509. *Unsaturated Carbohydrates. Part III.*[1] *A Rearrangement Reaction in the 2-Hydroxyglycal Series: Further Exceptions to Hudson's Isorotation Rule*

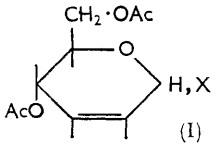
By R. J. Ferrier, W. G. Overend, and G. H. Sankey

Tetra-*O*-acetyl-2-hydroxy-D-glucal in boiling acetic acid undergoes a rearrangement to the anomeric 1,2,4,6-tetra-*O*-acetyl-2,3-didehydro-3-deoxy-D-*erythro*-hexoses (III) and (IV), which can be isolated by fractional crystallisation (α, 54%; β, 10%). On hydrogenation they give mixtures of 1,2,4,6-tetra-*O*-acetyl-3-deoxy-D-*ribo*- and -*arabino*-hexoses which reveal the anomeric configuration of the unsaturated esters, and which on deacetylation give the free 3-deoxyhexoses. The anomeric 1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-2,3-didehydro-3-deoxy-D-*erythro*-hexoses (VI) and (VII) (derived from tetra-*O*-benzoyl-2-hydroxy-D-glucal) and the acetates (III) and (IV) provide exceptions to Hudson's isorotation rules. A re-investigation of the configuration of the anomeric *p*-nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexosides has shown that at 589 mμ the more dextrorotatory isomer is the α-form, but that the rotatory dispersion curves cross at 285 mμ near the centre of Cotton effects. The conformations of the 2,3-unsaturated β-compounds are unexpectedly not H1.

The reaction undergone by esterified glycals when heated in water, namely, the allylic displacement of the C-3 ester grouping and the formation of 2,3-unsaturated compounds (pseudoglycals) is well known,[2] but the general nature of this type of rearrangement reaction has only recently become apparent.[1] Under the influence of suitable nucleophilic reagents, tri-*O*-acetyl-D-glucal may be converted into members of the series (I), and a furanoid glycal ester has been found to take part in similar reactions with great facility.[7] We now report that tetra-*O*-acetyl-2-hydroxy-D-glucal (II; R = Ac) and the corresponding benzoyl ester (II; R = Bz), when treated with boiling acetic acid, both undergo a reaction which is analogous to the glycal rearrangement.

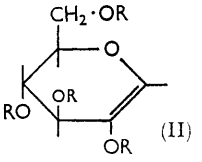
From the reaction of the acetate (II; R = Ac) two isomeric products were isolated by fractional crystallisation {(III), 54%, $[\alpha]_D$ +52°; (IV), 10%, $[\alpha]_D$ +156°}. Elemental and nuclear magnetic resonance (n.m.r.) spectroscopic analyses revealed that they were

[1] Part II, R. J. Ferrier, *J.*, 1964, 5443.
[2] B. Helferich, *Adv. Carbohydrate Chem.*, 1952, **7**, 209.

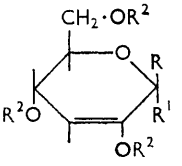


(I)

X = OH,[2] *O*-alkyl,[1] *O*-aryl,[3] *O*-Ac,[4] *S*-Ac,[5] theophyllyl [6]



(II)



	R	R^1	R^2
(III)	H	OAc	Ac
(IV)	OAc	H	Ac
(VI)	H	OAc	Bz
(VII)	OAc	H	Bz
(IX)	H	OH	Me

also isomeric with the initial glycal derivative (II; R = Ac), and both, on hydrogenation, gave mixtures of 1,2,4,6-tetra-*O*-acetyl-3-deoxy-D-*ribo*- and -D-*arabino*-hexose(-3-deoxy-D-glucose and -D-mannose). Neither n.m.r. spectroscopy nor polarimetry afforded reliable means for assigning anomeric configuration to the unsaturated acetates, but both methods, when applied to the hydrogenated derivatives, revealed clearly that the major product (despite the fact that it is the less dextrorotatory) was the α-isomer (III).

