419. *Methylene Derivatives of* L-*Fucose.*

By R. L. Nelson and Elizabeth Percival.

L-Fucose on treatment with paraformaldehyde yielded five methylene derivatives. Three of these have been separated and characterised as a di-*O*-methylene-L-fucose, and two mono-*O*-methylene-L-fucoses. 2-*O*-Methyl-L-fucose has been synthesised from methyl 3 : 4-*O*-*iso*propylidene-α-L-fucoside.

L-Fucose when treated with paraformaldehyde according to the method of Andrews, Hough, and Jones [1] gave chromatographic evidence that at least four compounds were formed. Crystals (I) were obtained from a rapidly-obtained chloroform extract of the neutralised product. The residual material, after further treatment with paraldehyde, was separated on cellulose into four fractions, and two of these fractions (III and IV) were investigated.

The crystals (I) (39·7% yield) which could not be detected on the paper chromatogram were non-reducing to Fehling solution and on hydrolysis gave L-fucose and 1·9 mol. of formaldehyde. They gave correct analytical results for a di-*O*-methylenefucose and on partial acid hydrolysis gave a mixture of L-fucose and fraction (IV). Separation on thick paper gave crystalline fraction (IV).

Fraction (IV) a mono-*O*-methylenefucose, was reducing and gave one mol. of formaldehyde on hydrolysis. Oxidation with periodate gave an uptake of 0·93 mol. of periodate and a release of 0·88 mol. of formic acid. Methylation and hydrolysis followed by separation on thick paper led to isolation of 2-*O*-methyl-L-fucose. Fraction (IV) must therefore be either the 3 : 5- or the 3 : 4-mono-*O*-methylene-L-fucose. Its high negative rotation ($[\alpha]_D^{20}$ −95°) is suggestive of a pyranose ring {cf. 2 : 3 : 4-tri-*O*-methyl-L-fucose, $[\alpha]_D$ −128°; [2] 2 : 3 : 5-tri-*O*-methyl-L-fucose, $[\alpha]_D^{20}$ +70° (*c*, 1·7 in H_2O) (unpublished work)}. If fraction (IV) is the 3 : 4-mono-*O*-methylene-L-fucose and not the 3 : 5-isomer, then fraction (I) is 1 : 2-3 : 4-di-*O*-methylene-L-fucose.

Fraction (III) was a reducing syrup; it gave approximately 1 mol. of formaldehyde on hydrolysis and was unaffected by periodate. Methylation followed by hydrolysis yielded a syrup which was shown to contain fucose, 3-*O*-methylfucose, and a substance with an R_F value slightly lower than that of 2 : 3 : 4-tri-*O*-methylfucose (paper chromatography). It would appear that the methylene group had been partly removed during methylation, and fraction (III) is tentatively identified as 2 : 5-mono-*O*-methylene-L-fucose.

Although fractions (II) and (V) were insufficient for complete investigation they both appeared to be mono-*O*-methylene derivatives. In contrast to rhamnose [1] no evidence for the presence of *O*-dimethyleneoxy-compounds was obtained.

Authentic crystalline 2-*O*-methyl-L-fucose has been synthesised from methyl 3 : 4-*O*-*iso*propylidene-α-L-fucoside by methylation followed by hydrolysis.

Experimental

Chromatography was carried out by the descending method on Whatman No. 1 filter paper, butane-1-ol–ethanol–water (40 : 11 : 19 v/v; upper layer) being used as mobile phase. L-Fucose and its derivatives were located on the chromatogram by spraying it with aniline oxalate. The rate of movement of compounds on the chromatogram is quoted relative to that of the solvent front (R_F value) and to that of L-fucose (R_{Fu} value).

