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NEW NEPLANOCIN ANALOGUES. 10. THE CONVERSION OF ADENOSINE TO NEPLANOCIN A, A CARBOCYCLIC NUCLEOSIDE ANTIBIOTIC WITH POTENT ANTIVIRAL ACTIVITY[1]

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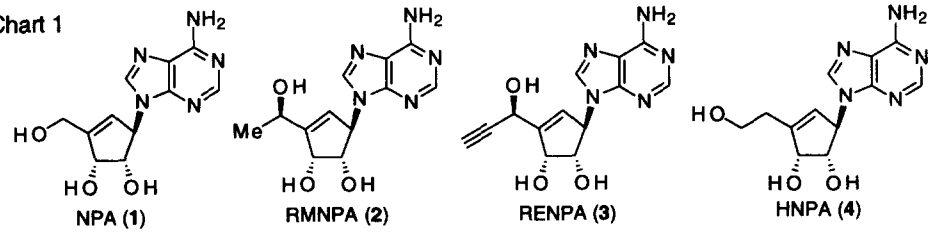
Abstract. Synthesis of neplanocin A, a potent antiviral carbocyclic nucleoside, from adenosine was achieved. An acyclic adeninenucleoside **21**, prepared from adenosine, was converted to 4'-keto acyclic derivative **27**. When **27** was treated with lithiotrimethylsilyldiazomethane in THF, a C-H insertion reaction at the 1'-position proceeded to give 6'-*O*-TBS-2',3'-*O*-isopropyrideneneplanocin A (**29**) along with its 1'-epimer **30**. © 1997 Elsevier Science Ltd.

S-Adenosylhomocysteine hydrolase (AdoHcy hydrolase), which is responsible for the hydrolysis of *S*-adenosyl-L-homocysteine to adenosine (Ado) and L-homocysteine (Hcy),[2,3] has been recognized as a good target for broad-spectrum antiviral agents.[2-4] Neplanocin A (NPA, **1**),[5] one of the most potent AdoHcy hydrolase inhibitors, has broad-spectrum antiviral activity.[6] However, NPA itself is apparently cytotoxic to host cells.[7] It has been recognized that the detrimental toxicity of NPA may be primarily due to the phosphorylation of the primary hydroxyl group at its 6'-position (the 6'-position of NPA corresponds to the 5'-position of Ado) by Ado kinase and subsequent metabolism by cellular enzymes.[7] NPA is also rapidly deaminated by Ado deaminase to a chemotherapeutically inactive inosine congener,[8] which may account for the reduced therapeutic potency of NPA, especially *in vivo*. Based on these observations, we studied structural modification of NPA[9] and found several potent antiviral derivatives of NPA, *e.g.* (6'*R*)-6'-*C*-methylneplanocin A (RMNPA, **2**),[9a-c] (6'*R*)-6'-*C*-ethynylneplanocin A (RENPA, **3**),[9i] 6'-homoneplanocin A (HNPA, **4**),[9f] which have excellent antiviral activities against various DNA and RNA viruses, yet show significantly less cytotoxicity than NPA.

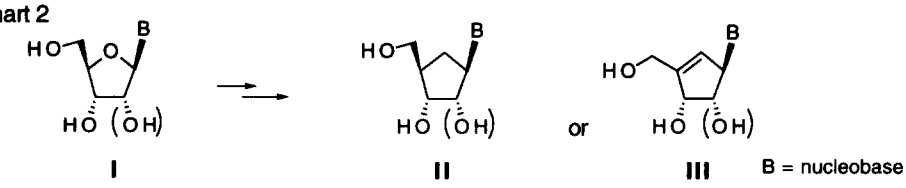
Chart 1



In these previous studies, NPA produced by *Ampullariella regularis* has been used as a starting material. However, its fermentation productivity is not efficient enough.[5a] On the other hand, the chemical synthesis of NPA has been extensively investigated, and several total syntheses have been achieved.[10] However, these

synthetic methods are not practical for providing enough NPA for use in chemical modification studies for biological evaluation. Therefore, an efficient alternative method for preparing NPA is needed.

Chart 2



The structures of carbocyclic nucleosides (**II** and **III**) are very similar to those of natural nucleosides (**I**), in which a tetrahydrofuran ring of the ribose moiety of natural nucleosides is replaced by a cyclopentane or cyclopentene ring (Chart 2). However, a synthesis of carbocyclic nucleosides from natural nucleosides has not been developed, probably due to the difficulty of constructing a carbocyclic moiety with the desired asymmetric centers. We describe here the conversion of adenosine to NPA *via* an intramolecular C-H insertion reaction of a methylidene carbene as a key step.

Chart 3

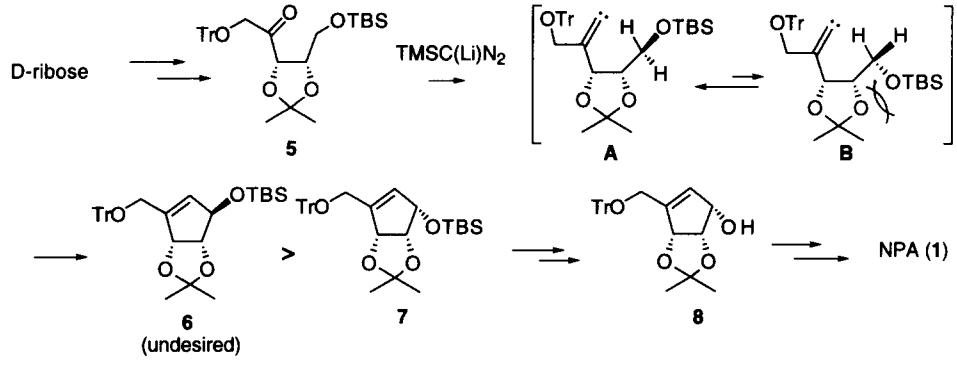
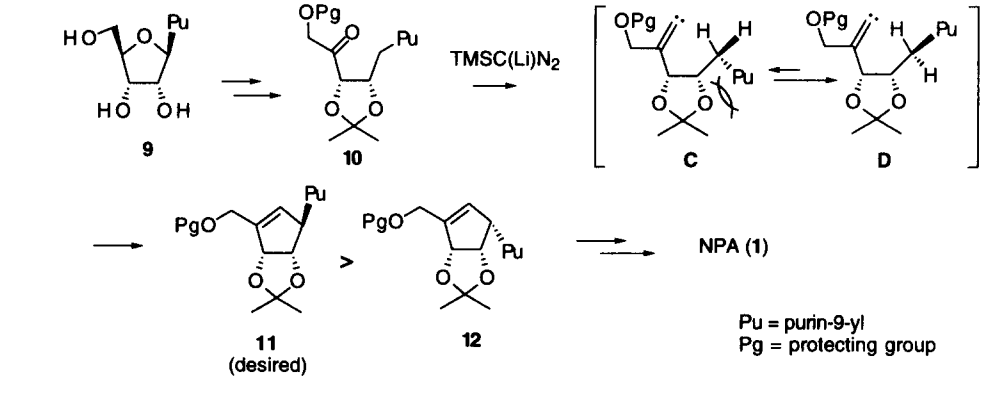
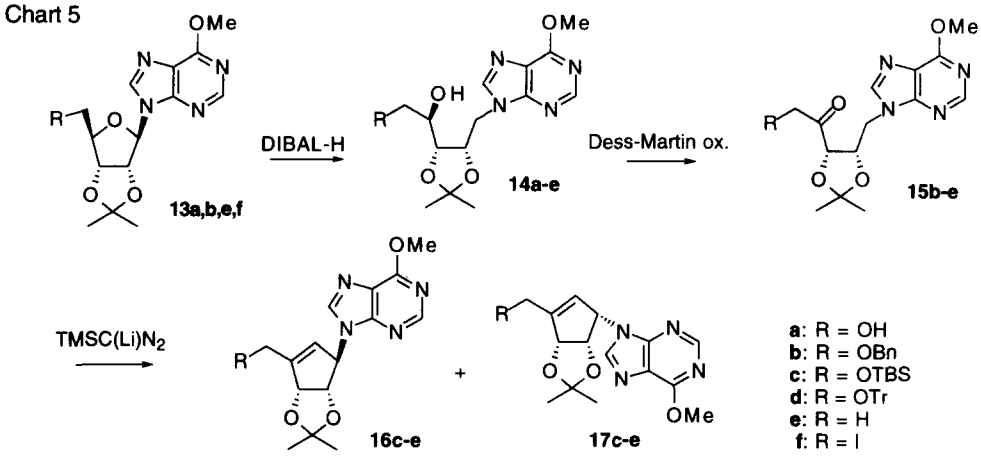


