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Systematic Syntheses and Inhibitory Activities of Bisubstrate-Type Inhibitors of Sialyltransferases

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Bisubstrate-type sialyltransferase inhibitors **1**/**2a**−**e**, having CMP−NeuAc and *N*-acetyllactosamine (or lactose) moieties connected by an alkanedithiol linker, were synthesized systematically. A uniform synthetic strategy was adopted that consists of consecutive couplings of three components (*N*-acetyllactosamine or lactose, sialic acid, and CMP), followed by oxidation. Due to the sensitivity of the compounds under alkaline conditions, final deprotection required careful monitoring by ^{1}H NMR. The inhibitory activities of **1**/**2a**−**e** toward ST6N and ST3N indicated that both the structure of the acceptor moiety and the distance between donor and acceptor moieties were important.

Introduction

Glycoconjugates, including O- and N-linked glycoproteins and glycosphingolipids, play critical roles in a variety of biological events. Well-recognized among them are cell−cell communication, bacterial adhesion, viral infection, signal transduction, protein folding/transport, and immune response.[1] Structures and compositions of glycan chains change dramatically during development, cell differentiation, and malignant transformation.[2] These are principally controlled by the expression levels, activities, and substrate specificities of glycosyltransferases (GTs). Since GTs usually have narrow specificities toward donor and acceptor substrates,[3] it is likely that both of them are recognized strictly in the enzyme binding pockets. Therefore, properly designed bisubstrate-like derivatives are expected to be specific and potent inhibitors of GTs.[4] Such compounds would be valuable in dissecting the active site structure of GTs and their mechanisms of action, which are largely unexplored.[5]

Sialic acid (*N*-acetylneuraminic acid, NeuAc), an important constituent of various glycoconjugates, typically resides at the nonreducing end of glycan chains. NeuAc-containing glycoconjugates play essential roles in a wide range of recognition events, particularly on mammalian cell surfaces.[6] Sialyltransferases (STs) are one of the largest and most important GT families and typically transfer NeuAc to galactose (Gal, Scheme 1) and *N*-acetylgalactosamine (GalNAc), and NeuAc. They use cytidine monophosphate−sialic acid (CMP−NeuAc) as the common donor substrate. So far, 20 different STs have been cloned, and they form one of four types of α-sialoside linkages, namely, NeuAcα2,6Gal, NeuAcα2,-3Gal, NeuAcα2,6GalNAc, and NeuAcα2,8NeuAc.[7]

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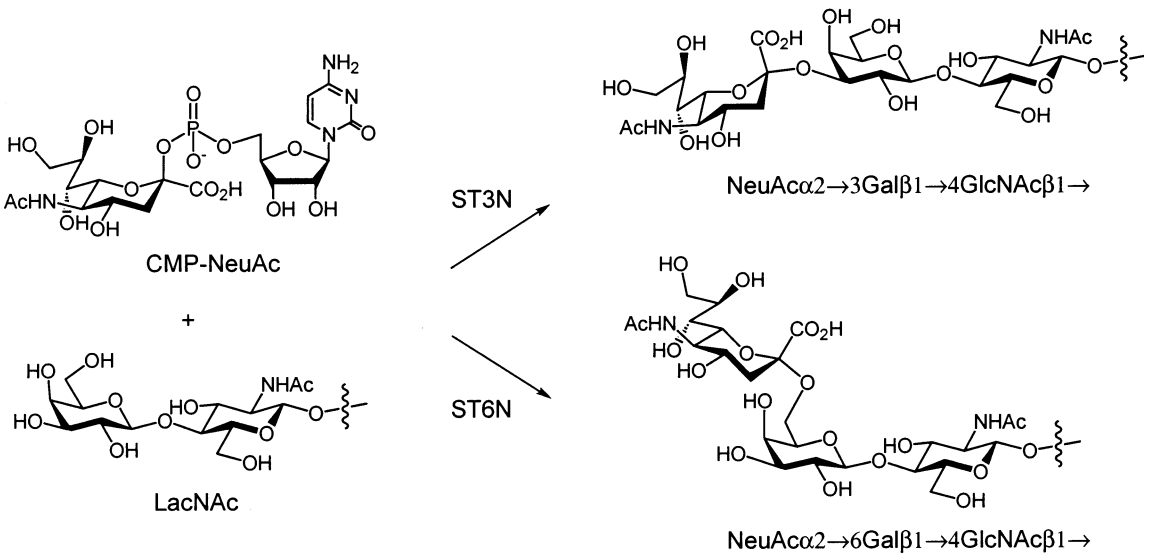
SCHEME 1



Among various STs, the most extensively studied are α-2,3-(N)-ST (ST3N) and α-2,6-(N)-ST (ST6N). These enzymes transfer NeuAc to the Gal residue of *N*-acetyllactosamine (Galβ1→4GlcNAc, LacNAc) either in an α2→3 or an α2→6 manner to form NeuAcα2→3Galβ1→4GlcNAc or NeuAcα2→6Galβ1→4GlcNAc and are responsible for the biosynthesis of complex-type asparagine-linked (N-linked) glycoproteins. These structures are also expressed in lacto-series glycosphingolipids and O-linked glycoproteins and are related intimately to important biomedical events such as inflammation,[8] cancer metastasis,[9] and the immune response.[10]

Interestingly, ST3N has a dual specificity to accept both LacNAc (K_m 2.7 mM) and Galβ1→3GlcNAc (K_m 0.6 mM) and is therefore referred to as Galβ1→3(4)GlcNAc α-2,3-sialyltransferase.[11] Lactose (Galβ1→4Glc; Lac) can also be a substrate for this enzyme, albeit with substantially lower affinity (K_m 9.4 mM).[11] On the other hand, ST6N is highly specific to LacNAc (K_m 1.6 mM); affinity toward lactose is low (129 mM), and Galβ1→3GlcNAc is a poor substrate for NeuAc transfer activity (∼1% of LacNAc).[11]

Although STs have previously been the subjects of intense research, an ST inhibitor of bisubstrate-type structures has not yet been reported.[12] Considering the paucity of information on the active site structure and the mode of action of the STs,[13] it would be highly desirable to establish a strategy by which the systematic preparation of various derivatives of bisubstrate-type inhibitors could be achieved in a uniform manner. Bisubstrate-like derivatives **1**/**2a**−**e** depicted in Figure 1A are one way to address this need. These compounds contain donor (CMP−NeuAc) and acceptor (LacNAc/Lac) components that are connected via sulfide bonds and separated by an alkyl linker of variable length. Distances between CMP−NeuAc and the acceptor can be varied simply by changing the length of alkanedithiol (n = 1∼5).

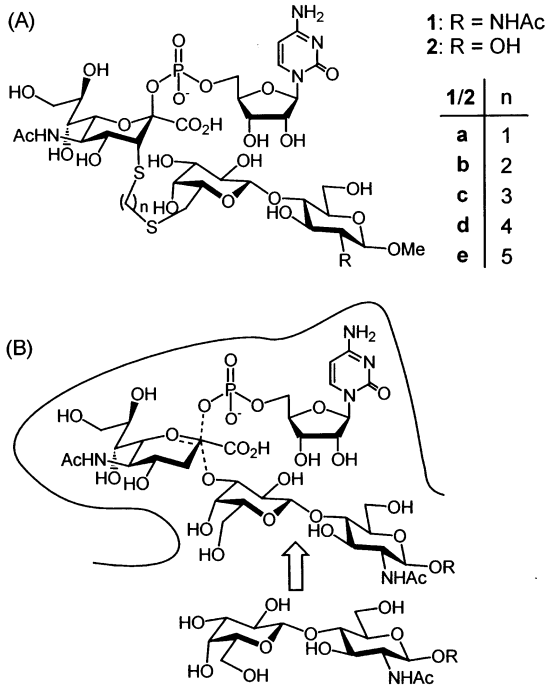


FIGURE 1. Bisubstrate-type inhibitors (A) and canonical transition state (B) of sialyltransferase-catalyzed reaction.

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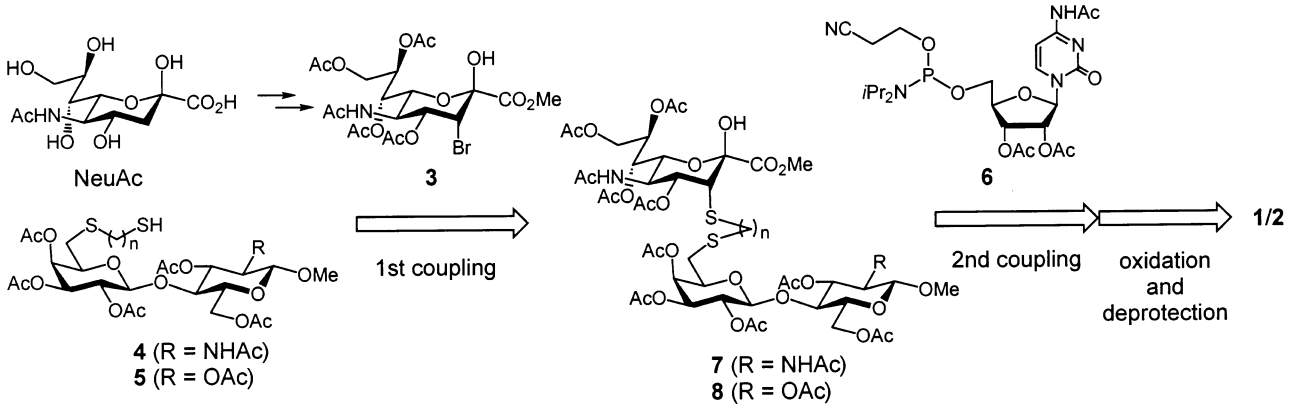
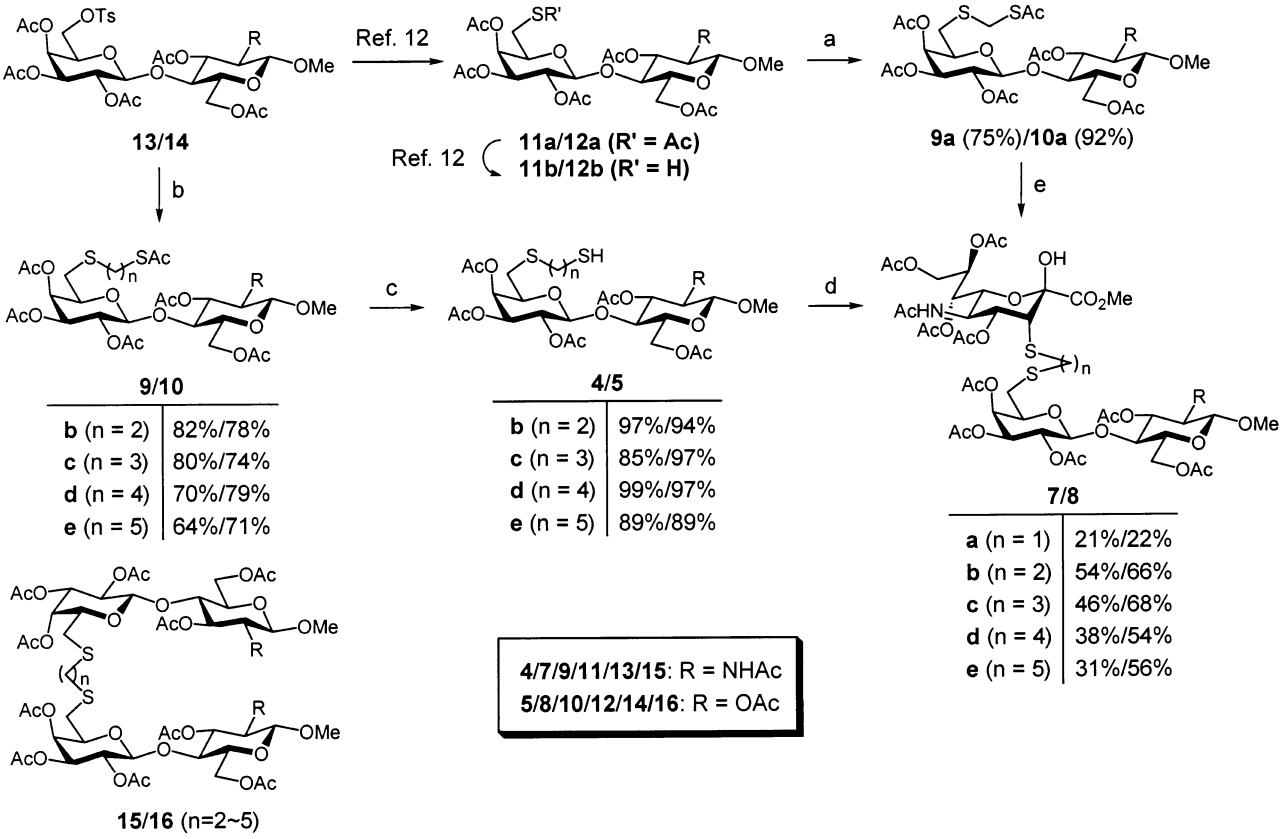
SCHEME 2



SCHEME 3[a]



9/10	
b (n = 2)	82%/78%
c (n = 3)	80%/74%
d (n = 4)	70%/79%
e (n = 5)	64%/71%

4/5	
b (n = 2)	97%/94%
c (n = 3)	85%/97%
d (n = 4)	99%/97%
e (n = 5)	89%/89%

7/8	
a (n = 1)	21%/22%
b (n = 2)	54%/66%
c (n = 3)	46%/68%
d (n = 4)	38%/54%
e (n = 5)	31%/56%

[a] Reagents and conditions: (a) (i) paraformaldehyde, HCl, CH_2Cl_2; (ii) KSAc, DMF, 80 °C. (b) (i) $HS(CH_2)_nSH$, TMS_2NK, THF, HMPA; (ii) Ac_2O, pyridine. (c) NH_2NH_2, AcOH, DMF. (d) **3**, TMS_2NK, THF, −78 to −10 °C. (e) **3**, TMS_2NK, MeOH, THF, −78 to −10 °C.

In all cases, acceptor components are linked to the C-3 position of CMP−NeuAc. Since NeuAc has a 3-deoxy structure, it was hoped that this position could be used for the linking of two components, without risking the critical functional group interactions. Furthermore, on the basis of canonical transition states of ST reactions (Figure 1B for ST3N), the acceptor portion was planned to be placed on the α-face of CMP−NeuAc.

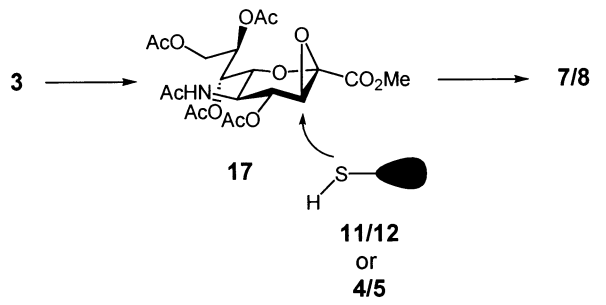
Our synthetic strategy shown in Scheme 2 consisted of consecutive couplings of three component precursors **3**, **4**/**5**, and **6** via **7**/**8** followed by oxidation and deprotection. Execution of this strategy to the preparation of a prototypical inhibitor **1a** was reported recently in a preliminary form.[14] Now, we wish to report herein the full detail of the systematic preparation of 10 compounds (**1/2a**−**e**). This was achieved from common intermediates (**3** and **13/14**; for the latter, see Scheme 3) in a divergent manner (vide infra).

