Reactions of saccharides catalyzed by molybdate ions XXXV.* Preparation of D-*erythro*-L-glucooctose and D-*erythro*-L-mannooctose

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Dedicated to Professor RNDr. V. Sutoris, CSc., in honour of his 60th birthday

Sodium salts of the epimeric 1-deoxy-1-nitrooctitols obtained by nitromethane synthesis with D-*glycero*-D-galactoheptose were converted by hydrogen peroxide under catalytic action of molybdate ions into D-*erythro*-L-glucooctose and D-*erythro*-L-mannooctose. Molybdate-catalyzed epimerization of D-*erythro*-L-mannooctose led to a mixture of epimeric aldooctoses in which D-*erythro*-L-glucooctose predominated. The aldooctoses occur in pyranoid structures in aqueous solutions and their complexing with molybdate ions induces furanoid structures.

Натриевые соли эпимерных 1-дезокси-1-нитрооктитолов, полученных посредством нитрометанового синтеза из D-*глицеро*-D-галактогептозы, были превращены действием перекиси водорода в присутствии молибдат-ионов в качестве катализатора в D-*эритро*-L-глюкооктозу и D-*эритро*-L-маннооктозу. Катализируемая молибдат-ионами эпимеризация D-*эритро*-L-маннооктозы приводит к образованию эпимерных альдооктоз, среди которых преобладала D-*эритро*-L-глюкооктоза. Альдооктозы имеют в водных растворах пиранозную структуру, а их комплексообразование с молибдат-ионами вызывает переход в фуранозную форму.

Of the large group of octoses, aldooctoses, in contrast to 2-octuloses (D-*glycero*-D-mannooctulose, D-*glycero*-L-galactooctulose), have not been reported to occur in natural material. Of 128 theoretically possible aldooctoses, only a few were prepared synthetically. The cyanohydrine synthesis with aldoheptoses leads to epimeric aldooctonic acids which are usually separated in the form of suitable salts and subsequently reduced to corresponding aldooctoses. This approach led to preparation of D-*erythro*-D-galactooctose [1], D-*erythro*-L-galactooctose, D-*erythro*-L-gulooctose, D-*erythro*-L-talooctose [2], D-*threo*-L-galactooctose [3], and D-*erythro*-L-mannooctose [4]. Nitromethane synthesis with D-*glycero*-D-galactoheptose gave sodium salt of 1-deoxy-1-nitro-D-*erythro*-L-

* For Part *XXXIV* see Ref. [12].

-mannooctitol which, on the Nef reaction (decomposition with sulfuric acid), gave D-*erythro*-L-mannooctose which was isolated as its phenylhydrazone [5]. Nitromethane synthesis was also employed for the preparation of D-*erythro*-L--galactooctose, D-*erythro*-L-talooctose, D-*threo*-L-galactooctose, and D-*threo*--L-talooctose, the sodium salts of 1-deoxy-1-nitrooctitols being decomposed by hydrogen peroxide under catalytic action of molybdate ions [6].

More recent procedures for the elongation of the carbon chain of aldoses involve the Wittig reaction leading to unsaturated saccharide derivatives which, on hydroxylation of the double bond and further processing, afford aldooctoses. This principle was used for preparing D-*threo*-L-galactooctose [7], D-*erythro*-D-galactooctose [8], 8-deoxy-D-*erythro*-D-galactooctose [9], and 1,2:3,4-di-*O*-isopropylidene derivatives of D-*erythro*-, L-*erythro*-, D-*threo*-, L-*threo*-D-galactooctopyranose [8] and 8-deoxy-1,2:3,4-di-*O*-isopropylidene-D-*erythro*-D-galactooctopyranose [8, 9].

In the present work we report on the preparation of D-*erythro*-L-glucooctose and D-*erythro*-L-mannooctose and on the form of their existence in aqueous solutions in the absence and in the presence of ammonium molybdate.

