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Integrating ReSET with Glycosyl Iodide Glycosylation in Step-Economy Syntheses of Tumor-Associated Carbohydrate Antigens and Immunogenic Glycolipids

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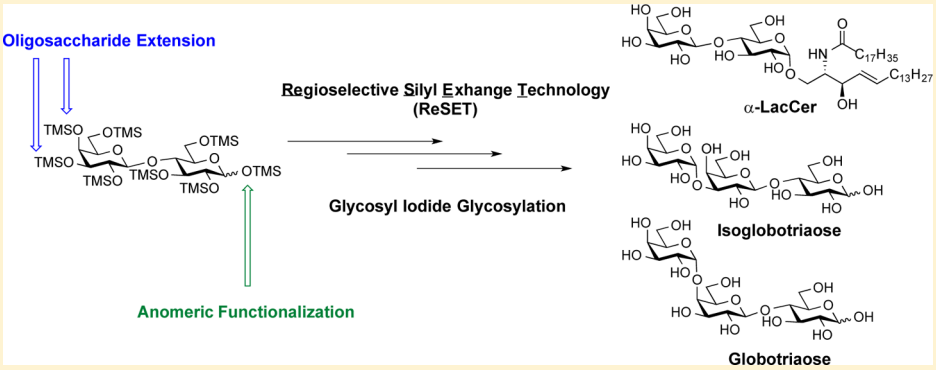
Supporting Information



ABSTRACT: Carbohydrates mediate a wide range of biological processes, and understanding these events and how they might be influenced is a complex undertaking that requires access to pure glycoconjugates. The isolation of sufficient quantities of carbohydrates and glycolipids from biological samples remains a significant challenge that has redirected efforts toward chemical synthesis. However, progress toward complex glycoconjugate total synthesis has been slowed by the need for multiple protection and deprotection steps owing to the large number of similarly reactive hydroxyls in carbohydrates. Two methodologies, regioselective silyl exchange technology (ReSET) and glycosyl iodide glycosylation have now been integrated to streamline the synthesis of the globo series trisaccharides (globotriaose and isoglobotriaose) and α-lactosylceramide (α-LacCer). These glycoconjugates include tumor-associated carbohydrate antigens (TACAs) and immunostimulatory glycolipids that hold promise as immunotherapeutics. Beyond the utility of the step-economy syntheses afforded by this synthetic platform, the studies also reveal a unique electronic interplay between acetate and silyl ether protecting groups. Incorporation of acetates proximal to silyl ethers attenuates their reactivity while reducing undesirable side reactions. This phenomenon can be used to fine-tune the reactivity of silylated/acetylated sugar building blocks.

INTRODUCTION

For the past five decades, cancer has been one of the top 10 causes of death in the United States, and the incidence rate is gradually increasing.[1,2] Cancer treatments and therapeutics to eradicate the disease are being intensively investigated in an effort to improve quality of life for those who suffer. Carbohydrate-based vaccine development is one promising approach to this end.[3−9] Cell membranes are decorated with carbohydrates in the form of glycolipids and glycoproteins with unique structures and aberrant glycosylation patterns that are correlated with tumor progression and metastases.[10−14] Vaccines based on the carbohydrate epitopes of these glycoconjugates are promising therapeutic targets, as are the more recently discovered bacterial derived glycolipids that stimulate immune response. Limited access to sufficient quantities of these biomolecules is a discovery roadblock making practical synthesis of complex carbohydrates a top priority in a recent National Academy of Sciences publication on the future of glycoscience.[15]

One major class of mammalian glycosphingolipids (GSLs) is the globo series tumor-associated carbohydrate antigens (TACAs).[3,4,10,14,16] Globotriaosyl ceramide (Gb3), isoglobotriaosyl ceramide (iGb3), Gb4, Gb5, and Globo H are the prominent members of this class (Figure 1). All of these biomolecules share a lactose core, which is diversified by galactosylation at either the 3′ or 4′ hydroxyls giving rise to iGb3 or Gb3, respectively. Gb3 in turn is the core structure shared by Globo H and Gb5. Given the centrality of the Gb3 core, its synthesis has been the focus of numerous investigations. Nicolaou and co-workers were the first to report the total synthesis of Gb3, and their approach remains one of the most efficient to date.[17,18] A total of eleven steps from commercially available lactose were required to prepare a protected globotriaose that served as a donor for the ceramide aglycon. Seven of those steps were focused on orthogonally

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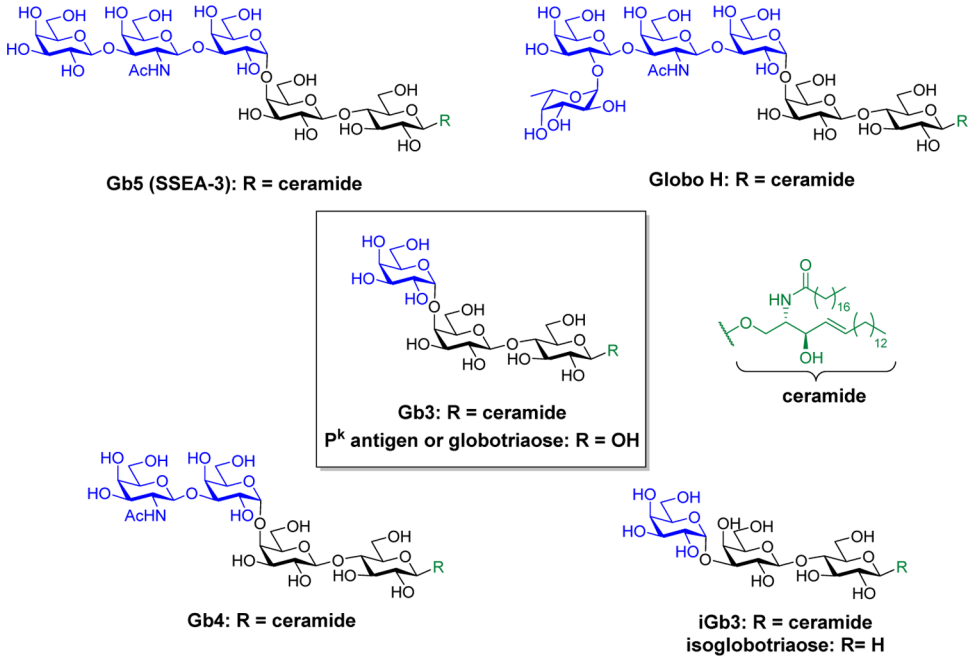

Figure 1. Globo series: A class of common TACAs.

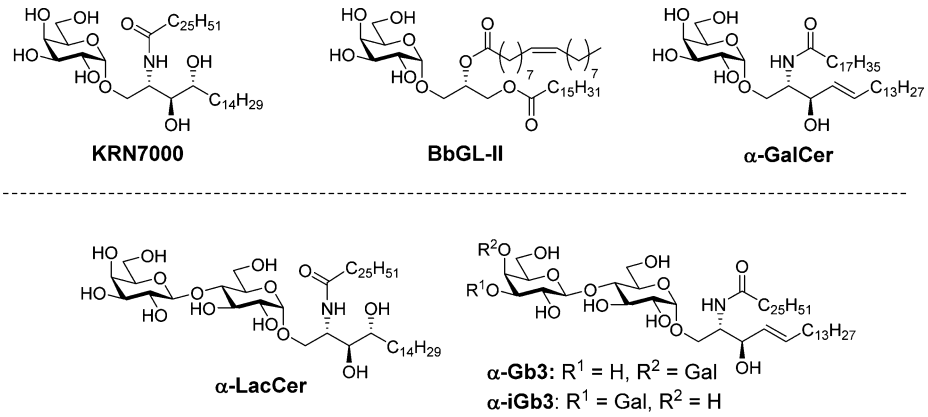

Figure 2. Examples of immunostimulatory glycolipids.

protecting lactose for 4′-galactosylation. Similarly, all syntheses of globotriaose/isoglobotraose that have engaged a lactosyl acceptor have required between 6 and 12 steps to prepare the disaccharide building block.[16−29]

While β-linked ceramides are known TACAs, bacterial derived α-linked analogues also stimulate an immune response and hold promise as vaccine adjuvants.[30−33] Isolating these glycolipids from their natural environments is a challenging process that can lead to decomposition or even rearrangement of the molecules of interest.[34] The lipid composition of the ceramide is also usually obtained as an inseparable and noncharacterizable mixture. For these reasons, chemical synthesis of α-linked ceramides is the primary source of pure and homogeneous materials for immunological studies. To meet this need, our group developed one-pot syntheses of KRN7000, BbGL-II and α-GalCer (Figure 2) and their glucosyl analogues,[35,36] while the Wang[37] and Savage[24] groups have reported syntheses of α-lactosylceramide, α-Gb3 and α-iGb3. These novel "sugar-capped" CD1d ligands for natural killer T (NKT) cells have been tested for their ability to stimulate cytokine release. The results established that the α-linkage is required for immune response and that the oligosaccharide structures serve as immunomodulators. These findings and biological evaluations of TACAs clearly point to an emerging area of immunotherapeutic discovery based upon α- and β-linked ceramides, and access to sufficient quantities of these glycoconjugates is a critical need.

Recently, the concept of step-economy was introduced and has subsequently been advocated among synthetic chemists.[38−41] Instead of the traditional linear synthesis or tour de force total synthesis, considerations of semisynthesis, diversity-oriented synthesis, function-oriented synthesis, and convergent synthesis can lead to high efficiencies in the production of drug leads. In applying this concept to glycoconjugate syntheses, eliminating the need for multiple protection/deprotection steps is an obvious starting point. Per-*O*-TMS protected monosaccharides have proven to be especially useful starting materials for step-economy protecting group manipulations.[42−44] We have exploited these readily available compounds in a process coined regioselective silyl exchange technology (ReSET).[45,46] In just two steps from free sugars, a wide range of partially acetylated/silylated carbohydrates can

