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Influence of the O3 Protecting Group on Stereoselectivity in the Preparation of *C*-Mannopyranosides with 4,6-*O*-Benzylidene Protected Donors

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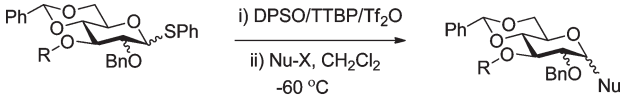
Received July 25, 2010

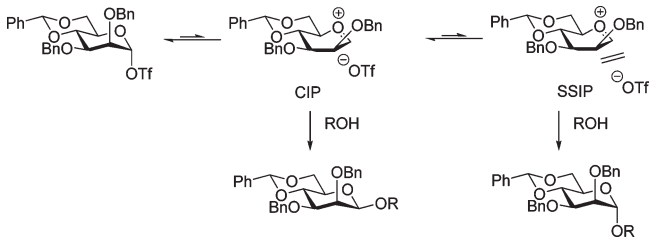


α-*C*-Glucopyranosides and mannopyranosides are obtained in 65−85% yields from 4,6-*O*-benzylidene-protected glucosyl and mannosyl thioglycosides bearing ester functionality at the 3-*O*-position by a coupling reaction with *C*-nucleophiles on activation with diphenyl sulfoxide, 2,4,6-tri-*tert*-butylpyrimidine, and trifluoromethanesulfonic anhydride.

Introduction

For some time, our laboratory has been interested in the stereocontrolled formation of *O*-glycosides, in particular the challenging β-mannopyranosides[1] and the α-sialosides.[2] In the mannopyranoside field, our extensive studies are consistent with a mechanistic picture in which an α-glycosyl triflate formed in situ serves as a reservoir for a series of transient contact (CIP) and solvent-separated (SSIP) ion pairs (Scheme 1). The CIP, in which the α-face of the glycosyl oxacarbenium ion is shielded by the proximal triflate anion, is viewed as the source of the β-mannopyranosides, while the SSIP, in whose chemistry the anomeric effect plays a dominant role, is the precursor to the α-mannopyranosides.[1b] While most of our work has focused on the formation of the *O*-glycosides, we were recently stimulated to investigate briefly *C*-glycoside formation. Working with a series of 4,6-*O*-benzylidene-protected manno- and glucopyranoside donors bearing non-participating benzyl ethers at the 2- and 3-positions, we found that simple allylsilanes and stannanes and silyl enol ethers as *C*-glycosyl acceptors gave the same overall trends as that of typical *O*-glycosyl acceptors.[3] Namely, high β-selectivity was observed in the mannose series while the converse was true in the glucose series. We concluded that there is a strong commonality of mechanism between the formation of *C*- and *O*-glycosides under the conditions practiced in our laboratory.

SCHEME 1. Mechanism of Benzylidene-Directed Mannosylation



Extending this study, as we report here, we have now directed attention at the intriguing case of the 4,6-*O*-benzylidene-protected mannosyl donors bearing an acyl group at the 3-position and find, as for *O*-glycoside formation,[4] that this switch of a single protecting group results in a complete

(1) (a) Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 4506–4507. (b) Crich, D. *Acc. Chem. Res.* **2010**, *43*, 1144–1153.

(2) (a) Crich, D.; Li, W. *Org. Lett.* **2006**, *8*, 959–962. (b) Crich, D.; Li, W. *J. Org. Chem.* **2007**, *72*, 2387–2391. (c) Crich, D.; Li, W. *J. Org. Chem.* **2007**, *72*, 7794–7797. (c) Crich, D.; Xu, B. *Org. Lett.* **2008**, *10*, 4033–4035. (e) Crich, D.; Navuluri, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 3049–3052.

(3) (a) Crich, D.; Sharma, I. *Org. Lett.* **2008**, *10*, 4731–4734. (b) For parallel work, see: McGarvey, G. J.; LeClair, C. A.; Schmidtmann, B. A. *Org. Lett.* **2008**, *10*, 4727–4730.

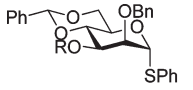
(4) (a) Crich, D.; Cai, W.; Dai, Z. *J. Org. Chem.* **2000**, *65*, 1291–1297. (b) Crich, D.; Yao, Q. *J. Am. Chem. Soc.* **2004**, *126*, 8232–8236. (c) Crich, D.; Picard, S. *J. Org. Chem.* **2009**, *74*, 9576–9579. (d) Ustyuzhanina, N.; Komarova, B.; Zlotina, N.; Krylov, V.; Gerbst, A.; Tsvetkov, Y.; Nifantiev, N. *Synlett* **2006**, 921–923.

DOI: 10.1021/jo101453y Published on Web 11/11/2010

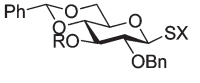
reversal of selectivity with the α-glycosides now being the predominant products. We are therefore reinforced in our notion of a common mechanism for *C*- and *O*-glycoside formation even if it is not clear at present how the group at O3 exerts such a major influence on the stereochemical outcome of these reactions. Also of interest and reported here is the effect of other groups at the 3-position, notably a sulfonyl ester[5] and a bulky silyl ether,[6] on the stereochemical outcome of *C*-glycosylation reactions in the 4,6-*O*-benzylidene-protected mannopyranose series.

Results and Discussion

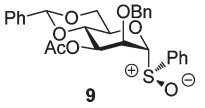
The thioglycosides **1**−**4**, **6**, and **7** were prepared as described in the literature,[7] and the alcohols **1** and **7** were further converted to the derivatives **5** and **8** by standard techniques as described in the Supporting Information. Compound **2** was oxidized with *m*-CPBA with the anticipated high stereoselectivity to the corresponding sulfoxide **9**.[8]



1: R = H
2: R = Ac
3: R = $CONBn_2$
4: R = Ts
5: R = TBDMS
6: R = Boc

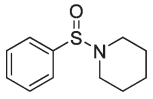


7: R = H, X = Et
8: R = Ac, X = Et

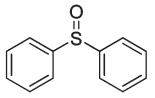


9

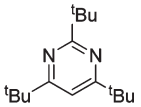
With the various donors in hand, a series of *C*-glycoside-forming reactions, with acceptors of varying nucleophilicity,[9] were conducted as reported in Table 1 with activation by the BSP/TTBP/Tf_2O cocktail[10] or the DPSO/TTBP/Tf_2O mixture recommended for the activation of thioglycosides by van Boom and co-workers or for the sulfoxide by Tf_2O/TTBP.[11]



BSP



DPSO



TTBP

The results of these reactions, for all donors carrying a carboxylate ester, carbonate, or carbamate group at *O*-3, correspond to the trend observed for the formation of *O*-glycosides under closely related reaction conditions. Thus, in the mannose series (entries 1−12), all reactions were highly α-selective as has been repeatedly found for the formation of the *O*-glycosides. As illustrated (Table 1, entry 1) for the somewhat less nucleophilic allylsilane, the reactions are temperature sensitive, giving reduced selectivity on warming to higher temperatures before completion. In the glucose series (Table 1, entries 13−15), the *C*-glycosylation reactions were also highly α-selective, somewhat in keeping with the formation of *O*-glycosides from other glucopyranosyl donors bearing esters at O-3 and ethers at O-2. In keeping with the work of Kim on the formation of *O*-glycosides,[5] a 3-*O*-sulfonyl mannopyranosyl donor also was found to be moderately *β*-selective in its reactions with allyltrimethylsilane and allyltributylstannnane (Table 1, entries 16 and 17).

The 3-*O*-silyl mannopyranosyl donor **5**, whose use typically results in poorly selective *O*-glycosylation reactions,[6,12] gave excellent *β*-selectivity with each of three nucleophiles: allyltrimethylsilane, allyltributylstannane, and acetophenone trimethylsilyl enol ether (Table 1, entries 18−20).

