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THE ACETALATION OF L-SORBOSE

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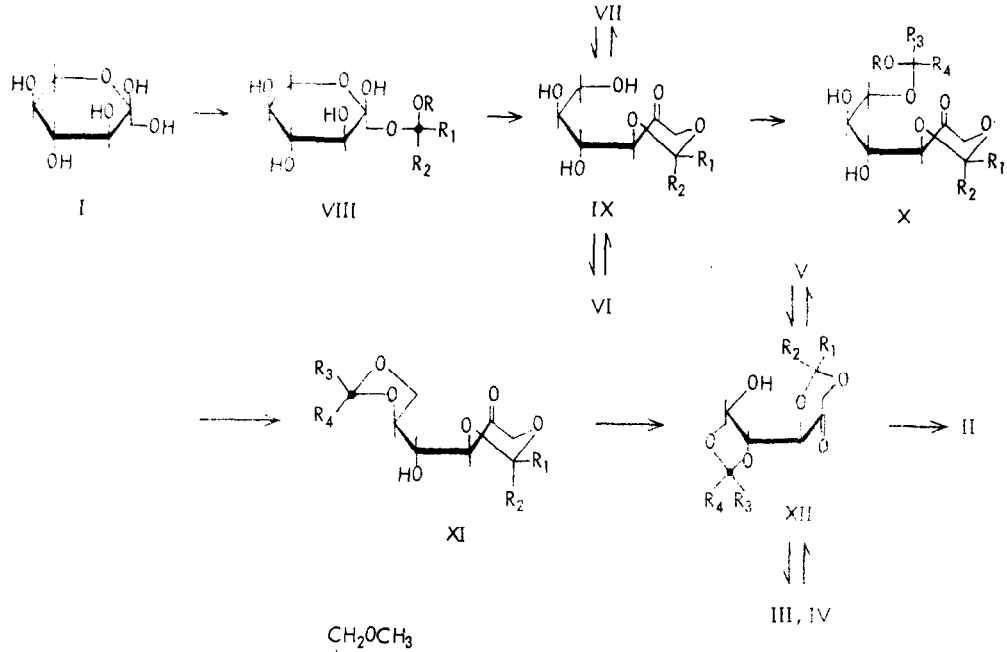
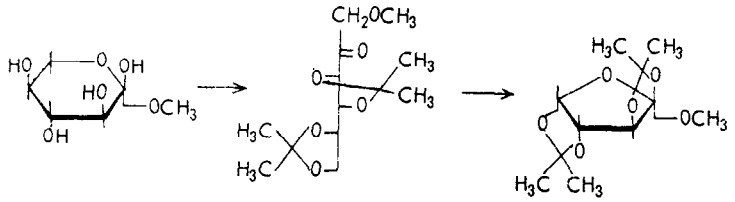
In previous communications, we reported that the acetonation of L-sorbose (I) with acetone dialkyl ketals afforded IIa-VIIa (1, 2) by a different mode than the acetonation with acetone (3). We have since investigated the reaction mechanisms of the former acetonation and concluded that the reaction proceeds through intermediate keto-forms as shown in Chart .

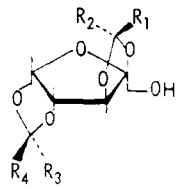
As a primary alcohol is more reactive than secondary and tertiary ones (4), acetone dialkyl ketals react with C_1-OH of I in the stable 1C conformation to afford VIII as an intermediate, which is easily converted into XI. It is quite obvious from the acetalation of glycerol (5) that IX exists in equilibrium with VI and VII. No isolation of VII would result from its instability, since one of two methyl groups is axial in the chair conformation of the six-membered O-isopropylidene group (6).