Each hydrogenated mixture showed two n.m.r. anomeric hydrogen signals as expected, and comparison of the chemical shifts and splittings of these with those of the

TABLE 1

Chemical shifts (δ; p.p.m. from tetramethylsilane) and coupling constants ($J_{1,2}$; c./sec.) of anomeric protons

Tetra-acetate of:	δ	$J_{1,2}$	Penta-acetate of:	δ [9]	$J_{1,2}$ [8]
3-Deoxy-β-D-glucopyranose ...	5·75	7·6	β-D-Glucopyranose	5·76	8
3-Deoxy-β-D-mannopyranose...	5·98	2·0	β-D-Mannopyranose	5·89	3
3-Deoxy-α-D-glucopyranose ...	6·28	3·5	α-D-Glucopyranose	6·31	3·2
3-Deoxy-α-D-mannopyranose...	6·04	<2·0	α-D-Mannopyranose	6·10	3

corresponding signals in the spectra of the glucose and mannose penta-acetates (Table 1) established that the dihydro-derivatives of ester (III) had the α-configuration. In particular, the presence of tetra-*O*-acetyl-3-deoxy-β-D-glucose in the products of hydrogenation of the anomer (IV) was readily detected by the characteristically large $J_{1,2}$ value,[8] and, furthermore, the compound was isolated from this mixture. Polarimetric measurements on the products of hydrogenation of the two unsaturated esters (III) and (IV) confirmed that they had the α- and β-configuration, respectively. Specific rotations of +72° and −10° are consistent only with this conclusion.

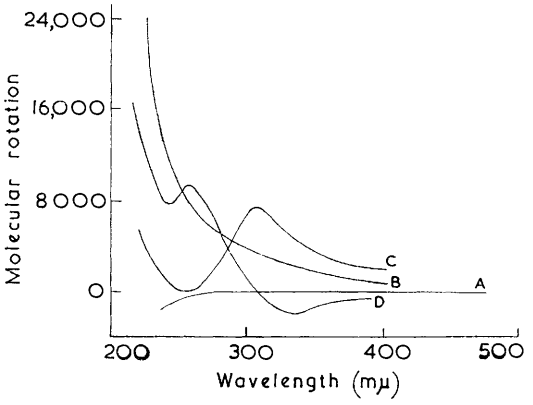
Deacetylation of the dihydro-derivatives of the acetates (III) and (IV) was carried out with sodium methoxide in methanol solution. Such treatment of aldose peracetates, in general, is complicated by the sensitivity of the sugars themselves to the reagent, but with 3-deoxyaldoses, where an elimination β to the reducing function cannot occur, the de-esterification proceeds without degradation of the free sugars. That it also occurs without epimerisation was illustrated by the fact that no 3-deoxymannose was formed during the methoxide treatment of tetra-*O*-acetyl-3-deoxy-β-D-glucose. The deoxyhexoses were separated on a column of cellulose powder and were obtained in crystalline form. From the major ester (III), 3-deoxy-glucose and -mannose were thus shown to have been produced in the ratio 66 : 34, and from the β-isomer (IV) in the ratio 24 : 76. Examination

[3] R. J. Ferrier, W. G. Overend, and A. E. Ryan, *J.*, 1962, 3667.
[4] D. M. Ciment, R. J. Ferrier, and W. G. Overend, unpublished results.
[5] S. Tegima, M. Haga, H. Nakamura, T. Maki, M. Sakata, and M. Akagi, Abs. of Papers, 145th National Meeting Amer. Chem. Soc., New York, 1963, p. 7D.
[6] W. A. Bowles and R. K. Robins, *J. Amer. Chem. Soc.*, 1964, **86**, 1252.
[7] R. K. Ness and H. G. Fletcher, *J. Org. Chem.*, 1963, **28**, 435.
[8] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, 1958, **80**, 6098.
[9] L. D. Hall, *T hedron Letters*, 1964, 1457.

of the intensities of the anomeric proton signals in the n.m.r. spectra of the mixtures of saturated acetates gave ratios of 63 : 37 and 23 : 77; the agreement confirms the validity of the n.m.r. signal assignments.

