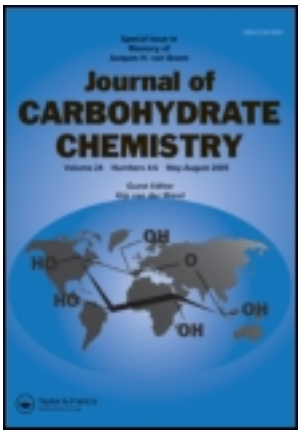

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SYNTHESIS OF THE METHYL GLYCOSIDES OF A DI- AND TWO TRISACCHARIDE FRAGMENTS SPECIFIC FOR THE *Shigella flexneri* SEROTYPE 2a *O*-ANTIGEN[1]

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ABSTRACT

The stereocontrolled synthesis of methyl α-D-glucopyranosyl-(1→4)-α-L-rhamnopyranoside (**EC**, **1**), methyl α-L-rhamnopyranosyl-(1→3)-[α-D-glucopyranosyl-(1→4)]-α-L-rhamnopyranoside (**B(E)C**, **3**) and methyl α-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranoside (**ECD**, **4**) is described; these constitute the methyl glycosides of branched and linear fragments of the *O*-specific polysaccharide of *Shigella flexneri* serotype 2a. Emphasis was put on the construction of the 1,2-cis **EC** glycosidic linkage resulting in the selection of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl fluoride (**8**) as the donor. Condensation of methyl 2,3-*O*-isopropylidene-4-*O*-trimethylsilyl-α-L-rhamnopyranoside (**11**) and **8** afforded the fully protected αE-disaccharide **20**, as a common intermediate in the synthesis of **1** and **3**, together with the corresponding βE-anomer **21**. Deacetalation and regioselective benzoylation of **20**, followed by glycosylation with 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate (**15**) afforded the branched trisaccharide **25**. Full deprotection of **20** and **25** afforded the targets **1** and **3**, respectively. The corresponding βE-disaccharide, namely, methyl β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranoside (**βEC**, **2**) was prepared analogously from **21**. Two routes to trisaccharide **4** were considered. Route 1 involved the coupling of a precursor to residue **E** and a disaccharide **CD**. Route 2 was based on the condensation of an appropriate **EC** donor and a precursor to residue **D**. The former route afforded a 1:2 mixture of the αE and βE condensation products which could not be separated, neither

at this stage, nor after deacetalation. In route 2, the required αE-anomer was isolated at the disaccharide stage and transformed into 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate (**48**) as the EC donor. Methyl 2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyran-oside (**19**) was preferred to its benzylidene analogue as the precursor to residue **D**. Condensation of **19** and **48** and stepwise deprotection of the glycosylation product afforded the target **4**.

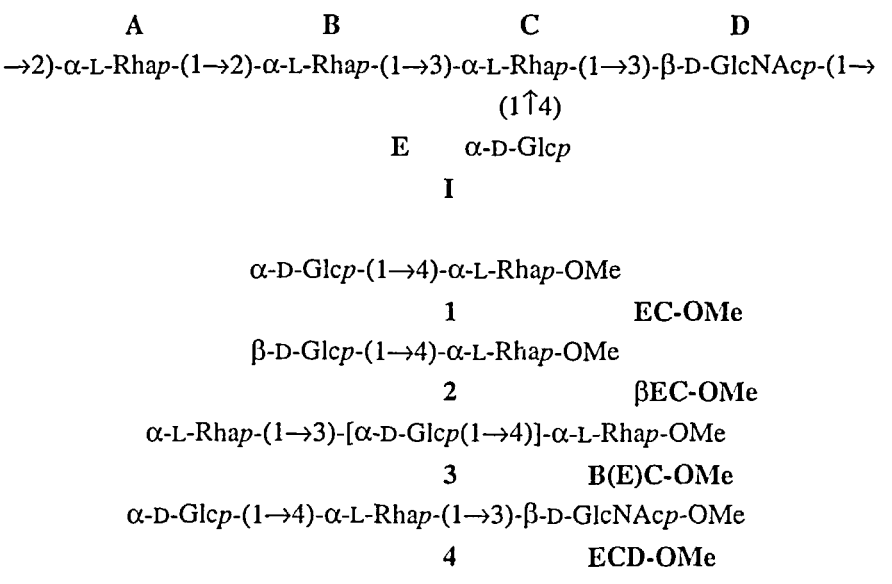
INTRODUCTION

Shigella flexneri serotype 2a is a common infective agent in humans that is responsible for the endemic form of shigellosis, a dysenteric syndrome characterised by bacterial invasion of the human colonic mucosa.[2] Despite several ongoing approaches in the development of a vaccine against this Gram-negative bacillus,[3-5] no licensed vaccine is available yet. However, shigellosis is a priority target as defined by the World Health Organisation (WHO), in its program for the development of vaccines against enteric diseases. Shigellosis causes a high rate of mortality among young infants (under two years of age) in developing countries. This is of high concern and has to be taken into consideration in any vaccine development program. For that matter, the vaccine subunit approach, based on the bacterial surface polysaccharide antigen, appears promising. Indeed, such an approach using protein conjugates of the bacterium's capsular polysaccharide (CP), has proven particularly efficient in infants, in the case of *Haemophilus influenza* type b.[6] In the case of nonencapsulated bacteria, increasing evidence supports the hypothesis that serum antibodies against their *O*-specific polysaccharides (*O*-SPs) may confer protective immunity in humans.[7] In particular, in the case of *S. flexneri*, field studies as well as studies on experimental models showed that protection against infection is specific for the serotype of the strain,[8-10] which is defined by the structure of the *O*-SP. More recently, it was suggested that protein conjugates of the *O*-SP of several enteropathogenic bacteria might offer protection against the homologous strain.[11] Indeed, such an approach, resulting in encouraging results, has been evaluated in the case of *Shigella flexneri* serotype 2a.[12] Nevertheless, optimal features for such conjugates are not well understood.

Furthermore, it was demonstrated on the model bacterium *S. flexneri* serotype 5a, that local anti-*O*-SP secretory IgA antibodies are sufficient to confer protection if present prior to infection.[13] For these reasons, we anticipated that chemically defined constructs incorporating easily accessible mimics of the *O*-SP as B-epitopes conjugated to a T-helper carrier would result in potential anti-*Shigella* vaccines. In this

approach, potentially optimal mimics of the *O*-SP would derive from the study of the molecular specificity of the complementarity between the *O*-SP and protective antibodies raised against *S. flexneri* serotype 2a. Thus, to help the design of optimal vaccine conjugates, such a study is under investigation in this laboratory. For that reason, several oligosaccharides representative of the *O*-SP of this bacterium were required in rather large quantities. Thus, in spite of the large amount of synthetic work on fragments of the *O*-SP of various bacteria of the *Shigella flexneri* family reported before by D. R. Bundle's group[14,15] and N. K. Kochetkov's group,[16,17] the synthesis of the required oligosaccharides was undertaken.

S. flexneri serotype 2a is defined by its branched pentasaccharide repeating unit[18,19] **I**, containing α-linked L-rhamnose, β-linked *N*-acetyl-D-glucosamine, and α-D-glucose branches as the monosaccharide constituents. As part of this project, we describe herein the synthesis of the **EC**, **B(E)C** and **ECD** fragments. They were synthesised as their methyl glycoside **1**,[20,21] **3**, and **4**, respectively, to allow binding studies in solution. To gain more insight in the *O*-SP:antibody recognition processes, the known β-anomer[21] **βEC-OMe (2)** was synthesised as well.



RESULTS AND DISCUSSION

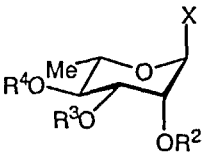
The approach used in this study is based on the synthesis of

heterofunctional, monosaccharide intermediates, which were then combined in a stepwise manner.

The monosaccharide intermediates.

D-Glucose: E unit. Commercially available 2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranose (**5**), allowing easy access to the bromide **6**,[22] the trichloroacetimidate **7**,[23,24] and the fluoride **8**,[25,26] was selected as the key precursor to residue **E**.

	X
5	OH
6	Br
7	$OC(NH)CCl_3$
8	F
9	$NHC(O)CCl_3$



	R^2	R^3	R^4	X
10	- iPr -		H	OMe
11	- iPr -		TMS	OMe
12	H	H	H	OAll
13	- iPr -		H	OAll
14	- iPr -		TMS	OAll
15	Bz	Bz	Bz	$OC(NH)CCl_3$
16	Ac	Ac	Ac	$OC(NH)CCl_3$

L-Rhamnose: C unit. Methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside[27] (**10**) has a temporary protecting group at position 2 and 3 which is easily removed in the presence of benzyl groups to allow chain elongation at position 3. Prepared in two steps from L-rhamnose, it was chosen as an appropriate precursor to the reducing end **C** residue. The corresponding trimethylsilylated **11** was also considered. As the anomeric allyl moiety is selectively removable, allyl α-L-rhamnopyranoside[28] (**12**) is a convenient precursor to residue **C** if involved in a block synthesis. It was converted into the 2,3-*O*-isopropylidene intermediate[29] **13**, which was eventually used as its trimethylsilylated analogue **14**.

L-Rhamnose: B unit. Based on the experience gained in the *S. flexneri* serotype 5a series,[30] the 2,3,4-tri-*O*-benzoyl-α-D-rhamnopyranosyl trichloroacetimidate[30,31] (**15**) was used as a chain terminator precursor, as well as the corresponding triacetate **16**.[32]

***N*-Acetyl-D-glucosamine: D unit.** Methyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**17**) was selectively converted into either its 4,6-*O*-benzylidene acetal[33] **18**,

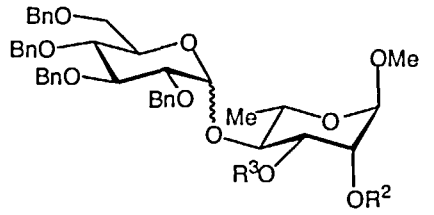
or the corresponding 4,6-*O*-isopropylidene acetal **19**. Both alcohols were used as precursors to residue **D**.

	R^3	R^4	R^6
17	H	H	H
18	H	- PhHC -	
19	H	- iPr -	

The E(B)C fragment, synthesis of disaccharide 1 and trisaccharide 3.

Considering the branched character of the glucose residue (**E**), special interest was put on the construction of the **EC** linkage. Optimised conditions were then applied to the synthesis of the branched trisaccharide **3**. For the latter, a retrosynthetic analysis showed that coupling of a donor **B** to a disaccharide **EC** was the most appropriate route. In that case, the α-D-glucopyranosyl linkage, the stereochemistry of which was the most difficult to control, was introduced first.

Assembly of disaccharide 1.

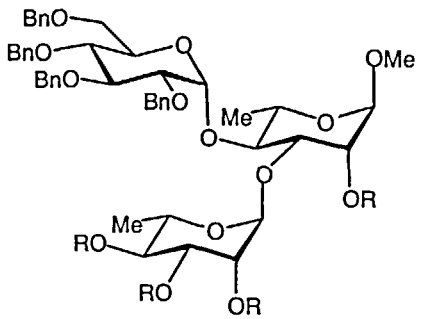


	R^2	R^3	α/β
20	- iPr -		α
21	- iPr -		β
22	H	H	α
23	H	H	β
24	Bz	H	α

Condensation of alcohol **10** was attempted with three different precursors to residue **E** following known procedures. Although successful in a closely related case,[34] Lemieux's procedure was not found satisfactory. Furthermore, use of the bromide **6**, in association with silver triflate as the promoter,[35] was found more promising than the combination of **6** and mercuric cyanide/mercuric bromide.[36] However, the 2:1 α/β selectivity of the coupling reaction was not satisfactory enough, nor was condensation of the trichloroacetimidate **7** and acceptor **10** in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf).[37] Next, emphasis was put on the fluoride **8**, a known convenient donor for the construction of α-D-glucopyranosidic linkages.[38] Attempted condensation with **10**, using TMSOTf or triflic anhydride (Tf_2O) as the promoter resulted in an acceptable α:β ratio but a rather

low yield. As reported earlier,[39] trimethylsilylation of the acceptor **10**, to give **11**, did overcome the poor nucleophilicity of the former. Overall, optimised coupling conditions yielded the α-D-disaccharide **20** in 56% yield, together with the β-anomer[40] **21** (24%). The α- and β-stereochemistry for the **EC** glycosidic linkage in **20** and **21**, respectively, was established by measuring the $^{1}J_{C\text{-}1,H\text{-}1}$ heteronuclear coupling constant. Compound **20** had $^{1}J_{C\text{-}1,H\text{-}1}$ equal to 173 Hz, and 169 Hz, whereas compound **21** had $^{1}J_{C\text{-}1,H\text{-}1}$ equal to 162 Hz, and 171 Hz, for residues **E** and **C**, respectively. Selective removal of the isopropylidene acetal of **20**, using 50% aq trifluoroacetic acid (TFA), afforded diol **22** (92%). The latter was debenzylated by conventional hydrogenolysis into the target disaccharide **1** (90%). Upon treatment with 80% aq AcOH, the fully protected **21** yielded diol **23** (83%), which was further hydrogenolyzed into the β-analogue **2** (88%).

Assembly of trisaccharide 3.



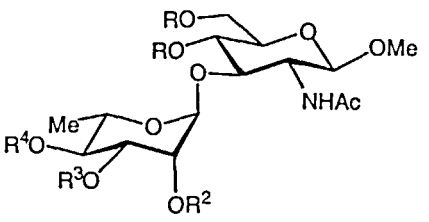
	R
25	Bz
26	H

The key diol intermediate **22** was regioselectively 2-*O*-benzoylated in two steps: (i) treatment with trimethyl *ortho*-benzoate under acid catalysis, and (ii) selective opening of the resulting 2,3-*O*-*ortho*-benzoate into **24** upon treatment with 50% aq TFA (86%). Glycosylation of the acceptor **24** with the trichloroacetimidate **15** under promotion by TMSOTf proceeded smoothly in diethyl ether to give the fully protected trisaccharide **25** in 93% yield. Debenzylation of the latter, using Pd-C as the catalyst, afforded the tetraol **26** (90%), which was debenzoylated into **3** (94%) under Zemplén conditions.

