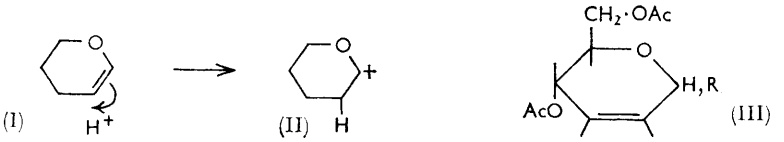
1038. *Unsaturated Carbohydrates. Part II.*[1] *Three Reactions Leading to Unsaturated Glycopyranosides.*

By R. J. Ferrier.

The influence of acid on reactions of glycals and their acetates is discussed. 3,4,6-Tri-*O*-acetyl-D-glucal reacts near 180° with methanol and ethanol to give methyl and ethyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-α,β-D-*erythro*-hexoside, respectively. The ethyl α-glycoside is readily isolated in crystalline form. Methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-[(methylthio)thiocarbonyl]-α-D-glucopyranoside (VIII) takes part in the Chugaev reaction to yield mainly the 2,3-unsaturated glycoside (IX), whilst the isomeric 3,4-unsaturated compound (XI) is the major product of the elimination which occurs on treatment of methyl 4,6-*O*-benzylidene-2-deoxy-3-oxo-α-D-*erythro*-hexoside toluene-*p*-sulphonylhydrazone (X; R = :N·NH·SO_2·C_6H_4·Me) with base.

2,3-Dihydropyran, in the presence of an acidic catalyst, reacts with water,[2] alcohols [2a,3] and phenols [4] to give 2-hydroxy-, 2-alkoxy-, and 2-aryloxy-tetrahydropyran. The glycals give 2-deoxyaldoses [5] and 2-deoxyglycosides [6] in analogous reactions. Thus, for example, methyl 2-deoxy-α-D-galactopyranoside can be prepared readily from D-galactal and this, in our experience, represents the most satisfactory synthesis of this glycoside. The *O*-acetylated glycals also take part in addition reactions with alcohols and phenols, and this same deoxy-glycoside has been prepared by treatment of 3,4,6-tri-*O*-acetyl-D-galactal with methanol in the presence of hydrochloric acid, followed by removal of the ester groups.[6b] Replacement of the methanol by phenol and of the hydrochloric acid by toluene-*p*-sulphonic acid gave phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranoside.[7] The mechanism of these additions involves, most probably, attack by the hydroxy-nucleophile on the stabilised carbonium ion (II) formed by β-protonation of the vinyl ether (I). Nitrogen analogues (the enamines) also protonate [8] and react with other electrophiles [9] at the β-carbon atom.



Under neutral conditions addition to the double bond does not occur. Glucal is stable in boiling water,[10] but its 3,4,6-tri-*O*-acetyl derivative suffers a displacement reaction to give the well-known 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexose [11] (4,6-di-*O*-acetyl-ψ-glucal; III; R = OH). Similar reactions occur with phenols [1] and with mercaptoacetic acid: [12] the aryl glycosides [III; R = OPh (α-isomer); R = O·C_6H_4·NO_2 (α- and β-isomers)] and the thio-ester [III; R = SAc (α-isomer)] are the products which

[1] Ferrier, Overend, and Ryan, *J.*, 1962, 3667, is considered to be Part I.
[2] (*a*) Paul, *Bull. Soc. chim. France*, 1934, **1**, 971; (*b*) Schniepp and Geller, *J. Amer. Chem. Soc.*, 1946, **68**, 1646.
[3] Woods and Kramer, *J. Amer. Chem. Soc.*, 1947, **69**, 2246.
[4] Parham and Anderson, *J. Amer. Chem. Soc.*, 1948, **70**, 4187.
[5] Whistler and Wolfrom, "Methods in Carbohydrate Chemistry," Vol. I, Academic Press, New York and London, 1962, p. 177; Overend and Stacey, *Adv. Carbohydrate Chem.*, 1953, **8**, 45.
[6] (*a*) Hughes, Overend, and Stacey, *J.*, 1949, 2846; (*b*) Overend, Shafizadeh, and Stacey, *J.*, 1951, 992.
[7] Wallenfels and Lehmann, *Annalen*, 1960, **635**, 166.
[8] Szmuszkovicz, "Advances in Organic Chemistry," Vol. 4, Interscience, New York, 1963.
[9] Stork, Brizzolara, Landesman, Szmuszkovicz, and Terrell, *J. Amer. Chem. Soc.*, 1963, **85**, 207.
[10] Laland Overend, and Stacey, *J.*, 1950, 738.
[11] Helferich, *Adv. Carbohydrate Chem.*, 1952, **7**, 209.
[12] Tejima, Haga, Nakamura, Maki, Sakata, and Akagi, 145th Meeting, American Chemical Society, September 1963.

