Reactions of saccharides catalyzed by molybdate ions. XXI.* Preparation of some ω-deoxyaldoses

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5-Deoxy-L-ribose, 6-deoxy-L-talose, 6-deoxy-D-talose, and 7-deoxy-L-*glycero*-L-taloheptose were prepared by molybdate catalyzed epimerization of the corresponding epimeric aldoses. 5-Deoxy-L-arabinose was obtained by oxidation of L-rhamnose with lead tetraacetate. 7-Deoxy-L-*glycero*-L-galactoheptose and 7-deoxy-L-*glycero*-L-taloheptose were prepared by nitromethane synthesis and oxidative decomposition of the corresponding nitroheptitols.

Описан синтез 5-деокси-L-рибозы, 6-деокси-L-талозы, 6-деокси-D-талозы, 7-деокси-L-*глицеро*-L-талогептозы из соответствующих эпимерных альдоз эпимеризацией катализированной молибдатными ионами. Из L-рамнозы была приготовлена 5-деокси-L-арабиноза окислением ацетатом Pb(IV). 7-Деокси-L-*глицеро*-L-галактогептоза и 7-деокси-L-*глицеро*-L-талогептоза были приготовлены при помощи нитрометанового синтеза и окислительного разложения соответствующих нитрогептитолов.

In recent years it was found that biological material contains in addition to frequently occurring L- and D-fucose [1] also their epimers, 6-deoxy-L- and 6-deoxy-D-talose. 6-Deoxy-L-talose is a constituent of the glycoside sarmentoside *A* of *Strophantus sarmentosus* [2], cell walls of *Actinomyces bovis* [3], *Streptococcus bovis* [4], and *Escherichia coli 045* [5]. 6-Deoxy-D-talose occurs in capsular polysaccharides of some gram-negative bacteria [6]. 6-Deoxytalose (L- or D-configuration not specified) was also found in lipopolysaccharides of *Citrobacter* [7], *Mycobacterium marianum* [8], *Escherichia coli*, and *Salmonella* [9].

In this paper we describe preparation of 6-deoxy-L- and 6-deoxy-D-talose by epimerization of L- and D-fucose. Attention is also devoted to epimerization of

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further ω-deoxyaldoses having *arabino* configuration, 5-deoxy-L-arabinose, and 7-deoxy-L-*glycero*-L-galactoheptose.

Epimerization of 5-deoxy-L-arabinose in mild acidic aqueous solutions under catalytic action of molybdate ions leads to an equilibrium mixture of 5-deoxy--L-arabinose and 5-deoxy-L-ribose in the ratio 3:1. Under the same conditions fucose gives a mixture of fucose and 6-deoxytalose in the ratio 4:1, and 7-deoxy-L-*glycero*-L-galactoheptose a mixture of 7-deoxy-L-*glycero*-L-galactoheptose and 7-deoxy-L-*glycero*-L-taloheptose in the ratio 9:1. A comparison of the composition of the equilibrium epimerization mixture of D-threose or D-erythrose (threose : erythrose 4:3) [10] with that of 5-deoxy-L-arabinose shows how the effect of the —CH_3 group at carbon C-4 is reflected. A similar shift of the equilibrium is evident when we compare the compositions of the equilibrium epimerization mixtures of L- or D-fucose and D-arabinose (arabinose : ribose 2:1) [11], and 7-deoxy-L-*glycero*-L-galactoheptose and D-galactose (galactose : talose 4:1) [12]. The epimerization of L- or D-fucose is, similarly as the epimerization of D-arabinose [11] or D-galactose [12], accompanied in a small extent by epimerization at carbon C-3. The epimerization mixtures of fucose contain besides 6-deoxytalose as the main product also 6-deoxygulose and 6-deoxysorbose. The presence of 6-deoxytagatose was not found. The fact that no evidence has been obtained for the formation of the corresponding ketoses during molybdate catalyzed epimerization of aldoses, serves as a proof that the catalysis by molybdate ions is selective for the epimerization reaction. This is in contrast to general acid-base catalyzed transformations of saccharides. The formation of 6-deoxysorbose may be ascribed to instability of the originally formed C-3 epimer, 6-deoxyidose, undergoing transformation also in acidic aqueous media [13].