Saturation of the enol groupings of the esters (III) and (IV) therefore gave the 1,2-*cis*-products preferentially. This is consistent with the results of hydrogenation (also palladium catalyst) of tetra-*O*-acetyl-2-hydroxy-D-glucal and -galactal [10] both of which contain stereochemically similar unsaturated groupings, and give mainly the 2,3-*cis*-1,5-anhydrohexitol derivatives. 2,3-Dimethylcyclohexene, which may be considered as a stereochemical model, hydrogenates to *cis*-2,3-dimethylcyclohexane predominantly.[11] Alternatively, with a platinum catalyst, tetra-*O*-acetyl-2-hydroxy-D-glucal apparently gives mainly tetra-*O*-acetyl-1,5-anhydro-D-glucitol, while tri-*O*-acetyl-2-hydroxy-D-xylal, which would be expected to behave like the glucal derivative, gives the 2,3-*trans*-product in high yield with a palladium catalyst.[10]

In the presence of strong acids the reactions of glycals leading to the 2,3-unsaturated compounds (I) are superseded by additions which give rise to 2-deoxyglycosyl derivatives.[1] With tetra-*O*-acetyl-2-hydroxy-D-glucal in acetic acid solution, however, methanesulphonic



Optical rotatory dispersion curves of 1,2,4,6-tetra-*O*-acetyl-2,3-didehydro-3-deoxy-α- and β-D-*erythro*-hexose (A and B) and *p*-nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-α- and -β-D-*erythro*-hexoside (C and D)

acid (in a concentration which would cause addition of acetic acid to the double bond of tri-*O*-acetyl-D-glucal) merely accelerated the rearrangement and the unsaturated acetates (III) and (IV) were obtained just as from the uncatalysed reaction. The presence of the C-2 acetoxyl group therefore apparently inhibited the protonation at this site which would be the first step in an addition process, and the added acid facilitated the removal of the C-3 acetoxyl group.

Although, in the acetic acid treatment of the acetate (II; R = Ac), the rearranged products were isolated in only 64% yield, evidence was obtained that finally no 1,2-unsaturated compounds remained since the non-crystalline portion on hydrogenation and deacetylation afforded only 3-deoxy-glucose and -mannose and no 1,5-anhydrohexitols (chromatographic determination). That the components of the final mixture were in equilibrium was indicated by the observation that the main component (III) reacted in boiling acetic acid to give a solution with the same optical activity as that of the original reaction mixture. Thus, the 2,3-unsaturated isomers are more stable than the hydroxy-glycal compounds, and the α-derivative (III) is more stable than its anomer.

Since at 589 mμ the α-unsaturated ester (III) is less dextrorotatory than the isomer (IV), this anomeric pair of compounds constitutes an exception to Hudson's isorotation rules,[12] and optical rotatory dispersion studies (Figure) demonstrated that the effect is not due to a fortuitous crossing of the o.r.d. curves since the same relationship holds over the

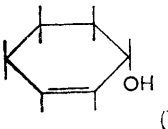
[10] M. G. Blair, *Adv. Carbohydrate Chem.*, 1954, **9**, 97.
[11] S. Siegel and G. V. Smith, *J. Amer. Chem. Soc.*, 1960, **82**, 6082.
[12] C. S. Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66.

range 230—400 mμ. Although they contravene the Hudson rule they do, however, conform with the (equally empirical) Mills' observation [13] that substituted cyclohexenols of structure (V) are less dextrorotatory than their epimers, and also with the wider generalisations of Bose and Chatterjee.[14]