Study on the ECD fragment, synthesis of trisaccharide 4.

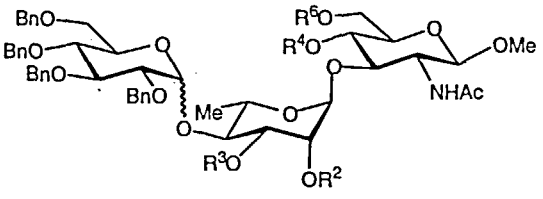
A retrosynthetic analysis showed that two routes to the target **4** could be considered, namely, the coupling of a donor **E** to a disaccharide **CD** (route 1), or the

condensation of a disaccharide donor **EC** to a **D** precursor (route 2). Both routes were undertaken, even though a mixture of αE and βE trisaccharide anomers could be anticipated in route 1.



	R^2	R^3	R^4	R,R
27	Bz	Bz	Bz	- PhHC -
28	H	H	H	- PhHC -
29	- iPr -		H	- PhHC -
30	Bz	Bz	Bz	- iPr -
31	Ac	Ac	Ac	- iPr -
32	H	H	H	- iPr -
33	- iPr -		H	- iPr -
34	Ac	Ac	Ac	- PhHC -

Route 1 is based on results obtained in the *S. flexneri* serotype 5a series.[30] In this series, the methyl α-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranoside trisaccharide was easily accessible upon extension of the chain at the nonreducing end. Analogously, the trichloroacetimidate **15** was condensed to the benzylidene precursor **18** in the presence of a catalytic amount of TMSOTf to afford the fully protected **CD** disaccharide **27** in 66% yield. Zemplén debenzoylation of **27** gave the triol **28** (97%), which was next selectively *O*-isopropylidenated into the intermediate **29** (75%). Attempted glycosylation of **29** with various precursors to residue **E**, namely compounds **8** and **9**, according to procedures that had proven successful at the disaccharide level, failed repeatedly. The starting acceptor **18** was always recovered, whereas the donor was either hydrolysed into the hemiacetal **5**, or transformed into the trichloroacetamide **9**. Formation of the latter rearrangement product, which had been reported before, was attributed to a highly unreactive acceptor.[41] These results were tentatively correlated to the structure of the acceptor. Indeed, the combination of the acetamido function and the benzylidene moiety renders **29** poorly soluble in diethyl ether. Although the solubility of **29** increased slightly when dichloromethane was used as the solvent, the products **35** (αE-anomer) and **36** (βE-anomer) resulting from the condensation of **29** and **7** were isolated as a mixture in a rather poor yield (14%). This result may be a consequence of the spatial arrangement of the acceptor, possibly leading to partial masking of HO-4_C. Indeed, based on an earlier observation[42] as well as on NMR data (see Table 1), it is assumed that **29** adopts a preferred conformation derived from the *exo*-anomeric effect.[43] This spatial arrangement resulted in anisotropic shielding of H-6_C by the phenyl ring of the benz-



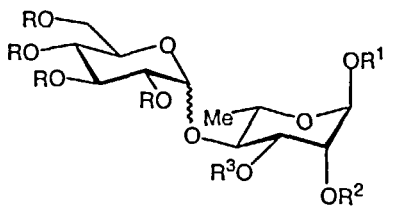
	R^2	R^3	R^4	R^6	α/β
35	-	iPr	- - CHPh	-	α
36	-	iPr	- - CHPh	-	β
37	-	iPr	- - iPr	-	α
38	-	iPr	- - iPr	-	β
39	Bz	Bz	- iPr	-	α
40	H	H	- iPr	-	α
41	H	H	H	H	α
42	H	H	H	H	β

ylidene moiety, which was confirmed by the upfield shift of the H-6_C doublet, as clearly seen in the ^{1}H NMR spectrum. It is assumed that this preferred conformation is not favourable for the introduction of the 2,3,4,6-tetra-*O*-α-D-benzyl glucopyranosyl moiety at position 4_C. Altogether, data show that the benzylidene moiety is not an appropriate protecting group for residue **D** in this particular case. For that reason, we turned to the preparation of the isopropylidene analogue **33** as the key precursor to block **CD** in the construction of the target **4**. Such a choice is supported by the fact that, analogous to the benzylidene moiety, the isopropylidene acetal can be easily introduced as a selective protecting group at *O*-4 and *O*-6 of the *N*-acetyl-D-glucosamine residue. Additional support derives from a previous comment stating that changing the benzylidene acetal for an isopropylidene one in a closely related **CD** construct, resulted in the disappearance of the upfield shift of the H-6_C.[44,45]

Table 1:

	H-6_C δ ppm (solvent)		H-6_C δ ppm (solvent)
27	0.75 ($CDCl_3$)	**30**	1.30 ($CDCl_3$)
34	0.60 ($CDCl_3$)[44]	**31**	1.15 ($CDCl_3$)
28	0.72 (DMSO-d_6)	**32**	1.05 (DMSO-d_6)
29	0.63 (DMSO-d_6)	**33**	1.06 (DMSO-d_6)

Conventional isopropylidenation of intermediate **17** using 2,2-dimethoxypropane gave acetal **19** in 71% yield. TMSOTf promoted condensation of **19** with either the tri-*O*-benzoylated donor **15** or the corresponding triacetate **16** gave the fully protected **CD** disaccharides **30** (87%) and **31** (81%), respectively. Zemplén debenzoylation of **30** resulted in the triol **32**, which was selectively blocked at *O*-2 and *O*-3 to give the di-*O*-isopropylidene acetal **33** (93% from **30**), which still proved to be



	R^1	R^2	R^3	R	α/β
43	All	- iPr -		Bn	α
44	All	- iPr -		Bn	β
45	All	H	H	Bn	α
46	All	OBz	OBz	Bn	α
47	H	OBz	OBz	Bn	α/β
48	$C(NH)CCl_3$	OBz	OBz	Bn	α

poorly soluble in diethyl ether. Thus, attempted glycosylation of the latter with the trichloroacetimidate donor **7**, was performed in anhydrous dichloromethane using a catalytic amount of TMSOTf as the promoter. The reaction proceeded smoothly to give the condensation products **37** and **38** as an inseparable mixture (73%). Conventional acidic hydrolysis of **37** and **38** resulted in a mixture of the corresponding tetraols **41** and **42** (74%). Again, separation of the two compounds at this stage was not possible. However, the approximate major/minor ratio could be extracted from the δ_{NH} in the ^1H NMR spectrum, while the correspondence major:β and minor:α was extracted from the ^{13}C NMR spectrum of the mixture by comparison with that of an authentic sample of **41**. The 1:2 ratio of **41** and **42** confirmed that route 1 was not the most appropriate for the preparation of the target **4**.

In route 2, the isopropylidene acceptor **19** was condensed to a convenient EC donor. Synthesis of the latter was inspired from the preparation of disaccharide **1**. Thus allyl α-L-rhamnopyranoside **12** was regioselectively isopropylidenated into the intermediate[29] **13**, which in turn was converted to the trimethylsilylated **14** (96%). Condensation of this precursor to residue **C** with the fluoride donor **8** was promoted by Tf_2O as described for the preparation of **20**, resulting in this case, in a 2.4:1 ratio of the αE[46] (**43**) and the βE (**44**) anomers, which were isolated in yields of 55% and 23%, respectively. One can notice that the yield of **43** is comparable to that obtained earlier using a different condensation procedure.[46] As in the methyl glycoside series, the stereochemistry of the EC linkage in **43** and **44** was ascertained based on the $^1J_{C\text{-}1,H\text{-}1}$ heteronuclear coupling constants. Data for compound **43** were 169 Hz and 169 Hz, data for compound **44** were 162 Hz and 168 Hz for residues **E** and **C**, respectively. Acidic hydrolysis of compound **43** then gave diol **45**,[46] resulting from the selective removal of the isopropylidene protecting group (95%). Conventional benzoylation of the latter furnished the fully protected intermediate **46** (90%), which was converted to the hemiacetal **47** (86%), following a two-step selective deallylation procedure involving (i) isomerisation of the allyl ether into the corresponding prop-1-enyl ether

using the cationic iridium complex and (ii) subsequent hydrolysis with mercury(II) bromide: mercury(II) oxide. Upon reaction with trichloroacetonitrile in the presence of a catalytic amount of DBU, the precursor **47** gave the crucial donor **48** (90%). Next, the trichloroacetimidate **48** was condensed to the 4,6-*O*-isopropylidene glucosaminyl intermediate **19** in the presence of a catalytic amount of TMSOTf as the promoter. When performed in anhydrous acetonitrile, the reaction proceeded smoothly to yield the fully protected trisaccharide **39** (74%). When $BF_3.Et_2O$ was used as the promoter, the glycosylation step was run in anhydrous dichloromethane to give the target **39** in a slightly improved yield of 81%. Zemplén debenzoylation of **39** gave diol **40** (98%), which was deacetalated into tetraol **41** upon aqueous acetic acid hydrolysis. Lastly, conventional debenzylation of **41**, using Pd-C as the catalyst afforded the target **4** (90%).

CONCLUSION

A **B** **C** **D'**

→2)-α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→3)-α-L-Rha*p*-(1→3)-α-D-GlcNAc*p*-(1→

(1↑4)

E α-D-Glc*p*

II

More recently, the structure of the repeating unit of the *O*-SP of *Serratia marcescens* O10 has been elucidated.[47] It is defined as the branched pentasaccharide **II**. It appears immediately that **I** and **II** only differ by the stereochemistry of the **DC** linkage. In fact, the C-1_D linkage is β in the *S. flexneri* series whereas it is α in the *S. marcescens* series. Consequently, fragments **1** and **3**, whose syntheses were described above are representative of fragments of both *O*-SPs. This could be of importance, as this once thought harmless Gram-negative bacterium is now known as being responsible for a number of serious infections occurring in hospitals. Thus, part of the work described herein may be relevant for similar studies concerning *S. marcescens* O10. In fact, while this work was in progress in our laboratory, a related synthetic approach was undertaken on the bacterium *S. marcescens* O10.[46]

EXPERIMENTAL

General Methods. General experimental methods not referred to in this section were as described previously.[30] Optical rotations were measured for $CHCl_3$ solutions at 25

°C, except where indicated otherwise, with a Perkin-Elmer automatic polarimeter, Model 241 MC. TLC on precoated slides of Silica Gel 60 F_{254} (Merck) was performed with solvent mixtures of appropriately adjusted polarity consisting of *A*, dichloromethane-methanol; *B*, cyclohexane-ethyl acetate, *C*, cyclohexane-acetone, *D*, cyclohexane-diethyl ether, *E*, toluene-ethyl acetate, *F*, toluene-acetone, *G*, water-acetonitrile. Detection was effected when applicable, with UV light, and/or by charring with orcinol (35 mM) in aq H_2SO_4 (4N). In the NMR spectra, of the two magnetically non-equivalent geminal protons at C-6, the one resonating at lower field is denoted H-6a and the one at higher field is denoted H-6b. Interchangeable assignments in the ^{13}C NMR spectra are marked with an asterisk in listing of signal assignments. Sugar residues in oligosaccharides are serially lettered according to the lettering of the repeating unit of the *O*-SP and identified by a subscript in listing of signal assignments. Low-resolution mass spectra were obtained by either chemical ionisation (CIMS) using NH_3 as the ionising gas or by electrospray mass spectrometry (ESMS).

Methyl 2-Acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (19). Camphorsulfonic acid (CSA, 650 mg, 2.8 mmol) was added to a suspension of methyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**17**, 2.68 g, 11.4 mmol) in a mixture of DMF (25 mL) and 2,2-dimethoxypropane (25 mL, 202 mmol), and the mixture was stirred at rt. After 4 h, TLC (solvent *A*, 17:3) showed that no starting material remained. Et_3N (5 mL) was added, stirring was pursued for 30 min, and volatiles were evaporated. The residue was column chromatographed (solvent *A*, 19:1) to give **19** (3.01 g, 96%) as a colourless foam; $[\alpha]_D$ –63° (*c* 1.0, methanol); ^1H NMR: δ 5.79 (d, 1H, $J_{NH,2}$ = 4.9 Hz, NH), 4.53 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1), 4.33 (d, 1H, $J_{OH,3}$ = 2.3 Hz, OH-3), 3.95 (dd, 1H, $J_{5,6a}$ = 5.8 Hz, H-6a), 3.92 (m, 1H, $J_{2,3}$ = 9.3 Hz, H-3), 3.81 (dd, 1H, $J_{6a,6b}$ = 10.4, $J_{5,6b}$ = 10.4 Hz, H-6b), 3.60 (dd, 1H, $J_{4,5}$ = 9.3 Hz, H-4), 3.51 (s, 3H, OCH_3), 3.47 (m, 1H, H-2), 3.31 (m, 1H, H-5), 2.01 (s, 3H, $C(=O)CH_3$), 1.54 (s, 3H, CCH_3), 1.45 (s, 3H, CCH_3). ^{13}C NMR: δ 172.1 (C=O), 101.7 (C-1), 99.8 (CHPh), 74.3 (C-4), 71.9 (C-3), 67.2 (C-5), 61.7 (C-6), 58.2 (C-2), 56.9 (OCH_3), 29.0 (CCH_3), 23.6 (NHAc), and 19.0 (CCH_3). CIMS for $C_{12}H_{21}NO_6$ (M, 275.3) *m/z* 276 $(M+H)^+$.

Anal. Calcd for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09%. Found: C, 52.15; H, 7.87; N, 5.11%.

Methyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (20) and Methyl (2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (21). (a) TMSOTf (90 μL, 0.46 mmol) was added to a solution of the acceptor[27] **10** (1.8 g, 8.25

mmol) and the trichloroacetimidate donor **7** (8.47 g, 12.38 mmol) in anhydrous diethyl ether (50 mL) at 0 °C, and the mixture was stirred at rt for 16 h. TLC (solvent *D*, 3:1) showed that the reaction was complete. The mixture was neutralised by addition of *sym*-collidine and concentrated. The residue was taken up in dichloromethane, washed successively with 5% aq $NaHCO_3$, 5% aq HCl, water and satd aq NaCl, dried and concentrated. Chromatography (solvent *D*, 17:3) gave the β-anomer **21** (659 mg, 11%). At this stage the α-anomer was contaminated by the rearrangement product[41] **9**. A new chromatography using solvent *C* (17:3) finally gave the fully protected disaccharide **20** (2.64 g, 43%), which crystallised on standing.

(b) A solution of alcohol **10** (3.47 g, 15.94 mmol) in dichloromethane (50 mL) was treated with pyridine (5.5 mL, 69.0 mmol) and trimethylsilyl chloride (6.11 mL, 47.8 mmol). After 2 h at rt, TLC (solvent *C*, 3:1) showed that the reaction was finished. Conventional work-up gave the crude trimethylsilylated **11** (4.53 g, 98%), which was used as such: ^{1}H NMR: δ 5.85 (s, 1H, H-1), 4.11 (d, 1H, $J_{2,3}$ = 5.8 Hz, H-2), 3.98 (dd, 1H, $J_{3,4}$ = 7.1 Hz, H-3), 3.57 (dq, 1H, H-5), 3.36 (s, 3H, OCH_3), 3.33 (dd, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 1.54 (s, 3H, CCH_3), 1.35 (s, 3H, CCH_3), 1.22 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 0.15 (s, 9H, $Si(CH_3)_3$).

Powdered MS (4Å, 60 g) were added to a solution of the fluoride **8** (13.17 g, 24.31 mmol) in anhydrous diethyl ether (90 mL), and the mixture was stirred for 1 h at rt, then cooled to 0 °C. Triflic anhydride (Tf_2O, 5.64 mL, 34.35 mmol) was added, and the mixture was then cooled to –25 °C. A solution of the acceptor **11** (4.53 g, 15.6 mmol) in anhydrous diethyl ether (90 mL) was added dropwise (1 h) at –25 °C, and stirring was continued for 16 h at 0 °C. TLC (solvent *D*, 3:1) showed complete disappearance of compound **11**. The mixture was neutralised by addition of *sym*-collidine, then filtered through a pad of Celite and the filtrate was concentrated. Usual work-up followed by chromatography (solvent *D*, 17:3) gave the β-anomer **21** (2.77 mg, 24%) as a colourless oil; $[\alpha]_D$ –13° (*c* 1.0), lit.[40] $[\alpha]_D$ –14° (*c* 2.5); ^{1}H NMR: δ 4.94 (dd, 1H, $J_{1,2}$ = 8.0 Hz, H-1_E), 4.93 (d, 1H, J = 11.1 Hz, OCH_2), 4.91 (d, 1H, J = 11.0 Hz, OCH_2), 4.89 (dd, 1H, H-1_C), 4.84 (d, 1H, J = 10.5 Hz, OCH_2), 4.79 (d, 1H, OCH_2), 4.71 (d, 1H, OCH_2), 4.64 (d, 1H, J = 12.3 Hz, OCH_2), 4.60 (d, 1H, OCH_2), 4.56 (d, 1H, OCH_2), 4.24 (dd, 1H, $J_{3,4}$ = 6.3 Hz, H-3_C), 4.11 (d, 1H, $J_{2,3}$ = 5.6 Hz, H-2_C), 3.77-3.64 (m, 6H, H-3_E, 4_E, $6a_E$, $6b_E$, 4_C, 5_C), 3.45-3.41 (m, 2H, H-2_E, 5_E), 3.41 (s, 3H, OCH_3), 1.48 (s, 3H, CCH_3), 1.36 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6_C), and 1.34 (s, 3H, CCH_3). ^{13}C NMR: δ 138.7-127.3 (Ph), 109.2 (CMe_2), 101.4 (C-1_E, $J_{C,H}$ = 162 Hz), 97.9 (C-1_C, $J_{C,H}$ = 171 Hz), 84.6 (C-4_C), 83.2 (C-2_E), 78.0 (2C, C-3_C, 3_E), 77.7 (C-4_E), 75.8 (C-2_C), 75.4 (OCH_2), 74.7 (2C, C-5_E, OCH_2), 74.7, 74.5 (2C, OCH_2), 68.5 (C-6_E), 64.1 (C-5_C), 54.7 (OCH_3), 27.7, 26.2 (2C, CCH_3), and 17.6 (C-6_C). CIMS for $C_{44}H_{52}O_{10}$ (M, 740.4) *m/z* 758 $(M+NH_4)^+$.

Eluted next was the target **20** (11.8 g, 56%); mp 85-86°C (from isopropyl ether:petroleum ether), $[\alpha]_D$ +35° (*c* 1.0); ^{1}H NMR: δ 7.41-7.15 (m, 20H, Ph), 4.98 (dd, 1H, H-1_E), 4.96 (d, 1H, J = 10.7 Hz, OCH_2), 4.86 (d, 1H, OH_2), 4.85 (d, 1H, J = 9.6 Hz, OCH_2), 4.83 (s, 1H, H-1_C), 4.80 (d, 1H, J = 12.0 Hz, OCH_2), 4.71 (d, 1H, OCH_2), 4.57 (d, 1H, J = 12.1 Hz, OCH_2), 4.53 (d, 1H, OCH_2), 4.50 (d, 1H, OCH_2), 4.05-4.12 (m, 3H, H-3_C, 5_E, 2_C), 3.98 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3_E), 3.81 (dd, 1H, $J_{6a,6b}$ = 10.1 Hz, H-$6a_E$), 3.79 (dd, 1H, $J_{4,5}$ = 9.7 Hz, H-4_E), 3.75 (dq, 1H, $J_{5,6}$ = 6.2 Hz, H-5_C), 3.66 (dd, 1H, $J_{5,6}$ = 1.8 Hz, H-$6b_E$), 3.60 (dd, 1H, $J_{1,2}$ = 3.6, $J_{2,3}$ = 9.8 Hz, H-2_E), 3.34 (s, 3H, OCH_3), 3.33 (dd, 1H, $J_{3,4}$ = 7.2, $J_{4,5}$ = 9.8 Hz, H-4_C), 1.44 (s, 3H, iPr), and 1.31 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6_C), 1.25 (s, 3H, iPr). ^{13}C NMR: δ 138.4-127.5 (Ph), 99.8 (C-1_C, $J_{C,H}$ = 169 Hz), 98.8 (C-1_E, $J_{C,H}$ = 173 Hz), 85.6 (C-4_C), 81.5 (C-3_E), 79.7 (C-2_E), 77.7 (C-4_E), 75.6, 75.00, 73.4, 73.3 (4C, OCH_2), 71.1 (C-5_E), 70.6 (C-2_C), 69.7 (C-3_C), 68.5 (C-6_E), 65.7 (C-5_C), 54.7 (OCH_3), and 17.7 (C-6_C). CIMS for $C_{44}H_{52}O_{10}$ (M, 740.4) *m/z* 758 $(M+NH_4)^+$.

Anal. Calcd for $C_{44}H_{52}O_{10}$: C, 71.35; H, 7.03%. Found: C, 71.21; H, 7.01%.

Methyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→ 4)-α-L-rhamnopyranoside (22). (a) Water (47 mL) was added to a solution of **20** (11.8 g, 15.9 mmol) in acetic acid (190 mL), and the mixture was stirred at 60 °C. After 4 h, TLC (solvent *C*: 4:1) showed that only a little starting material remained. The mixture was allowed to come back to rt, then concentrated to dryness by repeated coevaporation with toluene and cyclohexane. Chromatography of the residue (solvent *C*, 17:3) gave **22** (9.46 g, 85%) as a colourless oil.

(b) 50% Aq trifluoroacetic acid (TFA, 11 mL) was added, at 0 °C, to a solution of disaccharide **20** (1.58 g, 2.13 mmol) in dichloromethane (340 mL). The mixture was stirred vigorously at 0 °C for 3 h, when TLC (solvent *C*, 3:1) showed that only very little starting material remained. Volatiles were evaporated, and column chromatography (solvent *C*, 17:3) of the residue gave diol **22** (1.37 g, 92%); $[\alpha]_D$ +10° (*c* 1.0); ^{1}H NMR: δ 7.40-7.07 (m, 20H, Ph), 4.97 (d, 1H, J = 10.8 Hz, OCH_2), 4.83 (dd, 1H, $J_{1,2}$ = 3.5 Hz, H-1_E), 4.82 (d, 1H, J = 11.0 Hz, OCH_2), 4.81 (d, 1H, OCH_2), 4.76 (d, 1H, J = 11.9 Hz, OCH_2), 4.71 (s, 1H, H-1_C), 4.66 (d, 1H, OCH_2), 4.58 (d, 1H, J = 12.2 Hz, OCH_2), 4.51 (d, 1H, OCH_2), 4.49 (d, 1H, OCH_2), 4.03 (ddd, 1H, H-5_E), 3.99 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3_E), 3.86 (dd, 1H, $J_{2,3}$ = 9.3, $J_{3,4}$ = 9.3 Hz, H-2_C), 3.78-3.72 (m, 2H, H-3_C, 5_C), 3.67 (dd, 1H, H-$6a_E$), 3.63 (dd, 1H, $J_{5,6b}$ = 8.8, $J_{6a,6b}$ = 2.0 Hz, H-$6b_E$), 3.60 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2_E), 3.55 (dd, 1H, $J_{4,5}$ = 9.8 Hz, H-4_E), 3.38 (s, 3H, OCH_3), 3.35 (dd, 1H, $J_{3,4}$ = 9.1, $J_{4,5}$ = 9.1 Hz, H-4_C), 2.66, 2.65 (2 s, 2H, OH-2_C, OH-3_C), and 1.42 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6_C). ^{13}C NMR: δ 138.4-127.5 (Ph), 99.8 (C-1_C), 98.8 (C-1_E), 85.6 (C-4_C), 81.5 (C-3_E), 79.7 (C-2_E), 77.7 (C-4_E), 75.6, 75.0,

73.4, 73.3 (4C, OCH_2), 71.1 (C-5_E), 70.6 (C-2_C), 69.7 (C-3_C), 68.5 (C-6_E), 65.7 (C-5_C), 54.7 (OCH_3), and 17.7 (C-6_C). CIMS for $C_{41}H_{48}O_{10}$ (M, 700.3) *m/z* 718 $(M+NH_4)^+$.

Anal. Calcd for $C_{41}H_{48}O_{10}$: C, 70.27; H, 6.90%. Found: C, 70.24; H, 6.94%.

Methyl (2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-(1→ 4)-α-L-rhamnopyranoside (23). Water (3.5 mL) was added to a solution of **21** (863 mg, 1.16 mmol) in acetic acid (14 mL), and the mixture was stirred at 60 °C. After 4 h, TLC (solvent *C*: 4:1) showed that no starting material remained. The mixture was allowed to come back to rt, then concentrated to dryness by repeated coevaporation with toluene and cyclohexane. Chromatography of the residue (solvent *C*, 17:3) gave **23** (673 mg, 83%) as a colourless oil; $[\alpha]_D$ –208° (*c* 0.7); ^1H NMR: δ 7.35-7.13 (m, 20H, Ph), 4.96-4.54 (m, 8H, OCH_2), 4.68 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-1_C), 4.61 (d, overlapped, 1H, H-1_E), 3.90 (bs, 1H, H-2_C), 3.78 (dd, partially overlapped, 1H, H-3_C), 3.77-3.65 (m, 5H, H-$6a_E$, $6b_E$, 3_E, 4_E, 5_C), 3.53 (dd, 1H, $J_{3,4}$ = 10.3, $J_{4,5}$ = 9.8 Hz, H-4_C), 3.49 (dd, overlapped, 1H, H-2_E), 3.45 (m, 1H, H-5_E), 3.39 (s, 3H, OCH_3), 2.46 (bs, 1H, OH-2_C), 1.67 (s, 1H, OH-3_C), and 1.41 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6_C). ^{13}C NMR: δ 138.3-127.7 (Ph), 104.1 (C-1_E), 100.4 (C-1_C), 85.3 (C-3_E*), 83.6 (C-4_C), 82.3 (C-2_E), 78.0 (C-4_E*), 75.7, 75.6 (2C, OCH_2), 75.0 (2C, OCH_2, C-5_E), 73.5 (OCH_2), 71.4 (C-3_C), 70.8 (C-2_C), 68.6 (C-6_E), 66.2 (C-5_C), 54.9 (OCH_3), and 17.7 (C-6_C). CIMS for $C_{41}H_{48}O_{10}$ (M, 700.3) *m/z* 718 $(M+NH_4)^+$.

Anal. Calcd for $C_{41}H_{48}O_{10}$: C, 70.28; H, 6.86%. Found: C, 70.24; H, 6.88%.

