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Glycosylation

Synthesis of Disaccharide Nucleosides by the *O*-Glycosylation of Natural Nucleosides with Thioglycoside Donors

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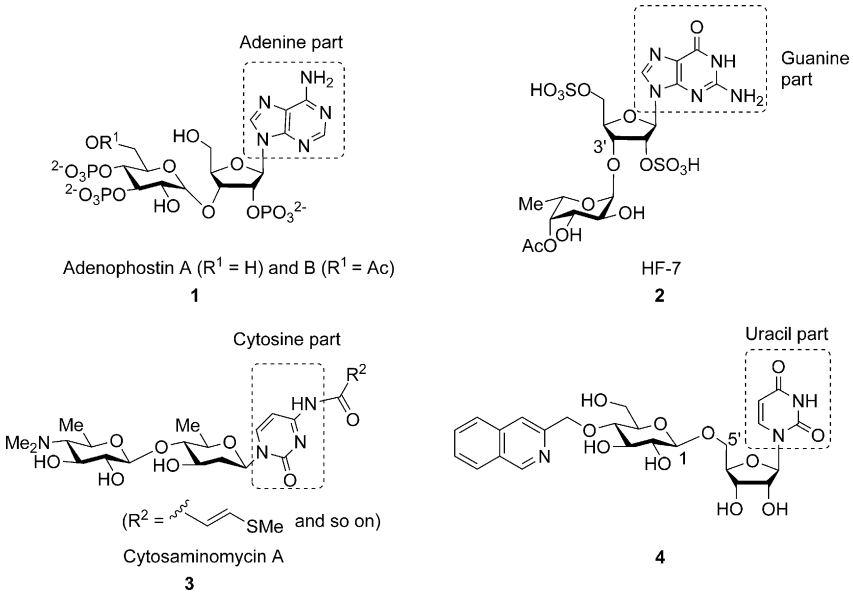
Abstract: Disaccharide nucleosides constitute an important group of naturally-occurring sugar derivatives. In this study, we report on the synthesis of disaccharide nucleosides by the direct *O*-glycosylation of nucleoside acceptors, such as adenosine, guanosine, thymidine, and cytidine, with glycosyl donors. Among the glycosyl donors tested, thioglycosides were found to give the corresponding disaccharide nucleosides in moderate to high chemical yields with the above nucleoside acceptors using *p*-toluenesulfenyl chloride (TolSCl) and silver triflate (AgOTf) as promoters. The interaction of these promoters with nucleoside acceptors was examined by ^{1}H NMR spectroscopic experiments.

Introduction

Disaccharide nucleosides constitute an important class of natural compounds that are found in tRNA, poly(ADP-ribose), antibiotics, and other biologically active compounds.[1] These compounds contain an external sugar moiety linked to one of the hydroxy groups of the nucleoside via an *O*-glycoside bond.[1,2] Typical examples include adenophostins **1**,[3] HF-7 **2**,[4] cytosaminomycins **3** and ezomycin derivatives,[6] and some candidates for inhibitors of chitin synthetase **4**,[7] which contain adenine, guanine, cytosine, and uracil moieties as the nucleobase moiety, respectively (Scheme 1). The efficient synthesis of these compounds and analogues continues to be a challenging task in synthetic organic chemistry.



Scheme 1. Typical examples of disaccharide nucleosides having adenine, guanine, cytosine, and uracil moieties.

Reports on the synthesis of disaccharide nucleosides, although limited, can be classified into the following three categories. The first is chemical *N*-glycosylation, in which glycosyl donors **5** (X = acyl or halide) are reacted with activated nucleobases to give the precursor of the disaccharide nucleoside **6** (Scheme 2a).[8] The drawbacks of this method include rather lower chemical yields (less than 50%), the necessity of preparing the rather unstable glycosyl halides **5**, and the use of toxic Hg salts for the activation of **5** (Koenigs–Knorr-type glycosylation).

The second method involves the *O*-glycosylation of nucleosides via the use of enzymes, specifically, glycosylases (Scheme 2b).[9] Typically, a reactive glycosyl donor such as *p*-nitrophenyl-β-D-galactoside is hydrolyzed by β-galactosidase in

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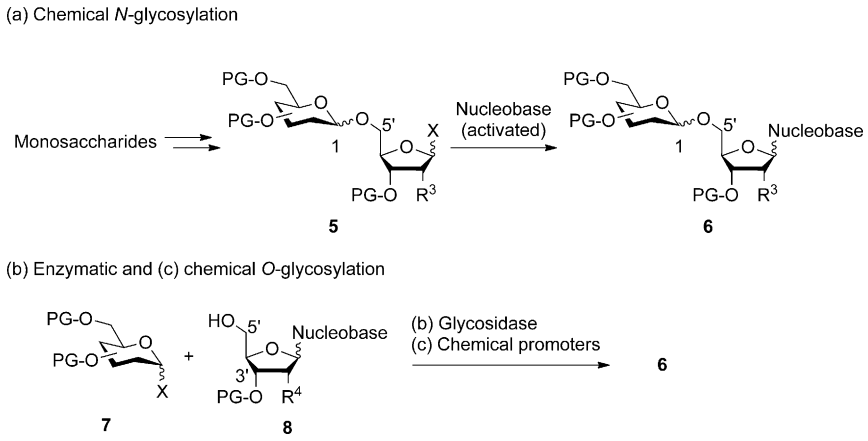


Scheme 2. Reported methodologies for the synthesis of disaccharide nucleosides (PG: protecting group).

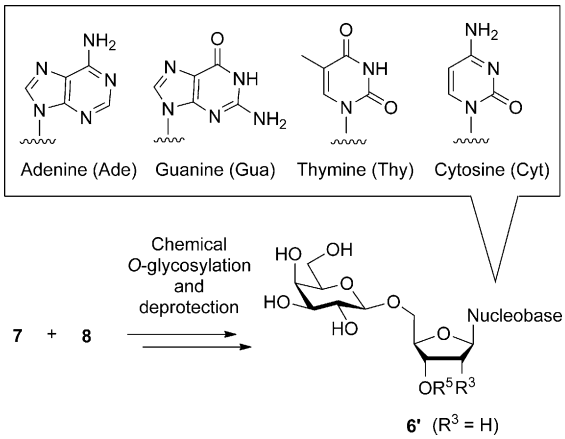
aqueous solution and then instantly reacts with nucleosides having adenine, uracil, thymine, and other nucleobase analogs. However, the application of this method is not widespread, due to the limited availability of specific glycosidases for the given glycosyl donors.

The third strategy is chemical *O*-glycosylation,[3c,10,11] as shown in Scheme 2c. This method has been applied to the synthesis of adenophostin A **1**,[12] which has a 10- to 100-fold more potent activity than inositol 1,4,5-trisphosphate ($Ins(1,4,5)P_3$) in releasing Ca^{2+} in living cells. Although this method would be expected to have widespread applications with respect to variations in substrates (donors and acceptors) and stereochemistry, one possible drawback would be the neutralization (inactivation) of promoters, which are generally Lewis acids or Brønsted acids, by the nucleobase units of nucleosides. In addition, side reactions such as the cleavage of the anomeric C–N bond of nucleosides and anomerization reactions under glycosylation conditions have also been reported.[13]

These findings prompted us to explore the general reaction conditions for the synthesis of disaccharide nucleosides **6′** via the *O*-glycosylation of nucleosides; glycosyl donors (**7**), nucleoside acceptors (**8**), promoters, solvent, and temperature (Scheme 3). In this manuscript, we report on the synthesis of disaccharide nucleosides by the direct *O*-glycosylation of Ade-, Gua-, Thy-, and Cyt-nucleosides[14] by the combined use of *p*-toluenesulfenyl chloride (TolSCl) and silver triflate (AgOTf).

Abstract in Japanese:

Disaccharide nucleoside は天然に存在する糖誘導体の重要な分子群のひとつである。今回我々は、adenosine (A)、guanosine (G)、thymidine (T)、cytidine (C)といったヌクレオシドアクセプターの *O*-グリコシル化反応による disaccharide nucleoside の化学的合成について報告する。グリコシル化反応の検討結果、チオグリコシドを糖供与体として、*p*-toluenesulfenyl chloride (TolSCl)と silver triflate (AgOTf)をグリコシル化活性化剤として用いると、対応する disaccharide nucleoside を良好な収率で与えることを見出した。また、グリコシル化活性化剤とヌクレオシドアクセプターとの相互作用を ^{1}H NMR により観測した。



Scheme 3. Synthesis of disaccharide nucleosides by the chemical *O*-glycosylation of nucleoside acceptors with glycosides.

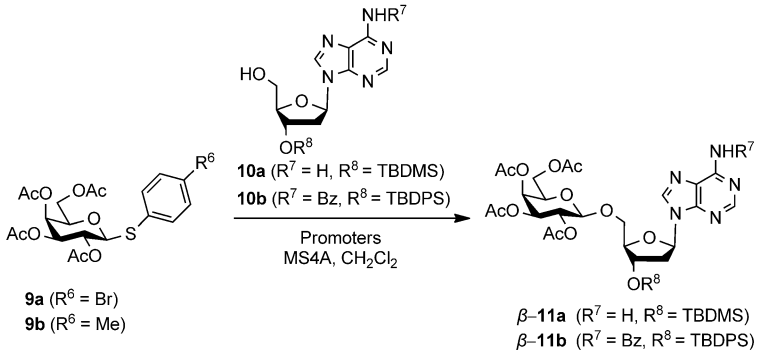
Results and Discussion

O-Glycosylation of nucleosides with thioglycosides and other glycosyl donors

We first attempted the glycosylation of 3′-*O*-TBDMS-deoxyadenosine **10a**[15] with thioglycosides **9a**[16] and **9b**,[17] because it is well known that thioglycosides are glycosyl donors that are stable, readily available, and can be easily modified. In addition, a variety of promoters for the activation of thioglycosides have been reported.[10,18]

As listed in entries 1–4 in Table 1, the findings showed that promoters such as NIS-TMSOTf,[19] DMTST,[20] NIS-AgOTf,[21] and NMPTC-Tf_2O[22] were insufficient in terms of producing the desired glycosides **11a** (NMPTC=*N*-(*p*-methylphenylthio)-ε-capro-

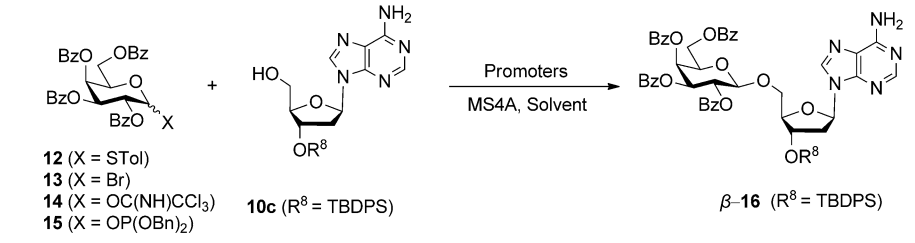
Table 1. The *O*-Glycosylation of nucleosides with thioglycosides and other glycosyl donors.



