Supporting Information
A New and Versatile Synthesis of 1,3-Dioxan-5-yl-Pyrimidine and Purine Nucleoside Analogues
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1. General Information

All reagents, solvents and other chemicals were used as purchased from Sigma-Aldrich without further purification unless otherwise specified. Air- or moisture-sensitive reactants and solvents were employed in reactions carried out under nitrogen atmosphere unless otherwise noted. Flash column chromatography purifications (medium pressure liquid chromatography) were carried out using Merck silica gel 60 (230-400 mesh, ASTM). The purity of compounds was determined by elemental analysis (C,H,N) that was performed on a Carlo Erba 1106 Analyzer instrument in the Microanalysis Laboratory of the Life Sciences Department of Università degli Studi di Modena e Reggio Emilia and the results are here reported. Melting points were determined with a Stuart SMP3 and they are uncorrected. The structures of all isolated compounds were ensured by Nuclear Magnetic Resonance (NMR) and Mass spectrometry. $^1$H and $^{13}$C NMR (1D and 2D experiments) spectra were recorded on a DPX-400 Avance (Bruker) spectrometer at 400 MHz. Chemical shifts are expressed in $\delta$ (ppm). $^1$H NMR chemical shifts are relative to tetramethylsilane (TMS) as internal standard. $^{13}$C NMR chemical shifts are relative to TMS at $\delta$ 0.0 or to the $^{13}$C signal of the solvent: CDCl$_3$, $\delta$ 77.04; CD$_3$OD, $\delta$ 49.8; DMSO-$d_6$, $\delta$ 39.5. $^1$H NMR data are reported as follows: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened), coupling constants (Hz), number of protons, and assignment (Ph, Phenyl; diox, 1,3-dioxane; Ts, Tosyl). $^1$H-$^1$H correlation spectroscopy (COSY), $^1$H-$^{13}$C Heteronuclear Single Quantum Coherence (HSQC) and Heteronuclear Multiple Bond Connectivity (HMBC) NMR 2D experiments were recorded to lay down $^1$H-$^1$H and $^1$H-$^{13}$C correlations respectively. Mass spectra were obtained by means of a QTOF mass spectrometer using electrospray ionization mode (HRMS-ESI) or atmosphere pressure chemical ionization (HRMS-APCI). The HPLC experimental conditions of the HPLC-MS system are: flow rate 0.1 ml/min, sample solution (100 pmol/ml) of the selected compound with 0.1% acetic acid, mobile phase consisting of acetonitrile (50%) and water (50%).
2. Protocols and Physical data of Compounds

Benzoyloxyacetaldehyde diethyl acetal (1)
Potassium benzoate (125.2 mmol, 20.0 g) was added to a solution of bromoacetaldehyde diethyl acetal (160.0 mmol, 24.4 mL) and 18-crown-6 ether (catalytic amount) in anhydrous DMF (25 mL) and the mixture was refluxed for 6 h. Then, after cooling to room temperature; water was added, and the mixture was extracted three times with ethyl acetate. The combined extracts were washed with water, dried (Na$_2$SO$_4$) and concentrated under vacuum. The residue was dried azeotropically with toluene to give benzoyloxyacetaldehyde diethyl acetal as a dark oily product (24.72 g, 104.0 mmol, 83%). This product was used in the next step without further purification.

$^1$H-NMR (400 MHz, CDCl$_3$) δ: 1.22 (t, J= 7.2 Hz, 6H, 2 x CH$_3$), 3.54-3.68 (m, 2H, CH$_2$CH$_3$), 3.68-3.80 (m, 2H, CH$_2$CH$_3$), 4.35 (d, J= 5.4 Hz, 2H, CH$_2$OCO), 4.84 (t, J= 5.4 Hz, 1H, CH), 7.43 (dd, J= 7.6, 7.7 Hz, 2H, CH-3, CH-5 Ph), 7.55 (t, J= 7.6 Hz, 1H, CH-4 Ph), 8.05 (d, J= 7.7 Hz, 2H, CH-2, CH-6 Ph).

$^{13}$C-NMR (100 MHz, CDCl$_3$) δ: 15.0 (2 CH$_3$), 62.2 (2 CH$_2$), 64.1 (CH$_2$OCO), 99.4 (CH), 128.1 (C-3, C-5 Ph), 129.4 (C-2, C-6 Ph), 129.7 (C-1 Ph), 132.8 (C-4 Ph), 166.0 (CO).

HRMS-APCI: calcd for C$_{13}$H$_{19}$O$_4^+$: [M+H]$^+$ 239.1278; found 239.1280.

(5-hydroxy-1,3-dioxan-2-yl)methyl benzoate (2)
To a solution of CoCl$_2$ (9.7 g, 75.0 mmol) in dry acetonitrile (100 mL), benzoyloxyacetaldehyde diethyl acetal (1) (33.3 g, 140.0 mmol), TMSCl (19.0 mL, 149.0 mmol) and glycerol (19.3 mL, 265.0 mmol) were added at room temperature, under stirring. After 12 h the reaction was stopped, the mixture was extracted three times with ethyl acetate and the extracts were collected and washed with NaHCO$_3$ 5%. The organic layer was dried (Na$_2$SO$_4$), filtered, and the solvent was evaporated under vacuum to give an oily residue. Purification and separation of two diastereoisomers 2a and 2b was achieved by flash column chromatography (70:30 cyclohexane:ethyl acetate): 5.00 g of cis isomer (2a, 21.0 mmol, 15%), 5.34 g of trans isomer (2b, 22.4 mmol, 16%) and 10.0 g of (4-(hydroxymethyl)-1,3-dioxolan-2-yl)methyl benzoate (2c, 42.0 mmol, 30%), as unseparable cis/trans diastereoisomeric mixture (50/50), were obtained. Molar ratio 1,3-dioxanes/1,3-dioxolanes: 55/45.

Cis-(5-hydroxy-1,3-dioxan-2-yl)methyl benzoate (2a)

$^1$H-NMR (400 MHz, CDCl$_3$) δ: 3.10 (br s, 1H, OH), 3.52-3.61 (m, 1H, CH-5 diox), 3.90-4.01 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.04-4.13 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.40 (d, J= 4.6 Hz, 2H, CH$_2$O), 4.96 (t, J= 4.6 Hz, 1H, CH-2 diox), 7.44 (dd, 2H, J= 7.4, 7.8 Hz, CH-3, CH-5 Ph), 7.57 (t, 1H, J= 7.4 Hz, CH-4 Ph), 8.01 (d, 2H, J= 7.8 Hz, CH-2, CH-6 Ph).
$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 64.0 (C-5 diox), 64.9 ($\text{CH}_2\text{OCO}$), 71.9 (C-4, C-6 diox), 98.9 (C-2 diox), 128.5 (C-3, C-5 Ph), 129.6 (C-1 Ph), 129.7 (C-2, C-6 Ph), 133.2 (C-4 Ph), 166.2 (CO).

HRMS-APCI: calcd for C$_{12}$H$_{15}$O$_5^+$: [M+H]$^+$ 239.0914; found 239.0917.

Trans-(5-hydroxy-1,3-dioxan-2-yl)methyl benzoate (2b)

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 3.02 (br s, 1H, OH), 3.42 (dd, J= 10.4, 10.8 Hz, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 3.81-3.91 (m, 1H, CH-5 diox), 4.22 (dd, J= 4.9, 10.4 Hz, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.35 (d, J= 4.6 Hz, 2H, CH$_2$O), 4.78 (t, J= 4.6 Hz, 1H, CH-2 diox), 7.43 (dd, 2H, J= 7.2, 7.8 Hz, CH-3, CH-5 Ph), 7.55 (t, 1H, J= 7.2 Hz, CH-4 Ph), 8.04 (d, 2H, J= 7.8 Hz, CH-2, CH-6 Ph).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 60.7 (C-5 diox), 64.4 ($\text{CH}_2\text{OCO}$), 70.8 (C-4, C-6 diox), 97.8 (C-2 diox), 128.2 (C-3, C-5 Ph), 129.2 (C-1 Ph), 129.5 (C-2, C-6 Ph), 133.1 (C-4 Ph), 166.1 (CO).

HRMS-APCI: calcd for C$_{12}$H$_{15}$O$_5^+$: [M+H]$^+$ 239.0914; found 239.0915.

[4-(Hydroxymethyl)-1,3-dioxan-2-yl]methyl benzoate (2c)

Trans isomer: $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 3.52-3.70 (m, 1H, CH$_2$OH), 3.69-3.88 (m, 2H, CH$_2$OH, CHa-5 dioxolane), 4.14 (dd, J= 6.7, 8.0 Hz, CHb-5 dioxolane), 4.22-4.26 (m, 1H, CH-4 dioxolane), 4.37 (d, J= 3.5 Hz, 2H, CH$_2$), 5.28 (t, J= 3.5 Hz, 1H, CH-2 dioxolane), 7.36-7.49 (m, 2H, CH-3, CH-5 Ph), 7.51-7.62 (m, 1H, CH-4 Ph), 8.01-8.14 (m, 2H, CH-2, CH-6 Ph).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 62.7 (CH$_2$OH), 64.2 ($\text{CH}_2\text{OCO}$), 66.2 (C-5 dioxolane), 66.4 (C-4 dioxolane), 101.6 (C-2 dioxolane), 128.2 (C-3, C-5 Ph), 129.2 (C-1 Ph), 129.3 (C-2, C-6 Ph), 133.0 (C-4 Ph), 166.1 (CO).

Cis isomer: $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 3.52-3.70 (m, 1H, CH$_2$OH), 3.69-3.88 (m, 1H, CH$_2$OH), 3.93 (dd, J= 6.1, 8.0 Hz, 1H, CHa-5 dioxolane), 4.01 (dd, J= 6.1, 8.0 Hz CHb-5 dioxolane), 4.28-4.32 (m, 1H, CH-4 dioxolane), 4.36 (d, J= 3.8 Hz, 2H, CH$_2$), 5.40 (t, J= 3.8 Hz, 1H, CH-2 dioxolane), 7.36-7.49 (m, 2H, CH-3, CH-5 Ph), 7.51-7.62 (m, 1H, CH-4 Ph), 8.01-8.14 (m, 2H, CH-2, CH-6 Ph).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 62.0 (CH$_2$OH), 64.0 ($\text{CH}_2\text{OCO}$), 66.2 (C-5 dioxolane), 66.4 (C-4 dioxolane), 101.4 (C-2 dioxolane), 128.1 (C-3, C-5 Ph), 129.2 (C-1 Ph), 129.3 (C-2, C-6 Ph), 132.9 (C-4 Ph), 165.9 (CO).