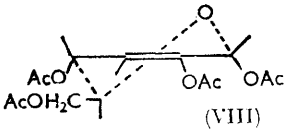
Work with the alkyl 2,3-didehydro-2,3-dideoxy-D-*erythro*- [1] and -D-*threo*- [4] hexopyranosides indicated that similar rotational anomalies also exist in these series, so we have re-investigated the configurations of the *p*-nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexosides,[3] the only other pair of 2,3-unsaturated anomers which has been described. The more dextrorotatory isomer ($[\alpha]_D$ +174°) on hydroxylation with neutral permanganate gave a syrup ($[\alpha]_D$ +110°) which on acetylation in pyridine solution afforded the known *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannoside, while the anomer ($[\alpha]_D$ +51°) when subjected to the same hydroxylation procedure gave a syrup with an optical rotation consistent only with the presence in it of β-glycosides ($[\alpha]_D$ −2·5°). This pair of compounds therefore conforms with the isorotation rules at 589 mμ, but the o.r.d. curves (Figure) cross near 285 mμ and these glycosides are therefore exceptional at shorter wavelengths. Both isomers exhibit Cotton effects centred around 285 mμ which are resultant, most probably, from the $n \longrightarrow \pi^*$ transition of the aromatic nitro-group. Optically active nitrobiphenyls [15] and alicyclic nitro-compounds [16] have both been found to give Cotton effects in this region.

Although the isorotation rules have been of great value in carbohydrate chemistry, and were reported as late as 1952 [17] as never having led to incorrect assignment of anomeric configuration, their reliability is becoming increasingly suspect when applied to compounds which bear chromophoric groupings attached directly to the anomeric centre. Several clear exceptions to the rules have been reported in the nucleoside series,[18] and indications that certain glycosylpyridinium salts also are anomalous have been given.[19]

From tetra-*O*-benzoyl-2-hydroxy-D-glucal the two 1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-2,3-didehydro-3-deoxy-D-*erythro*-hexoses (VI) and (VII) were obtained after heating in acetic acid {(VI), 63%, $[\alpha]_D$ +52°; (VII), 13%, $[\alpha]_D$ +91°}, and the major product, on hydrogenation, gave a crystalline 1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-3-deoxyhexose in 60% yield. De-esterification of this saturated product gave 3-deoxy-D-glucose, and it was shown to have the α-configuration by polarimetry ($[\alpha]_D$ +93°), and by n.m.r. spectroscopy ($J_{1,2}$ 3 c./sec.). The unsaturated ester (VI) must also have the α-anomeric configuration, and since its anomer (VII) is more dextrorotatory, this pair of compounds also represents an exception to the isorotation rules. It was not possible to hydrogenate the minor product (VII) under the conditions employed for the α-isomer (presumably because the large *trans*-related C-1 and C-4 ester groupings prevent the necessary contact with the catalyst; other workers have encountered difficulties in the hydrogenation of 2-hydroxyglycal benzoates [10]), so its structure was not established by chemical means.



(V)



(VIII)

Its n.m.r. spectrum (Table 2), however, revealed clearly that it bore the same relationship to the α-compound (VI) as did the β-acetate (IV) to the anomer (III). A possible alternative structure for this ester would be a 3-*O*-acetyl-2,4,6-tri-*O*-benzoyl-2-hydroxyglycal

[13] J. A. Mills, *J.*, 1952, 4976.
[14] A. K. Bose and B. G. Chatterjee, *J. Org. Chem.*, 1958, **23**, 1425.
[15] K. Mislow, E. Bunnenberg, R. Records, K. Wellman, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 1342.
[16] C. Djerassi, H. Wolf, and E. Bunnenberg, *J. Amer. Chem. Soc.*, 1963, **85**, 2835.
[17] W. A. Bonner, M. J. Kubitshek, and R. W. Drisko, *J. Amer. Chem. Soc.*, 1952, **74**, 5082.
[18] T. R. Emerson and T. L. V. Ulbricht, *Chem. and Ind.*, 1964, 2129.
[19] R. U. Lemieux and J. W. Lown, *Canad. J. Chem.*, 1963, **41**, 889.

formed by direct allylic displacement of the C-3 benzoyloxy-grouping, but since its coupling constant $J_{3,4}$ of 6 c./sec. requires it to be a 2-hydroxyglucal derivative, its optical rotation ($[\alpha]_D$ +91°) invalidates this possibility. Replacement of the C-3 benzoyl group of tetra-*O*-benzoyl-2-hydroxy-D-glucal ($[\alpha]_D$ −77°) by acetyl would have only a minor effect on optical activity.

