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Carbohydrate Research 262 (1994) 195–212

CARBOHYDRATE RESEARCH

Synthesis of the 5-aminopentyl glycoside of β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)-L-Fuc*p* and fragments thereof related to glycopeptides of human Christmas factor and the marine sponge *Microciona prolifera*

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Received 3 February 1994; accepted 25 March 1994

Abstract

The marine sponge *Microciona prolifera* and human coagulation factor IX (Christmas factor)-related mono- to tri-saccharide 5-aminopentyl glycosides β-D-Gal*p*-R (**5**), β-D-Glc*p*NAc-R (**16**), β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-R (**26**), β-D-Glc*p*NAc-(1 → 3)-β-L-Fuc*p*-R (**39**), β-D-Glc*p*NAc-(1 → 3)-α-L-Fuc*p*-R (**43**), β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)-β-L-Fuc*p*-R (**45**), and β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)-α-L-Fuc*p*-R (**47**), where R is a 5-aminopentyloxy spacer moiety, which allowed the construction of glycoconjugates, were prepared. Thus, 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl trichloroacetimidate (**10**) and 1,3,4,6-tetra-*O*-acetyl-2-chloroacetamido-2-deoxy-β-D-glucopyranose (**13**) were condensed with *N*-Z-protected 5-aminopentanol (**2**) followed by conversion of the coupling products into the corresponding *N*-acetylglucosamine derivatives, to give compound **16** after deblocking. Similarly, the donors **10** and **13** were coupled to position 3 of suitably protected aminopentyl β- (**32**) and α- (**37**) -L-fucopyranosides, to give the disaccharides **39** and **43**, respectively. Starting from lactose, *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzoyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl trichloroacetimidate (**23**) was prepared and used as an efficient disaccharide donor for the construction of ligand **26** from **2** and of the trisaccharide ligands **45** and **47** from fucosides **32** and **37**, respectively.

Key words: Christmas factor, human; Coagulation factor IX; Human marine sponge *Microciona prolifera*; Aminopentyl glycoside

SSDI 0008-6215(94)00126-Z

1. Introduction

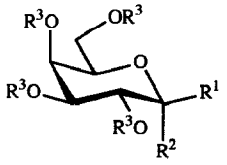
The unique trisaccharide fragment β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)-L-Fuc*p*, containing a 4,6-*O*-[1-(*R*)-carboxyethylidene] substituent at the terminal galactosyl unit, has been identified as part of a proteoglycan isolated from the marine sponge *Microciona prolifera* [1]. Monoclonal antibodies raised against the proteoglycan revealed that this trisaccharide was a major constituent of the glycan and, furthermore, was responsible for the Ca^{2+}-dependent reaggregation of dissociated cells of *Microciona prolifera* [1,2]. However, the anomeric configuration of the L-fucose residue, as well as whether this trisaccharide epitope was the repeating unit or represented a part of the repeating unit of the proteoglycan remained undetermined. Recently, the same trisaccharide sequence, α-(2 → 6) sialylated at the terminal galactose unit, has also been identified as an α-O-linked sugar moiety at serine 61 of human coagulation factor IX (Christmas factor) [3]. Nothing, however, is known so far about the distinct biological function of this rather unusual fucose-containing, serine-bound oligosaccharide.

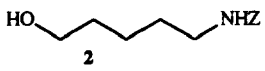
In this paper, syntheses of 5-aminopentyl mono- to tri-saccharide glycosides related to the title structure are presented in detail. The 5-aminopentyl aglycon was chosen for the fragments in order to confirm both a well defined anomeric α and β configuration of the L-fucose residue as well as to provide a "spacer-separated" amino group for the saccharides that allows the convenient preparation of the corresponding glycoconjugates for further biological studies. The ligand 5-aminopentyl 4,6-*O*-[1-(*R*)-carboxyethylidene]-β-D-galactopyranoside has recently been synthesized in our laboratory and was used both for the affinity purification of human serum amyloid P protein [4], and for the determination of the configuration of the pyruvic acetal of the *Microciona prolifera* proteoglycan via comparison of the NMR data [1].

2. Results and discussion

Previously, a series of 6-aminohexyl mono- and di-saccharides, including the β-D-galactopyranoside, 2-acetamido-2-deoxy-β-D-glucopyranoside, *N*-acetyl-β-D-lactosamine derivatives, have been prepared and successfully used as ligands for biological studies [5–9]. These glycosides were synthesized by mercuric cyanide [5,7,9] or silver carbonate [8] promoted condensation of the respective acetylated glycosyl halides with *N*-trifluoroacetyl [5,7,8] and *N*-Z-protected [1] [9] 6-aminohexanol, respectively. Similarly, 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**1**) was condensed here with 5-(benzyloxycarbonylamino)pentanol [10] (**2**) by promotion of $Hg(CN)_2$ and $HgBr_2$ to give first the blocked monosaccharide ligand **3** (28%). Deacetylation (Zemplén) of the latter afforded the crystalline Z-protected

[1] Z = benzyloxycarbonyl.





2

Compd	R^1	R^2	R^3
1	H	Br	Ac
3	$O(CH_2)_5NHZ$	H	Ac
4	$O(CH_2)_5NHZ$	H	H
5	$O(CH_2)_5NH_3^+Cl^-$	H	H

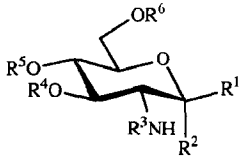
Scheme 1.

aminopentyl β-D-galactopyranoside **4** that was hydrogenolyzed to give the free ligand **5**.

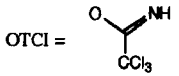
For the preparation of the aminopentyl GlcNAc derivative two efficient alternative procedures using the glucosamine donors **10** and **13** were applied for the glycosylation step with the alcohol **2**. Reacting 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-D-glucopyranosyl trichloroacetimidate (**10**) with **2** under boron trifluoride etherate catalysis afforded the glycoside **11** (95%). Sequential treatment of the latter with zinc in acetic acid followed by acetic anhydride in pyridine then gave the GlcNAc derivative **12** in 81% yield. The imidate **10** was obtained from the acetate **7** via bromide **8** and alcohol **9** as previously described [11]. An alternative procedure to the original preparation [12] of compounds **7** and **8** comprised the treatment of easily available [13] 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride (**6**) with 2,2,2-trichloroethoxycarbonyl chloride (Teoc-Cl) in a biphasic system, to give **7** in practically quantitative yield. This approach was especially useful because the glucosamine **6** also served as the starting material for 1,3,4,6-tetra-*O*-acetyl-2-chloroacetamido-2-deoxy-β-D-glucopyranose [14] (**13**).

Ferric chloride-promoted [14] condensation of **13** and **2** gave the *N*-chloroacetylated glycoside **14** (93%), reductive dehalogenation of which with Zn in acetic acid afforded compound **12** in 93% yield. Thus, the two procedures used here for the preparation of **12** from the relatively unreactive [15] alcohol **2** were equally well suited since the overall yields were excellent in both cases and, furthermore, all intermediates were crystalline compounds which facilitated their purification. The glucoside **12** was finally deacetylated (Zemplén) to give compound **15** which afforded the GlcNAc ligand **16** upon hydrogenolysis. In general, the application of *N*-chloroacetylated and Teoc-protected glucosamine donors seemed promising for the introduction of a β-D-GlcNAc moiety [11,14,16].

