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Synthesis of the sodium salts of methyl 2-O-α-L-fucopyranosyl-α-L-fucopyranoside 3- and 4-sulfate*

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ABSTRACT

Synthesis of methyl 2-*O*-α-L-fucopyranosyl-α-L-fucopyranoside 3- and 4-sulfate was accomplished through the use of a key glycosyl donor, methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside, with methyl 2,3-*O*-isopropylidene-α-L-fucopyranoside and methyl 4-*O*-acetyl-3-*O*-benzyl-α-L-fucopyranoside as acceptors.

INTRODUCTION

Fucoidan, a sulfated polymer of L-fucose, has been known to possess anticoagulant activity[2]. According to a recent report by Church *et al.*[3], fucoidan enhances the heparin cofactor II-thrombin reaction more than 3500-fold. It has also been reported that fucoidan and other sulfated polysaccharides, such as dextran sulfate, pentosan, heparin, and carageenans, act as potential inhibitors of various envelop viruses including the human immunodeficiency virus[4–6]. Thus, it was reasonable to assume that a variety of well-defined sulfated oligosaccharides having structures that occur as a part of such sulfated polysaccharides will be useful for various biological investigations. We are presently interested in the synthesis of such sulfated oligosaccharides, especially fragments of fucoidan. In this polysaccharide, an L-fucosyl residue is primarily α-linked to O-2 of an adjacent L-fucosyl residue, and sulfate groups are located either at C-3 or C-4. We report herein a facile synthesis of two sulfated disaccharides of L-fucose.

RESULTS AND DISCUSSION

Methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside (**2**), which is obtained from methyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside (**1**), is a versatile glycosyl donor for the synthesis of fucosylated oligosaccharides. Several routes have been described for its preparation. The reaction of 2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl bromide with thio-

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urea[7], followed by methylation of that β-1-thio derivative, or that of 1,2,3,4-tetra-*O*-acetyl-L-fucopyranose[8] are more commonly employed for the preparation of this glycosyl donor. The methyl 1-thio compound was an anomeric mixture from which the pure β-L anomer **1** could be isolated[8] by silica gel column chromatography in low yield (56%). Recently, we found that when 1,2,3,4-tetra-*O*-acetyl-L-fucopyranose was treated with (methylthio)trimethylsilane and trimethylsilyl triflate[9] in dichloromethane it produced the pure β anomer **1** in high yield (83%) after crystallization from chloroform–hexane. Our product had a m.p. of 140–141° which corresponded to that reported by Sato *et al.*[8].

For the synthesis of the title disaccharides, the readily accessible methyl 3,4-*O*-isopropylidene-α-L-fucopyranoside[10] (**3**) was the chosen intermediate. Reaction of **2** with methyl 3,4-*O*-isopropylidene-α-L-fucopyranoside in the presence of cupric bromide–tetrabutylammonium bromide[11] gave, in 79% yield after column chromatographic purifacation, the fully protected disaccharide derivative **8**, the ^{1}H-n.m.r. spectrum of which was in conformity with the overall structure expected. Cleavage of the isopropylidene group of **8** gave **9** which on hydrogenolytic cleavage furnished known methyl 2-*O*-α-L-fucopyranosyl-α-L-fucopyranoside[12] (**10**). The diol **9** was converted into its 3,4-(ethyl orthoacetate), which was hydrolyzed to give a key intermediate, methyl 4-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**11**), in 85% yield. The ^{1}H-n.m.r. spectrum of **11** exhibited a low field chemical shift at δ 2.12, confirming that compound **11** had been acetylated at O-4. Compound **11** was treated with sulfur trioxide–pyridine complex in *N,N*-dimethylformamide to give, in high yield (79%), **12** as its sodium salt after ion exchange.

O-Deacetylation of **12** in methanolic sodium methoxide, followed by removal of the benzyl ether protecting group exactly as described for **9** (to give **10**), afforded in 55% yield (on the basis of **12**) the sodium salt of methyl 2-*O*-α-L-fucopyranosyl-α-L-fucopyranoside 3-sulfate (**14**) as the dihydrate after cation-exchange resin treatment. The ^{13}C-n.m.r. spectrum of amorphous **14** was in accord with the structure assigned (see Table I).

