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Does Neighboring Group Participation by Non-Vicinal Esters Play a Role in Glycosylation Reactions? Effective Probes for the Detection of Bridging Intermediates

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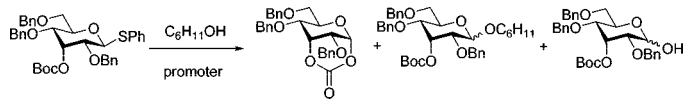

Neighboring group participation in glycopyranosylation reactions is probed for esters at the 3-*O*-axial and -equatorial, 4-*O*-axial and -equatorial, and 6-*O*-sites of a range of donors through the use *tert*-butoxycarbonyl esters. The anticipated intermediate cyclic dioxanyl cation is interrupted for the axial 3-*O*-derivative, leading to the formation of a 1,3-*O*-cyclic carbonate ester, with loss of a *tert*-butyl cation, providing convincing evidence of participation by esters at that position. However, no evidence was found for such a fragmentation of carbonate esters at the 3-*O*-equatorial, 4-*O*-axial and -equatorial, and 6-*O* positions, indicating that neighboring group participation from those sites does not occur under typical glycosylation conditions. Further probes employing a 4-*O*-(2-carboxy)benzoate ester and a 4-*O*-(4-methoxybenzoate) ester, the latter in conjunction with an ^{18}O quench designed to detect bridging intermediates, also failed to provide evidence for participation by 4-*O*-esters in galactopyranosylation.

Introduction

Neighboring group participation, or anchimeric assistance,[1] by 2-*O*-carboxylate esters is of fundamental importance to carbohydrate chemistry and is responsible for the facile, reliable, highly stereoselective synthesis of the 1,2-trans class of glycosidic bonds (β-glucosides and α-mannosides and related glycosidic bonds).[2] The intervention of 2-*O*-carboxylate esters in this manner is supported by the isolation of crystalline dioxalenium ions in some cases,[3] by the spectroscopic observation of the same species as intermediates in other cases,[4] by computational work,[5] by rate acceleration in the case of weakly activated donors,[3,6] and is implied by the highly 1,2-trans-selective nature of these reactions. Participation by other groups, such as the 2-*O*-(2-pyridyl)methyl ethers and several 2-*O*-(2-thio)ethyl ethers, has been demonstrated spectroscopically recently, [7] and the similar involvement of other groups such as the 2-*O*-phosphate esters,[8,9] the 2-deoxy-2-dibenzylamino systems,[10] and other bulky benzyl type ethers[11] has been suggested on the basis of stereochemical evidence.

In this paper, we address the possibility of neighboring group participation by carboxylate esters located on more remote positions, specifically on O3, O4, and O6 of glycopyranosyl donors. In 2000, we observed the thioglycoside **1**, with its 3-*O*-

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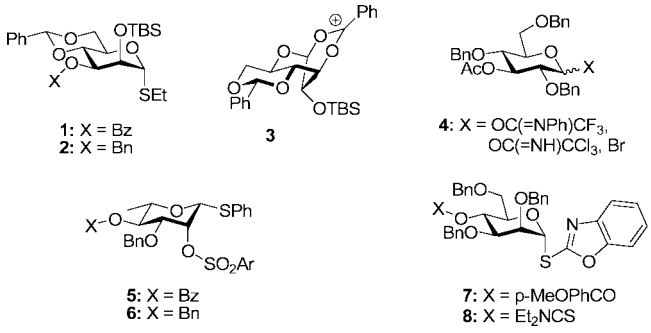
benzoate ester, to be highly α-selective,[12] in contrast with the excellent β-selectivity seen with the corresponding 3-*O*-benzyl ether **2**.[13] The phenomenon was subsequently extended to other esters at the 3-position of mannose and was successfully exploited in the synthesis of a complex oligosaccharide.[14] Our results are related to an earlier observation by van Boeckel and co-workers in which it was found that a 3-*O*-acetyl-protected mannopyranosyl bromide was less β-selective than the corresponding 3-*O*-benzyl derivative under insoluble silver salt conditions,[15,16] but they differ in that the changes are considerably greater in our work. At the time we speculated that the α-selectivity observed with **1** might be derived from neighboring group participation by the ester and invoked intermediates related to **3** that readily accommodate the trans-fused benzylidene acetal.[12] Subsequent work from our laboratory, however, has highlighted the high sensitivity of these 4,6-*O*-benzylidene-protected β-mannosylations to a range of substituents at the 3-position, causing us to doubt our original interpretation.[17]



Neighboring group participation by esters at the 3-position, both axial and equatorial, has previously been discussed by other groups,[15,18] most recently in the equatorial series by Nifantiev and co-workers for the donors **4**,[19] but the evidence rarely extends beyond stereochemical arguments. A similar situation pertains with respect to esters in the 4-*O*-position with numerous claims of neighboring group participation leading to improved synthesis of either α-galacto and fucosides,[20] or β-gluco and mannosides.[21] van Boeckel argued strongly that, at least for the systems studied in his laboratory using the insoluble silver salt method for the activation of glycosyl bromides, it is not necessary to invoke neighboring group participation by esters at the 3- and/or 4-positions of glucose and mannose in order to explain the selectivities observed.[15] In discussing the increased β-selectivities observed in rhamnopyranosylation reactions with donor **5**, as compared to **6**, under homogeneous activation conditions, we agreed with van Boeckel and inclined toward the effect of the ester being one of an electron-withdrawing group influencing the tightness of the ion pairs on activation of the donor.[9] In line with this hypothesis, Takahashi and co-workers observed excellent β-selectivity in a series of glycosylations conducted with a set of donors carrying electron-withdrawing but nonparticipating 4-*O*-sulfonate esters.[22] Demchenko and co-workers, on the other hand, recently came down strongly on the side of neighboring group participation from O4 with donors **6** and **7**, even though the best β-selectivity recorded was only 7:1.[21]

With respect to the effect of esters and related functions on O6 in glycosylation reactions, early work by the Schuerch group with glucosyl sulfonates as donors indicated that 6-*O*-(*N*-phenylcarbamates) afforded high selectivity for α-glucosides,[23] but the effect did not extend to the galactopyranosides.[24] However, rather than postulating neighboring group participation in the glucose series, the authors inclined toward the functionality at O6 influencing stereoselectivity by modulation of the tightness of the ion pair obtained on ionization of the glycosyl donor.[23] In another study by the Schuerch laboratory, investigation of a series of glucosyl donors carrying substituted 6-*O*-benzoates revealed that greater β-selectivity was observed with the more electron-rich esters, which was discussed in terms of the stabilization of the glycosyl oxocarbenium ion by the ester group, without the formation of a cyclic intermediate such as would be required by classical neighboring group participation.[25,26] In spite of this background, neighboring group participation by esters at O6, through seven-membered cyclic transition states and leading to the formation of α-glycosides, continues to be invoked frequently in the literature.[27]

The rational development of stereocontrolled oligosaccharide synthesis requires the resolution of these fundamental issues, and it is with this in mind that we advance here a series of probes capable of unambiguously establishing the presence of neighboring group participation in glycosylation reactions.

Results and Discussion

Concept. We conceived that participation by a carboxylate ester might be reliably established if the ester could be modified in such a way as to trap the intermediate dioxocarbenium ion by fragmentation. We considered that a *tert*-butoxycarbonyl (Boc) group would be a suitable system for use in this manner

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(25) Fréchet, J. M.; Schuerch, C. *J. Am. Chem. Soc.* **1972**, *94*, 604–609.
(26) Note that classical neighboring group participation from an O6 ester leading to β-glycosides is stereoelectronically improbable, as the intermediate would correspond to an inside,outside bicyclo[5.3.1]undecane-type system: (a) Alder, R. W.; East, S. P. *Chem. Rev.* **1996**, *96*, 2097–2111. (b) Kim, S.; Winkler, J. *Chem. Soc. Rev.* **1997**, *26*, 387–400.
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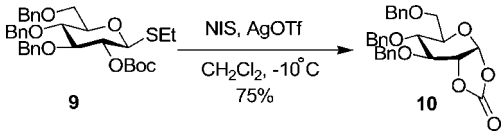
with loss of a *tert*-butyl-cation from the cyclic intermediate leading to the formation of a cyclic carbonate ester.

The capture of vicinal electrophilic centers by carbonate esters, especially *tert*-butoxycarbonates, leading to the formation of five-membered cyclic carbonates with the loss of an alkyl cation or equivalent is classical in organic synthesis,[28] and the comparable use of carbamates has found application in carbohydrate chemistry.[29] Although unusual, such chemistry has also been extended to the formation of a seven-membered cyclic carbonate through cyclization of a carbamate derived from a 4-pentenol with *N*-bromosuccinimide in a favorably conformationally constrained system.[30] More generally, the possibility of neighboring group participation in simple acyclic systems through six- and seven-membered cyclic dioxocarbenium ions has found some support in elegant labeling experiments conducted by Wilen and co-workers.[31] We note that the Hammett parameter, σ_p, for the CO_2Me group is +0.45, which is closely related to the +0.50 of the acetyl group,[32] from which we deduce that carbonate esters should be somewhat akin to acetate esters in their ability to take part in neighboring group participation. Likewise, the field effect parameter *F*, of the CO_2Me and COMe groups are very similar (0.34 and 0.33, respectively), indicating that both groups stabilize positive charge by field effects to a similar extent.[32]

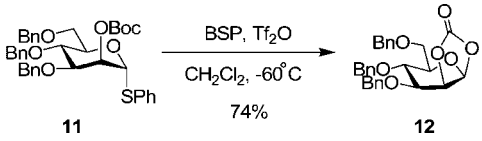
Proof of Concept. Activation of the 2-*O*-Boc protected thioglucoside **9**, readily available through reaction of ethyl 3,4,6-tri-*O*-benzyl-β-D-thioglucopyranoside and Boc_2O, with *N*-iodosuccinimide and silver triflate in dichloromethane at −10 °C afforded the cyclic carbonate **10** in 75% isolated yield (Scheme 1).

SCHEME 1. Cyclic Carbonate Formation from a 2-*O*-Boc Group: Glucose



The 2-*O*-mannosyl carbonate **11**, available from phenyl 3,4,6-tri-*O*-benzyl-α-D-thiomannopyranoside and Boc_2O, gave the cyclic carbonate **12** in 74% yield on treatment with 1-benzenesulfinyl piperidine (BSP)[33] and trifluoromethanesulfonic anhydride in dichloromethane at −60 °C (Scheme 2).

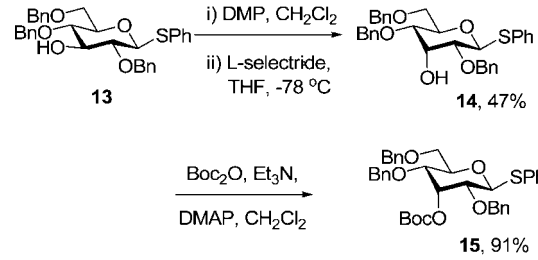
SCHEME 2. Cyclic Carbonate Formation from a 2-*O*-Boc Group: Mannose



These two experiments serve as proof of concept of cyclic carbonate formation from Boc esters in systems for which classical neighboring group participation by carboxylates is well-established.

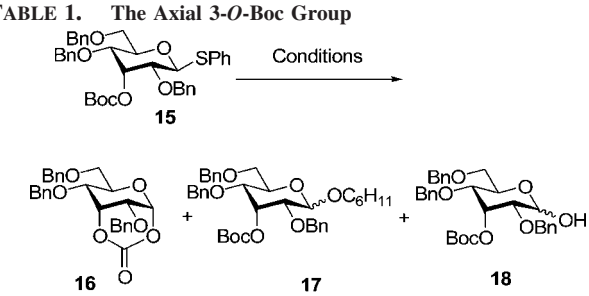
Axial 3-*O*-Esters. The possibility of participation by axial esters at O3 in the pyranose series was investigated with the allose donor **15**, which was obtained in a straightforward manner via Dess−Martin oxidation of the 2,4,6-tri-*O*-benzyl-β-D-thioglucoside **13**, reduction with L-Selectride, and condensation with Boc_2O (Scheme 3).

SCHEME 3. Preparation of a 3-*O*-Boc-Allopyranoside Donor



The activation of **15** was investigated under three sets of conditions. Treatment with BSP and trifluoromethanesulfonic anhydride at −60 °C in dichloromethane in the absence of an external nucleophile led to the isolation of the cyclic carbonate **16** in 70% yield (Table 1, entry 1). However, inclusion of the mild, non-nucleophilic base tri-*tert*-butylpyrimidine (TTBP)[34] in the reaction mixture and addition of cyclohexanol following activation resulted in the formation of the cyclohexyl glycoside **17** in 61% yield as an 11:1 β:α mixture, together with 7% of the expected cyclic carbonate **16** (Table 1, entry 2). Finally, activation by *N*-iodosuccinimide and trifluoromethanesulfonic anhydride in the absence of nucleophile gave the hydrolysis product **18** as the only isolable product (Table 1, entry 3) from a complex mixture in which the *tert*-butyl group was mostly retained as judged from the ^1H NMR spectrum of the crude reaction mixture.

