as also suggested by its mode of formation and behavior. The infrared spectrum (in Nujol) was consistent with this structure, showing bands at 1650 (-ONO_2 or ONO), 2280 (N≡N), 1610, 1580, 1500 (Ph), 1020–1090 cm^{-1} (BF_4).

Anal. Calcd for $C_{19}H_{24}O_3N_3BF_4$ (429.22): C, 49.50; H, 5.22; N, 9.10; F, 16.45. Found: C, 50.54; H, 5.17; N, 9.47; F, 17.05.[17]

The product was very unstable and decomposed rapidly without melting at about 120°, giving off a brown gas, while standing at 20–25° for several days gave a pale yellow solid, identified as the estrone 3-methyl ether 4-diazonium fluoroborate (IVb). In experiments where the initial precipitate of the diazonium fluoroborate nitrite ester was left stirring in the original reaction mixture for 1 hr at 15–25°, good yields (60–85%) of the 17-ketone (IVb) were obtained directly.[18] This could be converted into the 4-fluoroestrone methyl ether (Vb), as described above in 33% yield.

4-Fluoroestrone (VIIIb).—4-Fluoroestrone methyl ether (Vb, 500 mg) was mixed thoroughly with 5 g of pyridine hydrochloride and treated as described for the 4-fluoroestradiol methyl ether (VIb), yielding 100 mg (21%) of 4-fluoroestrone (VIIIb), mp 223–225°, $[\alpha]^{25}D$ +144° (*c* 1, chloroform). A thin layer chromatogram (alumina–chloroform) showed a single spot; uv, λ_{max}^{MeOH} 277.5 mμ (ε 1420) and 217 (8150). The infrared spectrum (in Nujol) was consistent with the structure VIIIb, with bands at 3200–3500 (OH), 1610, 1580, 1490 (Ph), 1730 cm^{-1} (17-C=O).

Anal. Calcd for $C_{18}H_{21}O_2F$ (288.37): C, 75.00; H, 7.33; F, 6.59. Found: C, 74.90; H, 7.40; F, 6.50.

Registry No.—Ia, 5976-73-8; Ib, 5976-74-9; IIa, 16223-65-7; IIb, 14846-62-9; IIIa, 13010-22-5; IIIb, 13010-21-4; IVa, 16222-59-6; IVb, 15091-55-1; IVc, 16222-60-9; Va, 16205-28-0; Vb, 16205-29-1; VIa, 16205-30-4; VIb, 16205-31-5; VIIa, 16205-32-6; VIIb, 1881-37-4; VIIIa, 16205-34-8; VIIIb, 1881-36-3.

Acknowledgments.—The authors wish to thank Dr. Byron H. Arison for interpretation of the nuclear magnetic resonance spectra, Mr. Robert W. Walker for the infrared spectra, Mr. Richard N. Boos and his staff for the elemental analyses, and Mr. Alec Kalowsky for the ultraviolet data.

(18) NOTE ADDED IN PROOF.—Subsequently this procedure was improved upon by filtering off the nitrite ester (IVc) and re-treating it with the original volumes of dioxane and aqueous fluoroboric acid at about 20°. After the evolution of gas had subsided, the estrone 3-methyl ether 4-diazonium fluoroborate (IVb) crystallized from the cooled (0°) reddish solution in 90% yield. This high yield indicates that this reaction proceeds by a mechanism quite different from the one suggested by Barton and coworkers[12-14] or authors cited by Barton, for the thermal decomposition of nitrite esters. Their mechanism requires the formation of equal amounts of ketone and the corresponding carbinol *via* an over-all disproportionation reaction, whereas we found no such alcohol. It is hoped that this subject can be expanded upon

$$2R_2CHO\text{—}N{=}O \longrightarrow R_2C{=}O + R_2CHOH + 2NO$$

in a planned forthcoming publication on low temperature decomposition of nitrite esters.

Synthesis of Optically Active 1-C-Phenylglycerols and Their Derivatives[1a]

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Received January 3, 1968

Addition of phenylmetallic reagents to 1,2-*O*-isopropylidene-D-glyceraldehyde leading to the formation of optically pure D-*erythro*- and D-*threo*-1-*C*-phenylglycerol was investigated. Oxidation of the newly formed hydroxyl group in the addition products by Moffatt's reagent gave the expected ketone, which was reduced by $LiAlD_4$ to yield a pair of optically active diastereomers, 2,3-*O*-isopropylidene-D-*erythro*-1-*C*-phenylglycerol-1-d_1 and 2,3-*O*-isopropylidene-D-*threo*-1-*C*-phenylglycerol-1-d_1. The absolute configuration of the phenylglycerols and their derivatives was established by conversion into compounds of known configuration and supported by infrared and nuclear magnetic resonance (nmr) spectrometric studies. The complex nmr splitting patterns of the 1-*C*-phenylglycerols and their acyclic derivatives are interpretable by their resemblance to simple first-order splitting patterns.

