The Photochemistry of Ketones Derived from Carbohydrates. Part 5.[1] Photochemical Cross-pinacolisation of Acetalised Pyranos-3-ulose Derivatives with Methanol; a Route to Branched-chain Sugar Derivatives

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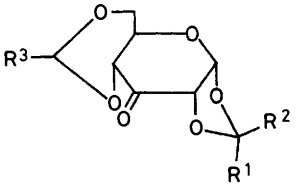
U.v. irradiation of methanolic solutions of the 4,6-*O*-ethylidene-1,2-*O*-isopropylidene derivative (1) and the 4,6-*O*-benzylidene-1,2-*O*-propylidene derivative (2) of *ribo*-hexos-3-ulose gave in each case the corresponding 1,2:4,6-substituted 3-*C*-hydroxymethyl-glucopyranose and -allopyranose derivatives. (3) and (4) and (11) and (12), from a cross-pinacolisation reaction, in combined yields of 42 and 55%, respectively. The *gluco*- [(3) and (11)] and *allo*- [(4) and (12)] structures were determined by ^1H and ^{13}C n.m.r. spectroscopy. In addition a little 1,2:4,6-diacetalised glucose and allose were produced by photoreduction, and significant amounts of 4,6-*O*-ethylidene-allono-δ-lactone (17) were formed from (1).

HYDROXYMETHYL branched-chain sugar derivatives are usually synthesised in two or more steps from osulose derivatives.[2,3] It occurred to us that application of the reported [4] photochemical cross-pinacolisation of 3,3,5,5-tetramethylcyclohexanone with methanol to pyrano-siduloses was worthy of study, since branched-chain sugars would thereby be produced in one step. This fitted in with our overall plans for synthesising biologically significant sugar derivatives by the irradiation of readily available photolabile carbohydrates.[1,5]

Most of our earlier photochemical studies with ketones were carried out on fully protected pyranosulose derivatives possessing free carbonyl groups at position 2 [6] or 4.[7] The products isolated from u.v. irradiations of these compounds in n-pentane, benzene, or acetonitrile arose by decarbonylation. Both types of osulose derivative gave furanoid products, and the 2-ulose derivatives also afforded olefinic products.

Attention was therefore given first to the irradiation of the 2- and 4-oxo-compounds in methanol. The results [8] were surprising because the products were virtually the same as those obtained in the non-protic solvents, except for a small amount of methyl esters formed by trapping of ketens. Chromatography indicated that there was little photochemical reduction and no significant cross-pinacolisation. Work with the available 2- and 4-osulose derivatives was therefore abandoned and the photochemical properties of some 1,2:4,6-diacetalised pyranos-3-uloses were examined. The compounds studied were the 4,6-*O*-ethylidene-1,2-*O*-isopropylidene derivative (1) and the 4,6-*O*-benzylidene-1,2-*O*-propylidene derivative (2) of *ribo*-hexopyranos-3-ulose. The former was prepared by a sequence of three well established reactions, whereas in the preparation of the latter compound five sequential reactions were used, including Gigg's method [9] for the construction of the 1,2-*O*-propylidene blocking group.

The photochemical behaviour of the derivatives (1) and (2) contrasted markedly with that of the compounds derived from the 2- and 4-uloses. In benzene the pyranos-3-ulose derivatives were transformed, relatively



(1) $R^1 = R^2 = R^3 = Me$

(2) $R^1 = H$ $R^2 = Et$, $R^3 = Ph$

slowly, into polar products with low t.l.c. mobilities, whereas in methanol there were products mobile on t.l.c. accompanied by some polar material. The less polar products are the subject of this study.

U.v. irradiation of a methanolic solution of the pyranos-3-ulose derivative (1) with the full arc of a medium-pressure mercury lamp gave products which were separated by p.l.c. into three pure compounds, R_F 0.27, 0.21, and 0.05, and a mixture of two isomers with R_F 0.41. All were identified initially from their elemental analysis and their i.r. and ^1H n.m.r. spectra. On this evidence the mixture with R_F 0.41 appeared to be composed of C-3 epimeric reduction products, contaminated with some starting material. This was confirmed by g.l.c. analysis in which the photoproducts were compared with the authentic derivatives of allose (15) and glucose (16), the former being obtained by reduction of the ketone (1) with lithium aluminium hydride.

[1] Part 4, P. M. Collins and B. R. Whitton, *J.C.S. Perkin I*, 1973, 1470.

[2] H. Grisbach and R. Schmid, *Angew. Chem. Internat. Edn.*, 1972, **11**, 159; W. G. Overend and N. R. Williams, *J. Chem. Soc.*, 1965, 3446; D. Horton and E. K. Just, *Carbohydrate Res.*, 1971, **18**, 81; J. H. Jordan and S. Smedley, *ibid.*, 1971, **16**, 177; H. Paulsen, V. Sinnwell, and P. Statler, *Angew. Chem. Internat. Edn.*, 1972, **11**, 149; J. M. J. Tronchet and J. M. Chalet, *Carbohydrate Res.*, 1972, **24**, 283; J. M. J. Tronchet, R. Graf, and R. Gurny, *Helv. Chim. Acta*, 1972, **55**, 613.

[3] B. Flaherty, S. Nahar, W. G. Overend, and N. R. Williams, *J.C.S. Perkin I*, 1973, 632.

[4] P. Yates, *Pure Appl. Chem.*, 1968, **16**, 107, and personal communication.

[5] P. M. Collins, N. N. Oparaeche, and V. R. N. Munasighe, *J.C.S. Perkin I*, 1975, 1700.

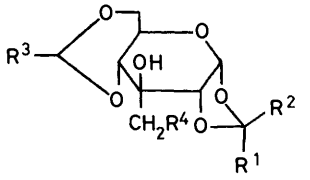
[6] P. M. Collins, P. Gupta, and R. Iyer, *Chem. Comm.*, 1970, 1261.

