An Alternative Route to Furanoid and Pyranoid Glycals [1]

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The reduction of suitably protected furanosyl and pyranosyl halides with sodium naphthalide in tetrahydrofuran gives furanoid and pyranoid glycals. Furanosyl halides with sodium or potassium in tetrahydrofuran give 3-*O*-furanosyl furanoid glycals as major products.

GLYCALS † are useful precursors in synthetic carbohydrate chemistry.[2] Pyranoid glycals are usually prepared [2] by modifications of the method discovered by Fischer and Zach,[3] but it has been shown [4] that these methods are not suitable for the preparation of furanoid glycals; a competing reaction predominates and low yields of the glycals are obtained. The preparation of furanoid glycals, which has been achieved [5] in neutral medium in high yield, is further complicated by their high reactivity.[4,5] Pyranoid glycals have also been prepared [6] by treating 2-deoxy-2-iodopyranosides with methyl-lithium, but the method has not been applied to furanoid glycals. We report an alternative route to furanoid and pyranoid glycals with base-stable protecting groups and the preparation of stable 3-*O*-furanosyl glycals.

The furanosyl chlorides (2) [7] and (8) [8] reacted with sodium naphthalide in tetrahydrofuran (THF) to give, on protonation with acetic acid, the furanoid glycals (11) (59%) and (12) (54%), respectively. Similarly, the pyranosyl halides (28) [prepared by chlorination of the rhamnose (27) [9]] and (29) [10] gave the pyranoid glycals (30) (46%) and (31) [11] (41%), respectively. Further, on quenching the reaction with methyl iodide, instead of acetic acid, the glycal (13) (60%) was obtained, instead of the glycal (11). Glycals (11)—(13) and (29) were readily identified from their spectral and analytical data.

The furanoid glycals (11)—(13) were purified by chromatography on silica gel with diethyl ether as eluant, but more polar solvents must be avoided: with benzene–acetone (7 : 1) as eluant isomerisation of the glycal (11) to compound (21) occurred to a considerable extent. The furanoid glycals can be stored at − 20° C without decomposition for at least 6 months; at 25 °C the glycal (12) decomposed [4] to the furan (22) after 7 days. The glycals (11) and (12) rearranged slowly in solution: catalytic hydrogenation of the freshly prepared glycals (11) and (12) gave not only their dihydroderivatives (16) (52%) and (17) (68%), respectively, but also traces of the aldose (23). Similarly, acetylation of glycal (11) with acetic anhydride in pyridine and then catalytic hydrogenation of the products, gave a mixture of the isomeric monoacetates (25) (62%) and (24) (6%); the monoacetates were obtained independently by acetylation of compounds (16) and (23), respectively. Hydrogenation of the glycal (13) gave only the dihydroderivative (18) (85%), demonstrating [4] the enhanced stability of furanoid glycals with poor leaving groups at C-3.

Chemical proof for the furanoid structure of the

† Used throughout this discussion to denote 1,4- or 1,5-anhydro-2-deoxyhex-1-enitols.

[1] Preliminary publication, S. J. Eitelman and A. Jordaan, *J.C.S. Chem. Comm.*, 1977, 552.

[2] R. J. Ferrier, *Adv. Carbohydrate Chem.*, 1965, **20**, 67; *Adv. Carbohydrate Chem. Biochem.*, 1969, **24**, 199.

[3] E. Fischer and K. Zach, *Sitz. ber. kgl. preuss, Akad. Wiss.*, 1913, **16**, 311.

[4] K. Bischofberger and R. H. Hall, *Carbohydrate Res.*, 1976, **52**, 223.

[5] R. K. Ness and H. G. Fletcher, jun., *J. Org. Chem.*, 1963, **28**, 435; M. Haga and R. K. Ness, *ibid.*, 1965, **30**, 158.

[6] M. Sharma and R. K. Brown, *Canad. J. Chem.*, 1966, **44**, 2825; 1968, **46**, 757; R. U. Lemieux, E. Fraga, and K. A. Watanabe, *ibid*, 1968, **47**, 61.

[7] (*a*) K. Freundenberg, A. Wolf, E. Knopf, and S. Zaheer, *Ber.*, 1928, **61**, 1743; (*b*) J. B. Lee and T. J. Nolan, *Tetrahedron*, 1967, **23**, 2798; (*c*) K. Takiura and S. Honda, *Chem. and Pharm. Bull. (Japan)*, 1970, **18**, 2125.

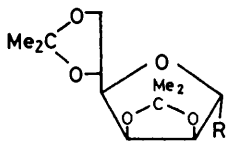
[8] B. D. Kohn, P. Kohn, and A. Dubin, *Carbohydrate Res.*, 1971, **18**, 349.

[9] S. J. Angyal, V. A. Pickles, and R. Ahluwalia, *Carbohydrate Res.*, 1967, **3**, 300.

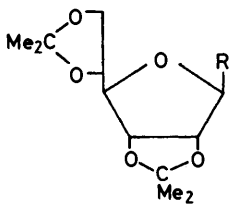
[10] M. L. Wolfrom and D. R. Husted, *J. Amer. Chem. Soc.*, 1937, **59**, 2559.

[11] E. L. Hirst and C. S. Woolvin, *J. Chem. Soc.*, 1931, 1131.

