Synthesis and Nuclear Magnetic Resonance Studies of some L-Fucosyl-containing Disaccharides

Herbert Baumann, Per-Erik Jansson and Lennart Kenne
Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden

Eleven disaccharides containing an L-fucosyl group have been synthesized and their ^1H and ^{13}C NMR spectra assigned. HSEA analysis has indicated which inter-residue atomic interactions are present in the disaccharides, some of which could be correlated with observed glycosylation shifts. The results give further knowledge about glycosylation shifts, valuable for the interpretation of NMR spectra of larger saccharides.

In a continuing study on relations between structure and ^1H and ^{13}C NMR chemical shifts of oligosaccharides,[1] a number of disaccharides containing an L-fucosyl group, *i.e.* a 6-deoxy-hexosyl sugar, have now been investigated. The results provide information on the relation between stereochemistry at the glycosidic bond and the chemical shifts. The data also provide an extension of the database in the computer program CASPER by which structural analysis of oligo- and poly-saccharides can be performed.[2]

Experimental

General Methods.—Data on coupling reactions, deprotection procedures, yields, physical constants and selected NMR chemical shifts are given in Table 1. Concentrations were performed under reduced pressure at bath temperatures <40 °C. ^1H NMR (270 and 400 MHz) and ^{13}C NMR spectra (67.5 and 100 MHz) were recorded for 0.04 and 0.2 mol dm^{-3} solutions, respectively, for D_2O solutions at 70 °C or for $CDCl_3$ solutions at ambient temperature, with a JEOL GSX 270 or GX 400 spectrometer. Chemical shifts are given in ppm using sodium 3-(trimethylsilyl)-[2,2,3,3-$^2H_4$]propanoate (TSP, δ_H 0.00), or dioxane (δ_C 67.40) for D_2O solutions and tetramethylsilane (δ_H, δ_C 0.00) for $CDCl_3$ solutions as internal references. For the assignment of signals, different H,H- and H,C-COSY experiments were used. Column chromatography was performed on silica gel. The purity and identity of intermediates and final products were determined as earlier described.[1] The compounds **1**, **2**, **5**, **8** and **10** are called α-glycosides referring to the central bond, and the remaining compounds β-glycosides.

Conformational Analysis.—The hard-spheres *exo*-anomeric (HSEA) program[3,4] was used to estimate minimum-energy conformations of the disaccharides. The torsional angles φ and ψ were defined by H(1′)–C(1′)–O(X)–C(X) and C(1′)–O(X)–C(X)–H(X), respectively, for which X represents the linkage position. The bond angle τ, defined by C(1′)–O(X)–C(X), was set at 117°. Co-ordinate sets of α-L-fucopyranose,[5] α-D-mannopyranose,[6] β-D-mannopyranose,[7] and methyl α-D-glucopyranoside[6] were obtained from crystal data. Those of methyl α-D-galactopyranoside, β-L-fucopyranose and methyl α-L-fucopyranoside were modified from the crystal data of α-D-galactopyranose,[8] methyl β-D-galactopyranoside,[9] and α-L-fucopyranose, respectively.

Glycosylation Methods.—Method A. Methyl trifluoromethanesulphonate (5 mol equiv.) was added to a stirred solution of a thioglycoside (1.3 mol equiv.) and suitably protected aglycone[10] at 0 °C in the solvent given in Table 1. The mixture was then allowed to reach 20 °C. When the reaction was complete, as indicated by TLC, triethylamine (10 mol equiv.) was added and the mixture was stirred for a further 30 min. The mixture was then diluted with dichloromethane, filtered through a layer of Celite, and washed successively with aq. 10% H_2SO_4, aq. $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and evaporated and the crude product was purified on a column of silica gel by using solvents given in Table 1.

Method B. The conditions used in this method were as described in method A but with the following additions: 2,6-di-*tert*-butyl-4-methylpyridine (5 mol equiv.) and 2,4,6-trimethylpyridine (5 mol equiv.) were added to the reaction mixture in the synthesis of compounds **24** and **25**, respectively.