Preparation of the Methylene Derivatives.—L-Fucose ($[\alpha]_D$ −74·5° in H_2O) (15 g.) was treated with paraformaldehyde according to the method of Andrews, Hough, and Jones.[1] After neutralisation with barium carbonate, the filtrate was rapidly extracted with chloroform (3 × 50 c.c.). The chloroform extracts were dried ($MgSO_4$) and evaporated to a syrup which was dissolved in water and rapidly extracted with chloroform. The chloroform extracts on

[1] Andrews, Hough, and Jones, *J. Amer. Chem. Soc.*, 1955, **77**, 125.
[2] O. T. Schmidt, Mayer, and Distelmaier, *Annalen*, 1943, **555**, 26.

concentration gave crystals (3·3 g.) of material which could not be detected on the paper chromatogram. Recrystallisation from ethanol and sublimation afforded *di*-O-*methylene*-L-*fucose* (I), m. p. 77°, $[\alpha]_D$ +58° (*c*, 0·7 in MeOH), +68° (*c*, 0·87 in H_2O) (Found: C, 51·3; H, 6·3. $C_8H_{12}O_5$ requires C, 51·1; H, 6·4%). The combined aqueous residues were extracted with chloroform during 18 hr. with continuous shaking. Evaporation of the dried ($MgSO_4$) chloroform extracts gave a syrup (*A*). This syrup smelled strongly of formaldehyde and trioxan sublimed from it when it was heated under reduced pressure. Chromatographic examination showed the presence of compounds with R_F 0·80, R_{Fu} 3·5 (II); R_F 0·70, R_{Fu} 3·0 (III); R_F 0·60, R_{Fu} 2·4 (IV). Continuous extraction of the aqueous mother liquors with chloroform for a further 24 hr. yielded a syrup (*B*) which on chromatographic examination was shown to contain fractions (III) and (IV) with a trace of a compound (V), R_F 0·50. The aqueous mother liquors on evaporation gave a yellow syrup consisting mainly of fucose (chromatography). This syrup together with fucose (2 g.) was treated with paraformaldehyde as before.[1] More of fraction (I) (3·6 g.) (total yield 6·9 g. from 17 g. of fucose) was obtained. The aqueous solution on evaporation gave a yellow syrup (*C*).

Syrups *A*, *B*, and *C* were combined and a portion (*ca.* 5 g.) was fractionated on a cellulose column with light petroleum (b. p. 100—120°)–butane-1-ol (70 : 30, changed in stages to 40 : 60 parts v/v) as the mobile phase; finally the fucose was eluted with ethanol. The following fractions were collected and treated with charcoal: (II) Crystalline (37 mg.), $[\alpha]_D^{20}$ +12° (*c*, 0·37 in H_2O), non-reducing to Fehling solution. (IIa) Syrup (26 mg.), a mixture of (II) and (III). (III) Syrup (248 mg.), $[\alpha]_D^{25}$ +16°, reducing. (IV) Crystalline (677 mg.), m. p. 96°, reducing to Fehling solution, $[\alpha]_D$ −124° (2 min.) ⟶ −90·5° (const., *c*, 5·8 in H_2O) (Found: C, 47·6; H, 6·7. $C_7H_{12}O_6$ requires C, 47·7; H, 6·8%). (V) (25 mg.), $[\alpha]_D$ −64° (*c*, 0·25 in H_2O).

Hydrolysis of the Methylene Derivatives.—The crystalline derivatives and the syrups were hydrolysed with N-sulphuric acid at 100° for 2 hr. [2N-H_2SO_4; 4 hr. for fraction (I)] giving fucose (detected chromatographically) and formaldehyde. In each case, formaldehyde was identified and estimated according to the method used by Andrews, Hough, and Jones.[1] Results are given in Table 1.

TABLE 1.

Compound or fraction	I	II	IIa	III	IV	V
M (calc.)	188	176	176	176	176	176
Wt. taken (mg.)	10·89	9·2	13	9·5	10·9	12·3
Yield of dimedone deriv. (mg.)	31·6	10·0	20·4	13·4	17·8	17·6
Yield of formaldehyde (mol.)	1·90	0·66	0·95	0·86	1·0	0·86

Periodate Oxidation.—To each compound (5—10 mg.) in water (5 c.c.) 0·2N-sodium metaperiodate (2 c.c.) was added, and the mixture was set aside in the dark. After 3 hr. the reaction mixture was treated according to one of the following methods: (i) Boric acid (2 g.) and saturated borax (5 ml.) were added and the mixture was set aside (3 min.). Potassium iodide (5 ml., 40%) was then added and the solution titrated with sodium arsenite. (ii) Ethylene glycol (1 c.c.) was added, and the formic acid liberated was titrated with 0·01N-sodium hydroxide. In order to hydrolyse the formyl esters which had been produced the formic acid titrations were completed on hot solutions. Results are given in Table 2.