Regioselective benzylation of known[13] methyl 2-*O*-allyl-α-L-fucopyranoside by the stannylidene procedure in the presence of tetrabutylammonium iodide produced the 2-*O*-allyl-3-*O*-benzyl derivative **5**, which was acetylated with pyridine–acetic anhydride to give the 4-*O*-acetyl compound **6**, and deallylation of **6** by palladium chloride and

TABLE I

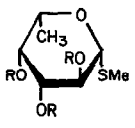
Proposed ^{13}C-n.m.r. chemical shifts[a]

Cpd.	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	OMe
10	99.31	75.66	71.38	74.15	69.24	17.99	99.60	70.79	72.17	74.66	69.78	17.99	57.66
14	99.55	74.81	78.67	72.92	68.94	18.03	99.69	70.90	72.20	73.12	69.81	18.13	57.84
18	99.71	76.10	70.86	83.63	68.57	18.10	99.71	70.25	72.24	74.70	69.88	18.57	57.86

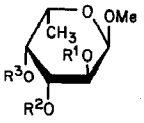
[a] For solutions in D_2O with Me_4Si as the external standard.

sodium acetate[14] furnished the key intermediate, methyl 4-*O*-acetyl-3-*O*-benzyl-α-L-fucopyranoside (**7**). The ^{1}H-n.m.r. spectra of both **6** and **7** contained signals in support of the overall structures expected. Thus, whereas the spectrum of **6** contained a one-proton resonance at δ 6.07–5.63, attributable to the allylic proton, that of **7** was devoid of such a resonance.

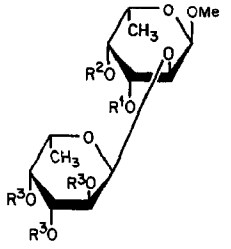
A similar glycosylation of **7** with **2** afforded the disaccharide derivative **15**, the ^{1}H-n.m.r. spectrum of which was, likewise, in accord with the overall structure expected. *O*-Deacetylation of **15** in methanolic sodium methoxide yielded **16** in high yield. Sulfation of **16**, in a manner analogous to that described for **11** (to give **12**), gave **17** as its sodium salt. Hydrogenolytic cleavage of the benzyl groups of **17** afforded the sodium salt of methyl 2-*O*-α-L-fucopyranosyl-α-L-fucopyranoside 4-sulfate (**18**) as a monohydrate after similar treatment as described for the preparation of **14**.



1 R = Ac
2 R = Bn



3 R^1 = H; R^2, R^3 = CMe_2
4 R^1 = $CH_2CH=CH_2$; R^2 = R^3 = H
5 R^1 = $CH_2CH=CH_2$; R^2 = Bn; R^3 = H
6 R^1 = $CH_2CH=CH_2$; R^2 = Bn; R^3 = Ac
7 R^1 = H; R^2 = Bn; R^3 = Ac



8 R^1, R^2 = CMe_2; R^3 = Bn
9 R^1 = R^2 = H; R^3 = Bn
10 R^1 = R^2 = R^3 = H
11 R^1 = H; R^2 = Ac; R^3 = Bn
12 R^1 = SO_3Na; R^2 = Ac; R^3 = Bn
13 R^1 = SO_3Na; R^2 = H; R^3 = Bn
14 R^1 = SO_3Na; R^2 = R^3 = H
15 R^1 = R^3 = Bn; R^2 = Ac
16 R^1 = R^3 = Bn; R^2 = H
17 R^1 = R^3 = Bn; R^2 = SO_3Na
18 R^1 = R^3 = H; R^2 = SO_3Na

^{13}C-N.m.r. assignments. — The assignements of the ^{13}C-n.m.r. resonances for the two sulfated disaccharides **14** and **18** were made by comparing their spectra with that of compound **10** reported in Table I. In the ^{13}C-n.m.r. spectrum of **14**, the resonance for C-3 showed a significant downfield shift of 7.29 p.p.m., by comparison to that of the parent disaccharide **10**, evidencing that O-3 was the site of sulfation[15]. The signals for C-2 and C-4 were observed at a field higher than that of the respective carbon atoms in **10** (see Table I) because of the β shift invariably observed with sulfation. However, in the spectra of **18**, an analogous downfield shift of 9.48 p.p.m. was observed for C-4, confirming that sulfation had occurred at O-4.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured at 25° with a Perkin–Elmer 241 polarimeter. T.l.c. was conducted on aluminum sheets, precoated with 0.2-mm layers of Silica Gel 60F-254 (E. Merk, Darmstadt, Germany); the components were located either by exposure to u.v. light or by spraying with 5% H_2SO_4 in ethanol (or both) and charring. Silica gel used for column chromatography was Baker Analyzed (60–200 mesh). ^{1}H-N.m.r. spectra were recorded at 25°; ^{1}H-n.m.r. spectra with a Varian EM-390, and ^{13}C-n.m.r. spectra with a Bruker AM-400 instrument, at 90 and 100.6 MHz, respectively; the chemical shifts (δ) are expressed from the tetramethylsilane signal. Solutions in organic solvents were generally dried with anhydrous Na_2SO_4. Dichloroethane and *N,N*-dimethylformamide were dried over 4A molecular sieves. Elemental analyses were performed by Robertson Laboratory, 29 Samson Ave., Madison, New Jersey 07940, U.S.A.

