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Glycosylation of Nucleosides

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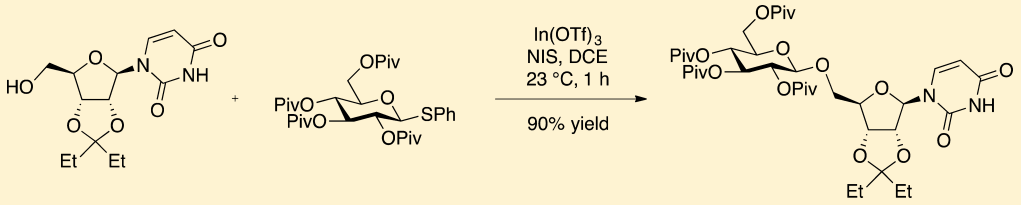
Supporting Information



ABSTRACT: Nucleoside *O*-glycosylation represents an archetypal problem in chemical selectivity, inasmuch as the nucleobase (an undesired site of reaction) is usually more nucleophilic than the hydroxyl (the desired site of reaction). Optimized reaction conditions have been developed for the efficient *O*-glycosylation of nucleoside hydroxyls. Both thioglycoside and Schmidt imidate donors (1.5 equiv) have been employed successfully. Interference by the nucleobase is minimized by the use of indium(III) triflate as the donor activating reagent; the $In(OTf)_3$ serves to promote apparent transfer of the donor glycosyl moiety from nucleobase to hydroxyl. Glycosylation of uridine triacetate gives products resulting from *O*- and *N*-glycosylation of the pyrimidine ring.

INTRODUCTION

Nucleoside disaccharides, various higher homologues, and other related modified complex nucleosides are an important class of natural products.[1,2] In particular, a stunning variety of complex nucleosides featuring the second glycosyl linkage, as well as components featuring lipid, heterocycle, sulfate, and amino acid subunits, have been found to show pronounced antibiotic and other activities. In many instances, this results from an effective inhibition of bacterial cell wall biosynthesis.[3−6] The chemical synthesis of nucleoside disaccharides and related compounds is quite challenging because of the complexity and density of functionality in these targets. Nevertheless, synthesis is often the best way to confirm structure and to provide material and analogues for medicinal and biological evaluation, including the investigation of biological pathways and metabolic modifications of nucleosides and (oligo)nucleotides. Synthetic studies also provide opportunities for valuable insight into issues of protecting group, heterocyclic, and glycosylation chemistry. For example, seemingly straightforward transformations, such as amide formation, C−C bond formation, and glycosylation, are often much more difficult in the presence of the nucleoside moiety.[7] Not surprisingly, the synthesis of the nucleoside disaccharide structural motif has been investigated by using not only the tactic of nucleosidation with pre-existing disaccharide donors but also the *O*-glycosylation of pre-existing nucleoside acceptors. The latter tactic, while synthetically more convergent, has an inherent problem: in most cases, the nucleoside heterocyclic base, a purine or a pyrimidine, features Lewis basic sites that are more reactive than the hydroxyl site where *O*-glycosylation is desired. There are several specific examples of complex nucleoside *O*-glycosylation in the literature in which glycosylation likely occurs preferentially on the nucleobase or other Lewis basic site, and completion of the reaction at the hydroxyl site requires a large excess of the donor.[8−10]

This is a fundamental issue in organic synthesis: how does one protect a more reactive site in a molecule so that the desired transformation can take place at a less reactive site? The attachment and subsequent cleavage of an effective protecting group, if one can be found, adds steps to the synthetic route. Some form of "transient protection" is more attractive.[11] In the case of nucleoside glycosylation, there are at least three "transient protection" scenarios by which the desired glycosylation selectivity could be achieved: (1) the donor, used in excess, reacts at both sites, and the glycosylated heterocycle portion is hydrolyzed during workup; (2) a Lewis acid, used in excess, blocks access to the more reactive nucleobase site; and (3) the Lewis acid promotes transfer of the glycosyl moiety from the nucleobase to the hydroxyl site. Because the glycosyl donor is typically more expensive than the Lewis acid, and sometimes considerably more so, options (2) and (3) are more attractive than (1). When this transformation occurs late in a total synthesis route, the freedom to optimize reaction conditions is limited by the amounts of starting materials available.

We began an investigation into the selective *O*-glycosylation of nucleosides with the restrictions that the amount and complexity of the donor should be limited, the Lewis acid should be inexpensive relative to the donor, and the reaction conditions should be mild. Furthermore, thioglycosides were initially used as glycosyl donors because of their multiple

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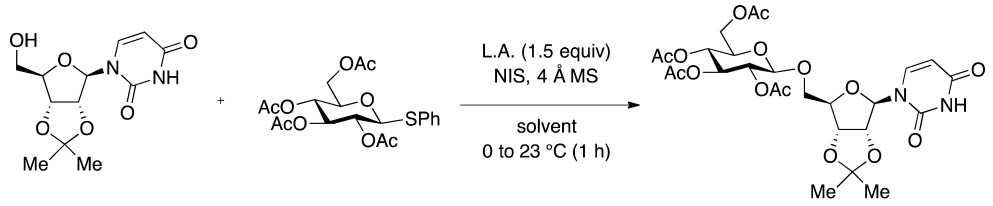
Table 1. Nucleoside Glycosylation−Lewis Acid Screen



1, 1 equiv **2**, 1.5 equiv **3**: % yield (HPLC)

entry	Lewis acid	solvent	HPLC yield (%)
1	TMS-OTf	1,2-dichloroethane	19
2	$BF_3{\cdot}OEt_2$	1,2-dichloroethane	34
3	AgOTf	1,2-dichloroethane	22
4	CuOTf	1,2-dichloroethane	32
5	$Cu(OTf)_2$	1,2-dichloroethane	37
6	$Bi(OTf)_3$	1,2-dichloroethane	trace
7	$Y(OTf)_3$	1,2-dichloroethane	15
8	$Ga(OTf)_3$	1,2-dichloroethane	33
9	$Sc(OTf)_3$	1,2-dichloroethane	26
10	**$Fe(OTf)_3$**	**1,2-dichloroethane**	**64**
11	**$In(OTf)_3$**	**1,2-dichloroethane**	**68**
12	$In(OTf)_3$	acetonitrile	42
13	$In(OTf)_3$	propionitrile	35
14	$In(OTf)_3$	dichloromethane	54
15	$In(OTf)_3$	ether	8
16	$In(OTf)_3$	THF	trace

advantages: they are easy to prepare, stable to storage and a variety of reaction conditions, and yet can be readily activated at modest temperatures with a wide range of electrophilic promoters.[12,13] Several syntheses of complex nucleoside antibiotics rely on thioglycoside intermediates to take advantage of these features.[14] A number of commendable glycosylation examples compliant with some of these criteria can be found in the literature.[15−26] However, even relatively successful nucleoside glycosylations are often optimized for the system at hand and, therefore, lack wide applicability. In fact, glycosylations in general are usually highly dependent on specific choices of donor, acceptor, promoter, solvent, and temperature. We sought a method that could more generally inform future complex nucleoside synthesis efforts. We found that, after some adjustment of reaction conditions and protecting groups, a protocol that features the Lewis acid indium(III) triflate proved to be particularly well suited to promote formation of nucleoside disaccharides by selective *O*-glycosylation.

RESULTS AND DISCUSSION

An initial screen (Table 1) of Lewis acid activators was performed with 2′,3′-*O*-isopropylidene)uridine[27] (**1**) as the acceptor and phenyl 1-thio-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside[28] **2** as the donor. Combinations of *N*-iodosuccinimide (NIS) and various Lewis acids were examined, and the formation of the O-5′-glycosylated nucleoside[29] (**3**) was monitored by HPLC. In all cases, the donor **2** was consumed, but unreacted acceptor **1** was returned in varying amounts. Under conventional conditions,[30] namely, 1.5 equiv each of trimethylsilyl trifluorosulfonate, NIS, and donor **2** in 1,2-dichloroethane solution for 1 h at room temperature, very little product **3** was formed (entry 1). This can be immediately attributed to interference, by the Lewis basic sites on the uracil base, with what should otherwise be an efficient *O*-glycosylation. Boron trifluoride etherate[31] offered a slight improvement (entry 2). Among a series of commercially available metal triflate activators (entries 3−11), two gave acceptable yields, iron(III) triflate and indium(III) triflate. Activation of thioglycosides by NIS in combination with metal triflates as a means to promote glycosylation of carbohydrate acceptors is known,[32] but the nucleoside case is more of a challenge. Further screening of several alternative solvents (entries 12−16) failed to improve on the combination of indium(III) triflate and 1,2-dichloroethane.[33]

At this point, two protecting group modifications were made to improve the glycosylation (Scheme 1). First, the isopropylidene protecting group of **1** was replaced by a 3-pentylidene acetal[34] (see **4**), which provides greater stability and solubility. Second, the acetyls of **2** were replaced by pivaloyls ("Piv"; see **5**), a refinement that minimizes interference by ortho ester formation during glycosylation of the primary hydroxyl.[35] As a result, product **7** could now be isolated in 90% yield, representing one of the best examples of such a nucleoside glycosylation.

With the amount of donor **5** held at 1.5 equiv, the amount of indium(III) triflate was varied in order to gain some insight into the role of the Lewis acid activator (Table 2). Yields, as determined by HPLC analysis, increase with the amount of In(III) triflate from 0.1 to 1.5 equiv (entries 1−4), but no additional benefit is observed beyond 1.5 equiv of activator. Without interence by the uracil base, a high glycosylation yield might have been expected with only catalytic In(III), since the Lewis acid can normally be recycled after initial NIS activation.[33c] Double glycosylation (once on the more reactive uracil ring and a second time on the 5′ hydroxyl), followed by hydrolysis of the glycosylated heterocycle on workup, corresponds to scenario 1 in the introduction above. As an exclusive path, this can be ruled out by the fact that yields

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Scheme 1. Improvement of Protecting Groups

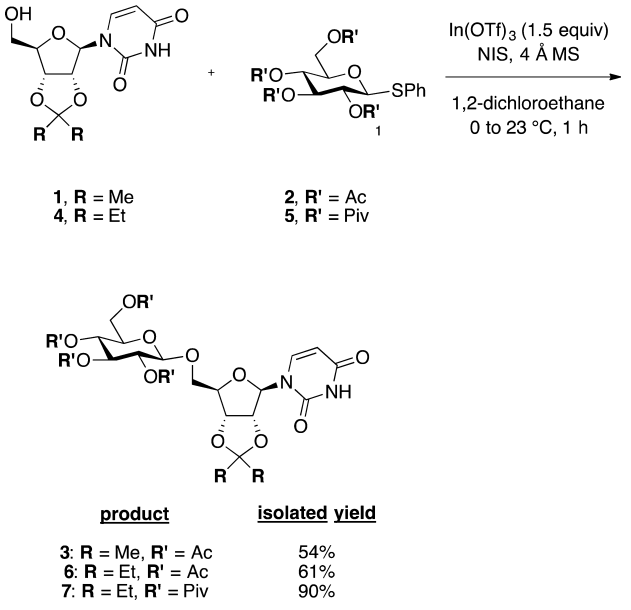
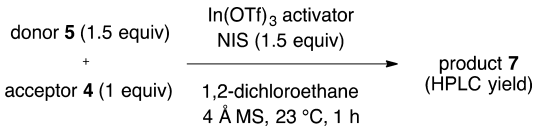


Table 2. Effect of the Amount of In(OTf)$_3$ Activator

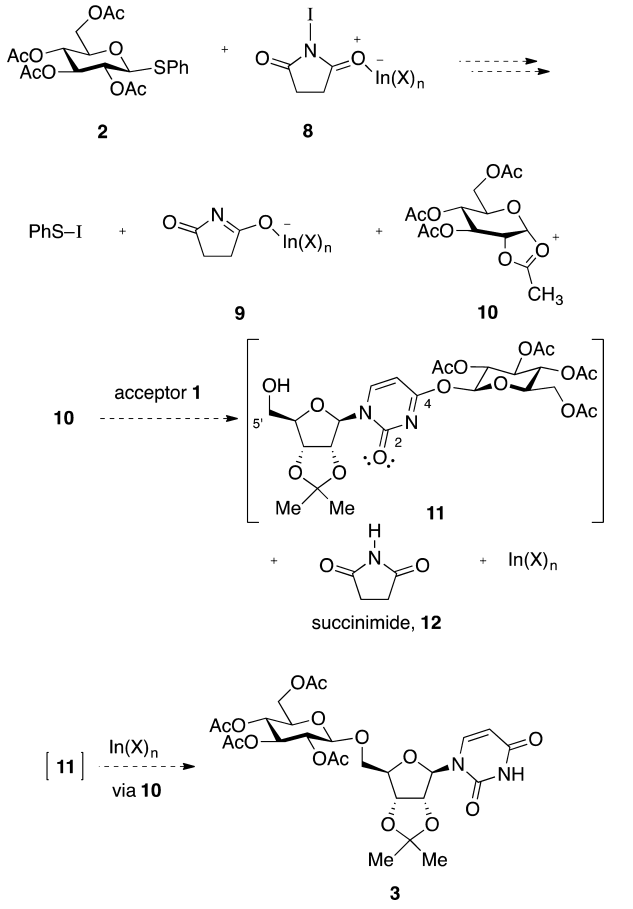


entry	In(OTf)$_3$ (equiv)	acceptor consumed (%)	HPLC yield (%)
1	0.1	27	23
2	0.5	82	77
3	1.0	92	85
4	**1.5**	**99**	**91**
5	2.0	95	87
6	3.0	92	85

exceed 75%, the maximum for double glycosylation when only 1.5 equiv of donor is employed. Scenario 2, namely, Lewis acid blockage of the more reactive site on the nucleobase, is also ruled out as an exclusive path because 0.5 equiv of In(III) would fail to block all the uracil sites and yet still leads to a 77% yield for the glycosylation. Scenario 3, however, is consistent with observations: glycosylation can occur first on the uracil ring, and in the presence of sufficient In(III) the glycosyl group can be transferred to the desired 5′-hydroxyl site.

A proposed mechanism reflecting this process is outlined in Scheme 2. Succinimide (**12**) serves as the eventual proton acceptor. The integrity of the indium−triflate bonds is left unspecified.[36] Initial glycosylation by the participated intermediate, **10**, or a functional equivalent, is suggested to occur at O-4 (see **11**, which itself resembles a glycosyl imidate donor), based on precedent that suggests that this site is the most Lewis basic on the neutral uracil ring. Analogies may be found in the kinetic reaction of the uracil ring of uridine derivatives at O-4 with silyl,[37] phosphoryl,[38] and sulfonyl[39] electrophiles. In contrast, N-3 glycosylation has been observed under Mitsunobu (i.e., basic) conditions,[40] which suggests that direct reaction at or isomerization to N-3 ought to be considered. In(III)-promoted intermolecular isomerization of **11** to product **3** may occur by, for example, coordination of the metal at O-2. The isomerization could be promoted by catalytic In(III) but

Scheme 2. Possible Mechanism for Nucleoside Glycosylation



favored by the presence of additional Lewis acid, which would account for the respectable yield at 0.5 equiv and improved yields at 1.0 and 1.5 equiv. The failure of other Lewis acids (Table 1), which ought to activate NIS anyway (see **8** and **9**), to give high yields of O-5′-glycosylated product **3** can be attributed to their inability to promote the O-4 to O-5′ isomerization of **11** as effectively. Any remaining O-4 glycosylated product **11** would be hydrolyzed back to acceptor **1** upon aqueous workup.

