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β-Selective glucosylation in the absence of neighboring group participation: influence of the 3,4-*O*-bisacetal protecting system

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Abstract—A 3,4-*O*-bisacetal 2,6-di-*O*-benzyl protected thioglucoside is converted to the corresponding glucosyl triflate with 1-benzenesulfinyl piperidine and trifluoromethanesulfonic anhydride. The moderate to excellent β-selectivity exhibited with this glucosyl triflate with a range of alcohols is generally higher than that observed with the more electronically disarmed corresponding 3,4-*O*-carbonate, for which a possible reason is advanced.
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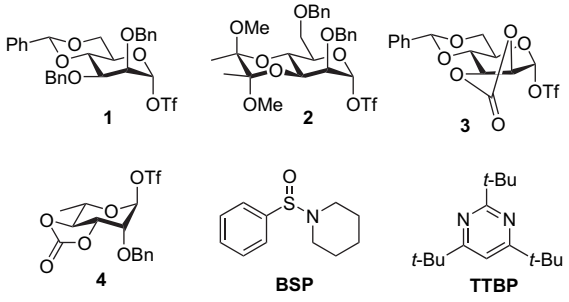
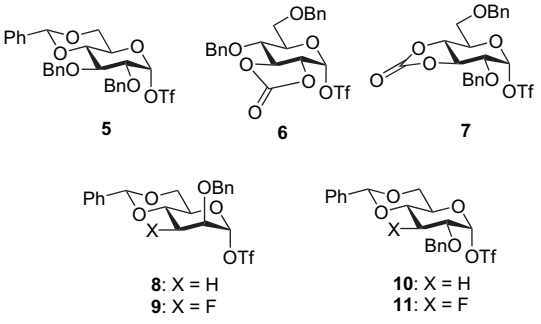
1. Introduction

The use of cyclic protecting groups to restrict conformational mobility can have dramatic effects on the stereoselectivity of glycosylation reactions.[1] This is illustrated by the glycosyl triflates **1**, **2**, **3**, and **4**, as generated from the corresponding thioglycosides with either 1-benzenesulfinyl piperidine (BSP) and triflic anhydride, or with benzenesulfinyl triflate, or from the corresponding sulfoxides with triflic anhydride, typically in the presence of a hindered base such as 2,6-di-*tert*-butyl-4-methylpyridine or 2,4,6-tri-*tert*-butylpyrimidine (TTBP).[2–5] With **1**, β-mannosides are obtained in a highly selective manner,[6–8] an observation that is attributed to the restriction of the C5–C6 bond to the most deactivating *trans-gauche* (*tg*) conformation, with the antiperiplanar C5–O5 and C6–O6 bonds,[9,10] by the presence of the benzylidene acetal.[11] This rationale is borne out by **2**, which is highly α-selective under the same reactions conditions.[12] Donor **3** is also highly α-selective,[12] a fact that we attribute to the imposition of a half-chair conformation on the pyranose ring by the cis-fused carbonate and which is sufficient to override the β-directing effect of the benzylidene acetal.[12,13] The 3,4-di-*O*-carbonate **4** on the other hand, which was investigated in L-6-deoxy-mannose (or L-rhamnose series), shows moderate β-selectivity.[14]



Different results are observed in the gluco-series wherein the benzylidene protected system **5** is α-selective,[15] the 2,3-di-*O*-carbonate **6** moderately β-selective,[16] and the 3,4-di-*O*-carbonate **7** somewhat unselective.[16] The 3-deoxy manno and gluco donors **8** and **10**,[17] as well as their 3-deoxy-3-fluoro counterparts **9** and **11**,[18] are all somewhat unselective prompting us to suggest that a key interaction in determining stereoselectivity in this series of glycosylation reactions is that between the C2–O2 and C2–O3 bonds.[17,18]



Keywords: Glycosylation; Bisacetal; Glycosyl triflate; Stereoselectivity; Protecting group.
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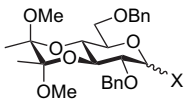
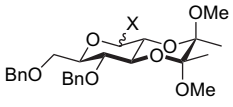
Here we describe our investigations of the influence of the bisacetal type protecting group on glycosylation stereoselectivity in the gluco-series through the use of thioglycosides **12** and **14**, and the corresponding triflates **13** and **15**.



12: X = β-SPh
13: X = α-OTf



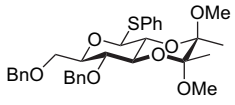
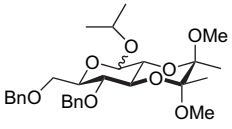
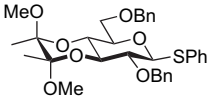
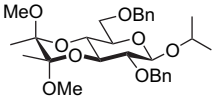
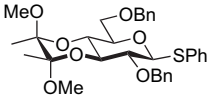
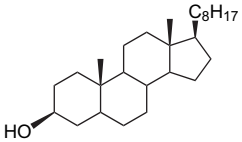
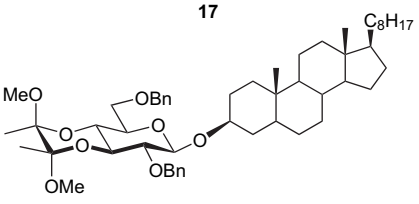
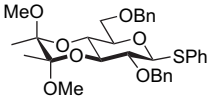
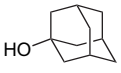
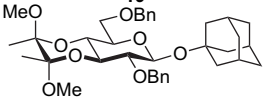
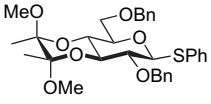
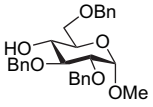
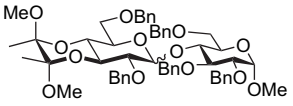
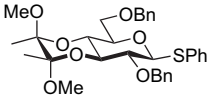
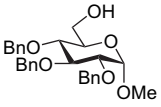
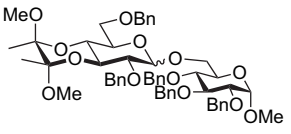
14: X = β-SPh
15: X = α-OTf

2. Results

Thioglycosides **12** and **14** were prepared as previously described[16] and converted to the corresponding triflates **13** and **15** in the standard manner with BSP and trifluoromethanesulfonic anhydride,[19,20] in the presence of TTBP[21] at −60 °C. Experiments conducted in deuteriochloroform in the NMR spectrometer revealed the formation of both triflates to be complete within minutes at −60 °C, with **13** characterized by an anomeric hydrogen resonating at δ 6.10, and **15** exhibiting the corresponding signal at δ 6.06. In variable temperature NMR experiments both **13** and **15** were found to undergo decomposition around −5 °C. Quenching of the 2,3-bisacetal protected triflate **15** with isopropanol gave the corresponding glucoside **16** in good yield, but with a disappointing anomeric selectivity of 3:1 in favor of the β-anomer (Table 1, entry 1). The 3,4-bisacetal protected triflate **13**, on the other hand, gave the β-glucoside **17** exclusively and in excellent yield (Table 1, entry 2). On the basis of these results no further couplings were undertaken in the 2,3-bisacetal series, however, a series of glycosylations were carried out with the preformed 3,4-bisacetal protected triflate **13** (Table 1, entries 3–10).

