** [R_f 0.40, hexanes–ethyl acetate (10:1); for the sultines,[10] R_f 0.20]: $[\alpha]^{20}_D$ +50.9° (*c* = 2.57, $CHCl_3$), also $[\alpha]^{20}_{578}$ +53.1°, $[\alpha]^{20}_{546}$ +60.2°, $[\alpha]^{20}_{436}$ +102°, $[\alpha]^{20}_{365}$ +161°; ^{1}H NMR (250 MHz) δ 7.34–7.26 (m, 5 H), 4.69, 4.40 (AB q, 2 H, *J* = 11.7 Hz), 3.93 (t, 1 H, *J* = 6.4 Hz), 3.73 (s, 3 H), 1.80–1.70 (m, 2 H), 1.50–1.20 (m, 16 H), 0.88 (t, 3 H, *J* = 7.0 Hz); ^{13}C NMR (62.89 MHz) δ 173.5, 137.6, 128.3, 128.0, 127.8, 78.1, 72.3, 51.7, 33.0, 31.9, 29.6, 29.45, 29.36, 29.3, 29.2, 25.3, 22.7, 14.1; IR (cm^{-1}) 3100 w, 3080 w, 3040 w, 2990 m, 2960 s, 2940 vs, 2870 s, 1770 vs, 1750 s, 1475 m, 1465 m, 1390 m, 1360 m, 1275 m, 1200 m, 1125 vs, 1080 m, 1030 m, and others.

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.86; H, 9.72.

(*R*)-2-(Benzyloxy)-1-dodecanol (8a). To a suspension of 120 mg (3.16 mmol) of lithium aluminum hydride in 50 mL of ether was added dropwise a solution of 1.00 g (3.12 mmol) of the ester **7** (oxathiane precursor de 98%) in 20 mL of dry ether over 10 min at room temperature. The excess $LiAlH_4$ was destroyed with sodium sulfate hydrate. The inorganic salts were filtered, and the filtrate was concentrated to give 0.88 g (97%) of **8a** as an oil: $[\alpha]^{20}_D$ −15.7° (*c* 3.42, $CHCl_3$), also $[\alpha]^{20}_{578}$ −16.4°, $[\alpha]^{20}_{546}$ −18.6°, $[\alpha]^{20}_{436}$ −31.4°, $[\alpha]^{20}_{365}$ −49.0° [lit.[5] for *R* isomer $[\alpha]^{20}_D$ −17.5° (no solvent given); for *S* isomer +17.1° (no solvent given) lit.[17] for *S* isomer +17.5° (*c* 1.0, $CHCl_3$)]; ^{1}H NMR (250 MHz) δ 7.40–7.20 (m, 5 H), 4.58, 4.54 (AB q, 2 H, *J* = 11.6 Hz) and others; ^{13}C NMR (62.89 MHz) δ 138.8, 128.4, 127.8, 527.7, 80.0, 71.6, 64.3, 32.0, 29.9, 29.7, 29.6, 29.4, 25.5, 22.7, 14.1.

2-(1(*R*)-Methoxyheptyl)-2 (22a). To a solution of 1.30 g (4.14 mmol) of 2-(1(*R*)-hydroxyheptyl)-**2**[10] in 100 mL of THF was added 0.49 g (20.4 mmol) of sodium hydride, followed by 5.88 g (2.6 mL, 41.4 mmol) of iodomethane at room temperature. The mixture was stirred for 1 day, and then the excess sodium hydride was quenched by dropwise addition of water. The organic layer was separated, dried ($MgSO_4$), and concentrated to give 1.22 g (90%) of the methyl ether as an oil after flash chromatography [hexanes–ethyl acetate (40:1)]: ^{1}H NMR (250 MHz) δ 4.98 (d, 1 H, *J* = 5.9 Hz), 3.48 (s, 3 H), 3.39 (dt, 1 H, *J* = 10.5, 4.3 Hz), 3.34–3.23 (m, 1 H), 1.41 (s, 3 H), 1.28 (s, 3 H), 0.92 (d, 3 H, *J* = 6.5 Hz), 0.88 (t, 3 H, *J* = 6.5 Hz), and others; ^{13}C NMR (25.2 MHz) δ 83.0, 82.1, 77.4, 59.4, 50.8, 42.9, 41.8, 34.8, 31.8, 31.5, 30.9, 29.7, 29.4, 25.4, 24.5, 22.9, 22.6, 22.1, 14.1.

2-(1(*S*)-(Methoxymethoxy)heptyl)-2 (22b) was prepared by the methoxymethylation (dimethoxymethane, phosphorus pentoxide, dichloromethane) of 2-(1(*S*)-hydroxyheptyl)-**2**:[10] ^{1}H NMR (150 MHz) δ 5.02 (d, 1 H, *J* = 3.9 Hz), 4.81, 4.67 (AB q, 2 H, *J* = 6.8 Hz), 3.72–3.66 (m, 1 H), 3.39 (s, 3 H), 3.37 (dt, 1 H, *J* = 10.5, 4.3 Hz), 1.41 (s, 3 H), 1.28 (s, 3 H), 0.91 (dt, 3 H, *J* = 6.5 Hz), 0.88 (t, 3 H, *J* = 6.5 Hz), and others; ^{13}C NMR (62.89 MHz) δ 96.5, 81.9, 79.2, 77.5, 55.7, 51.0, 42.8, 41.9, 34.8, 31.8, 31.6, 31.2, 29.8, 29.3, 25.5, 24.5, 22.8, 22.7, 22.1, 14.1.

2-(1(*S*)-((Benzyloxy)phenyl)methyl)-2 (23a) was prepared in 95% yield by the benzylation (benzyl bromide, sodium hydride, THF, reflux) of 2-(1(*S*)-(hydroxyphenyl)methyl)-**2**,[10] mp 77–78 °C: ^{1}H NMR (250 MHz) δ 7.39–7.24 (m, 10 H), 5.08 (d, 1 H, *J* = 6.8 Hz), 4.59, 4.32 (AB q, 2 H, *J* = 12.2 Hz), 4.41 (d, 1 H, *J* = 6.8 Hz), 3.23 (dt, 1 H, *J* = 10.5, 4.3 Hz), 1.38 (s, 3 H), 1.27 (s, 3

H), 0.85 (d, 3 H, J = 6.5 Hz), and others; ^{13}C NMR (62.89 MHz) δ 138.9, 137.8, 128.3, 128.22, 128.15, 128.0, 127.9, 127.5, 82.9, 82.4, 77.0, 70.9, 50.8, 42.7, 41.5, 34.7, 31.3, 29.7, 24.3, 22.9, 22.0; IR (cm^{-1}) 3040 m, 2960 vs, 2940 vs, 1460 vs, 1390 m, 1380 m, 1370 m, 1160 vs, 1120 vs, 1100 vs, 1070 vs, 1030 s, and others. Anal. Calcd for $C_{25}H_{32}O_2S$: C, 75.71; H, 8.13. Found: C, 75.87; H, 8.13.

2-(1(*S*)-((Methoxymethoxy)phenyl)methyl)-2 (23b) was prepared in 93% yield from the methoxymethylation (dimethoxymethane, phosphorus pentoxide, dichloromethane) of 2-(1-(*S*)-(hydroxyphenyl)methyl)-2: ^{1}H NMR (250 MHz) δ 7.40–7.27 (m, 5 H), 5.10 (d, 1 H, J = 6.7 Hz), 4.74 (d, 1 H, J = 6.7 Hz), 4.62, 4.54 (AB q, 2 H, J = 6.7 Hz), 3.40 (s, 3 H), 3.27 (dt, 1 H, J = 10.4, 4.2 Hz), 1.39 (s, 3 H), 1.27 (s, 3 H), 0.86 (dt, 3 H, J = 6.5 Hz), and others; ^{13}C NMR (62.89 MHz) δ 138.5, 127.4, 127.94, 127.88, 94.2, 82.8, 79.1, 77.1, 55.8, 50.8, 42.8, 41.5, 34.8, 31.4, 29.7, 24.4, 22.9, 22.0; IR (cm^{-1}) 3040 m, 2920 vs. 1450 m, 1370 s, 1200 s, 1185 s, 1150 vs, 1090 vs, 1070 vs, 1020 vs, and others.

