Nucleosides and Nucleotides. 186. Synthesis and Biological Activities of Pyrimidine Carbocyclic Nucleosides with a Hydroxyamino Group Instead of a Hydroxymethyl Group at the 4′-Position of the Sugar Moiety[1)]

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Pyrimidine carbocyclic nucleosides with a hydroxyamino group instead of a hydroxymethyl group at the 4′-position of the sugar moiety were designed as potential antitumor and/or antiviral agents. Pd (O)-catalyzed reactions of enantiomerically pure (+)-(1*R*,4*S*)-4-[(*tert*-butyldiphenylsilyl)oxy]-1-(ethoxycarbonyloxy)-2-cyclopentene (9) with *N*3-benzoylthymine and -uracil gave carbocyclic nucleosides 10 and 11. Subsequent Pd (O)-catalyzed reactions of *N*3-benzoyl-1-[(1*R*,4*S*)-4-(ethoxycarbonyloxy)-2-cyclopenten-1-yl]thymine (14) and -uracil (15) with *O*-benzylhydroxylamine smoothly gave the hydroxyamino-substituted carbocyclic nucleosides 16 and 17. From these nucleosides, the target compounds were prepared after deprotection or further reactions. The 2′,3′-didehydro-2′,3′-dideoxythymidine (D4T) analogue 20 was the most effective compound, with IC_{50} values of 27.3 and 34.5 μM against KB and L1210 cells *in vitro*. Carbocyclic analogues of uridine and cytidine (29 and 32) were less effective than 20 against both cell lines.

Key words carbocyclic nucleoside; hydroxylamine; antitumor activity; antiviral activity

Hydroxylamine derivatives have interesting chemical properties. They can be readily reduced to amines and readily oxidized to nitrones. Additionally, the oxidation of hydroxylamine by ceric sulfate[2)] and OH-radicals[3)] produces $NH_2O\cdot$ radicals. Therefore, if such a substituent can be introduced into the sugar moiety of a nucleoside, the result may be a unique nucleoside with a variety of biological activities. Recently, we synthesized several nucleosides with a hydroxyamino group instead of a hydroxyl group of the 2′ or 3′ position at the sugar moiety. Among them, 2′-deoxy-2′-hydroxyaminocytidine (2′-DHAC) and 3′-deoxy-3′-hydroxyaminocytidine (3′-DHAC) (Fig. 1) showed cytotoxicity against several tumor cell lines *in vitro*, and antileukemic activity against the mouse P388 model *in vivo*.[4,5)] We also detected 2′-NHO· radicals of 2′-DHAC in neutral aqueous solution at room temperature by ESR.[4)]

A nucleoside with a hydroxyamino group instead of a hydroxymethyl group at the 4′-position of the sugar moiety, such as **1**, (Fig. 1) would be expected to be a substrate of certain nucleoside kinases, since the hydroxyamino group may mimic to the hydroxymethyl group. However, substitution of the hydroxymethyl group of a D-ribose or 2-deoxy-D-ribose moiety by a hydroxyamino group would be difficult because that such nucleosides are not sufficiently stable. Therefore, we designed and synthesized carbocyclic nucleoside analogues with a hydroxyamino group at the carbocyclic moiety, such as **2**—**4** depicted in Fig. 1, and evaluated their cytotoxicity against tumor cells *in vitro* and their antiviral activities against human immunodeficiency virus type-1 (HIV-1) *in vitro*.

Chemistry

The synthetic route to the target compounds is outlined in Chart 1. The target compounds were straightforwardly synthesized using Pd-chemistry. Enantiomerically pure (+)-(1*R*,4*S*)-1-acetoxy-4-hydroxy-2-cyclopentene (**6**) was obtained by hydrolysis of the corresponding racemic diacetate **5** with porcine liver esterase in 99% ee.[6)] Compound **5** was protected with a *tert*-butyldiphenylsilyl (TBDPS) group, followed by deacetylation to give **8**, which was converted into an ethoxycarbonyl derivative **9**. Compound **9** was reacted with *N*3-benzoylthymine[7)] in the presence of $Pd_2(dba)_3\cdot CHCl_3$ and Ph_3P to smoothly give the desired thymine-carbocycle **10** in 94% yield. The configuration at the 1′-position was confirmed by nuclear Overhauser effect (NOE) experiments. When the 5′α-proton in **10** was irradiated, NOE enhancements of 18% and 16% were observed at the 1′ and 4′-protons, respectively. Therefore, *N*3-benzoylthymine was introduced *via* a double inversion, and **10** has the desired configuration at the 1′-position. To introduce nucleobases into similar carbocycles using Pd-chemistry, previous methods have used an acetoxy or benzoyloxy group as a leaving group.[8,9)] In our experiments, the ethoxycarbonyloxy group

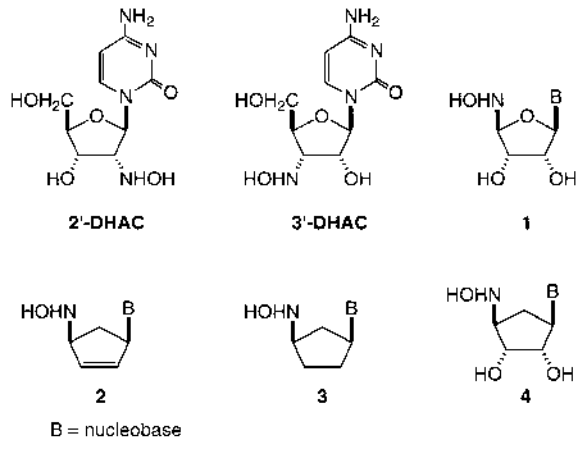

Fig. 1

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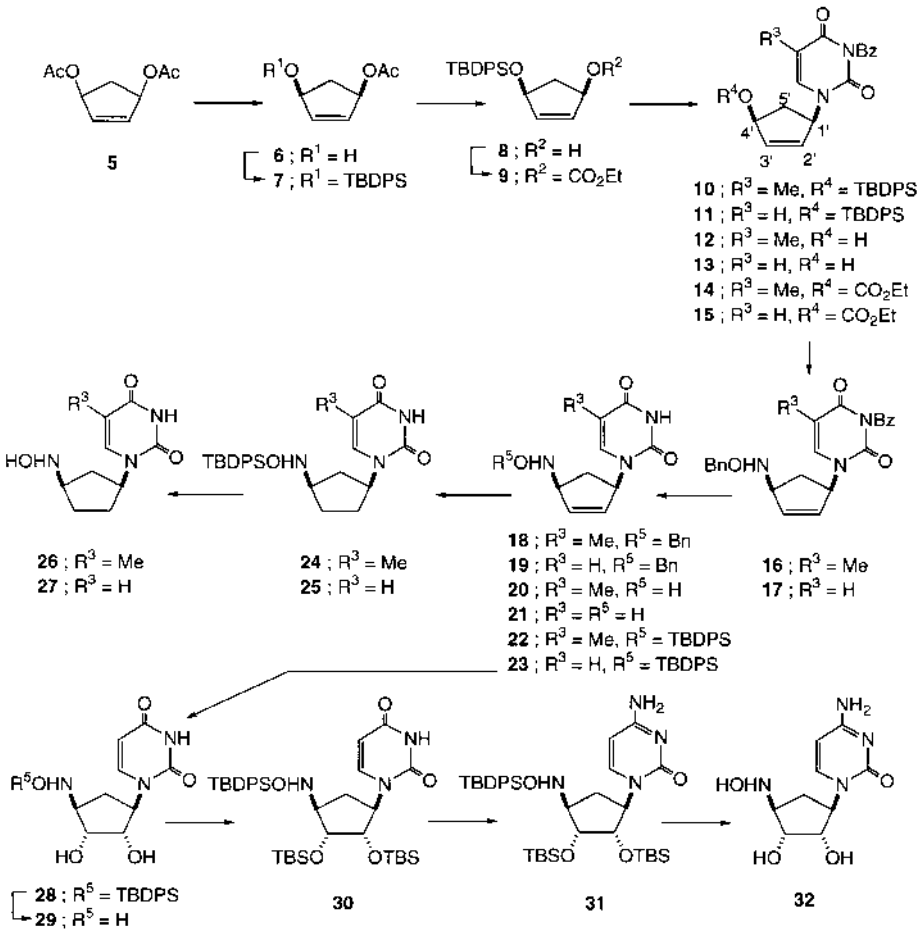

