

Synthesis and Conformational Analysis of C-4'-Modified (2-Oxabicyclo[3.1.0]hexyl)pyrimidine Nucleosides^[‡]

Julien Gagneron,^[a] Gilles Gosselin,^[a] and Christophe Mathé*^[a]

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We report on the synthesis of hitherto unknown pyrimidine nucleoside analogues bearing the 2-oxabicyclo[3.1.0]hexane scaffold (**5**, **6**, **8**, **13–17** and **19**) with various modifications at the C-4' position including methylene, azido, and arabino-like configuration. Conformational analysis on the nucleoside analogues **6**, **14** and **17** indicates that the conformation

of such C-4'-modified nucleoside analogues was restricted in the South-East hemisphere of the pseudorotation cycle (between a ⁰T₁ and a ²E conformation).

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Introduction

Over several decades, numerous nucleoside analogues with modifications in the sugar moiety have been designed with the hope of obtaining new antiviral and antitumor agents.^[1,2] Such nucleoside analogues generally have to be metabolized by cellular kinases to their 5'-triphosphate forms, which finally interact with viral or cellular polymerases, leading to a biological activity. In order to discover new nucleoside derivatives endowed with biological activities, modifications of the base and/or sugar moiety of natural nucleosides can be attempted.^[3] Recently, the conformational behaviour of natural as well as modified nucleosides, and in particular the sugar puckering, has been considered of great importance throughout their metabolic pathway, as well as in the final interaction with the target polymerases. Normally, the ribofuranose ring of natural nucleosides exists in a dynamic equilibrium covering a range of conformations, which can be easily described with the concept of the pseudorotation cycle.^[4] The North- (N-) and South- (S-) type conformations are the most relevant to the biological activities observed for nucleosides and nucleotides in association with various enzymes and receptors.^[5] For these reasons, the design of conformationally restricted nucleoside analogues has drawn considerable attention, because they adopt a determined conformation that can be useful in probing the conformational preferences of nucleoside/nucleotide-interacting enzymes and receptors.

In this regard, several nucleoside analogues with fixed furanose-ring puckering have been synthesized and evaluated for their biological activities. Numerous synthetic strategies have been used to lock the puckering of the furanose ring into a N-type or S-type conformation by adding various fused rings.^[6] As a part of our ongoing research on conformationally restricted nucleoside analogues, we have recently reported the synthesis of locked nucleosides built on the 2-oxabicyclo[3.1.0]hexane template and incorporating the canonical nucleic acid bases.^[7] Herein, we report on the synthesis of hitherto unknown pyrimidine nucleoside analogues bearing the 2-oxabicyclo[3.1.0]hexane scaffold (**5**, **6**, **8**, **13–17** and **19**) with various modifications at the C-4' position, including methylene, azido, and the *arabino*-like configuration (Figure 1). Additionally, the effect of such structural modifications on the resulting sugar conformation was studied on nucleosides **6**, **14** and **17** as model compounds by means of molecular modeling.

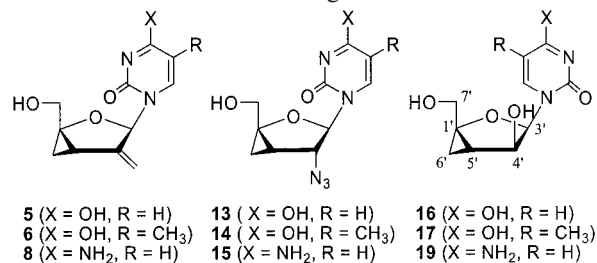


Figure 1. C-4'-modified pyrimidine nucleosides built on a 2-oxabicyclo[3.1.0]hexane scaffold. Numbering used as shown for **16–19**.

Results and Discussion

Chemical Synthesis

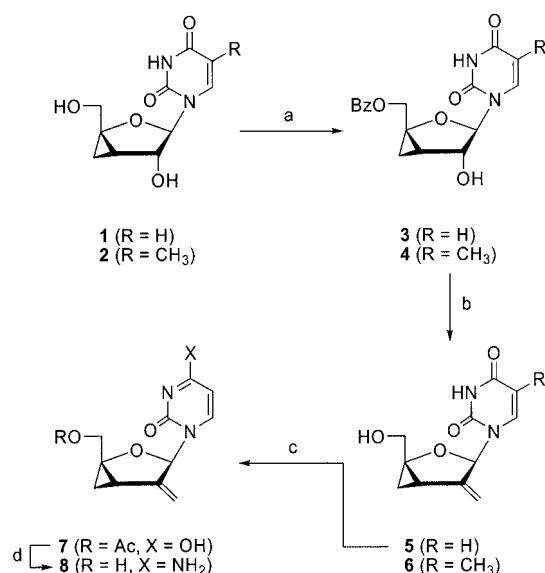
The synthesis of starting materials **1** and **2** was achieved through the preparation of a suitable sugar precursor bear-

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[a] Laboratoire de Chimie Organique Biomoléculaire de Synthèse, UMR 5625 CNRS-Université Montpellier II, Case courrier 008, Place Eugène Bataillon, 34095 Montpellier Cedex 5, France
Fax: +33-4-670042029
E-mail: cmathe@univ-montp2.fr

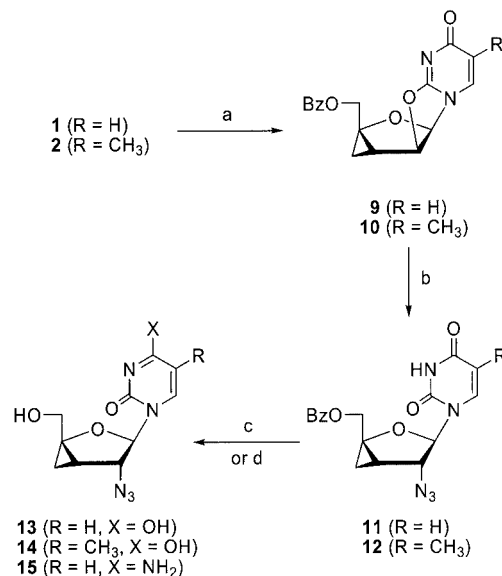
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ing the 2-oxabicyclo[3.1.0]hexane scaffold,^[7] followed by glycosylation reactions and deprotection (Scheme 1). Compounds **1** and **2** were selectively converted into their corresponding protected derivatives **3** and **4**, which were oxidized with the Dess–Martin periodinane reagent.^[8] The resulting 4'-keto nucleoside intermediates were not isolated but directly used in the Wittig reaction.^[9] The nucleosides **5** and **6** (Figure 1) were obtained after a final deprotection step and purification by silica gel column chromatography. The synthesis of the corresponding cytosine nucleoside **8** was accomplished in a two-step procedure from **5**. After an acetylation step, compound **7** was treated with Lawesson's reagent,^[10] to give a thioamide intermediate, which was treated with methanolic ammonia, affording nucleoside **8**. In order to prepare the target nucleosides **13–17** and **19** (Figure 1), compounds **1** and **2** were converted into the key anhydro derivatives **9** and **10** by a one-pot transformation involving a tandem Mitsunobu reaction (Scheme 2).^[11] Nucleophilic ring opening of the anhydro derivatives was achieved with sodium azide in the presence of 18-crown-6 and provided compounds **11** and **12**, which upon treatment with sodium methoxide in methanol gave the desired nucleosides **13** and **14**. The synthesis of the corresponding C-4'-azido cytosine nucleoside **19** was not accomplished with Lawesson's reagent. Indeed, the use of Lawesson's reagent on azido nucleosides has been reported to promote the reduction of the azido function.^[12] Instead, Sung's methodology,^[13] successfully applied in the conversion of uracil into cytosine azido nucleosides,^[14] was used. Thus, reaction of **11** with 4-chlorophenyl phosphorodichloridate, followed by sodium methylate, gave the cytosine derivative **15**. Finally, alkaline treatment of **9** and **10** (Scheme 3) yielded com-

