

Synthesis of galactosaminyl *D-chiro*-inositols

Georgia Marnera and Marc d'Alarcao*

Michael Research Building, Department of Chemistry, Tufts University, Medford, MA 02155, USA

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Abstract—All six isomeric *D*-galactosaminopyranosyl-*D-chiro*-inositols have been prepared by glycosylation of appropriate penta-*O*-benzyl-*D-chiro*-inositols. The three requisite protected *D-chiro*-inositols were prepared by SmI₂-promoted pinacol coupling of dialdehydes derived ultimately from L-arabinose.

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1. Introduction

Several glycosylated *chiro*-inositols have been isolated from natural sources, including plants,¹ fungi,² insects,³ and mammals.⁴ In plants, *chiro*-inositol-containing di- and trisaccharides are believed to confer desiccation tolerance to seeds,⁵ while in mammals, the inositol phosphoglycan (IPG) class of oligosaccharides are believed to be involved in insulin signal transduction.⁶ Because of their putative role in glucose homeostasis, the IPGs and their analogues are of considerable interest as possible treatments for Type II diabetes.

Two distinct classes of IPGs have been identified, one containing a glucosamine glycosidically linked to a *myo*-inositol,⁷ and the other containing a galactosamine glycosidically linked to a *D-chiro*-inositol.⁴ In the latter case, no information about the position or configuration of this terminal anomeric linkage has been published.

The chemical synthesis of glycosylated *D-chiro*-inositols is complicated by the relative difficulty in obtaining suitably protected *D-chiro*-inositols to serve as glycosyl acceptors.

While several differentially protected⁸ *chiro*-inositols have been synthesized,^{9–23} we sought a general strategy for the syntheses of a complete set of penta-*O*-benzyl-

D-chiro-inositols, each with a different unprotected hydroxyl group for glycosylation. Since *chiro*-inositol has a C₂ axis of symmetry, the set consists of only three different penta-*O*-benzyl-*chiro*-inositols: **8**, **9**, and **10**. With these three precursors in hand, all monoglycosylated *D-chiro*-inositol positional isomers may be prepared. Herein, we report a convenient synthesis of compounds **8**, **9**, and **10**, from 2,3,4-tri-*O*-benzyl-L-arabinopyranose (**1**), and demonstrate the utility of this set of precursors by preparing the peracetylated derivatives of all six possible isomers of 2-acetamido-2-deoxy-*D*-galactopyranosyl-*D-chiro*-inositol, **18 α,β** , **19 α,β** , and **20 α,β** . The complete set of pseudodisaccharides may be valuable as structurally defined standards for use in the elucidation of the position and configuration of the galactosaminyl-*D-chiro*-inositol linkage in natural IPGs. The α anomers of the unacetylated disaccharides have been previously prepared by other methods.^{20,21,24}

2. Results and discussion

The six-membered ring of the *D-chiro*-inositols **8**, **9**, and **10** was constructed using an intramolecular samarium diiodide coupling²⁵ of an appropriately protected 1,6-dialdehyde. SmI₂ is known to produce predominantly cis-diols that are trans-aligned with respect to neighboring alkoxy substituents²⁶ and has previously been used for the synthesis of *chiro*-inositols.^{17,18}

* Corresponding author. Tel.: +1 617 627 3686; fax: +1 617 627 3443; e-mail: marc.dalarcao@tufts.edu

The aldehydes needed for pinacol coupling were prepared as follows. 2,3,4-Tri-*O*-benzylarabinopyranose (**1**, Scheme 1), available in three steps from L-arabinose by a literature procedure,²⁷ was treated with 10 equiv of vinylmagnesium bromide in THF to give alcohols **2** (1.7:1 *syn:anti*). The resulting mixture was exhaustively silylated with *tert*-butylchlorodimethylsilane to produce **3**, which was treated with ozone, followed by NaBH₄, to give alcohols **4a**, **4b**, and **4c** (1.7:1.0:0.2). Presumably, alcohols **4a** and **4b** result from migration of the TBS group under the basic conditions of the borohydride reduction as has been previously observed.²⁸ At this stage the three isomers are easily separated, and either **4a** or **4c** can be carried on in the synthesis with the same outcome (*vide infra*).

Alkylation of either alcohol **4a** or **4c** gave compound **5** in good yield. It appears that the basic (NaH) alkylation conditions generate the same equilibrating mixture of alkoxy-silanes from either precursor (**4a** or **4c**) and that the subsequent alkylation occurs faster with the intermediate in which both silyl groups are on primary hydroxyl groups. Thus, alkylation of either **4a** or **4c** with benzyl bromide produces **5a**, while alkylation of **4a** or **4c** with *p*-methoxybenzyl bromide produces **5b**. The PMB-substituted compound **5b** is unstable on silica gel and, therefore, was carried on to the next step without purification.

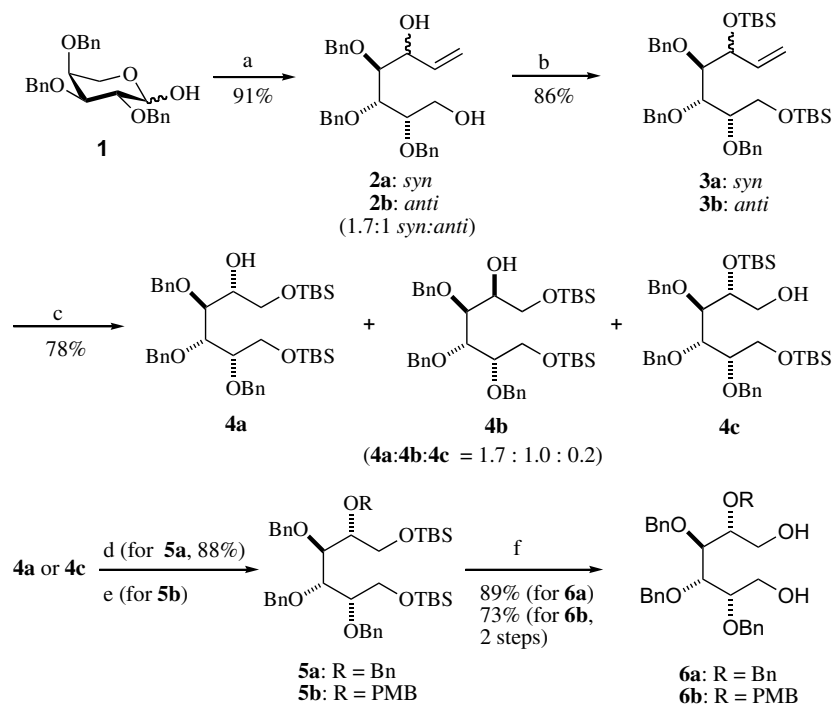
Treatment of either **5a** or **5b** with tetrabutylammonium fluoride resulted in removal of the TBS-groups

furnishing diols **6a** and **6b**, respectively. Each diol was subjected to a one-pot sequence of Swern oxidation, followed by SmI₂ pinacol coupling²⁹ (Scheme 2) affording *chiro*-inositols **7a** and **7b**.

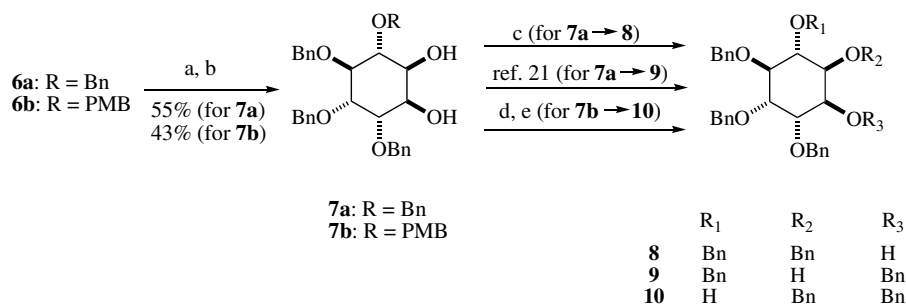
The structure of **7a** was confirmed by an independent synthesis of the same compound starting from L-xylose.³⁰ The structure of **7b** was confirmed by its transformation into **12**³⁰ and comparison with penta-*O*-benzyl-(–)-quebrachitol (**12'**),¹⁸ obtained by exhaustive benzylation of (–)-quebrachitol as shown in Scheme 3.

Selective benzylation of the equatorial hydroxyl group of **7a** via the dibutylstannyl ester (Scheme 2) afforded **8**¹⁶ without any detectable amount of the axially alkylated isomer (82% yield). The structure of **8** was established by ¹H NMR analysis of its acetyl derivative. Compound **9** was synthesized as previously described.³⁰ Exhaustive benzylation of **7b**, followed by oxidative (DDQ) removal of the *p*-methoxybenzyl group, provided compound **10**.