(*R*)-2-Methoxy-1-octanol (24a). To a mixture of 1.21 g (9.05 mmol) of *N*-chlorosuccinimide, 1.54 g (9.05 mmol) of silver nitrate, and 0.76 g (9.05 mmol) of sodium bicarbonate in 100 mL of 80% acetonitrile in water was added a solution of 1.00 g (3.04 mmol) of (*R*)-methyl ether **22a** (precursor de 98%) in 10 mL of acetonitrile all at once at room temperature. A white precipitate formed immediately. After 15 min of stirring, 1 mL of saturated sodium sulfite and 10 mL of saturated sodium chloride were added with an interval of 1 min. Silver chloride was filtered, and the filtrate was added dropwise to a suspension of 0.50 g (13.2 mmol) of sodium borohydride in 50 mL of ethanol at 0 °C over 10 min. The organic solvents were removed under reduced pressure, and the resulting aqueous solution was extracted continuously with 200 mL of ether overnight. Concentration of the ethereal extract, separation of the ether **24a** [R_f 0.28, hexanes–ethyl acetate (1:1)] from sultines[10] (R_f 0.63) by flash chromatography using hexanes–ethyl acetate (5:1) gave 0.19 g (39%) of **24a** as a colorless oil: $[\alpha]^{20}_D$ −26.8° (c = 0.68, $CHCl_3$), also $[\alpha]^{20}_{578}$ −27.9°, $[\alpha]^{20}_{546}$ −31.6°, $[\alpha]^{20}_{436}$ −52.7°, $[\alpha]^{20}_{365}$ −79.7°; $[\alpha]^{20}_D$ −1.5° (c 0.92, MeOH), also $[\alpha]^{20}_{578}$ −1.7°, $[\alpha]^{20}_{546}$ −2.0°, $[\alpha]^{20}_{436}$ −4.3°, $[\alpha]^{20}_{365}$ −8.3°. The proton NMR spectrum (250 MHz) of the methyl ether doped with Eu(hfc)$_3$ indicated an ee of 95%: ^{1}H NMR (250 MHz) δ 3.66, 3.49 (AB part of ABX, HOCH_2CH–, 2 H, J_{AB} = 11.6 Hz, J_{AX} = 3.1 Hz, J_{BX} = 6.2 Hz), 3.40 (s, 3 H), 3.30–3.21 (X part, HOCH$_2$CH–, m, 1 H), and others; ^{13}C NMR (62.89 MHz) δ 81.9, 64.0, 57.0, 31.8, 30.4, 29.5, 25.4, 22.6, 14.0.

(*S*)-2-(Methoxymethoxy)-1-octanol (24b) was similarly prepared in 34% yield from (*S*)-methoxymethyl ether **22b** (precursor de 86%): $[\alpha]^{20}_D$ +40.8° (c 2.24, $CHCl_3$), also $[\alpha]^{20}_{578}$ +42.6°, $[\alpha]^{20}_{546}$ +48.1°, $[\alpha]^{20}_{436}$ +79.4°, $[\alpha]^{20}_{365}$ +120°; $[\alpha]^{20}_D$ −13.0° (c 2.66, MeOH), also $[\alpha]^{20}_{578}$ −13.5°, $[\alpha]^{20}_{546}$ −15.2°, $[\alpha]^{20}_{436}$ −24.8°, $[\alpha]^{20}_{365}$ −36.7°. Examination of the proton NMR spectrum (250 MHz, $CDCl_3$) of **24b** doped with Eu(hfc)$_3$ showed an ee of 86%: ^{1}H NMR (250 MHz) δ 4.74, 4.69 (AB q, 2 H, J = 6.9 Hz), 3.62–3.50 (m, 3 H), 3.43 (s, 3 H), 3.14 (bs, 1 H), 1.60–1.15 (m, 10 H), 0.88 (t, 3 H, J = 6.5 Hz); ^{13}C NMR (62.89 MHz) δ 96.8, 81.3, 65.4, 55.5, 31.9, 31.8, 29.4, 25.6, 22.7. Anal. Calcd for $C_{10}H_{22}O_3$: C, 63.12; H, 11.65. Found: C, 62.81; H, 11.93.

(*S*)-2-(Benzyloxy)-2-phenyl-1-ethanol (25a) was similarly prepared in 61% yield from (*S*)-benzyl ether **23a** (precursor de 100%): $[\alpha]^{20}_D$ +104° (c 2.16, $CHCl_3$), also $[\alpha]^{20}_{578}$ +108°, $[\alpha]^{20}_{549}$, $[\alpha]^{20}_{436}$ +210°, $[\alpha]^{20}_{365}$ +331°; $[\alpha]^{20}_D$ +93.7° (c 2.01 MeOH), also $[\alpha]^{20}_{578}$ +98.0°, $[\alpha]^{20}_{546}$ +111°, $[\alpha]^{20}_{436}$ +189°, $[\alpha]^{20}_{365}$ +298°; ^{1}H NMR (250 MHz) δ 7.38–7.26 (m, 10 H), 4.52, 4.31 (AB q, 2 H, J = 11.6 Hz), 4.50 (X part of ABX, HOCH$_2$CH–, 1 H, J_{AX} = 8.3 Hz, J_{BX} = 3.9 Hz), 3.71, 3.60 (AB part of ABX, HOCH_2CH–, 2 H, J_{AB} = 11.7 Hz, J_{AX} = 8.3 Hz, J_{BX} = 3.9 Hz), 2.78 (bs, 1 H); ^{13}C NMR (62.89 MHz) δ 138.4, 137.9, 128.6, 128.4, 128.2, 127.9, 127.7, 127.0, 82.3, 70.7, 67.3; IR cm^{-1} 3620 m, 3100 w, 3040 m, 2880 m, 1640 m, 1460 m, 1400 m, 1355 m, 1330 w, 1100 vs, 1090 vs, 1060 vs, 1050 vs, 1030 s, and others. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.07; H, 7.12.

(*S*)-2-(Methoxymethoxy)-2-phenyl-1-ethanol (25b) was similarly prepared from (*S*)-methoxymethyl ether **23b** (precursor de 100%): $[\alpha]^{20}_D$ +196° (c 2.67, $CHCl_3$), also $[\alpha]^{20}_{578}$ +205°, $[\alpha]^{20}_{546}$ +233°, $[\alpha]^{20}_{436}$ +396°, $[\alpha]^{20}_{365}$ +623°; $[\alpha]^{20}_D$ +189° (c 1.86, MeOH), also $[\alpha]^{20}_{578}$ +197°, $[\alpha]^{20}_{546}$ +224°, $[\alpha]^{20}_{436}$ +381°, $[\alpha]^{20}_{365}$ +600°; ^{1}H NMR (250 MHz) δ 7.32 (s, 5 H), 4.70 (dd, 1 H, J = 7.8, 4.0 Hz), 4.62, 4.63 (AB q, 2 H, J = 5.2 Hz), 3.74–3.65 (m, 2 H), 3.37 (s, 3 H), 3.18 (bs, 1 H); ^{13}C NMR (62.89 MHz) δ 138.3, 128.5, 128.2, 126.9, 95.1, 80.3, 67.3, 55.6; IR cm^{-1} 3600 m, 3470 m, 3040 m, 2880 vs, 1440 m, 1380 m, 1350 m, 1200 m, 1150 m, 1090 s, 1070 s, 1020 vs, and others. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74. Found: C, 66.35; H, 7.70.

