Reactions of saccharides catalyzed by molybdate ions. XI.* Preparation of L-glycero-L-galacto- and L-glycero-L-taloheptose

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Epimeric aldoheptoses have been obtained by oxidative decomposition of a mixture of sodium salts of nitroheptitols prepared from L-mannose. The aldoheptoses have been characterized by p.m.r. spectroscopy and by gas—liquid chromatography of their per-*O*-trimethylsilyl derivatives.

Nitroalditols represent important derivatives used for many purposes in carbohydrate chemistry. *Pictet* and *Barbier* [1] introduced the nitromethane synthesis for extension of the carbon chain of aldoses; nitroalditols formed in the reaction afforded, after reduction and subsequent removal of the amino group, the corresponding alditols. The nitromethane synthesis found a general use in carbohydrate chemistry after *Sowden* [2] with his associates had elaborated optimum reaction conditions and employed the conversion of sodium salts of nitroalditols to aldoses by diluted mineral acids (Nef reaction). We have recently reported [3] that nitroalditols can as effectively be transformed into aldoses in alkaline medium with hydrogen peroxide under a catalysis with molybdate ions. This paper is devoted to the preparation of L-glycero-L-galacto- and L-glycero-L-taloheptose by oxidative decomposition of the corresponding nitroheptitols.

Condensation of D-mannose with nitromethane was carried out by *Sowden* and *Schaffer* [4] in methanol and led to 55% conversion to epimeric nitroalditols (lower yields were obtained in aqueous reaction medium [5]). By fractional crystallization they isolated 1-deoxy-1-nitro-D-glycero-D-galactoheptitol (37%) and 1-deoxy-1-nitro-D-glycero-D-taloheptitol (10%) which afforded on subsequent Nef reaction the corresponding aldoheptoses. Analogous treatment of L-mannose described herein gave a mixture of sodium salts of epimeric nitroheptitols, which, in the presence of hydrogen peroxide and a catalytic amount of molybdate ions, gave the corresponding L-aldoheptoses, sodium nitrite and nitrate. Excess of hydrogen peroxide was decomposed by Pd/C and sodium nitrite by acetic acid. Deionized mixture of aldoheptoses yielded on crystallization 33% of L-glycero-L-galactoheptose. Fractionation of the mother liquor on Dowex 50 W (Ba^{2+} form) led to recovery of additional 10% of L-glycero-L-galactoheptose and 12% of L-glycero-L-taloheptose. The separation of these epimeric aldoheptoses by ion-exchange chromatography was very effective, similarly to that of L-galactose and L-talose [3]. The elution volume of L-glycero-L-taloheptose was three times larger than that of L-glycero-L-galactoheptose.

Crystallization from a mixture water—methanol—ethanol gave L-glycero-L-galactoheptose monohydrate, m.p. 131—134°C, $[\alpha]_D^{21}$ −115.5° → −62° (equil.), from a mixture methanol—acetic acid L-glycero-L-taloheptose, m.p. 108—110°C, $[\alpha]_D^{21}$ −43° → −13.3° (equil.) (Table 1). Monitoring of the mutarotation in heavy water by p.m.r. spectroscopy

* For Part X see Ref. [3].

Table 1

Specific rotations and melting points of aldoheptoses

Time	L-Glycero-L-galactoheptose monohydrate	L-Glycero-L-taloheptose
	$[\alpha]_D^{21}$ (*c* 3, water)	
0	(−115.5)	(−43.0)
2.5 min	−113.1	−32.1
3	−112.6	−31.2
4	−111.6	−27.2
6	−109.6	−23.2
8	−108.3	−20.3
10	−106.1	−18.9
15	−102.9	−16.2
20	−99.8	−15.7
30	−94.1	−14.0
40	−88.0	−13.6
1 hr	−78.4	−13.4
1.5	−68.5	−13.3
2	−64.6	−13.3
3	−62.6	
24	−62.0	−13.3
	Melting points [°C] (Kofler)	
	131−134	108−110

Table 2

The p.m.r. data of the anomeric protons of aldoheptoses

Aldoheptose	Chemical shift (p.p.m.)		Coupling constants (Hz)	
	H-1 α-pyrano	H-1 β-pyrano	$J_{1,2}$ α-pyrano	$J_{1,2}$ β-pyrano
L-Glycero-L-galacto-	5.22	4.55	2.5	7.2
L-Glycero-L-talo-	5.23	4.78	2.0	1.3

