Synthesis of Neplanocin A Analog with 2′-"up"-*C*-Methyl Substituent as Potential Anti-HCV Agent

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2′-β-*C*-Methylneplanocin A (**3**) was synthesized *via* 2-β-*C*-methylribonolactone, prepared by a modified Whistler and BeMiller's method developed by our laboratory, as potential anti-HCV agent. Reduction of **14** with Dibal-H afforded **26** in a good yield with a trace of **25**, whereas a Luche reduction gave **26**/**25** = 4/1 mixture. Several attempts were made to chemoselectively remove TBS group in the presence of TBDPS group and treatment with both PPTS and TsOH showed the best result. Condensation of **26** with 6-chloropurine under Mitsunobu conditions produced an S_N2 product **27** along with an S_N2' product **28**.

Key Words: 2′-β-*C*-Methylneplanocin A, 2-β-*C*-Methylribonolactone, Chemoselective, HCV, PDC oxidation

Introduction

Hepatitis C virus (HCV), which was identified first in 1989 as a single-stranded, enveloped, positive sense RNA virus[1] and which is a major causative virus of chronic liver disease, has infected an estimated 170 million people worldwide.[2] To date, there is no vaccine available against HCV. The monotherapy with pergylated IFN-α (interferon alpha) and the combination therapy with pergylated IFN-α and ribavirin were approved by FDA for the treatment of HCV infection.[3,4] However, ribavirin causes side effects such as anemia and pergylated IFN-α does neuropsychiatirc adverse effects.[3] Judged from these adverse effects and an ability of viruses easily obtaining resistance to the drugs, there are urgent requirements to discover new and more effective anti-HCV agents.

Recently, 2′-β-*C*-methylribonucleoside derivatives including 2′-β-*C*-methyladenosine[5] (Fig. 1, EC_{50} = 0.3 μM in a cell-based, subgenomic HCV replicon assay) have been reported to exhibit very potent activity against HCV. Currently, valopicitabine,[6] a prodrug of 2′-β-*C*-methylcytidine, is in Phase II clinical trials for the treatment of HCV infection. It is reported that these nucleosides act as a terminator of the growing HCV's RNA chain. After the discovery of 2′-β-*C*-methyladenosine, numerous medicinal chemists have concentrated their attention on the synthesis of nucleosides with a branched sugar to find new anti-HCV agents.

2′-β-*C*-Methyladenosine was reported to display a strong preference for a *north* conformation (*P* = 15.6° in pseudorotational cycle),[7] which is one of two conformations that normal bicyclo[3.1.0]hexyl nucleosides can adopt. On the basis of the fact, recently we have synthesized *north*-bicyclo[3.1.0] hexyl nucleoside, **1**, with 2′-β-*C*-methyl group.[8] Disappointingly, it did not show any significant anti-HCV activity, indicating that cellular kinases might prefer a *south* conformation to the *north* conformation for conversion to the corresponding nucleotides.

It is well known that neplanocin A is a naturally occurring product possessing potent anticancer and antiviral activities.[9] Fluoroneplanocin A[10] and its cytosine congener **2**[11] exhibited more potent anticancer and antiviral activities. Considering that neplanocin A and its fluoro-substituted analogues showed good biological activities, the cyclopentene template of these nucleosides can be assumed to be a good template for phosphorylations by kinases. Therefore, as part of our continued effort to discover more potent HCV inhibitors,[12] it was of great interest to synthesize neplanocin A derivative with 2′-β-*C*-methyl substituent. We wish to report herein the synthesis of 2′-β-*C*-methylneplanocin A (**3**).

Results and Discussion

First of all, attempts were made to directly introduce a methyl substituent on the cyclopentenone template of **4** by a

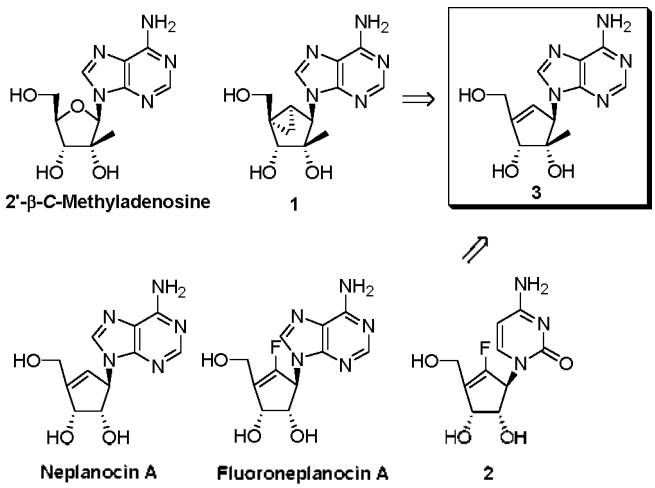
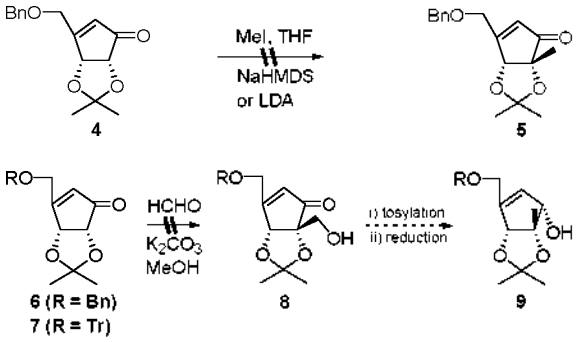
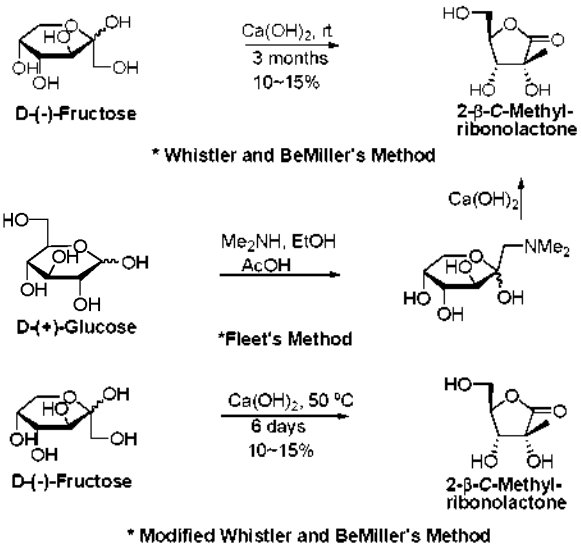


Figure 1. The rationale for the design of the desired nucleoside, **3**.

