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Stereocontrolled Synthesis of Ara-Type Cyclohexenyl Nucleosides

Jing Wang, Dolores Viña, Roger Busson, and Piet Herdewijn*

Laboratory of Medicinal Chemistry, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium

piet.herdewijn@rega.kuleuven.ac.be

Received March 18, 2003

A highly stereocontrolled synthesis of a new class of carbocyclic nucleosides, ara-type cyclohexenyl nucleosides, was developed. The key intermediate (±)-**9** was obtained after a series of transformations starting from easily available *endo*-bicyclo carboxylic acid (±)-**3**. The allylic hydroxyl group of (±)-**9** was masked via oxidation with manganese dioxide and released, after protection of the 2′-hydroxyl group, via reduction with $NaBH_4$ in the presence of $CeCl_3 \cdot 7H_2O$. The base moiety was introduced with use of the Mitsunobu methodology.

Introduction

Cyclohexenyl nucleosides are a newly emerging class of carbocyclic nucleosides in which the sugar ring of a natural nucleoside is replaced by a cyclohexene ring.[1−7] Cyclohexenyl nucleosides possess the properties of carbocyclic nucleosides, which due to the absence of an anomeric center are stable against chemical and enzymatic degradation. The presence of the double bond induces flexibility in the ring, similar to the flexibility of a furanose nucleoside. From a stereoelectronic point of view, the carbon−carbon double bond may take the function of the oxygen atom of a furanose. The resulting $\pi \rightarrow \sigma^*_{C1'-N}$ interaction mimics the anomeric effect of a natural nucleoside and considerably reduces the energy difference among the different conformers of a cyclohexene ring.[2] These nucleosides are therefore conformationally flexible and can be considered as the isosteres of natural nucleosides.

Previously, we have demonstrated that D-cyclohexenyl guanine is an interesting antiviral agent.[1] It shows selective anti-herpesvirus activity. Its activity profile is comparable to that of the known antiviral drug ganciclovir. This compound represents the most potent antiviral nucleoside with a six-membered carbohydrate moiety that has been reported.

Conformational analysis of these cyclohexenyl nucleosides shows that at the single molecular level they exist in an equilibrium between two-half-chair conformations ($^3H_2$ and $^2H_3$) and that the $^3H_2$ conformation with the base moiety in a pseudoaxial position predominates.[4] The $^3H_2$ and $^2H_3$ conformations resemble the 3′-*endo* and 3′-*exo* sugar conformations, respectively, of a natural nucleoside. It is generally accepted that conformational flexibility is important for potent antiviral activity,[8] because metabolic activation of a nucleoside (by enzymes) may require different conformations at the different phosphorylation steps. Therefore a rapid equilibrium between the different conformers of a nucleoside may support potent antiviral activity. Besides the remarkable antiviral activity of cyclohexenyl nucleosides, cyclohexenyl nucleic acids hybridize with both DNA and RNA, further demonstrating their conformational flexibility. They hold the promise as potential antisense candidates.[5]

In continuation of our study on cyclohexenyl nucleosides and to further understand their structure−activity relationship, we synthesized the ara-type cyclohexenyl nucleosides **2a**−**d** (Figure 1). The additional OH group

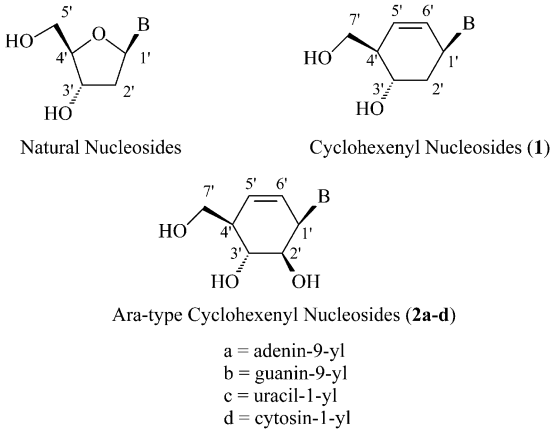


FIGURE 1. Structure of representative examples of cyclohexenyl nucleosides.

(1) Wang, J.; Froeyen, M.; Hendrix, C.; Andrei, G.; Snoeck, R.; De Clercq, E.; Herdewijn, P. *J. Med. Chem.* **2000**, *43(4)*, 736−745. References for related six-membered carbocyclic nucleosides are cited therein.

(2) Herdewijn, P.; De Clercq, E. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1591−1597.

(3) Wang, J.; Morral, J.; Hendrix, C.; Herdewijn, P. *J. Org. Chem.* **2001**, *66*, 8478−8482.

(4) Wang, J.; Herdewijn, P. *J. Org. Chem.* **1999**, *64* (21), 7820−7827

(5) Wang, J.; Verbeure, B.; Luyten, I.; Froeyen, M.; Hendrix, C.; Rosemeyer, H.; Seela, F.; Van Aerschot, A.; Herdewijn, P. *J. Am. Chem. Soc.* **2000**, *122* (36), 8595−8602.

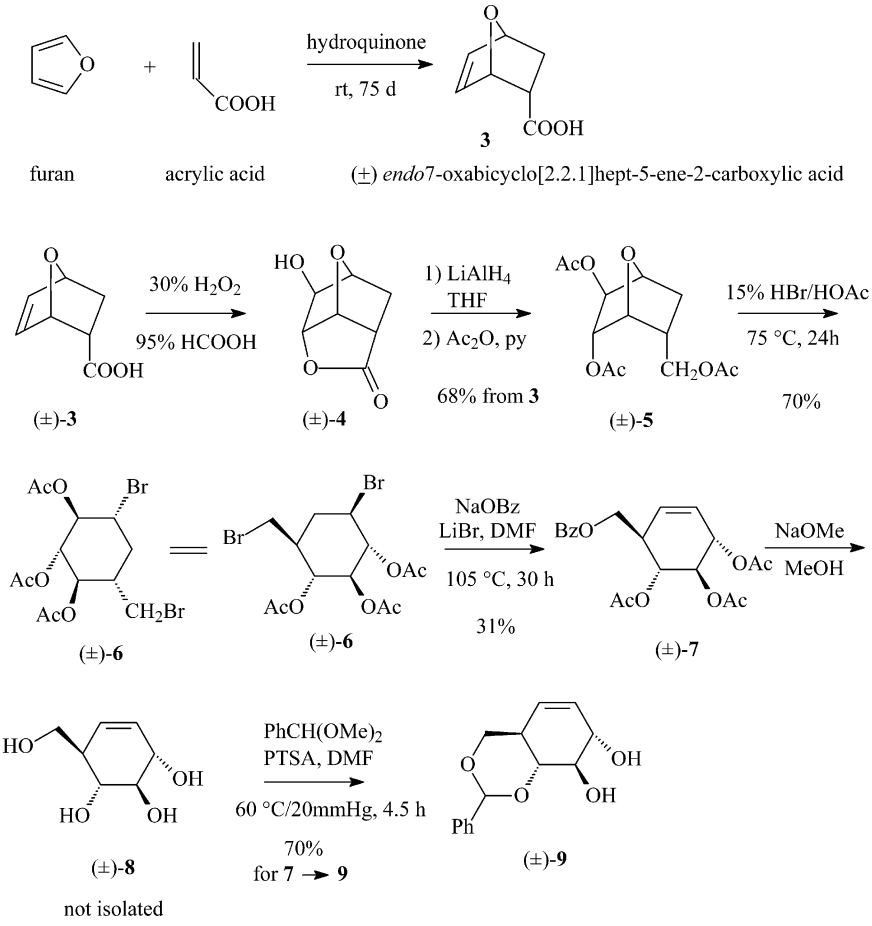
(6) Wang, J.; Herdewijn, P. *Perspectives in Nucleoside and Nucleic Acid Chemistry*; Verlag Helvetica Chimica Acta: Zürich, Switzerland, 2000; pp 95−108.

