stant value (12 hr. approx.). After 24 hr., titration of an aliquot revealed the consumption of 0.94 mole of periodic acid. An additional 24 hr. produced no further change in the periodate consumption.

The reaction mixture was neutralized ($BaCO_3$) and filtered. The filtrate was distilled at atmospheric pressure and the first 5 ml. of the distillate treated with a solution of dimedone (100 mg.) in ethanol (2 ml.). After standing several hours the white crystalline dimedone derivative of formaldehyde (10 mg.) was separated, m.p. and mixed m.p. 190° (after recrystallization from 50% ethanol).

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[CONTRIBUTION FROM THE DEPARTMENT OF AGRICULTURAL BIOCHEMISTRY, UNIVERSITY OF MINNESOTA]

Synthesis of D- and of L-α-*O*-Methylglycerol[1]

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The synthesis of D- and of L-α-*O*-methylglycerol is described.

During methylation studies on the reduced products of periodate oxidized pentosans, a substance believed to be an optically active α-*O*-methylglycerol was encountered. A literature search revealed that while the racemic modification of this substance has been known for many years[2,3] the preparation of either of its enantiomorphic forms has not been carried out, although an unsuccessful attempt to resolve the D,L-mixture by the use of optically active ketones (camphor and menthone) is reported.[2] α-*O*-Methylglycerol has been encountered but not characterized in studies on the glycosides of red algae (*Ceramium rubrum*).[4]

(1) Methyl 6-*O*-methyl-α-D-galactopyranoside

↓ Periodate oxidn.

D′-Methoxy-D-methoxymethyl-diglycolic aldehyde

↓ Reduction with H_2

D′-Methoxy-D-methoxymethyl-diethylene glycol

↓ Hydrolysis

D-α-*O*-Methylglycerol

(2) Methyl α-D-glucopyranoside

↓ Periodate oxidn.

D′-Methoxy-D-hydroxymethyl-diglycolic aldehyde

↓ Br_2 oxidn.

Strontium D′-methoxy-D-hydroxymethyl-diglycolate

↓ H^+, Ag_2O

Silver D′-methoxy-D-hydroxymethyl-diglycolate

↓ MeI + Ag_2O

D′-Methoxy-D-methoxymethyl-dimethyl-diglycolate

↓ $LiAlH_4$

D′-Methoxy-D-methoxymethyl-diethylene glycol

↓ Hydrolysis

D-α-*O*-Methylglycerol

This paper describes five different approaches to the preparation of optically active α-*O*-methylglycerol, two for the D- and three for the L-isomer; in each case the tedious process of resolution is avoided.

The D-isomer of α-*O*-methylglycerol was prepared by the two independent routes outlined.

The D-α-*O*-methylglycerol from the two experiments showed $[\alpha]^{21}D$ +5.9° and +5.4° (ethanol), respectively, and was characterized as the crystalline bis-*p*-nitrobenzoate. Its designation as the D-isomer follows the convention[5] which relates it to that form of glyceraldehyde into which the substance may be hypothetically oxidized without alteration or removal of substituents on the glycerol molecule.

By use of these procedures the configuration of each intermediate was known with certainty and hence it was possible to relate unambiguously the structure with sign of rotation, one of the purposes of this investigation. In addition, correlation with other species of known configuration was rendered unnecessary.

The three schemes employed for the synthesis of L-α-*O*-methylglycerol are shown.

The L-α-*O*-methylglycerol obtained by the three methods showed specific rotations in good agreement, numerically, with the values for the D-isomer.

Optically active 1,2-*O*-isopropylidene glycerol was used with great effectiveness by Baer and Fischer[6] for the preparation of optically active glycerides. These workers subjected the above compound to methylation to give 1,2-*O*-isopropylidene-L-3-*O*-methylglycerol from which L-α-*O*-methylglycerol was obtained by hydrolysis. The latter was not isolated and the authors, interested only in demonstrating the presence of adjacent hydroxyl groups, treated the hydrolyzed reaction mixture directly with periodic acid and reported a periodate consumption of one molecular proportion.

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(1) Paper No. 3585, Scientific Journal Series, Minnesota Agricultural Experiment Station, University of Minnesota, St. Paul, Minn.

