JOC Article

Conformational Restriction of Nucleosides by Spirocyclic Annulation at C4′ Including Synthesis of the Complementary Dideoxy and Didehydrodideoxy Analogues

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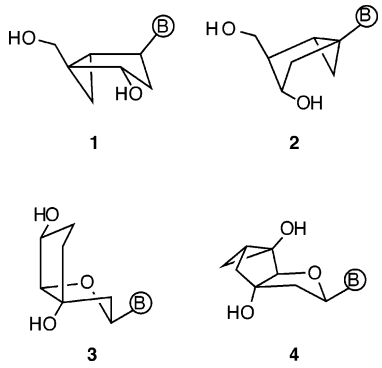
The concept of spirocyclic restriction, when generically applied to nucleoside mimics, allows for the preparation of diastereomeric pairs carrying either a syn- or anti-oriented hydroxyl at C-5′. Reported herein are convenient synthetic routes to enantiomerically pure 1-oxaspiro[4.4]nonanes featuring fully dihydroxylated end products as well as congeners having dideoxy and didehydrodideoxy substitution patterns. Notable use is made of the capacity for introducing unsaturation in the furanose sector via phenylsulfenylation and the incorporation of uracil and thymine by way of their silylated derivatives under catalysis with stannic chloride.

In recent years, attention has been increasingly focused on those structural modifications of nucleosides that feature restrictions in their conformational flexibility. These analogues include, but are not restricted to, the bicyclo[3.1.0]hexane-derived carbocyclic pseudosugars **1** and **2** devised by the Altmann[1] and Marquez groups,[2] Leumann's bi- and tricyclic networks **3** and **4**,[3] and Wengel's locked systems.[4] Eschenmoser's thorough investigation of homo-DNA oligonucleotides (constructed of hexose units rather than pentose)[5] is also exemplary. Our own thrust in this area involves detailed scrutiny of the level of structural preorganization attainable by spirocyclization at C4′ as featured in **5**−**8**. This choice has been motivated by several factors. Immediately apparent is the fact that the glycosyl torsion angle about the C4′−C5′ bond is now fixed, such that positioning of the hydroxyl functionality at R^1 or R^2 results in the adoption of rather different spatial orientations. Beyond this, extensive crystal structure data, most notably those for DNA and RNA fragments, reveal the existence of considerable void space in the region below C4′ of each nucleoside building block. The "empty space" (presumably occupied by water molecules) being referred to is sufficiently voluminous to accommodate more than the string of three methylene groups under consideration



1 **2** **3** **4**

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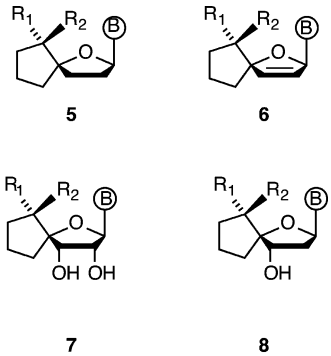
here. Accordingly, there are no pertinent concerns dealing with nonbonded steric superimposition. In this context, it is rather surprising that no C4′ α-homologated nucleosides were reported prior to 1992.[6] At the present time, molecules of this class are of high interest.[7]

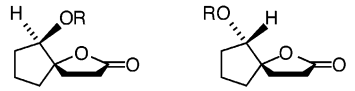
A final point to be mentioned here is the anticipated enhanced stability of **5**, **7**, and **8** to radical attack. DNA strand cleavage has been shown to occur because of the transient intervention of C4′ radicals resulting from hydrogen atom abstraction at that site.[8] Visual inspection of the spirocyclic systems reveals that the 4′-hydrogen is no longer present, being replaced by a carbon center that forms part of the cyclopentane ring. At the same time, the C5′ site is made neopentylic in nature, a feature that should certainly curtail competitive attack at that position as well for the usual steric reasons. Similar considerations lead to the added conclusion that phosphodiester linkages in nucleotides containing spirocyclic components such as **7** and **8** may not be as susceptible to degradation by cellular nucleases. Customarily, reduced hydrolysis rates translate into reduced levels of catabolic degradation.



5 **6** **7** **8**

a, R_1 = H, R_2 = OH; **b**, R_1 = OH, R_2 = H

In previous papers,[9] our long-standing interest in designing strategies for the synthesis of spirotetrahydrofuranyl networks has led us to develop expedient routes to γ-butyrolactones of general formula **9** and **10**. Key issues such as their production in enantiomerically pure form and with defined absolute configuration have equally been solved. Here, we report the conversion of these and related central building blocks into the broad range of spironucleosides defined by **5**, **6**, and **7**. Our ultimate expectation is that future work will establish that analogues of this type hold attraction as tools in molecular biology and as possible therapeutic agents. The synthesis of 2′-deoxy congeners **8** and designed assembly of the latter into spirocyclo-DNA oligomers are presently under active investigation.



9 **10**

Results and Discussion

The synthetic approach takes advantage of the feasibility of generating the phenylthio-substituted lactone **11** by the bis-α-functionalization of **9** (R = TBS) with phenyl benzenethiosulfonate and subsequent monoreduction with ethylmagensium bromide.[9a,10] As shown in Scheme 1, submission of **11** to diisobutylaluminum hydride reduction followed directly by acetylation gave in 94% yield an anomeric mixture of **12**. The coupling reactions between **12** and persilylated uracil or thymine were performed at −78 °C to room temperature in CH_2Cl_2 solutions containing $SnCl_4$.[11,12] Our expectation was that reliance could be placed on the transient intervention of an episulfonium ion intermediate[13] and/or complexation of the sulfur atom to the tin Lewis acid in advance of oxonium ion formation[14] to foster selective formation of

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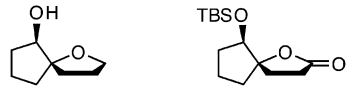
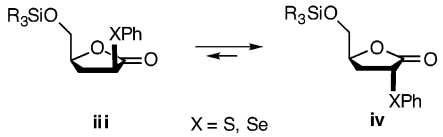
(10) The configuration of the carbinol center in **11** is well established from several perspectives. Thus, **11** is chemically derived from the known alcohol **i** (Dimitroff, M.; Fallis, A. G. *Tetrahedron Lett.* **1998**, *39*, 2531),



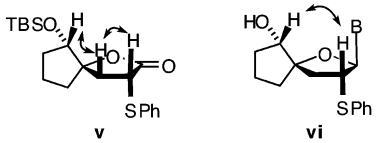
i **ii**

which was prepared by stereocontrolled reduction of the spiro ketone. The favored direction of hydride attack parallels the reaction course followed by other nucleophiles, for which X-ray crystallographic structural confirmation is available.[9a] The chemical conversion of **i** to **ii** earlier reported by us[9a] disturbs no resident stereocenters and provides confirmation that the prior assignment of stereochemistry made by Trost and co-workers (Trost, B. M.; Mao, M. K.-T.; Balkovec, J. M.; Buhlmayer, P. *J. Am. Chem. Soc.* **1986**, *108*, 4965) is in error. Direct spectral comparisons of samples of **ii** from both research groups provided convincing demonstration of their common anti arrangement. The configuration of the phenylthio substituent in **11** is likewise unambiguously based. As in less constrained nucleosides such as **iii** and **iv**, equilibration in the presence of a base such as DBU allows the ready interconversion of the $C_2\beta$ isomer with its thermodynamically more favored α diastereomer (Beach, J. W.; Kim, H. O.; Jeong, L. S.; Nampali, S.; Islam, Q.; Ahn, S. K.; Babu, J. R.; Chu, C. K. *J. Org. Chem*. **1992**, *57*, 3887).



iii **iv**

This useful protocol, which was utilized to prepare large amounts of **11**, is illustrated in more detail for the interconversion of **21** with **22** in Scheme 3. The spatial proximity of the three protons illustrated in **v** for **21** and the more direct interaction shown in **vi** for its analogues **25** and **27** are readily apparent from NOE analysis.



v **vi**

(11) Kawakami, H.; Ebata, T.; Koseki, K.; Matsumoto, K.; Matsushita, H.; Naoi, Y.; Itoh, K. *Heterocyles* **1991**, *32*, 2451.

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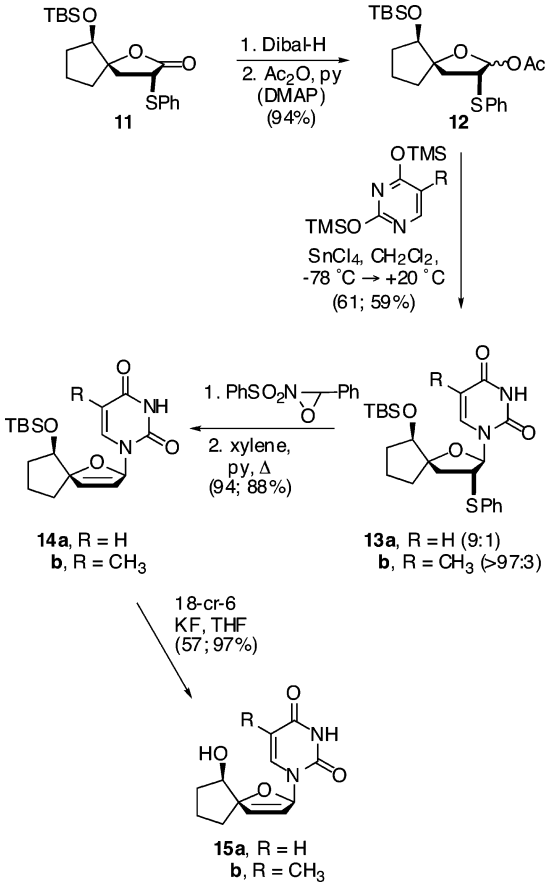
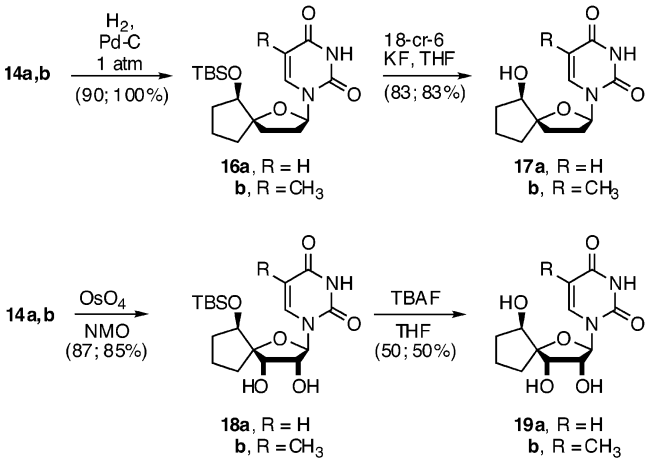
SCHEME 1



a 1,2-trans glycosyl bond.[15−18] In actuality, the β stereoisomer **13a** was isolated as a 9:1 mixture of anomers. With the somewhat more bulky thymine example, **13b** was the only product observed, in line with customary steric effects. The yield in both cases was approximately 60%.

