Highly Diastereoselective α-Mannopyranosylation in the Absence of Participating Protecting Groups

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S-Phenyl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside and its sulfoxide, following activation at −78 °C with benzenesulfenyl triflate or triflic anhydride, respectively, provide the corresponding α-mannosyl triflate as demonstrated by NMR spectroscopy. On addition of an acceptor alcohol α-mannosides are then formed. Similarly, *S*-phenyl 2,3-*O*-carbonyl-4,6-*O*-benzylidene-1-thia-α-D-mannopyranoside and ethyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-1-thia-α-D-mannopyranoside both provide α-mannosides on activation with benzenesulfenyl triflate followed by addition of an alcohol. These results stand in direct contrast to the highly β-selective couplings of comparable glycosylations with 2,3-di-*O*-benzyl-4,6-*O*-benzylidene protected mannosyl donors and draw attention to the subtle interplay of reactivity and structure in carbohydrate chemistry.

Introduction

We have recently described methods for the direct synthesis of β-mannopyranoside which proceed by means of α-mannosyl triflates generated in situ from glycosyl sulfoxides or thioglycosides with triflic anhydride or benzenesulfenyl triflate, respectively.[1−6] The stereoselectivity of these reactions is a function of the protecting groups on the mannose ring with the 2,3-di-*O*-benzyl-4,6-benzylidene system being highly β-selective as contrasted with the 2,3,4,6-tetra-*O*-benzyl one, which shows little or no selectivity.[1−5] We interpret this effect in terms of the ability of the protecting group set to stabilize the intermediate α-mannosyl triflate with respect to the corresponding ion pair. In effect, in Fraser-Reid's terminology,[7] the 4,6-benzylidene system torsionally disarms the covalent triflate toward collapse to the ion pair. This notion has been supported computationaly in a series of related glucopyranosyl pentenyl glycosides.[8] Thus, in the 4,6-benzylidene-protected system, the α-mannosyl triflate reacts predominantly via an S_N2-like[9] displacement, whereas in the tetrabenzyl system the ion pair is more accessible, which leads to a competing S_N1 process and the associated loss of stereoselectivity. We report below on the chemistry of an alternative bicyclo[4.4.0]decane-like system, in which the mannose 3- and 4-OH groups are spanned by Ley's bisacetal type protecting group,[10−13] and which leads with excellent selectivity to α-mannosides. Additionally, we report on the effect of a cyclic 2,3-*O*-carbonate protected system and also of a 3-*O*-benzoyl system, both of which overcome the β-directing influence of the 4,6-*O*-benzylidene group resulting in the highly selective formation of α-mannosides.

Results and Discussion

The 4,6-*O*-benzylidene protecting group is very versatile; it may be readily converted to the 6-*O*-benzyl-4-OH or the 4-*O*-benzyl-6-OH systems at will, or be cleaved to the 4,6-diol under hydrogenolytic or acidic conditions, or even transformed into the 6-bromo-6-deoxy-4-*O*-benzoyl system.[14,15] Nevertheless, the present requirement for this protecting group constitutes a limitation of our chemistry, especially insofar as it puts the β-L-rhamnopyranosides beyond our reach, and we are therefore driven to investigate alternative protecting systems.

We were attracted by the vicinal bisacetals, introduced by the Ley group,[10−13] as they permit the highly regioselective protection of the trans vicinal diols, to boot the 3,4-OH's in the mannopyranose series. Thus, the *S*-ethyl and *S*-phenyl thiomannosides (**1**) and (**2**) were exposed to butane-2,3-dione in the presence of trimethyl orthoformate and catalytic camphorsulfonic acid to give the corresponding 3,4-bisacetals (**3**) and (**4**), respectively. Exhaustive benzylation then provided **5** and **6**, which, on exposure to Oxone afforded the corresponding sulfoxides **7** and **8**. In line with precedent from this laboratory,[3] the oxidation of these axial thioglycosides was extremely

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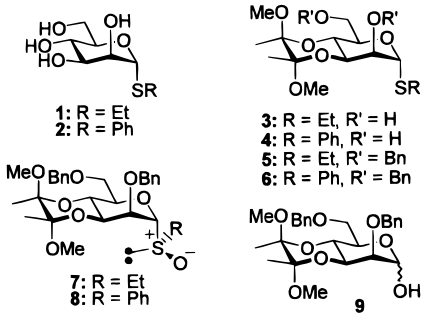
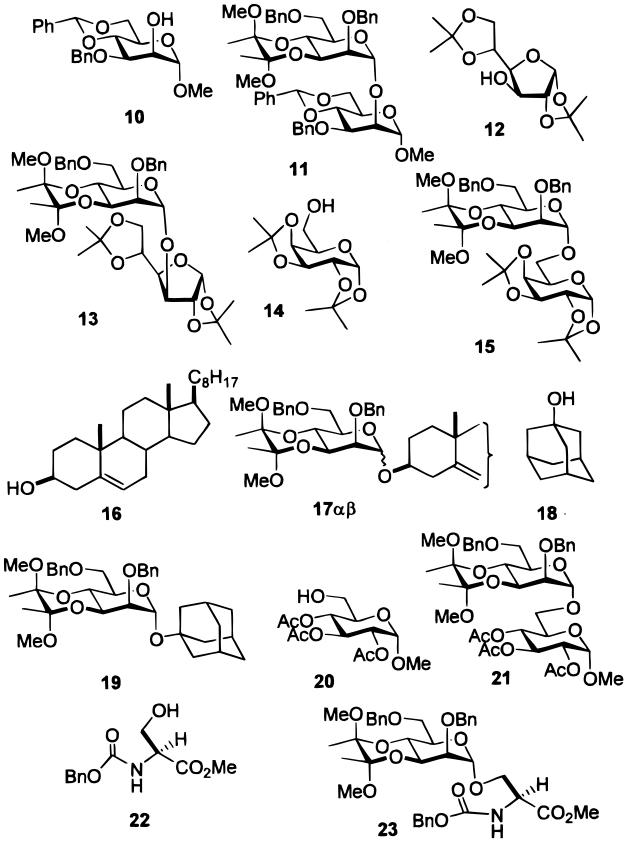
Table 1. Mannosylations with the 3,4-*O*-Bisacetals

donor	acceptor	product (% yield)	α/β ratio	recovered donor (%)
5	**10**	**11** (52), **9** (15)	>95/5	24
6	**12**	**13** (57), **9** (12)	>95/5	22
6	**14**	**15** (60), **9** (17)	>95/5	12
7	**16**	**17** (65), **9** (27)	5/1	0
8	**18**	**19** (88), **9** (8)	>95/5	0
8	**20**	**21** (62), **9** (30)	>95/5	0
8	**22**	**23** (55), **9** (29)	>95/5	0
26	**10**	**27** (56)	>95/5	33
26	**14**	**28** (82)	>95/5	10

selective, giving only one discernible stereoisomer, which we assign the S_R configuration on the basis of analogy.[16]



