Branched-chain Sugars. Part VIII.[1] A Contribution to the Chemistry of 2-*C*-Methyl-L-arabinose and -ribose

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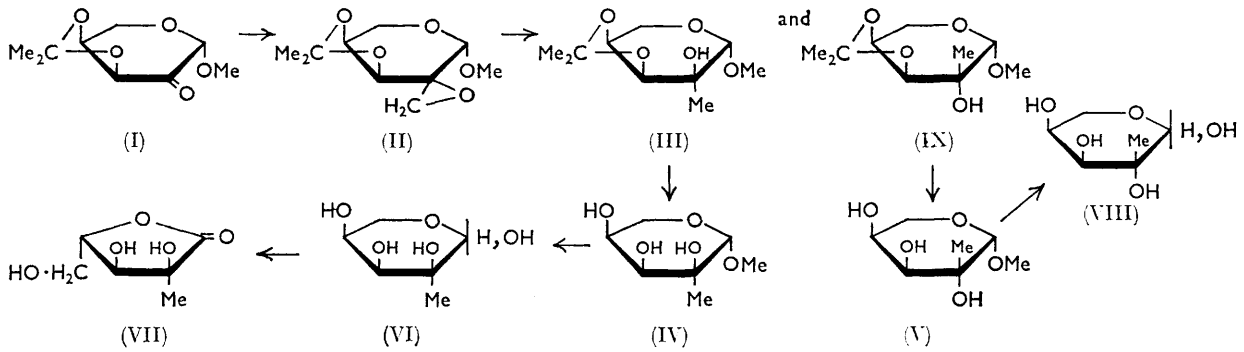
Treatment of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentosulopyranoside with diazomethane followed by lithium aluminium hydride yields two isomeric 2-*C*-methylpentoside derivatives: the preponderant product has the *ribo*-configuration. Evidence to support the configurations assigned to the products is provided. The stabilities of 2-*C*-methyl-L-ribose and -arabinose in acidic and basic media have been compared qualitatively with those of L-arabinose and D-ribose. Preliminary results on the treatment of methyl 2,2'-anhydro-2-*C*-hydroxymethyl-3,4-*O*-isopropylidene-β-L-pentoside (a mixture of the *arabino*- and *ribo*-isomers) with methanolic ammonia are noted.

PREVIOUSLY it was reported [2] that treatment of methyl 3,4-*O*-isopropylidene-β-D-*erythro*-pentosulopyranoside with a slight excess of diazomethane in diethyl ether–methanol gives a mixture of the two possible isomeric methyl 2,2'-anhydro-2-*C*-hydroxymethyl-3,4-*O*-isopropylidene-β-D-pentosides. The corresponding reaction has now been carried out in the L-series with methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentosulopyranoside (I).[3] Some reactions of epoxides of this type have been examined [4] and in this paper a further investigation is reported.

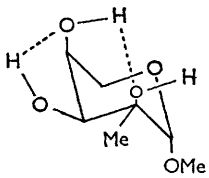
Treatment of the epoxide mixture (II; configuration at C-2 not defined) with lithium aluminium hydride (cf. ref. 1) afforded mainly a crystalline methyl 3,4-*O*-isopropylidene-2-*C*-methyl-β-L-pentoside (III) which on deacetonation gave a crystalline methyl 2-*C*-methyl-β-L-pentoside (IV). These products have now been shown to have the *ribo*-configuration. Partial hydrolysis of the mother liquors from the lithium aluminium hydride reaction gave an isomeric branched-chain glycoside (V), identical with the compound obtained by Burton *et al.*[3] from sequential treatment of compound (I) with methylmagnesium iodide and partial hydrolysis, and considered by them to be methyl 2-*C*-methyl-β-L-arabinoside. Products (IV) and (V) both consumed periodate (2·05 and 2·03 mol. respectively), which indicates that both contained three hydroxy-groups attached to contiguous carbon atoms and that epoxide cleavage had taken place as expected,[5] by attack of the hydride ion at the primary rather than at the tertiary carbon atom.

