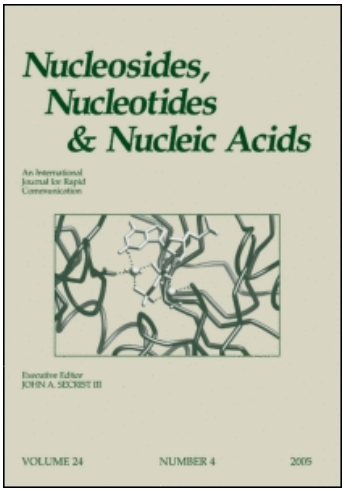

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A CONVERGENT APPROACH FOR THE SYNTHESIS OF ARA-NEPLANOCIN A ANALOGUES UNDER SUBZERO MICROWAVE ASSISTED CONDITIONS

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□ *A convergent strategy for the synthesis of ara-neplanocin A analogues has been developed. Microwave assisted Mitsunobu reaction proved to be an essential tool both for the 2′-β-hydroxy inversion and for the coupling reaction with the heterocyclic bases. The exploitation of the present approach allowed generating a family of ara-neplanocins which biological potential is still unexplored.*

Keywords Ara-neplanocin A analogues; convergent approach; microwave assisted synthesis

INTRODUCTION

Among the different members of the neplanocin family isolated from *Ampullariella regularis*,[1] neplanocin A **1** (NPA; Figure 1) has been extensively studied since it showed potent antiviral and anti-tumor activity both in vitro and *in* vivo.[2] The interesting biological activity of NPA seems to be in part due to an efficient inhibition of *S*-adenosylhomocysteine (AdoHcy) hydrolase.[3] However, the main drawback for the therapeutic utilization of NPA as an antiviral agent comes from its significant cytotoxicity. In contrast to NPA, ara-neplanocin A (**2**; ara-NPA) showed less cytotoxicity with still retaining reasonable antiviral activity.[4]

However, a thorough literature search indicated that little attention has been paid to the ara-neplanocin family of compounds. Apart from the adenine derivative **2** (ara-NPA), only the cytosine derivative **3** (ara-NPC) has

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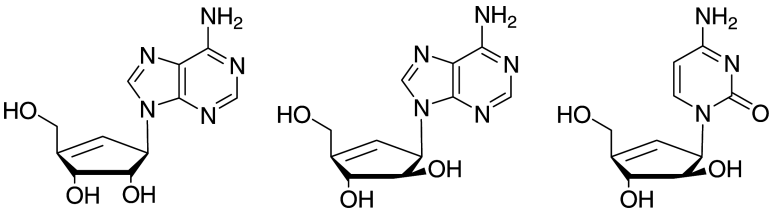


FIGURE 1 Neplanocin A (NPA, **1**) and known arabino analogues **2** (ara-NPA) and **3** (ara-NPC).

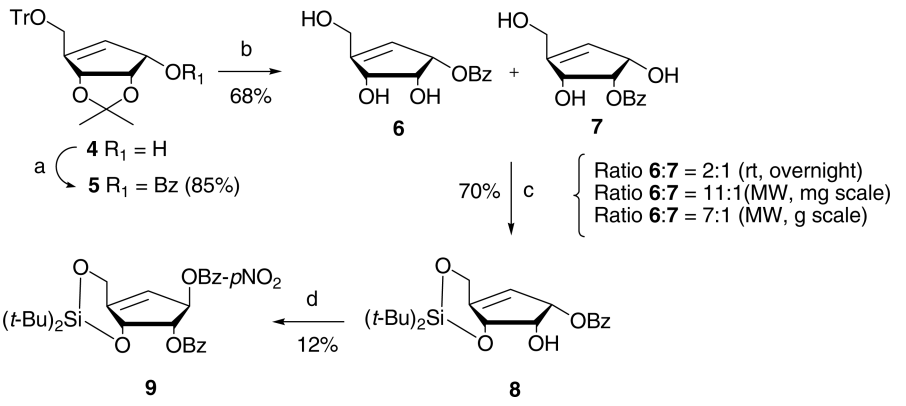
been reported so far, which was evaluated only for its antitumor activity.[5] While the ara-NPA was obtained from a divergent approach starting from NPA in four steps,[6] the ara-NPC was obtained from a 2,2′-anhydro-uridine intermediate, which was the byproduct of 2′-deoxygenation reaction. Considering the poor versatility of the reported approaches, we decided to develop a convergent synthetic strategy that allows to generate a family of base-modified ara-neplanocins of which biological potential have been unexplored. In addition, ara-neplanocins could be considered as an attractive template, giving access through appropriate chemical modifications of the 2′-α-hydroxy group as well as to new 2′-functionalized neplanocin-derivatives otherwise difficult to obtain.

RESULTS AND DISCUSSION

We have recently reported a practical and convenient methodology for the gram scale synthesis of the carbocyclic intermediate **4** in 52% overall yield after 8 steps.[7] The cyclopentenyl moiety **4** was therefore considered a good starting point for the construction of an arabino-type carbocyclic intermediate which could be coupled with different nucleobases in a convergent process.

Starting from **4,** different approaches (2,3-epoxide opening, 2-keto reduction) were tried for the inversion of the 2′-β-hydroxy group with no success, and ultimately we focussed on the Mitsunobu reaction (Scheme 1). The hydroxyl group in carbocyclic intermediate **4** was initially benzoylated to obtain compound **5,** which was treated with Dowex 50WX8–200 resin at room temperature to deprotect both trityl and acetonide groups. Using this method, both the trityl and acetonide protecting groups were removed, however, an undesired acid catalyzed benzoyl 1,2- migration results in 2:1 mixture of compounds **6** and **7** in 54% overall yield.

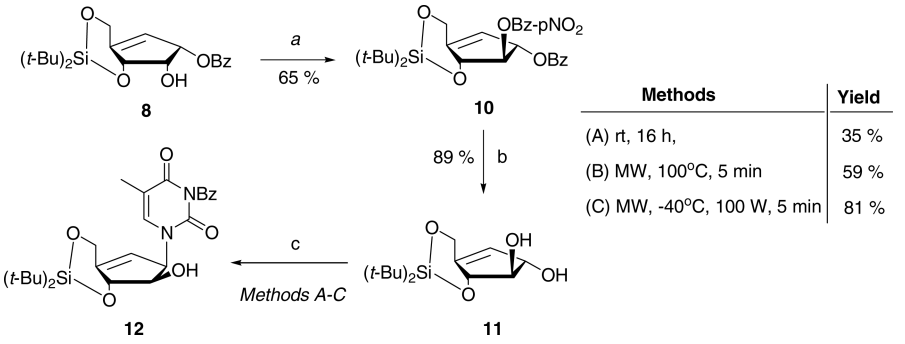
To avoid the acid catalyzed 1,2-migration, allyl and benzyl protecting groups were then used in place of the benzoyl. Unfortunaltely, subsequent studies showed that, in the presence of these two protecting groups, the Mitsunobu inversion at the C2 position was unsuccessful, proably due to



SCHEME 1 Reagents and conditions: a) BzCl, pyridine, room temperature, 2 hours; b) Dowex, MeOH, MW, open vessel, 65°C, 30 minutes (two cycles); (c) t-$Bu_2Si(OTf)_2$, DMF, 0°C, 30 minutes; (d) p-NO_2PhCO_2H, Ph_3P, DIAD, THF, room temperature, 16 hours.