With respect to the assignment of anomeric configuration, all *C*-glycosides bearing an acetyl group at the 3-position were converted by saponification and benzylation to the corresponding known[3a] 3-*O*-benzyl ethers. NOE measurements (Supporting Information) were employed to assign the configuration of the 3-*O*-silyl ethers **20** and **21** whose configuration was confirmed further by chemical correlation with compounds **10** and **12** (Scheme 2). In particular, it is noteworthy that desilylation of **21** derived from the coupling reaction (Table 1, entry 20) followed by acetylation gave the 3-*O*-acetyl derivative **12*β*** that differed from the sample **12α** obtained from the coupling process (Table 1, entry 4), thereby making both stereoisomers of **12** available for comparison of their spectral data. On the other hand, saponification of **12α** followed by silylation resulted in the formation of **21** with inversion of configuration at the anomeric center (Scheme 2). This inversion presumably takes place by a process involving enolization, *β*-elinination, and finally readdition as described previously for related *C*-glycosides prepared by Wittig olefination of anomeric hemiacetals.[13] As a general rule the equatorial *β*-*C*-glycosides had anomeric chemical shifts in the region $\delta_H(CDCl_3)$ 3.5−3.6, and, in silica gel chromatography, were less polar than the corresponding α-anomers which typically displayed anomeric chemical shifts of $\delta_H(CDCl_3)$ 4.0−4.1. The anomeric stereochemistry of the *O*-glycoside **18b** rests on the anomeric $^1J_{CH}$ and $^3J_{H1,H2}$ coupling constants of 171.9 and 3.5 Hz, respectively.

The underlying reason for the α-selectivity enforced by the presence of an ester group at the 3-position in these *C*-glycosylations, and indeed in their *O*-counterparts, remains obscure. The use of the 3-*O*-*tert*-butyloxycarbonyl-protected system with retention of the carbonate, as in the *O*-glycosylation series, argues strongly against neighboring group participation as we have discussed elsewhere.[14] In recent work from the Kim group,[5] with the 3-*O*-trichloroacetimidyl donor **22**, that mirrors a much earlier observation of Nicolaou with a 3-deoxy-3-acetamido donor **24**,[15] it was demonstrated that cyclic intermediates

(5) Baek, J. Y.; Lee, B.-Y.; Jo, M. G.; Kim, K. S. *J. Am. Chem. Soc.* **2009**, *131*, 17705–17713.
(6) Crich, D.; Dudkin, V. *Tetrahedron Lett.* **2000**, *41*, 5643–5646.
(7) (a) Crich, D.; Sun, S. *Tetrahedron* **1998**, *54*, 8321–8348. (b) Dubois, E.; Beau, J. M. *Carbohydr. Res.* **1992**, *228*, 103–120. (c) Ekeloef, K.; Oscarson, S. *Carbohydr. Res.* **1995**, *278*, 289–300.
(8) (a) Crich, D.; Mataka, J.; Sun, S.; Lam, K.-C.; Rheingold, A. R.; Wink, D. J. *Chem. Commun.* **1998**, 2763–2764. (b) Crich, D.; Mataka, J.; Zakharov, L. N.; Rheingold, A. L.; Wink, D. J. *J. Am. Chem. Soc.* **2002**, *124*, 6028–6036.
(9) The *N* values reported in Table 1 are taken from: Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66–77.
(10) (a) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020. (b) Crich, D.; Smith, M.; Yao, Q.; Picione, J. *Synthesis* **2001**, 323–326. (c) Crich, D.; Banerjee, A.; Li, W.; Yao, Q. *J. Carbohydr. Chem.* **2005**, *24*, 415–424.
(11) Codée, J. D. C.; van den Bos, L. J.; Litjens, R. E. J. N.; Overkleeft, H. S.; van Boeckel, C. A. A.; van Boom, J. H.; van der Marel, G. A. *Tetrahedron* **2004**, *60*, 1057–1064.
(12) Codée, J. D. C.; Hossain, L. H.; Seeberger, P. G. *Org. Lett.* **2005**, *7*, 3251–3254.
(13) Wang, Z.; Shao, H.; Lacroix, E.; Wu, S.-H.; Jennings, H. J.; Zou, W. *J. Org. Chem.* **2003**, *68*, 8097–8015.
(14) Crich, D.; Hu, T.; Cai, F. *J. Org. Chem.* **2008**, *73*, 8942–8953.

TABLE 1. Formation of *C*-Glycosides from the 3-*O*-Carboxylates and Other 3-*O*-Derivatives

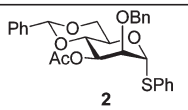
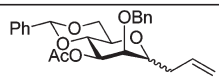
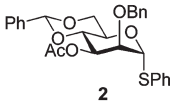
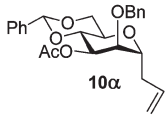
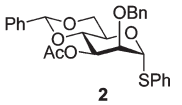
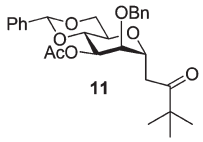
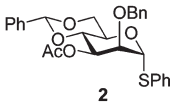
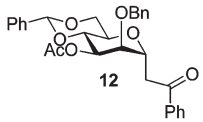
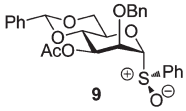
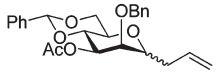
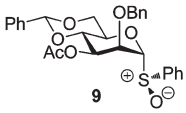
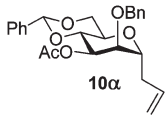
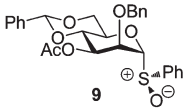
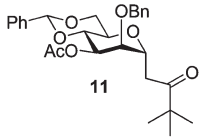
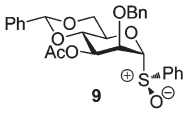
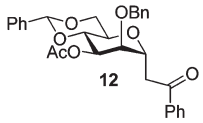
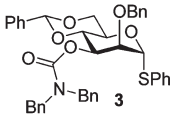
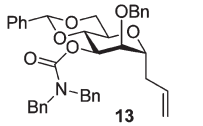
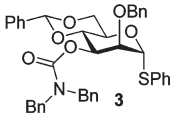
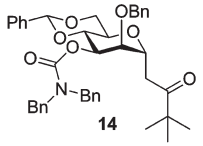
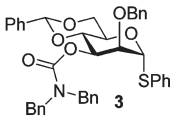
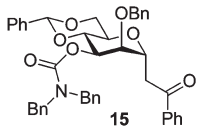
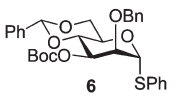
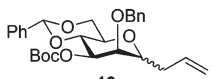
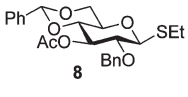
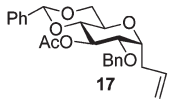
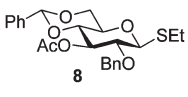
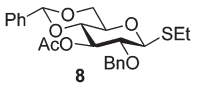
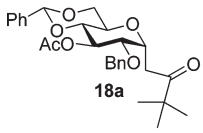
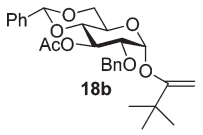
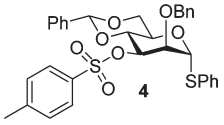
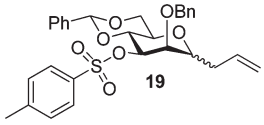
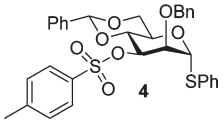
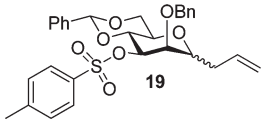
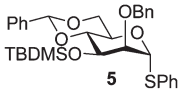
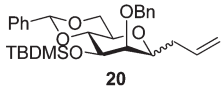
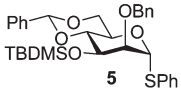
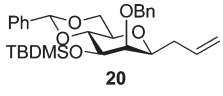
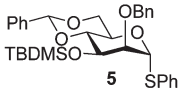
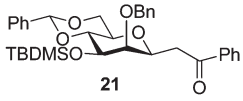
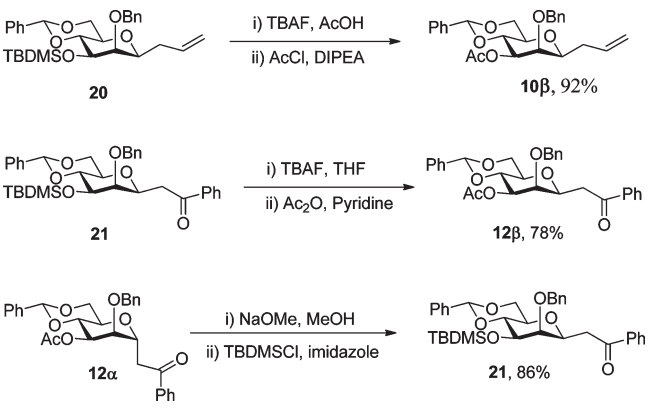
Entry	Donor	Acceptor	*N*-value	Coupled Product	Isolated Yield[a]	α:β Ratio[b]
1	 **2**		1.8	 **10**	67% 86%[d] 81%[e]	13:1 7:1[c] 3.52:1[c]
2	 **2**		5.5	 **10α**	71%	α only
3	 **2**		3.8	 **11**	76%	α only
4	 **2**		6.2	 **12**	79% 61%[e]	α only
5	 **9**		1.8	 **10**	65%	13:1
6	 **9**		5.5	 **10α**	69%	α only
7	 **9**		3.8	 **11**	74%	α only
8	 **9**		6.2	 **12**	84%	α only
9	 **3**		5.5	 **13**	73% 45%[e]	α only
10	 **3**		3.8	 **14**	76%	α only
11	 **3**		6.2	 **15**	86%	α only
12	 **6**		1.8	 **16**	44%	7.8:1
13	 **8**		1.8	 **17**	59%	α only
14	 **8**		5.5	**17**	63%	α only