(7) Wang, J.; Busson, R.; Blaton, N.; Rozenski, J.; Herdewijn, P. *J. Org. Chem.* **1998**, *63*, 3051−3058.

(8) Herdewijn, P. *Drug Discovery Today* **1997**, *2*, 235−242.

10.1021/jo0300946 CCC: $25.00
Published on Web 05/07/2003

SCHEME 1. Synthesis of the Nucleoside Precursor 9 Starting from (±)-*endo*-7-Oxabicyclo[2.2.1]hept-5-ene-2-carboxylic Acid (3)



at the C2′ position might influence the conformational behavior of the cyclohexene ring and drive the conformational equilibrium in the $^3H_2$ direction (in this conformation the 2′-OH group is equatorially oriented). Additionally, the extra hydroxyl group could increase the hydration and influence the stability of the polymeric structure once incorporated into the DNA skeleton. For the sake of clarity, we will use the nucleoside numbering system for compounds **2a**−**d** as indicated in Figure 1.

Results and Discussion

The synthesis of the *ara*-cyclohexenyl nucleosides is outlined in Schemes 1−3. Diels−Alder reaction of furan and acrylic acid in the presence of hydroquinone at room temperature under an inert atmosphere for 75 days provided the *endo*-bicyclo carboxylic acid **3** as the single isomer after recrystallization from ethanol (Scheme 1).[9] No attempts were made to reduce the initially described reaction time. Lactonization of **3** with H_2O_2 and formic acid, followed by reduction with $LiAlH_4$ and acetylation under standard conditions, gave rise to the triacetate **5**. Opening of the O-bridge was carried out with use of 15% HBr in acetic acid in a sealed tube at 75 °C for 24 h, generating dibromide **6**.[10] Elimination of the ring bromide and simultaneous replacement of the primary bromide by a OBz group, using LiBr/NaOBz in DMF at 130 °C for 30 h, gave directly the cyclohexenyl tetraacetate **7** in a moderate yield.[11] All intermediates were purified by crystallization without the use of chromatography.

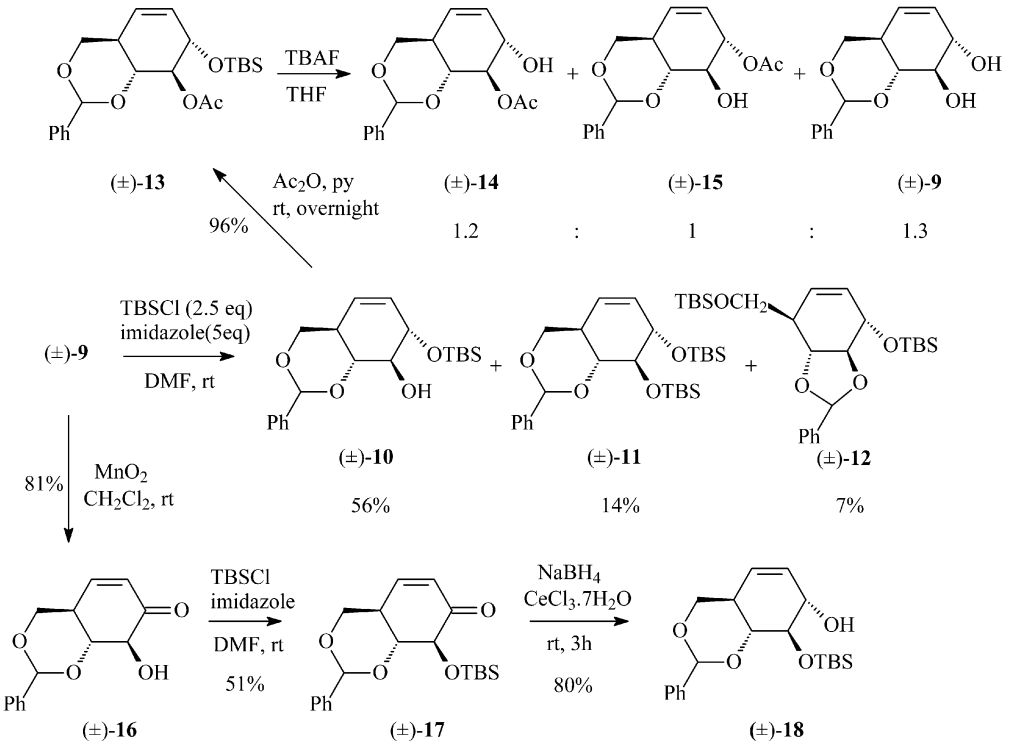
Deprotection of **7** by using NaOMe in MeOH yielded the free tetraol **8**. Selective protection of **8** as benzylidene acetal was carried out by using benzylidene dimethyl acetal in the presence of PTSA at 60 °C under reduced pressure (15−20 mmHg) for 4.5 h. Treatment of **9** with 2.5 equiv of *tert*-butyldimethylsilyl chloride in the presence of imidazole gave monosilylated **10** in 56% yield, together with bis-silyl ethers **11** (14%) and **12** (7%) (Scheme 2). The structural assignment of these three compounds was carried out by NMR experiments. Acetylation of **10** with Ac_2O in pyridine gave **13** in 96% yield. Removal of the TBS protecting group (see Scheme 2) by using TBAF was troublesome, giving rise to a 1.2:1:1.3 mixture of **14**, **15**, and **9**, respectively. While selective protection of one of the two hydroxyl groups of **9** proved difficult, the allylic hydroxyl group of **9** was oxidized to the corresponding enone **16** by using manganese dioxide in CH_2Cl_2 (81% yield). The remaining hydroxyl group was then protected as TBS ether under standard reaction conditions and reduction of enone **17** with $NaBH_4$ in the

(9) Suami, T.; Ogawa, S.; Nakamoto, K.; Kasahara, I. *Carbohydr. Res.* **1977**, *58*, 240

(10) Ogawa, S.; Kasahara, I.; Suami, T. *Bull. Chem. Soc. Jpn.* **1979**, *52* (1), 118−123.

(11) Ogawa, S.; Miyamoto, Y.; Nose, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2675−2680.

SCHEME 2. Synthetic Strategy for the Introduction of the *tert*-Butyldimethylsilyl Protecting Group



presence of $CeCl_3 \cdot 7H_2O$ gave the α-alcohol **18** as the sole isomer in 41% yield over two steps.

Introduction of the base moiety onto the cyclohexenyl ring was effected via a Mitsunobu reaction (Scheme 3). Treatment of **18** with adenine in the presence of PPh_3 and DEAD in dioxane at room temperature for 1 day gave rise to **19** in 43% yield. Complete deprotection of **19** with TFA/H_2O (3:1) at room temperature overnight afforded the adenine compound **2a** in 70% yield. The *ara*-cyclohexenyl guanine **2b** was synthesized by treatment of **18** with 2-amino-6-chloropurine under Mitsunobu reaction conditions and subsequent conversion of the purine-6-chloro group to the guanine function with TFA/H_2O (3:1) at room temperature for 2 days. In the process complete deprotection of the hydroxyl groups took place, giving directly the desired compound **2b** in 57% yield over the two steps.

Synthesis of the uracil derivative **2c** was carried out as above with use of N^3-benzoyluracil in the Mitsunobu reaction. Deprotection of the base-protecting group with a saturated ammonia solution in MeOH, followed by removal of the OH-protecting groups on the cyclohexenyl ring, generated **2c** in 16% overall yield over the three steps.