Nitromethane synthesis with D-*glycero*-D-galactoheptose in a solution of methanol and dimethyl sulfoxide in the presence of sodium methoxide gave sodium salts of the epimeric 1-deoxy-1-nitrooctitols which were oxidatively decomposed [10] to D-*erythro*-L-mannooctose and D-*erythro*-L-glucooctose. The aldooctoses were isolated from the reaction mixture by ion-exchange chromatography on a Dowex 50 W (Ba^{2+} form) column eluted with water. This step afforded chromatographically pure D-*erythro*-L-mannooctose, while D-*erythro*-L-glucooctose was obtained with some D-*glycero*-D-galactoheptose as admixture. Chromatographically homogeneous D-*erythro*-L-glucooctose was isolated from the mixture by crystallization from aqueous methanol. Referred to the starting D-*glycero*-D-galactoheptose, D-*erythro*-L-glucooctose and D-*erythro*-L-mannooctose were obtained in 20 % and 36 % yields, respectively. In terms of the Maltby rule, D-*erythro*-L-mannooctose was the main reaction product, similarly as in an analogous cyanohydrine synthesis [4].

In the molybdate-catalyzed epimerization D-*erythro*-L-mannooctose was converted to a mixture of epimeric aldooctoses in which D-*erythro*-L-glucooctose predominated. A part of this aldooctose was separated from the epimerization mixture by direct crystallization while the second portion of the sugar was obtained by ion-exchange chromatography on Dowex 50 W (Ba^{2+}). The overall yield of D-*erythro*-L-glucooctose, referred to the starting D-*erythro*-L-mannooctose, was 60 %.

D-*erythro*-L-Glucooctose has not been described yet in the literature. Crystallized from a methanol—water mixture it showed m.p. = 170—172 °C, α(D, 20 °C, 1 g dm^{-3}, water) = −59.2° (extrapol.) → −38.1° (equilibrium) or α(D, 20 °C,

Table 1

^{13}C NMR data of aldooctoses

Compound	Complex	Chemical shifts δ/ppm							
		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
D-*erythro*-L-Glucooctose									
Water									
Anomer *cis*		93.4	72.7	74.2	70.0	71.6	71.9	70.4	64.5
trans		97.2	74.7	75.4	69.0	77.2	68.9	70.4	64.5
Ammonium molybdate									
	I	99.8*	77.2	80.4	81.2	83.0	83.2	91.5	70.0
	II	98.8*	80.4	91.7	86.8	83.0	83.2	73.0	70.0
D-*erythro*-L-Mannooctose									
Water									
Anomer *cis*		95.1	72.5	74.6	66.9	74.9	69.2	71.8	64.5
trans		95.4	71.9	71.8	67.3	71.3	69.3	71.9	64.5
Ammonium molybdate									
Anomer *cis*	*III*	95.5	91.6	82.2	82.0	83.2	83.2	91.6	69.9
trans	*IV*	94.3	82.6	79.5	82.0	80.2	77.4	73.0	69.9
D-Arabinitol									
Water		64.2	71.5	71.7	72.2	64.3			
Ammonium molybdate**		63.8	82.8	82.9	91.5	70.2			

* The *cis* and *trans* forms are present in both types of complexes (*I*, *II*).

** The complex with the hydroxyl groups at C-2, C-3, and C-4.

Table 2

^{1}H NMR data of the acyclic parts of aldooctoses and D-arabinitol

Compound	Chemical shifts δ/ppm					Coupling constants J/Hz					
	H-5	H-6	H-7	H-8	H-8′	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8}$	$J_{7,8'}$	$J_{8,8'}$
D-*erythro*-L-Glucooctose											
Water											
Anomer *cis*	*					9.14					
trans	4.00	3.86	3.75	3.87	3.65	*	1.24	8.86	2.57	6.47	11.62
Ammonium molybdate	—	—	—	4.13	4.43	—	—	—	~0	2.24	9.70
D-*erythro*-L-Mannooctose											
Water											
Anomer *cis*	4.03					*	1.27				
trans	3.57	3.91	3.82	3.92	3.71	9.69	1.00	8.80	2.54	6.35	11.50
Ammonium molybdate	4.70	4.90	4.79	4.37	4.10	—	—	—	~0	3.00	10.00

