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Sequential Directed Epoxydation-Acidolysis from Glycals with MCPBA. A Flexible Approach to Protected Glycosyl Donors

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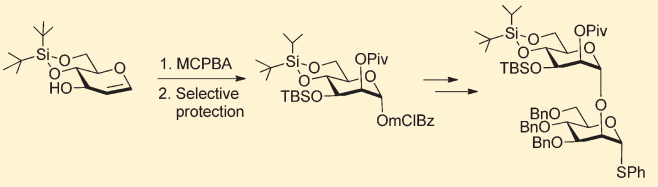
Supporting Information

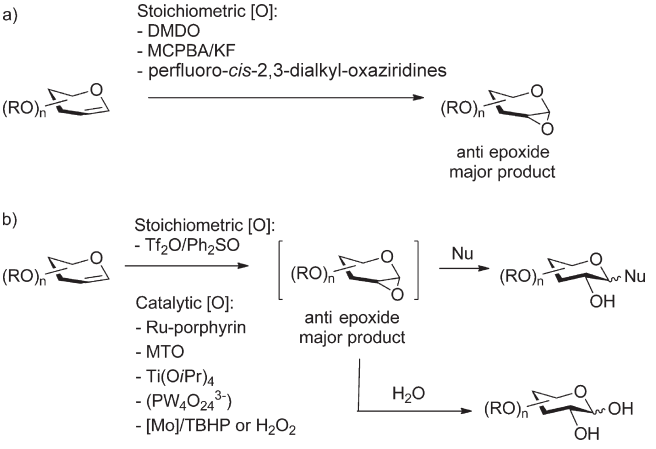
ABSTRACT: 4,6-Di-O-protected glucal and allal derivatives react with MCPBA to afford *manno*- and *allo*-1-*O*-*m*-chlorobenzoate derivatives, respectively, as a result of a syn epoxidation directed by the allylic hydroxyl group, and consecutive ring-opening by *m*-ClBzOH. When glucal and allal derivatives are fully protected, initial epoxidation proceeds mainly anti to the allylic group to give, after ring-opening, the corresponding pyranosyl chlorobenzoates. Stereoselectivity in the reaction of fully protected galactal derivatives was complete, although only a moderate increase in the syn epoxidation product was observed in 4,6- and 3,4-di-O-protected derivatives. 1-*O*-*m*-Chlorobenzoate **18** was selectively protected and activated as donor in the synthesis of disaccharide **21**.



INTRODUCTION

The synthesis of carbohydrate-based structures has become an important field of research and one of the biggest challenges of organic synthesis and medicinal chemistry.[1] In this context, efficient functionalization and selective protection procedures are key points in the synthesis of complex oligosaccharides.[1] Glycals have recently found a wide application as synthetic building blocks in the construction of various glycoconjugates.[2] One of the most direct strategies for activation of the double bond in glycals is epoxidation[3] to furnish 1,2-anhydrosugars, which are used as glycosyl donors, or as precursors of more stable glycosyl donors (Scheme 1a).[4] This transformation, however, suffers from several limitations due to the sensitive nature of the 1,2-anhydrosugar. On one hand, many epoxidation reactions lead to glycoside derivatives as a consequence of acid-catalyzed ring-opening of the labile anhydrosugar initially formed. Furthermore, an efficient epoxidation reaction of glycals must render the anhydrosugar free of any coproducts, as purification of the crude epoxide from a complex mixture is precluded. Practically the only reagent used for that purpose is dimethyldioxirane (DMDO).[3] 1,2-Anhydrosugars synthesized this way have been directly used in glycosylation events or transformed in a series of glycosyl donors, such as thioglycosides,[5] pentenyl glycosides,[6] amino glycosides,[7] glycosyl fluorides,[7] or glycosyl phosphates.[8] However, DMDO is unstable, has to be freshly prepared and poses serious safety problems, although the methods that generate it in situ[9] partially circumvent these problems. Other stoichiometric oxidants, namely MCPBA/KF[10] or perfluoro-*cis*-2,3-dialkyloxaziridines,[11] have been described to furnish highly pure sugar epoxides free of coproducts in a operationally easy way but have not found wide application in glycoconjugate synthesis, probably because of limited reaction scope or the use of nonconventional perfluorinated solvents/reagents.[12]

Scheme 1. (a) Stoichiommetric Epoxidation Methods of Glycals. (b) Tandem Epoxidation−Alcoholysis or Epoxidation−Glycosylation of Glycals



The elusive nature of 1,2-anhydro carbohydrates has motivated the development of *one-pot* epoxidation−glycosylation or epoxidation−hydrolysis of glycals in order to obtain stable glycosides or 1,2-sugar diols, that in turn are useful intermediates in several organic transformations. The stoichiometric system Tf_2O/diphenyl sulfoxide[13] promotes glycal oxidation via epoxidation−glycosylation processes. Interestingly, the use of Tf_2O−dibenzothiophene 5-oxide allows α-mannopyranosides to be obtained from glucal derivatives.

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The need for atomic economy and environmental awareness spurred the development of new catalytic epoxidation methods, but so far none have been able to provide sugar epoxides. Transition metal-based catalysts such as Ru-porphyrin,[14] CH_3ReO_3 (MTO),[15,16] Ti(O-*i*-Pr)$_4$,[17] Venturello's peroxotungstate ($PW_4O_{24}^{3}$),[17] and [Mo]/TBHP or H_2O_2[18] typically provide compounds resulting from sequential epoxidation−alcoholysis or hydrolysis[19] reactions (Scheme 1b). Most of these reactions have been explored with fully protected glucals and render the glucopyranoside derivatives as major products, as a consequence of initial sterically controlled epoxidation, mainly exerted by the substituent at C-3.

On the other hand, the synthesis of mannosylated structures[20] and related neoglycoconjugates mimicking natural systems is a hot spot in glycobiology. One of the goals is to obtain multivalent carbohydrate systems in order to enhance the weak affinity of individual carbohydrate−protein interactions. Another objective is the synthesis of oligosaccharides for biochemical studies. Both synthetic approaches rely on protection and deprotection strategies leading to multistep syntheses and too often represent the bottleneck of these synthetic strategies. Some examples of synthesis of orthogonally protected galactose,[21] *N*-acetyl glucosamine,[22] and mannose[23] derivatives have been described.

