Asymmetric Synthesis of C4′α-Carboxylated 2′-Deoxynucleosides. Preparation of Oxetanone Derivatives and Influence of Solvent on the Stereochemistry of Base Introduction

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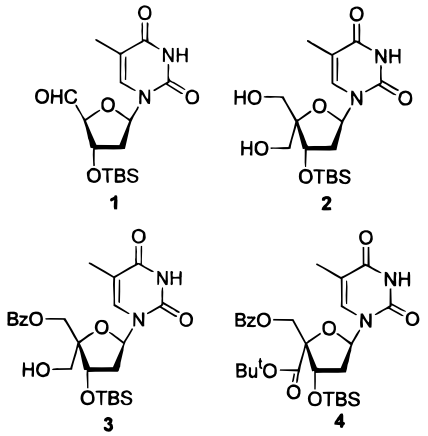
A synthesis of methyl 5-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-4α-methoxycarbonyl-2-deoxyribofuranoside from dimethyl L-tartrate is presented. Coupling of this substance with standard purine and pyrimidine bases, promoted by tin tetrachloride, provides the corresponding 4′α-methoxycarbonyl-nucleosides with moderate yield and selectivity. A series of related bicyclic donors, derived by forming a *β*-lactone between the 3-OH and the 4α-carboxy group, were prepared and assayed in coupling reactions. In nonpolar solvents good endo-selectivity is observed whereas in acetonitrile the exo-anomers are preferentially obtained. Methods for the removal of the 5′-*O*-benzyl ethers of the nucleosides are presented.

Introduction

C4′α-Homologated nucleotides, especially esters and ketones, are molecules of considerable current interest. One reason for this prominence arises from the ability of certain C4′α-ketones to block DNA polymerase and reverse transcriptase enzymes, such as the HIV-1 RT, and so their potential as antiviral agents.[1−4] Alternatively, the C4′α-selenol[5] and thiol esters[6] and the C4′α-*tert*-butylcarbonyl derivative[1] serve as convenient and unambiguous precursors to nucleotide C4′ radicals,[7] which are central to the degradation of oligonucleotides by bleomycin,[8,9] the enediyne antitumor antibiotics,[10,11] and ionizing radiation.[12] Nucleotide C4′ radicals are also key intermediates in DNA footprinting[13,14] and are convenient precursors to guanine radical cations.[15] The vast majority of work with these 2-deoxy-4′α-carbonyl-substituted nucleotides has been conducted with the thymidine series. Almost without fail, the synthesis[3,6,16,17] of these ramified thymidines can be traced back to original work by Jones on the Cannizzaro reaction of aldehyde **1** with formaldehyde giving the diol **2**.[18] The



reactivity profile of **2** is such that the α-OH is more readily protected than the *β*-OH,[19,20] which means that selective oxidation of the α-hydroxymethyl nucleoside **3** to the desired aldehyde or acid is typically preceded by a laborious three-step selective double-protection and mono-deprotection sequence.[3,6,16] This lengthy sequence, involving a minimum of nine steps from thymidine to a fully 3′,5′-protected 4′α-*tert*-butyloxycarbonylated system (**4**), is not readily applicable to the more sensitive purine nucleosides because of the necessary chromate oxidation step. This has the unfortunate consequence of limiting nucleoside and nucleotide C4′ chemistry and biochemis

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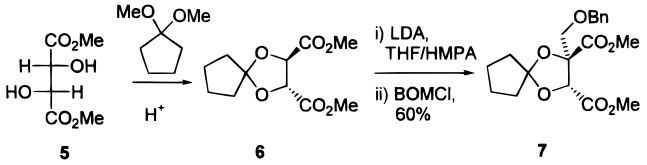
Scheme 1



try to the pyrimidine series. For a variety of reasons,[21] we are interested in studying C4′ homologues of the complete set of natural purine and pyrimidine nucleosides. Faced with the unattractive option of running through a greater than ten step sequence for each of the four DNA bases and with the need to develop much milder oxidizing conditions for the purine series, we opted instead to design and implement a de novo asymmetric synthesis. Ideally, this would have the flexibility to permit the incorporation of all bases, natural or unnatural, at an advanced stage, so providing a considerable economy of time and effort. Here, we describe in full the successful implementation of this design philosophy.[22] Additionally, we describe our attempts at using a β-lactone, formed by condensing the 3′-OH group with the 4′-acid, as a means of stereocontrol in the glycosidation step together with some interesting solvent effects in this coupling reaction.

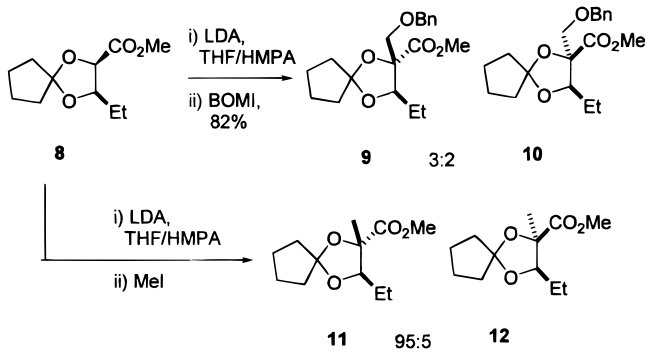
Results and Discussion

Retrosynthetic analysis pointed to L-tartaric acid as a cheap, readily available starting material, possessing the correct absolute stereochemistry, for the proposed synthesis. The dimethyl ester **5** was converted to the cyclopentylidene acetal **6**, on exposure to cyclopentanone dimethyl acetal and catalytic toluenesulfonic acid, in 90% yield. Taking advantage of Seebach's earlier demonstration that the alkylation of tartrate acetals takes place with retention of the configuration,[23] **6** was deprotonated with LDA in a mixture of THF and HMPA and the enolate quenched with freshly distilled benzyloxymethyl chloride (BOM-Cl). In this manner the monoalkylation product **7** could be isolated in 60% yield, as a single isomer (Scheme 1).

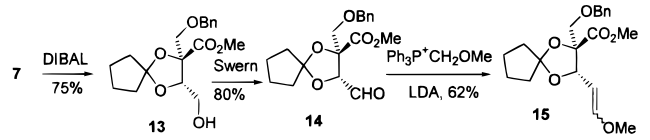
Hoffmann had earlier reported that the enolate derived from the related ester **8** was unreactive toward BOM-Cl but underwent alkylation with benzyloxymethyl iodide (BOM-I) to give a 3:2 mixture of diastereomers **9** and **10**. In contrast, he found that alkylation of **8** with methyl iodide gave a 95:5 mixture of diastereomers **11** and **12** (Scheme 2).[24] Evidently, the diastereoselectivity of such alkylations is a function of the alkylating agent with the more reactive ones being less selective. The stereochemistry of **7** was initially assigned by simple analogy with alkylations of diethyl tartrate acetonide conducted by the Seebach group; it was confirmed by subsequent steps in the synthesis as described below.

Controlled reduction of **7** with Dibal gave the alcohol **13** in 75% yield. This 4-hydroxy ester showed no tendency toward lactonization, which would have been the case for the stereoisomer, so providing strong support for the stereochemistry assigned to **7**. Swern oxidation then

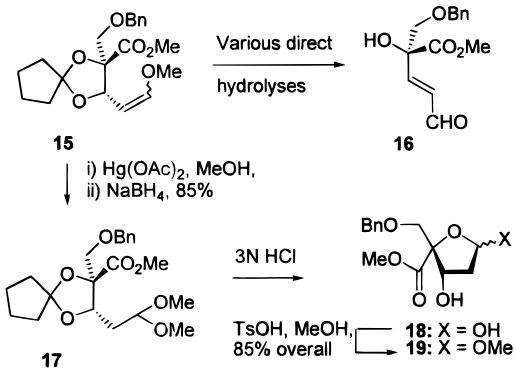
Scheme 2



Scheme 3



Scheme 4



afforded aldehyde **14** which was homologated using standard Wittig chemistry to give the enol ether **15**, a separable 1:1 mixture of *E*:*Z* isomers (Scheme 3).

Mild acid hydrolysis was expected to release the aldehyde and diol functions latent in **15**, followed by spontaneous cyclization to the furanose **18**. In the event, all such direct conversions assayed were marred by elimination and resulted in the formation of the α,β-unsaturated aldehyde **16**. After some experimentation we discovered, however, that **15** could be converted in excellent yield to the diacetal **17** by treatment with methanolic mercuric acetate followed by borohydride reduction. This species was then readily hydrolyzed to the desired ribofuranose **18** on exposure to 3 N HCl in THF. Crude **18** was converted to the methyl glycosides **19**, isolated in 85% overall yield from **17**, with methanolic TsOH (Scheme 4).

Silylation of **19** with TBDMSOTf gave **20**, which proved to be a suitable donor for coupling to the various bases. Thus, treatment of a room-temperature acetonitrile solution **20** with suitably protected forms of the four standard DNA bases and $SnCl_4$ as the promoter[25] provided the nucleosides in moderate-to-good yield as α:β mixtures (Scheme 5, Table 1). In each case the pairs of anomers were readily separated by chromatography over silica gel. In the guanosine series we also isolated minor amounts of both the α- and β-anomers of the *N*-7-

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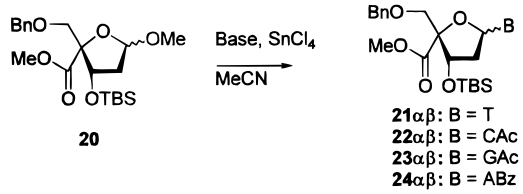
Scheme 5



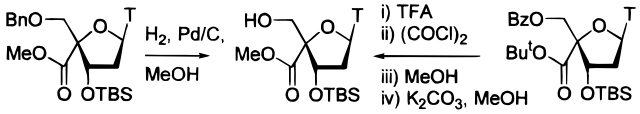
20

Table 1. Synthesis of Nucleosides from 20

base	product (% yield)	β:α[a]
T	**21** (70)	1:1
4-*N*-Ac−C	**22** (90)	5:7
2-*N*-Ac-G	**23** (83)	1:3
6-*N*-Bz-A	**24** (40)	1:1

[a] Anomeric ratios were determined by integrationof the ^{1}H NMR spectra of the crude reaction mixtures.

