ELSEVIER

Carbohydrate Research 291 (1996) 21–41

CARBOHYDRATE RESEARCH

Efficient, convergent syntheses of oligosaccharide allyl glycosides corresponding to the *Streptococcus* Group A cell-wall polysaccharide

France-Isabelle Auzanneau [1], Farzin Forooghian, B. Mario Pinto *

Department of Chemistry, Simon Fraser University, Burnaby, British Columbia, Canada V5A 1S6

Received 3 April 1996; accepted in revised form 5 May 1996

Abstract

Convergent syntheses of di-, tri, tetra-, penta-, and hexa-saccharide allyl glycosides corresponding to the β-hemolytic *Streptococcus* Group A cell-wall polysaccharide are described. The strategy relies on the preparation of related di- and tri-saccharide building blocks: β-D-Glc*p*NAc-(1-3)-α-L-Rha*p* and α-L-Rha*p*-(1-2)-[(β-D-Glc*p*NAc-(1-3)]-α-L-Rha*p*, which could be used either as glycosyl donors or acceptors in subsequent glycosylation reactions. The protecting groups were chosen to allow the selective removal of the allyl aglycon to access the intermediate glycosyl donors but also to allow their own removal without affecting the allyl group. The allyl group was intended for use in conjugation of the oligosaccharides to soluble protein carriers or solid supports for the preparation of antigens and immunoadsorbents, respectively. © 1996 Elsevier Science Ltd.

Keywords: *Streptococcus* Group A cell-wall oligosaccharides; Chemical glycosylation

1. Introduction

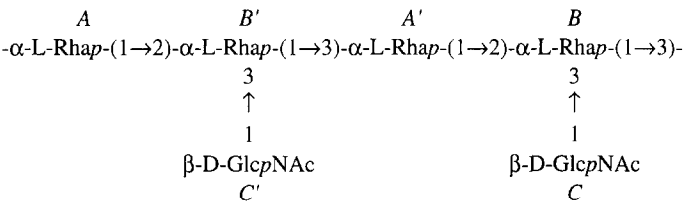
The β-hemolytic *Streptococcus* Group A is a common infective agent in humans, causing streptococcal pharyngitis (strep throat), some forms of pneumonia and toxic

* Corresponding author.

[1] Present address: Ecole Nationale de Chimie de Clermont-Ferrand, 24 avenue des Landais, BP 187, Ensemble Scientifique des Cézeaux, 63174 Aubière, France.

PII S0008-6215(96)00152-8

shock-like syndrome [1,2]. The infection by itself is a serious enough public health concern but it can also lead to the harmful sequelae of acute rheumatic fever, heart valve disease, or glomerulonephritis if untreated or treated improperly [1,3]. Complications such as rheumatic fever are thought to be the result of an autoimmune reaction [4–8] in which antibodies directed against streptococcal antigens lead the attack against host heart tissues. In this context, we have been actively pursuing a research program [9] to develop and characterize immunodiagnostic reagents and vaccines based on the *Streptococcus* Group A specific polysaccharide [10,11]:



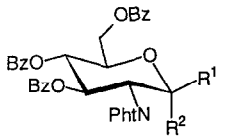
Thus far, we have reported the extensive syntheses of oligosaccharides corresponding to the cell-wall polysaccharide as well as their corresponding soluble glycoconjugates [12–16]. Although convergent, these syntheses were designed to furnish the final compounds as their propyl glycosides [12,13,15,16] for use as haptens in immunochemical studies, or as their (8-methoxycarbonyl) octyl glycosides, for the preparation of soluble glycoconjugates [14] via conjugation to protein carriers. We now report the syntheses of allyl glycosides that can be used not only for the preparation of higher oligosaccharides and haptens, but that can also be readily manipulated to give antigens and immunoadsorbents. The use of common precursors, namely the allyl glycosides of oligosaccharides, for the generation of haptens, antigens, and immunoadsorbents obviates the need for specialized syntheses of (8-methoxycarbonyl) octyl oligosaccharides for the last two applications and thus ensures economy of effort.

Retrosynthetic analysis had previously indicated [15] that a disconnection between the *B'* and *A'* rings gave the same branched trisaccharide $A(C')B'$ and $A'(C)B$. Therefore, the preparation of this key trisaccharide had allowed the convergent synthesis of the branched hexasaccharide $A(C')B'A'(C)B$. This strategy was also applied in our synthetic scheme but the intermediate protected mono- and di-saccharide analogues of *B'* and $C'B'$, respectively, were also used as glycosyl donors for the preparation of the tetra- and penta-saccharides $B'A'(C)B$ and $C'B'A'(C)B$. The synthesis of the tetrasaccharide has not hitherto been reported. In addition, the choice of protecting groups was made not only to allow the selective removal of the glycosidic allyl group to access the intermediate trichloroacetimidate glycosyl donors [15] but also to allow their selective removal without affecting the allyl aglycon which would be used for the conjugation of the oligosaccharides to soluble carriers or solid supports.

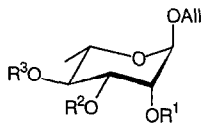
2. Results and discussion

The glycosyl bromide **2**, prepared from 1,3,4,6-tetra-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranose as previously described [15], was hydrolyzed in a 8:2 mixture of acetonitrile and H_2O to give the hemiacetal **3** which was, in turn, converted to the trichloroacetimidate glycosyl donor **4** by repeated treatments with trichloroacetonitrile in the presence of potassium carbonate. The glycosyl acceptor **5** was prepared from allyl α-L-rhamnopyranoside [17] in three steps: (1) preparation of the 2,3-*ortho*-acetate, (2) benzoylation of OH-4, and (3) selective opening of the *ortho*-acetate to give the 2-*O*-acetate. The glycosyl donor **8** was prepared from allyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside [18] in four steps: (1) acetylation of OH-3 to give the 3-*O*-acetate **6**, (2) isomerization of the allyl group with Wilkinson's catalyst and hydrolysis of the resulting propenyl glycoside [19] to give the hemiacetal **7** which, in turn, was converted to the trichloroacetimidate **8** by treatment with trichloroacetonitrile in the presence of DBU [20].

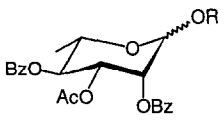
Glycosylation of the acceptor **5** with the trichloroacetimidate **4** was catalyzed by triethylsilyl trifluoromethanesulfonate (TESOTf) and gave the disaccharide **9** in 58% yield after partial purification. An analytically pure sample was obtained by flash chromatography followed by chromatography on Sephadex LH20 to allow full characterization of the intermediate disaccharide. However, the disaccharide **9** could be used directly in the subsequent reactions without these chromatographic purifications. Methanolysis of the 3-*O*-acetyl group [21] gave, after flash-chromatography, the disaccharide glycosyl acceptor **10** (81%) which was glycosylated with the trichloroacetimidate **8** in the presence of TESOTf. The glycosylation reaction was quantitative, as observed by TLC, but removal of trichloroacetamide (~ 3%) from the trisaccharide was difficult on a large scale (8 g). An analytically pure sample of the trisaccharide was obtained free of trichloroacetamide after a Sephadex LH20 chromatography and the remaining trisaccharide was used directly in the next steps. As described for the case of the disaccharide, methanolysis of the acetyl group of the trisaccharide **11** gave the glycosyl acceptor **12** which was obtained pure by flash chromatography (84%). Both the disaccharide **9** and trisaccharide **11** were submitted to conditions for the isomerization of the allyl group with Wilkinson's catalyst and for the hydrolysis of the resulting propenyl glycosides to give the hemiacetals **13** and **15**, respectively. Interestingly, while the disaccharide **13** was isolated in 74% yield, the trisaccharide **15** was only obtained in 54% yield. In the latter reaction, some unreacted starting allyl glycoside (13%) contaminated with some of the propyl glycoside (~ 2%) was also recovered. The hemiacetal **13** was converted to the glycosyl donor **14** using either potassium carbonate or DBU as bases and both reactions gave the trichloroacetimidate **14** in 76% yield. As reaction with DBU was observed to be slightly faster and the processing easier, this method was chosen to convert the hemiacetal **15** to the trisaccharide trichloroacetimidate **16** which was obtained in 75% yield.



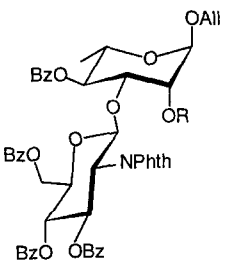
1 R^1 = OBz, R^2 = H
2 R^1 = Br, R^2 = H
3 R^1, R^2 = H, OH
4 R^1, R^2 = H, $OC(NH)CCl_3$



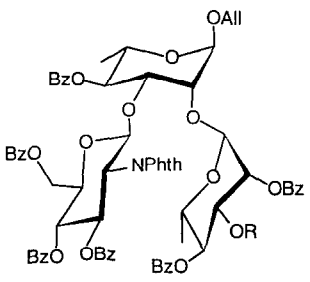
5 R^1 = Ac, R^2 = H, R^3 = Bz
6 R^1, R^3 = Bz, R^2 = Ac



