2,3-*O*-ISOPROPYLIDENE-L-ERYTHROTETRURONIC ACID AND -L-ERYTHROSE, AND THE METHYL D-ERYTHRO- AND D-THREO-TETROFURANOSIDES[1]

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ABSTRACT

Oxidation of 2,3-*O*-isopropylidene-β-L-rhamnose (I) with hypoiodite, followed by periodate cleavage of the derived aldonic acid, affords 2,3-*O*-isopropylidene-L-*erythro*tetruronic acid. Reduction of I with sodium borohydride and periodate oxidation of the resulting glycitol gives 2,3-*O*-isopropylidene-L-erythrose. Both products have been obtained in high yield, and are readily hydrolyzed to L-*erythro*tetruronic acid and L-erythrose, respectively.

Methyl α- and β-D-*erythro*- and D-*threo*-tetrofuranosides have been prepared by the Fischer glycoside synthesis from D-erythrose- and D-threose-formates, respectively. A notable anomeric difference in the lead tetraacetate oxidation behavior of the methyl D-threosides has been observed, the β-anomer being more reactive than the α-anomer.

In continuing earlier studies in this laboratory on the chemistry of the tetrose sugars (1, 2, 3, 4) several new tetrose derivatives have been prepared and are described in the current paper.

Stepwise degradation of D-glucuronic and D-galacturonic acids to D-*erythro*- and D-*threo*-tetruronic acids, respectively, by lead tetraacetate oxidation has been described previously (3). Since the L-isomers of these hexuronic acids are rare compounds, they do not provide practical sources of the L-tetruronic acids. The L-*threo*-isomer has been prepared by selective reduction of 2,3-di-*O*-acetyl-L-tartaric anhydride (5) and by oxidative degradation of D-glucosaccharo-γ-lactone (6), but the L-*erythro*-acid does not appear to have been reported. In the current paper a method is described for preparing L-*erythro*tetruronic acid from readily available 2,3-*O*-isopropylidene-L-rhamnose (7) (I). The latter derivative also has been utilized to prepare L-erythrose in high yield.

Acetonation of L-rhamnose in the presence of hydrogen chloride (7) appears to yield the 2,3-*O*-isopropylidene derivative almost exclusively. Two crystalline forms of monoacetone L-rhamnose have been described (8, 9) but only the β-anomer (9) has been isolated in the present study. The isopropylidene derivative (I) was oxidized with hypoiodite (10) to the L-rhamnonate (II) and the latter, which was not isolated, was degraded by periodate cleavage. From the reaction mixture crystalline 2,3-*O*-isopropylidene-L-*erythro*tetruronic acid (III) was isolated in about 75% yield. Chromatographically pure L-*erythro*tetruronic acid was readily obtained by autohydrolysis of III in aqueous solution.

Reduction of isopropylidene-β-L-rhamnose (I) to the rhamnitol derivative (IV), followed by periodate oxidation, afforded crystalline 2,3-*O*-isopropylidene-L-erythrose (V) in about 80% yield. The L-glycitol derivative (IV) was obtained as a syrup by catalytic hydrogenation but, with sodium borohydride reduction, attempts to isolate it resulted in partial hydrolysis of the isopropylidene group. For preparation of V, however, it was most convenient to carry out the reduction with borohydride and, after neutralizing the reaction mixture, to continue directly with the periodate cleavage step. Such a procedure was used by Ballou (11) in converting 3,4-*O*-isopropylidene-D-arabinose to the D-isomer