A series of coupling reactions was conducted in which either the thiomannoside **5** or **6** was activated with benzenesulfenyl triflate or the sulfoxide **7** or **8** was activated with triflic anhydride, before introduction of the acceptor. All experiments were conducted at −78 °C in dichloromethane in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) as a hindered base. It is immediately evident from the results presented in Table 1 that these couplings were not as high yielding as those previously reported with the 4,6-*O*-benzylidene-protected donors. Appreciable quantities of the hydrolysis product **9** were isolated from couplings using the sulfoxide donors (Table 1). The moderate yields in the case of the thioglycoside donors were the result of incomplete conversion of the donor (Table 1). The reactions were, however, selective giving, with one exception, a single anomer within the limits of our NMR detection. NOE experiments were not conclusive, and therefore, we turned to measurement of the $^1J_{CH}$ coupling between the anomeric carbon and its associated proton. It is widely appreciated that in standard chair conformers of *O*-glycopyranosides a value of approximately 173 Hz is diagnostic for the axial glycoside, whereas a coupling constant of around 163 Hz signifies an equatorial glycoside.[17] Indeed, this rule is nicely followed in the 4,6-benzylidene-protected mannopyranosides.[18] In the present series, we typically found coupling constants around 170 Hz and so suggestive of an α-linkage. In one instance, that of coupling to 3β-cholesterol, we typically obtained a 5/1 mixture of anomers and so were able to determine the anomeric $^1J_{CH}$ coupling for both the equatorial and the axial glycoside. The major cholesteryl glycoside had $^1J_{CH}$ of 165.9 Hz, while the minor one showed 155.9 Hz. We therefore assign the major isomer as the α-mannoside and similarly assign all the other coupling products. Consistent with this assignment is the fact that the α-cholesteryl mannoside has a more positive specific rotation than it's β-anomer.[3,19−21] The obvious conclusion to be drawn from this series of experiments is that the 3,4-bisacetal protecting system promotes highly α-selective couplings.



We considered the possibility that these α-selective mannosylations arose through an S_N2-like displacement of a β-mannosyl triflate (**24**), rather than on the anticipated intermediate α-mannosyl triflate (**25**). Indeed, in the glucopyranose series where α-selective coupling is seen even in the presence of the 4,6-*O*-benzylidene protecting group, we invoke such a displacement on a minor β-glucopyranosyl triflate through a Curtin−Hammett-type kinetic scheme.[22] As the anomeric effect is greater in mannopyranosides than in glucopyranosides,[23,24] such a pathway is not usually a problem with the 4,6-*O*-benzylidene-protected mannopyranosyl triflates. However, we reasoned that in the present instance the axial methoxy group on the α-face of the bisacetal protecting group might destabilize the α-triflate (**25**) with respect to the β-anomer (**24**) through an unfavorable electrostatic interaction. We therefore treated thioglycoside **6** with sodium cyanoborohydride and HCl in THF leading to the formation of **26** in 92% isolated yield. The stereochemistry of this reduction is explained in the usual manner by invoking axial attack by the hydride on the

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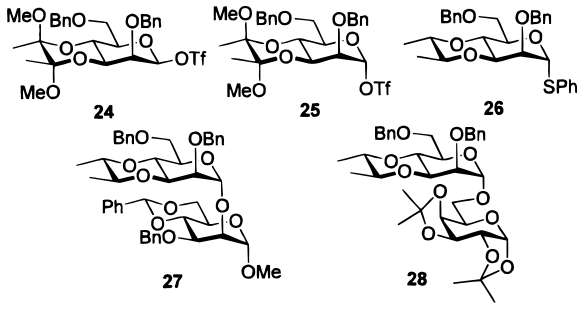
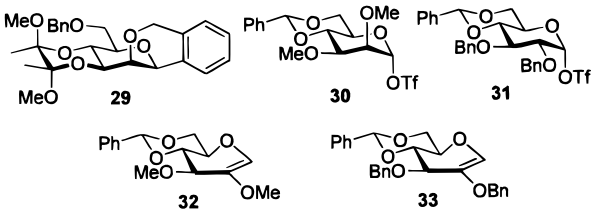
intermediate oxacarbenium ions. It was confirmed by NOE experiments, which established the spatial proximity of the newly introduced protons in the protecting group to either H3 or H4 of the mannose ring. Following activation by PhSOTf in the usual way, **26** was coupled to alcohols **10** and **14**. Again, as seen from Table 1, the yields were only moderate but the selectivity was high in favor of the α-mannoside, which negates this line of reasoning.

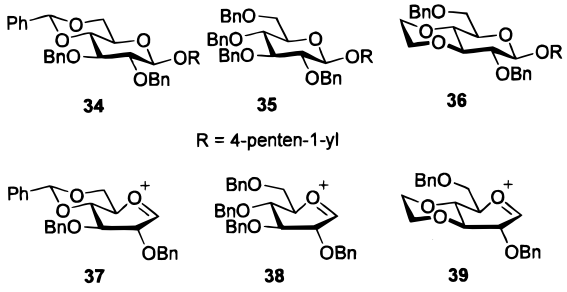


We therefore turned to an NMR investigation of the stability of the intermediate formed on activation of sulfoxide **7** by triflic anhydride. Thus, a solution of **7** and DTBMP in CD_2Cl_2 was cooled to −78 °C under Ar in the probe of the NMR spectrometer and a ^{1}H NMR spectrum recorded. The tube was then removed from the probe, and Tf_2O, precooled to −78 °C, was quickly added before the tube was returned to the cold probe and a new spectrum registered. This spectrum showed the sulfoxide to have been completely consumed in the time frame of this experiment (<5 min) and that one new very major carbohydrate-based species had been formed. The anomeric proton of this substance resonated at δ_H 6.03 in the form of a slightly broadened singlet. A ^{13}C NMR spectrum, also recorded at −78 °C, put the anomeric carbon at δ_C 105.0 and the value of the anomeric $^1J_{CH}$ coupling at 184.2 Hz. These values are entirely consistent with those recorded for a range of α-glycosyl triflates previously observed in this laboratory[5,22] and lead us to assign the first intermediate as the α-mannosyl triflate **25**. On gradual warming of the probe, this species was seen to be stable until approximately 5 °C, with decomposition being complete by 17 °C. The decomposition reaction was relatively clean and led to the isolation of one major product in 56% yield. The structure of this decomposition product was assigned as **29** on the basis of the spectroscopic data. Evidently, this species arises from the cyclization of an anomeric oxacarbenium ion onto the proximal 2-*O*-benzyl ether. We note that this mode of decomposition is different from that observed with the 4,6-*O*-benzylidene-protected α-mannosyl and α-glucosyl triflates **30** and **31**, which provided the glycals **32** and **33**, respectively.[5,22]



Given that α-mannosyl triflates are intermediates in these glycosylation reactions, as has been adequately demonstrated in this and previous work,[3,5,6] the question arises as to how such apparently minor changes in protecting groups wreck such major changes in stereoselectivity. Our current interpretation of the reaction[3,5] centers around the formation of β-mannosides via an S_N2-like[9] displacement of the α-mannosyl triflates, with the α-mannosides resulting from a dissociative pathway. On this basis, it seems likely that any change in selectivity may be the result of a shift in the relative energies of the covalent triflates, contact and solvent separated ion pairs provoked by the change in protecting groups. Such an interplay between both anomers of covalently bound glycosyl donors and the several ion pairs possible is a well-appreciated phenomenon in carbohydrate chemistry,[25] and indeed, in nucleophilic substitution in general.[26,27]

In support of this argument, we draw attention to the work of Fraser-Reid and collaborators who studied the bromonium ion promoted hydrolysis of a series of three glucosyl pentenyl glycosides **34**−**36**. The rates of hydrolysis were found to differ considerably, with **34** being the slowest and **36** the fastest.[8] Ab initio calculations, with slightly simplified model systems, indicated that the activation energies required to collapse the activated pentenyl glycosides to the corresponding oxacarbenium ions **37**−**39**, respectively, were highest for **34** and lowest for **36**, in agreement with the order of rates of hydrolysis.[8] This order of reactivity toward cation formation also corresponds directly with the sequence of β-selectivities observed with our series of similarly protected mannosyl donors and hints at the importance of cations related to **39** in the present α-selective couplings.