In this context, the aim of this work was to provide an easy access to orthogonally protected mannopyranoside derivatives. Here we present a systematic study of the epoxidation−glycosylation of glycals with MCPBA in order to obtain glycopyranosides. The idea is to use partially protected glycals with free hydroxyl groups in the allylic position in order to deliver the electrophilic oxygen to the sterically more congested glycal stereoface syn to the allylic alcohol, by promoting hydrogen bonding between the hydroxyl group and MCPBA. This transformation is anticipated to invert the typical stereoselectivity outcome of the oxidation reactions from fully protected glycals. The directed syn-oxidation of allylic alcohols with MCPBA has been widely documented, but it has not been systematically applied to unprotected glycals.[24]

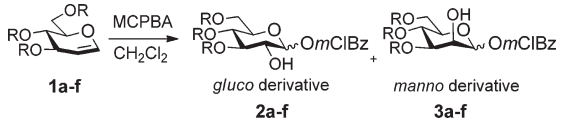
RESULTS AND DISCUSSION

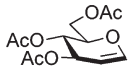
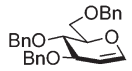
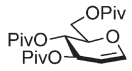
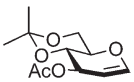
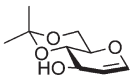
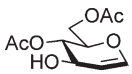
Oxidation of tri-*O*-acetyl-D-glucal (**1a**) with MCPBA in dichloromethane as the solvent afforded a mixture of *m*-chlorobenzoyl-*gluco*- (**2a**) and *manno*-pyranoside (**3a**) in a ratio 80:20 (Table 1, entry 1), as a result of glycal epoxidation to give the *gluco*- and *manno*-epoxides followed by ring-opening by the *m*-chlorobenzoate anion generated in situ (Scheme 2). Tri-*O*-benzyl-glucal (**1b**) provided a similar behavior, and the corresponding glycosides were obtained in quantitative yield and comparatively improved stereoselectivity, ratio gluco:manno = 84:16 (Table 1, entry 2). The use of bulkier protecting groups, such as pivaloate groups in glycal **1c**,[25] did not afford better stereoselectivities (Table 1, entry 3). Although α/β mixtures were obtained in all cases, the product derived from the α-epoxide (gluco), trans to the C-3 substituent, was the major one.

Oxidation of the conformationally more rigid glucal derivative **1d** furnished glycosides **2d** and **3d** with similar stereoselectivity to those of the previous examples (Table 1, entry 4). In order to reverse the stereoselectivity of the process, the directing effect of a hydroxyl group at the allylic position was explored. Gratifyingly, when partially protected glucal **1e**[26] reacted with MCPBA, glycoside **3e** derived from the *manno*-epoxide was exclusively obtained in 83% yield (Table 1, entry 5). In rigid systems such as this one, the directing effect can be conditional on conformational effects. The high level of stereoselectivity obtained in **1e**, however, is indicative of a directing effect, and actually the $^4H_5$ conformation of glycal **1e** seems to fit well with the postulated transition state model for MCPBA epoxidation of allylic alcohols, where the dihedral angle ranges 120−140° (Figure 1a).[27] Oxidation of 4,6-di-*O*-acetyl-D-glucal (**1f**)[28] was carried out in order to confirm the hydroxyl group directing effect in conformationally more flexible compounds (Table 1, entry 6). The product derived from the *manno*-epoxide **3f** was again preferentially obtained in 76% yield with a selectivity gluco:manno 10:90.

MCPBA oxidation of allal derivatives **4a** and **4b**,[29] with an allylic substituent in a pseudoaxial position, was also analyzed

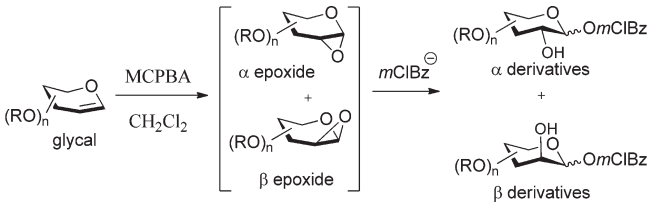
Table 1. MCPBA-Induced Stereoselective Tandem Epoxidation−Glycosylation of Glucals 1a−f



Entry[a]	Substrate	t (h)	Conv (%)	2a-f/3a-f[b]
1	 **1a**	1	>98	80 : 20[c]
2	 **1b**	1	>98	84 : 16[c]
3	 **1c**	5	>98	79 : 21[c]
4	 **1d**	3	>98	80 : 20[c]
5	 **1e**	1	>98	< 2 :98[d]
6	 **1f**	1	>98	10 : 90[d]

[a] Conditions: 0.36 mmol of glycal, 0.72 mmol of MCPBA, 11.5 mL of anhydrous CH_2Cl_2, rt. [b] Determined by NMR by integration of the anomeric protons of the crude reaction mixture. [c] Both compounds were obtained as α/β mixtures. [d] Only the α anomer was detected.

Scheme 2. MCPBA-Mediated Tandem Epoxidation-Ring-Opening of Glycals



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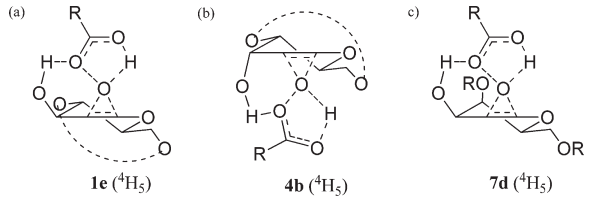
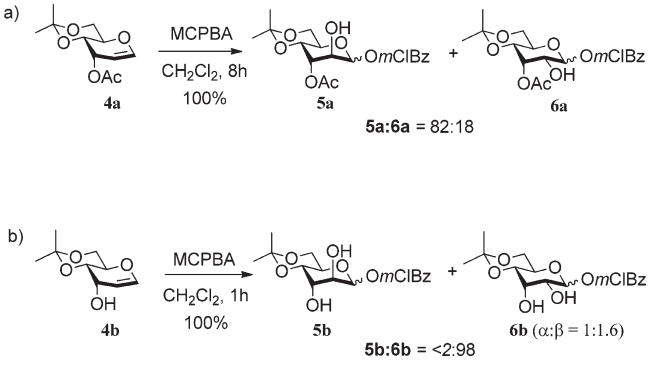


Figure 1. Proposed transition states for the 3-OH directed epoxidation with MCPBA of glucal **1e** (a), allal **4b** (b), and galactal **7d** (c).

Scheme 3. MCPBA-Mediated Epoxidation−Acidolysis of (a) Protected Allal 4a and (b) Partially Protected Allal 4b

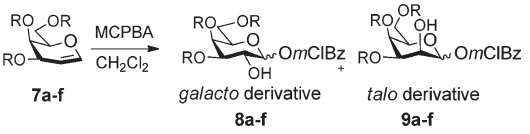


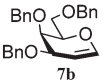
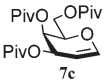
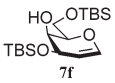
(Scheme 3). As expected, oxidation of fully protected allal **4a** rendered *altro*-glycoside **5a** as the major product, as a consequence of epoxidation on the more accessible glycal face. Reaction from partially protected allal **4b**, in contrast, furnished exclusively *allo*-glycoside **6b** in 90% yield, confirming the directing effect of the allylic hydroxyl group in the MCPBA-mediated oxidation of glycals (Figure 1b).

The effect of glycal configuration in the stereoselectivity of MCPBA-mediated epoxidation−glycosylation was extended to galactal derivatives (Table 2). Oxidation of tri-*O*-acetyl-D-galactal (**7a**) afforded galactoside **8a** as the major product (**8a**/**9a** ratio = 82:18) (Table 2, entry 1), similar to the selectivity obtained for the glucal analogue. Similarly, oxidation of tri-*O*-benzyl derivative **7b** furnished **8b** as the major product with a galacto:talo ratio = 85:15 (Table 2, entry 2), again similar to the selectivity obtained in the glucal analogue. Oxidation of tri-*O*-pivaloyl-D-galactal (**7c**)[25] afforded exclusively **8c** in 88% yield (Table 2, entry 3), improving the selectivity obtained with the gluco analogue **1c**. The axial substituent at C-4 plays a major role in the stereofacial bias of the glycal toward epoxidation, directing oxygen transfer preferentially from the opposite face.

