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Stereodirecting Effect of the Pyranosyl C-5 Substituent in Glycosylation Reactions

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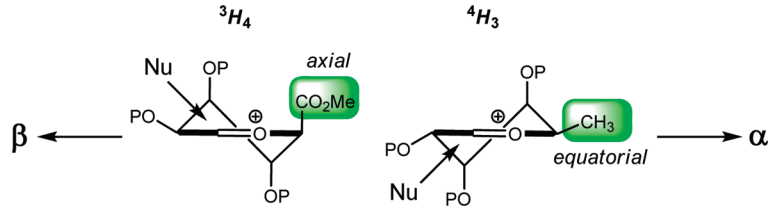

The stereodirecting effect of the glycosyl C-5 substituent has been investigated in a series of D-pyranosyl thioglycoside donors and related to their preferred positions in the intermediate $^3H_4$ and $^4H_3$ half-chair oxacarbenium ions. Computational studies showed that an axially positioned C-5 carboxylate ester can stabilize the $^3H_4$ half-chair oxacarbenium ion conformer by donating electron density from its carbonyl function into the electron-poor oxacarbenium ion functionality. A similar stabilization can be achieved by a C-5 benzyloxymethyl group, but the magnitude of this stabilization is significantly smaller than for the C-5 carboxylate ester. As a result, the preference of the C-5 benzyloxymethyl to occupy an axial position in the half-chair oxacarbenium ions is much reduced compared to the C-5 carboxylate ester. To minimize steric interactions, a C-5 methyl group prefers to adopt an equatorial position and therefore favors the $^4H_3$ half-chair oxacarbenium ion. When all pyranosyl substituents occupy their favored position in one of the two intermediate half-chair oxacarbenium ions, highly stereoselective glycosylations can be achieved as revealed by the excellent β-selectivity of mannuronate esters and α-selectivity of 6-deoxygulosides.

Introduction

Uronic acids, aldohexoses having their primary hydroxyl oxidized to a carboxylic acid, are widely spread constituents of naturally occurring polysaccharides.[1] For instance, the biologically important glycosaminoglycans are characterized by dimeric repeating units, in which one of the residues is either a D-glucuronic acid or a L-iduronic acid.[2] Alginate (composed of D-mannuronic acid and L-guluronic acid residues)[3] and pectin (D-galacturonic acid)[4] are examples of the class of homoglycuronans that contain solely uronic acids. Recently, we reported the syntheses of β-1,4-D-mannuronic acid[5] and α-1,4-L-guluronic acid[6] oligomers as fragments of the alginate polymer. In a sulfonium ion mediated preactivation glycosylation procedure,[7] the β-1,4-D-mannuronic acid linkages (**4**) were introduced with high stereoselectivity using a suitably protected thiomannuronate ester donor (e.g., **1**, Scheme 1). At the time, we assumed that in analogy with the thorough mechanistic studies of the group of Crich on the glycosylating properties of 4,6-*O*-benzylidene-thiomannoside donors, this stereochemical outcome can be explained by an S_N2-like attack of the nucleophile on the putative axial α-triflate **2** or on the corresponding contact ion

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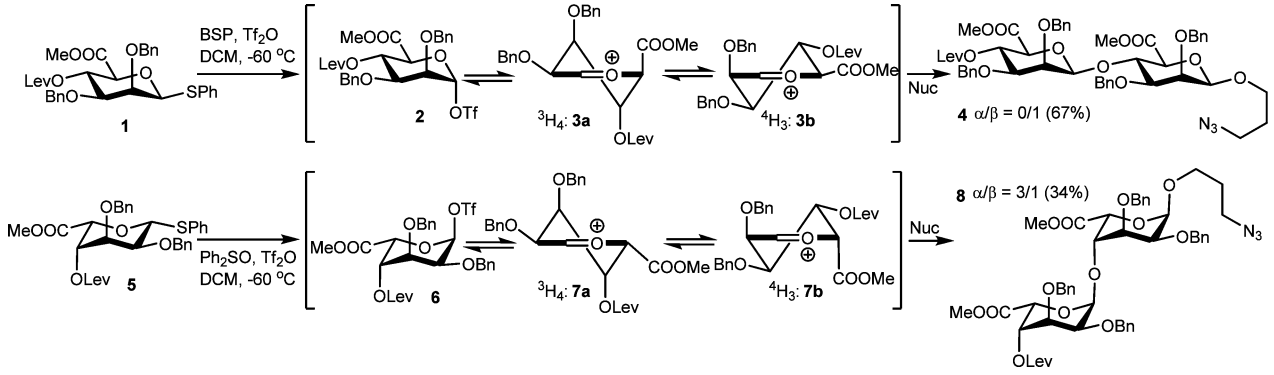
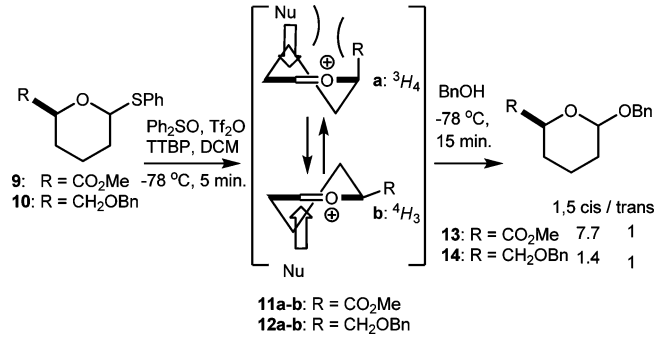
SCHEME 1. Glycosylations with Mannuronate and Guluronate Ester Donors



pair.[8] The electron-withdrawing capacity of the C-5 carboxylate[9] serves to destabilize the (solvent separated) oxocarbenium ion **3a**,**b**, resulting in a shift of the equilibrium to the side of the α-triflate **2**.[5]

Application of the same type of glycosylation procedure to the suitably protected thioguluronic ester donor **5** (the C-5 epimer of D-mannose) gave the α-linked product (**8**),[6] albeit with reduced stereoselectivity and yield. The stereochemical outcome of the glycosylation of **5** cannot be explained by invoking α-triflate **6** as the product-forming intermediate, since S_N2-like attack on the axial triflate **6** would result in the formation of the *β*-product (1,2-*trans*). Puzzled by the effect of the C-5 carboxylate ester on the stereochemistry of these glycosylations, our attention was attracted to the work of Woerpel and co-workers on the stereoselectivity of pyranosyl oxacarbenium ions in *C*-glycosylation reactions.[10] From their work it became apparent that the relative stability of the $^3H_4$ and $^4H_3$ half-chair conformers[11] of the intermediate oxacarbenium ions[12] is of prime importance for the stereochemical outcome of these reactions.[13] Provided that there are no prohibitive steric interactions in the transition state, the isomeric ratio of the addition products reflects the relative ground-state energies of the product-forming oxacarbenium ions.[14] The stability of the half-chair conformers is determined by the nature and the configuration of the substituents on the pyranose ring.[12c,15] Alkyl groups at C3 and C4 prefer to adopt pseudoequatorial positions, whereas electron-withdrawing substituents at these positions preferentially adopt an axial orientation, C-2 alkoxy substituents again prefer an equatorial orientation.[12c] To establish the stereodirecting effect of the C-5 carboxylate ester, we studied the condensations of pyranoside **9** (Scheme 2) having a single carboxylate subtituent at C-5 and its "non-oxidized" counterpart **10** having a methylene oxybenzyl group at this position.[16] It turned out that the C-5 ester is 1,5-*cis* directing, while the C-5 methylene oxybenzyl functionalized pyranose exhibits little selectivity. The stereochemical outcome of these glycosylations can be explained with the half-chair oxocarbenium ions **11** and **12** as product-forming intermediates. Attack of an incoming nucleophile on these ions occurs along a pseudoaxial trajectory with a facial selectivity which allows the formation of the lower energy chair product, as opposed to a twist-boat product originating from attack from the other side of the oxacarbenium ion.[14b] The formation of the 1,5-*cis*-products of **13** and **14** arises from the $^3H_4$ (**11a** and **12a**) conformer, indicating that the C-5 carboxylate prefers to occupy an axial position in the oxacarbenium ion intermediate.

SCHEME 2. Stereoselectivity of C-5-Functionalized Pyranosides



In the mannuronate ester $^3H_4$ oxacarbenium ion (**3a**), the axial preference of the C-5 ester can be accommodated keeping all other substituents in their most favorable orientations (Scheme 1). The $^3H_4$ conformer will therefore be substantially more stable than the corresponding $^4H_3$ half-chair (**3b**), and nucleophilic attack on **3a** leads to the formation of the 1,2-*cis* products. Thus, besides α-triflate **2** (Scheme 1), oxacarbenium ion **3a** can also be at the basis of the selectivity displayed by mannuronate esters. In the L-guluronate case, the C-5 ester can only adopt its

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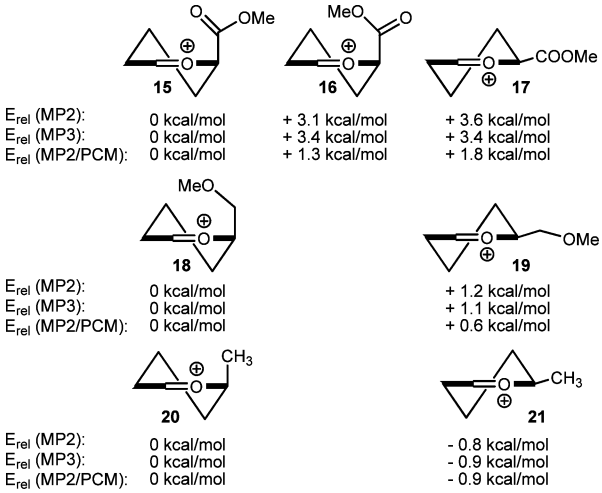

FIGURE 1. Calculated relative energies of C-5-substituted pyranosyl oxacarbenium ions. (a) The experimental error in these calculations is approximately ±1 kcal/mol.

favorable axial position in the $^4H_3$ half-chair (**7b**), in which all other substituents are in their disfavored positions (Scheme 1). In the alternative $^3H_4$ conformer (**7a**), the C-2, C-3, and C-4 are favorably oriented while placing the C-5 ester in the more destabilizing equatorial position. The guluronate ester oxacarbenium ion half-chairs will therefore be closer together in ground-state energy, and the selectivities of the glycosylations involving these intermediates is less pronounced. The effect of the C-5 ester does not outweigh the combined electronic effects of the substituents at C-2, C-3, and C-4,[12c] and therefore, the $^3H_4$ half-chair (**7a**), which leads to 1,2-*cis* selective condensations, is preferred over its $^4H_3$ counterpart (**7b**).

To investigate the magnitude of the stereodirecting effect of the C-5 substituent in glycosylations in more detail, we here present a study toward the glycosylation properties of a set of thioglycosides having a carboxylate methyl ester, a methylene benzyl ether, or a methyl group at C-5. To this end, D-manno-, D-gulo-, D-gluco-, and D-galacto-configured 1-thioglycosides, 1-thiouronic acids, and 1-thio-6-deoxythioglycosides were synthesized[17] and glycosidated with both a primary and a secondary glycosyl acceptor.

Results and Discussion

First, theoretical support was sought for the effect of ester, methylene ether,[18] and methyl functions at C-5 on the stability of the oxacarbenium ion half chairs (Figure 1). To this end, the geometries of the C-5-functionalized pyranosyl half-chair oxacarbenium ions were optimized and their relative energies calculated. Second-order Möller−Plesset (MP2) geometry optimizations[19] were performed using the 6-311+G** basis set in Spartan 04.[20] The MP2 and MP3 gas-phase energy calculations of the geometry- optimized conformers were performed using Gaussian 03.[21] The effect of the solvent (dichloromethane) was taken into account by application of the polarizable continuum model (PCM) at the MP2 level, which leveled the energy differences to some extent (vide infra). The results of the calculations are reported in Figure 1. Both the MP2 and MP3 calculations show that the methyl ester oxacarbenium ion $^3H_4$ conformer (**15** and **16**), in which the ester occupies an axial position, is more stable than the corresponding equatorial ester oxacarbenium ion (**17**). The orientation of the ester is also of importance: conformer **15**, in which the ester carbonyl is pointing toward the ring oxygen, was calculated to be approximately 3.5 kcal/mol more stable than the equatorial conformer, whereas conformer **16**, having the methoxy group oriented toward the oxacarbenium ion, is isoenergetic with the equatorial conformer.[22,23] The stability of **15** results from the donation of electron density from the carbonyl group to the electron-depleted oxacarbenium ion function. The axial preference of the C-5 ester with its carbonyl directed to the electron-depleted anomeric center, is of similar magnitude as the axial preference of C-3 and C-4 alkoxy groups.[12c] The axially oriented methyloxy methylene pyranosyl oxacarbenium **18**, with the alkoxy group situated above the ring,[10e] was also calculated to be the most stable conformer, although the difference between the axial and equatorial conformer was significantly smaller when compared to the C-5 ester system. The axially (**20**) and equatorially (**21**) oriented C-5 methyl oxacarbenium ions differ in energy by approximately 1 kcal/mol, in favor of the equatorial substituent. A similar value has previously been reported by Bowen and co-workers for the same system.[12c]

The trend[17] revealed by the calculations is in line with the experimental results described above in Scheme 2. The C-5 ester prefers to adopt an axial position in the oxacarbenium intermediate, thereby stabilizing the $^3H_4$ conformer relative to its $^4H_3$ counterpart. The stabilization is large enough to overrule the unfavorable steric interactions that develop in the transition state when the nucleophile approaches this half-chair conformer form the β-face. The 1,5-*cis* product is thus preferentially formed. The small preference of the methylene oxybenzyl group in pyranoside **18** to occupy an axial position does not lead to the selective formation of the 1,5-*cis* product. In this case, steric interactions between the incoming nucleophile and the C-5 substituent in the transition state counterbalance the ground-state preferences of the half-chair oxacarbenium ions.