Results and Discussion

Based on the synthetic plan depicted in Scheme 2, preparation of the acceptor component precursors **9**/**10a**

(14) Hinou, H.; Sun, X.-L.; Ito, Y. *Tetrahedron Lett.* **2002**, *43*, 9147−9150. Synthesis of bisubstrate analogues of syalyltransferase was announced: M. Izumi, H. Hashimoto et al. XXIst International Carbohydrate Symposium, July 7−12, 2002, Cairns, Australia; PP136.

SCHEME 4



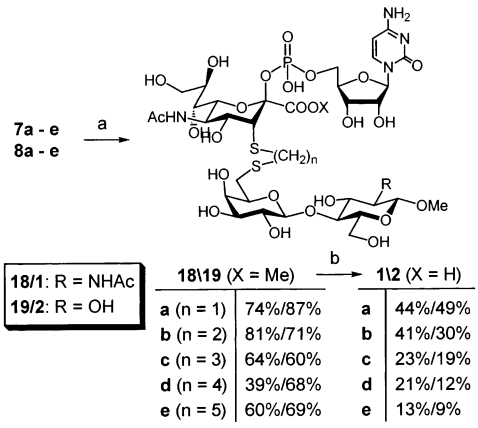
and **4**/**5b**−**e** was first examined (Scheme 3). C_1-Linker-carrying compounds **9a** and **10a** were prepared from known 6′-thio derivatives **11**[15] and **12**,[14] respectively, via S-chloromethylation (CH_2O, HCl[4c]) and Cl→S exchange with KSAc. On the other hand, C_2−C_5 derivatives were prepared by the reactions of 6′-*O*-tosylates **13**[15]/**14**[14] with dithiol $HS(CH_2)_nSH$ (n = 2−5). The products were isolated as *S*-acetates **9**/**10a**−**e** to facilitate the separation from concomitantly formed dimers **15**/**16b**−**e**. Subsequent treatment with hydrazine−acetic acid liberated thiol to afford **4**/**5b**−**e**.

Bromohydrin **3** was chosen as the NeuAc component, which was prepared from NeuAc via 2,3-dehydro derivative as described by Goto et al.[16] To our delight, coupling reactions with thiols **4**/**5b**−**e** proceeded stereoselectively to afford desired α-linked products[17] when TMS_2NK was used as a base and the reactions were conducted at low temperatures. For instance, reaction with **5b** gave **8b** as a single stereoisomer in 66% yield. That the coupling proceeded in an α-selective fashion may well be explained by posing the intermediacy of epoxide (Scheme 4).[18] In a likewise manner, LacNAc-linked **7b** was prepared from **4b**, again as an α-isomer (54%). Subsequently, C_3−C_5 derivatives **7**/**8c**−**e** were successfully prepared under identical conditions (Scheme 3).

Since hemithioacetals derived from the C_1 thioacetates **9**/**10a** are potentially labile, ligation with **3** was accomplished by tandem de-S-acetylation−substitution. Thus, **9**/**10a** were treated with **3** in the presence of KOMe. These conditions successfully afforded **7**/**8a**, although the yields were modest.

Thus obtained NeuAc−Lac/LacNAc conjugates have hemiketal OH and can be readily used for the subsequent coupling with CMP (Scheme 5). This task was achieved using Kajihara's excellent protocol developed for the preparation of CMP−NeuAc.[19] Namely, **7**/**8a**−**e** were reacted with phosphoramidite **6** in the presence of tetrazole. Subsequent oxidation with *tert*-butyl hydroperoxide (TBHP) was performed in the presence of Me_2S to avoid the risk of oxidation of the sulfide linker. Removal of the cyanoethyl group with DBU was followed

SCHEME 5[a]



18\19 (X = Me)		1\2 (X = H)	
a (n = 1)	74%/87%	a	44%/49%
b (n = 2)	81%/71%	b	41%/30%
c (n = 3)	64%/60%	c	23%/19%
d (n = 4)	39%/68%	d	21%/12%
e (n = 5)	60%/69%	e	13%/9%

[a] Reagents and conditions: (a) (i) 1*H*-tetrazole, MeCN, −40 °C to room temperature; (ii) *t*-BuOOH, Me_2S, MeCN, 0 °C to room temperature and then DBU; (iii) NaOMe, MeOH. (b) LiOH, D_2O.

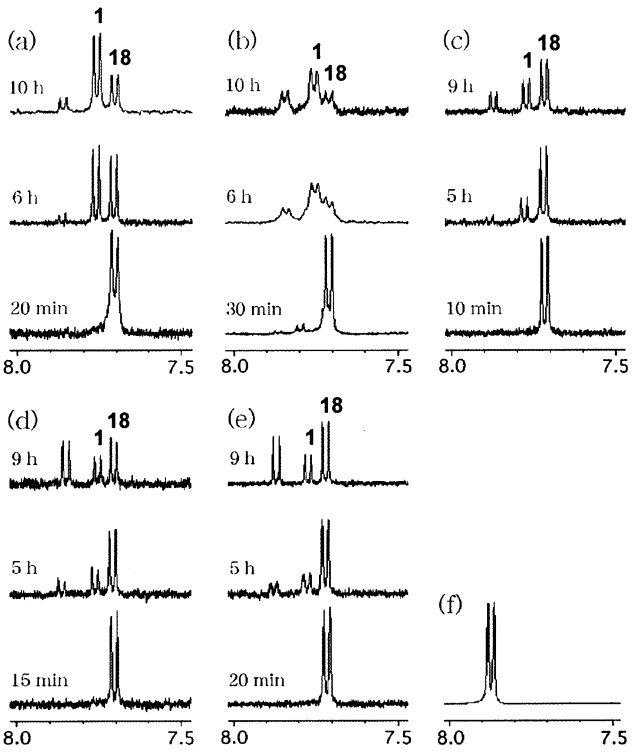


FIGURE 2. ^1H NMR monitoring of the saponification of **18** to **1** in 0.5 M LiOD/D_2O; (a) n = 1, (b) n = 2, (c) n = 3, (d) n = 4, (e) n = 5, and (f) CMP as a control.

by deacetylation with NaOMe to afford methyl esters **18**/**19a**−**e** having phosphodiester linkages.

Unexpectedly, final methyl ester saponification turned out to be challenging. As was the case for CMP−NeuAc,[19] one-pot addition−oxidation−deacetylation/saponification seemed to be reasonable. However, this option turned out to be completely unsatisfactory and all attempts to achieve these transformations in a single pot resulted in the complete cleavage of phosphodiester linkages to provide CMP. With these experiences, extensively purified **18**/**19a**−**e** was treated with LiOH in D_2O, with careful monitoring by ^1H NMR (Figure 2). Since prolonged treatment resulted in the phosphodiester hydroly-

(15) Kajihara, Y.; Kodama, H.; Wakabayashi, T.; Sato, K.; Hashimoto, H. *Carbohydr. Res.* **1993**, *247*, 179−193.
(16) Okamoto, K.; Kondo, T.; Goto, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 631−636.
(17) Ito, Y.; Ogawa, T. *Tetrahedron* **1990**, *46*, 89−102.
(18) Separately prepared epoxide **17** (ref 16) gave 3-α-sulfide under identical conditions.
(19) (a) Kajihara, Y.; Ebata, T.; Koseki, K.; Kodama, H.; Matsushita, H.; Hashimoto, H. *J. Org. Chem.* **1995**, *60*, 5732−5735. (b) Miyazaki, T.; Sato, H.; Sakakibara, T.; Kajihara, Y. *J. Am. Chem. Soc.***2000**, *122*, 5678−5694.

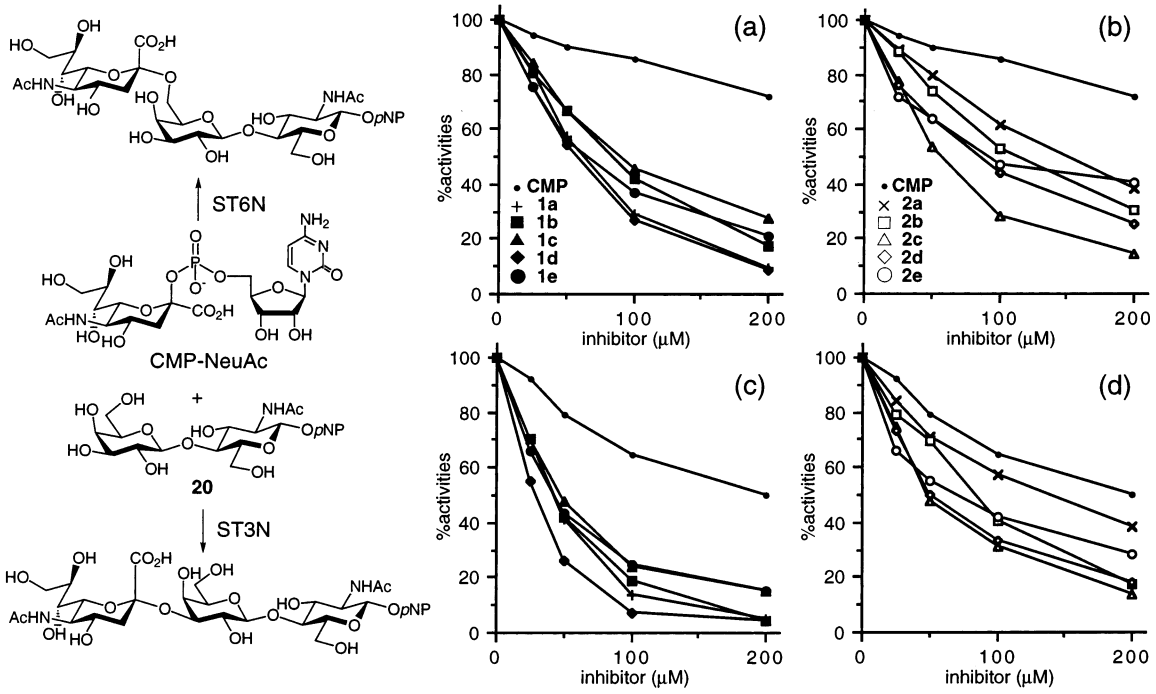


FIGURE 3. Inhibition curves of (a) ST6N by **1a**−**e**, (b) ST3N by **1a**−**e**, (c) ST6N by **2a**−**e**, (d) ST3N by **2a**−**e**, in the presence of inhibitors (0, 25, 50, 100, or 200 μM), CMP−NeuAc (200 μM), and *p*NP−LacNAc **20** (1.0 mM).

sis with liberation of CMP, reactions needed to be quenched immediately after maximum accumulation of the desired products **1**/**2a**−**e** was assessed to have been achieved.

It was noticed that the phosphodiester linkages became much more susceptible to hydrolysis after methyl ester saponification. This observation was in line with the report of Horenstein et al., which proposed the oxocarbenium ion-stabilizing effect of sialic acid carboxylate anion.[20] Noticeably, the yields of **1**/**2a**−**e** reflected their stability and correlated with the length of the linker; compounds with shorter chains were obtained in higher yields. Presumably, the sulfide linkers with longer alkyl chains (e.g., **1**/**2e**) effectively stabilize the C-2 carbenium ion by neighboring group participation and are more prone to repel the CMP, thereby weakening the glycosyl phosphate linkage. By contrast, similar participation by the shorter linkers was probably hindered for steric reasons.

In any event, the isolation of **1**/**2a**−**e** was successfully achieved by FPLC (Mono Q, Pharmacia) and their amounts were estimated by UV detection at 280 nm (cytidine as a standard). Inhibition activities toward ST6N and ST3N (rat recombinant)[21] were then evaluated. Assays were performed as described by Schmidt et al., using CMP−NeuAc (200 μM) and *p*-nitrophenyl LacNAc (**20**, 1.00 mM) as a donor and an acceptor substrate, respectively.[22] NeuAc transfer was measured in the presence of varying concentrations (0−200 μM) of inhibitors, and the results are shown in Figure 3. With kinetic constants summarized in Table 1, the followings were readily noticed: (1) the linker length seemed to be an important factor for inhibition, especially with **2a**−**e**, and (2) LacNAc-carrying derivatives are generally more potent than Lac-derived ones. For instance, compound **1a** carrying LacNAc with a minimum linker length was a potent inhibitor toward ST6N and ST3N; the K_i values against donor and acceptor were 10 and 13 μM, respectively, for both STs. Since K_m values of CMP−NeuAc and LacNAc for rat recombinant STs[11] are 42.7 μM and 2.38 mM for ST6N and 74.1 μM and 2.63 mM for ST3N, affinities of **1a** toward donor and acceptor sites of the enzymes were about 4-fold and 130-fold higher for ST6N and about 7-fold and 200-fold higher for ST3N than for natural substrates. In comparison, the Lac counterpart **2a** had a ca. 2-fold lower binding ability than CMP−NeuAc toward both ST6N and ST3N (Table 1). These results were in line with the specificity of the enzymes;

TABLE 1. K_i **Values of 1a**−**e and 2a**−**e toward ST6N and ST3N**

inhibitor or substrate	ST6N K_i (μM)		ST3N K_i (μM)	
	donor	acceptor	donor	acceptor
1a	10	13	10	13
1b	27	48	45	22
1c	207	217	243	226
1d	11	31	6	7
1e	11	96	29	110
2a	102	430	195	158
2b	85	271	111	324
2c	54	260	124	88
2d	42	114	40	78
2e	43	90	66	51
LacNAc[a,b]		2380		2630
CMP−NeuAc[a,b]	43		74	

[a] K_m values. [b] Taken from ref 11.

(20) (a) Kajihara's group (Yokohama City University, Japan) reported the enhanced stability of CDP−NeuAc methyl ester (81st Chemical Society of Japan National Meeting, Tokyo, March 2002). (b) Horenstein, B. A.; Bruner, M. *J. Am. Chem. Soc.* **1996**, *118*, 10371−10379.

(21) ST6N (EC 2.4.99.1), ST3N (EC 2.4.99.5); purchased from Calbiochem-Novabiochem Co.

(22) Schaub, C.; Müller, B.; Schmidt, R. R. *Glycoconjugate J.* **1998**, *15*, 345−354.

reported K_m values (native STs) of LacNAc/Lac[11] are 1.62 mM/129 mM for ST6N and 2.66 mM/9.40 mM for ST3N. While the suitable length (n) of the linker seems to be quite different between LacNAc series **1** ($1 \approx 4 > 5 > 2 > 3$) and Lac series **2** ($5 \approx 4 > 3 > 2 > 1$) derivatives, the general trends are quite similar between ST6N and ST3N (Figure 3, Table 1).

Conclusion

In summary, we have achieved the synthesis of a series of bisubstrate-type ST inhibitors. As summarized in Table 1, both the structures of the acceptor components (LacNAc vs Lac) and the distances between donor and acceptor components significantly affected the inhibitor activities. The advantage of our strategy is that these factors can be changed systematically, simply by using alkanedithiol linkers with different lengths. Because technically facile bromide−thiolate coupling was employed for the ligation of acceptor and NeuAc components, synthesis of a wider variety of analogues should be possible. For instance, incorporation of Galβ1→3GlcNAc as an acceptor component would be our immediate target. This disaccharide is known to be an excellent substrate for ST3N (better than LacNAc), but not for ST6N. Therefore, bisubstrate derivatives carrying Galβ1→3GlcNAc are expected to be potent inhibitors specific to ST3N. On the other hand, a major drawback of our approach is the lability of the glycosyl phosphate linkage of inhibitors. However, replacing the phosphate with a more stable functional group[23] might well circumvent this problem.

Further studies along these lines are in progress.

Experimental Section

General. Optical rotations were recorded using a 5 cm microcell. Melting points are uncorrected. ^{1}H NMR chemical shifts are given in parts per million and referenced to internal TMS (δ_H 0.00 in $CDCl_3$), $CHCl_3$ (δ_H 7.26 in $CDCl_3$), or HDO (δ_H 4.65 in D_2O). Flash column chromatography was performed on silica gel 60 (spherical type, particle size 40−100 μm) with the solvent systems specified.

