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Fluoridolysis of 5,6-epoxy carbohydrates: application to the synthesis of 5-fluoro lactosamine and isolactosamine glycosides

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Dedicated to Professor George Fleet on the occasion of his 65th birthday and in recognition of his numerous important contributions to the field of carbohydrate chemistry

ABSTRACT

The synthesis of 6-selenophenyl derivatives of β-1,3 and β-1,4 disaccharides has been explored for the purpose of extending our epoxide fluoridolysis methodology to the synthesis of 5-fluoro analogues of *N*-acetyl isolactosamine (isoLacNAc, lacto-*N*-biose) and *N*-acetyl lactosamine (LacNAc) glycosides. Successful synthesis of the C-6 selenium-containing disaccharides was achieved via Lewis acid-mediated donor and acceptor substrates, the latter containing a selectively protected C-6 hydroxyl group for ultimate conversion to the desired 6-selenophenyl disaccharides. In contrast, the use of selenium-containing acceptor substrates under a variety of conditions failed to yield the desired selenium-containing disaccharides. Oxidation of the 6-selenophenyl derivatives to the corresponding selenoxides followed by thermal elimination yielded the exocyclic olefins, which were converted to the 5,6-epoxides. Epoxide fluoridolysis yielded the desired target compounds, 5-fluoro β-octyl glycoside analogues of type 1 and type 2 glycans. The newly synthesized fluorine-containing disaccharides have potential application as fucosyltransferase substrates, both for mechanistic studies and in the chemoenzymatic synthesis of fluorine-containing oligosaccharides.

1. Introduction

The use of glycosyl fluorides to investigate enzyme catalysis of both glycosidases and glycosyltransferases has been exploited by Withers and colleagues.[1] Specifically, 2-deoxy-2-fluoro, 2-deoxy-2,2-difluoro, and 5-fluoro derivatives have been studied extensively to provide great insight into the catalytic mechanism and structural basis for catalysis for a large group of glycosidases.[2] In addition, 2-deoxy-2-fluoro derivatives of sugar nucleotides have been synthesized and used effectively to provide similar data for several glycosyltransferases.[3] In our own research on the mechanism and inhibition of glycosyltransferases, the use of similarly fluorinated derivatives of *N*-acetylglucosamine (GlcNAc) is of interest. Detailed investigation of the effect of fluorine, judiciously placed in donor or acceptor substrates, on reactions catalyzed by glycosyltransferases provide data that further our understanding of the mechanism of action (dissociative vs associative) of these enzymes. For the donor substrate of glycosyl transferase-catalyzed reactions, placing fluorine near a developing partial positive charge in the transition state may lead to enzyme inhibition due to destabilization of the transition state. Alternatively, in the acceptor substrate, it is anticipated that the pK_a of a proximal alcohol will be lowered significantly as the result of an adjacent fluorine substituent; for example, C_2H_5OH (pK_a 15.4) versus CH_2FCH_2OH (pK_a 14.4),[4] thereby affecting its nucleophilicity and possibly catalysis.[5] Since the acetamide group at C-2 is required for nearly all glycosyltransferases that use GlcNAc derivatives as substrates, the use of 2-fluoro derivatives was precluded. Therefore, the emphasis of our research in this area has been on the synthesis of 5-fluoro GlcNAc glycosides and pyrophosphates, and their use in enzymology.

In terms of methodology for the synthesis of 5-fluoro GlcNAc derivatives, most relevant is the description of 2-acetamido-2-deoxy-5-fluoro-α-L-idopyranosyl fluoride and its use in studying the mechanism of action of a β-*N*-acetylglucosaminidase (ExoII) from *Vibrio furnisii*.[6] The synthesis of this molecule involved the radical halogenation method pioneered by Ferrier and co-workers,[7] followed by halogen exchange to afford the 5-fluoro derivative in low yield, with the equatorial halogen (L-ido) predominating. More recently, a similar approach has been employed in the synthesis of 5-fluoro GlcNAc derivatives containing a 2-azidoacetyl group for use in proteomics research.[8] We have reported a new method, epoxide fluoridolysis, to synthesize 5-fluoro GlcNAc derivatives as analogues of both donor and acceptor substrates.[9] UDP-(5-F)-GlcNAc, was evaluated as a substrate for CLS (UDP-GlcNAc:GlcNAc-P-P-Dol *N*-acetylglucosaminyltransferase, EC 2.4.1.141).[10] The data indicated that the fluorinated donor served as a competitive inhibitor of UDP-GlcNAc and not as a substrate. The fact that the 5-fluoro analogue failed to act as a substrate but binds to the active site as a competitive inhibitor is consistent with the hypothesis that the adjacent electron-withdrawing fluorine destabilizes the postulated oxocarbenium ion-like transition state. Similarly,

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(5-F)-GlcNAc-β-octyl glycoside was evaluated as an alternate acceptor substrate for β-1,4 GalT (EC 2.4.1.38) from bovine milk.[10] In this case, there was a minimal effect on k_{cat} for the fluorinated vs non-fluorinated substrates, suggesting little bond formation between the acceptor and the UDP-Gal donor. This result supports a weakly associative ('exploded S_N2') transition state with minimal bond formation between the acceptor and donor substrates (Fig. 1).[10]

An extension of this approach would be to investigate the effect of positioning fluorine on glycosyltransferase acceptor substrates at varying distances from the nucleophilic hydroxyl group. To the best of our knowledge, this 'proximity effect' has not been investigated previously in reactions catalyzed by glycosyltransferases. Although other factors, such as relative stereochemistry of fluorine at C-5 versus the hydroxyl group at C-4 or C-3 (*syn* vs *anti*, gauche vs eclipsed) and the comparative structures of glycosyltransferase active sites, are surely significant, evaluation of the effect of 5-fluoro substitution on distal hydroxyl groups to act as acceptor substrates would provide valuable information. Herein, we describe the synthesis of 5-fluoro analogues of *N*-acetyllactosamine (LacNAc) and its 1,3-linked regioisomer, *N*-acetylisolactosamine (isoLacNAc, lacto *N*-biose). These fluorinated analogues are designed to assess the proximity effect in the reaction catalyzed by α-1,3/1,4-fucosyltransferase or FucT III (E.C. 2.4.1.65) (Fig. 2). FucT III is involved in the biosynthesis of Lewis B blood group antigens and fucosylates the free C-4 or C-3 hydroxyl groups of two GlcNAc-containing disaccharides, type 1 (isoLacNAc) and type 2 (LacNAc), respectively.[11]

FucT III has also been linked to an increase in tumor size in prostate cancer cell line PC-3 due to an increase in cellular adhesion in the stromal cells.[12] Therefore, additional details on the mechanism of FucT III-catalyzed glycosylation may lead to new inhibitors of this enzyme that could potentially impede prostate cancer progression. Two fluorinated analogues, **1** and **2** (Fig. 2), could aid in investigating the effects of fluorine on FucT III glycosyl acceptor substrates by differentially affecting the pK_a of the C-4 hydroxyl versus the C-3 hydroxyl and potentially affect their ability to act as acceptor substrates. The synthesis of isoLacNAc and LacNAc β-octyl glycosides (**3** and **4**, respectively) was pursued initially to obtain non-fluorinated substrates for comparative purposes in biochemical experiments. Ultimately, the non-fluorinated disaccharides proved to be key intermediates in the successful synthesis of the target 5-fluoro analogues, **1** and **2**. β-Octyl glycosides are commonly used in glycosyl transfer enzymology due to their facile separation from a radiolabeled donor substrate via binding to a reverse-phase solid support (Sep-Pak) in an assay to evaluate the enzymatic reaction.[13]

Extension of the previously reported epoxide fluoridolysis methodology[9] to a disaccharide framework should allow for the synthesis of more complex fluorinated carbohydrates, including the desired 5-fluoro isoLacNAc and LacNAc glycosides, **1** and **2** (Fig. 3). A 5,6-epoxide, **6,** obtained by dimethyldioxirane (DMDO)-mediated epoxidation of the corresponding exocyclic olefin,**7**, is opened with HF·pyridine to install the desired C-F bond at C-5. Oxidative elimination of a C-6 phenylselenide, **8**, in the presence of dihydropyran (DHP) results in the exocyclic olefin. Flexibil-

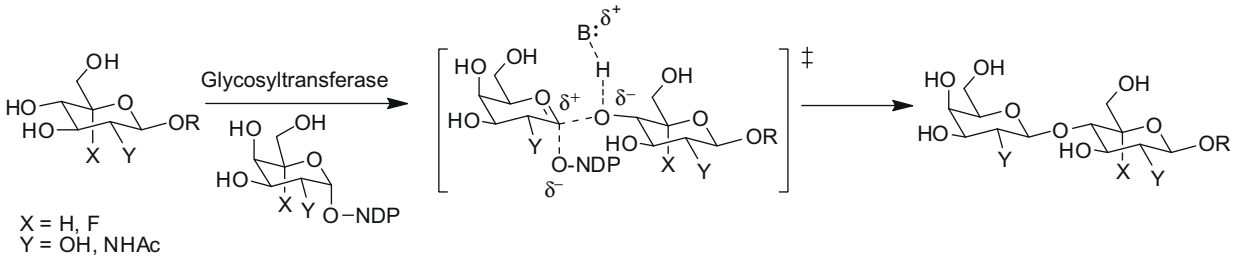


Figure 1. Proposed glycosyltransferase transition state.

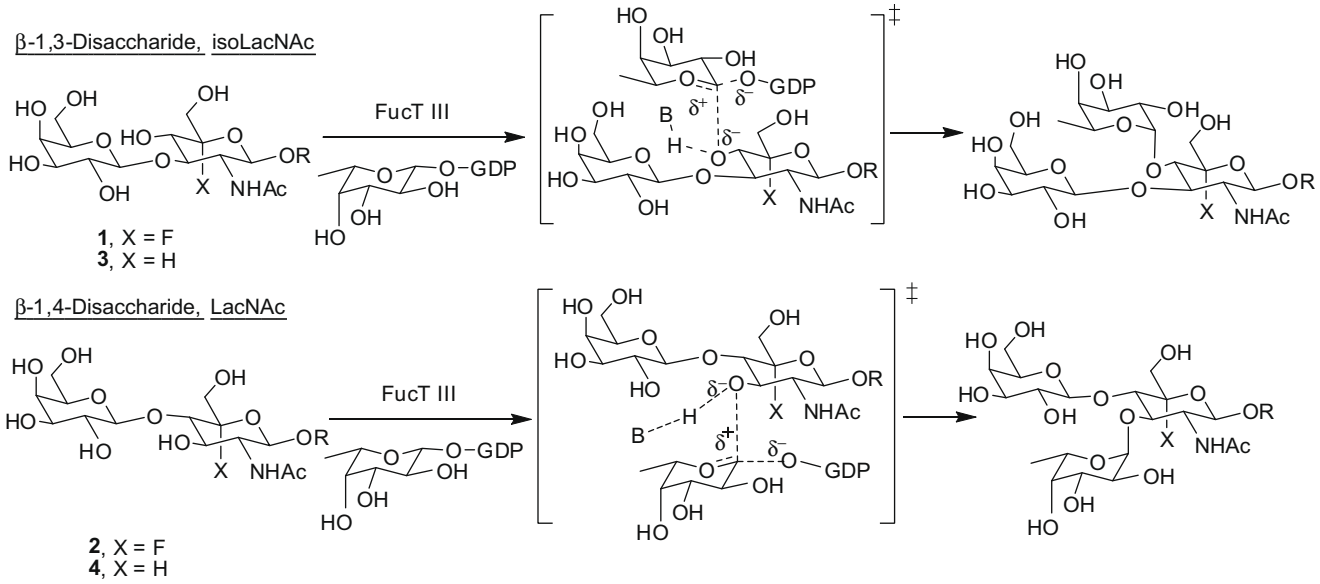


Figure 2. Proposed transition states for FucT III-catalyzed glycosyl transfer.

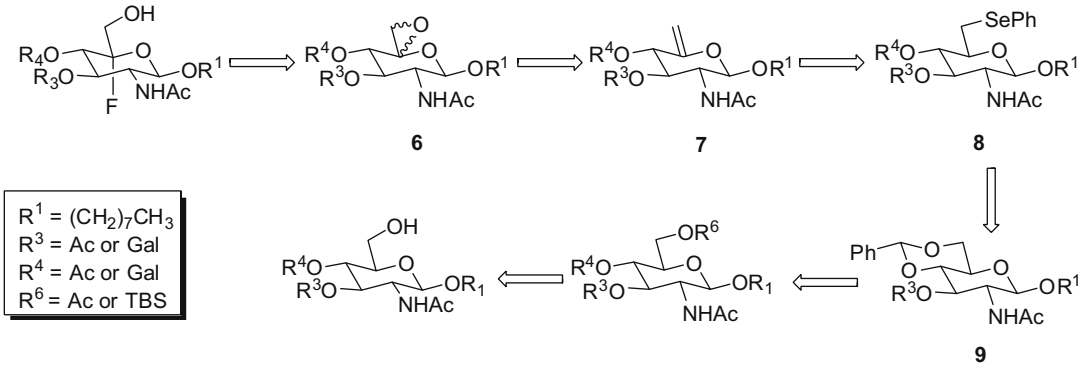


Figure 3. Epoxide fluoridolysis retrosynthetic analysis.

ity at C-3, C-4, and C-6 positions is achieved via an important benzylidene intermediate, **9**. Flexibility at the C-1 position is achieved using either an octyl glycoside or a *tert*-butyldimethyl silyl ether (TBS). Fluoridolysis in the GlcNAc series proceeds in good yields (72–83%).[9] However, epoxide fluoridolysis has not been reported in GlcNAc-containing disaccharides such as isoLacNAc and LacNAc, and is the subject of the research described in this paper.

In order to obtain the (5-fluoro) (iso)LacNAc glycosides, **1** and **2**, for evaluation as mechanistic probes of FucT III-catalyzed glycosylation, it is necessary to synthesize the C-6 phenylselenide-containing β-1,3 and β-1,4 octyl glycosides (Fig. 4). Formation of these target compounds proved synthetically challenging as glycosylation has not been reported using selenium-containing glycoside acceptors. There are two possibilities for forming the C-6 selenium-containing disaccharides. One option involves the coupling of phenylselenide monosaccharide acceptors **10** or **11** with a galactosyl donor.