The epimerization reaction is suitable for preparative purposes. A relatively simple procedure affords from the corresponding aldose 5-deoxy-L-ribose, 6-deoxy--L- or 6-deoxy-D-talose, and 7-deoxy-L-*glycero*-L-taloheptose in 19, 18, and 9% yield, respectively. Separation of epimeric aldoses in the equilibrium epimerization mixtures can be very effectively achieved by chromatography on ion exchanger Dowex 50 W in Ba^{2+} form [14]. The starting aldose can be recovered and reused for preparation of further amounts of the corresponding epimer.

L-Rhamnose was used as the starting compound for preparation of 5-deoxy--L-arabinose, 7-deoxy-L-*glycero*-L-galactoheptose, and 7-deoxy-L-*glycero*-L--taloheptose. Oxidation of L-rhamnose with lead tetraacetate at molar ratios 1:1, 1:2 or 1:3 results always in a cleavage of the linkage between carbons C-1 and C-2. After hydrolysis of 4-*O*-formyl-5-deoxy-L-arabinose, 5-deoxy-L-arabinose is obtained in 39% yield. Nitromethane synthesis with L-rhamnose followed by oxidative decomposition of the epimeric nitroheptitols gave in 49% yield a mixture of 7-deoxy-L-*glycero*-L-galactoheptose and 7-deoxy-L-*glycero*-L-taloheptose in the ratio 5:2.

Experimental

Specific rotations were measured with a Perkin—Elmer polarimeter, type 141 and melting points were determined on a Kofler stage. The composition of reaction mixtures as well as purity of isolated saccharides was examined by chromatography on Whatman No. 1 paper in the following solvent systems: S_1, *n*-butanol—ethanol—water (5:1:4); S_2, methyl ethyl ketone—*n*-butanol—water (7:2:1); S_3, ethyl acetate—acetic acid—water (saturated with boric acid) (9:1:1) (Table 1).

Table 1

Paper chromatography of ω-deoxysaccharides

Saccharide	Relative mobility		
	S_1	S_2	S_3
5-Deoxy-L-arabinose	1.93	3.67	2.88
5-Deoxy-L-ribose	2.03	3.68	3.28
D-Fucose	1.00	1.00	1.00
6-Deoxy-D-talose	1.61	2.66	2.98
6-Deoxy-D-gulose	1.26	1.54	1.39
6-Deoxy-D-sorbose	1.65	2.85	2.75
6-Deoxy-D-tagatose	1.55	2.40	3.10
L-Rhamnose	1.18	1.70	1.46
7-Deoxy-L-*glycero*-L-galactoheptose	0.85	0.72	0.87
7-Deoxy-L-*glycero*-L-taloheptose	1.37	2.00	2.01

S_1, S_2, and S_3 — solvent systems described in the text.