(17) See Supporting Information for experimental details.

(18) The methylene benzyloxy function of the glycosides used in this study are replaced by a methylene methoxy group in the pyranosyl oxacarbenium ions to simplify the calculations.

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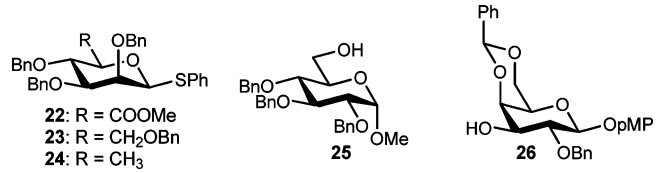
(22) It should be noted that the level of theory deployed in our study provides the relative energies with an error of approximately 1 kcal/mol. Therefore, care should be taken with the interpretation of small energy differences.

(23) The relative energies of the pyranosyl oxacarbenium ion, functionalized with a CF_3 substituent at C-5, were also calculated. MP2 and MP3 calculations showed the equatorial CF_3 to be the most stable by 0.23 and 0.25 kcal/mol, respectively. Application of the PCM model led to a difference in energy of 1.1 kcal/mol in favor of the equatorial conformer. These results indicate that the axial preference of C-5 carboxylate is a result of the stabilization of the positive charge at the anomeric center by the ester and is not caused by its electron-withdrawing nature. The small difference in stability of the C-5-CF_3 half chair oxacarbenium ions was translated in the stereochemical outcome of the condensation reaction of 1-phenylsulfanyl-5-trifluoromethyltetrahydropyran with benzyl alcohol, which proceeded without any selectivity to provide 1-benzyloxy-5-trifluoromethyltetrahydropyran as an α/β mixture (1:1.2).

TABLE 1. Study of the C-5 Substituent Effect in the Mannose Series



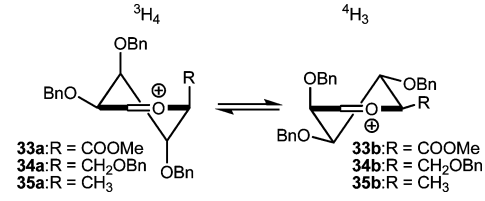
donor	acceptor	**22**: R = COOMe[a]	**23**: R = CH_2OBn[b]	**24**: R = CH_3[b]
mannose (**22**−**24**)	**25**	**27**: α/β = 0/1 (77%)	**28**: α/β = 1/2 (71%)	**29**: α/β = 1/1.7 (71%)
	26	**30**: α/β = 0/1 (58%)	**31**: α/β = 1/1.5 (52%)	**32**: α/β = 1/1 (65%)

[a] Reagents and conditions: Ph_2SO, TTBP, DCM, −60 °C to −45 °C, Tf_2O, 10 min, then −78 °C, nucleophile, to 0 °C. [b] Reagents and conditions: Ph_2SO, TTBP, DCM, −78 °C, Tf_2O, 10 min, nucleophile, to 0 °C.

Next, the stereodirecting effect of three C-5 substituents (methyl ester, methylene oxybenzyl, and methyl) on the glycosylation properties of a set of epimeric perbenzylated D-pyranosides was investigated. First, the mannose series was investigated. Phenyl 1-thio-β-D-mannuronate ester **22**, the corresponding D-mannose **23**, and 6-deoxy-D-mannose (D-rhamnose) **24** were condensed with both the primary alcohol **25** and the secondary alcohol **26** using a diphenylsulfoxide (Ph_2SO)−trifluoromethanesulfonic anhydride (Tf_2O) activation procedure. The coupling conditions for all three donors were identical except for the activation temperature: mannuronate ester **22** was activated starting at −60 °C and warming to −45 °C over a period of 15 min, before addition of the acceptor at −78 °C and very slow warming to 0 °C, at which temperature the reaction was quenched. The more reactive mannose donor **23** and rhamnose donor **24** were preactivated at −78 °C for 10 min after which the acceptor was added at the same temperature. The results of these condensations are summarized in Table 1.

Mannuronate ester **22** yielded solely the 1,2-*cis* (β-linked) products **27** and **30** independent of the nature of the acceptor. Tetrabenzylmannose **23** showed a significant drop in selectivity but maintained a slight preference for the formation of the 1,2-*cis* product. The *cis* selectivity for the glycosylation involving the primary acceptor **25** was slightly better than for the secondary acceptor **26**. Although the 1,2-*cis* selectivity of donor **23** is not unprecedented,[24] it stands in contrast to the perception that perbenzylated mannose donors are 1,2-*trans* selective (α-selective) in glycosylation reactions.[25] The condensations of D-rhamnose **24** showed a further decrease of 1,2-*cis* product formation, and also here the secondary acceptor gave more α-product. The anomeric ratios of the glycosylations in Table 1 reflect the expected stability differences of the respective oxacarbonium ion conformers (Scheme 3). In the $^3H_4$ conformer of mannuronic ester (**33a**) all substituents are situated in a favorable position, making this conformer considerably more stable than the $^3H_4$ half-chair. The ground-state energy difference of the mannuronate half-chair conformers is large enough to allow nucleophilic attack on the $^3H_4$ conformer, despite of the steric interactions that develop in the product-forming transition state, and the sole formation of the 1,2-*cis* product is observed. In mannose, the difference in stability between the $^3H_4$ conformer (**34a**) and its $^4H_3$ counterpart (**34b**) is less pronounced, and the nucleophilic attack more sensitive to steric effects. Because steric interactions in the transition state leading to the 1,2-*trans* product are smaller than in the transition state which leads to the 1,2-*cis*-linked dimer,[10d,e] a Curtin−Hammett/Winstein−Holness kinetic scenario,[26] in which product formation arises from the higher energy $^4H_3$ conformer (**34b**), can account for the formation of the 1,2-*trans* product in this case. Because the methyl group prefers an equatorial orientation in the oxacarbenium ion intermediate, the difference in stability between the $^3H_4$ (**35a**) and $^4H_3$ (**35b**) conformers of rhamnose is further minimized, and more product is formed from the $^4H_3$ oxacarbenium ion.

SCHEME 3. Mannosyl Oxacarbenium Ions



Execution of glycosylation reactions of **25** and **26** with D-gulose derivatives **36**−**38** shows an α-selectivity that increases slightly in going from the carboxylate methyl ester **36**, to methylene benzyl ether **37**, to 6-deoxy **38** (Table 2). For both tetrabenzyl (**37**) and the 6-deoxy (**38**) gulose the α-selectivity is slightly diminished when secondary alcohol **26** is used instead of primary acceptor **25**. On the contrary, for the guluronic acid methyl ester (**36**) glycosylations this effect is reversed.

The stereochemical outcome of the glycosylations in Table 2 can be rationalized with the oxacarbenium ions **45**−**47** (Scheme 4) as product-forming intermediates. Although the degree of influence of the substituents on the stereoselectivity seems to be reduced, the trend based on the relative stabilities of the $^3H_4$ and the $^4H_3$ conformers is again confirmed.[27] The gulosylations may proceed by an axial attack of the nucleophile on the $^4H_3$ conformer, leading to the *cis*-product (Scheme 4).[28] The $^4H_3$ oxacarbenium ion of 6-deoxygulose **47b** has all the substituents positioned in such a manner that they all contribute favorably to the stability of this conformer, and the gulosylations

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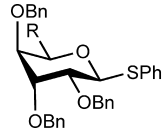
(25) (a) *Comprehensive Glycoscience*; KamerlingJ. P., Ed.; Elsevier: Oxford, 2007; Vol. 1. (b) *The Organic Chemistry of Sugars*; Levy, D. E..; Fügedi, P., Eds.; CRC Press: Boca Raton, 2006. (c) *Handbook of Chemical Glycosylation*—*Advances in Stereoselectivity and Therapeutic Relevance*; Demchenko, A. V., Ed.; Wiley-VCH: Weinheim, 2008. (d) Gouyette, C.; Neumann, J. M.; Fauve, R.; Huynh-Dinh, T. *Tetrahedron Lett.* **1989**, *30*, 6019–6022. (e) Babu, M. H.; Venugopal, R. G. *Tetrahedron* **1991**, *47*, 6435–6448. (f) Li, Z.-J.; Huang, H.-Q.; Cai, M.-S. *J. Carbohydr. Chem.* **1996**, *15*, 501–506. (g) Ding, X.; Yang, G.; Kong, F. *Carbohydr. Res.* **1998**, *310*, 135–140.

(26) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83–134.

(27) It is of interest to note that previous studies with L-gulose similar stereoselectivities were obtained, indicating that double stereo differentiation is no issue in these condensations (see ref 6).

TABLE 2. Study of the C-5 Substituent Effect in the Gulose Series

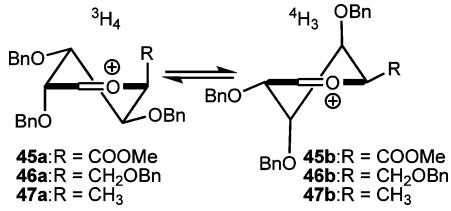


36: R = COOMe
37: R = CH_2OBn
38: R = CH_3

donor	acceptor	**36**: R = COOMe[a]	**37**: R = CH_2OBn[b]	**38**: R = CH_3[b]
gulose (**36**−**38**)	**25**	**39** α/β = 1/0.33 (86%)	**40** α/β = 1/0.10(76%)	**41** α/β = 1/0.08 (67%)
	26	**42** α/β = 1/0.17 (63%)	**43** α/β = 1/0.12 (70%)	**44** α/β = 1/0.15 (70%)

[a] Reagents and conditions: Ph_2SO, TTBP, DCM, −45 °C, Tf_2O 10 min, then −78 °C, nucleophile, to 0 °C. [b] Reagents and conditions: Ph_2SO, TTBP, DCM, −78 °C, Tf_2O 10 min, nucleophile, to 0 °C.

SCHEME 4. Gulosyl Oxacarbenium Ions



of this donor are therefore the most *cis* selective. The stereoselectivity of gulose **37** and in particular guluronic ester **36** is less pronounced, as in the $^4H_3$ conformer (**45b**) the carboxylic ester does not occupy its favored axial position (Scheme 4). The erosion in stereoselectivity caused by the unfavorable positioning of the C-5 substituent is considerably less in the gulose series than in the mannose series. This may be due to the difference in steric interactions that develop in the transition states of the nucleophilic additions to the respective oxacarbenium ions. Axial attack of a nucleophile on the mannose $^3H_4$ oxacarbenium ions **33a**−**35a** leads to 1,3-diaxial interactions with both the C-3 and C-5 substituents,[12c] which are absent in the transition state of the $^4H_3$ half-chairs **33b**−**35b** (Scheme 3). For gulose, both half-chair conformers give rise to one 1,3-diaxial interaction in the transition states and are therefore sterically equally demanding (Scheme 4).

The results reported above for mannuronic acid donor **22** and 6-deoxygulose donor **38** indicate that highly stereoselective glycosylations can be obtained when all the substituents occupy a favorable position in either the $^3H_4$ or the $^4H_3$ oxacabenium ion conformer. To further assess the effect of the substituent at C-5 on the stereochemical outcome of glycosylation reactions, three other epimers have been examined. D-Gluco-, D-allo-, and D-galacto-configured 1-thioglycosides and the corresponding 1-thiouronic acids were prepared and glycosidated with the same primary and secondary acceptor as used in the manno- and gulo-series. The results of these condensations are summarized in Table 3. Clearly, almost all of the condensations proceed with poor stereoselectivity.[24d,e,29,30] Furthermore, the nature of the acceptor has a profound effect on the stereochemical outcome of the glycosylations and no clear effect of the C-5 substituent can be distilled from the data reported in Table 3.