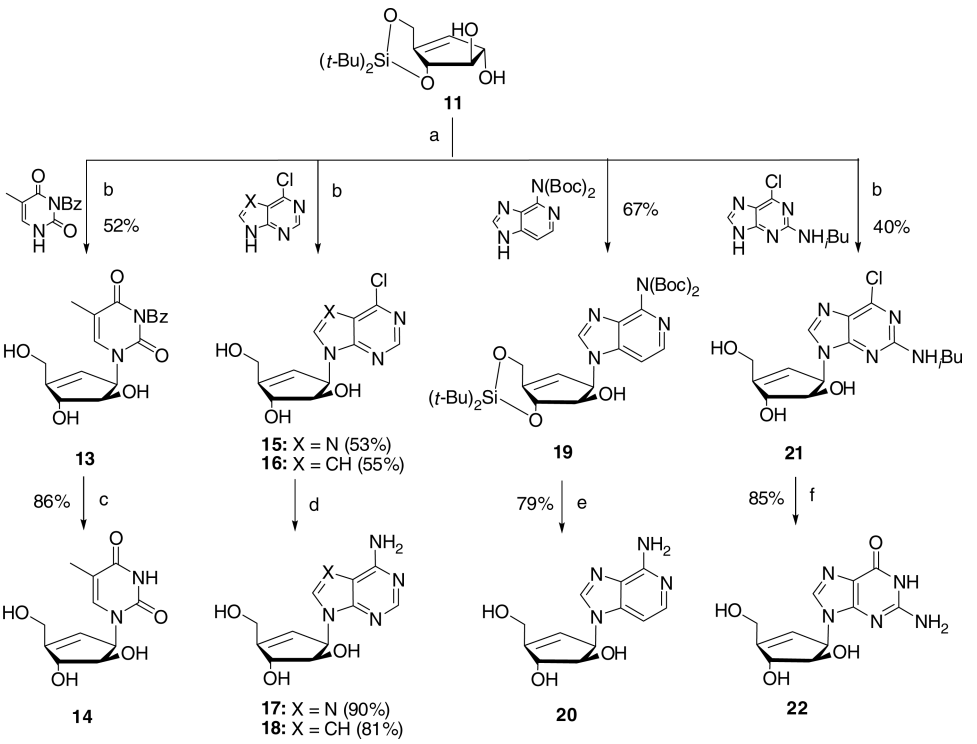
unfavorable stereoelectronic effects. Therefore, in order to study the effect of the electron withdrawing benzoyl group in the outcome of the Mitsunobu reaction, we went back to optimize the deprotection of compound **5** to improve the **6:7** ratio. Using the Dowex resin for deprotection in an open vessel under microwave assisted conditions, it was possible to significantly reduce the reaction time and the extent of acid catalyzed benzoyl migration. As described in Scheme 1, the mixture of compound **6** and **7** was thus obtained in a 11:1 ratio working in the milligram scale, while in the gram scale a 7:1 ratio was obtained. Reacting the mixture with di-tert-butylsilyl bis(trifluoromethanesulfonate), compound **8** was obtained after 30 minutes while **7** was recovered unreacted. Unfortunately, the attempted inversion of 2′-β-hydroxy group in compound **8** using the standard Mitsunobu reaction condition gave the undesired compound **9** as a result of the 1,2- benzoyl migration and subsequent Mitsunobu reaction on the anomeric hydroxy moiety. Surprisingly, running the Mitsunobu reaction on compound **8** under microwave assisted conditions, it was possible to cleanly invert the configuration of the C2-hydroxyl group (Scheme 2).

The choice of the solvent used in this reaction was crucial in determining the yield of the desired compound **10**, benzene (high boiling point) in place of THF provided less decomposed materials and better yields.[8] Compound **10** was then debenzoylated with lithium hydroxide to give the key intermediate **11,** which could be used in the coupling reaction with the appropriate heterocyclic bases. As depicted in Scheme 2, reacting compound **11** with N^3-benzoylthymine under the standard Mitsunobu reaction condition (room temperature), compound **12** was obtained in 35% yield after 16 hours. Due to the higher reactivity of the allylic hydroxy group, the desired compound **12** was obtained as single product and fully characterized by NMR experiments. Again, the use of microwave irradiation



SCHEME 2 Reagents and conditions:a) *p*-NO_2PhCO_2H, Ph_3P, DIAD, benzene, MW, 180°C, sealed tube, 5 minutes; b) THF/MeOH/H_2O (3:2:1), LiOH, room temperature, 30 minutes; c) N^3-benzoylthymine, Ph_3P, DIAD, THF (methods A-C).

was valuable in improving the outcome of the Mitsunobu reaction (Scheme 2). High temperature microwave assisted conditions (method B in Scheme 2) allowed to obtain the nucleoside **12** in 59% yield. However, subzero microwave assisted condition (−40°C), accessible by the use of a CEM Discover CoolMate system (method C in Scheme 2), furnished the desired compound **12** in 81% yield. The latter result can be rationalized with the production of less byproducts at low temperature. In addition, the comparison of methods B and C highlights that the acceleration of the coupling reaction under the Mitsunobu condition does not seems to be related to a thermal effect in the poor microwave absorbing THF but, most probably, to a specific microwave effect onto the charged transition state species.[9] Due to the difficulties encountered in the purification of compound **12** prompted us to develop a protocol for the one-pot Mitsunobu coupling reaction and deprotection of the silyl group of the carbocyclic moiety as the deprotected nucleoside can be more easily purified. According to this modified protocol, the key intermediate **11** was reacted for 5 minutes with the suitably protected nucleobase under the above desccribed subzero microwave assisted Mitsunobu condition, and the reaction mixture was treated with triethylamine trihydrofluoride at room temperature to deprotect silyl group in the same reaction vessel outside the microwave system for 30 minutes, affording the corresponding nucleosides **13**, **15**, **16**, and **21** (Scheme 3). Finally, deprotection or amination afforded the ara-neplanocin derivatives **14** (ara-NPT), **17** (ara-NPA), **18** (ara-7DNPA), and **22** (ara-NPG) in good overall yields. For the synthesis of the 3-deaza analogue **20**, 6-*N*,*N*-diBoc-3-deazaadenine has been used in the coupling reaction in order to avoid the formation of the N^7-derivative[10] which is a common side product in the synthesis of 3-deazapurine carbocyclic nucleosides.[11] The steric hindrance exerted by the bulky diBoc-protecting group during the coupling reaction, allowed to obtain the N^9-derivative **19** as a single product

