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Synthesis of Fluorinated Mucin Core 2 Branched Oligosaccharides with the Potential of Novel Substrates and Enzyme Inhibitors for Glycosyltransferases and Sulfotransferases

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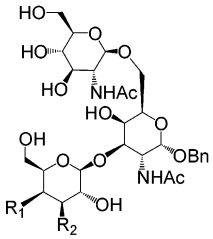

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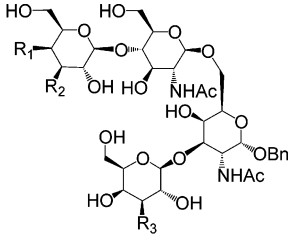

3: R_1 = F, R_2 = R_3 = OH
4: R_1 = R_2 = OH, R_3 = F
5: R_1 = R_3 = OH, R_2 = F

Syntheses of fluorinated mucin core 2 tri- and tetrasaccharides modified at the C-3 or C-4 position of the pertinent galactose residue are reported. These compounds were used for the study of sialyltransferases and 3-*O*-sulfotransferases involved in the biosynthesis of *O*-glycans. Our acceptor substrate specificity studies on three cloned sialyltransferases (Sia-Ts) revealed that a 3- or 4-fluoro substituent in β1,4Gal resulted in poor acceptors for α2,6(N)Sia-T and α2,3(N)Sia-T, whereas 4-fluoro-Galβ1,3GalNAcα was a good acceptor for α2,3(O)Sia-T. Uniquely, 4-F-Galβ1,4GlcNAcβ1,6(Galβ1,3)GalNAcα-OBn was an inhibitor of α2,6(N)Sia-T activity but not α2,3(N)Sia-T activity. Further we found that the activities of only Gal 3-*O*-sulfotransferases and not sialyltransferases were adversely affected by a C-3 fluoro substituent at the other Gal terminal of mucin core 2. The strategy of building branched mucin core 2 structures by three glycosidation sequence coupling three classes of glycosyl donors with the reactivity-matching acceptors proved to be successful in syntheses of modified mucin-type core structures of *O*-glycan. The relative poor yields of the glycosylations using fluorinated galactosyl donors indicated that the fluorine modification dramatically decreased the donor reactivity due to electron-withdrawing effect.

Introduction

The natural mucin ligands GlyCAM-1 and PSGL-1 for cell adhesion proteins[1] and various tumor-associated glycoproteins[2] are known to contain the core structure Galβ1→4GlcNAcβ1→6(Galβ1→3)GalNAcα-1 (Figure 1), which serves as a backbone for carrying glycan units playing an essential role in many biological processes.[3] However, the physiological roles of sialylated and sulfated mucin core 2 oligosaccharides in cancer, inflammation, and metastasis are yet to be elucidated in details. A knowledge of the detailed mechanism of enzymatic catalysis involved in glycosylation or sulfation on the C-3 or C-4 position of galactose residues of the mucin core 2 structure (Figure 1) in the formation of sialylated and sulfated *O*-glycan is needed for the design of metabolic inhibitors of these enzymes. In turn, the synthetic capability of these complex oligosaccharides will aid in the studies directed toward understanding the biosynthetic mechanism of these enzymes that catalyze the formation of these natural sialylated and sulfated *O*-glycans. Consequently, a tremendous effort has been made by various research groups

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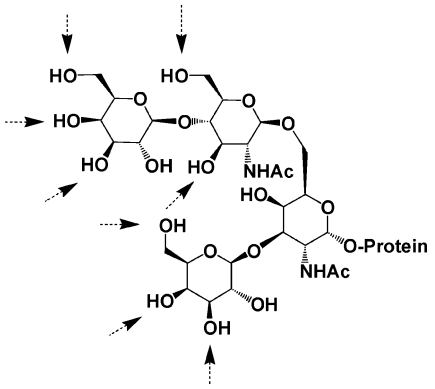

FIGURE 1. The possible positions modified by carbohydrate associated enzymes.

in developing a variety of synthetic methodologies including glycosyl bond formation and protection−deprotection strategies.[4]

Several laboratories reported the use of selectively fluorinated carbohydrate substrates as probes for studying enzymes involved in carbohydrate metabolism. Blood group A and B glycotransferases were shown to act on C-6 fluoro-substituted Gal whereas a C-3 fluoro substituent on Gal created competitive inhibitors for both enzymes.[5] van Dorst et al.[6] synthesized 3-F-Galβ1,-4GlcNAcβ1,2Manα-O$(CH_2)_7CH_3$ as a potential substrate probe for studing *N*-glycan biosynthesis. Scott and Viola[7] found that 3-fluoro and 4-fluoro analogues of D-glucose were higher affinity substrates than D-glucose for aldolase reductase but 2-fluoro and as well as 4-fluoro analogues of D-glucitol were inactive acceptors for sorbitol dehydrogenase. Tai et al.[8] synthesized a fluoro analogue of dolichol diphopho GlcNAc by replacing the acetamido group with fluorine. This compound was an inactive acceptor but a competitive inhibitor for GlcNAc transferase. Polyprenol monophosphomannosyl-dependent α1,6-Mannosyltransferase was able to utilize 2-fluoro Manα1,6Man as a substrate,[9] whereas 2,6-difluoro Manα1,6Man was neither an acceptor nor an inhibitor for this enzyme.[10]

Our laboratory has been engaged in the synthesis of complex oligosaccharide molecules, such as mucin core 2 branched sialylated and sulfated oligosaccharides for biochemical investigations. Substitution of the 3- or 4-hydroxyl group of the galactose residue in the sugar chain Galβ1→4GlcNAcβ1→6(Galβ1→3)GalNAcα− with a fluorine atom would have a differential effect on the acceptor substrate specificities of α2,3-sialyltransferase, 3-*O*-sulfotransferase, and α1,4-*N*-acetylglucosaminyltransferase during elongation of these mucin core 2 oligasaccharides. This approach may also provide useful information for devising highly effective inhibitors of these glycosyltransferases and sulfotransferases as well as metabolic inhibitors of glycoprotein synthesis. Herein, we first describe the effective syntheses and biochemical evaluation of fluorinated core 2 branched oligosaccharide analogues **1**−**5**.

Results and Discussion

Retrosynthesis. Scheme 1 outlines the retrosynthetic analysis of fluorinated mucin core 2 trisaccharides **1** and **2**. Retrosynthetic simplification of trisaccharides is rather straightforward, furnishing glucosamine donor **8** and C-3 or C-4 fluorinated disaccharide acceptors (**16** and **20**) bearing the mucin core 1 structure of Galβ1,3GalNAcα-1. In the forward sense, a highly regioselective *glycosylaion 1* of the primary hydroxyl group in the presence of the free secondary hydroxyl of the disaccharide acceptors would be expected to achieve the desired trisaccharides **1** and **2**. *N*-Phthalimido (*N*-Phth) protected glucosamine thioglycoside was chosen as a moderate glycosyl donor for *glcosylation 1* because of its potential of enhancing the regioselectivity toward the primary hydroxyl group of the disaccharide acceptors. Chemical modulations of galactose residues in mucin core 1 acceptors are involved in substitution of 3-OH or 4-OH of the galactose residue with fluorine. Retrosynthetic cleavage of the 1,3-glycosylic bond between galactosyl and *N*-acetylgalactosamine provides C-3 or C-4 fluorinated donors (**15**, **19**) and monosaccharide acceptor **7** as potential precursors. The hydroxyl group on the C-3 position of *N*-acetylgalactosamine is similar to the 4-OH of *N*-acetylglucosamines which are widely acknowledged to be among the most difficult alcohols to be glycosylated. On the basis of variable-temperature NMR studies, Crich et al.[11] suggested the intermolecular hydrogen bonding effects of the amide group which result in low reactivity toward *glycosylation 2* should be magnified at lower temperatures. *Glycosylation 2* carried out at a high temperature of 65 °C would be expected to achieve the desired fluorinated mucin core 1 structures by overcoming the hydrogen bonding effects of the amide group. To couple with the unreactive *N*-acetylgalactosamine acceptor **7** more efficiently, bromides (**15**, **19)** were selected to serve as glycosyl donors due to the matching reactivities. A sequence of straightforward functional group interconversions leads from 3-fluorinated donor **19** back to compound **10** and 4-fluorinated donor **15** back to the starting material **6**. The fluorination is carried out on the level of galactose, which minimizes the number of protecting groups that might interfere. In addition, the overall number of reaction steps would be limited.

The retrosynthetic analysis of fluorinated mucin core 2 tetrasaccharides **3**−**5** is outlined in Scheme 2. The employment of three classes of *glycosylations 1*, *2*, and *3* to carry out the desired structural transformations is the most distinguishing feature of the syntheses of the branched mucin core 2 tetrasaccharides. Retrosynthetic disconnection of tetrasaccharides **3**−**5** is most productive, for it furnishes lactosamine-type donors (**13**, **24**, **30**) and disaccharide acceptors (**12**, **20**). The *N*-phthalimido protected lactosamine thioglycoside serving as a glycosyl donor was found to be central to the success of the synthesis, which would minimize the synthetic steps by taking advantage of the thioglycoside, which can offer efficient temporary protection

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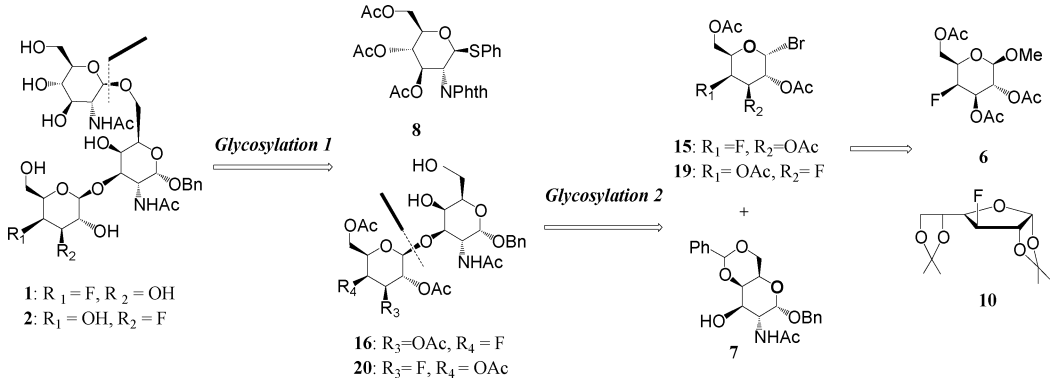
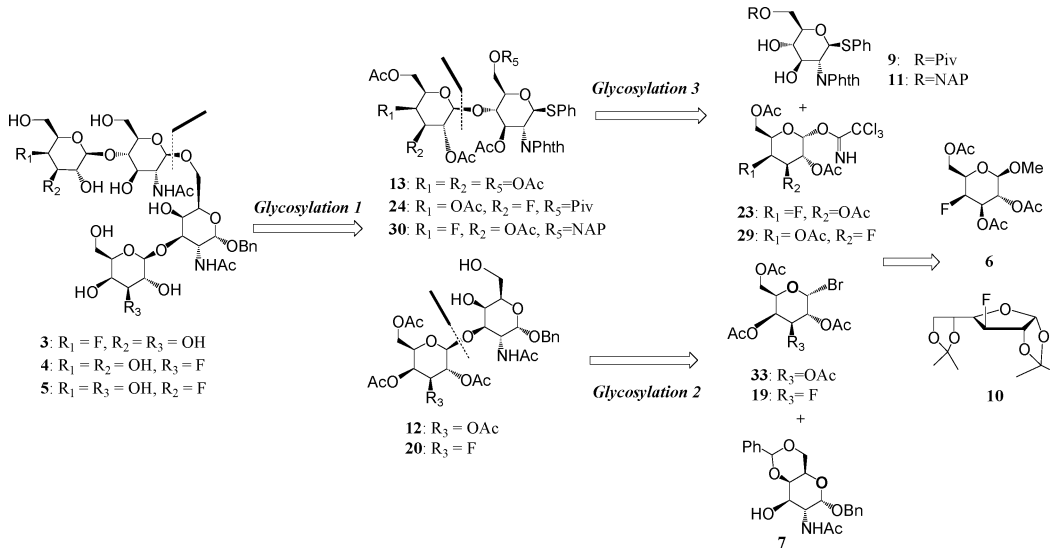
SCHEME 1. Retrosynthetic Analysis of Fluorinated Mucin Core 2 Trisaccharides 1 and 2