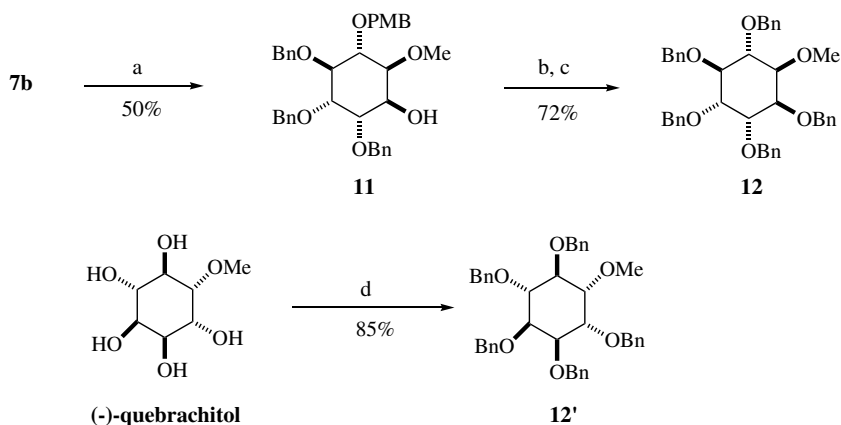
With the three suitably protected *chiro*-inositols in hand, we proceeded to prepare the galactosaminyl-*chiro*-inositol isomers. We found that the glycosylation reaction of each of the three different acceptors **8**, **9**, and **10** was optimally performed with a different glycosyl donor. In the case of acceptor **10**, glycosylation was most effectively accomplished with trichloroacetimidate **17** (Scheme 5), readily available from triacetyl-galactal as previously reported.³¹ Thus, treatment of *chiro*-inositol isomer **10** with **17** in the presence of trimethylsilyl triflate produced a 72% yield of a separable mixture of disac-



Scheme 1. Reagents and conditions: (a) vinylmagnesium bromide (10 equiv), THF, 0 °C to rt, 12 h; (b) *tert*-butylchlorodimethylsilane, imidazole, DMF, 12 h; (c) O₃, 3:1 MeOH–CH₂Cl₂, pyr (2 equiv), –78 °C; NaBH₄, –78 °C to rt; (d) NaH, BnBr, THF, TBAI, 12 h; (e) NaH, PMBCl, THF, TBAI, 2 d; (f) TBAF, THF, 2 h.



Scheme 2. Reagents and conditions: (a) (COCl)₂, DMSO, THF, -78 °C, 30 min; 2-Pr₂NEt, -78 °C to rt; (b) SnI₂ (6 equiv), THF, *t*-BuOH (3 equiv), -78 °C, 3 h; (c) Bu₂SnO, benzene, reflux; BnBr, Bu₄NBr, reflux, 45 min; (d) NaH, BnBr, DMF; (e) DDQ, CH₂Cl₂-H₂O, rt, 1.5 h.



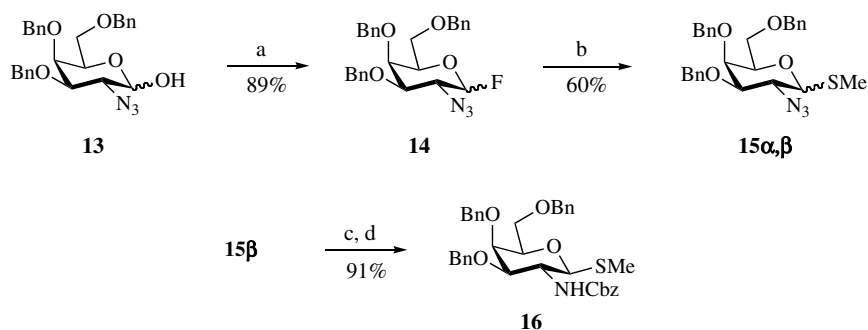
Scheme 3. Reagents and conditions: (a) Bu₂SnO, benzene, reflux; CH₃I, DMF, reflux; (b) DDQ, CH₂Cl₂-H₂O; (c) NaH, BnBr, DMF; (d) NaH, BnBr, Bu₄NI, DMF.

charides **22α** and **22β** in a ratio of 1:1.8. Each anomer was individually subjected to dissolving metal reduction followed by acetic anhydride to produce the acetylated galactosaminyl-(1→3)-*chiro*-inositol anomers **18α** and **18β**, respectively.

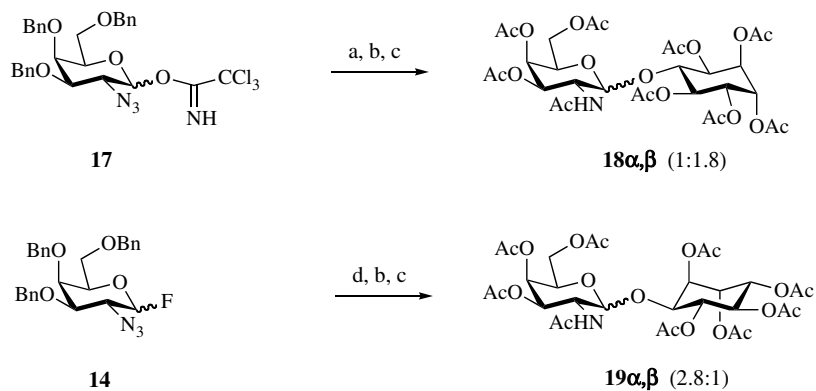
By contrast, with *chiro*-inositol acceptor **9**, the highest coupling yield was obtained by glycosylation with glycosyl fluoride **14**, readily available from known³² azide **13**, by treatment with DAST³³ (Scheme 4). Treatment of **14** with **9** in the presence of silver triflate and Cp₂ZrCl₂³⁴

produced an 89% yield of anomeric disaccharides **23α** and **23β** (2.8:1), each of which underwent clean reduction and acetylation as above to produce the acetylated galactosaminyl-(1→2)-*chiro*-inositol anomers **19α** and **19β**. The anomeric configuration was confirmed by examining the magnitude of the *J*_{H,C} coupling constant for the anomeric carbon in the ¹³C NMR spectrum according to the established method.^{35,36}

As expected, glycosylation of *chiro*-inositol **8** at its free axial hydroxyl group proved more difficult than



Scheme 4. Reagents and conditions: (a) DAST, THF, -42 °C to rt; (b) Bu₃SnSMe, SnCl₄, ClCH₂CH₂Cl, 0 °C; (c) H₂ (1 atm), Pd/CaCO₃/PbO; (d) CbzCl, py, CH₂Cl₂.

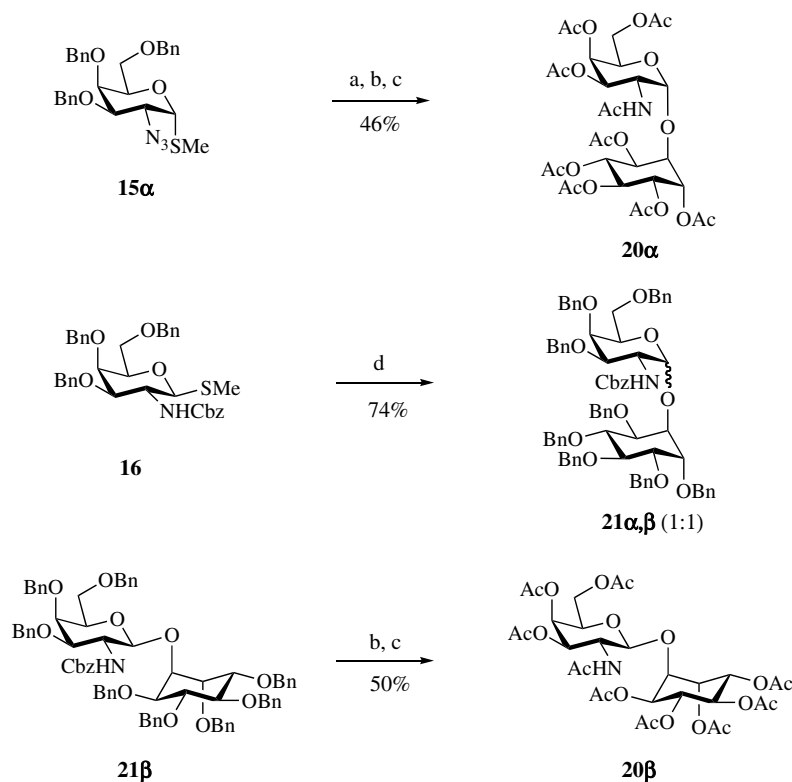


Scheme 5. Reagents and conditions: (a) **10**, TMSOTf, 4 Å MS, Et₂O, –78 °C (72% yield); (b) Na, NH₃ (l), –78 °C; (c) Ac₂O, Et₃N, DMAP, THF, DMF; (d) **9**, AgOTf, Cp₂ZrCl₂, toluene, 4 Å MS, –42 °C to rt (89% yield).

the others. In every case we attempted in which the glycosyl donor did not have a participating group at position 2, exclusive formation of the α -disaccharide was observed. This is consistent with earlier observations of complete α -selectivity in glycosylations of certain axial hydroxyl groups with 2-azido-2-deoxypyranosyl donors,³⁷ possibly representing a steric mismatch³⁸ in the transition state for the β -glycoside. The best yield of α disaccharide was obtained by glycosylation with methyl thioglycoside **15 α** , prepared as shown in Scheme 4. Thus, treatment of **8** with **15 α** in the presence of silver

triflate and phenylselenenyl chloride³⁹ (Scheme 6) produced the α disaccharide in 67% yield as the only anomer. Reduction and acetylation, as before, produced the acetylated α -D-galactosaminyl-(1 \rightarrow 1)-*chiro*-inositol **20 α** .