Chart 4



Recently, Ohira and co-workers reported a total synthesis of NPA starting from D-ribose, using a C-H insertion reaction of a methylidene carbene as a key step (Chart 3).[11] Although this is the shortest known method for the synthesis of NPA, the carbene insertion reaction gave the desired cyclopentene product **7** with a 1-α-configuration in only 15-18% yield, and the undesired diastereoisomer **6** was produced as a major product.[12] With regard to the alkylidene carbene intermediate in the C-H insertion reaction, two conformers, **A** and **B**, are conceivable, as shown in Chart 3; **B** would be unfavorable due to steric repulsion between the isopropylidene group and the bulky *t*-Bu(Me)$_2$SiO group, so that the undesired **6** would be produced predominantly *via* **A**. Based on this result, we hypothesized that NPA derivative **11** could be selectively obtained in a similar C-H insertion reaction of an alkylidene carbene with acyclic nucleoside **10** used as a substrate, since with regard to the alkylidene carbene intermediate, conformer **D** would be preferable to **C** due to the steric effect of the adenine group attached to the carbene inserting center, as shown in Chart 4. Substrate **10** was thought to be prepared from natural purine nucleosides *via* a reductive tetrahydrofuran-ring cleavage reaction of nucleosides with diisobutylaluminium hydride (DIBAL-H), recently developed by Kitade and co-workers.[13]

Chart 5



First, we used 6-methoxypurine nucleosides as substrates for derivatization: the 6-methoxypurine moiety is inert under various reaction conditions compared to the adenine moiety of adenosine itself, and can be converted to either an adenine or hypoxanthine residue after construction of the cyclopentene moiety. The synthetic scheme is shown in Chart 5. When 2',3'-*O*-isopropylidene-6-methoxypurine nucleoside **13a**, which was readily prepared from inosine, was treated with DIBAL-H in THF at room temperature,[13] the desired acyclic nucleoside **14a** was obtained in 62% yield. After the primary hydroxyl of **14a** was selectively protected by a *t*-butyldimethylsilyl (TBS) group, it was treated under Dess-Martin oxidation conditions[14] to give the ketone **15c**, a substrate for the C-H insertion reaction, quantitatively. Results of the C-H insertion reaction are summarized in Table 1. When **15c** was treated with 1.3 equiv of lithiotrimethylsilyldiazomethane in THF at 0 °C,[11] the C-H insertion reaction gave the carbocyclic nucleosides **16c** and **17c** in 22% yield as an epimeric mixture at the 1'-position. As expected, the reaction gave the desired β-isomer **16c** as the major product (α:β = 1:5). Reactions with an excess of lithiotrimethylsilyldiazomethane did not improve the yield of

the C-H insertion product (entries 2 and 3). However, a slightly better yield was observed with a much lower substrate concentration (entry 4).

Table 1. Synthesis of carbocyclic nucleosides by C-H insertion reaction of alkylidenecarbene

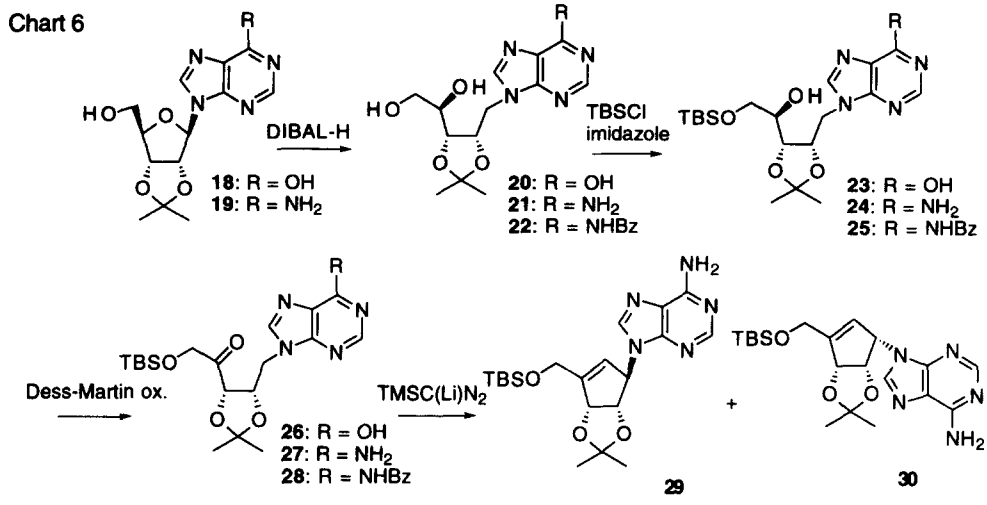
entry	substrate (concn)	TMSC(Li)N_2, equiv	product	% yield (α : β)
1	**15c** (0.1 M)	1.3	**16c,17c**	22 (1 : 5)
2	**15c** (0.1 M)	2.0	**16c,17c**	26 (1 : 5)
3	**15c** (0.1 M)	5.0	**16c,17c**	8 (1 : 5)
4	**15c** (0.02 M)	2.0	**16c,17c**	34 (1 : 5)
5	**15c** (0.005 M)	2.0	**16c,17c**	26 (1 : 5)
6	**15b** (0.02 M)	2.0	---	---
7	**15d** (0.02 M)	2.0	**16d,17d**	30 (1 : 2)
8	**15e** (0.02 M)	2.0	**16e,17e**	20 (1 : 10)
9	**26** (0.02 M)	2.0	---	---
10	**27** (0.02 M)	2.0	**29,30**	21 (1 : 4)
11	**28** (0.02 M)	2.0	---	---

[a]Reactions were parformed with 0.1 mmol of substrate at -78 °C and then 0 °C in THF.

