Bis(methyl 3-acetamido-4,6-di-O-acetyl-2,3-dideoxy-α-D-glucopyranosid-2-yl)amine (7)

The trihydrochloride **6** (121 mg), acetic anhydride (3.5 ml), and pyridine (7 ml) were magnetically stirred for 16 h at room temperature in a stoppered flask. Excess methanol was added and the mixture was evaporated. The residue was evaporated in succession with fresh methanol, several portions of toluene, and again with methanol. A solution of the resulting, brownish syrup in chloroform was washed with water to remove pyridine hydrochloride, dried over sodium sulfate, and evaporated with an ultimate addition of ethanol. Recrystallization of the semi-solid residue from absolute ethanol–petroleum ether gave **7** (68 mg, 40%) as colorless platelets: m.p. 328° (decomposition); $[\alpha]_D$ +123.5° (*c*, 0.8, chloroform); ν_{max} 3310 (NH), 1740 (ester CO), 1658 (amide I), and 1560 cm^{-1} (amide II); n.m.r. ($CDCl_3$): τ 3.27 (broadened doublet, amide NH), τ 5.15 (triplet, J = 9.5 Hz, H-4), τ 5.44 (doublet, J = 3 Hz, H-1), τ 5.6–6.3 (overlapping signals ascribable to H-3, H-5, H-6, and H-6′), τ 6.64 (singlet, OCH_3), τ 7.00 (multiplet, width ca. 18 Hz, H-2), τ 7.92, 7.95 (singlets, *O*-acetyl), τ 8.05 (singlet, *N*-acetyl), τ 8.27 (broadened signal of *sec.*-amine NH).

Anal. Calcd. for $C_{26}H_{41}N_3O_{14}$ (619.6): C, 50.40; H, 6.67; N, 6.78. Found: C, 50.26; H, 6.48; N, 6.79.

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Absolute configurations of the (−)-*erythro* and (−)-*threo*-2,3-dihydroxybutyric acids

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The absolute configurations of (−)-*erythro*-2,3-dihydroxybutyric acid and (−)-*threo*-2,3-dihydroxybutyric acid have been determined by optical rotatory dispersion and found to be 2(R), 3(R) for the *erythro* acid and 2(S), 3(R) for the *threo* acid.

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We recently found it necessary to determine the absolute configurations of the active *erythro*-2,3-dihydroxybutyric and *threo*-2,3-dihydroxybutyric acids for use in a stereospecific synthesis. Because of the inquiries which we have received regarding these compounds we felt it expedient to communicate this information prior to the completion of the synthetic problem.

The absolute configuration of (−)-*threo*-2,3-dihydroxybutyric acid has been indirectly determined by its production from L-threonine with nitrous acid (1). Since the stereochemistry of the deaminations of α-amino acids has been established to give unequivocably retention of configuration (2), this establishes the stereochemistry of the (−)-*threo*-dihydroxybutyric acid as being the same as L-threonine.

Erythro-2,3-dihydroxybutyric acid was prepared by hydroxylation of *trans*-crotonic acid with hydrogen peroxide and tungstic acid according to the method of Mugdan and Young (3). This acid was resolved through its quinine salt (4) to give (−)-*erythro*-2,3-dihydroxybutyric acid with a specific rotation of −9.5°.

The *threo*-isomer was prepared by a Milas oxidation of *trans*-crotonic acid with osmium tetroxide and hydrogen peroxide (5) and the dihydroxy acid resolved through its quinidine salt (6) to give (−)-*threo*-2,3-dihydroxybutyric acid with a specific rotation of −17.75°.

Because of the poor recovery of the resolved acids from their salts by previously reported procedures (4,6) the free acids were regenerated by their passage through a weak acid ion exchange column, a method recently communicated by us (7).