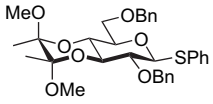
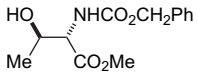
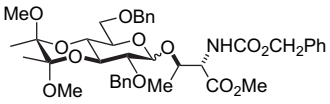
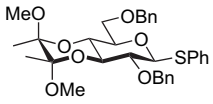
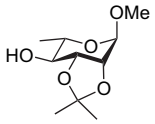
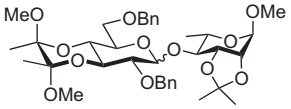
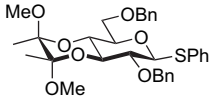
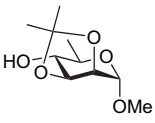
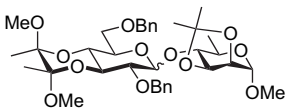
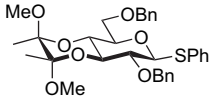
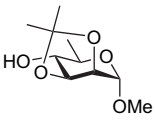
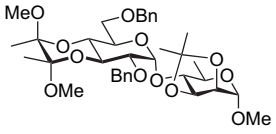
With 3β-cholestanol **18** as acceptor the β-glucoside **19** was formed exclusively (Table 1, entry 3), and a comparable result was observed with 1-adamantanol (Table 1, entry 4). With the glucose 4-OH acceptor **22** a ratio of 4:1 in favor of the β-glucoside **23** was observed (Table 1, entry 5). In view of this result, the poor ratio observed on coupling to the less hindered glucose 6-OH acceptor **24** was surprising

Table 1. Glycosylation of thioglycosides **12** and **14**

Entry	Donor	Acceptor	Product	β:α ratio[b]	Yield[a] (%)
1	 **14**		 **16**	3:1	78
2	 **12**		 **17**	β only	72
3	 **12**	 **18**	 **19**	β only	70
4	 **12**	 **20**	 **21**	β only	60
5	 **12**	 **22**	 **23**	4:1	80
6	 **12**	 **24**	 **25**	3:1	76

(*continued*)

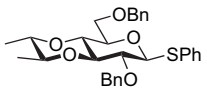
Table 1. (*continued*)

Entry	Donor	Acceptor	Product	β:α ratio[b]	Yield[a] (%)
7	 **12**	 **26**	 **27**	2:1	82
8	 **12**	 **28**	 **29**	1.5:1	78
9	 **12**	 **30**	 **31**	1.5:1	75
10	 **12**	 **30**	 **31**	α only[c]	70

[a] Isolated yields.
[b] Determined by the crude ^{1}H NMR analysis.
[c] Reaction was performed with NIS/TfOH activation.

(Table 1, entry 6). With the threonine derivative **26** the selectivity fell to 2:1 in favor of the β-anomer (Table 1, entry 7), and with either the L- or D-rhamnose 4-OH acceptors **28** and **30**,[22,23] respectively, the β:α selectivity was only 1.5:1 (Table 1, entries 8 and 9). In the β-mannosylation reactions conducted previously with donor **1**, as well as in β-rhamnosylation reactions with **4**, and, importantly, β-selective glucosylations with **6** and **7**, the secondary glucosyl acceptor **22** performs less well than the L-rhamnosyl acceptor **28** and the primary glucosyl acceptor **24**, perhaps suggesting that diastereoselective matching and/or mismatching plays a significant role in some of these glycosylation reactions.[24–26] Finally, donor **12** was activated with *N*-iodosuccinimide/trifluoromethanesulfonic acid combination[27] in the presence of acceptor **30**, when the disaccharide **31** was obtained with complete α-selectivity (Table 1, entry 10). The contrast in selectivity between entries 9 and 10 of Table 1 underlines the importance of the preformation of the glucosyl triflate **13** in the chemistry reported here. The change in selectivity on going from the BSP/trifluoromethanesulfonic anhydride activation method to promotion with *N*-iodosuccinimide and trifluoromethanesulfonic acid, or its silver salt, parallels similar observations made with a range of other thioglycosides in our laboratory.[28,29]

To probe the influence of the methoxy groups in the bisacetal system on the stereoselectivity of glycosylations, thioglycoside **12** was treated with sodium cyanoborohydride and HCl in THF,[30] when **32** was obtained in excellent yield, as a single diastereomer. The diequatorial disposition of the methyl groups in **32** follows from the mechanism of reduction and is supported by nuclear Overhauser measurements. The analogous stereoselectivity was previously observed in the mannose series when thioglycoside **33** was reduced cleanly to **34**.[12] Activation of **32** with BSP and triflic anhydride at −60 °C in dichloromethane, the standard conditions applied for glycosylation of **12**, followed by addition of acceptor **22** gave disaccharide **35** as a 1:1 mixture of α- and β-anomers in 50% yield. The methoxy groups in the bisacetal protecting system of **12**, therefore, play a significant role in determining the stereoselectivity of the glycosylation reaction.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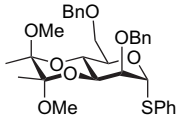
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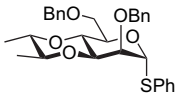
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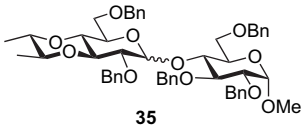
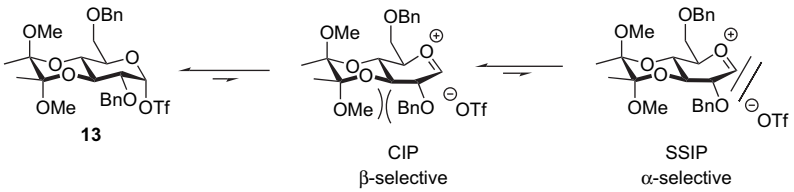

