JOC Article

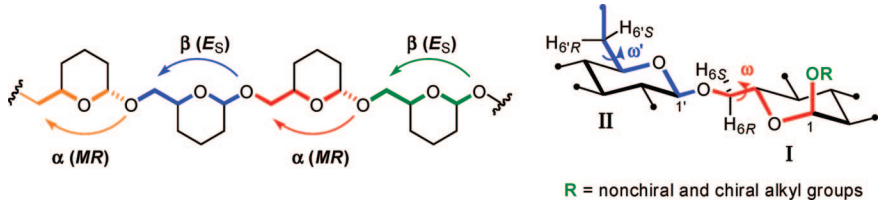
Conformational Domino Effect in Saccharides. 2. Anomeric Configuration Control

Alfredo Roën, Carlos Mayato, Juan I. Padrón, and Jesús T. Vázquez*

Instituto Universitario de Bio-Orgánica "Antonio González", Departamento de Química Orgánica, Universidad de La Laguna, 38206 La Laguna, Tenerife, Spain

jtruvaz@ull.es

Received June 2, 2008



A series of alkyl β-D-glucopyranosyl-(1→6)-α-D-glucopyranosides were synthesized and analyzed by NMR and CD techniques. As in their β-anomer series, the rotational populations of the hydroxymethyl group involved in the interglycosidic linkage (torsion angle ω) are shown to depend on the aglycon and the solvent. However, for this α-anomer series the rotational dependence arises directly from steric effects. Correlations between rotational populations and molar refractivity (*MR*) steric parameters, but not Taft's steric parameters (β-anomers), of the alkyl substituents were observed. The conformational domino effect previously predicted from alkyl β-(1→6)-diglucopyranosides is now supported by the conformational properties of their α-anomers, the anomeric configuration controlling the domino effect. In addition, the rotational populations around the C5′−C6′ bond (torsion angle ω') depend weakly on the structure of the aglycon and the anomeric configuration.

Introduction

Carbohydrates play a central role in a variety of important physiological events, including inflammation, metastasis, immune response, and bacterial and viral infection, which has led to an increased appreciation of these biomolecules.[1] To understand these events from a molecular point of view, not only their three-dimensional structure but also their conformational preferences in solution must be known. The conformation of an oligosaccharide in solution may be difficult to determine, owing to the flexibility of the glycosidic linkages and the rotation of the hydroxymethyl[2−23] and other pendant groups. Besides NMR[24] and X-ray diffraction,[25,26] molecular modeling has became another important tool for structural studies of carbo-

(1) Kiessling, L. L.; Carlson, E. E., Werz, D. B.; Seeberger, P. H. In *Advances in Sugar Chemistry in Chemical Biology*; Schreiber, S. L., Kapoor, T., Wess, G., Eds.; Wiley-VCH: Weinheim, 2007; Vol. 2, pp 635−691.
(2) Review Bock, K.; Duus, J. J. *Carbohydr. Chem.* **1994**, *184*, 513.
(3) Tvaroška, I.; Taravel, F. R.; Utille, J. P.; Carver, J. P. *Carbohydr. Res.* **2002**, *337*, 353.
(4) Kirschner, K. N.; Woods, R. J. *Proc. Nat. Acad. Sci. U.S.A.* **2001**, *98*, 10541.
(5) Molteni, C.; Parrinello, M. *J. Am. Chem. Soc.* **1998**, *120*, 2168.
(6) Brown, J. W.; Wladkowski, B. D. *J. Am. Chem. Soc.* **1996**, *118*, 1190.
(7) Tvaroška, I.; Carver, J. P. *J. Phys. Chem. B* **1997**, *101*, 2992.
(8) Hoffmann, M.; Rychlewski, J. *J. Am. Chem. Soc.* **2001**, *123*, 2308.
(9) Spieser, S. A. H.; Kuik, J. A. v.; Kroon-Batenburg, L. M. J.; Kroon, J. *Carbohydr. Res.* **1999**, *322*, 264.
(10) Senderowitz, H.; Parish, C.; Still, W. C. *J. Am. Chem. Soc.* **1996**, *118*, 2078.
(11) (a) Nishida, Y.; Ohrui, H.; Meguro, H. *Tetrahedron Lett.* **1984**, *25*, 1575. (b) Ohrui, H.; Nishida, Y.; Watanabe, M.; Hori, H.; Meguro, H. *Tetrahedron Lett.* **1985**, *26*, 3251. (c) Nishida, Y.; Hori, H.; Ohrui, H.; Meguro, H. *J. Carbohydr. Chem.* **1988**, *7*, 239.
(12) DeVries, N.; Buck, H. M. *Carbohydr. Res.* **1987**, *165*, 1.
(13) Nishida, Y.; Hori, H.; Ohrui, H.; Meguro, H.; Uzawa, J.; Reimer, D.; Sinnwell, V.; Paulsen, H. *Tetrahedron Lett.* **1988**, *29*, 4461.
(14) Poppe, L. *J. Am. Chem. Soc.* **1993**, *115*, 8421.
(15) Barrows, S. E.; Storer, J. W.; Cramer, C. J.; French, A. D.; Truhlar, D. G. *J. Comput. Chem.* **1998**, *19*, 1111.
(16) Yamada, H.; Harada, T.; Takahashi, T. *Tetrahedron Lett.* **1995**, *36*, 3185.
(17) Hori, H.; Nishida, Y.; Ohrui, H.; Meguro, H. *J. Carbohydr. Chem.* **1990**, *9*, 601.
(18) De Bruyn, A.; Anteunis, M. *Carbohydr. Res.* **1976**, *47*, 311.
(19) Jansson, P.-E.; Kenne, L.; Kolare, I. *Carbohydr. Res.* **1994**, *257*, 163.
(20) (a) Rockwell, G. D.; Grindley, T. B. *J. Am. Chem. Soc.* **1998**, *120*, 10953. (b) Kirschner, K. N.; Woods, R. J. *Proc. Nat. Acad. Sci. U.S.A.* **2001**, *98*, 10541. (c) Gonzalez-Outeriño, J.; Kirschner, K. N.; Thobhani, S.; Woods, R. J. *Can. J. Chem.* **2006**, *84*, 569.
(21) (a) Morales, E. Q.; Padrón, J. I.; Trujillo, M.; Vázquez, J. T. *J. Org. Chem.* **1995**, *60*, 2537. (b) Padrón, J. I.; Vázquez, J. T. *Chirality* **1997**, *9*, 626. (c) Padrón, J. I.; Vázquez, J. T. *Tetrahedron: Asymmetry* **1998**, *9*, 613. (d) Padrón, J. I.; Morales, E. Q.; Vázquez, J. T. *J. Org. Chem.* **1998**, *63*, 8247. (e) Nóbrega, C.; Vázquez, J. T. *Tetrahedron: Asymmetry* **2003**, *14*, 2793. (f) Mayato, C.; Dorta, R.; Vázquez, J. *Tetrahedron: Asymmetry* **2004**, *15*, 2385.
(22) Roën, A.; Padrón, J. I.; Vázquez, J. T. *J. Org. Chem.* **2003**, *68*, 4615.

10.1021/jo801184q CCC: $40.75 © 2008 American Chemical Society
Published on Web 08/27/2008

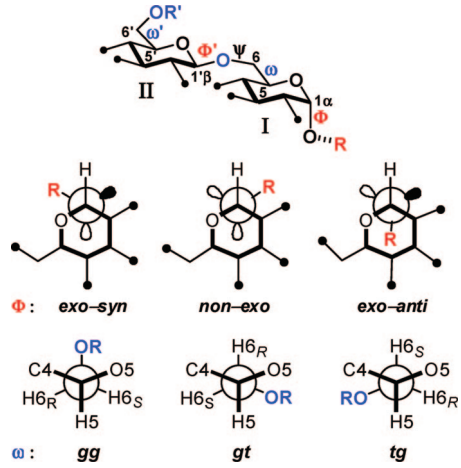


FIGURE 1. Torsion angle Φ around the O1−C1 bond and ω around C5−C6 (top). Newman projections of the idealized staggered rotamers around the O1−C1 (center) and C5−C6 bonds (bottom).

hydrates, permitting the range of attainable conformations to be evaluated in terms of the potential energy at each point specified by a pair of angles, ϕ (O5′−C1′−O6−C6) and Ψ (C1′−O6−C6−C5), for a 1→6 linkage.[26] In addition to these torsion angles, a third torsion angle ω (O5−C5−C6−O6) needs to be considered when the hydroxymethyl group is involved in the linkage. Rotation around the ϕ angle leads to the exo-syn, exo-anti, and non-exo rotamers, while that around the ω angle gives the *gauche-gauche* (*gg*), *gauche-trans* (*gt*) and *trans-gauche* (*tg*) rotamers (Figure 1).[27] This last torsion angle is also used to describe the conformation of unsubstituted hydroxymethyl groups.

The torsion angle ω of glycosides[21,23] has been proven to be conformationally dependent on the structure of the aglycon due to stereoelectronic and steric factors. Recent rotational studies with *C*-[28] and *S*-glycosides[29] have also shown it to be dependent on the aglycon. Besides these, stereochemical studies with methyl diglucopyranosides containing β-glycosidic linkages (1→2, 1→3, 1→4, and 1→6) also revealed that this angle depends on the glycosidic linkage type,[22] while studies with alkyl diglucopyranosides demonstrated that this interglycosidic ω angle depends on the structural nature of both the aglycon and the solvent.[20,22] These results pointed to a natural conformational domino effect in oligosaccharides, where the conformational properties of each (1→6) interglycosidic linkage depend on the structure of the previous residue or its aglycon (Figure 2).[23] Furthermore, correlations were observed between the Taft steric parameters[30] of the alkyl substituents (aglycon) versus the corresponding rotamer populations.

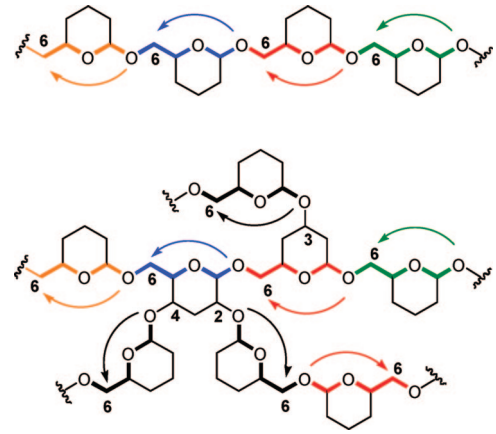


FIGURE 2. Schematic representation of a conformational domino effect in linear (top) or branched (bottom) oligosaccharides. The (1→2)-, (1→3)-, and (1→4)-bonded saccharides start a new domino effect; however, the (1→6)-interglycosidic linkages continue the domino effect.

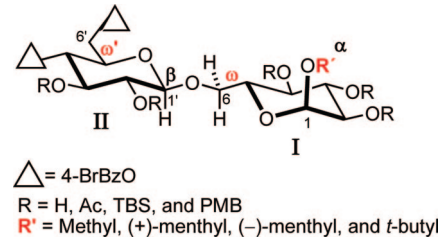


FIGURE 3. Model alkyl β-(1→6)-glucopyranosyl-α-D-glucopyranosides and ω torsion angles around the C5−C6 and C5′−C6′ bonds under study.

In this paper, we report the corresponding conformational study of alkyl β-D-glucopyranosyl-(1→6)-α-D-glucopyranosides in solution (Figure 3). This study revealed that the rotational populations of the hydroxymethyl group involved in the glycosidic linkage (residue I) depend on the structural nature of the aglycon and on the solvent. Furthermore, correlations were observed between the rotamer populations and molar refractivity (MR)[31] parameters of the alkyl substituents, which are used to measure the steric effects in proportion to the molar volume of the substituents; instead of with Taft's steric (E_S) parameters in the β-series. This shows how the anomeric configuration controls the rotational population behavior and therefore the domino effect.

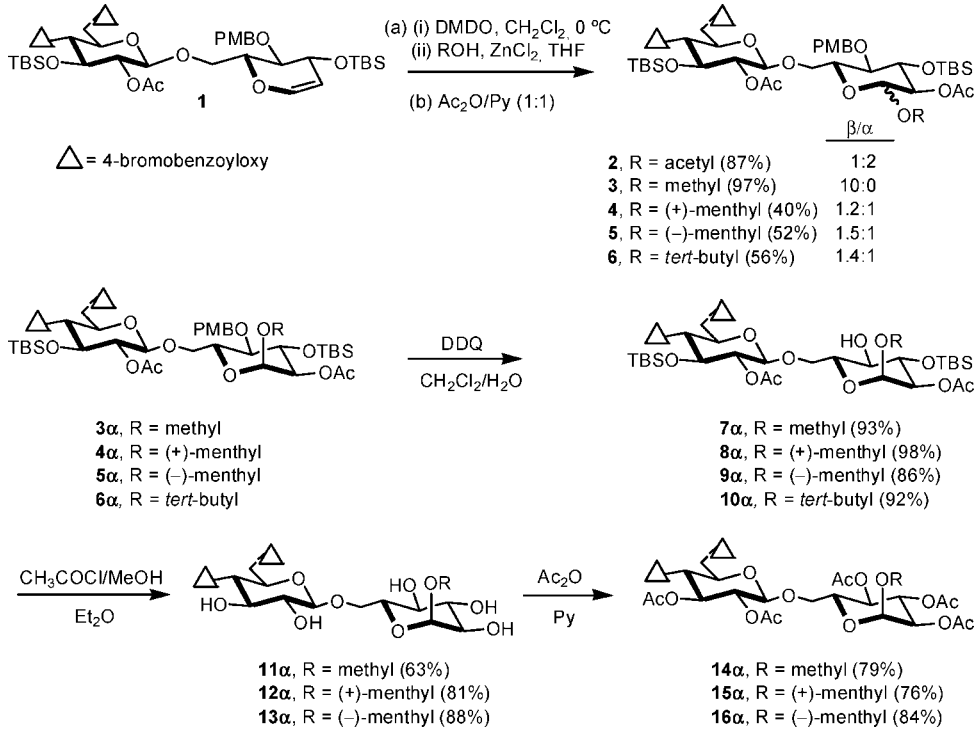
Results and Discussion

Synthesis. The α-anomer disaccharides were synthesized following the general strategy used to obtain their β-anomers,[23] namely by coupling different alcohols to the disaccharide **1** (Scheme 1) via the direct epoxidation of glycals and opening

(23) Roën, A.; Padrón, J. I.; Mayato, C.; Vázquez, J. T. *J. Org. Chem.* **2008**, *73*, 3351.
(24) Duus, J. Ø.; Gotfredsen, C. H.; Bock, K. *Chem. Rev.* **2000**, *100*, 4589.
(25) Jeffrey, G. A. *Acta Crystallogr.* **1990**, *B46*, 89.
(26) (a) Imberty, A.; Pérez, S. *Chem. Rev.* **2000**, *100*, 4567. (b) Wormald, M. R.; Petruscu, A. J.; Pao, Y-L.; Glithero, A.; Elliott, T.; Dwek, R. A. *Chem. Rev.* **2002**, *102*, 371.
(27) The first descriptor indicates the torsional relationship between O6 and O5 and the second that between O6 and C4.
(28) (a) Mayato, C.; Dorta, R. L.; Vázquez, J. T. *Tetrahedron: Asymmetry* **2007**, *18*, 931. (b) Mayato, C.; Dorta, R. L.; Vázquez, J. T. *Tetrahedron: Asymmetry* **2007**, *18*, 2803.
(29) Sanhueza, C. A.; Dorta, R. L.; Vázquez, J. T. *Tetrahedron: Asymmetry* **2008**, *19*, 258.
(30) (a) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1952**, *74*, 2729. (b) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1952**, *74*, 3120. (c) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 4532. (d) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 4538.