Chart 1

was found to be a good choice as the leaving group, as expected.

Deprotection of the TBDPS group by tetrabutylammonium fluoride (TBAF), followed by ethoxycarbonylation of the resulting hydroxyl group, gave a substrate **14** for the next Pd-catalyzed reaction to introduce a hydroxylamino group at the 4′-position. Compound **14** was treated with *O*-benzylhydroxylamine under conditions similar to those described above to give **16** in 84% yield. Removal of the benzoyl group at the *N*3-position using NaOMe and subsequently the *O*-benzyl group by BCl_3 gave **20** in 80% yield in two steps. Compound **20** provides a 4′-hydroxyaminated-carbocyclic equivalent of the anti-HIV agent 2′,3′-didehydro-2′,3′-dideoxythymidine (D4T). After protection of the hydroxyl group in **20** with a TBDPS group, the resulting **22** was hydrogenated in the presence of Pd/C in AcOEt to give cyclopentyl derivative **24** in 89% yield. When the same reaction was performed in MeOH, the N–O bond cleavage was also detected along with **24**. The TBDPS group in **24** was removed by treatment with HCl in a mixture of dioxane and MeOH to give **26** as a hydrochloride.

Uracil derivatives **21** and **27** were synthesized in a manner similar to that described for the synthesis of thymine analogues, as shown in Chart 1.

Compound **23** was *cis*-dihydroxylated using OsO_4 in the presence of 4-methylmorpholine *N*-oxide (NMO) to give **28** in 67% yield. The stereochemistry of **28** was determined using NOE experiments. Upon irradiation of the 1′-proton of **28**, 1.2% enhancement was observed at the 4′-proton, and 1.9% enhancement at the 2′-proton was detected upon irradiation of the 6-proton at the uracil moiety. Therefore, *cis*-dihydroxylation selectively occurred at the α-face of the carbocyclic ring. Deprotection of the TBDPS group in **28** with TBAF gave carbocyclic uridine derivative **29**.

Protection of the *cis*-hydroxyl group in **28** with a *tert*-butyldimethylsilyl (TBS) group gave **30**, which was further converted into a cytosine derivative **31** in a usual manner. Finally, **31** was deprotected with HCl in a mixture of dioxane and MeOH to give carbocyclic cytidine analogue **32** as a dihydrochloride.

Biological Activity

The cytotoxicities of 4′-hydroxyamino-substituted carbocyclic nucleosides **20**, **21**, **26**, **27**, **29** and **32** were investigated *in vitro* using mouse L1210 leukemia and human KB pharyngeal carcinoma cells.[10] The results are summarized in Table 1. Among the nucleosides, D4T analogue **20** was the most effective, with IC_{50} values of 27.3 and 34.5 μM against KB and L1210 cells *in vitro*, while uracil analogue **21** was only effective against L1210 cells, with an IC_{50} value of 88 μM. Cyclopentyl analogues **26** and **27** were devoid of any activities against both cell lines. Carbocyclic *ribo*-nucleoside analogues **29** and **32** were less cytotoxic than **20**, and cytosine analogue **32** was slightly more active than uracil analogue **29**.

The antiviral activities of the nucleosides against HIV-1

Table 1. Cytotoxic Effects against L1210 and KB Cells[a] and Anti-HIV-1 Activity[b] of Various 4′-Hydroxylamine-Substituted Uracil and Cytosine Carbocyclic Nucleosides

Compds	IC_{50} (μM)		EC_{50} (μM)	CC_{50} (μM)
	L1210	KB	HIV	MT-4
20	34.5	27.3	>0.34	0.34
21	88	>300	>0.35	0.35
26	>300	>300	>0.26	0.26
27	>300	>300	>300	>300
29	>300	57	ND[c]	ND
32	71	33	ND	ND
AZT	ND	ND	>0.0041	3.2

a) Tumor cell growth inhibitory activity assay *in vitro* was done following the method.[10] Each tumor cell (2×10^3 cells/well) was incubated in the presence or absence of compounds for 72 h. 3(4,5-dimethylthizol-2-yl)-2,5-dimethyltetrazolium bromide (MTT)-reagent was added to each well and plate was incubated for 4 h more, the resulting MTT-formazan was dissolved in DMSO and the OD (540 nm) was measured. Percent inhibition was calculated as follows: % inhibition=[1−OD (540 nm) of sample well/OD (540 nm) of control well]×100. IC_{50} (μg/ml) was given as the concentration at 50% inhibition of cell growth. *b*) To evaluate anti-HIV-1 activity, HIV-1 IIIb strain *vs*. MT-4 cells were used, respectively. Briefly, cells were infected with viruses at a multiplicity of infection (m.o.i.) of 0.02. Immediately after the virus infection, a cell suspension (100 μl) was placed into each well containing various concentrations of the compounds (100 μl). After 4 days of incubation at 36 °C, the number of viable cells was determined by the MTT method.[11] *c*) Not determined.

were also examined *in vitro* (Table 1).[11] However, **20**, **21**, and **26** were too cytotoxic to the host human T-leukemic MT-4 cells to measure their anti-HIV activities. Compound **27** showed no activity against HIV at up to 300 μM.

Although we do not have any direct evidence that these carbocyclic nucleosides became substrates of certain nucleoside kinases, based on the biological data shown in Table 1, there appears to be some nucleobase specificity for the cytotoxicity; thymine derivative **20** is more active than uracil derivative **21**, and cytosine derivative **32** is more active than uracil derivative **29**. These results could reflect the substrate specificities of thymidine kinase and uridine/cytidine kinase. Moreover, **20**, **21**, and **26** were more active against human leukemic MT-4 cells than against human KB cells, which are derived from solid tumors. These results could reflect that kinase activity is usually higher in T-leukemic cells than in cells derived from solid tumors. Therefore, it is likely that the hydroxyamino group may be a bioisostere of the hydroxymethyl group in nucleosides, and accepts a phosphate group by certain nucleoside kinases.

