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Ring Opening of Nucleoside 1′,2′-Epoxides with Organoaluminum Reagents: Stereoselective Entry to Ribonucleosides Branched at the Anomeric Position

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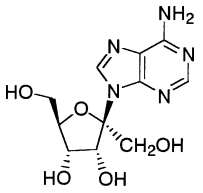
Epoxidation of 3′,5′-*O*-(di-*tert*-butylsilylene)-1′,2′-unsaturated uridine (**11**) with dimethyldioxirane proceeded from the α-face to give the 1′,2′-α-epoxide **12**. Upon reacting with organoaluminum reagents, the 1′,2′-α-epoxide **12** underwent preferential syn-opening of the epoxide ring to yield the *β*-anomers of 1′-methyl- (**13*β***), 1′-ethyl- (**14*β***), 1′-isobutyl- (**15*β***), 1′-ethynyl- (**16*β***), 1′-vinyl- (**17*β***), and 1′-phenyl- (**18*β***) uridine derivatives, although the corresponding α-anomers were also formed except for the reaction with triphenylaluminum. It was found, however, that protection of the N^3-position of **11** either with a benzyloxymethyl or benzoyl group led to the exclusive formation of the desired *β*-anomers. A possible explanation for the observed stereochemical outcome is presented. A similar strategy was found to be applicable to the synthesis of 1′-branched adenosine analogues, which include protected angustmycin C (**37**).

Introduction

The unique structure of the antitumor antibiotic angustmycin C (**1**)[1] has stimulated the synthesis of 1′-branched nucleoside analogues to explore novel nucleoside antimetabolites. Available synthetic methods for this type of analogue[2−5] mostly start with the construction of sugar components, which allow the introduction of various nucleobases. There is, however, an inherent limitation in this approach in terms of diversity at the anomeric substituents.



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In this context, we have reported the first example of anomeric manipulation of uracil nucleosides (Scheme 1),[6] which consists of two reaction steps: (1) stereoselective bromo-pivaloyloxylation of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pento-1-enofuranosyl]uracil (**2**) to give **3** and (2) nucleophilic *substitution* of **3** by the use of organosilicon reagents/$SnCl_4$ or organoaluminum reagents. The 1′-branched product **4** has been converted to the 2′-deoxy (**5**) and the arabinofuranosyl (**6**) derivatives, but synthesis of the ribofuranosyl counterparts (**7**) remained problematic.[7]

Although there have been several reports dealing with the *C*-glycoside synthesis from 1,2-epoxy sugar derivatives,[8,9] this approach has not been investigated in the field of nucleoside chemistry, despite the anticipated

(1) (a) Yüntsen, H.; Yonehara, H.; Ui, H. *J. Antibiot., Ser. A* **1954**, *7*, 113−115. (b) Yüntsen, H.; Ohkuma, K.; Ishii, Y. *J. Antibiot., Ser. A* **1956**, *9*, 195−201. (c) Schroeder, W.; Hoeksema, H. *J. Am. Chem. Soc.* **1959**, *81*, 1767−1768. (d) McCarthy, J. R.; Robins, R. K.; Robins, M. J. *J. Am. Chem. Soc.* **1968**, *90*, 4993−4999.

(2) From D-fructose: (a) Farkas, J.; Sorm, F. *Tetrahedron Lett.* **1962**, 813−814. (b) Farkas, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1963**, *28*, 882−886. (c) Hrebabecky, H.; Farkas, J.; Sorm. F. *Collect. Czech. Chem. Commun.* **1972**, *37*, 2059−2065. (d) Prisbe, E. J.; Smejkal, J.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1976**, *41*, 1836−1846. (e) Grouiller, A.; Chattopadhyaya, J. *Acta Chem. Scand.* **1984**, *B38*, 367−373. (f) Elliott, R. D.; Niwas, S.; Riordan, J. M.; Montgomery, J. A.; Secrist, J. A., III *Nucleosides Nucleotides* **1992**, *11*, 97−119. (g) Holy, A. *Nucleic Acids Res.* **1974**, *1*, 289−298. (h) Tatsuoka, T.; Imao, K.; Suzuki, K. *Heterocycles* **1986**, *24*, 617−620. (i) Yoshimura, Y.; Ueda, T.; Matsuda, A. *Tetrahedron Lett.* **1991**, *32*, 4549−4552. (j) Yoshimura, Y.; Otter, B. A.; Ueda, T.; Matsuda, A. *Chem. Pharm. Bull.* **1992**, *40*, 1761−1769.

(3) From 1-deoxy-1-nitro-*β*-D-ribofuranose: Mahmood, K.; Vasella, A.; Bernet, B. *Helv. Chim. Acta* **1991**, *74*, 1555−1584.

(4) From D-ribonolactone: (a) Faivre-Buet, V.; Grouiller, A.; Descotes, G. *Nucleosides Nucleotides* **1992**, *11*, 1411−1424. (b) Faivre-Buet, V.; Grouiller, A.; Descotes, G. *Nucleosides Nucleotides* **1992**, *11*, 1651−1660. (c) Hayakawa, H.; Miyazawa, M.; Tanaka, H.; Miyasaka, T. *Nucleosides Nucleotides* **1994**, *13*, 297−308. (d) Cappellacci, L.; Barboni, G.; Palmieri, M.; Pasqualini, M.; Grifantini, M.; Costa, B.; Martini, C.; Franchetti, P. *J. Med. Chem.* **2002**, *45*, 1196−1202.

(5) From D-ribofuranosyl cyanide: (a) Grouiller, A.; Buet, V.; Uteza, V.; Descotes, G. *Synlett* **1993**, 221−222. (b) Uteza, V.; Chen, G.-H.; Tuoi, J. L.-Q.; Descotes, G.; Fenet, B.; Grouiller, A. *Tetrahedron* **1993**, *49*, 8579−8588.

(6) Itoh, Y.; Haraguchi, K.; Tanaka, H.; Gen, E.; Miyasaka, T. *J. Org. Chem.* **1995**, *60*, 656−662.

(7) Stereoselective methods for the synthesis of ribofuranosyl uracil nucleosides have recently been reported: (a) Kodama, T.; Shuto, S.; Nomura, M.; Matsuda, A. *Chem. Eur. J.* **2001**, *7*, 2332−2340. (b) Kodama, T.; Shuto, S.; Ichikawa, S.; Matsuda, A. *J. Org. Chem.* **2002**, *67*, 7706−7715.

(8) (a) Collins, P. M.; Ferrier, R. J. *Monosaccharides: Their Chemistry and Their Roles in Natural Products*; John Wiley & Sons: Chichester, UK, 1995. (b) Postema, M. H. D. *C-glycoside Synthesis*; CRC Press: Boca Raton, FL, 1995.

(9) Allwein, S. P.; Cox, J. M.; Howard, B. E.; Johnson, H. W. B.; Rainier, J. D. *Tetrahedron* **2002**, *58*, 1997−2009.