(31) One of the parameters used to measure the steric effect is the molar refractivity (MR), which is a measure of the volume occupied by an atom or group of atoms. The greater the positive MR value of a substituent, the larger its steric or bulk effect. (a) Hansch, C.; Leo, A.; Unger, S. H.; Kim, K. H.; Kikaitani, D.; Lien, E. J. *J. Med. Chem.* **1973**, *16*, 1207. (b) Hansch, C.; Leo, A. *Exploring QSAR: Fundamentals and Applications in Chemistry and Biology*; American Chemical Society: Washington, DC, 1995; Vols. 1 and 2.

SCHEME 1. Synthesis of the Model Disaccharides



of the resulting epoxide by a nucleophile.[32,33] This procedure led to the anomer mixture of compounds **2** and **4**−**6**, the α-anomers being isolated and treated similarly to the *β*-anomers.[23]

To obtain the methyl disaccharide with the α anomeric configuration at C1, compound **3α**, an alternative procedure (Scheme 2) had to be used, since only the *β*-anomer was synthesized by the above procedure from compound **1** and MeOH as nucleophile (Scheme 1). As shown in Scheme 2, the methyl *β*-D-glucopyranosyl-(1→6)-α-D-glucopyranoside **22α** was produced similarly by coupling the glucosyl donor **21** to the monosaccharide **20**. This last monosaccharide was obtained in four steps from the methyl α-D-glucopyranoside through the known compounds **17**[34] and **18**.[35] Acetylation of **22α** led to the disaccharide **3α** with the desired α anomeric configuration.

The *tert*-butyl derivative **10α** under acetyl chloride/MeOH conditions led to undesired methanolysis. However, their protecting groups were successfully removed in two steps, first, the silyl groups by using the HF·Py complex in dry CH_3CN and then, the acetyl groups using *p*-TsOH, to arrive at the *tert*-butyl disaccharides **24α** (Scheme 3).[36,37] The *tert*-butyl penta-*O*-acetyldisaccharide **25α** was obtained by treating compound **23α** with acetic anhydride and pyridine.

Characterization and Spectroscopic Analysis. All of these compounds were characterized on the basis of their one- (^{1}H and ^{13}C) and two-dimensional (COSY, HMQC, and T-ROESY) NMR spectra. The anomeric configurations were assigned in each case by analyzing the coupling constant between H1 and H2 for each glucopyranosidic ring ($CDCl_3$, doublet, *β*-configuration: 7.8−8.1 Hz; α-configuration: 3.5−3.9 Hz) (Figure 4). The chemical shifts of C1 and H1 for compounds in the four sets of disaccharides were shielded (90.0−101.6 ppm) or deshielded (4.55−5.32 ppm), respectively, from methyl to *tert*-butyl derivatives. Furthermore, as occurred in alkyl glycosides[21] and the corresponding *β* series,[23] NMR data comparison between (−)- and (+)-menthyl disaccharides shows chemical shifts for the former compounds at higher fields for C1 (4.7−5.9 ppm) and for H1 (0.10−0.13 ppm).

The ^{1}H NMR signals of the prochiral protons at C6 and C6′ were differentiated according to the data in the literature[2,11] on their chemical shifts and coupling constants. Among the different types of Karplus equations,[38] those of Serianni[39] yield the most accurate representation of the rotameric populations in solution. In addition, since the *ω* population depends to some extent on solvation effects,[20] NMR measurements were performed in polar and nonpolar solvents.

(32) (a) Gervay, J.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 5448. (b) Bilodeau, Mark, T.; Danishefsky, S. J. Coupling of glycals: a new strategy for the rapid assembly of oligosaccharides. *Front. Nat. Prod. Res.* **1996**, *1*, 171(Modern Methods in Carbohydrare Synthesis). (c) Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1380. (d) Seeberger, P. H.; Danishefsky, S. J. *Acc. Chem. Res.* **1998**, *31*, 685, and references cited therein.

(33) (a) Hanessian, S.; Bacquet, C.; Lehong, N. *Carbohydr. Res.* **1980**, *80*, C17. (b) Mukaiyama, T.; Murai, Y.; Shoda, S. *Chem. Lett.* **1981**, 431. (c) Nicolau, K.; Seitz, S.; Papahatjis, D. *J. Am. Chem. Soc.* **1983**, *105*, 2430. (d) Kahne, D.; Walker, S.; Cheng, Y.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 6881. (e) Van Boom, J. *Tetrahedron Lett.* **1990**, *31*, 1331. (f) Sinaÿ, P.; Marra, A.; Esnault, J.; Veyrieres, A. *J. Am. Chem. Soc.* **1992**, *114*, 6354. (g) Schmidt, R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21. (h) Danishefsky, S.; Bilodeau, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1381. (i) Mukaiyama, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5590. (j) Crich, D.; Lim, L. B. L. *Org. React.* **2004**, *64*, 115.

(34) Hanessian, S.; Plessas, N. R. *J. Org. Chem.* **1969**, *34*, 1035.

(35) Xin-An, L.; Chien-Hung, C.; Cheng-Chung, W.; Shang-Cheng, H. *Synlett* **2003**, 1364.

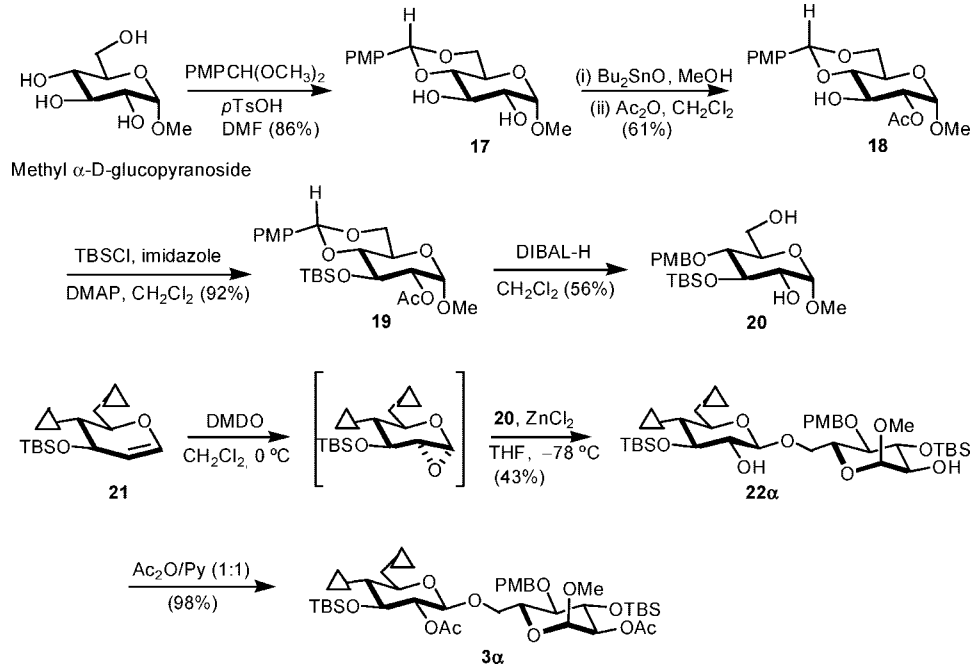
(36) Nicolau, K. C.; Webber, S. E. *Synthesis* **1986**, 453.

(37) Gonzalez, A. G.; Brouard, I.; Leon, F.; Padron, J. I.; Bermejo, J. *Tetrahedron Lett.* **2001**, *42*, 3187.

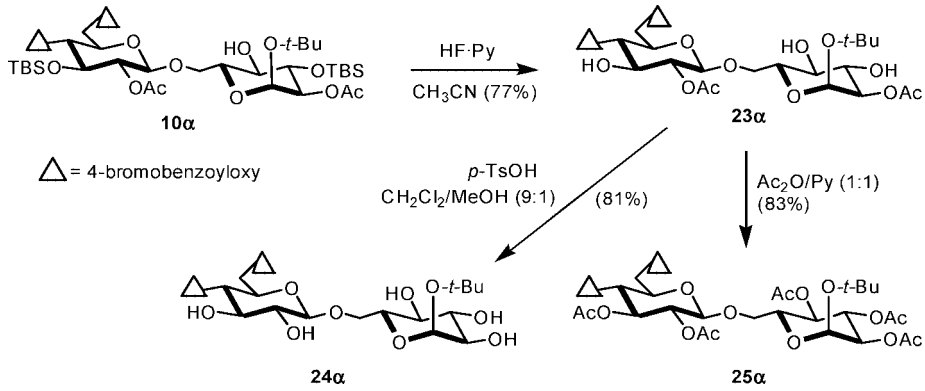
(38) (a) Haasnoot, C. A. G.; De Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783. (b) Manor, P. C.; Saenger, W.; Davies, D. B.; Jankowski, K.; Rabczenko, A. *Biochim. Biophys. Acta* **1974**, *340*, 472. (c) Stenutz, R.; Carmichael, I.; Widmalm, G.; Serianni, A. S. *J. Org. Chem.* **2002**, *67*, 949.

(39) (a) Thibaudeau, C.; Stenutz, R.; Hertz, B.; Klepach, T.; Zhao, S.; Wu, Q.; Carmichael, I.; Serianni, A. *J. Am. Chem. Soc.* **2004**, *121*, 15668. (b) Equations: (i) $2.8P_{gg} + 2.2P_{gt} + 11.1P_{tg} = J_{H5,H6proS}$; (ii) $0.9P_{gg} + 10.8P_{gt} + 4.7P_{tg} = J_{H5,H6proR}$; (iii) $P_{gg} + P_{gt} + P_{tg} = 1$.

SCHEME 2. Synthesis of the Disaccharide 3α



SCHEME 3. Synthesis of the *tert*-Butyl Disaccharides 24α and 25α



All model disaccharides contain CD exciton-coupled chromophores at C4′ and C6′,[40] namely *p*-bromobenzoates, in order to provide their CD spectra and less crowded NMR spectra. This approach allows the coupling constants to be determined more accurately under a first-order NMR analysis. Therefore, UV and CD spectroscopy were also used to characterize these compounds; the intramolecular charge-transfer band was around 245 nm in the UV, and the exciton Cotton effects were about 251 and 234 nm in the CD spectra.

Conformational Analysis. General Method. Stereoelectronic effects[41,42] have long been recognized to influence the conformation of carbohydrates. Both endo and exo anomeric effects are present in α-glucosides, while only the exo anomeric effect is present in *β*-glucosides (Figure 5). In α-glucosides, these two effects have opposing influences on the structural parameters of the bonds involved, and as a result, these parameters are only finely modified.[41,42] The plausible exo-syn and exo-anti rotamers around the Φ torsion angle (Figure 1) have a nonbonding electron pair located antiperiplanar to the C1−O5 bond, so only these two rotamers have the appropiate spatial disposition for the exo anomeric effect ($n_{O1} \rightarrow \sigma_{C1-O5}^*$). However, the axial configuration at C1 in the α-anomers leads

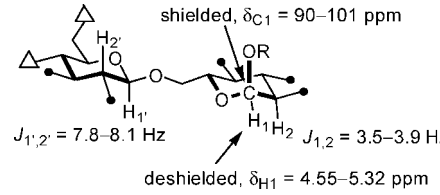


FIGURE 4. General NMR characteristics of model disaccharides.

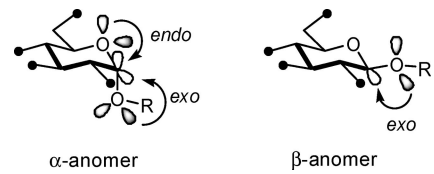


FIGURE 5. Orbitals involved in the exo- and endo anomeric effects in α- and *β*-glucosides.

(40) For a monograph on exciton CD spectroscopy, see: (a) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy. Exciton Coupling in Organic Stereochemistry*; University Science Books: California, 1983. (b) Nakanishi, K.; Berova, N. In *The Exciton Chirality Method in Circular Dichroism, Principles and Applications*; Nakanishi, K., Berova, N., Woody, R. W., Eds.; VCH Publishers: New York, 1994.

TABLE 1. Coupling Constants and Calculated Rotameric Populations (%) around the C5−C6 (Residue I) for the Pentahydroxy Disaccharides 11α−13α and 24α (DMSO-d_6)

compd	R	$J_{H5,H6R}$	$J_{H5,H6S}$[a]	P_{gg}	P_{gt}	P_{tg}	compd	$J_{H5,H6R}$	$J_{H5,H6S}$[a]	P_{gg}	P_{gt}	P_{tg}
11α	Me	6.8		44	56	0	**11*β***	6.8		44	56	0
12α	(+)-Mn	4.6		63	37	0	**12*β***	7.4		38	62	0
13α	(−)-Mn	6.4		47	53	0	**13*β***	6.6		46	54	0
24α	*tert*-Bu	6.0		50	50	0	**24*β***	7.2		40	60	0

[a] Not detected. An estimated value of 0.9 Hz was used for calculations.

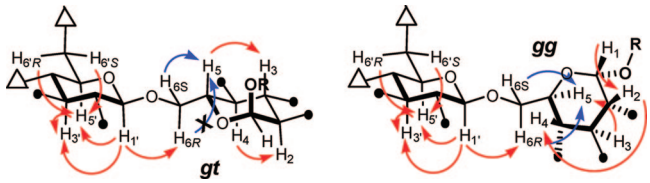


FIGURE 6. Main cross-peaks observed for the model disaccharides **11α−13α** and **24α** in the T-ROESY experiments (DMSO-d_6). Significant cross-peaks of the rotamers around the C5−C6 bond are shown in blue.

to strong nonbonded interactions between the aglycon (R) and the sugar ring under the exo-anti rotamer, which becomes very unstable or nonexistent and the exo-syn, free of these nonbonded interactions, the most stable. The rotameric populations around the Φ torsion angle will depend on the bulkiness of the aglycon, more precisely on the effective bulkiness involved in nonbonded interactions. We will discuss below how the molar refractivity[31] of the aglycons is correlated with the different rotational populations of the interglycosidic linkage, i.e., with those of the hydroxymethyl group around the C5−C6 bond (residue I).

Conformational Analysis of the Hydroxymethyl Group around the C5−C6 Bond (Residue I). The conformational study of the pentahydroxy disaccharides **11α−13α** and **24α** with an α configuration in C1 was carried out in a way similar to that of their *β* stereoisomers. NMR spectra were measured in DMSO-d_6, and the data are gathered in Table 1. The $J_{H5,H6R}$ values were between 4.6 and 6.8 Hz, while the $J_{H5,H6S}$ values could not be obtained, since the H6*S* signal appears as wide doublets, the doublet with greater coupling constant corresponding to the geminal coupling. These data point to very low values of the $J_{H5,H6S}$ coupling constants and therefore of the *tg* populations. The rotamer populations of the hydroxymethyl groups in solution were calculated using Serianni's equations.[39] To calculate the different rotational populations, a low value of 0.9 Hz was assigned to the $J_{H5,H6S}$ constant.[38c] The resulting calculated populations in DMSO (Table 1) showed that the *gt* rotamer was the most stable for the methyl and (−)-menthyl disaccharides, the *gg* for the (+)-menthyl derivative, and *gg* and *gt* equally populated for the *tert*-butyl disaccharide.

Besides confirming both anomeric configurations, the observed main cross-peaks in the T-ROESY experiments (Figure 6) showed intensities in accordance with the populations shown in Table 1. Thus, while a strong cross-peak was observed between H6*R* and H5 for the (+)-menthyl derivative **12α**, weak cross-peaks were observed for the methyl, (−)-menthyl, and *tert*-butyl derivatives, which possess higher *gt* populations than the former.