*Methyl 2,3,4-tri-*O*-acetyl-1-thio-β-*L*-fucopyranoside* (**1**). — *Method A.* To a stirred solution of 1,2,3,4-tetra-*O*-acetyl-L-fucopyranose (15 g) in dichloromethane (75 mL) was added (methylthio)trimethylsilane (15 mL) and trimethylsilyl triflate (7.5 mL). The mixture was stirred for 2 days at room temperature, and then treated with *N,N*-diisopropylethylamine. The residue was diluted with chloroform and washed with water, dried, and concentrated. The resulting product syrup crystallized from chloroform–hexane to give **1** (12.0 g, 83%), m.p. 140–141°, $[\alpha]_D^{25}$ +0.4° (*c* 1.3, chloroform); lit.[8] m.p. 139–141°, $[\alpha]_D$ −0.7° (*c* 1.0, chloroform).

Method B. To a solution of 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranose (3.1 g) in dichloromethane (40 mL) was added methyl iodide (1.8 ml) and *N,N*-diisopropyl ethylamine (2.3 ml), and the mixture was stirred for 1 h. The organic layer was washed with cold water, dried, and concentrated under diminished pressure. The resulting syrup crystallized from chloroform–hexane to give **1** (2.3 g, 72%), m.p. 139–140°, $[\alpha]_D^{25}$ +0.3° (*c* 1.1, chloroform).

*Methyl 2,3,4-tri-*O*-benzyl-1-thio-β-*L*-fucopyranoside* (**2**). — Compound **1** was converted into **2** by *O*-deacetylation with 0.01M methanolic sodium methoxide as described by Sato *et al.*[8], $[\alpha]_D^{25}$ +0.1° (*c* 1.2, chloroform); lit.[8] $[\alpha]_D^{25}$ −0.2° (*c* 1.5, chloroform).

*Methyl 2-*O*-allyl-3-*O*-benzyl-α-*L*-fucopyranoside* (**5**). — A mixture of methyl 2-*O*-allyl-α-L-fucopyranoside[13] (**4**; 10 g) and dibutyltin oxide (12 g) in benzene (500 mL) was heated for 20 h at reflux temperature with azeotropic distillation of water. The mixture was concentrated to about one-half its volume and, after addition of tetrabutylammonium iodide (28 g) and benzyl bromide (14 mL), the refluxing was continued for 5 h. Concentration of the mixture to dryness gave a residue which was purified in a column of silica gel with a solvent gradient of 20–30% ethyl acetate in hexane to afford **5** (13 g, 92%), amorphous, $[\alpha]_D^{25}$ −79° (*c* 1.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.43–7.13 (m, 5 H, arom.), 6.15–5.73 (m, 1 H, -C*H*=CH_2), 3.43 (s, 3 H, OMe), and 1.27 (d, 3 H, *J* 6 Hz, CMe).

Anal. Calc. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.09; H, 7.54.

Methyl 4-O-acetyl-2-O-allyl-3-O-benzyl-α-L-fucopyranoside (**6**). — Compound **5** (2.2 g) was stirred overnight in 1:2 acetic anhydride–pyridine (60 mL) at room temperature. The pyridine and acetic anhydride were evaporated under diminished pressure, the last traces being removed by coevaporation with several added portions of toluene. The residue was applied to a column of silica gel and eluted with 2:3 (v/v) ethyl acetate–hexane to give **6** (2.1 g, 84%), amorphous, $[\alpha]_D^{25}$ −100° (*c* 2.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.37–7.17 (m, 5 H, arom.), 6.07–5.63 (m, 1 H, -C*H*=CH_2), 3.37 (s, 3 H, OMe), 2.13 (s, 3 H, OAc), and 1.13 (d, 3 H, *J* 6 Hz, CMe).