Next, we performed the reaction with 5'-*O*-benzyl, 5'-*O*-trytyl (Tr), and 5'-deoxy derivatives (**15b**, **15d**, and **15e**, respectively) as substrates to investigate the influence of the protecting group of the 5'-hydroxyl on the C-H insertion reaction. 5'-*O*-Tr derivative **15d** was prepared from **14a** in a manner similar to that for preparing 5'-*O*-TBS derivative **15c**. 5'-*O*-Benzyl nucleoside **13b** was prepared from **13a** by a usual method. 5'-Deoxy-5'-iodo nucleoside **13f**, which was obtained by treating **13a** with an I_2/PPh_3/imidazole system[15] in benzene, was hydrogenated with Pd-charcoal to give the 5'-deoxy derivative **13e**. Dess-Martin oxidation of **14b** and **14e** gave the corresponding 4'-keto acyclic nucleosides **15b** and **15e**, respectively, which are substrates for the C-H insertion reaction. C-H insertion reactions were performed under the same reaction conditions as in entry 4 in Table 1. The reaction with 5'-*O*-Tr derivative **15d** gave a diastereomeric mixture of the cyclopentene products **16d** and **17d** in 30% yield (α:β = 1:2, entry 7). Although similar treatment of 5'-deoxy derivative **15e** gave the desired β-product with high selectivity (α:β = 1:10), the yield was not enough (entry 8). When the reaction was performed with 5'-benzyl derivative **15b**, none of the desired cyclopentene products were isolated.

We next investigated the C-H insertion reaction with substrates with a purine base, other than 6-methoxypurine; *i.e.*, namely, hypoxanthine derivative **26**, adenine derivative **27**,[13b] and N^6-benzoyladenine derivative **28**. These substrates were prepared starting from the corresponding nucleosides by a procedure similar to that described above (Chart 6). In the reaction of **26** and **28** with lithiotrimethylsilyldiazomethane, the corresponding carbocyclic nucleosides were not isolated. However, when adenine derivative **27** was subjected to the C-H insertion reaction, the protected NPA derivative **29** was obtained along with the corresponding α-diastereomer **30** in 20% yield in a ratio of 4:1 (entry 10). The spectral data of **29** were consistent with those of an authentic sample prepared from natural NPA.

Chart 6



In conclusion, we developed a convenient method for synthesizing NPA from adenosine. This is the first example of the conversion of a natural nucleoside into a carbocyclic nucleoside. Although further studies may be needed to develop a practical method for preparing NPA, this procedure provides NPA in only seven steps. Compound **29** (2,3-*O*-isopropylidene-6'-*O*-TBS-neplanocin A) can be used for synthetic study of 6'-modified analogues of neplanocin A .

Experimental Section

Melting points were determined on a Yanagimoto MP-3 micro-melting point apparatus and are uncorrected. The NMR spectra were recorded with a JEOL EX-270, -400 or, Bruker ARX-500 spectrometer with tetramethylsilane as an internal standard. Chemical shifts were reported in parts per million (δ), and signals are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). All exchangeable protons were detected by the addition of D_2O. Mass spectra were measured on a JEOL JMS-DX-303 spectrometer. Thin-layer chromatography was done on Merck coated plate $60F_{254}$. Silica gel column chromatography was done with Merck silica gel 5715.

9-(2,3-*O*-Isopropylidene-D-ribofuranosyl)-6-methoxypurine (13a). A solution of DMF (11.6 mL, 150 mmol) and thionyl chloride (21.9 mL, 300 mmol) in $CHCl_3$ (100 mL) was stirred at room temperature for 1 h. After a solution of 5'-*O*-acetyl-2',3'-*O*-isopropylideneinosine (10.6 g, 30 mmol) in $CHCl_3$ (200 mL) was added, the resulting mixture was heated under reflux for 2 h. The mixture was cooled and then poured into ice water. After the resulting solution was neutralized with Na_2CO_3, $CHCl_3$ was added. The $CHCl_3$ layer was dried over Na_2SO_4, and evaporated *in vacuo*. To a solution of the residue in MeOH (50 mL) was added NaOMe (1.3 M in MeOH, 50 mL, 65 mmol) at 0 °C, and the resulting mixture was stirred for 20 minutes at room temperature. AcOEt and water were added, and the mixture was partitioned. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$/MeOH, 20:1) to give **13a** (6.83 g, 71%) as a yellow oil. ^{1}H-NMR ($CDCl_3$) δ; 8.53 and 7.98 (each s, each 1 H, H-2 and -8), 6.00 (d, 1 H, OH, J = 11.2 Hz), 5.96 (d, 1 H, H-1', J = 4.6 Hz), 5.20 (t, 1 H, H-2', J = 4.6, 5.9 Hz), 5.12 (d, 1 H, H-3', J = 5.9 Hz), 4.55 (s, 1 H, H-4'),

4.21 (s, 3 H, OMe), 3.99 (d, 1 H, H-5'a, J = 11.2 Hz), 3.81 (t, 1 H, H-5'b, J = 11.2 Hz), 1.65 and 1.38 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 322 (M^+, 2%), 307 (M^+-Me), 264 (M^+-acetone), 233 (M^+-acetone-CH_2OH, base peak). Anal. Calcd for $C_{14}H_{18}N_4O_5$: C, 52.17; H, 5.63; N, 17.38. Found: C, 52.02; H, 5.69; N, 17.41.

9-[(2*S*,3*R*,4*R*)-(5,4-Dihydroxy-2,3-isopropylidenedioxy)pentyl]-6-methoxypurine (14a). DIBALH (0.95M in hexane, 48 mL) was added to a solution of **13a** (4.00 g, 12.4 mmol) in THF (65 mL) at 0 °C, and the mixture was stirred at room temperature for 13.5 h. MeOH was added to the mixture at 0 °C, and the resulting white precipitate was filtered off and washed with MeOH. The mixture of the filtrate and the washings were evaporated *in vacuo*, and the residue was purified by silica gel column chromatography ($CHCl_3$/MeOH, 10:1) to give **14a** (2.50 g, 62%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ; 8.54 and 8.10 (each s, each 1 H, H-8 and -2), 4.91 (dd, 1 H, H-1'a, J = 2.7, 14.4 Hz), 4.57 (ddd, 1 H, H-2', J = 2.7, 6.2, 9.0 Hz), 4.31 (dd, 1 H, H-1'b, J = 9.0, 14.4 Hz), 4.22 (dd, 1 H, H-3', J = 6.2, 9.1 Hz), 4.20 (s, 3 H, OMe), 3.90 (m, 1 H, H-5'a), 3.85-3.7 (m, 2 H, H-4' and -5'b), 3.49 and 2.62 (each bs, each 1 H, OH), 1.50 and 1.30 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 324 (M^+, 2%), 309 (M^+-Me), 293 (M^+-CH_2OH). HRMS (EI) calcd for $C_{14}H_{20}N_4O_5$ 324.1434, found 324.1454.