Methyl *O*-(2,3,4-Tri-*O*-acetyl-6-*S*-acetyl-6-β-D-galactopyranosyl)-(1→4)-2,3,5-tri-*O*-acetyl-β-D-glucopyanoside (12a). To a solution of methyl *O*-(2,3,4-tri-*O*-acetyl-6-*O*-*p*-toluenesulfonyl-β-D-galactopyranosyl)-(1→4)-2,3,5-tri-*O*-acetyl-β-D-glucopyanoside **14** (222 mg, 0.29 mmol) in DMF (2 mL) was added potassium thioacetate (332 mg, 2.91 mmol), and the mixture was stirred at 80 °C for 12 h. After cooling to ambient temperature, the mixture was concentrated, and the resulting residue was purified by flash column chromatography (hexane−acetone, 1:1) to give the title compound (180 mg, 93%) as an amorphous solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (d, 1H, J = 3.4 Hz), 5.20 (t, 1H, J = 8.0 Hz), 5.07 (t, 1H, J = 8.0 Hz), 4.93 (dd, 1H, J = 8.0, 3.4 Hz), 4.90 (t, 1H, J = 8.0 Hz), 4.50 (dd, 1H, J = 2.2, 11.4 Hz), 4.46 (d, 1H, J = 8.0 Hz), 4.40 (d, 1H, J = 8.0 Hz), 4.10 (dd, 1H, J = 11.4, 4.1 Hz), 3.83 (t, 1H, J = 9.1 Hz), 3.60−3.67 (m, 2H), 3.45 (s, 3H), 3.00 (d, 2H, J = 7.2 Hz), 2.32 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.96 (s, 3H). Anal. Calcd for $C_{27}H_{38}O_{17}S$: C, 48.79; H, 5.46; S, 4.82. Found: C, 48.76; H, 5.61; S, 4.59.

Methyl *O*-(2,3,4-Tri-*O*-acetyl-6-thio-β-D-galactopyranosyl)-(1→4)-2,3,5-tri-*O*-acetyl-β-D-glucopyanoside (12b). To a solution of **12a** (1.01 g, 1.52 mmol) in DMF (20 mL) at ambient temperature were added AcOH (87 μL, 1.5 mmol) and hydrazine monohydrate (74 μL, 1.5 mmol) successively. After stirring for 1 h, the mixture was concentrated to ca. 10 mL, diluted with EtOAc, washed with water, dried, and concentrated. Purification of the residue by flash column chromatography (hexanes−EtOAc, 1:1) afforded **12b** (912 mg, 97%) as an amorphous solid: $[\alpha]_D$ − 1.6° (c 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (d, 1H, J = 3.0 Hz), 5.18 (t, 1H, J = 8.0 Hz), 5.04 (dd, 1H, J = 8.0, 10.0 Hz), 4.92 (dd, 1H, J = 8.0, 3.0 Hz), 4.86 (t, 1H, J = 8.0 Hz), 4.49 (dd, 1H, J = 2.3 Hz), 4.43 (d, 1H, J = 8.0 Hz), 4.37 (d, 1H, J = 8.0 Hz), 4.07 (dd, 1H, J = 12.1, 4.6 Hz), 3.78 (t, 1H, J = 10.0 Hz), 3.58 (m, 2H, H-5, 5′), 3.44 (s, 3H), 2.66 (m, 1H), 2.44 (m, 1H), 2.14 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.93 (s, 3H), 1.66 (t, 1H, J = 8.0 Hz). Anal. Calcd for $C_{25}H_{36}O_{16}S$: C, 48.39; H, 5.20; S, 5.17. Found: C, 48.19; H, 5.45; S, 5.40.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-thioacetylmethyl-6-thio-β-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-β-D-glucopyanoside (9a). Hydrogen chloride was bubbled through a solution of **11b** (138 mg, 0.221 mmol) and paraformaldehyde (33 mg, 1.1 mmol) in CH_2Cl_2 (5 mL) at 0 °C for 20 min. The solution was allowed to stand for 3 h at 0 °C and then concentrated. The residue and potassium thioacetate (125 mg, 1.09 mmol) were dissolved in DMF (2 mL), and the mixture was stirred for 2 h at 50 °C. The reaction mixture was poured into water and extracted twice with EtOAc, and the combined extracts were washed with brine, dried, and concentrated. Purification of the residue by flash column chromatography (EtOAc) afforded **9a** (118 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (d, 1H, J = 9.5 Hz), 5.45 (d, 1H, J = 3.2 Hz), 5.08 (dd, 1H, J = 7.8, 10.5 Hz), 5.07 (t, 2H, J = 8.8, 8.1 Hz), 5.02 (dd, 1H, J = 3.2, 10.5 Hz), 4.53 (dd, 1H, J = 2.9, 12.0 Hz), 4.49 (d, 1H, J = 7.6 Hz), 4.37 (d, 1H, J = 7.1 Hz), 4.18 (dd, 1H, J = 4.9, 12.0 Hz), 4.11 (d, 1H, J = 14.2 Hz), 4.08 (dd, 1H, J = 7.1, 8.8 Hz), 3.96 (d, 1H, J = 14.2 Hz), 3.88 (t, 1H, J = 8.3 Hz), 3.77 (t, 1H, J = 6.4, 7.1 Hz), 3.69 (m, 1H), 3.46 (s, 3H), 2.73 (dd, 1H, J = 6.4, 14.2 Hz), 2.57 (dd, 1H, J = 7.1, 14.2 Hz), 2.42 (s, 3H), 2.17 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H); HRMS (FAB, NBA) calcd for $C_{28}H_{40}NO_{16}S_2$ ($M + H^+$) 712.1945, found 712.1956.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-thioacetylmethyl-6-thio-β-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-β-D-glucopyanoside (10a). The title compound was prepared as described for the preparation of **9a**. From 250 mg (0.400 mmol) of **12b**, 268 mg (92%) of **10a** was obtained as needles: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (d, 1H, J = 3.4 Hz), 5.20 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 8.1, 10.3 Hz), 5.00 (dd, 1H, J = 3.4, 10.3 Hz), 4.89 (dd, 1H, J = 7.8, 9.5 Hz), 4.52 (brd, 1H, J = 12.2 Hz), 4.49 (d, 1H, J = 8.1 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.15 (dd, 1H, J = 4.9, 12.2 Hz), 4.11 and 3.97 (d, 1H, J = 13.9 Hz), 3.88 (t, 1H, J = 9.3, 9.8 Hz), 3.77 (dd, 1H, J = 5.9, 7.6 Hz), 3.63 (m, 1H, H-5), 3.48 (s, 3H, OMe), 32.73 (dd, 1H, J = 5.9, 13.9 Hz), 2.57 (dd, 1H, J = 7.6, 13.9 Hz), 2.43 (s, 3H, SAc), 2.16 (s, 3H), 2.14 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H); MS (FAB, NBA) m/z 735 [M + H].

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(2-*S*-acetyl-2-thioethyl)-6-thio-β-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-β-D-glucopyanoside (9b). A 0.5 M solution of potassium bis(trimethylsilyl)amide (1.90 mL) in toluene was diluted with THF (4 mL) at −78 °C. After the mixture was degassed, 1,2-ethanedithiol (100 μL, 1.19 mmol) and HMPA (4 mL) were added successively to the mixture, and the mixture was degassed and stirred for 30 min. A solution of compound **13** (303 mg, 0.398 mmol) in THF (4 mL) was added at −78 °C. After being degassed, the mixture was gradually warmed to ambient temperature and stirred for 2 h, and acetic anhydride (1 mL) and pyridine (2 mL) were added to the solution. After the mixture was stirred for 12 h, the reaction was quenched with water and the mixture extracted with EtOAc. The organic layer was washed with brine, dried, and concentrated. The residue was purified by flash column

(23) Sato, K.; Seio, K.; Sekine, M. *J. Am. Chem. Soc.* **2002**, *124*, 12715−12724.

chromatography (EtOAc) to give **9b** (236 mg, 82%) and dimer **15b** (31 mg, 12%). **Compound 9b**: $[\alpha]_D^{28}$ −19° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (d, 1H, *J* = 9.5 Hz), 5.49 (d, 1H, *J* = 3.2 Hz), 5.12−5.07 (m, 2H), 5.01 (dd, 1H, *J* = 10.5 Hz), 4.51 (dd, 1H, *J* = 12.0 Hz), 4.51 (d, 1H, *J* = 7.8 Hz), 4.38 (d, 1H, *J* = 8.1 Hz), 4.18 (dd, 1H, *J* = 5.1, 12.0 Hz), 4.91 (dt, 1H, *J* = 8.3, 9.5 Hz), 3.86 (t, 1H, *J* = 8.1 Hz), 3.75 (t, 1H, *J* = 6.8 Hz), 3.70 (m, 1H), 3.46 (s, 3H), 3.08−3.01 (m, 2H), 2.85−2.60 (m, 4H), 2.36 (s, 3H), 2.17 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H). Anal. Calcd for $C_{29}H_{43}NO_{16}S_2$: C, 47.99; H, 5.97; N, 1.93; S, 8.84. Found: C, 48.06; H, 5.70; N, 2.03; S, 8.35. **Compound 15b**: $[\alpha]_D^{28}$ −15° (*c* 1.69, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (d, 2H, *J* = 9.5 Hz), 5.48 (d, 2H, *J* = 2.9 Hz), 5.12−5.07 (m, 4H), 5.03 (dd, 2H, *J* = 2.9, 10.5 Hz), 4.55 (d, 2H, *J* = 7.6 Hz), 4.50 (dd, 2H, *J* = 2.7, 12.0 Hz), 4.41 (d, 2H, *J* = 7.3 Hz), 4.16 (dd, 2H, *J* = 5.6, 12.0 Hz), 4.05 (dt, 2H, *J* = 7.3, 9.0 Hz), 3.86 (t, 2H, *J* = 8.2 Hz), 3.76 (t, 2H, *J* = 6.8 Hz), 3.71−3.67 (m, 2H), 3.46 (s, 6H), 2.85−2.72 (m, 6H), 2.59 (dd, 2H, *J* = 13.9 Hz), 2.16 (s, 6H), 2.12 (s, 6H), 2.10 (s, 6H), 2.06 (s, 6H), 1.98 (s, 6H), 1.97 (s, 6H).