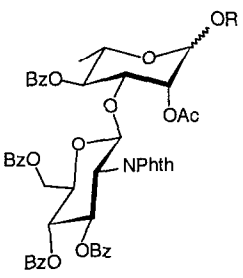
7 R = H
8 R = $C(NH)CCl_3$



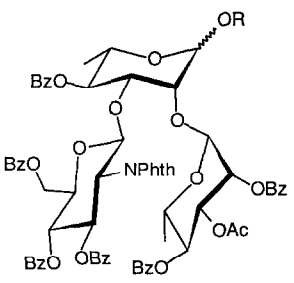
9 R = Ac
10 R = H



11 R = Ac
12 R = H



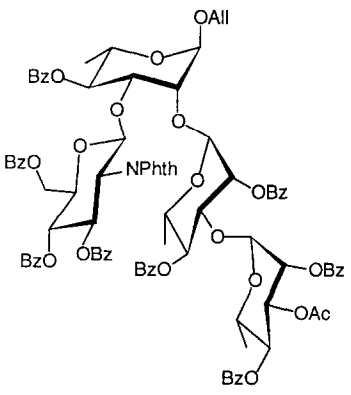
13 R = H
14 R = $C(NH)CCl_3$



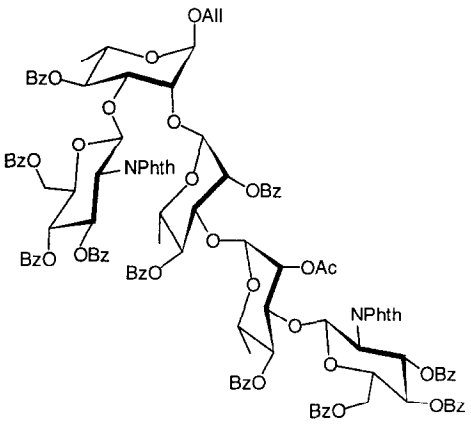
15 R = H
16 R = $C(NH)CCl_3$

The trisaccharide **12** was then glycosylated with the trichloroacetimidates **8**, **14**, and **16** under catalysis with TESOTf to give the tetra-, penta-, and hexa-saccharides **17**, **18**, and **19**, respectively. While the glycosylation with **8** and **14** proceeded easily with 0.09 equiv of TESOTf and 1.2 to 1.3 equiv of the glycosyl donors to give the tetrasaccharide **17** and the pentasaccharide **18** in 80% and 76% yield, respectively, the preparation of the hexasaccharide proved more difficult. Best results were obtained with a slight excess of the glycosyl acceptor (1.2 equiv) and by performing the reaction at room temperature for 24 h, with 0.23 equiv of the catalyst. The hexasaccharide **19** was then obtained in

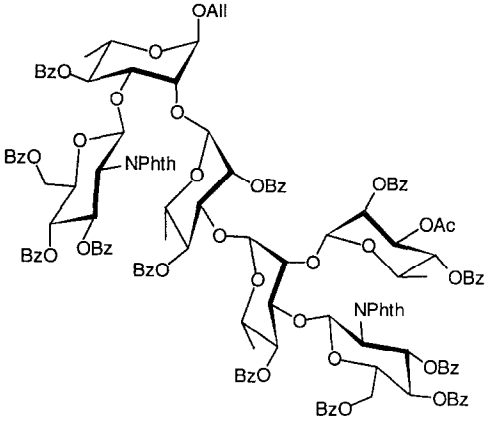
43% yield, while 37% of unreacted trisaccharide acceptor was recovered. Although the hexasaccharide appeared to be homogeneous on TLC and pure by NMR analysis, elemental analysis showed that it contained an impurity. An analytically pure sample was obtained by chromatography on a Sephadex LH20 column although the crude hexasaccharide was used directly in subsequent steps.



17



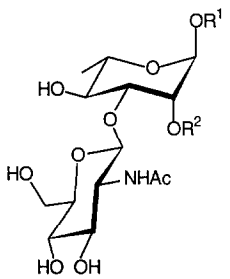
18



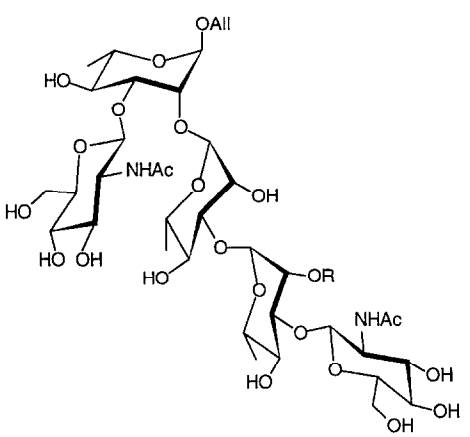
19

The protected di-, tri-, tetra-, penta-, and hexa-saccharides **9**, **11**, **17**, **18**, **19** were deprotected and *N*-acetylated in three steps to give the allyl glycosides **20**, **21**, **22**, **24**, and **25**, respectively. Thus, transesterification of the acetyl and benzoyl groups with sodium methoxide was followed by removal the phthalimido group by treatment with

ethylenediamine [22] and *N*-acetylation of the free amino group with acetic anhydride in methanol. The deprotected oligosaccharides **20** (68%), **21** (70%), **22** (88%), **24** (86%), and **25** (84%) were purified by successive flash chromatography and gel-permeation chromatography (Biogel P2) and were obtained as white amorphous powders after freeze-drying from water.



20 R^1 = All, R^2 = H
21 R^1 = All, R^2 = α-L-Rha
22 R^1 = All, R^2 = α-L-Rha-(1-3)-α-L-Rha
23 R^1 = Pr, R^2 = α-L-Rha-(1-3)-α-L-Rha



24 R = H
25 R = α-L-Rha

The tetrasaccharide **22** was converted quantitatively to the propyl glycoside **23** by hydrogenation in the presence of Pd/C. Purification of the tetrasaccharide only required filtration through a 22 μm Amicon filter to give the pure tetrasaccharide in 92% yield.

The deprotected oligosaccharides **20**, **21**, **22**, **24**, and **25** were characterized by ^{1}H and ^{13}C NMR spectroscopy and the chemical shifts and coupling constants for the ring protons as well as the chemical shifts for the ring carbons are reported in Tables 1 and 2, respectively.

The results described in the foregoing sections indicate that the use of acetyl, benzoyl, and phthalimido protecting groups ensure a limited number of protection and deprotection steps and allow the ready preparation of the mono-, di-, and tri-saccharide building blocks in large quantities. The syntheses reported here demonstrate once again [15,16] the versatility of the allyl group as a latent protecting group. In addition, the conjugation of the allyl glycosides to either solid supports or soluble protein carriers will allow the preparation of affinity columns and antigens which will be used as immunodiagnostic reagents or vaccines, respectively.

3. Experimental

General methods.—^{1}H NMR (400.13 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on a Bruker AMX-400 NMR spectrometer for solutions in $CDCl_3$ (internal standard, for ^{1}H: residual $CHCl_3$ δ 7.24; for ^{13}C: $CDCl_3$ δ 77.0) or D_2O [internal standard: sodium trimethylsilyl-(2,2,3,3-tetradeutero)propionate]. Chemical shifts and coupling constants were obtained from a first-order analysis of one-dimensional spectra and assignments of proton and carbon resonances were based on COSY and ^{13}C–^{1}H heteronuclear correlated experiments. The stereochemistry of the glycosidic linkages was determined from the $^{1}J_{C\text{-}1,H\text{-}1}$ coupling constants [23]. Optical rotations were measured on a Rudolph Research Autopol II automatic polarimeter. TLC was performed on precoated aluminum plates with Kieselgel Silica Gel 60 F_{254} (E. Merck) and detected with UV light and/or charred with a solution containing 1% $Ce(SO_4)_2$ and 1.5% molybdic acid in 10% aq H_2SO_4. Compounds were purified by flash chromatography [24] with Kieselgel Silica Gel 60 (230–400 mesh), solvents were distilled and dried according to standard procedures [25], and organic solutions were dried over Na_2SO_4 and concentrated below 40 °C, under reduced pressure. Gel permeation chromatography of protected compounds was performed using a Sephadex LH20 column (2.0 × 55 cm) with $CHCl_3$–MeOH (1:1) as eluent. Deprotected compounds were purified by gel permeation chromatography on a Biogel P2 column (1.5 × 90 cm) with H_2O as eluent. The high resolution fast atom bombardment (FAB) mass spectrum was recorded in thioglycerol at 8 kV on a Kratos Concept H Magnetic Instrument mass spectrometer.

3,4,6-Tri-O-benzoyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose (**3**).—1,3,4,6-Tetra-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranose [15] (8.0 g, 11 mmol) was dissolved in CH_2Cl_2 (50 mL) and a solution of 45% HBr in AcOH (15 mL) was added. The reaction mixture was stirred overnight at room temperature and concentrated. Residual traces of acid were co-evaporated with toluene (3 × 70 mL) to give the crude bromide **2** [15] that was dissolved in 80% aq CH_3CN (200 mL) and stirred for 18 h at room temperature. The hemiacetal **3** which had precipitated was removed by filtration and washed successively with H_2O until the washings were neutral, then with hexanes (3 × 20 mL), and dried under high vacuum (4.4 g, 64%). The filtrate and aqueous

Table 1
^{1}H NMR data [a] for compounds **20–25**

Ring protons	**20**	**21**	**22**	**23**	**24**	**25**
1B	4.76	4.83 (1.5)	4.81 (1.5)	4.75	4.81 (1.5)	4.80
2B	4.10 (3.0, 2.0)	4.11 (3.0, 2.0)	4.13 (3.0, 2.0)	4.13	4.12 (3.0, 2.0)	4.13
3B	3.78–3.63 (3.0, 2.0)	3.82	3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
4B	3.44 (9.5, 9.5)	3.54–3.35	3.54–3.35	3.54–3.35	3.54–3.35	3.55–3.33
5B	3.78–3.63	3.76–3.60	3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
6B	1.23 (6.5)	1.24 (6.5)	1.24 [b] (6.5)	1.25 [b] (6.0)	1.25 [b] (6.0)	1.26 [b] (6.0)
1C	4.62 (8.5)	4.64 (8.5)	4.63 (8.5)	4.62 (8.5)	4.62 [c] (8.5)	4.62 [c] (8.5)
2C	3.78–3.63	3.76–3.60	3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
3C	3.51	3.54	3.54	3.54	3.54	3.55
4C	3.40	↑ multiplet ↓	↑ multiplet ↓	↑ multiplet ↓	↑ multiplet ↓	↑ multiplet ↓
5C	3.40	3.35	3.35	3.35	3.40	3.33
6C	3.85 (11.5, –)	3.88 (11.5, –)	3.87 (12.0, –)	3.88 (12.0, –)	3.87	3.88
6′C	3.78–3.63	3.76–3.60	3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
1A′		5.10 (1.5)	5.00 (1.5)	5.00 (1.5)	5.11 (1.5)	5.12
2A′		4.00 (3.5, 2.0)	4.01	4.02 (2.5, 1.5)	4.03	4.03
3A′		3.76–3.60	3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
4A′		3.54–3.35	3.54–3.35	3.54–3.35	3.54–3.35	3.55–3.33
5A′		3.76–3.60	3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
6A′		1.22 (6.5)	1.22 [b] (6.5)	1.23 [b] (6.0)	1.22 [b] (6.0)	1.22 [b] (6.5)
1B′			5.12 (1.5)	5.13	4.99 (1.5)	5.06
2B′			4.05	4.04 (3.0, 2.0)	4.23 (3.5, 1.5)	4.24
3B′			3.84–3.63	3.84–3.65	3.87	3.94 (9.5, 3.0)
4B′			3.54–3.35	3.54–3.35	3.54–3.35	3.55–3.33
5B′			3.84–3.63	3.84–3.65	3.83–3.63	3.84–3.56
6B′			1.27 [b] (6.5)	1.27 [b] (6.5)	1.23 [b] (6.5)	1.24 [b] (6.0)
1C′					4.66 [c] (8.5)	4.68 [c] (8.5)
2C′					3.83–3.63	3.84–3.56
3C′					3.54	3.55
4C′					↑ multiplet ↓	↑ multiplet ↓
5C′					3.35	3.33

