Carbohydrate Research 380 (2013) 167–173

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Differential O-3/O-4 selectivity in the glycosylation of *N*-dimethylmaleoyl-protected hexosamine acceptors: effect of a conformationally armed (superarmed) glycosyl donor

F. Della Felice [a], Edmundo A. Rúveda [a], Carlos A. Stortz [b], María I. Colombo [a,*]

[a] Instituto de Química Rosario (CONICET-UNR), Facultad de Ciencias Bioquímicas y Farmacéuticas, Suipacha 531, 2000 Rosario, Argentina
[b] Departamento de Química Orgánica-CIHIDECAR, Facultad de Ciencias Exactas y Naturales, UBA, Ciudad Universitaria, Pab. 2, 1428 Buenos Aires, Argentina

ARTICLE INFO

Article history:
Received 23 May 2013
Received in revised form 23 July 2013
Accepted 3 August 2013
Available online 12 August 2013

ABSTRACT

An assessment of the relative O-3/O-4 reactivities of both α- and β-methyl glycosides of *N*-dimethylmaleoyl (DMM) glucosamine and allosamine acceptors protected at O-6 with a benzyl group using a D-glucopyranosyl conformationally armed donor (superarmed donor) counterpart is presented. The glycosylation of glucosamine derivatives followed the trends already observed for disarmed donors. On the other hand, the glycosylation of allosamine derivatives gave exclusively substitution on the equatorial O-4, in spite that with a disarmed donor the point of substitution is exclusively on the more hindered, electronically-preferred O-3.

1. Introduction

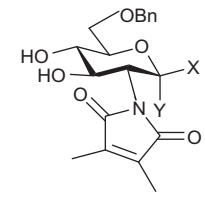
In the last years, the demands for reliable and easy synthetic approaches for oligosaccharides have expanded,[1] as their fundamental roles in biological processes were discovered. The mechanism of the glycosylation reaction has thus regained attention,[2,3] as the regio- and stereochemistry of the reaction define the final products, and their outcome, complicated to predicted and liable to subtle changes in the reaction medium, was attempted to be rationalized.[2–10] In this way, Vasella and co-workers[5,6] have shown the relevance of the acceptor hydrogen bonds in determining the regiochemistry of a glycosylation reaction of two secondary hydroxyl groups. This has been confirmed by experimental and theoretical calculations made on the charged reaction intermediates.[7,8] Fraser-Reid and co-workers have shown that the nature of the donor has an ultimate influence on the regioselectivity, introducing the concept of reciprocal donor–acceptor selectivity[9] by which 'armed' donors (i.e., those protected with electron-donating groups) react faster and in a different way (dependent on the acceptor) than 'disarmed' donors (i.e., those protected with electron-withdrawing groups). It has actually been shown that there are donors glycosylating faster than the armed ones, and others glycosylating at a slower rate than the disarmed ones, leading to the concept of superarmed and superdisarmed donors.[11]

Hexosamines are present in most of the glycoconjugates of natural origin; they are especially important in mammals.[12,13] Thus, the synthesis of relevant oligosaccharides, as those related to Le^x and peptidoglycan requires the manipulation of 6-O-protected, N-protected glucosamine 3,4-diols which should be specifically glycosylated. As disarmed donors tended to give exclusive 1→4 glycosylation and armed donors gave predominating 3-linked disaccharides,[14] sequential double-glycosylation of the acceptor diols (with no protection–deprotection scheme) were issued for the synthesis of Le^x-related oligosaccharides.[14,15] In any case, further work showed the influence of the anomeric configuration and protecting groups at O-6 of the *N*-dimethylmaleoyl (DMM) glucosamine acceptors on the regioselective outcome of the reaction.[16] From these reports it is obvious that no single reason for this typical regioselectivity holds under all glycosylation conditions. Besides electronic reasons, steric issues were used to explain exclusive glycosylations at O-4 with bulky donors.[17,18]

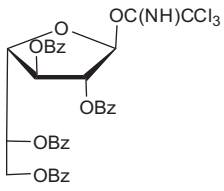
In a previous work,[16] we have assessed the regioselectivity of the isomeric α- and β- 6-O-benzylated *N*-dimethylmaleoyl (DMM) protected diols **1** and **2** when reacting with the disarmed donors **3** and **4**.

* Corresponding author. Tel./fax: +54 341 4370477.
E-mail address: colombo@iquir-conicet.gov.ar (M.I. Colombo).

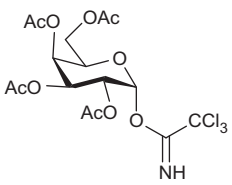
0008-6215/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.carres.2013.08.002



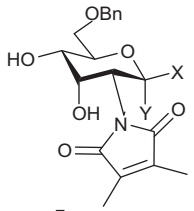
1 X=H; Y=OMe
2 X=OMe; Y=H



3

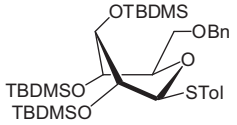


4



5 X=OMe; Y=H
6 X=H; Y=OMe

A marked difference in regioselectivity was found for the reaction with the furanosyl donor **3**: the α-anomer **1** gave rise to the 1→3 linked disaccharide preferentially (3.2:1), whereas the β-anomer **2** gave rise to the 1→4 disaccharide preferentially (2.9:1). The same reaction carried out with the less reactive donor **4** gave no regioselectivity for **1**, and complete O-4 selectivity for **2**.[16] When the allosamine derivatives **5** and **6** were allowed to react with the donor **4** complete O-3 selectivity was encountered,[8] in spite of the steric hindrance of this axial oxygen. DFT calculations strongly support this behavior from an electronic standpoint.[8] In continuation of these studies on the subtle factors acting on the regioselectivity of glycosylation of DMM-protected hexosamine acceptors, we have tried the reactions using the conformationally armed donor **7**. Within the superarmed donors,[11] compounds like **7** owe their high donating activity to the presence of bulky alkylsilyl groups which force the reagent to adopt a skew boat conformation (probably $^{3}S_{1}$) with axial or pseudoaxial silyloxy groups;[19,20] this conformation stabilizes markedly the intermediate oxacarbenium ion and thus, increases the rate of the glycosylation reaction[20] and generates a marked β-stereoselectivity in the products.[19]



$^{3}S_{1}$ TBDMS = $tBuMe_2Si$; Tol = p-tolyl

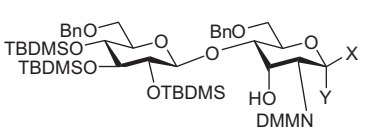
7

2. Results and discussion

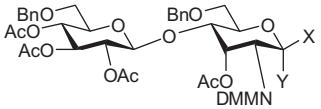
DMM-protected glucosamine acceptors **1** and **2**, were synthesized as described earlier,[16] whereas the allosamine acceptors (**5** and **6**) were obtained by reductive opening of the 4,6-*O*-benzylidene acetals[8] generated from inverting the C-3 configuration of the equivalent glucosamine derivatives.[21] The superarmed donor **7** was synthesized as described by Bols and co-workers.[20]

With these acceptors and donor in hand, we performed a number of coupling experiments. Glycosylations were carried out using the known methodologies of a thioglycoside as donor, activated by the addition of NIS and triflic acid at low temperatures. In our hands, the use of triflic acid gave variable yields. However, with TMSOTf a satisfactory reproducibility was obtained. The crude reaction mixtures were analyzed by TLC and ^{1}H NMR spectroscopy to establish the isomeric ratios. The results were confirmed by isolation of the disaccharides or derivatives by column chromatography, as explained for each coupling experiment. The type of linkage (1→3 or 1→4) was established in the ^{1}H NMR spectra by looking at the presence or absence of the signals corresponding to H(O)-3 and H(O)-4, and in the corresponding correlated HMBC spectra by observing the presence of H-1′–C-4/C-1′–H-4 or H-1′–C-3/C-1′–H-3 correlations. The disaccharides were characterized after removing the bulky alkylsilyl groups and then acetylating all the free hydroxyl groups. The results of the four coupling reactions are shown in Table 1.