Further acetonation must occur at the primary C_6-OH group of IX. Therefore, the reaction proceeds via the pathway IX → X → XI → XII → II. The acetonation of 1-O-methyl-L-sorbose (XIII) yielding 1-O-methyl-2,3:4,6-di-O-isopropylidene-α-L-sorbofuranose (XV) (7) via 1-O-methyl-3,4:5,6-di-O-isopropylidene-L-sorbose (XIV) suggests the pathway of IX → X → XI → XII → II. XII exists in equilibrium, V ⇌ XII ⇌ III, IV, similar to the case of IX. The fact that III, IV and V undergo rearrangements to II in the presence of acids supports the presence of the last step. The proposed pathway was also confirmed by thin-layer chromatographic and kinetic studies.

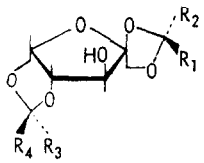
Isomeric diacetonated sorbofuranoses IIIa, IVa and Va were also obtained by careful isolation from the acetonation of I with acetone. Therefore, this acetonation is concluded to proceed in the above-described pathway, in which R in X is a L-sorbose residue because the reaction has been established as second order in VIa (3b). It is interesting that acetone ketals preferably react with IX. This might be caused by the difference in stabilities between the ketal forms of X (R: Alkyl or sorbose residue) from



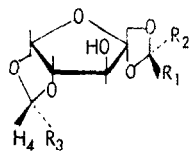




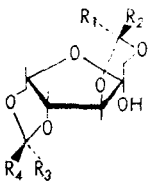
IIa, b, c, d, e



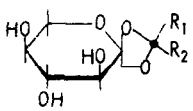
IIIa, d, e



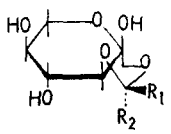
IVa, d, e



Va, b, d



VIa, b, d, e



VIIa, b

a: $R_1=R_2=R_3=R_4=CH_3$ b: $R_1=R_3=CH_3$, $R_2=R_4=H$ c: $R_2=R_3=CH_3$, $R_1=R_4=H$ d: $R_1=R_3=Ph$, $R_2=R_4=H$
e: $R_2=R_3=Ph$, $R_1=R_4=H$

acetone ketals and the hemiketal form of X (R: H) from acetone.