We have also briefly investigated the use of disarming protecting groups,[7] in conjunction with the 4,6-*O*-benzylidene group in the hope of improving the β-selectivity of the coupling even further. We directed our attention at the 2,3-*O*-carbonate **40** and the 3-*O*-benzoate **41**. Carbonate **40** in particular was thought promising in view of the fact that the similarly protected mannosyl bromide **42** has been used previously in β-selective mannosylations by the insoluble silver salt method.[28] The 3-*O*-benzoate **41** was targeted, as it was thought that an ester at this position would be moderately disarming[29,30] and unlikely to lead to neighboring group participation.

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Both substances were readily prepared from the corresponding diols **43** and **44**, respectively; **40** by treatment of **43** with phosgene and **41** by monobenzoylation of **44**, giving **45**, followed by silylation. Coupling reactions were carried out by activation of the thioglycosides in CH_2Cl_2, at −78 °C in the presence of DTBMP, with PhSOTf, followed by addition of **14** as acceptor. In both cases, the isolated yield of coupled product was moderate (60% and 69%) but the selectivities were high, and only one anomer was isolated. The products **46** and **47** from both reactions were readily converted to a single diol **48**, by either saponification or saponifaction followed by desilylation, respectively. As **48** is in the standard $^4C_1$ chair conformation, it was readily assigned as the α-mannoside on the basis of the anomeric $^1J_{CH}$ coupling of 170.4 Hz and the absence of the unusually upfield H5 multiplet (δ_H 3.1−3.3). This latter is diagnostic of the *β*-mannosides in the 4,6-*O*-benzylidene-protected series in the absence of disarming protecting groups.[3] Both coupling products **46** and **47** were therefore assigned as the α-mannosides, contrary to our initial expectations. This verification of stereochemistry, by conversion to **48**, was especially necessary in the case of the 2,3-*O*-carbonate **46** owing to its unusual conformation. Thus, the $^1J_{CH}$ anomeric coupling constant of the product **46** (171.2 Hz) is very close to that of authentic *β*-mannosides, with the same protecting group array **49** (170.9−172.0 Hz),[31] which implies that one or both of these compounds has a nonstandard conformation. Likewise, in both the α- and *β*-mannosides **46** and **49**, respectively, the mannose H5 signal resonates in the range δ_H 3.6−3.9, whereas we typically find it to be at δ 3.1−3.3 in 4,6-benzylidene-protected *β*-mannosides.[3] Taken as a whole, these data indicate that neither the α- nor the *β*-mannosides adopt the standard $^4C_1$ chair conformation when protected by the 2,3-*O*-carbonate group. On the basis of the NMR data for his *β*-mannosides, Kunz indicates that an $^0H_5$ half-chair is the preferred conformation and that this is enforced by the requirements of the cyclic carbonate group.[31] We see no reason to disagree with this conclusion and suggest that the mannose ring of **46** adopts a similar conformation. The corollary to this argument is that any α-triflate (**50**) derived from activation of **40** will also have the $^0H_5$ half-chair conformation leading, again, to a perturbation of any equilibrium with contact and solvent separated ion pairs and, so, a change in mechanism of displacement of the triflate.

With regard to the α-selectivity of the 3-*O*-benzoate, we suggest that, contrary to our initial expectation, neighboring group participation underlies the α-selectivity. Indeed, inspection of molecular models suggests that the pyranose ring can readily adopt a $^1S_5$ twist conformation, which permits the formation of the bridged cation without imposing undue strain on the fused 4,6-*O*-benzylidene ring.

Conclusion

Three different sets of protecting groups have been found to confer high α-selectivity on mannosylation reactions conducted by the triflate method.

Experimental Section[32]

General Method for the Preparation of the 3,4-*O*-Bisacetals. The thiomannopyranoside **1** or **2** (1.5 mmol) was dissolved in dry methanol (10 mL) followed by the addition of butane-2,3-dione (99.0 mg, 0.15 mL, 1.71 mmol), $HC(OMe)_3$ (0.88 g, 0.91 mL, 8.3 mmol), and camphor-10-sulfonic acid (34.0 mg, 0.15 mmol). The reaction mixture was then heated to reflux for 72 h before it was cooled to room temperature and quenched by addition of Et_3N (0.1 mL). The reaction mixture then was concentrated under vacuum, and the residue obtained was recrystalized from diethyl ether/hexane (1/3) to give **3** or **4**, respectively.

***S*-Ethyl 3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (3)** was prepared as an oil in 80% yield according to the general protocol: $[\alpha]_D = +217°$ (*c* 2.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.34 (s, 1 H), 4.15 (m, 2 H), 4.04 (m, 1 H), 4.00 (m, 1 H), 3.83 (m, 2 H), 3.29 (s, 3 H), 3.28 (s, 3 H), 2.63 (m, 2 H), 1.29 (s, 3 H), 1,27 (s, 3 H), 1.23 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 100.5, 99.9, 84.6, 71.2, 71.0, 68.9, 63.2, 61.2, 48.1, 48.0, 25.2, 17.8, 17.7, 14.9. Anal. Calcd for $C_{14}H_{26}O_7S$: C, 49.69; H, 7.74. Found: C, 49.86; H, 7.85.

***S*-Phenyl 3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (4)** was prepared as a white crystalline solid in 66% yield according to the general protocol: mp 201 °C; $[\alpha]_D = +282°$ (*c* 2.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 5.57 (s, 1 H), 4.28 (dt, $J = 2.2$, 6.0 Hz, 1 H), 4.23 (m, 1 H), 4.19 (t, $J = 6.0$ Hz, 1 H), 4.07 (dd, $J = 1.8$, 6.0 Hz, 1 H), 3.81 (m, 2 H), 3.34 (s, 3 H), 3.28 (s, 3 H), 1.36 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 131.9, 129.0, 127.6, 100.4, 99.8, 87.9, 71.4, 70.9, 68.6, 62.9, 60.9, 48.1, 47.9, 17.7, 17.6. Anal. Calcd for $C_{18}H_{26}O_7S$: C, 55.94; H, 6.78. Found: C, 55.94; H, 6.77.

General Method for the 2,6-Di-*O*-benzylation of the 3,4-*O*-Bisacetals. 3 or **4** (3.1 mmol) was dissolved in THF (30 mL), stirred vigorously, and treated with benzyl bromide (2.0 mL, 16.8 mmol) followed by portionwise addition of NaH (0.71 g, 17.8 mmol) at 0 °C. The so-obtained suspension was then heated to reflux with stirring for 3 h before it was cooled to room temperature and the reaction quenched by addition of ice−water (10 mL) and then EtOAc (50 mL). The organic phase was decanted off and the aqueous layer extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine and dried (Na_2SO_4), and the solvent was removed under vacuum to give an oil, which was purified by chromatography on silica gel eluting with EtOAc/hexane (1/5).

***S*-Ethyl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (5)**, a syrup, was prepared in 83% yield according to the general protocol: $[\alpha]_D = +156$ (*c* 2.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.31 (m, 10 H), 5.32 (d, $J = 1.1$ Hz, 1 H), 4.90 (d, $J = 12.1$ Hz, 1 H), 4.68 (d, $J = 12.1$ Hz, 1 H), 4.64 (d, $J = 12.0$ Hz, 1 H), 4.54 (d, $J = 12.0$ Hz,

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(32) For general experimental details see footnote 3.