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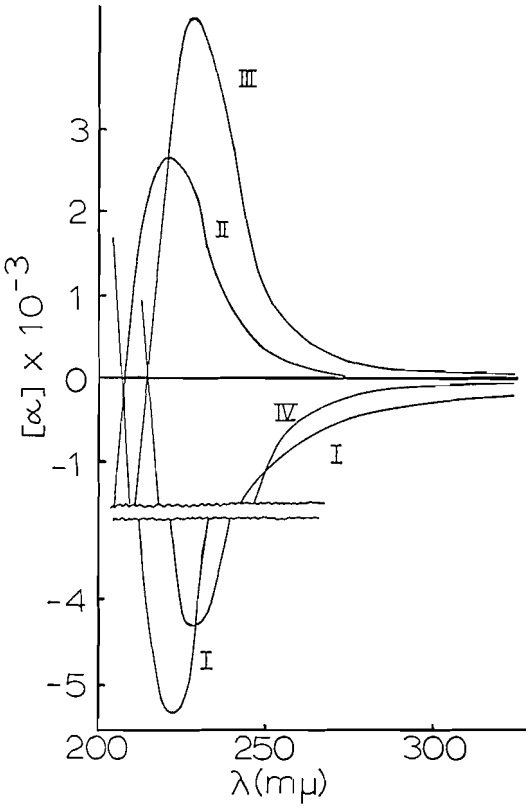
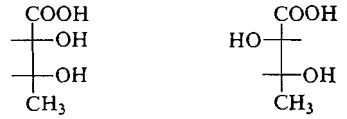


FIG. 1. Optical rotatory dispersion curves of: I, (−)-*erythro*-2,3-dihydroxybutyric acid; II, (−)-*threo*-2,3-dihydroxybutyric acid; III, (S)-(−)-tartaric acid; IV, (R)-(+)-tartaric acid.

Since the observation by Dirkx and Sixma (8) that the 210 mμ absorption band of active α-substituted acids is optically active the Cotton effects of a number of acids of known absolute configuration have been measured (8, 9). These workers have shown that α-hydroxy acids having the S-configuration at the α-carbon atom exhibit a positive Cotton effect in the region 220–235 mμ, depending on the solvent and the p*H*.

We have measured the optical rotatory dispersion curves of our resolved acids and these are shown in Fig. 1. The curves for (R)-(+)- and (L)-(−)-tartaric acids are included for comparison. As can be seen, (−)-*threo*-2,3-dihydroxybutyric acid exhibits a positive Cotton effect with an absorption maximum at 221 mμ and a specific rotation of +2640°. This acid therefore has the S-configuration at the α-carbon atom. On the other hand, (−)-*erythro*-2,3-dihydroxybutyric acid shows a negative Cotton effect with a trough at 221 mμ and a specific rotation of −5380°, and therefore has the R-configuration at the α-carbon atom.

From the stereospecific methods of preparation it then follows that the complete configuration for (−)-*erythro*-2,3-dihydroxybutyric acid (**1**) is 2(R), 3(R) and that for (−)-*threo*-2,3-dihydroxybutyric acid (**2**) is 2(S), 3(R).



1 **2**

Experimental

All rotations and optical rotatory dispersion (o.r.d.) measurements were taken on a Jasco ORD/UV-5 spectropolarimeter.

(±)-Erythro-2,3-dihydroxybutyric Acid

86 g (1 mole) of *trans*-crotonic acid was dissolved in 500 ml of hot water and the solution stirred vigorously. A 30% hydrogen peroxide solution (106 ml, 0.95 mole) containing 540 mg of tungstic acid was added portionwise in about 10 min. The temperature of the reaction mixture was raised to 70° and maintained for 4 h. The reaction mixture was cooled to room temperature, extracted with chloroform, and the chloroform extract washed with distilled water. The combined aqueous extracts were filtered to remove inorganic material, and the filtrate concentrated *in vacuo* at 50° to give a syrup. The syrup was dissolved in one part of boiling anhydrous ethyl acetate and treated with charcoal. The filtered solution, when cooled to 0°, deposited colorless crystals of (±)-*erythro*-2,3-dihydroxybutyric acid. Yield, 67.2 g (70%); m.p. 80–83° (over P_2O_5).

(±)-Threo-2,3-dihydroxybutyric Acid

50 ml of a 0.5% solution of osmium tetroxide in *tert*-butanol was added slowly and cautiously to a cooled solution of 86.0 g (1 mole) of *trans*-crotonic acid in 125 ml of 30% hydrogen peroxide, made up to a volume of 600 ml. The solution, which becomes very hot after complete addition of the osmium tetroxide solution, was allowed to stand for 2 h at room temperature. The reaction mixture was extracted 3 times with 300 ml of benzene to remove the osmium tetroxide and was further extracted with chloroform. The aqueous layer was evaporated to dryness *in vacuo* to a syrup. The syrup was dissolved in anhydrous ethyl acetate, treated with charcoal and filtered. The filtrate on cooling deposited crystalline (±)-*threo*-2,3-dihydroxybutyric acid. Yield, 74 g (64%); m.p. 73–74° (over P_2O_5).

