Reactions of saccharides catalyzed by molybdate ions. XIV.* Epimerization of pentuloses

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In acidic aqueous solutions under catalytic action of molybdate ions L-*erythro*-pentulose and D-*threo*-pentulose are converted into the corresponding epimeric pentuloses, aldoses, and dehydration products.

L-*эритро*-Пентулоза или D-*трео*-пентулоза в кислых водяных растворах в присутствии каталитического действия ионов молибденовой кислоты превращаются на соответствующие эпимерные пентулозы, альдозы и продукты дегидратации.

In acidic aqueous solutions 2-ketoses, in general, undergo dehydration reactions proceeding faster than those with corresponding aldoses [1, 2]. Aldoses also undergo reversion in diluted and transformations in more concentrated mineral acids (ribose and *erythro*-pentulose is formed from arabinose in 4.5 N or 9.0 N-H_2SO_4) [3]. In diluted aqueous solutions of molybdenic acid hexuloses epimerize without the formation of corresponding aldohexoses [4], and similarly, the epimerization of aldoses is in no case accompanied by the formation of corresponding 2-ketoses [5] or larger amounts of destruction products. Regarding the degree of conversion to the epimer, the efficiency of the molybdate catalyzed epimerization of 2-ketoses is lower than in the case of aldoses. The present paper deals with the epimerization of L-*erythro*-pentulose and D-*threo*-pentulose.

In 0.2% aqueous solution of molybdenic acid (pH 2.8) at 80°C, L-*erythro*-pentulose or D-*threo*-pentulose is converted to various by-products; 35% of pentuloses had reacted during a 4-hour incubation and 60% during a 12-hour incubation (Table 1). Evaluation of these reactions is rather difficult, since the epimerization reaction is accompanied by a transformation to aldopentoses and by a dehydration reaction (Table 2). Evidence has been obtained for the presence of 2-deoxyaldopentoses in the reaction mixture which pointed to a reduction process. A similar reaction carried out in diluted sulfuric acid (0.003 N-H_2SO_4, pH 2.8, 4 hrs) did not lead to the formation of dehydration products, and, in this case, only traces of aldopentoses were found in the reaction mixture. The epimerization of hexuloses catalyzed by molybdate ions leads to a change of the configuration at C-3 and C-4 (*e.g.* the epimerization of D-fructose gives D-sorbose (4.5%), tagatose (1%), and D-psicose (0.5%)) [4]. In the case of the epimerization of pentuloses, the configuration change at C-3 is reflected in the formation of epimeric pentulose. However, the change of the configuration

* For Part XIII see Ref. [5].

at C-4, in the sense of the D- and L-series, has not been evidenced. Absolute values of specific rotations of isolated epimeric pentuloses (D-*erythro*-pentulose $[\alpha]_D^{23}$ $-17 \pm 1°$ and L-*threo*-pentulose $[\alpha]_D^{23}$ $+31.5 \pm 0.5°$) are the same as the values of their antipodes prepared biochemically from the corresponding alditols [6, 7]. A fundamental difference in the behaviour of pentuloses and hexuloses consists in the fact that pentuloses cannot exist in a pyranoid form, which is a reason for their instability and readiness for transformation and dehydration reactions.

The epimerization of pentuloses can be used for preparative purposes. Particularly convenient way of the preparation of L-*erythro*-pentulose and D-*threo*-pentulose by dehydrogenation of ribitol and arabitol, respectively, by *Acetobacter* [6, 7] is not applicable for the preparation of their antipodes, which requires a more complicated chemical way. Thus the transformation of D-arabinose in a boiling pyridine solution gives D-*erythro*-pentulose [8], and L-*threo*-pentulose is formed under similar conditions from L-xylose [9, 10]. The yields of both pentuloses in these reactions are low (2.2—2.7%) and their isolation is rather pretentious due to additional products of the transformation reaction [11]. The epimerization of pentuloses catalyzed by molybdate ions gives epimeric pentuloses in higher yields (5.2—5.3%). By-products are separated from the reaction mixture by chromatography on cellulose and the separation of epimeric pentuloses is achieved by their fractionation on Dowex 50 W ion exchanger. Epimeric pentuloses are obtained in about 13% yield based on the amount of the starting pentulose recovered.

