Preparation of Some 2,6-Anhydroheptoses *via* Ozonolysis of Sodium 2,6-Anhydro-1-deoxyheptitol-1-nitronates

M. PETRUŠOVÁ, I. STRUČKOVÁ, M. MATULOVÁ, and L. PETRUŠ

Institute of Chemistry, Slovak Academy of Sciences, CS-842 38 Bratislava

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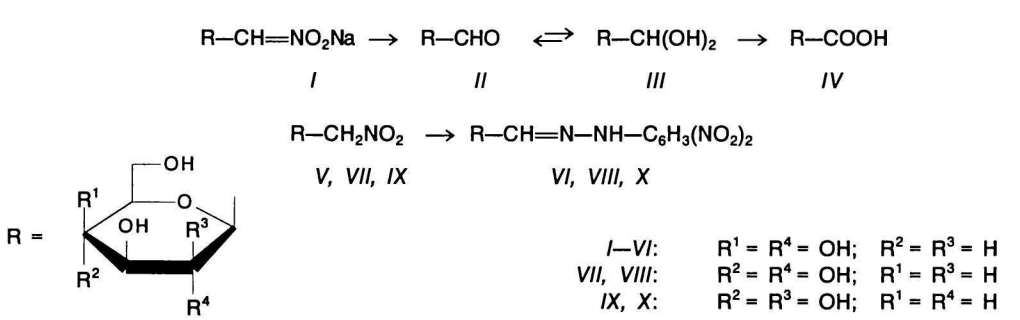
Ozonolysis of 2,6-anhydro-7-deoxy-7-nitro-L-*glycero*-L-*galacto*-heptitol*, 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol, and 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol, respectively, in aqueous sodium hydroxide at room temperature gave rise to the corresponding 2,6-anhydroheptoses. The products of the conversion were isolated as 2,4-dinitrophenylhydrazones and were characterized by ^{1}H and ^{13}C NMR spectroscopy.

The conversion of the nitromethyl group of 2,5- or 2,6-anhydro-1-deoxy-1-nitroalditols (glycosylnitromethanes) to the aldehydic one resulting in the formation of respective 2,5- or 2,6-anhydroaldoses continuously attracts attention. The reason is that these *C*-glycosylated formaldehydes are very interesting compounds for the synthesis of *C*-glycosyl compounds.

Recent extensive evaluation of reductive and oxidative procedures [2] has shown that the anhydronitroalditols resist such a simple conversion. It has been found however, that they can be easily converted to anhydroaldonic acids. *Martin et al.* [3] have succeeded to convert 2,6-anhydro-1-deoxy-1-nitroalditols in their per-*O*-acetylated silyl nitronate form to corresponding 2,6-anhydroaldoses by ozonolysis in dichloromethane at – 78 °C. We have shown that the treatment of 1-deoxy-1-nitroalditols [4] and 3,7-anhydro-2-deoxy-2-nitrooctitols [5] in aqueous sodium hydroxide with ozone at room temperature is an excellent method for their high yield conversion to corresponding carbonyl compounds. This contribution describes an analogically simple conversion of three 2,6-anhydro-1-deoxy-1-nitroheptitols to the corresponding 2,6-anhydroaldoses.

The treatment of an aqueous solution of 2,6-anhydro-7-deoxy-7-nitro-L-*glycero*-L-*galacto*-heptitol in its sodium nitronate form (*I*, Scheme 1 (*A*)) with ozone at room temperature within a few minutes resulted in the formation of 2,6-anhydro-D-*glycero*-L-*manno*-heptose (*II*). The derivative *II* occurs in an aqueous solution prevalently as hydrate *III* (*II* : *III* ≈ 1 : 4). During the conversion of *I* to *II*, a subsequent oxidation of *II* to 2,6-anhydro-D-*glycero*-L-*manno*-heptonic acid (*IV*, [5]) occurred. Thus, in the 75 MHz proton-decoupled ^{13}C NMR spectra of the reaction mixture, it was possible to observe signals at δ: 77.8 (CH_2NO_2, *I*), 172.1 (CHO, *II*), 89.4 ($CH(OH)_2$, *III*), and 178.0 (COOH, *IV*).