Originally it was planned to prepare the lactosamine ligand β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-$O(CH_2)_5NH_2$ by β-(1 → 4)-selective galactosylation of a suitable GlcNAc acceptor. This approach was previously described for the corresponding



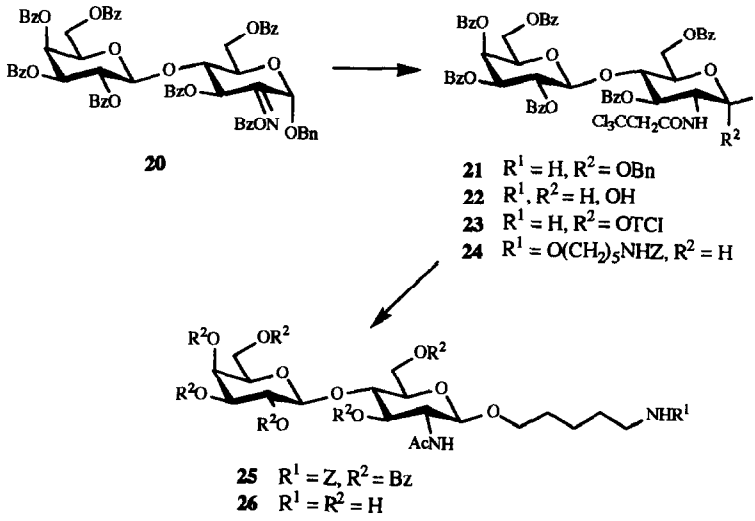
Compd	R^1	R^2	R^3	R^4	R^5	R^6
6	OAc	H	$H_2^+Cl^-$	Ac	Ac	Ac
7	OAc	H	CCl_3CH_2OCO	Ac	Ac	Ac
8	H	Br	CCl_3CH_2OCO	Ac	Ac	Ac
9	H	OH	CCl_3CH_2OCO	Ac	Ac	Ac
10	H	OTCI	CCl_3CH_2OCO	Ac	Ac	Ac
11	$O(CH_2)_5NHZ$	H	CCl_3CH_2OCO	Ac	Ac	Ac
12	$O(CH_2)_5NHZ$	H	Ac	Ac	Ac	Ac
13	OAc	H	$ClCH_2CO$	Ac	Ac	Ac
14	$O(CH_2)_5NHZ$	H	$ClCH_2CO$	Ac	Ac	Ac
15	$O(CH_2)_5NHZ$	H	Ac	H	H	H
16	$O(CH_2)_5NH_3^+OAc^-$	H	Ac	H	H	H
17	$O(CH_2)_5NHZ$	H	Ac	H	- PhCH -	
18	$O(CH_2)_5NHZ$	H	Ac	Bn	- PhCH -	
19	$O(CH_2)_5NHZ$	H	Ac	Bn	H	Bn



Scheme 2.

6-aminohexyl disaccharide [9]. Therefore, compound **15** was reacted with benzaldehyde and zinc chloride to give the 4,6-*O*-benzylidene derivative **17** (86%). The latter was benzylated at position 3, to give the fully blocked glucoside **18** (99%) which afforded the crystalline acceptor **19** (93%) upon regioselective reduction of the benzylidene acetal with sodium cyanoborohydride [17]. All attempts, however, to galactosylate compound **19** failed. Not even a trace of the desired disaccharide could be detected on TLC when **1** and **19** were treated under various conditions (no further details in the Experimental section), although the similar galactosylation of the corresponding 6-aminohexyl glycoside was reported to proceed in 89% yield [9].

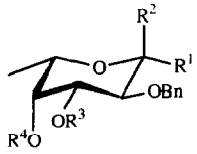
In order to circumvent the difficulties encountered so far in the preparation of the desired disaccharide ligand, an alternative approach via the donor **23** was chosen. The latter imidate was synthesized from benzyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzoyl-2-(benzoyloximino)-α-D-*arabino*-hexopyranoside [18] (**20**) which was obtained in 5 steps from hepta-*O*-benzoyl-α-lactosyl bromide via Lichtenthaler's 2-oximinoglycosyl bromide route [18–20]. Compound **20** was first reduced with diborane in THF as described [18], and the intermediate lactosamine derivative was treated with Teoc-Cl during workup. The urethane **21** (76%), thus obtained, was hydrogenolyzed to give crystalline **22** which



Scheme 3.

was converted into the imidate **23** in practically quantitative yield by reaction with trichloroacetonitrile and K_2CO_3. When the disaccharide donor **23** was treated with **2** and boron trifluoride etherate, as was performed for compound **11**, smooth condensation occurred, to give the protected aminopentyl glycoside disaccharide **24** (76%). Reductive cleavage of the trichloroethoxycarbonyl group of the latter with zinc followed by acetylation of the amino function then afforded the disaccharide **25** (78%). The final deblocking of the latter (first Zemplén *O*-deacylation, then catalytic hydrogenation) gave the 5-aminopentyl glycoside disaccharide **26** in 83% yield.

For the construction of the L-fucose-containing di- and tri-saccharide fragments suitably protected aminopentyl L-fucopyranosides were needed, an α-fucoside for saccharides related to human coagulation factor IX, and both α- and β-fucosides for the *Microciona prolifera*-related fragments, since no information about the anomeric configuration of the latter is yet available [21]. Starting from the known allyl 2,4-di-*O*-benzyl-α-L-fucopyranoside [22] (**27**), acetylation with acetic anhydride gave crude **28**, deallylation of which with $PdCl_2$ in acetic acid [4,23] followed by reacetylation of the anomeric hydroxyl afforded a 1:1 α,β-mixture of compounds **29** (78%). Treatment of the latter with ethanethiol and BF_3-etherate gave crude ethyl 3-*O*-acetyl-2,4-di-*O*-benzyl-1-thio-L-fucopyranoside (**30**) in 86% yield which was condensed with **2** under activation with *N*-iodosuccinimide and trifluoromethanesulfonic acid to give almost exclusively the β-product **31** (84%). The final *O*-deacetylation of position 3 afforded the desired acceptor **32** in 74% yield. The unexpectedly high β-selective glycosylation of the alcohol **2** implied that, on the other hand, the preparation of the corresponding aminopentyl α-L-fucopyranoside would be rather difficult. Indeed, the use of iodonium dicollidinium perchlorate (IDCP) [24] or $CuBr_2$–DMF–Bu_4NBr [25] as the activator,

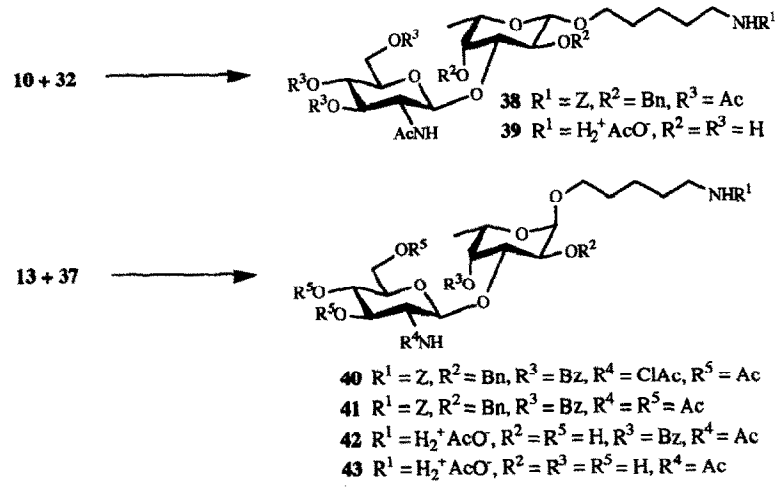


Compd	R^1	R^2	R^3	R^4
27	H	OAllyl	H	Bn
28	H	OAllyl	Ac	Bn
29	- H, OAc -		Ac	Bn
30	- H, SEt -		Ac	Bn
31	$O(CH_2)_5NHZ$	H	Ac	Bn
32	$O(CH_2)_5NHZ$	H	H	Bn
33	SEt	H	H	H
34	SEt	H	H	Bz
35	SEt	H	$ClCH_2CO$	Bz
36	- H, $O(CH_2)_5NHZ$ -		$ClCH_2CO$	Bz
37	H	$O(CH_2)_5NHZ$	H	Bz

