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A Concise Synthesis of Globotriaosylsphingosine

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Globotriaosylsphingosine (lysoCTH) is produced in the cell by deacylation of the *globo*-sphingolipid globotriaosylceramide. The latter compound is the major storage material encountered in Fabry patients, an inherited lysosomal storage disorder characterized by partially impaired α-galactosidase A (GLA) activity. Recent findings suggest that lysoCTH, next to its acylated precursor, is an important causative of Fabry disease symptoms. The glycolipid is thus a relevant synthetic target, and we here report on its efficient synthesis. Key to our strategy is the use of 4,6-*O*-di-*tert*-butylsilylene-protected D-galactose donors to yield D-Gal-α-D-Gal linkages with high stereoselectivity. In our optimized route we make use of acyl protecting groups to mask most of the hydroxy functions in the carbohydrate building blocks to facilitate straightforward global deprotection.

Introduction

Glycosphingolipids (GSLs) are a ubiquitous class of cellular components that partake in many biological processes. Glycosphingolipids that belong to the *globo* series have the D-Gal-α-D-Gal linkage as a characteristic substructure (Figure 1). This galabiose moiety is located in the hydrophilic part of the glycosphingolipid that protrudes from the cell membrane. The galabiose disaccharide is an important recognition site for both toxins and adhesive proteins, including bacterial lectins.[1,2] Moreover, some *globo* glycosphingolipids have been identified as tumor-specific antigens,[3] as is exemplified by the observed elevated globotriaosylceramide levels in Burkitt's lymphoma.[4]

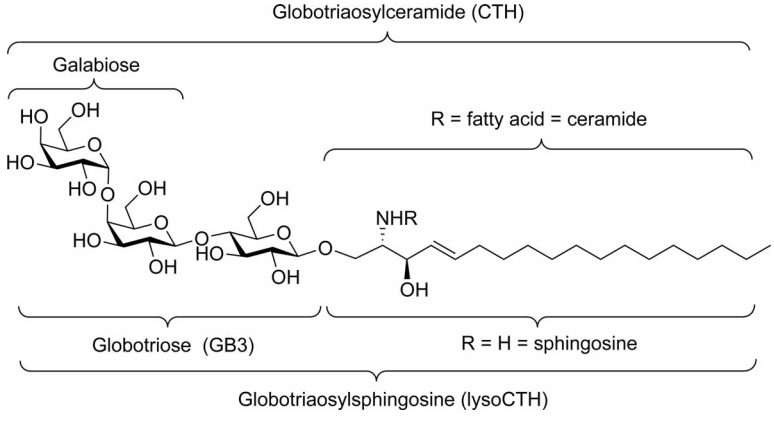

Figure 1. Globotriaosylceramide (R = fatty acid) and globotriaosylsphingosine (R = H).

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The metabolism of glycosphingolipids is a tightly controlled process, and disruption of any of the metabolic transformations is at the basis of several human diseases that belong to the family of lysosomal storage disorders.[5] For example, an inherited defect in gene encoding for the lysosomal hydrolase α-galactosidase A (GLA) is the underlying cause of Fabry disease.[6] This genetic defect results in

reduced GLA activity, with a concomitant accumulation of its substrate globotriaosylceramide (CTH).[7] Although the deficiency in enzyme activity is the undisputed cause of the disease, correlation between CTH levels and disease manifestations has yet to be observed. Recent findings have shown that another glycosphingolipid, namely, globotriaosylsphingosine (lysoCTH), which is the deacylated form of CTH, may be the actual storage material that causes disease manifestations in Fabry patients.[8,9] With the aim to get more insight in the physiological role of LysoCTH in Fabry disease we decided to embark on the development of an efficient synthesis of this glycosphingolipid. In this paper we report on our results in the development of a concise synthesis of globotriaosylsphingosine.

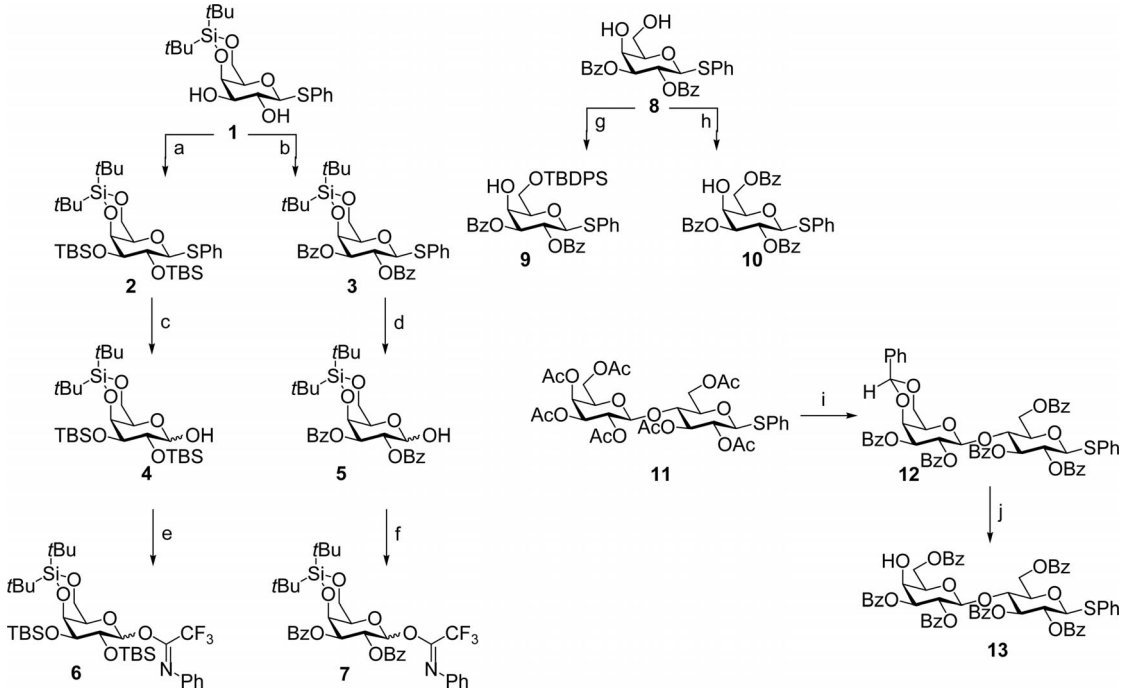
Results and Discussion

Dating back to the first reported synthesis of globotriose (Gb3) by Cox et al.[10] and globotriaosylceramide by Shapiro and Acher[11] in 1978, a handful of approaches towards the synthesis of Gb3 have been reported.[12] The most commonly used strategy for the assembly of Gb3 is to attach a galactose donor to a lactose acceptor, although condensation of a D-Gal-α-D-Gal disaccharide with a glucose acceptor has also been reported.[13] One-pot procedures[14] using either the "armed–disarmed" concept or in situ removable protecting groups have been utilized. Expeditious routes using fluorous protecting groups[15] to minimize the total assembly time have also been published.[16]

In the development of a robust and high-yielding synthetic route towards lysoCTH, both a high degree of stereoselectivity in the glycosylation reactions and minimal protecting group manipulations are of importance. With these considerations in mind, we first turned our attention to the stereoselective formation of the D-Gal-α-D-Gal linkage. Recent literature demonstrates that 4,6-*O*-di-*tert*-butylsilylene-protected D-galactose donors can be condensed with various acceptor molecules in a highly stereoselective fashion to provide the 1,2-*cis*-linked products.[17] It appears that the steric influence of the bulky *tert*-butyl groups (positioned above the anomeric position) overrules the *trans*-directing properties of participating groups at the C2-OH of a donor galactoside, with a high α-selectivity as a result. We reasoned that the use of the silylene protecting group would present an attractive alternative to the existing routes, which almost without exceptions employ a nonparticipating group (benzyl) at the C2-OH of the galactose donor to achieve high, or in some cases complete, α-selectivity.

As the first research objective we set out to investigate the α-directing effect of 4,6-*O*-di-*tert*-butylsilylene-protected D-galactose donors in the condensation with a number of galactose and lactose acceptors under a variety of glycosylation conditions. Donors **2**–**7** and acceptors **9**, **10**, and **13** used in these studies were prepared from readily available starting materials as depicted in Scheme 1.

The synthesis of the target donor galactosides was accomplished starting from known[17] phenyl 1-thio-4,6-*O*-di-*tert*-butylsilylene-thiogalactoside (**1**) as the common precur-



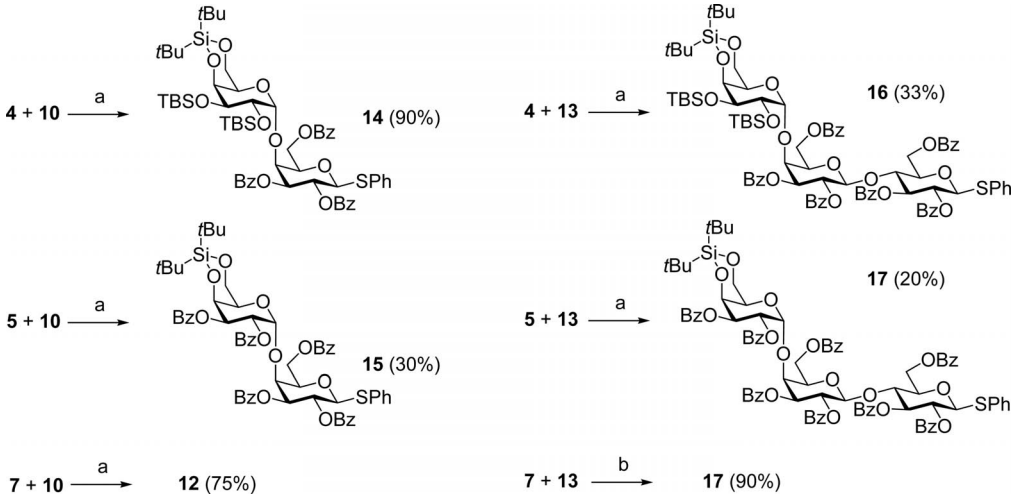
Scheme 1. Reagents and conditions: (a) TBDMSOTf, pyridine, DMAP, DMF, –40 °C, 45 min (93%); (b) BzCl, pyridine, 3 h (97%); (c) 1. NIS, TFA, CH_2Cl_2, 0 °C, 3 h, 2. Et_3N, 0 °C, 20 h (67%); (d) NIS, TFA, CH_2Cl_2, 0 °C, 3 h (78%); (e) $ClC(NPh)CF_3$, Cs_2CO_3, acetone, 0 °C, 2 h, (83%); (f) $ClC(NPh)CF_3$, Cs_2CO_3, acetone, 0 °C, 3 h, (83%); (g) TBDPSCl, imidazole, DMF, 0 °C to r.t. (80%); (h) BzCl, pyridine, 0 °C, 1 h (70%); (i) 1. NaOMe, MeOH, r.t., 20 h, 2. $PhCH(OMe)_2$, *p*-$TsOH{\cdot}H_2O$, MeCN, r.t., 20 h, 3. BzCl, pyridine, r.t., 20 h (66%); (j) 1. TFA, H_2O, CH_2Cl_2, 0 °C, 1 h (92%), 2. HOBt, BzCl, Et_3N, CH_2Cl_2, 0 °C, 5 h (63%).

sor. The *tert*-butyldimethylsilyl ether groups in **2** were introduced by using TBSOTf in pyridine with DMAP as the catalyst. Benzoylation of the diols in **1** afforded thio donor **3**.[17c] Hydrolysis of the thioacetals in **2** and **3** by using conditions we previously[18] disclosed [*N*-iodosuccinimide (NIS), trifluoroacetic acid (TFA), dichloromethane] provided hemiacetals **4** and **5**,[19] respectively, which in turn were transformed into acetimidate derivatives **6** and **7** by using standard conditions.[20] It should be noted that the NIS/TFA-mediated hydrolysis of **2** proceeded through the formation of the rather stable anomeric α-trifluoroacetate, which was hydrolyzed to the desired product after addition of triethylamine.