(2) J. C. Irvine, L. A. Macdonald and C. W. Soutar, *J. Chem. Soc.*, **107**, 337 (1915).

(3) H. S. Hill, M. S. Whelen and H. Hibbert, THIS JOURNAL, **50**, 2235 (1928).

(4) H. Bouveng, B. Lindberg and B. Wickberg, *Acta Chem. Scand.*, **9**, 807 (1955).

(5) H. O. L. Fischer and E. Baer, *Chem. Rev.*, **29**, 287 (1941).

(6) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463, 475 (1939).

(1) Methyl 6-*O*-trityl-α-D-glucopyranoside
$\downarrow \mathrm{NaIO_4}$
D′-Methoxy-D-triphenylmethoxymethyl-diglycolic aldehyde
$\downarrow \mathrm{NaBH_4}$
D′-Methoxy-D-triphenylmethoxymethyl-diethylene glycol
$\downarrow \mathrm{Ag_2O + MeI}$
D′-Methoxy-D-triphenylmethoxymethyl-di-*O*-methyl-diethylene glycol
$\downarrow$ Hydrolysis
L-α-*O*-Methylglycerol

(2) β-1,6-Anhydro-D-glucopyranose (β-glucosan)
$\downarrow \mathrm{HIO_4}$
L′-Oxy-D-methylene-diglycolic aldehyde
$\downarrow \mathrm{H_2}$ + Raney nickel
L′-Oxy-D-methylene-diethylene glycol
$\downarrow \mathrm{Ag_2O + MeI}$
L′-Oxy-D-Methylene-di-*O*-methyl-diethylene glycol
$\downarrow$ Hydrolysis
L-α-*O*-Methylglycerol

(3) 1,2;5,6-Di-*O*-isopropylidene-D-mannitol
$\downarrow \mathrm{Pb(OAc)_4}$; reduction
D-2,3-*O*-Isopropylideneglycerol
$\downarrow \mathrm{Ag_2O + MeI}$
1,2-*O*-Isopropylidene-L-3-*O*-methylglycerol
$\downarrow$ Hydrolysis
L-α-*O*-Methylglycerol

In the present work L-α-*O*-methylglycerol was characterized as a crystalline *p*-nitrobenzoate. The bis-*p*-nitrobenzoate of racemic α-*O*-methylglycerol melts about 25° higher than either of the optically active forms, a result in agreement with the general finding that in certain cases a racemic compound melts higher than either of the enantiomorphic forms.

This work has further shown that by controlling conditions the dialdehydes formed upon periodate oxidation of sugar glycosides may be used as intermediates in organic syntheses with complete retention of configuration.

Experimental

A. Synthesis of D-α-*O*-**Methylglycerol**. 1. **From Methyl 6-*O*-Methyl-α-D-galactopyranoside.** (a) **1,2;3,4-Di-*O*-isopropylidene-6-*O*-methyl-D-galactopyranose.**—A solution of 1,2;3,4-di-*O*-isopropylidene-D-galactose[7] (50 g., b.p. (bath temp.) 144–148° (0.005 mm.), n^{25}_{D} 1.4645, $[\alpha]^{25}_{\mathrm{D}}$ −56° in chloroform (*c* 2.5)) in acetone (95 ml.) was methylated with methyl sulfate (162 ml.) and 30% sodium hydroxide (405 ml.) in the usual way. Extraction with chloroform followed by distillation gave 1,2;3,4-di-*O*-isopropylidene-6-*O*-methyl-D-galactopyranose as a pale yellow liquid, b.p. (bath temp.) 125° (0.001–0.004 mm.), n^{25}_{D} 1.4525, $[\alpha]^{25}_{\mathrm{D}}$ −63.9° in chloroform (*c* 5) (yield 31 g.).[8]

(b) **6-*O*-Methyl-D-galactopyranose.**—To a solution of 1,2;3,4-di-*O*-isopropylidene-6-*O*-methyl-D-galactopyranose (30 g.) in acetone (100 ml.) was added water (20 ml.) and concentrated hydrochloric acid (7 ml.) and the reaction mixture heated at 97° (bath temp.) for 8 hr. when the optical rotation became constant.