When we consider the structures of the half-chair oxacarbenium ions involved in the condensations in Table 3 (Scheme 5), it can be seen that all of them have one or more substituents occupying an unfavorable position, making none of them highly favorable based on electronic grounds. In addition, destabilizing steric interactions are present in all oxacarbenium ions and in all product-forming transition states, except in the $^4H_3$ glucose half-chair **67b**. The stereochemical outcome of the glycosylations are thus a delicate balance between electronic and steric factors in both the ground state of the oxacarbenium ions and the resulting transition states. Furthermore, the reactivity of the acceptor is of decisive influence.[31]

Conclusion

The study described here investigated the stereodirecting capacity of glycosyl C-5 substituents in systems that were devoid of any other stereodirecting factors. In pyranosyl oxacarbenium ion intermediates possessing a half-chair conformation, a C-5 ester prefers to occupy a pseudoaxial position. As such it can donate electron density through space to the electron-depleted oxacarbenium ion, thereby stabilizing this intermediate. A C-5 methylene alkoxy substituent is also capable of such an energetically favorable interaction, but the magnitude of this stabilization is significantly smaller than that of the C-5 ester functionality. A C-5 alkyl group prefers to adopt an equatorial position because of steric reasons. When the stereodirecting effect of the C-5 substituent works in concert with the other functional groups on the pyranose ring, highly selective condensations are achieved. This is exemplified by the glycosidations of mannuronate ester **22** and 6-deoxy guloside **38**. In systems having conflicting substituent preferences, steric factors

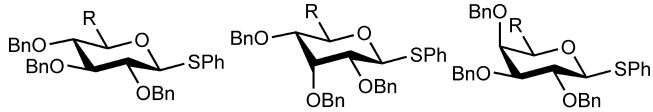
(28) The high α-selectivity of L-gulose has been observed in previous syntheses involving L-gulose donors. For examples of the synthesis of bleomycin, see: (a) Katano, K.; An, H.; Aoyagi, Y.; Overhand, M.; Sucheck, S. J.; Stevens, W. C., Jr.; Hess, C. D.; Zhou, X.; Hecht, S. M. *J. Am. Chem. Soc.* **1998**, *120*, 11285–11296. (b) Boger, D. L.; Honda, T. *J. Am. Chem. Soc.* **1994**, *116*, 5647–5656. See for the synthesis of an L-gulose alginate tetramer: (c) Chi, F.-C.; Kilkarni, S. S.; Zulueta, M. M. L.; Hung, S.-C. *Chem. Asian J.* **2009**, *3*, 386–390.

(29) Similar selectivities have been reported before in condensations of tetrabenzyl glucopyranosyl and tetrabenzyl galactopyranosyl donors. See, for example: (a) Milat, M. L.; Zollo, P. A.; Sinaÿ, P. *Carbohydr. Res.* **1982**, *100*, 263–271. (b) Hinklin, R. J.; Kiessling, L. L. *J. Am. Chem. Soc.* **2001**, *123*, 3379–3380. (c) Meloncelli, P. J.; Williams, T. M.; Hartmann, P. E.; Stick, R. V. *Carbohydr. Res.* **2007**, *342*, 1793–1804. (d) Mukaiyama, T.; Takeuchi, K.; Maeshima, H.; Saitoh, T. *Helv. Chem. Acta* **2000**, *83*, 1901–1918. (e) Choudhury, A. K.; Mukherjee, I.; Mukhopadhyay, B.; Roy, N. *J. Carbohydr. Chem.* **1999**, *18*, 361–367. (f) Kartha, K. P. R.; Aloui, M.; Field, R. A. *Tetrahedron Lett.* **1996**, *37*, 5175–5178.

(30) The high α-selectivity in the condensation of tetrabenzyl galactopyranosyl donors and the galactosyl C3-OH has been observed before. See, for example: (a) Wang, J.-Q.; Chen, X.; Zhang, W.; Zacharek, S.; Chen, Y.; Wang, G. P. *J. Am. Chem. Soc.* **1999**, *121*, 8174–8181. (b) Hanessian, S.; Huynk, H. K.; Reddy, G. V.; Duthaler, R. O.; Katopodis, A.; Streiff, M. B.; Kinzy, W.; Oehrlein, R. *Tetrahedron* **2001**, *57*, 3281–3290. (c) Ramos, D.; Rollin, R.; Klaffke, W. *J. Org. Chem.* **2001**, *66*, 2948–2956. (d) Litjens, R. E. J. N.; Hoogerhout, R.; Filippov, D. V.; Codée, J. D. C.; Van den Bos, L. J.; Van den Berg, R. J. B. H. N.; Overkleeft, H. S.; Van der Marel, G. A. *J. Carbohydr. Res.* **2005**, *24*, 755–769. (e) Ratcliffe, R. M.; Kamth, V. P.; Yeske, R. E.; Gregson, J. M.; Fang, Y. R.; Palcic, M. M. *Synthesis* **2004**, *14*, 2293–2296.

(31) (a) Belén Cid, M.; Alfonso, F.; Alonso, I.; Martín-Lomas, M. *Org. Biomol. Chem.* **2009**, *7*, 1471–1481. (b) Belén Cid, M.; Alfonso, I.; Alonso, F.; Bonilla, J. B.; López-Prados, J.; Martín-Lomas, M. *Eur. J. Org. Chem.* **2006**, 3947–3959. (c) Xia, C.; Yao, Q.; Schümann, J.; Rossy, E.; Chen, W.; Zhu, L.; Zhang, W.; De Libero, G.; Wang, P. G. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2195–2199. (d) Crich, D.; Dudkin, V. *J. Am. Chem. Soc.* **2001**, *121*, 6819–6825.

TABLE 3. Study of the C-5 Substituent Effect in the Glucose, Galactose, and Allose Series

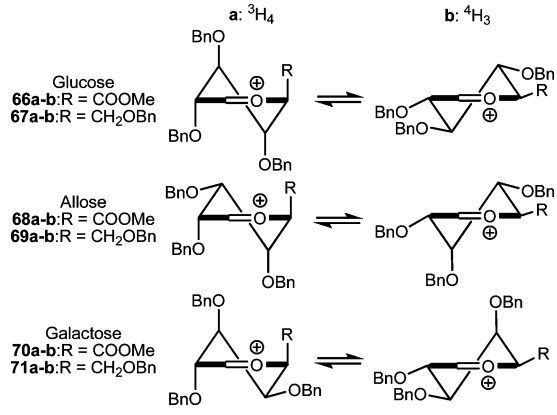


48: R = COOMe **54**: R = COOMe **60**: R = COOMe
49: R = CH_2OBn **55**: R = CH_2OBn **61**: R = CH_2OBn

donor	acceptor	R = COOMe[a]	R = CH_2OBn[b]
glucose (**48**, **49**)	**25**	**50**: α/β = 1/1.4 (68%)	**51**: α/β = 1/1.4 (75%)
	26	**52**: α/β = 1/0.6 (86%)	**53**: α/β = 1/1.7 (89%)
Allose (**54**, **55**)	**25**	**56**: α/β = 1/0.4 (91%)	**57**: α/β = 1/0.5 (92%)
	26	**58**: α/β = 1/0 (52%)	**59**: α/β = 1/0.6 (65%)
Galactose (**60**, **61**)	**25**	**62**: α/β = 1/2.3 (49%)	**63**: α/β = 1/3 (67%)
	26	**64**: α/β = 1/0.4 (86%)	**65**: α/β = 1/0.1 (72%)

[a] Reagents and conditions: Ph_2SO, TTBP, DCM, −45 °C, Tf_2O, 10 min, then −78 °C, nucleophile, to 0 °C. [b] Reagents and conditions: Ph_2SO, TTBP, DCM, −78 °C, Tf_2O, 10 min, nucleophile, to 0 °C.

SCHEME 5. Glucosyl, Galactosyl, and Allosyl Oxacarbenium Ions



in both the ground state of the oxacarbenium ion half-chair and product-forming transition states become important for the outcome of the reaction. The mechanistic insight described here can aid in the design of stereoselective glycosylation strategies.

Experimental Section

General Procedure for Glycosylations of Thioglycosides and 6-Deoxythioglycosides. A solution of donor, diphenyl sulfoxide (1.1 equiv), and tri-*tert*-butylpyrimidine (2.5 equiv) in DCM (0.05 M) was stirred over activated MS 3 Å for 30 min. The mixture was cooled to −78 °C before triflic acid anhydride (1.1 equiv) was added. The mixture was stirred for 10 min at −78 °C followed by addition of acceptor (1.5 equiv) in DCM (0.1 M). The reaction mixture was allowed to warm to 0 °C, and Et_3N (0.15 mL) was added. The reaction mixture was diluted with DCM and washed with $NaHCO_3$ (aq). The aqueous layer was extracted twice with DCM, and the collected organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by size-exclusion and column chromatography yielded the corresponding dimer.

General Procedure for Glycosylations of Thioglycuronates. A solution of donor, diphenyl sulfoxide (1.1 equiv), and tri-*tert*-butylpyrimidine (2.5 equiv) in DCM (0.05 M) was stirred over activated MS 3 Å for 30 min. The mixture was cooled to −60 °C before triflic acid anhydride (1.1 equiv) was added. The mixture was warmed to −45 °C and then cooled to −78 °C followed by addition of acceptor (1.5 equiv) in DCM (0.1 M). Stirring was continued, the reaction mixture was allowed to warm to 0 °C, and Et_3N (0.15 mL) was added. The reaction mixture was diluted with DCM and washed with $NaHCO_3$ (aq). The aqueous layer was extracted twice with DCM, and the collected organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by size-exclusion and column chromatography yielded the corresponding dimer.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(methyl 2,3,4-tri-*O*-benzyl-β-D-mannopyranosyluronate)-α-D-glucopyranoside (27). Donor **22** (86 mg, 0.15 mmol) was condensed with acceptor **25** according to the general procedure for glycosylations of thioglycuronates, yielding β-linked disaccharide **27** (80 mg, 58%) as an amorphous white solid: $[\alpha]^{22}_D = +9.4$ ($c = 0.016$, DCM); IR (neat) 729, 795, 860, 910, 1026, 1049, 1157, 1120, 1238, 1265, 1362, 1454, 1497, 1605, 1747, 2862, 2924, 3032 cm^{-1}; ^1H NMR (400 MHz) δ = 3.31 (s, 3H, C-1-OCH_3), 3.39−3.43 (m, 3H, H-3′, H-4, H-6), 3.50 (d, 1H, J = 9.2 Hz, H-2), 3.70−3.77 (m, 6H, CO_2CH_3, H-5, H-5′, H-2′), 4.01 (t, 1H, J = 8.8 Hz, H-3), 4.11−4.03 (m, 2H, H-1′, H-6), 4.21 (t, 1H, J = 9.2 Hz, H-4′), 4.47−4.56 (m, 4H, CH_2 Bn, H-1), 4.66 (d, 1H, J = 11.6 Hz, CH_2 Bn), 4.77−4.91 (m, 5H, CH_2 Bn), 4.96 (d, 1H, J = 10.0 Hz, CH_2 Bn), 5.02 (d, 1H, J = 10.8 Hz, CH_2 Bn), 7.20−7.46 (m, 30 H, H_{Ph}); ^{13}C NMR (100 MHz) δ = 52.4 (CO_2CH_3), 55.1 (C-1-OCH_3), 68.6 (C-6), 69.7 (C-5), 71.7 (CH_2 Bn), 73.3 (C-5′or C-2′), 73.4 (CH_2 Bn), 73.8 (CH_2 Bn), 74.8 (CH_2 Bn), 75.2 (CH_2 Bn), 75.3 (C-5′or C-2′), 75.8 (CH_2 Bn), 75.8 (C-4′), 77.6 (C-3′or C-4), 79.9 (C-2), 81.3 (C-3′or C-4), 82.2 (C-3), 97.8 (C-1), 102.1 (C-1′), 127.6−128.5 (CH arom), 138.0 (C_q Ph), 138.1 (C_q Ph), 1383 (C_q Ph), 138.3 (C_q Ph), 138.5 (C_q Ph), 138.88 (C_q Ph), 168.7 (C=O CO_2Me); ^{13}C-GATED NMR (100 MHz) δ = 97.8 ($J_{C\text{-}1,\ H\text{-}1}$ = 167 Hz, C-1), 102.1 ($J_{C\text{-}1',\ H\text{-}1'}$ = 155 Hz, C-1′); HRMS [M + Na]$^+$ calcd for $C_{56}H_{60}O_{12}Na$ 947.39770, found 947.39853.