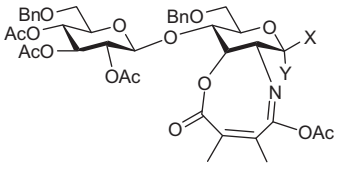
The reaction of donor **7** with the acceptor **5** gave exclusively the 4-linked disaccharide **8**, with a 54% yield. Some unreacted acceptor was found, but no other coupling product was detected by TLC or ^{1}H NMR. The determination of the anomeric configuration of disaccharide **8** could only be determined after removing the silyl protecting groups, with further acetylation. The removal of the silyl groups was first attempted by using tetrabutylammonium fluoride (TBAF) in THF solution. However, when this reaction was carried out and followed by acetylation of the free hydroxyl groups, the spectra of the product showed characteristics indicating that product **10** was not obtained, but instead, the unexpected product **12** was generated. The ^{13}C NMR and HMBC spectra confirmed the structure proposed for **12** and further, the $^{3}J_{H1',H2'}$ coupling constant (8.0 Hz) established the β-anomeric configuration of the disaccharide.



8: X=OMe, Y=H
9: X=H, Y=OMe



10: X=OMe, Y=H
11: X=H, Y=OMe



12: X=OMe, Y=H
13: X=H, Y=OMe

Table 1
Ratios[a] and yields of 3- and 4-linked disaccharides obtained after reaction of donor **7** and different acceptors, and comparison with the use of other donors

Acceptor	Ratio 1→3/1→4	Yield (%)	Ratio 1→3/1→4	
	With donor **7**		With donor **3**	With donor **4**
1 (GlcN, α)	2:1	65	3.2:1[b]	1:1[b]
2 (GlcN, β)	1:2.4	61	1:2.9[b]	0:1[b]
5 (AllN, β)	0:1	54	–	1:0[c]
6 (AllN, α)	0:1	57	–	1:0[c]

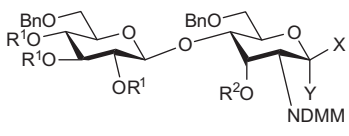
[a] Ratios were determined by ^{1}H NMR spectroscopy.
[b] From Ref. [16].
[c] From Ref. [8].

The formation of product **12** can be explained by rationalizing that the basic fluoride ion increases the nucleophilicity of O-3 allowing the attack to one of the carbonyl groups of DMM protecting group, followed by ring expansion and acetylation as shown in Scheme 1.

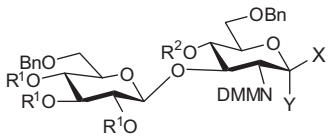
Changing the reaction conditions (i.e., using ethyl acetate as solvent, and adding acetic acid to reduce the basicity of the reagent) made possible to obtain a mixture of **10** (28%) and **12** (11%). By analysis of the ^{1}H NMR spectra of **10**, the anomeric configuration was established as β ($^3J_{H1',H2'}$ 7.8 Hz).

of reaction, determined that the product ratio was 2:1 favoring the 3-linked disaccharide (Table 1). Both disaccharides were fully characterized by their NMR spectra. Deprotection (removal of the silyl groups) with TBAF in EtOAc followed by acetylation, yielded the corresponding acetylated disaccharides **14b** and **15b**, for which the β-configuration was established ($^3J_{H1',H2'}$ 8.1 Hz and $^3J_{H1',H2'}$ 7.9 Hz, respectively).

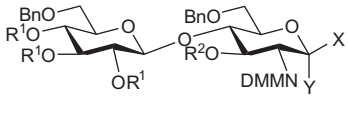
Coupling of **7** with acceptor **2** yielded a mixture of disaccharides **16a** and **17a**, not separable by column chromatography. Integration of the ^{1}H NMR signals of the crude reaction mixture indicated that the 4-linked disaccharide was prevalent, in a 2.4:1 ratio. The mixture could anyway be separated after acetylation by column chromatography to yield **16b** and **17b**. Removal of the silyl groups with TBAF in EtOAc, followed by acetylation, could only be possible with **17b**, yielding the corresponding acetylated disaccharide **17c**, for which the β-configuration was again established ($^3J_{H1',H2'}$ 7.9 Hz). Unfortunately, due to poor yields when obtaining disaccharide **16b**, removal of the silyl groups was not possible. Even so, according to the β-stereoselectivity previously described on all other disaccharides and taking into account that this selectivity is expected when using glucosyl superarmed donors,[19] it can be assumed that a β-stereochemistry was also obtained in **16b**.



8: X=OMe, Y=H, R^1=TBDMS, R^2=H
9: X=H, Y=OMe, R^1=TBDMS, R^2=H
10: X=OMe, Y=H, R^1=R^2=Ac



14a: X=H, Y=OMe, R^1=TBDMS, R^2=H
14b: X=H, Y=OMe, R^1=R^2=Ac
16a: X=OMe, Y=H, R^1=TBDMS, R^2=H
16b: X=OMe, Y=H,R^1=TBDMS, R^2=Ac

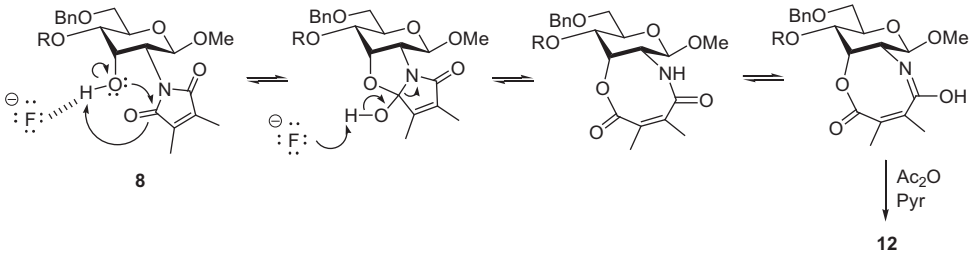


15a: X=H, Y=OMe, R^1=TBDMS, R^2=H
15b: X=H, Y=OMe, R^1=R^2=Ac
17a: X=OMe, Y=H, R^1=TBDMS, R^2=H
17b: X=OMe, Y=H, R^1=TBDMS, R^2=Ac
17c: X=OMe, Y=H, R^1=R^2=Ac

The coupling reaction of **7** and **6** also yielded exclusively the 4-linked disaccharide **9** (Table 1), as confirmed by NMR spectroscopy. As occurred for **8**, attempts of removal of the silyl groups with TBAF in THF resulted (after acetylation) in the anomalous product **13**, produced by attack of O-3 to one of the DMM carbonyl group. In this case, the reaction in EtOAc did not result in the expected generation of the desilylated disaccharide **11**. However, the β-stereochemistry of the disaccharide was again established by determining the $^3J_{H1',H2'}$ coupling constant in **13** (7.9 Hz).