TABLE 1. Continued

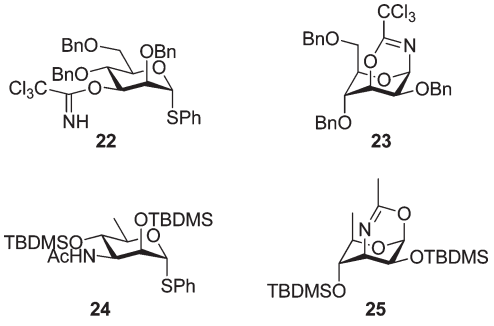
15	 **8**		3.8	 **18a** +  **18b**	**18a**, 41% **18b**, 21%	**18a**, α only **18b**, α only
16	 **4**		1.8	 **19**	53%	1:4
17	 **4**		5.5	 **19**	65%	1:5.5
18	 **5**		1.8	 **20**	68%	1:19
19	 **5**		5.5	 **20**	76%	β only
20	 **5**		6.2	 **21**	81%	β only

[a]Isolated yields after column chromatography. [b]Ratios were determined by ^{1}H NMR spectroscopy of crude reaction mixtures. [c]After addition of the nucleophile, the reaction mixture was slowly (~ 2 h) warmed to room temperature and quenched at the same temperature. [d]After addition of the nucleophile, the reaction mixture was immediately (~5 min) warmed to room temperature and quenched at the same temperature. [e]BSP was used instead of DPSO.

SCHEME 2. Correlation of the Anomeric Stereochemistry of Compounds 10*β* and 20 and of Compounds 12 and 21



(**23** and **25**, respectively) can be formed and trapped, leading them to the conclusion that the effect of the 3-*O*-ester can be explained by neighboring group participation. Amides and imidates are, however, considerably better nucleophiles than carboxylate esters,[16,17] and we question their use as probes for the latter in the present context. We continue to work toward a more satisfactory explanation for the effect of the 3-*O*-esters and will address the issue more fully in a subsequent paper.


22 **23** **24** **25**

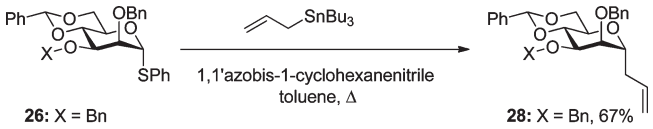
With respect to the 3-*O*-tosyl mannosyl donor **4** the moderate *β*-selectivity observed (Table 1, entries 16 and 17) is best explained in terms of the electron-withdrawing ability of the sulfonyl group stabilizing the covalent triflate and

(15) Nicolaou, K. C.; Daines, R. A.; Ogawa, Y.; Chakraborty, T. K. *J. Am. Chem. Soc.* **1988**, *110*, 4696–4705.

(16) Imidates react with a variety of electrophiles, including carboxylic anhydrides with which esters patently do not. (a) Roger, R.; Neilson, D. G. *Chem. Rev.* **1961**, *61*, 179–211. (b) Neilson, D. G. In *The Chemistry of Amidines and Imidates*; Patai, S., Ed.; Wiley-Interscience: London, 1975; Vol. 1; pp 385−489.

(17) For specific examples of the trapping of glycosyl oxocarbenium ions by amides in cases when esters are innocuous, see: Liao, L.; Auzanneau, F.-I. *J. Org. Chem.* **2005**, *70*, 6265–6273.

SCHEME 3. Formation of α-*C*-Glycosides by Radical Reactions



26: X = Bn
27: X = Bz

28: X = Bn, 67%
29: X = Bz, 78%

thereby reducing the concentration of ions pairs in the reaction mixture. We note that both the S−O and S═O single and double bonds are longer than their C−O and C═O counterparts and that the barrier for rotation about the SO_2−O bond is small compared to that for rotation about the CO−O bond in carboxylate esters.[18] As a consequence, we consider that alternative explanations to the electron-withdrawing character of the sulfonate ester are not required.

Interestingly, the use of pinacolone trimethylsilyl enol ether as nucleophile resulted in the formation of a significant amount of the *O*-glycoside **18b** when the 3-*O*-acetyl glucosyl donor **8** was employed (Table 1, entry 15), whereas with the corresponding mannosyl donor **2** and its close analogues **3** and **9** only the *C*-glycosides were isolated (Table 1, entries 3, 7, and 10). This situation closely follows that observed previously with the corresponding series of 3-*O*-benzyl donors, wherein a much higher yield of *O*-glycoside was observed for the gluco-configured donor than for the manno isomer.[3a] This difference presumably reflects the increased reactivity of the 4,6-*O*-benzylidene-protected glucopyranosyl donors over that of their mannopyranosyl counterparts on which we have remarked previously.[1b]

We have also very briefly investigated the formation of 4,6-*O*-benzylidene-protected *C*-mannosides by radical reactions employing allyltributylstannane[19] as reagent. As expected on the basis of literature precedent for similarly protected systems,[20] radicals generated from thioglycosides **26** and **27** obey the general rule[21] of α-selectivity in the quenching of pyranosyl radicals and gave the α-allyl *C*-glycosides **28** and **29** in good yield irrespective of the protecting group at the 3-position (Scheme 3). As 4,6-*O*-benzylidene-protected glucopyransoyl radicals are known[22] to adopt either $B_{2,5}$ or $^4H_5$ conformations that closely approximate the calculated conformations[23] of similarly protected oxocarbenium ions, the α-selectivity observed in the 3-*O*-benzyl series strongly supports the involvement of the counterion (in the CIP) in the β-selective formation of *C*- and *O*-glycosides under the typical ionic conditions.

