

Reactions of saccharides catalyzed by molybdate ions. XXVII.*

Epimerization of some aldoheptoses

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Molybdate catalyzed epimerization of *D-glycero-D-galactoheptose*, *D-glycero-D-taloheptose*, *D-glycero-D-guloheptose*, and *D-glycero-D-idoheptose* affords besides the C-2 epimeric aldoheptose also the complementary pair of C-3 epimeric aldoheptoses. In contrast to the epimerization of aldopentoses and aldohexoses, the epimerization of the four aldoheptoses is accompanied by formation of the corresponding heptuloses, *D-mannoheptulose* and *D-glucoheptulose*.

Эпимеризация, осуществленная в присутствии молибдатных ионов, *D-глицеро-D-галактогептозы*, *D-глицеро-D-талогептозы*, *D-глицеро-D-гулогептозы* и *D-глицеро-D-идогептозы* приводит к образованию, помимо C-2 эпимерной альдогептозы, дополнительной пары C-3 эпимерных альдогептоз. В отличие от альдопентоз и альдогексоз наблюдается в случае эпимеризации указанных четырех альдогептоз также образование соответствующих гептулоз: *D-манногептулозы* и *D-глюкогептулозы*.

Epimerization of aldoses catalyzed by molybdate ions has been employed as a simple procedure for preparation of C-2 epimeric aldoses. Epimerization of *L-arabinose* [1] or *D-galactose* [2] carried out already under mild reaction conditions offers besides C-2 epimeric aldoses (19% of *L-ribose* and 16% of *D-talose*, respectively) also the complementary pair of C-3 epimers (5%). Prolonged reaction time at increased concentration of the catalyst leads in the case of *D-arabinose* or any of the *D-aldopentoses* [3] to an equilibrium mixture of all four *D-aldopentoses* (34% of *D-xylose*, 29% of *D-arabinose*, 24% of *D-lyxose*, 13% of *D-ribose*). In the present work the epimerization of a group of aldoheptoses having *D-arabino* configuration at carbon atoms C-4, C-5, and C-6 was investigated in regard to inversion of the C-2 and C-3 hydroxyl groups.

Molybdate catalyzed epimerization of 1 M aqueous solutions of aldoheptoses (aldose : molybdic acid 1 mmol : 2 mg) at 95°C for 5 h, or *D-arabinose*, *D-galactose*, *D-glycero-D-galactoheptose*, and *D-glycero-D-guloheptose* at increased con-

* For Part XXVI see Ref. [3].

centration of molybdate ions (aldose : molybdic acid 1 mmol : 20 mg) for prolonged reaction time (14 h) gives a mixture of C-2 and C-3 epimeric aldoses. In the case of aldoheptoses the reaction mixtures also contained significant amounts of heptuloses. Relative proportions of aldoses and ketoses in the reaction mixtures were determined by gas chromatography after their conversion to per-*O*-acetyl derivatives of nitriles of the corresponding aldonic acids, and, occasionally, by paper chromatography (Table 1). To identify heptuloses in the epimerization mixtures D-mannoheptulose and D-glucoheptulose were prepared. From a mixture of saccharides obtained by isomerization of D-*glycero*-D-galactoheptose in pyridine (115°C, 4 h), D-mannoheptulose was isolated in 19% yield by chromatography on a polyethyleneimine ion exchanger. Analogous treatment of D-*glycero*-D-guloheptose gave D-glucoheptulose in 22% yield.

The degree of conversion of aldoheptoses having D-*arabino* configuration at carbon atoms C-4, C-5, and C-6 to C-2 epimeric aldoheptoses during the molybdate catalyzed epimerization increases in the order D-*glycero*-D-galactoheptose, D-*glycero*-D-taloheptose, D-*glycero*-D-guloheptose, and D-*glycero*-D-idoheptose. The proportion of the corresponding heptuloses in the reaction mixtures

Table 1

Composition of the reaction mixtures obtained by epimerization of aldoses catalyzed by molybdate ions