[7] P. M. Collins and P. Gupta, *J. Chem. Soc.* (*C*), 1971, 1965.

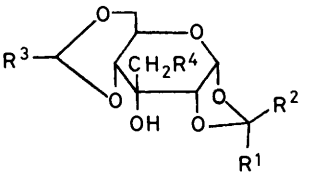
[8] A. S. Travis, unpublished experiments carried out in this laboratory.

[9] R. Gigg and C. D. Warren, *J. Chem. Soc.* (*C*), 1968, 1903.

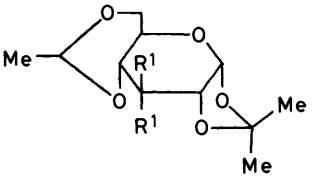
From the fraction with R_F 0.05, 4,6-*O*-ethylidene-D-allono-δ-lactone (17) crystallised. The lactone structure, which was assigned to this unexpected product from spectroscopic evidence, was confirmed by a hydroxamic acid test. Its *allo*-configuration was determined, after sequential reduction, hydrolysis, and pertrimethylsilylation, by g.l.c. analysis. The retention times of the mixture of silyl ethers formed were identical with those of the materials derived from D-allose and dissimilar to those of the pertrimethylsilyl derivatives formed from D-glucose.



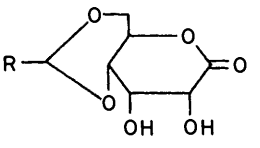
(3) $R^1 = R^2 = R^3 = Me, R^4 = OH$
(5) $R^1 = R^2 = R^3 = Me, R^4 = OAc$
(7) $R^1 = R^2 = R^3 = Me, R^4 = OTs$
(9) $R^1 = R^2 = R^3 = Me, R^4 = H$
(11) $R^1 = H, R^2 = Et, R^3 = Ph, R^4 = OH$
(13) $R^1 = H, R^2 = Et, R^3 = Ph, R^4 = OAc$



(4) $R^1 = R^2 = R^3 = Me, R^4 = OH$
(6) $R^1 = R^2 = R^3 = Me, R^4 = OAc$
(8) $R^1 = R^2 = R^3 = Me, R^4 = OTs$
(10) $R^1 = R^2 = R^3 = Me, R^4 = H$
(12) $R^1 = H, R^2 = Et, R^3 = Ph, R^4 = OH$
(14) $R^1 = H, R^2 = Et, R^3 = Ph, R^4 = OAc$



(15) $R^1 = H, R^2 = OH$
(16) $R^1 = OH, R^2 = H$



(17) R = Me
(18) R = Ph

The i.r. and ^1H n.m.r. data showed that the two products with R_F values 0.27 and 0.21 were alcohols, which contained four protons more than the starting material, two of which were exchangeable with D_2O, and the ^{13}C n.m.r. spectra showed that these products each contained one extra methylene carbon atom and a saturated quaternary carbon atom which replaced the ketone carbon atom present in (1). Consequently these compounds were the expected *C*-3-hydroxymethyl branched-chain sugar derivatives (3) and (4). The presence of a primary and a tertiary hydroxy-group was shown by the ready formation of monoacetoxy-alcohols (5) and (6) and monotosyloxy-alcohols (7) and (8). Upon treatment with lithium aluminium hydride these tosylates were converted into the *C*-methyl derivatives (9) and (10), respectively.

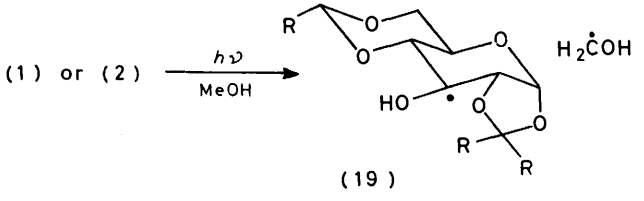
The assignment of configuration at the tertiary carbon atom in branched-chain sugar derivatives is not easy, particularly if the branching substituent contains a hydroxy-group. But in this work, since both stereoisomers were available, the problem was simplified and three methods were employed to determine the configuration at C-3. First a tentative assignment was made for (3) and (4) and related compounds from the proton shifts of the isopropylidene *endo*-methyl groups using the method of King and Overend.[10] The δ values for the *endo*-methyl signals [11] in the series of compounds (3), (5), and (7) are 1.55, 1.54, and 1.42, slightly lower than those for the *endo*-methyl groups in the C-3 epimers (4), (6), and (8) (1.59, 1.61, and 1.58). Therefore the former group can be assigned the *gluco*-structure, because in compounds with this configuration the *endo*-methyl groups are less deshielded by the pyranoid rings owing to conformational changes arising from steric interactions between the *cis*-branch substituent at C-3 and the *endo*-methyl of the isopropylidene group.

Secondly, the configuration at C-3 in (3) and (4) can be deduced from the configuration at this position in the less complex C-3 methyl derivatives (9) and (10). These compounds were hydrolysed to free sugars and their ^1H n.m.r. spectra were compared in the high-field region with that of the hydrolysate from methyl 4,6-*O*-benzylidene-3-*C*-methyl-α-D-allopyranoside, a compound whose configuration at C-3 was established earlier.[12] The chemical shift of the *C*-methyl protons in hydrolysed (10) was identical with that of the methyl group in the authentic 3-*C*-methylallose, whereas the methyl signal of the free sugar obtained from (9) appeared 10 Hz upfield from that of *C*-methylallose. The electro-

[10] R. D. King and W. G. Overend, *Carbohydrate Res.*, 1969, **9**, 423.
[11] N. Baggett, K. W. Buck, A. B. Foster, and J. M. Webber, *J. Chem. Soc.*, 1965, 3401.
[12] P. M. Collins and P. Gupta, *J.C.S. Perkin I*, 1972, 1670; G. B. Howarth, W. Szarek, and J. K. N. Jones, *Canad. J. Chem.*, 1968, **46**, 3575.