(*S*)-1,2-Dodecanediol (26) was obtained from the precursor (*S*)-**3** (87% de) as previously described for 1,2-octanediol,[10,27] yield 66%. The compound is a colorless solid, mp 71–72 °C, (lit.[5] mp 70–70.5 °C), $[\alpha]^{20}_D$ −10.1° (c 2.55, abs EtOH), also $[\alpha]^{20}_{578}$ −10.6°, $[\alpha]^{20}_{546}$ −11.9°, $[\alpha]^{20}_{436}$ −19.8°, $[\alpha]^{20}_{365}$ −30.1°; $[\alpha]^{20}_D$ +0.9° (c 2.83, $CHCl_3$), also $[\alpha]^{20}_{578}$ +1.0°, $[\alpha]^{20}_{546}$ +1.2°, $[\alpha]^{20}_{436}$ +2.0°, $[\alpha]^{20}_{365}$ +2.9°, $[\alpha]^{20}_D$ +0.5° (c 1.34, $CHCl_3$), also $[\alpha]^{20}_{578}$ +0.6°, $[\alpha]^{20}_{546}$ +0.7°, $[\alpha]^{20}_{365}$ +1.0°. Examination of a proton NMR spectrum (250 MHz) of the derived 2-phenyl-1,3-dioxolanes[28] doped with Eu(hfc)$_3$ showed an ee of 89%: ^{1}H NMR (250 MHz) δ 3.75–3.60 (m, 2 H), 3.50–3.37 (m, 1 H), 2.76 (bs, 2 H), 1.62–1.17 (m, 18 H), 0.88 (t, 3 H, J = 6.5 Hz); ^{13}C NMR (62.89 MHz) δ 72.4, 66.7, 33.2, 31.9, 29.7, 29.4, 25.6, 22.7, 14.1.

(*S*)-4-Decyl-1,3-dioxolane (27). A mixture of 0.12 g (0.593 mmol) of (*S*)-1,2-dodecanediol (**26**, precursor de 87%, optical purity 89%) and 0.02 g (0.67 mmol) of paraformaldehyde in 20 mL of benzene was refluxed in the presence of 5 mg of *p*-toluenesulfonic acid hydrate for 1 h. The usual workup, followed by Kugelrohr distillation (130–140 °C, 0.3 mmHg) gave 0.12 g (95%) of the product as an oil: $[\alpha]^{20}_D$ +7.6° (c 3.51, MeOH), also $[\alpha]^{20}_{578}$ +8.0°, $[\alpha]^{20}_{546}$ +9.4°, $[\alpha]^{20}_{436}$ +18.3°, $[\alpha]^{20}_{365}$ +33.4°; $[\alpha]^{20}_D$ +14.4° (c 3.24, $CHCl_3$) also $[\alpha]^{20}_{578}$ +15.1°, $[\alpha]^{20}_{546}$ +17.4°, $[\alpha]^{20}_{436}$ +31.9°, $[\alpha]^{20}_{365}$ +54.5°; ^{1}H NMR (250 MHz) δ 5.01, 4.86 (two s, 2 H), 4.00–3.93 (m, 2 H), 3.41 (apparent t, 1 H, J = 10 Hz), and others; ^{13}C NMR (62.89 MHz) δ 94.8, 76.4, 69.7, 33.1, 32.0, 29.7, 29.4, 25.9, 22.7, 14.1.

(*R*)-1-Methoxy-2-(benzyloxy)octane (28a). A mixture of 0.19 g (0.80 mmol) of (*R*)-2-(benzyloxy)-1-octanol[10] (precursor de 99%), 1.14 g (8 mmol) of iodomethane and 0.19 g (8 mmol) of sodium hydride in 50 mL of THF was stirred at room temperature until the starting alcohol disappeared. The usual workup followed by Kugelrohr distillation provided 0.18 g (90%) of the methyl ether as an oil: $[\alpha]^{20}_D$ +15.2° (c 1.74, $CHCl_3$), also $[\alpha]^{20}_{578}$ +15.8°, $[\alpha]^{20}_{546}$ +30.8°, $[\alpha]^{20}_{365}$ +49.0°; $[\alpha]^{20}_D$ +17.1° (c 1.60, MeOH), also $[\alpha]^{20}_{578}$ +18.4°, $[\alpha]^{20}_{546}$ +20.9°, $[\alpha]^{20}_{436}$ +35.6°, $[\alpha]^{20}_{365}$ +56.3°; ^{1}H NMR (250 MHz) δ 7.33–7.25 (m, 5 H), 4.66, 4.55 (AB q, 2 H, J = 11.8 Hz), 3.49–3.41 (m, 3 H), 3.34 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 139.1, 128.2, 127.7, 127.4, 78.1, 75.6, 71.9, 59.1, 31.9, 31.8, 29.4, 25.5, 22.7, 14.1. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 77.09; H, 10.04.

(*S*)-1-Methoxy-2-(methoxymethoxy)octane (28b) was similarly prepared from (*S*)-2-(methoxymethoxy)-1-octanol **24b** (precursor de 86%): $[\alpha]^{20}_D$ −8.8° (c 1.77, $CHCl_3$) also $[\alpha]^{20}_{578}$ −9.1°, $[\alpha]^{20}_{546}$ −10.2°, $[\alpha]^{20}_{436}$ −16.2°, $[\alpha]^{20}_{365}$ −23.8°; $[\alpha]^{20}_D$ −14.3° (c 14.3, MeOH), also $[\alpha]^{20}_{578}$ −14.8°, $[\alpha]^{20}_{546}$ −16.7°, $[\alpha]^{20}_{436}$ −27.0, $[\alpha]^{20}_{365}$ −39.9°; ^{1}H NMR (250 MHz) δ 4.75, 4.67 (AB q, 2 H, J = 6.8 Hz), 3.73–3.64 (m, 1 H), 3.41 (d, 2 H, J = 4.9 Hz), 3.39 (s, 3 H), 3.36 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 96.0, 76.2, 75.4, 59.0, 55.3, 32.0, 31.8, 29.4, 25.4, 22.6, 14.0. Anal. Calcd for $C_{11}H_{24}O_3$: C, 64.66; H, 11.84. Found: C, 64.88; H, 11.93.

(*R*)-1-Methoxy-2-(benzyloxy)-3-methylbutane (29) was similarly prepared from (*R*)-2-(benzyloxy)-3-methylbutanol[10] (precursor 96% de): $[\alpha]^{20}_D$ +23.6° (c 2.10, $CHCl_3$), also $[\alpha]^{20}_{578}$ +24.7°, $[\alpha]^{20}_{546}$ +28.1°, $[\alpha]^{20}_{436}$ +48.2°, $[\alpha]^{20}_{365}$ +77.3°; $[\alpha]^{20}_D$ +17.3° (c 2.70, MeOH), also $[\alpha]^{20}_{578}$ +18.1°, $[\alpha]^{20}_{546}$ +20.6°, $[\alpha]^{20}_{436}$ +35.2°, $[\alpha]^{20}_{365}$ +56.3°; ^{1}H NMR (250 MHz) δ 7.40–7.28 (m, 5 H), 4.71, 4.55 (AB q, 2 H, J = 11.7 Hz), 3.50–3.48 (m, 2 H), 3.36 (s, 3 H), 3.33–3.27 (m, 1 H), 1.90 (apparent octet, 1 H, J = 6.7 Hz), 0.95 (d, 3 H, J = 6.7 Hz), 0.93 (d, 3 H, J = 6.7 Hz); ^{13}C NMR (62.89 MHz) δ 139.2, 128.2, 127.6, 128.3, 83.2, 74.0, 72.6, 59.0, 30.2, 19.0, 18.1.