[6] showed that the crystalline aldoheptoses possess the α-pyranoid form. The p.m.r. spectra recorded at equilibrium did not contain explicit signals of other anomeric protons besides those of the α- and β-pyranoid form (Table 2). It is assumed therefore that the aldoheptoses are predominantly in the pyranoid form in the heavy water solutions. Gas—liquid chromatography of the trimethylsilyl derivatives of the crystalline preparations showed that the α-pyranoid form of L-glycero-L-galactoheptose and L-glycero-L-taloheptose is accompanied respectively with 3.6 and 2.5% of the β-pyranoid form.

Two additional unknown anomeric components were detected in pyridine solutions of both aldoheptoses (anomerization for 18 hrs at room temperature) (Table 3). In analogy

Table 3

Equilibrium states of aldoheptose anomers in pyridine solutions followed by gas—liquid chromatography

Aldoheptose		Column *A* RRT	Column *A* (%)	Column *B* RRT	Column *B* (%)
L-Glycero-L-galacto-	(F)	2.48	9.4	7.50	10.8
	(αP)	3.42	44.9	9.48	43.8
	(F)	3.63	6.1	10.81	6.3
	(βP)	4.85	39.6	14.50	39.1
L-Glycero-L-talo-	(F)	2.66	3.8	6.31	0.3
	(αP)	2.76	68.9	7.76	67.8
	(F)	3.12	15.9	8.91	16.7
	(βP)	4.26	12.0	12.30	15.2
Methyl-tetra-*O*-methyl-α,D-glucopyranoside		1.00 (t'_R 6.80 min, t_{CH_4} 7.8 min)		1.00	(t'_R 2.02 min)

(F) — furanoid form,
(P) — pyranoid form,
RRT — retention times of per-*O*-trimethylsilyl derivatives related to those of methyl-tetra-*O*-methyl-α,D-glucopyranoside,
% — percentage of individual components at equilibrium.

with the observation that furanoid forms are present in pyridine solutions of D-galactose [7, 8] and D-talose [8], one can assume that the unknown peaks on the chromatographic chart correspond to the furanoid forms of aldoheptoses.

Experimental

Specific rotations of saccharides were measured with an automatic Perkin—Elmer polarimeter, type 141 and melting points were determined on a Kofler stage.

The p.m.r. spectra of aldoheptoses were recorded with a Tesla 487 B (80 MHz) spectrometer in heavy water at 25 and 50°C using DSS as an internal standard (Table 2).

Gas—liquid chromatography was done with a Hewlett—Packard 5754 G gas chromatograph on a stainless steel capillary column (*A*) (45 m × 0.2 mm) packed with OV-17 at a temperature of 215°C and an inlet pressure of 0.7 atm. The temperature of the detector and injection port was 250°C, inlet splitter 1 : 100. Gas—liquid chromatography was performed also with a Hewlett—Packard 5711A equipment using a stainless steel column (*B*) (1.8 m × 3 mm) packed with 10% UC-W98 on Chromosorb W-HP (80—100 mesh) at a temperature of 212°C, flow rate 19.5 ml/min and a temperature of the detector and the injection port 250°C. In both cases flame ionization detector and nitrogen as a carrier gas were used.

Crystalline aldoheptoses were trimethylsilylated with a mixture trimethylchlorosilane—hexamethyldisilazane—pyridine (1 : 2 : 10) [13]. Equilibrium states of aldoheptoses in pyridine solutions were followed by gas—liquid chromatography. After 18-hr standing at room temperature, the solutions were treated with a mixture trimethylchlorosilane—hexamethyldisilazane (1 : 2) for 2 hrs and injected. Retention times of per-*O*-trimethylsilyl derivatives of aldoheptoses (Table 3) are related to an internal standard, methyl-tetra-*O*-methyl-α,D-glucopyranoside.

Preparation of L-*glycero*-L-*galactoheptose and* L-*glycero*-L-*taloheptose*

Nitromethane synthesis

A suspension of powdery L-mannose [3] (40 g) in methanol (300 ml) was mixed first with nitromethane (80 ml) and then with sodium methanolate (10 g of sodium in 300 ml of methanol) under stirring. After agitation for 8 hrs, the reaction mixture was left to stand at room temperature for 20 hrs. Separated sodium salts of nitroheptitols were filtered off and washed with methanol (3 × 50 ml).