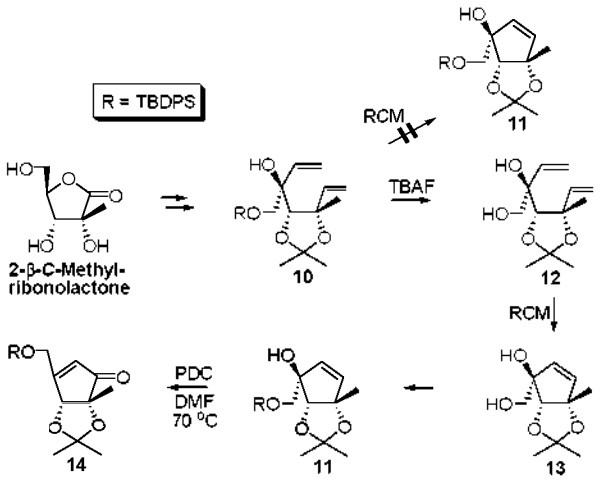
base-catalyzed methylation and following sequential procedures: i) stereoselective hydroxymethylation[13] using a Claisen-Schmidt reaction, ii) tosylation of the resulting hydroxyl group and iii) reduction of the tosylate[14] (Scheme 1). But, these reactions did not give any alkylated product.



Scheme 1. Attempts for introduction of methyl substituent into 5-β position of cyclopentenone/cyclopentenol



Scheme 2. Synthetic methods for D-2-β-*C*-methylribono-1,4-lactone

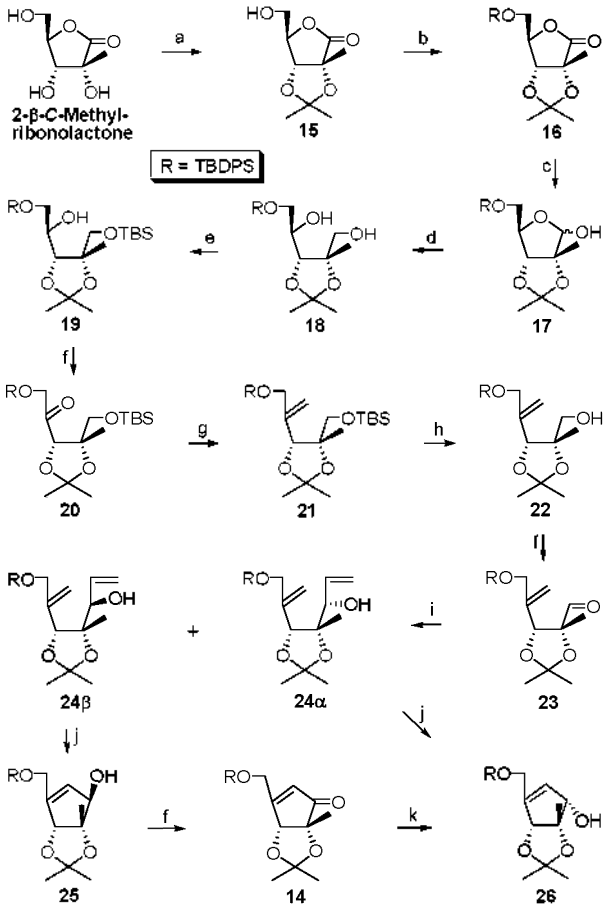


Scheme 3. Synthetic method for 5-methylcyclopentenone **14** *via* an oxidative rearrangement using PDC

Thus, 2-β-*C*-methylribonolactone, already bearing 2-β-*C*-methyl substituent, was used as key material, instead of the introduction of methyl substituent into cyclopentene template. First synthesis of 2-β-*C*-methylribonolactone was reported by Whistler and BeMiller (Scheme 2),[15] but too long reaction time was required and the yield was also low (10 ~ 15%). Due to these defects, new synthetic method has been required continuously. Recently, Fleet and coworkers reported a novel synthesis of 2-β-*C*-methylribonolactone starting from D-glucose (Scheme 2).[16] but the desired product was obtained in a less than 5% yield although 19% yield was reported in the literature. Therefore, our laboratory has developed a modified Whistler and BeMiller's method, which decreased the reaction time from three months to 6 d and gave a similar yield to that of the Whistler and BeMiller's method (Scheme 2). 2-β-*C*-Methylribonolactone was obtained in 15% yield by treatment of D-fructose with $Ca(OH)_2$ at an elevated temperature (50 °C) for 6 d.

It was envisioned that 5-β-*C*-methylcyclopentenone **14** (Scheme 3) would be an appropriate intermediate for the synthesis of 2′-β-*C*-methylneplanocin A (**3**). Attempts were made to use an oxidative rearrangement reaction with PDC for the synthesis of **14** (Scheme 3). First, in order to synthesize the substrate **11** for the oxidative rearrangement reaction, ring-closing metathesis (RCM)[17] with diene **10**, prepared from 2-β-*C*-methylribonolactone, was employed, but afforded only a trace of **11** along with the unreacted diene **10**. The low reactivity of the RCM reaction might be attributed to a steric hindrance between the bulky TBDPS and isopropylidene groups. Therefore, a RCM reaction was again conducted with TBDPS-deprotected diene **12**, and the desired RCM product, **13** was produced in a high yield within 2 h. A PDC-mediated oxidative rearrangement reaction[18] with **11**, obtained from silyation of **13**, gave the desired product in 50% yield along with unreacted starting material (41%), which has a quite similar R_f value to that of the product even if various combinations of several solvents were used as the developing solvent. This indicates that there is a difficulty in the purification unless the reaction proceeds completely.