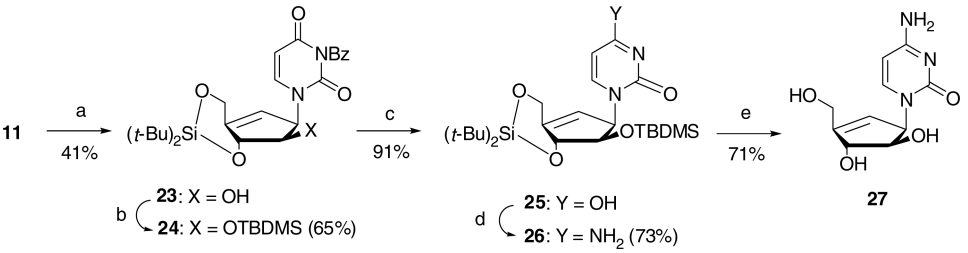


SCHEME 3 Reagents and conditions: a) Ph_3P, DIAD, THF, MW, −40°C, 100 W, 5 minutes; b) $Et_3N{\cdot}3HF$, room temperature, 30 minutes; c) Sat. NH_3 in MeOH, room temperature, 1 hour; d) Sat. NH_3 in MeOH, 90°C, 18 hours; e) 2N HCl/MeOH, 60°C 15 hours; f) i) formic acid, 90°C, MW, 5 minutes, ii) Sat. NH_3 in MeOH, room temperature, overnight.

which was finally deprotected with 2N HCl in methanol to give the desired ara-3DNPA **20** (Scheme 3).

For the synthesis of the cytosine analogue **27** (ara-NPC), N^3-benzoyluracil was coupled with **11** under Mitsunobu reaction (method C) to give nucleoside **23**, which was protected at the 2′-β-hydroxy group with *tert*-butyldimethylsilyl chloride, followed by debenzoylation with saturated methanolic ammonia at room temerature gave compound **25**. Ammination at C4 using tri-isopropylbenzene sulfonyl chloride/DMAP followed by reacting with ammnium hydroxide gave the cytosine analogue **26** (Scheme 4). Finally deprotection of silyl group with triethylamine trihydrofluoride gave the desired ara-NPC analogue **27**.

In conclusion, a convergent strategy for the synthesis of ara-neplanocin A analogues has been developed. The microwave accelerated Mitsunobu reaction proved to be an essential tool for both the synthesis of the key intermediate **11** and the coupling reaction with the heterocyclic bases. The exploitation of the present approach allowed to generate a family of ara-neplanocins of which biological potentials have not been explored. In



SCHEME 4 Reagents and conditions: a) Ph_3P, DIAD, THF, N^3-benzoyluracil, MW, −40°C, 100 W, 5 minutes; b) TBDMS-Cl, imidazole, CH_2Cl_2, 12 hours, 50°C; c) Saturated NH_3/MeOH, room temperature, 5 hours; d) 2,4,6-triisopropylbenzenesulfonyl chloride, DMAP, Et_3N, CH_3CN, 20 hours, then NH_4OH, 5 hours; e) $Et_3N{\cdot}3HF$, THF, 1 hour.

addition, ara-neplanocins could be considered as an attractive template giving access, through appropriate chemical modifications of the 2′-α-hydroxy group, to new series of 2′-functionalized derivatives otherwise difficult to obtain. Biological evaluation for all the synthesized compounds will be reported in due course.

EXPERIMENTAL SECTION

General Procedures

Melting points were determined on a Mel-temp II laboratory device and are uncorrected. NMR spectra were recorded on a Varian 500 MHz Fourier Transform spectrometer; chemical shifts are reported in parts per million-(δ), and signal are quoted as s (singlet), d (doublet), t (triplet), m (multiplet), and dd (double of doublets). UV spectra were obtained on a Beckman DU-650 spectrophotometer. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. TLC was performed on uniplates (silica gel) purchased from Analtech Co.(Newark, DE, USA) and elemental analysis were performed by Atlantic Microlab, Inc. (Norcross, GA, USA).

Microwave reactions were conducted using a CEM Benchmate Discover Synthesis Unit (CEM Corp., Matthews, NC, USA) consisting of a continuous focused microwave power delivery system with operator-selectable power output from 0 to 300W. The reactions were performed in 10 mL sealed vessel or in a 50 mL round bottom flack equipped with a tightly clamped condenser in open vessel mode. The temperature of the contents of the vessel was monitored using a calibrated infrared temperature control mounted under the reaction vessel. Subambient temperature microwave assisted reactions were conducted using a CEM-Coolmate apparatus connected to the Benchmate Discover unit. This system provides a jacketed low-temperature vessel that helps in maintaining low reaction temperature by means of a circulating cold microwave transparent fluid. Temperature

measurement is accomplished with an in situ fiber-optic probe. All experiments were performed using a stirring option whereby the contents of the vessel were stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel.

(1S,2S,3R)-1-Benzoyloxy-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)-4-cyclopentene (5): (1S,2S,3R)-1-Hydrxoy-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)-4-cyclopentene **4** (2.92 g, 6.81 mmol) was dissolved in anhydrous pyridine (20 mL) and benzoyl chloride (1.19 mL, 10.22 mmol) was added at 0°C. Reaction mixture was stirred at room temperature for 3 hours, and then diluted with diethyl ether, washed 3–4 times with 1N HCl solution, brine, dried over anhy. magnesium sulphate, and concentrated. The residue was purified over silica gel chromatography (10% EtOAc in hexane) to give compound **5** (3.08 g, 85%) as a white foam. M.p. 55°C (decomposition). $[\alpha]^{26}_{D}$ 16.37 (c 0.62, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.12 (d, $J = 7.32$ Hz, 2H), 7.58 (t, $J = 7.32$ Hz, 1H), 7.44–7.48 (m, 8H), 7.23–7.33 (m, 9H), 6.11 (s, 1H), 5.62 (m, 1H), 5.05 (d, $J = 5.86$ Hz, 1H), 4.92 (d, $J = 5.86$ Hz, 1H), 3.99 (d, $J = 14.65$ Hz, 1H), 3.76 (d, $J = 14.65$ Hz, 1H), 1.33 (s, 3H), 1.31 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 146.83, 143.85,133.01, 130.12, 129.89, 128.62, 128.37, 127.95, 127.18, 125.08, 112.99, 87.12, 83.39, 77.47, 76.05, 61.41, 27.49, 27.17; HR-FAB MS Obsd, m/z 273.1120; Calcd. for $C_{16}H_{17}O_4$, m/z 273.1127 $(M+H)^+$.

(1S,2S,3R)-1-Benzoyloxy-2,3-dihydroxy-4-hydroxymethyl-4-cyclopentene (6+7): To a solution of **5** (3.08 g, 5.79 mmol) in THF: MeOH (1:3, 30 mL), Dowex 50WX8-200 resin (9.24 g) was added and the resulting mixture was irradiated into the microwave at 100W (65°C) (2 × 30 minutes) under a continuous air cooling flow. The resin was filtered off, washed several times with MeOH and the filtrate was evaporated to dryness. The residue was purified by flash silica gel chromatography (CH_2Cl_2:MeOH 9:1) to give a 7:1 mixture of compounds **6+7** (1.15 g, 68%) which was directly used in the next step.

