Chapter 6

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

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 biological 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 glycuronans that contain solely uronic acids. Recently 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 were reported (see Chapter 5). 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 (for example 1, Scheme 1). 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 rationalized by an S\(_{N2}\)-like attack of the
nucleophile on the putative axial α-triflate 2 or on the corresponding contact ion pair. The electron withdrawing capacity of the C-5 carboxylate destabilizes the (solvent separated) oxocarbenium ion 3a-b, resulting in a shift of the equilibrium to the side of the α-triflate 2.

Scheme 1

Glycosylations with mannuronate and guluronate ester donors. Reagents and conditions: a) BSP, TTBP, DCM, -60 °C to -45 °C, Tf₂O 10 min, then -60 °C, nucleophile, to 0 °C. b) Ph₂SO, TTBP, DCM, -60 °C to -45 °C, Tf₂O 10 min, then -60 °C, nucleophile, to 0 °C.

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), albeit with reduced stereoselectivity and yield. The stereochemical outcome of the glycosylation of 5 can not 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 1,2-trans product. Puzzled by the effect of the C-5 carboxylate ester on the stereochemistry of these glycosylations, attention was attracted to the work of Woerpel and co-workers on the stereoselectivity of pyranosyl oxacarbenium ions in C-glycosylation reactions. From their work it is apparent that the relative stability of the 3H₄ and 4H₃ half-chair conformers of the intermediate oxacarbenium ions is of prime importance for the stereochemical outcome of C-glycosylations. 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.\textsuperscript{14} The stability of the half-chair conformers is determined by the nature and the configuration of the substituents on the pyranose ring.\textsuperscript{12c,15} Alkyl groups at C-3 and C-4 prefer to adopt pseudo equatorial positions, whereas electron withdrawing substituents at these positions preferentially adopt an axial orientation. C-2 Alkoxy substituents again prefer an equatorial orientation.\textsuperscript{12c} To establish the stereodirecting effect of the C-5 carboxylate ester Codée \textit{et al.} studied the condensations of pyranoside 9 (Scheme 2) having a single carboxylate substituent at C-5, and its “non-oxidized” counterpart 10 having a methyloxybenzyl group at this position.\textsuperscript{16} It turned out that the C-5 ester is 1,5-\textit{cis} directing, while the C-5 methyloxybenzyl functionalized pyranoside gives little selectivity. The stereochemical outcome of these glycosylations can be explained by taking into consideration the half chair oxocarbenium ions 11 and 12 as product forming intermediates. Attack of an incoming nucleophile on these ions occurs along a pseudo axial 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.\textsuperscript{14b} The formation of the 1,2-\textit{cis}-product 13 arises from the $^3\text{H}_4$ (11a) conformer, indicating that the C-5 carboxylate prefers to occupy an axial position in the oxacarbenium ion intermediate.

Scheme 2

![Scheme 2 Diagram](image)

Stereoselectivity of C-5 functionalized pyranosides. Reagents and conditions: a) Ph$_2$SO, TTBP, DCM, -78 °C, Tf$_2$O, 5 min, then BnOH, -78 °C, 15 min.

In the D-mannuronate ester $^3\text{H}_4$ oxocarbenium 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 $^3\text{H}_4$ conformer will therefore be substantially more stable than the corresponding $^4\text{H}_3$ half-chair (3b), and nucleophilic attack on 3a leads to the formation of the 1,2-\textit{cis} product. Thus, besides $\alpha$-triflate 2 (Scheme 1), oxocarbenium 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 favorable axial position in the $^4\text{H}_3$ half-chair (7b), in which all
other substituents are in disfavored positions (Scheme 1). In the alternative $^3\text{H}_4$ conformer (7a), the C-2, C-3 and C-4 substituents are favorably oriented, however the C-5 ester is in the more destabilizing equatorial position. 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, and therefore the $^4\text{H}_3$ half-chair (7b), which leads to 1,2-cis selective condensations, is preferred over its $^3\text{H}_4$ counterpart (7a). Because the guluronate ester oxacarbenium ion half chairs will be closer together in ground state energy the selectivity of glycosylations involving these intermediates is less pronounced.

To investigate the magnitude of the stereodirecting effect of the C-5 substituent in glycosylations in more detail, a study towards the glycosylation properties of a set of thioglycosides having a carboxylate methyl ester, a methylene benzyl ether or a methyl group at C-5 is presented in this Chapter. To this end, D-manno, D-gulo, D-gluco and D-galacto configured 1-thioglycosides, 1-thio uronic acids and 1-thio 6-deoxy thioglycosides were synthesized 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 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 were performed using the 6-311+G** basis set in Spartan 04. The MP2 and MP3 gas phase energy calculations of the geometry-optimized conformers were performed using Gaussian 03. 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 $^3\text{H}_4$ conformer (15), 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 of importance: conformer 15, in which the ester carbonyl is pointing towards the ring oxygen, was calculated to be approximately 3.6 kcal/mol more stable than the equatorial conformer, whereas conformer 16, having the methoxy group oriented towards the oxacarbenium ion, is isoenergetic with the equatorial conformer. 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 in conformer 15 is of similar magnitude as the axial preference of C-3 and C-4 alkoxy groups. The calculations show the axially oriented methyloxy methylene pyranosyl oxacarbenium 18 (with the alkoxy group situated above the ring) also 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.\textsuperscript{12c}

\textbf{Figure 1}

Calculated relative energies of C5-substituted pyranosyl oxacarbenium ions. The error in these calculations is approximately ± 1 kcal/mol.

The trend\textsuperscript{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 \textsuperscript{3}H\textsubscript{4} conformer relative to its \textsuperscript{4}H\textsubscript{3} counterpart leading to the preferential formation of the 1,5-\textit{cis} product. The slight preference of the methyloxybenzyl group in pyranoside 18 to occupy an axial position does not lead to the selective formation of the 1,5-\textit{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.

Next, the stereodirecting effect of three C-5 substituents (methyl ester, methyloxybenzyl 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\textsubscript{2}SO)-trifluoromethane sulphonic anhydride (Tf\textsubscript{2}O) 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 minutes, before adding 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 pre-activated at -78 °C for 10 minutes after which the acceptor was added at the same temperature. The results of these condensations are summarized in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Acceptor</th>
<th>22: R = COOMe&lt;sup&gt;a&lt;/sup&gt;</th>
<th>23: R = CH₃OBn&lt;sup&gt;b&lt;/sup&gt;</th>
<th>24: R = CH₃&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>27 α/β = 0/1 (77%)</td>
<td>28 α/β = 1/2 (71%)</td>
<td>29 α/β = 1/1.7 (71%)</td>
</tr>
<tr>
<td>26</td>
<td>30 α/β = 0/1 (58%)</td>
<td>31 α/β = 1/1.5 (52%)</td>
<td>32 α/β = 1/1 (65%)</td>
</tr>
</tbody>
</table>

Study of the C-5 substituent effect in the mannose series. Reagents and conditions: a) Ph₂SO, TTBP, DCM, -60 °C to -45 °C, Tf₂O 10 min, then -78 °C, nucleophile, to 0 °C; b) Ph₂SO, TTBP, DCM, -78 °C, Tf₂O 10 min, nucleophile, to 0 °C.

Mannuronate ester 22 yielded solely the β-linked products 27 and 30 independent of the nature of the acceptor. Tetrabenzyl mannose 23 showed a significant drop in selectivity, but maintained a slight preference for the formation of the β-product. The β-selectivity for the glycosylation involving the primary acceptor 25 was slightly better than for the secondary acceptor 26. Although the β-selectivity of donor 23 is not unprecedented<sup>23</sup>, it stands in contrast to the perception that perbenzylated mannose donors are α-selective in glycosylation reactions.<sup>24,25</sup> The condensations of d-rhamnose 24 showed a further decrease of β-product formation and also here the secondary acceptor gave more α-product. The anomeric ratios of the glycosylations in Table 1 follow the trend in the stability of the respective oxacarbonium ions (Scheme 3). In the 3H₄ conformer of mannuronic ester (33a) all substituents are situated in a favorable position, explaining the nucleophilic attack on this conformer and the sole formation of the cis product. In mannose the difference in stability between the 3H₄ conformer (34a) and its 4H₃ counterpart (34b) is less pronounced. Because steric interactions in the transition state leading to the α-product are smaller than in the transition state which leads to the β-linked dimer,<sup>10d,e</sup> a Curtin-Hammett/Winstein-Holness kinetic scenario,<sup>26</sup> in which product formation arises from the higher energy 4H₃ conformer (34b), can account for the formation of the 1,2-trans-product in the anomeric mixture. Because the methyl group prefers an equatorial orientation in the oxacarbonium ion intermediate, the difference in stability between the 3H₄ (35a) and 4H₃ (35b) conformers of rhamnose is further minimized, and more product is formed from the 4H₃ oxacarbonium ion.
Mannosyl oxacarbenium ions.

Execution of glycosylation reactions of 25 and 26 with D-gulose derivatives 36, 37 and 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. Contrary, for the guluronic acid methyl ester (36) glycosylations this effect is reversed.

Table 2

<table>
<thead>
<tr>
<th>Acceptor</th>
<th>36: R = COOMe&lt;sup&gt;a&lt;/sup&gt;</th>
<th>37: R = CH&lt;sub&gt;2&lt;/sub&gt;OBn&lt;sup&gt;b&lt;/sup&gt;</th>
<th>38: R = CH&lt;sub&gt;3&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>39 α/β = 1/0.33 (86%)</td>
<td>40 α/β = 1/0.10 (76%)</td>
<td>41 α/β = 1/0.08 (67%)</td>
</tr>
<tr>
<td>26</td>
<td>42 α/β = 1/0.17 (63%)</td>
<td>43 α/β = 1/0.12 (70%)</td>
<td>44 α/β = 1/0.15 (70%)</td>
</tr>
</tbody>
</table>

Study of the C-5 substituent effect in the gulose series. Reagents and conditions: a) Ph<sub>2</sub>SO, TTBP, DCM, -60 °C to -45 °C, Tf<sub>2</sub>O 10 min, then -78 °C, nucleophile, to 0 °C; b) Ph<sub>2</sub>SO, TTBP, DCM, -78 °C, Tf<sub>2</sub>O 10 min, nucleophile, to 0 °C.

