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A NEW ROUTE TO 6-DEOXY-6-HALO SUGARS

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Direct replacement of a hydroxyl group by a halogen atom in sugar derivatives excepting at an anomeric centre is convenient method of preparing halogenated sugars of interest as reactive intermediates and as potential metabolic inhibitors. However relatively few reagents are available for this purpose[1,2].

We have found, that the Pinner reaction[3] provides a new route to halogenated sugars. This S_N2 reaction[4] had been shown to proceed with particular ease in the case of imidate hydrohalides containing electron accepting substituents in the imino acid residue. The reaction has been used for instance in the synthesis of certain alkyl halides via unstable trichloroacetimidate hydrohalides[5,6]:

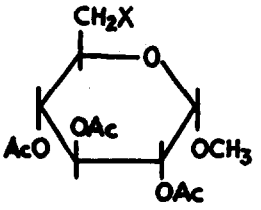
$$ROH + CCl_3CN + HHal \longrightarrow [CCl_3C(=NH\cdot HHal)OR] \longrightarrow RHal + CCl_3CONH_2$$

Using partially protected hexoses with a free primary hydroxyl group as alcohol component of the reaction we have obtained the corresponding 6-deoxy-6-halo sugars in good yields.

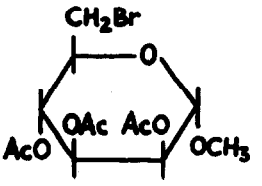
The general procedure is as follows. The protected sugar and CCl_3CN in chloroform solution is saturated with hydrogen halide at -15°. After keeping the sealed reaction mixture at room temperature for 10-15 hours (HBr) or for 2 days (HCl) and removing the volatile compounds and CCl_3CONH_2 the product is isolated by chromatography.

In this way we have synthesized methyl 2,3,4-tri-O-acetyl-6-chloro-6--deoxy- α-D-glucopyranoside (I)[7] in 85-90% yields, m.p. 97-98°, $[\alpha]_D^{20}$ + + 176° (c 0.1, chloroform), methyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy- α-D-

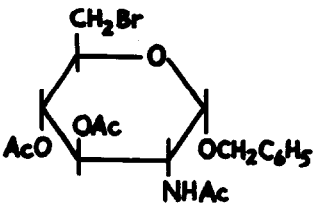
-glucopyranoside (II)[7] in 80-85% yields, m.p. 116-117°, $[\alpha]_D^{20}$ + 132° (c 0.1, chloroform), methyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy- α-D-manno-pyranoside (III)[8] in 77% yield, m.p. 77-78°, $[\alpha]_D^{20}$ + 53° (c 0.1, chloroform) and benzyl 2-acetamido-3,4-di-O-acetyl-6-bromo-2,6-dideoxy- α-D-glucopyranoside (IV) in 75% yield, m.p. 134-135°, $[\alpha]_D^{20}$ + 120° (c 0.2, chloroform). Calculated for $C_{19}H_{24}BrNO_7$: C,49.79 ; H,5.28 ; Br,17.44. Found: C,49.50 ; H,5.39 ; Br,17.11.



I: X = Cl
II: X = Br



III



IV

More drastic conditions are required for substitution of a secondary hydroxyl by halogen. This is now in the progress of investigation.

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