Deblocking and Purification Procedures.—Method C. The disaccharide derivative was dissolved in aq. 90% acetic acid (20 cm^3) and was hydrogenolysed at ~350 kPa over Pd/C (10%; 100–300 mg) for 16 h. The solution was filtered and concentrated to dryness, and the residue was purified by chromatography on a column of silica gel [ethyl acetate–acetic acid–methanol–water (12:3:3:2)] and then on a column of Bio-Gel P-2 with water as eluant. After freeze-drying, the product was obtained as an amorphous powder.

Method D. The disaccharide derivative was de-*O*-acylated with sodium methoxide in dichloromethane–methanol [0.025 mol dm^{-3}; (1:1), 10–30 cm^3]. The solution was neutralised with acetic acid or Dowex 50 (H^+), then evaporated, and the residual material was hydrogenolysed and purified as described above.

Method E. The isopropylidene group was removed by treatment with aq. 70% acetic acid at 100 °C. The solution was evaporated, and the residue was hydrogenolysed and purified as described in method C.

Results and Discussion

Synthesis of Disaccharides **1**–**11**.—The substances were numbered as follows:

1 α-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH
2 α-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH
3 β-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH
4 β-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH
5 α-L-Fuc*p*-(1 → 2)-α-L-Fuc*p*-OMe
6 β-L-Fuc*p*-(1 → 2)-α-D-Glc*p*-OMe
7 β-L-Fuc*p*-(1 → 3)-α-D-Glc*p*-OMe
8 α-L-Fuc*p*-(1 → 6)-α-D-Glc*p*-OMe
9 β-L-Fuc*p*-(1 → 6)-α-D-Glc*p*-OMe
10 α-L-Fuc*p*-(1 → 6)-α-D-Gal*p*-OMe
11 β-L-Fuc*p*-(1 → 6)-α-D-Gal*p*-OMe

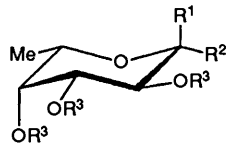
Data on coupling reactions, deprotection procedures, yields, physical constants and selected NMR chemical shifts are given

Table 1 Data on coupling reactions,[a] deprotection procedures,[a] yields, physical constants and selected NMR chemical shifts

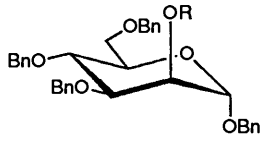
(a) Compd.	Aglycone precursor (mg)	Glycosyl donor (mg)	Glycosidation method[a] (solvent)[b]	TLC R_f (solvent)[c]	Column chromatography solvent	Yield (mg) (%)	δ_C C-1′	δ_C C-1
21	**15** (560)	**12** (720)	A (DE)	0.24 [P–E (5:1)]	T–E (8:1)	400 (53)	96.9	96.6
22	**15** (560)	**12** (720)	A (DE)	0.29 [P–E (5:1)]	T–E (8:1)	112 (15)	104.2	99.2
23	**16** (50)	**12** (150)	A (DE)	0.70 [T–E (1:1)]	T–E (3:1)	68 (50)	96.8	95.1
24	**17** (100)	**13** (140)	B (DM)	0.19 [T–E (3:1)]	T–E (3:1)	79 (45)	100.2	98.6
25	**18** (342)	**13** (324)	B (AN)	0.30 [P–E (2:1)]	P–E (2:1)	391 (66)	101.4	99.2
26	**19** (450)	**12** (700)	A (DE)	0.43 [I–E (2:1)]	I–E (7:2)	450 (52)	98.0	98.0
27	**19** (110)	**14** (170)	A (DE)	0.58 [T–E (4:1)]	P–E (3:2)	100 (46)	101.7	97.9
28	**20** (350)	**12** (540)	A (DE)	0.45 [I–E (2:1)]	I–E (3:1)	221 (33)	98.2	98.7
29	**20** (300)	**14** (500)	A (DE)	0.66 [T–E (3:1)]	T–E (15:1)	350 (59)	101.8	98.5