Method to bypass the troublesome oxidative rearrangement step was attempted as the next approach to the synthesis of 5-β-*C*-methylcyclopentenone **14**. Conversion of 2-β-*C*-methylribonolactone into a glycosyl donor **26** *via* **14** is described in Scheme 4. Isopropylidenation followed by silylation produced silyl ether **16**, which was reduced by successive two reducing reagents (Dibal-H and $NaBH_4$) to give diol **18** in a good yield. A TBS group was chosen for the regioselective protection of primary hydroxyl group and the reaction proceeded with a quantitative yield. Swern oxidation of the remaining hydroxyl group of **19** followed by a Wittig reaction of the resulting ketone **20** with (methylidene)triphenyl phosphorane afforded **21** in a good yield without any epimerization.[19] To carry out the selective deprotection of TBS group of **21** in the presence of TBDPS group,[20] first, LiCl, H_2O and DMF were treated,[21] but the yield and reaction time were unsatisfactory (Table 1). Secondly, $CeCl_3$ and NaI in CH_3CN were employed.[22] Although, at an elevated temperature (50 °C), the desired product was obtained, the yield was too low and the major product was a diol compound, generated from removal of both TBDPS and TBS groups. In case of treat-



Scheme 4. Reagents and conditions: (a) acetone, $CuSO_4$, *c*-H_2SO_4, rt, 3 h, 91%; (b) TBDPSCl, imidazole, CH_2Cl_2, rt, 2 h, 98%; (c) Dibal-H, CH_2Cl_2, -78 °C, 30 min, 98%; (d) $NaBH_4$, MeOH, reflux, 30 min, 94%; (e) TBSCl, imidazole, CH_2Cl_2, rt, 3 h, 99%; (f) $(COCl)_2$, DMSO, CH_2Cl_2, -78 °C, 1 h and then Et_3N, -78 °C -> rt, 99% for **20**, 97% for **23**, 86% for **14**; (g) CH_3PPh_3Br, *t*-BuOK, THF, rt, 1.5 h, 92%; (h) PPTS, *p*-TsOH, EtOH, rt, 7 h, 45%; (i) H_2C = $CHMgBr$, THF, -78 °C, 1 h, 64% for **24α**, 28% for **24β**; (j) 2nd generation Grubbs catalyst, CH_2Cl_2, rt, 7 h, 88% for **25**, 6 h, 86% for **26**; (k) Dibal-H, CH_2Cl_2, -78 °C, 30 min, 93%

ment with PPTS (pyridinium *p*-toluenesulfonate)[23] the reaction proceeded too slowly and in addition, when the reaction time was long, a ratio of the desired product **22** and the diol compound decreased. The best result was obtained by treatment with PPTS and TsOH in EtOH. In contrast to the treatment with PPTS only, addition of TsOH with PPTS accelated the reaction rate and the yield was also acceptable (45%, recovered yield: 83%). Maybe, low chemoselectivity between TBDPS and TBS in the various removal reactions results from an existence of TBDPS at the allylic position.

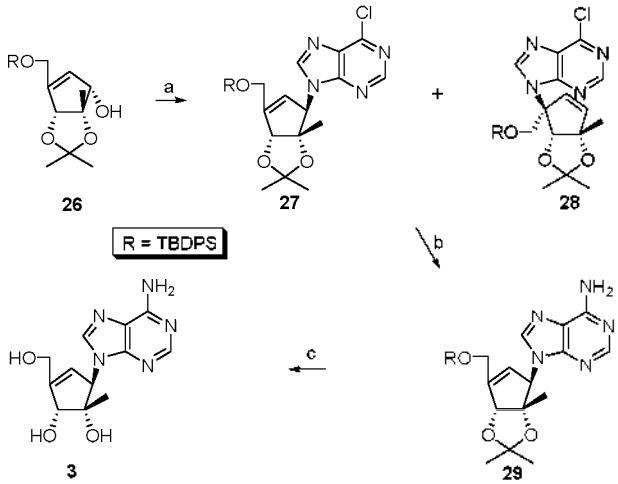
Swern oxidation of **22** followed by a Grignard reaction of the resulting aldehyde **23** gave dienes **24α** and **24β** (**24α** : **24β** = 2.3 : 1) as an easily separable diastereomeric mixture on a column chromatography. Each diastereomer **24β** and **24α** was subjected to a RCM reaction with a second Grubbs catalyst to afford β-cyclopentenol **25** and its α-isomer **26**, respectively. Conversion of **25** into **26** was examined. After an oxidation of **25**, a diastereo- and regioselective reduction of **14** was accomplished with a Luche reduction[24] using $NaBH_4$ in the presence

Table 1. Selective deprotection of TBS in the presence of TBDPS

Reagents and conditions	**21**	**22**	diol[a]
LiCl (50 eq.), H_2O, DMF, 90 °C, 2 d then 130 °C, 4 d	9%	55%	*NI*[b]
$CeCl_3$ (1.5 eq.), NaI (1.0 eq.), CH_3CN, rt, 3 d then 50 °C, 7 h	25%	18%	50%
PPTS (0.9 eq.), EtOH, rt, 3 d	60%	29%	8%
PPTS (0.9 eq.), *p*-TsOH (0.3 eq.), rt, 7 h	46%	43%	*NI*

[a]Compound in which both TBS and TBDPS groups of **21** are cleaved. [b]Not isolated.

Figure 2. ^1H NOE experiment data of 5-methylcyclopentenols, **25** and **26**.



Scheme 5. Reagents and conditions: (a) 6-chloropurine, PPh_3, DEAD, THF, rt, 1 h, 42% for **27**, 3% for **28**; (b) methanolic ammonia, MeOH, 80 °C, 7 h, 84%; (c) 4 *N* HCl, MeOH, rt, 6 h, 86%

of $CeCl_3$ to give **26**, along with **25** (**26**/**25** = 4/1). A Dibal-H reduction was chosen as an alternative method to improve the diastereoselectivity. Surprisingly, reduction of **14** with Dibal-H showed a superior diastereoselectivity to produce **26** in 93% yield with a trace of **25**. The stereochemistry of cyclopentenols **25** and **26** was confirmed by NOE experiments (Figure 2).

Upon the coupling reaction of **26** with 6-chloropurine under Mitsunobu conditions,[25] **27** was generated as the desired product in 42% yield, along with a migrated nucleoside **28** (3%), formed *via* an S_N2' mechanism (**27** : **28** = 14 : 1) (Scheme 5). 2′-β-*C*-Methylneplanocin A (**3**) was obtained from amination with methanolic ammonia and hydrolysis with 4 *N* HCl. Disappointingly, 2′-β-*C*-methylneplanocin A did not show significant activity against HCV and also recently Merck company published a paper related to the synthesis of the same final compound **3** as a communication form.[26] The lack of anti-HCV activity might result from a steric hindrance of 2′-β-*C*-methyl substituent

when 2′-β-*C*-methylneplanocin A and/or its phosphates interacted with kinases and/or polymerases. Biological evaluation against other viruses is currently underway, and will be reported in due course.