Scheme 4.

both of which had been reported to give satisfactory α-selectivities in similar fucosylations, did not improve the selectivity here (no further experimental details). However, it has been shown [26] that an electron-withdrawing acyl substituent at position 4 of a 1-thio-L-fucoside donor increased the $\alpha:\beta$ ratio of the glycosylation step due to favouring an S_N2-type mechanism during reaction with an alcohol [27]. Therefore, ethyl 2-*O*-benzyl-1-thio-β-L-fucopyranoside [28] (**33**) was converted with trimethyl orthobenzoate, according to the procedure of Pozsgay [29], into the 4-benzoate **34** (78%), acylation of which at position 3 with chloroacetic anhydride [30,31] afforded the crystalline compound **35** (98%). The *N*-iodosuccinimide-promoted condensation of the latter with alcohol **2** revealed the formation of a single spot on TLC. However, inspection of the NMR spectra of the isolated product **36** (92%) showed a 2:1 α,β-mixture of anomers which could not be separated. No further improvement of this coupling reaction could be achieved with IDCP as the promoter. Separation of the anomers was possible in part only after *O*-dechloroacetylation of **36** with thiourea. Thus, a 36% yield of pure α anomer **37** (and 38% of an anomeric mixture) was isolated from the mixture after a single chromatography.

For the synthesis of the respective disaccharide aminopentyl glycosides, the β-fucoside **32** was condensed with the donor **10**, followed by stepwise conversion of the trichloroethoxycarbonyl group to acetyl, to give the disaccharide **38** in 66% overall yield. Deblocking of the latter then afforded the target fragment **39**. Similarly, donor **13** was coupled with the α-fucoside **37** using ferric chloride, to give compound **40** (71%); dechlorination of the latter with zinc in acetic acid gave



Scheme 5.

41 (93%). Deblocking of **41** was, however, rather difficult. When compound **41** was deacylated (Zemplén) for 4 days at room temperature, followed by hydrogenolytic cleavage of the Z and benzyl groups, compound **42**, still containing a 4-*O*-benzoyl group, was obtained as the sole product in practically quantitative yield. Therefore, more drastic conditions for the deacylation step were required. Treatment of compound **41** with sodium methoxide for 2 days at 50°C removed the 4-*O*-benzoyl group and afforded the desired disaccharide fragment **43** (89%) after hydrogenolysis.

The remaining trisaccharide aminopentyl glycosides **45** and **47** were prepared in an almost identical sequence from the disaccharide imidate **23**. Condensation of **23** with either **32** or **37**, followed by stepwise treatment of the intermediates first with zinc in acetic acid and then with acetic anhydride in pyridine, gave the trisaccharides **44** (40%) and **46** (49%), respectively. Deblocking of the latter, as described for compound **16**, afforded the β-fucoside-containing target fragment **45** in 72% yield, and the α-fucoside-containing fragment **47** in 68% yield.

Biological studies with the mono- to tri-saccharide fragments related to human coagulation factor IX and the proteoglycan from *Microciona prolifera* thus prepared are now under investigation and results will be published elsewhere. Furthermore, syntheses of *M. prolifera*-related di- and tri-saccharide fragments containing a pyruvic acetal at the terminal galactose residue have also been performed according to the above strategies and results will be published in a forthcoming paper.

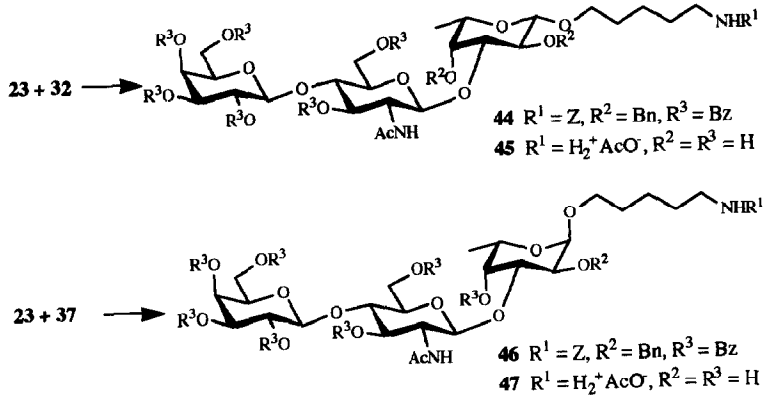
3. Experimental

General.—NMR data (Tables 1 and 2) were obtained from spectra measured in solutions of $CDCl_3$ for blocked compounds (with Me_4Si as an internal standard)

and of D_2O, acetone-d_6, Me_2SO-d_6, and CD_3OD for deblocked and partially deblocked compounds, respectively (with MeOH as an internal standard), at 25°C with a Bruker AC 250F spectrometer. Data in the first row refer to the first sugar residue. Proton-signal assignments were made by first-order analysis of the spectra. Of the two magnetically nonequivalent geminal protons at C-6 the one resonating at lower field was allocated H-6a and the one resonating at higher field H-6b. ^{13}C-Assignments were made by mutual comparison of the spectra, by DEPT spectra, and by comparison with spectra of related compounds. Optical rotations were measured at 25°C with a Perkin–Elmer automatic polarimeter, Model 241. Melting points were measured with a Büchi apparatus, Model SMP-20. Thin-layer chromatography (TLC) was performed on precoated plastic sheets, Polygram SIL UV_{254}, 40 × 80 mm (Macherey–Nagel) using appropriately adjusted mixtures of CCl_4–acetone for development. Detection was effected with UV light, where applicable, by I_2, and by charring with 5% H_2SO_4 in EtOH. Preparative chromatography was performed by elution from columns of Silica Gel 60 (Merck) using CCl_4–acetone. Solutions in organic solvents were dried with anhyd Na_2SO_4, and concentrated at 2 kPa, ≤ 40°C.

5-(Benzyloxycarbonylamino)pentyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (**3**).—A solution of compound **1** (5.14 g, 12.5 mmol), compound **2** (2.97 g, 12.5 mmol), $Hg(CN)_2$ (3.16 g, 12.5 mmol), and a catalytic amount of $HgBr_2$ (ca. 50 mg) in MeCN (50 mL) was stirred for 4 h at room temperature, diluted with CH_2Cl_2, washed with aq NaI and aq $Na_2S_2O_3$, and concentrated. Chromatography of the residue gave compound **3** (1.97 g, 28%); $[\alpha]_D$ −8.8° (*c* 2.1, $CHCl_3$). Anal. Calcd for $C_{27}H_{37}NO_{12}$: C, 57.14; H, 6.57; N, 2.47. Found: C, 56.87; H, 6.79; N, 2.43.

5-(Benzyloxycarbonylamino)pentyl β-D-galactopyranoside (**4**).—A solution of compound **3** (1.97 g, 3.47 mmol) in MeOH (50 mL) was treated with a solution of NaOMe in MeOH (1 M, 0.5 mL) for 24 h at room temperature. Dowex 1-X8 (H^+ form) was added until the solution became neutral. Filtration of the mixture, concentration of the filtrate and crystallization of the residue from EtOAc gave



Scheme 6.