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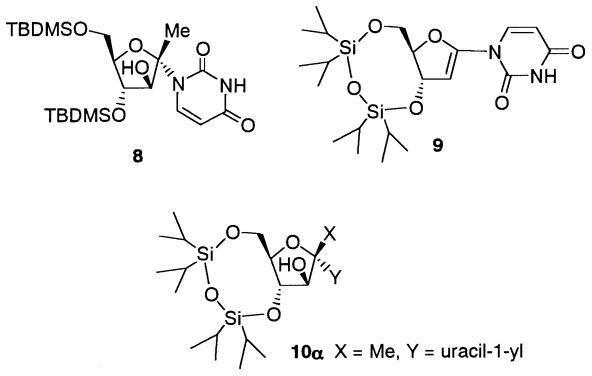
defined regiochemistry of incoming-nucleophiles. In this article, we describe a novel synthesis of 1′-branched ribofuranosyl nucleosides by way of ring opening of 1′,2′-α-epoxy nucleosides with organoaluminum reagents.

Results and Discussions

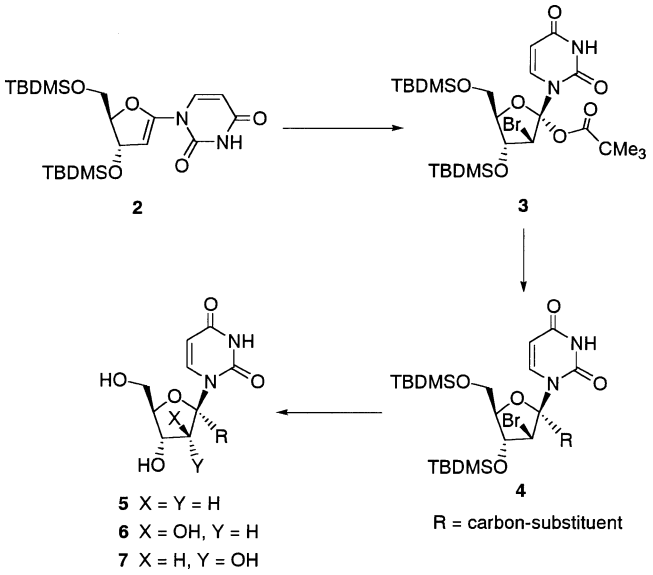
When the 1′,2′-unsaturated uridine protected with the *tert*-butyldimethylsilyl (TBDMS) group (**2**)[6] was oxidized with an acetone solution of dimethyldioxirane (DMDO, 1.2 equiv)[10] in CH_2Cl_2 at −30 °C for 0.5 h, complete disappearance of the starting material was confirmed by TLC analysis. Although DMDO oxidation of the 5,6-double bond of pyrimidine nucleosides has been reported,[11] formation of such a product was not observed under the above conditions throughout the present study. After evaporation of the solvents, the oxidation product was dissolved in CH_2Cl_2 and reacted with Me_3Al (3 equiv) at −30 °C for 4.5 h. From this reaction, only 1-[3,5-bis-*O*-TBDMS-1-methyl-α-D-arabinofuranosyl]uracil (**8**) was isolated in 44% yield. Evidence for the depicted stereochemistry of **8** was provided by NOE experiment: H-6/H-4′ (4.6%), CH_3-1′/H-3′ (1%), and H-2′/H-4′ (2.7%). Under similar reaction conditions, the TIPDS (1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-protected substrate (**9**)[12b] gave the arabinofuranosyl nucleosides **10α** (36%) and **10*β*** (6%). Apart from the stereochemistry of the introduced



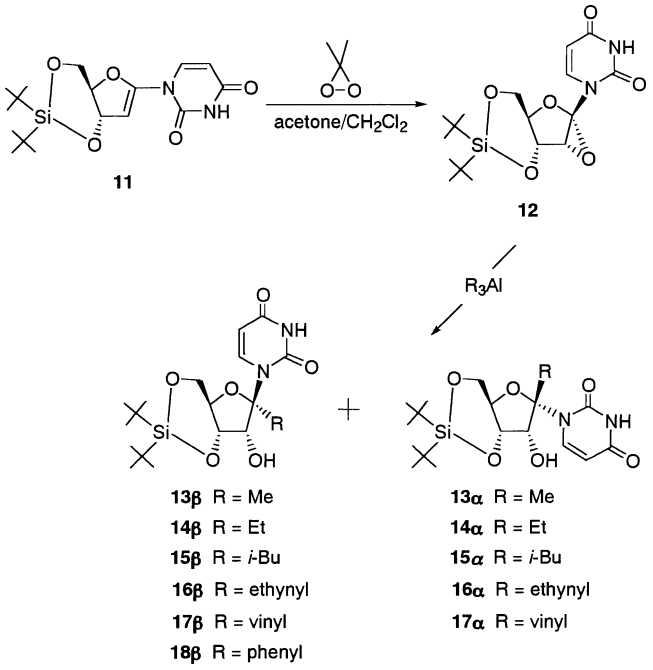
1′-methyl group, these results suggest that epoxidation of **2** and **9** had proceeded preferentially, if not exclusively, from the *β*-face of the 1-enofuranosyl structure.[13]

In the case of the DTBS (di-*tert*-butylsilylene)-protected 1′,2′-unsaturated uridine (**11**),[12b] the epoxide **12** obtained after evaporation of the oxidation mixture was found to be fairly stable in $CDCl_3$. Its ^1H NMR spectrum combined with NOE studies confirmed that the epoxide **12** was a single isomer with 1′,2′-α-epoxy stereochemistry, the observed NOE correlation being 15.4% between H-3′ and H-6. Upon reacting with Me_3Al in CH_2Cl_2 at −30 °C for 4.5 h,[14] **12** gave a mixture of **13*β*** and **13α** (**13*β***/**13α** = 5/1) in 86% yield (Scheme 2, entry 1 in Table 1).

SCHEME 1



SCHEME 2



Under similar reaction conditions, the 1′,2′-α-epoxide **12** reacted with a variety of organoaluminum reagents to give the respective 1′-carbon-substituted products (**14**−**18**) in good yields, except for the synthesis of the 1′-isobutyluridine derivative (**15**) in which dominant hydride attack took place to yield 3′,5′-*O*-(di-*tert*-butyl-

(10) (a) Adam, W.; Hadjiarapoglou, L.; Smerz, A. *Chem. Ber.* **1991**, *124*, 227−232. (b) Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.

(11) Saladino, R.; Bernini, R.; Crestini, C.; Mincione, E.; Bergamini, A.; Marini, S.; Palamara, A. T. *Tetrahedron* **1995**, *51*, 7561−7578.

(12) (a) Itoh, Y.; Haraguchi, K.; Tanaka, H.; Matsumoto, K.; Nakamura, K. T.; Miyasaka, T. *Tetrahedron Lett.* **1995**, *36*, 3867−3870. (b) Haraguchi, K.; Itoh, Y.; Matsumoto, K.; Hashimoto, K.; Nakamura, K. T.; Tanaka, H. *J. Org. Chem.* **2003**, *68*, 2006−2009.

(13) The stereochemistry of epoxides derived from **2** and **9** could not be determined by NOE experiment due to their instability.