Conclusions

We have synthesized 2′-β-*C*-methylneplanocin A (**3**) as potential anti-HCV agent starting from 2-β-*C*-methylribonolactone, obtained from employing the modified Whistler and BeMiller's method. PDC oxidation of **11** in DMF has afforded cyclopentenone **14**, but due to the purification problem of the product, the strategy could not be used in the large scale. RCM reaction of dienes **24α** and **24β** gave α-cyclopentenol **26** and β-cyclopentenol **25**, respectively and **25** could be converted into **26** by an oxidation and a diastereoselective reduction. It is noteworthy that the reduction of cyclopentenone **14** with Dibal-H gave much better diastereoselectivity than a Luche reduction. Attempts to deprotect TBS group in the presence of TBDPS group were made and the best result was obtained from a use of PPTS and TsOH together. It is also noteworthy that coupling of **26** with 6-chloropurine under Mitsunobu conditions gave **27** *via* an S_N2 mechanism and a migrated nucleoside **28** *via* an S_N2' mechanism. 2′-β-*C*-Methylneplanocin A did not show significant activity against HCV, implying that cellular kinases and/or HCV's polymerases might not accommodate the 2′-β-*C*-methyl substituent.

Experimental

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Varian Unity INOVA 400 and Varian Unity AS 500 instruments. Chemical shifts are reported with reference to the respective residual solvent or deuteriated peaks (δ_H 3.30 and δ_C 49.0 for CD_3OD, δ_H 7.27 and δ_C 77.0 for $CDCl_3$). Coupling constants are reported in hertz. The abbreviations used are as follows: s (singlet), d (doublet), m (multiplet), t (triplet), dd (doublet of doublet), br s (broad singlet). All the reactions described below were performed under argon or nitrogen atmosphere and monitored by TLC. All anhydrous solvents were distilled over CaH_2 or Na/benzophenone prior to use. Assignments of ^{1}H NMR data were conducted on the basis of nucleoside numbering.

Synthesis of D-2-β-*C*-methylribono-1,4-lactone: To D-fructose (100 g, 555.1 mmol) were added boiling water (1000 mL) and $Ca(OH)_2$ (10 g, 135.0 mmol) successively. The reaction mixture was stirred at room temperature for 5 h and at 50 °C for 3 d. Additional $Ca(OH)_2$ (40 g, 540.0 mmol) was added and the reaction mixture was stirred at 50 °C for additional 3 d. After cooling, the reaction mixture was filtered and to the filtrate was added oxalic acid dihydrate (38 g, 301.4 mmol). After being stirred vigorously for 10 min, the mixture was filtered through a pad of Celite. The filtrate was filtered again through Amberlite IR-120H ion-exchange resin under a gravity. After evaporation, the residue was purified by silica gel column chromatography. In the first silica gel column chromatography a co-solvent of methylene chloride and methanol (2:1) was used as the eluent and in the second one, ethyl acetate was used as the eluent to give D-2-β-*C*-methylribonolactone (10 ~ 15%) as a white solid. All spectral data were identical to those of the authentic sample.[15]

(3a*R*,6*R*,6a*R*)-Dihydro-6-(hydroxymethyl)-2,2,3a-trimethylfuro[3,4-*d*][1,3]dioxol-4(3a*H*)-one (15): 2-β-*C*-Methylribonolactone (1.03 g, 6.35 mmol) was converted to **15** (1.18 g, 91%) as a colorless oil according the reported procedure[25]: $[\alpha]_D^{25}$ -34.4 (*c* 1.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70-4.50 (m, 2 H), 3.97 (dd, 1 H, *J* = 3.2, 12.4 Hz), 3.80 (dd, 1 H, *J* = 2.8, 12.4 Hz), 2.61 (br s, 1 H), 1.63 (s, 3 H), 1.41 (s, 3 H), 1.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 113.1, 83.7, 83.1, 82.8, 62.3, 27.0, 26.9, 20.0; LRMS(FAB+) *m/z* 203 $(M + H)^+$.

(3a*R*,6*R*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-dihydro-2,2,3a-trimethylfuro[3,4-*d*][1,3]dioxol-4(3a*H*)-one (16): To a solution of **15** (1.18 g, 5.84 mmol) and imidazole (792 mg, 11.63 mmol) in anhydrous methylene chloride (15 mL) was added *tert*-butyldiphenylsilyl chloride (1.51 mL, 5.90 mmol) dropwise at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was extracted with methylene chloride. The organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (12:1) as the eluent to give silyl ether **16** (2.51 g, 98%) as a colorless oil: $[\alpha]_D^{25}$ +2.1 (*c* 1.31, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66-7.40 (m, 10 H), 4.53 (s, 1 H), 4.51 (t, 1 H, *J* = 3.5 Hz), 3.83 (d, 2 H, *J* = 3.5 Hz), 1.59 (s, 3 H), 1.45 (s, 3 H), 1.44 (s, 3 H), 1.07 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 135.8, 135.7, 132.6, 132.3, 130.3, 128.2, 113.3, 83.1, 82.6, 82.5, 63.8, 27.2, 27.1, 27.0, 20.6, 19.4; LRMS(FAB+) *m/z* 463 $(M + Na)^+$; HRMS(FAB+) *m/z* $C_{25}H_{32}O_5SiNa$ $(M+Na)^-$ calcd 463.1917, obsd 463.1924.

(3a*R*,6*R*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-tetrahydro-2,2,3a-trimethylfuro[3,4-*d*][1,3]dioxol-4-ol (17): To a stirred solution of **16** (2.74 g, 6.22 mmol) in anhydrous methylene chloride (25 mL) was added diisobutylaluminum hydride (Dibal-H, 6.6 mL, 6.6 mmol, 1.0 M solution in hexanes) at -78 °C, and the reaction mixture was stirred for 30 min at the same temperature. MeOH (6.6 mL), hexanes (13.2 mL) and ethyl acetate (13.2 mL) were added successively and the resulting mixture was stirred overnight, allowing it to reach room temperature. The generated gel was filtered off through a pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (7:1) as the eluent to give lactol **17** (2.70 g, 98%) as a colorless oil: $[\alpha]_D^{25}$ 7.0 (*c* 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.36 (m, 20 H), 5.19 (d, 1 H, *J* = 10.0 Hz), 5.09 (d, 1 H, *J* = 10.4 Hz), 4.51 (d, 1 H, *J* = 2.0 Hz), 4.45 (d, 1 H, *J* = 1.2 Hz), 4.21 (d, 1 H, *J* = 10.0 Hz), 4.19-4.17 (m, 1 H), 4.13-4.11 (m, 1 H), 3.80 (d, 1 H, *J* = 10.8 Hz), 3.77-3.63 (m, 4 H), 1.53 (s, 3 H), 1.48 (s, 3 H), 1.46 (s, 3 H), 1.45 (s, 3 H), 1.44 (s, 3 H), 1.43 (s, 3 H), 1.07 (s, 9 H), 1.05 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.9, 135.9, 135.8, 133.0, 132.8, 131.9, 131.7, 130.5, 130.4, 130.1, 130.1, 128.3, 128.1, 113.8, 112.9, 104.6, 102.3, 92.7, 88.2, 87.4, 87.1, 86.9, 82.5, 65.6, 65.2, 28.9, 28.1, 27.6, 27.5, 27.1, 22.2, 20.5, 19.4; LRMS(FAB+) *m/z* 465 $(M + Na)^+$; HRMS(FAB+) *m/z* $C_{25}H_{34}O_5SiNa$ (M +