Stereoselective addition of phenylmagnesium bromide to *aldehydro* and *keto* sugars and the determination of absolute configuration at the benzylic center was reported[2] recently. The steric difference between phenyllithium and phenylmagnesium bromide reagents was suggested as an explanation for the dramatic difference in diastereomeric product distribution, when these reagents added to *N*-benzyl-2,3-*O*-isopropylidene-D-glyceraldimine.[3] Addition of phenylmagnesium bromide to 2,3-di-*O*-benzoyl-D-glyceraldehyde was reported to yield a single optically active product, whose absolute configuration was not firmly established, but which was identified as "dibenzoyl-α-D-phenylglycerol" by the authors.[4] In this Article, we shall describe the synthesis of optically active 1-*C*-phenylglycerols; their derivatives, including some with a deuterium atom attached to the benzylic carbon; and the assignment of absolute configuration to these compounds.

When phenyllithium or phenylmagnesium bromide was allowed to react with 2,3-*O*-isopropylidene-D-glyceraldehyde,[5] the same pair of diastereomers, 2,3-*O*-isopropylidene-D-*threo*-1-*C*-phenylglycerol (**1**) and 2,3-*O*-isopropylidene-D-*erythro*-1-*C*-phenylglycerol (**4**), were obtained in good yield. Product analysis by glpc revealed that the phenyllithium addition gives almost the same diastereomeric distribution (62% *threo*, 38% *erythro*) as the phenylmagnesium bromide addition (58% *threo*, 42% *erythro*). The preponderant isomer in each case was the one predicted by Cram's rule of asymmetric induction.[6] Although the stereoselectivity of phenylmagnesium bromide reagent appears to be somewhat less than that observed for phenyllithium, no dramatic reversal of product distribution was noted in the course of this work, contrary to the reversal noted by Yoshimura, Ohgo, and Sato[3] for their work involving the addition of these two reagents to *N*-benzyl-2,3-*O*-

(1) (a) Presented at 155th National Meeting of the American Chemical Society, San Francisco, Calif., March 1968, Abstracts, p C2. (b) National Science Foundation Undergraduate Research Program Participant, Grant No. GY-817.

(2) T. D. Inch, R. V. Levy, and P. Rich, *Chem. Commun.*, 865 (1967).

(3) J. Yoshimura, Y. Ohgo, and T. Sato, *J. Amer. Chem. Soc.*, **86**, 3860 (1964).

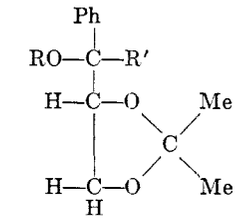
(4) M. Tiffeneau, I. Neuberg-Rabinovitch, and H. Cahnmann, *Bull. Soc. Chim. Fr.*, [v] **2**, 1866 (1935).

(5) E. Baer and H. O. L. Fisher, *J. Biol. Chem.*, **128**, 463 (1939).

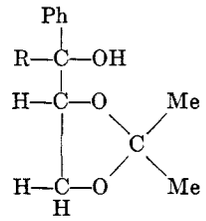
(6) (a) D. J. Cram and F. A. Abd. Elhafez, *J. Amer. Chem. Soc.*, **74**, 5828 (1952); (b) D. J. Cram and D. R. Wilson, *ibid.*, **85**, 1245 (1963).

isopropylidene-D-glyceraldimine, which is a nitrogen analog of 2,3-*O*-isopropylidene-D-glyceraldehyde.

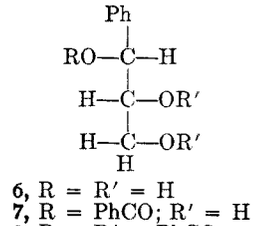
Assignment of structures to the two diastereomers was made by converting them into compounds of known configuration and supported by study of the intramolecular hydrogen bonding present in **1** and **4**. The absolute configuration of crystalline 2,3-*O*-isopropylidene-D-*threo*-1-*C*-phenylglycerol (**1**, mp 74–75°) was firmly established by benzoylation to give a monobenzoate (**2**), which was hydrolyzed by dilute acid to give 1-*O*-benzoyl-D-*threo*-1-*C*-phenylglycerol (**7**). Lead tetraacetate cleavage of **7** followed by lithium aluminum hydride reduction of the cleavage product gave optically pure L-(−)-1-phenyl-1,2-ethanediol (**14**), $[\alpha]^{23}D$ −57.8°. This compound with rotation of $[\alpha]^{28}D$ −47.1° was prepared by Eliel and Delmonte[7] by hydride reduction of D-(−)-mandelic acid of 82% optical purity. Assuming that the optical purity reported by Eliel and Delmonte is correct, simple calculation indicates that the L-(−)-1-phenyl-1,2-ethanediol from the degradation study is optically pure, which, in turn, suggests that all the steps in the reaction sequence from 2,3-*O*-isopropylidene-D-glyceraldehyde to L-(−)-1-phenyl-1,2-ethanediol proceeded with complete retention of configuration. This degradation study firmly established the configuration of the benzylic carbon; hence, the configuration of **1** must be D-*threo*, since the other asymmetric carbon was of known configuration and no evidence of racemization was noted in the reaction sequence.



