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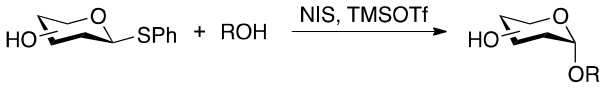

A simple, straightforward 1,2-*cis*-selective glycosidation method from an unprotected 1-thioglycoside is presented.

1,2-*cis* Alkyl Glycosides: Straightforward Glycosylation from Unprotected 1-Thioglycosyl Donors

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Abstract

A 1,2-*cis*-alkyl glycosidation protocol that makes use of unprotected phenyl 1-thioglycosyl donors is reported. Glycosylation of various functionalized alcohols was accomplished in moderate to high yield and selectivity to give the 1,2-*cis*-glycosides. In order to quickly develop optimum glycosylation conditions, an FIA (flow injection analysis)–ESI-TOF-MS method was developed that enabled rapid and quantitative evaluation of yield on small scale. This methodology, coupled with NMR spectroscopy, allowed for rapid evaluation of the overall reactions.

Introduction

As essential components in the cell membrane, carbohydrates and glycoconjugates serve many protective, stabilizing, organizational, barrier, and recognition functions.[1] The chemical synthesis of these glycoconjugates, including proteoglycans, glycolipids, and glycoproteins, is in great demand for biological studies of their functions as cell-wall components that are collectively termed the glycocalyx. Anomerically pure alkyl glycosides serving as fundamental building blocks are in demand to achieve the stereoselective synthesis of these cell-wall structures. Some

alkyl glycosides, such as propargyl[2] and allyl[3] glycosides are essential components in simple approaches for the construction of microarrays[4, 5] and glycodendrimers.[6]

Generally, 1,2-*trans*-alkyl glycosidation can be reliably achieved via neighboring-group participation of a C-2 acyl group on a glycosyl donor, while stereochemical control for 1,2-*cis*-alkyl glycosidation can be challenging.[7] The conventional Fischer glycosidation reaction, a straightforward way to afford short-chain, uncomplicated, thermodynamically favored 1,2-*cis*-alkyl glycosides, has been improved by using various acid catalysts,[8-10] microwave irradiation,[11] ultrasonication,[12] and ionic liquids.[13] Since free sugars have limited solubility in longer chain alcohols (acceptors), harsh conditions (e.g., high temperature, microwave, ultrasonication) are often required to push the reaction, which results in decomposition of the products,[8] formation of various side products, time-consuming separation processes, and low yields and poor stereoselectivities. Ether protecting groups, most often the benzyl group, are routinely used for protecting free hydroxyl groups in the synthesis of 1,2-*cis*-glycosides,[14] but benzyl deprotection by H_2/Pd will destroy a number of groups (alkene, alkyne, nitro, halogen) on functionalized alkyl glycosides.[15] The elegant intramolecular aglycon delivery (IAD) approach offers a stereospecific 1,2-*cis*-glycosidic syntheis, albeit from selectively protected intermediates.[16-19]

In principle, many of these issues can be circumvented through conversion of an unprotected glycosyl donor directly into the desired 1,2-*cis*-alkyl glycosides. Glycosylation by an unprotected sugar donor has several practical values:[20] the often tedious protection and deprotection process can be avoided;[21] unprotected donors possess higher reactivity compared to *O*-acyl-protected donors, and the better solubility of unprotected donors in short-chain alcohols (the acceptors) enables glycosylation at lower temperatures, which reduces the formation of by-products.

Mamidyala and Finn have reported glycosylation using unprotected alkynyl donors and $AuCl_3$ as an effective activator.[22, 23] Very recently, Nitz and co-workers reported glycosidation in relatively good yields using a protecting-group-free protocol with 1-*p*-toluenesulfonyl hydrazide and glycosyl chloride donors; however, anomeric selectivities were generally lacking.[24] Among the various classes of glycosyl donors,

phenyl 1-thioglycosyl compounds have been regarded as ideal choices for donor precursors (including precursors for light-induced glycosidation[21]) because they are stable, easily synthesized, and for the most part, crystalline.[25] Herein, we report a 1,2-*cis*-alkyl glycosidation protocol that makes use of unprotected phenyl 1-thioglycosyl donors.[21]

Results and discussion

A. Glycosidations

Phenyl 1-thio-β-D-galactopyranoside (**1a**)[26] and propargyl alcohol (**2a**) were selected as the unprotected glycosyl donor and acceptor–solvent, respectively, for the model glycosylation reaction (Table 1). Initially, the reaction was carried out between **1a**

Insert Table 1 here

and dry **2a** (40 equiv) under the activation of *N*-iodosuccinimide (NIS)/trimethylsilyl triflate (TMSOTf). The desired product was obtained in respectable yield and with high α stereoselectivity (Table 1, entry 1). TLC analysis of the crude product showed only the desired α,β anomers. Further experiments revealed other 1,2-*cis*-glycosidations that used the Lewis acids $BF_3{\cdot}OEt_2$[7] and TfOH[27] provided similar yields and stereoselectivities, while $H_2SO_4{\cdot}SiO_2$[9] gave a lower yield (a result also reported from another laboratory[28]) but higher stereoselectivity (compare entries 2−4). We surmise that the results may be due to the heterogeneity of the $H_2SO_4{\cdot}SiO_2$ catalyst. The bisulfate counterion would be trapped in the silica gel matrix, leading to the formation of a loosely solvent-separated ion pair (SSIP) between the bisulfate counterion and the oxocarbenium ion, suggesting a unimolecular (S_N1) favored transition state and better α selectivity due to the anomeric effect.[29-31] We also examined the activation by Lewis acids and *N*-bromosuccinimide (NBS). As anticipated, relatively lower yields and stereoselectivities were observed (entries 5 and 6), which could be attributed to the diminished electrophilic properties of the bromonium ion. Moreover, experimentation showed that glycosylation was most favored when the amount of alcohol was in the range of 40–60 equiv (entries 1–3 and 9 vs. entries 7–8 and 10). Experiments further

demonstrated neither TMSOTf nor NIS alone was able to trigger the glycosylation reaction (entries 11 and 12).

It is presumed that TMSOTf in excess alcoholic acceptor–solvent is hydrolyzing to trifluoromethanesulfonic acid (TfOH) and that the reagent provides a metered amount of acid. Varying amounts of TMSOTf were added to the reaction mixture of **1a** and **2a** as described in Table 1. When the amount of TMSOTf was increased to from 0.2 to 0.4 equiv, no improvement in yield or selectivity was observed; at 1.0 equiv, by-product formation became evident, and both yield and stereoselectivity were decreased to 52% and 5:1, respectively. Addition of 2.0 equiv of TMSOTf resulted in a series of by-products as observed on TLC.

B. Rapid high-throughput screening of reactions

In order to rapidly evaluate and identify optimum glycosylation conditions for a number of reactions, we adapted the concept of a high-throughput screening using mass spectrometry (MS) similar to that reported by Ito and co-workers, who employed MALDI-TOF-MS.[32, 33] In our reactions with small molecules, we used a coupled flow-injection system with ESI-TOF-MS (FIA–ESI-TOF-MS) that enabled quantitative evaluation of glycosylation yield with products of MW <500 amu. (For details, see Supplementary Information, section 1.) Furthermore, the method provided a more accurate estimation of yield in two ways: (1) An average value from a certain volume of sample (e.g., 2.5 μL with our flow-injection equipment) was evaluated rather than a tiny spot excited by the laser on MALDI. (2) Integration of the ion intensity peaks was used to calculate yield instead of the *m/z* peak height as in the MALDI method.[32, 33]

In order to provide an internal standard for the FIA–ESI-TOF-MS studies, propargyl α,β-D-galactopyranoside (**3a,** Scheme 1) was acetylated with Ac_2O-d_6 to

Insert Scheme 1 here

afford the per-deuterated glycosides; the α anomer (**4**) was separated out by column chromatography. While it is known that the ionizing properties of deuterated and nondeuterated glycosides are nearly identical.,[32] the fact was confirmed in this study specifically for these compounds. Details of the calibration work are provided in the

Supplementary Information, section 2. The FIA–ESI-TOF-MS responses were found essentially the same for either the ^{1}H- or ^{2}H-labeled compounds, thus facilitating a relatively uncomplicated rapid analysis of the reactions.

