Cellobiose from the Mixed α- and β-Cellobiose Octaacetates.—A suspension of 3.0 g. of the finely powdered cellobiose octaacetates in 150 cc. of methyl alcohol was deacetylated by barium methylate in the usual manner, The disaccharide (1.5 g., quantitative) was obtained in the form of prisms which melted with decomposition at 225–226° (cor.); a mixed melting point determination with authentic cellobiose showed no depression; an aqueous solution of the substance showed initial and final rotations of +16.2° and +34.9° (*c*, 1.0), respectively, in water, with a mutarotation rate of 0.0043 at 20°. Hudson and Yanovsky[11] reported an initial rotation of +16°, a final rotation of +35° and a mutarotation rate of 0.0047 for cellobiose. The over-all yield of cellobiose from epi-cellobiose octaacetate was 35%.

Anal. Calcd. for $C_{12}H_{22}O_{11}$: C, 42.10; H, 6.48. Found: C, 42.18; H, 6.53.

Summary

Synthetic epi-cellobiose octaacetate, prepared by the action of an acid-acetylating mixture on the condensation product of 2,3-isopropylidene-D-mannosan<1,5>β<1,6> with acetobromo-glucose, has been converted to the known cellobial hexaacetate by customary procedures. Cellobial hexaacetate, upon oxidation with perbenzoic acid, follows the rule proposed by Levene and Tipson, and adds the introduced hydroxyl at carbon two mainly in a *trans* position to the acetylated hydroxyl group on carbon three; the resulting reaction product is apparently chiefly cellobiose hexaacetate because, upon acetylation, it yields a mixture of crystalline α- and β-cellobiose octaacetates in 63% yield. Crystalline cellobiose was obtained in quantitative yield by deacetylation of the octaacetate mixture. The over-all yield of cellobiose from epi-cellobiose octaacetate was 35%. The results constitute the structurally definitive syntheses of epi-cellobiose and cellobiose from D-mannose and D-glucose; they are also total syntheses in the sense that they are finally referable solely to inorganic substances through Emil Fischer's total syntheses of the two hexoses.

(11) Hudson and Yanovsky, THIS JOURNAL, **39**, 1035 (1917).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

l-Glycidol

BY JOHN C. SOWDEN AND HERMANN O. L. FISCHER

The preparation of optically-active glycidol ("epihydrin alcohol," 2,3-epoxypropanol-1) was first reported by Abderhalden and Eichwald.[1] These authors obtained the enantiomorphic glycidols by a series of reactions from 1-amino-2,3-dibromopropane after having subjected this amine to resolution with *d*-tartaric acid. The glycidols were then employed, by reaction with fatty acids, to prepare the first examples of optically-active α-monoglycerides. Moreover, by the addition of ammonia to the glycidols, a reaction previously studied by L. Knorr and E. Knorr[2] for racemic glycidol, Abderhalden and Eichwald obtained the optically active forms of 1-aminopropanediol-2,3. These amino alcohols, in turn, were used to prepare enantiomorphic α,β-diglycerides and triglycerides. It is evident that the degree of optical purity of the α-monoglycerides, α,β-diglycerides and triglycerides thus obtained is limited by the degree of optical purity of the enantiomorphic glycidols employed for their preparation.

(1) E. Abderhalden and E. Eichwald, *Ber.*, **47**, 1856, 2880 (1914); **48**, 1847 (1915).

(2) L. Knorr and E. Knorr, *ibid.*, **32**, 750 (1899).

Previous publications from this Laboratory have described the use of the natural asymmetry of the mannitols for the preparation of *d*(+)-acetone-glycerol[3] and *l*(−)-acetone-glycerol.[4] These enantiomorphic acetone-glycerols were then employed to prepare optically active α-monoglycerides,[5] α,β-diglycerides,[6] triglycerides,[5,6] the α-glycerophosphoric acids,[7] and α-ethers of glycerol.[8]

The same general method has now been used in the preparation and proof of optical purity of *l*-glycidol[9] and *l*-1-aminopropanediol-2,3.[9]

Starting with *d*(+)-acetone-glycerol, the reactions involved are illustrated in Fig. 1. It can be

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

(4) E. Baer and H. O. L. Fischer, THIS JOURNAL, **61**, 761 (1939).

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

(6) J. C. Sowden and H. O. L. Fischer, THIS JOURNAL, **63**, 3244 (1941).

(7) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 491 (1939); **135**, 321 (1940).

(8) E. Baer and H. O. L. Fischer, *ibid.*, **140**, 397 (1941).