Alternatively, the phenylselenide is introduced after formation of the desired disaccharide linkage using the non-seleno precursors **12**[14] or **13**. Although the syntheses of the non-fluorinated disaccharides, **3** and **4**, have been reported previously in the literature,[15,16] those syntheses did not provide for differentiation of functionality at C-6. In the current research, synthesis of **3** and **4** has been achieved via routes that allow for incorporation of desired functionality at C-6.

2. Results and discussion

The C-6 bromide **14**[9] was displaced using PhSeH, NEt_3, and Bu_4NI (as a phase-transfer catalyst) to form the phenylselenides, **15** (Scheme 1). The addition of Bu_4NI dramatically decreased the reaction time from five days to overnight. The free C-3–OH groups were protected as a benzyloxymethyl (BOM) ether to form **16**.[†] The resulting differentially protected glycosides **16** were transformed to **17** by removal of the C-4 benzoyl protecting group with NaOMe.

In addition to the selenium-containing glycosyl acceptor substrates, the non-selenium-containing acceptor substrates were synthesized (Scheme 2). Beginning with compound **18**[14], the primary C-6 position was protected as a TBS ether to form **19**. Alternatively, the benzylidene **20**[14] was formed from **18** using $PhCH(OMe)_2$ and $pTsOH{\cdot}H_2O$. The C-3 alcohol of **20** was protected by acetylation to provide **21**. Benzylidene acetolysis followed by protection of the primary C-6 alcohol as a silyl ether (TBS) gave the acceptor, **22**.

The phenylselenide glycosyl acceptor substrates, **15** and **17**, were then used as acceptors in glycosylation reactions with two galactosyl donors (Table 1, **23**, X = Br or $OC(NH)CCl_3$) to form the desired β-1,3 disaccharide. Glycosylation of acceptors containing oxygen at C-6 (Table 1, entries 1–3 and 6) was explored under various reaction conditions using either a glycosyl bromide (Koenigs–Knorr conditions) or a trichloroacetimidate donor. Formation of the desired 1,3-disaccharide (Y = O) was observed in yields ranging from 30% to 83%, The highest yield in the shortest reaction time (Table 1, entry 6) was obtained using Lewis acid-mediated trichloroacetimidate donor activation. Unfortunately, all attempts to form the corresponding selenium-containing disaccharide (Y = Se) using various combinations of acceptors and donors under identical conditions (Table 1, entries 4, 5 and 7) failed. Acceptors were recovered in near quantitative amounts, along with the hydrolysis products derived from their respective donors.[‡]

Similarly, formation of the β-1,4-disaccharide was observed using oxygen-containing acceptors (X = O) (Table 2, entries 1, 4, and 5), albeit in somewhat lower yields (trace—59%) than observed in formation of the 1,3-disaccharides (Table 1).[17] In the case of the 1,4-disaccharides, use of a lower temperature was required due to the sensitivity of the protecting groups. Under a variety of less mild reaction conditions, loss of either the TBS or Ac protecting groups was observed. Again, all attempts to form the selenium-containing disaccharides (X = Se) failed under identical conditions (Table 2, entries 2, 3, and 6) shown to be effective for acceptors containing oxygen at C-6. In these experiments, unlike those described above for the 1,3-disaccharides, recovery of the acceptor was not always possible. It is possible that the nucleophilic 6-SePh substituent reacts with the donor to form a selenonium salt, which can react with any adventitious nucleophile (including water in the workup) in a non-productive manner.

In order to circumvent this problem, the second proposed synthetic route, outlined in Figure 4, involved installation of the 6-SePh substituent following formation of the 1,3- and 1,4-disaccharides. As shown in Scheme 3, the non-selenium containing disaccharide **28** (Table 1, entry 6) was converted to the C-6 phenylselenide under Hannessian–Hullar conditions via displacement of the C-6 bromide with PhSeH and NEt_3 to give **29**. In contrast to the positive rate effect observed in the synthesis of 6-SePh glucosamine derivatives (Scheme 1, **14**→**15**), the addition of Bu_4NI to reactions carried out in the pursuit of **29** resulted in significant formation of a C-6 methyl by-product, presumably formed via selenol-mediated reduction of the 6-iodomethyl intermediate.

[†] This reaction sequence is important in order to avoid formation of an undesired C-6 chloro by-product. The C-6 bromide must be displaced first by PhSeH. If the reaction sequence is reversed, release of chloride from BOM–Cl during formation of the 3-OBOM derivative results in a partial displacement of the C-6 bromide by chloride, leading to a 3:1 mixture of C-6 Br and C-6 Cl products.

[‡] The 8-(methoxycarbonyl)octyl (MCO) glycosides were synthesized by standard methods[18] and used in some experiments tabulated in Tables 1 and 2. However, the ester functionality of these glycosides was incompatible with hydrazinolysis conditions required for subsequent removal of the *N*-phthaloyl protecting group. Therefore, the MCO glycosides were not investigated further.

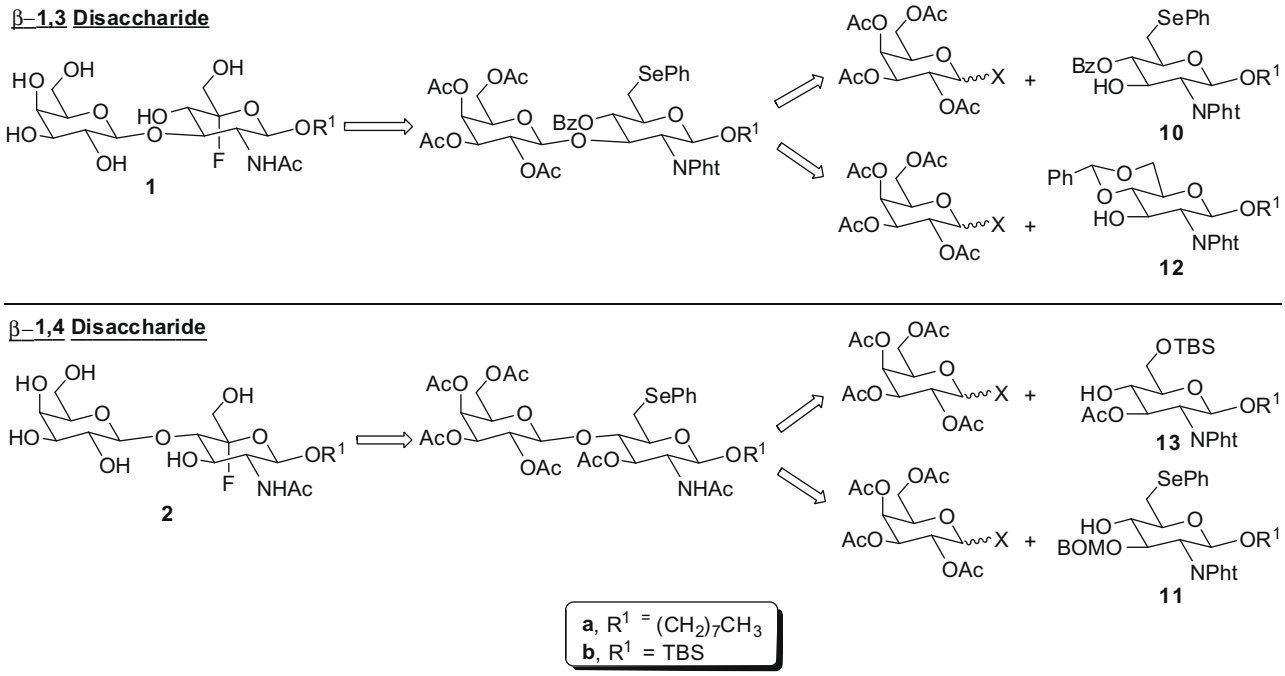
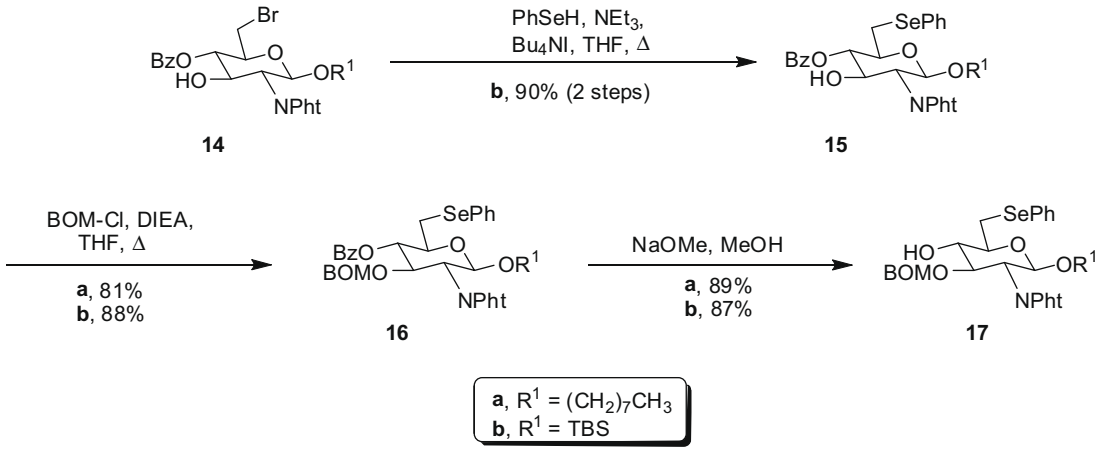


Figure 4. Disaccharide retrosynthetic analysis.



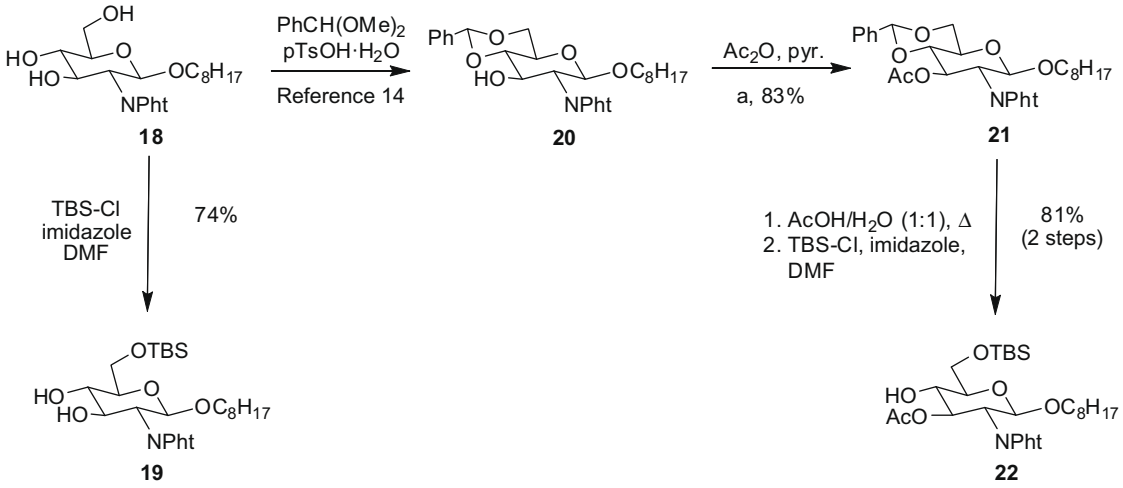
Scheme 1.

Therefore, use of Bu_4NI was avoided in the conversion of **28** to **29**. The *N*-phthaloyl, *O*-benzoyl, and *O*-acetyl protecting groups were removed by $H_2NNH_2{\cdot}H_2O$, followed by global *N*- and *O*-acetylation to yield the desired C-6 phenylselenide-containing disaccharide glycoside **30**. Formation of the non-fluorinated FucT III alternate substrate, **3** (Fig. 2), was effected by removal of the benzylidene and phthaloyl protecting groups to give **31**, followed by global *N* and *O*-acetylation, for ease of purification, and finally *O*-deacylation to give **3**.

In the β-1,4 disaccharide series, installation of the C-6 phenylselenide proceeded by the removal of the C-6 TBS ether of **32** (Table 2, entry 6) with HF·pyridine to give the free alcohol, **33** (Scheme 4). The C-6 phenylselenide, **34**, was successfully formed in modest yield using *N*-phenylseleno phthalimide (*N*-PSP) and PBu_3.[§,19] Removal of the phthaloyl and acetyl protecting groups, followed by *N*- and *O*-acetylation produced **35**. The non-fluorine containing FucT III alternate substrate, **4** (Fig. 2), was formed in a similar manner as that described for **3**. It is of interest to note that the TBS ether in **32** was removed under the hydrazinolysis conditions employed (EtOH, 100 °C).

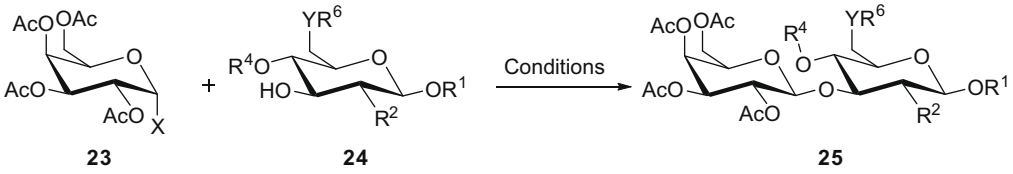
Installation of the 5,6 epoxide was performed in a three-step process from the C-6 phenylselenides **30** and **35** (Scheme 5). In the case of the β-1,3 isoLacNAc-β-octyl glycoside, **30**, spontaneous elimination of the selenoxide to the exocyclic olefin was observed during the course of the oxidation. If the reaction time was extended, complete elimination was observed to give the olefin, **37**, in 87% yield. Treatment of **37** with DMDO provided the epoxide **38** in excellent yield with a 1:1 diastereomeric ratio of D-Glc:L-Ido configurations. Spontaneous elimination of the selenoxide with direct formation of the olefin, as described in the previous section, was also observed in the β-1,4 disaccharide. However, elimination was less facile and complete conversion to the olefin was not observed. Therefore, the remaining selenoxide was thermally eliminated in the presence of DHP to afford the exocyclic olefin, **39**

§ Reaction of a model monosaccharide, *N*-phthaloyl-3,4-diacetyl-6-selenophenyl D-glucosamine β-octyl glycoside, with PSP under identical conditions as those described for the synthesis of **6d** led to the desired 6-SePh derivative in a yield of 60%.[18]



Scheme 2.

