Reaction of the Methyl 2,3-Anhydro-D-ribofuranosides with Nucleophiles

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IN continuation of a study of carbohydrate oxetans[1] we have found that when methyl 2,3-anhydro-β-D-ribofuranoside (I)[2] is treated with 1N-sodium hydroxide at 100° for 18 hr. methyl 3,5-anhydro-β-D-xylofuranoside (II), m.p. 63—64°, $[\alpha]_D$ −143° ($CHCl_3$), can be isolated in 57% yield. The reaction is reversible with the equilibrium strongly in favour of the 3,5-anhydride ($K > 20$). In the

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α-series conversion of the 2,3-anhydroriboside (V) to the 3,5-anhydroxyloside (VI) can be brought about under similar conditions, but is accompanied by considerable ring-opening. In the light of these experiments the anhydroribosides (I) and (V) have been treated with 5N-sodium methoxide in methanol at 65°. From (I) the major product was methyl 5-*O*-methyl-β-D-xylofuranoside, which was characterised by conversion into the crystalline 1,2-*O*-isopropylidene-5-*O*-methyl-α-D-xylofuranose;[3] methyl 3-*O*-methyl-β-D-xylofuranoside and a small amount of methyl 2-*O*-methyl-β-D-arabinofuranoside were also produced. It appears that attack by methoxide ion on the 2,3-epoxide is sterically hindered and that ring-opening at C-5 of the 3,5-epoxide (II) occurs more readily. Such attack of the 2,3-epoxides as does take place is at C-3 and this is in agreement with the behaviour of (I) towards aqueous ammonia[2,4] and sodium ethylmercaptide in methanol,[5] where the medium may not be sufficiently alkaline to cause epoxide migration. The major product when the 2,3-α-epoxide (V) was treated with methoxide ion was methyl 2-*O*-methyl-α-D-arabinofuranoside, characterised by acid hydrolysis and borohydride reduction to give crystalline 2-*O*-methyl-D-arabinitol;[6] a trace of the 3-*O*-methyl-D-xylo-compound was detectable, but no 5-methyl ether. In this case attack on the 2,3-epoxide ring is less hindered and no product arises *via* epoxide migration. Although the 2,3-α-epoxide (V) yields some of the 3-amino-compound with aqueous ammonia[2,4] the yields of crystalline products are poor and would not exclude the formation of the 2-amino-compound, even as the major product. Goodman[7] has reported that the epoxide ring of the 5-toluene-*p*-sulphonate of (V) undergoes reaction with sodium benzylmercaptide and with lithium aluminium hydride predominantly at C-2.

When the epoxide (V) was heated with an excess of aqueous potassium cyanide at 100° the lactone (IX)[8] was isolated in 57% yield after acidification. Although little is known about the reaction of vicinal epoxides with cyanide ion[9] it is reasonable to suppose that the cyanohydrin anions (IV) and (VII) would be capable of reverting to the parent epoxide (V). The 3-cyano-compound (VII) may, however, undergo hydrolysis as indicated by the intramolecular process in (VIII). A similar scheme has been proposed by Goodman to account for the reaction of (I) and (V) with thiocyanate ion.[7] When the epoxide (I) was treated with potassium cyanide in the same way, reaction was much slower and the 3,5-anhydride (II) could be detected by thin-layer chromatography. No lactone with properties similar to (IX) was detected after acidification. By analogy with the behaviour of the epoxide (I) towards methoxide ion it is believed that it is the anhydride (II) which reacts with cyanide ion to give the cyanide (III). The latter should be unstable to alkali as shown; Dr. N. A. Hughes[10] has informed us that 5′-cyano-5′-deoxy-2′,3′-*O*-isopropylideneuridine yields uracil on mild alkali treatment.

We are reporting this work now because of current interest in 3′,5′-anhydronucleosides.[11]

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