C. Optimization studies and scope of the reaction

Optimization studies were conducted as in the following paragraphs in which several solvents were examined. The conditions were those of Table 1, with variations. The effect of *N*,*N*-dimethylformamide (DMF) in the solvent on stereoselective α-glycosylation has been well documented,[34] and we anticipated that adding a catalytic amount of DMF might promote the formation of the 1,2-*cis*-glycosidic bond. After screening with added DMF, other solvents, including CH_2Cl_2, THF and Et_2O (0.2 equiv), were examined; however, no obvious improvement in yield or α selectivity was observed with any of these additives, and a further increase of the amount of solvent added (6 equiv) led to a general decrease in stereoselectivity and yield, which indicates that a neat alcohol environment is essential for optimum glycosylation under these conditions. Details of the above studies are provided in the Supplementary Information section, Table S2.

The reaction was performed on **1a** as in Table 1, entry 1, and the results were evaluated with different reaction times. Over a time course of 5 min to 2 h, essentially no changes in anomeric ratios of **3a** were observed. Yields, however, showed a trend of increasing with time up to 2 h as follows: 5 min, 67%, α/β 9.8:1; 30 min, 71%, α/β 9.8:1; 2 h, 75%, α/β 10:1. Reaction temperatures were also scrutinized. When NIS and TMSOTf were added at −30 °C, the solution turned maroon (black with propargyl alcohol, entry 1). When NIS and TMSOTf were added at −10–0 °C, the yield decreased slightly with a little faded maroon or black color obtained. But when NIS and TMSOTf were added at room temperature, the solution turned yellow, and a low yield (<30%) was obtained with most of the donor unreacted. The α/β selectivity remained essentially the same over these temperature ranges. For some alcohols so designated in Table 2 (i.e., those with higher mp's), a temperature range of −10–0 °C was selected (see Table 2, entries 2 and 5–8).

Insert Table 2 here.

With the appropriate conditions for 1,2-*cis*-alkyl glycosidation in hand, we investigated the scope of the reaction with several unprotected glycosyl donors and alcohols bearing various functional groups. (See Table 2.) The stereoselectivity of glycosylation with unprotected D-glucose, D-mannose and disaccharide donors and propargyl alcohol spanned from modest to high (Table 2, entries 1, 9−13). It is noteworthy that the major product from phenyl 1-thio-α-D-mannoside is the β (*cis*) anomer (Table 2, entry 10) that is formed. Glycosylation with various functionalized alcohols was accomplished without difficulty (Table 2, entries 2−8). A variety of groups on alcohols were tolerated to provide the corresponding 1,2-*cis*-substituted-alkyl glycosides. These results indicate the generality and applicability of the present glycosylation method.

A mechanistic explanation of the observed results from these glycosylations is no doubt complex, as numerous alcohol–substrate–Lewis acid reagent associations (including H-bonding interactions) are possible and difficult to sort out. We presume the role of NIS/TMSOTf follows that established for the activation of related systems.[35, 36] Perhaps noteworthy is the fact that we observed (Table 2, entry 13) that a 2-deoxy-1-thioglycoside (**1f**), an analog of **1a**, gives a significantly diminished α selectivity of only 1.7:1, possibly indicating a special role for the 2-OH group that might coordinate with the reagent alcohol and account for the generally higher *cis*-selectivities in the other examples. The role of such H-bonding in stereoselection in glycosylation has been addressed in numerous articles.[37-41] We, however, hasten to add that other factors, including a change in the anomeric effect, may also contribute to the observed change of the α:β ratio in the products.

D. Conclusions

In summary, a facile and general strategy for the direct construction of 1,2-*cis*-alkyl glycosides has been developed. Glycosylations between several unprotected phenyl 1-thioglycosyl donors and alcohols bearing various functional groups proceeds smoothly to give satisfying yields and 1,2-*cis* selectivity. Use of an FIA–ESI-TOF-MS/NMR protocol facilitated rapid and efficient optimization of conditions. We anticipate

that the synthetic procedures described herein will find application in a number of areas where enhanced 1,2-*cis* selectivity in glycosylated products is required.

Experimental Section

A. General methods.

All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Alcohols that were opened and stored for a period of time were pre-dried by Drierite® (anhyd calcium sulfate). Reagent grade dichloromethane (DCM), tetrahydrofuran (THF), ether (Et_2O), methanol (MeOH), *N*,*N*-dimethylformamide (DMF) and toluene were obtained from the Pure-Solv (Innovation Technologies) solvent system that uses alumina columns except for DMF, which was dried over a column of 5 Å molecular sieves. Pyridine was distilled over CaH_2 prior to use. All reactions were performed under anhydrous conditions unless otherwise noted. Reactions were monitored by thin-layer chomatography (TLC) on silica gel precoated aluminum plates. Zones were detected by UV irradiation using a 254 nm lamp and/or by heat/charring with *p*-anisaldehyde–sulfuric acid development reagent.[42] Column chomatography was performed on silica gel (40−63 μm). Optical rotation values were obtained at the sodium D line using a Perkin–Elmer 241 polarimeter. ^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded at room temperature with a Varian Inova 500 MHz instrument. Chemical shifts are reported in *δ*-units (ppm) relative to the residual ^{1}H $CDCl_3$ at *δ* 7.26 ppm and ^{13}C at *δ* 77.16 ppm. All two-dimensional experiments (gCOSY, gHSQC and gHMBC) were recorded on the same instrument using Varian protocols. Mass spectrometric analysis was performed on a QSTAR Elite quadrupole time-of-flight (QTOF) mass spectrometer with an ESI source.

B. General synthetic and analytical procedures.

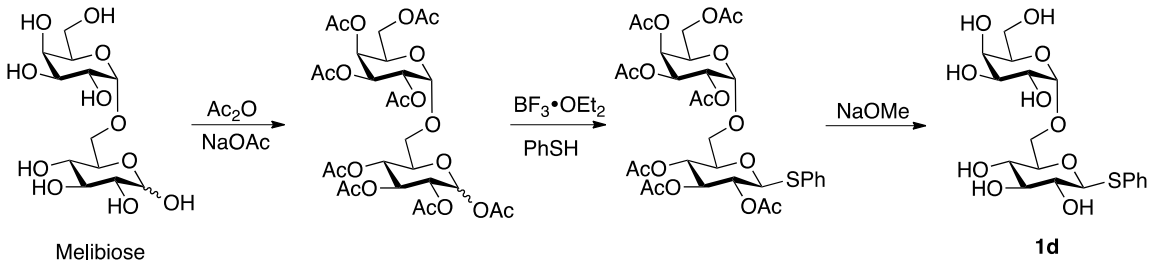
1. Synthesis of the phenyl thioglycoside donors 1a–1f.[26] The selected free sugar (5.00 g, 27.8 mmol for D-galactose, 1.0 g, 5.6 mmol for D-glucose and D-mannose, 1.0 g, 6.09 mmol for 2-deoxy-D-galactose, and 1.0 g, 2.9 mmol for a disaccharide) was suspended in a mixture of NaOAc (2.50 g, 30.5 mmol for D-galactose, 0.50 g, 6.1 mmol for the other monosaccharides) and Ac_2O (25 mL, 262.3 mmol for D-galactose, or 5.0 mL, 52.5 mmol for the other sugars), and the mixture was heated under an N_2

atmosphere at 70 °C. After 24 h, the yellow solution was cooled to room temperature, poured onto ice and quenched with satd aq $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The organic extract was washed successively with water and brine, dried over anhyd Na_2SO_4, and concentrated to afford the per-acetylated sugar as a solid that was used directly without further purification.

Thiophenol (3.60 mL, 35.2 mmol for the peracetylated D-galactose; amounts for the other sugars were adjusted correspondingly) was then added to a solution of per-acetylated sugar (10.6 g, 27.1 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C, and the mixture was stirred for 30 min. Then $BF_3{\cdot}Et_2O$ (10.3 mL, 81.3 mmol) was slowly injected into the mixture, which was allowed to warm to room temperature. After 5 h, the mixture was diluted by CH_2Cl_2, washed with satd aq $NaHCO_3$ and brine, dried over anhyd Na_2SO_4, concentrated in vacuo, and purified by column chomatography (hexanes–EtOAc 5:1, hexanes–EtOAc 2.5:1 for the disaccharides) to afford the per-acetylated phenyl thioglycoside as a colorless syrup.