That the main product (III) had the *ribo*-configuration was confirmed by complete hydrolysis to give a syrupy 2-*C*-methylpentose (VI) (characterised as its crystalline toluene-*p*-sulphonylhydrazone) which when oxidised with bromine [6] gave the crystalline enantiomorph (VII) of the known 'α'-*D*-glucosaccharinic acid lactone,[7] the structure of which has been established as 2-*C*-methyl-D-ribono-γ-lactone.[7,8] Additional evidence for configurational assignments of the glycosides was obtained from intramolecular hydrogen-bonding studies.[9] In carbon tetrachloride solutions intermolecular hydrogen-bonding between alcohol molecules is eliminated at concentrations less than 0·005M, and so in dilute solutions intramolecular hydrogen-bonding can be investigated by i.r. absorption spectroscopy. The OH stretching frequency of secondary alcohols occurs near 3630 cm.$^{-1}$ and reductions in this frequency can be related to the strengths of hydrogen bonds in which the hydrogens become involved. Bonding of a hydroxy-group on a saturated six-membered ring with a *gauche*-related neighbouring oxygen gives a five-membered ring and causes a decrease in the frequency of some 30—40 cm.$^{-1}$,



[1] Part VII, B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), 1966, 398.
[2] W. G. Overend and N. R. Williams, *J. Chem. Soc.*, 1965, 3446.
[3] J. S. Burton, W. G. Overend, and N. R. Williams, *J. Chem. Soc.*, 1965, 3433.
[4] See J. S. Burton, W. G. Overend, and N. R. Williams, *Proc. Chem. Soc.*, 1962, 181 and ref. 2 for treatment with sodium hydroxide.
[5] R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.
[6] Modification of the method of J. W. E. Glattfield and M. T. Hanke, *J. Amer. Chem. Soc.*, 1918, **40**, 989.
[7] J. C. Sowden, M. G. Blair, and D. J. Kuenne, *J. Amer. Chem. Soc.*, 1957, **79**, 6450.
[8] J. C. Sowden and D. R. Strobach, *J. Amer. Chem. Soc.*, 1960, **82**, 3707.
[9] M. Ticky, *Adv. Org. Chem.*, 1965, **5**, 115.

whereas an axial hydroxy-group bonded to a *syn*-axial oxygen atom forms a stronger six-membered ring and gives rise to considerably lower absorption frequencies. Thus the bonded hydroxy-group in cyclohexane-1,3-*cis*-diol absorbs at 3544 cm.$^{-1}$ and experience in carbohydrate chemistry [10-12] indicates that values near 3510 cm.$^{-1}$ are frequently found for this type of alcohol grouping. Clearly with three hydroxy-groups present the two 2-*C*-methylpentosides (IV and V) would be expected to give complex spectra which, however, are quite different and allow assignment of configuration at C-2. Whereas the arabinoside (V) gives a strong absorption at 3591 cm.$^{-1}$ with a shoulder at 3573 cm.$^{-1}$ indicative of weak bonds, the *ribo*-isomer (IV) shows absorptions at 3590 and 3570 cm.$^{-1}$ together with a more intense band at 3512 cm.$^{-1}$. This last absorption reveals the presence of a six-membered ring, and consequently an OH(2)—OH(4) interaction. Furthermore, it reveals that the illustrated conformation is assumed in carbon tetrachloride solution and suggests that the hydrogen-bonding pattern may, for example, be as shown.



Acid hydrolysis of the glycoside (V) gave syrupy 2-*C*-methyl-L-arabinose (VIII). No crystalline hydrazone could be prepared and the sugar was characterised by oxidation with bromine to the corresponding acid lactone, which with phenylhydrazine yielded a crystalline phenylhydrazide. An examination of the electrophoretic and chromatographic behaviour of compounds (IV), (V), (VI), and (VIII) gave supplementary evidence about their configurations. The results are shown in the Table and those particularly of electrophoresis in molybdate buffer, and of chromatography in the presence and absence of phenylboronic acid are striking. Complexing in molybdate buffer is specific for a *cis*,*cis*-triol system with the hydroxy-groups on a six-membered ring disposed axial–equatorial–axial.[13] Such a grouping can occur in L-ribose and in 2-*C*-methyl-L-ribose in either chair conformation but not in L-arabinose or in 2-*C*-methyl-L-arabinose. Addition of phenylboronic acid to the chromatographic solvent increases the mobility of pyranoid compounds containing, in a chair conformation, 1,3-diaxial diol groups with an oxygen atom in the central equatorial position.[10,14] As expected, this increase in mobility occurred with compounds (IV) and (VI), D-ribose, and methyl β-D-ribopyranoside, but not with the epimeric compounds.

[10] See R. J. Ferrier, W. G. Overend, Mrs. G. A. Rafferty, H. M. Wall, and N. R. Williams, *Proc. Chem. Soc.*, **1963**, **133**, and unpublished results.
[11] H. Spedding, *J. Chem. Soc.*, **1961**, **3617**; R. J. Ferrier, D. Prasad, A. Rudowski, and I. Sangster, *J. Chem. Soc.*, **1964**, **3330**.
[12] F. Korte, U. Claussen, and G. Snatzke, *Tetrahedron*, **1964**, **20**, 1477.