Experimental

Melting points were measured on a Yanagimoto MP-3 micromelting point apparatus (Yanagimoto, Japan) and are uncorrected. Fast atom bombardment mass spectrometry (FAB-MS) was done on a JEOL JMS-HX110 instrument at an ionizing voltage of 70 eV. The ^{1}H-NMR spectra were recorded on a JEOL JNM-GX 270 (270 MHz) or Bruker ARX 500 (500 MHz) spectrometer with tetramethylsilane as an internal standard. Chemical shifts are reported in parts per million (δ), and signals are expressed as s (singlet), d (doublet), t (triplet), m (multiplet), or br (broad). All exchangeable protons were detected by disappearance on the addition of D_2O. UV absorption spectra were recorded with a Shimadzu UV-240 spectrophotometer. IR spectra were recorded with a JEOL A-102 spectrometer. TLC was done on Merck Kieselgel F_{254} precoated plates (Merck, Germany). The silica gel used for column chromatography was YMC gel 60A (70—230 mesh) (YMC Co., Ltd., Japan).

(+)-(1*R*,4*S*)-1-Acetoxy-4-hydroxy-2-cyclopentene (6) Porcine liver esterase (45 g, purchased from Sigma) was added to a stirred solution of **5** (43.0 g, 233 mmol) in phosphate buffer (0.1 M, 200 ml, pH 7.0) at 37 °C. The mixture was stirred at 37 °C for 2 days and quenched by addition of EtOH (200 ml). The mixture was filtered through a Celite pad, which was washed with AcOEt. The combined filtrate and washings were concentrated *in vacuo*, and the residue was extracted with $CHCl_3$ (500 ml×5). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=2 : 1) to give **6** (11.2 g, 34% as a yellow oil): $[\alpha]_D^{25}$ 68.8° (*c*=1.02, $CHCl_3$); [lit.[6b]) $[\alpha]_D^{25}$ 68.0° (*c*=1.02, $CHCl_3$, 99% ee)].

(1*R*,4*S*)-4-[(*tert*-Butyldiphenylsilyl)oxy]-1-(ethoxycarbonyloxy)-2-cyclopentene (9) A mixture of **6** (5.60 g, 39.4 mmol), TBDPSCl (15.2 ml, 58.5 mmol), and imidazole (5.31 g, 78.0 mmol) in dimethylformamide (DMF, 100 ml) was stirred 24 h at 0 °C and diluted with Et_2O (500 ml). The mixture was washed with H_2O (200 ml×2) and brine (200 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give crude **7** as a colorless oil. A MeOH solution of NaOMe (28%, 1.27 ml) was added to the above oil in MeOH (100 ml), and the mixture was stirred for 24 h at room temperature. The mixture was neutralized with Dowex-50W X2 (H^+-form) and filtered. The filtrate was concentrated *in vacuo* to give crude **8** as a colorless oil, which was coevaporated several times with pyridine. $ClCO_2Et$ (11.2 ml, 117 mmol) was added to a solution of the above oil in pyridine (150 ml) at 0 °C under argon atmosphere. After the mixture was stirred for 1.5 h at room temperature, the reaction was quenched by addition of H_2O at 0 °C, and the solvent was removed *in vacuo*. The residue was dissolved in Et_2O (250 ml), which was washed with H_2O (250 ml×2) and brine (250 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=10 : 1) to give **9** (15.6 g, 97% as a colorless oil). ^{1}H-NMR (500 MHz, $CDCl_3$) 7.69—7.34 (10H, m, Ph), 5.91 (1H, d, H-2, *J*=5.6 Hz), 5.87 (1H, d, H-3, *J*=5.6 Hz), 5.29 (1H, dd, H-1, *J*=6.3, 6.3 Hz), 4.67 (1H, dd, H-4, *J*=5.9, 5.9 Hz), 4.20 (2H, q, $OC\underline{H}_2CH_3$, *J*=7.2 Hz), 2.68 (1H, ddd, H-5a, *J*=7.3, 7.3, 13.7 Hz), 1.83 (1H, ddd, H-5b, *J*=5.4, 5.4, 13.7 Hz), 1.32 (3H, t, $OCH_2C\underline{H}_3$, *J*=7.2 Hz), 1.04 (9H, s, *t*-Bu). FAB-LR-MS *m/z*: 411 ($(M+H)^+$, 11%). FAB-HR-MS *m/z*: 411.1978 (Calcd for $C_{24}H_{31}O_4Si$ $(M+H)^+$: 411.1990).

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-[(*tert*-butyldiphenylsilyl)oxy]-2-cyclopenten-1-yl]thymine (10)** A mixture of *N*3-benzoylthymine (3.50 g, 15.2 mmol), **9** (4.48 g, 4.48 mmol), $Pd_2(dba)_3\cdot CHCl_3$ (518 mg, 0.501 mmol), and PPh_3 (1.00 g, 3.81 mmol) in tetrahydrofuran (THF, 50 ml) was stirred for 30 min at room temperature under argon atmosphere, and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=3 : 1) to give **10** (5.70 g, 94% as a white foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 7.95—7.39 (16H, m, H-6, Ph), 6.06 (1H, ddd, H-2′, *J*=1.9, 1.9, 5.6 Hz), 5.80 (1H, dd, H-3′, *J*=2.4, 5.5 Hz), 5.55 (1H, ddd, H-1′, *J*=2.2, 5.0, 7.9 Hz), 4.78 (1H, ddd, H-4′, *J*=2.2, 2.2, 10.2 Hz), 2.66 (1H, ddd, H-5′a, *J*=7.2, 8.5, 15.1 Hz), 1.98 (3H, d, 5-Me, *J*=1.2 Hz), 1.73 (1H, ddd, H-5′b, *J*=2.8, 2.8, 15.0 Hz), 1.11 (9H, s, *t*-Bu). FAB-LR-MS *m/z*: 551 ($(M+H)^+$, 34%). *Anal*. Calcd for $C_{33}H_{34}N_4O_5Si\cdot H_2O$: C, 69.69; H, 6.38; N, 4.93. Found: C, 69.85; H, 6.09; N, 4.85.

