and nmr). On acidification of the alkaline extracts containing the acidic portion of the hydrolysis products, lactonization occurred to yield 1.80 g of the lactone of 4,4-dimethyl-5-phenyl-5-hydroxyheptanoic acid as a colorless oil: bp 125° (0.05 mm); ir 5.74 μ; nmr δ 0.50–0.96 (m, 6, >C(CH$_3$)(CH$_3$), CH$_2$CH$_3$), 1.09 (s, 3, >C(CH$_3$)(CH$_3$)), 1.20–2.79 (m, 6-CH$_2$CH$_2$–, –CH$_2$-CH$_3$), 7.30 (s, 5, aromatic).

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.6; H, 8.6. Found: C, 77.6; H, 8.6.

Pyrolysis of 1-Ethoxypropynyl Levulinate (19).—After 3.6 g of **19** was heated at 200° for 1 hr, 1.7 g (94%) of ethyl propionate was collected. The nonacidic residue was essentially lactone 19_{UL}, since 1.9 g (90%) of levulinic acid was obtained on treatment with aqueous sodium carbonate.

Ethyl α-(1-Phthalidyl)propionate (7).—A mixture of 15.0 g of phthalaldehydic acid, 17.2 g of ethyl iodide, 40 g of anhydrous potassium carbonate, and 400 ml of 2-butanone was held at reflux for 8 hr. Distillation of the neutral portion yielded 14.2 g (80%) of ethyl phthalaldehydate: bp 92–94° (5–6 mm);[17] ir 5.75 (CHO) and 5.81 μ (COOC$_2$H$_5$); nmr δ 10.61 (s, 1, CHO). The latter value establishes the aldehydo ester structure. A Reformatsky reaction involving 14.0 g of ethyl phthalaldehydate, 14.5 g of ethyl α-bromopropionate, 5.2 g of zinc, and 75 ml of 4:1 benzene–ether at reflux for 4 hr yielded 14.9 g (80%) of colorless **7**: bp 128–130° (0.1–0.2 mm); ir 5.63 and 5.76 μ; nmr δ 0.76–1.68 (m, 6, CHCH$_3$, –CH$_2$CH$_3$), 2.30–3.36 (m, 1, >CHCH$_3$), 3.73–4.55 (m, 2, –CH$_2$CH$_3$), 5.84 (d, J = 4.5 Hz, 1, –CH<), 7.30–8.15 (m, 4, aromatic).

Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.6; H, 6.0. Found: C, 66.5; H, 6.0.

This ester **7** proved identical with ester formed by pyrolysis of **4**, except for slight differences in content of the diastereomeric forms.

Ethyl α-(1-Methyl-1-phthalidyl)propionate (8).—Pure ethyl *o*-acetylbenzoate,[18] bp 100° (0.3–0.4 mm), ir 5.75 and 5.85 μ, nmr δ 2.40 (s, 3, CH$_3$CO), was obtained essentially as described for ethyl phthalaldehydate. By the Reformatsky route as described above for **7**, there was obtained 14.2 g of a crude product (from 17.1 g of ethyl *o*-acetylbenzoate) which showed (tlc) a small amount of product which moved faster than the main fraction. Chromatography on 350 g of neutral alumina (Woelm grade A) using petroleum ether yielded 11.5 g (52%) of **8**: bp 115–117° (0.2 mm); ir 5.62 and 5.77 μ; nmr δ 1.00–1.42 (m, 6, >CHCH$_3$, –CH$_2$CH$_3$), 1.75 (s, 3, CCH$_3$), 2.77–3.40 (m, 1, >CHCH$_3$), 3.88–4.39 (m, 2, –CH$_2$CH$_3$), 7.41–8.03 (m, 4, aromatic).

Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.7; H, 6.5. Found: C, 67.6; H, 6.4.

This ester **8** proved identical with ester formed by pyrolysis of **5**, except for slight differences in content of the diastereomeric forms.

Ethyl α-(1-Phenylphthalidyl)propionate (9).—A mixture of 5.08 g of ethyl *o*-benzoylbenzoate, 3.62 g of ethyl α-bromopropionate, 1.4 g of zinc, and 20 ml of 7:3 benzene–ether was held at reflux for 3 hr. After the usual work-up 6.4 g of crude neutral material was obtained. Chromatography over alumina (180 g) yielded 0.90 g (18%) of recovered ethyl *o*-benzoylbenzoate and 3.50 g (56%) of a mixture of solid and liquid isomers of **9**. The ir and nmr of the solid isomer were similar to that of the liquid which contained some of the solid isomer.

Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.4; H, 5.8. Found (for solid isomer): C, 73.5; H, 5.9. Found (for liquid isomer): C, 73.6; H, 5.9.

Both the solid and liquid isomers of **9** were identical with similar fractions obtained by pyroysis of **6** except for slight differences in content of diastereomeric forms in the liquid fraction of **9**.