TABLE 1. The Axial 3-*O*-Boc Group



entry	conditions	product, yield (%)	anomeric ratio (α:β)
1	BSP, Tf_2O, CH_2Cl_2, −60 °C	**16**, 70	–
2	TTBP, BSP, Tf_2O, cyclohexanol, CH_2Cl_2, −60 °C	**17**, 61; **16**, 7	1:11.2
3	NIS, Tf_2O, CH_2Cl_2, −60 °C	**18**, 55	–

The isolation of cyclic carbonate **16** on activation with BSP and Tf_2O (Table 1, entry 1) clearly demonstrates the possibility of participation by axial esters at the 3-*O*-position. The formation of the cyclohexyl glycosides **17** on inclusion of the nucleophile, however, strongly suggests that such neighboring group participation is not necessary for the selective formation of β-glycosides in this system and suggests that developing 1,3-diaxial interactions in transition state for formation of the α-glycoside are sufficient to explain the preferential formation

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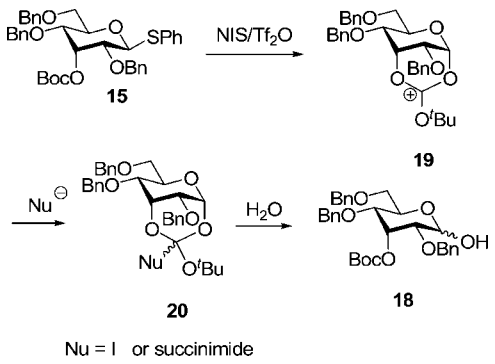
SCHEME 4. Possible Mechanisms for the Formation of 18

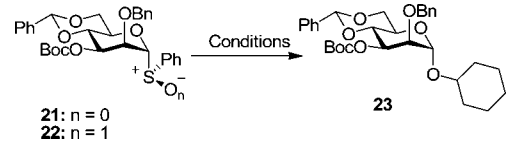


of β-glycosides in this type of system. The isolation of the hydrolysis product **18** on activation with NIS/Tf_2O presumably is due to trapping of a cyclic intermediate **19**, before loss of the *tert*-butyl group, by iodide or by succinimide (vide infra) to give an unstable orthocarbonate-type species (**20**), which undergoes hydrolysis on workup (Scheme 4). We prefer this mechanism over the trapping of the glycosyl oxocarbenium ion by iodide or succinimide, followed by hydrolysis on workup, as both glycosyl iodides[35] and succinimides[36] have been demonstrated on numerous occasions to be isolable substances that are readily handled under standard conditions.

Equatorial 3-*O*-Esters. A 3-*O*-Boc ester **21** was readily prepared from phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-thiomannoside, and a portion was converted to the sulfoxide **22**, which was formed as a single diastereomer, presumed to have the $(R)_S$ configuration on the basis of previous work.[37] When sulfoxide **22** was activated with Tf_2O at low temperature in dichloromethane followed by aqueous workup, a complex mixture was obtained that nevertheless retained the 3-*O*-Boc ester as determined from the ^1H NMR spectrum of the crude reaction mixture (Table 2, entry 1). On activation of the sulfoxide in the presence of TTBP followed by addition of cyclohexanol, the α-glycoside **23** was formed as a single α-anomer in 75% isolated yield (Table 2, entry 2). Activation of the thioglycoside **21** with BSP and Tf_2O followed by trapping with cyclohexanol gave the same glycoside with the same exquisite α-selectivity (Table 2, entry 3). In none of the experiments conducted with donors **21** and **22** were we able to find any evidence supporting the formation of a cyclic carbonate spanning positions 1 and 3 of the pyranose ring, and it is apparent that the α-selectivity observed by ourselves with donors carrying equatorial carboxylate esters on the 3-position of glycosyl donors does not arise from classical neighboring group participation.

Axial 4-*O*-Esters. A 4-*O*-Boc galactosyl donor **24** was readily obtained from ethyl 2,3,6-tri-*O*-benzyl-β-D-thiogalactopyranoside and activated with BSP and Tf_2O in ether at −60 °C.

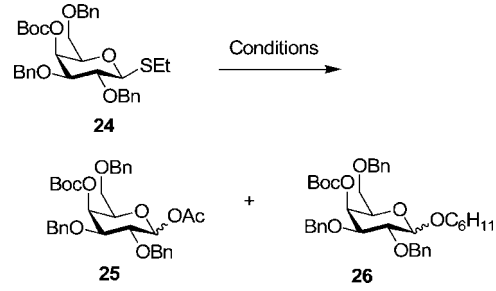
TABLE 2. The Equatorial 3-*O*-Boc Group



entry	conditions	product, yield (%)	anomeric ratio (α:β)
1	**22**, Tf_2O, CH_2Cl_2, −60 °C	complex mixture	–
2	**22**, TTBP, Tf_2O, $C_6H_{12}O$, CH_2Cl_2, −60 °C	**23**, 75	α only
3	**21**, TTBP, BSP, Tf_2O, $C_6H_{12}O$, CH_2Cl_2, −60 °C	**23**, 69	α only

Following workup, acetylation of the crude reaction mixture enabled isolation of the glycosyl acetates **25** as an anomeric mixture (Table 3, entry 1). When cyclohexanol was added as acceptor, the cyclohexyl glycosides **26** were obtained in high yield, with the anomeric ratio being dependent on the solvent, but favoring the β-anomer in both ether and dichloromethane (Table 3, entries 2 and 3). These results effectively rule out neighboring group participation from an axial ester at *O*-4.

TABLE 3. Axial 4-*O*-Boc Group



entry	conditions	product, yield (%)	anomeric ratio (α:β)
1	(i) BSP, Tf_2O, Et_2O, −60 °C; (ii) Ac_2O, py	**25**, 92	1:7.1
2	TTBP, BSP, Tf_2O, cyclohexanol, CH_2Cl_2, −60 °C	**26**, 88	1:3.9
3	TTBP, BSP, Tf_2O, cyclohexanol, Et_2O, −60 °C	**26**, 62	1:1.3

Equatorial 4-*O*-Esters. Two 4-*O*-Boc donors, **27** and **30**, were prepared in the usual manner from the corresponding alcohols and subjected to a series of activation and coupling reactions as set out in Table 4.

With the mannosyl donor **27**, activations were conducted by the NIS and BSP/Tf_2O methods with 2-propanol as acceptor (Table 4, entries 1−3) with no indication of the formation of a cyclic carbonate. In each case, the isopropyl glycoside **28** was isolated as an anomeric mixture slightly favoring the β-anomer, consistent with the general results of Demchenko with donors **7** and **8**. When the acceptor was omitted from the NIS-type activation, the ring-inverted α-glycosyl succinimide **29** was isolated in good yield (Table 4, entry 4), consistent with trapping of the glycosyl oxocarbenium ion being more rapid than any participation by the Boc group. With the 3-azido-2,3,6-trideoxy system **30**, anticipated to undergo more facile ring inversion than **27** and so to have a greater predisposition toward neighboring group participation from the 4-position,[38] no cyclic carbonate was found (Table 4, entries 5 and 6). When the

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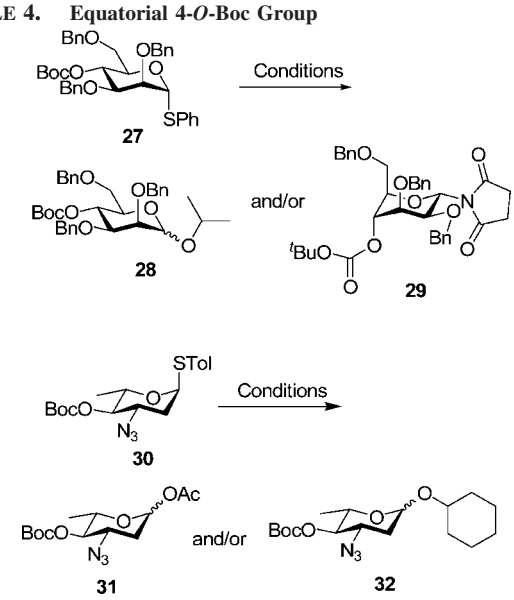
TABLE 4. Equatorial 4-*O*-Boc Group

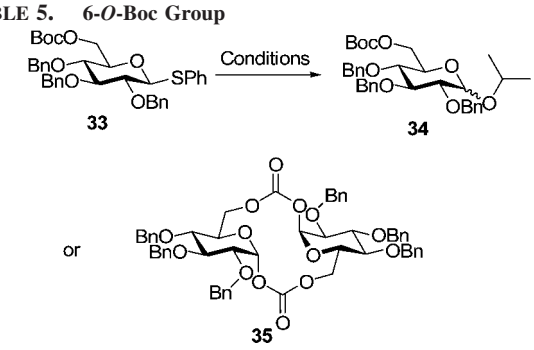


entry	donor	conditions	products yield (%)	anomeric ratio (α:β)
1	**27**	1.2 equiv of NIS, 0.3 equiv of AgOTf, 3 equiv of *i*PrOH, CH_2Cl_2, −10 °C	**28**, 72	0.9:1
2	**27**	1.2 equiv of BSP, 1.5 equiv of TTBP, 3 equiv of *i*PrOH, CH_2Cl_2, −40 °C	**28**, 76	0.8:1
3	**27**	1.2 equiv of BSP, 1.5 equiv of TTBP, 3 equiv of *i*PrOH, Et_2O, −60 °C	**28**, 65	0.7:1
4	**27**	1.2 equiv of NIS, 0.3 equiv of AgOTf, CH_2Cl_2, −10 °C	**29**, 59	α-only
5	**30**	(i) BSP, Tf_2O, CH_2Cl_2, −60 °C; (ii) Ac_2O, py	**31**, 73	1:1.7
6	**30**	TTBP, BSP, Tf_2O, cyclohexanol, CH_2Cl_2, −60 °C	**32**, 46	1:3.7

activation was conducted without acceptor, only the hydrolysis product was isolated, whereas quenching with cyclohexanol allowed isolation of the glycoside as an anomeric mixture favoring the β-isomer. Overall, the results obtained argue strongly against neighboring group participation by equatorial esters at *O*-4 as playing a significant role in glycosylation reactions.

6-*O*-Esters. With the 6-*O*-Boc glucosyl donor **33** and 2-propanol as acceptor, the glycoside **34** was obtained in high yield as an anomeric mixture, irrespective of whether the reaction was conducted in dichloromethane or ether (Table 5, entries 1 and 2). In the absence of acceptor, a crude reaction mixture containing predominantly one product, with an anomeric doublet at δ 6.21 (J = 3.0 Hz), was obtained. Chromatographic purification was accompanied by substantial decomposition; nevertheless, the same product was isolated in 16% yield and characterized on the basis of its NMR and mass spectrometric data as the macrocyclic bis-carbonate **35**. The symmetric α,α-nature of this macrolide strongly mitigates against its formation by dimerization of any monomeric cyclic carbonate, as this would necessarily require inversion of configuration at the anomeric center. Neighboring group participation by esters at *O*-6 is deemed unlikely on the basis of these results.

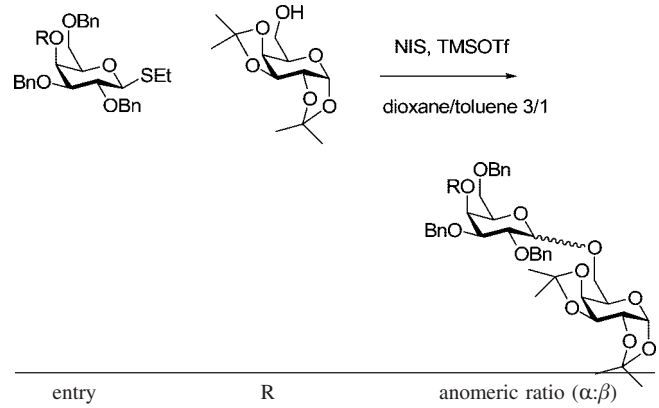
TABLE 5. 6-*O*-Boc Group



entry	conditions	product, yield (%)	anomeric ratio (α:β)
1	1.2 equiv of NIS, 0.3 equiv of TfOH, 3 equiv of *i*PrOH CH_2Cl_2, 0 °C	**34**, 80	1:1
2	1.2 equiv of NIS, 0.3 of equiv TfOH, 3 of equiv *i*PrOH, Et_2O, 0 °C	**34**, 74	1.5:1
3	1.2 equiv of NIS, 0.3 equiv of TfOH, CH_2Cl_2, 0 °C	**35**, 16	–

Axial Esters at O4 Revisited. One of the more supportive papers in the literature for neighboring group participation by remote groups is that of Boons and co-workers on a series of 4-*O*-acyl-galactosyl donors.[20c] This paper appears to provide evidence for a shift in mechanism between alkanoate and arylcarboxylate esters, as the data, some of which is reproduced in Table 6, clearly shows a jump in anomeric ratio between the acetate and the substituted benzoates. The situation, however, is complicated by the high α-selectivity obtained with the pivalate ester, particularly when it is realized that the Hammett σ_p value for a pivaloyl group is smaller than that of an acetyl group (σ_p pivaloyl = +0.32; σ_p acetyl = +0.50) and that the field effect parameter for pivaloyl is also smaller than that of an acetyl group (F pivaloyl = 0.26; F acetyl 0.33).[32] Apparently, steric effects are also at play here, as is the possibility of the intermediate glycosyl oxocarbenium ions assuming different conformations depending on the size of the group at O4.