have been isolated.* The mechanism of these reactions involves allylic displacement of the 3-acetoxy-group by the attacking nucleophile, and the poor "leaving properties" of the hydroxy-group explain the relative stability of parent glycals.

The acid catalyst is thus of fundamental importance in determining the course of the reaction of acetylated glycals. This was further indicated when the reaction leading to the unsaturated *p*-nitrophenyl glycosides (III; R = O·C_6H_4·NO_2)[1] was repeated, in benzene solution, but with added toluene-*p*-sulphonic acid. Despite considerable degradation and polymerisation, *p*-nitrophenyl 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside was isolated as the only crystalline product. The phenol–tri-*O*-acetyl-D-galactal results[7] are therefore corroborated qualitatively, but the fusion conditions employed by the German workers caused rapid and apparently complete polymerisation of tri-*O*-acetyl-D-glucal with the formation of a black elastic solid. Conversely, in the absence of added acid, 3,4,6-tri-*O*-acetyl-D-glucal reacted near 180° with dry methanol and ethanol to give unsaturated glycosides (III; R = OMe, OEt). From the ethanol reaction crystalline ethyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-α-D-*erythro*-hexoside [III; R = OEt (α-isomer)] was isolated (32%) after removal of the solvent and liberated acetic acid. The non-crystalline fraction yielded further quantities of this product (total 35%) after vacuum distillation. The crystalline material was identified with the compound obtained on treatment of 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexose with triethyl orthoformate.[10] On hydrogenation and de-*O*-acetylation it yielded the known ethyl 2,3-dideoxy-α-D-*erythro*-hexoside. The syrupy fraction showed only traces of slow-moving impurities on thin-layer chromatograms; the major component travelled as a discrete compound indistinguishable from the isolated crystalline material. It consumed hydrogen (1·05 mol.), and was shown by nuclear magnetic resonance (n.m.r.) spectroscopy to be an ethyl unsaturated glycoside diacetate. The observation that this syrup had the same optical activity as the crystalline product led us to investigate its nature more closely (see below).

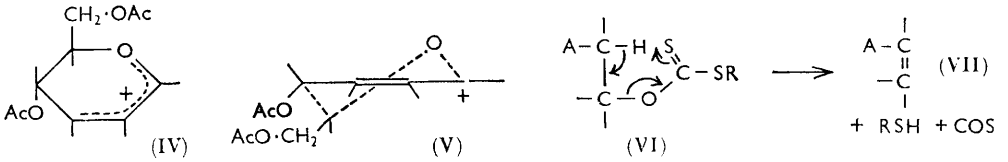
The product from the methanol reaction after distillation was shown to travel on thin-layer chromatograms as a discrete spot contaminated with only traces of slow-moving impurities. It consumed hydrogen (1·04 mol.) and gave satisfactory elemental and n.m.r. analyses for the methyl unsaturated glycoside (III; R = OMe). N.m.r. techniques clearly showed that the products from both the methanol and ethanol reactions were mixtures of isomers. The signal from the methoxyl protons (τ 6·55) in the spectrum of the methanol product was a sharp singlet. However, when the product was hydrogenated, this signal was resolved into two (τ 6·63, 6·51) of relative intensities 1·5 : 1 (total 3 protons) indicating the presence of two isomers, one having an axial methoxyl grouping (higher fields) and the other an equatorial.[13] The de-*O*-acetylated products (methyl 2,3-dideoxy-D-*erythro*-hexoside; examined in pyridine solution), also showed two methyl signals (τ 6·64, 6·52) of intensities 1·6 : 1. In the spectra of the saturated derivatives the signals from the equatorial anomeric hydrogen atoms could be distinguished clearly, and from their intensities it was calculated that the α : β-ratio was 1·6 : 1. Further, for the pure ethyl α-compound (III; R = OEt) the vinyl protons gave an unresolved sharp signal (τ 4·11) whilst there were two resonances (τ 4·10, 4·02) at this region in the spectrum of the mixed methyl glycosides (ratios 1·5 : 1; total 2 protons). The ratio of α : β-isomers is therefore 60 : 40. The presence of the double bond in these compounds requires that the methoxyl groups have *quasi*-axial and *quasi*-equatorial orientations and the proton signals of these are not resolved. A similar analysis of the spectra of the mixture of ethyl compounds (III; R = OEt) and of the saturated products indicated that the α : β-ratio was 55 : 45.