It is generally known that unstabilized aldehydes unlike *e.g.* aldoses are easily oxidable with oxygen to carboxylic acids. Therefore it was necessary to specify the end of the ozonolysis of *I* to *II*. Previously it has been shown [4] that ozonolysis of sodium nitronates affords besides corresponding carbonyl compounds also sodium nitrate. It means that the completion of the conversion caused a sudden change of a strongly alkaline to neutral pH of the reaction mixture and was easily detectable. Because of the subsequent oxidation of *II* to acid



Scheme 1

* The nomenclature used corresponds to that obviously used in *Carbohydrate Research* and is in accordance with the IUPAC rules (*cf.* rule Carb. 26, example 6 [1]).

IV, which is a stronger acid than *I*, it was necessary to use an excess of sodium hydroxide to keep the whole amount of *I* in activated nitronate form. In ad-

dition to sodium nitrate, sodium salt of *IV* was another product of the neutralization of the starting alkalinity. From the point of view of the maximum conversion of *I* to *II* trapped, the optimum conditions of the ozonolysis of *I* were found when 15 % molar excess of sodium hydroxide on *I* was used. Thus, a 75—80 % apparent conversion has been achieved. The final reaction mixture contained also 10—20 % of acid *IV* and 5—10 % of untreated starting material.

Compound *II* was isolated as a condensation product with 2,4-dinitrophenylhydrazine. Using the procedure, crystalline 2,6-anhydro-D-*glycero*-L-*manno*-heptose 2,4-dinitrophenylhydrazone (*VI*, Scheme 1 (*B*)) in an overall yield of 56 % was obtained from the starting 2,6-anhydro-7-deoxy-7-nitro-L-*glycero*-L-*galacto*-heptitol (*V*).

The same procedure applied to 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol (*VII*) and 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol (*IX*), at the optimum conditions for the conversion of *I* to *II*, afforded 49 % of 2,6-anhydro-D-*glycero*-D-*gulo*-heptose 2,4-dinitrophenylhydrazone (*VIII*) and 42 % of 2,6-anhydro-D-*glycero*-D-*galacto*-heptose 2,4-dinitrophenylhydrazone (*X*), respectively.

Compounds *VI*, *VIII*, and *X* were characterized by the ^{1}H and ^{13}C NMR spectroscopy (Table 1). The values of their proton coupling constants confirmed that the compounds have retained β-pyranose structure of the 2,6-anhydro ring of the starting material. As for the structure of the hydrazono group of these three compounds, the chemical shifts of the hydrogen atom H-1 and the carbon atom C-1 confirmed their acyclic, *i.e.* true hydrazono forms in pyridine solutions immediately after dissolution as well as after a few-day staying in the solution. A significant formation of cyclic hemiacetal forms was not observed either in aqueous solutions of the free 2,6-anhydroheptoses.

EXPERIMENTAL

Specific optical rotations were measured on a polarimeter 141 (Perkin—Elmer). Elemental analyses were obtained using an analyzer 240 (Perkin—Elmer). Melting points were measured on a Kofler stage and are uncorrected. Composition of reaction mixtures and purity of products were tested by TLC on Silufol plates (Lachema, Brno) detected with alkaline silver nitrate [6, 7]. Solvents were evaporated under diminished pressure at $\theta < 40$ °C. The ^{13}C NMR spectra (75.46 MHz) were recorded with a spectrometer AM 300 FT (Bruker) in D_2O (internal standard methanol, $\delta = 50.15$) and in C_5D_5N ($\delta = 123.0$) at 298 K using the DEPT pulse sequence. The ^{1}H NMR spectra (300.13 MHz) were recorded at 298 K using a 5 mm ^{1}H probe (internal standard sodium 3-(trimethylsilyl)propionate, $\delta = 0.00$) with the digital resolution 0.24 Hz/point. For the signal assignment and coupling constant determination in the ^{1}H NMR spectra, both 1D COSY and 1D relayed COSY experiments were used. The Gaussian soft pulse duration was 40 ms. An ozone generator 502 (Fischer) was used for the preparation of ozone from gaseous oxygen.

