Reactions of saccharides catalyzed by molybdate ions XXXVII*. Preparation of D-allose and D-altrose from D-glucose

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The molybdate-catalyzed epimerization of D-glucose in aqueous solutions carried out at 120—150 °C leads to a mixture of D-glucose, D-mannose, D-allose, and D-altrose, from which D-glucose and D-mannose are removed by yeast fermentation while D-allose and D-altrose are obtained in the ratio 3 : 2 in 14—17 % yield.

Катализируемая молибдат-ионами эпимеризация D-глюкозы в водных растворах, проводимая при 120—150 °C, приводит к образованию смеси D-глюкозы, D-маннозы, D-аллозы и D-альтрозы, из которой D-глюкоза и D-манноза устраняются дрожжевой ферментацией, в то время как D-аллоза и D-альтроза образуются в соотношении 3 : 2 с 14—17 % выходом.

Routes to D-allose and D-altrose are usually based on elongation of the carbon chain of D-ribose either by cyanohydrine [1] or nitromethane [2] synthesis. Important reaction for the preparation of D-allose is the nucleophilic substitution of the tosyl group in 1,2,4,6-tetra-*O*-benzoyl-3-*O*-(*p*-toluenesulfonyl)-β-D-glucopyranose by sodium benzoate [3]. Several other reactions affording D-allose and D-altrose from suitable derivatives of hexoses are in general more interesting from theoretical and stereochemical aspects than from a preparative point of view. The subject of the present work is a simple procedure for preparation of D-allose and D-altrose directly from D-glucose.

Epimerization of arbitrary aldose in aqueous solutions under mild conditions, *e.g.* in the presence of 0.1—1.0 % molybdenic acid at a temperature of 70—90 °C for 2—8 h, leads to an equilibrium mixture of C-2-epimeric aldoses. The aldose that possesses lower value of conformational stability in the preferred conformation predominates in the mixture [2]. Under the mentioned reaction conditions the epimerization of D-glucose [4], L-mannose [5] or L-rhamnose [6] gives an equilibrium mixture of the starting aldose and its 2-epimer. The formation of the corresponding 2-ketoses and complementary C-3-epimeric

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aldoses was not observed. Similarly, the epimerization of D-allose and D-altrose leads only to their interconversion without formation of the C-3-epimeric aldoses, D-glucose and D-mannose [2].

However, the epimerization under mild conditions of aldopentoses [7—9], D-galactose [10], D-talose [11], and aldoheptoses [12] affords in addition to the C-2-epimeric aldoses small amount of the complementary pair of the C-3-epimeric aldoses. It is assumed that the formation of the C-3-epimeric aldoses is conditioned by migration of hydrogen atoms between carbon atoms C-2 and C-3 [9,11, 13, 14]. The formation of the C-3-epimeric aldoses is envisaged as a reaction that can proceed only when the hydrogen atoms at C-2 and C-3 are in *trans*-diaxial arrangement [13, 14]. This would mean that arabinose can be converted to xylose [15] and D-galactose to D-idose [10] or *vice versa*, and that the C-3 epimerization is by two orders slower than the C-2 epimerization [15].

The molybdate-catalyzed epimerization of D-glucose to D-mannose at enhanced temperatures (120—150 °C) was found to be accompanied by formation of a significant amount of D-allose and D-altrose (14—17 %). The epimerization of D-glucose at carbon atoms C-2 and C-3 can be schematically illustrated as follows

$$\underset{(20\,\%)}{\text{D-mannose}} \rightleftharpoons \underset{(65\,\%)}{\text{D-glucose}} \rightleftharpoons \underset{(5\,\%)}{\text{D-altrose}} \rightleftharpoons \underset{(10\,\%)}{\text{D-allose}}$$

The results in Table 1 indicate that the same reaction time (2—3 h) gave about the same yield of D-allose and D-altrose at 150 °C as at 120 °C, however, at four

Table 1

Formation of D-allose and D-altrose during epimerization of 2 M D-glucose in aqueous 0.1 M solution of acetic acid containing different amounts of ammonium molybdate as a function of time at two different temperatures

Ammonium molybdate c/(mol dm^{-3})	D-Allose/% D-Altrose/%					
	120 °C			150 °C		
	t/h			t/h		
	2	4	6	2	4	6
0.001	3.5	5.3	7.7	10.1	8.8	8.4
	2.5	3.5	5.3	6.9	6.2	5.6
0.002	4.6	7.0	8.5	10.4	9.1	7.8
	3.2	4.8	5.6	7.1	6.3	5.2
0.004	8.9	8.4	8.1	8.8	8.4	7.6
	5.9	6.0	5.6	6.0	5.6	5.0
0.008	9.8	9.1	9.0	8.8	7.4	6.7
	6.4	6.0	6.0	5.7	4.9	4.6

times increased concentration of molybdate ions. Reaction times longer than 3 h did not lead to higher yields at temperatures of 140—150 °C because an increased decomposition of saccharides occurred.

The epimerization of D-glucose at enhanced temperatures can be applied for preparation of D-allose and D-altrose. D-Glucose and D-mannose can be removed from the reaction mixture by yeast fermentation, and D-allose is isolated from the residue by chromatography on a column of an ion exchanger containing the sulfo groups in Ca^{2+} form using elution with 50 % ethanol. D-Altrose is further purified by chromatography on a cellulose column in a neutral solvent system. The epimerization of D-glucose at enhanced temperatures is accompanied by formation of small amounts of reversion products, anhydrohexoses and aldopentoses as a consequence of the carbon chain cleavage. All these by-products were effectively removed during chromatographic fractionation.

