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Synthesis of 2-(β-D-glycopyranosyl)nitroethenes and -nitroethanes via aldehydo derivatives

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Abstract

pH-Controlled ozonolysis of the sodium nitronate forms of β-D-hexopyranosylnitromethanes (2,6-anhydro-1-deoxy-1-nitroheptitols) at room temperature produced the corresponding 2,6-anhydroheptoses. Without isolation, these glycosylated formaldehydes were converted by the conventional nitromethane route to the corresponding 2-(β-D-hexopyranosyl)nitroethenes (**8a–c**), via the intermediate acetylated 2-(β-D-hexopyranosyl)-2-hydroxynitroethanes. A spontaneous β-elimination of the acetoxy group vicinal to the nitro group occurred in acidic medium with the 2-acetamido-2-deoxy-β-D-glucopyranosyl derivative, but did not occur with the parent β-D-glucopyranosyl compound or its D-*galacto* or D-*manno* epimers. 2-*C*-Glycosylated nitroethenes were further transformed by a regioselective catalytic reduction to 2-(β-D-hexopyranosyl)nitroethanes.

Keywords: *C*-Glycosyl compounds; *aldehydo*-2,6-Anhydroheptoses; Nitroalkenes; β-Elimination; Ozonolysis

1. Introduction

Interest in *C*-glycosyl analogues of glycosylated amino acids [1,2] arises from (1) incorporation of glycosylated amino acids into peptide sequences by conventional means (e.g., [3–5]); (2) strong evidence that enzymes, specifically glycohydrolases, recognize *C*-glycosyl analogues of their normal substrates equally well as the substrates (e.g., [6]); (3) the stability of *C*-glycosyl compounds to acid-, base-, and enzyme-catalyzed

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hydrolysis; and (4) the potential long-lasting biological activity of peptides into which they are incorporated by reason of their hydrolytic stability, thus enhancing their functional properties and allowing greater opportunity for studying their interactions with receptors.

For preparation of *C*-glycosylated amino acids, at least two exocyclic carbon atoms are required — a methylene group replacing the glycosidic oxygen atom (or the imino group of a glycosylamine linkage) and a second carbon atom that is functionalized and can serve as the carbon atom of the amino acid that would normally bear a hydroxyl group or that would be the carbonyl carbon atom of an amide group. An aldol condensation between *C*-glycosylated nitromethane and formaldehyde has been used to obtain the required exocyclic group [7]. This paper describes conversion of *C*-glycosylnitromethanes (2,6-anhydro-1-deoxy-1-nitroalditols) into *C*-glycosylformaldehydes (2,6-anhydroaldoses) and their condensation with nitromethane for the same purpose.

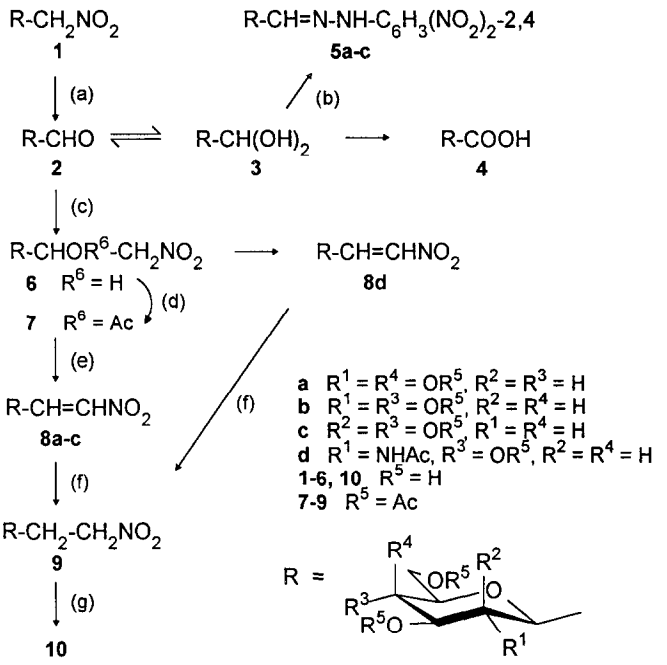
Conversion of the nitromethyl group of 2,5- or 2,6-anhydro-1-deoxy-1-nitroalditols to an aldehydo group can provide a readily available route to the respective 2,5- or 2,6-anhydroaldoses. Recent extensive evaluation of reductive and oxidative procedures [8] has shown that anhydronitroalditols resist such a simple conversion by means of the Nef reaction. Martin et al. [9] succeeded in converting 2,6-anhydro-1-deoxy-1-nitroalditols in their per-*O*-acetylated silyl nitronate forms to the corresponding 2,6-anhydroaldoses by ozonolysis in dichloromethane at −78 °C.

Ozonolysis of their nitro precursors in aqueous sodium hydroxide at room temperature is a convenient method of preparation of stabilized carbonyl structures. In this way, 1-deoxy-1-nitroalditols [10] and two epimeric 3,7-anhydro-2-deoxy-2-nitrooctitols [11] were converted in high yields to aldoses and 3,7-anhydro-D-*glycero*-L-*manno*-2-octulose, respectively; and in a preliminary study [12], three 2,6-anhydro-1-deoxy-1-nitroheptitols were successfully converted in > 70% yields to the corresponding 2,6-anhydroheptoses by pH-controlled ozonolysis. This paper describes that conversion in detail and its application for preparation of some 2-*C*-β-D-glycosylated nitroethenes and nitroethanes, and shows that the loss of acetic acid under acidic conditions to form a glycosylated nitroethene is unique to the peracetylated 3,7-anhydro-1-deoxy-1-nitroheptitol with the 2-acetamido-2-deoxy-β-D-glucopyranosyl ring structure [7].