Table 1
Synthesis of 1,3-disaccharides (isoLacNAc, Type 1)



Entry	X	R^1	R^2	Y	R^4	R^6	Activator	Solvent, temperature	Yield (%)
1	Br	MCO[a]	NHAc	O	>CHC_6H_5		AgOTf, 3 Å sieves	CH_2Cl_2, 0 °C rt	45
2	Br	MCO[a]	NHAc	O	>CHC_6H_5		$Hg(CN)_2$, $CaSO_4$	CH_2Cl_2, CH_3NO_2, 40 °C	75
3	Br	C_8H_{17}	NPht	O	>CHC_6H_5		$Hg(CN)_2$, $CaSO_4$	CH_2Cl_2, CH_3NO_2, 40 °C	30
4	Br	MCO[a]	NPht	Se	Bz	C_6H_5	$Hg(CN)_2$, $CaSO_4$	CH_2Cl_2, CH_3NO_2, 40 °C	0
5	Br	TBS	NPht	Se	Bz	C_6H_5	$Hg(CN)_2$, 3 Å sieves	CH_2Cl_2, CH_3NO_2, 40 °C	0
6	$OC(NH)CCl_3$	C_8H_{17}	NPht	O	>CHC_6H_5		TMS-OTf, 3 Å sieves	CH_2Cl_2, −20 °C→rt	83
7	$OC(NH)CCl_3$	TBS	NPht	Se	Bz	C_6H_5	TMS-OTf, 3 Å sieves	CH_2Cl_2, 0 °C	0

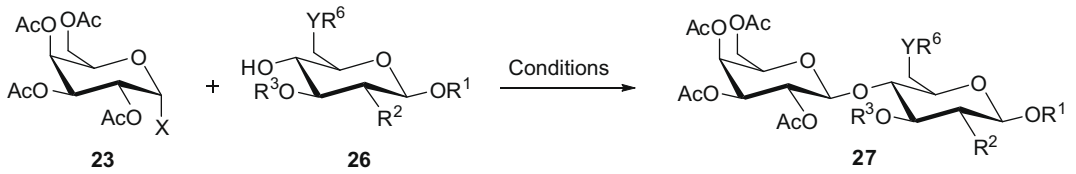
[a] MCO = 8-(Methoxycarbonyl)octyl.

(Scheme 5). Epoxidation proceeded in excellent yields to give **40** as a single diastereomer. Epoxide fluoridolysis of **38** (HF·pyridine) followed by removal of the acetate protecting groups with methanolic ammonia provided the (5-F)-isoLacNAc β-octyl glycoside, **1** (23%, two steps). Similarly, epoxide fluoridolysis of **40** (HF·pyridine), removal of the O-Ac protecting groups with methanolic ammonia afforded the (5-F)-LacNAc β-octyl glycoside, **2** (37%, two steps).

3. Conclusion

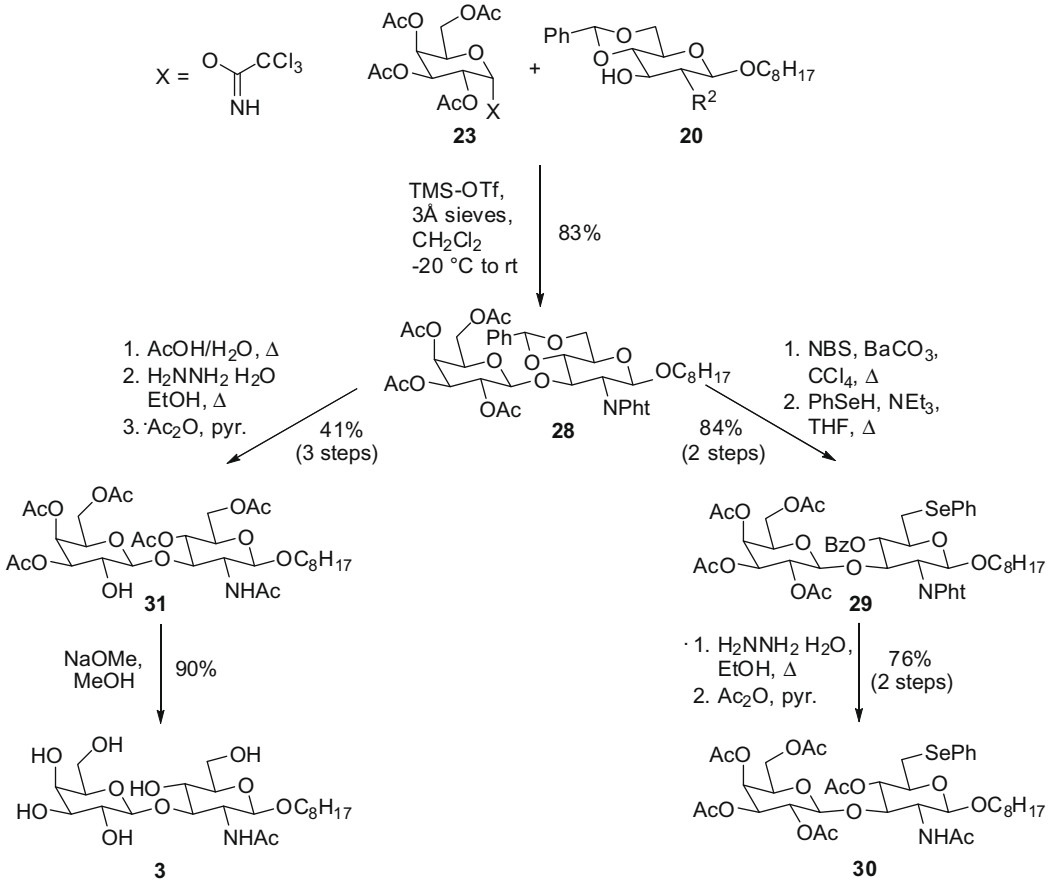
In conclusion, this report records the first synthesis of disaccharides containing fluorine selectively at one of the two C-5 positions, specifically (5-fluoro) (iso)LacNAc β-octyl glycosides. These (5-fluoro) glycosides were synthesized by the epoxide fluoridolysis method, using newly synthesized glycosyl epoxides, **38** and **40**. The epoxides were formed in a two-step oxidative elimination from the corresponding phenylselenide-containing disaccharides, **30** and **35**. The C-6 phenylseleno disaccharides, previously unreported in the literature,[20] were achieved in good yields only through the formation of (iso)LacNAc glycosides via non-selenium containing acceptor and donor substrates. Use of 6-phenylselenide-containing glycosides as glycosylation acceptors was not effective in formation of the desired disaccharide, presumably due to competing attack of the nucleophilic selenium on the glycosyl donor. Epoxidation of **37** and **39** proceeded in excellent yields, allowing for subsequent epoxide fluoridolysis at the C-5 position. These newly synthesized (5-fluoro) (iso)LacNAc glycosides are excellent candidates for use as mechanistic probes of the reaction catalyzed by the glycosyltransferase, FucT III, and other enzymes that use either isoLacNAc or LacNAc glycosides as substrates.

Table 2
Synthesis of 1,4-Disaccharides (LacNAc, Type 2)



Entry	X	R^1	R^2	R^3	Y	R^6	Activator	Solvent, temperature	Yield (%)
1	Br	MCO[a]	NHAc	Ac	O	Bn	AgOTf, TMU, 3 Å sieves	CH_2Cl_2, 0 °C→rt	Trace
2	Br	TBS	NPht	BOM	Se	C_6H_5	AgOTf, TMU, 3 Å sieves	CH_2Cl_2, 0 °C→rt	0
3	Br	TBS	NPht	BOM	Se	C_6H_5	$Hg(CN)_2$, $CaSO_4$	CH_2Cl_2·CH_3NO_2, 40 °C	0
4	$OC(NH)CCl_3$	C_8H_{17}	NHAc	Ac	O	TBS	TMS-OTf, 3 Å sieves	CH_2Cl_2, −30 °C→ rt	37[b]
5	$OC(NH)CCl_3$	C_8H_{17}	NPht	Ac	O	TBS	TMS-OTf, 3 Å sieves	CH_2Cl_2, −50 °C	13
6	$OC(NH)CCl_3$	C_8H_{17}	NPht	H	O	TBS	TMS-OTf, 3 Å sieves	CH_2Cl_2, −50 °C	56[c,d]
7	$OC(NH)CCl_3$	TBS	NPht	BOM	Se	C_6H_5	TMS-OTf, 3 Å sieves	CH_2Cl_2, −50 °C	0

[a] MCO = 8-(Methoxycarbonyl)octyl.
[b] Conversion to product is 51% after recovery of unreacted acceptor (28%).
[c] Following coupling, the free 3-hydroxy group was acetylated (Ac_2O, pyr) to afford the desired product, **32** (Scheme 4), in 34% overall yield (two steps).
[d] Use of BF_3·OEt_2, 3 Å sieves (CH_2Cl_2, −50 °C) as activator with this donor–acceptor pair for an extended reaction time (1.5 h) led to complete loss of the TBS group. Acetylation led to the peracetylated disaccharide, **36**, in 55% yield (two steps).

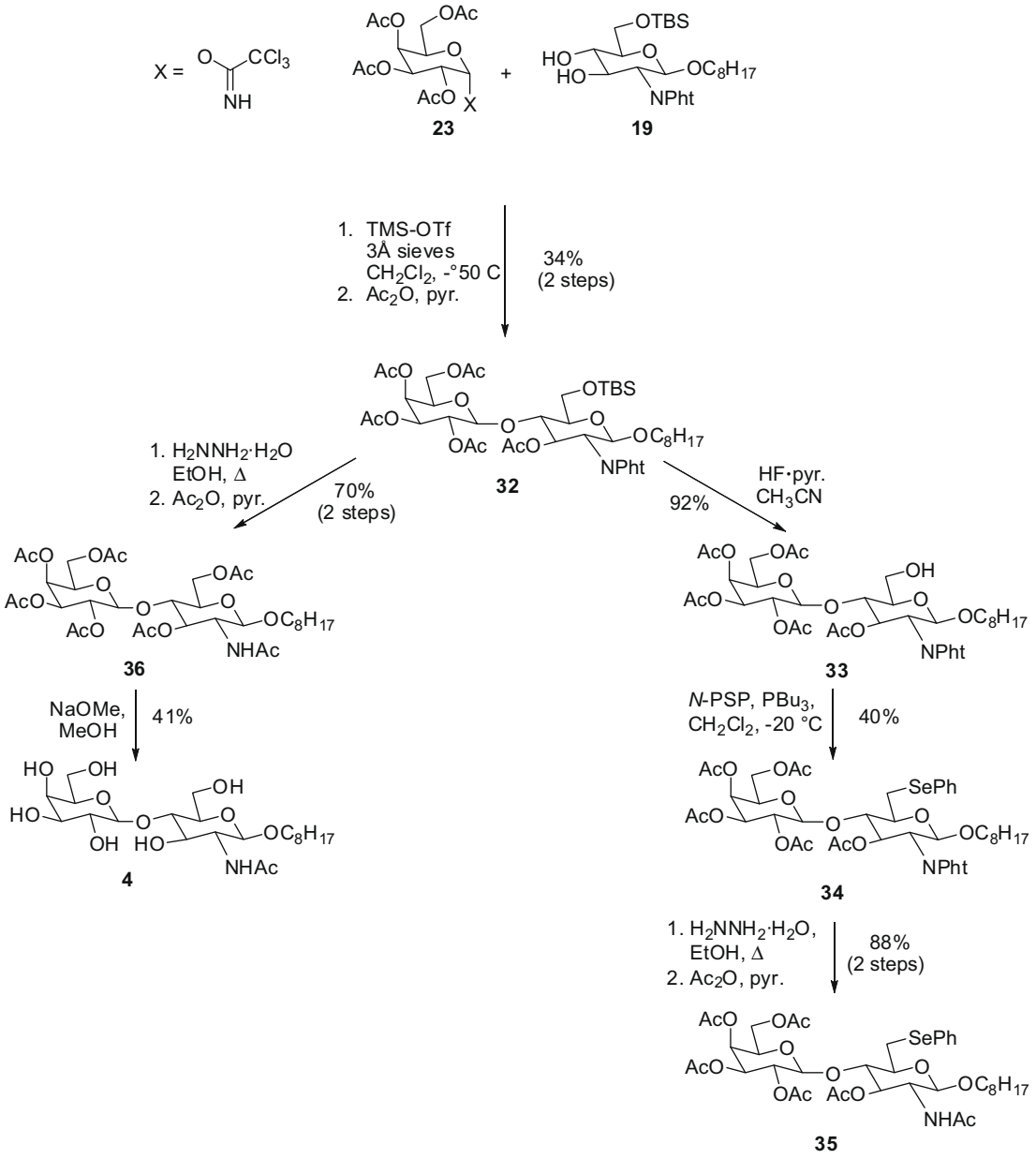


Scheme 3.