9-[(2*S*,3*R*,4*R*)-(5-*tert*-Butyldimethylsilyloxy-4-hydroxy-2,3-isopropylidenedioxy)-pentyl]-6-methoxypurine (14c). A solution of **14a** (973 mg, 3.00 mmol), imidazole (238 mg, 3.50 mmol), and TBSCl (528 mg, 3.50 mmol) in DMF (6 mL) was stirred at room temperature for 19 h. Imidazole (61 mg, 0.90 mmol) and TBSCl (136 mg, 0.90 mmol) were further added, and the resulting mixture was stirred at room temperature for 3 h. Saturated aqueous NH_4Cl and AcOEt were added, and the mixture was partitioned. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:1) to give **14c** (1.08 g, 82%) as a colorless solid. ^{1}H-NMR ($CDCl_3$) δ; 8.55 and 8.07 (each s, each 1 H, H-2 and -8), 4.96 (dd, 1 H, H-1'a, J = 2.5, 14.1 Hz), 4.56 (m, 1 H, H-2'), 4.21 (dd, 1 H, H-1'b, J = 10.0, 14.1 Hz), 4.19-4.10 (m, 4 H, OMe and H-3'), 3.9-3.7 (m, 3 H, H-5'a, -5'b, and -4'), 2.85 (d, 1 H, OH, J = 5.7 Hz), 1.49 and 1.67 (each s, each 3 H, isopropyl-Me), 0.92 (s, 9 H, *t*-Bu of TBS), 0.10 (s, 6 H, CH_3 of TBS). MS (EI): *m/z* 438 (M^+, 1.3%), 423 (M^+-Me), 381 (M^+-*t*-Bu, base peak), 323 (M^+-TBS). HRMS (EI) calcd for $C_{20}H_{34}N_4O_5Si$ 438.2298, found 438.2297.

9-[(2*S*,3*S*)-(5-*tert*-Butyldimethylsilyloxy-2,3-isopropylidenedioxy-4-pentanone)-1-yl]-6-methoxypurine (15c). 1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (747 mg, 1.78 mmol) was added to a solution of **14c** (386 mg, 0.88 mmol) in CH_2Cl_2 (18 mL), and the mixture was stirred at room temperature for 4.5 h. Saturated aqueous $NaHCO_3$ (12 mL) containing $Na_2S_2O_3$•$5H_2O$ (1.5 g), and then AcOEt were added at 0 °C. The mixture was partitioned, and the organic layer was washed with brine and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:1) to give **15c** (386 mg, quant.) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ; 8.51 and 7.98 (each s, each 1 H, H-8 and -2), 4.96 (d, 1 H, H-3', J = 7.4 Hz), 4.81 (ddd, 1 H, H-2', J = 2.8, 7.4, 9.8 Hz), 4.61 (dd, 1 H, H-1'a, J = 2.8, 14.3 Hz), 4.54 (d, 1 H, H-5'a, J = 19.0 Hz), 4.41 (d, 1 H, H-5'b, J = 19.0 Hz), 4.18 (s, 3 H, OMe), 3.93 (dd, 1 H, H-1'b, J = 9.8, 14.3 Hz), 1.62 and 1.32 (each s, each 3 H, isopropyl-Me), 0.93 (s, 9 H, *t*-Bu of TBS), 0.14 and 0.13 (each s, each 3 H, Me of TBS). MS (EI): *m/z* 436 (M^+, 1.5%), 421 (M^+-Me), 379 (M^+-*t*-Bu), 321 (M^+-TBS). Anal. Calcd for $C_{20}H_{32}N_4O_5Si$•$0.8H_2O$: C, 53.26; H, 7.51; N, 12.42. Found: C, 53.33; H, 7.35; N, 12.36.

A Typical Procedure for the C-H Insertion Reactions (Entry 4). BuLi (1.39 M hexane solution, 150 μL, 0.2o mmol) was added to a solution of $TMSCHN_2$ (2.0M hexane solution, 100μL, 0.20 mmol) in THF (4 mL) at -78 °C, and the mixture was stirred for 1 h. A solution of **15c** (44 mg, 0.10 mmol) in THF (1 mL) was added at -78 °C, and the mixture was stirred at same temperature for 1 h, and then at 0 °C

