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3,5-ANHYDRO-1,2-O-ISOPROPYLIDENE-α-D-GLUCOSE AND -β-L-IDOSE, TWO NEW CARBOHYDRATE OXETANES.

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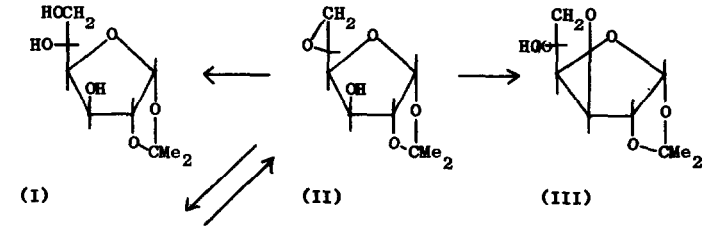
3,6-Anhydro-1,2-O-isopropylidene-α-D-glucose (III) is one of the products of alkali treatment of 5,6-anhydro-1,2-O-isopropylidene-α-D-glucose (II).[1] During an attempt to obtain an authentic sample of 3,6-anhydro-1,2-O-isopropylidene-β-L-idose (XIV) by similar treatment of the 5,6-anhydro-L-idose derivative (XIII) an unidentified anhydro compound was formed[2] together with 1,2-O-isopropylidene-β-L-idose (XVII).[3] The use of thin layer chromatography has enabled us to examine the reaction in more detail. Using Kieselgel G as adsorbent and ether as developing solvent the ketal (XVII) and a bimolecular compound (cf. ref.1) were detected at low R_F values together with the 3,6-anhydro-derivative (XIV)[4] and the new anhydro-compound at higher R_F values. When a 10% solution of the 5,6-anhydro-compound (XIII) in N-sodium hydroxide was heated at 100° for 7 minutes the new anhydro-compound was isolated, after chromatography on silica gel, in 10% yield. It is 3,5-anhydro-1,2-O-isopropylidene-α-D-glucose (XVI), m.p. 68-69°, $[\alpha]_D$ + 38.4° ($CHCl_3$). The time of heating is critical, because the anhydride is decomposed by alkali (see below). The structure followed from its elementary analysis and chemical behaviour. Acid hydrolysis (N-sulphuric acid; 100°) yielded first a reducing sugar of high R_F value

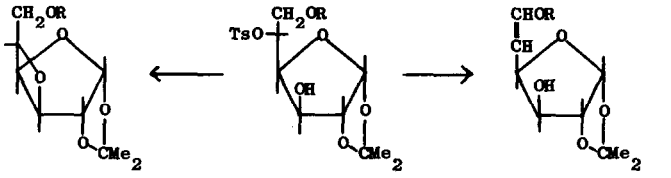
(probably 3,5-anhydro-glucose) which was then converted into idose, identified chromatographically. Under similar conditions 3,5-anhydro-1,2-O-isopropylidene-α-D-xylose (XIX)[5,6] was converted into a sugar of high R_F value (3,5-anhydro-xylose) and then into xylose (cf. ref. 7). Ring opening of an epoxide proceeds with inversion at that carbon atom which has been attacked.[8] The 3,5-anhydro-compound has therefore the D-gluco-configuration (XVI) and acid hydrolysis has occurred with inversion at $C_{(5)}$; no other hexose (e.g. D-allose, which would have arisen by attack on $C_{(3)}$) was detectable in the acid hydrolysate.

Alkaline hydrolysis (N-sodium hydroxide; 100°) of the 3,5-anhydro-compound (XVI) yielded the same mixture of products as that from alkali treatment of the 5,6-epoxide (XIII); 1,2-O-isopropylidene-β-L-idose (XVII) and its 3,6-anhydride (XIV) were isolated in crystalline form. Furthermore, 3,5-anhydro-1,2-O-isopropylidene-α-D-xylose (XIX) was hydrolysed to 1,2-O-isopropylidene-α-D-xylofuranose much more slowly under the same conditions, despite the presence of a primary carbon at $C_{(5)}$. These results can only be explained if the 3,5-anhydride (XVI) and the 5,6-anhydride (XIII) are interconvertible under alkaline conditions. We believe that this is the first case reported of a reversible "oxide migration"[9] involving a 3- and a 4-membered oxide ring.