SCHEME 2. Retrosynthetic Analysis of Fluorinated Mucin Core 2 Tetrasaccharide 3−5



of the anomeric center stable to the condition of *glycosylation 3.* Retrosynthetic disassembly of lactosamine-type donors by cleavage of the indicated bond provides fluorinated imidate donors (**23**, **29**) and diol thioglycosides (**9**, **11**) as glycosyl acceptors. In the synthetic direction, the bulky *N*-phthalimido protect group of thioglycosides was expected to serve two important roles in *glycosylation 3*. Not only would it block the neighbor hydroxyl at the C-3 position of the diol thioglycosides, but it would also enhance the reactivity of the hydroxyl group at the 4-position of glucosamine by masking the amide group to disturb its intermolecular hydrogen bonding, which effectively increases steric bulk around the nucleophilic alcohol.[11] Although *N*-trichloroethoxycarbonyl (*N*-Troc) functionality was found to afford greater glucosamine 4-OH reactivity than the comparable *N*-phthalimido protected acceptor in trichloroacetimidate coupling, an unexpected intermolecular aglycon transfer was observed in trimethylsilyl triflate (TMSOTf)-mediated glycosylation when using *N*-Troc protected thioglycoside as the glycosyl acceptor.[12] Therefore, the *N*-phthalimido protecting group could tune the reactivity of the anomeric center of the thioglycoside to a suitable extent under the condition of *glycosylation 3* in which the phenylthio functionality is completely stable. A sequence of straightforward functional group interconversions leads from 3-fluorinated imidate donors **29** and **19** back to compound **10** and 4-fluorinated imidate donor **23** back to the starting material **6**.

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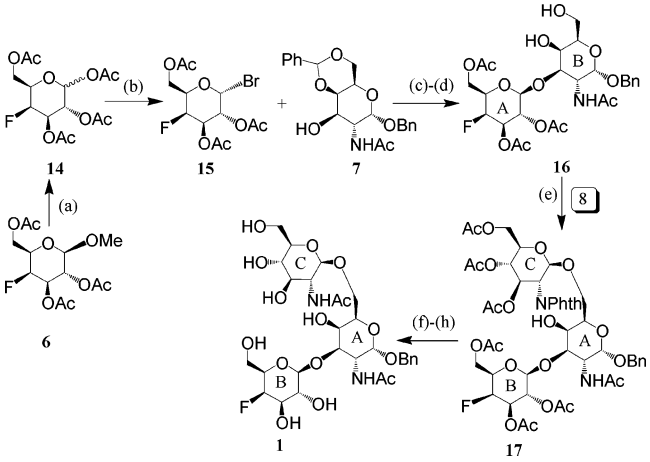
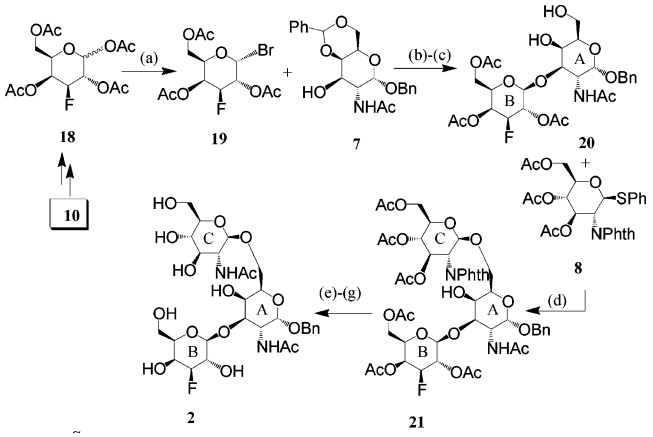
SCHEME 3[a]



[a] Reagents and conditions: (a) Ac_2O/H_2SO_4, 0−5 °C, 2 h, 58%; (b) HBr/HOAc, rt, 65%; (c) $Hg(CN)_2$, CH_3NO_2/benzene, 65 °C, 12 h; (d) 60% HOAc, 65 to 70 °C, 1.5 h, 28% over two steps; (e) NIS-TfOH/CH_2Cl_2, −65 °C, 48%; (f) NH_2-NH_2H_2O/CH_3OH (1/5), 90 °C, 6 h; (g) Ac_2O-pyridine (1/1), DMAP, rt, 12 h; (h) 1 M CH_3ONa in CH_3OH/CH_3OH−H_2O, rt, 12 h, 75% over three steps.

Synthesis. Syntheses of oligosaccharides **1** and **2** that commenced with two monosaccharide bromide donors (**15** and **19**) are illustrated in Schemes 3 and 4. Fluorinated compound **6** was prepared according to the literature method in a good

SCHEME 4[a]

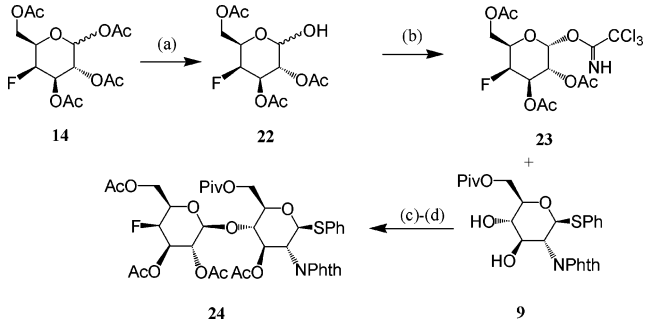


[a] Reagents and conditions: (a) HBr/HOAc, rt, 2 h, 71%; (b) $Hg(CN)_2$, CH_3NO_2/benzene, 65 °C, 12 h; (c) 60% HOAc, 65 to 70 °C, 1.5 h, 47% over two steps; (d) NIS-TfOH/CH_2Cl_2, −65 to −60 °C, 40%; (e) NH_2−NH_2·H_2O/CH_3OH (1/5), 90 °C, 6 h; (f) Ac_2O−pyridine (1:1), DMAP, rt, 12 h; (g) 1 M CH_3ONa in CH_3OH/CH_3OH in H_2O, rt, 12 h, 70% over three steps.

yield.[13] The conversion of a methyl group into an acetyl group was achieved by acetolysis of compound **6** with a catalytic amount of concentrated sulfuric acid in the presence of anhydrous acetic anhydride in an ice bath for 2 h in 58% yield. Bromide donor **15** was obtained upon treatment of tetraacetate **14** with 33% HBr−HOAc at room temperature for 2 h. Disaccharide **16** was then furnished through a $Hg(CN)_2$-promoted glycosylation in a poor yield of 28% over two steps. The relatively poor yield of the glycosylation with use of this fluorinated galactosyl bromide **15** compared with the 70% yield of reported glycosylation[14] with use of fully acetylated galactosyl bromide as donor indicated that the fluorine modification dramatically decreased the reactivity of the glycosyl donor due to its electron-withdrawing effect. Observation in our previous total synthesis of branched mucin core 2 sialylated and sulfated oligosaccharides[15] suggested that it is a plausible regioselective glycosylation of the 6-hydroxyl group of disaccharide acceptor **16** in the presence of a secondary 4-hydroxyl group. Coupling of disaccharide diol **16** with monosaccharide donor **8** at a low temperature of −65 °C provided trisaccharide **17** as the only glycosylated product in 48% yield. The stereochemical output of both the glycosidic and position connectivity of trisaccharide **17** was well established through two-dimensional NMR experiment including DQF-COSY, TOCSY, and ROESY. Structure **1** was then constructed by global deprotection of compound **17** in 75% yield over three steps: (1) removal of the *N*-Phth group from the glucosamine sugar residue, (2) complete acetylation with pyridine−acetic anhydride, and (3) removal of *O*-acetyl groups with 0.1 M sodium methoxide in methanol. The structure of compound **1** was established by a combination of electron-spray ionization high-resolution mass spectroscopy (ESI-HRMS) and two-dimensional NMR experiments (DQF-COSY and ROESY).

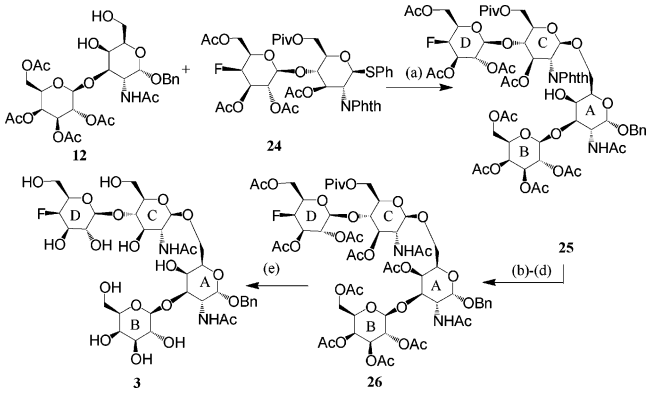
Synthesis of compound **2** is outlined in Scheme 4. Fluorinated monosaccharide bromide **19** was prepared in a good yield of

SCHEME 5[a]



[a] Reagents and conditions: (a) NH_2NH_2.HOAc/DMF, 50 °C, 2 h; (b) CCl_3CN/DBU, CH_2Cl_2, 0 to 25 °C, 80% over two steps; (c) TMSOTf/CH_2Cl_2, 4A-MS, −65 to −70 °C, 2 h; (d) Ac_2O/pyridine (1/1), DMAP, rt, 12 h, 63% over two steps.

SCHEME 6[a]



[a] Reagents and conditions: (a) NIS−TfOH/CH_2Cl_2, 4A-MS, − 65 to − 60 °C, 2 h, 76%; (b) Ac_2O/pyridine (1/1), DMAP, rt, 12 h, 80%; (c) NH_2−NH_2·H_2O/CH_3OH (1/5), 90 °C, 6 h; (d) Ac_2O/pyridine (1/1), DMAP, rt, 12 h; (e) 1 M CH_3ONa−CH_3OH/CH_3OH−H_2O, rt, 12 h, 45% over three steps.