Neutralization with sodium hydroxide, concentration of the reaction mixture and addition of ethanol with cooling caused the separation of sodium chloride which was filtered. Concentration *in vacuo*, followed by crystallization from aqueous ethanol gave 6-*O*-methyl-D-galactose, 10.3 g., as white flakes, m.p. and mixed m.p. with an authentic specimen 126.5–127.5°.

(c) **Methyl 6-*O*-Methyl-α-D-galactopyranoside.**—A solution of 6-*O*-methyl-D-galactopyranose (5.0 g.) in 2% methanolic hydrogen chloride (25 ml.) was boiled under reflux until the rotation became constant (13 hr.). The reaction mixture was neutralized with silver carbonate, filtered, and concentrated *in vacuo* to a thick sirup which readily crystallized in the form of white rosettes. After two recrystallizations from methanol, the methyl 6-*O*-methyl-α-D-galactopyranoside (3.0 g.), in the form of white flakes, had m.p. 137–138°, $[\alpha]^{23}_{\mathrm{D}}$ +165° in water (*c* 1).

Anal. Calcd. for $\mathrm{C_8H_{16}O_6}$: C, 46.2; H, 7.8; $\mathrm{OCH_3}$, 29.8. Found: C, 46.2; H, 7.5; $\mathrm{OCH_3}$, 29.8.

(d) **Oxidation of Methyl 6-*O*-Methyl-α-D-galactopyranoside with Periodic Acid.**—To an aqueous solution (25 ml.) containing methyl 6-*O*-methyl-α-D-galactopyranoside (1.87 g.) was added 0.4 *N* periodic acid (100 ml.) and the volume adjusted to 200 ml. After about 12 hr. the rotation became constant and titration of an aliquot of the reaction mixture revealed the uptake of 2.00 moles of periodic acid per mole of glycoside. The reaction mixture was neutralized with barium carbonate, filtered to remove barium iodate and periodate and concentrated *in vacuo* (bath temp. 40°) in the presence of barium carbonate (0.5 g.). The precipitated inorganic salts were removed by several extractions of the product with ethanol and the combined ethanolic extracts concentrated to yield a turbid solution which was treated with charcoal, filtered and concentrated *in vacuo*. Considerable difficulty was experienced in drying the dialdehyde to constant weight. The viscous orange sirup (1.69 g.) showed n^{25}_{D} 1.4615 and $[\alpha]^{21}_{\mathrm{D}}$ +143° in ethanol (*c* 1).

(e) **Catalytic Hydrogenation of the Dialdehyde.**—Raney nickel (5 g. approx.) was added to an ethanol solution (65 ml.) containing the dialdehyde (1.64 g.) obtained above, and hydrogenation carried out at room temperature with a pressure of hydrogen (1750 p.s.i.). After 1 hr. the temperature was raised to 110° and held there for an additional 7 hr.

After filtering the Raney nickel catalyst, the solution of the reduced dialdehyde was concentrated *in vacuo*, bath temperature 40–45°, to an orange sirup (1.335 g.) which was distilled giving D′-methoxy-D-methoxymethyl-diethylene glycol as a colorless mobile liquid (1.0732 g.), b.p. (bath temp.) 124–130° (0.002 mm.), n^{22}_{D} 1.4455 and $[\alpha]^{20}_{\mathrm{D}}$ −12° in water (*c* 1.2).

(f) **The Bis-*p*-nitrobenzoate of D′-Methoxy-D-methoxymethyl-diethylene Glycol.**—To a solution of the sirupy alcohol (51 mg.) in pyridine (3 ml.) was added *p*-nitrobenzoyl chloride (130 mg.). After heating for 0.5 hr. at 100°, the reaction mixture was poured with stirring into an ice-cold saturated sodium bicarbonate solution (75 ml.) when pale yellow granules precipitated. The product was filtered and washed with water. After recrystallizing twice from ethanol, the white powder (135 mg.) had m.p. 98–102°, $[\alpha]^{27}_{\mathrm{D}}$ −19° in chloroform (*c* 1).

Anal. Calcd. for $\mathrm{C_{21}H_{22}O_{11}N_2}$: C, 52.7; H, 4.6; N, 5.9. Found: C, 52.7; H, 5.3; N, 6.0.