Experimental

Monitoring of the conversion of D-*glucose to* D-*allose and* D-*altrose*

Sealed thick-wall glass test-tubes containing 5 cm^3 of aqueous solution of D-glucose (1.8 g; 10 mmol), 3×10^{-2} cm^3 (0.5 mmol) of acetic acid and 6.2, 12.4, 24.7 or 49.4 mg (5, 10, 20 or 40 μmol) of ammonium molybdate ($(NH_4)_6Mo_7O_{24} \cdot 4H_2O$) were heated on a silicone oil bath at 120 or 150 °C for 2, 4 or 6 h (Table 1). The content of the test-tubes was then mixed with 5 cm^3 of water and 10 cm^3 of a suspension of activated charcoal in water (2 g of charcoal in 100 cm^3 of water) and filtered. The filtrate was mixed with 20 cm^3 of a suspension of the yeast *Saccharomyces cerevisiae* (5 g of pressed yeast in 100 cm^3 of water) and incubated at room temperature until D-glucose and D-mannose completely disappeared (3 days). After filtering off the yeast, the solution was evaporated to dryness, the residue dissolved in 5 cm^3 of water and after addition of 5 cm^3 of methanol filtered. The filtrate was adjusted to 10 cm^3 with methanol and aliquots of 2×10^{-2} cm^3 were chromatographed on Whatman No. 1 paper in acetone—1-butanol—water ($\varphi = 7:2:1$) for 18—20 h at 23 °C. After detection of sugars with the anilinium hydrogen phthalate reagent for 5 min at 105 °C (1 cm^3 of aniline and 1.5 g of phthalic acid in 100 cm^3 of acetone) the areas corresponding to D-allose and D-altrose were cut out, eluted with 5 cm^3 of water (24 h at room temperature) and the absorbance of the eluates was measured at 308 nm in 1 cm cuvettes on a UNICAM SP 1700 spectrophotometer. The ratios of absorbances referred to known amounts of D-allose and D-altrose were found to correspond to the mass ratios of aldoses (Table 1). The chromatographic mobility of compounds related to that of D-glucose (1.00) was 1.11 for D-allose, 1.64 for D-altrose, and 1.29 for D-mannose.

Preparation of D-*allose and* D-*altrose from* D-*glucose*

A mixture of D-glucose monohydrate (198 g), ammonium molybdate (5 g), acetic acid (15 cm^3), and water (450 cm^3) was heated in a pressure vessel at 120 °C for 2 h. The

temperature was reached within 1 h. The mixture was then diluted with distilled water (1000 cm^3) and tap water (1000 cm^3) and, after addition of 30 g of pressed yeast (*Saccharomyces cerevisiae*), left to stand to remove D-glucose and D-mannose (3 days). The mixture was then filtered, concentrated to 500 cm^3, treated with activated charcoal and evaporated. The sirupy residue was chromatographed on a column (3.5 cm × 110 cm) of an Ostion KS 0210 ion exchanger in Ca^{2+} form using elution with 50 % ethanol. First 1500 cm^3 were collected at a flow rate of 100 $cm^3 h^{-1}$, further volume at a flow rate of 300 $cm^3 h^{-1}$. Fraction *1* (400—650 cm^3) contained reversion products and anhydroaldoses (6 g), fraction *2* (650—1250 cm^3) contained D-altrose plus small portion of reversion products (11 g), fraction *3* (1250—1750 cm^3) D-allose and D-altrose (6 g) in the ratio 1 : 1 and fraction *4* (1750—6000 cm^3) D-allose (14 g). D-Altrose was isolated from fraction *2* by rechromatography on a cellulose column (3.5 cm × 50 cm) in 1-butanol—ethanol—water ($\varphi = 5:1:4$). Chromatographically homogeneous aldoses were obtained by crystallization from alcohols. D-Allose crystallized from methanol showed m.p. = = 130—132 °C, $[\alpha]$ (D, 23 °C) = +14.1° ($c = 2$, water) or $[\alpha]$ (D, 23 °C) = −62° ($c = 1.5$, 4 % aqueous solution of ammonium molybdate). D-Altrose crystallized from anhydrous ethanol showed m.p. = 104—107 °C and $[\alpha]$ (D, 23 °C) = +31.5° ($c = 2$, water) or $[\alpha]$ (D, 23 °C) = +40° ($c = 1.5$, 4 % aqueous solution of ammonium molybdate). Ref. [16] gives for D-allose m.p. = 128—128.5 °C and $[\alpha]$ (D, 20 °C) = +14.4° ($c = 1.3$, water). Ref. [17] gives for D-altrose m.p. = 103—105 °C and $[\alpha]$ (D) = +32.6° ($c = 7.6$, water).

Fraction *1* from the ion-exchange chromatography containing reversion products and anhydroaldoses was rechromatographed on a cellulose column (3.5 cm × 50 cm) in 1-butanol—ethanol—water ($\varphi = 5:1:4$). Anhydroaldoses (3 g) were analyzed by chromatography on Whatman No. 1 paper in acetone—1-butanol—water ($\varphi = 7:2:1$) (6 h, 23 °C) followed by detection with the method of *Trevelyan* [18]. The mobility of compounds relative to that of D-glucose (1.00) was 2.7 for 1,6-anhydro-D-glucose, 3.0 for 1,6-anhydro-D-allose, and 3.3 for 1,6-anhydro-D-altrose.

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