HRMS-APCI: calcd for C$_{12}$H$_{15}$O$_5^+$: [M+H]$^+$ 239.0914; found 239.0916.

Cis-[5-(tosyloxy)-1,3-dioxan-2-yl]methyl benzoate (3a)

$p$-Toluenesulfonyl chloride (1.20 g, 6.3 mmol) was added at 0 °C to a solution of 2a (1.0 g, 4.2 mmol) and triethylamine (8.4 mmol, 1.17 mL) in dry CH$_2$Cl$_2$ (20 mL). The mixture was stirred at room temperature for 12 h. Ice and water were added and the mixture was extracted with CH$_2$Cl$_2$.
The organic extracts were collected and dried (Na₂SO₄). Crystallization from ethyl acetate/cyclohexane afforded the desired compound as a white solid (1.34 g, 3.4 mmol, 81%).
m.p.: 118-119 °C.

¹H-NMR (400 MHz, CDCl₃) δ: 2.47 (s, 3H, CH₃), 3.95 (dd, J= 1.4, 13.2 Hz, 2H, CH-4ax, CH-6ax diox), 4.19 (dd, J= 1.2, 13.2, 2H, CH-4eq, CH-6eq diox), 4.38 (d, J= 4.6 Hz, 2H, CH₂O), 4.47 (dd, J= 1.2, 1.4 Hz, 1H, CH-5 diox), 4.94 (t, J= 4.6 Hz, 1H, CH-2 diox), 7.35 (d, J= 8.0 Hz, 2H, CH-2, CH-6 Ph), 7.45 (dd, J= 7.6, 8.1 Hz, 2H, CH-3, CH-5 Ph), 7.58 (t, J= 7.6 Hz, 1H, CH-4 Ph), 7.84 (d, J= 8.3 Hz, 2H, CH-3, CH-5 Ts), 8.06 (d, J= 8.3 Hz, 2H, CH-2, CH-6 Ts).

¹³C-NMR (100 MHz, CDCl₃) δ: 21.4 (CH₃), 64.5 (CH₂OCO), 68.3 (C-4, C-6 diox), 71.9 (C-5 diox), 98.0 (C-2 diox), 127.4 (C-3, C-5 Ts), 128.1 (C-3, C-5 Ph), 129.3 (C-1 Ph), 129.5 (C-2, C-6 Ts), 129.7 (C-2, C-6 Ph), 133.6 (C-4 Ph), 133.8 (C-1 Ts), 144.7 (C-4 Ts), 166.1 (CO).

HRMS-APCI: calcd for C₁₀H₁₂O₇S⁺: [M+H]⁺ 393.1003; found 393.1004.

Trans-[5-(tosyloxy)-1,3-dioxan-2-yl]methyl benzoate (3b)

p-Toluenesulfonyl chloride (1.20 g, 6.3 mmol) was added at 0 °C to a solution of 2b (1.0 g, 4.2 mmol), triethylamine (8.4 mmol, 1.17 mL) in dry CH₂Cl₂ (20 mL). The mixture was stirred at room temperature for 12 h. Ice and water were added and the mixture was extracted with CH₂Cl₂. The organic extracts were collected and dried (Na₂SO₄). Crystallization from ethyl acetate/cyclohexane afforded the desired compound as a white solid (0.86 g, 2.2 mmol, 52%).
m.p.: 83-85 °C.

¹H-NMR (400 MHz, CDCl₃) δ: 2.46 (s, 3H, CH₃), 3.57 (dd, J= 10.4, 11.3 Hz, 2H, CH-4ax, CH-6ax diox), 4.14 (dd, J= 5.3, 11.3 Hz, 2H, CH-4eq, CH-6eq diox), 4.32 (d, J= 4.6 Hz, 2H, CH₂O), 4.45-4.58 (m, 1H, CH-5 diox), 4.78 (t, J= 4.5 Hz, 1H, CH-2 diox), 7.31-7.45 (m, 2H, CH-2, CH-6 Ph), 7.43-7.56 (m, 2H, CH-3, CH-5 Ph), 7.58-7.64 (m, 1H, CH-4 Ph), 7.81 (d, J= 8.4 Hz, 2H, CH-3, CH-5 Ts), 8.04 (d, J= 8.4 Hz, 2H, CH-2, CH-6 Ts).

¹³C-NMR (100 MHz, CDCl₃) δ: 21.4 (CH₃), 63.9 (CH₂OCO), 67.5 (C-5 diox), 67.9 (C-4, C-6 diox), 98.1 (C-2 diox), 127.6 (C-3, C-5 Ts), 128.1 (C-3, C-5 Ph), 129.5 (C-2, C-6 Ts), 129.2 (C-1 Ph), 129.9 (C-2, C-6 Ph), 133.4 (C-4 Ph), 133.7 (C-1 Ts), 145.3 (C-4 Ts), (165.8 (CO).

HRMS-APCI: calcd for C₁₀H₁₀O₇S⁺: [M+H]⁺ 393.1003; found 393.1006.

General Procedure A

To a suspension of selected pyrimidine/purine (1.2 mmol) and K₂CO₃ (1.2 mmol), in anhydrous DMF (10 mL), was added portion wise, under nitrogen, the tosylated compound (3a or 3b, 1 mmol) and 18-crown-6 ether (catalytic amount). The resulting mixture was stirred and refluxed for 24 h.
After cooling to room temperature the mixture was concentrated under vacuum. The residue was partitioned between ethyl acetate and water. The organic layer was separated and the aqueous phase was extracted with ethyl acetate. The extracts were combined, washed with water and dried (Na₂SO₄). The suspension was filtered and the solvent evaporated under vacuum. The residue obtained was purified by flash chromatography to yield the desired compound.

**Trans-{5-[2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (4a)**
The compound was obtained from 3a and uracil, following the general procedure A (0.045 g, 0.135 mmol, 14%).

\[^1\text{H-}	ext{NMR (400 MHz, CDCl}_3\text{)}\] δ: 4.21-4.32 (m, 4H, CH₂-4, CH₂-6 diox), 4.39-4.48 (m, 2H, CH₂O), 4.49-4.54 (m, 1H, CH-5, diox), 4.97 (t, J= 4.1 Hz, 1H, CH-2 diox), 5.77 (d, J= 8.4 Hz, 1H, CH-5 uracil), 7.22 (d, J= 8.4 Hz, 1H, CH-6 uracil), 7.42-7.48 (m, 2H, CH-3, CH-5 Ph), 7.53-7.58 (m, 1H, CH-4 Ph), 8.00-8.08 (m, 2H, CH-2, CH-6 Ph).

\[^{13}\text{C-NMR (100 MHz, CDCl}_3\text{)}\] δ: 47.8 (C-5 diox), 64.3 (CH₃OCO), 68.3 (C-4, C-6 diox), 99.1 (C-2 diox), 102.1 (C-5 uracil), 128.5 (C-3, C-5 Ph), 129.5 (C-1 Ph), 129.8 (C-2, C-6 Ph), 133.5 (C-4 Ph), 143.4 (C-6 uracil), 151.1 (C-2 uracil), 163.1 (C-4 uracil), 166.0 (CO).

HRMS-ESI: calcd for C\(_{16}\)H\(_{17}\)N\(_{2}\)O\(_{6}\)^+: [M+H]^+ 333.1081; found 333.1083.

**Cis-{5-[2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (4b)**
The compound was obtained from 3b and uracil, following the general procedure A (0.052 g, 0.156 mmol, 16% yield).

\[^1\text{H-}	ext{NMR (400 MHz, CDCl}_3\text{)}\] δ: 4.22-4.32 (m, 4H, CH₂-4, CH₂-6 diox), 4.41 (br s, 1H, CH-5 diox), 4.43-4.53 (m, 2H, CH₂O), 5.08 (t, J= 3.9 Hz, 1H, CH-2 diox), 5.62 (d, J= 8.1 Hz, 1H, CH-5 uracil), 7.42-7.53 (m, 2H, CH-3, CH-5 Ph), 7.56-7.65 (m, 1H, CH-4 Ph), 8.03-8.12 (m, 2H, CH-2, CH-6 Ph), 8.30 (d, J= 8.1 Hz, 1H, CH-6 uracil), 8.98 (br s, 1H, NH).

\[^{13}\text{C-NMR (100 MHz, CDCl}_3\text{)}\] δ: 47.7 (C-5 diox), 64.3 (CH₃OCO), 68.9 (C-4, C-6 diox), 99.0 (C-2 diox), 102.0 (C-5 uracil), 128.4 (C-3, C-5 Ph), 129.5 (C-1 Ph), 129.9 (C-2, C-6 Ph), 133.6 (C-4 Ph), 143.2 (C-6 uracil), 151.0 (C-2 uracil), 162.8 (C-4 uracil), 166.1 (CO).

HRMS-ESI: calcd. for C\(_{16}\)H\(_{17}\)N\(_{2}\)O\(_{6}\)^+: [M+H]^+ 333.1081; found 333.1079.

