Reactions of saccharides catalyzed by molybdate ions. XXIII.*
A contribution to the mechanism of the epimerization reaction

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In the presence of molybdic acid 2,6-anhydro-1-deoxy-1-nitro-D-galactitol undergoes conversion to its L-*ido* isomer which affords L-xylose on oxidative degradation. On example of this model compound representing 1-deoxy analogue of aldopyranoses, the mechanism of the epimerization reaction of aldoses is discussed in view of a simultaneous change of the configuration at carbon atoms C-2 and C-3.

2,6-Ангидро-1-дезокси-1-нитро-D-галактитол превращается в присутствии молибденовой кислоты в свой L-*идо*-изомер, из которого при окислительном отщеплении получается L-ксилоза. На этом примере модельного соединения, 1-дезокси-аналога альдопираноз, обсуждается механизм реакции эпимеризации альдоз с точки зрения одновременного изменения конфигурации на атомах углерода C-2 и C-3.

Under catalytic effect of molybdate ions aldoses epimerize to the corresponding epimeric aldoses. In the case of epimerization of aldopentoses [1] and some aldohexoses such as galactose, talose, gulose, and idose [2], the predominating inversion of the C-2 hydroxyl group was found to be accompanied by inversion of the hydroxyl group at carbon atom C-3. The present paper is devoted to investigation of the molybdate catalyzed inversion of hydroxyl groups in a model cyclic compound 2,6-anhydro-1-deoxy-1-nitro-D-galactitol.

The epimerization of arbitrary aldopentose and galactose or talose (reaction time 10 h at 95°C and aldose and molybdic acid weight ratio 100:1) leads to the formation of equilibrium mixtures containing two epimeric aldoses and low amounts of the complementary pair of epimeric aldoses (inversion of the C-3 hydroxyl group). The epimerization of 2,6-anhydro-1-deoxy-1-nitro-D-galactitol

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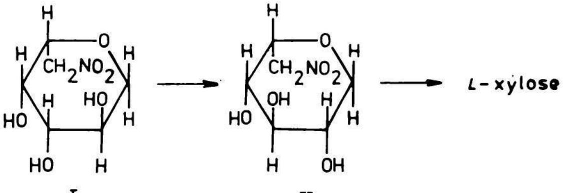
* For Part XXII see Ref. [3].

(*I*) was done at 95°C and higher amount of molybdic acid (*I* and molybdic acid weight ratio 5 : 2) for 16 h. Under these conditions a small part of anhydronitroalditols was transformed to aldopentoses. The anhydronitroalditols isolated from the reaction mixture were subjected to oxidative degradation to give D-lyxose and a small amount of L-xylose. While the oxidative decomposition of sodium salts of 1-deoxy-1-nitrohexitols led to the formation of aldohexoses [3], the same treatment of 2,6-anhydro-1-deoxy-1-nitrohexitols (-D-galactitol or -L-mannitol or -D-gulitol) afforded the corresponding aldopentoses (D-lyxose, L-arabinose, and D-xylose, respectively).

For investigation of the epimerization reaction it is more suitable to describe the chosen model compound *I* as 1,6-dideoxy-6-nitro-L-galactopyranose. In this nomenclature compound *I* possesses the same numbering of carbon atoms as aldoses, and since it does not contain hemiacetal hydroxyl group, it exists exclusively in the cyclic structure. Based on the fact that the reaction mixture obtained after epimerization of *I* and after subsequent oxidative decomposition of the mixture of anhydronitroalditols contained L-xylose, one may infer that the epimerization reaction involves a simultaneous configuration change at carbons C-2 and C-3 resulting in the formation of 1,6-dideoxy-6-nitro-L-idopyranose (*II*), *i.e.* 2,6-anhydro-1-deoxy-1-nitro-L-iditol (Scheme 1)



