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

\[
\text{D-mannose} \rightleftharpoons \text{D-glucose} \rightleftharpoons \text{D-altrose} \rightleftharpoons \text{D-allose}
\]

(20%) (65%) (5%) (10%)

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>
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<tr>
<th>Ammonium molybdate (c/(\text{mol dm}^{-3}))</th>
<th>(120°C)</th>
<th>(150°C)</th>
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<tr>
<td>(t/h)</td>
<td>(D-\text{Allose}/%)</td>
<td>(D-\text{Altrose}/%)</td>
</tr>
<tr>
<td>0.001</td>
<td>3.5</td>
<td>5.3</td>
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<tr>
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<tr>
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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 Ca2+ 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 cm³ of aqueous solution of D-glucose (1.8 g; 10 mmol), 3 × 10⁻² cm³ (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 [(NH₄)₆Mo₇O₂₄·4H₂O] 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 cm³ of water and 10 cm³ of a suspension of activated charcoal in water (2 g of charcoal in 100 cm³ of water) and filtered. The filtrate was mixed with 20 cm³ of a suspension of the yeast Saccharomyces cerevisiae (5 g of pressed yeast in 100 cm³ 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 cm³ of water and after addition of 5 cm³ of methanol filtered. The filtrate was adjusted to 10 cm³ with methanol and aliquots of 2 × 10⁻² cm³ were chromatographed on Whatman No. 1 paper in acetone—1-butanol—water (φ = 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 cm³ of aniline and 1.5 g of phthalic acid in 100 cm³ of acetone) the areas corresponding to D-allose and D-altrose were cut out, eluted with 5 cm³ 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 cm³), and water (450 cm³) 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 x 110 cm) of an Ostion KS0210 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 x 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-Allose 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 x 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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References


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