4. Experimental

4.1. General procedures

All chemicals used were from Aldrich or Acros, except for BOM–Cl from Tokyo Chemical Industry (TCI) America, Portland, Oregon and 8-methoxycarbonyl octanol from Toronto Research Chemicals (TRC), North York, Ontario, Canada. Water-sensitive reactions were conducted under an argon atmosphere and used oven-dried glassware, syringes and needles. Solvents were freshly distilled for moisture-sensitive reactions: THF from benzophenone ketyl, MeOH, NEt_3, CH_2Cl_2 and pyridine from CaH_2. $CHCl_3$ was purified

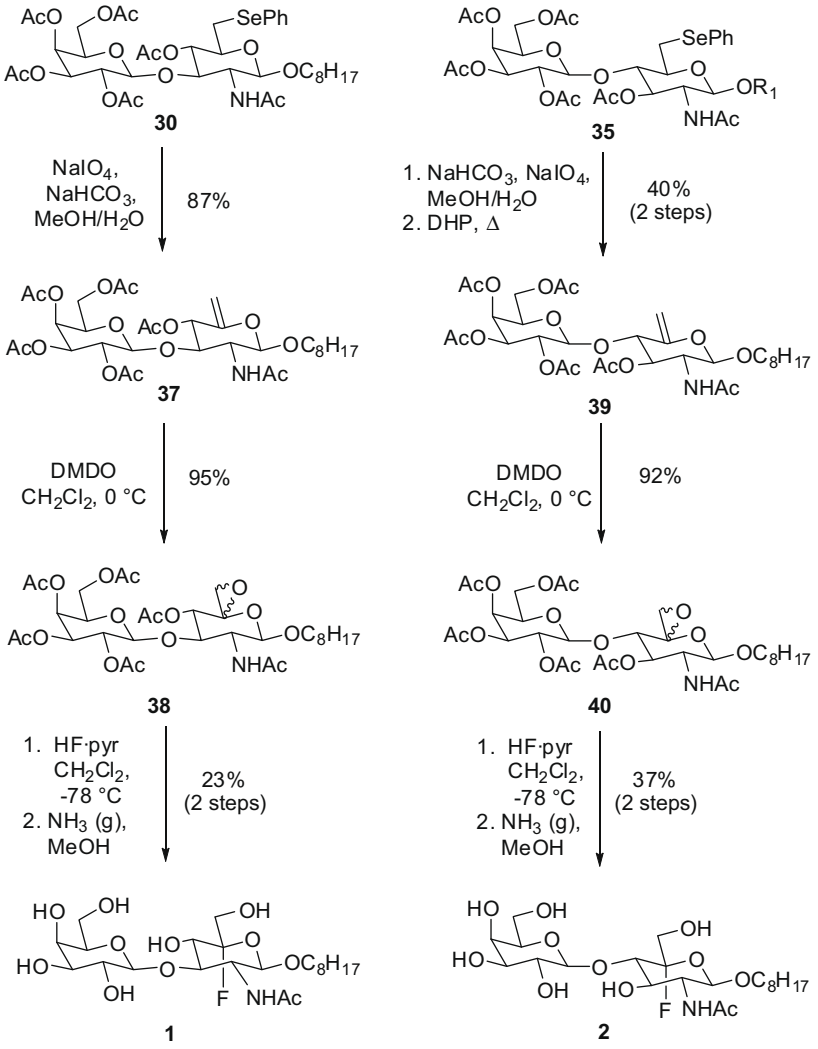


Scheme 4.

by passing through a column of activated Al_2O_3. AgOTf was purified by azeotropic removal of impurities with toluene. Flash column chromatography used 230–400 mesh Whatman silica gel. TLC was run on Whatman 250 μm silica plates with UV fluorescence detected by short wave UV. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 or 300 spectrometers or Varian 300 or 400 spectrometers. ^1H NMR chemical shifts (δ) for $CDCl_3$ or CD_3OD are in ppm using TMS as the reference at 0.00 ppm. ^1H NMR chemical shifts (δ) for spectra obtained in D_2O were referenced to HOD at 4.79 ppm. ^{13}C NMR chemical shifts (δ) for $CDCl_3$ or CD_3OD are in ppm using the center solvent peak of $CDCl_3$ at 77.00 ppm as the reference and CD_3OD at 49.00 ppm as the reference. ^{19}F NMR chemical shifts were referenced to TFA at 0 ppm as an external standard to TFA in $CDCl_3$. NMR assignments were based upon ^1H J values, ^1H COSY, and HETCOR. Diastereomeric ratio of 5,6 epoxides was determined by ^1H NMR and ^1H NOESY analysis. Mass spectra were recorded on a Micromass LCT Time-of-Flight mass spectrometer by electrospray ionization using sodium as the ion. Dimethyldioxirane (DMDO) was prepared as described.[21] The following carbohydrates were synthesized as described in the literature: **14a**,[14] **14b**,[9]**15a**,[9] **18**,[14] **20**,[14], **23** (X = Br),[22] and **23** (X = OC(NH)CCl_3).[22]

4.2. *t*-Butyldimethylsilyl 4-*O*-benzoyl-2,6-dideoxy-2-phthalamido-6-phenylseleno-β-D-glucopyranoside 15b

To compound **14b** (500 mg, 0.85 mmol) in 20 mL of THF were added NEt_3 (0.36 mL, 2.54 mmol), PhSeH (0.27 mL, 2.54 mmol), and NBu_4I (15 mg, 42 μmol), and the solution was brought to reflux. Additional portions of NEt_3 (0.36 mL, 2.54 mmol), PhSeH (0.27 mL, 2.54 mmol), and NBu_4I (15 mg, 42 μmol) were added after 18 h. After 44 h, the reaction mixture was cooled and diluted with 150 mL CH_2Cl_2. The solution was washed with 150 mL saturated $NaHCO_3$, H_2O, and saturated NaCl solutions. The solution was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude oil was purified using flash column chromatography



Scheme 5.

(hexanes/EtOAc, 3:1) to afford **15b** (510 mg, 90%) as a colorless solid: ^{1}H NMR ($CDCl_3$) δ 7.96 (d, 2H, NPht), 7.85 (m, 2H, NPht), 7.73 (m 2H, Bz), 7.60 (m, 1H, Bz), 7.49 (m, 2H, Bz), 7.44 (m, 2H, SePh), 7.22 (m, 3H, SePh), 5.49 (d, 1H, J = 8.0 Hz, H1), 5.09 (dd, 1H, J = 9.1 Hz, H4), 4.61 (m, 1H, J = 10.8, 6.2 Hz, H3), 4.27 (dd, 1H, J = 10.8, 8.0 Hz, H2), 4.00 (m, 1H, J = 8.6, 3.0 Hz, H5), 3.16 (m, 2H, H6), 2.57 (d, 1H, J = 6.3 Hz, OH), 0.73 (s, 9H, *t*Bu), 0.13 (s, 3H, CH_3-TBS), 0.04 (s, 3H, CH_3-TBS). ^{13}C NMR ($CDCl_3$) δ 166.92, 134.38, 133.93, 132.68, 131.89, 130.80, 130.14, 129.36, 129.21, 128.77, 127.20, 123,59, 109.82, 93.66, 74.08, 73.42, 59.58, 29.87, 25.55, 17.72, −3.82, −5.45. MS (ES, Na^+): m/z (relative intensity) 690.1 (100). HRMS (M+Na^+) calcd for $C_{33}H_{37}NO_7SeSiNa$, 690.1402; found 690.1403.

4.3. 4-*O*-Benzoyl-2-phthalamido-2,6-dideoxy-3-O-[(benzyloxy) methyl]-6-phenylseleno-octyl-β-D-glucopyranoside 16a

To a stirred solution of **15a** (125 mg, 0.19 mmol) in 5 mL THF were added DIEA (0.18 mL, 1.03 mmol) and BOMCl (0.13 mL, 0.94 mmol) and the reaction was brought to reflux. After 71 h, the reaction mixture was cooled and diluted with 25 mL CH_2Cl_2 and washed with 25 mL saturated $NaHCO_3$ solution and the aqueous layer was washed with 25 mL CH_2Cl_2. The combined organic layers were washed with 50 mL saturated NaCl solution, dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude oil was purified using flash column chromatography (hexanes/EtOAc, 3:1) to afford compound **16a** (120 mg, 81%) as a colorless oil/solid. ^{1}H NMR ($CDCl_3$) δ 8.02 (m, 2H, Pht), 7.98 (m, 2H, Pht), 7.60 (m, 2H, Bz), 7.72 (m, 3H, ArH of BOM), 7.84 (m, 2H, ArH of BOM), 7.33 (m, 5H, PhSe), 7.17 (m, 3H, Bz), 5.21 (m, 1H, J = 8.5 Hz, H1), 4.76 (m, 1H, H4), 4.64–4.60 (d, 2H, –O–CH_2-O-Bn), 4.50 (m, 1H, J = 7.2 Hz, H3), 4.36 (dd, 1H, J = 8.6 Hz, H2), 4.05 (d, 2H, –O–CH_2-Ph), 3.88 (m, 2H, CH_2, octyl), 3.47 (m, 1H, J = 12.5, 8.9, 6.2 Hz, H5), 3.16 (dd, 1H, J = 13.1, 9.0 Hz, H6), 3.06 (dd, 1H, J = 13.0, 2.5 Hz, H6), 1.24 (br s, 12H, CH_2-octyl), 0.81 (br s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ 165.21, 137.74, 136.98, 136.92, 133.91, 133.58, 133.44, 132.25, 131.45, 129.72, 128.94, 128.56, 128.45, 128.07, 127.96, 127.80, 127.77, 127.73, 127.54, 127.10, 126.78, 98.29, 95.98, 75.55, 74.15, 71.77, 69.57, 67.21, 64.00, 60.99, 55.73, 43.63, 31.57, 29.16, 29.10, 29.03, 25.72, 22.50, 14.13.

4.4. *t*-Butyldimethylsilyl 4-*O*-benzoyl-3-*O*-[(benzyloxy)methyl]-2,6-dideoxy-2-phthalamido-6-phenylseleno-β-D-glucopyranoside 16b

To a stirred solution of **15b** (500 mg, 0.75 mmol) in 15 mL of THF were added DIEA (0.72 mL, 4.12 mmol) and BOM–Cl (0.52 mL, 3.75 mmol) and the solution was brought to reflux. Addi-

tional portions of DIEA (0.72 mL, 4.12 mmol) and BOM–Cl (0.52 mL, 3.75 mmol) were added after 17 h. After 42 h, the reaction mixture was cooled and diluted with 100 mL CH_2Cl_2. The solution was washed with 100 mL saturated $NaHCO_3$ and the aqueous layer was washed with 100 mL CH_2Cl_2. The combined organic layers were washed with 100 mL saturated NaCl solution and was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude oil was purified using flash column chromatography (hexanes/EtOAc, 5:1) to afford **16b** (450 mg, 76%) as a colorless oil/solid: ^{1}H NMR ($CDCl_3$) δ 8.00 (m, 2H, Bz), 7.73 (br s, 2H, NPht), 7.62 (m, 2H, NPht), 7.46 (m 3H, Bz), 7.38 (m, 2H, Bz), 7.34 (m, 3H, ArH of BOM), 7.21 (m, 3H, SePh), 7.09 (m, 2H, SePh), 6.81 (m, 2H, ArH of BOM), 5.47 (d, 1H, J = 8.1 Hz, H1), 5.31 (dd, 1H, J = 9.5 Hz, H4), 4.80 (dd, 1H, J = 10.8, 8.9 Hz, H3), 4.76 (d, 1H, J = 7.2 Hz, O–C*H*$_2$-Ph/Bn), 4.63 (d, 1H, J = 7.2 Hz, O–C*H*$_2$-Ph/Bn), 4.39 (dd, 1H, J = 10.8, 8.1 Hz, H2), 4.08 (s, 2H, O–C*H*$_2$–O-Bn), 3.94 (ddd, 1H, J = 12.5, 9.5, 2.9 Hz, H5), 3.19 (m, 1H, H6), 3.10 (m, 1H, J = 12.9, 2.9 Hz, H6), 0.69 (s, 9H, *t*Bu), 0.14 (s, 3H, C*H*$_3$-TBS), 0.02 (s, 3H, C*H*$_3$-TBS). These spectral data are in agreement with those given in the literature.[9]

4.5. Octyl 3-*O*-[(benzyloxy)methyl]-2,6-dideoxy-2-phthalamido-6-phenylseleno-β-D-glucopyranoside 17a

To a stirred solution of **16a** (1.90 g, 2.42 mmol) in 100 mL of THF/MeOH (1:1) was added 0.5 M NaOMe solution (0.28 mL, 5.32 mmol). Two additional portions (0.28 mL, 5.32 mmol) of the NaOMe solution were added after 17 h and 23 h. After 45 h, the reaction mixture was quenched with 2.0 g of Dowex 50 W H^+ form resin (2.1 meq/mL) and stirred gently for 30 min. The mixture was filtered and the filtrate concentrated. The resulting oil was purified by flash column chromatography (hexanes/EtOAc, 3:1) to afford **17a** as a colorless oil (1.47 g, 89%). ^{1}H NMR ($CDCl_3$) δ 7.71 (d, 2H, NPht), 7.60 (m, 2H, NPht), 7.14 (m, 5H, SePh), 7.08 (m, 3H, ArH of BOM), 7.00 (m, 2H, ArH of BOM), 5.07 (d, 1H, J = 8.3 Hz, H1), 4.74 (d, 1H, J = 7.1 Hz, O–C*H*$_2$-Ph/Bn), 4.58 (d, 1H, J = 7.1 Hz, O–C*H*$_2$-Ph/Bn), 4.50 (d, 1H, J = 12.0 Hz, –OH), 4.33 (s, 2H, O–C*H*$_2$–O-Bn), 4.25 (d, 1H, J = 10.8 Hz, H4), 4.18 (dd, 1H, J = 8.3 Hz, H3), 3.69–3.62 (dd, 2H, H2/C*H*$_2$-octyl), 3.49–3.42 (dd, 2H, H5/C*H*$_2$-octyl), 3.31 (m, 1H, J = 13.2, 6.6 Hz,H6), 3.11 (m, 1H, J = 12.8, 8.3 Hz, H6), 1.32–1.31 (br s, 2H, C*H*$_2$-octyl), 1.16–0.97 (br s, 10H, C*H*$_2$-octyl), 0.88 (t, 3H, C*H*$_3$-octyl). ^{13}C NMR ($CDCl_3$) δ 171.00, 136.30, 133.93, 132.03, 131.52, 130.99, 128.87, 128.41, 127.92, 127.72, 126.45, 123.47, 123.01, 98.11, 96.06, 82.53, 75.46, 74.00, 70.31, 69.50, 60.26, 55.15, 31.54, 31.47, 29.68, 29.01, 25.70, 22.53, 22.48, 20.92, 14.09, 13.95. MS (ES, Na^+): m/z (relative intensity) 704.2 (100). HRMS (M+Na^+) calcd for $C_{36}H_{43}NO_7SeNa$, 704.2102; found 704.2103.

