Carbohydrate Research, 143 (1985) 249–255
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Efficient synthesis of methyl β-D-fucofuranoside and D-fucofuranose derivatives

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(Received October 16th, 1984; accepted for publication, February 10th, 1985)

Although the synthesis of a variety of fucopyranoside derivatives has been reported[1], there exist few reports[2] on the synthesis of fucofuranosides. Gardiner and Percival[2] reported that treatment of L-fucose with 0.8% methanolic hydrogen chloride at room temperature gave the best yield of methyl α- (20.6%) and β-L-fucofuranosides (44%) along with α- (15.4%) and β-L-fucofuranosides (20%). This report describes the efficient synthesis of 1-*O*-acyl-D-fucofuranoses also as a part of a program aimed at the total synthesis of gilvocarins[3] (anandimycins[4] and toromycins[5]).

Treatment[6] of D-fucose diethyl dithioacetal (**1**) with mercuric chloride and mercuric oxide in methanol at 0° gave methyl β-D-fucofuranoside (**2**) as a single product in 93% yield; no trace of the α anomer was found (by t.l.c. and ^{13}C-n.m.r. analysis). By the same reaction at 65°, a mixture of methyl α- and β-D-fucofuranosides was obtained that was readily separated by column chromatography on silica gel to afford methyl α-D-fucofuranoside (**3**, 12%) and the β anomer (**2**, 80%), respectively.

Benzylation of **2** was performed with benzyl bromide and sodium hydride in *N,N*-dimethylformamide. The anomerization of the product (**6**) was attained in 3% methanolic hydrogen chloride, giving methyl 2,3,5-tri-*O*-benzyl-α-D-fucofuranoside (**7**) and **6** in the ratio of 1:7. Hydrogenolysis of **7** gave a crystalline product identified by comparing its ^{13}C-n.m.r. spectrum with that of the α anomer (**3**).

The alkylated or acylated 1-*O*-(*p*-nitrobenzoyl)fucofuranoses are vital intermediates in a wide variety of syntheses, especially for glycosylation. Compound **6** was hydrolyzed in 1,4-dioxane solution with 0.5M sulfuric acid to give 2,3,5-tri-*O*-benzyl-D-fucofuranose (**8**). *p*-Nitrobenzoylation then afforded crystalline 2,3,5-tri-*O*-benzyl-1-α-(*p*-nitrobenzoyl)-α-D-fucofuranose (**10**) and the syrupy β anomer (**9**).

In order to prepare the acylated derivatives, methyl 2,3,5-tri-*O*-acetyl-β-D-

0008-6215/85/$ 03.30

fucofuranoside (**11**) (prepared from **2** by acetylation) was treated with acetic anhydride and conc. sulfuric acid in acetic acid to give a mixture of acetates **12**, **13**, and **14**. *p*-Nitrobenzoylation of **14** gave syrupy 2,3,5-tri-*O*-acetyl-1-*O*-(*p*-nitrobenzoyl)-β-D-fucofuranose (**15**) and the crystalline α anomer (**16**). Although the anomeric mixture of the tetraacetates **12** and **13** could not be separated, the pure β-acetate **12** was prepared from **8** via the following sequence of reactions: acetylation of the anomeric position and hydrogenolysis of the product (**17**), followed by acetylation.

Methylation of **2** with methyl iodide and sodium hydride in *N,N*-dimethylformamide afforded methyl 2,3,5-tri-*O*-methyl-β-D-fucofuranoside (**19**) as a distillable oil. Acid hydrolysis of **19**, followed by *p*-nitrobenzoylation, yielded 2,3,5-tri-*O*-methyl-1-*O*-(*p*-nitrobenzoyl)-β-D-fucofuranose (**21**).

In the ^{1}H-n.m.r. spectra, a sharp singlet for H-1 or the small coupling-constant ($J_{1,2}$) of the compounds **2, 4, 6, 9, 11, 12, 15, 17, 18, 19,** and **21** could be taken as an indication of the *trans* arrangement of the protons on the furanoid ring.

The synthetic avalability of compounds **9, 10, 12, 13, 15, 16,** and **21** provides a versatile series of intermediates for elaboration of *C*-fucofuranosyl derivatives.