Na)$^+$ calcd 465.2073, obsd 465.2060.

(*R*)-2-(*tert*-Butyl-diphenyl-silanyloxy)-1-((4*R*,5*S*)-5-(hydroxymethyl)-2,2,5-trimethyl-1,3-dioxolan-4-yl)ethanol (18): To a solution of **17** (2.46 g, 5.56 mmol) in MeOH (24.6 mL) were added sodium borohydride (210 mg, 5.56 mmol) and the mixture was stirred under reflux for 30 min. After cooling to room temperature, the reaction mixture was evaporated under reduced pressure until the volumn of solution became 5 mL and extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (2.5:1) as the eluent to give diol **18** (2.23 g, 94%) as a colorless oil: $[\alpha]_D^{25}$ -11.0 (*c* 1.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.36 (m, 10 H), 3.91-3.83 (m, 3 H), 3.76 (dd, 1 H, *J* = 6.0, 11.2 Hz), 3.69 (d, 1 H, *J* = 11.2 Hz), 3.52 (d, 1 H, *J* = 11.2 Hz), 2.71 (s, 2 H), 1.43 (s, 3 H), 1.33 (s, 6 H), 1.07 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 135.7, 133.1, 133.0, 130.2, 130.1, 128.1, 128.0, 108.1, 83.0, 81.4, 70.2, 65.8, 65.5, 28.6, 27.1, 26.8, 23.8, 19.5; LRMS(FAB+) *m/z* 467 (M + Na)$^+$; HRMS(FAB+) *m/z* $C_{25}H_{36}O_5SiNa$ (M + Na)$^+$ calcd 467.2230, obsd 467.2221.

(*R*)-(*tert*-Butyl-diphenyl-silanyloxy)-1-((4*R*,5*S*)-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-2,2,5-trimethyl-1,3-dioxolan-4-yl)ethanol (19): To a solution of **18** (2.90 g, 6.52 mmol) and imidazole (972 mg, 14.34 mmol) in anhydrous methylene chloride (63 mL) was added *tert*-butyldimethylsilyl chloride (1.08 g, 7.17 mmol) portionwise at 0 °C. After being stirred at room temperature for 3 h, the reaction mixture was extracted with methylene chloride. The organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (15:1) as the eluent to give silyl ether **19** (3.64 g, 99%) as a colorless oil: $[\alpha]_D^{25}$ -9.1 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73-7.34 (m, 10 H), 3.94-3.80 (m, 4 H), 3.74 (d, 1 H, *J* = 10.4 Hz), 3.60 (br s, 1 H), 3.30 (d, 1 H, *J* = 9.6 Hz), 1.41 (s, 3 H), 1.33 (s, 3 H), 1.31 (s, 3 H), 1.06 (s, 9 H), 0.91 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 135.6, 135.6, 133.6, 133.5, 129.6, 129.6, 127.6, 127.5, 107.5, 82.3, 81.1, 70.7, 66.1, 66.0, 27.4, 26.1, 25.6, 25.2, 22.9, 18.9, 18.0, -6.6; LRMS(FAB+) *m/z* 543 (M-CH_3)$^+$.

2-(*tert*-Butyl-diphenyl-silanyloxy)-1-((4*S*,5*S*)-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-2,2,5-trimethyl-1,3-dioxolan-4-yl)ethanone (20): To a stirred solution of oxalyl chloride (0.97 mL, 11.12 mmol) in dry methylene chloride (25 mL) was added dimethyl sulfoxide (1.71 mL, 24.10 mmol) at -78 °C, and the mixture was stirred at -78 °C for 30 min. To this mixture was added a solution of **19** (3.64 g, 6.51 mmol) in methylene chloride (20 mL), and the reaction mixture was stirred at -78 °C for 1 h. After the addition of triethylamine (6.30 mL, 45.20 mmol), the mixture was gradually warmed to room temperature. The reaction mixture was quenched with water and then extracted with methylene chloride. The organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (18:1) as the eluent to give ketone **20** (3.62 g, 99%) as a colorless oil: $[\alpha]_D^{25}$ -17.9 (*c* 2.04, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.36 (m, 10 H), 4.77 (d, 1 H, *J* = 18.0 Hz), 4.41 (d, 1 H, *J* = 18.0 Hz), 4.33 (s, 1 H), 3.52 (d, 1 H, *J* = 10.0 Hz), 3.44 (d, 1 H, *J* = 10.0 Hz), 1.46 (s, 3 H), 1.42 (s, 3 H), 1.32 (s, 3 H), 1.10 (s, 9 H), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 135.9, 135.8, 133.5, 133.1, 130.0, 123.0, 128.0, 127.9, 109.2, 84.7, 84.6, 68.7, 66.2, 27.8, 26.9, 26.7, 26.2, 24.0, 19.5, 18.7, -5.3, -5.6; LRMS(FAB+) *m/z* 579 (M+Na)$^+$; HRMS(FAB+) *m/z* $C_{31}H_{48}O_5Si_2Na$ (M + Na)$^+$ calcd 579.2938, obsd 579.2951.