for 15 min. Saturated aqueous NH_4Cl and AcOEt were added, and the mixture was partitioned. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt/hexane, 2:1-1:1) to give a mixture of **16c** and **17c** (15 mg, 34%). The ratio of **16c/17c** was 5:1, which was determined by ^{1}H-NMR. Analytical sample was purified by reverse-phase HPLC (column; YMC D-ODS-5, 2.5 x 25 cm; eluate, 80% aqueous MeOH). **9-[(1*S*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-(*tert*-butyldimethylsiloxymethyl)-4-cyclopenten-1-yl]-6-methoxypurine (16c).** ^{1}H-NMR ($CDCl_3$) δ; 8.57 and 7.81(each s, each 1 H, H-2 and -8), 5.78 (br s, 1 H, H-5'), 5.63 (br s, 1 H, H-1'), 5.32 (d, 1 H, H-3', *J* = 5.4 Hz), 4.71 (d, 1 H, H-2', *J* = 5.4 Hz), 4.5-4.4 (m, 2 H, H-6'a, b), 4.19 (s, 3 H, OMe), 1.48 and 1.35 (each s, each 3 H, isopropyl-Me), 0.92 (s, 9 H, *t*-Bu of TBS), 0.10 (s, 6 H, Me of TBS). MS (FAB): *m/z* 433 (M^++1). HRMS (FAB) calcd for $C_{21}H_{33}N_4O_4Si$ 433.2271, found 433.2251. **9-[(1*R*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-(*t*-butyldimethylsiloxy-methyl)-4-cyclopenten-1-yl]-6-methoxypurine (17c).** ^{1}H-NMR ($CDCl_3$) δ; 8.56 and 7.87 (each s, each 1 H, H-2 and -8), 5.85-5.75 (m, 2 H, H-1' and -5'), 5.05 (d, 1 H, H-3', *J* = 5.6 Hz), 4.97 (t, 1 H, H-2', *J* = 5.6 Hz), 4.50 (d, 1 H, H-6'a, *J* = 15.6 Hz), 4.37 (d, 1 H, H-6'b, *J* = 15.6 Hz), 4.20 (s, 3 H, OMe), 1.38 and 1.27 (each s, each 3 H, isopropyl CH_3). MS (EI): *m/z* 431 (M^+-1, 2%), 417 (M^+-Me). HRMS (EI) calcd for $C_{20}H_{29}N_4O_4Si$ (M^+-Me), 417.1958, found 417.1951. **9-[(1*S*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-(trityloxymethyl)-4-cyclopenten-1-yl]-6-methoxypurine (16d).** ^{1}H-NMR ($CDCl_3$) δ; 8.59 and 7.76 (each s, each 1 H, H-2 and -8), 7.5-7.2 (m, 15 H, Tr), 6.05 (br s, 1 H, H-5'), 5.68 (br s, 1 H, H-1'), 5.27 (d, 1 H, H-3', *J* = 5.7 Hz), 4.70 (d, 1 H, H-2', *J* = 5.7 Hz), 4.20 (s, 3 H, OMe), 4.11 (d, 1 H, H-6'a, *J* = 15.3 Hz), 4.05 (d, 1 H, H-6'b, *J* = 15.3 Hz), 1.45 and 1.32 (each s, each 3 H, isopropyl CH_3). MS (FAB): *m/z* 561 (M^++1). HRMS (FAB) calcd for $C_{34}H_{33}N_4O_4$ 561.2501, found 561.2496. **9-[(1*R*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-(trityloxymethyl)-4-cyclopenten-1-yl]-6-methoxypurine (17d).** ^{1}H-NMR ($CDCl_3$) δ; 8.56 and 7.84 (each s, each 1 H, H-2 and -8), 7.50-7.26 (m, 15 H, Tr), 5.96 (bs, 1 H, H-5'), 5.79 (br s, 1 H, H-1'), 5.01 (d, 1 H, H-3', *J* = 5.9 Hz), 4.92 (t, 1 H, H-2', *J* = 5.9 Hz), 4.20 (s, 3 H, OMe), 4.10-3.85 (m, 2 H, H-6'), 1.29 and 1.22 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 560 (M^+, 8%), 545(M^+-Me), 317 (M^+-Tr), 301 (M^+-TrO). HRMS (FAB) calcd for $C_{34}H_{32}N_4O_4$ 560.2423, found 560.2449. **9-[(1*S*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-methyl-4-cyclopenten-1-yl]-6-methoxypurine (16e).** ^{1}H-NMR ($CDCl_3$) δ; 8.56 and 7.77 (each s, each 1 H, H-2 and -8), 5.53-5.57 (m, 2 H, H-1' and -5'), 5.20 (d, 1 H, H-2', *J* = 5.9 Hz), 4.63 (d, 1 H, H-3', *J* = 5.3 Hz), 4.17 (s, 3 H, OMe), 1.97 (s, 3 H, H-6'), 1.46 and 1.35 (each s, each 3 H, isopropyl-Me). MS (FAB): 303 (M^++1). MS (EI): *m/z* 302 (M^+, 4%), 287 (M^+-Me), 244 (M^+-acetone). HRMS (FAB) calcd for $C_{15}H_{19}O_3N_4$ 303.145685, found 303.1445. **9-[(1*R*,2*S*,3*R*)-2,3-isopropylidenedioxy-4-methyl-4-cyclopenten-1-yl]-6-methoxypurine (17e).** ^{1}H-NMR ($CDCl_3$) δ; 8.53 and 7.86 (each s, each 1 H, H-2 and -8), 5.73 (br s, 1 H, H-5'), 5.50 (s, 1 H, H-1'), 4.85-5.00(m, 2 H, H-2' and -3'), 4.17 (s, 3 H, OMe), 1.95 (s, 3 H, H-6'), 1.36 and 1.26 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 302 (M^+, 6%), 287 (M^+-Me). HRMS (EI) calcd for $C_{15}H_{18}N_4O_3$ 302.1379, found 302.1422. **9-[(1*S*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-(*tert*-butyldimethylsiloxymethyl)-4-cyclopenten-1-yl]adenine (2',3'-*O*-isopropylidene-6'-*O*-*tert*-butyldimethylsilylneplanocin A, 29).** ^{1}H-NMR ($CDCl_3$) δ; 8.40 and 7.75 (each s, each 1 H, H-2 and -8), 6.12 (br s, 2 H, NH_2), 5.79 (br s, 1 H, H-5'), 5.61 (bs, 1 H, H-1'), 5.32 (d, 1 H, H-3', *J* = 5.5 Hz), 4.73 (d, 1 H, H-2', *J* = 5.5 Hz), 4.55-4.35 (m, 2 H, H-6'), 1.50 and 1.37 (each s, each 3 H, isopropyl-Me), 0.94 (s, 9 H, *t*-Bu of TBS), 0.12 (s, 6 H, Me of TBS). MS (EI): *m/z* 417 (M^+, 1.0%), 402 (M^+-Me), 360 (M^+-*t*-Bu), 302 (M^+-*t*-Bu-acetone). HRMS (EI) calcd for $C_{20}H_{31}N_5O_3Si$ 417.2196, found 417.2181. **9-[(1*R*,2*S*,3*R*)-2,3-isopropylidenedioxy-4-(*t*-butyldimethylsiloxymethyl)-4-cyclopenten-1-yl]adenine (30).** ^{1}H-NMR ($CDCl_3$) δ; 8.37 and 7.82 (each s, each 1 H, H-2 and -8), 6.25 (br s, 2 H, NH_2), 5.76 (m, 2 H, H-1' and -5'), 5.05 (d, 1 H, H-3', *J* =

5.4 Hz), 4.96 (t, 1 H, H -2', J = 5.4 Hz), 4.38 (d, 1 H, H-6'a, J = 15.6 Hz), 4.24 (d, 1 H, H-6'b, J = 15.6 Hz), 1.40 and 1.29 (each s, each 3 H, isopropyl CH_3), 0.93 (s, 9 H, *t*-Bu of TBS), 0.12 (s, 6 H, Me of TBS). MS (EI): *m/z* 417 (M^+, 1.3%), 402 (M^+-Me), 360 (M^+-*t*-Bu). HRMS (EI) calcd for $C_{20}H_{31}N_5O_3Si$ 417.2196, found 417.2183.

9-[(2*S*,3*R*,4*R*)-(5-Trityloxy-4-hydroxy-2,3-isopropylidenedioxy)pentyl]-6-methoxypurine (14d). A mixture of **14a** (1.00 g, 3.08 mmol) and TrCl (1.20 g, 4.30 mmol) in pyridine (20 mL) was stirred at 60 °C for 20 h. After the mixture was cooled to room temperature, saturated NH_4Cl and AcOEt were added, and the mixture was partitioned. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$, then $CHCl_3$/acetone, 10:1) to give **14d** (1.42 g, 81%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ; 8.55 and 8.05 (each s, each 1 H, H-2, and -8), 7.5-7.2 (m, 15 H, Tr), 4.91 (dd, 1 H, H-1'a, J = 2.5, 6.0 Hz), 4.55 (m, 1 H, H-2'), 4.3-4.1(m, 5 H, H-1'b, H-3' and OMe), 3.9-3.7 (m, 1 H, H-4'), 3.48 (dd, 1 H, H-5'a, J = 2.9, 9.7 Hz), 3.38 (dd, 1 H, H-5'b, J = 6.0, 9.7 Hz), 2.74 (d, 1 H, 4'-OH, J = 5.0 Hz), 1.41 and 1.26 (each s, each 3 H, isopropyl-Me). MS (FAB) : *m/z* 567 (MH^+, 29%). HRMS (FAB) calcd for $C_{33}H_{35}N_4O_5$ 567.2607, found 567.2609.