1 H), 4.40 (m. 2 H), 4.02 (m, 1 H), 3.78 (m, 3 H), 3.27 (s, 3 H), 3.20 (s, 3 H), 2.61 (m, 2 H), 1.35 (s, 3 H), 1.28 (s, 3 H), 1.24 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.7, 128.3, 127.9, 127.6, 100.1, 99.7, 83.7, 77.7, 73.4, 72.9, 71.1, 69.7, 68.9, 64.2, 48.0, 25.4, 17.9, 11.8. Anal. Calcd for $C_{28}H_{38}O_7S$: C, 64.84; H, 7.38. Found: C, 65.04; H, 7.43.

***S*-Phenyl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (6)**, a white crystalline solid, was prepared in 80% yield according to the general protocol: mp 210 °C; $[\alpha]_D$ = +164 (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 15 H), 5.54 (s, 1 H), 4.89 (d, J = 12.2 Hz, 1 H), 4.69 (d, J = 12.1 Hz, 1 H), 4.61 (d, J = 12.0 Hz, 1 H), 4.50 (d, J = 12.0 Hz, 1 H), 4.44 (dt, J = 3.7, 10.5 Hz, 1 H), 4.28 (t, J = 10.2 Hz, 1 H), 4.06 (dd, J = 2.7 Hz, 10.5 Hz, 1 H), 3.97 (dd, J = 1.5, 3 Hz, 1 H), 3.80 (d, J = 3.6 Hz, 2 H), 3.37 (s, 3 H), 3.21 (s, 3 H), 1.35 (s, 3 H), 1.31 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.7, 134.5, 131.9, 129.1, 128.3, 127.9, 127.6, 100.1, 99.8, 87.4, 77.7, 73.4, 72.8, 71.9, 69.6, 68.9, 64.1, 48.1, 17.9. Anal. Calcd for $C_{32}H_{38}O_7S$: C, 67.82; H, 6.76. Found: C, 67.90; H, 6.84.

General Protocol for the Oxidation of Thioglycosides to Glycosyl Sulfoxides. An aqueous solution (20 mL) of Oxone (0.62 g, 1 mmol) was added to **5** or **6** (2 mmol) in THF (20 mL) at 0 °C, and the reaction mixture was stirred for 3 h (TLC) and then worked up by addition of EtOAc (30 mL). The aqueous layer was extracted by EtOAc (2 × 10 mL), and the combined organic layers were concentrated to give a residue that was purified by chromatography, eluting with EtOAc/hexane (1:3) to give the sulfoxides (85%).

***S*-Ethyl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside *S*-oxide (7):** $[\alpha]_D$ = +153 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 10 H), 4.99 (d, J = 1.1 Hz, 1 H), 4.67 (d, J = 1.1 Hz, 1 H), 4.63 (m, 1 H), 4.53 (d, J = 2 Hz, 1 H), 4.49 (d, J = 1.2 Hz, 1 H), 4.36 (m, 1 H), 4.23 (m, 2 H), 3.82 (dt, J = 1.1, 6.3 Hz, 1 H), 3.62 (m, 1 H), 3.31 (s, 3 H), 3.20 (s, 3 H), 2.97 (m, 1 H), 2.70 (m, 1 H), 1.40 (s, 3 H), 1.29 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.6, 128.4, 128.3, 128.3, 127.7, 127.6, 127.5, 100.1, 99.9, 93.1, 77.0, 74.1, 73.6, 72.9, 69.2, 68.9, 63.1, 52.4, 48.4, 48.1, 43.8, 17.9, 5.9. Anal. Calcd for $C_{28}H_{38}O_8S$: C, 62.90; H, 7.16. Found: C, 63.42; H, 7.47.

***S*-Phenyl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside *S*-oxide (8):** $[\alpha]_D$ = +175 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.65−7.24 (m, 15 H), 4.92 (d, J = 10.8 Hz, 1 H), 4.62 (d, J = 10.8 Hz, 1 H), 4.46 (s, 2 H), 4.36 (m, 3 H), 4.23 (m, 2 H), 3.80 (d, J = 13.8 Hz, 1 H), 3.62 (dd, J = 6.0 Hz, 11.1 Hz, 1 H), 3.36 (s, 3 H), 3.21 (s, 3 H), 1.36 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 142.1, 138.4, 138.0, 131.4, 129.1, 128.4, 128.3, 128.0, 127.6, 124.8, 100.1, 99.9, 97.5, 74.0, 73.6, 73.0, 69.2, 69.0, 63.3, 48.5, 48.2, 17.9. Anal. Calcd for $C_{32}H_{38}O_8S$: C, 65.96; H, 6.57. Found: C, 66.15; H, 6.72.

General Procedure for the Coupling Reaction of Thioglycosides with Activation by PhSOTf. PhSCl (0.42 mg 0.3 mmol) in 1 mL of dry dichloromethane (2 mL) was added slowly to AgOTf (91 mg, 0.4 mmol) in dichloromethane (2 mL) containing pulverized 3A molecular sieves (20 mg) at −78 °C. After the mixture was stirred for 5 min, a solution of donor (0.1 mmol) and DTBMP (41 mg. 0.2 mmol) in dichloromethane (1 mL) was slowly added. After a further 15 min, the acceptor (0.2 mmol) in dichloromethane (1 mL) was added. The reaction was quenched after stirring for 2 h at −78 °C by addition of $NaHCO_3$ (satd, 1 mL). The reaction mixture then was diluted with EtOAc (20 mL), filtered over Na_2SO_4, and concentrated. The residue obtained was purified by chromatography on silica gel, eluting with EtOAc/hexane (1/5) or by preparative TLC.

General Procedure for the Coupling Reaction of Glycosyl Sulfoxides with Activation by Tf_2O. The sulfoxide (0.1 mmol) and DTBMP (41 mg, 0.2 mmol) were dissolved in dichloromethane (3 mL) under Ar and the solution cooled to −78 °C, followed by the rapid addition of Tf_2O (1 8μL, 0.12 mmol). The acceptor (0.2 mmol) in dichloromethane (2 mL) was added slowly after 10 min, after which time the reaction mixture was stirred for 2 h before it was quenched at −78 °C by addition of $NaHCO_3$ (satd, 0.5 mL). The resulting mixture was diluted with EtOAc (20 mL), dried over Na_2SO_4, and concentrated to give a residue that was purified by chromatography on silica gel eluting with EtOAc/hexane (1/5) or by preparative TLC.

2,6-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α/β-D-mannopyranose (9): $[\alpha]_D$ = +14.0 (*c* = 5.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 10 H), 5.21 (s, 1 H), 4.84 (d, J = 12.3 Hz, 1 H), 4.57 (m, 3 H), 4.23 (t, J = 10.2 Hz, 1 H), 3.95 (dd, J = 2.7, 10.5 Hz, 1 H), 3.72 (m, 4 H), 3.22 (s, 3 H), 3.19 (s, 1 H), 1.33 (s, 3 H), 1.27 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.7, 128.3, 127.9, 127.6, 127.5, 100.0, 99.7, 94.5, 75.6, 73.6, 73.1, 71.8, 68.9, 68.6, 63.7, 48.1, 17.9. Anal. Calcd for $C_{26}H_{33}O_8\cdot 0.33H_2O$: C, 64.71; H, 7.10. Found: C, 65.17; H, 6.98.