The cytosine compound **2d** was obtained via conversion of the uracil intermediate **22** into the cytosine derivative **23** upon treatment with $POCl_3$ and 1,2,4-triazole followed by ammonia gas. Deprotection of the OH groups gave rise to the cytosine compound **2d**.

The relative configuration of the *ara*-cyclohexenyl guanine was determined by NMR techniques. All proton and carbon signals were assigned with use of 1D and 2D NMR experiments. The β-configuration of the base moiety was established by a nOe experiment. Irradiation of H1′ of **2b** gave rise to an 11% increase of the H2′ signal, indicating the cis relationship between the guanine base and the 2′-OH group.

Conclusion

A highly stereocontrolled approach toward the synthesis of ara-type cyclohexenyl nucleosides was developed. It consists of 12 steps and proved to be useful for the synthesis of the pyridine as well as the purine nucleosides. The relative configuration was confirmed by nOe experiments. Only the guanine compound demonstrated marginal antiviral activity against herpes simplex virus type 1.[12]

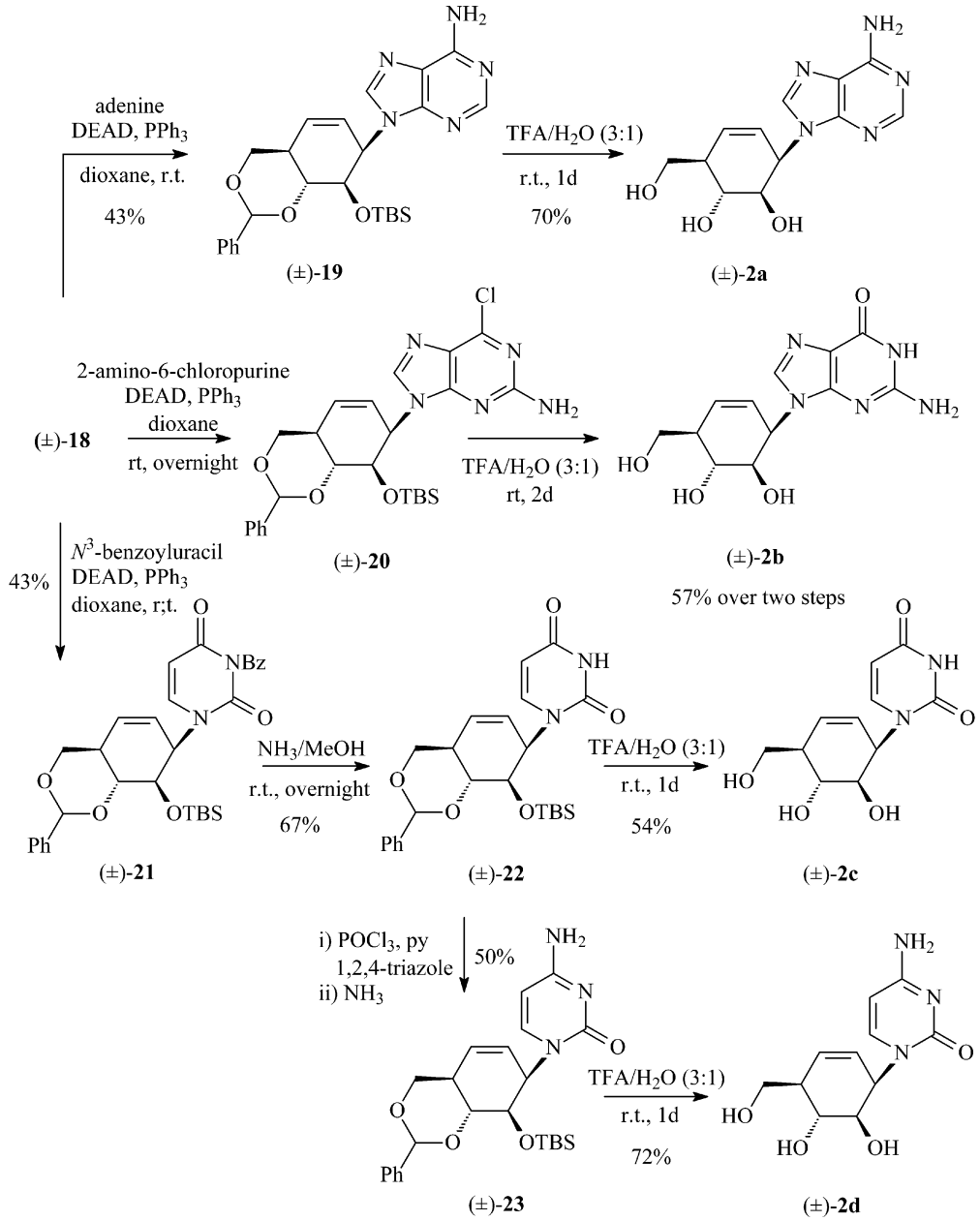
Experimental Section

Melting points were determined with a Büchi-Tottoli apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra were recorded with 200- and 500-MHz spectrometers. Chemical shifts are reported in δ (ppm) and are referred to TMS as internal standard. Liquid secondary ion mass spectra (LSIMS) were recorded with thioglycerol (THGLY) and 3-nitrobenzyl alcohol (NBA) as the matrix. All air-sensitive reactions were carried out under nitrogen. THF and Et_2O were distilled from sodium/benzophenone, 1,4-dioxane from CaH_2, and CH_2Cl_2 from P_2O_5. Precoated Alugram SIL G/UV_{254} plates were used for TLC and spots were examined with UV light and sulfuric acid/anisaldehyde spray. Elemental analysis were done at the University of Konstanz, Germany.

(±)-(4aα,7α,8aβ,8β)-2-Phenyl-4a,7,8,8a-tetrahydro-4*H*-1,3-benzodioxin-7,8-diol (9). To a mixture of **7**[11] (2.56 mmol, 1 g) in methanol (15 mL) at 0 °C was added dropwise a solution of 30% NaOMe in methanol (0.73 mL). The reaction was

(12) Compounds **2a**−**d** were evaluated for their inhibitory effect on the cytopathogenicity of herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), vaccinia virus, and vesicular stomatitis virus. The guanine analogue **2b** shows an EC_{50} value of 4 μg/mL against HSV-1 and 30 μg/mL against HSV-2.

SCHEME 3. Introduction of Nucleobases in the Allylic Position



stirred at 0 °C for 2 h and neutralized with Amberlite IR-120B (H^+) until pH <6. The clear solution was transferred and evaporated to give crude **8** (450 mg) as yellow solids. The crude **8** (450 mg) was dissolved into dry DMF (10 mL). $PhCH(OMe)_2$ (0.5 mL) and PTSA (6 mg) were added. The mixture was immersed into a 60 °C preheated oil bath and stirred under reduced pressure (15−20 mmHg) for 4.5 h. After the solution was cooled to room temperature, solid $NaHCO_3$ was added to quench the reaction. The resulting mixture was concentrated and the residue was chromatographed on silica gel (hexanes−EtOAc 1:1 then pure EtOAc) to give **9** (446 mg, 70% over two steps) as a white solid.