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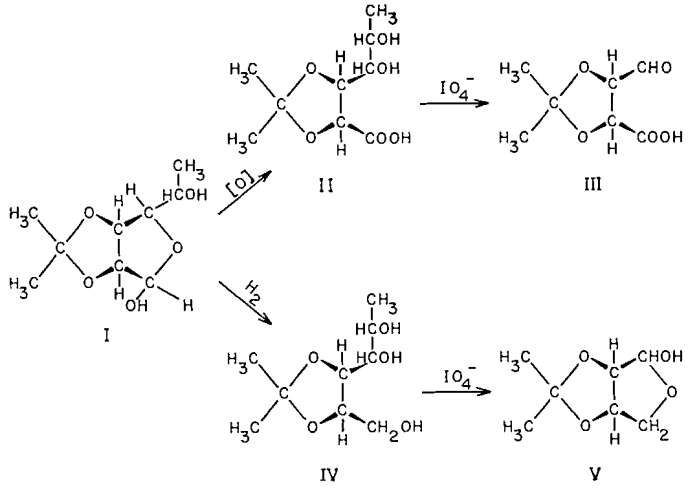
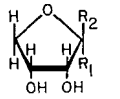


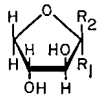
of V. Ballou's method, it will be noted, can also readily furnish V itself by starting with L-arabinose, but the required isopropylidene-pentose derivative is less readily prepared than is the monoacetone-L-rhamnose used in the current study.

Hydrolysis of 2,3-*O*-isopropylidene-L-erythrose with dilute acid afforded chromatographically pure L-erythrose. The calculated $[\alpha]_D$ of the latter sugar was +39°, somewhat higher numerically than most values reported earlier for the D- or L-isomer (see ref. 1 and references cited therein), but close to the value of $[\alpha]_D$ −41° found by Schaffer for D-erythrose derived from crystalline 2,4-*O*-ethylidene-D-erythrose dimer (12). These higher values, together with rotational data obtained by hydrolysis of the methyl D-erythrosides (see below), indicate that the specific rotation of D- or L-erythrose is −38° or +38° (±3°).

The current procedure for preparing L-erythrose may be found more satisfactory than previous means for obtaining this tetrose. Of other methods available the sulphone degradation (13) of diethyl dithio-L-arabinose affords the highest over-all yield of chromatographically pure L-erythrose (13), although the low specific rotation ($[\alpha]_D$ +23°) recorded for the syrupy product (13) suggests the presence of an undetected impurity.

Hockett and Maynard (15) found that D-erythrose reacts with methanolic hydrogen chloride (16) to form a mixture of the α- and β-furanosides (VII and VIII) rather than the dimethyl acetal or dimeric products, in this respect resembling more closely the higher-order sugars rather than DL-glycerose (17). In the current study it was of interest to isolate the isomeric tetrosides, which represent the simplest of the true glycosides. Di-*O*-formyl-D-erythrose (1), in 1% methanolic hydrogen chloride at room temperature, was rapidly deacylated and converted to a mixture of the glycosides. The anomeric compounds were readily distinguished on paper chromatograms (which showed also that





VI $R_1 = OCH_3$, $R_2 = H$ VIII $R_1 = OCH_3$, $R_2 = H$

VII $R_1 = H$, $R_2 = OCH_3$ IX $R_1 = H$, $R_2 = OCH_3$

other products were produced in only minor proportions), and were separated by chromatography on a cellulose column. The ratio of α- to β-anomer formed was about 1 to 3, whereas Hockett and Maynard found the ratio to be about 4 to 5 (15) and, recently, Ballou (18) has reported that the β-anomer is produced almost exclusively. In all three instances the reaction conditions used appear to have been similar and no explanation is offered to account for these wide variations. It may be noted, however, that the *trans*-β-glycoside always predominates in the mixtures.

Both glycosides were isolated as analytically pure syrups and characterized by optical properties and glycol-cleavage oxidation. Methyl β-D-erythroside was smoothly converted to a 2,3-cyclic carbonate, and a di-*p*-nitrobenzoate of the α-anomer was prepared. On hydrolysis with dilute aqueous acid each glycoside afforded chromatographically pure D-erythrose, the calculated specific rotation of the latter being $[\alpha]_D$ $-36°$ to $-39°$.