* An unsaturated nucleoside derivative has recently been isolated from the reaction between tri-*O*-acetyl-D-glucal and theophylline (Bowles and Robins, *J. Amer. Chem. Soc.*, 1964, **86**, 1252; see also Noval and Šorm, *Experientia*, 1962, **18**, 213).

[13] Barker, Homer, Keith, and Thomas, *J.*, 1963, 1538.

The observations that the crystalline (α-isomer) and non-crystalline (α- + β-isomers) fractions of the ethanol reaction products have almost the same optical rotations (105°, 110°), and that the mixed isomers obtained from the methanol reaction, and by methylation of 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexose [14] have high rotations (+139° and +143°, respectively) indicate that β-isomers in this series have anomalous optical rotatory properties. [This was not apparent with the *p*-nitrophenyl derivatives (III; R = O·C_6H_4·NO_2)].[1] That these effects are not caused by other factors (*e.g.*, by minor impurities) is suggested by the observation that the optical rotation of the methyl 2,3-dideoxy-α,β-D-*erythro*-hexosides derived from the methyl unsaturated compounds (III; R = OMe; α : β, 60 : 40) was found to be +83° (*c* 1 in H_2O). The calculated figure for this mixture is +78° (using the information obtained for the crystalline ethyl 2,3-dideoxy-α- and β-D-*erythro*-hexosides; $[\alpha]_D$, α +138°, β −29°) [15] or +93° (using the method of Whiffen).[16]

The α-isomers of the *p*-nitrophenyl glycoside (III; R = O·C_6H_4·NO_2) and the thioester (III; R = SAc) likewise predominate in the respective reaction products. Goering and his co-workers [17] showed that solvolyses of carboxylic esters of cyclohex-2-enol, the carbocyclic analogues of the glycal esters, involve alkyl–oxygen fission and the formation of a carbonium ion. In the case of 3,4,6-tri-*O*-acetyl-D-glucal the intermediate ion (IV) is stabilised by the ring oxygen atom, and the C-1 carbonium ion, which would exist in the H1 conformation (V),[18] would be the important reacting species. Since cyclic allylic



carbonium ions react preferentially to form *quasi*-axial bonds,[17] the nucleophiles would attack preferentially from the side of the ring on which C-5 is the out-of-plane atom, and the α-derivatives would therefore predominate amongst the initial reaction products. (We have not ascertained whether, under the conditions of the reaction, the products would interconvert). The n.m.r. spectrum of the products of the methanol reaction showed an absence of signals near τ 3·5, indicating that there were no C-1 vinyl protons present and therefore that no products arising from direct allylic displacement at C-3 had been formed.

Ness and Fletcher [19] reported a similar reaction between methanol and a furanoid glycal bearing a 3-benzoyloxy-group but, since it proceeded at room temperature, a striking difference exists between its rate and that of the tri-*O*-acetyl-D-glucal reaction. This difference is related to the ease with which the preferred geometry for rupture of the allylic bond (bond in a plane perpendicular to the double bond [17]) can be attained. The *quasi*-equatorial $C_{(3)}$–O bond in the six-membered glycal ester can achieve this orientation only after considerable ring distortion.[17] *