The coupling reaction of **7** and **1** yielded a mixture of 1→3 and 1→4 disaccharides (**14a** and **15a**, respectively) in a total yield of 65%, together with some unreacted material. The mixture of disaccharides was separated by column chromatography. Both the relative yield of each isolated disaccharide and integration of characteristic signals of the ^{1}H NMR spectrum of the crude mixture

All these results indicate that the behavior of the superarmed donor **7** in reaction with the anomeric allosamine acceptors **5** and **6** is completely different to that observed in the reactions with the disarmed donor **4**. The superarmed donor gave regiospecifically 4-linked disaccharides with either allosamine acceptor, whereas the disarmed donor gave exclusively the 3-linked disaccharides.[8] In spite that with both donors (different leaving groups and activation conditions) the mechanism of the glycosylation reaction could be different, it seems probably at first sight that the axial O-3, even activated by a strong hydrogen bond,[8] is too hindered to react with the bulky superarmed donor **7**. In this regard, Moitessier and coworkers recently observed that an armed donor preferentially glycosylated the more accessible hydroxyl group, whereas the reaction with a disarmed donor occurred on the most reactive hydroxyl group of a given acceptor.[22] Alternatively, if the ring expansion



Scheme 1.

observed during the deprotection (Scheme 1) occurs during the glycosylation reaction, it may well explain the regioselectivity observed.[†]

In clear contrast with the results observed with the anomeric allosamine acceptors **5** and **6**, the reaction of the superarmed donor **7** with the glucosamine derivatives **1** and **2**, showed the same trends as those observed previously in reactions with the disarmed donor **3**,[16] even though, as mentioned above, the glycosylations could occur through different mechanisms with both donors.

3. Experimental

Melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer for $CDCl_3$ solutions with Me_4Si as internal standard. Proton and carbon peaks assignments were performed with the aid of 2D NMR techniques (COSY, HSQC and HMBC). High resolution mass spectrometry (HRMS-ESI) was performed in a Bruker microTOF-Q II apparatus. Optical rotations were measured with a Jasco DIP-1000 polarimeter. Column chromatography was performed on silica gel 60 H, slurry packed, run under low pressure of nitrogen and employing increasing amounts of EtOAc in hexane as solvent. Analytical TLC was carried out using Kieselgel Merck GF254 with a thickness 0.20 mm. The homogeneity of all compounds prior to the high resolution mass spectral determination was carefully verified by TLC. Reactions were routinely run under a dry nitrogen atmosphere with magnetic stirring. All chemicals were used as purchased or purified according to standard procedures. The glycosyl acceptors **1**, **2**, **5** and **6**, and the donor **7** were synthesized and purified as described earlier.[8,15,19] Their chemical and spectral characterization matched those found in the literature.[8,15,19]

3.1. General procedure for the glycosylation and acetylation reactions

A suspension of the corresponding acceptor (**1** or **2**) (1 equiv), donor **7** (1.3 equiv) and activated 3 Å molecular sieves (740 mg/mmol donor) in anhydrous CH_2Cl_2 (5.0 mL) was stirred at room temperature. After 30 min, the mixture was cooled to −60 °C, NIS (1 equiv) and then TMSOTf (0.15 equiv) were added and the stirring continued for 55 min, when the solution turned red. The mixture was then neutralized by addition of Et_3N and filtered through a silica gel pad with copious washings with EtOAc. The filtrate was washed with satd aq Na_2SO_3, brine, dried (Na_2SO_4), evaporated and the residue was chromatographed to yield the corresponding disaccharides. The glycosylation of acceptors **5** or **6** was performed under the same reaction conditions except that 0.53 equiv of TfOH was used instead of TMSOTf, and the temperature was −50 °C. The acetylations were carried out under standard conditions: pyridine, DMAP, Ac_2O, room temperature, overnight.

3.1.1. Methyl 6-*O*-benzyl-2,3,4-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-allopyranoside (8)

54%; as a foam: $[\alpha]_D^{20}$ −29.3 (*c* 1.52, $CHCl_3$); R_f 0.67 (1:1 hexane:EtOAc). ^{1}H NMR *δ*: 7.37–7.33 (m, 5H, Ar*H*), 7.30–7.26 (m, 5H, Ar*H*′), 5.69 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 4.82 (d, 1H, $J_{1',2'}$ 4.3 Hz, H-1′), 4.66 (d, 1H, *J* 12.4 Hz, C*H*$_2$Ph), 4.57 (d, 1H, *J* 12.4 Hz, C*H*$_2$Ph), 4.46 (br s, 2H, C*H*$_2$Ph′), 4.33 (m, 1H, H-3), 4.10 (ddd, $J_{5,6b}$ 4.8 Hz, 1H, H-5), 3.95 (ddd, 1H, H-2), 3.92–3.82 (m, 2H, H-5′, H-6a), 3.77 (dd, with appearance of t, $J_{4',3'}$–$J_{4',5'}$ 2.8 Hz, 1H, H-4′), 3.73–3.68 (m, 2H, H-3′, H-4), 3.67–3.60 (m, 2H, H-2′, H-6b), 3.61–3.50 (m, 2H, H-6′), 3.49 (s, 3H, OC*H*$_3$), 3.32 (br s, 1H, O*H*), 1.87 (s, 6H, CC*H*$_3$ × 2), 0.86 (2s, 18H, C(C*H*$_3$)$_3$ × 2), 0.84 (s, 9H, C(C*H*$_3$)$_3$), 0.08 (s, 3H, Si-C*H*$_3$), 0.05 (s, 3H, Si-C*H*$_3$), 0.04 (s, 3H, Si-C*H*$_3$), 0.03 (s, 3H, Si-C*H*$_3$), 0.02 (s, 3H, Si-C*H*$_3$), −0.01 (s, 3H, Si-C*H*$_3$); ^{13}C NMR *δ*: 171.91 (*C*O × 2), 138.56 (*C*-Ar), 138.13 (*C*-Ar′), 136.99 (*C* × 2), 128.29, 127.44, 127.42 (*C*-Ar × 5, *C*-Ar′ × 5), 102.80 (C-1′), 97.09 (C-1), 78.25 (C-5′), 78.04 (C-4), 76.26 (C-3′), 76.20 (C-2′) 73.38 (*C*H$_2$Ph), 73.13 (*C*H$_2$Ph′), 72.58 (C-5), 70.99 (C-4′), 70.79 (C-6′), 69.81 (C-6, C-3), 56.71 (OC*H*$_3$), 55.38 (C-2), 25.84 (C(*C*H$_3$)$_3$ × 3), 17.91 (Si-*C*Me$_3$ × 3), 8.72 (CC*H*$_3$ × 2), −4.20, −4.28, −4.37, −4.42, −4.58, −4.94 (Si-*C*H$_3$ × 6); ESI-HMRS: calcd for $[C_{51}H_{83}NO_{12}Si_3 - H]^-$: 984.51503. Found, *m*/*z*: 984.51322. Unreacted acceptor **5** (28%).