^{1}H NMR (DMSO-d_6) δ 2.44 (m, 1H), 3.49−3.59 (m, 3H), 4.00 (m, 1H), 4.19 (dd, 1H, J = 10.4, 4.6 Hz), 5.07 (d, 1H, J = 2.4 Hz, OH), 5.08 (d, 1H, J = 3.4 Hz, OH), 5.31 (dt, 1H, J = 9.7, 2.0 Hz), 5.57 (dt, 1H, J = 9.7, 2.9 Hz), 5.59 (s, 1H), 7.35−7.39 (m, 3H), 7.47 (m, 2H). ^{13}C NMR ($CDCl_3$/DMSO-d_6) δ 38.4 (d, CH), 69.9 (t), 73.9 (d, CH), 75.4 (d, CH), 80.6 (d, CH), 102.0 (d, CH), 123.8 (d, CH), 126.3 (d, CH), 128.1 (d, CH), 128.9 (d, CH), 130.8 (d, CH), 137.9 (s, C). ES (isopropyl alcohol/water 1:1) 249 $(M + H)^+$; HRMS calcd for $C_{14}H_{17}O_4$ $(M + H)^+$ 249.1126, found 249.1115.

(±)-(4aα,7α,8a*β*,8*β*)-7-(*tert*-Butyldimethylsilyloxy)-2-phenyl-4a,7,8,8a-tetrahydro-4*H*-1,3 -benzodioxin-8-ol (10), (±)-(4aα,7α,8a*β*,8*β*)-7,8-Bis(*tert*-butyldimethyl-silyloxy)-2-phenyl-4a,7,8,8a-tetrahydro-4*H*-benzo-1,3-dioxine (11), and (±)-(3α*β*,4*β*,7aα,7α)-4,7-Bis(*tert*-butyl-dimethyl-silyloxy)-2-phenyl-3a,4,7,7a-tetrahydro-benzo-1,3-dioxole (12). To a solution of **9** (370 mg, 1.49 mmol) in DMF (10 mL) at 0 °C was added imidazole (507 mg, 7.45 mmol, 5 equiv), followed by TBSCl (564 mg, 3.74 mmol, 2.5 equiv) in portions. The reaction was stirred at 0 °C for 0.5 h and at room temperature overnight. Crashed ice was added to quench the reaction and the resulting mixture was concentrated. The residue was taken into EtOAc and washed with water and brine, dried over Na_2SO_4, and concentrated. The resulting light-yellow oil was chromatographed on silica gel (hexanes−EtOAc 10:1) and further by HPLC (hexanes−EtOAc 7:1) to afford **10** (300 mg, 56%) as colorless oil, **11** (100 mg, 14%) as a colorless oil, and **12** (65 mg, 9%) as a colorless oil.

10: R_f 0.44 (hexanes−EtOAc 5:1). ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 3H, CH_3Si), 0.16 (s, 3H, CH_3Si), 0.94 (s, 9H, $(CH_3)_3C$), 2.58 (d, 1H, J = 1.8 Hz, OH), 2.67 (m, 1H), 3.59 (dd, 1H, J = 10.6, 5.5 Hz), 3.64 (dd, 1H, J = 10.2, 8.0 Hz), 3.92 (ddd, 1H, J = 10.2, 7.0, 1.8 Hz), 4.29 (dd, 1H, J = 10.6, 4.6 Hz), 4.37 (m, 1H), 5.34 (dt, 1H, J = 9.9, 1.8 Hz), 5.60 (s, 1H, PhC*H*$(O)_2$), 5.56−5.64 (m, 1H), 7.38 (m), 7.50 (m). ^{13}C NMR ($CDCl_3$) δ −4.8 (q, CH_3Si), −4.5 (4q, CH_3Si), 18.1 (s, C), 25.8 (q, $(CH_3)_3C$), 38.1 (d, CH), 70.0 (t, CH_2), 74.8 (d, CH), 75.6 (d, CH), 81.0 (d, CH), 102.1 (d, CH, Ph*C*H), 123.4 (d, CH), 126.2 (d, CH), 128.3 (d, CH), 129.1 (d, CH), 132.0 (d, CH), 137.9 (s, C). ES (isopropyl alcohol/water 1:1) 363 $(M + H)^+$; HRMS calcd for $C_{20}H_{31}O_4Si$ $(M + H)^+$ 363.1991, found 363.1992.

11: R_f 0.60 (hexanes−EtOAc 5:1). ^{1}H NMR (500 MHz, DMSO-d_6) δ −0.10 (s, 3H, CH_3Si), −0.01 (s, 3H, CH_3Si), 0.09 (s, 3H, CH_3Si), 0.10 (s, 3H, CH_3Si), 0.77 (s, 9H, $(CH_3)_3C$), 0.89 (s, 9H, $(CH_3)_3C$), 2.52 (m, 1H), 3.56 (t, 1H, J = 10.7 Hz), 3.57 (t, 1H, J = 10.2 Hz), 3.81 (dd, 1H, J = 10.2, 6.8 Hz), 4.19 (dd, 1H, J = 10.7, 4.9 Hz), 4.28 (m, 1H), 5.39 (dt, 1H, J = 10.0, 1.7 Hz), 5.56 (dt, 1H, J = 10.0, 2.7 Hz), 5.57 (s, 1H, PhC*H*$(O)_2$), 7.35 (m), 7.42 (m, 2H). ^{13}C NMR (DMSO-d_6) δ −4.2 to −3.9 (4q, 4CH_3Si), 17.8 (s, C), 18.0 (s, C), 26.0 (two q, two $(CH_3)_3C$), 38.8 (d, CH), 69.2 (t, CH_2), 75.8 (d, CH), 76.6 (d, CH), 80.7 (d, CH), 101.8 (d, CH), 124.4 (d, CH), 126.6 (d, CH), 128.0 (d, CH), 128.9 (d, CH), 131.4 (d, CH), 138.4 (s, C). ES (isopropyl alcohol/water 1:1) 477 $(M + H)^+$; HRMS calcd for $C_{26}H_{45}O_4Si_2$ $(M + H)^+$ 477.2856, found 477.2847.

12: R_f 0.64 (hexanes−EtOAc 5:1). ^{1}H NMR (500 MHz, DMSO-d_6) δ −0.03 (s, 3H, CH_3Si), −0.01 (s, 3H, CH_3Si), 0.10 (s, 3H, CH_3Si), 0.11 (s, 3H, CH_3Si), 0.82 (s, 9H, $(CH_3)_3C$), 0.88 (s, 9H, $(CH_3)_3C$), 2.57 (m, 1H), 3.47 (t, 1H, J = 9.7 Hz), 3.56 (dd, 1H, J = 10.2, 6.3 Hz), 3.64 (dd, 1H, J = 9.7, 8.8 Hz), 3.77 (dd, 1H, J = 10.2, 4.0 Hz), 4.56 (m, 1H), 5.52 (dt, 1H, J = 8.2, 2.2 Hz), 5.64 (dt, 1H, J = 8.2, 1.7 Hz), 6.07 (s, 1H, PhC*H*$(O)_2$), 7.38 (m, 3H), 7.44 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ −5.6, −5.4, −4.8, −4.6 (4q, 4CH_3Si), 17.9 (s, C), 18.0 (s, C), 25.7 (two q, two $(CH_3)_3C$), 44.2 (d, CH), 63.0 (t, CH_2), 71.1 (d, CH), 74.3 (d, CH), 83.9 (d, CH), 103.9 (d, Ph-CH), 126.4 (d, CH), 128.0 (d, CH), 128.3 (d, CH), 129.0 (d, CH), 131.3 (d, CH), 139.3 (s, C). ES (isopropyl alcohol/water 1:1) 477 $(M + H)^+$; HRMS calcd for $C_{26}H_{45}O_4Si_2$ $(M + H)^+$ 477.2856, found 477.2844.

(±)-(4aα,7α,8a*β*,8*β*)-8-Acetoxy-7-(*tert*-butyldimethylsilyloxy)-2-phenyl-4a,7,8,8a-tetra hydro-4*H*-benzo-1,3-dioxine (13). Compound **10** (600 mg, 1.66 mmol) was treated with pyridine (20 mL) and Ac_2O (10 mL) at room temperature overnight. The reaction mixture was concentrated and the residue was chromatographed on silica gel (hexanes−EtOAc 10:1) to give **13** (640 mg, 96%) as a white solid.