Entry[a]	Donor	Acceptor	Promoters (eq against donor)	*T*	Product	Yield [%]
1	**9a**	**10a**	NIS (1.5 eq)/TMSOTf (cat.)	−60 °C to r.t.	–	trace
2	**9a**	**10a**	NIS (1.5 eq)/AgOTf (0.1 eq)	0 °C to r.t.	–	trace
3	**9a**	**10a**	DMTST (10 eq)	0 °C to r.t.	–	trace
4	**9b**	**10a**	NMPTC (1.2 eq)/Tf_2O (1.3 eq)	−40 °C to r.t.	–	trace
5	**9b**	**10a**	TolSCl (1.2 eq)/AgOTf (3.0 eq)	−40 °C	β-**11a**	9
6	**9b**	**10b**	TolSCl (1.2 eq)/AgOTf (3.0 eq)	−40 °C	–	trace

[a] All reactions were carried out in the presence of 1.2 equivalents of acceptors against glycosyl donors (**9a**–**9b**).

Table 2. Comparison of the reactivities of **12** and other glycosyl donors in the *O*-Glycosylation of **10c**.



Entry[a]	Donor	Promoters (eq. against donor)	Conditions (solvents, temperature)	Product	Yield [%]
1	**12**	TolSCl (1.3 eq) AgOTf (3.0 eq)	CH_2Cl_2 −40 °C	β-**16**	61
2	**12**	TolSCl (1.3 eq) AgOTf (3.0 eq)	CH_2Cl_2/1,4-Dioxane (3/1) −40 to30 °C	β-**16**	52
3	**12**	TolSCl (1.3 eq) AgOTf (3.0 eq)	CH_2Cl_2/Et_2O (3/1) −40 °C	β-**16**	67
4	**12**	*p*-NO_2PhSCl (1.3 eq) AgOTf (3.0 eq)	CH_2Cl_2 −40 °C to r.t.	β-**16**	74
5	**13**	$AgClO_4$ (1.5 eq) (exclusively α)	CH_2Cl_2 −40 °C to r.t.	β-**16**	complex mixture (< 40)
6	**14**	TMSOTf (1.5 eq) (exclusively α)	CH_2Cl_2 −40 °C	β-**16**	complex mixture (< 10)
7	**14**	$BF_3{\cdot}Et_2O$ (2.5 eq)	CH_2Cl_2 −40 °C	β-**16**	33
8	**15** ($\alpha:\beta = 1.8:1$)	$ZnCl_2$ (2.0 eq) AgOTf (4.0 eq)	CH_2Cl_2 −40 °C	–	trace
9	**15**	TMSOTf (2.5 eq)	CH_2Cl_2 −40 °C	–	trace

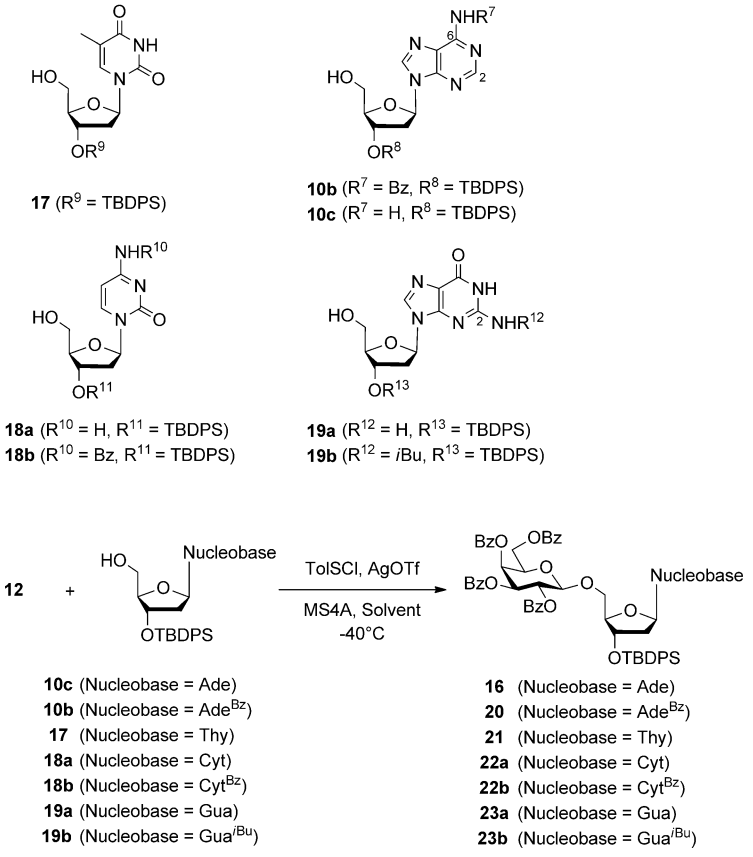
[a] All reactions were carried out in the presence of 1.2 equivalents of **10c** against glycosyl donors (**12**–**15**).

lactam). When a mixture of TolSCl and AgOTf[23] was used for the glycosylation with **9b**, the desired disaccharide **11a** was obtained in 9% yield (entry 5). The reaction of *N*-protected adenosine acceptor **10b**[24] and **9b** in the presence of the same promoters gave negligible product (entry 6). We assume that the low chemical yield in Table 1 is due to acyl-transfer from **9b** to **10a** or **10b** (5′-*O*-acetyl nucleosides were isolated in some cases) and/or the cleavage of TBDMS group of **10a,b** and/or **11a,b**.

Next, the *O*-glycosylation of the 3′-*O*-TBDPS-protected deoxyadenosine **10c**[25] was examined by using the thioglycoside **12**, the glycosyl bromide **13**,[26] the trichloroimidate **14**,[27] and the glycosyl phosphite **15**,[28] in which the hydroxy groups are protected with benzoyl groups to prevent transacylation. As listed in Table 2, glycosylation with **12** by using TolSCl and AgOTf gave a higher yield than the other glycosyl donors using their representative activators, when CH_2Cl_2, CH_2Cl_2/1,4-dioxane (3:1), and CH_2Cl_2/Et_2O (3:1) were used as the solvent (entries 1–3 vs. entries 5~9). We assume that low yields in entries 6–9 are possibly due to the cleavage of the *N*-glycosidic linkage under these conditions. Because the reaction conditions for the glycosylation of **10c** with **13**, **14**, and **15** have not been optimized in this work, we do not exclude the possibility that these glycosyl donors may afford **11a** under different reaction conditions. The reaction of **12** and **10c** using *p*-nitrobenzenesulfenyl chloride (*p*-NO_2PhSCl) and AgOTf[29] gave almost the identical result as that using TolSCl/AgOTf (entry 4 vs. entry 3).

The *O*-glycosylations of some other nucleosides with **12** were performed, and the results are summarized in Table 3. In entries 1 and 2, the reactions of thioglycoside **12** with unprotected **10c** and **10b**, in which the amino group is protected, gave the desired glycosides in 61% and 34% yields, respectively. Note that the reaction of adenosine using **10c** (entry 1), in which the adenosine moiety is not protected, gave a higher yield than that for the protected **10b** (entry 2) (this point is discussed below). In entry 3, the re-

Table 3. *O*-Glycosylation of other nucleosides with thioglycosides.



Entry	Donor	Acceptor[a]	Solvent	Product	Yield [%]
1[b]	**12**	**10c** (Ade)	CH_2Cl_2	β-**16**	61
2	**12**	**10b** (Ade^{Bz})	CH_2Cl_2	β-**20**	34
3	**12**	**17** (Thy)	CH_2Cl_2	β-**21**	88
4	**12**	**18a** (Cyt)	CH_2Cl_2	β-**22a**	49
5	**12**	**18b** (Cyt^{Bz})	CH_2Cl_2	β-**22b**	76
6	**12**	**19a** (Gua)	CH_2Cl_2	β-**23a**	14
7	**12**	**19b** (Gua^{iBu})	CH_2Cl_2	β-**23b**	46
8	**12**	**17** (Thy)	EtCN	β-**21**	62
9	**12**	**18b** (Cyt^{Bz})	EtCN	β-**22b**	26
10	**12**	**19b** (Gua^{iBu})	EtCN	β-**23b**	43

[a] All reactions were carried out in the presence of 1.2 equivalents of acceptors, 1.2–1.8 equivalents of TolSCl, and 3.0–3.5 equivalents of AgOTf against **12**. [b] Taken from entry 1 of Table 2.

action of the thioglycoside **12** with **17**[30] proceeded in CH_2Cl_2 to afford β-**21** in 88% yield.

In entries 4 and 5, the reactions of **12** with the unprotected and the protected Cyt-nucleoside acceptors, **18a**[25] and **18b**,[30] afforded the desired products in 49% and 76% yields, respectively. In entries 6 and 7, glycosylations with the unprotected and protected Gua-nucleoside acceptors, **19a** and **19b**,[30] afforded the desired glycosides in 14% and 46% yields, respectively. Therefore, the use of the protected Cyt- or Gua-nucleosides (**18b** and **19b**) rather than the unprotected ones (**18a** and **19a**) (entries 4 and 6 vs. entries 5 and 7) is an advantage in this type of synthesis. The chemical yields for the *O*-glycosylation in EtCN[31] (entries 8–10) were lower than those for reactions conducted in CH_2Cl_2 (entries 3, 5, and 7).

Reactions of the glucosaminyl donor **24**[32] with **10c**, **17**, **18b**, and **19b** gave the corresponding products (**25**–**28**) in acceptable yields, as listed in Table 4.

The glycosylation of the 3′-OH-free adenosine derivatives **29**[33] with **12** gave β-**30** exclusively in 52% yield (Scheme 4a). In addition, the reactions of **31**[34] and **33**[35] with **10c** afforded **32** and **34** in 46% (α/β = 3:1) and 57% (α/β = 2.5:1) yields, respectively (Scheme 4b and 4c). For comparison, the reaction of **10a**, which contains TBDMS at the 3′-OH group (see Table 1), with **33** resulted in a negligible yield of the desired product.

The deprotection of the representative glycosylation products, **16** and **21**, by treatment with TBAF[36] and then $MeNH_2$,[37] gave the deprotected compounds, **35** and **36**, respectively (Scheme 5a). The deprotection of α-**34** gave α-**37**, as shown in Scheme 5b.

Interaction of adenosyl acceptors with TolSCl and AgOTf studied by ^{1}H NMR spectroscopy

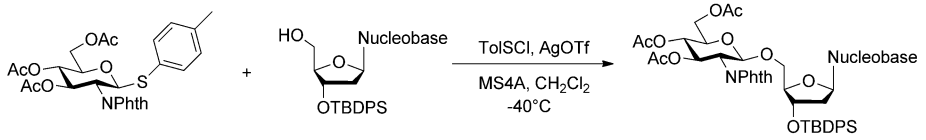
The results in entries 1 and 2 in Table 3 suggest that the adenosine derivative **10c**, in which the 6-NH_2 group is not protected, gives a better yield than that of *N*-protected adenosine derivative **10b**. To determine the reason for this, we collected ^{1}H NMR spectra of **38a**,[38] in which the 6-NH_2 group is not protected and the 3′- and 5′-OH groups are protected with TBDPS (to increase the solubility of the compound in an organic solvent), and 6-*N*-benzoyl-3′,5′-*O*-bis-TBDPS-2′-deoxyadenosine **38b**[39] in the absence and presence of TolSCl and AgOTf (in $CDCl_3$ at −40 °C).