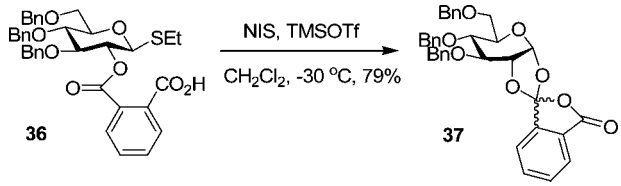
TABLE 6. Literature Data on 4-*O*-Acyl Galactosyl Donors



entry	R	anomeric ratio (α:β)
1	acetyl	7.2:1
2	4-nitrobenzoyl	14:1
3	benzoyl	17:1
4	4-methylbenzoyl	18:1
5	4-methoxybenzoyl	14:1
6	pivaloyl	16:1

For this reason, we believed it was important to develop an independent probe specifically for neighboring group participation by benzoate-type esters. We took inspiration from a seminal paper of Lemieux and Hindsgaul[39] in which it was demonstrated that 3,4,6-tri-*O*-acetyl-2-*O*-(carboxybenzoyl)-α-D-glucopyranosyl bromide underwent cyclization to an ortho-spiro ester (3,4,6-tri-*O*-acetyl-1,2-*O*-phthalidylidene-α-D-glucopyranose) on treatment with tetrabutylammonium bromide and 2,6-lutidine in 60% yield and, importantly, that one of these ortho-spiro esters could be isolated and fully characterized. Applying this concept, we prepared the hemiphthalate **36**, by reaction of the corresponding alcohol with sodium hydride and phthalic anhydride, and treated it with NIS and TMSOTf in dichloromethane at room temperature, leading to the isolation of ortho ester **37** in 79% yield as an inseparable mixture of two diastereomers (Scheme 5). In addition to the ^{1}H NMR spectrum with a characteristic anomeric hydrogen resonance at δ 6.10, compound **37** featured a strong IR carbonyl absorption at υ 1783 cm^{-1}.

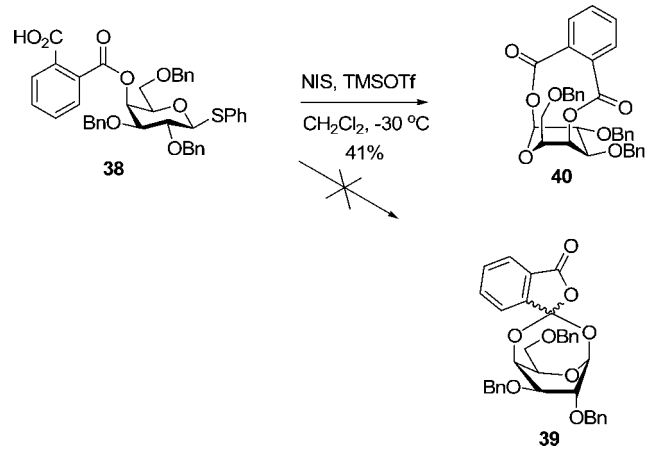
SCHEME 5. Proof of Concept for the Hemiphthalate Probe



With proof of concept established, we proceeded to prepare the galactosyl hemiphthalate **38** from phenyl 2,3,6-tri-*O*-benzyl-β-D-thiogalactopyranoside by treatment with sodium hydride and phthalic anhydride in DMF. On activation with *N*-iodosuccinimide and TMSOTf at −30 °C in dichloromethane, no evidence could be found for the formation of a bridged phthalide such as **39**, either by NMR or IR spectroscopy of the crude reaction mixture. Otherwise identical reactions run in CD_2Cl_2 with direct NMR examination also failed to provide evidence for the formation of **39**. However, it was possible to isolate from these reaction mixtures a compound to which we assign the $B_{3,O}$ diolide structure **40** (Scheme 6).[40,41] This compound might presumably arise by direct trapping of the glycosyl oxocarbenium ion by the acid group in **38**, but it is also conceivably the product of the rapid rearrangement of the putative intermediate **39**. This experiment was therefore deemed inconclusive and a further probe was sought.

To probe further the possibility of neighboring group participation by axial O4 esters, we conceived that the existence of bridging intermediates might be investigated by quenching with ^{18}O-enriched water and determination of the site of incorporation of the label (Scheme 7). The success of this experiment is predicated upon the kinetic mode of attack on the bridging cation taking place at the cationic carbon. This has been clearly demonstrated to be the case in our earlier work when, working in the presence of a non-nucleophilic base, we were able to monitor by ^{13}C NMR spectroscopy the formation of glycosyl orthoesters from preformed 2-phenyl-1,3-dioxalenium ions, rather than the glycosides observed on rearrangement.[4] Thus, we anticipated that low temperature activation of **41** in the absence of acceptors would lead to the glycosyl cation **42**, in equilibrium with the corresponding glycosyl triflate (not shown), and that this cation would be in equilibrium with the bridged cation **44** in the event that neighboring group participation occurs. Quenching of the glycosyl cation with ^{18}O-labeled water would lead to incorporation of the label solely at the anomeric center **43**, whereas quenching of the bridged cation **44** would ultimately lead to location of the label at the carbonyl carbon, as in **46**.

SCHEME 6. Application of an Axial 4-*O*-Hemiphthalate Probe



This experiment was conducted with the 4-methoxybenzoate **41**, with 95% ^{18}O-enriched water, leading to isolation of the hydrolysis product **43/46** in 82% yield, principally as the α-anomer. Unfortunately, this sample was not amenable to mass spectrometric analysis, and therefore, it was converted to the acetate **47**, isolated in 90% yield as a 4.1:1 α:β anomeric mixture. Mass spectrometry of **47** revealed the incorporation of one atom of ^{18}O to the extent of approximately 50%. Inspection by ^{13}C NMR spectroscopy revealed the presence of an isotopically shifted anomeric carbon and of a similarly shifted acetyl carbonyl group for both anomers. However, no isotopically shifted signals were apparent for either C-4 or the benzoyl carbonyl group, strongly suggesting incorporation of the label only at the anomeric site. Further confirmation of the location of the label was sought by treatment of the anomeric acetates **47** with thiophenol and $BF_3\cdot OEt_2$ in acetonitrile, resulting in the isolation of thioglycoside **41** in 97% yield as a 2.2:1 α:β-mixture. Interrogation of this mixture of anomeric thioglycosides by mass spectrometry revealed the absence of the ^{18}O label, leading to the conclusion that, in the quenching reaction, quenching only took place at the anomeric center.

Conclusion

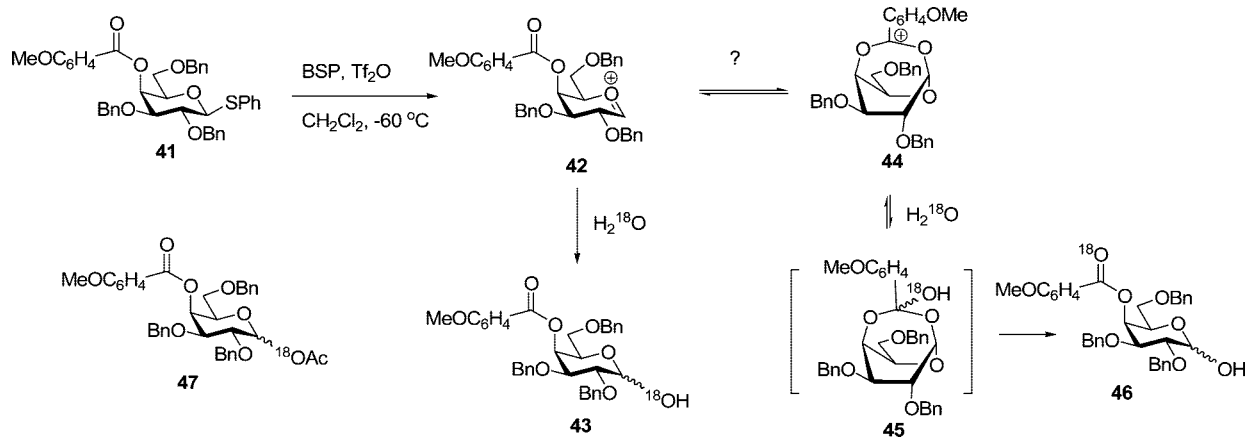
Our results unambiguously establish that neighboring group participation by axial esters at O3 is possible in the course of glycopyranosylation reactions, in general agreement with the work of Weisner and others.[18] On the other hand, no evidence was found in support of neighboring group participation by an equatorial O3 ester, by axial or equatorial O4 esters, or by esters at O6. In the case of axial O4 esters, for which the strongest case had been made in the literature, an isotopic labeling probe also failed to find evidence in support of a bridging intermediate. We conclude that participation by esters at these positions is

(39) Lemieux, R. U.; Hindsgaul, O. *Carbohydr. Res.* **1980**, *82*, 195–206.

(40) The structure of this compound is based on the examination of ^{1}H NMR data, which display $^3J_{1,2}$, $^3J_{2,3}$, and $^3J_{3,4}$ coupling constants of 4.0, 10.0, and 2.4 Hz, consistent with a $B_{3,O}$ conformation for the pyranose ring. The mass spectrum does not display a molecular ion, but has [M−phthalic anhydride]$^+$ (10%).

(41) A Chemical Abstracts search revealed 22 ten-membered diolides derived from phthalic anhydride, thereby indicating the accessibility of this structural class.

SCHEME 7. An Isotopic Labeling Probe



unlikely and that alternative explanations must be found for any stereochemical effects arising from the presence of esters at these positions.[42]

The elimination of neighboring group participation from consideration, particularly for the O3 equatorial, O4 axial, and O6 esters, ultimately requires the formulation of alternative hypotheses for the interesting stereochemical effects sometimes observed in the presence of these groups.[43,44] Remote protecting groups and/or substituents have long been known to influence the outcome of a variety of different reaction types,[45] as exemplified in glycopyranosylation by the influence of 4,6-*O*-alkylidene and silylene acetals, and have been variously attributed to conformational, inductive, stereoelectronic, and other effects.[13a,46] It is unlikely that one single effect will be found to be responsible for the effects of all remote esters in glycosylation reactions, but this remains to be determined by further investigation.

Experimental Section

General Procedure for Preparation of Boc-Protected Alcohols. To a solution of substrate (2.0 mmol) in CH_2Cl_2 (30 mL) were added Boc_2O (1.75 g, 8.0 mmol), Et_3N (362 μL, 2.6 mmol), and DMAP (24.4 mg, 0.2 mmol) followed by stirring at room temperature overnight. The mixture was washed with saturated $NaHCO_3$ and brine, dried, and concentrated. Chromatographic purification (eluent EtOAc/hexanes = 1/5) afforded the Boc protected donors.

General Procedure for Thioglycoside Activation by the BSP Method. The donor (0.1 mmol), BSP (0.12 mmol), TTBP (0.15 mmol), and activated 4 Å powdered molecular sieves (100 mg) were dissolved in dry CH_2Cl_2 (0.1 M) and stirred at −60 °C under N_2 atmosphere for 10 min, and then freshly distilled Tf_2O (0.15 mmol) was added. The reaction mixture was stirred at −60 °C for 1 h before quenching with saturated aqueous $NaHCO_3$. After extraction with CH_2Cl_2 (3 × 5 mL), the combined organic phase was washed with brine, dried, and concentrated. The crude reaction mixture was purified by chromatography on silica gel.

General Procedure for Thioglycoside Activation by the NIS Method. The donor (0.1 mmol), NIS (0.15 mmol), and activated 4 Å powdered molecular sieves (100 mg) were dissolved in dry CH_2Cl_2 (0.1 M) at room temperature and then stirred at −40 °C for 10 min before TMSOTf (0.01 mmol) was added dropwise at −40 °C. The reaction mixture was stirred at −40 °C for 1 h before quenching with $Na_2S_2O_3$ (20%) and extraction with CH_2Cl_2 (3 × 5 mL). The combined organic phase were washed with brine, dried, and concentrated. The crude reaction mixture was purified by chromatography on silica gel.

General Procedure for Glycosylation Reactions by the BSP/TTBP Method. The donor (0.1 mmol), BSP (0.12 mmol), TTBP (0.15 mmol), and activated 4 Å powdered molecular sieves (100 mg) were dissolved in dry CH_2Cl_2 (0.1 M) and stirred at −60 °C under N_2 atmosphere for 10 min, before redistilled Tf_2O (0.15 mmol) was added dropwise. After 10 min, the acceptor (0.15 mmol) was added and stirring maintained at −60 °C for 2 h. The reaction mixture was then allowed to warm to room temperature before it was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic phase was washed with brine, dried, and concentrated. The crude reaction mixture was purified by chromatography on silica gel.

General Procedure for Glycosylation Reactions by the NIS/AgOTf Method. A solution of donor (0.05 M), acceptor (1.5 equiv), and 3 Å molecular sieves in dry CH_2Cl_2 was stirred at room temperature for 0.5 h under argon before it was cooled to 0 °C. NIS (1 equiv) was then added followed by AgOTf or TMSOTf (0.3 equiv), and the resulting mixture was stirred for 30 min before it was filtered. The filtrate was washed by 20% $Na_2S_2O_3$ solution and brine. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was dried and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5−10/1) to afford the glycosylation products.