Methyl α-D-Glucopyranosyl-(1→4)-α-L-rhamnopyranoside (1). To a solution of the diol **22** (438 mg, 625 μmol) in a mixture of ethanol and acetic acid (20 mL, 9:1) was added 10% Pd-C catalyst (300 mg). The suspension was stirred under a hydrogen atmosphere. After 72 h, TLC (solvent *A*:, 3:1) showed that the reaction was complete. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. To eliminate any residual trace of catalyst, the residue was chromatographed on a short column of silica gel (solvent *A*, 4:1) to give the free disaccharide **1** (191 mg, 90%) as a colourless foam; $[\alpha]_D$ +41° (*c* 1.5, water), $[\alpha]_D$ +47° (*c* 1.5, MeOH), lit.[21] $[\alpha]_D$ +42° (*c* 1.0, water), $[\alpha]_D$ +38° (*c* 1.0, MeOH), lit.[20] $[\alpha]_D$ +43° (*c* 1.2, MeOH); the ^1H and ^{13}C NMR spectra were identical to those described in ref. 21. CIMS for $C_{13}H_{24}O_{10}$ (M, 340.3) *m/z* 358 $(M+NH_4)^+$.

Methyl β-D-Glucopyranosyl-(1→4)-α-L-rhamnopyranoside (2). The diol **23** (200 mg, 285 μmol) was hydrogenolyzed as described for the preparation of **1**. Column chromatography of the residue (solvent *A*, 4:1) gave the free β-anomer **2** (88 mg, 91%) as a white powder; $[\alpha]_D$ -32° (*c* 1.0, MeOH). The ^1H and ^{13}C NMR spectra were identical to those described in ref. 21. CIMS for $C_{13}H_{24}O_{10}$ (M, 340.3) *m/z* 358 $(M+NH_4)^+$.

Methyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-2-*O*-benzoyl-α-L-rhamnopyranoside (24). Trimethyl orthobenzoate (25.2 mL, 146.8 mmol) and CSA (2.65 g, 11.4 mmol) were added to a solution of **22** (20.56 g, 29.4 mmol) in anhydrous dichloromethane (150 mL). After stirring for 1 h at rt, TLC (solvent *C*, 7:3) showed the complete disappearance of **22** and the presence of a less polar product. The mixture was concentrated, and the residue was dissolved in $CHCl_3$ (50 mL). The solution was cooled to 0 °C, 50% aq trifluoroacetic acid (TFA, 5.0 mL, 32 mmol) was added, and the mixture was stirred for 15 min at this temperature. As TLC (solvent *C*, 3:1) showed that hydrolysis was completed, volatiles were evaporated. The residue was taken up in dichloromethane and washed successively with 5% aq $NaHCO_3$, water and satd aq NaCl. Concentration of the organic phase followed by chromatography of the residue (solvent *C*, 9:1) gave **24** (20.4 g, 86%) as a colourless foam. $[\alpha]_D$ +40° (*c* 1.0); ^1H NMR: δ 8.07-7.13 (m, 25H, Ph), 5.37 (dd, 1H, $J_{1,2}$ = 1.4 Hz, H-2_C), 4.97 (d, 1H, J = 10.9 Hz, OCH_2), 4.83 (m, 2H, 2 OCH_2), 4.81 (dd, 1H, $J_{1,2}$ = 2.59 Hz, H-1_E), 4.79 (d, 1H, J = 11.8 Hz, OCH_2), 4.77 (dd, 1H, H-1_C), 4.70 (d, 1H, OCH_2), 4.54 (d, 1H, J = 12.1 Hz, OCH_2), 4.47 (d, 1H, J = 11.0 Hz, OCH_2), 4.42 (d, 1H, OCH_2), 4.09 (m, 1H, H-5_E), 4.07 (dd, 1H, $J_{2,3}$ = 3.5 Hz, H-3_C), 3.98 (dd, 1H, $J_{2,3}$ = 9.3, $J_{3,4}$ = 9.3 Hz, H-3_E), 3.82 (dq, 1H, $J_{4,5}$ = 9.3 Hz, H-5_C), 3.63-3.58 (m, 3H, H-$6a_E$, $6b_E$, 2_E), 3.57 (dd, 1H, $J_{4,5}$ = 9.8 Hz, H-4_E), 3.49 (dd, 1H, $J_{3,4}$ = 9.1 Hz, H-4_C), 3.40 (s, 3H, OCH_3), and 1.45 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6_C). ^{13}C NMR (D_2O): δ 165.7 (C=0), 138.6-127.6 (Ph), 98.6 (C-1_E), 98.3 (C-1_C), 85.3 (C-4_C), 81.7 (C-3_E), 80.0 (C-2_E), 77.8 (C-4_E), 75.7, 75.1, 73.7, 73.5 (4C, CH_2Ph), 72.5 (C-2_C), 71.2 (C-5_E), 68.5 (C-6_E), 68.3 (C-3_C), 66.4 (C-5_C), 55.0 (OCH_3), and 18.0 (C-6_C). CIMS for $C_{48}H_{52}O_{11}$ (M, 804.4) *m/z* 822 $(M+NH_4)^+$.

Anal. Calcd for $C_{48}H_{52}O_{11}$: C, 71.64; H, 6.47%. Found: C, 71.59; H, 6.49%.

Methyl (2,3,4-Tri-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-[(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl-(1→4)]-2-*O*-benzoyl-α-L-rhamnopyranoside (25). TMSOTf (121 μL, 628 μmol) was added to a mixture of the disaccharide acceptor **24** (1.0 g, 1.24 mmol) and trichloroacetimidate donor[31] **15** (1.13 g, 1.86 mmol) in anhydrous diethyl ether (50 mL), at –50 °C. The mixture was stirred overnight while the cooling bath was slowly allowed to come back to 5 °C. TLC (solvent *B*, 7:3) showed the total disappearance of **24**. The mixture was neutralised by addition of *sym*-collidine, and volatiles were evaporated. Chromatography of the residue (solvent *E*, 99:1) gave the condensation product **25** (1.45 g, 93%) as a colourless foam; $[\alpha]_D$ +73° (*c* 1.0); ^1H NMR: δ 8.21-7.02 (m, 40H, Ph), 6.00 (dd, 1H, H-2_B), 5.70 (dd, 1H, $J_{2,3}$ = 3.0, $J_{3,4}$ = 10.0 Hz, H-3_B), 5.49 (dd, 1H, $J_{4,5}$ = 9.8 Hz, H-4_B), 5.43 (d, 1H, H-1_B), 5.40 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1_E), 5.33 (dd, 1H, $J_{1,2}$ = 1.9, $J_{2,3}$ = 3.3 Hz, H-2_C), 5.00 (d, 1H,

J = 11.0 Hz, OCH_2), 4.92 (d,1H, J = 11.3 Hz, OCH_2), 4.90 (s, 1H, H-1_C), 4.88 (d, 1H, OCH_2), 4.82 (d, 1H, OCH_2), 4.75 (d, 1H, J = 10.8 Hz, OCH_2), 4.37 (d, 1H, OCH_2), 4.32-4.26 (m, 3H, H-3_C, 2 OCH_2), 4.16 (m, 1H, $J_{4,5}$ = 10.2 Hz, H-5_E), 4.10 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-3_E), 3.97 (dq, 1H, $J_{4,5}$ = 9.7 Hz, H-5_B), 3.88-3.83 (m, 2H, H-5_C, 4_C), 3.72-3.67 (m, 3H, $J_{5,6}$ = 1.9 Hz, H-2_E, $6a_E$, $6b_E$), 3.50 (dd, 1H, $J_{3,4}$ = 9.5 Hz, H-4_E), 3.44 (s, 3H, OCH_3), 1.45 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6_C), and 1.15 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6_B). ^{13}C NMR: δ 166.1-164.8 (4C, C=O); 138.8-127.7 (Ph), 100.2 (C-1_B, $J_{C,H}$ = 170 Hz), 97.6 (C-1_C, $J_{C,H}$ = 171 Hz), 97.2 (C-1_E, $J_{C,H}$ = 170 Hz), 81.5 (C-3_E), 80.9 (C-2_E), 79.5 (C-3_C), 78.3 (C-4_C), 77.9 (C-4_E), 75.3, 74.8, 73.6 (3C, OCH_2), 73.0 (C-2_C), 72.5 (OCH_2), 71.6 (C-4_B), 71.4 (C-5_E), 70.3 (C-2_B), 70.0 (C-3_B), 68.9 (C-6_E), 67.2 (C-5_B), 66.9 (C-5_C), 54.9 (OCH_3), 18.6 (C-6_C), and 17.2 (C-6_B). CIMS for $C_{75}H_{74}O_{18}$ (M, 1262.5) *m/z* 1280.7 $(M+NH_4)^+$.

Anal. Calcd for $C_{75}H_{74}O_{18}$: C, 71.30; H, 5.90%. Found: C, 71.32; H, 5.93%.

Methyl (2,3,4-Tri-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-[(α-D-glucopyranosyl-(1→4)]-2-*O*-benzoyl-α-L-rhamnopyranoside (26). Compound **25** (604 mg, 478 μmol) was treated with 10% Pd-C catalyst (600 mg) in a 9:1 mixture of ethanol: acetic acid (24 mL) as described for the preparation of **1**. Column chromatography (solvent *A*, 4:1) afforded **26** (388 mg, 90%) as a colourless foam; $[\alpha]_D$ +118° (*c* 1.0); ^1H NMR: δ 8.21-7.20 (m, 20H, Ph), 5.93 (s, 1H, H-2_B), 5.63 (dd, 1H, $J_{2,3}$ = 2.9, $J_{3,4}$ = 10.0 Hz, H-3_E), 5.54 (dd, 1H, $J_{4,5}$ = 9.7 Hz, H-4_B), 5.47 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1_E), 5.34 (dd, 1H, H-2_C), 5.23 (s, 1H, H-1_B), 4.86 (d, 1H, $J_{1,2}$ = 1.3 Hz, H-1_C), 4.26 (dd, 1H, $J_{2,3}$ = 3.4, $J_{3,4}$ = 8.8 Hz, H-3_C), 4.08 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-4_C), 4.05 (s, 1H, OH), 4.03 (d, 1H, $J_{5,6b}$ = 9.02 Hz, H-$6b_E$), 4.02 (bs, 1H, OH), 4.00 (dq, 1H, H-5_B), 3.95 (ddd, 1H, H-5_E), 3.88 (dd, 1H, H-3_E), 3.88 (s, 1H, OH), 3.87 (d, 1H, $J_{6a,5}$ = 9.1 Hz, H-$6a_E$), 3.83 (dq, 1H, H-5_C), 3.66 (m, 2H, H-2_E, 4_E), 3.37 (s, 3H, OCH_3), 1.47 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6_C), and 1.13 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6_B); ^{13}C δ 166.5 (4C, C=O), 133.9-128.34 (Ph), 100.0 (C-1_B), 98.9 (C-1_E), 97.7 (C-1_C), 79.8 (C-3_C), 77.9 (C-4_C), 74.1 (C-3_E), 73.1 (2C, C-5_E, 2_C), 72.7 (C-2_E), 71.3 (C-4_B), 70.8 (C-2_B), 70.4 (C-3_B), 70.2 (C-4_E), 67.6 (C-5_B), 67.3 (C-5_C), 61.8 (C-6_E), 55.2 (OCH_3), 19.0 (C-6_C), and 17.3 (C-6_B). CIMS for $C_{47}H_{50}O_{18}$ (M, 902.3) *m/z* 920.5 $(M+NH_4)^+$.

Anal. Calcd for $C_{47}H_{50}O_{18}$: C, 62.52; H, 5.58%. Found: C, 62.59; H, 5.71%.

Methyl α-L-Rhamnopyranosyl-(1→3)-[α-D-glucopyranosyl-(1→4)]-α-L-rhamnopyranoside (3). 1M Methanolic sodium methoxide was added dropwise to a solution of **26** (435 mg, 0.48 mmol) in methanol (15 mL) until the mixture became alkaline (pH=10). After stirring at rt for 24 h, TLC (solvent *A*, 4:1) showed that the reaction was completed. The mixture was neutralised by addition of Amberlite IR-120 (H^+), then filtered and concentrated. The residue was taken up in water and extracted

several times with chloroform. The aqueous phase was lyophilised, and the residue was purified by reverse-phase chromatography (solvent *G*, gradient) to give the branched trisaccharide **3** (210 mg, 94 %) as a white powder; $[\alpha]_D$ +5° (*c* 1.0, methanol), $[\alpha]_D$ +4° (*c* 1.0, water); ^{1}H NMR (D_2O): δ 5.19 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1_E), 4.99 (s, 1H, H-1_B), 4.65 (d, 1H, $J_{1,2}$ = 2.1 Hz, H-1_C), 4.04 (m, 2H, H-2_C, 2_B), 3.94 (dd, 1H, $J_{2,3}$ = 3.1, $J_{3,4}$ = 9.0 Hz, H-3_C), 3.91-3.83 (m, 5H, H-5_E, 5_B, $6a_E$, $6b_E$, 5_C), 3.80 (dd, 1H, $J_{3,4}$ = 9.5, $J_{2,3}$ = 2.7 Hz, H-3_B), 3.75 (dd, 1H, $J_{4,5}$ = 10.0 Hz, H-4_C), 3.68 (dd, 1H, $J_{3,4}$ = 9.5 Hz, H-3_E), 3.55 (dd, 1H, $J_{2,3}$ = 10.0 Hz, H-2_E), 3.46 (dd, 1H, $J_{4,5}$ = 9.7 Hz, H-4_B), 3.45 (dd, 1H, $J_{4,5}$ = 9.5 Hz, H-4_E), 3.41 (s, 3H, OCH_3), 1.42 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6_B), and 1.28 (d, 1H, $J_{5,6}$ = 6.2 Hz, H-6_C); ^{13}C NMR (D_2O): δ 103.2 (C-1_B, $J_{C,H}$ = 170 Hz), 100.9 (C-1_C, $J_{C,H}$ = 170 Hz), 98.9 (C-1_E, $J_{C,H}$ = 170 Hz), 79.2 (C-3_C), 76.9 (C-4_C), 73.0 (C-3_E), 72.5 (2C, C-4_E, 5_E*), 71.9 (C-2_E), 70.7 (C-3_B), 70.5 (2C, C-2_B, 2_C), 69.8 (C-4_B), 69.7 (C-5_C*), 68.9 (C-5_B), 60.9 (C-6_E), 55.4 (OCH_3), 18.3 (C-6_C), and 17.0 (C-6_B); ESMS for $C_{19}H_{34}O_{14}$ (M, 486.2) *m/z* 504 $(M+NH_4)^+$.