The per-acetylated phenyl thioglycoside (22.5 mmol for the peracetylated phenyl 1-thio-D-galactoside; amounts for the other sugars were adjusted correspondingly) was then dissolved in dry MeOH (20 mL), followed by the addition of a small amount of NaOMe to afford pH 9. After 2 h the solution was quenched by the addition of Amberlite® IR-120 (H^+) resin. The resin was filtered off, and the solvent was removed in vacuo to afford the unprotected phenyl thioglycoside donor as a white powdery solid.

Literature reports for the phenyl thioglycosides **1a**–**c** and **1e** are as follows: phenyl 1-thio-β-D-galactopyranoside (**1a**),[26] phenyl 1-thio-β-D-glucopyranoside (**1b**),[43] phenyl 1-thio-α-D-mannopyranoside (**1c**),[44] and phenyl β-D-galactopyranosyl-(1→4)-1-thio-β-D-glucopyranoside (**1e**).[45] Phenyl *α*-D-galactopyranosyl-(1→6)-1-thio-β-D-glucopyranoside (**1d**), a new compound, was prepared as in the foregoing paragraphs and is characterized NMR spectroscopy and high-resolution MS in the following paragraph.



Phenyl α-D-galactopyranosyl-(1→6)-1-thio-β-D-glucopyranoside (1d). ^{1}H NMR (500 MHz, CD_3OD): *δ* 7.56–7.54 (m, 2H), 7.36–7.33 (m, 2H), 7.29–7.26 (m, 1H), 4.89 (d, *J* = 3.5 Hz, 1H, H-1'), 4.70 (d, *J* = 9.8 Hz, 1H, H-1), 3.92 (dd, *J* = 10.8, 6.1 Hz, 1H), 3.88 (ddd, *J* = 6.6, 5.6, 1.4 Hz, 1H), 3.83 (m, 1H), 3.80–3.73 (m, 3H), 3.70 (m, 2H), 3.59–3.56 (m, 1H), 3.43 (t, *J* = 8.8 Hz, 1H), 3.37 (m, 1H), 3.27 (dd, *J* = 9.8, 8.6 Hz, 1H). ^{13}C NMR (125 MHz, CD_3OD): *δ* 135.29, 132.15, 130.01, 128.26, 100.10, 89.04, 80.29, 79.65, 73.92, 72.11, 71.53, 71.49, 71.12, 70.38, 67.94, 62.84. HRESIMS: (*m/z*) $(M+Na)^+$ calcd for $C_{29}H_{38}O_{18}Na^+$ 457.1144; found 457.1146.

2. Glycosylation to give glycosides 3a–3m.

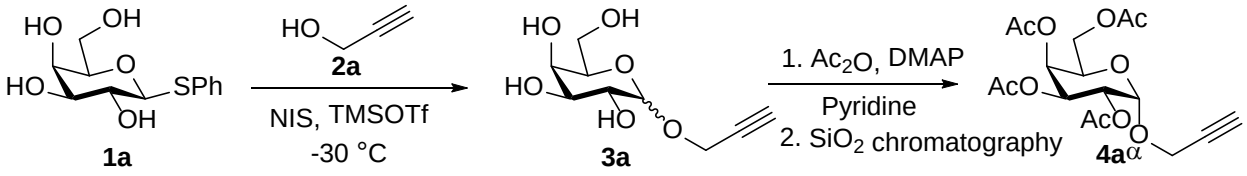
Phenyl 1-thiogalactoside donor **1a** (100 mg, 0.37 mmol) was dissolved in propargyl alcohol (**2a**, 0.87 mL, 0.82 g, 14.7 mmol), followed by the addition of pre-activated powdered 4 Å molecular sieves (150 mg), and stirring was continued for 1 h under nitrogen at room temperature. Then the mixture was cooled to −30 °C, and NIS (232 mg, 1.03 mmol) and TMSOTf (13.3 µL, 0.074 mmol) were added, which made a black (maroon with most other alcohols) solution. After 2 h, satd aq $Na_2S_2O_3$ was added to quench the reaction, and the dark color faded. The mixture was then filtered through Celite®, and the solution was concentrated in vacuo to give crude **3a**. Other alcohols were reacted in a similar manner to give glycosides **3b–3m**.

3. Acetylation of alkyl glycosides to give per-acetylated glycosides 4a–4c and 4e–4m.

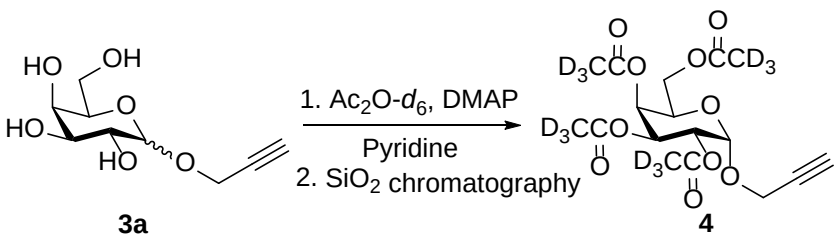
The residue from the foregoing step (**3a**) was dissolved in dry pyridine (10 mL), and 4-(dimethylamino)pyridine (DMAP, catalytic amt.) and Ac_2O (1 mL, 10.6 mmol) were added with stirring overnight at room temperature. After concentrating the mixture, the residue was partitioned between EtOAc and water, and the organic layer was

washed with satd aq $NaHCO_3$ and brine, dried over anhyd Na_2SO_4, and concentrated in vacuo to afford the crude product **4a**. In a similar manner compounds **4b**–**4c** and **4e–4m** were prepared. For the compounds in Table 2, the α anomers were typically separated and purified by column chromatography for characterization; yields were typically based on total acetylated products.

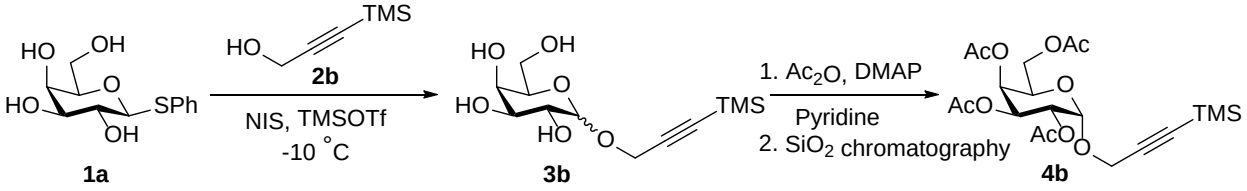
Experimental Data for Compounds 3d, 4, 4a–4c and **4e–4m**



Propargyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4a**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4:1, hexanes–EtOAc) to give **4a** (106.7 mg, 75.1%, α/β = 10:1) as a mixture of anomers. Data for **4aα:** R_f 0.23 (2.5:1, hexanes–EtOAc). $[\alpha]_D^{20}$ +148.5 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.46 (1H, dd, *J* = 3.4, 1.4 Hz, H-4), 5.36 (1H, dd, *J* = 10.9, 3.4 Hz, H-3), 5.32 (1H, d, *J* = 3.6 Hz, H-1), 5.17 (1H, dd, *J* = 10.9, 3.7 Hz, H-2), 4.27 (2H, dd, *J* = 2.4, 1.0 Hz, C*H*$_2$−C≡CH), 4.25 (1H, m, H-5), 4.11-4.09 (2H, m, H-6^a, H-6^b), 2.45 (1H, t, *J* = 2.4 Hz, CH$_2$−C≡C*H*), 2.14, 2.08, 2.04, 1.98 (12H, 4s, 4×COC*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): *δ*: 170.50, 170.48, 170.29, 170.05 (4×*C*OCH$_3$) 95.08 (C-1), 78.39 (CH$_2$−*C*≡CH), 75.32 (CH$_2$−C≡*C*H), 68.11 (C-4), 67.88 (C-2), 67.53 (C-3), 66.94 (C-5), 61.63 (C-6), 55.43 (*C*H$_2$−C≡CH), 20.91, 20.83, 20.78, 20.77 (4×COC*H*$_3$). HRESIMS: (*m/z*) calcd for $C_{17}H_{22}O_{10}Na^+$ (M+Na)$^+$ 409.1111; found 409.1114. Compound **4a** has been reported (NMR spectral data match those above) from the silica gel/H_2SO_4 glycosidation of the free sugar, a process we were unable to duplicate in yield and purity.[9] A similar problem has been reported by at least one other laboratory.[28]