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 3<sup>H</sup><sub>4</sub> and the 4<sup>H</sup><sub>3</sub> conformers, is again confirmed.<sup>27</sup> All gulosylations may proceed by an axial attack of the nucleophile on the 4<sup>H</sup><sub>3</sub> conformer, leading to the cis-product (Scheme 4). The 4<sup>H</sup><sub>3</sub> oxacarbenium ion of 6-deoxygulose 47b has the substituents positioned in such a manner that they all contribute favorably to the stability of this conformer and the glycosylations 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 4<sup>H</sup><sub>3</sub> 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 $^3$H$_4$ oxacarbenium ions 33a-35a leads to 1,3-diaxial interactions with both the C-3 and C-5 substituent, which are absent in the transition state of the $^4$H$_3$ 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).

Gulosyl oxacarbenium ions.

The results reported above for mannuronic acid donor 22 and 6-deoxy gulose donor 38 indicate that highly stereoselective glycosylations can be obtained when all the substituents occupy a favorable position in either the $^3$H$_4$ or the $^4$H$_3$ oxacarbenium ion conformer. To further assess the effect of the substituent at C-5 on the stereochemical outcome of glycosylation reactions, three other epimers were examined. D-gluco, D-allo and D-galacto configured 1-thioglycosides and the corresponding 1-thio uronic 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. Almost all of the condensations proceed with poor stereoselectivity. Furthermore, the nature of the acceptor appears to have a profound effect on the stereochemical outcome of the glycosylations. The low selectivities observed in the glucose (48 and 49) and galactose (60 and 61) series are in contrast to the previously reported highly $\alpha$-selective C-glycosylations of these epimers. No clear effect of the C-5 substituent can be distilled from the data reported in Table 3.
Stereodirecting Effect of the Pyranosyl C-5 Substituent in Glycosylation Reactions

Table 3

<table>
<thead>
<tr>
<th>Donor</th>
<th>Acceptor</th>
<th>$R = \text{COOMe}^a$</th>
<th>$R = \text{CH}_2\text{OBn}^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (48, 49)</td>
<td>25</td>
<td>$\alpha/\beta = 1/1.4$ (68%)</td>
<td>$\alpha/\beta = 1/1.4$ (75%)</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>$\alpha/\beta = 1/0.6$ (86%)</td>
<td>$\alpha/\beta = 1/1.7$ (89%)</td>
</tr>
<tr>
<td>Allose (54, 55)</td>
<td>25</td>
<td>$\alpha/\beta = 1/0.4$ (91%)</td>
<td>$\alpha/\beta = 1/0.5$ (92%)</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>$\alpha/\beta = 1/0$ (52%)</td>
<td>$\alpha/\beta = 1/0.6$ (65%)</td>
</tr>
<tr>
<td>Galactose (60, 61)</td>
<td>25</td>
<td>$\alpha/\beta = 1/2.3$ (49%)</td>
<td>$\alpha/\beta = 1/3$ (67%)</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>$\alpha/\beta = 1/0.4$ (86%)</td>
<td>$\alpha/\beta = 1/0.1$ (72%)</td>
</tr>
</tbody>
</table>

Study of the C-5 substituent effect in the glucose, galactose, and allose series. Reagents and conditions: a) Ph$_2$SO, TTBP, DCM, -60 °C to -45 °C, Tf$_2$O 10 min, then -78 °C, nucleophile, to 0 °C; b) Ph$_2$SO, TTBP, DCM, -78 °C, Tf$_2$O 10 min, nucleophile, to 0 °C.

Considering 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 $^{4}\text{H}_3$ 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.

Scheme 5

Glucosyl, galactosyl and allosyl oxacarbenium ions.
In 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 pseudo axial position. In this orientation it can donate electron density through space to the electron depleted oxacarbenium ion, thereby stabilizing this intermediate. A C-5 methoxyalkyl substituent is also capable of such an energetically favorable though space 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 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 glycosylation strategies.

Experimental

**General:** Dichloromethane was refluxed with P₂O₅ and distilled before use. Trifluoromethanesulfonic anhydride was distilled from P₂O₅. Traces of water in the donor and acceptor glycosides, diphenylsulfoxide and TTBP were removed by co-evaporation with toluene. All other chemicals (Acros, Fluka, Merck, Schleicher & Schue) were used as received. Column chromatography was performed on Merck silica gel 60 (0.040-0.063 mm). TLC analysis was conducted on HPTLC aluminum sheets (Merck, silica gel 60, F245). Size exclusion chromatography was performed on sephadex™ LH-20. Compounds were visualized by UV absorption (245 nm), by spraying with 20% H₂SO₄ in ethanol or with a solution of (NH₄)₆Mo₇O₂₄·4H₂O 25 g/L, (NH₄)₄Ce(SO₄)₂·2H₂O 10 g/L, 10% H₂SO₄ in H₂O followed by charring at +/- 140 °C. ¹H and ¹³C NMR spectra were recorded with a Bruker AV 400 (400 and 100 MHz respectively), AV 500 (500 and 125 MHz respectively) or a Bruker DMX 600 (600 and 150 MHz respectively). NMR spectra were recorded in CDCl₃ with chemical shift (δ) relative to tetramethylsilane unless stated otherwise. Optical rotations were measured on a Propol automatic polarimeter. High resolution mass spectra were recorded on a LTQ-orbitrap (thermo electron). IR spectra were recorded on a Shimadzu FTIR-8300 and are reported in cm⁻¹. The α/β ratio was determined using ¹H NMR and ¹³C-GATED NMR where applicable.

**Synthesis of Building Blocks:** β-Thio-D-allose was synthesized as described by Gómez *et al.* Thio-D-gulose was obtained as described in the previous Chapter using D-gulonolactone as starting material. To obtain the protected 1-thio glycosides the corresponding 1-thio tetraols were benzylated using BnBr and NaH in DMF yielding 23, 37, 49, 55 and 61 (Scheme 7). The uronic acids and 6-deoxy glycosides were synthesized by tritylating the C-6-OH and benzylating the remaining free hydroxyls by treatment with NaH and BnBr. The trityl group was then cleaved using pTsOH in methanol/DCM. Oxidation of the primary alcohol using the TEMPO/BAiB reagent combination and
ensuing methylation with MeI and K₂CO₃ in DMF gave the uronic acid methyl esters 22, 36, 48, 54 and 60. Treatment of the C-6-OH glycosides with PPh₃, iodine and imidazole in toluene at 70 °C and subsequent reduction of the iodine with LiAlH₄ yielded rhamnose 24 and 6-deoxy-D-gulose (antiarose) 38 (Scheme 7).

**Scheme 7**

![Scheme 7](image)

Synthesis of β-S-phenyl -glycosides, -uronic acid esters and -6-deoxy glycosides. Reagents and conditions: a) DMF, BnBr, NaH, 0 °C to rT; b) i. Pyridine, TrCl; ii. DMF, BnBr, NaH, 0 °C to rT; iii. MeOH, pTsOH (cat). iv. Toluene, PPh₃, Imidazole, I₂; v THF, LiAlH₄; c) i. Pyridine, TrCl; ii. DMF, BnBr, NaH, 0 °C to rT; iii. MeOH, pTsOH (cat). iv. DCM, H₂O, TEMPO, BAIB; v. DMF, K₂CO₃, MeI.

**General procedure for the synthesis of tetrabenzyl thioglycosides:** To a solution of thioglycoside in DMF (0.2 M) was added at 0 °C BnBr (4.8 eq.) and NaH (4.8 eq.). The mixture was allowed to warm to rT and stirred for several hours until TLC analysis showed total conversion into a higher running spot. The reaction was quenched by addition of MeOH at 0 °C, washed with H₂O and extracted three times with Et²O. The combined organic layers were dried over MgSO₄, filtered, and concentrated in vacuo. Column chromatography afforded the title compounds.

**General procedure for TEMPO/BAIB oxidations:** To a solution of thioglycoside in pyridine (0.2 M) was added trityl chloride (1.5 eq.) and a catalytic amount of DMAP. The reaction mixture was stirred until TLC analysis showed total conversion (several days). The reaction mixture was quenched by addition of MeOH and extracted with EtOAc. The combined organic layers were washed with HCl (1 M) and NaHCO₃ (aq., sat.), dried over MgSO₄, filtered, and concentrated in vacuo. The obtained yellow residue was dissolved in DMF (0.2 M) and at 0 °C was added BnBr (3.6 eq.) and NaH (3.6 eq.). The mixture was allowed to warm to rT and stirred for several hours until TLC analysis showed total conversion into a higher running spot. The reaction was quenched by addition of MeOH at 0 °C, washed with H₂O and extracted three times with Et₂O. The combined organic layers were dried over MgSO₄, filtered, and concentrated in vacuo. The obtained residues were dissolved in MeOH/DCM (4/1, v/v, 0.1 M) and a catalytic amount of pTsOH was added. The reaction mixture were stirred until TLC analysis showed total cleavage of the trityl protective group and the reaction mixture was neutralized with Et₃N and concentrated. Flash column chromatography yielded 6-OH thioglycoside which was dissolved in DCM/H₂O (2/1, 0.2 M in DCM) after which BAIB (2.5 eq.) and TEMPO (0.2 eq.) were added. After TLC analysis showed total conversion into a lower running spot. The reaction mixture was quenched by addition of Na₂S₂O₃ (aq). The organic layer was isolated and the aqueous
layer was extracted twice with EtOAc. The combined organic layers were dried over MgSO₄, filtered, concentrated, in vacuo. The resulting syrup was then dissolved in DMF (0.2 M), after which K₂CO₃ (5 eq.) and MeI (3 eq.) were added. The mixture was stirred for several hours until TLC analysis showed total conversion into a higher running spot. The mixture was washed with H₂O and extracted with Et₂O. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. Purification by column chromatography yielded the corresponding uronic acid esters.