To prepare the β anomer, we utilized glycosyl donor **16**, possessing the participating benzyloxycarbonyl (Cbz) protective group at position 2. Compound **16** was prepared as shown in Scheme 4. Treatment of **16** with **8**, silver triflate, and phenylselenenyl chloride, as above, produced a 1:1 mixture of anomeric disaccha-



Scheme 6. Reagents and conditions: (a) **8**, AgOTf, PhSeCl, 4 Å MS, toluene, –42 °C; (b) Na, NH₃ (l), –78 °C; (c) Ac₂O, Et₃N, DMAP, THF, DMF; (d) **8**, AgOTf, PhSeCl, 4 Å MS, 3:1 toluene–CH₂Cl₂, –42 °C.

rides (Scheme 6) in 76% yield. These were separated chromatographically, and the β anomer was reduced and acetylated as before to supply the acetylated β -D-galactosaminy-(1 \rightarrow 1)-*chiro*-inositol **20 β** . The lack of β selectivity despite the participating Cbz group probably reflects a strong steric mismatch³⁸ in the β transition state.

3. Conclusions

We have developed an enantiospecific synthesis for the three penta-*O*-benzyl-D-*chiro*-inositol isomers **8**, **9**, and **10** from L-arabinose. These partially protected cyclitols will be useful in the preparation of D-*chiro*-inositol-containing oligosaccharides. We have demonstrated this utility by preparing all of the six isomers in the 2-acetamido-2-deoxy-D-galactopyranosyl-D-*chiro*-inositol series. Since D-arabinose is also readily available, our synthesis may, in principle, also be used to prepare L-*chiro*-inositols and their derivatives.

4. Experimental

4.1. General methods

All reactions, with the exception of ozonolysis, were performed under an atmosphere of argon. Solvents and reagents obtained from commercial sources were used without further purification with the following exceptions. Tetrahydrofuran (THF) was distilled prior to use from sodium-benzophenone ketyl; pyridine and benzene were distilled from CaH₂; Ac₂O was fractionally distilled. Anhydrous reactions were performed with material dried by repeated coevaporation with toluene. TLC and preparative TLC were performed using J. T. Baker glass-backed silica gel plates (0.25 mm thickness) with 254-nm fluorescent indicator. The chromatograms were visualized by (a) ultraviolet illumination and (b) dipping in the Hanes-Isherwood solution (1 g of (NH₄)₆Mo₇O₂₄·4H₂O, 10 mL of 1 N HCl, 3 mL of HClO₄ in 90 mL of H₂O), followed by heating. Flash chromatography was performed on J. T. Baker silica gel (40 mesh). Ozone was generated using an ozone generator purchased from Ozone Pure Water, Inc. (model 2HD). NMR spectra were recorded on a Bruker AM 300 spectrometer using Me₄Si as an internal standard for ¹H in CDCl₃. Solutions of SmI₂ were titrated with I₂ prior to use.

4.2. (2*R*,3*S*,4*S*,5*R*/*S*)-2,3,4-Tri-*O*-benzyl-1,6-bis-*O*-(*tert*-butyldimethylsilyl)hexane-1,2,3,4,5,6-hexaol (**4a**/**4b**)

A solution of **1** (1.8 g, 4.3 mmol) in THF (27 mL) was slowly added over a period of 1 h to a stirred solution

of vinylmagnesium bromide in THF (25.2 mL of 1.7 M solution, 42.8 mmol) at 0 °C. After the solution was stirred at 0 °C for 8 h and then overnight at room temperature, satd aq NH₄Cl and 2 M HCl were added. The layers were separated, and the aqueous layer was extracted with Et₂O. The combined organic layers were washed, dried with MgSO₄ and evaporated. After chromatography of the residue on silica gel (2:1 hexanes–EtOAc), **2** (1.75 g, 91%) was obtained. The ratio was about 1.7:1 favoring the *syn*-diol as determined by ¹H NMR spectroscopy. Data for **2a**: ¹H NMR δ 7.35–7.22 (m, 15H, aromatic), 5.93 (ddd, 1H, *J* 17.1, 10.6, 5.6 Hz), 5.33 (dd, 1H, *J* 17.2, 3.0 Hz), 5.20 (dd, 1H, *J* 10.6, 3.0 Hz), 4.75–4.33 (m, 7H), 3.91–3.61 (m, 5H), 2.8 (br s, 1H, OH), 2.2 (br s, 1H, OH). Data for **2b**: ¹H NMR δ 7.25–7.22 (m, 15H, aromatic), 5.94 (ddd, 1H, *J* 17.2, 10.6, 5.4 Hz), 5.41 (ddd, 1H, *J* 17.2, 2.9, 1.4 Hz), 5.25 (ddd, 1H, *J* 10.6, 2.9, 1.5 Hz), 4.76–4.39 (m, 7H), 3.96–3.91 (m, 2H), 3.82–3.69 (m, 2H), 3.60 (dd, 1H, *J* 5.3, 3.3 Hz), 2.82 (d, 1H, OH), 2.20 (ψ t, 1H, OH).

To a solution of **2** (1.75 g, 3.9 mmol) in DMF (4.2 mL) were added imidazole (2.12 g, 31.2 mmol) and TBSCl (2.35 g, 15.6 mmol) at 0 °C and stirred for 12 h. Satd aq NaHCO₃ was added, the layers were separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were dried with MgSO₄ and evaporated. After chromatography of the residue on silica gel (29:1 hexanes–Et₂O), **3** (2.3 g, 86%) was obtained. Data for **3a**: ¹H NMR δ 7.35–7.22 (m, 15H, aromatic), 6.05 (ddd, 1H, *J* 17.2, 10.6, 5.1 Hz), 5.19 (ddd, 1H, *J* 17.2, 3.5, 1.7 Hz), 5.08 (ddd, 1H, *J* 10.6, 3.5, 1.6 Hz), 4.72–4.35 (m, 6H, CH₂Ph), 4.32 (ψ t, 1H, *J* 5.5 Hz), 3.98 (dd, 1H, *J* 11.1, 2.3 Hz), 3.87 (dd, 1H, *J* 5.6, 2.2 Hz), 3.78 (dd, 1H, *J* 5.5, 2.2 Hz), 0.88 (2s, 18H), 0.05 (2s, 12H). Data for **3b**: ¹H NMR δ 7.35–7.22 (m, 15H, aromatic), 5.99 (ddd, 1H, *J* 17.2, 10.3, 6.8 Hz), 5.25 (dd, 1H, *J* 17.2, 1.4 Hz), 5.16 (dd, 1H, *J* 10.3, 1.4 Hz), 4.77–4.43 (m, 6H, CH₂Ph), 4.32 (m, 1H), 3.96 (dd, 1H, *J* 11.2, 2.9 Hz), 3.89–3.83 (m, 2H), 3.72–3.66 (m, 2H), 0.88 (2s, 18H), 0.05 (2s, 12H).