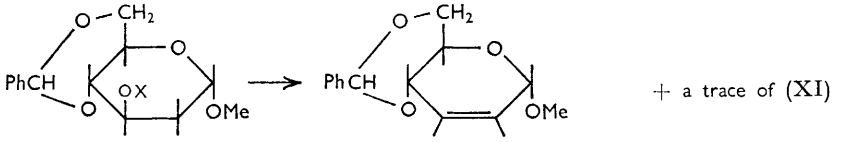
The Chugaev reaction, in which olefins are formed by the pyrolytic decomposition of

* In the carbocyclic series, allylic displacements occur much more readily from five- than from six-membered rings; 3-chlorocyclopentene is solvolysed 600 times faster than 3-chlorocyclohexene (Goering, Nevitt, and Silversmith, *J. Amer. Chem. Soc.*, 1955, **77**, 5026).

[14] Bergmann and Freudenberg, *Ber.*, 1931, **64**, 158.
[15] Bergmann, *Annalen*, 1925, **443**, 223.
[16] Whiffen, *Chem. and Ind.*, 1956, 964.
[17] Goering and Josephson, *J. Amer. Chem. Soc.*, 1962, **84**, 2779, and earlier Papers in this series.
[18] Ferrier and Overend, *Quart. Rev.*, 1959, **13**, 265.
[19] Ness and Fletcher, *J. Org. Chem.*, 1963, **28**, 435.

O-[(alkyltrio)thiocarbonyl] derivatives, has been attempted unsuccessfully in the carbohydrate series. The esters of 1,4:3,6-dianhydromannitol,[20] methyl 3,4-*O*-isopropylidene-β-D- and -L-arabinoside,[21] methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-altroside,[21] and of the di-*O*-isopropylidene derivatives of D-glucose, D-galactose, and D-mannose [22] all failed to yield unsaturated products. In some cases, rearrangement occurred to the corresponding (alkylthio)carbonylthio-derivatives (–O·CS·SR ⟶ –S·CO·SR), and this provides a route to specific deoxy-carbohydrate products.[23]

With alicyclic compounds the elimination proceeds generally by way of a concerted mechanism (VI) ⟶ (VII) involving the β-*cis*-hydrogen atom.[24] In the carbohydrate derivatives previously investigated, such atoms have been attached to carbon atoms bearing oxygen (VI; A = O-) the presence of which apparently prohibits this reaction,



(VIII ; X = CS·SMe) (IX)

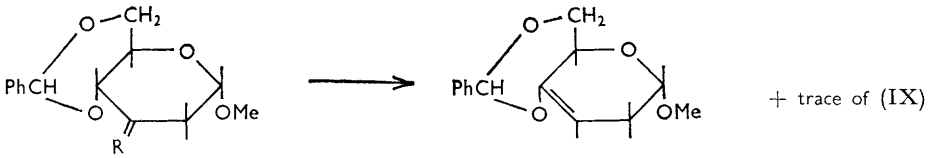
presumably because of mesomeric interaction between the unshared electrons of the oxygen (A) and the incipient π-bond. It is unlikely that steric factors [21] would alone be responsible for the lack of reactivity. The pyrolysis of methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-[(methylthio)thiocarbonyl]-α-D-glucopyranoside (VIII) in which there are two hydrogen atoms in the required orientation (only one being attached to a carbon atom bearing oxygen) was investigated. The major product, the only one which could be isolated, was the unsaturated glycoside (IX) so that O-4 stabilised H-4 relative to the axial hydrogen atom of the methylene group (H-2).* Thin-layer chromatography of the products revealed the presence of small amounts of the 3,4-unsaturated isomer (XI) showing that some elimination involving H-4 occurred. Although, in one experiment, direct pyrolysis gave the major product in 47% yield this could not be repeated, so that heating at 225° under nitrogen in diphenyl ether solution was preferred, and gave reproducible results (46%). The reaction could be followed conveniently by direct thin-layer chromatography of the diphenyl ether solution. The chromatograms were developed with an acidic solution of anisaldehyde,[25] a reagent which gives a wide variety of colours with different substituted carbohydrates and these also react at markedly different rates. Thus, the minor product of the pyrolysis, having slightly greater mobility than the 2,3-unsaturated compound and reacting relatively slowly with the spray reagent to give dark orange spots as opposed to blue-grey colours for the major product, could be identified with some degree of certainty by comparing its behaviour with that of a sample of the isomer (XI). The main product was identified with methyl 4,6-*O*-benzylidene-2,3-didehydro-2,3-dideoxy-α-D-*erythro*-hexoside (IX), prepared by treatment of the corresponding episulphide with triethyl phosphite.[26] This compound has also been prepared by other routes.[27]