4.6. *t*-Butyldimethylsilyl-3-*O*-[(benzyloxy)methyl]-2,6-dideoxy-2-phthalamido-6-phenylseleno-β-D-glucopyranoside 17b

To a stirred solution of **16b** (270 mg, 0.34 mmol) in 10 mL of THF/MeOH (1:1) was added 1 M NaOMe solution (0.35 mL, 0.35 mmol). After 6 h, the reaction mixture was quenched with 750 mg of Dowex 50 W H^+ form resin (2.1 meq/mL) and stirred gently for 15 min. The mixture was filtered and the filtrate concentrated. The resulting oil was purified by flash column chromatography (hexanes/EtOAc, 3:1) to afford **17b** as a colorless oil (200 mg, 87%): ^{1}H NMR ($CDCl_3$) δ 7.89 (d, 2H, NPht), 7.79 (m, 2H, NPht), 7.62 (m, 2H, SePh), 7.37–2.28 (m, 8H, SePh/ArH of BOM), 5.42 (d, 1H, J = 7.8 Hz, H1), 4.93 (d, 1H, J = 6.0 Hz, O–C*H*$_2$-Ph/Bn), 4.73 (d, 2H, O–C*H*$_2$-Ph/Bn/O–C*H*$_2$–O-Bn), 4.33 (s, 1H, O–C*H*$_2$–O-Bn), 4.47 (d, 1H, J = 1.4 Hz, –OH), 4.40 (d, 1H, J = 10.9, 8.0 Hz, H3), 4.31 (dd, 1H, J = 10.8, 7.8 Hz, H2), 3.79 (dd, 1H, J = 9.0, 2.4 Hz, H4), 3.62 (m, 2H, J = 5,7, 3.0, 2.0 Hz, H5/H6), 3.24 (m, 1H, J = 12.6, 8.8 Hz, H6), 0.75–0.0.71 (br s, 9H, TBS), 0.13 (m, 3H, TBS) 0.08 (m, 3H, TBS). ^{13}C NMR ($CDCl_3$) δ 168.80, 167.99, 136.53, 134.25, 132.11, 131.32, 129.17, 128.65, 128.16, 127.96, 127.86, 126.97, 123.58, 123.22, 96.29, 93.63, 82.48, 75.60, 74.38, 70.51, 57.43, 60.26, 30.07, −3.89, −5.57. MS (ES, Na^+): m/z (relative intensity) 706.1 (100). HRMS (M+Na^+) calcd for $C_{34}H_{41}NO_7SeSiNa$, 706.1715; found 706.1723.

4.7. Octyl 2-deoxy-2-phthalimido-6-*O*-*t*-butyldimethylsilyl-β-D-glucopyranoside 19

To a stirred solution of compound **18** (150 mg, 0.36 mmol) in 1.5 mL of DMF were added imidazole (72 mg, 1.07 mmol) and TBS–Cl (67 mg, 0.44 mmol). After 39 h, the reaction mixture was diluted with 10 mL of EtOAc and washed with 10 mL of H_2O and saturated NaCl solution. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude product was purified using a short silica gel plug (EtOAc) to afford **19** (140 mg, 74%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.82 (m, 2H, Pht), 7.69 (m, 2H, Pht), 5.17 (d, 1H, J = 8.4 Hz, H1), 4.32 (dd, 1H, J = 8.1 Hz, H4), 4.08 (dd, 1H, J = 8.5, 3.5 Hz, H2), 3.97 (dd, 1H, J = 10.3, 5.0 Hz, H3), 3.87 (m, 1H, H5), 3.75 (m, 1H, –C*H*$_2$-octyl), 3.73 (br s, 1H, –OH), 3.59 (m, 1H, H6), 3.51 (m, 1H, H6), 3.37 (m, 1H, –C*H*$_2$-octyl), 2.89 (d, 1H, J = 3.6 Hz, –OH), 1.23 (br s, 2H, C*H*$_2$-octyl), 1.16–1.00 (br s, 13H, C*H*$_2$-octyl), 0.98–0.78 (s, 12H, *t*Bu, C*H*$_3$-octyl), 0.07 (s, 6H, Me). ^{13}C NMR ($CDCl_3$) δ 168.28, 134.63, 133.33, 131.74, 123.96, 122.62, 98.78, 97.51, 75.81, 74.66, 74.14, 73.00, 72.17, 71.04, 69.64, 65.06, 56.70, 55.56, 30.25, 29.25, 28.23, 26.32, 25.32, 22.55, 21.52, 18.18, 14.50, 13.51, −5.04, −5.99. MS (ES, Na^+): m/z (relative intensity) 558.2 (100). HRMS (M+Na^+) calcd for $C_{28}H_{45}NO_7Na$, 558.2863; found 558.2869.

4.8. Octyl 2-deoxy-2-phthalimido-3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside 21

Compound **20** (2.25 g, 2.45 mmol) was dissolved in 10 mL of Ac_2O and 10 mL of pyridine. After 19 h, the reaction mixture was diluted to 75 mL of EtOAc and washed with 50 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude product was purified by flash column chromatography (hexanes/EtOAc, 3:1) to afford **21** (1.12 g, 83%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.81 (br s, 2H, NPht), 7.66 (br s, 2H, NPht), 7.43 (br s, 2H, Ph), 7.30 (br s, 3H, Ph), 5.89 (d, 1H, J = 9.8 Hz, H4), 5.51 (s, 1H, benzylidene), 5.43 (d, 1H, J = 8.4 Hz, H1), 4.37 (d, 1H, J = 10.2, 4.1 Hz, H3), 4.29 (dd, 1H, J = 9.1 Hz, H2), 3.83–3.74 (m, 3H, H6/H6/H5), 3.71 (m, 1H, C*H*$_2$-octyl), 3.42 (m, 1H, C*H*$_2$-octyl), 2.04 (s, 3H, OAc), 1.93 (s, 3H, NHAc), 1.58–1.55 (br s, 2H, C*H*$_2$-octyl), 1.28–1.21 (br s, 10H, C*H*$_2$-octyl), 0.85 (s, 3H, C*H*$_3$-octyl). ^{13}C NMR ($CDCl_3$) δ 170.03, 136.99, 134.28, 134.14, 128.14, 126.22, 123.44, 101.49, 98.65, 79.28, 77.50, 77.25, 76.99, 70.13, 69.76, 68.59, 66.18, 55.39, 31.55, 29.19, 29.14, 29.10, 29.01, 25.70, 22.50, 20.47, 14.01. MS (ES, Na^+): m/z (relative intensity) 574.2 (100). HRMS (M+Na^+) calcd for $C_{31}H_{37}NO_8Na$, 574.2417; found 574.2415.

4.9. Octyl 2-deoxy-2-phthalimido-3-*O*-acetyl-6-*O*-*t*-butyldimethylsilyl-β-D-glucopyranoside 22

Compound **21** (1.10 g, 1.99 mmol) was suspended in 50 mL of AcOH/H_2O (1:1) and heated to 100 °C. After 4.5 h, the reaction mixture was cooled and concentrated. The crude product was diluted in 75 mL of EtOAc and washed with 50 mL of saturated $NaHCO_3$ and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated to afford the diol (890 mg) as a colorless oil and taken on without any purification.

A portion of the crude diol (100 mg) was dissolved in 2.0 mL of DMF, to which TBS–Cl (40 mg, 0.27 mmol) and imidazole (44 mg, 0.65 mmol) were added. After 20 h, the DMF was concentrated. The crude product was diluted to 20 mL of EtOAc and washed with 10 mL of H_2O and saturated NaCl solution. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude product was purified using a short silica gel plug (EtOAc) to afford **22** (105 mg, 81%, two steps) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.86 (br s, 2H, NPht), 7.74 (br s, 2H, NPht), 5.65 (d, 1H, J = 10.6, 8.9 Hz, H4), 5.35 (d, 1H, J = 8.5 Hz, H1), 4.21 (dd, 1H, J = 10.6, 8.5 Hz, H3), 3.97–3.83 (m, 2H, H5/H2), 3.78 (m, 2H, H6/H6), 3.61 (m, 1H, CH_2-octyl), 3.42 (m, 1H, CH_2-octyl), 2.94 (d, J = 4.9 Hz, OH), 2.04 (s, 3H, OAc), 1.93 (s, 3H, NHAc), 1.58–1.55 (br s, 2H, CH_2-octyl), 1.28–1.21 (br s, 10H, CH_2-octyl), 0.85 (s, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 171.40, 170.32, 168.18, 167.78, 134.18, 134.11, 133.87, 131.37, 123.47, 123.41, 123.30, 98.09, 97.46, 76.23, 75.37, 73.77, 70.30, 70.07, 69.25, 69.04, 60.35, 55.42, 31.60, 29.29, 29.09, 25.87, 25.60, 22.52, 20.66, 17.94, 14.13. MS (ES, Na^+): m/z (relative intensity) calcd for $C_{30}H_{47}NO_8Na$, 512.3; found 512.3 (100).

4.10. Octyl 2-deoxy-2-phthalimido-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4,6-*O*-benzylidene-β-D-glucopyranoside 28

To a stirred solution of acceptor **20** (600 mg, 1.22 mmol) and donor **23** (X = OC(NH)CCl_3) (684 mg, 1.34 mmol) in 20 mL of CH_2Cl_2 at −20 °C were added 1.0 g 3 Å molecular sieves and freshly distilled TMS-OTf (50 μL, 0.30 mmol). The reaction mixture was allowed to warm to 0 °C for 3 h and then to room temperature. After 24 h, the reaction mixture was quenched with 0.05 mL of NEt_3 and filtered. The filtrate was washed with 20 mL of saturated $NaHCO_3$ and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude oil was purified using flash column chromatography (hexanes/EtOAc, 2:1) to afford **28** (840 mg, 83%) as a colorless foam: ^{1}H NMR ($CDCl_3$) δ 7.88 (s, 2H, Pht), 7.77 (s, 2H, Pht), 7.49 (s, 2H, Ph), 7.38 (s, 3H, Ph), 5.58 (s, 1H, benzylidene), 5.19 (d, 1H, J = 3.1 Hz, H4′), 5.14 (d, 1H, J = 8.5 Hz, H1), 4.99 (dd, 1H, J = 10.3, 8.0 Hz, H2′), 4.76–4.71 (m, 2H, H3/H3′), 4.55 (d, 1H, J = 8.0 Hz, H1′), 4.37 (dd, 1H, J = 10.5, 4.8 Hz, H4), 4.30 (dd, 1H, J = 10.4, 8.6 Hz, H2), 4.03 (dd, 1H, J = 11.0, 8.3 Hz, H6′), 3.86 (m, 1H, H6′), 3.82–3.77 (m, 3H, H6/H6/CH_2-octyl), 3.63 (m, 1H, H5), 3.49 (m, 1H, H5′), 3.38 (m, 1H, CH_2-octyl), 2.08 (s, 3H, OAc), 2.05 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.26–1.13 (br s, 3H, CH_2-octyl), 1.03–0.96 (br s, 9H, CH_2-octyl), 0.82 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 170.23, 170.01, 169.98, 168.82, 137.05, 134.18, 129.22, 128.31, 126.00, 101.43, 100.48, 98.74, 81.08, 75.69, 70.99, 70.28, 70.01, 69.19, 68.74, 66.63, 66.31, 60.76, 56.38, 31.60, 29.20, 29.03, 29.01, 25.70, 22.53, 20.56, 20.49, 20.39, 20.06, 14.15, 13.99. MS (ES, Na^+): m/z (relative intensity) 861.9 (100). HRMS (M+Na^+) calcd for $C_{43}H_{53}NO_{16}Na$, 862.3262; found 862.3259.

4.11. Octyl 2-deoxy-2-acetamido-3-*O*-(2,3,4,6-tetra-*O*-acetyl)-β-D-galactopyranosyl-4,6-*O*-diacetyl-β-D-glucopyranoside 31

A solution of **28** (22 mg, 26 μmol) in 1.0 mL AcOH/H_2O (1:1) was heated to reflux. After 2 h, the reaction mixture was cooled and concentrated. The crude reaction mixture was diluted with 30 mL of EtOAc and washed with 20 mL of saturated $NaHCO_3$ and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude product was purified with a short silica gel plug (EtOAc) to afford the diol (20 mg) as a colorless oil. To a stirred solution of this diol in 0.5 mL of EtOH in a Schlenk tube was added $H_2NNH_2{\cdot}H_2O$ (0.11 mL, 2.40 mmol). The reaction mixture was placed under a gentle vacuum, the tube sealed and heated to 100 °C. After 41 h, the reaction mixture was cooled, the tube opened and the reaction mixture concentrated and placed under vacuum for 6.5 h to afford the free isolactosamine (10 mg) as a colorless oil. The crude product, immediately taken on to the next step without any purification, was dissolved in 1.0 mL of pyridine and 1.0 mL of Ac_2O. After 18.5 h, the reaction mixture was diluted with 5 mL EtOAc and washed with 5 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The resulting light yellow oil was purified using preparative thin layer chromatography (hexanes/EtOAc, 1:1) to afford **31** (8 mg, 41%, three steps) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.65 (d, 1H, J = 7.1 Hz, NH), 5.33 (d, 1H, J = 3.3 Hz, H4′), 5.06 (dd, 1H, J = 10.3, 7.9 Hz, H2′), 4.98–4.91 (m, 3H, H1/H3/H3′), 4.56–4.52 (m, 2H, H4/H1′), 4.13–4.06 (m, 4H, H2/H5′/H6′/H6′), 3.87–3.81 (m, 2H, H6/H6), 3.66 (m, 1H, H5), 3.46 (m, 1H, CH_2-octyl), 3.13 (m, 1H, CH_2-octyl, 2.14 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.96 (s, 3H, NHAc), 1.55 (br s, 3H, CH_2-octyl), 1.25 (br s, 9H, CH_2-octyl), 0.85 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 170.73, 170.37, 170.27, 169.50, 168.90, 100.49, 98.96, 71.75, 71.03, 70.62, 70.05, 69.47, 69.11, 66.90, 62.55, 61.04, 60.35, 58.23, 53.37, 31.77, 29.44, 29.28, 25.87, 23.62, 22.60, 20.80, 20.61, 14.03. MS (ES, Na^+): m/z (relative intensity) 770.1 (100). HRMS (M+Na^+) calcd for $C_{34}H_{53}NO_{17}Na$, 770.3229; found 770.3211.