Registry No.—**4**, 30715-54-9; **5**, 30715-55-0; **6**, 30715-56-1; **7**, 30715-57-2; **8**, 30715-58-3; **9**, 30715-59-4; **15**, 30715-60-7; **15** (UL), 4055-00-9; **16**, 30708-61-3; **17**, 30788-19-3; **18**, 30788-20-6; **20**, 30788-21-7; **21**, 30788-22-8; **23**, 30708-62-4; **28**, 30708-63-5; 4,4-dimethyl-5-phenyl-5-hydroxyheptanoic acid lactone, 30708-64-6.

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(18) S. Gabriel, *Ber.*, **29**, 2521 (1896), reported bp 279°.

Configuration and Conformation of the Long-Chain Cyclic Acetals of Glycerol[1]

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The structural and geometrical isomers of long-chain cyclic acetals of glycerol were prepared by acid-catalyzed condensation of glycerol with *n*-hexadecanal followed by purification of the individual components by adsorption and gas–liquid chromatography. The structures of the four isomers were established by chemical and spectroscopic means. Configurations and conformations were determined by 100-MHz nmr spectroscopy aided by deuterium labeling. The isomers were identified as *cis*-2-pentadecyl-5-hydroxy-1,3-dioxane (**1a**), *trans*-2-pentadecyl-5-hydroxy-1,3-dioxane (**2a**), *cis*-2-pentadecyl-4-hydroxymethyl-1,3-dioxolane (**3a**), and *trans*-2-pentadecyl-4-hydroxymethyl-1,3-dioxolane (**4a**). The lower energy structures are those having cis configuration. It was found that the six-ring isomers **1a** and **2a** differ in the orientation of their substituents at C-5, while the long-chain alkyl groups remain locked in equatorial conformation.

Long-chain cyclic acetals of glycerol have been found in lipid extracts from various organisms. However, much controversy still exists whether cyclic glycerol acetals are natural lipid constituents[2] or rather artifacts[3] produced during hydrolysis of plasmalogen-type lipids.[4] It is interesting to note that smooth muscle contracting activities, similar to those known for prostaglandins, have recently been ascribed to cyclic glycerol acetal phospholipids,[5] and it appears intriguing to speculate on the possible role of glycerol acetals in plasmalogen biosynthesis. Present knowledge of the chemical and physical properties of cyclic glycerol acetals in general is scarce.[6] Difficulties in the separation of the long-chain homologs and in the correlation of isomers are responsible for much of the confusion persisting in this field.

In this communication we report the preparation and characterization of the four structurally or geometrically isomeric, long-chain cyclic acetals of glycerol and of

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(3) M. F. Frosolono, A. Kisic, and M. M. Rapport, *J. Org. Chem.*, **32**, 3998 (1967).

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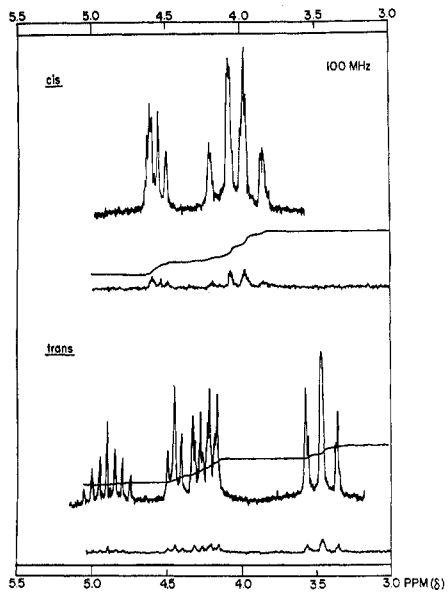


Figure 1.—100-MHz nmr spectra of *cis*-2-pentadecyl-5-acetoxy-1,3-dioxane (**1b**) (top) and *trans*-2-pentadecyl-5-acetoxy-1,3-dioxane (**2b**) (bottom).

some of their derivatives. Their structures as 1,3-dioxanes and 1,3-dioxolanes, as well as their configuration and conformation, were established.

Acid-catalyzed condensation of hexadecanal[7] with glycerol led quantitatively to a thermodynamically equilibrated mixture of cyclic glycerol acetals. In most experiments, these hydroxy compounds **1a–4a** were acetylated in order to facilitate fractionation. Preparative adsorption chromatography[10] of the acetates on silicic acid layers (tlc) yielded three fractions. The most polar and major fraction **1b** and the least polar and smallest one **2b** were shown to be uniform by gas chromatography (glc).[12] The fraction of medium mobility in tlc was separated by preparative glc into **3b** and **4b**. Some characteristic data of the individual acetates **1b–4b** are compiled in Table I. The mass spectra of **1b–4b** were in agreement with the molecular weight M = 356 and the ion fragments expected: *m/e* 43 (CH_3CO), 117 (M − $C_{15}H_{31}CO$), 145 (M − $C_{15}H_{31}$) 100%, 239 ($C_{15}H_{31}CO$), and 355 (M − 1).