76% starting from known compound **10** obtained from 1,2:5,6-diisopropylidene-α-D-gulose[16] over three steps: (1) fluorination of 1,2:5,6-disopropylidene-α-D-glucose with DAST,[17] (2) hydrolysis of resultant fluorinated compound in 60% acetic acid, and (3) acetylation of free hydroxyl groups with acetic anhydride in pyridine.[18] Fluorinated disaccharide diol **20** was then obtained by a $Hg(CN)_2$-catalyzed glycosylation of bromide donor **19** with acceptor **7**, followed by hydrolysis of the benzylidene group in 60% acetic acid. Compared with the 4-fluorine galactosyl bromide **15**, the 3-fluorine galactosyl bromide **19** exhibited increased reactivity to furnish disaccharide **20** in an improved yield. Regioselective glycosylation of the primary hydroxyl of diol **20** with phenylthio donor **8**, followed by full de-protection of resultant intermediate **21**, provided the targeted mucin core 2 trisaccharide **2**.

Synthesis of tetrasaccride **3** is outlined in Schemes 5 and 6. The fluorine-containing disaccharide donor **24** constitutes the first synthetic objective in the course of the synthesis of target **3**. Starting from the same tetraacetate **14** used for synthesis of

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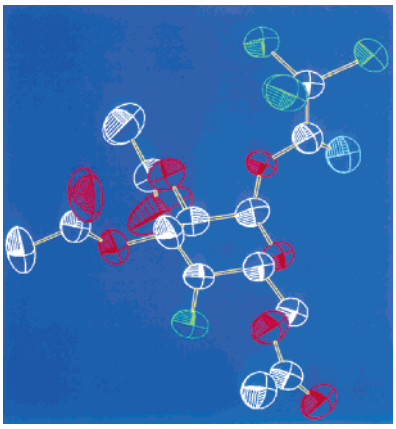


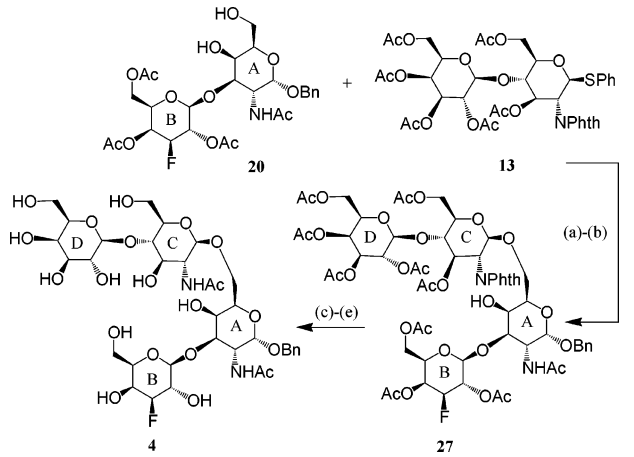
FIGURE 2. ORTEP[22] drawing of **23**.

bromide **15**, monosaccharide imidate **23** was obtained in an overall yield of 80% over two steps as illustrated in Scheme 5. The fluorination dramatically changed the physical property of the trichloroacetimidate **23**, which resulted in a well-crystallized form through a slow evaporation. The absolute configuration of fluorinated imidate donor was first characterized by X-ray analysis of compound **23** (Figure 2), which confirmed the trichloroacetimidate displaying the desired α-configuration. An attempt to couple acceptor **9** with imidate **23** at −45 to −40 °C led to a mixture of the β1,4- and β1,3-linkage of disaccharides that was difficult to separate by column chromatography. However, when the temperature was lowered to −70 to −65 °C, only β1,4-linkage disaccharide was obtained as the glycosylation product. Therefore, disaccharide **24** was prepared by coupling of the 4-hydroxyl of diol **9** with imidate **23** in a regioselective manner, followed by acetylation of the remaining free hydroxyl functionality in an overall yield of 63%. Substitution of 4-OH with a fluorine atom that has a strong electron-withdrawing negative effect seemed to reduce the glycosylation activity of imidate **23**. Regioselective glycosylation of the 6-hydroxyl group of diol **12** with lactosamine phenylthio donor **24** in a temperature-controlled manner provided tetrasacchride **25** in a high yield of 76%. The structure of tetrasaccharide **25** was established through 2D NMR experiments. Target **3** was obtained from the fully protected tetrasaccharide **26** by a similar procedure as described for de-protection of compound **17** to compound **1** in an overall yield of 39% over three steps. The structure and purity of compound **3** were also established by tremendous spectra experiments including ESI-HRMS, ^{19}F and ^{13}C NMR, 2D ^{1}H−^{1}H DQF-COSY, and 2D ROESY.

Synthesis of tetrasacchride **4** is described in Scheme 7. Regioselective glycosylation of 6-OH of the fluorinated disaccharide diol **20** with lactosamine donor **13** at low temperature afforded tetrasaccharide **27** in 65% yield. The resultant compound **27** was subjected to similar procedures as described for de-protection of the compound **21** to give compound **2**, and afforded targeted tetrasacchride **4** in an overall yield of 45% over three steps. The structure of compound **4** was fully established by ESI-HRMS, 2D DQF-COSY, and 2D ROESY.

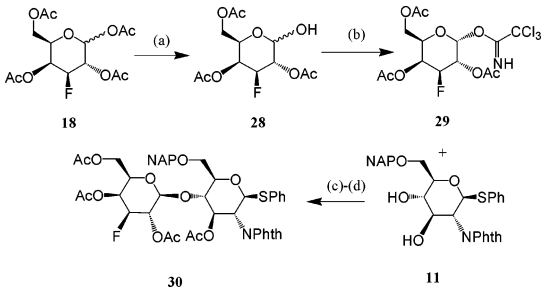
Synthesis of targeted oligosaccharide **5** is shown in Schemes 8 and 9. Regioselective glycosylation of the 4-hydroxyl group of acceptor **11** with the imidate donor **29** through a well-established glycosylation procedure from our laboratory[19g] provided a β1,4-linked disaccharide **30** in 32% yield. Coupling of disaccharide acceptor **12** with disaccharide donor **30** afforded a β1,6-linked tetrasaccharide **31** in a reasonable yield of 52%.

SCHEME 7[a]



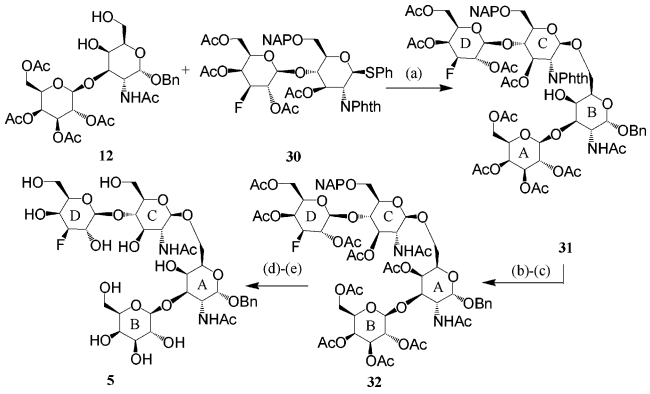
[a] Reagents and conditions: (a) NIS−TfOH/CH_2Cl_2, −45 to −40 °C, 65%; (b) Ac_2O/pyridine (1/1), DMAP, rt, 12 h, 80%; (c) NH_2−NH_2·H_2O/CH_3OH (1/5), 90 °C, 6 h; (d) Ac_2O/pyridine (1/1), DMAP, rt, 12 h; (e) 1 M CH_3ONa−CH_3OH/CH_3OH−H_2O, rt, 12 h, 45% over three steps.

SCHEME 8[a]



[a] Reagents and conditions: (a) NH_2−NH_2·HOAc/DMF, 50 °C, 2 h; (b) CCl_3CN/DBU, CH_2Cl_2, 0 to 25 °C, 32% over two steps; (c) TMSOTf/CH_2Cl_2, 4A-MS, −65 °C, 2 h, 43%; (d) Ac_2O/pyridine (1/1), DMAP, rt, 12 h, 76%.

SCHEME 9[a]



[a] Reagents and conditions: (a) NIS−TfOH/CH_2Cl_2, 4A-MS, −65 to −60 °C, 2 h, 52%; (b) Ac_2O/pyridine (1/1), DMAP, rt, 12 h, 45% over two steps; (b) NH_2−NH_2·H_2O/CH_3OH (1/5), 90 °C, 6 h; (c) Ac_2O/pyridine (1/1), DMAP, rt, 12 h; (d) DDQ in CH_2Cl_2/MeOH (4/1), rt, 18 h; (e) 1 M CH_3ONa−CH_3OH/CH_3OH−H_2O, rt, 12 h, 45% over four steps.

Target **5** was then obtained by complete de-protection of the resultant **31** in four steps. The structure and purity of tetrasacchride **5** were also established by tremendous spectra experiments including ESI-HRMS, ^{19}F and ^{13}C NMR, 2D ^{1}H−^{1}H DQF-COSY, and 2D ROESY.

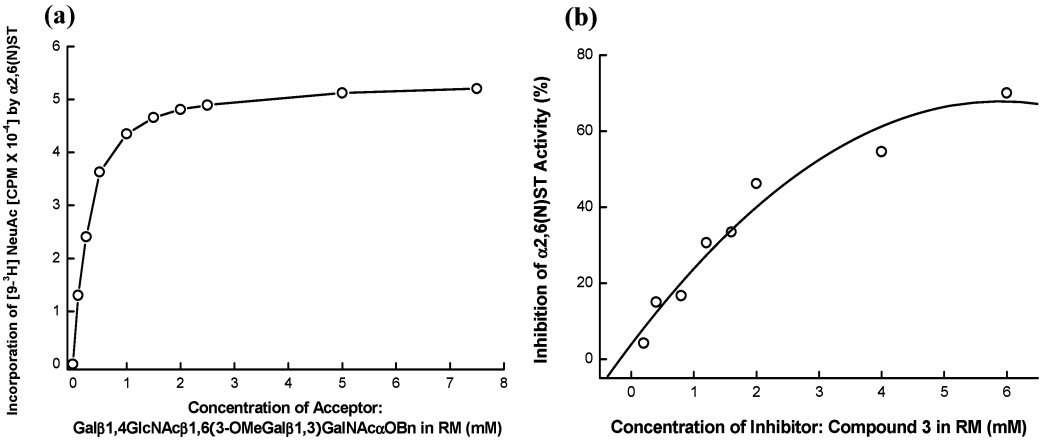


FIGURE 3. Inhibition of α2,6(N)Sia-T activity: (a) measurement of α2,6(N)Sia-T activity and (b) inhibition of α2,6(N)Sia-T activity by compound **3**.

3-*O*-Sulfo- and Sialyltransferase Activities. Sulfate and sialyl groups are located at various positions in glycoconjugates. A sulfated Lewis^x determinant was identified as a major structural motif in mucins produced by human colon carcinoma cells.[1b] Previous studies from our group[20a,b] indicated that two distinct Gal 3-*O*-sulfotransferases (Gal3STs) in tumor tissues and cancer cells exhibited distinct acceptor preferences. Enzymes from colon cancer cell lines and colon tumor tissues prefer to sulfate the C-3 position of Gal in the Galβ1,4GlcNAcβ moiety of the mucin core 2 structure. In contrast, enzymes from breast cancer cells prefer to act on the Galβ1,3GalNAcα moiety. Therefore, to determine the structural features of the mucin core 2 that influence Gal3ST activity, assay was undertaken with compounds **4** and **5** for various sulfotransferases.[20c] As compared to their activities toward the acceptor Galβ1,4GlcNAcβ1,6-(3-OMeGalβ1,3)GalNAcα-O-Bn, LS180 Gal3ST, Gal3ST-2, and Gal3ST-3 exhibited poor activity (12−16%) toward compound **4** and as anticipated, negligible activity (1−2%) toward compound **5**; Gal3ST4 showed only 23% activity with compound **5** as compared to its activity toward 3-OMeGalβ1,-4GlcNAcβ1,6(Galβ1,3)GalNAcα-OBn. Gal3ST2, Gal3ST3, and LS180 Gal3ST exhibited very little activity (1−2%) toward compound **5**. Thus it became evident that the sulfotransferases Gal3ST-2, Gal3ST-3, and LS180 GalST utilizing the Galβ1,-4GlcNAcβ terminal as acceptor acted poorly when there is a C-3 fluoro substituent on the β1,3 linked Gal of mucin core 2. Similarly, the sulfotransferase Gal3ST-4 specific for Galβ1,-3GalNAc terminal was adversely affected by a C-3 fluoro substituent on β1,4 linked Gal in mucin core 2.

