Note

3,6-Anhydro-D-glucal and its hydrolysis by acid

J. S. BRIMACOMBE, I. DA'ABOUL, AND L. C. N. TUCKER
Chemistry Department, The University, Dundee, DD1 4HN (Scotland)
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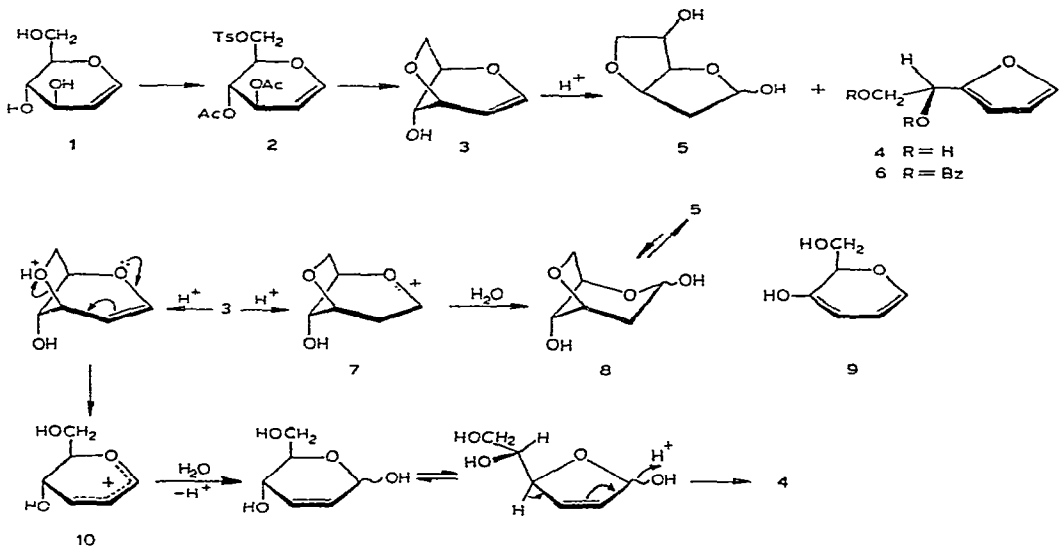
Our interest in the synthetic utilisation of unsaturated sugar sulphonates led us to prepare 3,4-di-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-D-glucal (**2**) by unimolar toluene-*p*-sulphonylation of D-glucal (**1**) and acetylation of the resulting 6-sulphonate. Nagabhushan[1] has recently reported an alternative preparation of **2** by the action of zinc dust on 2,3,4-tri-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranosyl bromide. Treatment of **2** with either methanolic sodium methoxide or, more conveniently, with Deacidite FF IP($^-$OH) resin rapidly converted it into a single product, which was formulated as 3,6-anhydro-D-glucal (**3**) on the basis of its elemental analyses and spectroscopic data; the product also formed a monoacetyl derivative.

3,6-Anhydro-D-glucal (**3**) was extremely labile under acidic conditions. On treatment with dilute hydrochloric acid at room temperature, it was rapidly converted into two products which were readily separated by chromatography on silica gel and identified as 2-(D-*glycero*-1,2-dihydroxyethyl)furan (**4**) and 3,6-anhydro-2-deoxy-D-*arabino*-hexose (**5**). The latter compound was the main product, and its molecular formula was revealed as $C_6H_{10}O_4$ by mass spectrometry and elemental analyses. Thus, it can be considered formally to be derived from **3** by the addition of the elements of water and, on this basis, its formulation as the 2-deoxy derivative **5** is reasonable. Evidence corroborating this structure was obtained by direct comparison with an authentic sample of **5**, prepared by the reaction of 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enose with methanolic barium methoxide[2], and by the formation of the known[2,3] *N*-benzyl-*N*-phenylhydrazone. The formation of **5** is readily rationalised by assuming that the carboxonium-ion intermediate **7** is attacked by water at C-1 to give the pyranoid-ring form **8**, which then undergoes ring-inversion to the furanoid form. Although this compound is usually formulated[4] in the pyranoid form **8**, it seems more likely[5] that the furanoid form **5**, containing two *cis*-fused, five-membered rings, would be favoured in the tautomeric equilibrium. The compound originally designated as "isoglucal" by Bergmann *et al.*[3] was recently shown[2] to have the structure **5**.