(1S,2S,3R)-1-Benzoyloxy-2-hydroxy-3,6-O-di-tert-butylsilanediyl-4-cycl- opentene (8): A solution of **6+7** (1.15 g, 4.60 mmol) in anhydrous DMF (15 mL) was cooled at 0°C and di-tert-butylsilyl bis(trifluoromethanesulfonate) (1.64 mL, 5.06 mmol) was added dropwise. The resulting mixture was stirred at 0°C for 30 minutes and then diluted with Et_2O, washed repeatedly with water, brine, dried over magnesium sulphate and concentrated. The residue was purified by flash silica gel chromatography (Hexane:EtOAc, 5:1) to give **8** (1.25 g, 70%) as a white solid: M.p. 72°C; $[\alpha]^{24}_{D}$ 32.01 (c 0.64, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.11 (d, $J = 7.81$ Hz, 2H), 7.59 (t, $J = 7.32$ Hz, 1H), 7.46 (t, $J = 7.32$ Hz, 2H), 5.89 (s, 1H), 5.76 (m, 1H), 4.92 (d, $J = 5.86$ Hz, 1H), 4.78 (m, 2H), 4.62 (q, 1H), 3.02 (d, $J = 7.32$ Hz, 1H), 1.11 (s, 9H), 1.04 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 145.08, 133.04, 130.00, 129.84, 128.33, 124.94, 75.82, 70.17,

63.96, 27.44, 27.06, 22.36, 20.59; HR-FAB MS Obsd, m/z 413.1801; Calcd. for $C_{21}H_{30}O_5Si$, m/z 413.1760 $(M+Na)^+$.

(1R,2S,3R)-1-(*p*-Nitro-benzoyl)-2-benzoyloxy-3,6-O-di-tert-butylsilanediyl-4-cyclopentene (9): To a solution of compound **8** (41 mg, 0.105 mmol), triphenylphosphine (55 mg, 021 mmol) and 4-nitrobenzoic acid (26 mg, 0.158 mmol) in dry THF (5 mL) at 0°C was added diisopropylazodicarboxylate (DIAD, 42 μL, 0.21 mmol) under nitrogen atmosphere. The mixture was stirred at room temperature for 24 hours, and then the solvent was removed under vacuum. The residue was purified by preparative TLC (10% EtOAc in Hexane) to give **9** (7 mg, 12%) as a pale yellow oil. ^{1}H-NMR ($CDCl_3$) δ 8.30 (d, J = 8.29 Hz, 2H), 8.21 (d, J = 8.29 Hz, 2H), 8.09 (d, J = 8.29 Hz, 2H), 7.57 (m, 1H), 7.44 (m, 2H), 6.13 (s, 1H), 5.94 (s, 1H), 5.63 (m, 1H), 5.43 (d, J = 3.8 Hz, 1H), 4.80 (d, J = 11.0 Hz, 1H), 4.72 (d, J = 11.0 Hz, 1H), 0.99 (s, 9H), 0.79 (s, 9H): ^{13}C NMR ($CDCl_3$) δ 150.72, 148.22, 135.08, 133.14, 130.91, 129.87, 129.67, 128.32, 123.64, 122.62, 83.45, 76.98, 75.37, 63.83, 27.00, 26.60, 22.31, 20.32; HR-FAB MS Obsd., m/z 540.2058; Calcd. for $C_{21}H_{30}O_5Si$, m/z 540.2053 $(M+H)^+$.

(1S,2R,3R)-1-Benzoyloxy-2-(p-nitro-benzoyl)-3,6-O-di-tert-butylsilanediyl-4-cyclopentene (10): In a microwave sealed vessel, diisopropylazodicarboxylate (DIAD, 778 μL, 3.97 mmol) was added dropwise to a solution of **8** (298 mg, 0.764 mmol), triphenylphosphine (1.16 g, 4.43 mmol) and 4-nitrobenzoic acid (612 mg, 3.66 mmol) in dry benzene (5 mL) under nitrogen atmosphere. The mixture was irradiated at 100 W (100°C) for 5 minutes then diluted with EtOAc, washed with water, brine, dried over magnesium sulphate, and concentrated. The residue was purified by flash silica gel chromatography (10% EtOAc in Hexane) to give **10** (726 mg, 65%) as a pale yellow solid: M.p. 64°C (decomposition); $[\alpha]^{27}_D$ 82.22 (c 0.47, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.23 (m, 2H), 8.19 (m, 2H), 7.99 (d, J = 7.32 Hz, 2H), 7.51 (t, J = 7.32 Hz, 1H), 7.39 (m, 2H), 5.84 (s, 1H), 5.73 (s, 1H), 5.65 (m, 1H), 5.12 (d, J = 3.91 Hz, 1H), 4.71 (d, J = 13.6 Hz, 1H), 4.61 (d, J = 13.6 Hz, 1H), 0.97 (s, 9H), 0.95 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 150.67, 144.29, 135.21, 133.36, 131.08, 129.85, 129.63, 128.50, 123.64, 123.59, 87.66, 80.63, 79.54, 63.28, 27.01, 26.98, 22.25, 20.22; HR-FAB MS Obsd, m/z 540.2058; Calcd. for $C_{21}H_{30}O_5Si$, m/z 540.2089 $(M+H)^+$.

(1S,2R,3R)-1,2-Dihydroxy-3,6-O-di-tert-butylsilanediyl-4-cyclopentene (11): To a solution of **10** (673 mg, 1.25 mmol) in a 3:2:1 mixture of THF/MeOH/H_2O (18 mL/12 mL/6 mL), lithium hydroxide monohydrate (183 mg, 4.37 mmol) was added and the resulting solution was stirred at room temperature for 30 minutes. The mixture was then concentrated under reduced pressure to a small volume, diluted with EtOAc, washed with water, brine, dried over magnesium sulphate, and concentrated. The residue was purified over flash silica gel (CH_2Cl_2:MeOH, 98:2) to give **11** (318 mg, 89%) as a white solid: M.p. 105°C; $[\alpha]^{27}_D$ -20.38 (c 0.55, $CHCl_3$);

^{1}H NMR (CD_3OD) δ 5.56 (s, 1H), 4.67–4.73 (m, 2H), 4.54 (d, J = 13.66 Hz, 1H), 4.31 (m, 1H), 3.97 (t, J = 5.37 Hz, 1H), 1.04 (s, 9H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 140.34, 126.86,, 89.57, 82.27, 77.79, 63.47, 21.98, 19.79; Anal. Calcd.. for $C_{14}H_{26}O_4Si$: C, 58.70; H, 9.15. Found: C, 58.69; H, 9.23.

(1S,2R,3R)-N^3-Benzoyl-1-[2-hydroxy-3,6-O-di-tert-butylsilanediyl-4-cycl- openten-1-yl]thymine (12): Method A: To a solution of **11** (1.0 mmol), triphenylphosphine (2.5 mmol) and N^3-benzoylthymine (1.5 mmol) in dry THF (7mL) at 0°C was added diisopropylazodicarboxylate (DIAD, 2.5 mmol) dropwise under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 24 hours. The residue was purified by preparative TLC (Hexane:EtOAc, 8:2) to give **12** (35%) as solid.