When sialyltransferases were examined,[21] the cloned enzymes α2,6(N)Sia-T and α2,3(N)Sia-T specific for Galβ1,4GlcNAc terminal exhibited good activities (78% and 97%, respectively) toward compound **4**; the cloned α2,3(O)Sia-T and prostate cancer cell LNCaP α2,3(O)Sia-T utilized compound **5** quite effectively (103% and 92%, respectively). Thus, in contrast to Gal 3-*O*-sulfortransferases, sialyltransferases were not affected by the C-3 fluoro substituent on the other Gal terminal of mucin core 2 structure. Compound **3** was also a good acceptor for cloned α2,3(O)Sia-T (102%) but a poor acceptor for cloned α2,3(N)Sia-T and α2,6(N)Sia-T (8% and 3%, respectively). When compound **3** was tested as an inhibitor as shown in Figure 3, α2,6(N)Sia-T activity was competitively inhibited by compound **3** (K_i 1.9 mM) whereas α2,3(N)Sia-T activity was not inhibited at all by compound **3**. Thus fluorination of acceptors resulted in entirely different effects on the ability of sulfo- and siayltransferases in utilizing these modified compounds as acceptors. In addition, C-4 fluorination of β1,4 linked Gal in mucin core 2 created a selective inhibitor, namely compound **3**, for α2,6(N)Sia-T, thus enabling a determination of α2,3(N)-Sia-T activity in the presence of α2,6(N)Sia-T activity.

In summary, fluorine-containing mucin core 2 oligosaccharide analogues **1**−**5** in which the fluorine atom located at different positions of galactose residue were synthesized in a convergent way for probing carbohydrates−enzyme interaction and carbohydrate-selection interaction.

Experimental Section

Assay of α2,3(N)Sia-T and α2,6(N)Sia-T Activity. Both α2,3-(N)Sia-T and α2,6(N)Sia-T were assayed with use of the acceptor Galβ1,4GlcNAcβ1,6(3-OMeGalβ1,3)GalNAcα-OBn.[21] For inhibition studies, an increasing concentration of compound **3** and a 2 mM concentration of the acceptor were taken in the reaction mixture (RM) run in duplicate. The inhibition constant K_i was determined by Lineweaver−Burke plot.

2,3,6-Tri-*O*-acetyl-4-deoxy-4-fluoro-α-D-galactopyranosyl Bromide (15). To a cold (ice-bath) solution of compound **6** (500 mg, 1.55 mmol) in anhydrous acetic anhydride (3.6 mL) was added dropwise anhydrous acetic anhydride (3.6 mL) containing concentrated sulfuric acid (80 μL). The reaction mixture was stirred at

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the same temperature for 2 h, quenched with sodium bicarbonate solution, and extracted with dichloromethane (3 × 20 mL). The organic phase was dried with Na_2SO_4 and concentrated to a crude residue that was passed through a column of silica gel eluted by hexane−ethyl acetate (4:1) to give pure compound **7** in quantitative yield. To a cold (ice-bath) solution of compound **14** (1.65 g, 47 mmol) in a mixture of dichloromethane (48 mL)−anhydrous acetic anhydride (1.4 mL) was added dropwise 33% HBr−HOAc (12 mL) with stirring at 0 to 25 °C for 2.5 h. The reaction mixture was quenched with saturated sodium bicarbonate solution and extracted with dichloromethane (3 × 100 mL). The organic phase was washed with saturated $NaHCO_3$ solution and brine, dried (Na_2SO_4), and concentrated to a crude residue that was passed through a short column of silica gel eluted with hexane−ethyl acetate (4:1) to give pure compound **15** (1.0 g) as a syrup: R_f 0.80 (hexane/ethyl acetate 2:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.60 (d, 1 H, J = 2.3 Hz, H-1), 5.50 (m, 1 H), 5.12−4.96 (m, 2 H, H-3), 4.43 (dd, 1 H), 4.23 (dd, 1 H), 4.15 (dd, 1 H), 2.14 (s, 6 H, Ac), 2.07 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.5 (C═O), 170.2 (C═O), 169.7 (C═O), 88.7 (C-1), 86.2 (d, $^1J_{C-F}$ = 192.6 Hz, C-4), 71.5 (d, $^3J_{C-F}$ = 5.4 Hz), 68.9 (d, $^2J_{C-F}$ = 20.1 Hz), 67.1 (d, $^2J_{C-F}$ = 17.3 Hz), 61.0, 20.87 (Ac), 20.78 (Ac), 20.70 (Ac); ^{19}F NMR ($CDCl_3$, 323.6 MHz) δ −172.00 ppm.

Benzyl(2,3,6-tri-*O*-acetyl-4-deoxy-4-fluoro-β-D-galactopyranosyl)-2-deoxy-2-acetamido-D-α-galactopyranoside (16). A mixture of compound **7**[19f] (684 mg, 1.71 mmol) and powdered $Hg(CN)_2$ in benzene/nitromethane (1:1, 100 mL) was heated until 50 mL of solvent had been distilled off. The temperature was then adjusted to 70 to 80 °C. Bromide donor **15** (951 mg, 2.57 mmol) was added and the stirring was continued for 12 h at the same temperature. The mixture was then diluted with benzene and washed with saturated $NaHCO_3$ aqueous solution, 10% KI, and water, and dried (Na_2SO_4), and concentrated. The crude residue was taken up in 60% aqueous acetic acid and stirred for 1.5 h at 60−65 °C. The solution was then concentrated under reduced pressure to a crude residue that was applied to a column of silica gel and eluted with dichloromethane−methanol (60:1) to give pure compound **16** (286 mg, 28%) as an amorphous solid: ^{1}H NMR (CD_3OD, 400 MHz) δ 7.38−7.35 (m, 5 H, ArH), 5.53 (t, 1 H), 5.20−5.16 (m, 2 H), 4.95 (d, 1 H, J = 3.4 Hz), 4.73 (d, 1 H, J_{gem} = 12.4 Hz, $PhCH_AO$, ABq), 4.68 (dd, 1 H, J = 3.4 Hz, J = 9.4 Hz), 4.67 (d, 1 H, $J_{1,2}$ = 8.7 Hz), 4.56−4.53 (m, 1 H), 4.46 (d, 1 H, J_{gem} = 11.4 Hz, $PhCH_BO$, ABq), 4.18−4.08 (m, 2 H), 3.90−3.78 (m, 3 H), 3.58−3.37 (m, 2 H), 2.16 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 1.95 (s, 3 H, Ac); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 170.9 (C═O), 170.6 (C═O), 170.3 (C═O), 164.1 (C═O), 137.0, 128.6, 128.5, 128.3, 101.0, 97.3, 88.5 (d, $^1J_{C-F}$ = 193.8 Hz, C^B-4), 77.5, 76.9, 70.4, 70.1, 70.0, 69.9, 69.8, 69.1, 67.3, 67.1, 61.9, 61.4, 48.0, 22.8 (NAc), 20.5 (2Ac), 20.4 (Ac). Anal. Calcd for $C_{27}H_{36}O_{12}NF\cdot H_2O$: C, 53.72; H, 6.34; F, 3.15. Found: C, 54.00; H, 6.10; F, 3.21.

Benzyl[(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopranosyl)]-(1→6)-[(2,3,6-tri-*O*-acetyl-4-deoxy-4-fluoro-β-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (17). A solution of compound **16** (80 mg, 0.133 mmol), compound **8** (74 mg, 0.140 mmol), and NIS (40 mg, 0.178 mmol) in dry dichloromethane (6 mL) containing 4 Å MS (2.0 g) was stirred for 1.5 h at −65°C. TfOH (27 uL) in dry dichloromethane (0.5 mL) was added and the solution was stirred for 1 h at the same temperature under N_2 atmosphere. The reaction was quenched with saturated sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with saturated 10% $Na_2S_2O_3$, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with dichloromethane/methanol (80:1) to give pure compound **17** (65 mg, 48%) as an amorphous solid: R_f 0.38 (CH_2Cl_2/MeOH 30:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.72−7.56 (m, 4 H, ArH), 7.36−7.29 (m, 5 H, ArH), 5.86−5.81 (m, 1 H), 5.49 (t, 1 H), 5.43 (d, 1 H), 5.49−5.31 (m, 1 H), 5.24−5.17 (m, 2 H), 4.60−4.53 (m, 3 H), 4.50−4.30 (m, 5 H), 4.28−4.17 (m, 3 H), 4.10−4.00 (m, 3 H), 4.00−3.70 (m, 5 H), 2.16 (s, 3 H, Ac), 2.15 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.05 (s, 3 H, Ac), 1.88 (s, 3 H, Ac), 1.86 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.5 (C═O), 170.2 (C═O), 169.7 (C═O), 169.5 (C═O), 168.2 (C═O), 134.4, 134.3, 128.8, 128.7, 128.7, 128.5, 128.4, 101.1 ($^3J_{C-F}$ = 10.9 Hz), 99.0, 97.2, 88.6 ($^1J_{C-F}$ = 194.0 Hz), 78.2, 72.2, 70.8, 70.7, 70.5, 70.4, 69.4, 69.2, 68.7, 66.8, 62.2, 61.6, 61.5, 54.9, 47.9, 23.5 (NAc), 21.0 (Ac), 20.9 (Ac), 20.86 (Ac), 20.85 (Ac), 20.64 (Ac), 20.62 (Ac). Anal. Calcd for $C_{47}H_{55}O_{21}N_2F$: C, 56.28; H, 5.53; F, 1.89. Found: C, 56.55; H, 5.73; F, 1.58.