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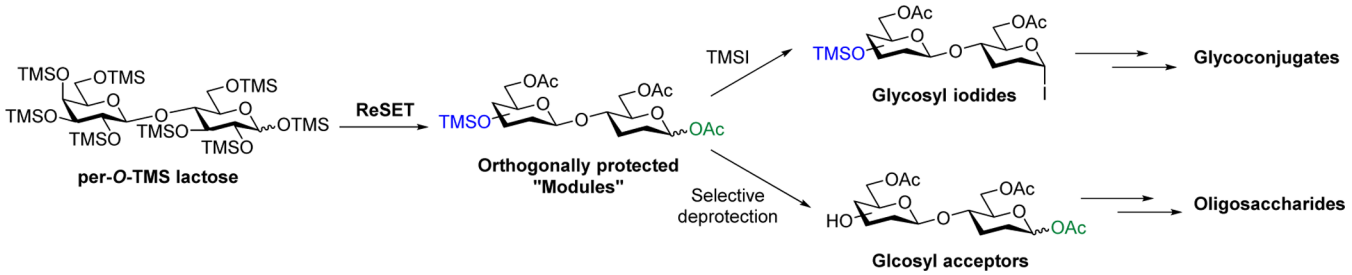
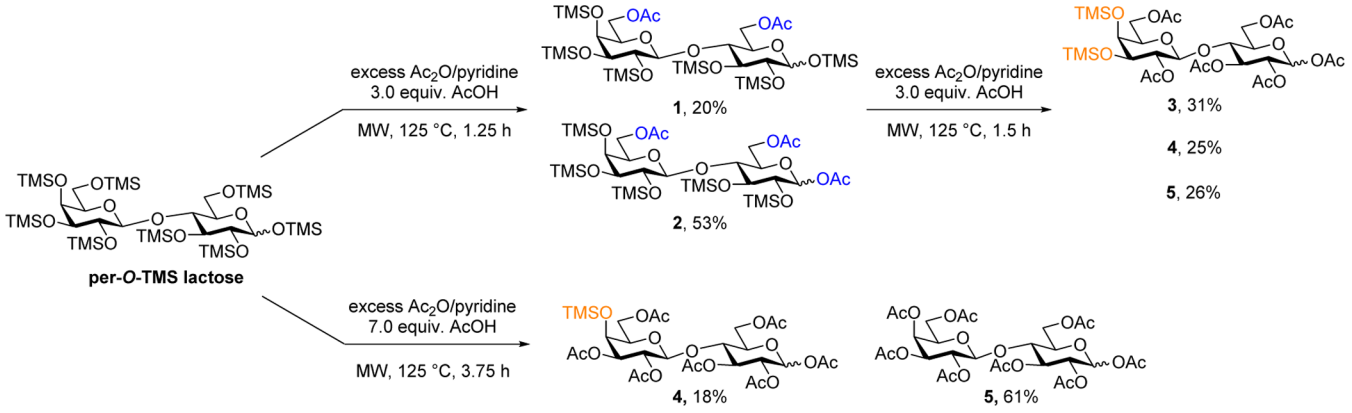


Figure 3. Application of ReSET to generate bifunctional modules for oligosaccharide and glycoconjugate syntheses.

Scheme 1. Tandem ReSET Affords Differentially Protected Lactose Modules



be prepared and readily transformed to either the corresponding glycosyl donor or acceptor (Figure 3). The introduction of electron-withdrawing acetate groups to silyl sugars affords bifunctional modules that are more stable than their per-*O*-TMS counterparts, yet highly reactive in glycosylation reactions. The anomeric acetate can be converted into various leaving groups including halides, thioethers and acetimidates. Efforts reported herein have concentrated on integrating glycosyl iodide glycosylation with a tandem ReSET strategy to accomplish step-economy syntheses of globo series trisaccharides and α-lactosylceramide. The dual methodology platform expands the current organic synthesis toolbox and provides new insight into the electronic interplay of acetate and silyl ether functionalities and their influence upon chemical reactivity.

RESULTS AND DISCUSSION

Tandem ReSET to Prepare Bifunctional Lactose Modules. ReSET begins with per-*O*-silylated sugars, which undergo selective exchange of silyl ethers for acetate protecting groups. The reactions are typically run in pyridine with excess acetic anhydride, and exchange is mediated by the addition of acetic acid. Regiocontrol is correlated with acetic acid stoichiometry and microwave reaction time. Typically, the reactions afford a mixture of products, all of which are useful in making a library of different analogues. For example, treating per-*O*-silylated lactose with 3.0 equiv of AcOH for 1.25 h leads to production of the di- and triacetylated compounds (**1** and **2**, Scheme 1) in 20 and 53% yields, respectively, whereas increasing the amount of acetic acid to 7 equiv forces the production of compound **4** having only one silyl ether at the 4′ position and per-*O*-Ac lactose (**5**) after 3.75 h.[46] Since the lactosyl 3′ and 4′ positions are the major glycosylation sites for globo series antigens, we attempted to establish conditions for preparing the disilyl ether analogue (**3**), but that compound could not be directly obtained in ReSET reactions of per-*O*-silylated lactose under any of the conditions evaluated. Previous studies in our lab indicated that proximal acetate groups facilitate silyl exchange;[46] thus, we reasoned that greater regiocontrol might be achieved using compounds **1** and **2** in a tandem process. To our delight, the reaction proceeded nicely to afford the desired analogues, **3** and **4**, in 31 and 25% yields, respectively. With these partially acetylated building blocks (**1**–**4**) in hand, focus shifted to employing them as either glycosyl donors or acceptors in oligosaccharide and glycoconjugate syntheses.

ReSET Products as Glycosyl Donors: α-Lactosylceramide Synthesis. Previous attempts to form and utilize per-*O*-TMS-lactosyl iodide led to complex reaction mixtures due to glycosidic bond cleavage and silyl exchange.[47] We later discovered that C-6 acetates protect glycosidic linkages from TMSI degradation.[48,49] Consistent with these findings, we were able to cleanly and quantitatively generate the lactosyl iodide from both **1** and **2** (Scheme 2A).[46] Synthetic ceramide (**7**)[36,50] was selected as the acceptor in the glycosylation studies due to its biological relevance. Iodide **6** was reconstituted in dry benzene and cannulated into a mixture of **7**, tetrabutylammonium iodide (TBAI) and diisopropylethylamine (DIPEA). After heating the reaction to 65 °C in anhydrous benzene overnight, the reaction mixture was concentrated and subjected to acidic methanolysis prior to per-*O*-acetylation for characterization purposes (Scheme 2B). A mixture of the per-*O*-acetylated isomers was isolated in 89% yield, and the ratio of primary adduct (**8**) to secondary adduct (**9**) was 1.5 to 1.0, respectively, as determined by anomeric proton integration values obtained by ^{1}H NMR.

The in situ anomerization process promoted by TBAI resulted in the exclusive formation of α-linked glycosides;

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Scheme 2. Synthesis of α-Lactosylceramide

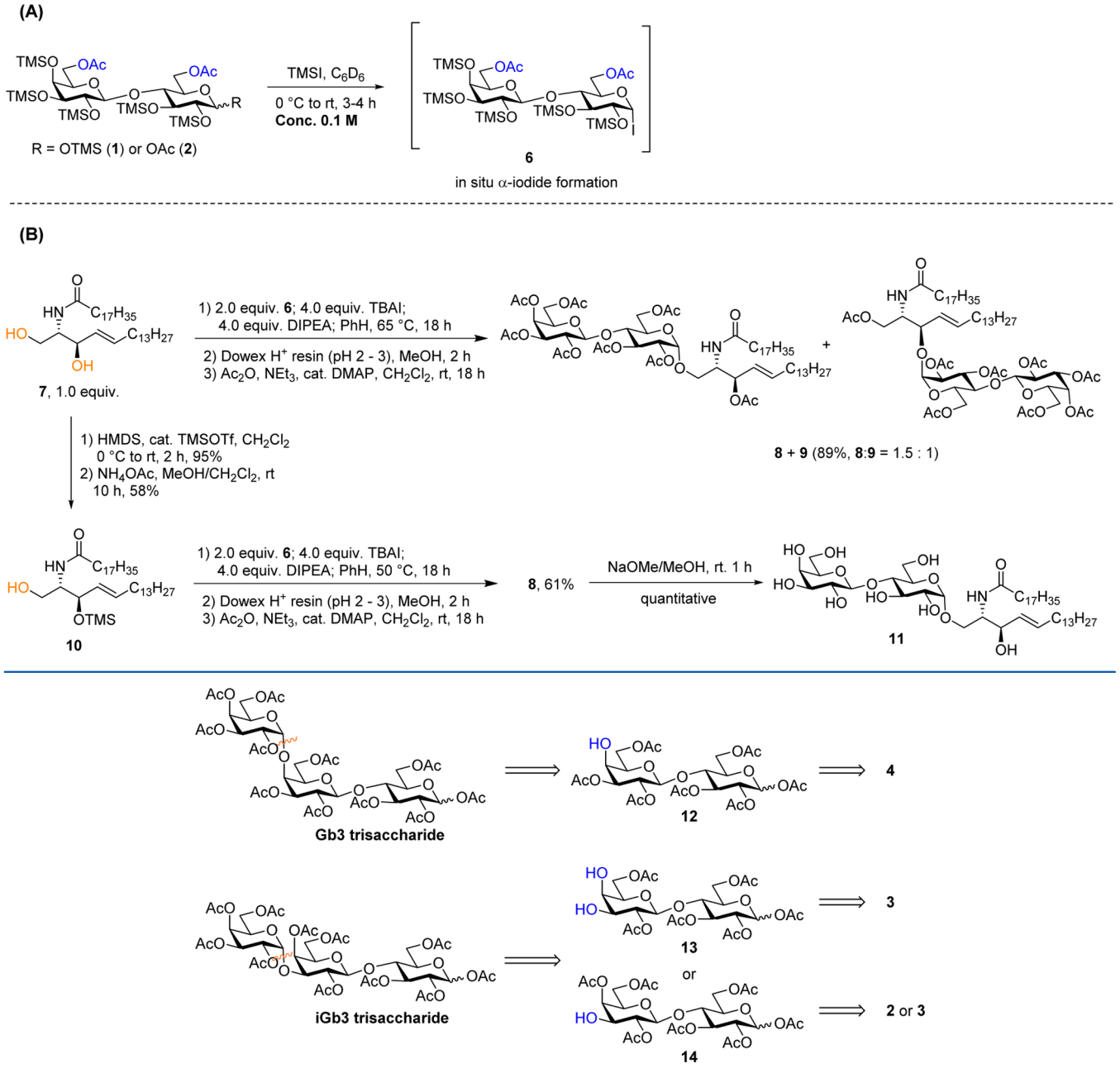

Figure 4. Retrosynthetic analysis of globo series trisaccharides.

however, multiple flash column chromatography purifications were required to separate **8** and **9**. To alleviate this complication, compound **10** was prepared by selective desilylation of di-*O*-TMS ceramide[42] according to a method recently published by Cui and co-workers.[51] Ceramide **10** was then coupled with **6** under the TBAI-promoted conditions (Scheme 2B). After acidic methanolysis and peracetylation, compound **8** was the only glycosylation product isolated. The glycosylation yield (61%) was slightly decreased compared to the glycosylation result of ceramide **7** (89%), possibly due to the result of increased steric hindrance from the secondary TMS ether. Nevertheless, deacetylation of **8** using NaOMe/MeOH led to fully deprotected α-lactosylceramide (**11**) in quantitative yield.