(*R*)-1-Methoxy-2-(benzyloxy)-2-cyclohexylethane (30) was similarly prepared from (*R*)-2-(benzyloxy)-2-cyclohexylethanol[10] (precursor de 96%): $[\alpha]^{20}_D$ +15.4° (c 2.67, $CHCl_3$), also $[\alpha]^{20}_{578}$ +16.2°, $[\alpha]^{20}_{546}$ +18.4°, $[\alpha]^{20}_{436}$ +31.9°, $[\alpha]^{20}_{365}$ +51.9°; $[\alpha]^{20}_D$ +12.9°

(27) Details of this preparation are described in the thesis of K.-Y. Ko, University of North Carolina at Chapel Hill, 1985, available from University Microfilms, Dissertation Copies, P.O. Box 1764, Ann Arbor, Michigan 48106.

(28) Eliel, E. L.; Ko, K.-Y. *Tetrahedron Lett.* **1983**, 3547.

(c 2.66, MeOH), also $[\alpha]^{20}_{578}$ +13.5°, $[\alpha]^{20}_{546}$ +15.4°, $[\alpha]^{20}_{436}$ +26.7°, $[\alpha]^{20}_{365}$ +43.2°; ^{1}H NMR (250 MHz) δ 7.39–7.25 (m, 5 H), 4.69, 4.52 (AB q, 2 H, J = 11.7 Hz), 3.51, 3.47 (AB part of ABX, J_{AB} = 10.1, J_{BX} = 4.0, J_{BX} = 5.4 Hz), 3.34 (s, 3 H), 3.28 (dd, 1 H, J = 5.4, 4.0 Hz), and others; ^{13}C NMR (62.89 MHz) δ 139.2, 128.1, 127.6, 127.2, 82.6, 73.8, 72.6, 59.0, 40.1, 29.4, 28.5, 26.6, 26.4, 26.3.

(*R*)-1-Methoxy-2-(benzyloxy)-3,3-dimethylbutane (31) was similarly prepared from (*R*)-2-(benzyloxy)-3,3-dimethylbutanol[10] (precursor de 100%): $[\alpha]^{20}_{D}$ +17.5° (c 2.28, $CHCl_3$), also $[\alpha]^{20}_{578}$ +18.2°, $[\alpha]^{20}_{546}$ +20.8°, $[\alpha]^{20}_{436}$ +36.1°, $[\alpha]^{20}_{365}$ +59.1°; $[\alpha]^{20}_{D}$ +8.7° (c 2.20, MeOH), also $[\alpha]^{20}_{578}$ +9.1°, $[\alpha]^{20}_{546}$ +10.4°, $[\alpha]^{20}_{436}$ +18.2°, $[\alpha]^{20}_{365}$ +30.6°; ^{1}H NMR (250 MHz) δ 7.39–7.24 (m, 5 H), 4.83, 4.55 (AB q, 2 H, J = 11.6 Hz), 3.64, 3.47 (AB part of ABX, 2 H, J_{AB} = 10.2, J_{AX} = 2.7, J_{BX} = 6.8 Hz), 3.35 (s, 3 H), 3.19 (dd, 1 H, J = 2.7, 6.8 Hz), 0.95 (s, 9 H); ^{13}C NMR (62.89 MHz) δ 139.5, 1281, 127.5, 127.1, 86.3, 74.8, 73.8, 58.9, 34.6, 26.5.

(2*R*,3*R*)- and (2*S*,3*R*)-3-(Benzyloxy)-2-tridecanol (32). To a solution of 0.9 mL (2.6 mmol) of 2.9 M methylmagnesium bromide in ether was added a solution of 3.2 mL (3.2 mmol) of 1 M chlorotitanium triisopropoxide in hexanes at 0 °C over 1 min. The solution became yellowish green. After 30 min of stirring, a solution of 0.25 g (0.87 mmol) of (*R*)-2-benzyloxydodecanal (**6a**) in 10 mL of ether was added over 5 min. The mixture was stirred for 2 h at −78 °C and then quenched with water. Acidification with dilute HCl and the usual workup gave 0.26 g (98% crude yield) of an oil. The ^{13}C NMR spectrum showed that the ratio of Cram product (2*R*,3*R*) to anti-Cram product (2*S*,3*R*) was 18:82. In contrast, the addition of methylmagnesium bromide to the aldehyde **6a** (ether, 0 °C) provided a mixture of Cram and anti-Cram product in a ratio of 87:13.

2*R*,3*R* isomer: ^{1}H NMR (250 MHz) δ 7.35–7.29 (m, 5 H), 4.65, 4.49 (AB q, 2 H, J = 11.3 Hz), 3.74 (apparent quintet, 1 H, J = 6.6 Hz), 3.21 (apparent quartet, 1 H, J = 5.9 Hz), 2.49 (bs, 1 H), 1.17 (d, 3 H, J = 6.4 Hz) and others; ^{13}C NMR (62.89 MHz) δ 138.5, 128.5, 127.9, 127.7, 84.2, 72.5, 69.0, 32.0, 30.3, 30.0, 29.6, 29.4, 25.0, 22.7, 19.1, 14.1.

2*S*,3*R* isomer: ^{1}H NMR (250 MHz) δ 7.35–7.24 (m, 5 H), 4.58 (s, 2 H), 3.99–3.90 (m, 1 H), 3.36–3.30 (m, 1 H), 2.38 (bs, 1 H), 1.15 (d, 3 H, J = 6.5 Hz), and others; ^{13}C NMR (62.89 MHz) δ 138.7, 128.4, 127.7, 127.6, 83.1, 72.2, 68.3, 31.9, 29.8, 29.6, 29.4, 29.3, 25.9, 22.7, 17.1, 14.1.

(4*R*,5*R*)- and (4*S*,5*R*)-1-Phenyl-5-(benzyloxy)-4-pentadecanol (9a). To a cold (−78 °C) solution of 10 mL of 0.4 M (3-phenylpropyl)magnesium bromide in ether was added a solution of 200 mg (0.82 mmol) of (*R*)-2-(benzyloxy)dodecanal (**6a**, oxathiane precursor de >98%) in 1 mL of ether over 10 min. The mixture was stirred for 1 h, then quenched with water at −78 °C. The usual workup, followed by purification [flash chromatography, hexanes–ethyl acetate (5:1)] gave 310 mg (94%) of a mixture of Cram product (4*R*,5*R* isomer) and anti-Cram product (4*S*,5*R* isomer) in a ratio of 94:6, as revealed by ^{13}C NMR. Separation of the major from the minor product by flash chromatography [hexanes–ethyl acetate (10:1)] gave 280 mg (84%) of the 4*R*,5*R* isomer. This isomer (syn) elutes faster than its 4*S*,5*R* epimer (anti).

4*R*,5*R* isomer: $[\alpha]^{20}_{D}$ +17.0° (c 1.56, MeOH), −9.1° (c 1.36, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.29–7.14 (m, 10 H), 4.61, 4.43 (AB q, 2 H, J = 11.3 Hz), 3.53 (bs, 1 H), 3.23 (apparent q, 1 H, J = 5.3 Hz), 2.61 (t, 2 H, J = 7.4 Hz), 2.36 (bs, 1 H, −OH), and others; ^{13}C NMR (62.89 MHz) δ 142.3, 138.5, 128.4, 128.2, 127.8, 127.7, 125.6, 82.3, 72.5, 72.4, 35.9, 33.1, 31.9, 30.4, 30.0, 29.6, 29.4, 27.5, 25.2, 22.7, 14.1.

4*S*,5*R* isomer: $[\alpha]^{20}_{D}$ +6.7° (c 1.86, MeOH), +4.2° (c 2.28, $CHCl_3$); ^{1}H NMR (150 MHz) δ 7.32–7.16 (m, 10 H), 4.55, 4.52 (AB q, 2 H, J = 11.5 Hz), 3.83–3.77 (m, 1 H), 3.35–3.29 (m, 1 H), 2.64 (t, 2 H, J = 7.6 Hz), and others; ^{13}C NMR (62.89 MHz) δ 142.3, 138.6, 128.4, 128.2, 127.8, 127.6, 125.7, 82.4, 72.0, 71.7, 35.9, 31.9, 31.6, 29.8, 29.6, 29.4, 28.8, 28.0, 25.8, 22.7, 14.1.