(b) Compd.	Protected precursor (mg; deprotection method)[a]	Yield (mg) (%)	Optical rotation $[\alpha]_{578}^{22}$ (*c* in water)	δ_{1-H} ($J_{1,2}$/Hz) 1′-H	δ_{1-H} ($J_{1,2}$/Hz) 1-H	δ_C C-1′	δ_C C-1
1[d]	**21** (376; C)	97 (59)	−117 (1.0)	4.99 (3.9)	5.29 (1.7)	98.80	92.49
2				5.07 (3.9)	4.96 (1.0)	102.15	94.84
3[d]	**22** (112; C)	49 (97)	0 (0.6)	4.54 (7.5)	5.41 (1.8)	105.34	94.08
4				4.52 (7.1)	4.86 (0.9)	104.71	93.79
5	**23** (68; E)	15 (44)	−223 (0.7)	5.02 (3.9)	4.96 (3.9)	97.64	97.84
6	**24** (79; D)	36 (86)	84 (0.8)	4.46 (7.8)	4.96 (3.2)	102.78	98.33
7	**25** (380; D)	77 (38)	102 (1.0)	4.60 (7.8)	4.86 (3.8)	104.06	99.86
8	**26** (350; C)	108 (80)	−17 (1.0)	4.93 (3.8)	4.80 (3.8)	100.07	100.33
9	**27** (350; D)	97 (75)	89 (1.0)	4.41 (7.8)	4.81 (3.7)	103.56	100.28
10	**28** (200; C)	57 (74)	−8 (0.8)	4.94 (3.7)	4.85 (3.3)	99.82	100.53
11	**29** (350; D)	82 (64)	113 (1.0)	4.40 (7.8)	4.84 (2.8)	103.70	100.49

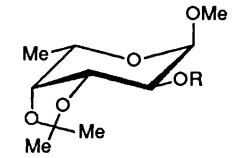
[a] Two coupling methods were used, A and B, and three deprotection methods, C, D and E. See Experimental section for details. [b] Different solvents are used in the glycosidation reactions, DE = diethyl ether, DM = dichloromethane, AN = acetonitrile. [c] TLC R_f-values are given for the solvent system used, T = toluene, E = ethyl acetate, P = light petroleum (b.p. 60–71 °C), I = 'isooctane' (2,2,4-trimethylpentane). [d] Deprotection of compounds **21** and **22**, respectively, gave anomeric mixtures and their NMR spectra are reported separately.



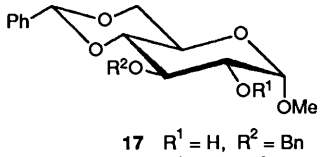
12 R^1 = H, R^2 = SEt, R^3 = Bn
12a R^1 = –, R^2 = H, R^3 = Bn
12b R^1 = H, R^2 = –, R^3 = Bn
13 R^1 = H, R^2 = SEt, R^3 = Ac
13a R^1 = H, R^2 = –, R^3 = Ac
14 R^1 = H, R^2 = SEt, R^3 = Bz
14a R^1 = H, R^2 = –, R^3 = Bz



