The Synthesis of L-glycero*Tetrulose and Related Compounds.**

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[Reprint Order No. 6164.]

L-*glycero*Tetrulose (L-erythrulose) has been prepared from D-fructose by two different routes. Syntheses of 5-deoxy-D-*threo*pentulose and 5 : 6-dideoxy-D-*threo*hexulose are also described. An attempted synthesis of L-*glycero*tetrulose 4-phosphate proved of little value as a preparative method.

Recent investigations have indicated the importance of tetroses in photosynthesis (Bassham, Benson, Kay, Harris, Wilson, and Calvin, *J. Amer. Chem. Soc.*, 1954, **76**, 1760) and in pentose phosphate metabolism (Horecker, Gibbs, Klenow, and Smyrniotis, *J. Biol. Chem.*, 1954, **207**, 393). The enzyme transketolase involved in these processes acts on various ketose substrates, including L-*glycero*tetrulose, to give rise to " active glycollaldehyde." This term is used to describe the two-carbon moiety that is transferred from hydroxypyruvate or from $C_{(1)}$ and $C_{(2)}$ of L-*glycero*tetrulose, D-fructose 6-phosphate, D-*altro*heptulose 7-phosphate, and D-*erythro*pentulose 5-phosphate, respectively, to aldoses by transketolase with thiamine pyrophosphate as coenzyme. Thus, from D-ribose 5-phosphate, the product is D-*altro*heptulose 7-phosphate, which contains two more carbon atoms than its aldose precursor. Methods for preparing tetruloses, and in particular their phosphate derivatives, have thus attracted our attention.

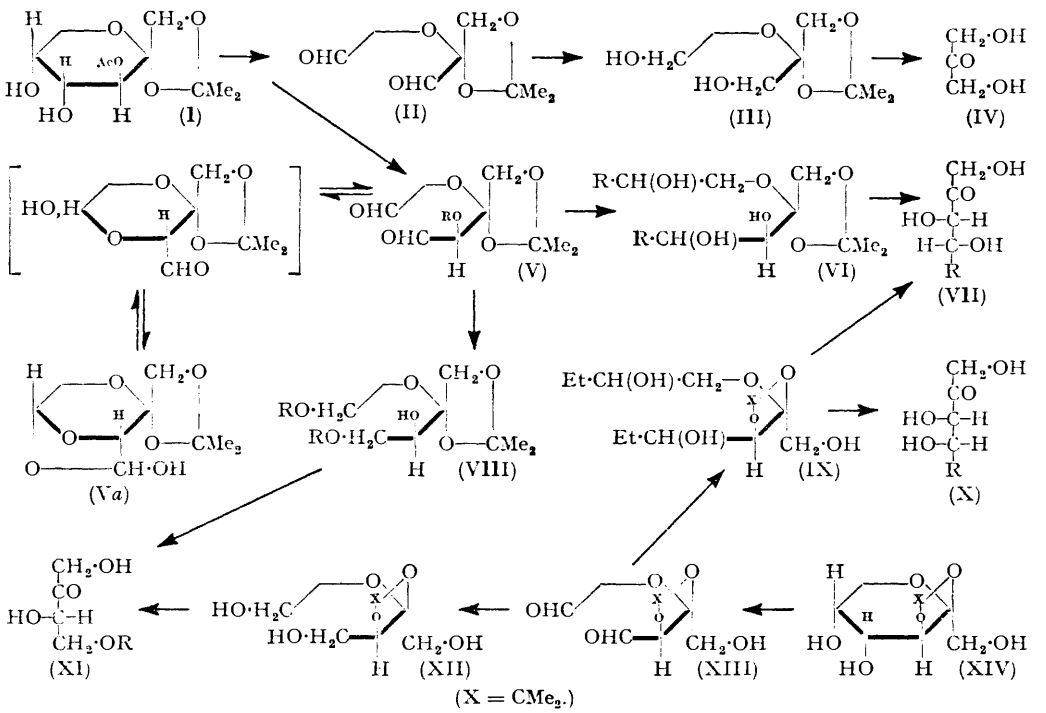
We have prepared L-*glycero*tetrulose (XI; R = H) from D-fructose since the structure of this tetrulose is pre-formed in this hexulose from $C_{(1)}$ to $C_{(4)}$. with the correct stereochemistry at $C_{(3)}$. By choice of suitably substituted D-fructopyranose derivatives, selective oxidative cleavage was caused to take place between $C_{(4)}$ and $C_{(5)}$ by using the α-glycol-splitting reagents, lead tetra-acetate or sodium metaperiodate. Reduction of the resultant aldehyde groups (from $C_{(4)}$ and $C_{(5)}$ of the original D-fructose), followed by removal of the protecting groups, yielded L-*glycero*tetrulose (XI; R = H). Two suitably protected compounds of D-fructopyranose are the 3-*O*-acetyl-1 : 2-*O*-*iso*propylidene (I) and the 2 : 3-*O*-*iso*propylidene (XIV) derivative, in which the 4- and 5-hydroxyl groups are available for α-glycol cleavage; the *iso*propylidene groups are stable under the oxidative conditions employed, yet are readily removed by mild acidic hydrolysis after the primary alcohol groups have been formed by reduction of the dialdehyde.