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(3-*S*-acetyl-3-thiopropyl)-6-thio-*β*-D-galactopyranosy]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (9c). The title compound was prepared as described for **9b** from **13** (303 mg, 0.398 mmol) and 1,3-propanedithiol (120 μL, 1.20 mmol) to give **9c** (235 mg, 80%) and dimer **15c** (26 mg, 10%). **Compound 9c**: $[\alpha]_D^{28}$ −27° (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (d, 1H, *J* = 9.5 Hz), 5.46 (d, 1H, *J* = 3.4 Hz), 5.10 (m, 2H), 5.01 (dd, 1H, *J* = 3.4, 10.5 Hz), 4.51 (dd, 1H, *J* = 3.2, 11.7 Hz), 4.49 (d, 1H, *J* = 8.1 Hz), 4.39 (d, 1H, *J* = 7.1 Hz), 4.17 (dd, 1H, *J* = 5.4, 11.7 Hz), 4.06 (dt, 1H, *J* = 7.1, 9.0 Hz), 3.85 (t, 1H, *J* = 8.1 Hz), 3.70 (t, 1H, *J* = 6.6, 7.3 Hz), 3.70 (m, 1H), 3.46 (s, 3H), 2.96 (t, 2H, *J* = 7.2 Hz), 2.71 (dd, 1H, *J* = 6.6, 13.7 Hz), 2.59 (t, 2H, *J* = 7.1 Hz), 2.54 (dd, 1H, *J* = 7.3, 13.7 Hz), 2.35 (s, 3H, SAc), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.85 (m, 2H). Anal. Calcd for $C_{30}H_{45}NO_{16}S_2$: C, 48.70; H, 6.13; N, 1.89; S, 8.67. Found: C, 48.40; H, 5.86; N, 2.01; S, 8.90. **Compound 15c**: $[\alpha]_D^{28}$ −19° (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (d, 2H, *J* = 9.5 Hz), 5.48 (d, 2H, *J* = 2.9 Hz), 5.11−5.07 (m, 4H), 5.02 (dd, 2H, *J* = 2.3, 10.5 Hz), 4.53 (d, 2H, *J* = 7.6 Hz), 4.50 (dd, 2H, *J* = 2.4, 12.0 Hz), 4.39 (d, 2H, *J* = 7.3 Hz), 4.17 (dd, 2H, *J* = 5.6 Hz), 4.05 (dt, 2H, *J* = 9.3 Hz), 3.84 (t, 2H, *J* = 8.1 Hz), 3.75 (t, 2H, *J* = 6.8 Hz), 3.71−3.68 (m, 2H), 3.46 (s, 6H), 2.75−2.65 (m, 6H), 2.57 (dd, 2H, *J* = 7.3, 13.9 Hz), 2.16 (s, 6H), 2.12 (s, 6H), 2.09 (s, 6H), 2.06 (s, 6H), 1.98 (s, 6H), 1.97 (s, 6H), 1.84 (m, 2H). Anal. Calcd for $C_{53}H_{78}N_2O_{30}S_2$: C, 49.45; H, 6.11; N, 2.18; S, 4.98. Found: C, 49.46; H, 6.07; N, 2.27; S, 5.18.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(4-*S*-acetyl-4-thiobutyl)-6-thio-*β*-D-galactpyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (9d). The title compound was prepared as described for **9b**. From **13** (303 mg, 0.398 mmol) and 1,4-butandithiol (139 μL, 1.18 mmol), **9d** (210 mg, 70.0%) and dimer **15d** (35 mg, 14%) were obtained**. Compound 9d**: $[\alpha]_D^{28}$ −21° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (d, 1H, *J* = 9.3 Hz), 5.48 (d, 1H, *J* = 3.4 Hz), 5.09 (m, 2H), 5.01 (dd, 1H, *J* = 3.4, 10.5 Hz), 4.51 (dd, 1H, *J* = 2.9, 11.8 Hz), 4.49 (d, 1H, *J* = 7.8 Hz), 4.39 (d, 1H, *J* = 7.1 Hz), 4.17 (dd, 1H, *J* = 5.2, 11.8 Hz, H-6b), 4.05 (dt, 1H, *J* = 7.1, 9.4 Hz, H-2), 3.84 (t, 1H, *J* = 8.1 Hz), 3.74−3.65 (m, 2H), 3.46 (s, 3H), 2.89 (t, 2H, *J* = 6.7 Hz), 2.70 (dd, 1H, *J* = 6.1, 13.7 Hz), 2.60−2.50 (m, 3H), 2.34 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.66 (m, 4H). Anal. Calcd for $C_{31}H_{47}NO_{16}S_2$: C, 49.39; H, 6.28; N, 1.86; S, 8.51. Found: C, 49.05; H, 6.11; N, 2.00; S, 8.63. **Compound 15d**: $[\alpha]_D^{28}$ −20° (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (d, 1H, *J* = 9.3 Hz), 5.47 (d, 2H, *J* = 2.9 Hz), 5.09 (t, 4H), 5.01 (dd, 2H, *J* = 2.9, 10.5 Hz), 4.50 (d, 2H, *J* = 7.8 Hz), 4.50 (dd, 2H, *J* = 12.0 Hz), 4.39 (d, 2H, *J* = 7.3 Hz), 4.16 (dd, 2H, *J* = 5.4, 12.0 Hz), 4.04 (dt, 2H, *J* = 7.3, 9.0 Hz), 3.83 (t, 2H, *J* = 8.9 Hz), 3.73−3.68 (m, 4H), 3.45 (s, 6H), 2.71 (dd, 2H, *J* = 6.1, 13.8 Hz), 2.58−2.52 (m, 6H), 2.16 (s, 6H), 2.12 (s, 6H), 2.09 (s, 6H), 2.06 (s, 6H), 1.98 (s, 6H), 1.97 (s, 6H), 1.67 (m, 4H). Anal. Calcd for $C_{54}H_{80}N_2O_{30}S_2$: C, 49.84; H, 6.20; N, 2.15; S, 4.93. Found: C, 49.45; H, 6.11; N, 2.23; S, 5.01.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(5-*S*-acetyl-5-thiopentyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (9e). The title compound was prepared as described for **9b**. From **13** (303 mg, 0.398 mmol) and 1,5-pentandithiol (160 μL, 1.19 mmol), **9e** (194 mg, 64%) and dimer **15e** (31 mg, 12%) were obtained. **Compound 9e**: $[\alpha]_D^{27}$ −21° (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (d, 1H, *J* = 9.3 Hz), 5.48 (d, 1H, *J* = 3.4 Hz), 5.09 (dd, 1H, *J* = 7.8, 10.5 Hz), 5.08 (dd, 2H, *J* = 9.0, 8.6 Hz), 5.01 (dd, 1H, *J* = 3.4, 10.5 Hz), 4.51 (dd, 1H, *J* = 3.2, 12.0 Hz), 4.48 (d, 1H, *J* = 7.8 Hz), 4.38 (d, 1H, *J* = 7.1 Hz), 4.16 (dd, 1H, *J* = 5.1, 12.0 Hz), 4.05 (dt, 1H, *J* = 7.1, 9.0, 9.3 Hz), 3.83 (t, 1H, *J* = 8.1 Hz), 3.72−3.64 (m, 2H), 3.46 (s, 3H), 2.87 (t, 2H, *J* = 7.2 Hz), 2.70 (dd, 1H, *J* = 6.1, 13.7 Hz), 2.54 (dd, 1H, *J* = 7.8, 13.7 Hz), 2.52 (t, 2H, *J* = 7.2 Hz), 2.33 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.63−1.55 (m, 4H), 1.48−1.42 (m, 2H). Anal. Calcd for $C_{32}H_{49}NO_{16}S_2$: C, 50.05; H, 6.43; N, 1.82; S, 8.35. Found: C, 49.77; H, 6.22; N, 1.98; S, 8.44. **Compound 15e**: $[\alpha]_D^{28}$ −20° (*c* 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (d, 2H, *J* = 9.5 Hz), 5.48 (d, 2H, *J* = 2.9 Hz), 5.08 (m, 4H), 5.01 (dd, 2H, *J* = 2.9, 10.5 Hz), 4.51 (dd, 2H, *J* = 2.0, 11.7 Hz), 4.49 (d, 2H, *J* = 7.6 Hz), 4.39 (d, 2H, *J* = 7.1 Hz), 4.16 (dd, 2H, *J* = 5.4, 11.7 Hz), 4.05 (dt, 2H, *J* = 7.1, 9.0, 9.5 Hz), 3.83 (t, 2H, *J* = 8.1 Hz), 3.71−3.63 (m, 4H), 3.45 (s, 6H), 2.70 (dd, 2H, *J* = 6.1, 13.7 Hz), 2.58−2.52 (m, 6H), 2.16 (s, 6H), 2.12 (s, 6H), 2.09 (s, 6H), 2.05 (s, 6H), 1.98 (s, 6H), 1.97 (s, 6H), 1.62−1.54 (m, 4H), 1.51−1.44 (m, 2H). Anal. Calcd for $C_{55}H_{82}N_2O_{30}S_2$: C, 50.22; H, 6.28; N, 2.13; S, 4.88. Found: C, 49.84; H, 6.17; N, 2.33; S, 5.29.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(2-*S*-acetyl-2-thioethyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (10b). Prepared as described for **9b**. From **14** (301 mg, 0.395 mmol), **10b** (224 mg, 78%) and dimer **16b** (37 mg, 15%) were obtained. **Compound 10b**: $[\alpha]_D^{28}$ −14° (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (d, 1H, *J* = 3.4 Hz, H-4′), 5.23 (t, 1H, *J* = 9.3 Hz), 5.08 (dd, 1H, *J* = 7.8, 10.3 Hz), 4.99 (dd, 1H, *J* = 3.4, 10.3 Hz), 4.91 (t, 1H, *J* = 9.3 Hz), 4.51 (dd, 1H, *J* = 3.1, 12.0 Hz), 4.50 (d, 1H, *J* = 7.8 Hz), 3.86 (t, 1H, *J* = 9.5 Hz), 4.40 (d, 1H, *J* = 8.1 Hz), 4.13 (dd, 1H, *J* = 4.9, 12.0 Hz), 3.75 (dd, 1H, *J* = 5.9, 7.8 Hz), 3.64 (m, 1H, *J* = 9.8, 4.9 Hz), 3.48 (s, 3H), 3.01−3.08 (m, 2H), 2.58−2.84 (m, 4H), 2.36 (s, 3H), 1.97 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 2.07 (s, 3H), 2.13 (s, 3H), 2.16 (s, 3H). Anal. Calcd for $C_{29}H_{42}O_{17}S_2$: C, 47.93; H, 5.82; S, 8.82. Found: C, 48.07; H, 5.82; S, 8.97. **Compound 16b**: $[\alpha]_D^{28}$ −15° (*c* 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (d, 2H, *J* = 3.2 Hz), 5.21 (t, 2H, *J* = 7.8 Hz), 5.06 (dd, 2H, *J* = 7.6, 10.3 Hz), 5.00 (dd, 2H, *J* = 10.3, 3.2 Hz), 4.90 (t, 2H, *J* = 9.3 Hz), 4.51 (d, 2H, *J* = 7.6 Hz), 4.50 (brd, 2H, *J* = 12.0 Hz), 4.39 (d, 2H, *J* = 7.8 Hz), 4.12 (dd, 2H, *J* = 4.9, 12.0 Hz), 3.86 (t, 2H, *J* = 9.5 Hz), 3.76 (t, 2H, *J* = 6.8 Hz), 3.62 (m, 2H, *J* = 4.9, 9.4 Hz), 3.48 (s, 6H), 2.73−2.85 (m, 6H), 2.57 (dd, 2H, *J* = 6.8, 13.9 Hz), 2.15 (s, 6H), 2.13 (s, 6H), 2.06 (s, 6H), 2.05 (s, 6H), 2.04 (s, 6H), 1.96 (s, 6H). Anal. Calcd for $C_{52}H_{74}O_{32}S_2$: C, 48.97; H, 5.85; S, 5.03. Found: C, 48.60; H, 5.74; S, 4.88.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(3-*S*-acetyl-3-thiopropyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (10c). Prepared as described for **9b**. From **14** (301 mg, 0.395 mmol) and 1,3-propanedithiol (119 μL, 1.19 mmol), **10c** (217 mg, 74%) and dimer **16c** (32 mg, 13%) were obtained. **Compound 10c**: $[\alpha]_D^{28}$ −16° (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 1H, *J* = 3.4 Hz), 5.22 (t, 1H, *J* = 9.5 Hz), 5.07 (dd, 1H, *J* = 7.6, 10.5 Hz), 4.98 (dd, 1H, *J* = 3.4, 10.5 Hz), 4.89 (dd, 1H, *J* = 7.8, 9.5 Hz), 4.51 (brd, 1H, *J* = 12.9 Hz), 4.49 (d, 1H, *J* = 7.6 Hz), 4.39 (d, 1H, *J* = 7.8 Hz), 4.12 (dd, 1H, *J* = 4.2, 12.9 Hz), 3.85 (t, 1H, *J* = 9.5 Hz), 3.68 (t, 1H, *J* = 7.1 Hz), 3.64 (m, 1H, *J* = 9.5, 4.2 Hz), 3.48 (s,

3H), 2.95 (t, 2H, J = 7.2 Hz), 2.70 (dd, 1H, J = 6.4, 13.4 Hz), 2.59 (t, 2H, J = 7.2 Hz), 2.53 (dd, 1H, J = 7.6, 13.4 Hz), 2.34 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.85 (m, 2H). Anal. Calcd for $C_{30}H_{42}O_{17}S_2$: C, 48.64; H, 5.99; S, 8.66. Found: C, 48.44; H, 5.93; S, 8.44. **Compound 16c**: $[\alpha]^{26}_D$ −17° (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 2H, J = 3.4 Hz), 5.21 (t, 2H, J = 9.5 Hz), 5.06 (dd, 2H, J = 7.8, 10.3 Hz), 4.50 (d, 2H, J = 7.8 Hz), 4.50 (brd, 2H, J = 12.0 Hz), 4.99 (dd, 2H, J = 3.4, 10.3 Hz), 4.89 (t, 2H, J = 9.5 Hz), 4.39 (d, 2H, J = 8.1 Hz), 4.12 (dd, 2H, J = 6.6, 12.0 Hz), 3.85 (t, 2H, J = 9.5 Hz), 3.76 (t, 2H, J = 6.6 Hz), 3.73 (ddd, 2H, J = 2.0, 5.1, 9.5 Hz), 3.48 (s, 6H), 2.65−2.74 (m, 6H), 2.57 (dd, 2H, J = 7.1, 13.9 Hz), 2.15 (s, 6H), 2.13 (s, 6H), 2.06 (s, 6H), 2.05 (s, 6H), 2.04 (s, 6H), 1.96 (s, 6H), 1.85 (m, 2H). Anal. Calcd for $C_{53}H_{76}O_{32}S_2$: C, 49.37; H, 5.94; S, 4.97. Found: C, 48.65; H, 5.85; S, 5.08.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(4-*S*-acetyl-4-thiobutyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (10d). Prepared as described for **9b**. From **14** (301 mg, 0.395 mmol) and 1,4-butandithiol (139 μL, 1.18 mmol), **10d** (235 mg, 79%) and dimer **16d** (27 mg, 11%) were obtained. **Compound 10d**: $[\alpha]_D^{28}$ −20° (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 1H, J = 2.7 Hz), 5.21 (t, 1H, J = 7.1 Hz), 5.06 (dd, 1H, J = 7.8, 10.5 Hz), 4.98 (dd, 1H, J = 2.7, 10.5 Hz), 4.89 (dd, 1H, J = 7.8, 9.5 Hz), 4.50 (dd, 1H, J = 2.0, 12.0 Hz), 4.49 (d, 1H, J = 7.8 Hz), 4.40 (d, 1H, J = 7.8 Hz), 4.12 (dd, 1H, J = 4.9, 12.0 Hz), 3.85 (t, 1H, J = 9.3 Hz), 3.68 (t, 1H, J = 6.1 Hz), 3.64 (ddd, 1H, J = 2.0, 4.9, 9.8 Hz), 3.48 (s, 3H), 2.89 (t, 2H, J = 7.1 Hz), 2.69 (dd, 1H, J = 6.1, 13.7 Hz), 2.50−2.57 (m, 3H, J = 13.7 Hz), 2.34 (s, 3H), 2.15 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.60−1.71 (m, 4H); HRMS (FAB, NBA) calcd for $C_{31}H_{45}O_{17}S_2$ (M − H)$^-$ 753.2098, found 753.2141. **Compound 16d**: $[\alpha]_D^{26}$ −21° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 2H, J = 3.4 Hz), 5.21 (t, 2H, J = 9.3 Hz), 5.06 (dd, 2H, J = 7.8, 10.3 Hz), 4.98 (dd, 2H, J = 3.4, 10.3 Hz), 4.89 (t, 2H, J = 9.3 Hz), 4.50 (dd, 2H, J = 2.7, 12.2 Hz), 4.49 (d, 2H, J = 7.8 Hz), 4.39 (d, 2H, J = 7.8 Hz), 4.12 (dd, 2H, J = 5.9, 12.2 Hz), 3.83 (t, 2H, J = 9.3 Hz), 3.69 (t, 2H, J = 7.1 Hz), 3.64 (ddd, 2H, J = 2.7, 5.9, 9.8 Hz), 3.48 (s, 6H), 2.70 (dd, 2H, J = 7.1, 13.9 Hz), 2.51−2.56 (m, 6H), 2.15 (s, 6H), 2.13 (s, 6H), 2.06 (s, 6H), 2.05 (s, 6H), 2.04 (s, 6H), 1.96 (s, 6H), 1.68 (m, 4H). Anal. Calcd for $C_{54}H_{78}O_{32}S_2$: C, 49.76; H, 6.03; S, 4.92. Found: C, 49.36; H, 5.98; S, 5.05.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(5-*S*-acetyl-5-thiopentyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (10e). Prepared as described for **9b** from **14** (301 mg, 0.395 mmol) and 1,5-pentandithiol (140 μL, 1.04 mmol) to give **10e** (216 mg, 71%) and **16e** (40 mg, 15%). **Compound 10e**: $[\alpha]^{28}_D$ −15° (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 1H, J = 3.4 Hz), 5.22 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 7.8, 10.5 Hz), 4.98 (dd, 1H, J = 3.4, 10.5 Hz), 4.90 (dd, 1H, J = 8.2, 9.5 Hz), 4.50 (dd, 1H, J = 2.0, 11.9 Hz), 4.47 (d, 1H, J = 7.8 Hz), 4.39 (d, 1H, J = 8.2 Hz), 4.12 (dd, 1H, J = 4.2, 11.9 Hz), 3.84 (t, 1H, J = 9.5 Hz), 3.67 (ddd, 2H, J = 2.0, 4.2, 9.5 Hz), 3.48 (s, 3H), 2.87 (t, 2H, J = 7.2 Hz), 2.69 (dd, 1H, J = 6.1, 13.7 Hz), 2.50−2.55 (m, 3H), 2.33 (s, 3H), 2.15 (s, 3H), 2.13 (s, 3H), 2.05 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.55−1.62 (m, 4H), 1.42−1.50 (m, 2H). Anal. Calcd for $C_{32}H_{48}O_{17}S_2$: C, 49.99; H, 6.29; S, 8.34. Found: C, 49.79; H, 6.08; S, 7.98. **Compound 16e**: $[\alpha]_D^{28}$ −17° (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 1H, J = 2.9 Hz), 5.21 (t, 1H, J = 9.3 Hz), 5.06 (dd, 1H, J = 8.1, 10.3 Hz), 4.98 (dd, 1H, J = 2.9, 10.3 Hz), 4.89 (dd, 1H, J = 7.9, 9.3 Hz), 4.50 (dd, 1H, J = 2.2, 11.7 Hz), 4.48 (d, 1H, J = 8.1 Hz), 4.39 (d, 1H, J = 7.9 Hz), 4.12 (dd, 1H, J = 4.5, 11.7 Hz), 3.83 (t, 1H, J = 9.5 Hz), 3.62−3.69 (m, 4H), 3.48 (s, 6H), 2.69 (dd, 2H, J = 6.1, 13.7 Hz), 2.51−2.56 (m, 6H), 2.15 (s, 3H), 2.13 (s, 3H), 2.05 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.55−1.62 (m, 4H), 1.46−1.51 (m, 2H). Anal. Calcd for $C_{55}H_{80}O_{32}S_2$: C, 50.15; H, 6.12; S, 4.87. Found: C, 49.87; H, 6.03; S, 4.83.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(2-thioethyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (4b). To a solution of **9b** (181 mg, 0.249 mmol) in DMF (3 mL) at ambient temperature was added hydrazine acetate (28 mg, 0.30 mmol), and the mixture was stirred for 1 h. The mixture was diluted with EtOAc, washed with water, dried, and concentrated. Purification of the residue by flash column chromatography (EtOAc) afforded **4b** (166 mg, 97%) as an amorphous solid: $[\alpha]^{28}_D$ −19° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (d, 1H, J = 9.3 Hz), 5.45 (d, 1H, J = 3.4 Hz), 5.09 (dd, 1H, J = 7.8, 10.3 Hz), 5.09 (t, 2H, J = 9.0 Hz), 5.01 (dd, 1H, J = 3.4, 10.3 Hz), 4.51 (dd, 1H, J = 3.2, 12.0 Hz), 4.51 (d, 1H, J = 7.8 Hz), 4.38 (d, 1H, J = 6.8 Hz), 4.17 (dd, 1H, J = 5.4, 12.0 Hz), 4.09 (dt, 1H, J = 6.8, 8.3 Hz), 3.86 (t, 1H, J = 8.0 Hz), 3.70 (brt, 1H, J = 5.6, 6.8 Hz), 3.70 (m, 1H), 3.46 (s, 3H), 2.83−2.69 (m, 5H), 2.58 (dd, 1H, J = 13.9 Hz), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.39 (t, 1H, J = 8.1 Hz). Anal. Calcd for $C_{27}H_{41}NO_{15}S_2$: C, 47.43; H, 6.04; N, 2.05; S, 9.38. Found: C, 47.49; H, 5.97; N, 2.14; S, 9.10.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(3-thiopropyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (4c). Prepared as described for **4b** from **9c** (222 mg, 0.300 mmol) to give **4c** (185 mg, 85.2%) as an amorphous solid: $[\alpha]^{28}_D$ −21° (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 (d, 1H, J = 9.5 Hz), 5.48 (d, 1H, J = 3.2 Hz), 5.09 (dd, 1H, J = 7.8, 10.5 Hz), 5.09 (t, 2H, J = 9.0 Hz), 5.01 (dd, 1H, J = 3.2, 10.5 Hz), 4.52 (dd, 1H, J = 3.4, 11.7 Hz), 4.48 (d, 1H, J = 7.8 Hz), 4.37 (d, 1H, J = 7.1 Hz), 4.17 (dd, 1H, J = 5.4, 11.7 Hz), 4.08 (dt, 1H, J = 7.1, 9.0 Hz), 3.84 (t, 1H, J = 7.8 Hz), 3.70 (brt, 1H, J = 6.3, 7.6 Hz), 3.70 (m, 1H), 3.46 (s, 3H), 2.72 (dd, 1H, J = 6.3, 13.7 Hz), 2.69−2.61 (m, 4H), 2.56 (dd, 1H, J = 7.6, 13.9 Hz), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.90−1.83 (m, 4H), 1.39 (t, 1H, J = 8.1 Hz). Anal. Calcd for $C_{28}H_{43}NO_{15}S_2$: C, 48.20; H, 6.21; N, 2.01; S, 9.19. Found: C, 48.12; H, 6.17; N, 2.15; S, 9.00.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(4-thiobutyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (4d). Prepared as described for **4b** from **9d** (185 mg, 0.245 mmol) to give **4d** (174 mg, 99%) as an amorphous solid: $[\alpha]^{28}_D$ −21° (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (d, 1 H, J = 9.5 Hz), 5.48 (d, 1H, J = 3.4 Hz), 5.10 (dd, 1H, J = 7.8, 10.3 Hz), 5.08 (t, 2H, J = 9.0 Hz), 5.00 (dd, 1H, J = 3.4, 10.3 Hz), 4.51 (dd, 1H, J = 3.2, 11.7 Hz), 4.47 (d, 1H, J = 7.8 Hz), 4.36 (d, 1H, J = 7.1 Hz), 4.16 (dd, 1H, J = 5.4, 11.7 Hz), 4.07 (dt, 1H, J = 7.1, 9.3 Hz), 3.83 (t, 1H, J = 7.8 Hz), 3.70 (m, 2H), 3.46 (s, 3H), 2.72 (dd, 1H, J = 13.9 Hz), 2.58−2.52 (m, 5H), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.72−1.67 (m, 4H), 1.38 (t, 1H, J = 7.8 Hz). Anal. Calcd for $C_{29}H_{45}NO_{15}S_2$: C, 48.93; H, 6.37; N, 1.97; S, 9.01. Found: C, 48.65; H, 6.25; N, 2.20; S, 8.89.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(5-thiopentyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyanoside (4e). Prepared as described for **4b** from **9e** (189 mg, 0.246 mmol) to give **4e** (160 mg, 89.4%) as an amorphous solid: $[\alpha]^{28}_D$ −21° (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (d, 1H, J = 9.5 Hz), 5.48 (d, 1H, J = 3.2 Hz), 5.09 (dd, 1H, J = 7.8, 10.5 Hz), 5.07 (t, 2H, J = 8.1, 8.8 Hz), 5.00 (dd, 1H, J = 3.2, 10.5 Hz), 4.51 (dd, 1H, J = 3.2, 11.7 Hz), 4.47 (d, 1H, J = 7.8 Hz), 4.36 (d, 1H, J = 7.1 Hz), 4.16 (dd, 1H, J = 5.4, 11.7 Hz), 4.07 (dt, 1H, J = 7.5, 9.5 Hz), 3.83 (t, 1H, J = 7.8 Hz), 3.67 (m, 2H), 3.46 (s, 3H), 2.72 (dd, 1H, J = 6.1, 13.7 Hz), 2.57−2.51 (m, 5H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.67−1.55 (m, 4H), 1.52−1.46 (m, 2H), 1.36 (t, 1H, J = 7.8 Hz). Anal. Calcd for $C_{30}H_{47}NO_{15}S_2$: C, 49.64; H, 6.53; N, 1.93; S, 8.84. Found: C, 49.42; H, 6.39; N, 2.10; S, 8.80.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(2-thioethyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (5b). Prepared as described for **4b** from **10b** (216 mg, 0.297 mmol) to give **5b** (191 mg, 94%) as an amorphous solid: $[\alpha]_D^{27}$ −15.9° (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (d, 1H, J = 3.4 Hz), 5.22 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J =