Scheme 6



21β **25** **26**

glycosylated isomers.[26] These were readily distinguished from the desired *N*-9 isomers by well-established spectroscopic methods.[26b,c,27]

NOE studies were largely inconclusive and ultimately the configuration of **21**β was confirmed by removal of the benzyl ether by hydrogenolysis over Pd/C, giving **25** (Scheme 6). This substance was found to be identical in every respect to an authentic sample obtained by debenzoylation and transesterification of **26**, which itself had been previously obtained from **2** via **3**.[6] This experiment, aside from establishing anomeric configuration, also nicely served to further confirm the stereochemical outcome of the initial alkylation (**6** → **7**). The anomeric configurations of **22**−**24**$\alpha\beta$ were assigned following close parallels in their ^{1}H NMR spectra with those of **21**$\alpha\beta$. Further supporting evidence for the configurational assignments in **22**−**24** was gleaned from specific rotations: at the sodium D line the β-anomers of the two pyrimidines (**21**β and **22**β) were found to be more dextrorotatory than their α-epimers, whereas the opposite was true for the two purines (**23**β and **24**β). This is exactly the pattern seen with the four natural DNA bases and their α-anomers.[28] It was also noted that all four β-anomers were eluting faster from silica gel than their α-isomers.

Although the above chemistry was satisfactory and met with our original objectives insofar as it provided a rapid asymmetric entry into the glycosyl donor **20** and subsequent introduction of both purine and pyrimidine bases, it was marred by the lack of selectivity in the final couplings. This is a very common problem in the area and is not seen as a major drawback coming as it does at the very end of the synthesis and giving readily separable anomers. However, the mixture of stereoisomers offended our sense of aesthetics and we resolved to search for a more selective coupling system. Premixing of the donor **20** with $SnCl_4$ prior to addition of the silylated heterocycle has been found to provide an element of stereocontrol in some systems,[29] but made little or no difference in the present instance. TMS iodide mediated coupling[30,31] of **20** with persilylated *N*-acetylcytosine in acetonitrile, followed by desilylation with the triethylamine−HF complex, was selective but in the wrong sense, giving the α-nucleoside **36**α in 45% overall yield. Replacement of TMSI as a mediator in this reaction by TMSOTf[32,33] gave a better yield (75%) but no selectivity (∼1:1). It was felt that more control would be gained by incorporating the glycosyl donor temporarily into a bicyclic system with stereodifferentiated concave and convex faces. Furthermore, it was felt that this might be achieved through the condensation of the 3′-OH with the 4′α-carboxylate group giving a β-lactone. 2-Oxetanones have a rich and interesting chemistry,[34−37] occur in natural products,[38] and have begun to be employed as intermediates in asymmetric synthesis.[39−41] However, we are not aware of any instances of their use as temporary control elements in the manner envisaged here. Of course, there is considerable literature covering the chemistry of the 3′,5′-anhydronucleosides,[42−45] but the oxetane is typically closed on a preformed nucleoside and does not appear to have been used as a stereocontrolling element in a coupling reaction. The anticipated use of the β-lactone function in turn required milder conditions for the actual glycosylation. To this end we elected to investigate Fraser−Reid's pentenyl glycosides,[46,47] thioglycosides, and Kahne's sulfoxide method.[48,49]

Three bicyclic glycosyl donors were prepared as outlined in Scheme 7. Thus, furanose **18** was condensed with 4-pentenol to give the pentenyl glycoside **27**, saponfication of which gave the acid **28**. Dehydration of this acid

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Scheme 7

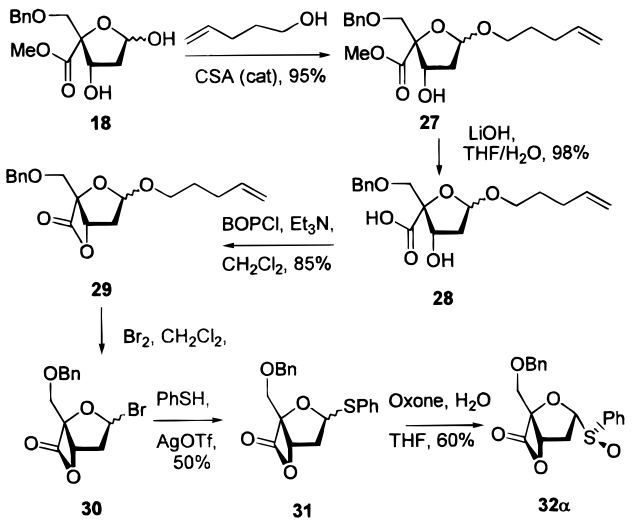
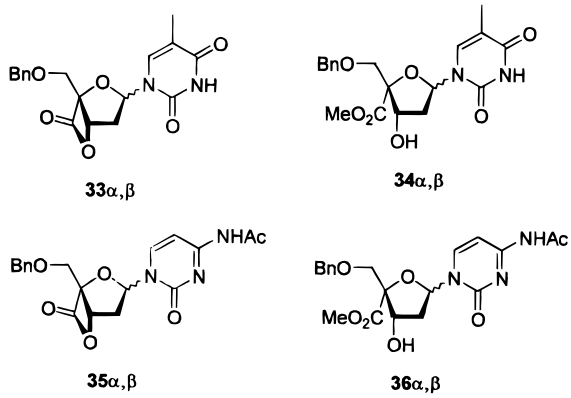


Table 2. Synthesis of Bicyclic Nucleosides

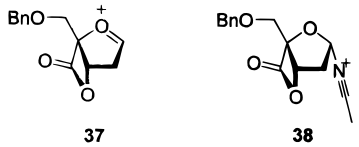
entry	substrate	base	activator	solvent	temp (°C)	product	% yield	β:α ratio
1	**29**	T	NIS/TfOH	MeCN	rt	**33**	47	5:1
2	**29**	T	NIS/TfOH	CH_2Cl_2	rt	**33**	50	1:1
3	**30**	T	AgOTf	MeCN	rt	**33**	40	5:1
4	**30**	T	AgOTf	CH_2Cl_2	rt	**33**	40	1:1
5	**30**	T	AgOTf	benzene	rt	**33**	45	<1:10
6	**32**α	T	Tf_2O	$MeCH_2CN$	−78	**33**	38	5:1
7	**32**α	T	Tf_2O	CH_2Cl_2	−78	**33**	<5	
8	**32**α	T	Tf_2O	toluene	−78	**33**	<5	
9	**29**	C^{Ac}	NIS/TfOH	MeCN	rt	**35**	40	3:1
10	**30**	C^{Ac}	AgOTf	MeCN	rt	**35**	30	3:1
11	**31**	C^{Ac}	NBS	CH_2Cl_2	rt	**35**	50	<1:10

with BOP-Cl[50] gave the β-lactone **29** in 85% yield. The formation of β-lactone **29**, as a stable entity enshrined within a bicyclo[3.2.0]heptane framework, provides the final and incontrovertible proof of the relative configuration of **7** (Scheme 1). Activation of **29** with bromine in dichloromethane provided the unstable bromide **30** which was converted to the thioglycosides **31** in 50% overall yield. We note in passing that the β-lactone moiety was stable to these Lewis-acid-promoted coupling reactions but that any exposure to thiophenol in the presence of a base inevitably resulted in opening to the thioester. Finally, oxidation of **31**α with oxone provided sulfoxide **32**α in 60% yield as a single diastereomer, which we tentatively assign S_R on the basis of related oxidations of α-thioglycosides in the pyranose series.[51]

Coupling of **29** with persilylated thymine in acetonitrile solution with activation by the NIS/TfOH couple resulted in a 47% isolated yield of a 5:1 β:α-anomers of **33** (Table 2, entry 1). Changing the solvent to dichloromethane afforded a similar yield of **33** but with only 1:1 selectivity (Table 2, entry 2). In situ generation of bromide **30** followed by AgOTf mediated coupling to persilylated thymine gave yields in the range 40−45% with selectivities ranging from 5:1 β:α to almost exclusively α, depending on the solvent (Table 2, entries 3−5). Activation of sulfoxide **32**α with Tf_2O at −78 °C in propionitrile followed by coupling with thymine again afforded a 5:1 mixture of β:α-anomers of **33** (Table 2, entry 6). Unfortunately, attempted coupling of **32** to thymine in dichloromethane or toluene solution resulted in complex reaction mixtures. The configurations of the two anomers of **33** were assigned by opening of the β-lactone with methanol, giving **34** and subsequent comparison to authentic samples obtained by desilylation of **21**. Less experiments were conducted with persilylated *N*-acetyl cytosine as the glycosyl acceptor but the results were similar to those obtained with thymine; the yields were moderate and the selectivities solvent dependent with acetonitrile favoring the β-anomer and dichloromethane the α-anomer (Table 2, entries 9−11). The stereochemistry of **35** was assigned similarly to that of **33** by conversion to **36**, which was independently accessible from **22**. All attempts at coupling any of the donors **29**−**32** with *N*-benzoyladenine or with *N*-acetylguanine unfortunately resulted in complex mixtures from which pure coupled products were not isolated.