Elimination of the 2-phenylthio substituent in **13** was next accomplished by controlled oxidation with the Davis oxaziridine reagent[19] and subsequent heating in xylene[11] to bring about the thermal elimination of phenylsulfenic acid. The first step generated diastereomeric pairs of sulfoxides (NMR analysis), which underwent conversion to **14** at different rates. The less reactive stereoisomer is presumed to be the one that necessarily projects its phenyl group under the furanoside ring during the E_i process. The transformations to **14** were therefore monitored by TLC until conversion to **15** was complete. In addition, pyridine was present to deter any possible deleterious side reactions capable of being brought on by the PhSOH byproduct. This step was notably efficient in both series (88−90%). The unprotected didehydrodideoxy nucleosides **15a** and **15b** were generated by reaction with potassium fluoride and 18-crown-6 in THF solution. The excellent yield of the thymidine example

SCHEME 2



reflects its exceptional stability under these conditions. In contrast, epimerization was encountered in both examples when recourse was made to TBAF for desilylation.

Saturation of the double bond in these systems was most efficaciously performed while the TBS group remained installed. The conversions of **14** to **16** proceeded in yields exceeding 90% (Scheme 2). Both dihydro products were deprotected with KF as previously described. Attempts were also made to generate **16** by the Raney nickel desulfurization of **13a** and **13b**. However, this reaction proved to be unserviceable due to its nonreproduciblity and degradative tendencies. Its utilization is not advised. In contrast, the OsO_4-promoted dihydroxylation of **14** proceeded very satisfactorily in the presence of NMO, thereby making possible targeted arrival at **19a** and **19b**.

The attractive features of the global approach detailed above prompted a companion investigation of the intrinsic reactivity resident in the epimeric α-C5′ series. Matters began well when **10** (R = TBS) was found to be responsive to bissulfenation and that product **20** underwent efficient reduction with ethylmagnesium bromide to give **21** and **22** (Scheme 3). Of comparable attractiveness were the discoveries that this lactone pair was chromatographically separable and that unwanted **22** could be equilibrated with **21** in THF solution containing DBU. The **21**/**22** equilibrium ratio of 7:1 played nicely into our hands and made feasible the acquisition of reasonable quantities of this key intermediate.

In view of existing precedent,[11] we envisioned that the reductive acetylation of **21**, as effected with diisobutylaluminum hydride/acetic anhydride, would be not at all problematic. However, experiments carried out at both −78 and −100 °C produced unacceptable amounts (up to 39%) of the overreduction product **24**. To prevent this undesired side reaction, the conversion to **23** was attempted with disiamylborane at room temperature.[20] Although these conditions are well-known to produce lactols without evidence of over-reduction, the problem persisted in this instance. Finally, it was uncovered that the co-addition of chlorotrimethylsilane to the Dibal-H reaction mixtures was reproducibly effective in suppress-

(15) Wilson, L. J.; Liotta, D. *Tetrahedron Lett.* **1990**, *31*, 1815.
(16) Montgomery, J. A.; Thomas, H. J. *J. Heterocycl. Chem.* **1979**, *16*, 353.
(17) Horton, D.; Sakata, M. *Carbohydr. Res.* **1976**, *48*, 41.
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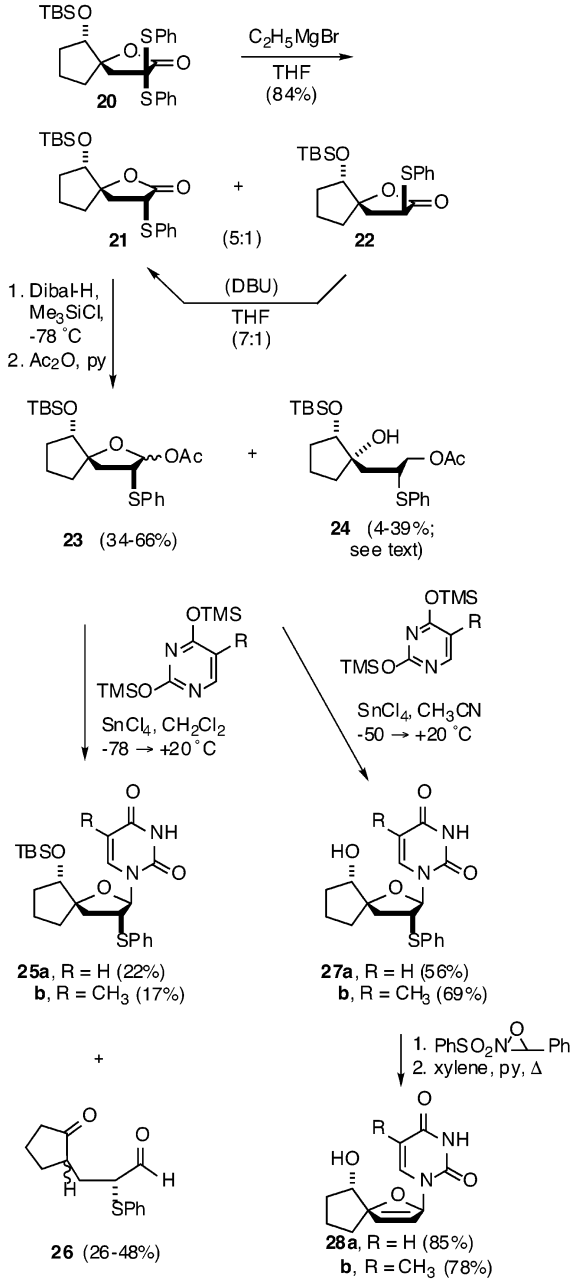
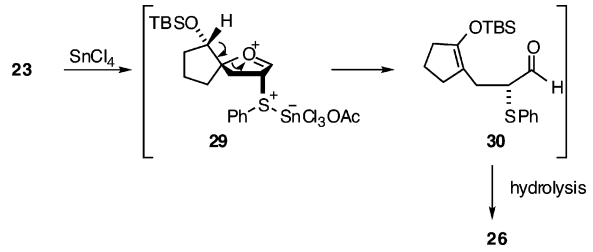
(20) Pedersen, C.; Jenson, H. S. *Acta Chem. Scand.* **1994**, *48*, 222.

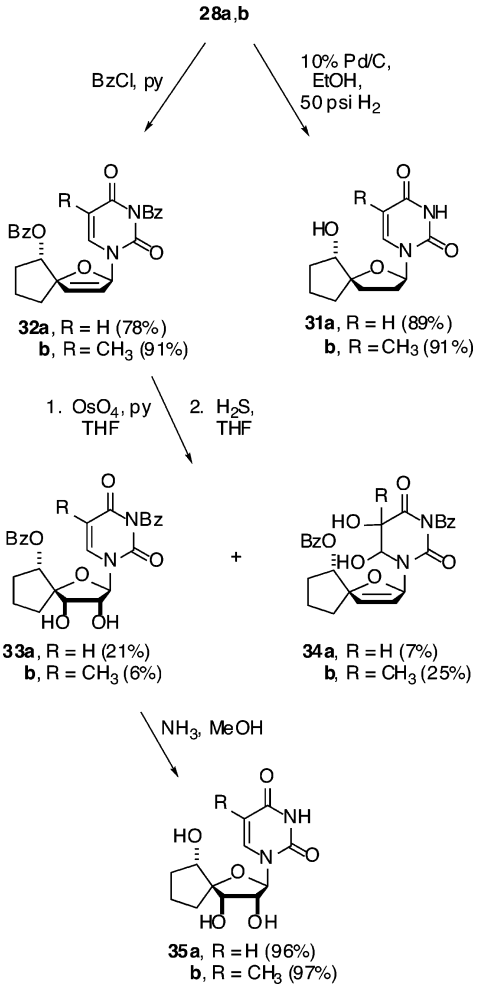
SCHEME 3



SCHEME 4



SCHEME 5



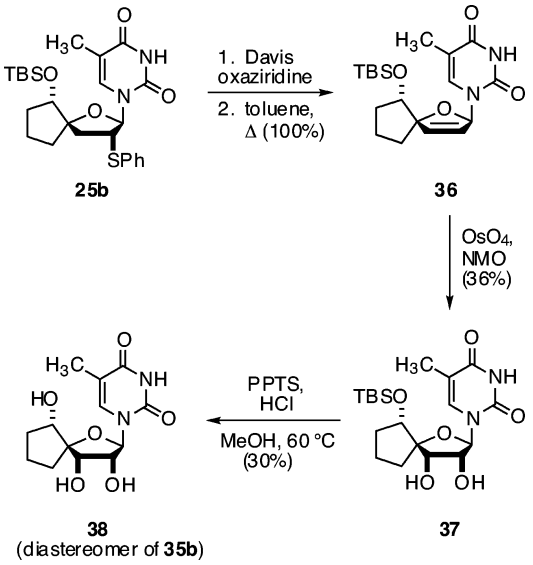
ing the generation of **24** to less than 5%. In situ silylation of the intermediate lactol aluminate in this fashion may prove to be a generally useful protocol.

In an attempt to achieve high-level β-selectivity in the glycosylation of **23**, combined use was again made of silylated bases and $SnCl_4$ in CH_2Cl_2 solution. The disappointing results were the same for both the uracil and the thymine examples. The yields of **25a** and **25b** were below the 25% level because of a competing fragmentation of the furanoside ring that delivered aldehyde **26**. In this stereoisomeric series, the stereoelectronic features resident in **29** are evidently conducive to operation of an E_2 elimination (Scheme 4). Once this irreversible step operates, the resulting silyl enol ether functionality in **30** becomes subject to hydrolysis during the aqueous workup with liberation of the cyclopentanone carbonyl group.

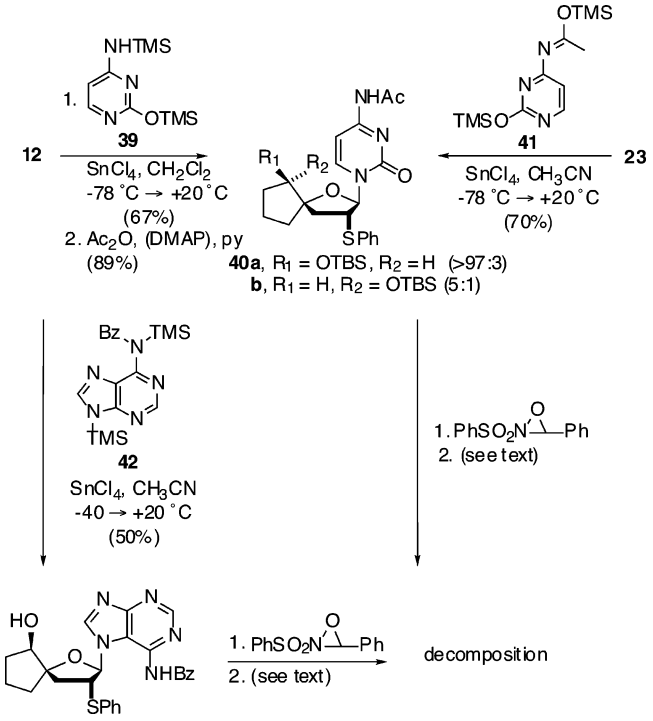
Matters were considerably improved when the glycosylation step was performed in acetonitrile solution at −50 °C to room temperature. This change in solvent was met with unexpected removal of the *tert*-butyldimethylsilyl protecting group. Although stereoselectivity was lowered, the isolated yields of **27a** and **27b** proved sufficiently elevated to be attractive. The advantages offered by this pathway were further reinforced by the finding that thermal elimination of the derived sulfoxides gave rise to **28a** and **28b** in an efficient manner. Saturation of the double bond in these substrates required an increase in pressure to 50 psi (Scheme 5).