8.1, 10.5 Hz), 4.97 (dd, 1H, J = 3.4, 10.5 Hz), 4.91 (t, 1H, J = 9.5 Hz), 4.51 (dd, 1H, J = 2.0, 12.0 Hz), 4.48 (d, 1H, J = 8.1 Hz), 4.40 (d, 1H, J = 8.1 Hz), 4.11 (dd, 1H, J = 12.0 Hz), 3.86 (t, 1H, J = 9.3 Hz), 3.68 (dd, 1H, J = 6.8, 7.1 Hz), 3.64 (ddd, 1H, J = 2.0, 4.9, 9.5 Hz), 3.48 (s, 3H), 2.70−2.83 (m, 5H), 2.57 (dd, 1H, J = 7.1, 13.7 Hz), 2.16 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H), 1.76 (t, 1H, J = 7.9 Hz); HRMS (FAB, NBA) calcd for $C_{27}H_{39}O_{16}S_2$ $(M - H)^-$ 683.1680, found 683.1678.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(3-thiopropyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (5c). Prepared as described for **4b** from **10c** (200 mg, 0.270 mmol) to give **5c** (183 mg, 97%) as an amorphous solid: $[\alpha]_D^{28}$ −17.3° (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 1H, J = 3.2 Hz), 5.22 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 7.8, 10.3 Hz), 4.97 (dd, 1H, J = 3.2, 10.3 Hz), 4.90 (dd, 1H, J = 7.8, 9.5 Hz), 4.51 (dd, 1H, J = 2.0, 12.0 Hz), 4.47 (d, 1H, J = 7.8 Hz), 4.40 (d, 1H, J = 7.8 Hz), 4.12 (dd, 1H, J = 5.1, 12.0 Hz), 3.85 (t, 1H, J = 9.5 Hz), 3.62−3.69 (m, 2H), 3.48 (s, 3H), 2.71 (dd, 1H, J = 6.3, 13.7 Hz), 2.61−2.69 (m, 4H), 2.54 (dd, 1H, J = 7.6, 13.7 Hz), 2.16 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H), 1.87 (q, 2H, J = 7.0 Hz), 1.38 (t, 1H, J = 7.9 Hz). Anal. Calcd for $C_{28}H_{42}O_{16}S_2$: C, 48.13; H, 6.06; S, 9.18. Found: C, 48.10; H, 5.83; S, 8.84.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(4-thiobutyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (5d). Prepared as described for **4b** from **10d** (214 mg, 0.284 mmol) to give **5d** (195 mg, 97%) as an amorphous solid: $[\alpha]_D^{28}$ −15° (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (d, 1H, J = 3.2 Hz), 5.22 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 7.8, 10.3 Hz), 4.97 (dd, 1H, J = 3.2, 10.3 Hz), 4.90 (dd, 1H, J = 7.8, 9.5 Hz), 4.50 (dd, 1H, J = 2.0, 12.0 Hz), 4.47 (d, 1H, J = 7.8 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.12 (dd, 1H, J = 4.9, 12.0 Hz), 3.84 (t, 1H, J = 9.3 Hz), 3.62−3.68 (m, 2H), 3.48 (s, 3H), 2.70 (dd, 1H, J = 6.1, 13.7 Hz), 2.51−2.58 (m, 5H), 2.16 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H), 1.65−1.73 (m, 4H), 1.38 (t, 1 H, J = 7.8 Hz); HRMS (FAB, NBA) calcd for $C_{29}H_{43}O_{16}S_2$ $(M - H)^-$ 711.1993, found 711.1986.

Methyl *O*-[2,3,4-Tri-*O*-acetyl-6-*S*-(5-thiopentyl)-6-thio-*β*-D-galactopyranosyl]-(1→4)-2,3,5-tri-*O*-acetyl-*β*-D-glucopyanoside (5e). Prepared as described for **4b** from **10e** (187 mg, 0.243 mmol) to give **5e** (157 mg, 89%) as an amorphous solid: $[\alpha]_D^{28}$ −16° (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47 (d, 1H, J = 3.4 Hz), 5.22 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 8.1, 10.5 Hz), 4.97 (dd, 1H, J = 3.4, 10.5 Hz), 4.90 (dd, 1H, J = 7.8, 9.3 Hz), 4.50 (dd, 1H, J = 1.7, 12.0 Hz), 4.46 (d, 1H, J = 8.1 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.12 (dd, 1H, J = 5.1, 12.0 Hz), 3.84 (t, 1H, J = 9.5 Hz), 3.62−3.67 (m, 2H), 3.48 (s, 3H), 2.69 (dd, 1H, J = 6.1, 13.7 Hz), 2.50−2.57 (m, 5H), 2.16 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H), 1.55−1.65 (m, 4H), 1.46−1.52 (m, 2H), 1.36 (t, 1H, J = 7.8 Hz). Anal. Calcd for $C_{30}H_{46}O_{16}S_2$: C, 49.58; H, 6.38; S, 8.82. Found: C, 49.56; H, 6.18; S, 8.58.

Compound 7a. To a degassed solution of **9a** (82 mg, 0.125 mmol), compound **3**[13] (65 mg, 0.114 mmol), and MeOH (6 μL, 0.15 mmol) in THF (1.4 mL) was added dropwise 0.5 M toluene solution of potassium bis(trimethylsilyl)amide (300 μL, 0.15 mmol) at −78 °C, and the mixture was warmed gradually to −10 °C. After the mixture was stirred for 2.5 h at −10 °C, the reaction was quenched with AcOH (50 μL) and diluted with EtOAc. The solution was washed with brine, dried, and concentrated. Flash column chromatography (acetone/hexane, 2:1→5:2) afforded the title compound **7a** (28 mg, 21%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (brs, 1H), 5.88 (d, 1H, J = 9.0 Hz), 5.74 (dd, 1H, J = 3.9, 9.8 Hz), 5.51 (m, 2H), 5.26 (m, 1H), 5.21 (t, 1H, J = 8.8 Hz), 5.14 (dd, 1H, J = 3.2, 10.5 Hz), 5.09 (dd, 1H, J = 7.3, 10.5 Hz), 4.73 (dd, 1H, J = 2.0, 12.2 Hz), 4.62 (d, 1H, J = 7.3 Hz), 4.55−4.46 (m, 2H), 4.43 (d, 1H, J = 7.3 Hz), 4.34 (brd, 1H, J = 12.0 Hz), 4.22 (dd, 1H, J = 5.6, 12.0 Hz), 4.15−4.07 (m, 2H), 4.02 (d, 1H, J = 3.9 Hz), 3.99−3.94 (m, 2H), 3.92 (d, 1H, J = 13.7 Hz), 3.85 (s, 3H), 3.81 (m, 1H), 3.70 (d, 1H, J = 13.7 Hz), 3.46 (s, 3H), 2.78 (dd, 1H, J = 9.0, 14.2 Hz), 2.48 (dd, 1H, J = 3.7, 14.2 Hz), 2.17 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.11 (s, 3H), 2.08 (s, 3H), 2.05 (s, 6H), 2.04 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H), 1.92 (s, 3H); HRMS (FAB, NBA) calcd for $C_{46}H_{65}N_2O_{28}S_2$ $(M - H)^-$ 1157.3165, found 1157.3169.

Compound 8a. Prepared as described for **7a** from **10a** (129 mg, 0.181 mmol), **3** (79 mg, 0.139 mmol), and MeOH (7 μL, 0.18 mmol) to give recovered **10a** (63 mg) and **8a** (47 mg, 22%): $[\alpha]_D^{28}$ −47° (*c* 0.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 (d, 1H, J = 9.3 Hz), 5.64 (dd, 1H, J = 3.9, 10.5 Hz), 5.45 (d, 1H, J = 2.7 Hz), 5.36 (m, 1H), 5.23 (m, 1H), 5.21 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 7.8, 10.3 Hz), 5.02 (dd, 1H, J = 2.7, 10.3 Hz), 4.89 (dd, 1H, J = 7.8, 9.5 Hz), 4.88 (m, 1H), 4.53 (d, 1H, J = 7.8 Hz), 4.50 (m, 1H), 4.46 (dt, 1H, J = 9.0, 10.5 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.32 (dd, 1H, J = 9.0 Hz), 4.14 (dd, 1H, J = 5.6, 11.7 Hz), 4.11 (dd, 1H, J = 8.5, 12.5 Hz), 3.86−3.79 (m, 4H), 3.83 (s, 3H), 3.70 (d, 1H, J = 13.4 Hz), 3.64 (m, 1H), 3.48 (s, 3H), 2.74 (dd, 1H, J = 7.3, 13.9 Hz), 2.62 (dd, 1H, J = 6.6 Hz, 2.18 (s, 3H), 2.17 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.05 (s, 6H), 2.04 (s, 6H), 1.96 (s, 3H), 1.91 (s, 3H); HRMS (FAB, NBA) calcd for $C_{46}H_{64}NO_{29}S_2$ $(M - H)^-$ 1158.3005, found 1158.3651.