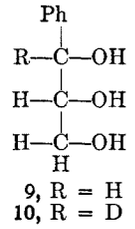
1, R = H; R′ = H
2, R = PhCO; R′ = H
3, R = H; R′ = D



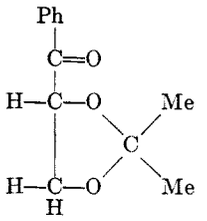
4, R = H
5, R = D



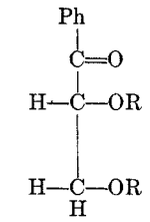
6, R = R′ = H
7, R = PhCO; R′ = H
8, R = R′ = PhCO



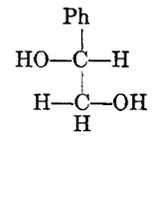
9, R = H
10, R = D



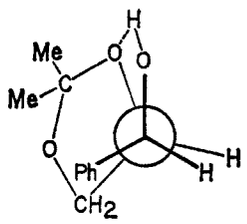
11



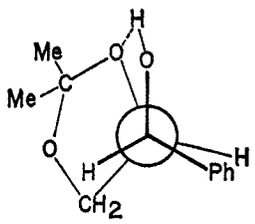
12, R = H
13, R = PhCO



14



4a, D-*erythro*



1a, D-*threo*

The structural assignment for the liquid 2,3-*O*-isopropylidene-D-*erythro*-1-*C*-phenylglycerol (**4**) was supported by dilute acid hydrolysis of the isopropylidene group to yield D-*erythro*-1-*C*-phenylglycerol (**9**) whose physical constants were identical with those reported for "α-D-phenylglycerol."[4] The diastereomeric relationship of **1** and **4** can be deduced from the fact that dicyclohexylcarbodiimide–dimethyl sulfoxide oxidation of **1** or a mixture of **1** and **4** yielded the same ketone (**11**). Also, lithium aluminum hydride reduction of the ketone (**11**) produced the diastereomers **1** and **4**, identical in all respects with the products obtained from the organometallic addition reactions. On the basis of acid hydrolysis, oxidation, and reduction studies described, it can be concluded that **4** must have the *erythro* configuration.

Additional support for the structural assignment of the *threo* configuration to **1** and the *erythro* configuration to **4** was obtained by an infrared spectrometric study of their intramolecular hydrogen bond strengths; in fact, tentative structural assignment was made on this basis. The Newman representation **1a** and **4a** of the diastereomers, drawn in the conformation most favorable for hydrogen bonding between the 1-hydroxyl hydrogen atom and the C-2 oxygen atom, clearly shows that in the D-*threo* isomer (**1a**) the phenyl group is aligned with a hydrogen, whereas in the D-*erythro* isomer (**4a**) the phenyl is aligned with C-3. Since repulsion between hydrogen and phenyl is less than between methylene and phenyl, the *threo* isomer provides the more favorable spatial arrangement for intramolecular hydrogen bonding. Infrared spectra of very dilute solutions of **1** and **4** in carbon tetrachloride provided $\Delta\nu$ values for the *threo* (35 cm^{-1}) and *erythro* (30 cm^{-1}) diastereomers. The frequency difference, $\Delta\nu$, is the distance (in cm^{-1}) between the free hydroxyl band and the bonded hydroxyl band. Kuhn[8] showed that a direct relationship exists between $\Delta\nu$ and the strength of the hydrogen bond; *e.g.*, he noted that a weaker hydrogen bond is formed in *meso*-butane-2,3-diol ($\Delta\nu$ = 39 cm^{-1}) than in *d*-butane-2,3-diol ($\Delta\nu$ = 45 cm^{-1}). Kuhn attributes the difference in hydrogen bond strength between these diastereomers to the fact that formation of an intramolecular hydrogen bond between the two hydroxyl groups requires a sterically unfavorable eclipsing of the two methyl groups in the *meso* isomer, whereas only hydrogen-methyl eclipsing is involved in the *d* isomer. By analogy, the crystalline diastereomer (**1**) having the larger $\Delta\nu$ value was assigned the D-*threo* configuration, since the molecule with this configuration would experience the least steric repulsion when it assumes the most favorable conformation for hydrogen bonding.

Ketone **11** was prepared by dicyclohexylcarbodiimide–dimethyl sulfoxide oxidation of either **1** or **4**. The ketone (**11**) provides a route for introducing a deuterium atom to the benzylic position of **1** and **4**. When **11** was reduced by lithium aluminum deuteride in anhydrous ether, 2,3-*O*-isopropylidene-D-*threo*-1-*C*-phenyglycerol-1-d_1 (**3**) and 2,3-*O*-isopropylidene-D-

(7) E. L. Eliel and D. Delmonte, *J. Org. Chem.*, **21**, 595 (1956).

(8) L. P. Kuhn, *J. Amer. Chem. Soc.*, **74**, 2492 (1952).