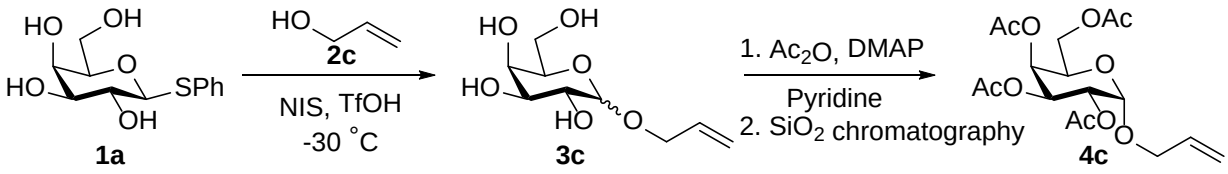


Propargyl 2,3,4,6-tetra-O-(acetyl-d_3)-α-D-galactopyranoside (**4**). Compound **3a** (64.3 mg, 0.295 mmol) was dissolved in dry pyridine (10 mL), and DMAP (catalytic amt.) and Ac_2O-d_6 (0.56 mL, 5.92 mmol) was added with stirring overnight at room temperature. After concentration, the residue was partitioned between CH_2Cl_2/water, and the organic layer was washed with satd aq $NaHCO_3$ and brine, dried over anhyd Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel chomatography (4:1 hexanes–EtOAc) to give **4** (106.1 mg, 90.4%) as a colorless syrup. R_f 0.23 (2.5:1, hexanes–EtOAc). $[\alpha]_D^{21}$ +148.2 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.46 (1H, dd, *J* = 3.4, 1.4 Hz, H-4), 5.36 (1H, dd, *J* = 10.9, 3.3 Hz, H-3), 5.31 (1H, d, *J* = 3.8 Hz, H-1), 5.16 (1H, dd, *J* = 10.9, 3.7 Hz, H-2), 4.26 (2H, dd, *J* = 2.4, 1.1 Hz, CH_2−C≡CH), 4.25 (1H, m, H-5), 4.10 (2H, m, H-6^a, H-6^b), 2.45 (1H, t, *J* = 2.4 Hz, CH_2−C≡C*H*). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.49 (×2), 170.30, 170.05 (4×*C*OCH_3) 95.06 (C-1), 78.38 (CH_2−*C*≡CH), 75.31 (CH_2−C≡*C*H), 68.06 (C-4), 67.83 (C-2), 67.48 (C-3), 66.93 (C-5), 61.58 (C-6), 55.42 (*C*H_2−C≡CH). HRESIMS: (*m/z*) calcd for $C_{17}H_{10}D_{12}O_{10}Na^+$ $(M+Na)^+$ 421.2050; found 421.2048.

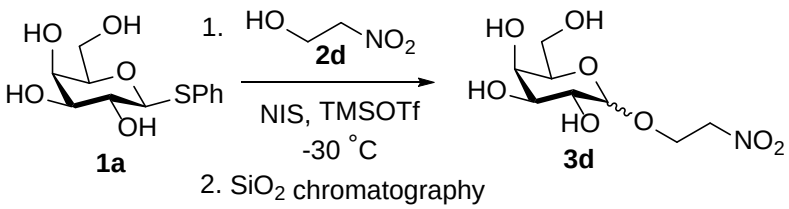


3-(Trimethylsilyl)propargyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4b**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4.5:1, hexanes–EtOAc) to give **4b** (104.9 mg, 62.2%, α/β = 10:1) as a mixture of anomers. Data for **4bα:** R_f 0.37 (2.5:1, hexanes–EtOAc). $[\alpha]_D^{20}$ 144.4 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500, $CDCl_3$ MHz): *δ* 5.46 (1H, dd, *J* = 3.4, 1.3 Hz, H-4), 5.38 (1H, dd, *J* = 10.9, 3.4 Hz, H-3), 5.34 (1H, d, *J* = 3.7 Hz, H-1), 5.16 (1H, dd, *J* = 10.9, 3.7

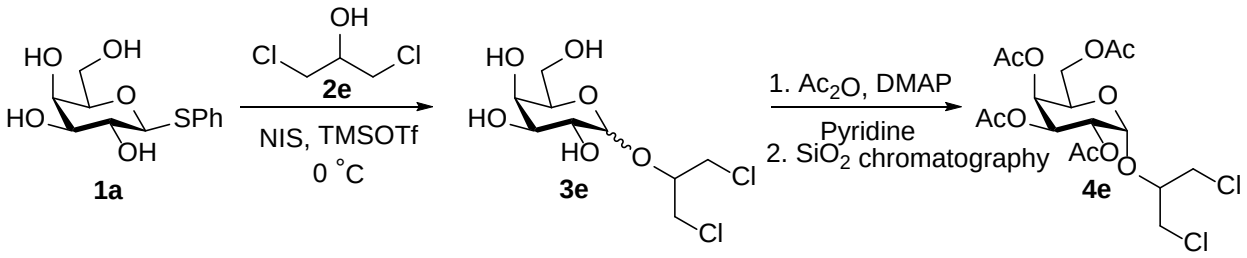
Hz, H-2), 4.26 (3H, m, CH_2−C≡CH, H-5), 4.14-4.05 (2H, m, H-6^a, H-6^b), 2.14, 2.09, 2.04, 1.99 (12H, 4s, 4×COCH_3), 0.17 (9H, s, −Si(CH_3)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.51, 170.36, 170.34, 170.11 (4×*C*OCH$_3$), 99.92 (CH$_2$−*C*≡C−TMS), 94.71 (C-1), 92.52 (CH$_2$−C≡*C*−TMS), 68.11 (C-4), 67.93 (C-2), 67.56 (C-3), 66.84 (C-5), 61.58 (C-6), 56.05 (*C*H$_2$−C≡C−TMS), 20.93, 20.83, 20.81, 20.79 (4×CO*C*H$_3$), -0.16 (−Si(*C*H$_3$)$_3$). HRESIMS: (*m/z*) calcd for $C_{20}H_{30}O_{10}SiNa^+$ (M+Na)$^+$ 481.1506; found 481.1507.



Allyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4c**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4:1, hexanes–EtOAc) to give **4c** (101. 2 mg, 70.9%, α/β = 7:1) as a mixture of anomers. Data for **4cα:** R_f 0.29 (2.5:1, hexanes–EtOAc). $[\alpha]_D^{20}$ +163.0 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.87 (1H, dddd, *J* = 17.2, 10.4, 6.1, 5.2 Hz, CH$_2$C*H*=CH$_2$) 5.45 (1H, dd, *J* = 3.4, 1.3 Hz, H-4), 5.38 (1H, dd, *J* = 12.0, 3.4 Hz, H-3), 5.31 (1H, dq, *J* = 17.2, 1.6 Hz, CH$_2$CH=C*H*$_2$), 5.22 (1H, dq, *J* = 10.4, 1.3 Hz, CH$_2$CH=C*H*$_2$), 5.15 (1H, d, *J* = 3.8 Hz, H-1), 5.12 (1H, m, H-2), 4.24 (1H, m, H-5), 4.18 (1H, ddt, 13.1, 5.2, 1.4 Hz, H-6^a/H-6^b), 4.09 (2H, m, C*H*$_2$CH=CH$_2$), 4.02 (1H, ddt, 13.1, 6.1, 1.4 Hz, H-6^a/H-6^b), 2.13, 2.07, 2.04, 1.97 (12H, 4s, 4×COC*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.50, 170.48, 170.33, 170.09 (4×*C*OCH$_3$), 133.34 (CH$_2$*C*H=CH$_2$), 118.12 (CH$_2$CH=*C*H$_2$), 95.47 (C-1), 68.90 (C-6), 68.25 (C-4), 68.21 (C-2), 67.73 (C-3), 66.49 (C-5), 61.86 (*C*H$_2$CH=CH$_2$), 20.91, 20.81, 20.78, 20.77 (4×CO*C*H$_3$). HRESIMS: (*m/z*) calcd for $C_{17}H_{24}O_{10}Na^+$ (M+Na)$^+$411.1267; found 411.1267. The β anomer of compound **4c** has been characterized.[46]