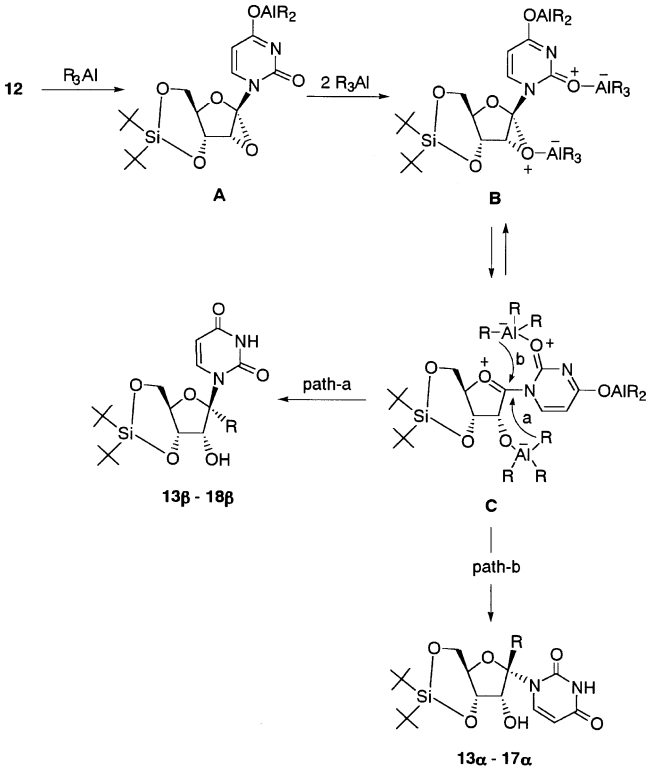
(14) When this reaction was conducted at room temperature, the combined yield of **13α** plus **13*β*** decreased to 55% due to further reaction of these products with Me_3Al to yield an elimination byproduct, 3,5-*O*-(di-*tert*-butylsilylene)-1-methylidene-D-ribofuranose: ^1H NMR ($CDCl_3$) δ 1.01 and 1.04 (18H, each as s), 2.37 (1H, br), 3.93 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{5'a,4'}$ = 10.7 Hz), 4.00 (1H, dd, $J_{3',4'}$ = 9.2 Hz and $J_{2',3'}$ = 4.4 Hz), 4.22 (1H, ddd, $J_{5'a,4'}$ = 10.7 Hz, $J_{5'b,4'}$ = 5.1 Hz, and $J_{3',4'}$ = 9.2 Hz), 4.36 (1H, d, J_{gem}= 2.2 Hz), 4.43 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'b}$ = 5.1 Hz), 4.46 (1H, d, $J_{2',3'}$ = 4.4 Hz), 4.50 (1H, d, J_{gem} = 2.2 Hz); FAB-MS *m*/*z* 287 ($M^+ + H$).

TABLE 1. Reactions of 12 with Organoaluminum Reagents[a]

entry	R_3Al (equiv)	products	yield (%)	ratio of β/α
1	Me_3Al (3)	**13*β***, **13α**	86	5/1
2	Et_3Al (3)	**14*β***, **14α**	90	4/1
3	*i*-Bu_3Al (6)	**15*β***, **15α**	35	9/1
4	$(HC{\equiv}C)_3Al$ (6)	**16*β***, **16α**	64	4/1
5	$(H_2C{=}CH)_3Al$ (6)	**17*β***, **17α**	90	32/1
6	Ph_3Al (6)	**18*β***	55	

[a] All reactions were carried out in CH_2Cl_2 at −30 °C for 4.5 h.

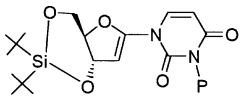
SCHEME 3



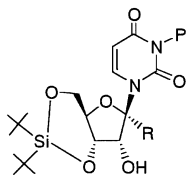
silylene)uridine (entry 3). Although preferential formation of the desired syn-ring-opened *β*-anomers was seen in entries 1−5, these products were always accompanied with the respective anti-opened α-anomers, except for entry 6.

In Scheme 3 is shown a possible reaction pathway for the reactions listed in Table 1. The epoxide **12**, upon reacting with R_3Al, could form an aluminum enolate **A** by dissociating acidic N^3-H. Coordination of R_3Al with the C^2-carbonyl of the base moiety as well as the oxygen atom of the epoxide ring results in the formation of **B**, which in turn forms the oxonium intermediate **C**. In cases where nucleophilic attack of the ligand R takes place from the 2′-*O*-aluminate (path a), only the syn-ring-opened products (**13*β*−18*β***) should result, whereas such attack of R from the base moiety (path b) would permit the formation of both anti- and syn-ring-opened products depending on the conformation about the $N^1{-}C^{1'}$ pivot bond.

On the basis of the above proposed reaction mechanism, we anticipated that the introduction of a sterically demanding protecting group to the N^3-position would lead to the sole formation of the *β*-anomer by preventing coordination of R_3Al to the C^2-carbonyl oxygen. This turned out to be the case. When the N^3-benzyloxymethyl 1′,2′-unsaturated uridine **19**, prepared from **11**, was oxidized with DMDO and then reacted with Me_3Al, **20*β*** was obtained in 93% yield without any trace amount of the α-isomer being formed. The exclusive syn-ring opening was also observed in the reaction with Et_3Al and *i*-Bu_3Al to give **21*β*** (75%) and **22*β*** (39%), respectively, as the sole product. Hydrogenolysis of **20*β*** in the presence of 5% Pd/C gave **13*β*** in excellent yield.



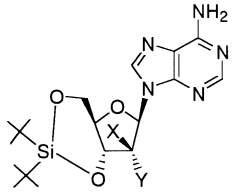
19 P = CH_2OCH_2Ph (BOM)
23 P = COPh (Bz)



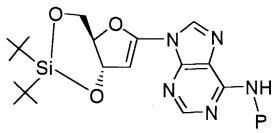
20β P = BOM, R = Me
21β P = BOM, R = Et
22β P = BOM, R = *i*-Bu
24β P = Bz, R = C≡CH
25β P = Bz, R = CH=CH_2
26β P = Bz, R = N_3
27β P = H, R = N_3

In cases where the 1′-substituents to be introduced are susceptible to hydrogenation conditions, the N^3-benzoylated substrate **23** was used. This substrate was prepared through benzoylation of 3′,5′-*O*-(di-*tert*-butylsilylene)-2′-deoxy-2′-phenylselenouridine[12] and subsequent oxidative syn elimination. The epoxide derived from **23** again underwent exclusive syn-ring opening upon reacting with $HC{\equiv}CAlEt_2$ (**24*β***, 53%), $(H_2C{=}CH)_3Al$ (**25*β***, 75%), and N_3AlEt_2 (**26b**, 52%). Debenzoylation of these products can be carried out with NH_3/MeOH to give the corresponding N^3-deprotected derivatives (**16*β***, **17*β***, and **27*β***) in quantitative yields.