Oxidative decomposition

To a solution of sodium salts of nitroheptitols in 0.05 M-NaOH (400 ml), sodium molybdate (2 g) was added followed by addition of 15% hydrogen peroxide (80 ml) at a rate to keep the temperature of the reaction mixture below 35°C. After standing at room temperature for 20 hrs, the mixture was treated with 5% Pd/C (*ca.* 0.5 g) for 24 hrs. Finally acetic acid (10 ml) was added and the solution was bubbled with air for 4 hrs, filtered, and deionized on columns of ion-exchangers in the order Wofatit SBW (acetate form, 4.5 × 100 cm), Wofatit KPS (H^+ form, 5 × 100 cm), and Wofatit SBW (acetate form, 3 × 90 cm). Water eluates (8 l) were evaporated to syrup which was dissolved in methanol, purified with charcoal, and evaporated again. Resulting syrup was dissolved in methanol (60 ml), mixed with acetic acid (30 ml), and crystallized at room temperature for 24 hrs to give a first portion of L-glycero-L-galactoheptose (15.6 g, *i.e.* 33.4%). The mother liquor was deprived of acetic acid by repeated evaporation with water and fractionated on a Dowex 50 W (X-8, 100—200 mesh, Ba^{2+} form) column (3.5 × 120 cm) using elution with water at a flow rate of 35 ml/hr. L-Glycero-L-galactoheptose (4.7 g, 10.1%) was isolated from the elution volume 580—740 ml, 1.9 g of the mixture of L-glycero-L-galactoheptose and L-mannose in the ratio 1 : 1 from the volume 740—810 ml, 3.2 g of L-mannose from the volume 810—960 ml and 5.7 g (12.2%) of L-glycero-L-taloheptose from the volume 1510—2100 ml.

L-Glycero-L-galactoheptose (A g) was dissolved in a mixture water—methanol—ethanol (1 : 1 : 1) (3 × A ml) and L-glycero-L-taloheptose (A g) in a mixture methanol—acetic acid (2 : 1) (3 × A ml). Resulting solutions were left to crystallize at room temperature for 3—4 days. Separated aldoheptoses (30—35%) were filtered off, washed with cold methanol, and dried over P_2O_5.

For L-glycero-L-galactoheptose monohydrate ($C_7H_{14}O_7 \cdot H_2O$) calculated: 36.83% C, 7.09% H; found: 36.84% C, 6.85% H.

For L-glycero-L-taloheptose ($C_7H_{14}O_7$) calculated: 40.00% C, 6.71% H; found: 39.87% C, 6.75% H.

For the D-antipodes of the aldoheptoses literature gives the following melting points and specific rotations in water: for α,D-glycero-D-galactoheptose Ref. [9] m.p. 140°C, Ref. [10] m.p. 145°C, $[\alpha]_D^{20}$ 124° → 69.0° (*c* 4); Ref. [4] m.p. 135—137°C, $[\alpha]_D^{25}$ 68.1° (*c* 3.5); for α,D-glycero-D-galactoheptose monohydrate Ref. [9, 11] m.p. 107°C, $[\alpha]_D^{20}$ 120° → 64.7°

(*c* 3.5), Ref. [10] m.p. 115—120°C, $[\alpha]_D^{20}$ 123.8° → 69.0° (*c* 4); for β,D-glycero-D-galactoheptose monohydrate Ref. [9, 11] m.p. 104°C, $[\alpha]_D^{20}$ 42.3° → 64.5° (*c* 4), Ref. [10] m.p. 104°C, $[\alpha]_D^{20}$ 52.9° → 68.8° (*c* 4); for D-glycero-D-taloheptose Ref. [12] m.p. 140°C, $[\alpha]_D$ 7.6° (*c* 5), and for α,D-glycero-D-taloheptose monohydrate Ref. [9] m.p. 83°C, $[\alpha]_D^{20}$ 45.7° → 14.7° (*c* 4) and Ref. [4] m.p. 83—84°C, $[\alpha]_D^{25}$ 15.8° (*c* 3.5).

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