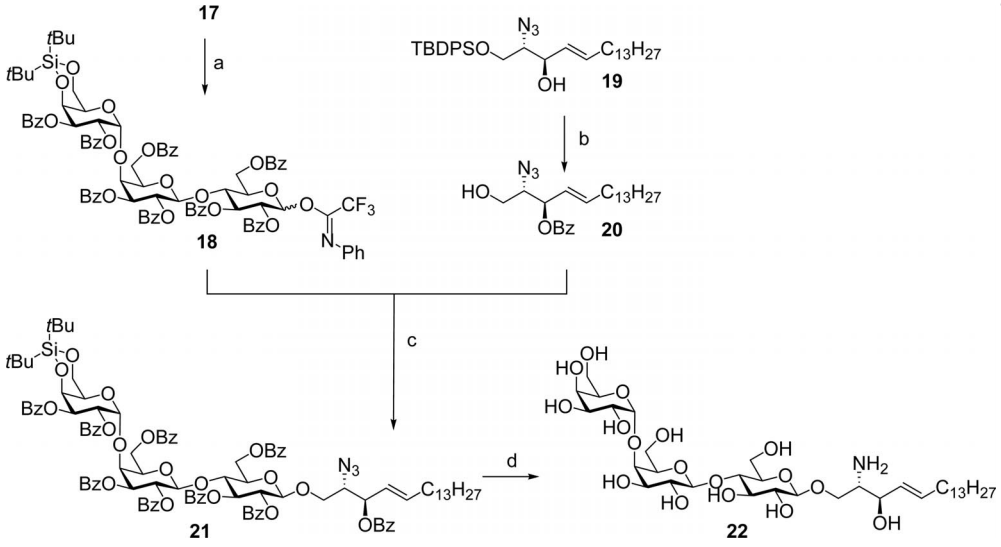
Acceptors **9** and **10** were synthesized from phenyl 2,3-di-*O*-benzoyl-1-thiogalactoside (**8**).[21] Regioselective protection of the C6-OH in **8** as the TBDPS ether or the benzoyl ester produced galactose acceptors **9** and **10**,[22] respectively. Acceptor lactoside **13**[23] was prepared from peracetylated thiolactoside **11**[24] in the following five-step sequence: (1) deacetylation, (2) installment of the *O*-4′-*O*-6′ benzylidene, (3) benzoylation of the remaining five hydroxy functions, (4) removal of the benzylidene protecting group, and (5) selective benzoylation of the primary alcohol.

With the set of donor and acceptor galactosides/lactosides in hand we turned our attention to the construction of the desired D-Gal-α-D-Gal linkage. To this end, we investigated the use of different donor–acceptor pairs and glycosylation conditions. The fruitful reactant/reagent combinations, with respect to productive coupling (isolated yields) and anomeric selectivity, are listed in Scheme 2. Hemiacetal donors **4** and **5** were both successfully condensed with phenyl 2,3,6-tri-*O*-benzoyl-1-thiogalactoside (**10**) under the agency of diphenyl sulfoxide and triflic anhydride to yield disaccharides **14** and **15**, respectively.[25] Both reactions yielded exclusively the D-Gal-α-D-Gal linkage, as evidenced by the observed 1′-H coupling constants ($J_{1',2'} \approx 3.5$ Hz). The important difference in these two experiments is the far more (90% as opposed to 30%) efficient glycosidation of acceptor **10** by silylated donor **4** in comparison to benzoylated donor **5** with otherwise the same reaction conditions. Imidate donor **7** gave, upon activation with trifluoromethanesulfonic acid[20] and subsequent addition of acceptor **10**, disaccharide **15** in 75% yield. In contrast to these results, condensation of persilylated imidate **6** with acceptor **10** (activating system triflic acid) proved unproductive. The same holds true when thioglycosides **2** or **3** (Ph_2SO, Tf_2O) was condensed with acceptor **10**.[26] Acceptor **9** featuring a bulky TBDPS substituent at O-6 proved resistant to galactosidation, and condensation with thiogalactoside **2**, hemiacetal **4** (in both cases, activating system Ph_2SO/Tf_2O), or imidate **6** (activated by triflic acid) failed to give the disaccharide. In the glycosylation experiments we performed that involved acceptor lactoside **13**, we observed productive couplings, again with exclusive formation (at least in isolated form) of the desired D-Gal-α-D-Gal linkage, employing hemiacetal **4**, hemiacetal **5**, or imidate donor **7**, in conjunction with the appropriate activator systems. The most efficient glycosylation in these series proved to be the one involving imidate **7**, providing trisaccharide **17** in 90% yield.

The final stages of our synthesis of the title compound are depicted in Scheme 3. Requisite partially protected D-*erythro*-sphingosine derivative **20** was prepared in two steps (benzoylation followed by liberation of the primary hydroxy) from known[27] sphingosine derivative **19**. It should be noted that in the final deprotection step we could not avoid partial migration of the benzoyl group from the secondary hydroxy group to the primary one, with 62% yield as a result.[28] Triflic acid mediated condensation of azidosphingosine **20** with trisaccharide **18**, prepared from **17** by hydrolysis of the thioacetal and ensuing installation of the imidate group, provided the title compound in fully protected form **21** in 80% yield and with no detectable formation of the α-anomer. Condensation of thioglycoside **17** (Ph_2SO, Tf_2O) with acceptor **20** provided the same product in much lower (32%) yield, whereas dehydrative condensation of the intermediate hemiacetal, obtained after hydrolysis of the thioacetal in **17**, provided **21** in 26% yield. Glo-



Scheme 2. Reagents and conditions: (a) Ph_2SO, Tf_2O, TTBP, DCM, –60 °C to r.t., (b) TfOH, DCM, 0 °C.



Scheme 3. Reagents and conditions: (a) 1. NIS, TFA, CH_2Cl_2, 0 °C, 3 h (86%), 2. $ClC(NPh)CF_3$, Cs_2CO_3, acetone, 0 °C, 2 h (92%); (b) 1. BzCl, pyridine, r.t. (93%), 2. TBAF, AcOH, THF, 0 °C, 1 h (62%); (c) TfOH (cat.), 0 °C, 1 h (80%); (d) 1. NaOMe, MeOH, r.t., 3 h, 2. H_2S, pyridine, AcOH, Et_3N, THF, r.t., 3 h, 3. $(HF)_3{\cdot}Et_3N$, pyridine, r.t., 20 h, 72%.

botriaosylsphingosine **22** was finally obtained after the following three-step sequence of events. (1) Global debenzoylation was performed using Zemplén conditions. (2) The partially deprotected Gb3 was purified by column chromatography prior to reduction of the azide with hydrogen sulfide to avoid acylation of the free amine. (3) The di-*tert*-butylsilylene protecting group was then removed with hydrogen fluoride in pyridine to give globotriaosylsphingosine **22** in 72% yield after HPLC purification.

Conclusions

In conclusion, we have described a straightforward synthesis of globotriaosylsphingosine. The optimized route of synthesis uses an α-directing galactosyl imidate bearing a 4,6-di-*tert*-butylsilylene protecting group for the formation of the D-Gal-α-D-Gal glycosidic linkage, giving access to phenyl 1-thioglobotrioside. The globotriaosyl donor was then transformed into the corresponding *N*-phenyl trifluoroimidate donor to achieve optimal yield in the condensation with an azidosphingosine acceptor. The protected globotriaosyl sphingosine was assembled in 57% yield over four steps from the 4,6-di-*tert*-butylsilylene galactosyl imidate. A mild deprotection sequence produced the desired globotriaosylsphingosine in 72% yield.

Experimental Section

General: Commercially available reagents and solvents (Acros, Fluka, or Merck) were used as received unless stated otherwise. Dichloromethane and THF were freshly distilled before use from P_2O_5 and Na/benzophenone, respectively. Triethylamine was distilled from calcium hydride and stored over potassium hydroxide. Trifluoromethanesulfonic anhydride was distilled from P_2O_5. Traces of water were removed from the starting compounds by co-evaporation with dichloroethane, dioxane, and/or toluene. All moisture-sensitive reactions were performed under an argon atmosphere. Molecular sieves (3 Å) were flame dried prior to use. Liquid column chromatography was performed using forced flow of the indicated solvent systems on Screening Devices Silica gel 60 (40–63 μm mesh). Analytical TLC was performed on aluminium sheets, precoated with silica gel (Merck, silica gel 60, F_{254}). Compounds were visualized using UV absorption (245 nm) or by spraying with 20% H_2SO_4 in ethanol, ammonium molybdate/cerium sulfate solution [$(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (25 g/L), $(NH_4)_4Ce(SO_4)_6{\cdot}2H_2O$ (10 g/L), 10% sulfuric acid in ethanol], or phosphomolybdic acid in EtOH (150 g/L) followed by charring (≈150 °C) or by spraying with potassium permanganate (1.6% in conc. sulfuric acid). IR spectra were recorded with a Shimadzu FTIR-8300. Optical rotations were measured with a Propol automatic polarimeter (sodium D line, λ = 589 nm). ^1H and ^{13}C NMR spectra were recorded with a Bruker AV 400 MHz spectrometer at 400.2 (^1H) and 100.6 (^{13}C) MHz or with a Bruker AV 600 MHz spectrometer at 600.0 (^1H) and 150.1 (^{13}C) MHz, respectively. Chemical shifts are reported as δ values (ppm) and directly referenced to TMS (δ =0.00 ppm) in $CDCl_3$ or to the solvent residual peak (D_2O). Coupling constants (J) are given in Hz and all ^{13}C spectra are proton decoupled. NMR assignments were made using COSY and HSQC and in some cases TOCSY experiments. LC–MS analyses were performed with a LCQ Advantage Max (Thermo Finnigan) equipped with a Gemini C_{18} column (Phenomenex, 50 × 4.6 mm, 3μ), utilizing the following buffers: A: H_2O, B: acetonitrile, and C: 1.0% TFA (aq.).

General Procedure for the Dehydrative Glycosylations: 1-Hydroxy-donor (0.12 mmol, 1.2 equiv.), diphenyl sulfoxide (0.26 mmol, 2.6 equiv.), and 2,4,6-tris-*tert*-butylpyrimidine (0.12 mmol, 1.2 equiv.), were dissolved in anhydrous DCM (3 mL) under an atmosphere of argon. Activated molecular sieves (3 Å) were added, and the mixture was stirred for 1 h at ambient temperature. The solution was then cooled to –60 °C and trifluoromethanesulfonic anhydride (0.130 mmol, 1.3 equiv.) was added. The mixture was warmed to –40 °C and stirred at this temperature for 1 h. The reaction was then cooled to –60 °C and the acceptor (0.10 mmol, 1.0 equiv.) was added as a solution in anhydrous DCM (2 mL). The reaction was stirred going to room temperature and was then quenched by addition of anhydrous triethylamine (1.0 mmol,

10 equiv.). The mixture was transferred to an extraction funnel using EtOAc, and the organics were washed with sat. aq. $NaHCO_3$ and brine. The water layers were extracted with EtOAc, and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo.

General Procedure for the Imidate Glycosylations: The imidate donor (0.12 mmol, 1.2 equiv.) and acceptor (0.1 mmol, 1 equiv.) were coevaporated two times in toluene and were then dissolved in anhydrous DCM (2 mL) and cooled to 0 °C before addition of a catalytic amount of TfOH (0.01 mmol, 0.1 equiv.). The reaction was stirred until TLC showed complete conversion of the acceptor. The reaction was then quenched by addition of triethylamine (1.0 mmol, 10 equiv.). The organics were transferred to an extraction funnel using EtOAc, and the organics were washed with sat. aq. $NaHCO_3$ and brine. The water layers were extracted with EtOAc, and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo.

Phenyl 4,6-*O*-Di-*tert*-butylsilanediyl-1-thio-β-D-galactopyranoside (1): Phenyl 1-thio-β-D-galactopyranoside (10.9 g, 40.0 mmol, 1.05 equiv.) was dried by coevaporation with anhydrous DMF (100 mL) and then dissolved in anhydrous DMF (160 mL). The mixture was cooled to –40 °C before dropwise addition of di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (12.3 mL, 38.1 mmol, 1.0 equiv.). The reaction was stirred at –40 °C for 30 min followed by addition of pyridine (9.24 mL, 114 mmol, 3.0 equiv.). The reaction was stirred for an additional 15 min and then transferred to an extraction funnel with diethyl ether (400 mL). The organics were washed with water (2 × 400 mL) and brine (300 mL). The aqueous layers were extracted with diethyl ether (300 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (5–20% acetone in DCM) afforded the title compound as a clear viscous oil (14.6 g, 35.4 mmol, 93%). R_f = 0.15 (20% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = –63 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.51 (m, 2 H, H_{arom}), 7.33–7.24 (m, 3 H, H_{arom}), 4.56 (d, J = 9.8 Hz, 1 H, 1-H), 4.42 (dd, J = 3.5, 1.1 Hz, 1 H, 4-H), 4.26 (dd, J = 12.5, 1.9 Hz, 1 H, 6_a-H), 4.22 (dd, J = 12.5, 2.2 Hz, 1 H, 6_b-H), 3.76 (dd, J = 9.8, 9.0 Hz, 1 H, 2-H), 3.55 (dd, J = 9.0, 3.5 Hz, 1 H, 3-H), 3.45 (m, 1 H, 5-H), 3.08 (br. s, 2 H, OH), 1.05 (s, 9 H, $CH_{3t\text{Bu-Si}}$), 1.04 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.2 ($C_{q\text{-arom}}$), 132.3, 128.8, 127.7 (CH_{arom}), 88.8 (C-1), 75.1 (C-5), 75.0 (C-3), 72.5 (C-4), 70.5 (C-2), 67.0 (C-6), 27.5, 27.3 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.2, 20.5 ($C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 3398, 2934, 2858, 1473, 1162, 1063, 826, 732, 649, 442 cm^{-1}. HRMS: calcd. for $[C_{20}H_{32}O_5SSi + Na]^+$ 435.1632; found 435.1629.