Compound	Chemical shifts δ/ppm							Coupling constants J/Hz							
	H-1	H-1′	H-2	H-3	H-4	H-5	H-5′	$J_{1,1'}$	$J_{1,2}$	$J_{1',2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$
D-Arabinitol															
Water	3.97	3.97	4.23	3.87	4.05	4.14	3.96	6.21	5.74	5.68	2.04	8.33	6.20	2.72	11.47
Ammonium molybdate	3.80	3.94	4.58	4.67	4.77	4.12	4.40	11.14	8.20	5.28	0.81	4.40	<0.2	2.20	10.26

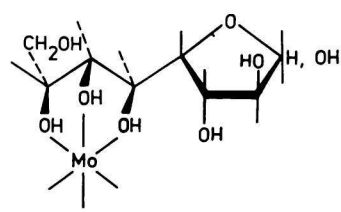
* Not assigned.

1 g dm^{-3}, 4 % aqueous solution of ammonium molybdate) = −80°. D-*erythro*-L-Mannooctose has already been described [4] as a crystalline compound, m.p. = 154 °C, α(D, 20 °C, 2 g dm^{-3}, water) = +11.7° (extrapol.) → −7.5° (equilibrium). Our attempts to crystallize D-*erythro*-L-mannooctose were unsuccessful despite the sugar was chromatographically homogeneous with α(D, 20 °C, 1 g dm^{-3}, water) = −6.4° ± 0.5° or α(D, 20 °C, 1 g dm^{-3}, 4 % aqueous solution of ammonium molybdate) = −23.5°.

The structural arrangements of D-*erythro*-L-glucooctose and D-*erythro*-L-mannooctose in aqueous solutions and in solutions of ammonium molybdate were studied by ^1H and ^{13}C NMR spectroscopy. The assignments for signals of the carbon atoms of the aldooctose rings were done on the basis of published data [11—15] (Table 1). The signals of the acyclic part of the molecules were assigned by using the spectral data of arabinitol recorded under the same conditions (Table 2). According to the chemical shifts in ^{13}C NMR spectra and the coupling constants of anomeric protons in ^1H NMR spectra ($J_{1,2(cis)} = 3.62$ Hz, $J_{1,2(trans)} = 7.9$ Hz for D-*erythro*-L-glucooctose; $J_{1,2(cis)} = 1.11$ Hz, $J_{1,2(trans)} = 1.8$ Hz for D-*erythro*-L--mannooctose), the aldooctoses occur in aqueous solutions in the pyranoid forms. Coupling constants for the acyclic parts of the molecules, $J_{5,6}$ to $J_{7,8}$, were almost identical with those of arabinitol, suggesting a similarity in their arrangement (Table 2).

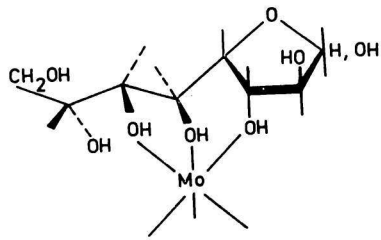
In the presence of ammonium molybdate the NMR spectra of aldooctoses showed significant changes both in chemical shifts and coupling constants. The ^{13}C NMR spectra showed that about 50 % of D-*erythro*-L-glucooctose and 90 % of D-*erythro*-L-mannooctose were complexed with molybdate. The uncomplexed portion of both aldooctoses occurred in the pyranoid forms.

^1H NMR spectra of aldooctose complexes with molybdate are very complicated and not all signals could be assigned. The complex formation was assessed mainly from the H-1 and H-2 signals indicating the interaction of molybdate with the hydroxyl groups of the furanoid ring [12]. On the other hand, the changes of chemical shifts and coupling constants of protons H-5 to H-8 served as an evidence for the complex formation with the hydroxyl groups of the side chain (Table 2). D-*erythro*-L-Glucooctose forms a complex through the hydroxyl groups at carbon atoms C-5, C-6, and C-7, which is accompanied by a conformational change of the side chain (*I*).