Benzyl[(β-D-galactopyranosyl)-(1→4)-(2-deoxy-2-acetamido-β-D-glucopranosyl)]-(1→6)-[(4-deoxy-4-fluoro-β-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (1). A solution of compound **17** (57 mg, 0.056 mmol) in dry methanol (10 mL) was treated with $NH_2-NH_2\cdot H_2O$ (2 mL) at 90 °C for 6 h. The reaction mixture was concentrated to a crude residue and coevaporated with dry toluene, dried, and acetylated with anhydrous acetic anhydride and dry pyridine (1:1, 6 mL) in the presence of DMAP (5 mg) overnight at room temperature, then concentrated to a crude residue that was purified by a short column of silica gel eluted with dichloromethane−methanol (80:1) to give a pure compound (48.3 mg) that was treated with 1 M sodium methoxide−methanol solution (102 μL) in a mixture of methanol−water (2 mL, 1:1) overnight at room temperature. The reaction mixture was concentrated to a crude residue and purified by a short column of silica gel eluted with i-C_3H_9OH/HOAc/H_2O (3:1:1) to give pure compound **1** (30 mg, 75%) as an amorphous solid: R_f 0.5 (i-C_3H_9OH/HOAc/H_2O 3:1:1); ^{1}H NMR (D_2O, DQF-COSY, and ROESY, 400 MHz) δ 7.45−7.20 (m, 5 H, ArH), 4.99 (d, 1 H, $J_{1,2}$ = 3.2 Hz, H^A-1), 4.84 (dd, 1 H, J = 2.8 Hz, J_{H-F} = 78 Hz, H^B-4), 4.72 (d, 1 H, J_{gem} = 12.4 Hz, $PhCH_AO$, ABq), 4.56 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H^C-1), 4.54 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^B-1), 4.53 (d, 1 H, J_{gem} = 12.7 Hz, $PhCH_BO$, ABq), 4.36 (dd, 1 H, J = 3.2 Hz, J = 9.6 Hz, H^A-2), 4.21 (d, 1 H, J = 2.8 Hz, H^A-4), 4.15 (dd, 1 H, H^A-5), 4.07 (dd, 1 H, H^A-6b), 4.05 (dd, 1 H, J = 2.8 Hz, J = 9.6 Hz, H^A-3), 4.94 (dd, 1 H, H^C-3), 3.85−3.66 (m, 5 H, H^C-6b, H^B-2, H^B-3, H^A-6a, H^C-6a), 3.64−3.41 (m, 6 H, H^B-6b, H^B-6a, H^C-5, H^B-2, H^B-5, H^C-4), 2.31 (s, 3 H, Ac), 2.21 (s, 3 H, Ac); ^{13}C NMR (D_2O, 100.6 MHz) δ 175.7 (C═O), 175.5 (C═O), 138.1, 130.1, 130.0, 129.7, 105.6, 102.8, 97.5, 90.7 (d, $^1J_{C-F}$ = 178.3 Hz), 78.4, 77.1, 75.2, 74.7 (d, $^2J_{C-F}$ = 17.1 Hz), 72.5 (d, $^2J_{C-F}$ = 18.9 Hz), 71.8, 71.2, 70.9, 70.7, 70.1, 62.0, 61.2, 61.10, 56.8, 49.8, 23.5 (NAc), 23.2 (NAc). ESI-HRMS calcd for $C_{29}H_{43}O_{15}N_2FNa$ (m/z): [MNa^+] 701.2540, found 701.2551.

2,3,6-Tri-*O*-acetyl-4-deoxy-4-fluorogalactosyl Trichloroacetimidate (23). Compound **14** (440 mg, 1.26 mmol) was treated with hydrazine acetic acid (150 mg, 1.66 mmol) in dry DMF (4 mL) at 50 °C for 2 h. The reaction mixture was concentrated to a crude residue, which was redissolved in ethyl acetate (100 mL). The organic phase was washed with saturated sodium bicarbonate solution (3 × 100 mL), dried with Na_2SO_4, and concentrated to a crude residue that was treated with CCl_3CN (0.76 mL) and DBU (38 μL) in dry dichloromethane (5 mL) at 0−25 °C for 2 h. The reaction mixture was concentrated to a crude residue that was passed through a short column of silica gel eluted with hexanes−ethyl acetate (2:1) to provide pure compound **23** in 80% yield as a white needle solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.96 (s, 1 H, NH), 6.62 (d, 1 H, J = 3.2 Hz, H-1), 5.45−5.30 (m, 2 H), 5.04 (dd, 1 H, J = 3.2 Hz, J = 1.8 Hz, $^2J_{H-F}$ = 50.6 Hz, H-4), 4.38−4.23 (m, 3 H), 2.15 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.03 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.5 (C═O), 170.4 (C═O), 170.0 (C═O), 93.6 (C-1), 86.5 (d, $^1J_{C-F}$ = 195.6 Hz, C-4), 69.5 (d, $^2J_{C-F}$ = 18.1 Hz), 68.3 (d, $^2J_{C-F}$ = 17.4 Hz), 66.9, 61.6, 61.5, 20.9 (Ac), 20.8 (Ac), 20.6 (Ac); ^{19}F NMR ($CDCl_3$, 323.6 MHz) δ −172.00 ppm.

Phenyl(2,3,6-tri-*O*-acetyl-4-deoxy-4-fluoro-β-D-galactopyranosyl)-(1→4)-2-deoxy-6-*O*-pivaloyl-3-*O*-acetyl-2-phthalimido-1-thio-β-D-glucopyranoside (24). A solution of compound **9**[17] (178

mg, 0.367 mmol) and compound **23** (174 mg, 0.385 mmol) in dry dichloromethane (6 mL) containing 4 Å MS (2.0 g) was stirred for 1.5−2 h at −65 to −70 °C. TMSOTf (14 μL) in dry dichloromethane (0.5 mL) was added and stirred for 1 h under N_2 atmosphere. Another portion of donor **23** (174 mg) was added and the solution was stirred for another 1.5 h. The reaction was quenched with saturated sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with saturated sodium bicarbonate, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with hexanes−ethyl acetate (1.5:1) to give a disaccharide (120 mg, 41%), which was further treated with anhydrous anhydride−pyridine (1:1, 6 mL) in the presence of DMAP (4 mg) overnight at room temperature. The reaction mixture was concentrated to a crude residue, which was purified by a short column of silica gel eluted with hexanes−ethyl acetate (2:1) to give pure compound **24** (80 mg, 63%) as an amorphous solid: ^{1}H NMR ($CDCl_3$, 400 MHz, DQF-COSY, TOCSY, and ROESY) δ 7.92−7.84 (m, 2 H, ArH), 7.76−7.72 (m, 2 H, ArH), 7.44−7.36 (m, 2 H, ArH), 7.32−7.20 (m, 3 H, ArH), 5.76−5.71 (m, 2 H, $J_{1,2}$ = 10.2 Hz, H^A-3, H^A-1), 5.17 (dd, 1 H, H^B-2), 4.87 (qd, 1 H, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 2.8 Hz, $^3J_{H-F}$ = 27.6 Hz, H^B-3), 4.79 (dd, 1 H, $J_{3,4}$ = 3.3 Hz, $^2J_{H-F}$ = 50.0 Hz, H^B-4), 4.53 (dd, 1 H, J = 14.3 Hz, H^A-6b), 4.51 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H^B-1), 4.31−4.26 (m, 1 H, H^B-6b), 4.23 (t, 1 H, J = 10.1 Hz, H^A-2), 4.17−4.12 (m, 3 H, H^B-6a, H^A-6a, H^A-5), 3.87−3.68 (m, 2 H, H^A-4, H^B-5), 2.08 (s, 6 H, 2Ac), 2.06 (s, 3 H, Ac), 1.87 (s, 3 H, Ac), 1.20 (s, 9 H, *t*-Bu); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 177.9 (C═O), 174.4 (C═O), 174.3 (C═O), 170.4 (C═O), 169.9 (C═O), 169.0 (C═O), 168.9 (C═O), 134.6, 134.4, 133.4, 129.1, 128.5, 123.9, 123.7, 100.8(C^B-1), 85.5 (d, $^1J_{C-F}$ = 187.1 Hz, C^B-4), 83.2 (C^A-1), 77.2, 76.6, 71.6 (d, $^2J_{C-F}$ = 17.1 Hz), 71.1 (d, $^2J_{C-F}$ = 18.4 Hz), 69.2, 62.5, 61.2 (d, $^3J_{C-F}$ = 5.1 Hz), 54.0, 31.7, 27.4 ($3CH_3$), 23.1 (Ac), 20.8 (Ac), 20.7 (Ac), 20.6 (Ac). Anal. Calcd for $C_{39}H_{44}O_{15}NSF$: C, 57.27; H, 5.42; F, 2.32. Found: C, 57.30; H, 5.42,; F, 2.41.

Benzyl[(2,3,6-tri-*O*-acetyl-4-deoxy-4-fluoro-*β*-D-galactopyranosyl)-(1→4)-(2-deoxy-6-*O*-pivaloyl-3-*O*-acetyl-2-phthalimido-*β*-D-glucopranosyl)]-(1→6)-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (25). A solution of compound **24** (62 mg, 0.074 mmol), compound **12** (45 mg, 0.070 mmol), and NIS (50 mg, 0.222 mmol) in dry dichloromethane (5 mL) containing 4 Å MS (2.0 g) was stirred for 1.5−2 h at −65 to −70 °C. TfOH (14 μL) in dry dichloromethane (0.5 mL) was added and the solution was stirred for 1 h at the same temperature under N_2 atmosphere. The reaction was quenched with saturated sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with saturated 10% $Na_2S_2O_3$, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with hexanes−ethyl acetate (1:4) to give pure compound **25** (72 mg, 76%) as an amorphous solid: ^{1}H NMR ($CDCl_3$, 600 MHz, DQF-COSY, TOCSY, and ROESY) δ 7.88−7.84 (m, 4 H, ArH), 7.40−7.28 (m, 3 H, ArH), 7.20−6.84 (m, 2 H, ArH), 5.75−5.71 (m, 1 H, H^C-3), 5.41 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H^C-1), 5.32 (d, 1 H, J = 9.3 Hz, NHAc), 5.29 (d, 1 H, J = 3.0 Hz, H^B-4), 5.21−5.10 (m, 2 H, H^D-2, H^B-2), 4.88 (qd, 1 H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 2.6 Hz, $^3J_{H-F}$ = 28.0 Hz, H^D-3), 4.80 (dd, 1 H, J = 2.1 Hz, $^2J_{H-F}$ = 55.6 Hz, H^D-4), 4.60 (d, 1 H, J = 3.8 Hz, H^A-1), 4.43 (ddd, 1 H, H^A-2), 4.39 (d, 1 H, $J_{1,2}$ = 7.7 Hz, H^D-1), 4.32−4.27 (m, 2 H, H^A-5, H^B-1), 4.24−4.14 (m, 4 H, $PhCH_AO$, H^D-6b, H^C-2, H^D-6a), 4.08−3.90 (m, 5 H, H^B-6b, H^B-6a, H^A-5), 3.91−3.50 (m, 9 H, H^C-4, $PhCH_BO$, H^A-4, H^A-6b, H^D-5, H^A-6a, H^B-5, H^A-3), 2.13 (s, 3 H, Ac), 2.09 (s, 6 H, 2Ac), 2.08 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.96 (s, 3 H, Ac), 1.88 (s, 3 H, Ac), 1.87 (s, 3 H, Ac), 1.26 (s, 9 H, *t*-Bu); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 181.0 (C═O), 178.1 (C═O), 174.5 (C═O), 170.6 (C═O), 170.5 (C═O), 170.4 (C═O), 170.3 (C═O), 170.6 (C═), 169.5 (C═O), 169.4 (C═O), 169.1 (C═O), 167.8 (C═O), 137.0, 134.7, 134.3, 128.6, 128.8, 128.7, 128.5, 123.9, 123.5, 101.6, 100.8, 98.5, 97.2, 85.5, 78.5, 71.1, 71.0, 71.0, 70.9, 70.9, 70.8, 69,6, 69.5, 69.5, 69.2, 69.0, 68.7, 68.4, 67.0, 62.1, 61.4, 61.2, 55.3, 47.8, 27.4, 23.4 (NAc), 20.87 (2Ac), 20.83 (2Ac), 20.78 (Ac), 20.75 (Ac), 20.71 (Ac), 20.68 (Ac). Anal. Calcd for $C_{62}H_{77}O_{30}N_2F$: C, 55.18; H, 5.75; N, 2.09. Found: C, 55.31; H, 5.58; N, 2.04.