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-[(*tert*-butyldiphenylsilyl)oxy]-2-cyclopenten-1-yl]uracil (11)** A mixture of **6** (6.77 g, 16.5 mmol), *N*3-benzoyluracil (4.60 g, 21.3 mmol), $Pd_2(dba)_3\cdot CHCl_3$ (735 mg, 0.71 mmol), and PPh_3 (1.46 g, 5.68 mmol) in THF (100 ml) was stirred for 3 h at room temperature under argon atmosphere. Work-up and purification were performed as described above to give **11** (8.45 g, 95% as a white foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 7.74 (1H, d, H-6, $J_{5,6}$=8.2 Hz), 7.96—7.39 (15H, m, Ph), 6.08 (1H, ddd, H-3′, *J*=1.8, 2.1, 5.6 Hz), 5.85 (1H, d, H-5, *J*=7.9 Hz), 5.80 (1H, dd, H-2′, *J*=2.3, 5.6 Hz), 5.54 (1H, m, H-1′), 4.80 (1H, ddd, H-4′, *J*=2.3, 2.3, 7.0 Hz), 2.65 (1H, ddd, H-5′a, *J*=7.0, 8.5, 15.0 Hz), 1.71 (1H, ddd, H-5′b, *J*=2.6, 2.9, 15.0 Hz), 1.09 (9H, s, *t*-Bu). ^{13}C-NMR (100 MHz, $CDCl_3$) 165.84, 161.94, 149.66, 141.35, 139.91, 135.43, 133.20, 131.33, 130.90, 130.30, 129.88, 129.86, 128.95, 127.72, 127.68, 102.46, 75.86, 58.81, 40.60, 26.96, 19.16. FAB-LR-MS *m/z*: 537 ($(M+H)^+$, 21%). *Anal*. Calcd for $C_{32}H_{32}N_2O_4Si$: C, 70.43; H, 6.10; N, 5.13. Found: C, 70.38; H, 6.00; N, 5.14.

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-hydroxy-2-cyclopenten-1-yl]thymine (12)** A mixture of **10** (5.30 g, 9.62 mmol) and TBAF (1 M in THF, 11.6 ml, 11.6 mmol) in THF (50 ml) was stirred at room temperature for 30 min, and the solvent was removed *in vacuo*. The residue was coevaporated several times with MeOH and purified by silica gel column chromatography ($CHCl_3$: EtOH=15 : 1) to give **12** (3.00 g, quant. as a white foam). ^{1}H-NMR (400 MHz, DMSO-d_6) 7.97—7.51 (6H, m, H-6, Ph), 6.18 (1H, m, H-2′), 5.88 (1H, m, H-3′), 5.36 (1H, m, H-1′), 5.29 (1H, br d, 4′-OH, *J*=6.1 Hz), 4.63 (1H, m, H-4′), 2.75 (1H, m, H-5′a), 1.84 (3H, s, 5-Me), 1.50 (1H, m, H-5′b). FAB-LR-MS *m/z*: 313 ($(M+H)^+$, 86%). *Anal*. Calcd for $C_{17}H_{16}N_2O_4$: C, 64.14; H, 5.28; N, 8.80. Found: C, 63.91; H, 5.34; N, 8.79.

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-hydroxy-2-cyclopenten-1-yl]uracil (13)** A mixture of **11** (2.14 g, 3.99 mmol) and TBAF (1 M in THF, 4.8 ml, 4.8 mmol)

in THF (30 ml) was stirred at room temperature for 4 h. Work-up and purification were performed as described above to give **13** (1.09 g, 91% as a pale yellow foam). ^{1}H-NMR (400 MHz, DMSO-d_6) 8.04—7.58 (6H, m, H-6, Ph), 6.19 (1H, m, H-3′), 5.93 (1H, dd, H-5, J=1.7, 8.2 Hz), 5.88 (1H, m, H-2′), 5.38—5.34 (2H, m, H-1′, 4′-OH), 4.64 (1H, m, H-4′), 2.75 (1H, ddd, H-5′a, J=7.7, 7.7, 14.8 Hz), 1.51 (1H, m, H-5′b). FAB-LR-MS m/z: 299 ((M+H)$^+$, 17%). *Anal*. Calcd for $C_{16}H_{14}N_2O_6$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.37; H, 4.85; N, 9.50.

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-(ethoxycarbonyloxy)-2-cyclopenten-1-yl]-thymine (14)** A mixture of **12** (1.60 g, 5.12 mmol) and $ClCO_2Et$ (1.47 ml, 15.4 mmol) in pyridine (30 ml) was stirred for 30 min at room temperature, and the solvent was removed *in vacuo*. The residue was coevaporated several times with toluene, and the residue dissolved in AcOEt (150 ml) was washed with H_2O (150 ml×2) and brine (150 ml). The organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=1 : 1) to give **14** (1.96 g, quant. as a yellow foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 7.94—7.48 (5H, m, Ph), 6.99 (1H, d, H-6, J=1.2 Hz), 6.33 (1H, ddd, H-2′, J=2.1, 2.1, 5.6 Hz), 6.02 (1H, ddd, H-3′, J=1.0, 2.3, 5.6 Hz), 5.69 (1H, m, H-1′), 5.59 (1H, m, H-4′), 4.25 (2H, q, $CO_2C\underline{H}_2CH_3$, J=7.2 Hz), 3.06 (1H, ddd, H-5′a, J=7.9, 7.9, 15.3 Hz), 1.96 (3H, d, 5-Me, J=1.2 Hz), 1.78 (1H, ddd, H-5′b, J=3.9, 3.9, 15.3 Hz), 1.35 (3H, t, $CO_2CH_2C\underline{H}_3$, J=7.2 Hz). FAB-LR-MS m/z: 385 ((M+H)$^+$, 60%). FAB-HR-MS m/z: 385.1374 (Calcd for $C_{20}H_{21}N_2O_6$ (M+H)$^+$: 385.1398).

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-(ethoxycarbonyloxy)-2-cyclopenten-1-yl]-uracil (15)** A mixture of **13** (2.94 g, 9.86 mmol) and $ClCO_2Et$ (2.83 ml, 29.6 mmol) in pyridine (50 ml) was stirred for 24 h at room temperature. Work-up and purification were performed as described above to give **15** (3.40 g, 93% as a pale yellow foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 7.96—7.49 (5H, m, Ph), 7.31 (1H, d, H-6, J=8.1 Hz), 6.36 (1H, ddd, H-2′, J=2.0, 2.0, 5.6 Hz), 6.04 (1H, dd, H-3′, J=2.4, 5.6 Hz), 5.87 (1H, d, H-5, J=8.1 Hz), 5.69 (1H, m, H-1′), 5.60 (1H, m, H-4′), 4.24 (2H, q, $OC\underline{H}_2CH_3$, J=6.6 Hz), 3.07 (1H, ddd, H-5′a, J=8.1, 8.1, 15.4 Hz), 1.79 (1H, ddd, H-5′b, J=3.4, 3.4, 15.4 Hz), 1.37 (3H, t, $OCH_2C\underline{H}_3$, J=6.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) 168.48, 161.62, 153.99, 149.49, 140.11, 135.90, 134.90, 134.05, 131.11, 130.21, 128.93, 102.86, 79.81, 64.33, 58.46, 37.21, 14.29. FAB-LR-MS m/z: 371 ((M+H)$^+$, 55%). FAB-HR-MS m/z: 371.1226 (Calcd for $C_{19}H_{19}N_2O_6$ (M+H)$^+$: 371.1242).