(9) The prefix *l*- here designates the optical relationship of the compounds to *l*-glyceraldehyde. Thus the terminal carbon atom to which the free hydroxyl group is bound in *l*-glycidol and *l*-1-aminopropanediol-2,3 is considered to be the potential aldehydic carbon atom of the glyceraldehyde, *e. g.*, *l*-glyceraldehyde, to which these compounds are related.

assumed that the reactions described in scheme A of Fig. 1 are such that no racemization occurs. Therefore, the reactions in scheme B must have also proceeded without racemization and the optical purity of the *l*-glycidol and *l*-1-aminopropanediol-2,3 is established.

The optically active glycidol reported herein is assigned to the *l*-series on the premise that no Walden inversion has occurred in the formation of the oxide ring. In scheme B of Fig. 1 it is evident that *no* Walden inversion has occurred in the over-all conversion of IV to VI. Thus, either *no* inversion has occurred in the individual reactions IV → V, V → VI, and V is *l*-glycidol, as illustrated, or complete inversion has occurred in *each* of these two reactions, and V is *d*-glycidol. Analogous reactions which have been recorded for sugar structures make it very unlikely that a two-fold Walden inversion has occurred in IV → VI. Thus, Ohle and co-workers[10] after extensive investigation report that 6-(*p*-toluenesulfonyl)-monoacetone-*d*-glucose under the influence of alkali yields 5,6-anhydro-monoacetone-*d*-glucose and not 5,6-anhydro-monoacetone-*l*-idose and that the addition of ammonia or amines to the anhydro sugar then yields derivatives of 6-amino-*d*-glucose. Moreover, recent work by Peat and Wiggins[11] and by Robertson and Myers[12] indicates that in the formation of an ethylene oxide ring, with inversion, by the elimination of *p*-toluenesulfonic acid, the inversion occurs on that carbon atom which held the *p*-toluenesulfonyl residue and that in the subsequent addition of ammonia to the oxide ring, inversion occurs on that carbon atom to which the amino group attaches. Therefore, no inversion is to be expected in ethylene oxide ring formation when the *p*-toluenesulfonyl group was attached to a non-asymmetric terminal carbon atom, or in the oxide ring opening with addition of ammonia when the amino residue attaches to the non-asymmetric terminal carbon.

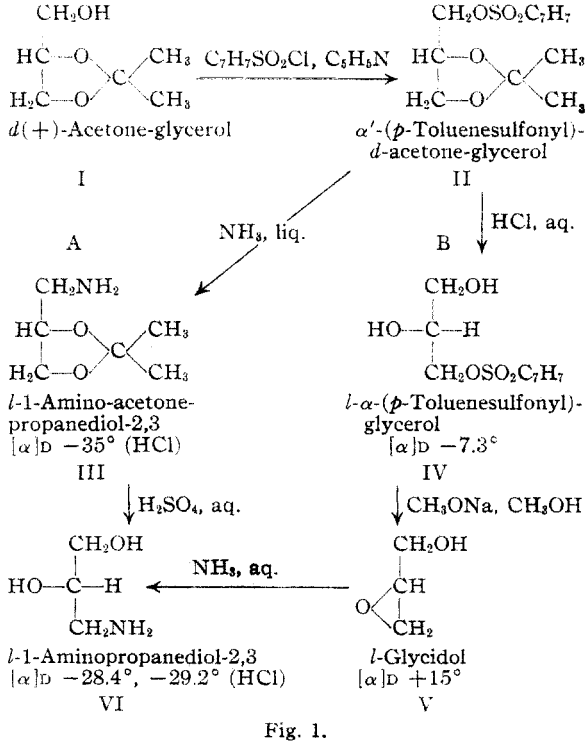

Fig. 1.

Experimental

***l*-α-(*p*-Toluenesulfonyl)-glycerol.**[13]—To a solution of 23.5 g. of *d*(+)-acetone-glycerol in 80 cc. of anhydrous pyridine was added, with cooling, 33.0 g. of *p*-toluenesulfonyl chloride. After standing for twenty-four hours at room temperature, ether was added to the reaction mixture and the resulting solution washed rapidly in succession with cold, dilute hydrochloric acid (80 cc. concentrated hydrochloric acid in 1 liter of water), water, saturated sodium bicarbonate solution, and water. After drying over anhydrous sodium sulfate, the ether extract was concentrated at reduced pressure to a sirupy residue of α'-(*p*-toluenesulfonyl)-*d*-acetone-glycerol. For the hydrolysis of the acetone group, 650 cc. of 0.5 *N* hydrochloric acid was added and the mixture heated, with stirring, at 75–80° for thirty-five minutes. On cooling, 21 g. of *l*-α-(*p*-toluenesulfonyl)-glycerol crystallized out. The filtrate from the first crop was saturated with sodium chloride and again cooled. After recrystallization from water, the second crop amounted to 10 g.; yield, 31.0 g., 71%. The ester, without further purification, showed m. p. 60–61°, $[\alpha]_D$ −7.3° (C_5H_5N, *c* 5.5). For pure *l*-α-(*p*-toluenesulfonyl)-glycerol, Fischer and Baer[13] record m. p. 63–64°, $[\alpha]_D$ −7.3° (C_5H_5N).

