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Radical-mediated stannylation of vinyl sulfones: access to novel 4′-modified neplanocin A analogues

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ABSTRACT

Synthesis of 4′-substituted (halogeno, phenyl, ethynyl, and cyano) neplanocin A analogues was carried out. A cyclopentenol derivative having a vinylstannane structure was designed as key-intermediate in this study, which was prepared based on radical-mediated sulfur-extrusive stannylation. The resulting stannylated cyclopentenol **15** was successfully condensed with 6-chloropurine through the Mitsunobu reaction, leading to the carbocyclic nucleoside **20**. Compound **20** was converted to its adenine counterpart **21** by treatment with NH_3/MeOH, during which the 4′-stannyl group remained intact. The title compounds were prepared by using **21** or the 4′-iodo derivative (**22**) mostly through the Stille reaction.

1. Introduction

Neplanocin A (NepA, **1** in Fig. 1) is an antibiotic isolated from *Ampullariella regularis*.[1] This compound has a wide range of antiviral activities[2] as well as antimalarial activity,[3] which are known to be associated with its inhibition of *S*-adenosyl-L-homocysteine hydrolase (SAH hydrolase).[4] On the other hand, because of its structural similarity to adenosine, NepA acts as a substrate for adenosine kinase and hence it shows cytotoxic effects.[5] In order for NepA to serve solely as an inhibitor against SAH hydrolase without showing cytotoxicity, removal of its 6′-hydroxyl group is certainly a rational approach to avoid metabolic transformation to the corresponding nucleotide. In this context, the 6′-deoxy analogues like **2**–**5** have already been synthesized either from NepA itself[6] or from carbohydrate precursors.[7] However, it has been reported that only **2**[7] retains the inhibitory activity against SAH hydrolase.[5,8]

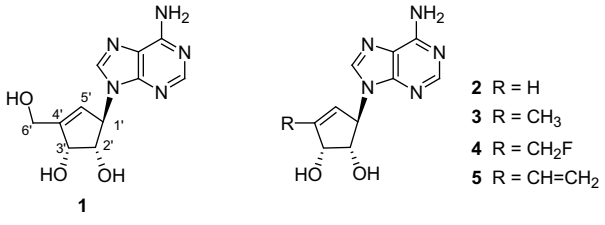

Figure 1. Structures of compounds **1**–**5**.

To further evaluate the NepA analogues lacking the 6′-hydroxyl group as SAH hydrolase inhibitors, we planned to develop a new synthetic approach, which allows the introduction of several carbon-functionalities into the 4′-position of **2**. Herein we report the synthesis of the 4′-halogeno, 4′-phenyl, 4′-ethynyl, and 4′-cyano analogues of **2** from a common vinylstannane intermediate, the preparation of which is based on radical-mediated stannylation of a vinyl sulfone.

2. Results and discussion

2.1. Synthetic plan

Our synthetic plan for the target compounds **A** is shown in Scheme 1. Compound **A** can be prepared from a common intermediate **B** by employing the Stille reaction.[9] A conventional S_N2 displacement of **C** will lead to **B** by the use of adenine or its synthetic equivalent as a nucleophile. Transformation of the vinyl sulfide or the vinyl sulfone **D** to the vinylstannane **C** is certainly a key-step in this synthetic scheme, and we expected that radical-mediated sulfur-extrusive stannylation would be applicable.[10,11]

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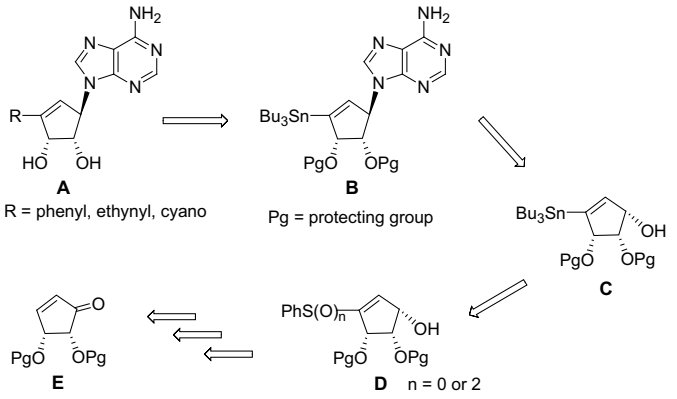
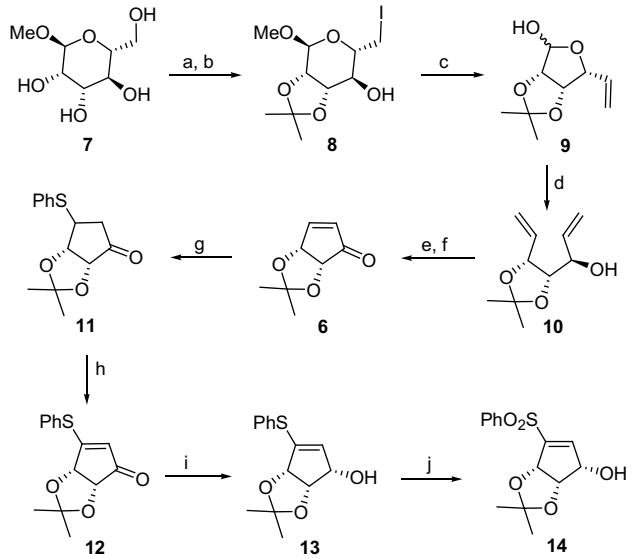
The preparation of **D** can be carried out starting with the known optically active cyclopentene **E** by following a sequence of reactions: 1,4-addition of benzenethiol, oxidation to regenerate an enone system, and selective 1,2-reduction.



Scheme 1. Synthetic plan.

2.2. Synthesis of the sulfur substrates (13 and 14) for radical-mediated stannylation

We selected the cyclopentenone **6**[7,12] for the preparation of **D** in Scheme 1. Compound **6** was prepared from **7** by the reported method with a slight modification. As shown in Scheme 2, commercially available methyl α-D-mannopyranoside **7** was converted to the iodide and then protected as an acetonide to yield **8**.[13] Treatment of **8** with Zn-powder in refluxing EtOH/H_2O gave the hemiacetal **9**[14] in quantitative yield. The Wittig reaction of **9** by using $Ph_3P{=}CH_2$ readily proceeded to give the diene **10**.[15] The requisite cyclopentenone **6** was obtained by ring closing metathesis of **10**[12a–d] and subsequent PDC oxidation of the resulting allyl alcohol in a one-pot manner.