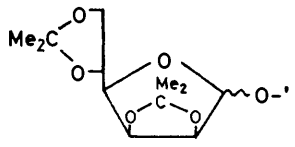
glycal (11) was obtained by hydrolysis of its dihydro-derivative (16) to give 1,4-anhydro-2-deoxy-D-arabinitol (26), which had physical properties different from those

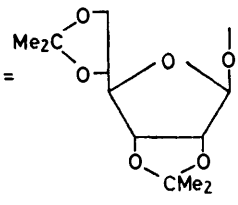


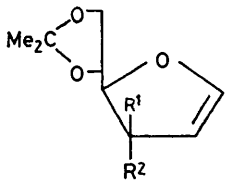
(1) R = OH
(2) R = Cl
(3) R = Br
(4) R = O·CHMe$_2$
(5) R = αM
(6) R = βM

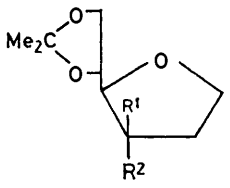


(7) R = OH
(8) R = Cl
(9) R = Br
(10) R = A

M = 

A = 

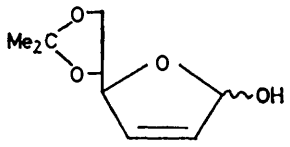




(11) R^1 = OH, R^2 = H
(12) R^1 = H, R^2 = OH
(13) R^1 = OMe, R^2 = H
(14) R^1 = αM, R^2 = H
(15) R^1 = H, R^2 = A
(16)
(17)
(18)
(19)
(20)

of the known [12] 1,5-anhydro-isomer. Further, compounds (23) and (24) were prepared by an independent synthesis. Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside [13] was catalytically hydrogenated, the product was deacetylated, and the resulting product was hydrolysed to give an unprotected aldose. Isopropylidenation of the aldose gave an acetal identical with compound (23) and acetylation of the acetal gave a monoacetate identical with compound (24).

With sodium or potassium metal in THF, in place of sodium naphthalide, the furanosyl bromide (3) [14] and the analogous chloride (2) [7] gave the 3-*O*-furanosyl glycal (14) as the major product. The glycoside (4) and the disaccharides (5) and (6) were obtained as by-products in low yield but no trace of the glycal (11) or its decomposition products,[4] compounds (21) and (22), was observed. Similarly, the furanosyl chloride (8) [8] and the analogous bromide (9), prepared in the same manner [14] as bromide (3), gave only the 3-*O*-furanosyl glycal (15) (69%) and a trace of the disaccharide (10). A low yield of the glycal (11) and its isomer (21) were obtained on treating the furanosyl bromide (3) with sodium sand in toluene at 70 °C. When lithium metal, magnesium turnings, or a zinc–copper couple [15] were used instead of sodium or potassium metal only the starting bromide (3) was recovered and the parent



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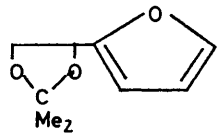

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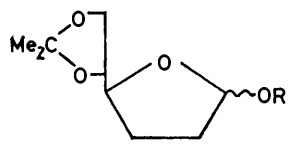
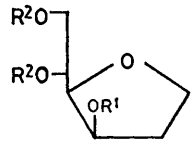
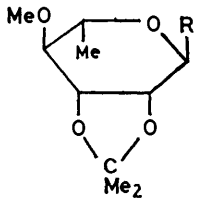


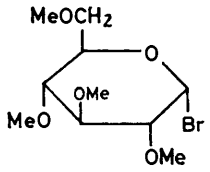
(23) R = H
(24) R = Ac



(25) R^1 = Ac; R^2,R^2 = CMe$_2$
(26) R^1 = R^2 = H



(27) R = OH
(28) R = Cl



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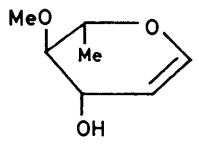
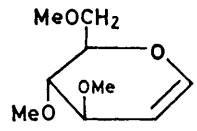


(30)



(31)

protected hexose (1) was obtained with the furanosyl bromide (3) and zinc in *NN*-dimethylformamide.

The glycals (14) and (15) were readily identified from

[12] M. Gehrke and F. Obst, *Ber.*, 1931, **64**, 1724.
[13] R. J. Ferrier and N. Prasad, *J. Chem. Soc.* (*C*), 1969, 570.
[14] S. Hanessian, M. M. Ponpipom, and P. Lavallee, *Carbohydrate Res.*, 1972, **24**, 45.
[15] L. M. Stephenson, R. V. Gemmer, and S. P. Current, *J. Org. Chem.*, 1977, **42**, 212.

their spectral and analytical data. Their n.m.r. spectra showed the typical [4,5] H-1 and -2 resonances of furanoid glycals and the absence of coupling between H-1′ and -2′ established [16] that these protons in the furanosyloxy group of both glycals were *trans*-oriented. The glycals (14) and (15) were more stable than the simple furanoid glycals (11) and (12), and they were purified by chromatography and high vacuum distillation. They can be stored at 25 °C for at least 90 days without appreciable decomposition. Hydrogenation of the glycals (14) and (15) gave the dihydro-derivatives (19) and (20), respectively, in high yield.