Methyl 3-*O*-benzyl-2-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranosyl]-4,6-*O*-benzylidene-α-D-mannopyranoside (11): $[\alpha]_D$ = +6.1 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 20 H), 5.60 (s, 1 H), 5.14 (s, 1 H), 4.74 (m, 3 H), 4.62 (m, 4 H), 4.24 (dd, J = 3.6, 8.8 Hz, 1 H), 4.14 (dd, J = 20, 9.6 Hz, 1 H), 4.08 (m, 4 H), 3.75 (m, 4 H), 3.75 (m, 4 H), 3.31 (s, 3 H), 3.20 (s, 3 H), 3.17 (s, 3 H), 1.33 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.8, 138.6, 138.4, 137.8, 137.6, 134.4, 129.7, 128.9, 128.8, 128.5, 128.3 128.1, 128.0, 127.9, 127.7, 127.6, 127.5, 127.4, 127.3, 127.1, 126.0, 101.7 ($^1J_{CH}$ = 171 Hz), 101.4 ($^1J_{CH}$ = 159 Hz), 100.9 ($^1J_{CH}$ = 173 Hz), 99.7, 99.5, 79.0, 76.0, 75.8, 73.3, 72.9, 72.8, 71.4, 69.0, 68.7, 63.9, 63.5, 54.6, 47.9, 47.8, 17.8. Anal. Calcd for $C_{47}H_{56}O_{13}$: C, 68.10; H, 6.81. Found: C, 67.84; H, 6.94.

3-*O*-[2,6-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranosyl]-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (13): $[\alpha]_D$ = +11.0 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.31(m, 10 H), 5.82 (d, J = 3.6 Hz, 1 H), 5.12 (d, J = 1.1 Hz, 1 H), 4.89 (d, J = 12.3 Hz, 1 H), 4.76 (d, J = 3.6 Hz, 1 H), 4.69 (d, J = 12.3 Hz, 1 H), 4.59 (d, J = 4.5 Hz, 2 H), 4.25 (d, J = 1.8 Hz, 1 H), 4.00 (m, 3 H), 3.96 (m, 3 H), 3.83 (dd, J = 6.3, 10.2 Hz, 1 H), 3.75 (d, J = 6.3 Hz, 1 H), 3.70 (m, 1 H), 3.27 (s, 3 H), 3.20 (s, 3 H), 1.50 (s, 3 H), 1.39 (s, 3 H), 1.35 (s, 3 H), 1.30 (s, 3 H), 1.29 (s, 3 H), 1.11 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.6, 129.1, 128.3, 127.9, 127.6, 127.5, 111.9, 109.3, 105.4, 100.7 ($^1J_{CH}$ = 171 Hz), 100.0, 99.8, 83.6, 81.4, 81.3, 75.6, 73.7, 73.1, 72.8, 71.9, 69.0, 67.8, 63.9, 52.4, 48.2, 48.0, 26.9, 26.1, 25.6, 17.9. Anal. Calcd for $C_{38}H_{52}O_{13}$: C, 63.67; H, 7.31. Found: C, 63.69; H, 7.49.

6-*O*-[2,6-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranosyl]-1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (15): $[\alpha]_D$ = +7.3 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 10 H), 5.50 (d, J = 4.8 Hz, 1 H), 4.94 (s, 1 H), 4.91 (d, J = 12.3 Hz, 1 H), 4.62 (m, 4 H), 4.29 (dd, J = 2.4, 4.9 Hz, 1 H), 4.22 (t, J = 10.2 Hz, 1 H), 4.16 (dd, J = 1.8, 8.1 Hz, 1 H), 4.06 (dd, J = 2.8, 10.3 Hz, 1 H), 3.99 (m, 2 H), 3.74 (m, 5 H), 3.31 (s, 3 H), 3.25 (s, 3 H), 1.53 (s, 3 H), 1.49 (s, 3 H), 1.37 (s, 6 H), 1.32 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.0, 138.8, 128.3, 127.9, 127.7, 127.4, 109.5, 108.7, 99.9, 99.7, 98.9 ($^1J_{CH}$ = 169 Hz), 96.4 ($^1J_{CH}$ = 178 Hz), 75.9, 73.5, 71.4, 71.0, 70.8, 69.2 68.8, 68.7, 65.4, 65.2, 63.8, 48.1, 48.0, 26.2, 26.1, 25.0, 24.7, 17.9. Anal. Calcd for $C_{38}H_{52}O_{13}$: C, 63.67; H, 7.31. Found: C, 62.49; H, 7.34.

3β-Cholesteryl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranoside (17α): $[\alpha]_D$ = +7.1 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 10 H), 5.24 (d, J = 4.7 Hz, 1 H), 4.96 (s, 1 H), 4.94 (d, J = 12.3 Hz, 1 H), 4.67 (d, J = 12.4 Hz, 1 H), 4.63 (d, J = 12 Hz, 1 H), 4.55 (d, J = 12 Hz, 1 H), 4.20 (t, J = 10 Hz, 1 H), 4.08 (dd, J = 2.8, 14.4 Hz, 1 H), 3.76 (d, J = 4.4 Hz, 2 H), 3.57 (d, J = 1.2 Hz, 1 H), 3.48 (m, 1 H), 3.29 (s, 3 H), 3.19 (s, 3 H), 2.35 (dd, J = 4.8 Hz, 13.2 Hz, 1 H), 2.27 (t, J = 12.0 Hz, 1 H), 1.90 (m, 5 H), 1.16 (s, 3 H), 1.15 (s, 3 H), 1.12 (m, 39 H); ^{13}C NMR ($CDCl_3$) δ 140.8, 139.0, 138.8, 128.3, 128.0, 127.6, 127.4, 127.3, 121.9, 99.9, 99.7, 97.4 ($^1J_{CH}$ = 165.9 Hz), 73.5, 73.2, 71.5, 70.0, 69.3, 64.2, 56.9, 56.3, 50.2, 48.2, 47.9, 42.5, 40.1, 39.9, 39.7, 37.2, 36.8, 36.4, 35.9, 32.0, 28.4, 28.2, 27.8, 24.5, 23.9, 22.9 22.7 21.2, 19.5, 18.9, 18.0, 12.0. Anal. Calcd for $C_{53}H_{78}O_8$: C, 75.50; H, 9.32. Found: C, 75.59; H, 9.22.

3β-Cholesteryl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-β-D-mannopyranoside (17β): $[\alpha]_D$ = +1.9 (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.37 (m, 10 H), 5.32 (d, J =

5.2 Hz, 1 H), 4.92 (s, 2 H), 4.62 (s, 2 H), 4.56 (s, 1 H), 4.03 (t, $J = 10$ Hz, 1 H), 3.87 (d, $J = 11.2$ Hz, 1 H), 3.66 (m, 5 H), 3.23 (s, 3 H), 3.18 (s, 3 H), 1.33 (s, 3 H), 1.27 (s, 3 H), 0.68−2.26 (m, 60 H); ^{13}C NMR ($CDCl_3$) δ 141.8, 139.0, 137.9, 134.8, 129.0, 128.1, 128.0, 127.6, 127.5, 127.2, 126.2, 122.0, 99.6, 96.4 ($^1J_{CH}$ = 155.9 Hz), 78.7, 74.9, 73.9, 73.4, 72.0, 70.0, 69.4, 68.9, 64.4, 64.0, 57.1, 56.8, 50.5, 48.3, 48.0, 42.5, 40.0, 39.6, 39.0, 38.0, 36.7, 36.3, 35.9, 32.3, 30.0, 28.5, 28.1, 24.4, 24.0, 23.0, 22.6, 21.4, 19.2, 18.0, 12.0. Anal. Calcd for $C_{53}H_{78}O_8$: C, 75.50; H, 9.32. Found: C, 75.59; H, 9.22.