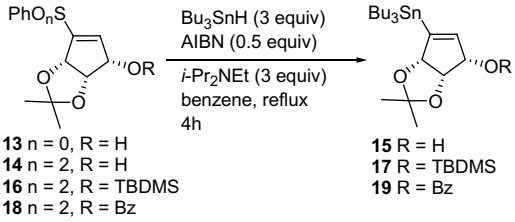


Scheme 2. Reagents and conditions: (a) I_2, Ph_3P, imidazole, THF, reflux; (b) 2,2-dimethoxypropane, TsOH, acetone, rt, (93% from **7**); (c) Zn-powder, EtOH, H_2O, 100 °C, (93%); (d) Ph_3PCH_3Br, NaH, DMSO, THF, reflux; (e) Grubbs first generation catalyst, CH_2Cl_2, rt; (f) PDC, CH_2Cl_2, (72% from **9**); (g) PhSH, Et_3N, CH_2Cl_2, rt, (81%); (h) NCS, CH_2Cl_2, rt, (94%); (i) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, −40 °C, (99%); (j) *m*-CPBA, CH_2Cl_2, rt, (100%).

The sulfide (**13**) and sulfone (**14**) to be used for radical stannylation were prepared as follows. Compound **6** was subjected to 1,4-addition of PhSH to give **11**. Treatment of **11** with NCS allowed regeneration of the double bond through the Pummerer type oxidation.[16] Stereoselective 1,2-reduction of the resulting enone **12** under the Luche conditions[17] gave the desired sulfide **13**. The sulfone **14** was prepared simply by oxidation of **13** with *m*-CPBA.

2.3. Radical-mediated stannylation of 13 and 14

Reaction of the sulfur functionalities in **13** and **14** with tributyltin radical was next examined (Scheme 3). These reactions were uniformly carried out in the presence of *i*-Pr_2NEt to prevent decomposition of the product as reported previously.[10e,11f] When the sulfide **13** was reacted with Bu_3SnH (3 equiv) in the presence of AIBN (0.5 equiv) and *i*-Pr_2NEt (3 equiv) in refluxing benzene for 4 h, only a trace amount of the stannylated product (**15**) was formed (Table 1, entry 1). The sulfone **14**, on the other hand, gave a higher yield of 52% (entry 2). Several attempts were made by increasing the amount of Bu_3SnH, prolonging the reaction time, and carrying out the reaction at higher temperature, but no significant improvement was seen in the yield of **15** from **14**.



Scheme 3. Sulfur-extrusive stannylation of **13**–**18**.

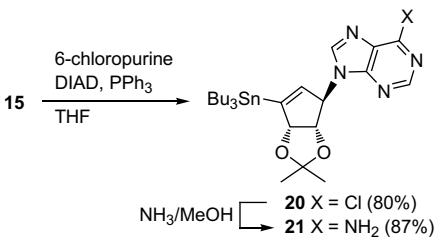
Table 1
Radical-mediated stannylation of **13**–**18**

Entry	Substrate	Yield (%) of the product	Recovery (%)
1	**13**	4 (**15**)	94 (**13**)
2	**14**	52 (**15**)	32 (**14**)
3	**16**	79 (**17**)[a]	21 (**16**)[a]
4	**18**	94 (**19**)[a]	6 (**18**)[a]

[a] Calculated by ^1H NMR spectroscopy.

It was found that the silyl protected vinyl sulfone **16** gave a higher yield of the stannylated product **17** (entry 3). When the benzoyl protected vinyl sulfone **18** was employed as a substrate, the highest yield of the product (**19**) was realized (entry 4). Practically, the requisite **15** can be obtained in 90% yield simply by evaporating the reaction mixture containing **19** and then treating the residue with NaOMe/MeOH.

Direct introduction of adenine base to **15** through the Mitsunobu reaction (DEAD/Ph_3P/THF)[18] was found to be discouraging, due to the difficulty to separate the resulting carbocyclic adenine-nucleoside **21** from diethyl 1,2-hydrazinedicarboxylate and Ph_3PO. The use of 6-chloropurine allowed the isolation of **20** in 80% yield after column chromatography (Scheme 4). The depicted N^9-substituted regiochemistry of **20** was confirmed by HMBC spectrum (correlation between H-1′ and C-4). Treatment of **20** with NH_3/MeOH in a sealed tube at 120 °C for 47 h gave the 4′-tributylstannyl derivatives (**21**) in 87% yield. Since we have experienced



Scheme 4. Mitsunobu reaction of **15** and further conversion of the product (**20**) to **21**.

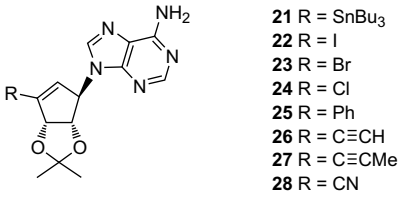
that a tributylstannyl group attached to an sp^2-hybridized carbon underwent protonolysis upon reacting with NH_3/MeOH,[19] the observed successful conversion from **20** to **21** under the above considerably forced reaction conditions was surprising.

Preparation of the 4′-halogeno, 4′-phenyl, 4′-ethynyl analogues was carried out by employing either **21** or the 4′-iodo derivative **22** (Table 2 and Fig. 2), the latter was readily obtained in quantitative yield by reacting **21** with iodine in THF (entry 1 in Table 2). Bromination and chlorination of **21** were performed by using NBS or NCS to give the respective 4′-halogeno derivative (**23**, 67%; **24**, 49%) (entries 2 and 3). The 4′-phenyl analogue **25** was prepared in a moderate yield through the Stille reaction between **21** and iodobenzene in DMF (entry 4). For the preparation of the ethynyl analogues (**26** and **27**), the cross-coupling reaction between the 4′-iodo derivative **22** and the respective organotin reagents was successfully applied (entries 5 and 6).

Table 2
Conversion of the 4′-tributylstannyl group of **21**

Entry	Substrate	Condition	Products (% yield by isolation)
1	**21**	I_2/THF, rt	**22** (100)
2	**21**	NBS/THF, rt	**23** (67)
3	**21**	NCS/THF, rt	**24** (49)
4	**21**	PhI, $(PPh_3)_2PdCl_2$, CuI/DMF, 120 °C	**25** (51)
5	**22**	$Bu_3SnC{\equiv}CH$, $Pd(PPh_3)_4$, CuI/THF, rt	**26** (83)
6	**22**	$Bu_3SnC{\equiv}CMe$, $Pd(PPh_3)_4$, CuI/THF, rt	**27** (100)
7[a]	**22**	Bu_3SnCN, $Pd(PPh_3)_4$, CuI/DMF, 120 °C	**28** (9), **21** (11)
8	**22**	Bu_3SnCN, $Pd(PPh_3)_4$/dioxane, 90 °C	**28** (25), **21** (20)
9[b]	**22**	Bu_3SnCN, $(PPh_3)_2PdCl_2$, CuI/DMF, 120 °C	**28** (73)

[a] The reaction was carried out in the presence of 0.2 equiv of CuI.
[b] CuI (1.0 equiv) was used.

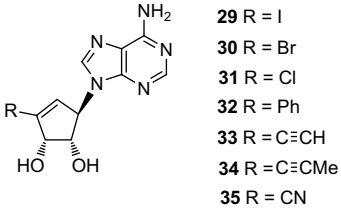


21 R = $SnBu_3$
22 R = I
23 R = Br
24 R = Cl
25 R = Ph
26 R = C≡CH
27 R = C≡CMe
28 R = CN

Figure 2. Structures of compounds **21**–**28**.

