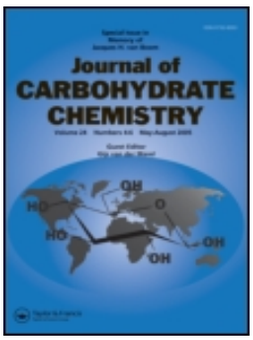

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SYNTHESIS, NMR, AND CONFORMATIONAL STUDIES OF FUCOIDAN FRAGMENTS 4: 4-MONO- AND 4,4'-DISULFATED (1→3)-α-l-FUCOBIOSIDE AND 4-SULFATED FUCOSIDE FRAGMENTS

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SYNTHESIS, NMR, AND CONFORMATIONAL STUDIES OF FUCOIDAN FRAGMENTS. IV.[1] 4-MONO- AND 4,4′-DISULFATED (1→3)-α-L-FUCOBIOSIDE AND 4-SULFATED FUCOSIDE FRAGMENTS

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ABSTRACT

Propyl 4-*O*-sulfonato- and 4,4′-di-*O*-sulfonato-3-*O*-α-L-fucopyranosyl-α-L-fucopyranosides, which are related to fragments of brown algal fucoidans, have been synthesized. Their spectral (^{1}H and ^{13}C NMR, NOE) and conformational properties have been studied in combination with molecular modeling and compared with the respective non-sulfated propyl fucobioside. Correlations between chemical shifts and conformational properties of these compounds were investigated.

INTRODUCTION

Fucoidans, a unique class of sulfated polysaccharides of brown seaweeds, consist mainly of L-fucose with some galactose, xylose, mannose, and uronic acid[2] as carbohydrate components. These biopolymers have been known for about a century, but their chemical structure, and especially their structural diversity in dependence on

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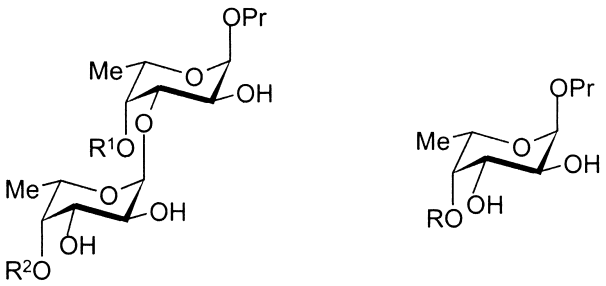
algal species, is poorly understood. Recent investigations have shown that (1 → 3)-linked α-L-fucopyranose 4-sulfate residue may be regarded as one of the principal structural units.

Although fucoidans have been extensively studied over the period of several decades due to their diverse biological activities, especially anticoagulant,[3] antiviral[4] and antiinflammatory,[5] the relationships between structure and biological activity are not clearly established.

The study presented here was performed as a part of the project aimed at the investigation of fucoidan structure and assessment of pharmacophores in their chains. Recently, we described[6] the synthesis and NMR studies of 2,3- and 3,4-branched α-L-fucotriosides which relate to non-sulfated vicinally branched fucoidan fragments. In this communication we report on the synthesis, NMR and conformational studies of propyl 3-*O*-α-L-fucopyranosyl-α-L-fucopyranoside **3**,[6] its 4-*O*-sulfonato- and 4,4′-di-*O*-sulfonato derivatives **1** and **2**. We also investigated the 4-sulfated monosaccharide **4** along with the non-sulfated analog **5**.[6]



1 $R^1=SO_3Na$, $R^2=H$ **4** $R=SO_3Na$

2 $R^1=R^2=SO_3Na$ **5** R=H

3 $R^1=R^2=H$

RESULTS AND DISCUSSION

Synthesis of compounds **1**, **2** and **4**. The preparation of target sulfated fucobiosides **1** and **2** was performed using the readily accessible disaccharide **6**[1] as the starting compound. Its treatment with sulfur trioxide–pyridine complex in DMF gave sulfated derivative **7** in 85% yield. The presence of a sulfate group at C-4 in **2** was confirmed by a downfield chemical shift of the H-4 signal to 5.28 ppm (Table 1) in its ^{1}H NMR spectrum.