Comparable results have been obtained with the acetalations of I. When I was treated with acetaldehyde dimethyl acetal in the presence of p-toluenesulfonic acid, Vb was mainly obtained, which was converted into IIb and IIc under more acidic conditions. The use of slightly acidic conditions afforded VIb and VIIb. Similarly, benzylidenation of I yielded predominantly Vd, which was converted into IId and IIe. Under slightly acidic conditions, the benzylidenation afforded dibenzylidene diastereoisomers IIId, IIIe, IVd and IVe and monobenzylidene ones VId and VIe. The structures of these newly isolated compounds were confirmed by chemical and NMR spectroscopic evidence, some of which were reported below. (Nmr were measured in $CDCl_3$ and chemical shifts were expressed in τ unit. Optical rotations were observed in $CHCl_3$ unless otherwise stated). IIb: m.p. 82-83°, $[\alpha]_D^{20}$ -9.5 (c, 0.972), NMR 4.83^q ($^{O_2}_{O_3}\!\!\times\!\!^{CH_3}_{\underline{H}}$), 5.35^q ($^{O_4}_{O_6}\!\!\times\!\!^{CH_3}_{\underline{H}}$). IIc: m.p. 58-59°, $[\alpha]_D^{20}$ -8.5 (c, 0.562), NMR 4.57^q ($^{O_2}_{O_3}\!\!\times\!\!^{CH_3}_{\underline{H}}$), 5.37^q ($^{O_4}_{O_6}\!\!\times\!\!^{CH_3}_{\underline{H}}$). IId: m.p. 129-131°, $[\alpha]_D^{24}$ -8.7 (c, 0.722), NMR 3.80^s ($^{O_2}_{O_3}\!\!\times\!\!^{Ph}_{\underline{H}}$), 4.58^s ($^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). IIe: syrup, $[\alpha]_D^{22}$ -10.0 (c, 0.993), NMR 4.07^s ($^{O_2}_{O_3}\!\!\times\!\!^{Ph}_{\underline{H}}$), 4.58^s ($^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). IIId: m.p. 114-115°, $[\alpha]_D^{22}$ -31.0 (c, 0.813), IR_{CCl_4} cm^{-1} 3556 (bonded OH), NMR of 3-O-acetate 4.61^s (H_3), 8.01 (OAc), 4.04^s ($^{O_1}_{O_2}\!\!\times\!\!^{Ph}_{\underline{H}}$), 4.55^s ($^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). IIIe: m.p. 122-125°, $[\alpha]_D^{24}$ +34.7 (c, 0.864), IR_{CCl_4} cm^{-1} 3557 (bonded OH), NMR of 3-O-acetate 4.76^s (H_3), 7.89^s (OAc), 4.21^s ($^{O_1}_{O_2}\!\!\times\!\!^{Ph}_{\underline{H}}$), 4.54^s ($^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). IVd: m.p. 186-194°, $[\alpha]_D^{24}$ +33.8 (c, 0.858, acetone), IR_{CCl_4} cm^{-1} 3629 (non-bonded OH), NMR of 3-O-acetate 4.60^s (H_3), 3.80^s ($^{O_1}_{O_2}\!\!\times\!\!^{Ph}_{\underline{H}}$), 4.60^s ($^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). IVe: m.p. 148-154°, $[\alpha]_D^{24}$ +175.4 (c, 1.037, acetone), IR_{CCl_4} cm^{-1} 3629 (non-bonded OH), NMR of 3-O-acetate 4.50^s (H_3), 3.97^s ($^{O_1}_{O_2}\!\!\times\!\!^{Ph}_{\underline{H}}$), 4.56^s ($^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). Vb: syrup, $[\alpha]_D^{24}$ +81.3 (c, 0.477), reduce Fehling solution, NMR 5.28^q, 5.35^q ($^{O_1}_{O_3}\!\!\times\!\!^{CH_3}_{\underline{H}}$, $^{O_4}_{O_6}\!\!\times\!\!^{CH_3}_{\underline{H}}$). Vd: m.p. 164-166°, $[\alpha]_D^{24}$ +48.8 (c, 0.934), reduce Fehling solution, NMR 4.47^s, 4.53^s ($^{O_1}_{O_3}\!\!\times\!\!^{Ph}_{\underline{H}}$, $^{O_4}_{O_6}\!\!\times\!\!^{Ph}_{\underline{H}}$). VIb (3,4,5-tri-O-acetate): syrup, $[\alpha]_D^{22}$ -45.5 (c, 0.341), NMR 4.95^d (H_3), 4.52^q (H_4), 5.00^m (H_5). VId (3,4,5-tri-O-acetate): m.p. 128-130°, $[\alpha]_D^{22}$ -125.2 (c, 0.956), NMR 4.87^d (H_3), 4.47^t (H_4), 4.98^m (H_5), 3.95^s ($^{O_1}_{O_2}\!\!\times\!\!^{Ph}_{\underline{H}}$). VIe (3,4,5-tri-O-acetate): m.p. 111-115°, $[\alpha]_D^{23}$ -89.2 (c, 0.937), NMR 4.82^d (H_3), 4.45^q (H_4), 4.95^m (H_5), 4.00^s ($^{O_1}_{O_2}\!\!\times\!\!^{Ph}_{\underline{H}}$). VIIb (4,5-O-diacetate): m.p. 110-112°, $[\alpha]_D^{22}$ -13 (c, 0.605), IR_{CHCl_3} cm^{-1} 3560 (OH), NMR 6.52^d (H_3), 4.54^t (H_4), 5.02^m (H_5), 5.28^q ($^{O_1}_{O_3}\!\!\times\!\!^{CH_3}_{\underline{H}}$). XIII: syrup, $[\alpha]_D^{24}$ -42.3 (c, 0.762, acetone). XIV: syrup, $[\alpha]_D^{24}$ +10.5 (c, 1.861, acetone), IR_{film} cm^{-1} 1738 (C=O).

It is reasonably concluded from the above results that our proposed mechanism for the acetonation can be applied to the acetalations.

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