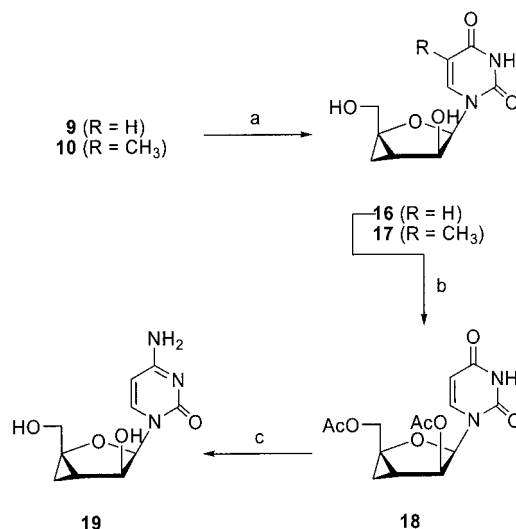


Scheme 1. a) BzCl, DMF, pyridine, 0 °C; b) i. periodinane, CH₂Cl₂, 0 °C; ii. C₂H₅C(CH₃)₂ONa, PPh₃MeBr, THF; iii. MeOH, MeONa; c) Ac₂O, pyridine; d) i. Lawesson's reagent, 1,2-dichloroethane, reflux; ii. MeOH/NH₃.

pounds **16** and **17** with the C-4' hydroxy group in the arabinoside configuration.^[15] After an acetylation step, derivative **18** was converted into the target nucleoside **19** by a thionation reaction with Lawesson's reagent and treatment of the resulting thioamide intermediate with methanolic ammonia.



Scheme 2. a) i. DEAD, PPh₃, BzOH, DMF; ii. DEAD, PPh₃; b) NaN₃, 18-crown-6, DMF, reflux; c) MeOH, MeONa; d) i. 1,2,4-triazole, pyridine, 4-chlorophenyl phosphorodichloridate; ii. NH₄OH, dioxane; iii. MeOH, MeONa.



Scheme 3. a) 1 N NaOH, MeOH; b) Ac₂O, pyridine; c) i. Lawesson's reagent, 1,2-dichloroethane, reflux; ii. MeOH/NH₃, 100 °C.

Conformational Analysis

Briefly, the definition of the conformational behaviour of natural, as well as modified nucleosides, involves the determination of three principal structural parameters.^[16] The glycosidic torsion angle χ determines the *syn* or *anti* disposition of the base relative to the sugar moiety (*syn* when the C-2 carbonyl of pyrimidines or N-3 of purines lies over the

sugar ring, *anti* when these atoms are oriented in the opposite direction). The torsion angle γ determines the orientation of the 5'-OH with respect to C-3', as represented by the three main rotamers $\gamma+$, γt and $\gamma-$. The conformation of the furanose ring and its deviation from planarity are described by the pseudorotational phase angle P (0–360°) and the maximal puckering amplitude $v_{\max}$ (0–50°). A conformationally unrestricted furanose ring in solution can adopt a number of envelope or twist forms, which are conveniently described by the value of P in the pseudorotation cycle (Figure 2). By convention, $P = 0^\circ$ corresponds to an absolute N conformation possessing a symmetrical twist form 3T_2 (C2'-*exo*-C3'-*endo*), whereas the S antipode twist, 2T_3 (C2'-*endo*-C3'-*exo*), corresponds to $P = 180^\circ$. Every 18°, the conformation of the furanose ring along the pseudorotation cycle alternates between envelope and twist conformations. For the typical N geometry, the conformations fluctuate between C2'-*exo* (2E) and C3'-*endo* (3E), whereas for an antipodal S geometry, the conformations range between C3'-*exo* (3E) and C2'-*endo* (2E). These two ranges are separated by two pseudorotational barriers that occur approximately in the Eastern (O4'-*endo*, 0E) and Western (O4'-*exo*, 0E) regions. Preference for any of these specific conformations in solution is determined by the interplay of important interactions resulting from steric and stereoelectronic effects. The latter consist mainly of the anomeric and gauche effects.^[17] Recently, we have reported the synthesis of conformationally locked nucleoside analogues built on a

2-oxabicyclo[3.1.0]hexane scaffold.^[7] This modification of the sugar moiety is able to restrict the dynamic equilibrium between the N-type and S-type geometry that normally characterizes the sugar moiety of standard nucleosides in solution. Using nucleoside **2** as a model compound, we have previously established that the conformation was restricted toward a 0T_1 conformation ($P = 107.2^\circ$, $v_{\max} = 17.2^\circ$, Table 1).^[7] Herein, the conformation of the thymine nucleosides **6**, **14** and **17** bearing various modifications at C-4' (including methylene, azido and the arabino configuration, respectively) were analyzed by molecular modeling and compared with compound **2**. An ab initio calculation was performed on the compound of interest by performing geometry optimization at the 3-21 G level with the basis set implemented in the HyperChem™ 7.5 software. A root-mean-square gradient termination cut-off of 0.05 kcal Å⁻¹ mol⁻¹ was used for geometry optimization with the Polak–Ribiere conjugate gradient algorithm. The torsion angles γ and χ on the nucleoside structure were initially located in the γ and *anti* ranges, respectively. The results of the calculations are illustrated in Table 1. Introduction of an exocyclic double bond in position 4' on the 2-oxabicyclo[3.1.0]hexane scaffold (compound **6**) drives the resulting conformation ($P = 156.6^\circ$ for **6** vs. 107.2° for **2**) toward a more markedly S-type conformation with a sugar puckering close to a C2'-*endo* envelope conformation (2E). Additionally, the double bond reduces the puckering amplitude ($v_{\max}$) to 10.9° , conferring a certain degree of planarity to the 2-oxabicy-