L-*glycero*Tetrulose (XI; R = H) has been prepared by bacterial oxidation of *meso*-erythritol (Bertrand, *Ann. Chim. Phys.*, 1904, **3**, 206, 259; Müller, Montigel, and Reichstein, *Helv. Chim. Acta*, 1937, **20**, 1468; Whistler and Underköfler, *J. Amer. Chem. Soc.*, 1938, **60**, 2507) whereas oxidation with chemical reagents gives DL-*glycero*tetrulose (Fenton and Jackson, *J.*, 1899, **7**; Neuberg, *Ber.*, 1902, **35**, 2627; Deniges, *Annalen*, 1909, **18**, 149, 168; Fischer and Tafel, *Ber.*, 1887, **20**, 1090). The latter was synthesised by Raphael (*J.*, 1952, 401) from but-2-ene-1 : 4-diol, and Iwadare (*Bull. Chem. Soc. Japan*, 1939, **14**, 131) synthesised the D-isomer *via* *iso*propylidene-D-glyceroyl chloride and the corresponding diazo-ketone. No wholly chemical synthesis of the L-isomer has been recorded.

* A summary of this paper was submitted at the 126th meeting of the American Chemical Society, New York, September 1954.

3-*O*-Acetyl-1 : 2-*O*-*iso*propylidene-β-D-fructopyranose (I) was prepared from 1 : 2-4 : 5-di-*O*-*iso*propylidene-β-D-fructose in improved yield (cf. Ohle and Schultz, *Ber.*, 1938, **71**, 2302) by acetylation with acetic anhydride in pyridine followed by selective hydrolysis of the product with 80% aqueous acetic acid at 37°. In an attempt to prepare the mono-*O*-acetyl dialdehyde (V; R = Ac), this derivative was oxidised with an excess of aqueous sodium metaperiodate, but further oxidation occurred with loss of the acetyl group to give the dialdehyde (II) (but see below). Reduction of this with ethereal lithium aluminium hydride gave the diol (III) which on acidic hydrolysis yielded dihydroxyacetone (IV) instead of the required L-*glycero*tetrulose (XI; R = H). Oxidation of 3-*O*-acetyl-1 : 2-*O*-*iso*propylidene-β-D-fructopyranose (I) with 1 mol. of metaperiodate gave a mixed product since on reduction and acidic hydrolysis a mixture of dihydroxyacetone (IV) and L-*glycero*tetrulose (XI; R = H) was obtained.

Oxidation of 3-*O*-acetyl-1 : 2-*O*-*iso*propylidene-β-D-fructopyranose (I) with lead tetra-acetate in glacial acetic acid produced, in poor yield, a crystalline hydroxy-dialdehyde (V; R = H) (from which a bis-2 : 4-dinitrophenylhydrazone was prepared), rather than the expected mono-*O*-acetyldialdehyde (V; R = Ac), owing to deacetylation during isolation. This " dialdehyde " (V; R = H) existed in a modified form, however, since it was almost



unoxidised by aqueous sodium metaperiodate, reacted with only slightly over 1 mol. of sodium hypoiodite, and gave an infrared absorption (in Nujol mull) devoid of carbonyl characteristics, thus suggesting that it exists mainly as the bicyclic hemiacetal (V*a*) (cf. Hurd, Baker, Holysz, and Saunders, *J. Org. Chem.*, 1953, **18**, 186). Reduction of this compound with an excess of ethereal lithium aluminium hydride gave the triol (VIII; R = H) which consumed 1 mol. of sodium metaperiodate with formation of 0·88 mol. of formaldehyde. Acidic hydrolysis of the triol (VIII; R = H) gave a mixture of L-*glycero*-tetrulose (XI; R = H) and ethylene glycol, from which the latter was removed by continuous chloroform-extraction.