With this possibility in mind, the action of alkali on the 5,6-anhydro-D-gluco-compound (II) has been reinvestigated using thin layer chromatography. Under the conditions of Reichstein and his coworkers[1] the 3,6-anhydride (III) was the sole product of high R_F value, but when the reaction time was reduced a new anhydro compound was observed which gradually disappeared as the reaction proceeded. 3,5-Anhydro-1,2-O-isopropylidene-β-L-idose (IV), m.p. 49°, $[\alpha]_D$ + 53.2° ($CHCl_3$) has been isolated after chromatography on silica gel. Acid hydrolysis (N-sulphuric acid; 100°)



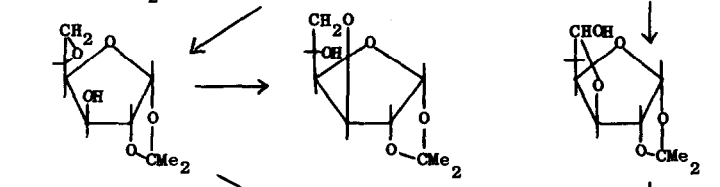
(I) (II) (III)



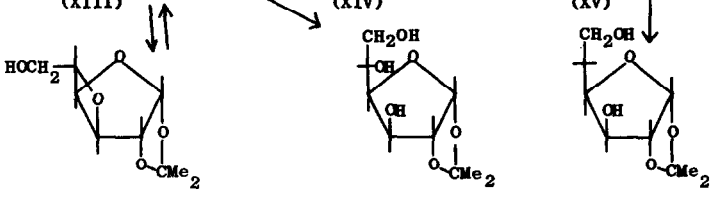
(IV; R = H)
(V; R = CPh_3)
(VI; R = CH_2Ph)

(VII; R = CPh_3)
(VIII; R = CH_2Ph)
(IX; R = H)

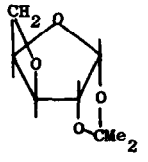
(X; R = CPh_3)
(XI; R = CH_2Ph)
(XII; R = H)



(XIII) (XIV) (XV)



(XVI) (XVII) (XVIII)



(XIX)

yielded finally glucose as the sole hexose, indicating specific attack at $C_{(5)}$. An alkaline hydrolysate was examined by thin layer chromatography. The starting material disappeared with formation of the ketal (I) and its 3,6-anhydride (III). This is strong evidence for the interconversion II $\rightleftarrows$ IV, another example of oxide migration involving an oxirane and an oxetane.

The 3,5-anhydro-compound (IV) has also been prepared by treatment of the sulphonate (VII) with sodium methoxide in methanol, and subsequent detritylation of the ether (V). The enol ether (X), m.p. 82-85°, is the major product of the reaction and can be removed by crystallisation or by chromatography on silica gel. Whistler and his colleagues[10] have found recently that treatment of the sulphonate (VIII) with methoxide ion gives a 95% yield of the enol ether (XI); the anhydride (VI) could not be detected. Detritylation of the ether (X) gave the syrupy 5-deoxy-1,2-O-isopropylidene-α-D-xylo-hexodialdo-1,4-furanose (XV) [2,4-dinitrophenylhydrazone, m.p. 184-185°, $[\alpha]_D$ - 17.4° (dioxane)]. Reduction of the sugar (XV) with sodium borohydride afforded 5-deoxy-1,2-O-isopropylidene-α-D-xylohexofuranose (XVIII), m.p. 94°, identical with an authentic sample[11,12] kindly supplied by Dr. E.J. Hedgley. We first encountered the sugar (XV) as a minor product (6%) in the preparation of the 5,6-anhydro-derivative (XIII) from the sulphonate (IX)[13] by treatment with methoxide ion,[3] presumably by way of (XII) as an intermediate.

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