Starting aldose	Aldoses in epimerization mixture (%) having configuration at C-2, C-3, and C-4				Conversion to 2-ketoses
	ribo	lyxo	arabino	xylo	
D- <i>glycero</i> -D-Galactoheptose ^a	9	1	90*	90	Traces* Traces of D-mannoheptulose
D- <i>glycero</i> -D-Taloheptose ^a	86	0	11*	11	0* 3% of D-mannoheptulose
D- <i>glycero</i> -D-Guloheptose ^a	Traces	73	3*	22	19* 5% of D-mannoheptulose and D-glucoheptulose (1:8)
D- <i>glycero</i> -D-Idoheptose ^a	Traces	60	5*	21	16* 19% of D-mannoheptulose and D-glucoheptulose (1:7)
D-Arabinose ^b	23	10	52	15	—
D-Galactose ^b	18	5*	81	76*	1 Traces of D-tagatose and D-sorbose
D- <i>glycero</i> -D-Galactoheptose ^b	10	3	81*	82	1* 5% of D-mannoheptulose and D-glucoheptulose (4:1)
D- <i>glycero</i> -D-Guloheptose ^b	4	38	37*	46	9* 12% of D-mannoheptulose and D-glucoheptulose (1:3)

Aldose (1.5 mmol) epimerized in: a) 1.5 ml of 0.2% molybdic acid at 95°C for 5 h; b) 1.5 ml of 2% molybdic acid at 95°C for 14 h.

Proportions of aldoses and ketoses in the reaction mixtures were determined by gas chromatography and paper chromatography (*).

increases in the same order. The greatest changes resulting from the epimerization occur with *D-glycero-D-idoheptose*, the ratio of *D-glycero-D-guloheptose* to *D-glycero-D-idoheptose* reaching the value 4 : 1. The same ratio of these aldohexoses obtained after epimerization of *D-glycero-D-guloheptose* showed that in both cases an equilibrium mixture of C-2 epimeric aldohexoses had been established. Epimerization of *D-glycero-D-galactoheptose* (or epimerization of *D-glycero-D-guloheptose* at carbon C-3, at enhanced amount of the catalyst) affords practically the same ratio of *D-glycero-D-galactoheptose* and *D-glycero-D-taloheptose* 9 : 1. From this it follows that during the epimerization of *D-glycero-D-taloheptose* under mild reaction conditions the equilibrium ratio of the starting aldose and its C-2 epimer has not been obtained yet. This may be rationalized by the fact that *D-glycero-D-taloheptose* being in the preferred C_1^4 conformation (conditioned by the bulky substituent at C-5 carbon atom) does not satisfy the basic requirement for the epimerization catalyzed by molybdate ions [4] which is *trans*-diequatorial arrangement of the hydroxyl groups at carbon atoms C-1 and C-2. (Epimerization of *D-mannose* proceeds slower than that of *D-glucose* for an analogous reason [5].)

The epimerization equilibrium ratio of C-2 epimeric aldoses formed under the same reaction conditions is shifted in the favour of aldose having arabino configuration at carbon atoms C-2, C-3, and C-4 in the order aldopentoses, aldohexoses, and aldohexoses (e.g. *D-arabinose*, *D-galactose*, and *D-glycero-D-galactoheptose* ratios to their C-2 epimers are 2 : 1, 4 : 1, and 9 : 1, respectively). In all cases the epimerization at carbon atom C-3 also takes place. The formation of 2-ketoheptoses is probably due to isomerization of conformationally unstable aldohexoses as a consequence of acidity of the reaction medium (an analogy to the formation of 6-deoxy-*D*-sorbose from 6-deoxy-*D*-idose [6]).

Experimental

Epimerization of aldoses

Aldoses were epimerized under the following conditions: *a*) A solution of 1.5 mmole of aldohexose (*D-glycero-D-galactoheptose*, *D-glycero-D-taloheptose*, *D-glycero-D-guloheptose*, *D-glycero-D-idoheptose*) and 3 mg of molybdic acid in 1.5 ml of water was heated at 95°C for 5 h; *b*) a solution of 1.5 mmole of aldose (*D-arabinose*, *D-galactose*, *D-glycero-D-galactoheptose*, *D-glycero-D-guloheptose*) and 30 mg of molybdic acid in 1.5 ml of water was heated at 95°C for 14 h. The reaction mixtures were deionized (Wofatit SBW in the carbonate form), evaporated and examined for the ratio of saccharides by gas chromatography or paper chromatography.