Table 1 (continued)

Ring protons	20	21	22	23	24	25
6C′					3.87	3.88
6′C′					3.83–3.63	3.84–3.56
1A						5.12
2A						3.99
3A						3.84–3.56
4A						3.55–3.33
5A						3.84–3.56
6A						1.20 [b]
						(6.5)

[a] The numbers in parentheses denote coupling constants in Hz.
[b,c] Assignments may be interchanged.

washings were combined, concentrated until two phases formed, and diluted with EtOAc (150 mL). The aqueous phase was decanted and the organic solution was washed successively with H_2O (100 mL), satd aq $NaHCO_3$ (100 mL), and satd aq NaCl (100 mL). The aqueous phases were re-extracted with EtOAc (2 × 70 mL) and the combined organic solutions were dried and concentrated. The residual solid was triturated with toluene–EtOAc 9:1 (~ 50 mL) and filtered. It was washed successively with toluene–EtOAc 9:1 (~ 30 mL), hexanes (2 × 30 mL), and dried (1.2 g, 18%). The hemiacetal **3** was obtained as a white amorphous powder which dissolved in $CDCl_3$ to give an anomeric mixture (α:β, 3:7). ^{1}H NMR ($CDCl_3$): δ 8.10–7.20 (m, 19 H, aromatics), 6.58 (dd, 1 Hα, *J* 11.5 and 9.0 Hz, H-3α), 6.33 (dd, 1 Hβ, *J* 11.0 and 9.5 Hz, H-3β), 5.85 (d, 1 Hβ, *J* 8.5 Hz, H-1β), 5.77 (dd, 1 Hα, *J* 10.0 and 9.0 Hz, H-4α), 5.73 (t, 1 Hβ, *J* 9.5 Hz, H-4β), 5.54 (bd, 1 Hα, H-1α), 4.92 (dd, 1 Hα, *J* 11.5 and 3.5 Hz, H-2α), 4.84 (m, 1 Hα, H-5α), 4.66 (dd, 1 Hβ, *J* 12.0 and 3.0 Hz, H-6β), 4.53 (dd, 1 Hβ, *J* 11.0 and 8.5 Hz, H-2β), 4.52–4.48 (m, 2 Hα and 1 Hβ, H-6α, H-6′α and H-6′β), 4.31 (ddd, 1 Hβ, *J* 10.0, 5.0 and 3.0 Hz, H-5β). Anal. Calcd for $C_{35}H_{27}NO_{10}$: C, 67.63; H, 4.38; N, 2.25. Found: C, 67.40; H, 4.44; N, 2.56.

3,4,6-Tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**4**).—Trichloroacetonitrile (7 mL, 4 equiv) and potassium carbonate (3.7 g, 1.5 equiv) were added to a solution of the hemiacetal **3** (10.9 g, 17.5 mmol) in anhyd CH_2Cl_2 (200 mL). The mixture was stirred under N_2 for 18 h at room temperature, filtered through Celite, and the solids were rinsed with CH_2Cl_2 (5 × 20 mL). The combined filtrate and washings were concentrated to an oily residue that was dissolved in anhyd CH_2Cl_2 (170 mL). Trichloroacetonitrile (7 mL, 4 equiv) and potassium carbonate (2 g, 0.8 equiv) were added and the reaction mixture was left under N_2 at room temperature for 18 h. The solids were filtered off, washed with CH_2Cl_2 (5 × 20 mL), and the combined filtrate and washings were concentrated. The dry residue was dissolved in toluene and chromatographed using toluene–EtOAc (9:1) as eluent. The trichloroacetimidate **4** was obtained as a colorless oil (10.3 g, 77%) that was used directly in the next step to prepare the disaccharide **10**. ^{1}H NMR data ($CDCl_3$): δ 8.70 (bs, 1 H, NH), 8.00–7.20 (m, 19 H, aromatics), 6.85 (d, 1 H, *J* 9.0 Hz, H-1), 6.41 (dd, 1 H, *J* 11.0 and 9.0 Hz,

Table 2
^{13}C NMR data [a] for compounds **20–22**, **24** and **25**

Ring carbons	**20**	**21**	**22**	**24**	**25**
1B	101.2	101.4	100.5	100.5	100.4
	(170)	(171)	(171)	(170)	(170)
2B	72.6	79.7	79.4	79.5	79.4
3B	82.7	82.6	82.8	82.8 [b]	82.6
4B	73.6	74.0	74.1 [b]	74.1 [c]	74.2
5B	71.6	71.9	71.9 [c]	71.9 [d]	71.9 [b]
6B	19.2	19.5	19.5 [d]	19.4 [e]	19.5 [c]
1C	105.5	105.3	105.3	105.4	105.3 [d]
	(161)	(162)	(162)	(160)	(164)
2C	58.4	58.8	58.8	58.8 [f]	58.7
3C	76.3	76.7	76.8	76.8 [c]	76.7
4C	72.4	73.0 [b]	72.7	72.7	72.7
5C	78.3	78.7	78.7	78.6 [g]	78.6
6C	63.2	63.8	63.8	63.7 [h]	63.7
1A′		104.5	104.9	104.2	104.4 [e]
		(173)	(171)	(173)	(174)
2A′		72.8 [b]	73.0	72.7	72.7
3A′		72.8 [b]	80.0	79.9	79.4
4A′		74.9	74.9 [b]	74.4 [c]	74.5
5A′		71.9	72.0 [c]	72.7 [d]	72.1 [b]
6A′		19.5	19.5 [d]	19.4 [e]	19.4 [c]
1B′			104.2	104.5	103.7
			(173)	(173)	(172)
2B′			72.8	72.7	79.1
3B′			73.1	82.7 [b]	82.5
4B′			74.4 [b]	73.8 [c]	74.0
5B′			72.2 [c]	72.2 [d]	72.1 [b]
6B′			19.7 [d]	19.7 [e]	19.6 [c]
1C′				105.4	105.2 [d]
				(160)	(164)
2C′				58.6 [f]	58.7
3C′				76.6 [c]	76.6
4C′				72.7	72.7
5C′				78.5 [g]	78.6
6C′				63.5 [h]	63.7
1A					104.2 [e]
					(172)
2A					72.7
3A					72.9
4A					74.9
5A					71.9 [b]
6A					19.4 [c]

[a] The numbers in parentheses denote the $^{1}J_{C,H}$ in Hz.
[b–h] Assignments may be interchanged.

H-3), 5.84 (dd, 1 H, *J* 10.0 and 9.5 Hz, H-4), 4.92 (dd, 1 H, *J* 11.0 and 9.0 Hz, H-2), 4.68 (dd, 1 H, *J* 12.0 and 3.0 Hz, H-6), 4.55 (dd, 1 H, *J* 12.0 and 5.0 Hz, H-6′), 4.47 (ddd, 1 H, *J* 10.0, 5.0 and 3.0 Hz, H-5).

Allyl 2-O-acetyl-4-O-benzoyl-α-L-rhamnopyranoside (**5**).—Allyl α-L-rhamnopyranoside was prepared as described previously [17] from L-rhamnose (5.0 g, 27 mmol) and dissolved in anhyd CH_3CN (40 mL). Trimethyl-*ortho*-acetate (7 mL, 2 equiv) and *p*-toluenesulfonic acid (40 mg) were added, and the solution was stirred under N_2 for 2 h at room temperature. Triethylamine (210 μL) was added to quench the reaction, solvents were evaporated, and residual traces of MeOH were co-evaporated with anhyd toluene (2 × 40 mL). The dry residue was dissolved in anhyd pyridine (30 mL), the stirred solution was cooled to 0 °C and benzoyl chloride (6.4 mL, 2 equiv) was added dropwise. The reaction mixture was allowed to reach room temperature and stirred for 1 h. MeOH (5 mL) was added to destroy the excess of reagents and the solvents were evaporated. The resulting oil was dissolved in EtOAc (70 mL) and washed successively with H_2O (60 mL), M HCl (60 mL), satd aq $NaHCO_3$ (60 mL) and satd aq NaCl (60 mL). The aqueous phases were re-extracted with EtOAc (2 × 60 mL), and the combined organic solutions were dried and concentrated. The residue was dissolved in 80% aq AcOH (50 mL), stirred for 1 h at room temperature and concentrated. Residual AcOH was co-evaporated with toluene (2 × 40 mL) and the alcohol **5** was purified by flash chromatography (hexanes–EtOAc, 8:2) and isolated as a colorless syrup (5.7 g, 59% calcd from L-rhamnose). $[\alpha]_D^{20}$ −46° (*c* 1.0, CH_2Cl_2); ^1H NMR data ($CDCl_3$): δ 8.10–7.40 (m, 5 H, aromatics), 5.92 (m, 1 H, $CH_2CH=$), 5.33, 5.24 (2m, 2 H, $CH_2=$), 5.15 (dd, 1 H, *J* 3.5 and 1.5 Hz, H-2), 5.12 (t, 1 H, *J* 10.0 Hz, H-4), 4.88 (d, 1 H, *J* 1.5 Hz, H-1), 4.20 (m, 2 H, H-3 and $CH_2CH=$), 4.01 (m, 2 H, H-5 and $CH_2CH=$), 2.17 (s, 3 H, CH_3CO), 1.28 (d, 3 H, *J* 6.0 Hz, H-6). Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.70; H, 6.33. Found: C, 61.47; H, 6.45.