4.12. Octyl 2-deoxy-2-acetamido-3-*O*-β-D-galactopyranosyl-β-D-glucopyranoside 3

To a stirred solution of **31** (5 mg, 6.7 μmol) in 0.5 mL of MeOH/THF (1:1) was added 0.5 M NaOMe solution (28 μL, 54 μmol). After 4 d, the reaction mixture was quenched with 0.050 g of Dowex 50 W H^+ form resin (2.1 meq/mL) and stirred gently for 20 min. The mixture was filtered and the filtrate concentrated. The resulting white powder was purified using a short silica gel plug with $CHCl_3$/MeOH (4:1) to afford **3** (3 mg, 90%) as a white powder: ^{1}H NMR (D_2O) δ 4.40 (d, 1H, J = 7.7 Hz, H1), 4.29 (d, 1H, J = 7.7 Hz, H1′), 3.79–3.74 (m, 3H, H2′/H3/H3′), 3.67–3.62 (m, 6H, H4′/H4/H2/H5/H6′/H6′), 3.57–3.43 (m, 2H, H6/H6), 3.41–3.34 (m, 3H, H5/-CH_2-octyl), 1.90 (s, 3H, NHAc), 1.40 (br s, 3H, CH_2-octyl), 1.14 (br s, 9H, CH_2-octyl), 0.72 (t, 3H, CH_3-octyl). ^{13}C NMR (D_2O) δ 174.48, 103.51, 100.87, 82.49, 75.35, 75.27, 72.49, 70.68, 70.59, 68.75, 68.53, 61.01, 60.77, 54.62, 31.08, 28.55, 28.47, 28.32, 25.07, 22.27, 22.00, 13.37. MS (ES, Na^+): m/z (relative intensity) 518.3 (100). HRMS (M+Na^+) calcd for $C_{22}H_{41}NO_{11}Na$, 518.2577; found 518.2576.

4.13. Octyl 2-deoxy-2-phthalamido-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-*O*-benzoyl-6-phenylseleno-β-D-glucopyranoside 29

To a stirred solution of **28** (700 mg, 0.83 mmol) in 35 mL of CCl_4 were added NBS (160 mg, 0.92 mmol) and $BaCO_3$ (483 mg, 2.45 mmol). The reaction mixture was heated to reflux and after a few minutes it turned to an orange color. As the reaction mixture progressed, it became white. After 45 min, the reaction was cooled, filtered, and the filtrated concentrated. The crude product was dissolved in 50 mL of CH_2Cl_2 and washed with 25 mL of H_2O three times and once with 25 mL of saturated NaCl solution. The organic extract was dried with Na_2SO_4, filtered and the filtrate concentrated to yield the bromide (750 mg) as a white powder and taken on without any purification: ^{1}H NMR ($CDCl_3$) δ 8.04 (m, 2H, Bz), 7.85 (d, 2H, NPht), 7.77 (m, 2H, NPht), 7.57 (m, 2H, Bz), 7.44 (m, 3H, Bz), 5.14 (m, 1H, H3), 5.11 (d, 1H, J = 8.5 Hz, H1), 4.97 (d, 1H, J = 4.2 Hz, H4′), 4.83 (dd, 1H, J = 10.5, 3.7 Hz, H3′), 4.54 (dd, 1H, J = 10.5, 3.5 Hz, H2′), 4.32 (m, 1H, H5′), 4.18 (d, 1H, J = 7.8 Hz,

H1′), 4.09 (dd, 1H, J = 4.1 Hz, H2), 3.94 (m, 1H, H4), 3.77 (m, 1H, CH_2-octyl), 3.53 (m, 2H, H6′/H6′), 3.49–3.31 (m, 4H, H5/H6/H6/CH_2-octyl), 2.09–1.75 (s, 12H, OAc), 1.41 (br s, 3H, CH_2-octyl), 1.14–0.98 (br s, 9H, CH_2-octyl), 0.80 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 169.92, 168.88, 164.58, 134.40, 133.32, 131.32, 129.91, 129.68, 128.25, 123.44, 100.09, 97.84, 74.64, 73.68, 72.43, 71.05, 70.65, 70.13, 66.77, 68.76, 66.09, 60.03, 55.54, 53.30, 31.46, 31.15, 28.99, 28.89, 25.58, 22.40, 20.22, 13.87. MS (ES, Na^+): m/z (relative intensity) calcd for $C_{43}H_{52}NO_{16}BrNa$, 940.2; found 940.2 (100).

To a stirred solution of the bromide (750 mg) in 30 mL of THF were added NEt_3 (0.37 mL, 2.69 mmol), PhSeH (0.24 mL, 2.45 mmol), and Bu_4NI (75 mg, 0.20 mmol). The reaction mixture was brought to reflux at 65 °C. After 16 h, the reaction was cooled and diluted to 100 mL of CH_2Cl_2 and washed with 100 mL of saturated $NaHCO_3$, H_2O, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered and the filtrate concentrated. The resulting yellow oil was purified using flash column chromatography (hexanes/EtOAc, 2:1) to afford **29** (700 mg, 84%, two steps) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.03 (m, 2H, Bz), 7.87 (d, 2H, NPht), 7.79 (m, 2H, NPht), 7.58 (m, 2H, Bz), 7.46 (m, 4H, Bz/SePh), 7.19 (m, 2H, SePh), 5.23 (m, 1H, H3′), 5.07 (d, 1H, J = 8.5 Hz, H1), 5.00 (d, 1H, J = 2.9 Hz, H4′), 4.86 (dd, 1H, J = 10.3, 7.8 Hz, H2′), 4.79 (dd, 1H, J = 10.7, 8.9 Hz, H3), 4.56 (m, 1H, H5′), 4.34 (dd, 1H, J = 10.7, 8.5 Hz, H2), 4.09 (d, 1H, J = 7.8 Hz, H1′), 3.94 (m, 1H, H4), 3.72 (m, 2H, H6′/H6′), 3.52 (m, 1H, H5), 3.44 (m, 1H, H6), 3.33 (m, 2H, CH_2-octyl), 3.13 (m, 1H, H6), 2.08 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.87 (s, 3H, OAc), 1.27–1.17 (br s, 3H, CH_2-octyl), 1.06–1.00 (br s, 9H, CH_2-octyl), 0.83 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 170.12, 170.04, 169.97, 169.00, 164.76, 134.49, 133.32, 132.19, 129.74, 128.99, 128.32, 126.79, 123.52, 100.23, 97.91, 74.97, 74.21, 70.81, 70.13, 69.65, 68.84, 66.18, 60.08, 55.74, 31.61, 29.05, 25.73, 22.56, 20.58, 20.36, 20.29, 14.03. MS (ES, Na^+): m/z (relative intensity) 1018.2 (100). HRMS (M+Na^+) calcd for $C_{49}H_{57}NO_{16}SeNa$, 1018.2740; found 1018.2745.

4.14. Octyl 2-deoxy-2-acetamido-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-*O*-acetyl-6-phenylseleno-β-D-glucopyranoside 30

To a stirred solution of **29** (45 mg, 45 μmol) in 1.0 mL of EtOH in a Schlenk tube was added $H_2NNH_2{\cdot}H_2O$ (0.19 mL, 4.070 mmol). The reaction mixture was placed under a gentle vacuum, the tube sealed and heated to 100 °C. After 18.5 h, the reaction mixture was cooled, the tube opened, and the reaction mixture concentrated and placed under vacuum for 6 h to afford the free isolactosamine (40 mg) as a colorless oil. The product, which was taken on to the next step without any purification, was dissolved in 3.0 mL of pyridine and 3.0 mL of Ac_2O. After 20.5 h, the reaction mixture was diluted with 10 mL of EtOAc and washed with 10 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The resulting light yellow oil was purified using preparative thin layer chromatography (hexanes/EtOAc, 1:4) to afford **30** (29 mg, 76%, two steps) as a colorless oil/solid: ^{1}H NMR ($CDCl_3$) δ 7.48 (m, 3H, SePh), 7.26 (m, 2H, SePh), 5.89 (d, 1H, J = 7.1 Hz, NH), 5.33 (d, 1H, J = 2.5 Hz, H4′), 5.04 (dd, 1H, J = 10.1 Hz, H2′), 4.96–4.90 (m, 2H, H3′/H1), 4.80 (dd, 1H, J = 9.1 Hz, H3), 4.55–4.48 (m, 3H, H1′/H4/H5′), 3.86 (dd, 1H, J = 12.9, 6.4 Hz, H6′), 3.66 (dd, 1H, J = 8.9, 6.1 Hz, H6′), 3.74 (m, 1H, H2), 3.42 (m, 1H, CH_2-octyl), 3.12 (m, 1H, CH_2-octyl), 3.03–2.97 (m, 3H, H5/H6/H6), 2.16 (s, 3H, OAc), 2.13 (br s, 15H, OAc/NHAc), 1.52 (br s, 3H, CH_2-octyl), 1.25 (br s, 9H, CH_2-octyl), 0.86 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 175.13, 171.13, 170.88, 170.39, 170.18, 170.11, 169.67, 169.01, 132.57, 129.01, 126.91, 100.53, 98.78, 73.73, 73.04, 71.06, 70.54, 69.87, 69.39, 66.92, 61.05, 60.36, 58.39, 31.79, 29.50, 29.44, 29.29, 25.89, 23.57, 22.61, 20.99, 20.89, 20.77, 20.60, 20.49, 14.15. MS (ES, Na^+): m/z (relative intensity) 868.2 (100). HRMS (M+Na^+) calcd for $C_{38}H_{55}NO_{17}SeNa$, 868.2635; found 868.2645.

4.15. Octyl 2-deoxy-2-phthalamido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-acetyl-6-*O*-*t*-butyldimethylsilyl-β-D-glucopyranoside 32

To a stirred solution of donor **23** (1.0 g, 2.0 mmol) and acceptor **19** (650 mg, 0.19 mmol) in 75 mL of CH_2Cl_2 was added 0.25 g 3 Å molecular sieves. The reaction mixture was refluxed for 1 h and then cooled to −50 °C and freshly distilled TMS-OTf (35 μL, 0.19 mmol) was added. After 15 min, the reaction mixture was quenched with 0.1 mL of NEt_3 and filtered. The filtrate was washed with 20 mL of saturated $NaHCO_3$ and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered and the filtrate concentrated to provide the desired product containing a free 3-hydroxyl group (590 mg, 56%). This product was dissolved in 10 mL of pyridine and 10 mL of Ac_2O. After 20 h, the reaction mixture was diluted to 50 mL of EtOAc and washed with 50 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude oil was purified using flash column chromatography (hexanes/EtOAc, 2:1) to afford **32** (210 mg, 34%, two steps) as a colorless oil/solid: ^{1}H NMR ($CDCl_3$) δ 7.79 (br s, 2H, Pht), 7.69 (s, 2H, Pht), 5.67 (dd, 1H, J = 10.7, 9.0 Hz, H3′), 5.31 (d, 1H, J = 3.1 Hz, H4′), 5.26 (d, 1H, J = 8.4 Hz, H1), 5.07 (dd, 1H, J = 10.3, 8.0 Hz, H2′), 4.91 (dd, 1H, J = 10.4, 3.5 Hz, H3), 4.69 (d, 1H, J = 7.9 Hz, H1′), 4.13–4.02 (m, 4H, H4/H2/H6/H6), 3.94–3.89 (m, 2H, H6′/H6′), 3.84 (m, 1H, H2), 3.81 (m, 1H, H5′), 3.71 (m, 1H, CH_2-octyl), 3.47 (m, 1H, Hz, H5), 3.36 (m, 1H, CH_2-octyl), 2.13–1.86 (s, 18H, NHAc, OAc), 1.67 (br s, 2H, CH_2-octyl), 1.24–1.00 (br s, 12H, CH_2-octyl), 0.87 (s, 12H, *t*Bu, CH_3-octyl), 0.06 (s, 6H, Me). ^{13}C NMR ($CDCl_3$) δ 171.08, 170.30, 170.17, 170.08, 170.05, 168.85, 167.93, 167.93, 167.57, 134.11, 133.94, 131.33, 123.38, 100.32, 97.61, 75.13, 75.08, 71.10, 70.96, 70.49, 69.40, 69.13, 68.67, 66.79, 66.35, 61.02, 60.95, 60.31, 54.99, 31.57, 29.23, 29.04, 25.84, 25.79, 22.50, 20.96, 20.66, 20.57, 20.49, 18.24, 14.11, 13.97, −4.97, −5.33. MS (ES, Na^+): m/z (relative intensity) 930.3 (100). HRMS (M+Na^+) calcd for $C_{38}H_{65}NO_{17}SiNa$, 930.3919; found 930.3926.

4.16. Octyl 2-deoxy-2-acetamido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3,6-*O*-acetyl-β-D-glucopyranoside 36

To a stirred solution of **32** (100 mg, 0.12 mmol) in 4.0 mL of EtOH in a Schlenk tube was added $H_2NNH_2{\cdot}H_2O$ (0.53 mL, 10.40 mmol). The reaction mixture was placed under a gentle vacuum, the tube sealed and heated to 100 °C. After 15 h, the reaction mixture was cooled, the tube opened, and the reaction mixture concentrated and placed under vacuum for 6 h to afford the free lactosamine (26 mg) as a colorless oil. The product was taken on to the next step without any purification. The crude product was dissolved in 3 mL of pyridine and 3 mL of Ac_2O. After 30 h, the reaction mixture was diluted with 20 mL of EtOAc and washed with 20 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The resulting yellow oil was purified using flash column chromatography (hexanes/EtOAc, 1:1) to afford **36** (60 mg, 70%, two steps) as a colorless oil/solid: ^{1}H NMR ($CDCl_3$) δ 5.63 (d, 1H, N-H), 5.35 (d, 1H, H4′), 5.23 (dd, 1H, J = 10.2 Hz, H2′), 5.19 (m, 1H, H3), 5.04 (dd, 1H, J = 10.8, 7.8 Hz, H3′), 4.82 (dd, 1H, J = 9.6 Hz, H4), 4.57 (d, 1H, J = 8.3 Hz, H1), 4.53 (dd, 1H, H2), 4.42 (d, 1H, J = 7.4 Hz, H1′), 4.10 (dd, 1H, H6′), 4.00 (m, 1H, H6′), 3.83–3.73 (m, 3H, H6/H6/CH_2-octyl), 3.64 (m, 1H, H5), 3.57 (m, 1H, Hz,

H5′), 3.40 (m, 1H, CH_2-octyl), 2.07–1.88 (s, 21H, NHAc, OAc), 1.53–1.51 (br s, 3H, CH_2-octyl), 1.30–1.10 (br s, 9H, CH_2-octyl), 0.85 (t, 3H, CH_3-octyl). MS (ES, Na^+): *m*/*z* (relative intensity) 770.3 (100). HRMS (M+Na^+) calcd for $C_{32}H_{53}NO_{17}Na$, 770.3211; found 770.3220.