The work presented here reinforces the notion of a commonality of mechanism for *C*- and *O*-glycoside formation and will likely be of use to workers interested in the effects of protecting groups[24] on glycosylation reactions and in *C*-glycoside synthesis from both the mechanistic[25] and preparative perspectives.[26]

Experimental Section

Phenyl 4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(*N*,*N*-dibenzylcarbonyl)-1-deoxy-1-thio-α-D-mannopyranoside (3). To a stirred solution of phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-α-D-mannopyranoside (**1**) (530 mg, 1.18 mmol) in dry DMF (5 mL) was added NaH (60% suspension in mineral oil, 57 mg, 1.42 mmol) at 0 °C. After 10 min, a solution of *N*,*N*-dibenzylchloroformamide (366 mg, 1.42 mmol) in dry DMF (1 mL) was added to the reaction mixture at 0 °C. The reaction mixture was stirred at rt for 1 h before it was quenched with saturated NH_4Cl solution and diluted with ethyl acetate. The organic layer was separated, washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (15% ethyl acetate/hexane) afforded the desired product (610 mg, 77%): $[\alpha]^{21}_D$ +54.8 (*c* = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.16 (m, 23H), 7.06 (t, *J* = 7.2 Hz, 2H), 5.59 (d, *J* = 9.6 Hz, 2H), 5.44 (dd, *J* = 9.6, 3.2 Hz, 1H), 4.66−4.58 (m, 3H), 4.51−4.45 (m, 2H), 4.34−4.19 (m, 4H), 3.90 (t, *J* = 7.8 Hz, 1H); ^{13}C NMR (100.9 MHz, $CDCl_3$) δ 155.1, 137.8, 137.6, 137.5, 137.3, 134.1, 132.0, 129.4, 129.3, 128.9, 128.8, 128.7, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 126.6, 102.1, 87.1, 78.9, 77.6, 76.9, 73.6, 72.4, 68.8, 65.5, 49.6, 49.3; ESI-HRMS calcd for $C_{41}H_{39}O_6NSNa$ $[M + Na]^+$ 696.2396, found 696.2348.

Phenyl 4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(4-methylbenzenesulfonyl)-1-deoxy-1-thio-α-D-mannopyranoside (4). To a stirred solution of phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-α-D-mannopyranoside (**1**) (255 mg, 0.57 mmol) in dry pyridine (5 mL) was added *p*-toluenesulfonyl chloride (475 mg, 2.50 mmol) followed by the addition of DMAP (61 mg, 0.50 mmol) at rt. After 8 h, pyridine was removed, and the reaction mixture was diluted with ethyl acetate. The organic layer was washed with 5% sodium carbonate solution, water, and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (20% ethyl acetate/hexane) afforded the desired product with a yield of 230 mg (76%): $[\alpha]^{22}_D$ +68.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.5 Hz, 2H), 7.42−7.25 (m, 15H), 7.11 (d, *J* = 8.0 Hz, 1H), 5.46 (s, 1H), 5.43 (d, *J* = 1.0 Hz, 1H), 4.85−4.83 (m, 2H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.35 (dd, *J* = 1.5, 3.5 Hz, 1H), 4.24−4.15 (m, 3H),

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3.84−3.80 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 144.9, 137.4, 137.2, 133.3, 133.2, 132.3, 129.8, 129.5, 129.2, 128.8, 128.5, 128.4, 128.3, 128.2, 126.4, 101.8, 87.4, 79.0, 77.9, 76.0, 74.4, 68.5, 65.7, 21.9; ESI-HRMS calcd for $C_{33}H_{32}O_7S_2Na$ $[M + Na]^+$ 627.1487, found 627.1475.

Phenyl 4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-1-deoxy-1-thio-α-D-mannopyranoside (5). To a stirred solution of phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-α-D-mannopyranoside (**1**) (230 mg, 0.51 mmol) and imidazole (200 mg, 2.94 mmol) in dry DMF (5 mL) was added *tert*-butyldimethylsilyl chloride (348 mg, 2.31 mmol) at rt. The reaction mixture was stirred at rt for 14 h before it was diluted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (10% ethyl acetate/hexane) afforded the desired product (245 mg, 85%): $[\alpha]^{26}_D$ +104.1 ($c = 1$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55−7.54 (m, 2H), 7.45−7.31 (m, 13H), 5.63 (s, 1H), 5.55 (s, 1H), 4.90 (d, $J = 12.0$ Hz, 1H), 4.74 (d, $J = 12.0$ Hz, 1H), 4.33−4.29 (m, 1H), 4.25−4.22 (m, 2H), 4.15 (t, $J = 9.5$ Hz, 1H), 4.0−3.99 (m, 1H), 3.89 (t, $J = 10.0$ Hz, 1H), 0.95 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 138.3, 137.9, 134.3, 131.8, 129.4, 129.1, 128.7, 128.3, 128.2, 128.1, 127.8, 126.5, 102.2, 87.9, 81.3, 79.5, 74.2, 71.1, 68.8, 65.9, 26.2, 18.6, −4.2, −4.5; ESI-HRMS calcd for $C_{32}H_{40}O_5SiSNa$ $[M + Na]^+$ 587.2263, found 587.2264.

Ethyl 4,6-*O*-Benzylidene-2-*O*-benzyl-1-deoxy-1-thio-β-D-glucopyranoside (7). To a solution of ethyl 4,6-*O*-benzylidene-1-deoxy-1-thio-β-D-glucopyranoside (312 mg, 1.0 mmol) and tetrabutylammonium hydrogensulfate (68 mg, 0.2 mmol) in methylene chloride (16 mL)/1 N NaOH (5 mL) was added benzyl bromide (143 μL, 1.2 mmol) at rt. The reaction mixture was heated to reflux at 45 °C for 24 h before it was cooled to rt and diluted with methylene chloride. The organic layer was separated, washed with water, saturated $NaHCO_3$ solution, and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (20% ethyl acetate/hexane) afforded the desired product (54 mg, 14%): $[\alpha]^{20}_D$ −32.8 ($c = 1$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50−7.31 (m, 10H), 5.54 (s, 1H), 4.96 (d, $J = 11.0$ Hz, 1H), 4.80 (d, $J = 10.5$ Hz, 1H), 4.70 (s, 1H), 4.58 (d, $J = 10.0$ Hz, 1H), 4.37−4.34 (m, 1H), 3.90 (dd, $J = 8.5, 9.5$ Hz, 1H), 3.77 (t, $J = 10.0$ Hz, 1H), 3.55 (t, $J = 9.0$ Hz, 1H), 3.49−3.45 (m, 1H), 3.40 (dd, $J = 8.0, 10.0$ Hz, 1H), 2.83−2.74 (m, 2H), 1.36−1.33 (m, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 138.2, 137.2, 129.5, 128.8, 128.6, 128.3, 127.9, 127.2, 126.5, 102.0, 85.8, 81.7, 80.7, 75.8, 75.5, 70.3, 68.9, 65.6, 25.5, 15.3; ESI-HRMS calcd for $C_{22}H_{26}O_5SNa$ $[M + Na]^+$ 425.1399, found 425.1384.

Ethyl 3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-β-D-glucopyranoside (8). To a stirred solution of ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-β-D-glucopyranoside (**7**) (50 mg, 0.12 mmol) and DIPEA (129 μL, 0.74 mmol) in dry methylene chloride (5 mL) was added acetyl chloride (44 μL, 0.62 mmol) at 0 °C. After 10 min, the reaction mixture was warmed to rt and stirred for 30 min before it was diluted with methylene chloride. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (20% ethyl acetate/hexane) afforded the desired product (54 mg, 98%): $[\alpha]^{21}_D$ −32.3 ($c = 1$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.43 (m, 2H), 7.38−7.31 (m, 8H), 5.48 (s, 1H), 5.38 (t, $J = 9.5$ Hz, 1H), 4.90 (d, $J = 11.0$ Hz, 1H), 4.64 (t, $J = 10.5$ Hz, 1H), 4.38−4.35 (m, 1H), 3.77 (t, $J = 10.5$ Hz, 1H), 3.61 (t, $J = 9.5$ Hz, 1H), 3.57−3.48 (m, 2H), 2.84−2.76 (m, 2H), 1.98 (s, 3H), 1.34 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.0, 137.9, 137.2, 129.3, 128.7, 128.5, 128.4, 128.2, 126.4, 101.6, 86.2, 80.1, 79.0, 75.6, 74.5, 70.6, 68.9, 25.8, 21.2, 15.3; ESI-HRMS calcd for $C_{24}H_{28}O_6SNa$ $[M + Na]^+$ 467.1504, found 467.1487.