Introduction of a cyano group was also carried out. Compound **22** was reacted with Bu_3SnCN in the presence of a catalytic amount of $Pd(PPh_3)_4$ and CuI in DMF according to the reported method (entry 7).[20a] This reaction, however, gave the desired 4′-cyano analogue **34** only in 9% yield. An additional product from this reaction was **21** (11%), apparently formed as a consequence of transfer of $SnBu_3$ group from the reagent. A similar trend was also observed when the reaction was carried out in the absence of CuI in refluxing dioxane (entry 8).[20b] Successful result was obtained by employing stoichiometric amount of CuI in combination with $PdCl_2(PPh_3)_2$ in DMF (entry 9).[10e]

Finally, the above synthesized compounds (**22**–**28**) were treated with 50% aqueous HCO_2H to give the respective free 4′-substituted Nep A analogues (**29**–**35**, Fig. 3) uniformly in high yields. Evaluation of antiviral and antimalarial activities of these compounds is a subject of our future studies.



29 R = I
30 R = Br
31 R = Cl
32 R = Ph
33 R = C≡CH
34 R = C≡CMe
35 R = CN

Figure 3. Compounds **29**–**35**.

3. Experimental section

3.1. General

^1H and ^{13}C NMR spectra were recorded either at 400 MHz or at 500 MHz. Chemical sifts are reported relative to Me_4Si. Mass spectra (MS) were taken in FAB mode with *m*-nitrobenzyl alcohol as a matrix. Column chromatography was carried out on silica gel. Thin-layer chromatography (TLC) was performed on precoated silica gel plate F_{254}. When necessary, analytical samples were purified by high performance liquid chromatography (HPLC). THF was distilled from benzophenone ketyl.

3.2. Methyl 6-deoxy-6-iodo-2,3-*O*-isopropylidene-α-D-mannopyranoside (8)

This compound was prepared by the reported method[17] with a slight modification. To a suspension of methyl α-D-mannopyranoside **7** (30.0 g, 155 mmol), imidazole (21.0 g, 309 mmol), and Ph_3P (60.9 g, 232 mmol) in THF (400 mL) was added I_2 (58.9 g, 232 mmol) in several portions. The resulting mixture was refluxed for 2 h, and then all the volatiles were evaporated. The residue was dissolved in a mixture of acetone (900 mL) and 2,2-dimethoxypropane (100 mL). To this was added $TsOH{\cdot}H_2O$ (17.6 g, 92.7 mmol) at 0 °C. After stirring for 5 min, the reaction mixture was allowed to warm to rt and stirred further 1 h. After addition of Et_3N (100 mL), approximately two-thirds of volatiles were evaporated. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=4/1) of the organic layer gave **8**[13] (49.4 g, 93%) as a solid.

3.3. 5,6-Dideoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hex-5-enofuranose (9)

A mixture of **8** (47.4 g, 138 mmol), Zn-powder (46.5 g), H_2O (80 mL), and EtOH (160 mL) was refluxed for 3 h. The mixture was filtered through a Celite pad and washed with EtOH. The filtrate was evaporated, and then partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=4/1) of the organic layer gave **9**[14,15] (23.8 g, 93%) as an oil.

3.4. (1*R*,4′*S*,5′*R*)-1-(2′,2′-Dimethyl-5′-vinyl[1′,3′]dioxol-4′-yl)prop-2-en-1-ol (10)

To a stirred suspension of NaH (60% oil-dispersion, 9.60 g, 255 mmol) in THF (500 mL) was added DMSO (26.6 mL, 375 mmol) at 0 °C. After stirring for 5 min, the mixture was allowed to warm to rt and stirred for 1 h, and then reacted with Ph_3PCH_3Br (91.0 g, 255 mmol) by adding at 0 °C and stirring for 1.5 h at rt. A THF (200 mL) solution of **9** (27.1 g, 150 mmol) was added to the above mixture at 0 °C and the resulting solution was refluxed for 4 h. After cooling the reaction mixture, approximately two-thirds of volatiles were evaporated. The reaction mixture was partitioned between Et_2O and saturated aqueous NH_4Cl. Column chromatography (hexane/EtOAc=4/1) of the organic layer gave **10**[12a,15] (22.2 g, 80%) as an oil.

3.5. (3a*R*,6a*R*)-2,2-Dimethyl-3a,6a-dihydrocyclopenta[1,3]-dioxol-4-one (6)

A mixture of **10** (9.70 g, 52.7 mmol) and Grubbs first generation catalyst (430 mg, 0.530 mmol) in CH_2Cl_2 (200 mL) was stirred at rt under positive pressure of dry Ar for 2 days. The reaction mixture was treated with PDC (39.7 g, 106 mmol) by stirrring at rt for further 2 days. After adding AcOEt (ca. 50 mL), the reaction mixture was filtered through a silica gel pad. The resulting filtrate was

evaporated and purified by column chromatography (hexane/EtOAc=2/1). This gave **6**[7,12](7.20 g, 89%) as a solid: $[\alpha]_D^{25}$ −69.3 (*c* 1.80, $CHCl_3$), [lit[12e] $[\alpha]_D^{25}$ −70.8 (*c* 0.92, $CHCl_3$)].

3.6. (2*R*,3*S*,4*S*)-2,3-Isopropylidenedioxy-4-(phenylthio)cyclopentan-1-one (11)

A mixture of **11** (376 mg, 2.44 mmol), PhSH (0.250 mL, 2.44 mmol), and Et_3N (14.0 μL, 0.100 mmol) in CH_2Cl_2 (4 mL) was stirred at 0 °C for 0.5 h, and then at rt for 2 h under positive pressure of dry Ar. The reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=20/1) of the organic layer gave **11** (520 mg, 81%) as a solid: mp 105–107 °C; $[\alpha]_D^{24}$ −214.7 (*c* 1.13, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.31 and 1.43 (6H, each as s, CMe_2), 2.30 (1H, dq, *J*=18.8 and 1.3 Hz, H-5), 3.09 (1H, ddd, *J*=18.8, 7.6 and 0.7 Hz, H-5), 3.97 (1H, d, *J*=7.6 Hz, H-4), 4.36 (1H, d, *J*=5.1 Hz, H-2), 4.69 (1H, d, *J*=5.1 Hz, H-3), 7.28–7.42 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 24.93, 26.72, 39.43, 42.47, 77.94, 80.79, 113.05, 127.86, 129.43, 131.51, 132.47, 210.96; FABMS *m*/*z* 265 (M^++H). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.63; H, 6.04.