2,6-Anhydro-D-*glycero*-L-*manno*-heptose 2,4-Dinitrophenylhydrazone (*VI*)

Ozone (30 mg min^{-1}) was passed at room temperature into a mixture of a solution of 2,6-anhydro-7-deoxy-7-nitro-L-*glycero*-L-*galacto*-heptitol (*V*, [7], 0.55 g, 2.5 mmol) in water (7.5 cm^3) and aqueous sodium hydroxide (c = 1 mol dm^{-3}, 2.9 cm^3) containing phenolphthalein (0.2 mg) until neutral reaction. The solution was immediately flushed with nitrogen for 5 min and concentrated under diminished pressure at

Table 1. ^{1}H and ^{13}C NMR Data of the Prepared Compounds

Compound	Chemical shift δ										
	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-7'	H-10	H-12	H-13
VI	8.31	4.56	4.74	4.28	4.70	4.23	4.54	4.47	9.01	8.29	7.97
VIII	8.26	4.62	4.25	4.26	4.33	4.12	4.62	4.41	9.03	8.31	7.98
X	8.52	4.70	4.66	4.31	4.63	4.07	4.65	4.40	9.05	8.36	7.97
	Coupling constant *J*/Hz										
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$	$J_{10,12}$	$J_{12,13}$	
VI	6.4	9.3	9.0	3.1	0.8	5.4	5.2	11.1	2.7	9.5	
VIII	6.4	9.4	8.7	9.2	8.5	2.3	5.3	12.0	2.6	9.4	
X	5.6	1.3	3.4	9.2	8.5	2.0	6.2	11.8	2.6	9.4	
	Chemical shift δ										
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13
VI	151.6	80.9	70.3	76.3	70.5	80.7	62.6	145.2	137.9	128.6	*	128.6	116.8
VIII	151.2	80.2	73.4	79.8	71.6	82.6	62.9	145.2	138.0	129.6	*	129.6	116.9
X	152.3	79.3	73.1	76.1	68.7	83.0	63.2	145.2	137.9	129.6	*	129.5	116.7

* Not ascribed (overlapped by a solvent signal); approximate value 123.2 [10].

40 °C. The residue was dissolved in a solution of 2,4-dinitrophenylhydrazine (1.3 g, 6.5 mmol) in methanol (150 cm^3) and left to stand for 20 h. The precipitate was collected by filtration, washed with a mixture of benzene—ethyl acetate (volume ratio = 7 : 3, 5 cm^3) and purified by chromatography (Silica gel, 40—100 μm, elution system S_1, acetone—methanol—chloroform—water, volume ratio = 75 : 10 : 10 : 5). Crystallization from methanol afforded *VI* (0.51 g, 56 %), m.p. = 157—159 °C, [α](D, 20 °C, ρ = 9.7 g dm^{-3}, pyridine) = + 101°, R_f = 0.75 (S_1). For $C_{13}H_{16}N_4O_9$ (M_r = 372.29) w_i(calc.): 41.94 % C, 4.33 % H, 15.05 % N; w_i(found): 41.70 % C, 4.12 % H, 14.71 % N.

2,6-Anhydro-D-*glycero*-D-*gulo*-heptose 2,4-Dinitrophenylhydrazone (*VIII*)

The procedure of the preparation of *VI* from *V* was applied to 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol (*VII*, [8], 0.55 g) and afforded *VIII* (0.45 g, 49 %), m.p. = 203—206 °C (methanol), [α](D, 20 °C, ρ = 11.5 g dm^{-3}, pyridine) = + 26°, R_f = 0.77 (S_1), w_i(found): 41.62 % C, 4.04 % H, 14.82 % N.

2,6-Anhydro-D-*glycero*-D-*galacto*-heptose 2,4-Dinitrophenylhydrazone (*X*)

The procedure of the preparation of *VI* from *V* was applied to 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol (*IX*, [9], 0.55 g) and afforded *X* (0.39 g, 42 %), m.p. = 207—209 °C (methanol), [α](D, 20 °C, ρ = 16.5 g dm^{-3}, pyridine) = + 22°, R_f = 0.71 (S_1), w_i(found): 41.73 % C, 4.31 % H, 14.94 % N.

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