It was of interest to attempt the preparations of 5-deoxypentuloses and 5 : 6-dideoxyhexuloses as reference compounds in enzymic syntheses. Thus, the " dialdehyde "

(V; R = H) when treated with ethereal methylmagnesium iodide and with ethereal ethylmagnesium bromide, gave, after acid hydrolysis, products containing mainly syrupy 5-deoxy-D-*threo*pentulose (VII; R = Me) and syrupy 5 : 6-dideoxy-D-*threo*hexulose (VII; R = Et) respectively. On paper chromatograms they gave single spots with R_F values and colour reactions indistinguishable from those of authentic specimens. Derived phenylosazones were indistinguishable from those prepared from 5-deoxy-D-xylose and 5 : 6-dideoxy-D-*xylo*hexose respectively. Authentic 5 : 6-dideoxy-D-*threo*hexose phenylosazone was prepared from 5 : 6-dideoxy-D-*xylo*hexose obtained by the acid hydrolysis of 5 : 6-dideoxy-1 : 2-*O*-*iso*propylidene-D-*xylo*hexose (McSweeney and Wiggins, *Nature*, 1951, **168**, 874). Clearly, in the Grignard reactions, asymmetric syntheses occurred which favoured the formation of the D-*threo*- (VII) rather than the L-*erythro*-configurations (X).

As an additional route for the preparation of L-*glycero*tetrulose (XI; R = H), 2 : 3-*O*-*iso*propylidene-β-D-fructopyranose (XIV), obtained by selective acid hydrolysis of 2 : 3-4 : 5-di-*O*-*iso*propylidene-β-D-fructose (Ohle and Koller, *Ber.*, 1924, **57**, 1566; Wolfrom, Shilling, and Binkley, *J. Amer. Chem. Soc.*, 1950, **72**, 4544) was oxidised with excess of sodium metaperiodate in aqueous solution. Continuous extraction with chloroform gave the syrupy dialdehyde (XIII) which gave a crystalline bis-2 : 4-dinitrophenylhydrazone and was reduced by ethereal lithium aluminium hydride to the triol (XII). Acidic hydrolysis of this triol gave syrupy L-*glycero*tetrulose (XI; R = H), characterised as its phenylosazone. This method of preparation gave a higher yield of L-*glycero*tetrulose than the foregoing preparation, and is more convenient.

These preparations provide methods for the synthesis of the sugar labelled with ^{14}C; thus [1-^{14}C]D-fructose would give [1-^{14}C]L-*glycero*tetrulose, and [3 : 4-$^{14}C_2$]D-fructose would give [3 : 4-$^{14}C_2$]L-*glycero*tetrulose.

Reaction of the dialdehyde (XIII) with ethylmagnesium bromide did not appear to be as stereospecific as the similar reaction with the hydroxy-dialdehyde (V; R = H). Treatment of the dialdehyde (XIII) (obtained by oxidation of 2 : 3-*O*-*iso*propylidene-β-D-fructopyranose) with ethereal ethylmagnesium bromide, followed by acid hydrolysis of the product (IX), gave a material which behaved like a 5 : 6-dideoxyhexulose on paper chromatograms. Since the optical rotation of this material differed from that of 5 : 6-dideoxy-D-*threo*hexulose and the derived 5 : 6-dideoxyhexose phenylosazone had a low indefinite m. p., it was probably a mixture of 5 : 6-dideoxy-L-*erythro*- (X; R = Et) and 5 : 6-dideoxy-D-*threo*-hexulose (VII; R = Et).

A preparation of L-*glycero*tetrulose 4-phosphate was attempted. L-*glycero*Tetrulose 1-phosphate has been produced from formaldehyde and hexose diphosphate by a rat-liver preparation (Charalampous and Mueller, *J. Biol. Chem.*, 1953, **201**, 161) and may act as a source of active glycolaldehyde. The triol (VIII; R = H) was treated in pyridine with 2 molar equivalents of diphenyl phosphorochloridate (Foster, Overend, and Stacey, *J.*, 1951, 980), which reacts preferentially with primary alcohol groups, giving the di(diphenyl phosphate) [VIII; R = $PO(OPh)_2$]. Catalytic hydrogenation in the presence of barium carbonate gave the barium diphosphate (VIII; R = PO_3Ba), which was hydrolysed in acid to a mixture, very probably of L-*glycero*tetrulose 4-phosphate (XI; R = PO_3Ba) and 2-hydroxyethyl dihydrogen phosphate, as indicated by their rates of movement and colour reactions on paper chromatograms. The yield of tetrulose phosphate was so poor that separation was not attempted. Alternative routes are being explored.