**Trans-{5-[5-chloro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (5a)**
The compound was obtained from 3a and 5-chlorouracil, following the general procedure A (0.041 g, 0.112 mmol, 11%).
\[ ^1 \text{H-NMR (400 MHz, DMSO)} \delta: 3.96 (dd, J = 10.6, 11.2 Hz, 2H, CH-4_{ax}, CH-6_{ax} \text{ diox}), 4.11 (dd, J = 4.9, 11.2 Hz, 2H, CH-4_{eq}, CH-6_{eq} \text{ diox}), 4.45 (d, J = 3.9 Hz, 2H, CH\text{\textsubscript{2}}O), 4.47-4.59 (m, 1H, CH-5 diox), 4.96 (t, J = 3.9 Hz, 1H, CH-2 diox), 7.47 (dd, J = 7.5, 7.9 Hz, 2H, CH-3, CH-5 Ph), 7.61 (t, J = 7.5 Hz, 1H, CH-4 Ph), 7.90 (s, 1H, CH-6 uracil), 7.95 (d, J = 7.9 Hz, 2H, CH-2, CH-6 Ph). \]

\[ ^13 \text{C-NMR (100 MHz, CDCl\textsubscript{3})} \delta: 48.3 (C-5 diox), 63.8 (CH\text{\textsubscript{3}}OCO), 66.4 (C-4, C-6 diox), 97.8 (C-2 diox), 106.6 (C-5 uracil), 128.7 (C-3, C-5 Ph), 128.8 (C-1 Ph), 129.4 (C-2, C-6 Ph), 134.0 (C-4 Ph), 140.1 (C-2 uracil), 150.5 (C-2 uracil), 160.3 (C-4 uracil), 166.3 (CO). \]

HRMS-ESI: calcd for C\text{\textsubscript{16}}H\text{\textsubscript{16}}ClN\text{\textsubscript{2}}O\textsubscript{6}: [M+H]\textsuperscript{+} 367.0691; found 367.0695.

**Cis-[5-[5-chloro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl]methyl benzoate (5b)**

The compound was obtained from 3b and 5-chlorouracil, following the general procedure A (0.046 g, 0.125 mmol, 12%).

\[ ^1 \text{H-NMR (400 MHz, CDCl\textsubscript{3})} \delta: 4.19-4.37 (m, 4H, CH\text{\textsubscript{2}}-4, CH\text{\textsubscript{2}}-6 diox), 4.50 (br s, 1H, CH-5 diox), 4.53 (d, J = 3.8 Hz, 2H, CH\text{\textsubscript{2}}O), 5.11 (t, J = 3.8 Hz, CH-2 diox), 7.53 (dd, J = 7.5, 8.0 Hz, 2H, CH-3, CH-5 Ph), 7.69 (dd, J = 1.3, 7.5 Hz, 1H, CH-4 Ph), 7.94 (dd, J = 1.3, 8.0 Hz, 2H, CH-2, CH-6 Ph), 8.65 (s, 1H, CH-6 uracil).

\[ ^13 \text{C-NMR (100 MHz, CDCl\textsubscript{3})} \delta: 48.5 (C-5 diox), 64.0 (CH\text{\textsubscript{3}}OCO), 68.5 (C-4, C-6 diox), 99.0 (C-2 diox), 108.7 (C-5 uracil), 128.3 (C-3, C-5 Ph), 129.6 (C-2, C-6 Ph), 129.9 (C-1 Ph), 133.2 (C-4 Ph), 139.6 (C-6 uracil), 149.2 (C-2 uracil), 157.8 (C-4 uracil), 166.1 (CO). \]

HRMS-ESI: calcd. for C\text{\textsubscript{16}}H\text{\textsubscript{16}}ClN\text{\textsubscript{2}}O\textsubscript{6}: [M+H]\textsuperscript{+} 367.0691; found 367.0692.

**Trans-[5-[5-fluoro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl]methyl benzoate (6a)**

The compound was obtained from 3a and 5-fluorouracil, following the general procedure A (0.048 g, 0.137 mmol, 13%).

\[ ^1 \text{H-NMR (400 MHz, DMSO)} \delta: 4.10-4.24 (m, 4H, CH\text{\textsubscript{2}}-4, CH\text{\textsubscript{2}}-6 diox), 4.33 (d, J = 4.3 Hz, 2H, CH\text{\textsubscript{2}}O), 4.49-4.59 (m, 1H, CH-5 diox), 5.09 (t, J = 4.3 Hz, 1H, CH-2 diox), 7.53 (dd, J = 7.3, 7.8 Hz, 2H, CH-3, CH-5 Ph), 7.68 (t, J = 7.8 Hz, 1H, CH-4 Ph), 8.01 (d, J = 7.3 Hz, 2H, CH-2, CH-6 Ph), 8.15 (d, J\textsubscript{H-F} = 6.5 Hz, 1H, CH-6 uracil).

\[ ^13 \text{C-NMR (100 MHz, CDCl\textsubscript{3})} \delta: 48.6 (C-5 diox), 64.2 (CH\text{\textsubscript{3}}OCO), 68.9 (C-4, C-6 diox), 99.6 (C-2 diox), 127.4 (d, J\textsubscript{C-F} = 34 Hz, C-6 uracil), 128.2 (C-3, C-5 Ph), 129.3 (C-1 Ph), 129.8 (C-2, C-6 Ph), 133.2 (C-4 Ph.), 140.0 (d, J\textsubscript{C-F} = 230 Hz, C-5 uracil), 149.8 (C-2 uracil), 157.0 (d, J\textsubscript{C-F} = 24 Hz, C-4 uracil), 166.1 (CO). \]
HRMS-ESI: calcd for C_{16}H_{16}FN_{2}O_{6}^+: [M+H]^+ 351.0987; found 351.0988.

Cis-{5-[5-fluoro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (6b)
The compound was obtained from 3b and 5-fluorouracil, following the general procedure A (0.040 g, 0.114 mmol, 11%).

{^1}H-NMR (400 MHz, CDCl₃) δ: 4.26-4.39 (m, 4H, CH₂-4, CH₂-6 diox), 4.50 (br s, 1H, CH-5 diox), 4.53 (d, J= 3.5 Hz, 2H, CH₂O), 5.10 (t, J= 3.5 Hz, CH-2 diox), 7.50 (dd, J= 7.2, 7.6 Hz, 2H, CH-3, CH-5 Ph), 7.62 (t, J= 7.6 Hz, 1H, CH-4 Ph), 7.94 (d, J= 7.2 Hz, 2H, CH-2, CH-6 Ph), 8.62 (d, J_{H,F}= 6.5 Hz, 1H, CH-6 uracil).

{^{13}}C-NMR (100 MHz, CDCl₃) δ: 48.4 (C-5 diox), 64.3 (CH₂OCO), 68.7 (C-4, C-6 diox), 98.9 (C-2 diox), 127.6 (d, J_{C,F}= 33 Hz, C-6 uracil), 128.3 (C-3, C-5 Ph), 129.1 (C-1 Ph), 129.5 (C-2, C-6 Ph), 133.1 (C-4 Ph), 139.1 (d, J_{C,F}= 232 Hz, C-5 uracil), 148.9 (C-2 uracil), 156.8 (d, J_{C,F}= 22 Hz, C-4 uracil), 166.0 (CO).

HRMS-ESI: calcd for C_{16}H_{16}FN_{2}O_{6}^+: [M+H]^+ 351.0987; found 351.0985.

Trans-{5-[5-bromo-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (7a)
The compound was obtained from 3a and 5-bromouracil, following the general procedure A (0.051 g, 0.124 mmol, 12%).

{^1}H-NMR (400 MHz, DMSO) δ: 4.01-4.25 (m, 4H, CH₂-4, CH₂-6 diox), 4.34 (d, J= 4.2 Hz, 2H, CH₂O), 4.44-4.56 (m, 1H, CH-5 diox), 4.97 (t, J= 4.2 Hz, 1H, CH-2 diox), 7.49 (dd, J= 7.3, 7.9 Hz, 2H, CH-3, CH-5 Ph), 7.62 (t, J= 7.3 Hz, 1H, CH-4 Ph), 7.94 (d, J= 7.9 Hz, 2H, CH-2, CH-6 Ph), 8.05 (s, 1H, CH-6 uracil).

{^{13}}C-NMR (100 MHz, CDCl₃) δ: 48.8 (C-5 diox), 66.5 (CH₂OCO), 68.5 (C-4, C-6 diox), 96.7 (C-5 uracil), 97.3 (C-2 diox), 128.3 (C-3, C-5 Ph), 129.0 (C-1 Ph), 129.9 (C-2, C-6 Ph), 133.4 (C-4 Ph), 142.5 (C-6 uracil), 149.4 (C-2 uracil), 157.6 (C-4 uracil), 166.1 (CO).

HRMS-ESI: calcd for C_{16}H_{16}BrN_{2}O_{6}^+: [M+H]^+ 411.0186; found 411.0183.

Cis-{5-[5-bromo-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (7b)
The compound was obtained from 3b and 5-bromouracil, following the general procedure A (0.062 g, 0.151 mmol, 15%).
$^{1}$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.26-4.40 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.46 (br s, 1H, CH-5 diox), 4.52 (d, J= 3.9 Hz, 2H, CH$_2$O), 5.11 (t, J= 3.9 Hz, 1H, CH-2 diox), 7.49 (dd, J= 7.4, 7.9 Hz, 2H, CH-3, CH-5 Ph), 7.61 (dt, J= 1.3, 7.4 Hz, 1H, CH-4 Ph), 7.95 (dd, J= 1.3, 7.9 Hz, 2H, CH-2, CH-6 Ph), 8.73 (s, 1H, CH-6 uracil).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 48.6 (C-5 diox), 64.1 (CH$_2$OCO), 68.5 (C-4, C-6 diox), 96.3 (C-5 uracil), 99.0 (C-2 diox), 128.3 (C-3, C-5 Ph), 129.1 (C-1 Ph), 129.6 (C-2, C-6 Ph), 133.1 (C-4 Ph), 142.1 (C-6 uracil), 149.2 (C-2 uracil), 157.6 (C-4 uracil), 165.9 (CO).

HRMS-ESI: calcd for C$_{16}$H$_{16}$BrN$_2$O$_6$: [M+H]$^+$ 411.0186; found 411.0185.

Trans-{$[5$-iodo-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (8a)

The compound was obtained from 3a and 5-iodouracil, following the general procedure A (0.046 g, 0.100 mmol, 10%).