Allyl 3-O-acetyl-2,4-di-O-benzoyl-α-L-rhamnopyranoside (**6**).—Acetic anhydride (50 mL) was added dropwise to a solution of allyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside [18] (38.7 g, 93 mmol) in pyridine (100 mL), stirred at 0 °C. The mixture was stirred 2 h at room temperature, concentrated, and the residual solvents were co-evaporated with toluene (2 × 100 mL). The resulting oil was dissolved in EtOAc (200 mL) and washed successively with M HCl (200 mL), satd aq $NaHCO_3$ (200 mL), and satd aq NaCl (200 mL). The aqueous phases were re-extracted with EtOAc (2 × 150 mL), and the combined organic solutions were dried and concentrated to give **6** as a colorless oil (41.6 g, 98%). $[\alpha]_D^{20}$ +76° (*c* 1.7, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.20–7.40 (m, 10 H, aromatics), 5.95 (m, 1 H, $CH_2CH=$), 5.65 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3), 5.55 (dd, 1 H, *J* 3.5 and 1.5 Hz, H-2), 5.48 (t, 1 H, *J* 10.0 Hz, H-4), 5.36, 5.26 (2m, 2 H, $CH_2=$), 4.98 (d, 1 H, *J* 1.5 Hz, H-1), 4.26 (m, 1 H, $CH_2CH=$), 4.11 (m, 1 H, H-5), 4.09 (m, 1 H, $CH_2CH=$), 1.87 (s, 3 H, CH_3CO), 1.32 (d, 3 H, *J* 6.0 Hz, H-6). Anal. Calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77. Found: C, 66.02; H, 5.82.

3-O-Acetyl-2,4-di-O-benzoyl-α,β-L-rhamnopyranose (**7**).—Tris(triphenylphosphine) rhodium chloride (1.26 g, 0.06 equiv) and 1,4-diazabicyclooctane (DABCO, 1.5 g, 0.6 equiv) were added to a solution of the allyl glycoside **6** (10.0 g, 22 mmol) in 90% aq EtOH (500 mL) and the stirred mixture was refluxed overnight. The reaction was cooled to room temperature and the solvents were evaporated. Residual H_2O was co-evaporated with toluene (3 × 100 mL) and the residue was dissolved in EtOAc (50 mL), filtered through silica, and eluted with EtOAc (500 mL). The eluate was concentrated to give a brownish oily residue which was dissolved in 90% aq acetone (500 mL). Yellow

mercuric oxide (5.25 g, 1.1 equiv) was added and a solution of mercuric chloride (6.57 g, 1.1 equiv) in 90% aq acetone (70 mL) was added dropwise to the stirred suspension. The reaction mixture was stirred overnight at room temperature, concentrated, and the residue was co-concentrated with MeOH (200 mL). The semi-solid residue was diluted with EtOAc (250 mL), filtered through Celite, and the solids were washed with EtOAc (3 × 100 mL). The combined filtrate and washings were washed successively with satd aq KI (2 × 200 mL), 5% aq sodium thiosulfate (2 × 100 mL), and satd aq NaCl (100 mL). The aqueous phases were re-extracted with EtOAc (2 × 100 mL) and the combined organic solutions were dried and concentrated. Chromatography (hexanes–EtOAc, 7:3) of the residue gave the hemiacetal **7** (7.4 g, 81%) which crystallized on standing. The crystals were triturated with hexanes–EtOAc (9:1) and filtered. The NMR spectrum in $CDCl_3$ showed an anomeric mixture $\alpha:\beta$, 8:2. ^{1}H NMR ($CDCl_3$): δ 8.20–7.40 (m, 10 H, aromatics), 5.71 (m, 1 Hα and 1 Hβ, H-3α and H-2β), 5.57 (dd, 1 Hα, *J* 3.5 and 1.8 Hz, H-2α), 5.49 (t, 1 Hα, *J* 10 Hz, H-4α), 5.42 (t, 1 Hβ, *J* 10 Hz, H-4β), 5.37 (bs, 1 Hα, H-1α), 5.35 (dd, *J* 10.0 and 3.0 Hz, H-3α), 5.14 (bs, 1 Hβ, H-1β), 4.36 (m, 1 Hα, H-5α), 3.81 (m, 1 Hβ, H-5β), 1.87 (s, 3 H, CH_3CO), 1.39 (d, 3 Hβ, *J* 6.0 Hz, H-6β), 1.32 (d, 3 Hα, *J* 6.0 Hz, H-6α). Anal. Calcd for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.80; H, 5.37.

3-O-Acetyl-2,4-di-O-benzoyl-α,β-L-rhamnopyranosyl trichloracetimidate (**8**).—Trichloroacetonitrile (3.75 mL, 3 equiv) and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, 450 μL, 0.25 equiv) were added to a solution of the hemiacetal **7** (5.0 g, 12 mmol) in anhyd CH_2Cl_2 (100 mL) and the reaction mixture was stirred overnight under N_2 at room temperature. Solvents were evaporated and flash chromatography (hexanes–EtOAc, 9:1) of the residue gave the pure trichloroacetimidate **8** (5.4 g, 80%) as a colorless glass that was used directly in the glycosylation reactions. ^{1}H NMR ($CDCl_3$), α-isomer: δ 8.80 (bs, 1 H, NH), 8.15–7.40 (m, 10 H, aromatics), 6.41 (d, 1 H, *J* 1.5 Hz, H-1), 5.75 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2), 5.68 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3), 5.57 (t, 1 H, *J* 10.0, H-4), 4.30 (m, 1 H, H-5), 1.87 (s, 3 H, CH_3CO), 1.38 (d, 3 H, H-6); ^{13}C NMR ($CDCl_3$), α-isomer: δ 95.06 (C-1, J_{C-H} 179 Hz).

Allyl 2-O-acetyl-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**9**).—A mixture of the donor **4** (10.3 g, 12.9 mmol) and the acceptor **5** (6.0 g, 1.3 equiv) in anhyd CH_2Cl_2 (160 mL) containing 4 Å activated molecular sieves (5 g) was stirred under N_2 for 0.5 h at room temperature and cooled to −75 °C. Triethylsilyl triflate (TESOTf, 180 μL, 0.06 equiv) was added, the mixture was stirred under N_2 at −75 °C for 3.5 h, then allowed to reach room temperature slowly and stirred overnight at room temperature. Triethylamine (160 μL) was added and the solids were filtered off and washed with CH_2Cl_2 (200 mL). The combined filtrate and washings were washed successively with H_2O (200 mL), 1 N HCl (200 mL), satd aq $NaHCO_3$ (200 mL), and satd aq NaCl (200 mL). The aqueous washings were re-extracted with CH_2Cl_2 (2 × 150 mL) and the combined organic solutions were dried and concentrated. Flash chromatography (hexanes:EtOAc, 7:3) of the residue gave the disaccharide **9** (7.5 g, 58%) as a colorless glass. TLC (toluene–EtOAc (9:1)) showed that the product was not pure. Nevertheless, its degree of purity (> 90%) was acceptable for direct use in the subsequent reactions. An analytically pure sample of the disaccharide **9** was obtained by successive flash chromatography

(toluene:EtOAc, 9:1) and chromatography on Sephadex LH20 to give a colorless glass. $[\alpha]_D^{20}$ +51° (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.12–7.10 (m, 24 H, aromatics), 6.11 (dd, 1 H, *J* 11.0 and 9.5 Hz, H-3C), 5.83 (m, 1 H, $CH_2CH=$), 5.69 (d, 1 H, *J* 8.5 Hz, H-1C), 5.64 (t, 1 H, *J* 9.5 Hz, H-4C), 5.40 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 5.26 (m, 1 H, $CH_2=$), 5.21 (t, 1 H, *J* 10.0 Hz, H-4B), 5.18 (m, 1 H, $CH_2=$), 4.76 (d, 1 H, *J* 1.5 Hz, H-1B), 4.57 (dd, 1 H, *J* 12.0 and 3.0 Hz, H-6C), 4.52 (dd, 1 H, *J* 11.0 and 8.5 Hz, H-2C), 4.45 (dd, 1 H, *J* 12.0 and 4.5 Hz, H-6′C), 4.26 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3B), 4.21 (m, 1 H, H-5C), 4.09 and 3.94 (2m, 2 H, $CH_2CH=$), 3.83 (m, 1 H, H-5B), 2.05 (s, 3 H, CH_3CO), 1.08 (d, 3 H, *J* 6.5 Hz, H-6B). Anal. Calcd for $C_{53}H_{47}NO_{16}$: C, 66.73; H, 4.97; N, 1.47. Found: C, 66.62; H, 5.03; N, 1.41.

