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Note

A facile synthesis of 2-acetamido-4,5,6-tri-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-*erythro*-*trans*-hex-2-enose

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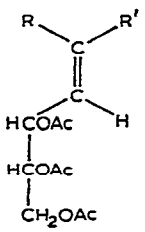
Acetolysis of di-*N*-acetylchitobiose with acetic anhydride–sulphuric acid, followed by neutralisation of the reaction mixture with aqueous sodium acetate, gives an unsaturated aldehyde, in low yield, which was tentatively formulated[1] as 2-acetamido-4,5,6-tri-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-*erythro*-*trans*-hex-2-enose (**1**). A synthesis of **1** starting from an anomeric mixture of isopropyl 2-acetamido-2-deoxy-D-glucosides is now described.

It was reasoned that **1** was formed from an acyclic precursor such as 2-amino-2-deoxy-D-glucose hepta-acetate, solvolysis of which would give first 2-amino-2-deoxy-*aldehydo*-D-glucose penta-acetate, which in turn would form **1** as a result of a β-elimination reaction. Since the conversion (under acetolysis conditions) of glycosides into hepta-acetates is facilitated when the aglycon has electron-repelling properties[2], increased yields of **1** were expected from isopropyl 2-acetamido-2-deoxy-D-glucoside; this was observed experimentally.



1 R = HC=O ; R' = NHAc
2 R = NHAc ; R'= HC=O

U.v. irradiation of **1** gave good yields of an isomer **2**, which was assigned the configuration in which the olefinic proton and aldehyde group are *cis*, on the basis of p.m.r. and u.v. spectral evidence. Thus, the olefinic proton in **2** resonated at lower field than that of **1**, due to its proximity to the aldehyde group[3]. The u.v. absorption of **2** is at appreciably longer wavelength than **1**, with a greater extinction coefficient which is presumably a reflection of the greater degree of orbital overlap possible in this isomer. Small proportions of **2** (up to 10%) were also found in crude **1** as extracted from the acetolysis mixture.

EXPERIMENTAL

2-Acetamido-2-deoxy-D-glucose was converted[4] into the anomeric mixture of isopropyl glycosides, and the product was crystallised from methanol–ether until free from starting material (t.l.c.).

The glycoside (1 g) was dissolved in ice-cold acetic anhydride (25 ml) containing 98% sulphuric acid (2.5 ml). After 6 h at 23°, the solution was poured into ice-cold, aqueous sodium acetate (300 ml, 25% w/v), and stored at 23° for 48 h. Crude **1** (1.3 g) was isolated by chloroform extraction (×4), followed by evaporation of the extracts to dryness with several additions of toluene. T.l.c. at this point (Silica Gel G; chloroform–ethyl acetate, 2:1) showed **1** as the major constituent (R_F 0.4), with a small proportion of **2** (R_F 0.55).

Elution of this product from Kieselgel (Merck, 0.05–0.2 mm) with 1:1 chloroform–light petroleum (b.p. 60–80°) gave first **2** (70 mg), m.p. 107° (from carbon tetrachloride), followed by **1** (1 g, 77%) as an oil which crystallised on storage; **1** had m.p. 96°. Recrystallisation from carbon tetrachloride gave material having m.p. 103°, $[\alpha]_D^{23}$ −30° (*c* 0.79, chloroform), $\lambda_{max}^{H_2O}$ 248 nm (ε 5.18×10^3). P.m.r. data (100 MHz, chloroform-*d*): τ 0.65 (*s*, 1 proton, CHO), 2.0 (*s*, 1 proton, exchangeable with D_2O, NH), 4.1 (*m*, 2 protons, H-3 and H-4), 4.65 (*m*, 1 proton, H-5), 5.7 (*m*, 2 protons, H-6), 7.9 (overlapping signals, 12 protons, 4Ac).

Anal. Calc. for $C_{14}H_{19}NO_8$: C, 51.06; H, 5.77; N, 4.25; mol. wt., 329 Found: C, 50.89; H, 5.43; N, 4.14; mol. wt. (mass spectrometry), 329.

The 2,4-dinitrophenylhydrazone of **1** had m.p. 121° (from methanol–ether), λ_{max}^{EtOH} 372 nm (ε 2.9×10^4).

Anal. Calc. for $C_{20}H_{23}N_5O_{11}$: C, 47.15; H, 4.52; N, 13.75. Found: C, 47.10; H, 4.46; N, 13.69.

Irradiation of a solution of **1** (400 mg) in dry benzene (70 ml) with light of wavelength >300 nm (Pyrex vessel, low-pressure mercury lamp) for 12 h gave ~50% conversion into a product with R_F identical to that of **2** in t.l.c. Isolation by preparative t.l.c. gave **2** (140 mg), m.p. 107° (from carbon tetrachloride), $\lambda_{max}^{H_2O}$ 267 nm (ε 5.73×10^3). P.m.r. data (60 MHz, chloroform-*d*): τ −0.1 (*s*, 1 proton, CHO), 2.1 (*s*, proton, exchangeable with D_2O, NH), 2.3 (*d*, 1 proton, J ~10 Hz, H-3), 3.6 (*q*, 1 proton, H-4), 4.7 (*q*, 1 proton, H-5), 5.7 (unsymmetrical *d*, 2 protons, H-6), 7.9 (overlapping signals, 12 protons, 4Ac).

Anal. Calc. for $C_{14}H_{19}NO_8$: C, 51.06; H, 5.77; N, 4.25; mol. wt., 329. Found: C, 50.93; H, 5.61; N, 4.20; mol. wt. (mass spectrometry), 329.

The mass spectra of **1** and **2** were identical.

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