O-Debenzoylation of **6** with methanolic sodium methoxide gave triol **8**. Its regioselective benzoylation with benzoyl chloride via the stannylidene procedure gave 3-*O*-benzoate **9** in 77% yield. A downfield chemical shift of the H-3 signal in the ^{1}H NMR spectrum of compound **9** (Table 1) indicated the location of a benzoate group at C-3.

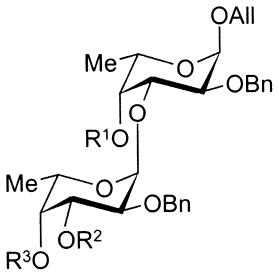
Treatment of compound **9** with sulfur trioxide–pyridine complex in DMF gave sulfated derivative **10** in 95% yield. Similarly, monohydroxy fucoside **11**[6] was

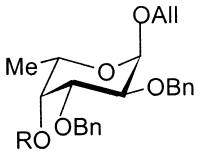
Table 1. ^{1}H NMR Shifts[a] for Protected Compounds **6**–**12**

Compound	Residue	H-1	H-2	H-3	H-4	H-5	H-6
6[6]	α-L-Fuc-OAll	5.10	4.03	4.17	3.91	4.03	1.34
	(1 → 3)-α-L-Fuc	5.06	3.96	4.14	5.47	4.35	1.01
7	α-L-Fuc-OAll	5.03	4.37	4.49	5.28		1.55
	(1 → 3)-α-L-Fuc	5.41	4.08	5.56	4.94		0.75
8	α-L-Fuc-OAll	4.85	3.79	4.00	3.65	3.91	1.29
	(1 → 3)-α-L-Fuc	4.82	3.70	3.94	3.65	4.15	1.10
9	α-L-Fuc-OAll	4.89	3.86	4.07	3.68	3.93	1.29
	(1 → 3)-α-L-Fuc	4.89	4.11	5.54	3.97	4.31	1.08
10	α-L-Fuc-OAll	4.96	4.01	4.28	4.89	3.96	1.30
	(1 → 3)-α-L-Fuc	5.50	4.13	5.67	4.57	4.52	1.15
11[6]	α-L-Fuc-OAll	4.78	3.48	3.82	3.90	1.21	4.78
12	α-L-Fuc-OAll	4.73	3.70	3.76	4.73	3.94	1.25

[a]In ppm, compounds **6**, **8**, **9**, **11** and **12** were recorded in $CDCl_3$; compounds **7** and **10** were recorded in CD_3OD. Other signals: $OCH_2CH{=}CH_2$ δ 5.13–5.41; $OCH_2CH{=}CH_2$ δ 5.78–6.05 and 5.70–5.87; $OCH_2CH{=}CH_2$ δ 4.22–4.45 and 4.00–4.15; $PhCH_2$ δ 4.50–4.80; $C_6H_5CH_2$ δ 6,90–8,20; C_6H_5CO δ 7.45–7.93.

sulfated to give **12**. Catalytic hydrogenolysis and subsequent saponification of compounds **7**, **10** and **12** gave target disaccharides **1** and **2** and fucoside **4** which were purified by gel filtration on a Sephadex G-10 column. The presence of the sulfate group at C-4 in compounds **1**, **2** and **4** was confirmed by downfield chemical shifts (Table 2) of the H-4 signals in the corresponding ^{1}H NMR spectra.





6 R^1=H, R^2=R^3=Bz

7 R^1=SO_3Na, R^2=R^3=Bz

8 R^1=R^2=R^3=H

9 R^1=R^3=H, R^2=Bz

10 R^1=R^3=SO_3Na, R^2=Bz

11 R=H

12 R=SO_3Na

Table 2. ^{1}H NMR Shifts[a] and Coupling Constants (Hz) for Oligosaccharides **1–5**