3.7. (2*R*,3*R*)-2,3-Isopropylidenedioxy-4-phenylthio-4-cyclopenten-1-one (12)

A mixture of **11** (200 mg, 0.760 mmol) and NCS (111 mg, 0.830 mmol) in CH_2Cl_2 (5 mL) was stirred at rt for 1 h under positive pressure of dry Ar. The reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=10/1) of the organic layer gave **12** (187 mg, 94%) as a solid: mp 144–146 °C; $[\alpha]_D^{24}$ −161.5 (*c* 0.805, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.45 and 1.48 (6H, each as s, CMe_2), 4.57 (1H, d, *J*=5.6 Hz, H-2), 5.20 (1H, d, *J*=5.6 Hz, H-3), 5.46 (1H, s, H-5), 7.43–7.51 (3H, m, Ph), 7.54–7.56 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 26.45, 27.46, 78.96, 79.42, 115.58, 124.11, 128.04, 130.07, 130.47, 134.50, 178.95, 198.03; FABMS *m*/*z* 263 (M^++H). Anal. Calcd for $C_{14}H_{14}O_3S$: C, 64.10; H, 5.38. Found: C, 64.01; H, 5.27.

3.8. (1*S*,2*S*,3*S*)-2,3-Isopropylidenedioxy-4-phenylthio-4-cyclopenten-1-ol (13)

To a solution of **12** (336 mg, 1.28 mmol) and $CeCl_3 \cdot 7H_2O$ (477 mg, 1.28 mmol) in MeOH (33 mL) was added $NaBH_4$ (58.0 mg, 1.54 mmol) at 40 °C in several portions. The reaction mixture was stirred for 1.5 h, quenched by adding AcOH (88.0 μL, 1.54 mmol), and diluted with acetone. Evaporation of the solvents was followed by partition of the residue between $CHCl_3$ and H_2O. The organic layer was dried (Na_2SO_4) and evaporated to give **13** (335 mg, 99%) as an oil: $[\alpha]_D^{25}$ −98.4 (*c* 1.115, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.42 and 1.53 (6H, each as s, CMe_2), 2.67 (1H, d, *J*=10.0 Hz, OH), 4.53 (1H, ddd, *J*=10.0, 5.6 and 2.0 Hz, H-1), 4.78 (1H, td, *J*=5.6 and 0.7 Hz, H-2), 4.96 (1H, d, *J*=5.6 Hz, H-3), 5.24 (1H, t, *J*=1.0 Hz, H-5), 7.35–7.39 (3H, m, Ph), 7.51–7.53 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 26.85, 27.71, 73.16, 78.19, 84.17, 113.19, 128.02, 128.83, 129.43, 130.82, 134.25, 143.33; FABMS *m*/*z* 303 (M^++K). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.38; H, 6.05.

3.9. (1*S*,2*S*,3*S*)-4-Benzenesulfonyl-2,3-isopropylidenedioxy-4-cyclopenten-1-ol (14)

To a solution of **13** (101 mg, 0.38 mmol) in CH_2Cl_2 (10 mL) was added *m*-CPBA (purity 65%, 203 mg, 0.760 mmol) at 0 °C in several portions. The reaction mixture was stirred at rt for 8 h, quenched by adding saturated aqueous $Na_2S_2O_3$, and then partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=1/1) of the organic layer gave **14** (116 mg, 100%) as a solid: mp 176–178 °C; $[\alpha]_D^{25}$ +129.1 (*c* 1.580, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0.89 and 1.29 (6H, each as s, CMe_2), 2.80 (1H, d, *J*=10.0 Hz, OH), 4.67 (1H, ddd, *J*=10.0, 5.5 and 1.8 Hz, H-1), 4.84 (1H, td, *J*=5.5 and 0.7 Hz, H-2), 5.26 (1H, d, *J*=5.5 Hz, H-3), 6.77 (1H, t, *J*=0.9 Hz, H-5), 7.53–7.57 (2H, m, Ph), 7.63–7.64 (1H, m, Ph), 7.97–8.00 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 26.46, 26.53, 72.45, 78.37, 81.17, 113.55, 128.86, 128.97, 133.75, 139.94, 144.76, 145.98; FABMS *m*/*z* 297 (M^++H). Anal. Calcd for $C_{14}H_{16}O_5S$: C, 56.74; H, 5.44. Found: C, 56.81; H, 5.37.

3.10. Radical reaction of 13 (entry 1 in Table 1)

A benzene (2 mL) solution of **13** (50.0 mg, 0.190 mmol), *i*-Pr_2NEt (100 μL, 0.570 mmol), Bu_3SnH (150 μL, 0.570 mmol), and AIBN (16.0 mg, 100 μmol) was heated at 80 °C for 4 h with stirring. Evaporation of the solvent followed by column chromatography (hexane/EtOAc=10/1) gave **15** (3.00 mg, 4%, oil) and **13** (47.0 mg, 94% recovery). Physical data of **15**: $[\alpha]_D^{24}$ +29.9 (*c* 0.650, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (9H, t, *J*=7.3 Hz, $Sn(CH_2)_3CH_3$), 0.95–0.99 (6H, m, $Sn(CH_2)_3$), 1.25–1.32 (6H, m, $Sn(CH_2)_3$), 1.36 and 1.38 (6H, each as s, CMe_2), 1.48–1.55 (6H, m, $Sn(CH_2)_3$), 2.62 (1H, d, *J*=10.3 Hz, OH), 4.57 (1H, ddd, *J*=10.3, 5.4 and 1.3 Hz, H-1), 4.69 (1H, t, *J*=5.4 Hz, H-2), 5.03 (1H, d, *J*=5.4 Hz, H-3), 5.89 (1H, t, *J*=15.4 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 9.4, 13.7, 27.0, 27.3, 27.9, 29.0, 76.8, 89.7, 111.9, 144.9, 147.7; FABMS *m*/*z* 485 (M^++K). Anal. Calcd for $C_{20}H_{38}O_3Sn$: C, 53.95; H, 8.60. Found: C, 54.25; H, 8.78.

3.11. Radical reaction of 14 (entry 2 in Table 1)

A mixture of **14** (967 mg, 3.26 mmol), *i*-Pr_2NEt (1.70 mL, 9.79 mmol), Bu_3SnH (2.63 mL, 9.79 mmol), and AIBN (268 mg, 1.63 mmol) in benzene (19 mL) was stirred at 80 °C for 4 h under positive pressure of dry Ar. Column chromatography (hexane/EtOAc=10/1) of the reaction mixture gave **15** (758 mg, 52%, oil) and **14** (329 mg, 32% recovery).