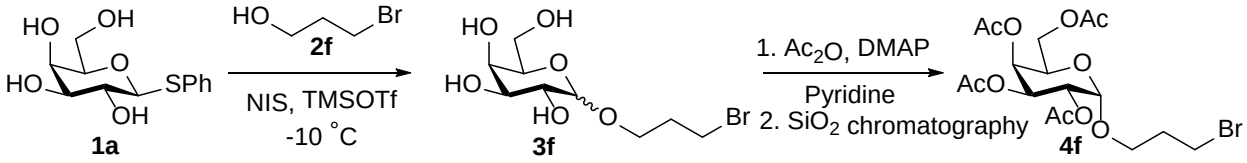


2-Nitroethyl α-D-galactopyranoside (**3d**). The compound was synthesized according to the general glycosylation procedure B.2, above. (The compound partially decomposed when subjected to the acetylation conditions.) The crude product was purified by silica gel chomatography (15:1 to 7:1, EtOAc–MeOH) to give **3d** (86.6 mg, 93.0%, α/β = 5:1) as a mixture of anomers. Data for **3dα:** R_f 0.43 (3:1, EtOAc–MeOH). $[\alpha]_D^{20}$ +24.7 (*c* 1.00, CH_3OH). ^{1}H NMR (500 MHz, CD_3OD): *δ* 4.94 (1H, d, *J* = 3.9 Hz, H-1), 4.78 (2H, m, $OCH_2CH_2NO_2$), 4.33 (1H, ddd, *J* = 11.9, 5.8, 4.6 Hz, $OCH_2CH_2NO_2$), 4.04 (1H, ddd, *J* = 11.9, 5.8, 4.6 Hz, $OCH_2CH_2NO_2$), 3.96 (1H, dd, *J* = 3.3, 1.2 Hz, H-4), 3.85 (1H, m, H-5), 3.82 (1H, m, H-2), 3.79–3.72 (3H, m, H-3, H-6^a, H-6^b). ^{13}C NMR (125 MHz, CD_3OD): *δ* 100.91 (C-1), 75.87 ($OCH_2CH_2NO_2$), 72.60 (C-5), 71.24 (C-3), 71.05 (C-4), 69.90 (C-2), 65.06 ($OCH_2CH_2NO_2$), 62.69 (C-6). HRESIMS: (*m/z*) calcd for $C_8H_{15}O_8NNa^+$ $(M+Na)^+$ 276.0695; found 276.0694. Compound **3d** has been reported.[47] Partial characterization was by ^{13}C NMR spectroscopy (reported only seven peaks) in DMSO-d_6.

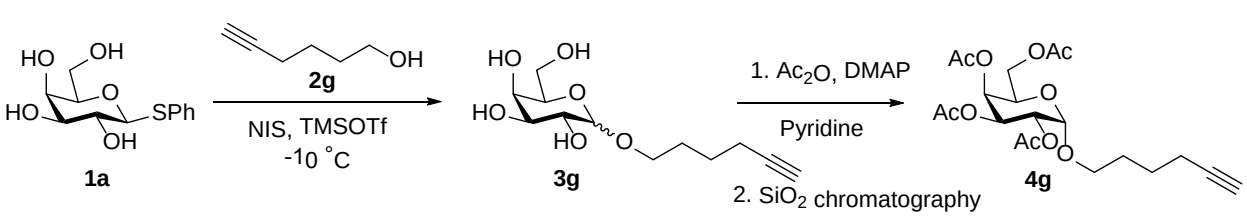


1,3-Dichloropropan-2-yl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4e**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4:1, hexanes–EtOAc) to give **4e** (143.1 mg, 84.9%, α/β = 5:1) as a mixture of anomers. Data for **4eα:** R_f 0.38 (2:1, hexanes–EtOAc). $[\alpha]_D^{22}$ +154.3 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.48 (1H, dd, *J* = 3.4, 1.3 Hz, H-4), 5.36 (1H, d, *J* = 3.9 Hz, H-1), 5.34 (1H, dd, *J* = 11.0, 3.4 Hz, H-3), 5.08 (1H, dd, *J* = 11.0, 3.9

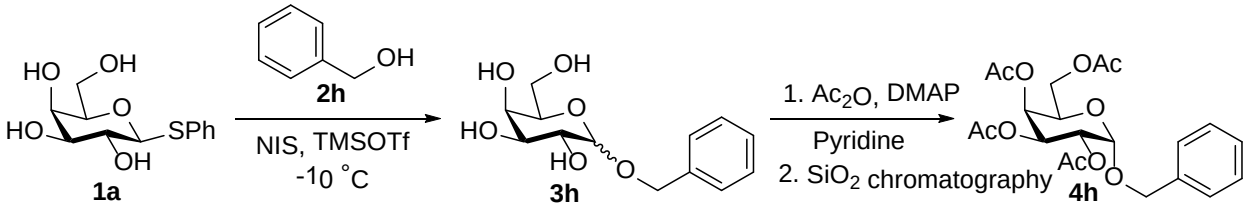
Hz, H-2), 4.45 (1H, ddd, *J* = 6.9, 5.6, 1.1 Hz, H-5), 4.10 (2H, m, H-6[a], H-6[b]), 4.00 (1H, m, C*H*($CH_2Cl)_2$), 3.74 (2H, d, *J* = 5.1 Hz, CH(C$H_2Cl)_2$), 3.66 (2H, m, CH(C$H_2Cl)_2$), 2.14, 2.08, 2.05, 2.00 (12H, 4s, 4×COCH_3). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.77, 170.49, 170.26, 170.07 (4×*C*OCH_3), 96.87 (C-1), 78.97 (*C*H($CH_2Cl)_2$), 68.14 (C-2, C-4), 67.44 (C-3), 67.34 (C-5), 62.14 (C-6), 44.16, 43.59 (CH(*C*$H_2Cl)_2$), 20.93, 20.80, 20.79, 20.75 (4×CO*C*H_3). HRESIMS: (*m/z*) calcd for $C_{17}H_{24}O_{10}Cl_2Na^+$ $(M+Na)^+$ 481.0644; found 481.0645, 483.0619, 485.0626 (ratio of molecular ion isotopic peak heights ≈ 9:6:1).



3-Bromopropyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4f**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4.5:1, hexanes–EtOAc) to give **4f** (96.5 mg, 56.0%, α/β = 3:1) as a mixture of anomers. **4fα:** R_f 0.37 (2:1, hexanes–EtOAc). $[\alpha]_D^{20}$ +98.6 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.45 (1H, dd, *J* = 3.4, 1.4 Hz, H-4), 5.34–5.31 (1H, m, H-3), 5.13 (1H, m, H-2), 5.12 (1H, d, *J* = 3.7 Hz, H-1), 4.23 (1H, m, H-5), 4.10 (2H, m, H-6[a], H-6[b]), 3.87 (1H, ddd, *J* = 9.9, 6.0, 5.0 Hz, one of OC$H_2CH_2CH_2Br$), 3.58–3.49 (3H, m, the other OC$H_2CH_2CH_2Br$ and two $OCH_2CH_2CH_2Br$), 2.17–2.10 (5H, m, $OCH_2CH_2CH_2Br$, CO*C*H_3), 2.08, 2.04, 1.98 (9H, 3s, 3 × CO*C*H_3). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.56, 170.49, 170.35, 170.20 (4 × *C*OCH_3), 96.63 (C-1), 68.26 (C-2), 68.19 (C-4), 67.69 (C-3), 66.56 (C-5), 65.96 (O*C*$H_2CH_2CH_2Br$), 61.91 (C-6), 32.15 ($OCH_2CH_2CH_2Br$), 30.17 ($OCH_2CH_2CH_2Br$), 20.93, 20.86, 20.81, 20.78 (4×CO*C*H_3). HRESIMS: (*m/z*) calcd for $C_{17}H_{25}O_{10}BrNa^+$ $(M+Na)^+$ 491.0529, 493.0511; found 491.0526, 493.0502 (ratio of molecular ion isotopic peak heights ≈ 1:1). Compound **4f** has been reported.[48] NMR spectral data match those above.