Experimental

Unless otherwise stated, optical rotations were measured at 20° in H_2O, evaporations were carried out under reduced pressure, and the solvent and spray reagents used for paper chromatography were butan-1-ol–ethanol–water (40 : 11 : 19 v/v) and a *ca.* 4% solution of *p*-anisidine hydrochloride in butan-1-ol–water. Rates of movement of spots on paper chromatograms were related to those of rhamnose, galactose, or the solvent front, and are denoted by R_{Rh}, R_{Gal}, and R_F respectively.

3-O-*Acetyl*-1 : 2-O-iso*propylidene*-β-D-*fructopyranose* (I).—1 : 2-4 : 5-Di-*O*-*iso*propylidene-α-D-fructose (112 g.) in pyridine (600 c.c.) containing acetic anhydride (150 c.c.) was kept at 37° for 16 hr., then poured into water (1 l.). The precipitated syrup was taken up in chloroform and

washed with successive portions of aqueous sodium hydrogen carbonate, N-sulphuric acid, and water, dried ($MgSO_4$), filtered, and evaporated. The syrupy 3-*O*-acetyl-1 : 2-4 : 5-di-*O*-*iso*propylidene-β-D-fructose was selectively hydrolysed at 37° for 20 hr. in 80% aqueous acetic acid (720 c.c.). The solution was evaporated until a white solid separated. Light petroleum (b. p. 60—80°; 500 c.c.) was added and the resulting precipitate filtered off (49 g.). The filtrate was evaporated to a syrup and hydrolysed with 80% aqueous acetic acid (500 c.c.) as described above (yield 29 g.). A third hydrolysis yielded a further 13 g. Recrystallisation of the combined material from benzene–light petroleum (b. p. 60—80°) gave the desired product (I) (85 g.), m. p. 149°, $[\alpha]_D$ −153° (*c*, 1·35) (Found: C, 50·4; H, 6·9. Calc. for $C_{11}H_{18}O_7$: C, 50·4; H, 6·9%).

Oxidation of 3-O-*Acetyl*-1 : 2-O-iso*propylidene*-β-D-*fructopyranose* (I).—(a) *With sodium metaperiodate.* The acetate (I) (0·5 g.) in phosphate buffer (pH 6) containing 0·15M-sodium metaperiodate (35 c.c.) was set aside for 48 hr. and then the solution was extracted thrice with ether. The combined extract was dried ($MgSO_4$) and filtered. The oxidation product was reduced in dry ethereal solution by an excess of lithium aluminium hydride (Lythgoe and Trippett, *J.*, 1950, 1983), and the product hydrolysed with 0·2N-sulphuric acid at 100° for 1 hr. After neutralisation ($BaCO_3$), filtration, and evaporation, the optically inactive product gave on paper chromatograms one discrete spot corresponding to dihydroxyacetone.

In a similar experiment, using 1 molar equivalent of sodium metaperiodate, the final product on examination on paper chromatograms showed the presence of dihydroxyacetone (IV) and *glycero*tetrulose (XI; R = H).

(b) *With lead tetra-acetate.* The acetate (I) (20 g.) in acetic acid (200 c.c.) was shaken with lead tetra-acetate (44 g., 1·3 mol.) for 24 hr. After treatment with ethylene glycol (0·82 c.c.), the solution was evaporated at 25° to *ca.* 100 c.c. It was added to water (500 c.c.), neutralised ($BaCO_3$), and filtered, and the filtrate extracted thrice with equal volumes of chloroform. The chloroform extract was dried ($MgSO_4$), filtered, and evaporated to a syrup which crystallised. Recrystallisation twice from ether gave the "*dialdehyde*" (V; R = H) (6·7 g.) as long prisms, m. p. 140—141°, $[\alpha]_D$ −37° (*c*, 0·94 in $CHCl_3$), −28° (*c*, 1·12) (Found: C, 49·7; H, 6·4%; *M*, 227, 226, as determined by the Menzies–Wright ebullition method, in chloroform and benzene respectively. $C_9H_{14}O_6$ requires C, 49·5; H, 6·4%; *M*, 218). The aldehyde (50 mg.) in ethanol (5 c.c.) containing 2 : 4-dinitrophenylhydrazine (86 mg., 1·9 mol.) was refluxed for 18 hr. On cooling, the yellow *bis*-2 : 4-*dinitrophenylhydrazone* separated and was recrystallised from ethanol {yield, 27 mg.; m. p. 104—106°, $[\alpha]_D$ −120° (*c*, 0·50 in $CHCl_3$)} (Found: C, 43·5; H, 4·0; N, 18·9. $C_{21}H_{22}O_{12}N_8$ requires C, 43·6; H, 3·8; N, 19·4%). The "dialdehyde" (V; R = H) after 1 hr. consumed only 0·16 mol. of sodium metaperiodate at pH 4. 1·14 Mol. of sodium hypoiodite was consumed at pH 11·4 in 18 hr. (cf. Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289).