A solution containing **3** (150 mg, 0.22 mmol) and pyridine (50 μ L) in CH₂Cl₂ (0.5 mL)–MeOH (1.5 mL) was treated with ozone at –78 °C until TLC (3:1 hexanes–Et₂O) showed complete disappearance of the starting material, at which point NaBH₄ (99.0 mg, 2.64 mmol) was added. The resulting mixture was allowed to reach room temperature. After stirring overnight at this temperature, the solvent was removed under reduced pressure. The residue was dissolved in Et₂O and washed with water. The aqueous layer was then extracted with Et₂O, and the combined organic extracts were dried over MgSO₄ and evaporated. Flash-column chromatography (14:1 hexanes–Et₂O) gave **4a** (66.9 mg), **4b** (43.6 mg), and **4c** (7.4 mg) (combined yield 78%). Data for **4a**: ¹H NMR δ 7.35–7.15 (m, 15H, aromatic), 4.76–4.54 (m,

6H, CH₂Ph), 3.98–3.92 (m, 2H), 3.87–3.77 (m, 4H), 3.59 (dd, 1H, *J* 6.3, 9.8 Hz), 3.49 (dd, 1H, *J* 6.3, 9.8 Hz), 2.8 (d, 1H, *J* 5.2 Hz, OH), 0.87 (2s, 18H), 0.05 (4s, 12H). HRESIMS: calcd for [C₃₉H₆₀NaO₆Si₂+Na]⁺, *m/z* 703.3821; found, *m/z* 703.3824. Data for **4b**: ¹H NMR δ 7.35–7.15 (m, 15H, aromatic), 4.82–4.41 (m, 6H, CH₂Ph), 4.08 (dd, 1H, *J* 11.2, 2.2 Hz), 4.04 (dd, 1H, *J* 7.2, 2.3 Hz), 3.89–3.72 (m, 5H), 3.69 (dd, 1H, *J* 10.2, 4.6 Hz), 2.75 (d, 1H), 0.87 (2s, 18H), 0.05 (4s, 12H). HRESIMS: calcd for [C₃₉H₆₀NaO₆Si₂+Na]⁺, *m/z* 703.3821; found, *m/z* 703.3810. Data for **4c**: ¹H NMR δ 7.35–7.15 (m, 15H, aromatic), 4.80–4.38 (m, 6H, CH₂Ph), 4.04–3.93 (m, 3H), 3.89 (dd, 1H, *J* 11.4, 4.6 Hz), 3.79–3.70 (m, 3H), 3.58 (m, 1H), 2.27 (ψt, 1H, *J* 6.2 Hz, OH), 0.87 (2s, 18H), 0.05 (4s, 12H).

4.3. 1,2,3,4,5-Penta-*O*-benzyl-*D*-chiro-inositol (**8**)¹⁶

To a solution of **4a** (56 mg, 0.082 mmol) in THF (450 μL) at 0 °C was added NaH (60%, 9.9 mg, 0.25 mmol), and the mixture was stirred at room temperature for 1 h. After cooling of the mixture to 0 °C, benzyl bromide (20 μL, 0.16 mmol) and TBAI (3 mg, 0.008 mmol) were added. The white slurry was stirred overnight at room temperature. Satd aq NH₄Cl was slowly added at 0 °C, the mixture was diluted with CH₂Cl₂, the layers were separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were dried with MgSO₄ and evaporated. Flash-column chromatography (24:1 hexanes–Et₂O) gave **5a** (55.8 mg, 88%). Data for **5a**: ¹H NMR δ 7.35–7.15 (m, 20H, aromatic), 4.84–4.39 (m, 8H, CH₂Ph), 4.06–3.82 (m, 4H), 3.74–3.66 (m, 4H), 0.85 (2s, 18H), 0.05 (4s, 12H).

To a solution of **5a** (570 mg, 0.74 mmol) in THF (2.8 mL) was added TBAF (3 mL of 1 M solution in THF, 3 mmol) at 0 °C, and the resulting solution was warmed to room temperature and stirred for 2 h. The mixture was then treated with satd aq NH₄Cl, diluted with water and extracted with EtOAc. The combined organic extracts were dried with MgSO₄ and concentrated. The residue was chromatographed on silica gel (2:1→1:1 hexanes–EtOAc) to afford diol **6a** (357 mg, 89%). Data for **6a**: ¹H NMR δ 7.4–7.2 (m, 20H, aromatic), 4.81–4.36 (m, 8H, CH₂Ph), 3.93 (ψt, 1H, *J* 4.8, 4.6 Hz), 3.87 (dd, 1H, *J* 12.2, 3.9 Hz), 3.82–3.76 (m, 2H), 3.74–3.66 (m, 3H), 3.54 (dd, 1H, *J* 13.2, 6 Hz), 2.35 (br s, 1H, OH), 2.15 (br s, 1H, OH).

To a solution of (COCl)₂ (54 μL, 0.62 mmol, 3 equiv) in THF (890 μL) at –78 °C was added dropwise DMSO (88 μL, 1.24 mmol, 6 equiv). After 10 min, a solution of **6a** (112 mg, 0.21 mmol) in THF (1.6 mL) was added dropwise via a cannula. After 30 min, *i*-Pr₂EtN (360 μL, 2.1 mmol, 10 equiv) was added, and the mixture was stirred for 30 min at –78 °C and for 2.5 h at room temperature. After this time, it was diluted with

6.9 mL THF and *t*-BuOH (59 μL, 0.62 mmol, 3 equiv). A freshly prepared⁴⁰ solution of SmI₂ (1.26 mmol, 6 equiv) in THF (12.6 mL) was slowly added via a cannula to the above mixture at –78 °C over a period of 30 min. The mixture was stirred for 3 h at –78 °C, after which time it was quenched with satd aq NaHCO₃ (25 mL), and the resulting white slurry was extracted with EtOAc (2 × 25 mL). The organic layer was washed with 10% Na₂S₂O₃ (25 mL) and dried with MgSO₄. Evaporation of the solvent and column chromatography (2:1 hexanes–EtOAc) afforded pure **7a**³⁰ (61 mg, 55% over two steps). Data for **7a**: ¹H NMR δ 7.4–7.22 (m, 20H, aromatic), 5.02, 4.81 (2d, 2H, *J*_{gem} 11.3 Hz, CH₂Ph), 4.99, 4.65 (2d, 2H, *J*_{gem} 10.5 Hz, CH₂Ph), 4.81, 4.65 (2d, 2H, *J*_{gem} 10.7 Hz, CH₂Ph), 4.72, 4.61 (2d, 2H, *J*_{gem} 11.7 Hz, CH₂Ph), 4.07–3.86 (m, 5H, CH-OR), 3.64 (ψt, 1H, *J*_{3,4} 9.1 Hz, H-3 or H-4), 2.31, 2.32 (2br d, 2OH).

A suspension of **7a**³⁰ (22.3 mg, 0.041 mmol) and dibutyltin oxide (0.045 mmol, 11.3 mg) in benzene (20 mL) was fitted with a distillation head and placed in an oil bath at 110 °C until most of the benzene had distilled. An additional portion of benzene (10 mL) was added to the residue, and the mixture was refluxed until again most of the benzene had distilled. The reaction mixture was cooled and treated with BnBr (0.082 mmol, 10 μL) and TBABr (0.045 mmol, 14.6 mg). The mixture was then refluxed for an additional 15 min. At the end of the reaction time, NaHCO₃ was added, and the mixture was extracted with CH₂Cl₂. The combined organic extracts were dried (MgSO₄) and concentrated to dryness. Preparative chromatography (1:1 hexanes–Et₂O) of the residue gave 21.3 mg of product **8**¹⁶ (82% yield). Data for **8**: ¹H NMR δ 7.35–7.25 (m, 25H, aromatic), 4.95–4.51 (m, 10H, CH₂Ph), 4.0–3.74 (m, 6H), 2.4 (s, 1H, OH).

A solution of **8** (3.3 mg, 0.005 mmol) in pyridine (192 μL) was treated with Ac₂O (0.035 mmol, 3.3 μL). After aqueous workup, 2.7 mg of the acetylated product was obtained. ¹H NMR (inositol numbering is the same as in **8**) δ 7.35–7.25 (m, 25H, aromatic), 5.33 (ψt, 1H, *J* 3.4 Hz, H-6), 4.94–4.47 (m, 10H, CH₂Ph), 3.95 (ψt, 1H, *J* 9.4 Hz), 3.89 (dd, 1H, *J* 9.7, 3.2 Hz), 3.76 (ψt, 1H, *J* 9.3 Hz), 3.72–3.69 (m, 2H), 2.0 (s, 3H, OAc).

4.4. 1,2,3,5,6-Penta-*O*-benzyl-*D*-chiro-inositol (**10**)

To a solution of **4b** (298 mg, 0.44 mmol) in THF (2.1 mL) at 0 °C was added NaH (60%, 69.9 mg, 1.76 mmol), and the mixture was stirred at room temperature for 1 h. After cooling of the mixture to 0 °C, *p*-methoxybenzyl chloride (237 μL, 1.76 mmol) and TBAI (81 mg, 0.22 mmol) were added. The resulting white slurry was stirred for 3 days at room temperature. Satd aq NH₄Cl was slowly added at 0 °C, the mixture was diluted with CH₂Cl₂, the layers were separated,

and the aqueous layer was extracted with CH_2Cl_2 . The combined organic layers were dried with MgSO_4 and evaporated. The residue was diluted with THF (1.7 mL) and treated with TBAF (1.75 mL of 1 M solution in THF, 1.75 mmol) at 0 °C. The resulting solution was warmed to room temperature and stirred for 2 h. The mixture was then treated with satd aq NH_4Cl , diluted with water, and extracted with EtOAc. The combined organic extracts were dried with MgSO_4 and concentrated. The residue was chromatographed on silica gel (2:1→1:1 hexanes–EtOAc) to afford diol **6b** (183 mg, 73% over two steps). Data for **6b**: ^1H NMR δ 7.35–7.2 (m, 17H, aromatic), 6.85 (d, 2H, aromatic), 4.81–4.36 (m, 8H, CH_2Ph), 3.92 (ψt , 1H, J 4.7 Hz), 3.88–3.65 (m, 6H), 3.78 (s, 3H, OCH_3), 3.54 (m, 1H), 2.28 (ψt , 1H, OH), 1.99 (ψt , 1H, OH).