The solvent effects on stereoselectivity observed with donors **29**−**32** suggest that, contrary to our initial expectation, an intermediate oxacarbenium ion **37** is attacked preferentially from the endo- (or α-) face in dichloromethane or benzene. The reversal of selectivity



in acetonitrile, or propionitrile, is then explained by a parallel endo-attack by the solvent to form the nitrilium ion **38**, which serves as an electrophile in a final S_N2-like displacement. Whatever the reason for the change in selectivity, it is clear that the fused β-lactone does not have the strong exo-biasing effect on stereochemistry that we had anticipated. It is evidently oversimplistic to make predictions on the stereoselectivity of reactions of fused bicyclic systems based uniquely on the concept of exo- and endo-surfaces as we,[52,53] and others,[23,54,55] have previously found in bicyclo[3.3.0]octane-type skeletons. At the very least the 5′-carbon, on the exo-surface, needs to be taken into consideration in the present system. Whatever the reason, the β-selectivities observed in

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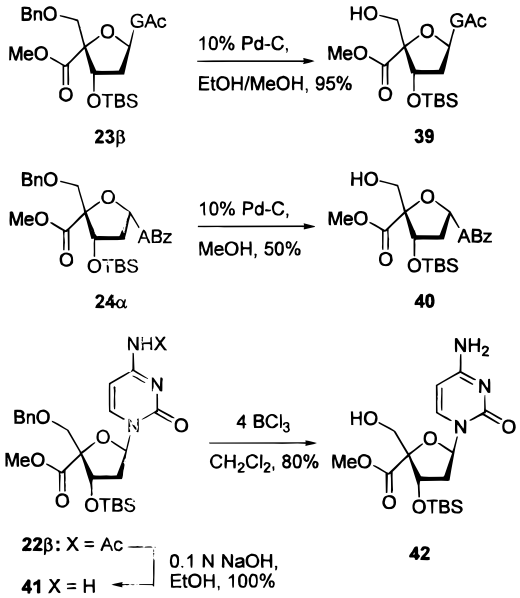
Scheme 8



coupling the pyrimidine bases to the various β-lactone donors in acetonitrile (Table 2) are superior to those obtained with the monocyclic donor **20** in the same solvent (Table 1).

Finally, we turned our attention to the removal of the 5′-*O*-benzyl ether, a somewhat unorthodox protecting group in nucleoside and nucleotide chemistry. As already noted in Scheme 6 standard hydrogenolytic cleavage is affected cleanly in the thymidine series. This was also the case with the β-guanosine (**23**β) and α-adenosine (**24**α) systems inspected (Scheme 8). However, attempted hydrogenolysis of the various cytidine derivatives resulted in competing reduction of the base, whether using hydrogen gas or cyclohexadiene in a transfer system.[56] Eventually conditions were discovered (Scheme 8) for satisfactory removal of the 5′-*O*-benzyl ether in the cytidine series involving initial saponification of the labile *N*-acetyl group followed by treatment with BCl_3.

Experimental Section

General. Unless otherwise stated NMR spectra were taken at 300 MHz (^{1}H) or 75 MHz (^{13}C) for $CDCl_3$ solutions. Chemical shifts are in ppm downfield from tetramethylsilane as the internal standard. Specific rotations were measured for chloroform solutions. All solvents were dried and degassed according to standard procedures. Microanalyses were conducted by Midwest Microlabs, Indianapolis, IN.

Dimethyl 2,3-*O*-Cyclopentylidene-L-tartrate (6). A mixture of dimethyl L-tartrate (**5**) (50 g, 0.28 mol), 1,1-dimethoxycyclopentane (60 g, 0.46 mol), and *p*-toluenesulfonic acid monohydrate (0.84 g, 4.4 mmol) was dissolved in benzene (500 mL) and refluxed for 12 h. After the resulting solution was cooled to room temperature, EtOAc (1 L) was added. The resulting solution was washed with saturated $NaHCO_3$, brine, and dried. Removal of the solvent followed by distillation (95 °C/2 mmHg) gave **6** as a colorless oil (57.8 g, 90%). $[\alpha]_D^{20}$ −38.4° (*c*, 4.2). ^{1}H NMR δ: 1.68−1.74 (m, 4 H), 1.81−1.91 (m, 4 H), 3.81 (s, 6 H), 4.76 (s, 2 H). ^{13}C NMR δ: 23.1, 36.2, 52.4, 76.5, 123.0, 169.7. Anal. Calcd. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 53.97; H, 6.71.

2*R*,3*R*-2-Benzyloxymethyl-2,3-bis(methoxycarbonyl)-1,4-dioxaspiro[4.4]nonane (7). To a stirred solution of **6** (24.4 g, 0.10 mol) and benzyl chloromethyl ether (37.5 g, 0.23 mol) in THF (0.5 L) and HMPA (100 mL) at −78 °C under Ar was added lithium diisopropylamide via cannula in THF (500 mL) for 1 h. [The LDA was generated from diisopropylamine (18.4 mL, 0.13 mol) and 2.5 M *n*-butyllithium (42 mL, 0.11 mol) at −78 °C for 30 min.] The mixture was stirred at −78 °C under Ar overnight and then warmed slowly to −5 °C. EtOAc (1.5 L) was added and the organic layer was washed with water and brine and then dried. Evaporation of the solvent followed by distillation (80−100 °C/1 mmHg) removed most of the starting materials and benzyl alcohol. The residue was purified by column chromatography on silica gel (eluent: EtOAc/Hexane, 1/7−1/5). **7** was obtained as a colorless oil (16.4 g, 60% based on recovered starting material 6.1 g). $[\alpha]_D^{20}$ −34.0° (*c* 2.8). ^{1}H NMR δ: 1.68−1.89 (m, 6 H), 1.96−2.06 (m, 6 H), 2.10−2.17 (m, 1 H), 3.63 (s, 3 H), 3.72 (s, 2 H), 3.85 (s, 3 H), 4.50 (s, 2 H), 5.01 (s, 1 H), 7.25−7.34 (m, 5 H). ^{13}C NMR δ: 22.9, 23.8, 36.7 (2 × C), 52.2, 52.9, 69.7, 73.6, 77.3, 84.8, 122.1, 127.4 (2 × C), 137.4, 168.6, 170.6. Anal. Calcd. for $C_{19}H_{24}O_7$: C, 62.63, H, 6.64. Found: C, 62.96, H, 6.66.

2*R*,3*S*-2-Benzyloxymethyl-3-hydroxymethyl-2-methoxycarbonyl-1,4-dioxaspiro[4.4]nonane (13). To a stirred solution of **7** (10 g, 27.5 mmol) in THF (250 mL) at −78 °C was added dropwise 1.5 M DIBAL-H in toluene (27.5 mL, 41.3 mmol) and then the reaction was warmed to 0 °C slowly and stirred at this temperature for 1 h. The reaction was quenched with 2 M HCl and diluted with EtOAc (0.5 L). The organic extracts were separated, washed, and dried. Removal of the solvent followed by column chromatography (eluent: EtOAc/Hexane, 3/1) gave **13** as a colorless oil (5 g, 75% based on 2.8 g of recovered starting material.). $[\alpha]_D^{20}$ −11.3 (*c*, 0.9). ^{1}H NMR δ: 1.65−1.94 (m, 8 H), 3.68 (dd, J = 22.1, 9.5 Hz, 2 H), 3.82 (s, 3 H), 3.82−3.92 (m, 2 H), 4.40 (t, J = 5.4 Hz, 1 H), 4.55 (dd, J = 15.2, 12.2 Hz, 2 H), 7.26−7.35 (m, 5 H). ^{13}C NMR δ: 23.0, 24.0, 36.4, 37.0, 52.6, 60.3, 70.1, 73.6, 79.4, 83.3, 119.8, 127.6 (2 × C), 127.8, 128.3 (2 × C), 137.1, 171.7. Anal. Calcd. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 63.97; H, 7.25.

2*R*,3*R*-2-Benzyloxymethyl-2-methoxycarbonyl-1,4-dioxaspiro[4.4]nonane-3-carboxaldehyde (14). To a well-stirred solution of anhydrous dichloromethane (580 mL) at −78 °C was added oxalyl chloride (16.1 mL, 0.18 mol). After 15 min, anhydrous DMSO (24.1 mL, 0.34 mol) was added dropwise. After the mixture stirred for 15 min, **13** (21.74 g, 64.7 mmol) in anhydrous dichloromethane (72 mL) was added followed by diisopropylethylamine (57 mL, 0.33 mol, after additional 30 min). The reaction mixture was allowed to warm to room temperature, water (300 mL) was added, and the organic layer was washed and dried. Removal of solvent followed by column chromatography gave **14** as a colorless oil (16 g, 80%). $[\alpha]_D^{20}$ −15.5° (*c*, 3.1). ^{1}H NMR δ: 1.69−1.86 (m, 6 H), 2.01−2.06 (m, 2 H), 3.66 (dd, J = 9.2, 5.7 Hz, 2 H), 3.82 (s, 3 H), 4.46 (dd, J = 16.3, 12.0 Hz, 2 H), 4.79 (s, 1 H), 7.24−7.36 (m, 5 H), 9.68 (s, 1 H). ^{13}C NMR δ: 23.1, 24.1, 36.8, 36.9, 53.3, 69.2, 73.6, 83.0, 85.9, 122.3, 127.8 (2 × C), 128.0, 128.6 (2 × C), 137.3, 170.7, 197.0. Anal. Calcd. for $C_{18}H_{22}O_6 \cdot H_2O$: C, 61.35; H, 6.86. Found: C, 61.62; H, 6.49.

2*R*,3*S*-2-Benzyloxymethyl-3-(*E*/*Z*-2-methoxyvinyl)-2-methoxycarbonyl-1,4-dioxaspiro[4.4]nonane (15). To a stirred suspension of methoxymethyltriphenylphosphonium chloride (4.31 g, 12.6 mmol) in THF (150 mL) at 0 °C was added lithium diisopropylamide via cannula in THF (150 mL) [LDA was generated from diisopropylethylamine (2.15 mL, 15.3 mmol) and 2.5 M *n*-butyllithium in hexane (5 mL, 12.5 mmol) at −78 °C for 30 min]. The mixture was stirred at 0 °C for 30 min before **14** (2.0 g, 6.0 mmol) in THF (150 mL) was added via cannula. After stirring at 0 °C for 30 min, the reaction mixture was poured into water (0.5 L) and extracted with EtOAc. The combined organic layers were dried, and removal of the solvent, followed by column chromatography (eluent: EtOAc/hexane, 1/3), gave two isomeric vinyl ethers

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15-*E* (0.7 g) and **15-*Z*** (0.65 g) as colorless oils (overall yield 62%). For **15-*E***: $[\alpha]_D^{20}$ −9.7° (*c*, 3.3). ^{1}H NMR *δ*: 1.68−2.05 (m, 8 H), 3.54 (s, 3 H), 3.64 (dd, *J* = 47.3, 9.7 Hz, 2 H), 3.77 (s, 3 H), 4.53−4.57 (m, 3 H), 4.75 (dd, *J* = 12.6. 9.1 Hz, 1 H), 6.63 (d, *J* = 12.5 Hz, 1 H), 7.26−7.35 (m, 5 H). ^{13}C NMR *δ*: 23.0, 23.9, 36.4, 37.3, 52.1, 56.1, 71.3, 73.4, 79.4, 84.6, 95.9, 119.6, 127.5 (3 × C), 128.2 (2 × C), 137.8, 152.6, 172.0. Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23; Found: C, 65.83; H, 7.17. For **15-*Z***: $[\alpha]_D^{20}$ +13.4° (*c* 2.4, $CHCl_3$). ^{1}H NMR *δ*: 1.67−2.02 (m, 8 H), 3.54 (d, *J* = 9.7 Hz, 1 H), 3.62 (s, 3 H), 3.75−3.78 (m, 4 H), 4.43 (dd, *J* = 9.5, 6.3 Hz, 1 H), 4.58 (dd, *J* = 16.7, 12.7 Hz, 2 H), 5.15 (d, *J* = 9.5 Hz, 1 H), 6.13 (d, *J* = 6.3 Hz, 1 H), 7.30 (s, 5 H). ^{13}C NMR *δ*: 23.1, 23.9, 36.5, 37.4, 52.3, 60.1, 71.2, 73.4, 73.9, 84.7, 99.0, 119.9, 127.4 (3 × C), 128.1 (2 × C), 138.0, 151.0, 172.0. Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.41; H, 7.24.