(4*S*,5*R*)-4-(*tert*-Butyl-dimethyl-silanyloxymethyl)-5-(3-*tert*-butyl-diphenyl-silanyloxyprop-1-en-2-yl)-2,2,4-trimethyl-1,3-dioxolane (21): To a stirred suspension of methyltriphenylphosphonium bromide (4.91 g, 13.74 mmol) in anhydrous tetrahydrofuran (60 mL) was added potassium *tert*-butoxide (1.68 g, 13.75 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h to give a yellow suspension. A solution of **20** (3.83 g, 6.88 mmol) in anhydrous THF (35 mL) was added dropwise at 0 °C, and the reaction mixture was allowed to reach room temperature. After being stirred for an additional 1.5 h, the reaction mixture was treated with saturated aqueous NH_4Cl solution (20 mL). The aqueous layer was extracted with diethyl ether and the organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (30:1) as the eluent to give olefin **21** (3.55 g, 92%) as a colorless oil: $[\alpha]_D^{25}$ -8.6 (*c* 2.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.35 (m, 10 H), 5.37 (s, 1 H), 5.22 (s, 1 H), 4.52 (s, 1 H), 4.24 (d, 1 H, *J* = 12.8 Hz), 4.18 (d, 1 H, *J* = 13.2 Hz), 3.47 (d, 1 H, *J* = 9.6 Hz), 3.17 (d, 1 H, *J* = 9.6 Hz), 1.43 (s, 3 H), 1.39 (s, 3 H), 1.32 (s, 3 H), 1.05 (s, 9 H), 0.79 (s, 9 H), -0.04 (s, 3 H), -0.07 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 135.8, 135.7, 133.7, 133.7, 129.9, 129.9, 127.9, 127.9, 110.8, 106.9, 82.2, 81.6, 65.8, 65.6, 28.6, 27.0, 26.6, 26.0, 22.3, 19.5, 18.5, -5.4, -5.5; LRMS(FAB+) *m/z* 577 (M+Na)$^+$; HRMS (FAB+) *m/z* $C_{32}H_{50}O_4Si_2Na$ (M+Na)$^+$ calcd 577.3145, obsd 577.3132.

((4*S*,5*R*)-5-(3-*tert*-Butyl-diphenyl-silanyloxyprop-1-en-2-yl)-2,2,4-trimethyl-1,3-dioxolan-4-yl)methanol (22): To a stirred solution of **21** (1.94 g, 3.53 mmol) in EtOH (60 mL) was added pyridinium *p*-toluene sulfonate (800 mg, 3.20 mmol) and *p*-toluene sulfonic acid (200 mg, 1.04 mmol) at room temperature. After being stirred at the same temperature for 7 h, the reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (6:1) as the eluent to give alcohol **22** (697 mg, 45%, recovered yield: 83%) as a colorless oil with staring material **21** (898 mg): $[\alpha]_D^{25}$ -14.2 (*c* 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.36 (m, 10 H), 5.43 (s, 1 H), 5.41 (s, 1 H), 4.40 (s, 1 H), 4.17 (d, 1 H, *J* = 13.6 Hz), 4.10 (d, 1 H, *J* = 13.6 Hz), 3.33 (dd, 1 H, *J* = 4.8, 11.2 Hz), 3.21 (dd, 1 H, *J* = 8.4, 11.2 Hz), 1.86-1.82 (m, 1 H), 1.46 (s, 3 H), 1.38 (s, 3 H), 1.31 (s, 3 H), 1.05 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 135.7, 133.2, 133.2, 130.1, 128.0, 112.6, 107.6, 82.1, 82.0, 65.5, 64.8, 28.5, 27.0, 26.7, 22.0, 19.4; LRMS (FAB+)

m/z 463 $(M + Na)^-$; HRMS(FAB+) *m/z* $C_{26}H_{36}O_4SiNa$ $(M + Na)^-$ calcd 463.2281, obsd 463.2267.

(4*R*,5*R*)-5-(3-*tert*-Butyl-diphenyl-silanyloxyprop-1-en-2-yl)-2,2,4-trimethyl-1,3-dioxolane-4-carbaldehyde (23): Compound **22** (808 mg, 1.83 mmol) was converted to **23** (780 mg, 97%) as a colorless oil in a similar procedure used for the synthesis of **20**: $[\alpha]_D^{25}$ -12.9 (*c* 2.16, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.36 (s, 1 H), 7.66-7.36 (m, 10 H), 5.35-5.34 (m, 2 H), 4.60 (s, 1 H), 4.13 (d, 1 H, *J* = 13.6 Hz), 4.07 (d, 1 H, *J* = 14.4 Hz), 1.47 (s, 3 H), 1.35 (s, 3 H), 1.24 (s, 3 H), 1.04 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 140.5, 135.7, 135.7, 133.3, 133.2, 130.1, 130.0, 128.0, 128.0, 113.1, 110.2, 85.3, 83.1, 64.6, 28.2, 27.0, 26.5, 19.5, 16.5; LRMS (FAB+) *m/z* 439 $(M + H)^+$; HRMS(FAB+) *m/z* $C_{26}H_{35}O_4Si$ $(M + H)^-$ calcd 439.2305, obsd 439.2312.

1-((4*S*,5*R*)-5-(1-*tert*-Butyl-diphenyl-silanyloxyvinyl)-2,2,4-trimethyl-1,3-dioxolan-4-yl)prop-2-en-1-ol (24): To a stirred solution of **23** (780 mg, 1.78 mmol) in tetrahydrofuran (20 mL) was added vinylmagnesium bromide (1 M solution in tetrahydrofuran, 3.56 mL, 3.56 mmol) at -78 °C, and the reaction mixture was stirred at -78 °C for 1 h. After being quenched with saturated ammonium chloride solution, the mixture was allowed to warm to room temperature, extracted with diethyl ether, dried over anhydrous magnesium sulfate, filtered, and concentrated to dryness. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (15:1) as the eluent to give diene **24α** (530 mg, 64%) and **24β** (230 mg, 28%) as a colorless oil: compound **24α**: $[\alpha]_D^{25}$ -44.9 (*c* 1.03, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70-7.37 (m, 10 H), 6.11-6.03 (m, 1 H), 5.59 (s, 1 H), 5.48 (s, 1 H), 5.35 (td, 1 H, *J* = 1.6, 17.2 Hz), 5.24 (td, 1 H, *J* = 1.6, 10.8 Hz), 4.34 (s, 1 H), 4.25 (d, 1 H, *J* = 13.2 Hz), 4.18 (d, 1 H, *J* = 13.2 Hz), 4.25-4.23 (m, 1 H), 2.21 (d, 1 H, *J* = 3.6 Hz), 1.48 (s, 3 H), 1.36 (s, 3 H), 1.24 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 136.7, 135.8, 135.8, 133.1, 133.1, 130.1, 128.0, 128.0, 116.2, 112.8, 107.4, 84.2, 82.9, 71.5, 65.1, 28.5, 27.0, 26.6, 19.4, 18.6; LRMS (FAB+) *m/z* 467 $(M+H)^-$; HRMS (FAB+) *m/z* $C_{28}H_{38}O_4SiNa$ $(M + Na)^+$ calcd 489.2437, obsd 489.2440: compound **24β**: $[\alpha]_D^{25}$ +4.0 (*c* 0.86, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67-7.36 (m, 10 H), 5.71-5.62 (m, 1 H), 5.48 (s, 1 H), 5.46 (s, 1 H), 5.25 (d, 1 H, *J* = 17.2 Hz), 5.10 (d, 1 H, *J* = 10.4 Hz), 4.44 (s, 1 H), 4.17 (d, 1 H, *J* = 14.4 Hz), 4.11 (d, 1 H, *J* = 14.4 Hz), 3.98 (d, 1 H, *J* = 6.4 Hz), 2.67 (s, 1 H), 1.53 (s, 3 H), 1.39 (s, 3 H), 1.15 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 135.7, 135.7, 135.6, 133.4, 133.3, 130.1, 128.0, 128.0, 118.0, 112.5, 107.6, 83.8, 82.4, 73.5, 64.8, 28.0, 27.0, 26.5, 20.9, 19.5; LRMS (FAB+) *m/z* 489 $(M+Na)^-$; HRMS (FAB+) *m/z* $C_{28}H_{39}O_4Si$ $(M + H)^+$ calcd 467.2618, obsd 467.2612.