phoretic mobilities, in borate buffer, of these free sugars agree with this structural relationship and consequently with the assignment of the *gluco*- and *allo*-structures to (9) and (10), respectively. Thirdly, the structures of (3) and (4) were confirmed by ^{13}C n.m.r. spectroscopy. The carbon atom of the hydroxymethyl group in compound (3) resonates 1.5 p.p.m. upfield from the corresponding atom in compound (4), which indicates an axial disposition for the substituent in the former compound and therefore the *gluco*-structure.[13] Also the quaternary pyranose carbon atom (C-3) is 1.6 p.p.m. more shielded in (4) than in (3). This indicates that (4) has the *allo*-configuration, since it has been shown [14] that a carbon atom in a six-membered ring carrying hydroxy and hydroxymethyl groups is shielded more in the configuration in which the hydroxy-group is axial, than in the alternative configuration.

U.v. irradiation of a methanolic solution of 4,6-*O*-benzylidene-1,2-*O*-propylidene-*ribo*-hexopyranos-3-ulose (2) gave photoproducts with t.l.c. properties similar to those of the products formed from (1). The material comprising the least mobile band, unlike the polar product (17) isolated from the photolysate of (1), could not be crystallised. Consequently it was not fully characterised, but appeared to be mainly 4,6-*O*-benzylidenehexono-δ-lactone [*e.g.* (18)]. The i.r., ^1H and ^{13}C n.m.r. spectra, and elemental analysis of the other two products isolated show them to be the expected branched-chain sugar derivatives (11) and (12). Both were converted into monohydroxy-monoacetates (13) and (14) confirming the presence of primary and tertiary alcohol groups in the photoproducts. Since further chemical transformations were not carried out on these branched-chain sugar derivatives, and because they did not possess an isopropylidene blocking group, two of the methods employed to determine the configuration at C-3 in (3) and (4) could not be used in the present case. However a comparison of the ^{13}C n.m.r. spectra of (3), (4), (11), and (12) showed that the chemical shifts of all the *C*-hydroxymethylhexosyl carbon atoms in (3) could be correlated with those in (11), and those in (4) with those in (12). Thus compound (11) was assigned the *gluco*-structure and (12) the *allo*-structure.



(19)

All the carbonyl addition products formed in these reactions probably arise from a common ketyl radical [*e.g.* (19)], formed when the photoexcited ulose abstracts a hydrogen atom from the methanol. A further hydrogen atom abstraction by this radical would give the reduction products [*e.g.* (15) and (16)], whereas cross-coupling with the hydroxymethyl radical yields branched-chain sugar derivatives [(3) and (4) or (11) and (12)]. Cross-pinacolisation between ketones and alcohols has been reported occasionally for systems in which one of the compounds is aromatic,[15] but it is rare when both are aliphatic.[4,16] Also the reaction is not general, since although 3,3,5,5-tetramethylcyclohexanone cross-pinacolises with methanol, the unsubstituted ketone does not.[4] Similarly, not all 4,6-acetalised pyranos-3-ulose derivatives add methanol; only those with 1,2-*O*-alkylidene protecting groups have been found to react significantly in this way.

Many reaction pathways can be devised for the conversion of ketones (1) and (2) into lactones (17) and (18). But little work has been undertaken to solve this problem. However it has been shown that the reduction product (15) is not involved in the conversion of (1) into (17): irradiation of (15) in methanol does not give (17) nor does the amount of (17) increase when (1) and (15) are irradiated together in methanol. The mechanism of this reaction is being investigated further.

EXPERIMENTAL

T.l.c., optical rotations, and i.r., u.v., and ^1H n.m.r. spectral measurements were carried out as described earlier.[1] ^{13}C N.m.r. spectra were measured with a JEOL FX60 instrument.[14] For g.l.c. a Varian Aerograph 2720 instrument, fitted with a 10 ft × 1/4 in column packed with 10% SE30 on Chromosorb W (60—80 mesh), was used, with hydrogen as carrier gas and a thermal conductivity detector. Mass spectra were measured with a A.E.I. MS902 instrument at an ionising voltage of 70 eV. Electrophoresis was carried out with a Shandon L24 instrument.

Preparation of Pyranos-3-uloses.—Propenyl 4,6-O-benzylidene-α-D-glucopyranoside. Hydrogen chloride gas (24 g) was added during 18 h to a stirred and heated mixture of D-glucose (400 g) and allyl alcohol (1 l). The mixture was cooled and neutralised with ammonia (s.g. 0.880), and the product isolated as a syrup (270 g). Column chromatography of a 1 g portion gave allyl α-D-glucopyranoside, m.p. 97—99° (lit.,[17] 101°).

The crude product (160 g) was acetalised with benzaldehyde in the presence of zinc chloride. Work-up afforded allyl 4,6-*O*-benzylidene α-D-glucoside (102 g), m.p. 130—131°, δ (60 MHz; $CDCl_3$) 4.87 (d, $J_{1,2}$ 3.0 Hz), 3.3—4.7 (m, H-2, -3, -4, -5, H_2-6, and OCH_2), 5.48 (s, PhC*H*), 7.3—7.6 (m, *Ph*C), 5.1—5.2 (m), 5.34br (d), and 5.6—6.1 (m, 3 vinylic H).