(4*R*,5*R*)- and (4*S*,5*R*)-1-Phenyl-5-(methoxymethoxy)-5-pentadecanol (9b) were similarly prepared by the addition of (3-phenylpropyl)magnesium bromide to (*R*)-2-(methoxymethoxy)dodecanal (**6b**). The two diastereomeric alcohols could not be separated by flash chromatography. Anal. Calcd for $C_{23}H_{38}O_3$: C, 75.78; H, 11.06. Found: C, 75.85; H, 10.88.

4*R*,5*R* isomer: ^{1}H NMR (250 MHz) δ 7.28–7.12 (m, 5 H), 4.66 (s, 2 H), 3.56–3.46 (m, 1 H), 3.35–3.26 (m, 1 H), 3.38 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 142.3, 128.4, 128.2, 125.6, 97.0, 83.1, 72.5, 55.7, 35.9, 32.8, 32.0, 31.0, 29.9, 29.7, 29.4, 27.4, 25.3, 22.7, 14.1.

4*S*,5*R* isomer: ^{1}H NMR (250 MHz) δ 7.29–7.10 (m, 5 H), 4.70, 4.61 (AB q, 2 H, J = 6.8 Hz), 3.64–3.42 (m, 2 H), 3.36 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 142.4, 128.4, 128.2, 125.6, 97.3, 84.2, 72.9, 55.7, 35.9, 32.9, 31.9, 31.1, 30.3, 29.7, 29.6, 29.3, 27.9, 26.0, 22.7, 14.1.

(4*R*,5*R*)-1-Phenyl-4,5-pentadecanediol (19) was prepared in 98% yield by the catalytic hydrogenolysis (5% Pd/C, methanol, 50 psi, 30 min) of the benzyl ether **9a** (oxathiane precursor de >98%): mp 64.5–65.0 °C, $[\alpha]^{20}_{D}$ +22.3° (c 0.43, MeOH), +19.1° (c 0.98, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.28–7.14 (m, 5 H), 3.35 (bs, 2 H), 2.91–2.83 (m, 2 H), 2.62 (t, 2 H, J = 7.4 Hz), and others; ^{13}C NMR (62.89 MHz) δ 142.2, 128.3, 128.2, 125.7, 74.5, 74.3, 35.8, 33.6, 33.1, 31.9, 29.71, 29.65, 29.4, 27.4, 25.7, 22.7, 14.1. Anal. Calcd for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 79.02; H, 11.24.

(4*R*,5*R*)-1-Phenyl-4,5-diacetoxypentadecane (20). A solution of 100 mg (0.313 mmol) of the diol **19** (oxathiane precursor de >98%) in 15 mL of acetic anhydride was treated with ca. 10 mg of 4-dimethylaminopyridine (DMAP) at room temperature. The whole mixture was stirred at room temperature overnight. Acetic anhydride was removed in vacuo and the residue was subject to flash chromatography [hexanes–ethyl acetate (5:1)] to give 120 mg (95%) of the diacetate **26** as an oil: $[\alpha]^{20}_{D}$ +21.3° (c 1.56, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.30–7.14 (m, 5 H), 5.10–4.98 (m, 2 H), 2.62 (t, 2 H, J = 7.3 Hz), 2.04 (s, 3 H), 2.01 (s, 3 H) and others; ^{13}C NMR (62.89 MHz) δ 170.3, 141.7, 128.4, 128.3, 125.8, 73.7, 73.5, 35.5, 31.9, 30.7, 30.2, 29.59, 29.55, 29.42, 29.35, 26.9, 25.2, 22.7, 20.8, 14.1; IR cm^{-1} 2920 s, 2860 m, 2740 vs, 1220 vs, and others.

(4*R*,5*R*)-1-Phenyl-4,5-(isopropylidenedioxy)pentadecane (21). A solution of 130 mg (0.41 mmol) of the diol **19** (oxathiane precursor de >98%) and 5 mg of *p*-toluenesulfonic acid hydrate in 10 mL of 2,2-dimethoxypropane was refluxed until TLC showed the absence of the starting diol. The excess 2,2-dimethoxypropane was removed in vacuo. The residue was dissolved in ether, and the ethereal solution was washed with sodium carbonate solution, dried, and concentrated. Kugelrohr distillation (150–160 °C, 0.05 mmHg) of the residue gave 130 mg (89%) of the acetonide as an oil: $[\alpha]^{20}_{D}$ +29.7° (c 1.48, MeOH), +21.0° (c 1.45, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.29–7.15 (m, 5 H), 3.64–3.48 (m, 2 H), 2.64 (t, 2 H, J = 6.8 Hz), 1.36 (s, 6 H), and others; ^{13}C NMR (62.89 MHz) δ 142.1, 128.4, 128.2, 125.7, 107.7, 80.9, 80.8, 35.9, 33.0, 32.4, 31.9, 29.8, 29.6, 29.5, 29.4, 27.8, 27.3, 26.2, 22.7, 14.1.

(6*R*,7*R*)- and (6*S*,7*R*)-7-(Benzyloxy)-heptadec-1-en-6-ol (10) were similarly prepared by the reaction of (*R*)-2-(benzyloxy)dodecanal (**6a**, oxathiane precursor de >98%) with 4-pentenylmagnesium bromide. The two diastereomeric alcohols were separable by flash chromatography [hexanes–ethyl acetate (10:1)]. The 6*R*,7*R* isomer (syn) elutes faster than the 6*S*,7*R* (anti).

6*R*,7*R* isomer: $[\alpha]^{20}_{D}$ +17.6° (c 2.28, MeoH), −10.5° (c 1.62, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.31–7.23 (m, 5 H), 5.78 (ddt, 1 H, J = 17.0, 10.2, 6.8 Hz), 4.99 (d, 1 H, J = 17 Hz), 4.93 (d, 1 H, J = 10.2 Hz), 4.66, 4.61 (AB q, 2 H, J = 11.4 Hz), 3.51 (bs, 1 H), 3.23 (apparent q, 1 H, J = 5.3 Hz), 2.48 (bs, 1 H, −OH), 2.09–2.04 (m, 2 H) and others; ^{13}C NMR (62.89 MHz) δ 138.7, 138.5, 128.4, 127.8, 127.6, 114.5, 82.4, 72.44, 72.39, 33.8, 32.9, 31.9, 30.3, 30.0, 29.6, 29.4, 25.2, 25.1, 22.7, 14.1.

6*S*,7*R* isomer: $[\alpha]^{20}_{D}$ +9.3° (c 1.74, MeOH), +4.9° (c 2.24 $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.32–7.20 (m, 5 H), 5.79 (ddt, 1 H, J = 17.0, 10.2, 6.7 Hz), 4.99 (d, 1 H, 17.0 Hz), 4.93 (d, 1 H, J = 10.2 Hz), 4.56, 4.51 (AB q, 2 H, J = 11.0 Hz), 3.78–3.72 (m, 1 H), 3.34–3.28 (m, 1 H), 2.35 (bs, 1 H), 2.10–2.04 (m, 2 H), and others; ^{13}C NMR (62.89 MHz) δ 138.63, 138.58, 128.3, 127.8, 127.6, 114.5, 82.4, 71.9, 71.7, 33.7, 31.9, 31.5, 29.8, 29.6, 29.3, 28.9, 25.8, 25.5, 22.7, 14.1.

(6*R*,7*R*)- and (6*S*,7*R*)-6-Acetoxy-7-(benzyloxy)-1-heptadecene (11) were prepared in 93% purified yield (Kugelrohr distillation, 170–175 °C, 0.05 mmHg) by acetylation (acetic anhydride, 4-(dimethylamino)pyridine) of the corresponding alcohols **10** (oxathiane precursor de >98%).