(3a*S*,4*R*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,6a-dihydro-2,2,3a-trimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4-ol (25): To a stirred solution of **24β** (230 mg, 0.49 mmol) in anhydrous methylene chloride (8 mL) was added Grubbs catalyst 2nd generation (25 mg, 0.03 mmol) at 0 °C, and the reaction mixture was stirred for 7 h at room temperature. After the volatiles were removed, the resulting residue was purified by column chromatography using hexanes and ethyl acetate (5:1) as the eluent to give β-cyclopentenol **25** (190 mg, 88%) as a colorless oil: $[\alpha]_D^{25}$ -24.6 (*c* 0.99, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.35 (m, 10 H), 5.85 (d, 1 H, *J* = 2.0 Hz), 4.67 (s, 1 H), 4.60 (d, 1 H, *J* = 7.5 Hz), 4.36 (d, 1 H, *J* = 16.0 Hz), 4.31 (d, 1 H, *J* = 16.0 Hz), 1.57 (d, 1 H, *J* = 7.0 Hz), 1.42 (s, 3 H), 1.39 (s, 3 H), 1.22 (s, 3 H), 1.09 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 135.8, 135.8, 133.5, 133.5, 130.0, 128.0, 127.9, 112.2, 90.6, 89.2, 81.6, 61.4, 29.3, 28.8, 27.0, 20.6, 19.5; LRMS (FAB+) *m/z* 461 $(M + Na)^-$; HRMS (FAB+) *m/z* $C_{26}H_{35}O_4Si$ $(M + H)^-$ calcd 439.2305, obsd 439.2319.

(3a*S*,4*S*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,6a-dihydro-2,2,3a-trimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4-ol (26): Method A. To a stirred solution of **24α** (400 mg, 0.91 mmol) in anhydrous methylene chloride (10 mL) was added Grubbs catalyst 2nd generation (15 mg, 0.02 mmol) at 0 °C, and the reaction mixture was stirred for 6 h at room temperature. After the volatiles were removed, the resulting residue was purified by column chromatography using hexanes and ethyl acetate (11:1) as the eluent to give α-cyclopentenol **26** (322 mg, 86%) as a colorless oil. **Method B.** To a stirred solution of **14** (14.1 mg, 0.03 mmol) in anhydrous methylene chloride (1.5 mL) was added diisobutylaluminum hydride (Dibal-H, 0.1 mL, 0.1 mmol, 1.0 M solution in hexanes) at -78 °C, and the reaction mixture was stirred for 30 min at the same temperature. MeOH (0.1 mL), hexanes (0.2 mL) and ethyl acetate (0.2 mL) were added successively and the resulting mixture was stirred overnight, allowing it to reach room temperature. The generated gel was filtered off through a pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (11:1) as the eluent to give α-cyclopentenol **26** (13 mg, 93%) as a colorless oil: $[\alpha]_D^{25}$ +19.5 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.68-7.32 (m, 10 H), 5.84 (d, 1 H, *J* = 1.6 Hz), 4.54 (s, 1 H), 4.34 (d, 1 H, *J* = 15.6 Hz), 4.25 (d, 1 H, *J* = 15.6 Hz), 4.20-4.16 (m, 1 H), 2.73 (d, 1 H, *J* = 9.6 Hz), 1.48 (s, 3 H), 1.40 (s, 3 H), 1.23 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 135.8, 135.8, 133.5, 130.1, 130.0, 127.9, 112.9, 88.4, 87.2, 79.1, 61.0, 29.6, 28.9, 27.0, 23.7, 19.5; LRMS (FAB+) *m/z* 461 $(M + Na)^-$; HRMS (FAB+) *m/z* $C_{26}H_{35}O_4Si$ $(M + H)^+$ calcd 439.2305, obsd 439.2312.

(3a*R*,6a*R*)-6-((*tert*-Butyl-diphenyl-silanyloxymethyl)-2,2,3a-trimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4(6a*H*)-one (14): To a stirred solution of oxalyl chloride (0.06 mL, 0.69 mmol) in dry methylene chloride (2.5 mL) was added dimethyl sulfoxide (0.1 mL, 1.41 mmol) at -78 °C, and the mixture was stirred at -78 °C for 30 min. To this mixture was added a solution of **25** (175 mg, 0.40 mmol) in methylene chloride (2.5 mL), and the reaction mixture was stirred at -78 °C for 1 h. After the addition of triethylamine (0.38 mL, 2.73 mmol), the mixture was gradually warmed to room temperature. The reaction mixture was quenched with water and then extracted with methylene chloride. The organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes and ethyl acetate (14:1) as the eluent to give cyclopentenone **14** (150 mg, 86%) as a colorless oil: $[\alpha]_D^{25}$ +4.8 (*c* 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.66-7.34 (m, 10 H), 6.35 (t, 1 H, *J* = 2.0 Hz), 4.67 (dd, 1 H, *J* = 1.6, 18.8 Hz),

4.61 (s, 1 H), 4.48 (dd, 1 H, J = 1.6, 18.8 Hz), 1.41 (s, 3 H), 1.37 (s, 3 H), 1.20 (s, 3 H), 1.07 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 175.9, 135.7, 135.6, 132.8, 132.7, 130.3, 128.1, 127.6, 115.2, 84.1, 83.9, 62.7, 28.9, 28.4, 26.9, 19.6, 19.5; LRMS (FAB+) *m/z* 437 $(M + H)^+$; HRMS (FAB+) *m/z* $C_{26}H_{33}O_4Si$ $(M + H)^+$ calcd 437.2148, obsd 437.2158.