To a solution of $(\text{COCl})_2$ (56 μL , 0.64 mmol, 3 equiv) in THF (1 mL) at -78 °C was added dropwise DMSO (91 μL , 1.28 mmol, 6 equiv). After 10 min, a solution of **6b** (122 mg, 0.21 mmol) in THF (1.6 mL) was added dropwise via a cannula. After 30 min, *i*-Pr₂EtN (370 μL , 2.1 mmol, 10 equiv) was added, and the mixture was stirred for 30 min at -78 °C and for 2.5 h at room temperature. After this time, it was diluted with THF (6.9 mL) and *t*-BuOH (61 μL , 0.63 mmol, 3 equiv). A freshly prepared⁴⁰ solution of SmI_2 (1.28 mmol, 6 equiv) in THF (12.8 mL) was slowly added via a cannula to the above mixture at -78 °C over a period of 30 min. The mixture was stirred for 3 h at -78 °C, after which time it was quenched with satd aq NaHCO_3 (25 mL), and the resulting white slurry was extracted with EtOAc (2×25 mL). The organic layer was washed with 10% $\text{Na}_2\text{S}_2\text{O}_3$ (25 mL), and dried with MgSO_4 . Evaporation of the solvent and column chromatography (2:1 hexanes–EtOAc) afforded pure **7b** (53 mg, 43% over two steps). Data for **7b**: ^1H NMR δ 7.35–7.2 (m, 17H, aromatic), 6.85 (d, 2H, aromatic), 5–5.57 (m, 8H, CH_2Ph), 4.05 (ψt , 1H, J 3.2 Hz), 3.97 (ψt , 1H, J 9.1 Hz), 3.92–3.91 (m, 2H), 3.86 (dd, 1H, J 9.4, 3.0 Hz), 3.78 (s, 3H, OCH_3), 3.62 (ψt , 1H, J 9.1 Hz), 2.5 (s, 1H, OH), 2.35 (s, 1H, OH).

A solution of **7b** (68.5 mg, 0.12 mmol) in DMF (1.1 mL) at 0 °C was treated with NaH (0.72 mmol, 29 mg of a 60% oil dispersion). After 0.5 h, the mixture was treated with benzyl bromide (0.6 mmol, 72 μL) and allowed to warm to room temperature. After overnight stirring, the mixture was cooled to 0 °C, and water was added. The aqueous layer was washed three times with CH_2Cl_2 , and the combined organic extracts were dried (MgSO_4) and concentrated under reduced pressure. A solution of the above residue in CH_2Cl_2 (3 mL) at 0 °C was treated with 330 μL of water and DDQ (0.12 mmol, 28.4 mg), and stirred at room temperature for 2 h. Satd aq NaHCO_3 was added, and the aqueous layer was separated from the organic layer and washed three times with CH_2Cl_2 . The combined or-

ganic extracts were dried with MgSO_4 and concentrated to dryness. Column chromatography (2:1 hexanes–Et₂O) gave 54.5 mg of **10** (72% yield for two steps). Data for **10**: ^1H NMR δ 7.4–7.10 (m, 25H, aromatic), 4.94–4.30 (m, 10H, CH_2Ph), 3.98 (m, 1H), 3.82–3.75 (m, 2H), 3.70–3.62 (m, 3H), 2.5 (s, 1H, OH). Racemic **10** has been previously reported.⁴¹

4.5. Methyl 3,4,6-tri-*O*-benzyl-2-benzyloxycarboxamido-2-deoxy-1-thio- β -D-galactopyranoside (**16**)

Compound **13**³² (191 mg, 0.40 mmol) was dissolved in THF (2.3 mL), and the resulting solution was cooled to -42 °C. DAST (59 μL , 0.60 mmol) was added, and the bath was removed immediately. The mixture was stirred at room temperature for 20 min, and the excess DAST was quenched with MeOH at -42 °C. CH_2Cl_2 (5 mL) was added, and the organic layer was washed with NaHCO_3 (2×3 mL) and dried with MgSO_4 . Purification via flash silica gel chromatography (9:1 hexanes–EtOAc) afforded 80.6 mg of **14 β** and 62 mg of **14 α** (89% combined yield). ^1H NMR (CDCl_3) of **14 β** : δ 7.40–7.20 (m, 15H, aromatic), 4.95 (dd, 1H, J 52.6, 7.6 Hz, H-1 β anomer), 4.89 (d, 1H, J 11.6 Hz, CH_2Ph), 4.72 (d, 1H, J 11.7 Hz, CH_2Ph), 4.66 (d, 1H, J 11.7 Hz, CH_2Ph), 4.56 (d, 1H, J 11.4 Hz, CH_2Ph), 4.48 (d, 1H, J 11.7 Hz, CH_2Ph), 4.41 (d, 1H, J 11.7 Hz, CH_2Ph), 3.99–3.89 (m, 2H), 3.64–3.60 (m, 3H), 3.52 (dd, 1H, J 10.4, 2 Hz). ^1H NMR (CDCl_3) of **14 α** : δ 7.40–7.20 (m, 15H, aromatic), 5.67 (dd, 1H, J 54.6, 2.6 Hz, H-1 α anomer), 4.89 (d, 1H, J 11.2 Hz, CH_2Ph), 4.76 (d, 1H, J 11.4 Hz, CH_2Ph), 4.70 (d, 1H, J 11.4 Hz, CH_2Ph), 4.54 (d, 1H, J 11.2 Hz, CH_2Ph), 4.52 (d, 1H, J 11.7 Hz, CH_2Ph), 4.43 (d, 1H, J 11.7 Hz, CH_2Ph), 4.11 (ψt , 1H, J 6.6 Hz), 4.09 (ψs , 1H), 4.04–3.90 (m, 2H), 3.58 (ψd , 2H, J 6.6 Hz).

A mixture of fluorides **14** (142 mg, 0.29 mmol) was dried by coevaporation with toluene and then cooled to 0 °C. Bu_3SnSMe in $\text{CH}_2\text{ClCH}_2\text{Cl}$ (0.44 mmol, 2 mL, of a 74 mg/mL stock solution) was added, and the resulting solution was stirred for 5 min. SnCl_4 in $\text{CH}_2\text{ClCH}_2\text{Cl}$ (0.44 mmol, 3.2 mL of a 37.1 mg/mL stock solution) was added, and stirring was continued for 30 min at 0 °C. The reaction was quenched by addition of 1 M NaHCO_3 (2 mL). The organic layer was separated from the aqueous layer, and the latter was extracted with CH_2Cl_2 (2×3 mL). The combined organic extracts were dried with MgSO_4 and concentrated. Purification via flash silica gel chromatography (6:1 hexanes–Et₂O) afforded 26.8 mg of **15 β** and 61.5 mg of **15 α** (60% combined yield). ^1H NMR (CDCl_3) of **15 β** : δ 7.40–7.25 (m, 15H, aromatic), 4.89 (d, 1H, J 11.6 Hz, CH_2Ph), 4.73 (d, 1H, J 11.6 Hz, CH_2Ph), 4.68 (d, 1H, J 11.6 Hz, CH_2Ph), 4.56 (d, 1H, J 11.6 Hz, CH_2Ph), 4.46 (d, 1H, J 11.7 Hz, CH_2Ph), 4.40 (d, 1H, J 11.7 Hz, CH_2Ph), 4.14 (d, 1H, J 10 Hz, H-1 β anomer),

3.96 (ψ d, 1H, J 2.6 Hz), 3.87 (ψ t, 1H, J 9.9 Hz), 3.61–3.52 (m, 3H), 3.42 (dd, 1H, J 9.7, 2.7 Hz), 2.20 (s, 3H, SCH₃). ¹H NMR (CDCl₃) of **15 α** : δ 7.40–7.25 (m, 15H, aromatic), 5.31 (d, 1H, J 5.5 Hz, H-1 α anomer), 4.88 (d, 1H, J 11.3 Hz, CH₂Ph), 4.71 (s, 2H, CH₂Ph), 4.52 (d, 1H, J 11.3 Hz, CH₂Ph), 4.50 (d, 1H, J 11.8 Hz, CH₂Ph), 4.41 (d, 1H, J 11.8 Hz, CH₂Ph), 4.36 (dd, 1H, J 10.5, 5.5 Hz), 4.24 (ψ t, 1H, J 6.4 Hz), 3.97 (ψ d, 1H, J 1.9 Hz), 3.76 (dd, 1H, J 10.5, 2.7 Hz), 3.59 (dd, 1H, J 9.3, 6.6 Hz), 3.54 (dd, 1H, J 9.3, 6.3 Hz), 2.21 (s, 3H, SCH₃).