As shown in Figure 1a–b, the ^{1}H NMR spectrum of **38a** remained essentially unchanged upon the addition of TolSCl + AgOTf, while **38b** was decomposed under identical conditions, as indicated in Figure 1c–e. The products produced from **38b** with AgOTf and TolSCl were isolated and identified as *N*-benzoyladenine **39** (as 1:1 and 2:1 complexes with Ag^+, as suggested by the FAB-mass spectrum in Figure S1 in the Supporting Information) and **40** (Scheme 6). This strongly suggests that the lower chemical yield in entry 2 of Table 3 compared to entry 1 is due to the depurination of **10b** and/or **20**.[40,41]

Conclusions

Herein, we report on the synthesis of disaccharide nucleosides by the direct *O*-glycosylation of nucleosides. The glycosylation of deoxyadenosine **10a** and **10c** with thioglycosides such as **9b** and **12** using a combination of TolSCl/AgOTf as glycosylation promoters gave the desired products in reasonable chemical yields. We synthesized disaccharide nucleosides by the direct *O*-glycosylation of Ade-, Gua-, Thy-, and Cyt-nucleosides

Table 4. *O*-Glycosylation of nucleosides with thioglycosides and other glycosyl donors.



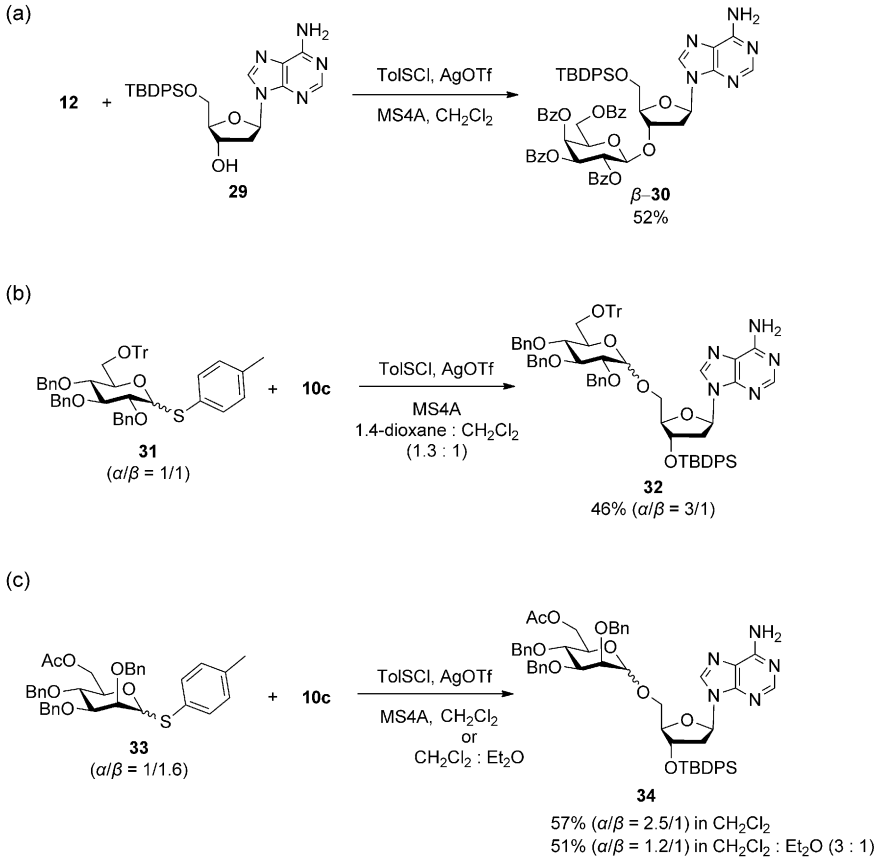
24

10c (Nucleobase = Ade)
17 (Nucleobase = Thy)
18b (Nucleobase = Cyt^{Bz})
19b (Nucleobase = Gua^{iBu})

25 (Nucleobase = Ade)
26 (Nucleobase = Thy)
27 (Nucleobase = Cyt^{Bz})
28 (Nucleobase = Gua^{iBu})

Entry[a]	Donor	Acceptor	Product	Yield [%]
1	**24**	**10c** (Ade)	β-**25**	63
2	**24**	**17** (Thy)	β-**26**	74
3	**24**	**18b** (Cyt^{Bz})	β-**27**	65
4	**24**	**19b** (Gua^{iBu})	β-**28**	37

[a] All reactions were carried out in the presence of 1.2 equivalents of acceptors, 1.2–1.8 equivalents of TolSCl, and 3.0–3.5 equivalents of AgOTf against **24**.



Scheme 4. Synthesis of **30**, **32**, and **34**.

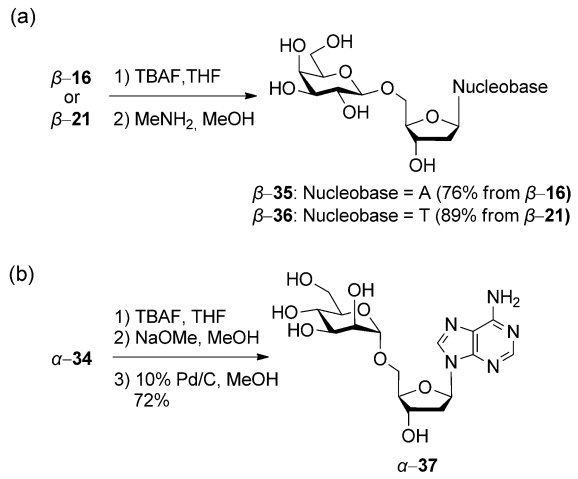
with **12** and the thioglucosaminide **24** and found that this method gives the desired products in moderate to good yields. The α-glycosylation of the thioglycoside **31** and deprotection of representative compounds **16**, **21**, and **34** were also demonstrated. ^{1}H NMR measurements of the adenosine derivatives **38a** and **38b** in the presence of TolSCl/AgOTf suggest that the 6-NH_2 protected adenosine derivatives **10b** and **38b** undergo C–N cleavage (depurination), resulting in lower glycosylation yields, while Thy- and Cyt-nucleoside acceptors have negligible interactions with TolSCl/AgOTf. These results afford important information regarding the glycosylation of nucleosides or other nucleobase-containing glycosyl acceptors for the synthesis of a variety of biologically relevant nucleoside disaccharide derivatives.

Experimental Section

General Information

Reagents and solvents were purchased at the highest commercial quality and were used without further purification. Anhydrous CH_2Cl_2 and $CDCl_3$ were prepared by distillation from calcium hydride, and propionitrile (EtCN) was prepared by distillation from calcium hydride and the successive distillation from phosphorus(V) oxide. All aqueous solutions were prepared using deionized water.

^{1}H (300 and 400 MHz) and ^{13}C (75 and 100 MHz) NMR spectra were recorded on a JEOL Always 300 and a JEOL Lambda 400 spectrometer, respectively. Tetramethylsilane (TMS) was used as an internal reference for ^{1}H and ^{13}C NMR measurements in $CDCl_3$, [D_6]DMSO and CD_3OD. 3-(Trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium (TSP) was used an internal reference for ^{1}H NMR measurements in D_2O. IR spectra were recorded on a PerkinElmer FTIR Spectrum 100 instrument at room temperature. MS measurements were performed on a JEOL JMS-SX102A and a Varian TQ-FT spectrometer. Thin-layer (TLC) and silica gel column chromatography was performed using Merck Silica gel 60 F_{254} plates and Fuji Silica Chemical FL-100D, respectively. GPC experiments were carried out using a system consisting of a POMP P-50 (Japan Analytical Industry Co., Ltd.), a UV/VIS DETECTOR S-3740 (Soma, Japan), a Manual Sample Injector 7725i (Rheodyne, USA) and a MDL-101 1 PEN RECORDER (Japan Analytical Industry Co., Ltd.), equipped with two GPC columns, JAIGEL-1H and JAIGEL-2 (Japan Analytical Industry Co., Ltd.) (20ϕ x 600 mm, No. A605201 and A605204).



Scheme 5. Deprotection reactions of **16**, **21**, and **34**.

Preparation of *p*-toluenesulfenyl chloride (TolSCl)[23]

Sulfuryl chloride (1.0 mL, 12 mmol) was added to a solution of toluenethiol (1.242 g, 10.00 mmol) in anhydrous hexane (5.0 mL) at 0 °C over a period of 5 min, followed by stirring at room temperature for 1 h. The reaction mixture was concentrated under reduced pressure and then distilled (54 °C, 1 mm Hg) to give the TolSCl as a red liquid (1.374 g, 87 %). This product was stored in the dark at −20 °C prior to use for periods of 1–3 months.

4-Bromophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (9 a)[16]

A mixture of 1,2,3,4,6-penta-*O*-acetyl-D-galactopyranose (500 mg, 1.3 mmol), *p*-bromothiophenol (290 mg, 1.5 mmol) and MS3A in anhydrous CH_2Cl_2 (8.0 mL) was stirred for 1 h at room temperature and then cooled to 0 °C, to which $BF_3{\cdot}OEt_2$ (1.7 mL, 6.4 mmol) was added at the same temperature. The reaction mixture was stirred for 30 min at 0 °C and allowed to warm to room temperature. After stirring overnight at room temperature, the reaction mixture was quenched by saturated aqueous $NaHCO_3$ and the resulting solution was diluted with $CHCl_3$. The suspension was filtered through Celite, and the filtrate was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography ($CHCl_3$) to give **9 a** as a colorless amorphous solid (668 mg, quant.): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 1.98$ (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H), 2.11 (s, 3H), 3.91 (t, $J = 6.6$ Hz, 1H), 4.07–4.21 (m, 2H), 4.65 (d, $J = 9.6$ Hz, 1H), 5.02 (dd, $J = 3.3$, 9.9 Hz, 1H), 5.17 (t, $J = 9.9$ Hz, 1H), 5.41 (d, $J = 3.0$ Hz, 1H), 7.38 (dd, $J = 1.8$, 7.2 Hz, 2H), 7.43 ppm (dd, $J = 1.8$, 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): $\delta = 20.1$, 20.1, 20.2, 20.3, 61.3, 66.7, 66.8, 71.4, 74.0, 85.2, 122.1, 130.8, 131.4, 133.9, 168.8, 169.4, 169.6, 169.7 ppm; HRMS (FAB+): calcd for $[M+Na]^+$, $C_{20}H_{23}{}^{79}BrO_9SNa$, 541.0144; found, 541.0145.