TABLE I
CHEMICAL SHIFTS AND COUPLING CONSTANTS 1-C-PHENYLGLYCEROLS AND DERIVATIVES

	Solvent	Chemical shifts, ppm				Coupling constants, Hz			
		H_1	H_2	H_3	H_3'	J_{12}	J_{23}	$J_{23'}$	$J_{33'}$
D-*threo*-1-*C*-Phenylglycerol (**6**)	D_2O	4.66	3.87	3.43	3.43	6.5	3.5	6.5	
D-*erythro*-1-*C*-Phenylglycerol (**9**)	D_2O	4.63	3.89	3.78	3.52	6.5	3.0	7.0	12
D-*erythro*-1-*C*-Phenylglycerol-1-d_1 (**10**)	D_2O		3.89	3.78	3.53		3.0	7.0	12
1,2,3-tri-*O*-Benzoyl-D-*threo*-1-*C*-phenylglycerol (**8**)	$DCCl_3$	6.53	6.05	4.67	4.33	7.0	4.0	5.5	12
(*R*)-α,β-Dihydroxypropiophenone (**12**)	$DCCl_3$		5.15	4.01	3.68		3.5	5.0	12
(*R*)-α,β-Dibenzoyloxypropiophenone (**13**)	$DCCl_3$		6.57	5.02	4.73		4.0	7.0	12

erythro-1-*C*-phenylglycerol-1-d_1 (**5**) were produced in the ratio of 67:33, respectively. The deuterated diastereomers have identical physical constants with their hydrogen counterparts. The nmr signals for the H_1 proton at δ 4.50 for the *threo* isomer and 4.85 for the *erythro* isomer were absent in the spectra of the deuterated isomers.

A benzene solution of the ketone (**11**) was reduced with lithium aluminum hydride to give the diastereomers **1** and **4** in the ratio of 60:40, respectively. Apparently, the product distribution is not altered drastically by the nature of the solvent. It is surprising to find that the synthesis of **1** and **4** either *via* the addition of phenyllithium or phenylmagnesium bromide to 2,3-*O*-isopropylidene-D-glyceraldehyde or *via* hydride reduction of ketone **11** favors the *threo* isomer. Cram and Allinger[9] demonstrated that the synthesis of 1,2-diphenyl-2-methyl-1-butanol *via* the addition of phenylmagnesium bromide to 2-methyl-2-phenylbutanal favored the formation of one diastereomer, whereas synthesis *via* hydride reduction of 1,2-diphenyl-2-methyl-1-butanone favored the other, which is in accordance with Cram's rule of asymmetric reduction.[6a]

Several model transition states have been proposed to help predict and correlate the addition to and the reduction of carbonyl compounds containing heteroatoms on the α position: the cyclic model,[6b] where the metal ion coordinates with the carbonyl oxygen and the heteroatom on the α position; the dipolar model,[10] where the substrate molecule assumes a conformation placing the carbonyl oxygen, and the heteroatom on the α position as far apart as possible; and the eclipsed model,[11] where the double bond of the carbonyl group eclipses the single bond of the α position giving the lowest energy transition state. After careful consideration of these model transition states, it was concluded that not one model can be chosen which could explain consistently the favored formation of **1** over **4** by both synthetic routes. Conceivably, the oxygen on C-3 may have an undetermined influence on these reactions. Since hydrogen bonding study seems to suggest that the predominating *threo* isomer (**1**) is more stable than the *erythro* isomer (**4**), perhaps, the stereoselectivity in this work is controlled by product stability, as proposed by Brown and Muzzio[12] for some acyclic ketones.

Magnetic nonequivalence resulting from molecular asymmetry was reviewed by Martin and Martin.[13] Some additional examples of nonequivalent methylene protons in nonrigid molecules were reported by Snyder.[14] The 1-*C*-phenylglycerols and their derivatives (Table I) having one or more asymmetric centers, gave complex splitting patterns. It was surprising to find, however, that the splitting pattern for all the acyclic 1-*C*-phenylglycerols and derivatives could be identified by their resemblance to first-order splitting. The values listed in Table I were obtained by the trial and error method suggested by Bible[15] and are found to match the spectra rather well; *e.g.*, see Figures 1 and 2. Correct assignment for proton resonance was aided by comparing the spectra of the phenylglycerols and the same isomers having a deuterium in place of a hydrogen at the benzylic carbon. The absence of the doublet in the δ 4.6 region (proton on C-1) and the deuterium quadrupole broadening of the multiplet at δ 3.8 (proton on C-2) in the spectra of the deuterated compound as compared to the spectra of its parent hydrogen compound permitted the assignment of the δ 4.6 region to the proton on C-1, δ 3.9 region to the proton on C-2, and δ 3.4–3.8 region to the geminal protons on C-3. It is interesting to note that the configurational difference at C-1 of the diastereomeric phenylglycerols is

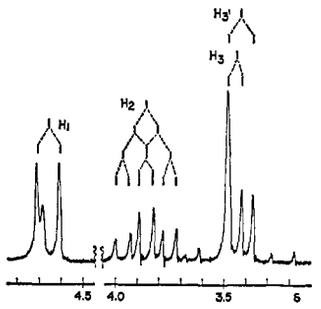


Figure 1.—A partial nmr spectrum (D_2O) at 60 MHz and the splitting pattern from first-order consideration of D-*threo*-1-*C*-phenylglycerol. The phenyl protons are not shown. Resonance peak at δ 4.7 is due to DOH.