2. Results and discussion

*Preparation of 2,6-anhydroaldoses (*C-β-D-*glycopyranosylformaldehydes).*—Treatment of an aqueous solution of 2,6-anhydro-7-deoxy-7-nitro-L-*glycero*-L-*galacto*-heptitol (**1a**) (β-D-galactopyranosylnitromethane) [1] in its sodium nitronate form with ozone at room temperature gave *aldehydo*-2,6-anhydro-D-*glycero*-L-*manno*-heptose (**2a**), which

[1] Although the alternative names in parentheses or brackets throughout the paper are the simplest in terms of comprehending structures and are systematic names, anhydroalditol and anhydroaldose names are given as the primary names for the purpose of straightforwardness of numbering carbon atoms in the presentation of NMR data. Compound **1a** is not named 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-L-*manno*-hepitol, which is more in keeping with the β-D-galactopyranosyl concept and the method of preparation, because of JCBN rule 2.2.2 which states that "the name selected is that which comes first in the alphabet".



(a) NaOH, H_2O, O_3, r.t.; (b) 2,4-DNPH, EtOH; (c) $MeNO_2$, NaOMe; (d) Ac_2O, H_2SO_4; (e) $NaHCO_3$, benzene, 80°C; (f) H_2, Pd/C, EtOAc; (g) NaOMe, MeOH

Scheme 1.

occurs in an aqueous solution predominately as hydrate **3a** (**2a**:**3a** ≈ 1:4), see Scheme 1. Because such unstabilized aldehydes (unlike aldoses) are easily oxidizable with oxygen to carboxylic acids, it was necessary to determine the end of the conversion of **1a** to **2a**. Ozonolysis of sodium nitronates affords, in addition to the corresponding carbonyl compounds, sodium nitrate [10]. Hence, the strong alkaline solution was neutralized as the reaction proceeded and the endpoint was easily detectable. Treatment with ozone for a longer time than was necessary to achieve the conversion of **1a** to **2a** resulted in oxidation of **2a** to 2,6-anhydro-D-*glycero*-L-*manno*-heptonic acid (**4a**) [11]. When equimolar amounts of starting **1a** and NaOH were used and the ozonization time was doubled, the ^{13}C NMR spectrum of the reaction mixture showed signals at δ 77.8 (CH_2NO_2, **1a**), 172.1 (*C*HO, **2a**), 89.4 [*C*H(OH)$_2$, **3a**], and 178.0 (*C*OOH, **4a**). Quantitative estimates of these signals were used for finding the optimal conditions of the conversion (Table 1).

Conditions for the conversion of **1a** to **2a** were optimum when a 10% molar excess of sodium hydroxide based on **1a** was used, as part of the starting alkalinity was consumed by acid **4a** subsequently formed by oxidation of **2a** by oxygen present in the ozone stream. In addition to about 85% of **2a** (including **3a**), the final reaction mixture

Table 1
Ozonolysis of (β-D-galactopyranosyl)nitromethane (**1a**) in its sodium nitronate form [a]

Reactants (mmol)		Reaction products (%) [b]			
1a	NaOH	**2a** (+**3a**)	**4a**	OA [c]	**1a**
1.0	1.0	80	10	t	10
1.0	1.1	85	10	t	5
1.0	1.2	75	25	t	0
1.0	1.3	65	35	t	0
1.0	1.4	55	45	t	0
1.0	1.5	40	60	t	0
2.0	2.4	65	30	5 [d]	0

[a] Total volume of reaction mixtures was 4 mL.
[b] Values estimated from ^{13}C NMR spectra.
[c] OA = oxidized aldolizates, t = trace.
[d] Isolated yield based on starting **1a**.

contained about 10% of acid **4a** and about 5% of starting **1a**. To avoid subsequent oxidation of **2a** to **4a**, the aldehyde was handled under a nitrogen atmosphere. Similar conversions were achieved with anhydronitroalditols **1b–d**.

For complete disappearance of starting anhydronitroalditols **1a–d**, a 20% excess of sodium hydroxide was used in the reaction mixtures. In spite of decreased yields of the corresponding aldehydo derivatives **2a–d** (to ca. 75%), these conditions were used to avoid mixtures of starting glycosylnitromethanes which were difficult to separate (**1a–d**) in the final products (2-β-D-glycosylated nitroethenes and nitroethanes). β-D-Glycosylated formaldehydes **2a–d** were isolated from reaction mixtures obtained under optimum conditions in even lower yields due to their instability. Therefore, to assure the efficient utility of aldehydes **2a–d**, reaction mixtures after ozonolysis, also containing sodium salts of the corresponding β-D-glycosylated formic acids (**4**) and nitric acid, but free of starting material, were used directly for condensation with nitromethane.

Concentrations of **1a–d** employed for ozonolysis were about 0.25 M. When the concentration of **1b** was doubled, oxidized aldol condensation products (up to 5%) were formed. Two pseudomolecular ions at *m/z* 763 and 779 in 1:4 ratio were present in FABMS spectra of the peracetates of these products. The structure R–CO–CH(OAc)–R resulting from aldol condensation of glycosylmethylnitronate and glycosylformaldehyde molecules and subsequent ozonolysis was ascribed to the former ion, and the structure HOOC–R′–CH(OAc)–R resulting from aldol condensation of two molecules of glycosylformaldehyde and subsequent oxidation (R corresponds to glycosyl residue, R′ to the glycosyl residue without an anomeric proton) was ascribed to the latter ion. The mixture was not analyzed further.