Compound 7b. To a degassed solution of **4b** (167 mg, 0.242 mmol) and **3** (106 mg, 0.147 mmol) in THF (2 mL) was added dropwise 0.5 M toluene solution of potassium bis(trimethylsilyl)amide (446 μL, 0.223 mmol) at −78 °C, and the mixture was warmed gradually to −10 °C. After the mixture was stirred for 3 h at −10 °C, the reaction was quenched with AcOH (50 μL) and diluted with EtOAc, and the solution was washed with brine, dried, and concentrated. Repeated purification by flash column chromatography (first, acetone/hexane, 1:1→3:2; second, EtOAc/acetone, 1:0→8:1) afforded recovered **4b** (29 mg) and the title compound **7b** (118 mg, 54%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (d, 1H, J = 8.8 Hz), 5.94 (d, 1H, J = 8.3 Hz), 5.66 (dd, 1H, J = 4.1, 9.8 Hz), 5.51 (d, 1H, J = 3.2 Hz), 5.35−5.28 (m, 1H), 5.10 (dd, 1H, J = 7.6, 10.3 Hz), 5.07 (dd, 1H, J = 3.2, 10.3 Hz), 5.01 (t, 1H, J = 9.0, 9.8 Hz), 4.79 (m, 1H), 4.56 (d, 1H, J = 7.6 Hz), 4.40−4.31 (m, 4H), 4.27 (dd, 1H, J = 6.1, 12.0 Hz), 4.13 (t, 1H, J = 9.3 Hz), 4.05−4.02 (m, 2H), 3.85 (m, 1H), 3.84 (s, 3H), 3.61 (m, 1H), 3.43 (s, 3H), 3.34 (d, 1H), 2.89−2.51 (m, 5H), 2.45 (dd, 1H, J = 4.6, 14.2 Hz), 2.16 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H), 1.87 (s, 3H); HRMS (FAB, NBA) calcd for $C_{47}H_{67}N_2O_{28}S_2$ $(M - H)^-$ 1171.3322, found 1171.3353.

Compound 7c. Prepared as described for **7b** from **4c** (166 mg, 0.237 mmol) and **3** (104 mg, 0.182 mmol) to give recovered **4c** (70 mg) and title compound **7c** (106 mg, 46%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (d, 1H, J = 9.7 Hz), 6.50 (d, 1H, J = 9.6 Hz), 5.60 (dd, 1H, J = 3.9, 10.3 Hz), 5.49 (d, 1H, J = 2.7 Hz), 5.36 (m, 1H), 5.27 (m, 1H), 5.10 (dd, 1H, J = 2.7, 10.5 Hz), 5.06 (t, 1H, J = 8.5 Hz), 5.05 (dd, 1H, J = 7.1, 10.5 Hz), 4.93 (m, 1H), 4.58 (d, 1H, J = 7.1 Hz), 4.46−4.37 (m, 3H), 4.30 (brd, 1H), 4.21 (dd, 1H, J = 5.9, 12.2 Hz), 4.14−4.03 (m, 2H), 4.13 (t, 1H, J = 8.8 Hz), 3.82 (m, 1H), 3.82 (s, 3H), 3.69 (m, 1H), 3.49 (d, 1H, J = 3.9 Hz), 3.46 (s, 3H), 2.8−2.5 (m, 6H), 2.18 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.10 (s, 3H), 2.09 (s, 6H), 2.07 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.98 (s, 3H), 1.87 (s, 3H), 1.79 (m, 2H); HRMS (FAB, NBA) calcd for $C_{48}H_{69}N_2O_{28}S_2$ $(M - H)^-$ 1185.3478, found 1185.3517.

Compound 7d. Prepared as described for **7b**. Reaction of **4d** (155 mg, 0.218 mmol) with **3** (96 mg, 0.168 mmol) gave recovered **3** and **4d** (129 mg, mixture) and title compound **7d** (77 mg, 38%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.0−6.2 (m, 2H), 5.60 (dd, 1H, J = 3.9, 10.5 Hz), 5.47 (brs, 1H), 5.33 (brs, 1H), 5.27 (m, 1H), 5.08 (m, 3H), 4.85 (dd, 1H, J = 2.2, 12.5 Hz), 4.58 (d, 1H, J = 7.6 Hz), 4.46 (dd, 1H, J = 2.4, 12.0 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.39 (m, 1H), 4.27 (brd, 1H, J = 10.5 Hz), 4.20 (dd, 1H, J = 5.9, 12.0 Hz), 4.13 (dd, 1H, J = 8.1, 12.5 Hz), 4.05 (dt, 1H, J = 8.3, 9.3 Hz), 3.88 (t, 1H, J = 8.5 Hz), 3.83 (s, 3H), 3.75 (t, 1H, J = 6.3 Hz), 3.68 (m, 1H), 3.49 (d, 1H, J = 3.9 Hz), 3.46 (s, 3H), 2.71 (dd, 1H, J = 6.3, 13.9 Hz),

2.6−2.5 (m, 5H), 2.17 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.07 (s, 6H), 2.05 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.97 (s, 3H), 1.93 (s, 3H), 1.65 (m, 4H); HRMS (FAB, NBA) calcd for $C_{49}H_{71}N_2O_{28}S_2$ $(M - H)^-$ 1199.3635, found 1199.3663.

Compound 7e. Prepared as described for **7b**. Reaction of **4e** (146 mg, 0.201 mmol) with **3** (90 mg, 0.157 mmol) gave recovered **4e** (96 mg) and title compound **7e** (59 mg, 31%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (d, 1H, J = 9.8 Hz), 5.97 (d, 1H, J = 9.0 Hz), 5.58 (dd, 1H, J = 4.2, 10.5 Hz), 5.50 (brs, 1H), 5.34 (dd, 1H, J = 2.0, 3.2 Hz), 5.26 (ddd, 1H, J = 2.2, 3.2, 8.1 Hz), 5.09−5.05 (m, 3H), 4.88 (dd, 1H, J = 2.2, 12.5 Hz), 4.50 (d, 1H, J = 8.1 Hz), 4.47 (dd, 1H, J = 2.4, 11.7 Hz), 4.38 (d, 1H, J = 7.6 Hz), 4.38 (m, 1H), 4.26 (dd, 1H, J = 2.0, 10.5 Hz), 4.17 (dd, 1H, J = 5.6 Hz), 4.14 (dd, 1H, J = 8.1, 12.5 Hz), 4.05 (dt, 1H, J = 7.6, 9.5 Hz), 3.81 (t, 1H), 3.81 (s, 3H), 3.76 (dd, 1H, J = 5.6, 8.1 Hz), 3.67 (m, 1H), 3.46 (s, 3H), 3.45 (d, 1H, J = 4.2 Hz), 2.72 (dd, 1H, J = 5.1, 13.7 Hz), 2.60−2.45 (m, 5H), 2.17 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.91 (s, 3H), 1.7−1.4 (m, 6H); HRMS (FAB, NBA) calcd for $C_{50}H_{73}N_2O_{28}S_2$ $(M - H)^-$ 1213.3791, found 1213.3821.

Compound 8b. Prepared as described for **7b** from **5b** (131 mg, 0.191 mmol) and **3** (84 mg, 0.147 mmol). Recovered **5b** (43 mg) and title compound **8b** (114 mg, 66%) were obtained**. Compound 8b**: $[\alpha]^{28}_D$ −24° (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (d, 1H, J = 9.8 Hz), 5.60 (dd, 1H, J = 3.9, 10.0 Hz), 5.48 (d, 1H, J = 2.9 Hz), 5.33 (m, 1H), 5.27 (m, 1H), 5.21 (t, 1H, J = 9.5 Hz), 5.07 (dd, 1H, J = 7.8, 10.3 Hz), 5.01 (dd, 1H, J = 2.9, 10.3 Hz), 4.99 (dd, 1H, J = 7.8 Hz), 4.84 (m, 1H), 4.52 (d, 1H, J = 7.8 Hz), 4.45 (m, 1H, J = 12.0 Hz), 4.39 (d, 1H), 4.34 (dt, 1H, J = 9.8, 10.7 Hz), 4.27 (dd, 1H, J = 2.0, 10.7 Hz), 4.17 (dd, 1H, J = 5.6 Hz), 4.11 (dd, 1H, J = 8.3, 10.2 Hz), 3.95 (dd, 1H, J = 8.9 Hz), 3.84 (s, 3H), 3.74 (brt, 1H, J = 5.4, 8.1 Hz), 3.64 (m, 1H), 3.47 (s, 3H), 3.43 (d, 1H, J = 3.9 Hz), 2.8−2.6 (m, 5H), 2.55 (dd, 1H, J = 8.1, 13.9 Hz), 2.18 (s, 3H), 2.17 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.90 (s, 3H); HRMS (FAB, NBA) calcd for $C_{47}H_{66}NO_{29}S_2$ $(M - H)^-$ 1172.3162, found 1172.3123.

Compound 8c. Prepared as described for **7b** from **5c** (116 mg, 0.166 mmol) and **3** (73 mg, 0.128 mmol). Recovered **5c** (30 mg) and title compound **8c** (104 mg, 68%) were obtained**. Compound 8c**: $[\alpha]^{28}_D$ −7.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.02 (d, 1H, J = 9.8 Hz), 5.57 (dd, 1H, J = 4.2, 10.5 Hz), 5.52 (d, 1H, J = 3.4 Hz), 5.34 (dd, 1H, J = 2.0, 3.9 Hz), 5.27 (ddd, 1H, J = 2.4, 3.9, 8.3 Hz), 5.18 (t, 1H, J = 9.5 Hz), 5.15 (dd, 1H, J = 3.4, 10.3 Hz), 5.03 (dd, 1H, J = 7.8, 10.3 Hz), 4.95 (dd, 1H, J = 2.4, 12.5 Hz), 4.93 (dd, 1H, J = 7.8, 9.5 Hz), 4.61 (d, 1H, J = 7.8 Hz), 4.39 (q, 1H, J = 10.5 Hz), 4.38 (d, 1H, J = 7.8 Hz), 4.34 (dd, 1H, J = 2.7, 11.7 Hz), 4.28 (dd, 1H, J = 6.6, 11.7 Hz), 4.27 (dd, 1H, J = 2.0, 10.5 Hz), 4.08 (dd, 1H, J = 8.3, 12.5 Hz), 3.95 (t, 1H, J = 9.5 Hz), 3.82 (s, 3 H), 3.80 (m, 1H, J = 5.6 Hz), 3.66 (m, 1H), 3.50 (d, 1H, J = 4.2 Hz), 3.48 (s, 3H, 2.8−2.5 (m, 6H), 2.18 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.96 (s, 3H), 1.91 (s, 3H), 1.5 (m, 2H); HRMS (FAB, NBA) calcd for $C_{48}H_{68}NO_{29}S_2$ $(M - H)^-$ 1186.3318, found 1186.2899.

Compound 8d. Prepared as described for **7b**. From **5d** (128 mg, 0.166 mmol) and **3** (79 mg, 0.128 mmol), recovered **5d** (59 mg) and title compound **8d** (73 mg, 56%) were obtained. **Compound 8d**: $[\alpha]^{28}_D$ −2.7° (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (d, 1H, J = 9.8 Hz), 5.55 (dd, 1H, J = 4.2, 10.5 Hz), 5.49 (d, 1H, J = 2.4 Hz), 5.32 (dd, 1H, J = 2.2, 3.7 Hz), 5.26 (ddd, 1 H, J = 2.4, 3.7, 8.3 Hz), 5.20 (t, 1H, J = 9.5 Hz), 5.08 (dd, 1H, J = 2.4, 10.0 Hz), 5.05 (dd, 1H, J = 7.3, 10.0 Hz), 4.90 (dd, 1H, J = 7.8, 9.5 Hz), 4.89 (dd, 1H, J = 2.4, 12.5 Hz), 4.52 (d, 1H, J = 7.3 Hz), 4.43 (dd, 1H, J = 2.0, 12.0 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.39 (m, 1H), 4.20 (dd, 1H, J = 2.2, 10.5 Hz), 4.18 (dd, 1H, J = 6.1, 12.0 Hz), 4.10 (dd, 1H, J = 8.3, 12.5 Hz), 3.84 (t, 1H, J = 9.7 Hz), 3.81 (s, 3H), 3.74 (brt, 1H, J = 5.9, 7.6 Hz), 3.65 (m, 1H), 3.48 (s, 3H), 3.46 (d, 1H, J = 4.2 Hz), 2.69 (dd, 1H, J = 5.9, 14.2 Hz), 2.6−2.5 (m, 5H), 2.18 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.03 (s, 3H), 1.96 (s, 3H), 1.91 (s, 3H), 1.64 (m, 4H); HRMS (FAB, NBA) calcd for $C_{49}H_{70}NO_{29}S_2$ $(M - H)^-$ 1200.3475, found 1200.3293.

Compound 8e. Prepared as described for **7b**. Reaction of **5e** (101 mg, 0.139 mmol) with **3** (61 mg, 0.107 mmol) gave recovered **5e** (30 mg) and title compound **8e** (91 mg, 54%): $[\alpha]^{28}_D$ −5.5° (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (d, 1H, J = 9.9 Hz), 5.57 (dd, 1H, J = 3.9, 10.3 Hz), 5.47 (d, 1H, J = 3.2 Hz), 5.32 (dd, 1H, J = 1.7, 3.7 Hz), 5.26 (ddd, 1H, J = 2.2, 3.7, 8.3 Hz), 5.20 (t, 1H, J = 9.5 Hz), 5.08 (dd, 1H, J = 3.2, 10.3 Hz), 5.05 (dd, 1H, J = 7.6, 10.3 Hz), 4.91 (dd, 1H, J = 7.8, 9.5 Hz), 4.89 (dd, 1H, J = 2.2, 12.5 Hz), 4.54 (d, 1H, J = 7.6 Hz), 4.5−4.4 (m, 2H), 4.38 (d, 1H, J = 7.8 Hz), 4.22 (dd, 1H, J = 1.7, 11.0 Hz), 4.19 (dd, 1H, J = 5.3, 12.0 Hz), 4.10 (dd, 1H, J = 8.3, 12.5 Hz), 3.90 (t, 1H, J = 9.5 Hz), 3.82 (s, 3H), 3.76 (brt, 1H, J = 6.3 Hz), 3.65 (m, 1H), 3.49 (d, 1H, J = 3.9 Hz), 3.48 (s, 3H), 2.70 (dd, 1H, J = 6.3, 13.9 Hz), 2.6−2.4 (m, 5H), 2.17 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.03 (s, 3H), 1.97 (s, 3H), 1.91 (s, 3H), 1.6−1.5 (m, 4H), 1.5−1.4 (m, 2H); HRMS (FAB, NBA) calcd for $C_{50}H_{72}NO_{29}S_2$ $(M - H)^-$ 1214.3631, found 1214.3585.

Compound 18a. Compound **7a** (20.1 mg, 17.3 μmol) and 2-cyanoethyl 2′,3′-*O*,*N*^{4}-triacetylcytidin-5′-yl *N*,*N*-diisopropylphosphoramidite **6** (29.6 mg, 52.0 μmol) were dried by coevaporation with dry EtOAc (two times). After addition of 1*H*-tetrazole (5.5 mg, 79 μmol), dry MeCN (0.8 mL) was instilled into the mixture with stirring at −40 °C under a nitrogen atmosphere and the mixture was warmed slowly to room temperature. After stirring for 30 min at room temperature, the mixture was diluted with EtOAc, washed with $NaHCO_3$ solution, dried, and concentrated. To the solution of the residue in MeCN (0.8 mL) were added Me_2S (120 μL, 1.73 mmol) and *t*-BuOOH (32 μL, 0.17 mmol) successively at 0 °C, and the mixture was stirred for 3 h at room temperature. After the mixture was cooled to 0 °C, DBU (7.8 μL, 52 μmol) was added, and the mixture was stirred for 5 min at 0 °C. Then, MeOH (1.6 mL) and 28% methanolic sodium methoxide (16 μL) were added. After stirring for 19 h at room temperature, the solution was concentrated to half volume in vacuo over a water bath (30 °C). The solution was applied to a column of Sephadex G-15 (1.5 × 60 cm) through a cotton plague and eluted with H_2O. Fractions containing the product were collected and concentrated. The residue was purified further by ODS column chromatography to afford **18a** [12.8 μmol (estimated by UV detection; cytidine at 280 nm), 74%]: ^{1}H NMR (400 MHz, D_2O) δ 7.86 (d, 1H, J = 7.6 Hz), 6.06 (d, 1H, J = 7.6 Hz), 5.86 (d, 1H, J = 3.2 Hz), 4.36 (d, 1H, J = 7.8 Hz), 4.35−4.33 (m, 2H), 4.19−4.04 (m, 7H), 3.87 (brd, 1H, J = 12.2 Hz), 3.84 (d, 1H, J = 3.2 Hz), 3.81−3.69 (m, 9H), 3.52−3.46 (m, 7H), 3.40 (dd, 1H, J = 8.1, 10.0 Hz), 3.39 (s, 3H), 3.33 (d, 1H, J = 9.8 Hz), 2.81−2.70 (m, 2H), 1.93 (s, 3H), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{37}H_{59}N_5O_{26}PS_2$ $(M - H)^-$ 1084.2627, found 1084.2664.