(g) **Hydrolysis of D′-Methoxy-D-methoxymethyl-diethylene Glycol and Isolation of D-α-*O*-Methylglycerol.**—A solution of the alcohol (1 g.) in water (50 ml.) containing sulfuric acid (0.7 ml.) was refluxed until the rotation became constant (45 min.). The solution was neutralized ($\mathrm{BaCO_3}$) filtered and evaporated *in vacuo* to a sirup. Distillation of the latter gave D-α-*O*-methylglycerol (0.33 g.) as a colorless liquid, b.p. (bath temp.) 95° (0.006 mm.), n^{25}_{D} 1.4424, and $[\alpha]^{21}_{\mathrm{D}}$ +5.9° in ethanol (*c*, 1.7).

Anal. Calcd. for $\mathrm{C_4H_{10}O_3}$: C, 45.3; H, 9.9. Found: C, 45.1; H, 9.8.

(h) **Bis-*p*-nitrobenzoate of** D-α-*O*-**Methylglycerol.**—A solution containing D-α-*O*-methylglycerol (25 mg.), *p*-nitrobenzoyl chloride (130 mg.) and pyridine (10 ml.) was heated on an oil-bath at 100° for 30 minutes. The cooled reaction mixture was then poured into an ice-cold saturated sodium

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[7] A. L. Raymond and E. F. Schroeder, THIS JOURNAL, **70**, 2785 (1948).

[8] K. Freudenberg and K. Smeykal, *Ber.*, **59**, 100 (1926).

bicarbonate solution to yield a turbid solution from which no crystals were deposited. The reaction mixture was therefore extracted with chloroform (five 20-ml. portions); the combined chloroform extracts were washed successively with water, dilute sulfuric acid, sodium bicarbonate solution and water, and dried over sodium sulfate. Evaporation of the chloroform extract produced a yellow sirup which was dissolved in ether (2 ml.) and treated with petroleum ether (b.p. 30–60°) until the first sign of turbidity; upon cooling crystallization occurred. A solution of the crystals (50 mg.) thus obtained in acetone (10 ml.) was treated with charcoal (0.5 g.), filtered and evaporated to a volume of about 1 ml. After adding ethanol and nucleating, crystalline bis-*O*-*p*-nitrobenzoyl-D-α-*O*-methylglycerol separated (45 mg.), m.p. 82–84°, $[\alpha]^{25}\mathrm{D}$ −45.2° in chloroform (*c* 1).

Anal. Calcd. for $C_{18}H_{16}O_9N_2$: C, 53.5; H, 4.0; N, 6.9. Found: C, 53.2; H, 3.8; N, 7.0.

2. **From D′-Methoxy-D-hydroxymethyl-diglycolic Acid.** (a) **D′-Methoxy-D-hydroxymethyl-diglycolic Acid.**—Oxidation of methyl α-D-glucopyranoside was effected with periodic acid and the dialdehyde oxidized with bromine in the presence of strontium carbonate.[9] The crystalline monohydrate of the strontium salt obtained in this manner showed $[\alpha]^{24}\mathrm{D}$ −46° in water (*c* 1).

(b) **D′-Methoxy-D-methoxymethyl-dimethyl-diglycolate.**—A solution of strontium D′-methoxy-D-hydroxymethyldiglycolate (1.94 g.) in water was percolated through a cation exchange resin (IR 120) and the column washed thoroughly with water. The eluate was neutralized with silver oxide, filtered and concentrated to dryness *in vacuo* at 30–35° (bath temp.) in the absence of light. The yellowish-white residue of silver salts was treated with methyl iodide (40 ml.) when a vigorous reaction (controlled by cooling) occurred. After the initial reaction was complete, silver oxide was added and the reaction mixture boiled under reflux for 7 hr. with vigorous shaking from time to time. After extracting the reaction mixture with ether, then methanol, the combined extracts were concentrated *in vacuo* to a yellow sirup which was dissolved in methyl iodide (25 ml.) and remethylated using silver oxide (3 g.). After three additional methylations in this manner, the yellow sirupy product was distilled giving D′-methoxy-D-methoxymethyl-dimethyl-diglycolate as a colorless liquid (975 mg.), b.p. (bath temp.) 143–148° (3 mm.), $n^{30}\mathrm{D}$ 1.4315, $[\alpha]^{29}\mathrm{D}$ +46.4° in ethanol (*c* 1).