(−)-Erythro-2,3-dihydroxybutyric Acid (1)

20 g (0.165 mole) of (±)-*erythro*-2,3-dihydroxybutyric acid was dissolved in 250 ml of water. The solution was heated to 50 °C and neutralized with 60 g (0.185 mole) of

quinine. The cooled solution was filtered to remove undissolved quinine and cooled to 0°. After two days the crystals formed were collected and washed with ice water. The crystals (30 g) were recrystallized twice from water and dried *in vacuo* over H_2SO_4. Yield, 29.0 g; m.p. 195°; $[\alpha]_D^{20}$ −115° (*c*, 5.04, H_2O); [lit. (4), $[\alpha]_D^{20}$ −113° (*c*, 5.0, H_2O)].

Concentration of the original filtrate gave a further 6 g of crystalline material.

The free acid was regenerated by passing an aqueous solution of the resolved quinine salt through a Bio-Rex-70 (H^+) resin column (7) yielding (−)-*erythro*-2,3-dihydroxybutyric acid, $[\alpha]_D^{25}$ −9.5° (*c*, 1.0, H_2O); [lit. (4), $[\alpha]_D^{20}$ −9.30° (*c*, 0.5, H_2O)].

Rotatory dispersion (*c*, 0.5, H_2O): $[\alpha]_{589}$ −9.5°, $[\alpha]_{250}$ −1060°, $[\alpha]_{221}$ −5380° (trough), $[\alpha]_{210}$ −1790°.

(−)-Threo-2,3-dihydroxybutyric Acid (2)

To a hot solution of 20 g (0.165 mole) of (±)-*threo*-2,3-dihydroxybutyric acid in 500 ml of water 60 g (0.185 mole) of quinidine was added. The hot solution was filtered and cooled. The crystalline salt (37.3 g) was dried in a vacuum desiccator over H_2SO_4. Concentration of the filtrate gave a further 2.0 g of material. After several recrystallizations from water, a salt with constant rotation was obtained, m.p. 117°; $[\alpha]_D^{20}$ +145.5° (*c*, 3.3, H_2O); [lit. (6), m.p. 114°, $[\alpha]_D^{18}$ +142.2°, (*c*, 3.31, H_2O)].

Regeneration of the free acid was accomplished in the same manner as with the *erythro* acid yielding (−)-*threo*-2,3-dihydroxybutyric acid as a syrup, $[\alpha]_D^{25}$ −17.75° (*c*, 1.0 H_2O); [lit. (6), $[\alpha]_D^{16}$ −13.51° (*c*, 6.0, H_2O)].

Rotatory dispersion (*c*, 0.5, H_2O): $[\alpha]_{589}$ −17.75°, $[\alpha]_{250}$ +360°, $[\alpha]_{221}$ +2640° (peak), $[\alpha]_{210}$ +880°.

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Chromatographic analysis of methyl ethers of 2-amino-2-deoxy-D-glucopyranose[1]

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The mono-, di-, and tri-*O*-methyl ether derivatives of 2-amino-2-deoxy-D-glucopyranose have been analyzed by gas–liquid chromatography of their fully acetylated 2-acetamido-2-deoxy-D-glucitol derivatives which were prepared from the glycoses by reduction with sodium borohydride followed by acetylation with acetic anhydride. The methyl ethers of 2-amino-2-deoxy-D-glucopyranose were also characterized by degradation with ninhydrin to the corresponding methyl ether derivatives of D-arabinose which were identified by paper chromatography.

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The identification of the methyl ether derivatives of 2-amino-2-deoxy-D-glucose from the hydrolyzates of methylated glycans containing 2-amino-2-deoxy-D-glucose units is usually a part of the procedure involved in the structural analysis of the original glycan. The paper chromatographic (1–6) method has been used for the identification of the methyl ethers of 2-amino-2-deoxy-D-glucose. However, in our experience, this method did not provide a satisfactory separation of the individual mono- and di-*O*-methyl derivatives. Gas–liquid chromatography (g.l.c.) has been used to identify some methyl ethers as their methyl 2-acetamido-2-deoxy-D-glucoside derivatives (7–9). A recent thin-layer chromatographic (t.l.c.) method for the separation of the methyl ethers of ethyl 2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranoside and of 2-deoxy-2-(2,4-dinitroanilino)-D-glucose (10) offers a practical procedure for the analysis of mixtures of the methyl ethers of 2-amino-2-deoxy-D-glucose. This note records a

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