Deacetylation of fractions **1b**, **2b**, and **3b** plus **4b** through $LiAlH_4$ reduction and extraction under alkaline conditions yielded uniform fractions of hydroxy compounds **1a** (R_f 0.49 in tlc, hexane–Et_2O, 40:60, v/v),

TABLE I
THE LONG-CHAIN CYCLIC ACETALS OF GLYCEROL

	Acetates			
Characteristics	**1b**	**2b**	**3b**	**4b**
Yield, %	42.0	20.2	20.7	17.1
R_f value[a]	0.35	0.68	0.46	0.46
R_t, min[b]	47	33	36	40
Mp, °C	87–89	61–63	33–34	41.5–43

[a] R_f values in adsorption thin layer chromatography;[10] developing solvent, hexane–Et_2O, 70:30 (v/v). [b] Retention times in gas–liquid chromatography.[12]

2a (R_f 0.62), and **3a** plus **4a** (R_f 0.56), respectively. Their physical properties, *i.e.*, behavior in tlc, melting points, as well as ir and mass spectral characteristics, were identical with those of the hydroxy compounds which had been isolated by repeated adsorption tlc from the original mixture of aldehyde–glycerol condensation products. Obviously, the long-chain cyclic acetals of glycerol do not suffer inversion or any other type of isomerization during acetylation, $LiAlH_4$ reduction, tlc on silicic acid, or as acetates in glc.

The structures of the cyclic acetals were determined. **1a**, **2a**, and **3a** plus **4a**, as obtained from the individual acetates through $LiAlH_4$ reduction, were each alkylated with hexadecylmethanesulfonate[8] and yielded the corresponding long-chain ethers **1c** (R_f 0.28, hexane–Et_2O, 95:5, v/v), **2c** (R_f 0.53), and **3c** plus **4c** (R_f 0.42), respectively. Acidic hydrolysis of **1c** and of **2c** in aqueous methanol–HCl and purification by tlc led to identical glycerol derivatives, namely 2-hexadecyl glycerol ether [mp 62–63° (lit.[13] 62.5–63.3°); ir spectra]. Hydrolysis of **3c** plus **4c** yielded 1-hexadecylglycerol ether [mp 63–64° (lit.[8] 65.5°); ir spectra] and none of the 2 isomer. The isomeric glycerol ethers were separable by chromatography on boric acid impregnated silicic acid layers[13,14] and shown to be identical with the authentic glycerol ether isomers. In addition, the five-membered ring structures of **3b** plus **4b** were established through synthesis from 2,2-dimethyl-4-acetoxymethyl-1,3-dioxolane (**5**) and hexadecanal. Thus, **1** and **2** were unequivocally identified as having the 1,3-dioxane skeleton, whereas **3** and **4** were shown to exist as 1,3-dioxolane derivatives.

The configuration and conformation of the individual, pure isomers **1b–4b** were determined. The 100-MHz nmr spectrum of acetate **2b**, as shown in Figure 1 (bottom), exhibits a symmetrical seven-line pattern centered at δ 4.89 ppm that can be correlated with an axial proton located next to an acetoxy group and vicinally to four methylene protons. This superimposed "triplet of triplets" for H_a-5 is caused through diaxial (J = 10.2 Hz) and axial–equatorial (J = 5.1 Hz) interaction with the methylene hydrogens H-4 and H-6. Similar signals were observed previously for axial protons in other cyclohexane-type systems in chair conformation.[15] In contrast, the nmr spectrum of **1b**, as shown in Figure 1 (top), does not exhibit the signals for an axial H-5.

The triplet at δ 4.46 (J = 5.0 Hz) in the spectrum of **2b** (Figure 1, bottom) as well as the partially embedded triplet at δ 4.54 ppm (J = 5.0 Hz) in **1b** (Figure 1, top)

(7) Hexadecanal was synthesized from alkylmethanesulfonate[8] by oxidation with dimethyl sulfoxide.[9]

(8) W. J. Baumann and H. K. Mangold, *J. Org. Chem.*, **29**, 3055 (1964).

(9) V. Mahadevan, F. Phillips, and W. O. Lundberg, *Lipids*, **1**, 183 (1966).

(10) Preparative adsorption chromatography was done on layers of silica gel H (Merck), 0.3 or 2 mm thick.[11] After chromatography in tanks lined with filter paper the lipid fractions were usually visible as opalescent bands without the use of an indicator; otherwise the fractions were made visible in uv light after spraying with a 0.2% solution of 2′,7′-dichlorofluorescein in ethanol. Bands of adsorbent were scraped off, the fractions were eluted with moist diethyl ether, the solvent was evaporated, and the products were dried *in vacuo* and kept in hexane solution.

(11) H. K. Mangold in "Thin-layer Chromatography. A Laboratory Handbook," E. Stahl, Ed., Springer-Verlag, Berlin, Heidelberg, New York, 1969, p 363; H. H. O. Schmid, L. L. Jones, and H. K. Mangold, *J. Lipid Res.*, **8**, 692 (1967).

(12) Gas chromatography was done using a Victoreen 4000 instrument equipped with flame ionization and thermoconductivity detectors. The column, 180 × 0.6 cm, packed with 18% ethylene glycol succinate (HiEff-2BP) on Gas Chrom P, 80–100 mesh (Applied Science Laboratories, Inc., State College, Pa.), was operated at 215°. Helium served as carrier gas at a pressure of 4.2 atm.