The synthesis of α-lactosylceramide has several salient features: (1) the glycosyl donor (**6**) can be prepared in three steps and 72% overall from free lactose; (2) the lactosyl iodide is reactive enough to couple with unprotected or partially protected ceramides, yet the inter-residue glycosidic bond is stable enough to survive glycosylation; (3) only the desired α-linkage is obtained in good yield; (4) only TMS ether and acetate protecting groups are utilized, allowing mild deprotection steps that are compatible with alkene and amide functionality in the ceramide component. This methodology nicely complements reactions of per-*O*-acetylated lactose, which afford the β-anomer due to neighboring group participation of the C-2 acetate.[52]

ReSET Products As Acceptors: Globo Series Trisaccharide Syntheses. Having demonstrated glycosylation

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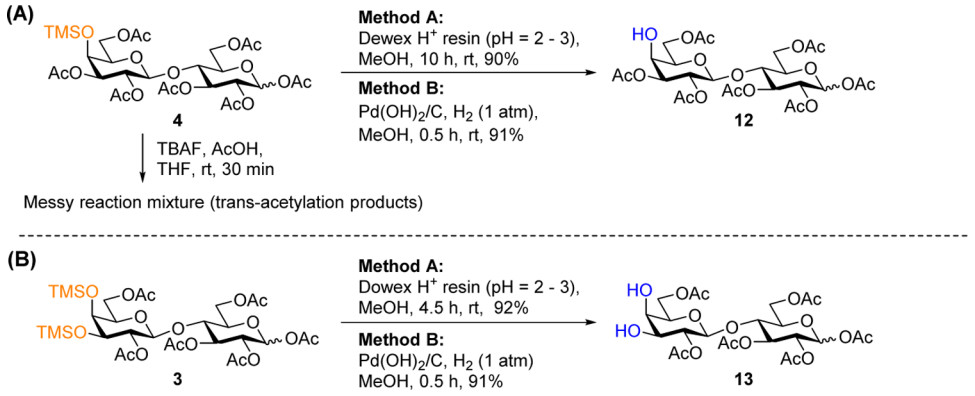
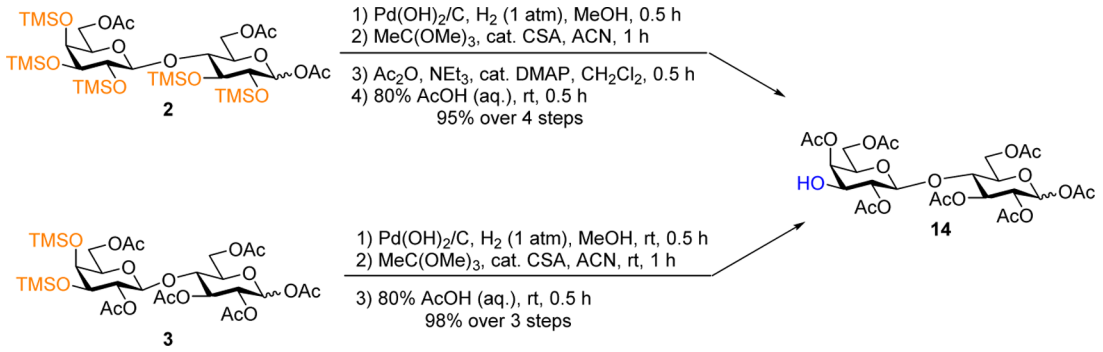
Scheme 3. Synthesis of Acceptors 12 and 13



Scheme 4. Synthesis of 3′-OH Acceptor 14



efficiency with partially acetylated silyl donors, we set our sights on exploiting these substrates as glycosyl acceptors. Chemical syntheses of the Globo series TACAs involve the construction of the crucial α-1,3 and α-1,4 glycosidic linkages. Yet a simple first order disconnection of globotriaose and isoglobotriaose at these linkages leads to 4′-OH acceptor **12**, 3′,4′-di-OH acceptor **13**, or 3′-OH acceptor **14** (Figure 4), which are all readily available from the tandem ReSET products **2**, **3**, and **4**.

To reduce the glycosylation strategy to practice, compound **4** was treated with Dowex acidic resin in MeOH to give the 4′-OH acceptor **12** in 90% yield (Scheme 3A). The long reaction time (10 h) was consistent with earlier results in our lab indicating that the rate of protodesilylation is attenuated with increasing numbers of acetate protecting groups.[46] In an attempt to shorten the reaction time, we initially subjected **4** to TBAF/AcOH, but the reaction led to unresolved trans-acetylation products. However, a report from Ikawa and co-workers[53,54] encouraged us to explore the deprotection of silyl ethers using Pd-catalyzed hydrogenolysis. Much to our delight, after 30 min under 1 atm H_2, **4** was transformed to 4′-OH acceptor **12** in 91% yield. In a similar manner, either acidic methanolysis or Pd-catalyzed hydrogenolysis was applied to **3**, leading to 3′,4′-di-OH compound **13** in 92 and 91% yields, respectively (Scheme 3B). To confirm the deprotection was the result of hydrogenolysis and not acidic catalysis, a control experiment without the introduction of H_2 gas was conducted. No reaction was observed after 2 h, indicating that H_2 gas is required for the Pd-catalyzed deprotection.

In order to prepare 3′-OH acceptor **14**, we looked to the work of Lin and co-workers, who published a one-pot procedure to selectively acetylate at the 4-position of galactose via 3,4-orthoester formation followed by selective acidic hydrolysis.[55] The procedure showed excellent results when applied to monosaccharides but not oligosaccharides, presumably because of solubility issues.[56] An adapted version of the methodology was applied to ReSET products **2** and **3** (Scheme 4). Compound **2** was first subjected to Pd-catalyzed hydrogenolysis and then concentrated to dryness. The resulting residue was reacted with trimethyl orthoacetate in the presence of catalytic camphor sulfonic acid (CSA) to form the cyclic orthoester at the 3′ and 4′ positions. After peracetylation, the orthoester was selectively hydrolyzed affording the 3′-OH acceptor (**14**) in almost quantitative yield. The four-step procedure was carried out in less than 3 h, and only one flash column chromatography purification was needed to obtain the target molecule. The consecutive hydrogenolysis−orthoester formation−acidic hydrolysis protocol was also applied to di-*O*-TMS compound **3**, leading to the same 3′-OH acceptor **14** in almost quantitative yield (Scheme 4).

With all the acceptors (**12**−**14**) in hand, we next examined the glycosylation reactions to form the globo series trisaccharides (Table 1). Wishing to achieve efficient α-galactosidation of the 4′-OH acceptor (**12**), we first tried using per-*O*-TMS galactosyl iodide promoted by TBAI in situ anomerization,[35,36] but the major product obtained was silylated acceptor. We previously observed similar trans-silylation complications, especially in cases where the acceptor is hindered or unreactive.[57,58] However, the per-*O*-benzyl galactosyl iodide derived from anomeric acetate **15**[59] was reactive when activated with AgOTf, and the presence of benzyl protecting groups conveniently allowed UV monitoring of the reaction progress. Importantly, only the desired α-1,4 linkage was obtained, which simplified the purification (Table 1, entry 1). The same reaction conditions with 1.5 and 2.5 equiv of

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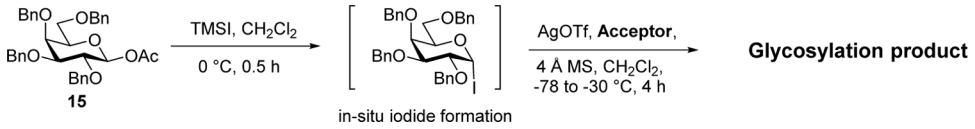
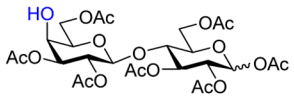
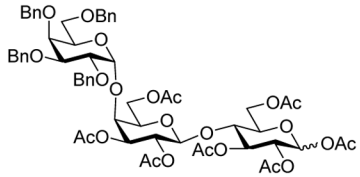
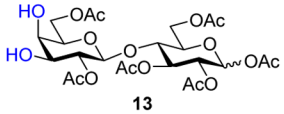
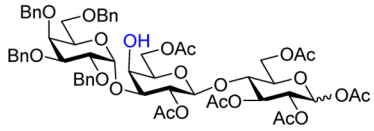
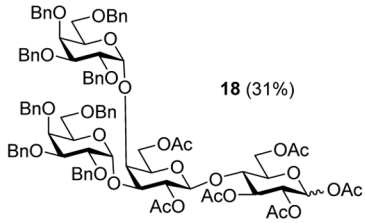
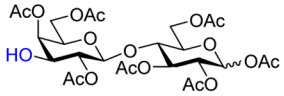
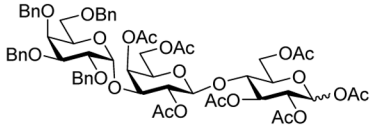
Table 1. Glycosyl Iodide Glycosylation Gave Gb3 and iGb3 Trisaccharide Scaffolds



Entry	Acceptor (limiting reagent)	Donor equiv.	Glycosylation product (yield)
1	 **12**	2.5 equiv.	 **16** (75%)
2	 **13**	1.5 equiv.	 **17** (44%)
3	**13**	2.5 equiv.	**17** (26%) +  **18** (31%)
4	 **14**	2.5 equiv.	 **19** (58%)
5*	**14**	2.5 equiv.	**19** (75%)

*Condition: 3.0 equiv of AgOTf, 3.0 equiv of tetramethylurea (TMU), 4 Å MS, CH_2Cl_2, −30 °C to rt, 24 h.

iodide were applied to the glycosylation reaction with acceptor **13** to examine the relative reactivity of the two hydroxyl groups. When 1.5 equiv of iodide was used, the desired protected isoglobotraose (**17**) was obtained, albeit in a lower yield of 44% (Table 1, entry 2). When 2.5 equiv of iodide was added, not only was **17** obtained in 26% yield, but also the digalactosylated product (**18**) was obtained in 31% yield (Table 1, entry 3).

To avoid over-galactosylation, the 3′-OH acceptor **14** was introduced. In this case, the desired product (**19**) was obtained in 58% yield (Table 1, entry 4). Side reactions, which we attributed to acyl migration, were also observed on the TLC plate. To minimize this possibility, an acid scavenger (tetramethylurea, TMU)[60] was added to the AgOTf-promoted glycosylation (Table 1, entry 5). The neutralized glycosylation procedure required higher temperature and longer time to complete; however, the target molecule (**19**) was obtained in 75% yield, indicating that the side reactions could be suppressed by the addition of weak base.

Debenzylation of compound **16** followed by reacetylation led to per-*O*-Ac globotriaose **20** in 95% yield (Scheme 5). Storing the trisaccharide in the peracetylated form was desired to increase stability. Moreover, the ^{1}H NMR signals of compound **20** were better resolved than the benzylated counterpart (**16**), making compound characterization and quality control more reliable. Acetate protecting groups are also preferred when generating the glycosyl iodide of the trisaccharides. When compound **16** was treated with TMSI, the reaction became messy and glycosidic bond cleavage products were observed in crude MS analyses; another example of electron donating protecting groups rendering the glycosidic linkage susceptible to cleavage. In contrast, peracetylated **20** readily transformed to the corresponding iodide (**22**) in situ, and subsequent reaction leads to β-linked glycoconjugates.

Global deprotection of **16** continued with Pd-catalyzed hydrogenolysis followed by deacetylation yielding globotriaose (**21**) in nearly quantitative yield (Scheme 5). The total synthesis of globotriaose required only four steps from free lactose to form the globotriaose scaffold, and two more consecutive protecting group manipulations (total six steps) to the natural product globotriaose (**21**).