The n.m.r. spectra of tetra-*O*-acetyl- and -*O*-benzoyl-2-hydroxy-D-glucal each contain (Table 2) a singlet (1 proton; H-1), a doublet (1 proton; H-3) and a quartet (1 proton; H-4), unresolved multiplets centred around δ 4·3 and 4·8 p.p.m., respectively [3 protons; H-5, H-6 (*eq*), and H-6 (*ax*)], and ester proton resonances. Comparison of the observed $J_{3,4}$ and $J_{4,5}$ values with those obtained from tri-*O*-acetyl-D-glucal (6·4 and 6·8 c./sec.) [20] reveals that introduction of the 2-ester groupings causes a slight alteration in molecular shape equivalent to a rotation about the 3,4- and 4,5-bonds which reduces each of the angles H-5–C-5–C-4–H-4 and H-4–C-4–C-3–H-3 by about 10°.

TABLE 2

N.m.r. parameters of unsaturated pyranoid compounds

Compound	Chemical shifts (δ scale; p.p.m. from T.M.S.) H-1	H-3	H-4	Coupling constants (c./sec.) $J_{3,4}$	$J_{4,5}$
Tri-*O*-acetyl-D-glucal [20]	6·53	5·34	5·20	6·4	6·8
Tetra-*O*-acetyl-2-hydroxy-D-glucal	6·69	5·62	5·26	4·0	6·0
Tetra-*O*-benzoyl-2-hydroxy-D-glucal	7·02	6·20	5·91	3·8	5·0
α-Acetate (III)	6·35	5·90	5·58	2·0	8·8
β-Acetate (IV)	6·44	6·01	5·35	5·5	1·5
α-Benzoate (VI)	6·64	6·30	6·02	2·0	*ca.* 10
β-Benzoate (VII)	6·75	6·41	5·81	5·8	1·5
p-Nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-α-D-*erythro*-hexoside	5·72	5·98	5·31	*ca.* 2	9·0
p-Nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-β-D-*erythro*-hexoside	5·80	6·08	5·06	*ca.* 2	*ca.* 2
Methylated enol (IX) [23]	5·65	5·14	4·17	2	8·5

The unsaturated acetates (III) and (IV) and benzoates (VI) and (VII) all gave spectra with H-1 singlets, H-3 doublets, H-4 quartets, and ester resonances as expected. In Table 2 chemical shifts and coupling constants derived from these spectra are listed, together with relevant information from the spectra of the anomeric *p*-nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexosides. With all these pairs of anomeric 2,3-unsaturated compounds a large $J_{4,5}$ was observed for the α-isomer, suggesting that each has a conformation close to the H1 half chair [21] [(VIII) for the α-acetate (III)]. Since the Karplus relationship cannot be applied to protons bonded to sp^2 hybridised carbon, $J_{3,4}$ values do not provide further information on detailed molecular geometry. The respective β-anomers show $J_{4,5}$ values quite inconsistent with this conformation, so inversion of a pseudo-axial C-1 substituent causes a gross effect on molecular shape which would have been unexpected on stereochemical grounds alone. It is suggested that the powerful anomeric effect [22] which is responsible, for example, for stabilising many C-1 axial compounds relative to their anomers, and for the existence of *trans*-2,5-dichloro-1,4-dioxan in the diaxial chair conformation may, in the present case, be the influence causing the apparent anomaly in the shape of the β-isomers.