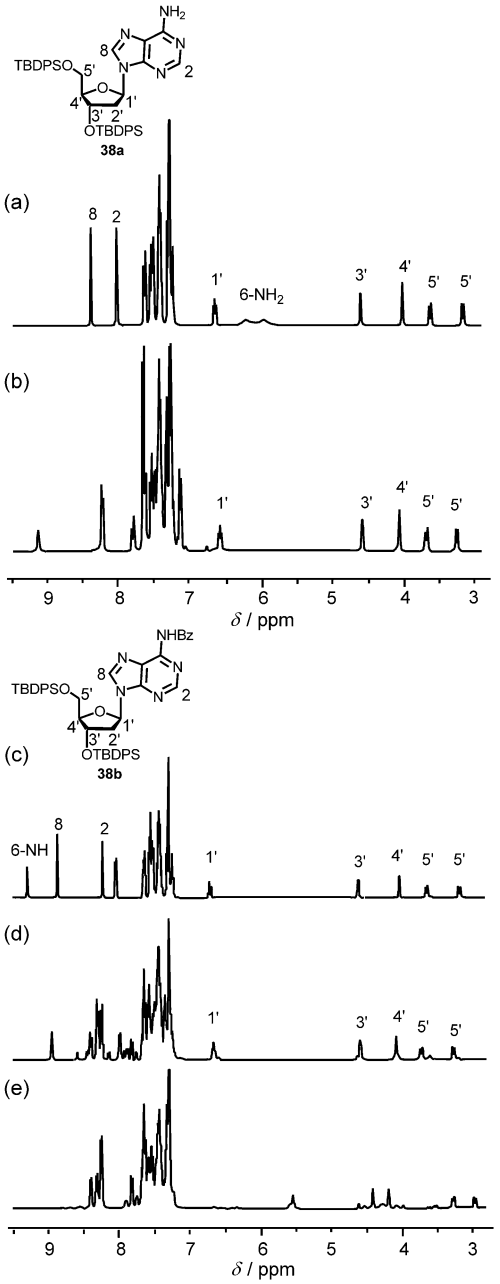
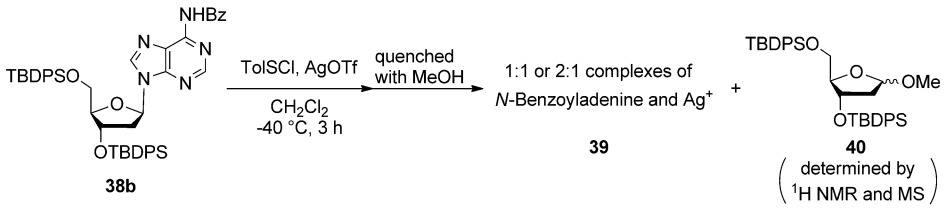


Figure 1. ^{1}H NMR spectra of **38 a** and **38 b** (14 mM) in $CDCl_3$ in the absence and presence of TolSCl (30 mM) and AgOTf (44 mM). (a) **38 a** at −40 °C, (b) **38 a** + TolSCl/AgOTf at −40 °C, (c) **38 b** at −40 °C, (d) **38 b** + TolSCl/AgOTf at −40 °C (10 min), (e) **38 b** at −40 °C + TolSCl/AgOTf at −40 °C (4 h).



Scheme 6. Reaction of **38 b** with TolSCl and AgOTf.

3′-*O*-*tert*-Butyldimethylsilyl-2′-deoxyadenosine (10a)[15a]

2′-Deoxyadenosine (462 mg, 1.8 mmol) was dried by co-evaporation with dry pyridine (three times), dissolved in dry pyridine (10 mL) and then cooled to 0 °C, to which 4,4′-dimethoxytrityl chloride

(751 mg, 2.2 mmol) was added.[15b] The reaction mixture was stirred for 30 min at 0 °C and was allowed to warm to room temperature. After stirring overnight, the reaction mixture was poured into water, extracted with $CHCl_3$, and the organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/AcOEt/MeOH = 100:2:1) to give the 5′-*O*-DMTritylated derivative[15b] as a pale yellow amorphous solid (694 mg, 68% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.01 (d, J = 3.6 Hz, 1H), 2.49–2.57 (m, 1H), 2.80–2.87 (m, 1H), 3.39 (t, J = 5.4 Hz, 1H), 3.78 (s, 6H), 4.10 (q, J = 4.5 Hz, 1H), 4.67–4.69 (m, 1H), 5.48 (brs, 2H), 6.41 (t, J = 6.6 Hz, 1H), 6.78 (td, J = 3.3, 9.0 Hz, 4H), 7.21–7.32 (m, 11H), 7.38–7.41 (m, 2H), 7.95 (s, 1H), 8.29 ppm (s, 1H).

The 5′-*O*-DMTritylated compound synthesized above (300 mg, 0.54 mmol) and imidazole (111 mg, 1.6 mmol) were dissolved in anhydrous DMF, to which *tert*-butyldimethyl chloride (123 mg, 0.81 mmol) was added.[15c] The reaction mixture was stirred at room temperature for 1 d, poured into water and extracted with $CHCl_3$. The organic layer was washed with saturated aqueous $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 100:1) to give the 3′-*O*-TBDMS-5′-*O*-DMTr-2′-deoxyadenosine[15c] as a colorless amorphous solid (332 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.01 (s, 3H), 0.05 (s, 3H), 0.86 (s, 9H), 2.38–2.45 (m, 1H), 2.69–2.78 (m, 1H), 3.25 (dd, J = 4.2, 10.5 Hz, 1H), 3.36 (dd, J = 4.5, 10.5 Hz, 1H), 3.79 (s, 6H), 4.08 (dd, J = 4.3, 7.8 Hz, 1H), 4.57 (td, J = 3.7, 5.7 Hz, 1H), 5.53 (brs, 2H), 6.40 (t, J = 6.4 Hz, 1H), 6.77 (td, J = 2.0, 8.7 Hz, 4H), 7.17–7.42 (m, 10H), 8.31 ppm (s, 1H).

TFA (90 μL, 1.2 mmol) was added to a solution of 3′-*O*-TBDMS-5′-*O*-DMTr-2′-deoxyadenosine (200 mg, 0.30 mmol) in CH_2Cl_2 at room temperature. The reaction mixture was stirred for 45 min at room temperature, quenched by the addition of aqueous 1N NaOH (1.0 mL), and then extracted with $CHCl_3$. The organic layer was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (AcOEt) to give **10a** as a white powder (87 mg, 80% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.12 (s, 6H), 0.93 (s, 9H), 2.16 (dd, J = 5.5, 13.0 Hz, 1H), 3.00–3.09 (m, 1H), 3.71 (t, J = 11.7 Hz, 1H), 3.94 (d, J = 12.8 Hz, 1H), 4.15 (s, 1H), 4.70 (d, J = 5.0 Hz, 1H), 5.68 (brs, 2H), 6.26 (dd, J = 5.1, 5.5 Hz, 1H), 6.52 (d, J = 11.2 Hz, 1H), 7.86 (s, 1H), 8.32 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = −4.8, 17.9, 25.9, 41.2, 63.1, 73.9, 87.5, 90.2, 121.0, 140.0, 148.5, 152.3, 156.2 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{16}H_{28}N_5O_3Si$, 366.1961; found, 366.1963.

3′-*O*-*tert*-Butyldimethylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-galactopyranosyl)-2′-deoxyadenosine (β-11a) (Entry 5 in Table 1)

A mixture of **9b** (45 mg, 0.10 mmol), **10a** (43 mg, 0.12 mmol) and MS4A in anhydrous CH_2Cl_2 (2.8 mL) was stirred for 1 h at room temperature and then cooled to −40 °C, to which AgOTf (64 mg, 0.25 mmol) and TolSCl (23 μL, 0.16 mmol) were added at the same temperature. The reaction mixture was stirred for 2 h at −40 °C and quenched by adding saturated aqueous $NaHCO_3$ (600 μL) and the resulting solution was diluted with CH_2Cl_2. The suspension was filtered through Celite, and the organic layer was washed with saturated $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 1:0 to 50:1) followed by GPC ($CHCl_3$) to give β-**11a** as a colorless amorphous solid (6 mg, 9% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.01 (s, 6H), 0.91 (s, 9H), 2.00 (s, 3H), 2.02 (s, 3H), 2.04 (s, 3H), 2.20 (s, 3H), 2.36–2.43 (m, 1H), 2.62–2.71 (m, 1H), 3.68 (dd, J = 3.6, 10.2 Hz, 1H), 3.91 (t, J = 6.3 Hz, 1H), 4.10–4.21 (m, 4H), 4.53–4.56 (m, 2H), 5.03 (dd, J = 3.3, 10.2 Hz, 1H), 5.25 (dd, J = 7.8, 10.5 Hz, 1H), 5.40 (d, J = 3.3 Hz, 1H), 5.72 (s, 2H), 6.48 (t, J = 6.6 Hz, 1H), 8.22 (s, 1H), 8.35 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = −5.0, −4.9, 17.8, 20.4, 20.5, 20.5, 20.6, 25.6, 40.9, 61.1, 66.8, 66.8, 68.4, 68.8, 70.6, 70.7, 72.2, 84.1, 85.9, 100.7, 119.7, 139.2, 149.4, 152,4, 155.5, 169.3, 170.0, 170.2, 170.2 ppm; IR (ATR): $\tilde{\nu}$ = 3013, 1666, 1541, 1465, 1347, 1221, 1154, 1076, 1020, 921, 851, 748, 579 cm^{-1}; HRMS (FAB+): calcd for $[M+H]^+$, $C_{30}H_{46}N_5O_{12}Si$, 696.2912; found, 696.2914.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-2′-deoxyadenosine (β-16) (Entry 1 in Table 2)

Reaction conditions for the synthesis of β-**16** were the same as those for β-**11a**. The resulting residue was purified by silica gel column chromatography (hexanes/AcOEt = 1:3 to 0:1) to give β-**16** as a colorless amorphous solid (30.3 mg, 61% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.00 (s, 9H), 2.40–2.52 (m, 2H), 2.75 (dd, J = 2.7, 10.5 Hz 1H), 3.91 (dd, J = 2.4, 10.2 Hz, 1H), 3.98–4.02 (m, 1H), 4.21 (t, J = 7.8 Hz, 1H), 4.31 (d, J = 4.8 Hz, 1H), 4.39 (dd, J = 7.2, 11.1 Hz, 1H), 4.43 (d, J = 8.1 Hz, 1H), 4.63 (dd, J = 6.3, 8.1 Hz, 1H), 5.58 (dd, J = 3.4, 10.3 Hz, 1H), 5.70 (s, 2H), 5.70 (t, J = 7.3 Hz 1H), 5.96 (d, J = 3.0 Hz, 1H), 5.62 (dd, J = 6.6, 8.4 Hz, 1H), 7.20–7.66 (m, 22H), 7.74–7.7.79 (m, 4H), 7.98 (d, J = 6.9 Hz, 2H), 8.12 (d, J = 7.5 Hz, 2H), 8.37 (s, 1H), 8.39 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.0, 26.8, 41.6, 61.8, 67.8, 69.6, 69.8, 71.1, 71.3, 74.3, 84.2, 86.9, 101.4, 119.8, 127.8, 128.3, 128.4, 128.5, 128.7, 128.9, 128.9, 129.3, 129.5, 129.7, 129.8, 129.8, 130.1, 130.2, 133.1, 133.3, 133.3, 133.4, 133.6, 135.6, 135.7, 139.4, 149.8, 152.7, 155.4, 165.2, 165.5, 165.5, 166.0 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{60}H_{58}N_5O_{12}Si$, 1068.3851; found, 1068.3854.

3′-*O*-*tert*-Butyldiphenylsilyl-2′-deoxyguanosine (19a)

Ethylenediamine (8.0 mL, 12 mmol) was added to a solution of **19b**[30] (173 mg, 0.30 mmol) in EtOH at room temperature. The reaction mixture was stirred for 3 h and then concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 97:3) to give **19a** as a white powder (140 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.11 (s, 9H), 2.18 (dd, J = 4.8, 12.4 Hz, 1H), 3.04 (t, J = 12.1 Hz, 1H), 3.66 (d, J = 12.8 Hz, 1H), 4.09 (s, 1H), 4.64 (d, J = 4.8 Hz, 1H), 6.03–6.31 (m, 3H), 7.36–7.51 (m, 7H), 7.62–7.68 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.0, 26.8, 40.7, 62.9, 74.9, 87.5, 89.7, 118.3, 127.9, 130.0, 133.2, 133.3, 135.5, 135.7, 149.8, 153.4, 158.9 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{26}H_{32}N_5O_4Si$, 506.2224; found, 506.2228.