Ethyl 3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyloxycarbonyl-1-thio-β-D-glucopyranoside (9). Compound **9** was formed from 3,4,6-tri-*O*-benzyl-β-D-thioglucopyranoside and Boc_2O by the general procedure in 78% yield as a colorless oil: $[\alpha]_D$ −0.8° (*c*, 1.2); ^1H

(42) Our conclusions largely parallel those of Woerpel in his recent investigation of the transannular participation of 4-thioethers in the reactions of cyclic tetrahydropyranyl oxocarbenium ions: Beaver, M. G.; Billings, S. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2082–2086.

(43) We consider the effect of the O4 equatorial esters to be satisfactorily explained by their effect on the equilibrium between the covalent glycosyl donors and the various ion pairs implicated in glycosylation, as discussed by van Boeckel.[15]

(44) An anonymous reviewer has offered the insightful suggestion that the effect of esters at O4 may be explained by their influence on the conformation about the C5−C6 bond, thereby affecting the proximity of the O6 group to the ring oxygen.

(45) (a) Barton, D. H. R.; McCapra, F.; May, P. J.; Thudium, F. *J. Chem. Soc.* **1960**, 1297–1311. (b) Magnus, N.; Magnus, P. *Tetrahedron Lett.* **1997**, *38*, 3491–3494. (c) Cieplak, A. S. *Chem. Rev.* **1999**, *99*, 1265–1336.

(46) (a) Fraser-Reid, B.; Wu, Z. C.; Andrews, W.; Skowronski, E. *J. Am. Chem. Soc.* **1991**, *113*, 1434–1435. (b) Imamura, A.; Ando, H.; Korogi, S.; Tanabe, G.; Muraoka, O.; Ishida, H.; Kiso, M. *Tetrahedron Lett.* **2003**, *44*, 6725–6728. (c) Jensen, H. H.; Nordstrom, M.; Bols, M. *J. Am. Chem. Soc.* **2004**, *126*, 9205–9213. (d) McDonnell, C.; López, O; Murphy, P. V.; Fernández Bolaños, J. G.; Hazell, R. G.; Bols, M. *J. Am. Chem. Soc.* **2004**, *126*, 12374–12385. (e) Pedersen, C. M.; Nordstrom, L. U.; Bols, M. *J. Am. Chem. Soc.* **2007**, *129*, 9222–9235. (f) Jensen, H. H.; Pedersen, C. M.; Bols, M. *Chem. Eur, J.* **2007**, *13*, 7576–7581. (g) Okada, Y.; Mukae, T.; Okajimia, K.; Taira, M.; Fujita, M.; Yamada, H. *Org. Lett.* **2007**, *8*, 1573–1576. (h) Okada, Y.; Nagata, O.; Taira, M.; Yamada, H. *Org. Lett.* **2007**, *9*, 2755–2758. (i) Jensen, H. H.; Bols, M. *Acc. Chem. Res.* **2006**, *39*, 259–265.

NMR δ 1.27 (t, J = 7.5 Hz, 3H), 1.49 (s, 9H), 2.72−2.76 (m, 2H), 3.48−3.51 (m, 1H), 3.67 (t, J = 9.0 Hz, 1H), 3.69−3.73 (m, 2H), 3.75 (dd, J = 2.0, 11.0 Hz, 1H), 4.40 (d, J = 10.0 Hz, 1H), 4.55 (d, J = 12.5 Hz, 1H), 4.56 (d, J = 11.0 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.78−4.82 (m, 4H), 7.16−7.29 (m, 15H); ^{13}C NMR δ 14.9, 23.9, 27.8 (3C), 68.9, 73.5, 75.0, 75.2, 75.4, 77.7, 79.5, 82.8, 83.5, 84.4, 127.6−128.5 (15C), 137.9, 138.2 (2C), 152.4; ESI HRMS calcd for $C_{34}H_{42}O_7SNa$ [M + Na]$^+$ 617.2544, found 617.2542.

3,4,6-Tri-*O*-benzyl-1,2-*O*-carbonyl-α-D-glucopyranose (10). Compound (**10**) was formed from compound (**9**) and NIS by the general procedure in 75% yield as a white solid: mp 60.1−61.2 °C; $[\alpha]_D$ +4.8° (*c*, 0.5) [lit.[47] mp 60−61 °C; $[\alpha]_D^{23}$ +4.9° (*c*, 4.8, $CHCl_3$)]; ^{1}H NMR δ 3.65−3.72 (m, 2H), 3.80−3.86 (m, 2H), 3.94 (t, J = 4.0 Hz, 1H), 4.43 (d, J = 11.5 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.59−4.71 (m, 4H), 6.07 (d, J = 6.5 Hz, 1H), 7.17−7.30 (m, 15H); ^{13}C NMR δ 68.4, 71.8, 72.7, 73.2, 73.3, 73.5, 75.9, 77.3, 97.4, 127.9−128.7 (15C), 136.9, 137.4, 137.6, 152.5; IR 1812 cm^{-1}.

Phenyl 2-*O*-*tert*-Butoxycarbonyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (11). Compound **11** was formed from 3,4,6-tri-*O*-benzyl-α-D-thiomannopyranoside and Boc_2O by the general procedure in 75% yield as a colorless oil: $[\alpha]_D$ = 98.0° (*c*, 0.3); ^{1}H NMR δ 1.47 (s, 9H), 3.74 (dd, J = 10.5, 2.0 Hz, 1H), 3.84 (dd, J = 10.5, 5.0 Hz, 1H), 3.92−3.97 (m, 2H), 4.34−4.37 (m, 1H), 4.47 (d, J = 12.0 Hz, 1H), 4.52 (d, J = 10.5 Hz, 1H), 4.61 (d, J = 11.0 Hz, 1H), 4.65 (d, J = 11.5 Hz, 1H), 4.76 (d, J = 11.0 Hz, 1H), 4.90 (d, J = 11.0 Hz, 1H), 5.37 (t, J = 2.5 Hz, 1H), 5.61 (d, J = 1.5 Hz, 1H), 7.19−7.38 (m, 18H), 7.49−7.51 (m, 2H); ^{13}C NMR δ 27.8, 69.0, 71.9, 72.5, 73.0, 73.4, 74.7, 75.3, 78.6, 82.7, 86.1, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.3, 128.37, 128.40, 129.0, 131.9, 133.8, 137.8, 138.3, 138.4, 153.1; IR 1097, 1277, 1740 cm^{-1}; ESI HRMS calcd for $C_{38}H_{42}O_7SNa$ [M + Na]$^+$ 665.2544, found 665.2548.

3,4,6-Tri-*O*-benzyl-1,2-*O*-carbonyl-α-D-mannopyranose (12). Compound **12** was formed from **11** and BSP by the general procedure in 74% yield as a colorless oil: $[\alpha]_D$ = −1.5° (*c*, 0.7); ^{1}H NMR δ 3.56−3.57 (m, 2H), 3.82−3.85 (m, 2H), 3.91 (t, J = 7.5 Hz, 1H), 4.50−4.53 (m, 3H), 4.73−4.79 (m, 4H), 5.79 (d, J = 5.0 Hz, 1H), 7,19−7.21 (m, 2H), 7.26−7.38 (m, 13H); ^{13}C NMR δ 69.4, 73.0 (2C), 73.6, 74.7, 75.3, 75.9, 76.8, 96.4, 127.8, 127.9, 128.0, 128.1, 128.2, 128.46, 128.50, 128.7, 137.2, 137.6, 137.7, 153.0; IR 1027, 1111, 1453, 1823 cm^{-1}; ESI HRMS calcd for $C_{28}H_{28}O_7Na$ [M + Na]$^+$ 499.1728, found 499.1724.

Phenyl 2,4,6-Tri-*O*-benzyl-1-thio-β-D-allopyranoside (14). To a stirred solution of **13**[48] (0.3 g, 0.55 mmol) in CH_2Cl_2 (5 mL) was added Dess−Martin periodinane (0.28 g, 0.66 mmol) followed by stirring at room temperature for 2 h. The reaction mixture was then diluted with CH_2Cl_2 (10 mL) and washed with saturated $NaHCO_3$ and brine. The organic layer was separated and concentrated and the residue was dissolved in THF (10 mL) before L-Selectride (1.1 mL, 1.1 mmol) was added at −78 °C. The reaction mixture was stirred at −78 °C for 20 min and then quenched with water, diluted with CH_2Cl_2 (10 mL), and washed with saturated $NaHCO_3$ and brine. The organic layer was dried and concentrated and purified by column chromatography (eluent EtOAc/hexanes = 1/4) to give **14** (0.14 g, 47%) as a colorless oil: $[\alpha]_D$ = 5.0° (*c*, 0.2); ^{1}H NMR δ 2.47 (s, 1H), 3.33 (dd, J = 12.2, 3.6 Hz, 1H), 3.53 (dd, J = 12.2, 3.4 Hz, 1H), 3.68−3.72 (m, 1H), 3.79 (dd, J = 13.5, 2.1 Hz, 1H), 3.94−3.98 (m, 1H), 4.33 (t, J = 3.5 Hz, 1H), 4.48−4.54 (m, 2H), 4.58−4.72 (m, 4H), 5.08 (d, J = 12.2 Hz, 1H), 7.22−7.37 (m, 18H), 7.56−7.58 (m, 2H); ^{13}C NMR δ 66.3, 69.2, 71.4, 72.3, 73.4, 74.0, 74.5, 76.4, 83.4, 127.3, 127.5, 127.7, 128.0, 128.1, 128.2, 128.3, 128.48, 128.53, 128.8, 132.0, 133.8, 137.4, 137.6, 138.4; IR 1066, 1283, 1454 cm^{-1}; ESI HRMS calcd for $C_{33}H_{34}O_5SNa$ [M + Na]$^+$ 565.2020, found 565.2009.

Phenyl 3-*O*-*tert*-Butoxycarbonyl-2,4,6-tri-*O*-benzyl-1-thio-β-D-allopyranoside (15). Compound **15** was formed from **14** and Boc_2O by the general procedure in 91% yield as a colorless oil: $[\alpha]_D$ = 12.3° (*c*, 0.13); ^{1}H NMR δ 1.42 (s, 9H), 3.38 (dd, J = 10.0, 3.0 Hz, 1H), 3.61 (dd, J = 10.0, 3.0 Hz, 1H), 3.71 (dd, J = 11.0, 4.0 Hz, 1H), 3.78 (dd, J = 10.5, 2.0 Hz, 1H), 3.93−3.96 (m, 1H), 4.40 (d, J = 10.5 Hz, 1H), 4.49−4.52 (m, 2H), 4.58−4.61 (m, 1H), 4.67−4.71 (m, 2H), 5.06 (d, J = 6.5 Hz, 1H), 5.75 (t, J = 3.0 Hz, 1H), 7.21−7.39 (m, 18H), 7.56−7.58 (m, 2H); ^{13}C NMR δ 27.7, 68.9, 69.0, 71.3, 71.8, 72.8, 73.4, 75.0, 75.4, 82.2, 83.6, 127.4, 127.5, 127.6, 127.9, 128.1, 128.2, 128.3, 128.7, 132.3, 133.3, 137.3, 137.5, 138.5, 153.5; IR 1091, 1280, 1369, 1454, 1740 cm^{-1}; ESI HRMS calcd for $C_{38}H_{42}O_7SNa$ [M + Na]$^+$ 665.2544, found 665.2539.

2,4,6-Tri-*O*-benzyl-1,3-*O*-carbonyl-α-D-allose (16). Compound **16** was formed from **15** and BSP by the general procedure in 70% yield as a colorless oil: $[\alpha]_D$ = 80.0° (*c*, 0.01); ^{1}H NMR δ 3.53 (t, J = 2.0 Hz, 1H), 3.69−3.78 (m, 4H), 3.82−3.85 (m, 1H), 4.45 (dd, J = 12.0, 6.0 Hz, 1H), 4.56−4.67 (m, 4H), 4.86 (d, J = 2.0 Hz, 1H), 5.57 (t, J = 2.5 Hz, 1H), 7.22−7.34 (m, 15H); ^{13}C NMR δ 67.1, 67.0, 69.5, 71.0, 71.6, 71.9, 73.6, 74.7, 96.2, 127.4, 127.8, 128.00, 128.02, 128.3, 128.51, 128.56, 128.63, 128.8, 129.3, 129.5, 136.1, 136.8, 137.5, 146.6; IR 1124, 1180, 1454, 1766 cm^{-1}; ESI HRMS calcd for $C_{28}H_{28}O_7Na$ [M + Na]$^+$ 499.1728, found 499.1711.