I *II*

Scheme 1

Our recent study of the mechanism of the epimerization reaction using tritium-labelled aldoses (at carbon atoms C-1 or C-2) has shown that the formation of epimeric aldose is a consequence of a mutual exchange of the C-1 and C-2 hydrogen atoms which is for obvious reasons possible only when the C—H bonds are in *trans* relationship [4]. The transformation of the cyclic model compound *I*, having *trans* arrangement of the hydrogen atoms at carbons C-2 and C-3, to compound *II* (affording L-xylose on oxidation) is in consonance with the interpretation of the epimerization mechanism. The molybdate complex formed with the C-2 and C-3 hydroxyl groups of *I* leads to such a deformation of the molecule (C-1, C-2, C-3, C-4, and the hydroxyl groups at C-2 and C-3 are situated in one plane) which is prerequisite for the mutual hydrogen atom exchange between carbon atoms C-2 and C-3 resulting in the formation of *II*. The results of *I* epimerization are also in agreement with that point of the proposed mechanism of epimerization of aldoses according to which aldoses epimerize in cyclic structures only [4]. It is known that acyclic saccharides do not epimerize under the conditions of epimerization of aldoses [5].

The formation of the mixture of four aldohexoses by epimerization of galactose can be then explained as follows. The formation of epimeric talose is a consequence of the exchange of hydrogen atoms between carbon atoms C-1 and C-2, the formation of idose is a result of a similar migration of hydrogen atoms between carbon atoms C-2 and C-3. The formation of gulose from idose is a process analogous to the formation of talose from galactose involving migration of hydrogen atoms at C-1 and C-2. Similarly can be explained the formation of all four aldopentoses by epimerization of any of them.

Experimental

2,6-Anhydro-1-deoxy-1-nitrohexitols used in this work were prepared according to [3] (-D-galactitol) and [6] (-L-mannitol and -D-gulitol).

Epimerization of 2,6-anhydro-1-deoxy-1-nitro-D-galactitol

A mixture of 2,6-anhydro-1-deoxy-1-nitro-D-galactitol (5 g), molybdic acid (2 g), and water (100 ml) was heated at 95°C for 16 h. The reaction mixture was then treated with activated charcoal, deionized (Wofatit SBW in the carbonate form) and, after being concentrated, chromatographed on a column (3 × 90 cm) of Dowex 1, X-8, 100—200 mesh ion exchanger in the acetate form using elution with water. Fraction *1* contained a mixture of aldopentoses and fraction *2* anhydronitrohexitols. Fraction *2* was concentrated under reduced pressure (at a temperature below 35°C, maintained also during subsequent concentration steps) and the distillation residue was crystallized from ethanol to give a part of 2,6-anhydro-1-deoxy-1-nitro-D-galactitol (1.5 g). The mother liquor was concentrated and the distillation residue of anhydronitrohexitols (1.1 g not containing aldopentoses) was dissolved in water (10 ml) and mixed with 10% aqueous solution of sodium molybdate (0.5 ml), 10% solution of sodium hydroxide (0.7 ml), and 30% aqueous solution of hydrogen peroxide (3 ml). After 24 h standing at room temperature the reaction mixture was deionized (Wofatit KPS in H^+ form, Wofatit SBW in acetate form), concentrated *in vacuo* and chromatographed on Whatman No. 3 papers in methyl ethyl ketone—*n*-butanol—water (16 : 2 : 1). Visualization of carbohydrates showed the presence of lyxose besides a small amount of xylose. The zone of xylose was eluted with a mixture water—methanol. Rechromatography of this material on Whatman No. 1 papers afforded L-xylose (35 mg) having $[\alpha]_D^{23}$ -18^c (*c* 1.7, water), and which gave a mixture of xylose and lyxose in the epimerization test with molybdic acid.

Control oxidative degradation of any of the three 2,6-anhydro-1-deoxy-1-nitrohexitols (-D-galactitol, -L-mannitol or -D-gulitol) under the conditions described for oxidative degradation of anhydronitrohexitols in fraction *2*, gave in all three cases only one, the corresponding aldopentose (D-lyxose, L-arabinose, and D-xylose, respectively):

References

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