EXPERIMENTAL

General methods. — Melting points were determined on a micro hot-stage and are uncorrected. T.l.c. was performed with 0.25-mm layers of Silica Gel 60 F_{254} (Merck) and with the following (v/v) solvent systems: (*A*) 5:1 ethyl acetate–2-propanol, (*B*) 4:1 hexane–ethyl acetate, (*C*) 2:1 hexane–ethyl acetate, (*D*) 1:1 hexane–ethyl acetate. Spots were located by u.v. light and by spraying with 1:2:100 anisaldehyde–sulfuric acid–acetic acid. Column chromatography was performed with silica gel (Merck No. 7734; 63–200 μm). Optical rotations were determined with a Jasco Model DIP-4 polarimeter. Elemental analyses were performed with a Perkin–Elmer Model 240 elemental analyzer. Proton and carbon magnetic resonance spectra were recorded with a JEOL FX-100 spectrometer. Proton–proton spin decoupling and proton–carbon selective decoupling experiments were performed with the FX-100 instrument. Chemical shifts are given on the δ scale and spin decouplings in Hz. Unless otherwise stated, n.m.r. spectra were measured at 25° in chloroform-*d*, with tetramethylsilane (δ 0.00) as the internal standard.

Synthesis of methyl D-*fucofuranosides from* D-*fucose diethyl dithioacetal.* — (*a*) *At 0°*. A mixture of D-fucose diethyl dithioacetal[7] (**1**) (2.0 g, 7.41 mmol), mercuric chloride (3.83 g, 14.11 mmol), and an excess of yellow mercuric oxide (3.0 g, 13.85 mmol) was mechanically stirred in methanol (50 mL) for 2 h at 0°. The mixture was filtered, and pyridine (0.9 mL) was added to the filtrate. After being kept overnight at 0°, the mixture was filtered and the filtrate concentrated under diminished pressure at 40° to a syrup. This was dissolved in a little cold water, and the solution was filtered from a small amount of the pyridine complex. The solution was evaporated *in vacuo* at 40°. The residue was leached with methanol, the mix-

ture filtered, and the filtrate evaporated. Repetition of this procedure (twice) gave methyl β-D-fucofuranoside (**2**) as a single product (R_F 0.54, solvent *A*); yield 1.23 g (93%), hygroscopic syrup; $[\alpha]_D^{28}$ −120.5° (*c* 1.4, methanol) [lit.[2] $[\alpha]_D^{18}$ +112° (*c* 7.0, water) for the L enantiomer]; ^{1}H-n.m.r. (D_2O, with sodium 4,4-dimethyl-4-silapentane-1-sulfonate as the internal standard): δ 1.24 (d, $J_{5,6}$ 6.4 Hz, H-6), 3.40 (s, OMe), 3.66–3.95 (m, $J_{4,5}$ 5.0 Hz, H-3,4,5), 4.89 (d, $J_{1,2}$ 1.7 Hz, H-1), and 4.02 (dd, $J_{2,3}$ 2.8 Hz, H-2).

The tris(*p*-nitrobenzoate) (**4**) of **2** had m.p. 157–158°, $[\alpha]_D^{27}$ −11.6° (*c* 0.3, chloroform); ^{1}H-n.m.r.: δ 1.56 (d, $J_{5,6}$ 6.6 Hz, H-6), 3.52 (s, OMe), 4.49 (dd, $J_{4,5}$ 4.8 Hz, H-4), 5.23 (s, H-1), 5.47 (br s, H-2), 5.52 (d, $J_{3,4}$ 5.5 Hz, H-3), 5.58 (dq, H-5), and 8.12–8.38 (m, arom.).

Anal. Calc. for $C_{28}H_{23}N_3O_{14}$: C, 53.76; H, 3.68; N, 6.72. Found: C, 53.81; H, 3.70; N, 6.75.