Compound 18b. Prepared as described for **18a**. Compound **7b** (20.7 mg, 17.6 μmol) was converted to compound **18b** (15.7 mg, 80.9%): ^{1}H NMR (400 MHz, D_2O) δ 7.78 (d, 1H, J = 7.6 Hz), 6.06 (d, 1H, J = 7.6 Hz), 5.86 (d, 1H, J = 2.2 Hz), 4.35 (d, 1H, J = 7.8 Hz), 4.33 (d, 1H, J = 7.8 Hz), 4.27 (dd, 1H, J = 4.2, 9.5 Hz), 4.17−4.04 (m, 6H), 4.02 (d, 1H, J = 10.5 Hz), 3.86 (brd, 1H, J = 12.6 Hz), 3.81 (d, 1H, J = 3.4 Hz), 3.81−3.73 (m, 5H), 3.70 (dd, 1H, J = 5.1, 12.6 Hz), 3.65−3.45 (m, 7H), 3.39 (dd, 1H, J = 7.8, 9.5 Hz), 3.37 (s, 3H), 3.34 (d, 1H, J = 4.2 Hz), 3.31 (d, 1H, J = 9.5 Hz), 2.72−2.65 (m, 6H), 1.91 (s, 3H), 1.89 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{38}H_{61}N_5O_{26}PS_2$ $(M - H)^-$ 1098.2784, found 1098.2799.

Compound 18c. Prepared as described for **18a**. Compound **7c** (27.8 mg, 23.4 μmol) was converted to compound **18c** (15.0 μmol, 64%): ^{1}H NMR (400 MHz, D_2O) δ 7.78 (d, 1H, J = 7.6 Hz), 5.98 (d, 1H, J = 7.6 Hz), 5.84 (d, 1H, J = 3.2 Hz), 4.35 (d, 1H, J = 7.8 Hz), 4.33 (d, 1H, J = 8.1 Hz), 4.26 (dd, 1H, J =

4.2, 9.5 Hz), 4.16−4.03 (m, 6H), 4.02 (d, 1H, J = 10.5 Hz), 3.86 (dd, 1H, J = 1.7, 12.2 Hz), 3.81 (d, 1H, J = 3.2 Hz), 3.78−3.73 (m, 5H), 3.70 (dd, 1H, J = 5.1 Hz), 3.65−3.46 (m, 7H), 3.39 (dd, 1H, J = 10.0 Hz), 3.37 (s, 3H), 3.30 (d, 1H, J = 9.5 Hz), 3.29 (d, 1H, J = 4.2 Hz), 2.68 (dd, 1H, J = 8.1, 14.2 Hz), 2.65 (dd, 1H, J = 5.9, 14.2 Hz), 2.58−2.51 (m, 4H), 1.91 (s, 3H), 1.89 (s, 3H), 1.73−1.66 (m, 2H); HRMS (FAB, glycerol) calcd for $C_{39}H_{63}N_5O_{26}PS_2$ $(M - H)^-$ 1112.2940, found 1112.2937.

Compound 18d. Prepared as described for **18a**. Compound **7d** (26.5 mg, 22.1 μmol) was converted to compound **18d** (6.2 μmol, 39%): ^{1}H NMR (400 MHz, D_2O) δ 7.79 (d, 1H, J = 7.6 Hz), 5.98 (d, 1H, J = 7.6 Hz), 5.84 (d, 1H, J = 2.4 Hz), 4.35 (d, 1H, J = 7.8 Hz), 4.33 (d, 1H, J = 7.8 Hz), 4.26 (dd, 1H, J = 4.2, 9.3 Hz), 4.15−4.03 (m, 6H), 4.02 (d, 1H, J = 10.5 Hz), 3.86 (brd, 1H, J = 12.2 Hz), 3.81 (d, 1H, J = 3.2 Hz), 3.78−3.74 (m, 5H), 3.70 (dd, 1H, J = 5.1, 12.2 Hz), 3.64−3.46 (m, 7H), 3.39 (t, 1H), 3.37 (s, 3H), 3.30 (d, 1H, J = 10.5 Hz), 3.30 (d, 1H, J = 4.2 Hz), 2.68 (dd, 1H, J = 8.1, 13.7 Hz), 2.65 (dd, 1H, J = 5.1 Hz), 2.53−2.43 (m, 4H), 1.91 (s, 3H), 1.90 (s, 3H), 1.50 (brs, 4H); HRMS (FAB, glycerol) calcd for $C_{40}H_{65}N_5O_{26}PS_2$ $(M - H)^-$ 1126.3097, found 1126.3051.

Compound 18e. Prepared as described for **18a** from compound **7e** (19.5 mg, 16.0 μmol), affording 9.6 μmol (60%) of compound **18e**: ^{1}H NMR (400 MHz, D_2O) δ 7.85 (d, 1H, J = 7.8 Hz), 6.03 (d, 1H, J = 7.8 Hz), 5.84 (d, 1H, J = 2.0 Hz), 4.34 (d, 1H, J = 7.8 Hz), 4.32 (d, 1H, J = 7.8 Hz), 4.26 (dd, 1H, J = 4.2, 9.3 Hz), 4.17−4.03 (m, 6H), 4.02 (d, 1H, J = 11.0 Hz), 3.86 (brd, 1H, J = 12.2 Hz), 3.81 (d, 1H, J = 3.2 Hz), 3.78−3.74 (m, 5H), 3.70 (dd, 1H, J = 5.1, 12.2 Hz), 3.64−3.45 (m, 7H), 3.39 (t, 1H, J = 10.0 Hz), 3.37 (s, 3H), 3.30 (d, 1H, J = 10.0 Hz), 3.29 (d, 1H), 2.68 (dd, 1H, J = 8.1, 13.7 Hz), 2.65 (dd, 1H, J = 5.4, 13.7 Hz), 2.52−2.42 (m, 4H), 1.91 (s, 3H), 1.89 (s, 3H), 1.48−1.39 (m, 4H), 1.34−1.27 (m, 2H); HRMS (FAB, glycerol) calcd for $C_{41}H_{67}N_5O_{26}PS_2$ $(M - H)^-$ 1140.3253, found 1140.3263.

Compound 19a. Prepared as described for **18a**. Compound **8a** (13.1 mg, 11.3 μmol) was converted to give 9.8 μmol (87%) of compound **19a**: ^{1}H NMR (400 MHz, D_2O) δ 7.83 (d, 1H, J = 7.6 Hz), 6.03 (d, 1H, J = 7.6 Hz), 5.83 (d, 1H, J = 2.0 Hz), 4.32 (m, 1H, J = 3.9 Hz), 4.31 (d, 1H, J = 8.1 Hz), 4.26 (d, 1H, J = 7.8 Hz), 4.2−4.0 (m, 7H), 3.87 (brd, 1H, J = 12.0 Hz), 3.81 (d, 1H, J = 2.7 Hz), 3.78−3.64 (m, 9H), 3.57 (d, 1H, J = 3.9 Hz), 3.52−3.46 (m, 5H), 3.43 (s, 3H), 3.38 (t, 1H, J = 10.0 Hz), 3.31 (d, 1H, J = 9.5 Hz), 3.17 (dd, 1H, J = 9.0 Hz), 2.77 (dd, 1H, J = 7.8, 13.9 Hz), 2.74 (dd, 1H, J = 5.6 Hz), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{35}H_{56}N_4O_{26}PS_2$ $(M - H)^-$ 1043.2362, found 1043.2390.

Compound 19b. Prepared as described for **18a**. Compound **8b** (12.4 mg, 10.6 μmol) was converted to 7.5 μmol (71%) of compound **19b**: ^{1}H NMR (400 MHz, D_2O) δ 7.79 (d, 1H, J = 8.1 Hz), 5.99 (d, 1H, J = 8.1 Hz), 5.83 (d, 1H, J = 2.9 Hz), 4.31 (d, 1H, J = 7.6 Hz), 4.27 (dd, 1H, J = 4.4, 9.5 Hz), 4.26 (d, 1H, J = 7.8 Hz), 4.2−4.0 (m, 7H), 3.84 (brd, 1H, J = 12.7 Hz), 3.80 (d, 1H, J = 3.4 Hz), 3.80−3.73 (m, 5H), 3.68−3.60 (m, 2H), 3.54−3.46 (m, 5H), 3.43 (s, 3H), 3.38 (dd, 1H, J = 9.2 Hz), 3.35 (d, 1H), 3.30 (d, 1H, J = 9.5 Hz), 3.18 (dd, 1H, J = 8.8 Hz), 2.75−2.63 (m, 6H), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{36}H_{58}N_4O_{26}PS_2$ $(M - H)^-$ 1057.2518, found 1057.2524.

Compound 19c. Prepared as described for **18a**. Compound **8c** (23.6 mg, 19.9 μmol) was converted to compound **19c** (12.0 μmol, 60%): ^{1}H NMR (400 MHz, D_2O) δ 7.76 (d, 1H, J = 7.8 Hz), 5.97 (d, 1H, J = 7.8 Hz), 5.84 (d, 1H, J = 2.9 Hz), 4.31 (d, 1H, J = 7.6 Hz), 4.25 (m, 2H), 4.15−3.99 (m, 7H), 3.84 (brd, 1H, J = 12.5 Hz), 3.80 (d, 1H, J = 3.4 Hz), 3.77−3.73 (m, 5H), 3.68−3.61 (m, 2H), 3.54−3.46 (m, 5H), 3.43 (s, 3H), 3.38 (t, 1H, J = 9.0 Hz), 3.30 (d, 1H, J = 4.9 Hz), 3.29 (d, 1H, J = 9.5 Hz), 3.17 (dd, 1H, J = 8.8 Hz), 2.69 (dd, 1H, J = 8.5, 13.9 Hz), 2.65 (dd, 1H, J = 5.1 Hz), 2.58−2.51 (m, 4H), 1.90 (s, 3H), 1.73−1.66 (m, 2H); HRMS (FAB, glycerol) calcd for $C_{37}H_{60}N_4O_{26}PS_2$ $(M - H)^-$ 1071.2675, found 1071.2640.

Compound 19d. Prepared as described for **18a**. From compound **8d** (12.6 mg, 10.5 μmol), 7.2 μmol (68%) of compound **19d** was obtained: ^{1}H NMR (400 MHz, D_2O) δ 7.82 (d, 1H, J = 7.6 Hz), 6.01 (d, 1H, J = 7.6 Hz), 5.84 (d, 1H, J = 3.2 Hz), 4.32 (d, 1H, J = 7.8 Hz), 4.26 (m, 2H), 4.16−4.00 (m, 7H), 3.85 (brd, 1H, J = 12.0 Hz), 3.82 (d, 1H, J = 3.4 Hz), 3.80−3.73 (m, 5H), 3.67 (dd, 1H, J = 3.9, 12.0 Hz), 3.63 (dd, 1H, J = 5.9, 8.3 Hz), 3.55−3.47 (m, 5H), 3.44 (s, 3H), 3.39 (dd, 1H, J = 9.0 Hz), 3.31 (d, 1H, J = 9.5 Hz), 3.30 (d, 1H, J = 4.9 Hz), 3.18 (dd, 1H, J = 8.8 Hz), 2.71 (dd, 1H, J = 8.3, 13.9 Hz), 2.65 (dd, 1H, J = 5.9, 13.9 Hz), 2.57−2.46 (m, 4H), 1.91 (s, 3H), 1.57−1.52 (m, 4H); HRMS (FAB, glycerol) calcd for $C_{38}H_{62}N_4O_{26}PS_2$ $(M - H)^-$ 1085.2831, found 1085.2847.

Compound 19e. Prepared as described for **18a**. From compound **8e** (15.1 mg, 12.4 μmol), 8.5 μmol (69%) of compound **19e** was obtained: ^{1}H NMR (400 MHz, D_2O) δ 7.76 (d, 1H, J = 7.6 Hz), 5.96 (d, 1H, J = 7.6 Hz), 5.83 (d, 1H, J = 3.2 Hz), 4.31 (d, 1H, J = 7.8 Hz), 4.23−4.27 (m, 2H), 4.15−3.98 (m, 7H), 3.84 (brd, 1H, J = 11.9 Hz), 3.80 (d, 1H, J = 3.4 Hz), 3.78−3.72 (m, 5H), 3.66 (dd, 1H, J = 3.9 Hz), 3.61 (dd, 1H, J = 5.6, 8.1 Hz), 3.54−3.45 (m, 5H), 3.42 (s, 3H), 3.38 (t, 1H, J = 10.0 Hz), 3.29 (d, 1H, J = 9.5 Hz), 3.27 (d, 1H, J = 4.4 Hz), 3.17 (t, 1H, J = 8.8 Hz), 2.69 (dd, 1H, J = 8.1, 13.9 Hz), 2.65 (dd, 1H, J = 5.6, 13.9 Hz), 2.53−2.40 (m, 4H), 1.90 (s, 3H), 1.48−1.38 (m, 4H), 1.32−1.26 (m, 4H); HRMS (FAB, glycerol) calcd for $C_{39}H_{64}N_4O_{26}PS_2$ $(M - H)^-$ 1099.2988, found 1099.2980.

Compound 1a. To a 0.5 M D_2O solution of compound **18a** (0.39 mL, 1.9 μmol) in a NMR tube was added lithium hydroxide (6.0 mg, 0.25 mmol) at room temperature, and saponification of the methyl ester of **18a** was monitored by a NMR spectrometer. At the maximum accumulation of **1a**, the solution was applied directly to a column of sephadex G-15 (1 × 25 cm) and eluted with 10 mM NH_4HCO_3 solution. The fractions containing **1a** were lyophilized. Purification of the residue by FPLC (mono Q; 50 mM NH_4HCO_3) afforded **1a** [0.85 μmol (estimated by UV detection; cytidine at 280 nm), 44%]: ^{1}H NMR (400 MHz, D_2O) δ 7.86 (d, 1H, J = 7.3 Hz), 6.01 (brd, 1H, J = 7.3 Hz), 5.86 (d, 1H, J = 3.9 Hz), 4.39 (d, 1H, J = 7.8 Hz), 4.36−4.33 (m, 2H), 4.23 (t, 1H, J = 4.4 Hz), 4.19 (t, 1H, J = 4.4 Hz), 4.13−4.08 (m, 3H), 4.05 (t, 1H, J = 11.5 Hz), 4.00 (d, 1H, J = 10.5 Hz), 3.89−3.70 (m, 8H), 3.63−3.47 (m, 7H), 3.39 (m, 1H), 3.38 (s, 3H), 3.22 (d, 1H, J = 9.5 Hz), 2.70 (dd, 1H, J = 4.2, 13.9 Hz), 2.67 (dd, 1H, J = 8.8, 13.9 Hz), 1.93(s, 3H), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{36}H_{57}N_5O_{26}PS_2$ $(M-H)^-$ 1070.2471, found 1070.2466.