No.	Residue	H-1	H-2	H-3	H-4	H-5	H-6	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
1	α-L-Fuc-OPr	4.99	3.98	4.07	4.81	4.23	1.34	3.8	10.3	3.4	<2	6.5
	α-L-Fuc(1 → 3)	5.17	3.80	3.96	3.87	4.37	1.26	4.0	10.3	3.5	<2	6.7
2	α-L-Fuc-OPr	4.92	3.92	4.03	4.76	4.18	1.28	3.9	10.4	2.8	<2	6.5
	α-L-Fuc(1 → 3)	5.13	3.78	4.00	4.60	4.44	1.26	3.9	10.4	2.9	<2	6.5
3[6]	α-L-Fuc-OPr	4.91	3.91	3.91	4.02	4.08	1.27	<3	nd[b]	nd[b]	nd[b]	6.7
	α-L-Fuc(1 → 3)	5.07	3.81	3.95	3.82	4.28	1.21	3.9	10.4	3.4	<2	6.7
4	α-L-Fuc-OPr	4.90	3.81	3.97	4.60	4.21	1.26	3.9	10.3	3.4	<2	6.7
5[6]	α-L-Fuc-OPr	4.88	3.78	3.86	3.80	4.10	1.22	3.8	10.2	3.5	<2	6.5

[a]In ppm, recorded at 40°C in D_2O with 0.05% acetone as internal standard. Signals of propyl aglycon: $OCH_2CH_2CH_3$ δ 0.92; $OCH_2CH_2CH_3$ δ 1.62–1.64; $OCH_2CH_2CH_3$ δ 3.49–3.84.
[b]Coupling constants not determined due to the overlapping of multiplets.

NMR analysis of compounds **1–5**. Tables 2 and 3 show the ^{1}H NMR and ^{13}C NMR chemical shifts for compounds **1**, **2** and **4** and parent non-sulfated **3** and **5**. Assignment of the ^{1}H NMR spectra (Table 2) of these compounds was made using a combination of ^{1}H–^{1}H COSY and 2D TOCSY experiments. ^{13}C NMR spectral assignments (Table 3) were made using 2D ^{1}H–^{13}C HMQC correlation spectroscopy.

To evaluate the influence of sulfate on ^{13}C NMR spectra of compounds **1**, **2** and **4** we calculated the sulfation effects (Δδ), which are the differences in chemical shifts of the respective signals in spectra of sulfated and non-sulfated compounds. As was expected, we observed substantial sulfation effects in ^{13}C NMR spectra (Table 4) on C-4 and C-3 atoms of the glycosylated unit and C-1′ atom of the glycosylating unit.

The values of ΔδC-4 for saccharides **1** and **2** are ca. 2 ppm larger than that for monosaccharide **4**. Sulfation effects in **4** are similar to those observed in the terminal residue of disaccharide **2** except for ΔδC-1′ value, which both in **1** and **2** are considerably positive. The sulfation effect on C-3 is negative in the monosaccharide which is obviously due to the so called β-effect, i.e., upfield shift of the β-carbon atom upon the introduction of an electronegative subtituent.[7] It is noteworthy that it

Table 3. ^{13}C NMR Shifts[a] for Oligosaccharides **1–5**

Compound	Residue	C-1	C-2	C-3	C-4	C-5	C-6
1	α-L-FucOPr	99.6	68.0	76.8	80.1	67.2	16.6
	α-L-Fuc(1 → 3)	99.1	69.7	71.2	73.2	68.3	17.1
2	α-L-FucOPr	99.5	67.8	76.6	80.0	67.1	17.0
	α-L-Fuc(1 → 3)	98.7	69.7	70.2	81.9	67.6	17.0
3[6]	α-L-FucOPr	99.5	67.6	75.8	69.3	67.5	16.5
	α-L-Fuc(1 → 3)	96.4	69.2	70.7	73.1	68.1	16.5
4	α-L-FucOPr	99.1	69.3	69.9	81.5	66.8	16.6
5[6]	α-L-FucOPr	99.5	69.2	70.9	73.1	67.7	16.5

[a]In ppm, recorded at 40°C in D_2O with 0.05% acetone as internal standard. Signals of propyl aglycon: $OCH_2CH_2CH_3$ δ 11.1; $OCH_2CH_2CH_3$ δ 23.2–23.3; $OCH_2CH_2CH_3$ δ 71.3.