The structure of the by-product (4) was confirmed by its independent synthesis from the furanosyl chloride (2) and potassium isopropoxide in propanol. Similarly, the disaccharides (5) and (6) were obtained in low yield by chromatographing the products of the reaction of the furanosyl chloride (2) and potassium 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyloxide in THF.[7a] The n.m.r. spectrum of compound (5) was much simpler than that of compound (6), indicating that the former was a symmetrical disaccharide and that the latter was the unsymmetrical α-D-,β-D-disaccharide (6). The $J_{1.2}$ and $J_{1'.2'}$ values (0 Hz) of the former compound indicated that it was the di-α-D-disaccharide (5). (This disaccharide had physical properties similar to those of the disaccharide of unspecified configuration reported by Freundenberg *et al.*[7a]) Further, in accord with Hudson's isorotation rules, the α-D-,β-D-compound (6) was less dextrorotatory than the di-α-D-compound (5). The simple n.m.r. spectrum of compound (10) similarly showed that it was the di-β-D-disaccharide.

The formation of the glycals (11)—(15), (30), and (31) can be rationalised by assuming the formation of an unstable C-1 anion from the glycosyl halide in the reducing medium and that this is followed by elimination of acetone, in the case of the glycals (11)—(15) and (30), to give 3-oxyanions, or, in the case of the glycal (31), by elimination of the C-2 methoxy-group. After reduction with sodium naphthalide as the reducing agent in THF, protonation gives the simple glycals (11), (12), and (30) and methylation gives the glycal (13). With sodium or potassium in THF the formation of the 3-*O*-oxyanions is slower and they attack unchanged halide to give the 3-*O*-furanosyl glycals as the major products. Acetone liberated on formation of the 3-*O*-oxyanions forms sodium isopropoxide and this attacks the halide to give the glycoside (4) in low yield. The formation of disaccharides (5), (6), and (10) must arise by attack of the reducing metal on free furanoses (1) and (7), present in the halides as impurity, giving furanosyl oxyanions which then attack unchanged halide: during these glycosylations, for which S_N1 character is assumed,[17] the bulky oxyanions attack mainly from the less hindered face of the halides.

Reactions of furanoid glycals are being investigated.

[16] J. D. Stevens and H. G. Fletcher, jun., *J. Org. Chem.*, 1968, **33**, 1799.

EXPERIMENTAL

All solvent extracts were dried (Na_2SO_4), filtered, and evaporated below 50 °C *in vacuo*. T.l.c. and column chromatography were performed on silica gel (Merck GF_{254}) (100 g of silica per g of residue for column separation). M.p.s were determined with a hot-stage apparatus. Unless otherwise stated, i.r. spectra were measured for thin films on sodium chloride with a Perkin-Elmer 237 spectrophotometer, and n.m.r. spectra with a Varian HA-100 instrument (tetramethylsilane as internal standard; solutions in $CDCl_3$). Optical rotations were measured for solutions in chloroform with a Perkin-Elmer 241 automatic polarimeter (*c* 1.0 ± 0.3) and mass spectra with an A.E.I. MS9 spectrometer by direct insertion. Where possible, samples of oils were distilled under high vacuum (Kugelröhr) for microanalysis. Where distillation was not possible, oils shown to be chromatographically homogeneous in several solvent systems were submitted for accurate mass determination.

Preparation of the Furanosyl and Pyranosyl Halides.—Compound (1) was treated with thionyl chloride; [7a] work-up gave the chloride (2), m.p. 36—38°, $[\alpha]_D^{20}$ +56° (Found: C, 51.7; H, 6.8; Cl, 12.7. Calc. for $C_{12}H_{19}ClO_5$: C, 51.7; H, 6.9; Cl, 12.7%), previously described [7] as an oil.

The chloride (8) [8] was prepared similarly.

The protected hexose (27) (3.77 g, 17.1 mmol) was chlorinated with thionyl chloride; [7a] work-up gave an oil. High-vacuum distillation gave the unstable chloride (28) (1.88 g, 47%) as a solid which could not be recrystallized; M^+ 238/236, τ 3.76 (1 H, s, H-1), 5.61 (1 H, d, $J_{2.3}$ 5 Hz, H-2), 5.72 (1 H, dd, $J_{3.2}$ 5, $J_{3.4}$ 7 Hz, H-3), 6.06 (1 H, m, H-5), 6.24 (3 H, s, OMe), 6.94 (1 H, dd, $J_{4.5}$ 10, $J_{4,3}$ 7 Hz, H-4), 8.45 and 8.62 (6 H, 2s, 2Me), and 8.64 (3 H, d, $J_{6.5}$ 6 Hz, H_3-6).

The bromide (3) was prepared as described by Hanessian *et al.*[14]

The protected hexose (7) (10.0 g, 38.5 mmol) was brominated by the method of Hanessian *et al.*[14] to give the unstable bromide (9) (7.1 g, 57%) as an oil, *m/e* 309/307 (M^+ − Me), τ 3.59 (1 H, s, H-1), 4.76 (1 H, d, $J_{2.3}$ 6 Hz, H-2), 4.98 (1 H, dd, $J_{3.2}$ 6, $J_{3.4}$ 1.5 Hz, H-3), 5.42 (1 H, m, H-5), 5.81 (1 H, dd, $J_{4.3}$ 1.5, $J_{4.5}$ 10 Hz, H-4), 5.82 (1 H, dd, $J_{6a.5}$ 6, $J_{6a.6b}$ 8.5 Hz, H_a-6), 6.04 (1H, dd, $J_{6b.5}$ 5, $J_{6b.6a}$ 8.5 Hz, H_b-6), and 8.53, 8.63, and 8.65 (12 H, 3s, 4Me).