4.17. Octyl 2-deoxy-2-acetamido-4-*O*-β-D-galactopyranosyl-β-D-glucopyranoside 4

To a stirred solution of **36** (55 mg, 74 μmol) in 3.0 mL of MeOH was added NaOMe powder (8.6 mg, 0.16 mmol). After 3 d, the reaction mixture was quenched with 0.10 g of Dowex 50 W H^+ form resin (2.1 meq/mL) and stirred gently for 20 min. The mixture was filtered and the filtrate concentrated. The resulting white powder was purified using a short silica gel plug ($CHCl_3$/MeOH, 4:1) to afford **4** (15 mg, 41%) as a white powder: ^{1}H NMR (D_2O) δ 4.70–4.60 (m, 2H, H1/H1′), 3.95–3.92 (m, 3H, H2′/H3/H3′), 3.79 (m, 6H, H4′/H4/H2/H5′/H6′/H6′), 3.54–3.45 (m, 5H, H6/H6/H5/-CH_2-octyl), 2.07 (s, 3H, NHAc), 1.63 (br s, 3H, CH_2-octyl), 1.32 (br s, 9H, CH_2-octyl), 0.89 (t, 3H, CH_3-octyl). ^{13}C NMR (D_2O) δ 133.86, 126.09, 101.71, 75.14, 72.53, 71.75, 70.86, 70.70, 68.86, 66.01, 62.66, 60.98, 56.79, 47.68, 31.10, 28.37, 25.25, 25.07, 22.00, 21.87, 19.95, 13.38. MS (ES, Na^+): *m*/*z* (relative intensity) 518.2 (100). HRMS (M+Na^+) calcd for $C_{22}H_{41}NO_{11}Na$, 518.2577; found 518.2582.

4.18. Octyl 2-deoxy-2-phthalamido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-acetyl-β-D-glucopyranoside 33

To a stirred 0 °C solution of **32** (220 mg, 0.24 mmol) in 8.0 mL of CH_3CN and pyridine (1.0 mL) in a Nalgene bottle was added 1.0 mL HF·pyridine. The reaction mixture was allowed to warm to room temperature. After 2.5 h, the reaction mixture was diluted to 25 mL of CH_2Cl_2 and washed with 25 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrated concentrated. The crude oil was purified using a short silica gel plug (EtOAc) to afford **33** (180 mg, 92%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.80 (br s, 2H, Pht), 7.76 (s, 2H, Pht), 5.47 (m, 1H, H3′), 5.36 (d, *J* = 8.3 Hz, H1), 5.32 (d, 1H, H4′), 5.28 (m, 2H, H3/H2′), 5.11 (m, 1H, H3), 4.99 (m, 1H, H4), 4.66 (d, 1H, *J* = 7.7 Hz, H1′), 4.16 (dd, 1H, *J* = 10.0 Hz, H2), 4.10–3.98 (m, 3H, H6/H6/CH_2-octyl), 3.94–3.88 (m, 2H, H6′/H6′), 3.78 (m, 2H, H5/H5′), 3.58 (m, 1H, CH_2-octyl), 3.40 (d, 1H, *J* = 8.0 Hz, –OH), 2.12–1.89 (s, 18H, NHAc, OAc), 1.67 (br s, 2H, CH_2-octyl), 1.24–1.12 (m, 10H, CH_2-octyl), 0.80 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 170.35, 170.21, 170.11, 169.87, 169.21, 167.97, 134.27, 132.65, 123.56, 100.97, 98.11, 75.61, 74.68, 71.36, 70.97, 70.48, 70.26, 69.21, 66.69, 60.76, 60.50, 55.03, 53.40, 31.59, 29.22, 29.06, 25.75, 22.54, 20.69, 20.64, 20.60, 20.58, 20.52, 14.01, 13.60. MS (ES, Na^+): *m*/*z* (relative intensity) 816.3 (100). HRMS (M+Na^+) calcd for $C_{38}H_{50}NO_{17}Na$, 816.3055; found 816.3079.

4.19. Octyl 2,6-dideoxy-2-phthalamido 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-acetyl-6-phenylseleno-β-D-glucopyranoside 34

To a stirred −20 °C solution of **33** (30 mg, 37 μmol) in 0.10 mL of CH_2Cl_2 were added *N*-PSP (22 mg, 75 μmol) and PBu_3 (18 μL, 75 μmol). The reaction mixture was warmed to 0 °C and the temperature maintained at 0 °C. After 41 h, the reaction mixture was diluted to 5 mL of CH_2Cl_2 and washed with 5 mL of H_2O and saturated NaCl solution. The organic extract was dried with Na_2SO_4, filtered, and the filtrated concentrated. The crude oil was purified using preparative thin layer chromatography (hexanes/EtOAc, 2:1) to afford **34** (14 mg, 40%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.83 (br s, 2H, Pht), 7.71 (m, 2H, Pht), 7.57 (m, 2H, SePh), 7.27 (m, 3H, SePh), 5.71 (dd, 1H, *J* = 10.6, 8.0 Hz, H2′), 5.33 (d, *J* = 8.4 Hz, H1), 5.27 (d, 1H, *J* = 3.4 Hz, H4′), 5.07 (dd, 1H, *J* = 10.4, 8.4 Hz, H2), 4.81 (dd, 1H, *J* = 10.4, 3.5 Hz, H3′), 4.46 (d, 1H, *J* = 8.0 Hz, H1′), 4.20 (dd, 1H, *J* = 10.6, 8.5 Hz, H3), 4.08 (m, 2H, H6′/H6′), 3.83 (m, 2H, H4/H5′), 3.75 (m, 1H, H5), 3.71 (m, 1H, CH_2-octyl), 3.43 (d, 1H, *J* = 12.4, 2.4 Hz, H6), 3.37 (m, 1H, CH_2-octyl), 3.14 (d, 1H, *J* = 12.3, 6.7 Hz, H6), 2.14–1.90 (s, 18H, NHAc, OAc), 1.41 (br s, 3H, CH_2-octyl), 1.24–1.03 (m, 9H, CH_2-octyl), 0.82 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 170.35, 170.18, 170.03, 169.84, 168.92, 132.93, 129.24, 127.27, 101.01, 97.79, 80.16, 74.13, 71.06, 70.92, 70.53, 69.91, 69.16, 66.61, 60.78, 55.14, 53.41, 31.64, 29.39, 29.22, 25.79, 22.58, 20.63, 20.57, 20.51, 14.04, 13.62. MS (ES, Na^+): *m*/*z* (relative intensity) 956.2 (100). HRMS (M+Na^+) calcd for $C_{44}H_{55}NO_{16}SeNa$, 956.2584; found 956.2607.

4.20. Octyl 2-deoxy-2-acetamido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-acetyl-6-phenylseleno-β-D-glucopyranoside 35

To a stirred solution of **34** (50 mg, 53 μmol) in 1 mL of EtOH in a Schlenk tube was added $H_2NNH_2{\cdot}H_2O$ (0.23 mL, 4.82 mmol). The reaction mixture was placed under a gentle vacuum, the tube sealed, and heated to 100 °C. After 15 h, the reaction mixture was cooled, the tube opened, and the reaction mixture concentrated and placed under vacuum for 6 h to afford the free amine as an oil/solid. The product, which was taken on to the next step without any purification, was dissolved in 1.0 mL of pyridine and 1.0 mL of Ac_2O. After 17.5 h, the reaction mixture was diluted with 10 mL of EtOAc and washed with 10 mL of saturated $CuSO_4$, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated. The resulting light yellow oil was purified using flash column chromatography (hexanes/EtOAc, 1:2) to afford **35** (40 mg, 88%, two steps) as a colorless oil/solid: ^{1}H NMR ($CDCl_3$) δ 7.58 (m, 3H, SePh), 7.35 (m, 2H, SePh), 5.60 (d, 1H, *J* = 9.5 Hz, N*H*), 5.29 (d, 1H, H4′), 5.04 (dd, 1H, *J* = 9.0 Hz, H2′), 4.82 (dd, 1H, *J* = 10.4, 3.3, Hz, H3′), 4.42 (d, 1H, *J* = 7.5 Hz, H1′), 4.37 (d, 1H, *J* = 8.0 Hz, H1), 4.08 (m, 2H, H6′/H6′), 4.04 (m, 1H, H5′), 3.81 (m, 1H, H3), 3.78–3.72 (m, 3H, H4/H2/H5), 3.64 (m, 1H, CH_2-octyl), 3.38 (m, 2H, H6/H6), 3.14 (m, 1H, CH_2-octyl), 2.17 (s, 3H, OAc), 2.13–1.91 (br s, 15H, OAc/NHAc), 1.52 (br s, 3H, CH_2-octyl), 1.25 (br s, 9H, CH_2-octyl), 0.87 (t, 3H, CH_3-octyl). ^{13}C NMR ($CDCl_3$) δ 170.67, 170.03, 169.21, 133.48, 132.19, 130.24, 129.19, 128.60, 127.95, 126.67, 100.44, 100.16, 74.77, 73.66, 72.88, 71.19, 70.19, 69.69, 68.45, 67.25, 66.05, 60.87, 53.73, 52.58, 29.39, 25.90, 23.75, 22.73, 21.36, 21.14, 21.02, 20.32, 20.10, 19.99. MS (ES, Na^+): *m*/*z* (relative intensity) 868.3 (100). HRMS (M+Na^+) calcd for $C_{38}H_{55}NO_{17}SeNa$, 868.2635; found 868.2671.

4.21. Octyl 2,6-dideoxy-2-acetamido-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-*O*-acetyl-5,6-dehydro-β-D-glucopyranoside 37

To a stirred solution of **30** (90 mg, 0.10 mmol) in 1.75 mL of MeOH/H_2O (6:1) were added $NaHCO_3$ (10 mg, 0.12 mmol) and $NaIO_4$ (34 mg, 0.16 mmol). A white precipitate formed during the course of the reaction. After 2 h, the reaction mixture was filtered and the filtrate concentrated to leave the H_2O. The filtrate had 5 mL of H_2O added and the aqueous extract was washed three times with 5 mL of EtOAc. The combined organic extracts were washed with 10 mL of saturated NaCl solution and dried with Na_2SO_4, filtered, and the filtrate concentrated. The crude product (55 mg), a mixture of selenoxides and olefin, was taken on without purification. Under an argon atmosphere, the crude product was dissolved

in 5.0 mL DHP and heated at reflux temperature. After 50 min, NMR analysis indicated a partial loss of O-acetyl groups. Therefore, Ac_2O (2 mL) and pyridine (2 mL) were added to re-acetylate the free hydroxyl groups. Standard workup resulted in a crude product that was purified using flash column chromatography (hexanes/EtOAc, 1:1) to afford **37** (46 mg, 63%) as a white oil/solid: ^{1}H NMR ($CDCl_3$) δ 6.03 (d, 1H, J = 9.8 Hz, N-*H*), 5.88 (d, 1H, J = 8.1 Hz, H1), 5.64 (m, 1H, H3), 5.37 (d, 1H, J = 3.2 Hz, H4′), 5.14 (dd, 1H, J = 10.3, 8.0 Hz, H2′), 5.01 (dd, 1H, J = 10.4, 3.4 Hz, H3′), 4.92 (dd, 2H, J = 3.1 Hz, H6/H6), 4.81 (d, 1H, J = 7.9 Hz, H1′), 4.65 (m, 1H, H4), 4.43–4.40 (m, 3H, J = 6.5 Hz, H5′/H6′/H6′), 3.92 (m, 1H, H2), 3.78 (m, 1H, C*H*$_2$-octyl), 3.45 (m, 1H, C*H*$_2$-octyl), 2.10 (s, 3H, OAc), 2.07–1.98 (br s, 15H, OAc/NHAc), 1.55 (br s, 3H, C*H*$_2$-octyl), 1.19 (br s, 9H, C*H*$_2$-octyl), 0.85 (t, 3H, C*H*$_3$-octyl). ^{13}C NMR ($CDCl_3$) δ 171.12, 170.37, 170.27, 170.06, 169.54, 169.09, 168.88, 150.88, 145.59, 121.66, 99.74, 95.28, 77.91, 70.98, 70.59, 69.84, 68.96, 68.62, 66.95, 66.42, 60.96, 60.34, 52.72, 31.77, 29.22, 29.13, 25.87, 23.97, 23.30, 22.58, 21.00, 20.93, 20.72, 20.64, 20.60, 20.53, 14.14, 14.05. MS (ES, Na^+): m/z (relative intensity) 710.3 (100). HRMS (M+Na^+) calcd for $C_{32}H_{49}NO_{15}Na$, 710.3000; found 710.2993.