35

3. Discussion

The β-selectivity observed with the 3,4-*O*-bisacetal protected glucosyl triflate **13** is significant in so far as it contrasts with the α-selectivity observed earlier[12] with the corresponding α-selective 3,4-*O*-bisacetal protected mannosyl triflate **2**. Even more significant, however, is the improved β-selectivity observed with triflate **13** over and above that has seen previously[16] with the corresponding 3,4-*O*-carbonate **7** as the more disarmed[31,32] carbonate was expected to be the more β-selective donor. Applying our standard mechanistic hypothesis for these glycosyl triflate based glycosylations,



Scheme 1. Glycosylation mechanism illustrating the influence of the 3,4-*O*-bisacetal group.

which is based on the classical Lemieux mechanism,[33] and for which we have provided substantial evidence,[7,34,35] the explanation must be found in the effect of the protecting groups on the equilibria between the covalent α-triflates, a transient contact ion pair (CIP) comprised of the glycosyl oxacarbenium ions and the triflate counter ion, and a related solvent separated ion pair (SSIP). In this hypothesis the covalent α-triflate serves as a reservoir for the transient CIP, which, with the triflate shielding the α-face from which it has just departed, is the source of the β-glycosides. In the SSIP the anomeric effect takes over, leading to the formation of the α-glycosides. β-Selectivity is the result of a protecting system that destabilizes the glycosyl oxacarbenium shifting the whole series of equilibria toward the covalent glycosyl triflate and thereby decreasing the concentration of the SSIP. α-Selectivity is the result of a higher concentration of the SSIP arising from increased glycosyl cation stability. In the case of triflate **13** (Scheme 1), as the covalent triflate collapses to the CIP with its glycosyl oxacarbenium ion in a conformation approximating to a $^4H_3$ half-chair,[36,37] the C2–O2 bond necessarily rotates down below the nominal pyranose plane leading to an increased steric interaction with the methoxy group of the bisacetal. We argue that it is this increased steric interaction, which is absent in the corresponding mannosyl triflate **2**, that destabilizes the glycosyl cation sufficiently to bring about the observed β-selectivity. With the 2,3-*O*-bisacetal protected triflate **15** this interaction is absent in the derived oxacarbenium ion, whether it adopts the $^4H_3$ or the closely related, isoenergetic ^3E conformer,[36,37] and the chemistry reverts to the more normal pattern with the more highly disarmed 2,3-*O*-carbonate being more β-selective than the acetal.

Strong support for this hypothesis is provided by the loss of stereoselectivity on glycosylation of the des-methoxy system **32**, when there is no longer a destabilizing steric interaction between the O2 protecting group and the cyclic protecting group spanning O3 and O4. Once again, it is appropriate to note the contrast with the mannose series wherein both the standard donor **33** and the des-methoxy analog **34** were α-selective.

4. Conclusion

Although several β-selective glucosylation reactions have been developed recently relying on the use of non-traditional methods of neighboring group participation,[38–40] the chemistry described here, together with that of the 2,3-*O*-carbonate **6**, provides a rare example of such a reaction that completely avoids such types of participation. The increased β-selectivity of **13**, as compared to the more electronically disarmed **6**, illustrates how subtle conformational effects and remote protecting groups can sometimes have major effects on reactivity.

5. Experimental

5.1. General experimental

NMR spectra were recorded in $CDCl_3$ solution, with chemicals shifts in parts per million downfield from tetramethylsilane at 500 and 125 MHz for ^1H and ^{13}C, respectively. Specific rotations were measured in $CHCl_3$ at room temperature. Mass spectra were recorded with electrospray ionization.

5.2. General procedure for glycosylation using the BSP/TTBP/Tf_2O system

To a stirred solution of phenyl 2,6-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-β-D-glucopyranoside (1 equiv), BSP (1.1 equiv), TTBP (1.5 equiv), and 4 Å molecular sieves in CH_2Cl_2 (0.05 M in substrate) at −60 °C under an Ar atmosphere was added Tf_2O (1.2 equiv). After stirring for 30 min at the same temperature, a solution of glycosyl acceptor (1.5 equiv) in CH_2Cl_2 (0.02 M in acceptor) was added slowly at −60 °C. The reaction was further stirred for 3 h at the same temperature and then allowed to reach room temperature before dilution with dichloromethane, filtration, and washing with excess CH_2Cl_2. The organic layer was then washed with saturated sodium bicarbonate solution, followed by saturated sodium chloride solution, then was dried over sodium sulfate, evaporated to dryness, and purified by silica gel column chromatography using EtOAc/hexanes as eluant to afford the corresponding β and α glucopyranosides.

5.2.1. Isopropyl 4,6-di-*O*-benzyl-2,3-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranoside (16β). $[\alpha]_D^{17}$ −103.0 (*c* 1.0); ^1H NMR δ: 1.19 (d, *J*=6.0 Hz, 3H), 1.27 (d, *J*=6.0 Hz, 3H), 1.32 (s, 3H), 1.36 (s, 3H), 3.29 (s, 3H), 3.30 (s, 3H), 3.48–3.55 (m, 2H), 3.60 (t, *J*=9.5 Hz, 1H), 3.65–3.68 (m, 1H), 3.74 (d, *J*=10.5 Hz, 1H), 3.88 (t, *J*=9.5 Hz, 1H), 3.95–3.98 (m, 1H), 4.53 (d, *J*=8.0 Hz, 1H), 4.56 (s, 2H), 4.60 (d, *J*=12.0 Hz, 1H), 4.92 (d, *J*=11.0 Hz, 1H), 7.23–7.33 (m, 10H); ^{13}C NMR δ: 17.7, 17.8, 22.3, 23.5, 47.8, 47.9, 69.4, 69.5, 72.5, 73.4, 74.0, 74.9, 75.0, 75.6, 99.3, 99.4, 99.5, 127.5, 127.6, 127.7, 128.0, 128.3, 128.4, 138.3, 138.4; HRMS calcd for $C_{29}H_{40}O_8Na$ $[M+Na]^+$: 539.2615, found 539.2610.

5.2.2. Isopropyl 4,6-di-*O*-benzyl-2,3-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranoside (16α). $[\alpha]_D^{17}$ +10.0 (*c* 1.0); ^1H NMR δ: 1.18 (d, *J*=6.0 Hz, 3H), 1.22

(d, J=6.5 Hz, 3H), 1.32 (s, 3H), 1.35 (s, 3H), 3.26 (s, 3H), 3.30 (s, 3H), 3.63 (d, J=10.0 Hz, 1H), 3.75–3.79 (m, 3H), 3.85 (d, J=9.5 Hz, 1H), 3.91–3.93 (m, 1H), 4.19 (t, J=10.0 Hz, 1H), 4.76 (d, J=8.5 Hz, 1H), 4.49 (d, J=7.0 Hz, 1H), 4.64 (d, J=12.5 Hz, 1H), 4.91 (d, J=11.5 Hz, 1H), 4.93 (d, J=4.0 Hz, 1H), 7.19–7.36 (m, 10H); ^{13}C NMR δ: 17.7, 18.1, 21.3, 23.1, 47.8, 47.9, 68.3, 68.5, 69.7, 70.5, 70.6, 73.4, 75.0, 75.3, 95.2, 99.3, 99.7, 127.6, 127.7, 127.9, 128.1, 128.3, 138.2, 138.5; HRMS calcd for $C_{29}H_{40}O_8Na$ [M+Na]$^+$: 539.2615, found 539.2610.

