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Note

Synthesis of a furanoid 2-aminoglycal derivative*

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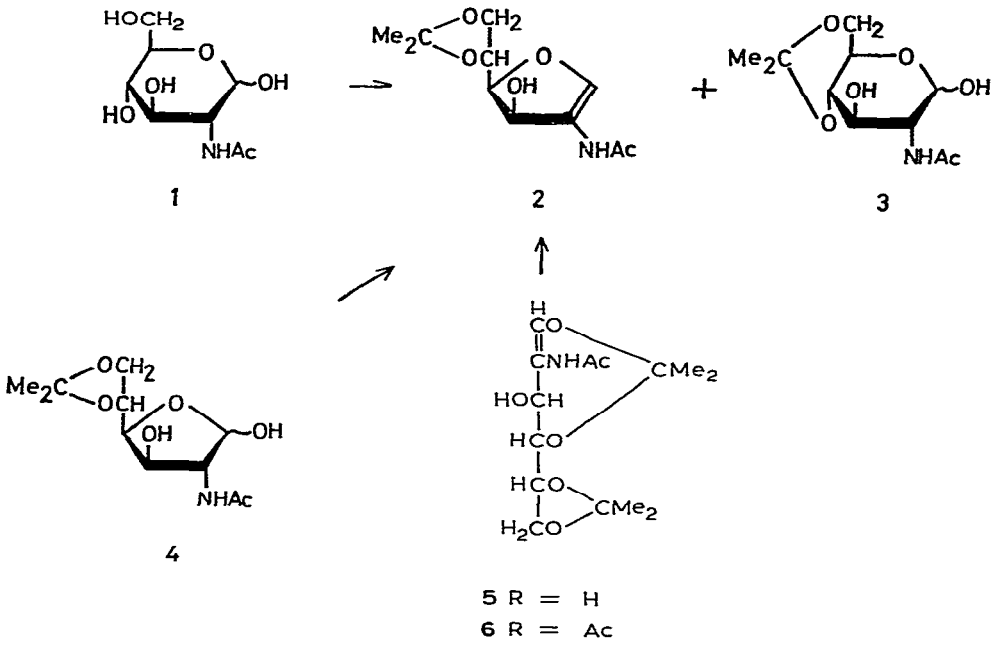
Furanoid as well as pyranoid glycals are useful intermediates in the synthesis of a variety of carbohydrate dervatives. Pyranoid glycals are usually prepared by modifications[2] of the method discovered by Fischer and Zach[3]. The first synthesis of a furanoid glycal was achieved by Ness and Fletcher[4] by treatment of 3,5-di-*O*-benzoyl-2-*O*-(*p*-nitrophenylsulfonyl)-β-D-ribofuranosyl bromide with sodium iodide, but this method will probably not often be employed for preparative work, because of the many steps involved in the preparation of furanosyl halide derivatives. Recently, Jordaan *et al.*[5] and Ireland *et al.*[6] reported an alternative route to furanoid glycals that involved treatment of furanosyl halides bearing a 2,3-*O*-isopropylidene group with sodium naphthalide or lithium–ammonia.

Our recent work[1,7–13] has shown that, for some aldoses, 2,2-dialkoxypropane–*N*,*N*-dimethylformamide–*p*-toluenesulfonic acid is a unique acetonating agent that may give unexpected, and potentially useful, products on changing such reaction conditions as the temperature, the reaction time, and the ratios of the acid, the 2,2-dialkoxypropane, and *N*,*N*-dimethylformamide. In the course of our studies of the reaction mechanism, formation of a new type of glycal, a furanoid 2-aminoglycal has been achieved. We report here a one-step synthesis of 2-acetamido-1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-D-*arabino*-hex-1-enitol (**2**) from 2-acetamido-2-deoxy-D-glucose (**1**), and discuss the mechanism of formation thereof.

A suspension of 2-acetamido-2-deoxy-D-glucose (**1**) in dry *N*,*N*-dimethylformamide was stirred at 10–15°, while large excesses of 2,2-dimethoxypropane and *p*-toluenesulfonic acid were added. The reaction was continued for 40 h at 10–15°, and the mixture was then treated with Amberlite IRA-410 ion-exchange resin for 3 h at 30°. 2-Acetamido-1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-D-*arabino*-hex-1-enitol[13] (**2**, 43%) and 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-D-glucopyranose[7] (**3**, 43%) were obtained as the main products.