The next targeted area of investigation, the dihydroxylation of **28a** and **28b**, quickly revealed that a significant reactivity difference exists when comparison is made with **14a** and **14b**. To facilitate handling, conversion to the dibenzoyl derivatives **32a** and **32b** was initially under-

SCHEME 6



SCHEME 7



taken. In the presence of catalytic quantities of osmium tetraoxide and various co-oxidants, no evidence of reaction was uncovered in either case. The application of forcing conditions simply induced hydrolysis of the benzoate ester. These problems were resolved in part by the use of stoichiometric amounts of the osmium reagent in 4:1 THF−pyridine as the reaction medium.[21] Early attempts to realize purification by chromatography of the osmate esters were soon abandoned as this operation did not resolve the considerable difficulty experienced in bringing about their hydrolytic degradation. However, exposure to gaseous hydrogen sulfide[22] proved to be serviceable and provided the opportunity for convenient product purification and characterization. When the base was uracil, the diol distribution favored **33a** over **34a** by a factor of 3:1. The electron-donating properties of the added methyl group in thymine proved sufficient to invert this ratio.[23] Although the yields are not elevated, it was possible to establish that dihydroxylation at either the dihydrofuran double bond or the nucleobase site gave rise to single diastereomers.

In an effort to realize more efficient access to these dihydroxylated products, an alternative approach via **25b** was explored as illustrated in Scheme 6. Following thermolysis of the sulfoxide and quantitative conversion to **36**, dihydroxylation to generate **37** could be achieved in 36% yield. Deprotection of the silyl ether under acidic conditions completed the crossing to **38**. In an unexpected development, **38** proved to be a diastereomer of **35b**. Although both members of this pair were in hand, we could not distinguish between the α,α- and β,β-isomers. As a result, the illustrated structures are not intended to force a distinction.

With these objectives met, our focus turned to introduction of the remaining nucleosidic bases. To this end, the acetate derivative **12** was subjected to the standard glycosylation conditions with persilylated cytosine **39** in CH_2Cl_2 as solvent. These conditions led to the generation of the targeted nucleoside in 67% yield and highly diastereoselective fashion (β/α > 97:3) (Scheme 7). Acetylation with acetic anhydride made available enantiomerically pure **40a** for further processing. The desired stereochemistry was also introduced upon coupling of **23** with **41** in acetonitrile in the presence of $SnCl_4$. This synthetic approach led directly to **40b**, the β isomer of which predominated by a factor of 5:1.

The glycosidation of **12** with persilylated benzoyladenine **42** proved to be particularly sensitive to the choice of solvent utilized in conjunction with $SnCl_4$. In several instances (e.g., ether, dichloromethane), mixtures of anomers were produced in addition to N^7 and N^9 adducts. Chromatographic separation under these circumstances was not feasible. When the use of acetonitrile was probed, **43** was found to be produced in 50% yield with appreciable β-selectivity (>97%). Although this conversion was found to proceed with loss of the *tert*-butyldimethylsilyl group, no N^9 isomer was detected. The practicality of these reaction conditions is obvious.

With **40a**, **40b**, and **43** in hand, oxidative elimination was the next requisite transformation. In line with our earlier studies, exposure of each of these nucleosides resulted in efficient formation of the epimeric sulfoxides. However, the thermolysis of these intermediates proved to be problematic, giving rise invariably to total degradation. This is not the first occasion where the removal of sulfide or sulfoxide proved unworkable when other cytidine and adenosine congeners were subjected to related chemical transformations.[24]

In conclusion, syntheses of the first spirocyclic nucleosides featuring both α- and β-hydroxyl substituents at C-5′ have been achieved for the nucleobases uracil and thymine. The chemical routing is concise for those nucleoside derivatives featuring three different substitu-

(21) Paquette, L. A.; Brand, S.; Behrens, C. *J. Org. Chem.* **1999**, *64*, 2010.
(22) Zhang, W.; Wang, C.; Jimenez, L. S. *Synth. Commun.* **2000**, *30*, 351.
(23) (a) Barvian, M. R.; Greenberg, M. M. *J. Org. Chem.* **1993**, *58*, 6151. (b) Iwai, S. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3874. (c) Deubel, D. V. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 1974.

tion plans at C-2′ and C-3′. The combination of these features makes possible ready assessment of the biological activity of the several end products. Such studies are in progress, as are efforts to develop a viable entry to the purine analogues.

Experimental Section

General Information. Consult ref 9a.

Reduction and Acetylation of 11. Lactone **11**[9a,10] (0.47 g, 1.20 mmol) was dissolved in CH_2Cl_2 (25 mL), cooled to −78 °C, and treated with Dibal-H (2.40 mL of 1.0 M, 2.40 mmol). After 30 min of stirring, a saturated solution of Rochelle's salt (40 mL) was introduced, the reaction mixture was allowed to warm to rt, and the separated aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The organic phases were combined, dried, and evaporated to leave an oil that was dissolved in CH_2Cl_2 (20 mL) and treated sequentially with pyridine (4.05 mL, 49.5 mmol), acetic anhydride (1.55 mL, 16.5 mmol), and a catalytic quantity of DMAP. After 30 min, the reaction mixture was poured into saturated $NaHCO_3$ solution (30 mL), and the separated aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with water (15 mL) and brine (15 mL) prior to drying and solvent evaporation. There was obtained 0.48 g (94%) of **12** as an anomeric mixture that was used without further purification.

General Glycosidation Procedure for 12. For the glycosidations of pyrimidine bases, CH_2Cl_2 is the solvent of choice. When purine bases are involved, CH_3CN is the preferred reaction medium. The sample of **12** and the heterocyclic base must be dissolved in the same solvent in order to realize good stereoselectivity. The persilylated base (1.5 equiv) was placed in the appropriate solvent (0.06 mmol/mL) and $SnCl_4$ (2.0 equiv) was added, at which time the base dissolved. The $SnCl_4$ used was 1 M in CH_2Cl_2 for thymine, cytosine, and uracil, and neat for adenine. The solution was stirred at rt for 1.5 h, cannulated into a cold (−78 °C) solution of **12** (0.03 mmol/mL), maintained at −78 °C for 30 min, warmed to rt, and stirred for 30 min prior to quenching with saturated $NaHCO_3$ solution. The separated aqueous layer was extracted with ethyl acetate, and the combined organic phases were dried and evaporated.

Product 13a. From 0.30 g (0.71 mmol) of **12** and 0.28 g (1.1 mmol) of persilylated uracil was obtained 0.22 g (61%) of **13a** as a 9:1 β/α anomeric mixture after chromatography on silica gel (elution with 3:2 hexane−ether): colorless syrup; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.06 (s, 1 H), 7.47−7.43 (m, 2 H), 7.28−7.22 (m, 4 H), 6.09 (d, J = 8.2 Hz, 1 H), 5.58 (dd, J = 8.1, 2.0 Hz, 1 H), 4.05 (t, J = 7.2 Hz, 1 H), 3.65 (dt, J = 10.6, 8.1 Hz, 1 H), 2.81 (dd, J = 12.9, 8.0 Hz, 1 H), 2.00−1.60 (m, 7 H), 0.93 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 150.3, 139.2, 133.4 (2C), 131.9, 129.0 (2C), 128.1, 102.8, 91.5, 88.5, 78.5, 50.3, 36.9, 35.6, 31.3, 25.8 (3C), 18.0, 17.9, −4.0, −4.7; ES HRMS m/z $(M + Na)^+$ calcd 497.1901, obsd 497.1913; $[\alpha]^{18}_D$ +8.8 (c 1.5, C_2H_5OH).

Anal. Calcd for $C_{24}H_{34}N_2O_4SSi$: C, 60.73; H, 7.22. Found: C, 60.83; H, 7.17.

Product 13b. From 0.30 g (0.71 mmol) of **12** and 0.29 g (1.1 mmol) of persilylated thymine (0.29 g, 1.1 mmol) was isolated 0.22 g (59%) of **13b** with a diastereomeric purity in excess of 97:3 after chromatography on silica gel (elution with 3:2 hexane−ether): colorless syrup; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1 H), 7.44−7.40 (m, 2 H), 7.27−7.21 (m, 3 H), 6.88 (d, J = 1.2 Hz, 1 H), 5.99 (d, J = 8.6 Hz, 1 H), 4.03 (t, J = 7.3 Hz, 1 H), 3.62 (dt, J = 10.8, 8.3 Hz, 1 H), 2.82 (dd, J = 12.8, 8.1 Hz, 1 H), 2.00−1.57 (m, 10 H), 0.94 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 150.3, 134.6, 133.5 (2C), 132.2, 129.0 (2C), 128.1, 111.2, 91.0, 88.3, 78.5, 49.6, 36.8, 36.1, 31.7, 25.9 (3C), 18.5, 18.0, 12.2, −3.9, −4.6; ES HRMS m/z $(M + Na)^+$ calcd 511.2057, obsd 511.2009; $[\alpha]^{18}_D$ −6.7 (c 0.6, C_2H_5OH).

General Procedure for Sulfoxidation and Thermolysis. The glycosidated sulfide (1.0 equiv) was dissolved in $CHCl_3$ (50 mL) and treated with the Davis oxaziridine (1.1 equiv). After 16−24 h of stirring, the solvent was evaporated to leave a residue that was taken up in xylenes (125 mL) containing 2−3 equiv of pyridine. The solution was refluxed for 4 h, cooled, and freed of solvent under reduced pressure. The residue was dissolved in ethyl acetate, washed with sodium thiosulfate solution, dried, and evaporated.

Product 14a. From 0.22 g (0.46 mmol) of **13a** was isolated 0.16 g (94%) of **14a** as a colorless syrup following chromatography on silica gel (elution with 3:2 hexane−ether): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.95 (br s, 1 H), 7.35 (d, J = 8.1 Hz, 1 H), 6.98 (t, J = 1.4 Hz, 1 H), 6.41 (dd, J = 5.9, 4.8 Hz, 1 H), 5.74−5.69 (m, 2 H), 3.99 (t, J = 5.3 Hz, 1 H), 2.09−1.54 (series of m, 6 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 150.8, 140.0, 138.9, 123.7, 102.7, 101.1, 89.2, 80.1, 35.2, 33.6, 25.7 (3C), 20.4, 17.9, −4.2, −4.7; ES HRMS m/z $(M + Na)^+$ calcd 387.1701, obsd 387.1745; $[\alpha]^{18}_D$ −39 (c 1.2, $CHCl_3$).

Product 14b. From 0.22 g (0.46 mmol) of **13b** was isolated 0.15 g (88%) of **14b** as a colorless syrup following chromatography on silica gel (elution with 3:2 hexane−ether): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (br s, 1 H), 7.26 (s, 1 H), 7.03 (s, 1 H), 6.43 (dd, J = 5.9, 1.6 Hz, 1 H), 5.72 (dd, J = 5.9, 0.9 Hz, 1 H), 3.93 (dd, J = 4.8, 2.7 Hz, 1 H), 2.12−1.58 (series of m, 9 H), 0.91 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4, 150.6, 139.2, 135.3, 124.0, 111.1, 101.2, 89.3, 80.6, 35.4, 34.1, 25.8 (3C), 21.3, 18.0, 17.5, −4.3, −4.8; ES HRMS m/z $(M + Na)^+$ calcd 401.1873, obsd 401.1852; $[\alpha]^{18}_D$ −34 (c 0.4, $CHCl_3$).