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-(*N*-benzyloxyamino)-2-cyclopenten-1-yl]-thymine (16)** $Pd_2(dba)_3\cdot CHCl_3$ (456 mg, 1.74 mmol) was added to a stirred solution of **14** (1.67 g, 4.34 mmol), PPh_3 (456 mg, 1.74 mmol), NaOH (267 mg, 6.53 mmol), and $NH_2OBn\cdot HCl$ (1.04 g, 6.53 mmol) in THF (20 ml) and H_2O (3 ml) at room temperature. After the mixture was stirred for 12 h at room temperature, the solvent was removed *in vacuo*. The residue was coevaporated several times with EtOH and purified by silica gel column chromatography (hexane : AcOEt=2 : 3) to give **16** (1.7 g, 94% as a yellow foam). ^{1}H-NMR (270 MHz, $CDCl_3$) 7.93—7.36 (11H, m, Ph), 6.15 (1H, ddd, H-3′, J=2.0, 2.0, 5.6 Hz), 5.80 (1H, ddd, H-2′, J=2.0, 2.0, 5.6 Hz), 5.71 (1H, br s, 4′-NH), 5.65 (1H, m, H-1′), 4.73 (2H, s, benzylic), 4.17 (1H, m, H-4′), 2.74 (1H, ddd, H-5′a, J=8.3, 8.3, 14.9 Hz), 1.75 (3H, d, 5-Me, J=1.0 Hz), 1.70 (1H, ddd, H-5′b, J=4.6, 4.6, 14.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) 169.37, 162.98, 149.38, 137.51, 137.27, 137.12, 134.82, 132.16, 131.58, 130.34, 129.00, 128.46, 128.44, 128.12, 110.90, 77.21, 76.98, 65.26, 59.29, 34.45, 12.38. FAB-LR-MS m/z: 418 ((M+H)$^+$, 100%). FAB-HR-MS m/z: 418.1760 (Calcd for $C_{24}H_{24}N_3O_4$ (M+H)$^+$: 418.1767).

***N*3-Benzoyl-1-[(1*R*,4*S*)-4-(*N*-benzyloxyamino)-2-cyclopenten-1-yl]-uracil (17)** A mixture of **15** (1.10 g, 2.97 mmol), $Pd_2(dba)_3\cdot CHCl_3$ (154 mg, 0.149 mmol), and PPh_3 (311 mg, 1.19 mmol) was added to a stirred solution of aqueous NaOH (2 M, 2.33 ml, 4.46 mmol) and $NH_2OBn\cdot HCl$ (711 mg, 4.46 mmol) in THF (20 ml) at room temperature. After the mixture was stirred for 7 h at room temperature, work-up and purification were performed as described above to give **17** (1.0 g, 84% as a pale yellow foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 7.94—7.33 (11H, m, H-6, Ph), 6.18 (1H, ddd, H-3′, J=2.0, 2.0, 5.6 Hz), 5.82 (1H, ddd, H-2′, J=2.2, 2.2, 5.4 Hz), 5.71 (1H, br s, 4′-NH), 5.64 (1H, m, H-1′), 5.47 (1H, d, H-5, J=8.1 Hz), 4.73, 4.69 (each 1H, each d, benzylic, each J=11.2 Hz), 4.19 (1H, m, H-4′), 2.75 (1H, ddd, H-5′a, J=9.3, 9.3, 14.7 Hz), 1.71 (1H, ddd, H-5′b, J=4.2, 4.2, 14.9 Hz). FAB-LR-MS m/z: 404 ((M+H)$^+$, 25%). FAB-HR-MS m/z: 404.1614 (Calcd for $C_{23}H_{22}N_3O_4$ (M+H)$^+$: 404.1609).

1-[(1*R*,4*S*)-4-(*N*-Benzyloxyamino)-2-cyclopenten-1-yl]thymine (18) A mixture of **16** (1.67 g, 4.00 mmol) in MeOH (30 ml) containing NaOMe (28%, 1 ml) was stirred for 24 h at room temperature, and neutralized by addition of aqueous HCl (1 M), and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$: AcOEt=1 : 1) to give **18** (1.21 g, 97% as a yellow foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 8.76 (1H, br s, 3-NH), 7.37—7.24 (6H, m, H-6, Ph), 6.13 (1H, ddd, H-3′, J=2.0, 2.0, 5.6 Hz), 5.78 (1H, ddd, H-2′, J=1.8, 1.8, 5.6 Hz), 5.69 (1H, br s, 4′-NH), 5.66 (1H, m, H-1′), 4.71 (2H, s, benzylic), 4.16 (1H, m, H-4′), 2.73 (1H, ddd, H-5′a, J=8.5, 8.5, 14.7 Hz), 1.74 (3H, d, 5-Me, J=1.2 Hz), 1.63 (1H, ddd, H-5′b, J=4.6, 4.6, 14.5 Hz). FAB-LR-MS m/z: 314 ((M+H)$^+$, 100%). FAB-HR-MS m/z: 314.1509 (Calcd for $C_{17}H_{20}N_3O_3$ (M+H)$^+$: 314.1504).

1-[(1*R*,4*S*)-4-(*N*-Hydroxyamino)-2-cyclopenten-1-yl]thymine (20) A mixture of **18** (1.2 g, 3.8 mmol) and BCl_3 (1 M in CH_2Cl_2, 20 ml) was stirred for 2 days at room temperature, and the reaction was quenched by addition of MeOH, and the solvent was removed *in vacuo*. The residue was coevaporated several times with MeOH, and purified by silica gel column chromatography ($CHCl_3$: MeOH=10 : 1) to give **20** (777 mg, 91% as a white foam). ^{1}H-NMR (270 MHz, MeOH-d_4) 7.35 (1H, d, H-6, J=1.0 Hz), 6.27 (1H, ddd, H-3′, J=2.0, 2.0, 5.6 Hz), 6.20 (1H, ddd, H-2′, J=2.0, 2.0, 5.6 Hz), 5.54 (1H, m, H-1′), 4.57 (1H, m, H-4′), 2.97 (1H, ddd, H-5′a, J=8.6, 8.6, 15.0 Hz), 1.97 (1H, ddd, H-5′b, J=5.0, 5.0, 14.9 Hz), 1.87 (3H, d, 5-Me, J=1.0 Hz). ^{13}C-NMR (100 MHz, MeOH-d_4) 166.15, 152.57, 139.56, 137.96, 132.99, 111.14, 67.46, 60.66, 24.90, 12.38; FAB-LR-MS m/z: 224 ((M+H)$^+$, 18%). *Anal*. Calcd for $C_{10}H_{14}ClN_3O_3\cdot 0.5H_2O$: C, 44.70; H, 5.63; N, 15.64. Found: C, 44.04; H, 5.51; N, 15.20.