1-Adamantanyl 2,6-di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranoside (19): $[\alpha]_D = +13.3$ (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.39 (m, 10 H), 5.19 (s, 1 H), 4.94 (d, $J = 12$ Hz, 1 H), 4.67 (s, 1 H), 4.62 (s, 1 H), 4.54 (d, $J = 12$ Hz, 1 H), 4.13 (m, 3 H), 3.74 (d, $J = 2.4$ Hz, 2 H), 3.52 (s, 1 H), 3.29 (s, 3 H), 3.12 (s, 3 H), 1.74 (m, 15 H), 1.33 (s, 3 H), 1.29 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.3, 139.0, 128.3, 128.0, 127.6, 127.4, 99.9, 99.7, 92.7 ($^1J_{CH}$ = 172 Hz), 74.6, 73.4, 73.0, 70.5, 69.3, 69.2, 64.3, 48.1, 47.9, 42.4, 36.4, 30.8, 18.1. Anal. Calcd for $C_{36}H_{48}O_8$: C, 71.03; H, 7.95. Found: C, 71.23; H, 8.13.

Methyl 2,3,4-tri-*O*-acetyl-6-*O*-[2,6-di-*O*-benzyl-3,4-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranosyl]-α-D-glucopyranoside (21): $[\alpha]_D = +10.5$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 10 H), 5.43 (t, $J = 0.3$ Hz, 1 H), 4.84 (m, 5 H), 4.60 (m, 3 H), 4.18 (t, $J = 10.8$ Hz, 1 H), 4.02 (dd, $J = 2.7$, 10.2 Hz, 1 H), 3.86 (m, 2 H), 3.70 (m, 3 H), 3.54 (dd, $J = 2.8$, 10.4 Hz, 1 H), 3.36 (s, 3 H), 3.26 (s, 3 H), 3.17 (s, 3 H), 2.06 (s, 3 H), 1.99 (s, 3 H), 1.94 (s, 3 H), 1.31 (s, 3 H), 1.25 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.3, 169.6, 138.9, 138.7, 128.3, 128.1, 127.6, 127.5, 99.9, 99.7, 99.4 ($^1J_{CH}$ = 170 Hz), 96.6 ($^1J_{CH}$ = 170 Hz), 75.6, 73.5, 73.2, 71.3, 71.1, 70.5, 69.5, 69.1, 68.9, 68.0, 65.5, 63.8 55.3, 48.0, 20.9, 20.8, 17.9. Anal. Calcd for $C_{39}H_{52}O_{16}\cdot 1H_2O$: C, 58.93; H, 6.85. Found: C, 58.28; H, 6.56.

***N*-Benzyloxycarbonyl-*O*-[2,6-di-*O*-benzyl-3,4-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannopyranosyl]-serine methyl ester (23):** $[\alpha]_D = +9.8$ (*c* 3.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.31 (m, 10 H), 5.80 (d, $J = 8.5$ Hz, 1 H), 5.10 (s, 2 H), 4.93 (d, $J = 12$ Hz, 1 H), 4.76 (s, 1 H), 4.58 (m, 4 H), 4.17 (m, 2 H), 3.90 (m, 2 H), 3.79 (m, 4 H), 3.72 (m, 3 H), 3.27 (s, 3 H), 3.18 (s, 3 H), 1.33 (s, 3 H), 1.27 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.6, 128.7, 128.4, 128.1, 127.9, 127.6, 127.5, 100.8 ($^1J_{CH}$ = 170 Hz), 99.9, 99.7, 75.7, 73.6, 73.4, 71.8, 69.2, 68.7, 67.2, 63.6, 54.5, 48.1, 48.0, 17.9. Anal. Calcd for $C_{38}H_{47}NO_{12}$: C, 64.30; H, 6.67; N, 1.97. Found: C, 64.48; H, 6.90; N, 1.75.

***S*-Phenyl 2,6-Di-*O*-benzyl-3,4-*O*-(butane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (26).** $NaCNBH_3$ (0.31 g, 5 mmol) was added to a THF solution (10 mL) of **6** (55.4 mg, 1 mmol) containing 3Å pulverized molecular sieves. After the solution was cooled to 0 °C, 1 N HCl in diethyl ether was added until the pH was 3−4. The reaction mixture was stirred at 0 °C for 2 h and then quenched by the addition of saturated $NaHCO_3$ (10 mL). The aqueous phase was separated and extracted by EtOAc (2 × 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by the chromatography on silica gel eluting with EtOAc/hexane (1/3) to give **26** (51.0 mg, 92%): $[\alpha]_D = +197$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 15 H), 5.57 (d, $J = 0.7$ Hz, 1 H), 4.83 (d, $J = 12.4$ Hz, 1 H), 4.72 (d, $J = 12.4$ Hz, 1 H), 4.64 (d, $J = 12$ Hz, 1 H), 4.50 (d, $J = 12$ Hz, 1 H), 4.35 (m, 1 H), 4.14 (dd, $J = 1.2$, 1.4 Hz, 1 H), 3.93 (dd, $J = 9.6$ Hz, 1 H), 3.87 (m, 3 H), 3.42 (m, 2 H), 1.19 (d, $J = 6$ Hz, 3 H), 1.12 (d, $J = 6$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.1, 134.1, 131.9, 128.9, 128.2, 128.1, 127.5, 127.4, 127.3, 127.2, 88.8, 77.9, 77.4, 77.0, 76.9, 76.6, 73.1, 72.4, 71.5, 71.4, 68.7, 17.4, 17.3. Anal. Calcd for $C_{30}H_{34}O_5S$: C, 71.12; H, 6.76. Found: C, 70.98; H, 6.75.

Methyl 3-*O*-benzyl-2-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(butane-2′,3′-diyl)-α-D-mannopyranosyl]-4,6-*O*-benzylidene-α-D-mannopyranoside (27): $[\alpha]_D = +24.4$ (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.45 (m, 20 H), 5.61 (s, 1 H), 5.21 (s, 1 H), 4.80 (s, 1 H), 4.77 (d, $J = 12$ Hz, 1 H), 4.64 (d, $J = 12$ Hz, 2 H), 4.63 (s, 1 H), 4.55 (m, 3 H), 4.26 (dd, $J = 4.4$, 10 Hz, 1 H), 4.10 (m, 1 H), 4.07 (dd, $J = 11.2$ Hz, 1 H), 3.94 (dd, $J = 3.2$, 6.8 Hz, 2 H), 3.85 (d, $J = 1$ 0 Hz, 2 H), 3.80 (m, 2 H), 3.77 (dd, $J = 4.4$, 14.4 Hz, 1 H), 3.73 (dd, $J = 6.8$, 10.4 Hz, 1 H), 3.37 (m, 2 H), 3.20 (s, 3 H), 1.17(d, $J = 6.8$ Hz, 3 H), 1.15 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.0, 138.4, 128.9, 128.4, 128.0, 127.6, 127.5, 127.3, 125.9, 101.4 ($^1J_{CH}$ = 158 Hz), 100.9 ($^1J_{CH}$ = 172 Hz), 79.1, 77.7, 75.9, 75.7, 73.2, 73.0, 72.6, 71.3, 69.2, 68.9, 63.6, 54.9, 17.4, 17.3. Anal. Calcd for $C_{45}H_{52}O_{11}$: C, 70.29; H, 6.82. Found: C, 70.31; H, 7.06.

