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Note

A convenient synthesis of D-idose

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Abstract

Addition of nitromethane to D-xylose leads to the formation of two epimeric deoxynitroalditols, namely 1-deoxy-1-nitro-D-iditol and 6-deoxy-6-nitro-L-glucitol. Conversion of the former, obtainable in good yield by direct crystallisation, by a modified Nef reaction in an argon atmosphere afforded 68% of D-idose, which may readily be converted into 1,6-anhydro-β-D-idopyranose ("D-idosan"). © 1998 Elsevier Science Ltd. All rights reserved

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In 1894, J. U. Nef [1] reported the successful transformation of α-hydroxynitroalkanes into aldehydes and ketones. Over 50 years later, J. C. Sowden et al. [2] showed that nitromethane addition to aldoses readily gives deoxynitroalditols ("Fischer-Sowden reaction") from which the corresponding higher aldoses may be obtained by use of the the Nef reaction [3]. The nitro compounds are generally transformed with base into their nitronate anions, which are then added dropwise to half-concentrated mineral acid. The solutions are made neutral and the ions removed. The resulting aldoses are isolated in yields of 58–84% [2].

In following the literature procedures [2], we found that the Nef reaction gave yields considerably lower than those reported. It was considered probable that oxygen from the air oxidises the intermediates or the desired products under the harsh conditions used, and therefore the reaction was carried out in an inert atmosphere. Increased yields were obtained and, in particular, this variation allows simple access to D-idose [4].

1. Results and discussion

In the present work addition of nitromethane to D-xylose (**1**) led to the formation of 1-deoxy-1-nitro-D-iditol (**2**) and 6-deoxy-6-nitro-L-glucitol (**3**) [5]. The yield of 47% of the former reported in the literature [5] was improved to 75% by extension of the reaction times and by multiple fractional crystallisations. The reaction of **2** under Nef conditions in an argon atmosphere afforded, in 68% yield, syrupy D-idose (**4**) containing traces of D-xylose (less than 1%) formed in a side reaction. Since **4** is not stable over a long period (the Lobry de Bruyn–Alberda van Ekenstein reaction transforms **4** into D-sorbose [6]), it was converted into 1,6-anhydro-β-D-idopyranose ("D-idosan", **5**) [7]. The overall yield of this anhydride from **2** was 52% (Scheme 1).

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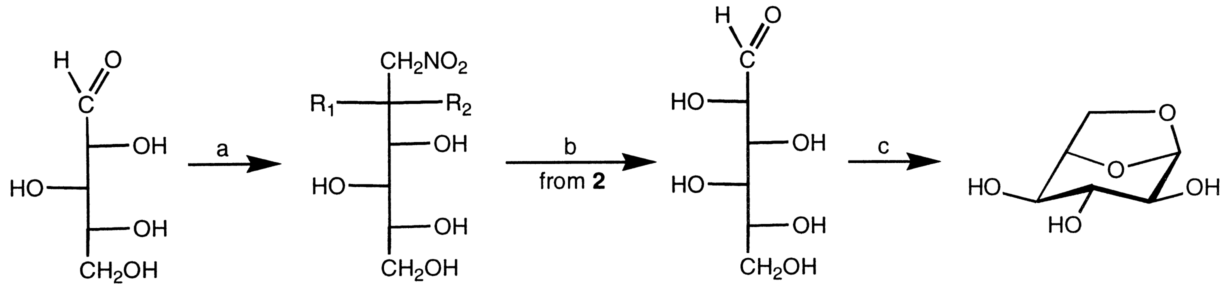

1

2: R^1 = OH, R^2 = H
3: R^1 = H, R^2 = OH

4

5

Scheme 1. Reagents and conditions: (a) $MeNO_2$, NaOMe, abs MeOH, 20 °C, 12 h; (b) NaOH (1–2 M, aq), then H_2SO_4 (8 M, aq), Ar, 10–20 °C, 1 h; (c) H_2SO_4 (dil, aq), reflux, 20 h.