Benzyl[(4-deoxy-4-fluoro-*β*-D-galactopyranosyl)-(1→4)-(2-deoxy-2-acetamido-*β*-D-gluco-ppranosyl)]-(1→6)-[(*β*-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (3). A solution of compound **25** (82 mg, 0.06 mmol) in dry methanol (10 mL) was treated with $NH_2-NH_2{\cdot}H_2O$ (2 mL) at 90 °C for 6 h. The reaction mixture was concentrated to a crude residue and coevaporated with dry toluene, dried, and acetylated with anhydrous acetic anhydride−dry pyridine (1:1, 6 mL) in the presence of DMAP (5 mg) overnight at room temperature, then it was concentrated to a crude residue, which was purified by a short column of silica gel eluted with dichloromethane−methanol (80:1) to give a pure compound that was treated with 1 M sodium methoxide−methanol solution in a mixture of methanol−water (2 mL, 1:1) overnight at room temperature. The reaction mixture was then concentrated to a crude residue, which was purified by a short column of silica gel eluted with *i*-C_3H_9OH/HOAc/H_2O (3:1:1) to give pure compound **3** (20 mg, 39%) as an amorphous solid: ^{1}H NMR (D_2O, DQF-COSY, TOCSY, and ROESY, 400 MHz) δ 7.50−7.00 (m, 5 H, ArH), 5.00 (d, 1 H, $J_{1,2}$ = 3.2 Hz, H^A-1), 4.87 (dd, 1 H, J = 2.8 Hz, $^2J_{H-F}$ = 52.0 Hz, H^D-4), 4.73 (d, 1 H, J_{gem} = 12.3 Hz, $PhCH_AO$, ABq), 4.59 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^D-1), 4.58 (d, 1 H, $J_{1,2}$ = 8.0 Hz, H^C-1), 4.53 (d, 1 H, J_{gem} = 12.4 Hz, $PhCH_BO$, ABq), 4.46 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H^B-1), 4.34 (dd, 1 H, H^A-2), 4.25 (d, 1 H, J = 2.8 Hz, H^A-4), 4.16 (dd, 1 H, H^A-5), 4.10 (dd, 1 H, H^A-6b), 4.08 (dd, 1 H, H^A-3), 4.02 (dd, 1 H), 3.92−3.80 (m, 6 H, H^C-4), 3.81 (dd, 1 H, H^D-3), 3.80−3.50 (m, 10 H, H^D-2, H^A-6a, H^C-3, H^D-2, H^C-2), 2.31 (s, 3 H, Ac), 2.29 (s, 3 H, Ac); ^{13}C NMR (D_2O, 100.6 MHz) δ 175.8 (C═O), 175.6 (C═O), 129.6, 129.4, 129.3, 105.9, 104.1, 102.8, 97.8, 79.8 (d, $^1J_{C-F}$ = 178.5 Hz), 76.1 (d, $^2J_{C-F}$= 50.6 Hz), 73.9, 72.1 (d, $^2J_{C-F}$ = 50.9 Hz), 71.5, 71.2, 70.2, 70.0, 62.2, 61.2, 56.2, 49.9, 23.5 (NAc), 23.2 (NAc); ^{19}F NMR ($CDCl_3$, 376.4 MHz) δ −172.95 ppm; ESI-HRMS calcd for $C_{35}H_{53}O_{20}N_2FNa$ (*m*/*z*) [MNa^+] 863.3068, found 863.3035.

1,2:5,6-Diisopropyl-3-deoxy-3-fluoro-α-D-galactose (10). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.92 (d, 1 H, J = 4.0 Hz, H-1), 4.80 (dd, 1 H, J = 4.3 Hz, J = 3.3 Hz, J_{H-F} = 67.7 Hz, H-3), 4.75 (d, 1 H, J = 3.2 Hz, H-4), 4.34 (dd, 1 H, J = 6.8 Hz, J = 7.3 Hz), 4.15−4.06 (m, 2 H), 3.83 (dd, 1 H), 1.55 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 114.0 (d, ketal carbon), 110.3 (d, $^4J_{C-F}$ = 2.8 Hz, ketal carbon), 105.2 (d, $^3J_{C-F}$ = 2.1 Hz, C-1), 94.4 (d, $^1J_{C-F}$ = 181.7 Hz, C-3), 85.1−84.6 (m, 2C), 75.2−75.1 (m, 1C), 65.8, 27.3 (CH_3), 26.7 (CH_3), 26.6 (CH_3), 25.4 (CH_3); ESI-HRMS calcd for $C_{12}H_{19}O_5FNa$ (*m*/*z*) [MNa^+] 285.1109, found 285.1110.

2,4,6-Tri-*O*-acetyl-3-deoxy-3-fluoro-α-D-galactopyranosyl Bromide (19). Compound **19** (yield 71%) was prepared from compound **18** according to the procedure for the preparation of compound **15**. R_f 0.36 (hexane/ethyl acetate 4:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.68 (t, 1 H, H-1), 5.68 (m, 1 H), 5.12−4.96 (m, 2 H, H-3), 4.43 (t, 1 H), 4.22 (dd, 1H), 4.10 (dd, 1 H), 2.16 (s, 6 H, Ac), 2.07 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.4 (C═O), 170.1 (C═O), 169.7 (C═O), 87.7 (d, $^3J_{C-F}$ = 8.0 Hz, C-1), 86.2 (d, $^1J_{C-F}$ = 192.6 Hz, C-3), 71.4 (d, $^3J_{C-F}$ = 5.4 Hz, H-4), 68.9 (d, $^2J_{C-F}$ = 20.1 Hz), 67.1 (d, $^2J_{C-F}$ = 17.3 Hz), 61.0, 20.9 (Ac), 20.8 (Ac), 20.7 (Ac); ^{19}F NMR ($CDCl_3$, 323.6 MHz) δ −172.00 ppm

Benzyl(2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-*β*-D-galactopyranosyl)-2-deoxy-2-acetamido-D-α-galactopyranoside (20). Compound **20** was prepared according to the procedure for the preparation of compound **16** with a yield of 47% over two steps. R_f 0.32 (dichloromethane-methanol: 20:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.35 (m, 5 H, ArH), 5.53 (t, 1 H), 5.20−5.16 (m, 2 H), 4.95 (d, 1 H, J = 3.4 Hz), 4.73 (d, 1 H, J_{gem} = 12.4 Hz, $PhCH_AO$, ABq), 4.68 (dd, 1 H, J = 3.4 Hz, J = 9.4 Hz), 4.67 (d, 1 H, $J_{1,2}$ = 8.7 Hz), 4.56−4.53 (m, 1 H), 4.46 (d, 1 H, J_{gem} = 11.4 Hz,

$PhCH_BO$, ABq), 4.18−4.08 (m, 3 H), 3.90−3.78 (m, 5 H), 3.58−3.37 (m, 2 H), 2.16 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 1.95 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$ + CD_3OD, 100.6 MHz) δ 170.9 (C═O), 170.7 (C═O), 170.3 (C═O), 164.2 (C═O), 137.0, 128.6, 128.5, 128.3, 101.0 (d, $^3J_{C-F}$ = 11.6 Hz, C^B-1), 97.4 (C^A-1), 88.5 (d, $^1J_{C-F}$ = 193.8 Hz, C^B-3), 77.5, 76.9, 70.4, 70.0, 69.9, 69.9, 69.1, 67.2, 67.1, 61.9, 48.1, 22.8 (NAc), 20.6 (NAc), 20.5 (NAc). Anal. Calcd for $C_{27}H_{36}O_{12}NF\cdot H_2O$: C, 53.72; H, 6.34; N, 2.33. Found: C, 53.43; H, 5.89; N, 2.12.

Benzyl[(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopranosyl)]-(1→6)-[(2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-*β*-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (21). A solution of compound **20** (50 mg, 0.073 mmol), compound **8** (45 mg, 0.085 mmol), and NIS (58 mg, 0.256 mmol) in dry dichloromethane (10 mL) containing 4 Å MS (1.5 g) was stirred for 1.0 h at −65 °C. TfOH (16 μL) in dry dichloromethane (0.5 mL) was added and the solution was stirred for 1 h at the same temperature under N_2 atmosphere. The reaction was quenched with saturated sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with saturated 10% $Na_2S_2O_3$, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with dichloromethane−methanol (100:1) to give pure compound **21** (32 mg, 40%) as an amorphous solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.72−7.56 (m, 4 H, ArH), 7.36−7.29 (m, 3 H, ArH), 7.20−7.12 (m, 2 H, ArH), 5.83 (m, 1 H, H^C-3), 5.48 (dd, 1 H, H^B-4), 5.43 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H^C-1), 5.36 (m, 1 H), 5.31 (d, 1 H, J = 7.6 Hz, H^B-1), 5.24−5.17 (m, 2 H, NHAc, H^C-4), 4.54 (d, 1 H, J = 3.2 Hz, H^A-1), 4.51 (dq, 1 H, H^B-3), 4.50−4.30 (m, 2 H, H^B-2, H^A-2), 4.28−4.17 (m, 4 H, H^C-6b, H^C-2, $PhCH_AO$, H^C-6a), 4.10−4.00 (m, 2 H, H^A-5), 4.00−3.70 (m, 5 H, H^A-4, H^C-5, H^A-6b, H^A-6a,), 3.60 (dd, 1 H, H^A-3), 3.59 (m, 1 H), 2.16 (s, 3 H, Ac), 2.15 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.05 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 1.88 (s, 3 H, Ac), 1.85 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.5 (C═O), 170.3 (C═O), 169.8 (C═O), 169.5 (C═O), 168.2 (C═O), 134.5, 134.4, 128.8, 128.8, 128.7, 128.6, 128.5, 101.1 ($^3J_{C-F}$ = 10.9 Hz), 99.0, 97.2, 88.7 ($^1J_{C-F}$ = 194.9 Hz), 78.2, 72.2, 70.9, 70.7, 70.5, 70.4, 69.4, 69.3, 68.8, 66.8, 62.3, 61.6, 61.6, 54.9, 47.9, 23.5 (NAc), 21.0 (Ac), 20.9 (Ac), 20.86 (Ac), 20.83 (Ac), 20.65 (Ac), 20.62 (Ac). Anal. Calcd for $C_{47}H_{55}O_{21}N_2F\cdot 2H_2O$: C, 54.32; H, 5.72. Found: C, 54.74; H, 5.73.