(13) R. Wood and F. Snyder, *Lipids*, **2**, 161 (1967).

(14) V. Prey, H. Berbalk, and M. Kausz, *Mikrochim. Acta*, 968 (1961).

(15) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965; D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.*, **86**, 2742 (1964).

TABLE II

NMR DATA OF 2-PENTADECYL-1,3-DIOXANES[a]

Compd	Configuration	Chemical shifts, δ[b] H-5	H_a-2[d]	H_e-4,6	H_a-4,6	Coupling constants, J[c] $J_{5,4e}$	$J_{5,4a}$	$J_{4\,gem} = J_{6\,gem}$
1b[e]	Cis	H_e = 4.60	4.54	4.12	3.93	1.5	1.5	12.7
2-d-**1b**[f]	Cis	H_e = 4.60[g]		4.12	3.93	1.5	1.5	12.7
2b[e]	Trans	H_a = 4.89[h]	4.46	4.25	3.47	5.1	10.2	10.4
2-d-**2b**[f]	Trans	H_a = 4.87[h]		4.21	3.41	5.1	10.2	10.4
1c[f,i]	Cis	H_e = 3.11	4.51	4.16	3.76	1.8	1.8	12.0
2c[f,i]	Trans	H_a ~ 3.4[j]	4.37	4.20	~3.4[j]	5.3	*j*	*j*

[a] Spectra of $CDCl_3$ solutions. Additional signals in the 100-MHz spectra are δ ~2.1 (s, 3, $COCH_3$), ~1.6 (broad s, 2, C-1′ CH_2), 1.28 (broad s, 26, internal CH_2 of chain), and 0.89 (t, 3, terminal CH_3). [b] Chemical shifts in parts per million downfield from tetramethylsilane. [c] Coupling constants in hertz. [d] Triplet due to coupling with exocyclic C-1′ CH_2; J = 5.0 Hz. [e] 100-MHz spectrum. [f] 60-MHz spectrum. [g] Quintuplet. [h] Septuplet. [i] Alkoxy H-1′ at 3.48 (t, 6.5). [j] Signals for H_a-4,6, H_a-5, and alkoxy H-1′ are poorly resolved.

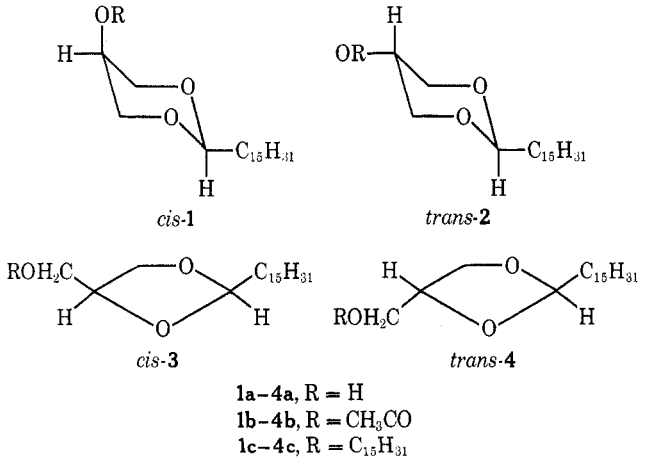
are due to the hydrogens at C-2. This was confirmed by specific deuteration at C-2,[16] *i.e.*, the absence of these triplets in the 2-deuterated dioxanes (see Table II). Both triplets, that of **1b** and **2b**, show identical coupling constants and almost identical chemical shifts, indicating identical H-2 orientation in both isomers. The magnitude of the chemical shifts strongly advocates axial hydrogens at C-2 in **1b** *and* **2b**. For an equatorial hydrogen at C-2 a shift of approximately δ 4.8 ppm would be expected.[17]

Elimination of the triplet for H_a-2 from the spectrum of **1b**, through specific C-2 deuteration, reveals a clear quintuplet at δ 4.60 ppm (J = 1.5 Hz) accounting for one hydrogen. This signal must be assigned to H_e-5. Obviously, due to the special situation in dioxane systems and probably as a result of shielding by ring oxygens, the equatorial H-5 absorbs at *higher* field than the corresponding axial hydrogen, quite in contrast to what is known to occur, *e.g.*, with steroids[18] and other cyclohexane systems.

The axial and equatorial hydrogens at C-4 in **1b** and **2b** are chemically equivalent with those at C-6. The four-line pattern in the 100-MHz spectrum of **2b** centered near 4.25 ppm represents a pair of doublets ($J_{4e,5a}$ = 5.1; $J_{4\,gem}$ = 10.4 Hz) and can be assigned to H_e-4 and H_e-6. The signals of H_a-4 and H_a-6 occur at 3.47 ppm as triplets due to the similar coupling constants $J_{4a,5a}$ = 10.2 and $J_{4\,gem}$ = 10.4 Hz. The spectrum of **1b** shows a pair of doublets centered at δ 4.12 and 3.93 ppm for H_e-4,6 and H_a-4,6, respectively (see Figure 1, top).