Analysis of the NMR data revealed higher *gt* and lower *gg* populations for the methyl group than the secondary or tertiary alkyl groups (menthyls and *tert*-butyl). The *gt* population decreased as the bulkiness of the aglycon increased, especially for the (+)-menthyl derivative, at the expense of the *gg* population. This behavior is just the opposite to that of their

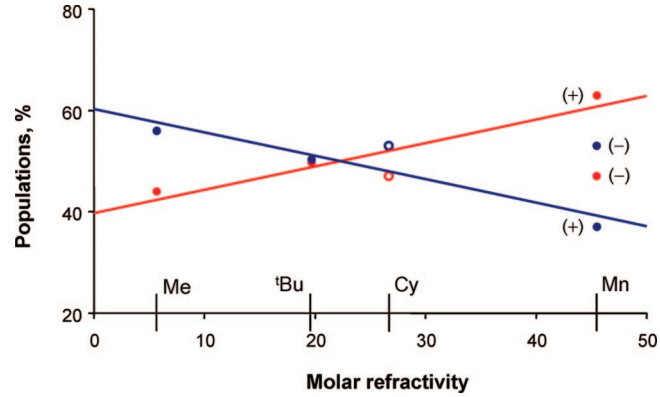


FIGURE 7. Plot of rotamer populations around the C5−C6 bond versus molar refractivity of the corresponding alkyl substituents of compounds **11α−13α** and **24α** (DMSO-d_6): P_{gg} (red line), P_{gt} (blue line).[43]

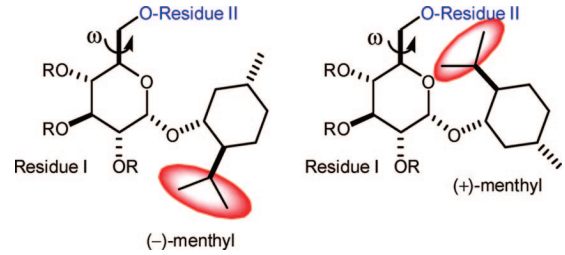


FIGURE 8. Drawings of (−)- and (+)-menthyl derivatives in their more stable exo-syn conformation, showing the anti or syn disposition, respectively, of the isopropyl group with respect to residue II.

β-stereoisomers **11*β*−13*β*** and **24*β*** (Table 1), where the *gt* population increased as the bulkiness of the aglycon increased. These data indicate nonbonded interactions are responsible for the rotational population differences for the α-series, and not entropy (steric hindrance to motions) and stereoelectronic effects, as in the *β*-series.[23] Plots of the rotamer populations against the molar refractivity of the alkyl substituents (cm^3/mol) (Figure 7) confirmed the different behavior of the two series. The *β*-series follows Taft's steric parameters[30] (steric hindrances to motions), while the α-series follows molar refractivity.[31] As can be observed in Figure 7, there is a linear correlation of the *gg* and *gt* rotational populations around the C5−C6 bond for compounds **11α**, **12α**, and **24α** with the corresponding molar refractivity parameters, but not for the (−)-menthyl derivative **13α**. For this last compound, an excellent correlation was obtained when the cyclohexyl group was used instead of applying its molar refractivity, signifying that the isopropyl group on this menthyl derivative was not involved in the nonbonded interactions (open circles in Figure 7). These results can be explained because the "effective volume" involved in nonbonded interactions between the aglycon and residue II in the (−)-menthyl derivative **13α** should not include the isopropyl group. Figure 8 shows how the isopropyl group affects the rotational populations of the hydroxymethyl group around

TABLE 2. Coupling Constants and Calculated Rotameric Populations (%) around the C5−C6 (Residue I) for the Penta-*O*-acetyl Disaccharides 14α−16α and 25α ($CDCl_3$)

compd	R	$J_{H5,H6R}$	$J_{H5,H6S}$	P_{gg}	P_{gt}	P_{tg}	compd	$J_{H5,H6R}$	$J_{H5,H6S}$	P_{gg}	P_{gt}	P_{tg}
14α	Me	6.5	2.0	45	55	0	**14*β***	7.4	1.8	36	64	0
15α	(+)-Mn	4.2	1.1	66	34	0	**15*β***	-[a]	-[a]			
16α	(−)-Mn	4.5	1.9	64	36	0	**16*β***	6.5	1.9	44	56	0
25α	*tert*-Bu	5.7	2.1	52	48	0	**25*β***	7.8	1.7	32	68	0

[a] H6*R* and H6*S* signals are isochronous.

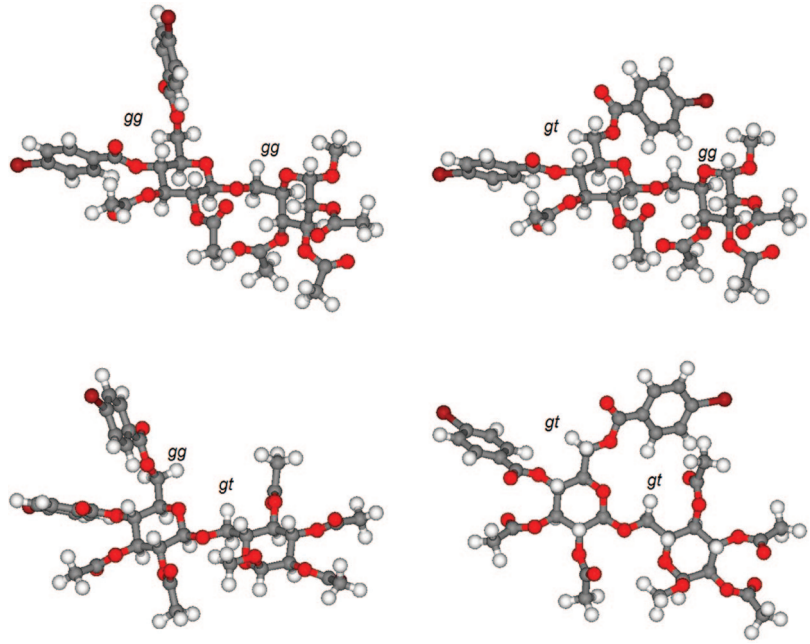


FIGURE 9. Perspective view of the methyl β-D-glucopyranosyl-(1→6)-α-D-glucopyranoside derivative **14α**.[44]

the C5−C6 bond by nonbonded interactions with residue II, so it is appropiate to apply the molar refractivity parameter of menthyl to the (+)-menthyl disaccharides. However, with the (−)-menthyl disaccharides, the molar refractivity of menthyl is too high, so that of cyclohexyl is more suitable since the isopropyl group in these disaccharides is not involved in nonbonded interactions with residue II.

NMR data of the penta-*O*-acetyl disaccharides **14α**−**16α** and **25α** (Table 2) led to rotamer populations similar to those obtained from their pentahydroxy disaccharide precursors (Table 1), except for the (−)-menthyl derivative. In this series, the presence of acetyl groups permits new steric interactions with the aglycon and possibly between the glucosidic rings. The increased *gg* population of the (−)-menthyl derivative could be due to additional steric factors. It is interesting to note the greater *gg* and smaller *gt* populations of all α-anomers versus the β-anomers.

Figure 9 shows four conformers of the methyl disaccharide **14α**, illustrating the disposition of the methyl group, or in general of any aglycon, with respect to residue II. While the *gg* rotamer around the C5−C6 bond allows the methyl group (aglycon) to be free from nonbonded interactions with residue II (top two conformers), the *gt* conformation locates the aglycon close to residue II (bottom two). The larger the structure of the aglycon, the greater the steric interactions and, therefore, the smaller the *gt* conformation.

Plots of the rotamer populations around the C5−C6 bond versus molar refractivity of the corresponding alkyl substituents of compounds **14α**−**16α** and **25α** indicate that the rotational behavior is governed by steric effects (nonbonded interactions), which depend on the aglycon and the solvent. Thus, Figure 10 shows excellent correlations between the rotational populations and their corresponding molar refractivity parameters obtained in chloroform and benzene, respectively, for the four compounds under study. However, in polar solvents (Figure 11), only three of the four show linearity, the (−)-menthyl derivative being clearly excluded. As occurred with the pentahydroxy disaccharides **11α**−**13α** and **24α** in DMSO-d_6, when the cyclohexyl molar refractivity parameter was used for the (−)-menthyl derivative (open circles) in all polar solvents, excellent linearities and high correlation coefficients were obtained in all cases. These results can be explained as above by considering the

(41) The stereoelectronic exo-anomeric effect consists of the conformational preference of glycosides for the gauche orientation (Lemieux, R. U.; Pavia, A. A.; Martin, J. C.; Watanabe, K. A. *Can. J. Chem.* **1969**, *47*, 4427) as a consequence of the stereoelectronic interaction between the p orbital of the interannular oxygen and the σ* orbital of the pyranose C1−O5 bond. Furthermore, this effect is responsible for the reduction and extension of C1−O1 and C1−O5 bonds, respectively, as observed in X-ray diffraction studies. Briggs, A. J.; Glenn, R.; Jones, P. G.; Kirby, A. J.; Ramaswamy, P. *J. Am. Chem. Soc.* **1984**, *106*, 6200).

(42) (a) Thatcher, G. R. J. In *Anomeric and Associated Stereoelectronic Effects. Scope and Controversy in the Anomeric Effect and Associated Stereoelectronic Effects*; Thatcher, G. R. J., Ed.; ACS Symposium Series 539; American Chemical Society: Washington, DC, 1993. (b) Juaristi, E.; Cuevas, G. In *The Anomeric Effect in New Directions in Organic and Biological Chemistry*; Rees, C. W., Ed.; CRC Press, Inc.: Boca Raton, FL, 1995.

(43) Regression line equations of Figure 8 (DMSO): $P_{gg} = 0.4645MR + 39.541$; $R^2 = 0.8401$; $P_{gt} = -0.4645MR + 60.459$; $R^2 = 0.8401$.

(44) The MMX force field was used to perform the molecular mechanics calculations (default dielectric constant $\epsilon = 1.5$). PCMODEL (v. 7.0). Serena Software.

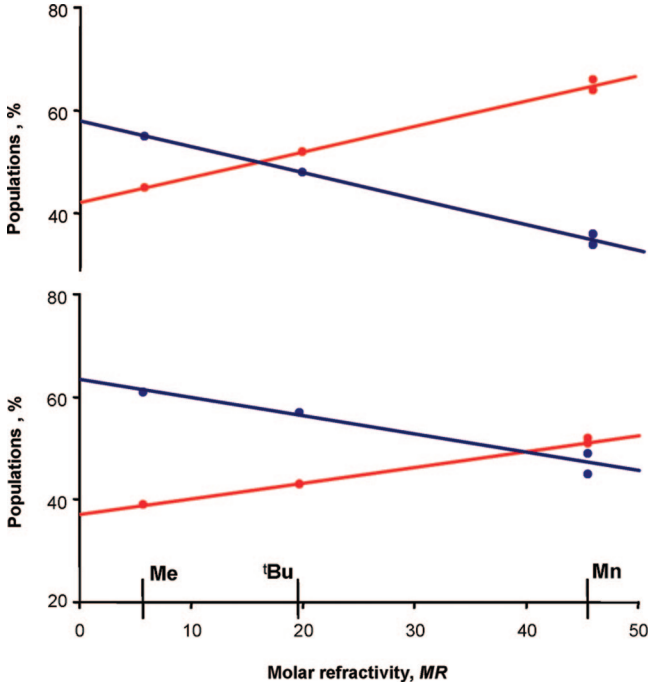


FIGURE 10. Plot of rotamer populations around the C5−C6 bond versus molar refractivity of the corresponding alkyl substituents of compounds **14α**−**16α** and **25α**: top, $CDCl_3$; bottom, C_6D_6; P_{gg}, red line; P_{gt}, blue line.[45]

"effective volume" involved in nonbonded interactions (Figure 8), thus confirming the origin of these rotational differences.

As shown in Figures 10 and 11, the rotational populations around the interglycosidic linkage depend on the structural nature of the solvent. A plot between the $J_{H5,H6R}$ of compounds **14α**−**16α** and **25α** and the dielectric constant of the solvents under study (Figure 12) reveals that (i) each aglycon exhibited different $J_{H5,H6R}$ and, therefore, *gt* rotational populations, (ii) in nonpolar solvents, (+)- and (−)-menthyl derivatives have similar $J_{H5,H6R}$ values (and *gt* populations), and (iii) in polar solvents the $J_{H5,H6R}$ values are further apart, especially for the menthyl derivatives **15α** and **16α**, which exhibit different values, and (iv) as the dielectric constant increases the $J_{H5,H6R}$ values (or *gt* populations) generally decrease.

Comparison of the pentahydroxy (Table 1) and penta-*O*-acetyl disaccharide anomers (Table 2) revealed higher $J_{H5,H6R}$ and lower $J_{H5,H6S}$ coupling constants and, therefore, larger *gt* and smaller *gg* populations for the disaccharides with the β anomeric configuration. This result is independent of the solvent. Figure 13 shows the plot of $J_{H5,H6R}$ coupling constants for the anomers at C1 of the methyl disaccharides **14α** and **14*β*** and *tert*-butyl disaccharides **25α** and **25*β*** against the dielectric constants of the solvents used in this study. It can be observed how the dashed lines (β-anomers) are above the solid lines (α-anomers), the differences being wider for the bulkier *tert*-butyl disaccharides.

Conformational Analysis of the Hydroxymethyl Group around the C5′−C6′ Bond (Residue II). Calculating the

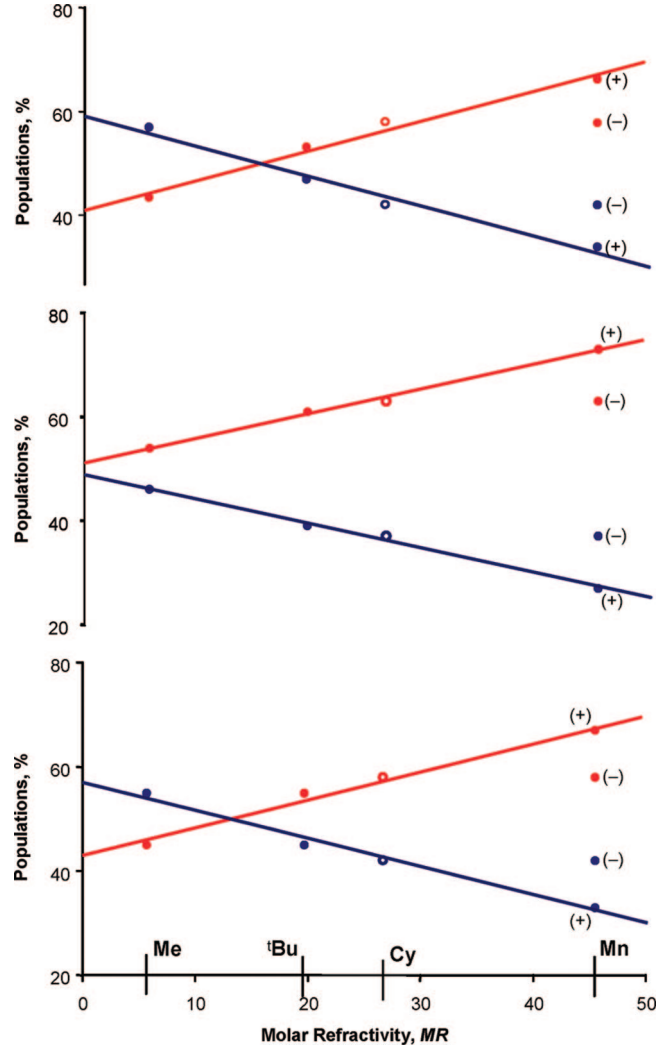


FIGURE 11. Plot of rotamer populations around the C5−C6 bond versus molar refractivity of the corresponding alkyl substituents of compounds **14α**−**16α** and **25α**: top, $(CD_3)_2CO$; middle, CD_3CN; bottom, DMSO-d_6; P_{gg}, red line; P_{gt}, blue line.[46]

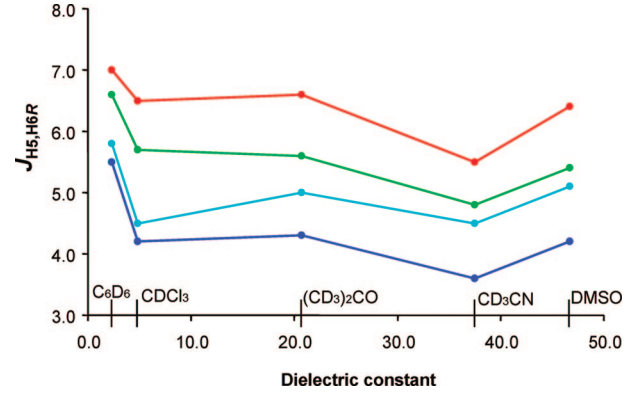


FIGURE 12. Plot of $J_{H5,H6R}$ coupling constants versus dielectric constants for disaccharides **14α**−**16α** and **25α**: methyl **14α** (red), *tert*-butyl **25α** (green), (−)-menthyl **16α** (light blue), and (+)-menthyl **15α** (dark blue).

populations around C5′−C6′ (torsion angle ω') for compounds **11α**−**16α**, **24α**, and **25α** from $J_{H5',H6'R}$ and $J_{H5',H6'S}$ coupling constants, the *gg* rotamer has the highest population (50−60%), then the *gt* (35−45%), and finally *tg* (3−10%). These proportions depend slightly on the solvent, the aglycon, and type of

(45) Regression line equations of Figure 10: (a) (top, $CDCl_3$): $P_{gg} = 0.5028MR + 42.119$; $R^2 = 0.9933$; $P_{gt} = -0.5028MR + 57.881$; $R^2 = 0.9933$; (b) (bottom, C_6D_6): $P_{gg} = 0.3172MR + 37.018$; $R^2 = 0.9949$; $P_{gt} = -0.3592MR + 63.452$; $R^2 = 0.9464$.