Anal. Calcd. for $C_9H_{16}O_7$: OCH_3, 52.5. Found: OCH_3, 52.2.

Treatment of D′-methoxy-D-methoxymethyl-dimethyldiglycolate (60 mg.) with methanolic ammonia in the usual way followed by removal of the solvent gave the diamide of D′-methoxy-D-methoxymethyl-diglycolic acid (39 mg.), m.p. 169.5–170.5° after recrystallization from ethanol.

Anal. Calcd. for $C_7H_{14}O_5N_2$: C, 40.8; H, 6.8; N, 13.6; OCH_3, 30.1. Found: C, 41.1; H, 6.5; N, 13.5; OCH_3, 30.8.

(c) **Reduction of D′-Methoxy-D-methoxymethyl-dimethyl-diglycolate, with Lithium Aluminum Hydride.**—Pulverized lithium aluminum hydride (1.2 g.) was added to dry diethyl ether (120 ml.) and the slurry refluxed for 30 min. A solution of D′-methoxy-D-methoxymethyl-dimethyl-diglycolate (750 mg.) in ether (3 ml.) was added dropwise to the above solution. After the initial vigorous reaction had subsided, the mixture was refluxed for 1 hr. The excess lithium aluminum hydride was decomposed by the dropwise addition of an ethereal solution of ethyl acetate. Dilute acetic acid was added until the reaction mixture was slightly acid (tested with congo red). The ethereal solution was concentrated *in vacuo* and the last traces of water removed by azeotropic distillation with ethanol. To the dry residue were added anhydrous sodium acetate (0.6 g.) and acetic anhydride (40 ml.). After boiling the reaction mixture under reflux for 3 hr., the excess of the acetic anhydride was distilled *in vacuo*. Water (100 ml.) was added and the product extracted with chloroform (five 25-ml. portions). The combined chloroform extracts were washed with water and dried over sodium sulfate. Concentration of the filtered solution yielded D′-methoxy-D-methoxymethyl-diethylene glycol diacetate (703 mg.) which showed $[\alpha]^{27}\mathrm{D}$ −18° in ethanol (*c* 5).

A solution of this diacetate (500 mg.) in 0.1 *N* alcoholic potassium hydroxide (50 ml.) was refluxed for 45 min. Titration of the reaction mixture and also a blank with 0.06 *N* hydrochloric acid gave a saponification equivalent of 260 (calcd. 264). After adding concentrated ammonia (0.5 ml.) to ensure against acid conditions, the reaction mixture was concentrated to dryness *in vacuo*. Extraction with acetone gave a yellow sirup which was distilled to give D′-methoxy-D-methoxymethyl-diethylene glycol (311 mg.) as a pale yellow sirup, b.p. (bath temp.) 160–165° (5 mm.), $n^{25}\mathrm{D}$ 1.4490, and $[\alpha]^{25}\mathrm{D}$ −15° in ethanol (*c* 1). Treatment of the alcohol with *p*-nitrobenzoyl chloride in pyridine in the usual way, yielded the bis-*p*-nitrobenzoate of D′-methoxy-D-methoxymethyl-diethylene glycol, m.p. and mixed m.p. 100–102°, $[\alpha]^{22}\mathrm{D}$ −21° in chloroform (*c* 1.1) (after recrystallization from acetone–ethanol).

(d) **Hydrolysis of D′-Methoxy-D-methoxymethyl-diethylene Glycol and Isolation of D-α-*O*-Methylglycerol.**—To a solution of D′-methoxy-D-methoxymethyldiethylene glycol (319 mg.) in water (15 ml.) and ethanol (1 ml.) was added Amberlite IR 120 cation exchange resin (1 g.). The reaction mixture was refluxed for 4 hr. After filtering the resin the filtrate was concentrated to a sirup (236 mg.) which showed $[\alpha]^{22}\mathrm{D}$ +3.4° in ethanol (*c* 4.7). Paper chromatographic analysis showed the presence of α-*O*-methylglycerol, besides unchanged starting material which appeared as a streak extending from one-quarter to one-half the length of the chromatogram from the starting line.