***p*-Methoxyphenyl 2-*O*-Menzyl-3-*O*-(methyl 2,3,4-tri-*O*-benzyl-β-D-mannopyranosyluronate)-4,6-benzylidene-β-D-galactopyranoside (30).** Donor **22** (86 mg, 0.15 mmol) was condensed with acceptor **26** according to the general procedure for glycosylations of thioglycuronates, yielding β-linked disaccharide **30** (107 mg, 77%) as an amorphous white solid: $[\alpha]^{22}_D = -8.5$ (c = 2, DCM); IR (neat) 729, 895, 1003, 1061 1096, 1219, 1265, 1366, 1508, 1747, 3055 cm^{-1}; ^1H NMR δ = 3.15 (d, 1H, J 9.2 Hz, H-3′), 3.53 (s, 1H, H-5), 3.62 (s, 1H, H-2′), 3.66−3.75 (m, 4H, H-5′, CO_2CH_3), 3.77 (s, 3H, CO_2CH_3), 3.84 (dd, 1H, J = 2.8 Hz, 9.6 Hz, H-3), 4.05−4.10 (m, 2H, H-2, H-6), 4.18 (t, 1H, J = 9.6 Hz, H-4′), 4.27 (d, 1H, J = 10.0 Hz, CH_2 Bn), 4.34−4.37 (m, 3H, H-4, H-6, CH_2 Bn), 4.60 (d, 1H, J, 10.4 Hz, CH_2 Bn), 4.70 (s, 1H, H-1′), 4.81−4.97 (m, 5H, H-1, CH_2 Bn), 5.61 (s, 1H, CHPh benzylidene), 6.83 (d, 2H, J = 8 Hz, H arom), 7.05−7.07 (m, 3H, H arom), 7.16−7.40 (m, 22H, H arom), 7.51−7.70 (m, 2H, H arom); ^{13}C NMR (100 MHz) δ = 52.3 (CO_2CH_3), 55.6 (OCH_3 *p*MP), 66.6 (C-5), 68.9 (C-6), 71.7 (C-2′), 71.7 (CH_2 Bn), 73.3 (CH_2 Bn), 75.2 (CH_2 Bn), 75.6 (C-4′), 75.8 (C-4, C-5), 77.7 (C-3), 79.1 (C-2), 82.0 (C-3′), 100.8 (CHPh benzylidene), 103.1 (C-1′, C-1), 114.5 (CH arom *p*MP), 118.8 (CH arom *p*MP), 126.3−128.8 (CH arom), 130.9 (C_q Ph), 151.4 (C_q Ph), 155.4 (C_q Ph), 168.7 (C=O CO_2Me); ^{13}C-

GATED NMR (100 MHz) δ = 100.8 ($J_{C\text{-}1,\ H\text{-}1}$ = 152 Hz, C-1), 103.2 ($J_{C\text{-}1',\ H\text{-}1'}$ = 155 Hz, C-1′); HRMS [M + Na]$^+$ calcd for $C_{55}H_{56}O_{13}Na$ 947.36131, found 947.36214.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-mannopyranoside)-α-D-glucopyranoside (28). Mannopyranoside **23** (95 mg, 0.15 mmol) was condensed with acceptor **25** according to the general procedure for glycosylations of thioglycosides, yielding disaccharide **28** (105 mg, 71%) as a mixture of anomers (α/*β*: 1/2): IR (neat) 729, 895, 1042, 1069, 1265, 1362, 1454, 1497, 2870 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.30 (s, 1.55 H, C-1α-OCH$_3$), 3.33 (s, 3H, C-1*β*-OCH$_3$), 3.36−3.47 (m, 5H), 3.51 (dd, 1H, *J* = 9.6 Hz, 3.2 Hz, H-3′*β*), 3.58−3.62 (m, 2H), 3.65−3.73 (m, 3H), 3.76−3.85 (m, 5H), 3.95−4.04 (m, 2H, H-4′, H-3), 4.11 (s, 1H, H-1′*β*), 4.16 (d, 1H, *J* = 10.8 Hz), 4.42−4.71 (m, 14H), 4.75−5.03 (m, 10H), 7.13−7.42 (m, 53 H); ^{13}C NMR (100 MHz) δ = 55.0 (OCH$_3$ *β*), 55.0 (OCH$_3$ α), 65.7, 68.2, 69.0, 69.7, 71.5, 71.8, 71.9, 72.0, 72.4, 73.6, 74.5, 74.7, 74.9, 75.0, 75.1, 75.6, 75.7, 75.9, 77.6, 79.5, 79.8, 79.9, 82.1, 82.2, 97.7 (C-1 *β*), 97.7 (C-1 α) 98.2 (C-1′α), 101.4 (C-1′ *β*), 127.3−128.4 (CH arom), 138.0 (C$_q$ Ph), 138.1 (C$_q$ Ph), 138.2 (C$_q$ Ph), 138.3 (C$_q$ Ph), 138.3 (C$_q$ Ph), 138.4 (C$_q$ Ph), 138.6 (C$_q$ Ph), 138.6 (C$_q$ Ph), 138.6 (C$_q$ Ph), 138.6 (C$_q$ Ph), 138.8 (C$_q$ Ph), 151.5 (C$_q$ Ph), 151.6 (C$_q$ Ph), 155.3 (C$_q$ Ph); ^{13}C-GATED NMR (100 MHz) δ = 98.2 (*J* = 164 Hz), 101.4 (*J* = 158 Hz); HRMS [M + NH$_4$]$^+$ calcd for $C_{62}H_{70}O_{11}N$ 1004.49434, found 1004.49572.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-mannopyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (31).** Mannopyranoside **23** (95 mg, 0.15 mmol) was glycosylated with acceptor **26** as described in the general procedure for glycosylations of thioglycosides, affording the title compound **31** (77 mg, 52%) as a mixture of anomers (α/*β*: 1/1.6): IR (neat) 729, 826, 899, 999, 1026, 1061, 1219, 1265, 1366, 1454, 1504, 2858 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.22 (dd, 1.6 H, *J* = 2.4 Hz, 9.2 Hz, H-3′*β*), 3.35−3.41 (m, 4H), 3.60 (d, 1H, *J* = 10.4 Hz), 3.67−3.73 (m, 4H), 3.77−3.84 (m, 13H), 3.88−3.910 (m, 1.6 H), 4.00−4.07 (m, 7H), 4.22−4.23 (m, 1.6 H), 4.27−4.40 (m, 10 H), 4.48−4.69 (m, 14 H), 4.76−4.79 (m, 3H), 4.82−4.88 (m, 3.5 H), 4.91−4.95 (m, 6H), 5.09 (s, 1H, H-1′α), 5.44 (s, 1H, CHPh α benzylidene), 5.58 (s, 1.6 H, CHPh *β* benzylidene), 6.80−6.83 (m, 4H, CH arom *p*MP), 7.01−7.40 (m, 27 H, 2 H arom Ph), 7.48−7.49 (m, 1H, H arom Ph), 7.53−7.58 (m, 1H, H arom Ph); ^{13}C NMR (100 MHz) δ = 55.6 (OCH$_3$ *p*MP), 66.2, 66.7, 68.1, 68.9, 69.0, 69.2, 69.9, 71.0, 71.3, 71.5, 72.1, 72.3, 72.7, 72.8, 73.3, 73.4, 74.3, 74.8, 74.9, 75.2, 75.7, 75.7, 76.1, 78.0, 78.9, 79.9, 82.8, 93.3 (C-1′α), 100.8 (CHPh benzylidene *β*), 101.0 (CHPh benzylidene α), 102.8 (C-1′ *β*), 103.1 (C-1), 114.4 (CH arom *p*MP), 114.5 (CH arom *p*MP), 118.8 (CH arom *p*MP), 118.9 (CH arom *p*MP), 126.3−139.0 (CH arom), 130.9 (CH arom), 137.7 (C$_q$ Ph), 138.0 (C$_q$ Ph), 138.0 (C$_q$ Ph), 138.1 (C$_q$ Ph), 138.2 (C$_q$ Ph), 138.2(C$_q$ Ph), 138.3 (C$_q$ Ph), 138.4 (C$_q$ Ph), 138.5 (C$_q$ Ph), 138.6 (C$_q$ Ph), 138.8 (C$_q$ Ph), 151.5 (C$_q$ Ph), 151.6 (C$_q$ Ph), 155.3 (C$_q$ Ph); ^{13}C-GATED NMR (100 MHz) δ = 93.3 (*J* = 171 Hz, C-1′α), 102.8 (*J* = 156 Hz, C-1′*β*); HRMS [M + NH$_4$]$^+$ calcd for $C_{61}H_{66}O_{12}N$ 1004.45795, found 1004.45932.