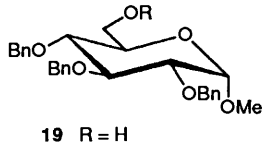
15 R = H
21 R = **12a**
22 R = **12b**



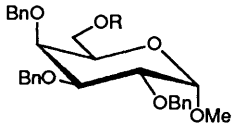
16 R = H
23 R = **12a**



17 R^1 = H, R^2 = Bn
18 R^1 = Bn, R^2 = H
24 R^1 = **13a**, R^2 = Bn
25 R^1 = Bn, R^2 = **13a**



19 R = H
26 R = **12a**
27 R = **14a**



20 R = H
28 R = **12a**
29 R = **14a**

in Table 1. Glycosylation of benzyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside **15** with ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **12** using methyl trifluoromethanesulphonate as promotor[10] gave a mixture of disaccharides **21** and **22** in the ratio 3.5:1. After separation, deprotection of anomer **21** gave the two anomers **1** and **2** in the ratio 1:1 as demonstrated by ^{1}H NMR spectroscopy. Compound **22** was deprotected analogously and gave, according to the ^{1}H NMR spectrum the products **3** and **4** in the ratio 2:1. Glycosylation of methyl 3,4-di-*O*-isopropylidene-α-L-fucopyranoside[11] **16**, methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[12] **19**, and methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranoside[12] **20** with thioglycoside **12** gave the disaccharide derivatives **23**, **26** and **28**, respectively, which after deprotection gave compounds **5**, **8** and **10**, respectively. The acetylated ethyl thiofucoside **13** was condensed with methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[13] **17** under methyl trifluoromethanesulphonate promotion and 2,6-di-*tert*-butyl-4-methylpyridine as acid scavenger (method B) to give compound **24**. Deprotection by treatment with acetic acid followed by hydrogenolysis gave compound **6**. Compound **25** was synthesized analogously to compound **24** except that the glycosyl acceptor was methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[13] **18** and the acid scavenger was 2,4,6-trimethylpyridine, to give compound **7** after deprotection. Reaction of thioglycoside **14** with glycosyl acceptors **19** and **20**, under methyl trifluoromethanesulphonate promotion, gave, after deprotection (method D), the 6-*O*-β-L-fucosyl disaccharides **9** and **11**, respectively.

HSEA Calculations for Disaccharides **1–7**.—The φ- and ψ-angles, and inter-residue atomic distances <3 Å for the minimum-energy conformations of disaccharides **1–7** are given in Table 2. The calculations gave, for all disaccharides, minimum-energy conformations with φ-angles of ~50° (α-L) or ~ −55° (β-L). The ψ-angle for disaccharides **1–7** varied to a

Table 2 Values for φ- and ψ-angles and inter-residue atomic distances < 3 Å in the minimum-energy conformations of disaccharides **1**–**7** obtained by HSEA calculations

	φ (°)	ψ (°)	1′-H[a]	5′-H	O-5′
α-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH **1**	50	20	2.46 (1-H), 2.50 (2-H)	2.54 (O-3)	2.60 (2-H)
α-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH **2**	45	15	2.64 (O-1), 2.31 (2-H)	2.50 (O-3)	2.61 (2-H)
β-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH **3**	−55	0	2.40 (2-H)		2.86 (1-H), 2.59 (2-H)
β-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH **4**	−55	−5	2.87 (O-3), 2.35 (2-H)		2.48 (2-H)
α-L-Fuc*p*-(1 → 2)-α-L-Fuc*p*-OMe **5**	50	25	2.54 (1-H), 2.56 (2-H)	2.71 (O-3)	2.59 (2-H)
β-L-Fuc*p*-(1 → 2)-α-D-Glc*p*-OMe **6**	−50	−25	2.48 (1-H), 2.47 (2-H)		2.44 (2-H)
β-L-Fuc*p*-(1 → 3)-α-D-Glc*p*-OMe **7**	−55	−5	2.99 (O-4), 2.42 (3-H)		2.54 (3-H)

[a] Primed label refers to the glycosyl group and unprimed to the aglycone.

much larger extent, from −25° to 25°. Minima other than those mentioned in Table 2 were also found for the β-linked disaccharides. These minima had φ-angles close to 180° with an energy of 8 kJ or more above that of the minimum-energy conformation and they are therefore much less populated and they will not be further discussed here. The O(6)–C(6) bond in the 6-*O*-fucosyl disaccharides **8**–**11** is very flexible and several energy minima are found[14] (data not shown).

The general observations for inter-residue atomic interactions were the same as those observed earlier,[1] *i.e.* that the atoms involved are 1′-H and O-5′ together with 5′-H in α-glycosides for the glycosyl group and X-H and one of the neighbouring equatorial atoms in the aglycone, X being the linkage position.

