Reactions of saccharides catalyzed by molybdate ions. VII.* Preparation of L-ribose, D- and L-lyxose

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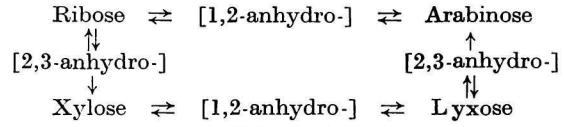
Received 6 July 1972

Epimerization of L-arabinose, D-xylose, or L-xylose catalyzed by molybdate ions gives besides the epimeric aldopentose also small amounts of the complementary pair of epimeric aldopentoses. A part of the starting aldose can be recovered from the reaction mixture by crystallization. The epimeric aldose (18—23%) is isolated either in the form of free sugar using ion-exchange chromatography on Dowex 50 W (Ba^{2+}) or in the form of *N*-phenylglycosylamine. Aldopentoses released upon hydrolysis of such derivatives crystallize without difficulties.

D-Xylose, L-arabinose, and D-ribose can be easily isolated from a suitable biological material, and D-arabinose and D-lyxose can be prepared simply by oxidation of the corresponding aldonic acids [2]. The procedures for preparation of L-ribose and L-lyxose are more complicated. L-Ribose was prepared by hydroxylation of L-arabinal by perbenzoic acid [3, 4] or by hydrogen peroxide under the catalytic action of molybdate ions [5]. L-Lyxose is usually obtained by the Ruff degradation of calcium L-galactonate [2] or from 2,3,4-tri-*O*-benzyl-D-galactitol by periodate oxidation followed by removal of the protecting groups [6]. *Jones* and *Nicholson* [7] prepared D-lyxose and D-ribose by an alkaline treatment of 2-*O*-tosyl-D-xylose and 2-*O*-mesyl-D-arabinose, respectively. 1,2-Anhydro sugars were proposed to be formed in the first step of this reaction [8].

In acidic solutions of molybdate ions aldoses epimerize under the formation of an equilibrium mixture of epimeric aldoses [1, 9—11]. In the case of the epimerization of aldopentoses, besides the epimeric aldose, also small amounts of the complementary pair of aldopentoses were formed [9]. The complexing of sugars with molybdate results probably in the formation of 1,2-anhydro, and, in a lesser extent also, 2,3-anhydro sugars (Scheme 1) which hydrolyze in the acidic medium giving thus all four aldopentoses.



Scheme 1

In the present work we concentrated on the preparative aspect of the epimerization of aldopentoses catalyzed by molybdate ions.

The epimerization of L-arabinose gave an equilibrium mixture of L-arabinose, L-ribose, L-xylose, and L-lyxose. A part of the starting L-arabinose (71%) was recovered from the reaction mixture by crystallization. The rest of the reaction mixture was used for the isolation of L-ribose either in free form by chromatography on Dowex 50 W (Ba^{2+})

* For Part VI see Ref. [1].

Table 1

Fractionation of the epimerization mixture of L-arabinose by ion-exchange chromatography

Fraction	Volume [ml]	Weight [g]	Saccharide present*
I	620	—	—
II	480	7.0	L-xylose, L-lyxose, L-arabinose
III	170	0.8	L-arabinose, 2-deoxy-L-*erythro*-pentose
IV	115	—	—
V	650	9.5 (19%)	L-ribose

* Examined by chromatography on Whatman No. 1 paper in *n*-butanol—ethanol—water (5 : 1 4 v/v) followed by detection with diphenylamine aniline reagent.

(19%) or in the form of *N*-phenyl-L-ribosylamine (18.6%). The chromatographic separation was more convenient for isolation of L-ribose than for that of L-xylose, L-lyxose, or L-arabinose (Table 1). However, the isolation *via* *N*-phenyl-L-ribosylamine [12] was simpler since L-ribose obtained after hydrolysis of this derivative and crystallization was chromatographically homogeneous. From the epimerization mixtures of D- or L-xylose, a part of the starting xylose was also recovered by crystallization (47—54%). Lyxose present in the filtrate was isolated as *N*-phenyllyxosylamine (18—23%). This derivative crystallized from aqueous ethanol easier and was also more stable than the analogous derivative of ribose. Its hydrolysis (during the water steam distillation) gave lyxose of a high purity.

It may be concluded that the above-described preparation of L-ribose, D- and L-lyxose including their isolation from the reaction mixtures *via* *N*-phenylglycosylamine represents a simple procedure for the preparation of these rare pentoses. Easy recovery of the starting aldopentoses points also to a good efficiency of the procedure.

Experimental

Preparation of L-*ribose*

A solution of L-arabinose (100 g) and molybdenic acid (1 g) in water (500 ml) was heated at 90—95°C for 9 hours. The mixture was then treated with charcoal and evaporated under reduced pressure. The obtained residue was dissolved in methanol (200 ml) and crystallized at 5°C for 24 hours. The crystalline L-arabinose (71 g) was filtered off, and the filtrate was concentrated and deionized on a Wofatit SBW column (4.6 × × 130 cm) in the acetate form. The eluate from the column (3 l) was evaporated to dryness in a vacuum (38.5 g). A half of the sirup obtained was used for the isolation of L-ribose by ion-exchange chromatography (procedure *A*), and the second half was processed to give *N*-phenyl-L-ribosylamine (procedure *B*).