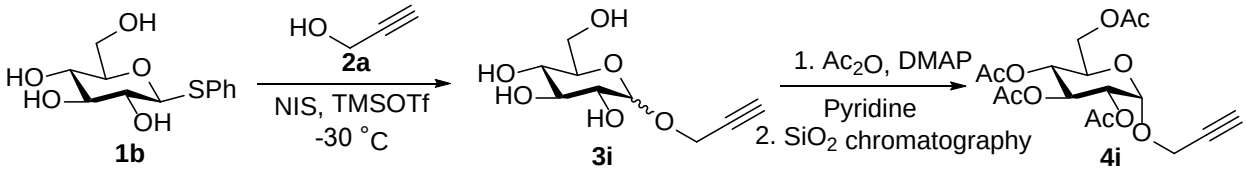


Hex-5-yn-1-yl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4g**) The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4.5:1, hexanes–EtOAc) to give **4g** (66.3 mg, 42.1%, α/β > 20:1) as a colorless syrup. Data for **4gα:** R_f 0.38 (2:1, hexanes–EtOAc). $[\alpha]_D^{20}$ +139.1 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.45 (1H, dd, *J* = 3.4, 1.3 Hz, H-4), 5.36–5.32 (1H, m, H-3), 5.12 (1H, m, H-2), 5.10 (1H, d, *J* = 3.4 Hz, H-1), 4.21 (1H, m, H-5), 4.10 (2H, m, H-6^a, H-6^b), 3.73 (1H, dt, *J* = 9.9, 6.1 Hz, one of OCH_2CH$_2$CH$_2$CH$_2$−C≡CH 3.45 (1H, dt, *J* = 9.9, 6.3 Hz, the other one of OCH_2CH$_2$CH$_2$CH$_2$−C≡CH), 2.23 (2H, tdd, *J* = 6.9, 2.7, 0.7 Hz, OCH$_2$CH$_2$CH$_2$CH_2−C≡CH), 2.14, 2.07, 2.04, 1.98 (12H, 4s, 4×COCH_3), 1.95 (1H, t, *J* = 2.6 Hz, OCH$_2$CH$_2$CH$_2$CH$_2$−C≡C*H*), 1.75–1.69 (2H, m, OCH$_2$CH_2CH$_2$CH$_2$−C≡CH), 1.64–1.59 (2H, m, OCH$_2$CH$_2$CH_2CH$_2$−C≡CH). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.56, 170.54, 170.37, 170.17 (4×*C*OCH$_3$), 96.29 (C-1), 84.10 (OCH$_2$CH$_2$CH$_2$CH$_2$−*C*≡CH), 68.85 (OCH$_2$CH$_2$CH$_2$CH$_2$−C≡*C*H), 68.36 (C-2), 68.26 (C-4), 68.16 (O*C*H$_2$CH$_2$CH$_2$CH$_2$−C≡CH), 67.80 (C-3), 66.39 (C-5), 61.96 (C-6), 28.45 (OCH$_2$*C*H$_2$CH$_2$CH$_2$−C≡CH), 25.21 (OCH$_2$CH$_2$*C*H$_2$CH$_2$−C≡CH), 20.93, 20.84, 20.81, 20.79 (4×CO*C*H$_3$), 18.23 (OCH$_2$CH$_2$CH$_2$*C*H$_2$−C≡CH). HRESIMS: (*m/z*) calcd for $C_{20}H_{28}O_{10}Na^+$ $(M+Na)^+$ 451.1580; found 451.1580.

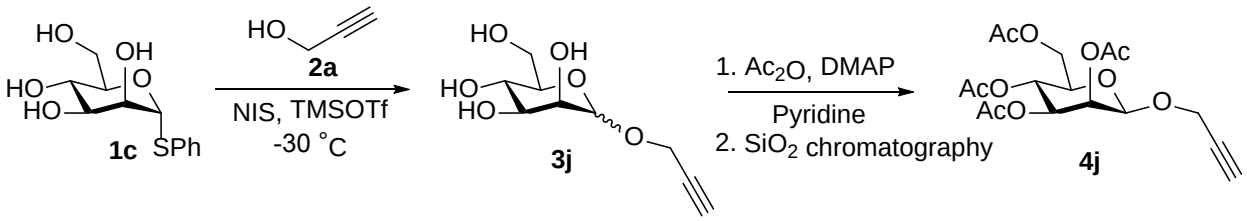


Benzyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4h**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4.5:1, hexanes–EtOAc) to give **4h** (116.5 mg, 72.3%, α/β = 3:1) as a mixture of anomers. Data for **4hα:** R_f 0.40 (2:1, hexanes–EtOAc). $[\alpha]_D^{21}$ +126.8 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.37–7.31 (5H, m, H_{arom}), 5.46 (1H, dd, *J* = 3.5, 1.3 Hz, H-4), 5.40 (1H, dd, *J* = 10.7, 3.4 Hz, H-3), 5.18 (1H, d, *J* = 3.7 Hz, H-1), 5.14 (1H, dd, *J* = 10.7, 3.7 Hz, H-2), 4.74–4.53 (2H, dd, *J* = 96.5, 12.1 Hz, CH_2Ph), 4.27 (1H, td, *J* = 6.7, 1.4 Hz, H-

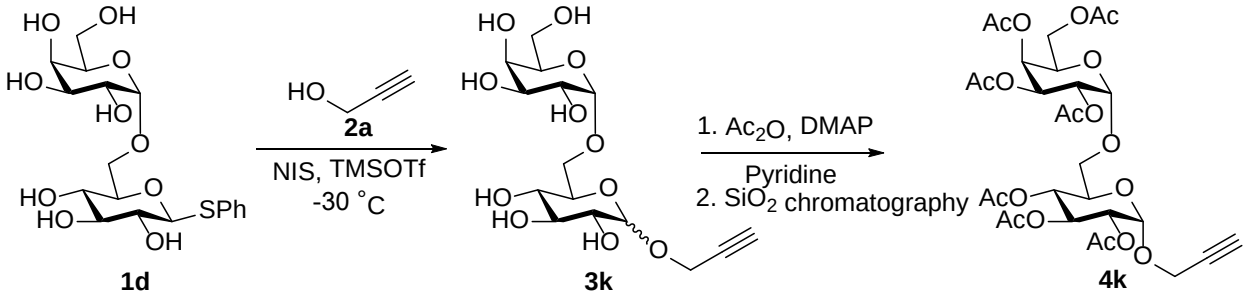
5), 4.08 (2H, qd, *J* = 11.2, 6.6 Hz, H-6[a], H-6[b]), 2.13, 2.05, 2.03, 1.98 (12H, 4s, 4×COC*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.50, 170.40, 170.33, 170.11 (4×*C*OCH$_3$), 136.90, 128.65, 128.24, 128.01 (C_{arom}), 95.52 (C-1), 70.09 (*C*H$_2$Ph), 68.23 (C-4), 68.20 (C-2), 67.78 (C-3), 66.63 (C-5), 61.81 (C-6), 20.86, 20.84, 20.79, 20.77 (4×COC*H*$_3$). HRESIMS: (*m/z*) calcd for $C_{21}H_{26}O_{10}Na^+$ $(M+Na)^+$ 461.1424; found 461.1426. Compound **4h** has been used in experiments apparently without characterization.[49] The β anomer is characterized in another paper.[50]



Propargyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**4i**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (5:1 to 4:1, hexanes–EtOAc) to give **4i** (112.8 mg, 79.4%, α/β = 7:1) as a mixture of anomers. Data for **4iα:** R_f 0.35 (2:1, hexanes–EtOAc). $[\alpha]_D^{21}$ +163.6 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.48 (1H, m, H-3), 5.28 (1H, d, *J* = 3.8 Hz, H-1), 5.08 (1H, dd, *J* = 10.1, 9.4 Hz, H-4), 4.91 (1H, dd, *J* = 10.3, 3.8 Hz, H-2), 4.27 (2H, d, *J* = 2.4 Hz, C*H*$_2$−C≡CH), 4.25-4.10 (2H, m, H-6[a], H-6[b]), 4.04 (1H, m, H-5), 2.44 (1H, t, *J* = 2.4 Hz, CH$_2$−C≡C*H*), 2.08, 2.07, 2.02, 2.00 (12H, 4s, 4×COC*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.75, 170.22, 170.14, 169.66 (4×*C*OCH$_3$) 94.69 (C-1), 78.28 (CH$_2$−*C*≡CH), 75.41 (CH$_2$−C≡*C*H), 70.56 (C-2), 70.04 (C-3), 68.52 (C-4), 67.94 (C-5), 61.82 (C-6), 55.52 (*C*H$_2$−C≡CH), 20.84, 20.79, 20.78, 20.72 (4×COC*H*$_3$). HRESIMS: (*m/z*) calcd for $C_{17}H_{22}O_{12}Na^+$ $(M+Na)^+$ 409.1111; found 409.1112. Compound **4i** has been reported.[46] The NMR data match those reported above.