Treatment of 2,3,4,6-tetra-*O*-methyl-D-glucose with lime water causes a β-elimination of methanol and the formation of the enol ether (IX) which has been obtained in crystalline form [23,24] and examined by n.m.r. spectroscopy.[23] The anomeric configuration could not be assigned from the spectrum since H-1 is not coupled with a neighbouring proton, but the $J_{3,4}$ and $J_{4,5}$ values obtained for this compound (Table 2), when considered with those

[20] L. D. Hall and L. F. Johnson, *Tetrahedron*, 1964, **20**, 883.
[21] R. J. Ferrier and W. G. Overend, *Quart. Rev.*, 1959, **13**, 265.
[22] R. U. Lemieux, "Molecular Rearrangements," ed. P. de Mayo, Interscience, New York, vol. II, 1964, p. 709.
[23] E. F. L. J. Anet, *Chem. and Ind.*, 1963, 1035.
[24] A. Klemer, H. Lukowski, and F. Zerhusen, *Chem. Ber.*, 1963, **96**, 1515.

determined in the present study, would indicate that the sugar had crystallised in the α-modification.

Experimental

N.m.r. spectra were obtained on a 60 Mc. Varian A-60 instrument for deuterochloroform solutions with tetramethylsilane as internal standard. The optical rotatory dispersion curves were measured on the Bellingham and Stanley/Bendix-Ericsson automatic recording spectropolarimeter. The concentrations of the methanolic solutions examined were *ca.* 0·2% for the acetates and *ca.* 0·004% for the *p*-nitrophenyl glycosides.

1,2,4,6-*Tetra*-O-*acetyl*-2,3-*didehydro*-3-*deoxy*-α- *and* -β-D-erythro-*hexose* (III) *and* (IV).—Tetra-*O*-acetyl-2-hydroxy-D-glucal (20 g., prepared by standard procedures [10]) was heated under reflux in glacial acetic acid (400 ml.) for 3 hr. during which time the optical rotation changed from −1·0° to +3·1° (const.). The solution was poured into water and extracted with methylene dichloride. The organic phase was washed with water, aqueous sodium hydrogen carbonate solution (which removed much of the coloured impurity), and again with water, and dried ($MgSO_4$). A brief treatment with activated charcoal removed most of the remaining colour and evaporation of the solvent gave a crystalline residue. Fractional crystallisation from aqueous ethanol (1 : 1, 100 ml.) afforded the α-*unsaturated acetate* (III) which was recrystallised from the same solvent (8·8 g., 44%), m. p. 66—67·4°, $[\alpha]_D$ +52° (*c* 1·0 in $CHCl_3$) (Found: C, 51·1; H, 5·5. $C_{14}H_{18}O_9$ requires C, 50·9; H, 5·5%). Removal of the solvent and treatment of the residue with ethanol afforded the β-*isomer* (IV) (2·0 g., 10%; recrystallised from ethanol), m. p. 81—83°, $[\alpha]_D$ +156° (*c* 1·0 in $CHCl_3$) (Found: C, 50·6; H, 5·4%). The n.m.r. spectra of these products revealed the presence in each of four acetyl groups, and one vinyl proton. Further quantities (2·0 g., 10%) of the α-acetate were subsequently obtained from the mother-liquors. The non-crystalline fraction (6·2 g., 31%) on hydrogenation (1·2 mol. gas absorbed), and deacetylation gave only 3-deoxy-glucose and -mannose (chromatographic analysis).

When the rearrangement was repeated with added methanesulphonic acid (0·002M), it proceeded at 100° (complete in 1 hr.), and gave a mixture with the same optical rotation as that of the non-catalysed reaction. The unsaturated esters (III) and (IV) were isolated in 55 and 10% yield.

1-O-*Acetyl*-2,4,6-*tri*-O-*benzoyl*-2,3-*didehydro*-3-*deoxy*-α- *and* -β-D-erythro-*hexose* (VI) *and* (VII).—Tetra-*O*-benzoyl-2-hydroxy-D-glucal (13 g.) was heated under reflux in glacial acetic acid (520 ml.) for 3 hr. during which time the rotation changed from −2·2° to +1·25° (const.). Removal of the solvent gave a solid residue from which the α-*unsaturated ester* (VI) was obtained (7·3 g., 63%), m. p. 151—153° (from ethanol), $[\alpha]_D$ +52° (*c* 1·0 in $CHCl_3$) (Found: C, 67·4; H, 4·7. $C_{29}H_{24}O_9$ requires C, 67·4; H, 4·7%). A second fraction on recrystallisation from ethanol afforded the β-*isomer* (VII) (1·5 g., 13%), m. p. 115—116·5°, $[\alpha]_D$ +91° (*c* 1·0 in $CHCl_3$) (Found: C, 67·3; H, 4·6%). The n.m.r. spectra of the esters (VI) and (VII) revealed the presence in each of one acetyl and three benzoyl groups, and one vinyl proton.