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-benzyl-α/*β*-D-rhamnopyranoside)-α-D-glucopyranoside (29). Rhamnopyranoside **24** (79 mg, 0.15 mmol) was glycosylated with acceptor **25** as described in the general procedure for glycosylations of thioglycosides, affording the title compound **29** (94 mg, 71%) as a mixture of anomers (α/*β*: 1/1.7): IR (neat) 732, 694, 1006, 1026, 1053, 1068, 1362, 1454, 2866 cm^{-1}; ^{1}H NMR (400 MHz) δ = 1.25 (d, 1.75 H, *J* = 4.8 Hz, C-6 α), 1.35 (d, 3 H, *J* = 6 Hz, C-6 *β*);^{13}C NMR (100 MHz) δ = 17.8 (C-6′ *β*), 17.9 (C-6 α′), 98.2(C-1′ α), 101.2 (C-1′ *β*); ^{13}C-GATED NMR (100 MHz) δ = 98.2 ($J_{C\text{-}1',\ H\text{-}1'}$ = 168 Hz, C-1′ α), 103.2 ($J_{C\text{-}1',\ H\text{-}1'}$ = 153 Hz, C-1′ *β*); HRMS [M + Na]$^+$ calcd for $C_{55}H_{60}O_{10}Na$ 903.4079, found 903.4077.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(2,3,4-tri-*O*-benzyl-α/*β*-D-rhamnopyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (32).** Rhamnopyranoside **24** (79 mg, 0.15 mmol) was glycosylated with acceptor **26** as described in the general procedure for glycosylations of thioglycosides, affording the title compound **32** (86 mg, 65%) as a mixture of anomers (α/*β*: 1/1): IR (neat) 694, 732, 995, 1026, 1061, 1218, 1454, 1504, 2341, 2873 cm^{-1}; ^{1}H NMR (400 MHz) δ = 1.26 (d, 3H, *J* = 4.8 Hz, C-6), 1.35 (d, 3H, *J* = 6 Hz, C-6); ^{13}C NMR (100 MHz) δ = 17.9 (C-6′ *β*), 18.0 (C-6′ α), 93.4 (C-1′ α), 102.5 (C-1′ *β*); ^{13}C-GATED NMR (100 MHz) δ = 97.7 ($J_{C\text{-}1,\ H\text{-}1}$ = 166 Hz, C-1′ α), 103.2 ($J_{C\text{-}1',\ H\text{-}1'}$ = 154 Hz, C-1′ *β*); HRMS [M + Na]$^+$ calcd for $C_{54}H_{56}O_{11}Na$ 903.3715, found 903.3712.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-L-gulopyranosyluronate)-α-D-glucopyranoside (39). Guluronic acid **36** (114 mg, 0.20 mmol) was glycosylated with glucoside **25** (139 mg, 0.30 mmol) as described in the general procedure for glycosylations of thioglycuronates, yielding **39** (115 mg, 73%) as a mixture of anomers (α/*β*: 1/0.33): IR (neat) 731, 808, 910, 1026, 1047, 1070, 1207, 1265, 1304, 1358, 1439, 1454, 1497, 1732, 1765, 2876, 3030 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.28 (s, 3H, CH$_3$ OMe), 3.33 (s, 1H, CH$_3$ OMe), 3.39 (dd, 1H, *J* = 3.6 Hz, 9.6 Hz), 3.49−3.53 (m, 0.3H), 3.59 (s, 3H, CH$_3$ COOMe), 3.61−3.65 (m, 1.3H), 3.66 (s, 1H, CH$_3$ COOMe), 3.68−3.73 (m, 1H), 3.75−3.77 (m, 2.2H), 3.80−3.82 (m, 1.6H), 3.85−3.87 (m, 1.3H), 3.90−4.02 (m, 3.6H), 4.22−4.99 (m, 18 H), 5.16 (d, 1H, *J* = 4 Hz, H-1′); ^{13}C NMR (100 MHz) δ = 51.9 (CH$_3$ COOMe), 51.9 (CH$_3$ COOMe), 54.8 (CH$_3$ OMe), 54.9 (CH$_3$ OMe), 67.4, 67.6, 68.2, 70.1, 70.3, 71.2, 72.5, 72.6, 72.9, 72.9, 73.0, 73.1, 73.2, 73.2, 73.4, 74.6, 74.7, 74.8, 75.5, 75.5, 75.7, 76.4, 76.9, 77.9, 78.1, 79.8, 80.0, 81.9, 82.0, 97.7 (C-1), 97.8 (C-1), 98.0 (C-1′ α), 101.0 (C-1′ *β*), 127.3−128.3 (CH arom), 137.4−138.8 (C$_q$ arom), 169.3 (C$_q$ COOMe), 170.0 (C$_q$ COOMe); HRMS [M + Na]$^+$ calcd for $C_{56}H_{60}O_{12}Na$ 947.3977, found 947.3985.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-L-gulopyranosyluronate)-4,6-benzylidene-*β*-D-galactopyranoside (42).** Guluronic acid **36** (114 mg, 0.20 mmol) was glycosylated with galactoside **26** (139 mg, 0.30 mmol) as described in the general procedure for glycosylations of thioglycuronates, yielding **42** (124 mg, 79%) as a mixture of anomers (α/*β*: 1/0.1): IR (neat) 731, 826, 908, 997, 1026 1065, 1078, 1175, 1217, 1265, 1306, 1366, 1439, 1454, 1506, 175, 2870, 3030 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.43 (s, 3H, CH$_3$ COOMe), 3.45 (bs, 1H), 3.72 (s, 3H, CH$_3$ *p*MP), 3.88−3.90 (m, 1H), 3.93−3.99 (m, 2H), 4.01−4.02 (m, 2H), 4.05−4.08 (m, 1H, H-6), 4.30−4.39 (m, 5H), 4.46 (m, 2H), 4.55−4.68 (m, 4H), 4.84−4.90 (m, 2H), 4.97 (d, 1H, *J* = 1.6 Hz), 5.39 (d, 1H, *J* = 3.6 Hz, H-1′), 5.56 (s, 1H, CHPh), 6.75−7.56 (m, 29H); ^{13}C NMR (100 MHz) δ = 51.6 (CH$_3$ COOMe), 55.5 (CH$_3$ OMe), 66.3, 67.6, 69.2, 70.9, 71.6, 72.4, 72.6, 73.3, 73.4, 74.6, 74.9, 76.3, 77.4, 92.9 (C-1′), 100.8 (CHPh), 103.0 (C-1), 114.3 (CH arom *p*MP), 118.9 (CH arom *p*MP), 126.2−128.7 (CH arom), 137.5−138.6 (C$_q$ arom), 151.6 (C$_q$ *p*MP), 155.1 (C$_q$ *p*MP), 169.7 (C$_q$ COOMe); HRMS [M + Na]$^+$ calcd for $C_{55}H_{56}O_{13}Na$ 947.36131, found 947.36184.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α/*β*-L-gulopyranoside)-α-D-glucopyranoside (40). Gulopyranoside **37** (127 mg, 0.20 mmol) was condensed with acceptor **25** according to the general procedure for glycosylations of thioglycosides, yielding disaccharide **40** (150 mg, 76%) as a mixture of anomers (α/*β*: 1/0.1): IR (neat) 733, 820, 908, 1026, 1047, 1069, 1194, 1207, 1310, 1327, 1360, 1454, 1497, 2870, 3030, 3063 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.28 (s, 3H, OMe), 3.41 (dd, 1H, *J* = 3.6 Hz, 9.6 Hz), 3.54 (m, 2H), 3.60 (bs, 1H), 3.66−3.78 (m, 3H), 3.81−3.82 (m, 2H), 3.95 (t, 1H, *J* = 9.2 Hz), 4.00 (dd, 1H, *J* = 4.0 Hz, 11.6 Hz), 4.34−4.56 (m, 8H), 4.63−4.71 (m, 4H), 4.75 (d, 1 H, *J* = 12 Hz, CH$_2$ Bn), 4.79 (d, 1 H, *J* = 10.8 Hz, CH$_2$ Bn), 4.93 (d, 1 H, *J* = 10.8 Hz, CH$_2$ Bn), 5.06 (bs, 1H, H-1′), 7.12−7.36 (m, 35H, H arom); ^{13}C NMR (100 MHz) δ = 54.9 (OMe), 65.7, 66.9, 68.7, 70.4, 70.9, 72.7, 73.1, 73.2, 73.2, 73.9, 74.8, 75.5, 75.6, 77.9, 70.1, 82.0, 97.7 (C-1 or C-1′), 97.9 (C-1 or C-1′),127.2−128.9 (CH arom), 137.9−139.0 (C$_q$ arom); HRMS [M + NH$_4$]$^+$ calcd for $C_{62}H_{70}O_{11}N$ 1004.49434, found 1004.49581.