***l*-Glycidol.**—To an ice-cold solution of 29.0 g. of *l*-α-(*p*-toluenesulfonyl)-glycerol (dried *in vacuo* over soda-lime) in 50 cc. of anhydrous ethyl ether and 25 cc. of absolute methanol was added 60 cc. of cold absolute methanol containing 2.60 g. of sodium. After standing for fifteen hours at 6°, the solution was filtered to remove the precipitated sodium *p*-toluenesulfonate, the salt was washed with absolute methanol, and the combined filtrates concentrated below 20° at reduced pressure to a sludge. Ethyl ether was added and the precipitated salt removed by filtration. After concentration of the ether filtrate at room temperature, distillation at reduced pressure yielded 5.9 g. (65%) of *l*-glycidol. The redistilled product showed b. p. 56–56.5° (11 mm.); d^{20}_4 1.117; n^{16}_D 1.4293.

(10) H. Ohle and L. v. Vargha, *Ber.*, **62**, 2435 (1929); H. Ohle and E. Euler, *ibid.*, **69**, 1022 (1936); H. Ohle, E. Euler and W. Malerczyk, *ibid.*, **69**, 1636 (1936); H. Ohle, H. Friedeberg and G. Haeseler, *ibid.*, **69**, 2311 (1936).

(11) S. Peat and L. F. Wiggins, *J. Chem. Soc.*, 1088, 1810 (1938).

(12) G. J. Robertson and W. H. Myers, *Nature*, **143**, 640 (1939).

(13) H. O. L. Fischer and E. Baer, *Naturwiss.*, **25**, 588 (1937).

Optical Rotation.—In substance, 1-dm. tube, $\alpha^{21}D$ +16.8°, $[\alpha]D$ +15°. Three successive preparations showed in a 1-dm. tube, αD +16.8°, +16.8°, +16.5°. Abderhalden and Eichwald[1] record for "*d*"-glycidol:[14] *d*, 1.1054; αD +8.50°; $[\alpha]^{18}D$ +7.69°, in substance.

Anal. Calcd. for $C_3H_6O_2$ (74.08): C, 48.6; H, 8.16. Found: C, 48.8; H, 8.30.

Some difficulty was encountered in obtaining satisfactory combustion data for *l*-glycidol. Thus, successive analyses on one preparation gave C, 48.2, 49.1; H, 8.22, 8.17.

***l*-Glycidol *p*-Nitrobenzoate.**—To 7.5 g. of *p*-nitrobenzoyl chloride in a mixture of 40 cc. of absolute chloroform and 12 cc. of absolute pyridine was added, at 0°, a solution of 3.0 g. of *l*-glycidol in 8 cc. of absolute chloroform. After standing for twenty-three hours at 6°, chloroform was added and the solution washed rapidly with cold dilute sulfuric acid (4.5 cc. of sulfuric acid in 400 cc. of water), water, saturated sodium bicarbonate solution, and water. After treatment with Drierite and decolorizing carbon, the solution was concentrated at room temperature to a crystalline mass. Recrystallization from a mixture of ether and petroleum ether (40–60°) produced 5.8 g. (64%) of pale lemon-colored needles. Pure *l*-glycidol *p*-nitrobenzoate, m. p. 59–60°, was obtained by recrystallization from anhydrous ether.

Optical Rotation.—In absolute chloroform, *c* 3.38, 1-dm. tube, $\alpha^{20}D$ +1.28°, $[\alpha]^{20}D$ +37.9°.

Anal. Calcd. for $C_{10}H_9O_5N$ (223.18): C, 53.8; H, 4.06; N, 6.28. Found: C, 54.1; H, 4.05; N, 6.24.

***d,l*-Glycidol *p*-Nitrobenzoate.**—This compound was prepared in 72% yield from racemic glycidol in the same manner as described above for the *l*-glycidol *p*-nitrobenzoate. Recrystallization from ether produced pale yellow needles; m. p. 56°.

Anal. Calcd. for $C_{10}H_9O_5N$ (223.18): C, 53.8; H, 4.06. Found: C, 54.0; H, 4.10.

***d,l*-α-(*p*-Nitrobenzoyl)-glycerol.**—One gram of *d,l*-glycidol *p*-nitrobenzoate was refluxed for six hours with a mixture of 15 cc. of water and 5 cc. of dioxane. The solution was concentrated to dryness *in vacuo* and the residue was recrystallized from chloroform. There was obtained 0.7 g. (66%) of *d,l*-α-(*p*-nitrobenzoyl)-glycerol, m. p. 106–107°, m. m. p. with authentic sample prepared by the method of Fischer, Bergmann and Bärwind[15] 106–107°.