2. Experimental

General methods.—All solvents were distilled before use. Amberlite IR-120 (H^+) cation exchange resin and Amberlite IRA-400 (OH^-) anion exchange resin were employed for deionisations. Melting points were determined on the hot stage of a Leitz Laborlux 12 microscope and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 MC polarimeter and the samples were dissolved 24 h before measurements to allow equilibration. The IR spectrum was recorded on a Philips PU 9706 spectrometer. The ^{1}H (300.1 MHz) and ^{13}C (75.5 MHz) NMR spectra were recorded with a Bruker AM 300 spectrometer. All samples were measured in D_2O, and resonances were referred to internal acetone (^{1}H δ 2.09, ^{13}C δ 30.5 CH_3).

*1-Deoxy-1-nitro-*D*-iditol* (**2**).—A solution of Na (10.5 g, 457 mmol) in abs MeOH (350 mL) was added to a suspension of dried D-xylose (50.0 g, 333 mmol) in abs MeOH (100 mL) and abs $MeNO_2$ (180 mL, 3.323 mol). The mixture was shaken on a mechanical shaker for 16 h at 20 °C. Diethyl ether (100 mL) was added to the suspension and the slurry cooled over 1 h to about −15 °C. The precipitate was filtered off and washed with cold Et_2O (50 mL) and cold MeOH (20 mL). The light-yellow sodium nitronate was dissolved in water (400 mL) and passed through a column of Amberlite IR-120 (H^+) resin. The eluate was concentrated at 35 °C under diminished pressure to a syrup. Multiple crystallisations from EtOH afforded **2** as a hemi hydrate (55.1 g, 75%) [5]: mp 89–90 °C, lit. 88 °C [5]; $[\alpha]_D^{20}$ $+3.4°$ (*c* 1, H_2O), lit. $[\alpha]_D^{20}$ $+3.8°$ (*c* 1.9, H_2O) [5]. The ^{13}C NMR and ^{1}H NMR data were identical to literature values [5,8].

D-*Idose* (**4**).—1-Deoxy-1-nitro-D-iditol (**2** [5], 2 g, 9.48 mmol) in degassed NaOH (M, aq, 10 mL) was added slowly under argon to H_2SO_4 (8 M, aq, 2.8 mL) with vigorous stirring, and with the temperature kept between 10 and 20 °C. The rate of addition was such that the blue colour of the immediately formed nitroso compound just disappeared. Stirring was continued for 1 h, Congo Red (~10 mg) was added, and the solution was diluted to double volume. $Ba(OH)_2$ (satd, aq) was then added until the indicator colour of the mixture turned from blue to pink (pH 3.0 to 5.2) and the neutralisation was continued to pH 6. Most of the precipitated $BaSO_4$ was separated by decantation, the residue was slurried with water and the solution again decanted. The combined turbid solution was filtered through a short column of silica gel 60, which was then washed with water (~30 mL). The filtrate was concentrated to about 100 mL at 40 °C in vacuo and subsequently deionised by use of cationic-, anionic-, and again cationic-exchange resins. The resins were filtered off and washed thoroughly after each step. The solvent was removed by distillation in vacuo and the resulting colourless syrup was dried under high vacuum to give **4** (1.36 g, 68%). The ^{13}C NMR of the mixture of pyranoses and furanoses matched the literature values [9].

*1,6-Anhydro-β-*D*-idopyranose ("*D*-idosan",* **5***)*.—1-Deoxy-1-nitro-D-iditol (**2** [5], 10 g, 47.4 mmol) in degassed NaOH (2 M, aq, 28 mL) was added, under the same conditions previously described for **4**, to degassed H_2SO_4 (8 M, aq, 32 mL). The reaction mixture was stirred for 1 h, diluted with water to 800 mL, and heated under reflux for 20 h. After cooling, the solution was concentrated to half its volume and neutralised with $Ba(OH)_2$ (satd, aq) and ion-exchange resins as for **4**. The filtrate was concentrated and the product crystallised from (3:1 ^{i}PrOH–EtOH), giving **5** (4.00 g, 52%): mp 128–129 °C, lit. 126–128 °C [7]; $[\alpha]_D^{20}$ −92.6° (*c* 2.00, H_2O), lit. $[\alpha]_D^{14}$ −92.6° ± 1° (*c* 2.052, H_2O) [7]; IR (KBr): ν 3600–3100 (O–H), 2960, 2900, 1425 (C–H), 1130, 1100, 1055, 1015 (C–O) cm^{-1}. The ^{13}C NMR matched the literature values [9].

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