Cyclohexyl 3-*O*-*tert*-Butoxycarbonyl-2,4,6-tri-*O*-benzyl-α-D-allopyranoside (17α) and Cyclohexyl 3-*O*-*tert*-Butoxycarbonyl-2,4,6-tri-*O*-benzyl-β-D-allopyranoside (17β). These glycosides were prepared by the general procedure with a combined yield of 61% (α:β = 1:11.2). Chromatographic separation on silica gel eluting with EtOAc/hexanes (1/6) enabled pure samples of the two anomers to be obtained. **17α**: colorless oil; yield 5%; $[\alpha]_D$ = 22.9° (*c*, 0.2); ^{1}H NMR δ 1.22−1.25 (m, 4H), 1.38−1.51 (m, 2H), 1.41 (s, 9H), 1.76−1.79 (m, 2H), 1.83−1.86 (m, 2H), 3.47−3.48 (m, 1H), 3.58−3.65 (m, 3H), 3.76−3.78 (m, 1H), 4.16 (d, J = 10.0 Hz, 1H), 4.34 (d, J = 12.0 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.55−4.61 (m, 2H), 4.68−4.73 (m, 2H), 4.97 (d, J = 4.0 Hz, 1H), 5.67 (s, 1H), 7.20−7.34 (m, 15H); ^{13}C NMR δ 23.8, 24.1, 25.8, 27.8, 31.3, 33.3, 65.7, 68.6 (2C), 70.5, 71.4, 72.6, 72.7, 73.6, 75.6, 81.7, 94.8, 127.66, 127.73, 127.9, 128.1, 128.2, 128.3, 128.4, 137.7, 138.0, 138.1, 154.2; IR 1100, 1284, 1367, 1454, 1735 cm^{-1}; ESI HRMS calcd for $C_{38}H_{48}O_8Na$ [M + Na]$^+$ 655.3242, found 655.3237. **17β**: colorless oil; yield 56%; $[\alpha]_D$ = 5.1° (*c*, 0.2); ^{1}H NMR δ 1.21−1.33 (m, 4H), 1.44 (s, 9H), 1.48−1.55 (m, 2H), 1.74−1.76 (m, 2H), 1.92−1.94 (m, 1H), 2.00−2.02 (m, 1H), 3.31 (dd, J = 8.0, 3.0 Hz, 1H), 3.52 (dd, J = 10.0, 3.0 Hz, 1H), 3.61−3.64 (m, 1H), 3.67−3.77 (m, 2H), 3.91 (dd, J = 10.0, 3.0 Hz, 1H), 4.35 (d, J = 11.0 Hz, 1H), 4.52−4.62 (m, 2H), 4.66−4.73 (m, 2H), 4.79 (d, J = 12.0 Hz, 1H), 4.86 (d, J = 7.5 Hz, 1H), 5.63 (t, J = 2.5 Hz, 1H), 7.22−7.38 (m, 15H); ^{13}C NMR δ 24.2, 24.5, 25.6, 27.8, 31.6, 33.4, 67.7, 68.8, 71.2, 72.2, 73.3, 73.7, 75.8, 75.9, 76.4, 82.1, 95.6, 127.4, 127.5, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 138.0, 138.5, 138.8, 153.4; IR 1097, 1280, 1741 cm^{-1}; ESI HRMS calcd for $C_{38}H_{48}O_8Na$ [M + Na]$^+$ 655.3242, found 655.3237.

3-*O*-*tert*-Butoxycarbonyl-2,4,6-tri-*O*-benzyl-D-allose (18). The donor **15** (17.8 mg, 0.028 mmol), NIS (7.5 mg, 0.033 mmol), and activated 4 Å powdered molecular sieves (80 mg) were dissolved in dried CH_2Cl_2 (0.1 M) at room temperature and then stirred at −60 °C for 10 min. Tf_2O (6.9 μL, 0.042 mmol) was then added dropwise at −40 °C. The reaction mixture was stirred at −40 °C for 1 h before it was quenched with $Na_2S_2O_3$ (20%). The reaction mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic phase was washed with brine, dried, and concentrated. Chromatographic purification (eluent EtOAc/hexanes = 1/4 then 1/2) then gave **18** (8.4 mg, 55%) as a colorless oil: $[\alpha]_D$ = 21.8° (*c*, 0.1); ^{1}H NMR major isomer δ 1.45 (s, 9H), 3.10 (d, J = 5.5

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Hz, 1H), 3.28 (dd, J = 8.0, 3.5 Hz, 1H), 3.59 (dd, J = 10.0, 3.0 Hz, 1H), 3.65 (dd, J = 10.5, 4.5 Hz, 1H), 3.71−3.73 (m, 1H), 3.96−3.99 (m, 1H), 4.36 (d, J = 10.5 Hz, 1H), 4.50 (d, J = 12.0 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.67 (d, J = 13.5 Hz, 1H), 4.76 (d, J = 12.0 Hz, 1H), 5.07 (dd, J = 7.5, 5.5 Hz, 1H), 5.71 (t, J = 3.0 Hz, 1H), 7.20−7.24 (m, 2H), 7.25−7.38 (m, 13H); minor isomer δ 1.43 (s, 9H), 3.53 (t, J = 2.0 Hz, 1H), 3.55−3.56 (m, 1H), 3.68−3.70 (m, 1H), 3.75−3.76 (m, 2H), 3.78−3.80 (m, 1H), 3.81−3.85 (m, 1H), 4.44−4.48 (m, 2H), 4.85−4.87 (m, 1H), 5.23 (dd, J = 9.5, 3.0 Hz, 1H), 5.58 (t, J = 2.0 Hz, 1H), 7.20−7.24 (m, 2H), 7.25−7.38 (m, 13H); ^{13}C NMR major isomer δ 27.7, 65.7, 68.9, 69.3, 71.5, 71.8, 72.8, 72.9, 73.6, 82.2, 94.4, 127.69, 127.72, 127.80, 127.85, 127.88, 127.95, 128.02, 128.04, 128.2, 128.3, 128.40, 128.43, 128.53, 128.55, 128.6, 128.8, 137.4, 137.7, 138.0, 153.5; minor isomer δ 27.6, 67.0, 67.1, 68.2, 69.5, 70.5, 71.0, 71.6, 82.9, 92.0, 95.5, 136.2, 136.8, 137.2, 137.5, 138.1, 146.6, 152.7; IR 1096, 1280, 1369, 1454, 1740 cm^{-1}; ESI HRMS calcd for $C_{32}H_{38}O_8Na$ [M + Na]$^+$ 573.2459, found 573.2448.

Phenyl 3-*O*-*tert*-Butoxycarbonyl-2-*O*-benzyl-4,6*O*-benzylidene-1-thio-α-D-mannopyranoside (21). This compound was formed by the general procedure in 98% yield as a white foam: $[\alpha]_D$ = 102.3° (*c*, 0.13); ^{1}H NMR δ 1.48 (s, 9H), 3.88 (t, J = 10.0 Hz, 1H), 4.23 (dd, J = 10.0, 5.0 Hz, 1H), 4.28−4.33 (m, 2H), 4.38−4.42 (m, 1H), 4.67 (s, 2H), 5.10 (dd, J = 10.0, 3.5 Hz, 1H), 5.52 (s, 1H), 5.59 (s, 1H), 7.28−7.37 (m, 11H), 7.41−7.43 (m, 2H), 7.50−7.51 (m, 2H); ^{13}C NMR δ 27.8, 65.3, 68.5, 73.3, 76.3, 77.6, 82.9, 86.8, 101.8, 126.3, 127.7, 128.0, 128.2, 128.5, 129.0, 129.2, 131.7, 133.7, 137.3, 137.4, 152.7; IR 1099, 1253, 1282, 1742 cm^{-1}; ESI HRMS calcd for $C_{31}H_{34}O_7SNa$ [M + Na]$^+$ 573.1918, found 573.1914.

Phenyl 3-*O*-*tert*-Butoxycarbonyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside *S*-Oxide (22). To a solution of **21** (137.9 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (77%, 56.1 mg) at −78 °C, after which the reaction mixture was warmed with stirring to −30 °C over 40 min before it was quenched with saturated $NaHCO_3$, washed with brine, and dried. After concentration, the crude reaction mixture was purified by column chromatography (eluent EtOAc/hexanes = 1/4) to give the sulfoxide (**22**) (127.8 mg, 90%) as a white foam: $[\alpha]_D$ = −61.5° (*c*, 0.2); ^{1}H NMR δ 1.48 (s, 9H), 3.73 (t, J = 9.5 Hz, 1H), 4.15−4.23 (m, 2H), 4.30 (t, J = 9.5 Hz, 1H), 4.50 (d, J = 10.5 Hz, 2H), 4.55 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 3.0 Hz, 1H), 5.43 (dd, J = 10.0, 3.5 Hz, 1H), 5.57 (s, 1H), 7.24−7.31 (m, 5H), 7.35−7.49 (m, 3H), 7.47−7.49 (m, 2H), 7.55−7.56 (m, 3H), 7.63−7.64 (m, 2H); ^{13}C NMR δ 27.7, 68.1, 68.9, 72.7, 73.0, 73.8, 75.5, 82.9, 97.6, 101.8, 124.6, 126.2, 128.1, 128.2, 128.4, 129.1, 129.5, 131.8, 136.9, 137.0, 141.4, 152.4; IR 1115, 1280, 1743 cm^{-1}; ESI HRMS calcd for $C_{31}H_{34}O_8SNa$ [M + Na]$^+$ 589.1867, found 589.1866.

Cyclohexyl 3-*O*-*tert*-Butoxycarbonyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (23). Compound **23** was formed from **21** and BSP or from sulfoxide **22** and Tf_2O in 69% (from **21**) or 75% (from **22**) yield as a colorless oil: $[\alpha]_D$ = 35.3° (*c*, 1.0); ^{1}H NMR δ 1.20−1.27 (m, 5H), 1.36−1.41 (m, 1H), 1.48 (s, 9H), 1.66−1.72 (m, 3H), 1.81−1.83 (m, 1H), 3.52−3.53 (m, 1H), 3.84 (t, J = 10.0 Hz, 1H), 3.94−3.98 (m, 2H), 4.19 (t, J = 10.0 Hz, 1H), 4.23−4.25 (m, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.76 (d, J = 12.0 Hz, 1H), 4.89 (s, 1H), 5.14 (dd, J = 10.5, 3.5 Hz, 1H), 5.57 (s, 1H), 7.28−7.42 (m, 7H), 7.46−7.50 (m, 2H), 7.56−7.59 (m, 1H); ^{13}C NMR δ 23.8, 24.0, 25.6, 27.8, 31.1, 33.2, 64.0, 68.8, 73.5, 73.9, 75.3, 82.5, 97.1, 101.6, 126.2, 127.6, 127.9, 128.1, 128.5, 128.8, 128.9, 129.4, 131.4, 133.6, 136.6, 137.4, 137.8, 152.9; IR υ 1070, 1274, 1451, 1720 cm^{-1}; ESI HRMS calcd for $C_{31}H_{40}O_8Na$ [M + Na]$^+$ 563.2616, found 563.2611.

Ethyl 4-*O*-*tert*-Butoxycarbonyl-2,3,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (24). Compound **24** was formed from 2,3,6-tri-*O*-benzyl-β-D-thiogalactopyranoside and Boc_2O by the general procedure in 90% yield as a colorless oil: $[\alpha]_D$ = 16.8° (*c*, 1.7); ^{1}H NMR δ 1.31 (t, J = 7.4 Hz, 3H), 1.49 (s, 9H), 2.70−2.80 (m, 2H), 5.57−3.72 (m, 5H), 4.46 (d, J = 9.3 Hz, 1H), 4.53 (s, 2H), 4.55 (d, J = 8.3 Hz, 1H), 4.79−4.84 (m, 3H), 5.43 (dd, J = 3.1, 0.7 Hz, 1H), 7.26−7.38 (m, 15H); ^{13}C NMR δ 15.1, 24.9, 27.7, 68.5, 69.7, 71.9, 73.9, 75.8, 75.9, 76.8, 81.2, 82.0, 85.3, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 137.8, 138.0, 138.3, 153.5; IR 1104, 1280, 1741 cm^{-1}; ESI HRMS calcd for $C_{34}H_{42}O_7SNa$ [M + Na]$^+$ 617.2544, found 617.2532.