In 1988, Nicolaou and co-workers published the first synthesis of Gb3, which is arguably the most efficient synthesis until now.[17] The approach required seven steps to prepare a selectively protected 4′-OH acceptor, which was glycosylated with per-*O*-Bn galactosyl fluoride under the activation of $AgCl_4$ and $SnCl_2$. During the process, seven protecting groups (OAc,

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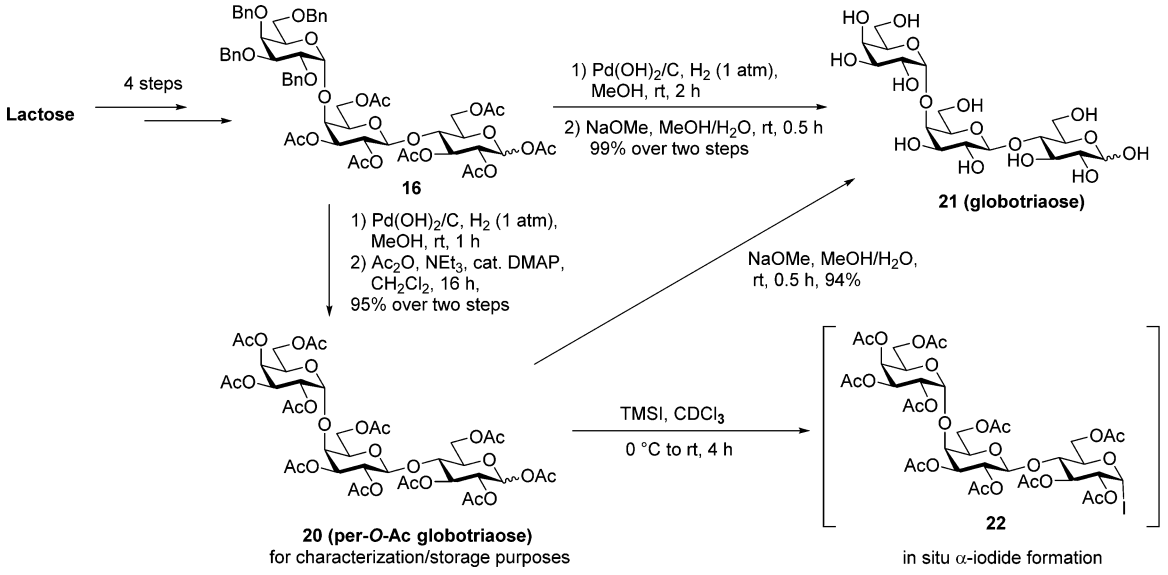
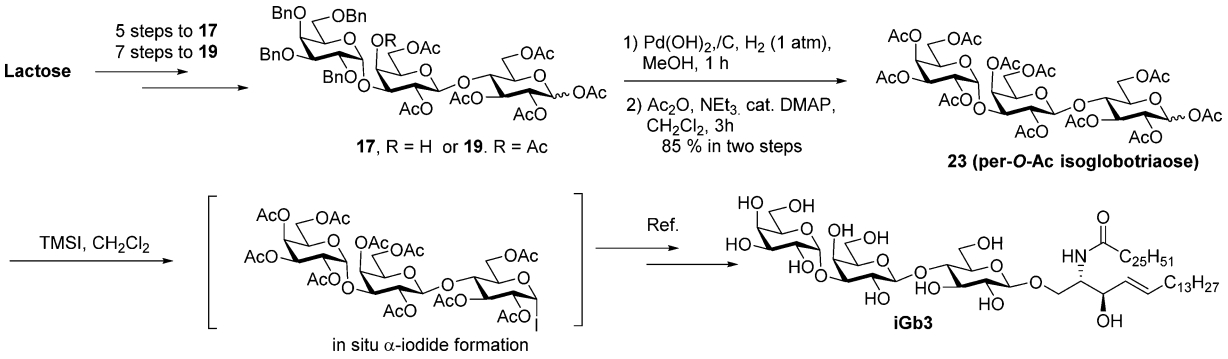
Scheme 5. Six-Step Synthesis of Globotriaose from Free Lactose



Scheme 6. Formal Synthesis of iGb3 from Compound 17



OBn, OBz, OPiv, SPh, F, and benzylidene) were utilized. In contrast, the simplified RESET/glycosyl iodide synthetic platform involves only three steps to prepare the 4′-OH glycosyl acceptor and arrives at the globotriaose scaffold in four steps. Moreover, the glycosyl iodides react under neutral conditions avoiding toxic tin reagents as the promoter for α-1,4 glycosylation.

Compounds **17** and **19** could be transformed to per-*O*-Ac isoglobotriaose (**23**) in 85% yield by hydrogenolysis and peracetylation (Scheme 6). In 2009, Castillon and co-workers published an efficient TBAI/AW-300 MS-promoted synthesis of iGb3 using per-*O*-Ac isoglobotriaose iodide and stannylceramide.[61] The group purchased isoglobotriaose and peracetylated it prior to generating the iodide. In the total synthesis approach to iGb3 reported here, both **23** and the in situ generated iodide intercept the Castillon synthesis, providing a formal synthesis of iGb3.

Among the published syntheses of isoglobotriaose scaffold using 3′,4′-di-OH acceptors, galactosylation typically suffers from low yields and poor stereoselectivity. Moreover, the 3′,4′-di-OH acceptors require at least six or seven steps to prepare from free lactose. When using acetylated galactosyl bromide[24] and trichloroacetimidate[26] donors, the glycosylation yields ranged from 28 to 31% with inseparable α-1,3 and β-1,3 isomers. In order to eliminate side reactions and increase donor reactivity, both Ogawa[25] and Schmidt[27] have introduced *O*-benzyl-protected galactosyl thiomethyl and trichloroacetimidate donors. These reactive donors provided increased yields but did not prevent the formation of β-linked isomers. In contrast, *O*-benzyl protected galactosyl iodide (Table 1, entries 2 and 3) readily reacts with acceptors **12**, **13**, and **14** to afford the α-linked products exclusively and in yields ranging from 44 to 75%.

Selectively protected 3′-OH acceptors generally afford better yields than 3′,4′-di-OH acceptors, since there is no competition between the two hydroxyl groups. However, 6−8 steps were required in order to prepare the 3′-OH acceptors. The protecting group manipulations involved OAc, OBn, OPiv, OPMB, and SPh groups, and the preparation took days to complete.[28,29] In comparison, the ReSET approach (Table 1, entry 4 and 5) required only three protecting groups (OBn, OAc, and OTMS) and 21 h to synthesize acceptor **14**. The optimized glycosylation of compound **14** reached 75% yield when coupled with per-*O*-Bn galactosyl iodide.

■ CONCLUSION

The combined ReSET/glycosyl iodide glycosylation strategy provides a step-economy platform for glycoconjugate synthesis that centers on the conversion of per-*O*-TMS-lactose into selectively protected modules with differential reactivities.[62] The orthogonally protected intermediates can be transformed into reactive glycosyl iodides in situ and coupled with

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unprotected or partially protected ceramides with high stereoselectivity in good yields. The marriage of these powerful platforms results in the exclusive formation of alpha-linked glycosides, which leads to increased efficiencies during the purification process. The bifunctional nature of these modules can be further exploited upon removal of the TMS groups yielding glycosyl acceptors ready for sugar chain elongation. When introduced into glycosylation reactions, the corresponding globo series tumor-associated carbohydrate antigens can be obtained in respectable yields. The TACA syntheses require only three protecting groups (OAc, OBn, and OTMS), which significantly reduces the number of protection/deprotection steps, not only in preparing the glycosyl acceptors, but also by direct activation of the anomeric acetate or silyl ether to the glycosyl iodide. These combined features characterize a versatile synthetic platform for the rapid assembly of biologically relevant glycolipids.

Beyond the time and step efficiencies of these methodologies, a unique interplay between acetate and silyl ether protecting groups is revealed. The acetate protecting groups help suppress side reactions such as silyl migration and interresidue glycosidic bond cleavage during TMSI-promoted iodide formation. Similarly, we find that proximal acetates significantly alter the reactivity of silyl ethers toward protodesilylation. This phenomenon is clearly evidenced in the acidic methanolysis of 4′-OTMS acetylated lactose (**4**), which took twice as long as analogue **3** having one less acetate, i.e., 3′,4′-di-OTMS acetylated lactose. We attribute the reactivity attenuation to acetate electron withdrawing effects, which inductively reduce the basicity of the ether and acetal oxygen atoms. Exquisite control is afforded by acetate incorporation, as shown in the contrasting behavior of per-*O*-silylated lactose and 6,6′-di-*O*-Ac-per-*O*-silyllactose (**1**) under the action of TMSI. Di- and trisaccharide substrates having no acetates undergo interresidue glycosidic bond cleavage, whereas incorporation of only two acetate groups at the C-6 positions directs reactivity toward the reducing end acetal resulting in the quantitative generation of the corresponding glycosyl iodides. These findings offer opportunities in systems removed from carbohydrate substrates where one could capitalize on the concept of attenuating ether reactivity by the inductive effects of proximal protecting groups.

EXPERIMENTAL SECTION

Procedure for Tandem Regioselective Silyl Exchange (ReSET) of Per-*O*-TMS Lactose (Scheme 1). In a 10 mL microwave reactor vessel with a dry stir bar, per-*O*-TMS lactose (500 mg, 0.54 mmol) was dissolved in anhydrous benzene (3 mL). The solvent was removed under rotary evaporation with argon backfilling. The azeotropic distillation was repeated two additional times to dryness affording viscous syrup. To the reaction flask was added anhydrous pyridine (2.0 mL/per mmol TMS sugar: 1.1 mL), Ac_2O (1.5 mL/per mmol TMS sugar: 8.1 mL), and AcOH (93 μL, 1.62 mmol, 3.0 equiv). The reaction vessel was subjected to microwave irradiation (standard mode, 100 W, 125 °C, ∼40 psi) for 1.25 h. Once TLC showed the reaction was complete, the reaction mixture was transferred into a 50 mL round-bottom flask, where it was azeotroped with copious amounts of anhydrous benzene to remove excess reagents and solvent. The crude mixture was immediately purified by gradient flash column chromatography (EA/Hex/NEt_3 = 5:85:10 to 14:85:1 to 29:70:1) to afford compound **1** (93 mg, 20%) and **2** (239 mg, 53%). Later on, compound **1** and **2** were combined. A mixture of compound **1** and **2** (194 mg, ∼0.23 mmol: calculated on the basis of compound **2**'s molecular weight; same as the following) was then treated with dry pyridine (0.35 mL), Ac_2O (0.46 mL) and AcOH (40 μL, 0.69 mmol, ∼3.0 equiv), followed by microwave irradiation (standard mode, 100 W, 125 °C, ∼40 psi) for 1.5 h. After the starting material was completely consumed, the reaction was azeotroped with dry benzene to remove excess reagents and solvent. The resulting residue was immediately purified by gradient flash column chromatography (EA/Hex = 40:60 to 60:40) to afford compound **3** (54 mg, ∼31%), compound **4** (41 mg, ∼25%) and compound **5** (42 mg, ∼26%) as white foams.