The allyl glucoside (45 g) was isomerised [9] in dry dimethyl sulphoxide (150 ml) at 100 °C with potassium t-butoxide [from potassium (5 g)] during 14 h to give the title compound (36 g), m.p. 145—146°, $\nu_{max.}$ 1 630 cm^{-1}

[13] G. W. Buchanan, J. B. Stothers, and S.-T. Wu, *Canad. J. Chem.*, 1969, **47**, 3113; A. M. Sepulchre, B. Septe, G. Lukacs, S. D. Gero, W. Voelter, and K. Breitmairer, *Tetrahedron*, 1974, **30**, 905; M. Miljkovic, M. Giligorijevic, T. Satoh, G. Glisin, and R. G. Pitcher, *J. Org. Chem.*, 1974, **30**, 3847.

[14] P. M. Collins and V. R. N. Munasighe, *Carbohydrate Res.*, submitted for publication.

[15] H. L. J. Backstrom, *Acta Chem. Scand.*, 1966, **20**, 2617; S. A. Weiner, *J. Amer. Chem. Soc.*, 1971, **93**, 425.

[16] S. P. Singh and J. Kagan, *Chem. Comm.*, 1969, 1121.

[17] E. A. Talley, M. D. Vale, and E. Yanovsky, *J. Amer. Chem. Soc.*, 1945, **67**, 2037.

(C=C), δ (60 MHz; $CDCl_3$) 5.09 (d, $J_{1,2}$ 3.5 Hz), 3.3—4.4 (m, H-2, -3, -4, -5, and H_2-6), 2.7—3.1 (2 HO), 5.54 (s, PhC*H*), 7.3—7.6 (m, *Ph*CH), 1.64 (q, *J* 6.5 and 2.0 Hz, CH_3), 6.12 (q, *J* 6.0 and 2.0 Hz, vinylic H), and 4.60 (quint, *J* 6.0 and 6.5 Hz, vinylic H).

4,6-O-*Benzylidene*-1,2-O-*propylidene*-α-D-*glucopyranose*. The propenyl glucoside (34 g), R_F 0.2 (EtOAc–CH_2Cl_2, 1 : 4) was heated at 150 °C as a melt under reduced pressure for 0.5 h, and then under reflux for 0.8 h in ethyl acetate (200 ml) containing toluene-*p*-sulphonic acid. The usual work-up gave the title *compound* (25 g, 72%), R_F 0.5 (EtOAc–CH_2Cl_2, 1 : 4), m.p. 116—117° [from ethyl acetate–light petroleum (b.p. 40—60 °C)], $\nu_{max.}$ 3 450 cm^{-1} (HO), δ (60 MHz; $CDCl_3$) 5.46 (d, $J_{1,2}$ 4.0 Hz), 2.95br (exchangeable, HO), 5.51 (s, PhC*H*), 7.3—7.6 (m, *Ph*CH), 4.94 (t, *J* 4.5 Hz, *H*CCH_2), 1.75br (oct, *J* 7.0 and 4.5 Hz, HCCH_2Me), 1.0br (t, *J* 7.0 Hz, CH_2*Me*), and a multiplet for 6 other protons (Found: C, 62.1; H, 6.6. $C_{16}H_{20}O_6$ requires C, 62.3; H, 6.5%). This compound was converted into a monoacetate, m.p. 75°, $\nu_{max.}$ 1 730 cm^{-1} (C=O), which had an n.m.r. spectrum similar to that of its hydroxy-precursor [except δ 2.1 (s, OAc) and 5.3 (d of d, *J* 3.5 and 7.0 Hz, H-3)].

4,6-O-*Benzylidene*-1,2-O-*propylidene*-α-D-ribo-*hexopyranos*-3-*ulose* (2). The 1,2:4,6-protected glucopyranose (10 g) in freshly distilled dichloromethane (50 ml) and carbon tetrachloride (200 ml) was oxidised during 1 h with ruthenium tetraoxide (from 6 g of the dioxide).[18] The usual work-up gave the *ulose* (2) (7.6 g, 78%), m.p. 129—130° (from ethanol), $\nu_{max.}$ 1 745 cm^{-1} (C=O), R_F 0.8, δ (220 MHz; $CDCl_3$) 5.81 (d, $J_{1,2}$ 4.5 Hz), 4.34 (d, $J_{2,1}$ 4.5 Hz), 4.32 (d, $J_{4,5}$ 9.0 Hz), 4.25 (t of d, $J_{5,6a}$ 4.5 Hz), 4.49 (d of d, $J_{6a,6b}$ 11.0 Hz), 3.85 (d of d $J_{6b,5}$ 10 Hz), 5.57 (s, PhC*H*), 7.38 and 7.50 (2 m, 3 H and 2 H, *Ph*CH), 5.10 (t, *J* 5.0 and 5.0 Hz, *H*CCH_2Me), 1.76 (m, HCCH_2Me), and 0.97 (t, *J* 7.0 Hz, Me) (Found: C, 62.9; H, 6.0. $C_{16}H_{18}O_6$ requires C, 62.7; H, 5.9%).

4,6-O-*Ethylidene*-1,2-O-*isopropylidene*-α-D-*glucopyranose* (16) (with F. Siavashy). Anhydrous glucose (90 g) (dried over phosphorus pentaoxide at reduced pressure) was treated for 3 days with paraldehyde (75 ml) containing sulphuric acid (0.5 ml). Ethanol (300 ml) and potassium hydroxide were added to bring the pH to 6.5. The mixture was heated, charcoal (5 g) added, and the solution filtered. On cooling, 4,6-*O*-ethylideneglucose (72 g) was obtained, m.p. 175° (lit.,[19] 178—179°), δ 1.30 (d, *J* 5.0 Hz, 4,6-*O*-ethylidene).