Desilylation of 14a. A solution of **14a** (0.07 g, 0.19 mmol) in THF (3 mL) was treated with the 18-crown-6−CH_3CN complex (0.18 g, 0.58 mmol) and potassium fluoride (0.03 g, 0.58 mmol), stirred at rt for 3 days, quenched with water (10 mL), and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were dried and evaporated to leave a residue that was chromatographed on silica gel. Elution with ether gave 0.04 g (57%) of **15a** as a white foam; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (br s, 1 H), 7.57 (d, J = 8.1 Hz, 1 H), 6.96 (t, J = 1.4 Hz, 1 H), 6.45 (dd, J = 5.9, 1.8 Hz, 1 H), 5.78 (dd, J = 5.9, 1.2 Hz, 1 H), 5.71 (dd, J = 8.1, 1.8 Hz, 1 H), 4.14−4.10 (m, 1 H), 2.27−1.59 (series of m, 6 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 150.7, 140.6, 137.3, 124.4, 102.5, 100.4, 89.7, 79.1, 34.9, 32.9, 19.6; ES HRMS m/z $(M + Na)^+$ calcd 273.0846, obsd 273.0866; $[\alpha]^{18}_D$ −13 (c 0.10, C_2H_5OH).

Desilylation of 14b. A solution of **14b** (0.13 g, 0.34 mmol) in THF (30 mL) was treated with the 18-crown-6−CH_3CN complex (1.05 g, 3.4 mmol) and potassium fluoride (0.20 g, 3.4 mmol), stirred at rot for 7 days, quenched with water (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were dried and evaporated to leave a residue that was chromatographed on silica gel. Elution with ether furnished 0.03 g (33%) of **15b** as a white foam and returned 0.09 g (68%) of unreacted **14b**.

For **15b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (br s, 1 H), 7.40 (d, J = 1.0 Hz, 1 H), 7.00 (s, 1 H), 6.49 (dd, J = 5.9, 1.7 Hz, 1 H), 5.83 (d, J = 5.9 Hz, 1 H), 4.19−4.16 (m, 1 H), 2.40−1.47 (series of m, 9 H) (OH not observed); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.7, 150.6, 137.8, 136.7, 125.2, 100.7, 90.0, 79.7, 35.4, 33.3, 30.8, 20.1, 12.9; ES HRMS m/z $(M + Na)^+$ calcd 287.1002, obsd 287.1011; $[\alpha]^{18}_D$ −3.0 (c 0.10, C_2H_5OH).

Hydrogenation of 14a. A 0.17 g (0.47 mmol) sample of **14a** was dissolved in ethanol (15 mL) and admixed with 5% palladium on charcoal (0.042 g). H_2 was bubbled through the suspension for 5 min, after which time a balloon of H_2 was

(24) (a) Kawakami, H.; Ebata, T.; Koseki, K.; Matsushita, H.; Naoi, Y.; Itoh, K. *Chem. Lett.* **1990**, 1459. (b) Kawakami, H.; Ebata, T.; Koseki, K.; Matsumoto, K.; Matsushita, H.; Naoi, Y.; Itoh, K. *Heterocycles* **1991**, *32*, 2451. (c) Kawakami, H.; Ebata, T.; Koseki, K.; Matsumoto, K.; Okano, K.; Matsushita, H. *Nucleosides Nucleotides* **1992**, *11*, 1673.

attached to the flask. The mixture was stirred for 24 h, filtered through a pad of Celite, and evaporated to give 0.13 g (90%) of **16a** as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (br s, 1 H), 7.68 (d, J = 8.1 Hz, 1 H), 6.08−6.06 (m, 1 H), 5.68 (d, J = 8.1 Hz, 1 H), 4.17 (t, J = 7.3 Hz, 1 H), 2.48−2.42 (m, 1 H), 2.27−2.20 (m, 1 H), 2.02−1.85 (m, 3 H), 1.76−1.45 (m, 5 H), 0.91 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 144.3, 140.0, 101.7, 94.9, 85.4, 77.9, 34.3, 32.5, 31.7, 27.7, 25.8 (3C), 18.3, 18.0, −4.0, −4.6; ES HRMS m/z (M + Na)$^+$ calcd 389.1867, obsd 389.1872; $[\alpha]^{18}_D$ −12 (c 0.2, $CHCl_3$).

Hydrogenation of 14b. Hydrogenation of **14b** (0.13 g, 0.34 mmol) in the predescribed manner for 24 h provided 0.13 g (100%) of **16b** as a white foam: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (br s, 1 H), 7.25 (s, 1 H), 6.07 (t, J = 5.9 Hz, 1 H), 4.10 (t, J = 6.4 Hz, 1 H), 2.47−2.24 (m, 2 H), 2.06−1.61 (series of m, 11 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 150.4, 135.2, 110.6, 94.3, 84.7, 77.9, 35.1, 32.0, 32.4, 29.2, 25.8 (3C), 19.1, 18.0, 12.6, −4.1, −4.7; ES HRMS m/z (M + Na)$^+$ calcd 403.2023, obsd 403.2044; $[\alpha]^{18}_D$ +17 (c 0.3, $CHCl_3$).

Desilylation of 16a. A solution of **16a** (0.09 g, 0.25 mmol) in THF (20 mL) was treated with the 18-crown-6−CH_3CN complex (0.77 g, 2.5 mmol) and potassium fluoride (0.15 g, 2.5 mmol), stirred at rt for 7 days, and worked up as described earlier. Elution with ether afforded 0.05 g (83%) of **17a**: ^{1}H NMR (500 MHz, CD_3OD) δ 7.95 (d, J = 8.1 Hz, 1 H), 6.03 (dd, J = 6.4, 4.1 Hz, 1 H), 5.66 (d, J = 8.1 Hz, 1 H), 4.11 (t, J = 7.1 Hz, 1 H), 2.51−2.42 (m, 1 H), 2.35−2.25 (m, 1 H), 2.12−2.00 (m, 2 H), 1.85−1.64 (m, 5 H), 1.58−1.50 (m, 1 H), (NH and OH not observed); ^{13}C NMR (125 MHz, CD_3OD) δ 166.4, 152.3, 142.4, 102.0, 96.2, 87.1, 77.6, 35.8, 33.1, 32.2, 28.7, 19.5; ES HRMS m/z (M + Na)$^+$ calcd 275.1002, obsd 275.1017; $[\alpha]^{18}_D$ +3.5 (c 0.4, C_2H_5OH).

Desilylation of 16b. A solution of **16b** (0.10 g, 0.26 mmol) in THF (30 mL) was treated with the 18-crown-6−CH_3CN complex (0.79 g, 2.6 mmol) and potassium fluoride (0.15 g, 2.6 mmol), stirred at rt for 7 days, and worked up as described earlier. Elution with ether gave **17b** (0.06 g, 83%): ^{1}H NMR (500 MHz, CD_3OD) δ 7.81 (d, J = 1.1 Hz, 1 H), 6.05 (dd, J = 6.5, 4.2 Hz, 1 H), 4.12 (t, J = 7.3 Hz, 1 H), 2.50−2.38 (m, 1 H), 2.33−2.25 (m, 1 H), 2.10−1.98 (m, 2 H), 1.87 (d, J = 1.1 Hz, 3 H), 1.80−1.62 (m, 5 H), 1.58−1.50 (m, 1 H) (NH and OH not observed); ^{13}C NMR (125 MHz, CD_3OD) δ 166.5, 152.4, 138.2, 111.0, 95.8, 86.7, 77.6, 35.8, 32.9, 32.1, 28.7, 19.4, 12.4; ES HRMS m/z (M + Na)$^+$ calcd 289.1159, obsd 289.1164; $[\alpha]^{18}_D$ −1.5 (c 0.8, C_2H_5OH).

General Procedure for Dihydroxylation. Either **14a** or **14b** (1 equiv) was dissolved in a 5:1 acetone−water mixture (15 mL), treated with osmium tetraoxide (30 mol %) and *N*-methylmorpholine-*N*-oxide (2.5 equiv), stirred for 48 h, quenched with a saturated solution of $Na_2S_2O_3$ (15 mL), and stirred for 30 min. The black mixture was extracted with ethyl acetate (3×), and the combined organic layers were dried and evaporated. Chromatography of the residue on silica gel (elution with hexane−ether 3:2) gave the desired diol.

18a. From a 0.14 g (0.40 mmol) of **14a** was isolated 0.13 g (87%) of **18a** as a colorless syrup: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.96 (br s, 1 H), 7.57 (d, J = 8.2 Hz, 1 H), 5.75 (d, J = 8.4 Hz, 1 H), 5.71 (d, J = 4.5 Hz, 1 H), 4.39 (br s, 1 H), 4.34−4.31 (m, 2 H), 4.06 (t, J = 6.9 Hz, 1 H), 3.03 (br s, 1 H), 2.05−1.96 (m, 1 H), 1.82−1.55 (m, 5 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 151.5, 139.7, 102.3, 97.2, 91.1, 79.0, 77.2, 71.1, 32.3, 29.0, 25.8 (3C), 18.7, 17.9, −4.0, −4.8; ES HRMS m/z (M + Na)$^+$ calcd 421.1765, obsd 421.1754; $[\alpha]^{18}_D$ −45 (c 1.4, $CHCl_3$).

18b. Reaction of 0.17 g (0.45 mmol) of **14b** afforded 0.14 g (85%) of **18b** as a colorless syrup: ^{1}H NMR (500 MHz, CD_3OD) δ 7.40 (s, 1 H), 5.80 (d, J = 7.4 Hz, 1 H), 4.27−4.25 (m, 1 H), 4.21 (d, J = 5.3 Hz, 1 H), 4.15−4.10 (m, 1 H), 2.29−2.24 (m, 1 H), 2.01−1.92 (m, 1 H), 1.84 (s, 3 H), 1.65−1.56 (m, 3 H), 1.55−1.45 (m, 1 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H) (OH and NH not observed); ^{13}C NMR (125 MHz, CD_3OD) δ 165.3, 151.9, 136.9, 110.9, 95.5, 88.1, 79.1, 74.0, 70.7, 32.7, 30.0, 25.6 (3C), 18.7, 18.0, 11.6, −4.7, −5.3; ES HRMS m/z (M + Na)$^+$ calcd 435.1928, obsd 435.1882; $[\alpha]^{18}_D$ −20 (c 0.20, C_2H_5OH).

Desilylation of 18a. A solution of **18a** (0.10 g, 0.25 mmol) in THF (20 mL) was treated with TBAF (1.25 mL of 1 M in THF, 1.25 mmol), stirred for 1 h, admixed with silica gel (0.05 g), and freed of solvent. The residue was placed atop a column of silica gel, and the product was eluted with ethyl acetate to give 0.02 g (50%) of **19a** as a white solid: mp 198−200 °C dec; ^{1}H NMR (300 MHz, CD_3OD) δ 7.82 (d, J = 8.1 Hz, 1 H), 5.93 (d, J = 7.0 Hz, 1 H),5.72 (d, J = 8.1 Hz, 1 H) 4.39 (dd, J = 7.0, 5.1 Hz, 1 H), 4.23 (d, J = 5.1 Hz, 1 H), 4.04 (t, J = 7.3 Hz, 1 H), 2.28−1.40 (series of m, 6 H) (3 OH and 1 NH not observed); ^{13}C NMR (125 MHz, CD_3OD) δ 166.1, 152.8, 142.6, 103.1, 96.6, 89.2, 78.9, 75.9, 71.7, 32.3, 30.7, 19.2; ES HRMS m/z (M + Na)$^+$ calcd 307.0901, obsd 307.0898; $[\alpha]^{18}_D$ −31 (c 0.5, C_2H_5OH).