(46) Regression line equations of Figure 11: (a) (top, acetone-d_6): $P_{gg} = 0.575MR + 40.97$; $R^2 = 0.9779$; $P_{gt} = -0.575MR + 59.03$; $R^2 = 0.9779$; (b) (middle, CD_3CN): $P_{gg} = 0.4727MR + 51.216$; $R^2 = 0.9945$; $P_{gt} = -0.4727MR + 48.784$; $R^2 = 0.9945$; (c) (bottom, DMSO-d_6): $P_{gg} = 0.5437MR + 42.983$; $R^2 = 0.9852$; $P_{gt} = -0.5437MR + 57.017$; $R^2 = 0.9852$.

TABLE 3. Coupling Constants and Calculated Rotameric Populations (%) around the C5′−C6′ Bond (Residue II) for the Pentahydroxy Disaccharides 11α−13α and 24α (DMSO-d_6)

compd	R	$J_{H5',H6'R}$	$J_{H5',H6'S}$	P_{gg}	P_{gt}	P_{tg}	compd	$J_{H5',H6'R}$	$J_{H5',H6'S}$	P_{gg}	P_{gt}	P_{tg}
11α	Me	4.8	3.0	58	37	5	**11*β***	4.7	3.1	58	36	6
12α	(+)-Mn						**12*β***	4.9	3.1	56	38	6
13α	(−)-Mn	5.6	2.8	51	46	3	**13*β***	4.9	2.9	57	39	4
24α	*tert*-Bu	5.1	2.8	56	41	3	**24*β***	5.1	3.0	54	40	6

TABLE 4. Coupling Constants and Calculated Rotameric Populations (%) around the C5′−C6′ Bond (Residue II) for the Penta-*O*-acetyl Disaccharides 14α−16α and 25α ($CDCl_3$)

compd	R	$J_{H5',H6'R}$	$J_{H5',H6'S}$	P_{gg}	P_{gt}	P_{tg}	compd	$J_{H5',H6'R}$	$J_{H5',H6'S}$	P_{gg}	P_{gt}	P_{tg}
14α	Me	4.8	3.3	55	36	9	**14*β***	4.9	3.2	55	37	8
15α	(+)-Mn	5.0	3.5	52	37	11	**15*β***	4.9	3.3	54	37	9
16α	(−)-Mn	4.8	3.5	54	35	11	**16*β***	4.9	3.3	54	37	9
25α	*tert*-Bu	5.0	3.4	52	38	10	**25*β***	5.1	3.2	53	39	8

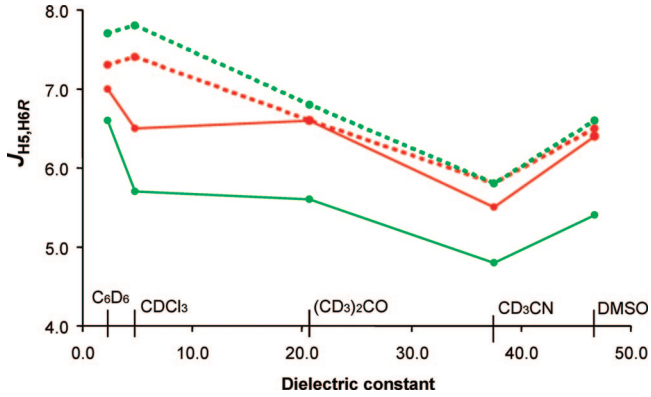


FIGURE 13. Plot of $J_{H5,H6R}$ coupling constants versus dielectric constants for disaccharides **14α** and **25α** and their respective *β*-anomers at C1 **14*β*** and **25*β***: methyl **14α** and **14*β*** (red), *tert*-butyl **25α** and **25*β*** (green); *β*-anomers (dashed lines), and α-anomers (solid lines).

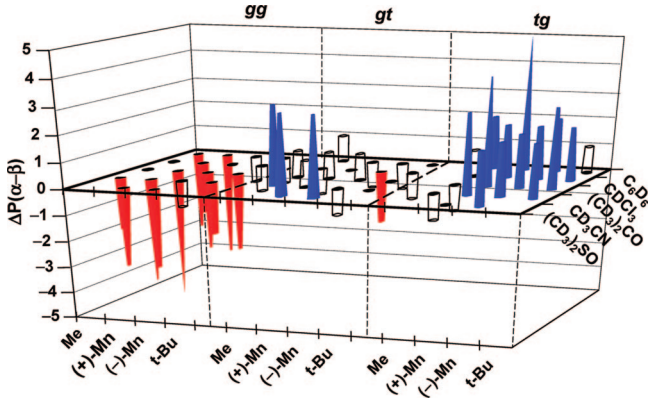


FIGURE 14. 3D plot of $\Delta P(\alpha - \beta)$ for the *gg*, *gt*, and *tg* rotamers of disaccharides **14α−16α** and **25α** in several solvents. Negative $\Delta P(\alpha - \beta)$ are represented by red cones, while positive values are blue. Colorless cones signify differences below two percent, while black spots mean zero differences.

substituents (Tables 3 and 4). As occurs with stereoisomers having a *β* configuration at C1, those with the α configuration at C1 exhibited stronger cross-peaks between H6′*S* and H5 than between H6′*R* and H5 in T-ROESY spectra, indicating greater *gt* populations around the C5′−C6′ bond than *tg*.

Anomer comparison analysis revealed that disaccharides having the α anomeric configuration at C1 did not exhibit any clear correlation unlike the *β*-series, which exhibited a linear correlation between the *gg* and *gt* populations at residue II and Taft's steric parameters for aliphatic substituents (aglycon, residue I). However, comparing the population differences ($\Delta P_{\alpha\text{-}\beta}$), α-anomers possess smaller *gg*, similar *gt*, and greater *tg* populations than their corresponding *β*-anomers. Figure 14 shows this result for the four disaccharides in five solvents.

TABLE 5. CD Data for the Pentahydroxy Disaccharides 11α−13α and 24α (EtOH)

compd	R	*1EC*	*2EC*	*A*	compd	*1EC*	*2EC*	*A*	$\Delta A_{\beta-\alpha}$
11α	Me	11.8	−3.7	15.5	**11*β***	13.3	−4.2	17.5	2.0
12α	(+)-Mn	11.1	−3.1	14.2	**12*β***	12.9	−3.9	16.8	2.6
13α	(−)-Mn	12.0	−3.1	15.1	**13*β***	13.0	−3.9	16.9	1.8
24α	*tert*-Bu	12.2	−3.9	16.1	**24*β***	12.8	−3.9	16.7	0.6

TABLE 6. CD Data for the Penta-*O*-acetyl Disaccharides 14α−16α and 25α (CH_3CN)

compd	R	*1EC*	*2EC*	*A*	compd	*1EC*	*2EC*	*A*	$\Delta A_{\beta-\alpha}$
14α	Me	15.0	−7.0	22.0	**14*β***	15.3	−7.0	22.3	0.3
15α	(+)-Mn	13.8	−6.7	20.5	**15*β***	14.6	−7.7	22.3	1.8
16α	(−)-Mn	15.1	−6.9	22.0	**16*β***	15.1	−6.9	22.0	0.0
25α	*tert*-Bu	14.4	−7.3	21.7	**25*β***	14.9	−7.0	21.9	0.2

Since the CD exciton chirality method[40] has proven to be an extremely sensitive technique commonly used for conformational analysis, the rotational populations around the C5′−C6′ bond were also analyzed by this technique. CD data for the model pentahydroxy disaccharides are shown in Table 5 (EtOH), while those for penta-*O*-acetyl disaccharides are shown in Table 6 (CH_3CN). Positive *A* values[47] were obtained for all these compounds, small differences being observed on changing the structure of the aglycon. Analysis of the pairwise interactions between the chromophores at C4′ and C6′ in the three rotamers around the C5′−C6′ bond (Figure 15)[48] did not reveal a clear pattern, in agreement with NMR results.

As mentioned above, NMR data comparison between anomers at C1 (Figure 14) revealed very similar rotational populations, although the α-anomers have very slightly lower *gg* and higher *tg* populations, especially in polar solvents. Analogous CD analysis of both anomeric configurations of the model pentahy-

(47) The amplitude (*A* value) of split CD Cotton effects is defined as $A = \Delta_1 - \Delta_2$ where $\Delta\epsilon_1$ and $\Delta\epsilon_2$ are intensities of the first and second Cotton effects, respectively. Occasionally the presence of a background ellipticity alters the intensity of the Cotton effects at short wavelengths. For this reason, the intensities of the second Cotton effects and the amplitudes (*A* values) of the CD spectra of our model compounds may not be precise; the intensities of the first Cotton effects are thus more accurate for comparative analysis.

(48) According to the CD exciton chirality method, the pairwise interaction between the chromophores at C4 and C6 in the three dispositions have a positive exciton contribution for the *gg* rotamer, negative for the *gt*, and null for the *tg*. Furthermore, the pairwise interaction for the *gg* rotamer is stronger due to the smaller distance between the chromophores in these positions and to a favorable dihedral angle.

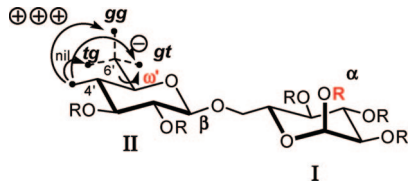


FIGURE 15. Sign and relative intensities for the pairwise interaction between the chromophores at C4′ and C6′ in the three rotamers.

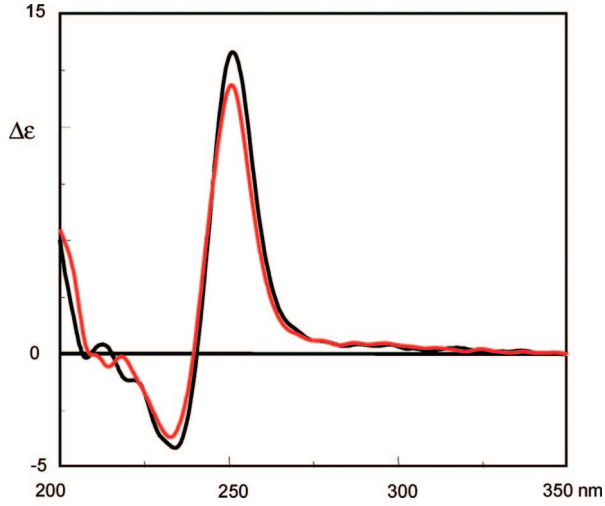


FIGURE 16. CD spectra of methyl disaccharides: **11α** (red line) and **11*β*** (black line) in EtOH.

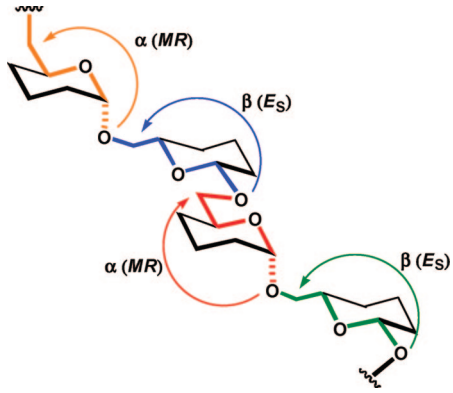


FIGURE 17. Schematic representation of a conformational domino effect in (1→6)-linked oligosaccharides.

droxy- or penta-*O*-acetyldisaccharides confirmed this. The results obtained showed very similar amplitudes (*A* values) between the two series, although the $\Delta A_{\beta-\alpha}$ values were between 0.0 and 2.6, confirming slight conformational differences in the hydroxymethyl group at residue II on varying the configuration in the first residue. According to the sign and relative intensity of the pairwise interaction between the chromophores at C4′ and C6′ in the three rotamers (Figure 15), smaller *gg* and/or larger *gt* populations should be expected for α-anomer disaccharides. The more intense Cotton effects for *β*-than α-anomers can be observed in the CD spectrum shown in Figure 16.

The results provide evidence for a remote conformational relay from the aglycon to the hydroxymethyl group at residue II. It is very small, due to the great distance between the groups, and follows a different pattern than the *β*-anomers, since no relationship was observed between the *gg* and *gt* populations and the Taft steric parameters of the aglycons. This differing anomer behavior confirms the separate origin of these conformational dependences, largely stereoelectronic and steric for the *β*-anomers, and only steric for the α-anomers.

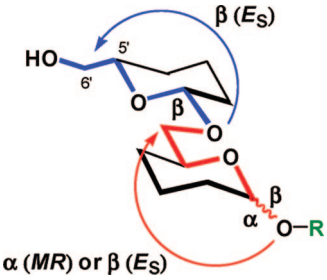


FIGURE 18. Schematic representation of the remote conformational effect in alkyl *β*-D-glucopyranosyl-(1→6)-*β*- and α-D-glucopyranosides.

Conclusions

A series of alkyl *β*-D-glucopyranosyl-(1→6)-α-D-glucopyranosides containing different aglycons were synthesized and analyzed by CD and NMR techniques. The results revealed that the rotational populations of the hydroxymethyl group involved in the interglycosidic linkage (torsion angle *ω*, O5−C5−C6−O6) depend on the structure of the aglycon and on the solvent; *gg* or *gt* being the most stable rotamers. Contrary to what happens with alkyl *β*-D-glucopyranosyl-(1→6)-*β*-D-glucopyranosides, where steric and stereoelectronic effects are responsible for the rotational populations of the hydroxymethyl group involved in the interglycosidic linkage, the populations of those with the α configuration at C1 depend only on steric effects. Besides this, while the populations of the alkyl *β*-D-glc-(1→6)-*β*-D-glc correlate with the Taft steric (E_S) parameter of the alkyl substituents, the rotational populations of their corresponding α-anomers (alkyl *β*-D-glc-(1→6)-α-D-glc) correlate with the molar refractivity (MR) parameters of the alkyl substituents. All these results support the predicted conformational domino effect in saccharides and show how important the anomeric configuration at each sugar residue is in determining the conformational populations of its glycosidic linkage with the next sugar residue (Figure 17).