1-[(1*R*,4*S*)-4-(*N*-Benzyloxyamino)-2-cyclopenten-1-yl]uracil (19) A mixture of **17** (1.60 g, 3.97 mmol) in MeOH (30 ml) containing NaOMe (28%, 1 ml) was stirred for 24 h at room temperature, and neutralized by addition of aqueous HCl (1 M), and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$: AcOEt=1 : 1) to give **19** (1.11 g, 3.71 mmol, 93% as a pale yellow foam). ^{1}H-NMR (500 MHz, $CDCl_3$) 8.95 (1H, br s, 3-NH), 7.82—7.31 (6H, m, H-6, Ph), 6.14 (1H, m, H-3′), 5.77 (1H, m, H-2′), 5.69 (1H, br s, 4′-NH), 5.65 (1H, m, H-1′), 5.40 (1H, d, H-5, J=8.0 Hz), 4.70, 4.67 (each 1H, each d, benzylic, each J=11.3 Hz), 4.16 (1H, m, H-4′), 2.73 (1H, ddd, H-5′a, J=8.6, 8.7, 14.9 Hz), 1.64 (1H, ddd, H-5b, J=4.1, 4.2, 14.8 Hz). FAB-LR-MS m/z: 300 ((M+H)$^+$, 100%). FAB-HR-MS m/z: 300.1344 (Calcd for $C_{16}H_{18}N_3O_3$ (M+H)$^+$: 300.1347).

1-[(1*R*,4*S*)-4-(*N*-Hydroxyamino)-2-cyclopenten-1-yl]uracil (21) A mixture of **19** (50 mg, 0.17 mmol) and BCl_3 (1 M in CH_2Cl_2, 2 ml) in CH_2Cl_2 (1 ml) was stirred for 24 h at room temperature at room temperature, work-up and purification were performed as described above to give **21** (30 mg, 86% as a white solid), mp 176—178 °C. ^{1}H-NMR (400 MHz, DMSO-d_6) 11.22 (1H, br s, 3-NH), 7.57 (1H, d, H-6, $J_{5,6}$=7.8 Hz), 7.28 (1H, br s, 4′-NHOH), 6.08 (1H, ddd, H-3′, J=2.0, 2.0, 5.3 Hz), 5.93 (1H, br s, 4′-NH), 5.78 (1H, ddd, H-2′, J=1.7, 1.7, 5.6 Hz), 5.57 (1H, d, H-5, $J_{5,6}$=8.1 Hz), 5.43 (1H, m, H-1′), 3.91 (1H, m, H-4′), 2.54 (1H, ddd, H-5′a, J=8.8, 8.8, 14.4 Hz), 1.50 (1H, ddd, H-5′b, J=4.4, 4.4, 14.4 Hz). ^{13}C-NMR (100 MHz, MeOH-d_4) 160.94, 152.42, 143.77, 137.59, 131.71, 102.73, 66.65, 62.01, 32.67. FAB-LR-MS m/z: 210 ((M+H)$^+$, 100%). *Anal*. Calcd for $C_9H_{11}N_3O_3\cdot 0.5H_2O$: C, 49.54; H, 5.54; N, 19.26. Found: C, 49.82; H, 5.33; N, 19.13.

1-[(1*R*,4*S*)-4-[*N*-(*tert*-Butyldiphenylsilyl)oxyamino]-2-cyclopenten-1-yl]thymine (22) A mixture of **20** (488 mg, 2.19 mmol), TBDPSCl (779 μl, 3.00 mmol), and imidazole (272 mg, 4.01 mmol) in DMF (10 ml) was stirred for 2 days at room temperature and diluted with AcOEt (15 ml), which was washed with H_2O (10 ml×3) and brine (10 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=1 : 1) to give **22** (523 mg, 52% as a white foam). ^{1}H-NMR (270 MHz, $CDCl_3$) 8.25 (1H, br s, 3-NH), 7.68—7.31 (10H, m, Ph), 6.99 (1H, s, H-6), 6.02 (1H, d, H-3′, J=5.6 Hz), 5.67 (1H, d, J=5.6 Hz), 5.54 (1H, m, H-1′), 5.22 (1H, br s, 4′-NH), 4.10 (1H, m, H-4′), 2.60 (1H, ddd, H-5′a, J=8.6, 8.6, 14.2 Hz), 1.66 (3H, s, 5-Me), 1.52 (1H, ddd, H-5′b, J=5.6, 5.6, 13.9 Hz), 1.08 (9H, s, *t*-Bu). FAB-LR-MS m/z: 462 ((M+H)$^+$, 100%). FAB-HR-MS m/z: 462.2190 (Calcd for $C_{26}H_{32}N_3O_3Si$ (M+H)$^+$: 462.2211).

1-[(1*R*,4*S*)-4-[*N*-(*tert*-Butyldiphenylsilyl)oxyamino]-2-cyclopenten-1-yl]uracil (23) A mixture of **21** (37 mg, 0.18 mmol), TBDPSCl (69 μl, 0.27 mmol) and imidazole (24 mg, 0.35 mmol) in DMF (1 ml) was stirred for 24 h at room temperature for 24 h. Work-up and purification were performed as described above to give **23** (70 mg, 88% as a white foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 8.50 (1H, br s, 3-NH), 7.68—7.36 (10H, m, Ph), 7.23 (1H, d, H-6, J=7.8 Hz), 5.99 (1H, m, H-3′), 5.63 (1H, m, H-1′), 5.58 (1H, m, H-2′), 5.40 (1H, d, H-5, J=8.1 Hz), 5.29 (1H, d, 4′-NH, J=3.9 Hz), 2.64 (1H, ddd, H-5′a, J=8.6, 8.6, 14.8 Hz), 1.58 (1H, m, H-5′b), 1.10 (9H, s, *t*-Bu). FAB-LR-MS m/z: 448 ((M+H)$^+$, 100%). FAB-HR-MS m/z: 448.2026 (Calcd for $C_{25}H_{29}N_3O_3Si$ (M+H)$^+$: 447.1978).

1-[(1*S*,4*R*)-4-[*N*-(*tert*-Butyldiphenylsilyl)oxyamino]cyclopent-1-yl]-thymine (24) A mixture of **22** (138 mg, 0.299 mmol) and 10% Pd–C (20 mg) in AcOEt (3 ml) was stirred for 24 h under H_2 atmosphere at room temperature and filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=1 : 1) to give **24** (117 mg, 84% as a white foam). ^{1}H-NMR (270 MHz, $CDCl_3$) 8.90 (1H, br s, 3-NH), 7.74—7.32 (10H, m, Ph), 7.02 (1H, s, H-6), 5.17 (1H, s, 4′-NH), 4.91 (1H, ddt, H-1′, *J*=7.6, 9.6, 17.2 Hz), 3.62 (1H, m, H-4′), 2.24 (1H, ddd, H-5′a, *J*=7.3, 9.6, 14.1 Hz), 1.80 (2H, m, H-3′), 1.72 (3H, s, 5-Me), 1.55 (1H, m, H-5′b), 1.21 (2H, m, H-2′), 1.11 (9H, s, *t*-Bu). FAB-LR-MS *m/z*: 464 ((M+H)$^+$, 100%). FAB-HR-MS *m/z*: 464.2383 (Calcd for $C_{26}H_{34}N_3O_3Si$ (M+H)$^+$: 464.2368).