Desilylation of 18b. Diol **18b** (60 mg, 0.15 mmol) was dissolved in THF (20 mL), treated with TBAF (1.25 mL of 1 M in THF, 1.25 mmol), stirred for 1 h, and processed in the predescribed manner to furnish 21 mg (50%) of **19b** as a white solid: mp 205−207 °C dec; ^{1}H NMR (500 MHz, CD_3OD) δ 7.88 (br s, 1 H), 7.65 (d, J = 1.1 Hz, 1 H), 5.91 (d, J = 7.1 Hz, 1 H), 4.40 (dd, J = 7.1, 5.2 Hz, 1 H), 4.22 (d, J = 5.2 Hz, 1 H), 4.05 (t, J = 7.4 Hz, 1 H), 2.40−2.30 (m, 1 H), 2.11−2.03 (m, 1 H), 1.89 (d, J = 1.1 Hz, 3 H), 1.75−1.65 (m, 3 H), 1.60−1.52 (m, 1 H) (3 OH not observed); ^{13}C NMR (125 MHz, CD_3OD) δ 166.3, 153.0, 138.3, 112.0, 96.3, 89.0, 78.9, 75.6, 71.6, 32.4, 30.7, 19.2, 12.4; ES HRMS m/z (M + Na)$^+$ calcd 321.1057, obsd 321.1061; $[\alpha]^{18}_D$ −11 (c 0.10, C_2H_5OH).

Bisulfide Lactone 20. Spirolactone **10** (5.00 g, 18.4 mmol) dissolved in dry THF (60 mL) was cooled to −78 °C, treated with lithium hexamethyldisilazide (45.0 mL of 1.0 M in THF, 45.0 mmol), and stirred for 1 h in the cold. After the introduction of phenyl benzenethiosulfonate (11.58 g, 47.2 mmol) as a solution in dry THF (40 mL), the reaction mixture was held at −78 °C for 3 h, allowed to warm to rt overnight, and quenched with saturated NH_4Cl solution (50 mL) prior to extraction with ether (3 × 100 mL). The combined organic phases were dried and concentrated to leave a residue that was purified by chromatography on silica gel (elution with 6% ether in hexane) to give **20** (7.74 g, 86%) as a colorless solid: mp 115.0−115.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73−7.64 (m, 4 H), 7.43−7.33 (m, 6 H), 3.61 (t, J = 7.1 Hz, 1 H), 2.64 (d, J = 14.3 Hz, 1 H), 2.17 (d, J = 14.3 Hz, 1 H), 2.09 (t, J = 9.3 Hz, 1 H), 1.83−1.69 (m, 3 H), 1.51−1.43 (m, 2 H), 0.86 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 136.4 (2C), 135.8 (2C), 131.1, 130.6, 130.0 (2C), 129.5 (2C), 129.0 (2C), 90.0, 77.4, 63.0, 42.8, 33.9, 30.2, 25.8 (3C), 18.2, 18.1, −4.4, −4.6; ES HRMS m/z (M + Na)$^+$ calcd 509.1616, obsd 509.1612; $[\alpha]^{20}_D$ −47.9 (c 1.09, $CHCl_3$).

Monophenylthio Lactones 21 and 22. To a solution of **20** (7.74 g, 15.8 mmol) in dry THF (100 mL) was added ethylmagnesium bromide (9.5 mL of 3.0 M in ether, 28.5 mmol) at −10 °C. After 2 h of stirring in the cold, the reaction mixture was quenched by the dropwise addition of saturated NH_4Cl solution (50 mL) and extracted with ether (3 × 100 mL). The combined organic layers were dried and concentrated to leave a residue that was purified by chromatography on silica gel. Elution with 4% ether in hexane provided **21** (3.75 g) and **22** (1.24 g) as colorless oils in a combined 83% yield.

For **21**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.50 (m, 2 H), 7.33−7.28 (m, 3 H), 4.18 (dd, J = 10.6, 9.3 Hz, 1 H), 3.83 (dd, J = 9.0, 7.4 Hz, 1 H), 2.53 (dd, J = 9.3, 9.0 Hz, 1 H), 2.20 (dd, J = 10.7, 12.0 Hz, 1 H), 1.86−1.78 (m, 4 H), 1.65−1.60 (m, 2 H), 0.83 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 132.9, 132.7 (2C), 129.1 (2C), 128.0, 90.7, 79.6, 46.4, 37.0, 33.1, 30.5, 25.7 (3C), 18.5, 17.8, −4.2, −5.1; ES HRMS m/z (M + Na)$^+$ calcd 401.1583, obsd 401.1588; $[\alpha]^{20}_D$ +26.2 (c 1.05, $CHCl_3$).

For **22**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.53 (m, 2 H), 7.35−7.29 (m, 3 H), 4.03 (t, J = 9.9 Hz, 1 H), 3.75 (t, J = 7.4 Hz, 1 H), 2.39 (dd, J = 13.0, 9.6 Hz, 1 H), 2.24 (dd, J = 13.0, 10.2 Hz, 1 H), 2.02−1.58 (series of m, 6 H), 0.86 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 133.0, 132.9 (2C), 129.4 (2C), 128.3, 91.1, 77.4, 46.4, 36.6, 33.8, 30.6, 26.1 (3C), 18.4, 18.3, −4.2, −4.4; ES HRMS m/z $(M + Na)^+$ calcd 401.1583, obsd 401.1595; $[\alpha]^{20}_D$ +19 (c 0.57, $CHCl_3$).

Equilibration of 22 with 21. A solution of **22** (1.34 g, 3.5 mmol) in THF (15 mL) was treated with DBU (0.05 mL, 0.3 mmol), stirred overnight at rt, diluted with 10% HCl (2 mL), and extracted with ethyl acetate (2 × 15 mL). The combined organic phases were washed with brine (3 mL), dried, and concentrated. Chromatography of the residue on silica gel (elution with 3% ether in hexanes) afforded **21** (1.10 g, 83%) in addition to unreacted **22** (0.15 g, 12%).

Reduction and Acetylation of 21. A solution of **21** (100 mg, 0.26 mmol) in dry CH_2Cl_2 (16 mL) was treated with Dibal-H (0.3 mL of 1 M, 0.30 mmol) at −78 °C, stirred at this temperature for 2 h, quenched with saturated Rochelle's salt solution (16 mL), and stirred overnight. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were dried and evaporated to provide the crude lactol that was immediately acetylated.

The above material was dissolved in pyridine (2 mL), treated with acetic anhydride (0.5 mL) at rt, stirred overnight, and evaporated to dryness under high vacuum. The residue was dissolved in ethyl acetate (10 mL), washed sequentially with saturated $CuSO_4$ solution (5 mL), water (5 mL), and brine (5 mL), dried, and concentrated. Purification of the residue by chromatography on silica gel (elution with 95:5 petroleum ether−ether) gave 38.7 mg (34%) of **23** and 43.7 mg (39%) of **24**, both as colorless oils.

For **23** (predominant anomer): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.38 (m, 2 H), 7.31−7.23 (m, 3 H), 6.22 (d, J = 1.7 Hz, 1 H), 3.90−3.85 (m, 1 H), 3.74−3.70 (m, 1 H), 2.37 (dd, J = 13.3, 7.6 Hz, 1 H), 2.25−1.50 (series of m, 10 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 134.3, 131.5 (2C), 128.9 (2C), 127.2, 102.4, 93.9, 78.1, 51.5, 37.3, 34.6, 30.8, 25.7 (3C), 21.3, 18.4, 18.1, −4.5, −4.7; ES HRMS m/z $(M + Na)^+$ calcd 445.1839, obsd 445.1814; $[\alpha]^{20}_D$ +28 (c 2.0, $CHCl_3$) (for the diastereomeric mixture).

For **24**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.44 (m, 2 H), 7.31−7.20 (m, 3 H), 4.24 (dd, J = 5.7, 1.1 Hz, 2 H), 3.76 (t, J = 6.9 Hz, 1 H), 3.68 (pent, J = 5.6 Hz, 1 H), 2.67 (s, 1 H), 2.02 (s, 3 H), 1.98−1.45 (series of m, 8 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 134.5, 132.1 (2C), 128.9 (2C), 127.1, 79.4, 78.6, 66.7, 43.1, 40.4, 35.3, 31.3, 25.8 (3C), 20.8, 19.4, 17.9, −4.3, −4.9; ES HRMS m/z $(M + Na)^+$ calcd 447.1996, obsd 447.1981; $[\alpha]^{19}_D$ +6.4 (c 2.9, $CHCl_3$).

Reduction of 21 with Minimized Overreduction. Treatment of a solution of **21** (50 mg, 0.13 mmol) and trimethylsilyl chloride (0.10 mL) in dry CH_2Cl_2 (8 mL) with Dibal-H (1.5 mL of 1 M in hexane, 0.15 mmol) at −78 °C was followed by application of the preceding procedure. There were isolated 32.1 mg (66%) of **23** and 2.2 mg (4%) of **24**.

General Glycosidation of 23 in CH_2Cl_2 Solution. The silylated base (1.0 mmol) and **23** (202 mg, 0.48 mmol) were dissolved in CH_2Cl_2 (2.5 mL), cooled to −78 °C, and treated with tin tetrachloride (1.9 mL of 1 M in CH_2Cl_2, 2 equiv). The reaction mixture was maintained at −78 °C for 15 min, allowed to warm to rt, quenched with saturated $NaHCO_3$ solution (3 mL), and extracted with CH_2Cl_2. The combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel (elution with 3:1 hexane−ether) to give the nucleoside.

For **25a**: 62.9 mg (22%) of the uridine and 36.2 mg (26%) of aldehyde **26**.

For **25b**: 30.1 mg (17%) of the thymidine and 66 mg (48%) of aldehyde **26**.

25a: colorless needles; mp 165.9−169.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 8.2 Hz, 1 H), 8.02 (br s, 1 H), 7.44−7.41 (m, 2 H), 7.28−7.23 (m, 3 H), 6.11 (d, J = 8.2 Hz, 1 H), 5.30 (dd, J = 2.1, 6.0 Hz, 1 H), 3.84 (dd, J = 2.3, 7.7 Hz, 1 H), 3.74 (dt, J = 7.5, 11.6 Hz, 1 H), 2.39−2.22 (m, 1 H), 2.17−2.08 (m, 1 H), 1.87−1.57 (series of m, 6 H), 0.93 (s, 9 H), 0.12 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 150.2, 140.8, 133.7 (2C), 132.2, 129.3 (2C), 128.4, 102.7, 89.8, 88.3, 80.3, 51.2, 38.1, 34.8, 30.7, 26.2 (3C), 18.4, 15.5, −4.2, −4.5; ES HRMS m/z $(M + Na)^+$ calcd 497.1901, obsd 497.1879; $[\alpha]^{19}_D$ +36 (c 0.71, $CHCl_3$).