For the preparation of methyl α- and β-D-*threo*-tetrofuranosides (IX and X), di-*O*-formyl-D-threose (2) was treated with methanolic hydrogen chloride as for the corresponding D-erythrose derivative. The specific rotation of the syrupy product and of the dialdehydes derived by periodate oxidation indicated that the α- and β-glycosides were formed in a ratio of about 3 to 2. The mixture was not well resolved on paper chromatograms and only a partial separation was effected on a cellulose column. Presence of two major components in the reaction mixture in the ratio given above was demonstrated more satisfactorily by gas–liquid chromatography* and small analytically pure samples of the α- and β-threosides were obtained by this chromatographic method. Methyl α-D-threoside was isolated also via the mixture of derived di-*p*-nitrobenzoates by fractional crystallization and deacylation.

The possibility of preparing methyl α-D-threoside by means of the Koenigs–Knorr reaction (20) was examined briefly. Extensive studies on the halides of *O*-acyl-pentofuranoses (21) have shown that the 1,2-*trans*-glycoside is generally formed starting with either the α- or β-halide. Applied to the D-*threo*furanose series, formation of the α-glycoside was to be expected. Tri-*O*-acetyl-D-threofuranose (22) was accordingly treated with hydrogen bromide in acetic acid, yielding an unstable syrupy product which appeared to contain both anomeric bromides. Reaction of this material with methanol, either in the presence or absence of silver oxide, led to formation of the mixed α- and β-glycosides, with the former predominating. Under the conditions used, therefore, the reaction was less stereospecific than usually encountered with the higher sugars and did not constitute a satisfactory preparative procedure.

The behavior of the various glycosides towards glycol scission by lead tetraacetate in acetic acid (23) was in general accord with the oxidation characteristics of related five-membered ring compounds. The steric arrangement of the *vic*-diol group of the D-erythrosides should correspond closely to that found in cyclopentane-*cis*-1,2-diol (24) and 1,4-anhydro erythritol (25) and, accordingly, these glycosides consumed oxidant extremely rapidly (Table I), as already shown for the mixed anomers (15). Similarly, as with cyclopentane-*trans*-1,2-diol (23) and 1,4-anhydro-L-threitol (26, 27), the D-threosides were attacked relatively slowly (Table I). The oxidation rates for the anomeric forms differed substantially, however, in contrast to the more uniform behavior of anomeric pyranose glycosides towards lead tetraacetate.†

**This technique has been shown to be highly effective for separating the anomeric forms of some methyl hexoside methyl ethers (19).*

†*A notable exception is the observation that the α-anomer of methyl 2-deoxy-D-erythropentopyranoside consumes lead tetraacetate almost twice as rapidly as does the β-anomer (28). In the periodate oxidation of* sterically rigid *bicyclic methyl glycosides, substantial anomeric differences have been observed (29).*

TABLE I

Properties of the methyl D-tetrofuranosides

Isomer	$[\alpha]_D^{25}$	$[\alpha]_D^{25}$ dialdehyde*	Oxidation rate (k)†
α-D-*Erythro*-(VII)	+133°	+121°	Fast (0°)‡
β-D-*Erythro*-(VIII)	−148°	−119°	Fast (0°)‡
α-D-*Threo*-(IX)	+97°	+113°	0.084 (25°)§
β-D-*Threo*-(X)	−193°	−116°	0.49 (25°)§

*D'- of L'-Methoxy-diglycolic aldehyde formed by periodate oxidation. Derived from crystalline methyl pentosides, these dialdehydes show $[\alpha]_D^{20}$ ±122–124° (37, 38).

†Rate of lead tetraacetate oxidation in mole^{-1} liter minute^{-1}. Cyclopentane-*trans*-1,2-diol gives $k_{20°}$ 12.8 (24).

‡One mole of oxidant per mole was consumed within 45 seconds.

§The compound was not hydrolyzed when kept in acetic acid at 25° C for 6 hours.