*(2,6-Di-O-acetyl-3,4-O-ditrimethylsilyl-β-D-galactopyranosyl)-(1−4)-O-(1,2,3,6-tetra-O-acetyl)-D-glucopyranoside (**3**).* Compound **3** (54 mg, ∼31%) was obtained from consecutive ReSET of per-*O*-TMS lactose (see ReSET procedure for reaction and purification conditions). The product consisted of inseparable α/β anomeric acetates and the major β-anomer is reported: TLC (EA/Hex = 40:60) R_f 0.38; ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.66 (d, *J* = 8.2 Hz, 1H, H-1), 5.21 (appt. t, *J* = 9.3 Hz, 1H, H-3), 5.06−5.00 (m, 2H, H-2, H-2′), 4.40 (dd, *J* = 12.0, 1.7 Hz, 1H, H-6a), 4.28 (d, *J* = 7.9 Hz, 1H, H-1′), 4.19−4.14 (m, 2H, H-6b, H-6′a), 4.10 (dd, *J* = 11.0, 6.6 Hz, 1H, H-6′b), 3.79 (appt. t, *J* = 9.3 Hz, 1H, H-4), 3.77−3.72 (m, 2H, H-4′, H-5), 3.57 (appt. t, *J* = 6.6 Hz, 1H, H-5′), 3.53 (dd, *J* = 9.8, 2.7 Hz, 1H, H3′), 2.11 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 0.12 (s, 9H), 0.11 (s, 9H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 170.6, 170.5, 169.8, 169.7, 168.9, 168.89, 101.1, 91.6, 74.9, 73.6, 72.9, 72.6, 72.4, 71.6, 71.1, 70.5, 62.5, 62.1, 21.1, 20.84, 20.82, 20.7, 20.6, 0.4, 0.2; HRMS (ESI-ion trap) *m*/*z* calcd for $[C_{30}H_{50}O_{17}Si_2 + NH_4^+]$ 756.2925, found 756.2947.

General Procedure for α-Lactosylceramide Synthesis (Scheme 2). In an oven-dried NMR tube, compound **2** (59 mg, 0.07 mmol) was added and dissolved in dry benzene-d_6 (0.7 mL). After TMSI (12 μL, 0.08 mmol) was introduced to the reaction vessel, the reaction was kept and 0 °C and gradually warmed to rt over 4−5 h. The reaction was monitored by proton NMR until the corresponding iodide (**6**) formed in situ. Next, compound **6** was transferred to a 25 mL pear-shape bottle, azeotroped with dry benzene (3 mL × 3) and dried under a high vacuum for 1 h to afford the iodide as a light yellow foam. *Note: The iodide is highly reactive and moisture sensitive. Column chromatography or aqueous workup should be avoided.* The compound **6** was next dissolved in dry benzene (2 mL) and kept under Ar. In a separate round-bottom flask, ceramide **7** (20 mg, 0.035 mmol), TBAI (52 mg, 0.14 mmol), DIPEA (25 mL, 0.14 mmol) and activated 4 Å molecular sieves (80 mg) were dissolved in dry bezene (2 mL) and stirred at rt under Ar. The iodide solution was transferred to the glycosyl acceptor solution via cannula dropwisely over 3 min at rt. Once transferred, the reaction mixture was gently heated to 65 °C overnight. Next, the reaction mixture was cooled to rt, filtered through a short Celite pad and concentrated under reduced pressure. The resulting residue was dissolved in MeOH (5 mL) and stirred with the Dowex acidic resin (pH = 2−3) at rt. After 2 h, the resin was filtered, and the solvent was evaporated under reduced pressure to afford a viscous orange oil. The resulting oil was then dissolved in CH_2Cl_2 (1 mL) under Ar. To the solution was then added Ac_2O (0.8 mL), NEt_3 (1.2 mL) and catalytic DMAP (∼2 mg), and the mixture was stirred at rt overnight. Next, the reaction mixture was concentrated under reduced pressure and was purified using flash column chromatography (EA/Hex = 50:50) to afford a mixture of isomers (compounds **8** and **9**) (39 mg, 89%) as a white foam. The mixture could be further purified by gradient flash column chromatography (EA/Hex = 40:60 to 60:40) to separate both isomers for characterization purpose. Mono-*O*-TMS protected ceramide **10** (19 mg, 0.03 mmol) could also be applied to the above reaction conditions but using 50 °C in the glycosylation step. Followed by desilylation and reacetylation, compound **8** (22 mg, 61%) was obtained as the only isomer.

*(2S,3R,4E)-3-O-Acetyl-1-O-(α-per-O-acetyl-D-lactopyranosyl)-2-(N-octadecanosylamino)octadec-4-ene-1,3-diol (**8**).* Compound **8** was obtained either from glycosyl iodide glycosylation using iodide **6**, and ceramide **7** or ceramide **10** (see general procedure for α-lactosylceramide synthesis for reaction and purification conditions): TLC (EA/Hex = 1/1) R_f 0.43; $[\alpha]^{24}_D$ +16.5 (c 0.26, $CHCl_3$); ^{1}H NMR (800 MHz, C_6D_6) δ 5.88 (appt. t, *J* = 9.5 Hz, 1H, H-3), 5.86−5.82 (m, 1H, alkene H-e), 5.55 (appt. t, *J* = 7.9 Hz, 1H, H-c), 5.52−5.47 (m, 3H, alkene H-d, H-2′, H-4′), 5.44 (d, *J* = 9.2 Hz, 1H, NH),

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5.14 (dd, J = 10.4, 3.4 Hz, 1H, H-3′), 5.10 (dd, J = 9.5, 3.7 Hz, 1H, H-2), 5.05 (d, J = 3.7 Hz, 1H, H-1), 4.73 (d, J = 10.4 Hz, 1H, H-6a), 4.63−4.58 (m, 1H, H-b), 4.39 (d, J = 7.8 Hz, 1H, H-1′), 4.22 (dd, J = 11.7, 6.4 Hz, 1H, H-6b), 4.14 (dd, J = 11.1, 6.6 Hz, 1H, H-6′a), 4.11−4.05 (m, 2H, H-5, H-6′b), 3.77 (dd, J = 10.7, 3.2 Hz, 1H, H-a), 3.67 (appt. t, J = 9.5 Hz, 1H, H-4), 3.50 (appt. t, J = 6.6 Hz, 1H, H-5′), 3.44 (dd, J = 10.7, 4.0 Hz, 1H, H-a′), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.95 (s, 3H), 1.87 (s, 3H), 1.74 (s, 3H), 1.69 (s, 3H), 1.66 (s, 3H), 1.55 (s, 3H), 1.35−1.26 (m, 52H, alkyl chain), 0.93−0.91 (m, 6H, terminal Me × 2); ^{13}C NMR (200 MHz, C_6D_6) δ 172.3, 170.3, 170.2, 170.1, 169.9, 169.8, 169.4, 169.2, 169.1, 137.3, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 126.1, 101.6, 96.8, 77.2, 73.1, 71.6, 71.5, 70.9, 70.7, 69.7, 69.2, 67.4, 67.0, 62.6, 61.1, 51.3, 36.5, 32.8, 32.38, 32.37, 30.3, 30.28, 30.26, 30.25, 30.24, 30.19, 30.18, 30.0, 29.88, 29.87, 29.77, 29.72, 29.4, 26.1, 23.2, 20.9, 20.7, 20.6, 20.5, 20.49, 20.2, 20.16, 19.8, 14.4; HRMS (ESI-ion trap) m/z calcd for $[C_{64}H_{107}NO_{21} + Na^+]$ 1248.7228, found 1248.7227.

*(2S,3R,4E)-1-O-Acetyl-3-O-(α-per-O-acetyl-D-lactopyranosyl)-2-(N-octadecanosylamino)octadec-4-ene-1,3-diol (**9**).* Compound **9** was obtained from the glycosyl iodide glycosylation using iodide **6** and ceramide 7 (see general procedure for α-lactosylceramide synthesis for reaction and purification conditions): TLC (EA/Hex = 1/1) R_f 0.40; $[\alpha]^{24}_D$ +21.6 (c 0.47, $CHCl_3$); ^{1}H NMR (800 MHz, C_6D_6) δ 5.88 (appt. t, J = 9.5 Hz, 1H, H-3), 5.69 (d, J = 8.6 Hz, 1H, NH), 5.60 (ddd, J = 18.6, 9.1, 3.4 Hz, 1H, alkene H-e), 5.55−5.52 (m, 1H, H-2′), 5.49 (d, J = 3.5 Hz, 1H, H-4′), 5.38 (dd, J = 15.5, 8.0 Hz, 1H, alkene H-d), 5.21 (d, J = 3.7 Hz, 1H, H-1), 5.15 (dd, J = 10.5, 3.5 Hz, 1H, H-3′), 5.06 (dd, J = 10.2, 3.7 Hz, 1H, H-2), 4.67 (dd, J = 11.8, 2.0 Hz, 1H, H-6a), 4.51 (d, J = 7.9 Hz, 1H, H-1′), 4.42 (ddd, J = 8.9, 7.4, 4.6 Hz, 1H, H-b), 4.36 (dd, J = 11.6, 6.0 Hz, 1H, H-a), 4.31 (dd, J = 11.9, 4.6 Hz, 1H, H-6b), 4.22−4.06 (m, 5H, H-5, H-6′ab, H-c, H-a′), 3.87−3.83 (m, 1H, H-4), 3.48 (appt. t, J = 7.0 Hz, 1H, H-5′), 2.01 (s, 3H), 1.98 (s, 3H), 1.91 (s, 3H), 1.83 (s, 3H), 1.78 (s, 1H), 1.74 (s, 3H), 1.64 (s, 3H), 1.53 (s, 3H), 1.43−1.22 (m, 52H, alkyl chain), 0.95−0.91 (m, 6H, terminal Me × 2); ^{13}C NMR (200 MHz, C_6D_6) δ 171.8, 171.1, 170.4, 170.1, 169.9, 169.8, 169.7, 169.2, 168.9, 136.1, 127.3, 101.6, 97.2, 81.8, 76.9, 72.2, 71.6, 70.9, 70.8, 69.9, 69.3, 66.9, 63.0, 62.2, 60.9, 52.6, 36.8, 32.6, 32.38, 32.37, 30.3, 30.27, 30.25, 30.23, 30.20, 30.18, 30.1, 30.0, 29.97, 29.9, 29.87, 29.80, 29.5, 26.0, 23.1, 20.9, 20.7, 20.6, 20.5, 20.4, 20.2, 20.1, 19.8, 14.4; HRMS (ESI-ion trap) m/z calcd for $[C_{64}H_{107}NO_{21} + Na^+]$ 1248.7228, found 1248.7272.