Table 4. Sulfation Effects (Δδ) in ^{13}C NMR Spectra of Compounds **1**, **2** and **4**

Compound	Residue	ΔδC-1	ΔδC-2	ΔδC-3	ΔδC-4	ΔδC-5	ΔδC-6
1	α-L-FucOPr	0.1	0.4	1.0	10.8	− 0.3	0.1
	α-L-Fuc(1 → 3)	2.7	0.5	0.5	0.1	0.2	0.6
2	α-L-FucOPr	0.0	0.2	0.8	10.7	− 0.4	0.5
	α-L-Fuc(1 → 3)	2.3	0.5	− 0.5	8.8	− 0.5	0.5
4	α-L-FucOPr	− 0.4	0.1	− 1.0	8.4	− 0.9	0.1

becomes slightly positive in disaccharides **1** and **2**, thus revealing that some other influence overcomes the β-effect. In order to explain the observed ΔδC we investigated conformations of these compounds.

Conformational analysis of compounds **1**–**3**. The common approach to investigate the conformational properties of oligosaccharides consists of building up a conformational map, i.e., plotting either potential energy or relative population based on it against φ and ψ angles around the glycoside linkage. Potential energy can be estimated according to one of the well established protocols using various molecular mechanics force fields.[8] Early investigators used algorithms of partial geometry optimisation leaving the carbohydrate ring rigid.[9] However, in recent years conformational analysis with full geometry optimisation has become the usual procedure.[10] The reliability of the obtained results is tested by comparison of an experimental physical property with the one calculated from the conformational map. Conformational modeling with the use of an MM3 force field[11] was shown to give better coincidence between calculated and experimental characteristics, particularly NOE values. The MM3 force field was also successfully used in conformational analysis of sulfated galactobiosides[12] and therefore was employed in conformational study of fucosides **1**–**3**.

To confirm the adequacy of the molecular modeling results we used the comparative analysis of theoretical and experimental NOE values for compounds **1**–**3** measured after the pre-irradiation of their H-1′ proton (Figure 1). Depending on the

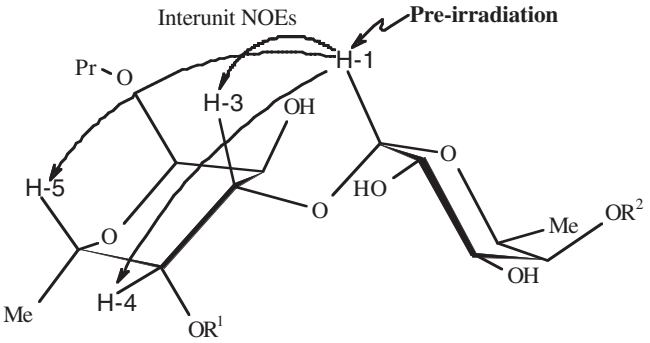


Figure 1. A schematic representation of the inter-unit NOE interactions observed for compound **1**–**3** (R^1, R^2═H or SO_3^-).

Table 5. Relative (%) Experimental and Calculated NOE Values for Trisaccharides **1–3** (Saturation of H-1′ of the Fucose Unit at ''Non-reducing'' End; Irradiation Time of 7.2 s)

Compound	Proton	Experimental NOE	Calculated NOE
1	H-2	0	− 0.3
	H-3	100	100
	H-4	41.5	49
	H-5	− 13.3	− 11.9
2	H-2	0	− 0.3
	H-3	100	100
	H-4	49.5	41.5
	H-5	− 10.2	− 12.0
3	H-2 + H-3	100[a]	100[a]
	H-4	88.8	85
	H-5	− 12.9	− 14.1

[a]Given for the sum of H-2 and H-3 due to the overlap of their signals in ^{1}H NMR spectrum of **3** (Table 2).

NMR technique used the NOE values can be measured in either steady-state or transient mode.[13] The values of the steady-state NOE are a function of all the inter-proton distances, and thus are very conformation dependent. The sensitivity of steady-state technique is higher.[13] The disadvantage of this method is that a resonance line should be irradiated selectively and during the longer time needed for the system to reach the new equilibrium state. Thus, the steady-state technique can be useful only for molecules with well resolved resonance lines in their ^{1}H NMR spectrum. As the H-1′ signal in ^{1}H NMR spectra of compounds **1–3** has separate location from other lines, we employed this technique to obtain steady-state NOE values (Table 5).