The generality of the optimized reaction conditions, namely, slight excess (1.5 equiv) each of donor, NIS, and indium(III) triflate at 23 °C for 1 h, was evaluated for additional donors and acceptors, as shown in Table 3 (donors are shown; acceptors, which are described in the Experimental Section, are apparent from the structure of the product). Galactopyranoside donor **13** proved to be almost as effective (87%) as the *gluco*-donor **5**, both using optimized uridine acceptor **4**. Ribofuranoside donor **15** was also employed successfully (80%). By mimicking uridine acceptor **4**, the analogous cytidine acceptor **45** gave a good yield (85%) of nucleoside disaccharide **17**. Ribofuranoside donor **15** worked almost as well (78%).

The relatively inaccessible[9b] secondary 2′-hydroxyl of an appropriately protected uridine acceptor (**56**) was glycosylated in 56% yield by using 2 equiv of the dependable donor **5**. The somewhat more activated donor, **20**, worked even better (64%).

The purine nucleosides are intrinsically difficult to *O*-glycosylate because they readily depurinylate, a process that occurs by way of competing N-7 glycosylation followed by loss

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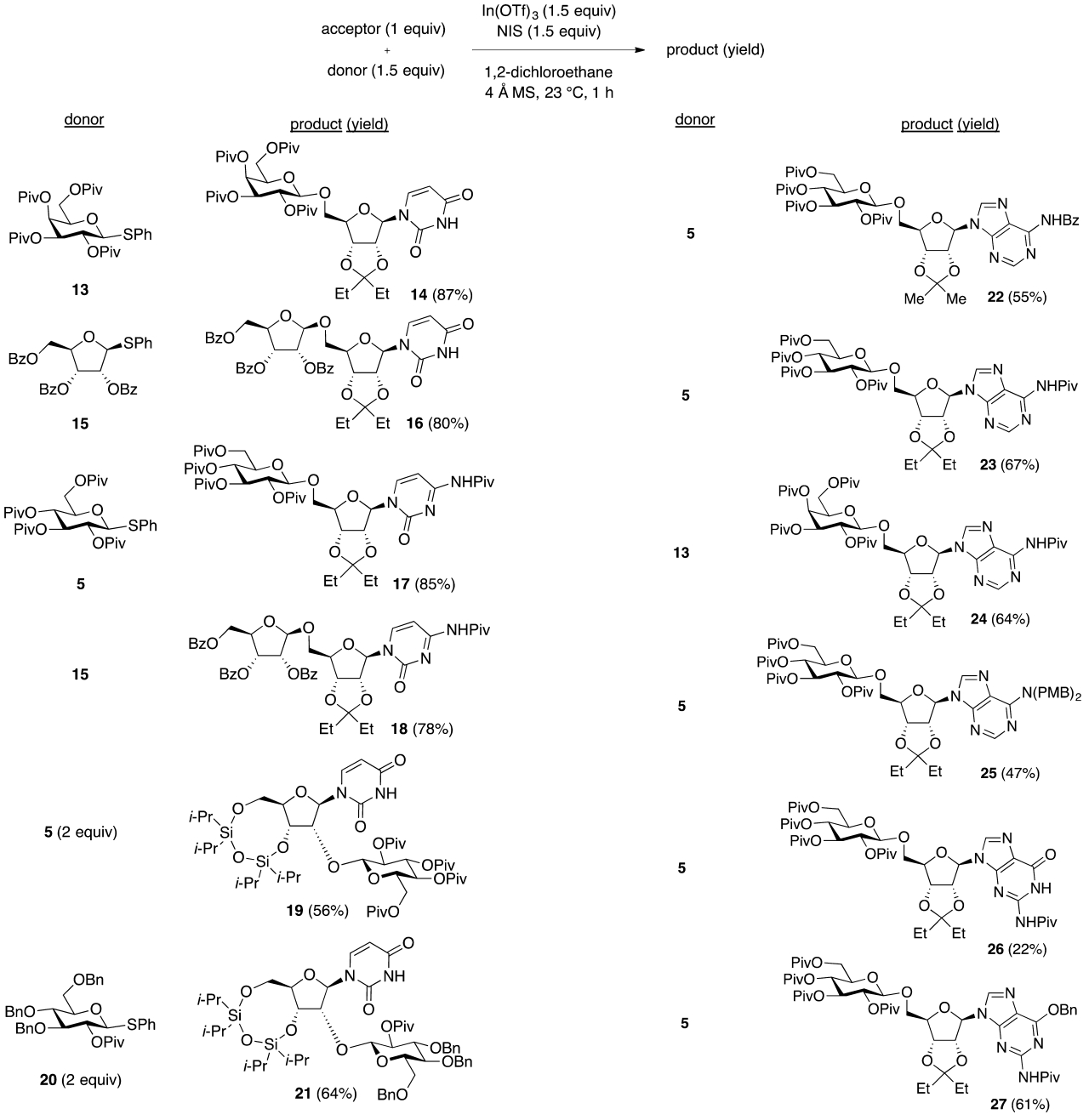
Table 3. Additional Thioglycoside Donors and Nucleoside Acceptors



of the ribofuranose at N-9.[9a,b,41] Additionally, the protecting group at the C-6 heteroatom (N or O) should be chosen with a view to minimizing its ability to act as a glycosyl accepting site itself. Thus, the adenosine (N-6)-benzoyl acceptor **52** was improved upon by switching to the (N-6)-pivaloyl version **47** (55% for **22** vs 67% yield for **23**). Galactopyranoside donor **13** also worked well (**24**, 64%), but the (N-6)-bis(*p*-methoxybenzyl) acceptor (**50**) was worse (**25**, 47%). An (N-2)-protected guanosine acceptor (**52**) performed poorly (**26**, 22%), but the situation was improved (**27**, 61%) by incorporation of an *O*-benzyl at C-6 (**55**), blocking glycosylation at that site.

Trichloroacetimidate (Schmidt) donors,[42] such as **28** (Table 4), are often preferred for glycosylations because of their high reactivity. Indium triflate ought to activate such donors by coordinating to the imidate nitrogen atom, but without the need for NIS. This idea was explored in the context of nucleoside glycosylation for three pyranose donors and three nucleoside acceptors (Table 4). In each case, the reaction required only 1 h at 0 °C. Donor **28**,[42] which is analogous to thioglycoside **2**, gave the disaccharide **3** in somewhat better yield than **2**. The "armed"[43] donor **29**[44] gave a good yield of 30, but without stereoselectivity (the two isomers of **30** were purified and characterized separately). A new Schmidt donor, **31**, worked well with both a pyrimidine acceptor (**4**) and a purine acceptor (**47**) and provided nucleoside disaccharides **32** and **33**, respectively. Overall, the results with Schmidt donors illustrate modest advantages over thioglycoside donors: the Schmidt donors demonstrate somewhat greater reactivity and embody the versatility of using the reducing sugar as the starting point for donor synthesis. As with thioglycoside donors (Table 3), indium(III) triflate-promoted transfer of the donor

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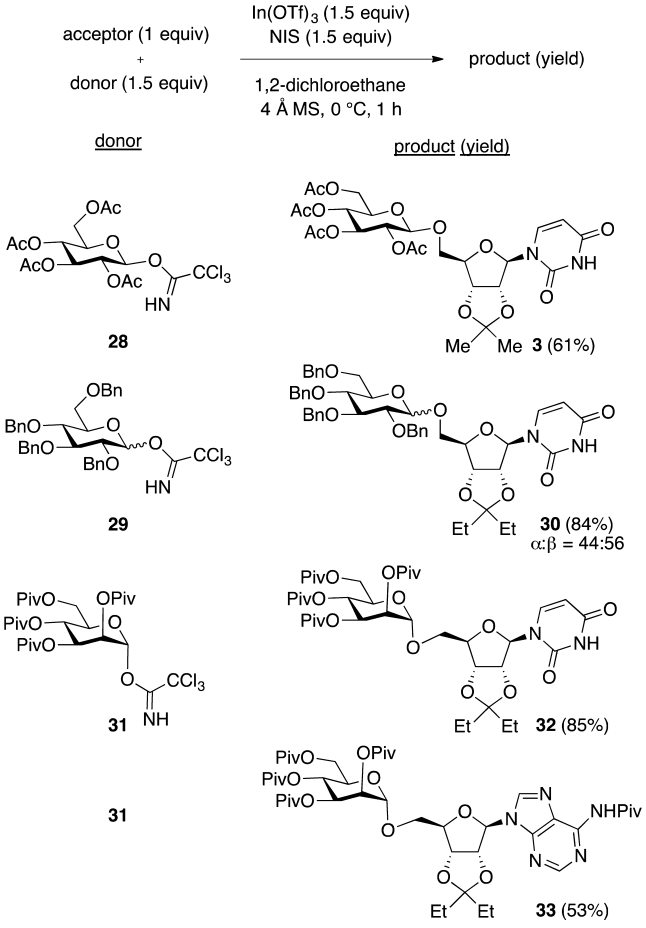
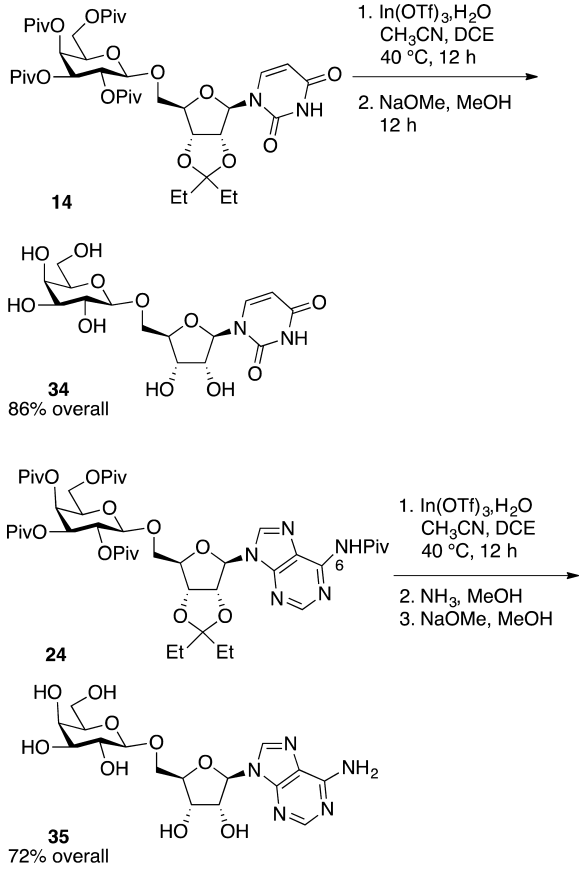
Table 4. Nucleoside *O*-Glycosylation with Schmidt Donors



Scheme 3. Deprotection of Nucleoside Disaccharides



moiety from nucleobase to hydroxyl appears to occur analogously in these examples, by way of the same probable intermediates (e.g., **11**).

We also demonstrate the deprotection of two of the nucleoside disaccharides (Scheme 3). Purification and isolation of such highly polar compounds can be challenging and is only occasionally done as part of literature reports, even though the ultimate synthetic targets must surely be the deprotected disaccharides themselves. Thus, hydrolysis of the 3-pentylidine acetal of **14**, followed by removal of the pivaloates under basic hydrolytic conditions and purification by reversed-phase chromatography, with aqueous acetonitrile as the eluant, gave the pyrimidine disaccharide **34**, matching the known compound,[45] in good overall yield. Indium(III) triflate was found to promote clean 3-pentylidene acetal hydrolysis in aq acetonitrile/dichloroethane solution, a reaction that was observed during these investigations when wet rather than dry acetonitrile was inadvertently used for a glycosylation reaction. Analogous hydrolysis reactions of other carbohydrate acetals are known.[46]

Similarly, hydrolysis of the 3-pentylidene acetal of **24**, and then sequential removal of the (N-6)-pivaloyl by ammonolysis, and the remaining pivaloates by methanolysis, gave the deprotected purine disaccharide **35**, matching the compound prepared previously.[45] Purification relied on reversed-phase chromatography as for **34**. The two-step procedure was used because methoxide treatment of (N-6)-acylated purines does not normally lead to successful deacylation, due to competing deprotonation at N-6.[47]

A focused effort was made to characterize possible nucleobase-glycosylated intermediates such as **11** (Scheme 2) that might serve as "ancillary donors," subject to indium(III) triflate-promoted intermolecular transfer of the glycosyl moiety to the ribose hydroxyl. Such intermediates were occasionally observed by TLC but could not be isolated from quenched reaction mixtures because they are readily hydrolyzed to give back the original acceptor. However, an increase in the quantity of donor (**37**, Scheme 4) and NIS relative to ribose-protected acceptor **36**, and a supply of just 0.02 equiv of iron(III) triflate as the activator, led to the accumulation of observable products. Direct preparative thin-layer chromatography of the crude reaction mixture allowed the isolation of the pyrimidine ring-glycosylated compounds **38** and **39**/**40**. (N-3)-Glycosylated uridine **38** matches the known compound, previously obtained from **36** by a Mitsunobu coupling reaction.[40b] It is stable to handling and shows no spontaneous tendency to hydrolyze back to **36**. In contrast, the *O*-glycosylated uridine products **39**/**40** were obtained as a moisture and storage-sensitive 5:1 mixture. Mass spectroscopic and proton and carbon NMR analysis indicates that they are a β/α pair of *O*-glucopyranoside derivatives of **36**. The respective H-1″ and C-1″ resonances [**39**: 6.22 ppm (J = 6.9 Hz) and 93.1 ppm; **40**: 6.76 ppm (J = 3.2 Hz) and 90.2 ppm] closely match the analogous β/α pairs of D-glucopyranoside tetra-acetates derived from 4-nitrophenol[48] and *N*-phenyltrifluoroacetimidate[49] and the Schmidt trichloroacetimidate donor **28**.[50] Furthermore, an (O-6)-β-D-glucopyranosyl guanosine derivatized as the hepta-acetate[51] shows H-1″/C-1″ signals [6.50 ppm, (J = 8.1 Hz) and 94.1 ppm] similar to those of **39**, and a series of four O-4 alkylated uridine triacetates shows ribofuranoside H-1′ and uridine H-5/

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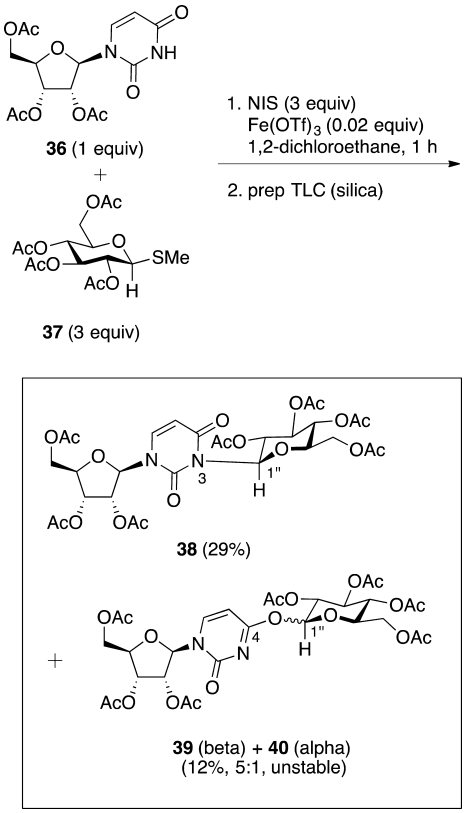
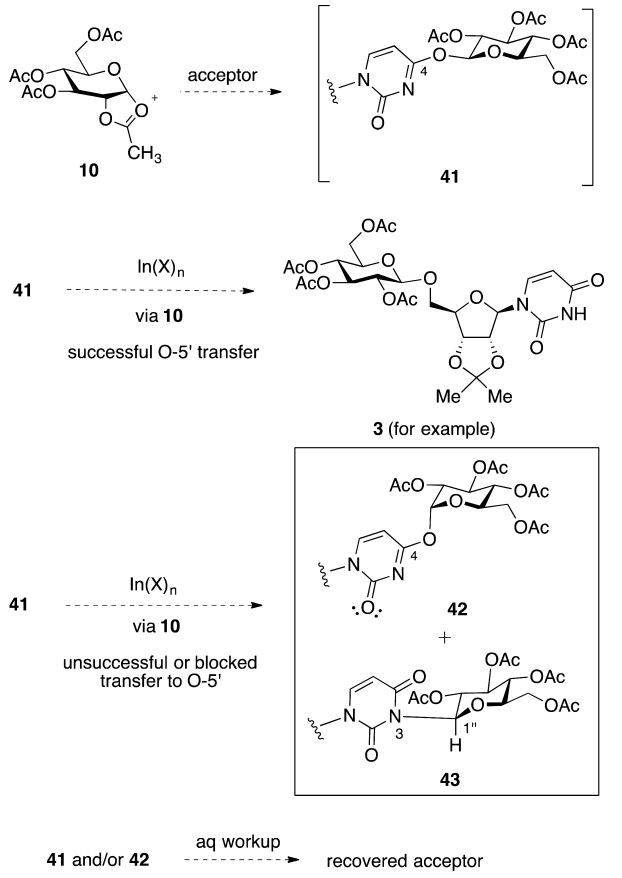
Scheme 4. Glycosylation of Uridine on the Pyrimidine Ring



Scheme 5. Uridine Nucleobase as "Ancillary Donor"



6 values in line with those of **39**/**40**.[52] The upfield position of C-5 of **39** (96.3 ppm) strongly suggests that glycosylation has occurred at O-4 (expected[53,54] for C-5: ~97 ppm) rather than the less reactive and more hindered O-2 (expected for C-5: ~108 ppm).