(*b*) *At 65°*. The diethyl dithioacetal (**1**, 2.0 g) was treated at 65°, by a method similar to that used in (*a*), to give an anomeric mixture of methyl D-fucofuranosides (crude yield 1.35 g), which was chromatographed (R_F 0.54 and 0.40, solvent *A*) to give **2** (1.05 g, 80%) and methyl α-D-fucofuranoside (**3**, 162 mg, 12%). Compound **3** had m.p. 124–125° (recrystallized from ethyl acetate); lit.[2] m.p. 127–128°; $[\alpha]_D^{27}$ +104.7° (*c* 0.3, methanol) [lit.[2] $[\alpha]_D^{18}$ −108° (*c* 2.0, water) for the L enantiomer]; ^{1}H-n.m.r. (D_2O), with sodium 4,4-dimethyl-4-silapentane-1-sulfonate as the internal standard): δ 1.19 (d, $J_{5,6}$ 6.1 Hz, H-6), 3.40 (s, OMe), 3.60 (dd, $J_{3,4}$ 6.8, $J_{4,5}$

TABLE I

^{13}C-N.M R. CHEMICAL SHIFTS OF THE CARBOHYDRATE MOIETY OF D-FUCOFURANOSIDE DERIVATIVES MEASURED AT 25 MHz.

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OMe-1*
2[a]	109.1	82.0	78.4	88.2	68.4	19.3	55.7
3[a]	103.0	77.8	76.1	86.4	70.6	18.6	56.0
4	106.4	77.8	82.9	83.0	70.5	16.1	55.2
5	100.9	78.1	75.8	81.1	72.0	16.0	55.8
6	106.8	84.2	83.1	88.2	73.5	15.9	54.6
7	101.2	81.7	83.7	84.5	77.0	15.5	55.0
9	101.8	87.0	83.3	88.2	74.1	15.7	
10	95.5	84.5	80.1	85.0	74.5	15.7	
11[b]	106.1	81.3	75.8	82.4	68.3	15.6	54.3
12	99.2	81.0	76.4	84.9	68.6	15.9	
13	93.1	73.8	75.6	82.3	69.8	15.8	
15	100.2	80.6	76.3	85.9	68.6	16.0	
16	95.2	73.9	76.0	83.1	69.7	16.0	
17	100.3	86.9	83.2	86.6	73.6	15.5	
18[a]	102.8	81.8	78.1	90.6	68.2	19.1	
19	105.9	89.2	85.2	83.6	75.8	14.4	53.8
21	101.1	88.8	85.3	87.5	76.2	14.7	

[a]Measured in D_2O with methanol (δ 49.8) as the internal standard. [b]Measured at 90 MHz (Nicolet 360 MHz spectrometer). The assignments were confirmed by ^{13}C–^{1}H two-dimensional correlation experiments.

7.8 Hz, H-4), 3.75 (dd, H-5), 3.92–4.18 (m, H-2, H-3), and 4.86 (d, $J_{1,2}$ 4.2 Hz, H-1).

Anal. Calc. for $C_7H_{14}O_5$: C, 47.19; H, 7.87. Found: C, 47.04; H, 7.95.

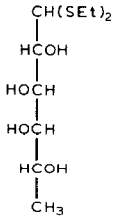
The tris(*p*-nitrobenzoate) (**5**) of **3** had m.p. 95–96°, $[\alpha]_D^{30}$ +69.2° (*c* 0.3 chloroform); ^{1}H-n.m.r.: δ 1.51 (d, $J_{5,6}$ 6.4 Hz, H-6), 3.47 (s, OMe), 4.38 (t, $J_{4,6}$ 6.0 Hz, H-4), 5.35 (d, $J_{1,2}$ 4.7 Hz, H-1), 5.48 (quint., H-5), 5.51 (dd, $J_{2,3}$ 7.0 Hz, H-2), 6.11 (dd, $J_{3,4}$ 6.0 Hz, H-3), 8.26, and 8.27 (s, arom.).

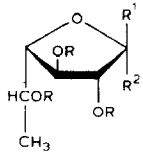
Anal. Calc. for $C_{28}H_{23}N_3O_{14}$: C, 53.76; H, 3.68; N, 6.72. Found: C, 53.51; H, 3.61; N, 6.74.