Phenyl 2,3-Di-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-di-*tert*-butylsilanediyl-1-thio-β-D-galacto-pyranoside (2): Phenyl 4,6-*O*-di-*tert*-butylsilanediyl-1-thio-β-D-galactopyranoside (1.73 g, 4.2 mmol, 1.0 equiv.) and DMAP (51 mg, 0.42 mmol, 0.1 equiv.) were dissolved in pyridine (20 mL) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (2.5 mL, 10.9 mmol, 2.6 equiv.) was added at 0 °C. The reaction was stirred at 0 °C for 15 min and then at room temperature overnight. The reaction was concentrated in vacuo, diluted with EtOAc (80 mL) and washed with 1 N HCl (100 mL), sat. aq. $NaHCO_3$ (100 mL), and brine (80 mL). The aqueous layers were extracted with EtOAc (80 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (0–40% DCM in petroleum ether) afforded the title compound as a clear oil (2.22 g, 3.46 mmol, 83%). R_f = 0.33 (40% DCM in petroleum ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (m, 2 H, H_{arom}), 7.29–7.19 (m, 3 H, H_{arom}), 4.56 (d, J = 9.4 Hz, 1 H, 1-H), 4.32 (dd, J = 2.8, 1.0 Hz, 1 H, 4-H), 4.19 (dd, J = 12.2, 1.9 Hz, 1 H, 6_a-H), 4.15 (dd, J = 12.2, 2.0 Hz, 1 H, 6_b-H), 4.01 (t, J = 8.9 Hz, 1 H, 2-H), 3.52 (dd, J = 8.6, 2.8 Hz, 1 H, 3-H), 3.33 (m, 1 H, 5-H), 1.12 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 1.04 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.96 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.95 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.26 (s, 3 H, $CH_{3\text{-TBS}}$), 0.15 (s, 3 H, $CH_{3\text{-TBS}}$), 0.12 (s, 3 H, $CH_{3\text{-TBS}}$), 0.10 (s, 3 H, $CH_{3\text{-TBS}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.8 ($C_{q\text{-arom}}$), 131.6, 128.6, 126.9 (3 CH_{arom}), 90.5 (C-1), 77.9 (C-3), 74.7 (C-5), 74.5 (C-4), 70.0 (C-2), 67.3 (C-6), 27.8, 27.4, 26.50, 26.46 (4 $CH_{3\text{-}t\text{Bu-Si}}$), 23.4, 20.7, 18.29, 18.28 (4 $C_{q\text{-}t\text{Bu-Si}}$), –2.0, –3.39, –3.42, –3.7 (4 $CH_{3\text{-TBS}}$) ppm. IR (neat): $\tilde{\nu}$ = 2932, 2856, 1473, 1254, 1080, 839, 772 cm^{-1}. HRMS: calcd. for $[C_{32}H_{60}O_5SSi_3 + H]^+$ 641.3542; found 641.3542.

Phenyl 2,3-Di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-1-thio-β-D-galactopyranoside (3): Phenyl 4,6-*O*-di-*tert*-butylsilanediyl-1-thio-β-D-galactopyranoside (3.30 g, 8.0 mmol, 1.0 equiv.) was dissolved in pyridine (20 mL) and benzoyl chloride (2.23 mL, 19.2 mmol, 2.4 equiv.) was added at room temperature. The reaction was stirred until TLC showed full conversion to a higher running product and was then quenched with MeOH (1 mL) and concentrated under reduced pressure. The residue was dissolved in EtOAc (50 mL) and washed with 1 N HCl (50 mL), sat. aq. $NaHCO_3$ (50 mL), and brine (40 mL). The aqueous layers were extracted with EtOAc (50 mL), and the combined organics were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (10% EtOAc in petroleum ether) afforded the title compound as a white solid (4.80 g, 7.7 mmol, 97%). R_f = 0.25 (10% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +121 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–7.96 (m, 4 H, H_{arom}), 7.55–7.45 (m, 4 H, H_{arom}), 7.42–7.35 (m, 4 H, H_{arom}), 7.28–7.24 (m, 3 H, H_{arom}), 5.92 (t, J = 10.0 Hz, 1 H, 2-H), 5.21 (dd, J = 9.6, 3.2 Hz, 1 H, 3-H), 4.95 (d, J = 10.0 Hz, 1 H, 1-H), 4.88 (d, J = 3.2 Hz, 1 H, 4-H), 4.40–4.30 (m, 2 H, 6_a-H and 6_b-H), 3.65 (br. s, 1 H, 5-H), 1.16 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.96 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.1, 165.4 (2 $C{=}O_{Bz}$), 133.8 ($C_{q\text{-arom}}$), 133.22, 133.15, 132.4, 129.79 (4 CH_{arom}), 129.77, 129.6 (2 $C_{q\text{-arom}}$), 129.4, 128.9, 128.4, 128.3, 127.8 (5 CH_{arom}), 87.5 (C-1), 75.4 (C-3), 75.0 (C-5), 70.4 (C-4), 68.1 (C-2), 67.1 (C-6), 27.5, 27.4 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.2, 20.7 (2 $C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 2934, 2858, 1720, 1273, 1169, 1084, 978, 826, 746 cm^{-1}. HRMS: calcd. for $[C_{34}H_{40}O_7SSi + H]^+$ 621.2337; found 621.2340.

2,3-Di-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-di-*tert*-butylsilanediyl-α/β-D-galactopyranose (4): Phenyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-di-*tert*-butylsilanediyl-1-thio-β-D-galactopyranoside (1.90 g, 2.96 mmol, 1.0 equiv.) was dissolved in DCM (30 mL). *N*-iodosuccinimide (1.33 g, 5.93 mmol, 2.0 equiv.) was added at 0 °C, before addition of trifluoroacetic acid (0.23 mL, 2.96 mmol, 1.0 equiv.). The reaction was left stirring at 0 °C under exposure to the atmosphere. Initially TLC showed full conversion to a higher running product (anomeric TFA adduct, which could be isolated). Triethylamine (1.25 mL, 8.89 mmol, 3.0 equiv.) was added, and the reaction showed full conversion to a lower running product after 5 h. The mixture was then transferred to an extraction funnel with EtOAc (70 mL). The organics were washed with sodium thiosulfate (20% aq., 100 mL), sat. aq. $NaHCO_3$ (100 mL), and brine (80 mL). The aqueous layers were extracted with EtOAc (100 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (5–20% EtOAc in petroleum ether) afforded the title compound as a clear oil (1.09 g, 1.99 mmol, 67%). R_f = 0.30 (10% EtOAc in petroleum ether). NMR assignment of major isomer (α): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.18 (d, J = 3.5 Hz, 1 H, 1-H), 4.30 (d, J = 2.9 Hz, 1 H, 4-H), 4.23 (dd, J = 12.4, 1.7 Hz, 1 H, 6_a-H), 4.17 (dd, J = 12.4, 1.7 Hz, 1 H, 6_b-H), 4.07 (dd, J = 9.3, 3.5 Hz, 1 H, 2-H), 3.89 (br.

s, 1 H, 5-H), 3.79 (dd, J = 9.3, 2.9 Hz, 1 H, 3-H), 2.99 (br. s, 1 H, OH), 1.04 (br. s, 18 H, 2 $CH_{3t\text{Bu-Si}}$), 0.94 (s, 9 H, $CH_{3t\text{Bu-Si}}$), 0.92 (s, 9 H, $CH_{3t\text{Bu-Si}}$), 0.13 (s, 3 H, $CH_{3\text{-TBS}}$), 0.11 (s, 3 H, $CH_{3\text{-TBS}}$), 0.10 (s, 6 H, 2 $CH_{3\text{-TBS}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 94.0 (C-1), 74.6 (C-3), 71.3 (C-4), 70.1 (C-5), 67.9 (C-2), 67.4 (C-6), 27.42, 27.35, 26.04, 25.99 (4 $CH_{3\text{-}t\text{Bu-Si}}$), 23.4, 20.7, 18.07, 18.05 (4 $C_{q\text{-}t\text{Bu-Si}}$), –4.0, –4.1, –4.3, –4.8 (4 $CH_{3\text{-TBS}}$) ppm. IR (neat): $\tilde{\nu}$ = 2932, 2858, 1472, 1253, 1102, 833, 774, 648 cm^{-1}. HRMS: calcd. for $[C_{26}H_{56}O_6Si_3 + H]^+$ 549.3458; found 549.3453. Data for the anomeric TFA adduct trifluoroacetyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-di-*tert*-butylsilandiyl-1-thio-α-D-galacto-pyranoside: R_f = 0.95 (10% EtOAc in petroleum ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.38 (d, J = 3.3 Hz, 1 H, 1-H), 4.45 (d, J = 2.2 Hz, 1 H, 4-H), 4.34 (dd, J = 9.5, 3.3 Hz, 1 H, 2-H), 4.27 (d, J = 12.7 Hz, 1 H, 6_a-H), 4.20 (d, J = 12.7 Hz, 1 H, 6_b-H), 3.91 (dd, J = 9.5, 2.7 Hz, 1 H, 3-H), 3.85 (br. s, 1 H, 5-H), 1.09 (br. s, 18 H, 2 $CH_{3t\text{Bu-Si}}$), 0.98 (s, 9 H, $CH_{3t\text{Bu-Si}}$), 0.90 (s, 9 H, $CH_{3t\text{Bu-Si}}$), 0.15 (s, 3 H, $CH_{3\text{-TBS}}$), 0.14 (s, 6 H, 2 $CH_{3\text{-TBS}}$), 0.13 (s, 3 H, $CH_{3\text{-TBS}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.2 (q, J = 42.5 Hz, C=O), 114.6 (q, J = 286.1 Hz, CF_3), 98.0 (C-1), 74.2 (C-3), 71.11 (C-5), 71.06 (C-4), 68.0 (C-2), 66.6 (C-6), 27.4, 27.3, 26.1, 25.8 (4 $CH_{3t\text{Bu-Si}}$), 23.4, 20.8, 18.1, 17.8 (4 $C_{q\text{-}t\text{Bu-Si}}$), –4.2, –4.4, –4.5, –4.7 (4 $CH_{3\text{-TBS}}$) ppm.

2,3-Di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α/β-D-galacto-pyranose (5): Phenyl 2,3-di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-1-thio-β-D-galactopyranoside (5.49 g, 8.85 mmol, 1.0 equiv.) was dissolved in DCM (85 mL). *N*-iodosuccinimide (3.98 g, 17.7 mmol, 2.0 equiv.) was added at 0 °C, before addition of trifluoroacetic acid (0.68 mL, 8.85 mmol, 1.0 equiv.). The reaction was left stirring under exposure to the atmosphere until TLC showed full conversion. The mixture was then transferred to an extraction funnel with EtOAc (150 mL) and washed with sodium thiosulfate (20% aq., 200 mL), sat. aq. $NaHCO_3$ (200 mL), and brine (150 mL). The aqueous layers were extracted with EtOAc (150 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (0–10% ethyl ether, 40% DCM in petroleum ether) afforded the title compound as a white solid (3.67 g, 6.9 mmol, 78%). R_f = 0.25 (20% EtOAc in petroleum ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.97 (m, 4 H, CH_{arom}), 7.56–7.49 (m, 2 H, CH_{arom}), 7.42–7.35 (m, 4 H, CH_{arom}), 5.77 (dd, J = 10.5, 3.5 Hz, 0.7 H, 2_α-H), 5.72 (m, 0.7 H, 1_α-H), 5.66 (m, 1 H, 3_α-H and 2_β-H), 5.31 (dd, J = 10.2, 3.2 Hz, 0.3 H, 3_β-H), 4.91–4.85 (m, 1 H, 4_α-H and 1_β-H), 4.83 (d, J = 3.0 Hz, 0.3 H, 4_β-H), 4.38–4.31 (m, 1.3 H, $6_{a\text{-}\alpha}$-H, $6_{a\text{-}\beta}$-H, and $6_{b\text{-}\alpha}$-H), 4.22 (dd, J = 12.6, 1.6 Hz, 0.7 H, $6_{b\text{-}\beta}$-H), 4.19 (m, 0.7 H, 5_α-H), 3.68 (m, 0.3 H, 5_β-H), 3.63 (d, 0.3 H, OH_β), 2.81 (s, 0.7 H, OH_α), 1.15 (s, 2.7 H, $CH_{3\text{-}t\text{Bu-Si-}\beta}$), 1.13 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si-}\alpha/\beta}$), 0.98 (s, 6.3 H, $CH_{3\text{-}t\text{Bu-Si-}\alpha}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.4, 166.21, 166.15, 166.10 (4 $C{=}O_{Bz}$), 133.5, 133.33, 133.29, 133.1, 129.9, 129.8, 129.74, 129.71 (8 CH_{arom}), 129.42, 129.40, 129.1 (3 $C_{q\text{-arom}}$), 128.43, 128.37 (2 CH_{arom}), 96.3 (C-1_β), 91.2 (C-1_α), 73.4 (C-3_β), 71.9 (C-2_β), 71.7 (C-5_β), 71.3 (C-4_α), 70. 6 (C-3_α), 70.5 (C-4_β), 68.9 (C-2_α), 67.04 (C-6_α), 67.03 (C-5_α), 66.9 (C-6_β), 27.5, 27.43, 27.36, 27.2 (CH_3, 4 $CH_{3\text{-}t\text{Bu-Si-}\alpha/\beta}$), 23.28, 23.26, 20.8, 20.7 (4 $C_{q\text{-}t\text{Bu-Si-}\alpha/\beta}$) ppm. IR (neat): $\tilde{\nu}$ = 3473, 2935, 2860, 1719, 1267, 1100, 1073, 997, 708, 441 cm^{-1}. HRMS: calcd. for $[C_{28}H_{36}O_8Si + H]^+$ 529.2252; found 529.2249.