5.2.3. Isopropyl 2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranoside (17β). White solid, mp 98 °C; $[\alpha]_D^{17}$ +94.0 (c 1.0); ^{1}H NMR δ: 1.23 (d, J=6.0 Hz, 3H), 1.29 (s, 3H), 1.31 (d, J=6.5 Hz, 3H), 1.35 (s, 3H), 3.19 (s, 3H), 3.30 (s, 3H), 3.41 (dd, J=8.7 and 7.5 Hz, 1H), 3.61–3.68 (m, 3H), 3.77–3.81 (m, 2H), 3.98–4.00 (m, 1H), 4.46 (d, J=7.5 Hz, 1H), 4.61 (q, J=4.0 Hz, 2H), 4.77 (d, J=11.0 Hz, 1H), 4.86 (d, J=11.5 Hz, 1H), 7.25–7.28 (m, 2H), 7.30–7.35 (m, 6H), 7.39–7.40 (m, 2H); ^{13}C NMR δ: 17.7, 17.8, 22.3, 23.7, 47.9, 48.0, 66.4, 68.7, 72.5, 72.7, 73.5, 73.7, 74.7, 79.2, 99.5, 102.6, 127.4, 127.5, 127.7, 128.2, 128.3, 138.5, 139.0; HRMS calcd for $C_{29}H_{40}O_8Na$ [M+Na]$^+$: 539.2615, found 539.2618.

5.2.4. 3β-Cholestanyl 2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranoside (19β). White solid, mp 128 °C; $[\alpha]_D^{17}$ +84.0 (c 0.75); ^{1}H NMR δ: 0.59–0.63 (m, 1H), 0.65 (s, 3H), 0.83 (s, 3H), 0.86–1.39 (m, 36H), 1.47–1.57 (m, 4H), 1.64–1.73 (m, 2H), 1.80–1.81 (m, 1H), 1.96–1.98 (m, 2H), 3.19 (s, 3H), 3.30 (s, 3H), 3.40 (dd, J=9.5 and 7.5 Hz, 1H), 3.61–3.67 (m, 4H), 3.78 (t, J=9.5 Hz, 2H), 4.50 (d, J=7.5 Hz, 1H), 4.60 (q, J=4.0 Hz, 2H), 4.77 (d, J=11.5 Hz, 1H), 4.86 (d, J=11.5 Hz, 1H), 7.24–7.33 (m, 8H), 7.39–7.41 (m, 2H); ^{13}C NMR δ: 12.1, 12.3, 17.7, 17.8, 18.7, 21.3, 22.6, 22.8, 23.8, 24.2, 28.0, 28.3, 28.8, 29.7, 32.1, 34.8, 35.5, 35.6, 35.8, 36.2, 37.1, 39.5, 40.1, 42.6, 44.8, 47.8, 47.9, 54.4, 56.3, 56.5, 66.5, 68.7, 72.5, 73.5, 73.7, 74.7, 79.4, 99.5, 102.4, 127.4, 127.5, 127.8, 128.2, 128.3, 138.5, 139.0; HRMS calcd for $C_{53}H_{80}O_8Na$ [M+Na]$^+$: 867.5751, found 867.5758.

5.2.5. 1-Adamantyl 2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranoside (21β). $[\alpha]_D^{17}$ +85.0 (c 1.0); ^{1}H NMR δ: 1.28 (s, 3H), 1.34 (s, 3H), 1.59–1.62 (m, 6H), 1.81–1.84 (m, 3H), 1.91–1.93 (m, 3H), 2.14 (s, 3H), 3.19 (s, 3H), 3.29 (s, 3H), 3.39 (dd, J=9.5 and 7.5 Hz, 1H), 3.59–3.63 (m, 3H), 3.78–3.80 (m, 2H), 4.59 (s, 2H), 4.69 (d, J=7.5 Hz, 1H), 4.75 (d, J=11.5 Hz, 1H), 4.87 (d, J=1.5 Hz, 1H), 7.24–7.27 (m, 2H), 7.29–7.34 (m, 6H), 7.39–7.41 (m, 2H); ^{13}C NMR δ: 17.6, 17.8, 30.7, 36.3, 42.7, 47.9, 66.7, 69.0, 72.7, 73.3, 73.4, 74.7, 75.2, 79.2, 96.5, 99.5, 127.3, 127.4, 127.8, 128.1, 128.2, 138.5, 139.1; HRMS calcd for $C_{36}H_{48}O_8Na$ [M+Na]$^+$: 631.3241, found 631.3243.

5.2.6. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (23β). $[\alpha]_D^{17}$ +72.0 (c 1.0); ^{1}H NMR δ: 1.27 (s, 3H), 1.34 (s, 3H), 3.19 (s, 3H), 3.29 (s, 3H), 3.37 (s, 3H), 3.43–3.47 (m, 4H), 3.53–3.58 (m, 1H), 3.68–3.81 (m, 5H), 3.88–3.92 (m, 2H), 4.34 (d, J=12.5 Hz, 1H), 4.43 (q, J=7.5 Hz, 2H), 4.49–4.60 (m, 4H), 4.71–4.78 (m, 3H), 4.87 (d, J=11.5 Hz, 1H), 5.06 (d, J=11.5 Hz, 1H), 7.37–7.19 (m, 25H); ^{13}C NMR δ: 17.6, 17.8, 47.9, 48.0, 55.3, 66.2, 68.2, 68.4, 70.0, 73.1, 73.2, 73.4, 73.6, 74.1, 74.7, 75.3, 78.9, 79.6, 80.5, 98.4, 99.6, 102.8, 127.0, 127.2, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.4, 138.0, 138.4, 138.7, 138.9, 139.7; HRMS calcd for $C_{54}H_{64}O_{13}Na$ [M+Na]$^+$: 943.4239, found 943.4260.