$^{1}$H-NMR (400 MHz, DMSO) $\delta$: 3.98 (dd, J= 10.3, 11.2 Hz, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.13 (dd, J= 4.6, 11.2 Hz, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.37 (d, J= 4.2 Hz, 2H, CH$_2$O), 4.44-4.54 (m, 1H, CH-5 diox), 5.09 (t, J= 4.2 Hz, 1H, CH-2 diox), 7.51 (dd, J= 7.4, 8.0 Hz, 2H, CH-3, CH-5 Ph), 7.62 (d, J= 7.4 Hz, 1H, CH-4 Ph), 8.02 (d, J= 8.0 Hz, 2H, CH-2, CH-6 Ph), 8.23 (s, 1H, CH-6 uracil).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 48.4 (C-5 diox), 63.9 (CH$_2$OCO), 67.8 (C-4, C-6 diox), 71.0 (C-5 uracil), 98.3 (C-2 diox), 128.1 (C-3, C-5 Ph), 129.1 (C-1 Ph), 129.5 (C-2, C-6 Ph), 133.1 (C-4 Ph), 146.5 (C-6 uracil), 149.9 (C-2 uracil), 158.8 (C-4 uracil), 166.1 (CO).

HRMS-ESI: calcd for C$_{16}$H$_{16}$IN$_2$O$_6$: [M+H]$^+$ 459.0048; found 459.0050.

Cis-{$[5$-iodo-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl}methyl benzoate (8b)

The compound was obtained from 3b and 5-iodouracil, following the general procedure A (0.052 g, 0.114 mmol, 11%).

$^{1}$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.25-4.40 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.45 (br s, 1H, CH-5 diox), 4.52 (d, J= 4.1 Hz, 2H, CH$_2$O), 5.11 (t, J= 4.1 Hz, 1H, CH-2 diox), 7.47 (dd, J= 7.3, 7.9 Hz, 2H, CH-3, CH-5 Ph), 7.59 (d, J= 7.3 Hz, 1H, CH-4 Ph), 7.99 (d, J= 7.9 Hz, 2H, CH-2, CH-6 Ph), 8.80 (s, 1H, CH-6 uracil).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 48.6 (C-5 diox), 64.2 (CH$_2$OCO), 68.5 (C-4, C-6 diox), 71.1 (C-5 uracil), 99.1 (C-2 diox), 128.2 (C-3, C-5 Ph), 129.2 (C-1 Ph), 129.8 (C-2, C-6 Ph), 133.2 (C-4 Ph), 147.1 (C-6 uracil), 149.6 (C-2 uracil), 158.6 (C-4 uracil), 165.8 (CO).

HRMS-ESI: calcd for C$_{16}$H$_{16}$IN$_2$O$_6$: [M+H]$^+$ 459.0048; found 459.0048.
Trans-\{5-[5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl\}methyl benzoate (9a)

The compound was obtained from 3a and thymine, following the general procedure A (0.049 g, 0.141 mmol, 14%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 1.99 (s, 3H, CH$_3$), 4.12 (dd, $J = 10.6$, 11.1 Hz, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.31 (dd, $J = 4.7$, 11.1 Hz, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.43 (d, $J = 4.6$ Hz, 2H, CH$_2$O), 4.55-4.69 (m, 1H, CH-5 diox), 5.00 (t, $J = 4.6$ Hz, 1H, CH-2 diox), 7.11 (s, 1H, CH-6 thymine), 7.51 (dd, $J = 7.3$, 7.9 Hz, 2H, CH-3, CH-5 Ph), 7.60 (t, $J = 7.3$ Hz, 1H, CH-4 Ph), 8.11 (d, $J = 7.9$, 2H, CH-2, CH-6 Ph), 9.11 (br s, 1H, NH).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 12.3 (CH$_3$), 46.1 (C-5 diox), 63.8 (CH$_2$OCO), 66.6 (C-4, C-6 diox), 98.6 (C-2 diox), 111.5 (C-5 thymine), 128.1 (C-3, C-5 Ph), 128.9 (C-1 Ph), 129.5 (C-2, C-6 Ph), 133.0 (C-4 Ph), 137.0 (C-6 thymine), 149.8 (C-2 thymine), 162.4 (C-4 thymine), 165.9 (CO).

HRMS-ESI: calcd for $C_{17}H_{19}N_2O_5^+$: [M+H]$^+$ 347.1238; found 347.1241.

Cis-\{5-[5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl\}methyl benzoate (9b)

The compound was obtained from 3b and thymine, following the general procedure A (0.044 g, 0.127 mmol, 13%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 1.85 (s, 3H, CH$_3$), 4.22-4.33 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.47 (br s, 1H, CH-5 diox), 4.49 (d, $J = 3.8$ Hz, 2H, CH$_2$O), 5.07 (t, $J = 3.8$ Hz, 1H, CH-2 diox), 7.47 (dd, $J = 7.4$, 7.8 Hz, 2H, CH-3, CH-5 Ph), 7.60 (t, $J = 7.4$ Hz, 1H, CH-4 Ph), 7.99-8.16 (m, 3H, CH-2, CH-6 Ph, CH-6 thymine), 8.66 (br s, 1H, NH).

$^{13}$C-NMR (100 MHz, DMSO) $\delta$: 12.3 (CH$_3$), 47.4 (C-5 diox), 64.1 (CH$_2$OCO), 68.7 (C-4, C-6 diox), 98.8 (C-2 diox), 110.4 (C-5 thymine), 128.2 (C-3, C-5 Ph), 129.1 (C-1 Ph), 129.5 (C-2, C-6 Ph), 133.1 (C-4 Ph), 138.7 (C-6 thymine), 151.0 (C-2 thymine), 163.5 (C-4 thymine), 165.9 (CO).

HRMS-ESI: calcd for $C_{17}H_{19}N_2O_6^+$: [M+H]$^+$ 347.1238; found 347.1240.

Trans-\{5-[4-amino-2-oxopyrimidin-1(2H)-yl]-1,3-dioxan-2-yl\}methyl benzoate (10a)

The compound was obtained from 3a and cytosine, following the general procedure A (0.050 g, 0.151 mmol, 15%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.14 (dd, $J = 10.2$, 11.4 Hz, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.28 (dd, $J = 5.2$, 10.2 Hz, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.41 (d, $J = 4.0$ Hz, 2H, CH$_2$O), 4.47-4.56 (m, 1H, CH-5 diox), 5.02 (t, $J = 4.3$ Hz, 1H, CH-2 diox), 5.66 (d, $J = 7.5$ Hz, 1H, CH-5 cytosine), 7.44 (dd, $J = 7.3$, 7.9 Hz, 2H, CH-2 diox), 8.76 (d, $J = 8.0$ Hz, 1H, CH-6 diox), 9.11 (br s, 1H, NH).

HRMS-ESI: calcd for $C_{17}H_{19}N_2O_5$: [M+H]$^+$ 347.1238; found 347.1240.

5-([5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl]-1,3-dioxan-2-yl]methyl benzoate (10b)

The compound was obtained from 3b and cytosine, following the general procedure A (0.050 g, 0.151 mmol, 15%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.14 (dd, $J = 10.2$, 11.4 Hz, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.28 (dd, $J = 5.2$, 10.2 Hz, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.41 (d, $J = 4.0$ Hz, 2H, CH$_2$O), 4.47-4.56 (m, 1H, CH-5 diox), 5.02 (t, $J = 4.3$ Hz, 1H, CH-2 diox), 5.66 (d, $J = 7.5$ Hz, 1H, CH-5 cytosine), 7.44 (dd, $J = 7.3$, 7.9 Hz, 2H, CH-2 diox), 8.76 (d, $J = 8.0$ Hz, 1H, CH-6 diox), 9.11 (br s, 1H, NH).

HRMS-ESI: calcd for $C_{17}H_{19}N_2O_5$: [M+H]$^+$ 347.1238; found 347.1240.
7.7 Hz, 2H, CH-3, CH-5 Ph), 7.58 (t, J= 7.3 Hz, 1H, CH-4 Ph), 7.61 (d, J= 7.7 Hz, 1H, CH-6 cytosine), 8.07 (d, J= 7.7 Hz, 2H, CH-2, CH-6 Ph).

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\): 48.3 (C-5 dioix), 64.2 (CH\(_2\)OCO), 68.1 (C-4, C-6 dioix), 94.3 (C-5 cytosine), 99.1 (C-2 dioix), 128.8 (C-3, C-5 Ph), 129.3 (C-1 Ph), 129.7 (C-2, C-6 Ph), 133.2 (C-4 Ph), 144.1 (C-6 cytosine), 149.3 (C-2 cytosine), 161.2 (C-4 cytosine), 166.0 (CO).

HRMS-ESI: calcd for \(C_{16}H_{18}N_{3}O_5^+\): [M+H]\(^+\) 332.1241; found 332.1240.

**Cis-\{5-[4-amino-2-oxoprimidin-1(2H)-yl]-1,3-dioxan-2-yl\}methyl benzoate (10b)**

The compound was obtained from 3b and cytosine, following the general procedure A (0.047 g, 0.142 mmol, 14% yield).

\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\): 4.24-4.40 (m, 4H, CH\(_2\)-4, CH\(_2\)-6 dioix), 4.51 (d, J= 3.8 Hz, 2H, CH\(_2\)O), 4.59 (br s, 1H, CH-5 dioix), 5.12 (t, J= 3.4 Hz, 1H, CH-2 dioix), 5.72 (d, J= 7.4 Hz, 1H, CH-5 cytosine), 7.47 (dd, J= 7.4, 7.8 Hz, 2H, CH-3, CH-5 Ph), 7.62 (t, J= 7.4 Hz, 1H, CH-4 Ph), 7.94 (d, J= 7.8 Hz, 2H, CH-2, CH-6 Ph), 8.11 (d, J= 7.4 Hz, 1H, CH-6 cytosine).

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\): 48.6 (C-5 dioix), 64.2 (CH\(_2\)OCO), 68.5 (C-4, C-6 dioix), 93.8 (C-5 cytosine), 98.8 (C-2 dioix), 128.5 (C-3, C-5 Ph), 129.5 (C-1 Ph), 129.8 (C-2, C-6 Ph), 133.5 (C-4 Ph), 144.2 (C-6 cytosine), 149.4 (C-2 cytosine), 161.0 (C-4 cytosine), 165.8 (CO).

HRMS-ESI: calcd for \(C_{16}H_{18}N_{3}O_5^+\): [M+H]\(^+\) 332.1241; found 332.1243.

**Trans-\{5-[4-amino-5-fluoro-2-oxoprimidin-1(2H)-yl]-1,3-dioxan-2-yl\}methyl benzoate (11a)**

The compound was obtained from 3a and 5-fluorocytosine, following the general procedure A (0.052 g, 0.149 mmol, 15%).