3.12. (1*S*,2*S*,3*S*)-4-Benzenesulfonyl-1-*tert*-butyldimethylsilyloxy-2,3-isopropylidenedioxy-4-cyclopentene (16)

A mixture of **14** (300 mg, 1.01 mmol), imidazole (206 mg, 3.03 mmol), DMAP (124 mg, 1.01 mmol), and TBDMSCl (305 mg, 2.02 mmol) in MeCN (10 mL) was stirred at rt for 24 h. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=2/1) of the organic layer gave **16** (237 mg, 57%) as a solid: mp 126–129 °C; $[\alpha]_D^{23}$ +108.0 (*c* 0.685, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.09 (3H, s, SiMe), 0.13 (3H, s, SiMe), 0.79 (3H, s, Me), 0.90 (9H, s, SiBu-*t*), 1.23 (3H, s, Me), 4.70–4.72 (2H, m, H-2 and H-3), 5.16–5.18 (1H, m, H-1), 6.73–6.74 (1H, m, H-5), 7.50–7.64 (2H, m, Ph), 7.57–7.63 (1H, m, Ph), 7.98–8.00 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ −4.8, −4.6, 18.4, 25.8, 26.3, 26.6, 73.8, 79.7, 80.9, 113.0, 128.9, 133.6, 140.1, 145.0, 145.7; FABMS *m*/*z* 411(M^++H). Anal. Calcd for $C_{20}H_{30}O_5SSi$: C, 58.50; H, 7.36. Found: C, 58.85; H, 7.51.

3.13. (1*S*,2*S*,3*S*)-4-Benzenesulfonyl-1-benzoyloxy-2,3-isopropylidenedioxy-4-cyclopentene (18)

To a mixture of **14** (5.50 g, 18.6 mmol), DMAP (2.74 g, 22.3 mmol), and *i*-Pr_2NEt (6.48 mL, 37.2 mmol) in CH_2Cl_2 (100 m L) was added BzCl (2.83 mL, 24.2 mmol) at 0 °C. The resulting mixture was stirred at rt for 3 h. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=1/4) of the organic layer gave **18** (6.10 g, 82%) as a solid: mp 212–215 °C; $[\alpha]_D^{25}$ +159.2 (*c* 0.990, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.07 (3H, s, Me), 1.23 (3H, s, Me), 5.12 (1H, t, *J*=5.6 Hz,

H-2), 5.31 (1H, d, *J*=5.6 Hz, H-3), 5.68–5.69 (1H, m, H-1), 6.90–6.91 (1H, m, H-5), 7.42–7.47 (2H, m, Ph), 7.56–7.59 (2H, m, Ph), 7.64–7.68 (1H, m, Ph); High resolution FABMS (*m*/*z*) calcd for $C_{21}H_{21}O_6S$: 401.1059, found: 401.1090 (M^++H).

3.14. Radical reaction of 16 to yield 17 (entry 3 in Table 1)

A benzene (5 mL) solution of **16** (200 mg, 0.490 mmol), *i*-Pr_2NEt (260 μL, 1.47 mmol), Bu_3SnH (0.380 mL, 1.47 mmol), and AIBN (40.0 mg, 0.250 mmol) was heated at 80 °C for 4 h with stirring. The yield of **17** was calculated based on ^{1}H NMR spectroscopy by integrating H-5.

3.15. Radical reaction of 18 to yield 19 (entry 4 in Table 1) and subsequent conversion to 15

A mixture of **18** (260 mg, 0.650 mmol), *i*-Pr_2NEt (340 μL, 1.95 mmol), Bu_3SnH (525 μL, 1.95 mmol), and AIBN (54.0 mg, 0.330 mmol) in benzene (4 mL) was stirred at 80 °C for 4 h under positive pressure of dry Ar. The reaction mixture was evaporated. The yield of **19** was calculated based on ^{1}H NMR spectroscopy by integrating H-5. The residue was dissolved in MeOH (15 mL), to which NaOMe (176 mg, 3.25 mmol) was added at 0 °C. The mixture was stirred at rt for 2 h and partitioned between CH_2Cl_2 and saturated aqueous NH_4Cl. Column chromatography (hexane/EtOAc=10/1) of the organic layer gave **15** (260 mg, 90%) as an oil.

3.16. 6-Chloro-9-[(1*R*,2*S*,3*S*)-2,3-isopropylidenedioxy-4-tributylstannyl-4-cyclopenten-1-yl]purine (20)

To a THF (40 mL) solution of PPh_3 (1.60 g, 6.10 mmol) was added DEAD (40% toluene solution, 2.65 mL, 6.10 mmol) dropwise at 0 °C under positive pressure of dry Ar. The resulting solution was stirred for 15 min, and then was added to a mixture of **15** (1.06 g, 2.44 mmol) and 6-chloropurine (0.570 g, 3.66 mmol) in THF (20 mL). After being stirred for 0.5 h, the reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (hexane/EtOAc=8/1) of the organic layer gave **20** (1.14 g, 80%) as an oil: $[\alpha]_D^{24}$ −16.0 (*c* 0.775, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.91 (9H, t, *J*=7.3 Hz, $Sn(CH_2)_3CH_3$), 0.97–1.15 (6H, m, $Sn(CH_2)_3$), 1.30–1.39 (6H, m, $Sn(CH_2)_3$), 1.36 and 1.44 (6H, each as s, CMe_2), 1.48–1.64 (6H, m, $Sn(CH_2)_3$), 4.66 (1H, d, *J*=5.4 Hz, H-2′), 5.56 (1H, dt, *J*=5.4 and 1.0 Hz, H-3′), 5.72 (1H, s, H-1′), 5.89–5.96 (1H, m, H-5′), 7.95 (1H, s, H-8), 8.77 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 9.68, 13.68, 26.07, 27.25, 27.48, 29.03, 67.52, 83.83, 90.93, 111.99, 132.14, 135.30, 143.28, 151.10, 151.45, 152.09, 158.04; FABMS *m*/*z* 583 (M^++H). Anal. Calcd for $C_{25}H_{39}ClN_4O_2Sn$: C, 51.61; H, 6.76; N, 9.63. Found: C, 51.74; H, 6.74; N, 9.52.

3.17. 9-[(1*R*,2*S*,3*S*)-2,3-Isopropylidenedioxy-4-tributylstannyl-4-cyclopenten-1-yl]-adenine (21)

A THF (10 mL) solution of **20** (3.20 g, 5.69 mmol) and NH_3/MeOH (saturated at 0 °C, 40 mL) were placed in a sealed tube and the whole was heated at 120 °C for 2 days. The reaction mixture was evaporated and purified by column chromatography (hexane/EtOAc=1/1). This gave **21** (2.70 g, 87%) as an oil: $[\alpha]_D^{23}$ −22.6 (*c* 0.645, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.91 (9H, t, *J*=7.3 Hz, $Sn(CH_2)_3CH_3$), 0.96–1.15 (6H, m, $Sn(CH_2)_3$), 1.30–1.39 (6H, m, $Sn(CH_2)_3$), 1.35 and 1.43 (6H, each as s, CMe_2), 1.46–1.65 (6H, m, $Sn(CH_2)_3$), 4.63 (1H, d, *J*=5.4 Hz, H-2′), 5.51 (1H, dt, *J*=5.4 and 1.2 Hz, H-3′), 5.66 (1H, s, H-1′), 5.87 (2H, br, NH_2), 5.90–5.97 (1H, m, H-5′), 7.61 (1H, s, H-8), 8.39 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 9.6, 13.7, 26.1, 27.5, 29.1, 66.7, 84.1, 90.8, 111.8, 120.1, 136.3, 138.4, 149.9, 153.2, 155.4, 156.8; FABMS *m*/*z* 564 (M^++H). Anal. Calcd for $C_{25}H_{41}N_5O_2Sn$: C, 53.40; H, 7.35; N, 12.45. Found: C, 53.44; H, 7.45; N, 12.38.