2,6-Anhydroaldoses **2a–c** were previously characterized as their crystalline 2,4-dinitrophenylhydrazones (**5a–c**) [12]. Proton coupling constants confirmed that the carbon skeletons of the products were identical to those of the starting materials. The chemical shifts of the anomeric proton and C-1 confirmed that the hydrazones were acyclic in

pyridine solution immediately after dissolution as well as after a few days. Neither was significant cyclic hemiacetal formation observed in aqueous solutions of the free 2,6-anhydroheptoses (**2a–d**).

It was expected that aldehydes (**2**) would anomerize in alkaline solution. No evidence of anomerization was found. However, any one of the aldehydes was in the presence of strong base for only a very few minutes, all four compounds were already in thermodynamically most stable forms with an equatorial anomeric substituent, and **2a**, **2b**, and **2d** have the more stable 1,2-*trans* configuration; so while the potential for anomerization may have been present, no actual anomerization was evident.

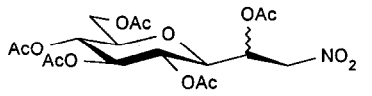
*Preparation of 2-(β-*D*-glycopyranosyl)nitroethenes and -nitroethanes.*—Addition of nitromethane to 2,6-anhydroaldoses (**2**) in the presence of sodium methoxide afforded the corresponding epimeric nitroalcohols (**6**) in 72 to 80% yields. Following reaction, a sulfonic acid-type cation-exchange resin in the H^+ form was used simultaneously with a strongly basic anion-exchange resin in the HCO_3^- form both to remove sodium ions and to trap anions of both nitric and 2,6-anhydroaldonic acids produced during ozonolysis. For all four products (**6a–d**), the ratio of the two epimers at the new chiral carbon atom was approximately 2:1 as determined by ^{13}C NMR spectroscopy (comparison of their well resolved CH_2OH signals). No other CH_2OH signal nor signals characteristic of species **2** or **3** were present in these spectra. No further characterization of **6a–d** was carried out.

Because we wanted to prevent base-catalyzed elimination of the acetoxy group vicinal to the nitro group that commonly occurs with nitro sugars, epimeric nitroalcohols **6a–d** were acetylated under acidic conditions. Treatment of methanolic solutions of **6a–d** with a mixture of acetic anhydride and sulfuric acid assured good temperature control and thus mild per-*O*-acetylation so that colourless reaction mixtures were obtained. Simultaneously formed methyl acetate was easily removed by evaporation, and 85–90% yields of epimeric mixtures of **7a–c** were obtained by the conventional isolation procedure. The major epimers were crystalline. However, washing the $CHCl_3$ extracts with aqueous $NaHCO_3$ had to be avoided because of formation of **8a–c** and subsequent addition of water to give underacetylated species. For the actual preparation of nitroalkenes **8a–c**, solutions of **7a–c** were heated several hours at the reflux temperature of dry benzene in the presence of sodium hydrogencarbonate. The corresponding 2-*C*-glycosylated nitroethenes **8a–c** were obtained in 90–95% yields.

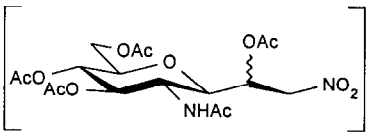
The conventional isolation procedure failed, however, in the isolation of the two epimers of **7d**. Soon after pouring the reaction mixture into a mixture of ice and water, a precipitate identified as per-*O*-acetylated nitroalkene **8d** appeared, then disappeared after a few minutes. Extraction did not provide the expected product, but a brown mixture of partially *O*-acetylated, uncharacterized products. When a calculated amount of sodium hydrogencarbonate was used to neutralize sulfuric acid, **8d**, which remained as an insoluble substance, could be isolated from the reaction mixture as the only product (79% yield).

The nitroalkenes had the *E* configuration almost exclusively (*E*:*Z* > 95:5). The chemical shift of the vinylic proton H-2 (*E* isomers: δ C*H*=CHNO$_2$ 7.0–7.2 ppm; *Z* isomers: 5.7–5.8 ppm) clearly established [9,13] the configuration of the 1,2-disubstituted double bond of compounds **8a–d**. ^{13}C NMR signals of the double bond of the *E*

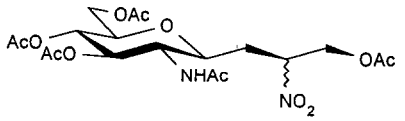
isomers of **8a–d** were observed at 140–142 (C-1) and 134–137 ppm (C-2). Signals for the *Z* isomer of **8a** were clearly observed at 130.7 and 129.6 ppm.



7b



7d



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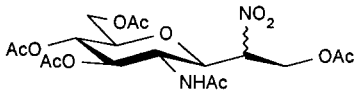

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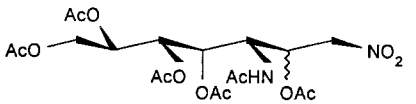

13

Spontaneous β-elimination of an acetoxy group in acetylated nitrosugars has been observed before and has been ascribed to several stereochemical factors, *e.g.*, to the $A^{(1,2)}$-strain present in six-membered cyclic nitroalkenes with an equatorial oxygen functionality [14]. A factor similar to the $A^{(1,2)}$-strain is not likely to be operating in otherwise stereochemically similar structures **7a–d**, as the only difference between structures **7b** and **7d** is the substitution of an acetamido group for the acetoxy group at C-2.