To calculate the theoretical steady-state NOE value for a single conformation we employed the iterative Noggle and Shirmer[14] Eq. 1. The obtained NOE values for conformers were further averaged over the multiple minima on the conformational map according to a Boltzman distribution. In every minimum the computed NOE was multiplied by Boltzman factor $e^{-E/RT}$, and the sum of all the obtained values was then divided by the sum of their Boltzman factors.

$$f_i^k = \frac{1}{2} \cdot (r_{ik})^{-6} - \frac{1}{2} \cdot \sum_d (r_{kd})^{-6} \cdot f_i^d \quad (1)$$

The conformational maps for disaccharides **1–3** were built via a grid search procedure using 10° steps both in φ and ψ directions. These compounds were characterized by the presence of two main minima: broad minimum **A** located around point φ = 40°, ψ = 40°, and narrow minimum **B** located near the point φ = 20°, ψ = − 50° (Figure 2). Minimum **A** corresponds to the conformation with spatial proximity of the anomeric proton H-1′ of the glycosylating residue and proton H-4 of the glycosylated fucose unit (Figure 3A). In conformation **B**, H-1′ is close to H-3 (Figure 3B). The conformational map of compound **2** had also a minimum **C** (φ = 40°, ψ = − 60°).

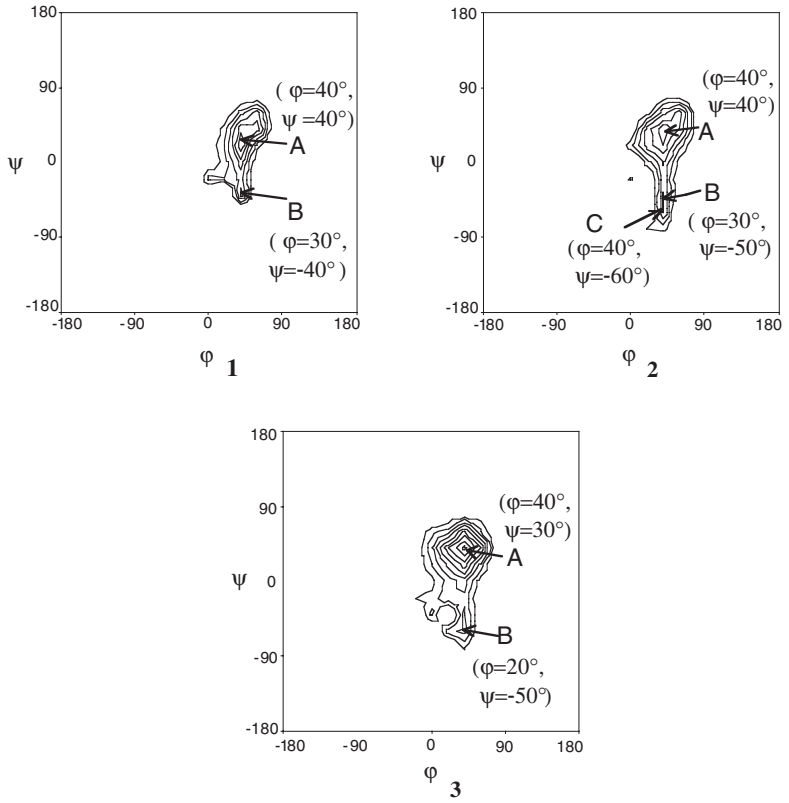


Figure 2. Conformational maps of compounds **1**–**3**. Population levels are presented every 10%.

In the case of non-sulfated compound **3**, the population ratio for local minima **A** and **B** is 1.6:1 as calculated according to Boltzman distribution. For 4-*O*-sulfated compound **1** the ratio of population of minimum **A** to the sum of populations of minima **B** and **C** is 1:1.4, showing the tendency for H-1′ to stay in proximity with H-3 rather than H-4. This can be explained by the presence of the sulfate moiety at C-4.