The bromide (29) was prepared as described by Wolfrom *et al.*[10]

1,4-*Anhydro*-2-*deoxy*-5,6-O-*isopropylidene*-D-arabino-*hex*-1-*enitol* (11).—A solution of naphthalene (0.5 g) in dry THF (50 ml) was purged with dry nitrogen (½ h). Sodium wire (*ca.* 1 g) was pressed into the solution and the mixture was vigorously stirred, under nitrogen, at 25 °C until it had the intense green colour of sodium naphthalide (*ca.* ½ h). A solution of the chloride (2) (1.0 g, 3.6 mmol) in dry THF (25 ml) was added dropwise at such a rate that there was always an excess of sodium naphthalide (green colour) throughout the addition. T.l.c. then indicated that all the starting material had reacted. The sodium wire was removed, dry diethyl ether (50 ml) was added, and the mixture was exposed to the atmosphere. When it had lost its green colour (<5 min) it was neutralized with acetic acid and filtered through a pad of silica gel. The solvent was removed to give an oil, containing naphthalene, which was chromatographed (diethyl ether) to give the *hex*-1-*enitol* (11) (0.4 g, 59%) as an oil, $[\alpha]_D^{20}$ −48°, $\nu_{max.}$ 3 450 (OH)

[17] G. Wulfe and G. Röhle, *Angew. Chem. Internat. Edn.*, 1974, **13**, 157.

and 1 620 cm^{-1} (C=C), M^+ 186, τ 3.44 (1 H, d, $J_{1,2}$ 3 Hz, H-1), 4.77 (1 H, t, $J_{2,1}$ 3, $J_{2,3}$ 3 Hz, H-2), 5.10br (1 H, m, $J_{3,2}$ 3, $J_{3,4}$ 6.5 Hz, sharpens on addition of D_2O, H-3), 5.30—6.10 (4 H, m, H-4 and -5 and H_2-6), 7.96br (1 H, s, exchanges with D_2O, OH), and 8.55 and 8.62 (6 H, 2s, 2Me) (Found: *m/e* 171.065. $C_8H_{11}O_4$ requires M^+ — Me, 171.066).

Chromatography of the crude mixture with benzene–acetone (7 : 1) as eluant gave the hex-1-enitol (11) (15%) and then 2,3-*dideoxy*-5,6-O-isopropylidene-αβ-D-erythro-*hex*-2-*enofuranose* (21) (37%) as an oil, $\nu_{max.}$ 3 500 cm^{-1} (OH), *m/e* 171 (M^+ — Me), τ *ca.* 4.00 (2 H, m, H-2 and -3), 5.10—6.30 (6 H, m, changes on addition of D_2O, H-1, -4, and -5, H_2-6, OH), and 8.60 and 8.68 (6 H, 2s, 2Me) (Found: *m/e* 171.066. $C_8H_{11}O_4$ requires M^+ — Me, 171.066).

Hydrogenation (45 lb in^{-2}) of the hex-1-enitol (11) over Pd–C (5%) in diethyl ether gave an oil. Chromatography (diethyl ether) gave an oil which on acetylation (acetic anhydride–pyridine) gave a monoacetate (4%), identical (i.r. and mass spectra and R_F) with an authentic sample of the monoacetate (24) (see later). Further elution gave the *hexitol* (16) (52%) as an oil, $[\alpha]_D^{20}$ −26°, $\nu_{max.}$ 3 450 cm^{-1} (OH), *m/e* 173 (M^+ — Me), τ 5.54 (1 H, m, sharpens on addition of D_2O, H-3), 5.65—6.44 (6 H, m, H_2-1, H-4, -5, H_2-6), 7.38br (1 H, exchanges with D_2O, OH), 7.70—8.10 (2 H, m, H_2-2), and 8.60 and 8.66 (6 H, 2s, 2 Me) (Found: *m/e* 173.081. $C_8H_{13}O_4$ requires M^+ — Me, 173.081).

Acetylation (acetic anhydride–pyridine) of the hex-1-enitol (11) gave a mixture which was hydrogenated (26 lb in^{-2}) over Pd–C (5%) in diethyl ether. Work-up and chromatography with benzene–diethyl ether (1 : 1) as eluant gave a monoacetate (6%), identical (i.r. and mass spectra and R_F) with an authentic sample of the monoacetate (24) (see later). Further elution gave the *hexitol* (25) (62%) as an oil, $[\alpha]_D^{20}$ −52°, $\nu_{max.}$ 1 740 cm^{-1} (CO), *m/e* 215 (M^+ — Me), τ 4.62 (1 H, septet, H-3), 5.64—6.30 (6 H, m, H_2-1, H-4, -5, H_2-6) 7.52—8.20 (2 H, m, H_2-2), 7.96 (3 H, s, OAc), and 8.64 and 8.70 (6 H, 2s, 2 Me) (Found: *m/e* 215.093. $C_{10}H_{15}O_5$ requires M^+ — Me, 215.091).