Phenyl 3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-α-D-mannopyranoside *S*-Oxide (9). To a stirred solution of phenyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-α-D-mannopyranoside (**2**) (400 mg, 0.81 mmol) in methylene chloride (20 mL) was added *m*-CPBA (77%, 182 mg, 0.81 mmol) at −78 °C. The reaction mixture was allowed to warm to −20 °C naturally over 1.5 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The organic layer was separated, washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (40% ethyl acetate: hexane) afforded the desired product (368 mg, 89%): $[\alpha]^{22}_D$ −57.1 ($c = 1$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69−7.67 (m, 2H), 7.60−7.58 (m, 3H), 7.48−7.46 (m, 2H), 7.39−7.37 (m, 3H), 7.31−7.30 (m, 3H), 7.17−7.16 (m, 2H), 5.62 (d, $J = 6.5$ Hz, 1H), 5.58 (s, 1H), 4.53−4.51 (m, 3H), 4.33 (d, $J = 12.0$ Hz, 1H), 4.27−4.24 (m, 3H), 3.77−3.73 (m, 1H), 2.01 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.1, 141.4, 137.2, 137.0, 132.0, 129.8, 129.4, 128.7, 128.5, 128.4, 126.5, 124.9, 102.2, 97.3, 75.6, 73.4, 72.6, 70.7, 70.2, 68.5, 21.1; ESI-HRMS calcd for $C_{28}H_{28}O_7SNa$ $[M + Na]^+$ 531.1453, found 531.1461.

General Procedure 1 for Glycosylation Using the Diphenyl Sulfoxide/TTBP/Tf_2O System. To a stirred solution of donor (1 equiv), diphenyl sulfoxide (1.2 equiv), TTBP (1.5 equiv), and 4 Å molecular sieves in CH_2Cl_2 (0.05 M in substrate) at −55 °C under an argon atmosphere was added Tf_2O (1.2 equiv). After 30 min of stirring at −55 °C, a solution of the glycosyl acceptor (5.0 equiv) was slowly added. The reaction mixture was stirred for a further 2−12 h at −55 °C before it was quenched with $NaHCO_3$ solution at the same temperature. The reaction mixture was diluted with CH_2Cl_2, and the molecular sieves were filtered off. The organic layer was washed with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel, eluting with hexanes/ethyl acetate or hexanes/methyl *tert*-butyl ether mixtures, afforded the corresponding coupled products.

3-*O*-Acetyl-1-allyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-α-D-mannopyranose (10α) and 3-*O*-Acetyl-1-allyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-β-D-mannopyranose (10β). Prepared by general procedure 1 with a combined yield of 104 mg (81%, 3.52:1 α/β). Both anomers were separated by flash column chromatography on silica gel (10% methyl *tert*-butyl ether/hexane). **10α**: $[\alpha]^{23}_D$ +13.8 (*c*, 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48−7.46 (m, 2H), 7.39−7.31 (m, 8H), 5.77−5.71 (m, 1H), 5.60 (s, 1H), 5.24−5.13 (m, 4H), 4.68 (d, $J = 12.0$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 4.26−4.21 (m, 2H), 4.10 (t, $J = 7.0$ Hz, 1H), 3.91 (dd, $J = 1.5, 3.5$ Hz, 1H), 3.84 (t, $J = 10.0$ Hz, 1H), 3.76−3.71 (m, 1H), 2.63−2.57 (m, 1H), 2.42−2.37 (m, 1H), 2.05 (s, 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.8, 137.9, 137.6, 133.3, 129.3, 128.7, 128.5, 128.4, 128.2, 126.4, 118.6, 102.0, 76.8, 76.7, 76.4, 73.0, 70.8, 69.4, 66.0, 33.9, 21.3; ESI-HRMS calcd for $C_{25}H_{28}O_6Na$ $[M + Na]^+$ 447.1784, found 447.1775. **10β**: colorless oil; $[\alpha]^{20}_D$ −39.6 (*c*, 0.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.41−7.33 (m, 8H), 5.78−5.70 (m, 1H), 5.58 (s, 1H), 5.11−5.07 (m, 3H), 4.76 (d, $J = 11.0$ Hz, 1H), 4.62 (d, $J = 12.0$ Hz, 1H), 4.31−4.28 (m, 1H), 4.18 (t, $J = 10.0$ Hz, 1H), 4.03−4.01 (m. 1H), 3.97 (m, $J = 2.0$ Hz, 1H), 3.84 (t, $J = 10.5$ Hz, 1H), 3.63 (t, $J = 7.0$ Hz, 1H), 3.52−3.47 (m, 1H), 2.53−2.47 (m, 1H), 2.34−2.29 (m, 1H), 2.06 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.9, 137.6, 137.7, 134.1, 129.2, 128.7, 128.5, 128.4, 128.2, 126.4, 118.1, 101.9, 79.5, 76.9, 76.6, 75.8, 74.9, 72.2, 68.9, 35.6, 21.3; ESI-HRMS calcd for $C_{25}H_{28}O_6Na$ $[M + Na]^+$ 447.1784, found, 447.1772.

3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-(3,3-dimethyl-2-oxobutyl)-α-D-mannopyranose (11). Prepared by general procedure 1 (eluent 15% ethyl acetate/hexane) with a yield of 37 mg (76%): $[\alpha]^{22}_D$ −23.6 ($c = 1.0$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.46 (m, 2H), 7.41−7.31 (m, 8H),

5.59 (s, 1H), 5.12 (dd, J = 11.0, 4.0 Hz, 1H), 4.82 (d, J = 12.0 Hz, 1H), 4.76 (t, J = 7.0 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H),4.25−4.21 (m, 2H), 3.84 (t, J = 10.0 Hz, 1H), 3.80 (dd, J = 1.0, 3.5 Hz, 1H), 3.69−3.65 (m, 1H), 2.96 (s, 1H), 2.95 (s, 1H), 1.98 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 212.6, 170.7, 138.0, 137.5, 129.3, 128.6, 128.5, 128.1, 126.4, 101.9, 76.4, 72.9, 72.4, 70.4, 69.3, 67.4, 44.8, 36.1, 26.3, 21.2; ESI-HRMS calcd for $C_{28}H_{34}O_7Na$ $[M + Na]^+$ 505.2202, found 505.2210.