**General procedure for the synthesis of 6-deoxy glycosides:** To a solution of thioglycoside in pyridine (0.2 M) was added trityl chloride (1.5 eq.) and a catalytic amount of DMAP. The reaction mixture was stirred until TLC analysis showed total conversion (several days). The reaction mixture was quenched by addition of MeOH and extracted with EtOAc. The combined organic layers were washed with HCl (1 M) and NaHCO₃ (aq., sat.), dried over MgSO₄, filtered, and concentrated in vacuo. The obtained yellow residue was dissolved in DMF (0.2 M) and at 0 °C was added BnBr (3.6 eq.) and NaH (3.6 eq.). The mixture was allowed to warm to rT and stirred for several hours until TLC analysis showed total conversion into a higher running spot. The reaction was quenched by addition of MeOH at 0 °C, washed with H₂O and extracted three times with Et₂O. The combined organic layers were dried over MgSO₄, filtered, and concentrated in vacuo. The obtained residues were dissolved in MeOH/DCM (4/1, v/v, 0.1 M) and a catalytic amount of pTsOH was added. The reaction mixture were stirred until TLC analysis showed total cleavage of the trityl protective group and the reaction mixture was neutralized with Et₃N and concentrated. Flash column chromatography yielded the 6-OH thioglycoside which was dissolved in Toluene (0.05 M) and degassed with argon for 1 h. Then PPh₃ (1.5 eq.), imidazole (2 eq.) and I₂ (1.4 eq.) were added. The mixture was then heated to 70 °C. After TLC analysis showed total conversion into a higher running spot, the reaction mixture was quenched by addition of Na₂S₂O₃ (aq) and NaHCO₂⁻ (aq). The organic layer was isolated and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over MgSO₄, filtered, and concentrated in vacuo. Purification by column chromatography yielded the corresponding 6-iodo compounds which were then dissolved in THF (0.2 M). At 0 °C LiAlH₄ (2 eq.) was added and the mixture was then heated to 70 °C. When TLC analysis showed total conversion of starting material the reaction was cooled to rT and quenched with EtOAc, filtered and concentrated in vacuo. Purification by column chromatography yielded the corresponding 6 deoxy glycosides.

**General procedure for glycosylations of thioglycosides and 6-deoxy thioglycosides:** A solution of donor, diphenyl sulfoxide (1.1 eq) and tri-tert-butylypyrimidine (2.5 eq) in DCM (0.05 M) was stirred over activated MS 3Å for 30 min. The mixture was cooled to -78 °C before triflic anhydride (1.1) was added. The mixture was stirred for 10 min. at -78 °C followed by addition of acceptor (1.5 eq) in DCM (0.1 M). The reaction mixture was allowed to warm to 0 °C and Et₃N (0.15 ml) was added. The reaction mixture was diluted with DCM and washed with NaHCO₃ (aq). The aqueous layer was extracted twice with DCM and the collected organic layers were dried over MgSO₄, 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 eq) and tri-tert-butylypyrimidine (2.5 eq) in DCM (0.05 M) was stirred over activated MS 3Å for 30 min. The mixture was cooled to -60 °C before triflic anhydride (1.1 eq) was added. The mixture was warmed to -45 °C then cooled to -78 °C followed by addition of acceptor (1.5 eq) in DCM (0.1
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M). Stirring was continued and the reaction mixture was allowed to warm to 0 °C and Et₃N (0.15 ml) was added. The reaction mixture was diluted with DCM and washed with NaHCO₃ (aq). The aqueous layer was extracted twice with DCM and the collected organic layers were dried over MgSO₄, filtered and concentrated in vacuo. Purification by size exclusion and column chromatography yielded the corresponding dimer.

**Methyl (phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-mannopyranosyluronate) (22):** The title compound was prepared according to the general procedure for the synthesis of uronate esters starting from phenyl-1-thio-β-D-mannopyranoside (2.54 g, 9.35 mmol) yielding 22 as a white solid (2.15 g, 40%). [α]D = -65 (c = 1, DCM); IR (neat): 725, 829, 883, 1007, 1026, 1045, 1076, 1138, 1207, 1238, 1393, 1454, 1732, 2037, 2191, 2341, 2361; ¹H NMR (400 MHz): δ = 3.62 (dd, 1H, J = 9.6 Hz, H-3), 3.72 (s, 3H, CO₂CH₃), 3.87 (d, 1H, J = 9.6 Hz, H-5), 4.14 (d, 1H, J = 2.0 Hz, H-2), 4.31 (t, 1H, J = 9.6 Hz, H-4), 4.68-4.75 (m, 3H, CH₂ Bn), 4.78 (s, 1H, H-1), 4.85-4.88 (m, 2H, CH₂ Bn), 5.05 (d, 1H, J = 11.6 Hz, CH₂ Bn), 7.24-7.37 (17 H, 1 H Arom), 7.45-7.49 (m, 3H, H Arom); 13C NMR (100 MHz): δ = 52.5 (CO₂CH₃), 72.8 (CH₂ Bn), 75.2 (CH₂ Bn), 75.3 (CH₂ Bn), 75.6 (C-4), 77.3 (C-2), 78.9 (C-5), 83.4 (C-3), 88.9 (C-1), 127.4-129.0 (CH Arom), 130.9 (CH Arom), 135.2 (C_q Ph), 137.9 (C_q Ph), 138.1 (C_q Ph), 168.3 (C=O, CO₂Me); 13C-GATED NMR (100 MHz): δ = 88.94 (J_C-1, H-1 = 152 Hz, C-1); HRMS: C₃₄H₃₄O₆S + NH₄⁺ requires: 588.2414, found 588.2428.

**Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 2,3,4-tri-O-benzyl-β-D-mannopyranosyluronate)-β-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 a white solid. [α]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; ¹H NMR (400 MHz): δ = 3.31 (s, 3H, C-1-OCH₃), 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, CO₂CH₃, H-5, H-5', H-2'), 4.01 (t, 1H, J = 9.2 Hz, H-4'), 4.47-4.56 (m, 4H, CH₂ Bn, H-1), 4.66 (d, 1H, J = 9.2 Hz, H-2), 4.77-4.91 (m, 5H, CH₂ Bn), 4.96 (d, 1H, J = 10.0 Hz, CH₂ Bn), 7.20-7.46 (m, 30 H, HArom); 13C NMR (100 MHz): δ = 52.4 (CO₂CH₃), 55.1 (C-1-OCH₃), 68.6 (C-6), 69.7 (C-5), 71.7 (CH₂ Bn), 73.3 (C-5’ or C-2’), 73.4 (CH₂ Bn), 73.8 (CH₂ Bn), 74.8 (CH₂ Bn), 75.2 (CH₂ Bn), 75.3 (C-5’ or C-2’), 75.8 (CH₂ 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 CO₂Me); 13C-GATED NMR (100 MHz): δ = 97.8 (J_C-1, H-1 = 167 Hz, C-1), 102.1 (J_C-1’, H-1’ = 155 Hz, C-1’); HRMS: C₅₆H₆₀O₁₂ + Na⁺ requires: 947.39770, found 947.39853.

**para-Methoxyphenyl-2-O-benzyl-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 a white solid. [α]D = - 8.5 (c = 2, DCM); IR (neat): 729, 895, 1003, 1061 1096, 1219, 1265, 1366, 1508, 1747, 3055; 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’,
Phenyl-2,3,4,6-tetra-O-benzyl-1-thio-β-D-mannopyranoside (23): The title compound was prepared according to the general procedure for the synthesis of tetrabenzyld thioglycosides starting from phenyl-1-thio-β-D-mannopyranoside (0.5 g, 1.84 mmol) yielding 23 as white solid (704 mg, 60%). IR (neat): 733, 841, 907, 945, 999, 1026, 1072, 1130, 1207, 1254, 1273, 1308, 1362, 1396, 1454, 1481, 1497, 1582, 2858, 3028; 1H NMR (400 MHz): δ = 3.54 (m, 1H, H-5), 3.63 (dd, 1H, J = 9.6 Hz, J = 3.2 Hz, H-3), 3.73 (dd, 1H, J = 6.4 Hz, 6.4 Hz, H-6), 3.76 (dd, 1H, J = 9.6 Hz, H-4), 4.15 (d, 1H, J = 2.4 Hz, H-2), 4.54-4.61 (m, 3H, CH2 Bn), 4.67 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.73 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.77 (s, 1H, H-1), 4.87 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.89 (d, 1H, J = 10.8 Hz, CH2 Bn), 5.05 (d, 1H, J = 11.6 Hz, CH2 Bn), 7.19-7.36 (m, 23H, H Arom), 7.44-7.52 (m, 2H, H Arom); 13C NMR (100 MHz): δ = 69.8 (C-6), 72.6 (CH2 Bn), 73.4 (CH2 Bn), 74.9 (C-4), 75.0 (CH2 Bn), 75.2 (CH2 Bn), 77.5 (C-2), 80.1 (C-5), 84.3 (C-3), 87.6 (C-1), 127.0-130.52 (CH Arom), 135.7 (Cq SPh), 138.0 (Cq Ph), 138.2 (Cq Ph), 138.2 (Cq Ph), 138.5 (Cq Ph).