This work has shown that treatment of the glycosulopyranoside (I) with diazomethane and cleavage of the resultant epoxide (II) with lithium aluminium hydride

Electrophoretic and chromatographic mobilities

	M_G in borate buffer at pH 9·2 *	M_S in molybdate buffer at pH 5·0 †	R_F ‡ in solvent A	R_F in solvent B
L-Arabinose	0·91	0·15	0·18	0·13
D-Ribose §	0·72	0·48	0·27	0·54
2-*C*-Methyl-L-arabinose	0·85	0·15	0·37	0·34
2-*C*-Methyl-L-ribose	0·70	0·61	0·39	0·71
Methyl β-L-arabinopyranoside	0·29	<0·1	0·40	0·31
Methyl β-D-ribopyranoside	0·44	<0·1	0·55	0·86
Methyl 2-*C*-methyl-β-L-arabinopyranoside	0·23	<0·1	0·58	0·52
Methyl 2-*C*-methyl-β-L-ribopyranoside	0·30	<0·1	0·74	0·92

* M_G = Rate of migration relative to D-glucose. Results were corrected by measuring the electro-endosmotic flow of 2,3,4,6-tetra-*O*-methyl-D-glucose. For details of buffer see J. L. Frahn and J. A. Mills, *Chem. and Ind.*, 1956, 578. † M_S = Rate of migration relative to sorbitol (glucitol) corrected by measuring the electro-endosmotic flow of glycerol. For buffer see E. J. Bourne, D. H. Hutson, and H. Weigel, *J. Chem. Soc.*, 1960, 4252. ‡ R_F = Mobility relative to solvent front. § Use of the D-isomer should not affect the mobility or vitiate comparisons.

is an alternative procedure to treatment with either methylmagnesium iodide [3] or methyl-lithium [15] for the introduction of a methyl branch at C-2 in compound (I). Like treatment with methyl-lithium, but unlike that with methylmagnesium iodide, this reaction leads mainly to a product with the L-*ribo*-configuration.[16] Although Burton *et al.*[3] isolated only methyl 3,4-*O*-isopropylidene-2-*C*-methyl-β-L-arabinoside (IX) and then, by hydrolysis, compound (V) from the reaction of compound (I) with methylmagnesium iodide, a careful re-examination of this reaction has shown that in fact both compounds (III) and (IX) are produced, although the former is formed only in small amount.

The 2-*C*-methylpentoses (VI and VIII) showed considerable stability in both acids and bases. For example, they could still be detected chromatographically (and in fact were the only detectable components) after being heated under reflux for 4 hr. with 4N-hydrochloric acid: this treatment destroyed both D-ribose and L-arabinose. Furthermore, these branched-chain sugars on chromatograms react more slowly than the pentoses with spray reagents containing an aromatic amine and an acid, which suggests that the furan derivatives arising under these conditions,[17] which lead to coloured products, are

[13] H. Weigel, *Adv. Carbohydrate Chem.*, **1963**, **18**, 61.
[14] E. J. Bourne, E. M. Lees, and H. Weigel, *J. Chromatography*, **1963**, **11**, 253.
[15] A. A. J. Feast, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), **1966**, **303**.
[16] The direction of addition reactions to glycosulopyranosides will form the subject of a separate publication. See P. M. Collins, Ph.D. Thesis, University of London, 1963.
[17] See C. D. Hurd and L. L. Isenhour, *J. Amer. Chem. Soc.*, **1932**, **54**, 317; M. L. Wolfrom, R. D. Schuetz, and L. F. Cavalieri, *J. Amer. Chem. Soc.*, **1948**, **70**, 514; **1949**, **71**, 3518.

less readily formed. 2-*C*-Methyl-L-arabinose also failed to give a positive Molisch test and 2-*C*-hydroxymethyl-D-ribose (hamamelose) was shown to be reasonably stable in 4N-hydrochloric acid at 100°, a result at variance with a report by Fischer and Freudenberg [18] that hamamelose is more sensitive to hot mineral acids than glucose and other aldohexoses.