Gas chromatography

Starting aldoses or the distillation residues of the epimerization mixtures (10–20 mg) were dissolved in 10% solution of hydroxylamine hydrochloride in pyridine (0.2 ml) and heated first for 10 min and, after addition of acetic acid anhydride (0.4 ml), for 20 min at 120°C (these solutions were directly used for injection). Analysis was carried out on a Hewlett—Packard 5450 gas chromatograph provided with a double flame ionization detector using a 3 m long column (2 mm diameter) packed with 5% QF-1 on Supelcoporte (100–120 mesh), at a temperature rise programmed from 200°C (8 min) to 240°C (6°C min⁻¹), a nitrogen flow rate of 14 ml min⁻¹, and an injector temperature of 250°C. Relative retention times $r_{i,s}$ of pentoses (s — D-ribose, 13.46 min): D-lyxose 1.05, D-arabinose 1.08, D-xylose 1.15; $r_{i,s}$ of hexoses (s — D-talose, 19.61 min): D-gulose and D-galactose 1.15, D-idose 1.20, D-tagatose 0.71, D-sorbose 0.79; $r_{i,s}$ of heptoses (s — D-glycero-D-taloheptose, 30.69 min): D-glycero-D-guloheptose 1.14, D-glycero-D-idoheptose 1.21, D-glycero-D-galactoheptose 1.23, D-mannoheptulose 0.67, D-glucoheptulose 0.72.

Paper chromatography

Epimerization mixtures of aldoses were chromatographed on Whatman No. 1 paper in 1-butanol—ethanol—water (5 : 1 : 4) (20–23°C, 80–120 h). Relative ratios of pentoses and hexoses were determined after detection with the anilinium hydrogen phthalate reagent, and that of heptoses after detection with the urea reagent (3 g of urea in 100 ml of acetone and 10 ml of 85% phosphoric acid, heating at 100°C for 2–4 min) by scanning the chromatograms with an ERI-10 densitometer. Mobilities of saccharides relative to that of D-glucose (1.00) are for D-arabinose 1.26, D-xylose 1.51, D-lyxose 1.58, D-ribose 1.75, D-galactose 0.83, D-gulose 1.19, D-talose 1.47, D-idose 1.55, D-sorbose 1.16, D-tagatose 1.34, D-glycero-D-galactoheptose 0.65, D-glycero-D-guloheptose 0.82, D-glycero-D-taloheptose 1.18, D-glycero-D-idoheptose 1.30, D-mannoheptulose 0.98, and D-glucoheptulose 1.10.

Preparation of D-mannoheptulose and D-glucoheptulose

A mixture of D-glycero-D-galactoheptose [7] (20 g) and pyridine (400 ml) was heated at 115°C for 4 h, then evaporated and crystallized from ethanol to give a part (ca. 50%) of the starting aldoheptose. Fractionation of the mother liquor on a column (120 × 2 cm) of a polyethyleneimine ion exchanger in the Cl cycle [8] using elution with water gave in fraction 1 (190–360 ml) D-mannoheptulose (3.8 g) which, after crystallization from ethanol, showed m.p. 149–152°C (Kofler) and $[\alpha]_D^{25} = +28.6^\circ$ (c 2, water) or $[\alpha]_D^{25} = -141.8^\circ$ (c 2, 4% aqueous solution of ammonium molybdate), and in fraction 2 (370–900 ml) starting aldose and a small amount of D-glycero-D-taloheptose.

The procedure described above for the preparation of D-mannoheptulose carried out with D-glycero-D-guloheptose [9] gave in 22% yield D-glucoheptulose, m.p. 170—174°C (Kofler), $[\alpha]_D^{25} = +65.6^\circ$ (c 2, water).

Ref. [10] gives for D-mannoheptulose m.p. 152°C and $[\alpha]_D^{20} = +29^\circ$ (c 2, water), and Ref. [11] for D-glucoheptulose m.p. 171—174°C and $[\alpha]_D^{20} = +67.5^\circ$ (c 2.5, water).

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