Finally, we turned our attention to the synthesis of 1′-substituted adenosines. The substrate **31** for DMDO oxidation was prepared from 3′,5′-*O*-DTBS-adenosine **28**.[15] Thus, treatment of **28** with I_2/Ph_3P/imidazole in refluxing dioxane gave 2′-deoxy-2′-iodo-arabinofuranosyl nucleoside **29** (72%) after acidic hydrolysis of the resulting N^6-phosphorane.[16] Elimination reaction of **29** was effected with DBN in refluxing CH_3CN to give **30** (68%). To prevent oxidation at the N^1-position with DMDO,[17] **30** was further converted to the N^6-pivaloyl derivative **31** (90%).



28 X = H, Y = OH
29 X = I, Y = H



30 P = H
31 P = $COCMe_3$

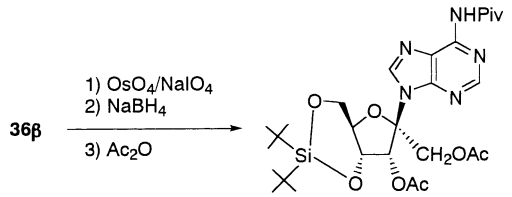
Epoxidation of **31** with DMDO was carried out under the same reaction conditions as the case for the 1′,2′-unsaturated uridine **11**. Although no attempt was made to analyze the diastereomeric purity of the resulting

(15) Furusawa, K.; Ueno, K.; Katsura, T. *Chem. Lett.* **1990**, 97−100.
(16) Gimisis, T.; Ialongo, G.; Chatgilialoglu, C. *Tetrahedron* **1998**, *54*, 573−592.
(17) DMDO oxidation at the base moiety of adenosine derivatives has been reported: Saladino, R.; Crestini, C.; Bernini, R.; Mincione, E.; Ciafrino, R. *Tetrahedron Lett.* **1995**, *36*, 2665−2668.

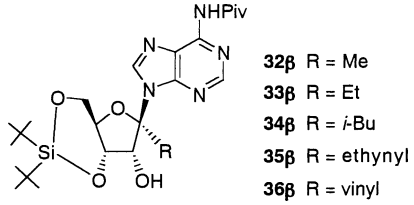
TABLE 2. Synthesis of 32β-36β from the Epoxide Derived from 31

entry	R_3Al (equiv)	time (h)	temp (°C)	product	yield (%)
1	Me_3Al (3)	4.5	−30	**32β**	80
2	Et_3Al (3)	4.5	−30	**33β**	59
3	*i*-Bu_3Al (6)	4.5	−30	**34β**	37
4	$(HC{\equiv}C)_3Al$ (6)	7.0	−30 to rt	**35β**	39
5	$(H_2C{=}CH)_3Al$ (6)	4.5	−30	**36β**	68

SCHEME 4



epoxide, its reaction with Me_3Al gave the 1′-methyladenosine derivative **32β** in 80% yield (entry 1 in Table 2). Under similar reaction conditions, Et_3Al, *i*-Bu_3Al, $(HC{\equiv}C)_3Al$, and $(H_2C{=}CH)_3Al$ also effected the stereoselective C−C bond formation at the anomeric position to give **33β**−**36β** (entries 2−5). No formation of the



corresponding α-anomers was observed throughout these reactions. The 1′-vinyl derivative **36β** could be transformed to protected angustmycin C (**37**) through oxidative cleavage of the double bond with $OsO_4/NaIO_4$, hydride reduction of the resulting aldehyde, and acetylation of the diol. This is the first example that protected angustmycin C was synthesized from adenosine. In conclusion, we have developed a novel method for the synthesis of ribofuranosyl nucleosides having a carbon substituent at the anomeric position by way of nucleophilic ring opening of 1′,2′-epoxy nucleoside with aluminum reagents. The epoxides were prepared by DMDO oxidation of 3′,5′-*O*-DTBS-protected 1′, 2′-unsaturated nucleosides. Although nucleophilic ring opening of the 1′,2′-α-epoxyuridine derivative **12** gave a mixture of β- and α-anomers, benzyloxymethyl or benzoyl protection at the N^3-position completely suppressed the formation of the α-anomer. This synthetic method enabled us to introduce a variety of carbon substituents as well as an azido group at the amomeric position of uridine. A similar approach was successfully adopted to 3′,5′-*O*-DTBS-protected 1′,2′-unsaturated N^6-pivaloyladenosine **31**. Evaluation of the biological activities of deprotected 1′-branched nucleoside analogues is in progress.

Experimental Section

Melting points are uncorrected. ^1H NMR was measured at 400 or 500 MHz. Chemical shifts are reported relative to Me_4Si. Mass spectra (MS) were taken in FAB mode (*m*-nitrobenzyl alcohol as a matrix). Column chromatography was carried out on silica gel (Silica Gel 60, Merck). Thin-layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck). HPLC was carried out on a Shimadzu LC-6AD with a shim-pack PREP-SIL(H)·KIT column (2 × 25 cm^2).

***N*³-Benzyloxymethyl-1-[3,5-*O*-(di-*tert*-butylsilylene)-2-deoxy-D-*erythro*-pento-1-enofuranosyl]uracil (19).** A stirred DMF (30 mL) solution of **11** (500 mg, 1.4 mmol) was treated with DBU (0.5 mL, 2.8 mmol) and then with benzyloxymethyl chloride (0.4 mL, 2.8 mmol) at 0 °C. After being stirred for 3.5 h at room temperature, the reaction mixture was partitioned between EtOAc/H_2O. Column chromatography (hexane/EtOAc = 3/1) of the organic layer gave **19** (614 mg, 93%) as a foam: UV (MeOH) λ_{max} 268 nm (ε 10 000), λ_{min} 247 nm (ε 9 000); ^1H NMR ($CDCl_3$) δ 0.96 and 0.99 (18H, each as s), 4.10 (1H, dd, $J_{4',5'a}$ = 11.0 Hz and $J_{5'a,5'b}$ = 8.3 Hz), 4.17 (1H, ddd, $J_{4',5'a}$ = 11.0 Hz, $J_{4',5'b}$ = 4.6 Hz, and $J_{3',4'}$ = 10.4 Hz), 4.40 (1H, dd, $J_{5'a,5'b}$ = 8.3 Hz and $J_{4',5'b}$ = 4.6 Hz), 4.62 (2H, s), 5.23 (1H, dd, $J_{3',4'}$ = 10.4 Hz and $J_{2',3'}$ = 1.7 Hz), 5.42 (2H, s), 5.70 (1H, d, $J_{5,6}$ = 8.2 Hz), 5.77 (1H, d, $J_{2',3'}$ = 1.7 Hz), 7.16−7.30 (5H, m), 7.42 (1H, d, $J_{5,6}$ = 8.2 Hz); FAB-MS *m*/*z* 487 (M^+ + H). Anal. Calcd for $C_{25}H_{34}N_2O_6Si$: C, 61.70; H, 7.04; N, 5.76. Found: C, 61.57; H, 7.18; N, 5.67.