\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\): 4.13 (dd, J= 10.0, 11.2 Hz, 2H, CH-4\(_{ax}\), CH-6\(_{ax}\) dioix), 4.30 (dd, J= 4.5, 10.0 Hz, 2H, CH-4\(_{eq}\), CH-6\(_{eq}\) dioix), 4.51 (d, J= 4.3 Hz, 2H, CH\(_2\)O), 4.56-4.71 (m, 1H, CH-5 dioix), 5.09 (t, J= 4.3 Hz, 1H, CH-2 dioix), 7.31 (d, J\(_{HH}=\) 7.6 Hz, 1H, CH-6 cytosine), 7.41-7.54 (m, 2H, CH-3, CH-5 Ph), 7.55-7.68 (m, 1H, CH-4 Ph), 7.98-8.16 (m, 2H, CH-2, CH-6 Ph).

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\): 48.4 (C-5 dioix), 64.1 (CH\(_2\)OCO), 68.8 (C-4, C-6 dioix), 98.8 (C-2 dioix), 128.4 (C-3, C-5 Ph), 128.2 (d, J\(_{CF}=\) 30 Hz, C-6 cytosine), 129.2 (C-1 Ph), 129.8 (C-2, C-6 Ph), 133.4 (C-4 Ph), 137.4 (d, J\(_{CF}=\) 240 Hz, C-5 cytosine), 153.1 (C-2 cytosine), 156.3 (d, J\(_{CF}=\) 20 Hz, C-4 cytosine), 159.9 (CO).

HRMS-ESI: calcd for \(C_{16}H_{17}F_{N_{3}}O_5^+\): [M+H]\(^+\) 350.1147; found 350.1140.

**Cis-\{5-[4-amino-5-fluoro-2-oxoprimidin-1(2H)-yl]-1,3-dioxan-2-yl\}methyl benzoate (11b)**
The compound was obtained from 3b and 5-fluorocytosine, following the general procedure A (0.048 g, 0.137 mmol, 14% yield).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.26-4.44 (m, 4H, CH$_2$-4, CH$_2$-6 dioxygen), 4.51 (d, J= 4.0 Hz, 2H, CH$_2$O), 4.73 (br s, 1H, CH-5 dioxygen), 5.12 (t, J= 4.0 Hz, 1H, CH-2 dioxygen), 7.44 (dd, J= 7.3, 7.8 Hz, 2H, CH-3, CH-5 Ph), 7.61 (t, J= 7.3 Hz, 1H, CH-4 Ph), 7.91 (d, J$_{H,F}$= 7.4 Hz, 1H, CH-6 cytosine), 8.09 (d, J= 7.8 Hz 2H, CH-2, CH-6 Ph).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 48.6 (C-5 dioxygen), 64.3 (CH$_2$OCO), 68.5 (C-4, C-6 dioxygen), 99.0 (C-2 dioxygen), 128.4 (C-3, C-5 Ph), 128.7 (d, J$_{C,F}$= 33 Hz, C-6 cytosine), 129.7 (C-1 Ph), 129.9 (C-2, C-6 Ph), 133.6 (C-4 Ph), 137.8 (d, J$_{C,F}$= 242 Hz, C-5 cytosine), 153.4 (C-2 cytosine), 156.0 (d, J$_{C,F}$= 18 Hz, C-4 cytosine), 166.1 (CO).

HRMS-ESI: calcd for C$_{16}$H$_{17}$FN$_3$O$_5^+$: [M+H]$^+$ 350.1147; found 350.1151.

**Trans-[5-(6-chloro-9H-purin-9-yl)-1,3-dioxan-2-yl]methyl benzoate (12a)**

The compound was obtained from 3a and 6-chloropurine, following the general procedure A (0.065 g, 0.174 mmol, 17%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.48-4.59 (m, 6H, CH$_2$O, CH$_2$-4, CH$_2$-6 dioxygen), 4.89-5.01 (m, 1H, CH-5 dioxygen), 5.17 (t, J= 4.4 Hz, 1H, CH-2 dioxygen), 7.48 (dd, J= 7.4, 7.9 Hz, 2H, CH-3, CH-5 Ph), 7.61 (t, J= 7.4 Hz, 1H, CH-4 Ph), 8.06-8.18 (m, 3H, CH-2, CH-6 Ph, CH-8 purine), 8.71 (s, 1H, CH-2 purine).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 49.3 (C-5 dioxygen), 64.2 (CH$_2$OCO), 67.6 (C-4, C-6 dioxygen), 98.7 (C-2 dioxygen), 128.4 (C-3, C-5 Ph), 129.4 (C-1 Ph), 129.8 (C-2, C-6 Ph), 130.9 (C-5 purine), 133.4 (C-4 Ph), 145.2 (C-8 purine), 151.5 (C-4 purine), 151.7 (C-6 purine), 152.1 (C-2 purine), 166.2 (CO).

HRMS-ESI: calcd for C$_{17}$H$_{16}$ClN$_3$O$_4^+$: [M+H]$^+$ 375.0855; found 375.0861.

**Cis-[5-(6-chloro-9H-purin-9-yl)-1,3-dioxan-2-yl]methyl benzoate (12b)**

The compound was obtained from 3b and 6-chloropurine, following the general procedure A (0.059 g, 0.158 mmol, 15%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.30-4.38 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ dioxygen), 4.39-4.46 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ dioxygen), 4.49 (d, J= 4.3 Hz, 2H, CH$_2$O), 4.82 (br s, 1H, CH-5 dioxygen), 5.21 (t, J= 4.3 Hz, 1H, CH-2 dioxygen), 7.48 (dd, J= 7.5, 7.8 Hz, 2H, CH-3, CH-5 Ph), 7.60 (dd, J= 1.2, 7.5 Hz, 1H, CH-4 Ph), 8.07 (dd, J= 1.2, 7.8 Hz, 2H, CH-2, CH-6 Ph), 8.73 (s, 1H, CH-2 purine), 8.92 (s, 1H, CH-8 purine).

$^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 48.5 (C-5 dioxygen), 64.6 (CH$_2$OCO), 69.0 (C-4, C-6 dioxygen), 99.4 (C-2 dioxygen), 128.5 (C-3, C-5 Ph), 129.3 (C-1 Ph), 129.8 (C-2, C-6 Ph), 131.0 (C-5 purine), 133.5 (C-4
Ph), 145.4 (C-8 purine), 151.1 (C-4 purine), 151.5 (C-6 purine), 151.8 (C-2 purine), 166.1 (CO). HRMS-ESI: calcd for $C_{17}H_{16}ClN_{3}O_{4}^{\pm}$: [M+H]$^{\pm}$ 375.0855; found 375.0862.

**Trans-[5-(2-amino-6-chloro-9H-purin-9-yl)-1,3-dioxan-2-yl]methyl benzoate (13a)**

The compound was obtained from 3a and 6-chloro-2-amino-purine, following the general procedure A (0.056 g, 0.144 mmol, 14%).

$^1$H-NMR (400 MHz, CDC$_3$Cl) $\delta$: 4.33-4.42 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.49 (d, J= 4.0 Hz, 2H, CH$_2$O), 3.76 (br s, 1H, CH-5 diox), 5.11 (t, J= 4.0 Hz, CH-2 diox), 5.25 (br s, 2H, NH$_2$), 7.49 (dd, J= 7.4, 7.7 Hz, 2H, CH-3, CH-5 Ph), 7.62 (t, J= 7.4 Hz, 1H, CH-4 Ph), 7.74 (s, 1H, CH-8 purine), 8.11 (d, J= 7.8 Hz, 2H, CH-2, CH-6 Ph).

$^{13}$C-NMR (100 MHz, CDC$_3$Cl) $\delta$: 48.3 (C-5 diox), 64.8 (CH$_2$OCO), 68.0 (C-4, C-6 diox), 128.4 (C-3, C-5 Ph), 129.5 (C-1 Ph), 129.8 (C-2, C-6 Ph), 130.6 (C-5 purine), 133.2 (C-4 Ph), 139.5 (C-8 purine), 151.4 (C-6 purine), 152.9 (C-4 purine), 159.2 (C-2 purine), 159.9 (CO). HRMS-ESI: calcd for $C_{17}H_{15}ClN_{3}O_{4}^{\pm}$: [M+H]$^{\pm}$ 390.0964; found 390.0958.

**Cis-[5-(2-amino-6-chloro-9H-purin-9-yl)-1,3-dioxan-2-yl]methyl benzoate (13b)**

The compound was obtained from 3b and 6-chloro-2-amino-purine, following the general procedure A (0.063 g, 0.162 mmol, 16%).

$^1$H-NMR (400 MHz, CDC$_3$Cl) $\delta$: 4.30-4.44 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.50 (d, J= 4.2 Hz, 2H, CH$_2$O), 4.69 (br s, 1H, CH-5 diox), 5.05 (br s, 2H, NH$_2$), 5.18 (t, J= 4.2 Hz, 1H, CH-2 diox), 7.51 (dd, J= 7.4, 7.8 Hz, 2H, CH-3, CH-5 Ph), 7.62 (t, J= 7.4 Hz, 1H, CH-4 Ph), 8.09 (d, J= 7.8 Hz, 2H, CH-2, CH-6 Ph), 8.77 (s, 1H, CH-8 purine).

$^{13}$C-NMR (100 MHz, CDC$_3$Cl) $\delta$: 48.8 (C-5 diox), 64.4 (CH$_2$OCO), 68.8 (C-4, C-6 diox), 128.9 (C-3, C-5 Ph), 129.4 (C-1 Ph), 129.9 (C-2, C-6 Ph), 130.8 (C-5 purine), 133.5 (C-4 Ph), 139.6 (C-8 purine), 151.5 (C-6 purine), 152.7 (C-4 purine), 159.1 (C-2 purine), 166.0 (CO). HRMS-ESI: calcd for $C_{17}H_{15}ClN_{3}O_{4}^{\pm}$: [M+H]$^{\pm}$ 390.0964; found 390.0969.