2,3-Di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galacto-pyranoside *N*-Phenyl-2,2,2-trifluoroacetimidate (7): 2,3-Di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α/β-D-galactopyranose (1.85 g, 3.5 mmol, 1.0 equiv.) was dissolved in acetone (20 mL) and cooled to 0 °C. Cesium carbonate (1.71 g, 5.25 mmol, 1.5 equiv.) was added followed by chloro *N*-phenyl-trifluoroimidate (1.09 g, 5.25 mmol, 1.5 equiv.), and the reaction was stirred at 0 °C for 2 h. The reaction mixture was filtered and concentrated in vacuo. Purification by silica gel column chromatography, using silica gel that was neutralized by running an eluent of 3% NEt_3 in petroleum ether (100 mL) through the column (0–5% EtOAc, 20% DCM in petroleum ether) produced the title compound as a white solid (1.90 g, 2.72 mmol, 78%). R_f = 0.64 (0.58 for β-anomer; 10% EtOAc and 20% DCM in petroleum ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06–7.98 (m, 4 H, H_{arom}), 7.61–7.50 (m, 2 H, H_{arom}), 7.46–7.35 (m, 4 H, H_{arom}), 7.12 (t, J = 7.7 Hz, 2 H, $H_{arom\text{-}NPh}$), 7.00 (t, J = 7.7 Hz, 1 H, $H_{arom\text{-}NPh}$), 6.87 (br. s, 1 H, 1-H), 6.40 (br. s, 2 H, $H_{arom\text{-}NPh}$), 6.02 (br. d, J = 9.2 Hz, 1 H, 2-H), 5.65 (dd, J = 10.6, 3.3 Hz, 1 H, 3-H), 5.00 (s, 1 H, 4-H), 4.40–4.26 (m, 2 H, 6_a-H and 6_b-H), 4.15 (br. s, 1 H, 5-H), 1.13 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.98 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.1, 165.6 (2 $C{=}O_{Bz}$), 143.0 ($C{=}N_{NPh}$), 133.5, 133.3, 129.8, 129.7 (4 CH_{arom}), 129.5, 129.0 (2 $C_{q\text{-arom}}$), 128.6, 128.5, 128.4 (3 CH_{arom}), 124.2, 119.1 (2 $CH_{arom\text{-}NPh}$), 93.4 (br., C-1), 70.74 (C-3), 70.65 (C-4), 69.8 (C-5), 67.2 (C-2), 66.6 (C-6), 27.5, 27.2 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.3, 20.8 (2 $C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 2948, 2862, 1732, 1276, 1208, 1119, 994, 786, 707, 443 cm^{-1}. HRMS: calcd. for $[C_{36}H_{40}F_3NO_8Si + H]^+$ 700.2548; found 700.2549.

Phenyl 2,3-Di-*O*-benzoyl-β-D-galactopyranoside (8):[21] Phenyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (2.12 g, 3.92 mmol, 1.0 equiv.) was dissolved in acetic acid (40 mL) and heated to 80 °C. The reaction was stirred until TLC showed full conversion to a lower running product (≈3 h) and was then concentrated in vacuo. Purification by silica gel column chromatography (20–40% EtOAc in petroleum ether) afforded the title compound as a white solid (1.33 g, 2.8 mmol, 74%). R_f = 0.35 (50% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +105 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.90 (m, 4 H, H_{arom}), 7.59–7.49 (m, 4 H, H_{arom}), 7.40–7.24 (m, 7 H, H_{arom}), 5.81 (dd, J = 10.0, 9.9 Hz, 1 H, 2-H), 5.33 (dd, J = 9.9, 3.0 Hz, 1 H, 3-H), 4.98 (d, J = 10.0 Hz, 1 H, 1-H), 4.43 (d, J = 2.8 Hz, 1 H, 4-H), 4.02 (dd, J = 11.9, 5.9 Hz, 1 H, 6_a-H), 3.93 (dd, J = 11.9, 4.5 Hz, 1 H, 6_b-H), 3.82 (t, J = 5.1 Hz, 1 H, 5-H), 2.65 (br. s, 2 H, OH) ppm. ^{13}C NMR (101 MHz, CDCl3): δ = 165.8, 165.3 (2 $C{=}O_{Bz}$), 133.4, 133.2, 132.4, 129.83, 129.77 (5 CH_{arom}), 129.3 ($C_{q\text{-arom}}$), 129.0 (CH_{arom}), 128.9 ($C_{q\text{-arom}}$), 128.42, 128.35, 128.1 (3 CH_{arom}), 86.6 (C-1), 78.1 (C-5), 75.5 (C-3), 68.4 (C-4), 67.9 (C-2), 62.7 (C-6) ppm. IR (neat): $\tilde{\nu}$ = 3470, 3063, 2942, 2878, 1718, 1275, 1093, 1069, 1027, 734, 708, 691 cm^{-1}. HRMS: calcd. for $[C_{26}H_{24}O_7S + H]^+$ 481.1316; found 481.1313.

Phenyl 2,3-Di-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (9): Phenyl 2,3-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (1.79 g, 3.73 mmol, 1.0 equiv.) and imidazole (0.38 g, 5.59 mmol, 1.5 equiv.) were dissolved in anhydrous DMF (20 mL) and cooled to 0 °C. *tert*-Butyldiphenylchlorosilane (1.13 g, 4.10 mmol, 1.1 equiv.) was dissolved in anhydrous DMF (10 mL) and added to the cooled solution. The reaction was stirred, going to ambient temperature overnight and was then quenched with methanol (1 mL). The mixture was transferred to an extraction funnel with EtOAc (100 mL) and washed with water (2 × 100 mL) and brine (80 mL). The aqueous layers were extracted with EtOAc (100 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (5–10% EtOAc in petroleum ether) afforded the title compound as a white solid (2.15 g, 2.99 mmol, 80%). R_f = 0.60 (20% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +70 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02–7.95 (m, 4 H, H_{arom}), 7.77–7.68 (m, 4 H, H_{arom}), 7.52–7.29 (m, 10 H, H_{arom}), 7.26–7.19 (m, 2 H, H_{arom}), 5.83 (t, J = 9.9 Hz, 1 H, 2-H), 5.33 (dd, J = 9.9, 2.9 Hz, 1 H, 3-

H), 4.95 (d, J = 9.9 Hz, 1 H, 1-H), 4.49 (br. s, 1 H, 4-H), 4.05 (dd, J = 10.9, 5.0 Hz, 1 H, 6_a-H), 4.00 (dd, J = 10.9, 4.7 Hz, 1 H, 6_b-H), 3.80 (t, J = 4.7 Hz, 1 H, 5-H), 3.02 (br. d, J = 3.7 Hz, 2 H, OH), 1.08 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.9, 165.2 (2 $C{=}O_{Bz}$), 135.6, 135.5, 134.7, 133.3, 133.1 (5 CH_{arom}), 132.71, 132.65, 132.42 (3 $C_{q\text{-}arom}$), 132.38, 129. 9, 129.8, 129.7 (4 CH_{arom}), 129.5, 129.1 (2 $C_{q\text{-}arom}$), 128.8, 128.33, 128.28, 127.82, 127.80, 127.6 (6 CH_{arom}), 86.7 (C-1), 77.9 (C-5), 75.7 (C-3), 68.5 (C-4), 67.9 (C-2), 64.0 (C-6), 26.8 ($CH_{3\text{-}t\text{Bu-Si}}$), 19.1 ($C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 3483, 3078, 2930, 2856, 1720, 1275, 1105, 1093, 1069, 1026, 740 cm^{-1}. HRMS: calcd. for $[C_{42}H_{42}O_7SSi + Na]^+$ 741.2313; found 741.2312.