4-*O*-*tert*-Butoxycarbonyl-2,3,6-*O*-tribenzyl-α-D-galactopyranosyl Acetate (25α) and 4-*O*-*tert*-Butoxycarbonyl-2,3,6-*O*-benzyl-β-D-galactopyranosyl Acetate (25β). To a solution of compound **24** (32.4 mg, 0.054 mmol), BSP (13.7 mg, 0.065 mmol), and 4Å powdered molecular sieves (100 mg) in Et_2O (1.0 mL) was added Tf_2O (11.0 μL, 0.065 mmol) at −60 °C under N_2. The reaction mixture was stirred at −60 °C for 30 min and then quenched with saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic phase washed with brine, dried, and concentrated. The residue was dissolved in Ac_2O (1.0 mL), pyridine (1.0 mL) was added, and the mixture was stirred at room temperature overnight. After removal of the solvent, the residue was dissolved in CH_2Cl_2 (5 mL) and washed with saturated $NaHCO_3$, and the organic phase was washed with brine and dried. After concentration the crude reaction mixture was purified by column chromatography (eluent EtOAc/hexanes = 1/4) to give **25** (29.7 mg, 92%, α:β = 1:7.1) as a colorless oil. **25α**: yield 10%; $[\alpha]_D$ = 14.7° (*c*, 0.2); ^{1}H NMR δ 1.47 (s, 9H), 2.10 (s, 3H), 3.51−3.59 (m, 2H), 3.90−3.97 (m, 2H), 4.16 (t, J = 7.5 Hz, 1H), 4.50 (s, 2H), 4.59 (d, J = 11.0 Hz, 1H), 4.66−4.73 (m, 2H), 4.81 (d, J = 10.5 Hz, 1H), 5.49 (s, 1H), 6.35 (d, J = 3.0 Hz, 1H),7.20−7.38 (m, 15H); ^{13}C NMR δ 21.0, 27.7, 68.2, 70.2, 70.3, 72.1, 73.6, 73.9, 74.7, 76.0, 82.3, 90.6, 127.5, 127.6, 127.8, 127.9, 128.1, 128.3, 128.4, 137.7, 138.1, 138.2, 153.2, 169.3; IR 1108, 1279, 1369, 1454, 1744 cm^{-1}; ESI HRMS calcd for $C_{34}H_{40}O_9Na$ [M + Na]$^+$ 615.2565, found 615.2559. **25β**: yield 71%; $[\alpha]_D$ = 11.2° (c, 0.2); ^{1}H NMR δ 1.48 (s, 9H), 2.04 (s, 3H), 3.56 (t, J = 8.5 Hz, 1H), 3.65 (t, J = 10.0 Hz, 2H), 3.79 (t, J = 8.5 Hz, 1H), 3.85 (t, J = 5.0 Hz, 1H), 4.51 (s, 2H), 4.55 (d, J = 11.5 Hz, 1H), 4.69 (d, J = 11.0 Hz, 1H), 4.82−4.86 (m, 2H), 5.44 (s, 1H), 5.59 (d, J = 8.0 Hz, 1H), 7.26−7.35 (m, 15H); ^{13}C NMR δ 21.0, 27.8, 67.7, 69.1, 72.1, 72.8, 73.9, 75.5, 77.6, 79.8, 82.3, 94.0, 127.69, 127.72, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 137.6, 137.8, 138.4, 153.3, 169.3; IR 1105, 1280, 1368, 1454, 1743 cm^{-1}; ESI HRMS calcd for $C_{34}H_{40}O_9Na$ [M + Na]$^+$ 615.2565, found 615.2560.

Cyclohexyl 4-*O*-*tert*-Butoxycarbonyl-2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (26α) and Cyclohexyl 4-*O*-*tert*-Butoxycarbonyl-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (26β). These glycosides were obtained by the general procedure with a combined yield of 88% (α:β = 1:3.9). When the reaction was conducted in diethyl ether as solvent, the yield was 62% and the α:β ratio 1:1.3. **26α**: colorless oil; yield 18%; $[\alpha]_D$ = 88.6° (*c*, 0.2); ^{1}H NMR δ 1.15−1.26 (m, 3H), 1.31−1.38 (m, 1H), 1.44−1.53 (m, 11H), 1.71−1.78 (m, 2H), 1.86−1.91 (m, 2H), 3.54−3.59 (m, 3H), 3.82 (dd, J = 10.0, 3.5 Hz, 1H), 3.98 (dd, J = 9.5, 3.0 Hz, 1H), 4.21 (t, J = 6.0 Hz, 1H), 4.49−4.54 (m, 2H), 4.59−4.65 (m, 2H), 4.78−4.82 (m, 2H), 4.99 (d, J = 3.5 Hz, 1H), 5.42 (s, 1H), 7.20−7.38 (m, 15H); ^{13}C NMR δ 24.2, 24.5, 25.6, 27.8, 31.6, 33.4, 67.7, 68.8, 71.2, 72.2, 73.3, 73.7, 75.8, 75.9, 76.4, 82.1, 95.7, 127.4, 127.5, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.0, 138.6, 138.8, 153.4; IR 1102, 1279, 1453, 1741 cm^{-1}; ESI HRMS calcd for $C_{38}H_{48}O_8Na$ [M + Na]$^+$ 655.3242, found 655.3245. **26β**: colorless oil; yield 70%; $[\alpha]_D$ = 17.4° (*c*, 0.4); ^{1}H NMR δ 1.22−1.30 (m, 4H), 1.40−1.53 (m, 11H), 1.74−1.76 (m, 2H), 1.90−1.97 (m, 2H), 3.55 (dd, J = 9.5, 3.5 Hz, 1H), 3.60−3.69 (m, 5H), 4.48 (d, J = 8.0 Hz, 1H), 4.54 (d, J = 2.5 Hz, 2H), 4.57 (d, J = 11.0 Hz, 1H), 4.72 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 11.5 Hz, 1H), 4.92 (d, J = 10.5 Hz, 1H), 5.34 (d, J = 3.5 Hz, 1H), 7.26−7.39 (m, 15H); ^{13}C NMR δ 24.0, 24.1, 25.7, 27.8, 31.9, 33.7, 68.7, 69.8, 72.2, 73.9, 75.3, 76.8, 77.7, 79.0, 79.6, 81.9, 102.0, 127.5, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 138.0, 138.2, 138.9, 153.6; IR 1080,

1280, 1454, 1741 cm^{-1}; ESI HRMS calcd for $C_{38}H_{48}O_8Na$ [M + Na]$^+$ 655.3242, found 655.3231.

Phenyl 2,3,6-Tri-*O*-benzyl-4-*O*-*tert*-butyloxycarbonyl-1-thio-α-D-mannopyranoside (27). Compound **27** was formed from 2,3,6-tri-*O*-benzyl-α-D-thiomannopyranoside and Boc_2O by the general procedure in 76% yield as a colorless oil: $[\alpha]_D$ +49.0° (*c*, 1.45); ^1H NMR δ 1.47 (s, 9H), 3.68 (dd, J = 3.0, 11.0 Hz, 1H), 3.73 (dd, J = 6.0, 11.0 Hz, 1H), 3.85 (dd, J = 3.0, 9.5 Hz, 1H), 4.00 (d, J = 2.0, 2.5 Hz, 1H), 4.43−4.47 (m, 1H), 4.53 (d, J = 10.0 Hz, 1H), 4.54 (s, 2H), 4.57 (d, J = 10.0 Hz, 1H), 4.64 (d, J = 12.0 Hz, 1H), 4.70 (d, J = 12.0 Hz, 1H), 5.24 (t, J = 10.0 Hz, 1H), 5.57 (d, J = 1.5 Hz, 1H), 7.19−7.39 (m, 13H), 7.49 (d, J = 7.5 Hz, 2H); ^{13}C NMR δ 27.8 (3C), 69.6, 71.2, 71.8, 71.9, 72.1, 73.4, 75.8, 77.5, 82.5, 85.8, 127.4−128.5 (18C), 129.0, 131.9, 134.0, 137.8, 138.0, 138.3, 152.7; ESI HRMS calcd for $C_{38}H_{42}O_7$ SNa [M + Na]$^+$ 665.2544, found 665.2540.

Isopropyl 2,3,6-Tri-*O*-benzyl-4-*O*-*tert*-butyloxycarbonyl-α-D-mannopyranoside (28α) and Isopropyl 2,3,6-Tri-*O*-benzyl-4-*O*-*tert*-butyloxycarbonyl-*β*-D-mannopyranoside (28*β*). 28α: $[\alpha]_D$ +21.6° (*c*, 0.3); ^1H NMR δ 1.06 (d, J = 6.0 Hz, 3H), 1.16 (d, J = 6.0 Hz, 3H), 1.42 (s, 9H), 3.60−3.68 (m, 2H), 3.73 (t, J = 2.5 Hz, 1H), 3.88−3.98 (m, 3H), 4.54 (dd, J = 4.5, 12.0 Hz, 2H), 4.60 (dd, J = 1.5, 12.0 Hz, 2H), 4.67 (d, J = 12.0 Hz, 1H), 4.78 (d, J = 12.5 Hz, 1H), 4.93 (d, J = 1.5 Hz, 1H), 5.16 (t, J = 10.0 Hz, 1H), 7.20−7.40 (m, 15H); ^{13}C NMR δ 21.2, 23.2, 27.7, 69.0, 69.8, 70.2, 72.0, 72.2, 72.8, 73.4, 74.6, 77.7, 82.2, 95.9, 127.3−128.3 (15C), 138.4 (3C), 152.7; IR 1746 cm^{-1}; ESI HRMS calcd for $C_{35}H_{44}O_8Na$ [M + Na]$^+$ 615.2929, found 615.2930. **28*β***: $[\alpha]_D$ −54.3° (*c*, 0.3); ^1H NMR δ 1.16 (d, J = 6.0 Hz, 3H), 1.30 (d, J = 6.0 Hz, 3H), 1.46 (s, 9H), 3.46 (dd, J = 3.0, 9.5 Hz, 1H), 3.56−3.59 (m, 1H), 3.67−3.74 (m, 2H), 3.84 (d, J = 3.0 Hz, 1H), 4.01 (m, 1H), 4.35 (d, J = 12.0 Hz, 1H), 4.44 (d, J = 12.0 Hz, 1H), 4.47 (br. s, 1H), 4.54 (d, J = 12.0, 1H), 4.61 (d, J = 12.0 Hz, 1H), 4.88 (d, J = 12.5 Hz, 1H), 4.96 (d, J = 12.5 Hz, 1H), 5.04 (t, J = 10.0 Hz, 1H), 7.20−7.49 (m, 15H); ^{13}C NMR δ 21.8, 23.6, 27.7 (3C), 70.4, 71.3, 71.5, 72.2, 73.6, 73.7, 74.3, 76.4, 78.1, 79.8, 82.4, 99.4, 126.7−128.9 (15C), 138.1, 138.3, 138.6, 152.7; ESI HRMS calcd for $C_{35}H_{44}O_8Na$ [M + Na]$^+$ 615.2929, found 615.2925.

***N*-(2′,3′,6′-Tri-*O*-benzyl-4′-*O*-*tert*-butyloxycarbonyl-α-D-mannopyranosyl)succinimide (29).** $[\alpha]_D^{23}$ +62.0° (*c*, 0.5); ^1H NMR δ 1.49 (s, 9H), 2.48−2.56 (m, 2H), 3.67 (dd, J = 5.0, 11.0 Hz, 1H), 3.78 (dd, J = 6.5, 11.0 Hz, 1H), 3.96 (t, J = 2.5 Hz, 1H), 4.36 (d, J = 12.0 Hz, 1H), 4.43 (t, J = 5.0 Hz, 1H), 4.48 (d, J = 12.0 Hz, 1H), 4.54 (s, 2H), 4.71 (d, J = 12.0 Hz, 1H), 4.75 (d, J = 12.0 Hz, 1H), 4.78 (dd, J = 3.0, 8.0 Hz, 1H), 4.94 (dd, J = 3.0, 5.0 Hz, 1H), 5.77 (d, J = 9.0 Hz, 1H), 7.18−7.40 (m, 17H); ^{13}C NMR δ 27.8, 28.0, 68.2, 71.6, 71.8, 72.1, 72.3, 73.4, 74.4, 75.3, 83.0, 127.6−128.4 (15C), 137.8, 138.1 (2C), 152.6, 176.7 (2C); IR 1711, 1720, 1739 cm^{-1}; ESI HRMS calcd for $C_{36}H_{41}O_9NNa$ [M + Na]$^+$ 654.2674, found 654.2669.

***p*-Tolyl 4-*O*-*tert*-Butoxycarbonyl-3-azido-2,3,6-trideoxy-1-thio-α-L-lyxopyranoside (30).** Compound **30** was formed by the general procedure in 98% yield as a colorless oil: $[\alpha]_D$ = −287.1° (*c*, 0.24); ^1H NMR δ 1.21 (d, J = 6.0 Hz, 3H), 1.53 (s, 9H), 2.12 (td, J = 13.5, 5.5 Hz, 1H), 2.33 (s, 3H), 2.36 (dd, J = 13.5, 5.5 Hz, 1H), 3.89−3.95 (m, 1H), 4.34−4.37 (m, 1H), 4.43 (t, J = 9.5 Hz, 1H), 5.49 (d, J = 5.5 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H); ^{13}C NMR δ 17.2, 21.1, 27.7, 36.0, 58.3, 66.7, 78.7, 83.2, 83.4, 129.9, 130.3, 132.1, 137.8, 152.7; IR 1097, 1274, 1750, 2104 cm^{-1}; ESI HRMS calcd for $C_{18}H_{25}N_3O_4SNa$ [M + Na]$^+$ 402.1458, found 402.1456.