3.1.2. Methyl 6-*O*-benzyl-2,3,4-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α-D-allopyranoside (9)

57%; as a foam: R_f 0.59 (7:3 hexane:EtOAc). ^{1}H NMR *δ*: 7.36–7.28 (m, 10H, Ar*H*, Ar*H*′), 5.21 (br d, 1H, $J_{OH,H-3}$ 1.4 Hz, O*H*), 4.92 (d, 1H, $J_{1',2'}$ 6.0 Hz, H-1′), 4.73 (br s, 1H, H-1), 4.71 (d, 1H, *J* 10.1 Hz, C*H*$_2$Ph), 4.56–4.48 (m, 4H, C*H*$_2$Ph, C*H*$_2$Ph′, H-3), 4.45–4.36 (m, 1H, H-5), 4.30 (dd, 1H, *J* 3.6; 2.4 Hz, H-2), 4.00 (ddd, 1H, *J* 1.2; 6.8; 7.3 Hz, H-5′), 3.93–3.83 (m, 1H, H-4′), 3.88–3.78 (m, 2H, H-4, H-6a), 3.76–3.71 (m, 3H, H-2′, H-3, H-6b), 3.63 (d, with appearance of s, 1H, H-6a′), 3.60 (d, with appearance of s, 1H, H-6b′), 3.33 (s, 3H, OC*H*$_3$), 1.95 (s, 6H, CC*H*$_3$ × 2), 0.91 (s, 9H, C(C*H*$_3$)$_3$), 0.87 (s, 9H, C(C*H*$_3$)$_3$), 0.85 (s, 9H, C(C*H*$_3$)$_3$), 0.11 (s, 3H, Si-C*H*$_3$), 0.10 (s, 6H, Si-C*H*$_3$ × 2), 0.06 (s, 3H, Si-C*H*$_3$), 0.04 (s, 3H, Si-C*H*$_3$), 0.02 (s, 3H, Si-C*H*$_3$); ^{13}C NMR *δ*: 172.37 (*C*O × 2), 138.56 (*C*-Ar), 137.49 (*C*-Ar′, *C* × 2), 128.25, 128.19, 127.40, 127.31 (*C*-Ar × 5, *C*-Ar′ × 5), 102.28 (C-1′), 98.47 (C-1), 80.02 (C-5′), 79.39 (C-4′), 77.19 (C-2′), 75.12 (C-4), 73.26 (*C*H$_2$Ph), 73.10 (*C*H$_2$Ph′), 71.34 (C-6′), 70.97 (C-3′), 69.48 (C-3), 68.94 (C-6), 66.16 (C-5), 55.86 (OC*H*$_3$), 54.88 (C-2), 25.93 (C(*C*H$_3$)$_3$), 25.88 (C(*C*H$_3$)$_3$ × 2), 17.92 (Si-*C*Me$_3$ × 3), 8.90 (CC*H*$_3$ × 2), −3.70, −3.90, −4.45, −4.75, −4.77 (Si-*C*H$_3$ × 6); ESI-HMRS: calcd for $[C_{51}H_{83}NO_{12}Si_3 + K]^+$: 1024.48547. Found: *m*/*z*: 1024.48113. Unreacted acceptor **6** (24%).

3.1.3. Methyl 6-*O*-benzyl-2,3,4-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1→3)-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α-D-glucopyranoside (14a) and methyl 6-*O*-benzyl-2,3,4-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α-D-glucopyranoside (15a)

3.1.3.1. Disaccharide 14a. 43%; as a foam: $[\alpha]_D^{31}$ +49.9 (*c* 0.54, $CHCl_3$); R_f 0.61 (7:3 hexane:EtOAc). ^{1}H NMR *δ*: 7.40–7.21 (m, 10H, Ar*H*, Ar*H*′), 5.12 (dd, 1H, $J_{3,4}$ 8.6 Hz, $J_{3,2}$ 11.1 Hz, H-3), 5.08 (s, 1H, O*H*), 4.91 (d, 1H, $J_{1',2'}$ 5.2 Hz, H-1′), 4.69 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 4.65 (d, 1H, *J* 12.4 Hz, C*H*$_2$Ph), 4.61 (d, 1H, *J* 12.4 Hz, C*H*$_2$Ph), 4.54 (d, 1H, *J* 11.9 Hz, C*H*$_2$Ph′), 4.51 (d, 1H, *J* 11.9 Hz, C*H*$_2$Ph′), 4.14 (dd, 1H, H-2), 4.13–4.08 (m, 1H, H-5′), 3.88–3.79 (m, 3H, H-4′, H-5, H-6a), 3.74 (dd, 1H, *J* 5.9; 10.8 Hz, H-6b), 3.68 (br s, 1H, H-3′), 3.66–3.59 (m, 2H, H-6′), 3.57 (br d, 1H, H-2′), 3.50, (ddd, 1H, $J_{4,5}$ 9.1 Hz, H-4), 3.28 (s, 3H, OC*H*$_3$), 1.92 (br s, 6H, CC*H*$_3$ × 2), 0.88 (s, 9H, C(C*H*$_3$)$_3$), 0.86 (s, 9H, C(C*H*$_3$)$_3$), 0.78 (s, 9H, C(C*H*$_3$)$_3$), 0.04 (s, 6H, Si-C*H*$_3$ × 2), 0.03 (s, 6H, Si-C*H*$_3$ × 2), 0.00 (s, 3H, Si-C*H*$_3$), −0.11 (s, 3H, Si-C*H*$_3$); ^{13}C NMR *δ*: 172.71, 171.47 (*C*O × 2), 138.60 (*C*-Ar), 138.27 (*C*), 138.11 (*C*-Ar′), 136.14 (*C*), 128.25, 127.69, 127.52, 127.47, 127.34 (*C*-Ar × 5, *C*-Ar′ × 5), 100.37 (C-1′), 98.45 (C-1), 78.80 (C-3′), 78.75 (C-5′), 76.82 (C-2′), 75.82 (C-3), 73.45 (*C*H$_2$Ph), 73.29 (*C*H$_2$Ph′), 71.22 (C-5), 71.04 (C-4′), 70.78 (C-6′), 70.01 (C-4), 69.70 (C-6), 55.01 (C-2, OC*H*$_3$), 25.85 (C(*C*H$_3$)$_3$), 25.81 (C(*C*H$_3$)$_3$), 25.63 (C(*C*H$_3$)$_3$), 17.85 (Si-*C*Me$_3$ × 2), 17.70 (Si-*C*Me$_3$), 8.74 (CC*H*$_3$ × 2), −3.78, −4.48, −4,58, −4.68, −4.73, −4.97 (Si-*C*H$_3$ × 6). ESI-HMRS: calcd for $[C_{51}H_{83}NO_{12}Si_3 + Na]^+$: 1008.51153. Found: *m*/*z*: 1008.50806.

[†] We thank an anonymous reviewer for the suggestion that the ring expansion could occur during the glycosylation reaction.

3.1.3.2. Disaccharide 15a. 24%; as a foam: $[\alpha]_D^{31}$ +72.7 (*c* 0.43, $CHCl_3$); R_f 0,66 (7:3 hexane:EtOAc). ^1H NMR δ: 7.35–7.31 (m, 5H, Ar*H*), 7.28–7.23 (m, 5H, Ar*H*′), 4.99 (dd, 1H, $J_{3,2}$ 11.3 Hz, $J_{3,4}$ 8.7 Hz, H-3), 4.83 (d, 1H, $J_{1',2'}$ 6.0 Hz, H-1′), 4.69 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 4.68 (d, 1H, *J* 12.4 Hz, CH_2Ph), 4.53 (d, 1H, *J* 12.4 Hz, CH_2Ph), 4.49 (d, 1H, *J* 11.9 Hz, CH_2Ph′), 4.44 (d, 1H, *J* 11.9 Hz, CH_2Ph′), 4.35 (br s, 1H, O*H*), 4.10 (dd, 1H, H-2), 4.04 (ddd, 1H, *J* 1.0; 6.9 (×2) Hz, H-5′), 3.89–3.83 (m, 2H, H-4′, H-5), 3.79–3.71 (m, 3H, H-3′, H-6), 3.67–3.60 (m, 2H, H-2′, H-4), 3.59 (br s, 1H, H-6a′), 3.57 (br s, 1H, H-6b′), 3.31 (s, 3H, OCH_3), 1.94 (s, 6H, CCH_3 × 2), 0.91 (s, 9H, C(CH_3)$_3$), 0.88 (s, 9H, C(CH_3)$_3$), 0.83 (s, 9H, C(CH_3)$_3$), 0.10 (2s, 6H, Si-CH_3 × 2), 0.07 (s, 3H, Si-CH_3), 0.04 (s, 3H, Si-CH_3), 0.02 (s, 3H, Si-CH_3), −0.01 (s, 3H, Si-CH_3); ^{13}C NMR δ: 171.97 (*C*O × 2), 138.34 (*C*-Ar), 138.09 (*C*-Ar′), 136.98 (*C* × 2), 128.27, 128.21, 127.62, 127.44, 127.37, 127.30 (*C*-Ar × 5, *C*-Ar′ × 5), 101.75 (C-1′), 98.63 (C-1), 80.09 (C-5′), 79.32 (C-4), 78.81 (C-3′), 77.30 (C-2′), 73.40 (*C*H$_2$Ph), 73.28 (*C*H$_2$Ph′), 70.86, 70.83 (C-4, C-6′), 69.84 (C-5), 68.33 (C-6), 65.16 (C-3), 56.17 (C-2), 55.48 (OCH_3), 25.89 (C(*C*H$_3$)$_3$), 25.80 (C(*C*H$_3$)$_3$), 25.77 (C(*C*H$_3$)$_3$), 17.87 (Si-*C*Me$_3$ × 3), 8.76 (C*C*H$_3$ × 2), −3.63, −4.03, −4.41, −4.55, −4,87, −4,95 (Si-*C*H$_3$ × 6); ESI-HMRS: calcd for $[C_{51}H_{83}NO_{12}Si_3 + Na]^+$: 1008.51153. Found: *m*/*z*: 1008.50648. Unreacted acceptor **1** (24%).