6*R*,7*R* isomer: $[\alpha]^{20}_{D}$ +21.7° (c 1.50 MeOH), +14.5° (c 1.26, $CHCl_3$); ^{1}H NMR (150 MHz) δ 7.31–7.20 (m, 5 H), 5.74 (ddt, 1 H, J = 17, 10.1, 6.6 Hz), 5.06–5.01 (m, 1 H), 4.99 (dt, 1 H, J = 17 Hz), 4.93 (dt, 1 H, J = 10.1 Hz), 4.57 (s, 2 H), 3.41–3.39 (m,

1 H), 2.08–2.04 (m, 2 H), 2.00 (s, 3 H) and others; ^{13}C NMR (62.89 MHz) δ 170.4, 138.6, 138.2, 128.2, 127.9, 127.5, 114.8, 79.2, 74.0, 72.4, 33.5, 32.0, 29.9, 29.7, 29.64, 29.57, 29.4, 29.0, 25.7, 25.0, 22.7, 21.0, 14.1.

6S,7R isomer: $[\alpha]^{20}_D$ +6.1° (c 2.16, $CHCl_3$); ^1H NMR (250 MHz) δ 7.34–7.24 (m, 5 H), 5.78 (ddt, 1 H, J = 17, 10.2, 6.7 Hz), 5.10–5.04 (m, 1 H + 1 H), 4.96 (dt, 1 H, J = 10.2 Hz), 4.66, 4.47 (AB q, 2 H, J = 11.5 Hz), 3.45–3.42 (m, 1 H), 2.05 (s, 3 H) and others; ^{13}C NMR (62.89 MHz) δ 170.6, 138.6, 138.3, 128.3, 127.9, 127.5, 114.8, 80.2, 74.9, 72.3, 33.5, 31.9, 30.7, 29.4, 28.8, 25.9, 25.1, 22.7, 21.2, 14.1.

(5R,6R)- and (5S,6R)-5-Acetoxy-6-(benzyloxy)hexadecanal (12). Through a solution of 0.70 g (1.74 mmol) of (6R,7R)-acetate 11 (oxathiane precursor de >98%) in 100 mL of dry dichloromethane was passed a stream of ozone in oxygen at −78 °C until the pale blue color of ozone appeared. Excess ozone was removed by bubbling dry nitrogen through the solution which was then warmed to room temperature and treated with 2 mL of dimethyl sulfide. After stirring for 1 h, the solvent and the excess sulfide was removed in vacuo. Flash chromatography [hexanes–ethyl acetate (5:1)] of the residue gave 0.56 g (80% yield) of the aldehyde 12 as an oil. The 5S,6R isomer was prepared similarly in 80% yield.

5R,6R isomer: $[\alpha]^{20}_D$ +12.9° (c 2.01, $CHCl_3$); ^1H NMR (250 MHz) δ 9.70 (t, 1 H, J = 1.4 Hz), 7.31–7.22 (m, 5 H), 5.05–4.98 (m, 1 H), 4.59, 4.57 (AB q, 2 H, J = 11.7 Hz), 3.45–3.38 (m, 1 H), 2.42–2.36 (m, 2 H), 2.05 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 201.5, 170.5, 138.3, 128.2, 127.8, 127.5, 79.0, 73.6, 72.3, 43.3, 31.8, 29.7, 29.5, 29.44, 29.36, 29.2, 28.8, 25.5, 22.5, 20.9, 18.2, 14.0; IR (cm^{-1}) 2920 vs, 2860 s, 1740 vs, 1720 vs, 1380 m, and others.

5S,6R isomer: $[\alpha]^{20}_D$ +1.7° (c 1.72, $CHCl_3$); ^1H NMR (250 MHz) δ 9.74 (t, 1 H, J = 1.4 Hz), 7.31–7.25 (m, 5 H), 5.06–5.02 (m, 1 H), 4.64, 4.48 (AB q, 2 H, J = 11.2 Hz), 3.48–3.42 (m, 1 H), 2.48–2.39 (m, 2 H), 2.05 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 201.5, 170.5, 138.5, 128.3, 127.9, 127.6, 80.2, 74.7, 72.4, 43.5, 31.9, 30.8, 29.7, 29.61, 29.55, 29.3, 28.9, 25.8, 22.7, 21.1, 18.4, 14.1.

(5R,6R)- and (5S,6R)-5-Acetoxy-6-(benzyloxy)hexadecanoic Acid (13). A solution of 0.55 g (1.36 mmol) of the (5R,6R)-aldehyde 12 and 2 mL of 2-methyl-2-butene (chlorine scavenger) in 50 mL of *tert*-butyl alcohol was treated with a solution of 1.10 g (purity 80%, 9.9 mmol) of sodium chlorite and 1.23 g of potassium dihydrogen phosphate (KH_2PO_4), in 30 mL of water over 10 min at room temperature. The stirring was continued for an additional 30 min, and then the organic solvent was removed under reduced pressure. The resulting aqueous solution was extracted with ether (3 × 50 mL). The combined ethereal solution was dried ($MgSO_4$) and concentrated to give 0.55 g (96%) of the acid as an oil. Similarly the 5S,6R isomer was prepared from the corresponding aldehyde.

5R,6R isomer: ^1H NMR (250 MHz) δ 10.63 (bs, 1 H), 7.32–7.27 (m, 5 H), 5.06–5.00 (m, 1 H), 4.58 (s, 2 H), 3.46–3.39 (m, 1 H), 2.34–2.29 (m, 2 H), 2.03 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 178.8, 170.8, 138.4, 128.3, 128.0, 127.6, 79.1, 73.8, 72.4, 33.7, 31.9, 29.9, 29.6, 29.5, 29.4, 28.9, 25.6, 22.7, 21.0, 20.9, 14.1.

5S,6R isomer: ^1H NMR (250 MHz) δ 7.32–7.23 (m, 5 H), 5.08–5.04 (m, 1 H), 4.65, 4.48 (AB q, 2 H, J = 11.7 Hz), 3.48–3.42 (m, 1 H), 2.38–2.32 (m, 2 H), 2.05 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 178.8, 170.8, 138.5, 128.3, 127.9, 127.6, 80.1, 74.8, 72.4, 33.7, 31.9, 30.7, 29.61, 29.56, 29.3, 28.8, 25.7, 22.7, 21.1, 21.0, 14.1.

(5R,6R)- and (5S,6R)-6-(Benzyloxy)-5-hexadecanolide (18). Saponification of acetate 13 (oxathiane precursor de >98%) with NaOH (methanol/water, reflux, 1 H), followed by lactonization of the resulting 5-hydroxy acid (p-TsOH, benzene, room temperature, 1 h) and purification by flash column chromatography [hexanes–ethyl acetate (1:2)] gave the lactone 18 in 86% yield. The 5S,6R isomer and the 5R,6S isomer were similarly prepared from the corresponding acids.

5R,6R isomer: $[\alpha]^{20}_D$ +3.4° (c 1.57, $CHCl_3$); ^1H NMR (250 MHz) δ 7.32–7.25 (m, 5 H), 4.65, 4.60 (AB q, 2 H, J = 11.5 Hz), 4.41–4.34 (m, 1 H), 3.51–3.44 (m, 1 H), 2.64–2.34 (m, 2 H), and others; ^{13}C NMR (62.89 MHz) δ 171.3, 138.4, 128.3, 127.9, 127.7, 81.1, 80.2, 73.1, 31.9, 29.7, 29.6, 29.3, 25.7, 23.3, 22.7, 18.6, 14.1; IR cm^{-1} 2920 vs, 1730 s, 1420 s, 1190 vs, 1040 s, 920 s, and others.

