Reactions of Saccharides Catalyzed by Molybdate Ions XLVII.* Effect of Molybdate Ions on Transformation of Lower Aldoses

J. KÖNIGSTEIN and V. BÍLIK

Institute of Chemistry, Slovak Academy of Sciences, CS-842 38 Bratislava

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Formation of the corresponding 2-ketoses and dehydration products of D-erythrose, D-threose, 5-deoxy-L-ribose, 5-deoxy-L-arabinose, and DL-glyceraldehyde on epimerization catalyzed by molybdate ions was examined by polarography. Transformation of D-erythrose and D-threose was accompanied, in addition to their mutual epimerization, also with formation of the corresponding 2-ketose and a product of dehydration. On the other hand, transformations of 5-deoxy-L-ribose and 5-deoxy-L-arabinose were associated with origination of the respective dehydration and epimerization products only. The course of transformations of aldoses under investigation was compared with the conversion of DL-glyceraldehyde.

Epimerization of D-threose or D-erythrose catalyzed by molybdate ions afforded an equilibrium mixture of the corresponding aldotetroses in a 4 : 3 ratio; one third of the starting aldose was simultaneously converted into by-products [1]. Similarly, epimerization of 5-deoxy-L-arabinose produced an equilibrium mixture of the starting aldose and 5-deoxy-L-ribose in a 3 : 1 ratio and one fourth of the reactant was converted into by-products [2]. Epimerization of 4-deoxy-D-*xylo*-hexose led to 4-deoxy-D-*lyxo*-hexose (14 %) and a greater amount (33 %) of by-products [3]. The catalytical epimerization of DL-(1-^{13}C)glyceraldehyde furnished only a small amount of DL-(2-^{13}C)glyceraldehyde, the (1-^{13}C)dihydroxyacetone being the main product [3]. Conversion of DL-glyceraldehyde was investigated from the viewpoint of kinetics, too [4]. Some reducing disaccharides with (1→4) linkage (lactose, epilactose, maltose, epimaltose) did not undergo epimerization. Stronger conditions (an enhanced amount of molybdic acid, an extended reaction time) epimerized lactose into epilactose in trace amounts only [5]. As found, celtrobiose (4-*O*-β-D-glucopyranosyl-D-altrose) did epimerize to epiceltrobiose [6]. 3-Deoxy-D-*arabino*-hexose or 3-deoxy-D-*ribo*-hexose were transformed quantitatively into 3-deoxy-D-*erythro*-hexulose [7]. Molybdate ions-catalyzed epimerization of aldopentoses and higher aldoses did not lead to formation of meaningful amounts of by-products under mild conditions.

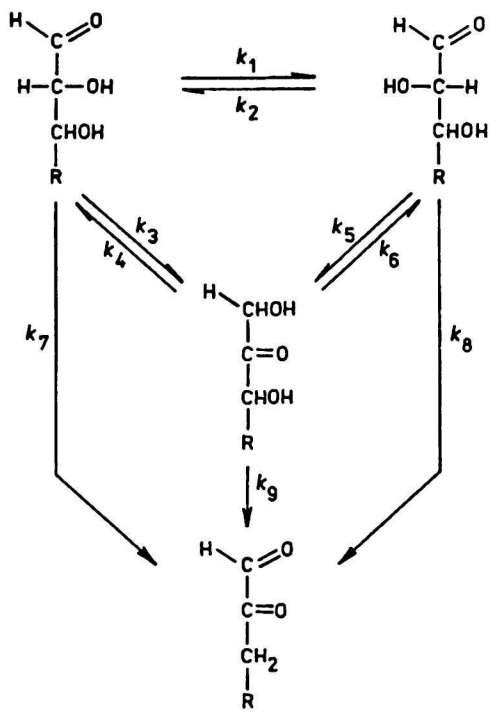
D-Erythrose, D-threose, 5-deoxy-L-arabinose, and 5-deoxy-L-ribose form molybdate complexes with ammonium molybdate as evidenced by NMR spectroscopy [8, 9]. It is assumed that the epimerization process is subject to production of a transition molybdate complex in which aldose entered the binuclear molybdate complex through the carbonyl group and three vicinal hydroxyl groups [3, 10, 11]. The epimerization of DL-(1-^{13}C)glyceraldehyde, 4-deoxy-D-*arabino*-hexose [3], and celtrobiose [6] showed that the hydroxyl group at C-4 of the aldose is not essential for the epimerization process. Absence of the C-3 hydroxyl group of an aldose was exclusively manifested by isomerization to the corresponding 2-ketose without epimerization [7].