Method B: In a microwave sealed vessel, diisopropylazodicarboxylate (DIAD, 2.5 mmol) was added dropwise to a solution of **11** (1.0 mmol), triphenylphosphine (2.5 mmol) and N^3-benzoylthymine (1.5 mmol) in dry THF (7 mL) under nitrogen atmosphere. The mixture was irradiated at 100 W (100°C) for 5 minutes then concentrated. The residue was purified by preparative TLC (Hexane:EtOAc, 8:2) to give **12** (59%) as solid.

Method C: To a solution of **11** (100 mg, 0.349 mmol), triphenylphosphine (229 mg, 0.873 mmol) and N^3-benzoylthymine (141 mg, 0.698 mmol) in dry THF (7 mL) was added diisopropylazodicarboxylate (DIAD, 171 μL, 0.873 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −40°C (initial cooling fluid temperature = −50°C, fluid speed max) for 5 minutes at 100W then diluted with EtOAc washed with water, brine, dried over magnesium sulphate, and concentrated. The residue was purified by preparative TLC (Hexane:EtOAc, 8:2) to give **12** (141 mg, 81%) as a white solid: M.p. 88°C (decomposition); $[\alpha]^{28}_D$ -39.99 (c 0.55, $CHCl_3$); UV ($CHCl_3$) λ_{max} 254 nm; ^{1}H-NMR ($CDCl_3$) δ 7.93 (d, J = 7.32 Hz, 2H), 7.63 (m, 1H), 7.48 (m, 2H), 6.87 (s, 1H), 5.62 (s, 1H), 5.54 (m, 1H), 4.99 (s, 1H), 4.86 (d, J = 14.16 Hz, 1H), 4.72 (d, J = 14.16 Hz, 1H), 4.44 (m, 1H), 2.85 (s, 1H), 1.07 (s, 9H), 0.95 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 151.09, 148.69, 137.40, 135.06, 131.54, 130.49, 129.20, 121.02, 110.19, 83.89, 78.70, 63.45, 60.80, 27.09, 26.91, 22.25, 20.22, 12.69; HR-FAB MS Obsd, m/z 499.2285; Calcd.. for $C_{26}H_{34}N_2O_6Si$, m/z 499.2264 $(M+H)^+$.

(1S,2R,3R)-N^3-Benzoyl-1-[2,3-dihydroxy-4-hydroxymethyl-4-cyclopen- ten-1-yl]thymine (13): To a solution of **11** (30 mg, 0.113 mmol), triphenylphosphine (74 mg, 0.281 mmol) and N^3-benzoylthymine (46 mg, 0.225 mmol) in dry THF (5 mL) was added diisopropylazodicarboxylate (DIAD, 55 μL, 0.281 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −40°C (initial cooling fluid temperature = −50°C, fluid speed max) for 5 minutes at 100W then triethylamine trihydrofluoride (37 μL, 0.225 mmol) was added and the reaction stirred outside at room temperature for 30 minutes. Reaction mixture was neutralized with minimum satd. $NaHCO_3$, and evaporated. The residue was purified by preparative TLC (CH_2Cl_2:MeOH, 98:2) to give

13 (20 mg, 52%) as a pale yellow solid; M.p. 70°C (decomposition); $[\alpha]^{26}_{D}$ 5.54 (c 0.50, MeOH); UV (MeOH) λ_{max} 252 nm; ^{1}H NMR (CD_3OD) δ 7.97 (m, 2H), 7.72 (t, $J = 7.32$ Hz, 1H), 7.55 (m, 2H), 7.28 (s, 1H), 5.76 (s, 1H), 5.61 (m, 1H), 4.56 (s, 1H), 4.31 (m, 2H), 4.23 (m, 1H), 1.91 (s, 3H); ^{13}C NMR (CD_3OD) δ 150.86, 140.04, 135.07, 131.89, 130.37, 129.17, 121.98, 108.63, 81.01, 77.29, 61.59, 58.81, 11.13; HR-ESI MS Obsd. m/z 345.1083; Calcd.. for $C_{17}H_{16}N_2O_6$, m/z 345.1087 $(M+H)^+$.

(1S,2R,3R)-1-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl] thy- mine (14): Compound **13** (40 mg, 0.117 mmol) was dissolved in saturated methanolic ammonia (10 ml) and stirred at room temperature for 1 hour. The solvent was evaporated under vacuum and the residue was purified on preparative TLC (CH_2Cl_2:MeOH, 85:15) to **14** (24 mg, 86%) as a white solid: M.p. 65°C (decomposition); $[\alpha]^{26}_{D}$ 25.54 (c 0.50, MeOH); UV (MeOH) λ_{max}, nm: 273 (pH 2), 273.5 (pH 11), 272.0 (pH 7); ^{1}H NMR (CD_3OD) δ 7.12 (s, 1H), 5.70 (s, 1H), 5.61–5.63 (m, 1H), 4.53 (s, 1H), 4.28 (m, 2H), 4.22–4.24 (m, 1H), 1.85 (s, 3H); ^{13}C NMR (CD_3OD) δ 165.64, 152.31, 151.98, 139.95, 122.75, 108.4, 81.0, 77.2, 61.1, 58.8, 11.14; Anal. Calcd.. for $C_{11}H_{14}N_2O_5 \cdot 0.6H_2O$: C, 49.85; H, 5.78; N, 10.57. Found: C, 49.97; H, 5.93; N, 10.06.

(1S,2R,3R)-9-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl]6-chlo- ropurine (15): To a solution of **11** (120 mg, 0.45 mmol), triphenylphosphine (295 mg, 1.13 mmol) and 6-chloropurine (139 mg, 0.90 mmol) in dry THF (7mL) was added Diisopropylazodicarboxylate (DIAD, 221μL, 1.13 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −40°C (initial cooling fluid temperature = −50°C, fluid speed max) for 5 minutes at 100 W then triethylamine trihydrofluoride (147μL, 0.90 mmol) was added and the reaction stirred at room temperature for 30 minutes. Reaction mixture was neutralized with minimum satd. $NaHCO_3$ and evaporated. The residue was purified by flash silica gel chromatography (CH_2Cl_2:MeOH, 9:1) to give **15** (68 mg, 53%) as a pale yellow solid: M.p. 182°C; $[\alpha]^{27}_{D}$ -89.22 (c 0.44, MeOH); UV (MeOH) λ_{max} 265 nm; ^{1}H NMR (CD_3OD) δ 8.80 (s, 1H), 8.40 (s, 1H), 5.96 (s, 1H), 5.87 (m, 1H), 4.78 (m, 1H), 4.40 (m, 3H); ^{13}C NMR (CD_3OD) δ 153.18, 152.46, 151.44, 149.48, 146.49, 130.95, 120.72, 80.36, 77.86, 59.95, 58.54; HR-ESI MS Obsd, m/z 283.0589; Calcd. for $C_{11}H_{11}ClN_4O_3$, m/z 283.0599 $(M+H)^+$.