Partially protected galactal derivatives having free hydroxyl groups at positions 3, 4, or 6 (**7d**−**f**) were also tested. When compound **7d**,[28] with a free allylic hydroxyl group, was treated with MCPBA, the galacto derivative **8d** was still the major product although the percentage of the talo derivative **9d** increased significantly (galacto:talo ratio = 67:33) (Table 2, entry 4). The presence of an axial substituent at C-4 may destabilize the transition state that involves the complexation of MCPBA to the 3-OH (Figure 1c). Virtually the same selectivity was obtained from oxidation of glycal **7e**,[30] with a a free hydroxyl group at position 6 (Table 2, entry 5), although implication of a directing effect of the distal hydroxyl group is rather unlikely, especially if the $^4H_5$ half-chair conformation of the glycal is considered. Oxidation of

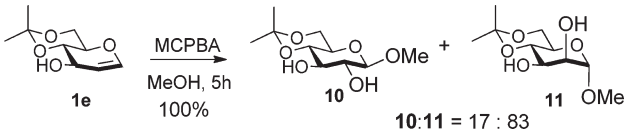
Table 2. MCPBA-Induced Stereoselective Tandem Epoxidation−Glycosylation of Galactal Derivatives 7a−f



Entry[a]	Substrate	t (h)	Conv (%)	**8a-f/9a-f**[b,c]
1	 **7a**	1	>98	82 : 18
2	 **7b**	1	>98	85 : 15
3	 **7c**	5	>98	> 98 : 2
4	 **7d**	2	>98	67 : 33
5	 **7e**	3	>98	72 : 28
6	 **7f**	2	>98	90 : 10

[a] Conditions: 0.36 mmol of glycal, 0.72 mmol of MCPBA, 11.5 mL of anhydrous CH_2Cl_2, rt. [b] Determined by NMR by integration of the anomeric protons of the crude reaction mixture. [c] Both compounds were obtained as α/β mixtures.

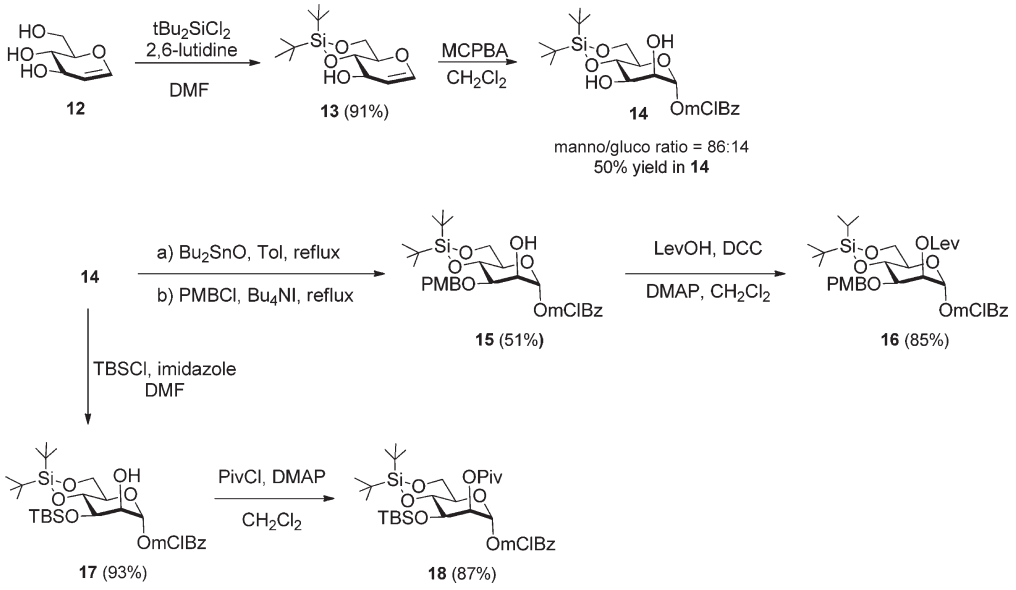
Scheme 4. MCPBA-Mediated Epoxidation of Partially Protected Glucal 1e



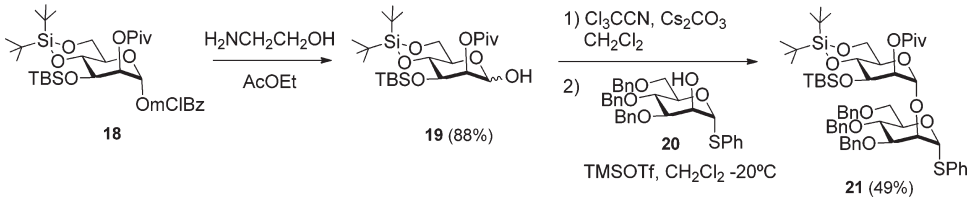
galactal **7f**[31] led to the galacto derivative **8f** in 85% yield with an excellent stereoselectivity (**8f**/**9f** ratio = 90:10). Homoallylic hydroxyl groups can direct epoxidation in cyclic systems, especially if they occupy axial positions. Probably the presence of bulky groups at positions 3 and 6 limits the coordination of MCPBA to the hydroxyl group. Thus, the directing effect of a hydroxyl group in the oxidation of galactals is rather weak and is very sensitive to steric interferences.

Tandem epoxidation−alcoholysis has been reported using mainly metal catalysts.[15−17] We explored this tandem reaction using MCPBA in methanol as a solvent. Under these conditions, methyl glycosides **10** and **11**[32] were obtained (Scheme 4) in a 17:83 ratio, with a manno stereoselectivity partially eroded with respect to its analogous reaction in CH_2Cl_2 (compare with Table 1, entry 5, where only the manno derivative was detected). The use of polar alcoholic solvents may partially cancel this syn-directing effect by disturbing the hydrogen bonding. Epoxidation−methanolysis of tri-*O*-acetyl-D-glucal

Scheme 5. Synthesis of Orthogonally Protected α-Mannopyranoside Building Blocks



Scheme 6. Synthesis of Disaccharide 21



with methyltrioxorhenium (MTO) or supported MTO derivatives and urea hydrogen peroxide adduct in ionic liquids have been described to give, at best, 36:64 mixtures of the gluco: manno methyl glycosides,[15,16] whereas the analogous reaction with Ti(O-*i*-Pr)$_4$ provided highly stereoselectivity (gluco/manno ratio = 6:94) although it required long reaction times (170 h) and did not lead to full conversion.[17]

The usefulness of the directed tandem epoxidation−glycosylation procedure developed in this paper was demonstrated by the straightforward synthesis of the *manno*-glycosyl donors **16** and **18** (Scheme 5). Compound **13** was prepared from D-glucal (**12**) following reported procedures.[33] The reaction of **13** with MCPBA under the previously reported conditions afforded compound **14** in 50% yield. Monoprotection of the equatorial hydroxyl function in **14** by forming first the stannyl acetal and consecutive addition of *p*-methoxybenzyl chloride afforded compound **15**.[34] Subsequent acylation of the free hydroxyl group at position 2 with levulinic acid/DCC gave orthogonally protected mannopyranoside **16** in 43% yield (two steps).[35] Compound **18** was prepared from diol **14** via sequential silylation and pivaloylation following the Seeberger procedure.[36] Orthogonally protected chlorobenzyl α-mannopyranosides **16** and **18** were synthesized in five and four steps from D-glucal in overall yields of 20% and 37%, respectively.