Anal. Calc. for $C_{19}H_{26}O_6$: C, 65.12; H, 7.48. Found: C, 65.38; H, 7.21.

Methyl 4-O-acetyl-3-O-benzyl-α-L-fucopyranoside (**7**). — A mixture of **6** (2.0 g, 5.7 mmol), $PdCl_2$ (4.5 g, 25.4 mmol), and sodium acetate trihydrate (7.0 g, 51.5 mmol) in 19:1 glacial acetic acid–water was stirred for 1.5 h at 50°. It was then filtered through Celite and concentrated under diminished pressure, the last traces being removed by coevaporation with several portions of toluene. The residue was dissolved in ethyl acetate and washed with aq. $NaHCO_3$, water, dried, and concentrated. Chromatography of the residue in a silica gel column with 3:2 hexane–ethyl acetate gave **7** (1.5 g, 85%), $[\alpha]_D^{25}$ −168° (*c* 1.6, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.37–7.07 (m, 5 H, arom.), 3.37 (s, 3 H, OMe), 2.21 (s, 3 H, OAc), and 1.10 (d, 3 H, *J* 6 Hz, CMe).

Anal. Calc. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.66; H, 6.98.

Methyl 3,4-O-isopropylidene-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**8**). — A solution of **2** (5.0 g, 10.8 mmol) and **3** (2.1 g, 9.6 mmol) in 5:1 dichloroethane–*N*,*N*-dimethylformamide (120 mL) was stirred for 0.5 h with 4A molecular sieves (15 g) under protection from light and moisture. Tetrabutylammonium bromide (5.4 g, 16.7 mmol) and $CuBr_2$ (4.0 g, 17.1 mmol) were added, and the mixture was stirred for 16 h at room temperature. The mixture was filtered through Celite, the solids were thoroughly washed with chloroform, and the filtrate and washings combined, and washed with aq. $NaHCO_3$, and water, dried, and concentrated under diminished pressure. The residue was applied to a column of silica gel and eluted with a solvent gradient consisting of 20–25% ethyl acetate in hexane. On concentration, the fractions corresponding to the product gave **8** (4.8 g, 79%), as a colorless syrup, $[\alpha]_D^{25}$ −101° (*c* 2.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.50–7.23 (m, 15 H, arom.), 4.93 (d, 1 H, *J* 3.4 Hz, H-1′), 3.38 (s, 3 H, OMe), 1.49 and 1.33 (each s, 3 H, CMe), 1.20 (d, 3 H, *J* 6.8 Hz, H_3-6), and 1.10 (d, 3 H, *J* 6.5 Hz, H_3-6).

Anal. Calc. for $C_{37}H_{46}O_9$: C, 70.01; H, 7.30. Found: C, 70.36; H, 7.09.

Methyl 2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**9**). — Compound **8** (2.0 g) was stirred in 60% aqueous acetic acid (50 mL) for 1.5 h at 50°. Acetic acid was evaporated under diminished pressure, the last traces being removed by coevaporation with several added portions of toluene. The residue was purified in a column of silica gel with 9:1 (v/v) chloroform–acetone as eluent. On concentration, the fractions corresponding to the product gave a solid which was dissolved in a little chloroform. Addition of hexane caused the precipitation of **9** (1.3 g, 70%), amorphous, $[\alpha]_D^{25}$ −100° (*c* 1.4, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.36–7.31 (m, 15 H, arom.), 4.80 (d,

1 H, *J* 3.6 Hz, H-1'), 3.36 (s, 3 H, OMe), 1.28 (d, 3 H, *J* 6.5 Hz, H_3-6), and 1.14 (d, 3 H, *J* 6.4 Hz, H_3-6).

Anal. Calc. for $C_{34}H_{42}O_9$: C, 68.66; H, 7.12. Found: C, 68.69; H, 7.17.