Reduction of Dialdehyde (V; R = H).—Lithium aluminium hydride (0·4 g.) was carefully added to a solution of the dialdehyde (V; R = H) (3·6 g.) in boiling dry ether (250 c.c.), the whole heated under reflux for 15 min., and excess of reagent destroyed by addition of ethyl acetate. Water (500 c.c.) was added, organic solvents were evaporated, and dilute sulphuric acid was added to neutralise the solution. The precipitate was filtered off, and the filtrate evaporated to *ca.* 200 c.c. and then continuously extracted with chloroform. The extract was dried ($MgSO_4$), filtered, and evaporated to a syrupy *triol* (VI; R = H) (3·43 g.), $[\alpha]_D$ −35° (*c*, 2·45 in $CHCl_3$) (Found: C, 48·3; H, 8·1. $C_9H_{18}O_6$ requires C, 48·6; H, 8·1%). The triol on oxidation with sodium metaperiodate, buffered ($NaHCO_3$) or unbuffered (*ca.* pH 4), consumed 0·98 mol. of reagent; formic acid could not be detected. Following Bell's method (*J.*, 1948, 992), oxidation of the triol with metaperiodate gave 0·88 mol. of formaldehyde. Acetylation of the triol (132 mg.) in pyridine–acetic anhydride (2 + 0·4 c.c.) for 16 hr. at 20° gave a syrupy *triacetate* (184 mg.), $[\alpha]_D$ −48° (*c*, 3·36 in $CHCl_3$) (Found: C, 52·1; H, 6·9; Ac, 36·5. $C_{15}H_{24}O_9$ requires C, 51·7; H, 6·9; Ac, 37·1%).

L-glycero*Tetrulose* (XI; R = H).—The triol (VI; R = H) (1·01 g.) in 0·05N-sulphuric acid 10 c.c.) was heated at 100° for 1 hr., neutralised ($BaCO_3$), and filtered, and the filtrate extracted continuously with chloroform to remove ethylene glycol. Evaporation of the aqueous solution gave L-*glycero*tetrulose (XI; R = H) as a syrup (350 mg.), $[\alpha]_D$ +7° (*c*, 1·62). Müller, Montigel, and Reichstein (*loc. cit.*) and Whistler and Underköfler (*loc. cit.*) record $[\alpha]_D$ +12°. Iwadare (*loc. cit.*) records $[\alpha]_D^{15}$ −11° for the D-isomer. On the paper chromatogram the syrup gave a yellow-brown spot with R_{Rh} 1·00. L-*glycero*Tetrulose phenylosazone was obtained by treating an aqueous solution (10 c.c.) of the syrup (163 mg.) with phenylhydrazine (0·4 c.c.) and acetic acid (1·5 c.c.) at 50° for 18 hr. The product was filtered off, dried, washed with benzene, and

with water, and recrystallised from aqueous ethanol. The osazone (165 mg.) had m. p. 162°, $[\alpha]_D$ +32° (10 min.) ⟶ 0° (24 hr.; const.) (*c*, 0·75 in C_5H_5N–EtOH, 3 : 2 v/v) (Found: N, 18·6. Calc. for $C_{16}H_{18}O_2N_4$: N, 18·8%).