5S,6R isomer: $[\alpha]^{20}_D$ +1.9° (c 1.15, $CHCl_3$); ^1H NMR (250 MHz) δ 7.30–7.20 (m, 5 H), 4.65, 4.58 (AB q, 2 H, J = 11.3 Hz), 4.31–4.25 (m, 1 H), 3.63–3.58 (m, 1 H), 2.60–2.31 (m, 2 H), and others; ^{13}C NMR (62.89 MHz) δ 171.1, 138.6, 128.3, 127.8, 127.5, 82.5, 80.5, 73.4, 31.9, 31.0, 29.9, 29.7, 29.6, 29.5, 29.3, 25.5, 22.7, 22.5, 18.5, 14.1.

5R,6S isomer: $[\alpha]^{20}_D$ −1.9° (c 1.10, $CHCl_3$).

(5R,6R)- and (5S,6R)-6-Hydroxy-5-hexadecanolide (17) were prepared by the catalytic hydrogenolysis (5% Pd/C, methanol, 45 psi, 2 h) of the benzyl ethers 18 (oxathiane precursor de >98%) in 93% yield after Kugelrohr distillation (175–180 °C, 0.05 mmHg).

5R,6R isomer: mp 70–71 °C; ^1H NMR (250 MHz) δ 4.22–4.14 (m, 1 H), 3.58–3.51 (m, 1 H), 2.65–2.32 (m, 2 H), 2.96 (bs, 1 H) and others; ^{13}C NMR (62.89 MHz) δ 171.4, 83.2, 73.3, 32.7, 31.9, 29.7, 29.6, 29.3, 25.5, 24.2, 22.7, 18.5, 14.1; IR cm^{-1} 2900 s, 1740 s, 1440 m, 1160 m, 1040 m, and others.

5S,6R isomer: mp 67–68 °C (lit.[3] 66.5–68 °C); ^1H NMR (250 MHz) δ 4.33–4.27 (m, 1 H), 3.90–3.83 (m, 1 H), 2.70–2.39 (m, 2 H) and others; ^{13}C NMR (62.89 MHz) δ 172.3, 83.7, 71.9, 31.7, 31.4, 29.6, 29.4, 29.2, 25.8, 22.6, 20.6, 18.1, 14.1. The proton spectrum agrees with that reported.[6]

(5R,6R)- and (5S,6R)-6-Acetoxy-5-hexadecanolide (1) were prepared by the acetylation (acetic anhydride, DMAP) of the alcohols 17 (oxathiane precursor de >98%) in 87–94% yield. Similarly, the 5R,6S isomer 1a (natural pheromone) was prepared from the (5R,6S)-alcohol (see below—oxathiane precursor de >98%).

5R,6R isomer: $[\alpha]^{20}_D$ +14.4° (c 1.06, $CHCl_3$) [lit.[4] +14.6°, lit.[5] +14.4°); ^1H NMR (250 MHz) δ 5.01–4.94 (m, 1 H), 4.40–4.32 (m, 1 H), 2.66–2.34 (m, 2 H), 2.08 (s, 3 H), and others; ^{13}C NMR (62.89 MHz) δ 170.6, 170.4, 79.8, 73.9, 31.9, 30.0, 29.64, 29.57, 29.5, 29.4, 29.3, 25.4, 24.2, 22.7, 20.9, 18.4, 14.1; IR cm^{-1} 2900 vs, 2850 s, 1760 vs, 1750 vs, 1370 m, 1160 s, 1030 s, and others. The proton spectrum agrees with that reported in ref 4b; the signal at 3.69 ppm reported in ref 6 is evidently due to an extraneous impurity.[29]

5S,6R isomer: $[\alpha]^{20}_D$ +37.5° (c 0.90, $CHCl_3$) (lit.[3] +38.8°, lit.[4] +37.2°, lit.[8] +39.1°, lit.[9] +42.0°, lit.[5] +38.0°); ^1H NMR (250 MHz) δ 5.02–4.95 (m, 1 H), 4.39–4.31 (m, 1 H), 2.67–2.38 (m, 2 H), 2.08 (s, 3 H), 1.8–2.0 (m), 1.6–1.8 (m), 1.3 (broad m), 0.89 (t) agree with those reported.[2,4,6]

^{13}C NMR (62.89 MHz) δ 170.8, 170.4, 80.5, 74.4, 31.9, 29.6, 29.4, 29.3, 25.3, 23.6, 22.7, 21.0, 18.3, 14.1.

5R,6S isomer: $[\alpha]^{20}_D$ −37.2° (c 2.07, $CHCl_3$) (lit.[3] −36.2°, lit.[4] −37.4°, lit.[8] −39.2°, lit.[9] −37.6°).

(5R)-1-Phenyl-5-(benzyloxy)-4-pentadecanone (15a). A solution of 1.96 g (24.8 mmol) of pyridine in 50 mL of dry dichloromethane was treated with 1.24 g (12.4 mmol) of dry chromium trioxide in small portions. The resulting dark red suspension was stirred for 15 min and then treated with a solution of 0.85 g (1.07 mmol) of the alcohol 9a (oxathiane precursor de >98%) in 10 mL of dichlormethane all at once followed by stirring for $^1/_2$ h. Chromium salts were removed by passing through a short column of Florisil. The eluent was washed with dilute HCl solution, dried (Na_2SO_4), and concentrated. Purification by flash chromatography [hexanes–ethyl acetate (20:1)] gave 0.72 g (85%) of the ketone as an oil: $[\alpha]^{20}_D$ +37.4° (c 2.09, $CHCl_3$), also $[\alpha]^{20}_{578}$ +39.3°, $[\alpha]^{20}_{546}$ +45.2°, $[\alpha]^{20}_{436}$ +85.7°, $[\alpha]^{20}_{365}$ +177°; ^1H NMR (250 MHz) δ 7.32–7.13 (m, 10 H), 4.49, 4.37 (AB q, 2 H, J = 11.6 Hz), 3.75 (t, 1 H, J = 6.3 Hz), 2.30 (t, 2 H, J = 6.3 Hz), 2.53 (t, 2 H, J = 7.3 Hz), 1.89 (apparent quintet, 2 H, J = 7.3 Hz), and others; ^{13}C NMR (62.89 MHz) δ 212.8, 141.6, 137.6, 128.4, 128.3, 127.8, 125.9, 85.0, 72.4, 36.8, 35.1, 32.2, 31.9, 29.6, 29.4, 29.3, 25.2, 24.7, 22.7, 14.1; IR (cm^{-1}) 3040 m, 2920 vs, 1715 vs, 1450 s, and others.

(5R)-1-Phenyl-5-(methoxymethoxy)-4-pentadecanone (15b) was similarly prepared in 84% yield by Collins oxidation of the alcohols 9b (oxathiane precursor de >98%): $[\alpha]^{20}_D$ +27.2° (c 1.78, $CHCl_3$) also $[\alpha]^{20}_{578}$ +28.5°, $[\alpha]^{20}_{546}$ +32.0°, $[\alpha]^{20}_{436}$ +51.6°, $[\alpha]^{20}_{365}$ +77.3°; ^1H NMR (250 MHz) δ 7.27–7.11 (m, 5 H), 4.58, 4.57 (AB q, 2 H, J = 6.9 Hz), 3.94 (t, 1 H, J = 6.2 Hz), 3.30 (s, 3 H), 2.60 (t, 2 H, J = 7.5 Hz), 2.49 (t, 2 H, J = 7.2 Hz), 1.90 (apparent q, 2 H, J = 7.4 Hz), and others; ^{13}C NMR (62.89 MHz) δ 211.2, 141.6, 128.4, 128.1, 125.9, 96.4, 82.6, 55.8, 37.5, 35.1, 32.1, 31.9, 29.6, 29.44, 29.36, 25.2, 24.7, 22.7, 14.1. Anal. Calcd for $C_{23}H_{38}O_3$: C, 76.20;

(29) Mori, K., personal communication.

H, 10.56. Found: C, 76.64; H, 10.81.