A mixture of **15 β** (70.7 mg, 0.14 mmol) and Lindlar's catalyst (141 mg) in THF (16.5 mL) was stirred at room temperature under an H₂ atmosphere for 7 h. The reaction mixture was filtered through Celite, rinsed with EtOAc, and concentrated. The residue (34.3 mg) was dissolved in CH₂Cl₂ (390 μ L), and Cbz-Cl (12.2 μ L, 0.086 mmol) was added, followed by slow addition of pyridine (7 μ L). The mixture was stirred for 2 h at room temperature, after which time it was diluted with CH₂Cl₂ (4 mL), and the organic phase was washed with 1 M NaHCO₃ (1 mL), dried with MgSO₄, and concentrated. Purification via flash silica gel chromatography (3:1 hexanes–EtOAc) afforded 40.1 mg of **16** (91% yield over two steps). ¹H NMR (CDCl₃) of **16**: δ 7.40–7.20 (m, 20H, aromatic), 5.14 (s, 2H, CH₂Ph), 4.95 (d, 1H, J 11.6 Hz, CH₂Ph), 4.84 (m, 1H), 4.68 (d, 1H, J 11.8 Hz, CH₂Ph), 4.65 (br s, 1H), 4.62 (d, 1H, J 11.6 Hz, CH₂Ph), 4.50 (d, 1H, J 11.8 Hz, CH₂Ph), 4.48 (d, 1H, J 11.8 Hz, CH₂Ph), 4.45 (d, 1H, J 11.7 Hz, CH₂Ph), 4.04 (m, 1H), 3.87–3.86 (m, 2H), 3.64–3.62 (m, 3H), 2.21 (s, 3H, SCH₃). HRESIMS: calcd for [C₃₆H₃₉NO₆S+Na]⁺, m/z 636.2390; found, m/z 636.2405.

4.6. 3-*O*-(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy- α,β -D-galactopyranosyl)-1,2,4,5,6-penta-*O*-benzyl-D-*chiro*-inositol (**22 α,β**)

To a pre-dried mixture of **10** (5.2 mg, 0.0082 mmol) and **17**³¹ (11.3 mg, 0.0182 mmol) were added 4 Å MS and 290 μ L anhyd Et₂O. The reaction mixture was cooled to –78 °C, and TMSOTf (15 μ L of 10 μ L TMSOTf/mL of Et₂O solution) was added. The resulting mixture was stirred at –78 °C for 10 min and was quenched by the addition of 1 M NaHCO₃ (2 mL). It was filtered through Celite, the organic layer was separated from the aqueous layer, and the latter was extracted with Et₂O (3 \times 3 mL). The combined organic extracts were dried with MgSO₄ and concentrated. Purification via preparative TLC (4:1 hexanes–EtOAc) yielded 2.3 mg of the α anomer, **22 α** , and 4.1 mg of the β anomer, **22 β** (72% combined yield). Data for **22 α** : ¹H NMR (CDCl₃) δ 7.4–7.05 (m, 40H, aromatic), 5.63 (d, 1H, J 3.3 Hz, H-1 α anomer), 5.01 (d, 1H, J 10.4 Hz, CH₂Ph), 4.84 (d, 1H, J 10.4 Hz, CH₂Ph), 4.79 (d, 1H, J 11.4 Hz,

CH₂Ph), 4.66–4.24 (m, 14H), 4.16 (dd, 1H, J 9.4, 9.2 Hz), 3.96 (dd, 1H, J 9.7, 9.2 Hz), 3.88–3.73 (m, 5H), 3.56–3.43 (m, 4H). HRESIMS: calcd for [C₆₈H₆₉N₃O₁₀+Na]⁺, m/z 1110.4875; found, m/z 1110.4893. Data for **22 β** : ¹H NMR (CDCl₃) δ 7.4–7.05 (m, 40H, aromatic), 4.99 (d, 1H, J 10 Hz, CH₂Ph), 4.96 (d, 1H, J 11.2 Hz, CH₂Ph), 4.83 (d, 1H, J 8 Hz, H-1 β anomer), 4.74–4.14 (m, 15H), 3.95–3.55 (m, 10H), 3.29 (dd, 1H, J 10.4, 2.8 Hz). HRESIMS: calcd for [C₆₈H₆₉N₃O₁₀+Na]⁺, m/z 1110.4875; found, m/z 1110.4888.

4.7. 3-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- α -D-galactopyranosyl)-1,2,4,5,6-penta-*O*-acetyl-D-*chiro*-inositol (**18 α**)

Sodium (43 mg, 1.87 mmol) was added to NH₃ [(l), ~5 mL] at –78 °C, and the mixture was stirred for 2 min under N₂ to form a blue solution, into which was added compound **22 α** (8.8 mg, 0.0081 mmol) in dry THF (2 mL). The resulting mixture was stirred for 20 min at –78 °C, and then the reaction was quenched with abs MeOH (1.5 mL) at –78 °C. The NH₃ was removed with a stream of air, and additional MeOH was added to bring the total volume of solution in the reaction flask to ~10 mL. After neutralization with Dowex-50 X8 (407 mg), the mixture was filtered, rinsed with satd NH₃ in MeOH (20 mL), and concentrated under reduced pressure. The crude product was further dissolved in DMF–THF (470 μ L, 1:1), and DMAP (small amount), Et₃N (235 μ L), and finally Ac₂O (80 μ L) were added. The mixture was stirred for 24 h at room temperature and then diluted with EtOAc (10 mL). It was washed with water (2 \times 3 mL), dried with MgSO₄, and concentrated under reduced pressure. Purification via preparative TLC (EtOAc) gave 3.1 mg of **18 α** (53% over two steps). The ¹H NMR spectrum was identical to that published.²⁴ HRESIMS: calcd for [C₃₀H₄₁O₁₉N+H]⁺, m/z 720.2351; found, m/z 720.2369.

4.8. 3-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-galactopyranosyl)-1,2,4,5,6-penta-*O*-acetyl-D-*chiro*-inositol (**18 β**)

Sodium (28.5 mg, 1.24 mmol) was added to NH₃ [(l), ~5 mL] at –78 °C, and the mixture was stirred for 2 min under N₂ to form a blue solution, into which was added compound **22 β** (4.1 mg, 0.0038 mmol) in dry THF (2 mL). The resulting mixture was stirred for 20 min at –78 °C, and then the reaction was quenched with abs MeOH (2 mL) at –78 °C. The NH₃ was removed with a stream of air, and additional MeOH was added to bring the total volume of solution in the reaction flask to ~10 mL. After neutralization with Dowex-50 X8 (270 mg), the mixture was filtered, rinsed with satd NH₃ in MeOH (20 mL), and concentrated under reduced pressure. The crude product was further dis-

solved in 1:1 DMF–THF (220 μ L), and DMAP (small amount), Et₃N (110 μ L), and finally Ac₂O (35 μ L) were added. The mixture was stirred for 24 h at room temperature and then diluted with EtOAc (10 mL). It was washed with water (2 \times 2 mL), dried with magnesium sulfate, and concentrated under reduced pressure. Purification via preparative TLC (EtOAc) gave 1.5 mg of **18 β** (56% over two steps). ¹H NMR (CDCl₃): δ 5.79 (dd, 1H, *J* 11.2, 3.3 Hz), 5.51 (d, 1H, *J* 7 Hz, H-1 β anomer), 5.37 (dd, 1H, *J* 11.4, 3.3 Hz), 5.36 (dd, 1H, *J* 4.3, 3.8 Hz), 5.3–5.22 (m, 5H), 4.25 (dd, 1H, *J* 9.6, 4.7 Hz), 4.12 (m, 1H), 4.08–3.98 (m, 2H), 3.17 (m, 1H, NHAc), 2.20 (s, 3H, Ac), 2.18 (s, 3H, Ac), 2.12 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.88 (s, 3H, Ac). HRESIMS: calcd for [C₃₀H₄₁O₁₉N+H]⁺, *m/z* 720.2351; found, *m/z* 720.2335.