These spectral data are consistent with the following energetic and steric considerations. In 1,3-dioxanes the differences in enthalpies between chair and skew-boat are known to be in the same order of magnitude (7.1 kcal/mol) as they are for cyclohexane (5.9 kcal/mol.[19,20] Introduction of oxygens into the ring system of cyclohexane results in shorter distances between an axial C-2 substituent and H_a-4 or H_a-6 (from 2.29 to 1.94 Å),[21] *i.e.*, the dioxane chair is slightly puckered in the O, C-2, O region and flattened at C-4, C-5, C-6. Consequently, equatorial methyl substitution at C-2 is favored by approximately 4.0 kcal/mol[19,20] as compared with axial substitution; equatorial methyl substitution at C-5 is favored by 0.8 kcal/mol only,[21] because little interaction occurs between an axial C-5 substituent and the "axial" electron pairs of the ring oxygens[19] and due to the flattened chair. Ring systems bearing bulky substituents usually exist predominantly in one conformation in which the bulky "anchor group" is equatorially oriented. Furthermore, hydroxy groups in heterocyclic systems often prefer the axial position where they can exert a stabilizing effect through hydrogen bonding. Therefore, the chair form, C-2 alkyl substitution in equatorial orientation, and isomerism about C-5 may be expected for the dioxanes **1** and **2** and was confirmed in the present study.

In contrast to the dioxanes the degree of puckering in dioxolanes is quite small; consequently, the symmetry in dioxolanes does not deviate much from that of a planar system, and a number of conformations of very similar free energy are possible. The 100-MHz nmr spectra, therefore, are time averages of those of several conformers and show a multitude of poorly resolved signals for H-4,5 (3.4–4.4 ppm) and for the acetoxymethyl protons near 4.13 (**3b**) or 4.17 ppm (**4b**). The spectra



1a–4a, R = H
1b–4b, R = CH_3CO
1c–4c, R = $C_{15}H_{31}$

permit, however, the distinction of cis and trans isomers on the basis of the shifts observed for the H-2 triplets. The latter were unequivocally correlated by specific deuteration.[16] The closer proximity of the 4-acetoxymethyl group and H-2 in the trans 2,4-disubstituted dioxolane should lead to mutual deshielding and, therefore, to a shift of the H-2 signal to lower field than for the cis isomer, similar or more pronounced than that re-

(16) 2-Deuterio-2-pentadecyl-5-acetoxy-1,3-dioxanes were prepared as follows: $LiAlD_4$ reduction of methyl hexadecanoate gave 1,1-dideuteriohexadecanol that was converted to its methanesulfonate. Dimethyl sulfoxide oxidation gave 1-deuteriohexadecanal, which was treated with glycerol, acetylated, and fractionated by preparative tlc as described for the nondeuterated acetals.

(17) K. Pihlaja and P. Äyräs, *Acta Chem. Scand.*, **24**, 204 (1970).

(18) E. L. Eliel, *Angew. Chem.*, **77**, 784 (1965); *ibid., Int. Ed. Engl.*, **4**, 761 (1965).

(19) K. Pihlaja, *Acta Chem. Scand.*, **22**, 716 (1968).

(20) E. L. Eliel, *Accounts Chem. Res.*, **3**, 1 (1970).

(21) F. G. Ridell and M. J. T. Robinson, *Tetrahedron*, **23**, 3417 (1967).

ported for the diastereoisomeric 2,4-dimethyl-1,3-dioxolanes.[22] Actually, the chemical shift for the triplet of H-2 in **3b** is found to be δ 4.88 ppm (J = 4.5 Hz) and thus is identical with the H-2 signal of the nonsubstituted 2-pentadecyl-1,3-dioxolane.[23] The corresponding signal of **4b** is shifted to lower field strength (δ 4.99 ppm, J = 4.5 Hz). Therefore, cis configuration must be assigned to **3b** and trans configuration to **4b**.

This interpretation is in agreement with infrared data. It has been shown that the ring breathing vibration of *cis*-2,4-dimethyl-1,3-dioxolane occurs at 935 cm^{-1}, whereas that of the trans isomer is lowered to 926 cm^{-1}.[24] A similar difference between the isomeric pairs was reported for 2,2-dimethyl-4-methoxymethyl-1,3-dioxolanes, but both bands had been shifted to higher frequencies (953, 933 cm^{-1}). These findings agree well with our observations; the spectrum of *cis*-2-pentadecyl-4-acetoxymethyl-1,3-dioxolane (**3b**) shows the ring breathing vibration at 980 cm^{-1}, the trans isomer **4b** exhibits a stronger band at 951 cm^{-1}.

These data demonstrate that the isomers dioxane **1** and dioxolane **3** occur in cis configuration, and dioxane **2** and dioxolane **4** occur in trans configuration. For both, dioxanes and dioxolanes, the more thermodynamically stable isomers are those having cis configuration. Interestingly, cis dioxane **1b** is more polar than the trans isomer **2b**, whereas for dioxolanes the situation is reversed.