***N*³-Benzyloxymethyl-3′,5′-*O*-(di-*tert*-butylsilylene)-1′-methyluridine (20β).** This compound was prepared from **19** (50 mg, 0.1 mmol) through DMDO oxidation followed by the reaction with Me_3Al (6 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography (hexane/EtOAc = 3/1) of the organic layer gave **20β** (49.8 mg, 93%, foam): UV (MeOH) λ_{max} 267 nm (ε 9400), λ_{min} 234 nm (ε 1500); ^1H NMR ($CDCl_3$) δ 1.03 and 1.05 (18H, each as s), 1.75 (3H, s), 2.57 (1H, br), 3.76 (1H, dd, $J_{3',4'}$ = 9.0 Hz and $J_{2',3'}$ = 4.6 Hz), 3.93 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'a}$ = 10.4 Hz), 4.12 (1H, ddd, $J_{4',5'a}$ = 10.4 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.0 Hz), 4.48 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'b}$ = 5.1 Hz), 4.66 (1H, d, $J_{2',3'}$ = 4.6 Hz), 4.73 (2H, s), 5.48 (2H, s), 5.70 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.23−7.37 (5H, m), 7.64 (1H, d, $J_{5,6}$ = 8.4 Hz); NOE experiment, CH_3-1′/H-4′(1.8%), H-6/H-5′a (1.6%), H-6/H-3′ (2.4%); FAB-MS *m*/*z* 520 (M^+ + H). Anal. Calcd for $C_{26}H_{38}N_2O_7Si$: C, 60.21; H, 7.38; N, 5.40. Found: C, 60.21; H, 7.54; N, 5.14.

***N*³-Benzyloxymethyl-3′,5′-*O*-(di-*tert*-butylsilylene)-1′-ethyluridine (21β).** This compound was prepared from **19** (50 mg, 0.1 mmol) through DMDO oxidation followed by the reaction with Et_3Al (3 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 3/1) gave **21β** (40.9 mg, 75%, foam): UV (MeOH) λ_{max} 267 nm (ε 9100), λ_{min} 234 nm (ε 1200); ^1H NMR ($CDCl_3$) δ 0.71 (3H, t, *J* = 7.5 Hz), 1.03 and 1.05 (18H, each as s), 2.00 (1H, dt, *J* = 7.5 Hz and J_{gem} = 7.3 Hz), 2.52 (1H, br), 2.63 (1H, dt, *J* = 7.5 Hz and J_{gem} = 7.3 Hz), 3.77 (1H, dd, $J_{3',4'}$ = 9.7 Hz and $J_{2',3'}$ = 4.8 Hz), 3.95 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'a}$ = 10.6 Hz), 4.09 (1H, ddd, $J_{4',5'a}$ = 10.6 Hz, $J_{4',5'b}$ = 4.9 Hz, and $J_{3',4'}$ = 9.7 Hz), 4.49 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'b}$ = 4.9 Hz), 4.68 (1H, d, $J_{2',3'}$ = 4.8 Hz), 4.72 (2H, s), 5.49 (2H, s), 5.69 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.24−7.38 (5H, m), 7.60 (1H, d, $J_{5,6}$ = 8.4 Hz); NOE experiment, CH_3CH_{2a}-1′/H-4′ (4.4%), H-6/H-5′a (4.9%), H-6/H-3′ (3.7%); FAB-MS *m*/*z* 533 (M^+ + H). Anal. Calcd for $C_{27}H_{40}N_2O_7Si\cdot{}^1/_{10}H_2O$: C, 60.67; H, 7.58; N, 5.24. Found: C, 60.77; H, 7.67; N, 4.95.

***N*³-Benzyloxymethyl-3′,5′-*O*-(di-*tert*-butylsilylene)-1′-isobutyluridine (22β).** This compound was prepared from **19** (50 mg, 0.1 mmol) through DMDO oxidation followed by the reaction with *i*-Bu_3Al (6 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 3/1) gave **22β** (22.3 mg, 39%, foam): UV (MeOH) λ_{max} 267 nm (ε 10 500), λ_{min} 236 nm (ε 4 000); ^1H NMR ($CDCl_3$) δ 0.79 (3H, d, *J* = 6.6 Hz), 0.90 (3H, d, *J* = 6.8 Hz), 1.03 and

1.05 (18H, each as s), 1.47 (1H, m), 1.81 (1H, dd, J = 7.0 Hz and J_{gem} = 15.2 Hz), 2.46 (1H, br), 2.65 (1H, dd, J = 5.3 Hz and J_{gem} = 15.2 Hz), 3.75 (1H, dd, $J_{3',4'}$ = 9.6 Hz and $J_{2',3'}$ = 4.4 Hz), 3.95 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'a}$ = 10.3 Hz), 4.12 (1H, ddd, $J_{4',5'a}$ = 10.3 Hz, $J_{4',5'b}$ = 4.9 Hz, and $J_{3',4'}$ = 9.6 Hz), 4.50 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'b}$ = 4.9 Hz), 4.61 (1H, d, $J_{2',3'}$ = 4.4 Hz), 4.70 (2H, s), 5.49 (2H, s), 5.72 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.26−7.37 (5H, m), 7.66 (1H, d, $J_{5,6}$ = 8.4 Hz); NOE experiment, CH_3CH_{2a}-1′/H-4′ (1.9%), H-6/H-5′a (5.1%), H-6/H-3′ (2.1%); FAB-MS *m*/*z* 561 (M^+ + H). Anal. Calcd for $C_{29}H_{44}N_2O_7Si \cdot {}^1/_{10}H_2O$: C, 61.92; H, 7.92; N, 4.98. Found: C, 61.81; H, 8.05; N, 4.72.

Hydrogenolysis of 20*β* To Yield 13*β*. A mixture of **20*β*** (43 mg, 0.08 mmol) and 5% Pd/C (15 mg) in MeOH (4 mL) was stirred at room temperature for 6 h under positive pressure of H_2. Removal of the catalyst by filtration was followed by evaporation of the solvent. This gave **13*β*** (33 mg, 100%), which was identical by ^{1}H NMR spectroscopy with that prepared from **12**.

***N*³-Benzoyl-1-[3,5-*O*-(di-*tert*-butylsilylene)-2-deoxy-D-*erythro*-pento-1-enofuranosyl]uracil (23).** To a mixture of 3′,5′-*O*-(di-*tert*-butylsilylene-2′-deoxy-2′-phenylselenouridine[12b] (1.25 g, 2.4 mmol) and *i*-Pr_2NEt (2.5 mL, 14.3 mmol) in CH_2Cl_2 (50 mL) was added benzoyl chloride (1.7 mL, 14.3 mmol) at 0 °C. After being stirred for 2 h at room temperature, the reaction mixture was partitioned between CH_2Cl_2 and sat. aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc = 5/1) of the organic layer gave the N^3-benzoyl derivative (1.38 g, 92%) as a pale yellow foam. Oxidation of this product (937 mg, 1.49 mmol) was carried out by reacting it with *m*-CPBA (468 mg, 2.09 mmol) in CH_2Cl_2 (5 mL) at 0 °C for 2 h. Neutralization of the oxidation mixture with Et_3N was followed by partition between CH_2Cl_2/sat. aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc = 1/3) of the organic layer gave the corresponding selenoxide (896 mg, 93%, foam). Compound **23** (338 mg, 56%, foam) was formed by heating the above selenoxide (825 mg, 1.28 mmol) in THF (15 mL) containing Et_3N (0.72 mL, 5.13 mmol) at 50 °C for 4 h. Isolation of **23** was carried out by column chromatography (hexane/EtOAc = 5/1).