(1S,2R,3R)-9-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl]6-chl- oro-7-deazapurine (16): To a solution of **11** (288 mg, 1.00 mmol), triphenylphosphine (527 mg, 2.01 mmol) and 6-chloropurine (232 mg, 1.50 mmol) in dry THF (7 mL) was added diisopropylazodicarboxylate (DIAD, 404μL, 2.01 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −40°C for 5 minutes at 100W then triethylamine trihydrofluoride (486 μL, 3.01 mmol) was added and the reaction stirred at room temperature for 30 minutes. Reaction mixture was neutralized

with minimum satd. $NaHCO_3$ and evaporated. The residue was purified by silica gel chromatography (CH_2Cl_2:MeOH, 9:1) to give **16** (140 mg, 55%) as a pale yellow solid: M.p. 140°C; $[\alpha]^{27}_D$ -72.50 (c 0.23, MeOH); UV (MeOH) λ_{max} 275 nm; ^{1}H-NMR (DMSO-d_6) δ 8.62 (s, 1H), 7.40 (d, J = 3.5 Hz, 1H), 6.11 (d, J = 3.0 Hz, 1H), 5.81 (dd, J = 2.0, 4.5 Hz, 1H), 5.70 (d, J = 1.5 Hz, 1H), 5.25 (d, J = 6.0 Hz, 1H), 5.11 (d, J = 5.5 Hz, 1H), 4.92 (m, 1H), 4.16 (m, 3H); ^{13}C NMR (DMSO-d_6) δ 153.92, 151.68, 150.66, 150.42, 130.89, 121.08, 117.45, 98.24, 80.21, 78.51, 59.46, 58.73; HR-ESI MS Obsd, m/z 281.0536; Calcd. for $C_{12}H_{12}ClN_3O_3$, 281.0567 $(M+H)^+$.

(1S,2R,3R)-9-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl]-ade- nine (17): Compound **15** (120 mg, 0.425 mmol) was dissolved in methanol (10 mL) and saturated with ammonia for 20 minutes at 0°C and heated at 90°C for 18 hours in a steel bomb. The solvent was evaporated under reduced pressure and the residue was purified using C_{18} reverse phase silica gel column chromatography (methanol:water = 20:80) to give **17** (100 mg, 90%) as a white solid: M.p. 230°C; $[\alpha]^{23}_D$ -95.83 (c 0.4, MeOH); UV (MeOH) $\lambda_{max,}$ nm: 219, 260 (pH 11), 210, 260 (pH 2), 210, 260 (pH 7); ^{1}H NMR (DMSO-d_6) δ 8.17 (s, 1H), 7.83 (d, J = 2 Hz, 1H), 7.30 (brs, 2H), 5.73 (d, J = 1.5 Hz, 1H), 5.53 (m, 1H), 5.24 (m, 2H), 4.92 (brs, 1H), 4.56 (brs, 1H), 4.15 (m, 3H); ^{13}C NMR (DMSO-d_6) δ 156.0, 152.68, 151.66, 150.42, 129.89, 121.08, 117.45, 98.24, 80.21, 78.51, 59.46, 58.73; HR-ESI MS Obsd, m/z 264.1086; Calcd. for $C_{11}H_{13}N_5O_3$, 264.1097 $(M+H)^+$; Anal. Calcd. for $C_{11}H_{13}N_5O_3 \cdot 0.33H_2O$: C, 49.13; H, 5.00; N, 26.04; Found: C, 49.01; H, 5.01; N, 25.97.

(1S,2R,3R)-9-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl]-7-deazaadenine (18): Compound **16** (127 mg, 0.451 mmol) was dissolved in methanol (10 mL) and saturated with ammonia for 20 minutes at 0°C and heated at 90°C for 18 hours in a steel bomb. The solvent was evaporated under reduced pressure and the residue was purified using flash silica gel column chromatography (methanol: $CHCl_3$ = 1:5) to give **18** (96 mg, 81%) as a white solid: M.p. 140°C; $[\alpha]^{23}_D$ -70.27 (c 0.12, MeOH); UV (MeOH) $\lambda_{max,}$ nm: 230, 275 (pH 2), 227, 273 (pH 11), 210, 273 (pH 7); ^{1}H-NMR (DMSO-d_6) δ 8.12 (s, 1H), 7.30 (brs, 2H), 6.91 (d, J = 3.5 Hz, 1H), 6.58 (d, J = 3.5 Hz, 1H), 5.69 (d, J = 7.0 Hz, 1H), 5.66 (s, 1H), 5.21 (d, J = 6.5 Hz, 1H), 5.03 (d, J = 5.5 Hz, 1H), 4.92 (t, J = 5.5 Hz, 1H), 4.52 (m, 1H), 4.12 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 157.92, 152.77, 149.89, 149.53, 124.44, 121.88, 102.70, 88.99, 80.17, 78.61, 58.67, 58.43; HR-ESI MS Obsd, m/z 263.1142; Calcd. for $C_{12}H_{14}N_4O_3$, 263.1145 $(M+H)^+$; Anal. Calcd. for $C_{12}H_{14}N_4O_3 \cdot 0.2H_2O$: C, 54.21; H, 5.46; N, 21.07; Found: C, 54.23; H, 5.49; N, 21.12.

(1S,2R,3R)-1-[2-Hydroxy-3,6-O-di-tert-butylsilanediyl-4-cyclopenten-1-yl]-4-(*N,N*-di-*tert*-butyloxycarbonylamino)-imidazo[4,5-*c*]pyridine (19): To a solution of **11** (285 mg, 0.99 mmol), triphenylphosphine (391 mg, 1.49 mmol) and *N*,*N*-diBoc-3-deazaadenine (400 mg, 1.19 mmol) in dry

THF (7 mL) was added diisopropyl-azodicarboxylate (DIAD, 0.29 mL, 1.49 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −40°C (initial cooling fluid temperature = −50°C, fluid speed max) for 5 minutes at 100 W then diluted with EtOAc washed with water, brine, dried over $MgSO_4$, and concentrated. The residue was purified over flash silica gel chromatography (Hexane:EtOAc, 7:3) to give **19** (400 mg, 67%) as a white solid: M.p. 201°C; $[\alpha]^{28}_D$ -88.99 (c 0.25, MeOH); UV ($CHCl_3$) λ_{max} 211, 264 nm; ^{1}H NMR ($CDCl_3$) δ 8.21 (d, J = 6 Hz, 1H), 7.77 (s, 1H), 7.25 (d, J = 5.5 Hz, 1H), 5.83 (brs, 1H), 5.42 (d, J = 6.5 Hz, 1H), 5.08 (d, J = 3.0 Hz, 1H), 4.90 (d, J = 14 Hz, 1H), 4.75 (d, J = 14 Hz, 1H), 4.57 (q, 1H), 2.50 (d, J = 5 Hz, 1H), 1.43 (s, 18H), 1.07 (s, 9H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 151.56, 147.55, 144.19, 143.77, 141.48, 140.64, 136.56, 121.37, 106.3, 83.7, 83.0, 79.3, 63.4, 60.2, 27.9, 27.8, 27.1, 26.9, 22.3, 20.2; HR-FAB MS Obsd, m/z 603.3132; Calcd. for $C_{30}H_{46}N_4O_7Si$, m/z 603.3214 $(M+H)^+$.