9-((3a*S*,4*R*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,6a-dihydro-2,2,3a-trimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)-6-chloro-9*H*-purine (27) and **9-((3a*S*,6*R*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-6,6a-dihydro-2,2,3a-trimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-6-yl)-6-chloro-9*H*-purine (28):** To a stirred solution of cyclopentenol **26** (121 mg, 0.28 mmol), triphenyl phosphine (145 mg, 0.56 mmol) and 6-chloropurine (86 mg, 0.56 mmol) in tetrahydrofuran (5 mL) was added dropwise diethyl azodicarboxylate (0.09 mL, 0.56 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 1 h. The volatiles were evaporated *in vacuo* and the resulting residue was purified by silica gel column chromatography using hexanes and ethyl acetate (4.7:1) as the eluent to give the protected 6-chloropurine nucleoside **27** (67 mg, 42%) as a colorless oil and migrated product **28** (5 mg, 3%) as a colorless oil: compound **27**: UV (CH_2Cl_2) λ_{max} 266.0 nm; $[\alpha]_D^{25}$ -32.8 (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1 H), 7.83 (s, 1 H), 7.70-7.36 (m, 10 H), 5.89-5.86 (m, 1 H), 5.75-5.72 (m, 1 H), 4.83 (s, 1 H), 4.50 (d, 1 H, J = 17.2 Hz), 4.46 (d, 1 H, J = 17.2 Hz), 1.40 (s, 3 H), 1.34 (s, 3 H), 1.08 (s, 9 H), 0.91 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 152.6, 152.4, 151.5, 143.8, 135.7, 133.2, 133.2, 132.1, 130.3, 130.2, 128.1, 128.1, 121.4, 113.4, 90.0, 89.5, 67.6, 61.4, 29.1, 28.9, 27.0, 20.9, 19.5; LRMS (FAB+) *m/z* 575 $(M + H)^+$; HRMS (FAB+) *m/z* $C_{31}H_{36}ClN_4O_3Si$ $(M+H)^+$ calcd 575.2245, obsd 575.2240; compound **28**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (s, 1 H), 7.92 (s, 1 H), 7.73-7.40 (m, 10 H), 6.13 (t, 1 H, J = 2.0 Hz), 5.94 (d, 1 H, J = 2.0 Hz), 4.77 (s, 1 H), 4.55- 4.47 (m, 2 H), 1.63 (s, 3 H), 1.42 (s, 3 H), 1.11 (s, 9 H), 0.93 (s, 3 H).

9-((3a*S*,4*R*,6a*R*)-6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,6a-dihydro-2,2,3a-trimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)-9*H*-purin-6-amine (29): A solution of **27** (57 mg, 0.10 mmol) in methanolic ammonia (2 mL) was heated to 80 °C in a glass bomb for 7 h. After cooling to room temperature, the volatiles were removed *in vacuo*. The resulting residue was purified by silica gel column chromatography using hexanes and ethyl acetate (1:2) as the eluent to give protected adenine nucleoside **29** (47 mg, 84%) as a white solid: mp 155.4-157.4 °C; UV (CH_2Cl_2) λ_{max} 261 nm; $[\alpha]_D^{25}$ -27.3 (*c* 0.63, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1 H), 7.52 (s, 1 H), 7.70-7.35 (m, 10 H), 5.88-5.85 (m, 1 H), 5.68-5.65 (m, 1 H), 4.81 (s, 1 H), 4.49 (d, 1 H, J = 15.6 Hz), 4.44 (d, 1 H, J = 15.6 Hz), 2.13 (br s, 2 H), 1.39 (s, 3 H), 1.32 (s, 3 H), 1.07 (s, 9 H), 0.93 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 153.7, 151.8, 150.9, 139.0, 135.7, 133.3, 133.3, 130.2, 128.1, 112.2, 120.1, 113.1, 90.2, 89.6, 66.9, 61.4, 29.2, 28.9, 27.0, 20.9, 19.5; LRMS (FAB+) *m/z* 556 $(M + H)^+$; HRMS (FAB+) *m/z* $C_{31}H_{38}N_5O_3Si$ $(M + H)^+$ calcd 556.2744, obsd 556.2734.

(1*S*,2*R*,5*R*)-5-(6-Amino-9*H*-purin-9-yl)-3-(hydroxymethyl)-1-methylcyclopent-3-ene-1,2-diol (3): To a stirred solution of **29** (47 mg, 0.08 mmol) in MeOH (0.5 mL) was added 4 *N*-HCl (1 mL) at room temperature. After being stirred at the same temperature for 6 h, the reaction mixture was evaporated under reduced pressure until the volumn of solution became 0.5 mL, neutralized with basic resin, and filtered. The filtrate was concentrated *in vacuo* and the resulting residue was purified by silica gel column chromatography using methylene chloride and MeOH (7:1) as the eluent to give 2′-β-*C*-methylneplanocin A (**3**) (20 mg, 86%) as a white solid: mp = 212.5 - 213.7 °C; UV (MeOH) λ_{max} 261.0 nm; $[\alpha]_D^{25}$ -134.0 (*c* 0.52, DMF); ^{1}H NMR (500 MHz, CD_3OD) δ 8.22 (s, 1 H), 7.98 (s, 1 H), 5.94 (s, 1 H), 5.49 (d, 1 H, J = 1.5 Hz), 4.47 (s, 1 H), 4.36 (d, 1 H, J = 15.5 Hz), 4.32 (d, 1 H, J = 15.5 Hz), 0.87 (s, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 156.2, 152.7, 152.0, 150.0, 140.0, 121.9, 119.1, 79.3, 79.0, 67.1, 59.0, 21.4; LRMS (FAB+) *m/z* 278 $(M + H)^+$.

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