Bamford and Stevens [28] first showed that toluene-*p*-sulphonylhydrazones of aliphatic

* In a related experiment methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-[(methylthio)thiocarbonyl]-β-D-alloside gave the 5,6-olefin specifically (Ryan, Arzoumanian, Acton, and Goodman, *J. Amer. Chem. Soc.*, 1964, **86**, 2503).

[20] Bladon and Owen, *J.*, 1950, 585.
[21] Wolfrom and Foster, *J. Amer. Chem. Soc.*, 1956, **78**, 1399.
[22] Freudenberg and Wolf, *Ber.*, 1927, **60**, 232.
[23] Hough, Priddle, and Theobald, *Adv. Carbohydrate Chem.*, 1960, **15**, 91.
[24] Nace, *Org. Reactions*, 1962, **12**, 57.
[25] Stahl and Kaltenbach, *J. Chromatog.*, 1961, **5**, 351.
[26] Christensen and Goodman, *J. Amer. Chem. Soc.*, 1961, **83**, 3827.
[27] Bolliger and Prins, *Helv. Chim. Acta*, 1946, **29**, 1061; Richards, *J.*, 1954, 4511; Newth, *J.*, 1956, 471; Horton and Turner, *Tetrahedron Letters*, 1964, 2531.
[28] Bamford and Stevens, *J.*, 1952, 4735.

or alicyclic carbonyl compounds take part in base-catalysed elimination reactions to yield olefins. By this method cyclohexene, for example, can be obtained in high yield from cyclohexanone. A new class of carbohydrate carbonyl compounds has become available since methods for oxidising secondary hydroxyl groups on partly substituted pyranoside rings have been developed.[29] The elimination undergone by the toluene-*p*-sulphonylhydrazone (X; R = :N·NH·SO_2·C_6H_4·Me) of one member of this class, methyl 4,6-*O*-benzylidene-2-deoxy-3-oxo-α-D-*erythro*-hexoside (X; R = O),[30] has been investigated. Again, in this reaction, elimination could occur to give either the 2,3-olefin (IX) or the substituted enol (XI), and again both glycosides were detected amongst the products. In this case the 3,4-unsaturated compound was the major product and the only one isolated (56%). It was shown by n.m.r. spectroscopy to be structurally isomeric with the known olefin



(X; R = :N·NH·SO_2·C_6H_4·Me) (XI)

(IX) and to contain only one vinyl proton. It reduced permanganate and, on hydrogenation, consumed 3 mol. of hydrogen without production of a discrete product after 1 mol. had been absorbed, so that saturation and hydrogenolysis of the acetal ring occurred simultaneously. Complete hydrolysis of the hydrogenated products gave two compounds with the chromatographic properties of 2,3-dideoxy-*erythro*- and -*threo*-hexose.

The mechanism of such eliminations has been shown to involve preliminary ionisation of the conjugate base, in this case (X; R = :N·$\bar{N}$·SO_2·C_6H_4·Me), to a diazo-compound (X; R = :$\overset{+}{N}$=$\bar{N}$)[31] which undergoes thermal decomposition, chiefly to unsaturated products, by way of a carbene intermediate. Strong evidence for the presence of such an intermediate in the decomposition of butan-2-one toluene-*p*-sulphonylhydrazone has been provided.[32] Unsaturated products arise by intramolecular insertion of the carbenoid group into neighbouring C–H bonds, in the case under examination the $C_{(2)}$–H or $C_{(4)}$–H bonds. The finding of the 3,4-enolic compound (XI) as the major product is consistent with the observations that diethyl ether and furan suffer preferential carbene (methylene) insertion at the α-C–H bonds.[33] Attachment of oxygen to carbon therefore activates to some extent C–H bonds to reactions with carbenes. Steric factors will also influence the course of this carbohydrate reaction.