3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-(2-oxo-2-phenylethyl)-α-D-mannopyranose (12α). Prepared by general procedure 1 (eluent 15% ethyl acetate/hexane) with a yield of 40 mg (79%): $[\alpha]^{22}_D$ −17.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98−7.96 (m, 2H), 7.64−7.61 (m, 1H), 7.53−7.44 (m, 6H), 7.38−7.31 (m, 6H), 5.60 (s, 1H), 5.23 (dd, J = 11.0, 4.0 Hz, 1H), 4.94−4.90 (m, 1H), 4.86 (d, J = 12.0 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.28−4.23 (m, 2H), 3.97 (dd, J = 1.5, 3.0 Hz, 1H), 3.85 (t, J = 10.0 Hz, 1H), 3.79−3.76 (m, 1H), 3.52 (dd, J = 5.0, 17.50 Hz, 1H), 3.37 (dd, J = 8.5, 17.5 Hz, 1H), 1.99 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 196.7, 170.8, 138.0, 137.5, 136.7, 134.6, 134.0, 129.3, 129.2, 129.1, 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 126.4, 102.0, 76.9, 76.6, 73.0, 72.6, 70.4, 69.3, 67.3, 38.1, 21.2; ESI-HRMS calcd for $C_{30}H_{30}O_7Na$ $[M + Na]^+$ 525.1889, found 525.1866.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(*N*,*N*-dibenzylcarbonyl)-1-deoxy-1-allyl-α-D-mannopyranose (13). Prepared by the general procedure 1 (eluent 10% ethyl acetate/hexane) with a yield of 33 mg (73%): $[\alpha]^{22}_D$ −16.3 (c = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49−7.15 (m, 18H), 7.04 (t, J = 7.5 Hz, 2H), 5.77−5.70 (m, 1H), 5.59 (s, 1H), 5.36 (dd, J = 3.5, 10.5 Hz, 1H), 5.20−5.12 (m, 2H), 4.70−4.59 (m, 4H), 4.29−4.18 (m, 4H), 4.11 (t, J = 8.0 Hz, 1H), 4.08 (dd, J = 2.0, 3.5 Hz, 1H), 3.86−3.76 (m, 2H), 2.68−2.62 (m, 1H), 2.44−2.39 (m, 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 156.3, 138.1, 137.7, 137.4, 137.3, 133.5, 129.2, 128.8, 128.6, 128.5, 128.2, 128.0, 127.9, 127.7, 126.5, 118.4, 102.0, 73.4, 72.5, 69.4, 65.9, 49.5, 49.3, 33.9; ESI-HRMS calcd for $C_{38}H_{39}NO_6Na$ $[M + Na]^+$ 628.2675, found 628.2616.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(*N*,*N*-dibenzylcarbonyl)-1-deoxy-1-(3,3-dimethyl-2-oxo-butyl)-α-D-mannopyranose (14). Prepared by the general procedure **1** (eluent 15% ethyl acetate/hexane) with a yield of 37 mg (76%): $[\alpha]^{22}_D$ −17.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.40−7.39 (m, 3H), 7.33−7.31 (m, 2H), 7.27−7.267 (m, 5H), 7.20−7.15 (m, 6H), 7.05−7.02 (m, 2H), 5.59 (s, 1H), 5.31 (dd, J = 3.0, 10.0 Hz, 1H), 4.81−4.78 (m, 2H), 4.67 (d, J = 16.5 Hz, 1H), 4.60−4.57 (m, 2H), 4.30−4.15 (m, 4H), 4.02 (d, J = 2.0 Hz, 1H), 3.84 (t, J = 10.0 Hz, 1H), 3.76−3.71 (m, 1H), 3.10 (dd, J = 6.0, 17.5 Hz, 1H), 2.88 (dd, J = 8.0, 17.5 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 212.5, 156.3, 138.3, 137.7, 137.4, 137.3, 129.2, 128.9, 128.7, 128.5, 128.2, 127.9, 127.7, 127.6, 126.5, 101.9, 78.3, 73.3, 72.9, 72.1, 69.3, 67.3, 49.5, 49.3, 44.8, 36.1, 26.4; ESI-HRMS calcd for $C_{41}H_{45}NO_7Na$ $[M + Na]^+$ 686.3094, found 686.3115.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(*N*,*N*-dibenzylcarbonyl)-1-deoxy-1-(2-oxo-2-phenylethyl)-α-D-mannopyranose (15). Prepared by the general procedure **1** (eluent 20% ethyl acetate/hexane) with a yield of 44 mg (86%): $[\alpha]^{20}_D$ −9.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.0 Hz, 2H), 7.62 (t, J = 7.0 Hz, 1H), 7.53−7.50 (m, 5H), 7.41−7.25 (m, 10H), 7.20−7.15 (m, 5H), 7.03 (t, J = 7.5 Hz, 2H), 5.60 (s, 1H), 5.41 (dd, J = 3.0, 10.0 Hz, 1H), 4.97 (t, J = 6.5 Hz, 1H), 4.83 (d, J = 12.0 Hz, 1H), 4.70−4.65 (m, 2H), 4.57 (d, J = 15.5 Hz, 1H), 4.31 (dd, J = 9.0, 10.5 Hz, 1H), 4.25−4.19 (m, 3H), 4.16−4.15 (m, 2H), 3.85−3.83 (m, 2H), 3.58 (dd, J = 6.0, 17.5 Hz, 1H), 3.40 (dd, J = 8.0, 17.0 Hz, 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 196.6, 156.3, 138.2, 137.7, 137.4, 137.3, 136.7, 133.9, 129.3, 129.1, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 126.5, 102.0, 78.3, 73.3, 73.0, 72.1, 69.3, 67.3, 49.6, 49.3, 38.2; ESI-HRMS calcd for $C_{43}H_{41}NO_7Na$ $[M + Na]^+$ 706.2781, found 706.2772.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-*tert*-butoxycarbonyl-1-deoxy-1-allyl-α-D-mannopyranose (16α) and 4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-*tert*-butoxycarbonyl-1-deoxy-1-allyl-β-D-mannopyranose (16β). Prepared by the general procedure 1 with a combined yield of 44 mg (44%, 7.8:1 α/β). Both anomers were separated by flash column chromatography on silica gel (10% methyl *tert*-butyl ether/hexane). **16α**: $[\alpha]^{23}_D$ −0.174 (c = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51−7.49 (m, 2H), 7.40−7.29 (m, 8H), 5.74−5.66 (m, 1H), 5.59 (s, 1H), 5.16−5.10 (m, 2H), 5.04 (dd, J = 3.0, 10.0 Hz, 1H), 4.66 (q, J = 12.0 Hz, 2H), 4.28−4.22 (m, 2H), 4.08 (t, J = 7.5 Hz, 1H), 3.97 (dd, J = 1.5, 3.0 Hz, 1H), 3.83 (t, J = 10.0 Hz, 1H), 3.74−3.69 (m, 1H), 2.61−2.55 (m, 1H), 2.37−2.31 (m, 1H), 1.49 (s, 9H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 153.2, 138.0, 137.6, 133.3, 129.2, 18.6, 128.4, 128.3, 128.1, 126.4, 118.4, 101.9, 82.9, 77.1, 76.9, 76.3, 73.6, 73.4, 69.3, 65.9, 33.8, 28.0; ESI-HRMS calcd for $C_{28}H_{34}O_7Na$ $[M + Na]^+$ 505.2202, found 505.2206. **16β**: $[\alpha]^{23}_D$ −35.50 (c = 0.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51−7.49 (m, 2H), 7.42−7.31 (m, 8H), 5.74−5.65 (m, 1H), 5.58 (s, 1H), 5.07−5.04 (m, 2H), 4.92−4.88 (m, 2H), 4.56 (d, J = 11.0 Hz, 1H), 4.30 (dd, J = 4.5, 10.5 Hz, 1H), 4.21 (t, J = 10.0 Hz, 1H), 4.03 (d, J = 3.0 Hz, 1H), 3.84 (t, J = 10.0 Hz, 1H), 3.58 (t, J = 7.0 Hz, 1H), 3.51−3.46 (m, 1H), 2.50−2.44 (m, 1H), 2.28−2.23 (m, 1H), 1.51 (s, 9H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 153.3, 138.0, 137.7, 134.2, 129.2, 128.7, 128.6, 128.4, 128.2, 126.5, 117.9, 101.8, 83.0, 79.5, 77.8, 76.6, 76.1, 75.6, 72.1, 68.8, 35.6, 28.0; ESI-HRMS calcd for $C_{28}H_{34}O_7Na$ $[M + Na]^+$ 505.2202, found 505.2208.

3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-allyl-α-D-glucopyranose (17). Prepared by the general procedure **1** (eluent 10% ethyl acetate/hexane) with a yield of 30.0 mg (63%): $[\alpha]^{23}_D$ +13.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46−7.45 (m, 2H), 7.38−7.30 (m, 8H), 5.80−5.71 (m, 1H), 5.48 (s, 1H), 5.43 (t, J = 9.0 Hz, 1H), 5.16−5.09 (m, 2H), 4.64 (s, 2H), 4.26 (dd, J = 10.0, 4.5 Hz, 1H), 4.13−4.11 (m, 1H), 3.75−3.71 (m, 2H), 3.66 (t, J = 10.0 Hz, 1H), 3.60 (t, J = 9.5 Hz, 1H), 2.65−2.58 (m, 1H), 2.55−2.52 (m, 1H), 2.08 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.4, 138.0, 137.3, 134.2, 129.2, 128.7, 128.5, 128.2, 128.0, 126.4, 117.7, 101.7, 80.2, 77.9, 74.9, 73.1, 71.5, 69.7, 63.7, 31.0, 21.3; ESI-HRMS calcd for $C_{25}H_{28}O_6Na$ $[M + Na]^+$ 447.1784, found 447.1791.