6-*N*-Benzoyl-3′-*O*-*tert*-butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-2′-deoxyadenosine (β-20) (Entry 2 in Table 3)

Reaction conditions for the synthesis of β-**20** were the same as those for β-**11a**. The resulting residue was purified by silica gel column chromatography (hexanes/$CHCl_3$ = 1:4 to 0:1, then hexanes/AcOEt = 2/1) to give β-**20** as a colorless amorphous solid (34.4 mg, 34% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.08 (s, 9H), 2.40–2.54 (m, 2H), 3.10 (dd, J = 3.6, 10.8 Hz 1H), 3.40 (dd, J = 3.3, 10.2 Hz, 1H), 4.11–4.15 (m, 1H), 4.33 (dd, J = 5.7, 10.8 Hz, 1H),

4.42 (dt, J=2.1, 6.3 Hz, 1H), 4.45–4.51 (m, 1H), 4.53–4.59 (m, 2H), 5.39 (dd, J=4.5, 6.3 Hz, 1H), 5.74 (dd, J=2.7, 4.2 Hz, 1H), 5.94 (d, J=4.8 Hz, 1H), 6.62 (t, J=6.9 Hz 1H), 7.28–7.63 (m, 27H), 7.89–8.02 (m, 8H), 8.19 (s, 1H), 8.75 (s, 1H), 9.05 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ=19.0, 26.9, 41.0, 62.3, 63.5, 66.4, 68.9, 69.5, 69.9, 73.3, 74.3, 84.7, 86.5, 98.2, 120.1, 123.2, 125.8, 127.9, 127.9, 128.4, 128.4, 128.5, 128.8, 128.9, 129.1, 129.4, 129.7, 129.8, 129.8, 129.9, 130.1132.7, 133.0, 133.0, 133.2, 133.4, 133.6, 133.7, 135.7, 135.7, 136.0, 141.6, 149.4, 151.6, 152.6, 164.6, 165.2, 165.2, 165.9 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{67}H_{62}N_5O_{13}Si$, 1172.4113; found, 1172.4110.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-thymidine (β-21) (Entry 3 in Table 3)

Reaction conditions for the synthesis of β-**21** were the same as those for β-**11a**. The resulting residue was purified by silica gel column chromatography (hexanes/AcOEt=2:1) to give β-**21** as a colorless amorphous solid (133 mg, 88% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.93 (s, 9H), 1.78–1.88 (m, 1H), 2.04–2.14 (m, 4H), 2.43 (dd, J=1.5, 10.6 Hz 1H), 3.84–3.88 (m, 1H), 3.96 (dd, J=1.5, 10.5 Hz, 1H), 4.06 (d, J=5.4, 1H), 4.18–4.23 (m, 2H), 4.37 (d, J=6.9, 10.8 Hz, 1H), 4.62 (dd, J=6.6, 11.4 Hz, 1H), 5.56–5.68 (m, 2H), 5.95 (d, J=2.4 Hz 1H), 6.50 (dd, J=5.4, 9.3 Hz, 1H), 7.22–7.50 (m, 20H), 7.55–7.81 (m, 3H), 7.72–7.80 (m, 4H), 7.98–8.03 ppm (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ=12.7, 18.9, 26.7, 40.3, 61.6, 68.0, 69.5, 69.9, 70.9, 71.5, 74.0, 84.7, 86.5, 102.1, 111.3, 127.9, 128.3, 128.5, 128.5, 128.6, 128.7, 128.8, 129.2, 129.3, 129.7, 129.7, 129.9, 130.0, 132.9, 133.3, 133.4, 133.6, 133.8, 135.6, 135.7, 136.2, 150.5, 163.7, 165.2, 165.5, 165.5, 166.0 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{60}H_{59}N_2O_{14}Si$, 1059.3736; found, 1059.3735.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-2′-deoxycytidine (β-22a) (Entry 4 in Table 3)

Reaction conditions for the synthesis of β-**22a** were the same as those for β-**11a**. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH=200:1 to 50:1) to give β-**22a** as a colorless amorphous solid (24.7 mg, 49% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.96 (s, 9H), 1.73–1.79 (m, 3H), 2.43 (ddd, J=1.3, 5.9, 13.7 Hz, 1H), 2.59 (dd, J=1.5, 10.3 Hz, 1H), 3.86–3.93 (m, 2H), 4.15 (d, J=6.2 Hz, 1H), 4.20 (t, J=7.0 Hz, 1H), 4.28 (d, J=7.3 Hz, 1H), 4.39 (dd, J=6.6, 11.4 Hz, 1H), 4.59 (dd, J=6.6, 11.4 Hz, 1H), 5.53–5.66 (m, 3H), 5.95 (dd, J=0.9, 3.0 Hz, 1H), 6.55 (dd, J=5.9, 8.1 Hz, 1H), 7.20–7.34 (m, 7H), 7.38–7.65 (m, 15H), 7.75 (dd, J=1.2, 6.9 Hz, 4H), 7.89 (d, J=7.3 Hz, 1H), 7.98–8.06 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ=18.9, 26.8, 41.9, 46.1, 61.8, 68.1, 69.0, 69.6, 71.1, 71.3, 73.7, 86.1, 86.4, 94.4, 101.3, 127.8, 128.3, 128.5, 128.6, 128.7, 128.8, 129.0, 129.3, 129.4, 129.7, 129.8, 129.9, 130.0, 133.1, 133.4, 133.5, 133.8, 135.6, 135.7, 141.7, 155.9, 165.2, 165.4, 165.5, 165.5, 166.0 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{59}H_{58}N_3O_{13}Si$, 1044.3739; found, 1044.3742.

4-*N*-Benzoyl-3′-*O*-*tert*-butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-2′-deoxycytidine (β-22b) (Entry 5 in Table 3)

Reaction conditions for the synthesis of β-**22b** were the same as those for β-**11a**. The resulting residue was purified by silica gel column chromatography (hexanes/AcOEt=2:1 to 3:2) to give β-**22b** as a colorless amorphous solid (76 mg, 76% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.97 (s, 9H), 1.85–1.95 (m, 1H), 2.54–2.60 (m, 2H), 3.92–3.96 (m, 2H), 4.16 (d, J=5.9 Hz, 1H), 4.21 (t, J=6.8 Hz, 1H), 4.29 (d, J=7.3 Hz, 1H), 4.42 (dd, J=6.8, 11.2 Hz, 1H), 4.69 (dd, J=6.6, 11.4 Hz, 1H), 5.54–5.67 (m, 2H), 5.97 (d, J=2.2 Hz, 1H), 6.54 (dd, J=5.9, 8.1 Hz, 1H), 7.18–7.35 (m, 6H), 7.38–7.62 (m, 20H), 7.72–7.77 (m, 4H), 7.81–7.85 (m, 2H), 8.01–8.04 (m, 4H), 8.25 (d, J=7.5 Hz, 1H), 8.60 ppm (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ=18.9, 26.8, 42.2, 61.8, 67.9, 69.1, 69.6, 71.0, 71.5, 74.0, 87.2, 97.1, 101.5, 127.6, 127.9, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.4, 129.4, 129.7, 129.8, 129.9, 130.0, 130.1, 132.9, 133.0, 133.4, 133.4, 133.5, 133.6, 135.6, 135.7, 145.0, 154.7, 162.0, 165.0, 165.5, 165.6, 166.0 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{66}H_{62}N_3O_{14}Si$, 1148.4001; found, 1148.4001.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-2′-deoxyguanosine (β-23a) (Entry 6 in Table 3)

Reaction conditions for the synthesis of β-**23a** were the same as those for β-**11a**. The resulting residue was purified by NH silica gel column chromatography ($CHCl_3$/MeOH=100:1 to 10:1) to give β-**23a** as a colorless amorphous solid (7.0 mg, 14% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.99 (s, 9H), 2.27–2.44 (m, 2H), 2.82 (d, J=9.0 Hz, 1H), 3.91–4.01 (m, 2H), 4.20–4.45 (m, 4H), 4.60–4.69 (m, 1H), 5.56 (dd, J=3.3, 10.2 Hz, 1H), 5.71 (dd, J=7.9, 10.4 Hz, 1H), 5.95 (d, J=3.3 Hz, 1H), 6.31 (t, J=7.2 Hz, 1H), 7.20–7.64 (m, 22H), 7.74–7.82 (m, 4H), 7.96–8.00 (m, 3H), 8.09 ppm (d, J=6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ=19.0, 26.9, 29.7, 41.0, 46.0, 50.8, 61.8, 67.8, 69.3, 69.7, 71.2, 74.2, 77.2, 83.8, 86.7, 101.3, 117.3, 127.8, 128.3, 128.4, 128.5, 128.7, 128.9, 129.0, 129.3, 129.5, 129.8, 130.0, 130.1, 130.1, 133.1, 133.3, 133.4, 133.8, 135.6, 135.7, 136.2, 151.8, 153.6, 159.2, 165.2, 165.5, 165.6, 166.1 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{60}H_{58}N_5O_{13}Si$, 1084.3801; found, 1084.3802.

2-*N*-Isobutyryl-3′-*O*-*tert*-butyldiphenylsilyl-5′-*O*-(2″,3″,4″,6″-tetra-*O*-benzoyl-β-D-galactopyranosyl)-2′-deoxyguanosine (β-23b) (Entry 6 in Table 3)

Reaction conditions for the synthesis of β-**23b** were the same as those for β-**11a**. The resulting residue was purified by NH silica gel column chromatography ($CHCl_3$/MeOH=1:0 to 200:1) to give β-**23b** as a colorless amorphous solid (22.9 mg, 46% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.91 (d, J=6.7 Hz, 3H), 0.98 (s, 9H), 1.13 (d, J=6.7 Hz, 3H), 1.99 (dd, J=54.9, 12.9 Hz, 1H), 2.48 (tt, J=6.6, 6.9 Hz, 1H), 2.69 (dd, J=3.0, 11.4 Hz, 1H), 2.92 (ddd, J=5.7, 10.2, 13.0 Hz, 1H), 3.95–3.98 (m, 2H), 4.17–4.36 (m, 4H), 4.62 (dd, J=6.0, 11.1 Hz, 1H), 5.54 (dd, J=3.6, 7.8 Hz, 1H), 5.70 (dd, J=7.8, 10.5 Hz, 1H), 5.96 (d, J=2.7 Hz, 1H), 6.13 (dd, J=4.8, 10.2 Hz, 1H), 7.22–7.28 (m, 4H), 7.33–7.70 (m, 18H), 7.71–7.81 (m, 4H), 7.95–8.01 (m, 3H), 8.07 (dd, J=1.5, 8.4 Hz, 2H), 9.33 (s, 1H), 12.08 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ=18.5, 18.9, 19.0, 26.8, 36.3, 39.0, 61.6, 67.7, 68.5, 70.0, 71.2, 71.3, 73.7, 85.3, 86.7, 101.2, 122.5, 127.9, 128.0, 128.3, 128.5, 128.6, 128.6, 128.8, 129.0, 129.3, 129.4, 129.6, 129.8, 129.9, 130.0, 130.2, 133.1, 133.3, 133.4, 133.5, 133.9, 134.1, 135.6, 135.8, 139.1, 147.4, 148.5, 155.6, 165.5, 165.5, 166.1, 166.1, 178.5 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{64}H_{64}N_5O_{14}Si$, 1154.4219; found, 1154.4223.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(3″,4″,6″-tri-*O*-acetyl-2″-deoxy-2″-phthalimido-β-D-glucopyranosyl)-2′-deoxyadenosine (β-25) (Entry 1 in Table 4)