Experimental

D-*threo*-Pentulose and L-*erythro*-pentulose were prepared by microbial dehydrogenation of D-arabitol by *Acetobacter pasterianus BS 1775* [7] and of ribitol by *Acetobacter suboxidans BS 2356* [6], respectively. Starting compounds and reaction products were

Table 1

Polarographic determination of the conversion of pentuloses in aqueous solution of molybdenic acid (%)

Reaction conditions	Starting compound	
	L-*erythro*-Pentulose	D-*threo*-Pentulose
Reaction time, hrs (80°C)		
1	90	89
2	83	82
3	75	73
4	68	66
8	51	50
12	39	37
Reaction temperature, °C (4 hrs)		
60	100	100
70	86	83
80	69	68
90	60	56

identified by paper chromatography in three solvent systems (Table 3), polarographically using a Radelkis polarograph, type OH 102 (Budapest), by optical rotations measured with a Perkin—Elmer polarimeter, type 141 and by melting points determined on a Kofler stage. The pH values of solutions were measured using a Radiometer Titrator, type TTT 2 (Copenhagen).

Effect of molybdenic acid on the conversion of pentuloses

A solution of pentulose (500 mg) and molybdenic acid (10 mg) in water (5 ml) was heated at 80°C. At definite time intervals, samples were taken and diluted with water to give 5×10^{-4} M concentration of the starting pentulose. Polarographic determination of pentuloses (Table 1) was carried out in 0.1 M isobutylamine buffer (0.1 M isobutylamine and 0.1 M isobutylammonium chloride) in the presence of 0.01 M *o*-phenylenediamine. In this medium, the epimeric pentuloses exhibit a well developed polarographic wave ($E_{1/2} = -1.73$ to -1.75 V, referred to SCE) which, however, cannot be distinguished one from another. Aldopentoses themselves give polarographic waves at more negative potentials than the one corresponding to exclusion of the basic electrolyte. Dehydration products of the type of α-dicarbonyl compounds condense with *o*-phenylenediamine to derivatives of chinoxaline ($E_{1/2} = -0.9$ V). Aldopentoses and 2-deoxypentoses react with isobutylamine with a formation of corresponding imines ($E_{1/2} = -1.4$ V). The quoted types of compounds do not interfere with the determination of pentuloses.

The effect of temperature (60, 70, 80, and 90°C) on the conversion of D-*threo*-pentulose was followed polarographically under similar concentration conditions (Table 1).

Epimerization of D-*threo-pentulose*

A mixture of D-*threo*-pentulose (8 g), water (80 ml), and molybdenic acid (160 mg) was heated at 80°C for 4 hrs. The reaction solution was then deionized on an ion exchanger (Wofatit SBW in the acetate form), the eluate was evaporated under reduced pressure (temperature up to 40°C) to sirupy residue which was fractionated on a cellulose column (3.8 × 140 cm) using solvent system S_1, to separate dehydration products with admixtures of 2-deoxy-D-xylose (0.42 g, elution volume 1800—2390 ml) from 2-ketopentoses (5.72 g, elution volume 2590—3190 ml) and aldopentoses (0.29 g, elution volume 3420—3890 ml).

Examination of the fraction of dehydration products by paper chromatography in the solvent system S_1 indicated the presence of compounds having R_{xyl}, 3.45 and 4.55 (yellow and red colour, respectively, with the aniline—hydrogen phthalate reagent) and 2-deoxypentoses. 2-Deoxypentose isolated by chromatography on Whatman No. 3 paper has $[\alpha]_D^{23}$ −5° (*c* 1, water) and, after reduction with $NaBH_4$, exhibited identical chromatographic mobility as 2-deoxyxylitol (Table 1). For 2-deoxy-D-xylose the values $[\alpha]_D^{19}$ −1.9° (*c* 0.5, water) were reported [12].