5.2.7. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranosyl]-α-D-glucopyranoside (23α). $[\alpha]_D^{17}$ +82.5 (c 0.8); ^{1}H NMR δ: 1.28 (s, 3H), 1.30 (s, 3H), 3.17 (s, 3H), 3.27 (s, 3H), 3.38 (s, 3H), 3.52 (dd, J=9.5 and 3.5 Hz, 2H), 3.55–3.59 (m, 2H), 3.68 (d, J=9.0 Hz, 1H), 3.76–3.83 (m, 4H), 3.94 (t, J=9.5 Hz, 1H), 4.02 (t, J=9.0 Hz, 1H), 4.11 (t, J=9.5 Hz, 1H), 4.38 (d, J=12.0 Hz, 1H), 4.47–4.58 (m, 6H), 4.67 (d, J=12.5 Hz, 1H), 4.81–4.88 (m, 3H), 5.66 (d, J=4.0 Hz, 1H), 7.16–7.31 (m, 25H); ^{13}C NMR δ: 17.7, 17.9, 47.9, 48.0, 55.2, 65.8, 67.8, 69.4, 69.6, 70.4, 73.3, 73.3, 73.5, 73.7, 74.1, 74.4, 76.3, 80.1, 81.8, 97.7, 98.1, 99.3, 99.4, 126.8, 126.9, 127.3, 127.4, 127.5, 127.6, 127.8, 128.1, 128.2, 128.2, 128.4, 138.0, 138.1, 138.3, 138.6, 139.2; HRMS calcd for $C_{54}H_{64}O_{13}Na$ [M+Na]$^+$: 943.4239, found 943.4258.

5.2.8. Methyl 2,3,6-tri-*O*-benzyl-6-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (25β). $[\alpha]_D^{17}$ +61.1 (c 1.65); ^{1}H NMR δ: 1.28 (s, 3H), 1.32 (s, 3H), 3.17 (s, 3H), 3.29 (s, 3H), 3.33 (s, 3H), 3.47–3.59 (m, 4H), 3.65–3.69 (m, 3H), 3.75–3.79 (m, 3H), 3.97 (t, J=9.5 Hz, 1H), 4.15 (d, J=11.0 Hz, 1H), 4.35 (d, J=7.0 Hz, 1H), 4.51 (d, J=11.0 Hz, 1H), 4.58 (d, J=6.0 Hz, 2H), 4.62 (d, J=3.5 Hz, 1H), 4.65–4.69 (m, 3H), 4.78 (dd, J=12.5 and 4.5 Hz, 1H), 4.82 (s, 2H), 4.96 (d, J=11.0 Hz, 1H), 7.13–7.36 (m, 25H); ^{13}C NMR δ: 13.8, 13.9, 44.0, 44.1, 51.3, 62.3, 64.7, 64.8, 66.0, 69.0, 69.5, 69.6, 70.1, 70.9, 71.0, 71.8, 73.9, 74.1, 74.8, 75.9, 78.2, 94.2, 95.7, 100.1, 123.4, 123.5, 123.6, 123.7, 123.8, 123.9, 124.0, 124.1, 124.3, 124.4, 124.5, 124.6, 134.4, 134.5, 134.6, 134.9, 135.1; HRMS calcd for $C_{54}H_{64}O_{13}Na$ [M+Na]$^+$: 943.4239, found 943.4208.

5.2.9. Methyl 2,3,6-tri-*O*-benzyl-6-*O*-[2,6-di-*O*-benzyl-3,4-di-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranosyl]-α-D-glucopyranoside (25α). $[\alpha]_D^{17}$ +81.0 (c 0.5); ^{1}H NMR δ: 1.27 (s, 3H), 1.32 (s, 3H), 3.18 (s, 3H), 3.24 (s, 3H), 3.29 (d, J=8.0 Hz, 1H), 3.33 (s, 3H), 3.39 (dd, J=10.0 and 4.0 Hz, 1H), 3.57–3.69 (m, 4H), 3.73–3.77 (m, 3H), 3.89–3.96 (m, 2H), 4.19 (t, J=10.0 Hz, 1H), 4.49–4.57 (m, 4H), 4.63–4.70 (m, 3H), 4.78–4.86 (m, 3H), 4.93 (d, J=11.0 Hz, 1H), 5.03 (d, J=4.0 Hz, 1H), 7.16–7.34 (m, 25H); ^{13}C NMR δ: 17.7, 17.9, 47.8, 47.9, 54.9, 65.6, 66.2, 68.1, 68.9, 69.8, 70.5, 72.8, 73.3, 73.4, 75.0, 75.7, 76.6, 77.9, 80.2, 82.1, 97.8, 97.9, 99.4, 99.5, 127.2, 127.3, 127.4, 127.5, 127.6, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.4, 138.2, 138.3, 138.5, 138.9, 139.0; HRMS calcd for $C_{54}H_{64}O_{13}Na$ [M+Na]$^+$: 943.4239, found 943.4227.

5.2.10. *N*-Benzyloxycarbonyl 2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranosyl-L-threonine methyl ester (27β). $[\alpha]_D^{17}$ +66.9 (c 1.3); ^{1}H NMR δ: 1.28 (d, J=6.5 Hz, 6H), 1.34 (s, 3H), 3.18 (s, 3H), 3.29

(s, 3H), 3.34–3.37 (m, 1H), 3.50–3.51 (m, 1H), 3.65 (s, 3H), 3.67–3.78 (m, 4H), 4.34 (dd, J=9.0 and 3.5 Hz, 1H), 4.38 (d, J=7.5 Hz, 1H), 4.41–4.43 (m, 1H), 4.50 (q, J=12.0 Hz, 2H), 4.77 (s, 2H), 5.13 (dd, J=17.5 and 12.5 Hz, 2H), 5.76 (d, J=9.0 Hz, 1H), 7.23–7.37 (m, 15H); ^{13}C NMR δ: 17.7, 17.8, 47.9, 48.0, 52.4, 58.8, 65.6, 67.1, 68.2, 72.6, 73.6, 73.7, 74.8, 75.0, 78.6, 99.6, 101.8, 127.5, 127.6, 127.8, 128.1, 128.3, 128.5, 136.4, 138.2, 138.6, 156.8, 170.8; HRMS calcd for $C_{39}H_{49}NO_{12}Na$ [M+Na]$^+$: 746.3147, found 746.3166.