3.1.4. Methyl 6-*O*-benzyl-2,3,4-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1→3)-4-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranoside (16b) and methyl 6-*O*-benzyl-2,3,4-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranoside (17b)

3.1.4.1. Disaccharide 16b. 4% (from **2**), as a foam: R_f 0.53 (7:3 hexane:EtOAc). ^1H NMR δ: 7.37–7.27 (m, 10H, Ar*H*, Ar*H*′), 4.90–4.85 (m, 2H, H-3, H-4), 4.75 (d, 1H, $J_{1,2}$ 8.33 Hz, H-1), 4.56 (t, 4H, CH_2Ph, CH_2Ph′), 4.41, (d, 1H, $J_{1',2'}$ 6.2 Hz, H-1′), 4.07 (dd, 1H, $J_{2,3}$ 10.4 Hz, H-2), 3.82 (br d, 1H, *J* 3.1 Hz, H-4′), 3.79–3.74 (m, 1H, H-5′), 3.73–3.69 (m, 1H, H-5), 3.68–3.64 (m, 1H, H-6a′), 3.63–3.60 (m, 1H, H-3′), 3.60–3.56 (m, 3H, H-6b′, H-6), 3.40 (s, 3H, OCH_3), 3.35 (d, 1H, H-2′), 1.92 (2s, 9H, COCH_3, CCH_3 × 2), 0.85 (s, 9H, C(CH_3)$_3$), 0.82 (s, 9H, C(CH_3)$_3$), 0.79 (s, 9H, C(CH_3)$_3$), 0.06 (s, 3H, Si-CH_3), 0.03 (s, 3H, Si-CH_3), 0.02 (s, 6H, (Si-CH_3) × 2), −0.03 (2s, 6H, (Si-CH_3) × 2); ^{13}C NMR δ: 169.58 (*C*O × 3), 138.36, 138.10 (*C*-Ar, *C*-Ar′), 137.33 (*C* × 2), 128.33, 128.26, 127.76, 127.64, 127.57, 127.50 (*C*-Ar × 5, *C*-Ar′ × 5), 100.00 (C-1′), 99.30 (C-1), 80.70 (C-5′), 78.67 (C-3′), 78.10 (C-2′), 73.72 (C-5), 73.51 (*C*H$_2$Ph), 73.16 (*C*H$_2$Ph′), 71.31 (C-6′), 70.74 (C-4, C-4′), 70.42 (C-3), 69.54 (C-6), 56.52 (OCH_3), 55.63 (C-2), 25.90 (C(*C*H$_3$)$_3$), 25.80 (C(*C*H$_3$)$_3$ × 2), 21.10 (COCH_3), 17.89 (Si-*C*Me$_3$ × 2), 17.83 (Si-*C*Me$_3$), 8.90 (C*C*H$_3$ × 2), −3.89, −4.13, −4.64, −4.84, −4,88, −4.98 (Si-CH_3 × 6). ESI-HMRS: calcd for $[C_{53}H_{85}NO_{13}Si_3 + Na]^+$: 1050.52209. Found: *m*/*z*: 1050.51737.

3.1.4.2. Disaccharide 17b. 14% (from **2**), as a foam: $[\alpha]_D^{32}$ +10.9 (*c* 0.42, $CHCl_3$); R_f 0.48 (7:3 hexane:EtOAc). ^1H NMR δ: 7.37–7.26 (m, 10H, Ar*H*, Ar*H*′), 5.51 (dd, 1H, $J_{3,2}$ 10.8 Hz, $J_{3,4}$ 8.9 Hz, H-3), 5.10 (d, 1H, $J_{1,2}$ 8.6 Hz, H-1), 4.73 (d, 1H, $J_{1',2'}$ 6.4 Hz, H-1′), 4.64 (d, 1H, *J* 12.1 Hz, CH_2Ph), 4.56 (d, 1H, *J* 12.1 Hz, CH_2Ph), 4.52 (d, 1H, *J* 11.9 Hz, CH_2Ph′), 4.49 (d, 1H, *J* 11.9 Hz, CH_2Ph′), 4.02 (dd, 1H, H-2), 3.97–3.88 (m, 2H, H-4, H-5′), 3.88–3.83 (m, 2H, H-3′, H-6a), 3.72–3.67 (m, 2H, H-4′, H-6b), 3.66–3.63 (m, 1H, H-5), 3.62–3.53 (m, 2H, H-6′), 3.47 (br d, 1H, H-2′), 3.42 (s, 3H, OCH_3), 1.94 (s, 6H, CCH_3 × 2), 1.87 (s, 3H, COCH_3), 0.89 (s, 9H, C(CH_3)$_3$), 0.85 (s, 9H, C(CH_3)$_3$), 0.84 (s, 9H, C(CH_3)$_3$), 0.08 (s, 6H, Si-CH_3 × 2), 0.06 (s, 3H, Si-CH_3), 0.03 (s, 3H, Si-CH_3), 0.01 (s, 3H, Si-CH_3), −0.02 (s, 3H, Si-CH_3); ^{13}C NMR δ: 171.55, 170.41 (*C*O × 3), 138.36, 138.24 (*C*-Ar, *C*-Ar′), 128.30, 128.25, 127.57, 127.52, 127.37 (*C*-Ar × 5, *C*-Ar′ × 5), 100.79 (C-1′), 98.92 (C-1), 80.67 (C-5′), 78.67 (C-4′), 77.85 (C-2′), 75.17 (C-5), 73.54 (C-4), 73.24 (*C*H$_2$Ph), 73.08 (*C*H$_2$Ph′), 71.35 (C-6′), 71.31 (C-3), 70.66 (C-3′), 68.20 (C-6), 56.62 (OCH_3), 54.65 (C-2), 25.90 (C(*C*H$_3$)$_3$), 25.84 (C(*C*H$_3$)$_3$), 25.74 (C(*C*H$_3$)$_3$), 20.77 (COCH_3), 17.92 (Si-*C*Me$_3$), 17.89 (Si-*C*Me$_3$), 17.81 (Si-*C*Me$_3$), 8.77 (C*C*H$_3$ × 2), −3.81, −3.89, −4.62, −4.66, −4.92, −5.04 (Si-CH_3 × 6); ESI-HMRS: calcd for $[C_{53}H_{85}NO_{13}Si_3 + Na]^+$: 1050.52209. Found: *m*/*z*: 1050.51686. Unreacted acceptor **2** (10%).