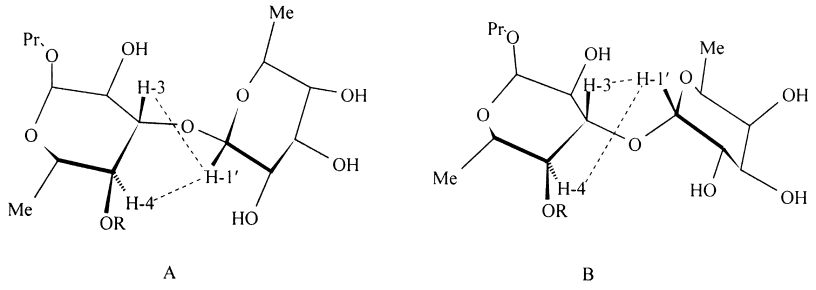


Figure 3. Inter-proton interactions in conformations **A** and **B** in compounds **1**–**3** (R═H or SO_3^-).

NOE values for compounds **1** and **3** were calculated based on the above statistical ratios. These values are consistent with the experimental data (Table 5).

The conformational map of disaccharide **1** (Figure 2) contained a number of almost equally populated conformations lying between conformations **A** and **B**. Therefore we could not correctly select any of them to estimate an NOE. To overcome this problem we varied energy limits (percent from the global minimum energy) within which lay the points to include in the calculation of an NOE. It was thus empirically determined that satisfactory coincidence with the experimental data can be obtained by setting this limit to 10% of the energy of the minimum. It was further found that NOEs for compounds **2** and **3** computed in the same manner with the same limit also coincided with the experimental values (Table 5).

According to Table 5 both experimental NOE and calculated relative NOE on H-4 in compounds **1** and **2** are nearly twofold lower than in compound **3**. This leads to the suggestion that mono-4-*O*-sulfation of the disaccharide increases the weight of the conformation in which protons H-1′ and H-3 are spatially close. This result is similar to that obtained by Stortz and Cerezo[12] for 4-*O*-sulfated galactobioside. Experimental NOE values for compounds **1** and **2** did not reflect considerable differences in conformations, but theoretical calculations showed that compound **1** was probably more flexible than **2**.

Our calculations did not indicate any substantial change in the conformation of sugar rings. It is also in accordance with the fact that coupling constants in the studied disaccharides do not change significantly (Table 2).

Using these results we tried to explain the difference in sulfation effects ($\Delta\delta$C, Table 4) for glycosylating and glycosylated units in ^{13}C NMR spectra of disaccharides **1** and **2**. We regarded sulfate groups in disaccharides as anions and assumed their free rotation. These assumptions allowed us to neglect possible anisotropy of the sulfates. Both disaccharides were characterized by the considerable weight of the conformation with close H-1′ and H-3 protons (Figure 3B, Table 6). In terms of the Grant and Cheney conception[15] the interaction between these protons causes a downfield shift of C-3 and C-1′ signals. The significance of this effect is demonstrated by the fact that the chemical shift of C-3 becomes positive in the disaccharides **1** and **2** while the β-effect makes it negative in monosaccharide **4** and in the glycosylating residue of disulfated disaccharide **2**. The downfield shift of C-1′ of over 2 ppm is also observed for disaccharides **1** and **2**.

Interaction between H-1′ and H-4 causes a strong upfield shift of C-4 in conformations of type **A** (Figure 3A), and a slight downfield shift of the same signal in conformation **B** (Figure 3B). Due to the increase of the statistical weight of the conformation

Table 6. H-1′–H-3 and H-1′–H-4 Distances (Å) in Conformations **A** and **B** for Trisaccharides **1–3**

	H-1′–H-3		H-1′–H-4	
Compound	**A**	**B**	**A**	**B**
1	2.56	2.27	2.21	3.92
2	2.55	2.26	2.21	3.43
3	2.56	2.21	2.22	3.72

of type **B** in compounds **1** and **2**, the sulfation effect on atom C-4 becomes about 2 ppm larger than in monosaccharide **4** or in the glycosylating residue in compound **2**.

CONCLUSIONS

Several 4-*O*-sulfated (1 → 3)-linked fucobiosides were synthesized and investigated by ^{1}H and ^{13}C NMR spectroscopy. Conformational analysis of these compounds and of parent non-sulfated fucobioside using combined molecular mechanics and steady-state NOE experiments showed the interaction between protons located around inter-residue linkage (H-1′, H-3 and H-4). The correlation between these interactions and ^{13}C NMR chemical shift values has been investigated. This information will be of use in the analysis of fucoidan NMR spectra.