Infrared spectroscopy of unsaturated pyranose derivatives is helpful in determining the position of the double bonds. Those compounds having an oxygen atom attached to one of the vinyl carbon atoms, *e.g.*, the glycals, their acetyl derivatives, and the glycoside (XI), show intense, sharp absorptions for C=C stretching near 1650 $cm.^{-1}$. Those with electronically more symmetrical double bonds, either without enolic systems [*e.g.*, compound (IX)] or with both vinyl carbon atoms linked to oxygen (*e.g.*, the 2-hydroxyglycal esters), show barely perceptible absorptions at these frequencies.

Experimental

In thin-layer chromatography, silica gel G was the adsorbent, benzene–methanol (100 : 1) was the solvent, and acidic anisaldehyde [25] [anisaldehyde–ethanol–concentrated sulphuric acid

[29] Burton, Overend, and Williams, *Chem. and Ind.*, 1961, 175.
[30] Ferrier, Flaherty, Overend, and Williams, unpublished results.
[31] Powell and Whiting, *Tetrahedron*, 1959, **7**, 305; Friedman and Shechter, *J. Amer. Chem. Soc.*, 1959, **81**, 5512.
[32] Frey and Stevens, *J. Amer. Chem. Soc.*, 1962, **84**, 2647.
[33] Doering, Knox, and Jones, *J. Org. Chem.*, 1959, **24**, 136.

(1 : 20 : 1)] the spray reagent. The n.m.r. spectra were obtained on a 60 Mc. Varian A-60 instrument for deuterochloroform solutions (unless otherwise noted) with tetramethylsilane as internal standard. Hydrogenations were carried out over a palladium–charcoal catalyst.

p-*Nitrophenyl* 3,4,6-*Tri*-O-*acetyl*-2-*deoxy*-α-D-*glucopyranoside*.—Tri-*O*-acetyl-D-glucal (3·5 g.), *p*-nitrophenol (7·0 g.), and toluene-*p*-sulphonic acid (0·15 g.) were heated under reflux in benzene (20 ml.) for 30 min. (The unsaturated products are obtained in this way if the acid is omitted.) The solution became black and a spongy polymeric precipitate was formed. Benzene (100 ml.) was added, the solids were removed by filtration, and the solution was treated with aqueous sodium hydroxide until the excess of phenol had been removed. After washing with water and drying, the solution was treated with decolourising charcoal and evaporated to dryness to leave a residue from which *p*-nitrophenyl 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside (0·3 g.) was isolated as the only crystalline product, m. p. and mixed m. p. 142—143°, $[\alpha]_D$ +167° (MeOH) {lit.,[34] m. p. 140—141°, $[\alpha]_D$ +170° (MeOH)}.

Fusion reactions at 110° for short periods of time between *p*-nitrophenol and tri-*O*-acetyl-D-glucal in the presence of small amounts of toluene-*p*-sulphonic acid or methanesulphonic acid gave intractable black rubbery products from which no carbohydrate material could be extracted.