In addition, the rotational populations around the C5′−C6′ bond (torsion angle *ω*′) in alkyl *β*-D-glc-(1→6)-α-D-glc are shown to depend weakly on the structural nature of the aglycon (residue I) and the solvent, the *gg* rotamer being the most stable in all cases (Figure 18). Anomer comparison analysis between the rotational populations around the C5′−C6′ bond indicated that, in general, independently of the solvent, the *gg* population is slightly smaller, the *gt* is similar, and *tg* slightly higher in the α series that in the *β*. This observation agrees with CD data, where smaller amplitudes were obtained for the α-anomers. This tiny remote conformational dependence in the second sugar residue, through simply changing the anomeric configuration in the first residue, supports the above-mentioned domino effect in (1→6)-linked oligosaccharides.

Experimental Section

General Procedure for Preparation of Disaccharides 2α, 4α−6α, and 22α. A solution of dimethyldioxirane in acetone (2 equiv) was added to a stirred solution of disaccharide **1** in dry CH_2Cl_2 (5 mL/mmol) at 0 °C under an argon atmosphere, and the reaction was stirred for 30 min. The 1,2-anhydrosugar thus obtained was concentrated under reduced pressure and left under vacuum for 2 h. It was then dissolved in dry THF (10 mL/mmol) under

argon, and molecular sieves 3 Å and the corresponding nucleophile were added. The reaction mixture was cooled to −78 °C, and then 0.5 equiv of a 1.0 M solution of $ZnCl_2$ in diethyl ether was added. The reaction was allowed to warm to room temperature and stirred overnight. The mixture was diluted with EtOAc, filtered, and washed with water, the combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. After this, 2 mL of a 1:1 solution of dry pyridine/acetic anhydride was added at room temperature and stirred overnight. Excess solvent was removed under reduced pressure and the residue purified with column chromatography.

General Procedure for Debenzylation. DDQ (2.5 equiv) at room temperature was added to a stirred solution of the starting material in CH_2Cl_2/H_2O (9:1, 50 mL/mmol). This was then diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 twice, the combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was purified with column chromatography.

General Procedure for Deprotection of Silyl and Acetyl Groups. A solution of starting material in dry diethylether (40 mL/mmol) was added to a stirred solution of acetyl chloride (40 equiv) in dry methanol (40 mL/mmol). When the reaction was completed, it was concentrated under vacuum, and the residue was purified by Sephadex column chromatography (*n*-hexane/$CHCl_3$/MeOH, 2:1:1).

1,2-Di-*O*-acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-*β*-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-α-D-glucopyranose (2α). Following the general procedure for preparation of disaccharides, 130 mg (0.12 mmol) of compound **1** was epoxidized and treated with 500 μL of water giving, after acetylation, compound **2** (127 mg, 0.11 mmol) as a mixture α/β = 2:1 with a 87% yield, isolated after column chromatography (*n*-hexane/EtOAc, 8:2). Thus, 85.6 mg of α- and 41.7 mg of β-anomer were obtained. Compound **2α**: colorless syrup; ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, *J* = 8.5 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.24 (d, *J* = 3.5 Hz, H-1), 5.34 (t, *J* = 9.2 Hz, H-4′), 5.02 (t, *J* = 8.4 Hz, H-2′), 4.81 (dd, *J* = 3.6, 9.8 Hz, H-2), 4.72 (d, *J* = 10.7 Hz, 1H), 4.52 (d, *J* = 7.9 Hz, H-1′), 4.48 (d, *J* = 10.7 Hz, 1H), 4.47 (dd, *J* = 3.7, 12.1 Hz, H-6′$_{proS}$), 4.34 (dd, *J* = 5.0, 12.1 Hz, H-6′$_{proR}$), 4.05 (t, *J* = 9.0, H-3), 4.04 (dd, *J* = 1.6, 10.9 Hz, H-6$_{proS}$), 3.99 (t, *J* = 8.9 Hz, H-3′), 3.87 (m, H-5′, H-5), 3.78 (s, 3H), 3.60 (dd, *J* = 5.5, 10.9 Hz, H-6$_{proR}$), 3.37 (t, *J* = 8.8 Hz, H-4), 2.10 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 0.89 (s, 9H), 0.71 (s, 9H), 0.08 (s, 6H), −0.01 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (δ, $CDCl_3$): 169.9 (s), 169.1 (s), 165.4 (s), 164.3 (s), 159.3 (s), 131.8−128.2, 113.8 (2d), 100.8 (d, C-1′), 89.6 (d, C-1), 78.2 (d, C-4), 74.8 (t), 73.3 (d, C-2′), 72.9 (d, C-5), 72.9 (d, C-3′), 72.5 (d, C-2), 72.3 (d, C-4′), 71.8 (d, C-3), 71.7 (d, C-5′), 67.3 (t, C-6), 63.6 (t, C-6′), 55.3 (q), 25.7 (3q), 25.4 (3q), 21.1 (q), 20.8 (q), 18.0 (s), 17.7 (s), −4.0 (q), −4.4 (2q), −4.5 (q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ (Δε) 251 (13.8), 234 nm (−5.8). Anal. Calcd for $C_{52}H_{70}Br_2O_{17}Si_2$: C, 52.79; H, 5.96. Found: C, 52.90; H, 6.05.

Methyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-*β*-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (3α). Compound **22α** (179 mg, 0.17 mmol) was dissolved in 6 mL of a 1:1 solution of dry pyridine/acetic anhydride. Excess solvent was removed under reduced pressure to give, after column chromatography (*n*-hexane/EtOAc, 8:2), compound **3α** (188.8 mg, 98% yield): TLC R_f = 0.38 (*n*-hexane/EtOAc, 7:3); mp = 144.4−145.0 °C; $[\alpha]^{25}_D$ = +26.4 (*c* 0.39, $CHCl_3$); MS (FAB) 1179, 1177, 1175 (0.1, 0.1, 0.1, $[M + Na]^+$), 687, 685, 683 (2, 4, 2, $[C_{28}H_{33}SiBr_2O_8]$), 185, 183 (10, 10, [BrBz]), 121 (100, $[C_8H_9O]$); ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, *J* = 8.6 Hz, 2H), 7.75 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.34 (t, *J* = 9.3 Hz, H-4′), 5.06 (t, *J* = 8.5 Hz, H-2′), 4.83 (d, *J* = 3.6 Hz, H-1), 4.73 (d, *J* = 10.9 Hz, 1H), 4.63 (dd, *J* = 3.6, 9.7 Hz, H-2), 4.48 (d, *J* = 8.0 Hz, H-1′), 4.44 (dd, *J* = 2.7, 12.1 Hz, H-6′$_{proS}$), 4.43 (d, *J* = 11.3 Hz, 1H), 4.35 (dd, *J* = 4.9, 12.1 Hz, H-6′$_{proR}$), 4.06 (t, *J* = 9.2 Hz, H-3), 4.04 (dd, *J* = 1.7, 10.5 Hz, H-6$_{proS}$), 3.99 (t, *J* = 8.9 Hz, H-3′), 3.83 (m, H-5′), 3.78 (s, 3H), 3.76 (m, H-5), 3.53 (dd, *J* = 6.1, 10.5 Hz, H-6$_{proR}$), 3.30 (s, 3H), 3.26 (t, *J* = 9.4 Hz, H-4), 2.11 (s, 3H), 2.06 (s, 3H), 0.89 (s, 9H), 0.72 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H), −0.01 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.4 (s), 169.0 (s), 165.4 (s), 164.3 (s), 159.2 (s), 131.8−128.4, 113.8 (2d), 101.0 (d, C-1′), 96.6 (d, C-1), 79.1 (d, C-4), 74.5 (t), 74.3 (d, C-2), 73.4 (d, C-2′), 72.9 (d, C-3′), 72.4 (d, C-4′), 71.9 (d, C-3), 71.7 (d, C-5′), 69.6 (d, C-5), 68.1 (t, C-6), 63.7 (t, C-6′), 55.3 (q), 54.9 (q), 25.8 (3q), 25.4 (3q), 21.3 (2q), 18.0 (s), 17.7 (s), −4.0 (q), −4.2 (q), −4.5 (2q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ (Δε) 251 (13.7), 234 nm (−3.3). Anal. Calcd for $C_{51}H_{70}Br_2O_{16}Si_2$: C, 53.0; H, 6.1. Found: C, 53.01; H, 6.30.

(+)-Menthyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-*β*-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (4α). Following the general procedure, 136 mg (0.13 mmol) of compound **1** was epoxidized and treated with 100 mg of (+)-menthol (0.64 mmol, 5 equiv) to provide, after column chromatography (*n*-hexane/EtOAc, 9.5:0.5), 65 mg of compound **4** (0.05 mmol) with a 40% yield as anomer mixture (β/α = 1.2:1). Compound **4α**: TLC R_f = 0.61 (*n*-hexane/EtOAc, 7:3); mp = 142.1−144.4 °C; $[\alpha]^{25}_D$ = +48.7 (*c* 1.4, $CHCl_3$); MS (FAB) 1280, 1278, 1276 (0.1, 0.1, 0.1 $[M + Na]^+$), 687, 685, 683 (3, 5, 2, $[C_{28}H_{33}SiBr_2O_8]$), 185, 183 (9, 10, [BrBz]), 121 (100, $[C_8H_9O]$; ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.33 (t, *J* = 9.1 Hz, H-4′), 5.14 (d, *J* = 3.8 Hz, H-1), 5.10 (d, *J* = 8.3 Hz, H-2′), 4.76 (d, *J* = 10.5 Hz, 1H), 4.56 (dd, *J* = 3.8, 9.8 Hz, H-2), 4.50 (d, *J* = 10.7 Hz, 1H), 4.45 (d, *J* = 7.8 Hz, H-1′), 4.42 (dd, *J* = 3.8, 12.0 Hz, H-6′$_{proS}$), 4.33 (dd, *J* = 5.3, 12.0 Hz, H-6′$_{proR}$), 4.04 (t, *J* = 9.1 Hz, H-3), 3.99 (m, H-6$_{proS}$, H-3′), 3.84 (m, H-5′), 3.80 (s, 3H), 3.77 (m, H-5), 3.75 (dd, *J* = 3.0, 10.3 Hz, H-6$_{proR}$), 3.44 (t, *J* = 9.3 Hz, H-4), 3.31 (m, 1H), 2.13 (m, 1H), 2.06 (s, 3H), 2.05 (s, 3H), 1.83 (m, 1H), 1.62 (m, 2H), 1.25 (m, 3H), 0.90 (s, 9H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.72 (s, 9H), 0.68 (d, *J* = 6.9 Hz, 3H), 0.10 (s, 3H), 0.09 (s, 3H), −0.01 (s, 3H), −0.18 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.3 (s), 168.8 (s), 165.4 (s), 164.3 (s), 159.3 (s), 131.8−128.2, 113.9 (2d), 100.7 (d, C-1′), 92.8 (d, C-1), 78.6 (d, C-4), 77.0 (d), 74.5 (t), 74.4 (d, C-2), 73.3 (d, C-2′), 73.0 (d, C-3′), 72.4 (d, C-4′), 72.0* (d, C-3), 71.9 (d, C-5′), 69.9 (d, C-5), 67.2 (t, C-6), 63.9 (t, C-6′), 55.3 (q), 47.7 (d), 40.2 (t), 34.4 (t), 31.2 (d), 25.8 (3q), 25.4 (3q), 25.4 (d), 22.6 (t), 22.3 (q), 21.3 (q), 21.2 (q), 21.1 (q), 18.0 (s), 17.7 (s), 15.2 (q), −4.0 (q), −4.2 (q), −4.4 (2q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ (Δε) 251 (12.0), 234 nm (−4.0). Anal. Calcd for $C_{60}H_{86}Br_2O_{16}Si_2$: C, 56.30; H, 6.80. Found: C, 56.28; H, 7.23.

(−)-Menthyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-*β*-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (5α). Following the general procedure for preparation of disaccharides, 140 mg (0.13 mmol) of compound **1** was epoxidized and treated with 100 mg of (−)-menthol (0.64 mmol, 5 equiv) to give, after column chromatography (*n*-hexane/EtOAc, 9.5:0.5), 87 mg (0.07 mmol) of compound **5** in 52% yield as an anomer mixture (β/α = 1.5:1). Compound **5α**: TLC R_f = 0.50 (*n*-hexane/EtOAc, 8:2); mp = 142.1−144.4 °C; $[\alpha]^{25}_D$ = +27.1 (*c* 0.92, $CHCl_3$); MS (FAB) 1280, 1278, 1276 (0.1, 0.1, 0.1 $[M + Na]^+$), 687, 685, 683 (3, 5, 2, $[C_{28}H_{33}SiBr_2O_8]$), 185, 183 (10, 11, [BrBz]), 121 (100, $[C_8H_9O]$); ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.33 (t, *J* = 9.2 Hz, H-4′), 5.08 (t, *J* = 8.4 Hz, H-2′), 5.04 (d, *J* = 3.6 Hz, H-1), 4.77 (d, *J* = 10.8 Hz, 1H), 4.57 (dd, *J* = 3.6,

9.9 Hz, H-2), 4.50 (d, J = 10.8 Hz, 1H), 4.46 (d, J = 7.8 Hz, H-1′), 4.45 (dd, J = 3.8, 12.0 Hz, H-6′$_{proS}$), 4.34 (dd, J = 5.1, 12.0 Hz, H-6′$_{proR}$), 4.13 (t, J = 9.2 Hz, H-3), 4.02 (br d, J = 10.5 Hz, H-6$_{proS}$), 3.99 (t, J = 8.9 Hz, H-3′), 3.89 (m, H-5), 3.82 (m, H-5′), 3.80 (s, 3H), 3.72 (dd, J = 3.8, 10.6 Hz, H-6$_{proR}$), 3.39 (t, J = 9.3 Hz, H-4), 3.18 (m, 1H), 2.15 (m, 2H), 2.08 (s, 3H), 2.05 (s, 3H), 1.63 (m, 2H), 1.26 (m, 2H), 0.90 (s, 9H), 0.87 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H), 0.72 (s, 9H), 0.69 (d, J = 7.0 Hz, 3H), 0.09 (s, 3H), 0.07 (s, 3H), −0.01 (s, 3H), −0.19 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.3 (s), 168.80 (s), 165.4 (s), 164.3 (s), 159.20 (s), 131.8−128.2, 113.8 (2d), 100.9 (d, C-1′), 97.5 (d, C-1), 81.8 (d), 78.9 (d, C-4), 74.6 (d, C-2), 74.4 (t), 73.4 (d, C-2′), 73.0 (d, C-3′), 72.4 (d, C-4′), 71.8 (C-5′, C-3), 69.8 (d, C-5), 67.4 (t, C-6), 63.8 (t, C-6′), 55.3 (q), 48.6 (d), 42.7 (t), 34.3 (t), 31.5 (d), 25.8 (3q), 25.4 (3q), 25.2 (d), 23.1 (t), 22.3 (q), 21.3 (q), 21.0 (2q), 18.0 (s), 17. (s), 16.10 (q), −4.0 (q), −4.2 (q), −4.4 (2q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ ($\Delta\varepsilon$) 251 (13.5), 234 nm (−4.4). Anal. Calcd for $C_{60}H_{86}Br_2O_{16}Si_2$: C, 56.30; H, 6.80. Found: C, 56.26; H, 7.10.