Physical data for **23**: foam; ^{1}H NMR ($CDCl_3$) δ 1.03 and 1.05 (18H, each as s), 4.19 (1H, dd, $J_{4',5'a}$ = 11.0 Hz and $J_{5'a,5'b}$ = 8.3 Hz), 4.26 (1H, ddd, $J_{4',5'a}$ = 11.0 Hz, $J_{4',5'b}$ = 4.6 Hz, and $J_{3',4'}$ = 10.8 Hz), 4.50 (1H, dd, $J_{5'a,5'b}$ = 8.3 Hz and $J_{4',5'b}$ = 4.6 Hz), 5.30 (1H, dd, $J_{3',4'}$ = 10.8 Hz and $J_{2',3'}$ = 1.7 Hz), 5.82 (1H, d, $J_{2',3'}$ = 1.7 Hz), 5.89 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.49−7.93 (5H, m), 7.93 (1H, d, $J_{5,6}$ = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 20.24, 22.52, 27.19, 27.42, 66.50, 79.70, 82.56, 96.46, 102.88, 129.22, 130.47, 131.08, 135.30, 138.75, 145.03, 146.03, 146.97, 161.04, 167.84; FAB-HRMS *m*/*z* calcd for $C_{24}H_{31}N_2O_6Si$ 471.1951, found 471.1992 (M^+ + H).

N*³-Benzoyl-3′,5′-*O*-(di-*tert*-butylsilylene)-1′-ethynyluridine (24*β*).** This compound was prepared from **23** (50 mg, 0.11 mmol) through DMDO oxidation followed by the reaction with $HC{\equiv}CAlEt_2$ (6 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 5/1) gave **24*β (28.9 mg, 53%, foam): ^{1}H NMR ($CDCl_3$) δ 1.03 and 1.06 (18H, each as s), 2.88 (1H, s), 3.02 (1H, br), 3.97 (1H, dd, $J_{3',4'}$ = 9.7 Hz and $J_{2',3'}$ = 4.8 Hz), 4.00 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'a}$ = 10.2 Hz), 4.13 (1H, ddd, $J_{4',5'a}$ = 10.2 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.7 Hz), 4.53 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'b}$ = 5.1 Hz), 4.71 (1H, d, $J_{2',3'}$ = 4.8 Hz), 5.86 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.48−7.68 and 7.91−7.93 (5H, m), 7.82 (1H, d, $J_{5,6}$ = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 20.39, 22.71, 27.08, 27.28, 66.86, 74.93, 75.04, 76.40, 78.27, 93.66, 102.29, 129.23, 130.50, 130.55, 131.24, 135.29, 138.07, 148.63, 161.76, 168.20; FAB-HRMS *m*/*z* calcd for $C_{26}H_{33}N_2O_7Si$ 513.2057, found 513.2064 (M^+ + H).

N*³-Benzoyl-3′,5′-*O*-(di-*tert*-butylsilylene)-1′-vinyluridine (25*β*).** This compound was prepared from **23** (75 mg, 0.16 mmol) through DMDO oxidation followed by the reaction with trivinylaluminum (6 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 4/1) gave **25*β (61.5 mg, 75%, foam): UV (MeOH) λ_{max} 254 nm (ϵ 20 800), λ_{min} 226 nm (ϵ 6 100); ^{1}H NMR ($CDCl_3$) δ 1.01 and 1.08 (18H, each as s), 2.57 (1H, br), 3.96 (1H, dd, $J_{3',4'}$ = 9.6 Hz and $J_{2',3'}$ = 4.6 Hz), 4.03 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'a}$ = 10.6 Hz), 4.16 (1H, ddd, $J_{4',5'a}$ = 10.6 Hz, $J_{4',5'b}$ = 4.9 Hz, and $J_{3',4'}$ = 9.6 Hz), 4.56 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'b}$ = 4.9 Hz), 4.90 (1H, d, $J_{2',3'}$ = 4.6 Hz), 5.46 (1H, dd, $J_{CH_{2a}=CH}$ = 10.8 and J_{gem} = 1.1 Hz), 5.58 (1H, dd, $J_{CH_{2b}=CH}$ = 17.2 Hz and J_{gem} = 1.1 Hz), 5.81 (1H, d, $J_{5,6}$ = 8.5 Hz), 6.54 (1H, dd, $J_{CH_2=CH}$ = 17.2 and 10.8 Hz), 7.48−7.68 and 7.89−7.91 (5H, m), 7.78 (1H, d, $J_{5,6}$ = 8.5 Hz); NOE experiment, $CH_2{=}CH$-1′/H-4′ (0.9%), H-6/H-5′a (2.9%); FAB-MS *m*/*z* 516 (M^+ + H). Anal. Calcd for $C_{26}H_{34}N_2O_7Si$: C, 60.68; H, 6.66; N, 5.44. Found: C, 60.49; H, 6.64; N, 5.40.

Preparation of Trivinylaluminum (0.25 M Solution). To a stirred CH_2Cl_2 (16.7 mL) solution of $AlCl_3$ (1.0 g, 7.5 mmol) was added vinylmagnesium chloride (1.7 M in THF solution) at 0 °C under Ar atmosphere and the mixture was stirred overnight. The resulting solution was used for the vinylation reaction.

1′-Azido-*N*³-benzoyl-3′,5′-*O*-(di-*tert*-butylsilylene)-uridine (26*β*). This compound was prepared from **23** (75 mg, 0.16 mmol) through DMDO oxidation followed by the reaction with N_3AlEt_2 (toluene solution, 3 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 4/1) gave **26*β*** (44.2 mg, 52%, foam): ^{1}H NMR ($CDCl_3$) δ 1.04 and 1.07 (18H, each as s), 2.95 (1H, br), 3.97 (1H, dd, $J_{3',4'}$ = 9.8 Hz and $J_{2',3'}$ = 4.8 Hz), 3.99 (1H, dd, $J_{5'a,5'b}$ = 9.1 Hz and $J_{4',5'a}$ = 10.7 Hz), 4.43 (1H, ddd, $J_{4',5'a}$ = 10.7 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.8 Hz), 4.57 (1H, dd, $J_{5'a,5'b}$ = 9.1 Hz and $J_{4',5'b}$ = 5.1 Hz), 4.97 (1H, d, $J_{2',3'}$ = 4.8 Hz), 5.84 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.49−7.69 and 7.90−7.93 (5H, m), 7.77 (1H, d, $J_{5,6}$ = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 20.44, 22.72, 27.03, 27.24, 66.66, 75.23, 75.63, 75.95, 102.60, 105.91, 129.28, 130.47, 131.10, 135.36, 137.76, 148.71, 161.59, 168.08; NOE experiment, 2′-OH/H-4′ (1.1%), H-6/H-5′a (3.8%), H-6/H-3′ (2.8%); FAB-HRMS *m*/*z* calcd for $C_{24}H_{32}N_5O_7Si$ 530.2071, found 530.2108 (M^+ + H); IR (neat) 2136 cm^{-1}.