Mass-spectral data and elemental analyses on the minor product obtained from treatment of **3** with acid showed that it was isomeric with the starting material, while the presence of unsaturated linkages was revealed by n.m.r. spectroscopy and by the rapid decolorisation of bromine water. This product afforded a dibenzoate



[m.p. 85–86°, $[\alpha]_D$ +65° (*c* 1, methanol)], thereby showing it to be a diol. In trying to identify the diol, we were able to clarify a somewhat enigmatic situation concerning the identity of the products formed on treatment of D-glucal with acids. The reactions of D-glucal and D-galactal with 5% sulphuric acid at room temperature were reported by Stacey and co-workers[6] to give mainly the 2-deoxyhexoses, together with a minor product to which they assigned the structure 3-hydroxy-2-(hydroxymethyl)-2-pyran (**9**); this diol afforded a dibenzoate having m.p. 85°, $[\alpha]_D$ +64° (*c* 1.6, methanol). More recently, Horton and Tsuchiya[7a] have shown that D-glucal is converted into 2-(D-*glycero*-1,2-dihydroxyethyl)furan (**4**) (dibenzoate **6**, m.p. 84°) on heating with aqueous acetic acid; the diol **4** also resulted[7b] when methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside was treated similarly. The dibenzoate derived from our diol was identical with that obtained from D-glucal following the route of Stacey *et al.*[6], whereas the n.m.r. spectrum of the diol itself was unquestionably the same as that recorded by Horton and co-workers[7b] for the diol **4**. It was clear at this point that the diols prepared by the various routes were the same, and this conclusion was re-inforced by comparison of the melting points of the dibenzoyl derivatives. Subsequently, n.m.r. spectroscopy of all the diols proved that they were identical. The diol in question undoubtedly has the structure **4**, since it has been shown[7] to consume one molar equivalent of periodic acid with the formation of 2-furaldehyde and formaldehyde; the n.m.r. spectrum is completely in accord with this assignment. Thus, the minor product resulting from the action of dilute sulphuric acid on D-glucal (and D-galactal) is 2-(D-*glycero*-1,2-dihydroxyethyl)furan (**4**), and the evidence on which the structure **9** is based[6] must be regarded as equivocal. It is pertinent to note that the diacetate of **4** is now considered[8] to be one of the products of the acid-catalysed rearrangement of 3,4,6-tri-*O*-acetyl-D-galactal although originally it was tentatively assigned[9] a pyranoid structure based on **9**.

There is no information to indicate how 3,6-anhydro-D-glucal (**3**) is converted into **4**, although the rearrangement may proceed through the carboxonium ion **10** since this intermediate could conceivably also be formed when D-glucal[6,7a] and methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[7b] are treated with acid. However, the pathway suggested for the transformation of this ion into 2-(D-*glycero*-1,2-dihydroxyethyl)furan (**4**) is wholly speculative.

EXPERIMENTAL

Thin-layer chromatography (t.l.c.) was performed on Kieselgel G, and detection was effected with vanillin–sulphuric acid[10]. N.m.r. spectra were obtained with a Perkin–Elmer R-10 spectrometer for deuteriochloroform solutions with tetramethylsilane as internal reference; infrared spectra were recorded with a Perkin–Elmer Infracord spectrometer. Mass spectra were measured on a MS9 mass spectrometer. The basic resin used for deacylation was prepared by washing the freshly regenerated hydroxide-form of the resin with dry methanol.

*3,4-Di-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-*D*-glucal* (**2**). — A solution of 3,4,6-tri-*O*-acetyl-D-glucal[11] (10 g) in methanol (100 ml) was stirred for 2 h with Deacidite FF IP($^-$OH) resin (*ca.* 10 ml), whereupon t.l.c. (aceone–light petroleum, 1:2) revealed that deacetylation to give D-glucal (**1**) was complete. The resin was filtered off, the filtrate was concentrated to a syrup to which pyridine (10 ml) was added, and the solution was again concentrated. This process was repeated, after which the residue was dissolved in pyridine (100 ml) and treated at room temperature for 2 h with a solution of toluene-*p*-sulphonyl chloride (9.5 g, 1.5 mol.) in methylene chloride (100 ml). Water (10 ml) was then added, and the solution was kept (0°) for 30 min before being partitioned between water and methylene chloride. The organic layer was washed with a solution of sodium hydrogen carbonate, dried ($MgSO_4$), and concentrated to a syrup which was acetylated by using acetic anhydride (25 ml) and pyridine (25 ml) in the usual way. The resulting product was decolourised by filtering a methanolic solution (100 ml) through a charcoal pad, which was then washed with methanol (100 ml). On storage at 0°, the filtrate deposited colourless crystals of **2** (6.5 g, 46%), m.p. 108°, $[\alpha]_D$ +30° (*c* 1, chloroform). The product was indistinguishable (t.l.c. and n.m.r. spectroscopy) from an authentic sample [m.p. 103°, $[\alpha]_D$ +30° (*c* 1.1, chloroform)] prepared by an alternative route[1].