Anal. Calcd for $C_{19}H_{34}O_{14}\cdot H_2O$: C, 45.24; H, 7.19%. Found: C, 44.96; H, 6.97%.

Methyl (2,3,4-Tri-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-benzylidene-β-D-glucopyranoside (27). TMSOTf (110 μL) was added, at 0 °C, to a mixture of the known benzylidene alcohol[33] **18** (1.0 g, 3.15 mmol) and the trichloroacetimidate donor[31] **15** (2.44 g, 4.0 mmol) in anhydrous dichloromethane (75 mL). The reaction mixture was stirred at rt for 16 h, after which time, TLC (solvent *A*, 24:1) showed that very little **18** remained. Et_3N (500 μL) was added, and volatiles were evaporated. Chromatography of the residue (solvent *F*, 4:1) gave the fully protected disaccharide **27** (1.63 g, 66%) as a colourless foam which could be crystallised from diethyl ether; mp 248.0-248.5 °C, $[\alpha]_D$ +66° (*c* 1.0); ^{1}H NMR: δ 8.07-7.21 (m, 20H, Ph), 6.00 (d, 1H, $J_{NH,2}$ = 6.9 Hz, NH), 5.78 (dd, 1H, $J_{2,3}$ = 3.4, $J_{3,4}$ = 10.1 Hz, H-3_C), 5.63 (s, 1H, PhCH), 5.56 (dd, 1H, $J_{4,5}$ = 10.0 Hz, H-4_C), 5.33 (dd, 1H, $J_{1,2}$ = 1.6 Hz, H-2_C), 5.11 (d, 1H, H-1_C), 5.08 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1_D), 4.67 (dd, 1H, $J_{2,3}$ = 9.2, $J_{3,4}$ = 9.3 Hz, H-3_D), 4.40 (m, 2H, H-5_C, $6a_D$), 3.84 (dd, 1H, $J_{5,6}$ = 9.7, $J_{6a,6b}$ = 10.2 Hz, H-$6b_D$), 3.68 (m, 2H, H-4_D, 5_D), 3.53 (s, 3H, OCH_3), 3.27 (ddd, 1H, H-2_D), 2.08 (s, 3H, C(=O)CH_3), and 0.75 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6_C). ^{13}C NMR: δ 171.7 (NC=O), 165.9, 165.8, 165.7 (3C, OC=O), 137.3-126.5 (Ph), 102.2 (PhCH), 100.9 (C-1_D), 97.6 (C-1_C), 80.6 (C-4_D), 74.8 (C-3_D), 71.8 (C-2_C*), 71.5 (C-4_C*), 70.0 (C-3_C), 69.0 (C-6_D), 66.7 (C-5_C), 66.2 (C-5_D), 59.5 (C-2_D), 57.4 (OCH_3), 23.7 (C(=O)CH_3), and 16.8 (C-6_C). CIMS for $C_{43}H_{43}NO_{13}$ (M, 781.3) *m/z* 799.3 $(M+NH_4)^+$.

Anal. Calcd for $C_{43}H_{43}NO_{13}$: C, 66.06; H, 5.54; N, 1.79%. Found C, 66.02; H, 5.56; N, 1.86%.

Methyl α-L-Rhamnopyranosyl-(1→ 3)-2-acetamido-2-deoxy-4,6-*O*-benzylidene-β-D-glucopyranoside (28). 1M Methanolic sodium methoxide was added to a solution of disaccharide **27** (1.63 g, 2.08 mmol) in methanol (50 mL) until pH 10, and the solution was stirred at rt overnight. After neutralisation with Amberlite IR-120 (H^+), filtration, evaporation of the volatiles, purification of the crude product was achieved by column chromatography (solvent *A*, 9:1). The triol **28** (0.95 g, 97%) was isolated as a colourless solid; $[\alpha]_D$ −140° (*c* 1.0); ^{1}H NMR (DMSO-d_6): δ 8.04 (d, 1H, $J_{NH,2}$ = 8.2 Hz, NH), 7.45-7.36 (m, 5H, Ph), 5.64 (s, 1H, PhCH), 4.69 (bs, 2H, H-1_C, OH-2_C), 4.52 (d, 1H, $J_{OH,3}$ = 3.4 Hz, OH-3_C), 4.41 (d, 1H, $J_{1,2}$ = 7.4 Hz, H-1_D), 4.23 (dd, 1H, $J_{6a,6b}$ = 10.2, $J_{5,6a}$ = 4.8 Hz, H-$6a_D$), 3.80-3.73 (m, 3H, H-2_D, 3_D, $6b_D$), 4.64 (dq, 1H, $J_{4,5}$ = 9.2 Hz, H-5_C), 3.58-3.52 (m, 2H, H-2_C, 4_D), 3.46-3.39 (m, 5H, H-3_C, 5_D, OCH_3), 3.27 (ddd, 1H, $J_{4,5}$ = 9.3 Hz, H-4_C), 1.85 (s, 3H, C(=O)CH_3), and 0.72 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6_C). ^{13}C NMR (DMSO-d_6): δ 171.4 (NC=O), 137.5-126.1 (Ph), 101.9 (C-1_D), 101.1 (C-1_C), 100.3 (PhCH), 79.2 (C-4_D), 76.4 (C-3_D), 71.8 (C-4_C), 70.4 (C-2_C), 70.3 (C-3_C), 68.2 (C-5_C), 67.7 (C-6_D), 65.9 (C-5_D), 56.0 (OCH_3), 55.1 (C-2_D), 22.8 (C(=O)CH_3), and 17.4 (C-6_C). CIMS for $C_{22}H_{31}NO_{10}$ (M, 469.2) *m/z* 470 $(M+H)^+$.

Anal. Calcd for $C_{22}H_{31}NO_{10}$: C, 56.28; H, 6.66; N, 2.98%. Found C, 56.13; H, 6.82; N, 2.95%.

Methyl (2,3-*O*-Isopropylidene-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-benzylidene-β-D-glucopyranoside (29). Camphorsulfonic acid (CSA, 18 mg, 75 μmol) was added to a solution of triol **28** (710 mg, 1.5 mmol) in a mixture of DMF (10 mL) containing 2,2-dimethoxypropane (1.3 mL, 10.9 mmol), and the mixture was stirred at rt. After 2 h, TLC (solvent *A*, 19:1) showed that no starting material remained. Et_3N (100 μL) was added, volatiles were evaporated, and the residue was column chromatographed (solvent *A*, 24:1) to give **29** (580 mg, 75%) as a white solid, together with 160 mg (21%) of **29** contaminated by a slightly more polar product; $[\alpha]_D$ +89° (*c* 1.0); ^{1}H NMR (DMSO-d_6): δ 8.10 (d, 1H, $J_{NH,2}$ = 8.9 Hz, NH), 7.45-7.35 (m, 5H, Ph), 5.64 (s, 1H, PhCH), 5.04 (d, 1H, $J_{OH,4}$ = 6.2 Hz, OH-4_C), 5.00 (s, 1H, H-1_C), 4.44 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1_D), 4.26 (dd, 1H, $J_{6a,6b}$ = 10.2, $J_{5,6a}$ = 4.8 Hz, H-$6a_D$), 3.91 (d, 1H, J2,3 = 5.7 Hz, H-2_C), 3.81-3.73 (m, 4H, H-2_D, 4_D, $6b_D$, 3_C), 3.59 (dd, 1H, $J_{2,3}$ = 9.2 Hz, H-3_D), 3.52 (m, 1H, H-5_C), 3.47 (m, 1H, H-5_D), 3.35 (s, 3H, OCH_3), 3.27 (ddd, 1H, $J_{3,4}$ = 10.0, $J_{4,5}$ = 9.5 Hz, H-4_C), 1.82 (s, 3H, C(=O)CH_3), 1.37, 1.23 (2s, 6H, CCH_3), and 0.63 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6_C). ^{13}C NMR (DMSO-d_6): δ 169.1 (NC=O), 137.4-126.1 (Ph), 107.8 (CMe_2), 101.7 (C-1_D), 100.5 (PhCH),

97.3 (C-1_C), 78.9 (C-3_D), 77.7 (C-3_C*), 76.7 (C-4_D*), 75.4 (C-2_C), 73.3 (C-4_C), 67.7 (C-6_D), 65.9 (C-5_D), 65.6 (C-5_C), 56.0 (OCH_3), 55.2 (C-2_D), 27.8, 26.1 (CCH_3), 22.7 (C(=O)CH_3), and 16.8 (C-6_C). CIMS for $C_{25}H_{35}NO_{10}$ (M, 509.2) *m/z* 510 $(M+H)^+$.

Anal. Calcd or $C_{25}H_{35}NO_{10}$: C, 58.93; H, 6.92; N, 2.75%. Found C, 58.81; H, 7.10; N, 2.70%.

Methyl (2,3,4-Tri-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (30). A mixture of the alcohol **19** (317 mg, 1.15 mmol) and the trichloroacetimidate donor[31] **15** (927 mg, 1.49 mmol) in anhydrous dichloromethane (15 mL) was treated with TMSOTf (20 μL, 103 μmol) as described for the preparation of **27**. After 16 h, TLC (solvent *A*, 24:1) showed the total disappearance of **19**. Et_3N (500 μL) was added, and volatiles were evaporated. Chromatography of the residue (solvent *F*, 98.5:1.5) gave the fully protected disaccharide **30** (717 mg, 87%) as a colourless foam; $[\alpha]_D$ +84° (*c* 1.0); ^1H NMR: δ 8.10-7.25 (m, 15H, Ph), 6.16 (bs, 1H, NH), 5.80 (dd, 1H, $J_{2,3}$ = 3.3, $J_{3,4}$ = 10.1 Hz, H-3_C), 5.67 (dd, 1H, $J_{4,5}$ = 9.9 Hz, H-4_C), 5.56 (dd, 1H, $J_{1,2}$ = 1.9, $J_{2,3}$ = 3.3 Hz, H-2_C), 5.12 (bs, 1H, H-1_C), 4.98 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1_D), 4.49 (m, 2H, H-3_D, 5_C), 3.99 (dd, 1H, $J_{5,6a}$ = 5.4, $J_{6a,6b}$ = 10.8 Hz, H-$6a_D$), 3.84 (dd, 1H, $J_{5,6b}$ = 10.4 Hz, H-$6b_D$), 3.69 (dd, 1H, $J_{3,4}$ = 9.4, $J_{4,5}$ = 9.4 Hz, H-4_D), 3.50 (s, 3H, OCH_3), 3.44 (m, 1H, H-5_D), 3.28 (m, 1H, H-2_D), 2.08 (s, 3H, C(=O)CH_3), 1.57, 1.43 (2s, 6H, CCH_3), and 1.30 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6_C). ^{13}C NMR: δ 171.6 (NC=O), 165.7 (3C, OC=O), 133.5-128.3 (Ph), 100.8 (C-1_D), 99.4 (CMe_2), 97.7 (C-1_C), 76.1 (C-3_D), 73.3 (C-4_D), 71.8 (C-4_C), 71.5 (C-2_C), 71.0 (C-3_C), 67.0 (C-5_D), 66.6 (C-5_C), 62.3 (C-6_D), 59.1 (C-2_D), 57.2 (OCH_3), 29.2 (CCH_3), 23.6 (C(=O)CH_3), 19.4 (CCH_3), and 17.5 (C-6_C). CIMS for $C_{39}H_{43}NO_{13}$ (M, 733.3) *m/z* 752.4 $(M+NH_4)^+$.

Anal. Calcd for $C_{39}H_{43}NO_{13}$: C, 63.84; H, 5.91; N, 1.91%. Found C, 63.77; H, 5.98; N, 1.96%.

Methyl (2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (31). A mixture of the alcohol **19** (2.3 g, 8.36 mmol) and the trichloroacetimidate donor[32] **16** (5.4 g, 12.54 mmol) in anhydrous dichloromethane (75 mL) was treated with TMSOTf (162 μL, 0.84 mmol) as described for the preparation of **26**. After 16 h, TLC (solvent *A*, 95:5) showed the total disappearance of **19**. Et_3N (500 μL) was added, and volatiles were evaporated. Chromatography of the residue (solvent *A*, 97:3) gave the fully protected disaccharide **31** (3.70 g, 81%) as a colourless foam; $[\alpha]_D$ −70° (*c* 1.0); ^1H NMR: δ 6.04 (d, 1H, $J_{NH,2}$ = 7.4 Hz, NH), 5.27 (dd, 1H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 10.1 Hz, H-3_C), 5.11 (dd, 1H, $J_{1,2}$ = 1.7 Hz, H-2_C), 5.04 (dd, 1H, $J_{4,5}$ = 9.9 Hz, H-4_C), 4.86 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1_D), 4.80 (d, 1H, H-1_C), 4.30 (dd, 1H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 9.4 Hz, H-3_D), 4.14 (dq, 1H, H-

5_C), 3.94 (dd, 1H, $J_{5,6a}$ = 5.4, $J_{6a,6b}$ = 10.8 Hz, H-$6a_D$), 3.77 (dd, 1H, $J_{5,6b}$ = 10.4 Hz, H-$6b_D$), 3.57 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-4_D), 3.47 (s, 3H, OCH_3), 3.37 (m, 1H, H-5_D), 3.18 (ddd, 1H, H-2_D), 2.12, 2.07, 1.99 (3s, 12H, C(=O)CH_3), 1.49, 1.39 (2s, 6H, CCH_3), and 1.15 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6_C). ^{13}C NMR: δ 171.2 (NC=O), 170.1, 170.0, 169.8 (3C, OC=O), 100.6 (C-1_D), 99.2 (CMe_2), 97.5 (C-1_C), 76.1 (C-3_D), 73.0 (C-4_D), 70.9 (C-4_C), 70.1 (C-2_C), 68.8 (C-3_C), 66.8 (C-5_D), 66.1 (C-5_C), 62.0 (C-6_D), 58.5 (C-2_D), 56.9 (OCH_3), 28.9 (CCH_3), 23.3, 20.7, 20.6, 20.5 (4C, C(=O)CH_3), 19.1 (CCH_3), and 17.1 (C-6_C). CIMS for $C_{24}H_{37}NO_{13}$ (M, 547.2) *m/z* 565 $(M+NH_4)^+$.