Methyl 2-O-α-L-fucopyranosyl-α-L-fucopyranoside (**10**). — A solution of **9** (1.5 g) in 95% aqueous ethanol (60 ml) was shaken under H_2 at 345 kPa for 2 d. The suspension was filtered through a bed of Celite, the solid thoroughly washed with 20% aqueous ethanol, and the filtrate and washings were combined, and concentrated under diminished pressure. The crude product was purified in a column of silica gel with 4:1 (v/v) chloroform–methanol as the eluent. Concentration of the fractions containing the product gave a solid residue that crystallized from ethanol (75%), m.p. 189–190°, $[\alpha]_D^{25}$ −224° (*c* 0.8, methanol); ^{1}H-n.m.r. (D_2O): δ 5.03 (d, 1 H, *J* 3.6 Hz, H-1') and 3.42 (s, 3 H, OMe); lit.[12], m.p. 190–192, $[\alpha]_D$ −227°, (*c* 0.57, methanol).

Methyl 4-O-acetyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**11**). — To a solution of **9** (1.1 g, 1.85 mmol) in dry benzene (32 mL) were added triethyl orthoacetate (8.0 mL) and 4-toluenesulfonic acid monohydrate (2 mg). The solution was stirred for 1.5 h at room temperature, triethylamine was added, and the solution was washed with cold water, dried, and concentrated under diminished pressure to give the 3,4-orthoester in quantitative yield. This was dissolved in 80% aqueous acetic acid (50 mL) and the solution stirred for 1 h at room temperature. Acetic acid was evaporated under diminished pressure, the last traces being removed by coevaporation with several added portions of toluene. The crude product was applied to a column of silica gel and eluted with a solvent gradient consisting of 30–40% ethyl acetate in hexane. Concentration of the fractions corresponding to the product gave **11** (1.0 g, 85%), $[\alpha]_D^{25}$ −87° (*c* 0.8, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.40–7.13 (m, 15 H, arom.), 3.33 (s, 3 H, OMe), 2.12 (s, 3 H, OAc), and 1.10 (d, 6 H, *J* 6 Hz, 2 H_3-6).

Anal. Calc. for $C_{36}H_{44}O_{10}$: C, 67.90; H, 6.96. Found: C, 67.82; H, 6.94.

Sodium [methyl 4-O-acetyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside] 3-sulfate (**12**). — To a stirred solution of **11** (1.1 g, 1.7 mmol) in dry *N,N*-dimethylformamide (25 mL) was added dropwise a solution of SO_3–pyridine complex (1.3 g, 8.2 mmol) in *N,N*-dimethyl formamide (20 mL). Stirring was continued for an additional 1.5 h at room temperature, and the excess of reagent was destroyed by the addition of methanol. The solvent was evaporated, and the residue was dissolved in chloroform and washed with cold water. Evaporation of chloroform gave a white solid which was dissolved in methanol and passed through Amberlite IR-120P (Na^+) in methanol. Solvent removal afforded **12** (1.1 g, 79%), amorphous solid, $[\alpha]_D^{25}$ −138° (*c* 1.4, methanol); ^{1}H-n.m.r. [($^2H_3$)Me_2SO]: δ 7.37–7.10 (m, 15 H, arom.), 3.30 (s, 3 H, OMe), 1.98 (s, 3 H, OAc), and 1.03 (d, 6 H, *J* 6 Hz, 2 H_3-6).

Anal. Calc. for $C_{36}H_{43}NaO_{13}S$: C, 58.52; H, 5.87. Found: C, 58.34; H, 5.75.

Sodium (methyl 2-O-α-L-fucopyranosyl-α-L-fucopyranoside) 3-sulfate (**14**). — Compound **12** (0.6 g) was stirred in 0.1 M methanolic sodium methoxide (100 ml) for 16 h at room temperature. The solution was de-ionized with Amberlite IR-120 (H^+) cation-exchange resin, the resin filtered off, and the filtrate concentrated under diminished pressure. The intermediate **13** was dissolved in 95% ethanol (40 mL) and treated with

10% Pd–C (0.6 g) under H_2 at 345 kPa for 2 days. The suspension was filtered through a bed of Celite, and the solids were thoroughly washed with 20% aqueous ethanol. The filtrate and washings were combined and evaporated. The residue was purified in a column of silica gel with 5:4:1 (v/v) chloroform–methanol–water as the eluent. The fractions corresponding to **14** were combined and concentrated and the residue so obtained was dissolved in water and passed through Amberlite IR-120P (Na^+) cation-exchange resin. Lyophilization of the fractions corresponding to **14** gave a hygroscopic, amorphous powder (0.19 g, 55%, on the basis of **12**), $[\alpha]_D^{25}$ −156° (*c* 1.2, methanol).