One possible explanation for this phenomenon is an interaction of the nitro and acetamido groups that disrupts the resonance in the acetamido group and, thereby, enhances the basicity of its imino moiety which intramolecularly catalyzes β-elimination of the 2-acetoxy group of **7d**. However, anhydronitrononitol (**11**) [15] and anhydronitrooctitol (**12**) [16] epimers, which also offer the possibility of interaction of their nitro and acetamido groups, were stable under acidic and neutral conditions. To initiate β-elimination of their acetoxy groups, treatment with an external base was necessary. Another pair of model compounds containing the acetamido group, epimeric peracetylated nitroheptitols **13**, underwent only partial β-elimination. Thus, a 55:45 mixture of epimeric nitroalditols, obtained by the Henry reaction with *N*-acetyl-D-glucosamine, afforded, under identical acetylation conditions, a 55:30:15 mixture of **13** epimers and their corresponding nitroalkene [estimated from the ^{13}C NMR spectra by integration of

their well-resolved CH_2OR (R = H or Ac) and CHNHAc carbon signals] (other data not given). All these observations taken together suggest that the acetamido group was somehow responsible for the unexpected β-elimination (in strongly acidic medium) of the acetoxy group vicinal to the nitro group in both **7d** epimers, that another specific structure is also required, and that neither alone is sufficient to effect elimination. The latter required structure might be one that produces a repulsion of the acetoxy group to be eliminated by a neighboring substituent, e.g., the free electron pairs of the ring oxygen atom. Such repulsion is quite possible in epimers **7d**, partial in epimers **13**, and absent in epimers **11** and **12**.

Selective reduction [17] of the alkene double bond of **8a–d** furnished 2-(β-D-glycosyl)nitroethanes **9a–d** in high yields (> 90%). Appearance of two signals at 70–70.5 (C-1) and 28.5–29.5 ppm (C-2) in the ^{13}C NMR spectra, instead of the signals of the double bond in **8a–d**, proved the structure of the nitroalkane moiety of **9a–d**. Also, the ability of *O*-deacetylated **9a–d** to exchange both CH_2NO_2 protons in slightly alkaline D_2O, as do 1-deoxy-1-nitroalditols [18], additionally confirmed the presence of the nitromethyl group in **9a–d**. The consequences of the proton–deuterium exchange were observed also in the ^{13}C NMR spectra, i.e., the signal of the C-1 carbon atom was missing and that of C-2 was changed into a triplet after exchange.

3. Experimental

General methods and materials.—Melting points were measured on a Kofler stage. Microanalyses were obtained using a Perkin–Elmer 240 instrument. Optical rotations were obtained at 20 °C using a Perkin–Elmer 141 polarimeter. ^{13}C NMR (75.46 MHz, internal methanol, δ 50.15) and ^{1}H NMR spectra [300.13 MHz, internal sodium 3-(trimethylsilyl)propionate, δ 0.00] were obtained at 20 °C using a General Electric or a Bruker AM-300 spectrometer. Positive-ion FABMS spectra were recorded on a Kratos MS50 spectrometer using DTT/DTE matrix. Flash chromatography was performed on silica gel pads in a sintered glass filter funnel by elution with 4:3 v/v EtOAc–hexane. Silica gel TLC plates were developed with the same solvent; alkaline silver nitrate or sulfuric acid charring was used to detect components. A Fisher 502 ozone generator was used for the preparation of ozone from gaseous oxygen. Solvents were evaporated under diminished pressure at < 40 °C. 2,6-Anhydro-7-deoxy-7-nitro-L-*glycero*-L-*galacto*-heptitol [(β-D-galactopyranosyl)nitromethane, **1a**], 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol [(β-D-glucopyranosyl)nitromethane, **1b**], 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol [(β-D-mannopyranosyl)nitromethane, **1c**], and 2-acetamido-2,6-anhydro-1,2-dideoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol [(2-acetamido-2-deoxy-β-D-glucopyranosyl)nitromethane, **1d**] were prepared according to literature methods [19–21].

Ozonolysis of β-D-*hexopyranosylnitromethanes* (**1**) *to 2,6-anhydroheptoses* (**2**).—(a) Ozone (20 mg/min) was introduced at ambient temperature into a solution of **1a** (223 mg, 1.0 mmol), M NaOH (1.0–1.5 mL), and water (2.5–3.0 mL; total volume of the solution 4 mL) until pH 7 was reached (usually 2–3 min). Then, the reaction mixture was immediately flushed with nitrogen (5 min), evaporated, and submitted to ^{13}C NMR

spectroscopic examination (Table 1). (b) Ozone (60 mg/min) was introduced at ambient temperature into a solution of **1** (5 mmol) in water (14 mL) and M NaOH (6.0 mL) until pH 7 of the reaction mixture was reached (ca. 7 min). Then, the reaction mixture was immediately flushed with nitrogen (5 min) and evaporated to a glass (1.4–1.6 g) containing **2** (and **4**).

Nitromethane addition to **2**.—The residue containing **2** was dissolved in deaerated methanol (50 mL). Nitromethane (2 mL) and a freshly prepared solution of sodium methoxide in MeOH (1.5 M, 7.5 mL) were added under stirring at ambient temperature. After standing overnight in the dark at 5 °C, most of the MeOH was evaporated, and crushed dry ice (50 mL), Amberlite IR-120 (H^+, 25 mL), Amberlite IRA-400 (OH^-, 15 mL), and water (50 mL) were added sequentially and rapidly; and the stirred mixture was maintained in a bath at 20 °C for 10 min. The neutral mixture was filtered and washed with water (3 × 30 mL). The filtrate and washings were concentrated, and the residue was dried by repeated evaporation of EtOH from it to afford a solid foam of anhydronitroalditols **6** (2.6–2.9 mmol, 52–58% based on starting **1**, epimeric ratio 2:1 by ^{13}C NMR spectroscopy).