A more complete picture of the nucleoside glycosylation process now emerges, as illustrated in Scheme 5 for the reaction of acetoxy-participated glucopyranose-derived dioxalenium donor **10** or a functionally similar species such as the α triflate[55] or iodide,[56] with a uridine acceptor. Initial reaction of the donor species with an acceptor heteroatom on the pyrimidine can be expected to provide the ancillary donor, O-4 β glucopyranoside **41**. In the presence of a suitable Lewis acid such as indium(III) triflate, **41** can transfer the donor glycosyl moiety (e. g., **10**) to the hydroxyl accepting atom in an intermolecular fashion to give a disaccharide product such as **3**. During this glycosyl-transfer process, some amount of intermediate that is doubly glycosylated at O-4 and O-5′ may be formed, but further glycosyl transfer would still lead to **3**. Alternatively, should transfer of **10** to the hydroxyl be slow or blocked, **41** can rearrange to the more stable *alpha* isomer, **42**. By comparison, a donor species generated from acetobromo-α-D-glucose and silver triflate reacts with tetramethylurea on the oxygen atom to give the α-D-glucopyranosyl oxonium adduct only.[57] Acetamido *O*-glycosylations, some of them observed during attempted disaccharide formation, have also been described, and the amide can be protected against glycosylation by prior *O*-alkylation.[58] A β-L-fucopyranoside donor reacts on the amide oxygen with an acceptor acetamido substituent to give the α (equatorial) *O*-glycosylated product. Larger amounts of the silver(I) perchlorate activator, however, lead instead to the isomeric, and presumably more stable, β (axial) glycosylated product.[59] The possibility that some **42** is formed initially cannot be ruled out, but donor species related to **10** are reliable for producing only the β glycoside with a variety of acceptors, including the nucleoside hydroxyl acceptors described in this work, under conditions where equilbration to α is unlikely.

Indium(II) triflate-promoted rearrangement of either **41** or **42** to the (N-3)-glycosylated product **43** can occur subsequently if no other acceptor site is more reactive. The *N*-glycoside **43** is observed to be quite stable to isolation and is presumably less reactive than **41** or **42** to serve as an activatable donor species to give **3**. The fact that **43** is obtained as only the β isomer suggests that this isomer forms first and does not isomerize to α under the reaction or isolation conditions.

CONCLUSION

Mild and general experimental conditions have been developed for the efficient *O*-glycosylation of nucleoside ribofuranose hydroxyls despite competition from more Lewis basic sites on the purine or pyrimidine nucleobase. Indium(III) triflate serves both to activate the glycosyl donor, either a thioglycoside or glycosyl trichloroacetimidate, and to promote the isomerization of ancillary donor, heterocycle-glycosylated, intermediates to the desired nucleoside disaccharide. The isolation and characterization of (O-4)- and (N-3)-2″,3″,4″,6″-tetra-O-acetyl-D-glucopyranosyl derivatives of uridine 2′,3′,5′-triacetate provides evidence for the susceptibility of these sites to unintended or temporary glycosylation.

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EXPERIMENTAL SECTION

General Methods. Reagents and solvents were purchased from commercial suppliers and used without purification. ^{1}H and ^{13}C NMR spectra are referenced to the residual solvent signal. Purification by column chromatography on silica gel refers to the use of an automated MPLC instrument with prepacked silica gel columns. The products were monitored at a wavelength of 260 nM. Analytical LC−MS was conducted with a Waters Xterra MS C-18 (2.1 × 20 mm, 3.5 μM) IS column; 10 μL injection; gradient of 10% to 100% acetonitrile (with 0.05% TFA) in water (with 0.05% TFA) over 3.75 min at 1 mL/min, 5.5 min analysis time, 7 min total run time, monitored at 254 nM; 62−1500 amu mass range; electrospray ionization with positive-ion detection. Analytical TLC employed precoated Analtech #21511 silica plates.

General Glycosylation Procedure. A 10 mL vial was charged with the nucleoside acceptor (0.15 mmol), indium triflate (84 mg, 0.15 mmol), activated 4 Å molecular sieves (150 mg), the sugar donor (0.1 mmol), and 1,2-dichloroethane (1 mL). The mixture was stirred at 0 °C or room temperature for 15 min. The reaction mixture was then treated with *N*-iodosuccinimide (34 mg, 0.15 mmol) and allowed to stir at 0 °C or room temperature for 45 min. The reaction mixture was filtered through a 0.45 μM PTFE syringe filter and then rinsed with dichloromethane (2× 5 mL). The organic solution was washed with 10 mL of saturated aq sodium bisulfite, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by using a prepacked silica gel column or preparative silica thin-layer chromatography plate to afford the glycosylation product.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(((3aR,4R,6R,6aR)-6-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-dimethyltetrahydrofuro-[3,4-d][1,3]dioxol-4-yl)methoxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3**).* By following the general procedure, donor **2** (66 mg, 0.15 mmol) was combined with acceptor **1** (28 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 3:2 hexane/ethyl acetate as the eluant afforded **3** (33 mg, 54%) as a white solid: mp 122−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (br s, 1 H), 7.56 (d, 1 H, *J* = 6.4 Hz), 5.92 (d, 1 H, *J* = 2.0 Hz), 5.83 (d, 1 H, *J* = 6.4 Hz), 5.26 (d, 1 H, *J* = 7.6 Hz), 5.09 (dd, 1 H, *J* = 7.6 and 8.0 Hz), 4.96 (dd, 1 H, *J* = 6.8 and 8.0 Hz), 4.78 (dd, 1 H, *J* = 2.0 and 4.8 Hz), 4.70 (dd, 1 H, *J* = 2.4 and 4.8 Hz), 4.56 (d, 1 H, *J* = 6.4 Hz), 4.42 (d, 1 H, *J* = 2.4 Hz), 4.32 (dd, 1 H, *J* = 3.6 and 10.0 Hz), 4.21 (dd, 1 H, *J* = 2.0 and 8.8 Hz), 4.15 (dd, 1 H, *J* = 1.6 and 10.0 Hz), 3.70−3.76 (m, 2 H), 2.13 (s, 3 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 3 H), 1.60 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 170.4, 169.5, 164.0, 150.5, 141.8, 114.4, 102.3, 100.8, 93.1, 85.1, 84.9, 80.8, 72.4, 72.1, 71.3, 69.5, 68.4, 61.9, 27.2, 25.3, 20.8, 20.69, 20.67, 20.64; HR-ESI-MS $[M + H]^+$ calcd for $C_{26}H_{35}N_2O_{15}$ 615.2037, found 615.2029.

*Acceptor **4** for Preparing **7**, **14**, **16**, **30**, and **32**: 1-((3aR,4R,6R,6aR)-2,2-Diethyl-6-(hydroxymethyl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)pyrimidine-2,4(1H,3H)-dione (**4**).*[60] Acceptor **4** was prepared by following the literature method.[61] Trimethyl orthoformate (3.18 g, 30.0 mmol) and *p*-toluenesulfonic acid monohydrate (0.38 g, 2.0 mmol) were added to a solution of uridine (2.44 g, 10.0 mmol) in 20 mL of 3-pentanone. The reaction was allowed to stir at room temperature for 2 h and then was concentrated. A solution of the residue in 10 mL of dimethyl sulfoxide was chromatographed with a prepacked C18 reversed-phase column (120 g), eluting with 5% to 90% acetonitrile/water. The fractions containing product were combined and lyophilized to afford **4** (2.65 g, 85% yield) as a white solid: mp 167−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (broad, 1 H), 7.39 (d, 1 H, *J* = 6.4 Hz), 5.76 (d, 1 H, *J* = 6.4 Hz), 5.62 (d, 1 H, *J* = 2.0 Hz), 5.07 (dd, 1 H, *J* = 2.0 and 5.2 Hz), 4.99 (dd 1 H, *J* = 2.8 and 5.2 Hz), 4.33 (d, 1 H, *J* = 2.8 Hz), 3.94 (dd, 1 H, *J* = 2.0 and 9.6 Hz), 3.84 (dd, 1 H, *J* = 3.2, 9.6 Hz), 2.46 (br s, 1H), 1.81 (q, 2 H, *J* = 6.0 and 11.6 Hz), 1.65 (q, 2 H, *J* = 6.0 Hz), 1.01 (t, 3 H, *J* = 6.0), 0.91 (t, 3 H, *J* = 6.0 Hz); ^{13}C NMR (125 Hz, DMSO) δ 163.4, 150.5, 142.2, 117.4, 101.9, 91.7, 86.9, 84.2, 81.1, 61.6, 29.2, 28.8, 8.4, 7.7; HR-ESI-MS $[M + H]^+$ calcd for $C_{14}H_{21}N_2O_6$ 313.1400, found 313.1390.

*(2S,3R,4S,5R,6R)-2-(Phenylthio)-6-((pivaloyloxy)methyl)-tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**5**).*[62] Sodium methoxide (122 mg, 2.27 mmol) was added to a solution of phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (2.5 g, 5.67 mmol) in methanol (50 mL). The reaction mixture was allowed to stir overnight and then was neutralized with Dowex 50 × 8−100 acidic resin. The resin was filtered, and the filtrate was concentrated to afford the crude tetraol as a white residue, which was dried azeotropically with toluene (3 × 5 mL) and taken to the next step without further purification.

Pivaloyl chloride (7.5 mL, 56.7 mmol) was added dropwise to a solution of the tetraol (5.67 mmol) and 4-(dimethylamino)pyridine (345 mg, 2.84 mmol) in pyridine (50 mL). The mixture was heated at reflux for 24 h, cooled to room temperature, and then quenched with methanol (10 mL). Concentration gave a residue that was dissolved in 150 mL of dichloromethane. The organic solution was washed sequentially with 2 N HCl (150 mL) and saturated aqueous sodium bicarbonate (3 × 150 mL). The organic layer was dried over sodium sulfate, concentrated, and then purified by flash chromatography, eluting with 10% ethyl acetate in hexane, to afford the donor **5** (3.03 g, 88% over two steps) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.53 (m, 2 H), 7.29−7.34 (m, 3 H), 5.37 (dd, 1 H, *J* = 7.2 and 7.6 Hz), 5.11 (d, 1 H, *J* = 8.0 Hz), 5.05 (dd, 1 H, *J* = 7.6 and 8.0 Hz), 4.75 (d, 1 H, *J* = 8.0 Hz), 4.27 (dd, 1 H, *J* = 1.6 and 10.0 Hz), 4.07 (dd, 1 H *J* = 4.8 and 9.6 Hz), 3.78 (m, 1 H), 1.24 (s, 9 H), 1.23 (s, 9 H), 1,17 (s, 9 H), 1.12 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.8, 176.9, 176.3, 176.1, 132.7, 132.3, 128.9, 128.2, 86.4, 76.4, 73.3, 69.5, 67.6, 62.2, 38.8, 38.7, 38.6, 27.1, 27.1, 27.0; LC-ESI-MS $[M + H]^+$ calcd for $C_{32}H_{49}O_9S$ 609.31, found 609.32.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(((3aR,4R,6R,6aR)-6-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-diethyltetrahydrofuro-[3,4-d][1,3]dioxol-4-yl)methoxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**6**).* By following the general procedure, donor **2** (66 mg, 0.15 mmol) was combined with acceptor **4** (31 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 3:2 hexane/ethyl acetate as the eluant afforded **6** (39 mg, 61%) as a white solid: mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (br s, 1 H), 7.54 (d, 1 H, *J* = 6.8 Hz), 5.94 (d, 1 H, *J* = 2.4 Hz), 5.82 (d, 1 H, *J* = 6.8 Hz), 5.26 (d, 1 H, *J* = 7.6 Hz), 5.10 (dd, 1 H, *J* = 7.6 and 8.0 Hz), 4.97 (d, 1 H, *J* = 7.2 Hz), 4.79 (dd, 1 H, *J* = 2.0 and 5.2 Hz), 4.71 (dd, 1 H, *J* = 2.0 and 5.2 Hz), 4.55 (d, 1 H, *J* = 6.4 Hz), 4.44 (d, 1 H, *J* = 2.4 Hz), 4.32 (dd, 1 H, *J* = 3.6 and 10.0 Hz), 4.21 (dd, 1 H, *J* = 2.0 and 8.8 Hz), 4.15 (dd, 1 H, *J* = 1.6 and 10.0 Hz), 3.70−3.76 (m, 2 H), 2.13 (s, 3 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 3 H), 1.81 (q, 2 H, *J* = 6.0 and 12.0 Hz), 1.63 (q, 2 H, *J* = 6.0 and 12.0 Hz), 1.01 (t, 3 H, *J* = 6.0 Hz), 0.90 (t, 3 H, *J* = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 170.4, 169.5, 169.5, 163.6, 150.7, 141.8, 118.9, 102.4, 100.9, 93.3, 85.4, 85.3, 81.2, 72.5, 72.2, 71.3, 69.7, 68.5, 61.9, 29.7, 29.6, 20.9, 20.8, 20.7, 20.7, 8.5, 8.0; HR-ESI-MS $[M + H]^+$ calcd for $C_{28}H_{39}N_2O_{15}$ 643.2350, found 643.2340.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-6-(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-diethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**7**).* By following the general procedure, donor **5** (91 mg, 0.15 mmol) was combined with acceptor **4** (31 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 65:35 hexane/ethyl acetate as the eluant afforded **7** (73.0 mg, 90%) as a white solid: mp 112−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (br s, 1 H), 7.57 (d, 1 H, *J* = 6.4 Hz), 5.97 (d, 1 H, *J* = 2.0 Hz), 5.85 (d, 1 H, *J* = 6.4 Hz), 5.36 (t, 1 H, *J* = 7.6 Hz), 5.10 (dd, 1 H, *J* = 7.6 and 8.0 Hz), 4.96 (dd, 1 H, *J* = 6.8 and 7.6 Hz), 4.74 (dd, 1 H, *J* = 2.0 and 5.2 Hz), 4.68 (dd, 1 H, *J* = 2.4 and 5.2 Hz), 4.54 (d, 1 H, *J* = 6.4 Hz), 4.39 (dd, 1 H, *J* = 2.0 and 4.4 Hz), 4.22 (dd, 1 H, *J* = 1.2 and 10.0 Hz), 4.18 (dd, 1 H, *J* = 2.0 and 8.4 Hz), 4.09 (dd, 1 H, *J* = 4.4 and 10.0 Hz), 3.73−3.76 (m, 1 H), 3.64 (dd, 1 H, *J* = 2.8 and 4.4 Hz), 1.79 (q, 2 H, *J* = 6.0 and 12.0 Hz), 1.58 (q, 2 H, *J* = 6.0 and 12.0 Hz), 1.23 (s, 9 H), 1.16 (s, 9 H), 1.15 (s, 9 H), 1.13 (s, 9 H), 0.99 (t, 3 H, *J* = 6.0 Hz), 0.86 (t, 3 H, *J* = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 177.3, 176.8, 176.5, 164.4, 150.4, 142.2, 118.9, 102.3, 100.9, 92.8, 85.2, 85.1, 80.8, 72.6, 71.9, 71.3, 69.2, 68.0, 61.9, 39.0, 38.8, 38.8, 38.8, 29.4, 29.3,

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27.19, 27.16, 27.12, 27.10, 8.3, 7.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{40}H_{63}N_2O_{15}$ 811.4228, found 811.4219.