*(2S,3R,4E)-3-O-Trimethylsilyl-2-(N-octadecanosylamino)octadec-4-ene-1,3-diol (**10**).* To a 0 °C CH_2Cl_2 (3 mL) solution of compound **7** (150 mg, 0.27 mmol) was added 1,1,1,3,3,3-hexamethyldisilazane (HMDS, 121 μL, 0.58 mmol) and TMSOTf (∼5 μL, 0.03 mmol), and the mixture was gradually warmed to rt in 2 h (based on Wang's method).[63] The reaction mixture was then diluted with EA/Hex (v/v =1:1, 20 mL) and washed with water and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduce pressure to afford per-*O*-TMS ceramide (179 mg, 95%) as a white powder. Per-*O*-TMS ceramide (179 mg, 0.25 mmol) was dissolved in a well-stirred CH_2Cl_2/MeOH (v/v = 1:1, 3 mL) solution. To the solution was added NH_4OAc (38 mg, 0.5 mmol), and the reaction was stirred at rt for 10 h. The reaction mixture was concentrated and purified using flash column chromatography (EA/Hex = 1/4 to 1/2) to afford mono-*O*-TMS-protected ceramide **10** (91 mg, 58%) as a white amorphous solid: TLC (EA/Hex = 1/5) R_f 0.20; $[\alpha]^{24}_D$ −15.0 (c 0.02, MeOH); ^{1}H NMR (600 MHz, C_6D_6) δ 5.94 (d, J = 7.4 Hz, 1H, NH), 5.63 (ddd, J = 7.9, 6.8, 3.4 Hz, 1H, H-5), 5.42 (dd, J = 15.4, 6.1 Hz, 1H, H-4), 4.56−4.49 (m, 1H, H-3), 4.06 (d, J = 11.5 Hz, 1H, H-1a), 3.97 (dt, J = 7.2, 3.5 Hz, 1H, H-2), 3.65−3.55 (m, 1H, H-1b), 3.06 (d, J = 7.0 Hz, 1H, OH), 1.96−1.93 (m, 4H, H-6ab, H-2′ab), 1.70 (dd, J = 14.1, 7.0 Hz, 2H, H-7ab), 1.46−1.17 (m, 52H, alkyl chain), 0.97−0.85 (m, 6H, terminal Me × 2), 0.14−0.03 (s, 9H, TMS); ^{13}C NMR (150 MHz, C_6D_6) δ 172.3, 133.1, 130.2, 75.7, 62.5, 55.2, 36.7, 32.6, 32.4, 30.24, 30.20, 30.16, 30.1, 29.98, 29.92, 29.9, 29.8, 29.7, 29.6, 26.0, 23.1, 14.4, 0.2; HRMS (ESI-ion trap) m/z calcd for $[C_{39}H_{79}NO_3Si + H^+]$ 638.5902, found 638.5930.

*(2S,3R,4E)-3-O-Acetyl-1-O-(α-D-lactopyranosyl)-2-(N-octadecanosylamino)octadec-4-ene-1,3-diol (**11**).* Compound **8** (17 mg, 0.012 mmol) was dissolved in dry MeOH (2 mL) and treated with 25% NaOMe in MeOH solution (∼5 μL) at rt. After 1 h, Dowex acidic resin was added to the reaction mixture until pH = 7. The mixture was then filtered through a short Celite plug and concentrated under reduced pressure to afford compound **11** (15 mg, >98%) as a white powder: TLC (EA/MeOH/H_2O = 7:2:1) R_f 0.77; $[\alpha]^{24}_D$ +2.7 (c 0.40, MeOH); ^{1}H NMR (800 MHz, pyridine-d_5) δ 8.48 (d, J = 8.5 Hz, 1H, NH), 6.01−5.99 (m, 2H, alkene H × 2), 5.37 (d, J = 3.7 Hz, 1H, H-1), 5.09 (d, J = 7.8 Hz, 1H, H-1′), 4.88−4.85 (m, 1H, H-c), 4.82−4.80 (m, 1H, H-b), 4.57−4.39 (m, 8H, H-3, H-2′, H-4′, H-6ab, H-6′ab, H-a), 4.37−4.34 (m, 1H, H-5), 4.32−4.30 (m, 1H, H-a′), 4.25 (appt. t, J = 9.3 Hz, H-4), 4.16−4.14 (m, 2H, H-3′, H-5′), 4.13 (dd, J = 3.7, 9.3 Hz, 1H, H-2), 2.44 (appt. t, J = 7.5, 2H, H-g, H-g′), 2.11−2.08 (m, 2H, H-f, H-f′), 1.88−1.81 (m, 2H, H-h, H-h′), 1.39−1.22 (m, 52H, alkyl chain), 0.90−0.87 (m, 6H, terminal Me × 2); ^{13}C NMR (200 MHz, pyridine-d_5) δ 174.0, 133.0, 132.5, 106.3, 101.7, 83.1, 77.7, 75.7, 74.0, 73.9, 73.2, 73.0, 72.9, 70.6, 69.6, 62.8, 62.6, 55.6, 37.3, 33.3, 32.6, 30.54, 30.51, 30.50, 30.45, 30.43, 30.41, 30.37, 30.29, 30.25, 30.1, 26.9, 23.4, 14.8; HRMS (ESI-ion trap) m/z calcd for $[C_{48}H_{91}NO_{13} + H^+]$ 890.6563, found 890.6569.

*(2,6-Di-O-acetyl-3,4-diol-β-D-galactopyranosyl)-(1−4)-O-(1,2,3,6-tetra-O-acetyl)-D-glucopyranoside (**13**).* Method A: To a MeOH (3 mL) solution of compound **3** (41 mg, 0.06 mmol) was added Dowex H^+ resin (∼80 mg) until the pH = 2−3. The suspension was allowed to stir at rt for 4.5 h until the starting material was completely consumed. Next, the Dowex acidic resin was removed via filtration, and the filtrate was concentrated to afford a viscous oil. The resulting residue was immediately purified by flash column chromatography (100% EA) to obtain compound **13** (30 mg, 92%) as a white foam. Method B: To a MeOH solution of compound **3** (115 mg, 0.16 mmol) was added $Pd(OH)_2$/C (20% Pd, 100 mg). The reaction mixture was allowed to stir under H_2 gas (1 atm) at rt for 0.5 h until the starting material was completely consumed. Next, the Pd-catalyst was removed by a short plug of MeOH-packed Celite. The filtrate was concentrated to afford a viscous oil. The resulting residue was purified by flash column chromatography (100% EA) to obtain compound **13** (85 mg, 91%) as a white foam. The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (100% EA) R_f 0.36; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.67 (d, J = 8.8 Hz, 1H, H-1), 5.23 (appt. t, J = 8.8 Hz, 1H, H-3), 5.07 (appt. t, J = 8.8 Hz, 1H, H-2), 4.81 (appt. t, J = 8.4 Hz, 1H, H-2′), 4.46 (d, J = 12.4 Hz, 1H, H-6a), 4.38-.34 (m, 2H, H-1′, H-6b), 4.28−4.22 (m, 1H, H-6′a), 4.22 (m, 1H, H-6′b), 3.84−3.77 (m, 3H, H-4, H-5, H-4′), 3.69−3.54 (m, 2H, H-3′, H-5′), 2.13 (s, 3H), 2.12 (s, 3H), 2.11 (s, 3H) 2.10 (s, 3H), 2.06 (s, 2H), 2.03 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.9, 171.0, 170.4, 169.9, 169.5, 168.9, 100.5, 91.7, 75.6, 74.1, 73.7, 72.9, 72.4, 72.0, 70.4, 68.1, 62.1, 61.9, 20.9, 20.84, 20.82, 20.8, 20.76, 20.6; HRMS (ESI-ion trap) m/z calcd for $[C_{24}H_{34}O_{17} + NH^+]$ 612.2134, found 612.2134.

*(2,6-Di-O-acetyl-β-D-galactopyranosyl)-(1−4)-O-(1,2,3,6-tetra-O-acetyl)-D-glucopyranoside (**14**).* Method A: To a MeOH (3 mL) solution of compound **2** (70 mg, 0.08 mmol) was added $Pd(OH)_2$/C (20% Pd, 50 mg). The reaction mixture was allowed to stir under H_2 (1 atm) at rt for 0.5 h. Next, the reaction mixture was filtered through a MeOH-packed Celite pad to remove the Pd catalyst, and the filtrate was concentrated under reduced pressure. The resulting residue was then dissolved in dry acetonitrile (2 mL) and treated with trimethyl orthoacetate (32 μL, 0.25 mmol) and catalytic camphorsulfonic acid (∼4 mg, 0.02 mmol). After 1 h, NEt_3 (∼0.1 mL) was added to quench the reaction, and the reaction mixture was concentrated under reduced pressure. The resulting residue was then dissolved in CH_2Cl_2 (2 mL) and treated with Ac_2O (50 μL, 0.50 mmol), NEt_3 (105 μL, 0.75 mmol) and catalytic DMAP (∼2 mg). After 0.5 h, the solvent was evaporated, and the dry residue was treated with 80% $AcOH_{(aq)}$ at rt with vigorous stirring for another 0.5 h. The reaction mixture was then azeotroped with benzene to remove excess reagents, and the resulting residue was purified using flash column chromatography (EA/Hex = 3/1 to 4/1) to afford compound **14** (52 mg, 95%) as a white foam. Method B: To a MeOH (3 mL) solution of compound **3** (65 mg, 0.088 mmol) was added $Pd(OH)_2$/C (20% Pd, 60 mg). The reaction

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mixture was allowed to stir under H_2 (1 atm) at rt for 0.5 h. Next, the reaction mixture was filtered through a MeOH-packed Celite pad to remove the Pd catalyst, and the filtrate was concentrated under reduced pressure. The resulting residue was then dissolved in dry ACN (2 mL) and treated with trimethyl orthoacetate (35 μL, 0.26 mmol) and catalytic CSA (~4 mg, 0.02 mmol). After 1 h, NEt_3 (~0.1 mL) was added to quench the reaction, and the reaction mixture was concentrated under reduced pressure. The resulting residue was treated with 80% $AcOH_{(aq)}$ at rt with vigorous stirring for another 0.5 h. The reaction mixture was then azeotroped with benzene to remove the excess reagents, and the resulting residue was purified using flash column chromatography (EA/Hex = 3/1 to 4/1) to afford compound **14** (57 mg, 98%) as a white foam. The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 2/1) R_f 0.28; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.68 (d, J = 8.4 Hz, 1H, H-1), 5.30 (d, J = 2.9 Hz, 1H, H-4′), 5.24 (appt. t, J = 9.3 Hz, 1H, H-3), 5.06 (dd, J = 9.3, 8.4 Hz, 1H, H-2), 4.85 (dd, J = 10.0, 7.9 Hz, 1H, H-2′), 4.47 (dd, J = 12.1, 1.8 Hz, 1H, H-6a), 4.42 (d, J = 7.9 Hz, 1H, H-1′), 4.20 (dd, J = 12.1, 4.9 Hz, 1H, H-6b), 4.15−4.04 (m, 2H, H-6′ab), 3.86−3.73 (m, 4H, H-4, H-5, H-3′, H-5′), 2.46 (d, J = 6.3 Hz, 1H, OH), 2.18 (s, 3H), 2.13 (s, 3H), 2.12 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.2, 170.7, 170.5, 170.4, 169.7, 169.5, 100.6, 91.6, 75.7, 73.6, 73.1, 72.5, 71.8, 71.0, 70.4, 69.1, 61.9, 61.4, 20.84, 20.81, 20.75, 20.73, 20.67, 20.5; HRMS (ESI-ion trap) m/z calcd for $[C_{26}H_{36}O_{18} + NH_4^+]$ 654.2240, found 654.2289.