Reaction conditions for the synthesis of β-**25** were the same as those for β-**11 a**. The resulting residue was purified by silica gel column chromatography (hexanes/AcOEt = 1:1 to 1:3) followed by GPC ($CHCl_3$) to give β-**25** as a colorless amorphous solid (31 mg, 63% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.97 (s, 9H), 1.85 (s, 3H), 2.03 (s, 3H), 2.10 (s, 3H), 2.23–2.31 (m, 2H), 2.73 (dd, J = 4.2, 10.8 Hz, 1H), 3.74–3.80 (m, 2H), 3.91–3.94 (m, 1H), 4.09–4.28 (m, 4H), 5.03 (d, J = 8.4 Hz, 1H), 5.13 (t, J = 9.3 Hz, 1H), 5.77–5.84 (m, 3H), 6.43 (t, J = 7.2 Hz, 1H), 7.31–7.48 (m, 10H), 7.62–7.71 (m, 4H), 8.03 (s, 1H), 8.33 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 18.8, 20.3, 20.5, 20.7, 41.2, 54.3, 61.8, 68.9, 69.4, 70.1, 71.7, 73.9, 84.4, 86.8, 98.0, 120.0, 123.4, 127.8, 127.9, 129.9, 130.0, 130.9, 132.9, 134.3, 135.4, 135.5, 139.5, 149.2, 151.0, 154.6, 167.3, 169.4, 170.0, 170.7 ppm; IR (ATR): $\tilde{\nu}$ = 2935, 1747, 1716, 1633, 1594, 1471, 1427, 1385, 1365, 1334, 1222, 1104, 1075, 1033, 948, 900, 823, 798, 743, 721, 702, 647, 504 cm^{-1}; HRMS (FAB+): calcd for $[M+H]^+$, $C_{46}H_{51}N_6O_{12}Si$, 907.3334; found, 907.3334.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(3″,4″,6″-tri-*O*-acetyl-2″-deoxy-2″-phthalimido-β-D-glucopyranosyl)-thymidine (β-26) (Entry 2 in Table 4)

Reaction conditions for the synthesis of β-**26** were the same as those for β-**11 a**. The resulting residue was purified by silica gel column chromatography (hexanes/AcOEt = 2:1 to 1:1) to give β-**26** as a colorless amorphous solid (76 mg, 74% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.92 (s, 9H), 1.55 (ddd, J = 5.0, 8.5, 14.2 Hz, 1H), 1.86 (s, 3H), 2.02–2.11 (m, 10H), 2.25 (dd, J = 1.8, 10.1 Hz, 1H), 3.74–3.82 (m, 3H), 3.88 (d, J = 5.5 Hz, 1H), 4.07 (dd, J = 2.2, 12.5 Hz, 1H), 4.13 (dd, J = 8.4, 10.8 Hz, 1H), 4.35 (dd, J = 4.4, 12.5 Hz, 1H), 4.90 (d, J = 8.4 Hz, 1H), 5.10 (dd, J = 9.1, 10.8 Hz, 1H), 5.83 (dd, J = 9.2, 10.8 Hz, 1H), 6.40 (dd, J = 5.4, 9.2 Hz, 1H), 7.32–7.49 (m, 11H), 7.61–7.79 (m, 4H), 8.21 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 12.5, 18.8, 20.4, 20.5, 20.6, 26.7, 40.5, 54.4, 61.6, 68.8, 69.5, 70.0, 72.0, 74.0, 84.9, 86.5, 98.2, 111.3, 123.4, 127.9, 127.9, 129.9, 130.1, 130.8, 132.8, 133.0, 134.5, 135.4, 135.5, 135.5, 150.4, 163.7, 167.3, 169.3, 170.0, 170.5 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{46}H_{52}N_3O_{14}Si$, 898.3219; found, 898.3218.

4-*N*-Benzoyl-3′-*O*-*tert*-butyldiphenylsilyl-5′-*O*-(3″,4″,6″-tri-*O*-acetyl-2″-deoxy-2″-phthalimido-β-D-glucopyranosyl)-2′-deoxycytidine (β-27) (Entry 3 in Table 4)

Reaction conditions for the synthesis of β-**27** were the same as those for β-**11 a**. The resulting residue was purified by silica gel column chromatography (hexanes/$CHCl_3$ = 1:3 to 0:1) to give β-**27** as a colorless amorphous solid (32.5 mg, 65% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.94 (s, 9H), 1.49–1.58 (m, 1H), 1.85 (s, 3H), 2.04 (s, 3H), 2.16 (s, 3H), 2.38–2.50 (m, 2H), 3.74–3.85 (m, 3H), 3.95 (d, J = 6.0 Hz, 1H), 4.09–4.19 (m, 2H), 4.39 (dd, J = 4.2, 12.6 Hz, 1H), 4.96 (d, J = 8.7 Hz, 1H), 5.16 (t, J = 9.3 Hz 1H), 5.82 (dd, J = 9.0, 10.8 Hz, 1H), 6.39 (dd, J = 5.4, 8.1 Hz, 1H), 7.30–7.75 (m, 18H), 7.93 (d, J = 6.9 Hz, 2H), 8.01 (d, J = 7.5 Hz, 1H), 8.69 ppm (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 18.9, 20.4, 20.6, 20.8, 26.8, 42.2, 54.4, 61.7, 68.8, 69.3, 70.1, 72.1, 74.0, 87.2, 87.3, 97.0, 98.1, 123.5, 127.6, 127.9, 128.0, 129.0, 129.9, 130.1, 130.9, 132.8, 133.1, 133.1, 133.3, 134.6, 135.5, 135.6, 144.5, 162.0, 167.3, 169.4, 170.1, 170.8 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{52}H_{55}N_4O_{14}Si$, 987.3484; found, 987.3484.

2-*N*-Isobutyryl-3′-*O*-*tert*-butyldiphenylsilyl-5′-*O*-(3″,4″,6″-tri-*O*-acetyl-2″-deoxy-2″-phthalimido-β-D-glucopyranosyl)-2′-deoxyguanosine (β-28) (Entry 4 in Table 4)

Reaction conditions for the synthesis of β-**28** were the same as those for β-**11 a**. The resulting residue was purified by NH silica gel column chromatography (hexanes/$CHCl_3$ = 1:4, then $CHCl_3$/MeOH = 100:1) to give β-**28** as a colorless amorphous solid (18.4 mg, 37% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.96 (s, 9H), 1.27–1.30 (m, 7H), 1.86 (s, 3H), 2.03 (s, 3H), 2.09 (s, 3H), 2.43–2.53 (m, 1H), 2.61–2.71 (m, 2H), 3.65–3.79 (m, 2H), 3.89 (s, 1H), 4.07–4.28 (m, 4H), 5.03 (d, J = 8.4 Hz, 1H), 5.10 (t, J = 9.6 Hz, 1H), 5.78 (dd, J = 9.0, 10.2 Hz, 1H), 6.09 (dd, J = 4.8, 9.6 Hz, 1H), 7.31–7.49 (m, 10H), 7.65–7.75 (m, 5H), 8.87 (s, 1H), 12.02 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.0, 19.0, 19.1, 20.4, 20.6, 20.8, 26.8, 29.7, 36.5, 39.6, 54.4, 61.8, 68.8, 68.9, 70.4, 71.9, 73.7, 84.5, 86.5, 97.9, 122.0, 123.5, 127.9, 128.1, 130.0, 130.2, 130.9, 132.9, 133.0, 134.6, 135.4, 135.6, 138.0, 147.3, 148.1, 155.5, 167.6, 169.3, 170.0, 170.8, 178.4 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{50}H_{57}N_6O_{14}Si$, 993.3702; found, 993.3702.

3′-*O*-(2″,3″,4″,6″-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-5′-*O*-*tert*-butyldiphenylsilyl-2′-deoxyadenosine (β-30) (Scheme 4 a)

Reaction conditions for the synthesis of β-**30** were the same as those for β-**11 a**. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 100:1 to 50:1) followed by GPC ($CHCl_3$) to give β-**30** as a colorless amorphous solid (52 mg, 52% yield): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.03 (s, 9H), 2.73–2.94 (m, 2H), 3.66 (dd, J = 4.0, 11.0 Hz, 1H), 3.83 (dd, J = 6.0, 11.0 Hz, 1H), 3.99–4.21 (m, 1H), 4.23 (t, J = 6.8 Hz, 1H), 4.41 (dd, J = 6.3, 11.5 Hz, 1H), 4.62–4.68 (m, 2H), 4.82 (d, J = 8.1 Hz, 1H), 5.54–5.60 (m, 3H), 5.79 (dd, J = 8.1, 10.3 Hz, 1H), 5.98 (d, J = 3.3 Hz, 1H), 6.27 (t, J = 7.0 Hz, 1H), 7.23–7.68 (m, 22H), 7.78–7.97 (m, 7H), 8.11 (dd, J = 1.3, 8.2 Hz, 2H), 8.23 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 19.2, 26.9, 38.0, 62.0, 63.1, 68.0, 69.6, 71.5, 80.3, 84.6, 85.1, 101.4, 120.2, 127.9, 127.9, 128.3, 128.4, 128.5, 128.7, 128.7, 129.0, 129.1, 129.3, 129.6, 129.8, 130.0, 130.1, 130.1, 132.9, 133.3, 133.4, 133.7, 135.5, 135.5, 139.3, 149.5, 152.5, 155.3, 165.2, 165.6, 165.6, 165.9 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{60}H_{58}N_5O_{12}Si$, 1068.3851; found, 1068.3846.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(2″,3″,4″-tri-*O*-benzyl-6″-*O*-trityl-D-glucopyranosyl)-2′-deoxyadenosine (32) (Scheme 4b)

Reaction conditions for the synthesis of **32** were the same as those for β-**11 a**. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 200:1 to 50:1) to give **32** as a colorless amorphous solid (22.8 mg, 46% yield, α/β = 3:1): ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 1.06 (s, 6.7H), 1.11 (s, 2.3H), 2.33–2.38 (m, 1.5H), 2.48–2.52 (m, 0.5H), 3.03 (dd, J = 2.6, 10.1 Hz, 0.75H), 3.13–3.38 (m, 3.75H), 3.42–3.68 (m, 2.5H), 3.76 (t, J = 9.2 Hz, 0.75H), 3.87 (t, J = 9.4 Hz, 0.25H), 4.22–4.30 (m, 2H), 4.36–4.41 (m, 1H), 4.55–4.60 (m, 1H, H-1″ of β-anomer and other proton of α and β-anomers), 4.62–4.81 (m, 3.5H, H-1″ of α-anomer and other protons of α and β-anomers), 4.88–4.96 (m, 1.25H), 5.28 (s, 0.5H), 5.55 (s, 1.5H), 6.61 (t, J = 7.0 Hz, 0.25H, H-1′ of β-anomer), 6.68 (t, J = 7.2 Hz, 0.75H, H-1′ of α-anomer) 6.82–6.88 (m, 2H), 7.08–7.48 (m, 35.75H), 7.53–7.58 (m, 3H), 7.62–7.68 (m, 1.25H), 8.20 (s, 0.25H), 8.27 (s, 0.25H), 8.35 (s, 0.75H), 8.57 ppm (s, 0.75H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 18.9, 19.0, 26.9, 29.6, 41.7, 41.9, 61.7, 62.4, 67.6, 69.2, 72.1, 73.2, 74.7, 74.8, 74.9, 75.0, 75.8, 75.8, 77.4, 77.7, 79.3, 81.9, 82.4, 83.8, 84.6, 84.8, 86.2, 86.3, 86.4, 86.9, 97.5,

103.1, 119.6, 119.9, 126.8, 126.9, 127.5, 127.6, 127.7, 127.7, 127.8, 127.9, 127.9, 128.0, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 128.7, 129.9, 130.0, 130.1, 132.8, 133.0, 133.2, 135.5, 135.6, 135.6, 135.7, 138.0, 138.3, 138.4, 139.9, 143.8, 149.5, 149.9, 152.5, 152.7, 155.2, 155.3 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{72}H_{74}N_5O_8Si$, 1164.5307; found, 1164.5308.