This paper presents results of isomerization of D-erythrose, D-threose, 5-deoxy-L-ribose, 5-deoxy-L-arabinose, and DL-glyceraldehyde obtained by means of polarographic analytical method [4], which records the different reactivity of aldoses and ketoses (not possessing hemiacetal or hemiketal structures) with primary aliphatic amines. Aldoses form quantitatively aldimines at suitable conditions, whilst ketoses do virtually not react. Products of dehydration – 1,2-dicarbonyl derivatives – react quantitatively with 1,2-phenylenediamine to give stable quinoxaline derivatives. Owing to the replacement of >C=O groups for >C=N ones the half-wave potentials of cathodic polarographic waves associated with the polarographic reduction shifted towards the more positive values with respect to the original carbonyl compounds (aldoses); as a result, the polarographic waves are well developed and sufficiently resolved. This method, described for trioses and tetroses, was now applied for 5-deoxypentoses. Diffuse character of the polarographic current was evidenced; dependence

* For Part *XLVI* see Ref. [9].

of its magnitude on the square root of the mercury level height was linear with the correlation coefficient r = 0.9969. Temperature coefficient ΔT = 1.86 % °C^{-1} in the interval 20—50 °C at 5 x 10^{-4} mol dm^{-3} aldose concentration in 0.3 M isobutylamine buffer solution in the presence of 0.01 M 1,2-phenylenediamine. The calibration graphs showing relationship between the magnitude of polarographic waves and concentration of 5-deoxyaldopentoses (i_d = f(c)) in the 10^{-4}—10^{-3} mol dm^{-3} concentration range (correlation coefficients $r \geq$ 0.9925, intercepts $a \leq$ 4.4 mm at the relative standard deviation s_r = 2.6 %) were evaluated. Results obtained indicated the linearity of the function under examination and suitability of aldimines for polarographic analytical determination of both 5-deoxyaldopentoses; these results are in accordance with those of trioses and tetroses [4].

The expression conversion of lower aldoses involves all changes proceeding in the given reaction medium. Convenient reaction conditions (by *ca.* 2 orders lower concentrations of the starting compounds than usual with aldolizations, an absence of redox substances) hinder aldolizations (second-order reactions) and oxidation-reduction disproportionations. The course of transformation of lower aldoses can be, then, illustrated by Scheme 1. The over-all rate constants $k = (k_1 - k_2) + (k_3 - k_4) + k_7$ are expressed approximately,



Scheme 1

Conversion of lower aldoses; R = H, CH_2OH, $CH(OH)CH_3$; k_1 to k_9 are the respective rate constants.

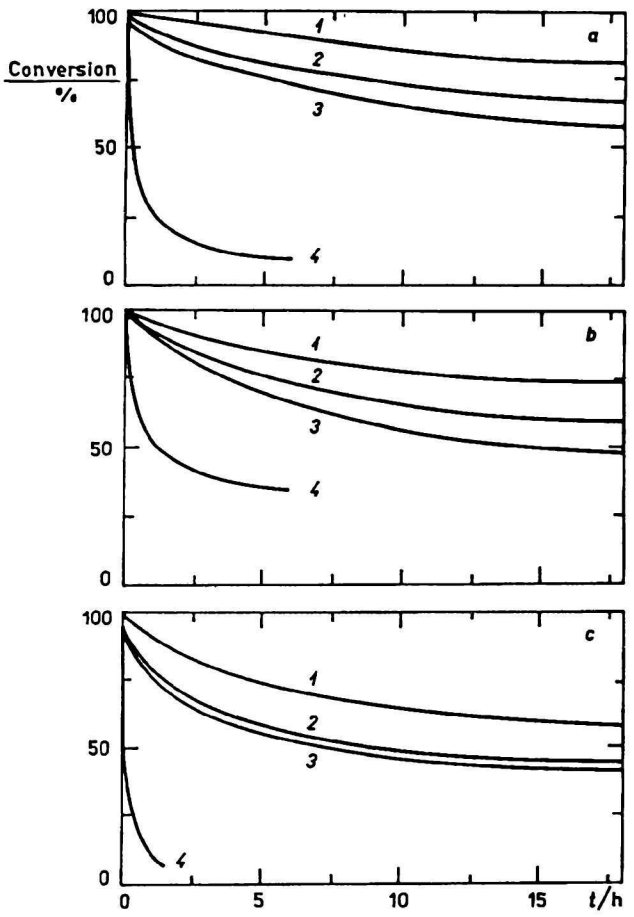


Fig. 1. Conversion courses of lower aldoses (*a*) D-threose, *b*) 5-deoxy-L-arabinose, *c*) DL-glyceraldehyde) at 70 °C in *1.* acetate buffer (pH = 4.6), *2.* ammonium molybdate (pH = 5.1), *3.* ammonium molybdate (pH = 3.1), *4.* carbonate buffer (pH = 10.2).