EXPERIMENTAL

General methods. TLC was performed on Silica Gel 60 F_{254} (Merck) with EtOAc–toluene (A, 1:2), CH_2Cl_2–MeOH (B, 5:1, C, 10:1); spots were detected by charring with H_3PO_4. Column chromatography of non-sulfated compounds was performed on Silica Gel 0.063–0.2 μm (Fluka) by gradient elution with toluene–EtOAc. Gel chromatography was performed on a Sephadex G-10 column (2 × 20 cm) by elution with water at a flow rate of 1 mL/min, and a Sephadex LH-20 column (2 × 40 cm) by elution with MeOH at a flow rate of 1 mL/min. Optical rotations were determined with a Jasco DIP-360 digital polarimeter at 26–30°C. All solvents used for syntheses were purified according to conventional procedures.[16]

NMR spectra for substituted compounds **7**–**10** and **12** were recorded on Bruker spectrometers WM-250 and AMX-300 at 303 K. ^{1}H and ^{13}C NMR spectra for oligosaccharides **1**, **2** and **4** were recorded in D_2O on a Bruker spectrometer DRX-500 with 0.05% acetone as reference (^{1}H 2.225 ppm; ^{13}C 31.45 ppm). Gradient enhanced 2D gCOSY, gNOESY and gHSQC experiments as well as TOCSY experiments were used for resonance assignment. Experimental NOE were measured by differential spectroscopy on a Bruker DRX-500 instrument in D_2O (99.98% D, Merck) solutions at 303 K.

Computations were performed using the TINKER program with the implemented MM3 force field. The dielectric constant ε was set to 81. All sulfate groups were treated as anions. Parameters for their modeling were based on published work[17] with slight modifications. No solvent molecules were considered in the calculation. The starting structures were produced by geometry optimization with MM+ (HyperChem[18]). For each point of a conformational map the same starting geometry was used, and the dihedral angles were restrained with force constant of 10 kcal/deg^2 before the optimization.

Sodium Allyl 3-*O*-(3,4-Di-*O*-benzoyl-2-*O*-benzyl-α-L-fucopyranosyl)-2-*O*-benzyl-4-*O*-sulfonato-α-L-fucopyranoside (7). A solution of **6** (100 mg, 0.14 mmol) in DMF (1 mL) was treated with SO_3·Py complex (176 mg, 0.9 mmol) for 1h at rt, then quenched with $NaHCO_3$ (100 mg) and stirred for 1 h. The solid was filtered off and washed with MeOH (10 mL). The filtrate was treated with KU-2 (Na^+) cation-

exchange resin for 20 min, the resin was filtered off, and the filtrate was concentrated. Gel chromatography on a Sephadex LH-20 column in MeOH afforded amorphous **7** (95 mg, 85%): $[\alpha]_D - 220°$ (*c* 2, MeOH); R_F 0.36 (solvent C). The ^{1}H NMR data for **7** are presented in Table 1.

Anal. Calcd for $C_{43}H_{45}NaO_{14}S$ (840.87): C, 61.42%; H, 5.39%. Found: C, 61.33%; H, 5.36%.

Allyl 3-*O*-(2-*O*-Benzyl-α-L-fucopyranosyl)-2-*O*-benzyl-α-L-fucopyranoside (8). A solution of **7** (248 mg, 0.33 mmol) in 2 mL of 0.1M MeONa in MeOH was kept for 1 h at rt and then neutralized with KU-2 (H^+) resin, filtered, and concentrated to dryness. Column chromatography of the residue gave triol **8** (151 mg, 85%): $[\alpha]_D - 142°$ (*c* 2, EtOAc); R_F 0.14 (solvent A). The ^{1}H NMR data for **8** are presented in Table 1.

Anal. Calcd for $C_{29}H_{38}O_9$ (530.62): C, 65.66%; H, 7.17%. Found: C, 65.65%; H, 6.95%.