EXPERIMENTAL

Paper chromatography was carried out using as solvents (A) ethyl acetate – acetic acid – formic acid – water (18:3:1:4), (B) butan-1-ol – ethanol – water (40:11:19), and (C) ethyl acetate – pyridine – water (100:40:30).

Gas–liquid chromatography was carried out as described by Craig and Murty (30), using a succinate – ethylene glycol polyester on Chromosorb W at a column temperature of 205° and a helium flow of 60 ml/minute.

Solutions were concentrated *in vacuo* at 40° C. Melting points are corrected. Boiling points cited are air-bath temperatures. Optical rotations were measured at approximately 25°.

2,3-O-Isopropylidene-L-*rhamnose* (I)

A slight modification of the procedure of Fischer (16) was used. L-Rhamnose hydrate (30 g) was dehydrated by heating *in vacuo* at 100° C for 3 hours. Dry acetone (300 ml) was added, followed by a solution of acetone (20 ml) containing hydrogen chloride (1.5 g), and the mixture was shaken at room temperature until the solid dissolved (1–2 hours). Excess ammonia was bubbled into the solution, the ammonium chloride filtered off, and the filtrate concentrated. The syrupy residue was dissolved in water (50 ml), extracted twice with ethyl acetate (100 ml), and the extract was washed twice with water (25 ml), dried over sodium sulphate, and concentrated. Weight, 19.0 g, $[\alpha]_D$ +6° (c, 4.3, H_2O). Paper chromatographic examination of the syrupy product and of the aqueous fractions indicated that the former consisted almost exclusively of monoacetone L-rhamnose (R_F 0.9, solvent B) and the latter mainly of L-rhamnose. Five grams of 2,3-*O*-isopropylidene-β-L-rhamnose, m.p. 88–90° C, $[\alpha]_D$ +17° (equilibrium value) (c, 2, H_2O), was obtained from a solution of the syrup in ether–hexane, but prolonged storage of the mother liquor in the cold failed to yield additional crystalline material. (For further examination of the syrupy residue, see below.)

2,3-O-Isopropylidene-L-*erythruronic Acid* (III)

2,3-*O*-Isopropylidene-β-L-rhamnose (1.0 g) was dissolved in water (50 ml), 0.1 N iodine (110 ml containing 2.4 g of potassium iodide) was added, and the solution cooled in an ice bath. Sodium hydroxide (N, 17.0 ml) was added dropwise with good stirring during a period of 15 minutes. At 45 minutes, titration of a portion of the reaction mixture showed that the consumption of hypoiodite was 1.0 mole/mole. A few drops of 0.1 N thiosulphate was added to decolorize the solution, silver acetate (7.0 g) was added and the suspension stirred at room temperature for 15 minutes, and sodium chloride solution

then added to remove excess silver ion. The suspension was filtered, the filtrate cooled to 5° C, and powdered sodium periodate (1.0 g) added. After 30 minutes, the oxidation mixture (which gave a faint test for excess periodate) was concentrated to a volume of 200 ml, acidified with Amberlite IR-120, and the solution and resin were extracted 5 times with ethyl acetate (50 ml). The combined extract was washed twice with water (25 ml) and dried over sodium sulphate. Evaporation of the solvent afforded a syrup which rapidly solidified (weight, 0.65 g), m.p. 92–98° C. (R_F 0.85, solvent A, yellow color with *p*-anisidine hydrochloride spray (31).) Recrystallized from ethyl acetate – hexane, the product had a melting point of 103–104° C, $[\alpha]_D$ +1.4° (*c*, 1.4, H_2O). Calculated for $C_7H_{10}O_5$: C, 48.27%; H, 5.79%. Found: C, 48.05%; H, 5.76%.