Compound 1b. Prepared as described for **1a**. From compound **18b** (3.73 μmol), 0.97 μmol (41%) of compound **1b** (0.97 μmol, 41%) was obtained: ^{1}H NMR (400 MHz, D_2O) δ 7.85 (d, 1H, J = 7.6 Hz), 6.04 (brs, 1H), 5.85 (d, 1H, J = 3.9 Hz), 4.37 (d, 1H, J = 7.8 Hz), 4.34 (d, 1H, J = 7.8 Hz), 4.26 (dd, 1H, J = 4.2, 9.3 Hz), 4.21 (t, 1H, J = 4.9 Hz), 4.19−4.05 (m, 4H), 4.02 (t, 1H, J = 10.0 Hz), 3.98 (d, 1H, J = 10.5 Hz), 3.89−3.47 (m, 12H), 3.40 (m, 1H), 3.38 (s, 3H), 3.27 (d, 1H, J = 4.1 Hz), 3.23 (d, 1H, J = 9.5 Hz), 2.75−2.65 (m, 6H), 1.92 (s, 3H), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{37}H_{59}N_5O_{26}PS_2$ $(M - H)^-$ 1084.2623, found 1084.2628.

Compound 1c. Compound **15c** (2.41 μmol) was treated in a manner as described for the preparation of **1a** to give compound **1c** (0.55 μmol, 23%): ^{1}H NMR (400 MHz, D_2O) δ 7.85 (d, 1H, J = 7.6 Hz), 6.00 (brd, 1H, J = 7.4 Hz), 5.85 (d, 1H, J = 4.2 Hz), 4.37 (d, 1H, J = 7.8 Hz), 4.34 (d, 1H, J = 7.8 Hz), 4.26 (dd, 1H, J = 4.2, 10.0 Hz), 4.22 (t, 1H, J = 4.9 Hz), 4.19 (t, 1H), 4.12−4.05 (m, 3H), 4.03 (t, 1H, J = 10.5 Hz), 3.98 (d, 1H, J = 10.5 Hz), 3.88−3.83 (m, 3H), 3.75 (brd, 1H, J = 10.3 Hz), 3.71 (dd, 1H, J = 4.9, 12.5 Hz), 3.67−3.46 (m, 7H), 3.39 (m, 1H), 3.38 (s, 3H), 3.24 (d, 1H, J = 4.2 Hz), 3.23 (d, 1H, J = 9.5 Hz), 2.70−7.62 (m, 2H), 2.61−2.52 (m, 4H), 1.92 (s, 3H), 1.91 (s, 3H), 1.73−1.68 (m, 2H); HRMS (FAB, glycerol) calcd for $C_{38}H_{61}N_5O_{26}PS_2$ $(M - H)^-$ 1198.2784, found 1098.2781.

Compound 1d. Compound **18d** (2.76 μmol) was treated in a manner as described for the preparation of **1a** to give compound **1c** (0.57 μmol, 21%): ^{1}H NMR (400 MHz, D_2O) δ 7.84 (d, 1H, J = 7.6 Hz), 5.99 (d, 1H), 5.84 (d, 1H, J = 4.2 Hz), 4.35 (d, 1H, J = 7.8 Hz), 4.33 (d, 1H, J = 7.8 Hz), 4.24 (dd, 1H, J = 4.2 Hz), 4.22 (t, 1H, J = 4.6 Hz), 4.18 (t, 1H, J = 4.2 Hz), 4.11−4.03 (m, 3H), 4.03 (t, 1H, J = 10.3 Hz), 3.98 (d, 1H,

J = 10.7 Hz), 3.88−3.83 (m, 3H), 3.75 (brd, 1H, J = 10.3 Hz), 3.71 (dd, 1H, J = 4.9, 12.5 Hz), 3.67−3.46 (m, 7H), 3.39 (dd, 1H), 3.38 (s, 3H), 3.23 (d, 1H), 3.23 (d, 1H, J = 9.5 Hz), 2.70−7.62 (m, 2H), 2.55−2.43 (m, 4H), 1.91(s, 3H), 1.90 (s, 3H), 1.52 (brs, 4H); HRMS (FAB, glycerol) calcd for $C_{39}H_{63}N_5O_{26}PS_2$ (M − H)$^-$ 1112.2940, found 1112.2949.

Compound 1e. Compound **18e** (2.51 μmol) was treated in a manner as described for the preparation of **1a** to give compound **1e** (0.32 μmol, 13%): ^{1}H NMR (400 MHz, D_2O) δ 7.84 (d, 1H, J = 7.6 Hz), 5.99 (brd, 1H), 5.84 (d, 1H, J = 4.2 Hz), 4.34 (d, 1H, J = 7.6 Hz), 4.33 (d, 1H, J = 7.2 Hz), 4.23 (dd, 1H, J = 4.0, 10.5 Hz), 4.21 (t, 1H, J = 4.9 Hz), 4.17 (t, 1H, J = 4.9 Hz), 4.12−4.07 (m, 3H), 4.00 (t, 1H, J = 10.7 Hz), 3.97 (d, 1H, J = 10.7 Hz), 3.85 (brd, 1H, J = 12.2 Hz), 3.82−3.79 (m, 2H), 3.74 (brd, 1H, J = 11.8 Hz), 3.70 (dd, 1H, J = 4.9, 12.2 Hz), 3.64−3.45 (m, 7H), 3.38 (dd, 1H), 3.37 (s, 3H), 3.22 (d, 1H, J = 4.6 Hz), 3.22 (d, 1H, J = 9.3 Hz), 2.72−7.63 (m, 2H), 2.55−2.42 (m, 4H), 1.91 (s, 3H), 1.89 (s, 3H), 1.50−1.40 (m, 4H), 1.36−1.28 (m, 2H); HRMS (FAB, glycerol) calcd for $C_{40}H_{65}N_5O_{26}PS_2$ (M − H)$^-$ 1126.3097, found 1126.3075.

Compound 2a. Compound **19a** (2.36 μmol) was treated in a manner as described for the preparation of **1a** to give compound **2a** (1.14 μmol, 49%): ^{1}H NMR (400 MHz, D_2O) δ 7.83 (d, 1H, J = 7.6 Hz), 5.99 (brd, 1H, J = 7.4 Hz), 5.83 (d, 1H, J = 4.2 Hz), 4.34 (d, 1H, J = 8.1 Hz), 4.32 (dd, 1H, J = 4.4, 9.8 Hz), 4.26 (d, 1H, J = 8.1 Hz), 4.20 (t, 1H, J = 5.1 Hz), 4.17 (t, 1H, J = 4.9 Hz), 4.10−4.00 (m, 4H), 3.99 (d, 1H, J = 10.3 Hz), 3.86−3.65 (m, 8H), 3.55 (dd, 1H, J = 3.4, 10.0 Hz), 3.52−3.48 (m, 5H), 3.43 (s, 3H), 3.38 (t, 1H, J = 9.8 Hz), 3.23 (d, 1H, J = 9.8 Hz), 3.17 (dd, 1H, J = 8.7 Hz), 2.82 (dd, 1H, J = 4.8, 13.9 Hz), 2.77 (dd, 1H, J = 8.8, 13.9 Hz), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{34}H_{54}N_4O_{26}PS_2$ (M − H)$^-$ 1029.2205, found 1029.2253.

Compound 2b. Compound **19b** (3.22 μmol) was treated in a manner as described for the preparation of **1a** to give compound **2b** (0.95 μmol, 30%): ^{1}H NMR (400 MHz, D_2O) δ 7.83 (d, 1H, J = 7.6 Hz), 5.98 (d, 1H, J = 7.6 Hz), 5.83 (d, 1H, J = 4.2 Hz), 4.33 (d, 1H, J = 7.8 Hz), 4.26 (d, 1H, J = 7.8 Hz), 4.25 (m, 1H), 4.20 (t, 1H, J = 4.9 Hz), 4.17 (t, 1H, J = 5.0 Hz), 4.12−4.04 (m, 3H), 4.01 (d, 1H, J = 10.0 Hz), 3.97 (d, 1H, J = 10.5 Hz), 3.86−3.78 (m, 3H), 3.74 (brd, 1H, J = 12.0 Hz), 3.68−3.63 (m, 2H), 3.54 (dd, 1H, J = 3.4, 10.0 Hz), 3.53−3.45 (m, 4H), 3.43 (s, 3H), 3.38 (dd, 1H), 3.26 (d, 1H, J = 4.2 Hz), 3.22 (d, 1H, J = 10.0 Hz), 3.19 (dd, 1H, J = 8.8 Hz), 2.77−2.65 (m, 6H), 1.91 (s, 3H); HRMS (FAB, glycerol) calcd for $C_{35}H_{56}N_4O_{26}PS_2$ (M − H)$^-$ 1043.2362, found 1043.2317.

Compound 2c. Compound **19c** (1.77 μmol) was treated in a manner as described for the preparation of **1a** to give compound **2c** (0.34 μmol, 19%): ^{1}H NMR (400 MHz, D_2O) δ 7.84 (d, 1H, J = 7.6 Hz), 5.99 (brd, 1H, J = 6.9 Hz), 5.84 (d, 1H, J = 4.4 Hz), 4.33 (d, 1H, J = 7.8 Hz), 4.26 (d, 1H, J = 8.1 Hz), 4.25−4.20 (m, 2H), 4.17 (t, 1H, J = 4.9 Hz), 4.12−4.02 (m, 3H), 4.01 (t, 1H, J = 10.3 Hz), 3.97 (d, 1H, J = 10.5 Hz), 3.86−3.78 (m, 3H), 3.75 (brd, 1H, J = 12.0 Hz), 3.68−3.63 (m, 2H), 3.54 (dd, 1H, J = 3.4, 10.0 Hz), 3.53−3.45 (m, 4H), 3.43 (s, 3H), 3.38 (dd, J = 8.0, 9.8 Hz, 1H), 3.23 (d, 1H, J = 4.2 Hz), 3.22 (d, 1H, J = 10.5 Hz), 3.19 (t, 1H, J = 8.5 Hz), 2.70 (dd, 1H, J = 7.6, 10.0 Hz), 2.68 (dd, 1H, J = 6.1 Hz), 2.60−2.51 (m, 4H), 1.91 (s, 3H), 1.75−1.70 (m, 2H); HRMS (FAB, glycerol) calcd for $C_{36}H_{58}N_4O_{26}PS_2$ (M − H)$^-$ 1057.2518, found 1057.2518.

Compound 2d. Compound **19d** (1.64 μmol) was treated in a manner as described for the preparation of **1a** to give compound **2d** (0.20 μmol, 12%): ^{1}H NMR (400 MHz, D_2O) δ 7.84 (d, 1H, J = 7.6 Hz), 5.99 (brd, 1H, J = 6.8 Hz), 5.84 (d, 1H, J = 4.2 Hz), 4.32 (d, 1H, J = 7.8 Hz), 4.26 (d, 1H, J = 7.8 Hz), 4.25−4.20 (m, 2H), 4.17 (t, 1H, J = 4.9 Hz), 4.12−4.06 (m, 3H), 4.00 (d, 1H, J = 10.0 Hz), 3.96 (d, 1H, J = 10.5 Hz), 3.86−3.80 (m, 3H), 3.74 (brd, 1H, J = 12.0 Hz), 3.68−3.61 (m, 2H), 3.55−3.45 (m, 5H), 3.43 (s, 3H), 3.38 (dd, 1H, J = 9.8 Hz), 3.23−3.21 (m, 2H), 3.18 (t, 1H, J = 9.3 Hz), 2.70 (dd, 1H, J = 7.8, 14.2 Hz), 2.67 (dd, 1H, J = 5.6, 14.2 Hz), 2.57−2.45 (m, 4H), 1.91 (s, 3H), 1.53 (brs, 4H); HRMS (FAB, glycerol) calcd for $C_{37}H_{60}N_4O_{26}PS_2$ (M − H)$^-$ 1071.2675, found 1071.2698.

Compound 2e. Compound **19e** (1.93 μmol) was treated in a manner as described for the preparation of **1a** to give compound **2e** (0.18 μmol, 9.2%): ^{1}H NMR (400 MHz, D_2O) δ 7.84 (d, 1H, J = 7.6 Hz), 5.99 (brd, 1H, J = 6.6 Hz), 5.84 (d, 1H, J = 3.2 Hz), 4.32 (d, 1H, J = 7.8 Hz), 4.26 (d, 1H, J = 7.8 Hz), 4.23 (m, 2H), 4.17 (t, 1H, J = 4.6 Hz), 4.11−4.05 (m, 3H), 4.00 (t, 1H, J = 10.5 Hz), 3.96 (d, 1H, J = 10.5 Hz), 3.86−3.80 (m, 3H), 3.74 (brd, 1H, J = 12.0 Hz), 3.68−3.61 (m, 2H), 3.54−3.42 (m, 5H), 3.43 (s, 3H), 3.38 (dd, 1H, J = 9.8 Hz), 3.22 (m, 2H), 3.18 (dd, 1H, J = 9.3 Hz), 2.72−7.62 (m, 2H), 2.53−2.42 (m, 4H), 1.91 (s, 3H), 1.49−1.39 (m, 4H), 1.36−1.28 (m, 4H); HRMS (FAB, glycerol) calcd for $C_{38}H_{62}N_4O_{26}PS_2$ (M − H)$^-$ 1085.2831, found 1085.2837.

Sialyltransferase Assay. Rat recombinant α(2,6)-sialyltransferase expressed in *Spodoptera frugiperda* (EC 2.4.99.1) and rat recombinant α(2,3)-sialyltransferase expressed in *S. frugiperda* (EC 2.4.99.5) were purchased from Calbiochem−Novabiochem Co. Kinetic parameters were calculated by fitting the initial rates to the Michaelis−Menten equation. In all assays the consumption of CMP−NeuAc was limited to less than 15% under the following conditions.

Inhibition curves of **1**/**2a**−**e** shown in Figure 3 were determined using five different concentration of inhibitors from 0−200 μM as mentioned in Figure 3. The assay mixtures contained 25 mM sodium cacodylate (pH 6.5), 0.25% Triton X-100, 1 mg/mL BSA, 200 μM CMP−NeuAc **18**, 1.00 mM *p*NP LacNAc **20**, and sialyltransferase in a total volume of 30 μL. The assay tubes were incubated at 37 °C for 30 min and heated over an oil bath at 95 °C for 2 min. Each sample was analyzed by HPLC as described in ref 22.

The kinetic parameters of **1**/**2a**−**e** for the donor shown in Table 1 were determined at three different concentrations of inhibitor, 100, 50, and 0 μM, and CMP−NeuAc 200, 100, and 50 μM. The assay mixtures contained 25 mM sodium cacodylate (pH 6.5), 0.25% Triton X-100, 1 mg/mL BSA, 1.00 mM *p*NP LacNAc, and sialyltransferase in a total volume of 30 μL. The assay tubes were incubated at 37 °C for 30 min and heated over oil bath at 95 °C for 2 min. Each sample was analyzed by HPLC as described in ref 22.

The kinetic parameters of **1**/**2a**−**e** for the acceptor shown in Table 1 were determined at three different concentrations of inhibitor, 100, 50, and 0 μM, and *p*NP LacNAc, 2.00, 1.00, and 0.50 mM. The assay mixtures contained 25 mM sodium cacodylate (pH 6.5), 0.25% Triton X-100, 1 mg/mL BSA, 200 μM CMP−NeuAc, and sialyltransferase in a total volume of 30 μL. The assay tubes were incubated at 37 °C for 30 min and heated over an oil bath at 95 °C for 2 min. All samples were analyzed by HPLC as described in ref 22.

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Supporting Information Available: ^{1}H NMR spectra of compounds **1a**−**e**, **2a**−**e**, **5b**, **5d**, **7a**−**e**, **8a**−**e**, **9a**, **10a**, **10d**, **15b**, **18a**−**e**, and **19a**−**e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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