3.2. Reactions for deprotection of the *tert*-butyldimethylsilyl groups

3.2.1. Attempt of deprotecting disaccharide 8

Tetrabutylammonium fluoride (TBAF, 1 M solution in THF, 240 μL, 0.24 mmol) was added dropwise to a solution of **8** (17.2 mg, 17.44 μmol) in THF (1.0 mL) in an ice-water bath, and the mixture was allowed to reach room temperature during 1 h. After 16 h (TLC) the solvent was evaporated and the residue was acetylated and chromatographed yielding compound **12** (5.3 mg, 38%) as a foam: R_f 0.22 (1:1 hexane:EtOAc). ^1H NMR δ: 7.42–7.33 (m, 5H, Ar*H*′), 7.32–7.27 (m, 5H, Ar*H*), 5.63 (dd, 1H, $J_{3,2}$–$J_{3,4}$ 3.0 Hz, H-3), 5.12–5.04 (m, 2H, H-3′, H-4′), 4.90 (dd, 1H, $J_{2',1'}$ 8.0 Hz, $J_{2',3'}$ 9.7 Hz, H-2′), 4.78 (d, 1H, $J_{1,2}$ 8.3 Hz, H-1), 4.69 (d, 1H, *J* 12.1, CH_2Ph), 4.56 (d, 1H, CH_2Ph), 4.53 (d, 1H, *J* 12.1, CH_2Ph′), 4.51 (d, 1H, H-1′), 4.46 (d, 1H, *J* 12.1, CH_2Ph′), 4.03–3.88 (m, 3H, H-2, H-4, H-5), 3.71 (dd, 1H, $J_{6a,6b}$ 10.7 Hz, $J_{6a,5}$ 1.0 Hz, H-6a), 3.66 (dd, 1H, $J_{6b,5}$ 3.6 Hz, H-6b), 3.54 (br s, 3H, H-5′, H-6′), 3.49 (s, 3H, OCH_3), 2.07 (s, 3H, COCH_3), 1.99 (br s, 3H, C(N)CCH_3), 1.97 (s, 3H, COCH_3), 1.93 (s, 3H, COCH_3), 1.92 (br s, 3H, C(O)CCH_3), 1.86 (s, 3H, COCH_3); ^{13}C NMR δ: 170.31, 169.90, 169.45, 169.19 (*C*O × 4), 167.87 (*C*(O)CMe), 154.89 (*C*(N)O), 145.83 (C(N)*C*Me), 138.17 (*C*-Ar′), 138.01 (*C*-Ar), 132.86 (C(O)*C*Me), 128.50, 128.27, 127.78, 127.49 (*C*-Ar × 5, *C*-Ar′ × 5), 101.16 (C-1), 100.86 (C-1′), 73.74 (*C*H$_2$Ph), 73.62 (*C*H$_2$Ph′), 73.53 (C-4), 73.07 (C-5), 73.00 (C-3′, C-5′), 71.53 (C-2′), 71.05 (C-3), 69.12 (C-4′), 68.62 (C-6′), 68.47 (C-6), 60.48 (C-2), 56.64 (OCH_3), 20.87 (COCH_3), 20.63 (COCH_3 × 3), 10.00 (C(N)CCH_3), 9.09 (C(O)CCH_3); ESI-HMRS: calcd for $[C_{41}H_{49}NO_{16} + H]^+$: 812.31241. Found: *m*/*z*: 812.31103.

3.2.2. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-allopyranoside (10)

Tetrabutylammonium fluoride (TBAF, 1 M solution in THF, 240 μL, 0.24 mmol) was added dropwise to a solution of **8** (25.1 mg, 24.4 μmol) in EtOAc (2.0 mL) with AcOH (9.6 μL, 0.17 mmol) at −20 °C, and the mixture was allowed to reach room temperature during 1 h. After 16 h (TLC) the solvent was evaporated and the residue was acetylated and chromatographed yielding compound **10** (5.7 mg, 28%) as a foam and the anomalous compound **12** (2.3 mg, 11%).

3.2.2.1. Disaccharide 10. R_f 0.40 (1:1 hexane:AcOEt). ^1H NMR δ: 7.39–7.34 (m, 5H, Ar*H*′), 7.33–7.29 (m, 5H, Ar*H*), 5.57 (dd, 1H, H-3), 5.55 (d, 1H, $J_{1,2}$ 8.6 Hz, H-1), 5.10–5.04 (m, 2H, H-3′, H-4′), 4.88 (dd, 1H, $J_{2',1'}$ 7.8 Hz, $J_{2',3'}$ 9.8 Hz, H-2′), 4.69 (d, 1H, *J* 12.1 Hz, CH_2-Ph′), 4.55 (d, 1H, CH_2Ph′), 4.52 (d, 1H, CH_2Ph), 4.50 (d, 1H, H-1′), 4.46 (d, 1H, *J* 11.9 Hz, CH_2Ph), 4.01 (dd, 1H, $J_{2,3}$ 2.5 Hz, H-2), 3.98 (br s, 2H, H-4, H-5), 3.71 (d, 1H, $J_{6a,6b}$ 10.8 Hz, H-6a), 3.66 (dd, 1H, $J_{6b,5}$ 2.7 Hz, H-6b), 3.56–3.47 (m, 3H, H-5′, H-6), 3.46 (s, 3H, OCH_3), 1.99 (s, 3H, COCH_3), 1.97 (s, 3H, COCH_3), 1.93 (s, 3H, COCH_3), 1.90 (br s, 6H, CCH_3 × 2), 1.87 (s, 3H, COCH_3); ^{13}C NMR δ: 171.63, 170.61, 170.32, 169.42, 169.16 (*C*O × 6), 138.10, 138.01 (*C*-Ar × 2, *C* × 2), 128.51, 128.31, 127.88, 127.79, 127.55 (*C*-Ar × 5, *C*-Ar′ × 5), 100.85 (C-1′), 97.48 (C-1), 73.73 (C-4, *C*H$_2$Ph′), 73.59 (*C*H$_2$Ph), 73.21 (C-5), 73.10 (C-5′), 72.98 (C-4′), 71.44 (C-2′), 70.98 (C-3), 68.95 (C-3′), 68.37 (C-6, C-6′), 56.76 (OCH_3), 54.42 (C-2), 20.80 (COCH_3),

20.62 ($COCH_3 \times 3$), 8.77 ($CCH_3 \times 2$); ESI-HMRS: calcd for $[C_{41}H_{49}NO_{16} + Na]^+$: 834.29436. Found: *m*/*z*: 834.29312.