***tert*-Butyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (6α).** Following the general procedure, 151 mg (0.14 mmol) of compound **1** was epoxidized and treated with 1 mL of *tert*-butyl alcohol to give, after column chromatography (*n*-hexane/EtOAc, 9:1), 84 mg (0.07 mmol) of compound **6** with a 56% yield as anomer mixture (β/α = 1.4:1). Compound **6α**: TLC R_f = 0.49 (*n*-hexane/EtOAc, 7.5:2.5); mp = 140.7−142.2 °C; $[\alpha]^{25}_D$ = +43.7 (*c* 1.3, $CHCl_3$); MS (FAB) 1221, 1219, 1217 (0.1, 0.2, 0.1 [M + Na]$^+$), 687, 685, 683 (3, 5, 3, [$C_{28}H_{33}SiBr_2O_8$]), 185, 183 (11, 11, [BrBz]), 121 (100, [C_8H_9O]); ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, J = 8.5 Hz, 2H), 7.74 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 5.34 (t, J = 9.2 Hz, H-4′), 5.24 (d, J = 3.7 Hz, H-1), 5.10 (t, J = 8.5 Hz, H-2′), 4.74 (d, J = 10.6 Hz, 1H), 4.51 (d, J = 7.8 Hz, H-1′), 4.51 (dd, J = 3.7, 9.8 Hz, H-2), 4.46 (d, J = 10.9 Hz, 1H), 4.45 (dd, J = 3.7, 12.0 Hz, H-6′$_{proS}$), 4.34 (dd, J = 5.0, 12.0 Hz, H-6′$_{proR}$), 4.10 (t, J = 9.2 Hz, H-3), 4.03 (dd, J = 1.8, 10.5 Hz, H-6$_{proS}$), 3.97 (m, H-3′, H-5), 3.83 (m, H-5′), 3.78 (s, 3H), 3.68 (dd, J = 4.8, 10.5 Hz, H-6$_{proR}$), 3.30 (dd, J = 8.9, 9.8 Hz, H-4), 2.08 (s, 3H), 2.07 (s, 3H), 1.15 (s, 9H), 0.90 (s, 9H), 0.71 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), −0.02 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.3 (s), 168.8 (s), 165.4 (s), 164.3 (s), 159.2 (s), 131.8−128.2, 113.8 (2d), 100.6 (d, C-1′), 90.1 (d, C-1), 79.2 (d, C-4), 75.0 (d, C-2), 74.6 (t), 73.2 (d, C-2′), 73.1* (d, C-3′), 72.4 (d, C-4′), 71.8 (C-5′, C-3), 69.6* (d, C-5), 67.8 (t, C-6), 63.7 (t, C-6′), 55.2 (q), 29.3 (3q), 25.8 (3q), 25.5 (3q), 21.3 (q), 21.1 (q), 18.0 (s), 17.7 (s), −4.0 (q), −4.3 (q), −4.5 (2q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) 112 ($\Delta\varepsilon$) 251 (13.8), 234 nm (−3.4). Anal. Calcd for $C_{54}H_{76}Br_2O_{16}Si_2$: C, 54.20; H, 6.40. Found: C, 54.23; H, 6.81.

Methyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (7α). Following the general procedure for debenzylation, 123 mg (0.11 mmol) of compound **3α** yielded 106.2 mg of compound **7α** (93%): TLC R_f = 0.31 (*n*-hexane/EtOAc, 7:3); mp = 88.5−90.1 °C; $[\alpha]^{25}_D$ = +45.2 (*c* 1.09, $CHCl_3$); MS (FAB) 1059, 1057, 1055 (0.2, 1, 0.3, [M + Na]$^+$), 687, 685, 683 (21, 41, 18, [$C_{28}H_{33}SiBr_2O_8$]), 185, 183 (98, 100, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.83 (d, J = 8.5 Hz, 2H), 7.82 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.9 Hz, 2H), 7.53 (d, J = 8.9 Hz, 2H), 5.36 (t, J = 9.4 Hz, H-4′), 5.05 (dd, J = 8.2, 8.9 Hz, H-2′), 4.86 (d, J = 3.6 Hz, H-1), 4.62 (dd, J = 3.6, 9.8 Hz, H-2), 4.58 (d, J = 8.0 Hz, H-1′), 4.50 (dd, J = 3.4, 12.2 Hz, H-6′$_{proS}$), 4.35 (dd, J = 4.5, 12.2 Hz, H-6′$_{proR}$), 4.09 (br d, J = 8.4 Hz, H-6$_{proS}$), 4.01 (t, J = 9.0 Hz, H-3′), 3.94 (t, J = 8.7 Hz, H-3), 3.88 (m, H5′), 3.75−3.68 (H-6$_{proR}$, H5), 3.43 (m, H-4), 3.32 (s, 3H), 2.34 (d, J = 4.0 Hz, 1H), 2.11 (s, 3H), 2.10 (s, 3H), 0.86 (s, 9H), 0.71 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.00 (s, 3H), - 0.19 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.4 (s), 169.3 (s), 165.5 (s), 164.3 (s), 131.8−128.4, 101.2 (d, C-1′), 96.9 (d, C-1), 73.8 (d, C2), 73.5 (d, C2′), 73.0 (d, C3′), 72.5 (d, C3), 72.0 (2d, C4, C4′), 71.9 (d, C5′), 69.7 (d, C5), 68.6 (t, C6), 63.2 (t, C6′), 55.0 (q), 25.7 (3q), 25.4 (3q), 21.2 (q), 21.1 (q), 18.1 (s), 17.7 (s), −4.4 (q), −4.5 (3q). Anal. Calcd for $C_{43}H_{62}Br_2O_{15}Si_2$: C, 49.90; H, 6.04. Found: C, 49.89; H, 6.15.

(+)-Menthyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl]-β-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (8α). Following the general procedure for debenzylation, 125 mg (0.10 mmol) of compound **4α** yielded 112 mg of compound **8α** (98%): TLC R_f = 0.42 (*n*-hexane/EtOAc, 8:2); mp = 86.4−87.5 °C;$[\alpha]^{25}_D$ = +54.3 (*c* 1.15, $CHCl_3$); MS (FAB) 1183, 1181 (0.3, 0.2, [M + Na]$^+$), 687, 685, 683 (24, 47, 18, [$C_{28}H_{33}SiBr_2O_8$]), 185, 183 (100, 99, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 5.35 (t, J = 9.3 Hz, H-4′), 5.15 (d, J = 3.9 Hz, H-1), 5.04 (d, J = 8.7 Hz, H-2′), 4.57−4.55 (H-2, H-1′), 4.48 (dd, J = 3.3, 12.1 Hz, H-6′$_{proS}$), 4.38 (dd, J = 4.6, 12.1 Hz, H-6′$_{proR}$), 4.01 (t, J = 9.3 Hz, H-3′), 3.97 (dd, J = 2.6, 10.7 Hz, H-6$_{proS}$), 3.92 (m, H-3, H-5′), 3.81 (dd, J = 3.1, 10.7 Hz, H-6$_{proR}$), 3.74 (m, H-5), 3.54 (br t, J = 9.5, H-4), 3.32 (dt, J = 3.8, 10.5, 1H), 2.46 (s, 1H), 2.16 (m, 1H), 2.10 (s, 3H), 2.07 (s, 3H), 1.82 (m, 1H), 1.65 (m, 2H), 0.86 (m, 15H), 0.71 (m, 12H), 0.12 (s, 3H), 0.09 (s, 3H), −0.00 (s, 3H), −0.19 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.4 (s), 169.2 (s), 165.5 (s), 164.3 (s), 131.9−128.3, 101.3 (d, C-1′), 93.0 (d, C-1), 76.9 (d), 74.0 (d, C-2), 73.6 (d, C-2′), 73.0 (d, C-3′), 72.3* (d, C-4′), 72.1* (d, C-5′), 72.0* (d, C-3), 71.7* (d, C-4), 69.9 (d, C-5), 68.4 (t, C-6), 63.4 (t, C-6′), 47.7 (d), 40.1 (t), 34.4 (t), 31.3 (d), 25.7 (3q), 25.5 (d), 25.4 (3q), 22.7 (t), 22.3 (q), 21.2 (q), 21.1 (q), 21.0 (q), 18.1 (s), 17.7 (s), 15.3 (q), −4.4 (q), −4.5 (2q), −4.5 (q). Anal. Calcd for $C_{52}H_{78}Br_2O_{15}Si_2$: C, 53.88; H, 6.78. Found: C, 53.87; H, 6.44.

(−)-Menthyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (9α). Following the general procedure for debenzylation, 83 mg (0.07 mmol) of compound **5α** yielded 64.8 mg of compound **9α** (86% yield): TLC R_f = 0.39 (*n*-hexane/EtOAc, 8:2); mp = 85.8−87.8 °C; $[\alpha]^{25}_D$ = +36.8 (*c* 0.55, $CHCl_3$); MS (FAB) 1183, 1181, 1179 (0.2, 0.4, 0.1, [M + Na]$^+$), 687, 685, 683 (17, 41, 18, [$C_{28}H_{33}SiBr_2O_8$]), 185, 183 (82, 100, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.85 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 5.36 (t, J = 9.4 Hz, H-4′), 5.04 (m, H-2′, H-1), 4.60 (m, H-2), 4.59 (d, J = 8.0 Hz, H-1′), 4.56 (dd, J = 3.7, 12.2 Hz, H-6′$_{proS}$), 4.30 (dd, J = 4.1, 12.2 Hz, H-6′$_{proR}$), 4.04−3.94 (H-3′, H-6$_{proS}$, H-3), 3.87−3.80 (H-5′, H-6$_{proR}$, H-4), 3.46 (m, H-5), 3.18 (dt, J = 4.2, 10.5 Hz, 1H), 2.50 (d, J = 4.6 Hz, 1H), 2.13 (m, 2H), 2.10 (s, 3H), 2.05 (s, 3H), 1.54 (m, 2H), 1.25 (m, 3H), 0.86 (15H), 0.71 (12H), 0.12 (s, 3H), 0.09 (s, 3H), −0.01 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.2 (s), 169.2 (s), 165.5 (s), 164.3 (s), 131.9−128.4, 101.3 (d, C-1′), 97.8 (d, C-1), 81.9 (d), 74.3 (d, C-2), 73.7 (d, C-2′), 73.1 (d, C-3′), 72.3 (d, C-3), 72.0* (d, C-4), 72.0* (d, C-4′), 72.0* (d, C-5), 70.2 (d, C-5′), 68.5 (t, C-6), 63.0 (t, C-6′), 48.6 (d), 42.8 (t), 34.2 (t), 31.5 (d), 25.7 (3q), 25.4 (3q), 25.1 (d), 23.1 (t), 22.3 (q), 21.3 (q), 21.0 (q), 20.9 (q), 18.1 (s), 17.7 (s), 16.1 (q), −4.3 (q), −4.4 (q), −4.5 (q), −4.5 (q). Anal. Calcd for $C_{52}H_{78}Br_2O_{15}Si_2$: C, 53.88; H, 6.78. Found: C, 53.91; H, 6.94.

***tert*-Butyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (10α).** Following the general procedure for debenzylation, 90 mg (0.08 mmol) of compound **6α** yielded 74.4 mg of compound **10α** (92%): TLC R_f = 0.45 (*n*-hexane/EtOAc, 7:3); mp = 83.3−84.7 °C; $[\alpha]^{25}_D$ = +52.3 (*c* 0.79, $CHCl_3$); FAB-MS: 1101, 1099, 1197 (1, 2, 1, [M + Na]$^+$), 687, 685, 683 (52, 95, 41, [$C_{28}H_{33}SiBr_2O_8$]), 185, 183 (100, 99, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, J = 8.5 Hz, 2H), 7.81

(d, J = 8.5 Hz, 2H), 7.54 (t, J = 8.5 Hz, 2H), 7.52 (t, J = 8.5 Hz, 2H), 5.36 (t, J = 9.3 Hz, H-4′), 5.25 (d, J = 3.5 Hz, H-1), 5.05 (t, J = 8.5 Hz, H-2′), 4.59 (d, J = 8.0 Hz, H-1′), 4.49 (m, H-2, H-6′$_{proS}$), 4.36 (dd, J = 4.5, 12.1 H-6′$_{proR}$), 4.00 (m, H-3′, H-6$_{proS}$), 3.93 (t, J = 8.9 Hz, H-3), 3.87 (m, H-5, H-5′), 3.75 (dd, J = 4.8, 10.4 Hz, H-6$_{proR}$), 3.44 (dt, J = 3.2, 9.0, H-4), 2.34 (d, J = 3.2 Hz, 1H), 2.10 (s, 3H), 2.05 (s, 3H), 1.17 (s, 9H), 0.87 (s, 9H), 0.71 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), −0.01 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.4 (s), 169.2 (s), 165.5 (s), 164.3 (s), 131.9−128.4, 101.1 (d, C-1′), 90.4 (d, C-1), 75.2 (s), 74.1 (d, C-2), 73.5 (d, C-2′), 73.1 (d, C-3′), 72.4 (d, C-3), 72.2 (d, C-4′), 72.1 (d, C-4), 71.9 (d, C-5), 69.5 (d, C-5′), 68.5 (t, C-6), 63.4 (t, C-6′), 29.7 (q), 29.3 (q), 28.4 (3q), 25.7 (3q), 25.4 (3q), 21.3 (q), 21.0 (q), 18.1 (s), 17.7 (s), −4.5 (4q). Anal. Calcd for $C_{46}H_{68}Br_2O_{15}Si_2$: C, 51.30; H, 6.36. Found: C, 51.42; H, 6.53.

Methyl 6-*O*-[4,6-Bis-*O*-(4-bromobenzoyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (11α). Following the general procedure for desilylation and deacetylation, 35 mg (0.08 mmol) of compound **7α** yielded 17.3 mg of compound **11α** (63%): TLC R_f = 0.17 (CH_2Cl_2/MeOH, 9:1); mp = 160.2−161.5 °C; $[\alpha]^{25}_D$ = +74.6 (c 0.39, $CHCl_3$); MS (FAB) 745 (0.4, $[M + Na]^+$), 531, 529, 527 (3, 7, 4, $[C_{20}H_{17}Br_2O_7]$), 307 (17, $[C_{12}H_{19}O_9]$), 185, 183 (30, 29, [BrBz]), 154 (100); ^{1}H NMR (δ, DMSO) 7.89 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.6 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 5.49 (d, J = 5.6 Hz, 1H), 5.38 (d, J = 4.9 Hz, 1H), 5.05 (d, J = 6.4 Hz, 1H), 5.02 (t, J = 9.6 Hz, H-4′), 4.88 (br s, 1H), 4.76 (d, J = 6.3 Hz, 1H), 4.55 (d, J = 3.6 Hz, H-1), 4.51 (d, J = 7.8 Hz, H-1′), 4.39 (dd, J = 3.0, 12.0 Hz, H-6′$_{proS}$), 4.32 (dd, J = 4.8, 12.0 Hz, H-6′$_{proR}$), 4.00 (br d, J = 11.0, H-6$_{proS}$), 3.96 (m, H5′), 3.68 (dd, J = 6.8, 11.3 Hz, H-6$_{proR}$), 3.62 (m, H5, H3′), 3.42 (m, H-3), 3.30 (s, 3H), 3.22 (m, H-2, H-2′), 3.11 (m, H-4); ^{13}C NMR (δ, DMSO) 165.7 (s), 165.4 (s), 132.8−128.4, 104.6 (d, C-1′), 100.6 (d, C-1), 74.6* (d, C-3′), 74.5* (d, C-2′), 74.2 (d, C-3), 73.2 (d, C-4′), 72.8* (d, C-2), 72.2* (d, C-5), 71.6 (d, C-5′), 71.3 (d, C-4), 70.3 (t, C-6), 64.5 (t, C-6′), 55.4 (q); UV (EtOH) λ_{max} 245 nm; CD (EtOH) λ ($\Delta\varepsilon$) 251 (11.8), 234 nm (−3.7). Anal. Calcd for $C_{27}H_{30}Br_2O_{13}$: C, 44.90; H, 4.19. Found: C, 44.91; H, 4.54.