Ethyl 4,6-*Di*-O-*acetyl*-2,3-*didehydro*-2,3-*dideoxy*-α-D-erythro-*hexoside*.—3,4,6-Tri-*O*-acetyl-D-glucal (6 g.) was dissolved in ethanol (18 ml.) (dried over a molecular sieve) and heated in sealed tubes in a heating block at 180° under an atmosphere of nitrogen for 4 hr. (optical rotation constant). (Although the solution was below the surface of the block, later experiments suggested that it may not have attained 180°.) The pale yellow solution was taken to dryness and the last traces of solvent, which gave an acidic reaction and had the smell of acetic acid, were removed at 0·5 mm. The residue deposited crystals (1·71 g.) on standing overnight, which were readily separated from the non-crystallisable fraction with the aid of an unglazed tile. Recrystallisation from aqueous alcohol gave the ethyl unsaturated glycoside (1·5 g.), m. p. 78—79°, $[\alpha]_D$ +105° (*c* 1·0 in C_6H_6) {lit.,[10] m. p. 78—79°, $[\alpha]_D$ +107° (in C_6H_6) for the compound prepared from 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexose and triethyl orthoformate}. The infrared spectra of samples prepared by both routes were identical. The product (0·71 g.) absorbed hydrogen (1·03 mol.) and gave a syrupy product which, on deacetylation with sodium methoxide, yielded ethyl 2,3-dideoxy-α-D-*erythro*-hexoside (0·35 g.), m. p. 68—70°, $[\alpha]_D$ +135° (H_2O), +151° (EtOH) {lit.,[10] m. p. 67—69°, $[\alpha]_D$ +140° (H_2O). Bergmann [15] gives m. p. 72°, $[\alpha]_D$ +138° (H_2O), +156° (EtOH)}. The fraction obtained by chloroform extraction of the tile was a mobile oil (3·75 g.), $[\alpha]_D$ +109° (C_6H_6) which gave a colourless product (2·98 g.), b. p. 98—100°/0·01 mm., $[\alpha]_D$ +110° (C_6H_6) on distillation. From this further quantities (0·15 g., total 35%) of the ethyl α-glycoside were obtained. Despite further attempted purification by distillation no other crystalline products were isolated. The n.m.r. spectrum showed the presence of an ethyl, a vinyl, and two acetyl groups.

Methyl 4,6-*Di*-O-*acetyl*-2,3-*didehydro*-2,3-*dideoxy*-α,β-D-erythro-*hexoside*.—Tri-*O*-acetyl-D-glucal (2·0 g.) was treated with dry methanol as above. Removal of the solvent and the liberated acetic acid gave a light brown syrup which, on distillation, gave the colourless methyl hexoside (1·5 g.), b. p. 78—82°/0·03 mm., $[\alpha]_D$ +139° (*c* 1·0 in C_6H_6), n_D^{22} 1·4560 (Found: C, 53·3; H, 6·4; OMe, 12·2. Calc. for $C_{11}H_{16}O_6$: C, 54·1; H, 6·6; OMe, 12·7%). Bergmann and Feudenberg [14] give $[\alpha]_D$ +143° (C_6H_6), n_D^{20} 1·4579 for the syrup obtained by methylation of 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexose. The n.m.r. spectrum showed the presence of three methoxyl, six acetyl, and two vinyl protons.

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-3-O-[(*methylthio*)*thiocarbonyl*]-α-D-*glucopyranoside* (VIII).—Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (3·0 g.) was heated under reflux in ether (150 ml.) over sodium powder (5 g.) for 9 hr. and set aside at room temperature for 12 hr. A white powder precipitated which was readily brought into suspension by agitation and removed with the solvent by decantation. To the ethereal suspension and ether washings, carbon disulphide (20 ml.) was added and the gel which formed immediately was heated under reflux for 4 hr. Methyl iodide (20 ml.) was added and the heating was continued for 1 hr. The precipitated sodium iodide (1·44 g., 85%) and the solvent were removed to leave a solid residue from which the xanthate ester (3·1 g., 77%) was obtained by crystallisation from light petroleum (b. p. 60—80°). Optical rotation measurements and thin-layer chromatography indicated

[34] Shafizadeh and Stacey, *J.*, 1957, 4612.

that this product contained 10% of the unesterified starting material which was readily removed by fractionation on a column of silica gel eluted with benzene–methanol (50 : 1). The final product was recrystallised from light petroleum (b. p. 60—80°) to give the *xanthate*, m. p. 152—153°, $[\alpha]_D$ +51° (*c* 1·2 in $CHCl_3$) (Found: C, 53·9; H, 5·2; S, 18·0; OMe, 8·6. $C_{16}H_{20}O_5S_2$ requires C, 53·9; H, 5·6; S, 17·9; OMe, 8·7%).

Methyl 4,6-O-*Benzylidene*-2,3-*didehydro*-2,3-*dideoxy*-α-D-erythro-*hexoside* (IX).—(*a*) The foregoing ester (0·71 g.) was heated at 220°/15 mm. for 20 min. during which time the colour of the melt darkened. The cooled mixture was extracted with light petroleum (b. p. 60—80°). Removal of the solvent and sublimation of the residue afforded the 2,3-unsaturated glycoside (0·23 g., 47%), m. p. 118—119° (from ethanol), $[\alpha]_D$ +125° (*c* 1·0 in $CHCl_3$) {lit.,[26] m. p. 117—119°, $[\alpha]_D$ +126° ($CHCl_3$)}. The infrared spectrum was identical to that of the compound prepared from methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epithio-α-D-allopyranoside with triethyl phosphite.[26] (Dr. S. McNally is thanked for providing this spectrum). The synthesis could not be effected reproducibly by this method.