4.9. 2-*O*-(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy- α,β -D-galactopyranosyl)-1,3,4,5,6-penta-*O*-benzyl-D-*chiro*-inositol (**23 α,β**)

To a pre-dried mixture of donor **14** (6.8 mg, 0.014 mmol; see Experimental for **16** for preparation of **14**) and acceptor **9** (13.6 mg, 0.022 mmol) were added 4 Å MS, toluene (1.3 mL), and Cp₂ZrCl₂ (20.7 mg, 0.071 mmol). The mixture was cooled to –42 °C, and AgOTf (36.5 mg, 0.14 mmol) was added. It was stirred for 5 min at –42 °C and then allowed to warm to room temperature. The reaction was stirred at room temperature for 2.5 h, after which time it was quenched by the addition of 1 M NaHCO₃ (2 mL), diluted with 6 mL of CH₂Cl₂, and filtered through Celite. The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 \times 3 mL). The combined organic extracts were dried with MgSO₄ and concentrated. Purification via preparative TLC (4:1 hexanes–EtOAc) afforded 10.1 mg of **23 α** and 3.6 mg of **23 β** (89% combined yield). Data for **23 α** : ¹H NMR (CDCl₃) δ 7.35–7.10 (m, 40H, aromatic), 4.95 (d, 1H, *J* 11.7 Hz, CH₂Ph), 4.91 (d, 1H, *J* 10.6 Hz, CH₂Ph), 4.89 (d, 1H, *J* 4 Hz, H-1 α anomer), 4.79 (d, 1H, *J* 10.9 Hz, CH₂Ph), 4.78 (d, 1H, *J* 10.5 Hz, CH₂Ph), 4.75 (d, 1H, *J* 10.1 Hz, CH₂Ph), 4.70 (d, 1H, *J* 11.8 Hz, CH₂Ph), 4.67 (d, 1H, *J* 12.2 Hz, CH₂Ph), 4.65–4.28 (m, 9H), 4.24 (dd, 1H, *J* 6.5, 6.7 Hz), 4.11 (dd, 1H, *J* 9.5, 2.4 Hz), 3.96–3.77 (m, 5H), 3.73–3.65 (m, 3H), 3.53–3.43 (m, 2H). HRESIMS: calcd for [C₆₈H₆₉N₃O₁₀+Na]⁺, *m/z* 1110.4881; found, *m/z* 1110.4865. Data for **23 β** : ¹H NMR (CDCl₃) δ 7.40–7.10 (m, 40H, aromatic), 4.95 (d, 1H, *J* 10.9 Hz, CH₂Ph), 4.93 (d, 1H, *J* 11.3 Hz, CH₂Ph), 4.91 (d, 1H, *J* 10.6 Hz, CH₂Ph), 4.88 (d, 1H, *J* 10.2 Hz, CH₂Ph), 4.84–4.35 (m, 13H), 4.13 (dd, 1H, *J* 9.5, 2.9 Hz), 3.99–3.82 (m, 6H), 3.60 (t, 1H, *J* 7.1 Hz), 3.55 (dd, 1H, *J* 4.2, 2.4 Hz), 3.48–3.39 (m, 2H), 3.30 (dd, 1H, *J* 10.3, 2.8 Hz). HRESIMS: calcd for [C₆₈H₆₉N₃O₁₀+Na]⁺,

m/z 1110.4881; found, *m/z* 1110.4892. ¹H-Coupled ¹³C NMR (CDCl₃) of **23 β** : δ 102.78 (d, *J* 163 Hz), which confirmed the presence of the β -glycosidic bond.^{35,36}

4.10. 2-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- α -D-galactopyranosyl)-1,3,4,5,6-penta-*O*-acetyl-D-*chiro*-inositol (**19 α**)

Sodium (41.4 mg, 1.8 mmol) was added to NH₃ [(l), ~5 mL] at –78 °C, and the mixture was stirred for 2 min under N₂ to form a blue solution, into which was added compound **23 α** (10 mg, 0.0092 mmol) in dry THF (2 mL). The resulting mixture was stirred for 20 min at –78 °C, and then the reaction was quenched with abs MeOH (3.5 mL) at –78 °C. The NH₃ was removed with a stream of air, and additional MeOH was added to bring the total volume of solution in the reaction flask to ~10 mL. After neutralization with Dowex-50 X8 (391 mg), the mixture was filtered, rinsed with satd NH₃ in MeOH (20 mL), and concentrated under reduced pressure. The crude product was further dissolved in 1:1 DMF–THF (560 μ L), and DMAP (small amount), Et₃N (280 μ L), and finally Ac₂O (90 μ L) were added. The mixture was stirred for 24 h at room temperature and then diluted with EtOAc (10 mL). It was washed with water (2 \times 3 mL), dried with MgSO₄, and concentrated under reduced pressure. Purification via preparative TLC (EtOAc) gave 3.5 mg of **19 α** (53% over two steps). ¹H NMR (CDCl₃): δ 6.12 (d, 1H, *J* 9.3 Hz), 5.64–5.26 (m, 6H), 5.03 (d, 1H, *J* 3.5 Hz, H-1 α anomer), 4.91 (dd, 1H, *J* 11.6, 3.2 Hz), 4.57 (ddd, 1H), 4.23–4.04 (m, 3H), 3.93 (dd, 1H, *J* 10.4, 5.4 Hz), 2.25 (s, 3H, Ac), 2.20 (s, 3H, Ac), 2.15 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.02 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.97 (s, 3H, Ac), 1.96 (s, 3H, Ac). HRESIMS: calcd for [C₃₀H₄₁O₁₉N+H]⁺, *m/z* 720.2351; found, *m/z* 720.2377.

4.11. 2-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-galactopyranosyl)-1,3,4,5,6-penta-*O*-acetyl-D-*chiro*-inositol (**19 β**)

Sodium (20.1 mg, 0.87 mmol) was added to NH₃ [(l), ~5 mL] at –78 °C, and the mixture was stirred for 2 min under N₂ to form a blue solution, into which was added compound **23 β** (4.7 mg, 0.0043 mmol) in dry THF (2 mL). The resulting mixture was stirred for 20 min at –78 °C, and then the reaction was quenched with abs MeOH (2 mL) at –78 °C. The NH₃ was removed with a stream of air, and additional MeOH was added to bring the total volume of solution in the reaction flask to ~10 mL. After neutralization with Dowex-50 X8 (270 mg), the mixture was filtered, rinsed with satd NH₃ in MeOH (20 mL), and concentrated under reduced pressure. The crude product was further dissolved in 1:1 DMF–THF (260 μ L), and DMAP (small

amount), Et₃N (130 μ L), and finally Ac₂O (40 μ L) were added. The mixture was stirred for 24 h at room temperature and then diluted with EtOAc (10 mL). It was washed with water (2 \times 2 mL), dried with MgSO₄, and concentrated under reduced pressure. Purification via preparative TLC (EtOAc) gave 1.3 mg of **19 β** (42% over two steps). ¹H NMR (CDCl₃): δ 5.54 (dd, 1H, *J* 11.2, 3.4 Hz), 5.48–5.32 (m, 5H), 5.23 (dd, 1H, *J* 10.1, 3.2 Hz), 5.10 (d, 1H, *J* 8.1 Hz, H-1 β anomer), 4.25 (dd, 1H, *J* 9.5, 3.4 Hz), 4.19–4.13 (m, 2H), 4.08 (dd, 1H, *J* 11.2, 5.8 Hz), 3.94 (m, 1H), 3.53 (m, 1H, NHAc), 2.22 (s, 3H, Ac), 2.21 (s, 3H, Ac), 2.18 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.95 (s, 3H, Ac). HRESIMS: calcd for [C₃₀H₄₁O₁₉N+H]⁺, *m/z* 720.2351; found, *m/z* 720.2320.

4.12. 1-*O*-(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy- α -D-galactopyranosyl)-2,3,4,5,6-penta-*O*-benzyl-D-*chiro*-inositol (**24**)

To a flame-dried flask were added 4 Å MS, phenylselenium chloride (5.6 mg, 0.029 mmol), and toluene (220 μ L). The mixture was cooled to –42 °C and AgOTf (9.1 mg, 0.035 mmol) was added. A solution of **15 α** (14.8 mg, 0.029 mmol) and **8** (7.4 mg, 0.012 mmol) in toluene (850 μ L) was added to the vigorously stirred mixture. After 1.5 h, 1 M NaHCO₃ (1 mL) was added slowly to the reaction mixture. It was filtered through Celite, the organic layer was separated from the aqueous layer, and the latter was extracted with CH₂Cl₂ (3 \times 3 mL). The combined organic layers were dried with MgSO₄, filtered, and concentrated. Purification via preparative TLC (4:1 hexanes–EtOAc) gave 8.6 mg of **24** (67% yield). ¹H NMR (CDCl₃): δ 7.45–7.15 (m, 40H, aromatic), 4.92 (d, 1H, *J* 10.5 Hz, CH₂Ph), 4.89 (d, 1H, *J* 10.6 Hz, CH₂Ph), 4.86–4.59 (m, 10H), 4.51 (d, 1H, *J* 12.1 Hz, CH₂Ph), 4.50 (d, 1H, *J* 11.1 Hz, CH₂Ph), 4.43 (d, 1H, *J* 12.1 Hz, CH₂Ph), 4.28 (dd, 1H, *J* 8.3, 5.8 Hz), 4.25 (d, 1H, 11.7 Hz, CH₂Ph), 4.19 (d, 1H, *J* 11.6 Hz, CH₂Ph), 4.03 (m, 1H), 3.97 (dd, 1H, *J* 10, 2.7 Hz), 3.92–3.84 (m, 3H), 3.85 (dd, 1H, *J* 7.7, 3.1 Hz), 3.81–3.70 (m, 3H), 3.50 (ψ t, 1H, *J* 8.5 Hz), 3.28 (dd, 1H, *J* 8.5, 5.4 Hz). HRESIMS: calcd for [C₆₈H₆₉N₃O₁₀+Na]⁺, *m/z* 1110.4875; found, *m/z* 1110.4846. ¹H-Coupled ¹³C NMR (CDCl₃): δ 97.02 (d, *J* 168.5 Hz) confirmed the presence of the α -glycosidic bond.^{35,36}