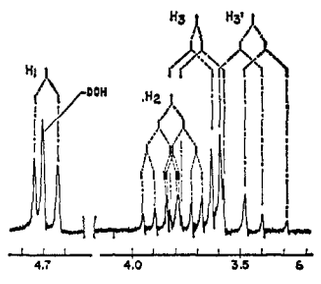


Figure 2.—A partial nmr spectrum (D_2O) at 60 MHz and the splitting pattern from first-order consideration of D-*erythro*-1-*C*-phenylglycerol. The phenyl protons are not shown.

(9) D. J. Cram and J. Allinger, *J. Amer. Chem. Soc.*, **76**, 4516 (1954).
(10) J. W. Cornforth, R. H. Cornforth, and K. K. Mathews, *J. Chem. Soc.*, 112 (1959).
(11) G. J. Karabetsos, *J. Amer. Chem. Soc.*, **89**, 1367 (1967).
(12) H. C. Brown and J. Muzzio, *ibid.*, **88**, 2811 (1966).
(13) L. Martin and J. Martin, *Bull. Soc. Chim. Fr.*, 2117 (1966).
(14) E. I. Snyder, *J. Amer. Chem. Soc.*, **88**, 1155 (1966).
(15) R. H. Bible, "Interpretation of NMR Spectra—An Empirical Approach," Plenum Press, New York, N. Y., 1965.

manifested in the nmr spectra (Figures 1 and 2). The methylene region (δ ~3.4–3.8) is more complex for D-*erythro*- than for the D-*threo*-phenylglycerol. Apparently, the chemical shifts of the geminal protons of the D-*threo* isomer are very similar, thereby giving a simpler splitting pattern in comparison to the *erythro* isomer. The low intensity doublets, centered at δ 3.2 and 3.6 of the nmr spectrum for the *threo* isomer (Figure 1), could be the remnant of the outside lines for a more complex splitting pattern of the geminal protons.

Experimental Section[16]

The hydrogen bonding study was carried out in CCl_4 in a decimeter quartz cell using the Beckman IR-12 infrared spectrometer. Nuclear magnetic resonance spectra were obtained with a Varian A-60 instrument. All rotations were obtained in a decimeter cell in a Rudolph 80 polarimeter.

Gas chromatographic analyses were carried out using an Aerograph Model 328, thermal-conductivity instrument employing a 10 ft × 0.25 in. o.d. copper column. Helium flow was kept between 80 and 100 cc/min, column temperature was 190°, and the injection port temperature was maintained at 270°. Samples were collected in a glass U tube.

All column chromatographic purifications were carried out with a 20-mm diameter column of silicic acid (100–200 mesh), prepared by pouring a benzene slurry of the silicic acid (80 g) into a 20-mm i.d. glass column and permitting the silicic acid to settle undisturbed for 1 hr. The sample (dissolved in the minimal quantity of benzene and/or chloroform, if necessary) was added carefully to the column and eluted with 120-ml portions of solvent, which were applied to the column in order of increasing elution capacity. The eluent was collected in 60-ml fractions. The eluting solvent systems and the order of addition were benzene, benzene–chloroform (3:1, v/v), benzene–chloroform (1:1 v/v), benzene–chloroform (1:3 v/v), chloroform, chloroform–ethyl acetate (3:1, v/v), chloroform–ethyl acetate (1:1 v/v), chloroform–ethyl acetate (1:3 v/v), ethyl acetate, ethyl acetate–acetone (3:1 v/v), ethyl acetate–acetone (1:1 v/v), ethyl acetate–acetone (1:3 v/v), and acetone. The solvent system, which is listed for a given chromatographic purification, is the eluting solvent passing through the column when the major portion of the desired compound was eluted from the column. The eluent fractions were examined for contents by thin layer chromatography (tlc), which were conducted on 1 × 3 in. glass plates covered with a layer of Adsorbosil-3[17] using the solvent systems specified. The components were detected by iodine vapor.

Condensation of 2,3-*O*-Isopropylidene-D-glyceraldehyde[5] with Phenyllithium.—Bromobenzene (30 ml, 0.29 mol) was added dropwise to an ether (300 ml) suspension of finely cut lithium ribbon (4.0 g, 0.57 g-atom) in a 500-ml flask, which was equipped with a condenser and drying tube. After all the bromobenzene was added, the suspension was stirred for 2 hr. 2,3-*O*-Isopropylidene-D-glyceraldehyde (17.0 g, 0.13 mol), dissolved in 30 ml of diethyl ether, was added slowly to the phenyllithium suspension with vigorous stirring. After stirring for 3 hr, the reaction mixture was poured into ice–water. The organic layer was washed twice with 100-ml portions of water and dried over anhydrous sodium sulfate. Solvent removal under reduced left 27 g of an amber syrup. Gas chromatography of the syrup showed two major components with slightly different retention times. The relative ratio of the peak areas is 38:62 in favor of the isomer with the longer retention time. After cooling overnight, long needles formed in the syrup, which were collected on a sintered glass funnel and washed with *n*-hexane (8.4 g, mp 70–73°). Gas chromatography of the mother liquor again indicated the presence of two major components with identical retention times as the original syrup, but the peak area ratio (65:35) is now in favor of the faster moving component. The change in peak area ratio suggests that the isomer with the longer retention time is the crystalline one.