When the 2-*C*-methylpentoses (VI and VIII) were heated with pyridine, under conditions which caused epimerisation of unbranched pentoses, no isomerisation could be detected chromatographically. In N-sodium hydroxide at 100° the branched-chain sugars again behaved differently to pentoses. Whereas L-arabinose and D-ribose gave a number of products including lactones, and retained no trace of starting material, the 2-*C*-methylpentoses were almost unchanged and gave no detectable lactones, although spraying a chromatogram of the alkaline solution of 2-*C*-methyl-L-arabinose with universal indicator solution revealed an acidic component moving at the same rate as lactic acid. A reverse aldolisation of a 2-*C*-methylpentose would give lactaldehyde and glyceraldehyde and the latter is known to isomerise under basic conditions to lactic acid.[19] This type of change has been proposed for the formation of lactic acid and other short chain fragments from hexoses [20] but no direct evidence for it is available. When solutions of L-arabinose or 2-*C*-methyl-L-arabinose in methanol (one part) and 0·025N-aqueous sodium hydroxide (two parts) were heated under reflux for 2 hr. titration indicated that acidic products were produced from both substances, but not so readily from the branched-chain pentose as from L-arabinose (0·16 and 1·5 equiv. of acid respectively). Likewise in an excess of 0·01N-sodium hydroxide at room temperature the two sugars behaved differently. Whereas there was virtually no change in the titre with acid of the solution of the 2-*C*-methylpentose over 16 days, during the same period the titre of the solution of L-arabinose decreased by an amount equivalent to the production from the pentose of 1·5 mol. of acid. Apparently the absence of the α-hydrogen atom makes the 2-*C*-methylpentoses much more stable than the unbranched pentoses in both acidic and basic media.

The epoxide (II) was also treated with methanolic ammonia and afforded a crystalline product which had the correct analysis for a methyl 2-aminomethyl-3,4-*O*-isopropylidene-β-L-pentoside. Mild acetylation gave a gummy product which contained no *O*-acetyl group, so presumably epoxide cleavage had occurred to give a primary amino-group and a tertiary hydroxy-group rather than a product containing a primary hydroxy-group, *i.e.* cleavage occurs of the same bond as when the epoxide (II) is treated with lithium aluminium hydride. Reactions of this type are being investigated further as part of a programme of work on the synthesis of branched-chain amino-sugars.[21]

EXPERIMENTAL

Methods.—Analytical paper chromatograms were prepared under as near identical conditions as possible by the descending flow method on Whatman no. 1 paper. Spray reagents were (i) silver nitrate–sodium hydroxide,[22] (ii) aniline hydrogen phthalate,[23] and (iii) hydroxylamine–ferric chloride.[24] For glycosides or sugar alcohols which, in the presence of phenylboronic acid could not be detected by the above reagents, the method (iv) incorporating hydrogen fluoride developed by Britton [25] for the detection of carbohydrates in the presence of borate was used. Chromatograms for preparative purposes were made with Whatman no. 3 paper. Solvent systems were (A) the upper phase of n-butanol–ethanol–water (4 : 1 : 5 v/v), and (B) phenylboronic acid (5 g.) in solvent A (100 ml.) containing sufficient additional ethanol (*ca.* 2·5 ml.) to maintain homogeneity.

The enclosed strip technique [26] was used for paper electrophoresis with Whatman no. 3 paper as support. Generally spots were located with spray (i). T.l.c. was carried out with plates prepared according to Stahl.[27] Spots were detected by spraying either with concentrated sulphuric acid in ethanol or with an anisaldehyde spray.[28]

Qualitative i.r. spectra were measured with a Perkin-Elmer Infracord 137 spectrophotometer. Syrupy samples were prepared as smears on potassium bromide discs and solids as potassium bromide discs containing *ca.* 1% of the material. High resolution i.r. spectra were measured with a Unicam SP 700 spectrophotometer, on 0·005M solutions in carbon tetrachloride in 1 cm. cells.

Methyl 2,2′-Anhydro-2-C-hydroxymethyl-3,4-O-isopropylidene-β-L-pentoside mixture (II).—Diazomethane (3 g.) in ethanolic ether (200 ml.) was added to a solution of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentosulopyranoside (9 g.) in methanol (200 ml.) at 0°. Nitrogen was evolved and after storage overnight the solvent was evaporated to a syrup (9·2 g.), b.p. 72°/0·2 mm., $[\alpha]_D^{20}$ +195° (*c* 1·1 in MeOH), no C=O absorption. Burton *et al.*[4] give b.p. 76°/0·1 mm., $[\alpha]_D^{20}$ +196° (in MeOH) but have not yet described the preparation. The i.r. absorption spectrum of our compound was identical with that of the sample prepared earlier in this laboratory.[4]

Methyl 3,4-O-Isopropylidene-2-C-methyl-β-L-riboside (III).—Lithium aluminium hydride (1·9 g.) was added in portions with stirring to dry ether (500 ml.). Methyl 2,2′-anhydro-2-*C*-hydroxymethyl-3,4-*O*-isopropylidene-β-L-pentoside (2 g.) in ether (50 ml.) was added in one portion, and the mixture was heated under reflux for 3 hr. and cooled in ice. The excess of hydride was destroyed by dropwise addition of wet ethyl acetate followed by water. The ethereal layer was separated and the aqueous phase was extracted with ether (3 × 10 ml.). The combined extracts were dried