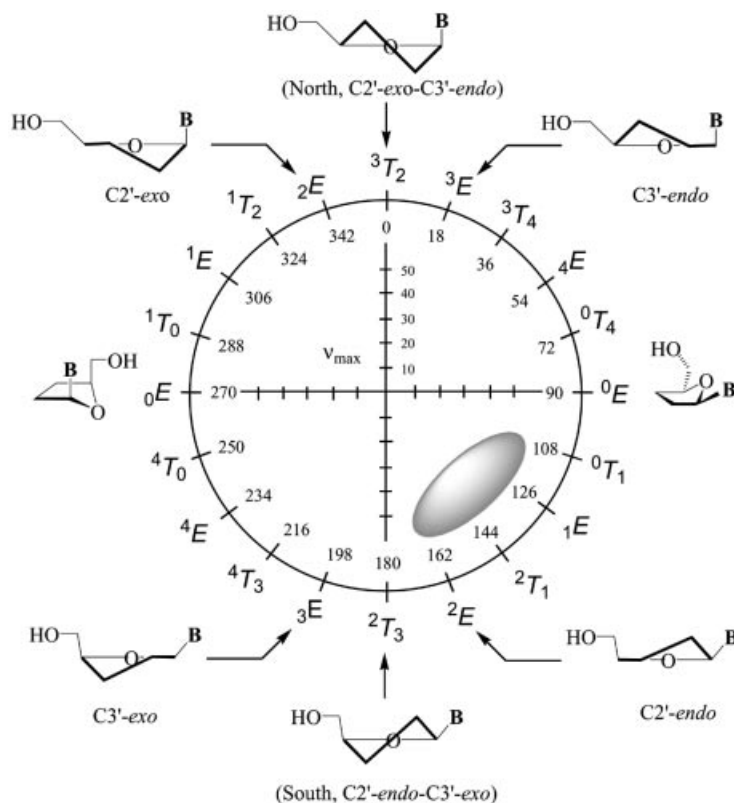


Figure 2. Pseudorotation cycle for nucleosides showing the characteristic North, South, East and West conformations. The units of P and $v_{\max}$ values are degrees. Envelope (E) and twist (T) forms alternate every 18°. The shaded area indicates the preferred pseudorotational region for nucleosides **2**, **6**, **14** and **17**.

Table 1. Selected torsion angles, pseudorotational phase angle P and maximum torsion angle $\nu_{\max}$ of compound **2**, **6**, **14** and **17**, as determined from ab initio calculations.

Analogue	ν_0 [°]	ν_1 [°]	ν_2 [°]	ν_3 [°]	ν_4 [°]	$\nu_{\max}$ [°] ^[22]	P [°] ^[22]
2 ^[7]	− 17.2	13.8	− 5.1	− 5.5	14.1	17.2	107.2
6	− 7.2	10.7	− 10.0	5.6	1.0	10.9	156.6
14	− 19.1	16.6	− 7.8	− 4.0	14.3	19.2	114.0
17	− 23.1	24.9	− 16.0	0.9	14.4	25.9	128.1

clo[3.1.0]hexane scaffold. An increase of the planarity has been recently reported in the case of methanocarbanucleosides built on a bicyclo[3.1.0]hexane template following the introduction of a double bond within the bicyclic ring system.^[18] Introduction of an azido function (compound **14**) in place of the hydroxy group (compound **2**) at C-4' in a ribo-like configuration (4' *R*) afforded similar sugar puckering ($P = 114^\circ$ for **14** vs. 107.2° for **2**) and $\nu_{\max}$ (19.2° for **14** vs. 17.2° for **2**), and both conformations are close to a 0T_1 conformation. In this case, the presence of the azido function does not greatly influence the sugar puckering and the $\nu_{\max}$. In the case of compound **17**, inversion of stereochemistry at C-4' (4' *R* $\rightarrow$ 4' *S*, ribo- to arabino-like configuration) drives the resulting conformation ($P = 128^\circ$ for **17** vs. 107.2° for **2**) toward a sugar puckering close to a C1'-*exo* envelope conformation (${}_1E$) with a larger puckering amplitude ($\nu_{\max} = 25.9^\circ$ for **17** vs. 17.2° for **2**). This ${}_1E$ type conformation may be ascribed to a preferential pseudo-axial orientation of the hydroxy group in regard to a favourable O2'-C3'-C4'-O4' gauche effect^[19] and a preferential pseudo-equatorial orientation of the base due to the 2-oxabicyclo[3.1.0]hexane scaffold, leading to minimal steric hindrance between the base and the hydroxymethyl residue in position 1. The vicinal (${}^3J_{H4'-H3'}$) coupling constants were estimated^[20] from the torsion angles φ (H3'-C3'-C4'-H4') obtained from molecular modeling of selected nucleoside analogues **2** and **17** (Table 2), according to the Diez-Altona-Donders equation, as implemented in the MestRe-J program.^[21] A good agreement was observed between estimated and experimental ${}^3J_{H4'-H3'}$ values, showing that the solution conformations of nucleosides **2** and **17** match the lowest energy structure from molecular modeling.

Table 2. Torsion angles of lowest energy structures from ab initio calculations and estimated and experimental ${}^3J_{H3'-H4'}$ values of selected compounds **2** and **17**.

Analogue	φ H3'-C3'-C4'-H4' [°]	${}^3J_{\text{estd.}}, \text{H3'-H4'}$ [Hz]	${}^3J_{\text{exp.}}, \text{H3'-H4'}$ [Hz]
2	133	5.1	5.0 ^[a]
17	27	4.7	4.8

[a] Data from ref.^[7]

Conclusions

The synthesis of conformationally restricted pyrimidine nucleoside analogues with various structural modifications at the C-4' position (including methylene, azido and the arabino-like modifications) was achieved, starting from their corresponding 2-oxabicyclo[3.1.0]hexane parent nucle-

osides. Models (**6**, **14** and **17**) bearing the thymine base suggest that the conformations of such C-4'-modified 2-oxabicyclo[3.1.0]hexane nucleoside analogues were restricted into the S-E hemisphere of the pseudorotation cycle (between a 0T_1 and a 2E conformation). Thus, through appropriate chemical modifications at the C-4' position, we have modulated by degrees the conformation of the resulting nucleosides. These new nucleoside analogues built on a 2-oxabicyclo[3.1.0]hexane scaffold may find wider applicability to probe the conformational preferences of nucleoside/nucleotide-converting enzymes and receptors.