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-α/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; 1H NMR (400 MHz): δ = 3.30 (s, 1.55 H, C-1α-OCH3), 3.33 (s, 3H, C-1β-OCH3), 3.36-3.47 (m, 5H), 3.51 (dd, 1H, J = 9.6 Hz, 3.2 Hz, H-3β), 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), 13C NMR (100 MHz): δ = 55.0 (OCH3 β), 55.0 (OCH3 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, 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 (Cq Ph), 138.1 (Cq Ph), 138.2 (Cq Ph), 138.3 (Cq Ph), 138.3 (Cq Ph), 138.4 (Cq Ph), 138.4 (Cq Ph), 138.6 (Cq Ph), 138.6 (Cq Ph), 138.6 (Cq Ph), 138.8 (Cq Ph), 151.5 (Cq Ph), 151.6 (Cq Ph), 155.3 (Cq Ph). 13C-GATED NMR (100 MHz): δ = 98.2 (J = 164 Hz), 101.4 (J = 158 Hz); HRMS: C55H56O13 + Na+ requires: 942.3613, found 947.3621.
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*para*-Methoxyphenyl-2-O-benzyl-3-O-(2,3,4,6-tetra-O-benzyl-a/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 (a/β: 1/1.6). IR (neat): 729, 826, 899, 999, 1026, 1061, 1219, 1265, 1366, 1454, 1504, 2858; 1H 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), 3.88-3.91 (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 pMP), 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); 13C NMR (100 MHz): δ = 55.6 (OCH3 pMP), 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 pMP), 114.5 (CH Arom pMP), 118.8 (CH Arom pMP), 118.9 (CH Arom pMP), 126.3-139.0 (CH Arom), 130.9 (CH Arom), 137.7 (Cq Ph), 138.0 (Cq Ph), 138.0 (Cq Ph), 138.2 (Cq Ph), 138.2 (Cq Ph), 138.3 (Cq Ph), 138.4 (Cq Ph), 138.5 (Cq Ph), 138.6 (Cq Ph), 138.8 (Cq Ph), 151.5 (Cq Ph), 151.6 (Cq Ph), 155.3 (Cq Ph). 13C-GATED NMR (100 MHz): δ = 93.3 (J = 171 Hz, C-1′α), 102.8 (J = 156 Hz, C-1′β); HRMS: C61H62O12 + NH4+ requires: 1004.4580, found 1004.4593.

Phenyl-2,3,4-tri-O-benzyl-1-thio-β-D-rhamnose (24): Rhamnopyranoside 24 was prepared from Phenyl-1-thio-β-D-mannopyranoside (1.63 g, 6 mmol) according to the general procedure for the synthesis of 6-deoxy glycosides and 24 was obtained as a clear oil (0.66 g, 21%). IR (neat): 694, 734, 1026, 1080, 1732, 2870; 1H NMR (400 MHz): δ = 1.34 (d, 3H, J = 6.4 Hz, H-6), 3.69 (t, 1H, J = 9.2 Hz, H-4), 3.84 (dd, 1H, J = 2.8 Hz, 9.2 Hz, H-3), 3.98 (dd, 1H, J = 2 Hz, 3.2 Hz, H-2), 4.12-4.19 (m, 1H, H-5), 4.56 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.58-4.70 (m, 5H, CH2 Bn), 5.49 (d, 1H, J = 1.6 Hz, H-1), 7.12-7.34 (m, 20H, H Arom); 13C NMR (100 MHz): δ = 17.8 (C-6), 69.2 (C-5), 70.2 (CH2 Bn), 72.0 (CH2 Bn), 75.3 (CH2 Bn), 76.5 (C-2), 79.9 (C-3), 80.4 (C-4), 85.7 (C-1), 127.1-128.9 (CH Arom), 131.2 (CH Arom), 134.6 (Cq Arom), 137.9-138.4 (Cq Arom); HRMS: C33H34O4S + Na+ requires: 549.2070, found 549.2059.

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 (a/β: 1/1.7). IR (neat): 732, 694, 1006, 1026, 1053, 1068, 1362, 1454, 2866; 1H 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); 13C NMR (100 MHz): δ = 17.8 (C-6′ β), 17.9 (C-6′ α), 98.2(C-1′ α), 101.2 (C-1′ β); 13C-GATED NMR (100 MHz): δ = 98.2 (Jc-1′, h-1′ = 168 Hz, C-1′ α), 103.2 (Jc-1′, h-1′ = 153 Hz, C-1′ β); HRMS: C55H60O12 + Na+ requires: 903.4079, found 903.4077.
**para-Methoxyphenyl-2-O-benzyl-3-O-(2,3,4-tri-O-benzyl-
α-D-ribofuranosyl)-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; ¹H NMR 
(400 MHz): δ = 1.26 (d, 3H, J = 4.8 Hz, C-6), 1.35 (d, 3H, J = 6 Hz, C-6); ¹³C NMR (100 MHz): δ = 
17.9 (C-6′ α), 18.0 (C-6′ β), 93.4 (C-1′ α), 102.5 (C-1′ β); ¹³C-GATED NMR (100 MHz): δ = 127.7 
(J_C-1, H-1 = 166 Hz, C-1′ α), 103.2 (J_C-1′, H-1′ = 154 Hz, C-1′ β); HRMS: C₅₄H₅₆O₁₁ + Na⁺ requires: 
903.3715, found 903.3712.

**Methyl (phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-galactopyranosyluronate) (36):** The title compound was prepared according to the general procedure for the 
synthesis of uronate esters starting from phenyl-1-thio-β-D-galactopyranoside 
(0.348 mg, 1.28 mmol) yielding 36 as a white solid (433 mg, 59%). [α]D = -17.0 
(c = 0.02, DCM); IR (neat): 731, 897, 814, 939, 1026, 1074, 1126, 1209, 1265, 1304, 1358, 1420, 
1439, 1454, 1477, 1497, 1734, 1765, 2876; ¹H NMR (400 MHz): δ = 3.72-3.75 (m, 4H, H-3, 
CO₂CH₃), 3.83 (dd, 1H, J = 3.2 Hz, 10 Hz, H-2), 3.91 (dd, 1H, J = 3.6 Hz, 1.6 Hz, H-4), 4.31 (d, 1H, 
J = 12.0 Hz, CH₂ Bn), 4.39 (d, 1H, J = 12.0 Hz, CH₂ Bn), 4.41 (d, 1H, J = 12.0 Hz, CH₂ Bn), 4.56 (d, 1H, 
J = 12 Hz, CH₂ Bn), 4.60 (s, 1H, H-5), 4.61 (d, 1H, J = 12.0 Hz, CH₂ Bn), 4.71 (d, 1H, J = 12.4 
Hz, CH₂ Bn), 5.23 (d, 1H, J = 10.0 Hz, H-1); ¹³C NMR (100 MHz): δ = 52.1 (CO₂CH₃), 72.5 (CH₂ 
Bn), 72.7 (CH₂ Bn), 72.9 (C-2), 74.7 (C-5), 76.2 (C-4), 84.4 (C-1), 127.2-128.6 (CH Arom), 132.4 (CH Arom), 133.7 (Cₗₜ Ph), 137.4 (Cₗₜ Ph), 137.7 (Cₗₜ Ph), 137.8 (Cₗₜ Ph), 169.1 (CO₂CH₃); HRMS: C₃₄H₃₄O₆S + Na⁺ requires: 593.1968, found 593.1975.

**Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 2,3,4-tri-O-
benzyl-β-D-galactopyranosyl)-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; ¹H NMR (400 MHz): δ = 3.28 (s, 3H, CH₃ OMe), 
3.33 (s, 1H, CH₃ OMe), 3.39 (dd, 1H, J = 3.6 Hz, 9.6 Hz), 3.49-3.53 (m, 0.3H), 3.59 (s, 3H, CH₃ 
COOMe), 3.61-3.65 (m, 1.3H), 3.66 (s, 1H, CH₃ CH₂ OMe), 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, 3.7H), 4.22-4.99 (m, 18 H), 5.16 (d, 1H, J = 
4 Hz, H-1′); ¹³C NMR (100 MHz): δ = 51.9 (CH₃ COOMe), 51.9 (CH₃ COOMe), 54.8 (CH₃ OMe), 
54.9 (CH₃ OMe), 67.4, 67.6, 68.2, 70.1, 70.3, 71.2, 72.5, 72.6, 72.9, 73.0, 73.1, 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, 80.1, 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 (Cₗₜ Arom), 169.3 (Cₗₜ COOMe), 
170.0 (Cₗₜ COOMe); HRMS: C₅₆H₆₀O₁₂ + Na⁺ requires: 947.3977, found 947.3985.
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**para-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; 1H NMR (400 MHz): δ = 3.43 (s, 3H, CH3 COOMe), 3.45 (bs, 1H), 3.72 (s, 3H, CH3 pMP), 3.88-3.90 (m, 1H), 3.93-3.99 (m, 1H), 4.01-4.02 (m, 1H), 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); 13C NMR (100 MHz): δ = 51.6 (CH3 COOMe), 55.5 (CH3 pMP), 66.3, 67.6, 69.2, 70.9, 71.6, 72.4, 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 pMP), 118.9 (CH Arom pMP), 126.2-128.7 (CH Arom), 137.5-138.6 (Cq Arom), 151.6 (Cq pMP), 155.1 (Cq pMP), 169.7 (Cq COOMe); HRMS: C55H56O13 + Na+ requires: 947.3613, found 947.3618.

**Phenyl-2,3,4,6-tetra-O-benzyl-1-thio-β-D-gulopyranoside (37):** The title compound was prepared according to the general procedure for the synthesis of tetrabenzyl thioglycosides starting from phenyl-1-thio-β-L-gulopyranoside (1.37 g, 5 mmol) yielding 37 as transparent oil (2.41 g, 89%). [α]D = -9.17 (c = 0.02, DCM). IR (neat); 741, 1001, 1028, 1076, 1101, 1207, 1360, 1439, 1454, 1497, 2866, 3032, 3061; 1H NMR (400 MHz): δ = 3.51 (m, 1H, H-4), 3.57-3.67 (m, 2H, H-6), 3.71 (t, 1H, J = 3.2 Hz, H-3), 3.75 (dd, 1H, J = 2.8 Hz, 10.0 Hz, H-2), 4.13 (t, 1H, J = 6.4 Hz, H-5), 4.26 (d, 1H, J = 12.0 Hz, CH2 Bn), 4.31 (d, 1H, J = 12.0 Hz, CH2 Bn), 4.37 (d, 1H, J = 10.8 Hz, CH2 Bn), 4.40 (d, 1H, J = 8.8 Hz, CH2 Bn), 4.47-4.52 (m, 2H, CH2 Bn), 4.59 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.66 (d, 1H, J = 12.0 Hz, CH2 Bn), 5.23 (d, 1H, J = 10.0 Hz, H-1), 7.08-7.10 (m, 2H, H Arom), 7.12-7.35 (m, 21 H, H Arom), 7.51-7.60 (m, 2H, H Arom); 13C NMR (100 MHz): δ = 69.0 (C-6), 72.4 (CH2Ph), 72.8 (CH2Ph), 73.1 (C-3), 73.2 (CH2Ph), 73.4 (CH2Ph), 74.5 (C-4), 74.7 (C-2), 74.9 (C-4), 84.3 (C-1), 126.8-128.6 (CH Arom), 131.4 (CH Arom), 138.2 (Cq Ph); HRMS: C40H40O5S + Na+ requires: 655.2489, found 655.2487.