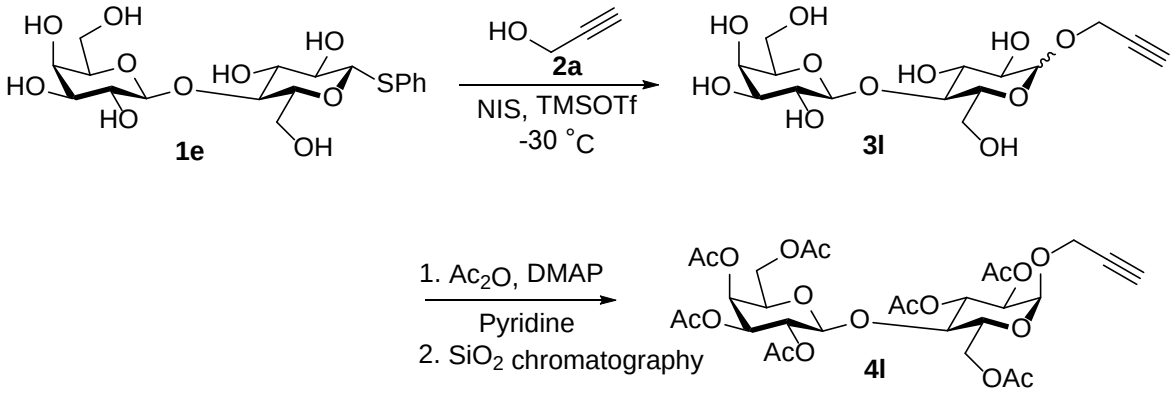


Propargyl 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranoside (**4j**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (4:1 to 2.5:1, hexanes–EtOAc) to give **4j** (115.6 mg, 81.4%, α/β = 1:2) as a mixture of anomers. Data for **4jβ:** R_f 0.18 (2:1, hexanes–EtOAc). $[\alpha]_D^{20}$ −82.8 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.48 (1H, dd, *J* = 3.3, 1.1 Hz, H-2), 5.26 (1H, t, *J* = 9.9 Hz, H-4), 5.09 (1H, dd, *J* = 10.0, 3.3 Hz, H-3), 4.94 (1H, d, *J* = 1.1 Hz, H-1), 4.38 (2H, m, C*H*$_2$−C≡CH), 4.31 (1H, dd, *J* = 12.3, 5.3 Hz, H-6^a), 4.16 (1H, dd, *J* = 12.3, 2.5 Hz, H-6^b), 3.69 (1H, ddd, *J* = 9.9, 5.3, 2.6 Hz, H-5), 2.48 (1H, t, *J* = 2.4 Hz, CH$_2$−C≡C*H*), 2.17, 2.08, 2.03, 1.98 (12H, 4s, 4×COC*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.79, 170.36, 170.10, 169.68 (4×*C*OCH$_3$), 95.76 (C-1, $J_{C1\text{-}H1}$ = 158.76 Hz), 77.94 (CH$_2$−*C*≡CH), 76.09 (CH$_2$−C≡*C*H), 72.66 (C-5), 71.21 (C-3), 68.85 (C-2), 66.08 (C-4), 62.45 (C-6), 55.91 (*C*H$_2$−C≡CH), 20.95, 20.88, 20.81, 20.69 (4×CO*C*H$_3$). HRESIMS: (*m/z*) calcd for $C_{17}H_{22}O_{12}Na^+$ $(M+Na)^+$ 409.1111; found 409.1111. The $J_{C1\text{-}H1}$ cited above is in line with that generally expected for a β-D-mannoside.[51] A recent example is that of Demchenko and co-workers.[52]



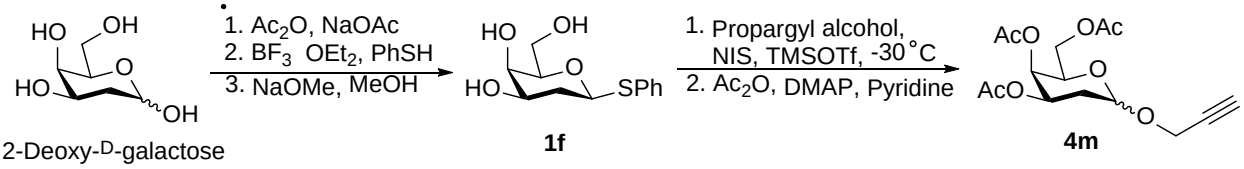
Propargyl 6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (**4k**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (2:1, hexanes–EtOAc) to give **4k** (172.1 mg, 69.4%, α/β = 8:1) as a mixture of anomers. Data for **4kα:** R_f 0.29 (1:1, hexanes–EtOAc). $[\alpha]_D^{20}$ +166.2 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 5.48 (1H, dd, *J* = 10.3, 9.3 Hz, H-3), 5.45 (1H, dd, *J* = 3.4, 1.3 Hz, H-4'), 5.34 (1H, dd, *J* = 10.8, 3.3 Hz, H-3'), 5.24 (1H, d, *J* = 3.7 Hz, H-1), 5.16 (1H, d, *J* = 3.7 Hz, H-1'), 5.11 (1H, dd, *J* = 10.8, 3.6 Hz, H-2'), 5.05 (1H, dd, *J* = 10.2, 9.3 Hz, H-4), 4.85 (1H, dd, *J* = 10.3, 3.8 Hz, H-2),

4.28 (2H, dd, *J* = 2.5, 0.7 Hz, C*H*$_2$−C≡CH), 4.25 (1H, m, H-5'), 4.07 (2H, m, H-6'^{a,b}), 4.02 (1H, m, H-5), 3.72 (1H, dd, *J* = 11.3, 5.4 Hz, H-6^a), 3.55 (1H, dd, *J* = 11.3, 2.4 Hz, H-6^b), 2.49 (1H, t, *J* = 2.4 Hz, CH$_2$−C≡C*H*), 2.13, 2.11, 2.07, 2.04, 2.03, 2.00, 1.97 (21H, 7s, 7×COC*H*$_3$). ^{13}C NMR (125 MHz, CDCl$_3$): *δ* 170.66, 170.52, 170.32, 170.27, 170.19, 170.00, 169.64 (7×*C*OCH$_3$), 96.39 (C-1'), 94.49 (C-1), 78.31 (CH$_2$−*C*≡CH), 75.57 (CH$_2$−C≡*C*H), 70.63 (C-2), 70.09 (C-3), 69.16 (C-4), 68.93 (C-5), 68.27 (C-4'), 68.25 (C-2'), 67.60 (C-3'), 66.58 (C-5'), 66.31 (C-6), 61.90 (C-6'), 55.51 (*C*H$_2$−C≡CH), 20.94, 20.86, 20.82, 20.81 (×2), 20.79, 20.78 (7×COC*H*$_3$). HRESIMS: (*m/z*) calcd for $C_{29}H_{38}O_{18}Na^+$ $(M+Na)^+$ 697.1956; found 697.1956.



Propargyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (**4l**). The compound was synthesized according to the general glycosylation and acetylation procedures B.2 and B.3, above. The crude product was purified by silica gel chomatography (2:1 to 1.5:1, hexanes–EtOAc) to give **4l** (140.6 mg, 56.7%, α/β = 12:1) as a mixture of anomers. Data for **4lα:** R_f 0.22 (1:1, hexanes–EtOAc). $[\alpha]_D^{22}$ +59.7 (*c* 1.00, CHCl$_3$). ^{1}H NMR (500 MHz, CDCl$_3$): *δ* 5.47 (1H, dd, *J* = 10.3, 9.2 Hz, H-3), 5.34 (1H, dd, *J* = 3.6, 1.2 Hz, H-4'), 5.20 (1H, d, *J* = 3.8 Hz, H-1), 5.10 (1H, dd, *J* = 10.4, 7.9 Hz, H-2'), 4.95 (1H, dd, *J* = 10.4, 3.5 Hz, H-3'), 4.83 (1H, dd, *J* = 10.3, 3.8 Hz, H-2), 4.48 (1H, d, *J* = 7.9 Hz, H-1'), 4.45 (1H, dd, *J* = 12.0, 2.1 Hz, H-6^a), 4.25 (2H, dd, *J* = 3.3, 2.4 Hz, C*H*$_2$−C≡CH), 4.14 (2H, m, H-6^b, H-6'^{a}), 4.07 (1H, dd, *J* = 11.1, 7.5 Hz, H-6'^{b}), 3.96 (1H, m, H-5), 3.86 (1H, ddd, *J* = 7.5, 6.3, 1.2 Hz, H-5'), 3.76 (1H, dd, *J* = 10.1, 9.2 Hz, H-4), 2.43 (1H, t, *J* = 2.4 Hz, CH$_2$−C≡C*H*), 2.14, 2.12, 2.06, 2.05, 2.04, 2.04, 1.95 (21H, 7s, 7×COC*H*$_3$). ^{13}C NMR (125 MHz, CDCl$_3$): *δ* 170.50, 170.48, 170.47, 170.30, 170.21, 169.59, 169.13 (7×*C*OCH$_3$), 101.16 (C-1'), 94.41 (C-1),

78.30 (CH_2−*C*≡CH), 76.42 (C-4), 75.37 (CH_2−C≡*C*H), 71.19 (C-3'), 70.79 (C-2), 70.77 (C-5'), 69.76 (C-3), 69.27 (C-2'), 68.85 (C-5), 66.74 (C-4'), 61.86 (C-6), 60.94 (C-6'), 55.30 (*C*H_2−C≡CH), 21.00 (×2), 20.84, 20.78 (×2), 20.77, 20.64 (7×CO*C*H_3). HRESIMS: (*m/z*) calcd for $C_{29}H_{38}O_{18}Na^+$ $(M+Na)^+$ 697.1956; found 697.1956. Compound **4l** has been reported.[12] However, the NMR data differ from those we report and assign above. Our assignments are based on 2D NMR data. See the NMR spectra in the Supplementary Information section.



Propargyl 3,4,6-tri-O-acetyl-2-deoxy-α,β-D-*lyxo*-hexopyranoside (4m). In addition, the thiophenyl glycoside (donor) of 2-deoxy-D-*lyxo*-hexopyranose (phenyl 2-deoxy-1-thio-β-D-*lyxo*-hexopyranoside, **1f**) was also synthesized and applied in this glycosylation reaction to afford propargyl 3,4,6-tri-*O*-acetyl-2-deoxy-α,β-D-*lyxo*-hexopyranoside (alias: "propargyl 3,4,6-tri-*O*-acetyl-2-deoxy-α,β-D-galactopyranoside," **4m**).[53] However, a moderate yield (67%) and low stereoselectivity (α:β = 1.7:1) were achieved. The acetylated mixture **4m** was not further separated into its anomers..

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Supplementary Information. Supplementary Information is available online at…….

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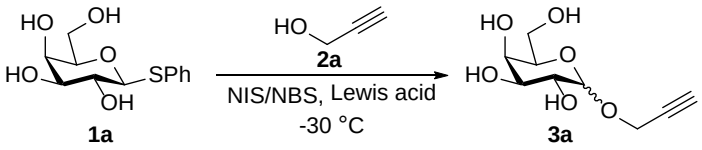
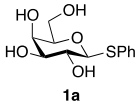
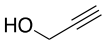
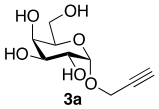
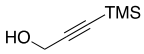
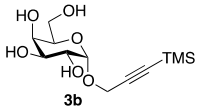
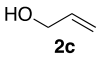
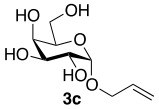
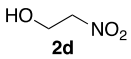
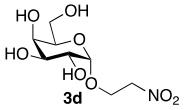
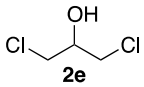
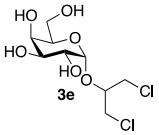
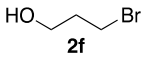
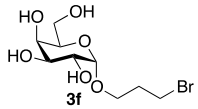
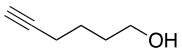
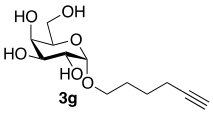
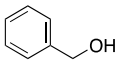
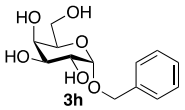
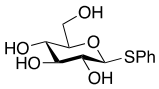
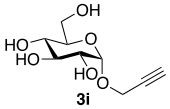
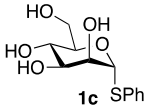
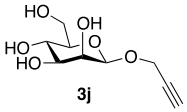
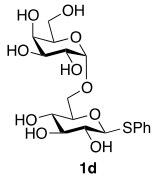
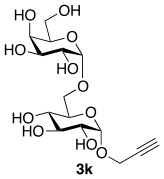
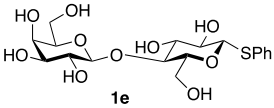
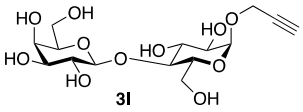
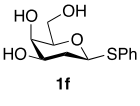
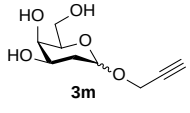
Table 1 Optimization of reaction conditions[a]



entry	Lewis acid	halogen source	propargyl alcohol (mol equiv)	yield (%)[b]	α:β[c]
1	TMSOTf	NIS	40	75	10:1
2	$BF_3{\cdot}OEt_2$	NIS	40	74	10:1
3	TfOH	NIS	40	76	9:1
4	$H_2SO_4{\cdot}SiO_2$	NIS	40	52	15:1
5	TMSOTf	NBS	40	59	5:1
6	$BF_3{\cdot}OEt_2$	NBS	40	38	5:1
7	TMOSTf	NIS	20	50	7:1
8	TMSOTf	NIS	30	53	10:1
9	TMSOTf	NIS	60	76	10:1
10	TMSOTf	NIS	100	58	11:1
11	TMSOTf	None	40	0	—
12	None	NIS	40	0	—

[a]The reaction was conducted using 0.37 mmol of **1a**, 1.03 mmol (2.8 equiv) of NIS/NBS, and 0.07 mmol (0.20 equiv) of Lewis acid for 2 h. [b]The yield was determined after acetylation of **3a** by FIA–ESI-TOF-MS. [c]The anomeric ratio was determined by integration of H-1 in the ^{1}H NMR spectrum of the crude product **3a**.

Table 2 Scope of the reaction.[a]

Entry	Donor	Acceptor	α Product	% Yield[b]	α:β[c]
1	 **1a**	 **2a**	 **3a**	75	10:1
2[d]	**1a**	 **2b**	 **3b**	62	10:1
3	**1a**	 **2c**	 **3c**	71	7:1
4	**1a**	 **2d**	 **3d**	93[e]	5:1[f]
5[g]	**1a**	 **2e**	 **3e**	85	5:1
6[d]	**1a**	 **2f**	 **3f**	56	3:1
7[d]	**1a**	 **2g**	 **3g**	42	> 20:1
8[d]	**1a**	 **2h**	 **3h**	72	3:1
9	 **1b**	**2a**	 **3i**	79	7:1
10	 **1c**	**2a**	 **3j**	81	1:2
11	 **1d**	**2a**	 **3k**	69	8:1
12	 **1e**	**2a**	 **3l**	57	12:1
13	 **1f**	**2a**	 **3m**	67[h]	1.7:1

Footnotes to Table 2

[a] For details of the synthetic procedures, see the Experimental Section. Reaction time = 2 h, and temperature = −30 °C, unless otherwise noted. [b] Isolated yield after acetylation and chromatographic separation of the products to give **4a**–**4m**. [c] The anomeric ratio was determined by integrating the ^{1}H NMR spectrum of the crude product. [d] The reaction was performed at −10 °C. [e] Isolated yield without acetylation. [f] The anomeric ratio was determined from isolated products. [g] The reaction was performed at 0 °C. [h]Anomeric mixture; anomers not separated.

Scheme 1 Synthesis of deuterated glycoside substrate as the internal standard