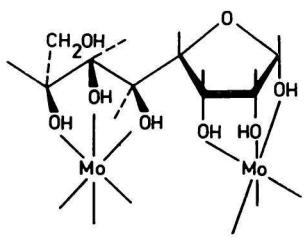
I

In addition to the signals of H-8 and H-8′ of D-*erythro*-L-glucooctose in the absence of molybdate (Table 2) the ^{1}H NMR spectrum recorded in the presence of molybdate contains new H-8 and H-8′ signals ($\delta = 4.38$ ppm (d) and 4.54 ppm (q)) with coupling constants $J_{8,8'} = 10.5$ Hz and $J_{7,8} = 3.1$ Hz. These data suggest that the complex formation involves two hydroxyl groups of the side chain (C-5 and C-6) and one of the furanoid ring (C-3) (*II*).

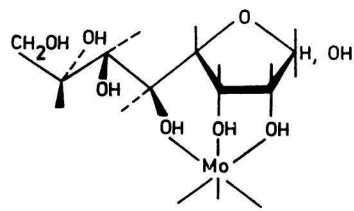


II

Steric conditions for the formation of a similar complex are fulfilled also in the case of D-*erythro*-L-mannooctose. Analysis of the spectra of D-*erythro*-L-mannooctose pointed out, however, that other two molybdate complexes predominate (*III*, *IV*).



III



IV

One complex (*IV*) involves the hydroxyl groups at C-2, C-3, and C-5, forcing thus the *trans*-anomer ($J_{1,2} < 0.2$ Hz). In the other, clearly predominating, D-*erythro*-L-mannooctose complexes with two molybdate ions through the hydroxyl groups at C-1, C-2, C-3 and at C-5, C-6, C-7 (*III*).

The different structural arrangement of the studied aldooctoses in water (pyranoid structures) and in aqueous solution of ammonium molybdate (furanoid structures) is mainly caused by the fact that molybdate complexes are preferentially formed with the hydroxyl groups at C-5, C-6, and C-7 (*I*). Moreover, in the case of D-erythro-L-mannooctose, the two to one complex is formed (*III*) together with

additional recombinant complexes (*II* and *IV*) in which the furanoid structure of aldooctoses remains preserved.

Experimental

^{1}H NMR spectra of aldooctoses and of D-arabinitol were measured with an FT-NMR Bruker AM-300 spectrometer (300.13 MHz) at a temperature of 294 K in D_2O in the absence and in the presence of ammonium molybdate (m(molybdate) : m(saccharide) = = 2 : 1). Methanol was used as internal standard ($\delta = 3.40$ ppm) and homocorrelated spectra (COSY45) were employed for the assignments of proton signals. Digital resolution was 0.18 Hz per point. ^{13}C NMR spectra (75.46 MHz) were measured under the same conditions using again methanol as internal standard ($\delta = 50.15$ ppm). Digital resolution was 2.5 Hz per point.

Melting points were determined on a Kofler stage and optical rotations were measured with an automatic Perkin—Elmer 141 polarimeter. Water or 4 % aqueous solution of ammonium molybdate were used as the solvents.

Composition of reaction mixtures and purity of saccharides was followed by chromatography on Whatman No. 1 paper eluted with n-butanol—ethanol—water mixture (volume ratio = 5 : 1 : 4) for 50—70 h at 20—24 °C. The relative mobility referred to that of D-*glycero*-D-galactoheptose (1.00) is 0.82 for D-*erythro*-L-glucooctose and 1.14 for D-*erythro*-L-mannooctose.

Preparation of D-*erythro*-L-*glucooctose and* D-*erythro*-L-*mannooctose*

Nitromethane synthesis

A solution of D-*glycero*-D-galactoheptose [16] (100 g) in a mixture of dimethyl sulfoxide (200 cm^3) and methanol (300 cm^3) was mixed with nitromethane (200 cm^3) and methanolic solution of sodium methoxide (23 g of sodium in 750 cm^3 of methanol) added in portions under stirring. The mixture was agitated for 7 h and then left to stand at room temperature for 20 h. The sodium salts of nitrooctitols were filtered off and washed with methanol (3×50 cm^3).