2*S*-Methyl 2-Benzyloxymethyl-2-hydroxy-5-oxa-3-*E*-pentenoate (16). To a stirred solution of **15** (36 mg, 0.1 mmol) in dichloromethane (1 mL) were added trifluoroacetic acid (0.5 mL) and water (0.05 mL). The reaction mixture was stirred at room temperature for 1 h and then the reaction quenched with saturated $NaHCO_3$ solution. The organic layer was separated, washed, and dried. Removal of the solvent followed by column chromatography (eluent: EtOAc/Hexane, 2/1) gave **16** as a white crystalline solid (21 mg, 80%). $[\alpha]_D^{20}$ −18.1° (*c*, 1.9). ^{1}H NMR *δ*: 3.50 (d, *J* = 9.5 Hz, 1 H), 3.76 (s, 1 H), 3.84−3.89 (m, 4 H), 4.60 (dd, *J* = 31.8, 12.2 Hz, 2 H), 6.55 (dd, *J* = 15.6, 7.7 Hz, 1 H), 6.80 (d, *J* = 15.6 Hz, 1 H), 7.26−7.39 (m, 5 H), 9.59 (d, *J* = 7.7 Hz, 1 H). ^{13}C NMR *δ*: 53.6, 73.6, 74.1, 78.3, 127.2 (2 × C), 127.9, 128.4 (2 × C), 132.9, 137.1, 150.9, 171.6, 192.5. Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.27; H, 6.14.

2*R*,3*S*-2-Benzyloxymethyl-3-[2,2-di(methoxy)ethyl]-2-methoxycarbonyl-1,4-dioxaspiro[4.4]nonane (17). To a stirred solution of **15** (3.62 g, 10 mmol) in methanol (50 mL) was added mercuric acetate (3.50 g, 11 mmol). Stirring was continued at room temperature until no more starting material was detectable by TLC, then the reaction mixture was cooled to 0 °C, and $NaBH_4$ (0.42 g, 11 mmol) was added in portions. After addition, the suspension was stirred at 0 °C for 30 min and at room temperature for 30 min. The reaction mixture was decanted and the residue was washed with additional solvent. The combined organic solutions were concentrated and the residue was partitioned between dichloromethane and water. The organic layer was separated, washed, and dried. Removal of the solvent followed by column chromatography (eluent: EtOAc/Hexane, 1/1) gave **17** as a colorless oil (3.23 g, 85%). $[\alpha]_D^{20}$ −13.9° (*c*, 2.6). ^{1}H NMR *δ*: 1.63−2.11 (m, 10 H), 3.32 (s, 3 H), 3.33 (s, 3 H), 3.52 (d, *J* = 9.3 Hz, 1 H), 3.72 (d, *J* = 10.6 Hz, 1 H), 3.76 (s, 3 H), 4.22 (dd, *J* = 10.6, 2.7 Hz, 1 H), 4.50−4.61 (m, 3 H), 7.26−7.35 (m, 5 H). ^{13}C NMR *δ*: 23.4, 24.2, 32.2, 36.8, 37.5, 52.7, 53.6, 70.7, 73.7, 78.3, 84.0, 102.0, 119.8, 127.8 (3 × C), 128.5 (2 × C), 137.9, 171.9. HRMS Calcd for $C_{21}H_{30}O_7$: 394.1992. Found: 394.1996 ($M^{+\cdot}$).

Methyl 5-*O*-Benzyl-2-deoxy-4α-methoxycarbonyl-α,*β*-D-*ribo*-pentofuranoside (19α,*β*). To a solution of **17** (0.9 g, 2.4 mmol) in THF (50 mL) was added 3 M HCl (50 mL). The mixture was stirred at room temperature for 6 h and then extracted with EtOAc. The combined organic layers were washed and dried. Removal of the solvent gave a colorless oil, which was placed in a 100 mL flask with methanol (50 mL) and *p*-toluenesulfonic acid (0.1 g). This reaction mixture was stirred at room temperature for 3 h, before it was poured into saturated $NaHCO_3$ solution (50 mL), and extracted with dichloromethane (3 × 60 mL). The combined organic layers were dried and concentrated in vacuo to leave an oil. Column chromatography gave **19**α (0.43 g) and **19***β* (0.15 g) as colorless oils (yield: 85%). For **19**α: $[\alpha]_D^{20}$ −42.0° (*c*, 2.7). ^{1}H NMR *δ*: 2.14−2.28 (m, 2 H), 2.62 (d, *J* = 4.6 Hz, 1 H), 3.38 (s, 3 H), 3.63 (d, *J* = 9.8 Hz, 1 H), 3.80 (s, 3 H), 3.83 (d, *J* = 9.9 Hz, 1 H), 4.47 (dd, *J* = 11.1, 6.4 Hz, 1 H), 4.60 (dd, *J* = 15.3, 12.4 Hz, 2 H), 5.27 (dd, *J* = 5.0, 2.8 Hz, 1 H), 72.8−7.36 (m, 5 H). ^{13}C NMR *δ*: 40.5, 52.8, 55.7, 73.2, 73.8, 74.2, 90.2, 105.6, 127.9 (3 × C), 128.4 (2 × C), 138.0, 171.5. Anal. Calcd. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.53; H, 6.76. For **19***β*: $[\alpha]_D^{20}$ +107.3° (*c*, 1.6). ^{1}H NMR *δ*: 2.04−2.09 (m, 1 H), 2.24 (dt, *J* = 13.5, 4.9 Hz, 1 H), 3.22 (d, *J* = 11.4 Hz, 1 H), 3.54 (s, 3 H), 3.64 (d, *J* = 9.9 Hz, 1 H), 3.71−3.77 (m, 4 H), 4.19 (dd, *J* = 11.3, 5.3 Hz, 1 H), 4.56 (dd, *J* = 14.8, 12.3 Hz, 2 H), 5.25 (d, *J* = 4.4 Hz, 1 H), 7.26−7.36 (m, 5 H). ^{13}C NMR *δ*: 41.0, 52.1, 55.2, 72.5, 73.5, 75.0, 93.3, 106.6, 127.5 (2 × C), 127.6, 128.3 (2 × C), 137.6, 170.5. Anal. Calcd. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.70; H, 6.76.

Methyl 5-*O*-Benzyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4α-methoxycarbonyl-α,*β*-D-*ribo*-pentofuranoside (20α). To a stirred solution of **19**α (633 mg, 2.1 mmol), and 2,6-lutidine (0.54 mL, 4.6 mmol) in dichloromethane (5 mL) at room temperature was added TBDMSOTf (0.61 mL, 2.7 mmol) dropwise. After 1 h, the reaction mixture was poured into brine and diluted with dichloromethane. The organic layer was separated, washed, and dried. Removal of the solvent followed by column chromatography (eluent: EtOAc/Hexane, 1/7) gave **20**α as a colorless oil (840 mg, 96%). $[\alpha]_D^{20}$ −25.9° (*c*, 2.7). ^{1}H NMR *δ*: 0.015 (s, 3 H), 0.021 (s, 3 H), 0.83 (s, 9 H), 2.13−2.19 (m, 2 H), 3.38 (s, 3 H), 3.63 (d, *J* = 10.2 Hz, 1 H), 3.72 (s, 3 H), 3.92 (d, *J* = 10.2 Hz, 1 H), 4.45 (t, *J* = 71. Hz, 1 H), 4.63 (s, 2 H), 5.28−5.30 (m, 1 H), 7.28−7.34 (m, 5 H). ^{13}C NMR *δ*: −5.1, −4.8, 17.9, 25.7 (3 × C), 41.2, 52.1, 55.4, 72.3, 73.8, 73.9, 90.3, 105.4, 127.6, 127.8 (2 × C), 128.4 (2 × C), 138.4, 170.6. Anal. Calcd for $C_{21}H_{34}O_6Si$: C, 61.43; H, 8.35. Found: C, 61.50; H, 8.42.

General Method for the Coupling Reaction between 20 and Bases. Properly protected base (2.2 equiv) in freshly distilled acetonitrile under Ar was stirred with *N*,*O*-bis-(trimethylsilyl)-acetamide at 80 °C for 30 min. The reaction mixture was cooled to 0 °C and **20** (1.0 equiv) and $SnCl_4$ (10 equiv) were added. The reaction mixture was then stirred at room temperature until the disappearance of **20**. The reaction was diluted with EtOAc, washed, and dried. Removal of the solvent followed by gradient elution from silica gel (EtOAc/hexane, 1/4−6/1) gave the α- and *β*-anomers of the nucleosides, respectively.