5-Deoxy-L-arabinose

A solution of L-rhamnose (25 g, 0.15 mole) in water (30 ml) was mixed with acetic acid (1500 ml), cooled at 15—18°C and lead tetraacetate (90 g, 0.2 mole) was added by portions during 10—15 min. After standing at room temperature for 20 min, the mixture was mixed with 0.5 M solution of oxalic acid in acetic acid (400 ml) to remove lead ions. After filtration, the solution was evaporated under reduced pressure (temperature below 40°C). The sirupy residue was dissolved in ethyl acetate (750 ml) and the solution was extracted with cold water (2 × 50 ml). The ethyl acetate solution was evaporated *in vacuo* and the sirupy distillation residue was dissolved in 0.05 M-H_2SO_4 (125 ml) and then heated at 35—40°C for 5 h. After deionization (Wofatit SBW in HCO_3^- form) and concentration, the solution was fractionated on a column (4 × 120 cm) of cellulose eluted with acetone—*n*-butanol—water (7:2:1) to give in fraction *1* 5-deoxy-L-arabinose (8 g) sirup having $[\alpha]_D^{23}$ −6.7° (*c* 2, water) and $[\alpha]_D^{23}$ −32 ± 1° (*c* 2, 4% aqueous solution of ammonium molybdate), and in fraction *2* L-rhamnose (0.3 g). Ref. [15] gives for 5-deoxy-L-arabinose sirup $[\alpha]_D^{21}$ −8° (15 min) → −3° (14 h) (*c* 4.5, water), Ref. [16] $[\alpha]_D$ −6.9° (*c* 2.16, water), and Ref. [17] for 5-deoxy-D-arabinose $[\alpha]_D^{18}$ +7.0° (*c* 1.46, water).

5-Deoxy-L-ribose

A solution of 5-deoxy-L-arabinose (8 g) and molybdic acid (0.16 g) in water (80 ml) was heated at 80°C for 4 h, then treated with charcoal, deionized (Wofatit SBW in acetate form), concentrated under reduced pressure to sirup which was fractionated on a column (3.5 × 120 cm) of Dowex 50 W (X-8, 100—200 mesh) in Ba^{2+} form using elution with water at a rate of 45 ml/h. Fraction *1* (elution volume 1200—1700 ml) contained 5-deoxy-L-arabinose (4.7 g) and fraction *2* (2100—2600 ml) 5-deoxy-L-ribose (1.5 g) isolated as sirup, $[\alpha]_D^{23}$ −11.9 ± 0.5° (*c* 2, water) and $[\alpha]_D^{23}$ − 52.6 ± 1° (*c* 2, 4% aqueous solution of ammonium molybdate). Ref. [18] gives for sirupy 5-deoxy-D-ribose $[\alpha]_D^{23}$ +11° (*c* 4, water).

6-Deoxy-D-talose

A solution of D-fucose (10 g) and molybdic acid (0.1 g) in water (50 ml) was heated at 90°C for 8 h and then processed and fractionated as described in the procedure for preparation of 5-deoxy-L-ribose. Fraction *1* (elution volume 700—1300 ml) contained D-fucose (7.6 g) and small amount of 6-deoxy-D-gulose and 6-deoxy-D-sorbose (*ca.* 5%). Fraction *2* (1800—2800 ml) contained 6-deoxy-D-talose (1.8 g) which, after crystallization from ethanol, showed m.p. 120—122°C and $[\alpha]_D^{20}$ +25.7° (4 min) → +24.0° (6 min) → +22.8° (8 min) → +21.9° (10 min) → +19.8° (20 min) → +18.8 ± 0.5° (24 h) (*c* 2, water), or $[\alpha]_D^{23}$ +26.2 ± 1.5° (*c* 2, 4% aqueous solution of ammonium molybdate). Ref. [6] gives for 6-deoxy-D-talose m.p. 129—131°C and $[\alpha]_D^{23}$ +20.6° (*c* 3.2, water).

A part of D-fucose (*ca.* 4 g) was removed from fraction *1* by crystallization from methanol. Chromatography of the mother liquor on Whatman No. 3 paper with solvent system S_2 yielded 6-deoxy-D-gulose, $[\alpha]_D^{23}$ −32.1° (*c* 5, water), and 6-deoxy-D-sorbose, $[\alpha]_D^{23}$ +22.4° (*c* 4, water). Ref. [19] gives for 6-deoxy-D-gulose m.p. 130—131°C and $[\alpha]_D^{29}$ −42.3° (30 min) → −38.0° (water), and Ref. [20] for 6-deoxy-L-sorbose m.p. 88°C and $[\alpha]_D^{22}$ −27.7 ± 0.5° (*c* 3.75, water).

