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Note

Synthesis of L-fucose

MARTA DEJTER-JUSZYNSKI AND HAROLD M. FLOWERS
Department of Biophysics, Weizmann Institute of Science, Rehovoth (Israel)
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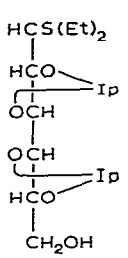
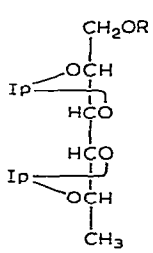
L-Fucose is a sugar of considerable biological interest and wide natural occurrence. Its isolation from the Fucus species of seaweed is not difficult[1]. However, it is a relatively expensive sugar and the only synthesis described afforded an overall yield of 1% from L-arabinose[2]. Our approach, which affords a good yield of L-fucose from the readily available D-galactose, is also of theoretical interest in that it involves the formal inversion of the D-galactose molecule to produce derivatives of L-galactose. Furthermore, the open-chain intermediates prepared may be utilized in the synthesis of disaccharides of L-fucose which we are investigating at present. The secondary hydroxyl groups in acyclic derivatives are expected to be more reactive than the more sterically hindered hydroxyl groups attached to a pyran ring.

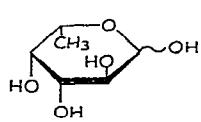
The conversion of D-galactose into L-fucitol pentaacetate[3] and 2,3:4,5-di-*O*-isopropylidene-D-galactose diethyl dithioacetal[4] (**1**) have been described. By adaptations of these methods, 2,3:4,5-di-*O*-isopropylidene-L-fucitol (**2**) was prepared, in 29% yield from D-galactose, as a crystalline product which gave a crystalline *p*-toluenesulfonate (**3**) in good yield. Oxidation of **2** with dimethyl sulfoxide–phosphoric acid–dicyclohexylcarbodiimide[5] gave a mixture which was hydrolyzed directly with acetic acid. After column chromatography, L-fucose (**4**), was obtained from the hydrolyzate in 15% overall yield from D-galactose. A small amount of unoxidized L-fucitol (1% yield based on D-galactose) was also obtained.



1



2 R = H
3 R = Tosyl



4

EXPERIMENTAL

For general methods see Ref. 6.

*6-Deoxy-2,3:4,5-di-*O*-isopropylidene-*L*-galactitol* (*2,3:4,5-di-*O*-isopropylidene-*L*-fucitol*) (**2**). — 2,3:4,5-Di-*O*-isopropylidene-D-galactose diethyl dithioacetal (**1**) was prepared as described in Ref. 4; t.l.c. (4:1 benzene–ether) showed the presence of two acetal products, the major spot having the smaller R_F value. They were separated by column chromatography on silica gel and the major fraction was eluted with 4:1 benzene–ether (76% yield from D-galactose diethyl dithioacetal). This homogeneous material (**1**, 5 g) and Raney nickel catalyst[3] (60 g) were heated at reflux overnight in 70% ethanol (400 ml). The nickel was removed by filtration and washed several times with hot ethanol. The combined solutions and washings were evaporated *in vacuo*, and the residue was dissolved in benzene and chromatographed on a column of silica gel. The combined homogeneous fractions eluted with 2:1 benzene–ether gave an amorphous solid on evaporation of the solvent (2.8 g, 81%). Crystallization from petroleum ether afforded needles, m.p. 52–54°; $[\alpha]_D^{23}$ 0° (*c* 1.0, chloroform).

Anal. Calc. for $C_{12}H_{22}O_5$: C, 58.51; H, 9.00. Found: C, 58.35; H, 8.90.

The minor fraction was presumably 2,3:5,6-di-*O*-isopropylidene-D-galactose[4].

*6-Deoxy-2,3:4,5-di-*O*-isopropylidene-1-*O*-p-tolylsulfonyl-*L*-galactitol* (**3**). — To a portion of **2** (0.35 g, 1.0 mmole) dissolved in pyridine (5 ml) was added *p*-toluenesulfonyl chloride (0.21 g, 1.1 mmole). The reaction mixture was kept overnight at room temperature and, after addition of water, extracted with chloroform. The organic layer was washed successively with cold hydrochloric acid, a saturated solution of sodium hydrogen carbonate, and water, dried with calcium chloride, and evaporated *in vacuo* to a syrup (0.45 g, 75.5%). Crystallization from 80% ethanol afforded **3**, m.p. 75–77°; n.m.r. data: τ 2–2.75 (m, 4H, aromatic), 7.54 (3H, C_6H_4–Me), 8.56–8.76 (m, 15H, CH–Me and 2 C–Me_2).

Anal. Calc. for $C_{19}H_{28}O_7S$: C, 56.99; H, 7.05; S, 8.01. Found: C, 57.52; H, 6.90; S, 7.99.

*6-Deoxy-*L*-galactose* (L-*fucose*) (**4**). — A solution of dicyclohexylcarbodiimide (6.2 g, 30 mmoles) in benzene (10 ml) and anhydrous orthophosphoric acid (5 ml of a M solution in dimethyl sulfoxide, 5 mmoles) were added to a solution of **2** (2.46 g, 10 mmoles) in dimethyl sulfoxide (40 ml). The reaction mixture was kept overnight at room temperature, the dicyclohexylurea removed by filtration, the filtrate evaporated *in vacuo* to a syrup, and the crude product hydrolyzed with 60% acetic acid (100 ml) at 100° for 2 h. The solution was evaporated *in vacuo* and water was added and evaporated several times. The residue (1.26 g) was dissolved in 3:1 ethyl acetate–methanol and chromatographed on silica gel. An earlier fraction (0.30 g) eluted from the column was stable to hot 60% acetic acid solution and was not investigated further; a second fraction gave **4** (0.80 g, 50% from **2**), identical with an authentic specimen of L-fucose on t.l.c. in 9:1 acetone–methanol and 3:1 ethyl acetate–methanol and on paper chromatography in 4:5:1 butanol–ethanol–water, 8:2:1 ethyl acetate–pyridine–water, and 18:3:1:4 ethyl acetate–acetic acid–formic acid–water. Crystallization from

absolute ethanol afforded prisms, m.p. 137–139°; $[\alpha]_D^{23}$ −75° (equilibrium, *c* 0.8, water); lit.[1]: m.p. 140–141°; $[\alpha]_D^{17}$ −76° (equilibrium, *c* 2.0, water).

Anal. Calc. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 44.14; H, 7.23.

A third fraction eluted from the column (60 mg, 3.6% from **2**) was shown to be L-fucitol.

A portion of **4** was converted into the methylphenylhydrazone[1], m.p. 180–182°; $[\alpha]_D^{23}$ +6.0° (*c* 5.0, pyridine); lit.[1]: m.p. 172°; $[\alpha]_D$ +5.0 (*c* 5.0, pyridine).

Anal. Calc. for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44. Found: C, 58.08; H, 7.29; N, 10.42.

A specimen of L-fucose methylphenylhydrazone prepared from authentic L-fucose showed m.p. 180–182°; $[\alpha]_D^{23}$ +6.0° (*c* 5.2, pyridine).

Anal. Calc. for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44. Found: C, 57.98; H, 7.62; N, 10.53.

No depression of m.p. was observed on admixture of the derivatives prepared from **4** and from authentic L-fucose. The n.m.r. spectra of the two hydrazones were identical: τ 2.67 (5H, N–Ph), 6.48 (3H, N–Me), 8.74 (d, *J* 6.5 Hz, 3H, CH–Me).

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