Anal. Calcd for $C_{24}H_{37}NO_{13}$: C, 52.65; H, 6.81; N, 2.56%. Found C, 52.49; H, 6.90; N, 2.57%.

Methyl (2,3-*O*-Isopropylidene-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (33). 1M Methanolic sodium methoxide was added to a solution of disaccharide **30** (700 mg, 0.98 mmol) in methanol (10 mL) until pH 10, and the solution was stirred at rt overnight. After neutralisation with Amberlite IR-120 (H^+), filtration, evaporation of the volatiles, purification of the crude product was achieved by column chromatography (solvent *A*, 88:12). The triol **32** (235 mg, 58%) was isolated as a colourless solid; ^{1}H NMR (DMSO-d_6): δ 7.96 (d, 1H, $J_{NH,2}$ = 9.1 Hz, NH), 4.69 (d, 1H, $J_{OH,2}$ = 3.7 Hz, OH-2_C), 4.62 (bs, 1H, H-1_C), 4.60 (d, 1H, $J_{OH,4}$ = 5.1 Hz, OH-4_C), 4.50 (d, 1H, $J_{OH,3}$ = 5.6 Hz, OH-3_C), 4.34 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1_D), 3.82 (dd, 1H, $J_{6a,6b}$ = 10.6, $J_{6a,5}$ = 5.5 Hz, H-$6a_D$), 3.75-3.64 (m, 3H, H-5_C, 2_D, $6b_D$), 3.56 (dd, 1H, H-3_D), 3.51-3.45 (m, 3H, H-2_C, 3_D, 4_D), 3.38 (m, overlapped, 1H, H-3_C), 3.32 (s, 3H, OCH_3), 3.21 (m, 1H, H-5_D), 3.13 (m, 1H, H-4_C), 1.82 (s, 3H, C(=O)CH_3), 1.43, 1.29 (2s, 6H, OCH_3), and 1.05 (d, 3H, $J_{6,5}$ = 6.0 Hz, H-6_C). ^{13}C NMR (DMSO-d_6): δ 169.0 (NC=O), 101.9 (C-1_D), 101.0 (C-1_C), 98.7 (CMe_2), 76.5 (C-3_D), 72.3 (C-4_D*), 71.8 (C-4_C), 70.6 (2C, C-2_C*, 3_C), 68.2 (C-5_C), 66.9 (C-5_D), 61.6 (C-6_D), 55.9 (OCH_3), 55.1 (C-2_D), 28.9 (CCH_3), 22.9 (C(=O)CH_3), 19.1 (CCH_3), and 17.6 (C-6_C). CIMS for $C_{18}H_{31}NO_{10}$ (M, 421.2) *m/z* 422.3 $(M+H)^+$.

(a) CSA (20 mg, 86 μmol) was added to a suspension of the triol **32** (130 mg, 0.30 mmol)in 2,2-dimethoxypropane (5 mL) containing a slight amount of DMF (1 mL), and the mixture was stirred for 1 h. TLC (solvent *A*, 88:12) showed that no starting triol remained, and Et_3N (50 μL) was added. Volatiles were evaporated, and the crude residue was chromatographed to give the di-*O*-isopropylidene derivative **33** (115 mg, 81%).

(b) The crude triol **32**, prepared as described above from **30** (1.94 g, 2.71 mmol), was dissolved in the minimum amount of DMF, and 2,2-dimethoxypropane (10 mL, 10.9 mmol) was added. CSA (100 mg, 432 μmol) was added to the solution and the mixture

was processed as described for the preparation of **29**. The residue was column chromatographed (solvent *A*, 93:7) to give **33** (1.17 g, 93% from **30**) as a white solid which crystallised on standing; mp 269-270 °C (from AcOEt:MeOH), $[\alpha]_D$ –61° (*c* 1.0); ^{1}H NMR (DMSO-d_6): δ 8.03 (d, 1H, $J_{NH,2}$ = 9.1 Hz, NH), 5.11 (d, 1H, $J_{OH,4}$ = 6.4 Hz, OH-4$_C$), 4.97 (bs, 1H, H-1$_C$), 4.37 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1$_D$), 3.89 (bd, 1H, $J_{2,3}$ = 5.7 Hz, H-2$_C$), 3.85-3.61 (m, 6H, H-3$_C$, 2$_D$, 5$_C$, 6a$_D$, 6b$_D$, 3$_D$), 3.54 (dd, 1H, $J_{3,4}$ = 9.2, $J_{4,5}$ = 9.2 Hz, H-4$_D$), 3.33 (s, 3H, OCH_3), 3.25 (m, 1H, H-5$_D$), 2.97 (m, 1H, H-4$_C$), 1.80 (s, 3H, C(=O)CH_3), 1.43, 1.39, 1.30, 1.23 (4*s*, 12H, CCH_3), and 1.06 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6$_C$). ^{13}C NMR (DMSO-d_6): δ 169.0 (NC=O), 107.8 (CMe_2), 101.7 (C-1$_D$), 98.7 (CMe_2), 97.2 (C-1$_C$), 78.0 (C-3$_C$), 76.9 (C-3$_D$), 75.4 (C-2$_C$), 73.4 (C-4$_C$), 71.9 (C-4$_D$), 66.8 (C-5$_D$), 65.5 (C-5$_C$), 61.4 (C-6$_D$), 55.9 (OCH_3), 55.1 (C-2$_D$), 28.9, 27.9, 26.1 (3C, CCH_3), 22.7 (C(=O)CH_3), 19.1 (CCH_3), and 17.3 (C-6$_C$). CIMS for $C_{21}H_{35}NO_{18}$ (M, 461.2) *m/z* 462 $(M+H)^+$.

Anal. Calcd for $C_{21}H_{35}NO_{18}$: C, 54.65; H, 7.64; N, 3.03%. Found C, 54.70; H, 7.80; N, 2.91%.

Methyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (39). (a) TMSOTf (150 μL, 772 μmol) was added, at 0 °C, to a solution of acceptor **19** (1.27 g, 4.62 mmol) and trichloroacetimidate donor **48** (7.2 g, 6.92 mmol) in anhydrous acetonitrile (20 mL), and the mixture was stirred at rt. After 1.5 h, TLC (solvent *B*, 3:2) showed that no starting acceptor remained. Et_3N (750 μL) was added, and volatiles were evaporated. Chromatography of the residue (solvent *B*,: 17:3) gave the fully protected trisaccharide **39** (4.0 g, 74 %) as a colourless foam.

(b) Powdered MS 4Å (2.8 g) was added to a solution of the acceptor **19** (1.0 g, 3.63 mmol) and the trichloroacetimidate donor **48** (5.65 g, 5.45 mmol) in anhydrous dichloromethane (55 mL). The mixture was stirred for 1 h at rt, then cooled to –25 °C. A 2M solution of $BF_3.Et_2O$ in anhydrous dichloromethane (64 mL) was added dropwise at –25 °C, then the mixture was stirred overnight at –10 °C. TLC (solvent *B*, 3:2) showed that little starting material remained. The mixture was neutralised by addition of Et_3N (5 mL), then filtered through a pad of Celite, and the filtrate was concentrated. Work-up as described for compound **30**, followed by chromatography (solvent *B*, 17:3) gave **39** (3.45 g, 81%) as a colourless foam; $[\alpha]_D$ +89° (*c* 1.0); ^{1}H NMR: δ 8.04-7.02 (m, 30H, Ph), 6.15 (d, 1H, $J_{NH,2}$ = 7.3 Hz, NH), 5.60 (dd, 1H, $J_{2,3}$ = 3.6, $J_{3,4}$ = 9.5 Hz, H-3$_C$), 5.46 (dd, 1H, $J_{1,2}$ = 1.8 Hz, H-2$_C$), 5.01 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1$_D$), 5.00 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1$_E$), 4.97 (d, 1H, H-1$_C$), 4.91-4.64 (m, 6H, OCH_2), 4.46 (dd, 1H, $J_{3,4}$ = 9.5, $J_{2,3}$ = 9.3 Hz, H-3$_D$), 4.34 (d, 1H, J = 10.9 Hz, OCH_2), 4.29 (dq, partially overlapped, 1H, H-5$_C$), 4.24 (d, 1H, J = 12.1 Hz, OCH_2),

3.99-3.74 (m, 4H, H-6a$_D$, 3$_E$, 4$_C$, 6b$_D$), 3.69-3.60 (m, 2H, H-5$_E$, 4$_E$), 3.61 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-4$_D$), 3.50 (m, 4H, $J_{2,3}$ = 9.6 Hz, H-2$_E$, OCH_3), 3.43 (m, 1H, H-5$_D$), 3.33 (dd, 1H, $J_{6a,6b}$ = 10.1 Hz, H-6a$_E$), 3.12 (m, 1H, H-2$_D$), 3.04 (d, 1H, H-6b$_E$), 2.02 (s, 3H, C(=O)CH_3), 1.50 (s, 3H, CCH_3), 1.44 (d, 3H, $J_{5,6}$ = 5.8 Hz, H-6$_C$), and 1.37 (CCH_3). ^{13}C NMR: δ 170.4 (NC=O), 165.7, 165.6 (2C, OC=O), 138.7-127.5 (m, Ph), 100.7 (C-1$_D$, $J_{C,H}$ undetermined), 99.6 (CMe_2), 99.3 (C-1$_E$, $J_{C,H}$ = 168 Hz), 97.8 (C-1$_C$, $J_{C,H}$ = 171 Hz), 81.6 (C-3$_E$), 80.4 (C-2$_E$), 79.5 (C-4$_C$), 77.3 (C-4$_E$), 76.2 (C-3$_D$), 75.4, 74.7, 74.0 (3C, OCH_2), 73.3 (2C, OCH_2, C-4$_D$), 71.3 (2C, C-2$_C$, 3$_C$), 71.2 (C-5$_E$), 67.7 (C-5$_C$), 67.6 (C-6$_E$), 67.0 (C-5$_D$), 62.3 (C-6$_D$), 59.3 (C-2$_D$), 57.2 (OCH_3), 29.0 (CCH_3), 23.4 (C(=O)CH_3), 19.2 (CCH_3), and 18.2 (C-6$_C$). CIMS for $C_{66}H_{73}NO_{17}$ (M, 1151.5) *m/z* 1169.4 $(M+NH_4)^+$.

Anal. Calcd for $C_{66}H_{73}NO_{17}$: C, 68.80; H, 6.39; N, 1.22%. Found C, 66.93; H, 6.78; N, 1.53%.

Methyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (40). 1M Methanolic sodium methoxide was added dropwise to a solution of **39** (2.36 g, 2.03 mmol) in methanol (50 mL) until pH 10 was reached. The mixture was stirred overnight at rt. As TLC (solvent *F*, 3:2) showed complete reaction, the mixture was neutralised by addition of Amberlite IR-120 (H^+) then filtered and concentrated. Flash chromatography of the crude material (solvent *C*, 11:9) gave **40** (1.90 g, 98%) as a colourless foam; $[\alpha]_D$ +8° (*c* 1.0); ^{1}H NMR: δ 7.57-7.07 (m, 20H, Ph), 5.81 (d, 1H, $J_{NH,2}$ = 8.6 Hz, NH), 4.94 (d, 1H, J = 10.9 Hz, OCH_2), 4.90 (d, 1H, $J_{1,2}$ = 4.7 Hz, H-1$_E$), 4.88 (bs, 1H, H-1$_C$), 4.85-4.44 (m, 7H, OCH_2), 4.62 (d, overlapped, 1H, H-1$_D$), 4.08 (m, 1H, H-5$_C$), 4.05-3.92 (m, 5H, H-6a$_D$, 5$_E$, 3$_D$, 3$_E$, 2$_C$), 3.80 (dd, 1H, $J_{6a,6b}$ = 10.4 Hz, H-6b$_D$), 3.74 (dd, 1H, $J_{3,4}$ = 12.4 Hz, H-3$_C$), 3.65-3.47 (m, 6H, H-2$_D$, 6a$_E$, 6b$_E$, 4$_D$, 2$_E$, 4$_E$), 3.47 (s, 3H, OCH_3), 3.36 (m, 1H, H-5$_D$), 3.31 (m, 1H, $J_{4,5}$ = 9.3 Hz, H-4$_C$), 2.82 (bs, 1H, OH-2$_C$), 2.02 (s, 3H, C(=O)CH_3), 1.74 (bs, 1H, OH-3$_C$), 1.48 (s, 3H, CCH_3), 1.40 (s, 3H, CCH_3), and 1.34 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6$_C$). ^{13}C NMR: δ 170.5 (NC=O), 138.4-127.7 (m, Ph), 101.6 (C-1$_D$), 99.8 (C-1$_C$), 99.5 (CMe_2), 98.6 (C-1$_E$), 85.4 (C-4$_C$), 81.4 (C-3$_E$), 79.8 (C-2$_E$), 77.7 (C-4$_E$), 76.6 (C-3$_D$), 75.4, 75.0, 73.4, 73.2 (4C, OCH_2), 72.8 (C-4$_D$), 71.2 (C-5$_E$), 70.9 (C-2$_C$), 69.5 (C-3$_C$), 68.5 (C-6$_E$), 67.2 (C-5$_D$), 66.2 (C-5$_C$), 62.3 (C-6$_D$), 57.3 (C-2$_D$), 56.8 (OCH_3), 29.1 (CCH_3), 23.4 (C(=O)CH_3), 19.3 (CCH_3), and 17.6 (C-6$_C$). CIMS for $C_{52}H_{65}NO_{15}$ (M, 943.4) *m/z* 961.6 $(M+NH_4)^+$.