In the 2-linked disaccharide **1** a strong interaction of 1′-H with a proton (1-H) is instead to an oxygen (O-1) in compound **2**. This was not observed for the β-L-fucosyl disaccharides **3** and **4** in which 1′-H is directed towards O-3 and is thereby not affected by the substituent(s) on C-1. The interactions calculated for the L-Fuc*p*-(1 → 2)-D-Man*p* disaccharides **1**–**4** were also predicted for D-Glc*p*-(1 → 2)-L-Rha*p* disaccharides which have been investigated previously.[1] These disaccharides have the same relative stereochemistry at the glycosidic linkage and therefore the same interactions should be present. Only minor differences (<0.15 Å) in calculated inter-residue atomic distances are found for the four pairs of disaccharides. Such an analogy has also been observed for 1,3-linked *galacto*- and *manno*-derivatives.[15]

The proton on the linkage carbon in the aglycone interacts in compounds **1**–**7** with both 1′-H and O-5′ in the glycosyl group.

^{1}H *NMR Glycosylation Shifts.*—The ^{1}H NMR chemical shifts and the induced chemical-shift differences (glycosylation shifts, $\Delta\delta$) relative to the chemical shifts of the corresponding monomers are given in Table 3.

In the glycosyl group significant glycosylation shifts (>0.05 ppm) are only observed for some of the signals from 1′-, 2′- and 5′-H. The signal from the anomeric proton (1′-H) has a large upfield shift (−0.13 to −0.27 ppm) for the α-glycosides, whereas the shift for the β-glycosides is smaller (0.05 to −0.15 ppm). This correlates with calculated short distances between 1′-H and protons in the aglycone for most of the compounds. For compounds **2** and **4**, however, short distances to oxygens were also calculated but an upfield shift was still observed. The 5′-H signals from the α-glycosides are shifted either downfield (by 0.05–0.16 ppm) as in compounds **1**, **2** and **5** or upfield (−0.12 to −0.11 ppm) as in compounds **8** and **10**. The downfield shift is correlated with a calculated short distance between 5′-H and O-3, and the upfield shift to a calculated proximity to one or more hydrogens in the methyl glycoside residue[14] (data not shown). The downfield shift for the 2′-H signal from the β-glycosides (0.05–0.16 ppm) seems to be general.[1]

The significant glycosylation shifts for signals from the aglycone were observed mainly for protons at or next to the glycosidic linkage and vary significantly (−0.20 to 0.24 ppm). The signal from the proton on the linkage carbon in the β-glycosides is shifted more downfield than that in the corresponding α-glycoside. This correlates with a shorter calculated distance between this proton and O-5′ in the β-glycosides than that in the α-glycosides.

The similar stereochemistry around the glycosidic bond of the 2-linked L-fucosyl-D-mannosides **1**–**4** and the 2-linked D-glucosyl-L-rhamnosides[1] as discussed above is reflected in glycosylation shifts for these pairs which are similar in signal magnitude.

As has also been observed for other 6-linked disaccharides,[14] only a marginal change of the glycosylation shifts occurs in the methyl glycoside residue for disaccharides with *gluco*- and with *galacto*-configuration **8** ⟶ **10** and **9** ⟶ **11**, respectively.

^{13} *NMR Glycosylation Shifts.*—The ^{13}C NMR chemical shifts and glycosylation shifts $\Delta\delta$ are given in Table 4.

As for most of the earlier investigated disaccharides,[1] significant glycosylation shifts (>0.5 ppm) are observed for signals from atoms at or near the glycosidic linkage. For disaccharides **1**–**11** the glycosylation shifts for signals from linkage carbons, C-1′ and C-X (X = 2, 3 or 6), range from 4.5 to 9.7 ppm. The lowest values (4.5–5.7 ppm) are observed for the anomeric carbon signal (C-1′) in disaccharides **1**, **5** and **6** that, as indicated by the energy calculations, have an interaction between 1′-H and 1-H (the γ-*gauche* effect).[16] In addition the C-1 signal from those compounds has a large upfield shift (−2.6 to −1.9 ppm).