9-[(2*S*,3*S*)-(2,3-Isopropylidenedioxy-5-trityloxy-4-pentanone)-1-yl]-6-methoxypurine (15d). The procedure described for **15c** was employed. From **14d** (1.13 g, 2.00 mmol), **15d** was obtained as a colorless oil (1.04 g, 92%). ^{1}H-NMR ($CDCl_3$) δ; 8.50 and 7.87 (each s, each 1 H, H-2 and -8), 7.60-7.29 (m, 15 H, Tr), 4.90-4.75 (m, 2 H, H-2' and -3'), 4.56 (d, 1 H, H-1'a, J = 14.1 Hz), 4.26 (d, 1 H, H-5'a, J = 18.7 Hz), 4.19 (s, 3 H, OMe), 4.01 (d, 1 H, H-5'b, J = 18.7 Hz), 3.67 (dd, 1 H, H-1'b, J = 8.5, 14.1 Hz), 1.41 and 1.23 (each s, each 3 H, isopropyl-Me). MS (EI): m/z 564 (M^+, 0.07%), 549 (M^+-Me, 0.4%), 321 (M^+-Tr), 291 (M^+-$TrOCH_2$), 263 (M^+-$TrOCH_2CO$), 243 (Tr^+, base). HRMS (EI) calcd for $C_{33}H_{32}N_4O_5$ 564.2373, found 564.2347.

9-(5-*O*-Benzyl-2,3-*O*-isopropylidene-1-β-D-ribofuranosyl)-6-methoxypurine (13b). To a suspensin of NaH (60% in oil, 40 mg, 1.0 mmol) in THF (0.5 mL) and DMF (0.25 mL) was added **13a** (161 mg, 0.50 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h . To the mixture was added BnBr (120 μL, 1.00 mmol) at 0 °C and the resulting mixture was stirred at room temperature for 24 h. Saturated aqueous NH_4Cl and AcOEt were added, and the mixture was partitioned. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:2-1:1) to give **13b** (140 mg, 68%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ; 8.53 and 8.15 (each s, each 1 H, H-2 and -8), 7.4-7.1 (m, 5 H, $C_6H_5CH_2$), 6.23 (d, 1 H, H-1', J = 2.5 Hz), 5.34 (dd, 1 H, H-2', J = 2.5, 6.1 Hz), 4.99 (dd, 1 H, H-3', J = 6.1, 2.3 Hz), 4.55 (ddd, 1 H, H-4', 2.3, 3.5, 4.4 Hz), 4.47 (s, 2 H, $C_6H_5CH_2$), 4.20 (s, 3 H, OMe), 3.70 (dd, 1 H, H-5'a, J = 10.4, 3.5 Hz), 3.62 (dd, 1 H, H-5'b, J = 10.4, 4.4 Hz), 1.65 and 1.41 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 412 (M^+, 2.6%), 397 (M^+-Me), 354 (M^+-acetone), 321 (M^+-Bn). HRMS (EI) calcd for $C_{21}H_{24}N_4O_5$ 412.1747, found 412.1723.

9-(5-Deoxy-5-iodo-2,3-*O*-isopropylidene-1-β-D-ribofuranosyl)-6-methoxypurine (13f). A mixture of **13a** (1.97 g, 6.00 mmol), imidazole (1.02 g, 15.0 mmol), triphenylphosphine (3.93 g, 15.0 mmol), and iodine (3.05 g, 12.0 mmol) in benzene (60 mL) was stirred at room temperature for 1.5 h. Saturated aqueous $Na_2S_2O_3$, and then AcOEt were added. The mixture was partitioned, and the organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:1) to give **13f** (1.49 g, 56%) as a colorless solid. ^{1}H-NMR ($CDCl_3$) δ; 8.56 and 8.06 (each s, each 1 H, H-2 and -8), 6.17 (d, 1 H, H-1', J = 2.1 Hz), 5.50 (dd, 1 H, H-2', J = 2.1, 6.4 Hz), 5.11 (dd, 1 H, H-3', J = 6.4, 2.9 Hz), 4.44 (ddd, 1 H, H-4', J = 2.9, 8.2, 5.3 Hz), 4.20 (s, 3 H, OMe), 3.44 (dd, 1 H, H-5'a, J = 8.2, 10.1 Hz), 3.27 (dd, 1 H, H-5'b, J = 10.1, 5.3 Hz), 1.63

and 1.41 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 432 (M^+, 2.6%), 417 (M^+-Me), 374 (M^+-acetone), 247 (M^+-acetone-I), 233 (M^+-acetone-CH_2I). Anal. Calcd for $C_{14}H_{17}IN_4O_4$: C, 38.91; H, 3.96; N, 12.96; I, 29.36. Found: C, 38.97; H, 3.96; N, 12.74; I, 29.33.

9-(5-Deoxy-2,3-*O*-isopropylidene-D-ribofuranosyl)-6-methoxypurine (13e). A mixture of **13f** (847 mg, 1.96 mmol), Et_3N (330 μL), dry ice (about 1 g), and 10% Pd-C (50 mg) in MeOH (10 mL) was vigorously stirred at room temperature under hydrogen atmosphere (1 atm) for 20 h. The insoluble solid was filtered off, and the filtrate was evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:1) to give **13e** (520 mg, 87%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ; 8.58 and 8.04 (each s, each 1 H, H-2 and -8), 6.09 (d, 1 H, H-1', *J* = 2.3 Hz), 5.52 (dd, 1 H, H-2', *J* = 2.3, 6.4 Hz), 4.80 (dd, 1 H, H-3', *J* = 3.5, 6.4 Hz), 4.41 (dq, 1 H, H-4', *J* = 3.5, 6.6 Hz), 4.21 (s, 3 H, isopropyl-Me), 1.63 and 1.41 (each s, each 3 H, isopropyl-Me), 1.38 (d, 3 H, H-5', *J* = 6.6 Hz). MS (EI): m/z 306 (M^+, 1.6%), 291 (M^+-Me), 248 (M^+-acetone), 233 (M^+-acetone-Me). HRMS (EI) calcd for $C_{14}H_{18}N_4O_4$ 306.1328, found 306.1355.

9-[(2*S*,3*R*,4*R*)-(5-Benzyloxy-4-hydroxy-2,3-isopropylidenedioxy)pentyl]-6-methoxypurine (14b). The procedure described for **14a** was employed. From **13b** (242 mg, 0.587 mmol), **14b** was obtained as a light yellow oil (138 mg, 57%). ^{1}H-NMR ($CDCl_3$) δ; 8.56 and 8.07 (each s, each 1 H, H-2 and -8), 7.5-7.4 (m, 5 H, $C_6H_5CH_2$), 4.95 (dd, 1 H, H-1'a, *J* = 14.1, 2.5 Hz), 4.62 (s, 2 H, $C_6H_5CH_2$), 4.57 (ddd, 1 H, H-2', *J* = 2.5, 6.0, 9.5 Hz), 4.3-4.1 (m, 5 H, H-1'b, H-3' and OMe), 4.0-3.9 (m, 1 H, H-4'), 3.80 (dd, 1 H, H-5'a, *J* = 2.8, 9.7 Hz), 3.64 (dd, 1 H, H-5'b, *J* = 6.0, 9.7 Hz), 2.82 (d, 1 H, 4'-OH, *J* = 5.1 Hz), 1.50 and 1.29 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 414 (M^+, 2.2%), 399 (M^+-Me), 307 (M^+-BnO), 293 (M^+-$BnOCH_2$). HRMS (EI) calcd for $C_{21}H_{26}N_4O_5$ 414.1903, found 414.1917.