Acetylation of **6**.—The residue containing **6** was dissolved in MeOH (2.5 mL) and added dropwise into acetic anhydride (45 mL) containing concentrated H_2SO_4 (4 drops) at 30–40 °C with stirring. After the final addition, the mixture was stirred for an additional 4 h. The clear solution was then poured into ice and water (300 mL), and the mixture was stirred for 3 h. The water was extracted with $CHCl_3$ (3 × 60 mL), and the extract was washed with water until neutral (usually 7 ×), dried (Na_2SO_4), and evaporated, yielding pentaacetates **7a–c** (ca. 1.1 g, 85%, epimeric ratio 2:1 by ^{13}C NMR spectroscopy).

*(*E*)-4-Acetamido-5,6,8-tri-*O*-acetyl-1,2,4-trideoxy-1-nitro-*D*-glycero-*D*-gulo-oct-1-enitol [(*E*)-2-(2-acetamido-2-deoxy-β-*D*-glucopyranosyl)nitroethene triacetate,* **8d***].*—Immediately after pouring the reaction mixture from acetylation of **6d** into an ice and water mixture, 0.5 M $NaHCO_3$ (5.4 mL) was added. An identical isolation procedure to that described for **7a–c** afforded **8d** (1.1 g, 89%); mp 179–181 °C (1:1 v/v EtOAc–hexane); $[\alpha]_D^{25}$ −36.5° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.20 (dd, 1 H, $J_{1,2}$ 13.3 Hz, H-1), 7.14 (dd, 1 H, $J_{2,3}$ 3.3 Hz, H-2), 5.73 (bd, 1 H, $J_{4,NH}$ 8.8 Hz, NH), 5.19 (t, 1 H, $J_{5,6}$ 9.4 Hz, H-5), 5.12 (t, 1 H, $J_{6,7}$ 9.6 Hz, H-6), 4.23 (dd, 1 H, $J_{8,8'}$ 12.4 Hz, H-8), 4.22 (ddd, 1 H, $J_{3,4}$ 10.3 Hz, H-3), 4.18 (dd, 1 H, H-8′), 3.99 (td, 1 H, $J_{4,5}$ 10.2 Hz, H-4), 3.74 (ddd, 1 H, $J_{7,8}$ 2.4, $J_{7,8'}$ 4.8 Hz, H-7), 2.12, 2.08, 2.07, 1.99 (4 s, 12 H, 4 CH_3 of Ac); ^{13}C NMR ($CDCl_3$): δ 171.4, 170.6, 170.5, 169.2 (4 CO of Ac), 140.8 (C-1), 136.1 (C-2), 75.9 (C-3), 75.0 (C-7), 73.3 (C-5), 67.9 (C-6), 61.9 (C-8), 53.7 (C-4), 23.2, 20.7, 20.6, 20.5 (4 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{22}N_2O_{10}$: C, 47.76; H, 5.51, N, 6.96. Found: C, 47.39; H, 5.58; N, 6.79.

Dehydroacetylation of **7a–c**.—Solutions of pentaacetates **7a–c** (1 g) in dry benzene (20 mL) containing $NaHCO_3$ (1 g) were heated at the reflux temperature for 5 h. The cooled mixtures were filtered and evaporated. The products, nitroalkenes **8a–c**, were crystallized from 1:1 v/v EtOAc–hexane.

*(*E*)-1,3,4,5-Tetra-*O*-acetyl-2,6-anhydro-7,8-dideoxy-8-nitro-*L*-glycero-*L*-galacto-oct-7-enitol [(*E*)-2-(β-*D*-galactopyranosyl)nitroethene tetraacetate,* **8a***].*—Yield 0.80 g (92%); mp 179–181 °C; $[\alpha]_D^{25}$ −2.1° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.20 (dd, 1

H, $J_{7,8}$ 13.3 Hz, H-8), δ 7.07 (dd, 1 H, $J_{6,7}$ 4.1 Hz, H-7), 5.47 (dd, 1 H, $J_{2,3}$ 3.0 Hz, H-3), 5.16 (t, 1 H, $J_{4,5}$ 9.6 Hz, H-5), 5.11 (dd, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 4.22 (ddd, 1 H, $J_{1,1'}$ 11.5 Hz, H-1), 4.17 (dd, 1 H, $J_{1,2}$ 7.0, $J_{1',2}$ 7.1 Hz, H-2), 4.12 (dd, 1 H, $J_{5,6}$ 5.9 Hz, H-6), 4.00 (ddd, 1 H, H-1'), 2.17, 2.11, 2.07, 2.00 (4 s, 12 H, 4 CH_3 of Ac); ^{13}C NMR ($CDCl_3$): δ 170.4, 170.1, 170.0, 169.4 (4 CO of Ac), 141.2 (C-8), 134.9 (C-7), 74.6 (C-6), 74.3 (C-2), 71.7 (C-4), 68.1 (C-3), 67.3 (C-5), 61.5 (C-1), 20.7, 20.6 (2 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{21}NO_{11}$: C, 47.64; H, 5.25, N, 3.47. Found: C, 47.35; H, 5.32; N, 3.11.