5.2.11. *N*-Benzyloxycarbonyl 2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranosyl-L-threonine methyl ester (27α). $[\alpha]_D^{17}$ +100.0 (c 1.0); ^{1}H NMR δ: 1.28 (d, J=6.0 Hz, 6H), 1.31 (s, 3H), 3.17 (s, 3H), 3.25 (s, 3H), 3.54 (s, 3H), 3.64 (dd, J=11.0 and 2.0 Hz, 2H), 3.67–3.72 (m, 1H), 3.74 (d, J=10.0 Hz, 1H), 3.93–3.96 (m, 1H), 4.07 (t, J=10.0 Hz, 1H), 4.24–4.25 (m, 1H), 4.32–4.33 (m, 1H), 4.54 (dd, J=12.0 and 6.5 Hz, 2H), 4.66 (d, J=12.0 Hz, 1H), 4.77 (d, J=12.0 Hz, 1H), 4.86 (d, J=3.5 Hz, 1H), 5.07–5.14 (m, 2H), 5.96 (d, J=8.0 Hz, 1H), 7.23–7.34 (m, 15H); ^{13}C NMR δ: 17.6, 17.8, 19.2, 47.9, 52.3, 58.9, 65.9, 66.9, 67.9, 69.3, 70.2, 73.4, 73.5, 75.7, 76.2, 98.9, 99.5, 99.6, 1274, 127.5, 127.7, 127.9, 128.0, 128.2, 128.4, 136.4, 138.0, 138.5, 156.7, 171.0; HRMS calcd for $C_{39}H_{49}NO_{12}Na$ [M+Na]$^+$: 746.3147, found 746.3171.

5.2.12. Methyl 4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranosyl]-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (29β). $[\alpha]_D^{17}$ +47.0 (c 0.85); ^{1}H NMR δ: 1.28 (s, 3H), 1.31 (s, 3H), 1.32 (d, J=6.5 Hz, 3H), 1.34 (s, 3H), 1.45 (s, 3H), 3.21 (s, 3H), 3.29 (s, 3H), 3.36 (d, J=9.5 Hz, 1H), 3.39 (s, 3H), 3.57–3.55 (m, 1H), 3.66–3.63 (m, 1H), 3.77–3.69 (m, 4H), 3.82 (t, J=10.0 Hz, 1H), 4.07 (d, J=6.0 Hz, 1H), 4.21 (t, J=6.5 Hz, 1H), 4.56 (d, J=12.0 Hz, 1H), 4.62 (d, J=12.5 Hz, 1H), 4.77 (d, J=12.0 Hz, 1H), 4.84 (d, J=11.5 Hz, 2H), 4.94 (d, J=6.5 Hz, 1H), 7.40–7.41 (m, 2H), 7.25–7.32 (m, 8H); ^{13}C NMR δ: 17.6, 17.7, 17.8, 26.4, 27.8, 47.9, 48.0, 54.8, 64.3, 66.1, 68.2, 72.4, 73.5, 73.8, 74.3, 75.9, 77.9, 78.2, 79.1, 98.1, 99.6, 101.7, 109.2, 127.2, 127.4, 127.5, 128.0, 128.3, 138.5, 139.3; HRMS calcd for $C_{36}H_{50}O_{12}Na$ [M+Na]$^+$: 697.3194, found 697.3176.

5.2.13. Methyl 4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranosyl]-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (29α). $[\alpha]_D^{17}$ +88.0 (c 0.37); ^{1}H NMR δ: 1.22 (s, 3H), 1.29 (d, J=6.5 Hz, 3H), 1.30 (s, 3H), 1.35 (s, 3H), 1.39 (s, 3H), 3.21 (s, 3H), 3.31 (s, 3H), 3.33 (s, 3H), 3.61–3.67 (m, 2H), 3.69–3.73 (m, 2H), 3.74–3.76 (m, 1H), 3.92 (t, J=10.0 Hz, 1H), 4.04 (d, J=5.5 Hz, 1H), 4.10–4.17 (m, 3H), 4.57 (s, 2H), 4.69 (d, J=12.0 Hz, 1H), 4.81 (s, 1H), 4.90 (d, J=12.0 Hz, 1H), 4.99 (d, J=3.5 Hz, 1H), 7.25–7.35 (m, 10H); ^{13}C NMR δ: 17.4, 17.8, 18.0, 26.3, 28.1, 48.0, 48.1, 54.6, 64.8, 65.7, 67.3, 68.8, 70.5, 73.6, 74.1, 75.9, 80.8, 97.9, 98.8, 99.5, 99.6, 108.8, 127.4, 127.5, 127.8, 128.2, 128.3, 138.2, 138.7; HRMS calcd for $C_{36}H_{50}O_{12}Na$ [M+Na]$^+$: 697.3194, found 697.3183.

5.2.14. Methyl 4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranosyl]-2,3-*O*-isopropylidene-α-D-rhamnopyranoside (31β). $[\alpha]_D^{17}$ +78.0 (c 1.0); ^{1}H NMR δ: 1.26 (s, 3H), 1.28 (s, 3H), 1.33 (d, J=6.0 Hz, 3H), 1.34 (s, 3H), 1.46 (s, 3H), 3.19 (s, 3H), 3.29 (s, 3H), 3.37 (s, 3H), 3.45–3.51 (m, 2H), 3.58–3.61 (m, 1H), 3.67–3.82 (m, 5H), 4.09 (d, J=5.5 Hz, 1H), 4.32 (t, J=6.5 Hz, 1H), 4.55–4.62 (m, 3H), 4.79 (s, 2H), 4.82 (s, 1H), 7.27–7.38 (m, 10H); ^{13}C NMR δ: 17.6, 17.8, 17.9, 26.2, 28.0, 47.9, 48.0, 54.8, 64.6, 66.0, 68.4, 72.9, 73.4, 73.9, 74.8, 75.8, 79.3, 82.2, 98.2, 99.5, 99.6, 103.3, 108.9, 127.4, 127.5, 127.6, 127.8, 128.2, 128.2, 138.4, 138.7; HRMS calcd for $C_{36}H_{50}O_{12}Na$ [M+Na]$^+$: 697.3194, found 697.3191.

5.2.15. Methyl 4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranosyl]-2,3-*O*-isopropylidene-α-D-rhamnopyranoside (31α). $[\alpha]_D^{17}$ +132.0 (c 1.0); ^{1}H NMR δ: 1.29 (s, 3H), 1.30 (d, J=6.5 Hz, 3H), 1.34 (s, 3H), 1.35 (s, 3H), 1.53 (s, 3H), 3.19 (s, 3H), 3.32 (s, 3H), 3.34 (s, 3H), 3.55–3.65 (m, 3H), 3.69–3.78 (m, 3H), 3.91–3.92 (m, 1H), 4.04–4.08 (m, 2H), 4.33 (t, J=6.0 Hz, 1H), 4.56 (q, J=8.5 Hz, 2H), 4.84 (s, 1H), 4.77–4.81 (m, 2H), 5.59 (d, J=4.0 Hz, 1H), 7.24–7.32 (m, 8H), 7.41–7.42 (m, 2H); ^{13}C NMR δ: 17.7, 18.0, 18.5, 26.3, 28.0, 47.9, 48.1, 54.7, 63.7, 66.2, 67.9, 69.4, 69.8, 73.2, 73.6, 76.0, 76.4, 78.5, 78.6, 96.5, 98.1, 99.4, 99.6, 109.2, 127.4, 127.5, 127.6, 128.2, 128.3, 138.1, 138.9; HRMS calcd for $C_{36}H_{50}O_{12}Na$ [M+Na]$^+$: 697.3194, found 697.3198.