3.18. 9-[(1*R*,2*S*,3*S*)-4-Iodo-2,3-isopropylidenedioxy-4-cyclopenten-1-yl]adenine (22)

A mixture of **21** (1.35 g, 2.40 mmol) and iodine (1.22 g, 4.80 mmol as I_2) in THF (40 mL) was stirred at rt for 7 h. The reaction mixture was quenched by adding saturated aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2. Column chromatography (CH_2Cl_2/MeOH=20/1) of the extract gave **22** (957 mg, 100%) as a solid: mp 223–226 °C; $[\alpha]_D^{25}$ −31.2 (*c* 0.510, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 and 1.52 (6H, each as s, CMe_2), 4.70 (1H, d, *J*=5.5 Hz, H-2′), 5.46 (1H, dt, *J*=5.5 and 1.2 Hz, H-3′), 5.49 (1H, t, *J*=2.0 Hz, H-1′), 5.78 (2H, br, NH_2), 6.29–6.30 (1H, m, H-5′), 7.69 (1H, s, H-8), 8.38 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 26.26, 27.40, 65.83, 83.31, 89.71, 106.95, 113.02, 120.03, 135.89, 138.32, 149.62, 153.37, 155.57; High resolution FABMS (*m*/*z*) calcd for $C_{13}H_{15}IN_5O_2$: 400.0251, found: 400.0271 (M^++H).

3.19. 9-[(1*R*,2*S*,3*S*)-4-Bromo-2,3-isopropylidenedioxy-4-cyclopenten-1-yl]adenine (23)

A mixture of **21** (50 mg, 0.09 mmol) and NBS (23 mg, 0.13 mmol) in THF (2 mL) was stirred at rt for 1 h. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (CH_2Cl_2/MeOH=40/1) of the organic layer gave **23** (21.0 mg, 67%) as a solid: mp 199–202 °C; $[\alpha]_D^{24}$ −67.7 (*c* 0.830, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 and 1.53 (6H, each as s, CMe_2), 4.77 (1H, dt, *J*=5.6 and 0.5 Hz, H-2′), 5.44 (1H, ddd, *J*=5.6, 1.7 and 1.0 Hz, H-3′), 5.49 (1H, t, *J*=2.1 Hz, H-1′), 5.66 (2H, br, NH_2), 6.07 (1H, dd, *J*=2.1 and 1.0 Hz, H-5′), 7.71 (1H, s, H-8), 8.38 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 26.1, 27.3, 64.4, 83.5, 86.8, 113.4, 119.7, 128.2, 131.6, 138.4, 149.6, 152.3, 155.6; FABMS *m*/*z* 352 and 354 (M^++H). Anal. Calcd for $C_{13}H_{14}BrN_5O_2 \cdot 1/10H_2O$: C, 44.11; H, 4.04; N, 19.78. Found: C, 44.39; H, 3.86; N, 19.52.

3.20. 9-[(1*R*,2*S*,3*S*)-4-Chloro-2,3-isopropylidenedioxy-4-cyclopenten-1-yl]adenine (24)

A mixture of **21** (60.0 mg, 0.110 mmol) and NCS (28.0 mg, 0.210 mmol) in THF (2 mL) was stirred at rt for 48 h. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (CH_2Cl_2/MeOH=40/1) of the organic layer gave **24** (16.0 mg, 49%) as a foam: $[\alpha]_D^{21}$ −115.6 (*c* 0.270, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 and 1.54 (6H, each as s, CMe_2), 4.79 (1H, d, *J*=5.6 Hz, H-2′), 5.38–5.40 (1H, m, H-3′), 5.54 (1H, t, *J*=2.1 Hz, H-1′), 5.81 (2H, br, NH_2), 5.88–5.90 (1H, m, H-5′), 7.72 (1H, s, H-8), 8.38 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 26.08, 27.31, 63.26, 83.49, 85.18, 113.47, 120.06, 123.93, 138.39, 141.70, 149.64, 153.32, 155.58; High resolution FABMS (*m*/*z*) calcd for $C_{13}H_{15}ClN_5O_2$: 308.0914, found: 308.0932 (M^++H).

3.21. 9-[(1*R*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-phenyl-4-cyclopenten-1-yl]adenine (25)

A mixture of **21** (149 mg, 0.270 mmol) and $(Ph_3P)_2PdCl_2$ (37.0 mg, 53.0 μmol) in DMF (3 mL) was heated at 120 °C for 1 h under positive pressure of dry Ar. To this solution were added CuI (50.0 mg, 0.270 mmol) and PhI (61.0 μL, 0.530 mmol). The reaction mixture was heated at 120 °C for 24 h, and then partitioned between EtOAc and H_2O. Column chromatography (CH_2Cl_2/MeOH=50/1) of the organic layer gave **25** (47 mg, 51%) as a foam: $[\alpha]_D^{23}$ +4.4 (*c* 0.730, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.43 and 1.47 (6H, each as s, CMe_2), 4.84 (1H, d, *J*=5.9 Hz, H-2′), 5.76 (1H, t, *J*=1.2 Hz, H-3′), 5.84 (1H, dd, *J*=5.9 and 1.2 Hz, H-1′), 5.87 (1H, br, NH_2), 6.22 (1H, d, *J*=2.7 Hz, H-5′), 7.39–7.45 (3H, m, Ph), 7.70–7.73 (2H, m, Ph), 7.74 (1H, s, H-8), 8.39 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 25.89, 27.31, 64.96, 84.41, 84.47, 112.77, 119.51, 121.60, 126.99, 128.72, 132.65, 134.50, 139.37, 148.71, 149.69, 153.54, 155.26; High resolution

FABMS (*m*/*z*) calcd for $C_{19}H_{19}N_5O_2$: 350.1617, found: 350.1634 (M^++H).