Anhydrous copper(II) sulphate (600 g) was added in portions during 1 h to a solution of the product (30 g) in acetone (4.0 l) which was heated under reflux. The reaction was continued for a further 3 h and then filtered. The filtrate was evaporated and the residue was triturated with dichloromethane. The unchanged 4,6-*O*-ethylideneglucose (20 g) was filtered off and the solution evaporated to give a syrup (10 g) which contained (16) and di-*O*-isopropylideneglucofuranose in the ratio 9 : 1 (g.l.c.). Crystallisation from di-isopropyl ether gave *compound* (16) (8.4 g, 70% conversion), m.p. 84—85° (from di-isopropyl ether), $[\alpha]_D^{22}$ +89° (*c* 1.0), R_F 0.4, t_R 4.5 min (215 °C), $\nu_{max.}$ 3 475 cm^{-1} (OH), δ (100 MHz; $CDCl_3$) 5.48 (d, $J_{1,2}$ 4.5 Hz), 4.14 (d of d, *J* 9.0 and 5.0 Hz), 3.24 (t, *J* 8.0 Hz), 3.14 (t, *J* 8.0 Hz), and 3.60—4.05 (3 H, m) (H-2, -3, -4, -5, and H_2-6), 1.52 and 1.36 (2 s, 2 Me), 1.34 (d, *J* 5.0 Hz, HC*Me*), and 4.68 (q, *J* 5.0 Hz, *H*CMe) (Found: C, 53.7; H, 7.3. $C_{11}H_{18}O_6$ requires C, 53.7; H, 7.4%).

The 3-*acetate* (80% yield), had m.p. 123—124°, $[\alpha]_D^{20}$ +10°, 1 740 cm^{-1} (C=O) (Found: C, 54.4; H, 6.9. $C_{13}H_{20}O_7$ requires C, 54.2; H, 7.0%), δ 2.11 (OAc) and 5.19 (d of d, *J* 4.5 and 8.0 Hz, H-3).

4,6-O-*Ethylidene*-1,2-O-*isopropylidene*-α-D-ribo-*hexopyranos*-3-*ulose* (1). 4,6-*O*-Ethylidene-1,2-*O*-isopropylideneglucose (16) (2 g), when oxidised in the usual way,[18] gave *compound* (1) (1.6 g, 80%), m.p. 76—78°, $\nu_{max.}$ 1 740 cm^{-1} (C=O), $[\alpha]_D^{20}$ +95° (*c* 1.0), $\lambda_{max.}$ (EtOH) 273.5 nm (ε 650), R_F 0.6, t_R 4.7 min (215 °C), δ (220 MHz; $CDCl_3$) 5.72 (d, $J_{1,2}$ 5.0 Hz), 4.25 (d, $J_{2,1}$ 5.0 Hz), 3.4—3.7 (1 H, m) and 4.0—4.4 (3 H, m) (H-4, -5, and H_2-6), 4.68 (q, *J* 5.0 Hz. *H*CMe), 1.38 (d, *J* 5.0 Hz, HC*Me*), and 2.1 and 2.4 (2 s, Me_2C) (Found: C, 53.9; H, 6.6. $C_{11}H_{16}O_6$ requires C, 54.1; H, 6.6%).

U.v. Irradiation of 4,6-O-*Ethylidene*-1,2-O-*isopropylidene*-ribo-*hexopyranos*-3-*ulose* (1).—The 3-ulose (1) (1.55 g) in methanol (100 ml) was irradiated for 1.5 h through quartz with a 450 W medium-pressure mercury arc. The solution was evaporated under reduced pressure to give a syrup, which was separated into the following five fractions either by column chromatography or by p.l.c.: (i) unchanged (1) (0.23 g), R_F 0.64 (EtOAc–CH_2Cl_2, 1 : 4), $\nu_{max.}$ 1 740 cm^{-1} (C=O); (ii) a mixture (0.09 g, 7%), R_F 0.41, $\nu_{max.}$ 3 450 cm^{-1} (HO) comprising 4,6-*O*-ethylidene-1,2-*O*-isopropylidene derivatives of α-D-glucose (16) and α-D-allose (15) with t_R values identical with those of authentic samples of (15) and (16); (iii) 4,6-O-*ethylidene*-1,2-O-*isopropylidene*-3-C-*hydroxymethyl*-α-D-*glucopyranose* (3) (0.3 g, 20%), R_F 0.27, t_R 7.10 min (215 °C), m.p. 129—130° [from di-isopropyl ether–light petroleum (b.p. 40—60 °C)], $[\alpha]_D^{20}$ +5° (*c* 0.6), $\nu_{max.}$ 3 340 and 3 140 cm^{-1} (HO), *m/e* 275 (1%, $M^+ - H$), 261 (29, $M^+ - CH_3$), and 245 (11, $M^+ - CH_2OH$), δ_H (100 MHz; $CDCl_3$) 5.54 (d, $J_{1,2}$ 4.0 Hz), 4.13 (d, $J_{2,1}$ 4.0 Hz), 3.28—4.40 (m, H-4, -5, H_2-6, 3-CH_2, and 2 HO), 4.72 (q, *J* 5.0 Hz, C*H*Me), 1.36 (d, *J* 5.0 Hz, CH*Me*), and 1.34 and 1.56 (2 s, CMe_2), δ_C($CDCl_3$) 96.2, 79.9, 70.8, 84.9, 61.1, 69.3, 63.8 (C-1, -2, -3, -4, -5, -6, and 3-CH_2), 108.8 (*C*Me_2), 99.9 (*C*Me), 25.4 and 27.0 [C(*C*H_3)$_2$], and 20.4 (C*C*H_3) (Found: C, 51.7; H, 7.4. $C_{12}H_{20}O_7$ requires C, 52.2; H, 7.3%); (iv) 4,6-O-*ethylidene*-1,2-O-*isopropylidene*-3-C-*hydroxymethyl*-α-D-*allopyranose* (4) (0.33 g, 22%), R_F 0.21, t_R 9.30 min, m.p. 109—110° (recrystallised), $[\alpha]_D^{20}$ +97° (*c* 0.6), $\nu_{max.}$ 3 340 cm^{-1} (HO) [mass spectrum similar to that of compound (3)], δ_H (100 MHz; $CDCl_3$) 5.50 (d, $J_{1,2}$ 5.0 Hz), 4.70 (q, 5.0 Hz, C*H*Me), 2.9br (s, 2 HO), 1.30 (d, *J* 5.0 Hz, CH*Me*), 1.34 and 1.58 (2 s, CMe_2), 3.20—3.80 (4 H), and 3.95—4.20 (3 H), δ_C($CDCl_3$) 97.3, 72.0, 69.2, 76.6, 58.2, 68.8, and 65.3 (C-1, -2, -3, -4, -5, -6, and 3-CH_2), 108.2 (*C*Me_2), 99.8 (*C*Me), 26.4 and 26.4 [C(*C*H_3)$_2$], and 20.4 (C*C*H_3) (Found: C, 51.7; H, 7.2. $C_{12}H_{20}O_7$ requires C, 52.2; H, 7.3%); (v) 4,6-O-*ethylidene*-D-*allono*-δ-*lactone* (17) (0.33 g, 30%), R_F 0.05, m.p. 210—211°, $\nu_{max.}$ 1 738, 1 755, and 3 400 cm^{-1} (δ-lactone C=O and HO), δ_H (220 MHz; C_6D_5N) 5.20 (d, $J_{2,3}$ 6.5 Hz), 4.76 (d of d, $J_{3,4}$ 4.5 Hz), 4.01 (d of d, $J_{4,5}$ 10.0 Hz), 4.53 (t of d, $J_{5,6a}$ 10.0 Hz), 4.34 (d of d, $J_{6e,5}$ 5.0 Hz), 3.62 (t, $J_{6a,6e}$ 10.0 Hz), 4.78 (q, *J* 5.0 Hz, C*H*Me), 1.36 (d, *J* 5.0 Hz, CH*Me*), 4.95br (s, 2 HO), *m/e* 203 (8%, $M^+ - H$), 189 (17, $M^+ - Me$), 160 (65, $M^+ -$ AcH), 143 (33, $M^+ -$ AcOH) (Found: C, 46.8; H, 5.8. $C_8H_{12}O_6$ requires C, 47.1; H, 5.9%). Compound (17) gave