Oxidative decomposition

The sodium salts of nitrooctitols were added in portions in the course of 5—10 min to a mixture of 0.5 M aqueous solution of sodium hydroxide (1000 cm^3), 30 % aqueous hydrogen peroxide (100 cm^3), and ammonium molybdate (4 g). Because of heat development, the mixture was cooled during the first two hours to keep the temperature below 30 °C. After 20 h standing at room temperature, the mixture was mixed with acetic acid (10 cm^3) and immediately air-bubbled for 2—3 h. After addition of a small amount of 5 % Pd/C, the mixture was left to stand for 24 h and then filtered. The filtrate was deionized on 500 cm^3 of Ostion KS 0210 cation exchanger in H^+ form and on 500 cm^3 of Ostion

AT 0209 anion exchanger in HCO_3^- form. The deionized solution was concentrated and fractionated by chromatography.

Isolation

One fifth of the distillation residue was fractionated on a column (3.5 cm × 120 cm) of Dowex 50 W (X-8, 75—150 μm, Ba^{2+} form) eluted with water at a rate of 35 $cm^3 h^{-1}$. Fraction 1 (elution volume 325—610 cm^3) contained D-*erythro*-L-glucooctose and D-*glycero*-D-galactoheptose in the mass ratio 2 : 1 (6.9 g). Fraction 2 (elution volume 630—800 cm^3) contained chromatographically homogeneous D-*erythro*-L-mannooctose (8.3 g), which did not crystallize from mixtures methanol—water, ethanol—water, and acetic acid—water. Sirupy D-*erythro*-L-mannooctose (dried over P_2O_5) had α(D, 20 °C, 1 g dm^{-3}, water) = −6.4° ± 0.5° or α(D, 20 °C, 1 g dm^{-3}, 4 % aqueous solution of ammonium molybdate) = −23.5° ± 0.5°. Ref. [4] gives for D-*erythro*-L-mannooctose crystallized from a mixture acetic acid—water (volume ratio = 5 : 1) m.p. = 154 °C and α(D, 20 °C, 2 g dm^{-3}, water) = +11.7° (extrapol.)→ +10.5° (5 min)→ −6.2° (230 min)→ −6.9° (292 min)→ −7.5° (equilibrium).

Crystallization of fraction 1 from a mixture methanol—water (volume ratio = 5 : 1) afforded chromatographically homogeneous D-*erythro*-L-glucooctose, m.p. = 170—172 °C and α(D, 20 °C, 1 g dm^{-3}, water) = −59.2° (extrapol.)→ −58.8° (1.5 min)→ −58.1° (3 min)→ −57.8° (5 min)→ −38.1° (48 h, equilibrium) or α(D, 20 °C, 1 g dm^3, 4 % aqueous solution of ammonium molybdate) = −80° ± 1.5°.

For D-*erythro*-L-glucooctose ($C_8H_{16}O_8$) w_i(calc.): 39.99 % C, 6.71 % H; w_i(found): 39.94 % C, 6.82 % H.

Preparation of D-*erythro*-L-*glucooctose*

A solution of D-*erythro*-L-mannooctose (10 g) and molybdic acid (0.25 g) in water (100 cm^3) was heated at 90—100 °C for 10 h, deionized by addition of an anion exchanger (Ostion AT 0209 in HCO_3^- form, 10 cm^3) and evaporated. The residue was crystallized from a mixture methanol—water to give the first crop of crystalline D-*erythro*-L-glucooctose (2.5 g). The fractionation of the mother liquor on a Dowex 50 W (Ba^{2+}) column gave the second portion of D-*erythro*-L-glucooctose (3.5 g) as well as D-*erythro*-L-mannooctose (4 g).

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