Experimental Section

General Remarks: Evaporation of solvents was carried out with a rotary evaporator under reduced pressure. Melting points were determined in open capillary tubes with a Gallenkamp MFB-595–010 M apparatus and are uncorrected. UV spectra were recorded with a Uvikon 931 (Kontron) spectrophotometer. NMR spectra were recorded at 400 MHz (${}^1\text{H}$) and 100 MHz (${}^{13}\text{C}$) in $(\text{CD}_3)_2\text{SO}$ at ambient temperature with a Bruker DRX 400 spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm), referenced to the residual solvent peak at 2.49 δ (${}^1\text{H}$) and 39.5 δ (${}^{13}\text{C}$) relative to tetramethylsilane (TMS). Deuterium exchange and COSY experiments were performed in order to confirm proton assignments. Coupling constants, J , are reported in Hz. 2D ${}^1\text{H}$ - ${}^{13}\text{C}$ heteronuclear COSY was performed for the attribution of ${}^{13}\text{C}$ signals. FAB mass spectra were recorded in the positive-ion or negative-ion mode with a JEOL SX 102 spectrometer. The matrix was a mixture (50:50, v/v) of glycerol and thioglycerol (G-T), or 3-nitrobenzyl alcohol (NBA). IR spectra were recorded with a Perkin-Elmer FT-IR paragon 1000 spectrometer. Specific rotations were measured with a Perkin-Elmer Model 241 spectropolarimeter (path length 1 cm) and are given in units of $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$. Elemental analyses were carried out by the Service de Microanalyses du CNRS, Division de Vernaison (France). Thin-layer chromatography was performed on precoated aluminium sheets of Silica Gel 60 F₂₅₄ (Merck, Art. 5554), and product spots were visualised by UV absorbency followed by charring with 5% ethanolic sulfuric acid. Column chromatography was carried out on Silica Gel 60 (Merck, Art. 9385). All moisture-sensitive reactions were carried out under rigorous anhydrous conditions under an argon atmosphere in oven-dried glassware. Solvents were dried and distilled prior to use, and solids were dried with P_2O_5 under reduced pressure.

[(1S,3R,4R,5S)-3-[2,4-Dioxo-3,4-dihydro-1(2H)-pyrimidinyl]-4-hydroxy-2-oxabicyclo[3.1.0]hex-1-yl]methyl Benzoate (3): Yield 710 mg (50%). M.p. 69°C . $[\alpha]_{\text{D}}^{20} = -88.6$ ($c = 0.44$, DMSO). ${}^1\text{H}$ NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): $\delta = 11.38$ (br. s, 1 H, NH), 8.04–7.53 (m, 6 H, C_6H_5 , 6-H), 5.52 (m, 3 H, 5-H, 3'-H and 4'-OH), 4.80 (m, 2 H, 4'-H and 7'a-H), 4.50 (d, $J = 12.7$ Hz, 1 H, 7'b-H), 1.96 (m, 1 H, 5'-H), 1.35 (t, $J = 5.4$ Hz, 1 H, 6'a-H), 0.95 (dd, $J =$

6.5, 9.4 Hz, 1 H, 6'-b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 165.6 (C=O), 162.9 (C-4), 150.2 (C-2), 141.5 (C-6), 133.5–128.8 (C_{ar}), 102.3 (C-5), 90.6 (C-3'), 75.1 (C-1'), 67.8 (C-4'), 66.3 (C-7'), 23.6 (C-5'), 12.7 (C-6') ppm. FAB-MS: m/z = 345 $[\text{M} + \text{H}]^+$. HRMS: calcd. for $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 345.1087; found 345.1073.

[(1*S*,3*R*,4*R*,5*S*)-4-Hydroxy-3-[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-2-oxabicyclo[3.1.0]hex-1-yl]methyl Benzoate (4): Yield 505 mg (50%). M.p. 177 °C. $[\alpha]_{\text{D}}^{20}$ = -97 (c = 1.00, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 11.36 (br. s, 1 H, NH), 8.04–7.53 (m, 5 H, C_6H_5), 7.37 (d, J = 1.1 Hz, 1 H, 6-H), 5.52 (m, 2 H, 3'-H and 4'-OH), 4.70 (m, 2 H, 4'-H and 7'a-H), 4.49 (d, J = 12.7 Hz, 1 H, 7'b-H), 1.94 (m, 1 H, 5'-H), 1.62 (s, 3 H, CH_3), 1.36 (t, J = 6.6 Hz, 1 H, 6'a-H), 0.94 (dd, J = 6.6, 9.1 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 165.6 (CO), 163.5 (C-4), 150.4 (C-2), 136.5 (C-6), 133.5–128.8 (C_{ar}), 110.2 (C-5), 89.2 (C-3'), 74.8 (C-4'), 67.2 (C-1'), 66.1 (C-7'), 23.2 (C-5'), 12.3 (C-6'), 11.7 (CH_3) ppm. FAB-MS: m/z = 359 $[\text{M} + \text{H}]^+$. $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_6$ (358.35): calcd. C 60.33, H 5.06, N 7.82; found C 60.16, H 5.27, N 7.61.

1-[(1*S*,3*R*,5*S*)-1-(Hydroxymethyl)-4-methylene-2-oxabicyclo[3.1.0]hex-3-yl]-2,4(1*H*,3*H*)-pyrimidinedione (5): Yield 140 mg (36% from 3). UV (EtOH 95%): λ_{max} (ϵ) = 260 nm (9100). $[\alpha]_{\text{D}}^{20}$ = -28.6 (c = 0.14, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 11.39 (br. s, 1 H, NH), 7.50 (d, J = 8.1 Hz, 1 H, 6-H), 6.33 (s, 1 H, 3'-H), 5.69 (d, J = 8.1 Hz, 1 H, 5-H), 5.32 (d, J = 1.8 Hz, 1 H, $\text{CH}=\text{CH}_2$), 5.06 (t, J = 6.1 Hz, 1 H, 7'-OH), 4.82 (s, 1 H, $\text{CH}=\text{CH}_2$), 3.95 (dd, J = 6.1, 12.7 Hz, 1 H, 7'a-H), 3.48 (dd, J = 5.1, 12.7 Hz, 1 H, 7'b-H), 2.22 (dd, J = 4.5, 9.6 Hz, 1 H, 5'-H), 1.18 (t, J = 5.2 Hz, 1 H, 6'a-H), 1.08 (dd, J = 5.9, 9.6 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 163.0 (C-4), 150.6 (C-2), 148.6 (C-4'), 141.3 (C-6), 108.3 ($\text{CH}=\text{CH}_2$), 102.7 (C-5), 84.8 (C-3'), 71.9 (C-1'), 61.8 (C-7'), 23.5 (C-5'), 18.4 (C-6') ppm. FAB-MS: m/z = 237 $[\text{M} + \text{H}]^+$. $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_4$ (0.1 dioxane, 254.04): calcd. C 55.88, H 5.27, N 11.43; found C 55.73, H 5.23, N 11.22.