Experimental Section

Melting points were determined on a Kofler hot stage and are corrected. Elemental analyses were carried out by I. Beetz, Mikroanalytisches Laboratorium, Kronach, Germany. Infrared spectra were taken with a Perkin-Elmer Model 21 spectrophotometer. Carbon disulfide served as solvent, except in the ranges 2400–2000 and 1650–1400 cm^{-1}, where tetrachloroethylene was used.[25] Mass spectra were recorded on a Hitachi Perkin-Elmer single-focusing instrument, RMU-6D, at 70-eV ionization potential. Abundances of ions are given as percentages relative to the most prominent peak. Nuclear magnetic resonance (nmr) spectra were recorded on Varian A-60A and HA-100 spectrometers, using deuteriochloroform as solvent. Nmr absorptions are reported in parts per million (ppm) downfield from tetramethylsilane.

Preparation of Cyclic Glycerol Acetals (1a–4a).—Hexadecanal[7] (0.96 g, 4 mmol), 0.92 g (10 mmol) of glycerol, 0.5 g of *p*-toluenesulfonic acid, and 250 ml of dry benzene were placed in a three-necked flask equipped with water separation head, reflux condenser, inlet and outlet tubes for dry nitrogen, and stirrer. The reaction mixture was kept at reflux temperature for 2 hr, while the water formed was continuously removed by azeotropic distillation; then most of the benzene was distilled off. After cooling, ice-cold 1% aqueous K_2CO_3 was added, and the products were extracted with three 150-ml portions of diethyl ether. The organic phase was washed with two 50-ml portions of water, dried (Na_2SO_4), and concentrated *in vacuo*, yielding 1.08 g (86%) of glycerol acetals.

Separation into three fractions **1a**, **2a**, and **3a** plus **4a** was achieved by repeated preparative tlc[10] using hexane–Et_2O (40:60, v/v) for developing of the chromatoplates (method A).

Alternatively, pure hydroxy acetals **1a–4a** were prepared more conveniently from the individual acetates **1b–4b** through $LiAlH_4$ reduction (method B) in diethyl ether (3 hr), decomposition of the excess reagent with moist ether, and extraction from the basic medium, followed by tlc purification. The following products were obtained by either procedure.

cis-**2-Pentadecyl-5-hydroxy-1,3-dioxane** (**1a**): mp 69.5–71° (**1a** as prepared by method A, mp 69–70.5°; mmp 70–71°); ir (CS_2, C_2Cl_4)[25] 3542 (m), 3440, 1461 (m), 1404, 1388 (m), 1364 (m), 1299, 1234 (m), 1225 (m), 1145 (s), 1107, 1088 (m), 1056 (m), 996 (m), 983, 938, 892, 826, 812 cm^{-1} (m). *Anal.* Calcd for $C_{19}H_{38}O_3$: C, 72.56; H, 12.18; O, 15.26. Found: C, 72.22; H, 12.13; O, 14.98.

trans-**2-Pentadecyl-5-hydroxy-1,3-dioxane** (**2a**): mp 84–86° (**2a** as prepared by method A, mp 84–85°; mmp 84–85°); ir (CS_2, C_2Cl_4)[25] 3600 (m), 3455, 1460 (sh), 1404, 1329, 1261, 1223, 1145 (s), 1113, 1065 (s), 1057 (s), 1045 (s), 959, 900, 802 cm^{-1}. *Anal.* Calcd for $C_{19}H_{38}O_3$: C, 72.56; H, 12.18; O, 15.26. Found: C, 72.45; H, 12.54; O, 15.26.

2-Pentadecyl-4-hydroxymethyl-1,3-dioxolane (**3a**,**4a**): mp 30–32°; ir (CS_2, C_2Cl_4)[25] 3560 (m), 3460, 1408, 1395, 1348, 1225, 1200, 1138 (s), 1121 (s), 1100 (sh), 1040 (s), 972, 962 cm^{-1}. *Anal.* Calcd for $C_{19}H_{38}O_3$: C, 72.56; H, 12.18; O, 15.26. Found: C, 72.31; H, 12.23; O, 15.66.

Acetylation of 1 g of cyclic glycerol acetals was done in a mixture of 10 ml of absolute pyridine and 100 ml of acetic anhydride for 2 hr at 80°. Most of the acetic anhydride was removed under reduced pressure. The cold mixture was poured into ice water, neutralized with K_2CO_3, and extracted with hexane. The extract was washed with 2% K_2CO_3 solution and water, dried (K_2CO_3), and concentrated *in vacuo*, yielding a mixture of acetates **1b–4b**. Fractionation was done by preparative tlc[10] (hexane–Et_2O, 70:30, v/v) and by preparative glc[12] for the separation of **3b** and **4b**. Some of the characteristic data of the individual acetates **1b–4b** are listed in Table I.