3.22. 9-[(1*R*,2*S*,3*R*)-4-Ethynyl-2,3-isopropylidenedioxy-4-cyclopenten-1-yl]adenine (26)

A mixture of **22** (261 mg, 0.650 mmol), $Pd(PPh_3)_4$ (38.0 mg, 33 μmol), CuI (6.00 mg, 33 μmol), and $Bu_3SnC{\equiv}CH$ (376 μL, 1.30 mmol) in THF (5 mL) was stirred at rt for 1 h under positive pressure of dry Ar. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (CH_2Cl_2/MeOH=40/1) of the organic layer gave **26** (162 mg, 83%) as a solid: mp 235 °C (decomp.); IR (neat) 2140 cm^{-1} (C≡CH); $[\alpha]_D^{25}$ −57.7 (*c* 0.170, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.39 and 1.54 (6H, each as s, CMe_2), 3.30 (1H, s, C≡CH), 4.75 (1H, d, *J*=5.6 Hz, H-2′), 5.48 (1H, d, *J*=5.6 Hz, H-3′), 5.64 (1H, s, H-1′), 5.70 (2H, br, NH_2), 6.17 (1H, t, *J*=1.3 Hz, H-5′), 7.68 (1H, s, H-8), 8.39 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 25.90, 27.31, 64.70, 77.19, 83.61, 83.72, 86.00, 113.20, 120.09, 132.29, 133.78, 138.46, 149.81, 153.42, 155.40; FABMS *m*/*z* 298 (M^++H). Anal. Calcd for $C_{15}H_{15}N_5O_2{\cdot}1/3H_2O$: C, 59.41; H, 5.20; N, 23.09. Found: C, 59.39; H, 4.96; N, 22.95.

3.23. 9-[(1*R*,2*S*,3*R*)-2,3-Isopropylidenedioxy-4-methylethynyl-4-cyclopenten-1-yl]-adenine (27)

A mixture of **22** (100 mg, 0.250 mmol), $Pd(PPh_3)_4$ (15.0 mg, 13 μmol), CuI (3.00 mg, 13 μmol), and $Bu_3SnC{\equiv}CMe$ (165 mg, 0.500 mmol) in THF (2 mL) was stirred at rt for 1 h under positive pressure of dry Ar. The reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. Column chromatography (CH_2Cl_2/MeOH=40/1) of the organic layer gave **27** (80.0 mg, 100%) as a solid: mp 190–192 °C; IR (neat) 2330 cm^{-1} (C≡CMe); $[\alpha]_D^{25}$ −36.0 (*c* 0.830, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.38 and 1.54 (6H each as s, CMe_2), 2.07 (3H, s, C≡CMe), 4.70 (1H, d, *J*=5.6 Hz, H-2′), 5.37 (1H, d, *J*=5.4 Hz, H-3′), 5.63 (1H, s, H-1′), 5.84 (2H, br, NH_2), 5.98 (1H, d, *J*=2.7 Hz, H-5′), 7.68 (1H, s, H-8), 8.39 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 4.7, 25.9, 27.3, 64.7, 73.6, 83.8, 86.1, 93.2, 113.0, 120.1, 130.6, 133.7, 138.4, 149.8, 153.4, 155.4; FABMS *m*/*z* 312 (M^++H). Anal. Calcd for $C_{16}H_{17}N_5O_2{\cdot}1/6CH_2Cl_2$: C, 59.62; H, 5.36; N, 21.50. Found: C, 59.71; H, 5.18; N, 21.36.

3.24. 9-[(1*R*,2*S*,3*R*)-4-Cyano-2,3-isopropylidenedioxy-4-cyclopenten-1-yl]adenine (28)

A mixture of Bu_3SnCN (238 mg, 0.750 mmol) and $(Ph_3P)_2PdCl_2$ (53.0 mg, 75 μmol) in DMF (4 mL) was heated at 120 °C for 1 h under positive pressure of dry Ar. To this solution were added **22** (150 mg, 0.380 mmol) and CuI (72.0 mg, 0.380 mmol). The reaction mixture was heated at 120 °C for 24 h and partitioned between EtOAc and H_2O. Column chromatography (CH_2Cl_2/MeOH=40/1) of the organic layer gave **28** (83.0 mg, 74%) as a solid: mp 172–175 °C; IR (neat) 2230 cm^{-1} (C≡N); $[\alpha]_D^{25}$ −128.1 (*c* 1.650, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 and 1.53 (6H, each as s, CMe_2), 4.90 (1H, d, *J*=5.5 Hz, H-2′), 5.61 (1H, t, *J*=1.8 Hz, H-3′), 5.77 (1H, d, *J*=5.5 Hz, H-1′), 5.96 (2H, br, NH_2), 6.59 (1H, d, *J*=2.7 Hz, H-5′), 7.73 (1H, s, H-8), 8.32 (1H, s, H-2); ^{13}C NMR ($CDCl_3$) δ 25.8, 27.2, 65.0, 82.9, 85.2, 113.8, 119.9, 123.2, 138.8, 142.2, 149.5, 153.3, 155.7; FABMS *m*/*z* 299 (M^++H). Anal. Calcd for $C_{14}H_{14}N_6O_2{\cdot}2/5H_2O$: C, 55.04; H, 4.88; N, 27.51. Found: C, 55.22; H, 4.58; N, 27.27.

3.25. Preparation of 9-[(1*R*,2*S*,3*S*)-2,3-Dihydroxy-4-iodo-4-cyclopenten-1-yl]adenine (29): general procedure for removal of the isopropylidene group

Compound **22** (50.0 mg, 0.125 mmol) in 50% aqueous HCO_2H (6 mL) was stirred at rt for 24 h. The reaction mixture was evaporated to dryness and the residue was dissolved in aqueous NH_3. Evaporation of the solvent followed by column chromatography (CH_2Cl_2/MeOH=13/1) of the residue gave **29** (43.0 mg, 96%) as a solid: mp 214–216 °C; $[\alpha]_D^{24}$ −85.8 (*c* 0.825, MeOH); ^1H NMR (DMSO-d_6) δ 4.41–4.47 (2H, m, H-2′ and H-3′), 5.31 (1H, dt, *J*=5.1 and 1.8 Hz, H-1′), 5.39 (1H, br, OH), 5.48 (1H, br, OH), 6.49 (1H, d, *J*=1.8 Hz, H-5′), 7.23 (2H, br, NH_2), 8.11 (1H, s, H-8), 8.12 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 59.7, 75.1, 79.5, 95.4, 104.2, 119.1, 139.8, 149.5, 152.4, 156.0; FABMS *m*/*z* 360 (M^++H). Anal. Calcd for $C_{10}H_{10}IN_5O_2{\cdot}1/7CH_2Cl_2$: C, 32.83; H, 2.79; N, 18.88. Found: C, 33.01; H, 2.50; N, 18.77.

3.26. 9-[(1*R*,2*S*,3*S*)-4-Bromo-2,3-dihydroxy-4-cyclopenten-1-yl]adenine (30)

Obtained in 96% yield as a solid: mp 230–232 °C; $[\alpha]_D^{25}$ −109.7 (*c* 0.460, MeOH); ^1H NMR (DMSO-d_6) δ 4.46–4.47 (2H, m, H-2′ and H-3′), 5.32–5.35 (1H, m, H-1′), 5.37 (1H, d, *J*=6.6 Hz, OH), 5.46 (1H, d, *J*=6.8 Hz, OH), 6.27 (1H, d, *J*=2.0 Hz, H-5′), 7.18 (2H, br, NH_2), 8.10 (1H, s, H-8), 8.11 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 64.3, 75.2, 76.7, 119.1, 127.8, 132.1, 139.8, 149.5, 152.3, 156.0; FABMS *m*/*z* 312 and 314 (M^++H). Anal. Calcd for $C_{10}H_{10}BrN_5O_2{\cdot}1/20CH_2Cl_2$: C, 38.15; H, 3.22; N, 22.14. Found: C, 38.13; H, 3.02; N, 21.86.