5′-*O*-Benzyl-3′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-thymidine (21*β*) and the Anomer (21α). These were prepared from thymine and **20** according to the general method. Chromatography eluent: EtOAc/hexane, from 1/4 to 3/1. The α- and *β*-anomers were both obtained as foams (α/*β*, 1/1, yield 70%). For **21***β*: $[\alpha]_D^{20}$ +27.2° (*c*, 2.2). ^{1}H NMR *δ*: 0.05 (s, 3 H), 0.07 (s, 3 H), 0.85 (s, 9 H), 1.57 (s, 3 H), 2.16−2.25 (m, 1 H), 2.39−2.47 (m, 1 H), 3.74 (s, 3 H), 3.84 (d, *J* = 10.5 Hz, 1 H), 4.04 (d, *J* = 10.5 Hz, 1 H), 4.57 (dd, *J* = 11.8, 5.1 Hz, 2 H), 4.69 (dd, *J* = 6.8, 4.8 Hz, 1 H), 6.57 (t, *J* = 6.4 Hz, 1 H), 7.26−7.38 (m, 5 H), 7.56 (s, 1 H), 8.77 (br, 1 H). ^{13}C NMR *δ*: −7.0, −6.7, 10.3, 15.9, 23.7, 39.1, 50.4, 68.4, 71.4, 72.0, 83.9, 89.0, 109.1, 125.9, 126.4, 126.9, 134.1, 135.3, 148.1, 161.5, 168.0. Anal. Calcd for $C_{25}H_{36}N_2O_7Si$: C, 59.50; H, 7.19. Found: C, 59.68; H, 7.30. For **21**α: $[\alpha]_D^{20}$ +3.2° (*c*, 1.8). ^{1}H NMR *δ*: 0.00 (s, 3 H), 0.03 (s, 3 H), 0.78 (s, 9 H), 1.93 (d, *J* = 1.1 Hz, 3 H), 2.04−2.10 (m, 1 H), 2.71−2.77 (m, 1 H), 3.71 (dd, *J* = 13.4, 10.2 Hz, 2 H), 3.75 (s, 3 H), 4 45 (dd, *J* = 5.5, 2.5 Hz, 1 H), 4.58 (s, 2 H), 6.31 (dd, *J* = 7.0, 3.2 Hz, 1 H), 7.26−7.38 (m, 5 H), 8.19 (s, 1 H), 8.80 (br, 1 H). ^{13}C NMR *δ*: −5.3, −4.8, 12.9, 17.8, 25.5, 42.2, 52.6, 72.0, 74.1, 74.7, 87.3, 94.1, 110.0, 127.9, 128.2 (2 × C), 128.8 (2 × C), 137.5, 137.6, 150.6, 164.2, 169.5. Anal. Calcd for $C_{25}H_{36}N_2O_7Si$: C, 59.50; H, 7.19. Found: C, 59.33; H, 7.15.

4-*N*-Acetyl-5′-*O*-benzyl-3′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-cytidine (22*β*) and the Anomer (22α). These were prepared from N^4-acetylcytosine and **20** according to the general procedure. Chromatography eluent: EtOAc/hexane, from 3/1 to 6/1. The α-anomer was obtained as a foam and the *β*-anomer as a crystal (α/*β*, 7/5, yield 90%). For **22***β*: mp 169−172 °C; $[\alpha]_D^{20}$ +99.7° (*c*, 3.8). ^{1}H NMR *δ*: 0.02 (s, 6 H), 0.84 (s, 9 H), 2.12−2.20 (m, 1 H), 2.23 (s, 3 H), 2.65−2.75 (m, 1 H), 3.75 (s, 3 H), 3.95 (dd, *J* = 34.8, 10.6 Hz, 2 H), 4.95 (s, 2 H), 4.62 (t, *J* = 6.8 Hz, 1 H), 6.48 (dd, *J* = 7.0, 4.4 Hz, 1 H), 7.10 (d, *J* = 7.5 Hz, 1 H), 7.31−7.42 (m, 5 H), 8.37 (d, *J* = 7.6 Hz, 1 H), 8.66 (br, 1 H). ^{13}C NMR *δ*: −5.4, −5.0, 17.6, 24.7, 25.4 (3 × C), 41.3, 52.1, 69.1, 71.9, 73.8, 87.5, 90.7, 96.7, 128.0 (2 × C), 128.3, 128.6 (2 × C),

136.8, 144.7, 154.8, 163.1, 169.7, 171.4. Anal. Calcd. for $C_{26}H_{37}N3O_7Si$: C, 58.74; H, 7.01. Found: C, 58.69; H, 7.01. For **22**α: $[\alpha]_D^{20}$ −36.2° (*c*, 2.5). ^{1}H NMR *δ*: −0.11 (s, 3 H), −0.03 (s, 1 H), 0.70 (s, 9 H), 2.15−2.25 (m, 4 H), 2.80−2.90 (m, 1 H), 3.71 (dd, *J* = 15.0, 10.1 Hz, 2 H), 3.79 (s, 3 H), 4.40 (d, *J* = 3.5 Hz, 1 H), 4.57 (s, 2 H), 6.26 (d, *J* = 5.2 Hz, 1 H), 72.6−7.42 (m, 6 H), 8.84 (d, *J* = 7.5 Hz, 1 H), 8.93 (br, 1 H). ^{13}C NMR *δ*: −5.5, −4.9, 17.6, 24.8, 25.3 (3 × C), 42.2, 52.5, 72.0, 73.8, 74.8, 89.4, 95.2, 96.3, 127.7 (2 × C), 128.0, 128.5 (2 × C), 137.2, 146.3, 155.2, 163.2, 169.2, 171.3. Anal. Calcd. for $C_{26}H_{37}N_3O_7Si$: C, 58.74; H, 7.01. Found: C, 58.62; H, 6.94.

2-*N*-Acetyl-5′-*O*-Benzyl-3′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-guanosine (23*β*) and the Anomer (23α). These were prepared from 2-acetylamino-6-hydroxy-purine and **20** according to the general method. Chromatography eluent: $CHCl_3/CH_3OH$, from 20/1 to 10/1. Both anomers were obtained crystalline. (α/*β*, 3/1, yield 83%). For **23***β*: mp 229−232 °C; $[\alpha]_D^{20}$ +12.2° (*c*, 0.8). ^{1}H NMR *δ*: 0.05 (s, 3 H), 0.06 (s, 3 H), 0.83 (s, 9 H), 2.24 (s, 3 H), 2.45−2.53 (m, 1 H), 2.55−2.64 (m, 1 H), 3.74−3.80 (m, 4 H), 3.98 (d, *J* = 10.6 Hz, 1 H), 4.55 (dd, *J* = 18.8, 11.9 Hz, 2 H), 4.81 (t, *J* = 5.5 Hz, 1 H), 6.47 (t, *J* = 6.2 Hz, 1 H), 7.24−7.34 (m, 5 H), 7.95 (s, 1 H). ^{13}C NMR *δ*: −5.0, −4.7, 18.0, 24.7, 25.7, 41.2, 52.4, 70.1, 73.6, 74.1, 84.4, 91.5, 121.6, 128.1 (2 × C), 128.3, 128.8 (2 × C), 137.4, 137.6, 147.2, 148.0, 156.1, 170.3, 171.4. Anal. Calcd. for $C_{27}H_{37}N_5O_7Si$: C, 56.72; H, 6.52. Found: C, 57.14; H, 6.70. For **23**α: mp 156−158 °C; $[\alpha]_D^{20}$ +31.3° (*c*, 1.4). ^{1}H NMR *δ*: −0.08 (s, 3 H), −0.01 (s, 3 H), 0.81 (s, 9 H), 2.14 (s, 3 H), 2.28−2.35 (m, 1 H), 2.81−2.90 (m, 1 H), 3.71 (s, 3 H), 3.83 (dd, *J* = 19.8, 10.2 Hz, 2 H), 4.53−4.57 (m, 3 H), 3.20 (dd, *J* = 7.4, 4.2 Hz, 1 H), 7.26−7.35 (m, 5 H), 8.37 (s, 1 H), 9.55 (br, 1 H). ^{13}C NMR *δ*: −5.2, −4.8, 18.0, 24.4, 25.7 (3 × C), 29.9, 41.8, 52.6, 72.3, 74.2, 75.1, 84.7, 93.7, 120.9, 128.1 (2 × C), 128.4, 128.8 (2 × C), 137.3, 138.9, 156.3, 169.5, 172.6. Anal. Calcd. for $C_{27}H_{37}N_5O_7Si$: C, 56.72; H, 6.52. Found: C, 56.68; H, 6.61.

5′-*O*-Benzyl-6-*N*-benzoyl-3′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-adenosine (24*β*) and the Anomer (24α). These were prepared from N^6-benzoyladenine and **20** according to the general method. The chromatography eluent was EtOAc/hexane, from 1/1 to 6/1. Two anomers were obtained as foams (α/*β*, 1/1, yield 40%). For **24***β*: $[\alpha]_D^{20}$ +6.2° (*c*, 3.3). ^{1}H NMR *δ*: 0.05 (s, 3 H), 0.08 (s, 3 H), 0.86 (s, 9 H), 2.57−2.67 (m, 1 H), 2.75−2.84 (m, 1 H), 3.76 (s, 3 H), 4.03 (dd, *J* = 40.5, 7.1 Hz, 2 H), 4.56 (s, 2 H), 4.90 (t, *J* = 6.1 Hz, 1 H), 6.73 (t, *J* = 6.7 Hz, 1 H), 7.23−7.34 (m, 5 H), 7.50 (t, *J* = 7.0 Hz, 2 H), 7.59 (t, *J* = 7.3 Hz, 1 H), 8.02 (d, *J* = 7.1 Hz, 1 H), 8.37 (s, 1 H), 8.74 (s, 1 H), 9.10 (br, 1 H). ^{13}C NMR *δ*: −5.3, −5.0, 14.1, 17.7, 25.4 (3 × C), 40.6, 52.1, 69.8, 73.3, 85.0, 91.1, 123.3, 127.8 (3 × C), 127.9, 128.4 (2 × C), 128.8 (2 × C), 132.7, 133.6, 137.1, 142.0, 149.3, 151.2, 152.4, 164.5, 170.0. Anal. Calcd. for $C_{32}H_{39}N_5O_6Si$: C, 62.22; H, 6.36. Found: C, 62.25; H, 6.47. For **24**α: $[\alpha]_D^{20}$ +28.7° (*c*, 2.5). ^{1}H NMR *δ*: −0.13 (s, 3 H), −0.01 (s, 3 H), 0.70 (s, 9 H), 2.48 (d, *J* = 13.9 Hz, 1 H), 2.92−3.00 (m, 1 H), 3.74−3.76 (m, 4 H), 3.87 (d, *J* = 10.2 Hz, 1 H), 4.56−4.61 (m, 3 H), 6.68 (dd, *J* = 7.0, 2.6 Hz, 1 H), 7.30−7.40 (m, 5 H), 7.51 (t, *J* = 7.0 Hz, 2 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 8.02 (d, *J* = 7.4 Hz, 2 H), 8.80 (s, 1 H), 8.86 (s, 1 H), 9.1 (br, 1 H). ^{13}C NMR *δ*: −5.6, −5.2, 17.5, 25.2 (3 × C), 25.4, 42.2, 52.3, 71.8, 73.9, 75.0, 86.1, 94.1, 122.8, 127.6 (2 × C), 127.7 (2 × C), 127.9, 128.5 (2 × C), 128.7 (2 × C), 132.6, 133.8, 137.2, 142.7, 149.1, 151.0, 151.3, 164.5, 169.2. Anal. Calcd. for $C_{32}H_{39}N_5O_6Si$: C, 62.22; H, 6.36. Found: C, 62.43; H, 6.56.