4-*O*-*tert*-Butoxycarbonyl-3-azido-2,3,6-trideoxy-1-L-lyxopyranosyl Acetate (31). Application of the BSP protocol to compound **30** gave 4-*O*-*tert*-butoxycarbonyl-3-azido-2,3,6-trideoxy-1-α-L-lyxopyranose in 30% yield as a colorless oil with ^1H NMR δ 1.21 (d, J = 6.0 Hz, 3H), 1.52 (s, 9H), 1.79 (td, J = 13.0, 3.5 Hz, 1H), 2.05 (dd, J = 13.0, 5.0 Hz, 1H), 3.75−3.78 (m, 1H), 3.86−3.91 (m, 1H), 4.42 (t, J = 10.0 Hz, 1H), 5.12 (d, J = 3.0 Hz, 1H); ^{13}C NMR δ 17.4, 27.7, 34.8, 57.2, 66.5, 76.4, 91.4, 96.1, 152.6; IR 1132, 1255, 1749, 2103 cm^{-1}. Acetylation of this pyranose according to the procedure used for **25** gave the title compound **31** in 73% combined yield (α:β = 1:1.7) as a colorless oil: $[\alpha]_D$ = −21.9° (*c*, 0.2); ^1H NMR (400 MHz) major isomer (β) δ 1.27 (d, J = 6.0 Hz, 3H), 1.51 (s, 9H), 1.73−1.82 (m, 1H), 2.12 (s, 3H), 2.23−2.28 (m, 1H), 3.57−3.67 (m, 2H), 4.43 (t, J = 9.6 Hz, 1H), 5.72 (dd, J = 9.6, 1.6 Hz, 1H); minor isomer (α) δ 1.22 (d, J = 6.0 Hz, 3H), 1.57 (s, 9H), 1.85−1.89 (m, 1H), 2.09 (s, 3H), 2.15−2.20 (m, 1H), 3.86−3.93 (m, 2H), 4.46 (t, J = 10.0 Hz, 1H), 6.15 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz) δ major isomer (β) 17.5, 21.2, 27.9, 35.2, 59.6, 71.9, 77.4, 83.5, 91.5, 152.8, 169.2; minor isomer (α) δ 17.6, 31.1, 34.3, 57.4, 68.5, 78.1, 83.7, 90.6, 152.1, 169.1; IR 1259, 1752, 2101 cm^{-1}; ESI HRMS calcd for $C_{13}H_{21}N_3O_6Na$ [M + Na]$^+$ 338.1328, found 338.1322.

Cyclohexyl 4-*O*-*tert*-Butoxycarbonyl-3-azido-2,3,6-trideoxy-L-lyxopyranoside (32). Compound **32** was formed from **30** by the general procedure in 46% yield (α:β = 1:3.7) as a colorless oil: $[\alpha]_D$ = −3.3° (*c*, 0.15); ^1H NMR major isomer δ 1.26 (d, J = 6.5 Hz, 3H), 1.22−1.32 (m, 4H), 1.34−1.41 (m, 2H), 1.51 (s, 9H), 1.69−1.77 (m, 3H), 1.85−1.94 (m, 2H), 2.17−2.21 (m, 1H), 3.41−3.46 (m, 1H), 3.52−3.57 (m, 1H), 3.61−3.66 (m, 1H), 4.36−4.42 (m, 1H), 4.62 (dd, J = 9.5, 2.0 Hz, 1H); minor isomer δ 1.19 (d, J = 6.5 Hz, 3H), 1.55 (s, 9H), 2.09−2.13 (m, 1H), 3.88−3.97 (m, 2H), 3.52−3.57 (m, 1H), 5.00 (d, J = 3.0 Hz, 1H); ^{13}C NMR δ 17.5, 24.0, 24.2, 25.6, 27.7, 31.8, 33.5, 36.8, 59.9, 70.6, 76.4, 77.3, 78.0, 78.1, 83.2, 96.1, 97.2, 152.6; IR 1130, 1749, 2103 cm^{-1}; ESI HRMS calcd for $C_{17}H_{29}N_3O_5Na$ [M + Na]$^+$ 378.2000, found 378.2005.

Phenyl 2,3,4-Tri-*O*-benzyl-6-*O*-*tert*-butyloxycarbonyl-1-thio-*β*-D-glucopyranoside (33). Compound **33** was formed from 2,3,4-tri-*O*-benzyl-β-D-thioglucopyranoside and Boc_2O by the general procedure in 80% yield as a colorless oil: $[\alpha]_D$ +2.7° (*c*, 0.8); ^1H NMR δ 1.53 (s, 9H), 3.55 (t, J = 9.0 Hz, 1H), 3.60−3.64 (m, 2H), 3.74−3.79 (m, 1H), 4.33 (dd, J = 5.0 Hz, 1H), 4.39 (dd, J = 1.5, 10.0 Hz, 1H), 4.63 (d, J = 10.5 Hz, 1H), 4.70 (d, J = 10.0 Hz, 1H), 4.77 (d, J = 10.0 Hz, 1H), 4.89 (d, J = 10.0 Hz, 1H), 4.90 (d, J = 10.0 Hz, 1H), 4.94−4.99 (m, 2H), 7.26−7.50 (m, 18H), 7.61 (d, J = 7.5, 1H); ^{13}C NMR δ 27.9, 65.7, 75.3, 75.6, 75.9, 77.0, 77.7, 80.9, 82.3, 86.7, 87.7, 127.6−129.0 (18C), 132.0 (2C), 133.8, 137.7, 138.0, 138.3, 153.5; ESI HRMS calcd for $C_{38}H_{42}O_7SNa$ [M + Na]$^+$ 665.2544, found 665.2539.

Isopropyl 2,3,4-Tri-*O*-benzyl-6-*O*-*tert*-butyloxycarbonyl-α-D-glucopyranoside (34α) and Isopropyl 2,3,4-Tri-*O*-benzyl-6-*O*-*tert*-butyloxycarbonyl-*β*-D-glucopyranoside (34*β*). Compounds **34α** and **34*β*** were formed from **33** by the general NIS procedure in 80% yield (α:β = 1:1, dichloromethane) or 74% yield (α:β = 1.5:1, diethyl ether) as a colorless oily mixture: ESI HRMS calcd for $C_{35}H_{44}O_8Na$ [M + Na]$^+$ 615.2929, found 615.2922. **34α**: ^1H NMR δ 1.18 (d, J = 6.0 Hz, 3H), 1.22 (d, J = 6.0 Hz, 3H), 1.46 (s, 9H), 3.54−3.57 (m, 1H), 3.87 (m, J = 6.0 Hz, 1H), 3.91 (m, 1H), 4.01 (t, J = 9.0 Hz, 1H), 4.19 (dd, J = 2.0, 12.0 Hz, 1H), 4.28 (m, 1H), 4.33 (dd, J = 4.5, 11.5 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 4.69 (d, J = 10.5 Hz, 1H), 4.76 (d, J = 12.0 Hz, 1H), 4.82 (d, J = 10.5 Hz, 1H), 4.84 (d, J = 3.0 Hz, 1H), 4.88 (d, J = 11.0 Hz, 1H), 5.02 (d, J = 11.0 Hz, 1H), 7.21−7.29 (m, 15H); ^{13}C NMR δ 21.4, 23.4, 28.0 (3 C), 65.7, 68.9, 69.5, 73.4, 75.5, 78.0, 80.1, 82.2, 82.3, 95.0, 127.8−128.7 (15 C), 138.2, 138.4, 139.1, 153.7. **34*β***:^1H NMR δ 1.23 (d, J = 6.0 Hz, 3H), 1.28 (d, J = 6.0 Hz, 3H), 1.47 (s, 9H), 3.42 (t, J = 8.0 Hz, 1H), 3.46−3.54 (m, 3H), 3.64 (t, J = 9.0 Hz, 1H), 4.00 (m, 1H), 4.27 (m, 1H), 4.46 (d, J = 8.0 Hz), 4.56 (d, J = 10.5 Hz, 1H), 4.64 (d, J = 12.0 Hz, 1H), 4.78 (d, J = 10.5 Hz, 1H), 4.85 (d, J = 10.5 Hz, 1H), 4.93 (d, J = 12.5 Hz, 1H), 4.96 (d, J = 12.0 Hz, 1H), 7.21−7.29 (m, 15H); ^{13}C NMR δ 22.4, 23.9, 28.0 (3 C), 66.0, 72.6, 73.1, 75.1, 75.3, 75.9, 78.1, 82.4, 85.0, 102.3, 127.8−128.7 (15 C), 138.0, 138.7, 138.8, 153.6.

Di-(2,3,4-tri-*O*-benzyl-D-glucopyranoside)-(1,6),(6,1)-dicarbonate (35). $[\alpha]_D$ +88.7° (*c*, 0.3); ^1H NMR (C_6D_6) δ 3.12 (t, J = 9.0 Hz, 2H), 3.53 (ddd, J = 1.2, 4.0, 9.0 Hz, 2H), 4.14 (t, J = 9.0

Hz, 2H), 4.22 (t, J = 9.0 Hz, 2H), 4.33 (t, J = 9.0 Hz, 2H), 4.48 (dd, J = 12.0, 20.0 Hz, 4H), 4.61 (d, J = 11.5 Hz, 2H), 4.68 (d, J = 11.0 Hz, 2H), 4.81 (d, J = 11.5 Hz, 2H), 4.93 (d, J = 11.5 Hz, 2H), 6.21 (d, J = 3.0 Hz, 2H), 7.14−7.37 (m, 30H); ^{13}C NMR δ 67.0, 72.5, 72.6, 75.4, 77.3, 78.7, 81.7, 93.6, 127.6−128.4 (30C), 138.0, 138.1, 139.1, 153.0; IR 1768 cm^{-1}; ESI HRMS calcd for $C_{56}H_{56}O_{14}Na$ [M + Na]$^+$ 975.3568, found 975.3582.

Ethyl 3,4,6-Tri-*O*-benzyl-2-*O*-(2-carboxybenzoyl)-1-thio-β-D-glucopyranoside (36). To a solution of ethyl 3,4,6-tri-*O*-benzyl-β-D-thioglucopyranoside (460 mg, 0.92 mmol) in dry DMF (10.0 mL) was added NaH (60%, 73.6 mg, 1.84 mmol) at room temperature. The reaction mixture was stirred for 10 min, and then phthalic anhydride (272.5 mg, 1.84 mmol) was added and the mixture was stirred at room temperature overnight. After removal of the solvent, the residue was taken up in 5% HCl (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with brine and dried. After concentration, the residue was purified by column chromatography (eluent EtOAc/hexanes = 1/1) to give the compound **36** in 37% yield as a colorless oil: $[\alpha]_D$ = 15.9° (*c*, 4.3); ^{1}H NMR (400 MHz) δ 1.27 (t, J = 7.6 Hz, 3H), 2.70−2.80 (m, 2H), 3.59 (dd, J = 9.6, 2.4 Hz, 1H), 3.70−3.80 (m, 3H), 3.88 (t, J = 8.8 Hz, 1H), 4.55−4.64 (m, 4H), 4.76−4.82 (m, 3H), 5.29−5.36 (m, 1H), 7.15−7.35 (m, 15H), 7.51−7.57 (m, 2H), 7.76−7.84 (m, 2H), 9.22 (br. s, 1H); ^{13}C NMR (100 MHz) δ 15.1, 24.0, 69.1, 73.5, 73.7, 75.3, 75.3, 78.1, 79.7, 83.4, 84.2, 127.82, 127.84, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.61, 128.64, 129.5, 130.2, 130.7, 131.4, 132.0, 132.7, 138.2, 138.3, 138.4, 165.7, 172.6; IR 1070, 1266, 1454, 1704, 1729 cm^{-1}; ESI HRMS calcd for $C_{37}H_{38}O_8SNa$ [M + Na]$^+$ 665.2185, found 665.2186.

3,4,6-Tri-*O*-benzyl-1,2-*O*-phthalidylidene-α-D-glucopyranose (37) (endo and exo mixture). Compound **37** was formed from **36** and NIS by the general procedure in 79% yield as a colorless oil: $[\alpha]_D$ = 48.2° (*c*, 0.6); ^{1}H NMR (400 MHz) major isomer δ 3.70−3.81 (m, 3H), 4.02 (t, J = 3.6 Hz, 1H), 4.10−4.14 (m, 1H), 4.40 (d, J = 11.6 Hz, 1H), 4.51−4.63 (m, 4H), 4.71−4.76 (m, 2H), 6.09−6.11 (m, 1H), 7.18−7.20 (m, 2H), 7.26−7.34 (m, 13H), 7.61−7.67 (m, 3H), 7.86−7.88 (m, 1H); minor isomer δ 3.85 (dd, J = 10.8, 3.2 Hz, 1H), 4.19−4.23 (m, 1H), 4.43−4.46 (m, 1H), 4.81−4.87 (m, 2H), 7.21−7.23 (m, 2H), 7.57 (d, J = 7.2 Hz, 1H), 7.75 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz) major isomer δ 69.4, 71.4, 72.2, 73.2, 73.8, 74.8, 75.8, 80.4, 82.8, 98.9, 123.6, 125.5, 127.94, 127.99, 128.03, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.8, 132.4, 135.0, 137.3, 137.8, 138.2, 140.9, 165.7; minor isomer δ 68.4, 72.1, 73.5, 74.9, 75.0, 101.7, 123.1, 125.4, 127.89, 132.2, 135.1, 138.0, 138.4, 142.6; IR 891, 1061, 1108, 1283, 1453, 1783 cm^{-1}; ESI HRMS calcd for $C_{35}H_{32}O_8Na$ [M + Na]$^+$ 603.1995, found 603.1994.

Phenyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2-carboxybenzoyl)-1-thio-β-D-galactopyranoside (38). Compound **38** was formed from phenyl 2,3,6-tri-*O*-benzyl-β-D-thiogalactopyranoside and phthalic anhydride by the same procedure as compound **36** in 48% yield as a colorless oil: $[\alpha]_D$ = 16.2° (*c*, 1.1); ^{1}H NMR (400 MHz) δ 3.67−3.77 (m, 4H), 3.84 (t, J = 6.0 Hz, 1H), 4.49−4.56 (m, 3H), 4.71−4.79 (m, 3H), 4.82 (d, J = 11.2 Hz, 1H), 5.85 (d, J = 1.6 Hz, 1H), 7.15−7.38 (m, 18H), 7.49−7.58 (m, 4H), 7.68 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz) δ 68.7, 69.0, 72.3, 73.9, 76.0, 76.6, 77.0, 81.5, 88.0, 127.6, 127.98, 128.02, 128.1, 128.3, 128.5, 128.61, 128.63, 128.7, 129.1, 129.67, 129.74, 130.4, 131.3, 131.5, 131.8, 132.0, 132.1, 133.9, 137.8, 138.1, 138.4, 166.9, 171.1; IR 1067, 1102, 1280, 1728 cm^{-1}; ESI HRMS calcd for $C_{41}H_{38}O_8SNa$ [M + Na]$^+$ 713.2185, found 713.2191.