**General procedure B**

The selected pyrimidine/purine derivative (0.136 mmol) was dissolved in concentrated aqueous ammonia solution (15 mL) and stirred for 5 h in a Pyrex pressure tube. After evaporation of the solvent under vacuum, the residue was crystallized from methanol/diethyl ether to give the desired compound.

**Trans-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (14a)**
The compound was obtained from compound 4a following the general procedure B (0.025 g, 0.110 mmol, 81%).
m.p.: 256-258 °C.
$^1$H-NMR (400 MHz, DMSO) δ: 3.31-3.42 (m, 2H, CH$_2$OH), 3.89-4.05 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.32-4.51 (m, 1H, CH-5 diox), 4.54 (t, J= 3.9 Hz, 1H, CH-2 diox), 4.82 (t, J= 5.8 Hz, 1H, OH), 5.61 (d, J= 7.5 Hz, 1H, CH-5 uracil), 7.72 (d, J= 7.5 Hz, 1H, CH-6 uracil), 11.37 (br s, 1H, NH).
$^{13}$C-NMR (100 MHz, DMSO) δ: 48.0 (C-5 diox), 65.5 (CH$_2$OH), 66.7 (C-4, C-6 diox), 101.2 (C-2 diox), 101.8 (C-5 uracil), 143.1 (C-6 uracil), 151.2 (C-2 uracil), 163.5 (C-4 uracil).
Anal. Calcd for C$_9$H$_{12}$N$_2$O$_5$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.43; H, 5.52; N, 12.11.
HRMS-ESI: calcd for C$_9$H$_{13}$N$_2$O$_5^+$: [M+H]$^+$ 229.0819; found 229.0818.

**Cis-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (14b)**
The compound was obtained from compound 4b following the general procedure B (0.026 g, 0.114 mmol, 73%).
m.p.: 198-200 °C.
$^1$H-NMR (400 MHz, DMSO) δ: 3.32-3.46 (m, 2H, CH$_2$OH), 4.01-4.13 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.15-4.23 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.29 (br s, 1H, CH-5 diox), 4.68 (t, J= 4.3 Hz, 1H, CH-2 diox), 4.86 (t, J= 6.3 Hz, 1H, OH), 5.58 (d, J= 8.0 Hz, 1H, CH-5 uracil), 8.15 (d, J= 8.0 Hz, 1H, CH-6 uracil), 11.32 (br s, 1H, NH).
$^{13}$C-NMR (100 MHz, DMSO) δ: 47.4 (C-5 diox), 62.5 (CH$_2$OH), 67.8 (C-4, C-6 diox), 100.7 (C-2 diox), 101.3 (C-5 uracil), 143.8 (C-6 uracil), 160.1 (C-2 uracil), 163.3 (C-4 uracil).
Anal. Calcd for C$_9$H$_{12}$N$_2$O$_5$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.59; H, 5.70; N, 12.31.
HRMS-ESI: calcd for C$_9$H$_{13}$N$_2$O$_5^+$: [M+H]$^+$ 229.0819; found 229.0821.

**Trans-5-chloro-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (15a)**
The compound was obtained from compound 5a following the general procedure B (0.023 g, 0.088 mmol, 79%).
m.p.: 189-191 °C.
$^1$H-NMR (400 MHz, DMSO) δ: 3.33-3.44 (m, 2H, CH$_2$OH), 3.90-4.09 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.41-4.52 (m, 1H, CH-5 diox), 4.54 (t, J= 4.0 Hz, 1H, CH-2 diox), 4.80 (t, J= 5.8 Hz, 1H, OH), 8.13 (s, 1H, CH-6 uracil), 11.21 (br s, 1H, NH).
$^{13}$C-NMR (100 MHz, DMSO) δ: 48.1 (C-5 diox), 65.3 (CH$_2$OH), 66.8 (C-4, C-6 diox), 101.3 (C-2 diox), 107.6 (C-5 uracil), 139.9 (C-6 uracil), 151.3 (C-2 uracil), 163.7 (C-4 uracil).
Anal. Calcd for C$_9$H$_{11}$ClN$_2$O$_5$: C, 41.16; H, 4.22; N, 10.67. Found: C, 40.93; H, 4.19; N, 10.33.
HRMS-ESI: calcd for C$_{9}$H$_{12}$ClN$_{2}$O$_{5}$$^{+}$: [M+H]$^{+}$ 263.0429; found 263.0432.

**Cis-5-chloro-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (15b)**
The compound was obtained from compound **5b** following the general procedure B (0.026 g, 0.099 mmol, 79%).
m.p.: 207-209 °C.
$^{1}$H-NMR (400 MHz, DMSO) δ: 3.34-3.47 (m, 2H, CH$_{2}$OH), 4.01-4.12 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.13-4.21 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.31 (br s, 1H, CH-5 diox), 4.71 (t, J= 4.1 Hz, 1H, CH-2 diox), 4.95 (t, J= 6.0 Hz, 1H, OH), 8.47 (s, 1H, CH-6 uracil), 11.30 (br s, 1H, NH).
$^{13}$C-NMR (100 MHz, DMSO) δ: 47.5 (C-5 diox), 62.4 (CH$_{2}$OH), 68.0 (C-4, C-6 diox), 100.6 (C-2 diox), 108.3 (C-5 uracil), 141.2 (C-6 uracil), 160.3 (C-2 uracil), 163.4 (C-4 uracil).
Anal. Calcd for C$_{9}$H$_{11}$ClN$_{2}$O$_{5}$: C, 41.16; H, 4.22; N, 10.67. Found: C, 41.05; H, 4.14; N, 10.41. HRMS-ESI: calcd for C$_{9}$H$_{12}$ClN$_{2}$O$_{5}$$^{+}$: [M+H]$^{+}$ 263.0429; found 263.0428.

**Trans-5-fluoro-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (16a)**
The compound was obtained from compound **6a** following the general procedure B (0.022 g, 0.089 mmol, 65%).
m.p.: 173-175 °C.
$^{1}$H-NMR (400 MHz, DMSO) δ: 3.23-3.40 (m, 2H, CH$_{2}$OH), 3.81-4.04 (m, 4H, CH$_{2}$-4, CH$_{2}$-6 diox), 4.39-4.49 (m, 1H, CH-5 diox), 4.51 (t, J= 4.2 Hz, 1H, CH-2 diox), 4.80 (t, J= 6.2 Hz, 1H, OH), 8.11 (d, J$_{H-F}$= 6.3 Hz, 1H, CH-6 uracil), 11.81 (br s, 1H, NH).
$^{13}$C-NMR (100 MHz, DMSO) δ: 47.9 (C-5 diox), 62.6 (CH$_{2}$OH), 66.7 (C-4, C-6 diox.), 101.8 (C-2 diox), 126.3 (d, J$_{C-F}$ = 33 Hz, C-6 uracil), 139.6 (d, J$_{C-F}$ = 232 Hz, C-5 uracil), 149.8 (C-2 uracil), 158.2 (d, J$_{C-F}$= 24 Hz, C-4 uracil).
Anal. Calcd for C$_{9}$H$_{11}$FNN$_{2}$O$_{5}$: C, 43.91; H, 4.50; N, 11.38. Found: C, 43.99; H, 4.51; N, 11.55. HRMS-ESI: calcd for C$_{9}$H$_{12}$FN$_{2}$O$_{5}$$^{+}$: [M+H]$^{+}$ 247.0725; found 247.0726.

**Cis-5-fluoro-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (16b)**
The compound was obtained following the general procedure B from compound **6b** (0.020 g, 0.081 mmol, 71%).
m.p.: 188-190 °C.
$^{1}$H-NMR (400 MHz, DMSO) δ: 3.27-3.44 (m, 2H, CH$_{2}$OH), 4.07-4.14 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.15-4.28 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.30 (br s, 1H, CH-5 diox), 4.71 (t, J= 4.2 Hz, 1H,
CH-2 diox), 4.91 (t, J= 6.1 Hz, 1H, OH), 8.37 (d, J_H,F= 6.5 Hz, 1H, CH-6 uracil), 11.65 (br s, 1H, NH).

$^1$C-NMR (100 MHz, DMSO) δ: 47.6 (C-5 diox), 62.3 (CH$_2$OH), 67.9 (C-4, C-6 diox), 100.8 (C-2 diox), 125.5 (d, J_C:F = 32 Hz, C-6 uracil), 139.9 (d, J_C:F = 230 Hz, C-5 uracil), 149.9 (C-2 uracil) 157.0 (d, J_C:F= 26 Hz, C-4 uracil).


**Trans-5-bromo-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (17a)**

The compound was obtained from compound 7a following the general procedure B (0.026 g, 0.085 mmol, 69%).

m.p.: 155-157 °C.

$^1$H-NMR (400 MHz, DMSO) δ: 3.31-3.52 (m, 2H, CH$_2$OH), 3.92-4.12 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.39-4.49 (m, 1H, CH-5 diox), 4.52 (t, J= 4.4 Hz, 1H, CH-2 diox), 4.84 (t, J= 6.0 Hz, 1H, OH), 8.20 (s, 1H, CH-6 uracil), 11.79 (br s, 1H, NH).

$^1$C-NMR (100 MHz, DMSO) δ: 47.8 (C-5 diox), 62.5 (CH$_2$OH), 66.8 (C-4, C-6 diox), 96.2 (C-5 uracil), 101.2 (C-2 diox), 143.1 (C-6 uracil), 150.0 (C-2 uracil), 159.2 (C-4 uracil).


**Cis-5-bromo-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (17b)**

The compound was obtained from compound 7b following the general procedure B (0.030 g, 0.098 mmol, 65%).

m.p.: 171-173 °C.

$^1$H-NMR (400 MHz, DMSO) δ: 3.28-3.43 (m, 2H, CH$_2$OH), 4.09-4.16 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.18-4.30 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.32 (br s, 1H, CH-5 diox), 4.70 (t, J= 3.9 Hz, 1H, CH-2 diox), 4.96 (t, J= 6.4 Hz, 1H, OH), 8.45 (s, 1H, CH-6 uracil), 11.82 (br s, 1H, NH).