Phenyl 2,3,6-Tri-*O*-benzoyl-β-D-galactopyranoside (10): Phenyl 2,3-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (4.81 g, 10 mmol, 1.0 equiv.) was dissolved in pyridine (30 mL) and cooled to 0 °C followed by addition of benzoyl chloride (1.28 mL, 11.0 mmol, 1.1 equiv.). The reaction was stirred for 1 h at 0 °C and was then quenched with methanol (1 mL). The mixture was concentrated in vacuo and transferred to an extraction funnel with EtOAc (100 mL). The organics were washed with 1 N HCl (100 mL), sat. aq. $NaHCO_3$ (100 mL), and brine (80 mL). The aqueous layers were extracted with EtOAc (100 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (10–20% EtOAc in petroleum ether) afforded the title compound as a white solid (4.10 g, 7.01 mmol, 70%). R_f = 0.64 (40% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +90 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06–8.00 (m, 2 H, H_{arom}), 7.99–7.93 (m, J = 7.3 Hz, 4 H, H_{arom}), 7.58 (m, 1 H, H_{arom}), 7.53–7.41 (m, 6 H, H_{arom}), 7.40–7.28 (m, 4 H, H_{arom}), 7.23 (m, 1 H, H_{arom}), 7.18–7.12 (m, 2 H, H_{arom}), 5.84 (t, J = 9.9 Hz, 1 H, 2-H), 5.41 (dd, J = 9.9, 3.0 Hz, 1 H, 3-H), 5.00 (d, J = 10.1 Hz, 1 H, 1-H), 4.70 (dd, J = 11.7, 5.3 Hz, 1 H, 6_a-H), 4.64 (dd, J = 11.7, 6.6 Hz, 1 H, 6_b-H), 4.43 (m, 1 H, 4-H), 4.15 (br. t, J = 6.1 Hz, 1 H, 5-H), 2.78 (br. d, J = 5.2 Hz, 2 H, OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.4, 165.8, 165.3 (3 $C{=}O_{Bz}$), 133.5, 133.3, 133.2 (3 CH_{arom}), 132.9 ($C_{q\text{-}arom}$), 132.2, 129.81, 129.76, 129.75 (4 CH_{arom}), 129.5, 129.3, 128.84 (3 $C_{q\text{-}arom}$), 128.82, 128.41, 128.40, 128.3, 127.9 (5 CH_{arom}), 86.8 (C-1), 76.3 (C-5), 75.2 (C-3), 67.9 (C-4), 67.6 (C-2), 63.5 (C-6) ppm. IR (neat): $\tilde{\nu}$ = 3483, 3078, 2930, 2856, 1720, 1275, 1105, 1093, 1069, 1026, 740 cm^{-1}. HRMS: calcd. for $[C_{42}H_{42}O_7SSi + Na]^+$ 741.2313; found 741.2312.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-benzylidene-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside (12): Phenyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside[2] (16.8 g, 23.0 mmol, 1.0 equiv.) was dissolved in methanol (250 mL) and sodium methoxide (30% in methanol, 0.64 mL, 4.60 mmol, 0.2 equiv.) was added at ambient temperature. The reaction was run overnight giving full conversion to a lower running product (TLC; 30% MeOH in EtOAc, R_f = 0.32). The reaction was neutralized with Amberlite H^+, filtered, and concentrated in vacuo, producing a white solid that was used without further purification. The solids were dried by means of a vacuum pump overnight. The crude phenyl 4-*O*-(β-D-galactopyranosyl)-1-thio-β-D-glucopyranoside was then suspended in anhydrous acetonitrile (300 mL) and placed under an atmosphere of argon. Benzaldehyde dimethylacetal (5.18 mL, 34.5 mmol, 1.5 equiv.) was added followed by p-TsOH·H_2O (0.219 g, 1.15 mmol, 0.05 equiv.). The reaction was left stirring at ambient temperature overnight, giving a clear solution (TLC; 10% MeOH in EtOAc, R_f = 0.33). The reaction was quenched by addition of triethylamine (1.62 mL, 11.5 mmol, 0.5 equiv.) and was then concentrated under reduced pressure. The residue was dissolved in EtOAc (200 mL) and washed with sat. aq. $NaHCO_3$ (200 mL) and brine (200 mL). The aqueous layers were extracted with EtOAc (200 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude phenyl 4-*O*-(4,6-benzylidene-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside was dissolved in anhydrous pyridine (150 mL) followed by addition of benzoyl chloride (16.0 mL, 138 mmol, 6.0 equiv.) at ambient temperature. The reaction was stirred overnight, quenched by addition of MeOH (2 mL), and concentrated in vacuo. Crystallization from DCM/petroleum ether produced the title compound as a white cotton like solid (10.6 g, 10.2 mmol, 44%). The mother liquor was then purified by silica gel column chromatography (0–10% EtOAc, 40% DCM in petroleum ether) for additional product (5.2 g, 5.0 mmol, 22%) in a total yield of 66% over three steps. R_f = 0.80 (50% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +107 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.86 (m, 10 H, H_{arom}), 7.60 (t, J = 7.4 Hz, 1 H, H_{arom}), 7.51 (t, J = 7.4 Hz, 1 H, H_{arom}), 7.47–7.41 (m, 4 H, H_{arom}), 7.40–7.35 (m, 4 H, H_{arom}), 7.34–7.26 (m, 10 H, H_{arom}), 7.21–7.13 (m, 3 H, H_{arom}), 7.04 (m, J = 7.6 Hz, 2 H, H_{arom}), 5.84 (t, J = 9.1 Hz, 1 H, 3-H), 5.78 (dd, J = 10.4, 7.9 Hz, 1 H, 2′-H), 5.31 (t, J = 9.7 Hz, 1 H, 2-H), 5.28 (s, 1 H, $CH_{benzylidene}$), 5.16 (dd, J = 10.4, 3.6 Hz, 1 H, 3′-H), 4.91 (d, J = 10.0 Hz, 1 H, 1-H), 4.83 (d, J = 7.9 Hz, 1 H, 1′-H), 4.66 (dd, J = 11.9, 1.9 Hz, 1 H, 6_a-H), 4.39 (dd, J = 11.9, 5.1 Hz, 1 H, 6_b-H), 4.31 (d, J = 3.3 Hz, 1 H, 4′-H), 4.13 (dd, J = 9.7, 9.1 Hz, 1 H, 4-H), 3.89 (ddd, J = 9.7, 5.1, 1.9, Hz, 1 H, 5-H), 3.71 (d, J = 11.5 Hz, 1 H, $6'_a$-H), 3.56 (d, J = 11.5 Hz, 1 H, $6'_b$-H), 2.99 (m, 1 H, 5′-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.1, 165.5, 165.3, 165.0, 164.8 (5 $C{=}O_{Bz}$), 137.4 ($C_{q\text{-}arom}$), 133.3, 133.2, 133.1, 133.03, 133.01 (5 CH_{arom}), 131.6 ($C_{q\text{-}arom}$), 129.88, 129.86, 129.7, 129.6 (4 CH_{arom}), 129.5, 129.3, 128.92, 128.87 (4 $C_{q\text{-}arom}$), 128.8, 128.7, 128.32, 128.26, 128.1, 127. 9, 126.3 (7 CH_{arom}), 101.5 (C-1′), 100.6 ($CH_{benzylidene}$), 85.6 (C-1), 76.8 (C-4 and C-5), 75.0 (C-3), 73.0 (C-4′), 72.6 (C-3′), 70.8 (C-2), 69.5 (C-2′), 67.9 (C-6′), 66.5 (C-5′), 62.6 (C-6) ppm. IR (neat): $\tilde{\nu}$ = 3070, 2942, 2862, 1717, 1452, 1276, 1113, 1027, 706 cm^{-1}. HRMS: calcd. for $[C_{60}H_{50}O_{15}S + Na]^+$ 1065.2763; found 1065.2765.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside: Phenyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-benzylidene-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside (6.8 g, 6.5 mmol, 1.0 equiv.) was dissolved in DCM (250 mL) and cooled to 0 °C. Trifluoroacetic acid (2.50 mL, 32.5 mmol, 5.0 equiv.) was added followed by water (1 mL). The reaction was run until TLC showed full conversion to a lower running spot. The reaction mixture was transferred to an extraction funnel and washed with sat. aq. $NaHCO_3$ (200 mL) and brine (150 mL). The aqueous layers were extracted with EtOAc (200 mL), and the combined organics were dried (Na_2SO_4) and concentrated under reduced pressure. Purification by column chromatography (5–20% EtOAc, 40% DCM in petroleum ether) produced the title compound as a white solid (5.7 g, 5.97 mmol, 92%). R_f = 0.35 (50% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +78 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.97 (m, 2 H, H_{arom}), 7.96–7.92 (m, 4 H, H_{arom}), 7.92–7.88 (m, 4 H, H_{arom}), 7.61 (tm, J = 7.4 Hz, 1 H, H_{arom}), 7.56–7.50 (m, 2 H, H_{arom}), 7.49–7.43 (m, 3 H, H_{arom}), 7.42–7.36 (m, 6 H, H_{arom}), 7.34–7.28 (m, 3 H, H_{arom}), 7.23–7.15 (m, 3 H, H_{arom}), 7.06 (tm, J = 7.6 Hz, 1 H, H_{arom}), 5.76 (t, J = 8.9 Hz, 1 H, 3-H), 5.73 (t, J = 10.4, 7.9 Hz, 1 H, 2′-H), 5.39 (t, J = 9.6 Hz, 1 H, 2-H), 5.09 (dd, J = 10.4, 3.1 Hz, 1 H, 3′-H), 4.92 (d, J = 9.9 Hz, 1 H, 1-H), 4.78 (d, J = 7.9 Hz, 1 H, 1′-H), 4.65 (dd, J = 11.9, 1.9 Hz, 1 H, 6_a-H), 4.43 (dd, J = 11.9, 5.7 Hz, 1 H, 6_b-H), 4.20 (d, J = 3.1 Hz, 1 H, 4′-H), 4.10 (dd, J = 9.4, 8.9 Hz, 1 H, 4-H), 3.89 (ddd, J = 9.4, 5.7, 1.9, Hz, 1 H, 5-H), 3.41–3.33 (m, 2 H, 5′-H and $6'_a$-H), 3.26 (dd, J = 11.8, 5.0 Hz, 1

H, 6′$_b$-H), 1.70 (br. s, 2 H, 2 OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.82, 165.75, 165.4, 165.2, 165.0 (5 C=O_{Bz}), 133.5, 133.32, 133.25, 133.2, 133.0 (5 CH_{arom}), 131. 8 ($C_{q\text{-}arom}$), 129.85, 129.81, 129.74 (3 CH_{arom}), 129.70 ($C_{q\text{-}arom}$), 129.64, 129.55 (2 CH_{arom}), 129.2, 129.0, 128.80 (3 $C_{q\text{-}arom}$), 128.77, 128.6, 128.42, 128.39, 128.38, 128.36, 128.1 (7 CH_{arom}), 101.3 (C-1′), 85.8 (C-1), 76.9 (C-5), 76.5 (C-4), 74.6 (C-3), 74.3 (C-5′), 74.2 (C-3′), 70. 5 (C-2), 69.7 (C-2′), 68.1 (C-4′), 62.9 (C-6), 62.4 (C-6′) ppm. IR (neat): $\tilde{\nu}$ = 3490, 3064, 2948, 2872, 1722, 1269, 1069, 1027, 707 cm^{-1}. HRMS: calcd for $[C_{53}H_{46}O_{15}S + Na]^+$ 977.2450; found 977.2448.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside (13):[23] Benzoyl chloride (0.51 mL, 4.4 mmol, 1.1 equiv.) was added dropwise to a solution of hydroxybenzotriazole (0.60 g, 4.4 mmol, 1.1 equiv.) and triethylamine (0.62 mL, 4.4 mmol, 1.1 equiv.) in anhydrous DCM (16 mL). When TLC showed full conversion to the activated ester. Phenyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-β-D-galactopyranosyl)-1-thio-β-D-glycopyranoside (3.82 g, 4.00 mmol, 1.0 equiv.), dissolved in DCM (5 mL) was added followed by triethylamine (0.62 mL, 4.4 mmol, 1.1 equiv.). The reaction was stirred until no more conversion to product was seen and transferred to an extraction funnel with EtOAc (80 mL). The organics were washed with sat. aq. $NaHCO_3$ (100 mL) and brine (80 mL). The aqueous layers were extracted with EtOAc (100 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (5–15% EtOAc, 40% DCM in petroleum ether) produced the title compound as a white solid (2.68 g, 2.53 mmol, 63%). R_f = 0.12 (20% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +55 (c = 1.0, $CHCl_3$). NMR spectroscopic data are identical to those previously reported.[3] IR (neat): $\tilde{\nu}$ = 3487, 3062, 2950, 2868, 1722, 1265, 1093, 1069, 1026, 706 cm^{-1}. HRMS: calcd. for $[C_{60}H_{50}O_{16}S + Na]^+$ 1081.2712; found 1081.2709.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-(2,3-bis-*O*-*tert*-butyldimethylsilyl-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (14): Galactose hydroxy donor **4** (66 mg, 0.12 mmol, 1.2 equiv.), diphenyl sulfoxide (53 mg, 0.26 mmol, 2.6 equiv.), and 2,4,6-tris-*tert*-butylpyrimidine (75 mg, 0.300 mmol, 3.0 equiv.) were dissolved in anhydrous DCM (4 mL) under an atmosphere of argon. Activated molecular sieves (3 Å) were added, and the mixture was stirred for 1 h at ambient temperature. The solution was then cooled to –60 °C and trifluoromethanesulfonic anhydride (22 μL, 0.13 mmol, 1.3 equiv.) was added. The mixture was warmed to –40 °C and stirred at this temperature for 1 h. The reaction was then cooled to –60 °C and galactose acceptor **10** (59 mg, 0.10 mmol, 1.0 equiv.) was added as a solution in anhydrous DCM (2 mL). The reaction was stirred for 3 h going to room temperature and was then quenched by addition of anhydrous triethylamine (140 μL, 1.0 mmol, 10 equiv.). The mixture was transferred to an extraction funnel using EtOAc (40 mL), and the organics were washed with sat. aq. $NaHCO_3$ (40 mL) and brine (40 mL). The water layers were extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (10–30% ethyl ether in petroleum ether) produced the title compound as a white solid (100 mg, 90 μmol, 90%). R_f = 0.31 (15% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +54 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.09 (m, 2 H, H_{arom}), 8.07–8.02 (m, 2 H, H_{arom}), 7.95–7.91 (m, 2 H, H_{arom}), 7.61 (m, 1 H, H_{arom}), 7.54–7.45 (m, 7 H, H_{arom}), 7.38–7.31 (m, 4 H, H_{arom}), 7.16 (br. t, J = 7.3 Hz, 2 H, H_{arom}), 5.57 (t, J = 9.9 Hz, 1 H, 2-H), 5.47 (dd, J = 10.2, 2.3 Hz, 1 H, 3-H), 4.90 (d, J = 10.2 Hz, 1 H, 1-H), 4.89 (d, J = 3.2 Hz, 1 H, 1′-H), 4.77 (dd, J = 12.2, 3.3 Hz, 1 H, 6$_a$-H), 4.69 (dd, J = 12.2, 7.6 Hz, 1 H, 6$_b$-H), 4.36 (d, J = 1.4 Hz, 1 H, 4-H), 4.31 (dd, J = 12.6, 1.5 Hz, 1 H, 6$_a$′-H), 4.27 (d, J = 2.3 Hz, 1 H, 4′-H), 4.20 (dd, J = 7.8, 3.1 Hz, 1 H, 5-H), 4.11–4.05 (m, 2 H, 2′-H and 6$_b$′-H), 3.94 (dd, J = 9.7, 2.8 Hz, 1 H, 3′-H), 3.58 (br. s, 1 H, 5′-H), 1.06 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.97 (s, 18 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.83 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.21 (s, 3 H, $CH_{3\text{-TBS}}$), 0.18 (s, 3 H, $CH_{3\text{-TBS}}$), 0.05 (s, 3 H, $CH_{3\text{-TBS}}$), 0.00 (s, 3 H, $CH_{3\text{-TBS}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.0, 165.9, 164.9 (3 C=O_{Bz}), 133.8, 133.4, 133.14, 133.07 (4 CH_{arom}), 131.7 ($C_{q\text{-}arom}$), 130.1 (CH_{arom}), 130.0 ($C_{q\text{-}arom}$), 129.81, 129.73 (2 CH_{arom}), 129.4 ($C_{q\text{-}arom}$), 129.2 (CH_{arom}), 128.7 ($C_{q\text{-}arom}$), 128.5, 128.44, 128.37, 128.28, 127.9, 127.6 (6 CH_{arom}), 101.3 (C-1′), 85.6 (C-1), 77.5 (C-5), 76.1 (C-4), 74.9 (C-4′), 74.7 (C-3), 70.9 (C-3′), 70.3 (C-2′), 68.9 (C-5′), 67.7 (C-2), 67.1 (C-6′), 64.9 (C-6), 27.5, 27.3, 26.2 (4 $CH_{3\text{-}t\text{Bu-Si}}$), 23.4, 20.7, 18.3, 18.2 (4 $C_{q\text{-}t\text{Bu-Si}}$), –3.9, –4.2, –4.3, –4.7 (4 $CH_{3\text{-TBS}}$) ppm. IR (neat): $\tilde{\nu}$ = 3070, 2932, 2857, 1729, 1270, 1093, 1069, 837, 709 cm^{-1}. HRMS: calcd. for $[C_{59}H_{82}O_{13}SSi_3 + Na]^+$ 1137.4676; found 1137.4676.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (15)