1-[(1*S*,4*R*)-4-[*N*-(*tert*-Butyldiphenylsilyl)oxyamino]cyclopent-1-yl]-uracil (25) A mixture of **23** (89 mg, 0.20 mmol) and 10% Pd–C (10 mg) in AcOEt (2 ml) was stirred for 20 h under H_2 atmosphere at room temperature and filtrated through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=1 : 1) to give **25** (80 mg, 89% as a white foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 8.56 (1H, br s, 3-NH), 7.71—7.35 (10H, m, Ph), 7.03 (1H, d, H-6, *J*=8.1 Hz), 5.44 (1H, d, H-5, *J*=8.1 Hz), 5.18 (1H, br s, 4′-NH, *J*=3.9 Hz), 4.92 (1H, ddt, H-1′, *J*=8.8, 9.0, 9.0 Hz), 3.66 (1H, m, H-4′), 2.24 (1H, ddd, H-5′a, *J*=7.1, 9.5, 15.1 Hz), 1.81 (2H, m, H-3′), 1.59 (2H, m, H-2′), 1.19 (1H, m, H-5′b), 1.10 (9H, s, *t*-Bu). FAB-LR-MS *m/z*: 450 ((M+H)$^+$, 100%). FAB-HR-MS *m/z*: 450.2203 (Calcd for $C_{25}H_{32}N_3O_3Si$ (M+H)$^+$: 450.2211).

1-[(1*S*,4*R*)-4-(*N*-Hydroxyamino)cyclopent-1-yl]thymine Hydrochloride (26) A mixture of **24** (90 mg, 0.19 mmol) in MeOH (1.5 ml) and HCl (4 M in 1,4-dioxane, 1.5 ml) was stirred for 24 h at room temperature, and the solvent was removed *in vacuo*. The residue was dissolved in H_2O (15 ml), which was washed with $CHCl_3$ (10 ml×3). The aqueous layer was concentrated *in vacuo* to give **26** (48 mg, 94% as a white foam). ^{1}H-NMR (400 MHz, MeOH-d_4) 7.56 (1H, d, H-6, *J*=1.1 Hz), 4.74 (1H, ddd, H-1′, *J*=7.8, 8.9, 16.7 Hz), 3.90 (1H, m, H-4′), 2.53 (1H, ddd, H-5′a, *J*=8.0, 8.7, 14.2 Hz), 2.25—2.03 (5H, m, H-2′, H-3′, H-5′b), 1.89 (3H, d, 5-Me, *J*=1.1 Hz). ^{13}C-NMR (100 MHz, MeOH-d_4) 166.00, 152.57, 141.00, 111.67, 62.26, 59.35, 32.62, 28.83, 26.75, 12.39. FAB-LR-MS *m/z*: 226 ((M+H)$^+$, 50%). *Anal*. Calcd for $C_{10}H_{15}N_3O_3 \cdot HCl \cdot 0.5H_2O$: C, 44.37; H, 6.33; N, 15.52. Found: C, 44.67; H, 6.17; N, 15.16.

1-[(1*S*,4*R*)-4-(*N*-Hydroxyamino)cyclopent-1-yl]uracil Hydrochloride (27) A mixture of **25** (61 mg, 0.14 mmol) in MeOH (1 ml) and HCl (4 M in 1,4-dioxane, 1 ml) was stirred for 24 h at room temperature, and the solvent was removed *in vacuo*. The residue was dissolved in H_2O (15 ml), which was washed with $CHCl_3$ (15 ml×3). The aqueous layer was concentrated *in vacuo* to give **27** (33 mg, 98% as a white foam). ^{1}H-NMR (400 MHz, DMSO-d_6) 11.60 (1H, br s, 4′-NH_2OH), 11.3, 10.9 (each 1H, each s, 3-NH, 4′-NHOH), 7.87 (1H, d, H-6, *J*=8.3 Hz), 5.65 (1H, d, H-5, *J*=8.1 Hz), 4.92 (1H, ddt, H-1′, *J*=7.6, 7.6, 7.6 Hz), 3.78 (1H, m, H-4′), 2.35 (1H, ddd, H-5′a, *J*=8.1, 8.1, 12.3 Hz), 2.11—1.83 (5H, m, H-2′, H-3′, H-5′b). ^{13}C-NMR (100 MHz, MeOH-d_4) 172.67, 160.58, 151.42, 111.35, 68.44, 63.75, 41.28, 37.76, 34.24. FAB-LR-MS *m/z*: 212 ((M+H)$^+$, 38%). *Anal*. Calcd for $C_9H_{13}N_3O_3 \cdot HCl$: C, 43.64; H, 5.70; N, 16.97. Found: C, 43.57; H, 5.59; N, 16.72.

1-[(1*R*,2*S*,3*R*,4*S*)-4-[*N*-(*tert*-Butyldiphenylsilyl)oxyamino]-2,3-dihydroxycyclopent-1-yl]uracil (28) A mixture of **23** (400 mg, 0.89 mmol), NMO (210 mg, 1.79 mmol) and OsO_4 (5 mg/ml in *tert*-BuOH containing 1% *tert*-BuOOH, 6 ml, 0.12 mmol) in THF (2 ml) and H_2O (2 ml) was stirred for 2 h at room temperature and further amounts of NMO (100 mg, 0.852 mmol) and OsO_4 (3 ml, 0.06 mmol) were added to the mixture at 0 °C. After the mixture was stirred for further 2 h at room temperature, the reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$, and the mixture was extracted with AcOEt (50 ml). The organic layer was washed with H_2O (30 ml), saturated aqueous $NaHCO_3$ (20 ml), saturated aqueous $Na_2S_2O_3$ (30 ml), and brine (30 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$: MeOH=20 : 1) to give **28** (288 mg, 67% as a white foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 9.50 (1H, br s, 3-NH), 7.69—7.24 (10H, m, Ph), 6.87 (1H, d, H-6, *J*=7.8 Hz), 5.51 (1H, d, H-5, *J*=8.1 Hz), 5.48 (1H, br s, 4′-NH), 4.66 (1H, ddd, H-1′, *J*=8.3, 8.6, 8.7 Hz), 3.98 (1H, m, H-3′), 3.86 (1H, br s, 3′-OH), 3.78 (1H, m, H-2′), 3.49 (1H, m, H-4′), 3.18 (1H, br s, 2′-OH), 2.25 (1H, ddd, H-5′a, *J*=8.5, 8.5, 14.0 Hz), 1.28 (1H, m, H-5′b), 1.10 (9H, s, *t*-Bu). FAB-LR-MS *m/z*: 482 ((M+H)$^+$, 64%). FAB-HR-MS *m/z*: 482.2119 (Calcd for $C_{25}H_{32}N_3O_5Si$ (M+H)$^+$: 482.2109).

