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Note

Preparative synthesis of 2-acetamido-2,6-dideoxy-L-galactose (*N*-acetyl-L-fucosamine)*

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2-Acetamido-2,6-dideoxy-L-galactose (*N*-acetyl-L-fucosamine, **6**) is a constituent of the O-chain of the antigenic lipopolysaccharide of the *Pseudomonas aeruginosa*[1–3], Fisher immunotype 2, Lanyí types 0:7ab and 011, and of the polysaccharides of certain enteric bacteria[4]. L-Fucosamine has been obtained by the acidic hydrolysis of *Pneumococcus* Type V (ref. 5) and Type XII (ref. 6) capsular polysaccharides. In connection with work on the structure and biological activity of *Pseudomonas aeruginosa* antigens, certain derivatives of *N*-acetyl-L-fucosamine were needed. Four syntheses[7–10] of this sugar or its derivatives are known, but because of low yields, none of these methods was preparatively useful. Moreover, certain dervatives required for our proposed stereocontrolled oligosaccharide synthesis were not accessible by the literature procedures. To circumvent the limitations of the published procedures, we have developed a new and straightforward synthesis of *N*-acetyl-L-fucosamine by azidonitration[11] of a glycal precursor.

In the present synthesis, 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-*lyxo*-hex-1-enitol (3,4-di-*O*-acetyl-L-fucal, **1**) was converted into 3,4-di-*O*-acetyl-2-azido-2,6-dideoxy-α-L-galactopyranosyl nitrate (**2**) and 3,4-di-*O*-acetyl-2-azido-2,6-dideoxy-L-galactose (**3**) in 95% combined yield by reaction with ceric ammonium nitrate and sodium azide. It is noteworthy that products **2** and **3** have the azido group at the 2-position in the equatorial (L-*galacto*) orientation, and this is to be expected[11] owing to the quasiaxial orientation of the 4-acetoxy group of **1**. The formation of **3** possibly occurs by way of **2**, as it was found that a solution of pure **2** in aqueous acetone changed into **3** on being kept.

Acetolysis of the crude azidonitration products gave 1,3,5-tri-*O*-acetyl-2-azido-2,6-dideoxy-L-galactopyranose (**4**) as an anomeric mixture. The same anomeric mixture **4** was also obtained by the conventional acetylation of **3**. The

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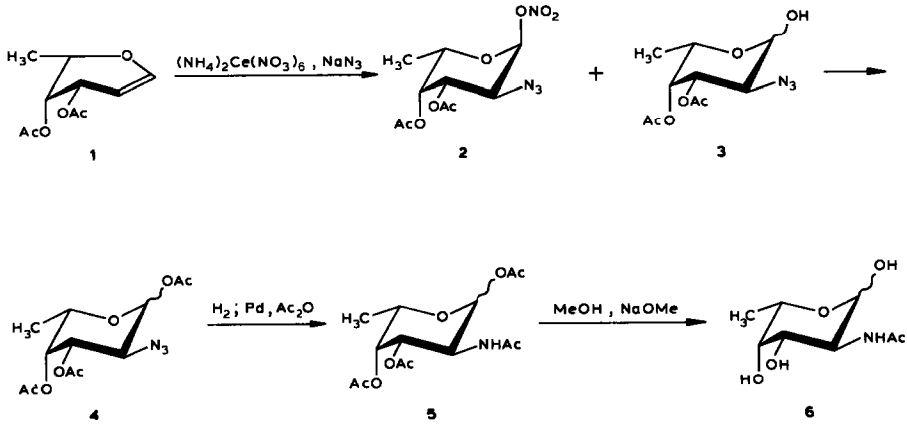
^{1}H-n.m.r. spectrum of **4** indicated that it has an α/β ratio of 5:1 and the pure α-L anomer of **4** was obtained by crystallization from a solution of the anomeric mixture in diethyl ether. Catalytic hydrogenation of **4** in the presence of acetic anhydride gave 1,3,5-tri-*O*-acetyl-2-acetamido-2,6-dideoxy-α,β-L-galactopyranose (**5**) as an anomeric mixture in quantitative yield, from which the pure β-L anomer was obtained by crystallization. *O*-Deacetylation of **5** gave *N*-acetyl-L-fucosamine (**6**) in 76% net yield from the glycal **1**.