Allyl 4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**10**).—A methanolic solution of HCl (1.04 N, 90 mL), prepared by adding acetyl chloride (8 mL) to freshly distilled MeOH (100 mL), was added to a solution of the disaccharide **9** (7.4 g, 7.8 mmol) in freshly distilled MeOH (60 mL) and the solution was stirred at 48–54 °C for 1.5 h. The solution was cooled to 0 °C and NEt_3 (14 mL) was added dropwise to neutralize the HCl. The solution was concentrated to a semi-solid residue that was dissolved in CH_2Cl_2 (500 mL) and washed successively with 1 N HCl (200 mL), satd aq $NaHCO_3$ (200 mL), and H_2O (200 mL). The aqueous washings were re-extracted with CH_2Cl_2 (2 × 150 mL) and the combined organic solutions were dried and concentrated. Flash chromatography (hexanes–toluene–EtOAc; 5:3:2, 500 mL; 4:3:3, 1500 mL) of the residue, followed by a second flash chromatography (hexanes–toluene–EtOAc, 4:3:3) of the impure fractions gave the alcohol **10** (5.7 g, 81%) as a colorless glass. $[\alpha]_D^{20}$ +32° (*c* 1.1, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 8.12–7.10 (m, 24 H, aromatics), 6.16 (dd, 1 H, *J* 11.0 and 9.0 Hz, H-3C), 5.81 (m, 1 H, $CH_2CH=$), 5.74 (d, 1 H, *J* 8.5 Hz, H-1C), 5.59 (dd, 1 H, *J* 10.0 and 9.5 Hz, H-4C), 5.26 (m, 2 H, $CH_2=$ and H-4B), 5.20 (m, 1 H, $CH_2=$), 4.73 (m, 1 H, H-6C), 4.70 (m, 1 H, H-1B), 4.59 (dd, 1 H, *J* 11.0 and 8.5 Hz, H-2C), 4.46 (dd, 1 H, *J* 12.0 and 6.5 Hz, H-6′C), 4.31 (m, 1 H, H-5C), 4.17 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 4.09 (m, 1 H, $CH_2CH=$), 4.07 (m, 1 H, H-3B), 3.87 (m, 1 H, $CH_2CH=$), 3.81 (m, 1 H, H-5B), 1.07 (d, 3 H, *J* 6.5 Hz, H-6B). Anal. Calcd for $C_{51}H_{45}NO_{15}$: C, 67.17; H, 4.97; N, 1.54. Found: C, 66.76; H, 5.03; N, 1.45.

Allyl 2-O-(3-O-acetyl-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**11**).—A mixture of the acceptor **10** (5.6 g, 6.1 mmol) and the trichloroacetimidate **8** (4.1 g, 1.2 equiv) in anhyd CH_2Cl_2 (150 mL) containing 4 Å activated molecular sieves (5 g) was stirred under N_2 for 2 h at room temperature and cooled to −75° C. TESOTf (125 μL, 0.09 equiv) was added and the mixture was stirred under N_2 at −75° C for 0.5 h then at room temperature for 2 h. Triethylamine (115 μL) was added and the solids were filtered off and washed with CH_2Cl_2 (200 mL). The combined filtrates were washed successively with H_2O (200 mL), 1 N HCl (200 mL), satd aq $NaHCO_3$ (200 mL), and satd aq NaCl (200 mL). The aqueous washings were re-extracted with CH_2Cl_2 (2 × 200 mL) and the combined organic solutions were dried and concentrated. Flash chromatography (hexanes–toluene–EtOAc, 5:3:2) of the residue gave the trisaccharide **11** (8.0 g) as a colorless glass. Although elemental analysis and the NMR spectrum of the compound showed that it contained some residual trichloroacetamide (≈ 3%), the

trisaccharide was used directly in the next reactions. An analytically pure sample of the trisaccharide **11** was obtained by further purification on Sephadex LH20 to give a colorless glass. $[\alpha]_D^{20}$ +40° (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.32–7.10 (m, 34 H, aromatics), 6.22 (dd, 1 H, *J* 11.0 and 9.0 Hz, H-3C), 5.88 (t, 1 H, *J* 10.0 Hz, H-4C), 5.79 (m, 2 H, $CH_2CH=$ and H-3A′), 5.73 (d, 1 H, *J* 8.5 Hz, H-1C), 5.64 (d, 1 H, *J* 1.5 Hz, H-1A′), 5.61 (dd, 1 H, *J* 3.0 and 2.0 Hz, H-2A′), 5.53 (t, 1 H, *J* 10.0 Hz, H-4A′), 5.27 (m, 1 H, $CH_2=$), 5.22 (dd, 1 H, *J* 11.0 and 8.5 Hz, H-2C), 5.20 (m, 2 H, $CH_2=$ and H-4B), 4.79 (d, 1 H, *J* 1.5 Hz, H-1B), 4.66 (dd, 1 H, *J* 12.0 and 3.0 Hz, H-6C), 4.43 (dd, 1 H, *J* 12.0 and 6.0 Hz, H-6′C), 4.36 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 4.27 (m, 1 H, H-5C), 4.24 (dd, 1 H, *J* 9.5 and 3.5 Hz, H-3B), 4.18 (m, 1 H, H-5A′), 4.11 and 3.94 (2m, 2 H, $CH_2CH=$), 3.85 (m, 1 H, H-5B), 1.95 (s, 3 H, CH_3CO), 1.20 (d, 3 H, *J* 6.5 Hz, H-6A′), 1.14 (d, 3 H, *J* 6.5 Hz, H-6B). Anal. Calcd for $C_{73}H_{65}NO_{22}$: C, 67.02; H, 5.01; N, 1.07. Found: C, 66.87; H, 5.02; N, 1.30.

*Allyl 4-O-benzoyl-2-O-(2,4-di-O-benzoyl-α-*L*-rhamnopyranosyl)-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-α-*L*-rhamnopyranoside* (**12**).—Deacetylation of the trisaccharide **11** (2.4 g, 1.8 mmol) as well as work up of the reaction were accomplished as described for the preparation of disaccharide **10**. Flash chromatography (hexanes–toluene–EtOAc; 5:3:2, 200 mL; 4.5:3:2.5, 200 mL; 4:3:3, 300 mL) gave the alcohol **12** (1.95 g, 84%) as a colorless glass. $[\alpha]_D^{20}$ +20° (*c* 1.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 8.32–6.90 (m, 34 H, aromatics), 6.28 (dd, 1 H, *J* 11.0 and 9.0 Hz, H-3C), 6.00 (dd, 1 H, *J* 10.0 and 9 Hz, H-4C), 5.79 (m, 1 H, $CH_2CH=$), 5.70 (d, 1 H, *J* 8.5 Hz, H-1C), 5.69 (m, 1 H, H-2A′), 5.49 (d, 1 H, *J* 1.5 Hz, H-1A′), 5.39 (t, 1 H, *J* 10.0 Hz, H-4A′), 5.28 (m, 1 H, $CH_2=$), 5.25 (dd, 1 H, *J* 10.5 and 8.5 Hz, H-2C), 5.19 (m, 1 H, $CH_2=$), 5.15 (t, 1 H, *J* 10 Hz, H-4B), 4.82 (d, 1 H, *J* 1.5 Hz, H-1B), 4.71 (dd, 1 H, *J* 12.0 and 3.0 Hz, H-6C), 4.47 (m, 2 H, H-3A′ and H-6′C), 4.34 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 4.29 (m, 1 H, H-5C), 4.24 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3B), 4.19 (m, 1 H, H-5A′), 4.11 and 3.95 (2m, 2 H, $CH_2CH=$), 3.84 (m, 1 H, H-5B), 1.24 (d, 3 H, *J* 6.5 Hz, H-6A′), 1.12 (d, 3 H, *J* 6.5 Hz, H-6B). Anal. Calcd for $C_{71}H_{63}NO_{21}$: C, 67.34; H, 5.01; N, 1.11. Found: C, 67.08; H, 5.07; N, 1.32.

*2-O-Acetyl-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-α,β-*L*-rhamnopyranose* (**13**).—Tris(triphenylphosphine) rhodium chloride (204 mg, 0.06 equiv) and DABCO (250 mg, 0.6 equiv) were added to a solution of the allyl glycoside **9** (3.5 g, 3.7 mmol) in 90% aq EtOH (100 mL) and the mixture was refluxed under N_2 for 7 h. The mixture was cooled to room temperature and the solvents were evaporated. The residual H_2O was co-evaporated with toluene (50 mL) and the residue was dissolved in EtOAc (15 mL), filtered through silica, and eluted with EtOAc (300 mL). The eluate was concentrated to give a brownish oily residue which was dissolved in 90% aq acetone (80 mL). Yellow mercuric oxide (874 mg, 1.1 equiv) was added followed by a solution of mercuric chloride (1.0 g, 1.0 equiv) in 90% aq acetone (20 mL). The reaction mixture was stirred overnight at room temperature, filtered over Celite, and the solids were washed successively with acetone (2 × 100 mL) and EtOAc (100 mL). The combined filtrate and washings were concentrated to a residue that was dissolved in EtOAc (200 mL) and washed successively with satd aq KI (200 mL), 10% aq sodium thiosulfate (2 × 200 mL), and satd aq NaCl (200 mL). The aqueous phases were re-extracted with EtOAc (2 × 150 mL) and the combined organic solutions were

dried and concentrated. Flash chromatography (hexanes–EtOAc, 1:1) of the residue gave the hemiacetal **13** (2.6 g, 74%) as a colorless glass. An NMR spectrum in $CDCl_3$ showed that compound **13** was present mostly as one anomer, assumed to be the more stable α-anomer. ^{1}H NMR ($CDCl_3$): (8.20–7.20 (m, 24 H, aromatics), 6.15 (dd, 1 H, *J* 11.0 and 9.0 Hz, H-3C), 5.71 (d, 1 H, *J* 8.5 Hz, H-1C), 5.64 (t, 1 H, *J* 9.5 Hz, H-4C), 5.44 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 5.22 (t, 1 H, *J* 10.0 Hz, H-4B), 5.16 (bs, 1 H, H-1B), 4.64 (dd, 1 H, *J* 12.0 and 3.0 Hz, H-6C), 4.53 (dd, 1 H, *J* 11.0 and 8.5 Hz, H-2C), 4.46 (dd, 1 H, *J* 12.0 and 5.0 Hz, H-6′C), 4.36 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3B), 4.23 (m, 1 H, H-5C), 4.08 (m, 1 H, H-5B), 2.10 (s, 3 H, CH_3CO), 1.08 (d, 3 H, *J* 6.5 Hz, H-6B).