The product was retreated with the cation exchange resin in the same manner for 5 hr. Removal of the resin and solvent followed by distillation gave D-α-*O*-methylglycerol (121 mg.) which showed $[\alpha]^{23}\mathrm{D}$ +5.4° in ethanol (*c* 1.7). Treatment with *p*-nitrobenzoyl chloride in the usual manner gave the characteristic bis-*p*-nitrobenzoate, m.p. and mixed m.p. with a specimen prepared as in A,1 (see above) 82–84°, $[\alpha]^{25}\mathrm{D}$ −45° in chloroform (*c* 1).

B. **Synthesis of L-α-*O*-Methylglycerol.** 1. **From β-1,6-Anhydro-D-glucopyranose (β-Glucosan).**—(a) β-Glucosan[10] was oxidized with periodic acid as previously described[11] to give L-oxy-D-methylenediglycolic aldehyde.

(b) **Reduction of L′-Oxy-D-methylene-diglycolic Aldehyde.**—Raney nickel (10 g.) was added to a solution of the sirupy dialdehyde (1.4 g.) in ethanol (60 ml.) and hydrogenation commenced at a pressure of hydrogen, 1250 p.s.i. at room temperature. After 1 hr. the temperature was raised to 100° and held there for 12 hr. After filtering the catalyst, the filtrate was concentrated *in vacuo* and the residue distilled to give L′-oxy-D-methylene-diethylene glycol (1.27 g.) as a colorless mobile liquid, b.p. (bath temp.) 102–110° (0.001 mm.), $[\alpha]^{23}\mathrm{D}$ +12.6° in ethanol (*c* 1.3) and $n^{22}\mathrm{D}$ 1.4685.

To a solution of L′-oxy-D-methylene-diethylene glycol (478 mg.) in pyridine (20 ml.), tosyl chloride (1.5 g.) was added. After standing at room temperature for 48 hr., the reaction mixture was poured with stirring into a saturated solution of sodium bicarbonate. After two recrystallizations from acetone–ethanol, the silky white needles (635 mg.) of the bis-*p*-toluenesulfonate showed $[\alpha]^{23}\mathrm{D}$ −0.7° in chloroform (*c* 21) and m.p. 86–87°.

Anal. Calcd. for $C_{19}H_{22}O_8S_2$: C, 51.6; H, 5.0; S, 14.5. Found: C, 51.8; H, 5.3; S, 13.8.

(c) **Methylation of L′-Oxy-D-methylene-diethylene Glycol.**—Silver oxide (5 g.) was added to a solution of the sirupy alcohol (644 mg.) in methyl iodide (25 ml.) and the reaction mixture was refluxed for 5.5 hr. After extracting with ether and concentrating the extract *in vacuo*, the product was remethylated in the same way. After three such methylations the product yielded upon distillation L-oxy-D-methylene-di-*O*-methyldiethylene glycol (618 mg.) as a mobile, colorless liquid, b.p. (bath temp.) 95–100° (3 mm.), $[\alpha]^{25}\mathrm{D}$ +4° in ethanol (*c* 1.6) and $n^{24}\mathrm{D}$ 1.4265.

Anal. Calcd. for $C_7H_{14}O_4$: C, 51.8; H, 8.7. Found: C, 51.6; H, 8.7.

(d) **L-α-*O*-Methylglycerol.**—Concentrated sulfuric acid (0.1 ml.) was added to a solution of L′-oxy-D-methylene-di-*O*-methyl-diethylene glycol (298 mg.) in 50% ethanol (25 ml.). After boiling the reaction mixture under reflux for 4.5 hr., it was neutralized with barium carbonate, filtered, and concentrated *in vacuo* to a yellow sirup (136 mg.).

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(9) E. L. Jackson and C. S. Hudson, This Journal, **59**, 994 (1937).

(10) Edna M. Montgomery, N. K. Richtmyer and C. S. Hudson *ibid.*, **65**, 3 (1943).

(11) E. L. Jackson and C. S. Hudson, *ibid.*, **62**, 958 (1940).