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a positive ester test upon treatment sequentially with hydroxylamine and acidified iron(III) chloride.

C-3 *Branched-chain Sugar Derivatives of* 4,6-O-*Ethylidene*-1,2-O-*isopropylidene-allo- and -gluco-pyranose prepared from Compounds* (3) *and* (4).—3-C-*Acetoxymethyl derivatives* (5) *and* (6). The 3-*C*-hydroxymethyl derivatives (3) and (4) (*ca.* 50 mg each) were separately treated in pyridine (5 ml) with acetic anhydride (0.5 ml) during 16 h at 22 °C. The usual work-up of the experiment with (3) gave a syrupy monoacetate (5) (54 mg), $[\alpha]_D^{20}$ +6° (*c* 0.2), $\nu_{max.}$ 1 740 and 3 570 cm^{-1} (C=O and HO), δ (220 MHz; $CDCl_3$) 5.51 (d, $J_{1.2}$ 4.0 Hz), 4.05 (d, $J_{2.1}$ 4.0 Hz), 3.58 (d, $J_{4.5}$ 10.0 Hz), 3.90 (t of d, $J_{5.6a}$ 10.0 Hz), 4.18 (d of d, $J_{6e.5}$ 5.0 Hz), 3.40 (t, $J_{6a.6e}$ 10.0 Hz), 4.40 (s, CH_2OAc), 4.66 (q, *J* 5.0 Hz, C*H*Me), 1.30 (d, *J* 5.0 Hz, CH*Me*), 1.33 and 1.54 (2 s, CMe_2), 2.10 (s, Ac), and 2.87 (s, HO).

The experiment with (4) gave the monoacetate (6) (55 mg, 94%), m.p. 80—82° (from ethanol), $[\alpha]_D^{20}$ +90° (*c* 0.2), $\nu_{max.}$ 1 740 and 3 550 cm^{-1} (C=O and HO), δ (220 MHz; $CDCl_3$) 5.57 (d, $J_{1.2}$ 5.5 Hz), 4.04 (d, $J_{2.1}$ 5.5 Hz), 4.02 (d, J_{gem} 11 Hz, 3-CH_a), 4.14 (d, J_{gem} 11 Hz, 3-CH_b), 4.71 (q, *J* 5.0 Hz, C*H*Me), 1.39 (d, *J* 5.0 Hz, CH*Me*), 3.0 (s, HO), 1.61 and 1.40 (2 s, CMe_2), and 2.10 (s, Ac) [the signals at 4.16—4.30 (2 H) and 3.30—3.55 (2 H) for the remaining protons were second order].

3-C-*Tosyloxymethyl derivatives* (7) *and* (8). The 3-*C*-hydroxymethyl derivatives (3) and (4) (100 and 40 mg, respectively) were separately treated in anhydrous pyridine (3 ml) with toluene-*p*-sulphonyl chloride (3 mol. equiv.) during 15 h at 22 °C. The usual work-up gave from (3) the monotosylate (7) (114 mg, 66%), m.p. 134—136°, R_F 0.6, $\nu_{max.}$ 3 570 cm^{-1} (HO), δ (100 MHz; $CDCl_3$) 5.54 (d, $J_{1.2}$ 4.0 Hz), 4.08 (d, $J_{2.1}$ 4.0 Hz), 3.62 (d, $J_{4.5}$ 9.5 Hz), 3.86 (t of d, $J_{5.6a}$ 9.5 Hz), 3.42 (t, $J_{6a.6e}$ 9.5 Hz), 4.16 (d of d, $J_{6e.5}$ 4.5 Hz), 4.36br (s, CH_2OTs), 4.68 (t, *J* 5.0 Hz, C*H*Me), 3.30br (s, HO), 1.33 (d, *J* 5.0 Hz, CH*Me*), 1.36 and 1.42 (2 s, CMe_2), 2.51 (s, MeC_6H_4), and 7.84 and 7.42 (2 d, C_6H_4).