cis-**2-Pentadecyl-5-acetoxy-1,3-dioxane** (**1b**): ir (CS_2, C_2Cl_4)[25] 1731 (s), 1408, 1372 (s), 1348, 1240 (s), 1151 (s), 1103 (m), 1072 (m), 1009 (m), 972, 946, 924, 780 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 356 (0.7), 355 (2.5), 145 (100), 117 (22), 43 (47). *Anal.* Calcd for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31; O, 17.95. Found: C, 70.27; H, 11.04; O, 17.70.

trans-**2-Pentadecyl-5-acetoxy-1,3-dioxane** (**2b**): ir (CS_2, C_2Cl_4)[25] 1742 (s), 1406, 1368 (m), 1327, 1299, 1231 (s), 1151 (s), 1115 (m), 1075 (sh), 1049 (s), 962 (m), 885, 690 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 356 (0.4), 355 (1.9), 145 (100), 117 (25), 43 (63). *Anal.* Calcd for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31; O, 17.95. Found: C, 70.41; H, 11.06; O, 17.64.

cis-**2-Pentadecyl-4-acetoxymethyl-1,3-dioxolane** (**3b**): ir (CS_2, C_2Cl_4)[25] 1739 (s), 1367 (m), 1229 (s), 1140 (s), 1123 (m), 1041 (s), 980, 961 cm^{-1} (sh); mass spectrum (70 eV) *m/e* (rel intensity) 356 (0.5), 355 (1.0), 145 (100), 117 (4.8), 43 (44).

trans-**2-Pentadecyl-4-acetoxymethyl-1,3-dioxolane** (**4b**): ir (CS_2, C_2Cl_4)[25] 1739 (s), 1370 (m), 1231 (s), 1140 (s), 1123 (m), 1041 (s), 980, 961 cm^{-1} (m); mass spectrum (70 eV) *m/e* (rel intensity) 356 (0.5), 355 (0.9), 145 (100), 117 (5.2), 43 (36).

Anal. Calcd for $C_{21}H_{40}O_4$ (mixture of **3b** and **4b**, mp 36–38°): C, 70.74; H, 11.31; O, 17.95. Found: C, 70.43; H, 11.04; O, 17.64.

Alternatively, **3b** and **4b** were prepared by transacetalation of isopropylideneglycerol acetate **5** with hexadecanal.[7]

2,2-Dimethyl-4-acetoxymethyl-1,3-dioxolane (**5**).—2,2-Dimethyl-4-hydroxymethyl-1,3-dioxolane (1,2-isopropylidene glycerol, Aldrich Chemical Co., Inc., Milwaukee, Wis.) was treated with a tenfold amount of acetic anhydride–pyridine, 10:1, in a sealed ampoule for 2 hr at 80° and was worked up as described above. Distillation yielded **5**: bp 47–48° (1 mm); mass spectrum (70 eV) *m/e* (rel intensity) 159 (34, M − CH_3), 101 (19, M − CH_2OCOCH_3), 73 (3, CH_2OCOCH_3), 43 (100, CH_3CO), 42 (6, CH_2CO). *Anal.* Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10; O, 36.74. Found: C, 54.98; H, 8.41; O, 36.73.

2-Pentadecyl-4-acetoxymethyl-1,3-dioxolane (**3b**, **4b**).—Hexadecanal[7] (0.48 g, 2 mmol), 0.61 g (3.5 mmol) of **5**, 0.5 g of *p*-toluenesulfonic acid, and 150 ml of dry benzene were placed in a three-necked flask equipped with condenser, inlet for dry nitrogen, and stirrer. Most of the solvent was distilled off continuously over a period of 2 hr. Extraction with diethyl ether and drying, as described above, and purification by preparative tlc (hexane–Et_2O, 70:30, v/v) yielded 0.39 g (55%) of **3b** plus **4b**, R_f 0.46, consisting of 66.7% **3b** (R_t 36 min) and 33.3% **4b** (R_t 40 min).[12]

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(25) Relative intensities of ir absorption bands are given: s, strong; m, medium; sh, shoulder; weak bands (w) are without designation. The following bands associated with vibrations of the aliphatic chains occur in all the spectra quoted and are not listed for each compound: 2925–2915 (s) and 2850–2845 cm^{-1} (s), ν CH of CH_2; near 1470 (m), δ CH of CH_2; 1448–1445 (sh) or (w) and 1380–1375 (m), asymmetrical and symmetrical δ CH of CCH_3, respectively; 719–717 (m), CH rocking vibration of $(CH_2)_n$.

The cyclic acetals **1a–4a** were alkylated with hexadecyl methanesulfonate in the presence of KOH in xylene according to established procedures[8] of glycerol ether synthesis, and each of the reaction products was purified by preparative tlc[10] (hexane–Et_2O, 95:5, v/v). For nmr data, see Table II.

cis-**2-Pentadecyl-5-hexadecyloxy-1,3-dioxane** (**1c**): mp 95–96°; ir (CS_2, C_2Cl_4)[25] 2715, 2652, 1408, 1339 (m), 1284, 1244, 1161 (s), 1139, 1116 (s), 1099 (s), 1006 (s), 955, 893, 804 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 538 (1.0), 537 (1.7), 327 (100), 57 (49). *Anal.* Calcd for $C_{35}H_{70}O_3$: C, 78.00; H, 13.09; O, 8.91. Found: C, 77.85; H, 12.87; O, 9.20.