L-*Erythrotetruronic Acid*

Monoacetone L-erythruronic acid (28 mg) in water (2.0 ml) was heated on the steam bath: α_D +0.02° (1 dm, initial) → α_D −0.20° (60 minutes, constant); $[\alpha]_D$ −18° (calc.). (D-Erythruronic acid has $[\alpha]_D$ +18° (3).) Chromatographic examination of the hydrolyzate indicated the presence of one component travelling at the rate of D-*erythro*tetruronic acid (R_{gal} 1.4, solvent A) and giving an intense yellow color (which appears in the cold and intensifies on heating) with *p*-anisidine hydrochloride spray.

D-*Erythrono-γ-lactone*

Monoacetone L-erythruronic acid (0.3 g) was reduced with sodium borohydride (0.3 g) in water–methanol (2:1). The isopropylidene group of the syrupy product was hydrolyzed at 100° C in 80% acetic acid for 1.5 hours, affording D-erythrono-γ-lactone (0.1 g), which, recrystallized from ethanol, had a melting point of 100–102° C, undepressed, $[\alpha]_D$ −73° (*c*, 2.4, H_2O). (Lit. (1): m.p. 103–104° C; $[\alpha]_D$ −72°.) Calculated for $C_4H_6O_4$: C, 40.68%; H, 5.12%. Found: C, 40.69%; H, 5.16%.

2,3-O-Isopropylidene-L-*erythrose* (V)

2,3-*O*-Isopropylidene-L-rhamnose (2.0 g) in water (80 ml) was added dropwise to a well-stirred solution of sodium borohydride (0.8 g) in ice water (40 ml). After 4 hours at room temperature, acetic acid was added slowly to destroy excess borohydride and to adjust the pH to 6. The solution was cooled externally to 10° C, and powdered sodium periodate (2.2 g) was added portionwise over a period of 15 minutes. The reaction mixture was kept at 25° C for 3 hours (it then gave a faintly positive test for periodate), then concentrated to a volume of about 25 ml, and the slurry extracted 4 times with ethyl acetate (50 ml). After the extract was washed twice with water (15 ml) and dried over sodium sulphate, the solvent was evaporated off affording a clear, colorless syrup* (1.3 g) (R_F 0.8, solvent B) which solidified almost completely when stored overnight at 3° C. The crystalline material melted at 27–30° C. After distillation (60–70° C (bath) at 10 mm) the product still contained a small proportion of liquid, and the crystalline material melted at 29–31° C, $[\alpha]_D$ +72° (*c*, 2.4, CH_3OH) (no mutarotation observed). Calculated for $C_7H_{12}O_4$: C, 52.49%; H, 7.55%. Found: C, 52.53%; H, 7.56%.

2,3-O-Isopropylidene-L-*erythrose from Syrupy Monoacetone* L-*Rhamnose*

A sample (1.0 g) of the material remaining after crystallization of I (above) was treated with sodium borohydride followed by periodate oxidation, as in the preparation of V. The syrupy product (0.8 g) was distilled (50–70° C (bath) at 2 mm) affording a colorless syrup which solidified almost completely at 3° C. The melting point of the crystalline

**This product is moderately volatile, and hence should not be dried for a prolonged period in vacuo.*

material was 27–31° C. In addition to V, the product was found chromatographically to contain a minor component (R_F 0.9, solvent B) that was detected with aniline oxalate but did not give the tetrose color. Attempts to purify the monoacetone-L-erythrose by recrystallization from various solvent systems were unsuccessful.

L-Erythrose

2,3-*O*-Isopropylidene-L-erythrose (19.3 mg) in 0.1 *N* sulphuric acid (1 ml) was heated on the steam bath: α_D +1.22° (1 dm, initial) → +0.97° (30 minutes, constant); $[\alpha]_D$ +39° (calc.). After neutralization with Dowex-1 resin (bicarbonate form) the hydrolyzate was found chromatographically (solvent C) to contain a single component travelling at the rate of D-erythrose and giving the typical tetrose fluorescence under ultraviolet with aniline oxalate spray (32). The infrared absorption spectrum (potassium bromide disk) of the product was indistinguishable from that of D-erythrose. Reduction of the product with aqueous sodium borohydride yielded chromatographically pure erythritol, m.p. 118–120° C, undepressed. Calculated for $C_4H_{10}O_4$: C, 39.34%; H, 8.25%. Found: C, 39.43%; H, 8.30%.