General Procedure for Constructing Globotriaose and Isoglobotriaose (Table 1). To a 0 °C CH_2Cl_2 solution of compound **15** (conc. 0.1−0.2 M, 2.5 equiv) was added TMSI (2.8 equiv) under argon atmosphere. After stirring for 30 min, the reaction mixture was azeotroped with anhydrous benzene (5 mL × 3) and dried under a high vacuum system for 1 h to afford the corresponding glycosyl iodide as a light yellow foam. The iodide was then dissolved in CH_2Cl_2 (1 mL) under argon and cooled to −78 °C. In a separate flask, AgOTf (3.2 equiv), acceptor (compound **12**, **13**, or **14**; ~0.10 mmol scale; 1.0 equiv) and activated 4 Å molecular sieves (~200 mg) were allowed to stir in a CH_2Cl_2 (2 mL) solution under argon atmosphere at rt for 30 min. The acceptor solution was then cooled to −78 °C, and the cooled glycosyl iodide solution was transferred dropwisely to the acceptor flask via cannula. After 4 h, the reaction mixture was gradually warmed from −78 to −30 °C, diluted with EA (10 mL), and quenched by NEt_3 (~1 mL). The suspension was filtered through a well-packed Celite pad and washed with EA (~30 mL). The filtrate was washed with saturated $NaHCO_{3(aq)}$ (20 mL × 1) and brine (20 mL × 2), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by gradient flash column chromatography (EA/Hex) to obtain corresponding oligosaccharides (compound **16**, **17**, **18**, or **19**) as white foams.

(2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl)-(1−4)-O-(2,3,6-tri-O-acetyl-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-D-glucopyranoside (**16**). Following the general procedure for constructing the globotriaose, compound **15** (510 mg, 0.88 mmol) and TMSI (142 μL, 0.97 mmol) were used for galactosyl iodide formation. The forming iodide CH_2Cl_2 solution (1 mL) was then cannulated to the CH_2Cl_2 solution (1.5 mL) of 4′-OH acceptor **12** (220 mg, 0.35 mmol) under the activation of AgOTf (270 mg, 1.05 mmol) at −78 to −30 °C for 4 h with the presence of activated 4 Å molecular sieves (800 mg). After workup, the reaction mixture was then purified by gradient flash column chromatography (EA/Hex = 2/3 to 1/1) to obtain **16** (300 mg, 75%) as a white foam (Table 1, entry 1). The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 1/1) R_f 0.43; ^{1}H NMR (800 MHz, $CDCl_3$) δ 7.43−7.24 (m, 20H, ArH), 5.65 (d, J = 8.9 Hz, 1H, H-1), 5.20 (appt. t., J = 8.9 Hz, 1H, H-3), 5.13 (dd, J = 10.2, 7.9 Hz, 1H, H-2′), 5.04 (appt. t, J = 8.9 Hz, 1H, H-2), 4.92 (d, J = 12.0 Hz, 1H, PhCH), 4.86−4.80 (m, 2H, $PhCH_2$), 4.76−4.73 (m, 3H, H-1″, H-3′, PhCH), 4.67 (d, J = 12 Hz, 1H, PhCH), 4.56 (d, J = 12 Hz, 1H, PhCH), 4.50−4.40 (m, 4H, H-6a, H-6′ab, PhCH × 2), 4.39 (d, J = 7.9 Hz, 1H, H-1′), 4.27 (dd, J = 9.0, 4.7 Hz, 1H, H-5″), 4.16 (s, 1H, H-4″), 4.10 (dd, J = 12.3, 4.6 Hz, 1H, H-6b), 4.05 (m, 1H, H-2″), 3.97 (d, J = 2.3, 1H), 3.77 (appt. t, J = 8.9 Hz, 1H, H-4), 3.72 (dd, J = 10.0, 4.7 Hz, 1H, H-5), 3.64 (appt. t, J = 6.8 Hz, 1H, H-5′), 3.61 (appt. t, J = 8.6 Hz, 1H, H-6″a), 3.42 (dd, J = 8.6, 4.9 Hz, 1H, H-6″b), 2.11 (s, 3H), 2.09 (s, 3H), 2.04 (s, 6H), 2.03 (s, 3H), 2.02 (s, 3H), 1.86 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 170.7, 170.4, 170.3, 169.8, 169.5, 168.9, 168.7, 138.8, 138.7, 138.1, 137.9, 128.4, 128.33, 128.30, 128.2, 128.15, 128.11, 128.0, 127.7, 127.6, 127.4, 127.36, 127.34, 101.4, 101.0, 91.7, 79.1, 76.0, 75.5, 75.3, 75.0, 74.6, 74.2, 73.6, 73.3, 72.8, 72.5, 72.3, 72.2, 70.3, 69.6, 69.4, 67.6, 61.7, 61.0, 20.84, 20.82, 20.6, 20.5; HRMS (ESI-ion trap) m/z calcd for $[C_{60}H_{70}O_{23} + Na^+]$ 1181.4200, found 1181.4241.

(2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl)-(1−3)-O-(2,6-di-O-acetyl-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-D-glucopyranoside (**17**). Following the general procedure for constructing the isoglobotriaose scaffold, compound **15** (183 mg, 0.32 mmol) and TMSI (50 μL, 0.36 mmol) were used for galactosyl iodide formation. The CH_2Cl_2 solution (1.5 mL) of forming iodide was then cannulated to the CH_2Cl_2 solution (1.5 mL) of 3′,4′-di-OH acceptor **13** (75 mg, 0.13 mmol) under the activation of AgOTf (103 mg, 0.42 mmol) at −78 to −30 °C for 4 h with the presence of activated 4 Å molecular sieves (300 mg). After workup, the reaction mixture was then purified by flash column chromatography (EA/Hex = 50:50) to obtain **17** (37 mg, 26%) as a white amorphous foam and compound **18** (63 mg, 31%) as a colorless oil (Table 1, entry 3). The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 1/1) R_f 0.43; ^{1}H NMR (800 MHz, $CDCl_3$) δ 7.41−7.34 (m, 5H, ArH), 7.34−7.20 (m, 15H, ArH), 5.64 (d, J = 8.3 Hz, 1H, H-1), 5.21 (appt. t, J = 9.4 Hz, 1H, H-3), 5.06−5.03 (m, 2H, H-2, H-2′), 4.88 (d, J = 11.6 Hz, 1H, PhCH), 4.86 (d, J = 11.4, 1H, PhCH), 4.74 (s, 2H, $PhCH_2$), 4.68 (d, J = 3.7 Hz, 1H, H-1″), 4.63 (d, J = 11.6 Hz, 1H, PhCH), 4.52 (d, J = 11.4 Hz, 1H, PhCH), 4.46−4.40 (m, 2H, H-6a, PhCH), 4.33 (d, J = 11.9 Hz, 1H, PhCH), 4.30−4.24 (m, 3H, H-1′, H-6′ab), 4.15−4.09 (m, 1H, H-6b), 4.01 (dd, J = 9.6, 3.8 Hz, 1H, H-2″), 3.95−3.89 (m, 2H, H-4′, H-3″), 3.81−3.78 (m, 2H, H-4, H-5″), 3.76−3.69 (m, 2H, H-5, H-4′), 3.60−3.55 (m, 2H, H-5′, H-3′), 3.43−3.36 (m, 2H, H-6″ab), 2.14 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 170.8, 170.4, 169.9, 169.6, 169.5, 168.9, 138.3, 137.6, 137.4, 128.6, 128.57, 128.46, 128.4, 128.3, 128.27, 128.24, 127.9, 127.8, 127.7, 127.66, 127.5, 100.4, 96.5, 91.7, 79.6, 78.5, 75.3, 74.9, 74.8, 74.7, 74.3, 73.7, 73.5, 72.9, 72.1, 71.9, 70.7, 70.4, 70.1, 68.8, 65.0, 63.1, 61.8, 20.9, 20.8, 20.7, 20.67, 20.63; HRMS (ESI-ion trap) m/z calcd for $[C_{58}H_{68}O_{22} + NH_4^+]$ 1134.4540, found 1134.4445.

(2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl)-(1−3)-O-(2,3,6-tri-O-acetyl-4-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-D-glucopyranoside (**18**). Compound **18** (63 mg, 31%) was obtained as a colorless oil (Table 1, entry 3; see compound **17** and general procedure for constructing isoglobotriaose for reaction and purification conditions). The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 1/1) R_f 0.63; ^{1}H NMR (600 MHz, methanol-d_4) δ 5.71 (d, J = 8.3 Hz, 1H, H-1), 5.29−5.20 (m, 2H), 5.07 (appt. t, J = 8.9 Hz, 1H), 4.98−4.92 (m, 3H), 4.80 (d, J = 11.2 Hz, 1H), 4.77−4.70 (m, 2H), 4.65 (d, J = 11.3 Hz, 2H), 4.59−4.23 (m, 18H), 4.20 (d, J = 8.3 Hz, 1H), 4.13 (dd, J = 12.3, 5.1 Hz, 1H), 4.10−3.98 (m, 5H), 3.97−3.75 (m, 8H), 3.71−3.60 (m, 5H), 3.51 (appt. t, J = 8.8 Hz, 1H), 3.44−3.38 (m, 1H), 2.07 (s, 3H), 2.05 (s, 3H), 2.00 (s, 6H), 1.97 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (150 MHz, methanol-d_4) δ 172.5, 172.3, 171.5, 171.2, 171.1, 170.4, 140.5, 140.3, 140.23, 140.20, 140.0, 139.9, 139.6, 129.7, 129.4, 129.38, 129.32, 129.24, 129.21, 129.20, 129.16, 129.14, 128.9, 128.8, 128.61, 128.56, 128.53, 128.46, 128.41, 103.2, 102.2, 100.6, 92.9, 79.9, 79.8, 78.8, 78.4, 76.8, 76.8, 76.3, 76.1, 76.0, 74.9, 74.4, 74.2, 74.1, 73.2, 73.0, 71.9, 71.4, 70.8, 69.4, 65.3, 63.4, 49.4, 49.3, 49.1, 49.0, 48.9, 48.7, 48.6, 32.8, 23.7, 21.5, 21.2, 20.9, 20.7, 20.6, 20.5, 14.4; HRMS (ESI-ion trap) m/z calcd for $[C_{92}H_{102}O_{27} + NH_4^+]$ 1656.6947, found 1656.6932.

(2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl)-(1−3)-O-(2,4,6-tri-O-acetyl-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-D-glucopyranoside (**19**). Following the general procedure for constructing the isoglobotriaose scaffold, compound **15** (75 mg, 0.13

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mmol) and TMSI (20 μL, 0.15 mmol) were used for galactosyl iodide formation. The CH_2Cl_2 solution (1.5 mL) of the forming iodide was then cannulated to the CH_2Cl_2 solution (1.5 mL) of 4′-OH acceptor **14** (33 mg, 0.05 mmol) under the activation of AgOTf (42 mg, 0.16 mmol) at −30 °C to rt for 24 h with the presence of activated 4 Å molecular sieves (300 mg) and tetramethylurea (TMU, 20 μL, 0.16 mmol). After workup, the reaction mixture was then purified by flash column chromatography (EA/Hex = 50:50) to obtain **19** (45 mg, 75%) as a white amorphous foam (Table 1, entry 5). The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 1/1) R_f 0.40; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39−7.23 (m, 20H, ArH), 5.66 (d, J = 8.2 Hz, 1H, H-1), 5.42 (d, J = 3.0 Hz, 1H, H-4′), 5.22 (appt. t, J = 9.0 Hz, 1H, H-3), 5.09 (dd, J = 10.1, 7.9 Hz, 1H, H-2′), 5.04−5.01 (m, 2H, H-2, H-1″), 4.90 (d, J = 11.4 Hz, 1H, PhCH), 4.81 (d, J = 11.8 Hz, 1H, PhCH), 4.71−4.67 (m, 2H, PhCH × 2), 4.63 (d, J = 11.6 Hz, 1H, PhCH), 4.50−4.47 (m, 2H, PhCH × 2), 4.42−4.37 (m, 2H, PhCH, H-6a), 4.31 (d, J = 7.9 Hz, 1H, H-1′), 4.10 (dd, J = 12.0, 5.1 Hz, 1H, H-6b), 4.07−4.01 (m, 2H, H-6′ab), 3.98 (dd, J = 10.0, 3.4 Hz, 1H, H-2″), 3.87−3.71 (m, 6H, H-4, H-3′, H-5′, H-3″, H-4″, H-5″), 3.66 (appt. t, iJ = 6.7 Hz, 1H, H-5), 3.55−3.45 (m, 2H, H-6″ab), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.92 (s, 3H), 1.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4, 170.3, 170.2, 169.6, 169.5, 168.8, 168.7, 138.7, 138.67, 138.61, 138.0, 128.4, 128.35, 128.2, 128.15, 128.13, 127.9, 127.7, 127.6, 127.56, 127.50, 127.4, 100.9, 95.1, 91.6, 78.4, 75.7, 75.2, 75.1, 74.8, 73.6, 73.3, 73.2, 73.0, 72.6, 71.1, 70.5, 69.9, 68.5, 64.8, 61.4, 20.8, 20.8, 20.7, 20.68, 20.66, 20.59, 20.4; HRMS (ESI-ion trap) m/z calcd for $[C_{60}H_{70}O_{23} + Na^+]$ 1181.4200, found 1181.4279.