*(2S,3R,4S,5S,6R)-2-(Phenylthio)-6-((pivaloyloxy)methyl)-tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**13**).*[63] Donor **13** was prepared by following the procedure for **5** (83% yield overall) and was obtained as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.54 (m, 2 H), 7.30−7.33 (m, 3 H), 5.42 (d, 1 H, J = 2.4 Hz), 5.22 (dd, 1 H, J = 7.6 and 8.0 Hz), 5.13 (dd, 1 H, J = 2.4 and 8.0 Hz), 4.73 (d, 1 H, J = 8.0 Hz), 4.20 (dd, 1 H, J = 7.6 and 11.2 Hz), 4.01−4.05 (m, 2 H), 1.23 (s, 9 H), 1.20 (s, 9 H), 1,18 (s, 9 H), 1.01 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 177.4, 177.0, 176.6, 133.7, 129.0, 128.6, 86.1, 75.0, 72.4, 67.1, 66.8, 61.7, 27.3, 27.3, 27.2, 27.1; LC-ESI-MS $[M + H]^+$ calcd for $C_{32}H_{49}O_9S$ 609.31, found 609.30.

*(2R,3R,4S,5S,6R)-2-(((3aR,4R,6R,6aR)-6-(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-diethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**14**).* By following the general procedure, donor **13** (91 mg, 0.15 mmol) was combined with acceptor **4** (31 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 65:35 hexane/ethyl acetate as the eluant afforded **14** (70 mg, 87%) as a white solid. An analogous, larger scale, reaction starting with 200 mg of **4**, and with purification by flash chromatography on a prepacked silica gel column (40 g) eluting with 3:1 hexane/ethyl acetate, provided 425 mg (82%) of **14**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (br s, 1 H), 7.54 (d, 1 H, J = 6.4 Hz), 6.01 (d, 1 H, J = 2.0 Hz), 5.78 (dd, 1 H, J = 2.0 and 6.8 Hz), 5.41 (d, 1 H, J = 1.6 Hz), 5.13−5.19 (m, 2 H), 4.74 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.72 (dd, 1 H, J = 2.8 and 5.2 Hz), 4.54 (d, 1 H, J = 5.6 Hz), 4.36−4.38 (m, 1 H), 4.20 (dd, 1 H, J = 1.6 and 8.0 Hz), 4.18 (dd, 1 H, J = 4.8 and 8.4 Hz), 3.97−4.04 (m, 2 H), 3.65 (dd, 1 H, J = 2.8 and 8.4 Hz), 1.79 (q, 2 H, J = 6.0 and 12.0 Hz), 1.58 (q, 2 H, J = 6.0 and 12.0 Hz), 1.28 (s, 9 H), 1.18 (s, 9 H), 1.16 (s, 9 H), 1.12 (s, 9 H), 0.99 (t, 3 H, J = 6.0), 0.86 (t, 3 H, J = 6.0); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 177.3, 177.0, 163.6, 150.5, 141.7, 118.9, 102.8, 101.2, 92.3, 85.97, 84.95, 80.7, 71.3, 70.7, 69.3, 69.0, 66.7, 61.1, 39.2, 38.91, 38.88, 38.82, 29.43, 29.41, 27.18, 27.28, 27.20, 8.4, 8.0; HR-ESI-MS $[M + H]^+$ calcd for $C_{40}H_{63}N_2O_{15}$ 811.4228, found 811.4213.

*(2R,3R,4R,5S)-2-((Benzoyloxy)methyl)-5-(phenylthio)-tetrahydrofuran-3,4-diyl Dibenzoate (**15**).*[64] Thiophenol (0.5 mL, 4.88 mmol) was added to a stirred solution of commercial 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (1.01 g, 2.00 mmol) in dichloromethane (20 mL) at 0 °C. Boron trifluoride etherate (0.46 mL, 3.66 mmol) was added dropwise. After the mixture was stirred at 0 °C for 3 h, the reaction was quenched by the addition of triethylamine (0.6 mL, 4.30 mmol) and then concentrated. The residue was purified by flash chromatography, eluting with 20% ethyl acetate in hexane, to afford donor **15** (815 mg, 73%) as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.08−8.10 (m, 2 H), 8.02−8.03 (m, 2 H), 7.93−7.94 (m, 2 H), 7.54−7.61 (m, 5 H), 7.41−7.46 (m, 4 H), 7.36−7.39 (m, 2 H), 7.24−7.31 (m, 3 H), 5.77 (dd, 1 H, J = 4.0 Hz), 5.72 (dd, 1 H, J = 4.0 Hz), 5.65 (d, 1 H, J = 4.0 Hz), 4.66−4.72 (m, 2 H), 4.55 (dd, 1 H, J = 3.2 and 5.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 165.5, 165.2, 133.9, 133.7, 133.6, 133.3, 131.4, 130.02, 129.99, 129.9, 129.7, 129.2, 129.1, 128.6, 128.6, 88.3, 80.6, 74.8, 72.5, 64.4; LC-ESI-MS $[M + H]^+$ calcd for $C_{32}H_{27}O_7S$ 555.15, found 555.12.

*(2R,3R,4R,5R)-2-((Benzoyloxy)methyl)-5-(((3aR,4R,6R,6aR)-6-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-dimethyltetrahydrofuro-[3,4-d][1,3]dioxol-4-yl)methoxy)tetrahydrofuran-3,4-diyl Dibenzoate (**16**).* By following the general procedure, donor **15** (83 mg, 0.15 mmol) was combined with acceptor **4** (31 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 7:3 hexane/ethyl acetate as the eluant afforded **16** (61 mg, 80%) as a white solid: mp 82−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (br s, 1 H), 8.00−8.04 (m, 4 H), 7.90−7.92 (m, 2 H), 7.58−7.61 (m, 2 H), 7.52−7.55 (m, 2 H), 7.33−7.45 (m, 6 H), 5.80−5.85 (m, 3 H), 5.72 (d, 1 H, J = 3.6 Hz), 5.31 (s, 1 H), 4.90 (dd, 1 H, J = 2.0 and 5.2 Hz), 4.83 (dd, 1 H, J = 3.2 and 5.2 Hz), 4.77 (dd, 1 H, J = 4.4 and 8.0 Hz), 4.66 (dd, 1 H, J = 3.6 and 9.6 Hz), 4.59 (dd, 1 H, J = 4.4 and 9.6 Hz), 4.32−4.59 (m, 1 H), 4.11 (dd, J = 2.8 and 9.2 Hz), 3.73 (dd, 1 H, J = 4.0 and 8.8 Hz), 1.77 (q, 2 H, J = 6.0), 1.61 (q, 2 H, J = 6.0 Hz), 0.98 (t, 3 H, J = 6.0 Hz), 0.88 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 165.4, 165.3, 163.7, 150.3, 141.9, 133.7, 133.6, 133.3, 129.89, 129.85, 129.6, 129.1, 128.9, 128.6, 128.5, 119.1, 106.1, 103.0, 93.7, 85.8, 84.8, 80.9, 79.1, 75.4, 72.2, 68.4, 64.8, 29.5, 29.3, 8.5, 7.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{40}H_{41}N_2O_{13}$ 757.2609, found 757.2592.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-2,2-Diethyl-6-(2-oxo-4-pivalamidopyrimidin-1(2H)-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**17**).* According to the general procedure, donor **5** (91.3 mg, 0.15 mmol, 1.5 equiv) was reacted with acceptor **45** (40 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 94:6 dichloromethane/methanol as the eluant afforded **17** (76 mg, 85%) as a white solid: mp 113−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, 1 H, J = 6.0 Hz), 7.66 (d, 1 H, J = 6.0 Hz), 5.93 (d, 1 H, J = 2.0 Hz), 5.34 (d, 1 H, J = 7.6 Hz), 5.11 (dd, 1 H, J = 7.6 and 8.0 Hz), 4.81−4.84 (m, 2 H), 4.67 (dd, 1 H, J = 1.6 and 4.8 Hz), 4.61 (d, 1 H, J = 2.0 Hz), 4.52 (d, 1 H, J = 6.4 Hz), 4.21−4.25 (m, 3 H), 3.75−3.79 (m, 1 H), 3.65 (dd, 1 H, J = 2.4 and 8.4 Hz), 3.52 (br s, 1 H), 1.79 (q, 2 H, J = 6.0 Hz), 1.59 (q, 2 H, J = 6.0 Hz), 1.36 (s, 9 H), 1.25 (s, 9 H), 1.18 (s, 9 H), 1.14 (s, 9 H), 1.11 (s, 9 H), 1.00 (t, 3 H, J = 6.0 Hz), 0.88 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 177.3, 177.1, 176.9, 176.35, 161.43, 148.9, 118.4, 100.8, 96.1, 96.0, 87.3, 86.3, 81.7, 73.0, 71.8, 71.0, 69.1, 68.3, 62.1, 41.3, 39.0, 38.90, 38.88, 29.4, 29.2, 27.30, 27.28, 27.25, 27.19, 27.18, 27.13, 27.11, 26.6, 8.4, 7.8; HR-ESI-MS $[M + H]^+$ calcd for $C_{45}H_{72}N_3O_{15}$ 894.4963, found 894.4951.

*(2R,3R,4R,5R)-2-((Benzoyloxy)methyl)-5-(((3aR,4R,6R,6aR)-2,2-diethyl-6-(2-oxo-4-pivalamidopyrimidin-1(2H)-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)tetrahydrofuran-3,4-diyl Dibenzoate (**18**).* By following the general procedure, donor **15** (83 mg, 0.15 mmol) was combined with acceptor **45** (40 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 94:6 dichloromethane/methanol as the eluant afforded the **18** (66 mg, 78%) as a white solid: mp 56−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06−8.07 (m, 2 H), 8.01−8.03 (m, 2 H), 7.94−7.96 (m, 2 H), 7.70 (br s, 1 H), 7.54−7.61 (m, 3 H), 7.36−7.45 (m, 6 H), 5.83 (br s, 1 H), 5.78 (dd, 1 H, J = 4.0 and 5.2 Hz), 5.67 (d, 1 H, J = 3.6 Hz), 5.30 (s, 1 H), 4.99 (d, 1 H, J = 5.2 Hz), 4.78 (dd, 1 H, J = 3.2 and 4.4 Hz), 4.73 (dd, 1 H, J = 3.2 and 9.2 Hz), 4.60 (dd, 1 H, J = 4.4 and 9.6 Hz), 4.49 (m, 1 H), 4.12 (dd, 1 H, J = 2.4 and 9.2 Hz), 3.76 (dd, 1 H, J = 5.2 and 9.2 Hz), 1.78 (q, 2 H, J = 6.0 Hz), 1.62 (q, 2 H, J = 6.0 Hz), 1.31 (s, 9 H), 0.99 (t, 3 H, J = 6.0 Hz), 0.89 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 165.6, 165.5, 162.2, 148.1, 133.8, 133.7, 133.5, 130.02, 129.97, 129.9, 129.7, 129.2, 129.0, 128.7, 128.6, 128.62, 128.60, 119.0, 106.4, 96.5, 87.5, 85.7, 81.3, 79.4, 75.4, 72.2, 68.9, 64.7, 41.1, 29.6, 29.3, 26.7, 8.5, 7.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{45}H_{50}N_3O_{13}$ 840.3344, found 840.3327.

*(2S,3R,4S,5R,6R)-2-(((6aR,8R,9R,9aR)-8-(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2,4,4-tetraisopropyltetrahydro-6H-furo[3,2-f]-[1,3,5,2,4]trioxadisilocin-9-yl)oxy)-6-((pivaloyloxy)methyl)-tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**19**).* By following the general procedure, donor **5** (121.7 mg, 0.20 mmol, 2.0 equiv) was combined with acceptor **56** (see the SI, 49 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 4:1 hexane/ethyl acetate as the eluant afforded **19** (55 mg, 56%) as a white solid: mp 108−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1 H); 7.87 (d, J = 8.1 Hz, 1 H), 6.10 (s, 1 H), 5.66 (dd, 1 H, J = 1.5 and 8.1 Hz), 5.29 (t, 1 H, J = 8.9 Hz), 5.09−5.17 (m, 2 H), 4.21−4.26 (m, 3 H), 4.09 (d, 1 H, J = 9.2 Hz), 4.02 (dd, 1 H, J = 5.8 and 12.3 Hz), 3.92 (dd, 1 H, J = 1.5 and 13.7 Hz), 3.81 (dd, 1 H, J = 4.9 and 10.0 Hz), 0.83−1.17 (m, 64 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 177.3, 176.6, 176.4, 163.7, 149.8, 140.2, 101.6, 100.8, 88.8, 81.7, 81.5, 72.9, 72.4, 71.4, 68.4, 68.2, 62.2, 59.4, 38.93, 38.89, 38.85, 38.76, 27.4, 27.3, 27.2, 27.1, 17.63, 17.55, 17.5, 17.4, 17.2, 17.1, 17.0, 13.4, 13.0, 12.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{47}H_{81}N_2O_{16}Si_2$ 985.5125, found 985.5119.

*(2S,3R,4S,5R,6R)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-(phenylthio)tetrahydro-2H-pyran-3-yl Pivalate (**20**).*[65,66] A 33%

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hydrobromic acid solution in acetic acid (3.18 mL, 53.1 mmol) was added dropwise to a stirred solution of α-D-glucopyranose pentabenzoate (6.20 g, 8.85 mmol) in 50 mL of dry dichloromethane. The reaction mixture was allowed to stir under argon for 16 h at room temperature and then was diluted with 100 mL of dichloromethane. The organic solution was washed sequentially with 100 mL of water, saturated aqueous sodium bicarbonate, and water. The organic phase was dried over magnesium sulfate and concentrated, and the resulting residue was dissolved in 50 mL of nitromethane. Activated molecular sieves (4 Å, 1.50 g) were added, and the resulting mixture was stirred under argon for 1 h. The flask was then covered with foil and treated sequentially with γ-collidine (1.50 mL, 11.36 mmol), dry methanol (0.34 mL, 8.9 mmol), and *tert*-butylammonium bromide (5.0 mmol, 1.62 g). After 16 h of stirring, triethylamine (0.4 mL) was added, the solution was filtered, and the filtrate was washed with 100 mL of saturated aqueous sodium bicarbonate. The organic layer was separated, and the aqueous layer was back extracted with 2 × 50 mL of dichloromethane. The combined organic solution was washed with water, dried over magnesium sulfate, and then concentrated. The product was sequentially debenzoylated and benzylated by using the reported procedure.[67] The product was purified by column chromatography on silica gel, eluting with 20−40% ethyl acetate/hexane, to afford the known orthoester (3.57 g, 6.28 mmol, 71% yield) as a light yellow gel.