3′-*O*-(*tert*-Butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-thymidine (25) from 21*β*. To a solution of **21***β* (20 mg, 0.04 mmol) in methanol (0.5 mL) was added Pd/C (10%, 2 mg). The reaction mixture was stirred at room temperature under H_2 until TLC showed the disappearance of the starting material. The reaction mixture was filtered and washed with MeOH. Removal of the solvent gave **25** (16 mg, 98%) as a white foam. $[\alpha]_D^{20}$ +28.0° (*c*, 0.5). ^{1}H NMR *δ*: 0.08 (s, 6 H), 0.86 (s, 9 H), 1.91 (s, 3 H), 2.35−2.38 (m, 1 H), 2.54−2.61 (m, 1 H), 3.76 (s, 3 H), 3.89−3.94 (m, 1 H), 4.00−4.07 (m, 1 H), 4.78 (dd, *J* = 7.1, 4.5 Hz, 1 H), 6.20 (t, *J* = 6.7 Hz, 1 H), 7.21 (s, 1 H). ^{13}C NMR *δ*: −5.0, −4.7, 12.6, 18.0, 25.7 (3 × C), 39.8, 52.4, 63.7, 73.3, 90.0, 91.8, 111.4, 138.3, 150.3, 163.6, 170.8. Anal. Calcd. for $C_{18}H_{30}N_2O_7Si$: C, 52.15; H, 7.29. Found: C, 52.19; H, 7.27.

Preparation of Authentic 25 from 26. To a solution of **26** (11 mg, 0.02 mmol) in dichloromethane (0.5 mL) was added trifluoroacetic acid (64 μL) at 0 °C. The reaction mixture was stirred at room temperature for 1 h. The solvent and volatiles were coevaporated with benzene. The crude acid was then taken up with benzene (0.5 mL) and treated with 1,1-dichloromethyl methyl ether (36 μL). The reaction mixture was heated to gentle reflux for 1 h. After cooling to room temperature, the solvent was removed under vacuum. The resulting acid chloride was taken up with dry dichloromethane (0.3 mL) and treated with MeOH (8.1 μL, 0.2 mmol), followed by DMAP (3 mg, 0.025 mmol). After the mixture was stirred at room temperature for 12 h, the solvent was removed and the crude reaction mixture was dissolved in MeOH (0.5 mL) and K_2CO_3 (5 mg, 0.022 mmol) was added. After 30 min, the solvent was removed and column chromatography on silica gel (eluent, EtOAc/Hexane, 2/1) gave **25** (7 mg, 90%) as a white foam, whose spectral data were identical in every aspect to those of the sample obtained above.

Coupling of 20 with *N*-Acetylcytosine Mediated by TMS Iodide: 4-*N*-Acetyl-1-(*2S*,*3S*,*5S*-*2*-benzyloxymethyl-3-hydroxy-2-methoxycarbonyl-5-tetrahydrofuranyl)cytosine. (36α). To a solution of **20** (50 mg, 0.12 mmol) in acetonitrile (1 mL) at 0 °C was added TMSI (21 μL, 0.14 mmol) dropwise. After 5 min a solution of persilylated *N*-acetylcytosine (0.24 mmol) in acetonitrile (0.5 mL) was added. The reaction mixture was allowed to warm to room temperature and was then stirred for 5 h before the reaction was quenched with 3 N HCl and the solution extracted with EtOAc. The extracts were washed with saturated $NaHCO_3$, and brine, and dried. Removal of the solvent and filtration on silica gel (eluent: EtOAc) gave a mixture of **22**α and a trimethylsilylated derivative (30 mg). This mixture (27 mg) was dissolved in THF (1 mL), treated with $Et_3N{\cdot}3HF$ (81 μL, 0.5 mmol), and then heated to reflux under Ar for 3 h. Removal of the solvent followed by chromatography on silica gel (eluent: EtOAc/MeOH 40/1) gave anomerically pure **36**α (19 mg, 45% overall) which was identical to the sample described below.

4-Pentenyl 5-*O*-Benzyl-2-deoxy-4α-methoxycarbonyl-α,*β*-D-*ribo*-pentofuranoside (27α and 27*β*). To a solution of **18**, obtained by hydrolysis of **17** as described in the preparation of **19** above (1.82 g, 6.5 mmol) in 4-pentenol (8 mL) was added camphor 10-sulfonic acid (89 mg, 0.4 mmol) followed by stirring at room temperature for 4 h. The excess 4-pentenol was then recovered by distillation and the residue was partitioned between saturated sodium bicarbonate solution and EtOAc. The organic layer was washed with brine and dried over sodium sulfate. Removal of the solvent followed by column chromatography (eluent: EtOAc/hexane, 1/1) gave **27**α (0.72 g) and **27***β* (1.44 g) as colorless oils (combined yield: 95%). For **27**α: $[\alpha]_D^{20}$ −35.3° (*c*, 2.7). ^{1}H NMR *δ*: 1.56−1.65 (m, 2 H), 2.02−2.09 (m, 2 H), 2.18−2.22 (m, 2 H), 2.95 (d, *J* = 4.6 Hz, 1 H), 3.37−3.45 (m, 1H), 3.62 (d, *J* = 9.8 Hz, 1 H), 3.71−3.82 (m, 1 H), 3.79 (s, 3 H), 3.84 (d, *J* = 9.8 Hz, 1 H), 4.42−4.48 (m, 1 H), 4.58 (dd, *J* = 17.8, 12.3 Hz, 2 H), 4.92−5.02 (m, 2 H), 5.36 (dd, *J* = 5.1, 3.0 Hz, 1 H), 5.73−5.83 (m, 1 H), 7.24−7.35 (m, 5 H). ^{13}C NMR *δ*: 28.9, 30.4, 40.5, 52.4, 52.7, 67.8, 73.3, 73.8, 74.3, 90.1, 104.5, 114.9, 127.8, 138.0, 171.5. Anal. Calcd. For $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.98; H, 7.45. For **27***β*: $[\alpha]_D^{20}$ +93.7° (*c*, 1.3). ^{1}H NMR *δ*: 1.66−1.73 (m, 2 H), 2.04−2.14 (m, 3 H), 2.20−2.26 (m, 1 H), 3.30 (d, *J* = 11.7 Hz, 1 H), 3.42−3.49 (m, 1 H), 3.64 (d, *J* = 9.9 Hz, 1 H), 3.74 (d, *J* = 9.9 Hz, 1 H), 3.76 (s, 3 H), 4.10−4.22 (m, 2 H), 4.54 (d, *J* = 1.6 Hz, 2 H), 4.94−5.05 (m, 2 H), 7.25−7.35 (m, 5 H). ^{13}C NMR *δ*: 28.9, 30.5, 41.3, 52.3, 67.6, 72.8, 73.9, 75.5, 93.5, 105.6, 114.9, 127.8, 137.9, 138.3, 170.7. Anal. Calcd. for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.88; H, 7.48.

1*R*,3*R*,5*S*-1-(Benzyloxymethyl)-2,6-dioxa-7-oxo-3-(4-pentenyloxy)bicyclo[3.2.0]heptane (29α). To a solution of **27**α (700 mg, 2 mmol) in THF (10 mL) was added 1 M aqueous LiOH (10 mL, 10 mmol) and the mixture was stirred at room temperature for 6 h before it was neutralized with 2 N HCl to

pH 7. The THF was removed under reduced pressure and the residue re-acidified to pH 2 with 2 N HCl. The mixture was extracted with EtOAc and the organic layer was washed with brine and dried over sodium sulfate. Removal of the solvent gave **28**α as a colorless oil (630 mg, 99%). To a solution of this crude acid (480 mg, 1.4 mmol) in dichloromethane (20 mL) at room temperature were added Et_3N (0.64 mL, 4.6 mmol) and BOP-Cl (550 mg, 2.2 mmol). The resulting mixture was stirred at room temperature for 3 h before the solvent was removed under reduced pressure. Column chromatography of the residue on silica gel (eleunt: EtOAc/hexane, 1/9) gave the title compound as a colorless oil (320 mg, 85%). $[\alpha]_D^{20}$ −78.5° (*c*, 2.5). ^{1}H NMR δ: 1.57−1.71 (m, 2 H), 2.00−2.13 (m, 3 H), 2.48 (d, J = 15.2 Hz, 1H), 3.38−3.45 (m, 1 H), 3.71−3.82 (m, 2 H), 3.90 (d, J = 10.7 Hz, 1 H), 4.69 (s, 2 H), 4.94−5.04 (m, 2 H), 5.05 (d, J = 5.2 Hz, 1 H), 5.50 (d, J = 5.2 Hz, 1 H), 5.73−5.87 (m, 1 H), 7.28−7.38 (m, 1 H). ^{13}C NMR δ: 28.6, 30.3, 37.3, 52.4, 65.6, 68.2, 74.1, 77.0, 79.1, 97.0, 107.2, 115.0, 127.9, 128.7, 137.4, 138.3, 170.7. υ ($CHCl_3$): 1843 cm^{-1}. Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.96. Found: C, 68.01; H, 7.01.