$^1$C-NMR (100 MHz, DMSO) δ: 47.5 (C-5 diox), 62.4 (CH$_2$OH), 68.0 (C-4, C-6 diox), 96.6 (C-5 uracil), 100.9 (C-2 diox), 143.8 (C-6 uracil), 150.0 (C-2 uracil), 159.0 (C-4 uracil).


**Trans-5-iodo-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (18a)**
The compound was obtained from compound 8a following the general procedure B (0.026 g, 0.073 mmol, 73%).

m.p.: 174-176 °C.

$^1$H-NMR (400 MHz, DMSO) $\delta$: 3.31-3.49 (m, 2H, CH$_2$OH), 3.95-4.14 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.42-4.58 (m, 1H, CH-5 diox), 4.61 (t, J= 4.1 Hz, 1H, CH-2 diox), 4.89 (t, J= 6.3 Hz, 1H, OH), 8.22 (s, 1H, CH-6 uracil), 11.75 (br s, 1H, NH).

$^{13}$C-NMR (100 MHz, DMSO) $\delta$: 47.9 (C-5 diox), 62.6 (CH$_2$OH), 66.8 (C-4, C-6 diox), 78.0 (C-5 uracil), 102.2 (C-2 diox), 143.1 (C-6 uracil), 151.2 (C-2 uracil), 160.2 (C-4 uracil).

Anal. Calcd for C$_9$H$_{11}$N$_2$O$_5$: C, 30.53; H, 3.13; N, 7.91. Found: C, 30.31; H, 3.02; N, 7.84.

HRMS-ESI: calcd for C$_9$H$_{12}$N$_2$O$_5^+$: [M+H]$^+$ 354.9785; found 354.9789.

Cis-5-iodo-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidine-2,4(1H,3H)-dione (18b)

The compound was obtained from compound 8b following the general procedure B (0.029 g, 0.082 mmol, 72%).

m.p.: 190-192 °C.

$^1$H-NMR (400 MHz, DMSO) $\delta$: 3.29-3.42 (m, 2H, CH$_2$OH), 3.99-4.11 (m, 2H, CH-4$_{ax}$, CH-6$_{ax}$ diox), 4.13-4.23 (m, 2H, CH-4$_{eq}$, CH-6$_{eq}$ diox), 4.33 (br s, 1H, CH-5 diox), 4.68 (t, J= 4.0 Hz, 1H, CH-2 diox), 4.98 (t, J= 6.7 Hz, 1H, OH), 8.61 (s, 1H, CH-6 uracil), 11.77 (br s, 1H, NH).

$^{13}$C-NMR (100 MHz, DMSO) $\delta$: 47.6 (C-5 diox), 62.3 (CH$_2$OH), 67.8 (C-4, C-6 diox), 77.5 (C-5 uracil), 100.7 (C-2 diox), 151.6 (C-6 uracil), 151.1 (C-2 uracil), 160.0 (C-4 uracil).

Anal. Calcd for C$_9$H$_{11}$N$_2$O$_5$: C, 30.53; H, 3.13; N, 7.91. Found: C, 30.51; H, 3.15; N, 7.97.

HRMS-ESI: calcd for C$_9$H$_{12}$N$_2$O$_5^+$: [M+H]$^+$ 354.9785; found 354.9792.

Trans-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]-5-methylpyrimidine-2,4(1H,3H)-dione (19a)

The compound was obtained from compound 9a following the general procedure B (0.025 g, 0.103 mmol, 73%).

m.p.: 190-192 °C.

$^1$H-NMR (400 MHz, DMSO) $\delta$: 1.78 (s, 3H, CH$_3$), 3.34-3.46 (m, 2H, CH$_2$OH), 3.89-4.02 (m, 4H, CH$_2$-4, CH$_2$-6 diox), 4.41-4.58 (m, 1H, CH-5 diox), 4.62 (t, J= 4.3 Hz, 1H, CH-2 diox), 4.93 (t, J= 6.1 Hz, 1H, OH), 7.62 (s, 1H, CH-6 thymine), 11.27 (br s, 1H, NH).

$^{13}$C-NMR (100 MHz, DMSO) $\delta$: 12.0 (CH$_3$), 47.1 (C-5 diox), 62.5 (CH$_2$OH), 66.6 (C-4, C-6 diox), 101.0 (C-2 diox), 109.1 (C-5 thymine), 138.2 (C-6 thymine), 150.9 (C-2 thymine), 163.5 (C-4 thymine).
Anal. Calcd for C\textsubscript{10}H\textsubscript{14}N\textsubscript{2}O\textsubscript{5}: C, 49.58; H, 5.83; N, 11.56. Found: C, 49.63; H, 5.89; N, 11.61. HRMS-ESI: calcd for C\textsubscript{10}H\textsubscript{15}N\textsubscript{2}O\textsubscript{5}: [M+H]\textsuperscript{+} 243.0975; found 243.0974.

Cis-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]-5-methylpyrimidine-2,4(1\textsubscript{H},3\textsubscript{H})-dione (19b)
The compound was obtained from compound 9b following the general procedure B (0.021 g, 0.087 mmol, 68%).
m.p.: 209-211 °C.
\textsuperscript{1}H-NMR (400 MHz, DMSO) \(\delta\): 1.81 (s, 3H, CH\textsubscript{3}), 3.30-3.42 (m, 2H, CH\textsubscript{2}OH), 4.02-4.12 (m, 2H, CH-4\textsubscript{ax}, CH-6\textsubscript{ax} diox), 4.13-4.23 (m, 2H, CH-4\textsubscript{eq}, CH-6\textsubscript{eq} diox), 4.31 (br s, 1H, CH-5 diox), 4.65 (t, J= 4.2 Hz, 1H, CH-2 diox), 4.96 (t, J= 6.0 Hz, 1H, OH), 8.04 (s, 1H, CH-6 thymine), 11.31 (br s, 1H, NH).
\textsuperscript{13}C-NMR (100 MHz, DMSO) \(\delta\): 12.5 (CH\textsubscript{3}), 47.2 (C-5 diox), 62.6 (CH\textsubscript{2}OH), 68.0 (C-4, C-6 diox), 101.1 (C-2 diox), 108.0 (C-5 thymine), 139.5 (C-6 thymine), 151.1 (C-2 thymine), 163.8 (C-4 thymine).
Anal. Calcd for C\textsubscript{10}H\textsubscript{15}N\textsubscript{2}O\textsubscript{5}: C, 49.58; H, 5.83; N, 11.56. Found: C, 49.61; H, 5.77; N, 11.31. HRMS-ESI: calcd for C\textsubscript{10}H\textsubscript{15}N\textsubscript{2}O\textsubscript{5}: [M+H]\textsuperscript{+} 243.0975; found 243.0977.

Trans-4-amino-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidin-2(1\textsubscript{H})-one (20a)
The compound was obtained from compound 10a following the general procedure B (0.021 g, 0.092 mmol, 61%).
m.p.: 165-167 °C.
\textsuperscript{1}H-NMR (400 MHz, DMSO) \(\delta\): 3.32-3.45 (m, 2H, CH\textsubscript{2}OH), 3.89-4.02 (m, 4H, CH\textsubscript{2}-4, CH\textsubscript{2}-6 diox), 4.43-4.59 (m, 1H, CH-5 diox), 4.62 (t, J= 4.0 Hz, 1H, CH-2 diox), 4.91 (t, J= 6.3 Hz, 1H, OH), 5.66 (d, J= 7.5 Hz, 1H, CH-5 cytosine), 7.10 (br s, 2H, NH\textsubscript{2}), 7.61 (d, J= 7.5 Hz, 1H, CH-6 cytosine).
\textsuperscript{13}C-NMR (100 MHz, DMSO) \(\delta\): 48.6 (C-5 diox), 62.6 (CH\textsubscript{2}OH), 67.4 (C-4, C-6 diox), 94.5 (C-5 cytosine), 101.3 (C-2 diox), 143.3 (C-6 cytosine), 156.1 (C-2 cytosine), 165.5 (C-4 cytosine).
Anal. Calcd for C\textsubscript{9}H\textsubscript{13}N\textsubscript{3}O\textsubscript{4}: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.73; H, 5.86; N, 18.63. HRMS-ESI: calcd for C\textsubscript{9}H\textsubscript{13}N\textsubscript{3}O\textsubscript{4}: [M+H]\textsuperscript{+} 228.0979; found 228.0982.

Cis-4-amino-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidin-2(1\textsubscript{H})-one (20b)
The compound was obtained from compound 10b following the general procedure B (0.023 g, 0.101 mmol, 71%).
m.p.: 200-202 °C.
\(^1\)H-NMR (400 MHz, DMSO) \(\delta\): 3.31-3.44 (m, 2H, CH\(_2\)OH), 3.99-4.10 (m, 2H, CH-4\(_{ax}\), CH-6\(_{ax}\) diox), 4.13-4.23 (m, 2H, CH-4\(_{eq}\), CH-6\(_{eq}\) diox), 4.30 (br s, 1H, CH-5 diox), 4.67 (t, J= 4.1 Hz, 1H, CH-2 diox), 4.90 (t, J= 6.0 Hz, 1H, OH), 5.70 (d, J= 7.6 Hz, 1H, CH-5 cytosine), 6.97 (br s, 2H, NH\(_2\)), 8.11 (d, J= 7.6 Hz, 1H, CH-6 cytosine).

\(^13\)C-NMR (100 MHz, DMSO) \(\delta\): 48.0 (C-5 diox), 62.7 (CH\(_2\)OH), 68.0 (C-4, C-6 diox), 93.0 (C-5 cytosine), 101.1 (C-2 diox), 144.6 (C-6 cytosine), 155.6 (C-2 cytosine), 165.5 (C-4 cytosine).

Anal. Calcd for C\(_9\)H\(_{13}\)N\(_3\)O\(_4\): C, 47.57; H, 5.77; N, 18.49. Found: C, 47.19; H, 5.51; N, 18.25. HRMS-ESI: calecd for C\(_9\)H\(_{14}\)N\(_3\)O\(_4^+\): [M+H]\(^+\) 228.0979; found 228.0981.

**Trans-4-amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidin-2(IH)-one (21a)**
The compound was obtained from compound 11a following the general procedure B (0.025 g, 0.102 mmol, 68%).

m.p.: 189-191 °C.