Table 1
^{1}H NMR data [a]

Comp.	Chemical shifts (δ), multiplicities, and coupling constants (Hz)							
	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6a}$)	H-6a ($J_{5,6b}$)	H-6b ($J_{6a,6b}$)	Others
3	4.45d	5.20dd	5.01dd	5.38dd	4.05–3.87m	4.18dd	4.11dd	5.09s Z
	(7.8)	(10.5)	(3.4)	(0.8)	(6.7)	(6.7)	(−11.2)	
12	4.66d	3.92–3.75m	5.31t	5.06t	3.67ddd	4.26dd	4.12dd	5.10 s Z
	(8.3)	(9.7)	(9.7)	(9.5)	(4.7)	(2.4)	(−12.2)	
14	4.74d	3.92–3.80m	5.38t	5.07t	3.71ddd	4.27dd	4.14dd	5.09 s Z
	(8.2)	(9.5)	(9.5)	(9.5)	(4.8)	(2.3)	(−12.4)	3.98d $ClCH_2$
18	4.94d	3.52bdd	4.25t	3.66t	3.85ddd	4.33dd	3.78bt	5.55s PhCH
	(8.3)	(9.6)	(9.6)	(9.2)	(5.0)	(10.3)	(−10.3)	5.08s Z
21	4.99d	3.93–3.77m	5.42t	4.19t	3.93–3.77m	4.39–3.98m	4.39–3.98m	4.70d, 4.48d
	(3.7)	(9.9)	(9.9)	(10.0)	(−)	(−)	(−)	(−11.9) Bn
	4.89d	5.70dd	5.39dd	5.75dd	3.93–3.77m	4.39–3.98m	4.39–3.98m	4.65d, 4.53d
	(7.9)	(10.4)	(3.6)	(<1)	(−)	(−)	(−)	(−12.1) $ClCH_2$
23	6.43d	4.05–3.87m	5.75t	4.32t	4.05–3.87m	4.72–4.39m	4.17bd	4.66d, 4.56d
	(3.7)	(9.9)	(9.9)	(9.9)	(−)	(−)	(−)	(−12.0) CH_2CCl_3
	4.94d	5.71dd	5.40dd	5.77bd	4.05–3.87m	4.72–4.39m	4.72–4.39m	
	(7.9)	(10.2)	(3.3)	(<1)	(−)	(−)	(−)	
24	4.90d	3.76–3.42m	5.68dd	4.24bt	3.92–3.82m	4.62bd	4.34bdd	5.09s Z
	(7.8)	(10.0)	(10.2)	(9.5)	(−)	(−)	(−11.9)	4.47d, 4.54d
	4.90d	5.68dd	5.35dd	5.57bd	3.76–3.42m	4.62bd	4.09dd	(−12.1) CH_2CCl_3
	(7.8)	(10.2)	(3.3)	(<1)	(−)	(−)	(−12.9)	
32	4.29d	3.56–3.41m	3.56–3.41m	3.56–3.41m	3.93dt	1.23d	–	5.07s Z
	(7.4)	(−)	(−)	(9.4)	(6.4)	(−)		
34	4.48d	3.60t	3.88dt	5.38dd	3.75dq	1.23d	–	4.97d, 4.70d
	(9.6)	(9.4)	(3.6)	(0.7)	(6.4)	(−)		(−10.7) Bn
35	4.58d	3.75t	5.16dd	5.49dd	3.89dq	1.26d	–	3.87d, 3.76d
	(9.7)	(9.7)	(3.4)	(0.6)	(6.7)	(−)		(−14.9) CH_2Cl
37	4.88d	4.26bd	3.81dd	5.47bd	4.12dd	1.16d	–	4.70d, 4.65d
	(3.5)	(10.0)	(3.5)	(<1)	(6.5)	(−)		(−11.9) Bn

[a] For solutions in $CDCl_3$. Data in the 1st row of each entry refer to sugar residue 1; data in the 2nd row refer to sugar residue 2.

Table 2
^{13}C NMR data [a]

Comp.	Chemical shifts (δ)						
	C-1	C-2	C-3	C-4	C-5	C-6	Others
3	101.3	68.9 [b]	70.9	67.1 [b]	70.6	61.3	69.6 Z, 66.6 OCH_2, 40.9 NCH_2
4 [c]	106.2	77.8 [b]	76.2 [b]	71.8 [b]	71.5 [b]	63.7	73.8 OCH_2, 68.5 Z, 42.9 NCH_2
5 [d]	105.6	78.0 [b]	75.7 [b]	73.6 [b]	71.5 [b]	63.8	72.8 OCH_2, 42.3 NCH_2
11	100.7	56.3	71.9	71.7	68.7	62.1	74.4 CH_2CCl_3, 91.9 CCl_3, 69.8 OCH_2
12	100.7	54.8	72.3	71.7	68.7	62.1	69.5 OCH_2, 67.3 Z, 40.9 NCH_2
14	100.4	55.2	71.8	68.7	71.8	62.1	69.7 OCH_2, 66.6 Z, 42.5 $ClCH_2$
15 [e]	102.7	57.4	76.1	72.1	77.9	62.8	70.3 OCH_2, 67.3 Z, 41.8 NCH_2
16 [d]	104.0	58.4	76.6	72.9	78.7	63.6	72.8 OCH_2, 42.2 NCH_2
17 [f]	105.8	62.5	70.8	86.5	75.7	73.3	106.3 PhCH, 74.2 OCH_2
18	100.5	57.9	76.5	82.8	65.9	66.6	101.2 PhCH, 74.5 Bn, 69.7 OCH_2, 68.8 Z
19	99.9	56.9	80.4	73.2	73.8	69.2	74.2, 73.6 Bn, 70.6 OCH_2, 66.5 Z
21	96.4	54.3	69.1	76.2	71.6 [b]	60.9	70.4 Bn, 76.3 CH_2CCl_3, 95.2 CCl_3
	101.2	70.0	71.9	67.4	71.3 [b]	62.2	
23	90.7	54.2	71.0	74.5	71.0	61.0	95.1, 94.7 CCl_3, 75.2 Cl_3CCH_2
	101.3	70.0	71.8	67.4	71.4	61.8	
24	101.3 [b]	56.3	72.8	76.2	73.3	61.1	95.5 CCl_3, 74.4 Cl_3CCH_2
	101.0 [b]	70.0	71.9	67.5	71.4	62.4	69.6 OCH_2, 66.5 Z, 40.9 NCH_2
25	101.2 [b]	58.0	72.7	75.8	73.2	61.1	69.2 OCH_2, 66.4 Z, 40.9 NCH_2
	101.0 [b]	70.0	71.7	67.5	71.4	62.5	
26 [d]	104.0	58.0	78.3	81.4	75.4 [b]	63.0	73.0 OCH_2, 42.2 NCH_2
	105.8	73.9	75.3 [b]	71.5	77.7	64.0	
31	103.7	77.3 [b]	66.6	67.6	75.6 [b]	16.6	74.6 OCH_2, 69.6 Z, 41.0 NCH_2
32	103.6	79.4 [b]	74.4	78.4 [b]	70.5	16.9	75.3, 74.5, 69.4 2×Bn, OCH_2, 41.0 NCH_2
34	84.8	78.7	74.0 [b]	73.6 [b]	73.4 [b]	16.7	75.5 Bn
35	85.2	76.5	75.9	73.0	71.2	16.6	75.6 Bn, 40.6 CH_2Cl
37	96.9	76.7	73.8	73.8	65.1	16.3	72.7 OCH_2, 68.2 Bn, 66.6 Z, 41.0 NCH_2
38	103.7	79.5	78.0	78.0	71.8	16.9	75.0, 74.2 2×Bn, 69.5 OCH_2, 66.5 Z
	98.7	55.7	71.8	70.2	68.7	61.9	41.0 NCH_2
39 [d]	105.2	78.7	82.8	72.7	71.7	18.3	72.8 OCH_2, 42.2 NCH_2
	101.6	58.5	73.3	71.3	76.5	63.5	
40	97.2	72.9	74.3	64.7	71.1	16.2	73.2 Bn, 68.3 OCH_2, 66.5 Z
	98.2	54.9	71.7	68.7	72.2	62.0	42.1 CH_2Cl, 40.9 NCH_2
41	95.8	73.4	73.7	64.5	70.9	16.2	73.3 OCH_2, 68.4 Bn, 65.6 Z
	98.3	54.0	71.9	68.6	72.7	62.0	40.9 NCH_2
42 [d]	101.1 [b]	76.5	78.6	72.9	68.5	18.2	71.0 OCH_2, 42.2 NCH_2
	100.3 [b]	58.3	73.8	69.7	76.1	63.6	137.3, 132.8, 131.9 C_{Ph}
43 [d]	100.9	78.8	80.0	72.0	69.4 [b]	18.2	70.8 OCH_2, 42.2 NCH_2
	101.7	58.6	72.9	69.2 [b]	76.5	63.7	
45 [d]	105.7	73.6	82.6	71.3 [b]	71.2 [b]	18.2	72.7 OCH_2, 42.1 NCH_2
	105.1	57.9	78.2	81.2	77.6	63.8	
	101.4	73.8	75.1	71.6	77.6	62.8	
47 [d]	100.8	71.4	79.9	69.4 [b]	69.2 [b]	18.2	70.8 OCH_2, 42.2 NCH_2
	105.8	58.1	78.3	81.4	75.4	63.0	
	101.5	73.8	75.2	71.9	77.7	63.9	