EXPERIMENTAL

General methods. — Melting points were measured with a Thomas–Hoover "Unimelt" apparatus, and are not corrected. Specific rotations were measured with a Perkin–Elmer Model 141 polarimeter. T.l.c. was performed on Silica Gel $60F_{254}$ (Merck) and column chromatography with Silica Gel 60 (230–400 mesh, Merck). I.r. spectra were recorded with a Perkin–Elmer 137 spectrometer. N.m.r. spectra were recorded with a Bruker WP-200 or AM-500 spectrometers. Solutions were evaporated under diminished pressure.

*3,4-Di-*O*-acetyl-2-azido-2,6-dideoxy-α-*L*-galactopyranosyl nitrate* (**2**) *and 3,4-di-*O*-acetyl-2-azido-2,6-dideoxy-*L*-galactose* (**3**). — $(NH_4)_2Ce(NO_3)_6$ (4 g) and NaN_3 (0.5 g) were added to a solution of 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-*lyxo*-hex-1-enitol[12] (850 mg) in dry acetone (20 mL), and the mixture was stirred for 8 h at −15°. T.l.c. of the supernatant solution with 3:1 hexane–ethyl acetate no longer showed the presence of the glycal **1**. The mixture was partitioned between water and diethyl ether, and the organic layer was separated, dried (Na_2SO_4), and evaporated. The syrupy residue was divided into two equal portions, which were subjected separately to column chromatography and acetolysis. Elution of one portion from a column of silica gel with 6:1 hexane–ethyl acetate gave **2** (155 mg, 30%) as a crystalline solid. Compound **2** was recrystallized from ether–hexane; m.p. 115°, $[\alpha]_D^{22}$ −160° (*c* 0.5, chloroform); ν_{max}^{film} 2120 (N_3), 1750 (OAc), and 1650 cm^{-1} (ONO_2).



Anal. Calc. for $C_{10}H_{14}N_4O_8$: C, 37.74; H, 4.43; N, 17.60. Found: C, 37.75; H, 4.48; N, 17.57.

The second fraction eluted from the column gave **3** (350 mg, 65%) as a syrup; ν_{max}^{film} 3400 (OH), 2120 (N_3), and 1750 cm^{-1} (OAc). Compound **3** was characterized as its 1-acetate **4**.

The preparative value of the azidonitration reaction was also demonstrated on a larger scale. Thus, at the level of 22.0 g of **1**, this reaction yielded **2** (7.8 g, 30%), and **3** (17.84 g, 66%).

1,3,5-Tri-O-acetyl-2-azido-2,6-dideoxy-α,β-L-galactopyranose (**4**). — (*a*) *From* **3** *by acetylation.* Conventional acetylation of **3** (350 mg) with acetic anhydride in pyridine gave **4** (395 mg, 98%) as a crystalline solid; m.p. 149–152°; ν_{max}^{film} 2120 (N_3) and 1750 cm^{-1} (OAc); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 6.28 (d, $J_{1,2}$ 3.2 Hz, H-1α), 5.53 (d, $J_{1,2}$ 8.5 Hz, H-1β), 1.21 (d, $J_{5,6}$ 6.4 Hz, H-6β), and 1.18 (d, $J_{5,6}$ 6.5 Hz, H-6α); the ratio of α to β was 5:1.

Anal. Calc. for $C_{12}H_{17}N_3O_7$: C, 45.72; H, 5.43; N, 13.33. Found: C, 45.64; H, 5.45; N, 13.29.

Crystallization of the anomeric mixture of **4** (200 mg) from diethyl ether yielded the pure α-L anomer (100 mg); m.p. 155°, $[\alpha]_D^{25}$ −130° (*c* 0.5, chloroform); ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{12}H_{17}N_3O_7$: C, 45.72; H, 5.43; N, 13.33. Found: C, 45.81; H, 5.49; N, 13.31.