(+)-Menthyl 6-*O*-[4,6-Bis-*O*-(4-bromobenzoyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (12α). Following the general procedure for desilylation and deacetylation, 45.5 mg (0.04 mmol) of compound **8α** yielded 27.3 mg of compound **12α** (81%): TLC R_f = 0.37 (CH_2Cl_2/MeOH, 9:1); mp = 158.3−159.7 °C; $[\alpha]^{25}_D$ = +7.5 (c 0.43, $CHCl_3$); MS (FAB) 871, 869, 867 (1, 1, 1, $[M + Na]^+$), 531, 529, 527 (5, 10, 5, $[C_{20}H_{17}Br_2O_7]$), 307 (26, $[C_{12}H_{19}O_9]$), 185, 183 (16, 17, [BrBz]), 154 (100); ^{1}H NMR (δ, DMSO) 7.89 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 8.6 Hz, 2H), 7.75 (d, J = 8.6 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 5.50 (d, J = 5.7 Hz, 1H), 5.28 (d, J = 4.9 Hz, 1H), 5.01 (d, J = 5.6 Hz, 1H), 5.00 (t, J = 9.6 Hz, H-4′), 4.86 (d, J = 3.8 Hz, H-1), 4.82 (d, J = 4.4 Hz, 1H), 4.47 (d, J = 6.8 Hz, 1H), 4.45 (d, J = 8.1 Hz, H-1′), 4.35 (d, J = 4.0 Hz, H-6′$_{proS}$, H-6′$_{proR}$), 3.96 (m, H-5′), 3.92 (d, J = 10.0 Hz, H-6$_{proS}$), 3.71 (dd, J = 4.6, 10.8 Hz, H-6$_{proR}$), 3.64−3.59 (m, H-5, H-3′), 3.42−3.32 (m, H-3), 3.30 (m, H-4), 3.25−3.20 (m, H-2, H-2′), 2.22 (m, 1H), 2.10 (br d, J = 12.2 Hz, 1H), 1.61 (m, 2H), 1.33 (m, 1H), 1.21 (m, 1H), 1.05 (m, 1H), 0.91 (d, J = 6.4 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.69 (d, J = 6.8 Hz, 3H); ^{13}C NMR (δ, DMSO) 165.6 (s), 165.4 (s), 132.7−128.4, 104.2 (d, C-1′), 95.7 (d, C-1), 75.3* (d, C-3), 74.7* (d, C-5), 74.5* (d, C-2′), 74.0* (d), 73.3 (d, C-4′), 72.5* (d, C-2), 72.5* (d, C-3′), 71.5 (d, C-5′), 70.5* (d, C-4), 69.3 (t, C-6), 64.6 (t, C-6′), 48.6 (d), 40.4 (t), 35.0 (t), 31.7 (d), 25.6 (d), 23.3 (t), 23.2 (q), 22.1 (q), 16.3 (q); UV (EtOH) λ_{max} 245 nm; CD (EtOH) λ ($\Delta\varepsilon$) 251 (11.1), 234 nm (−3.1). Anal. Calcd for $C_{36}H_{46}Br_2O_{13}$: C, 51.08; H, 5.48. Found: C, 51.08; H, 5.64.

(−)-Menthyl 6-*O*-[4,6-Bis-*O*-(4-bromobenzoyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (13α). Following the general procedure for desilylation and deacetylation, 33.0 mg (0.03 mmol) of compound **9α** yielded 21.0 mg of compound **13α** (88% yield): TLC R_f = 0.35 (CH_2Cl_2/MeOH, 9:1); mp = 157.7−158.9 °C; $[\alpha]^{25}_D$ = +43.4 (c 0.32, $CHCl_3$); MS (FAB) 531, 529, 527 (0.8, 3, 1, $[C_{20}H_{17}Br_2O_7]$), 307 (9, $[C_{12}H_{19}O_9]$), 185, 183 (9.60, 11, [BrBz]), 154 (100); ^{1}H NMR (δ, DMSO) 7.89 (d, J = 8.6 Hz, 2H), 7.86 (d, J = 8.6 Hz, 2H), 7.76 (d, J = 8.6 Hz, 2H), 7.72 (d, J = 8.6 Hz, 2H), 5.53 (d, J = 5.3 Hz, 1H), 5.30 (d, J = 4.7 Hz, 1H), 4.99 (d, J = 7.0 Hz, 1H), 4.98 (t, J = 9.6 Hz, H-4′), 4.86 (br s, 1H), 4.73 (d, J = 3.7 Hz, H-1), 4.64 (d, J = 5.6 Hz, 1H), 4.46 (d, J = 7.8 Hz, H-1′), 4.40 (dd, J = 2.8, 12.0 Hz, H-6′$_{proS}$), 4.28 (dd, J = 5.6, 10.8 Hz, H-6′$_{proR}$), 3.98 (m, H-5′), 3.98 (d, J = 10.1 Hz, H-6$_{proS}$), 3.80 (m, H-5), 3.69 (dd, J = 6.4, 11.0 Hz, H-6$_{proR}$), 3.64 (m, H-3′), 3.42 (br t, J = 7.5 Hz, H-3), 3.26−3.19 (m, H-2, H-2′, 1H), 3.12 (m, H-4), 2.43 (m, 1H), 2.25 (br d, J = 12.2 Hz, 1H), 1.57 (m, 2H), 1.35 (m, 2H), 1.14 (m, 1H), 0.95 (m, 2H), 0.89 (d, J = 6.5 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H), 0.78 (m, 1H), 0.73 (d, J = 6.9 Hz, 3H); ^{13}C NMR (δ, DMSO) 165.8 (s), 165.5 (s), 132.7−128.4, 104.8 (d, C-1′), 101.6 (d, C-1), 81.3* (d), 74.6* (d, C-2), 74.6* (d, C-3′), 73.9 (d, C-3), 73.4 (d, C-4′), 73.2* (d, C-2′), 72.5 (d, C-5), 71.6 (d, C-5′), 70.3 (d, C-4), 70.8 (t, C-6), 64.7 (t, C-6′), 49.4 (d), 43.4 (t), 34.9 (t), 32.1 (d), 24.9 (d), 23.5 (t), 23.3 (q), 21.9 (q), 17.0 (q); UV (EtOH) λ_{max} 245 nm; CD (EtOH) λ ($\Delta\varepsilon$) 251 (12.0), 234 nm (−3.1). Anal. Calcd for $C_{36}H_{46}Br_2O_{13}$: C, 51.08; H, 5.48. Found: C, 51.07; H, 5.64.

Methyl 2,3,4-Tri-*O*-acetyl-6-*O*-[2,3-di-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (14α). Compound **11α** (65 mg, 0.09 mmol) was dissolved in 1 mL of a 1:1 solution of dry pyridine/acetic anhydride. Excess solvent was removed under reduced pressure to give, after column chromatography (n-hexane/EtOAc, 8:2), compound **14α** (66.0 mg) in 79% yield: TLC R_f = 0.36 (n-hexane/EtOAc, 1:1); mp = 230.5−232.9 °C dec; $[\alpha]^{25}_D$ = +46.7 (c 1.63, $CHCl_3$); MS (FAB) 933 (0.6, $[M]^+$), 615, 613, 611 (9, 17, 8, $[C_{24}H_{21}Br_2O_9]$), 307 (25, $[C_{12}H_{19}O_9]$), 185, 183 (21, 22, [BrBz]), 154 (100); ^{1}H NMR (δ, $CDCl_3$) 7.81 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 4H), 5.45 (t, J = 9.6 Hz, H-4′), 5.42 (t, J = 9.4 Hz, H-3′), 5.39 (t, J = 9.4 Hz, H-3), 5.10 (t, J = 8.0 Hz, H-2′), 4.92 (d, J = 3.5 Hz, H-1), 4.91 (t, J = 9.4 Hz, H-4), 4.84 (dd, J = 3.5, 10.2 Hz, H-2), 4.66 (d, J = 7.9 Hz, H-1′), 4.53 (dd, J = 3.3, 12.1 Hz, H-6′$_{proS}$), 4.39 (dd, J = 4.8, 12.1 Hz, H-6′$_{proR}$), 3.97−3.92 (H-5′, H-5, H-6$_{proS}$), 3.57 (dd, J = 6.5, 11.1 Hz, H-6$_{proR}$), 3.38 (s, 3H), 2.07 (s, 6H), 1.99 (s, 6H), 1.90 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.1 (2s), 170.0 (s), 169.6 (s), 169.3 (s), 165.3 (s), 164.4 (s), 132.0−127.6, 101.1 (d, C-1′), 96.5 (d, C-1), 72.3 (d, C-3), 71.8 (d, C-5′), 71.1 (d, C-2′), 70.9 (d, C-2), 70.1 (d, C-4′), 69.9 (d, C-3′), 69.0 (d, C-4), 68.2 (d, C-5), 68.2 (t, C-6), 63.1 (t, C-6′), 55.3 (q), 20.6 (4q), 20.5 (q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ ($\Delta\varepsilon$) 251 (15.0), 234 nm (−7.0). Anal. Calcd for $C_{37}H_{40}Br_2O_{18}$: C, 47.66; H, 4.32. Found: C, 47.67; H, 4.49.

(+)-Menthyl 2,3,4-Tri-*O*-acetyl-6-*O*-[2,3-di-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (15α). Compound **12α** (15 mg, 0.02 mmol) was dissolved in 1 mL of a 1:1 solution of dry pyridine/acetic anhydride. Excess solvent was removed under reduced pressure to give, after column chromatography (n-hexane/EtOAc, 8:2), compound **15α** (14.5 mg, 0.05 mmol) in 76% yield: TLC R_f = 0.35 (n-hexane/EtOAc, 6:4); mp = 236.3−238.7 °C (dec); $[\alpha]^{25}_D$ = +77.6 (c 1.02, $CHCl_3$); MS (FAB) 1077 (0.4, $[M + Na]^+$), 903, 901, 899 (5, 10, 4, $[C_{37}H_{44}Br_2O_{17}]$), 615, 613, 611 (43, 83, 42, $[C_{24}H_{21}Br_2O_9]$), 185, 183 (97, 100, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.80 (d, J = 8.6 Hz, 2H), 7.76 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H), 7.50 (d, J = 8.6 Hz, 2H), 5.45−5.35 (m, H-4′, H-3, H-3′), 5.24 (d, J = 3.9 Hz, H-1), 5.08 (dd, J = 7.9, 9.4 Hz, H-2′), 5.01 (t, J = 9.8 Hz, H-4), 4.78 (dd, J = 3.9, 10.4 Hz, H-2), 4.59 (d, J = 7.9 Hz, H-1′), 4.50 (dd, J = 3.5, 12.1 Hz, H-6′$_{proS}$), 4.40 (dd, J = 4.9, 12.1 Hz, H-6′$_{proR}$), 4.01−3.90 (m, H-5′, H-6$_{proS}$, H-5), 3.50 (dd, J = 4.2, 10.5 Hz, H-6$_{proR}$), 3.38 (dt, J = 3.9, 10.5 Hz, 1H), 2.18 (m, 1H), 2.09 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.90 (s, 3H), 1.83 (m, 1H), 1.70 (m, 2H), 1.31 (m, 2H), 0.92 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 6.5 Hz, 3H), 0.70 (d, J = 6.9 Hz, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.1 (3s), 169.5 (s), 169.4 (s), 165.3 (s), 164.4 (s),

131.9−127.6, 100.9 (d, C-1′), 92.4 (d, C-1), 77.2 (d), 72.4* (d, C-4′), 71.7* (d, C-5), 71.1 (d, C-2′), 70.9 (d, C-2), 70.2* (d, C-3′), 69.9* (d, C-3), 68.9 (d, C-4), 68.1* (d, C-5′), 67.8 (t, C-6), 63.2 (t, C-6′), 47.6 (d), 40.0 (t), 34.2 (t), 31.2 (d), 25.4 (d), 22.6 (t), 22.2 (q), 21.2 (q), 20.7 (q), 20.6 (3q), 20.5 (q), 15.2 (q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ ($\Delta\varepsilon$) 251 (13.8), 234 nm (−6.7). Anal. Calcd for $C_{46}H_{56}Br_2O_{18}$: C, 52.28; H, 5.34. Found: C, 52.28; H, 5.41.

(−)-Menthyl 2,3,4-Tri-*O*-acetyl-6-*O*-[2,3-di-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (16α). Compound **13α** (14.0 mg, 0.02 mmol) was dissolved in 1 mL of a 1:1 solution of dry pyridine/acetic anhydride. Excess solvent was removed under reduced pressure to give, after column chromatography (*n*-hexane/EtOAc, 8:2), compound **16α** (14.7 mg) in 84% yield: TLC R_f = 0.37 (*n*-hexane/EtOAc, 6:4); mp = 230.2−231.8 °C dec; $[\alpha]^{25}_D$ = +38.4 (*c* 1.14, $CHCl_3$); MS (FAB) 1077 (2, $[M + Na]^+$), 903, 901, 899 (3, 4, 2, $[C_{37}H_{44}Br_2O_{17}]$), 615, 613, 611 (39, 70, 36, $[C_{24}H_{21}Br_2O_9]$), 185, 183 (99, 100, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.80 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 5.48 (t, *J* = 9.8 Hz, H-3), 5.41 (m, H-4′, H-3′), 5.13 (d, *J* = 3.7 Hz, H-1), 5.09 (t, *J* = 8.5 Hz, H-2′), 4.99 (t, *J* = 9.5 Hz, H-4), 4.79 (dd, *J* = 3.7, 10.0 Hz, H-2), 4.62 (d, *J* = 7.9 Hz, H-1′), 4.52 (dd, *J* = 3.5, 12.1 Hz, H-6′$_{proS}$), 4.41 (dd, *J* = 4.8, 12.1 Hz, H-6′$_{proR}$), 4.11 (m, H-5), 3.99 (dd, *J* = 2.4, 10.8 Hz, H-6$_{proS}$), 3.96 (m, H-5′), 3.54 (dd, *J* = 4.5, 10.8 Hz, H-6$_{proR}$), 3.25 (dt, *J* = 4.10, 10.3 Hz, 1H), 2.17 (m, 1H), 2.10 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.90 (s, 3H), 1.62 (m, 2H), 1.39 (m, 1H), 1.27 (m, 2H), 0.99 (m, 1H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H), 0.82 (m, 1H), 0.67 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.3 (s), 170.1 (s), 170.0 (s), 169.5 (s), 169.4 (s), 165.3 (s), 164.4 (s), 131.9−127.6, 101.1 (d, C-1′), 97.4 (d, C-1), 82.5 (d), 72.4 (d, C-4′), 71.8 (d, C-5′), 71.2 (d, C-2′), 71.1 (d, C-2), 70.3 (d, C-3), 69.9 (d, C-3′), 69.1 (d, C-4), 68.0 (t, C-6), 67.9 (d, C-5), 63.2 (t, C-6′), 48.5 (d), 42.8 (t), 34.1 (t), 31.5 (d), 24.9 (d), 22.8 (t), 22.3 (q), 21.0 (q), 20.7 (q), 20.6 (2q), 20.5 (2q), 15.8 (q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ ($\Delta\varepsilon$) 251 (15.1), 234 nm (−6.9). Anal. Calcd for $C_{46}H_{56}Br_2O_{18}$: C, 52.28; H, 5.34. Found: C, 52.29; H, 5.35.