^{1}H NMR ($CDCl_3$) δ 0.09 (s, 3H, CH_3Si), 0.11 (s, 3H, CH_3Si), 0.90 (s, 9H, $(CH_3)_3C$), 2.10 (s, 3H, CH_3CO), 2.79 (m, 1H), 3.63 (t, 1H, J = 11.0 Hz), 3.69 (t, 1H, J = 11.0 Hz), 4.28 (dd, 1H, J = 11.0, 4.5 Hz), 4.49 (m, 1H), 5.35 (dd, 1H, J = 11.0, 7.7 Hz), 5.36 (dm, 1H, J = 9.9 Hz), 5.54 (s, 1H, PhC*H*$(O)_2$), 5.61 (dt, 1H, J = 9.9, 2.6 Hz), 7.35 (m, 3H), 7.45 (m, 2H). ^{13}C NMR ($CDCl_3$) δ −4.9 (q, CH_3Si), −4.7 (q, CH_3Si), 17.9 (s, C), 21.0 (q, CH_3CO), 25.5 (q, $(CH_3)_3C$), 38.7 (d, CH), 69.9 (t, CH_2), 72.5 (d, CH), 75.8 (d, CH), 78.8 (d, CH), 101.6 (d, CH, Ph*C*H), 123.7 (d, CH), 126.0 (d, CH), 128.2 (d, CH), 128.8 (d, CH), 131.6 (d, CH), 137.9 (s, C), 170.0 (s, CH_3COO). ES (isopropyl alcohol/water 1:1) 405 $(M + H)^+$; HRMS calcd for $C_{22}H_{32}O_5Si$ $(M + H)^+$ 405.2097, found 405.2091.

(±)- (4aα,7α,8a*β*,8*β*)-8-Acetoxy-2-phenyl-4a,7,8,8a-tetrahydro-4*H*-benzo-1,3-dioxin-7-ol (14) and (±)-(4aα,7α,-8a*β*,8*β*)-7-Acetoxy-2-phenyl-4a,7,8,8a-tetrahydro-4*H*-benzo-1,3-dioxin-8-ol (15). To a solution of **13** (620 mg, 1.53 mmol) in THF (15 mL) at 0 °C was added slowly a 1 M TBAF in THF solution (4.59 mL, 4.59 mmol, 3 equiv). After remaining at 0 °C for 0.5 h, the reaction was brought to room temperature and stirred for 1 h. TLC showed the completion of the reaction. Ice was added to quench the reaction. The mixture was diluted with EtOAc, washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel (hexanes−EtOAc 1:2) to give a 1.2:1:1.3 ratio of **14** as a colorless residue, **15** as a colorless residue, and **9** as a white solid.

14 (145 mg, 0.5 mmol, 32%): R_f 0.37 (hexanes−EtOAc 1:2). ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3H, CH_3COO), 2.75 (m, 1H), 3.35 (br s, 1H, OH), 3.65 (t, 1H, J = 11.0 Hz), 3.77 (t, 1H, J = 10.6 Hz), 4.30 (dd, 1H, J = 10.6, 4.6 Hz), 4.40 (m, 1H), 5.13 (dd, 1H, J = 11.0, 7.0 Hz), 5.42 (dd, 1H, J = 9.9, 1.4 Hz), 5.57 (s, 1H, PhC*H*$(O)_2$), 5.75 (dm, 1H, J = 9.9 Hz), 7.36 (m, 3H), 7.47 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 21.0 (q, CH_3CO), 38.0 (d, CH), 69.8 (t, CH_2), 72.8 (d, CH), 78.2 (d, CH), 78.4 (d, CH), 101.6 (d, CH, Ph*C*H), 124.6 (d, CH), 126.1 (d, CH), 128.2 (d, CH), 128.9 (d, CH), 130.1 (d, CH), 137.8 (s, C), 172.4 (s, CH_3COO). ES (isopropyl alcohol/water 1:1) 291 $(M + H)^+$; HRMS calcd for $C_{16}H_{18}O_5$ $(M + H)^+$ 291.1232, found 291.1227.

15 (119 mg, 0.4 mmol, 27%): R_f 0.50 (hexanes−EtOAc 1:2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.13 (s, 3H, CH_3COO), 2.66 (m, 1H), 2.93 (br s, 1H, OH), 3.64−3.70 (m, 2H), 4.10 (dd, 1H, J = 10.5, 7.2 Hz), 4.30 (dd, 1H, J = 11.0, 4.4 Hz), 5.46 (m, 1H), 5.49 (dt, 1H, J = 9.8, 1.7 Hz), 5.61 (s, 1H, PhC*H*$(O)_2$), 5.67 (dt, 1H, J = 9.8, 3.0 Hz), 7.38 (m, 3H), 7.51 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (q, CH_3CO), 37.8 (d, CH), 69.7 (t, CH_2), 72.7 (d, CH), 76.8 (d, CH), 80.9 (d, CH), 102.2 (d, CH, Ph*C*H), 126.2 (d, CH), 126.4 (d, CH), 127.0 (d, CH), 128.3 (d, CH), 129.1 (d, CH), 137.6 (s, C), 171.0 (s, CH_3COO). ES (isopropyl alcohol/water 1:1) 291 $(M + H)^+$; HRMS calcd for $C_{16}H_{18}O_5$ $(M + H)^+$ 291.1232, found 291.1222.

9 (134 mg, 0.54 mmol, 35%): R_f 0.25 (hexanes−EtOAc 1:2).

(±)-(4aα,8a*β*,8*β*)-8-Hydroxy-2-phenyl-4,4a,8,8a-tetrahydro-benzo-1,3-dioxin-7-one (16). A mixture of **9** (650 mg, 2.62 mmol) and MnO_2 (2.28 g, 26.2 mmol, 10 equiv) in dry CH_2Cl_2 (40 mL) was stirred vigorously at room temperature overnight. The reaction mixture was filtered through Celite and washed with CH_2Cl_2. The filtrate was concentrated to give **16** (460 mg, 71%) as a red solid.

^{1}H NMR ($CDCl_3$) δ 3.01 (m, 1H), 3.83 (t, 1H, J = 11.2 Hz), 3.92 (dd, 1H, J = 11.2, 9.1 Hz), 4.38 (d, 1H, J = 11.2 Hz), 4.45 (dd, 1H, J = 11.2, 4.7 Hz), 5.64 (s, 1H, PhC*H*$(O)_2$), 6.26 (dd, 1H, J = 10.3, 3.4 Hz), 6.67 (dd, 1H, J = 10.3, 2.0 Hz), 7.39 (m, 3H), 7.55 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 39.1 (d, CH), 68.7 (t, CH_2), 76.4 (d, CH), 82.5 (d, CH), 101.8 (d, CH), 126.3 (d, CH), 128.3 (d, CH), 129.2 (d, CH), 129.3 (d, CH), 137.2 (s, C), 146.3 (d, CH), 197.6 (s, C, CO).

(±)-(4aα,8a*β*,8*β*)-8-(*tert*-Butyldimethylsilyloxy)-2-phenyl-4,4a,8,8a-tetrahydro-benzo-1,3-dioxin-7-one (17). To a solution of **16** (200 mg, 0.81 mmol) in DMF (5 mL) at 0 °C under N_2 was added imidazole (276 mg, 2.05 mmol, 5 equiv), followed by TBSCl (306 mg, 2.03 mmol, 2.5 equiv) in portions. The reaction mixture was stirred at 0 °C for 0.5 h and at room temperature for 3 h. Crushed ice was added to quench the reaction and the resulting mixture was concentrated. The residue was taken into EtOAc, washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel (hexanes−EtOAc 10:1, 5:1) to give **17** (150 mg, 51%) as a reddish oil.