A pure sample of the crystalline compound (**1**) was obtained by two recrystallizations from *n*-hexane: mp 74–75°; $[\alpha]^{23}D$ −30.0° (*c* 3.0, CH_3OH); infrared absorption (5 × $10^{-3}M$ CCl_4), ν_{OH} 3623 and $\nu_{OH}..O$ 3588 cm^{-1}; nmr signals ($DCCl_3$) at δ 1.4 (-CH_3), 2.9 (-OH), 3.7 (H_3), 4.2 (H_2), 4.5 (H_1), 7.2 (ArH).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.19; H, 7.74. Found: C, 69.30; H, 7.62.

A pure sample of the liquid isomer (**4**) was obtained by repeated injections of 25-μl portions of an acetone solution of the isomeric mixture to a column (0.25 in × 10 ft) of 10% QF-1[18] on ABS-70/80[19] at 190°: $[\alpha]^{23}D$ +4.5° (*c* 4.0, CH_3OH); infrared absorption (5 × 10^{-3} *M*, CCl_4), ν_{OH} 3626 and $\nu_{OH}..O$ 3596 cm^{-1}; nmr signals ($DCCl_3$) at δ 1.14 (-CH_3), 2.6 (-OH), 3.9 (H_3), 4.2 (H_2), 4.9 (H_1), 7.3 (Ar-H).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.19; H, 7.74. Found: C, 69.29; H, 7.74.

Condensation of 2,3-*O*-Isopropylidene-D-glyceraldehyde with Phenylmagnesium Bromide.—The Grignard reagent was prepared by reacting magnesium metal (4.8 g, 0.19 g-atom) with bromobenzene (24 ml, 0.23 mol) in 300 ml of anhydrous ether. To the Grignard reagent was added 17.0 g of 2,3-*O*-isopropylidene-D-glyceraldehyde in small portions. The same reaction time and procedure used for the phenyllithium reaction was followed. Gas chromatography showed two major components in a ratio of 58:42 in favor of the crystalline isomer.

Benzoylation of the Crystalline Isomer (1).—The monobenzoate (**2**) was formed by dropwise addition of 2.6 ml of benzoyl chloride to 4.0 g of **1** in pyridine (30 ml). After standing overnight the reaction mixture was poured into ice–water from which **2** crystallized to yield 5.9 g, 98%. Recrystallization from ethanol gave a pure sample (5.5 g, 91%): mp 71.5–72.5°; $[\alpha]^{23}D$ +11.7° (*c* 3.6, $HCCl_3$).

Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.17; H, 6.68.

Determination of the Configuration of the Crystalline Isomer (1).—The isopropylidene group was hydrolyzed from 1 g of **2** by refluxing for 20 min in ethanol (40 ml) containing 2 ml of 3 *N* HCl. After neutralizing the acid, 1-*O*-benzoyl-1-*C*-phenylglycerol (**7**) was isolated as a syrup, which was purified by Biosil A[20] column chromatography, eluting with chloroform–ethyl acetate (3:1); tlc showed one spot, R_f 0.38 (chloroform). A 10-ml benzene solution of compound **7** (0.5 g) was allowed to react for 10 min with lead tetraacetate (3.2 g). After the excess lead tetraacetate was destroyed by adding 1 ml of ethylene glycol to the reaction mixture, the inorganic salts were removed by filtration. The filtrate was diluted with 50-ml of diethyl ether, washed twice with 10% aqueous bicarbonate solution, dried over anhydrous sodium sulfate, and concentrated *in vacuo* to a syrup. The syrup, dissolved in 5 ml of ether, was added to 0.2 g of $LiAlH_4$ suspended in 15 ml of anhydrous ether. After 3 hr, sufficient water was added carefully to the reaction mixture to destroy the excess hydride and cleave the complex, without forming a distinct aqueous layer. After removal of inorganic salts by filtration, the ethereal filtrate was concentrated *in vacuo* to a syrup. The crude syrup was chromatographed on a column of Bio-sil A (80 g), eluting with chloroform–ethyl acetate (1:3 v/v) to give chromatographically pure syrup (0.14 g, 56%) which slowly crystallized from a small volume of ether–pentane (1:3 v/v); tlc showed one spot, R_f 0.65 (ethyl acetate). Pure crystalline L-(−)-1-phenyl-1,2-ethanediol (**14**) was obtained by recrystallization from ether–pentane (1:3 v/v): mp 66–67°, $[\alpha]^{23}D$ −57.8° (*c* 3.2, ether) {lit. mp 67°, $[\alpha]^{20}D$ −47.1° (ether), from hydride reduction of D-(−)-mandelic acid of 82% optical purity[7]}.