Allyl 3-*O*-(3-*O*-Benzoyl-2-*O*-benzyl-α-L-fucopyranosyl)-2-*O*-benzyl-α-L-fucopyranoside (9). A mixture of triol **8** (64 mg, 0.12 mmol), Bu_2SnO (33 mg, 0.13 mmol) and toluene (1.7 mL) was refluxed until complete dissolution and then concentrated to the volume of 0.7 mL. BzCl (0.02 mL, 0.17 mmol) was added, the solution was kept at rt for 3 h and concentrated in vacuo. Column chromatography of the residue gave amorphous **9** (59 mg, 77%): $[\alpha]_D - 166°$ (*c* 2, EtOAc); R_F 0.39 (solvent A). The ^{1}H NMR data for **9** are presented in Table 1.

Anal. Calcd for $C_{36}H_{42}O_{10}$ (634.72): C, 68.12%; H, 6.67%. Found: C, 68.20%; H, 6.69%.

Sodium Allyl 3-*O*-(Sodium 4-*O*-Sulfonato-3-*O*-benzoyl-2-*O*-benzyl-α-L-fucopyranosyl)-2-*O*-benzyl-4-*O*-sulfonato-α-L-fucopyranoside (10). Sulfation of **9** (43 mg, 0.07 mmol) by SO_3·Py complex (0.7 mmol) as described for **7**, gave **10** (58 mg, 95%): $[\alpha]_D - 151°$ (*c* 2.5, MeOH); R_F 0.29 (solvent B). The ^{1}H NMR data for **10** are presented in Table 1.

Anal. Calcd for $C_{36}H_{40}Na_2O_{16}S_2$ (838.80): C, 51.55%; H, 4.81%. Found: C, 51.63%; H, 4.89%.

Sodium Allyl 2,3-Di-*O*-benzyl-4-*O*-sulfonato-α-L-fucopyranoside (12). Sulfation of **11**[6] (35 mg, 0.09 mmol) by SO_3·Py complex (72 mg, 0.45 mmol) as described for **7**, gave **12** (41 mg, 93%). The ^{1}H NMR data for **12** are presented in Table 1.

Anal. Calcd for $C_{23}H_{27}NaO_8S$ (486.51): C, 56.78%; H, 5.59%. Found: C, 56.62%; H, 5.66%.

Sodium Propyl 3-*O*-(α-L-Fucopyranosyl)-4-*O*-sulfonato-α-L-fucopyranoside (1). A solution of **7** (46.1 mg, 0.06 mmol) in MeOH (3 mL) was subjected to catalytic hydrogenolysis with 10% Pd–C at 20°C and atm. pressure for 2 h. The

mixture was filtered through Celite, and the solvent was evaporated in vacuo. The residue was dissolved in water (1 mL), 0.1M NaOH (0.5 mL) was added. The mixture was kept for 1 h at rt and then was subjected to gel filtration on a Sephadex G-10 column in water to give amorphous **1** (20 mg, 75%): $[\alpha]_D - 103°$ (*c* 0.675, H_2O). The ^1H and ^{13}C NMR data for **1** are presented in Tables 2 and 3.

Anal. Calcd for $C_{15}H_{27}NaO_{12}S$ (454.42): C, 39.65%; H, 5.99%. Found: C, 39.53%; H, 5.88%.

Sodium Propyl 3-*O*-(Sodium-4-*O*-sulfonato-α-L-fucopyranosyl)-4-*O*-sulfonato-α-L-fucopyranoside (2). Debenzylation and debenzoylation of **10** (56 mg, 0.067 mmol), as described for **1**, yielded amorphous **2** (28 mg, 75%), $[\alpha]_D - 185°$ (*c* 1, H_2O). The ^1H and ^{13}C NMR data for **2** are presented in Tables 2 and 3.

Anal. Calcd for $C_{15}H_{26}Na_2O_{15}S_2$ (556.46): C, 32.38%; H, 4.71%. Found: C, 32.43%; H, 4.89%.

Sodium Propyl 4-*O*-Sulfonato-α-L-fucopyranoside (4). Debenzylation of **12** (40 mg, 0.08 mmol), as described for **1**, yielded amorphous **4** (18 mg, 75%): $[\alpha]_D - 74°$ (*c* 0.725, H_2O). The ^1H and ^{13}C NMR data for **4** are presented in Tables 2 and 3.

Anal. Calcd for $C_9H_{17}NaO_8S$ (308.28): C, 35.07%; H, 5.56%. Found: C, 35.13%; H, 5.76%.

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