(*b*) *From a mixture of* **2** *and* **3** *by acetolysis.* One half of the crude azidonitration product obtained from 850 mg of **1** was dissolved in acetic anhydride (2 mL) and mixed with a solution (2 mL) of H_2SO_4 (0.2 mL) in acetic acid (10 mL). The mixture was kept for 18 h at 4°, stirred with sodium acetate (2 g), and partitioned

TABLE I

^{1}H-N.M.R. CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (Hz) FOR COMPOUNDS **1**, **4α**, AND **5β**[a]

Compound	*H-1* ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3* ($J_{3,4}$)	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6*	*OAc and NAc*
1	6.30d	4.07dd	5.25dd	5.34dd	4.30dq	1.18d	2.20
	(4.1)	(11.3)	(3.2)	(0.9)	(6.6)		2.07
4α	6.29d	3.90ddd	←5.34–5.31m→		4.20q	1.14d	2.07
							2.16
	(3.60)	(11.8)	(3.2)	(~0)	(6.7)		2.18
5β	5.67d	4.42ddd	5.05dd	5.20dd	3.90dq	1.22d	1.94
							2.02
	(7.7)	(11.2)	(3.3)	(0.8)	(6.4)		2.12
							2.19

[a]For solutions in (^{2}H)chloroform recorded at 500 MHz.

TABLE II

^{13}C-N.M.R. CHEMICAL SHIFTS (δ) FOR COMPOUNDS **1**, **4α**, AND **5β**[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OAc*	*NAc*	*C=O*
1	97.42	55.87	68.93	69.69	68.06	15.81	20.46 20.49		169.45 170.03
4α	90.74	56.82	77.04	77.29	76.79	15.91	20.56 20.64 20.94		168.97 169.94 170.37
5β	93.16	49.79	70.61	70.61	69.47	16.12	20.70 20.94	23.35	169.76 169.22 170.60 170.86

[a]For solutions in (^{2}H)chloroform recorded at 125 MHz.

between water and chloroform. The organic layer was dried and evaporated, and the residue was eluted from a column of silica gel with 4:1 hexane–ethyl acetate to give **4** (590 mg, 94%) as a crystalline solid identical with **4** obtained by method (*a*). This product was used for the next reaction.

1,3,5-Tri-O-acetyl-2-acetamido-2,6-dideoxy-α,β-L-galactopyranose (**5**). — A solution of **4** (590 mg) in methanol (25 mL) containing acetic anhydride (1 mL) was hydrogenated at 60 lb.in.$^{-2}$ (0.42 MPa) in the presence of 10% Pd–C (500 mg) for 20 h. The mixture was filtered, the filtrate evaporated, and the residue eluted from a column of silica gel with 10:1 chloroform–acetone to give **5** (550 mg, 90%) as a glass; $[\alpha]_D^{22}$ −80° (*c* 0.5, chloroform); ^{1}H-n.m.r. (500 MHz, $CDCl_3$): δ 6.20 (d, $J_{1,2}$ 3.1 Hz, H-1α) and 5.67 (d, $J_{1,2}$ 7.7 Hz, H-1β).

Anal. Calc. for $C_{14}H_{21}NO_8$: C, 50.75; H, 6.39; N, 4.22. Found: C, 50.82; H, 6.41; N, 4.21.

The β anomer of **5** was obtained from the anomeric mixture in diethyl ether by crystallization; m.p. 172°, $[\alpha]_D^{20}$ −15° (*c* 0.5, chloroform); for ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

2-Acetamido-2,6-dideoxy-L-galactose (**6**). — To a solution of **5**, anomeric mixture (200 mg), in methanol (2 mL) was added 0.1M methanolic sodium methoxide solution (0.5 mL). The mixture was kept for 18 h at 0°, diluted with methanol, made neutral with Dowex 50W-X4 (H^+) resin, and evaporated. The residue crystallized from ethanol to give pure **6** (110 mg, 95%); m.p. 198–199°, $[\alpha]_D^{23}$ −115 → −82° (equil., water); lit.[10] m.p. 195–198° and $[\alpha]_D$ −116 → −83° (water). The ^{1}H-n.m.r. spectrum of **6** was identical with that[13] of its D enantiomer; ^{1}H-n.m.r. (200 MHz, chloroform): δ 5.07 (d, $J_{1,2}$ 3.5 Hz, H-1α), 4.5 (d, $J_{1,2}$ 8.1 Hz, H-1β), 1.93 (s, NAc), 1.15 and 1.10 (2 d, H-6α,6β).

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