The addition of water to *l*-glycidol *p*-nitrobenzoate, by refluxing with a mixture of water and dioxane, yielded products of various melting points and rotations, and it was apparent that considerable racemization accompanied the reaction.

***l*-1-Amino-acetonepropanediol-2,3.**—Fifteen grams of α′-(*p*-toluenesulfonyl)-*d*-acetone-glycerol (purified by distillation from a Hickman type still at a bath temperature of 130° at 0.002 mm.), was allowed to react with 25 cc. of anhydrous liquid ammonia in a sealed tube at room temperature for ninety-eight hours. After evaporation of the ammonia, anhydrous ether was added and the ammonium *p*-toluenesulfonate was filtered off. The ether solution was concentrated at room temperature and the product was distilled at reduced pressure. Redistillation yielded 3.75 g. (55%) of *l*-1-amino-acetonepropanediol-2,3; b. p. 54–55° (8 mm.); d^{20}_4 1.009; $n^{20}D$ 1.4378.

Optical Rotation.—In substance, 1-dm. tube, αD +14.5°, $[\alpha]D$ +14.4°. In excess hydrochloric acid, 10 minutes $[\alpha]D$ −35.4°, 80 minutes $[\alpha]D$ −25.2°, 130 minutes $[\alpha]D$ −22.8°, 450 minutes $[\alpha]D$ −21.1° (constant).

Anal. Calcd. for $C_6H_{13}O_2N$ (131.17): C, 54.9; H, 9.99; 7.63 cc. 0.1 *N* HCl per 100 mg. Found: C, 54.9; H, 10.05; 7.58 cc. 0.1 *N* HCl per 100 mg.

l-1-Aminopropanediol-2,3

I. From *l*-1-Amino-acetonepropanediol-2,3.—Three and one-half grams of *l*-1-amino-acetonepropanediol-2,3 was refluxed for two hours with 50 cc. of 0.1 *N* sulfuric acid. The sulfuric acid was then precipitated with barium hydroxide and the filtered solution concentrated to dryness at reduced pressure. Absolute ethanol was added and the distillation repeated. The residue was dissolved in absolute ethanol and the solution, after being dried over potassium carbonate, concentrated at reduced pressure. Two distillations of the residue yielded 1.9 g. (78%) of *l*-1-aminopropanediol-2,3, b. p. 95–98° at 0.003 mm.

Optical Rotation.—In 5 *N* HCl, *c* 5.87, 1-dm. tube, αD −1.67°, $[\alpha]D$ −28.4°; in H_2O, *c* 5.09, 1-dm. tube, αD −0.12°, $[\alpha]D$ −2.4°. Abderhalden and Eichwald[1] record for *l*-aminopropanediol: in dilute HCl, $[\alpha]D$ −14.08°; in H_2O, $[\alpha]D$ −1.34°.

Anal. Calcd. for $C_3H_9O_2N$ (91.11): C, 39.5; H, 9.95; N, 15.4; 10.98 cc. 0.1 *N* HCl per 100 mg. Found: C, 39.4; H, 10.00; N, 15.3; 10.88 cc. 0.1 *N* HCl per 100 mg.

II. From *l*-Glycidol.—Four and one-half grams of *l*-glycidol was added to 400 cc. of cold concentrated (28%) aqueous ammonia. After standing fourteen hours in the icebox, the solution was concentrated at reduced pressure, below 30°, to a volume of 15–20 cc. Absolute ethanol (120 cc.) was added and the solution dried over potassium carbonate. Concentration of the solution and two distillations of the residue yielded 4.43 g. (80%) of *l*-1-aminopropanediol-2,3.

Optical Rotation.—In 5 *N* HCl *c* 7.47, 1-dm. tube, αD −2.18°, $[\alpha]D$ −29.2°. In H_2O, *c* 7.33, 1-dm. tube, αD −0.18°, $[\alpha]D$ −2.5°.

Anal. Calcd. for $C_3H_9O_2N$ (91.11): C, 39.5; H, 9.95; 10.98 cc. 0.1 *N* HCl per 100 mg. Found: C, 39.7; H, 10.20; 10.86 cc. 0.1 *N* HCl per 100 mg.

l-1-Aminopropanediol-2,3 crystallizes completely if cooled to −80° and warmed again gradually to room temperature. It then shows m. p. 55–57°. The amino alcohol rapidly absorbs moisture or carbon dioxide.

Summary

The natural asymmetry of *d*-mannitol has been employed to prepare optically pure *l*-glycidol and *l*-1-aminopropanediol-2,3, using *d*(+)-acetone-glycerol as an intermediary.

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(14) The prefix "*d*"- is used by Abderhalden and Eichwald to designate direction of rotation and not optical classification.

(15) E. Fischer, M. Bergmann and H. Bärwind, *Ber.*, **53**, 1589 (1920).