9-[(2*S*,3*S*)-(5-Benzyloxy-2,3-isopropylidenedioxy-4-pentanone)-1-yl]-6-methoxypurine (15b). The procedure described for **15c** was employed. From **14b** (212 mg, 0.536 mmol), **15b** was obtained as a light yellow oil (201 mg, 90%). ^{1}H-NMR ($CDCl_3$) δ; 8.53 and 7.94 (each s, each 1 H, H-2 and -8), 7.5-7.3 (m, 5 H, $C_6H_5CH_2$), 4.87 (d, 1 H, H-3', *J* = 7.5 Hz), 4.80 (ddd, 1 H, H-2', *J* = 2.5, 7.5, 9.2 Hz), 4.65-4.55 (m, 3 H, $C_6H_5CH_2$ and H-1'a), 4.41 and 4.28 (each d, each 1 H, H-5', *J* = 18.4 Hz), 3.89 (dd, 1 H, H-1'b, *J* = 9.2, 14.1 Hz), 1.59 and 1.30 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 397 (M^+-Me, 3.5%).

9-[(2*S*,3*S*)-(2,3-Isopropylidenedioxy-4-pentanone)-1-yl]-6-methoxypurine (15e). The procedure described for **14e** was employed. From **13e** (156 mg, 0.51 mmol), **14e** was obtained as a colorless oil (92 mg). The oil and 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (254.5 mg, 0.30 mmol) was dissolved in CH_2Cl_2 (3 mL), and the mixture was stirred at room temperature for 4.5 h. Saturated aqueous $NaHCO_3$ containing $Na_2S_2O_3$•$5H_2O$ was added at 0 °C, and then AcOEt was added, and the mixture was partitioned. The organic layer was washed with brine and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt, 1:3) to give **15e** (63 mg, 40% from **14e**) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ; 8.56 and 8.05 (each s, each 1 H, H-2 and -8), 4.74 (ddd, 1 H, H-2', *J* = 2.5, 7.6, 9.6 Hz), 4.64 (dd, 1 H, H-1'a, *J* = 2.5, 14.3 Hz), 4.62 (d, 1 H, H-3', *J* = 7.6 Hz), 4.20 (s, 3 H, OMe), 3.95 (dd, 1 H, H-1'b, *J* = 9.6, 14.3 Hz), 2.31 (s, 3 H, COMe), 1.64 and 1.33 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 306 (M^+, 15%), 291 (M^+-Me), 263 (M^+-CH_3CO), 248 (M^+-acetone). HRMS (EI) calcd for $C_{14}H_{18}N_4O_4$ 306.1328, found 306.1307.

***N*^{6}-Benzoyl-9-[(2*S*,3*R*,4*R*)-(5-hydroxy-4-hydroxy-2,3-isopropylidenedioxy)-pentyl]adenine (22)**. A mixture of **21**[13] (1.87 g, 6.00 mmol) and TMSCl (6.0 mL, 36.0 mmol) in pyridine (90 mL) was stirred at room temperature for 2 h. Benzoyl chloride (5.6 mL, 36.0 mmol) was added to the solution, and the mixture was further stirred at room temperature for 2 h. To the mixture, water (9 mL)

was added, and the mixture was stirred at room temperature for 0.5 h, and then saturated aqueous NH_3 (18 mL) was added, and the resulting mixture was stirred for 1 h. The mixture was extracted with $CHCl_3$, and the organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$/MeOH, 20 :1) to give **22** (1.93 g, 78%) as a colorless solid. ^{1}H-NMR ($CDCl_3$) δ; 9.24 (br s, 1 H, NH), 8.82 (br s, 1 H, H-2), 8.20 (s, 1 H, H-8), 8.1-8.0 (m, 2 H, Bz), 8.7-8.5 (m, 3 H, Bz), 4.96 (dd, 1 H, H-1'a, *J* = 2.7, 14.4 Hz), 4.58 (ddd, 1 H, H-2', *J* = 2.7, 6.2, 9.2 Hz), 4.31 (dd, 1 H, H-1b', *J* = 9.2, 14.4 Hz), 4.22 (dd, 1 H, H-3', *J* = 6.2, 9.3 Hz), 3.93 (dd, 1 H, H-5'a, *J* = 2.9, 11.0 Hz), 3.9-3.8 (m, 1 H, H-4'), 3.77 (dd, 1 H, H-5'b, *J* = 5.5, 11.0 Hz), 1.78 (bs, 2 H, OH), 1.50 and 1.30 (each s, each 3 H, isopropyl-Me). MS (EI): *m/z* 413 (M^+), 398 (M^+-Me). HRMS (EI) calcd for $C_{20}H_{23}N_5O_5$ 413.1698, found 413.1702.

9-[(2*S*,3*R*,4*R*)-(5-*tert*-Butyldimethylsilyloxy-4-hydroxy-2,3-isopropylidenedioxy)-pentyl]hypoxanthine (23). A solution of **20**[13] (1.24 g, 4.01 mmol), imidazole (468 mg, 6.80 mmol), and TBSCl (906. mg, 6.00 mmol) in DMF (9 mL) was stirred at room temperature for 8 h, and then saturated aqueous NH_4Cl and AcOEt were added. The mixture was partitioned, the organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$/MeOH, 18:1) to give **23** (1.61 g, 94%) as a colorless solid. ^{1}H-NMR ($CDCl_3$) δ; 12.83 (br s, 1 H, NH), 8.13 (s, 1 H, H-2), 7.97 (s, 1 H, H-8), 4.89 (dd, 1 H, H-1'a, *J* = 2.3, 14.1 Hz), 4.54 (ddd, 1 H, H-2', *J* = 2.3, 6.2, 10.2 Hz), 4.2-4.1 (m, 2 H, H-1'b and H-3'), 3.95-3.70 (m, 3 H, H-4' and -5'a, b), 2.82 (d, 1 H, 4'-OH, *J* = 5.3 Hz), 1.51 and 1.29 (each s, each 3 H, isopropyl-Me), 0.93 (s, 9 H, *t*-Bu of TBS), 0.12 (s, 6 H, Me of TBS). MS (EI): *m/z* 409 (M^+-Me), 367 (M^+-*t*-Bu), 309 (M^+-TBS). Anal. Calcd for $C_{19}H_{32}N_4O_5Si$: C, 53.75; H, 7.60; N, 13.20. Found: C, 53.51; H, 7.57; N, 13.01.

9-[(2*S*,3*R*,4*R*)-(5-*tert*-Butyldimethylsilyloxyl-4-hydroxy-2,3-isopropylidenedioxy)-pentyl]adenine (24). The procedure described for **23** was employed. From **21** (618 mg, 2.00 mmol), **24** was obtained as a colorless solid (764 mg, 90%). ^{1}H-NMR ($CDCl_3$) δ; 8.37 and 7.96 (each s, each 1 H, H-2 and -8), 5.68 (brs, 2 H, NH_2), 4.91 (dd, 1 H, H-1'a, *J* = 2.5, 14.3 Hz), 4.57 (ddd, 1 H, H-2', *J* = 2.5, 6.1, 9.8 Hz), 4.17 (dd, 1 H, H-1'b, *J* = 9.8, 14.3 Hz), 4.18 (t, 1 H, H-3', *J* = 6.1 Hz), 3.9-3.7 (m, 3 H, H-4' and H-5'a, b), 3.0 (brs, 1 H, OH), 1.50 and 1.28 (each s, each 3 H, isopropyl-Me), 0.92 (s, 9 H, *t*-Bu of TBS), 0.10 (s, 6 H, Me of TBS). MS (EI): *m/z* 423 (M^+), 408 (M^+-Me), 366 (M^+-*t*-Bu), 308 (M^+-TBS). HRMS (EI) calcd for $C_{19}H_{33}N_5O_4Si$ 423.2302, found 423.2278.