Methyl 2-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-(*p*-methoxybenzyliden)-α-D-glucopyranoside (19). Compound **18** (492 mg, 1.39 mmol) was dissolved in dry CH_2Cl_2 (10 mL) under an argon atmosphere and treated with imidazole (379 mg, 5.56 mmol), *tert*-butyldimethylsilyl chloride (419 mg, 2.77 mmol), and DMAP as catalyst. When the reaction was completed, it was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 twice, the combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was then purified by column chromatography (*n*-hexane/EtOAc, 8:2) to lead to compound **19** (601 mg, 1.28 mmol, 92%): TLC R_f = 0.42 (*n*-hexane/EtOAc, 8:2); colorless syrup; $[\alpha]^{25}_D$ = −16.7 (*c* 2.7, $CHCl_3$); MS (FAB) 469 (53, [M]++1), 411 (54, $[C_4H_9]$), 154 (13, $[C_8H_{10}O_3]$), 137 (19, $[C_8H_9O_2]$), 121 (17, $[C_8H_9O]$), 73 (100, $[C_5H_{13}]$); ^{1}H NMR (δ, $CDCl_3$) 7.40 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.47 (s, 1H), 4.90 (d, *J* = 3.7 Hz, H-1), 4.78 (dd, *J* = 3.8, 9.4 Hz, H-2), 4.25 (dd, *J* = 4.4, 9.8 Hz, H-6$_{proR}$), 4.12 (t, *J* = 9.2 Hz, H-3), 3.81 (m, H-5), 3.80 (s, OCH_3), 3.72 (t, *J* = 10.1 Hz, H-6$_{proS}$), 3.48 (t, *J* = 9.2 Hz, H-4), 3.38 (s, OCH_3), 2.12 (s, 3H), 0.82 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 170.4 (s), 160.0−113.4, 101.8 (d), 97.8 (d, C-1), 82.1 (d, C-4), 74.3 (d, C-2), 69.5 (d, C-3), 68.9 (t, C-6), 62.2 (d, C-5), 55.2 (2q), 25.6 (3q), 21.0 (q), 18.1 (s), −4.3 (q), −4.7 (q). Anal. Calcd for $C_{23}H_{36}O_7Si$: C, 58.95; H, 7.74. Found: C, 58.70; H, 7.86.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-4-*O*-(*p*-methoxybenzyl)-α-D-glucopyranoside (20). To a solution of compound **19** (714 mg, 1.52 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under argon a 1.0 M solution of DIBAL-H (6.01 mL) was added dropwise. The reaction was quenched with the addition of methanol (3 mL), diluted with EtOAc, and washed with saturated NH_4Cl solution. The aqueous layer was extracted with EtOAc (3 times), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (*n*-hexane/EtOAc, 7:3) of the residue gave **20** (364 mg) in 56% yield: TLC R_f = 0.23 (*n*-hexane/EtOAc, 6:4); colorless syrup; $[\alpha]^{25}_D$ = +108.1 (*c* 0.58, $CHCl_3$); MS (FAB) 428 (6, $[M]^+$), 411 (7, $[C_4H_9]$), 154 (15, $[C_8H_{10}O_3]$), 137 (9, $[C_8H_9O_2]$), 121 (100, $[C_8H_9O]$); ^{1}H NMR (δ, $CDCl_3$) 7.26 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.81 (d, *J* = 11.1 Hz, 1H), 4.73 (d, *J* = 3.8 Hz, H-1), 4.54 (d, *J* = 11.1 Hz, 1H), 3.83 (t, *J* = 9.4 Hz, H-3), 3.80 (s, OCH_3), 3.75 (m, H-6$_{proS}$), 3.65 (m, H-6$_{proR}$), 3.59 (m, H-5), 3.46 (dt, *J* = 3.8, 9.4 Hz, H-2), 3.39 (s, OCH_3), 3.36 (t, *J* = 9.4 Hz, H-4), 1.88 (d, *J* = 9.4 Hz, OH), 1.68 (br s, OH), 0.95 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 159.3−113.8, 99.5 (d, C-1), 77.9 (d, C-4), 76.1 (d, C-3), 74.6 (t), 73.4 (d, C-2), 71.0 (d, C-5), 61.9 (t, C-6), 55.3 (q), 55.2 (q), 26.0 (3q), 18.6 (s), −4.0 (q), −4.2 (q). Anal. Calcd for $C_{21}H_{36}O_7Si$: C, 58.85; H, 8.47. Found: C, 58.91; H, 8.63.

Methyl 6-*O*-[4,6-Bis-*O*-(4-bromobenzoyl)-3-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (22α). The methyl glucopyranosyl glucopyranoside **22α** (213.0 mg) was obtained in 43% yield by coupling the glucosyl donor **21** (290 mg, 0.46 mmol) with 2 equiv of the glucosyl aceptor **20** (400 mg, 0.93 mmol) according to the general procedure: TLC R_f = 0.30 (*n*-hexane/EtOAc, 7:3); colorless syrup; $[\alpha]^{25}_D$ = +0.6 (*c* 0.59, $CHCl_3$); MS (FAB) 1095, 1093, 1091 (0.1, 0.1, 0.1 $[M + Na]^+$), 185, 183 (11, 11, [BrBz]), 121 (100, $[C_8H_9O]$); ^{1}H NMR (δ, $CDCl_3$) 7.82 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.26 (t, *J* = 9.5 Hz, H-4′), 4.83 (d, *J* = 11.0 Hz, 1H), 4.75 (d, *J* = 3.8 Hz, H-1), 4.51 (d, *J* = 10.9 Hz, 1H), 4.45 (dd, *J* = 3.6, 12.0 Hz, H-6′$_{proS}$), 4.34 (dd, *J* = 5.1, 12.0 Hz, H-6′$_{proR}$), 4.32 (d, *J* = 7.7 Hz, H-1′), 4.09 (dd, *J* = 2.0, 11.0 Hz, H-6$_{proS}$), 3.84−3.75 (H-3′, H-5′, H-3, H-5), 3.79 (s, 3H), 3.68 (dd, *J* = 5.2, 11.1 Hz, H-6$_{proR}$), 3.54 (br t, *J* = 8.3 Hz, H-2′), 3.47 (dt, *J* = 3.9, 9.3 Hz, H-2), 3.39 (s, 3H), 3.32 (t, *J* = 9.3 Hz, H-4), 1.88 (d, *J* = 9.3 Hz, 1H), 1.67 (br s, 1H), 0.94 (s, 9H), 0.72 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), −0.12 (s, 3H); ^{13}C NMR (δ, $CDCl_3$) 165.4 (s), 164.5 (s), 159.1 (s), 131.8−128.2, 113.8 (2d), 103.4 (d, C-1′), 99.4 (d, C-1), 78.5 (d, C-4), 76.1* (d, C-3′), 75.1* (d, C-5′), 74.5 (t), 74.2 (d, C-2′), 73.2 (d, C-2), 72.4 (d, C-4′), 71.7* (d, C-3), 70.1* (d, C-5), 68.7 (t, C-6), 63.9 (t, C-6′), 55.3 (2q), 26.0 (3q), 25.6 (3q), 18.2 (s), 18.0 (s), −3.9 (q), −4.2 (2q), −4.8 (q). Anal. Calcd for $C_{47}H_{66}Br_2O_{14}Si_2$: C, 52.71; H, 6.21. Found: C, 52.73; H, 6.39.

***tert*-Butyl 2-*O*-Acetyl-6-*O*-[2-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (23α).** Compound **10α** (50.0 mg, 0.05 mmol) was dissolved in 3 mL of dry acetonitrile under an argon atmosphere at 0 °C, treated with 10 μL of HF-Py (0.12 mmol), and left at room temperature. When the reaction was completed, it was diluted with CH_2Cl_2 and washed with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (2 times). The combined extracts were dried over $MgSO_4$, filtered, and concentrated. Sephadex chromatography of the residue (*n*-hexane/$CHCl_3$/MeOH, 2:1:1) furnished **23α** (30.5 mg) in 77% yield: TLC R_f = 0.52 (CH_2Cl_2/MeOH, 9:1); colorless syrup; $[\alpha]^{25}_D$ = +58.7 (*c* 0.78, $CHCl_3$); MS (FAB) 873, 871, 869 (5, 13, 4, $[M + Na]^+$), 777, 775, 773 (7, 11, 5, $[M - C_4H_9O]$), 573, 571, 569 (19, 29, 19, $[C_{22}H_{19}Br_2O_8]$), 307 (42, $[C_{12}H_{19}O_9]$), 185, 183 (97, 100, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.85 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 5.30 (t, *J* = 9.7 Hz, H-4′), 5.27 (d, *J* = 3.8 Hz, H-1), 4.97 (dd, *J* = 7.9, 9.3 Hz, H-2′), 4.66 (d, *J* = 7.8 Hz, H-1′), 4.61 (dd, *J* = 3.0, 12.1 H-6′$_{proS}$), 4.56 (dd, *J* = 3.8, 10.1, H-2), 4.40 (dd, *J* = 5.1, 12.1 H-6′$_{proR}$), 4.02 (dd, *J* = 2.8, 10.7 Hz, H-6$_{proS}$), 3.98−3.92 (H-3, H-5, H-5′), 3.91 (t, *J* = 9.3 Hz, H-3′), 3.82 (dd, *J* = 4.8, 10.7 Hz, H-6$_{proR}$), 3.53 (t, *J* = 9.3 Hz, H-4),

2.14 (s, 3H), 2.10 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (δ, $CDCl_3$) 171.0 (2*s*), 165.5 (s), 165.3 (s), 131.8−127.9, 100.9 (d, C-1′), 90.3 (d, C-1), 75.4 (s), 74.0 (d, C-2′), 73.6 (d, C-2), 73.6* (d, C-3′), 72.2 (d, C-4′), 71.8* (d, C-5), 71.4* (d, C-5′), 71.2 (d, C-4), 69.5* (d, C-3), 68.9 (t, C-6), 63.3 (t, C-6′), 25.3 (3q), 20.9 (2q). Anal. Calcd for $C_{34}H_{40}Br_2O_{15}$: C, 48.13; H, 4.75. Found: C, 48.17; H, 4.92.

***tert*-Butyl 6-*O*-[4,6-Bis-*O*-(4-bromobenzoyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (24α).** Compound **23α** (15.0 mg, 0.02 mmol) was dissolved in 2 mL of CH_2Cl_2/MeOH (9:1) and *p*-TsOH-H_2O (6.9 mg, 0.04 mmol) added. When the reaction was completed, it was diluted with CH_2Cl_2 and washed with a saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (two times). The combined extracts were dried over $MgSO_4$, filtered, and concentrated. Sephadex chromatography of the residue (*n*-hexane/$CHCl_3$/MeOH, 2:1:1) led to **24α** (11.2 mg) in 81% yield: TLC R_f = 0.29 (CH_2Cl_2/MeOH, 9:1); mp = 152.3−154.0 °C; $[\alpha]^{25}_D$ = +69.0 (*c* 0.40, $CHCl_3$); MS (FAB) 789, 787, 785 (0.4, 1, 0.2, [M + Na]$^+$), 531, 529, 527 (3, 5, 3, [$C_{20}H_{17}Br_2O_7$]), 307 (16, [$C_{12}H_{19}O_9$]), 185, 183 (14, 15, [BrBz]), 154 (100); ^{1}H NMR (δ, DMSO) 7.81 (d, J = 8.6 Hz, 2H), 7.79 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 5.42 (d, J = 5.7 Hz, 1H), 5.23 (d, J = 5.0 Hz, 1H), 4.94 (t, J = 9.7 Hz, H-4′), 4.90 (d, J = 5.3 Hz, 1H), 4.86 (d, J = 3.7 Hz, H-1), 4.68 (d, J = 4.5 Hz, 1H), 4.41 (d, J = 7.8 Hz, H-1′), 4.32 (dd, J = 3.0, 12.0 Hz, H-6′$_{proS}$), 4.26 (dd, J = 5.1, 12.0 Hz, H-6′$_{proR}$), 4.24 (d, J = 7.1 Hz, 1H), 3.90 (m, H5′), 3.87 (d, J = 11.5, H-6$_{proS}$), 3.75 (m, H5), 3.63 (dd, J = 6.0, 11.1 Hz, H-6$_{proR}$), 3.56 (m, H3′), 3.34 (m, H-3), 3.29−3.07 (H-2, H-2′, H-4), 1.14 (s, 9H); ^{13}C NMR (δ, DMSO) 165.2 (s), 164.9 (s), 132.3−127.9, 104.1 (d, C-1′), 93.4 (d, C-1), 74.4 (d), 74.1 (d, C-3′), 74.1* (d, C-4), 73.7 (d, C-3), 72.8 (d, C-4′), 72.2* (d, C-2′), 71.4 (d, C-5), 71.0 (d, C-5′), 70.8* (d, C-2), 69.9 (t, C-6), 64.1 (t, C-6′), 28.8 (3q); UV (EtOH) λ_{max} 245 nm; CD (EtOH) λ ($\Delta\varepsilon$) 251 (12.2), 234 nm (−3.9). Anal. Calcd for $C_{30}H_{36}Br_2O_{13}$: C, 47.14; H, 4.75. Found: C, 47.15; H, 5.05.

***tert*-Butyl 2,3,4-Tri-*O*-acetyl-6-*O*-[2,3-di-*O*-acetyl-4,6-bis-*O*-(4-bromobenzoyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (25α).** Compound **23α** (11.3 mg, 0.01 mmol) was dissolved in 1 mL of a 1:1 solution of dry pyridine/acetic anhydride. Excess solvent was removed under reduced pressure to give, after column chromatography (*n*-hexane/EtOAc, 8:2), compound **25α** (10.7 mg) in 83% yield: TLC R_f = 0.43 (*n*-hexane/EtOAc, 1:1); mp = 227.5−230.2 °C dec; $[\alpha]^{25}_D$ = +55.7 (*c* 0.79, $CHCl_3$); MS (FAB) 903, 901, 899 (4, 8, 5, [$C_{37}H_{44}Br_2O_{17}$]), 615, 613, 611 (21, 49, 21, [$C_{24}H_{21}Br_2O_9$]), 185, 183 (97, 100, [BrBz]); ^{1}H NMR (δ, $CDCl_3$) 7.81 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 2H), 5.46 (t, J = 9.4 Hz, H-3), 5.40 (m, H-4′, H-3′), 5.32 (d, J = 3.6 Hz, H-1), 5.09 (t, J = 7.9 Hz, H-2′), 4.91 (t, J = 9.5 Hz, H-4), 4.72 (dd, J = 3.6, 10.3 Hz, H-2), 4.63 (d, J = 7.9 Hz, H-1′), 4.53 (dd, J = 3.4, 12.2 Hz, H-6′$_{proS}$), 4.39 (dd, J = 4.9, 12.2 Hz, H-6′$_{proR}$), 4.15 (m, H-5), 3.94 (m, H-5′), 3.91 (dd, J = 2.1, 10.8 Hz, H-6$_{proS}$), 3.52 (dd, J = 5.7, 10.8 Hz, H-6$_{proR}$), 2.07 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.90 (s, 3H), 1.20 (s, 9H); ^{13}C NMR (δ, $CDCl_3$) 170.2 (2*s*), 170.1 (s), 169.7 (s), 169.3 (s), 165.3 (s), 164.4 (s), 132.0−127.6, 100.8 (d, C-1′), 90.0 (d, C-1), 76.0 (s), 72.5* (d, C-4′), 71.8 (d, C-5′), 71.1 (d, C-2′, C-2), 70.3 (d, C-3), 69.9* (d, C-3′), 69.3 (d, C-4), 68.1 (t, C-6), 67.8 (d, C-5), 63.2 (t, C-6′), 28.3 (3q), 20.7 (2q), 20.6 (2q), 20.5 (q); UV (CH_3CN) λ_{max} 245 nm; CD (CH_3CN) λ ($\Delta\varepsilon$) 251 (14.4), 234 nm (−7.3). Anal. Calcd for $C_{40}H_{46}Br_2O_{18}$: C, 49.30; H, 4.76. Found: C, 49.30; H, 4.79.

Acknowledgment. This research was supported by the Ministerio de Educación y Ciencia (Spain) through Grant No. CTQ2007-67532-C02-02/BQU. A.R. and C.M. thank Banco Santander and the Consejería de Educación y Deportes (Gobierno de Canarias), respectively, for fellowships. J.I.P. thanks the Spanish MCYT-FSE for a Ramón y Cajal contract.

Supporting Information Available: Tables containing NMR and CD data for disaccharides **2α**−**16α** and **23α**−**25α**, atom coordinates of the rotamers of the disaccharide **14α**, as well as ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801184Q