*Methyl 2,3,5-tri-*O*-benzyl-β-*D*-fucofuranoside* (**6**). — Methyl β-D-fucofuranoside (**2**, 2.7 g) was benzylated with benzyl bromide (15.6 g) and sodium hydride (50% dispersion in oil, 4.38 g) in *N,N*-dimethylformamide (25 mL) at room temperature for 6 h under nitrogen. The mixture was processed conventionally (ether extraction), and the product chromatographed (solvent *B*), giving syrupy **6** (5.39 g, 94%); $[\alpha]_D^{15}$ −63.8° (*c* 1.8, methanol); ^{1}H-n.m.r.: δ 1.25 (d, $J_{5,6}$ 6.8 Hz, H-6), 3.41 (s, OMe), 3.73 (dq, $J_{4,5}$ 3.5 Hz, H-5), 3.95–4.12 (m, H-3, H-4), 4.02 (s, H-2), 4.50, 4.52 and 4.59 (q, J_{benzylic} 12 Hz, benzyl), 5.00 (s, H-1), 7.27, and 7.33 (s, arom.).

Anal. Calc. for $C_{28}H_{32}O_5$: C, 75.00; H, 7.14. Found: C, 74.73; H, 7.14.

*Methyl 2,3,5-tri-*O*-benzyl-α-*D*-fucofuranoside* (**7**). — The benzyl ether (**6**, 550 mg) was dissolved in 3% methanolic hydrogen chloride (20 mL; prepared from 20 mL of dry methanol and 1 mL of acetyl chloride), and the solution kept for 3 days at room temperature. The acid was neutralized by addition of solid sodium carbonate, and the solution was concentrated and extracted with chloroform. The com-





1

2 R = R^2 = H, R^1 = OMe
3 R = R^1 = H, R^2 = OMe
4 R = *(p)*$NO_2C_6H_4CO$, R^1 = OMe, R^2 = H
5 R = *(p)*$NO_2C_6H_4CO$, R^1 = H, R^2 = OMe
6 R = Bzl, R^1 = OMe, R^2 = H
7 R = Bzl, R^1 = H, R^2 = OMe
8 R = Bzl, R^1, R^2 = H, OH
9 R = Bzl, R^1 = *(p)*$NO_2C_6H_4CO_2$, R^2 = H
10 R = Bzl, R^1 = H, R^2 = *(p)* $NO_2C_6H_4CO_2$
11 R = Ac, R^1 = OMe, R^2 = H
12 R = Ac, R^1 = OAc, R^2 = H
13 R = Ac, R^1 = H, R^2 = OAc
14 R = Ac, R^1, R^2 = H, OH
15 R = Ac, R^1 = *(p)*$NO_2C_6H_4CO_2$, R^2 = H
16 R = Ac, R^1 = H, R^2 = *(p)*$NO_2C_6H_4CO_2$
17 R = Bzl, R^1 = OAc, R^2 = H
18 R = R^2 = H, R^1 = OAc
19 R = Me, R^1 = OMe, R^2 = H
20 R = Me, R^1, R^2 = H, OH
21 R = Me, R^1 = *(p)*$NO_2C_6H_4CO_2$, R^2 = H

bined extracts were dried over sodium sulfate and evaporated to give an anomeric mixture (the ratio was ~6:1 by ^{13}C-n.m.r. analysis), that was chromatographed (R_F 0.46 and 0.40, solvent *B*) to give recovered **6** (455 mg) and methyl 2,3,5-tri-*O*-benzyl-α-D-fucofuranoside **7** (65 mg). Compound **7** had $[\alpha]_D^{20}$ +20.2° (*c* 1.2, methanol); ^{1}H-n.m.r.: δ 1.14 (d, $J_{5,6}$ 6.4 Hz, H-6), 3.31 (s, OMe), 3.57 (t, $J_{4,5}$ 6.4 Hz, H-5), 3.85 (t, $J_{3,4}$ 6.8, $J_{2,3}$ 6.8 Hz, H-3), 3.95–4.20 (m, H-2,4), 4.59 and 4.65 (s, q, benzyl), 4.72 (d, $J_{1,2}$ 3.7 Hz, H-1), 7.28, 7.31, and 7.34 (s, arom.).

Anal. Calc. for $C_{28}H_{32}O_5$: C, 75.00; H, 7.14. Found: C, 74.43; H, 7.17.