Hydrolysis of **1c** in aqueous hydrochloric acid–methanol[8] and purification by tlc (hexane–Et_2O, 10:90, v/v) yielded 2-hexadecyl glycerol ether: mp 62° (lit.[13] 62.5–63.3°); migration rate on boric acid impregnated plates (chloroform–methanol, 98:2, v/v) was identical with that of a standard.

trans-**2-Pentadecyl-5-hexadecyloxy-1,3-dioxane** (**2c**): mp 86–87°; ir (CS_2, C_2Cl_4)[25] 2660, 1369, 1327, 1297, 1271, 1222, 1150 (m), 1138 (sh), 1116 (s), 1042 (m), 962 (m), 900, 802, 680, 665 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 538 (0.4), 537 (1.7), 327 (100), 57 (39). *Anal.* Calcd for $C_{35}H_{70}O_3$: C, 78.00; H, 13.09; O, 8.91. Found: C, 78.00; H, 12.95; O, 9.10.

Hydrolysis of **2c** and purification, as described above, yielded 2-hexadecyl glycerol ether, mp 63°.

2-Pentadecyl-4-hexadecyloxymethyl-1,3-dioxolanes (**3c**, **4c**): mp 71–73°; ir (CS_2, C_2Cl_4)[25] 1411, 1350, 1302, 1258, 1140 (m), 1119 (s), 1045 (m), 960, 803 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 538 (0.6), 537 (0.9), 327 (100), 57 (41). *Anal.* Calcd for $C_{35}H_{70}O_3$: C, 78.00; H, 13.09; O, 8.91. Found: C, 78.00; H, 12.83; O, 9.29.

Hydrolysis of the mixture of **3c** plus **4c**, and purification, as described above, yielded 1-hexadecyl glycerol ether: mp 63–64° (lit.[8] 65.5°); migration rate on boric acid impregnated plates (chloroform–methanol, 98:2, v/v) was identical with that of a standard.

Registry No.—**1a**, 30889-22-6; **1b**, 30889-23-7; **1c**, 30889-24-8; **2a**, 30889-25-9; **2b**, 30889-26-0; **2c**, 30889-27-1; **3a**, 30889-28-2; **3b**, 30889-29-3; **3c**, 30889-30-6; **4a**, 30889-31-7; **4b**, 30889-32-8; **4c**, 30889-33-9; **5**, 14739-11-8.

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Conformational Analysis. LXXIV. Studies on Phenol and Anisole Derivatives[1-3]

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The orientation of the hydroxyl or methoxyl in a number of ortho-substituted phenols and anisoles has been studied by experimental (dipole moment) and theoretical (molecular mechanics) methods. The phenolic hydroxyl is coplanar with the ring, even in di-*o*-*tert*-butylphenol. The rotational barrier about the C_{Ar}–O bond in anisole is negligibly small. Di-*o*-methylanisole has the methoxyl perpendicular to the ring plane.

Conformational properties of phenols have been studied in some detail *via* their infrared spectra. The hydroxyl overtone region was observed at an early date by Wulf.[5] An ortho halogen on a phenol may interact (hydrogen bond) with the hydroxyl, and Pauling[6] interpreted the doublet in the O–H stretching overtone region as due to the existence of cis and trans orientations of the hydroxyl, which lies in the plane of the benzene ring. Baker,[7] in his study of the fundamental hydroxyl stretching region, reaffirmed and more fully explained the observed shifts.

Similar shifts result when other groups such as nitro or carbonyl are placed ortho to the phenol, since hydrogen bonding again takes place.[8]

While most phenolic hydroxyls which are not hydrogen bonded absorb at 3608 ± 2 cm^{-1}, important exceptions include those phenols which are alkylated in the ortho position. In particular, di-*o*-*tert*-butyl substitution shifts the free hydroxyl to a much higher frequency (3643 cm^{-1}).[9] The increase seems too large to be accounted for by resonance or inductive contributions of the alkyl group alone. It might be reasonably attributed to twisting of the O–H bond out of the plane of the benzene ring. This would decrease the resonance interaction between the oxygen and the ring, raise the electron density on oxygen, and increase the bond strength of the O–H bond, thereby increasing the absorption frequency. That this is probably not the case, however, was deduced by Ingold[10] when, by using the σ values derived by Taft[11] for ortho substituents, he found that the frequencies of the O–H bands for 4-substituted phenols and 4-substituted 2,6-di-*tert*-butylphenols can be correlated by a Hammett σ–ρ relationship. A plot of the σ values of the two types of phenols *vs.* absorption frequency gave two parallel straight lines. The conclusion was that both types of phenols had similar structures. From a study of models, Ingold calculated that with the cis phenolic hydrogen selectively placed in the most favorable coplanar position, a maximum compression energy with the *tert*-butyl group of the order of 0.1–0.2 kcal/mol is present, which is rather small compared with the 7.0-kcal/mol resonance energy postulated from maintaining the O–H bond in the plane of the ring.

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