Oxidation of Compounds 1 and 4 to 4-(*R*)-Benzoyl-2,2-dimethyldioxolane (11).—Moffatt's reagent[21] was prepared by carefully adding dicyclohexylcarbodiimide (7.5 g), pyridine (1 ml), and trifluoroacetic acid (0.5 ml) to 30 ml of cold benzene–dimethyl sulfoxide (1:1 v/v). To the prepared reagent, a 10-ml benzene solution of compound **1** (0.55 g) was added and stored overnight at room temperature. After removal of the solid material by filtration, the filtrate was diluted by adding diethyl

(16) Elemental Analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind. All melting points are uncorrected.

(17) Silicic acid with 10% binder, 10–18 Å, Applied Science Laboratories, Inc., State College, Penn.

(18) A fluorosilicone polymer, Analabs, Inc., Hamden, Conn.

(19) Acid- and base-washed, silanized diatomaceous earth, 70/80 mesh, Analabs, Inc., Hamden, Conn.

(20) Chromatographic grade silicic acid, 100–200 mesh, Bio-Rad Laboratories, Richmond, Calif.

(21) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, **87**, 5670 (1965).

ether (50 ml). The ethereal solution was washed twice with 10% aqueous oxalic acid, followed by a 10% aqueous sodium bicarbonate washing, then dried over sodium sulfate. Solvent removal *in vacuo* left a residual syrup (0.50 g), which crystallized on adding pentane and cooling. The crystals were removed by filtration and washed with a little cold pentane (0.26 g, 47%; mp 58–60°). Some difficulty was noted in removing the decomposition by-products from **11**.

Using this procedure, isomeric mixtures of compounds **1** and **4** were were oxidized to compound **11** in comparable yield.

A pure sample of compound **11** was obtained by three crystallizations from pentane: mp 61–62°; $[\alpha]^{23}D$ +15.3° (*c* 3.6, CH_3OH); nmr signals ($DCCl_3$) at δ 1.4 ($-CH_3$), 4.3 (H_3), 5.2 (H_2), 7.4 and 8.0 (Ar–H).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.76; H, 6.91.

2,3-*O*-Isopropylidene-D-*threo*-1-*C*-phenylglycerol-1-d_1 (3) and 2,3-*O*-Isopropylidene-D-*erythro*-1-*C*-phenylglycerol-1-d_1 (5) from Compound 11.—An ether solution (10 ml) of compound **11** (0.40 g) was added slowly to a suspension of $LiAlD_4$ (0.15 g) in ether (50 ml). After 24 hr, moist ether was added to destroy the excess $LiAlD_4$ and the inorganic solids were removed by filtration. The filtrate was concentrated *in vacuo* to a syrup (0.37 g). Gas chromatography indicated the presence of two components with the same retention times as **1** and **4**. The isomeric distribution was 67:33 in favor of the crystalline isomer (**3**).

On standing overnight in a little pentane, compound **3** crystallized from solution. The crystals (0.11 g) were isolated by filtration and washed with a little cold pentane. Pure 2,3-*O*-isopropylidene-D-*threo*-1-*C*-phenylglycerol-1-d_1 (**3**) was obtained by sublimation at 0.05 mm (60° bath): mp 74–75°; admixture with compound **1**, mp 74–75°; $[\alpha]^{23}D$ −28.1° (*c*, 3.6, CH_3OH); nmr signals ($DCCl_3$) at δ 1.4 ($-CH_3$), 2.9 (–OH), 3.7 (H_3), 4.2 (H_2), 7.4 (Ar–H).

Anal. Calcd for $C_{12}H_{15}DO_3$: C, 68.87; H + D, 8.19. Found: C, 69.09; H + D, 8.04.

A pure sample of 2,3-*O*-isopropylidene-D-*erythro*-1-*C*-phenylglycerol-1-d_1 (**5**) was obtained by preparative glpc. Although chromatographically pure, the syrup could not be induced to crystallize: $[\alpha]^{23}D$ +4.3° (*c* 2.5, CH_3OH); nmr signals ($DCCl_3$) at δ 1.4 ($-CH_3$), 2.5 (–OH), 3.9 (H_3), 4.3 (H_2), 7.3 (Ar–H).

Lithium Aluminum Hydride Reduction of 11 in Benzene.—A benzene solution (1 ml) of **11** (.043 g) was added dropwise to a suspension of $LiAlH_4$ (0.1 g) in benzene (10 ml). The reaction conditions and procedure of the previous experiment were followed. Product analysis by glpc indicated that the reduction favored the crystalline over the liquid isomer in the ratio of 6:4. The crystalline and liquid products were identified as compounds **1** and **4**, respectively, by glpc and ir and nmr spectroscopy.

D-*threo*-1-*C*-Phenylglycerol (6) from 1.—A solution of compound **1** (1.0 g) and 3 *N* HCl (1 ml) in ethanol (20 ml) was refluxed for 1 hr. The solution was neutralized with Ag_2CO_3 and the solids removed by filtration; the filtrate was concentrated *in vacuo* to a syrup (0.71 g), which could not be induced to crystallize. The syrup (0.71 g) was applied to a column of Bio-sil A (80 g), eluting with ethyl acetate–acetone (3:1 v/v) to yield chromatographically pure D-*threo*-1-*C*-phenylglycerol (0.51 g, 62%): tlc, one spot, R_f 0.56 (ethyl acetate); $[\alpha]^{23}D$ −38.6° (*c* 3.5, CH_3OH); nmr signals (D_2O) at δ 3.4 (H_3), 3.9 (H_2), 4.7 (H_1), 7.4 (Ar–H).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.26; H, 7.19. Found: C, 64.38; H, 7.27.