6-*O*-[2,6-Di-*O*-benzyl-3,4-*O*-(butane-2′,3′-diyl)-α-D-mannopyranosyl]-1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (28): $[\alpha]_D = +20.0$ (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 10 H), 5.52 (d, $J = 5.0$ Hz, 1 H), 4.91 (s, 1 H), 4.83 (d, $J = 12.5$ Hz, 1 H), 4.70 (d, $J = 12.5$ Hz, 1 H), 4.69 (d, $J = 12.5$ Hz, 1 H), 4.59 (dd, $J = 3.5$, 8 Hz, 1 H), 4.52 (d, $J = 12.5$ Hz, 1 H), 4.31 (dd, $J = 2.4$, 5.0 Hz, 1 H), 4.18 (dd, $J = 1.8$, 7.9 Hz, 1 H), 3.95 (m, 1 H), 3.71 (m, 5 H), 3.35 (m, 2 H), 1.50 (s, 3 H), 1.45 (s, 3 H), 1.32 (s, 6 H), 1.18 (d, $J = 5.6$ Hz, 3 H), 1.08 (d, $J = 5.6$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.0, 128.1, 127.4, 127.2, 110.0, 109.0, 98.5 ($^1J_{CH}$ = 171 Hz), 96.2 ($^1J_{CH}$ = 174 Hz), 77.4, 76.4, 75.4, 75.0, 72.8, 72.6, 71.0, 70.9, 70.5, 68.6, 65.6, 25.9, 25.8, 24.8, 24.4, 17.3, 17.2. Anal. Calcd for $C_{36}H_{48}O_{11}$: C, 65.84; H, 7.37. Found: C, 65.19; H, 7.35.

Generation and Decomposition of Triflate 25. Isolation of Decomposition Product 29. Sulfoxide **7** (5.1 mg, 0.01 mmol) was mixed with DTBMP (4.5 mg, 0.02 mmol) and dissolved in CH_2Cl_2-d_2 (0.5 mL) in an NMR tube under an Ar atmosphere and the ^{1}H NMR spectrum recorded at −78 °C. Cold Tf_2O (5 μL, 0.012 mmol) was then injected at −78 °C. The ^{1}H NMR spectrum, taken immediately at the same temperature, revealed **7** sulfoxide to have been completely-consumed and a major new compound formed with an anomeric proton chemical shift of $\delta = 6.03$ (br s). The ^{13}C NMR spectrum revealed the anomeric carbon to resonate at δ = 105.0 with $^1J_{CH}$ = 184.2 Hz. The temperature of the probe was then raised in 10 K steps, with observation by ^{1}H NMR until decomposition was complete around 290 K. On a slightly larger preparative scale, the decomposition product **29** was isolated in 56% yield: $[\alpha]_D = +9.0$ (*c* 2.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 9 H), 5.04 (d, $J = 15.5$ Hz, 1 H), 4.78 (d, $J = 15.2$ Hz, 1 H), 4.57 (d, $J = 12.0$ Hz, 1 H), 4.53 (d, $J = 12.9$ Hz, 1 H), 4.34 (s, 1 H), 4.06 (t, $J = 12.0$ Hz, 1 H), 3.99 (dd, $J = 3.3$, 10.2 Hz, 1 H), 3.90 (dd, $J = 0.9$, 3.1 Hz, 1 H), 3.82 (m, 2 H), 3.68 (dd, $J = 6.6$, 11.2 Hz, 1 H), 3.32 (s, 3 H), 3.18 (s, 3 H), 1.42 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.6, 135.5, 131.9, 130.8, 128.9, 128.3, 127.8, 127.5, 127.0, 124.2, 100.5, 99.8, 78.5, 74.2, 73.6, 72.2, 71.0, 69.4, 68.4, 63.9, 48.3, 48.0, 18.0. Anal. Calcd for $C_{26}H_{32}O_7$: C, 68.40; H, 7.07. Found: C, 68.04; H, 7.14.

***S*-Phenyl 2,3-*O*-Carbonyl-4,6-*O*-benzylidene-1-thia-α-D-mannopyranoside (40).** A solution of **43** (2.0 g, 5.55 mmol) in pyridine (12 mL) was cooled to 0 °C before phosgene (7.0 mL, 6.66 mmol) in hexane was added dropwise in 10 min. After completion, the reaction mixture was poured slowly into a mixture of ice−water and saturated $NaHSO_3$. The organic layer was separated. After drying on Na_2SO_3, concentration and trituration with Et_2O afforded the carbonate **40** (1.8 g, 4.81 mmol, 87%): ^{1}H NMR ($CDCl_3$) δ 7.30−7.50 (m, 10 H), 5.90 (s, 1 H), 5.60 (s, 1 H), 4.86−5.00 (m, 2 H), 4.18−4.35 (m, 2 H), 3.89−4.00 (m, 1 H), 3.75 (t, $J = 10.0$ Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 153.2, 136.6, 136.6, 131.1, 129.7, 129.6, 129.1, 128.6, 126.3, 102.1, 82.9, 79.0, 77.4, 75.1, 68.4, 61.1; ν 1818 cm^{-1}; MS (electrospray) *m/z* 408.9 (M + Na). Anal. Calcd for $C_{20}H_{18}O_6S$: C, 62.16; H, 4.70. Found: C, 62.22; H, 4.73.

6-*O*-[2,3-*O*-Carbonyl-4,6-*O*-benzylidene-α-D-mannopyranosyl]-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (46). A solution of AgOTf (250 mg, 0.90 mmol) in CH_2Cl_2 (6 mL) was cooled under Ar to −78 °C. PhSCl (130 mg, 0.90 mmol) in CH_2Cl_2 (2 mL) was added dropwise in 10 min. After being stirred 10 min, a solution of **40** (104 mg, 0.30 mmol) and DTBMP (185 mg, 0.90 mmol) in CH_2Cl_2 (3 mL) was added dropwise. After another 10 min, a solution of acceptor **14** (156 mg, 0.60 mmol) in CH_2Cl_2 (3 mL) was added. The reaction was stirred for a further 1 h and then allowed to warm to 0 °C, before it was quenched with two drops of saturated $NaHSO_3$. The mixture was filtered on Celite and then washed with aqueous $NaHSO_3$ and brine. After drying on Na_2SO_4 and concentration, chromatography on silica gel (eluent: hexane/

EtOAc 8/1) gave **46** (96 mg, 60%): ^{1}H NMR ($CDCl_3$) δ 7.35−7.51 (m, 5 H), 5.50 (d, J = 5.0 Hz, 1 H), 5.16 (s, 1 H), 4.85 (t, J = 7.2 Hz, 1 H), 4.71 (d, J = 7.0 Hz, 1 H), 4.60 (dd, J = 2.3, 8.0 Hz, 1 H), 4.35 (m, 2 H), 4.20 (m, 1 H), 3.78−4.00 (m, 3 H), 3.68−3.78 (m, 2 H), 1.52 (s, 3 H), 1.46 (s, 3 H), 1.35 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 153.4, 136.7, 129.5, 128.5, 126.3, 109.7, 108.9, 102.0, 96.5, 95.9 ($^1J_{CH}$ = 171.2 Hz), 78.7, 76.6, 75.3, 71.1, 70.8, 70.5, 68.7, 67.1, 66.1, 59.6, 52.4, 29.8, 26.3, 26.1, 25.0, 24.7; MS (electrospray) m/z 567.0 (M + 1). Anal. Calcd for $C_{26}H_{32}O_{12}\cdot 1H_2O$: C, 56.31; C, 6.18. Found: C, 56.32; H, 6.35.