1,4-*Anhydro*-2-*deoxy*-5,6-O-*isopropylidene*-D-ribo-*hex*-1-*enitol* (12).—The chloride (8) (1.68 g, 6.03 mmol) was treated as described for the preparation of compound (11), to give the *hex*-1-*enitol* (12) (610 mg, 54%) as an oil, $[\alpha]_D^{20}$ +127°, $\nu_{max.}$ 3 380 (OH) and 1 615 cm^{-1} (C=C), M^+ 186, τ 3.53 (1 H, dd, $J_{1,2}$ 3, $J_{1,3}$ 1 Hz, H-1), 4.86 (1 H, t, $J_{2,1} = J_{2,3}$ 3 Hz, H-2), 5.1br (1 H, m, sharpens on addition of D_2O, H-3), 5.70—6.20 (4 H, m, H-4, -5, H_2-6), 7.00br (1 H, s, exchanges with D_2O, OH), and 8.57 and 8.67 (6 H, 2s, 2 Me) (Found: *m/e* 171.066. $C_8H_{11}O_4$ requires M^+ — Me, 171.066).

Hydrogenation of the hex-1-enitol (12) as described for the hex-1-enitol (11) gave the monoacetate (24) (7%) and the *hexitol* (17) (68%) as an oil, $[\alpha]_D^{20}$ +18°, $\nu_{max.}$ 3 450 cm^{-1} (OH), *m/e* 173 (M^+ — Me), τ 5.65 (1 H, quintet, sharpens on addition of D_2O, H-3), 5.80—6.40 (6 H, m, H_2-1, H-4, -5, H_2-6), 7.34br (1 H, exchanges with D_2O, OH), *ca.* 8.00 (2 H, m, H_2-2), and 8.60 and 8.68 (6 H, 2s, 2 Me) (Found: *m/e* 173.081. $C_8H_{13}O_4$ requires M^+ — Me, 173.081).

After 7 days at 25 °C the hex-1-enitol (12) had decomposed completely (t.l.c.). Chromatography with benzene–ethyl acetate (20 : 1) as eluant gave (*R*) 1-(2-furyl)-1,2-*O*-isopropylidene-ethane-1,2-diol (22) (42%), an oil, $[\alpha]_D^{20}$ +23°, M^+ 168, τ 2.26 (1 H, t, $J_{5,4} = J_{5,3}$ = 0.5 Hz, furyl H-5), 3.64 (2 H, m, furyl H-3, -4), 4.94 (1 H, dd, $J_{1,2a}$ 7, $J_{1,2b}$ 8 Hz, H-1), 5.80 (1 H, dd, $J_{2a,1}$ 7, $J_{2a,2b}$ 8.5 Hz, H_a-2), 5.96 (1 H, dd, $J_{2b,1}$ 8, $J_{2b,2a}$ 8.5 Hz, H_b-2), and 8.53 and 8.58 (6 H, 2s, 2 Me).

1,4-*Anhydro*-2-*deoxy*-5,6-O-*isopropylidene*-3-O-*methyl*-D-arabino-*hex*-1-*enitol* (13).—The chloride (2) (700 mg, 2.5 mmol) was reduced with sodium naphthalide in THF as previously described. After removal of the excess of sodium, while the solution was still green, methyl iodide (2 ml) was added and the solvents were removed to leave an oil which was chromatographed (hexane) to remove naphthalene. Further elution with diethyl ether gave the *hex*-1-*enitol* (13) (320 mg, 60%), $[\alpha]_D^{20}$ −70°, $\nu_{max.}$ 1 620 cm^{-1} (C=C), *m/e* 185 (M^+ — Me), τ 3.41 (1 H, d, $J_{1,2}$ 3 Hz, H-1), 4.69 (1 H, t, $J_{2,1} = J_{2,3}$ = 3 Hz, H-2), 5.40—6.18 (5 H, m, H-3, -4, -5, H_2-6), 6.72 (3 H, s, OMe), and 8.54 and 8.61 (6 H, 2s, 2 Me) (Found: *m/e* 185.080. $C_9H_{13}O_4$ requires M^+ — Me, 185.081).

Hydrogenation of the hex-1-enitol (13) as described for the hex-1-enitol (11) gave the *hexitol* (18) (85%) as an oil, $[\alpha]_D^{20}$ −41°, *m/e* 187 (M^+ — Me), τ 5.75 (1 H, q, H-3), 5.90—6.40 (6 H, m, H_2-1, H-4, -5, H_2-6), 6.66 (3 H, s, OMe), *ca.* 8.00 (2 H, m, H_2-2), and 8.61 and 8.67 (6 H, 2s, 2 Me) (Found: *m/e* 187.095. $C_9H_{15}O_4$ requires M^+ — Me, 187.097).