3′-*O*-*tert*-Butyldiphenylsilyl-5′-*O*-(6″-*O*-acetyl-2″,3″,4″-tri-*O*-benzyl-D-mannopyranosyl)-2′-deoxyadenosine (34) (Scheme 4c)

Reaction conditions for the synthesis of **34** were the same as those for β-**11a**. The resulting residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 1:0 to 100:1) to give **34** as a colorless amorphous solid (31.9 mg, 57% yield, α/β = 2.5:1): α-**34**; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.09 (s, 9H), 2.00 (s, 3H), 2.24 (m, 1H), 2.39 (m, 1H), 3.56 (m, 2H), 3.84 (t, J = 9.3 Hz, 1H), 4.06–4.16 (m, 3H), 4.51–4.56 (m, 5H, H-1″ of α-anomer and other protons), 4.64–4.70 (m, 2H), 4.87 (d, J = 10.8 Hz, 1H), 5.70 (s, 2H), 6.41 (t, J = 6.0 Hz, 1H, H-1′ of α-anomer), 7.19–7.38 (m, 25H), 7.62–7.65 (m, 6H), 8.32 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.0, 20.8, 19.0, 26.9, 40.9, 63.0, 67.0, 70.2, 71.8, 72.8, 73.6, 73.9, 74.8 75.1, 77.2, 79.4, 84.3 (C-1′ of α-anomer), 86.0, 98.2 (C-1″ of α-anomer), 120.0, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.3, 128.4, 130.2, 130.2, 132.8, 132.9, 134.8, 135.6, 135.7, 138.1, 138.2, 138.2, 138.5, 149.6, 153.0, 155.4, 170.8 ppm; β-**34**; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.07 (s, 9H), 2.00 (s, 3H), 2.30–2.44 (m, 1H), 2.45–2.55 (m, 1H), 3.26–3.59 (m, 2H), 3.41 (dd, J = 2.8, 9.0 Hz, 1H), 3.77 (d, J = 2.6 Hz, 1H), 3.85–3.92 (m, 2H), 4.20–4.26 (m, 3H, H-1″ of β-anomer and other protons), 4.32 (dd, J = 2.2, 12.1 Hz, 1H), 4.47 (d, J = 3.9 Hz, 1H), 4.52–4.58 (m, 2H), 4.67 (s, 2H), 4.89 (d, J = 10.5 Hz, 1H), 5.88 (br s, 2H), 6.46 (t, J = 7.2 Hz, 1H, H-1′ of β-anomer), 7.14–7.46 (m, 20H), 7.65 (d, J = 7.5 Hz, 5H), 8.10 (s, 1H), 8.29 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.0, 20.9, 26.9, 40.7, 63.6, 69.5, 71.6, 73.7, 73.8, 74.1, 74.2, 74.4, 75.2, 76.6, 77.2, 82.1, 84.4 (C-1′ of β-anomer), 86.4, 101.2 (C-1″ of β-anomer), 127.4, 127.5, 127.7, 127.8, 127.9, 128.0, 128.1, 128.1, 128.4, 128.4, 130.1, 133.1, 133.2, 135.7, 135.8, 137.9, 138.0, 138.3, 139.7, 152.7, 155.3, 171.0 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{55}H_{62}N_5O_9Si$, 964.4317; found, 964.4318.

5′-*O*-β-D-Galactopyranosyl-2′-deoxyadenosine (β-35) (Scheme 5a)

1 M Bu_4NF in THF (44.5 μL, 44.5 μmol) was slowly added to an ice-cooled solution of β-**16** (47.5 mg, 44.5 μmol) in THF (1.3 mL). The mixture was stirred on an ice bath under an argon atmosphere for 4 h. After removing the solvent by evaporation, the residue was dissolved in CH_2Cl_2, the solution washed with H_2O and brine, dried over Na_2SO_4 and concentrated. The residue purified by silica gel column chromatography ($CHCl_3$/MeOH = 100:2 to 100:3) to give the desilylated compound as a colorless amorphous solid (36.9 mg): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.38–2.42 (m, 2H), 2.67–2.77 (m, 1H), 3.85 (dd, J = 2.7, 7.8 Hz, 1H), 4.08–4.14 (m, 1H), 4.23 (dd, J = 3.6, 10.8 Hz, 3H), 4.35 (t, J = 4.8 Hz, 1H), 4.45 (dd, J = 4.8, 8.4 Hz, 1H), 4.53–4.58 (m, 1H), 4.71 (dd, J = 1.8, 8.4 Hz, 1H), 4.88 (d, J = 8.0 Hz, 1H), 5.55 (brs, 2H), 5.67 (dd, J = 2.7, 8.1 Hz, 1H), 5.82 (dd, J = 6.3, 10.8 Hz, 1H) 6.01 (d, J = 1.8 Hz, 1H), 6.45 (t, J = 5.1 Hz, 1H) 7.22–7.27 (m, 2H), 7.35–7.46 (m, 5H), 7.49–7.54 (m, 4H), 7.64 (t, J = 5.7 Hz, 1H), 7.78 (dd, J = 0.9, 6.6 Hz, 2H), 7.93 (dd, J = 0.9, 6.3 Hz, 2H), 8.00 (dd, J = 0.9, 6.3 Hz, 2H), 8.14 (dd, J = 1.2, 6.6 Hz, 2H), 8.25 (s, 1H), 8.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 40.7, 61.9, 68.0, 69.9, 69.9, 71.2, 71.6, 72.3, 84.0, 85.4, 101.6, 120.0, 128.3, 128.5, 128.5, 128.7, 128.7, 128.9, 129.0, 129.3, 129.7, 129.8, 129.8, 130.1, 133.4, 133.5, 133.6, 139.3, 149.6, 152.8, 155.5, 165.5, 165.6, 166.1 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{44}H_{40}N_5O_{12}Si$, 830.2674; found, 830.2672.

The desilylated compound (31.4 mg, 37.8 μmol) was treated with 2.0 mL of methylamine in MeOH (10 M) for 6 h under an argon atmosphere at room temperature. After evaporation of the solvent, the oily residue was dissolved in water and the *N*-methylbenzamide was removed by successive washing of the aqueous phase with CH_2Cl_2. The aqueous layer was concentrated under reduced pressure, and resulting yellow suspension was centrifuged and washed with ethanol to give β-**35** as a colorless amorphous solid (11.9 mg, 76% from β-**16**): ^{1}H NMR (400 MHz, D_2O, TSP): δ = 2.63 (ddd, J = 4.1, 6.4, 14.2 Hz, 1H), 2.91 (dt, J = 6.3, 13.5 Hz, 1H), 3.52 (dd, J = 7.7, 9.9 Hz, 1H), 3.59–3.64 (m, 2H), 3.72–3.74 (m, 2H), 3.84 (dd, J = 5.4, 11.5 Hz, 1H), 3.91 (d, J = 3.4 Hz, 1H), 4.16 (dd, J = 3.4, 11.5 Hz, 1H), 4.29–4.32 (m, 1H), 4.38 (d, J = 7.8 Hz, 1H), 4.60–4.94 (m, 1H), 6.52 (t, J = 6.6 Hz, 1H), 8.26 (s, 1H), 8.42 ppm (s, 1H); ^{13}C NMR (100 MHz, D_2O, 1,4-dioxane): δ = 38.7, 61.0, 68.7, 69.4, 70.8, 71.1, 72.8, 75.2, 83.9, 85.7, 103.1, 118.8, 140.0, 148.6, 152.5, 155.4 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{16}H_{24}N_5O_8Si$, 414.1629; found, 414.1622.

5′-*O*-β-D-Galactopyranosyl-2′-thymidine (β-36) (Scheme 5a)

1 M Bu_4NF in THF (38 μL, 38.0 μmol) was slowly added to a solution of β-**21** (40.2 mg, 38.0 μmol) in THF (1.0 mL) at 0 °C. The mixture was stirred at 0 °C under an argon atmosphere for 4 h. After removing solvent by evaporation, the residue was dissolved in CH_2Cl_2, and the resulting solution was washed with H_2O and brine, dried over Na_2SO_4 and concentrated. The remaining residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 200:1 to 50:1) to give the desilylated compound as a colorless amorphous solid (27.8 mg): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.03–2.09 (m, 5H), 2.18 (brs, 1H), 3.73 (dd, J = 2.3, 10.5 Hz, 1H), 4.05 (d, J = 2.6 Hz, 1H), 4.21–4.26 (m, 1H), 4.25–4.49 (m, 3H), 4.72 (dd, J = 6.2, 11.0 Hz, 1H), 4.85 (d, J = 7.7 Hz, 1H), 5.71 (dd, J = 3.5, 10.5 Hz, 1H), 5.80 (dd, J = 7.7, 10.5 Hz, 1H), 6.02 (dd, J = 0.8 Hz, 3.5 Hz, 1H), 6.37 (t, J = 7.1 Hz, 1H), 7.22–7.28 (m, 2H), 7.37–7.68 (m, 11H), 7.77 (dd, J = 1.2, 8.3 Hz, 2H), 7.91–8.08 (m, 4H), 8.44 ppm (brs, 1H).

The desilylated compound (27.6 mg, 33.6 μmol) was treated with 2.0 mL of methylamine in MeOH (10 M) for 6 h under an argon atmosphere at room temperature. After evaporation of the solvent, the resulting oily residue was dissolved in water and the *N*-methylbenzamide was removed by successive washing of the aqueous phase with CH_2Cl_2. The aqueous phase evaporated to dryness, and the resulting yellow foam was centrifuged and washed with methanol to give β-**36** as a colorless amorphous solid (13.4 mg, 89% from β-**21**): ^{1}H NMR (400 MHz, D_2O, TSP): δ = 1.91 (s, 3H), 2.32–2.46 (m, 2H), 3.55–3.89 (m, 6H), 3.93 (d, J = 3.2 Hz, 1H), 4.17–4.22 (m, 2H), 4.46 (d, J = 7.8 Hz, 1H), 4.51–4.56 (m, 1H), 6.32 (t, J = 5.1 Hz, 1H), 7.63 ppm (s, 1H); ^{13}C NMR (100 MHz, D_2O, 1,4-dioxane): δ = 11.6, 38.3, 61.1, 68.6, 69.5, 70.9, 70.9, 72.8, 75.3, 85.2, 85.4, 103.2, 111.6, 137.5, 151.7, 166.6 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{16}H_{25}N_2O_{10}$, 405.1510, found, 405.1509.

