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Carbohydrate Research 270 (1995) 93–96

CARBOHYDRATE RESEARCH

Note

A novel synthesis of L-fucose from D-galactose

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Received 13 October 1994; accepted 2 December 1994

Keywords: Synthesis; L-Fucose; D-Galactose

L-Fucose is ubiquitous in nature and its presence in glycoconjugates and other biologically important moieties plays an important role in the activity of these substances [1]. However, it is a quite expensive sugar. In the course of synthesis of some biologically active oligosaccharides, it was therefore deemed pertinent to develop an easy route for the synthesis of L-fucose from a readily available source.

Several methods for the synthesis of L-fucose have been reported [2–5]. Two of these methods used D-galactose as the starting material. The first one [4] involved a lengthy reaction sequence and low yield. The second method [5] had a shorter route but utilized expensive reagents and involved syrupy intermediates. The purpose of this communication is to report an easy and inexpensive route for the synthesis of L-fucose from D-galactose in good yield using inexpensive reagents and involving mostly crystalline intermediates.

D-Galactose diethyl dithioacetal [6] (**1**), obtained from D-galactose, was reduced [7] with Raney nickel in the presence of zinc granules and sodium hydroxide to afford L-fucitol (**2**). The use of zinc and NaOH reduced the requirement of Raney nickel to one-half while the yield increased threefold. L-Fucitol (**2**), thus obtained, was partially acetylated [8] with acetic anhydride (1.2 equiv) and pyridine, giving 1-*O*-acetyl-L-fucitol (**3**). The tetrabenzoate (**4**), obtained by benzoylation of **3**, was then deacetylated [9] with

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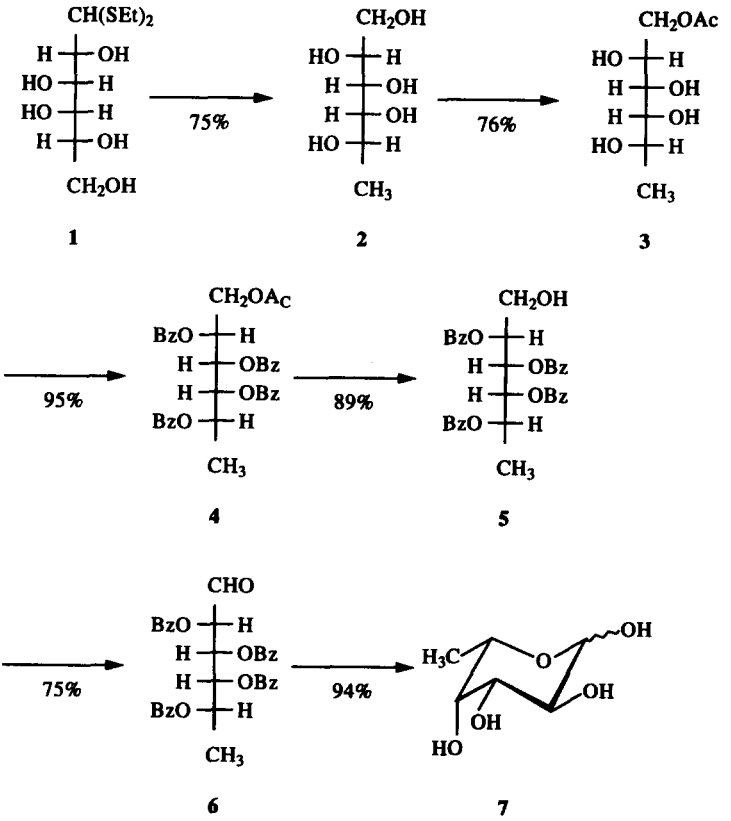
SSDI 0008-6215(94)00004-2



Scheme 1.

methanolic HCl, affording 2,3,4,5-tetra-*O*-benzoyl-L-fucitol (**5**). This compound was found to be identical with the compound obtained by tritylation of **2** followed by benzoylation and detritylation of the product. The L-fucitol derivative (**5**) was oxidized with Me_2SO/acetic anhydride [10] to give 2,3,4,5-tetra-*O*-benzoyl-*aldehydo*-L-fucose (**6**) which on treatment with methanolic sodium methoxide gave L-fucose (**7**). The overall yield of L-fucose based on D-galactose diethyl dithioacetal was 34%.

Experimental

Reactions were monitored by TLC on Silica Gel G (Merck). Column chromatography was performed using 100–200 mesh silica gel (SRL, India), and all solvents were removed below 40°C under reduced pressure unless stated otherwise. Optical rotations were measured with a Perkin–Elmer 241 MC polarimeter. The ^1H and ^{13}C NMR spectra were recorded with a Jeol FX100 spectrometer. Melting points were determined on a

paraffin oil bath and are uncorrected. GLC of alditol acetates was performed on a Hewlett–Packard model 5730A gas chromatograph fitted with a glass column (1.83 m × 6 mm) packed with 3% ECNSS-M on Gas Chrom Q (100–120 mesh), at 170°.