The experiment with (4) gave the monotosylate (8) (51 mg, 78%), m.p. 137—139°, R_F 0.9, $\nu_{max.}$ 3 510 cm^{-1} (HO), δ (100 MHz; $CDCl_3$) 5.63 (d, $J_{1.2}$ 5.5 Hz), 4.20 (d, $J_{2.1}$ 5.5 Hz), 3.86 (d, $J_{4.5}$ 9.5 Hz), 3.0br (HO), 4.58 (q, *J* 5.0 Hz, C*H*Me), 3.20—3.60 (2 H) and 4.00—4.40 (3 H), 1.24 (d, *J* 5.0 Hz, CH*Me*), 1.40 and 1.58 (2 s, CMe_2), 2.44 (s, MeC_6H_4), and 7.46 and 7.90 (2 d, C_6H_4).

3-C-*Methyl derivatives* (9) *and* (10). The 3-*C*-tosyloxymethyl derivatives (7) and (8) (80 and 43 mg, respectively) were separately reduced with lithium aluminium hydride (120 and 80 mg) in tetrahydrofuran (10 ml) under reflux for 15 h. Ethanol (2 ml) and water (2 ml) were added and after 1 h the mixtures were filtered and the inorganic salts washed with dichloromethane. The combined filtrates were evaporated and the residues were taken up in dichloromethane; the solutions were washed with water, dried, and evaporated to give products, which were purified by p.l.c. on silica gel (EtOAc–CH_2Cl_2, 1 : 9) using iodine vapour to locate the fractions. From the compound (7) the 3-*C*-methyl derivative (9) was obtained (29 mg, 60%), R_F 0.29 (EtOAc–CH_2Cl_2, 1 : 9), δ (100 MHz; $CDCl_3$) 5.66 (d, $J_{1.2}$ 4.5 Hz), 4.08 (d, $J_{2.1}$ 4.5 Hz), 3.47 (d, $J_{4.5}$ 10.0 Hz), 3.86 (t of d, $J_{5.6e}$ 5.0 Hz), 4.26 (d of d, $J_{6e.6a}$ 10.0 Hz), 3.47 (t, $J_{6a.5}$ 10.0 Hz), 2.28br (HO), 4.82 (q, *J* 5.0 Hz, C*H*Me), 1.36 (d, *J* 5.0 Hz, CH*Me*), 1.40 and 1.42 (2 s, CMe_2), and 1.57 (s, CMe).

From the experiment with (8), material believed to be compound (10) was obtained after p.l.c. (8 mg; R_F 0.3).

Partial ^{1}H *N.m.r. Spectra of* 3-C-*Methyl*-D-*allose and* -D-*glucose*.—The 3-*C*-methyl-glucose and -allose derivatives (9) and (10) and methyl 4,6-*O*-benzylidene-3-*C*-methyl-α-D-allopyranoside [12] (*ca.* 8—20 mg of each) were dissolved in 2M-DCl in D_2O (*ca.* 0.6 ml) in three separate n.m.r. tubes and their ^{1}H 100 MHz spectra were measured in the region δ 2.5—0.5. The solutions were heated at 70 °C and the spectra remeasured at intervals during 7 h. After this period there was no further change and in each case intense sharp *C*-methyl singlets remained in the high-field regions. A small quantity of methanol was added to each tube as an internal standard and the positions of the *C*-methyl signals, relative to the *O*-methyl standard signal, were determined. The branched-chain sugar obtained from (9) exhibited its *C*-methyl signal 212 Hz upfield from the internal standard, whereas the *C*-methyl signal of the isomer obtained from both (10) and the other source was 202 Hz to higher field than the reference signal.

The hydrolysates were also examined by electrophoresis in 0.05M-sodium borate at 4 KV. The two samples of 3-*C*-methylallose had identical mobilities, whereas the *gluco*-isomer moved faster, the mobility ratio being 0.8 : 1 [similar to the ratio of M_G values (83 and 100) reported [20] for D-allose and D-glucose in this buffer].

Reduction and Hydrolysis of 4,6-O-*Ethylidene*-D-*allono*-δ-*lactone* (17).—Sodium borohydride (4 mg) in water (2 ml) was added during 1 h to a stirred, cooled (*ca.* 3 °C) solution of the lactone (17) (20 mg) in water (3 ml), while the pH was maintained between 3 and 4 by addition of M-sulphuric acid.[21] An excess of acid (0.5 ml) was then added to destroy borohydride, the sodium cations were removed with an ion-exchange resin [IR 120 (H^+)], and the boric acid was volatilised as its methyl ester. The 4,6-*O*-ethylidene blocking group was removed from the crude product by warming with M-hydrochloric acid at 100 °C for 1.5 h and the free sugar so obtained was trimethylsilylated [22] with 'Tri-sil' (Me_3SiCl in pyridine) at 60 °C during 5 min. The mixture was kept in a desiccator at 0.1 mmHg over phosphorus pentaoxide to remove excess of reagent and pyridine. The residue was dissolved in n-hexane and the solution analysed by g.l.c. It exhibited three significant peaks with t_R (200 °C) 14.4, 16.8, and 20.0 min, identical with those obtained from pertrimethylsilylated D-allose but differing from those obtained with the D-glucose derivatives (t_R 18.6 and 25.4 min).