Anal. Calcd for $C_{52}H_{65}NO_{15}\cdot 0.5H_2O$: C, 65.53; H, 6.98; N, 1.47%. Found C, 65.62; H, 6.99; N, 1.45%.

Methyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranoside (41). (a) A solution of

the disaccharide acceptor **33** (230 mg, 0.5 mmol) and the trichloroacetimidate donor **7** (513 mg, 0.75 mmol) in anhydrous dichloromethane was stirred at –80 °C. TMSOTf (10 μL, 52 μmol) was added, and stirring was continued overnight while the reaction temperature slowly came back to rt. TLC (solvent *A*, 19:1) showed that completion of the reaction was close to 80%. More **7** (103 mg, 0.25 mmol) was added, and after an additional 4 h, hardly any starting **33** remained. As observed for the attempted preparation of **35** and **36** (not described), a large amount of rearrangement product[41] **9** was present in the reaction mixture (solvent *B*, 13:7). Et_3N (50 μL) was added, and volatiles were evaporated. Column chromatography (solvent *A*, 49:1) of the residue gave the fully protected trisaccharide methyl (2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→ 4)-(2,3-*O*-isopropylidene-α-L-rhamnopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (**37**) and the corresponding β-D-glucopyranosyl anomer (**38**) (360 mg, 73%) as an α:β mixture, which could not be separated; CIMS for $C_{55}H_{69}O_{15}$ (M, 983.5) *m/z* 1001.4 $(M+NH_4)^+$.

Anal. Calcd for $C_{55}H_{69}O_{15}$: C, 67.12; H, 7.07; N, 1.42%. Found C, 67.17; H, 7.23; N, 1.28%.

The above mixture of trisaccharides **37** and **38** (230 mg, 0.23 mmol) dissolved in AcOH (2.4 mL) was treated with water (600 μL) at 60 °C. After 4.5 h at this temperature, no more progress of the reaction could be seen on TLC plates (solvent *A*, 9:1). The mixture was worked-up as described for the preparation of **22**, and the residue was chromatographed (solvent *A*, 95:5) to give **41** and methyl (2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-(1→4)-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranoside (**42**) as a 1:2 mixture (154 mg, 74%). Characteristic NMR data were: ^{13}C NMR: δ 103.8 (C-1β), 101.8 (C-1β), 101.4 (C-1α_C) 101.3 (C-1β), 101.1 (C-1α_D), 99.2 (C-1α_E); CIMS for $C_{49}H_{61}NO_{15}$ (M, 903.4) *m/z* 921.4 $(M+NH_4)^+$.

(b) Water (5 mL) was added to a solution of compound **40** (1.0 g, 1.12 mmol) in acetic acid (14 mL), and the reaction mixture was processed as described for the preparation of compound **22**. Chromatography of the crude material on a short column of silica gel (solvent *B*, 1:1) gave pure **41** as colourless foam; $[\alpha]_D$ +19° (*c* 1.0); ^1H NMR: δ 7.33-7.13 (m, 20H, Ph), 5.76 (d, 1H, $J_{NH,2}$ = 8.8 Hz, NH), 4.95 (d, 1H, J = 10.9 Hz, OCH_2), 4.89 (bs, 1H, H-1$_C$), 4.88 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1$_E$), 4.86-4.71 (m, 3H, OCH_2), 4.72 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1$_D$), 4.66-4.44 (m, 4H, OCH_2), 4.05-3.88 (m, 7H, H-3$_D$, 5$_E$, 3$_E$, 5$_C$, 6a$_D$, 6b$_D$, 2$_C$), 3.80 (d, 1H, H-3$_C$), 3.64 (dd, 1H, $J_{6a,6b}$ = 9.6 Hz, H-6a$_E$), 3.60-3.43 (m, 8H, H-2$_E$, 6b$_E$, 5$_D$, 4$_D$, 4$_E$, OCH_3), 3.38 (m, 1H, H-4$_C$), 3.33 (m, 1H, H-2$_D$), 2.97 (bs, 1H, OH), 2.39 (bs, 1H, OH), 2.18 (s, 3H, C(=O)CH_3), 1.81 (bs, 2H, OH), and 1.42 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6$_C$). ^{13}C NMR: δ 170.5 (C=O), 138.5-127.7 (m, Ph),

101.3 (C-1_C), 100.9 (C-1_D), 99.3 (C-1_E), 85.0 (2C, C-3_D, 4_C), 81.5 (C-3_E), 79.7 (C-2_E), 77.7 (C-4_E), 75.7 (OCH_2), 75.1 (C-4_D), 75.0, 73.6, 73.5 (3C, OCH_2), 71.3 (C-5_E), 70.9 (2C, C-2_C, 5_D), 69.4 (C-3_C), 68.7 (C-6_E), 67.7 (C-5_C), 62.8 (C-6_D), 57.0 (OCH_3), 56.3 (C-2_D), 23.6 (C(=O)CH_3), and 17.7 (C-6_C). CIMS for $C_{55}H_{69}NO_{15}$ (M, 943.4) *m/z* 921.4 $(M+NH_4)^+$.

Anal. Calcd for $C_{55}H_{69}NO_{15}$: C, 65.10; H, 6.80; N, 1.55%. Found C, 65.05; H, 6.99; N, 1.41%.

Allyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→ 4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (43) and Allyl (2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (44). The allyl glycoside **13** (5.0 g, 20.5 mmol) was treated with TMSCl (8.83 mL, 65.6 mmol) and pyridine (7.5 mL, 91.0 mmol) as described for the preparation of **11**. Conventional work-up gave the corresponding trimethylsilyl precursor **14** (6.22 g, 96%) as a colourless oil; ^{1}H NMR: δ 5.90 (m, 1H, C*H*=CH_2), 5.29 (m, 1H, J = 9.8 Hz, CH=CH_2) 5.19 (m, 1H, J = 10.5 Hz, CH=CH_2), 5.00 (bs, 1H, H-1), 4.15 (m, 1H, OCH_2), 4.13 (d, 1H, $J_{2,3}$ = 5.5 Hz, H-2), 4.00 (dd, H-3), 3.99 (m, 1H, OCH_2), 3.62 (m, 1H, H-5), 3.31 (m, 1H, H-4), 1.45 (s, 3H, CCH_3), 1.34 (s, 3H, CCH_3), and 1.20 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6), 0.14 (s, 9H, $Si(CH_3)_3$).

Next, a mixture of the crude **14** (6.22 g, 19.68 mmol) and the fluoride donor **8** (16 g, 29.52 mmol) in anhydrous diethyl ether (450 mL) was treated with Tf_2O (7.4 mL, 45.0 mmol) in the presence of powdered MS 4Å (68 g) as described for the preparation of **20** (method b). Chromatography of the residue (solvent *F*: 99:1) gave the β-anomer **44** as the first eluting product (3.17 g, 23%); $[\alpha]_D$ -19° (*c* 1.0); ^{1}H NMR: δ 7.39-7.17 (m, 20H, Ph), 5.93 (m, 1H, C*H*=CH_2), 5.33 (m, 1H, J = 1.4, J = 17.0 Hz, CH=CH_2) 5.24 (m, 1H, J = 10.2 Hz, CH=CH_2), 5.03 (bs, 1H, H-1_C), 4.95 (d, 1H, J = 11.0 Hz, OCH_2), 4.94 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1_E), 4.93 (d, 1H, J = 10.8 Hz, OCH_2), 4.83 (d, 1H, OCH_2), 4.78 (d, 1H, OCH_2), 4.75 (d, 1H, J = 12.9 Hz, OCH_2), 4.66 (d, 1H, OCH_2), 4.62 (d, 1H, J = 12.2 Hz, OCH_2), 4.55 (d, 1H, OCH_2), 4.24 (dd, 1H, $J_{3,4}$ = 5.6 Hz, H-3_C), 4.21 (m, 1H, OCH_2), 4.14 (dd, $J_{2,3}$ = 5.6 Hz, H-2_C), 4.03 (m, 1H, OCH_2), 3.75-3.63 (m, 6H, H-$6a_E$, $6b_E$, 3_E, 5_C, 4_C, 4_E), 3.44-3.38 (m, 2H, H-5_E, 2_E), 1.47 (s, 3H, CCH_3), 1.34 (d, partially overlapped, 3H, H-6_C), and 1.32 (s, 3H, CCH_3). ^{13}C RMN: δ 138.6-127.5 (Ph, All), 117.8 (All), 109.1 (CMe_2), 101.7 (C-1_E), 96.2 (C-1_C), 84.8 (C-4_C), 82.5 (C-2_E), 78.3 (C-3_E), 78.2 (C-3_C), 77.9 (C-4_E), 76.1 (C-2_C), 75.6 (OCH_2), 74.9 (2C, OCH_2, C-5_E), 74.8, 73.5 (2C, OCH_2), 68.7 (C-6_E), 68.0 (OCH_2), 64.5 (C-5_C), 27.9, 26.3 (2C, CCH_3), and 17.8 (C-6_C). CIMS for $C_{46}H_{54}O_{10}$ (M, 766.4) *m/z* 784.6 $(M+NH_4)^+$.

Anal. Calcd for $C_{46}H_{54}O_{10}$: C, 72.04; H, 7.10%. Found C, 72.01; H, 7.07%.

Eluted next was the α-anomer **43** (8.7 g, 55%); $[\alpha]_D$ +30° (*c* 1.0); ^{1}H NMR: δ 7.36-7.16 (m, 20H, Ph), 5.90 (m, 1H, C*H*=CH$_2$), 5.29 (m, 1H, CH=C*H*$_2$), 5.20 (m, 1H, CH=C*H*$_2$), 4.99 (d, 1H, H-1$_C$), 4.98 (d, 1H, partially overlapped, H-1$_E$), 4.97 (d, 1H, OCH$_2$), 4.86 (d, 1H, J = 10.8 Hz, OCH$_2$), 4.84 (d, 1H, J = 10.8 Hz, OCH$_2$), 4.81 (d, 1H, J = 12.8 Hz, OCH$_2$), 4.71 (d, 1H, OCH$_2$), 4.63 (d, 1H, J = 11.9 Hz, OCH$_2$), 4.53 (d, 1H, OCH$_2$), 4.50 (d, 1H, OCH$_2$), 4.18-4.07 (m, 4H, OCH$_2$, H-3$_C$, 2$_C$, 5$_E$), 3.98 (dd, 1H, $J_{3,4}$ = 9.5 Hz, H-3$_E$), 3.95 (m, 1H, OCH$_2$), 3.83-3.77 (m, 3H, H-6a$_E$, 5$_C$, 4$_E$), 3.66 (dd, 1H, $J_{6a,6b}$ = 10.5, $J_{5,6b}$ = 1.8 Hz, H-6b$_E$), 3.59 (dd, 1H, $J_{2,3}$ = 8.9 Hz, H-2$_E$), 3.34 (dd, 1H, $J_{3,4}$ = 6.8, $J_{4,5}$ = 10.1 Hz, H-4$_C$), 1.44 (s, 3H, CCH$_3$), 1.31 (d, 3H, $J_{6,5}$ = 6.8 Hz, H-6$_C$), and 1.26 (s, 3H, CCH$_3$). ^{13}C NMR: δ 138.6-127.6 (Ph), 117.9 (All), 109.0 (CMe$_2$), 98.4 (C-1$_E$, $J_{C,H}$ = 169 Hz), 96.0 (C-1$_C$, $J_{C,H}$ = 169 Hz), 82.3 (C-3$_E$), 80.9 (C-4$_C$), 79.9 (C-2$_E$), 77.9 (C-4$_E$), 76.9 (C-2$_C$), 76.1 (C-3$_C$), 75.6, 75.2, 74.3, 73.6 (4C, OCH$_2$), 70.3 (C-5$_E$), 68.0 (C-6$_E$), 67.8 (OCH$_2$), 65.6 (C-5$_C$), 28.2, 26.4 (2C, CCH$_3$), and 17.5 (C-6$_C$). CIMS for $C_{46}H_{54}O_{10}$ (M, 766.4) *m/z* 767.4 $(M+H)^+$.

Anal. Calcd for $C_{46}H_{54}O_{10}$: C, 72.04; H, 7.10%. Found C, 72.01; H, 7.07%.

Allyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-α-L-rhamnopyranoside (45). The fully protected α-anomeric disaccharide **43** (2.99 g, 3.9 mmol) was solubilised in 80% aq AcOH (48 mL) and processed as described for the preparation of diol **22** (method a). Column chromatography of the residue (solvent *C*, 17:3) gave diol **45** (2.43 g, 95%) as a colourless oil; $[\alpha]_D$ +6° (*c* 1.0); ^{1}H NMR: δ 7.32-7.12 (m, 20H, Ph), 5.93 (m, 1H, C*H*=CH$_2$), 5.31 (m, 1H, CH=C*H*$_2$), 5.21 (m, 1H, CH=C*H*$_2$), 4.97 (d, 1H, J = 10.9 Hz, OCH$_2$), 4.91 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1$_E$), 4.85 (bs, 1H, H-1$_C$), 4.86-4.45 (m, 7H, OCH$_2$), 4.20 (m, 1H, OCH$_2$), 4.03-3.93 (m, 4H, OCH$_2$, H-5$_C$, 2$_C$, 3$_E$), 3.78 (m, 2H, H-3$_C$, 5$_C$), 3.67 (dd, 1H, $J_{6a,6b}$ = 10.4, $J_{5,6a}$ = 2.1 Hz, H-6a$_E$), 3.58 (m, 2H, H-6b$_E$, 2$_E$), 3.52 (dd, 1H, $J_{3,4}$ = 9.9, $J_{4,5}$ = 9.3 Hz, H-4$_E$), 3.35 (dd, 1H, $J_{3,4}$ = 9.0, $J_{4,5}$ = 9.1 Hz, H-4$_C$), 2.64 (d, 2H, $J_{OH,2}$ = 1.7, $J_{OH,3}$ = 1.7 Hz, OH-2, OH-3), and 1.40 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6$_C$). ^{13}C NMR: δ 138.7-127.6 (Ph, All), 117.4 (All), 98.9 (C-1$_C$), 98.2 (C-1$_E$), 85.7 (C-4$_C$), 81.5 (C-3$_E$), 79.8 (C-2$_E$), 77.7 (C-4$_E$), 75.6, 75.0, 73.4, 73.3 (4C, OCH$_2$), 71.1 (C-5$_E$), 70.8 (C-2$_C$), 69.8 (C-3$_C$), 68.5 (C-6$_E$), 67.9 (OCH$_2$), 66.0 (C-5$_C$), and 17.7 (C-6$_C$). CIMS for $C_{43}H_{50}O_{10}$ (M, 726.3) *m/z* 727.4 $(M+H)^+$.