The above orthoester (1.2 g, 2.11 mmol) was stirred with activated molecular sieves (4 Å, 500 mg) and acetonitrile (10 mL) under an argon atmosphere for 1 h. Thiophenol (2.35 g, 21.3 mmol) and mercury(II) bromide (0.076 g, 0.211 mmol) were added, and the mixture was heated at reflux for 2.5 h. The reaction mixture was filtered, the filtrate was concentrated, and the residue was dissolved in dichloromethane (20 mL). The organic solution was washed sequentially with 1% aq sodium hydroxide (30 mL) and water (30 mL), dried over magnesium sulfate, and concentrated. The residue was purified by column chromatography on silica gel, eluting with 10% ethyl acetate in hexane, to afford the thioglycoside (976 mg, 71% yield) as white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.05 (m, 2 H), 7.61−7.80 (m, 1H), 7.44−7.50 (m, 4 H), 7.19−7.36 (m, 13 H), 7.11−7.14 (m, 5 H), 5.29 (dd, 1 H, *J* = 7.6 and 8.0 Hz), 4.82 (d, 1 H, *J* = 9.2 Hz), 4.79 (d, 1 H *J* = 8.4 Hz), 4.73 (d, 1 H, *J* = 8.8 Hz), 4.64 (d, 1 H, *J* = 8.4 Hz), 4.56−4.61 (m, 3 H), 3.82−3.87 (m, 2 H), 3.73−3.78 (m, 2 H), 3.61−3.64 (m, 1 H, 1.56 (br s, 1 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 165.4, 138.4, 138.1, 137.8, 133.4, 133.1, 132.7, 130.1, 130.0, 129.0, 128.62, 128.60, 128.5, 128.4, 128.19, 128.16, 127.9, 127.8, 127.7, 86.3, 84.5, 79.7, 76.2, 75.2, 73.7, 72.6, 69.2; LC-ESI-MS $[M + H]^+$ calcd for $C_{40}H_{39}O_6S$ 647.25, found 646.98.

Sodium methoxide (7.5 mg, 0.14 mmol) was added to a solution of the thioglycoside (900 mg, 1.39 mmol) in methanol (15 mL), and the reaction mixture was allowed to stir for 3 h. The solution was neutralized with Dowex 50 × 8−100 acidic resin, the resin was filtered, and the filtrate was concentrated. The residue was dried azeotropically with toluene (2 × 5 mL) and taken to the next step without further purification.

Pivaloyl chloride (0.20 mL, 1.50 mmol) was added dropwise to a solution of the crude carbinol (1.39 mmol) and 4-(dimethylamino)-pyridine (168 mg, 1.39 mmol) in pyridine (10 mL). The mixture was heated at 60 °C for 24 h and then cooled to room temperature and quenched with methanol (1 mL). After concentration, the residue was dissolved in 20 mL of dichloromethane, and the organic solution was washed sequentially with 2 N HCl (10 mL) and saturated aqueous sodium bicarbonate (2 × 10 mL). The organic layer was dried over sodium sulfate, concentrated, and purified by flash chromatography, eluting with 10% ethyl acetate in hexane, to afford the thioglycoside donor **20** (705 mg, 81% over two steps) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.53 (m, 2 H), 7.21−7.31 (m, 16 H), 7.16−7.18 (m, 2 H), 5.10 (t, 1 H, *J* = 9.8 Hz), 4.75−4.78 (m, 2 H), 4.61−4.70 (m, 2 H), 4.53−4.58 (m, 2 H), 3.80 (dd, 1 H, *J* = 1.5 and 11.0 Hz), 3.66−3.75 (m, 2 H), 3.55−3.58 (m, 1 H), 1.24 (s, 9 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 176.7, 138.3, 138.1, 138.0, 133.5, 132.3, 128.9, 128.5, 128.4, 128.0, 127.9, 127.8, 127.75, 127.71, 127.6, 127.4, 86.7, 84.8, 79.5, 77.8, 75.3, 75.11; 73.6, 71.7, 69.1, 38.9, 27.3; LC-ESI-MS $[M + H]^+$ calcd for $C_{38}H_{43}O_6S$ 627.28, found 627.00.

*(2S,3R,4S,5R,6R)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-((((6aR,8R,9R,9aR)-8-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2,4,4-tetraisopropyltetrahydro-6H-furo[3,2-f][1,3,5,2,4]-trioxadisilocin-9-yl)oxy)tetrahydro-2H-pyran-3-yl Pivalate (**21**).* By following the general procedure, donor **20** (125 mg, 0.20 mmol, 2.0 equiv) was combined with acceptor **56** (49 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 9:1 hexane/ethyl acetate as the eluant afforded **21** (65 mg, 64%) as a white solid: mp 71−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (br s, 1 H), 7.78 (d, 1 H, *J* = 8.2 Hz), 7.26−7.30 (m, 13 H), 7.16−7.18 (m, 2 H), 5.93 (s, 1 H), 5.61 (d, 1 H, *J* = 8.1 Hz), 5.30 (d, 1 H, *J* = 1.2 Hz), 5.17 (t, 1 H, *J* = 8.0 Hz), 5.02 (d, 1 H, *J* = 7.9 Hz), 4.78 (d, 1 H, *J* = 11.2 Hz), 4.73 (d, 1 H, *J* = 11.1 Hz), 4.67 (d, 1 H, *J* = 11.2 Hz), 4.62 (d, 1 H, *J* = 11.2 Hz), 4.55 (d, 1 H, *J* = 10.7 Hz), 4.54 (d, 1 H, *J* = 10.8 Hz), 4.37 (d, 1 H, *J* = 4.2 Hz), 4.28 (dd, 1 H, *J* = 3.6 and 5.9 Hz), 4.21 (d, 1 H, *J* = 13.5 Hz), 4.07−4.15 (m, 1 H), 3.91 (d, 1 H, *J* = 13.6 Hz), 3.73−3.79 (m, 2 H), 3.66 (t, 1 H, *J* = 9.2 Hz), 3.55−3.57 (m, 1 H), 0.83−1.27 (m, 37 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 163.2, 149.4, 140.7, 138.5, 138.3, 138.1, 128.6, 128.5, 128.4, 128.1, 128.0, 127.7, 127.4, 101.4, 100.4, 90.0, 83.7, 81.3, 79.5, 78.0, 75.4, 75.0, 74.9, 73.5, 73.1, 68.9, 68.8, 59.5, 38.9, 29.8, 27.4, 17.6, 17.6, 17.5, 17.43, 17.37, 17.2, 17.13, 17.05, 13.5, 13.3, 13.0, 12.8; HR-ESI-MS $[M + H]^+$ calcd for $C_{53}H_{75}N_2O_{13}Si_2$ 1003.4807, found 1003.4821.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-6-(6-Benzamido-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**22**).* By following the general procedure, donor **5** (92 mg, 0.15 mmol) was combined with commercial N^6-benzoyl-2′,3′-*O*-isopropylideneadenosine (49 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 93:7 dichloromethane/methanol as the eluant afforded **22** (50 mg, 55%) as a white solid: mp 88−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1 H), 8.61 (s, 1 H), 8.17 (d, 2 H, *J* = 6.0 Hz), 7.65 (dd, 1 H, *J* = 5.6 and 6.0 Hz), 7.57 (dd, 1 H, *J* = 5.6 and 6.4 Hz), 6.33 (d, 1 H, *J* = 2.0 Hz), 5.26−5.31 (m, 2 H), 5.21 (dd, 1 H, *J* = 7.6 Hz), 4.81 (dd, 1 H, *J* = 1.2 and 4.8 Hz), 4.65−4.68 (m, 2 H), 4.48 (d, 1 H, *J* = 7.2 Hz), 4.23 (dd, 1 H, *J* = 1.2 and 8.0 Hz), 4.15 (dd, 1 H, *J* = 4.8 and 9.6 Hz), 3.70−3.74 (m, 1 H), 3.63 (dd, 1 H, *J* = 2.0 and 8.4 Hz), 1.68 (s, 3 H), 1.41 (s, 3 H), 1.22 (s, 9 H), 1.17 (s, 9 H), 1.10 (s, 9 H), 1.06 (s, 9 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 178.3, 177.3, 176.7, 176.5, 165.3, 151.8, 151.3, 149.0, 142.8, 133.3, 133.0, 129.0, 128.7, 122.4, 114.4, 100.5, 93.0, 86.0, 85.4, 81.9, 77.5, 72.9, 71.9, 71.1, 69.1, 68.1, 62.1, 39.0, 38.94, 38.86, 38.83, 27.3, 27.31, 27.29, 27.28, 27.21, 25.5; HR-ESI-MS $[M + H]^+$ calcd for $C_{46}H_{64}N_5O_{14}$ 910.4450, found 910.4433.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-2,2-Diethyl-6-(6-pivalamido-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**23**).* By following the general procedure, donor **5** (91 mg, 0.15 mmol) was combined with acceptor **47** (42 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 93:7 dichloromethane/methanol as the eluant afforded **23** (62 mg, 67%) as a white solid: mp 75−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1 H), 8.68 (s, 1 H), 6.34 (d, 1 H, *J* = 1.2 Hz), 5.27−5.30 (m, 2 H), 5.13 (dd, 1 H, *J* = 7.6 and 8.0 Hz), 4.82 (d, 1 H, *J* = 4.8 Hz), 4.69 (dd, 1 H, *J* = 6.4 and 7.6 Hz), 4.66 (s, 1 H), 4.45 (d, 1 H, *J* = 6.4 Hz), 4.17−4.22 (m, 2 H), 4.10 (dd, 1 H, *J* = 5.2 and 10.0 Hz), 3.69−3.72 (m, 1 H), 3.62 (dd, 1 H, *J* = 2.4 and 8.4 Hz), 1.87 (q, 2 H, *J* = 6.0 Hz), 1.66 (q, 2 H, *J* = 6.0 Hz), 1.45 (br s, 1 H), 1.22 (s, 9 H), 1.18 (s, 9 H), 1.17 (s, 9 H), 1.03 (s, 18 H), 1.06 (t, 3 H, *J* = 6.0 Hz), 0.92 (t, 3 H, *J* = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 177.3, 176.8, 176.7, 151.8, 150.7, 148.4, 143.1, 121.7, 118.9, 100.6, 92.9, 86.5, 85.5, 82.1, 72.9, 71.9, 71.1, 69.3, 68.3, 62.5, 39.04, 38.95, 38.86, 29.6, 29.4, 27.29, 27.25, 27.23, 27.20, 8.5, 7.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{46}H_{72}N_5O_{14}$ 918.5076, found 918.5059.

(2R,3R,4S,5S,6R)-2-(((3aR,4R,6R,6aR)-2,2-Diethyl-6-(6-pivalamido-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-

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*((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**24**).* By following the general procedure, donor **13** (92 mg, 0.15 mmol) was combined with acceptor **47** (42 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 97:3 dichloromethane/methanol as the eluant afforded **23** (59 mg, 64%) as a white solid: mp 86−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1 H), 8.56 (br s, 1 H), 8.32 (s, 1 H), 6.27 (d, 1 H, J = 2.0 Hz), 5.41 (d, 1 H, J = 2.4 Hz), 5.28 (dd, 1 H, J = 2.0 and 5.2 Hz), 5.23 (dd, 1 H, J = 6.4 and 8.4 Hz), 5.11 (dd, 1 H, J = 2.4 and 8.4 Hz), 4.93 (dd, 1 H, J = 2.0 and 4.8 Hz), 4.51−4.52 (m, 2 H), 4.15 (dd, 1 H, J = 5.2 and 8.8 Hz), 4.11 (dd, 1 H, J = 2.4 and 8.4 Hz), 4.02 (dd, 1 H, J = 4.8 and 8.8 Hz), 3.95 (app t, 1 H, J = 5.2 Hz), 3.68 (dd, 1 H, J = 4.0 and 8.4 Hz), 1.85 (q, 2 H, J = 6.0 and 12.0 Hz), 1.64 (q, 2 H, J = 6.0 Hz), 1.42 (s, 9 H), 1.30 (s, 9 H), 1.28 (s, 9 H), 1.12 (s, 9 H), 1.21 (s, 9 H), 1.05 (t, 3 H, J = 6.0 Hz), 0.90 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 177.3, 177.0, 176.9, 175.7, 153.0, 151.3, 149.8, 142.0, 123.1, 119.0, 101.2, 91.0, 85.5, 85.0, 81.8, 71.2, 70.8, 69.5, 68.8, 66.7, 61.1, 40.7, 39.2, 38.9, 38.8, 29.5, 29.4, 27.5, 27.3, 27.20, 27.17, 27.14, 8.5, 8.0; HR-ESI-MS $[M + H]^+$ calcd for $C_{46}H_{72}N_5O_{14}$ 918.5076, found 918.5058.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-6-(6-(Bis(4-methoxybenzyl)-amino)-9H-purin-9-yl)-2,2-diethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**25**).* By following the general procedure, donor **5** (92 mg, 0.15 mmol) was reacted with acceptor **50** (58 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 95:5 dichloromethane/methanol as the eluant afforded **25** (51 mg, 47%) as a white solid: mp 58−91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1 H), 7.95 (s, 1 H), 7.23 (d, 4 H, J = 6.8 Hz), 6.87 (d, 4 H, J = 6.8 Hz), 6.19 (d, 1 H, J = 2.0 Hz), 5.35 (dd,1 H, J = 2.0 and 5.2 Hz), 5.31 (dd, 1 H, J = 7.6 and 8.0 Hz), 5.12 (dd, 1 H, J = 7.6 and 8.0 Hz), 5.04 (dd, 1 H, J = 6.4 and 7.8 Hz), 4.96 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.52 (d, 1 H, J = 6.4 Hz), 4.46 (m, 1 H), 4.20 (d, 1 H, J = 8.8 Hz), 4.12 (dd, 1 H, J = 3.2 and 8.4 Hz), 4.04 (dd, 1 H, J = 4.4 and 9.6 Hz), 3.82 (s, 6 H), 3.73 (dd, 1 H, J = 4.8 and 8.4 Hz), 3.68 (dd, 1 H, J = 2.8 and 8.0 Hz), 1.85 (q, 2 H, J = 6.0 Hz), 1.65 (q, 2 H, J = 6.0 Hz), 1.21 (s, 9 H), 1.18 (s, 9 H), 1.12 (s, 9 H), 1.09 (s, 9 H), 1.05 (t, 3 H, J = 6.0 Hz), 0.91 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 177.3, 176.7, 176.5, 159.1, 155.0, 152.9, 150.7, 137.7, 129.4, 120.0, 118.9, 114.1, 101.1, 90.7, 85.5, 84.7, 81.9, 72.6, 72.2, 71.2, 69.6, 68.0, 61.9, 55.4, 29.6, 29.4, 27.3, 27.24, 27.19, 27.13, 8.5, 8.0; HR-ESI-MS $[M + H]^+$ calcd for $C_{57}H_{80}N_5O_{15}$ 1074.5651, found 1074.5646.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-2,2-Diethyl-6-(6-hydroxy-2-pivalamido-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**26**).* According to the general procedure, donor **5** (92 mg, 0.15 mmol) was reacted with acceptor **52** (44 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 92:8 dichloromethane/methanol as the eluant afforded **26** (21 mg, 22%) as a white solid: mp 65−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1 H), 8.61 (s, 1 H), 8.00 (s, 1 H), 8.17 (d, 2 H, J = 6.0 Hz), 6.01 (d, 1 H, J = 2.4 Hz), 5.36 (dd, 1 H, J = 7.6 Hz), 5.17 (dd, 1 H, J = 2.4 and 5.2 Hz), 5.10 (dd, 1 H, J = 7.6 and 8.0 Hz), 5.02 (dd, 1 H, J = 6.8 and 7.2 Hz), 4.85 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.52 (d, 1 H, J = 6.4 Hz), 4.41 (m, 1 H), 4.27 (d, 1 H, J = 9.2 Hz), 4.06 (dd, 1 H, J = 2.8 and 8.4 Hz), 4.02 (dd, 1 H, J = 4.8 and 10.0 Hz), 3.72 (m, 1 H), 3.62 (dd, 1 H, J = 2.8 and 8.4 Hz), 1.83 (q, 2 H, J = 6.0 Hz), 1.63 (q, 2 H, J = 6.0 Hz), 1.53 (s, 9 H), 1.19 (s, 9 H), 1.17 (s, 18 H), 1.14 (s, 9 H), 1.04 (t, 3 H, J = 6.0 Hz), 0.90 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.0, 178.2, 177.3, 177.0, 176.5, 155.5, 148.2, 148.0, 137.6, 122.0, 119.2, 100.9, 90.2, 84.6, 84.6, 81.1, 72.8, 72.0, 71.2, 68.6, 68.1, 61.9, 40.5, 39.0, 39.99, 38.95, 38.93, 29.6, 29.4, 27.4, 27.32, 27.26, 27.24, 27.21, 8.6, 8.1; HR-ESI-MS $[M + H]^+$ calcd for $C_{46}H_{72}N_5O_{15}$ 934.5025, found 934.5007.