6-Deoxy-L-talose

L-Fucose (9.5 g) was epimerized and further processed as described in the procedure for preparation of 6-deoxy-D-talose. Crystallization from ethanol gave 6-deoxy-L-talose, m.p. 131—133°C, $[\alpha]_D^{20}$ −26.4° (4 min) → −24.7° (6 min) → −23.4° (8 min) → −22.4° (10 min) → −20.1° (20 min) → −18.8 ± 0.5° (24 h) (*c* 3, water). Ref. [2] m.p. 116—118°C, $[\alpha]_D^{18}$ −20.2° (10 min) → −18.9 ± 2° (3 h) (*c* 1.5, water); Ref. [21] m.p. 126—127°C, $[\alpha]_D$ −20.5 ± 1.4° (*c* 2.3, water).

7-Deoxy-L-glycero-L-taloheptose

A mixture of 7-deoxy-L-*glycero*-L-galactoheptose (20 g), molybdic acid (0.2 g), and water (100 ml) was heated at 90°C for 8 h, then purified with charcoal, deionized (Wofatit SBW in acetate form) and evaporated. The resulting sirup was crystallized from methanol to give 7-deoxy-L-*glycero*-L-galactoheptose (11 g). The mother liquor was fractionated on ion exchanger Dowex 50 W. Fraction *1* (700—1400 ml) contained

7-deoxy-L-*glycero*-L-galactoheptose (6.3 g) and fraction *2* (1800—2800 ml) 7-deoxy--L-*glycero*-L-taloheptose (1.8 g) isolated as a sirup having $[\alpha]_D^{23} -1.9 \pm 0.5°$ (*c* 2, water) or $[\alpha]_D^{23} -29.9 \pm 1°$ (*c* 2, 4% aqueous solution of ammonium molybdate). For $C_7H_{14}O_6$ calculated: 43.30% C, 7.27% H; found: 43.42% C, 7.34% H.

7-Deoxy-L-glycero-L-galactoheptose and 7-deoxy-L-glycero-L-taloheptose

A solution of L-rhamnose (50 g) in methanol (200 ml) was mixed with nitromethane (100 ml) and methanolic solution of sodium methanolate (12.5 g of sodium in 350 ml of methanol) added by portions. After 20 h, sodium salts of nitroheptitols were filtered off and dissolved in water (500 ml). After addition of sodium molybdate (2.5 g) and, by portions, 15% aqueous solution of hydrogen peroxide (100 ml) to keep the temperature of the reaction mixture below 30°C, the whole mixture was left to stand for 24 h. After treatment for 24 h with 5% palladised charcoal (*ca.* 0.5 g), the solution was mixed with acetic acid (12 ml) and bubbled with air for 4 h. The solution was filtered, deionized (first on catex, then on anex in acetate form) and evaporated to sirup, which was crystallized from methanol (70 ml) to give the first portion of 7-deoxy-L-*glycero*-L-galactoheptose (15 g). Fractionation of the mother liquor on Dowex 50 W ion exchanger gave in fraction *1* (750—1050 ml) a mixture of 7-deoxy-L-*glycero*-L-galactoheptose and rhamnose (11 g) in the ratio 1 : 1, and in fraction *2* (1450—2500 ml) 7-deoxy-L-*glycero*-L-taloheptose (8.4 g). Crystallization of fraction *1* from methanol afforded further portion of 7-deoxy-L-*glycero*-L-galactoheptose which was recrystallized from a mixture methanol—water (3 : 1), m.p. 186—189°C, $[\alpha]_D^{23}$ $-109.4°$ (4 min) → $-107.7°$ (6 min) → $-105.6°$ (8 min) → $-103.8°$ (10 min) → $-94.7°$ (20 min) → $-59.6 \pm 0.5°$ (24 h) (*c* 3, water). Ref. [22] gives for 7-deoxy--L-*glycero*-L-galactoheptose m.p. 186.5—187.5°C and $[\alpha]_D^{20} -128.6° \rightarrow -62.5°$ (*c* 2.48, water).