(*b*) The xanthate ester (0·1 g.) was heated at 225° in diphenyl ether (1 ml.) under nitrogen. Samples of the solution were examined by thin-layer chromatography, which showed that pyrolytic decomposition was complete in 1 hr. The reaction was repeated using ester (1·02 g.) and solvent (5 ml.). The ether was removed by distillation (b. p. 64°/0·07 mm.) and the product (0·49 g.) was isolated by sublimation, (0·33 g., 46%), m. p. 118—119° [from light petroleum (b. p. 60—80°)], $[\alpha]_D$ +123° (*c* 0·5 in $CHCl_3$). Small amounts of the isomeric 3,4-unsaturated compound were detected in the mother liquors by thin-layer chromatography.

Methyl 4,6-O-*Benzylidene*-3,4-*didehydro*-2,3-*dideoxy*-α-D-glycero-*hexoside* (XI).—Methyl 4,6-*O*-benzylidene-2-deoxy-3-oxo-α-D-*erythro*-hexoside was obtained by oxidation of the secondary alcohol, and converted into the toluene-*p*-sulphonylhydrazone in high yield.[30] The hydrazone (1·4 g.) was dissolved in *N*-methyl-2-pyrrolidone (10 ml.) and 3·0N-methanolic sodium methoxide (1·1 ml., 1·0 mol), was added. The solution, which darkened on addition of the base, was heated at 180° for 7 min., by which time all the gases had been evolved and the colour had deepened considerably. After removal of the solvent at 50° the residue was extracted with benzene and the insoluble portion (0·64 g.) was dissolved in water. Acidification of the solution caused precipitation of toluene-*p*-sulphinic acid, m. p. 85—86° (lit.,[35] 86°. The derived *p*-tolyl-2,4-dinitrophenylsulphone had m. p. 187—188° (lit.,[35] 187—188°).

The benzene extract was evaporated to dryness and the dark residue solidified. Adhering brown oily material was removed with the aid of unglazed tile and the remaining solid was treated with boiling light petroleum (b. p. 60—80°) which dissolved all but the coloured impurities. From this solution colourless needles were obtained (m. p. 71—73°) which on recrystallisation from the same solvent gave the $\Delta^{3,4}$-*hexoside* (0·45 g., 56%), m. p. 74—75°, $[\alpha]_D$ +162° (*c* 0·8 in $CHCl_3$) (Found: C, 67·4; H, 6·3; OMe, 12·2. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5; OMe, 12·5%). The n.m.r. spectrum confirmed the presence of 3 methoxyl, 5 phenyl, and 1 vinyl protons. The crystalline product (0·20 g.) was hydrogenated in ethyl acetate over palladium–charcoal. The reaction was stopped when 1·1 mol. hydrogen had been consumed, and thin-layer chromatography showed that considerable amounts of starting material remained, and that several products were present. The hydrogenation was completed (total, 2·9 mol. absorbed) and the mixture was shown to consist of two components only. Hydrolysis of the products was carried out by heating in aqueous solution in the presence of acidic resin, and the free sugars were identified chromatographically as 2,3-dideoxy-*erythro*- and -*threo*-hexose [butan-1-ol–ethanol–water (4 : 1 : 5)].

The author thanks Dr. A. B. Foster for a sample of ethyl 2,3-dideoxy-α-D-*threo*-hexoside and Messrs. B. Flaherty and P. J. Beynon for methyl 4,6-*O*-benzylidene-2-deoxy-3-oxo-α-D-*erythro*-hexoside. He is also indebted to Dr. P. M. Collins and other members of this department for helpful discussions and to Professor W. G. Overend for his interest.

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Malet Street, London W.C.1. [*Received, January 1st*, 1964.]

[35] Loudon, *J.*, 1935, 537.