***S*-Ethyl 3-*O*-Benzoyl-4,6-*O*-benzylidene-1-thia-α-D-mannopyranoside (45).** To a solution of diol **44** (1.0 g, 3.19 mmol) in pyridine (10 mL) at −45 °C was added benzoyl chloride (0.41 mL, 3.50 mmol). The mixture was stirred at that temperature for 40 min before concentration and chromatography on silica gel (eluent: hexane/ethyl acetate = 6/1) gave the title compound **45** (615 mg, 46%): $[\alpha]^{20}_D$ = +52.4 (c = 1.85, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.05 (m, 2 H), 7.50−7.60 (m, 1 H), 7.25−7.50 (m, 7 H), 5.61 (s, 1 H), 5.51 (dd, J = 3.2 Hz, 10.0 Hz, 1 H), 5.36 (s, 1 H), 4.21−4.45 (m, 4 H), 3.91 (t, J = 10.3 Hz, 2 H), 2.52−2.80 (m, 3 H), 1.32 (t, J = 7.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.6, 137.3, 133.5, 129.9, 129.7, 129.2, 128.6, 128.4, 126.3, 101.9, 85.2, 76.6, 71.9, 71.4, 68.8, 64.6, 25.3, 15.0. Anal. Calcd For $C_{22}H_{24}O_6S$: C, 63.45, H5.81. Found: C, 63.63, H, 5.80.

***S*-Ethyl 3-*O*-Benzoyl-4,6-*O*-benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-1-thia-α-D-mannopyranoside (41).** A solution of alcohol **45** (300 mg, 0.72 mmol), *tert*-butyldimethylsilyl triflate (0.34 mL, 1.44 mmol), and *N*,*N*-diisopropylethylamine (0.54 mL, 3.10 mmol) in CH_2Cl_2 (6 mL) was stirred at −5 °C for 30 min and then 2 h at room temperture, quenched with saturated aqueous $NaHCO_3$ and brine, and then dried (Na_2SO_4). Concentration and chromatography on silica gel (eluent: hexane/ethyl acetate = 25/1) gave the title compound as an oil (284 mg, 74%): $[\alpha]^{20}_D$ = +24 (c = 0.74, CH_3Cl); ^{1}H NMR ($CDCl_3$) δ 8.05 (m, 2 H), 7.30−7.58 (m, 8 H), 5.66 (s, 1 H), 5.46 (dd, J = 3, 9.6 Hz, 1 H), 5.20 (s, 1 H), 4.50 (dd J = 1.2, 3.0 Hz, 1 H), 4.40 (m, 3 H), 3.98 (t, J = 10.0 Hz, 3 H), 2.70 (m, 2 H), 1.36 (t, J = 7.5 Hz, 3 H), 0.98 (s, 9 H), 0.09 (s, 3 H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.8, 137.3, 132.9, 129.9, 129.7, 128.8, 128.2, 128.1, 126.1, 101.8, 86.2, 76.4, 66.7, 64.7, 25.6, 25.2, 17.9, 14.9. Anal. Calcd for $C_{28}H_{38}O_6SSi$: C, 63.36; H, 7.22. Found: C, 63.58; H, 7.44.

6-*O*-[3-*O*-Benzoyl-4,6-*O*-benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-α-D-mannopyranosyl]-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (47). A solution of AgOTf (172 mg, 0.69 mmol) in CH_2Cl_2 (6 mL) was cooled under Ar to −78 °C. PhSCl (100 mg, 0.69 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min. After the mixture was stirred for 10 min, a solution of **41** (121 mg, 0.23 mmol) and DTBMP (141 mg, 0.69 mmol) in CH_2Cl_2 (3 mL) was added dropwise. After another 10 min, a solution of acceptor **14** (120 mg, 0.46 mmol) in CH_2Cl_2 (3 mL) was added. The reaction was stirred for a further 1 h and then allowed to warm to 0 °C before it was quenched by two drops of saturated $NaHSO_3$. The mixture was filtered on Celite and then washed with aqueous $NaHSO_4$ and brine. After drying on Na_2SO_4 and concentration, chromatography on silica gel (eluent: hexane/EtOAc 8/1) gave **47** (115 mg, 69%): ^{1}H NMR ($CDCl_3$) δ 8.06 (d, J = 8 Hz, 2 H), 7.55 (m, 1 H), 7.35−7.49 (m, 4 H), 7.25−7.35 (m, 3 H), 5.65 (s, 1 H), 5.55 (dd, J = 3.0, 9.0 Hz, 1 H), 5.50 (dd, J = 3.0, 12 Hz, 1 H), 4.80 (s, 1 H), 4.68 (dd, J = 3.0, 10.0 Hz, 1 H), 4.20−4.42 (m, 6 H), 4.01 (m, 2 H), 3.86 (m, 2 H), 3.75 (t, J = 8.0 Hz, 1 H), 1.60 (s, 3 H), 1.48 (s, 3 H), 1.40 (s, 6 H), 0.92 (s, 9 H), 0.15 (s, 3 H), −0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.9, 137.3, 132.9, 130.0, 129.7, 128.8, 128.2, 128.2, 128.2, 126.0, 109.2, 108.6, 101.6, 101.5 ($^1J_{CH}$ = 171.1 Hz), 96.2, 76.1, 71.5, 70.7, 70.5, 70.2, 66.9, 66.2, 65.7, 65.7, 26.1, 25.9, 25.8, 24.8, 24.5, 17.9; MS (electrospray), m/z 746.1 (M^+ + 1). Anal. Calcd for $C_{38}H_{52}O_{12}$-Si: C, 62.62; H, 7.19. Found: C, 62.78; H, 7.34.

6-*O*-[4,6-*O*-Benzylidene-α-D-mannopyranosyl]-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (48). From Carbonate 46. To a solution of **46** (20 mg) and THF (2 mL) was added three drops of LiOH in water solution. The reaction mixture was stirred for about 2 h until all the starting material was consumed. $MgSO_4$ powder was added into the solution, and then the organic solvent was filtered and concentrated to give the diol **48**.

From Benzoate 47. To a solution of **47** (20 mg) in MeOH (2 mL) was added a catalytic amount of sodium, after which the reaction mixture was stirred for 4 h. After the starting material had disappeared, the solvent was removed under vacuum. The residue was taken up in $CHCl_3$, and then two drops of water and brine were added into the solution. The organic layer was dried with $MgSO_4$ and concentrated. To the residue were added CH_2Cl_2 (2 mL) and TBAF (0.05 mL), followed by stirring for 5 h. After completion, the reaction mixture was filtered on Celite, diluted with water, and extracted by CH_2Cl_2 three times. Drying and concentration gave compound **48**: ^{1}H NMR ($CDCl_3$) δ 7.35−7.50 (m, 5 H), 5.55 (s, 1 H), 5.22 (d, J = 5 Hz, 1 H), 4.89 (s, 1 H), 4.61 (dd, J = 2.4, 8 Hz, 1 H), 4.31 (dd, J = 2.4, 5 Hz, 1 H), 4.25 (t, J = 8 Hz, 2 H), 4.05 (m, 2 H), 3.67−4.00 (m, 6 H), 2.90 (br.s, 2 H), 1.39 (s, 3 H), 1.33 (s, 3H), 1.25 (br.s, 6 H), ^{13}C NMR ($CDCl_3$) δ 137.4, 129.4, 128.5, 126.5, 109.6, 108.8, 102.4, 100.4 ($^1J_{CH}$ = 170.4 Hz), 96.5, 79.0, 71.1, 70.8, 70.7, 68.9, 68.7, 68.3, 66.6, 66.2, 63.4, 29.9, 26.3, 26.1, 25.8, 25.1, 24.7; MS (electrospray): m/z 510, and 517.9 (M + H_2O); FABHRMS found 509.2021, calcd for $C_{25}H_{33}O_{11}$ (M − H^+) 509.2023.

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Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra of disaccharide **48**. This material is available free of charge via the Internet at http://pubs.acs.org.

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