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Some Benzylidene and Cyclohexylidene Derivatives of 3-Deoxy-3-nitro-α-D-glucopyranose[1]

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In a previous paper[2] we reported that methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-glucopyranoside reacts smoothly with theophylline and 2,6-dichloropurine in the presence of sodium hydrogen carbonate to give, *via* 3-nitro-2-enoside, the corresponding 2-purinyl-glucosides in excellent yields. This finding urged us to attempt the similar reaction with 2-nitro sugars. To our knowledge, the only example belonging to this class of compounds, except 2-nitroalditols, has been described by Lemieux *et al.*[3], *i.e.* per-*O*-acetyl-2-nitro-D-glucal, -galactal and -xylal, derived from the corresponding acetylated glycals with dinitrogen tetraoxide. But all attempts to obtain 2′-nitro nucleosides from the reaction mixtures of these compounds with some purine homologues have been hitherto unsuccessful in our laboratory.

On the other hand, we have studied on the oxidative C^1-C^2 fission of 3-deoxy-3-nitro-D-glucose (**2**) with periodate or lead tetraacetate with the aim of preparing and characterizing 2-nitro sugars, but the desired product (**7**) is likely too unstable to isolate, giving only the degradated product (**8**). In this paper, we wish to present thereof and some acetal derivatives of **2** obtained throughout this work.

Phenyl 3-deoxy-3-nitro-β-D-glycopyranoside (**1**), almost selectively prepared by successive oxidation and nitromethane condensation of phenyl β-D-glucopyranoside,[4] was hydrolyzed (4 N HCl, 100°C, 2 hr) to give the reducing 3-deoxy-3-nitro-D-glucose (**2**).[5] Treatment of **2** with benzaldehyde and zinc chloride yielded the 4,6-*O*-benzylidene derivative (**3**). Compounds **2** and **3** were isolated in high yields as an α-form (downward-mutarotating). Acetylation of **3** with acetic anhydride in pyridine gave the 1,2-di-*O*-acetate (**4**), which was deduced to be an α-anomer on the basis of its NMR spectra: (1) a relatively small value of $J_{1,2}$-(3.8 Hz)[6]; (2) an axial *O*-acetyl signal resonating at 7.84 τ(CDCl$_3$).[6,7]

On an acetal exchange reaction[8] with 1,1-diethoxycyclohexane in the presence of *p*-toluenesulfonic acid (50°C/~20 mmHg), **2** gave the 1,2;4,6-di-*O*-cyclohexylidene derivative (**5**). The α-*pyranose* structure of **5** was proved by comparison of the chemical shifts and coupling constants of its ring protons[9] with those of 4,6-*O*-benzylidene-1,2-*O*-cyclohexylidene derivative (**6**), prepared by the analogous treatment of **3** (*cf.*

Table 1. 100 MHz NMR spectra in CDCl$_3$ (TMS as an internal standard)

Comp.	Chemical shifts in τ								Coupling constants in Hz						
	H^1	H^2	H^3	H^4	H^5	H^{6e}	H^{6a}	PhCH	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6e}$	$J_{5,6a}$	$J_{6e,6a}$
4	3.61	4.49	4.97	5.90	5.8 ~6.2	5.65	6.13	4.45	3.5	10.5	10	9	3.5	~10	10
5	4.41	5.52	5.34	5.92	6.09	5.93	6.12	—	4.5	7	10	10	2.5	~11	11
6	4.38	5.46	5.18	6.00	5.92	5.59	6.27	4.48	4.5	6.5	10.5	11	3	~10	11
8	O–CHO(2.02); H^3(5.09); H^{4e}(5.58); H^{4a}(6.32)							4.47	$J_{2,3}$(10); $J_{3,4e}$(5); $J_{3,4a}$(10); $J_{4a,4e}$(11)						

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1) From the Master Dissertation, T. Sakakibara, Tokyo Institute of Technology, February 1970.

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2) T. Nakagawa, T. Sakakibara, and S. Kumazawa, *Tetrahedron Lett.*, **1970**, 1645.

3) R. U. Lemieux, T. L. Nagabhushan, and I. K. O'Neill, *Can. J. Chem.*, **46**, 413 (1968).

4) T. Nakagawa, Y. Sato, T. Takamoto, F. W. Lichtenthaler, and N. Majer, This Bulletin, **43**, 3866 (1970).

5) This compound was just described by Baer *et al.*, who prepared it by acid hydrolysis (6 N HCl, 100°C, 1 hr) of methyl 3-deoxy-3-nitro-β-D-glucopyranoside [H. H. Baer, W. Rank, and F. Kienzle, *Can. J. Chem.*, **48**, 1302 (1970)].