25b: white solid; mp 167.2−168.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (br s, 1 H), 7.55 (d, J = 1.2 Hz, 1 H) 7.43−7.40 (m, 2 H), 7.24−7.22 (m, 3 H), 6.08 (d, J = 8.8 Hz, 1 H), 3.82 (t, J = 7.4 Hz, 1 H), 3.74−3.65 (m, 1 H), 2.35 (dd, J = 12.9, 7.4 Hz, 1 H), 2.09 (t, J = 12.9 Hz, 1 H), 1.85−1.53 (series of m, 6 H), 1.81 (d, J = 1.2 Hz, 3 H), 0.96 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 150.2, 135.3, 133.5 (2C), 132.2, 129.0 (2C), 128.1, 111.0, 88.7, 87.3, 79.9, 50.2, 37.7, 34.3, 30.2, 29.7, 26.0 (3C), 18.2, 12.2, −4.2, −4.7; ES HRMS m/z $(M + Na)^+$ calcd 511.2057, obsd 511.2055; $[\alpha]^{20}_D$ +44 (c 0.50, $CHCl_3$).

26: colorless oil; inseparable 4:3 mixture of diastereomers; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48−9.47 (m,1 H), 7.42−7.38 (m, 2 H), 7.31−7.24 (m, 3 H), 3.95 (td, J = 7.4, 3.0 Hz, 0.5 H), 3.76 (td, J = 7.5, 3.1 Hz, 0.5 H), 2.43−1.99 (series of m, 4 H), 1.86−1.73 (series of m, 2 H), 1.71−1.47 (series of m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 219.9, 219.7, 194.7, 194.4, 133.4 (2C), 133.3 (2C), 131.8, 131.4, 129.2 (4C), 128.5, 128.4, 55.1, 55.0, 46.4, 45.8, 37.8 (2C), 30.1, 29.9, 28.1, 27.7, 20.6, 20.5; HRMS m/z $(M + Na)^+$ calcd 271.0763, obsd 271.0762.

General Glycosidation of 23 in Acetonitrile Solution. The silylated base (1.4 mmol) and anomeric acetate **23** (300 mg, 0.71 mmol) were dissolved in dry acetonitrile (3.0 mL), cooled to −78 °C, treated with tin(IV) chloride (2.8 mL of 1 M in CH_2Cl_2, 2.8 mmol), allowed to warm to rt over the course of 4 h, and stirred overnight. The reaction mixture was quenched with saturated $NaHCO_3$ solution (6 mL), the aqueous phase was extracted with ethyl acetate (3 × 20 mL), and the combined organic layers were dried and freed of solvent. The residue was chromatographed on silica gel (elution with 4:3 ethyl acetate−hexane) to give 144 mg (56%) of **27a** or 179 mg (69%) of **27b**.

For **27a**: white solid; mp 187.2−190.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (br s, 1 H), 7.44−7.41 (m, 2 H), 7.33 (d, J = 8.1 Hz, 1 H), 7.27−7.24 (m, 3 H), 5.73 (d, J = 8.0 Hz, 1 H), 5.53 (dd, J = 8.1, 1.5 Hz, 1 H), 4.21−4.09 (m, 1 H), 3.90 (q, J = 7.3 Hz, 1 H), 2.55 (dd, J = 13.1, 7.9 Hz, 1 H), 2.09−1.92 (m, 3 H), 1.86−1.52 (series of m, 4 H)(OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 150.0, 141.7, 133.0 (2C), 131.9, 129.3 (2C), 128.3, 102.7, 93.8, 90.3, 78.1, 47.8, 38.7, 35.6, 31.4, 18.8; ES HRMS m/z $(M + Na)^+$ calcd 383.1036, obsd 383.1016; $[\alpha]^{19}_D$ +65 (c 0.53, $CHCl_3$−CH_3OH 1:1).

For **27b**: white solid; mp 201.1−202.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (br s, 1 H), 7.44−7.39 (m, 2 H), 7.26−7.22 (m, 3 H), 6.92 (d, J = 1.2 Hz, 1 H), 5.60 (d, J = 8.1 Hz, 1 H), 4.27 (dt, J = 10.6, 8.3 Hz, 1 H), 3.89 (q, J = 7.1 Hz, 1 H), 3.04 (d, J = 7.1 Hz, 1 H), 2.56 (dd, J = 13.0, 8.0 Hz, 1 H), 2.04−1.93 (m, 3 H), 1.75 (d, J = 1.2 Hz, 3 H), 1.74−1.52 (m, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 150.1, 137.7, 132.9 (2C), 132.1, 129.1 (2C), 128.1, 110.9, 94.9, 90.2, 78.1, 47.1, 38.7, 35.7, 31.4, 18.9, 12.3; ES HRMS m/z $(M + Na)^+$ calcd 397.1192, obsd 397.1163; $[\alpha]^{20}_D$ +12 (c 0.95, CH_3-OH−$CHCl_3$ 9:1).

For the diastereomer of **27b**: white solid; mp 117.4−119.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (br s, 1 H), 7.35 (d, J = 1.1 Hz, 1 H), 7.29−7.16 (m, 5 H), 6.33 (d, J = 5.1 Hz, 1 H), 4.42 (dt, J = 7.9, 5.0 Hz, 1 H), 3.77 (dd, J = 13.4, 6.6 Hz, 1 H), 2.69 (dd, J = 13.9, 7.9 Hz, 1 H), 2.28−2.22 (m, 1 H), 2.20−2.05 (m, 2 H), 1.96 (d, J = 1.1 Hz, 3 H), 2.02−1.56 (series of m, 4 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 149.8, 135.9, 133.5, 129.9 (2C), 128.9 (2C), 127.3, 109.4, 90.7,

86.9, 78.2, 49.3, 39.4, 35.5, 31.3, 19.0, 12.7; ES HRMS *m/z* (M + Na)$^+$ calcd 397.1192, obsd 397.1202.

Oxidative Elimination of 27a. A solution of **27a** (122 mg, 0.34 mmol) in $CHCl_3$ (10.0 mL) was treated at rt with the Davis oxaziridine (98 mg, 0.37 mmol), stirred for 4 h, concentrated under reduced pressure, and redissolved in pyridine (1 mL), diluted with xylene (4 mL), refluxed for 4 h, and freed of solvent. The residue was chromatographed on silica gel (elution with 1:1 hexane−ethyl acetate) to give **28a** (79.1 mg, 85%) as a white solid: mp 84.7−86.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (br s, 1 H), 7.68 (d, J = 8.1 Hz, 1 H), 7.09 (t, J = 1.5 Hz, 1 H), 6.26 (dd, J = 5.9, 1.9 Hz, 1 H), 5.75 (dd, J = 5.9, 1.3 Hz, 1 H), 5.69 (dd, J = 8.1, 1.4 Hz, 1 H), 4.03 (q, J = 7.2 Hz, 1 H), 2.32 (d, J = 9.4 Hz, 1 H), 2.12−2.05 (m, 1 H), 1.95−1.82 (m, 2 H), 1.76−1.58 (series of m, 2 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 151.0, 140.9, 139.1, 124.6, 102.4, 98.6, 89.1, 76.8, 34.9, 32.4, 19.0; $[\alpha]^{19}_D$ +24 (*c* 0.60, CH_3OH).

Oxidative Elimination of 27b. Entirely comparable treatment of **27b** (127 mg, 0.34 mmol) afforded 70 mg (78%) of **28b** as a white solid: mp 228.1−229.0 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (br s, 1 H), 7.46 (d, J = 1.2 Hz, 1 H), 7.10 (t, J = 1.5 Hz, 1 H), 6.26 (dd, J = 5.9, 1.9 Hz, 1 H), 5.74 (dd, J = 5.9, 1.2 Hz, 1 H), 4.08−4.00 (m, 1 H), 2.26 (d, J = 9.6 Hz, 1 H), 2.13−2.04 (m, 1 H), 1.95−1.72 (m, 2 H), 1.87 (s, 3 H), 1.70−1.57 (m, 2 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 150.9, 138.9, 136.4, 124.8, 110.9, 98.3, 88.9, 76.9, 34.9, 32.4, 19.1, 12.3; ES HRMS *m/z* (M + Na)$^+$ calcd 287.1002, obsd 287.1014; $[\alpha]^{20}_D$ +76 (*c* 0.92, $CHCl_3$).

Hydrogenation of 28a. A solution of **28a** (13.9 mg, 0.054 mmol) in ethanol (3 mL) was treated with 10% palladium on carbon (2.6 mg), stirred overnight under 50 psi of H_2 in a pressure reactor, and filtered through a pad of Celite (rinsed with 3 × 5 mL of methanol). Since reaction was incomplete, the sample was submitted two more times to the above protocol. The solvent was evaporated, and the residue was purified by chromatography on silica gel (elution with 3:2 ethyl acetate−hexane) to give 12.1 mg (89%) of **31a** as a white solid: mp 272.1−273.5 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74 (br s, 1 H), 7.82 (d, J = 7.5 Hz, 1 H), 6.17 (dd, J = 3.4, 2.1 Hz, 1 H), 5.74 (d, J = 7.2 Hz, 1 H), 3.94 (t, J = 7.0 Hz, 1 H), 2.52−1.57 (series of m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 150.4, 140.6, 102.3, 92.7, 85.7, 77.1, 34.8, 32.2, 31.8, 31.7, 18.7; ES HRMS *m/z* (M + Na)$^+$ calcd 275.1002, obsd 275.0994; $[\alpha]^{20}_D$ +17 (*c* 0.82, CH_3OH).

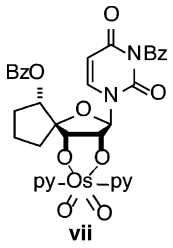
Hydrogenation of 28b. A solution of **28b** (15.8 mg, 0.060 mmol) in ethanol (3 mL) was hydrogenated similarly over 10% palladium on carbon (2.9 mg). Only one pass was necessary to deliver **31b** (14.6 mg, 92%) as a white solid: mp 172.3 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.5, 1.4 Hz, 2 H), 7.91 (dd, J = 8.5, 1.3 Hz, 2 H), 7.63 (t, J = 1.1 Hz, 1 H), 6.98 (t, J = 1.4 Hz, 1 H), 6.40 (dd, J = 5.9, 1.9 Hz, 1 H), 5.79 (dd, J = 5.9, 1.2 Hz, 1 H), 5.46 (t, J = 7.9 Hz, 1 H), 2.22−1.93 (m, 5 H), 1.77−1.74 (m, 1 H), 1.27 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 166.3, 150.1, 138.5, 135.7, 135.2, 133.8, 131.8, 130.7 (2C), 129.9 (2C), 129.8 (2C), 129.3 (2C), 128.9, 125.5, 111.2, 97.4, 89.1, 76.9, 35.6, 29.0, 19.0, 11.9; ES HRMS *m/z* (M + Na)$^+$ calcd 495.1527, obsd 495.1517; $[\alpha]^{20}_D$ −44 (*c* 0.87, $CHCl_3$).

Benzoylation of 28a and 28b. The spironucleoside (0.11 mmol) was dissolved in dry pyridine (4 mL), treated with benzoyl chloride (0.5 mL), and stirred overnight. The volatiles were removed, and the residue was dissolved in CH_2Cl_2 (30 mL) and washed with brine. The combined organic phases were dried and evaporated to leave a residue that was purified by chromatography on silica gel. Elution with 2:1 hexane−ethyl acetate gave **32a** (39 mg, 78%) as well as **32b** (47.2 mg, 91%).