Anal. Calc. for $C_{13}H_{23}NaO_{12}S \cdot 2H_2O$: C, 33.76; H, 5.88. Found: C, 33.50; H, 5.82.

Methyl 4-O-acetyl-3-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**15**). — Compound **7** (1.5 g, 4.8 mmol) was condensed with **2** (2.8 g, 6.0 mmol) in 5:1 dichloroethane–*N,N*-dimethylformamide (120 mL) in the presence of tetrabutylammonium bromide (2.9 g, 9.0 mmol), $CuBr_2$ (2.1 g, 9.0 mmol), and 4A molecular sieves (10 g) in a manner analogous to that described for **3** (to give **8**). After the processing described earlier, the crude reaction product was applied to a column of silica gel and eluted with a solvent gradient consisting of 20–25% ethyl acetate in hexane. Evaporation of the fractions corresponding to the product yielded **15** (2.2 g, 62.5%), $[\alpha]_D^{25}$ −95° (*c* 1.9, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.38–7.20 (m, 20 H, arom.), 4.89 (d, 1 H, *J* 4.1, H-1′), 3.40 (s, 3 H, OMe), 2.12 (s, 3 H, OAc), 1.16 (d, 3 H, *J* 6.5 Hz, H_2-6), and 0.73 (d, 3 H, *J* 6.5 Hz, H_3-6).

Anal. Calc. for $C_{43}H_{50}O_{10}$: C, 71.09; H, 6.93. Found: C, 71.26; H, 6.86.

Methyl 3-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**16**). — This compound was obtained by *O*-deacetylation of **15** (2.0 g) in 0.1M methanolic sodium methoxide (200 ml), followed by column chromatographic purification on silica gel using a solvent gradient consisting of 30–40% ethyl acetate in hexane, amorphous (1.8 g, 95.5%), $[\alpha]_D^{25}$ −88° (*c* 1.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.40–7.20 (m, 20 H, arom.), 4.95 (d, 1 H, *J* 3.5 Hz, H-1′), 3.37 (s, 3 H, OMe), 1.29 (d, 3 H, *J* 6.5 Hz, H_3-6), and 0.91 (d, 3 H, *J* 6.4 Hz, H_3-6).

Anal. Calc. for $C_{41}H_{48}O_9$: C, 71.91; H, 7.06. Found: C, 71.81; H, 7.09.

Sodium [methyl 3-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside] 4-sulfate (**17**). — Compound **16** (1.0 g, 1.46 mmol) was treated with SO_3–pyridine complex (1.2 g, 7.5 mmol) exactly as described for **11** (to give **12**). After processing as just described for the preparation of **12**, the residue was dissolved in methanol and passed through an Amberlite IR-120P (Na^+) cation-exchange resin column. The fractions corresponding to **17** were concentrated and the residue was dissolved in methanol. Addition of ether precipitated **17** (1.1 g, 95%), amorphous, $[\alpha]_D^{25}$ −144° (*c* 1.0, methanol); ^{1}H-n.m.r. [($^2H_3$)Me_2SO]: δ 7.40–7.03 (m, 20 H, arom.), 3.17 (s, 3 H, OMe), 1.17 (d, 3 H, *J* 6 Hz. H_3-6), and 0.77 (d, 3 H, *J* 6 Hz, H_3-6).

Anal. Calc. for $C_{41}H_{47}O_{12}SNa$: C, 62.58; H, 6.02. Found: C, 62.29; H, 6.08.

Sodium (methyl 2-O-α-L-fucopyranosyl-α-L-fucopyranoside) 3-sulfate (**18**). — Compound **17** (0.5 g) was hydrogenated in the presence of 10% Pd–C (0.5 g) as just described. After purification in a silica gel column with 5:4:1 (v/v) chloroform–methanol–water as the eluent, **18** (0.18 g, 66%) was obtained as the sodium salt by passage

through Amberlite IR-120P (Na^+) cation-exchange resin, $[\alpha]_D^{25}$ $-160°$ (*c* 0.9, methanol).

Anal. Calc. for $C_{13}H_{23}NaO_{12}S \cdot H_2O$: C, 35.13; H, 5.67. Found: C, 35.37; H, 5.39.

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