^{1}H NMR ($CDCl_3$) δ 0.09 (s, 3H, CH_3Si), 0.21 (s, 3H, CH_3Si), 0.94 (s, 9H, $(CH_3)_3C$), 2.91 (m, 1H), 3.80 (t, 1H, J = 11.2 Hz), 3.93 (dd, 1H, J = 11.2, 9.2 Hz), 4.33 (d, 1H, J = 11.2 Hz), 4.44 (dd, 1H, J = 11.2, 4.6 Hz), 5.63 (s, 1H, PhC*H*$(O)_2$), 6.15 (dd, 1H, J = 10.0, 2.9 Hz), 6.52 (dd, 1H, J = 10.0, 1.9 Hz), 7.38 (m, 3H), 7.53 (m, 2H). ^{13}C NMR ($CDCl_3$) δ −5.3 (q, CH_3Si), −4.6 (q, CH_3Si), 18.7 (s, C), 25.7 (q, $(CH_3)_3C$), 39.3 (d, CH), 68.9 (t, CH_2), 78.1 (d, CH), 82.5 (d, CH), 101.4 (d, CH), 126.1 (d, CH), 128.1 (d, CH), 128.8 (d, CH), 131.0 (d, CH), 137.6 (s, C), 143.7 (d, CH), 197.0 (s, CO).

(±)-(4aα,8a*β*,8*β*)-8-(*tert*-Butyldimethylsilyloxy)-2-phenyl-4,4a,8,8a-tetrahydro-benzo-1,3-dioxin-7-ol (18). To a solution of **17** (240 mg, 0.67 mmol) in MeOH (10 mL) was added $CeCl_3 \cdot 7H_2O$ (369 mg, 0.99 mmol, 1.5 equiv). The mixture was stirred at room temperature for 0.5 h until a homogeneous solution was obtained. $NaBH_4$ (30 mg, 0.80 mmol, 1.2 equiv)

was added in portions. The reaction mixture was stirred at room temperature for 3 h. Ice was added to the reaction mixture and the mixture was concentrated. The residue was taken into EtOAc, washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel (hexanes−EtOAc 10:1, then 5:1) to afford **18** (210 mg, 87%) as a colorless oil.

^{1}H NMR ($CDCl_3$) δ 0.02 (s, 3H, CH_3Si), 0.13 (s, 3H, CH_3Si), 0.89 (s, 9H, $(CH_3)_3C$), 2.22 (d, 1H, J = 4.4 Hz, OH), 2.66 (m, 1H), 3.60 (dd, 1H, J = 10.6, 4.4 Hz), 3.65 (dd, 1H, J = 10.2, 7.0 Hz), 3.90 (dd, 1H, J = 10.2, 7.0 Hz), 4.24 (dd, 1H, J = 10.6, 4.8 Hz), 4.32 (m, 1H), 5.37 (dt, 1H, J = 9.9, 2.0 Hz), 5.57 (s, 1H, PhC*H*$(O)_2$), 5.70 (dt, 1H, J = 9.9, 2.8 Hz), 7.37 (m, 3H), 7.51 (m, 2H). ^{13}C NMR ($CDCl_3$) δ −4.9 (q, CH_3Si), −4.3 (q, CH_3-Si), 18.2 (s, C), 25.8 (q, $(CH_3)_3C$), 39.1 (d, CH), 70.0 (t, CH_2), 75.4 (d, CH), 77.0 (d, CH), 80.9 (d, CH), 102.3 (d, CH), 124.5 (d, CH), 126.3 (d, CH), 128.0 (d, CH), 128.8 (d, CH), 130.4 (d, CH), 138.0 (s, C). ES (isopropyl alcohol/water 1:1) 363 $(M + H)^+$; HRMS calcd for $C_{20}H_{30}O_4Si$ $(M + H)^+$ 363.1991, found 363.1982.

(±)-2′-*O*-*tert*-Butyldimethylsilyl-3′,7′-*O*-benzylidene-*ara*-cyclohexenyl-adenine (19). To a mixture of **18** (140 mg, 0.39 mmol), adenine (111 mg, 0.78 mmol), and Ph_3P (216 mg, 0.78 mmol) in dry dioxane (6 mL) under N_2 at room temperature was added a solution of DEAD (136 μL, 0.78 mmol) in dry dioxane (2.5 mL) over a period of 30 min. The reaction mixture was stirred at room temperature overnight and concentrated. The resulting residue was chromatographed on silica gel (CH_2Cl_2/MeOH, 98:2) to yield **19** (80 mg, 43%) as a white solid.

Mp 225−227 °C. ^{1}H NMR ($CDCl_3$) δ −0.07 (s, 3H, CH_3Si), −0.08 (s, 3H, CH_3Si), 0.49 (s, 9H, $(CH_3)_3C$), 2.71 (m, 1H, H4′), 3.86 (t, 1H, J = 11.0 Hz, H7′a), 3.89 (t, 1H, J = 9.8 Hz, H3′), 4.37 (dd, 1H, J = 10.2, 6.8 Hz, H2′), 4.42 (dd, 1H, J = 10.9, 4.5 Hz, H7′b), 5.58 (br, 2H, NH_2), 5.59 (obs, 1H, H1′), 5.62 (s, 1H, PhC*H*$(O)_2$), 5.77 (dt, 1H, J = 9.5, 1.5 Hz, H5′), 5.86 (1H, ddd, J = 9.5, 4.0, 3.1 Hz, H6′), 7.36 (m, 3H), 7.49 (m, 2H), 7.87 (s, 1H, H8), 8.37 (s, 1H, H2). ^{13}C NMR ($CDCl_3$) δ −4.9 (CH_3Si), −4.7 (CH_3Si), 17.9 (C), 25.2 $(CH_3)_3$, 39.1 (CH, C4′), 53.8 (CH, C1′), 70.0 (CH_2, C7′), 70.7 (CH, C2′), 79.6 (CH, C3′), 102.8 (Ph*C*H$(O)_2$), 119.5 (C5), 126.1 (CH, C6′), 126.4 (CH_o), 128.1 (CH_m), 128.5 (CH, C5′), 128.9 (CH_p), 137.7 (C,Ci), 140.5 (CH, C8), 151.1 (C, C4), 152.8 (CH, C2), 155.3 (C, C6). Assignments based on 2D COSY, GHSQC- and GHMBC-spectra. HRMS calcd for $C_{25}H_{33}N_5O_3Si$ $(M + H)^+$ 480.2353, found 480.2433.

(±)-*ara*-Cyclohexenyl-adenine (2a). 19 (150 mg, 0.31 mmol) was treated with TFA−H_2O (3:1, 6 mL) at room temperature overnight. The reaction mixture was concentrated and coevaporated with toluene (3×). The residue was chromatographed on silica gel such as eluent CH_2Cl_2/MeOH (10: 0.5, 10:1, 10:2) to afford **2a** (60 mg, 70%) as a white solid.