6-Deoxy-D-tagatose

1-Deoxy-D-altritol (500 mg) prepared by reduction of 6-deoxy-D-talose with $NaBH_4$ was dehydrogenated biochemically by *Acetobacter pasteurianus* BS 1775 [23]. Sirupy 6-deoxy--D-tagatose (160 mg), $[\alpha]_D^{22} -0.8°$ (*c* 4.3, water), was isolated from the reaction medium by chromatography on Whatman No. 3 paper with solvent system S_2. Ref. [24] gives for 6-deoxy-D-tagatose sirup $[\alpha]_D^{18} -2 \pm 2°$ (*c* 2, water).

References

1. Dutton, G. G. S., *Advan. Carbohyd. Chem.* ***28,*** 12 (1973).
2. Schmitz, J., *Helv. Chim. Acta* ***31,*** 1719 (1948).
3. McLennan, A. P., *Biochim. Biophys. Acta* ***48,*** 600 (1961).
4. Pazur, J. H., Kane, J. A., Dropkin, D. J., and Jackman, L. M., *Arch. Biochem. Biophys. Acta* ***150,*** 382 (1972).
5. Gaugler, R. W., *Diss. Abstr. Int.* ***34B,*** 3084 (1974).
6. Markowitz, A., *J. Biol. Chem.* ***237,*** 1767 (1962).

7. Keleti, J., Lüderitz, O., Mlynarčík, D., and Sedlák, J., *Eur. J. Biochem.* ***20,*** 237 (1971).
8. Chaput, M., Michel, G., and Lederer, E., *Experientia* ***17,*** 107 (1961).
9. Oerskov, F., Oerskov, I., Jann, B., Mueller-Seitz, E., and Westphal, O., *Acta Pathol. Microbiol. Scand.* ***71,*** 339 (1967); *Chem. Abstr.* ***68,*** 9426*u* (1968).
10. Bílik, V. and Stankovič, Ľ., *Chem. Zvesti* ***27,*** 544 (1973).
11. Bílik, V., *Chem. Zvesti* ***26,*** 372 (1972).
12. Bílik, V., Voelter, W., and Bayer, E., *Justus Liebigs Ann. Chem.* ***1974,*** 1162.
13. Wolfrom, M. L. and Hanessian, S., *J. Org. Chem.* ***27,*** 1800 (1962).
14. Bílik, V., Petruš, L., and Alföldi, J., *Chem. Zvesti* ***30,*** 698 (1976).
15. Kuhn, R., Bister, W., and Defeldecker, W., *Justus Liebigs Ann. Chem.* ***617,*** 115 (1958).
16. Hough, L. and Taylor, J. T., *J. Chem. Soc.* ***1955,*** 3544.
17. Zinner, H., Wessely, K., and Kristen, H., *Chem. Ber.* ***92,*** 1618 (1959).
18. Schunk, C. H., Lavigne, J. B., and Folkers, K., *J. Amer. Chem. Soc.* ***77,*** 2210 (1955).
19. Levene, P. A. and Compton, J., *J. Biol. Chem.* ***111,*** 339 (1935).
20. Müller, H. and Reichstein, T., *Helv. Chim. Acta* ***21,*** 263 (1938).
21. Collins, P. M. and Overend, W. G., *J. Chem. Soc.* ***1965,*** 1912.
22. Jackson, E. L. and Hudson, C. S., *J. Amer. Chem. Soc.* ***75,*** 3000 (1953).
23. Stankovič, Ľ., Linek, K., and Fedoroňko, M., *Carbohyd. Res.* ***35,*** 243 (1974).
24. Barnett, J. and Reichstein, T., *Helv. Chim. Acta* ***20,*** 1529 (1937).

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