6) L. D. Hall, *Advan. Carbohyd. Chem.*, **19**, 51 (1964).

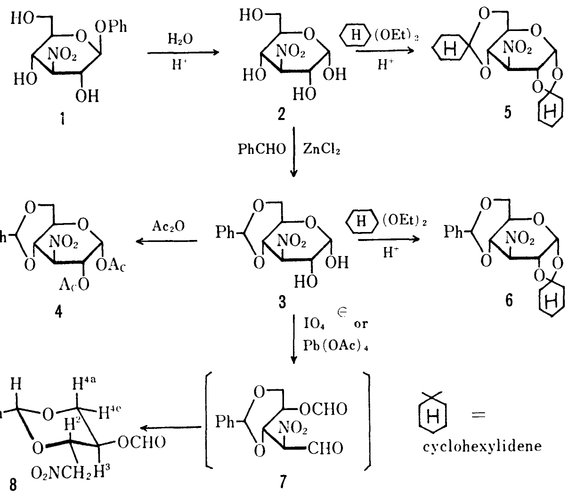
7) F. W. Lichtenthaler and P. Emig, *Carbohyd. Res.*, **7**, 121 (1968).

8) F. H. Bissett, M. E. Evans, and F. W. Parrish, *ibid.*, **5**, 184 (1967).

9) Moreover, if compound **5** had a *furanose* structure, $J_{2,3}$ should be $\geq$0.5 Hz. *Cf.* R. J. Abraham, L. D. Hall, L. Hough, and K. A. McLauchlan, *Chem. Ind.* (London), **1962**, 213; *J. Chem. Soc.*, **1962**, 3699.

Table 1).

Oxidation of **3** with periodate or lead tetraacetate gave no 2-nitro sugar **7** but a successive de-*C*-formylation occurred to form 2,4-*O*-benzylidene-1-deoxy-3-*O*-formyl-1-nitro-D-erythritol (**8**), whose structure was confirmed by its NMR spectra (Table 1).



Experimental

Melting points were determined in capillaries and are uncorrected. IR spectra were obtained with a Hitachi EPI-S2 instrument. NMR spectra were taken with a JEOLCO JNM-4H-100 spectrometer, using an internal TMS standard. Optical rotations were measured with a Carl Zeiss photoelectric polarimeter.

3-Deoxy-3-nitro-α-D-glucose (2). A mixture of phenyl 3-deoxy-3-nitro-β-D-glucopyranoside[4] (10.0 g) and 4 N hydrochloric acid was refluxed for 2 hr and the resulting solution was evaporated. The residue was dissolved in hot water (*ca.* 50 m*l*), treated with active charcoal and filtered. The filtrate was evaporated, and the residue was coevaporated several times with water and then crystallized from ethanol. After washing with ethyl acetate, the crystals (colorless, 5.5 g, 75%) may be used for a synthetic purpose without further purification. A sample for analysis was recrystallized from methanol/ethyl acetate: mp 174—174.5°C (decomp.) [*lit*,[5] 176—177°C (decomp.)]; $[\alpha]^{20}_{\mathrm{D}}$ +114° (t=0 min) → +108.5° (5 min) →+93.2° (30 min) →+79.5° (22 hr; const.) (c 1, H_2O)[*lit*,[5] $[\alpha]_{\mathrm{D}}$ +99.6° (6 min) →+73.9° (130 min, const.) (c 1, H_2O)].

Found: C, 34.44; H, 5.10; N, 6.72%. Calcd for $C_6H_{11}O_7N$: C, 34.45; H, 5.30; N, 6.70%.

4,6-O-Benzylidene-3-deoxy-3-nitro-α-D-glucopyranose (3). A mixture of **2** (2.7 g), zinc chloride (4 g), and benzaldehyde (13 m*l*) was stirred for 2 days and then poured into a mixture of ice water and petroleum ether with vigorous stirring. The precipitates were collected by filtration, washed well with water and petroleum ether, and recrystallized from ethanol/water: Yield 2.9 g (76%); mp 149.5—150.5°C; $[\alpha]^{20}_{\mathrm{D}}$ +34.3° (t=0 min) →+31.0° (2 hr 15 min) →+22.6° (24 hr) →+15.8° (3 days) →+12.2° (7 days) →+8.9° (15 days, const.)(c 1, dioxane). IR(KBr): 3400 cm⁻¹ (OH); 1565 cm⁻¹ (NO_2).