(7*R*)-7-(Benzyloxy)heptadec-1-en-6-one (14) was prepared similarly in 85% yield by the Collins oxidation of the alcohols **10** (oxathiane precursor de >98%): $[\alpha]^{20}_{D}$ +42.9° (*c* 2.13, $CHCl_3$), also $[\alpha]^{20}_{578}$ +45.0°, $[\alpha]^{20}_{546}$ +51.6°, $[\alpha]^{20}_{436}$ +96.4%, $[\alpha]^{20}_{365}$ +194°; ^1H NMR (250 MHz) δ 7.36–7.29 (m, 5 H), 5.75 (ddt, 1 H, *J* = 17.0, 10.3, 6.6 Hz), 5.04–4.93 (m, 2 H), 4.54, 4.39 (AB q, 2 H, *J* = 11.7 Hz), 3.76 (dd, 1 H, *J* = 7.5, 5.3 Hz), 2.53 (t, 2 H, *J* = 7.3 Hz), 2.05 (apparent q, 2 H, *J* = 7 Hz), 1.73–1.58 (m, 2 H), and others; ^{13}C NMR (62.89 MHz) δ 212.6, 137.9, 137.7, 128.4, 127.8, 115.1, 85.1, 72.4, 36.8, 33.2, 32.2, 31.9, 29.6, 29.4, 29.3, 25.3, 22.7, 22.3, 14.1; IR cm^{-1} 2920 vs, 2860 s, 1720 vs, 1460 s, 1100 s, and others.

(6*R*,7*S*)-6-(Benzyloxy)-7-(benzyloxy)-1-heptadecene (16). To a mixture of 0.35 g (0.97 mmol) of (6*R*,7*S*)-7-(benzyloxy)-heptadec-1-en-6-ol (**10**, oxathiane precursor de >98%), 0.24 g (1.97 mmol) of benzoic acid and 0.51 g (1.94 mmol) of triphenylphosphine in 5 mL of dry THF was added 0.36 g (1.96 mmol) of diethyl azodicarboxylate (DEAD) over 5 min at 0 °C. The yellow color of DEAD disappeared. The solution was stirred for 1 h at 0 °C. THF was removed under vacuum, and 50 mL of hexanes was added to the residue to dissolve the products soluble in hexanes. The hexanes solution was decanted and concentrated. The residue was subject to flash chromatography [hexanes–ethyl acetate (40:1)] to give 0.35 g (78%) of the benzoate **16** as an oil: $[\alpha]^{20}_{D}$ -8.1° (*c* 0.60, $CHCl_3$); ^1H NMR (250 MHz) δ 8.04 (d, 2 H, *J* = 7.9 Hz), 7.56–7.38 (m, 3 H), 7.32–7.18 (m, 5 H), 5.76 (ddt, 1 H, *J* = 17.0, 10.3, 6.6 Hz), 5.30 (dt, 1 H, *J* = 9.4, 3.0 Hz), 4.99 (d, 1 H, *J* = 17.0 Hz), 4.93 (d, 1 H, *J* = 10.2 Hz), 4.69, 4.50 (AB q, 2 H, *J* = 11.6 Hz), 3.60–3.57 (m, 1 H), 2.14–2.01 (m, 2 H) and others; ^{13}C NMR (62.89 MHz) δ 166.2, 138.6, 138.3, 132.8, 130.5, 129.6, 128.3, 128.2, 127.9, 127.5, 114.8, 80.4, 75.9, 72.5, 33.5, 31.9, 31.0, 29.6, 29.3, 28.7, 25.9, 25.1, 22.7, 14.1; IR (cm^{-1}) 2900 vs, 2860 vs, 1730 s, 1720 vs, 1440 m, 1270 vs, 1170 m, and others.

(6*S*,7*S*)-6-(Benzyloxy)-7-(benzyloxy)-1-heptadecene (16) was prepared by the benzoylation (benzoic anhydride, pyridine) of the (6*S*,7*S*)-alcohol **10**: ^1H NMR (250 NMR) δ 8.04 (d, 2 H, *J* = 8.0 Hz), 7.58–7.42 (m, 3 H), 7.34–7.28 (m, 5 H), 5.76 (ddt, 1 H, *J* = 17.0, 10.2, 6.7 Hz), 5.31 (dt, 1 H, *J* = 8.5, 4.4 Hz), 4.99 (d, 1 H, *J* = 17.0 Hz), 4.94 (d, 1 H, *J* = 10.2 Hz), 4.65, 4.62 (AB q, 2 H, *J* = 11.6 Hz), 3.60–3.53 (m, 1 H), 2.12–2.03 (m, 2 H) and others.

(5*R*,6*S*)-5-(Benzyloxy)-6-(benzyloxy)hexadecanal (33) was prepared in 81% yield by ozonolysis of (6*R*,7*S*)-6-(benzyloxy)-7-(benzyloxy)-1-heptadecene (**16**): $[\alpha]^{20}_{D}$ -6.1° (*c* 1.65, $CHCl_3$); ^1H NMR (250 MHz) δ 9.71 (t, 1 H, *J* = 1.3 Hz), 8.06 (d, 1 H, *J* = 7.9 Hz), 7.57–7.40 (m, 3 H), 7.33–7.22 (m, 5 H), 5.29 (dt, 1 H, *J* = 9.4, 3.0 Hz), 4.71, 4.52 (AB q, 2 H, *J* = 11.5 Hz), 3.63–3.60 (m, 1 H), 2.50–2.42 (m, 2 H), and others; ^{13}C NMR (62.89 MHz) δ 201.7, 166.1, 138.5, 132.9, 130.3, 129.6, 128.4, 128.3, 127.9, 127.5, 80.3, 75.6, 72.6, 43.5, 31.9, 29.6, 29.3, 28.8, 25.8, 22.7, 18.4, 14.1; IR cm^{-1} 2920 vs, 2860 s, 1730 vs, 1720 s, 1450 m, 1270 s, 1170 m, and others.

(5*R*,6*S*)-5-(Benzyloxy)-6-(benzyloxy)hexadecanoic acid (34) was prepared by the sodium chlorite oxidation of (5*R*,6*S*)-aldehyde **33**: ^1H NMR (250 MHz) δ 8.06 (d, 2 H, *J* = 7.9 Hz), 7.58–7.40 (m, 3 H), 7.30–7.24 (m, 5 H), 5.32–5.26 (m, 1 H), 4.71,4.52 (AB q, 2 H, *J* = 11.5 Hz), 3.64–3.58 (m, 1 H), 2.41–2.36 (m, 1 H), and others.

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Selective Reactions of Azide-Substituted α-Diazo Amides with Olefins and Alcohols Using Rhodium(II) Catalysts

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The synthesis and addition of azide-substituted α-diazo amides such as *N*-(4-azidophenyl)-α-diazoacetamide and *N*-(4-azido-2-hydroxyphenyl)-α-diazoacetamide to olefins and alcohols using either rhodium(II) acetate or preferably rhodium(II) pivalate provided cyclopropanecarboxamides and α-alkoxy amides, respectively, without disrupting the azide functionality. These azide-bearing α-diazo amides are potentially useful in the preparation of photoaffinity cross-linking reagents for studying the mechanism of action of natural products.

In connection with the development of photoaffinity reagents[1] for studying the mechanism of action of natural products, we required a synthesis of various α-diazo amide reagents **1** bearing an aryl azide group and possessing the capacity for radioiodination.[2] The selection of the α-diazo amide functionality rather than the corresponding α-diazo ester functionality was based on the anticipated stability of the amide linkage relative to the ester linkage in the ultimate products of the cross-linking experiments. Although the reactions of α-diazo esters with olefins[3] and alcohols[4] have been investigated in some detail, the analogous synthesis and reactions of α-diazo amides **1** have been largely neglected.[5] As a consequence, we needed to develop an acceptable route to azide-substituted α-diazo amides **1** and to demonstrate the selective manipulation of the α-diazo amide functionality in the presence of an azide group.

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