Hydrogenolysis of **7**. — Hydrogenolysis of the benzyl ether (**7**, 65 mg) over 10% Pd–C (15 mg) and one drop of acetic acid in methanol for 48 h afforded crystalline **3** (18.6 mg, 72%), identical with the sample **3** prepared by glycosidation from **1**.

*2,3,5-Tri-*O*-benzyl-1-*O*-acetyl-β-*D*-fucofuranose* (**17**). — Methyl 2,3,5-tri-*O*-benzyl-β-D-fucofuranoside (**6**, 470 mg) was dissolved in 10 mL of 1,4-dioxane, and 0.5M sulfuric acid (10 mL) was added. The solution was boiled for 30 min, ~15 mL of distillate being collected. More 1,4-dioxane (10 mL) and 0.5M sulfuric acid (10 mL) were then added and the process was repeated to give a solution showing a spot having R_F 0.44 (solvent *C*). The solution was then cooled and made neutral with aqueous sodium carbonate. The solvent was removed *in vacuo* and the residue extracted with chloroform, the extract then being washed with water and dried with sodium sulfate. Upon removal of solvent, a syrup was obtained that was chromatographed to give 2,3,5-tri-*O*-benzyl-D-fucose (**8**, 340 mg, 75%).

This product was acetylated in acetic anhydride (3 mL) and pyridine (2 mL) at room temperature to afford syrupy 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-β-D-fucofuranose (**17**) as a single product; $[\alpha]_D^{28}$ −36.9° (*c* 1.5, methanol); ^{1}H-n.m.r.: δ 1.19 (d, $J_{5,6}$ 6.4 Hz, H-6), 2.07 (s, OAc), 3.69 (quintet, $J_{4,5}$ 5.2 Hz, H-5), 3.95 (d, $J_{3,4}$ 5.2 Hz, H-3), 4.02 (s, $J_{2,3}$ 0 Hz, H-2), 4.20 (t, H-4), 4.40 and 4.55 (s, benzyl), 4.60 (q, benzyl), 6.25 (s, H-1), 7.25, 7.28, and 7.32 (s, arom.).

Anal. Calc. for $C_{29}H_{32}O_6$: C, 73.10; H, 6.72. Found: C, 72.70; H, 6.70.

*The two anomeric 2,3,5-tri-*O*-benzyl-1-*O*-(p-nitrobenzoyl)-β- and α-D-fucofuranoses* (**9** *and* **10**). — A solution of 2,3,5-tri-*O*-benzyl-D-fucose (**8**, 340 mg) and *p*-nitrobenzoyl chloride (140 mg) in dry pyridine (2 mL) was stirred overnight at room temperature. After removal of pyridine *in vacuo* the residue was chromatographed (solvent *B*) to give the syrupy β anomer (**9**, R_F 0.51, 230 mg); $[\alpha]_D^{30}$ −53.2° (*c* 1.1, chloroform) and crystalline α anomer (**10**, R_F 0.42, 205 mg); m.p. 70.5–71°, $[\alpha]_D^{30}$ +21.4° (*c* 0.4, chloroform). ^{1}H-N.m.r. of **9**: δ 1.23 (d, $J_{5,6}$ 6.4 Hz, H-6), 3.80 (quintet, $J_{4,5}$ 5.0 Hz, H-5), 4.07 (br d, $J_{2,3}$ 1.0 Hz, H-3), 4.19 (br s, H-2), 4.36 (t, $J_{3,4}$ 5.0 Hz, H-4), 4.46 and 4.62 (s, benzyl), 4.64 (d, benzyl), 6.53 (s, H-1), 7.27, 7.30, and 7.33 (s, arom.), and 8.10 (s, arom.). ^{1}H-N.m.r. of **10**: δ 1.25 (d, $J_{5,6}$ 6.3 Hz, H-6), 3.63 (dq, $J_{4,5}$ 4.5 Hz, H-5), 4.00 (dd, $J_{2,3}$ 4.5, $J_{3,4}$ 6.0 Hz, H-3), 4.30–4.50 (m, H-2,4), 4.40–4.85 (m, benzyl), 6.51 (d, $J_{1,2}$ 3.4 Hz, H-1), 7.24, 7.26 and 7.31 (s, arom.), and 8.02 (s, arom.).