*(2R,3R,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-6-(6-(Benzyloxy)-2-pivalamido-9H-purin-9-yl)-2,2-diethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**27**).* By following the general procedure, donor **5** (92 mg, 0.15 mmol) was combined with acceptor **55** (53 mg, 0.10 mmol) at 0 °C for 15 min and then 23 °C for 45 min. After workup, purification by thin-layer chromatography with 96:4 dichloromethane/methanol as the eluant afforded **27** (63 mg, 61%) as a white solid: mp 81−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1 H), 8.02 (br s, 1 H), 7.55−7.56 (m, 2 H), 7.32−7.38 (m, 3 H), 6.15 (s, 1 H), 5.66 (s, 2 H), 5.34 (d, 1 H, J = 5.2 Hz), 5.27 (app t, 1 H, J = 7.6 Hz), 5.21 (dd, 1 H, J = 2.4 and 4.8 Hz), 5.10 (dd, 1 H, J = 7.6 and 8.0 Hz), 4.97 (dd, 1 H, J = 6.8 and 7.2 Hz), 4.44−4.48 (m, 2 H), 4.14 (d, 1 H, J = 10.0 Hz), 4.05 (dd, 1 H, J = 2.0 and 8.4 Hz), 3.99 (dd, 1 H, J = 4.0 and 8.8 Hz), 3.73 (dd, 1 H, J = 4.2 and 8.4 Hz), 3.62 (dd, 1 H, J = 3.6 and 8.0 Hz), 1.82 (q, 2 H, J = 6.0 Hz), 1.65 (q, 2 H, J = 6.0 Hz), 1.37 (s, 9 H), 1.17 (s, 9 H), 1.14 (s, 9 H), 1.10 (s, 9 H), 1.05 (s, 9 H), 1.03 (t, 3 H, J = 6.0 Hz), 0.89 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 177.4, 176.7, 176.4, 175.2, 161.0, 152.5, 141.1, 136.1, 128.7, 128.6, 128.3, 118.6, 101.1, 90.6, 86.6, 84.8, 81.8, 72.4, 72.2, 71.2, 70.1, 69.1, 67.9, 61.8, 40.4, 40.0, 38.86, 38.85, 38.79, 29.49, 29.46, 27.7, 27.4, 27.3, 27.23, 27.18, 27.1, 8.5, 8.0; HR-ESI-MS $[M + H]^+$ calcd for $C_{53}H_{78}N_5O_{15}$ 1024.5494, found 1024.5484.

*1-((3aR,4R,6R,6aR)-2,2-Diethyl-6-(((((2R/2S,3R,4S,5R,6R)-3,4,5-tris-(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-methyl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)pyrimidine-2,4-(1H,3H)-dione (**30α/β**).* By following the general procedure, commercially available donor **29** (102.8 mg, 0.15 mmol 1.5 equiv) was combined with acceptor **4** (31.2 mg, 0.10 mmol) at 0 °C for 60 min. After workup, purification by thin-layer chromatography using 4:1 hexane/ethyl acetate as the eluant afforded **30*α*** (30.9 mg, 37%) as a white solid, R_f = 0.21, mp 65−93 °C, and **30*β*** (39 mg, 47%) as a white solid, R_f = 0.28, mp 62−78 °C. For **30*α***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (broad, 1 H), 7.83 (d, 1 H, J = 6.4 Hz), 7.29−7.41 (m, 18 H), 7.14−7.28 (m, 2 H), 6.09 (d, 1 H, J = 2.4 Hz), 5.53 (d, 1 H, J = 6.4 Hz), 4.98 (d, 1 H, J = 8.8 Hz), 4.85 (d, 1 H, J = 9.2 Hz), 4.81 (d, 1 H, J = 10.0 Hz), 4.78 (dd, 1 H, J = 2.8 and 5.2 Hz), 4.71 (d, 1 H, J = 2.8 Hz), 4.68 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.63 (d, 1 H, J = 5.2 Hz), 4.61 (d, 1 H, J = 5.2 Hz), 4.51 (d, 1 H, J = 1.2 Hz), 4.49 (d, 1 H, J = 2.4 Hz), 4.41 (dd, 1 H, J = 2.4 and 5.2 Hz), 3.92 (dd, 1 H, J = 2.8 and 8.8 Hz), 3.87 (dd, 1 H, J = 6.4 and 6.8 Hz), 3.60−3.73 (overlapped, 6 H), 1.83 (q, 2 H, J = 6.0 and 12.0 Hz), 1.64 (q, 2 H, J = 6.0, 12.0 Hz), 1.04 (t, 3 H, J = 6.0 Hz), 0.91 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.12, 150.21, 141.67, 138.66, 138.14, 138.02, 137.95, 128.87, 128.72, 128.70, 128.68, 128.49, 128.28, 128.19, 128.15, 128.13, 128.05, 128.00, 119.35, 103.10, 97.87, 91.47, 85.16, 84.72, 82.08, 80.58, 80.07, 77.73, 75.94, 75.45, 73.93, 73.74, 70.99, 68.48, 68.07, 29.59, 8.61, 8.14; HR-ESI-MS $[M + H]^+$ calcd for $C_{48}H_{55}N_2O_{11}$ 835.3806, found 835.3790. For **30*β***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (br s, 1 H), 7.63 (d, 1 H, J = 6.4 Hz), 7.29−7.36 (m, 18 H), 7.18−7.20 (m, 2 H), 5.99 (d, 1 H, J = 1.5 Hz), 5.72 (d, 1 H, J = 6.5 Hz), 4.92 (d, 1 H, J = 8.8 Hz), 4.86 (d, 1 H, J = 8.6 Hz), 4.84 (d, 1 H, J = 8.8 Hz), 4.81 (d, 1 H, J = 8.8 Hz), 4.79 (d, 1 H, J = 8.7 Hz), 4.75 (dd, 1 H, J = 1.2 and 5.2 Hz), 4.63 (d, 1 H, J = 9.8 Hz), 4.58 (d, 1 H, J = 9.8 Hz), 4.56 (d, 1 H, J = 9.8 Hz), 4.52 (br d, 1 H, J = 2.2 Hz), 4.46 (d, 1 H, J = 6.3 Hz), 4.26 (dd, 1 H, J = 2.1 and 8.6 Hz), 3.74−3.78 (m, 2 H), 3.63−3.72 (m, 3 H), 3.48 (dd, 1 H, J = 3.3 and 7.3 Hz), 3.40 (t, 1 H, 6 H J = 6.4 Hz), 1.81 (q, 2 H, J = 6.0 Hz), 1.57 (q, 2 H, J = 6.0 Hz), 1.02 (t, 3 H, J = 6.0 Hz), 0.87 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 150.1, 141.7, 138.5, 138.2, 138.1, 138.0, 128.5, 128.5, 128.1, 128.04, 127.95, 127.92, 127.90, 127.84, 127.75, 118.8, 103.4, 102.0, 93.9, 86.1, 85.7, 84.8, 82.2, 81.2, 77.8, 75.8, 75.2, 75.1, 75.0, 73.6, 69.8, 68.7, 29.5, 29.3, 8.5, 7.9. HR-ESI-MS $[M + H]^+$ calcd for $C_{48}H_{54}N_2O_{11}$ 835.3809, found 835.3790.

*(2R,3R,4S,5S,6R)-2-((Pivaloyloxy)methyl)-6-(2,2,2-trichloro-1-iminoethoxy)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**31**).* Donor **31** was prepared by following the literature method.[68] A solution of pivaloyl chloride (10.65 mL, 86.50 mmol), pyridine (10.05 mL, 125 mmol), and D-(+)-mannose (2.50 g, 14.00 mmol) in 20 mL of chloroform was stirred at room temperature for 2 days and then was transferred to a separatory funnel along with 200 mL of ethyl acetate. The organic phase was separated and washed sequentially with water (100 mL) and 1 N HCl (2 × 100 mL). The organic phase was dried over anhydrous sodium sulfate and concentrated to afford a sticky solid. The product was crystallized

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twice from methanol to give 3.05 g (36% yield) of the pentapivaloate as a white solid.

A solution of the above solid (3.0 g, 4.99 mmol) and hydrazine acetate (1.07 g, 11.47 mmol) in dimethylformamide (50 mL) was heated at 50 °C under a nitrogen atmosphere for 48 h. The reaction mixture was cooled to room temperature and diluted with 200 mL of ethyl acetate. The organic portion was washed sequentially with water (100 mL) and brine (100 mL), dried over sodium sulfate, and then concentrated. The residue was purified by chromatography, eluting with 10−60% ethyl acetate in hexane, to afford 1.55 g (61% yield) of the reducing sugar as a light yellow oil.

A solution of the reducing sugar (1.54 g, 2.98 mmol) in dichloromethane (50 mL) was treated with trichloroacetonitrile (1.20 mL, 11.92 mmol), and then sodium hydride (0.11 g, 2.98 mmol) was added at room temperature with vigorous stirring. The reaction mixture was allowed to stir for 2 h, filtered through Celite, and then concentrated. The residue was purified by flash chromatography, eluting with 10% ethyl acetate/hexane, to afford **31** (1.20, 59% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.77 (s, 1 H), 6.20 (d, 1 H, J = 1.2 Hz), 5.58 (dd, 1 H, J = 8.0 and 8.4 Hz), 5.47 (dd, 1 H, J = 1.2 and 2.0 Hz), 5.43 (dd, 1 H, J = 2.4 and 8.0 Hz), 4.18−4.21 (m, 3 H), 1.28 (s, 9 H), 1.21 (s, 9 H), 1,17 (s, 9 H), 1.12 (s, 9 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.7, 177.0, 176.6, 176.5, 159.8, 94.7, 71.6, 69.3, 69.2, 67.8, 64.4, 61.5, 38.9, 38.8, 38.7, 27.1, 27.1, 27.1; HR-ESI-MS $[M-CCl_3CONH]^+$ calcd for $C_{26}H_{43}O_9^+$ 499.2907, found 499.2902.

*(2S,3S,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-6-(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-diethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**32**).* By following the general procedure, donor **31** (99 mg, 0.15 mmol) was combined with acceptor **4** (31 mg, 0.10 mmol) at 0 °C for 60 min. After workup, purification by thin-layer chromatography with 3:2 hexane/ethyl acetate as the eluant afforded **32** (69 mg, 85%) as a white solid: mp 97−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (br s, 1 H), 7.31 (d, 1 H, J = 6.4 Hz), 5.82−5.84 (m, 2 H), 5.49 (dd, 1 H, J = 8.0 Hz), 5.31 (dd, 1 H, J = 2.4 and 8.0 Hz), 5.26 (m, 1 H), 4.94 (dd, 1 H, J = 2.0 and 6.4 Hz), 4.88 (dd, 1 H, J = 3.6 and 5.2 Hz), 4.81 (s, 1 H), 4.29 (dd, 1 H, J = 3.2 and 6.0 Hz), 4.12−4.18 (m, 2 H), 4.01 (d, 1 H, J = 8.0 Hz), 3.91 (dd, 1 H, J = 3.2 and 9.2 Hz), 1.79 (q, 2 H, J = 6.0 and 12.0 Hz), 1.63 (q, 2 H, J = 6.0 and 12.0 Hz), 1.25 (s, 9 H), 1.22 (s, 9 H), 1.14 (s, 9 H), 1.11 (s, 9 H), 0.99 (t, 3 H, J = 6.0 Hz), 0.88 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 177.5, 177.1, 176.6, 163.8, 150.3, 141.8, 119.3, 103.2, 98.29, 93.28, 85.2, 84.7, 80.7, 69.6, 69.4, 69.1, 67.6, 64.9, 61.8, 38.9, 38.8, 29.5, 29.3, 27.18, 27.16, 27.13, 27.11, 8.5, 7.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{40}H_{63}N_2O_{15}$ 811.4228, found 811.4239.

*(2S,3S,4S,5R,6R)-2-(((3aR,4R,6R,6aR)-2,2-Diethyl-6-(6-pivalamido-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl Tris(2,2-dimethylpropanoate) (**33**).* By following the general procedure, donor **31** (99 mg, 0.15 mmol) was combined with acceptor **47** (42 mg, 0.10 mmol) at 0 °C for 60 min. After workup, purification by thin-layer chromatography with 94:6 dichloromethane/methanol as the eluant afforded **33** (49 mg, 53%) as a white solid: mp 106−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1 H), 8.66 (br s, 1 H), 8.08 (s, 1 H), 6.19 (d, 1 H, J = 1.2 Hz), 5.62 (dd, 1 H, J = 1.2 and 4.8 Hz), 5.42 (dd, 1 H, J = 8.0 and 8.4 Hz), 5.31 (s, 1 H), 5.18 (dd, 1 H, J = 2.4 and 8.0 Hz), 5.09 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.98 (dd, 1 H, J = 1.2 and 6.4 Hz), 4.67 (d, 1 H, J = 1.2), 4.57−4.59 (m, 1 H), 4.99 (dd, 1 H, J = 2.8 and 10.0 Hz), 3.75−3.83 (m, 3 H), 3.70 (dd, 1 H, J = 3.6 and 8.8 Hz), 1.85 (q, 2 H, J = 6.0 Hz), 1.71 (q, 2 H, J = 6.0 Hz), 1.41 (s, 9 H), 1.25 (s, 9 H), 1.20 (s, 9 H), 1.13 (s, 9 H), 1.09 (s, 9 H), 1.05 (t, 3 H, J = 6.0 Hz), 0.96 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 177.2, 177.1, 176.6, 175.9, 153.2, 151.1, 150.1, 142.0, 123.9, 119.1, 98.2, 92.0, 86.5, 84.7, 82.2, 69.4, 69.2, 69.0, 68.3, 64.9, 61.7, 40.7, 39.1, 39.0, 38.93, 38.88, 29.8, 29.3, 27.5, 27.31, 27.28, 27.24, 27.21, 8.7, 7.9; HR-ESI-MS $[M + H]^+$ calcd for $C_{46}H_{72}N_5O_{14}$ 918.5076, found 918.5066.