***p*-Methoxyphenyl 2-*O*-Benzyl-(2,3,4,6-tetra-*O*-benzyl-α/*β*-L-gulopyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (43).** Gulopyranoside **37** (127 mg, 0.20 mmol) was glycosylated with acceptor **26** according to the general procedure for glycosylations of thioglycosides, yielding disaccharide **43** (138 mg, 70%) as a mixture of anomers (α/*β*: 1/0.12): IR (neat) 731, 824, 872, 910, 997, 1026, 1065, 1080, 1173, 1217, 1265, 1308, 1367, 1454, 1506, 2866, 3030 cm^{-1}; ^1H NMR (400 MHz) $\delta = 3.30$ (s, 1H), 3.37 (dd, 1H, $J = 6$ Hz, 10 Hz), 3.53 (bs, 1H), 3.61 (dd, 1H, $J = 7.2$ Hz, 10.4 Hz), 3.74 (s, 3H, CH_3 *p*MP), 3.88−3.92 (m, 2H), 4.00−4.08 (m, 3H), 4.22 (d, 1 H, $J = 12$ Hz, CH_2 Bn), 4.28−4.46 (m, 8H), 4.57−4.64 (m, 3H), 4.68 (d, 1 H, $J = 10.8$ Hz, CH_2 Bn), 4.77 (m, 2H), 4.86 (d, 1 H, $J = 10.8$ Hz, CH_2 Bn), 5.32 (d, 1 H, $J = 3.2$ Hz, H-1′), 5.51 (s, 1H, CHPh), 6.77−7.54 (m, 34H, H arom); ^{13}C NMR (100 MHz) $\delta = 55.5$ (OCH_3 *p*MP), 65.2, 66.3, 69.1, 69.3, 70.6, 71.3, 72.4, 72.5, 72.6, 73.3, 73.7, 74.6, 74.7, 76.0, 76.3, 91.9 (C-1′), 101.0 (CHPh), 102.9 (C-1), 114.3 (CH arom *p*MP), 118.9 (CH arom *p*MP), 126.3−128.8 (CH arom), 137.7−139.1 (C_q arom), 151.8 (C_q *p*MP), 155.1(C_q *p*MP); HRMS $[M + Na]^+$ calcd for $C_{61}H_{62}O_{12}Na$ 1009.41335, found 1009.41396.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-benzyl-α/*β*-D-antiaropyranoside)-α-D-glucopyranoside (41). Antiaromatic pyranoside **38** (79 mg, 0.15 mmol) was glycosylated with acceptor **25** as described in the general procedure for glycosylations of thioglycosides, affording the title compound **41** (89 mg, 67%) as a mixture of anomers (α/*β*: 1/0.08): IR (neat) 633, 694, 1026, 1069, 1358, 2341, 2870, 3028 cm^{-1}; ^1H NMR (400 MHz) $\delta = 1.07$ (d, 3H, $J = 6.4$ Hz, H-6′), 3.29 (s, 3H, CH_3 OMe), 3.31−3.33 (m, 1H), 3.43 (dd, 1H, $J = 3.6$ Hz, 9.6 Hz), 3.66−3.78 (m, 3H), 3.81−3.82 (m 2H), 3.93−4.00 (m 2H), 4.30 (dq, 1H, $J = 1.2$ Hz, 6.4 Hz, H-5′), 4.39 (d, 1H, $J = 12$ Hz, CH_2 Bn), 4.47−4.81 (m, 12H), 4.93 (d, 1H, $J = 10.8$ Hz, CH_2 Bn), 5.00 (d, 1H, $J = 2.8$ Hz, H-1′), 7.13−7.38 (m, 30H, H arom); ^{13}C NMR (100 MHz) $\delta = 15.6$ (C-6′), 54.9 (CH_3 OMe), 62.7 (C-5′), 66.9 (C-6), 70.1, 71.1, 72.7, 73.1, 73.3, 73.5, 73.9, 74.8, 75.5, 77.7, 77.9, 80.1, 82.0, 97.8 (C-1′), 97.9 (C-1), 127.0−128.8 (CH arom), 137.9−139.0 (C_q arom); HRMS $[M + Na]^+$ calcd for $C_{55}H_{60}O_{10}Na$ 903.4079, found 903.4073.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(2,3,4-tri-*O*-benzyl-α/*β*-D-antiapyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (44).** Antiaromatic pyranoside **38** (79 mg, 0.15 mmol) was glycosylated with acceptor **26** as described in the general procedure for glycosylations of thioglycosides, affording the title compound **44** (93 mg, 70%) as a mixture of anomers (α/*β*: 1/0.15): IR (neat) 694, 733, 995, 1026, 1060, 1219, 1454, 1504, 2341, 2870 cm^{-1}; ^1H NMR (400 MHz) $\delta = 0.91$ (d, 3H, $J = 6.8$ Hz, H-6′), 3.24 (d, 1H, $J = 2.4$ Hz), 3.45 (s, 1H), 3.73 (s, 3H, CH_3 *p*MP), 3.87−3.92 (m, 2H), 3.96 (dd, 1H, $J = 3.6$ Hz, 10 Hz), 4.03−4.07 (m, 2H), 4.32−4.39 (m, 4H), 4.45 (q, 1H, $J = 6$ Hz, H-5′), 4.49 (d, 1H, $J = 12$ Hz, CH_2 Bn), 4.57 (d, 1H, $J = 12$ Hz, CH_2 Bn), 4.62 (d, 1H, $J = 11.6$ Hz, CH_2 Bn), 4.69 (d, 1H, $J = 10.8$ Hz, CH_2 Bn), 4.73 (d, 1H, $J = 10.8$ Hz, CH_2 Bn), 4.85 (d, 1H, $J = 11.6$ Hz, CH_2 Bn), 4.90 (d, 1H, $J = 7.6$ Hz, H-1), 5.24 (d, 1H, $J = 3.6$ Hz, H-1′), 5.52 (s, 1H, CHPh), 6.76−7.54 (m, 29H, H arom); ^{13}C NMR (100 MHz) $\delta = 55.5$ (CH_3 *p*MP), 65.2 (C-5′), 66.3, 69.1, 69.3, 70.6, 71.3, 72.4, 72.5, 72.6, 73.3, 73.7, 74.6, 74.7, 76.0, 76.3, 91.9 (C-1′), 101.0 (CHPh), 102.9 (C-1), 114.3 (CH *p*MP), 118.9 (CH *p*MP), 126.3−128.8 (CH arom), 137.7−139.1 (C_q arom), 151.8 (C_q *p*MP), 155.1 (C_q *p*MP); HRMS $[M + Na]^+$ calcd for $C_{54}H_{56}O_{11}Na$ 903.3715, found 903.3712.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-D-glucopyranosyluronate)-α-D-glucopyranoside (50). Donor **48** (114 mg, 0.2 mmol) was condensed with acceptor **25** following the general procedure for glycosylations of thioglycuronates, giving disaccharide **50** (0.14 mmol, 68%) as a mixture of anomers (α/*β*: 1/1.4): IR (neat) 737, 914, 1030, 1072, 1088, 1157, 1138 1200, 1285, 1358, 1454, 1497, 1751, 2912, 3032, 3063 cm^{-1}; ^1H NMR (400 MHz) $\delta = 3.35$ (s, 3H, CO_2CH_3 *β*), 3.37 (s, 1.9 H, CO_2CH_3 α), 3.42−3.60 (m, 1.6 H), 3.48−3.56 (m, 3.5 H), 3.57−3.65 (m, 5 H), 3.67 (s, 3H, OCH_3 *β*), 3.67−3.86 (m, 6H), 3.94−4.01 (m, 2.5 H), 4.12 (dd, 1H, $J = 1.6$ Hz, 10.8 Hz), 4.29 (d, 0.7 H, $J = 10.0$ Hz), 4.38 (d, 1.1 H, $J = 7.6$ Hz, H-1′*β*), 4.50 (d, $J = 11.6$ Hz), 4.55−4.60 (m, 4.6 H), 4.72−4.83 (m, 4.2 H), 4.72−4.83 (m, 8.9 H), 4.88−4.98 (m, 6 H), 7.17−7.35 (m, 55H, H arom); ^{13}C NMR (100 MHz) $\delta = 52.3$ (CO_2CH_3 α or *β*), 52.3 (CO_2CH_3 α or *β*), 66.5 (C-6 α or *β*), 68.8 (C-6 α or *β*), 69.7 (OCH_3 α or *β*), 70.3 (OCH_3 α or *β*), 72.5, 73.2, 73.3, 74.4, 74.8, 74.8, 74.9, 74.9, 75.5, 75.6, 75.6, 77.9, 79.1, 79.3, 79.5, 79.8, 78.0, 80.8, 81.5, 81.8, 82.0, 83.8, 97.7 (C-1′α), 97.9 (C-1 α and *β*), 104.0 (C-1′*β*), 127.5−128.4 (CH arom Ph), 137.8 (C_q Ph), 138.0 (C_q Ph), 138.1 (C_q Ph), 138.2 (C_q Ph), 138.2 (C_q Ph), 138.7 (C_q Ph), 168.7 (C═O CO_2Me); HRMS $[M + Na]^+$ calcd for $C_{56}H_{60}O_{12}Na$: 947.39770, found 947.39850.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-D-glucopyranosyluronate)-4,6-benzylidene-*β*-D-galactopyranoside (52).** Donor **48** (114 mg, 0.2 mmol) was glycosylated with acceptor **26** as described as in the general procedure for glycosylations of thioglycuronates, yielding disaccharide **52** (159 mg, 86%) as a mixture of anomers (α/*β*: 1/0.6): IR (neat) 737, 826, 914, 991, 1030, 1088, 1180, 1219, 1288, 1366, 1454, 1508, 1747, 2203, 2870, 3032 cm^{-1}; ^1H NMR (400 MHz) $\delta = 3.49$ (s, 1.2 H), 3.53 (s, 0.6 H), 3.54−3.67 (m, 4.6 H), 3.70−3.73 (m, 3.2 H), 3.75−3.83 (m, 6.7 H), 3.85−3.87 (d, $J = 6.8$ Hz), 3.97 (dd, 1.5 H, $J = 3.6$ Hz, $J = 10$ Hz, H-3′α), 4.05 (dd, 0.7 H, $J = 3.6$ Hz, $J = 10$ Hz, H-3′*β*), 4.10−4.25 (m, 5H), 4.37−4.42 (m, 3.4 H), 4.80−4.88 (m, 3.6 H), 4.91−5.10 (m, 2.5 H), 5.13 (d, 0.6 H, $J = 7.3$ Hz, H-1′*β*), 5.29 (d, 1H, $J = 3.6$ Hz, H-1′α), 5.60 (s, 1H, CHPh benzylidene α), 5.67 (s, 0.6 H, CHPh benzylidene *β*), 6.85−6.88 (m, 3.7 H, H arom *p*MP), 7.09−7.40 (m, 47 H, H arom), 7.45−7.48 (m, 2.4 H, H arom), 7.62−7.64 (m, 3.6 H, H arom); ^{13}C NMR (100 MHz) $\delta = 52.2$ (CO_2CH_3 α), 52.3 (CO_2CH_3 *β*), 55.5 (OCH_3 *p*MP), 66.2, 66.5, 68.8, 69.2, 70.2, 71.2, 72.1, 74.1, 74.4, 74.7, 74.9, 75.0, 74.4, 75.0, 75.5, 75.7, 75.9, 76.5, 78.6, 78.8, 79.2, 79.7, 80.9, 81.0, 83.5, 92.7 (C-1′α), 100.6, 101.3, 103.0 (C-1 α and *β*), 103.1, 103.4 (C-1′α), 114.4 (CH arom *p*MP), 118.8 (CH arom *p*MP), 126.2−129.0 (CH arom Ph), 137.5 (C_q Ph), 137.7 (C_q Ph), 137.8 (C_q Ph), 138.0 (C_q Ph), 138.0 (C_q Ph), 138.1 (C_q Ph), 138.2 (C_q Ph), 138.3 (C_q Ph), 138.4 (C_q Ph), 151.4 (C_q Ph), 151.5 (C_q Ph), 155.2 (C_q Ph), 155.3 (C_q Ph), 169.1 (C═O CO_2Me *β*), 170.3 (C═O CO_2Me α); HRMS $[M + Na]^+$ calcd for $C_{55}H_{56}O_{13}Na$ 947.36131, found 947.36208.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-glucospyranoside)-α-D-glucopyranoside (51). Donor **49** (127 mg, 0.2 mmol) was glycosylated with acceptor **25** in the same way as described in the general procedure for glycosylations of thioglycosides, affording the title compound **51** (148 mg, 75%) as a mixture of anomers (α/*β*: 1/1.4): IR (neat) 737, 826, 910, 1042, 1069, 1157, 1207, 1265, 1327, 1362, 1454, 1497, 1585, 2870, 2905, 3032, 3063 cm^{-1}; ^1H NMR (400 MHz) $\delta = 3.29$ (s, 5.1 H, OCH_3), 3.41−3.44 (m, 1 H), 3.47−3.52 (m, 5.4 H, OCH_3), 3.54−3.63 (m, 4H), 3.71−4.00 (m, 10 H), 4.14 (d, 1H, $J = 10$ Hz), 4.31 (d, 1 H, $J = 7.6$ Hz, H-1′*β*), 4.34−4.44 (m, 3.6 H), 4.50−4.63 (m, 6.6 H), 4.75−4.86 (m, 6.5 H), 4.90−4.97 (m, 4H), 5.00 (d, 1.4 H, $J = 3.2$ Hz, H-1′α), 7.15−7.32 (m, 35 H, 35 × H arom); ^{13}C NMR (100 MHz) $\delta = 55.0$ (OCH_3 α), 55.1 (OCH_3 *β*), 66.3, 68.5, 68.6, 68.9, 69.3, 69.8, 70.2, 72.4, 72.7, 72.8, 73.2, 73.3, 73.4, 73.5, 74.5, 74.7, 74.7, 74.9, 75.0, 75.1, 75.6, 75.6, 76.5, 77.9, 78.1, 78.2, 78.2, 78.8, 80.1, 81.9, 82.0, 82.2, 97.8 (C-1′α), 104.2 (C-1′*β*), 127.3- 128.3 (CH arom), 137.8 (C_q Ph), 138.0 (C_q Ph), 138.1 (C_q Ph), 138.1 (C_q Ph), 138.3 (C_q Ph), 138.4 (C_q Ph), 138.7 (C_q Ph), 138.7 (C_q Ph), 138.8 (C_q Ph); HRMS $[M + NH_4]^+$ calcd for $C_{62}H_{70}O_{11}N$: 1004.49434, found 1004.49587.