[a] For solutions in $CDCl_3$ unless otherwise indicated. Data in the 1st row of each entry refer to sugar residue 1; data in the 2nd and 3rd row, if present, refer to sugar residues 2 and 3, respectively.
[b] Assignments may be reversed.
[c] For solutions in acetone-d_6.
[d] For solutions in D_2O.
[e] For solutions in CD_3OD.
[f] For solutions in Me_2SO-d_6.

compound **4** (1.33 g, 96%); mp 136°C; $[\alpha]_D$ −9.5° (*c* 0.4, MeOH). Anal. Calcd for $C_{19}H_{29}NO_8$: C, 57.13; H, 7.32; N, 3.51. Found: C, 57.09; H, 7.33; N, 3.30.

5-Aminopentyl β-D-galactopyranoside (**5**).—A suspension of compound **4** (1.0 g, 2.5 mmol), AcOH (1 mL), and a catalytic amount of Pd (10% on charcoal, 100 mg) in 1:1 water–MeOH (20 mL) was treated with H_2 for 24 h at room temperature. The mixture was filtered and the filtrate was concentrated. Chromatography of the residue on Bio-Gel P2 with water followed by elution of the lyophilized carbohydrate-containing fractions from a Dowex 1-X8 (Cl^- form) column gave compound **5** (0.75 g, 99%); $[\alpha]_D$ −5.5° (*c* 1.1, H_2O). Anal. Calcd for $C_{11}H_{24}ClNO_6$: C, 43.78; H, 8.02; N, 4.64; Cl, 11.75. Found: C, 43.83; H, 8.00; N, 4.47; Cl, 10.26.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranose (**7**).—2,2,2-Trichloroethoxycarbonyl chloride (3.8 g, 18.0 mmol) was added to a mixture of compound **6** [13] (5.0 g, 13.0 mmol) in CH_2Cl_2 (100 mL) and $NaHCO_3$ (4.2 g, 50.0 mmol) in water (50 mL), and the mixture was vigorously stirred for 1 h at room temperature. The organic layer was separated, washed with aq HCl and aq $NaHCO_3$, and concentrated, to give crude compound **7** (6.79 g, 100%), that was homogeneous (TLC) and used without further purification for the preparation of compounds **8**–**10** as previously described [11,12].

5-(Benzyloxycarbonylamino)pentyl 3,4,6-tri-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (**11**).—BF_3-etherate (251 μL, 2.0 mmol) was added at 0°C to a solution of compound **10** [11] (1.25 g, 2.0 mmol) and compound **2** (0.45 g, 1.89 mmol) in CH_2Cl_2 (20 mL), and the mixture was stirred for 0.5 h at 0°C. The mixture was neutralized by addition of pyridine, washed with aq $NaHCO_3$, and concentrated. Chromatography of the residue gave compound **11** (1.25 g, 95%); mp 74–75°C (acetone–hexane), $[\alpha]_D$ +0.2° (*c* 0.2, $CHCl_3$). Anal. Calcd for $C_{28}H_{36}Cl_3N_2O_{12}$: C, 48.12; H, 5.19; N, 4.01; Cl, 15.22. Found: C, 48.01; H, 5.36; N, 3.96; Cl, 15.17.

5-(Benzyloxycarbonylamino)pentyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (**12**).—(*a*) A suspension of compound **11** (1.10 g, 1.57 mmol) and Zn (2.0 g, 30.5 mmol) in AcOH (50 mL) was stirred for 0.5 h at room temperature, filtered through a layer of Celite, and concentrated by repeated coevaporation of toluene. The residue was dissolved in pyridine (20 mL) and treated with Ac_2O (10 mL) for 24 h at 4°C. The mixture was diluted with a small amount of water in order to destroy the excess of Ac_2O and partitioned between water and CH_2Cl_2. The organic layer was separated, washed with aq HCl and aq $NaHCO_3$, and concentrated. Chromatography of the residue gave compound **12** (0.72 g, 81%); mp 139°C (acetone–hexane); $[\alpha]_D$ −8.0° (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{27}H_{38}N_2O_{11}$: C, 57.24; H, 6.76; N, 4.94. Found: C, 56.95; H, 6.73; N, 4.74.

(*b*) Treatment of compound **14** (see below, 2.65 g, 4.3 mmol) with Zn (4.0 g, 60.9 mmol) in AcOH (50 mL) for 1 h at room temperature, as described under (*a*) but without subsequent acetylation, gave compound **12** (2.28 g, 94%).

5-(Benzyloxycarbonylamino)pentyl 3,4,6-tri-O-acetyl-2-chloroacetamido-2-deoxy-β-D-glucopyranose (**14**).—$FeCl_3$ (0.97 g, 6.0 mmol) was added in one portion at room temperature to a suspension of compound **13** [14] (2.5 g, 5.9 mmol), 3A molecular sieves (0.5 g), and compound **2** (1.42 g, 6.0 mmol) in CH_2Cl_2 (20 mL),

and the mixture was stirred for 3 h. The suspension was filtered through a layer of Celite, washed with aq HCl and aq $NaHCO_3$, and concentrated. Crystallization of the residue from acetone–hexane gave compound **14** (3.30 g, 93%); mp 125°C; $[\alpha]_D$ −9.1° (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{27}H_{37}ClN_2O_{11}$: C, 53.96; H, 6.21; N, 4.66; Cl, 5.90. Found: C, 53.73; H, 6.26; N, 4.58; Cl, 6.09.

*5-(Benzyloxycarbonylamino)pentyl 2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**15**).—Treatment of compound **12** (3.0 g, 5.3 mmol) with a solution of NaOMe in MeOH (10 mM, 30 mL), as described for compound **4**, gave compound **15** (2.25 g, 96%); mp 150–155°C (EtOH), $[\alpha]_D$ −15.2° (*c* 0.4, MeOH). Anal. Calcd for $C_{21}H_{32}N_2O_8 \cdot H_2O$: C, 56.11; H, 7.40; N, 6.23. Found: C, 56.50; H, 7.40; N, 6.17.

*5-Aminopentyl 2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**16**).—Hydrogenolysis of compound **15** (0.5 g, 1.14 mmol) with Pd (10% on charcoal, ca. 50 mg) in 5:5:1 MeOH–water–AcOH (11 mL), as described for compound **5**, but without final exchange of acetate to chloride, gave compound **16** (415 mg, 99.7%); $[\alpha]_D$ −17.7° (*c* 0.2, H_2O). FABMS: Calcd for $C_{13}H_{27}N_2O_6$: 307 ($M - AcO^-$).