Compound **18** was then selected to test its potential use as donor in glycosylation reactions. Thus, the treatment of **18** with 2-aminoethanol afforded mannose derivative **19** in 88% yield. Then, **19** was reacted with trichloroacetonitrile to form the corresponding thichloroacetamidite, which was treated in situ with the acceptor **20** and TMSOTf as activator. The reaction was conducted for 2 h to afford disaccharide **21** in 49% yield (Scheme 6).

CONCLUSION

Partially unprotected glycals with free hydroxyl groups in the allylic position direct the stereoselectivity of the epoxidation with MCPBA to give the *syn*-epoxide, which is opened in situ under the reaction conditions to give glycosylated compounds. The reaction was completely stereoselective when glucal **1e** and allal **4b** derivatives were the starting materials and very stereoselective with glucal **1f**. Oxidation of galactal derivatives proceeded with much lower stereocontrol, probably due to destabilization of the transition state by the presence of an axial substituent at C-4. When the allyl hydroxyl group was protected, products derived from the *anti*-epoxide were obtained. Orthogonally protected *manno*-glycosyl donors **16** and **18** have been synthesized using this procedure in only five and four steps in 20% and 37% overall yields, respectively. Compound **18** was hydrolyzed, activated as the trichloroacetimidate, and used as a donor to afford disaccharide **21**, which demonstrates that this compound can be used as glycosyl donor.

EXPERIMENTAL SECTION

General Experimental Methods. All chemicals used were reagent grade and used as supplied. Glucals **1a**,**b** and galactals **7a**,**b** were commercially available. Glycals **1d** and **4a** were obtained through a

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conventional procedure for acetylation. All other glycals were synthesized according to literature procedures: **1c**,[25] **1e**,[26] **1f**,[28] **4b**,[29] **7c**,[25] **7d**,[28] **7e**,[30] **7f**,[31] **13**.[33] HPLC grade dichloromethane (CH_2Cl_2), tetrahydrofuran (THF), dimethylformamide (DMF), and diethyl ether were dried using a solvent purification system. The other solvents were purified using standard procedures.[37] ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent at 400 and 100 MHz, respectively, with chemical shifts (δ) referenced to internal standards $CDCl_3$ (7.27 ppm ^1H, 77.23 ppm ^{13}C) or Me_4Si as an internal reference (0.00 ppm), unless otherwise specified. The 2D correlation spectra (TOCSY, gCOSY, NOESY, gHSQC, gHMBC) were visualized using VNMR program. Optical rotations were measured at 598 nm at room temperature with 10 cm cells. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F_{254} glass or aluminum plates. Compounds were visualized by UV (254 nm) irradiation or dipping the plate in a suitable developing solution. Flash column chromatography was carried out using forced flow or by gravity of the indicated solvent on silica gel 60 (230−400 mesh). Radial chromatography was performed on 1, 2, or 4 mm plates of 60 PF_{254} silica gel, depending on the amount of product.

General Procedure for MCPBA Epoxidation. To a solution of glycal (0.36 mmol) in dry CH_2Cl_2 (11.5 mL) was added MCPBA (180 mg, 0.72 mmol). The mixture was stirred at room temperature. The reaction was monitored by TLC until the starting material was consumed. The solution was extracted with CH_2Cl_2 and washed successively with saturated aqueous $NaHCO_3$ and water. The solution was dried over $MgSO_4$, and then the solvent was removed under reduced pressure. The resulting residue was analyzed by ^1H NMR.

1-*O*-(3-Chlorobenzoyl)-4,6-*O*-isopropylidene-α-D-mannopyranoside (3e). Following the general procedure, **1e** (0.05 g, 0.27 mmol) was reacted with MCPBA (0.07 g, 0.54 mmol) to furnish compound **3e** as a white solid (0.08 g, 0.22 mmol, 83%), after purification by flash chromatography (hexane/EtOAc 1:2). Mp 175−177 °C.

Data for **3e**: $[\alpha]^{25}_D$ +17.8 (*c* 1.18, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 7.99 (bs, 1H), 7.94 (dd, 1H, *J* = 8.0, 1.2 Hz), 7.59 (ddd, 1H, *J* = 8.0, 1.2, 1.2 Hz), 7.43 (dd, 1H, *J* = 8.0, 8.0 Hz), 6.37 (d, 1H, *J* = 1.2 Hz), 4.18 (bs, 1H), 4.09 (d, 1H, *J* = 5.2 Hz), 3.91−3.76 (m, 4H), 1.54 (s, 3H), 1.45 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 163.4, 135.0, 134.0, 131.0, 130.2, 130.0, 128.3, 100.5, 94.5, 70.9, 70.2, 69.3, 66.8, 62.1, 29.3, 19.5. FT-IR (neat) ν in cm^{-1}: 3418, 3291, 2994, 2925, 1730, 1252, 1083, 961, 856, 744. HRMS (ESI^+) *m*/*z* calcd for $C_{16}H_{19}ClNaO_7$ [M − Na]: 381.0717, found: 381.0703.

4,6-Di-*O*-acetyl-1-*O*-(3-chlorobenzoyl)-α-D-mannopyranoside (3f). Following the general procedure, **1f** (0.03 g, 0.13 mmol) was reacted with MCPBA (0.05 g, 0.26 mmol) to afford a 1:9 mixture of compounds **2f** and **3f**. Purification by radial chromatography (hexane/EtOAc 1:2) afforded compound **3f** as a white solid (0.04 g, 0.10 mmol, 76%). Mp 140−142 °C.

Data for **3f**: $[\alpha]^{25}_D$ +4.79 (*c* 0.7, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 7.98 (s, 1H), 7.92 (d, 1H, *J* = 8.0 Hz), 7.60 (ddd, 1H, *J* = 8.0, 1.2, 1.2 Hz), 7.44 (dd, 1H, *J* = 8.0, 8.0 Hz), 6.43 (d, 1H, *J* = 2.0 Hz), 5.19 (dd, 1H, *J* = 9.6, 9.6 Hz), 4.38 (dd, 1H, *J* = 12.4, 4.4 Hz), 4.14 (dd, 1H, *J* = 9.6, 2.0 Hz), 4.16−4.05 (m, 3H), 2.17 (s, 3H), 2.09 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 172.1, 171.1, 163.2, 134.2, 134.2, 130.9, 130.3, 130.0, 128.3, 94.0, 70.8, 70.5, 70.0, 69.5, 62.4, 21.2, 21.0. FT-IR (neat) ν in cm^{-1}: 3424, 3303, 2931, 1733, 1250, 1084, 964, 858, 744. HRMS (ESI^+) *m*/*z* calcd for $C_{17}H_{19}ClNaO_9$ [M − Na]: 425.0615, found: 425.0606.