*1-((2R,3R,4S,5R)-3,4-Dihydroxy-5-((((2R,3R,4S,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)methyl)-tetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione (**34**).* A solution of nucleoside disaccharide **14** (110 mg, 0.14 mmol), indium triflate (114 mg, 0.20 mmol, and one drop of water in 1 mL of 1,2-dichloroethane and 1 mL of acetonitrile was allowed to stir at 40 °C for 12 h. Twenty milliliters of water was added, and the mixture was extracted with ethyl acetate (3 × 20 mL). The organic extract was dried over anhydrous sodium sulfate and concentrated to provide 102 mg of crude diol product. A solution of the crude product in 2 mL of methanol was treated with freshly prepared 1 M sodium methoxide (methanol solution, 0.55 mL, 0.544 mmol) at 0 °C. The solution was allowed to warm to room temperature and stir at this temperature for 12 h. The pH of the resulting solution was adjusted to approximately 7 by the addition of solid carbon dioxide. The solvent was removed and the residue obtained was dissolved 2 mL of dimethyl sulfoxide. This solution was loaded onto a C-18 reversed-phase column (40 g) eluting with 0% to 60% acetonitrile/water. The desired fraction was collected and concentrated by lyophilization to afford **34** (47 mg, 0.117 mmol, 86% overall) as a white solid: mp 146−159 °C; ^{1}H NMR (400 MHz, D_2O) δ 3.49 (dd, 1 H, J = 6.4, 8.0 Hz), 3.58 (dd, 1 H, J = 2.8 and 8.0 Hz), 3.62 (dd, 1 H, J = 3.2 and 6.4 Hz), 3.67 (dd, 1 H, J = 3.6 and 9.6 Hz), 3.72 (dd, 1 H, J = 6.4 and 9.6 Hz), 3.81 (dd, 1 H, J = 2.8 and 9.2 Hz), 3.86 (d, 1 H, J = 2.4 Hz), 4.16 (d, 1 H, J = 2.0 Hz), 4.19−4.21 (m, 1 H), 4.26 (dd, 1 H, J = 4.0 Hz), 4.30 (dd, 1 H, J = 3.6 and 4.0 Hz), 4.39 (d, 1 H, J = 6.4 Hz), 5.83 (d, 1 H, J = 3.6 Hz), 5.85 (s, 1 H), 7.88 (d, 1 H, J = 6.4 Hz); ^{13}C NMR (125 MHz, D_2O) δ 168.8, 153.7, 144.2, 105.0, 104.3, 91.4, 85.2, 77.3, 75.9, 74.9, 73.0, 71.8, 70.7, 70.6, 63.2; LC-ESI-MS $[M + H]^+$ calcd for $C_{15}H_{23}N_2O_{11}$ 407.13, found 407.10.

*(2R,3R,4S,5R,6R)-2-(((2R,3S,4R,5R)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methoxy)-6-(hydroxymethyl)-tetrahydro-2H-pyran-3,4,5-triol (**35**).* Nucleoside disaccharide **24** (92 mg, 0.10 mmol) was hydrolyzed as for **14** (above). A solution of the crude diol product in 2 mL of 7 N ammonia in methanol was allowed to stir at room temperature for 12 h. The resulting reaction was concentrated, and the residue obtained was further dried with high vacuum pump for overnight to afford 81 mg of white solid.

A solution of the above product in 2 mL of methanol was treated with freshly prepared 1 M methanolic sodium methoxide (0.3 mL, 0.30 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stir for 12 h. The pH of the resulting solution was adjusted to about 7 by the addition of solid carbon dioxide. The solvent was removed, and the crude product was dissolved in 2 mL of dimethyl sulfoxide. This solution was chromatographed as for **34** (above) to provide **35** (31 mg, 0.07 mmol, 72% overall) as a white solid: mp 198 °C (dec); ^{1}H NMR (400 MHz, D_2O) δ 8.39 (s, 1H), 8.18 (s, 1 H), 6.03 (d, 1 H, J = 4.0 Hz), 4.67 (m, 1H), 4.42 (dd, 1 H, J = 3.6 and 4.0 Hz), 4.37 (d, 1 H, J = 6.4 Hz), 4.28−4.31 (m, 1 H), 4.15 (dd, 1 H, J = 2.4 and 9.6 Hz), 3.85 (dd, 1 H, J = 3.2 and 8.8 Hz), 3.83 (d, 1 H, J = 3.2 Hz), 3.69 (dd, 1 H, J = 6.4 and 9.6 Hz), 3.65 (dd, 1 H, J = 3.6 and 9.6 Hz), 3.62 (dd, 1 H, J = 3.6 and 6.4 Hz), 3.55 (dd, 1 H, J = 2.8 and 8.0 Hz), 3.47 (dd, 1 H, J = 6.4 and 8.0 Hz); ^{13}C NMR (125 MHz, D_2O) δ 155.5, 152.0, 150.6, 143.0, 120.6, 105.3, 89.9, 85.8, 77.4, 76.3, 74.9, 73.0, 72.4, 71.1, 70.8, 63.2; LC-ESI-MS $[M + H]^+$ calcd for $C_{16}H_{24}N_5O_9$ 430.16, found 430.12.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(3-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)-2,6-dioxo-3,6-dihydropyrimidin-1(2H)-yl)tetrahydro-2H-pyran-3,4,5-triyl Triacetate, (2R,3R,4S,5R)-2-(Acetoxymethyl)-6-((1-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate, and (2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-((1-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**38**, **39**, and **40**, Respectively).* A solution of 2′,3′,5′-tri-*O*-acetyluridine (37 mg, 0.10 mmol) and methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (113.5 mg, 0.30 mmol) in 2 mL of 1,2-dichloroethane was treated with 3 Å molecular sieves (100 mg) and *N*-iodosuccinimide (67.5 mg, 0.30 mmol), and the mixture was allowed to stir at room temperature for 15 min. Iron(III) triflate (1.0 mg, 0.002 mmol) was

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added, and the reaction mixture was allowed to stir at room temperature for 1 h. The reaction mixture was directly applied to a thin-layer chromatography plate; double elution with 95:5 dichloromethane/methanol afforded **38** (R_f = 0.37, 20.3 mg, 0.029 mmol, 29% yield) and **39**/**40** (R_f = 0.40, 8.4 mg, 0.012 mmol, 12% yield) as white solids. For **38**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, 1 H, J = 8.2 Hz), 6.17 (d, 1 H, J = 5.8 Hz), 6.06 (d, 1 H, J = 4.8 Hz), 5.76 (d, 1 H, J = 8.2 Hz), 5.29−5.36 (m, 3 H), 5.17 (t, 1 H, J = 9.9 Hz), 4.42−4.14 (m, 5H), 3.83 (dd, 1 H, J = 3.0 and 8.2 Hz), 2.15 (s, 3 H), 2.13 (s, 6 H), 2.08 (s, 3 H), 2.04 (s, 3 H), 2.00 (s, 3 H), 1.91 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.2, 170.1, 170.0, 169.8, 169.7, 169.6, 149.2, 138.3, 101.7, 86.5, 80.2, 79.3, 77.4, 74.9, 73.7, 72.6, 70.4, 68.1, 68.0, 63.4, 62.1, 20.9, 20.9, 20.8, 20.7, 20.7, 20.6, 20.5; LC-ESI-MS [M + H]$^+$ calcd for $C_{29}H_{36}N_2O_{18}$ 701.20, found 701.04. For **39**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, 1 H, J = 7.5 Hz), 7.79 (d, 1 H, J = 7.4 Hz), 6.22 (d, 1 H, J = 6.9 Hz), 6.04 (d, 1 H, J = 3.8 Hz), 5.99 (d, 1 H, J = 7.4 Hz), 5.37 (t, 1 H, J = 4.6 Hz), 5.28 (t, 1 H, J = 5.4 Hz), 5.21−5.25 (m, 1 H), 5.12−5.16 (m, 1 H), 4.36−3.38 (m, 3 H), 4.29 (dd, 1 H, J = 3.8 and 12.6 Hz), 4.08−4.11 (m, 2 H), 3.92 (d, 1 H, J = 9.7 Hz), 2.11 (s, 3 H), 2.10 (s, 3 H), 2.08 (s, 3 H), 2.07 (s, 3 H), 2.02 (s, 3 H), 1.99 (s, 3 H), 1.98 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.2, 170.1, 170.0, 169.6, 169.5, 169.5, 169.5, 154.9, 144.0, 154.9, 144.0, 96.3, 93.1, 89.6, 80.0, 73.7, 72.9, 72.6, 70.5, 69.8, 69.8, 62.9, 61.4, 20.84, 20.79, 20.67, 20.66, 20.56, 20.55; LC-ESI-MS [M + H]$^+$ calcd for $C_{29}H_{36}N_2O_{18}$ 701.20, found, 701.06. For **40**: ^{1}H NMR (400 MHz, $CDCl_3$) δ (minor resonances identifiable in the mixture with **39**) 7.83 (d, 1 H, J = 7.5 Hz), 6.76 (d, 1 H, J = 3.2 Hz), 6.24 (obscured d), 6.05 (obscured d), 5.52 (t, 1 H, J = 9.8 Hz), 5.07 (t, 1 H, J = 10 Hz), 4.87 (dd, 1 H, J = 3.3 and 10 Hz), 4.24 (dd, 1 H, J = 4 and 10 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ (minor resonances identifiable in the mixture with **39**) 154.6, 143.6, 90.2, 62.1, 60.5.

Acceptor 45 for Preparing 17 and 18: *N*-(1-((3a*R*,4*R*,6*R*,6a*R*)-2,2-Diethyl-6-(hydroxymethyl)tetrahydrofuro[3,4-*d*][1,3]-dioxol-4-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)pivalamide (45). The 3-pentylidene acetal (**44**) was prepared from cytidine by following the procedure for **4** (622 mg, 83% yield) as a white solid: mp 146−150 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.18 (d, 1 H, J = 6.4 Hz), 6.11 (d, 1 H, J = 6.4 Hz), 5.89 (d, 1 H, J = 2.0 Hz), 4.83 (dd, 1 H, J = 2.0 and 5.2 Hz), 4.38 (m, 1 H), 3.80 (dd, 1 H, J = 2.8 and 5.2 Hz), 3.72 (dd, 1 H, J = 3.6 and 6.4 Hz), 1.78 (q, 2 H, J = 6.0 Hz), 1.64 (q, 2 H, J = 6.0 Hz), 1.00 (t, 3 H, J = 6.0), 0.89 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, DMSO) δ 160.3, 147.9, 145.4, 116.9, 93.8, 93.3, 88.1, 84.8, 81.0, 61.3, 29.0, 28.7, 8.3, 7.6; LC-ESI-MS [M + H]$^+$ calcd for $C_{14}H_{21}N_3O_5$ 312.15, found 312.11.

A solution of **44** (622 mg, 2.0 mmol) in 20 mL of pyridine was treated with pivaloyl chloride (2.49 mL, 20.0 mmol) and added dropwise at room temperature, and the mixture was allowed to stir overnight. The reaction was cooled to 0 °C, quenched with 5 mL of methanol, and then concentrated. The residue was purified by using a prepacked C-18 reversed-phase column (120 g), eluting with 5% to 90% acetonitrile/water. The fractions containing product were collected and lyophilized to afford **45** (640 mg, 77% yield) as a white solid: mp 129−165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (br s, 1 H), 7.73 (d, 1 H, J = 6.0 Hz), 7.49 (d, 1 H, J = 6.0 Hz), 5.54 (d, 1 H, J = 2.0 Hz), 5.28 (dd, 1 H, J = 2.0 and 5.2 Hz), 5.16 (dd, 1 H, J = 2.8 and 5.2 Hz), 4.41 (m, 1 H), 3.97 (dd, 1 H, J = 2.0 and 9.6 Hz), 3.86 (dd, 1 H, J = 2.8 and 9.6 Hz), 1.82 (q, 2 H, J = 6.0 Hz), 1.65 (q, 2 H, J = 6.0 Hz), 1.31 (s, 9 H), 1.03 (t, 3 H, J = 6.0), 0.91 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 155.3, 147.7, 118.5, 98.2, 96.6, 88.7, 84.8, 80.9, 62.8, 40.5, 29.5, 29.2, 27.7, 27.1, 8.5, 7.9; HR-ESI-MS [M + H]$^+$ calcd for $C_{19}H_{30}N_3O_6$ 396.2135, found 396.2126.

Acceptor 47 for Preparing 23, 24, and 33: *N*-(9-((3a*R*,4*R*,6-*R*,6a*R*)-2,2-Diethyl-6-(hydroxymethyl)tetrahydrofuro[3,4-*d*]-[1,3]dioxol-4-yl)-9*H*-purin-6-yl)pivalamide (47). The 3,3-pentylidene acetal **46** was prepared from adenosine by following the procedure for **4** (84% yield) as a white solid: ^{1}H NMR (400 MHz, CD_3OD) δ 8.40 (s, 1 H), 8.26 (s, 1 H), 6.22 (d, 1 H, J = 2.4 Hz), 5.33 (dd, 1 H, J = 2.4 and 5.2 Hz), 5.05 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.39 (m, 1 H), 3.77 (dd, 1 H, J = 3.2 and 10.0 Hz), 3.70 (dd, 1 H, J = 3.6 and 9.6 Hz), 1.85 (q, 2 H, J = 6.0 Hz), 1.68 (q, 2 H, J = 6.0 Hz), 1.05 (t, 3 H, J = 6.0 Hz), 0.91 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, DMSO) δ 154.8, 150.9, 148.7, 140.5, 119.0, 117.3, 89.9, 87.2, 83.9, 81.7, 61.6, 28.9, 28.7, 8.3, 7.7; LC-ESI-MS [M + H]$^+$ calcd for $C_{15}H_{22}N_5O_4$ 336.16, found 336.10.

N-Pivaloyl derivative **47** was prepared from **46** by following the procedure for **45** (75% yield) as a white solid: mp 90−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (br s, 1 H), 8.72 (s, 1 H), 8.11 (s, 1 H), 6.11 (d, 1 H, J = 3.2 Hz), 5.21 (dd, 1 H, J = 3.6 and 4.8 Hz), 5.13 (dd, 1 H, J = 1.2 and 5.2 Hz), 4.53 (s, 1 H), 3.96 (dd, 1 H, J = 1.2 and 6.0 Hz), 3.81 (dd, 1 H, J = 2.0 and 6.0 Hz), 1.86 (q, 2 H, J = 6.0 Hz), 1.65 (q, 2 H, J = 6.0 Hz), 1.40 (s, 9 H), 1.24 (s, 1 H), 1.05 (t, 3 H, J = 6.0), 0.89 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 152.4, 150.7, 150.5, 142.6, 124.2, 118.9, 93.8, 86.9, 83.8, 81.6, 63.3, 40.7, 29.5, 29.2, 27.5, 27.3, 8.7, 8.2; HR-ESI-MS [M + H]$^+$ calcd for $C_{20}H_{30}N_5O_5$ 420.2247, found 420.2237.