Distillation of the product gave L-α-*O*-methylglycerol (82 mg.), $[\alpha]^{28}\mathrm{D}$ −5.3° in ethanol (*c* 1.7).

A solution containing L-α-*O*-methylglycerol (51.7 mg.) and *p*-nitrobenzoyl chloride (200 mg.) in pyridine (5 ml.) was heated at 85° for 30 min. The cooled reaction mixture was poured with stirring into an ice-cold solution of sodium bicarbonate (100 ml.). The yellow precipitate which separated was filtered, washed with water, and recrystallized from acetone–ethanol to give the bis-*O*-*p*-nitrobenzoyl derivative of L-α-*O*-methylglycerol, as yellow needles, m.p. and mixed m.p. with a specimen synthesized from 1,2-*O*-isopropylideneglycerol as in B, 3 (see below) 82–84°, $[\alpha]^{27}\mathrm{D}$ +44.8° in chloroform (*c* 1.2).

2. **From Methyl 6-*O*-Trityl-α-D-glucopyranoside.** (a) **D′-Methoxy-D-trityloxymethyl-diglycolic Aldehyde.**—To a solution of methyl 6-*O*-trityl-α-D-glucopyranoside[12] (10.0 g.), in acetone (600 ml.) was added 0.4 *N* sodium periodate solution (125 ml., 26% excess). The volume was adjusted to 1 l. with water and the reaction allowed to proceed at room temperature until the rotation (initial value $\alpha\mathrm{D}$ (1 dm.) +0.60°) became constant (final value $\alpha\mathrm{D}$ +0.24° after 6 days). The periodate consumption had then reached a maximum of 1.70 moles and the formic acid production amounted to 0.5 mole per mole of trityl compound. The reaction mixture was extracted with four 200-ml. portions of benzene. After drying (Na_2SO_4) the combined benzene extracts were evaporated *in vacuo* (bath temp. 40–45°) to give a colorless sirup (8.06 g.) which showed $[\alpha]^{25}\mathrm{D}$ +30.3° in ethanol (*c* 1) and gave a positive test with Schiff and Fehling solutions.

(b) **D′-Methoxy-D-trityloxymethyl-diethylene Glycol.**—To a solution of the dialdehyde (8.05 g.) in methanol (50 ml.) was added a solution of sodium borohydride (1.5 g.) in methanol (50 ml.). The vigorous bubbling which ensued was moderated by cooling in an ice-bath. After 10 hr. the reaction mixture was neutralized with dilute acetic acid. Water (200 ml.) was added and the neutralized solution was extracted with four 100-ml. portions of ether. The combined ethereal extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the dihydric alcohol as a colorless, non-reducing sirup (8.09 g.) showing $[\alpha]^{23}\mathrm{D}$ −12.7° in ethanol (*c* 1.4) and $n^{23}\mathrm{D}$ 1.5640.

(c) **D′-Methoxy-D-trityloxymethyl-diethylene Glycol Dimethyl Ether.**—The alcohol (3.9 g.) obtained in (b) was dissolved in acetone (25 ml.) and methylated with methyl sulfate (100 ml.) and 40% potassium hydroxide (300 ml.), the reagents being added in 5 portions over a 50-minute period at room temperature. At this stage a light brown oil collected on the surface of the reaction mixture. A distillation head was attached to the apparatus and the acetone was distilled off at 55°. The yellow reaction mixture was extracted with ether (five 50-ml. portions) and the combined ethereal extracts dried (Na_2SO_4). Filtration and concentration *in vacuo* yielded a yellow sirup which was dissolved in acetone (50 ml.) and subjected to two more methlations using methyl sulfate (22 ml.) and 30% sodium hydroxide (66 ml.) at room temperature.

After drying (Na_2SO_4), the ethereal extracts from the third methylation were concentrated *in vacuo* (bath temp. 50°) to yield a yellow sirup which was treated with silver oxide (7 g.) and methyl iodide (25 ml.) under reflux for 5.5 hr. with stirring. Extraction with ether and concentration *in vacuo* gave an orange liquid (3.2 g.), $n^{24}\mathrm{D}$ 1.5542. The product showed no rotation in ethanol or in chloroform (*c* 1.5) (Found: OCH_3, 20.5, 21.0).