3-*Deoxy*-D-ribo- *and* -arabino-*hexose*.—(*a*) *From the unsaturated* α-*acetate* (III). This ester, like the others, showed a strong tendency to absorb significantly more than 1 mol. of hydrogen (presumably as a result of hydrogenolysis of the allylic ester groupings), but under the conditions noted they consumed the amount necessary for simple saturation of the unsaturated bond. The α-ester (2·0 g.) was hydrogenated under atmospheric pressure and at room temperature in ethyl acetate solution (100 ml.) with a palladium catalyst (5% on barium sulphate, 0·5 g.). Removal of the catalyst and solvent left, in theoretical amount, a colourless syrupy mixture of tetra-*O*-acetyl-3-deoxy-α-D-*ribo*- and -*arabino*-hexose, $[\alpha]_D$ +72·5° (*c* 1·0 in $CHCl_3$). N.m.r. analysis confirmed these structures and revealed that the isomers were present in the ratio 63 : 37. Deacetylation of the syrup was carried out at room temperature for 1 hr. with methanolic sodium methoxide (25 ml.; 0·1M). Removal of the sodium ions with resin (Amberlite IR-120, H^+ form), and of the solvent afforded the mixed 3-deoxyhexoses (0·975 g., 98%) which were applied to a column of powdered cellulose and eluted with butan-1-ol–ethanol–water (4 : 1 : 5). Three fractions were collected. Fraction (i) (0·09 g., 9%) was 3-deoxy-D-*arabino*-hexose m. p. 141—142° (from ethanol), $[\alpha]_D$ +45° ⟶ +53° (*c* 2·0 in H_2O). Rembarz [25] gives m. p. 141—142°, $[\alpha]_D$ +46° ⟶ +53° (H_2O). Fraction (ii) (0·458 g., 47%) was shown chromatographically to consist of a mixture of both sugars. The optical rotation,

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$[\alpha]_D$ +42·5° (H_2O) indicated that the ratio of the two components was 1 : 1. Fraction (iii) (0·405 g., 41%) had m. p. 106—107° (from ethanol), $[\alpha]_D$ +80° ⟶ +32° (*c* 1·0 in H_2O) [lit.,[26] for 3-deoxy-D-*ribo*-hexose, m. p. 105·5—107°, $[\alpha]_D$ +102° (extrapolated) ⟶ +32°]. All three fractions afforded the same 2,4-dinitrophenylosazone, m. p. 265° (decomp.) (undepressed on admixture with the derivative of 3-deoxy-D-*ribo*-hexose synthesised by an alternative route [27]). Corbett [28] gives m. p. 263—264° and Kenner and Richards [29] give m. p. 266° for this compound. This fractionation indicates that the *ribo*- and *arabino*-isomers were present in the ratio 66 : 34.