*(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-(1−4)-O-(2,3,6-tri-O-acetyl-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-D-glucopyranoside (per-O-Ac globotriaose, **20**).* To a MeOH (5 mL) solution of compound **16** (186 mg, 0.16 mmol) was added $Pd(OH)_2$/C (20% Pd, 180 mg). The reaction mixture was allowed to stir under H_2 gas (1 atm) at rt for 1 h. Next, the reaction mixture was filtered through a MeOH-packed Celite pad to remove the Pd catalyst, and the filtrate was concentrated under reduced pressure. The resulting residue was then dissolved in CH_2Cl_2 (4 mL) and treated with Ac_2O (0.3 mL, 3.2 mmol), NEt_3 (0.4 mL, 3.2 mmol) and catalytic DMAP (6 mg, 0.05 mmol). After stirring overnight, the reaction mixture was concentrated under reduced pressure and purified using flash column chromatography (EA/Hex = 2:1) to afford **20** (147 mg, 95%) as a white foam. The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 2/1) R_f 0.33; ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.68 (d, J = 8.3 Hz, 1H, H-1), 5.58 (d, J = 3.2 Hz, 1H, H-4″), 5.39 (dd, J = 11.0, 3.4 Hz, 1H, H-3″), 5.24 (appt. t, J = 9.2 Hz, 1H, H-3), 5.18 (dd, J = 11.0, 3.6 Hz, 1H, H-2″), 5.10 (dd, J = 10.8, 7.8 Hz, 1H, H-2′), 5.05 (dd, J = 9.2, 8.3 Hz, 1H, H-2), 4.98 (d, J = 3.6 Hz, 1H, H-1″), 4.72 (dd, J = 10.8, 2.6 Hz, 1H, H-3′), 4.52−4.47 (m, 2H, H-1′, H-5″), 4.45−4.42 (m, 2H, H-6a, H-6′a), 4.20−4.08 (m, 4H, H-6b, H-6′b, H-6″ab), 4.01 (s, 1H, H-4′), 3.84 (dd, J = 19.8, 9.2 Hz, 1H, H-4), 3.79−3.75 (m, 2H, H-5, H-5′), 2.13 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 170.6, 170.5, 170.4, 170.3, 170.0, 169.6, 169.5, 168.8, 168.7, 100.9, 99.6, 91.5, 75.8, 73.4, 72.9, 72.7, 71.8, 70.5, 68.8, 68.7, 67.8, 67.1, 67.0, 61.8, 61.3, 60.2, 20.9, 20.8, 20.7, 20.6, 20.59, 20.54, 20.4; HRMS (ESI-ion trap) m/z calcd for $[C_{40}H_{54}O_{27} + Na^+]$ 989.2745, found 989.2771.

*α-D-Galactopyranosyl-(1−4)-β-D-galactopyranosyl-(1−4)-D-glucopyranose (globotriaose, **21**).* To a MeOH solution of compound **16** (63 mg, 0.054 mmol) was added $Pd(OH)_2$/C (20% Pd, 63 mg) and stirred under H_2 gas (1 atm) for 2 h. After the disappearance of starting material on TLC, the $Pd(OH)_2$/C was removed by passing through a MeOH-packed Celite pad. The filtrate was concentrated and redissolved in anhydrous MeOH (3 mL) followed by addition of NaOMe/MeOH solution (25 wt %, 40 μL). Some white suspension formed after 15 min, and H_2O (1.0 mL) was added to dissolve the suspension. The reaction mixture was stirred for another 15 min and was acidified to pH = 6 by adding Dowex H^+ resin. The solution was filtered through a plug of C_{18} reverse-phrase silica gel and washed with MeOH and water to remove the resin and desalt. The filtrate was concentrated and lyophilized to afford compound **21** (27 mg, 99%) as a white fluffy foam: TLC (EA/2-propanol/H_2O = 2:2:1) R_f 0.22; ^{1}H NMR (800 MHz, D_2O) δ 5.22 (d, J = 3.7 Hz, 0.4 H), 4.94 (d, J = 3.7 Hz, 1H), 4.66 (d, J = 8.0 Hz, 0.4 H), 4.50 (dd, J = 7.8, 1.7 Hz, 1H), 4.35 (s, 1H), 4.06−4.01 (m, 2H), 3.98−3.54 (m, 14H), 3.27 (appt. t, J = 8.6 Hz, 0.4 H); ^{13}C NMR (200 MHz, D_2O) δ 103.90, 103.86, 101.0, 96.4, 92.4, 79.3, 79.2, 78.0, 75.5, 74.5, 72.8, 71.5, 70.8, 69.8, 69.6, 69.22, 69.20, 61.1, 61.0, 60.7, 60.6 (Assignment matches with literature);[64] HRMS (ESI0-ion trap) m/z calcd for $[C_{18}H_{32}O_{16} + NH_4^+]$ 522.2029, found 522.2012.

*(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-(1−4)-O-(2,3,6-tri-O-acetyl-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-D-glucopyranosyl iodide (**22**).* In an oven-dried NMR tube, compound **20** (20 mg, 0.02 mmol) was added and dissolved in dry $CDCl_3$ (0.2 mL). After TMSI (4 μL, 0.03 mmol) was introduced to the reaction vessel, the reaction was kept and 0 °C and gradually warmed to rt over 4−5 h. The reaction was monitored by proton NMR until its corresponding iodide (**22**) formed: in situ ^{1}H NMR (800 MHz, $CDCl_3$) δ 6.90 (d, J = 4.3 Hz, 1H, H-1), 5.58 (d, J = 3.2 Hz, 1H, H-4″), 5.45 (appt. t, J = 9.5 Hz, 1H, H-3), 5.39 (dd, J = 11.0, 3.2 Hz, 1H, H-3″), 5.17 (dd, J = 11.0, 3.5 Hz, 1H, H-2″), 5.11 (dd, J = 10.8, 7.8 Hz, 1H, H-2′), 4.98 (d, J = 3.5 Hz, 1H, H-1″), 4.72 (dd, J = 10.8, 2.6 Hz, 1H, H-3′), 4.53 (d, J = 7.8 Hz, 1H, H-1′), 4.50−4.41 (m, 3H, H-5″, H-6a, H-6′a), 4.20−4.07 (m, 5H, H-2, H-6b, H-6′b, H-6″ab), 4.01 (d, J = 1.8 Hz, 1H, H-4′), 3.98−3.95 (m, 1H, H-5), 3.89 (appt. t, J = 9.5 Hz, 1H, H-4), 3.78 (appt. t, J = 6.7 Hz, 1H, H-5′), 2.12 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.057 (s, 3H), 2.053 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H); in situ ^{13}C NMR (200 MHz, $CDCl_3$) δ 170.7, 170.6, 170.5, 170.4, 170.3, 170.1, 169.8, 169.5, 169.2, 168.8, 100.7, 99.5, 75.5, 74.7, 72.8, 72.6, 71.8, 71.3, 70.4, 68.8, 67.8, 67.1, 66.9, 61.4, 61.0, 60.2, 20.9, 20.84, 20.80, 20.75, 20.72, 20.67, 20.64, 20.61, 20.58, 20.55.

*(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-(1−3)-O-(2,4,6-tri-O-acetyl-β-O-D-galactopyranosyl)-(1−4)-O-1,2,3,6-tetra-O-acetyl-β-D-glucopyranoside (per-O-Ac isoglobotriaose, **23**).* To a MeOH (5 mL) solution of compound **17** (32 mg, 0.03 mmol) was added $Pd(OH)_2$/C (20% Pd, 30 mg). The reaction mixture was allowed to stir under H_2 gas (1 atm) at rt for 1 h. Next, the reaction mixture was filtered through a MeOH-packed Celite pad to remove the Pd catalyst, and the filtrate was concentrated under reduced pressure. The resulting residue was then dissolved in CH_2Cl_2 (2 mL) and treated with Ac_2O (0.3 mL, 3.2 mmol), NEt_3 (0.4 mL, 3.2 mmol) and catalytic DMAP (∼2 mg). After stirring for 3 h, the reaction mixture was concentrated under reduced pressure and purified using flash column chromatography (EA/Hex = 70:30) to afford **23** (23 mg, 85%) as a white foam. The product consisted of inseparable α/β anomeric acetates, and the major β-anomer is reported: TLC (EA/Hex = 70:30) R_f 0.41; ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.67 (d, J = 8.4 Hz, 1H, H-1), 5.45 (dd, J = 3.1, 1.4 Hz, 1H, H-4″), 5.32 (d, J = 2.4 Hz, 1H, H-4′), 5.27−5.21 (m, 3H, H-3, H-1″, H-2″), 5.16 (dd, J = 10.3, 7.9 Hz, 1H, H-2′), 5.09 (dd, J = 10.9, 3.2 Hz, 1H, H-3″), 5.04 (dd, J = 9.4, 8.4 Hz, 1H, H-2), 4.46−4.38 (m, 2H, H-6a, H-1′), 4.22−4.01 (m, 6H, H-6b, H-6′ab,, H-5″, H-6″ab), 3.87−3.74 (m, 4H, H-4, H-5, H-3′, H-5′), 2.16 (s, 3H), 2.14 (s, 3H), 2.13 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H), 2.061 (s, 3H), 2.057 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 170.6, 170.5, 170.4, 170.3, 170.1, 169.9, 169.8, 169.7, 169.0, 168.8, 101.1, 93.5, 91.6, 75.5, 73.6, 72.9, 72.7, 70.9, 70.6, 69.7, 67.3, 66.9, 66.6, 64.7, 61.9, 61.3, 61.1, 21.0, 20.97, 20.93, 20.91, 20.88, 20.84, 20.77, 20.73, 20.6; HRMS (ESI-ion trap) m/z calcd for $[C_{40}H_{54}O_{27} + NH_4^+]$ 984.3191, found 984.3215.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General information and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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