***N*^{6}-Benzoyl-9-[(2*S*,3*R*,4*R*)-(5-*tert*-Butyldimethylsilyloxyl-4-hydroxy-2,3-isopropylidenedioxy)pentyl]adenine (25).** The procedure described for **23** was employed. From **22** (1.24 g, 3.00 mmol), **25** was obtained as a colorless solid (1.50 g, 95%). ^{1}H-NMR ($CDCl_3$) δ; 9.14 (br s, 1 H, NH), 8.82 and 8.22 (each s, each 1 H, H-2 and 8), 8.1-8.0 (m, 2 H, 2 H of Bz), 7.7-7.5 (m, 3 H, 3 H of Bz), 5.02 (dd, 1 H, H-1'a, *J* = 2.4, 14.2 Hz), 4.58 (ddd, 1 H, H-2', *J* = 2.4, 6.1, 10.2 Hz), 4.25 (dd, 1 H, H-1'b, *J* = 10.2, 14.2 Hz), 4.18 (dd, 1 H, H-3', *J* = 6.1, 9.4 Hz), 3.95-3.70 (m, 3 H, H-4' and -5'a, b), 3.85 (br s, 1 H, OH), 1.50 and 1.29 (each s, each 3 H, isopropyl-Me), 0.93 (s, 9 H, *t*-Bu of TBS), 0.12 (s, 6 H, Me of TBS). MS (EI): *m/z* 527 (M^+, 0.6%), 512 (M^+-Me), 498, 470 (M^+-*t*-Bu), 412 (M^+-TBS). HRMS (EI) calcd for $C_{26}H_{37}N_5O_5Si$ 527.2562, found 527.2537

9-[(2*S*,3*S*)-(5-*tert*-Butyldimethylsilyloxy-2,3-isopropylidenedioxy-4-pentanone)-1-yl]hypoxanthine (26). The procedure described for **15c** was employed. From **23** (42 mg, 0.10 mmol), **26** was obtained as an amorphous solid (42 mg, qunat.). ^{1}H-NMR ($CDCl_3$) δ; 13.00 (br s, 1 H, NH), 8.15 and 7.88 (each s, each 1 H, H-2 and -8), 4.97 (d, 1 H, H-3', *J* = 7.4 Hz), 4.78 (ddd, 1 H, H-2', *J* = 2.7, 9.8, 7.4 Hz), 4.54 (d, 1 H, H-5'a, *J* = 19.0 Hz), 4.53 (dd, 1 H, H-1'a, *J* = 14.0, 2.7 Hz), 4.42 (d, 1 H, H-5'b, *J* = 19.0 Hz), 3.89 (dd, 1 H, H-1'b, *J* = 9.8, 14.0 Hz), 1.63 and 1.34 (each s, each 3 H, isopropyl-Me), 0.94 (s, 9 H, *t*-Bu of TBS), 0.14 and 0.13 (each s, each 3 H, Me of TBS). MS (FAB): m/z 423 (MH^+).

HRMS (FAB) calcd for $C_{19}H_{31}N_4O_5Si$ 423.2063, found 423.2093.

9-[(2*S*,3*S*)-(5-*tert*-Butyldimethylsilyloxy-2,3-isopropylidenedioxy-4-pentanone)-1-yl]adenine (27). The procedure described for **15c** was employed. From **24** (847 mg, 2.00 mmol), **27**[13b] was obtained a light yellow solid (597 mg, 71%). ^{1}H-NMR ($CDCl_3$) δ; 8.32 and 7.88 (each s, each 1 H, H-2 and -8), 6.0 (bs, 2 H, NH_2), 4.97 (d, 1 H, H-3', *J* = 7.4 Hz), 4.82 (ddd, 1 H, H-2', *J* = 2.8, 7.4, 9.5 Hz), 4.57 (dd, 1 H, H-1'a, *J* = 2.8, 14.1 Hz), 4.55 (d, 1 H, H-5'a, *J* = 19.0 Hz), 4.43 (d, 1 H, H-5'b, *J* = 19.0 Hz), 3.90 (dd, 1 H, H-1'b, *J* = 9.5, 14.1 Hz), 1.63 and 1.34 (each s, each 3 H, isopropyl-Me), 0.94 (s, 9 H, *t*-Bu of TBS), 0.14 and 0.15 (each s, each 3 H, Me of TBS). MS (EI): *m/z* (M^+,3.6%), 406 (M^+-Me), 364 (M^+-*t*-Bu), 306 (M^+-TBS). HRMS (EI) calcd for $C_{19}H_{31}N_5O_4Si$ 421.2145, found 421.2130.

***N*^{6}-Benzoyl-9-[(2*S*,3*S*)-(1-*tert*-Butyldimethylsilyloxy-2,3-isopropylidenedioxy-4-pentanone)-1-yl]adenine (28).** The procedure described for **15c** was employed. From **25** (530 mg, 1.00 mmol), **28** was obtained as a colorless solid (543 mg, quant.). ^{1}H-NMR ($CDCl_3$) δ; 9.10 (br s, 1 H, NH), 8.77 and 8.08 (each s, each 1 H, H-2 and -8), 8.05-8.00 (m, 2 H, Bz), 7.65-7.45 (m, 3 H, Bz), 5.00 (d, 1 H, H-3', *J* = 7.6 Hz), 4.83 (ddd, 1 H, H-2', *J* = 2.7, 7.6, 9.8 Hz), 4.66 (dd, 1 H, H-1'a, *J* = 2.7, 14.3 Hz), 4.56 (d, 1 H, H-5'a, *J* = 19.0 Hz), 4.45 (d, 1 H, H-5'b, *J* = 19.0 Hz), 3.96 (dd, 1 H, H-1'b, *J* = 9.8, 14.3 Hz), 1.64 and 1.34 (each s, each 3 H, isopropyl-Me), 0.96 (s, 9 H, *t*-Bu of TBS), 0.16 (s, 6 H, Me of TBS). MS (FAB): *m/z* 526 (MH^+, base peak). HRMS (FAB) calcd for $C_{26}H_{36}N_5O_5Si$ 526.2486, found 526.2478.

Synthesis of authentic 2,3-O-isopropylidene-6'-*O*-*t*-butyldimethylsilylneplanocin A (29). The procedure described for **23** was employed. From 2',3'-*O*-isopropylidenenepanocina A[9a] (48 mg, 0.15 mmol), **29** was obtained as a colorless solid (32 mg, 50%).

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References and Notes

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