3.2.3. Attempt of deprotecting disaccharide 9

The reaction for compound **9** (86.9 mg, 88.1 μmol) was carried out as described for compound **8** in THF solution, yielding compound **13** (1.4 mg, 1.72 μmol) as a foam: R_f 0.75 (1:1 hexane:EtOAc). ^{1}H NMR δ: 7.41–7.26 (m, 10H, Ar*H*, Ar*H*′), 5.64 (unresolved dd, 1H, $J_{3,4}$–$J_{3,2}$ 3.3 Hz, H-3), 5.11–5.00 (m, 2H, H-3′, H-5′), 4.88 (dd, 1H, $J_{2',1'}$ 7.9 Hz, $J_{2',3'}$ 9.4 Hz, H-2′), 4.77 (d, 1H, $J_{1,2}$ 4.2 Hz, H-1), 4.72 (d, 1H, *J* 12.0 Hz, C*H*$_2$Ph), 4.53 (d, 1H, *J* 11.9 Hz, C*H*$_2$Ph′), 4.52 (d, 1H, *J* 12.0 Hz, C*H*$_2$Ph), 4.50 (d, 1H, H-1′), 4.49 (d, 1H, *J* 11.9 Hz, C*H*$_2$Ph′), 4.18–4.12 (m, 2H, H-2, H-5), 3.96 (dd, 1H, $J_{4,5}$ 10.1 Hz, H-4), 3.74–3.64 (m, 2H, H-6), 3.58–3.48 (m, 3H, H-4′, H-6′), 3.38 (s, 3H, OC*H*$_3$), 2.10 (s, 3H, COC*H*$_3$), 2.04 (d, 3H, *J* 1,2 Hz, C(N)CC*H*$_3$), 1.97 (s, 3H, COC*H*$_3$), 1.94 (d, 3H, *J* 1.2 Hz, C(O)CC*H*$_3$), 1.93 (s, 3H, COC*H*$_3$), 1.88 (s, 3H, COC*H*$_3$); ^{13}C NMR δ: 170.82, 170.32, 169.50, 169.05 (*C*O × 4), 167.74 (*C*(O)CMe), 154.20 (*C*(N)O), 146.27 (C(N)*C*Me), 138.07 (*C*-Ar′), 137.93 (*C*-Ar), 132.83 (C(O)*C*Me), 128.60, 128.27, 127.97, 127.93, 127.71, 127.49 (*C*-Ar × 5, *C*-Ar′ × 5), 100.66 (C-1′), 98.60 (C-1), 73.80 (*C*H$_2$Ph), 73.51 (*C*H$_2$Ph′), 73.14 (C-4′), 72.98 (C-3′), 72.61 (C-4), 71.57 (C-2′), 70.06 (C-3), 69.36 (C-5′), 68.92 (C-6′), 68.28 (C-6), 65.52 (C-5), 58.30 (C-2), 55.80 (O*C*H$_3$), 21.25 (COC*H*$_3$), 20.62 (COC*H*$_3$ × 3), 10.19 (C(N)CC*H*$_3$), 9.12 (C(O)CC*H*$_3$); ESI-HMRS: calcd for $[C_{41}H_{49}NO_{16} + Na]^+$: 834.29436. Found: *m*/*z*: 834.29352.

3.2.4. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)-4-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α-D-glucopyranoside (14b)

The reaction for compound **14a** (15.2 mg, 14.41 μmol) was carried out as described for compound **8** in EtOAc and AcOH solution, yielding compound **14b** (4.4 mg, 35%) as a foam: R_f 0.37 (1:1 hexane:EtOAc). ^{1}H NMR δ: 7.42–7.29 (m, 10 H, Ar*H* × 5 Ar*H*′ × 5), 5.18–5.06 (m, 2H, H-3, H-4′), 5.05–4.94 (m, 2H, H-3′,H-4), 4.71 (dd, 1H, $J_{2',1'}$–$J_{2',3'}$ 8.1 Hz, H-2′), 4.62 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 4.53 (br s, 2H, C*H*$_2$Ph′), 4.48 (d, 1H, H-1′), 4.47 (d, 1H, *J* 11.6 Hz, C*H*$_2$Ph), 4.39 (d, 1H, *J* 11.6 Hz, C*H*$_2$Ph), 4.23 (dd, 1H, $J_{2,3}$ 10.9 Hz, H-2), 4.00–3.92 (m, 1H, H-5), 3.60–3.49 (m, 5H, H-5′, H-6′, H-6), 3.31 (s, 3H, O*C*H$_3$), 2.02 (br s, 3H, CC*H*$_3$), 1.96 (br s, 3H, CC*H*$_3$), 1.94 (s, 3H, COC*H*$_3$), 1.92 (s, 3H, COC*H*$_3$), 1.83 (s, 3H, COC*H*$_3$), 1.77 (s, 3H, COC*H*$_3$); ^{13}C NMR δ: 172.25, 172.14, 170.60, 169.68, 169.37, 168.84 (*C*O × 6), 138.83 (*C*), 137.88 (*C*-Ar), 137.40 (*C*-Ar′), 135.99 (C), 128.36, 128.33, 128.01, 127.80, 127.61 (*C*-Ar × 5, *C*-Ar′ × 5), 99.03 (C-1′), 98.70 (C-1), 73.51 (*C*H$_2$Ph′), 73.27 (C-3, *C*H$_2$Ph), 73.03 (C-3′), 72.55 (C-5′), 71.85 (C-2′), 69.70 (C-4), 69.30 (C-4′), 68.99 (C-6′), 68.89 (C-5), 68.47 (C-6), 55.32 (O*C*H$_3$), 55.12 (C-2), 20.63 (COC*H*$_3$ × 2), 20.57 (COC*H*$_3$), 20.31 (COC*H*$_3$), 8.82 (CC*H*$_3$ × 2). ESI-HMRS: calcd for $[C_{41}H_{49}NO_{16} + Na]^+$: 834.29436. Found: *m*/*z*: 834.29399.

3.2.5. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α-D-glucopyranoside (15b)

The reaction for compound **15a** (15.8 mg, 16.1 μmol) was carried out as described for compound **8** in EtOAc and AcOH solution, yielding compound **15b** (4.9 mg, 37%) as a foam: R_f 0.32 (1:1 hexane:EtOAc). ^{1}H NMR δ: 7.45–7.27 (m, 10H, Ar*H* × 5, Ar*H*′ × 5), 6.23 (dd, 1H, $J_{3,2}$ 11.7 Hz, $J_{3,4}$ 8.3 Hz, H-3), 5.04 (dd, 1H, $J_{4',3'}$–$J_{4',5'}$ 9.2 Hz, H-4′), 4.97 (dd, 1H, $J_{3',2'}$ 9.2 Hz, H-3′), 4.84–4.76 (m, 2H, H-2′, C*H*$_2$Ph), 4.70 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 4.49 (d, 1H, *J* 12,0 Hz, C*H*$_2$Ph), 4.45 (d, 1H, *J* 11.6 Hz, C*H*$_2$Ph′), 4.44 (d, 1H, $J_{1',2'}$ 7.9 Hz, H-1′), 4.40 (d, 1H, *J* 11.6 Hz, C*H*$_2$Ph′), 4.32 (dd, 1H, H-2), 3.91–3.86 (m, 2H, H-4, H-5), 3.82 (br d, 1H, $J_{6a,6b}$ 10.2 Hz, H-6a), 3.65 (br d, 1H, H-6b), 3.53 (dd, 1H, $J_{6'a,5'}$ 3.0 Hz, $J_{6'a,6'b}$ 10.3 Hz, H-6a′), 3.46 (dd, 1H, $J_{6'b,5'}$ 4.4 Hz, H-6b′), 3.40–3.33 (m, 1H, H-5′), 3.29 (s, 3H, O*C*H$_3$), 1.97 (s, 3H, COC*H*$_3$), 1.93 (s, 6H, CC*H*$_3$ × 2), 1.92 (s, 3H, COC*H*$_3$), 1.89 (s, 3H, COC*H*$_3$), 1.86 (s, 3H, COC*H*$_3$); ^{13}C NMR δ: 171.16, 170.46, 169.40, 169.18, 168.66 (*C*O × 6), 137.48 (*C*-Ar, *C*-Ar′), 137.14 (*C* × 2), 128.72, 128.39, 128.27, 127.81 (*C*-Ar × 5, *C*-Ar′ × 5), 99.76 (C-1′), 98.67 (C-1), 76.10 (C-4), 73.77 (*C*H$_2$Ph), 73.48 (*C*H$_2$Ph′), 73.26 (C-3′), 72.61 (C-5′), 71.93 (C-2′), 69.85 (C-5), 69.19 (C-4′), 68.63 (C-6′), 67.24 (C-6), 66.92 (C-3), 55.29 (O*C*H$_3$), 53.63 (C-2), 20.86 (COC*H*$_3$), 20.66 (COC*H*$_3$ × 2), 20.61 (COC*H*$_3$), 8.84 (CC*H*$_3$ × 2); ESI-HMRS: calcd for $[C_{41}H_{49}NO_{16} + K]^+$: 850.26829. Found: *m*/*z*: 850.27111.