1,5-*Anhydro*-2,6-*dideoxy*-4-O-*methyl*-L-arabino-*hex*-1-*enitol* (30).—The chloride (28) was treated as described for the preparation of compound (11). Work-up gave an oil which was chromatographed with ethyl acetate–hexane (1 : 1) as eluant to give the *hex*-1-*enitol* (30) (360 mg, 46%), m.p. 75—77° (hexane), $[\alpha]_D^{20}$ −1°, $\nu_{max.}$ (KBr) 3 250 (OH) and 1 650 cm^{-1} (C=C), M^+ 144, τ 3.68 (1 H, dd, $J_{1,2}$ 6, $J_{1,3}$ 2 Hz, H-1), 5.28 (1 H, dd, $J_{2,1}$ 6, $J_{2,3}$ 2.5 Hz, H-2), 5.72 (1 H, dt, $J_{3,2}$ 2.5, $J_{3,4}$ 7, $J_{3,5}$ 2 Hz, sharpens on addition of D_2O, H-3), 6.10 (1 H, m, H-5), 6.28 (3 H, s, OMe), 6.86 (1 H, dd, $J_{4,3}$ 7, $J_{4,5}$ 9.5 Hz, H-4), 7.72br (1 H, exchanges with D_2O, OH), and 8.60 (3 H, d, $J_{6,5}$ Hz, H_3-6) (Found: C, 58.4; H, 8.2. $C_7H_{12}O_3$ requires C, 58.3; H, 8.4%).

Compound (30) was also obtained in *ca.* 20% yield on treating the chloride (28) with an excess of potassium in THF.

1,5-*Anhydro*-2-*deoxy*-3,4,6-*tri*-O-*methyl*-D-arabino-*hex*-1-*enitol* (31).—The bromide (29) (6.0 g, 2 mmol) was treated as described for the preparation of compound (11) and the mixture was worked up to give a semi-crystalline solid which was taken up in chloroform (100 ml). The solution was washed with aqueous sodium hydrogen carbonate and evaporated to give a solid. Chromatography ($CHCl_3$) removed naphthalene and elution with chloroform–ethyl acetate (1 : 1) gave an oil which was distilled (*ca.* 20 mmHg; 120 °C) to give the hex-1-enitol (31) (1.54 g, 41%), identical (i.r., n.m.r., and mass spectra) with an authentic sample.[11]

1-O-*Acetyl*-2,3-*dideoxy*-5,6-O-*isopropylidene*-αβ-D-erythro-*hexofuranose* (24).—Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[13] (500 mg, 1.9 mmol) was hydrogenated [Pd–C (5%); 25 lb in^{-2}; ethyl acetate (100 ml)], the product was deacetylated with sodium methoxide in methanol, and the glycosydic bond was hydrolysed (M-HCl; 50 °C; 3 h) to give a syrup. Acetalization with acetone and sulphuric acid (16 h; 25 °C) gave an oil (23) [$\nu_{max.}$ 3 410 cm^{-1} (OH), *m/e* 173 (M^+ — Me)] which was purified by chromatography with benzene–acetone (6 : 1) as eluant. Acetylation (acetic anhydride–pyridine) of compound (23) gave the *monoacetate* (24) (135 mg, 30% overall) as an oil, $\nu_{max.}$ 1 740 cm^{-1} (CO), *m/e* 215 (M^+ — Me), τ 3.76 (1 H, m, H-1), 5.80—6.30 (4 H, m, H-4, -5, H_2-6),

7.70—8.20 (7 H, m, H_2-2, H_2-3, OAc), and 8.60—8.66 (6 H, 2s, 2 OMe) (Found: *m/e* 215.093. $C_{10}M_{15}O_5$ requires M^+ − Me, 215.092).

1,4-*Anhydro*-2-*deoxy*-D-arabino-*hexitol* (26).—The hexitol (16) (196 mg, 1 mmol) was heated with aqueous acetic acid (70%; 30 min; 100 °C) and the solvents were evaporated off to give the *hexitol* (26) (147 mg, 95%), m.p. 94—95° (ethyl acetate); $[\alpha]_D^{20}$ −127° (H_2O), $\nu_{max.}$ (KBr) 3 250 cm^{-1} (OH), *m/e* 149 (M^+ + H), 130 (M^+ − H_2O), τ [$(CD_3)_2SO$] 5.42 (1 H, d, *J* 5 Hz, exchanges with D_2O, OH), 5.55 (1 H, d, *J* 5 Hz, exchanges with D_2O, OH), 5.73 (2 H, m, changes on addition of D_2O, OH, H-3), 6.00—6.90 (6 H, m, sharpens on addition of D_2O, H_2-1, H-4, -5, H_2-6), and *ca.* 8.10 (2 H, m, H_2-2) (Found: C, 48.4; H, 8.1. $C_6H_{12}O_4$ requires C, 48.6; H, 8.1%).

1,4-*Anhydro*-2-*deoxy*-5,6-O-*isopropylidene*-3-O-(2,3:5,6-*di*-O-*isopropylidene*-α-D-*mannofuranosyl*)-D-arabino-*hex*-1-*enitol* (14).—A freshly cut pellet of sodium (*ca.* 2.5 g, 108 mmol) was added to a solution of the bromide (3) (17.5 g, 54 mmol) in THF (100 ml) and the mixture was stirred vigorously, under nitrogen at 25 °C for 3 h. The excess of sodium was removed, diethyl ether (200 ml) was added, and the mixture was filtered through a pad of silica gel. Evaporation gave an oil which was chromatographed (mixed fractions were rechromatographed) with benzene–acetone (7 : 1) as eluant to give the glycoside (4) (560 mg, 7%), identical (i.r., n.m.r., and mass spectra) with an authentic sample (see later).