Additional glycosylation shifts are observed for the C-2′ signal from β-glycosides (−1.4 to −0.7 ppm) and for the C-5′ signal from α-glycosides (0.4–1.0 ppm). These shifts seem to be general for α- and β-glycosides, respectively.[1]

As discussed above, the 2-linked mannosides **1**–**4** have their mirror counterparts in a set of D-Glc*p*-(1→2)-L-Rha*p*-OMe disaccharides. The ^{13}C NMR glycosylation shifts are similar within each pair of disaccharides with one exception, and that is the C-2 signal from compounds **2** and **4** which is shifted ~2 ppm more downfield than in the corresponding rhamnosides. This is not correlated with any changes in calculated short distances but may be due to the fact that the rhamnosides are methyl glycosides and compounds **2** and **4** are reducing disaccharides.

On comparison of glycosylation shifts from the methyl glucosides with those from the methyl galactosides, **8** ⟶ **10**

Table 3 ^{1}H NMR chemical shifts and glycosylation shifts[a] of the disaccharides **1–11** obtained at 70 °C relative to internal TSP (δ_H 0.00)

Substance	1′-H	2′-H	3′-H	4′-H	5′-H	6′-H	1-H	2-H	3-H	4-H	5-H	6-H[a]	6-H[b]	OMe
α-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH	4.99	3.79	3.92	3.82	4.36	1.22	5.29	3.92	3.97	3.75	3.81	3.83	3.83	
1	−0.21	0.03	0.06	0.01	0.16	0.01	0.11	−0.02	0.11	0.07	−0.01	0.09	−0.03	
α-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH	5.07	3.85	3.95	3.83	4.36	1.22	4.96	4.00	3.72	3.60	3.40	3.76	3.91	
2	−0.13	0.08	0.09	0.02	0.16	0.01	0.07	0.05	0.06	0.00	0.02	0.01	0.00	
β-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH	4.54	3.56	3.65	3.74	3.78	1.26	5.41	4.02	3.93	3.73	3.81	3.84	3.84	
3	−0.01	0.10	0.02	0.00	−0.01	0.00	0.23	0.08	0.07	0.05	−0.01	0.10	−0.02	
β-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH	4.52	3.62	3.68	3.77	3.86	1.28	4.86	4.13	3.75	3.66	3.41	3.74	3.90	
4	−0.03	0.16	0.05	0.03	0.07	0.02	−0.03	0.18	0.09	0.06	0.01	−0.01	−0.01	
α-L-Fuc*p*-(1 → 2)-α-L-Fuc*p*-OMe	5.02	3.79	3.91	3.82	4.25	1.22	4.95	3.85	3.92	3.84	4.04	1.24		3.42
5	−0.18	0.02	0.05	0.01	0.05	0.01	0.19	0.05	0.14	0.06	0.04	0.02		0.01
β-L-Fuc*p*-(1 → 2)-α-D-Glc*p*-OMe	4.46	3.54	3.64	3.76	3.80	1.27	4.96	3.74	3.77	3.47	3.65	3.76	3.86	3.34
6	−0.09	0.08	0.01	0.02	0.01	0.01	0.15	0.18	0.09	0.06	0.01	0.00	−0.01	−0.09
β-L-Fuc*p*-(1 → 3)-α-D-Glc*p*-OMe	4.60	3.57	3.68	3.76	3.82	1.29	4.86	3.65	3.85	3.61	3.67	3.77	3.87	3.44
7	0.05	0.11	0.05	0.02	0.03	0.03	0.05	0.09	0.17	0.20	0.03	0.01	0.00	0.01
α-L-Fuc*p*-(1 → 6)-α-D-Glc*p*-OMe	4.93	3.80	3.87	3.81	4.09	1.23	4.80	3.57	3.68	3.47	3.75	3.77	3.94	3.44
8	−0.27	0.03	0.01	0.00	−0.11	0.02	−0.01	0.01	0.00	0.06	0.11	0.01	0.07	0.01
β-L-Fuc*p*-(1 → 6)-α-D-Glc*p*-OMe	4.41	3.52	3.65	3.75	3.79	1.27	4.81	3.57	3.68	3.52	3.77	3.93	4.07	3.44
9	−0.14	0.06	0.02	0.01	0.00	0.01	0.00	0.01	0.00	0.11	0.13	0.17	0.20	0.01
α-L-Fuc*p*-(1 → 6)-α-D-Gal*p*-OMe	4.94	3.79	3.84	3.82	4.08	1.23	4.85	3.85	3.82	4.01	4.06	3.74	3.86	3.44
10	−0.26	0.02	−0.02	0.01	−0.12	0.02	0.00	0.01	0.01	0.02	0.17	−0.02	0.10	0.01
β-L-Fuc*p*-(1 → 6)-α-D-Gal*p*-OMe	4.40	3.51	3.64	3.75	3.78	1.27	4.84	3.84	3.83	4.04	4.07	3.86	4.00	3.44
11	−0.15	0.05	0.01	0.01	−0.01	0.01	−0.01	0.00	0.02	0.05	0.18	0.10	0.24	0.01