4.22. Octyl 2,6-dideoxy-2-acetamido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-acetyl-5,6-dehydro-β-D-glucopyranoside 39

To a stirred solution of **35** (40 mg, 50 μmol) in 7.0 mL of MeOH/H_2O (6:1) were added $NaHCO_3$ (5 mg, 58 μmol) and $NaIO_4$ (17 mg, 80 μmol). A white precipitate formed during the course of the reaction. After 2.5 h, the reaction mixture was filtered and the filtrate concentrated to leave the H_2O. The filtrate had 5.0 mL of H_2O added and the aqueous extract was washed three times with 5.0 mL of EtOAc. The combined organic extracts were washed with 10 mL of saturated NaCl solution and dried with Na_2SO_4, filtered, and the filtrate concentrated. The resulting mixture of olefin and selenoxides (31 mg) was taken on without any purification, dissolved in 3.0 mL of DHP, and heated to reflux at 100 °C. After 45 min, the reaction mixture was cooled and diluted with 5.0 mL of CH_2Cl_2 and washed with 5.0 mL of H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic extract was dried with Na_2SO_4, filtered and, the filtrate concentrated. The crude product was purified using flash column chromatography (hexanes/EtOAc, 1:1) to afford **39** (12 mg, 40%, two steps) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.55 (d, 1H, J = 9.6 Hz, N-*H*), 5.37 (d, 1H, J = 3.0 Hz, H4′), 5.29 (d, 1H, H1), 5.20 (dd, 1H, J = 8.0 Hz, H2′), 5.06 (dd, 1H, J = 10.5, 3.4 Hz, H3′), 4.92 (s, 1H, H6′), 4.88 (s, 1H, H6′), 4.68 (s, 1H, H6), 4.63 (s, 1H, H6), 4.54 (d, 1H, J = 7.9 Hz, H1′), 4.30 (m, 1H, H4), 4.21 (dd, 1H, J = 4.9 Hz, H3), 4.13 (m, 1H, H5′), 3.89 (m, 1H, H2), 3.75 (m, 1H, C*H*$_2$-octyl), 3.36 (m, 1H, C*H*$_2$-octyl), 2.17 (s, 3H, OAc), 2.09–1.96 (br s, 15H, OAc/NHAc), 1.53 (br s, 3H, C*H*$_2$-octyl), 1.35 (br s, 9H, C*H*$_2$-octyl), 0.86 (t, 3H, C*H*$_3$-octyl). ^{13}C NMR ($CDCl_3$) δ 171.13, 170.17, 170.09, 169.95, 169.33, 149.46, 103.87, 101.85, 97.76, 73.29, 70.86, 70.28, 69.44, 68.59, 68.05, 66.57, 60.88, 46.82, 31.82, 29.42, 29.32, 29.29, 26.10, 22.88, 22.63, 21.04, 20.85, 20.64, 14.18. MS (ES, Na^+): m/z (relative intensity) 710.3 (100). HRMS (M+Na^+) calcd for $C_{32}H_{49}NO_{15}Na$, 710.3000; found 710.3006.

4.23. Octyl 2-deoxy-2-acetamido-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-*O*-acetyl-5,6-epoxy-β-D-glucopyranoside 38

To a stirred 0 °C solution of **37** (45 mg, 65 μmol) in 2.0 mL of CH_2Cl_2 was added DMDO (approximately 8 mL). After 13 h, the reaction mixture was dried with Na_2SO_4, filtered, and the filtrate was concentrated to afford **38** (44 mg, 95%) as a colorless oil: ^{1}H NMR (C_6D_6) δ 5.78 (m, 1H, H3′), 5.56 (d, 1H, H4′), 5.50 (dd, 1H, H2′), 5.31 (d, 1H, H1), 5.02 (m, 1H, H3), 4.44 (d, 1H, H1′), 4.30 (m, 1H, H4), 4.18 (m, 1H, H5′), 3.75 (m, 2H, Hz, H6′/H6′), 3.43 (m, 1H, H2), 3.43 (m, 1H, C*H*$_2$-octyl), 3.13 (m, 1H, C*H*$_2$-octyl), 2.78 (d, 1H, H6), 2.53 (d, 1H, H6), 2.12–1.69 (br s, 18H, OAc/NHAc), 1.62 (br s, 3H, C*H*$_2$-octyl), 1.25 (br s, 9H, C*H*$_2$-octyl), 0.90 (t, 3H, C*H*$_3$-octyl). ^{13}C NMR (C_6D_6) δ 170.61, 170.44, 170.23, 78.43, 71.66, 69.93, 69.58, 68.09, 67.64, 63.07, 61.58, 33.56, 32.55, 30.44, 30.17, 30.05, 26.65, 26.54, 23.39, 21.20, 21.12, 21.02, 20.64, 20.41, 20.28, 20.21, 14.67, −1.71. MS (ESI) m/z (relative intensity): 726.3 ([M+Na^+], 100).

4.24. Octyl 2-deoxy-2-acetamido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-acetyl-5,6-epoxy-β-D-glucopyranoside 40

To a stirred 0 °C solution of **39** (11 mg, 16 μmol) in 2.0 mL of CH_2Cl_2 was added DMDO (approximately 8 mL). After 1 h, the reaction mixture was dried with Na_2SO_4, filtered, and the filtrate was concentrated to afford **40** (11 mg, 92%) as a colorless oil: ^{1}H NMR (C_6D_6) δ 6.37 (d, 1H, J = 9.7 Hz, N-*H*), 5.60 (m, 1H, H3), 5.49 (d, 1H, J = 3.0 Hz, H4′), 5.27 (d, 1H, J = 8.7 Hz, H1), 5.25 (dd, 1H, J = 10.6, 3.4 Hz, H3′), 4.82 (dd, 1H, J = 2.8 Hz, H2′), 4.79 (m, 1H, H5′), 4.74 (d, 1H, J = 7.9 Hz, H1′), 4.12 (m, 2H, Hz, H6′/H6′), 3.85 (m, 1H, H4), 3.54 (m, 1H, C*H*$_2$-octyl), 3.36 (m, 1H, H2), 3.18 (m, 1H, C*H*$_2$-octyl), 2.82 (d, 1H, J = 4.7 Hz, H6), 2.43 (d, 1H, J = 4.7 Hz, H6), 2.01–1.61 (br s, 18H, OAc/NHAc), 1.53 (br s, 3H, C*H*$_2$-octyl), 1.28 (br s, 9H, C*H*$_2$-octyl), 0.91 (t, 3H, C*H*$_3$-octyl). ^{13}C NMR (C_6D_6) δ 171.06, 170.41, 170.00, 169.56, 169.22, 103.69, 101.62, 79.06, 74.08, 71.96, 71.49, 71.08, 69.91, 69.73, 67.49, 61.45, 51.45, 49.24, 32.51, 30.11, 30.06, 30.01, 26.64, 23.39, 23.20, 21.04, 20.76, 20.56, 20.48, 20.23, 14.67, −1.73. MS (ESI) m/z (relative intensity): 726.3 ([M+Na^+] 100).

4.25. Octyl 2-deoxy-2-acetamido-3-*O*-β-D-galactopyranosyl-5-fluoro-β-D-glucopyranoside 1

To a −78 °C stirred solution of **38** (18 mg, 25 μmol) in 1.0 mL of CH_2Cl_2 was added HF·pyridine (10 μL). After 1.75 h, the reaction mixture was quenched with 0.01 mL of NEt_3 and the resulting light yellow solution was diluted to 5 mL of CH_2Cl_2 and washed with 5 mL of H_2O and saturated NaCl solution. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated to afford the (5-F) glycoside (30 mg) which was taken on without any purification. NH_3 was bubbled through a stirred methanolic solution (2 mL) of the resulting (5-F) glycoside at 0 °C. After 10 min, the flask was sealed and warmed to room temperature. After 1.5 h, the solvent and NH_3 were removed with a stream of nitrogen. The resulting product was purified using preparative thin layer chromatography (EtOAc/MeOH, 5:1) to afford **1** (3 mg, 23% two steps) as a white powder: ^{1}H NMR (D_2O) δ 3.92 (m, 1H, H1), 3.76–3.58 (d, 4H, H1′/H2′/H3/H3′), 3.42–3.28 (m, 6H, H4′/H4/H2/H5′/H6′/H6′), 3.41–3.34 (m, 2H, –C*H*$_2$-octyl), 2.19–2.06 (m, 2H, H6/H6), 1.86 (s, 3H, NHAc), 1.48 (br s, 3H, C*H*$_2$-octyl), 1.29 (br s, 9H, C*H*$_2$-octyl), 0.91 (t, 3H, C*H*$_3$-octyl). ^{13}C NMR (D_2O) δ 174.73, 105.84, 90.69, 77.37, 72.32, 69.80, 61.53, 60.38, 55.56, 46.61, 40.64, 35.13, 29.38, 25.71, 21.58, 10.79. ^{19}F NMR (D_2O) δ 89.6. MS (ES, Na^+): m/z (relative intensity) calcd for; found 536.2 (100). HRMS (M+Na^+) calcd for $C_{22}H_{40}NO_{11}FNa$, 536.2483; found 536.2457.

4.26. Octyl 2-deoxy-2-acetamido-4-*O*-β-D-galactopyranosyl-5-fluoro-β-D-glucopyranoside 2

To a −78 °C stirred solution of **7d** (11 mg, 15 μmol) in 1.0 mL of CH_2Cl_2 was added HF·pyridine (0.01 mL). After 2 h, the reaction mixture was quenched with 0.01 mL of NEt_3 and the resulting light

yellow solution was washed with 5 mL of H_2O and saturated NaCl solution. The organic extract was dried with Na_2SO_4, filtered, and the filtrate concentrated to afford the (5-F) glycoside (20 mg) and taken on without any purification. NH_3 was bubbled through a stirred methanolic solution (2 mL) of the resulting (5-F) glycoside at 0 °C. After 10 min, the flask was sealed and warmed to room temperature. After 1.5 h, the solvent and NH_3 were removed with a stream of nitrogen. The resulting product was purified using flash column chromatography (EtOAc/MeOH, 5:1) to afford **2** (3 mg, 37% two steps) as a white powder: ^{1}H NMR (D_2O) δ 4.12 (d, 1H, J = 7.1 Hz, H1), 3.91 (m, 1H, H1′), 3.73–3.57 (m, 3H, H2′/H3/H3′), 3.44–2.93 (m, 8H, H4′/H4/H2/H5′/H6′/H6′/-CH_2-octyl), 2.00–1.95 (m, 2H, H6/H6), 2.00 (s, 3H, NHAc), 1.47 (br s, 3H, CH_2-octyl), 1.32 (br s, 9H, CH_2-octyl), 0.84 (t, 3H, CH_3-octyl). ^{13}C NMR (D_2O) δ 173.64, 103.26, 90.68, 75.41, 72.49, 71.01, 69.31, 68.61, 61.94, 61.06, 56.48, 42.26, 31.11, 28.49, 25.05, 22.03, 21.31, 13.42, 10.55. ^{19}F NMR (D_2O) δ 69.5. MS (ES, Na^+): m/z (relative intensity) calcd for; found 536.2 (100). HRMS (M+Na^+) calcd for $C_{22}H_{40}NO_{11}F$-Na, 536.2483; found 536.2485.

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References

1. Williams, S. J.; Withers, S. G. *Carbohydr. Res.* **2000**, *327*, 27–48.
2. Rempel, B. P.; Withers, S. G. *Glycobiology* **2008**, *18*, 570–586.
3. Lairson, L. L.; Henrissat, B.; Davies, G. J.; Withers, S. G. *Ann. Rev. Biochem.* **2008**, *77*, 521–555.
4. Timperley, C. M.; White, W. E. *J. Fluorine Chem.* **2003**, *123*, 65–70.
5. Richard, J. P.; Heo, C. K.; Toteva, M. M. *J. Phys. Org. Chem.* **2008**, *21*, 531–537.
6. Vocadlo, D. J.; Mayer, C.; He, S. M.; Withers, S. G. *Biochemistry* **2000**, *39*, 117–126.
7. Somsak, L.; Ferrier, R. J. *Adv. Carbohydr. Chem. Biochem.* **1991**, *49*, 37–92.
8. Stubbs, K. A.; Scaffidi, A.; Debowski, A. W.; Mark, B. L.; Stick, R. V.; Vocadlo, D. J. *J. Am. Chem. Soc.* **2008**, *130*, 327–335.
9. Hartman, M. C. T.; Coward, J. K. *J. Am. Chem. Soc.* **2002**, *124*, 10036–10053.
10. Hartman, M. C. T.; Jiang, S.; Rush, J. S.; Waechter, C. J.; Coward, J. K. *Biochemistry* **2007**, *46*, 11630–11638.
11. Sun, H.-Y.; Lin, S.-W.; Ko, T.-P.; Pan, J.-F.; Liu, C.-L.; Lin, C.-N.; Wang, A. H.-J.; Lin, C.-H. *J. Biol. Chem.* **2007**, *282*, 9973–9982.
12. Homeister, J. W.; Thall, A. D.; Petryniak, B.; Maly, P.; Rogers, C. E.; Smith, P. L.; Kelly, R. J.; Gersten, K. M.; Askari, S. W.; Cheng, G. Y.; Smithson, G.; Marks, R. M.; Misra, A. K.; Hindsgaul, O.; von Andrian, U. H.; Lowe, J. B. *Immunity* **2001**, *15*, 115–126.
13. Palcic, M. M.; Heerze, L. D.; Pierce, M.; Hindsgaul, O. *Glycoconjugate J.* **1988**, *5*, 49–63.
14. Barresi, F.; Hindsgaul, O. *Can. J. Chem.* **1994**, *72*, 1447.
15. Fort, S.; Kim, H. S.; Hindsgaul, O. *J. Org. Chem.* **2006**, *71*, 7146–7154.
16. Ding, Y. L.; Fukuda, M.; Hindsgaul, O. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1903–1908.
17. Crich, D.; Dudkin, V. *J. Am. Chem. Soc.* **2001**, *123*, 6819–6825.
18. Hagena, T. L., Ph.D. Thesis, University of Michigan, 2008.
19. Grieco, P. A.; Jaw, J. Y.; Claremon, D. A.; Nicolaou, K. C. *J. Org. Chem.* **1981**, *46*, 1215–1217.
20. Witczak, Z. J.; Czernecki, S. *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 143–199.
21. Murray, R. W.; Singh, M. *Org. Synth.* **1998**, *IX*, 288–293.
22. Bukowski, R.; Morris, L. M.; Woods, R. J.; Weimar, T. *Eur. J. Org. Chem.* **2001**, 2697–2705.