(1S,2R,3R)-9-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl]-3-deazaadenine (20): A mixture of **19** (180 mg, 0.299 mmol), 2N HCl in methanol (10 mL) was heated to 60°C for 15 hours. The mixture was evaporated under reduced pressure and co-evaporated with methanol (3 × 50 mL). The residue was dissolved in methanol (10 mL), neutralized with IRA-400 (OH) resin, filtered the solution, concentrated and purified using amine functionalized silica gel column chromatography (CH_2Cl_2:MeOH, 9:1) to give **20** (62 mg, 79%) as a white solid: M.p. 244°C; $[\alpha]^{23}_D$ -102.88 (c 0.16, MeOH); UV (H_2O) $\lambda_{max,}$ nm: 216, 266 (pH 2), 220, 266 (pH 11), 215, 266 (pH 7); ^{1}H NMR (CD_3OD) δ 8.00 (s, 1H), 7.72 (d, J = 6 Hz, 1H), 6.99 (d, J = 6 Hz, 1H), 5.98 (s, 1H), 5.54 (m, 1H), 4.69 (m, 1H), 4.38 (s, 2H); ^{13}C NMR (CD_3OD) δ 152.3, 150.7, 146.7, 142.7, 131.7, 128.7, 127.0, 102.5, 80.17, 78.61, 58.67, 58.43; HR-ESI MS Obsd, m/z 263.1142; Calcd. for $C_{12}H_{14}N_4O_3$, 263.1145 $(M+H)^+$; Anal. Calcd. for $C_{12}H_{14}N_4O_3 \cdot 0.2H_2O$: C, 54.21; H, 5.46; N, 21.07; Found: C, 54.23; H, 5.49; N, 21.12.

(1S,2R,3R)-N^2-Isopropylamino-9-[2,3-dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl]6-chloropurine (21): To a solution of **11** (111 mg, 0.417 mmol), triphenylphosphine (274 mg, 1.043 mmol) and 6-chloro-N^2-isobutyrylpurine (200 mg, 0.834 mmol) in dry THF (7 mL) was added diisopropylazodicarboxylate (DIAD, 204μL, 1.043 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −20°C (initial cooling fluid temperature = −50°C, fluid speed max) for 30 minutes at 300W then triethylamine trihydrofluoride (136 μL, 0.834 mmol) was added and the reaction stirred at room temperature for 30 minutes. Reaction mixture was neutralized with minimum satd. $NaHCO_3$ and evaporated. The residue was purified by preparative TLC (CH_2Cl_2: MeOH, 9:1) to give **21** (62 mg, 40%) as a yellow solid: M.p. 123.5°C (decomposition); $[\alpha]^{26}_D$ -7.47 (c 0.49, MeOH); UV (MeOH) λ_{max} 233 nm; ^{1}H NMR (CD_3OD) δ 8.24 (s, 1H), 5.93 (s, 1H), 5.83 (m, 1H), 4.82 (m, 1H), 4.38–4.42 (m, 3H), 2.83

(m, 1H), 1.27 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (CD_3OD) δ 153.28, 153.17, 152.13, 149.76, 145.57, 127.60, 120.50, 80.04, 78.13, 59.62, 58.54, 35.58, 18.31; HR-ESI MS Obsd, m/z 368.1103; Calcd. for $C_{15}H_{18}ClN_5O_4$, 368.1126 $(M+H)^+$.

(1S,2R,3R)-1-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl] guanine (22): In a microwave sealed vessel, a mixture of **21** (57 mg, 0.155 mmol) and formic acid (2 mL) was irradiated at 90°C for 5 minutes under a continuous air cooling flow and then concentrated in vacuum. The residue was dissolved in a solution of methanol (10 mL) saturated with ammonia and stirred at room temperature overnight. The mixture was then evaporated to dryness, dissolved in a small amount of methanol and precipitated by addition of diethyl ether. The solid was filtered off and washed with diethyl ether to give **22** (37 mg, 85%) as a brown solid: M.p. 198°C; $[\alpha]^{26}_D$ -95.2 (c, 0.12, H_20); UV (H_2O) λ_{max}, nm: 254 (pH 2), 256 (pH 11), 252 (pH 7); ^{1}H NMR (D_2O) δ 7.65 (s, 1H), 5.98 (s, 1H), 5.46 (m, 1H), 4.77 (m, 1H), 4.38–4.42 (m, 3H); ^{13}C NMR (D_2O) δ 161.88; 156.83, 153.57, 141.58, 124.96, 119.00, 82.50, 80.58, 61.36, 61.18; Anal. Calcd. for $C_{11}H_{13}N_5O_4$: C, 47.31; H, 4.69; N, 25.08; Found: C, 47.29; H, 4.58; N, 24.92.

(1S,2R,3R)-N^3-Benzoyl-1-[2-hydroxy-3,6-O-di-tert-butylsilanediyl-4-cyclopenten-1-yl]uracil (23): To a solution of **11** (360 mg, 1.25 mmol), triphenylphosphine (824 mg, 3.14 mmol) and N^3-benzoyluracil (472 mg, 2.51 mmol) in dry THF (70 mL) was added diisopropylazodicarboxylate (DIAD, 632 μL, 3.14 mmol) dropwise under nitrogen atmosphere. The resulting solution was irradiated at −40°C (initial cooling fluid temperature = −50°C, fluid speed max) for 5 minutes at 100 W then diluted with EtOAc washed with water, brine, dried over magnesium sulphate and concentrated under reduced pressure The residue was purified by silica gel column chromatography (Hexane:EtOAc, 8:2) to give **23** (250 mg, 41%) as a white solid: M.p. 102°C (decomposition); $[\alpha]^{28}_D$ -39.99 (c 0.55, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 7.98 (m, 2H), 7.67 (m, 1H), 7.51 (m, 2H), 7.09 (d, J = 8.0 Hz, 1H), 5.80 (d, J = 8.0 Hz, 1H), 5.63 (s, 1H), 5.59 (m, 1H), 5.01 (brs, 1H), 4.88 (dd, J = 2.0, 14 Hz, 1H), 4.75 (d, J = 14 Hz, 1H), 4.47 (m, 1H), 2.96 (s, 1H), 1.07 (s, 9H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 168.78, 162.21, 150.99, 149.17, 141.61, 135.12, 131.44, 130.50, 129.82, 129.03, 128.03, 120.59, 101.54, 83.80, 78.64, 63.39, 60.87, 27.09, 26.91, 22.25, 20.22; HR-ESI MS Obsd, m/z 485.2106; Calcd. for $C_{25}H_{32}N_2O_6Si$, m/z 485.2109 $(M+H)^+$.