and conversions involve mutual transformations of epimeric aldoses, aldoses and the corresponding 2-ketose, as well as the irreversible formation of 1,2-dicarbonyl compounds – primary products of dehydration. The over-all constants are expressed after elimination of aldolization and disproportionation reactions in such a way that further partial reactions of the total consecutive-competitive system (characterized by k_5, k_6, k_8, k_9) are considered more significant in the further conversion course, especially after reaching equilibrium in the system; our attention was more pointed towards the former reaction course.

The conversion process of DL-glyceraldehyde, D-erythrose, 5-deoxy-L-ribose, D-threose, and 5-deoxy-L-arabinose was examined in four various reaction media (Fig. 1) aiming to compare both the catalytical effect of molybdate ions and the acid-base catalysis. These media were molybdate solutions of pH = 5.1 and 3.1 (Fig. 1, curves *2*, *3*) and equimolar buffer solutions – acetate of pH = 4.6 and carbonate of pH = 10.2 (Fig. 1, curves *1*,

Table 1. Rate Constants for Conversions of Lower Aldoses ($k \cdot 10^6/s^{-1}$, θ = 70 °C)

Saccharide	Mo^{VI}		Buffer solution	
	pH 3.1	pH 5.1	pH 4.6	pH 10.2
D-Erythrose	3.0	2.8	1.9	173
5-Deoxy-L-ribose	3.1	2.3	1.3	292
D-Threose	5.3	5.0	4.0	228
5-Deoxy-L-arabinose	3.3	2.8	2.2	272
DL-Glyceraldehyde	13.1	8.8	2.4	508

4). Further conditions (temperature 70 °C and aldose concentrations 10^{-2} mol dm^{-3}) were selected as optimal as far as the rate and the preferred course direction were considered. D-Threose, 5-deoxy-L-arabinose, and DL-glyceraldehyde have a similar reaction course; D-erythrose and 5-deoxy-L-ribose are analogous in comparison with the two adducts (Fig. 1). All aldoses were found to react most rapidly in alkaline medium due to the specific base catalysis, which was, together with the reaction mechanism, already examined with trioses in more detail [12]. Shoulder at the curves indicated two stages of this process; the first one was associated with approaching the equilibrium and the second one with its irreversible interference caused by dehydration (Scheme 1). Conversion at equal molybdate concentrations proceeded faster at pH = 3.1, the reason for this could be the specific acid-catalyzed dehydration. The conversion course of aldoses in acetate buffer solution of pH = 4.6 (Fig. 1, curve *1*) does not lie between those in molybdate media; it is the slowest as a result of specific acid catalysis only. Of aldoses under investigation DL-glyceraldehyde was generally found to be converted most rapidly. Reactivity of other aldoses was comparable.

A more comprehensive and global sight on the reactivity of lower aldoses under study as far as their conversions are concerned is offered by the over-all rate constants (Table 1). They do not characterize especially the particular type of conversions, but they make an over-all view and mutual comparison possible. The over-all rate constants do not point out any preferential type of conversions in a certain phase of the reaction course and therefore, some differences appeared on comparison with the reaction courses. These were observed during 18 h, the over-all constants within 96 h. It emerged that tetroses are more reactive, D-threose being more than D-erythrose; reactivities of 5-deoxy-L-arabinose and 5-deoxy-L-ribose displayed virtually no difference.

Estimation of reaction products of all aldoses under study in all four reaction media after 3 h of reacting demonstrated more the character of conversions (Table 2). The total amount of reaction

Table 2. Yields (%) of 2-Ketoses (*a*) and Products of Dehydration (*b*) from Conversions of Lower Aldoses after 3 h Reaction Time at 70 °C