L-*Fucitol* (**2**).—D-Galactose diethyl dithioacetal (**1**) [6] was prepared from D-galactose. To a solution of **1** (10 g, 35 mmol) in 70% EtOH (250 mL), Raney nickel (30 g), zinc granules (5 g), and NaOH (10 g) were added and the mixture was refluxed for 2 h. The mixture was filtered through a Celite bed. The filtrate was treated with Dowex 50 (H^+) and Rexin 300 (OH^-) resins in succession and filtered again. The filtrate was concentrated to a glassy material which was crystallized from ethanol to give L-fucitol (**2**; 4.35 g, 75%); mp 151–152°C; $[\alpha]_D$ 0° (*c* 1, water); lit. [5] mp 154°C; $[\alpha]_D$ + 0.8° (water); ^{1}H NMR (CD_3OD): δ 1.02 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_6H_{14}O_5$: C, 43.36; H, 8.49. Found: C, 43.22; H, 8.59.

1-O-*Acetyl*-L-*fucitol* (**3**).—To a solution of L-fucitol (**2**) (4 g, 24 mmol) in pyridine (40 mL) cooled to −40°C was added acetic anhydride (2.6 mL, 28 mmol), and the mixture was kept at that temperature for 2 h. The temperature was then raised to −5°C. After 18 h, the mixture was evaporated to dryness and purified by column chromatography using 2:1 toluene–EtOAc. The major product crystallized from MeOH–EtOAc to give pure 1-*O*-acetyl-L-fucitol (**3**; 3.8 g, 76%); mp 159–160°C; $[\alpha]_D$ +19.5° (*c* 0.9, MeOH); ^{1}H NMR (CD_3OD): δ 1.22 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 2.06 (3 H, OAc). Anal. Calcd for $C_8H_{16}O_6$: C, 46.15; H, 7.74. Found: C, 46.03; H, 7.89.

1-O-Acetyl-2,3,4,5-tetra-O-benzoyl-L-*fucitol* (**4**).—Compound **3** was benzoylated conventionally with benzoyl chloride and pyridine, yielding **4** (95%); mp 101–102°C (EtOH); $[\alpha]_D$ −0.64° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.4 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 1.84 (s, 3 H, CH_3CO), 7.53–8.15 (m, 20 H, 4 Ph). Anal. Calcd for $C_{36}H_{32}O_{10}$: C, 69.2; H, 5.16. Found: C, 69.1; H, 5.33.

2,3,4,5-Tetra-O-benzoyl-L-*fucitol* (**5**).—To a solution of **4** (5 g) in MeOH (25 mL) was added acetyl chloride (5 mL) and the mixture was left at 22°C for 16 h. The product, separated as a white precipitate, was collected by filtration and washed with MeOH to give **5** (4.1 g, 89%); mp 116–118°C (EtOH); $[\alpha]_D$ −1° (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.32 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 7.5–8.2 (m, 20 H, 4 Ph). Anal. Calcd for $C_{34}H_{30}O_9$: C, 70.09; H, 5.18. Found: C, 69.98; H, 5.29.

2,3,4,5-Tetra-O-benzoyl-aldehydo-L-*fucose* (**6**).—To a solution of **5** (3.5 g, 6 mmol) in Me_2SO (18 mL) was added acetic anhydride (12 mL), and the mixture was stirred vigorously at 40°C under N_2 for 3 h. The reagents were then removed by evaporation and the product was purified by column chromatography using 6:1 toluene–ether to afford pure **6** (2.6 g, 75%); $[\alpha]_D$ +7.3° (*c* 0.95, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.41 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 5.4–5.9 (m, 2 H, H-4 and H-5), 6.05 (dd, 1 H, $J_{2,3}$ 8.5, $J_{3,4}$ 6 Hz, H-3), 6.35 (dd, 1 H, $J_{1,2}$ 0.3 Hz, H-2), 7.5–8.2 (m, 20 H, 4 Ph), 9.5 (d, 1 H, H-1). Anal. Calcd for $C_{34}H_{28}O_9$: C, 70.3; H, 4.86. Found: C, 70.2; H, 4.98.

L-*Fucose* (**7**).—Compound **6** (2 g, 3 mmol) was treated with 0.05 M NaOMe in MeOH (30 mL) at room temperature for 4 h. The mixture was then stirred with Dowex 50 (H^+) resin for 30 min, the resin filtered off and washed with MeOH, and the solution concentrated to afford L-fucose. Compound **7** was crystallized from dry EtOH (0.5 g, 94%); mp 138–140°C; $[\alpha]_D$ −74.6° (*c* 1, equil. in H_2O); lit. [4] mp 137–139°C; $[\alpha]_D$ −75° (H_2O).

Acknowledgment

One of the authors (S.S.) thanks C.S.I.R., New Delhi, for financial assistance.

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