1*R*,3*S*,5*S*-1-(Benzyloxymethyl)-2,6-dioxa-7-oxo-3-(4-pentenyloxy)bicyclo[3.2.0]heptane (29*β*). **29**β was prepared from **27**β analogously to the α-anomer above. $[\alpha]_D^{20}$ +76.8° (*c*, 1.4). ^{1}H NMR δ: 1.63−1.72 (m, 2 H), 1.95−2.13 (m, 3 H), 2.60 (dd, J = 15.2, 4.8 Hz, 1 H), 3.49−3.56 (m, 1 H), 3.71 (d, J = 10.4 Hz, 1 H), 3.76−3.83 (m, 1 H), 3.89 (d, J = 10.4 Hz, 1 H), 4.62 (dd, J = 15.5, 12.1 Hz, 2 H), 4.96−5.04 (m, 2 H), 5.09 (d, J = 5.3 Hz, 1 H), 5.38 (dd, J = 6.3, 4.7 Hz, 1 H), 5.74−5.83 (m, 1 H), 7.27−7.38 (m, 5 H). ^{13}C NMR δ: 28.9, 30.2, 37.3, 65.9, 69.9, 74.0, 58.5, 96.4, 107.3, 115.3, 127.9, 128.2, 128.7, 137.4, 138.0, 169.5. υ ($CHCl_3$): 1837 cm^{-1}. Anal. Calcd. for $C_{18}H_{22}O_5$:C, 67.91; H, 6.96. Found: C, 67.70; H, 6.98.

1*R*,3*R*,5*S*-1-(Benzyloxymethyl)-2,6-dioxa-7-oxo-3-phenylthiobicyclo[3.2.0]heptane (31α) and the 3*S* Diastereomer (31*β*). To a solution of **29**α (115 mg, 0.36 mmol) in dichloromethane (5 mL) was added a solution of bromine in dichloromethane dropwise at 0 °C under Ar until a brown color persisted. The solvent was then removed under reduced pressure and the resulting solid dried for 20 min under vacuum and then redissolved in dichloromethane (2 mL). This solution and PhSH (41 μL, 0.4 mmol) were added at the same time to a stirred solution of AgOTf (111 mg, 0.43 mmol) in dichloromethane (2 mL) at −78 °C under Ar. The reaction mixture was allowed to warm to 0 °C, then diluted with aqueous $NaHCO_3$, and extracted with EtOAc. The combined organic layers were washed and dried. Removal of the solvent followed by column chromatography on silica gel (eluent: EtOAc/hexane, 1/7) gave pure **31**β (30 mg) and **31**α mixed with an inseparable impurity (60 mg, 50% purity) (overall yield: 50%). For **31**β: mp 64−66 °C. $[\alpha]_D^{20}$ −84.4° (*c*, 1.0). ^{1}H NMR δ: 1.86−1.96 (m, 1 H), 2.67 (d, J = 14.9, 5.0 Hz, 1 H), 3.76 (d, J = 10.6 Hz, 1 H), 3.95 (d, J = 10.6 Hz, 1 H), 4.62 (s, 2 H), 5.07 (d, J = 4.7 Hz, 1 H), 5.50 (dd, J = 10.7, 5.0 Hz, 1 H), 7.25−7.39 (m, 8 H), 7.48−7.51 (m, 2 H). ^{13}C NMR δ: 36.7, 65.4, 74.2, 79.4, 86.4, 98.9, 128.0, 128.7, 129.3, 132.3, 137.2, 169.0. υ ($CHCl_3$): 1833 cm^{-1}. Anal. Calcd. for $C_{19}H_{18}O_4S$: C, 66.65; H, 5.30. Found: C, 66.64; H, 5.40. **31**α was characterized by an anomeric signal at δ 6.01 in the ^{1}H spectrum. It was used as obtained in the next step because of the difficulties with purification.

1*R*,3*R*,5*S*-1-(Benzyloxymethyl)-2,6-dioxa-7-oxo-3-phenylthiobicyclo[3.2.0]heptane *S*-Oxide (32α). To the solution of the impure **31**α (60 mg, 0.09 mmol) in THF (1 mL) at 0 °C was added dropwise Oxone (54 mg, 0.09 mmol) in water (0.2 mL) after which the reaction mixture was stirred at 0 °C for 30 min and then diluted with EtOAc (5 mL). The organic layer was washed and dried. Removal of the solvent followed by column chromatography on silica gel (eluent: EtOAc/hexane, 3/1) gave **32**α (19 mg, 60%) as a single diastereomer at *S*. mp 103−105 °C. $[\alpha]_D^{20}$ +67.7° (*c*, 0.7). ^{1}H NMR δ: 2.42−2.52 (m, 1 H), 3.32 (d, J = 16.7 Hz, 1 H), 3.67 (d, J = 10.8 Hz, 1 H), 3.87 (d, J = 10.8 Hz, 1 H), 4.57 (s, 2 H), 4.92 (d, J = 7.4 Hz, 1 H), 5.28 (d, J = 5.0 Hz, 1 H), 7.26−7.37 (m, 5 H), 7.52−7.57 (m, 3 H), 7.68−7.72 (m, 2 H). ^{13}C NMR δ: 32.1, 64.8, 74.3, 80.1, 100.8, 101.1, 125.3, 128.1, 128.4, 128.8, 129.4, 132.0, 136.9, 141.8, 168.4. υ ($CHCl_3$): 1831 cm^{-1}. Anal. Calcd. for $C_{19}H_{18}O_5S$: C, 63.67; H, 5.06. Found: C, 63.88; H, 5.29.

General Procedure for the Preparation of Persilylated Bases.[33] A mixture of base (0.2 mmol) and ammonium sulfate (1 crystal) in hexamethyldisilazide (1 mL) was refluxed under Ar for 8 h before the solvent was removed under vacuum. After the mixture was dried under high vacuum for a further 2 h, the crude preparation was used directly in the coupling reaction.

General Procedure for Coupling with Donors 29α*β* Promoted by NIS and TfOH. Pentenyl glycoside **29**α or **29**β (32 mg, 0.1 mmol), silylated base (0.2 mmol), NIS (24 mg, 0.11 mmol), and activated powdered 4A molecular sieves (100 mg) in anhydrous solvent (2 mL) were stirred under Ar for 5 min before TfOH (11 μL, 0.12 mmol) was added. The reaction mixture was then stirred at room temperature for 2 h after which it was diluted with EtOAc (5 mL). The organic layer was washed with $Na_2S_2O_3$, $NaHCO_3$, and brine and dried over sodium sulfate. Removal of the solvent followed by column chromatography gave the desired nucleosides, as αβ mixtures, which were converted immediately to the methyl esters as set out in the general protocol.

General Procedure for Coupling with Bromide 30. To a solution of **29**α or **29**β (32 mg, 0.1 mmol) in dichloromethane (1 mL), bromine solution in dichloromethane was added dropwise at 0 °C under Ar until a brown color persisted. The solvent was then removed under reduced pressure and the residue dried under high vacuum for 20 min before it was dissolved in the dry reaction solvent (1 mL). This solution was then added dropwise to a mixture of silylated base (0.2 mmol) and AgOTf (31 mg, 0.12 mmol) in dichloromethane (1 mL) containing 100 mg of powered activated 4A molecular sieves at room temperature (Table 2). The reaction mixture was stirred at room temperature for 2 h and then diluted with EtOAc (10 mL). The resulting mixture was washed with saturated aqueous $NaHCO_3$ and brine and dried over sodium sulfate. Removal of the solvent followed by column chromatography gave the desired nucleosides, as αβ mixtures of isomers, which were converted immediately to the methyl esters as set out in the general protocol.

General Procedure for Coupling with Thioglycosides 31α and 31*β*. To a solution of **31**α or **31**β (34 mg, 0.1 mmol) and powdered 4A molecular sieves (50 mg) in dichloromethane (1 mL) at room temperature under Ar was added silylated *N*-acetyl cytosine (31 mg, 0.2 mmol) in dichloromethane (1 mL). After the mixture was stirred for 20 min, NBS (24 mg, 0.13 mmol) in dichloromethane (0.5 mL) was added and the reaction mixture allowed to stand overnight before the reaction was quenched with sodium bicarbonate solution and the solvent extracted with dichloromethane. It was then worked up as above to give the crude nucleoside β-lactones, which were converted immediately to the methyl esters as set out below.

General Procedure for Coupling with Sulfoxide 32α. To a solution of sulfoxide **32**α (36 mg, 0.1 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (41 mg, 0.2 mmol) in the anhydrous reaction solvent (1 mL) at −78 °C under Ar was added Tf_2O (21 μL, 0.12 mmol), followed by stirring for 5 min. Silylated thymine (0.2 mmol) in the same solvent (1 mL) was then added and the mixture was allowed to warm to room temperature. After standing overnight, the reaction was quenched with $NaHCO_3$ and worked up as above for coupling with bromide **30** to give the crude nucleoside β-lactones which were immediately converted to the methyl esters as set out in the general protocol.

General Procedure for the Conversion of the *β*-Lactone Nucleosides into Methyl Esters. The αβ mixtures of isomers obtained from the coupling reactions were treated with triethylamine (1 equiv) in MeOH for 30 min at room temperature. Removal of the volatiles under reduced pressure and column chromatography then gave **34**α and **34**β, or **36**α and **36**β, which were identical to authentic samples obtained by desilylation of **21**α and **21**β, or **22**α and **22**β, respectively.

General Procedure for Desilylation of 21α, 21*β* and 22α, 22*β*. The nucleoside (1 mmol) in THF (1 mL) was treated with triethylamine trihydrofluoride (10 equiv) at room tem-

perature for 12 h. Removal of the volatiles and chromatography over silica gel then gave the desilylated compound.