Benzyl[(2-deoxy-2-acetadimido-*β*-D-glucopranosyl)]-(1→6)-(3-deoxy-3-fluoro-*β*-D-galactopyranosyl)-2-deoxy-2-acetamido-D-α-galactopyranoside (2). Compound **2** was obtained from compound **21** according to the procedure described for compound **17** in 75% yield. ^{1}H NMR (D_2O, DQF-COSY and ROESY, 400 MHz) δ 7.60−7.20 (m, 5 H, ArH), 4.98 (d, 1 H, J = 3.4 Hz, H^A-1), 4.76 (d, 1 H, J_{gem} = 12.6 Hz, $PhCH_AO$, ABq), 4.55 (d, 1 H, J = 8.4 Hz, H^C-1), 4.54 (dq, 1 H, H^B-3), 4.51 (d, 1 H, J_{gem} = 12.3 Hz, $PhCH_BO$, ABq), 4.48 (d, 1 H, J = 7.6 Hz, H^B-1), 4.33 (dd, 1 H, H^A-2), 4.23 (d, 1 H, J = 2.8 Hz, H^A-4), 4.20 (dd, 1 H, H^B-4), 4.15 (dd, 1 H, H^A-5), 4.07 (dd, 1 H, H^A-6b), 4.03 (dd, 1 H, H^A-3), 3.94 (dd, 1 H, H^C-3), 3.86−3.60 (m, 7 H, H^B-2, H^C-6b, H^C-2, H^A-6a, H^B-5, H^B-6b, H^B-6a), 3.60−3.40 (m, 3 H, H^C-5, H^C-6a, H^C-4), 1.96 (s, 3 H, Ac), 1.93 (s, 3 H, Ac); ^{13}C NMR (CD_3COOD, 100.6 MHz) δ 175.3 (C═O), 175.1 (C═O), 138.1, 129.9, 129.9, 129.6, 105.0 ($^3J_{C-F}$ = 12.2 Hz), 102.7, 97.5, 94.0 ($^1J_{C-F}$ = 183.9 Hz), 80.6, 78.4, 77.1, 75.1, 74.9, 71.2, 70.8, 70.7, 70.6, 70.5, 70.4, 69.9, 67.9, 61.9, 61.8, 56.8, 49.7, 23.5 (NAc), 23.1 (NAc); ^{19}F NMR ($CDCl_3$, 376.4 MHz) δ −175.4 ppm; ESI-HRMS calcd for $C_{29}H_{43}O_{15}N_2FNa$ (*m*/*z*) [MNa^+] 701.2540, found 701.2543.

Benzyl[(3,4,6-tri-*O*-acetyl-D-*β*-galactosyl)-(1→4)-2-deoxy-2-phthalimido-*β*-D-glucopranosyl)]-(1→6)-[(2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-*β*-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (27). A solution of compound **20** (124 mg, 0.183 mmol), compound **13** (148 mg, 0.192 mmol), and NIS (130 mg, 0.57 mmol) in dry dichloromethane (5−6 mL) containing 4 Å MS (3.0 g) was stirred for 1.5 h at −65 °C then TfOH (37 μL) in dry dichloromethane (0.5 mL) was added and the solution was stirred for 1 h at the same temperature under N_2 atmosphere. The reaction was quenched with saturated sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with saturated 10% $Na_2S_2O_3$, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with dichloromethane−methanol (60:1) to give pure compound **27** (64 mg, 26%) as an amorphous solid: R_f 0.15 (CH_2Cl_2/MeOH 40:1) ^{1}H NMR ($CDCl_3$, 600 MHz, DQF-COSY, TOCSY, and ROESY) δ 7.88−7.28 (m, 4 H, ArH), 7.20−6.84 (m, 5 H, ArH), 5.75−5.72 (m, 1 H), 5.41 (d, 1 H), 5.32 (d, 1 H, J = 9.3 Hz, NHAc), 5.29 (d, 1 H, J = 3.0 Hz), 5.21−5.08 (m, 2 H), 4.88 (qd, 1 H), 4.80 (dd, 1 H), 4.61 (d, 1 H, J = 3.8 Hz, H^A-1), 4.45 (ddd, 1 H, H^A-2), 4.40 (d, 1 H, $J_{1,2}$ = 7.7 Hz, H^D-1), 4.32−4.25 (m, 2 H), 4.24−4.14 (m, 4 H), 4.09−3.90 (m, 5 H), 3.91−3.51 (m, 9 H), 2.13 (s, 3 H, Ac), 2.09 (s, 6 H, 2Ac), 2.08 (s, 6 H, 2Ac), 2.04 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.95 (s, 3 H, Ac), 1.89 (s, 3 H, Ac), 1.88 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 181.0 (C═O), 178.1 (C═O), 174.5 (C═O), 170.6 (C═O), 170.45 (C═O), 170.41 (C═O), 170.38 (C═O), 170.6 (C═), 169.5 (C═O), 169.4 (C═O), 169.1 (C═O), 137.0, 134.7, 134.3, 128.7, 128.8, 128.7, 128.5, 123.9, 123.5, 101.6, 100.8, 98.5, 97.3, 85.6, 78.5, 71.1, 71.08, 71.03, 70.93, 70.90, 70.8, 69,6, 69.54, 69.51, 69.2, 69.0, 68.7, 68.4, 67.0, 62.2, 61.4, 61.3, 61.2, 55.3, 47.8, 23.4 (NAc), 20.88 (Ac), 20.84 (Ac), 20.79 (Ac), 20.76 (Ac), 20.72 (Ac), 20.69 (Ac). Anal. Calcd for $C_{59}H_{71}O_{30}N_2F$: C, 54.19; H, 5.47; F, 1.45. Found: C, 54.25; H, 5.38; F, 1.31.

Benzyl[(*β*-D-galactopyranosyl)-(1→4)-(2-deoxy-2-acetamido-*β*-D-glucopranosyl)]-(1→6)-[(3-deoxy-3-fluoro-*β*-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (4). Compound **4** (28 mg, 80**%**) was obtained from compound **27** according to procedure described for compound **17**. R_f 0.5 (*i*-C_3H_9OH/HOAc/H_2O 3:1:1); ^{1}H NMR (D_2O, DQF-COSY and ROESY, 400 MHz) δ 7.50−7.20 (m, 5 H, ArH), 4.99 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H^A-1), 4.72 (d, 1 H, J_{gem} = 12.6 Hz, $PhCH_AO$, ABq), 4.61 (dq, 1 H, H^B-3), 4.58 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^B-1), 4.53 (d, 1 H, J_{gem} = 12.4 Hz, $PhCH_BO$, ABq), 4.49 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H^C-1), 4.48 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^D-1), 4.35 (dd, 1 H, H^A-2), 4.23 (d, 1 H, J = 2.8 Hz, H^A-4), 4.20 (dd, 1 H, H^B-4), 4.15 (dd, 1 H, H^A-5), 4.07 (dd, 1 H, H^A-6b), 4.04 (dd, 1 H, H^A-3), 4.01 (dd, 1 H), 3.94 (d, 1 H, J = 2.7 Hz, H^D-4), 3.90−3.50 (m, 15 H, H^B-2, H^D-2), 2.31 (s, 3 H, Ac), 2.21 (s, 3 H, Ac); ^{13}C NMR (D_2O, 100.6 MHz) δ 175.7 (C═O), 175.5 (C═O), 138.2, 130.1, 129.9, 129.7, 105.1 (d, $^3J_{C-F}$ = 11.3 Hz), 104.2, 102.7, 97.6, 94.1 (d, $^1J_{C-F}$ = 183.4 Hz), 79.9, 78.5, 76.6, 76.1, 75.0, 74.9, 73.9, 73.8, 72.3, 70.9, 70.8, 70.7, 70.6 (d, $^2J_{C-F}$ = 18.6 Hz), 69.9 (d, $^2J_{C-F}$ = 20.4 Hz), 62.3, 61.9, 61.8, 61.4, 56.4, 49.8, 23.5 (NAc), 23.2 (NAc); ESI-HRMS calcd for $C_{35}H_{53}O_{20}N_2FNa$ (*m*/*z*) [MNa^+] 863.3068, found 863.3037.

2,4,6-Tri-*O*-acetyl-3-deoxy-3-fluorogalactosyl Trichloroacetimidate (29). A solution of compound **18** (2.34 g, 6.94 mmol) in DMF (8 mL) was treated with hydrazine acetic acid (922 mg) at 50 °C for 2 h. The reaction mixture was concentrated to a crude residue, which was redissolved in ethyl acetate (100 mL) and washed with saturated sodium bicarbonate solution (3 × 100 mL) and the organic phase was dried with Na_2SO_4 and concentrated to a crude residue that was treated with CCl_3CN (2 mL) and DBU (200 μL) in dry dichloromethane (10 mL) at 0−25 °C for 2 h. The reaction mixture was concentrated to a crude residue, which was passed through a short column of silica gel eluted with hexanes−ethyl acetate (2:1) to provide pure compound **29** (984 mg) in 32% as an amorphous solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.95 (s, 1 H, NH), 6.70 (d, 1 H, J = 3.1 Hz, H-1), 5.45−5.30 (m, 2 H), 5.04 (m, 1 H), 4.38−4.23 (m, 3 H), 2.15 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.03 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.5 (C═O), 170.4 (C═O), 170.1 (C═O), 93.6 (C-1), 86.4 (d, $^1J_{C-F}$ = 195.6 Hz, C-3), 69.5 (d, $^2J_{C-F}$ = 18.2 Hz), 68.3 (d, $^2J_{C-F}$ = 17.8 Hz), 66.9, 61.6, 61.5, 20.9 (Ac), 20.8 (Ac), 20.6 (Ac); ^{19}F NMR ($CDCl_3$, 323.6 MHz) δ −172.15 ppm.

Phenyl(2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-*β*-D-galactopyranosyl)-(1→4)-2-deoxy-6-*O*-naphthylmethyl (NAP)-3-*O*-acetyl-2-

phthalimido-1-thio-β-D-glucopyranoside (30). A solution of compound **11**[19f] (368 mg, 0.77 mmol) and compound **29** (354 mg, 0.808 mmol) in dry dichloromethane (10 mL) containing 4 Å MS (4.0 g) was stirred for 1.5−2 h at −45 °C. TMSOTf (38 μL) in dry dichloromethane (0.5 mL) was added and the solution was stirred for 1 h under N_2 atmosphere. The reaction was quenched with sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with sodium bicarbonate, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with hexanes−ethyl acetate (2:1) to give a disaccharide (275 mg, 43%), which was further treated with anhydrous anhydride−pyridine (1:1, 6 mL) in the presence of DMAP (5 mg) overnight at room temperature. The reaction mixture was concentrated to a crude residue that was purified by a short column of silica gel eluted with hexanes−ethyl acetate (2:1) to give pure compound **30** (210 mg, 76%) as an amorphous solid: R_f 0.16 (hexane/ethyl acetate 2:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.92−7.80 (m, 9 H, ArH), 7.60−7.40 (m, 5 H, ArH), 7.28−7.20 (m, 2 H, ArH), 5.74−5.68 (m, 2 H), 5.29−5.28 (m, 1 H), 5.04−4.99 (m, 1 H), 4.95 (d, 1 H, J_{gem} = 13.1 Hz, $ArCH_AO$, ABq), 4.66 (d, 1 H, J_{gem} = 13.0 Hz, $ArCH_BO$, ABq), 4.35−4.29 (m, 2 H), 4.13−3.94 (m, 4 H), 3.86−3.85 (m, 2 H), 3.70 (dt, 1 H), 3.47−3.44 (m, 1 H), 2.08 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 1.99 (s, 3 H, Ac), 1.84 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.5 (C═O), 170.1 (C═O), 170.1 (C═O), 168.8 (C═O), 135.5, 134.6, 134.4, 133.2, 129.1, 128.5, 128.4, 128.02, 127.9, 127.2, 126.7, 126.5, 126.3, 123.9, 123.7, 99.9 (d, $^3J_{C-F}$ = 10.7 Hz, C^B-1), 88.9 (d, $^1J_{C-F}$ = 193.9 Hz, C^B-3), 88.5 (C^A −1), 79.1, 75.5, 73.9, 72.1, 70.5, 70.2 (d, $^2J_{C-F}$ = 19.4 Hz), 67.5, 66.7 (d, $^2J_{C-F}$ = 16.7 Hz), 61.0, 54.2, 20.9 (Ac), 20.8 (Ac), 20.7 (Ac), 20.7 (Ac). Anal. Calcd for $C_{45}H_{44}O_{14}NFS$: C, 61.84; H, 5.07; F, 2.17. Found: C, 61.77; H, 5.12; F, 1.95.