Method A: Galactose hydroxy donor **5** (63 mg, 0.12 mmol, 1.2 equiv.), diphenyl sulfoxide (53 mg, 0.26 mmol, 2.6 equiv.), and 2,4,6-tris-*tert*-butylpyrimidine (30 mg, 0.12 mmol, 1.2 equiv.) were dissolved in anhydrous DCM (3 mL) under an atmosphere of argon. Activated molecular sieves (3 Å) were added, and the mixture was stirred for 1 h at ambient temperature. The solution was then cooled to –60 °C and trifluoromethanesulfonic anhydride (22 μL, 0.13 mmol, 1.3 equiv.) was added. The mixture was warmed to –40 °C and stirred at this temperature for 1 h. The reaction was then cooled to –60 °C and galactose acceptor **10** (59 mg, 0.10 mmol, 1.0 equiv.) was added as a solution in anhydrous DCM (2 mL). The reaction was stirred for 3 h going to room temperature and was then quenched by addition of anhydrous triethylamine (140 μL, 1.0 mmol, 10 equiv.). The mixture was transferred to an extraction funnel using EtOAc (40 mL), and the organics were washed with sat. aq. $NaHCO_3$ (40 mL) and brine (40 mL). The water layers were extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (5–20% EtOAc in petroleum ether) produced the title compound as a white solid (33 mg, 30 μmol, 30%).

Method B: Galactoside imidate donor **7** (105 mg, 0.15 mmol, 1.5 equiv.) and galactose acceptor **10** (59 mg, 0.10 mmol, 1.0 equiv.) were coevaporated twice with anhydrous toluene (4 mL) and then dissolved in anhydrous DCM (3 mL). The solution was cooled to 0 °C and trifluoromethansulfonic acid (0.9 μL, 10 μmol, 0.1 equiv.) was added. The reaction was stirred for 2 h at 0 °C and was then quenched by addition of triethylamine (140 μL, 1.0 mmol, 10 equiv.). The organics were transferred to an extraction funnel using EtOAc (40 mL), and the organics were washed with sat. aq. $NaHCO_3$ (40 mL) and brine (40 mL). The water layers were extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (5–20% EtOAc in petroleum ether) produced the title compound as a white solid (82 mg, 75 μmol, 75%). R_f = 0.18 (15% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +51 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.05 (m, 2 H, H_{arom}), 8.05–8.02 (m, 2 H, H_{arom}), 7.96–7.91 (m, 4 H, H_{arom}), 7.78–7.74 (m, 2 H, H_{arom}), 7.67–7.63 (m, 2 H, H_{arom}), 7.54–7.47 (m, 4 H, H_{arom}), 7.44–7.30 (m, 12 H, H_{arom}), 7.22 (br. t, J = 7.7 Hz, 2 H, H_{arom}), 5.73 (dd, J = 10.7, 3.6 Hz, 1 H, 2′-H), 5.51 (dd, J = 10.7, 3.1 Hz, 1 H, 3′-H), 5.50–5.44 (m, 2 H, 2-H and 3-H), 5.37 (d,

J = 3.6 Hz, 1 H, 1′-H), 4.89 (d, J = 8.3 Hz, 1 H, 1-H), 4.86 (dd, J = 11.1, 6.3 Hz, 1 H, 6_a-H), 4.75 (d, J = 3.1 Hz, 1 H, 4′-H), 4.42 (dd, J = 11.1, 6.5 Hz, 1 H, 6_b-H), 4.26 (br. s, 1 H, 4-H), 4.21 (dd, J = 13.1, 1.7 Hz, 1 H, 6_a′-H), 4.10 (t, J = 6.5 Hz, 1 H, 5-H), 3.98 (dd, J = 13.1, 2.2 Hz, 1 H, 6_b′-H), 3.41 (br. s, 1 H, 5′-H), 1.07 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.99 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.3, 166.0, 165.9, 165.6, 164.8 (5 $C{=}O_{Bz}$), 135.6, 133.5, 133.3, 133.2, 133.04, 133.02, 130.2 (7 CH_{arom}), 123.0, 129.9 (2 $C_{q\text{-}arom}$), 129.73, 129.70, 129.67, 129.6 (4 CH_{arom}), 129.4, 129.2, 128.8 (3 $C_{q\text{-}arom}$), 128.70 (CH_{arom}), 128.67 ($C_{q\text{-}arom}$), 128.5, 128.39, 128.35, 128.34, 128.2 (5 CH_{arom}), 98.7 (C-1′), 84.8 (C-1), 76.7 (C-4), 76.3 (C-5), 74.4 (C-3), 71.1 (C-4′), 70.5 (C-3′), 69.5 (C-2′), 67.9 (C-5′), 67.6 (C-2), 66.7 (C-6′), 62.2 (C-6), 27.5, 27.2 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.3, 20.7 (2 $C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 3072, 2935, 2858, 1718, 1269, 1093, 1070, 1027, 707 cm^{-1}. HRMS: calcd. for $[C_{61}H_{62}O_{15}SSi + Na]^+$ 1117.3471; found 1117.3477.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-[2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-bis-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galactopyranosyl)-β-D-galactopyranosyl]-1-thio-β-D-glucopyranoside (16): Galactose hydroxy donor **4** (66 mg, 0.12 mmol, 1.2 equiv.), diphenyl sulfoxide (53 mg, 0.26 mmol, 2.6 equiv.) and 2,4,6-tris-*tert*-butylpyrimidine (75 mg, 0.30 mmol, 3.0 equiv.) were dissolved in anhydrous DCM (4 mL) under an atmosphere of argon. Activated molecular sieves (3 Å) were added, and the mixture was stirred for 1 h at ambient temperature. The solution was then cooled to –60 °C and trifluoromethanesulfonic anhydride (22 μL, 0.13 mmol, 1.3 equiv.) was added. The mixture was warmed to –40 °C and stirred at this temperature for 1 h. The reaction was then cooled to –60 °C and lactose acceptor **13** (106 mg, 0.10 mmol, 1.0 equiv.) was added as a solution in anhydrous DCM (2 mL). The reaction was stirred for 3 h going to room temperature and was then quenched by addition of anhydrous triethylamine (140 μL, 1.00 mmol, 10 equiv.). The mixture was transferred to an extraction funnel using EtOAc (40 mL), and the organics were washed with sat. aq. $NaHCO_3$ (40 mL) and brine (40 mL). The water layers were extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (10–30% ethyl ether in petroleum ether) produced the title compound as a white solid (53 mg, 33 μmol, 33%). R_f = 0.28 (15% EtOAc in petroleum ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (br. d, J = 7.9 Hz, 2 H, H_{arom}), 7.98 (br. d, J = 8.0 Hz, 2 H, H_{arom}), 7.89 (br. d, J = 7.6 Hz, 6 H, H_{arom}), 7.75 (br. d, J = 7.9 Hz, 2 H, H_{arom}), 7.58–7.49 (m, 3 H, H_{arom}), 7.46–7.28 (m, 12 H, H_{arom}), 7.24–7.06 (m, 6 H, H_{arom}), 7.02 (br. t, J = 8.0 Hz, 2 H, H_{arom}), 5.80 (t, J = 9.2 Hz, 1 H, 3-H), 5.61 (dd, J = 10.7, 8.0 Hz, 1 H, 2′-H), 5.32 (dd, J = 10.7, 2.3 Hz, 1 H, 3′-H), 5.25 (t, J = 9.5 Hz, 1 H, 2-H), 4.95–4.88 (m, 2 H, 1′-H and 1′′-H), 4.78 (d, J = 9.9 Hz, 1 H, 1-H), 4.71–4.62 (m, 2 H, 6_a-H and 6_a′-H), 4.51 (dd, J = 11.9, 5.5 Hz, 1 H, 6_b-H), 4.38 (d, J = 11.4 Hz, 1 H, 6_a′′-H), 4.33 (m, 1 H, 4′′-H), 4.29–4.21 (m, 2 H, 4′-H and 6_b′′-H), 4.09–4.03 (m, 2 H, 5′′-H and 2′′-H), 3.94 (m, 1 H, 5-H), 3.85 (m, 2 H, 5′-H and 3′′-H), 1.03 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.97 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.90 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.73 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.04 (s, 3 H, $CH_{3\text{-TBS}}$), 0.03 (s, 3 H, $CH_{3\text{-TBS}}$), –0.05 (s, 3 H, $CH_{3\text{-TBS}}$), –0.07 (s, 3 H, $CH_{3\text{-TBS}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.9, 165.8, 165.72, 165.65, 165.2, 165.0 (6 $C{=}O_{Bz}$), 133.4, 133.3, 133.19, 133.16, 132.8 (5 CH_{arom}), 131.9 ($C_{q\text{-}arom}$), 129.84, 129.81, 129.64, 129.61, 129.59 (5 CH_{arom}), 129.53, 129.49, 129.2, 128.9 (4 $C_{q\text{-}arom}$), 128.8 (CH_{arom}), 128.7 ($C_{q\text{-}arom}$), 128.6, 128.38, 128.36, 128.3, 128.0 (5 CH_{arom}), 101.2 (C-1′′), 94.2 (C-1′), 85.7 (C-1), 77.0 (C-5), 76.3 (C-4), 75.1 (C-4′), 74.2 (C-4′′), 74.1 (C-5′), 72.7 (C-3), 71.0 (C-3′), 70.4 (C-2), 69.7 (C-3′′), 68.9 (C-5′′), 67.7 (C-2′), 67.2 (C-2′′), 66.7 (C-6′′), 62.7 (C-6′), 61.8 (C-6), 27.4, 27.3, 26.22, 26.16 (4 $CH_{3\text{-}t\text{Bu-Si}}$), 23.4, 20.7, 18.2, 18.1 (4 $C_{q\text{-}t\text{Bu-Si}}$), –4.0, –4.2, –4.5, –4.6 (4 $CH_{3\text{-TBS}}$) ppm.

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-[2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galactopyranosyl)-β-D-galactopyranosyl]-1-thio-β-D-glucopyranoside (17)

Method A: Galactose hydroxy donor **5** (63 mg, 0.12 mmol, 1.2 equiv.), diphenyl sulfoxide (53 mg, 0.26 mmol, 2.6 equiv.), and 2,4,6-tri-*tert*-butylpyrimidine (30 mg, 0.12 mmol, 1.2 equiv.) were dissolved in anhydrous DCM (3 mL) under an atmosphere of argon. Activated molecular sieves (3 Å) were added, and the mixture was stirred for 1 h at ambient temperature. The solution was then cooled to –60 °C and trifluoromethanesulfonic anhydride (22 μL, 0.13 mmol, 1.3 equiv.) was added. The mixture was warmed to –40 °C and stirred at this temperature for 1 h. The reaction was then cooled to –60 °C and lactose acceptor **13** (106 mg, 0.10 mmol, 1.0 equiv.) was added as a solution in anhydrous DCM (3 mL). The reaction was stirred for 3 h going to room temperature and was then quenched by addition of anhydrous triethylamine (140 μL, 1.0 mmol, 10 equiv.). The mixture was transferred to an extraction funnel using EtOAc (40 mL), and the organics were washed with sat. aq. $NaHCO_3$ (40 mL) and brine (40 mL). The water layers were extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (2–8% EtOAc, 20% DCM in petroleum ether) produced the title compound as a white solid (32 mg, 20 μmol, 20%).