***p*-Methoxyphenyl-2-*O*-Benzyl-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-glucospyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (53).** Donor **49** (127 mg, 0.2 mmol) was condensed with acceptor **26** according to the general procedure for glycosylations of thioglycosides, delivering disaccharide **53** (176 mg, 89%) as a mixture of anomers (α/*β*: 1/1.7): IR (neat) 737, 826, 1003, 1030, 1065, 1219, 1362, 1454, 1504, 2866, 3032 cm^{-1}; ^1H NMR (400 MHz) $\delta = 3.37$−3.41 (m, 3H), 3.48−3.59 (m, 5H), 3.61−3.69 (m, 3.8 H),

3.73 (s, 3H, OCH_3 β), 3.74 (s, 1.8 H, OCH_3 α), 3.90 (dd, 0.8 H, J = 3.6 Hz, 10.0 Hz), 3.97−4.01 (m, 2.2 H), 4.03−4.06 (d, 0.8 H, J = 8.0 Hz), 4.10−4.19 (m, 3.3 H), 4.26−4.35 (m, 4.3 H), 4.44−4.51 (m, 4H), 4.54−4.60 (m, 3.6 H), 4.78−4.89 (m, 8.9 H), 4.95−5.04 (m, 4.8 H), 5.21 (d, 1H, J = 3.6 Hz, H-1′α), 5.55 (s, 0.6 H, CHPh benzylidene α), 5.60 (s, 1H, CHPh benzylidene β), 6.79−6.82 (m, 3.7 H, H arom *p*MP), 7.03−7.36 (m, 60 H, H arom), 7.60−7.62 (m, 3.6 H, H arom); ^{13}C NMR (100 MHz) δ = 55.5 (OCH_3 *p*MP β), 55.5 (OCH_3 *p*MP α), 66.3, 66.6, 68.3, 68.8, 68.9, 69.8, 71.2, 71.8, 73.0, 74.1 (α), 74.4 (CH_2Ph α), 74.4 (CH_2 Bn β), 74.4 (CH_2 Bn β), 74.8 (β), 74.9 (CH_2 Bn α), 74.9 (CH_2 Bn β), 75.5 (CH_2 Bn β), 75.6 (CH_2 Bn α), 75.6 (CH_2 Bn α), 75.9 (β), 76.2 (β), 76.5 (α), 77.5 (α), 77.7 (β), 78.7 (β), 79.2 (α), 81.6 (β), 81.9 (α), 84.4 (β), 92.0 (1′ α), 100.6 (CHPh benzylidene), 101.4 (CHPh benzylidene), 103.2 (C-1 β), 103.2 (C-1 α), 103.5 (C-1′ β); HRMS $[M + Na]^+$ calcd for $C_{61}H_{62}O_{12}Na$ 1009.41335, found 1009.41410.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-D-allopyranosyluronate)-α-D-glucopyranoside (56). Alluronic acid **54** (86 mg, 0.15 mmol) was condensed with glucoside **25** (105 mg, 0.225 mmol, 1.5 equiv) following the general procedure for glycosylations of thioglycuronates, yielding **56** (126 mg, 76%) as a mixture of anomers (α/β: 1/0.4): IR (neat) 737, 914, 1026, 1072, 1088, 1161, 1204, 1281, 1327, 1362, 1454, 1497 1747, 2905, 3032, 3063 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.26 (s, 3H, C-1-$OCH_3\alpha$), 3.30 (s, 1.1 H, C-1-OCH_3 β), 3.37 (dd, 1H, J = 3.6 Hz, 9.6 Hz), 3.45−3.53 (m, 2H), 3.56 (dd, 1H, J = 2.4 Hz, 9.6 Hz), 3.67−3.68 (m, 4H), 3.70 (s, 3H, CO_2CH_3 α), 3.91−3.99 (m, 2H), 4.06−4.17 (m, 0.4 H), 4.15 (m, 1H), 4.38 (d, 1H, J = 12.0 Hz, CH_2 Bn), 4.42−4.70 (m, 10H), 4.73−4.98 (m, 3H), 5.08 (d, 1H, J = 4.0 Hz, H-1α), 7.10−7.37 (m, 45H, 4 H arom); ^{13}C NMR (100 MHz) δ = 52.1 (OCH_3 β), 52.1 (OCH_3 α), 54.9 (CO_2CH_3 α), 55.1 (CO_2CH_3 β), 67.1 (α), 67.2 (C-6 α), 68.5 (C-6 β), 69.9 (β), 70.4 (Cα), 70.8 (CH_2 Bn α), 71.2 (CH_2 Bn α), 71.9 (CH_2 Bn β), 72.5 (β), 72.9 (CH_2 Bn β), 73.2 (β), 73.3 (CH_2 Bn β), 74.0 (CH_2 Bn β), 74.5 (β), 75.0 (CH_2 Bn α, 76.0 (α), 76.9 (α), 77.2 (β), 77.8 (α), 77.9 (β), 78.3 (β), 79.7 (β), 80.1 (α), 82.0 (α), 97.8 (C-1′α), 97.9 (C-1 α), 101.3 (C-1′ β); ^{13}C GATED NMR (100 MHz) δ = 97.8 ($J_{C\text{-}1'\alpha,\ H\text{-}1'\alpha}$ = 167 Hz, C-1′α), 97.9 ($J_{C\text{-}1\alpha,\ H\text{-}1\alpha}$ = 166 Hz, C-1α); HRMS $[M + NH_4]^+$ calcd for $C_{56}H_{64}O_{12}N$ 942.44230, found 942.44368.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-allopyranosyluronate)-4,6-benzylidene-*β*-D-galactopyranoside (58).** Alluronic acid **54** (86 mg, 0.15 mmol) was glycosylated with galactoside **26** (105 mg, 0.225 mmol, 1.5 equiv) as described in the general procedure for glycosylations of thioglycuronates giving α-linked disaccharide **58** (72 mg, 52%) as transparent oil: $[\alpha]^{22}_D$ = +26.3 (c = 0.2, DCM); IR (neat) 729, 826, 895, 999,1030, 1061, 1096, 1180, 1215, 1265, 1366, 1454, 1508, 1744, 2866, 3055 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.46 (s, 1H, H-5), 3.54 (s, 3H, CO_2CH_3), 3.58 (t, 1H, J = 3.6 Hz, H-2′), 3.61 (dd, 1H, J = 9.6 Hz, 2.4 Hz, H-4′), 3.75 (s, 3H, OCH_3 *p*MP), 3.99−4.09 (m, 3H, H-2, H-4, H-6), 4.27 (m, 1H, H-3′), 4.34−4.40 (m, H-3, H-6, CH_2 Bn), 5.52 (d, 1H, J = 11.6 Hz, CH_2 Bn), 4.56 (d, 1H, J = 10.4 Hz, CH_2 Bn), 4.61 (d, 1H, J = 11.2 Hz, CH_2 Bn), 4.71 (d, 1H, J = 10.4 Hz, CH_2 Bn), 4.80 (d, 1H, J = 11.6 Hz, CH_2 Bn), 4.89−4.95 (m, 3H, H-5′, H-1, CH_2 Bn), 5.33 (d, 1H, J = 4.0 Hz, H-1′), 5.55 (s, 1H, CHPh benzylidene), 6.77 (d, 2H, J = 9.2 Hz, H arom), 7.00 (d, 2H, J = 6.8 Hz, H arom), 7.02−7.30 (m, 23H, 2 H arom), 7.51−7.58 (m, 2H, H arom); ^{13}C NMR (100 MHz) δ = 52.1 (CO_2CH_3), 55.6 (OCH_3 *p*MP), 66.3 (C-5), 67.0 (C-5′), 69.3 (C-6), 70.8 (CH_2 Bn), 71.0 (CH_2 Bn), 71.5 (C-3), 73.2 (C-3′), 74.1 (CH_2 Bn), 75.0 (CH_2 Bn), 75.4 (C-2), 76.0 (C-4), 76.3 (C-2′), 77.0 (C-4′), 92.5 (C-1′), 101.0 (CHPh benzylidene), 102.8 (C-1), 114.3 (CH arom *p*MP), 118.8 (CH arom *p*MP), 126.3, 137.1−128.9 (CH arom), 137.7−139.0 (C_q arom), 151.7 (C_q *p*MP), 155.1 (C_q *p*MP), 171.5 (C═O CO_2Me); ^{13}C-GATED NMR (100 MHz) δ = 92.4 ($J_{C\text{-}1',\ H\text{-}1'}$ = 164 Hz, C-1′), 102.7 ($J_{C\text{-}1,\ H\text{-}1}$ = 160 Hz, C-1); HRMS $[M + NH_4]^+$ calcd for $C_{55}H_{60}O_{13}N$ 942.40592, found 942.40719.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-allopyranoside)-α-D-glucopyranoside (57). Allopyranoside **55** (95 mg, 0.15 mmol) was condensed with acceptor **25** according to the general procedure for glysolylations of thioglycosides, yielding disaccharide **57** (136 mg, 92%) as a mixture of anomers (α/β: 1/0.5): IR (neat) 729, 910, 1026, 1049, 1072, 1207, 1265, 1327, 1362, 1454, 1497, 2870, 3032 cm^{-1}; ^{1}H NMR (600 MHz) δ = 3.26 (s, 3H), 3.31−3.33 (m, 2H), 3.39 (dd, 0.5 H, J = 3.6 Hz, 9.6 Hz, H-2α), 3.43−3.46 (m, 1.6 H), 3.51 (dd, 1H, J = 3.6 Hz, 9.6 Hz, H-2β), 3.55−3.60 (m, 2.5 H), 3.65−3.74 (m, 6.3 H), 3.93 (t, 1H, J = 9.0 Hz), 3.97−4.00 (m, 1.5 H), 4.11 (m, 0.4 H), 4.17−4.18 (m, 1.5 H), 4.23−4.25 (m, 1H), 4.37 (d, 1H, J = 7.6 Hz), 4.37 (d, 0.5 H, J = 7.6 Hz), 4.44 (d, 1H, J = 8.0 Hz), 4.48−4.69 (m, 13 H), 4.73 (d, 0.5 H), 4.77−4.85 (m, 4.3 H), 4.90−4.97 (m, 3.2 H), 5.1 (d, 1H, J = 3.0 Hz, H-1′ α), 7.07−7.36 (m, 53H, 5 H arom); ^{13}C NMR (125 MHz) δ = 54.9 (OCH_3 β), 55.1 (OCH_3 α), 66.2 (α), 66.6, 68.1, 68.6, 69.4, 69.9, 70.4, 70.6, 70.8 (CH_2 Bn α), 71.5 (CH_2Ph β), 72.6 (CH_2 Bn β), 72.8 (α), 73.3 (CH_2 Bn β), 73.3 (CH_2 Bn α), 73.4 (CH_2 Bn α), 73.5 (CH_2 Bn α), 74.0 (CH_2 Bn α), 74.4 (α), 74.5 (CH_2 Bn α), 74.6 (β), 74.8 (CH_2 Bn α), 75.0 (CH_2 Bn β), 75.5 (CH_2 Bn α), 75.6 (β), 75.6 (α), 75.6 (CH_2 Bn β), 76.7 (β), 77.8 (β), 77.8 (α), 79.0 (β), 79.6 (β), 80.1 (α), 82.0 (α), 97.6 (C-1′α), 97.9 (C-1 α), 98.0 (C-1 β), 101.1 (C-1′β), 127.0−128.4 (CH arom), 137.8 (C_q Ph), 138.1 (C_q Ph), 138.1 (C_q Ph), 138.3 (C_q Ph), 138.3 (C_q Ph), 138.4 (C_q Ph), 138.5 (C_q Ph), 138.7 (C_q Ph), 138.8 (C_q Ph), 138.9 (C_q Ph), 139.0 (C_q Ph), 137.4 (C_q Ph); ^{13}C-GATED NMR (100 MHz) δ = 97.6 ($J_{C\text{-}1'\alpha,\ H\text{-}1'\alpha}$ = 167 Hz), 101.1 ($J_{C\text{-}1'\beta,\ H\text{-}1'\beta}$ = 162 Hz); HRMS $[M + NH_4]^+$ calcd for $C_{62}H_{70}O_{11}N$ 1004.49434, found 1004.49594.

***p*-Methoxyphenyl 2-*O*-Benzyl-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-allopyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (59).** Allopyranoside **55** (95 mg, 0.15 mmol) was condensed with acceptor **26** according to the general procedure for glycosylations of thioglycosides, affording disaccharide **59** (105 mg, 71%) as a mixture of anomers (α/β: 1/0.56). α Isomer: $[\alpha]^{22}_D$ = +11.3 (c = 0.6, DCM); IR (neat) 729, 826, 907, 999, 1026, 1061, 1096, 1146, 1180, 1219, 1265 1366, 1393, 1454, 1504, 2866, 3032 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.40−3.45 (m, 3H, H-5, H-6′, H-6′), 3.56−3.59 (m, 2H, H-2′, H-4′), 3.76 (s, 3H, OCH_3 *p*MP), 3.98−4.00 (m, 2H, H-3, H-2), 4.08 (d, 1H, J = 11.2 Hz, CH_2 Bn), 4.32−4.59 (m, 10H, H-4, H-3′, H-5′, CH_2 Bn), 4.66 (d, 1H, J = 11.6 Hz, CH_2 Bn), 4.78−4.83 (m, 2H, H-1, CH_2 Bn), 4.99 (d, 1H, J = 11.6 Hz, CH_2 Bn), 5.30 (d, 1H, J = 4.0 Hz, H-1′), 5.57 (s, 1H, CHPh benzylidene), 6.78−6.80 (m, 2H, H arom), 7.02−7.36 (m, 28H, H arom), 7.44−7.47 (m, 2H, H arom), 7.55−7.57 (m, 2H, H arom); ^{13}C NMR (100 MHz) δ = 55.6 (OCH_3 *p*MP), 65.9 (C-5′), 66.4 (C-5), 68.7 (C-6′), 69.3 (C-6), 70.6 (CH_2 Bn), 70.6 (CH_2 Bn), 71.6 (C-4), 73.0 (CH_2 Bn), 73.5 (C-3), 74.2 (CH_2 Bn), 74.6 (C-4′or C-2′), 74.7 (C-3 or C-2), 74.8 (CH_2 Bn), 76.2 (C-3 or C-2), 76.8 (C-2′ or C-4′), 92.4 (C-1′), 100.9 (CHPh benzylidene), 103.1 (C-1), 114.3 (CH arom *p*MP), 118.9 (CH arom *p*MP), 126.3−129.1 (CH arom), 137.7 (C_q Ph), 138.0 (C_q Ph), 138.2 (C_q Ph), 138.4 (C_q Ph), 138.5 (C_q Ph), 139.4 (C_q Ph), 151.8 (C_q *p*MP), 155.1 (C_q *p*MP); ^{13}C-GATED NMR (100 MHz) δ = 92.4 ($J_{C\text{-}1',\ H\text{-}1'}$ = 162 Hz, C-1′), 103.1 ($J_{C\text{-}1,\ H\text{-}1}$ = 154 Hz, C-1); HRMS $[M + NH_4]^+$ calcd for $C_{61}H_{66}O_{12}N$ 1004.45795, found 1004.45933. β Isomer: $[\alpha]^{22}_D$ = +32.3 (c = 1.2, DCM); IR 737, 826, 1003, 1092 1223, 1366, 1454, 1504, 2866 cm^{-1}; ^{1}H NMR (400 MHz) δ = 3.31 (dd, 1H, J = 7.6 Hz, 2.4 Hz, H-2′), 3.42−3.46 (m, 2H, H-4′, H-5), 3.65 (dd, 1H, J = 4.8 Hz, 10.8 Hz, H-6′), 3.73 (dd, 1H, J = 10.8 Hz, 2.0 Hz, H-6), 3.76 (s, 3H, OCH_3 *p*MP), 3.96−3.99 (m, 2H, H-3, H-6), 4.04−4.14 (m, 3H, H-5′, H-2, H-3′), 4.29−4.34 (m, 2H, H-6, H-4), 4.43 (d, 1H, J = 11.6 Hz, CH_2 Bn), 4.49 (d, 1H, J = 8.8 Hz, CH_2 Bn), 4.58 (d, 1H, J = 12.4 Hz, CH_2 Bn), 4.76 (d, 1H, J = 12.0 Hz, CH_2 Bn), 4.80−4.93 (m, 6H, H-1, CH_2 Bn), 5.42 (d, 1H, J = 8.0 Hz, H-1′), 5.56 (s, 1H, CHPh benzylidene), 6.79 (d, 2H, J = 6.8 Hz, H arom), 7.02−7.39 (m, 32H, 3 H arom), 7.39−7.61 (m, 2H, H arom); ^{13}C NMR (100 MHz) δ = 55.6 (OCH_3 *p*MP), 66.6 (C-4′), 69.0 (C-6), 69.53 (C-6′), 71.4 (CH_2 Bn), 72.0 (C-5′), 72.9 (CH_2 Bn),