TABLE 2.

Compound or fraction	II	III	IV	Compound or fraction	II	III	IV
M (calc.)	176	176	176	Wt. taken (mg.)	9·0	9·5	7·70
Wt. taken (mg.)	9·0	9·5	6·8	Formic acid yield (c.c. of			
Periodate uptake (c.c. of 0·01N)	2·73	2·2	7·10	0·01N)	nil	0·5	3·0
,, (mol.)	0·25	0·19	0·93	,, ,, (mol.)	nil	0·13	0·88

Partial Hydrolysis of Di-O-*methylene*-L-*fucose* (I).—The compound (333 mg.) was heated at 100° in 0·01N-sulphuric acid and the hydrolysis followed polarimetrically: $[\alpha]_D$ +225° (initial), +219° (15 min.), +210° (2 hr.). The concentration of acid was increased to 0·02N and heating continued. The rotations observed were +180° (5 hr.), +141° (10 hr.), +110° (13 hr.). Aliquot portions were removed after (*a*) 5 hr., (*b*) 10 hr., and (*c*) 13 hr. Neutralisation, concentration, and chromatographic examination showed (*a*) a single faint spot, R_F 0·60, R_{Fu} 0·24 (cf. fraction IV), (*b*) a spot R_F 0·60, and a faint spot corresponding to fucose, (*c*) the same two

spots as (*b*). The remaining solution afforded a syrup after cooling, neutralisation ($BaCO_3$), and concentration. Separation of this syrup on thick paper gave two fractions: (1) R_F 0·60, R_{Fu} 0·24, crystalline, m. p. and mixed m. p. with compound (IV) 96°, $[\alpha]_D^{18}$ −95° (*c*, 0·25 in H_2O); (2) crystalline fucose, m. p. 140—142°.

Fraction (III).—This syrup (100 mg.) was methylated thrice with Purdie reagents. Hydrolysis with N-sulphuric acid for 2 hr., neutralisation ($BaCO_3$), and concentration gave a syrup (48 mg.) which gave spots corresponding to fucose (trace), 3-*O*-methylfucose, and a dark red spot with R_F 0·66 [cf. 2 : 3 : 4-tri-*O*-methylfucose, R_f 0·70; 2 : 3 : 5-tri-*O*-methylfucose, R_F 0·87 (unpublished work)] similar in colour to other spots given by fucofuranose derivatives.

3 : 4-O-*Methylene*-L-*fucose* (IV).—This compound (280 mg.) was methylated thrice with Purdie reagents. The addition of methanol (2 c.c.) was necessary to dissolve the material in the first methylation. The product, a syrup (n_D^{18} 1·4650), was hydrolysed for 1 hr. with N-sulphuric acid at 100° and the neutralised solution ($BaCO_3$) filtered and concentrated to syrup. Chromatographic examination showed this to be 2-*O*-methylfucose contaminated with a trace of fucose. Separation on thick paper gave crystalline 2-*O*-methyl-L-fucose, m. p. and mixed m. p. 150°

Synthesis of 2-O-*Methylfucose* (With Miss B. Guarco).—Methyl 3 : 4-*O*-*iso*propylidene-α-L-fucoside was prepared by Percival and Percival's method [3] from L-fucose. Four methylations with Purdie reagents followed by distillation (bath temp. 90—100°/0·04 mm.) gave a syrup, n_D^{16} 1·4555°. Hydrolysis with 4% sulphuric acid at 100° for 6 hr. afforded crystalline 2-O-*methylfucose*, m. p. 150—152°, $[\alpha]_D^{18}$ −87° (*c*, 1·0 in H_2O) (Found: C, 48·0; H, 7·6; OMe, 17·55. $C_7H_{14}O_5$ requires C, 47·2; H, 7·8; OMe, 17·4%).

The authors thank Professor E. L. Hirst, F.R.S., for his interest and advice, the Institute of Seaweed Research, Inveresk, for the gift of fucose, and the Distillers Company Limited and Imperial Chemical Industries Limited for grants.

Department of Chemistry, University of Edinburgh. [*Received, January 7th*, 1957.]

[3] Percival and Percival, *J.*, 1950, 690.