1-[(1*S*,3*R*,5*S*)-1-(Hydroxymethyl)-4-methylene-2-oxabicyclo[3.1.0]hex-3-yl]-5-methyl-2,4(1*H*,3*H*)-pyrimidinedione (6): Yield 120 mg (36% from 3). UV (EtOH 95%): λ_{max} (ϵ) = 263 nm (8900). $[\alpha]_{\text{D}}^{20}$ = -100.0 (c = 0.6, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 11.38 (br. s, 1 H, NH), 7.38 (d, J = 1.2 Hz, 1 H, 6-H), 6.33 (s, 1 H, 3'-H), 5.31 (d, J = 1.9 Hz, 1 H, $\text{CH}=\text{CH}_2$), 5.09 (t, J = 6.4 Hz, 1 H, 7'-OH), 4.79 (d, J = 0.9 Hz, 1 H, $\text{CH}=\text{CH}_2$), 3.96 (dd, J = 5.8, 12.7 Hz, 1 H, 7'a-H), 3.49 (dd, J = 5.0, 12.7 Hz, 1 H, 7'b-H), 2.22 (dd, J = 4.5, 9.6 Hz, 1 H, 5'-H), 1.75 (d, J = 1.2 Hz, 3 H, CH_3), 1.17 (t, J = 5.2 Hz, 1 H, 6'a-H), 1.08 (dd, J = 5.8, 9.6 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 162.8 (C-4), 149.7 (C-2), 147.8 (C-4'), 135.9 (C-6), 109.2 (C-5), 107.3 ($\text{CH}=\text{CH}_2$), 83.7 (C-3'), 70.9 (C-1'), 60.9 (C-7'), 22.7 (C-5'), 17.6 (C-6'), 11.3 (CH_3) ppm. FAB-MS: m/z = 251 $[\text{M} + \text{H}]^+$. $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_4$ (0.3 H_2O , 255.66): calcd. C 56.38, H 5.76, N 10.96; found C 56.20, H 5.48, N 10.91.

[(1*S*,3*R*,5*S*)-3-[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-4-methylene-2-oxabicyclo[3.1.0]hex-1-yl]methyl Acetate (7): To a solution of compound 5 (150 mg, 0.635 mmol) in pyridine (4 mL) was added acetic anhydride (0.9 mL, 9.5 mmol). After 12 h, the solution was evaporated, co-evaporated with toluene, and the residue was purified by silica gel column chromatography (CH_2Cl_2 /methanol, 97:3) to give compound 7 (170 mg, 96%) as a colourless syrup. $[\alpha]_{\text{D}}^{20}$ = -163 (c = 0.92, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 11.41 (br. s, 1 H, NH), 7.35 (d, J = 8.1 Hz, 1 H, 6-H), 6.28 (s, 1 H, 3'-H), 5.74 (d, J = 8.1 Hz, 1 H, 5-H), 5.38 (d, J = 1.9 Hz, 1 H, $\text{CH}=\text{CH}_2$), 4.86 (s, 1 H, $\text{CH}=\text{CH}_2$), 4.47 (d, J = 12.8 Hz, 1 H, 7'a-H), 4.20 (d, J = 12.8 Hz, 1 H, 7'b-H), 2.36 (dd, J = 5.1, 9.2 Hz, 1

H, 5'-H), 2.01 (s, 3 H, CH_3), 1.18 (t, J = 5.2 Hz, 1 H, 6'a-H), 1.10 (dd, J = 5.8, 9.6 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 170.7 (COCH_3), 163.5 (C-4), 150.5 (C-2), 146.8 (C-4'), 141.5 (C-6), 109.7 ($\text{CH}=\text{CH}_2$), 102.8 (C-5), 85.5 (C-3'), 68.3 (C-1'), 65.8 (C-7'), 24.2 (C-5'), 20.5 (CH_3CO), 19.1 (C-6') ppm. FAB-MS: m/z = 279 $[\text{M} + \text{H}]^+$. HRMS: calcd. for $\text{C}_{13}\text{H}_{15}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ 279.0981; found 279.0969.

4-Amino-1-[(1*S*,3*R*,5*S*)-1-(hydroxymethyl)-4-methylene-2-oxabicyclo[3.1.0]hex-3-yl]-2(1*H*)-pyrimidinone (8): Yield 50 mg (50%). UV (EtOH 95%): λ_{max} (ϵ) = 269 nm (9000). $[\alpha]_{\text{D}}^{20}$ = -94.9 (c = 0.59, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 7.49 (d, J = 7.4 Hz, 1 H, 6-H), 7.25 (d, J = 13.6 Hz, 2 H, NH_2), 6.39 (s, 1 H, 3'-H), 5.75 (d, J = 7.4 Hz, 1 H, 5-H), 5.34 (d, J = 1.9 Hz, 1 H, $\text{CH}=\text{CH}_2$), 5.04 (t, J = 5.8 Hz, 1 H, 7'-OH), 4.65 (s, 1 H, $\text{CH}=\text{CH}_2$), 3.95 (dd, J = 6.2, 12.6 Hz, 1 H, 7'a-H), 3.49 (dd, J = 5.2, 12.6 Hz, 1 H, 7'b-H), 2.19 (dd, J = 4.5, 9.3 Hz, 1 H, 5'-H), 1.12 (t, J = 5.2 Hz, 1 H, 6'a-H), 1.07 (dd, J = 5.9, 9.3 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 165.50 (C-4), 155.1 (C-2), 149.9 (C-4'), 142.1 (C-6), 107.3 ($\text{CH}=\text{CH}_2$), 94.9 (C-5), 85.5 (C-3'), 71.4 (C-1'), 61.9 (C-7'), 23.6 (C-5'), 18.3 (C-6') ppm. FAB-MS: m/z = 471 $[\text{2M} + \text{H}]^+$, 236 $[\text{M} + \text{H}]^+$. HRMS: calcd. for $\text{C}_{11}\text{H}_{14}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$ 236.1035; found 236.1027.

[(5*aR*,6*aS*,7*aS*,7*bS*)-2-Oxo-5*a*,7*a*,7*b*-tetrahydro-2*H*,6*aH*-cyclopropa[4',5']furo[2',3':4,5][1,3]oxazolo[3,2-*a*]pyrimidin-6*a*-yl]methyl Benzoate (9): Yield 504 mg (59%). UV (EtOH 95%): λ_{max} (ϵ) = 252 nm (8000). $[\alpha]_{\text{D}}^{20}$ = -134 (c = 0.94, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 7.80 (d, J = 7.4 Hz, 1 H, 6-H), 7.40–7.71 (m, 5 H, C_{ar}), 6.09 (d, J = 5.5 Hz, 1 H, 3'-H), 5.81 (d, J = 8.0 Hz, 1 H, 5-H), 5.58 (d, J = 5.5 Hz, 1 H, 4'-H), 4.83 (d, J = 12.9 Hz, 1 H, 7'a-H), 4.21 (d, J = 12.9 Hz, 1 H, 7'b-H), 2.23 (dd, J = 5.6, 10.5 Hz, 1 H, 5'-H), 1.29 (dd, J = 5.6, 6.5 Hz, 1 H, 6'a-H), 1.14 (t, J = 7.2 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 170.9 (CO), 165.2 (C-4), 159.5 (C-2), 136.7 (C-6), 128.7–133.4 (C_{ar}), 108.9 (C-5), 93.2 (C-3'), 84.7 (C-4'), 70.0 (C-1'), 64.4 (C-7'), 23.7 (C-5'), 17.0 (C-6') ppm. FAB-MS: m/z = 327 $[\text{M} + \text{H}]^+$. $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_5$ (326.31): calcd. C 62.57, H 4.32, N 8.59; found C 62.27, H 4.33, N 8.34.