3.2.6. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α-D-glucopyranoside (17c)

The reaction for compound **16b** (20.1 mg, 20.38 μmol) was carried out as described for compound **8** in EtOAc and AcOH solution, yielding compound **17c** (8.0 mg, 50%) as a foam: R_f 0.52 (1:1 hexane:EtOAc). ^{1}H NMR δ: 7.40–7.27 (m, 10H, Ar-*H*), 5.48 (dd, 1H, $J_{3,2}$ 10.7 Hz, $J_{3,4}$ 9.0 Hz, H-3), 5.09 (d, 1H, $J_{1,2}$ 8.6 Hz, H-1), 5.07 (t, 1H, $J_{4',3'}$–$J_{4',5'}$ 9.5 Hz, H-4′), 5.00 (t, 1H, $J_{3',2'}$–$J_{3',4'}$ 9.3 Hz, H-3′), 4.81 (t, 1H, $J_{2',1'}$–$J_{2',3'}$ 8.6 Hz, H-2′), 4.77, 4.51 (2 d, 1H each, *J* 12.1 Hz, C*H*$_2$Ph × 2), 4.48 (d, 1H, *J* 7.8 Hz, H-1′), 4.46, 4.39 (2 d, 1H each, *J* 11.9 Hz, C*H*$_2$Ph′ × 2), 3.99 (dd, 1H, H-2), 3.97 (t, 1H, $J_{4,3'}$–$J_{3,5}$ 9.5 Hz, H-4), 3.81–3.70 (m, 2H, H-6), 3.59–3.55 (m, 1H, H-5), 3.54 (d, 1H, *J* 3.1 Hz, H-6a′), 3.48 (d, 1H, *J* 4.3 Hz, H-6b′), 3.43 (s, 3H, O*C*H$_3$), 3.41–3.35 (m, 1H, H-5′), 1.97 (s, 3H, COC*H*$_3$), 1.93 (s, 9H, COC*H*$_3$, CC*H*$_3$ × 2), 1.88 (s, 3H, COC*H*$_3$), 1.87 (s, 3H, COC*H*$_3$); ^{13}C NMR δ: 171.43, 170.40, 170.23, 169.40, 168.82 (*C*O × 6), 137.75, 137.42 (*C*-Ar, *C*-Ar′), 137.37–137.07 (*C* × 2), 128.61, 128.42, 128.09, 127.90, 127.81 (*C*-Ar × 5, *C*-Ar′ × 5), 99.87 (C-1′), 99.14 (C-1), 75.32 (C-4), 74.59 (C-5), 73.68 (*C*H$_2$Ph*), 73.35 (C-3′, *C*H$_2$-Ph′*), 72.64 (C-5′), 71.76 (C-2′), 70.92 (C-3), 69.07 (C-4′), 68.49 (C-6′), 67.26 (C-6), 56.85 (O*C*H$_3$), 54.65 (C-2), 20.61 (COC*H*$_3$ × 3), 20.47 (COC*H*$_3$), 8.78 (CC*H*$_3$ × 2); ESI-HMRS: calcd for $[C_{41}H_{49}NO_{16} + Na]^+$: 834.29436. Found: *m*/*z*: 834.29556. Unreacted disaccharide **16b** (7%).

Acknowledgments

We thank Dr. Manuel González-Sierra for spectral determinations and helpful discussions. Financial support from UNR, UBA, and CONICET is also acknowledged. M.I.C., C.A.S., and E.A.R. are Research Members of the National Research Council of Argentina (CONICET).

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2013.08.002.

References

1. Zhu, X.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 1900–1934.
2. Mydock, L. K.; Demchenko, A. V. *Org. Biomol. Chem.* **2010**, *8*, 497–510.
3. Whitfield, D. M. *Adv. Carbohydr. Chem. Biochem.* **2009**, *62*, 83–159.
4. Crich, D. *Acc. Chem. Res.* **2010**, *43*, 1144–1153.
5. Bozó, E.; Vasella, A. *Helv. Chim. Acta* **1994**, *77*, 745–753.
6. Muddasani, P. R.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1994**, *77*, 334–350.
7. Cid, M. B.; Alfonso, F.; Alonso, I.; Martín-Lomas, M. *Org. Biomol. Chem.* **2009**, *7*, 1471–1481.
8. Colombo, M. I.; Rúveda, E. A.; Stortz, C. A. *Org. Biomol. Chem.* **2011**, *9*, 3020–3025.
9. Uriel, C.; Gómez, A. M.; López, C. J.; Fraser-Reid, B. *Eur. J. Org. Chem.* **2009**, 403–411.
10. Bohn, M. L.; Colombo, M. I.; Rúveda, E. A.; Stortz, C. A. *Org. Biomol. Chem.* **2008**, *6*, 554–561.
11. Premathilake, H. D.; Demchenko, A. V. *Top. Curr. Chem.* **2011**, *301*, 189–221.

12. Werz, D. B.; Ranzinger, R.; Herget, S.; Adibekian, A.; Von der Lieth, C.-W.; Seeberger, P. H. *ACS Chem. Biol.* **2007**, *2*, 685–691.
13. Bongat, A. F. G.; Demchenko, A. V. *Carbohydr. Res.* **2007**, *342*, 374–406.
14. Ellervik, U.; Magnusson, G. *J. Org. Chem.* **1998**, *63*, 9314–9322.
15. Lay, L.; Manzoni, L.; Schmidt, R. R. *Carbohydr. Res.* **1998**, *310*, 157–171.
16. Bohn, M. L.; Colombo, M. I.; Pisano, P. L.; Stortz, C. A.; Rúveda, E. A. *Carbohydr. Res.* **2007**, *342*, 2522–2536. and references cited therein.
17. Gourmala, C.; Zhu, Z.; Luo, Y.; Bo, T. F.; Ghalem, S.; Hu, Y.; Zhang, Y. *Tetrahedron: Asymmetry* **2005**, *16*, 3024–3029.
18. Zhang, Y.; Fechter, E. J.; Wang, T.-S. A.; Barrett, D.; Walker, S.; Kahne, D. E. *J. Am. Chem. Soc.* **2007**, *129*, 3080–3081.
19. Okada, Y.; Mukae, T.; Okajima, K.; Taira, M.; Fujita, M.; Yamada, H. *Org. Lett.* **2007**, *9*, 1573–1576.
20. Pedersen, C. M.; Nordstrøm, L. U.; Bols, M. *J. Am. Chem. Soc.* **2007**, *129*, 9222–9235.
21. Colombo, M. I.; Stortz, C. A.; Rúveda, E. A. *Carbohydr. Res.* **2011**, *346*, 569–576.
22. Lawandi, J.; Rocheleau, S.; Moitessier, N. *Tetrahedron* **2011**, *67*, 8411–8420.