Next eluted was the *hex*-1-*enitol* (14) (7.33 g, 63%), m.p. 53—55° (from hexane), $[\alpha]_D^{20}$ +13°, $\nu_{max.}$ (KBr) 1 610 cm^{-1} (C=C), *m/e* 415 (M^+ − Me), τ(C_6D_6) 3.76 (1 H, d, $J_{1.2}$ 3 Hz, H-1), 4.79 (1 H, s, H-1'), 4.91 (1 H, t, $J_{2.1}$ = $J_{2.3}$ 3 Hz, H-2), 5.37—6.08 (11 H, m, H-3, -4, -5, H_2-6, H-2', -3', -4', -5', H_2-6'), and 8.53, 8.60, 8.66, 8.68, and 8.92 (18 H, 5s, 6 Me) (Found: C, 59.1; H, 7.6. $C_{21}H_{32}O_9$ requires C, 58.9; H, 7.5%). This was followed by the disaccharide (5) (272 mg, 2%) and then the disaccharide (6) (530 mg, 4%), identical (i.r., n.m.r. and mass spectra) with authentic samples (see later). Last eluted was the hexose (1) (143 mg, 1%), identical (m.p. and mixed m.p.) with an authentic sample.

Similar results were obtained by replacing the bromide (3) with the chloride (2) or sodium with potassium.

Hydrogenation [50 lb in^{-2}; Pd–C (5%); ethyl acetate] of the hex-1-enitol (14) gave an oil which on chromatography with benzene–acetone (7 : 1) as eluant gave the *hexitol* (19) (83%) as an oil, $[\alpha]_D^{20}$ +14°, *m/e* 430 (M^+), τ 4.82 (1 H, s, H-1'), 5.24 (1 H, dd, $J_{3'.2'}$ 6, $J_{3'.4'}$ 3.5 Hz, H-3'), 5.42 (1 H, d, $J_{2'.3'}$ 6 Hz, H-2'), 5.48—6.43 (11 H, m, H_2-1, H-3, -4, -5, H_2-6, H-4', -5', H_2-6'), *ca.* 7.90 (2 H, m, H_2-2), and 8.56, 8.62, 8.64, 8.67, and 8.69 (18 H, 5s, 6 Me) (Found: C, 59.0; H, 8.0. $C_{21}H_{34}O_9$ requires C, 58.6; H, 8.0%).

Reduction of the Bromide (3) *with Sodium Sand in Toluene.*—Reduction at 75 °C for 4 h and work-up gave an oil which was chromatographed, with benzene–acetone (7 : 1) as eluant, to give, in order of elution, the hex-1-enitol (14) (9%). the hex-1-enitol (11) (11%), and finally compound (21) (10%).

Reduction of the Bromide (3) *with Zinc in* NN-*Dimethylformamide.*—Reduction at 50 °C for 16 h and work up gave an oil, which was chromatographed with benzene–acetone (7 : 1) as eluant, to give, in order of elution, the hexose (1) (40%), the hex-1-enitol (11) (<1%), and finally compound (21) (6%).

1,4-*Anhydro*-2-*deoxy*-5,6-O-*isopropylidene*-3-O-(2,3:5,6-*di*-O-*isopropylidene*-β-D-*allofuranosyl*)-D-ribo-*hex*-1-*enitol* (15).—The bromide (9) (640 mg, 1.97 mmol) was treated as described for the preparation of the hex-1-enitol (14) to give an oil. Chromatography with benzene–acetone (5 : 1) as eluant gave the *hex*-1-*enitol* (15) (290 mg, 69%), m.p. 108—110° (from ethyl acetate–hexane), $[\alpha]_D^{20}$ +52°, $\nu_{max.}$ (KBr) 1 610 cm^{-1} (C=C), *m/e* 413 (M^+ − Me), τ 3.52 (1 H, dd, $J_{1.2}$ 2.5, $J_{1.3}$ 1 Hz, H-1), 4.79 (1 H, s, H-1'), 5.01 (1 H, t, $J_{2.1}$ = $J_{2.3}$ = 2.5 Hz, H-2), 5.16 (2 H, m and d, $J_{2'.3'}$ 6 Hz, H-2', -3), 5.43 (1 H, d, $J_{3'.2'}$ 6 Hz, H-3'), 5.79—6.20 (8 H, m, H-4, -5, H_2-6, H-4', -5', H_2-6'), and 8.55, 8.59, 8.68, and 8.71 (18 H, 4s, 6 Me) (Found: C, 58.1; H, 7.6. $C_{21}H_{32}O_9$ requires C, 57.9; H, 7.5%).

Again, similar results were obtained by replacing the bromide (9) with the chloride (8) or sodium with potassium.