1-*O*-(3-Chlorobenzoyl)-4,6-*O*-isopropylidene-α-D-allopyranoside (6bα) and 1-*O*-(3-Chlorobenzoyl)-4,6-*O*-isopropylidene-β-D-allopyranoside (6bβ). Following the general procedure, **4b** (0.04 g, 0.21 mmol) was reacted with MCPBA (0.11 g, 0.42 mmol) to afford **6b** (0.07 g, 0.19 mmol, 90%) as a mixture α:β = 48:52. Compound **6bβ** was obtained in a pure form by purification by radial chromatography (hexane/EtOAc 2:1) as a white solid. Mp 88−90 °C.

Data for **6bβ**: $[\alpha]^{25}_D$ −15.65 (*c* 0.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 8.08 (dd, 1H, *J* = 1.6, 1.6 Hz), 7.99 (d, 1H, *J* = 8.0 Hz), 7.56 (ddd, 1H, *J* = 8.0, 1.2, 1.2 Hz), 7.40 (dd, 1H, *J* = 8.0, 8.0 Hz), 6.07 (d, 1H, *J* = 8.4 Hz), 4.32 (dd, 1H, *J* = 2.8, 2.4 Hz), 4.03−3.96 (m, 2H), 3.81 (dd, 1H, *J* = 8.4, 3.6 Hz), 3.77−3.69 (m, 2H), 1.53 (s, 3H), 1.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 164.3, 134.8, 133.9, 131.1, 130.3, 130.0, 128.5, 100. 0, 94.3, 71.3, 70.6, 69.6, 64.9, 62.3, 29.1, 19.4. FT-IR (neat) ν in cm^{-1}: 3390, 2941, 1734, 1250, 1066, 1024, 747. HRMS (ESI^+) *m*/*z* calcd for $C_{16}H_{19}ClNaO_7$ [M − Na]: 381.0717, found: 381.0679.

Spectroscopic data of **6bα** from the α/β mixture: ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 8.05 (d, 1H, *J* = 1.6 Hz), 7.97 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.61 (d, 1H, *J* = 8.0 Hz), 7.45 (dd, 1H, *J* = 8.0, 7.6 Hz), 6.56 (d, 1H, *J* = 4.0 Hz), 5.57 (dd, 1H, *J* = 3.2, 1.2 Hz), 5.41 (dd, 1H, *J* = 10.4, 3.2 Hz), 4.38 (dd, 1H, *J* = 7.2, 6.8 Hz), 4.27 (dd, 1H, *J* = 10.4, 4.0 Hz), 4.11 (dd, 1H, *J* = 10.8, 6.8 Hz), 4.05 (dd, 1H, *J* = 10.8, 7.2 Hz), 1.28 (s, 9H), 1.22 (s, 9H), 1.13 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 178.9, 178.0, 177.0, 164.0, 135.1, 134.1, 130.9, 130.3, 130.1, 128.2, 93.2, 70.7, 69.7, 67.3, 67.2, 61.1, 39.3, 39.2, 38.9, 27.4, 27.3, 27.2.

1-*O*-(3-Chlorobenzoyl)-3,4,6-tri-*O*-pivaloyl-α-D-galactopyranoside (8cα) and 1-*O*-(3-Chlorobenzoyl)-3,4,6-tri-*O*-pivaloyl-β-D-galactopyranoside (8cβ). Following the general procedure for MCPBA epoxidation, **8cα** and **8cβ** were synthesized from **7c** (0.08 g, 0.2 mmol) and MCPBA (0.10 g, 0.4 mmol). The final products **8cα** and **8cβ** were obtained in a ratio 21:79, respectively. Purification by radial chromatography (hexane/EtOAc 9:1) afforded compounds **8cα** (0.03 g, 0.06 mmol, 27%) and **8cβ** (0.07 g, 0.12 mmol, 61%) as colorless syrups (overall yield 88%).

Data for **8cα**: $[\alpha]^{25}_D$ +30.5 (*c* 0.74, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 8.05 (d, 1H, *J* = 1.6 Hz), 7.97 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.61 (d, 1H, *J* = 8.0 Hz), 7.45 (dd, 1H, *J* = 8.0, 7.6 Hz), 6.56 (d, 1H, *J* = 4.0 Hz), 5.57 (dd, 1H, *J* = 3.2, 1.2 Hz), 5.41 (dd, 1H, *J* = 10.4, 3.2 Hz), 4.38 (dd, 1H, *J* = 7.2, 6.8 Hz), 4.27 (dd, 1H, *J* = 10.4, 4.0 Hz), 4.11 (dd, 1H, *J* = 10.8, 6.8 Hz), 4.05 (dd, 1H, *J* = 10.8, 7.2 Hz), 1.28 (s, 9H), 1.22 (s, 9H), 1.13 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 178.9, 178.0, 177.0, 164.0, 135.1, 134.1, 130.9, 130.3, 130.1, 128.2, 93.2, 70.7, 69.7, 67.3, 67.2, 61.1, 39.3, 39.2, 38.9, 27.4, 27.3, 27.2. FT-IR (neat) ν in cm^{-1}: 3462, 2970, 1738, 1365, 1217. FT-IR (neat) ν in cm^{-1}: 3462, 2970, 1738, 1365, 1229, 1217, 1023, 748. HRMS (ESI^+) *m*/*z* calcd for $C_{28}H_{39}ClNaO_{10}$ [M − Na]: 593.2129, found: 593.2101.

Data for **8cβ**: $[\alpha]^{25}_D$ +9.39 (*c* 1.94, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 8.09 (dd, 1H, *J* = 2.0, 2.0 Hz), 8.01 (dd, 1H, *J* = 7.6, 2.0 Hz), 7.57 (dd, 1H, *J* = 8.0, 2.0 Hz), 7.41 (dd, 1H, *J* = 8.0, 7.6 Hz), 5.87 (d, 1H, *J* = 8.0 Hz), 5.48 (d, 1H, *J* = 3.2 Hz), 5.16 (dd, 1H, *J* = 10.4, 3.2 Hz), 4.24−4.03 (m, 4H), 1.29 (s, 9H), 1.20 (s, 9H), 1.18 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 178.4, 178.1, 177.0, 163.9, 134.8, 134.0, 130.9, 130.3, 130.2, 128.5, 95.2, 73.2, 72.3, 69.3, 66.9, 61.0, 39.3, 39.1, 38.9, 27.4, 27.3, 27.2. FT-IR (neat) ν in cm^{-1}: 3447, 2970, 1739, 1365, 1217, 1066, 746. HRMS (ESI^+) *m*/*z* calcd for $C_{28}H_{39}ClNaO_{10}$ [M − Na]: 593.2129, found: 593.2096.

3,6-Di-*O*-*tert*-butyldimethylsilyl-1-*O*-(3-chlorobenzoyl)-α-D-galactopyranoside (8fα) and 3,6-Di-*O*-*tert*-butyldimethylsilyl-1-*O*-(3-chlorobenzoyl)-β-D-galactopyranoside (8fβ). Following the general procedure, **7f** (0.08 g, 0.16 mmol) was reacted with MCPBA (0.10 g, 0.32 mmol) to afford **8f** (0.07 g, 0.14 mmol, 85%) as a mixture α:β = 57:43, from a mixture of diastereoisomers galacto/talo = 90:10. Products **8fα** and **8fβ** were obtained in a pure form by purification by radial chromatography (hexane/EtOAc 3:1) as colorless syrups.