On the other hand, the acetonation of **1** with the reagent under the conditions

*The Behavior of Some Aldoses with 2,2-Dialkoxypropane–*N*,*N*-Dimethylformamide–*p*-Toluenesulfonic Acid, Part VII. For Part VI, see ref. 1. For a preliminary report, see ref. 13.



just described, except that, after completion of the reaction, the mixture was stirred with Amberlite IR-45 ion-exchange resin (to remove the acid), instead of the Amberlite IRA-410 resin used in the foregoing experiment, gave compound **3** (44%), 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose[12] (**4**, 14%), and a labile compound, namely, 2-acetamido-2-deoxy-1,4:5,6-di-*O*-isopropylidene-D-*arabino*-hex-1-enitol (**5**, 30%). It is interesting that, in the former experiment, significant amounts of the furanoid 2-aminoglycal derivative (**2**) were obtained, but none of the compounds **4** and **5** was isolated. These results show that compounds **4** and **5** were converted into the furanoid 2-aminoglycal derivative (**2**) during stirring of the reaction mixture with the Amberlite IRA-410 resin to remove the acid.

In order to verify this conclusion, the following experiments were performed. Treatment of compound **4** in methanol with Amberlite IRA-410 (OH^-) ion-exchange resin gave compound **2** in good yield, as expected. It seems likely that the formation of furanoid 2-aminoglycals from a variety of 2-(acylamino)-2-deoxyfuranoses and their derivatives by use of basic resins should be expected. Acetylation of the labile compound **5** gave a fairly stable, syrupy monoacetate (**6**), which was characterized by i.r. and n.m.r. spectroscopy and f.d. mass spectrometry; the presence of an acetamido, an *O*-acetyl, and two *O*-isopropylidene groups and a double bond was shown by the i.r. and n.m.r. spectra.

Configurational assignments were confirmed by decoupling techniques and treatment with D_2O, and the major peaks in the f.d. mass spectrum [*m/e* 344 $(M + 1)^+$, 343 (M^+), 101, and 43] support structure **6** well. Treatment of compounds **5** and **6** in *N*,*N*-dimethylformamide with Amberlite IRA-410 (OH^-) ion-exchange resin gave the furanoid 2-aminoglycal derivative **2** in good yield.

EXPERIMENTAL

General. — Melting points were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were determined with a Yanagimoto OR-50 polarimeter. N.m.r. spectra were recorded at 90 MHz with a Hitachi R-22 spectrometer. Mass spectra were recorded with a Jeol D-300 spectrometer. Preparative chromatography was performed on 300-mesh silica gel (Waco Co.) with the solvent systems specified. *N,N*-Dimethylformamide was distilled, and dried over Drierite (W.A. Hammond Drierite Co.). Evaporations were conducted *in vacuo*.

*Acetonation of 2-acetamido-2-deoxy-*D*-glucose* (**1**). — (*A*) *Treatment with Amberlite IRA-410 (OH^-) ion-exchange resin.* A suspension of 2-acetamido-2-deoxy-D-glucose (**1**) (10.0 g) in *N,N*-dimethylformamide (100 mL) was stirred at 10–15°, while 2,2-dimethoxypropane (30 mL) and *p*-toluenesulfonic acid monohydrate (3.0 g) were added; stirring was continued for 40 h at 10–15°. Amberlite IRA-410 (OH^-) ion-exchange resin (40 g) was added to the mixture, which was then stirred for 3 h at 30°, and the resin filtered off and washed with *N,N*-dimethylformamide. The filtrate and washings were combined, and evaporated at 50° (bath). Crystallization was spontaneous, and, when evaporation was complete, the mass was cooled, and stirred with chloroform (200 mL); after further cooling, the product was removed by filtration. The crystalline product (2.9 g, 25%) was identical with 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-D-glucopyranose[7] (**3**). The filtrate was concentrated, and the concentrate chromatographed on a column of silica gel (200 g) with (*a*) 70:1, (*b*) 40:1, and (*c*) 20:1 chloroform–methanol. Eluant (*a*) gave 2-acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal[1] (480 mg, 3.1%); eluant (*b*) yielded 2-acetamido-1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-D-*arabino*-hex-1-enitol (**2**; 4.7 g, 43%) [m.p. 152°, $[\alpha]_D^{25}$ −1° (*c* 0.5, methanol); lit.[13] m.p. 152°, $[\alpha]_D^{25}$ −1° (methanol)]: and eluant (*c*) afforded compound **3** (2.2 g, 19%) [total yield of **3**, 5.1 g (43%)].