(*b*) *From the unsaturated* β-*acetate* (IV). The hydrogenation of this ester (1·0 g.) was carried out as above and the n.m.r. spectrum of the products {1·0 g., $[\alpha]_D$ −9·5 ($CHCl_3$)} was consistent with that of a 23 : 77 mixture of tetra-*O*-acetyl-3-deoxy-β-D-*ribo*- and -*arabino*-hexoses. Nucleation of the mixture afforded a small amount of the *ribo*-isomer, m. p. and mixed m. p. 127—128° (lit.,[26] 129—130°) which gave 3-deoxy-D-*ribo*-hexose alone on deacetylation. The de-esterification of the acetate mixture and the resolution of the products (0·443 g.) were carried out as before. Three fractions were again collected. Fraction (i) (0·291 g., 66%) was 3-deoxy-D-*arabino*-hexose, m. p. and mixed m. p. 140—141°, $[\alpha]_D$ +46° ⟶ +53·5° (*c* 2·0 in H_2O). Fraction (ii) (0·105 g., 24%) was a mixture of the deoxyhexoses with $[\alpha]_D$ +38·8° (*c* 1·0 in H_2O); it therefore contained 32% of the D-*arabino*-isomer. Fraction (iii) (0·034 g., 8%) m. p. and mixed m. p. 105—107°, $[\alpha]_D$ +32° (*c* 1·0 in H_2O) was 3-deoxy-D-*ribo*-hexose. Fractions (i) and (iii) both gave the previously prepared 2,4-dinitrophenylosazone. This fractionation indicates that the *ribo*- and *arabino*-isomers were present in ratio of 24 : 76.

(*c*) *From the unsaturated* α-*acetate benzoate* (VI). Hydrogenation of this ester (2·0 g.) was effected in ethyl acetate solution with palladium–charcoal (0·2 g., 5%) as catalyst. Removal of the catalyst and solvent and crystallisation from ethanol (50 ml.) gave 1-O-*acetyl*-2,4,6-*tri*-O-*benzoyl*-3-*deoxy*-α-D-ribo-*hexose* (1·2 g., 60%) m. p. 100—102°, $[\alpha]_D$ +93° (*c* 1·0 in $CHCl_3$) (Found: C, 67·4; H, 5·3. $C_{29}H_{26}O_9$ requires C, 67·2; H, 5·1%). The n.m.r. spectrum revealed the presence of one acetyl, three benzoyl, and a methylene group. De-esterification was effected as before, and the product was extracted with light petroleum. The residue crystallised with difficulty from ethanol, m. p. 106—107°, $[\alpha]_D$ +62° ⟶ +32° (*c* 2·0 in H_2O). It was further characterised as 3-deoxy-D-*ribo*-hexose by its conversion, with sodium acetate and acetic anhydride, into the β-tetra-acetate, m. p. and mixed m. p. 127—128°, $[\alpha]_D$ −13° (*c* 1·0 in $CHCl_3$){lit.,[26] m. p. 129—130°, $[\alpha]_D$ −14° ($CHCl_3$)}. The infrared spectrum of the acetate was identical with that of tetra-*O*-acetyl-3-deoxy-β-D-*ribo*-hexose.

Hydroxylation of the p-*Nitrophenyl* 4,6-*Di*-O-*acetyl*-2,3-*didehydro*-2,3-*dideoxy*-D-erythro-*hexosides*.—The α-isomer (1·0 g.) was dissolved in acetone (30 ml.) and aqueous potassium permanganate (20 ml., 2%) was added with stirring at 10° over 1 hr. During the addition, carbon dioxide was passed through the suspension. Ethanol was added to reduce the excess of permanganate, and solids were removed by filtration. Cations were then removed from the filtrate with resin (Amberlite IR-120, H^+ form) and the solvents evaporated to leave a syrup (0·7 g.), $[\alpha]_D$ +110° (EtOH) Acetylation was effected over 20 hr. with acetic anhydride (4 ml.) in pyridine (8 ml.) and the solution was poured into water. Extraction with methylene dichloride gave a syrup (0·55 g.) from which *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannoside (0·20 g.) was obtained, m. p. 154° (from ethanol), $[\alpha]_D$ +103° (*c* 1 in $CHCl_3$) {lit.,[30] m. p. 156—157°, $[\alpha]_D$ +103° ($CHCl_3$)}. On hydrolysis, mannose was obtained as the only free sugar (chromatographic determination).

The unsaturated β-glycoside (0·4 g.) was hydroxylated similarly and gave a syrup (0·33 g.), $[\alpha]_D$ −2·5° (EtOH) which, on acetylation, afforded a product (0·15 g.), $[\alpha]_D$ +22° ($CHCl_3$) which could not be crystallised.

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