U.v. Irradiation of 4,6-O-*Benzylidene*-1,2-O-*propylidene*-ribo-*hexopyranos*-3-*ulose* (2).—(i) *In methanol.* Irradiation of (2) (0.4 g) in methanol as described previously gave, after work-up, a syrup, which was separated by p.l.c. into five bands; R_F 0.82, 0.75, 0.4, 0.35, and 0.05 (C_6H_6–EtOAc–MeOH, 16 : 3 : 1). The fraction of R_F 0.05 gave a glassy material which would not crystallise. It was believed to be 4,6-*O*-benzylidenehexono-δ-lactone (18) (presumably with the *allo*-configuration), $\nu_{max.}$ 1 740 and 3 500 cm^{-1} (C=O and HO), showing ^{1}H n.m.r. signals for a benzylidene residue, and giving a positive lactone test. The fraction with R_F 0.75 was unchanged (2) (70 mg).

The fractions with R_F 0.35 and 0.40 were eluted together and then rechromatographed (p.l.c.; EtOAc–CH_2Cl_2, 1 : 4).

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[21] M. L. Wolfrom and A. Thompson, *Methods Carbohydrate Chem.*, 1963, **2**, 65.
[22] C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Amer. Chem. Soc.*, 1963, **85**, 2497.

The less mobile component, R_F 0.2, was 4,6-O-*benzylidene*-3-C-*hydroxymethyl*-1,2-O-*propylidene*-α-D-*glucose* (11) (110 mg, 30%), m.p. 117—119° (from butan-2-ol), $[\alpha]_D^{20}$ +33° (*c* 0.2), δ_H (100 MHz; $CDCl_3$) 5.54 (d, $J_{1.2}$ 4.5 Hz), 3.5—4.2 (6 H), 4.36 (d of d, $J_{6a.6e}$ 9.5, $J_{6a.5}$ 4.0 Hz), 4.78 (t, *J* 4.5 Hz, *H*CEt), 1.78 (q of d, *J* 4.5 and 7.0 Hz, $MeCH_2$), 1.0 (t, *J* 7.0 Hz, CH_2CH_3), 3.20br (2 H, exchangeable, 2 HO), 5.45 (s, PhC*H*), and 7.2—7.6 (5 H, aromatic), $\delta_C(CDCl_3)$ 96.4, 84.9, 71.2, 80.6, 60.9, 69.8, and 63.8 (C-1, -2, -3, -4, -5, -6, 3-CH_2), 104.8 (*C*Et), 102.1 (*C*Ph), 27.0 (CH_2), 8.1 (CH_3), and 126.3, 128.3, 129.2, and 137.1 (Ph) (Found: C, 60.1; H, 6.6. $C_{17}H_{22}O_7$ requires C, 60.3; H, 6.6%). The monoacetate (13) (64 mg, 95%) showed $[\alpha]_D^{20}$ +28° (*c* 0.2), $\nu_{max.}$ 1 740 and 3 450 cm^{-1} (C=O and HO), δ (100 MHz; $CDCl_3$) 5.57 (d, $J_{1.2}$ 4.5 Hz), 3.5—4.5 (5 H), 4.44 and 4.60 (2 d, J_{gem} 12.0 Hz, 3-CH_2), 4.83 (t, *J* 5.0 Hz, *H*CEt), 1.80 (q of d, CH_2Me), 1.02 (t, *J* 7.0 Hz, CH_2CH_3), 3.42 (s, exchangeable, HO), 5.50 (s, PhC*H*), 7.6—7.2 (5 H, aromatic), and 2.06 (s, OAc).

The mobile component, 4,6-O-*benzylidene*-3-C-*hydroxymethyl*-1,2-O-*propylidene*-α-D-*allopyranose* (12) (90 mg, 25%), R_F 0.3, was a waxy solid, m.p. 128—130° (from $CHCl_3$–C_6H_{14}), $[\alpha]_D^{21}$ +43° (*c* 0.2), $\nu_{max.}$ 3 450 cm^{-1} (HO), δ_H (100 MHz; $CDCl_3$) 5.38 (d, $J_{1.2}$ 5.5 Hz), 4.07 (d, $J_{2.1}$ 5.5 Hz), 3.2—3.8 (4 H) and 4.2—4.5 (2 H) (H-4, -5, H_2-6, and 3-CH_2), 4.92 (t, *J* 5.0 Hz, *H*CEt), 1.83 (m, *J* 5.0 and 7.0 Hz, $MeCH_2$), 1.04 (t, *J* 7.0 Hz, CH_2CH_3), 3.0br (exchangeable, 2 HO), 5.52 (s, PhC*H*), and 7.2—7.6 (Ph), $\delta_C(CDCl_3)$ 98.0, 76.9, 69.3, 71.1, 59.4, 69.3, and 64.7 (C-1, -2, -3, -4, -5, -6, and 3-CH_2), 102.7 (*C*Et), 102.0 (*C*Ph), 26.8 (CH_2), 8.3 (CH_3), and 126.3, 128.3, 129.2, and 137.1 (Ph) (Found: C, 60.4; H, 6.9. $C_{17}H_{22}O_7$ requires C, 60.3; H, 6.6%).

The monoacetate (14) (86 mg, 95%) showed $[\alpha]_D^{20}$ +38° (*c* 0.2), $\nu_{max.}$ 1 740 and 3 450 cm^{-1} (C=O and HO), δ (100 MHz; $CDCl_3$) 5.43 (d, $J_{1.2}$ 5.5 Hz), 3.98 (d, $J_{2.1}$ 5.5 Hz), 4.06 (d, J_{gem} 11.0 Hz, 3-CH_a), 4.29 (d, J_{gem} 11.0 Hz, 3-CH_b), 4.2—4.6 (2 H, m), 3.4—3.8 (3 H, m), 4.93 (t, *J* 5.0 Hz, *H*CEt), 1.84 (m, $MeCH_2$), 1.04 (t, *J* 6.5 Hz, CH_2CH_3), 5.53 (s, PhC*H*), 7.3—7.6 (m, Ph), and 2.06 (s, Ac).

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