Anal. Calcd for $C_{43}H_{50}O_{10}\cdot H_2O$: C, 69.34; H, 7.02%. Found: C, 69.17; H, 7.02%.

Allyl (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzoyl-α-L-rhamnopyranoside (46). Benzoyl chloride (6.8 mL, 58.5 mmol) was added dropwise to a solution of diol **45** (14.14 g, 19.47 mmol) in pyridine (35 mL) at 0 °C. The mixture was stirred for 72 h, at rt and methanol was added. Conventional

work-up followed by chromatography of the residue (solvent *B*, 9:1) gave the di-*O*-benzoyl intermediate **46** (16.5 g, 90%) as a colourless oil; $[\alpha]_D$ +89° (*c* 1.0); ^{1}H NMR: δ 8.05-6.98 (m, 30H, Ph), 6.14 (m, 1H, C*H*=CH$_2$), 5.70 (dd, 1H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 9.3 Hz, H-3$_C$), 5.61 (dd, 1H, $J_{1,2}$ = 1.7 Hz, H-2$_C$), 5.40 (m, 1H, CH=C*H*$_2$), 5.29 (m, 1H, CH=C*H*$_2$), 4.99 (bs, 1H, H-1$_C$), 4.98 (d, 1H, partially overlapped, H-1$_E$), 4.97-4.68 (m, 5H, OCH$_2$), 4.38 (m, 1H, J = 10.9 Hz, OCH$_2$), 4.32-4.25 (m, 2H, OCH$_2$), 4.12-4.05 (m, 2H, OCH$_2$, H-5$_C$), 3.97-3.87 (m, 3H, OCH$_2$, H-3$_E$, 4$_C$), 3.71 (m, 1H, H-5$_E$), 3.67 (dd, 1H, $J_{3,4}$ = 10.4, $J_{4,5}$ = 10.4 Hz, H-4$_E$), 3.53 (dd, 1H, $J_{1,2}$ = 3.4, $J_{2,3}$ = 10.4 Hz, H-2$_E$), 3.37 (dd, 1H, $J_{5,6a}$ = 1.2 Hz, H-6a$_E$), 3.09 (dd, 1H, $J_{6a,6b}$ = 10.9, $J_{5,6a}$ = 1.1 Hz, H-6b$_E$), and 1.49 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6$_C$). ^{13}C NMR: δ 165.4 (2C, C=O), 138.9-127.4 (Ph, All), 117.9 (All), 99.2 (C-1$_C$*), 96.2 (C-1$_E$*), 81.5 (C-3$_E$), 80.2 (C-2$_E$), 79.6 (C-4$_C$), 77.2 (C-4$_E$), 75.4, 74.7, 74.0, 73.3 (4C, OCH$_2$), 71.2 (C-3$_C$), 71.1 (C-5$_E$), 70.7 (C-2$_C$), 68.2 (OCH$_2$), 67.5 (2C, C-6$_E$, 5$_C$), and 18.2 (C-6$_C$). CIMS for $C_{57}H_{58}O_{12}$ (M, 934.4) *m/z* 935.4 $(M+H)^+$.

Anal. Calcd for $C_{57}H_{58}O_{12}$: C, 73.22; H, 6.25%. Found C, 73.12; H, 6.27%.

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl-(1→ 4)-2,3-di-*O*-benzoyl-α-L-rhamnopyranose (47). Compound **46** (1.70 g, 1.83 mmol) was dissolved in anhydrous THF (20 mL). The solution was degassed and placed under Ar. 1,5-Cyclooctadiene-bis(methyldiphenylphosphine)iridium hexafluorophosphate (150 mg, 177 mmol) was added, and the solution was degassed again. The catalyst was activated by passing over a stream of hydrogen until the solution had turned yellow (ca. 5 min). The reaction mixture was degassed again and stirred under an Ar atmosphere for 2 h, then concentrated to dryness. The residue was dissolved in acetone (18 mL), then water (2 mL), mercuric chloride (745 mg, 2.74 mmol) and mercuric oxide (794 mg, 3.66 mmol) were added successively. The mixture protected from light was stirred at rt for 1 h and acetone was evaporated. The resulting suspension was taken up in CH_2Cl_2, washed twice with 50% aq KI, water and satd aq NaCl, dried and concentrated. Purification of the crude material was effected by silica gel chromatography (solvent *E*, 97:3) to furnish the hemiacetal **47** (1.22 g, 86%) as a mixture of α- and β-anomers. Crystallisation of an analytical sample gave the α-anomer as pure material; mp (98.0-98.5 °C, from isopropyl ether:petroleum ether); $[\alpha]_D$ +119° (*c* 1.0); ^{1}H NMR: δ 8.06-6.92 (m, 30H, Ph), 5.70 (dd, 1H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 9.3 Hz, H-3$_C$), 5.56 (dd, 1H, $J_{1,2}$ = 1.8 Hz, H-2$_C$), 5.23 (dd, 1H, H-1$_C$), 4.95 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1$_E$), 4.89 (d, 1H, J = 10.9 Hz, OCH$_2$), 4.80 (d, 1H, J = 11.8 Hz, OCH$_2$), 4.79 (d, 1H, OCH$_2$), 4.69 (d, 1H, J = 10.8 Hz, OCH$_2$), 4.65 (d, 1H, OCH$_2$), 4.35 (d, 1H, OCH$_2$), 4.26 (dq, partially overlapped, 1H, H-5$_C$), 4.22 (d, 1H, J = 11.9 Hz, OCH$_2$), 3.92 (d, 1H, OCH$_2$), 3.91 (dd, 1H, $J_{3,4}$ = 9.6 Hz, H-3$_E$), 3.85 (dd, 1H, $J_{4,5}$

= 9.3 Hz, H-4$_C$), 3.67 (m, 1H, H-5$_E$), 3.64 (dd, 1H, $J_{4,5}$ = 9.3 Hz, H-4$_E$), 3.48 (d, 1H, $J_{2,3}$ = 9.8 Hz, H-2$_E$), 3.37 (dd, 1H, $J_{5,6a}$ = 1.6, $J_{6a,6b}$ = 10.8 Hz, H-6a$_E$), 3.09 (dd, 1H, $J_{5,6b}$ = 1.5 Hz, H-6b$_E$), 3.03 (d, 1H, $J_{OH,1}$ = 3.91 Hz, OH-1$_C$), and 1.50 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6$_C$). ^{13}C NMR: δ 165.4 (2C, C=O), 138.8-127.5 (m, Ph), 99.2 (C-1$_E$), 91.9 (C-1$_C$), 81.5 (C-3$_E$), 80.3 (C-2$_E$), 79.6 (C-4$_C$), 77.2 (C-4$_E$), 75.4, 74.7, 73.9, 73.2 (4C, OCH_2), 71.2 (C-5$_E$), 71.0 (C-2$_C$), 70.9 (C-3$_C$), 67.6 (2C, C-6$_E$, 5$_C$), and 18.3 (C-6$_C$). CIMS for $C_{54}H_{56}O_{13}$ (M, 894.4) *m/z* 895.4 $(M+H)^+$.

Anal. Calcd for $C_{54}H_{56}O_{13}\cdot H_2O$: C, 71.04; H, 6.18%. Found: C, 71.22; H, 6.02%.

(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→ 4)-2,3-di-*O*-benzoyl-α-L-rhamnopyranosyl Trichloroacetimidate (48). Trichloroacetonitrile (12.8 mL, 127.4 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 185 μL, 1.2 mmol) were added to a solution of the hemiacetal **47** (11.32 g, 12.46 mmol) in anhydrous dichloroethane (30 mL) at 0 °C. The mixture turned brownish and then dark brown while being stirred at 0 °C. After 30 min, TLC (solvent *B*, 7:3 containing Et_3N 0.1%) showed that only little starting material remained. The mixture was concentrated, coevaporated repeatedly with toluene, and the residue was purified by flash-chromatography (solvent *B*, 75:15 containing 10% dichloromethane and 0.1% Et_3N) on a short column of silica gel to afford **48** (10.8 g, 83%) as a colourless oil; $[\alpha]_D$ +72° (*c* 1.0); ^{1}H NMR: δ 8.75 (s, 1H, NH), 8.07-7.00 (m, 30H, Ph), 6.39 (dd, 1H, $J_{1,2}$ = 1.8 Hz, H-1$_C$), 5.78 (dd, 1H, H-2$_C$), 5.71 (dd, 1H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 9.3 Hz, H-3$_C$), 4.96 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1$_E$), 4.91 (d, 1H, J = 10.7 Hz, OCH_2), 4.82 (d, 1H, J = 11.7 Hz, OCH_2), 4.81 (d, 1H, OCH_2), 4.71 (d, 1H, J = 10.7 Hz, OCH_2), 4.66 (d, 1H, OCH_2), 4.35 (d, 1H, OCH_2), 4.23 (d, 1H, J = 12.0 Hz, OCH_2), 4.21 (dq, partially overlapped, 1H, H-5$_C$), 3.95-3.90 (m, 3H, OCH_2, H-4$_C$, 3$_E$) 3.71 (m, 1H, H-5$_E$), 3.65 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-4$_E$), 3.50 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2$_E$), 3.40 (dd, 1H, $J_{5,6a}$ = 1.4 Hz, H-6a$_E$), 3.05 (dd, 1H, $J_{5,6b}$ = 1.2, $J_{6a,6b}$ = 10.9 Hz, H-6b$_E$), and 1.55 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6$_C$). ^{13}C NMR: δ 165.5, 165.2, (2C, C=O), 160.4 (C=NH), 133.8-127.4 (m, Ph), 99.5 (C-1$_E$), 94.7 (C-1$_C$), 90.8 (CCl_3), 81.3 (C-3$_E$), 80.1 (C-2$_E$), 79.0 (C-4$_C$), 77.1 (C-4$_E$), 75.3, 74.7, 73.8, 73.1 (4C, OCH_2), 71.1 (C-5$_E$), 70.7 (C-3$_C$), 70.4 (C-5$_C$), 68.9 (C-2$_C$), 67.3 (C-6$_E$), and 18.1 (C-6$_C$).

Anal. Calcd for $C_{56}H_{54}Cl_3NO_{12}$ (M, 1039.4): C, 64.71; H, 5.24; N, 1.35%. Found C, 64.61; H, 5.25; N, 1.33%.

Methyl α-D-Glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranoside (4). A solution of **41** (633 mg, 711 mmol) in a 9:1 mixture of ethanol and acetic acid (35 mL) was treated with 10% Pd-C catalyst (2 g) as described for the preparation of **1**. The residue was taken up in water and

extracted several times with chloroform. The aqueous phase was lyophilised, and the residue was purified by reverse phase chromatography (solvent *G*, gradient) to give, after lyophilisation, the linear trisaccharide **4** (340 mg, 90%); $[\alpha]_D$ +4° (*c* 1.0, water), $[\alpha]_D$ +5° (*c* 1.0, MeOH), ^{1}H NMR (D_2O): δ5.03 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1_E), 4.83 (bs, 1H, H-1_C), 4.48 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1_D), 4.08 (dq, 1H, $J_{4,5}$ = 9.6 Hz, H-5_C), 3.99 (m, 1H, H-5_E), 3.93 (d, 1H, H-$6a_D$), 3.82-3.71 (m, 6H, H-3_C, 2_D, $6a_E$, 2_C, $6b_E$, $6b_D$), 3.68 (dd, 1H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 9.6 Hz, H-3_E), 3.60-3.43 (m, 9H, H-3_D, 2_E, OCH_3, 4_D, 5_D, 4_C, 4_E), 2.05 (s, 3H, C(=O)CH_3), and 1.31 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6_C). ^{13}C NMR (D_2O): δ 175.0 (C=O), 102.1 (C-1_C), 102.0 (C-1_D), 100.5 (C-1_E), 82.8 (C-3_D), 81.8 (C-4_C); 76.7 (C-2_E), 73.5 (C-3_E), 72.5 (C-5_E), 72.3 (C-4_D), 71.8 (C-2_C), 70.1 (C-4_E), 69.7 (C-3_C), 69.3 (C-5_D), 68.8 (C-5_C), 61.5 (C-6_D), 60.8 (C-6_E), 57.8 (OCH_3), 55.9 (C-2_D), 22.7 (C(=O)CH_3), and 17.3 (C-6_C). CIMS for $C_{21}H_{37}NO_{15}$ (M, 543.2) *m/z* 544 $(M+H)^+$.

Anal. Calcd for $C_{21}H_{37}NO_{15}$: C, 46.41; H, 6.86; N, 2.58%. Found C, 46.55; H, 6.72; N, 1.88%.

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