For **32a**: pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (dd, J = 6.1, 1.1 Hz, 2 H), 7.91 (dd, J = 8.2, 1.2 Hz, 2 H), 7.66−7.61 (m, 2 H), 7.59−7.50 (m, 4 H), 7.45 (d, J = 1.9 Hz, 1 H), 6.97 (t, J = 1.5 Hz, 1 H), 6.34 (dd, J = 5.9, 1.9 Hz, 1 H), 5.78 (dd, J = 5.8, 1.3 Hz, 1 H), 5.49 (t, J = 8.0 Hz, 1 H), 5.22 (d, J = 8.2 Hz, 1 H), 2.21−1.42 (series of m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 166.5, 162.9, 150.1, 140.3, 138.5, 135.5, 134.2, 133.1, 130.9 (2C), 130.2 (2C), 130.1, 129.5 (2C), 129.1 (2C), 126.2, 102.8, 98.1, 89.4, 77.7, 35.6, 28.7, 19.1; ES HRMS *m/z* (M + Na)$^+$ calcd 481.1370, obsd 481.1371; $[\alpha]^{20}_D$ −25 (*c* 0.96, $CHCl_3$).

For **32b**: white solid; mp 161.2−162.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.2, 1.3 Hz, 2 H), 7.90 (dd, J = 8.3, 1.2 Hz, 2 H), 7.68−7.53 (m, 2 H), 7.51−7.42 (m, 4 H), 7.03 (d, J = 1.2 Hz, 1 H), 6.97−6.91 (m, 1 H), 6.39 (dd, J = 5.9, 2.0 Hz, 1 H), 5.80 (dd, J = 5.9, 1.3 Hz, 1 H), 5.45 (t, J = 7.9 Hz, 1 H), 2.22−1.93 (m, 5 H), 1.77−1.69 (m 1 H), 1.28 (d, J = 1.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 166.4, 162.8, 138.3, 135.5, 134.9, 133.5, 131.7, 130.6 (2C), 129.7 (2C), 129.6, 129.1 (2C), 128.5 (2C), 125.4, 111.4, 97.2, 88.9, 76.8, 35.4, 28.8, 18.9, 11.7; ES HRMS *m/z* (M + Na)$^+$ calcd 495.1527, obsd 495.1517; $[\alpha]^{20}_D$ −17 (*c* 0.92, $CHCl_3$).

Dihydroxylation of 32a. A 96.0 mg (0.209 mmol) sample of **32a** was dissolved in THF (12 mL) containing pyridine (3 mL) and treated with a solution of osmium tetraoxide (53.6 mg, 0.211 mmol) in pyridine (1 mL). After 18 h of stirring, the volatiles were removed under reduced pressure. This material was used directly. An analytical sample was purified by chromatography on silica gel (elution with hexane−ethyl acetate 1:1 to 100% ethyl acetate) to furnish the osmate ester **vii** as a brown oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 4 H), 8.11 (t, J = 8.0 Hz, 3 H), 7.95 (d, J = 7.5 Hz, 4 H), 7.61 (q, J = 7.2 Hz, 2 H), 7.56 (s, 4 H), 7.50 (t, J = 7.9 Hz, 2 H), 7.45−7.42 (m, 2 H), 6.45 (d, J = 4.9 Hz, 1 H), 6.05 (t, J = 2.8 Hz, 1 H), 5.65 (d, J = 8.2 Hz, 1 H), 5.23 (t, J = 5.4 Hz, 1 H), 4.89 (d, J = 6.0 Hz, 1 H), 2.21−1.50 (series of m, 6 H); ES HRMS *m/z* (M − py + Na)$^+$ calcd 816.1203, obsd 816.1218.



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The osmate ester was dissolved in THF (12 mL), and H_2S was bubbled through the solution for 15 min, during which time a black precipitate formed and TLC indicated the consumption of starting material. This mixture was purged with N_2 for 5 min, filtered through a pad of Celite, rinsed with ether, and concentrated. The residue was chromatographed on silica gel (elution with hexane−ethyl acetate 1:1) to give 21.7 mg (21%) of **33a** and 7.2 mg (7%) of **34a**.

For **33a**: white solid; mp 102.4−103.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 1.4 Hz, 2 H), 7.94 (d, J = 4.3 Hz, 1 H), 7.88 (dd, J = 7.2, 1.1 Hz, 2 H), 7.65−7.60 (m, 2 H), 7.47 (q, J = 8.2 Hz, 4 H), 6.03 (d, J = 4.3 Hz, 1 H), 5.71 (t, J = 6.9 Hz, 1 H), 5.52 (d, J = 8.3 Hz, 1 H), 4.49−4.44 (m, 1 H), 3.66 (d, J = 8.1 Hz, 1 H), 2.38−1.64 (series of m, 6 H) (neither OH observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 167.2, 163.0, 149.9, 141.6, 135.1, 131.5, 130.5 (2C), 127.8 (2C), 129.1 (2C), 128.7, 128.6 (2C), 100.8, 91.8, 84.8, 77.2, 74.5, 71.6, 35.2, 29.7, 29.2, 19.1; ES HRMS *m/z* (M + Na)$^+$ calcd 515.1424, obsd 515.1458; $[\alpha]^{20}_D$ +41 (*c* 0.53, $CHCl_3$).

For **34a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dd, J = 8.4, 1.4 Hz, 2 H), 7.92 (dd, J = 8.4, 1.3 Hz, 2 H), 7.64−7.56 (m, 2 H), 7.50−7.43 (m, 4 H), 6.82 (t, J = 1.6 Hz, 1 H), 6.24 (dd, J = 5.9, 2.0, 1 H), 5.94 (dd, J = 5.9, 1.2 Hz, 1 H), 5.45−5.38 (m, 2 H), 4.45 (d, J = 3.2 Hz, 1 H), 3.45 (br s, 1 H), 2.87 (br s, 1 H), 2.19−2.02 (m, 4 H), 1.85−1.75 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 167.2, 163.0, 149.7, 136.7, 134.9, 133.4, 130.5 (2C), 129.8, 129.7 (2C), 129.1 (2C), 128.7 (2C), 127.4, 126.0, 96.5, 88.9, 77.3, 73.3, 69.5, 34.6, 28.8, 9.1; ES HRMS *m/z* (M + Na)$^+$ calcd 515.1424, obsd 515.1417; $[\alpha]^{17}_D$ +78 (*c* 0.52, $CHCl_3$).

Dihydroxylation of 32b. A 94 mg (0.199 mmol) sample of **32b** was dissolved in THF (12 mL) containing pyridine (3 mL) and treated with a solution of osmium tetraoxide (51.1 mg, 0.201 mmol) in pyridine (1 mL). After 18 h of stirring, the volatiles were removed under reduced pressure. This osmate ester was dissolved in THF (12 mL), and H_2S was bubbled through the solution for 15 min, during which time a black precipitate formed and TLC indicated the consumption of starting material. This mixture was purged with N_2 for 5 min, filtered through a pad of Celite, rinsed with ether, and concentrated. The residue was chromatographed on silica gel (elution with hexane−ethyl acetate 1:1) to give 5.7 mg (6%) of **33b** and 25.1 mg (25%) of **34b**.

For **33b**: colorless gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 7.1 Hz, 2 H), 7.87 (d, J = 7.3 Hz, 2 H), 7.66−7.59 (m, 3 H), 7.46 (q, J = 7.7 Hz, 4 H), 6.00 (d, J = 5.0 Hz, 1 H), 5.75 (t, J = 6.3 Hz, 1 H), 4.51−4.49 (m, 1 H), 4.13−4.12 (m, 1 H), 3.76 (br d, J = 5.5 Hz, 1 H), 2.24 (br s, 1H), 2.23−2.01 (m, 3 H), 1.84−1.80 (m, 1H), 1.74 (s, 3H), 1.60−1.48 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 162.8, 150.0, 137.7, 134.9, 133.6, 131.6, 130.4 (2C), 129.8 (2C), 129.1 (2C), 128.6 (2C), 109.5, 91.7, 84.8, 77.2, 74.7, 71.6, 35.1, 29.7, 19.4, 12.2; ES HRMS m/z $(M + Na)^+$ calcd 529.1581, obsd 529.1566; $[\alpha]^{19}_D$ +27 (c 0.65, $CHCl_3$).

For **34b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 7.3 Hz, 2 H), 7.93 (d, J = 7.3 Hz, 2 H), 7.61−7.54 (m, 2 H), 7.45 (t, J = 7.7 Hz, 4 H), 6.83 (s, 1 H), 6.20 (dd, J = 5.9, 1.9 Hz, 1 H), 5.92 (d, J = 5.9 Hz, 1 H), 5.37 (t, J = 6.5 Hz, 1H), 5.13 (s, 1 H), 2.19−1.76 (series of m, 6 H), 2,03 (s, 3H) (2 OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 167.9, 166.5, 149.8, 135.7, 134.9, 133.3, 131.9, 130.4 (2C), 130.1 (2C), 129.1 (2C), 128.5 (2C), 128.4, 126.9, 96.2, 88.3, 77.6, 77.2, 72.7, 34.0, 28.2, 21.9, 18.5; ES HRMS m/z $(M + Na)^+$ calcd 529.1581, obsd 529.1600; $[\alpha]^{19}_D$ +44 (c 0.78, $CHCl_3$).

Saponification of 33a. A solution of **33a** (21.7 mg, 0.044 mmol) in methanol (10 mL) was saturated with NH_3 by bubbling ammonia gas into the solution for 1 h at rt. The reaction vessel was sealed with a rubber septum and allowed to stir for 12 h. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (elution with ethyl acetate) to give 12.0 mg (96%) of **35a** as a colorless gum: ^{1}H NMR (300 MHz, CD_3OD) δ 8.25 (d, J = 8.1 Hz, 1 H), 6.02 (d, J = 4.1 Hz, 1 H), 5.63 (d, J = 8.1 Hz, 1 H), 4.29 (t, J = 4.3 Hz, 1 H), 4.24−4.20 (m, 2 H), 2.17−1.56 (series of m, 6 H) (1 NH and 3 OH not observed); ^{13}C NMR (75 MHz, CD_3OD) δ 166.6, 152.3, 144.5, 100.6, 89.9, 86.2, 74.9, 73.1, 72.7, 35.3, 31.7, 19.8; ES HRMS m/z $(M + Na)^+$ calcd 307.0900, obsd 307.0913; $[\alpha]^{19}_D$ +39 (c 0.70, CH_3OH).

Saponification of 33b. A solution of **33b** (5.7 mg, 0.011 mmol) in methanol (5 mL) was saturated with NH_3 by bubbling ammonia gas into the solution for 1 h at rt. The reaction vessel was sealed with a rubber septum and allowed to stir for 12 h. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (elution with ethyl acetate) to give 3.3 mg (97%) of **35b**: ^{1}H NMR (300 MHz, CD_3OD) δ 8.14 (d, J = 1.1 Hz, 1 H), 6.04 (d, J = 4.0 Hz, 1 H), 4.30 (t, J = 4.3 Hz, 1 H), 4.26−4.23 (m, 2 H), 2.03−2.00 (m, 1 H), 1.90 (d, J = 1.1 Hz, 3 H), 1.88−1.85 (m, 4 H), 1.68−1.61 (m, 1 H) (1 NH and 3 OH not observed); ^{13}C NMR (125 MHz, CD_3OD) δ 165.7, 151.5, 139.4, 108.2, 92.1, 85.0, 74.0, 72.2, 71.7, 34.3, 30.8, 18.8. 11.5; ES HRMS m/z $(M + Na)^+$ calcd 321.1057, obsd 321.1068; $[\alpha]^{17}_D$ +31 (c 0.43, CH_3OH).