Data for **8fα**: $[\alpha]^{25}_D$ +40.57 (*c* 0.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 7.93 (dd, 1H, *J* = 2.0, 2.0 Hz), 7.86 (d, 1H, *J* = 7.6 Hz), 7.53 (ddd, 1H, *J* = 7.6, 2.0, 0.8 Hz), 7.36 (dd, 1H, *J* = 7.6, 7.6 Hz), 6.43 (d, 1H, *J* = 4.0 Hz), 4.12−4.09 (m, 1H), 3.99−3.95 (m, 2H), 3.92−3.83 (m, 2H), 3.73 (dd, 1H, *J* = 10.0, 5.2 Hz), 2.65 (bs, 1H), 0.90 (s, 9H), 0.81 (s, 9H), 0.20 (s, 6H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$,

100.6 MHz) δ in ppm: 164.3, 134.9, 133.7, 131.8, 130.1, 130.0, 128.1, 93.7, 72.9, 72.5, 69.5, 68.7, 62.1, 26.0, 25.9, 18.5, 18.4, −4.2, −4.4, −5.2, −5.3. FT-IR (neat) ν in cm^{-1}: 3447, 2927, 1735, 1253, 1099, 835, 778. HRMS (ESI^+) m/z calcd for $C_{25}H_{43}ClNaO_7Si_2$ [M − Na]: 569.2134, found: 569.2123.

Spectroscopic data of **8f*β*** from the reaction crude product: ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 7.96−7.87 (m, 2H), 7.64−7.55 (m, 2H), 5.77 (d, 1H, J = 8.0 Hz), 4.20−3.73 (m, 6H), 0.95 (s, 9H), 0.88 (s, 9H), 0.17 (s, 6H), 0.08 (s, 6H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 164.3, 134.7, 133.6, 131.4, 129.9, 128.1, 128.0, 95.2, 75.4, 75.3, 71.1, 70.8, 68.8, 61.5, 26.0, 25.8, 18.4, 18.3, −4.4, −4.6, −5.1, −5.2.

Methyl 4,6-*O*-Isopropylidene-*β*-D-glucopyranoside (10) and Methyl 4,6-*O*-Isopropylidene-*α*-D-mannopyranoside (11).[32] To a solution of **1e** (0.06 g, 0.32 mmol) in dry MeOH (10 mL) was added MCPBA (144 mg, 0.64 mmol). The mixture was stirred at room temperature. The reaction was monitored by TLC until the starting material was consumed. After 5 h, the solution was extracted with EtOAc and washed successively with saturated aqueous $NaHCO_3$ and water. The solution was dried over $MgSO_4$, and then the solvent was removed under reduced pressure to afford a 17:83 mixture of compounds **10** and **11**. Purification by radial chromatography (hexane/EtOAc 1:2), afforded compounds **10** (0.06 g, 0.26 mmol, 80%) and **11** (0.01 g, 0.04 mmol, 13%) as white solids (overall yield 93%).

Data for **10**: Mp 74−76 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 4.29 (d, 1H, J = 8.0 Hz), 3.95 (dd, 1H, J = 10.8, 5.6 Hz), 3.81 (dd, 1H, J = 10.8, 10.4 Hz), 3.69 (dd, 1H, J = 9.2, 8.8 Hz), 3.58 (dd, 1H, J = 10.0, 9.2 Hz), 3.57 (s, 3H), 3.46 (dd, 1H, J = 8.8, 8.0 Hz), 3.29 (ddd, 1H, J = 10.0, 10.0, 5.6 Hz), 1.52 (s, 3H), 1.45 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 104.3, 100.0, 74.9, 73.7, 73.3, 67.5, 62.2, 57.7, 29.9, 29.2.

Data for **11**: Mp 107−109 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 4.74 (d, 1H, J = 1.2 Hz), 4.02 (dd, 1H, J = 3.2, 1.2 Hz), 3.97−3.91 (m, 2H), 3.90−3.80 (m, 2H), 3.66−3.60 (m, 1H), 3.37 (s, 3H), 1.53 (s, 3H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 101.4, 100.3, 71.5, 71.1, 69.3, 63.9, 62.4, 55.2, 29.4, 19.5.

4,6-Di-*O*-(*tert*-butyl)silanediyl-1-*O*-(3-chlorobenzoyl)-*α*-D-mannopyranoside (14). Following the general procedure, **13** (0.68 g, 2.36 mmol) was reacted with MCPBA (1.16 g, 4.72 mmol) to afford a 14:86 mixture of compounds β-gluco and α-manno **14**. Purification by radial chromatography (hexane/EtOAc 1:2) afforded compound **14** as a white solid (0.2 g, 0.44 mmol, 50%). Mp 125−127 °C.

Data for **14**: $[\alpha]^{25}_D$ +31.44 (c 0.63, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 7.97 (d, 1H, J = 2.0 Hz), 7.91 (ddd, 1H, J = 8.0, 0.8, 0.8 Hz), 7.59 (ddd, 1H, J = 8.0, 2.0, 0.8 Hz), 7.43 (dd, 1H, J = 8.0, 8.0 Hz), 6.36 (d, 1H, J = 1.6 Hz), 4.21−4.16 (m, 2H), 4.14 (dd, 1H, J = 10.0, 4.8 Hz), 4.02 (dd, 1H, J = 9.6, 3.6 Hz), 3.97 (dd, 1H, J = 10.0, 10.0 Hz), 3.89 (ddd, 1H, J = 10.0, 9.6, 4.8 Hz), 2.90 (bs, 1H), 2.77 (bs, 1H), 1.08 (s, 9H), 1.02 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 163.2, 135.1, 134.0, 131.2, 130.2, 130.1, 128.1, 93.9, 74.3, 71.9, 69.7, 69.5, 66.3, 27.6, 27.1, 22.9, 20.2. FT-IR (neat) ν in cm^{-1}: 3504, 3270, 2933, 2858, 1737, 1253, 1104, 959, 855, 825, 763. HRMS (ESI^+) m/z calcd for $C_{21}H_{31}ClNaO_7Si$ [M − Na]: 481.1425, found: 481.1417.

4,6-Di-*O*-(*tert*-butyl)silanediyl-1-*O*-(3-chlorobenzoyl)-3-*O*-(4-methoxybenzyl)-*α*-D-mannopyranoside (15).[34] A mixture of **14** (137.4 mg, 0.32 mmol) and dibutyltin oxide (89.2 mg, 0.35 mmol) in toluene (8.6 mL) was refluxed under Dean−Stark conditions for 3 h. The reaction mixture was allowed to cool to room temperature, and DMF (0.3 mL) was added to the mixture. 4-Methoxybenzyl chloride (46 μL, 0.35 mmol) and TBAI (122.2 mg, 0.35 mmol) were added, and the mixture was heated at reflux for 3 h. Then, the mixture was diluted with EtOAc (5 mL), washed with H_2O (2 × 5 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure, followed by flash chromatography on silica gel (hexane/EtOAc 3:1), affording the title compound as a colorless oil (88.9 mg, 0.16 mmol, 51%).