73.4 (CH_2 Bn), 74.2 (CH_2 Bn), 74.4 (C-2), 75.2 (CH_2 Bn), 75.7 (C-5), 77.0 (C-4), 77.3 (C-4), 78.3 (C-3′), 78.7 (C-2′), 100.8 (CHPh benzylidene), 101.9 (C-1′), 103.3 (C-1), 114.4 (CH arom *p*MP), 119.1 (CH arom *p*MP), 126.4−128.7 (CH arom), 137.8 (C_q Ph), 138.2 (C_q Ph), 138.3 (C_q Ph), 138.4 (C_q Ph), 138.7 (C_q Ph), 139.1 (C_q Ph), 151.7 (C_q *p*MP), 155.3 (C_q *p*MP); HRMS $[M + NH_4]^+$ calcd for $C_{61}H_{66}O_{12}N$ 1004.45795, found 1004.45938.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-D-galactopyranosyluronate)-α-D-glucopyranoside (62). Galacturonic acid **60** (114 mg, 0.20 mmol) was condensed with glucoside **25** (139 mg, 0.30 mmol) as described in the general procedure for glycosylations of thioglycuronates yielding **62** (91 mg, 49%) as a mixture of anomers (α/*β*: 1/2.3): IR (neat) 733, 818, 914, 1026, 1049, 1068, 1092, 1211, 1269, 1358, 1454, 1497, 1605, 1732, 1767, 2870, 3032 cm^{-1}; ^1H NMR (400 MHz) δ = 3.28 (s, 3 H, OCH_3 α), 3.29 (s, 8 H, OCH_3 *β*), 3.40 (dd, 1H, *J* = 3.6 Hz, *J* = 9.6 Hz), 3.44−54 (m, 10 H), 3.58 (s, 3H, CO_2CH_3 α), 3.62 (s, 7H, OCH_3 *p*MP, CO_2CH_3 *β*), 3.65 (dd, 2H, *J* = 5.6 Hz, 10.8 Hz), 3.85−3.89 (m, 7H), 3.91−4.02 (m, 5H), 4.06 (dd, 1H, *J* = 3.6 Hz, 9.6 Hz), 4.20−4.23 (m, 6H), 4.29 (d, 2H, *J* = 8.0 Hz), 4.40 (bs, 1H), 4.50−4.72 (m, 16 H), 4.73−4.83 (m, 4 H), 4.97 (dd, 6H, *J* = 2.0 Hz, 10.8 Hz), 5.07 (d, 1H, *J* = 3.6 Hz, H-1′α), 7.18−7.36 (m, 16 H, H arom Ph); ^{13}C NMR (100 MHz) δ = 53.0 (OCH_3 C-1-OCH_3), 55.0 (OCH_3 CO_2CH_3), 66.8 (C-6 α), 68.6 (C-6 *β*), 69.9 (*β*), 70.1 (α), 70.7 (α), 72.7 (CH_2 Bn α), 72.9 (CH_2 Bn α), 73.2 (CH_2 Bn α), 73.2 (CH_2 Bn *β*), 73.8 (*β*), 74.4, 74.7 (CH_2 Bn α), 74.9 (*β*), 75.0 (CH_2 Bn *β*), 75.5 (CH_2 Bn *β*), 75.6 (CH_2 Bn α), 75.8 (α), 76.5 (α), 77.2 (α), 77.8 (α), 79.8 (*β*), 78.0 (α), 81.3 (*β*), 81.9 (*β*), 82.0 (α), 97.7 (C-1 *β*), 97.7 (C-1 α), 98.1 (C-1′α), 103.7 (C-1′*β*), 137.3−128.3 (CH arom), 138.0−138.8 (C_q arom), 168.4 (C═O CO_2CH_3 *β*), 169.2 (C═O CO_2CH_3 α); HRMS $[M + NH_4]^+$ calcd for $C_{56}H_{64}O_{12}N$ 942.44230, found 942.44373.

***p*-Methoxyphenyl 2-*O*-Benzyl-3-*O*-(methyl 2,3,4-tri-*O*-benzyl-α/*β*-D-allopyranosyluronate)-4,6-benzylidene-*β*-D-galactopyranoside (64).** Galacturonic acid **60** (114 mg, 0.20 mmol) was glycosylated with glucoside **26** (139 mg, 0.30 mmol, 1.5 equiv) as described in the general procedure for glycosylations of thioglycuronates yielding **64** (159 mg, 86%) as a mixture of anomers (α/*β*: 1/0.4): IR (neat) 737, 826, 922, 999, 1030, 1065, 1096 1219, 1366, 1396, 1454, 1504, 1759, 2870, 3032 cm^{-1}; ^1H NMR (400 MHz) δ = 3.31 (s, 0.7 H, *p*MP *β*), 3.41−3.44 (m, 2H), 3.45 (s, 3H, *p*MP α), 3.56 (s, 1H, CO_2CH_3 *β*), 3.72 (s, 3H, CO_2CH_3 α), 3.83 (s, 0.4 H), 3.87 (dd, 1H, *J* = 3.2 Hz, *J* = 10.0 Hz), 3.95 (dd, 1H, *J* = 2.8 Hz, 10.0 Hz), 4.01−4.07 (m, 3H), 4.09−4.17 (m, 3H), 4.28−4.32 (m, 2H), 4.34 (d, 0.4 H, *J* = 3.6 Hz), 4.50−4.55 (m, 1.4 H), 4.60 (d, 3H, *J* = 12.0 Hz), 4.67 (d, 2H, *J* = 11.2 Hz, CH_2 Bn), 4.74−4.92 (m, 6H), 4.97 (d, 0.4 H, *J* = 8.0 Hz, H-1′*β*), 4.53 (d, 1 H, *J* = 11.2 Hz, CH_2 Bn α), 5.05 (d, 0.4 H, *J* = 11.6 Hz, CH_2 Bn *β*), 5.28 (d, 1H, *J* = 3.6 Hz, H-1′α), 0.55 (s, 1H, CHPh benzylidene α), 5.61 (s, 0.4 H, CHPh benzylidene *β*), 6.78 (d, 3H, *J* = 2.0 Hz, H arom *p*MP α, *p*MP *β*), 6.80 (s, 3H, *J* = 2.0 Hz, H arom *p*MP α, *p*MP *β*), 7.02−7.39 (m, 38.5 H, H arom), 7.54−7.56 (m, 2H, H arom), 7.60−7.60 (m, 0.8 H, H arom); ^{13}C NMR (100 MHz) δ = 51.7 (OCH_3 *p*MP α), 52.0 (OCH_3 *p*MP *β*), 55.5 (CO_2CH_3 α, CO_2CH_3 *β*), 66.3 (α), 66.6 (*β*), 68.7 (CH_2 Bn *β*), 69.1 (CH_2 Bn α), 70.5 (α), 71.3 (α), 72.2 (CH_2 Bn), 73.2 (CH_2 Bn), 73.8 (α), 74.3 (CH_2 Bn), 74.6 (CH_2 Bn), 74.7 (CH_2 Bn), 75.1 (*β*), 75.2 (CH_2 Bn), 75.3 (α), 75.5 (*β*), 76.2 (α), 76.8 (α), 77.6 (α), 78.3 (*β*), 79.1 (*β*), 81.0 (*β*), 93.0 (C-1′α), 100.5 (CHPh benzylidene *β*), 101.1 (CHPh benzylidene α), 103.0 (C-1′*β*), 103.1 (C-1 α, C-1*β*), 114.3 (CH arom *p*MP), 118.6 (CH arom *p*MP), 126.1−128.8 (CH arom), 137.6−138.5 (C_q arom), 151.4 (C_q *p*MP), 155.2 (C_q *p*MP), 168.8 (C═O CO_2Me α); HRMS $[M + NH_4]^+$ calcd for $C_{55}H_{60}O_{13}N$ 942.40592, found 942.40733.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-galactopyranoside)-α-D-glucopyranoside (63). Galactoside **61** (127 mg, 0.20 mmol) was condensed with glucoside **25** (139 mg, 0.30 mmol, 1.5 equiv) according to the general procedure for glycosylations of thioglycosides, yielding **63** (132 mg, 67%) as a mixture of anomers (α/*β*: 1/3): IR (neat) 733, 818, 910, 1026, 1065, 1092, 1157, 1207, 1265, 1362, 1454, 1497, 1585, 1605, 1956, 2870, 3032, 3063 cm^{-1}; ^1H NMR (400 MHz) δ = 3.33 (s, 3H, OCH_3 *β*), 3.35 (s, 1H, OCH_3 α), 3.43−3.73 (m, 12 H), 3.71−3.84 (m, 1.7 H), 3.96−4.02 (m, 1.7 H), 4.18 (d, 1H, *J* = 10.4 Hz, CH_2 Bn), 4.35 (d, 1H, *J* = 8.0 Hz, H-1′ *β*), 4.40−4.47 (m, 0.7 H), 4.50−4.66 (m, 8 H), 4.69−4.84 (m, 8 H), 4.91 (m, 1.6 H, CH_2 Bn), 4.97 (m, 2 H, CH_2 Bn and C-1′ α), 7.13−7.42 (m, 59H, 5 H arom); ^{13}C NMR (100 MHz) δ = 55.1 (OCH_3 α), 55.1 (OCH_3 *β*), 66.0, 68.4, 68.5, 69.8, 70.2, 70.3, 72.3 (CH_2 Bn), 73.3 (CH_2 Bn), 74.8 (CH_2 Bn), 74.9 (CH_2 Bn), 75.0, 75.4 (CH_2 Bn), 75.6 (CH_2 Bn), 75.6 (CH_2 Bn), 77.5, 77.7, 77.8, 77.9, 79.7, 79.9, 80.1, 81.6, 81.9, 82.0, 84.7, 97.2 (C-1′α), 97.9 (C-1 α), 98.0 (C-1 *β*), 103.7 (C-1′*β*), 127.5−128.4 (CH arom), 138.0 (C_q Ph), 138.1 (C_q Ph), 138.1 (C_q Ph), 138.2 (C_q Ph), 138.3 (C_q Ph), 138.3 (C_q Ph), 138.5 (C_q Ph), 138.8 (C_q Ph); HRMS $[M + NH_4]^+$ calcd for $C_{62}H_{70}O_{11}N$ 1004.49434, found 1004.49583.

***p*-Methoxyphenyl 2-*O*-Benzyl-(2,3,4,6-tetra-*O*-benzyl-α/*β*-D-galactospyranoside)-4,6-benzylidene-*β*-D-galactopyranoside (65).** Galactoside **61** (127 mg, 0.20 mmol) was glycosylated with galactoside **26** (139 mg, 0.30 mmol, 1.5 equiv) following the general procedure for glycosylations of thioglycosides, giving disaccharide **65** (0.142 mg, 72%) as a mixture of anomers (α/*β*: 1/0.1): IR (neat) 737, 826, 907, 999, 1061, 1099, 1223, 1312, 1366, 1454, 1504, 2168, 2866, 3032 cm^{-1}; ^1H NMR (400 MHz) δ = 5.24 (d, 1H, *J* = 3.6 Hz, H-1′α), 5.50 (s, 1H, CHPh-α benzylidene), 5.55 (s, 0.1 H, CHPh-*β* benzylidene). α Anomer: 3.25−3.29 (m, 2H, H-5, H-6′), 3.53−3.57 (m, 1H, H-6′), 3.69 (d, 1H, *J* = 2.0 Hz, H-4′), 3.73 (s, 3H, OCH_3 *p*MP), 3.88 (dd, 1H, *J* = 3.2 Hz, 10.0 Hz, H-3), 3.92−3.99 (m, 2H, H-3′, H-6), 4.07 (d, 1H, *J* = 3.6 Hz, H-2′), 4.09−4.14 (m, 1H, H-2), 4.18 (t, 1H, *J* = 6.4 Hz, H-5′), 4.26−4.29 (m, 4H, H-6, H-4, CH_2 Bn), 4.53 (d, 1H, *J* = 11.6 Hz, CH_2 Bn), 4.58 (m, 2H, CH_2 Bn), 4.66 (d, 1H, *J* = 12.0 Hz, CH_2 Bn), 4.76−4.81 (m, 3H, H-1, CH_2 Bn), 4.92 (d, 1 H, CH_2 Bn), 5.01 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 5.24 (d, 1H, *J* = 3.6 Hz, H-1′α), 5.50 (s, 1H, CHPh-α benzylidene), 6.79 (d, 2H, *J* = 2.0 Hz, H arom *p*MP), 6.81 (d, 2H, *J* = 2.0 Hz, H arom *p*MP), 7.01−7.37 (m, 28 H, 2 H arom Ph), 7.52−7.55 (m, 2H, H arom Ph); ^{13}C NMR (100 MHz) δ = 55.5 (OCH_3 *p*MP), 66.2 (C-5 or C-5′), 69.3 (C-5 or C-5′), 69.2 (C-6 or C-6′), 69.3 (C-6 or C-6′), 71.3 (C-4), 71.9 (CH_2 Bn), 72.6 (CH_2 Bn), 72.9 (CH_2 Bn), 73.7 (C-3), 74.6 (CH_2 Bn), 75.1 (C-4), 75.2 (CH_2 Bn), 76.0 (C-2′), 76.8 (C-2), 78.5 (C-3), 92.6 (C-1′ α), 100.5 (C-1′*β*), 101.2 (CHPh benzylidene), 103.1 (C-1 α), 103.6 (C-1 *β*); HRMS $[M + NH_4]^+$ calcd for $C_{61}H_{66}O_{12}N$ 1004.45795, found 1004.45943.

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Supporting Information Available: General experimental procedures, synthesis of the glycosyl donors, and NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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