Found: C, 52.47; H, 4.81; N, 4.72%. Calcd for $C_{13}H_{15}O_7N$: C, 52.52; H, 5.09; N, 4.71%.

1,2-Di-O-acetyl-4,6-O-benzylidene-3-deoxy-3-nitro-α-D-glucopyranose (4). To a solution of **3** (0.89 g) in pyridine (9 m*l*) was added acetic anhydride (6 m*l*) under ice cooling. The reaction mixture was allowed to stand for 2 hr at room temperature and then poured into ice water. The precipitates were collected by filtration, washed well with water, and recrystallized from acetone/ethanol: Yield 1.13 g (99.2%); mp 220°C (decomp.); $[\alpha]^{20}_{\mathrm{D}}$ +65.9° (c 1, $CHCl_3$). IR (KBr): 1755 cm⁻¹ (C=O); 1565 cm⁻¹ (NO_2). NMR ($CDCl_3$): 7.84 τ (3H-*s*, *ax*. *O*-Ac on C^1); 7.99 τ (3H-*s*, *eq*. *O*-Ac on C^2).[6,7]

Found: C, 53.39; H, 4.93; N, 3.71%. Calcd for $C_{17}H_{19}O_9N$: C, 53.54; H, 5.02; N, 3.67%.

1,2;4,6-Di-O-cyclohexylidene-3-deoxy-3-nitro-α-D-glucopyranose (5). A solution of **2** (0.63 g), 1,1-diethoxycyclohexane[10] (2 m*l*), and *p*-toluenesulfonic acid (0.01 g) in DMF (6 m*l*) was boiled at 50°C/~20 mmHg, with use of a fine stream of dry air to promote steady ebullition.[8] After 1.5 hr, the reaction mixture was neutralized with sodium hydrogencarbonate, the undissolved material was filtered off, the filtrate was evaporated *in vacuo*, and the residue was recrystallized from ethanol/petroleum ether: Yield 0.5 g (45%); mp 121—123.5°C; $[\alpha]^{20}_{\mathrm{D}}$ +122° (c 1, $CHCl_3$). IR (KBr): 1560 cm⁻¹ (NO_2).

Found: C, 58.36; H, 7.09; N, 3.78%. Calcd for $C_{18}H_{27}O_7N$: C, 58.52; H, 7.37; N, 3.79%.

4,6-O-Benzylidene-1,2-O-cyclohexylidene-3-deoxy-3-nitro-α-D-glucopyranose (6). A solution of **3** (0.89 g), 1,1-diethoxycyclohexane[10] (12 m*l*), and *p*-toluenesulfonic acid (0.01 g) in dioxane (20 m*l*) was treated for 5 hr similarly as described above. The product was recrystallized from acetone/ethanol: 0.69 g (61%); mp 155.5—156.5°C; $[\alpha]^{20}_{\mathrm{D}}$ +95.5° (c 1, $CHCl_3$). IR (KBr): 1550 cm⁻¹ (NO_2).

Found: C, 60.18; H, 5.87; N, 3.82%. Calcd for $C_{19}H_{23}O_7N$: C, 60.47; H, 6.14; N, 3.71%.

2,4-O-Benzylidene-1-deoxy-3-O-formyl-1-nitro-D-erythritol (8). a) Periodate Oxidation: Into a solution of sodium metaperiodate (0.70 g) in water (50 m*l*) was added **3** (0.89 g) and stirred at room temperature. After 6 hr, sodium hydrogencarbonate (0.25 g) was added to it and them ixture was stirred for 3 days. The precipitates were collected by filtration, washed with water, and recrystallized from ethanol/petroleum ether: colorless needles (0.404 g, 50.5%); mp 113°C; $[\alpha]^{20}_{\mathrm{D}}$ −47.2° (c 1, EtOAc). IR (KBr): 1725 cm⁻¹ (C=O); 1560 cm⁻¹ (NO_2); no absorption of OH.

Found: C, 53.93; H, 4.76; N, 5.23%. Calcd for $C_{12}H_{13}O_6N$: C, 53.93; H, 4.90; N, 5.24%.

b) Lead Tetraacetate Oxidation: In a solution of lead tetraacetate (1.46 g) in dry benzene (30 m*l*) was stirred **3** (0.89 g) at room temperature for 2 hr, the precipitates were filtered off, the filtrate was evaporated, and the residue was recrystallized from ethanol/petroleum ether to give over 70% yield of colorless needles, mp and mixed mp 113°C. IR and NMR spectra were identical with those of the product obtained under (*a*).

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