3.27. 9-[(1*R*,2*S*,3*S*)-4-Chloro-2,3-dihydroxy-4-cyclopenten-1-yl]adenine (31)

Obtained in 97% yield as a solid: mp 232–234 °C; $[\alpha]_D^{25}$ −139.0 (*c* 0.285, MeOH); ^1H NMR (DMSO-d_6) δ 4.44 (1H, ddd, *J*=11.0, 5.9 and 1.7 Hz, H-2′), 4.47 (1H, t, *J*=5.9 Hz, H-3′), 5.38 (1H, dt, *J*=5.1 and 1.7 Hz, H-1′), 5.43 (1H, d, *J*=6.6 Hz, OH), 5.56 (1H, d, *J*=6.3 Hz, OH), 6.10 (1H, d, *J*=1.7 Hz, H-5′), 7.21 (2H, br, NH_2), 8.11 (1H, s, H-8), 8.13 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 63.64, 75.18, 72.26, 119.16, 127.89, 137.42, 139.86, 149.51, 152.32, 156.00; FABMS *m*/*z* 268 (M^++H). Anal. Calcd for $C_{10}H_{10}ClN_5O_2{\cdot}2/5H_2O$: C, 43.70; H, 3.96; N, 25.48. Found: C, 43.54; H, 3.74; N, 25.39.

3.28. 9-[(1*R*,2*S*,3*R*)-2,3-Dihydroxy-4-phenyl-4-cyclopenten-1-yl]adenine (32)

Obtained in 72% yield as a solid: mp 228–230 °C; $[\alpha]_D^{25}$ −22.5 (*c* 0.405, MeOH); ^1H NMR (DMSO-d_6) δ 4.51 (1H, q, *J*=6.1 Hz, H-2′), 4.91 (1H, t, *J*=6.1 Hz, H-3′), 5.18 (1H, *J*=6.1 Hz, H-1′), 5.33 (1H, d, *J*=7.3 Hz, OH), 5.56 (1H, d, *J*=6.6 Hz, OH), 6.43 (1H, d, *J*=1.7 Hz, H-5′), 7.20 (2H, br, NH_2), 7.32 (1H, t, *J*=7.3 Hz, Ph), 7.39 (2H, t, *J*=7.3 Hz, Ph), 7.65 (2H, d, *J*=7.3 Hz, Ph), 8.12 (1H, s, H-8), 8.18 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 64.54, 72.57, 76.78, 119.28, 126.23, 126.32, 128.08, 128.42, 134.16, 139.89, 144.59, 149.77, 152.27, 156.03; FABMS *m*/*z* 309 (M^++H). Anal. Calcd for $C_{16}H_{15}N_5O_2{\cdot}2/5H_2O$: C, 60.71; H, 5.03; N, 22.13. Found: C, 61.00; H, 4.88; N, 21.82.

3.29. 9-[(1*R*,2*S*,3*R*)-4-Ethynyl-2,3-dihydroxy-4-cyclopenten-1-yl]adenine (33)

Obtained in quantitative yield as a solid: mp 233 °C (decomp.); IR (KBr) 2120 cm^{-1} (C≡CH); $[\alpha]_D^{25}$ −49.0 (*c* 0.270, MeOH); ^1H NMR (DMSO-d_6) δ 4.20 (1H, s, C≡CH), 4.37 (1H, q, *J*=6.3 Hz, H-2′), 4.44 (1H, t, *J*=6.3 Hz, H-3′), 5.26 (1H, d, *J*=7.0 Hz, OH), 5.32 (1H, d, *J*=6.4 Hz, OH), 5.44 (1H, dd, *J*=6.3 and 1.1 Hz, H-1′), 6.29 (1H, d, *J*=2.1 Hz, H-5′), 7.16 (2H, br, NH_2), 8.09 (1H, s, H-8), 8.10 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 64.20, 74.94, 75.78, 79.80, 84.65, 119.16, 128.64, 138.31, 140.01, 149.54, 152.32, 155.94; FABMS *m*/*z* 258 (M^++H). Anal. Calcd for $C_{12}H_{11}N_5O_2{\cdot}1/4H_2O$: C, 55.06; H, 4.43; N, 26.76. Found: C, 54.90; H, 4.16; N, 26.81.

3.30. 9-[(1*R*,2*S*,3*R*)-2,3-Dihydroxy-4-methylethynyl-4-cyclopenten-1-yl]adenine (34)

Obtained in quantitative yield as a solid: mp 225 °C (decomp.); IR (KBr) 2220 cm^{-1} (C≡CMe); $[\alpha]_D^{23}$ −88.4 (*c* 0.380, MeOH); ^1H NMR (DMSO-d_6) δ 2.01 (3H, s, C≡CMe), 4.33 (1H, q, *J*=6.2 Hz, H-2′), 4.39 (1H, t, *J*=6.2 Hz, H-3′), 5.23 (1H, d, *J*=7.1 Hz, OH), 5.26 (1H, d, *J*=6.1 Hz, OH), 5.41 (1H, d, *J*=6.2 Hz, H-1′), 6.08 (1H, d, *J*=2.0 Hz, H-5′), 7.18 (2H, br, NH_2), 8.08 (1H, s, H-8), 8.10 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 4.05, 64.26, 75.16, 75.89, 76.05, 90.57, 119.17, 129.92, 135.14, 139.85, 149.54, 152.26, 155.99; FABMS *m*/*z* 272 (M^++H). Anal. Calcd for $C_{13}H_{13}N_5O_2\cdot 3/4MeOH$: C, 55.92; H, 5.46; N, 23.72. Found: C, 55.87; H, 5.48; N, 23.68.

3.31. 9-[(1*R*,2*S*,3*R*)-4-Cyano-2,3-dihydroxy-4-cyclopenten-1-yl]adenine (35)

Obtained in 83% yield as a foam: IR (KBr) 2230 cm^{-1} (C≡N); $[\alpha]_D^{26}$ +28.7 (*c* 0.215, MeOH); ^1H NMR (DMSO-d_6) δ 4.41 (1H, t, *J*=5.9 Hz, H-2′), 4.67 (1H, d, *J*=5.9 Hz, H-3′), 5.56 (1H, d, *J*=6.3 Hz, H-1′), 7.14 (1H, d, *J*=1.5 Hz, H-5′), 7.25 (2H, br, NH_2), 8.11 (1H, s, H-8), 8.13 (1H, s, H-2); ^{13}C NMR (DMSO-d_6) δ 64.14, 73.48, 75.28, 115.87, 119.07, 140.19, 148.70, 149.45, 152.44, 156.05; High resolution FABMS (*m*/*z*) calcd for $C_{11}H_{11}N_6O_2$: 259.0943, found: 259.0960 (M^++H).

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