*(E)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-1-nitro-*D-glycero-D-gulo-*oct-1-enitol [(E)-2-(β-*D*-glucopyranosyl)nitroethene tetraacetate,* **8b***].*—Yield 0.78 g (90%); mp 98–100 °C; $[\alpha]_D^{25}$ −21.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.19 (dd, 1 H, $J_{1,2}$ 13.3 Hz, H-1), 7.06 (dd, 1 H, $J_{2,3}$ 4.1 Hz, H-2), 5.27 (t, 1 H, $J_{5,6}$ 9.4 Hz, H-5), 5.14 (t, 1 H, $J_{6,7}$ 9.7 Hz, H-6), 4.95 (t, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.2–4.3 (m, 2 H, H-3, H-8), 4.18 (dd, 1 H, $J_{8,8'}$ 12.5 Hz, H-8'), 3.78 (ddd, 1 H, $J_{7,8}$ 2.4, $J_{7,8'}$ 4.8 Hz, H-7), 2.11, 2.09, 2.05, 2.02 (4 s, 12 H, 4 Me of Ac); ^{13}C NMR ($CDCl_3$): δ 170.3, 169.9, 169.7, 169.6 (4 CO of Ac), 141.3 (C-1), 134.6 (C-2), 76.1 (C-7), 73.9 (C-3), 73.7 (C-5), 70.9 (C-4), 67.8 (C-6), 61.8 (C-8), 20.7, 20.6, 20.5 (3 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{21}NO_{11}$: C, 47.64; H, 5.25, N, 3.47. Found: C, 47.67; H, 5.32; N, 3.17.

*(E)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-1-nitro-*D-glycero-D-galacto-*oct-1-enitol [(E)-2-(β-*D*-mannopyranosyl)nitroethene tetraacetate,* **8c***].*—Yield 0.82 g (94%); mp 121–123 °C; $[\alpha]_D^{25}$ −53.8° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.20 (dd, 1 H, $J_{1,2}$ 13.2 Hz, H-1), 7.01 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 5.53 (dd, 1 H, $J_{4,5}$ 3.4 Hz, H-4), 5.27 (t, 1 H, $J_{6,7}$ 10.0 Hz, H-6), 5.13 (dd, 1 H, $J_{5,6}$ 10.1 Hz, H-5), 4.52 (dd, 1 H, $J_{3,4}$ 1.9 Hz, H-3), 4.27 (dd, 1 H, $J_{8,8'}$ 12.4 Hz, H-8), 4.22 (dd, 1 H, H-8'), 3.75 (ddd, 1 H, $J_{7,8}$ 2.6, $J_{7,8'}$ 5.9 Hz, H-7), 2.13, 2.12, 2.07, 2.01 (4 s, 12 H, 4 Me of Ac); ^{13}C NMR ($CDCl_3$): δ 170.5, 170.2, 169.5, 169.1 (4 CO of Ac), 141.6 (C-1), 134.9 (C-2), 76.3 (C-7), 73.4 (C-3), 71.5 (C-5), 68.3 (C-4), 65.2 (C-6), 62.3 (C-8), 20.7, 20.6, 20.4 (3 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{21}NO_{11}$: C, 47.64; H, 5.25, N, 3.47. Found: C, 47.26; H, 5.41; N, 3.62.

Reduction of **8** *to* **9**.—A solution of crude 2-glycosylnitroethene peracetate **8** (0.5 g) in EtOAc (100 mL) was stirred vigorously with 10% Pd/C (180 mg) under hydrogen at ambient temperature and pressure for 10 min [15]. Gas uptake was rapid and showed a sharp decrease in rate after 25 mL had been consumed. Following filtration, the filtrate was evaporated to give a crystalline residue (0.45–0.48 g). Recrystallization from anhydrous ethanol afforded nitroalkane **9**.

*1,3,4,5-Tetra-*O*-acetyl-2,6-anhydro-7,8-dideoxy-8-nitro-*L-glycero-L-galacto-*octitol [2-(β-*D*-galactopyranosyl)nitroethane tetraacetate,* **9a***].*—Yield 0.40 g (80%); mp 45–46 °C; $[\alpha]_D^{25}$ +1.0° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.43 (d, 1 H, $J_{2,3}$ 3.0 Hz, H-3), 5.10 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 5.02 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 4.4–4.7 (m, 2 H, H-8, H-8'), 4.13 (dd, 1 H, $J_{1,1'}$ 11.4 Hz, H-1), 4.04 (dd, 1 H, H-1'), 3.87 (t, 1 H, $J_{1,2}$ 6.4, $J_{1',2}$ 7.1 Hz, H-2), 3.54 (dt, 1 H, $J_{5,6}$ 9.3 Hz, H-6), 2.36 (dddd, 1 H, H-7), 2.0–2.2 (m, 1 H, H-7'), 2.16, 2.09, 2.06, 1.99 (4 s, 12 H, 4 Me of Ac); ^{13}C NMR ($CDCl_3$): δ 169.9, 169.8, 169.2 (4 CO of Ac), 74.7 (C-6), 74.3 (C-2), 71.6 (C-4), 71.0 (C-8), 68.8 (C-3), 67.5 (C-5), 61.4 (C-1), 28.9 (C-7), 20.5 (s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{23}NO_{11}$: C, 47.41; H, 5.72, N, 3.46. Found: C, 47.28; H, 5.67; N, 3.77.