Method B: Imidate donor **7** (1.78 g, 2.6 mmol, 1.5 equiv.) and lactose acceptor **13** (1.80 g, 1.7 mmol, 1.0 equiv.) were coevaporated two times with toluene (10 mL) and then dissolved in anhydrous DCM (17 mL) and cooled to 0 °C before addition of a catalytic amount of TfOH (15 μL, 0.17 mmol, 0.1 equiv.). The reaction was stirred until TLC showed complete conversion of the lactose acceptor (≈4 h). The reaction mixture was then transferred to an extraction funnel with EtOAc (30 mL) and washed with sat. aq. $NaHCO_3$ (50 mL) and brine (40 mL). The aqueous layers were then extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by size exclusion column chromatography, followed by silica gel column chromatography (2–8% EtOAc, 20% DCM in petroleum ether) produced the title compound as a white solid (2.46 g, 1.57 mmol, 92%). R_f = 0.41 (20% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +49 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (br. d, J = 7.9 Hz, 2 H, H_{arom}), 8.05 (br. d, J = 8.0 Hz, 2 H, H_{arom}), 8.01 (br. d, J = 7.9 Hz, 2 H, H_{arom}), 7.95 (br. d, J = 8.0 Hz, 2 H, H_{arom}), 7.90 (br. d, J = 7.9 Hz, 2 H, H_{arom}), 7.88 (br. d, J = 8.0 Hz, 2 H, H_{arom}), 7.68 (br. d, J = 7.9 Hz, 2 H, H_{arom}), 7.58–7.51 (m, 4 H, H_{arom}), 7.50–7.43 (m, 4 H, H_{arom}), 7.42–7.16 (m, 19 H, H_{arom}), 7.14–7.05 (m, 4 H, H_{arom}), 5.78 (t, J = 9.2 Hz, 1 H, 3-H), 5.72 (dd, J = 10.7, 3.7 Hz, 1 H, 2′′-H), 5.61 (dd, J = 10.8, 7.8 Hz, 1 H, 2′-H), 5.50 (dd, J = 10.7, 3.1 Hz, 1 H, 3′′-H), 5.39 (t, J = 9.7 Hz, 1 H, 2-H), 5.36 (d, J = 3.6 Hz, 1 H, 1′′-H), 5.27 (dd, J = 10.7, 2.1 Hz, 1 H, 3′-H), 5.09 (d, J = 3.0 Hz, 1 H, 4′′-H), 4.89 (d, J = 10.0 Hz, 1 H, 1-H), 4.80 (d, J = 7.8 Hz, 1 H, 1′-H), 4.59 (dd, J = 12.1, 2.1 Hz, 1 H, 6_a-H), 4.52 (dd, J = 12.9, 1.8 Hz, 1 H, 6_a′′-H), 4.48–4.41 (m, 2 H, 6_b-H and 6_b′′-H), 4.36 (br. s, 1 H, 5′′-H), 4.11–4.05 (m, 2 H, 4-H and 4′-H), 3.95 (dd, J = 10.9, 5.5 Hz, 1 H, 6_a′-H), 3.87 (ddd, J = 10.0, 5.4, 2.0 Hz, 1 H, 5-H), 3.76 (dd, J = 10.9, 7.7 Hz, 1 H, 6_b′-H), 3.57 (dd, J = 7.7, 5.5 Hz, 1 H, 5′-H), 1.06 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.99 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.2, 166.0, 165.8, 165.7, 165.14, 165.05, 164.83, 164.77 (8 $C{=}O_{Bz}$), 133.4, 133.2, 133.16, 133.13, 133.08, 133.0, 132.9 (7 CH_{arom}), 131.7 ($C_{q\text{-}arom}$), 130.1, 129.98 (2 CH_{arom}),

129.94 ($C_{q\text{-arom}}$), 129.8, 129.66, 129.62 (3 CH_{arom}), 129.60, 129.56 (2 $C_{q\text{-arom}}$), 129.52, 129.4 (2 CH_{arom}), 129.2, 129.0 (2 $C_{q\text{-arom}}$), 128.7 (CH_{arom}), 128.64, 128.56, 128.52 (3 $C_{q\text{-arom}}$), 128.46, 128.43, 128.36, 128.32, 128.18, 128.09 (6 CH_{arom}), 101.5 (C-1′), 98.7 (C-1′′), 85.7 (C-1), 76.95 (C-5), 76.84 (C-4), 76.3 (C-4′), 74.2 (C-3), 72.78 (C-3′), 72.72 (C-5′), 71.2 (C-3′′), 71.0 (C-4′′), 70.4 (C-2), 69.7 (C-2′), 69.6 (C-2′′), 68.3 (C-5′′), 66.9 (C-6′′), 62.6 (C-6), 60.5 (C-6′), 27.5, 27.2 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.2, 20.7 (2 $C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 3070, 2934, 2860, 1722, 1266, 1069, 706 cm^{-1}. HRMS: calcd. for $[C_{88}H_{84}O_{23}SSi + Na]^+$ 1591.4786; found 1591.4795.

2,3,6-Tri-*O*-benzoyl-4-*O*-[2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-glucopyranoside *N*-Phenyl-2,2,2-Trifluoroacetimidate (18): Phenyl thioglycotrioside **17** (2.24 g, 1.43 mmol, 1.0 equiv.) was dissolved in DCM (30 mL) and cooled to 0 °C. *N*-Iodosuccinimide (0.35 g, 1.57 mmol, 1.1 equiv.) was added followed by addition of trifluoroacetic acid (0.12 mL, 1.57 mmol, 1.1 equiv.). The reaction was left stirring under exposure to the atmosphere until TLC showed full conversion (≈3 h). The mixture was then transferred to an extraction funnel with EtOAc (50 mL) and washed with sodium thiosulfate (20% aq., 70 mL), sat. aq. $NaHCO_3$ (70 mL), and brine (60 mL). The aqueous layers were extracted with EtOAc (70 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (0–10% acetone, 40% DCM in petroleum ether) afforded the title compound as a white solid (1.82 g, 1.23 mmol, 86%). R_f = 0.55 and 0.60 (20% acetone in petroleum ether). NMR assignment for the major isomer (α): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.22 (br. d, J = 7.6 Hz, 2 H, H_{arom}), 8.10–8.03 (m, 4 H, H_{arom}), 8.02–7.88 (m, 6 H, H_{arom}), 7.76–7.70 (m, 2 H, H_{arom}), 7.62–7.26 (m, 22 H, H_{arom}), 7.26–7.19 (m, 2 H, H_{arom}), 7.16 (br. t, J = 7.8 Hz, 2 H, H_{arom}), 6.17 (t, J = 9.6 Hz, 1 H, 3-H), 5.75 (dd, J = 10.6, 3.5 Hz, 1 H, 2′′-H), 5.68 (m, 1 H, 2′-H), 5.63 (d, J = 3.5 Hz, 1 H, 1-H), 5.55 (dd, J = 11.0, 3.3 Hz, 1 H, 3′′-H), 5.41 (d, J = 3.5 Hz, 1 H, 1′′-H), 5.32 (d, J = 10.1 Hz, 1 H, 3′-H), 5.23 (dd, J = 10.2, 3.5 Hz, 1 H, 2-H), 5.11 (m, 1 H, 4′′-H), 4.90 (d, J = 7.8 Hz, 1 H, 1′-H), 4.60–4.30 (m, 6 H, 6_a-H, 6_b-H, 6_a′′-H, 6_b′′-H, 5-H and 5′′-H), 4.23–4.07 (m, 3 H, 4-H, 4′-H and 6_a′-H), 3.87 (m, 1 H, 6_b′-H), 3.58 (m, 1 H, 5′-H), 1.09 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 1.03 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.3, 166.1, 165.99, 165.98, 165.8, 165.1, 164.9 (2) (8 C=O_{Bz}), 133.5, 133.4, 133.2, 133.1, 133.01, 132.96, 130.1, 129.9, 129.68, 129.66, 129.5, 129.4 (12 CH_{arom}), 129.1, 129.0, 128.9, 128.7, 128.6 (5 $C_{q\text{-arom}}$), 128.49, 128.45, 128.40, 128.37, 128.3, 128.1 (6 CH_{arom}), 101.5 (C-1′), 98.7 (C-1′′), 90.2 (C-1), 76.9 (C-4), 76.1 (C-4′), 73.0 (C-3′), 72.7 (C-5′), 72.2 (C-2), 71.2 (C-3′′), 71.1 (C-4′′), 70.3 (C-3), 69.9 (C-2′′), 69.6 (C-2′), 68.4 (C-5′′), 68.3 (C-5), 66.9 (C-6′′), 62.3 (C-6), 60.5 (C-6′), 27.6 27.3 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.3, 20.8 (2 $C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 3070, 2934, 2855, 1722, 1452, 1266, 1093, 1069, 1027, 706 cm^{-1}. HRMS: calcd. for $[C_{82}H_{80}O_{24}Si + Na]^+$ 1499.4701; found 1499.4707. The protected globotriaosyl hemiacetal (1.80 g, 1.22 mmol, 1.0 equiv.) was dissolved in acetone (30 mL) and cooled to 0 °C. Cesium carbonate (0.60 g, 1.83 mmol, 1.5 equiv.) was added followed by chloro *N*-phenyl-trifluoroimidate (0.38 g, 1.83 mmol, 1.5 equiv.), and the reaction was stirred at 0 °C for 2 h. The reaction mixture was filtered and concentrated in vacuo. Purification by silica gel column chromatography, which initially was neutralized by running an eluent of 3% NEt_3 in petroleum ether (200 mL) through the column (0–10% EtOAc, 20% DCM in petroleum ether) produced the title compound as a white solid (1.85 g, 1.12 mmol, 92%). R_f = 0.47 and 0.42 (10% EtOAc and 20% DCM in petroleum ether). NMR assignment of major isomer: ^1H NMR (400 MHz, $CDCl_3$): δ = 8.22 (br. d, J = 7.2 Hz, 2 H, H_{arom}), 8.08–8.02 (m, 4 H, H_{arom}), 7.98 (br. d, J = 7.5 Hz, 2 H, H_{arom}), 7.93 (br. d, J = 7.9 Hz, 4 H, H_{arom}), 7.69 (br. d, J = 7.8 Hz, 2 H, H_{arom}), 7.57–7.51 (m, 4 H, H_{arom}), 7.50–7.43 (m, 4 H, H_{arom}), 7.42–7.25 (m, 16 H, H_{arom}), 7.12 (br. t, J = 7.8 Hz, 2 H, H_{arom}), 7.05 (br. t, J = 7.8 Hz, 2 H, $H_{arom\text{-}NPh}$), 6.94 (br. t, J = 7.4 Hz, 1 H, $H_{arom\text{-}NPh}$), 6.71 (br. s, 1 H, C-1), 6.36 (br. s, 2 H, $H_{arom\text{-}NPh}$), 6.14 (t, J = 9.2 Hz, 1 H, 3-H), 5.75 (dd, J = 10.7, 3.6 Hz, 1 H, 2′′-H), 5.69 (dd, J = 10.8, 7.8 Hz, 1 H, 2′-H), 5.54 (dd, J = 10.7, 3.0 Hz, 1 H, 3′′-H), 5.49 (m, 1 H, 2-H), 5.40 (d, J = 3.6 Hz, 1 H, 1′′-H), 5.30 (dd, J = 10.9, 2.1 Hz, 1 H, 3′-H), 5.11 (d, J = 3.1 Hz, 1 H, 4′′-H), 4.90 (d, J = 7.8 Hz, 1 H, 1′-H), 4.64–4.35 (m, 5 H, 6_a-H, 6_b-H, 6_a′′-H, 6_b′′-H and 5′′-H), 4.31–4.21 (m, 2 H, 4-H, 5-H), 4.15–4.09 (m, 1 H, 4′-H), 4.05 (dd, J = 10.9, 5.1 Hz, 1 H, 6_a′-H), 3.81 (m, 1 H, 6_b′-H), 3.55 (dd, J = 8.0, 5.4 Hz, 1 H), 1.07 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 1.01 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.2, 166.0, 165.7, 165.6, 165.4, 164.80, 164.77, 164.7 (8 C=O_{Bz}), 142.8 (C=N), 133.6, 133.4, 133.2, 133.14, 133.10, 133.06, 132.95, 132.87, 130.1, 129.94 (10 CH_{arom}), 129.91 ($C_{q\text{-arom}}$), 129.89, 129.63, 129.59, 129.57, 129.5 (5 CH_{arom}), 129.4 ($C_{q\text{-arom}}$), 129.3 (CH_{arom}), 129.0, 128.6 (2 $C_{q\text{-arom}}$), 128.53, 128.50 (2 CH_{arom}), 128.48 ($C_{q\text{-arom}}$), 128.44, 128.40, 128.36, 128.35, 128.3, 128.1, 128.0 (7 CH_{arom}), 124.2, 119.0 (2 $CH_{arom\text{-}NPh}$), 115.8 (q, J = 285.7 Hz, CF_3), 101.8 (C-1′), 98.8 (C-1′′), 92.1 (C-1, br.), 76.4 (C-4), 76.1 (C-4′), 72.9 (C-3′), 72.7 (C-5′), 71.3 (C-3′′), 71.2 (C-5), 71.0 (C-4′′), 70.2 (C-2 and C-3), 69.8 (C-2′), 69.5 (C-2′′), 68.3 (C-5′), 66.9 (C-6′′), 61.7 (C-6), 60.1 (C-6′), 27.5, 27.2 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.2, 20.7 (2 $C_{q\text{-}t\text{Bu-Si}}$) ppm. IR (neat): $\tilde{\nu}$ = 3069, 2936, 2860, 1718, 1452, 1266, 1093, 1070, 907, 730, 705 cm^{-1}. HRMS: calcd. for $[C_{90}H_{84}F_3NO_{24}Si + Na]^+$ 1670.4997; found 1670.5009.

