

Reactions of saccharides catalyzed by molybdate ions XXXVI*. A contribution to the epimerization of D-glucose to D-mannose

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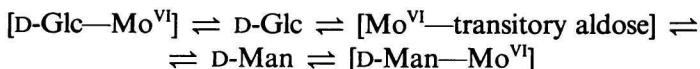
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The epimerization of D-glucose catalyzed by molybdate ions carried out at D-glucose to water amount of substance ratios 1 : 1 and 1 : 4, and at a temperature of 90—125 °C for 20—40 min, afforded a mixture of D-glucose and D-mannose in the ratio 3 : 1.

Эпимеризация D-глюкозы, катализируемая молибдат-ионами, проводимая в водных растворах с соотношением D-глюкоза : вода 1 : 1 и 1 : 4 при температуре 90—125 °C в течение 20—40 минут, приводила к образованию смеси D-глюкозы и D-маннозы в соотношении 3 : 1.

The molybdate-catalyzed epimerization of D-glucose to D-mannose described in 1972 [1] was the first example of a general 2-epimerization of aldoses. The reaction was applied for preparation of D-mannose from D-glucose [1], L-glucose from L-mannose [2], and α -methyl D-mannopyranoside from D-glucose [3]. The present paper is devoted to efficiency of the preparation of D-mannose regarding its large quantities required.

The 2-epimerization of D-glucose or D-mannose is an intramolecular rearrangement leading to an equilibrium mixture of D-glucose and D-mannose in the ratio 73 : 27. The sequence of reactions during the epimerization can be schematically demonstrated as follows [4—6]:



Aldoses form complexes with molybdate ions in mild acidic solutions. The complex formation proceeds well with aldoses of the homomorphous series of ribose, worse with aldoses of the homomorphous series of lyxose and poorly with homomorphous series of arabinose and xylose [7—9]. The existence of the molybdate complexes of D-glucose and D-mannose ($[\text{D-Glc-Mo}^{\text{VI}}]$, $[\text{D-Man-Mo}^{\text{VI}}]$) was established by CD measurements [10]. By NMR spectroscopy it was demonstrated that D-mannose enters the complex as β -D-mannopyranose through the hydroxyl groups at carbon atoms C-1, C-2, and C-3 [11]. It is assumed, however, that the epimerization requires

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Table 1

Epimerization of D-glucose ($c = 1 \text{ mol dm}^{-3}$) and D-mannose ($c = 1 \text{ mol dm}^{-3}$) in the presence of acetic acid ($c = 0.1 \text{ mol dm}^{-3}$) and ammonium molybdate ($c = 10^{-3} \text{ mol dm}^{-3}$) depending on time and temperature

Epimerized aldose	$\theta/^\circ\text{C}$		t/h									
			0	0.25	0.5	0.75	1	2	3	5	10	
D-Glucose	70	$w(\text{Glc})/\%$	100	94	91	89	87	83	80	77	73	
		$w(\text{Man})/\%$	0	6	9	11	13	17	20	23	27	
	80	$w(\text{Glc})/\%$	100	88	84	81	79	75	74	73	—	
		$w(\text{Man})/\%$	0	12	16	19	21	25	26	27	—	
	90	$w(\text{Glc})/\%$	100	82	78	75	74	73	—	—	—	
		$w(\text{Man})/\%$	0	18	22	25	26	27	—	—	—	
D-Mannose	70	$w(\text{Glc})/\%$	0	2	3	5	6	10	14	22	41	
		$w(\text{Man})/\%$	100	98	97	95	94	90	86	78	59	
	80	$w(\text{Glc})/\%$	0	3	6	9	12	25	36	52	66	
		$w(\text{Man})/\%$	100	97	94	91	88	75	64	48	34	
	90	$w(\text{Glc})/\%$	0	10	18	26	33	54	62	67	73	
		$w(\text{Man})/\%$	100	90	82	74	67	46	38	33	27	

Table 2

Epimerization of D-glucose monohydrate (1 mol) in the presence of acetic acid (2×10^{-2} mol) and ammonium molybdate (10^{-3} or 2×10^{-3} mol) depending on water content, time, and temperature

$n(\text{H}_2\text{O})/\text{mol}$	$\theta/^\circ\text{C}$	t/min	Regenerated D-glucose w/%	<i>N</i> -Phenyl-D-mannosylamine Yield/%
1	125	40	41	24
1.6	120	30	40	24
2.1	120	20	38	25
2.1 ^a	90	40	39	24
2.6	115	25	28	25
2.6 ^a	90	40	29	24
3	110	30	22	25.5
3 ^a	90	40	23	25
4	105	35	10	26
4 ^a	90	40	9	25.5
4.6	105	35	1	26.5

a) 2×10^{-3} mol of ammonium molybdate.

a different type of the aldose-molybdate complex (Mo^{VI} —transitory aldose complex). In one case it has been proposed that the aldose bound in such an active complex occurs in the pyranoid form and that the epimerization involves a migration of hydrogen atoms between atoms C-1 and C-2 [4]. According to different authors [5, 6], aldose enters the complex in acyclic structure and the epimerization involves a recombination of C-1 and C-2 carbon atoms together with the corresponding hydrogen atoms. Since three types of complexes can be considered to be formed in the reaction medium, kinetic evaluation of D-glucose or D-mannose epimerization is unusually difficult.