Oxidative Elimination of 25b. A solution of **25b** (0.12 g, 0.25 mmol) in $CHCl_3$ (10 mL) was treated with Davis oxaziridine (0.07 g, 0.27 mmol), stirred for 16 h, and quenched with water (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic phases were washed with 1 M HCl (10 mL), dried, and evaporated to leave the sulfoxide that was dissolved in toluene (100 mL) containing calcium carbonate (100 mg). The suspension was heated overnight at reflux, cooled, and filtered. The filtrate was washed with saturated $Na_2S_2O_4$ solution, dried, and evaporated to leave a residue that was chromatographed on silica gel. Elution with 3:1 hexanes−ethyl acetate furnished 0.09 g (100%) of **36** as a white foam: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (br s, 1 H), 7.70 (d, J = 1.1 Hz, 1 H), 6.83 (t, J = 1.4 Hz, 1 H), 6.05 (dd, J = 5.9, 1.9 Hz, 1 H), 5.91 (dd, J = 5.9, 1.1 Hz, 1 H), 4.06 (t, J = 7.1 Hz, 1 H), 2.07−1.70 (m, 9 H), 0.88 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 153.5, 136.6 (2 C), 127.1, 109.9, 98.8, 89.4, 77.2, 36.4, 33.7, 25.8 (3 C), 18.6, 18.3, 12.7, −4.3, −4.5; ES HRMS m/z $(M + Na)^+$ calcd 401.1867, obsd 401.1886.

Dihydroxylation of 36. To a solution of **36** (0.10 g, 0.26 mmol) in 8:1 acetone−water (6 mL) were added osmium tetraoxide (0.008 g, 0.032 mmol) and NMO (0.092 g, 0.80 mmol). The yellow reaction mixture was stirred for 24 h, quenched with saturated $Na_2S_2O_4$ solution, and agitated for a final 30 min. After extraction with ethyl acetate (3 × 5 mL), the combined organic layers were dried and evaporated. The residue was purified by chromatography on silica gel (elution with 1.5 hexanes−ethyl acetate) to give **37** (0.04 g, 36%) as a white solid: mp 122−123.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (br s, 1 H), 7.80 (d, J = 1.2 Hz, 1 H), 5.76 (d, J = 5.7 Hz, 1 H), 4.90 (br s, 1 H), 4.34 (t, J = 5.3 Hz, 1 H), 4.08 (d, J = 5.1 Hz, 1H), 3.96 (dd, J = 10.3, 7.2 Hz, 1 H), 3.24 (br s, 1 H), 2.08−1.61 (m, 9 H), 0.84 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 152.0, 136.6, 109.8, 96.6, 91.3, 77.6, 77.2, 74.8, 313, 29.2, 25.7 (3 C), 18.0, 17.9, 12.7, −4.5, −4.9; ES HRMS m/z $(M + Na)^+$ calcd 435.1922, obsd 435.1936.

Desilylation of 37. A solution of **37** (0.02 g, 0.05 mmol) in absolute ethanol (4 mL) was treated with pyridinium *p*-toluenesulfonate (0.02 g, 0.084 mmol) followed by one drop of concentrated HCl. The reaction mixture was heated overnight at 60 °C, cooled, admixed with silica gel (0.3 g), and freed of solvent under reduced pressure. The residue was loaded atop a column of silica gel. Elution with 9:1 ethyl acetate−methanol afforded 6 mg (60%) of **38** as a white solid: mp 254.5−257.5 °C dec; IR (CH_3CN, cm^{-1}) 3628, 3537, 1695, 1634; ^{1}H NMR (300 MHz, CD_3OD) δ 8.11 (d, = 1.2 Hz, 1H), 5.92 (d, J = 6.1 Hz, 1 H), 4.33 (dd, J = 5.8, 5.3 Hz, 1 H), 4.01 (d, J = 5.1 Hz,1 H), 3.91 (t, J = 8.0 Hz, 1 H) 2.09−1.54 (m, 9 H) (3 OH and NH protons not observed); ^{13}C NMR (75 MHz, CD_3OD) δ 166.6, 153.1, 139.5, 111.5, 94.8, 89.8, 77.2, 75.6, 74.5, 32.3, 31.1, 19.4, 12.6; ES HRMS m/z $(M + Na)^+$ calcd 321.1057, obsd 321.1037; $[\alpha]^{18}_D$ +12 (c 1.0, C_2H_5OH).

Generation of 40a from 12. The general glycosylation procedure for **12** was followed. From 0.30 g (0.71 mmol) of **12**, 0.28 g (1.1 mmol) of persilylated cytosine **39**, and 1.40 mL of 1 M $SnCl_4$ in CH_2Cl_2 was produced 0.23 g (67%) of **40a** (>97:3 β/α isomeric purity) after chromatography on silica gel (elution with benzene−ethyl acetate 1:1): colorless gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.38 (m, 2 H), 7.26 (d, J = 7.4 Hz, 1 H), 7.22−7.15 (m, 3 H), 6.18 (d, J = 7.6 Hz, 1 H), 5.79 (d, J = 7.4 Hz, 1 H), 4.01 (t, J = 6.4 Hz, 1 H), 3.61 (q, J = 8.0 Hz, 1 H), 2.75 (dd, J = 13.0, 7.9 Hz, 1 H), 1.98−1.25 (series of m, 7 H), 0.87 (s, 9 H), 0.06 (s, 6 H) (NH_2 protons not seen); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 155.9, 140.0, 133.0, 132.9 (2C), 129.0 (2C), 127.6, 95.6, 91.8, 88.8, 78.4, 51.1, 37.2, 35.8, 31.7, 25.8 (3C), 18.6, 17.9, −4.0, −4.7; ES HRMS m/z $(M + Na)^+$ calcd 496.2061, obsd 496.2046; $[\alpha]^{18}_D$ +20 (c 1.9, C_2H_5OH).

The above nucleoside (0.16 g, 0.34 mmol) was dissolved in CH_2Cl_2 (20 mL), treated with acetic anhydride (0.13 mL, 1.4 mmol), pyridine (0.28 mL, 3.4 mmol), and DMAP (8 mg − catalytic), and stirred for 1 h prior to quenching with saturated $NaHCO_3$ solution (30 mL). The product was extracted with ethyl acetate (3 × 15 mL), the combined organic phases were dried and evaporated, and the residue was chromatographed on silica gel. Elution with hexane−ether 1:2 furnished 0.16 g (89%) of **40a** as a white solid: mp 190−192 °C dec; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.33 (br s, 1 H), 7.72 (d, J = 7.6 Hz, 1 H), 7.43−7.22 (m, 6 H), 6.19 (d, J = 7.2 Hz, 1 H), 4.10 (t, J = 6.9 Hz, 1 H), 3.70 (q, J = 7.9 Hz, 1 H), 2.78 (dd, J = 13.1, 7.9 Hz, 1 H), 2.28 (s, 3 H), 2.05−1.40 (series of m, 7 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

171.5, 162.9, 155.0, 144.0, 133.0 (2C), 132.9, 129.1 (2C), 127.9, 97.2, 93.1, 89.9, 78.4, 52.0, 37.3, 35.8, 31.6, 25.9 (3C), 24.9, 18.5, 17.9, −4.0, −4.6; ES HRMS *m/z* $(M + Na)^+$ calcd 538.2166, obsd 538.2165; $[\alpha]^{18}_D$ +45 (*c* 2.8, $CHCl_3$).

Generation of 40b from 23. The general glycosidation procedure in acetonitrile was utilized to give **40b** in 70% yield as a white solid: mp 79.8−81.7 °C following chromatographic purification (elution with 2% CH_3OH in CH_2Cl_2): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.31 (br s, 1 H), 8.67 (d, J = 7.5 Hz, 1 H), 7.46−7.43 (m, 2 H), 7.30 (d, J = 7.5 Hz, 1 H), 7.27−7.21 (m, 3 H), 6.28 (d, J = 6.9 Hz, 1 H), 3.84 (t, J = 7.5 Hz, 1 H), 3.71 (dt, J = 7.1, 7.0 Hz, 1 H), 2.35 (dd, J = 13.1, 7.3 Hz, 1 H), 2.29 (s, 3 H), 2.10 (dd, J = 13.1, 9.4 Hz, 1 H), 1.99−1.57 (series of m, 6 H), 0.93 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 162.9, 155.2, 145.3, 133.3 (2C), 132.9, 129.0 (2C), 127.9, 97.0, 91.1, 88.7, 79.3, 53.0, 38.3, 34.7, 30.5, 25.9 (3C), 24.9, 18.2, 18.1, −4.5, −4.7; ES HRMS *m/z* $(M+Na)^+$ calcd 538.2166, obsd 538.2138; $[\alpha]^{20}_D$ +89.6 (*c* 1.32, $CHCl_3$).

Generation of 43 from 12. Into a solution of persilylated benzoyladenine **42** (0.11 g, 0.36 mmol) in dry acetonitrile (10 mL) was introduced neat $SnCl_4$ (0.11 mL, 0.96 mmol), and this mixture was stirred for 1 h before being slowly added to a −40 °C solution of **12** (0.10 g, 0.24 mmol) in the same solvent (15 mL). After 30 min, warming to rt was allowed to occur slowly and stirring was maintained for another 6 h prior to quenching with saturated $NaHCO_3$ solution (20 mL). The separated aqueous layer was extracted with ethyl acetate (3 × 15 mL), and the combined organic solutions were dried and evaporated. Chromatography of the residue on silica gel (elution with 1:1 benzene−ethyl acetate) furnished 60 mg (50%) of **43** as a colorless syrup: ^{1}H NMR (500 MHz, C_6D_6) δ 8.53 (br s, 1 H), 7.70−7.68 (m, 2 H), 7.27 (s, 1 H), 7.05−7.02 (m, 3 H), 6.95−6.92 (m, 3 H), 6.73−6.69 (m, 3 H), 5.54 (d, J = 8.0 Hz, 1 H), 5.04−5.00 (m, 1 H), 4.27 (t, J = 8.7 Hz, 1 H), 3.04 (dd, J = 12.6, 7.5 Hz, 1 H), 2.03−1.89 (m, 3 H), 1.59−1.51 (m, 1 H), 1.41−1.32 (m, 3 H) (OH not observed); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 152.0, 150.2, 143.0, 139.5, 133.0, 132.2 (2C), 131.8, 129.0 (2C), 128.9 (2C), 128.3, 128.0, 127.8 (2C), 94.1, 93.1, 78.0, 48.5, 38.5, 36.0, 28.6, 17.4 (C4 of adenine not observed); ES HRMS *m/z* $(M + Na)^+$ calcd 510.1577, obsd 510.1626; $[\alpha]^{19}_D$ −14 (*c* 0.30, $CHCl_3$).

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Supporting Information Available: Copies of the high-field ^{1}H NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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