3,6-Anhydro-D-glucal (**3**). — A solution of **2** (5 g) in methanol (100 ml) was stirred with Deacidite FF IP($^-$OH) resin (*ca.* 25 ml) for 1 h, whereafter the resin was filtered off and the solution was concentrated to yield the crude product. This was sublimed at 60°/0.1mmHg to give the anhydro sugar **3** (1.1 g, 66%), m.p. 93–94°, $[\alpha]_D$ +49° (*c* 1, methanol), ν_{max} 1625 cm^{-1} (C=C) (Found: C, 56.1; H, 6.25. $C_6H_8O_3$ calc.: C, 56.25; H, 6.25%). N.m.r. data: τ 3.50 (doublet, $J_{1,2}$ 5.5 Hz, H-1) and 5.00 (multiplet, H-2).

Acetylation of **3** (0.5 g), in the usual way, gave 4-*O*-acetyl-3,6-anhydro-D-glucal (0.4 g, 60%), b.p. 60°/0.2 mmHg, $[\alpha]_D$ −93° (*c* 1, methanol), ν_{max} 1780 (acetate) and 1650 cm^{-1} (C=C) (Found: C, 56.5; H, 5.9. $C_8H_{10}O_4$ calc.: C, 56.7; H, 5.9%).

Treatment of 3,6-anhydro-D-glucal (**3**) *with acid and characterisation of the products.* — A solution of **3** (1.5 g) in 0.1M hydrochloric acid (25 ml) was set aside for 1 h at room temperature, during which time complete reaction had occurred. Concentration of the neutralised ($NaHCO_3$) solution left a solid residue which was extracted with acetone. The extract was concentrated, and the mixture of products was chromatographed on silica gel (elution with acetone–methylene chloride, 1:1) to give first 2-(D-*glycero*-1,2-dihydroxyethyl)furan (**4**) (0.14 g), b.p. 80–90° (bath)/0.1 mmHg, $[\alpha]_D$ +17° (*c* 1, methanol) (Found: C, 55.85; H, 7.0. Mol. wt., 128.0474. $C_6H_8O_3$ calc.: C, 56.3; H, 6.3%. Mol. wt., 128.0473). N.m.r. data: τ 2.60 (1-proton multiplet, H-5), 3.67 (narrow multiplet, 2 protons, H-3 and H-4), 5.20 (1-proton triplet, methine group, $J_{1,2}$ ~5.5 Hz), and 6.16 (2-proton doublet, methylene group, $J_{1,2}$ ~5.5 Hz). Continued elution gave 3,6-anhydro-2-deoxy-D-*arabino*-hexose (**5**) (0.42 g), which crystallised after distillation [b.p. 80–90°(bath)/0.1 mmHg] and had m.p. 46–47°, $[\alpha]_D$ +45° (*c* 1, water) (Found: C, 49.0; H, 6.8. Mol. wt., 146.0582. $C_6H_{10}O_4$ calc.: C, 49.3; H, 6.9%. Mol. wt., 146.0579).

Compound **5** was shown to be identical (n.m.r. and i.r. spectroscopy) with an authentic sample prepared[2] by treatment of 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enose with methanolic barium methoxide. Bergmann and Schotte[12] recorded m.p. 49–50°, $[\alpha]_D$ +45.6° (water), for "isoglucal"[3], which has the same structure[2]. The *N*-benzyl-*N*-phenylhydrazone derived from **5** had m.p. and mixed m.p. 123–124°, $[\alpha]_D$ −22° (*c* 1, methanol) [lit., m.p. 121° (ref. 2), and m.p. 121–122°, $[\alpha]_D$ −21.9° (methanol) (ref. 12)], and the 2,4-dinitrophenylhydrazone had m.p. 165–165.5° (dec.) (Found: C, 44.4; H, 4.5; N, 16.8. $C_{12}H_{14}N_4O_7$ calc.: C, 44.2; H, 4.3; N, 17.2%). The melting point of the latter derivative did not coincide with that [m.p. 122–123° (dec.)] previously reported[2], but repetition of the literature procedure afforded a 2,4-dinitrophenylhydrazone having m.p. and mixed m.p. 165–165.5° (dec.).

The diol **4** was indistinguishable (n.m.r. and i.r. spectroscopy, t.l.c.) from a sample prepared according to the procedure described by Stacey *et al.*[6], who reported b.p. 120–130° (bath)/0.01 mmHg for this compound; the n.m.r. spectrum was also indistinguishable from that recently recorded[7b] for an authentic sample of 2-(D-*glycero*-1,2-dihydroxyethyl)furan. Benzoylation gave 2-(D-*glycero*-1,2-dibenzoyloxyethyl)furan (**6**) as needles having m.p. 85–86°, $[\alpha]_D$ +65° (*c* 1, methanol), $[\alpha]_D$ +67° (*c* 1, chloroform), in good agreement with the literature values of m.p. 85°, $[\alpha]_D$ +64° (*c* 1.6, methanol) (ref. 6); m.p. 84° (corrected, ref. 7*a*); and m.p. 79.5–80.5°, $[\alpha]_D$ +72 ±0.7° (*c* 1.9, chloroform) (ref. 7*b*).

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