1,2,3-tri-*O*-Benzoyl-D-*threo*-1-*C*-phenylglycerol (8) from 6.—Benzoyl chloride (0.7 ml) was added dropwise to a solution of **6** (0.3 g) in pyridine (15 ml) and the mixture stored at room temperature overnight. Crystalline **8** was obtained, when the reaction mixture was poured into water and stirred to yield 0.8 g, 93%. Two recrystallizations from benzene–pentane gave pure **8**: mp 139–140°; $[\alpha]^{23}D$ +12.2° (*c* 4.42, $HCCl_3$); nmr signals ($DCCl_3$) at δ 4.5 (H_3), 6.1 (H_2), 6.5 (H_1), 7.4 and 8.0 (Ar–H) (lit.[4] mp 110° for *dl-threo*-tribenzoate).

Anal. Calcd for $C_{30}H_{24}O_6$: C, 74.98; H, 5.03. Found: C, 74.54; H, 5.07.

D-*erythro*-1-*C*-Phenylglycerol (9).—The syrupy product (3.0 g), obtained from the phenyllithium addition to 2,3-*O*-isopropylidene D-glyceraldehyde, 3 *N* HCl (4 ml), and ethanol (35 ml) were heated under reflux for 1.5 hr. After neutralization of the acid with Ag_2CO_3 and filteration to remove the inorganic solids, the filtrate was concentrated *in vacuo* to give a syrup (2.3 g) which was dissolved in a small volume of chloroform. Compound **9** crystallized from the chloroform solution and was removed by filtration (0.7 g, mp 97–104°). D-*erythro*-1-*C*-Phenylglycerol was purified by two recrystallizations from acetone: mp 106–107°; $[\alpha]^{23}D$ +19.6° (*c* 6.34, H_2O); nmr signals (D_2O) at δ 3.6 (H_3), 3.8 (H_2), 4.6 (H_1), 7.3 (Ar–H) [lit.[4] mp 105–106°, $[\alpha]D$ +18.4° (10% aqueous), for α-D-phenylglycerol].

D-*erythro*-1-*C*-Phenylglycerol-1-d_1 (10) from 5.—A chromatographically pure sample of **5** (25 mg) and 3 *N* HCl (0.1 ml) were dissolved in ethanol (3.0 ml) and the solution was heated under reflux for 1 hr. The same work-up described for the preparation of **9** was followed to yield 16 mg of syrup, which crystallized upon adding acetone and cooling: mp 106–107°; admixture with **9**, mp 106–107°; $[\alpha]^{23}D$ +19.0° (*c* 1.6, D_2O); nmr signals (D_2O) at δ 3.5 (H_3), 3.8 (H_2), 7.3 (Ar–H).

(*R*)-α,β-Dihydroxypropiophenone (12) from 11.—An acetone solution (5 ml) of **11** (0.20 g) and 1 *N* HCl (0.25 ml) was heated under reflux for 5 min. After neutralization of the acid with Ag_2CO_3 and removal of the solids by filtration, the filtrate was concentrated *in vacuo* to give a syrup (0.12 g). A pure sample of **12** was obtained by chromatographing the syrup (0.12 g) on a column of Bio-sil A (80 g), eluting with ethyl acetate: tlc, one spot, R_f 0.71 (ethyl acetate); $[\alpha]^{23}D$ +72.1° (*c* 8.0, H_2CCl_2); nmr signals ($DCCl_3$) at δ 3.7 (H_β), 4.5 (–OH), 5.1 (H_α), 7.4 and 7.9 (Ar–H).

(*R*)-α,β-Dibenzoyloxypropiophenone (13) from 12.—Standard benzoylation procedure using benzoyl chloride in methylene chloride–pyridine solution converted **12** (0.10 g) into the dibenzoate, which was purified by chromatographing on a Bio-sil A (80 g) column, eluting with benzene–chloroform (1:1 v/v); tlc showed one spot, R_f 0.50 (benzene). Compound **13** could not be induced to crystallize: $[\alpha]^{23}D$ −51.4° (*c* 2.7, H_2CCl_2); nmr signals ($DCCl_3$) at δ 4.8 (H_β), 6.6 (H_α), 7.5 and 8.0 (Ar–H).

Anal. Calcd for $C_{23}H_{18}O_5$: C, 73.79; H, 4.85. Found: C, 73.67; H, 4.72.

Registry No.—**1**, 16354-89-5; **2**, 16355-01-4; **3**, 16354-90-8; **4**, 16354-91-9; **5**, 16354-92-0; **6**, 16354-93-1; **8**, 16354-94-2; **9**, 16354-95-3; **10**, 16354-96-4; **11**, 16354-97-5; **12**, 16354-98-6; **13**, 16354-99-7; **14**, 16355-00-3.