5-*Deoxy*-D-threo*pentulose* (VII; R = Me).—The dialdehyde (V; R = H) (713 mg.) was dissolved in boiling dry ether (200 c.c.), and an excess of methylmagnesium iodide [from magnesium (398 mg.) and methyl iodide (1·48 g.) in ether (20 c.c.)] added. After 15 min., water (50 c.c.) was added, and the aqueous layer neutralised with dilute sulphuric acid and filtered, and the filtrate extracted thrice with chloroform (50 c.c.). The combined extracts were dried ($MgSO_4$), filtered, and evaporated to a syrupy 5-deoxypentulose derivative (VI; R = Me) (200 mg.), $[\alpha]_D$ −45° (*c*, 2·00 in $CHCl_3$). On paper chromatograms it gave a single spot (R_F 0·86), yellow with *p*-anisidine hydrochloride and pink with orcinol–trichloroacetic acid (Klevstrand and Nordal, *Acta Chem. Scand.*, 1950, **4**, 1320). The syrup (VI; R = Me) (190 mg.) was hydrolysed with 0·05N-sulphuric acid at 100° for 1 hr. After neutralisation ($BaCO_3$), filtration, and evaporation, paper-chromatographic analysis of the product indicated the presence of 5-deoxy-D-*threo*pentulose (VII; R = Me); propane-1 : 2-diol, expected from the hydrolysis of the 5-deoxypentulose derivative (VI; R = Me), was not detected. Purification of the 5-deoxy-D-*threo*pentulose by chromatography on Whatman No. 1 filter-paper sheets (Flood, Hirst, and Jones, *Nature*, 1947, **160**, 86), followed by elution of the product from the appropriate sections of the filter papers with water, gave syrupy 5-deoxy-D-*threo*pentulose (97 mg.), $[\alpha]_D$ −1° (*c*, 1·94), −15° (*c*, 1·94 in MeOH); Gorin, Hough, and Jones (*J.*, 1953, 2140) record $[\alpha]_D$ −4° (in MeOH). The phenylosazone was prepared by warming the deoxypentulose (48 mg.) in water (5 c.c.) containing phenylhydrazine (0·12 c.c.) and acetic acid (0·5 c.c.) for 6 hr. at 50°. The osazone was filtered off, dried, washed with benzene and water, and recrystallised from aqueous ethanol. The product (15 mg.) had m. p. 171—173°, undepressed on admixture with 5-deoxy-D-*threo*pentose phenylosazone and depressed with 5-deoxy-L-*erythro*pentose phenylosazone. The *X*-ray powder photograph of the product was identical with that of an authentic specimen. Our specimen had $[\alpha]_D$ +73° (10 min.) ⟶ +7° (24 hr., const.) (*c*, 0·55 in C_5H_5N–EtOH, 3 : 2 v/v) (Found: C, 65·4; H, 6·4. Calc. for $C_{17}H_{20}O_2N_4$: C, 65·4; H, 6·4%).

5 : 6-*Dideoxy*-D-threo*hexulose* (VII; R = Et).—The dialdehyde (V; R = H) (700 mg.) was treated with ethylmagnesium bromide as for the foregoing preparation. The 5 : 6-dideoxyhexulose derivative so obtained was a syrup (VI; R = Et) (434 mg.), $[\alpha]_D$ −11° (*c*, 2·17 in $CHCl_3$), which gave on the paper chromatogram a yellow spot with R_F 0·90. The syrup (400 mg.) was hydrolysed as in the preparation of 5-deoxy-D-*threo*pentulose (VII; R = Me) and yielded a product which on paper chromatograms gave a yellow spot (R_{Rh} 2·2; slightly faster than that of 5 : 6-dideoxy-D-*xylo*hexose). Butane-1 : 2-diol was not detected with the ammoniacal silver nitrate spray. Purification by chromatography on Whatman No. 1 filter-paper sheets gave syrupy 5 : 6-dideoxy-D-*threo*hexulose (VII; R = Et) (200 mg.), $[\alpha]_D$ +6° (*c*, 2·50), −8° (*c*, 2·50 in MeOH). The dideoxyhexulose (47 mg.) was dissolved in water (10 c.c.) containing acetic acid (0·5 c.c.), phenylhydrazine (0·12 c.c.) was added, and the solution warmed at 50° for 6 hr. The product was filtered off, dried, washed with benzene, then water, and recrystallised from aqueous ethanol. The osazone (18 mg.) had m. p. 164—165°, undepressed on admixture with 5 : 6-dideoxy-D-*threo*hexose phenylosazone. This gave an *X*-ray powder photograph identical with that of an authentic specimen (see below) and had $[\alpha]_D$ +44° (10 min.) ⟶ +15° (24 hr.; const.) (*c*, 0·55 in C_5H_5N–EtOH, 3 : 2 v/v) (Found: C, 66·6; H, 6·7. Calc. for $C_{18}H_{22}O_2N_4$: C, 66·3; H, 6·7%).

5 : 6-*Dideoxy*-D-xylo*hexose and its Phenylosazone*.—5 : 6-Dideoxy-1 : 2-*O-iso*propylidene-D-*xylo*hexose (McSweeney and Wiggins, *loc. cit.*) (42 mg.) was hydrolysed in 0·1N-sulphuric acid (2 c.c.) at 100° for 1 hr. The solution was neutralised ($BaCO_3$), filtered, and evaporated to a syrup which had $[\alpha]_D$ +2° (*c*, 0·90 in EtOH). Treatment of the aldose (30 mg.) in water (2 c.c.) with phenylhydrazine (0·1 c.c.) and acetic acid (0·3 c.c.) at 80° for 1 hr. gave an *osazone*, which was collected, dried, and washed with benzene and then water. It (13 mg.) had m. p. 167—168° and $[\alpha]_D$ +47° (10 min.) ⟶ +20° (24 hr.; const.) (*c*, 0·60 in C_5H_5N–EtOH, 3 : 2 v/v) (Found: C, 66·1; H, 6·4. $C_{18}H_{22}O_2N_4$ requires C, 66·3; H, 6·7%).