3,4,6-Tri-*O*-benzyl-1,4-*O*-phthaloyl-α-D-galactopyranose (40). Compound **40** was formed from **38** and NIS by the general procedure in 41% yield as a colorless oil: $[\alpha]_D$ = 80.0° (*c*, 0.3);^{1}H NMR (400 MHz) δ 3.19−3.27 (m, 2H), 3.71 (dd, J = 10.0, 2.4 Hz, 1H), 3.79−3.81 (m, 1H), 4.13 (d, J = 12.0 Hz, 1H), 4.32 (dd, J = 10.0 4.4 Hz, 1H), 4.35 (d, J = 12.0 Hz, 1H), 4.68 (d, J = 12.4 Hz, 1H), 4.81 (d, J = 10.4 Hz, 1H), 4.87 (d, J = 10.4 Hz, 1H), 4.93 (d, J = 13.2 Hz, 1H), 5.85 (d, J = 2.4 Hz, 1H), 6.58 (d, J = 4.0 Hz, 1H), 6.97−6.99 (m, 3H), 7.03−7.04 (m, 2H), 7.09 (d, J = 8.0 Hz, 1H), 7.20−7.31 (m, 6H), 7.39−7.43 (m, 5H), 7.51−7.54 (m, 1H), 8.30 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 Hz) δ 67.0, 68.6, 69.9, 70.9, 73.8, 74.9, 75.2, 75.7, 77.4, 93.1, 125.7, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.47, 128.51, 128.8, 129.6, 132.0, 133.0, 135.9, 137.4, 138.3, 138.6, 164.0, 167.1; IR 1067, 1105, 1261, 1724 cm^{-1}; ESI HRMS calcd for $C_{27}H_{28}O_5SNa$ [M − $C_8H_4O_3$ (phthalic anhydride) + Na]$^+$ 455.1834, found 455.1855.

Phenyl 2,3,6-Tri-*O*-benzyl-4-*O*-(4-methoxybenzoyl)-1-thio-β-D-galactopyranoside (41). To a solution of 4-methoxybenzoic acid (102.1 mg, 0.76 mmol) in dry CH_3CN (5 mL) was added 1,1′-carbonyldiimidazole (129.2 mg, 0.80 mmol) under N_2. The reaction mixture was stirred at 60−70 °C for 2 h and then cooled to room temperature before phenyl 2,3,6-tri-*O*-benzyl-β-D-thiogalactopyranoside (196.6 mg, 0.36 mmol) in CH_3CN (4 mL) was added dropwise followed by DBU (121.0 μL, 0.76 mmol). The reaction mixture was stirred at 60 °C overnight, cooled, poured into saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with brine, dried, and concentrated. The residue was purified by column chromatography (eluent EtOAc/hexanes = 1/4) to give the **41** in 93% yield as a colorless oil: $[\alpha]_D$ = 22.5° (*c*, 2.2); ^{1}H NMR δ 3.60 (dd, J = 10.0, 6.5 Hz, 1H), 3.69−3.78 (m, 3H), 3.89 (d, J = 7.5 Hz, 1H), 3.91 (s, 3H), 4.46−4.55 (m, 3H), 4.72 (d, J = 9.5 Hz, 1H), 4.76 (s, 2H), 4.87 (d, J = 11.5 Hz, 1H), 5.88 (d, J = 3.0 Hz, 1H), 6.93−6.96 (m, 2H), 7.24−7.41 (m, 18H), 7.65−7.67 (m, 2H), 7.96−7.99 (m, 2H); ^{13}C NMR δ 55.7, 67.3, 68.8, 72.0, 74.0, 75.9, 76.6, 76.9, 81.7, 87.4, 113.9, 122.4, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 128.56, 128.58, 128.6, 129.1, 132.3, 133.1, 133.3, 137.90, 137.92, 138.5, 163.8, 165.6; IR 1102, 1257, 1454, 1605, 1716 cm^{-1}; ESI HRMS calcd for $C_{41}H_{40}O_7SNa$ [M + Na]$^+$ 699.2392, found 699.2397.

2,3,6-Tri-*O*-benzyl-4-*O*-(4-methoxybenzoyl)-D-[1-$^{16/18}$O]-galactopyranosyl Acetate (47). To a solution of donor **41** (35.7 mg, 0.053 mmol), BSP (13.2 mg, 0.063 mmol), and activated 4 Å molecular sieves (100 mg) in dichloromethane (1 mL) was added Tf_2O (13.3 μL, 0.079 mmol) at −60 °C. The mixture was stirred at −60 °C for 2 h before $H_2{}^{18}O$ (95% ^{18}O, 50 μL) was added. The reaction mixture was filtered, dried, and concentrated. The residue was purified by column chromatography (eluent EtOAc/hexanes = 1/2) to give 2,3,6-tri-*O*-benzyl-4-*O*-(4-methoxybenzoyl)-α-D-[1-$^{16/18}$O]-galactopyranose (**43**) (38.1 mg, 82%) as a colorless oil: from the ^{13}C NMR, ^{16}O/^{18}O is around 4:1; $[\alpha]_D$ = 98.3° (*c*, 1.0); ^{1}H NMR δ 3.49 (d, J = 6.5 Hz, 2H), 3.89 (s, 3H), 3.95 (dd, J = 10.0, 3.5 Hz, 1H), 4.13 (dd, J = 10.0, 3.5 Hz, 1H), 4.36 (d, J = 12.5 Hz, 1H), 4.44 (d, J = 11.5 Hz, 1H), 4.56 (d, J = 11.5 Hz, 1H), 4.60 (t, J = 6.0 Hz, 1H), 4.68−4.71 (m, 2H), 4.86 (d, J = 11.5 Hz, 1H), 5.35 (d, J = 3.5 Hz, 1H), 5.83 (d, J = 2.5 Hz, 1H), 6.90 (d, J = 8.5 Hz, 2H), 7.19−7.27 (m, 13H), 7.32 (d, J = 6.5 Hz, 2H), 7.96 (d, J = 9.0 Hz, 2H); ^{13}C NMR δ 55.7, 68.7, 68.9, 69.2, 71.8, 73.5, 73.8, 75.0, 76.6, 94.1(94.050, 94.072), 113.8, 122.7, 127.6, 127.69, 127.73, 127.9, 128.06, 128.08, 128.4, 128.45, 128.50, 132.2, 138.1, 138.5, 138.7, 163.7, 165.7; IR 1100, 1257, 1454, 1605, 1717 cm^{-1}. This pyranose was dissolved in Ac_2O, pyridine was added, and the mixture was stirred at 80 °C overnight. After removal of the solvents, the residue was dissolved in CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, and dried. After concentration, the crude reaction mixture was purified by column chromatography (eluent EtOAc/hexanes = 1/4) to give compound **47** (90%, α:β = 4.1:1) as a colorless oil: from the ^{13}C NMR, the ^{16}O/^{18}O ratio is ∼1:1; mass spectrometry also displayed a 1:1 ^{16}O/^{18}O ratio for the sodiated molecular ion; $[\alpha]_D$ = 40.9° (*c*, 0.5); ^{1}H NMR major isomer δ 3.48−3.56 (m, 3H), 3.88 (s, 3H), 3.98−4.03 (m, 2H), 4.25 (t, J = 6.5 Hz, 1H), 4.39−4.41 (m, 1H), 4.46−4.50 (m, 1H), 4.54−4.59 (m, 1H), 4.66−4.70 (m, 3H), 4.87 (d, J = 11.5 Hz, 2H), 5.91 (s, 1H), 6.41 (d, J = 3.0 Hz, 1H), 6.92 (d, J = 9.0 Hz, 2H), 7.21−7.33 (m, 15H), 7.97 (d, J = 9.0 Hz, 2H); minor isomer δ 3.60−3.62 (m, 1H), 3.89 (s, 3H), 3.95 (t, J = 6.0 Hz, 1 Hz), 4.81 (d, J = 12.0 Hz, 1H), 5.67 (d, J = 7.5 Hz, 1H), 5.86 (d, J =

2.5 Hz, 1H), 6.94 (d, $J = 9.0$ Hz, 2H), 7.21−7.36 (m, 15H), 8.05 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR major isomer δ 21.4, 55.7, 67.8, 68.5, 70.8, 72.0, 74.0, 74.6, 76.4, 80.1, 91.0 (high resolution: 90.991, 91.020), 113.9, 127.9, 128.0, 128.07, 128.14, 128.18, 128.23, 128.3, 128.4, 128.52, 128.55, 128.59, 132.2, 137.8, 138.2, 138.3, 163.79, 165.6, 169.7 (169.739, 169.752); minor isomer δ 21.2, 66.8, 67.9, 72.1, 73.5, 73.86, 73.90, 75.6, 77.8, 94.3 (94.243, 94.267), 122.4, 127.7, 132.3, 137.7, 137.9, 138.5, 163.83, 156.5, 169.4; IR υ 1100, 1257, 1605, 1717, 1750 cm^{-1}; ESI HRMS calcd for $C_{37}H_{38}O_9Na$ $[M + Na]^+$ 649.2414, found 649.2404; ESI HRMS calcd for $C_{37}H_{38}O_8{}^{18}ONa$ $[M + Na]^+$ 651.2456, found 651.2465.

Phenyl 2,3,6-Tri-*O*-benzyl-4-*O*-(4-methoxybenzoyl)-1-thio-α,*β*-D-galactopyranoside (41α and 41*β*). To a solution of phenyl 2,3,6-tri-*O*-benzyl-4-*O*-(4-methoxybenzoyl)-D-[1-$^{16/18}$*O*]-galactopyranosyl acetate (**47**) (13.9 mg, 0.022 mmol) in CH_3CN (1 mL) were added thiophenol (34 μL, 0.033 mmol) and $BF_3 \cdot Et_2O$ (9.3 μL, 0.07 mmol) under N_2 at room temperature. The reaction mixture was stirred at room temperature overnight then was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phase was washed with brine and dried. Concentration and purification of the residue by column chromatography (eluent EtOAc/hexanes = 1/4) gave **41** (α:β = 2.2:1) in 97% yield as a colorless oil: $[\alpha]_D = 58.4°$ (*c*, 0.5); ^{1}H NMR major isomer δ 3.48−3.53 (m, 2H), 3.67−3.76 (m, 1H), 3.80 (s, 3H), 3.87 (dd, $J = 10.0$, 3.0 Hz, 1H), 4.15 (dd, $J = 10.0$, 5.05 Hz, 1H), 4.38−4.43 (m, 1H), 4.56 (d, $J = 11.5$ Hz, 1H), 4.66−4.80 (m, 3H), 4.78 (d, $J = 12.0$ Hz, 1H), 5.65 (d, $J = 5.5$ Hz, 1H), 5.79 (d, $J = 3.0$ Hz, 1H), 6.83−6.86 (m, 2H), 7.13−7.27 (m, 16H), 7.29−7.31 (m, 2H), 7.46−7.48 (m, 2H), 7.90−7.91 (m, 2H); minor isomer δ 3.67−3.76 (m, 1H), 3.83 (s, 3H), 4.38−4.43 (m, 2H), 4.44- 4.46 (m, 1H), 4.62 (d, $J = 9.0$ Hz, 1H), 4.77 (d, $J = 11.0$ Hz, 1H), 5.79 (d, $J = 3.0$ Hz, 1H), 6.83−6.86 (m, 2H), 7.13−7.27 (m, 16H), 7.29−7.31 (m, 2H), 7.56−7.58 (m, 2H), 7.87−7.89 (m, 2H); ^{13}C NMR major isomer δ 55.70, 68.5, 69.0, 69.3, 72.2, 73.1, 73.7, 75.5, 76.8, 88.1, 113.9, 122.5, 127.5, 127.7, 127.8, 127.9, 127.95, 127.97, 128.06, 128.12, 128.2, 128.3, 128.4, 128.46, 128.52, 128.56, 128.61, 129.10, 132.2, 132.5, 133.0, 138.2, 138.3, 163.7, 165.6; minor isomer δ 55.73, 67.2, 68.8, 71.9, 73.9, 75.9, 76.6, 77.0, 81.7, 87.4, 122.4, 129.1, 132.3, 133.2, 134.2, 137.8, 138.0, 138.5, 163.7, 165.6; IR 1101, 1256, 1605, 1716 cm^{-1}; ESI HRMS calcd for $C_{41}H_{40}O_7SNa$ $[M + Na]^+$ 699.2392, found 699.2372. Inspection by ^{13}C NMR spectroscopy revealed no isotopically shifted signal for the anomeric carbon. No evidence was found by mass spectrometry for the presence of ^{18}O.

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Supporting Information Available: General experimental methods and copies of spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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