1′-Azido-3′,5′-*O*-(di-*tert*-butylsilylene)uridine (27*β*): Debenzoylation of 26*β* as a Typical Procedure. Compound **26*β*** (28 mg) in NH_3/MeOH (7 mL) was stirred for 1 h at room temperature. Evaporation followed by column chromatography (hexane/EtOAc = 2/1) of the reaction mixture gave **27*β*** (22 mg, 100%, foam): ^{1}H NMR ($CDCl_3$) δ 1.05 (18H, each as s), 3.91 (1H, dd, $J_{3',4'}$ = 9.7 Hz and $J_{2',3'}$ = 4.7 Hz), 3.96 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'a}$ = 10.3 Hz), 4.34 (1H, br), 4.57 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'b}$ = 5.1 Hz), 4.49 (1H, ddd, $J_{4',5'a}$ = 10.3 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.7 Hz), 4.77 (1H, d, $J_{2',3'}$ = 4.7 Hz), 5.77 (1H, d, $J_{5,6}$ = 8.3 Hz), 7.70 (1H, d, $J_{5,6}$ = 8.3 Hz), 9.65 (1H, br); ^{13}C NMR ($CDCl_3$) δ 22.40, 22.73, 27.06, 27.30, 66.99, 74.93, 75.50, 75.63, 102.03, 106.16, 139.14, 150.05, 163.34; NOE experiment, H-6/H-3′ (0.9%), H-6/H-5′a (3.8%); FAB-HRMS *m*/*z* calcd for $C_{17}H_{28}N_5O_6Si$ 426.1809, found 426.1821 (M^+ + H); IR (neat) 2123 cm^{-1}.

3′,5′-*O*-(Di-*tert*-butylsilylene)-1′-methyl-*N*⁶-pivaloyladenosine (32*β*). This compound was prepared from **31** (50 mg, 0.11 mmol) through DMDO oxidation followed by the reaction with Me_3Al (3 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 2/1) gave **32*β*** (42.5 mg, 80%, foam): ^{1}H NMR ($CDCl_3$) δ 0.99 and 1.03 (18H, each as s), 1.41 (9H, s), 1.95 (3H, s), 3.26 (1H, br), 3.98 (1H, dd, $J_{3',4'}$ = 9.5 Hz and $J_{2',3'}$ = 4.2 Hz), 4.02 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'a}$ = 10.4 Hz), 4.29 (1H,

ddd, $J_{4',5'a}$ = 10.4 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.5 Hz), 4.56 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'b}$= 5.1 Hz), 4.93 (1H, d, $J_{2',3'}$ = 4.2 Hz), 8.23 (1H, s), 8.51 (1H, br), 8.74 (1H, s); ^{13}C NMR ($CDCl_3$) δ 20.26, 22.17, 22.52, 27.18, 27.31, 40.33, 67.55, 73.72, 74.58, 76.28, 98.49, 124.39, 140.36, 149.53, 150.14, 152.10, 175.68; NOE experiment, 2′-OH/H-4′ (1.3%), CH_3-1′/H-4′ (1.2%), H-2/H-5′a (2.8%); FAB-HRMS *m/z* calcd for $C_{24}H_{40}N_5O_5Si$ 506.2799, found 506.2834 (M^+ + H).

3′,5′-*O*-(Di-*tert*-butylsilylene)-1′-ethyl-*N*^{6}-pivaloyladenosine (33*β*). This compound was prepared from **31** (50 mg, 0.11 mmol) through DMDO oxidation followed by the reaction with Et_3Al (3 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 2/1) gave **33*β*** (32.3 mg, 59%, foam): ^{1}H NMR ($CDCl_3$) δ 0.58 (3H, t, J = 7.4 Hz), 0.98 and 1.03 (18H, each as s), 1.41 (9H, s), 2.30 (1H, dt, J = 7.4 Hz and J_{gem} = 7.3 Hz), 2.62 (1H, dt, J = 7.4 Hz and J_{gem} = 7.3 Hz), 2.99 (1H, br), 3.94 (1H, dd, $J_{3',4'}$ = 9.7 Hz and $J_{2',3'}$ = 4.4 Hz), 4.01 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'a}$ = 10.6 Hz), 4.25 (1H, ddd, $J_{4',5'a}$ = 10.6 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.7 Hz), 4.57 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'b}$ = 5.1 Hz), 5.01 (1H, d, $J_{2',3'}$ = 4.4 Hz), 8.20 (1H, s), 8.51 (1H, s), 8.74 (1H, s); ^{13}C NMR ($CDCl_3$) δ 5.78, 20.36, 22.61, 25.98, 27.19, 27.24, 27.41, 40.44, 67.72, 74.01, 74.58, 76.21, 100.59, 124.27, 141.41, 150.14, 152.29, 175.70; NOE experiment, 2′-OH/H-4′ (1.3%), H-2/H-5′a (1.7%), H-2/H-3′ (1.0%); FAB-HRMS *m/z* calcd for $C_{25}H_{42}N_5O_5Si$ 520.2955, found 520.2979 (M^+ + H).

3′,5′-*O*-(Di-*tert*-butylsilylene)-1′-isobutyl-*N*^{6}-pivaloyladenosine (34*β*). This compound was prepared from **31** (50 mg, 0.11 mmol) through DMDO oxidation followed by the reaction with *i*-Bu_3Al (3 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 3/1) gave **34*β*** (21.6 mg, 37%, foam): UV (MeOH) λ_{max} 274 nm (ϵ 19 000),λ_{min} 236 nm (ϵ 5 900); ^{1}H NMR ($CDCl_3$) δ 0.49 (3H, d, J = 6.6 Hz), 0.90 (3H, d, J = 6.6 Hz), 0.98 and 1.04 (18H, each as s), 1.19 (1H, m), 1.41 (9H, s), 2.13 (1H, dd, J = 7.5 Hz and J_{gem} = 15.2 Hz), 2.65 (1H, dd, J = 4.8 Hz and J_{gem} = 15.2 Hz), 2.81 (1H, br), 3.89 (1H, dd, $J_{3',4'}$ = 9.8 Hz and $J_{2',3'}$ = 4.3 Hz), 4.01 (1H, dd, $J_{5'a,5'b}$ = 9.1 Hz and $J_{4',5'a}$ = 10.5 Hz), 4.27 (1H, ddd, $J_{4',5'a}$ = 10.5 Hz, $J_{4',5'b}$ = 4.9 Hz, and $J_{3',4'}$ = 9.8 Hz), 4.56 (1H, dd, $J_{5'a,5'b}$ = 9.1 Hz and $J_{4',5'b}$ = 4.9 Hz), 4.84 (1H, d, $J_{2',3'}$ = 4.3 Hz), 8.18 (1H, s), 8.50 (1H, br), 8.76 (1H, s); NOE experiment, 2′-OH/H-4′ (1.5%), H-2/H-5′a (1.9%), H-6/H-3′ (1.0%); FAB-MS *m/z* 548 (M^+ + H). Anal. Calcd for $C_{27}H_{45}N_5O_5Si\cdot{}^1/_3H_2O$: C, 58.56; H, 8.31; N, 12.65. Found: C, 58.74; H, 8.47; N, 12.42.