Oxidation of 2 : 3-O-iso*Propylidene*-β-D-*fructopyranose* (XIV) *with Sodium Metaperiodate*.—2 : 3-*O-iso*Propylidene-α-D-fructopyranose (XIV) (860 mg.) in aqueous sodium metaperiodate (4%; 50 c.c.), buffered at pH 6 with 0·7M-potassium dihydrogen phosphate (10 c.c.), was kept for 2 hr. and then continuously extracted with chloroform. The extract was dried ($MgSO_4$), filtered, and evaporated to the dialdehyde (XIII; 838 mg.) as a colourless syrup with $[\alpha]_D$ +21° (*c*, 3·35 in $CHCl_3$), which gave on a paper chromatogram a light yellow spot (R_F 0·87). The

syrupy dialdehyde (160 mg.) and 2 : 4-dinitrophenylhydrazine (266 mg., 1·9 mol.) were boiled under reflux in ethanol (50 c.c.) for 20 hr. and, on cooling, the solution yielded yellow crystals which were recrystallised from ethanol to give the *bis*-2 : 4-*dinitrophenylhydrazone* (94 mg.), m. p. 109—113°, $[\alpha]_D$ −10° (*c*, 0·52 in $CHCl_3$) (Found : C, 43·5; H, 3·8. $C_{21}H_{22}O_{12}N_8$ requires C, 43·6; H, 3·8%).

Reduction of the Dialdehyde (XIII).—The dialdehyde (480 mg.) in dry ether (10 c.c.) was added to an excess of lithium aluminium hydride (0·1 g.) in ether (10 c.c.); after 10 min., excess of reagent was destroyed by ethyl acetate. Water (50 c.c.) was then added, organic solvents were evaporated, and the remaining aqueous white sludge was titrated to neutrality with dilute hydrochloric acid. The solution was filtered and extracted continuously with chloroform. The extract was dried ($MgSO_4$), filtered, and evaporated to a syrupy triol (XII) (471 mg.), $[\alpha]_D$ +59° (*c*, 3·74 in $CHCl_3$). This gave on a paper chromatogram a light yellow spot (R_F 0·75).

L-glycero*Tetrulose* (XI; R = H).—The triol (XII) (216 mg.) was hydrolysed in 0·1N-sulphuric acid (2 c.c.) at 100° for 1 hr. The solution was neutralised ($BaCO_3$), filtered, and extracted continuously with chloroform to remove ethylene glycol. The aqueous portion was evaporated to a syrup (110 mg.), $[\alpha]_D$ +5° (*c*, 1·7). L-*glycero*Tetrulose (30 mg.) in water (4 c.c.) containing acetic acid (0·5 c.c.) and phenylhydrazine (0·1 c.c.) was kept for 2 hr. at 50°. The osazone was filtered off, dried, washed with benzene, then water, and dried. It had m. p. 160—161° and $[\alpha]_D$ +32° (10 min.) ⟶ 0° (const.; 24 hr.) (*c*, 0·50 in C_5H_5N–EtOH, 3 : 2 v/v) (Found : C, 64·1; H, 6·0; N, 19·2. Calc. for $C_{16}H_{18}O_2N_4$: C, 64·4; H, 6·0; N, 18·8%).

Reaction of the Dialdehyde (XIII) *with Ethylmagnesium Bromide*.—The dialdehyde (549 mg.) in dry ether (10 c.c.) was treated under reflux with excess of ethylmagnesium bromide [prepared from magnesium (800 mg.) and ethyl bromide (2·5 c.c.) in ether (10 c.c.)], then refluxed for 15 min. Water (40 c.c.) was added and the aqueous layer neutralised with dilute sulphuric acid. The solution was filtered and extracted continuously with chloroform. The extract was dried ($MgSO_4$), filtered, and evaporated to a syrup (IX) (588 mg.) which had $[\alpha]_D$ +33° (*c*, 5·6 in $CHCl_3$) and gave a yellow spot (R_F 0·90) on a paper chromatogram. The syrup (520 mg.) was hydrolysed with 0·1N-sulphuric acid (5 c.c.) at 100° for 30 min., neutralised ($BaCO_3$), filtered, and evaporated. The syrupy residue gave on a paper chromatogram mainly a yellow-brown spot (R_{Rh} 2·2, corresponding to 5 : 6-dideoxy*threo*hexulose) with traces of *glycero*tetrulose. The product was purified by chromatography on Whatman No. 1 filter-paper sheets to give a syrup (177 mg.), $[\alpha]_D$ −14° (*c*, 2·53 in MeOH), −8° (*c*, 2·53). 5 : 6-Dideoxy-D-*threo*hexulose has $[\alpha]_D$ −8° (*c*, 2·50 in MeOH) and $[\alpha]_D$ +6° (*c*, 2·50). The syrup [(VII) + (X); R = Et] (170 mg.) in water (10 c.c.) containing phenylhydrazine (0·35 c.c.) and acetic acid (2 c.c.) was warmed at 50° for 3 hr. The osazone which separated on cooling was collected, washed with water, and recrystallised from benzene–light petroleum (b. p. 60—80°). The product had a m. p. range 80—110°, indicating a mixture of isomeric phenylosazones (Found : C, 66·3; H, 6·6. Calc. for $C_{18}H_{22}O_2N_4$: C, 66·3; H, 6·7%).