2,3-O-Isopropylidene-L-rhamnitol

2,3-*O*-Isopropylidene-L-rhamnose (0.5 g) in absolute ethanol (10 ml) was heated at 100° C for 8 hours at a pressure of 1400 p.s.i. of hydrogen in the presence of Raney nickel catalyst (0.3 g). The catalyst was filtered off and the filtrate evaporated, affording a colorless syrup (0.5 g) which gave a single spot on a paper chromatogram (R_F 0.7, solvent B, ammoniacal silver nitrate spray (33)), $[\alpha]_D$ +5.5° (*c*, 4.1, CH_3OH). Presence of an isopropylidene group was indicated by the infrared absorption spectrum. The product consumed 1.0 mole of periodate per mole, affording 2,3-*O*-isopropylidene-L-erythrose. Acetylation and benzoylation gave amorphous products.

Reaction of Di-O-formyl-D-erythrose with Methanolic Hydrogen Chloride

Di-*O*-formyl-D-erythrose syrup (1) (3.2 g) in methanol (50 ml) (α_D +0.14°) was treated with 2.5% methanolic hydrogen chloride (35 ml) at 25° C, the observed rotation changing to α_D −1.65° (5 minutes, constant). Excess silver carbonate was added, the neutral filtrate was treated with hydrogen sulphide and again filtered, and the solution was concentrated to yield a colorless syrup (2.2 g), $[\alpha]_D$ −49° (*c*, 4.4, CH_3OH). Examined by paper chromatography (solvent B), the syrup was found to contain two main components (R_F 0.59 (major) and R_F 0.66), a small proportion of free erythrose, and two trace components (R_F 0.74 and R_F 0.79).

Methyl β-D-Erythrotetrofuranoside (II)

Methyl D-erythroside syrup (5.5 g) was chromatographed on a cellulose column using benzene–ethanol–water (500:50:1) as solvent. The component (R_F 0.59) was eluted from the column first and isolated as a colorless syrup (3.5 g), b.p. 80–90° C at 0.5 mm; n_D 1.4630, $[\alpha]_D$ −148° (*c*, 1.5, H_2O). (Ballou reports $[\alpha]_D$ −149° (*c*, 1, $CHCl_3$) (18).) Calculated for $C_5H_{10}O_4$: C, 44.77%; H, 7.52%. Found: C, 44.30%; H, 7.62%.

The glycoside was hydrolyzed with 0.1 *N* sulphuric acid at 100° C to constant rotation in 30 minutes. Calculated for chromatographically pure D-erythrose formed $[\alpha]_D$ −36° (in the acid solution, and after treatment with Dowex-1 resin (bicarbonate form)).

Oxidized with sodium periodate, the uptake by the glycoside was 1.0 mole/mole, and the observed rotation changed from α_D −2.55° (*c*, 1.75) to −2.06° (20 minutes, constant). Calculated for dialdehyde formed $[\alpha]_D$ −119°.

Methyl β-D-Erythrofuranoside-2,3-carbonate

Methyl β-D-erythroside (0.9 g) was dissolved in pyridine (30 ml) and to the stirred solution was added dropwise a solution of phosgene (0.75 g) in toluene (35 ml) (34). After 18 hours the solid pyridine hydrochloride was filtered off, the filtrate concentrated, and the residue taken up in chloroform. The chloroform solution was washed twice with copper sulphate solution, then with bicarbonate solution, twice with water, dried over sodium sulphate, and concentrated. The syrupy product (1.0 g) solidified, and recrystallization was effected from ethyl acetate – hexane, m.p. 73° and $[\alpha]_D$ −152° (*c*, 2.4, $CHCl_3$). Calculated for $C_6H_8O_5$: C, 45.00%; H, 5.01%. Found: C, 44.81%; H, 5.01%. The infrared absorption spectrum showed a major broad peak at 1790–1795 cm^{-1}, characteristic of a cyclic, rather than acyclic, carbonate group (35).