*5-(Benzyloxycarbonylamino)pentyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-*D*-glucopyranoside* (**17**).—Freshly molten $ZnCl_2$ (5 g) was added at room temperature to a suspension of compound **15** (1.65 g, 3.75 mmol) in benzaldehyde (15 mL) and the mixture was vigorously stirred for 16 h. Water (50 mL) and hexane (100 mL) were added with stirring and the precipitate was collected by filtration. Recrystallization of the solid material from EtOH (containing a few drops of Et_3N in order to ensure basic conditions) gave compound **17** (1.70 g, 86%); mp 222–223°C; $[\alpha]_D$ −44.7° (*c* 0.2, $CHCl_3$). Anal. Calcd for $C_{28}H_{36}N_2O_8 \cdot H_2O$: C, 62.56; H, 6.94; N, 5.21. Found: C, 62.71; H, 6.76; N, 4.98.

*5-(Benzyloxycarbonylamino)pentyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-*D*-glucopyranoside* (**18**).—To a suspension of compound **17** (1.40 g, 2.65 mmol), BaO (6.7 g, 43.7 mmol), and $Ba(OH)_2 \cdot 8H_2O$ (2.75 g, 8.5 mmol) in DMF (45 mL) was added at 0°C benzyl bromide (6.7 mL and 3.3 mL after 0.5 h) and the mixture was warmed to room temperature. More benzyl bromide (3.3 mL) was added and stirring was continued for 3 h. The excess of benzyl bromide was destroyed by addition of MeOH (10 mL) at 0°C followed by stirring for 2 h at room temperature. CH_2Cl_2 (100 mL) was added, the mixture was filtered through a layer of Celite, the filtrate was washed with water and aq $NaHCO_3$, and concentrated. Crystallization of the residue from acetone–hexane gave compound **18** (1.62 g, 99%); mp 203°C; $[\alpha]_D$ −2.7° (*c* 0.6, $CHCl_3$). Anal. Calcd for $C_{35}H_{42}N_2O_8$: C, 67.94; H, 6.84; N, 4.53. Found: C, 68.00; H, 6.88; N, 4.27.

*5-(Benzyloxycarbonylamino)pentyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**19**).—Ethereal HCl solution was added in small portions at room temperature to a vigorously stirred solution of compound **18** (1.25 g, 2.0 mmol) and $NaCNBH_3$ (1.45 g, 23 mmol) in THF (50 mL) until the evolution of H_2 ceased. CH_2Cl_2 (100 mL) was added, and the mixture was washed with aq HCl and aq $NaHCO_3$, and concentrated. Crystallization of the residue from acetone–hexane gave compound **19** (1.61 g, 93%); mp 127°C; $[\alpha]_D$ −3.6° (*c* 0.3, $CHCl_3$); ^1H NMR (significant signals): δ 5.07 (s, 2 H, $PhCH_2O$), 4.79 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1). Anal.

Calcd for $C_{35}H_{44}N_2O_8$: C, 67.72; H, 7.14; N, 4.51. Found: C, 67.64; H, 7.01; N, 4.31.

Benzyl O-*(2,3,4,6-tetra*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)-3,6-di*-O-*benzoyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α*-D-*glucopyranoside* (**21**).—BH_3 (1 M in THF, 15 mL, 15 mmol) was added under Ar at −10°C to a solution of compound **20** [18] (1.47 g, 1.26 mmol) in THF (20 mL), and the solution was stirred for 3 h at room temperature. MeOH (12 mL) was added at 0°C, followed by Et_3N (12 mL) and 2,2,2-trichloroethoxycarbonyl chloride (1.0 mL) after 0.5 h. The mixture was stirred for 2 h at room temperature and concentrated. The residue was filtered with MeOH over a column of Dowex 1-X8 (OH^- form) and carbohydrate-containing fractions were pooled and concentrated. Chromatography of the residue gave compound **21** (1.18 g, 76%); $[\alpha]_D$ +57.3° (*c* 0.2, $CHCl_3$). Anal. Calcd for $C_{64}H_{54}Cl_3NO_{18}$: C, 62.42; H, 4.42; N, 1.14. Found: C, 62.32; H, 4.68; N, 0.92.

O-*(2,3,4,6-Tetra*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)-3,6-di*-O-*benzoyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α*-D-*glucopyranose* (**22**).—A suspension of compound **21** (0.58 g, 0.47 mmol) and a catalytic amount of Pd (10% on charcoal, 12 mg) in AcOH (20 mL) was treated for 24 h with H_2. Filtration of the mixture, concentration of the filtrate, and crystallization of the residue from acetone–hexane gave compound **22** (0.5 g, 93%); mp 135–142°C (with softening at 133°C); $[\alpha]_D$ +54.1° (*c* 0.3, $CHCl_3$ + 1 drop of pyridine, after 1 h standing at room temperature); NMR (significant signals of the α anomer): δ 5.76 (d, 1 H, $J_{1,2}$ 2.8 Hz, H-1^1), 92.9 (C-1^1), 4.78 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1^2), 101.2 (C-1^2), 95.7 (CCl_3). Anal. Calcd for $C_{57}H_{48}Cl_3NO_{18}$: C, 59.98; H, 4.24; N, 1.23; Cl, 9.32. Found: C, 60.07; H, 4.42; N, 1.25; Cl, 9.47.

O-*(2,3,4,6-Tetra*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)-3,6-di*-O-*benzoyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α*-D-*glucopyranosyl trichloroacetimidate* (**23**).—A suspension of compound **22** (0.45 g, 0.39 mmol), trichloroacetonitrile (1 mL), and finely ground K_2CO_3 (1 g) in CH_2Cl_2 (10 mL) was stirred for 3 h at room temperature, filtered through a layer of Celite, and concentrated. Chromatography of the residue gave compound **23** (0.50 g, 99.7%); $[\alpha]_D$ +64.9° (*c* 0.4, $CHCl_3$). Anal. Calcd for $C_{59}H_{48}Cl_6N_2O_{18}$: C, 55.12; H, 3.76; N, 2.18; Cl, 16.54. Found: C, 55.00; H, 3.80; N, 2.03; Cl, 16.04.

5-(Benzyloxycarbonylamino)pentyl O-*(2,3,4,6-tetra*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)-3,6-di*-O-*benzoyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β*-D-*glucopyranoside* (**24**).—BF_3-etherate (30 μL, 0.25 mmol) was added at 0°C to a solution of compound **23** (0.25 g, 0.19 mmol) and compound **2** (47.5 mg, 0.2 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred at 0°C for 15 min, neutralized with pyridine, and concentrated. Chromatography of the residue gave compound **24** (196.3 mg, 76%); $[\alpha]_D$ +28.4° (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{70}H_{65}Cl_3N_2O_{20}$: C, 61.79; H, 4.82; N, 2.06; Cl, 7.82. Found: C, 61.55; H, 4.76; N, 2.01; Cl, 8.10.

5-(Benzyloxycarbonylamino)pentyl O-*(2,3,4,6-tetra*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)-2-acetamido-3,6-di*-O-*benzoyl-2-deoxy-β*-D-*glucopyranoside* (**25**).—Treatment of compound **24** (190 mg, 0.14 mmol) with Zn in AcOH followed by acetic anhydride in pyridine, as described for compound **12** (*a*), and chromatography gave compound **25** (134 mg, 78%); $[\alpha]_D$ +27.3° (*c* 0.3, $CHCl_3$); ^1H NMR

(significant signals): δ 4.91 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1[1]), 5.02 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1[2]). Anal. Calcd for $C_{69}H_{66}N_2O_{19}$: C, 67.53; H, 5.42; N, 2.28. Found: C, 67.35; H, 5.42; N, 2.05.