2-Azido-3-*O*-benzoyl-D-*erythro*-sphingosine-1-yl 2,3,6-Tri-*O*-benzoyl-4-*O*-[2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-α-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-glucopyranoside (21): Globotriaosylimidate donor **18** (180 mg, 0.11 mmol, 1.2 equiv.) and sphingosine acceptor **20** (39 mg, 0.09 mmol, 1.0 equiv.) were coevaporated twice with toluene (5 mL) and then dissolved in anhydrous DCM (3 mL). Activated molecular sieves (3 Å) were added, and the mixture was stirred for 1 h at ambient temperature and then cooled to 0 °C before addition of a catalytic amount of trifluoromethanesulfonic acid (0.8 μL, 9.1 μmol, 0.1 equiv.). The reaction was stirred at 0 °C until TLC showed complete conversion of the sphingosine acceptor (≈2 h). The reaction was quenched by addition of triethylamine (0.13 mL, 0.91 mmol, 10 equiv.). The organics were then transferred to an extraction funnel with EtOAc (40 mL) and washed with sat. aq. $NaHCO_3$ (40 mL) and brine (30 mL). The aqueous layers were extracted with EtOAc (40 mL), and the combined organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (10–20% EtOAc and 10% DCM in petroleum ether) produced the title compound as an amorphous solid (138 mg, 0.07 mmol, 80%). R_f = 0.35 (20% EtOAc in petroleum ether). $[\alpha]_D^{22}$ = +29 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.17 (br. d, J = 7.2 Hz, 2 H, H_{arom}), 8.07–7.99 (m, 4 H, H_{arom}), 7.97 (br. d, J = 7.6 Hz, 4 H, H_{arom}), 7.89 (br. d, J = 7.4 Hz, 4 H, H_{arom}), 7.69 (br. d, J = 7.2 Hz, 2 H, H_{arom}), 7.57 (br. d, J = 7.2 Hz, 2 H, H_{arom}), 7.54–7.42 (m, 8 H, H_{arom}), 7.41–7.27 (m, 15 H, H_{arom}), 7.21 (br. t, J = 7.6 Hz, 2 H, H_{arom}), 7.11 (br. t, J = 7.7 Hz, 2 H, H_{arom}), 5.78 (t, J = 9.1 Hz, 1 H, 3-H), 5.73 (dd, J = 10.7, 3.6 Hz, 1 H, 2′′-H), 5.67 (m, 1 H, 5_{Sp}-H), 5.62 (dd, J = 11.2, 7.7 Hz, 1 H, 2′-H), 5.55–5.48 (m, 2 H, 3′′-H and 3_{Sp}-H), 5.47–5.38 (m, 2 H, 2-H and 4_{Sp}-H), 5.38 (d, J = 3.4 Hz, 1 H, 1′′-H), 5.28 (dd, J = 10.9, 2.1 Hz, 1 H, 3′-H), 5.10 (d, J = 2.8 Hz, 1 H, 4′′-H), 4.83 (d, J = 7.8 Hz, 1 H, 1′-H), 4.71 (d, J = 7.6 Hz, 1 H, 1-H), 4.57–4.48 (m, 2 H, 6_a-H and H6_a′′), 4.46–4.39 (m, 2 H,

6_b-H and H$6_b''$), 4.37 (br. s, 1 H, 5′′-H), 4.21 (t, J = 9.4 Hz, 1 H, 4-H), 4.09 (br. s, 1 H, 4′-H), 3.98 (dd, J = 10.9, 5.4 Hz, 1 H, $6_a'$-H), 3.91–3.77 (m, 4 H, $1_{a–Sp}$-H, 2_{Sp}-H, 5-H and $6_b'$-H), 3.58–3.48 (m, 2 H, 5′-H and $1_{b–Sp}$-H), 1.87 (m, 2 H, 6_{Sp}-H), 1.33–1.12 (m, 22 H, 7_{Sp}-H to 17_{Sp}-H), 1.06 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 1.00 (s, 9 H, $CH_{3\text{-}t\text{Bu-Si}}$), 0.88 (t, J = 6.8 Hz, 3 H, 18_{Sp}-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.2, 166.0, 165.8, 165.7, 165.1, 165.0, 164.9, 164.81, 164.78 (9 C=O_{Bz}), 138.9 (C-5_{Sp}), 133.4, 133.2, 133.1, 133.04, 132.98, 132.9, 130.1, 130.0 (8 CH_{arom}), 129.93, 129.89 (2 $C_{q\text{-}arom}$), 129.8, 129.7, 129.63, 129.56, 129.51 (5 CH_{arom}), 129.46 ($C_{q\text{-}arom}$), 129.4 (CH_{arom}), 129.3, 129.1, 128.6, 128.53, 128.50 (5 $C_{q\text{-}arom}$), 128.48, 128.4, 128.3, 128.2, 128.1 (5 CH_{arom}), 122.3 (C-4_{Sp}), 101.4 (C-1′), 100.6 (C-1), 98.7 (C-1′′), 76.7 (C-4), 76.2 (C-4′), 74.8 (C-3_{Sp}), 73.1 (C-3), 73.0 (C-5), 72.8 (C-3′), 72.7 (C-5′), 71.7 (C-2), 71.2 (C-3′′), 71.0 (C-4′′), 69.7 (C-2′), 69.5 (C-2′′), 68.6 (C-5′′), 68.1 (C-1_{Sp}), 66.9 (C-6′′), 63.4 (C-2_{Sp}), 62.2 (C-6), 60.5 (C-6′), 32.2 (C-6_{Sp}), 31.9, 29.64, 29.61 (2), 29.59, 29.5, 29.31, 29.30, 29.1, 28.5 (10 $CH_{2\text{-}Sp}$), 27.5, 27.2 (2 $CH_{3\text{-}t\text{Bu-Si}}$), 23.2 ($C_{q\text{-}t\text{Bu-Si}}$), 22.7 ($CH_{2\text{-}Sp}$), 20.7 ($C_{q\text{-}t\text{Bu-Si}}$), 14.1 (C-$18_{Sp}$) ppm. IR (neat): $\tilde{\nu}$ = 3070, 2926, 2856, 2104, 1722, 1451, 1265, 1093, 1069, 909, 704 cm^{-1}. HRMS: calcd. for $[C_{107}H_{117}N_3O_{26}Si + Na]^+$ 1910.7587; found 1910.7584.

Globotriaosylsphingosine (22): Protected globotriaosylsphingosine **21** (70 mg, 0.04 mmol, 1.0 equiv.) was dissolved in DCM/MeOH (1:4, 5 mL) and sodium methoxide (30% in MeOH, 5 μL, 0.04 mmol, 1.0 equiv.) was added. The reaction was stirred overnight at ambient temperature, and the progression of the reaction was followed by analytical HPLC–MS. The reaction was then quenched with Amberlite H^+, filtered, and concentrated in vacuo. The crude reaction mixture was then dissolved in pyridine (4 mL) and HF·pyridine (8 μL, 8.0 equiv. based on HF) was added. The reaction was run overnight at ambient temperature and was then concentrated in vacuo. The residue was then roughly purified over a short silica column and eluted with MeOH/$CHCl_3$ (1:3). The residue was then dissolved in a pyridine/Et_3N/MeOH mixture (2:1:1, 8 mL) and bubbled with H_2S at 0 °C for 30 min. The reaction was then stirred at ambient temperature overnight, and the completion of the reaction was monitored by analytical HPLC–MS. The reaction mixture was purged with argon gas and was then concentrated in vacuo. Purification by HPLC–MS (24–46% B, 3 CV, following the general procedure for HPLC–MS purifications) produced the title compound (TFA-salt) as a white powder after lyophilization (24 mg, 27 μmol, 72%). $[\alpha]_D^{22}$ = +32 (c = 0.1, MeOH). ^{1}H NMR (600 MHz, [D_4]methanol): δ = 5.87 (dtd, J = 15.4, 6.8, 1.3 Hz, 1 H, 5_{Sp}-H), 5.49 (ddt, J = 15.4, 6.8, 1.5 Hz, 1 H, 4_{Sp}-H), 4.94 (d, J = 3.9 Hz, 1 H, 1′′-H), 4.40 (d, J = 6.9 Hz, 1 H, 1′-H), 4.37 (d, J = 7.8 Hz, 1 H, 1-H), 4.32 (ddd, J = 6.8, 4.7, 1.3 Hz, 1 H, 3_{Sp}-H), 4.25 (ddd, J = 7.1, 5.2, 1.3 Hz, 1 H, 5′′-H), 4.01–3.96 (m, 2 H, 4′-H and $1_{a–Sp}$-H), 3.94 (dd, J = 11.9, 2.6 Hz, 1 H, 6_a-H), 3.93–3.91 (m, 2 H, 4′′-H and $1_{b–Sp}$-H), 3.89 (dd, J = 7.7, 4.1 Hz, 1 H, 6_b-H), 3.88–3.81 (m, 3 H, $6_a'$-H, $6_b'$-H and 2′′-H), 3.77 (dd, J = 10.2, 3.2 Hz, 1 H, 3′′-H), 3.74 (dd, J = 11.1, 7.1 Hz, 1 H, $6_a''$-H), 3.71–3.66 (m, 2 H, 5′-H and $6_b''$-H), 3.58–3.51 (m, 4 H, 4-H, 3-H, 3′-H and 2′-H), 3.47 (m, 1 H, 5-H), 3.40 (ddd, J = 8.5, 4.7, 3.6 Hz, 1 H, 2_{Sp}-H), 3.30 (t, J = 7.7 Hz, 1 H, 2-H), 2.10 (q, J = 7.0 Hz, 2 H, 6_{Sp}-H), 1.42 (m, 2 H, 7_{Sp}-H), 1.36–1.25 (m, 20 H, 8_{Sp}-H to 17_{Sp}-H), 0.90 (t, J = 7.0 Hz, 3 H, 18_{Sp}-H) ppm. ^{13}C NMR (151 MHz, [D_4]methanol): δ = 136.8 (C-5_{Sp}), 128.3 (C-4_{Sp}), 105.4 (C-1′), 103.7 (C-1), 102.7 (C-1′′), 80.8 (C-4), 79.8 (C-4′), 76.6 (C-5′ and C-5), 76.3 (C-2′), 74.7 (C-3), 74.6 (C-2), 72.8 (C-5′′), 72.6 (C-3′), 71.3 (C-6′′), 71.0 (C-4′′), 70.8 (C-3_{Sp}), 70.5 (C-2′′), 67.1 (C-1_{Sp}), 62.7 (C-6′′), 61.6 (C-6), 61.5 (C-6′), 56.7 (C-2_{Sp}), 33.4 (C-6_{Sp}), 33.1, 30.79 (3), 30.76, 30.74, 30.6, 30.5, 30.4, 30.2, 23.7 (11 $CH_{2\text{-}Sp}$), 14.4 (C-18_{Sp}) ppm. IR (neat): $\tilde{\nu}$ = 3344 (br., s), 2925, 2855, 1674, 1202, 1134, 1067, 1027, 974, 801, 721 cm^{-1}. HRMS: calcd for $[C_{36}H_{67}NO_{17} + H]^+$ 786.4482; found 786.4485.

Supporting Information (see footnote on the first page of this article): NMR spectra of all new compounds.

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