Mp 143−145 °C. ^{1}H NMR (DMSO) (500 MHz) δ 2.22 (m, 1H, H4′), 3.69 (m, 3H, H7′a, H7′b, H3′), 3.78 (dt, 1H, J = 8.3, 5.1 Hz, H2′), 4.87 (t, 1H, J = 5.0 Hz, 7′-OH), 4.92 (d, 1H, J = 4.4 Hz, 3′-OH), 5.10 (d, 1H, J = 5.1 Hz, 2′-OH), 5.32 (m, 1H, H1′), 5.74 (ddd, 1H, J = 10.0, 3.9, 2.4 Hz, H6′), 5.97 (dt, 1H, J = 10.0, 2.2 Hz, H5′), 7.11 (br, 2H, NH_2), 7.95 (s, 1H, H8), 8.12 (s, 1H, H2). ^{13}C NMR (DMSO) (500 MHz) δ 46.4 (CH,C4′), 52.2 (CH, C1′), 61.4 (CH, C7′), 67.2 (CH, C3′), 70.2 (CH, C2′), 118.7 (C, C5), 123.2 (CH, C6′), 133.5 (CH, C5′), 140.4 (CH, C8), 150.3 (C, C4), 152.1 (CH, C2), 156.0 (C, C6). HRMS calcd for $C_{12}H_{15}N_50_3$ $(M + H)^+$ 278.1175, found 278.1253. Anal. Calcd for $C_{12}H_{15}N_5O_3$ (MW 277.1175): C, 51.96; H, 5.46; N, 25.27. Found: C, 51.64; H, 5.84; N, 25.59.

(±)-*ara*-Cyclohexenyl-guanine (2b). To a mixture of **18** (165 mg, 0.46 mmol), PPh_3 (241 mg, 0.92 mmol, 2 equiv), and 2-amino-6-chloropurine (156 mg, 0.92 mmol, 2 equiv) in dry dioxane (5 mL) under nitrogen at room temperature was added a solution of DIAD (182 μL, 0.92 mmol, 2 equiv) in dioxane (3 mL) very slowly. The reaction mixture was stirred further at room temperature overnight. The mixture was diluted with dioxane and filtered and the solid washed with CH_2Cl_2. The filtrate and washings were concentrated and the residue was chromatographed on silica gel (CH_2Cl_2−EtOAc 1:1) to give the crude **20** (560 mg) asa yellow foam.

The crude **20** (560 mg) was treated with TFA/water (3:1, 10 mL) at room temperature for 2 days. The reaction mixture was concentrated and coevaporated with toluene. The residue was chromatographed on reverse HPLC (5% CH_3CN in water containing 0.1% TFA) to afford **2b** (78 mg, 57% over two steps) as a white foam.

^{1}H NMR (500 MHz, D_2O) δ 2.47 (m, 1H, H4′), 3.72 (dd, 1H, J = 9.8, 7.8 Hz, H3′), 3.85 (dd, 1H, J = 10.2, 2.4 Hz, H7a′), 3.89 (dd, 1H, J = 10.2, 3.4 Hz, H7b′), 4.14 (dd, 1H, J = 10.3, 5.2 Hz, H2′), 5.47 (t-br, 1H, J = 5.2 Hz, H1′), 5.87 (ddd, 1H, J = 9.7, 5.2, 2.4 Hz, H6′), 6.19 (ddd, 1H, J = 9.7, 2.4, 1.4 Hz, H5′), 8.64 (s, 1H, H8). ^{13}C NMR (125 MHz, D_2O) δ 48.5 (CH, C4′), 57.2 (CH, C1′), 63.6 (CH2, C7′), 69.3 (CH, C3′), 72.9 (CH, C2′), 117.9 (C, C5), 124.1 (CH, C6′), 138.8 (CH, C5′), 139.9 (CH, C8), 153.8 (C, C4), 157.8 (C, C2), 158.4 (C, C6). ES (isopropyl alcohol/water 1:1) 294 $(M + H)^+$; HRMS calcd for $C_{12}H_{16}N_5O_4$ $(M + H)^+$ 294.1202, found 294.1207. Anal. Calcd for $C_{12}H_{15}N_5O_3$ (MW 293.112): C, 49.13; H, 5.16; N, 23.89. Found: C, 49.07; H, 4.98; N, 23.57.

(±)-2′-*O*-*tert*-Butyldimethylsilyl-3′,7′-*O*-benzylidene-*ara*-cyclohexenyl-*N*^{1}-benzoyluracil (21). To a mixture of **18** (380 mg, 1.05 mmol), N^3-benzoyluracil (283 mg, 1.3 mmol), and Ph_3P (330, 1.3 mmol) in dry dioxane (10 mL) was slowly added a solution of DEAD (0.2 mL, 1.3 mmol) in dry dioxane (1 mL). The mixture was stirred at room temperature overnight and the solvent was evaporated. The residue was chromatographed on silica gel (*n*-hexane/EtOAc, 9:1, 8:2, 7:3, 5:5). Evaporation afforded compound **21** (250 mg, 43%) as a yellow foam.

^{1}H NMR ($CDCl_3$) δ 0.005 (s, 6H, $(CH_3)_2Si$), 0.77 (s, 9H, $(CH_3)_3C$), 2.61 (m, 1H, H4′), 3.65 (t, 1H, J = 9.9 Hz, H3′), 3.79 (t, 1H, J = 11.0 Hz, H7′a), 4.30 (dd, 1H, J = 9.9, 7.3 Hz, H2′), 4.39 (dd, 1H, J = 11.0, 4.5 Hz, H7′b), 5.61 (s, 1H, PhCH$(O)_2$), 5.67−5.79 (m, 3H, H1′, H5′, H6′), 5.86 (d, 1H, J = 8.1 Hz, H5), 7.33−7.68 (3m, 10H 2 ar), 7.97 (d, 1H, J = 8.1 Hz, H6). ^{13}C NMR ($CDCl_3$) δ −6.3 (CH_3Si), −6.1 (CH_3Si), 16.7 (C), 24.2 $(CH_3)_3C$), 36.9 (CH, C4′), 53.0 (CH, C1′), 68.5 (CH_2, C7′), 68.8 (CH, C2′), 78.2 (CH, 3′), 100.1 (CH, C5), 101.5 (Ph, CH$(O)_2$), 125.1 (2(CH, C6′ + Pho)), 126.8 (CH), 127.7 (CH), 128.5 (CH,-C5′), 129.3 (CH), 130.2 (C), 133.6 (CH), 136.2 (C), 141.4 (CH, C6), 149.1 (C═O, C2), 161.0 (C═O, C4). HRMS calcd for $C_{31}H_{36}N_2O_6Si$ $(M + H)^+$ 561.2343, found 561.2435.

(±)-2′-*O*-*tert*-Butyldimethylsilyl-3′,7′-*O*-benzylidene-*ara*-cyclohexenyl-uracil (22). 21 (370 mg, 0.66 mmol) was treated with NH_3/MeOH (25 mL) at room temperature overnight. Evaporation left an oil, which was purified on silica gel (CH_2Cl_2/MeOH, 99:1) to afford **22** as a white solid (200 mg, 67%).

Mp 200−202 °C. ^{1}H NMR ($CDCl_3$) δ −0.04 (s, 3H, CH_3Si), 0.03 (d, 3H, CH_3Si), 0.73 (s, 9H, $(CH_3)_3C$), 2.60 (m, 1H, H4′), 3.56 (t, 1H, J = 9.8 Hz, H3′), 3.76 (t, 1H, J = 11.0 Hz, H7′a), 4.25 (dd, 1H, J = 10.2, 7.4 Hz, H2′), 4.39 (dd, 1H, J = 11.0, 4.6 Hz, H7′b), 5.58 (s, 1H, PhCH$(O)_2$), 5.64−5.81 (3m, 4H, H1′, H5′, H6′, H5), 7.27 (m, 2H), 7.36 (m, 2H), 7.49 (m, 2H), 8.40 (s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ −5.1 (CH_3Si), −4.8 (CH_3Si), 18.0 (C), 25.5 ($(CH_3)_3C$), 38.1 (CH, C4′), 53.7 (CH, C1′), 69.9 (CH_2, C7′), 70.2 (CH, C2′), 79.5 (CH, C3′), 101.6 (CH, C5), 102.9 (CH, Ph CH$(O)_2$), 126.4 (2CH, C6′ and CHO), 128.2 (CH, CH_m), 129.1 (CH, C5′), 129.8 (CH, CH_p), 137.5 (C, Ci), 142.6 (CH, C6), 151.2 (C═O, C2), 162.9 (C═O, C4). HRMS calcd for $C_{24}H_{32}N_2O_5Si$ $(M + H)^+$ 457.2081, found 457.2166.