Attempted Preparation of L-glycero*Tetrulose* 4-*Phosphate* (VII; R = PO_3Ba).—The triol (VIII; R = H) (829 mg.) in pyridine (2·7 c.c.) was treated at 0° with diphenyl phosphorochloridate (2·22 g., 2·2 mol.). After 10 min. at 0° and 18 hr. at 20°, the solution was poured into aqueous sodium hydrogen carbonate (50 c.c.), and the solution extracted twice with equal volumes of chloroform. The combined extract was shaken with water, dried ($MgSO_4$), filtered, and evaporated to a syrup [VIII; R = $PO(OPh)_2$] (2·58 g.), $[\alpha]_D$ −14° (*c*, 2·18 in MeOH) (Found : P, 8·8. $C_{33}H_{36}O_{12}P_2$ requires P, 9·0%). The *bis*(*diphenyl phosphate*) [VIII; R = $PO(OPh)_2$] (871 mg.) was boiled under reflux in methanol (20 c.c.) containing activated charcoal (0·5 g.) for 10 min. to remove catalyst poisons. The solution was filtered and made up to 50 c.c. with methanol. Water (16 c.c.), barium carbonate (2 g.), and Adams catalyst (150 mg.) were added and the mixture was shaken in hydrogen at 1 atm. After 4 hr., when uptake of hydrogen had ceased, the solution was filtered and evaporated to a white solid (VIII; R = PO_3Ba) (697 mg.), $[\alpha]_D$ −15° (*c*, 0·57).

In order to find suitable conditions for hydrolysis of the *iso*propylidene groups and not the phosphate, a portion (32·6 mg.) was dissolved in 0·1N-sulphuric acid (30 c.c.), barium sulphate was centrifuged off, and the residue heated at 80°. At intervals samples were taken and the amount of inorganic phosphate liberated estimated by the method of Foster, Overend, and Stacey (*loc. cit.*). After 4 hr., 8% of the total phosphate was liberated. The salt (VIII; R = PO_3Ba) (138 mg.) was partially hydrolysed in 0·1N-sulphuric acid (15 c.c.) at 80° for 4 hr. It was titrated to pH 7 with aqueous barium hydroxide, the solution filtered, and the filtrate evaporated to a small volume. An excess of acetone was added and the precipitated material collected, triturated with ethanol, and recovered. The product (23 mg.) was examined on

paper chromatograms (Whatman No. 542; ethyl acetate–acetic acid–formic acid–water, 18 : 3 : 1 : 4 v/v). The presence of two compounds was indicated. The slower-moving material (R_{Gal} 0·74) (L-*glycero*tetrulose 4-phosphate ?) gave a blue colour with the ammonium molybdate–perchloric acid phosphate spray (Hanes and Isherwood, *Nature*, 1949, **164**, 1107) and a yellow colour with the *p*-anisidine hydrochloride spray. The faster-moving material (2-hydroxyethyl dihydrogen phosphate ?) gave a blue spot (R_{Gal} 1·3) with the phosphate spray and no colour with the *p*-anisidine hydrochloride spray. The original compound (VIII; R = PO_3Ba) which gave yellow and blue spots (R_{Rh} 1·2) with the *p*-anisidine hydrochloride and phosphate sprays respectively, was not present.

The authors thank Dr. R. N. Jones of the National Research Laboratories, Ottawa, Canada, for determining the infrared spectrum of the bicyclic hemiacetal (V*a*), and the Chemical Society for a grant. One of them (P. A. J. G.) thanks the City of Bristol Education Authorities for a Scholarship.

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