(*B*) *Treatment with Amberlite IR-45 (OH^-) ion-exchange resin.* Acetonation of **1** (10.0 g) with 2,2-dimethoxypropane (30 mL) and *p*-toluenesulfonic acid monohydrate (3.0 g) in *N,N*-dimethylformamide (100 mL) was performed under the conditions described in (*A*); after the reaction, the mixture was stirred for 1 h with Amberlite IR-45 resin (40 g) to remove the acid. After removal of the resin, the solution was evaporated at 40° (bath) to a syrup which crystallized from chloroform (200 mL). The product was identical with compound **3**: wt. 3.8 g (32%). The filtrate was concentrated, and the concentrate chromatographed on a column of silica gel (200 g) with (*a*) 70:1, (*b*) 50:1, and (*c*) 20:1 chloroform–methanol. Eluant (*a*) gave 2-acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal[1] (500 mg, 3.2%); eluant (*b*) yielded **5** (4.2 g, 31%) as an unstable syrup which was characterized after acetylation (see next section). Elution with 20:1 chloroform–methanol afforded **4** (1.7 g, 14%), m.p. 145–147°, $[\alpha]_D^{25}$ +9° (*c* 1.0, methanol: equil.) [lit.[1] m.p. 145–147°, $[\alpha]_D$ +9° (methanol)] and compound **3** (1.4 g, 12%); total yield of **3**, 5.2 g (44%).

*2-Acetamido-3-O-acetyl-2-deoxy-1,4:5,6-di-O-isopropylidene-*D-arabino-*hex-1-enitol* (**6**). — A sample of **5** (3.8 g) was treated with pyridine (10 mL) and acetic an-

hydride (8 mL), and the solution was kept overnight at —5°, and then evaporated at 30° to a syrup. Chromatography of the syrup on a column of silica gel (100 g) with 150:1 chloroform–methanol afforded compound **6** (2.1 g, 48%) as a colorless syrup, $[\alpha]_D^{25}$ —30.5° (*c* 0.3, methanol); ν_{max}^{film} 3230 (NH), 1760 (ester), 1676 (C=C), 1650 and 1510 (amide), and 840 cm^{-1} (Me_2C); n.m.r. data at 90 MHz (in chloroform-*d*): τ 2.67 (s, 1 H, H-1), 3.16 (s, 1 H, NH), 5.62 (d, 1 H, $J_{3,4}$ 8.0 Hz, H-3), 5.85–6.13 (m, 3 H, H-5,6), 6.32 (near t, 1 H, $J_{3,4'} = J_{4,5} = 8.0$ Hz, H-4), 7.89, 7.99 (2 s, 6 H, AcO, AcN), 8.61 (s, 6 H, Me_2C), and 8.65 and 8.69 (2 s, 6 H, Me_2C); mass data (f.d. emitter; current 14 mA): *m/e* 344 [25, $(M + 1)^+$], 343 [100, M^+], 101 [12, $(Me_2C_3H_3O^+)$], and 43 [28, $(MeCO^+)$].

Anal. Calc. for $C_{16}H_{25}NO_7$: C, 55.96; H, 7.34; N, 4.08. Found: C, 55.92; H, 7.58; N, 4.21.

2-Acetamido-1,4-anhydro-2-deoxy-5,6-O-isopropylidene-D-arabino-*hex-1-enitol* (**2**). — (*A*) *From compound* **4**. A misture of compound **4** (1.0 g), *N,N*-dimethylformamide (10 mL), and Amberlite IRA-410 (OH^-) ion-exchange resin (10 g) was stirred for 8 h at room temperature, by which time, the starting material was no longer detectable by t.l.c. After filtration to remove the resin, the filtrate was evaporated, to give crystalline **2** (720 mg, 77%). Recrystallized from ether, the product was obtained as colorless plates, m.p. 152°, $[\alpha]_D^{25}$ —1° (*c* 0.5, methanol). The i.r. and n.m.r. spectra were identical with those of an authentic sample of **2**.

(*B*) *From compound* **5**. A mixture of compound **5** (200 mg), *N,N*-dimethylformamide (4 mL), and Amberlite IRA-410 (OH^-) resin (1.0 g) was stirred for 3 h at room temperature. The product was chromatographed on a column of silica gel, with 50:1 chloroform–methanol as the eluant, to give compound **2** (120 mg, 75%).

(*C*) *From compound* **6**. A mixture of compound **6** (200 mg), *N,N*-dimethylformamide (3 mL), and Amberlite IRA-410 (OH^-) resin (2.0 g) was stirred for 30 h at room temperature. After filtration to remove the resin, the filtrate was evaporated, to give crystalline **2** (130 mg, 92%).

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