5.3. Activation of donor 12 with *N*-iodosuccinimide/trifluoromethanesulfonic acid

To a stirred 0.05 M solution of **12** and acceptor **30** (1.5 equiv) in dry dichloromethane under argon was added *N*-iodosuccinimide (1.2 equiv) at 0 °C, followed by trifluoromethanesulfonic acid (0.1 equiv). After stirring for 0.5 h at 0 °C, the reaction mixture was then diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate. The combined organic portion was washed with aqueous sodium thiosulfate and then brine, dried over sodium sulfate, and evaporated to dryness. Purification by silica gel chromatography gave **31α** in 70% yield, with spectroscopic data identical to those described above.

5.4. Phenyl 2,6-di-*O*-benzyl-3,4-*O*-(butane-2,3-diyl)-1-thio-β-D-glucopyranoside (32)

Sodium cyanoborohydride (0.33 g, 15.0 mmol) was added to a stirred solution of donor **12** (0.2 g, 1.0 mmol) in THF (10.0 mL) under an inert atmosphere. The solution was cooled to 0 °C and 2.0 M HCl in diethyl ether was added until the pH was 3–4. The reaction mixture was stirred at room temperature for 24 h, maintaining the same pH, then was quenched by the addition of saturated $NaHCO_3$.The aqueous phase was extracted with EtOAc (50 mL) and the organic layer was washed with water and then brine. After drying over sodium sulfate, the extracts were evaporated to dryness and purified by column chromatography using EtOAc/hexanes as eluant to give **32** (0.13 g, 70%). $[\alpha]_D^{17}$ −4.7 (c 1.0); ^{1}H NMR δ: 1.10 (d, J=6.0 Hz, 3H), 1.17 (d, J=6.0 Hz, 3H), 3.30–3.39 (m, 3H), 3.43 (t, J=9.5 Hz, 1H), 3.54 (t, J=9.0 Hz, 1H), 3.58 (d, J=8.0 Hz, 1H), 3.65 (dd, J=11.0 and 4.5 Hz, 1H), 3.82 (d, J=10.0 Hz, 1H), 4.55 (d, J=12.0 Hz, 1H), 4.63 (d, J=12.5 Hz, 1H), 4.72 (d, J=9.5 Hz, 1H), 4.76 (d, J=11.0 Hz, 1H), 4.83 (d, J=11.0 Hz, 1H), 7.58–7.60 (m, 2H), 7.45–7.47 (m, 2H), 7.23–7.37 (m, 11H); ^{13}C

NMR δ: 17.3, 17.4, 68.8, 73.4, 73.9, 75.1, 77.6, 77.7, 77.8, 82.9, 87.2, 127.4, 127.5, 127.6, 127.7, 128.2, 128.3, 128.8, 132.1, 133.7, 138.4, 138.5; HRMS calcd for $C_{30}H_{34}O_5S$: $C_{30}H_{34}O_5S$ $[M+Na]^+$: 529.2019, found 529.2019.

5.5. Glycosylation of des-methoxy donor 32

Activation of **32** according to the standard BSP protocol and treatment with acceptor **22** gave **35** (50%) as a 1:1 α/β mixture. Column chromatography on silica gel eluting with EtOAc/hexanes gave **35**β and **35**α.

5.5.1. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(butane-2,3-diyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (35β). $[\alpha]_D^{21}$ +20.0 (*c* 0.45); ^{1}H NMR δ: 1.07 (d, *J*=6.0 Hz, 3H), 1.15 (d, *J*=5.5 Hz, 3H), 3.29–3.33 (m, 4H), 3.37 (s, 3H), 3.39–3.46 (m, 4H), 3.58 (d, *J*=10.5 Hz, 1H), 3.65 (d, *J*=9.5 Hz, 1H), 3.69 (d, *J*=11.5 Hz, 1H), 3.82 (d, *J*=3.0 Hz, 1H), 3.86 (t, *J*=9.0 Hz, 2H), 3.91 (d, *J*=10.0 Hz, 1H), 4.37–4.49 (m, 5H), 4.55 (d, *J*=3.5 Hz, 1H), 4.59 (d, *J*=12.0 Hz, 1H), 4.69 (d, *J*=12.0 Hz, 1H), 4.76 (dd, *J*=11.0 and 7.5 Hz, 1H), 4.83 (d, *J*=11.5 Hz, 1H), 5.06 (d, *J*=11.0 Hz, 1H), 7.21–7.41 (m, 25H); ^{13}C NMR δ: 17.3, 17.4, 55.3, 68.2, 68.5, 69.9, 73.1, 73.3, 73.7, 74.2, 74.3, 74.5, 75.3, 77.5, 78.9, 79.6, 80.5, 80.9, 98.4, 102.6, 127.1, 127.2, 127.4, 127.5, 127.6, 127.7, 127.7, 127.8, 128.0, 128.1, 128.2, 128.4, 138.0, 138.4, 138.8, 138.9, 139.6; HRMS calcd for $C_{52}H_{60}O_{11}$: $C_{52}H_{60}O_{11}$ $[M+Na]^+$: 883.4028, found 883.4021.