Benzyl[(2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-β-D-galactopyranosyl)-(1→4)-(2-deoxy-6-*O*-naphthylmethyl-3-*O*-acetyl-2-phthalimido-β-D-glucopranosyl)]-(1→6)-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (31). A solution of compound **12**[17] (150 mg, 0.234 mmol), compound **30** (216 mg, 0.246 mmol), and NIS (166 mg, 0.738 mmol) in dry dichloromethane (6 mL) containing 4 Å MS (3.0 g) was stirred for 1.5−2 h at −65 °C. TfOH (47 μL) in dry dichloromethane (0.5 mL) was added and the solution was stirred for 1 h at the same temperature under N_2 atmosphere. The reaction was quenched with saturated sodium bicarbonate solution. The solids were filtered off and the organic layer was washed with saturated 10% $Na_2S_2O_3$, dried with Na_2SO_4, and concentrated. The crude residue was passed through a short column of silica gel eluted with dichloromethane−methanol (60:1) to give pure compound **31** (170 mg, 52%) as an amorphous solid: R_f 0.47 (CH_2Cl_2/MeOH 30:1); ^{1}H NMR ($CDCl_3$, DQF-COSY, TOCSY, and ROESY, 600 MHz) δ 7.80−7.48 (m, 11 H, ArH), 7.36−7.28 (m, 3H, ArH), 7.20−7.12 (m, 2 H, ArH), 5.71−5.65 (m, 1 H, H^C-3), 5.41 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H^C-1), 5.37 (d, 1 H, J = 10.4 Hz, NHAc), 5.29 (d, 1 H, J = 2.8 Hz, H^B-4), 5.20−4.87 (m, 5 H, H^D-3, H^B-2, $PhCH_AO$, H^D-2, H^B-3), 4.62 (d, 1 H, J_{gem} = 12.3 Hz, $PhCH_BO$, ABq), 4.59 (d, 1 H, $J_{1,2}$ = 2.1 Hz, H^A-1), 4.45 (ddd, 1 H, H^A-2), 4.39 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^B-1), 4.34−4.24 (m, 3 H, H^C-2), 4.18 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^D-1), 4.12−3.52 (m, 16 H), 3.36 (t, 1 H), 2.12 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 1.96 (s, 3 H, Ac), 1.88 (s, 3 H, Ac), 1.83 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.5 (C═O), 170.4 (C═O), 170.2 (C═O), 170.1 (C═O), 169.6 (C═O), 168.9 (C═O), 137.1, 134.6, 134.3, 128.9, 128.8, 128.7, 128.6, 128.1, 128.0, 126.9, 126.8, 126.6, 102.5, 99.9 (d, $^3J_{C-F}$ = 10.3 Hz), 98.8, 97.3, 88.9 (d, $^1J_{C-F}$ = 193.4 Hz), 75.3, 75.7, 74.7, 74.1, 71.2, 71.1, 70.9, 69.9, 69.8, 69.6, 69.1, 68.8, 68.6, 67.4, 67.1, 61.6, 61.2, 55.9, 47.9, 23.6 (NAc), 20.99 (Ac), 20.96 (Ac), 20.91 (Ac), 20.87 (Ac), 20.82 (Ac), 20.80 (Ac). Anal. Calcd for $C_{68}H_{77}O_{28}N_2F$: C, 58.78; H, 5.59; F, 1.37. Found: C, 57.37; H, 5.41; F 1.40.

Benzyl[(2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-β-D-galactopyranosyl)-(1→4)-(2-deoxy-6-*O*-naphthylmethyl-3-*O*-acetyl-2-acetadimido-β-D-glucopranosyl)]-(1→6)-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)]-2-deoxy-2-acetamido-D-α-galactopyranoside (32). A solution of compound **31** (141 mg, 0.10 mmol) in dry methanol (10 mL) was treated with $NH_2-NH_2\cdot H_2O$ (2 mL) at 85−90 °C for 6 h. The reaction mixture was concentrated to a crude residue and coevaporated with dry toluene, dried, and acetylated with anhydrous acetic anhydride and dry pyridine (1:1, 8 mL) in the presence of DMAP (5 mg) overnight at room temperature, then concentrated to a crude residue, which was purified by a short column of silica gel eluted with dichloromethane−methanol (80:1) to give pure compound **32** (103 mg, 93%) as an amorphous solid: R_f 0.16 (CH_2Cl_2/MeOH 30:1); ^{1}H NMR ($CDCl_3$, DQF-COSY, and ROESY, 400 MHz) δ 7.88−7.81 (m, 4 H, ArH), 7.54−7.48 (m, 3 H, ArH), 7.37−7.31 (m, 5 H, ArH), 5.64 (d, 1 H, J = 9.9 Hz, NHAc), 5.61 (d, 1 H, J = 9.5 Hz, NHAc), 5.33 (d, 2 H, J = 3.4 Hz, H^B-4, H^A-4), 5.23 (dd, 1 H, H^D-4), 5.09 (dd, 1 H, J = 7.7 Hz, J = 8.5 Hz, H^B-2), 5.04−4.90 (m, 4 H, H^C-3, H^A-1, H^D-2, H^B-3), 4.71 (d, 1 H, J_{gem} = 11.4 Hz, $PhCH_AO$, ABq), 4.58 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^D-1), 4.54 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H^B-1), 4.54 (dd, 1 H, H^A-2), 4.43 (d, 1 H, J = 8.4 Hz, H^C-1), 4.39 (d, 1 H, J_{gem} = 11.0 Hz, $PhCH_BO$, ABq), 4.20−3.76 (m, 14 H, H^C-2, H^A-3, H^D-3), 3.50−3.38 (m, 4 H, H^C-5, H^D-5), 2.11 (s, 6 H, 2Ac), 2.09 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 1.97 (s, 3 H, Ac), 1.95 (s, 6 H, 2Ac), 1.86 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.1 (C═O), 170.6 (C═O), 170.5 (C═O), 170.4 (C═O), 170.3 (C═O), 170.2 (C═O), 170.1 (C═O), 170.0 (C═O), 169.9 (C═O), 169.8 (C═O), 169.1 (C═O), 137.1, 135.5, 133.4, 133.3, 130.2, 129.6, 129.3, 128.9, 128.8, 128.7, 128.6, 128.5, 128.0, 127.9, 127.4, 126.8, 126.6, 126.5, 101.7, 100.92, 99.8 (d, $^3J_{C-F}$ = 11.4 Hz), 97.1, 88.7 (d, $^1J_{C-F}$ = 195.0 Hz), 74.8, 74.7, 73.9, 73.4, 72.8, 71.1, 70.9, 69.9, 69.8, 69.2, 68.9, 68.9, 67.4, 67.0, 66.8, 66.7, 61.4, 61.2, 61.1, 53.8, 49.1, 23.5 (NAc), 23.5 (NAc), 21.0 (Ac), 20.87 (Ac), 20.86 (Ac), 20.81(Ac), 20.78 (Ac), 20.74 (Ac). Anal. Calcd for $C_{62}H_{77}O_{27}N_2F$: C, 57.22; H, 5.96; F, 1.46. Found: C, 56.90; H, 5.85; F, 1.30.

Benzyl[(3-deoxy-3-fluoro-β-D-galactopyranosyl)-(1→4)-2-deoxy-2-acetadimido-β-D-glucopranosyl)]-(1→6)-(β-D-galactopyranosyl)-2-deoxy-2-acetamido-D-α-galactopyranoside (5). To a solution of compound **32** (78 mg, 0.06 mmol) in a mixture of dichloromethane−methanol (10 mL, 4:1) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (87 mg, 0.38 mmol), and the reaction mixture was concentrated and taken up in dichloromethane (10 mL), which was washed with saturated $NaHCO_3$ (2 × 10 mL), dried (Na_2SO_4), and concentrated. The crude residue was applied to a column of silica gel eluted with hexanes/ethyl acetate (2:1) to give a pure compound that was treated with 1 M sodium methoxide−methanol solution (20 μL) in a mixture of methanol−water (0.5 mL, 1:1) overnight at room temperature. The reaction mixture was concentrated to a crude residue and purified by a short column of silica gel eluted with *i*-C_3H_9OH/HOAc/H_2O (3:1:1) to give pure compound **5** (38 mg, 75%) as an amorphous solid: R_f 0.5 (*i*-C_3H_9OH/HOAc/H_2O 3:1:1); ^{1}H NMR (D_2O, DQF-COSY and ROESY, 400 MHz) δ 7.50−7.20 (m, 5 H, ArH), 4.99 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H^A-1), 4.73 (d, 1 H, J_{gem} =12.6 Hz, $PhCH_AO$, ABq), 4.61 (dq, 1 H, J = 2.8 Hz, J = 9.6 Hz, $^2J_{H-F}$ =68.0 Hz, H^D-3), 4.58 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^D-1), 4.55 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H^C-1), 4.52 (d, 1 H, J_{gem} = 12.5 Hz, $PhCH_BO$), 4.46 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H^B-1), 4.33 (dd, 1 H, H^A-2), 4.24 (d, 1 H, J = 2.8 Hz, H^A-4), 4.03 (d, 1 H, J = 3.2 Hz, H^D-4), 4.16 (m, 1 H, H^A-5), 4.07 (dd, 1 H, H^A-6b), 4.04 (dd, 1 H, H^A-3), 4.00 (dd, 1 H, H^C-3), 3.91 (d, 1 H, J = 2.8 Hz, H^B-4), 3.91−3.72 (m, 9 H), 3.64 (m, 2 H, H^C-5, H^B-3), 3.52 (dd, 1 H, H^B-2), 2.31 (s, 3 H, Ac), 2.28 (s, 3 H, Ac); ^{13}C NMR (D_2O, 100.6 MHz) δ 175.8 (C═O), 175.5 (C═O), 138.2, 130.1, 129.9, 129.7, 105.9, 103.4 (d, $^3J_{C-F}$ = 12.7 Hz), 102.7, 97.6, 94.1 (d, $^1J_{C-F}$ = 183.9 Hz), 79.8, 78.3, 76.2 (d, $^2J_{C-F}$ = 17.8 Hz), 75.3 (d, $^3J_{C-F}$ = 6.8 Hz), 73.8, 73.7, 71.9, 71.1, 70.9, 70.8,

70.7, 70.1, 69.9, 68.2, 67.9, 62.3, 61.99, 61.97, 61.3, 56.4, 49.8, 23.6 (NAc), 23.3 (NAc); ESI-HRMS calcd for $C_{35}H_{53}O_{20}N_2FNa$ (*m*/*z*) [MNa^+] 863.3068, found 863.3088.

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Supporting Information Available: General experimental methods, X-ray crystallographic data (including structure factors), 1D or 2D NMR spectra of key compounds, and ESI-HRMS of compounds **1**−**5** and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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