4.13. 1-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- α -D-galactopyranosyl)-2,3,4,5,6-penta-*O*-acetyl-D-*chiro*-inositol (**20 α**)

Sodium (36.3 mg, 1.58 mmol) was added to NH₃ [(l), ~5 mL] at –78 °C, and the mixture was stirred for 2 min under N₂ to form a blue solution, into which

was added compound **24** (8.6 mg, 0.0079 mmol) in dry THF (2 mL). The resulting mixture was stirred for 20 min at –78 °C, and then the reaction was quenched with abs MeOH (3 mL) at –78 °C. The NH₃ was removed with a stream of air, and additional MeOH was added to bring the total volume of solution in the reaction flask to ~10 mL. After neutralization with Dowex-50 X8 (280 mg), the mixture was filtered, rinsed with satd NH₃ in MeOH (20 mL), and concentrated under reduced pressure. The crude product was further dissolved in 1:1 DMF–THF (470 μ L), and DMAP (small amount), Et₃N (235 μ L), and finally Ac₂O (75 μ L) were added. The mixture was stirred for 24 h at room temperature and then diluted with EtOAc (10 mL). It was washed with water (2 \times 3 mL), dried with MgSO₄, and concentrated under reduced pressure. Purification via preparative TLC (EtOAc) gave 3.8 mg of **20 α** (68% over two steps). ¹H NMR (CDCl₃): δ 6.11 (d, 1H, *J* 9.2 Hz), 5.48 (dd, 1H, *J* 2.2, 1.1 Hz), 5.41 (dd, 1H, *J* 9.6, 8.6 Hz), 5.41–5.35 (m, 2H), 5.30–5.26 (m, 2H), 5.22 (dd, 1H, *J* 11.7, 11.2 Hz), 4.98 (d, 1H, *J* 3.5 Hz, H-1 α anomer), 4.69 (ddd, 1H, *J* 12.3, 9.2, 3.5 Hz), 4.40 (t, 1H, *J* 6.8 Hz), 4.15–4.09 (m, 2H), 4.02 (dd, 1H, *J* 11.2, 6.2 Hz), 2.17 (s, 3H, Ac), 2.16 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.04 (s, 6H, Ac), 2.01 (s, 3H, Ac). HRESIMS: calcd for [C₃₀H₄₁O₁₉N+H]⁺, *m/z* 720.2351; found, *m/z* 720.2346.

4.14. 1-*O*-(3,4,6-Tri-*O*-benzyl-2-benzoyloxycarboxamido-2-deoxy- α , β -D-galactopyranosyl)-2,3,4,5,6-penta-*O*-benzyl-D-*chiro*-inositol (**21 α , β**)

To a flame-dried flask were added 4 Å MS, phenylselenium chloride (12.9 mg, 0.067 mmol), and toluene (500 μ L). The mixture was cooled to –42 °C, and AgOTf (20.8 mg, 0.081 mmol) was added. Slowly a solution of **16** (25.7 mg, 0.042 mmol) and **8** (17 mg, 0.027 mmol) in 3:1 toluene–CH₂Cl₂ (1.9 mL, total) was added to the vigorously stirred mixture. After stirring at –42 °C for 45 min, 1 M NaHCO₃ (2 mL) was added to the reaction mixture. The resulting solution was filtered through Celite, the organic layer was separated from the aqueous layer, and the latter was extracted with CH₂Cl₂ (3 \times 4 mL). The combined organic layers were dried with MgSO₄, filtered, and concentrated. Purification via preparative TLC (7:3 hexanes–EtOAc) gave 10.8 mg of **21 α** and 11.4 mg of **21 β** (combined yield 74%). Data for **21 α** : ¹H NMR (CDCl₃) δ 7.35–7.20 (m, 45H, aromatic), 5.13 (d, 1H, *J* 12.2 Hz, CH₂Ph), 4.91 (d, 1H, *J* 11.5 Hz, CH₂Ph), 4.91–4.81 (m, 3H), 4.78 (d, 1H, *J* 10.4 Hz, CH₂Ph), 4.72–4.39 (m, 14H), 4.30 (m, 1H), 4.22 (s, 1H, CH₂Ph), 4.03 (m, 1H), 3.98 (t, 1H, *J* 3.3 Hz), 3.85 (t, 1H, *J* 9.8 Hz), 3.79 (dd, 1H, *J* 9.8, 2.9 Hz), 3.72 (t, 1H), 3.67–3.51 (m, 4H), 3.33 (dd, 1H, *J* 8.7, 5.5 Hz). HRESIMS: calcd for

$[C_{76}H_{77}NO_{12}+Na]^+$, m/z 1218.5338; found, m/z 1218.5307. 1H -Coupled ^{13}C NMR ($CDCl_3$): δ 97.87 (d, J 172 Hz), which confirmed the presence of the α -glycosidic bond.^{35,36} Data for **21 β** : 1H NMR ($CDCl_3$) δ 7.40–7.15 (m, 45H, aromatic), 5.10 (d, 1H, J 12.2 Hz, CH_2Ph), 5.0 (d, 1H, J 11.8 Hz, CH_2Ph), 4.93 (d, 1H, J 10.7 Hz, CH_2Ph), 4.85–4.47 (m, 17H), 4.45 (m, 1H), 3.99 (m, 1H), 3.96 (m, 1H), 3.95–3.80 (m, 6H), 3.61–3.50 (m, 2H), 3.45 (m, 1H). HRESIMS: calcd for $[C_{76}H_{77}NO_{12}+Na]^+$, m/z 1218.5338; found, m/z 1218.5322. 1H -Coupled ^{13}C NMR ($CDCl_3$): δ 102.69 (d, J 163 Hz), which confirmed the presence of the β -glycosidic bond.^{35,36}

4.15. 1-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-galactopyranosyl)-2,3,4,5,6-penta-*O*-acetyl-D-*chiro*-inositol (**20 β**)

Sodium (43.8 mg, 1.9 mmol) was added to NH_3 [(l), ~ 5 mL] at $-78^\circ C$, and the mixture was stirred for 2 min under N_2 to form a blue solution, into which was added compound **21 β** (11.4 mg, 0.0095 mmol) in dry THF (2 mL). The resulting mixture was stirred for 20 min at $-78^\circ C$, and then the reaction was quenched with abs MeOH (5 mL) at $-78^\circ C$. The NH_3 was removed with a stream of air, and additional MeOH was added to bring the total volume of solution in the reaction flask to ~ 10 mL. After neutralization with Dowex-50 X8 (670 mg), the mixture was filtered, rinsed with satd NH_3 in MeOH (20 mL), and concentrated under reduced pressure. The crude product was further dissolved in 1:1 DMF–THF (580 μ L), and DMAP (small amount), Et_3N (290 μ L), and finally Ac_2O (100 μ L) were added. The mixture was stirred for 24 h at room temperature and then diluted with EtOAc (10 mL). It was washed with water (2×3 mL), dried with $MgSO_4$, and concentrated under reduced pressure. Purification via preparative TLC (EtOAc) gave 3.4 mg of **20 β** (50% over two steps). 1H NMR ($CDCl_3$): δ 5.75 (dd, 1H, J 11.3, 3.4 Hz), 5.69 (t, 1H, J 7.6 Hz), 5.55–5.37 (m, 5H), 5.26 (dd, 1H, J 10.1, 2.7 Hz), 5.16 (d, 1H, J 8.2 Hz), 4.19 (t, 1H, J 3.3 Hz), 4.18–4.09 (m, 2H), 3.96 (t, 1H, J 6.5 Hz), 3.52 (m, 1H, NHAc), 2.22 (s, 3H, Ac), 2.19 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.05 (s, 6H, Ac), 2.04 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.02 (s, 3H, Ac). HRESIMS: calcd for $[C_{30}H_{41}O_{19}N+H]^+$, m/z 720.2351; found, m/z 720.2365.

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Supplementary data

Images of NMR spectra for compounds within this paper are available in Supplementary data. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.03.031.

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