[18] E. Fischer and K. Freudenberg, *Ber.*, 1912, **45**, 2709.
[19] J. U. Nef, *Annalen*, 1904, **335**, 247.
[20] J. C. Sowden, *Adv. Carbohydrate Chem.*, 1957, **12**, 35.
[21] See S. W. Gunner, W. G. Overend, and N. R. Williams, *Chem. and Ind.*, 1964, 1523; S. W. Gunner, Ph.D. Thesis, University of London, 1964; R. King, S. McNally, W. G. Overend, and N. R. Williams, unpublished results.
[22] W. E. Trevelyan, D. P. Procter, and J. S. Harrison, *Nature*, 1950, **166**, 444.
[23] S. M. Partridge, *Nature*, 1949, **164**, 443.
[24] M. Abdel-Akher and F. Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.
[25] H. G. Britton, *Biochem. J.*, 1959, **73**, 19P.
[26] A. B. Foster, *Chem. and Ind.*, 1952, 1050.
[27] E. Stahl, *Chem.-Ztg.*, 1958, **82**, 323.
[28] E. Stahl and U. Kaltenbach, *J. Chromatography*, 1961, **5**, 351.

(anhydrous K_2CO_3) and evaporated. The colourless platelets of *methyl* 3,4-O-*isopropylidene*-2-C-*methyl*-β-L-*riboside* (1 g., 50%) had m.p. 69—70° [from light petroleum (b.p. 40—60°)], $[\alpha]_D^{20}$ +140° (*c* 1 in EtOH), $\nu_{max.}$ 3500 cm.$^{-1}$ (OH) (Found: C, 54·7; H, 8·0; O, 36·5. $C_{10}H_{18}O_5$ requires C, 55·0; H, 8·3; O, 36·7%).

Methyl 2-C-*Methyl*-β-L-*arabinoside* (V) *and* -*riboside* (IV).—(*a*) The syrupy mother liquors (0·5 g.) from the lithium aluminium hydride reaction with compound (II) in methanol (20 ml.) containing water (0·25 ml.) and concentrated hydrochloric acid (0·2 ml.) were heated under reflux for 3 hr. After neutralisation ($PbCO_3$), filtration, and evaporation, a syrup was obtained which was extracted with ethyl acetate (20 ml.). The filtered extract was concentrated to a syrup which crystallised when nucleated with methyl 2-*C*-methyl-β-L-arabinoside. The *C*-methylarabinoside (90 mg.) had m.p. 97—98° (from ethyl acetate), mixed m.p. with an authentic sample 96—97°, $[\alpha]_D^{20}$ +125° (*c* 0·47 in EtOH) (lit.,[3] m.p. 100°, $[\alpha]_D^{20}$ +124° in EtOH).

(*b*) Methyl 3,4-*O*-isopropylidene-2-*C*-methyl-β-L-riboside (0·2 g.) in methanol (25 ml.) was shaken with Amberlite IR-120 (H^+) resin (0·8 g.) until spectrophotometric measurements at 263 mμ indicated that no more acetone was being produced (18 hr.). The supernatant liquid was decanted and the resin washed with methanol. Alternatively, the isopropylidene derivative (0·5 g.) in methanol (20 ml.) containing concentrated hydrochloric acid (0·2 ml.) and water (0·25 ml.) was heated under reflux for 3 hr. The solution was neutralised ($PbCO_3$). In either case, the product was isolated by evaporation of the solvent, but from the deacetonation with hydrochloric acid the product was syrupy. *Methyl* 2-*C*-*methyl*-β-L-*riboside* (0·11 g., 68%) had m.p. 58—59° (from ether), $[\alpha]_D^{20}$ +173·8° (*c* 0·5 in MeOH), $\nu_{max.}$ 3500 cm.$^{-1}$ (OH) (Found: C, 47·0; H, 7·7; OMe, 16·5. $C_7H_{14}O_5$ requires C, 47·2; H, 7·9; OMe, 17·4%).