Starting material	Mo^{VI}				Buffer solution			
	pH 3.1		pH 5.1		pH 4.6		pH 10.2	
	a	*b*	*a*	*b*	*a*	*b*	*a*	*b*
D-Erythrose	6	9	3	4	0	4	22	63
5-Deoxy-L-ribose	0	77	0	13	0	10	19	34
D-Threose	7	12	5	10	0	5	18	68
5-Deoxy-L-arabinose	0	21	0	18	0	9	29	32
DL-Glyceraldehyde	20	17	23	11	0	20	0	100

products corresponded with conclusions already presented. A meaningful finding is that no isomerization products of all aldoses in acetate buffer solution were observed at the given conditions. Conversion of both aldotetroses in acid medium in the presence of molybdate ions was accompanied by isomerization to form 2-ketotetroses. 5-Deoxyaldopentoses did not furnish isomerization products. We suppose that the observed phenomenon is due to catalytical action of molybdate ions giving rise to reaction intermediates (transition complexes), which influence variously the rate of the particular reaction types responsible for conversion of the starting aldoses. Formation of the common reaction intermediate is fast. After that considerably slower and therefore rate-determining steps – dehydration and isomerization – came into effect, both being comparable with aldotetroses. On the other hand, dehydration proceeding much faster is preferred with 5-deoxyaldopentoses due to steric reasons and consequently, the isomerization product had no chance to originate. The dehydration products (1,2-dicarbonyl derivatives) were transformed into stable quinoxaline derivatives and therefore, their consecutive changes could not be traced. A relatively higher temperature promoted the dehydration.

EXPERIMENTAL

The conversions of aldoses were carried out in flasks equipped with joint stoppers at a 10 cm^3 reaction volume and (70 ± 0.1) °C; this temperature was kept constant with an MLW TB 75 (Prüfgeräte, Medingen) thermostat. The reaction media were aqueous equimolar (pH = p*K*) solutions of 0.1 M acetate buffer according to Michaelis (pH = 4.6), 0.1 M carbonate buffer (pH = 10.2), 0.1 M ammonium molybdate (pH = 5.1), and 0.1 M ammonium molybdate adjusted with 0.5 M acetic acid to pH = 3.1. All reaction media contained aldoses and 1,2-phenylenediamine in concentrations 0.01 mol dm^{-3} and 0.2 mol dm^{-3},

respectively. The pH values of solutions used were measured with a pH-meter PHM 82 (Radiometer-Standard) possibly coupled with Titrator TTT 80 and a magnetic valve MNV-2 (for pH adjustment of ammonium molybdate) and measuring glass (type EA 109 H) and reference calomel (type EA 404, Metrohm) electrodes. Samples for analysis (0.5 cm^3) were withdrawn from the rapidly cooled solution by an automatic pipette P 500 (Gilson) in nominal times. Polarograph OH-105 (Radelkis, Budapest) and polarographic jacketed cell with separated saturated calomel electrode were used for polarographic and analytical measurements. The aqueous samples were determined at a 5×10^{-4} mol dm^{-3} concentration (calculated per the starting aldoses) in 0.3 M equimolar isobutylamine buffer (pH = pK = 10.4) in the presence of 0.001 M 1,2-phenylenediamine at (20 ± 0.1) °C (thermostated by the U 1 apparatus (Prüfgeräte, Medingen)).

Linear regression method was employed for numerical processing of experimental data from the conversion courses, computation of rate constants (first-order over-all constants), processing of calibration data for analytical determinations and their evaluation using the PC Commodore 16.

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REFERENCES

1. Bílik, V. and Stankovič, Ľ., *Chem. Zvesti 27,* 544 (1973).
2. Bílik, V., Petruš, Ľ., Stankovič, Ľ., and Linek, K., *Chem. Zvesti 32,* 372 (1978).
3. Hayes, M. L., Pennings, N. J., Serriani, A. S., and Barker, R. J., *J. Am. Chem. Soc. 104,* 6764 (1982).
4. Königstein, J., *Collect. Czechoslov. Chem. Commun. 43,* 1152 (1978).
5. Bílik, V., Jurčová, E., and Sutoris, V., *Chem. Zvesti 32,* 252 (1978).
6. Angyal, S. J., private communication.
7. Bílik, V. and Petruš, Ľ., *Collect. Czechoslov. Chem. Commun. 43,* 1159 (1978).
8. Bílik, V., Alföldi, J., and Soókyová, E., *Chem. Zvesti 38,* 499 (1984).
9. Matulová, M. and Bílik, V., *Chem. Papers 46,* 253 (1992).
10. Clark, E. L., Jr., Hayes, M. L., and Barker, R., *Carbohydr. Res. 153,* 263 (1986).
11. Bílik, V. and Matulová, M., *Chem. Papers 44,* 257 (1990).
12. Fedoroňko, M. and Königstein, J., *Collect. Czechoslov. Chem. Commun. 34,* 3881 (1969).

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