A. Isolation by chromatography

The mixture of saccharides (19.2 g) was chromatographed on a column (3.5 × 120 cm) of Dowex 50Wx8 (100—200 mesh, Ba^{2+}) using elution with water at a rate 20 ml/hour. Five fractions were collected (Table 1). Fraction II was concentrated *in vacuo* and

crystallized to furnish L-arabinose. L-Lyxose was isolated from the filtrate *via* *N*-phenyl-L-lyxosylamine.

Fraction *III* was chromatographed on Whatman No. 3 paper in *n*-butanol—ethanol—water (5 1 4 v/v) to separate L-arabinose from a deoxypentose (30—50 mg) identified as 2-deoxy-L-*erythro*-pentose, $[\alpha]_D^{24}$ +59.6° (*c* 1.76, methanol).

Fraction *V* was evaporated *in vacuo* and the residue was dried by three successive evaporations with anhydrous ethanol (3 × 10 ml). The sirup was dissolved in anhydrous ethanol (10 ml), seeded with L-ribose, and crystallized at room temperature for 24 hours to give L-ribose (6.5 g).

B. Isolation via N-phenyl-L-ribosylamine

The saccharide mixture (19.2 g) was dissolved in water (5 ml); then aniline (7.5 ml) and ethanol (17.5 ml) were added before the mixture was left to stand at room temperature for 24 hours. The separated *N*-phenyl-L-ribosylamine (14 g) was filtered off, washed with 25% aqueous ethanol (3 × 8 ml) and dried in air. The obtained product (m.p. 93—95°C), $[\alpha]_D^{24}$ −8.0° (*c* 2.0, methanol) was suspended in water (300 ml), ethanol (100 ml) was added and the mixture was subjected to water steam distillation (above 1 l of distillate was collected). The solution free of aniline was treated with charcoal and evaporated to sirup. This was further dried by successive evaporations with anhydrous ethanol. The dry sirupy L-ribose (9.3 g, *i.e.* 18.6%) was crystallized from anhydrous ethanol (10 ml) to give 5.5 g of crystalline product.

Preparation of D-*lyxose*

A solution of D-xylose (50 g) and molybdenic acid (0.5 g) in water (250 ml) was kept at 90—95°C for 12 hours and then treated with charcoal. The filtrate was deionized on an Amberlite 402 (OH^-) column (3.1 × 90 cm). The column eluate (5 l) was evaporated *in vacuo* to sirupy residue which was further dissolved in methanol (50 ml), seeded with D-xylose and left to crystallize at room temperature for 48 hours. Crystalline D-xylose (27 g) was filtered off and the filtrate was evaporated. Water (5.5 ml), aniline (11.5 ml), and ethanol (4.0 ml) were added to the residue and the resulting mixture was left to stand at room temperature for 20 hours. Separated *N*-phenyl-D-lyxosylamine (16.5 g), (m.p. 148—150°C), $[\alpha]_D^{24}$ −24° (3 min) → −17° (2 hours, equilibrium) (*c* 2.0, methanol) was then treated in the manner used for isolation of L-ribose (see procedure *B*). Sirupy D-lyxose (11.6 g, *i.e.* 23.2%) was crystallized from anhydrous ethanol (10 ml) to give 6.6 g of crystalline product.

Preparation of L-*lyxose*

The epimerization of L-xylose (30 g; prepared as described previously [2]) carried out in the same way as that of D-xylose led to recovery of the starting L-xylose (14 g) and to isolation of *N*-phenyl-L-lyxosylamine (7.9 g), m.p. 149—150°C, $[\alpha]_D^{24}$ +78° (3 min) → +17° (2 hours, equilibrium) (*c* 2.0, methanol). Hydrolysis of *N*-phenyl-L-lyxosylamine gave sirupy L-lyxose (5.4 g, *i.e.* 18%) which was crystallized from anhydrous ethanol.

Recrystallization of L-*ribose*, D- *and* L-*lyxose*

Aldopentose (*A* g) was dissolved under heating in anhydrous ethanol (3 × *A* ml). After 24-hour standing at room temperature the crystalline portion of the aldopentose was filtered off (70—75%), washed with anhydrous ethanol, and dried.

The melting points and the optical rotatory data of the pentoses in question are presented in Table 2.

Table 2

Characterization of recrystallized pentoses

Time of mutarotation	L-Ribose $[\alpha]_D^{24}$	D-Lyxose (*c* 2.0, water)*	L-Lyxose
3 min	15.7	−5.5	4.5
5 min	16.9	−8.0	9.0
10 min	17.9	−11.5	12.0
2 hours	19.5	−13.0	13.0
24 hours	19.5	−13.0	13.0
M.p. [°C] (Kofler)	82−83	103−104	103−104

* Measured with a Perkin−Elmer automatic polarimeter, type 141. Ref. [2] gives for L-ribose m.p. 85−87°C, $[\alpha]_D^{20}$ + 23° (water), for D-lyxose $[\alpha]_D^{20}$ −14° (*c* 7.7, water) and for L-lyxose $[\alpha]_D^{20}$ −6° → +13.5° (water).

Acknowledgements. We wish to thank Mr F. Javorský for technical assistance.

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Translated by P. Biely