Data for **15**: $[\alpha]^{25}_D$ +65.6 (c 2.76, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ in ppm: 7.93 (s, 1H); 7.86 (d, 1H, J = 7.6 Hz); 7.60 (dt, 1H, J = 7.6, 1.0, 1.0 Hz); 7.43 (t, 1H, J = 7.6 Hz); 7.35 (d, 2H, J = 8.4 Hz); 6.90 (d, 2H, J = 8.4 Hz); 6.32 (d, 1H, J = 1.6 Hz); 4.96 (d, 1H, J = 11.2 Hz); 4.78 (d, 1H, J = 11.2 Hz); 4.39 (t, 1H, J = 10.0 Hz); 4.12 (dd, 1H, J = 10.0, 4.6 Hz); 4.02 (dd, 1H, J = 3.6, 1.6 Hz); 3.98 (t, 1H, J = 10.0 Hz); 3.88 (td, 1H, J = 10.0, 4.6 Hz), 3.82−3.76 (m, 4H); 2.93 (bs, 1H), 1.11 (s, 9H), 1.04 (s, 9H). ^{13}C NMR ($CDCl_3$) δ in ppm: 162.9, 159.5, 134.6, 133.8, 131.1, 130.0, 130.0, 129.8, 129.7, 127.9, 114.5, 93.8, 76.8, 74.6, 73.5, 69.8, 69.3, 66.4, 55.3, 27.5, 27.1, 22.7, 20.0. FT-IR (neat) ν in cm^{-1}: 3416, 2960, 2923, 2890, 2858, 1735, 1251, 1094, 1026, 853, 823, 763. HRMS (ESI^+) m/z calcd for $C_{29}H_{39}ClNaO_8Si$ [M − Na]: 601.1995, found: 601.1937.

4,6-Di-*O*-(*tert*-butyl)silanediyl-1-*O*-(3-chlorobenzoyl)-2-*O*-levulinoyl-3-*O*-(4-methoxybenzyl)-*α*-D-mannopyranoside (16):[35] 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (50.6 mg, 0.25 mmol) and DMAP (21.3 mg, 0.17 mmol) were added under argon to a solution of **15** (50.0 mg, 0.09 mmol) and levulinic acid (15.3 mg, 0.13 mmol) in dichloromethane (1.2 mL). The reaction mixture was stirred at room temperature overnight. Then the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (hexane/EtOAc 3:1) to give the desired product as a colorless oil (37.3 mg, 0.09 mmol, 85%).

Data for **16**: $[\alpha]^{25}_D$ +33.8 (c 1.87, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ in ppm: 7.88 (t, 1H, J = 1.6 Hz); 7.77 (dt, 1H, J = 8.0, 1.6 Hz); 7.59 (dt, 1H, J = 8.0, 1.6 Hz); 7.41 (t, 1H, J = 8.0 Hz); 7.33 (d, 2H, J = 8.4 Hz); 6.89 (d, 2H, J = 8.4 Hz); 6.20 (d, 1H, J = 1.6 Hz); 5.31 (dd, 1H, J = 3.6, 1.6 Hz); 4.73 (s, 2H); 4.26 (t, 1H, J = 9.6 Hz); 4.09 (dd, 1H, J = 10.0, 4.6 Hz); 3.96 (t, 1H, J = 10.0 Hz); 3.86−3.77 (m, 5H); 2.81−2.69 (m, 4H); 2.18 (s, 3H); 1.09 (s, 9H), 1.01 (s, 9H). ^{13}C NMR ($CDCl_3$) δ in ppm: 206.3, 172.1, 162.7, 159.5, 134.0, 134.0, 130.9, 130.2, 130.2, 130.0, 129.7, 128.1, 114.0, 92.2, 74.8, 74.4, 72.5, 70.3, 69.3, 66.5, 55.3, 55.4, 38.2, 28.2, 27.6, 27.2, 22.9, 20.1. FT-IR (neat) ν in cm^{-1}: 2933, 2893, 2859, 1742, 1721, 1471, 1104, 1081, 1065, 1033, 859, 824, 1033. HRMS (ESI^+) m/z calcd for $C_{34}H_{45}ClNaO_{10}Si$ [M − Na]: 699.2363, found: 699.2322.

3-*O*-*tert*-Butyldimethylsilyl-4,6-di-*O*-(*tert*-butyl)silanediyl-1-*O*-(3-chlorobenzoyl)-*α*-D-mannopyranoside (17):[36] Compound **14** (259.8 mg, 0.57 mmol) was azeotropically dried with toluene (3 × 5 mL) and taken up in DMF (7 mL). Imidazole (93.5 mg, 1.43 mmol) and *tert*-butyldimethylsilyl chloride (99.1 mg, 0.69 mmol) were added, and the reaction mixture was stirred overnight. Diethyl ether (15 mL) was added and washed with 5 mL of each of the following: $NaHCO_3$ (aq, s), H_2O, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (from hexane/EtOAc 10:1 to 3:1) to give the desired product as a colorless oil (283.6 mg, 0.53 mmol, 93%).

Data for **17**: $[\alpha]^{25}_D$ +0.30 (c 4.57, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ in ppm: 7.98 (t, 1H, J = 1.8 Hz); 7.77 (dt, 1H, J = 8.0, 1.6 Hz); 7.60 (dt, 1H, J = 8.0, 1.6 Hz); 7.45 (t, 1H, J = 8.0 Hz); 6.39 (d, 1H, J = 1.6 Hz); 4.13 (t, 1H, J = 9.4 Hz); 4.12 (dd, 1H, J = 10.0, 4.6 Hz); 3.98 (dd, 1H, J = 9.4, 3.4 Hz); 3.92 (t, 1H, J = 9.4 Hz); 3.92 (m, 1H); 3.87 (td, 1H, J = 9.4, 4.6 Hz); 1.06 (s, 9H); 1.02 (s, 9H); 0.95 (s, 9H); 0.22 (s, 3H); 0.19 (s, 3H). ^{13}C NMR ($CDCl_3$) δ in ppm: 163.2, 135.1, 133.9, 131.3, 130.2, 130.1, 128.0, 93.7, 74.5, 72.8, 71.1, 69.7, 66.5, 27.7, 27.2, 26.0, 22.9, 20.1, 18.3, −4.0, −4.7. FT-IR (neat) ν in cm^{-1}: 3563, 2933, 2891, 2858, 1740, 1471, 1094, 861, 837, 825, 765. (ESI^+) m/z calcd for $C_{27}H_{49}ClNO_7Si_2$ [M − NH_4]: 590.2736, found: 590.2741.