(d) **L-α-*O*-Methylglycerol.**—A solution of the methylated trityl compound (2.5 g.) in 0.57 *N* ethereal solution of hydrogen chloride (50 ml.) was kept in the refrigerator for 1.5 hr. The reaction mixture was allowed to come to room temperature and poured with stirring into ice-water (45 ml.). The ethereal layer was separated and re-extracted with 40 ml. of water. The combined aqueous extracts were boiled for 5 hr., neutralized ($PbCO_3$), filtered, and concentrated *in vacuo* to give an orange sirup containing inorganic salts which were separated by extracting the product with absolute ethanol. The reddish sirup obtained (423 mg.) consisted of L-α-*O*-methyl-glycerol and L-3,4-di-*O*-methylerythritol. Distillation of the sirupy product gave a colorless mobile liquid (295 mg.), b.p. (bath temp.) 100–102° (0.15 mm.), $n^{24}\mathrm{D}$ 1.4455, $[\alpha]^{24}\mathrm{D}$ −4° in ethanol (*c* 2).

A chromatogram of the distillate using 1-butanol:ethanol:water (5:1:4) as the irrigating solvent and a Tollens spray reagent showed two spots corresponding to (A) L-α-*O*-methylglycerol (R_f 0.63) and (B) L-3,4-di-*O*-methylerythritol (R_f 0.69). The distillate was applied to the top of a cellulose–hydrocellulose column[13] and separation effected with ethyl methyl ketone–water azeotrope using an automatic fraction collector adjusted so as to change receivers every 10 minutes. Spotting the contents of each tube on a piece of Whatman No. 1 filter paper and spraying with Tollens solution so as to reveal the presence of reducing compounds located the two components B, tubes 52–64, and A, tubes 70–96. The contents of tubes 70–96 were pooled and concentrated *in vacuo* to give a pale yellow sirup which upon distillation afforded L-α-*O*-methylglycerol (103 mg.), $[\alpha]^{22}\mathrm{D}$ −5.4° in ethanol (*c* 1). The bis-*p*-nitrobenzoate, prepared in the usual manner, had m.p. 81–83° and showed $[\alpha]^{22}\mathrm{D}$ +45° in chloroform (*c* 1).

Component B was later identified as L-3,4-di-*O*-methylerythritol. A discussion of this compound and the significance of its formation will constitute the subject of another paper.

3. **From D-2,3-*O*-Isopropylideneglycerol.**—A solution of 1,2-*O*-isopropylidene-L-3-*O*-methylglycerol, obtained from methylating 0.75 g. of D-1,2-*O*-isopropylideneglycerol[6] in 0.5 *N* sulfuric acid (25 ml.), was refluxed for 5 hr. Neutralization ($BaCO_3$), filtration, and concentration *in vacuo* yielded a yellow sirup which upon distillation gave L-α-*O*-methylglycerol as a mobile liquid b.p. (bath temp.) 97–100° (1.4 mm.)(0.320 g.), $n^{24}\mathrm{D}$ 1.4423, $[\alpha]^{21}\mathrm{D}$ −5.4° in ethanol (*c* 3).

To a solution (15 ml.) of L-α-*O*-methylglycerol (0.055 g.) in pyridine (15 ml.) was added *p*-nitrobenzoyl chloride (0.250 g.). The mixture was heated on an oil-bath (100°) for 30 minutes, cooled and poured into an ice-cold saturated solution of sodium bicarbonate. Vigorous stirring caused crystallization. Filtration yielded the bis-*p*-nitrobenzoate of L-α-*O*-methylglycerol as a yellowish powder (0.160 g.) which had m.p. 82–82.5°. Recrystallization from acetone–ethanol produced pale yellow needles, m.p. 82–84°, $[\alpha]^{27}\mathrm{D}$ +44.3° in chloroform (*c* 1).

Anal. Calcd. for $C_{18}H_{16}O_9N_2$: C, 53.5; H, 4.0; N, 6.9. Found: C, 53.7; H, 4.1; N, 6.6.

The bis-*p*-nitrobenzoate of racemic α-*O*-methylglycerol, made by mixing equal parts of the enantiomorphs, had m.p. 109°.

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