3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-(3,3-dimethyl-2-oxo-butyl)-α-D-glucopyranose (18α). Prepared by the general procedure 1 (eluent 15% ethyl acetate/hexane) with a yield of 33 mg (41%): $[\alpha]^{22}_D$ +21.2 (c = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46−7.44 (m, 2H), 7.38−7.27 (m, 8H), 5.48 (s, 1H), 5.33 (t, J = 9.0 Hz, 1H), 4.94−4.91 (m, 1H), 4.58 (d, J = 11.5 Hz, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.25−4.23 (m, 1H), 3.76−3.73 (m, 1H), 3.70−3.67 (m, 2H), 3.61 (t, J = 9.0 Hz, 1H), 2.98 (dd, J = 5.5, 17.5 Hz, 1H), 2.88 (dd, J = 7.0, 17.5 Hz, 1H), 2.07 (s, 3H), 1.12 (s, 9H); ^{13}C NMR (125.9 MHz, $CDCl_3$) δ 212.5, 170.5, 137.7, 129.3, 128.6, 128.5, 128.2, 126.3, 101.7, 79.9, 73.0, 71.6, 71.5, 69.6, 65.1, 44.7, 34.4, 26.3, 21.3; ESI-HRMS calcd for $C_{28}H_{34}O_7Na$ $[M + Na]^+$ 505.2202, found 505.2213.

(3,3-Dimethyl-2-buten-2-yl) 3-*O*-acetyl-2-*O*--benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (18β). Prepared by the general procedure 1 (eluent 10% ethyl acetate/hexane) with a yield of 17 mg (21%); $[\alpha]^{22}_D$ +42.2 (c = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.45 (m, 2H), 7.37−7.30 (m, 8H), 5.61 (t, J = 10.0 Hz, 1H), 5.48 (s, 1H), 5.36 (d, J = 3.5 Hz, 1H), 4.64 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.28−4.24 (m, 1H), 4.22 (d, J = 2.0 Hz, 1H), 4.13 (d, J = 2.5 Hz, 1H), 3.89−3.84 (m, 1H), 3.71−3.64 (m, 2H), 3.58 (t, J = 10.0 Hz, 1H), 2.09 (s, 3H), 1.17 (s, 9H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.0, 169.3, 138.0, 137.3, 129.2, 128.7, 128.4, 128.1, 127.8, 126.4, 101.7, 94.8, 82.6, 79.8, 77.7, 72.5, 71.0, 69.3, 63.2, 36.5, 28.5, 21.3; ESI-HRMS calcd for $C_{28}H_{34}O_7Na$ $[M + Na]^+$ 505.2202, found 505.2158.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(4-methylbenzenesulfonyl)-1-deoxy-1-allyl-α-D-mannopyranose (19α) and 4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-(4-methylbenzenesulfonyl)-1-deoxy-1-allyl-*β*-D-mannopyranose (19*β*). Prepared by the general procedure 1 with a combined yield of 42 mg (53%, 1:4 α/*β*). Both anomers were separated by flash column chromatography on silica gel (15% methyl tert-butyl ether/hexane). **19α**: $[\alpha]^{22}_D$ −35.5 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.75 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 7.0 Hz, 2H), 7.39−7.32 (m, 6H), 7.24 (d, *J* = 7.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.65−5.60 (m, 1H), 5.46 (s, 1H), 5.13−5.09 (m, 2H), 4.84 (d, *J* = 12.0 Hz, 1H), 4.80 (dd, *J* = 3.0, 10.5 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.22−4.16 (m, 2H), 4.04−4.01 (m, 2H), 3.77 (t, *J* = 10.0 Hz, 1H), 3.61−3.56 (m, 1H), 2.49−2.45 (m, 1H), 2.36 (s, 3H), 2.33−2.27 (m, 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) *δ* 144.7, 137.8, 137.3, 133.7, 132.9, 129.7, 129.1, 128.7, 128.6, 128.2, 126.4, 118.7, 101.8, 78.3, 77.8, 76.4, 74.2, 69.1, 66.1, 33.8, 21.9; ESI-HRMS calcd for $C_{30}H_{32}O_7SNa$ $[M + Na]^+$ 559.1766, found 559.1750. **19*β***: $[\alpha]^{22}_D$ −7.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.75 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 6.5 Hz, 2H), 7.40−7.31 (m, 6H), 7.21 (d, *J* = 7.0 Hz, 2H), 7.05 (d, *J* = 8.5 Hz, 2H), 5.69−5.62 (m, 1H), 5.42 (s, 1H), 5.12−5.03 (m, 3H), 4.75 (d, *J* = 11.5 Hz, 1H), 4.66 (dd, *J* = 3.0, 10.0 Hz, 1H), 4.24−4.21 (m, 1H), 4.14−4.10 (m, 2H), 3.78−3.74 (m, 1H), 3.53 (t, *J* = 6.5 Hz, 1H), 3.36−3.31 (m, 1H), 2.49−2.43 (m, 1H), 2.35 (s, 3H), 2.25−2.19 (m, 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) *δ* 144.8, 137.9, 137.3, 133.9, 133.4, 129.7, 129.1, 129.0, 128.6, 128.3, 128.2, 126.4, 118.1, 101.8, 82.0, 79.7, 77.4, 76.1, 75.9, 72.1, 68.7, 35.5, 21.9; ESI-HRMS calcd for $C_{30}H_{32}O_7SNa$ $[M + Na]^+$ 559.1766, found 559.1754.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-1-deoxy-1-allyl-*β*-D-mannopyranose (20). Prepared by the general procedure 1 (eluent 10% ethyl acetate/hexane) with a yield of 28 mg (76%): $[\alpha]^{22}_D$ −52.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.52−7.50 (m, 2H), 7.45−7.43 (m, 2H), 7.39−7.29 (m, 6H), 5.77−5.69 (m, 1H), 5.58 (s, 1H), 5.16 (d, *J* = 11.5 Hz, 1H), 5.08 (t, *J* = 3.5 Hz, 1H), 5.05 (s, 1H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.28−4.25 (m, 1H), 4.03 (t, *J* = 9.0 Hz, 1H), 3.96 (dd, *J* = 3.0, 10.0 Hz, 1H), 3.82 (t, *J* = 10.0 Hz, 1H), 3.68 (d, *J* = 1.5 Hz, 1H), 3.53 (t, *J* = 7.0 Hz, 1H), 3.41−3.37 (m, 1H), 2.52−2.46 (m, 1H), 2.35−2.29 (m, 1H), 0.92 (s, 9H), 0.14 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) *δ* 139.0, 137.9, 134.6, 129.1, 128.5, 128.3, 127.8, 126.5, 117.7, 102.2, 79.7, 79.5, 75.7, 75.5, 72.2, 69.0, 35.8, 26.2, 18.6, −4.1, −4.5; ESI-HRMS calcd for $C_{29}H_{40}O_5SiNa$ $[M + Na]^+$ 519.2543, found 519.2564.

Correlation of Compounds 10*β* and 20. To a stirred solution of **20** (28 mg, 0.056 mmol) in dry THF (0.5 mL) was added acetic acid (25 *μ*L) followed by the addition of TBAF (1 M in THF, 0.56 mL, 0.56 mmol) at rt under nitrogen atmosphere. The reaction mixture was stirred at rt for 1 h before it was quenched with saturated NH_4Cl solution. The reaction mixture was diluted with ethyl acetate followed by washing with water and brine, dried over sodium sulfate and concentrated under reduced pressure. Chromatographic purification (20% ethyl acetate: hexane) afforded the alcohol (21 mg, 97%). To a stirred solution of the alcohol (21 mg, 0.054 mmol) and DIPEA (94 *μ*L, 0.54 mmol) in dry methylene chloride (1 mL) was added acetyl chloride (19 *μ*L, 0.27 mmol) at 0 °C. After 10 min, the reaction mixture was warmed up to rt and stirred for 30 min before it was diluted with methylene chloride. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (15% ethyl acetate/hexane) gave a compound (22 mg, 98%), whose spectral data were identical with those of compound **10*β*** reported above.