*2-O-Acetyl-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-α,β-*L*-rhamnopyranosyl trichloroacetimidate* (**14**).—*Method A.*— Trichloroacetonitrile (45 μL, 3 equiv) and K_2CO_3 (31 mg, 1.5 equiv) were added to a solution of the hemiacetal **13** (137 mg, 0.15 mmol) in anhyd CH_2Cl_2 (5 mL) and the mixture was stirred for 24 h under N_2 at room temperature. The solids were filtered off and washed with CH_2Cl_2 (≈ 10 mL) and the combined filtrate and washings were concentrated. Flash chromatography (hexanes–toluene–EtOAc, 4:4:2) gave the trichloroacetimidate **14** (120 mg, 76%) as a colorless glass.

Method B.— Trichloroacetonitrile (45 μL, 3 equiv) and a solution (100 μL, 0.25 equiv) of DBU in CH_2Cl_2 (5.6 μL/mL) were added to a solution of the hemiacetal **13** (139 mg, 0.15 mmol) in anhyd CH_2Cl_2 (5 mL) and the mixture was stirred overnight under N_2 at room temperature. More DBU in CH_2Cl_2 (50 μL, 0.12 equiv) and more trichloroacetonitrile (20 μL, 1.5 equiv) were added and the reaction was left to proceed for an additional 7 h at room temperature. The solvents were evaporated and flash chromatography (as described above) gave the trichloroacetimidate **14** (116 mg, 76%) as a colorless glass. ^{1}H NMR ($CDCl_3$): δ 8.70 (s, 1 H, NH), 8.10–7.10 (m, 24 H, aromatics), 6.24 (d, 1 H, *J* 2 Hz, H-1B), 6.15 (dd, 1 H, *J* 11.0 and 9.5 Hz, H-3C), 5.74 (d, 1 H, *J* 8.5 Hz, H-1C), 5.68 (t, 1 H, *J* 9.5 Hz, H-4C), 5.60 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 5.32 (t, 1 H, *J* 10.0 Hz, H-4B), 4.58 (dd, 1 H, *J* 12.0 and 3.5 Hz, H-6C), 4.54 (dd, 1 H, *J* 11.0 and 8.0 Hz, H-2C), 4.45 (dd, 1 H, *J* 12.0 and 4.0 Hz, H-6′C), 4.34 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3B), 4.24 (m, 1 H, H-5C), 4.03 (m, 1 H, H-5B), 2.15 (s, 3 H, CH_3CO), 1.12 (d, 3 H, *J* 6.0 Hz, H-6B).

*2-O-(3-O-Acetyl-2,4-di-O-benzoyl-α-*L*-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-α,β-*L*-rhamnopyranose* (**15**).— Isomerization of the allyl glycoside **11** (3.5 g, 2.7 mmol), followed by hydrolysis of the resulting propenyl glycoside to give the hemiacetal **15** were accomplished as described for the preparation of the hemiacetal **13**. Flash chromatography (hexanes–EtOAc, 1:1) gave unreacted starting material (638 mg, 15%) and the hemiacetal **15** (1.85 g, 54%) which was obtained as a colorless glass. An NMR spectrum in $CDCl_3$ showed that compound **15** was present mostly as one anomer, presumed to be the more stable α-anomer for which the NMR data are reported below. ^{1}H NMR ($CDCl_3$): δ 8.38–6.90 (m, 34 H, aromatics), 6.24 (dd, 1 H, *J* 10.5 and 9.0 Hz, H-3C), 5.90 (t, 1 H, *J* 10.0 Hz, H-4C), 5.77 (dd, 1 H, *J* 10.0 and 3.0 Hz, H-3A′), 5.72 (d, 1 H, *J* 8.0 Hz, H-1C), 5.60 (m, 2 H, H-1A′ and H-2A′), 5.52 (t, 1 H, *J* 10.0 Hz, H-4A′), 5.24 (dd, 1 H, *J* 10.5 and 8.5 Hz, H-2C), 5.20 (m, 1 H, H-4B), 5.17 (m, 1 H, H-1B), 4.72 (dd, 1 H, *J* 12.0 and 3.0

Hz, H-6C), 4.40 (m, 2 H, H-6'C and H-2B), 4.31 (dd, 1 H, *J* 9.5 and 3.5 Hz, H-3B), 4.28 (m, 1 H, H-5C), 4.17 (m, 1 H, H-5A'), 4.08 (m, 1 H, H-5B), 1.95 (s, 3 H, CH_3CO), 1.21 (d, 3 H, *J* 6.0 Hz, H-6A'), 1.13 (d, 3 H, *J* 6.5 Hz, H-6B).

2-O-(3-O-Acetyl-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α,β-L-rhamnopyranosyl trichloroacetimidate (**16**).—Trichloroacetonitrile (120 μL, 3 equiv) and DBU (20 μL, 0.34 equiv) were added to a solution of the hemiacetal **15** (501 mg, 0.39 mmol) in anhyd CH_2Cl_2 (20 mL) and the mixture was stirred overnight under N_2 at room temperature. The solvents were evaporated and the residue was dissolved in toluene (5 mL), filtered through silica, and eluted with hexanes–toluene–EtOAc (4:3:3) to give the trichloroacetimidate **16** (419 mg, 75%) as a colorless glass. ^{1}H NMR ($CDCl_3$): δ 8.68 (s, 1 H, NH), 8.30–7.10 (m, 34 H, aromatics), 6.25 (d, 1 H, *J* 2.0 Hz, H-1B), 6.22 (dd, 1 H, *J* 10.5 and 9.0 Hz, H-3C), 5.91 (t, 1 H, *J* 9.0 Hz, H-4C), 5.80 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3A'), 5.76 (d, 1 H, *J* 8.0 Hz, H-1C), 5.67 (d, 1 H, *J* 1.5 Hz, H-1A'), 5.62 (dd, 1 H, *J* 3.0 and 2.0 Hz, H-2A'), 5.53 (t, 1 H, *J* 10.0 Hz, H-4A'), 5.32 (t, 1 H, *J* 9.5 Hz, H-4B), 5.17 (dd, 1 H, *J* 10.5 and 8.0 Hz, H-2C), 4.6% (dd, 1 H, *J* 12.0 and 3.0 Hz, H-6C), 4.57 (dd, 1 H, *J* 3.5 and 2.0 Hz, H-2B), 4.37 (dd, 1 H, *J* 12.0 and 5.0 Hz, H-6'C), 4.29 (m, 1 H, H-3B), 4.25 (m, 2 H, H-5A' and H-5C), 4.06 (m, 1 H, H-5B), 1.58 (s, 3 H, CH_3CO), 1.24 (d, 3 H, *J* 6.5 Hz, H-6A'), 1.19 (d, 3 H, *J* 6.5 Hz, H-6B).

Allyl 2-O-(3-O-(3-O-acetyl-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**17**).—Glycosylation of the acceptor **12** (515 mg, 0.4 mmol) with the trichloroacetimidate **8** (267 mg, 1.2 equiv) as well as work up of the reaction were performed as described for the preparation of **11**. Flash chromatography (toluene:EtOAc, 9:1) gave **17** (538 mg, 79.5%) as a colorless glass. $[\alpha]_D^{20}$ +61° (*c* 1.1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 8.42–6.89 (m, 44 H, aromatics), 6.24 (dd, 1 H, *J* 10.5 and 9.5 Hz, H-3C), 6.05 (bt, 1 H, *J* 9.5 Hz, H-4C), 5.78 (m, 1 H, $CH_2CH=$), 5.74 (d, 1 H, *J* 8.5 Hz, H-1C), 5.69 (t, 1 H, *J* 10.0 Hz, H-4A'), 5.65 (m, 2 H, H-1A' and H-2A'), 5.52 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3B'), 5.38 (t, 1 H, *J* 10.0 Hz, H-4B'), 5.35 (m, 1 H, H-2B'), 5.32 (m, 1 H, H-2C), 5.29 (m, 1 H, H-1B'), 5.26 and 5.19 (2m, 2 H, $CH_2=$), 5.16 (m, 1 H, H-4B), 4.78 (d, 1 H, *J* 1.5 Hz, H-1B), 4.57 (m, 1 H, H-6C), 4.67 (m, 1 H, H-3A'), 4.50 (dd, 1 H, *J* 12.5 and 5.5 Hz, H-6'C), 4.38 (dd, 1 H, *J* 3.5 and 1.5 Hz, H-2B), 4.34 (m, 1 H, H-5B'), 4.28 (m, 1 H, H-5C), 4.20 (dd, 1 H, *J* 9.5 and 3.5 Hz, H-3B), 4.15 (m, 1 H, H-5A'), 4.10 and 3.93 (2m, 2 H, $CH_2CH=$), 3.84 (m, 1 H, H-5B), 1.76 (s, 3 H, CH_3CO), 1.32 (d, 3 H, *J* 6.0 Hz, H-6B'), 1.25 (d, 3 H, *J* 6.0 Hz, H-6A'), 1.13 (d, 3 H, *J* 6.0 Hz, H-6B). Anal. Calcd for $C_{93}H_{83}NO_{28}$: C, 67.18; H, 5.03; N, 0.84. Found: C, 66.92; H, 5.01; N, 0.95.