(*c*) To a stirred ethereal suspension of methylmagnesium iodide, [from magnesium (7·22 g.) and methyl iodide (32 g.)] a solution was added of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentosulopyranoside (15 g.) in the minimum amount of ether. The mixture was stirred for 1·5 hr. and water was added; when no further reaction occurred the ethereal solution was decanted and the residue was washed with ether. Concentration gave an oil (14·47 g., 89%), b.p. 50—55°/0·1 mm., which was heated for 3 hr. under reflux in dry methanol (270 ml.) with conc. hydrochloric acid (2·7 ml.) and water (3·4 ml.). The cooled solution was neutralised ($PbCO_3$) and filtered, and the residue was washed with methanol. The filtrate and washings were evaporated and the residue was extracted with warm ethyl acetate. Evaporation to dryness gave crystals of methyl 2-*C*-methyl-β-L-arabinoside which were separated from a syrup by washing with ethyl acetate. The pure arabinoside (7·3 g., 66%) had m.p. 98—99° (from ethyl acetate), $[\alpha]_D^{23}$ +124·6° (*c* 1 in EtOH), +140° (*c* 1·1 in H_2O). Acetylation [acetic anhydride–pyridine (1 : 2; 6 ml.), 2 days, room temperature] of this glycoside (0·5 g.), isolation of the product by pouring into water (70—80 ml.), and extraction with chloroform gave a colourless *diacetate* (0·4 g., 54%), b.p. 90°/0·1 mm., $[\alpha]_D^{20}$ +155° (*c* 1·2 in MeOH), $\nu_{max.}$ 3500 (OH) and 1750 (C=O) cm.$^{-1}$ (Found: C, 50·2; H, 6·9; OMe, 11·7; Ac, 32·3. $C_{11}H_{18}O_7$ requires C, 50·4; H, 6·9; OMe, 11·8; Ac, 32·8%). The acetyl groups were assigned to positions 3 and 4 on the basis of the known resistance of tertiary hydroxy-groups to base-catalysed esterification.[29]

The syrup obtained after removal of the crystalline arabinoside was shown by chromatography in solvent A to contain three components which corresponded to methyl β-L-arabinoside, methyl 2-*C*-methyl-β-L-arabinoside and methyl 2-*C*-methyl-β-L-riboside. The last compound was eluted from a chromatogram (0·08 g. from 0·5 g. of mixture) and was identified by chromatographic comparison [solvents A and B; sprays (i) and (iv)] with authentic material prepared as described above. After hydrolysis (N-hydrochloric acid, 100°, 6 hr.) the riboside gave a sugar indistinguishable chromatographically from 2-*C*-methyl-L-ribose (see below) in solvents A and B [sprays (i) and (iv)].

Methyl 2-*C*-methyl-β-L-riboside (0·0086 g.) and -arabinoside (0·0081 g.) were oxidised at room temperature with 0·015M-periodate; the consumption of oxidant was followed spectrophotometrically.[30] Methyl α-D-glucoside (0·0084 g.) was oxidised as a control. Final uptakes of oxidant (mol.) after 42 hr. were:

methyl 2-*C*-methyl-β-L-riboside	2·05
methyl 2-*C*-methyl-β-L-arabinoside	2·03
methyl α-D-glucopyranoside	2·07

2-C-*Methyl*-L-*ribose* (VI).—Methyl 2-*C*-methyl-β-L-riboside (0·47 g.) in water (20 ml.) was stirred and heated in the presence of Amberlite IR-120 (H^+) resin (1·8 g.) until chromatography indicated that the solution was free from starting material. The supernatant liquid was decanted, stirred with charcoal, filtered, and evaporated to a pale yellow viscous syrup (0·25 g.), $[\alpha]_D^{20}$ +111° (*c* 0·9 in EtOH), R_F 0·35 (chromatographically homogeneous). A portion (0·07 g.) of the syrup and toluene-*p*-sulphonylhydrazine (0·07 g.) were heated together in methanol (1 ml.) for 1 hr. A solid which separated from the cooled solution was collected and gave 2-C-*methyl*-L-*ribose toluene*-p-*sulphonylhydrazone*, m.p. 169—170° (decomp.) (from methanol), $[\alpha]_D^{20}$ +9·3° (*c* 1·1 in pyridine) (Found: C, 47·0; H, 6·2; N, 8·3; S, 9·9. $C_{13}H_{20}N_2O_6S$ requires C, 47·0; H, 6·1; N, 8·4; S, 9·7%) [lit.,[31] m.p. 169·5—170°, $[\alpha]_D^{22}$ +1·8° (in pyridine), for the D-isomer].