4,6-*O*-Benzylidene-2-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-1-deoxy-1-(2-oxo-2-phenylethyl)-α-D-mannopyranose (21). Prepared by the general procedure 1 (eluent 10% ethyl acetate/hexane) with a yield of 99 mg (81%); $[\alpha]^{22}_D$ −17.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.84−7.82 (m, 2H), 7.60−7.56 (m, 1H), 7.52−7.50 (m, 2H), 7.46−7.43 (m, 2H), 7.40−7.35 (m, 3H), 7.32−7.31 (m, 2H), 7.22−7.20 (m, 2H), 7.14−7.11 (m, 1H), 5.58 (s, 1H), 5.09 (d, *J* = 11.5 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.25−4.21 (m, 2H), 4.09 (dd, *J* = 3.0, 9.5 Hz, 1H), 4.02 (t, *J* = 9.5 Hz, 1H), 3.91−3.90 (m, 1H), 3.79 (t, *J* = 10.0 Hz, 1H), 3.49−3.44 (m, 1H), 3.25 (dd, *J* = 5.0, 17.5 Hz, 1H), 3.14 (dd, *J* = 7.5, 17.5 Hz, 1H), 0.93 (s, 9H), 0.17 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) *δ* 197.7, 138.7, 137.9, 136.9, 133.5, 129.1, 128.8, 128.7, 128.6, 128.3, 127.9, 126.5, 102.3, 79.7, 79.2, 75.9, 75.7, 75.1, 72.1, 68.9, 40.0, 26.2, 18.6, −4.1, −4.4; ESI-HRMS calcd for $C_{34}H_{42}O_6SiNa$ $[M + Na]^+$ 597.2648, found 597.2621.

3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-(2-oxo-2-phenylethyl)-*β*-D-mannopyranose (12*β*). To a stirred solution of **21** (28 mg, 0.049 mmol) in dry THF (0.5 mL) was added TBAF (1 M in THF, 0.49 mL, 0.49 mmol) at room temperature under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 15 min before it was quenched with saturated NH_4Cl solution. The reaction mixture was diluted with ethyl acetate, washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (20% ethyl acetate/hexane) afforded the desilylated alcohol (21 mg), which was taken up in pyridine (1 mL) and treated with acetic anhydride (0.5 mL) at room temperature. After 2 h, the solvents were removed under vacuum and the product was subjected to chromatographic purification (15% ethyl acetate/hexane) to give **12*β*** (19 mg, 78%): $[\alpha]^{22}_D$ −28.2 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.84 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.49−7.20 (m, 12H), 5.59 (s, 1H), 5.27 (dd, *J* = 10.0, 3.5 Hz, 1H), 4.83 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.31−4.26 (m, 2H), 4.20−4.16 (m, 2H), 3.85 (t, *J* = 10.0 Hz, 1H), 3.61−3.58 (m, 1H), 3.31 (dd, *J* = 5.5, 17.50 Hz, 1H), 3.06 (dd, *J* = 7.0, 17.5 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) *δ* 197.0, 170.68, 137.8, 137.6, 136.7, 133.6, 129.3, 128.8, 128.7, 128.6, 128.4, 128.3, 126.4, 101.9, 76.7, 76.6, 75.9, 75.6, 74.4, 72.0, 68.8, 39.8, 21.3; ESI-HRMS calcd for $C_{30}H_{30}O_7Na$ $[M + Na]^+$ 525.1889, found 525.1871.

Conversion of Compound 12α to 21 with Inversion of Anomeric Configuration. To a stirred solution of **12α** (40 mg, 0.08 mmol) in methanol was added 25% sodium methoxide in methanol (50 *μ*L) at rt. The reaction mixture was stirred at rt for 30 min before it was diluted with ethyl acetate The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure to provide the crude alcohol. To a stirred solution of the crude alcohol (0.08 mmol) and imidazole (27 mg, 0.4 mmol) in dry DMF (1 mL) was added *tert*-butyldimethylsilyl chloride (48 mg, 0.32 mmol) at rt. The reaction mixture was stirred at rt for 12 h before it was diluted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification (10% ethyl acetate: hexane) afforded a compound (39 mg, 86%) whose spectral data were identical to those of compound **21** reported above.

Phenyl 4,6-*O*-Benzylidene-3-*O*-benzoyl-2-*O*-benzyl-1-deoxy-1-thio-α-D-mannopyranoside (27). To a stirred solution of phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thio-α-D-mannopyranoside (**1**) (300 mg, 0.66 mmol) in dry pyridine (5 mL) was added benzoyl chloride (387 *μ*L, 3.33 mmol) followed by the addition of DMAP (81 mg, 0.66 mmol) at rt. After 3 h, pyridine was removed, and the reaction mixture was diluted with ethyl acetate. The organic layer was washed with 5% sodium carbonate solution, water, and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatographic purification on silica gel (eluent 10% ethyl acetate/hexane) afforded the desired product with a yield of 336 mg (91%): $[\alpha]^{21}_D$ +27.3 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.13

(d, $J = 7.0$ Hz, 2H), 7.64−7.20 (m, 18H), 5.70 (s, 1H), 5.65 (s, 1H), 5.62 (dd, $J = 3.5$, 10.0 Hz, 1H), 4.72 (d, $J = 12.0$ Hz, 1H), 4.60 (d, $J = 11.5$ Hz, 1H), 4.55−4.48 (m, 2H), 4.43 (dd, $J = 2.5$, 3.5 Hz, 1H), 4.33 (dd, $J = 5.0$, 11.0 Hz, 1H), 3.99 (t, $J = 10.0$ Hz, 1H); ^{13}C NMR (100.9 MHz, $CDCl_3$) δ 166.1, 137.5, 137.4, 134.0, 132.1, 130.2, 130.1, 129.5, 129.3, 128.7, 128.6, 128.5, 128.3, 128.2, 126.4, 102.0, 86.9, 78.1, 77.1, 76.6, 73.4, 71.4, 68.8, 65.7; ESI-HRMS calcd for $C_{33}H_{30}O_6SNa$ $[M + Na]^+$ 577.1661, found 577.1636.

General Procedure 2 for Radical Reactions. A stirred solution of thioglycoside (1.0 equiv), allyltributylstannane (3.0 equiv), and 1,1′-azobis(cyclohexanecarbonitrile) (0.2 equiv) in dry degassed toluene was heated to reflux under nitrogen at 113 °C. Three further portions of 1,1′-azobis(cyclohexanecarbonitrile) (0.2 equiv) were added at intervals of 2 h, and the reaction mixture then was stirred under reflux for 5 h. The solvents were removed, and the crude reaction mixture was purified over silica gel eluting with 15% ethyl acetate/hexanes.

4,6-*O*-Benzylidene-3-*O*-benzoyl-2-*O*-benzyl-1-deoxy-1-allyl-α-D-mannopyranose (29). Prepared by the general procedure **2** with a yield of 89 mg (78%, α only). **28**: $[\alpha]^{21}_D$ −56.8 ($c = 1.0$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, $J = 7.0$ Hz, 2H), 7.62−7.18 (m, 13H), 5.80−5.73 (m, 1H), 5.66 (s, 1H), 5.50 (dd, $J = 3.5$, 11.0 Hz, 1H), 5.24−5.15 (m, 2H), 4.65 (d, $J = 11.5$ Hz, 1H), 4.57 (d, $J = 12.0$ Hz, 1H), 4.42 (t, $J = 10.0$ Hz, 1H), 4.31−4.28 (m, 1H), 4.16 (t, $J = 7.5$ Hz, 1H), 4.05 (d, $J = 2.0$ Hz, 1H), 3.90 (t, $J = 10.0$ Hz, 1H), 3.85−3.80 (m, 1H), 2.70−2.64 (m, 1H), 2.50−2.44 (m, 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 166.3, 137.8, 137.6, 133.4, 130.1, 129.2, 128.6, 128.4, 128.2, 128.1, 126.3, 118.7, 101.9, 76.9, 76.5, 73.1, 71.4, 69.4, 66.1, 33.9; ESI-HRMS calcd for $C_{30}H_{30}O_6Na$ $[M + Na]^+$ 509.1940, found 509.1903.

Acknowledgment. We thank the NIH (GM62160) for support of this work.

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