(±)-*ara*-Cyclohexenyl-uracil (2c). 22 (100 mg, 0.22 mmol) was treated with TFA−H_2O (3:1, 6 mL) at room temperature for 24 h. The reaction mixture was concentrated and coevaporated with toluene (3×). The residue was chromatographed on silica gel (CH_2Cl_2/MeOH 99:1) to afford **2c** (30 mg, 54%) as a white solid, which was crystallizated from MeOH.

Mp 223 °C. ^{1}H NMR (DMSO) (500 MHz) δ 2.15 (m, 1H, H4′), 3.54 (ddd, 1H, J = 10.2, 5.6, 2.0 Hz, H7′a), 3.61 (m, 1H, H7′a), 3.64 (m, 1H, H3′), 3.70 (m, 1H, H2′), 4.80 (t, 1H, J = 5.6 Hz, 7′OH), 4.99 (d, 1H, J = 4.2 Hz, 3′OH), 5.23 (d, 1H, J = 5.6 Hz, 2′OH), 5.26 (td, J = 5.4, 2.7 Hz, H1′), 5.49 (d, 1H, J = 8.1 Hz, H5), 5.50 (m, 1H, H6′), 5.95 (dt, J = 10.2, 2.7 Hz, H5′), 7.35 (d, 1H, J = 8.1 Hz, H6), 11.16 (s, 1H, NH). ^{13}C NMR (DMSO) (500 MHz) δ 45.7 (CH, C4′), 52.5 (CH, C1′), 61.6 (CH_2, C7′), 67.5 (CH, C3′), 68.8 (CH, C2′), 99.9 (CH, C5), 122.9 (CH, C6′), 133.7 (CH, C5′), 144.1 (CH, C6), 151.4 (C=O, C2), 163.6 (C=O, C4). Assignments based on 2D COSY, GHSQC- and GHMBC-spectra. HRMS calcd for $C_{11}H_{14}N_2O_5$ $(M + H)^+$ 255.0903, found 255.0972. Anal. Calcd for $C_{11}H_{14}N_2O_5$ (MW 254.093): C, 51.95; H, 5.55%, N, 11.02. Found: C, 52.16; H, 5.44; N, 11.21.

(±)-2′-*O*-*tert*-Butyldimethylsilyl-3′,7′-*O*-benylidene-*ara*-cyclohexenyl-cytosine (23). 22 (200 mg, 0.44 mmol) was added to a premixed solution of 68 μL of phosphorus oxychloride and 1,2,4-triazole (205 mg, 2.96 mmol) in anhydrous pyridine (15.35 mL). The reaction mixture was stirred for 24 h at room temperature. The reaction mixture was cooled to 0 °C and ammonia gas was bubbled through the mixture for 15 min. The reaction mixture was further stirred for 15 min at room temperature, evaporated, and coevaporated with toluene. The residue was suspensed in 100 mL of CH_2Cl_2/MeOH (1:1) and filtered over a small layer of Celite to remove most of the inorganic salts. The filtrate was evaporated, dissolved in CH_2Cl_2, and washed with water to remove 1,2,4-triazole. The organic residue was evaporated and purified by column chromatography (CH_2Cl_2/MeOH 97:3) to afford **23** (100 mg, 50%) as a yellow oil.

^{1}H NMR ($CDCl_3$) δ 0.09 (d, 6H, 2 × CH_3Si), 0.72 (s, 9H, $(CH_3)_2C$), 2.58 (m, 1H, H4′), 3.58 (t, 1H, J = 9.9 Hz, H3′), 3.74 (t, 1H, J = 11.2 Hz, H7′a), 4.28 (dd, 1H, J = 9.9 and 8.1 Hz, H2′), 4.37 (dd, 1H, J = 11.2 and 4.8 Hz, H7′b), 5.55 (s, 1H, $PhCH(O)_2$), 5.66 (s, 2H, H1′, H5′), 5.72 (d, 1H, J = 7.3 Hz, H5), 5.95 (dm, 1H, J = 7.7 Hz, H6′), 7.26−7.52 (3m, 6H, H6, 5CH). ^{13}C NMR ($CDCl_3$) δ −5.2 (CH_3Si), −4.9 (CH_3Si), 18.0 (C), 25.4 ($(CH_3)_3C$), 37.8 (CH, C4′), 54.2 (CH, C1′), 70.0 (CH_2, C7′), 70.3 (CH, C2′), 79.9 (CH, C3′), 94.1 (CH, C5), 102.7 (CH, Ph $CH(O)_2$), 126.4 (CH, CHO), 127.6 (CH, C5′), 128.2 (CH, CH_m), 128.5 (CH, C6′), 129.1 (CH, CH_p), 137.7 (C, Ci), 144.5 (CH, C6), 157.2 (C=O, C2), 165.0 (C=O, C4). HRMS calcd for $C_{24}H_{33}N_3O_4Si$ $(M + H)^+$ 456.2240, found 456.2317.

(±)-*ara*-Cyclohexenyl-cytosine (2d). 23 (100 mg, 0.22 mmol) was treated with TFA−H_2O (3:1, 6 mL) at room temperature overnight. The mixture was concentrated and coevaporated with toluene (3×). The residue was chromatographed on silica gel (CH_2Cl_2/MeOH, 96:4, 95:5, 93:7, 90:10, 5:2) to afford **2d** as a white solid (40 mg, 72%).

Mp 124−126 °C. ^{1}H NMR (DMSO) δ 2.19 (m, 1H, H4′), 3.39 (br, 2′, 3′, 7′-OH and HOD), 3.52 (dd, 1H, J = 10.2, 5.6 Hz, H7′a), 3.62 (dd, 1H, J = 10.2, 5.6 Hz, H7′b), 3.68 (dd, J = 6.0, 3.7 Hz, H-3′), 3.75 (t, 1H, J = 5.5 Hz, H2′), 5.30 (m, 1H, H1′), 5.49 (dm, 1H, J = 10.3 Hz, H6′), 6.00 (m, 2H, H5′, H5), 7.66 (d, 1H, J = 7.6 Hz, H6), 8.72 (s, 1H, NH_2), 9.32 (s, 1H, NH_2). ^{13}C NMR (DMSO) δ 45.6 (CH, C4′), 54.0 (CH, C1′), 61.7 (CH_2, C7′), 67.4 (CH, C3′), 68.0 (CH, C2′), 92.6 (CH, C5), 121.9 (CH, C6′), 134.1 (CH, C5′), 148.33 (CH, C6), 148.6 (C=O, C2), 159.7 (C=O, C4). HRMS calcd for $C_{11}H_{15}N_3O_4$ $(M + H)^+$ 254.1063, found 254.1136. Anal. Calcd for $C_{11}H_{15}N_3O_4$ (MW 253.106): C, 52.15; H, 5.97; N, 16.60. Found: C, 51.93; H, 6.28; N, 16.56.

Acknowledgment. This research was financially supported by a grant from the Katholieke Universiteit Leuven (GOA 97/11). The authors thank Dr. Erik De Clercq for antiviral data.

JO0300946