Acceptor 50 for Preparing 25: ((3a*R*,4*R*,6*R*,6a*R*)-6-(6-(Bis(4-methoxybenzyl)amino)-9*H*-purin-9-yl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methanol (50).[69] A solution of adenosine 3-pentylidene acetal **46** (1.20 g, 3.58 mmol) in 35 mL of dimethylformamide was treated with *tert*-butyldimethylsilyl chloride (1.08 g, 7.06 mmol) and imidazole (0.73 g, 10.74 mmol). The reaction was allowed to stir at room temperature overnight. The reaction mixture was diluted with 100 mL of water and extracted with ethyl acetate (3 × 100 mL). The combined organic solution was dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography, eluting with 1:1 ethyl acetate/hexane, to afford the O-5′ silyl ether **48** (1.57 g, 97% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1 H), 8.06 (s, 1 H), 6.21 (d, 1 H, J = 2.0 Hz), 5.58 (br s, 1 H), 5.38 (dd, 1 H, J = 2.0 and 5.2 Hz), 5.01 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.46 (m, 1 H), 3.88 (dd, 1 H, J = 3.6 and 8.8 Hz), 3.78 (dd, 1 H, J = 3.6 and 8.8 Hz), 1.87 (q, 2 H, J = 6.0 Hz), 1.71 (q, 2 H, J = 12.0 Hz), 1.08 (t, 3 H, J = 6.0), 0.95 (t, 3 H, J = 6.0 Hz), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 153.4, 149.7, 139.7, 120.3, 118.7, 91.7, 88.0, 85.3, 82.0, 63.8, 29.8, 29.5, 26.1, 18.5, 8.6, 8.0, −5.2, −5.3; LC-ESI-MS [M + H]$^+$ calcd for $C_{21}H_{36}N_5O_4Si$ 450.25, found 450.21.

Sodium hydride (0.30 g, 7.40 mmol) was added to a stirred solution of **48** (1.57 g, 3.50 mmol) in 35 mL of tetrahydrofuran at 0 °C, followed by 4-(methoxy)benzyl chloride (1.16 g, 7.4 0 mmol). The mixture was stirred at room temperature overnight and then quenched with 100 mL of saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate (3 × 100 mL), and the combined organic solution was dried over anhydrous sodium sulfate and then concentrated. The residue was purified by flash chromatography, eluting with 15% ethyl acetate/hexane, to afford the *N*,*N*-bis(*p*-methoxybenzyl) ether **49** (1.62 g, 66% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1 H), 7.93 (s, 1 H), 7.23 (d, 4 H, J = 6.8 Hz), 6.86 (d, 4 H, J = 6.8 Hz), 6.21 (d, 1 H, J = 1.6 Hz), 5.42 (dd, 1 H, J = 2.0 and 5.2 Hz), 5.03 (dd, 1 H, J = 2.0 and 5.2 Hz), 4.43 (m, 1 H), 3.88 (dd, 1 H, J = 3.6 and 8.8 Hz), 3.83 (s, 6 H), 3.78 (dd, 1 H, J = 4.8 and 8.8 Hz), 1.87 (q, 2 H, J = 6.0 Hz), 1.71 (q, 2 H, J = 6.0 Hz), 1.07 (t, 3 H, J = 6.0 Hz), 0.95 (t, 3 H, J = 6.0 Hz), 0.87 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 155.0, 152.9, 150.7, 137.6, 129.4, 120.4, 118.6, 114.2, 91.5, 87.9, 85.1, 82.1, 63.8, 55.5, 29.8, 29.5, 26.2, 26.1, 18.6, 8.6, 8.0, −5.2, −5.3; LC-ESI-MS [M + H]$^+$ calcd for $C_{37}H_{52}N_5O_6Si$ 690.93, found 690.87.

A tetrabutylammonium fluoride solution in tetrahydrofuran (2.50 mL, 2.50 mmol) was added to a solution of **49** (1.62 g, 2.35 mmol) in 20 mL of THF. The mixture was allowed to stir at room temperature for 30 min, concentrated, and then purified by flash chromatography, eluting with 60% ethyl acetate/hexane to afford **50** (1.26 g, 93% yield) as a white foam: mp 69−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1 H), 7.77 (s, 1 H), 7.22 (d, 4 H, J = 6.8 Hz), 6.87 (d, 4 H, J = 6.8 Hz), 5.92 (d, 1 H, J = 3.6 Hz), 5.31 (dd, 1 H, J = 3.6 and 5.2 Hz), 5.21 (dd, 1 H, J = 1.2 and 5.2 Hz), 4.58 (m, 1 H), 4.02 (d, 1 H, J = 10.4 Hz), 3.86 (dd, 1 H, J = 1.2 and 10.4 Hz), 3.83 (s, 6 H), 1.89 (q, 2 H, J = 6.0 Hz), 1.71 (q, 2 H, J = 6.0 Hz), 1.09 (t, 3 H, J = 6.0 Hz), 0.93 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 156.8, 152.0, 150.7, 140.6, 131.5, 131.0, 121.9, 120.4, 115.7, 93.3, 89.0, 86.3, 83.7,

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64.3, 56.4, 31.0, 30.8, 9.5, 9.0; HR-ESI-MS $[M + H]^+$ calcd for $C_{31}H_{38}N_5O_6$ 576.2822, found 576.2809.

Acceptor 52 for Preparing 26: *N*-(9-((3a*R*,4*R*,6*R*,6a*R*)-2,2-Diethyl-6-(hydroxymethyl)tetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-6-oxo-6,9-dihydro-1*H*-purin-2-yl)pivalamide (52).[3] The 3-pentylidene acetal of guanosine (**51**) was prepared by following the procedure for **4** (81% yield) and was obtained as a white solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.96 (s, 1 H), 6.05 (d, 1 H, J = 2.0 Hz), 5.27 (dd, 1 H, J = 2.0 and 5.2 Hz), 5.05 (dd, 1 H, J = 2.4 and 5.2 Hz), 4.32 (m, 1 H), 3.76 (dd, 1 H, J = 3.6 and 9.6 Hz), 3.70 (dd, 1 H, J = 3.6 and 9.6 Hz), 1.83 (q, 2 H, J = 6.0 Hz), 1.68 (q, 2 H, J = 6.0 Hz), 1.05 (t, 3 H, J = 6.0 Hz), 0.91 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, DMSO) δ 156.7, 153.7, 150.7, 136.0, 117.2, 116.5, 88.6, 87.2, 84.0, 81.5, 61.7, 28.9, 28.6, 8.3, 7.7; LC-ESI-MS $[M + H]^+$ calcd for $C_{15}H_{22}N_5O_5$ 352.16, found 352.07.

Acceptor **52** was prepared from **51** by following the procedure for **45** (45% yield) and was obtained as a white solid: mp 111−128 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.41 (s, 1 H), 8.11 (s, 1 H), 6.14 (d, 1 H, J = 1.6 Hz), 5.26 (dd, 1 H, J = 1.6 and 5.2 Hz), 5.01 (dd, 1 H, J = 2.0 and 5.2 Hz), 4.44 (m, 1 H), 3.77 (dd, 1 H, J = 2.8 and 9.6 Hz), 3.71 (dd, 1 H, J = 3.6, 9.6 Hz), 1.82 (q, 2 H, J = 6.0 Hz), 1.69 (q, 2 H, J = 6.0 Hz), 1.33 (s, 9 H), 1.03 (t, 3 H, J = 6.0 Hz), 0.92 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ 183.8, 157.3, 151.2, 140.2, 120.6, 120.0, 93.9, 90.2, 87.5, 83.9, 63.8, 42.2, 31.0, 30.8, 27.7, 9.4, 8.7; HR-ESI-MS $[M + H]^+$ calcd for $C_{20}H_{30}N_5O_6$ 436.2196, found 436.2188.

Acceptor 55 for Preparing 27: *N*-(6-(Benzyloxy)-9-((3a*R*,4*R*,6-*R*,6a*R*)-2,2-diethyl-6-(hydroxymethyl)tetrahydrofuro[3,4-*d*]-[1,3]dioxol-4-yl)-9*H*-purin-2-yl)pivalamide (55).[70] A stirred solution of guanosine (1.45 g, 5.0 mmol) in dry dimethylformamide (20 mL) was treated with imidazole (2.7 g, 40.0 mmol) and *tert*-butyldimethylsilyl chloride (4.5 g, 30.0 mmol). The reaction mixture was allowed to stir at room temperature overnight, diluted with ethyl acetate (150 mL), and then washed sequentially with water (3 × 50 mL), saturated aqueous ammonium chloride, and brine. The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated to afford the tris(silyl ether) as a white solid (3.0 g). This product was further dried overnight under high vacuum and then was dissolved in anhydrous tetrahydrofuran (40 mL). Triphenylphosphine (1.97 g, 7.5 mmol) was added, followed by benzyl alcohol (1.03 mL, 10 mmol). The mixture was cooled to 0 °C, and diisopropyl azodicarboxylate (1.48 mL, 7.5 mmol) was added dropwise. The solution was allowed to stir at room temperature for 4 h and then concentrated. The residue was purified by flash column chromatography, eluting with 5% ethyl acetate/hexane, to afford the *O*-benzyl derivative (**53**, 2.0 g, 57% over two steps) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1 H), 7.51−7.49 (m, 2 H), 7.38−7.26 (m, 3 H), 5.92 (d, 1 H, J = 4.0 Hz), 5.56 (s, 2 H), 5.96 (br s, 2 H), 4.52 (dd, 1 H, J = 3.6 and 4.0 Hz), 4.30 (d, 1 H, J = 3.2 Hz), 4.01 (m, 1 H), 3.98 (dd, 1 H, J = 3.2 and 9.2 Hz), 3.78 (dd, 1 H, J = 2.0 and 8.8 Hz), 0.95 (s, 9 H), 0.94 (s, 9 H), 0.83 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.12 (s, 6 H), −0.02 (s, 3 H), −0.14 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 159.7, 154.1, 137.7, 136.7, 128.7, 128.48, 128.46, 128.4, 128.4, 128.3, 128.0, 115.7, 87.4, 85.6, 76.7, 72.5, 68.0, 62.9, 26.0, 25.8, 25.6, 18.7, 18.3, 18.0, −4.1, −4.55, −4.57, −4.9, −5.2, −5.3; LC-ESI-MS $[M + H]^+$ calcd for $C_{35}H_{62}N_5O_5Si_3$ 716.40, found 716.40.

A solution of **53** (2.0 g, 2.80 mmol) in pyridine (20 mL) was treated with pivaloyl chloride (1.01 g, 8.40 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (0.17 g, 1.40 mmol) at room temperature. The mixture was allowed to stir at room temperature for 5 h and then was concentrated. The residue was diluted with ethyl acetate (100 mL), and the organic solution was washed sequentially with 0.2 N HCl (3 × 50 mL) and brine. The organic solution was dried over anhydrous sodium sulfate, filtered, and concentrated to provide the *N*-pivaloyl derivative as a white solid (2.1 g). The white solid was dissolved in 20 mL tetrahydrofuran, and the solution was treated with tetra-*n*-butylammonium fluoride tetrahydrofuran solution (9.0 mL, 9.00 mmol). The reaction mixture was allowed to stir at room temperature for 30 min and then was concentrated. The residue was purified by flash column chromatography, eluting with ethyl acetate, to afford triol **54** (680 mg, 54% over two steps) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1 H), 7.81 (s, 1 H), 7.49−7.47 (m, 2 H), 7.36−7.29 (m, 3 H), 5.76 (d, 1 H, J = 5.2 Hz), 5.67 (d, 2 H, J = 9.6 Hz), 5.46 (d, 2 H, J = 9.6 Hz), 4.83 (dd, 1 H, J = 4.0 and 5.2 Hz), 4.34 (t, 1 H, J = 4.4 Hz), 3.85 (dd, 1 H, J = 2.0 and 10.0 Hz), 3.70 (dd, 1 H, J = 2.4 and 10.0 Hz), 1.35 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6, 160.3, 151.7, 151.2, 141.6, 135.6, 128.8, 128.6, 128.5, 118.5, 91.4, 87.7, 74.5, 72.9, 69.2, 62.9, 40.4, 27.6; LC-ESI-MS $[M + H]^+$ calcd for $C_{22}H_{28}N_5O_6$ 458.20, found 458.03.

The 3-pentylidene acetal of **54** was prepared by following the procedure for **4** (85% yield), affording acceptor **55** as a white solid: mp 92−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (br s, 1 H), 7.84 (s, 1 H), 7.55−7.57 (m, 2 H), 7.32−7.38 (m, 3 H), 5.95 (d, 1 H, J = 2.8 Hz), 5.65−5.71 (m, 2 H), 5.37 (dd, 1 H, J = 2.0 and 5.2 Hz), 5.21 (dd, 1 H, J = 2.8 and 5.2 Hz), 4.90 (dd, 1 H, J = 2.8 and 8.0 Hz), 4.48 (m, 1 H), 3.94−3.97(m, 1 H), 3.77−3.82 (m, 1 H), 1.85 (q, 2 H, J = 6.0 Hz), 1.66 (q, 2 H, J = 6.0 Hz), 1.37 (s, 9 H), 1.05 (t, 3 H, J = 6.0 Hz), 0.90 (t, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 161.2, 151.9, 151.7, 141.5, 135.9, 128.8, 128.5, 128.3, 119.6, 118.5, 92.5, 87.5, 81.4, 69.2, 62.8, 40.4, 29.4, 29.3, 27.5, 8.5, 8.1; HR-ESI-MS $[M + H]^+$ calcd for $C_{27}H_{36}N_5O_6$ 526.2666, found 526.2656.

Acceptor 56 for Preparing 19 and 21: 1-((6a*R*,8*R*,9*R*,9a*S*)-9-Hydroxy-2,2,4,4-tetraisopropyltetrahydro-6*H*-furo[3,2-*f*]-[1,3,5,2,4]trioxadisilocin-8-yl)pyrimidine-2,4(1*H*,3*H*)-dione (56).[71] 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (3.52 mL, 11.00 mmol) was added dropwise and with vigorous stirring to a solution of uridine (2.5 g, 10.25 mmol) in pyridine (100 mL) at 0 °C. The mixture was allowed to warm to room temperature and stir overnight. The solution was concentrated, and the residue was partitioned between dichloromethane and water. The organic layer was washed with brine, and then dried over anhydrous sodium sulfate. Concentration gave a residue that was purified by silica gel chromatography, eluting with 40% ethyl acetate/hexanes, to afford acceptor **56** (4.50 g, 9.23 mmol, 91%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1 H), 7.68 (d, 1 H, J = 8.16 Hz), 5.73 (s, 1 H), 5.69 (dd, 1 H, J = 1.6 and 8.0 Hz), 4.37 (dd, 1 H, J = 5.0 and 8.7 Hz), 4.17−4.21 (m, 2 H), 4.09−4.11 (m, 1 H), 3.99 (dd, 1 H, J = 2.6 and 13.1 Hz), 3.06 (br s, 1 H), 1.02−1.11 (28 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 150.3, 140.1, 102.1, 91.1, 82.1, 75.3, 69.0, 60.4, 17.6, 17.5, 17.4, 17.4, 17.2, 17.09, 17.05, 17.0, 13.5, 13.09, 13.06, 12.7; LC-ESI-MS $[M + H]^+$ calcd for $C_{21}H_{39}N_2O_7Si_2$ 487.23, found 487.24.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02852.

^{1}H and ^{13}C NMR spectra of numbered compounds (PDF)

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Notes

The authors declare no competing financial interest.

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