Allyl 2-O-(3-O-(2-O-acetyl-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranosyl)-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**18**).—Glycosylation of the acceptor **12** (159 mg, 0.13 mmol) with the trichloroacetimidate **14** (170 mg, 1.3 equiv) was performed as described for the preparation of **11**. The reaction was allowed to proceed under N_2 for 15 min at −75 °C, then for 24 h at room temperature, and the mixture was processed as described for the preparation of **11**. Flash chromatography (hexanes–toluene–EtOAc, 4:3:3) gave

the pentasaccharide **18** (207 mg, 76%) as a colorless glass. $[\alpha]_D^{20}$ +54° (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.40–6.90 (m, 58 H, aromatics), 6.19 (dd, 1 H, *J* 10.5 and 9.0 Hz, H-3C), 6.04 (dd, 1 H, *J* 10.5 and 9.0 Hz, H-3C'), 5.87 (dd, 1 H, *J* 10.0 and 9.0 Hz, H-4C), 5.76 (m, 1 H, $CH_2CH=$), 5.72 (d, 1 H, *J* 8.0 Hz, H-1C), 5.67 (dd, 1 H, *J* 3.0 and 2.0 Hz, H-2A'), 5.63 (t, 1 H, *J* 10.0 Hz, H-4A'), 5.58 (bs, 1 H, H-1A'), 5.54 (t, 1 H, *J* 9.5 Hz, H-4C'), 5.37 (d, 1 H, *J* 8.5 Hz, H-1C'), 5.26 (m, 1 H, $CH_2=$), 5.20–5.10 (m, 6 H, $CH_2=$, H-4B, H-2C, H-1B', H-2B' and H-4B'), 4.78 (d, 1 H, *J* 1.0 Hz, H-1B), 4.66 (dd, 1 H, *J* 12.0 and 2.5 Hz, H-6C), 4.51–4.40 (m, 3 H, H-6'C, H-3A', H-2C'), 4.36 (dd, 1 H, *J* 3.5 and 1.5 Hz, H-2B), 4.27 (m, 1 H, H-5C), 4.23–4.05 (m, 5 H, $CH_2CH=$, H-3B, H-5A', H-3B', H-6C'), 4.02–3.88 (m, 3 H, $CH_2CH=$, H-5B', H-6'C'), 3.83 (m, 1 H, H-5B), 1.84 (s, 3 H, CH_3CO), 1.22 (d, 3 H, *J* 6.0 Hz, H-6A'), 1.13 (d, 3 H, *J* 6.5 Hz, H-6B), 0.94 (d, 3 H, *J* 6.5 Hz, H-6B'). Anal. Calcd for $C_{121}H_{104}N_2O_{36}$: C, 67.21; H, 4.85; N, 1.30. Found: C, 67.27; H, 4.83; N, 1.52.

Allyl 2-O-(3-O-(2-O-(2-O-acetyl-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranosyl)-2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-3-O-(3,4,6-tri-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**19**).—A mixture of the acceptor **12** (456 mg, 1.22 equiv) and the trichloroacetimidate **16** (417 mg, 0.295 mmol) in anhyd CH_2Cl_2 (8 mL) containing 4 Å activated molecular sieves (800 mg) was stirred under N_2 for 1 h at room temperature. A solution of TESOTf in anhyd CH_2Cl_2 (50 μL/mL, 200 μL, 0.15 equiv) was added and the mixture was stirred overnight under N_2 at room temperature. More TESOTf in CH_2Cl_2 (50 μL/mL, 100 μL, 0.075 equiv) was added to the reaction mixture in two portions within a 2 h period, and the reaction was allowed to proceed at room temperature under N_2 for 24 h. Triethylamine (25 μL) was added, and the sieves were filtered and washed with CH_2Cl_2 (2 × 5 mL). The combined supernatant and washings were concentrated. Flash chromatography (hexanes–EtOAc; 6:4, 250 mL; 1:1, 250 mL) of the residue gave the unreacted glycosyl acceptor **12** (275 mg) and the hexasaccharide **19** (429 mg). Although TLC in hexanes–EtOAc (6:4), showed homogeneous spots in both cases, TLC in toluene–EtOAc (5:1) showed that both the unreacted acceptor **12** and the hexasaccharide **19** were slightly impure. The acceptor **12** was obtained pure (169 mg, 37%) following flash chromatography (toluene:EtOAc, 7:1). The hexasaccharide **19** was purified by further flash chromatography (toluene:EtOAc, 5:1) and was obtained as a colorless glass (322 mg, 43%). An analytically pure sample was obtained by chromatography on Sephadex LH20. $[\alpha]_D^{20}$ +57° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.50–6.94 (m, 68 H, aromatics), 6.20 (dd, 1 H, *J* 10.5 and 9.0 Hz, H-3C), 6.13 (dd, 1 H, *J* 10.5 and 9.0 Hz, H-3C'), 5.87 (dd, 1 H, *J* 10.0 and 9.0 Hz, H-4C), 5.81–5.68 (m, 5 H, $CH_2CH=$, H-3A, H-2A', H-1C and H-4C'), 5.63 (bs, 1 H, H-1A), 5.58 (t, 1 H, *J* 10.0 Hz, H-4A'), 5.57 (bs, 1 H, H-1A'), 5.51–5.46 (m, 2 H, H-1C' and H-2A), 5.45 (t, 1 H, *J* 10.0 Hz, H-4A), 5.26 (m, 1 H, $CH_2=$), 5.21–5.12 (m, 6 H, $CH_2=$, H-4B, H-2C, H-1B', H-4B' and H-2C'), 4.77 (bs, 1 H, H-1B), 4.65 (dd, 1 H, *J* 12.0 and 2.5 Hz, H-6C), 4.62 (dd, 1 H, *J* 12.5 and 2.5 Hz, H-6C'), 4.49 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3A'), 4.44 (dd, 1 H, *J* 12.0 and 5.5 Hz, H-6'C), 4.36 (dd, 1 H, *J* 3.5 and 1.5 Hz, H-2B), 4.28 (m, 1 H, H-2B'), 4.25 (m, 1 H, H-5C), 4.22 (dd, 1 H, *J* 10.0 and 3.5 Hz, H-3B), 4.16–4.03 (m, 6 H, $CH_2CH=$, H-5A, H-5A', H-3B', H-5B', H-6'C'), 3.93 (m, 1 H, $CH_2CH=$), 3.84 (m,

1 H, H-5B), 3.75 (m, 1 H, H-5C′), 1.92 (s, 3 H, CH_3CO), 1.155 (d, 3 H, *J* 6.0 Hz, H-6B′), 1.15 (d, 3 H, *J* 6.0 Hz, H-6A′), 1.10 (d, 3 H, *J* 6.5 Hz, H-6B), 0.88 (d, 1 H, *J* 6.0 Hz, H-6A). Anal. Calcd for $C_{141}H_{123}N_2O_{42}$: C, 67.29; H, 4.89; N, 1.11. Found: C, 67.15; H, 4.82; N, 0.93.

Allyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**20**).—The protected disaccharide **9** (310 mg, 0.324 mmol) was suspended in freshly distilled MeOH (18 mL), a solution of sodium methoxide (M, 2 mL) was added, and the mixture was stirred overnight at room temperature. More sodium methoxide in MeOH (500 μL) was added and the reaction was allowed to proceed for an additional 24 h. The solution was de-ionized with Rexyn 101 (H^+), the resin was filtered, and then rinsed with MeOH (16 mL). The combined filtrate and washings were concentrated, the residue was co-concentrated with toluene (3 × 15 mL), and then dissolved in EtOH (15 mL). Ethylenediamine (2.5 mL) was added, and the stirred mixture was refluxed overnight and then allowed to cool to room temperature. The solvent was evaporated and the residue was co-concentrated with toluene (3 × 15 mL) and dissolved in MeOH (15 mL). Acetic anhydride (1.5 mL) was added, the solution was left at room temperature for 1.5 h, and concentrated. Solvents were evaporated and the residue was co-concentrated with toluene (2 × 15 mL). Flash chromatography of the residue ($CHCl_3$–MeOH; 9:1, 200 mL; 85:15, 200 mL; 8:2, 200 mL), followed by gel permeation chromatography of the semi-pure disaccharide (Biogel P2, H_2O), and finally flash chromatography (EtOAc–MeOH–H_2O, 7:1.3:1) of the product gave the disaccharide **20** (90 mg, 68%) which was isolated as an amorphous powder upon freeze-drying (TLC, EtOAc–MeOH–H_2O, 6:3:1, R_f 0.8). $[\alpha]_D^{20}$ −54° (*c* 1.1, MeOH). NMR data for the ring protons and carbons are reported in Tables 1 and 2, respectively. ^{1}H NMR (D_2O): δ 5.91 (m, 1 H, CH_2CH=), 5.30 and 5.23 (2m, 2 H, CH_2=), 4.10 and 4.01 (2m, 2 H, CH_2CH=), 1.98 (s, 3 H, CH_3CON); ^{13}C NMR (D_2O): δ 177.5 (CO), 135.9 (CH_2CH=), 121.2 (CH_2=), 70.9 (CH_2CH=), 24.8 (CH_3CON). Anal. Calcd for $C_{17}H_{29}NO_{10}$,0.5H_2O: C, 49.03; H, 7.26; N, 3.36. Found: C, 49.39; H, 6.95; N, 3.65.

Allyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**21**).—The trisaccharide **11** (151 mg, 0.114 mmol) was deprotected and *N*-acetylated as described for the preparation of **20**. The trisaccharide **21** (TLC, EtOAc–MeOH–H_2O, 6:3:1, R_f 0.7) was purified by two successive flash chromatographies using EtOAc–MeOH–H_2O (7:1.3:1) as eluent for the first, and $CHCl_3$–MeOH (8:2, R_f 0.0) followed by EtOAc–MeOH–H_2O (6:3:1) for the second column. The trisaccharide **21** (44 mg, 70%) was finally obtained pure and free of salts after chromatography on a Biogel P2 column (H_2O) and was isolated as a white amorphous powder after freeze-drying. $[\alpha]_D^{20}$ −57° (*c* 0.9, MeOH); NMR data for the ring protons and carbons are reported in Tables 1 and 2, respectively. ^{1}H NMR (D_2O): δ 5.91 (m, 1 H, CH_2CH=), 5.31 and 5.27 (2m, 2 H, CH_2=), 4.18 and 4.03 (2m, 2 H, CH_2CH=), 1.98 (s, 3 H, CH_3CON); ^{13}C NMR (D_2O): δ 177.5 (CO), 136.1 (CH_2CH=), 121.5 (CH_2=), 71.0 (CH_2CH=), 25.1 (CH_3CON). Anal. Calcd for $C_{23}H_{39}NO_{14}$: C, 49.90; H, 7.10; N, 2.53. Found: C, 49.54; H, 7.18; N, 2.65

Allyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-O-(3-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**22**).—The tetrasaccharide **17** (476.6 mg, 0.287 mmol) was deprotected and *N*-acetylated as described for the

preparation of the disaccharide **20**. The tetrasaccharide **22** (TLC, EtOAc–MeOH–H_2O, 6:3:1, R_f 0.55) was purified by flash chromatography using $CHCl_3$–MeOH (8:2, R_f 0.0) followed by EtOAc–MeOH–H_2O (6:3:1). The tetrasaccharide **22** (176 mg, 88%) was finally obtained pure and free of salts after chromatography on a Biogel P2 column (H_2O), and was isolated as a white amorphous powder after freeze-drying. $[\alpha]_D^{20}$ −75° (*c* 1.0, MeOH); NMR data for the ring protons and carbons are reported in Tables 1 and 2, respectively. ^{1}H NMR (D_2O): δ 5.91 (m, 1 H, CH_2CH=), 5.31 and 5.26 (2m, 2 H, CH_2=), 4.18 and 4.03 (2m, 2 H, CH_2CH=), 1.96 (s, 3 H, CH_3CON); ^{13}C NMR (D_2O): δ 177.3 (CO), 136.1 (CH_2CH=), 121.5 (CH_2=), 71.0 (CH_2CH=), 25.1 (CH_3CON). Anal. Calcd for $C_{29}H_{49}NO_{18}$: C, 49.78; H, 7.06; N, 2.00. Found: C, 49.36; H, 7.11; N, 1.90.

Propyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-O-(3-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**23**).—The allyl glycoside **22** (33 mg, 0.047 mmol) was dissolved in MeOH (4 mL), 10% palladium-on-carbon catalyst (50% in H_2O, 17 mg) was added and the stirred mixture was hydrogenated overnight at 52 lb · in.$^{-2}$ at room temperature. The catalyst was filtered off, rinsed with MeOH (4 mL) and the combined filtrates were concentrated to dryness. The residue was dissolved in H_2O and filtered through a 22 μm Amicon filter to give the pure tetrasaccharide **23** (30 mg, 92%) that was obtained as a white powder upon freeze-drying. NMR data for the ring protons are reported in Table 1. ^{1}H NMR (D_2O): δ 3.84–3.65 (m, 1 H, $OCH_2CH_2CH_3$), 3.54–3.35 (m, 1 H, $OCH_2CH_2CH_3$), 1.97 (s, 3 H, CH_3CON), 1.57 (m, 2 H, $OCH_2CH_2CH_3$), 0.87 (t, 3 H, *J* 7.5 Hz, $OCH_2CH_2CH_3$). HRMS. Calcd for $C_{29}H_{52}NO_{18}$ (M + H): 702.3184. Found: 702.3200.

Allyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-O-(3-O-(3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**24**).—The pentasaccharide **18** (135 mg, 0.06 mmol) was deprotected and *N*-acetylated as described for the preparation of **20**. The pentasaccharide **24** (TLC, EtOAc–MeOH–H_2O, 6:3:1, R_f 0.3) was purified by flash chromatography using $CHCl_3$–MeOH (8:2, R_f 0.0) followed by EtOAc–MeOH–H_2O (6:3:1). The pentasaccharide **26** was finally obtained pure and free of salts (48 mg, 86%) after chromatography on a Biogel P2 column (H_2O), and was isolated as a white amorphous powder after freeze-drying. $[\alpha]_D^{20}$ −59° (*c* 0.7, MeOH). NMR data for the ring protons and carbons are reported in Tables 1 and 2, respectively. ^{1}H NMR (D_2O): δ 5.91 (m, 1 H, CH_2CH=), 5.30 and 5.25 (2m, 2 H, CH_2=), 4.18 and 4.03 (2m, 2 H, CH_2CH=), 1.98 and 1.96 (2s, 2 × 3 H, 2 × CH_3CON). ^{13}C NMR (D_2O): δ 177.7 and 177.3 (CO), 136.1 (CH_2CH=), 121.5 (CH_2=), 71.1 (CH_2CH=), 25.1 (CH_3CON). Anal. Calcd for $C_{37}H_{62}N_2O_{23}$: C, 49.22; H, 6.92; N, 3.10. Found: C, 48.68; H, 6.85; N, 3.05.

Allyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-O-(3-O-(3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**25**).—The protected hexasaccharide (320 mg, 0.13 mmol) **19** was suspended in freshly distilled MeOH (11 mL), a solution of sodium methoxide (M, 1.5 mL) was added, and the mixture was stirred overnight at room temperature. More aliquots of the methanolic solution of sodium methoxide (500 μL, 150 μL, 100 μL, and 2 × 50 μL) were added over the following three days while the reaction was allowed to proceed at room temperature. The solution was de-ionized

with Rexyn 101 (H^+), the resin was filtered and then rinsed with MeOH (16 mL). The combined filtrate and washings were concentrated and the residue was co-concentrated with toluene (3 × 15 mL) and dissolved in EtOH (8 mL). Subsequent removal of the phthalimido group and acetylation of the free amino group were performed as described for the preparation of **20**. The hexasaccharide **25** was purified by flash chromatography using $CHCl_3$–MeOH (8:2, R_f 0.0) followed by EtOAc–MeOH–H_2O (6:3:1, R_f 0.4). The hexasaccharide **25** (112 mg, 84%) was finally obtained pure and free of salts after chromatography on a Biogel P2 column (H_2O), and was isolated as a white amorphous powder after freeze-drying. $[\alpha]_D^{20}$ −59° (*c* 1.1, MeOH). NMR data for the ring protons and carbons are reported in Tables 1 and 2, respectively. ^{1}H NMR (D_2O): δ 5.90 (m, 1 H, CH_2CH=), 5.30 and 5.25 (2m, 2 H, CH_2=), 4.17 (m, 1 H, CH_2CH=), 4.06–3.97 (m, 1 H, CH_2CH=), 1.98 and 1.97 (2s, 2 × 3 H, 2 × CH_3CON); ^{13}C NMR (D_2O): δ 177.5 and 177.3 (CO), 136.0 (CH_2CH=), 121.5 (CH_2=), 71.0 (CH_2CH=), 25.1 (CH_3CON). Anal. Calcd for $C_{43}H_{72}N_2O_{27}$: C, 49.23; H, 6.92; N, 2.67. Found: C, 48.87; H, 7.03; N, 2.89.

Acknowledgements

We are grateful to the Heart and Stroke Foundation of B.C. and Yukon and the Natural Sciences and Engineering Research Council of Canada for financial support. We also thank D. McGillivray for recording the mass spectrum.

References

[1] A.L. Bisno, in G.L. Mandell, R.G. Douglas, and J.E. Benett (Eds.), *Principles and Practice of Infectious Diseases*, 2nd ed., Wiley, New York, 1985, pp 1133–1142.
[2] V.A. Fischetti, *Sci. Am.*, (1991) 59–65.
[3] J. Rotta, in R. Bell and G. Torrigiani (Eds.), *Towards Better Carbohydrate Vaccines*, John Wiley & Sons, New York, 1986, pp 203–218.
[4] M.W. Cunningham, S.M. Antone, J.M. Guliza, M.B. McManus, V.A. Fischetti, and C.J. Gauntt, *Proc. Natl. Acad. Sci. USA*, 89 (1992) 1320–1324.
[5] V.A. Fischetti, *Clin. Microbiol. Rev.*, 2 (1989) 285–314.
[6] J.B. Dale and E.H. Beachey, *J. Exp. Med.*, 162 (1985) 583–591.
[7] I. Goldstein, P. Rebeyrotte, J. Parlebas, and B. Halpern, *Nature*, 219 (1968) 866–868.
[8] I. Goldstein, L. Scebat, J. Renais, P. Hadjinsky, and J. Dutartre, *Israel J. Med. Sci.*, 19 (1983) 483–490.
[9] B.M. Pinto, *ACS Symp. Ser.*, 519 (1992) ch. 9, 111–131.
[10] J.E. Colingan, T.J. Kindt, and R.M. Krause, *Immunochemistry*, 15 (1978) 755–760.
[11] D.H. Huang, N.R. Krishna, and D.G. Pritchard, *Carbohydr. Res.*, 155 (1986) 193–199.
[12] K.B. Reimer and B.M. Pinto, *J. Chem. Soc., Perkin Trans 1*, (1988) 2103–2111.
[13] J.S. Andrews and B.M. Pinto, *J. Chem. Soc., Perkin Trans 1*, (1990) 1785–1792.
[14] B.M. Pinto, K.B. Reimer, and A. Tixidre, *Carbohydr. Res.*, 210 (1991) 199–219.
[15] K.B. Reimer, S.L. Harris, V. Varma, and B.M. Pinto, *Carbohydr. Res.*, 228 (1992) 399–414.
[16] J.R. Mariño-Albernas, S.L. Harris, V. Varma, and B.M. Pinto, *Carbohydr. Res.*, 245 (1993) 245–257.
[17] B.M. Pinto, D.G. Morissette, and D.R. Bundle, *J. Chem. Soc., Perkin Trans 1*, (1987) 9–14.
[18] G.O. Aspinall, A.M. Crane, D.W. Gammon, I.H. Ibrahim, N.K. Khare, D. Chatterjee, B. Rivoire, and P.J. Brennan, *Carbohydr. Res.*, 216 (1991) 337–355.

[19] P.A. Gent and R. Gigg, *J. Chem. Soc., Chem. Commun.*, (1974) 277–278.
[20] S. Sato, Y. Ito, T. Nukuda, Y. Nakahara, and T. Ogawa, *Carbohydr. Res.*, 167 (1987) 197–210.
[21] N.E. Byramova, M.V. Ovchinnikov, L.V. Backinowski, and N.K. Kochetkov, *Carbohydr. Res.*, 124 (1983) c8–c10.
[22] O. Kanie, S.C. Crawley, M.M. Palcic, and O. Hindsgaul, *Carbohydr. Res.*, 243 (1993) 139–164.
[23] K. Bock and C. Pedersen, *J. Chem. Soc., Perkin Trans. 2*, (1974) 293–297.
[24] D.R. Bundle, T. Iversen, and S. Josephson, *Am. Lab.*, 12 (1980) 93–98.
[25] D.D. Perrin and W.L.F. Armarego, *Purification of Laboratory Chemicals*, 3rd ed., Pergamon Press, London, 1988.