(1S,2R,3R)-N^3-Benzoyl-1-[2-(*tert*-butyl-dimethylsilyloxy)-3,6-O-di-tert-butylsilanediyl-4-cyclopenten-1-yl]uracil (24): To a solution of **23** (250 mg, 0.51 mmol), imidazole (140 mg, 2.06 mmol) in anhydrous CH_2Cl_2 (5 mL), was added *tert*-butyldimethylsilyl chloride (116 mg, 0.77 mmol) at room temperature and stirred for 12hours at 50°C. The solvent was evaporated under reduced pressure and purified using silica gel column chromatography (EtOAc:hexane = 3:7) to give **24** (202 mg, 65%) as white solid: M.p. 188°C; $[\alpha]^{23}_D$ -42.02 (c 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.94

(m, 2H), 7.64 (m, 1H), 7.48 (m, 2H), 6.97 (d, J = 8.5 Hz, 1H), 5.77 (d, J = 8.5 Hz, 1H), 5.72 (m, 1H), 5.61 (brs, 1H), 4.92 (brs, 1H), 4.81 (m, 1H), 4.68 (d, J = 13.5 Hz, 1H), 4.39 (m, 1H), 1.05 (s, 3H), 0.95 (s, 3H), 0.89 (s, 3H), 0.15 (s, 3H), 0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.0, 162.5, 150.5, 148.0, 142.6, 135.2, 131.7, 130.7, 129.2, 122.3, 101.0, 85.1, 79.1, 63.7, 60.2, 27.2, 27.1, 27.0, 25.9, 22.4, 20.3, 18.1, −4.0, −4.5; HR-ESI MS Obsd, m/z 599.2381; Calcd. for $C_{31}H_{46}N_2O_6Si_2$, m/z 599.2972 $(M+H)^+$.

(1S,2R,3R)-1-[2-(*tert*-Butyl-dimethylsilyloxy)-3,6-O-di-tert-butylsilanediyl -4-cyclopenten-1-yl]uracil (25): Compound **24** (200 mg, 0.334 mmol) was dissolved in a solution of methanolic ammonia (10mL) at 0°C and stirred for 5 hours at room temperature. The solvent was evaporated under reduced pressure and the residue was purified on silica gel chromatography (CH_2Cl_2: MeOH, 85:15) to give **25** (150 mg, 91%) as a white solid: M.p. 195°C; $[\alpha]^{23}_D$ −50.67 (c 0.47, $CHCl_3$); UV (MeOH) λ_{max} 267 nm; ^{1}H NMR ($CDCl_3$) δ 8.48 (s, 1H), 6.88 (d, J = 8 Hz, 1H), 5.72 (m, 1H), 5.65 (dd, J = 2.5, 8.0 Hz, 1H), 5.58 (d, J = 1 Hz, 1H), 4.86 (t, J = 1 Hz, 1H), 4.81 (m, 1H), 4.67 (d, J = 14.5 Hz, 1H), 4.38 (m, 1H), 1.04 (s, 9H), 0.95 (s, 9H), 0.82 (s, 9H), 0.12 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.2; 157.2, 153.1, 147.8, 127.6, 106.5, 90.4, 84.3, 68.9, 65.2, 32.4, 32.3, 31.0, 27.7, 25.6, 23.3, 0.5, −0.0; HR-ESI MS Obsd, m/z 495.2697; Calcd. for $C_{24}H_{42}N_2O_5Si_2$, m/z 495.2711 $(M+H)^+$.

(1S,2R,3R)-1-[2-(*tert*-Butyl-dimethylsilyloxy)-3,6-O-di-tert-butylsilanediyl -4-cyclopenten-1-yl]cytosine (26): A mixture of **25** (250 mg, 0.53 mmol) and 4-dimethylaminopyridine (DMAP) (131 mg, 1.07 mmol) in anhydrous acetonitrile (15 mL), was added triethylamine (0.149 mL, 1.07 mmol) followed by 2,4,6-triisopropylbenzenesulfonyl chloride (324 mg, 1.07 mmol) at room temperature under nitrogen. After being stirred for 20 hours, NH_4OH (30%, 20 mL) was added and stirred for 5 hours. The mixture was diluted with chloroform and washed with saturated aqueous NH_4Cl (3 × 20 mL) solution. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified using silica gel column chromatography (CH_2Cl_2: MeOH, 96:4) to give **26** (182 g, 73%) as a solid: M.p. 192°C; $[\alpha]^{23}_D$ -56.25 (c 0.5, $CHCl_3$); UV (MeOH) λ_{max} 275 nm; ^{1}H NMR ($CDCl_3$) δ 6.94 (d, J = 7.0 Hz, 1H), 5.91 (d, J = 6.5 Hz, 1H), 5.82 (d, J = 5.5 Hz, 1H), 5.58 (s, 1H), 4.87 (s, 1H), 4.78 (d, J = 14 Hz, 1H), 4.65 (d, J = 13.5 Hz, 1H), 4.38 (dd, J = 3.5, 7.5 Hz, 1H), 1.05 (s, 9H), 0.95 (s, 9H), 0.80 (s, 9H), 0.10 (s, 3H), 0.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.21, 157.0, 146.3, 143.6, 123.9, 93.8, 85.5, 78.8, 63.7, 60.5, 27.1, 26.9, 25.6, 22.3, 20.2, 18.0, −4.9, −5.3; HR-ESI MS Obsd., m/z 494.2870; Calcd. for $C_{24}H_{43}N_3O_4Si_2$, m/z 494.2871 $(M+H)^+$.

(1S,2R,3R)-1-[2,3-Dihydroxy-4-hydroxymethyl-4-cyclopenten-1-yl] cyto- sine (27): To a solution of **26** (152 mg, 0.327 mmol) in THF (5 mL), $Et_3N{\cdot}3HF$ (0.168 mL, 1.04 mmol) was added and stirred at room temperature for 1 hour. Reaction mixture was evaporated and the residue

was dissolved in methanol and neutralized with IRA-400 (OH) resin. The resin was filtered and the filtrate concentrated and purified using amine functionalized silica gel column chromatography (CH_2Cl_2: MeOH, 5:1) to give **27** (53 mg, 71%) as a white solid: M.p. 262°C (decomposition); $[\alpha]^{24}_D$ + 48.2 (c 0.3, MeOH); ^{1}H NMR (DMSO-d_6) δ 8.84 (brs, 1H), 8.02 (brs, 1H), 7.28 (d, J = 7.0 Hz, 1H), 5.85 (d, J = 5.5 Hz, 1H), 5.54 9m, 2H), 5.28–4.94 (3 × brs, 3 × OH), 4.33 (s, 1H), 4.07 (m, 3H); ^{13}C NMR (CD_3OD) δ 165.1, 157.0, 146.2, 143.5, 124.1, 93.8, 81.0, 77.8, 61.1, 56.5; HR-ESI MS Obsd., m/z 240.0982; Calcd. for $C_{10}H_{13}N_3O_4$, m/z 240.0985 $(M+H)^+$; Anal. Calcd. for $C_{10}H_{13}N_3O_4$: C, 50.20; H, 5.48; N, 17.57. Found: C, 49.92; H, 5.50; N, 17.39.

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