3′,5′-*O*-(Di-*tert*-butylsilylene)-1′-ethynyl-*N*^{6}-pivaloyladenosine (35*β*). This compound was prepared from **31** (80 mg, 0.17 mmol) through DMDO oxidation followed by the reaction with triethynylaluminum (5 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 2/1) gave **35*β*** (51.3 mg, 59%, foam): ^{1}H NMR ($CDCl_3$) δ 1.06 (18H, each as s), 1.40 (9H, s), 3.06 (1H, s), 3.67 (1H, br), 4.05 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'a}$ = 10.4 Hz), 4.35 (1H, ddd, $J_{4',5'a}$ = 10.4 Hz, $J_{4',5'b}$ = 5.1 Hz, and $J_{3',4'}$ = 9.6 Hz), 4.52 (1H, dd, $J_{5'a,5'b}$ = 9.2 Hz and $J_{4',5'b}$ = 5.1 Hz), 4.58 (1H, dd, $J_{3',4'}$ = 9.6 Hz and $J_{2',3'}$ = 4.9 Hz), 5.12 (1H, d, $J_{2',3'}$ = 4.9 Hz), 8.40 (1H, s), 8.49 (1H, br), 8.76 (1H, s); ^{13}C NMR ($CDCl_3$) δ 20.37, 22.67, 27.15, 27.27, 27.40, 40.49, 67.07, 74.94, 75.52, 76.46, 79.57, 92.03, 124.20, 140.86, 149.82, 150.31, 152.58, 175.63; NOE experiment, H-3′/H-2 (1.6%), H-2/H-5′a (2.7%), H-2/H-2′ (0.5%); FAB-HRMS *m/z* calcd for $C_{25}H_{38}N_5O_5Si$ 516.2642, found 516.2594 (M^+ + H).

3′,5′-*O*-(Di-*tert*-butylsilylene)-*N*^{6}-pivaloy-1′-vinyladenosine (36*β*). This compound was prepared from **31** (36 mg, 0.08 mmol) through DMDO oxidation followed by the reaction with trivinylaluminum (5 equiv). The procedures employed were essentially the same as those described for the preparation of **8** from **2**. The Celite filtrate was partitioned between $CHCl_3$/H_2O. Column chromatography of the organic layer (hexane/EtOAc = 1.5/1) gave **36*β*** (22.4 mg, 68%, foam): UV (MeOH) λ_{max} 273 nm (ϵ 18 200), λ_{min} 235 nm (ϵ 5 800); ^{1}H NMR ($CDCl_3$) δ 1.01 and 1.03 (18H, each as s), 1.40 (9H, s), 2.95 (1H, br), 4.03 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'a}$ = 10.4 Hz), 4.19 (1H, dd, $J_{3',4'}$ = 9.7 Hz and $J_{2',3'}$ = 4.2 Hz), 4.29 (1H, ddd, $J_{4',5'a}$ = 10.4 Hz, $J_{4',5'b}$ = 4.9 Hz, and $J_{3',4'}$ = 9.7 Hz), 4.59 (1H, dd, $J_{5'a,5'b}$ = 9.0 Hz and $J_{4',5'b}$ = 4.9 Hz), 5.27 (1H, d, $J_{2',3'}$ = 4.2 Hz), 5.37 (1H, dd, J = 17.1 Hz and J_{gem} = 0.8 Hz), 5.43 (1H, dd, J = 10.7 Hz and J_{gem} = 0.8 Hz), 6.58 (1H, dd, J = 17.1 Hz and 10.7 Hz), 8.20 (1H, s), 8.49 (1H, s), 8.74 (1H, s); NOE experiment, 2′-OH/H-4′ (2.8%), H-2/H-5′a (2.2%), H-2/H-3′ (1.0%); FAB-MS *m/z* 518 (M^+ + H). Anal. Calcd for $C_{25}H_{39}N_5O_5Si$: C, 57.60; H, 7.61; N, 13.45. Found: C, 57.78; H, 7.78; N, 13.19.

9-[1,3-Di-*O*-acetyl-4,6-*O*-(di-*tert*-butylsilylene)-*β*-D-psicofuranosyl]-*N*^{6}-pivaloyladenine (37). To a stirred 75% dioxane (5 mL) solution of **36*β*** (53.5 mg, 0.10 mmol) and $NaIO_4$ (110.6 mg, 0.52 mmol) was added a 2% OsO_4 solution (0.13 mL, 0.01 mmol) and the mixture was stirred for 4 h at room temperature. After the reaction mixture was evaporated to dryness, $NaBH_4$ (3.9 mg, 0,10 mmol) was added to a stirred EtOH (5 mL) solution of the residue and the mixture was stirred for 30 min. The reaction mixture was filtered through Celite and the filtrate was partitioned between AcOEt/sat. NaCl and the organic layer was purified by preparative TLC ($CHCl_3$/MeOH = 12/1) to give the diol. To a stirred pyridine (2 mL) solution of the diol was added Ac_2O (0.03 mL) at 0 °C and the mixture was stirred at room temperature for 9 h. The reaction mixture was partitioned between AcOEt/sat. $NaHCO_3$ and silica gel column chromatography ($CHCl_3$/MeOH = 40/1) of the organic layer gave **37** (17.1 mg, 27%) as a foam: ^{1}H NMR ($CDCl_3$) δ 0.96 and 1.00 (18H, each as s), 1.41 (9H, s), 1.87 and 2.25 (6H, each as s), 4.01 (1H, dd, $J_{5'a,5'b}$ = 9.4 Hz and $J_{4',5'a}$ = 10.3 Hz), 4.06 (1H, dd, $J_{3',4'}$ = 9.9 Hz and $J_{2',3'}$ = 4.4 Hz), 4.25 (1H, ddd, $J_{4',5'a}$ = 10.3 Hz, $J_{4',5'b}$ = 4.9 Hz, and $J_{3',4'}$ = 9.9 Hz), 4.58 (1H, dd, $J_{5'a,5'b}$ = 9.4 Hz and $J_{4',5'b}$ = 4.9 Hz), 4.79 (2H, s), 6.57 (1H, d, $J_{2',3'}$ = 4.4 Hz), 8.19 (1H, s), 8.48 (1H, br), 8.74 (1H, s); ^{13}C NMR ($CDCl_3$) δ 20.31, 20.54, 20.76, 22.70, 27.05, 27.20, 27.53, 40.46, 62.88, 67.37, 73.85, 75.02, 75.43, 95.68, 124.00, 140.76, 149.47, 150.49, 152.54, 168.03, 169.75, 175.52; FAB-HRMS *m/z* calcd for $C_{28}H_{44}N_5O_8Si$ 606.2959, found 606.2949 (M^+ + H).

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Supporting Information Available: Experimental procedures and full characterization for compounds **8**−**18b** and **29**−**31**. This material is available free of charge via the Internet at http://pubs.acs.org.

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