5′-*O*-α-D-Mannopyranosyl-2′-deoxyadenosine (α-37) (Scheme 5b)

1 M Bu_4NF in THF (21 μL, 21 μmol) was slowly added to a solution of α-**34** (20.0 mg, 20.7 μmol) in THF (0.7 mL) at 0 °C. The mixture was stirred at 0 °C under an argon atmosphere for 2 h. After removing solvent by evaporation, the residue was dissolved in CH_2Cl_2, the solution washed with H_2O and brine, dried over Na_2SO_4

and concentrated. The remaining residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 100:1 to 98:2) to give the desilylated compound as a colorless amorphous solid (13.9 mg): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.04 (s, 3H), 2.45 (m, 1H), 2.64 (m, 1H), 3.01 (brs, 1H), 3.65 (dd, J = 4.8, 11.1 Hz, 1H), 3.72–3.95 (m, 5H), 4.12 (d, J = 4.0 Hz, 1H), 4.21 (dd, J = 5.9, 11.7 Hz, 1H), 4.31 (dd, J = 1.8, 11.7 Hz, 1H), 4.55–4.78 (m, 6H), 4.85 (t, J = 11.0 Hz, 2H), 5.67 (s, 2H), 6.36 (t, J = 5.9 Hz, 1H), 7.27–7.40 (m, 15H), 7.97 (s, 1H), 8.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 20.9, 40.4, 63.8, 67.0, 70.2, 71.3, 72.0, 73.0, 74.6, 74.8, 75.3, 77.2, 79.8, 84.6, 85.2, 98.5, 127.7, 127.7, 128.0, 128.3, 128.3, 128.4, 137.9, 138.1, 138.2, 138.9, 149.4, 152.9, 155.4, 171.1 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{39}H_{44}N_5O_9$, 726.3139; found, 726.3138.

The desilylated compound (7.0 mg, 9.6 μmol) was dissolved in 0.1 M a solution of sodium methoxide in MeOH (150 μL) and stirred for 6 h under an argon atmosphere at room temperature. The solution was neutralized with 0.1 N HCl aq., extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and evaporated in vacuo to give the deacetylated compound as a colorless amorphous solid (5.5 mg): ^{1}H NMR (300 MHz, CD_3OD, TMS): δ = 0.89 (brs, 1H), 1.28 (s, 1H), 2.48 (m, 2H), 3.48 (m, 1H), 3.59–3.94 (m, 8H), 4.12 (dd, J = 3.3, 6.6 Hz, 1H), 4.40 (d, J = 11.7 Hz, 1H), 4.52–4.68 (m, 5H), 4.82 (d, J = 10.6 Hz, 1H), 6.37 (t, J = 6.2 Hz, 1H), 7.11–7.39 (m, 17H), 8.21 (s, 1H), 8.25 ppm (s, 1H); ^{13}C NMR (100 MHz, CD_3OD, TMS): δ = 41.8, 54.8, 62.5, 68.1, 72.6, 72.6, 74.3, 74.4, 75.7, 76.0, 76.6, 80.7, 86.2, 87.4, 99.4, 120.6, 128.6, 128.7, 128.8, 129.0, 129.2, 129.3, 129.4, 139.6, 139.8, 140.5, 150.2, 153.9, 157.3 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{37}H_{42}N_5O_8$, 684.3033; found, 684.3036.

A mixture of the deacetylated compound (21.9 mg, 0.032 mmol), 10% Pd/C (70 mg) and MeOH/H_2O (10/1) (1.1 mL) was vigorously stirred under a H_2 atmosphere at room temperature for 2 days. The mixture was filtered through Celite with MeOH/H_2O (5:1 to 0:1), and the filtrate was concentrated under reduced pressure to give α-**37** as a colorless amorphous solid (12.2 mg, 72% from α-**34**): ^{1}H NMR (300 MHz, D_2O, TSP): δ = 2.58–2.64 (m, 1H), 2.82–2.89 (m, 1H), 3.22 (m, 1H), 3.55–3.97 (m, 7H), 4.09 (dd, J = 3.1, 11.5 Hz, 1H), 4.26 (m, 1H), 4.58–4.69 (m, 1H), 6.43 (t, J = 6.6 Hz, 1H), 8.64 (s, 1H), 8.45 ppm (s, 1H); ^{13}C NMR (75 MHz, D_2O, 1,4-dioxane): δ = 39.5, 58.8, 61.7, 70.0, 71.0, 72.0, 73.6, 77.0, 84.6, 86.5, 101.0, 119.4, 140.9, 149.4, 153.4, 156.3 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{16}H_{24}N_5O_8$, 414.1625, found, 414.1626.

6-*N*-Benzoyl-3′,5′-*O*-bis-*tert*-butyldiphenylsilyl-2′-deoxyadenosine (38b)[39]

Benzoyl chloride (60 μL, 1.03 mmol) was slowly added to a solution of **38a** (125 mg, 0.17 mmol) in dry pyridine (1.5 mL) at 0 °C. The mixture was stirred at 0 °C under an argon atmosphere for 4 h, to which H_2O (0.35 mL) and conc. aqueous NH_3 (0.70 mL) were added. The mixture was stirred at room temperature under an argon atmosphere for 1.5 h. After removing solvent by evaporation, the residue was dissolved in $CHCl_3$, washed with H_2O and brine, dried over Na_2SO_4 and concentrated. The remaining residue was purified by silica gel column chromatography (hexanes/$CHCl_3$ = 1:1 to 0:1) to give compound **38b** as a colorless amorphous solid (135 mg, 96%): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.93 (s, 9H), 1.11 (s, 9H), 2.46 (m, 2H), 3.37 (dd, J = 3.6, 11.4 Hz, 1H), 3.67 (dd, J = 3.6, 11.4 Hz, 1H), 4.14 (q, J = 3.6 Hz, 1H), 4.14–4.18 (m, 1H), 6.58 (t, J = 7.2 Hz, 1H), 7.25–7.67 (m, 23H), 8.00 (d, J = 8.7 Hz, 2H), 8.11 (s, 1H), 8.76 (s, 1H), 9.03 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.0, 19.1, 26.8, 26.9, 41.1, 63.7, 73.7, 77.12, 84.5, 88.2, 123.1, 127.7, 127.8, 127.9, 128.6, 128.8, 129.4, 129.8, 129.8, 130.0, 132.5, 132.6, 132.8, 132.9, 133.1, 133.1, 133.7, 134.0, 135.4, 135.5, 135.7, 135.8,141.2, 143.2, 149.39, 151.4, 152.0, 152.6, 164.6, 172.2 ppm; HRMS (FAB+): calcd for $[M+H]^+$, $C_{49}H_{54}N_5O_4Si_2$ 832.3714; found, 832.3719.

^{1}H NMR measurements of nucleoside derivatives in the presence of glycosylation promoters

To a solution of the nucleoside derivative (0.010 mmol) in anhydrous $CDCl_3$ (700 μL), AgOTf (7.9 mg, 0.030 mmol) and/or TolSCl (3.2 mg, 2.7 μL, 0.020 mmol) were added at −40 °C. NMR spectra were then recorded at −40 °C by using a NMR spectrometer (at 400 MHz for ^{1}H NMR spectra).

Reaction of 38b with TolSCl + AgOTf that affords 1:1 or 2:1 complexes of *N*-benzoyladenine and Ag^+ (39), methyl 3′,5′-*O*-bis-*tert*-butyldiphenylsilyl-D-2′-deoxyriboside (40) (Scheme 6)

To a solution of **38b** (35 mg, 0.042 mmol) in CH_2Cl_2 (1.0 mL), TolSCl (10 mg, 9.1 μL, 0.063 mmol) and AgOTf (32 mg, 0.13 mmol) were added at −40 °C. The reaction mixture was stirred for 3 h at −40 °C and quenched by adding MeOH (several drops). The mixture was concentrated in vacuo. The residue was washed with Et_2O to give **39** as a white solid (25 mg, mixture) (see Figure S5 in the Supporting Information): ^{1}H NMR (300 MHz, [D_6]DMSO, TMS): δ = 7.21–7.79 (m, 7H), 8.12 (d, J = 7.5 Hz, 2H), 8.75 (s, 1H), 8.88 (s, 1H), 11.91 ppm (brs, 1H); HRMS (FAB+): calcd for $[M+Ag]^+$, $C_{12}H_9N_5O^{107}Ag$: 345.9858, $C_{12}H_9N_5O^{109}Ag$: 347.9855; found, 345.9858, 347.9855. HRMS (FAB+): calcd for $[M+Ag]^+$, $[C_{12}H_9N_5O]_2{}^{107}Ag$: 585.0665, $[C_{12}H_9N_5O]_2{}^{109}Ag$: 587.0662; found, 585.0665, 587.0661.

The supernatant fraction was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexanes/$CHCl_3$ = 10:1 to 1:1) to give compound **40** as a colorless amorphous solid (15 mg, 58%, α/β = 1:1): ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.95 (d, J = 9.0 Hz, 9H), 1.03 (s, 9H), 1.86–1.87 (m, 1H), 1.91–1.92 (m, 1H), 3.25 (s, 1.5H), 3.31 (dd, J = 4.4, 11.4 Hz, 0.5H), 3.41 (s, 1.5H), 3.45 (d, J = 5.9 Hz, 1H), 3.56 (dd, J = 2.6, 11.0 Hz, 0.5H), 4.06–4.10 (m, 0.5), 4.13–4.17 (m, 0.5H), 4.27–4.33 (m, 0.5H), 4.36–4.41 (m, 0.5H), 4.96 (dd, J = 2.2, 5.9 Hz, 0.5H), 5.09 (dd, J = 3.3, 5.5 Hz, 0.5H), 7.25–7.43 (m, 12H), 7.53–7.65 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 19.1, 19.2, 26.7, 26.9, 41.6, 41.9, 54.8, 55.2, 63.9, 65.0, 72.9, 73.7, 77.2, 85.6, 87.3, 105.0, 105.5, 127.5, 127.6, 127.6, 127.6, 127.7, 127.7, 129.5, 129.7, 129.7, 133.5, 133.5, 133.5, 133.5, 133.8, 133.8, 133.9, 135.6, 135.6, 135.6, 135.7, 135.7, 135.8, 135.9 ppm; HRMS (FAB+): calcd for $[M+Na]^+$, $C_{38}H_{48}O_4Si_2Na$ 647.2989; found, 647.2990.

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[41] The ^{1}H NMR spectra of Thy-acceptor **17** and Cyt-acceptor **18b** suggest that the interaction of these nucleoside acceptors with TolSCl and AgOTf is not so strong (only a small change was observed in the aromatic region of **18b**, as shown in Figures S3 and S4 in the Supporting Information). The addition of TolSCl and AgOTf to Gua-acceptors **19a** and **19b** induced considerable spectral change (Figure S5), and the structures of the complexes are yet to be studied.

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