Methyl α-D-Erythrotetrofuranoside (I)

Following elution of the β-glycoside from the cellulose column, a fraction consisting mainly of the α-anomer was obtained (0.6 g), rechromatographed on the cellulose column, and distilled (b.p. 65–85° C at 0.2 mm); n_D 1.4665, $[\alpha]_D$ +133° (*c*, 1.2, H_2O). Calculated for $C_5H_{10}O_4$: methoxyl, 23.1%. Found: methoxyl, 22.8%.

On hydrolysis with 0.1 *N* sulphuric acid at 100° C to constant rotation, the observed value corresponded to $[\alpha]_D$ −37° for chromatographically pure D-erythrose formed; after neutralization with Dowex-1 (bicarbonate form), $[\alpha]_D$ −39°.

Treated with sodium periodate, the glycoside consumed 1.0 mole/mole, the observed rotation changing from α_D +1.71° → +1.48° (10 minutes, constant). Calculated for the dialdehyde formed, $[\alpha]_D$ +121°.

Methyl α-D-Erythrofuranoside Di-p-nitrobenzoate

Methyl α-D-erythroside (0.10 g) in pyridine (5 ml) was treated with *p*-nitrobenzoyl chloride (0.65 g) at 55° C for 4 hours. On addition of aqueous sodium bicarbonate, a solid product was obtained (0.30 g) and was recrystallized from ethyl acetate – hexane, m.p. 109–110° C and $[\alpha]_D$ −17.3° (*c*, 1.7, $CHCl_3$). Calculated for $C_{19}H_{16}O_{10}N_2$: C, 52.78%; H, 3.73%. Found: C, 52.84%; H, 3.60%.

Reaction of D-Threose Formate with Methanolic Hydrogen Chloride

D-Threose formate syrup (2) (4.5 g), treated with methanolic hydrogen chloride as described above, afforded a colorless syrup (2.6 g). Purified by distillation (b.p. 75–90° C at 0.2 mm) the product had $[\alpha]_D$ +7.9° (*c*, 2.4, H_2O) and, examined by paper chromatography (solvent B), was found to contain two major tetrose components (R_F 0.65 and 0.62; overlapping, with the former predominant) and a minor tetrose component (R_F 0.75). On treatment with periodate the mixture consumed 0.9 mole of oxidant per mole, the calculated value of $[\alpha]_D$ +33° for the dialdehydes formed corresponding to an α,β-mixture of about 3 to 2. Calculated for $C_5H_{10}O_4$: methoxyl, 23.1%. Found: methoxyl, 24.6%.

Methyl α- and β-D-Threotetrofuranosides

Vapor phase chromatography of the syrupy mixture of D-threosides readily separated the two major components from each other, and showed them to be present in a ratio of about 3 to 2 (α- to β-). On a preparative scale, 50–100 mg of each component was isolated by repeated chromatographic runs, and purified by distillation.

The first of the two components to emerge from the column was the *β-anomer* (R_F 0.62, b.p. 80–90°/0.2 mm), $[\alpha]_D$ −193° (*c*, 1.1, H_2O). The glycoside consumed 1.0 mole of

periodate per mole, affording a dialdehyde having $[\alpha]_D$ −116° (calculated). Calculated for $C_5H_{10}O_4$: C, 44.77%; H, 7.52%. Found: C, 44.60%; H, 7.48%.

The *α-anomer* (R_F 0.65, b.p. 85–100°/0.2 mm) had $[\alpha]_D$ +97° (*c*, 1.6, H_2O). It consumed 1.0 mole of periodate per mole, yielding a dialdehyde having $[\alpha]_D$ +113° (calculated). Calculated for $C_5H_{10}O_4$: C, 44.77%: H, 7.52%. Found: C, 44.73%; H, 7.31%.