Hydrogenation of the crude oil obtained on treating the bromide (9) with sodium metal in THF gave an oil which on chromatography with benzene–ethyl acetate (4 : 1) as eluant gave the *disaccharide* (10) (2%), m.p. 215° (sublimes; from methanol), $[\alpha]_D^{20}$ −60°, *m/e* 487 (M^+ − Me), τ 4.81 (2 H, s, H-1, -1'), 5.15 (2 H, d, $J_{3.2}$ 6 Hz, H-3, -3'), 5.30 (2 H, d, $J_{2.3}$ 6 Hz, H-2, -2'), 5.82—6.20 (8 H, m, H-4, -5, H_2-6, H-4,' -5,' H_2-6'), and 8.53, 8.57, 8.65, and 8.69 (24 H, 4s, 8 Me) (Found: C, 57.5; H, 7.6. $C_{24}H_{38}O_{11}$ requires C, 57.4; H, 7.6%).

Further elution gave the *hexitol* (20) (66%), m.p. 86° (from ethanol), $[\alpha]_D^{20}$ −34°, *m/e* 415 (M^+ − Me), τ 4.81 (1 H, s, H-1'), 5.12 (1 H, d, $J_{3'.2'}$ 6 Hz, H-3'), 5.38 (1 H, d, $J_{2'.3'}$ 6 Hz, H-2'), 5.60—6.40 (11 H, m, H_2-1, H-3, -4, -5, H_2-6, H-4', -5', H_2-6'), *ca.* 8.00 (2 H, m, H_2-2), and 8.51, 8.53, 8.56, and 8.66 (18 H, 4s, 6 Me) (Found: C, 58.6; H, 8.0. $C_{21}H_{34}O_9$ requires C, 58.6; H, 8.0%).

Isopropyl 2,3:5,6-*Di*-O-*isopropylidene*-α-D-*mannofuranoside* (4).—Potassium (*ca.* 1 g) was dissolved in dry isopropyl alcohol (50 ml) at 25 °C and a solution of the chloride (2) (837 mg, 3 mmol) in dry isopropyl alcohol (20 ml) was added. After stirring for 16 h the mixture was filtered and evaporated to give an oil. Chromatography with benzene–acetone (7 : 1) as eluant gave the *glycoside* (4) (910 mg, 72%) as an oil, $[\alpha]_D^{20}$ + 54°, *m/e* 287 (M^+ − Me), τ 4.94 (1 H, s, H-1), 5.26 (1 H, dd, $J_{3.2}$ 3.0, $J_{3.4}$ 6.5 Hz, H-3), 5.48 (1 H, d, $J_{2.3}$ 6.5 Hz, H-2), 5.62 (1 H, sextet, H-4), 5.85—6.30 (3 H, m, H-4, H_2-6), and 8.58—8.91 (19 H, 4 Me, $CHMe_2$) (Found: C, 59.7; H, 8.4. $C_{15}H_{26}O_6$ requires C, 59.6; H, 8.7%).

(2,3:5,6-*Di*-O-*isopropylidene*-α-D-*mannofuranosyl*)-2,3:5,6-*di*-O-*isopropylidene*-α-D-*mannofuranoside* (5) *and its* αβ-*Analogue* (6).—Potassium (*ca.* 2 g) was added to a solution of the protected hexose (1) (500 mg, 1.9 mmol) in dry THF (25 ml) at 25 °C. After hydrogen evolution had ceased (4 h), the excess of potassium was removed and a solution of the chloride (2) (0.53 g, 1.9 mmol) in dry THF (25 ml) was added with stirring. The solution was refluxed (16 h) and evaporated to give an oil. Chromatography with benzene–ethyl acetate (9 : 1) as eluant gave unchanged chloride (2) (100 mg, 20%).

Further elution gave the αα-*disaccharide* (5) (130 mg, 13%), m.p. 187—188° (from methanol), $[\alpha]_D^{20}$ +63°, *m/e* 487 (M^+ − Me), τ 4.79 (2 H, s, H-1, -1'), 5.22 (2 H, dd, $J_{3.2}$ 6, $J_{3.4}$ 4 Hz, H-3, -3'), 5.44 (2 H, d, $J_{2.3}$ 6 Hz, H-2, -2'), 5.52—6.18 (8 H, m, H-4, -5, H_2-6, H-4', -5', H_2-6'), and 8.54, 8.56, 8.63, and 8.67 (24 H, 4s, 8 Me) (Found: C, 57.1; H, 7.6. $C_{24}H_{38}O_{11}$ requires C, 57.3; H, 7.6%).

Further elution gave the αβ-*disaccharide* (6) (90 mg, 10%)

as an oil, $[\alpha]_D^{20}$ +18°, *m/e* 487 (M^+ − Me), τ 4.84 (1 H, s, H-1), 5.11 (1 H, d, $J_{1',2'}$ 3 Hz, H-1'), 5.14—5.43 (4 H, m, H-2, -3, -2', -3'), 5.50—5.70 (2 H, m, H-5, -5'), 5.80—6.13 (5 H, *m*, H-4, H_2-6, H-4', H_a-6'), 6.45 (1 H, dd, H_b-6'), and 8.48, 8.55, 8.57, 8.64, and 8.68 (24 H, 5s, 8 Me) (Found: C, 57.4; H, 7.5. $C_{24}H_{38}O_{11}$ requires C, 57.3; H, 7.6%).

Finally eluted was the protected hexose (1) (150 mg, 30%).

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