[(5*aR*,6*aS*,7*aS*,7*bS*)-3-Methyl-2-oxo-5*a*,7*a*,7*b*-tetrahydro-2*H*,6*aH*-cyclopropa[4',5']furo[2',3':4,5][1,3]oxazolo[3,2-*a*]pyrimidin-6*a*-yl]methyl Benzoate (10): Yield 475 mg (60%). M.p. 238 °C. UV (EtOH 95%): λ_{max} (ϵ) = 263 nm (7000). $[\alpha]_{\text{D}}^{20}$ = -97 (c = 1.00, DMSO). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 7.50–7.40 (m, 6 H, C_6H_5 and 6-H), 6.08 (d, J = 5.1 Hz, 1 H, H-3'), 5.55 (d, J = 5.1 Hz, 1 H, 4'-H), 4.87 (d, J = 12.9 Hz, 1 H, 7'a-H), 4.18 (d, J = 12.9 Hz, 1 H, 7'b-H), 2.22 (dd, $J_{\text{H}5'-\text{H}6'a}$ = 5.5, 10.2 Hz, 1 H, 5'-H), 1.65 (s, 3 H, CH_3), 1.28 (dd, J = 6.4, 10.2 Hz, 1 H, 6'b-H), 1.12 (t, J = 5.8 Hz, 1 H, 6'a-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 171.3 (CO), 165.2 (C-4), 159.0 (C-2), 128.6–133.3 (C-6 and C_{ar}), 117.1 (C-5), 93.7 (C-3'), 84.2 (C-4'), 69.8 (C-1'), 64.2 (C-7'), 23.9 (C-5'), 17.0 (C-6'), 13.3 (CH_3) ppm. FAB-MS: m/z = 341 $[\text{M} + \text{H}]^+$. $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_5$ (340.33): calcd. C 63.52, H 4.74, N 8.23; found C 63.37, H 4.40, N 8.48.

[(1*S*,3*R*,4*R*,5*S*)-4-Azido-3-[2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-2-oxabicyclo[3.1.0]hex-1-yl]methyl Benzoate (11): Yield 50 mg (44%). UV (EtOH 95%): λ_{max} (ϵ) = 260 (10500). ^1H NMR (300 MHz, $[\text{D}_6]\text{DMSO}$): δ = 11.45 (br. s, 1 H, NH), 8.00–7.63 (m, J = 8.0 Hz, 6 H, C_6H_5 and 6-H), 5.62 (d, J = 5.2 Hz, 1 H, 3'-H), 5.53 (d, J = 8.0 Hz, 1 H, H-5), 5.00 (t, J = 5.6 Hz, 1 H, 4'-H), 4.67 (d, J = 12.7 Hz, 1 H, 7'a-H), 4.63 (d, J = 12.7 Hz, 1 H, 7'b-H), 2.20 (m, 1 H, 5'-H), 1.38 (t, J = 5.5 Hz, 1 H, 6'a-H), 1.11 (dd, J = 6.8, 9.1 Hz, 1 H, 6'b-H) ppm. ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 165.5 (C=O), 162.8 (C-4), 149.9 (C-2), 140.9 (C-6), 133.5–128.8

(C_{ar}), 102.4 (C-5), 89.5 (C-3'), 68.7 (C-1'), 66.5 (C-4'), 65.8 (C-7'), 21.3 (C-5'), 13.9 (C-6') ppm. FAB-MS: *m/z* = 369 [M+H]⁺. IR: $\tilde{\nu}_{\text{N}_3}$ = 2108 cm⁻¹. C₁₇H₁₅N₅O₅ (369.33): calcd. C 55.28, H 4.09, N 18.96; found C 55.07, H 3.89, N 18.78.

[(1S,3R,4R,5S)-4-Azido-3-[5-methyl-2,4-dioxo-3,4-dihydro-1(2H)-pyrimidinyl]-2-oxabicyclo[3.1.0]hex-1-yl]methyl Benzoate (12): Yield 150 mg (53%). UV (EtOH 95%): λ_{max} (ϵ) = 263 nm (10300). [α]_D²⁰ = -105.5 (c = 0.54, DMSO). ¹H NMR (300 MHz, [D₆]DMSO): δ = 11.4 (br. s, 1 H, NH), 8.05–7.53 (m, 5 H, C₆H₅), 7.35 (d, J = 1.1 Hz, 1 H, 6-H), 5.64 (d, J = 5.7 Hz, 1 H, 3'-H), 4.98 (t, J = 5.8 Hz, 1 H, 4'-H), 4.77 (d, J = 12.8 Hz, 1 H, 7'a-H), 4.54 (d, J = 12.8 Hz, 1 H, 7'b-H), 2.19 (m, 1 H, 5'-H), 1.59 (d, J = 1.1 Hz, 3 H, CH₃), 1.43 (t, J = 5.6 Hz, 1 H, 6'a-H), 1.10 (dd, J = 6.8, 9.1 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 165.6 (C=O), 163.5 (C-4), 150.0 (C-2), 135.9 (C-6), 133.6–128.8 (C_{ar}), 110.5 (C-5), 87.8 (C-3'), 68.0 (C-1'), 66.2 (C-4'), 65.7 (C-7'), 20.9 (C-5'), 13.3 (CH₃), 11.8 (C-6') ppm. FAB-MS: *m/z* = 384 [M+H]⁺. IR: $\tilde{\nu}_{\text{N}_3}$ = 2107 cm⁻¹. C₁₈H₁₇N₅O₅ (383.36): calcd. C 56.39, H 4.47, N 18.27; found C 56.07, H 4.49, N 17.98.