Methyl α-D-Threofuranoside Di-p-nitrobenzoate and Methyl α-D-Threofuranoside

The mixture of α- and β-D-threosides (0.5 g) was treated with *p*-nitrobenzoyl chloride as described above, and the amorphous product (1.2 g) was taken up in ethyl acetate – hexane. Crystalline material (0.6 g) was deposited and recrystallized twice from the same solvent, m.p. 131–133° C and $[\alpha]_D$ −115° (*c*, 2.0, $CHCl_3$). Calculated for $C_{19}H_{16}O_{10}N_2$: C, 52.78%; H, 3.78%. Found: C, 52.80%; H, 3.65%.

The di-*p*-nitrobenzoate (0.3 g) suspended in methanol (20 ml) was treated under reflux with sodium methoxide (0.1 *N*, 2 ml). Acetic acid was added to neutrality, the methanol evaporated off, and the residue taken up in water and extracted three times with benzene. The aqueous layer was concentrated, and the product distilled, $[\alpha]_D$ +96° (*c*, 2.2, H_2O). The infrared absorption spectrum of the syrup was indistinguishable from that of methyl α-D-threoside and different from that of the β-glycoside.

Methyl β-D-Threofuranoside Di-p-nitrobenzoate

A syrup consisting mainly of methyl β-D-threofuranoside ($[\alpha]_D$ −165°) was obtained by partial separation of the mixed threosides on a cellulose column using benzene–ethanol–water (1000:15:0.5). Treatment with *p*-nitrobenzoyl chloride afforded a di-*p*-nitrobenzoate which, when crystallized from ethyl acetate – pentane, had a melting point of 55–57° C, $[\alpha]_D$ −213° (*c*, 1.6, $CHCl_3$). Calculated for $C_{19}H_{16}O_{10}N_2$ (containing a mole of ethyl acetate): C, 53.05%; H, 4.62%; N, 5.38%; acetyl, 8.27%. Found: C, 53.03%; H, 4.63%; N, 5.21%; acetyl, 7.81%.

Preparation of the Methyl D-Threosides via Acetobromo-D-threose

Tri-*O*-acetyl D-threose (22) (0.50 g) in chloroform (4 ml) ($[\alpha]_D$ +35°) was treated with hydrogen bromide (2 ml, 40% in acetic acid). Within 5 minutes the observed rotation was constant, giving a calculated value of $[\alpha]_D$ −10°. The solution was quickly concentrated, toluene being added 4 times in completing the evaporation of solvent, affording a pale yellow syrup (0.54 g). (Attempts to dry a portion thoroughly for analysis resulted in rapid darkening, and no crystalline product could be isolated from cold ether–hexane.)

The syrup (0.1 g) in methanol (5 ml) was shaken for 18 hours with silver oxide (0.3 g) and Drierite (0.7 g). Found: $[\alpha]_D$ −5° (calculated for methyl tetroside). In the absence of silver oxide and Drierite the observed rotation of the solution was constant in 10 minutes, $[\alpha]_D$ −6° (calculated for methyl tetroside). Both products were deacylated with sodium methoxide, and found by paper chromatography to contain mainly methyl threoside, $[\alpha]_D$ +25° (*c*, 1, H_2O). The infrared absorption spectra of the deacetylated products were closely similar to that of methyl α-D-threoside. Examined by vapor phase chromatography the α- and β-anomers were detected in the products in a ratio of about 3 to 1.

Lead Tetraacetate Oxidations

The methyl D-erythrosides (40 mg) in 5 ml of acetic–propionic acid mixture (75:25) (2) were each treated at 0° C with lead tetraacetate solution (50 mg in 4 ml of the same solvent). Oxidation of the methyl D-threosides was carried out in acetic acid at 25° C,

using the same concentration of reactants. Reaction rates were measured as described by Criegee (36).

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