4,5,6,8-Tetra-O-*acetyl-3,7-anhydro-1,2-dideoxy-1-nitro*-D-glycero-D-gulo-*octitol [2-(β-D-glucopyranosyl)nitroethane tetraacetate,* **9b**].—Yield 0.41 g (82%); mp 110–112 °C; $[\alpha]_D^{25}$ −8.4° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.19 (t, 1 H, $J_{5,6}$ 10.0 Hz, H-5), 5.04 (t, 1 H, $J_{6,7}$ 9.7 Hz, H-6), 4.90 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.4–4.6 (m, 2 H, H-1, H-1′), 4.22 (dd, 1 H, $J_{8,8'}$ 12.4 Hz, H-8), 4.08 (dd, 1 H, H-8′), 3.64 (ddd, 1 H, $J_{7,8}$ 2.3, $J_{7,8'}$ 5.2 Hz, H-7), 3.56 (dt, 1 H, $J_{3,4}$ 9.6 Hz, H-3), 2.3–2.5 (m, 1 H, H-2), 2.0–2.2 (m, 1 H, H-2′), 2.10, 2.08, 2.04, 2.01 (4 s, 12 H, 4 Me of Ac); ^{13}C NMR ($CDCl_3$): δ 170.6, 170.2, 169.8, 169.5 (4 CO of Ac), 75.7 (C-7), 74.3 (C-3), 73.7 (C-5), 71.4 (C-4), 70.9 (C-1), 68.2 (C-6), 61.9 (C-8), 28.8 (C-2), 20.7, 20.6 (2 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{23}NO_{11}$: C, 47.41; H, 5.72, N, 3.46. Found: C, 47.01; H, 5.76; N, 3.06.

4,5,6,8-Tetra-O-*acetyl-3,7-anhydro-1,2-dideoxy-1-nitro*-D-glycero-D-galacto-*octitol [2-(β-D-mannopyranosyl)nitroethane tetraacetate,* **9c**].—Yield 0.41 g (82%); mp 116–118 °C; $[\alpha]_D^{25}$ −39.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.37 (dd, 1 H, $J_{4,5}$ 3.5 Hz, H-4), 5.22 (t, 1 H, $J_{6,7}$ 10.0 Hz, H-6), 5.06 (t, 1 H, $J_{5,6}$ 10.1 Hz, H-5), 4.4–4.6 (m, 2 H, H-1, H-1′), 4.26 (dd, 1 H, H-8), 4.08 (dd, 1 H, H-8′), 3.77 (ddd, 1 H, $J_{7,8}$ 4.6 Hz, H-7), 3.63 (ddd, 1 H, $J_{3,4}$ 2.3 Hz, H-3), 1.9–2.2 (m, 2 H, H-2, H-2′), 2.20, 2.11, 2.05, 1.98 (4 s, 12 H, 4 Me of Ac); ^{13}C NMR ($CDCl_3$): δ 170.7, 170.4, 170.2, 169.7 (4 CO of Ac), 76.1 (C-7), 73.8 (C-3), 71.2 (C-5), 71.0 (C-1), 68.2 (C-4), 65.0 (C-6), 62.3 (C-8), 28.8 (C-2), 20.8, 20.7, 20.6 (3 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{23}NO_{11}$: C, 47.41; H, 5.72, N, 3.46. Found: C, 47.06; H, 5.75; N, 3.26.

4-Acetamido-5,6,8-tri-O-*acetyl-3,7-anhydro-1,2,4-trideoxy-1-nitro*-D-glycero-D-gulo-*octitol [2-(2-acetamido-2-deoxy-β-D-glucopyranosyl)nitroethane triacetate,* **9d**].—Yield 0.43 g (86%); mp 194–195 °C; $[\alpha]_D^{25}$ −42.6° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.58 (bd, 1 H, $J_{4,NH}$ 8.6 Hz, NH), 5.07 (t, 1 H, $J_{5,6}$ 9.7 Hz, H-5), 4.99 (t, 1 H, $J_{6,7}$ 9.7 Hz, H-6), 4.61 (ddd, 1 H, $J_{1,2}$ 5.5, $J_{1,2'}$ 4.9, $J_{1,1'}$ 13.8 Hz, H-1), 4.49 (td, 1 H, H-1′), 4.22 (dd, 1 H, $J_{8,8'}$ 12.3 Hz, H-8), 4.09 (dd, 1 H, H-8′), 4.04 (q, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.58 (ddd, 1 H, $J_{7,8}$ 2.4, $J_{7,8'}$ 5.3 Hz, H-7), 3.40 (dt, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 2.4–2.5 (m, 1 H, H-2), 2.0–2.2 (m, 1 H, H-2′), 2.10, 2.06, 2.04, 1.98 (4 s, 12 H, 4 Me of Ac); ^{13}C NMR ($CDCl_3$): δ 171.6, 170.8, 170.6, 169.4 (4 CO of Ac), 75.5 (C-3), 75.4 (C-7), 73.6 (C-5), 71.3 (C-1), 68.5 (C-6), 62.1 (C-8), 53.1 (C-4), 29.1 (C-2), 20.7, 20.6 (2 s, 12 H, 4 Me of Ac). Anal. Calcd for $C_{16}H_{24}N_2O_{10}$: C, 47.52; H, 5.98, N, 6.93. Found: C, 47.14; H, 6.07; N, 6.83.

Deacetylation of **9**.—A suspension of a nitroalkane peracetate **9** (0.4 g) in 0.1 M NaOMe (20 mL) was stirred for 1 h. Then, Amberlite IR-120 (H^+, 5 mL, prewashed with MeOH) was added and stirring was continued for 15 min. The neutral mixture was filtered, and the filtrate evaporated to give 2-glycosylnitroethane **10**.

2,6-Anhydro-7,8-dideoxy-8-nitro-L-glycero-L-galacto-*octitol [2-(β-D-galactopyranosyl)nitroethane,* **10a**].—Yield 0.22 g (94%); mp 121–122 °C; $[\alpha]_D^{25}$ +3.6° (*c* 2.4, H_2O); ^{13}C NMR (D_2O): δ 80.8 (C-6), 78.8 (C-2), 76.7 (C-4), 73.9 (C-8), 72.9 (C-3), 71.4 (C-5), 64.0 (C-1), 31.5 (C-7). Anal. Calcd for $C_8H_{15}NO_7$: C, 40.50; H, 6.37, N, 5.90. Found: C, 40.79; H, 6.69; N, 5.55.