1-[(1S,3R,4R,5S)-4-Azido-1-(hydroxymethyl)-2-oxabicyclo[3.1.0]hex-3-yl]-2,4(1H,3H)-pyrimidinedione (13): Yield 130 mg (90%). M.p. 178 °C. UV (EtOH 95%): λ_{max} (ϵ) = 260 nm (9800). [α]_D²⁰ = -95.3 (c = 0.64, DMSO). ¹H NMR (300 MHz, [D₆]DMSO): δ = 11.41 (br. s, 1 H, NH), 7.79 (d, J = 8.1 Hz, 1 H, 6-H), 5.71 (d, J = 8.1 Hz, 1 H, 5-H), 5.61 (d, J = 4.7 Hz, 1 H, 3'-H), 5.09 (t, J = 5.3 Hz, 1 H, 7'-OH), 4.83 (t, J = 4.7 Hz, 1 H, 4'-H), 3.89 (dd, J = 6, 12.7 Hz, 1 H, 7'a-H), 3.49 (dd, J = 4.8, 12.7 Hz, 1 H, 7'b-H), 1.94 (m, 1 H, 5'-H), 1.15 (dd, J = 5.2, 6.6 Hz, 1 H, 6'a-H), 0.88 (dd, J = 6.6, 9.0 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 163.0 (C-4), 150.0 (C-2), 140.7 (C-6), 102.4 (C-5), 89.2 (C-3'), 72.6 (C-1'), 67.7 (C-4'), 61.7 (C-7'), 20.5 (C-5'), 13.6 (C-6') ppm. FAB-MS: *m/z* = 266 [M+H]⁺. C₁₀H₁₁N₅O₄ (265.23): calcd. C 45.28, H 4.18, N 26.41; found C 45.24, H 4.10, N 26.25.

1-[(1S,3R,4R,5S)-4-Azido-1-(hydroxymethyl)-2-oxabicyclo[3.1.0]hex-3-yl]-5-methyl-2,4(1H,3H)-pyrimidinedione (14): Yield 60 mg (69%). UV (EtOH 95%): λ_{max} (ϵ) = 264 nm (11700). [α]_D²⁰ = -123.5 (c = 0.51, DMSO). ¹H NMR (300 MHz, [D₆]DMSO): δ = 11.40 (br. s, 1 H, NH), 7.66 (d, J = 1.1 Hz, 1 H, 6-H), 5.62 (d, J = 5.0 Hz, 1 H, 3'-H), 5.12 (t, J = 5.5 Hz, 1 H, 7'-OH), 4.81 (t, J = 5.0 Hz, 1 H, 4'-H), 3.90 (dd, J = 6.0, 12.7 Hz, 1 H, 7'a-H), 3.51 (dd, J = 5.0, 12.7 Hz, 1 H, 7'b-H), 1.94 (m, 1 H, 5'-H), 1.79 (s, 3 H, CH₃), 1.17 (t, J = 5.8 Hz, 1 H, 6'a-H), 0.89 (dd, J = 6.8, 9.0 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 163.6 (C-4), 150.0 (C-2), 136.2 (C-6), 110.0 (C-5), 88.4 (C-3'), 72.2 (C-1'), 67.5 (C-4'), 61.7 (C-7'), 20.4 (C-5'), 13.3 (CH₃), 12.1 (C-6') ppm. FAB-MS: *m/z* = 280 [M+H]⁺. C₁₁H₁₃N₅O₄ (279.25): calcd. C 47.31, H 4.69, N 25.08; found C 47.47, H 4.70, N 24.77.

4-Amino-1-[(1S,3R,4R,5S)-4-azido-1-(hydroxymethyl)-2-oxabicyclo[3.1.0]hex-3-yl]-2(1H)-pyrimidinone (15): To a cooled (ice/water bath) solution of compound **11** (120 mg, 0.325 mmol) in dry pyridine (2 mL) was added 1,2,4-triazole (295 mg, 4.27 mmol) followed by the addition of 4-chlorophenyl phosphorodichloridate (0.231 mL, 1.43 mmol). The reaction mixture was stirred at room temperature for 48 h, and the solvent was evaporated to dryness. The residue was dissolved in CH₂Cl₂ (30 mL) and washed with water. The organic layer was dried (Na₂SO₄), concentrated to dryness, and the residue was purified by silica gel column chromatography with a stepwise gradient of MeOH (3–5%) in CH₂Cl₂ to afford the 4-triazolyl intermediate (85 mg). This compound was then dissolved in NH₄OH/dioxane (2.7 mL, 1:3, v/v), and the reaction mixture was stirred overnight at room temperature. The mixture was evaporated, and the crude product was purified by silica

gel column chromatography with a stepwise gradient of MeOH (6–10%) in CH₂Cl₂. The appropriate fractions were collected (50 mg) and treated with sodium methylate (22 mg, 0.41 mmol) in methanol (2.2 mL). The reaction mixture was stirred at room temperature overnight and neutralized with a 2 N HCl solution and evaporated to dryness. The residue was purified by silica gel column chromatography with a stepwise gradient of MeOH (10–16%) in CH₂Cl₂ to give compound **15** (30 mg, 29% overall yield from **11**), which was lyophilized from water. UV (EtOH 95%): λ_{max} (ϵ) = 270 nm (9400). ¹H NMR (300 MHz, [D₆]DMSO): δ = 7.74 (d, J = 7.4 Hz, 1 H, 6-H), 7.26 (br. s, 2 H, NH₂), 5.61 (d, J = 7.4 Hz, 1 H, 5-H), 5.61 (d, J = 4.7 Hz, 1 H, 3'-H), 5.04 (t, J = 5.5 Hz, 1 H, 7'-OH), 4.70 (t, J = 4.7 Hz, 1 H, 4'-H), 3.89 (dd, J = 5.9, 12.6 Hz, 1 H, 7'a-H), 3.48 (dd, J = 5.0, 12.6 Hz, 1 H, 7'b-H), 1.92 (m, 1 H, 5'-H), 1.10 (t, J = 5.0 Hz, 1 H, 6'a-H), 0.89 (dd, J = 6.5, 9.0 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 165.6 (C-4), 154.6 (C-2), 141.6 (C-6), 94.6 (C-5), 90.5 (C-3'), 72.2 (C-1'), 68.2 (C-4'), 61.8 (C-7'), 20.7 (C-5'), 13.7 (C-6') ppm. FAB-MS: *m/z* = 265 [M+H]⁺. HRMS: calcd. for C₁₀H₁₃N₆O₃ [M+H]⁺ 265.1049; found 265.1052.

1-[(1S,3R,4S,5S)-4-Hydroxy-1-(hydroxymethyl)-2-oxabicyclo[3.1.0]hex-3-yl]-2,4(1H,3H)-pyrimidinedione 16: Yield 120 mg (80%). M.p. 173 °C. UV (EtOH 95%): λ_{max} (ϵ) = 260 nm (11800). [α]_D²⁰ = +85.4 (c = 1.03, DMSO). ¹H NMR (300 MHz, [D₆]DMSO): δ = 11.23 (br. s, 1 H, NH), 7.64 (d, J = 8.1 Hz, 1 H, 6-H), 5.79 (d, J = 4.7 Hz, 1 H, 3'-H), 5.56 (d, J = 8.1 Hz, 1 H, 5-H), 5.44 (d, J = 4.7 Hz, 1 H, 4'-OH), 4.97 (t, J = 5.0 Hz, 1 H, 7'-OH), 4.24 (t, J = 4.7 Hz, 1 H, 4'-H), 3.87 (dd, J = 5.2, 12.5 Hz, 1 H, 7'a-H), 3.60 (dd, J = 4.8, 12.5 Hz, 1 H, 7'b-H), 1.49 (dd, J = 4.9, 9.7 Hz, 1 H, 5'-H), 0.89 (t, J = 5.4 Hz, 1 H, 6'a-H), 0.72 (dd, J = 6.6, 9.7 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 163.3 (C-4), 150.1 (C-2), 143.2 (C-6), 99.6 (C-5), 86.4 (C-3'), 70.9 (C-4'), 69.7 (C-1'), 61.8 (C-7'), 23.3 (C-5'), 11.6 (C-6') ppm. FAB-MS: *m/z* = 241 [M+H]⁺. C₁₀H₁₂N₂O₅ (240.21): calcd. C 50.00, H 5.04, N 11.66; found C 49.94, H 5.03, N 11.56.