2-C-*Methyl*-L-*ribonolactone* (VII).—2-*C*-Methyl-L-ribose (0·2 g.) was shaken for 18 hr. with bromine (0·09 ml.), lead carbonate (0·35 g.), and water (8 ml.). After filtration [residues well washed with water (3 × 10 ml.)] the combined filtrate and washings were concentrated to a solid which was extracted with water (2 × 3 ml.). Evaporation of the filtered extract to 1 ml. and then passage of the solution through a column (21 × 2 cm.) of Amberlite IR-120 (H^+) resin, followed by evaporation, gave a syrup which was dissolved in glacial acetic acid. Removal of solvent left a colourless syrup (0·17 g., 86%) which later crystallised and gave 2-*C*-methyl-L-ribono-γ-lactone, m.p. 159—160° (from acetonitrile), $[\alpha]_D^{20}$ −91·1° (*c* 1·2 in H_2O), $\nu_{max.}$ 3500 (OH) and 1770 (C=O) cm.$^{-1}$. The *X*-ray powder diffraction pattern and i.r. absorption spectrum of this product were identical with those of the D-enantiomorph {m.p. 162—163° (from water), $[\alpha]_D^{25}$ +93·6° (in water) [7]} (supplied by the late Prof. J. C. Sowden) as were the R_F values of the lactones (both 0·55 in a solvent A) and the corresponding ammonium salts [0·26 in pyridine–n-butanol–water (8 : 8 : 4 v/v)].

[29] See F. Shafizadeh, *Adv. Carbohydrate Chem.*, 1956, **11**, 263; A. B. Foster, T. D. Inch, J. Lehmann, L. F. Thomas, J. M. Webber, and J. A. Wyer, *Proc. Chem. Soc.*, 1962, 254.

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2-C-*Methyl*-L-*arabinose* (VIII).—A solution of methyl 2-*C*-methyl-β-L-arabinoside (1 g.) in N-hydrochloric acid (25 ml.) was heated under reflux for 6 hr. After cooling, neutralisation ($BaCO_3$), treatment with charcoal, filtration, and evaporation, a syrupy residue was obtained which was extracted with ethanol. Concentration of the filtered extract gave syrupy 2-*C*-methyl-L-arabinose (0·87 g.), $[\alpha]_D$ −2·4° (*c* 3·1 in MeOH) which was chromatographically pure but did not crystallise. It had M_G 0·85, R_F 0·37 (solvent A) and 0·34 (solvent B). [The hydrolysis could also be achieved by heating under reflux with N-sulphuric acid or Amberlite IR-120 (H^+) resin suspended in water, but a less pure product resulted in the former case, and a longer hydrolysis time was needed with the resin.] This branched-chain sugar (0·2 g.) was oxidised with bromine (0·08 ml.) in water (8·8 ml.) by shaking for 18 hr. in the presence of lead carbonate (0·4 g.). More bromine (0·08 ml.) was then added and shaking was continued for another 48 hr. The 2-*C*-methyl-L-arabonolactone was isolated in the usual manner and was obtained as a syrup which did not crystallise. This syrup (0·19 g.) was heated with phenylhydrazine (0·15 ml.) on a water bath for 30 min. The melt initially obtained soon solidified, and the cooled residue gave the *phenylhydrazide* as colourless crystals, m.p. 188—189° (from methanol), $[\alpha]_D$ 0·0° (*c* 0·5 in MeOH) (Found: C, 52·8; H, 6·7; N, 10·1. $C_{12}H_{18}N_2O_5$ requires C, 53·3; H, 6·7; N, 10·4%).

Stability of 2-C-*Methylpentoses*.—(a) *In acids*. (i) 4N-Hydrochloric acid (1 ml.) was added to separate samples of L-arabinose (11·6 mg.), D-ribose (4·6 mg.), 2-*C*-methyl-L-arabinose (11·5 mg.), and 2-*C*-methyl-L-ribose (5 mg.). The solutions were heated simultaneously under reflux for 4 hr. The solutions of pentoses darkened and then became pale again with deposition of black solid. The 2-*C*-methylpentoses became only very slightly coloured. The cooled solutions were diluted with water (2 ml.) and neutralised with lead carbonate. The clear filtrates were evaporated to dryness and the residues extracted with methanol (*ca.* 0·5 ml.) and examined chromatographically with starting materials as references [solvents A and B, sprays (i) and (iv)]. Arabinose and ribose were completely destroyed by the treatment but the 2-*C*-methylpentoses were unchanged.

In another experiment samples of D-ribose (7·8 mg.), 2-*C*-methyl-L-ribose (6·5 mg.), and D-hamamelose (2-*C*-hydroxymethyl-D-ribose) (7·5 mg.) were treated with 4N-hydrochloric acid as described above. The hamamelose solution darkened sooner than that of 2-*C*-methyl-L-ribose, but chromatograms [solvent A, spray (i)] showed that although both hamamelose and 2-*C*-methyl-L-ribose were still present in their solutions, the ribose had been completely destroyed.