Refractionation of the fraction of pentuloses on an ion-exchange column of Dowex 50 W, X-8 (100—200 mesh) in a Ba^{2+} form (3.8 × 140 cm) using elution with water afforded D-*threo*-pentulose (4.97 g, *i.e.* 62.1%, in the elution volume 950—1300 ml) and D-*erythro*-pentulose (0.43 g, *i.e.* 5.3%, in the elution volume 1360—1900 ml). D-*erythro*-Pentulose was chromatographically homogeneous and had $[\alpha]_D^{23}$ −17 ± 1° (*c* 1.0—1.2, water). Ref. [8] gives for D-*erythro*-pentulose $[\alpha]_D^{21}$ −16.3° (*c* 2, water).

Crystallization of the fraction of aldopentoses from methanol gave D-xylose with m.p.

Table 2

Composition of the reaction mixtures after epimerization of pentuloses in 0.2% aqueous solution of molybdenic acid at 80°C for 4 hrs

Isolated compounds %	Epimerization of	
	L-*erythro*-Pentulose	D-*threo*-Pentulose
Starting pentulose	54.8	62.1
Epimeric pentulose	5.2	5.3
Aldopentoses	4.9	3.6
Dehydration products of the above saccharides with admixture of 2-deoxyaldopentoses	10.5	5.2

Table 3

Paper chromatography of saccharides

Compound	Relative mobility			Colour reaction*
	S_1	S_2	S_3	
threo-Pentulose	1.66	1.38	—	Redbrown
erythro-Pentulose	1.66	1.56	—	Redbrown
Xylose	1.00	1.00	—	Red
Arabinose	0.84	1.00	—	Red
Lyxose	1.08	1.00	—	Red
Ribose	1.24	1.25	—	Red
2-Deoxyribose	2.72	—	—	Yellow
2-Deoxyxylose	2.52	—	—	Yellow
threo-3-Pentulose	1.24	1.38	—	Yellow
erythro-3-Pentulose	1.28	1.56	—	Yellow
Xylitol	—	—	1.00	—
Arabitol	—	—	1.22	—
Ribitol	—	—	1.55	—
2-Deoxyxylitol	—	—	2.53	—
2-Deoxyribitol	—	—	2.78	—
3-Deoxyxylitol	—	—	0.59	—

Chromatography on Whatman No. 1 paper in solvent systems: S_1 — methyl ethyl ketone—butanol—water 7 : 2 : 1; S_2 — chloroform—acetic acid (1.4 ml H_2O/100 ml of the system) 7 : 2; S_3 — cyclohexanol—pyridine—water (saturated with boric acid) 6 : 5 : 2.

* Detection with the anilinium hydrogen phthalate reagent. Alditols were visualized with the periodate—benzidine reagent.

149—151°C and $[\alpha]_D^{23}$ +19° (*c* 2, water), while in [13] m.p. 153°C and $[\alpha]_D^{25}$ +20° (*c* 1, water) are reported. Paper chromatography of the mother liquor showed D-lyxose besides D-xylose, and, after reduction with $NaBH_4$, D-xylitol and arabitol.

Epimerization of L-*erythro-pentulose*

L-*erythro*-Pentulose (8 g) was epimerized and further treated identically as D-*threo*--pentulose. Fractionation of the reaction mixture on a cellulose column resulted in a separation of pentuloses (5.12 g) from the dehydration products (0.84 g) and aldopentoses (0.39 g). Refractionation of pentuloses on a column of an ion exchanger afforded L-*threo*-pentulose (0.44 g) and L-*erythro*-pentulose (4.38 g). L-*threo*-Pentulose was chromatographically homogeneous and had $[\alpha]_D^{23}$ $+31.5 \pm 0.5°$ (*c* 1.0—1.2, water) as compared to $[\alpha]_D^{21}$ $+31°$ (*c* 1, water) [14].

Paper chromatography of the fraction of dehydration products revealed the presence of compounds having R_{xyl} 3.45 and 4.55, and 2-deoxyribose, which were proved also polarographically. Ribose and arabinose were identified chromatographically in the fraction of aldopentoses. Reduction with $NaBH_4$ gave ribitol and arabitol.

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