1-[(1S,3R,4S,5S)-4-Hydroxy-1-(hydroxymethyl)-2-oxabicyclo[3.1.0]hex-3-yl]-5-methyl-2,4(1H,3H)-pyrimidinedione (17): Yield 220 mg (86%). M.p. 75 °C. UV (EtOH 95%): λ_{max} (ϵ) = 263 nm (9500). [α]_D²⁰ = +66.9 (c = 1.21, DMSO). ¹H NMR (300 MHz, [D₆]DMSO): δ = 11.25 (br. s, 1 H, NH), 7.53 (d, J = 1.1 Hz, 1 H, 6-H), 5.78 (d, J = 4.8 Hz, 1 H, 3'-H), 5.41 (d, J = 4.8 Hz, 1 H, 4'-OH), 5.00 (t, J = 5.8 Hz, 1 H, 7'-OH), 4.24 (t, J = 4.8 Hz, 1 H, 4'-H), 3.89 (dd, J = 5.9, 12.6 Hz, 1 H, 7'a-H), 3.62 (dd, J = 5.7, 12.6 Hz, 1 H, 7'b-H), 1.76 (d, J = 1.1 Hz, 3 H, CH₃), 1.49 (dd, J = 4.9, 9.7 Hz, 1 H, 5'-H), 0.87 (t, J = 5.4 Hz, 1 H, 6'a-H), 0.72 (dd, J = 6.6, 9.7 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 163.9 (C-4), 150.1 (C-2), 138.9 (C-6), 106.7 (C-5), 86.4 (C-3'), 71.0 (C-4'), 69.7 (C-1'), 61.8 (C-7'), 23.4 (C-5'), 12.1 (CH₃), 11.7 (C-6') ppm. FAB-MS: *m/z* = 509 (2M+H)⁺, 255 [M+H]⁺. C₁₁H₁₄N₂O₅ (254.24): calcd. C 51.97, H 5.55, N 11.02; found C 51.86, H 5.55, N 10.83.

[(1S,3R,4S,5S)-4-(Acetyloxy)-3-[2,4-dioxo-3,4-dihydro-1(2H)-pyrimidinyl]-2-oxabicyclo[3.1.0]hex-1-yl]methyl acetate (18): To a solution of compound **16** (120 mg, 0.5 mmol) in pyridine (3 mL) was added acetic anhydride (0.7 mL, 7.4 mmol). After stirring overnight, the solution was evaporated, co-evaporated with toluene, and the crude product was purified by silica gel column chromatography with a stepwise gradient of MeOH (3–5%) in CH₂Cl₂ to give compound **18** (140 mg, 86%) as a white foam. ¹H NMR (300 MHz, [D₆]DMSO): δ = 11.37 (br. s, 1 H, NH), 7.50 (d, J = 8.1 Hz, 1 H, 6-H), 6.06 (d, J = 4.8 Hz, 1 H, 3'-H), 5.70 (d, J = 8.1 Hz, 1 H, 5-H), 5.30 (d, J = 4.8 Hz, 1 H, 4'-H), 4.47 (s, 2 H, 7'a-H and 7'b-H),

2.09 (s, 3 H, CH₃), 1.94 (s, 3 H, CH₃), 1.77 (dd, $J = 5.1$, 10.1 Hz, 1 H, 5'-H), 1.38 (dd, $J = 5.1$, 7.1 Hz, 1 H, 6'a-H), 1.00 (dd, $J = 7.1$, 10.1 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): $\delta = 170.2$ (COCH₃), 168.9 (COCH₃), 162.8 (C-4), 149.6 (C-2), 141.2 (C-6), 100.9 (C-5), 84.5 (C-3'), 72.6 (C-4'), 66.9 (C-1'), 64.6 (C-7'), 21.4 (C-5'), 20.6 (CH₃CO), 20.4 (CH₃CO), 12.3 (C-6') ppm. FAB-MS: $m/z = 649$ [2M + H]⁺, 325 [M + H]⁺. HRMS: calcd. for C₁₄H₁₇N₂O₇ [M + H]⁺ 325.1036; found 325.1045.

4-Amino-1-[(1S,3R,4S,5S)-4-hydroxy-1-(hydroxymethyl)-2-oxabicyclo[3.1.0]hex-3-yl]-2(1H)-pyrimidinone (19): Yield 70 mg (83%). UV (EtOH 95%): λ_{max} (ϵ) = 270 nm (9100). [α]_D²⁰ = +86.6 ($c = 0.78$, DMSO). ¹H NMR (300 MHz, [D₆]DMSO): $\delta = 7.61$ (d, $J = 7.4$ Hz, 1 H, 6-H), 7.37 (br. s, 1 H, NH), 7.16 (br. s, 1 H, NH), 5.79 (d, $J = 4.5$ Hz, 1 H, 3'-H), 5.71 (d, $J = 7.4$ Hz, 1 H, 5-H), 5.29 (d, $J = 5.3$ Hz, 1 H, 4'-OH), 4.92 (t, $J = 5.6$ Hz, 1 H, 7'-OH), 5.09 (t, $J = 4.5$ Hz, 1 H, 4'-H), 3.83 (dd, $J = 5.7$, 12.5 Hz, 1 H, 7'a-H), 3.66 (dd, $J = 5.5$, 12.5 Hz, 1 H, 7'b-H), 1.51 (dd, $J = 4.9$, 9.7 Hz, 1 H, 5'-H), 0.87 (t, $J = 6.6$ Hz, 1 H, 6'a-H), 0.71 (dd, $J = 6.6$, 9.7 Hz, 1 H, 6'b-H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): $\delta = 164.9$ (C-4), 154.0 (C-2), 144.0 (C-6), 92.2 (C-5), 86.8 (C-3'), 70.3 (C-4'), 69.1 (C-1'), 61.9 (C-7'), 23.6 (C-5'), 11.2 (C-6') ppm. FAB-MS: $m/z = 240$ [M + H]⁺. HRMS: calcd. for C₁₀H₁₄N₃O₄ [M + H]⁺ 240.0984; found 240.1021.

Supporting Information (see also the footnote on the first page of this article): Typical procedure for the synthesis of compounds **3–6**, **8–14**, **16**, **17** and **19**.

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