[a] Primed labels refer to the fucopyranosyl group and unprimed to the aglycone. Glycosylation shifts are calculated by subtraction of chemical shifts for signals from the corresponding hexose for the glycosyl group and the corresponding hexose or methyl hexoside for the aglycone, and a positive difference indicates a downfield shift.

Table 4 ^{13}C NMR chemical shifts and glycosylation shifts[a] of the disaccharides **1–11** obtained at 70 °C relative to internal dioxane (δ_C 67.40)

Substance	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
α-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH	98.80	68.95	70.39	72.77	67.85	16.05	92.49	77.84	70.62	67.80	73.58	61.62	
1	5.68	−0.14	0.10	−0.02	0.75	−0.28	−2.45	6.15	−0.63	−0.14	0.24	−0.37	
α-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH	102.15	69.63	70.53	72.77	68.12	16.13	94.84	81.37	73.26	67.77	77.12	61.75	
2	9.03	0.54	0.24	−0.02	1.02	−0.20	0.29	9.24	−0.77	0.08	0.12	−0.24	
β-L-Fuc*p*-(1 → 2)-α-D-Man*p*-OH	105.34	72.07	73.94	72.21	71.73	16.17	94.08	80.96	71.22	68.35	73.30	61.98	
3	8.19	−0.66	0.01	−0.14	0.09	−0.16	−0.86	9.27	−0.03	0.41	−0.04	−0.01	
β-L-Fuc*p*-(1 → 2)-β-D-Man*p*-OH	104.71	71.84	73.84	72.12	72.15	16.05	93.79	81.86	73.99	68.09	77.24	61.95	
4	7.56	−0.89	−0.09	−0.23	0.51	−0.28	−0.76	9.73	−0.04	0.40	0.24	−0.04	
α-L-Fuc*p*-(1 → 2)-α-L-Fuc*p*-OMe	97.64	68.99	70.50	72.78	67.81	16.05	97.84	74.14	69.02	72.80	67.13	16.12	55.73
5	4.52	−0.10	0.21	−0.02	0.71	−0.28	−2.60	5.17	−1.62	0.08	−0.04	0.00	−0.23
β-L-Fuc*p*-(1 → 2)-α-D-Glc*p*-OMe	102.78	71.29	73.83	72.14	71.90	16.19	98.33	79.40	72.83	70.62	72.26	61.58	55.69
6	5.63	−1.44	−0.10	−0.21	0.26	−0.14	−1.86	7.17	−1.27	−0.06	−0.26	−0.09	−0.24
β-L-Fuc*p*-(1 → 3)-α-D-Glc*p*-OMe	104.06	71.91	73.81	72.14	71.88	16.16	99.86	70.92	83.65	69.88	72.31	61.51	55.82
7	6.91	−0.82	−0.12	−0.21	0.24	−0.17	−0.33	−1.31	9.55	−0.80	−0.21	−0.16	−0.11
α-L-Fuc*p*-(1 → 6)-α-D-Glc*p*-OMe	100.07	69.20	70.59	72.75	67.52	16.06	100.33	72.18	74.02	70.65	71.84	68.12	56.16
8	6.96	0.11	0.30	−0.04	0.42	−0.27	0.13	−0.05	−0.08	−0.02	−0.68	6.45	0.24
β-L-Fuc*p*-(1 → 6)-α-D-Glc*p*-OMe	103.56	71.48	73.90	72.22	71.71	16.18	100.28	72.17	73.90	70.48	71.32	68.90	56.13
9	6.41	−1.25	−0.03	−0.13	0.07	−0.15	0.09	−0.06	−0.20	−0.19	−1.20	7.22	0.21
α-L-Fuc*p*-(1 → 6)-α-D-Gal*p*-OMe	99.82	69.02	70.62	72.72	67.58	16.05	100.53	69.08	70.36	70.36	70.24	68.06	56.25
10	6.70	−0.07	0.33	−0.07	0.49	−0.28	0.18	−0.10	−0.10	0.18	−1.28	6.01	0.30
β-L-Fuc*p*-(1 → 6)-α-D-Gal*p*-OMe	103.70	71.40	73.92	72.23	71.71	16.21	100.49	69.09	70.11	70.31	69.62	69.26	56.21
11	6.55	−1.32	−0.01	−0.12	0.07	−0.12	0.14	−0.09	-0.35	0.13	−1.89	7.21	0.25