**Methyl 2,3,4,6-tetra-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-β-L-gulopyranoside)-α-D-glucopyranoside (40):** Glucopyranoside 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, 1360, 1454, 1497, 2870, 3030, 3063; 1H NMR (400 MHz): δ = 3.28 (s, 3H, OMe), 3.41 (dd, 1H, J = 3.6 Hz, 9.6 Hz), 3.54 (m, 2H, CH3 pMP), 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, 1H, J = 12 Hz, CH2 Bn), 4.79 (d, 1H, J = 10.8 Hz, CH2 Bn), 4.93 (d, 1H, J = 10.8 Hz, CH2 Bn), 5.06 (bs, 1H, H-1’), 7.12-7.36 (m, 35H, H Arom); 13C NMR (100 MHz): δ = 54.9 (OMe), 65.7, 66.9, 68.7, 70.4, 70.9, 72.7, 73.1, 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 (Cq Arom); HRMS: C62H66O11 + Na+ requires: 1004.4943, found 1004.4958.
para-Methoxyphenyl-2-O-benzyl-(2,3,4,6-tetra-O-benzyl-a/b/L-gulopyranoside)-4,6-benzylidene-b-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 (a/b: 1/0.12). IR (neat): 731, 824, 910, 977, 1026, 1065, 1080, 1173, 1217, 1265, 1308, 1367, 1454, 1506, 2866, 3030; 1H NMR: (400 MHz): δ = 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, CH3 pMP), 3.88-3.92 (m, 2H), 4.00-4.08 (m, 3H), 4.22 (d, 1H, J = 12 Hz, CH2 Bn), 4.28-4.46 (m, 8H), 4.57-4.64 (m, 3H), 4.68 (d, 1H, J = 10.8 Hz, CH2 Bn), 5.32 (d, 1H, J = 3.2 Hz, H-1’), 5.51 (s, 1H, CHPh), 6.77-7.54 (m, 34H, H Arom); 13C NMR (100 MHz): δ = 55.5 (OCH3 pMP), 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), 118.9 (CH Arom pMP), 114.3 (CH Arom pMP), 115.1 (Cq pMP), 126.3-128.8 (CH Arom), 137.7-139.1 (Cq Arom), 151.8 (Cq pMP), 155.1(Cq pMP); HRMS: C61H62O12 + Na+ requires: 1009.4134, found 1009.4140.

Phenyl-2,3,4-tri-O-benzyl-1-thio-b-D-antiarose (38): Antiaropyranoside 38 was prepared from Phenyl-1-thio-b-D-gulopyranoside (2.82 g, 10.3 mmol) according to the general procedure for the synthesis of 6-deoxy glycosides and 38 was obtained as a clear oil (1.53 g, 28%). IR (neat): 694, 733, 1026, 1072, 1732, 1870; 1H NMR (400 MHz): δ = 1.20 (d, 3H, J = 6.4 Hz, H-6), 3.19 (d, 1H, J = 3.2 Hz, H-4), 3.71-3.77 (m, 2H, H-2, H-3), 4.02 (q, 1H, J = 6.4 Hz, H-5), 4.28 (d, 1H, J = 12.0 Hz, CH2 Bn), 4.32 (d, 1H, J = 12.0 Hz, CH2 Bn), 4.35 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.47 (d, 1H, J = 12.4 Hz, CH2 Bn), 4.57 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.68 (d, 1H, J = 12.4 Hz, CH2 Bn), 5.20 (d, 1H, J = 10.0 Hz, H-1), 7.11-7.59 (m, 20H, H Arom); 13C NMR (100 MHz): δ = 16.2 (C-6), 71.2 (C-5), 72.3 (CH2 Bn), 72.6 (CH2 Bn), 73.1 (CH2 Bn), 73.2 (C-3), 74.4 (C-2), 77.4 (C-4), 84.0 (C-1), 126.6-128.8 (CH Arom), 131.3 (CH Arom), 134.4 (Cq Arom), 137.8-138.1 (Cq Arom); HRMS: C33H34O4S + Na+ requires: 549.2070, found 549.2061.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4-tri-O-benzyl-a/b-D-antiaropyranoside)-a-D-glucopyranoside (41): Rhamnopyranoside 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 (a/b: 1/0.08). IR (neat): 633, 694, 1026, 1069, 1358, 2341, 2870, 3028; 1H NMR: (400 MHz): δ = 1.07 (d, 3H, J = 6.4 Hz, H-6’), 3.29 (s, 3H, CH3 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, CH2 Bn), 4.47-4.81 (m, 12H), 4.93 (d, 1H, J = 10.8 Hz, CH2 Bn), 5.00 (d, 1H, J = 2.8 Hz, H-1’), 7.13-7.38 (m, 30H, H Arom); 13C NMR (100 MHz): δ = 15.6 (C-6’), 54.9 (CH3 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 (Cq Arom); HRMS: C55H66O12 + Na+ requires: 903.4079, found 903.4073.
Stereodirecting Effect of the Pyranosyl C-5 Substituent in Glycosylation Reactions

**para-Methoxyphenyl-2-O-benzyl-3-O-(2,3,4-tri-O-benzyl-α/β-D-antiapynanoside)-4,6-benzylidene-β-D-galactopyranoside (44):**

Rhamnopyranoside 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; 1H NMR: (400 MHz): δ = 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, CH3 pMP), 3.87-3.92 (m, 2H), 3.96 (dd, 1H, J = 3.6 Hz, H-1', 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, CH2 Bn), 4.57 (d, 1H, J = 12 Hz, CH2 Bn), 4.62 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.69 (d, 1H, J = 10.8 Hz, CH2 Bn), 4.73 (d, 1H, J = 10.8 Hz, CH2 Bn), 4.85 (d, 1H, J = 11.6 Hz, CH2 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); 13C NMR (100 MHz): δ = 55.5 (CH3 pMP), 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 pMP), 118.9 (CH pMP), 126.3-128.8 (CH Arom), 137.7-139.1 (Cq Arom), 151.8 (Cq pMP), 155.1 (Cq pMP); HRMS: C54H56O11 + Na+ requires: 903.3715, found 903.3712.

**Methyl (phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-glucopyranosyluronate) (48):** The title compound was prepared according to the general procedure for the synthesis of uronate esters starting from phenyl-1-thio-β-D-glucopyranoside (4.08 g, 15.0 mmol) yielding 48 as a white solid (5.5 g, 62%). [α]D = - 8.9 (c = 2, DCM); IR (neat): 745, 818, 868, 910, 980, 1026, 1076, 1153, 1207, 1288, 1358, 1439, 1454, 1497, 1740, 2905; 1H NMR: (400 MHz): δ = 3.52 (t, 1H, J = 9.6 Hz, H-2), 3.69-3.72 (m, 4H, H-3, CO2CH3), 3.84 (t, 1H, J = 9.2 Hz, H-4), 3.92 (d, 1H, J = 9.6 Hz, H-5), 4.61 (d, 1H, J = 10.8 Hz, CH2 Bn), 4.68 (d, 1H, J = 10.0 Hz, H-1), 4.72 (d, 1H, J = 10.4 Hz, CH2 Bn), 4.87 (d, 1H, J = 10.8 Hz, CH2 Bn), 4.83-4.90 (m, 3H, 2H, CH2 Bn), 7.21-7.38 (m, 18H, H Arom), 7.55 (d, 2H, J = 7.2 Hz, H Arom); 13C NMR: δ = 52.5 (CO2CH3), 75.1 (CH2 Bn), 75.5 (CH2 Bn), 75.9 (CH2 Bn), 77.9 (C-5), 79.2 (C-4), 80.2 (C-2), 85.8 (C-3), 88.3 (C-1), 127.8-129.0 (CH Arom), 132.2 (CH Arom), 133.1 (Cq SPh), 137.7 (Cq Ph), 137.8 (Cq Ph), 138.1 (Cq Ph), 168.6 (C=O CO2CH3); HRMS: C34H34O6S + Na+ requires: 593.1968, found 593.1950.

**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; 1H NMR (400 MHz): δ = 3.35 (s, 3H, CO2CH3), 3.37 (s, 1.9 H, CO2CH3 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, OCH3 α), 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' α), 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); 13C NMR (100 MHz): δ = 52.3 (CO2CH3 α or β), 52.3 (CO2CH3 α or β), 66.5 (C-6 α or β), 68.8 (C-6 α or β), 69.7 (OCH3 α or β), 70.3 (OCH3 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), 137.7-139.1 (Cq Arom), 151.8 (Cq pMP), 155.1 (Cq pMP); HRMS: C54H56O11 + Na+ requires: 903.3715, found 903.3712.
137.8 (C\textsubscript{q} Ph), 138.0 (C\textsubscript{q} Ph), 138.1 (C\textsubscript{q} Ph), 138.2 (C\textsubscript{q} Ph), 138.7 (C\textsubscript{q} Ph), 168.7 (C=O CO\textsubscript{2}Me); HRMS: C\textsubscript{56}H\textsubscript{60}O\textsubscript{12} + Na\textsuperscript{+} requires: 947.3977, found 947.3985.