5-Aminopentyl O-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**26**).—Deblocking of compound **25** (125 mg, 0.1 mmol) with a catalytic amount of NaOMe for 24 h at room temperature as described for compound **4**, but with chromatography (silica gel, 10:1 CH_2Cl_2–MeOH) of the intermediate, followed by hydrogenolysis, as described for compound **16**, gave compound **26** (44.7 mg, 83%); $[\alpha]_D$ −14.5° (*c* 4.4, H_2O). FABMS: Calcd for $C_{19}H_{37}N_2O_{11}$: 469 ($M - AcO^-$).

Allyl 3-O-acetyl-2,4-di-O-benzyl-α-L-fucopyranoside (**28**).—A mixture of compound **27** [22] (2.5 g, 6.5 mmol) and Ac_2O (5 mL) in pyridine (15 mL) was stirred for 7 h at room temperature, poured into water, stirred for 16 h, and extracted with CH_2Cl_2. The combined organic layers were washed with aq HCl and aq $NaHCO_3$, and concentrated. Chromatography of the residue gave crude compound **28** (2.36 g) that was used without further purification.

1,3-Di-O-acetyl-2,4-di-O-benzyl-L-fucopyranose (**29**).—A solution of crude compound **28** (2.36 g) and $PdCl_2$ (150 mg, 0.85 mmol) in degassed aq 90% AcOH (100 mL) was heated for 15 h at 95°C while N_2 was bubbled through the solution. The mixture was concentrated, the residue was suspended in CH_2Cl_2 (100 mL), and filtered through a layer of Celite. The material obtained after removal of the solvent was dissolved in pyridine (20 mL) and treated for 7 h at room temperature with Ac_2O (10 mL). Work-up, as described for compound **28**, and chromatography gave compound **29** (2.17 g, 88% from **27**), as a 1:1 anomeric mixture; NMR (significant signals): δ 6.38 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1α), 5.59 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1β), 94.2 (C-1β), 90.5 (C-1α). Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.37; H, 6.64.

Ethyl 3-O-acetyl-2,4-di-O-benzyl-1-thio-L-fucopyranoside (**30**).—A solution of compound **29** (1.17 g, 2.7 mmol), ethanethiol (0.22 mL, 3.0 mmol), and BF_3-etherate (0.38 mL, 3.0 mmol) in CH_2Cl_2 (20 mL) was stirred for 0.5 h at room temperature, washed with aq $NaHCO_3$, and concentrated, to give crude compound **30** (1.0 g, 85%), as an anomeric mixture that was used without further purification.

5-(Benzyloxycarbonylamino)pentyl 3-O-acetyl-2,4-di-O-benzyl-β-L-fucopyranoside (**31**).—Trifluoromethanesulfonic acid (27.5 μL, 0.3 mmol) was added under Ar at −30°C to a suspension of crude compound **30** (1.0 g, 2.3 mmol), compound **2** (0.71 g, 3.0 mmol), 3A molecular sieves (0.5 g), and *N*-iodosuccinimide (0.67 g, 3.0 mmol) in CH_2Cl_2 (30 mL), and the mixture was stirred for 45 min at −30°C. Pyridine was added, the mixture was filtered through a layer of Celite, and the filtrate was washed with aq $Na_2S_2O_3$ and aq $NaHCO_3$. Concentration of the solution and chromatography of the residue gave, first, compound **31** (1.17 g, 84%); $[\alpha]_D$ −38.7° (*c* 0.4, $CHCl_3$); ^1H NMR (significant signals): δ 4.36 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 1.20 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6). Anal. Calcd for $C_{35}H_{43}NO_8$: C, 69.40; H, 7.16; N, 2.31. Found: C, 69.01; H, 7.15; N, 2.24.

Eluted next was a mixture of anomers of compound **31** (0.21 g, 15%).

5-(Benzyloxycarbonylamino)pentyl 2,4-di-O-benzyl-β-L-fucopyranoside (**32**).—Treatment of compound **31** (0.75 g, 1.2 mmol) with methanolic NaOMe (10 mM, 10 mL) as described for compound **4**, and chromatography gave compound **32** (0.5 g, 74%); $[\alpha]_D$ −13.4° (*c* 0.3, $CHCl_3$). Anal. Calcd for $C_{33}H_{41}NO_7$: C, 70.32; H, 7.33; N, 2.48. Found: C, 70.07; H, 7.44; N, 2.45.

Ethyl 4-O-benzoyl-2-O-benzyl-1-thio-β-L-fucopyranoside (**34**).—A solution of compound **33** [28] (2.98 g, 10 mmol), trimethyl orthobenzoate (5 mL), and a catalytic amount of *p*-toluenesulfonic acid (ca. 20 mg) in DMF (25 mL) was treated as described in ref [29], to give compound **34** (3.15 g, 78%); $[\alpha]_D$ −38.6° (*c* 0.8, $CHCl_3$). Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.65; H, 6.51. Found: C, 65.70; H, 6.59.

Ethyl 4-O-benzoyl-2-O-benzyl-3-O-chloroacetyl-1-thio-β-L-fucopyranoside (**35**).—A suspension of compound **34** (1.87 g, 4.6 mmol), chloroacetic anhydride (1.71 g, 10.0 mmol), and $NaHCO_3$ (1.0 g) in DMF (20 mL) was stirred for 2 h at room temperature, poured into water, and extracted with CH_2Cl_2. The combined organic layers were washed with aq $NaHCO_3$ and concentrated. Chromatography of the residue gave compound **35** (2.15 g, 98%) that crystallized slowly; mp 103°C (without recrystallisation); $[\alpha]_D$ −63.1° (*c* 0.4, $CHCl_3$). Anal. Calcd for $C_{24}H_{27}ClO_6S$: C, 60.18; H, 5.68; Cl, 7.40; S, 6.69. Found: C, 60.02; H, 5.80; Cl, 7.41; S, 6.62.

5-(Benzyloxycarbonylamino)pentyl 4-O-benzoyl-2-O-benzyl-3-O-chloroacetyl-L-fucopyranoside (**36**).—Trifluoromethanesulfonic acid (11 μL, 0.12 mmol) was added under Ar at 0°C to a suspension of compound **35** (1.14 g, 2.38 mmol), compound **2** (0.83 g, 3.5 mmol), 3A molecular sieves (0.5 g), and *N*-iodosuccinimide (0.68 g, 3.0 mmol) in CH_2Cl_2/Et_2O (1:10, 15 mL), and the mixture was stirred for 15 min at 0°C. Work-up as described for compound **31** gave compound **36** (1.43 g, 92%) as a 2:1 α,β-anomeric mixture; ^{13}C NMR (significant signals): δ 103.6 (C-1β), 97.5 (C-1α). Anal. Calcd for $C_{35}H_{40}ClNO_9$: C, 64.26; H, 6.16; N, 2.14. Found: C, 64.51; H, 6.30; N, 2.14.

5-(Benzyloxycarbonylamino)pentyl 4-O-benzoyl-2-O-benzyl-α-L-fucopyranoside (**37**).—A solution of compound **36** (1.43 g, 2.19 mmol) and thiourea (0.38 g, 5.0 mmol) in MeOH (20 mL) was stirred for 3 days at 40°C and concentrated. Chromatography of the residue gave, first, compound **37** (0.45 g, 36%); $[\alpha]_D$ −92.8° (*c* 0.3, $CHCl_3$). Anal. Calcd for $C_{35}H_{39}NO_8$: C, 68.61; H, 6.81; N, 2.42. Found: C, 68.85; H, 6.77; N, 2.34.

Eluted next was a 1:1 anomeric mixture of compound **37** (0.48, 38%).