5.5.2. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3,4-*O*-(butane-2,3-diyl)-α-D-glucopyranosyl]-α-D-glucopyranoside (35α). $[\alpha]_D^{21}$ +21.0 (*c* 0.50); ^{1}H NMR δ: 1.06 (d, *J*=6.0 Hz, 3H), 1.13 (d, *J*=6.0 Hz, 3H), 3.27–3.45 (m, 4H), 3.37 (s, 3H), 3.49–3.55 (m, 2H), 3.64–3.74 (m, 3H), 3.76 (t, *J*=9.5 Hz, 1H), 3.84–3.87 (m, 1H), 3.93 (t, *J*=10.0 Hz, 1H), 4.03 (t, *J*=9.0 Hz, 1H), 4.32 (d, *J*=12.5 Hz, 1H), 4.48 (q, *J*=9.5 Hz, 2H), 4.54–4.60 (m, 5H), 4.67 (d, *J*=12.0 Hz, 1H), 4.78 (d, *J*=12.0 Hz, 1H), 4.82 (d, *J*=11.5 Hz, 1H), 4.94 (d, *J*=11.5 Hz, 1H), 5.74 (d, *J*=3.5 Hz, 1H), 7.18–7.33 (m, 25H); ^{13}C NMR δ: 17.3, 17.5, 55.1, 67.3, 69.5, 69.8, 73.1, 73.2, 73.3, 73.4, 73.5, 73.7, 74.3, 75.9, 77.3, 77.9, 80.3, 82.0, 97.7, 97.9, 126.8, 127.0, 127.4, 127.4, 127.5, 127.5, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 138.0, 138.2, 138.3, 138.4, 139.1; HRMS calcd for $C_{52}H_{60}O_{11}$: $C_{52}H_{60}O_{11}$ $[M+Na]^+$: 883.4028, found 883.4027.

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References and notes

1. Review on the effect of cyclic protecting groups in glycosylation: Litjens, R. E. J. N.; van den Bos, L. J.; Codée, J. D. C.; Overkleeft, H. S.; van der Marel, G. *Carbohydr. Res.* **2007**, *342*, 419–429.
2. Crich, D.; Lim, L. B. L. *Org. React.* **2004**, *64*, 115–251.
3. Crich, D. Chemistry of Glycosyl Triflates: Synthesis of β-Mannopyranosides. In *Glycochemistry: Principles, Synthesis, and Applications*; Wang, P. G., Bertozzi, C. R., Eds.; Dekker: New York, NY, 2001; pp 53–75.
4. Crich, D. *J. Carbohydr. Chem.* **2002**, *21*, 663–686.
5. Review on bisacetal chemistry: Ley, S. V.; Baeschlin, D. K.; Dixon, D. J.; Foster, A. C.; Ince, S. J.; Priepke, H. W. M.; Reynolds, D. J. *Chem. Rev.* **2001**, *101*, 53–80.
6. Crich, D.; Sun, S. *J. Org. Chem.* **1997**, *62*, 1198–1199.
7. Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217–11223.
8. Crich, D.; Sun, S. *Tetrahedron* **1998**, *54*, 8321–8348.
9. Rao, V. S. R.; Qasba, P. K.; Balaji, P. V.; Chandrasekaran, R. *Conformation of Carbohydrates*; Harwood Academic: Amsterdam, 1998.
10. Grindley, T. B. Structure and Conformation of Carbohydrates. *Glycoscience: Chemistry and Chemical Biology*; Fraser-Reid, B., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin, 2001; Vol. 1, pp 3–51.
11. Jensen, H. H.; Nordstrom, M.; Bols, M. *J. Am. Chem. Soc.* **2004**, *126*, 9205–9213.
12. Crich, D.; Cai, W.; Dai, Z. *J. Org. Chem.* **2000**, *65*, 1291–1297.
13. Crich, D.; Vinod, A. U.; Picione, J.; Wink, D. J. *ARKIVOC* **2005**, 339–344.
14. Crich, D.; Vinod, A. U.; Picione, J. *J. Org. Chem.* **2003**, *68*, 8453–8458.
15. Crich, D.; Cai, W. *J. Org. Chem.* **1999**, *64*, 4926–4930.
16. Crich, D.; Jayalath, P. *J. Org. Chem.* **2005**, *70*, 7252–7259.
17. Crich, D.; Vinogradova, O. *J. Org. Chem.* **2006**, *71*, 8473–8480.
18. Crich, D.; Li, L. *J. Org. Chem.* **2007**, *72*, 1681–1690.
19. Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020.
20. Crich, D.; Banerjee, A.; Li, W.; Yao, Q. *J. Carbohydr. Chem.* **2005**, *24*, 415–424.
21. Crich, D.; Smith, M.; Yao, Q.; Picione, J. *Synthesis* **2001**, 323–326.
22. Martín, A.; Butters, T. D.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **1999**, *10*, 2343–2360.
23. Nishio, T.; Miyake, Y.; Kubota, K.; Yamai, M.; Miki, S.; Ito, T.; Oku, T. *Carbohydr. Res.* **1996**, *280*, 357–363.
24. Paulsen, H. Selectivity and Reactivity in Oligosaccharide Synthesis. In *Selectivity—A Goal for Synthetic Efficiency*; Bartmann, W., Trost, B. M., Eds.; Chemie: Weinheim, 1984; pp 169–190.
25. Spijker, N. M.; van Boeckel, C. A. A. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 180–183.
26. Fraser-Reid, B.; López, J. C.; Gómez, A. M.; Uriel, C. *Eur. J. Org. Chem.* **2004**, 1387–1395.
27. Veeneman, G. H.; van Leeuwen, S. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331–1334.
28. Crich, D.; de la Mora, M.; Vinod, A. U. *J. Org. Chem.* **2003**, *68*, 8142–8148.
29. Crich, D.; Pedersen, C. M.; Bowers, A. A.; Wink, D. J. *J. Org. Chem.* **2007**, *72*, 1553–1565.
30. Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97–101.
31. Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583–5584.
32. Green, L. G.; Ley, S. V. Protecting Groups: Effects on Reactivity, Glycosylation Stereoselectivity, and Coupling.

Carbohydrates in Chemistry and Biology; Ernst, B., Hart, G. W., Sinaÿ, P., Eds.; Wiley-VCH: Weinheim, 2000; Vol. 1, pp 427–448.
33. Lemieux, R. U.; Hendriks, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.* **1975**, *97*, 4056–4062.
34. Crich, D.; Chandrasekera, N. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5386–5389.
35. Review on mechanisms of glycoside bond hydrolysis and formation: Horenstein, N. A. *Adv. Phys. Org. Chem.* **2006**, *41*, 275–314.
36. Nukuda, T.; Bérces, A.; Wang, L.; Zgierski, M. Z.; Whitfield, D. M. *Carbohydr. Res.* **2005**, *340*, 841–852.
37. Nukada, T.; Berces, A.; Whitfield, D. M. *Carbohydr. Res.* **2002**, *337*, 765–774.
38. Kim, J.-H.; Yang, H.; Boons, G.-J. *Angew. Chem., Int. Ed.* **2005**, *44*, 947–949.
39. Kim, J.-H.; Yang, H.; Park, J.; Boons, G.-J. *J. Am. Chem. Soc.* **2005**, *127*, 12090–12097.
40. Smoot, J. T.; Pornsuriyasak, P.; Demchenko, A. V. *Angew. Chem., Int. Ed.* **2005**, *44*, 7123–7126.