**para-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 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; \textsuperscript{1}H NMR (400 MHz): δ = 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 pMP), 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); \textsuperscript{13}C NMR (100 MHz): δ = 52.2 (CO\textsubscript{2}CH\textsubscript{3} α), 52.3 (CO\textsubscript{2}CH\textsubscript{3} β), 55.5 (OCH\textsubscript{3} pMP), 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 pMP), 117.5 (C\textsubscript{q} Ph), 137.5 (C\textsubscript{q} Ph), 137.7 (C\textsubscript{q} Ph), 137.8 (C\textsubscript{q} Ph), 138.0 (C\textsubscript{q} Ph), 138.1 (C\textsubscript{q} Ph), 138.2 (C\textsubscript{q} Ph), 138.3 (C\textsubscript{q} Ph), 138.4 (C\textsubscript{q} Ph), 151.4 (C\textsubscript{q} Ph), 151.5 (C\textsubscript{q} Ph), 155.2 (C\textsubscript{q} Ph), 155.3 (C\textsubscript{q} Ph), 169.1 (C=O CO\textsubscript{2}Me β), 170.3 (C=O CO\textsubscript{2}Me α); HRMS: C\textsubscript{55}H\textsubscript{56}O\textsubscript{13} + Na\textsuperscript{+} requires: 947.3613, found 947.3621.

**Phenyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-glucospyranoside (49):** The title compound was prepared according to the general procedure for the synthesis of tetrabenzyl thioglycosides starting from phenyl-1-thio-β-D-glucospyranoside (6.81 g, 25 mmol) yielding 49 as white crystals (15.4 g, 94%). \textsuperscript{1}H NMR (400 MHz): δ = 3.47-3.54 (m, 2H, H-2, H-5), 3.63-3.78 (m, 4H, H-3, H-4, H-6), 4.50 (d, 1H, J = 12.0 Hz, CH\textsubscript{2} Bn), 4.56-4.60 (m, 2H, CH\textsubscript{2} Bn), 4.67 (d, 1H, J\textsubscript{1,2} = 9.5 Hz, H-1), 4.72 (d, 1H, J = 10.0 Hz, CH\textsubscript{2} Bn), 4.81-4.91 (m, 4H, CH\textsubscript{2} Bn), 7.04-7.39 (m, 23 H, H Arom), 7.56-7.61 (m, 2H, H Arom); \textsuperscript{13}C NMR (100 MHz): δ = 68.8 (C-6), 73.2 (CH\textsubscript{2} Bn), 74.8 (CH\textsubscript{2} Bn), 75.2 (CH\textsubscript{2} Bn), 75.6 (CH\textsubscript{2} Bn), 77.6 (C-3 or C-4), 78.9 (C-5), 80.6 (C-2), 86.6 (C-3 or C-4), 87.2 (C-1), 127.2-128.7 (CH Arom), 131.7 (CH Arom), 133.7 (C\textsubscript{q} Ph), 137.9 (C\textsubscript{q} Ph), 138.1 (C\textsubscript{q} Ph), 138.2 (C\textsubscript{q} Ph).

**Methyl 2,3,4,6-tetra-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-α/β-D-glucopyranoside)-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; \textsuperscript{1}H NMR (400 MHz): δ = 3.29 (s, 5.1 H, OCH\textsubscript{3}), 3.41-3.44 (m, 1 H), 3.47-3.52 (m, 5.4 H, OCH\textsubscript{3}), 3.54-3.63 (m, 4H), 3.71-4.00 (m, 10 H), 4.14 (d, 1H, J = 10 Hz), 4.31 (d, 1H, 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 x H Arom), 7.56-7.61 (m, 2H, H Arom); \textsuperscript{13}C NMR (100 MHz): δ = 55.0 (OCH\textsubscript{3} α), 55.1 (OCH\textsubscript{3} β), 66.3, 68.5, 68.6, 68.9, 69.3, 69.8, 70.2, 72.4,
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72.7, 72.8, 73.2, 73.3, 73.4, 73.5, 74.5, 74.7, 74.9, 75.0, 75.1, 75.6, 76.5, 77.9, 78.1, 78.2, 78.8, 80.1, 81.9, 82.0, 82.2, 97.8 (C-1'), 104.2 (C-1'), 127.3-128.3 (CH Arom), 137.8 (Cq Ph), 138.0 (Cq Ph), 138.1 (Cq Ph), 138.3 (Cq Ph), 138.4 (Cq Ph), 138.7 (Cq Ph), 138.8 (Cq Ph); HRMS: C_{62}H_{66}O_{11} + NH_{4}^+ requires: 1004.4943, found 1004.4959.

para-Methoxyphenyl-2-O-benzyl-(2,3,4,6-tetra-O-benzyl-D-glucopyranoside)-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; 1H NMR (400 MHz): δ = 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$_3$ Ph), 3.74 (s, 1.8 H, OCH$_3$ Ph), 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), 4.78-4.89 (m, 8.9 H), 4.95-5.04 (m, 4.8 H), 5.21 (d, 1H, J = 3.6 Hz, H-1'), 5.55 (s, 0.6 H, CHPh benzylidene), 5.60 (s, 1H, CHPh benzylidene); 13C NMR (100 MHz): δ = 55.5 (OCH$_3$ Ph), 55.5 (OCH$_3$ Ph), 66.3, 66.6, 68.3, 68.8, 68.9, 69.8, 71.2, 71.8, 73.0, 74.1 (α), 74.4 (CH$_2$Ph α), 74.4 (CH$_2$Bn β), 74.8 (β), 74.9 (CH$_3$ Bn α), 74.9 (CH$_3$ Bn β), 75.5 (CH$_3$ Bn α), 75.6 (CH$_3$ 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: C$_{61}$H$_{62}$O$_{12}$ + Na$^+$ requires: 1009.4134, found 1009.4141.

Methyl (phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-allopyranosyluronate) (54): The title compound was prepared according to the general procedure for the synthesis of uronate esters starting from phenyl-1-thio-β-D-allopyranoside (1.22 g, 4.50 mmol) yielding 54 as a white solid (1.30 g, 51%). [α]$_D$ = + 2.27 (c = 0.06, CH$_2$Cl$_2$); IR (neat): 729, 895, 1026, 1076, 1207, 1265, 1358, 1439, 1497, 1747, 2882, 3055; 1H NMR (400 MHz): δ = 3.31 (dd, 1H, J = 2.4 Hz, 9.6 Hz, H-2), 3.62 (dd, 1H, J = 9.6 Hz, 2.4 Hz, H-4), 3.71 (s, 3H, CO$_2$CH$_3$), 4.08 (t, 1H, J = 2.4 Hz, H-3), 4.40 (d, 1H, J = 11.6 Hz, CH$_2$ Bn), 4.44-4.51 (m, 3H, H-5, CH$_2$ Bn), 4.57 (d, 1H, J = 11.6 Hz, CH$_2$ Bn), 4.77 (d, 1H, J = 12.8 Hz, CH$_2$ Bn), 4.80 (d, 1H, J = 12.8 Hz, CH$_2$ Bn), 5.22 (d, 1H, J = 10.0 Hz, H-1), 7.19-7.33 (m, 18H, 1 H Arom), 7.34 (d, 2H, J = 3.2 Hz, H Arom), 13C NMR (100 MHz): δ = 52.2 (CO$_2$CH$_3$), 71.8 (CH$_2$ Bn), 72.3 (CH$_2$ Bn), 73.2 (C-3), 74.2 (CH$_2$ Bn), 74.5 (C-5), 77.0 (C-2), 77.2 (C-4), 84.2 (C-1), 127.3-128.7 (CH Arom), 131.9 (CH Arom), 133.2 (Cq Ph), 137.3 (Cq Ph), 137.4 (Cq Ph), 138.4 (Cq Ph), 169.5 (C=O CO$_2$CH$_3$); 13C-GATED NMR (125 MHz): 84.4 (J$_{C-1, H-1}$ = 160 Hz, C-1); HRMS: C$_{34}$H$_{34}$O$_6$S + Na$^+$ requires: 593.1968, found 593.1965.

Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 2,3,4-tri-O-benzyl-β-D-allopyranosyluronate)-α-D-glucopyranoside (56): Donor glycoside 54 (86 mg, 0.15 mmol) was condensed with glycoside 25 (105 mg, 0.225 mmol, 1.5 eq.) 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; 1H NMR (400 MHz): δ = 3.26 (s, 3H, C-1-OCH$_3$α), 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, CO2CH3 α), 3.91-3.99 (m, 2H), 4.06-4.17 (m, 1H), 4.15 (d, 1H, J = 12.0 Hz, CH2 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); 13C NMR (100 MHz): δ = 52.1 (OCH3 β), 52.1 (OCH3 α), 54.9 (CO2CH3 α), 55.1 (CO2CH3 β), 67.1 (α), 67.2 (C-6 α), 68.5 (C-6 β), 69.9 (β), 70.4 (Ca), 70.8 (CH2 Bn α), 71.2 (CH2 Bn α), 71.9 (CH2 Bn β), 72.5 (β), 72.9 (CH2 Bn β), 73.2 (β), 73.3 (CH2 Bn β), 74.0 (CH2 Bn β), 74.5 (β), 75.0 (CH2 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). 13C-GATED NMR (100 MHz): δ = 97.8 (%C-1’, H-1’α = 167 Hz, C-1’α), 97.9 (J/C-1α, H-1α = 166 Hz, C-1α); HRMS: C56H60O12 + NH4+ requires: 942.4423, found 942.4437.