[a] Primed labels refer to the fucopyranosyl group and unprimed to the aglycone. Glycosylation shifts are calculated by subtraction of chemical shifts for signals from the corresponding hexose for the glycosyl group and the corresponding hexose or methyl hexoside for the aglycone, and a positive difference indicates a downfield shift.

and **9** ⟶ **11**, respectively, only a small difference is observed. The largest difference is observed for the C-5 signal which is shifted 0.6 ppm more upfield in the galactosides **10** and **11** compared with the glucosides **8** and **9**.

Acknowledgements

This work was supported by grants from the Swedish Natural Science Research Council and the Swedish National Board for Technical Development. Ms Suzanne Sallander, Ms Anna Börje and Mrs Pia Mickols are gratefully acknowledged for their technical assistance.

References

1 P.-E. Jansson, L. Kenne and H. Ottoson, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2011 and references therein.
2 P.-E. Jansson, L. Kenne and G. Widmalm, *Carbohydr. Res.*, 1989, **188**, 169.
3 R. U. Lemieux, K. Bock, L. T. J. Delbaere, S. Koto and V. S. Rao, *Can. J. Chem.*, 1980, **58**, 631.
4 H. Thøgersen, R. U. Lemieux, K. Bock and B. Meyer, *Can. J. Chem.*, 1982, **60**, 44.
5 W. J. Cook and C. E. Bugg, *Biochim. Biophys. Acta*, 1975, **389**, 428.
6 G. A. Jeffrey, R. K. McMullan and S. Takagi, *Acta Crystallogr., Sect. B*, 1977, **33**, 728.
7 V. Warin, F. Baert, R. Fouret, G. Strecker, G. Spik, B. Fournet and J. Montreuil, *Carbohydr. Res.*, 1979, **76**, 11.

8 B. Sheldrick, *Acta Crystallogr., Sect. B*, 1976, **32**, 1016.
9 S. Takagi and G. A. Jeffrey, *Acta Crystallogr., Sect. B*, 1979, **35**, 902.
10 P. Fügedi, P. J. Garegg, H. Lönn and T. Norberg, *Glycoconj. J.*, 1987, **4**, 97.
11 E. E. Percival and E. G. V. Percival, *J. Chem. Soc.*, 1950, 690.
12 M. Ek, P. J. Garegg, H. Hultberg and S. Oscarson, *J. Carbohydr. Chem.*, 1983, **2**, 305.
13 P. J. Garegg, T. Iversen and S. Oscarson, *Carbohydr. Res.*, 1976, **50**, C12.
14 I. Kolare, P.-E. Jansson and L. Kenne, manuscript in preparation.
15 H. Baumann, P.-E. Jansson and L. Kenne, *J. Chem. Soc., Perkin Trans. 1*, 1988, 209.
16 F. W. Wehrli and T. Wirthlin in *Interpretation of Carbon-13 NMR Spectra*, Heyden, London, 1976, p. 22.

Paper 1/01267C
Received 18*th March* 1991
Accepted 20*th May* 1991