5′-Benzyl-2′-deoxy-4′α-methoxycarbonyl-D-thymidine (34*β*). $[\alpha]_D^{20}$ +6.4° (*c*, 2.4). ^{1}H NMR *δ*: 1.60 (s, 3 H), 2.24−2.33 (m, 1 H), 2.42−2.50 (m, 1 H), 3.49 (br s, 1 H), 3.79 (s, 3 H), 4.01 (d, *J* = 10.3 Hz, 1 H), 4.06 (d, *J* = 10.3 Hz, 1 H), 4.60 (dd, *J* = 16.8, 11.7 Hz, 2 H), 4.68−4.74 (m, 1 H), 6.60 (t, *J* = 7.4 Hz, 1 H), 7.27−7.37 (m, 5 H), 7.54 (s, 1 H), 9.26 (br s, 1 H). ^{13}C NMR *δ*: 12.3, 40.2, 52.9, 71.6, 74.1, 86.0, 91.5, 111.4, 127.8 (2 × C), 128.4, 128.8 (2 × C), 136.1, 137.2, 150.6, 164.1, 170.7. Anal. Calcd. for $C_{19}H_{22}N_2O_7 \cdot 0.25H_2O$: C, 57.79; H, 5.74. Found: C, 57.55; H, 5.72.

1-(2*S*,3*S*,5*S*-2-Benzyloxymethyl-3-hydroxy-2-methoxycarbonyl-5-tetrahydrofuranyl)thymine (34α). $[\alpha]_D^{20}$ +11.1° (*c*, 1.2). ^{1}H NMR *δ*: 1.77 (s, 3 H), 2.47−2.52 (m, 1 H), 2.64−2.73 (m, 1 H), 3.68 (dd, *J* = 20.6, 10.1 Hz, 1 H), 3.81 (s, 3 H), 4.37−4.46 (m, 2 H), 4.55 (s, 2 H), 6.19−6.22 (m, 1 H), 7.26−7.36 (m, 5 H), 8.14 (s, 1 H). ^{13}C NMR *δ*: 12.6, 41.4, 52.7, 72.4, 73.7, 88.3, 94.8, 109.2, 127.8 (2 × C), 128.1, 128.7 (2 × C), 137.5, 138.6, 151.2, 165.0, 169.8. Anal. Calcd. for $C_{19}H_{22}N_2O_7 \cdot 0.75H_2O$: C, 56.50; H, 5.86. Found: C, 56.56; H, 5.58.

4-*N*-Acetyl-5′-*O*-benzyl-2′-deoxy-4′α-methoxycarbonyl-D-cytidine. (36*β*). $[\alpha]_D^{20}$ +64.1° (*c*, 1.9). ^{1}H NMR *δ*: 2.13−2.20 (m, 1 H), 2.24 (s, 3 H), 2.79−2.88 (m, 1 H), 3.78 (s, 3 H), 3.88 (d, *J* = 10.3 Hz, 1 H), 3.96 (d, *J* = 10.3 Hz, 1 H), 4.60 (s, 2 H), 4.67 (t, *J* = 4.4 Hz, 1 H), 6.53 (t, *J* = 6.2 Hz, 1 H), 7.22 (d, *J* = 7.5 Hz, 1 H), 7.26−7.40 (m, 5 H), 8.24 (d, *J* = 7.5 Hz, 1 H). ^{13}C NMR *δ*: 25.0, 41.4, 52.8, 71.0, 73.4, 74.1, 88.3, 91.9, 96.8, 128.2 (2 × C), 128.5, 128.9 (2 × C), 137.0, 145.1, 15.5, 162.7, 170.5, 171.0. Anal. Calcd. for $C_{20}H_{23}N_3O_7 \cdot 0.75H_2O$: C, 57.74; H, 5.73. Found: C, 55.86; H, 5.60.

4-*N*-Acetyl-1-(2*S*,3*S*,5*S*-2-benzyloxymethyl-3-hydroxy-2-methoxycarbonyl-5-tetrahydrofuranyl)cytosine. (36α). $[\alpha]_D^{20}$ −86.0° (*c*, 2.5). ^{1}H NMR *δ*: 2.15 (s, 3 H), 2.02−2.09 (m, 1 H), 2.73−2.78 (m, 1 H), 3.63 (d, *J* = 10.0 Hz, 1 H), 3.74 (d, *J* = 10.0 Hz, 1 H), 3.76 (s, 3H), 4.43 (d, *J* = 4.1 Hz, 1 H), 4.54 (dd, *J* = 16.5, 12.6 Hz, 2 H), 4.70 (br s, 1 H), 6.11 (d, *J* = 6.7 Hz, 1 H), 7.20−7.34 (m, 5 H), 7.42 (d, *J* = 7.5 Hz, 1 H), 8.79 (d, *J* = 7.5 Hz, 1 H), 9.58 (br s, 1 H). ^{13}C NMR *δ*: 24.9, 41.7, 52.8, 72.4, 73.8, 73.9, 90.3, 95.7, 96.2, 127.8 (2 × C), 128.1, 128.7 (2 × C), 137.4, 146.8, 155.7, 162.6, 169.9, 171.0. Anal. Calcd. for $C_{20}H_{23}N_3O_7 \cdot H_2O$: C, 55.16; H, 5.79. Found: C, 55.20; H, 5.79.

2-*N*-Acetyl-3′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-guanosine (39). To a solution of **23***β* (50 mg, 0.09 mmol) in a mixture of EtOAc (2 mL) and MeOH (2 mL) was added Pd−C (10%, 50 mg) and then hydrogen was bubbled through the solution until TLC showed the disappearance of the starting material. After filtration and removal of the solvent, the residue was triturated with dry ether to give **39** as a white solid (40 mg, 95%). mp 242−244 °C. $[\alpha]^{20}_D$ = +15.3° (*c*, 1.1, MeOH). ^{1}H NMR *δ*: 0.08 (s, 3 H), 0.13 (s, 3 H), 0.85 (s, 9 H), 2.27 (s, 3 H), 2.27−2.36 (m, 1 H), 2.85−2.95-(m, 1 H), 3.73 (s, 3 H), 3.90−4.10 (m, 2 H), 4.79 (br s, 1 H), 5.14(br s, 1 H), 6.37 (t, *J* = 6.9 Hz, 1 H), 7.90 (s, 1 H). ^{13}C NMR *δ*: −5.0, −4.7, 18.0, 24.6, 25.7 (3 × C), 40.9, 52.3, 63.9, 74.1, 86.4, 93.0, 122.1, 139.2, 147.7, 155.5, 170.4, 172.8. Anal. Calcd. for $C_{20}H_{31}N_5O_7Si \cdot 0.5H_2O$: C, 48.96; H, 6.57. Found: C, 48.96; H, 6.57.

6-*N*-Benzoyl-1-[2*S*,3*S*,5*S*-2-benzyloxymethyl-3-(*tert*-butyldimethylsiloxy)-2-methoxycarbonyl-5-tetrahydrofuranyl]adenine (40). Prepared from **24**α by hydrogenolysis as described for **39** above with the difference that removal of the solvent was followed by chromatography on silica gel (eluent: MeOH/$CHCl_3$, 1/10) which gave **39** as a white foam (yield: 50%). $[\alpha]_D^{20}$ +39.8° (*c*, 0.8). ^{1}H NMR *δ*: −0.01 (s, 3 H), 0.05 (s, 3 H), 0.74 (s, 9 H), 2.56−2.63 (m, 1 H), 2.85−2.94 (m, 1 H), 3.75 (s, 3 H), 3.88 (s, 2 H), 4.71 (dd, *J* = 5.7, 3.7 Hz, 1 H), 6.65 (dd, *J* = 6.8, 3.7 Hz, 1 H), 7.41−7.62 (m, 3 H), 8.04 (d, *J* = 7.1 Hz, 2 H), 8.78 (s, 1 H), 8.86 (s, 1 H), 9.29 (br s, 1 H). ^{13}C NMR *δ*: −5.1, −4.8, 17.9, 25.6 (3 × C), 41.5, 52.7, 64.6, 74.4, 85.3, 93.6, 123.0, 128.2, 128.5, 129.0, 130.2, 132.9, 134.0, 142.8, 149.6, 151.5, 152.7, 165.5, 170.4. Anal. Calcd. for $C_{25}H_{33}N_5O_6Si$: C, 56.91; H, 6.30. Found: C, 56.74; H, 6.36.

3′-*O*-(*tert*-Butyldimethylsilyl)-2′-deoxy-4′α-methoxycarbonyl-D-cytidine (42). A solution of **22***β* (54 mg, 0.1 mmol) in MeOH (2 mL) and 0.1 N NaOH (2 mL, 0.2 mmol) was stirred at room temperature for 1 h and then the MeOH was removed under vacuum. The remaining aqueous phase was acidified to pH 2 and the solvent extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), and evaporated down to give a white foam (49 mg, 100%) which was dissolved in dichloromethane (1 mL) at −78 °C under Ar amd treated dropwise with 1 M boron trichloride (0.4 mL, 0.4 mmol) in dichloromethane. The reaction mixture was allowed to warm to 0 °C gradually and then MeOH (2 mL) was added to quench the reaction. The volatiles were removed under reduced pressure and the residue triturated with dry ether to give **42** as a white solid (32 mg, 80%). mp 164−166 °C. $[\alpha]_D^{20}$ +74.5° (*c*, 0.6). ^{1}H NMR (CD_3OD) *δ*: 0.09 (s, 3 H), 0.10 (s, 3 H), 0.88 (s, 9 H), 2.21−2.29 (m, 1 H), 2.39−2.47 (m, 1 H), 3.73 (s, 3 H), 3.89 (s, 2 H), 4.67 (dd, *J* = 6.5, 4.4 Hz, 1 H), 5.90 (d, *J* = 7.5 Hz, 1 H), 6.45 (t, *J* = 6.5 Hz, 1 H), 7.96 (d, *J* = 7.5 Hz, 1 H). ^{13}C NMR *δ*: −4.6, −4.3, 19.1, 26.6, 42.7, 53.0, 64.5, 75.2, 89.5, 94.0, 96.6, 143.7, 158.5, 168.1, 172.6. Anal. Calcd. for: $C_{17}H_{29}N_3O_6Si \cdot 0.5H_2O$: C, 49.98; H, 7.40. Found: C, 49.96; H, 7.40.

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