**para-Methoxyphenyl-2-O-benzyl-3-O-(Methyl 2,3,4-tri-O-benzyl-D-allopyranosyluronate)-4,6-benzylidene-D-galactopyranoside (58):** Alluronic acid 54 (86 mg, 0.15 mmol) was glycosylated with galactoside 26 (105 mg, 0.225 mmol, 1.5 eq.) as described in the general procedure for glycosylations of thioglycuronates giving β-linked disaccharide 58 (72 mg, 52%) as transparent oil. [α]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; 1H NMR (400 MHz): δ = 3.46 (s, 1H, H-5), 3.54 (s, 3H, CO2CH3), 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, OCH3 pMP), 3.99-4.09 (m, 3H, H-2, H-4, H-6), 4.27 (d, 1H, J = 11.6 Hz, CH2 Bn), 5.52 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.56 (d, 1H, J = 10.4 Hz, CH2 Bn), 4.61 (d, 1H, J = 11.2 Hz, CH2 Bn), 4.71 (d, 1H, J = 10.4 Hz, CH2 Bn), 4.80 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.89-4.95 (m, 3H, H-5’, H-1, CH2 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); 13C NMR (100 MHz): δ = 52.1 (CO2CH3), 55.6 (OCH3 pMP), 66.3 (C-5), 67.0 (C-5’), 69.3 (C-6), 70.8 (CH2 Bn), 71.0 (CH2 Bn), 71.5 (C-3), 73.2 (C-3’), 74.1 (CH2 Bn), 75.0 (CH2 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 pMP), 118.8 (CH Arom pMP), 126.3, 137.1-128.9 (CH Arom), 137.7-139.0 (Cq Arom), 151.7 (Cq pMP), 155.1 (Cq pMP), 171.5 (C=O CO2Me); 13C-GATED NMR (100 MHz): δ = 92.4 (J/C-1’, H-1’α = 164 Hz, C-1’α), 102.7 (J/C-1α, H-1α = 160 Hz, C-1α); HRMS: C55H56O13 + NH4+ requires: 942.4059, found 942.4072.

**Phenyl-2,3,4,6-tetra-O-benzyl-1-thio-D-allopyranoside (55):** The title compound was prepared according to the general procedure for the synthesis of tetrabenzyl thioglycosides starting from phenyl-1-thio-D-allopyranoside (1 g, 3.67 mmol) yielding 55 as white solid (1.66 g, 72%). [α]D = -1.16 (c = 0.06, CH2Cl2); IR (neat): 729, 910, 1045, 1072, 1207, 1265, 1354, 1454, 1497, 1585, 2870, 3032; 1H NMR (400 MHz): δ = 3.31 (dd, 1H, J = 2.0 Hz, 9.6 Hz, H-2), 3.48 (dd, 1H, J = 1.6 Hz, 9.6 Hz, H-4), 3.71 (dd, 1H, J = 4.4 Hz, 10.8 Hz, H-6), 3.79 (d, 1H, J = 10.0 Hz, H-6), 4.10 (m, 2H, H-3, H-5), 4.39 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.46-4.60 (m, 5H, CH2 Bn), 4.77 (d, 1H, J = 12.0 Hz, CH2 Bn), 4.82 (d, 1H, J = 12.0 Hz, CH2 Bn), 5.26 (d, 1H, J = 10.0 Hz, H-1), 7.11-7.56 (m, 23H, H Arom), 7.57-7.59 (m, 2H, H Arom); 13C NMR (100 MHz): δ = 52.1 (C-1’), 102.7 (J/C-1α, H-1α = 160 Hz, C-1α); HRMS: C55H56O13 + NH4+ requires: 942.4059, found 942.4072.
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Ph), 138.7 (Cq Ph); 13C-GATED NMR (100 MHz): 83.6 (JC-1, H-1 = 158 Hz, C-1); HRMS: C40H40O5S + Na+ requires: 655.2489, found 655.2486.

**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 glycosylations 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, 1265, 1287, 1297, 1362, 1454, 1497, 2870, 3032; 1H NMR (600 MHz): δ = 3.26 (s, 3H), 3.31-3.33 (m, 2H), 3.39 (dd, 0.5 H, J = 3.6 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), 3.97-4.18 (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, 1H, J = 3.0 Hz), 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′), 7.07-7.36 (m, 53H, 5 H Arom); 13C NMR (125 MHz): δ = 54.9 (OCH3), 55.1 (OCH3), 66.2 (α), 66.6, 68.1, 68.6, 69.4, 69.9, 70.4, 70.6, 70.8 (CH2 Bn α), 71.5 (CH2Ph β), 72.6 (CH2 Bn β), 72.8 (α), 73.3 (CH2 Bn β), 73.3 (CH2 Bn α), 73.4 (CH2 Bn α), 73.5 (CH2 Bn β), 74.0 (CH2 Bn α), 74.4 (α), 74.5 (CH2 Bn α), 74.6 (β), 74.8 (CH2 Bn α), 75.0 (CH2 Bn β), 75.5 (CH2 Bn α), 75.6 (β), 75.6 (α), 75.6 (CH2 Bn β), 76.7 (β), 77.8 (β), 77.8 (α), 79.0 (β), 79.6 (β), 80.1 (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 (Cp Ph), 138.1 (Cp Ph), 138.1 (Cp Ph), 138.3 (Cp Ph), 138.3 (Cp Ph), 138.4 (Cp Ph), 138.5 (Cp Ph), 138.7 (Cp Ph), 138.8 (Cp Ph), 138.9 (Cp Ph), 139.0 (Cp Ph), 137.4 (Cp Ph); 13C-GATED NMR (100 MHz): δ = 97.6 (JC-1′-H-1′= 167 Hz), 101.1 (JC-1′-H-1′= 162 Hz); HRMS: C62H66O11 + NH4+ requires: 1004.4943, found 1004.4959.

**para-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]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. 1H 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, OCH3 pMP), 3.98-4.00 (m, 2H, H-3, H-2), 4.08 (d, 1H, J = 11.2 Hz, CH2 Bn), 4.32-4.59 (m, 10H, H-3′, H-5′, CH2 Bn), 4.66 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.78-4.83 (m, 2H, H Arom), 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); 13C NMR (100 MHz): δ = 65.9 (C-5′), 66.4 (C-5), 68.7 (C-6′), 69.3 (C-6), 70.6 (CH2 Bn), 70.6 (CH2 Bn), 71.6 (C-4), 73.0 (CH2 Bn), 73.5 (C-3), 74.2 (CH2 Bn), 74.6 (C-4′ or C-2′), 74.7 (C-3 or C-2), 74.8 (CH2 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 pMP), 118.9 (CH Arom pMP), 123.0-129.1 (CH Arom), 137.7 (Cq Ph), 138.0 (Cq Ph), 138.2 (Cq Ph), 138.4 (Cq Ph), 138.5 (Cq Ph), 139.4 (Cq Ph), 151.8 (Cp pMP), 155.1 (Cp pMP); 13C-GATED NMR (100 MHz): δ = 92.4 (JC-1′, H-1′ = 162 Hz, C-1′), 103.1 (JC-1, H-1 = 154 Hz, C-1). HRMS: [M+NH4]+ calcd for C61H66O12N: calcd: 1004.45795, found 1004.45933. [α]D = + 32.3 (c = 1.2, DCM); IR: 737, 826, 1003, 1092 1223, 1366, 1454, 1504, 2866; 1H 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, OCH₃ pMP), 3.96-3.99 (m, 2H, H-3, H-6), 4.04-4.14 (m, 3H, H-2, H-3'), 4.29-4.34 (m, 4H, H-1, CH₂ Bn), 4.43 (d, 1H, J = 11.6 Hz, CH₂ Bn), 4.49 (d, 1H, J = 8.8 Hz, CH₂ Bn), 4.58 (d, 1H, J = 12.4 Hz, CH₂ Bn), 4.76 (d, 1H, J = 12.0 Hz, CH₂ Bn), 4.80-4.93 (m, 6H, H-1,  CH₂ 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); 13C NMR (100 MHz): δ = 55.6 (OCH₃ pMP), 66.6 (C-4'), 69.0 (C-6), 69.53 (C-6'), 71.4 (CH₂ Bn), 72.0 (C-5'), 72.9 (CH₂ Bn), 73.4 (CH₂ Bn), 74.2 (CH₂ Bn), 74.4 (C-2), 75.2 (CH₂ 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 pMP), 119.1 (CH Arom pMP), 126.4-128.7 (CH Arom), 137.8 (Cq Ph), 138.2 (Cq Ph), 138.3 (Cq Ph), 138.4 (Cq Ph), 138.7 (Cq Ph), 151.7 (Cq pMP), 155.3 (Cq pMP); HRMS: C₆₁H₆₂O₁₂ + NH₄⁺ requires: 1004.4580, found 1004.4594.

Methyl (phenyl 2,3,4-tri-O-benzyl-1-thio-β-d-galactopyranosyluronate) (60): The title compound was prepared according to the general procedure for the synthesis of uronate esters starting from phenyl-1-thio-β-D-galactopyranoside (3.08 g, 11.3 mmol) yielding 60 as a white solid (5.25 g, 78%). IR (neat): 694, 733, 1026, 1080, 1732, 2855; 1H NMR (400 MHz): δ = 3.64 (m, 1H, H-3), 3.69 (s, 3H, CO₂CH₃), 3.94 (t, 1H, J = 9.6 Hz, H-2), 4.05 (s, 1H, H-5), 4.31 (d, 1H, J = 1.2 Hz, H-4), 4.60 (d, 1H, J = 9.6 Hz, H-1), 4.63 (d, 1H, J = 12.8 Hz, CH₂ Bn), 4.70-4.76 (m, 3H, CH₂ Bn), 4.81 (d, 1H, J = 10.4 Hz, CH₂ Bn), 4.90 (d, 1H, J = 11.6 Hz, CH₂ Bn), 7.20-7.39 (m, 18H, 1 H Arom), 7.63-7.64 (m, 2H, H Arom); 13C NMR (100 MHz): δ = 52.1 (CO₂CH₃), 72.8 (CH₂ Bn), 74.4 (CH₂ Bn), 75.0 (C-4), 75.6 (CH₂ Bn), 76.6 (C-2), 83.3 (C-3), 87.8 (C-8), 127.5-128.8 (CH Arom), 132.4 (CH Arom), 133.5 (Cq Ph), 137.9 (Cq Ph), 138.1 (Cq Ph), 151.7 (Cq pMP), 153.3 (Cq pMP); HRMS: C₅₇H₆₀O₁₂ + NH₄⁺ requires: 1004.4580, found 1004.4594.

Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 2,3,4-tri-O-benzyl-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): 694, 733, 818, 914, 1026, 1049, 1068, 1092, 1211, 1269, 1358, 1454, 1497, 1605, 1732, 1767, 2870, 3032; 1H NMR (400 MHz): δ = 3.28 (s, 3 H, OCH₃ α), 3.29 (s, 8 H, OCH₃ β), 3.40 (dd, 1H, J = 3.6 Hz, J = 9.6 Hz), 3.44-54 (m, 10 H), 3.58 (s, 3H, CO₂CH₃ α), 3.62 (s, 7H, OCH₃ pMP, CO₂CH₃ 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'), 7.18-7.36 (m, 16 H, H Arom Ph); 13C NMR (100 MHz): δ = 53.0 (OCH₃ C-1-OCH₃), 55.0 (OCH₃ CO₂CH₃), 66.8 (C-6 α), 68.6 (C-6 β), 69.9 (β), 70.1 (α), 70.7 (α), 72.7 (CH₂ Bn α), 72.9 (CH₂ Bn α), 73.0 (CH₂ Bn α), 73.2 (CH₂ Bn β), 74.4, 74.7 (CH₂ Bn β), 74.9 (β), 75.0 (CH₂ Bn β), 75.5 (CH₂ Bn β), 76.0 (CH₂ Bn β), 76.5 (α), 76.5 (α), 77.2 (α), 77.8 (α), 78.8 (β), 79.9 (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 (Cq Arom), 168.4 (C=O CO₂CH₃ β), 169.2 (C=O CO₂CH₃ α); HRMS: C₅₇H₆₀O₁₂ + NH₄⁺ requires: 942.4423, found 942.4437.
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**para-Methoxyphenyl-2-0-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 eq.) 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, 1395, 1454, 1504, 1579, 2870, 3032; 1H NMR (400 MHz): δ = 3.31 (s, 0.7 H, pMP α), 3.41-3.44 (m, 2H), 3.45 (s, 3H, pMP α), 3.56 (s, 1H, CO2CH3 β), 3.72 (s, 3H, CO2CH3 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, J = 10.0 Hz), 4.01-4.07 (m, 3H), 4.60 (d, 3H, J = 12.0 Hz), 4.67 (d, 2H, J = 11.2 Hz, CH2 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, CH2 Bn α), 5.05 (d, 0.4 H, J = 11.6 Hz, CH2 Bn β), 5.28 (d, 1H, J = 3.6 Hz, H-1′α), .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 pMP α, pMP β), 6.80 (s, 3H, J = 2.0 Hz, H Arom pMP α, pMP β), 7.02-7.39 (m, 38.5 H, H Arom), 7.54-7.56 (m, 2H, H Arom pMP), 114.3 (CH Arom pMP), 118.6 (CH Arom pMP), 126.1-128.8 (CH Arom), 137.6-138.5 (C q Arom), 151.4 (C q pMP), 155.2 (C q pMP), 168.8 (C=O CO2Me α); HRMS: C55H56O13 + NH4 + requires: 942.4059, found 942.4073.

**Phenyl-2,3,4,6-tetra-O-benzyl-1-thio-β-D-galactopyranoside (61):** The title compound was prepared according to the general procedure for the synthesis of tetrabenzyl thioglycosides starting from phenyl-1-thio-β-D-galactopyranoside (6.81 g, 25 mmol) yielding (61) as white solid (15.0 g, 92%). [α]D = + 13.1 (c = 0.2, DCM); IR (neat): 737, 810, 841, 880, 914, 941, 988, 1015, 1049, 1080, 1146, 1219, 1269, 1292, 1369, 1454, 1477, 1497, 1582, 2882, 3032, 3059; 1H NMR (400 MHz): δ = 3.59-3.66 (m, 4H, H-3, H-5, H-6), 3.93 (t, 1H, J = 9.2 Hz, H-2), 3.98 (d, 1H, J = 2.8 Hz, H-4), 4.41 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.47 (d, 1H, J = 11.6 Hz, CH2 Bn), 4.60 (d, 1H, J = 11.2 Hz, CH2 Bn), 4.64 (d, 1H, J = 9.6 Hz, H-1), 4.69-4.75 (m, 3H, CH2 Bn), 4.78 (d, 1H, J = 10.0 Hz, CH2 Bn), 4.96 (d, 1H, J = 11.2 Hz, CH2 Bn), 7.14-7.31 (m, 23H, 2 H Arom), 7.52-7.59 (m, 2H, H Arom); 13C NMR (100 MHz): δ = 51.7 (OCH3 pMP α), 52.0 (OCH3 pMP β), 55.5 (CO2CH3 α, CO2CH3 β), 66.3 (α), 66.6 (β), 68.7 (CH2 Bn β), 69.1 (CH2 Bn α), 70.5 (α), 71.3 (α), 72.2 (CH2 Bn), 73.2 (CH2 Bn), 73.8 (α), 74.3 (CH2 Bn), 74.6 (CH2 Bn), 74.7 (CH2 Bn), 75.1 (β), 75.2 (CH2 Bn), 75.3 (α), 75.5 (β), 76.2 (α), 76.8 (β), 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, C-19), 114.3 (CH Arom pMP), 118.6 (CH Arom pMP), 126.1-128.8 (CH Arom), 137.6-138.5 (C q Arom), 151.4 (C q pMP), 155.2 (C q pMP), 168.8 (C=O CO2Me α); HRMS: C55H55O13 + Na+ requires: 655.2489, found 655.2486.

**Methyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-galactopyranoside (63):** Galactoside (61) (127 mg, 0.20 mmol) was condensed with glucoside (25) (139 mg, 0.30 mmol, 1.5 eq.) according to the general procedure for glycosylations of thioglycosides, yielding (63) (132 mg, 67%) as a mixture of anomers (α/β: 1/3). [α]D = + 13.1 (c = 0.2, DCM); IR (neat): 737, 810, 841, 880, 914, 941, 988, 1015, 1049, 1080, 1146, 1219, 1269, 1292, 1369, 1454, 1477, 1497, 1582, 2882, 3032, 3059; 1H NMR (400 MHz): δ = 3.33 (s, 3H, OCH3 β), 3.35 (s, 1H, OCH3 α), 3.43-3.73 (m, 12 H), 7.14-7.31 (m, 23H, 2 H Arom), 7.52-7.59 (m, 2H, H Arom); 13C NMR (100 MHz): δ = 68.7 (C-6), 72.7 (CH2 Bn), 73.5 (C-4), 73.5 (CH2 Bn), 74.4 (CH2 Bn), 75.6 (CH2 Bn), 77.2 (C-2 + C-5), 84.1 (C-3), 87.7 (C-1); HRMS: C40H40O5S + Na+ requires: 655.2489, found 655.2486.
3.96-4.02 (m, 1.7 H), 4.18 (d, 1H, J = 10.4 Hz, CH₂ 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, CH₂ Bn), 4.97 (m, 2 H, CH₂ Bn and C-1’ α), 7.13-7.42 (m, 59H, 5 H Arom); ¹³C NMR (100 MHz): δ = 55.1 (OCH₃), 66.0, 68.4, 68.5, 69.8, 70.2, 70.3, 72.3 (CH₂ Bn), 73.3 (CH₂ Bn), 74.8 (CH₂ Bn), 74.9 (CH₂ Bn), 75.0, 75.4 (CH₂ Bn), 75.6 (CH₂ 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’ β), 97.9 (C-1 α), 98.0 (C-1 β), 103.7 (C-1’ β), 127.5-128.4 (CH Arom), 138.0 (C₆ Ph), 138.1 (C₆ Ph), 138.1 (C₆ Ph), 138.2 (C₆ Ph), 138.3 (C₆ Ph), 138.3 (C₆ Ph), 138.5 (C₆ Ph), 138.8 (C₆ Ph); HRMS: C₆₀H₆₆O₁₁ + NH₄⁺ requires: 1004.4943, found 1004.4958.

**para-Methoxyphenyl-2-O-benzyl-(2,3,4,6-tetra-O-benzyl-α-β-D-galactopyranoside)-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 eq.) 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, 1454, 1504, 2168, 2866, 3032; ¹H NMR (400 MHz): δ = 5.24 (d, 1H, J = 3.6 Hz, H-1’ α), 5.50 (s, 1H, CHPh-benzylidene), 5.55 (s, 0.1 H, CHPh-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, OCH₃), 3.88 (dd, 1H, J = 3.2 Hz, 10.0 Hz, H-3), 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, CH₂ Bn), 4.53 (d, 1H, J = 11.6 Hz, CH₂ Bn), 4.58 (m, 2H, CH₂ Bn), 4.66 (d, 1H, J = 12.0 Hz, CH₂ Bn), 4.76-4.81 (m, 3H, 2H Arom Ph), 5.01 (d, 1H, J = 10.8 Hz, CH₂ 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 pMP), 6.81 (d, 2H, J = 2.0 Hz, H Arom pMP), 7.01-7.37 (m, 28 H, 2 H Arom Ph), 7.52-7.55 (m, 2H, H Arom Ph); ¹³C NMR (100 MHz): δ = 55.5 (OCH₃), 66.2 (C-5 or C-5’), 69.3 (C-5 or C-5’), 69.2 (C-6 or C-6’), 71.3 (C-4), 71.9 (CH₂ Bn), 72.6 (CH₂ Bn), 72.9 (CH₂ Bn), 73.7 (C-3), 74.6 (CH₂ Bn), 75.1 (C-4), 75.2 (CH₂ Bn), 76.0 (C-2’), 76.8 (C-2), 78.5 (C-3), 92.6 (C-1’ β), 100.5 (C-1’ β), 110.1 (CHPh benzylidene), 103.1 (C-1 α), 103.6 (C-1 β); HRMS: C₆₁H₆₁O₁₁ + NH₄⁺ requires: 1004.4580, found 1004.4594.

**References and Notes**


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17 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.


19 Spartan’04 Wavefunction, Inc. Irvine, CA, U.S.A.

Chapter 6


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.

The relative energies of the pyranosyl oxacarbenium ion, functionalized with a CF₃ substituent at C-5 were also calculated. MP2 and MP3 calculations showed the equatorial CF₃ to be the most stable by respectively 0.23 and 0.25 kcal/mol. 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-CF₃ 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).


It is of interest to note that previous in studies with L-gulose similar stereoselectivities were obtained, indicating that double stereodifferentiation is no issue in these condensations (See ref 5).