5-(Benzyloxycarbonylamino)pentyl (2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzyl-β-L-fucopyranoside (**38**).—Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (6.6 μL, 0.04 mmol) was added under Ar at −20°C to a solution of compound **32** (352.5 mg, 0.625 mmol) and compound **10** (437.5 mg, 0.7 mmol) in CH_2Cl_2 (12 mL), and the mixture was stirred for 0.5 h at −20°C, neutralized by the addition of pyridine, and concentrated. The residue was dissolved in AcOH (10 mL) and treated with Zn followed by Ac_2O in pyridine as described for compound **12**. Chromatography gave compound **38** (366.1 mg, 66%); $[\alpha]_D$ −6.7° (*c* 0.2, $CHCl_3$); ^1H NMR (significant signals): δ 4.30 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1^1), 5.20 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1^2), 1.19 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6^1). Anal.

Calcd for $C_{47}H_{60}N_2O_{15}$: C, 63.22; H, 6.77; N, 3.14. Found: C, 63.02; H, 6.75; N, 3.13.

5-Aminopentyl O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-β-L-fucopyranoside (**39**).—Treatment of compound **38** (244 mg, 0.27 mmol) with methanolic NaOMe (10 mM, 10 mL) for 24 h at room temperature, followed by hydrogenolysis as described for compound **26**, gave compound **39** (132.8 mg, 96%); $[\alpha]_D$ −13.2° (*c* 0.5, H_2O). FABMS: Calcd for $C_{18}H_{36}N_2O_{10}$: 453 ($M - AcO^-$).

5-(Benzyloxycarbonylamino)pentyl O-(3,4,6-tri-O-acetyl-2-chloroacetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-4-O-benzoyl-2-O-benzyl-α-L-fucopyranoside (**40**).—Treatment of compound **37** (0.26 g, 0.45 mmol) and compound **13** (0.21 g, 0.5 mmol) with $FeCl_3$ (113.5 mg, 0.7 mmol) in CH_2Cl_2 (10 mL) for 24 h at room temperature, as described for compound **14**, and chromatography gave compound **40** (0.30 g, 71%); $[\alpha]_D$ −48.5° (*c* 0.5, $CHCl_3$); ^1H NMR (significant signals): δ 4.78 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1^1), 4.93 (d, 1 H, $J_{1,2}$ 9.0 Hz, H-1^2), 1.11 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6^1). Anal. Calcd for $C_{47}H_{57}ClN_2O_{16}$: C, 59.96; H, 6.10; Cl, 3.77; N, 2.98. Found: C, 59.92; H, 6.20; Cl, 4.06; N, 2.83.

5-(Benzyloxycarbonylamino)pentyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-4-O-benzoyl-2-O-benzyl-α-L-fucopyranoside (**41**).—Treatment of compound **40** (0.30 g, 0.32 mmol) with Zn (0.5 g) in AcOH (5 mL) for 3 h at room temperature, as described for compound **12** (*b*), and chromatography gave compound **41** (0.27 g, 93%); $[\alpha]_D$ −56.9° (*c* 0.6, $CHCl_3$); ^1H NMR (significant signals): δ 4.79 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1^1), 5.12 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1^2), 1.12 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6^1). Anal. Calcd for $C_{47}H_{58}N_2O_{16}$: C, 62.24; H, 6.45; N, 3.09. Found: C, 62.14; H, 6.47; N, 2.99.

5-Aminopentyl O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-α-L-fucopyranoside (**42**).—Treatment of compound **41** (236 mg, 0.25 mmol) with methanolic NaOMe (10 mM, 10 mL) for 4 days at room temperature, followed by hydrogenolysis as described for compound **26**, gave compound **42** (155 mg, 100%); $[\alpha]_D$ −67.2° (*c* 0.7, H_2O). FABMS: Calcd for $C_{28}H_{40}N_2O_{11}$: 557 ($M - AcO^-$).

5-Aminopentyl O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-α-L-fucopyranoside (**43**).—Treatment of compound **41** (180 mg, 0.18 mmol) with methanolic NaOMe (5 mM, 10 mL) for 2 days at 50°C, followed by hydrogenolysis as described for compound **26**, gave compound **43** (87 mg, 89%); $[\alpha]_D$ −53.8° (*c* 0.7, H_2O). FABMS: Calcd for $C_{19}H_{37}N_2O_{10}$: 453 ($M - AcO^-$).

5-(Benzyloxycarbonylamino)pentyl O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-benzoyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzyl-β-L-fucopyranoside (**44**).—TMSOTf (6.6 μL, 0.04 mmol) was added under Ar at 0°C to a solution of compound **32** (225.5 mg, 0.4 mmol) and compound **23** (433.9 mg, 0.337 mmol) in CH_2Cl_2 (6 mL), and the mixture was stirred for 0.5 h at 0°C, neutralized by addition of pyridine, and concentrated. The residue was dissolved in AcOH (10 mL) and treated with Zn followed by Ac_2O in pyridine as described for compound **12**. Chromatography gave compound **44** (215.3 mg, 40%); $[\alpha]_D$ +20.0° (*c* 0.3, $CHCl_3$); ^{13}C NMR (significant signals): δ 103.6 (C-1^3), 100.8 (C-1^2), 99.3 (C-1^1), 54.8 (C-2^2), 16.8 (C-6^1). Anal. Calcd for $C_{89}H_{88}N_2O_{23}$: C, 68.80; H, 5.71. Found: C, 68.80; H, 5.65.

5-Aminopentyl O-*β*-D-*galactopyranosyl-(1 → 4)*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-L-*fucopyranoside* (**45**).—Treatment of compound **44** (200 mg, 0.129 mmol) with methanolic NaOMe (1 mM, 100 mL) followed by hydrogenolysis as described for compound **26**, gave compound **45** (63 mg, 72%); $[\alpha]_D$ −12.4° (*c* 0.3, H_2O). FABMS: Calcd for $C_{25}H_{47}N_2O_{15}$: 615 ($M - AcO^-$).

5-(Benzyloxycarbonylamino)pentyl O-*(2,3,4,6-tetra*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*(2-acetamido-3,6-di*-O-*benzoyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-4*-O-*benzoyl-2*-O-*benzyl-α*-L-*fucopyranoside* (**46**).—TMSOTf (5.5 μL, 0.03 mmol) was added under Ar at −20°C to a solution of compound **37** (214.9 mg, 0.372 mmol) and compound **23** (303.5 mg, 0.236 mmol) in CH_2Cl_2 (4.5 mL), the mixture was stirred for 45 min at −20°C, neutralized by addition of pyridine, and concentrated. The residue was dissolved in AcOH (10 mL) and treated with Zn followed by Ac_2O in pyridine as described for compound **12**. Chromatography gave compound **46** (181.3 mg, 49%); $[\alpha]_D$ −14.5° (*c* 0.1, $CHCl_3$); ^{13}C NMR (significant signals): δ 100.9 (C-1^3), 98.4 (C-1^2), 96.5 (C-1^1), 53.8 (C-2^2), 16.3 (C-6^1). Anal. Calcd for $C_{89}H_{86}N_2O_{24}$: C, 68.19; H, 5.53. Found: C, 68.10; H, 5.53.

5-Aminopentyl O-*β*-D-*galactopyranosyl-(1 → 4)*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-α*-L-*fucopyranoside* (**47**).—Treatment of compound **46** (127 mg, 0.082 mmol) with methanolic NaOMe (1 mM, 20 mL) for 2 days at 50°C followed by hydrogenolysis, as described for compound **26**, gave compound **47** (37.5 mg, 68%); $[\alpha]_D$ −12.4° (*c* 0.3, H_2O). FABMS: Calcd for $C_{25}H_{47}N_2O_{15}$: 615 ($M - AcO^-$).

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