1-[(1*R*,2*S*,3*R*,4*S*)-2,3-Dihydroxy-4-(*N*-hydroxyamino)cyclopent-1-yl]-uracil Hydrochloride (29) A solution of **28** (29 mg, 0.06 mmol) in MeOH (0.5 ml) and HCl (4 M in 1,4-dioxane, 0.5 ml) was stirred for 24 h at room temperature, and the solvent was removed *in vacuo*. The residue was co-evaporated several times with dioxane to give **29** (16 mg, 95% as a white powder). ^{1}H-NMR (400 MHz, DMSO-d_6) 11.80 (2H, br s, 4′-NH_2OH), 11.30, 10.00 (each 1H, each br s, 3-NH, 4′-NH_2OH), 7.83 (1H, d, H-6, *J*=8.1 Hz), 7.66 (1H, d, H-5, *J*=8.1 Hz), 4.73 (1H, ddd, H-1′, *J*=9.5, 9.5, 9.8 Hz), 4.40 (1H, dd, H-2′, *J*=5.4, 9.5 Hz), 4.20 (1H, dd, H-3′, *J*=5.1, 5.1 Hz), 3.48 (1H, m, H-4′), 2.34 (1H, ddd, H-5′a, *J*=9.1, 9.1, 13.1 Hz), 1.78 (1H, m, H-5′b). ^{13}C-NMR (100 MHz, MeOH-d_4) 166.04, 152.71, 145.53, 102.75, 73.53, 70.71, 65.49, 63.88, 26.67. FAB-LR-MS *m/z*: 244 ((M+H)$^+$, 14%). FAB-HR-MS *m/z*: 244.0934 (Calcd for $C_9H_{14}N_3O_5Si$ (M+H)$^+$: 244.0932).

1-[(1*R*,2*S*,3*R*,4*S*)-2,3-Bis[(*tert*-butyldimethylsilyl)oxy]-4-[*N*-(*tert*-butyldiphenylsilyl)oxyamino]cyclopent-1-yl]uracil (30) A mixture of **28** (96 mg, 0.20 mmol), TBSCl (90 mg, 0.60 mmol), and imidazole (68 mg, 1.0 mmol) in DMF (2 ml) was stirred for 2 h at room temperature, and further amounts of TBSCl (60 mg, 0.40 mmol) and imidazole (54 mg, 0.80 mmol) were added to the mixture at 0 °C. After the mixture was stirred for 24 h at room temperature, the mixture was diluted with AcOEt (15 ml), which was washed with H_2O (15 ml×3) and brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane : AcOEt=3 : 1) to give **30** (128 mg, 90% as a white foam). ^{1}H-NMR (400 MHz, $CDCl_3$) 8.15 (1H, br s, 3-NH), 7.65—7.30 (10H, m, Ph), 6.97 (1H, d, H-6, *J*=8.0 Hz), 5.45 (1H, d, H-5, *J*=8.0 Hz), 5.36 (1H, d, 4′-NH, *J*=6.7 Hz), 4.52 (1H, m, H-1′), 4.14 (1H, m, H-2′), 4.10 (1H, m, H-3′), 3.32 (1H, m, H-4′), 2.35 (1H, ddd, H-5′a, *J*=8.4, 10.6, 14.7 Hz), 1.27 (1H, m, H-5′b), 1.03 (9H, s, *t*-Bu), 0.82, 0.75 (each 9H, each s, *t*-Bu), 0.01, −0.07, −0.13, −0.24 (each 3H, each s, Me). FAB-LR-MS *m/z*: 710 ((M+H)$^+$, 29%). FAB-HR-MS *m/z*: 710.3841 (Calcd for $C_{37}H_{60}N_3O_5Si_3$ (M+H)$^+$: 710.3837).

1-[(1*R*,2*S*,3*R*,4*S*)-2,3-Bis[(*tert*-butyldimethylsilyl)oxy]-4-[*N*-(*tert*-butyldiphenylsilyl)oxyamino]cyclopent-1-yl]cytosine (31) A mixture of **30** (110 mg, 0.155 mmol), 2,4,6-triisopropylbenzenesulfonyl chloride (TPSCl, 141 mg, 0.465 mmol), Et_3N (65 μl, 0.47 mmol), and dimethylaminopyridine (DMAP, 8 mg, 0.064 mmol) in CH_3CN (1 ml) was stirred for 1.5 h at room temperature, then NH_4OH (28%, 1 ml) was added to the mixture at room temperature. After 3 h, the resulting mixture was diluted with AcOEt (25 ml), which was washed with H_2O (25 ml) and brine (25 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography ($CHCl_3$: MeOH=50 : 1) to give **31** (62 mg, 56% as a pale yellow foam). ^{1}H-NMR (400 MHz, $CDCl_3$–D_2O) 7.73—7.33 (10H, m, Ph), 7.14 (1H, d, H-6, *J*=7.2 Hz), 5.50 (1H, d, H-5, *J*=7.2 Hz), 4.71 (1H, m, H-1′), 4.28 (1H, m, H-3′), 4.17 (1H, m, H-2′), 3.23 (1H, m, H-4′), 2.28 (1H, ddd, H-5′a, *J*=8.0, 11.0, 14.8 Hz), 1.72 (1H, ddd, H-5′b, *J*=6.8, 6.8, 15.2 Hz), 1.10 (9H, s, *t*-Bu), 0.84, 0.83 (each 9H, each s, *t*-Bu), 0.05, 0.00, −0.01, −0.04 (each 3H, each s, Me). FAB-LR-MS *m/z*: 709 ((M+H)$^+$, 100%). FAB-HR-MS *m/z*: 709.4003 (Calcd for $C_{37}H_{61}N_4O_4Si_3$ (M+H)$^+$: 709.3997).

1-[(1*R*,2*S*,3*R*,4*S*)-2,3-Dihydroxy-4-(*N*-hydroxyamino)cyclopent-1-yl]-cytosine Dihydrochloride (32) A mixture of **31** (52 mg, 0.07 mmol) in MeOH (0.5 ml) and HCl (4 M in 1,4-dioxane, 0.5 ml) was stirred for 5 h at room temperature, and the solvent was removed *in vacuo*. The residue was coevaporated several times with EtOH, which was dissolved in H_2O (15 ml), and the aqueous layer was washed with $CHCl_3$ (15 ml×3) and concentrated *in vacuo*. The residue was coevaporated several times with EtOH and Et_2O, and the resulting crystals were collected by filtration to give **32** (23 mg, quant. as a white crystalline), mp 145—148 °C. ^{1}H-NMR (400 MHz, MeOH-d_4) 8.05 (1H, d, H-6, *J*=7.8 Hz), 6.15 (1H, d, H-5, *J*=7.8 Hz), 4.62 (1H, ddd, H-1′, *J*=8.3, 8.3, 10.0 Hz), 4.50 (1H, dd, H-2′, *J*=6.0, 8.0 Hz), 4.37 (1H, dd, H-3′, *J*=3.8 , 5.5 Hz), 3.71 (1H, ddd, H-4′, *J*=3.7, 8.2, 8.4 Hz), 2.57 (1H, ddd, H-5′a, *J*=8.4, 8.4, 13.5 Hz), 2.22 (1H, ddd, H-5′b, *J*=8.4, 10.3, 13.5 Hz). ^{13}C-NMR (100 MHz, MeOH-d_4) 160.88, 149.36, 148.97, 94.92, 73.31, 70.52, 65.24, 65.20, 26.38. FAB-LR-MS *m/z*: 243 ((M+H)$^+$). *Anal*. Calcd for $C_9H_{16}Cl_2N_4O_4 \cdot HCl \cdot 1/4Et_2O$: C, 32.45; H, 5.31; N, 15.14. Found: C, 32.93; H, 5.43; N, 15.24.

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