3,7-Anhydro-1,2-dideoxy-1-nitro-D-glycero-D-gulo-*octitol [2-(β-D-glucopyranosyl)nitroethane,* **10b**].—Yield 0.21 g (90%); glassy foam; $[\alpha]_D^{25}$ −6.5° (*c* 0.7, H_2O); ^{13}C NMR (D_2O): δ 80.8 (C-7), 78.5 (C-3), 77.6 (C-5), 74.5 (C-4), 73.5 (C-1),

71.1 (C-6), 62.1 (C-8), 30.2 (C-2). Anal. Calcd for $C_8H_{15}NO_7$: C, 40.50; H, 6.37, N, 5.90. Found: C, 40.65; H, 6.70; N, 5.67.

3,7-Anhydro-1,2-dideoxy-1-nitro-D-glycero-D-galacto-*octitol [2-(β-D-mannopyranosyl)nitroethane,* **10c** *].*—Yield 0.20 g (85%); glassy foam; $[\alpha]_D^{25}$ −38.2° (*c* 2.0, H_2O); ^{13}C NMR (D_2O): δ 81.3 (C-7), 76.3 (C-3), 75.4 (C-5), 73.8 (C-1), 72.1 (C-4), 68.0 (C-6), 62.5 (C-8), 29.6 (C-2). Anal. Calcd for $C_8H_{15}NO_7$: C, 40.50; H, 6.37, N, 5.90. Found: C, 40.84; H, 6.58; N, 5.61.

4-Acetamido-3,7-anhydro-1,2,4-trideoxy-1-nitro-D-glycero-D-gulo-*octitol [2-(2-acetamido-2-deoxy-β-D-glucopyranosyl)nitroethane* **10d** *].*—Yield 0.26 g (94%); mp 187–188 °C; $[\alpha]_D^{25}$ −40.2° (*c* 0.6, H_2O); ^{13}C NMR (D_2O): δ 177.4 (CO of Ac), 82.3 (C-7), 78.3 (C-3), 77.9 (C-5), 75.0 (C-1), 72.9 (C-6), 63.7 (C-8), 57.9 (C-4), 31.7 (C-2), 25.0 (Me of Ac). Anal. Calcd for $C_{10}H_{18}N_2O_7$: C, 43.16; H, 6.52, N, 10.07. Found: C, 42.86; H, 6.77; N, 9.84.

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References

[1] L. Petruš and J.N. BeMiller, *Carbohydr. Res.*, 230 (1992) 197–200.
[2] V. Wittman and H. Kessler, *Peptides 1992, Proc. Eur. Peptide Symp.*, 22 (1993) 369–370.
[3] H. Kunz, *Angew. Chem. Int. Ed. Engl.*, 26 (1987) 294–308.
[4] H. Paulsen, *Angew. Chem. Int. Ed. Engl.*, 29 (1990) 823–839.
[5] H. Franzyk, M. Meldal, H. Paulsen, and K. Bock, *J. Chem. Soc., Perkin Trans. 1*, (1995) 2883–2898.
[6] J.N. BeMiller, R.J. Gilson, R.W. Myers, M.M. Santoro, and M.P. Yadav, *Carbohydr. Res.*, 250 (1993) 93–100.
[7] M. Petrušová, J.N. BeMiller, and L. Petruš, *Tetrahedron Lett.*, 37 (1996) 2341–2344.
[8] P. Köll and H. Dromowicz, *Abstr. Eur. Carbohydr. Symp., 6th, Edinburgh, 1991*, B56.
[9] O.R. Martin, F.E. Khamis, and S.P. Rao, *Tetrahedron Lett.*, 30 (1989) 6143–6146.
[10] E. Lattová, M. Petrušová, and L. Petruš, *Chem. Pap.*, 45 (1991) 823–827.
[11] M. Petrušová, E. Lattová, M. Matulová, and L. Petruš, *Chem. Pap.*, 46 (1992) 120–123.
[12] M. Petrušová, I. Strucková, E. Lattová, and L. Petruš, *Chem. Pap.*, 47 (1993) 195–197.
[13] G. Descotes, Y. Bahurel, M. Bourillot, G. Pingeon, and R. Rostaing, *Bull. Soc. Chim. Fr.*, (1970) 282–289.
[14] P.A. Wade and R.M. Giuliano, in H. Feuer and A.T. Nielsen (Eds.), *Nitro Compounds. Recent Advances in Synthesis and Chemistry*, VCH, New York, 1990, pp 137–265.
[15] L. Petruš, M. Petrušová, and J.N. BeMiller, *Abstr. Int. Carbohydr. Symp., 17th, Ottawa, 1994*, B1.104.
[16] L. Petruš, M. Petrušová, and J.N. BeMiller, *Abstr. Eur. Carbohydr. Symp., 8th, Seville, 1995*, A67.
[17] H.H. Baer and T. Neilson, *Can. J. Chem.*, 43 (1965) 840–846.
[18] P. Köll, H. Brandenburg, W. Seelhorst, C. Stenns, and H. Kogelberg, *Liebigs Ann. Chem.*, (1991) 207–211.
[19] L. Petruš, S. Bystrický, T. Sticzay, and V. Bílik, *Chem. Zvesti*, 36 (1982) 103–110.
[20] A. Förtsch, H. Kogelberg, and P. Köll, *Carbohydr. Res.*, 164 (1987) 391–402.
[21] M. Petrušová, M. Fedoronko, and L. Petruš, *Chem. Pap.*, 44 (1990) 267–271.