(ii) Paper chromatograms were prepared from equal quantities of L-arabinose, D-ribose, 2-*C*-methyl-L-arabinose, and 2-*C*-methyl-L-ribose, in solvent A. Spray (i) readily detected all the sugars. With spray (ii) under the usual conditions (paper heated up to 5 min. at 105—110°) the branched-chain sugars showed up more slowly than the simple pentoses, and gave a light brown instead of a dark red-brown spot. The branched-chain sugars were more clearly seen by heating the paper at 120—130° for several min. Similar results were obtained with the benzidine [32] and *p*-anisidine [33] spray reagents; the former was the most sensitive of the aromatic amine sprays tried.

(b) *In bases*. (ii) Deoxygenated aqueous pyridine (1 ml.) prepared by passing nitrogen through a mixture of water (one part) and pyridine (nine parts) for 0·5 hr. was added to separate samples of L-arabinose (8·3 mg.), 2-*C*-methyl-L-arabinose (7·9 mg.), 2-*C*-methyl-L-ribose (7·1 mg.), and D-ribose (7·2 mg.), and the solutions were heated for 3·5 hr. in an atmosphere of nitrogen. Chromatographic examination [solvents A and B, sprays (i) and (iv)] of the solutions indicated that the pentoses gave epimers and other unidentified products whereas the 2-*C*-methylpentoses were unchanged.

(ii) N-Sodium hydroxide (1 ml. through which nitrogen had been bubbled for 0·5 hr.) was added to L-arabinose (9·4 mg.), 2-*C*-methyl-L-arabinose (9·4 mg.), 2-*C*-methyl-L-ribose (6·3 mg.), and D-ribose (6·7 mg.). Nitrogen was passed through the solutions, which were heated at 100° for 1 min. Zeocarb 225 (H^+) resin was added to the cooled solutions until they became acid. The filtered solutions were evaporated and the residues were examined chromatographically [solvents A and B, sprays (i), (iii), and (iv)]. From both pentoses a number of spots were detected, some of which were lactones: no arabinose or ribose remained. From the 2-*C*-methylpentoses fast-moving spots had been formed which could not be detected with the lactone spray (iii), but appreciable quantities of starting materials were still present.

In 0·01N-sodium hydroxide (50 ml.), 2-*C*-methyl-L-arabinose (36·5 mg.) was stable for 16 days as shown by titration of aliquot samples (5 ml.) with 0·01N-hydrochloric acid. On the other hand aliquots (5 ml.) of a solution of L-arabinose (15·3 mg.) in 0·01N-sodium hydroxide (25 ml.) showed a decrease in titre equivalent to the production of 1·5 equiv. of acid in the same time.

0·025N-Sodium hydroxide (10 ml.) was added to methanolic solutions (5 ml.) of known amounts of L-arabinose and 2-*C*-methyl-L-arabinose (10—20 mg.). The mixtures were heated under reflux for 2 hr. (soda-lime guard tubes). When cool, the condensers were rinsed with boiling water (5 ml.) and the solutions were titrated with 0·01N-hydrochloric acid. It was found that on a molar basis the L-arabinose had neutralised 1·5 equiv. of base whereas the 2-*C*-methyl-L-arabinose had neutralised only 0·16 equiv.

Treatment of Compound (II) *with Methanolic Ammonia*.—Methyl 2,2′-anhydro-2-*C*-hydroxymethyl-3,4-*O*-isopropylidene-β-L-pentoside (2·5 g.) was dissolved in a mixture of methanol (20 ml.) and aqueous ammonia (*d* 0·880; 20 ml.). The solution was heated in a sealed tube under pressure at 110° for 21 hr. It was then cooled, stirred with charcoal, filtered, and evaporated to yield a syrup which was extracted with light petroleum (b.p. 40—60°). From the extract a *methyl* 2-C-*aminomethyl*-3,4-O-*isopropylidene*-β-L-*pentoside* (0·99 g., 34%) was obtained as white plates, m.p. 94—95°, $[\alpha]_D^{20}$ +167·3° (*c* 1·04 in EtOH), $\nu_{max.}$ 3500 (OH), and 3280 and 1590 (NH) $cm.^{-1}$ (Found: C, 51·6; H, 8·3; N, 5·9; OMe, 13·5. $C_{10}H_{19}NO_5$ requires C, 51·5; H, 8·2; N, 6·0; OMe, 13·3%). The substance (0·825 g.) was acetylated with acetic anhydride (3·5 ml.) in pyridine (6·5 ml.) for 48 hr. at room temperature, and the product isolated in the usual way to give a gum (0·36 g.), b.p. 100—104°/0·1 mm., $[\alpha]_D^{20}$ +136·7° (*c* 1 in MeOH) (Found: *O*-Ac, 0·35%).

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