The rate of D-glucose and D-mannose epimerization was followed in a solution of acetic acid ($c = 0.1 \text{ mol dm}^{-3}$) to ensure a constant pH of the medium (pH 3.3). Aqueous solutions of aldoses of the homomorphous series of ribose and lyxose tend to decrease pH values at a sufficient ammonium molybdate concentration. The results showed that the rate of D-glucose or D-mannose epimerization increased 2.5—3 times with a temperature rise by 10°C . The epimerization of D-mannose was much slower than that of D-glucose (Table 1). When the epimerization was done at 28°C for 270 days, D-glucose was converted to a mixture containing 76% of D-glucose and 24% of D-mannose, while D-mannose gave 52% of D-glucose and 48% of D-mannose. The sugar mixture, 73% of D-glucose and 27% of D-mannose, obtained on epimerization of D-glucose at 95°C for 5 h, did not change on further incubation at 28°C even for 270 days. This observation indicated that the equilibrium ratio of the epimeric aldoses is independent of the temperature in the range 28°C — 90°C .

The conditions of D-glucose epimerization were modified by decreasing the portion of water in the reaction mixture and by increasing the reaction temperature to more than 100°C at the atmospheric pressure. As a result of these changes, a mixture of D-glucose and D-mannose in the ratio 3:1 was obtained within 20–40 min (Table 2). At an amount of substance ratio of D-glucose and water 1:1.6 to 1:2.6, 30–40 % of the starting D-glucose was recovered from the reaction mixture by direct crystallization from alcohols. D-Mannose was then isolated from the mother liquor in 24–25 % in the form of crystalline *N*-phenyl-D-mannosylamine. Lower content of water complicated the processing of the reaction mixtures while more diluted reaction mixtures were less suitable for the recovery of D-glucose (Table 2).

Experimental

Monitoring of D-glucose and D-mannose epimerization

A reaction vessel containing 100 cm³ of D-glucose or D-mannose (18.0 g; 0.1 mol) solution in water and 0.6 cm³ (10⁻² mol) of acetic acid was heated in a thermostat at a temperature of 70°C, 80°C or 90°C ($\pm 0.5^\circ\text{C}$) or kept in the dark at 28°C. To the mixture 2.0 cm³ of 6 % aqueous solution of ammonium molybdate ((NH₄)₆Mo₇O₂₄·4H₂O, 124 mg, 10⁻⁴ mol) was added and at time intervals 1 cm³ aliquots were taken and adjusted to 4 % solution of ammonium molybdate containing 1.5 % of aldose. D-Glucose [α]_(D, 23^\circ\text{C}) = +52° (water) and +56° (4 % solution of ammonium molybdate). The corresponding values of D-mannose are +14.5° and -35° [9]. After 20–24 h standing at room temperature, specific rotations of the samples were measured with an automatic Perkin—Elmer polarimeter, type 141A. The values of optical rotations were used to calculate the proportion in percentage of D-glucose and D-mannose in the epimerization mixtures (Table 1).

Epimerization of D-glucose at various water content

A mixture of D-glucose monohydrate (198 g; 1 mol), acetic acid (1.1 cm³; 2 × 10⁻² mol), ammonium molybdate (1.25 g or 2.5 g of (NH₄)₆Mo₇O₂₄·4H₂O; 10⁻³ mol or 2 × 10⁻³ mol), and water (10.8–66.6 cm³; 0.6–3.7 mol) was heated at 90–125°C for 20–40 min (Table 2). After cooling to 70–85°C and addition of methanol (100 cm³) and ethanol (100 cm³), the mixture was seeded with solid D-glucose and crystallized at room temperature for 48 h. Separated D-glucose was filtered off, washed with a mixture of methanol and ethanol ($\phi_r = 1:1$) and dried. The filtrate was made up to 650 cm³ with the methanol—ethanol mixture, mixed with aniline (80 cm³) and left to stand at room temperature for 24 h. Crystalline *N*-phenyl-D-mannosylamine was collected by filtration and washed with a mixture methanol—ethanol ($\phi_r = 1:1$) (Table 2).

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