3-*O*-*tert*-Butyldimethylsilyl-4,6-di-*O*-(*tert*-butyl)silanediyl-1-*O*-(3-chlorobenzoyl)-2-*O*-pivaloyl-*α*-D-mannopyranoside (18):[36] Compound **17** (286.3 mg, 0.50 mmol) was azeotropically dried with toluene (3 × 5 mL) and taken up in CH_2Cl_2 (3.8 mL). DMAP (159 mg, 1.30 mmol) and pivaloyl chloride (0.73 mL, 0.62 mmol) were added, and the reaction was stirred for 2 h. CH_2Cl_2 was added and washed

with saturated $NaHCO_3$, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by column chromatography (from hexane to hexane/EtOAc 15:1) to afford **18** as a colorless oil (283.1 mg, 0.44 mmol, 87%).

Data for **18**: $[\alpha]^{25}_D$ +21.43 (*c* 4.60, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ in ppm: 7.99 (t, 1H, *J* = 1.9 Hz), 7.90 (dt, 1H, *J* = 8.0, 1.2 Hz), 7.62 (ddd, 1H, *J* = 8.0, 2.2, 1.0 Hz), 7.46 (t, 1H, *J* = 8.0 Hz), 6.16 (d, 1H, *J* = 1.9 Hz), 5.21 (dd, 1H, *J* = 3.0, 2.0 Hz), 4.22−4.09 (m, 3H), 3.92 (t, 1H, *J* = 10.0 Hz), 3.85 (td, 1H, *J* = 8.4, 4.8 Hz), 1.26 (s, 9H), 1.08 (s, 9H), 1.01 (s, 9H), 0.92 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H). ^{13}C NMR ($CDCl_3$) δ in ppm: 177.2, 163.0, 135.1, 134.0, 131.1, 130.3, 130.1, 127.9, 92.4, 74.7, 70.9, 70.9, 70.3, 66.9, 39.1, 27.7, 27.3, 27.2, 25.9, 23.0, 20.1, 18.4, −4.4, −4.8. FT-IR (neat) ν in cm^{-1}: 2932, 2894, 2859, 1741, 1473, 1113, 854, 838, 825, 746. (ESI^+) *m*/*z* calcd for $C_{32}H_{53}ClNaO_8Si_2$ [M − Na]: 679.2865; found: 679.2813.

3-*O*-*tert*-Butyldimethylsilyl-4,6-di-*O*-(*tert*-butyl)silanediyl-2-*O*-pivaloyl-α-D-mannopyranose (19):[38] Compound **18** (253.0 mg, 0.42 mmol) was dissolved in EtOAc (1.7 mL). 2-Aminoethanol (84 μL, 1.43 mmol) was added, and the mixture was stirred at room temperature for 2 h. The solvent was evaporated in vacuo, and the crude product was purified by column chromatography (from hexane to hexane/EtOAc 9:1) to afford **19** as a colorless oil (176 mg, 0.37 mmol, 88%).

Data for **19**: ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 5.00−4.93 (m, 2H), 4.01 (dd, 1H, *J* = 9.7, 4.7 Hz), 3.97−3.90 (m, 2H), 3.86 (ddd, 1H, *J* = 8.6, 8.0, 4.8 Hz), 3.82−3.75 (m, 1H), 2.78 (s, 1H), 1.12 (s, 9H), 0.96 (s, 9H), 0.91 (s, 9H), 0.78 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 177.8, 93.2, 75.3, 72.6, 70.2, 68.0, 67.3, 39.1, 27.8, 27.4, 27.2, 25.9, 23.1, 20.1, 18.3, −4.3, −4.7. FT-IR (neat) ν in cm^{-1}: 3422, 2931, 2858, 1738, 1714, 1473, 1159, 1123, 1107, 1082, 1022, 865, 838, 825. HRMS (ESI^+) *m*/*z* calcd for $C_{25}H_{51}O_7Si_2$ [M − NH_4]: 519.3173, found: 519.3150.

Phenyl 2-*O*-(3-*O*-*tert*-Butyldimethylsilyl-4,6-di-*O*-(*tert*-butyl)silanediyl-2-*O*-pivaloyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (21):[39] Powdered 4 Å molecular sieves (51 mg) and trichloroacetonitrile (102 μL, 0.97 mmol) were added to a solution of compound **19** (102 mg, 0.20 mmol) in CH_2Cl_2 (2.2 mL) at room temperature. The reaction mixture was stirred for 10 min followed by the addition of cesium carbonate (71 mg, 0.20 mmol), and stirring was continued for another 45 min. The reaction mixture was then filtered over Celite, and the solvent was removed under reduced pressure. The crude product was used in the glycosylation reaction without further purification.

A solution of trichloroacetimidate donor, thiophenyl acceptor **20** (326 mg, 0.61 mmol), and 4 Å molecular sieves (1.2 g) in dry CH_2Cl_2 (51 mL) was stirred at room temperature for 30 min. After cooling to −20 °C, TMSOTf (10 μL, 0.05 mmol) was added. The resulting mixture was stirred for 2 h and then diluted with CH_2Cl_2. Saturated aqueous $NaHCO_3$ was added to quench the reaction. The molecular sieves were filtered off through a Celite pad. The filtrate was washed with brine, dried over Mg_2SO_4, and concentrated. The residue was purified by column chromatography (from hexane to hexane/CH_2Cl_2 3:2) to afford **21** (102 mg, 0.10 mmol, 49%) as a white syrup.

Data for **21**: $[\alpha]^{25}_D$ +0.66 (*c* 3.58, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ in ppm: 7.50−7.14 (m, 20H), 5.47 (d, 1H, *J* = 1.7 Hz), 5.20 (t, 1H, *J* = 2.1 Hz), 4.93 (d, 1H, *J* = 1.6 Hz), 4.84 (d, 1H, *J* = 10.7 Hz), 4.74−4.65 (m, 2H), 4.59 (d, 1H, *J* = 12.1 Hz), 4.53 (d, 1H, *J* = 9.5 Hz), 4.50 (d, 1H, *J* = 11.9 Hz), 4.33−4.26 (m, 1H), 4.20 (t, 1H, *J* = 2.3 Hz), 4.07−3.96 (m, 2H), 3.89 (dd, 1H, *J* = 9.0, 2.6 Hz), 3.87−3.64 (m, 6H), 1.20 (s, 9H), 1.04 (s, 9H), 0.95 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ in ppm: 177.2, 138.4, 138.3, 138.2, 134.2, 133.7, 132.1, 129.3, 128.7, 128.6, 128.5, 128.3, 128.0, 128.0, 127.8, 127.7, 126.8, 99.5, 87.8, 80.3, 75.5, 75.3, 75.1, 75.1, 73.4, 73.0, 72.6, 72.1, 70.5, 69.4, 68.6, 67.1, 39.0, 27.7, 27.4, 27.2, 25.9, 23.0, 20.1, 18.3, −4.4, −4.7. FT-IR (neat) ν in cm^{-1}: 3063, 3031, 2928, 2857, 1737, 1473, 1454, 1362, 1251, 1084, 1026, 864, 839. HRMS (ESI^+) *m*/*z* calcd for $C_{58}H_{86}NO_{11}SSi_2$ [M + NH_4]: 1060.5460, found: 1060.5476.

■ ASSOCIATED CONTENT

Supporting Information. Copies of NMR spectra of compounds **3e**, **3f**, **6bβ**, **8cα**, **8cβ**, **8fα**, **10**, **11**, **14**−**19**, **21**. This material is available free of charge via the Internet at http://pubs.acs.org.

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