Anal. Calc. for $C_{34}H_{33}NO_8$: C, 69.97; H, 5.70; N, 2.40. Found for **10**: C, 69.91; H, 5.66; N, 2.38.

Methyl 2,3,5-tri-O-acetyl-β-D-fucofuranoside (**11**). — The β anomer (**11**) was quantitatively obtained by treatment of **2** with acetic anhydride in pyridine; $[\alpha]_D^{19}$ −61.8° (*c* 1.3, methanol); ^{1}H-n.m.r. (measured at 360 MHz): δ 1.27 (d, $J_{5,6}$ 7.0 Hz, H-6), 2.03 and 2.05 (s, OAc), 3.34 (s, OMe), 4.02 (dd, $J_{3,4}$ 6.2, $J_{4,5}$ 4.5 Hz, H-4), 4.86 (s, H-1), 4.94 (dd, $J_{2,3}$ 2.0 Hz, H-3), 4.96 (br s, H-2), and 5.10 (dq, H-5).

1,2,3,5-Tetra-O-acetyl-β- and α-D-fucofuranoses (**12** *and* **13**) *and 2,3,5-tri-O-acetyl-D-fucofuranose* (**14**). — (*a*) *From* **11**. On treatment of **11** (1.43 g) with sulfuric acid (0.38 mL) and acetic anhydride (2.6 mL) in acetic acid (1.2 mL) at 0° for 10 min, a syrupy mixture was obtained that was chromatographed (R_F 0.52 and 0.28, solvent *D*) to afford an anomeric mixture of **12** and **13** (1.02 g, 65%) (12:13 = 2:1, by ^{13}C-n.m.r. analysis) and **14** (360 mg, 23%) (β:α = 3:1, by ^{13}C-n.m.r. analysis).

(*b*) *From* **17**. Hydrogenolysis of **17** was performed under the same conditions as used for **7** to give, after chromatography (10:1 ethyl acetate–2-propanol), syrupy 1-*O*-acetyl-β-D-fucofuranose (**18**). Compound **18** was acetylated with acetic anhydride in pyridine to give crystalline tetra-*O*-acetyl-β-D-fucofuranose (**12**); m.p. 67–68°, $[\alpha]_D^{27}$ −59.7° (*c* 0.9, chloroform); ^{1}H-n.m.r.: δ 1.31 (d, $J_{5,6}$ 7.0 Hz, H-6), 2.10 and 2.14 (s, OAc), 4.18 (dd, $J_{3,4}$ 5.0, $J_{4,5}$ 4.5 Hz, H-4), 5.07 (dd, $J_{2,3}$ 2.0 Hz, H-3), 5.16 (d, H-2), 5.05–5.23 (m, H-5), and 6.18 (s, H-1).

Anal. Calc. for $C_{14}H_{20}O_9$: C, 50.60; H, 6.02. Found: C, 50.62; H, 6.01.

The two anomeric 2,3,5-tri-O-acetyl-1-O-(p-nitrobenzoyl)-β- and α-D-fucofuranoses (**15** *and* **16**). — Treatment of **14** (1.11 g) with *p*-nitrobenzoyl chloride (782 mg) in dry pyridine (4 mL) at room temperature for 12 h, gave a syrupy anomeric mixture as one spot on t.l.c. (R_F 0.58, solvent *D*), which was chromatographed through a short column to give a crystalline product (1.61 g, 96%). The ^{13}C-n.m.r. spectrum indicated the presence of an anomeric mixture [δ 100.7 for the β anomer (80%) and 95.2 for the α anomer (20%)].

Three further crystallizations from hexane–ethyl acetate gave the pure α anomer (**16**); m.p. 177–178°, $[\alpha]_D^{32}$ +63.8° (*c* 0.4, chloroform); ^{1}H-n.m.r.: δ 1.26 (d, $J_{5,6}$ 6.6 Hz, H-6), 1.98, 2.04 and 2.13 (s, OAc), 4.09 (t, $J_{4,5}$ 6.4, $J_{3,4}$ 6.4 Hz, H-4), 5.15 (quintet, H-5), 5.48 (dd, $J_{2,3}$ 7.0 Hz, H-2), 5.62 (dd, H-3), 6.58 (d, $J_{1,2}$ 4.5 Hz, H-1), 8.28, and 8.30 (s, arom.).

Anal. Calc. for $C_{19}H_{21}NO_{11}$: C, 51.94; H, 4.82; N, 3.19. Found: C, 51.98; H, 4.79; N, 3.11.

The β anomer (**15**) was obtained by preparative t.l.c. (0.75-mm silica gel on the plate) [R_F 0.42 (α anomer) and 0.38 (β anomer); 4:1 benzene–ether]; $[\alpha]_D^{25}$ −39.2° (*c* 1.1, chloroform); ^{1}H-n.m.r.: δ 1.34 (d, $J_{5,6}$ 6.7 Hz, H-6), 2.18 and 2.11 (s, OAc), 4.34 (t, $J_{4,5}$ 4.9 Hz, H-4), 5.18 (d, $J_{3,4}$ 4.9 Hz, H-3), 5.19 (q, H-5), 5.35 (br s, H-2), 6.47 (s, H-1), 8.26, and 8.29 (s, arom.).

Methyl 2,3,5-tri-O-methyl-β-D-fucofuranoside (**19**). — To a stirred suspension of sodium hydride (60% dispersion in oil, 726 mg) in dry *N,N*-dimethylformamide (5 mL) under nitrogen was added a solution of **2** (898 mg) in dry *N,N*-dimethylformamide (5 mL). After stirring for 30 min at room temperature, methyl iodide

(1.41 mL) was added at 0° and the mixture was stirred for 2 h at room temperature. Water (20 mL) was added and the mixture extracted with ether. Conventional processing gave the title compound (720 mg, 65%) as a colorless oil; b.p. 75–77°/1 mmHg; $[\alpha]_D^{30}$ −111.4° (*c* 0.6, chloroform); ^{1}H-n.m.r.: δ 1.20 (d, $J_{5,6}$ 6.4 Hz, H-6), 3.41 (s, OMe), 3.42–3.63 (m, H-3,5), 3.68 (d, $J_{2,3}$ 2.0 Hz, H-2), 3.88 (t, $J_{3,4}$ 5.4, $J_{4,5}$ 5.4 Hz, H-4), and 4.90 (s, H-1).

Anal. Calc. for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 54.28; H, 9.17.

2,3,5-Tri-O-methyl-1-O-(p-nitrobenzoyl)-β-D-fucofuranose (**21**). — Acid hydrolysis of **19** by a method similar to that used for **6** yielded 2,3,5-tri-*O*-methyl-D-fucose **20** ($\beta:\alpha = 3:2$ by ^{13}C-n.m.r. analysis), which was acylated as for the preparation of **9** and **10** to give, after chromatography (R_F 0.62 and 0.52, solvent *D*), the β anomer (**21**) as a syrup (83% yield); $[\alpha]_D^{33}$ −51.2 g (*c* 1.5, chloroform) and an unknown compound (**22**); m.p. 161–161.5°, $[\alpha]_D^{30}$ −31.8° (*c* 0.5, chloroform). ^{1}H-N.m.r. of **21**: δ 1.22 (d, $J_{5,6}$ 6.4 Hz, H-6), 3.44, 3.45 and 3.52 (s, OMe), 3.68 (d, $J_{3,4}$ 5.9 Hz, H-3), 3.95 (br s, H-2), 3.30–3.59 (m, H-5), 4.16 (t, $J_{4,5}$ 5.9 Hz, H-4), and 6.46 (s, H-1).

Anal. Calc. (for **22**) $C_{16}H_{21}NO_8$: C, 54.08; H, 5.95; N, 3.94. Found: C, 54.11; H, 5.95; N, 3.86.

ACKNOWLEDGMENTS

The authors are greatly indebted to Mr. Junichi Goda for the elemental analyses and to Dr. T. Iwashita (Suntory Institute for Bioorganic Research) for recording the ^{13}C and ^{1}H-n.m.r. spectra of compound **11** at 360 MHz with a Nicolet 360 spectometer.

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