\(^1\)H-NMR (400 MHz, DMSO) \(\delta\): 3.32-3.46 (m, 2H, CH\(_2\)OH), 3.88-4.02 (m, 4H, CH\(_2\)-4, CH\(_2\)-6 diox), 4.45-4.61 (m, 1H, CH-5 diox), 4.65 (t, J= 4.0 Hz, 1H, CH-2 diox), 4.92 (t, J= 6.0 Hz, 1H, OH), 7.70 (br s, 2H, NH\(_2\)), 8.03 (d, J\(_{H-F}\)= 7.4 Hz, 1H, CH-6 cytosine).

\(^13\)C-NMR (100 MHz, DMSO) \(\delta\): 48.7 (C-5 diox), 62.5 (CH\(_2\)OH), 67.5 (C-4, C-6 diox.), 101.2 (C-2 diox.), 128.4 (d, J\(_{C-F}\)= 32 Hz, C-6 cytosine), 137.9 (d, J\(_{C-F}\)= 242 Hz, C-5 cytosine), 153.5 (C-2 cytosine), 156.9 (d, J\(_{C-F}\)= 14 Hz, C-4 cytosine).

Anal. Calcd for C\(_9\)H\(_{12}\)FN\(_3\)O\(_4\): C, 44.08; H, 4.93; N, 17.14. Found: C, 44.36; H, 5.01; N, 17.33. HRMS-ESI: calecd for C\(_9\)H\(_{13}\)FN\(_3\)O\(_4^+\): [M+H]\(^+\) 246.0885; found 246.0887.

**Cis-4-amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-dioxan-5-yl]pyrimidin-2(IH)-one (21b)**
The compound was obtained from compound 11b following the general procedure B (0.020 g, 0.082 mmol, 60%).

m.p.: 250-252 °C.

\(^1\)H-NMR (400 MHz, DMSO) \(\delta\): 3.41 (dd, 2H, J= 4.1, 6.0 Hz, CH\(_2\)OH), 4.00-4.13 (m, 2H, CH-4\(_{ax}\), CH-6\(_{ax}\) diox), 4.14-4.25 (m, 2H, CH-4\(_{eq}\), CH-6\(_{eq}\) diox), 4.30 (br s, 1H, CH-5 diox), 4.71 (t, J= 4.1 Hz, 1H, CH-2 diox), 4.93 (t, J= 6.0 Hz, 1H, OH), 7.61 (br s, 2H, NH\(_2\)), 8.28 (d, J\(_{H-F}\)= 7.5 Hz, 1H, CH-6 cytosine).

\(^13\)C-NMR (100 MHz, DMSO) \(\delta\): 48.2 (C-5 diox), 62.6 (CH\(_2\)OH), 67.8 (C-4, C-6 diox), 101.1 (C-2 diox), 128.9 (d, J\(_{C-F}\)= 32 Hz, C-6 cytosine), 138.5 (d, J\(_{C-F}\)= 239 Hz, C-5 cytosine), 153.6 (C-2 cytosine), 157.2 (d, J\(_{C-F}\)= 13 Hz, C-4 cytosine).

HRMS-ESI: calcd for C₉H₁₃F₃N₂O₅⁺: [M+H]⁺ 246.0885; found 246.0881.

Trans-[5-(6-amino-9H-purin-9-yl)-1,3-dioxan-2-yl]methanol (22a)

Compound 12a (0.060 g, 0.160 mmol) was dissolved in concentrated aqueous ammonia solution (15 mL) and placed in reactor at 100 °C for 12 h. After solvent evaporation under vacuum, the residue was crystallized from methanol/diethyl ether to give the desired compound as a yellow solid (0.028 g, 0.111 mmol, 69%).
m.p.: 218-220 °C.

1H-NMR (400 MHz, DMSO) δ: 3.37-3.48 (m, 2H, CH₂OH), 4.17-4.32 (m, 4H, CH₂-4, CH₂-6 diox), 4.61-4.82 (m, 2H, CH-2, CH-5 diox), 4.94 (t, J= 6.2 Hz, 1H, OH), 7.23 (br s, 2H, NH₂), 8.10 (s, 1H, CH-2 purine), 8.21 (s, 1H, CH-8 purine).

13C-NMR (100 MHz, DMSO) δ: 49.3 (C-5 diox), 62.6 (CH₂OH), 67.8 (C-4, C-6 diox), 101.4 (C-2 diox), 118.8 (C-5 purine), 139.2 (C-8 purine), 149.0 (C-4 purine), 152.6 (C-2 purine), 156.0 (C-6 purine).

Anal. Calcd for C₁₀H₁₄N₃O₅: C, 47.81; H, 5.22; N, 27.87. Found: C, 47.96; H, 5.31; N, 27.93.


Cis-[5-(6-amino-9H-purin-9-yl)-1,3-dioxan-2-yl]methanol (22b)

Compound 12b (0.055 g, 0.147 mmol) was dissolved in concentrated aqueous ammonia solution (15 mL) and placed in reactor at 100 °C for 12 h. After solvent evaporation under vacuum, the residue was crystallized from methanol/diethyl ether to give the desired compound as a yellow solid (0.025 g, 0.100 mmol, 68%).
m.p.: 255-257 °C.

1H-NMR (400 MHz, DMSO) δ: 3.47 (dd, 2H, J= 4.0, 6.2 Hz, CH₂O), 4.02-4.16 (m, 2H, CH-4ax, CH-6ax diox), 4.18-4.32 (m, 2H, CH-4eq, CH-6eq diox), 4.51 (br s, 1H, CH-5 diox), 4.69 (t, J= 4.0 Hz, 1H, CH-2 diox), 4.90 (t, J= 6.2 Hz, 1H, OH), 7.17 (br s, 2H, NH₂), 8.08 (s, 1H, CH-2 purine), 8.40 (s, 1H, CH-8 purine).

13C-NMR (100 MHz, DMSO) δ: 49.3 (C-5 diox), 62.5 (CH₂OH), 67.9 (C-4, C-6 diox), 101.3 (C-2 diox), 118.9 (C-5 purine), 139.4 (C-8 purine), 149.5 (C-4 purine), 153.0 (C-2 purine), 156.3 (C-6 purine).

Anal. Calcd for C₁₀H₁₄N₃O₅: C, 47.81; H, 5.22; N, 27.87. Found: C, 47.86; H, 5.44; N, 28.03.


Trans-2-amino-9-[2-(hydroxymethyl)-1,3-dioxan-5-yl]-1H-purin-6(9H)-one (23a)
Compound 13a (0.052 g, 0.133 mmol) was dissolved in methanol and 40% NaOH aqueous solution was added. The reaction mixture was refluxed at 100 °C for 5 h, after the solvent was removed under vacuum. The solid residue was then dissolved in DMF and the insoluble was removed by filtration. DMF was evaporated under vacuum to give a black oil. Crystallization from methanol/diethyl ether afforded the desired compound as a yellow solid (0.030 g, 0.112 mmol, 84%).

m.p.: 278-280 °C.

1H-NMR (400 MHz, DMSO) δ: 3.32-3.46 (m, 2H, CH₂OH), 4.21-4.34 (m, 4H, CH₂-4, CH₂-6 diox), 4.31-4.60 (m, 2H, CH-2, CH-5 diox), 4.64 (t, J= 6.0 Hz, 1H, OH), 7.19 (br s, 2H, NH₂), 7.63 (s, 1H, CH-8 purine).

13C-NMR (100 MHz, DMSO) δ: 49.5 (C-5 diox), 62.7 (CH₂OH), 68.0 (C-4, C-6 diox), 101.6 (C-2 diox), 116.7 (C-5 purine), 134.6 (C-8 purine), 151.1 (C-4 purine), 155.4 (C-6 purine), 158.5 (C-2 purine).


HRMS-ESI: calcd for C₁₀H₁₂N₄O₄⁺: [M+H]⁺ 268.1040; found 268.1038.

Cis-2-amino-9-[2-(hydroxymethyl)-1,3-dioxan-5-yl]-1H-purin-6(9H)-one (23b)

Compound 13b (0.060 g, 0.154 mmol) was dissolved in methanol and 40% NaOH aqueous solution was added. The reaction mixture was refluxed at 100 °C for 5 h, after the solvent was removed under vacuum. The solid residue was then dissolved in DMF and the insoluble was removed by filtration. DMF was evaporated under vacuum to give a black oil. Crystallization from methanol/diethyl ether afforded the desired compound as a yellow solid (0.035 g, 0.131 mmol, 85%).

m.p.: 280-282 °C.

1H-NMR (400 MHz, DMSO) δ: 3.41-3.49 (m, 2H, CH₂OH), 4.01-4.13 (m, 2H, CH-4ax, CH-6ax diox), 4.19-4.31 (m, 3H, CH-5, CH-4eq, CH-6eq diox), 4.69 (t, J= 4.2 Hz, 1H, CH-2 diox), 4.81-4.92 (m, 1H, OH), 6.52 (br s, 2H, NH₂), 7.88 (s, 1H, CH-8 purine).

13C-NMR (100 MHz, DMSO) δ: 49.3 (C-5 diox), 62.5 (CH₂OH), 67.9 (C-4, C-6 diox), 101.3 (C-2 diox), 116.6 (C-5 purine), 134.9 (C-8 purine), 151.3 (C-4 purine), 155.8 (C-6 purine), 158.6 (C-2 purine).


3. Biological Assays

Anti-HIV activity

The anti-HIV activity and cytotoxicity of the compounds were evaluated against wild-type HIV-1 strain IIIB, and HIV-2 strain ROD in MT-4 cell cultures using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method. Briefly, stock solutions (10 x final concentration) of test compounds were added in 25 µL volumes to two series of triplicate wells so as to allow simultaneous evaluation of their effects on mock- and HIV-infected cells at the beginning of each experiment. Serial 5-fold dilutions of test compounds were made directly in flat-bottomed 96-well microtiter trays using a Biomek 3000 robot (Beckman instruments). Untreated control HIV- and mock-infected cell samples were included for each sample. Virus stock (50.0 µL) at 100-300 CCID₅₀ (50.0% cell culture infectious dose) or culture medium was added to either the virus-infected or mock-infected wells of the microtiter tray. Mock-infected cells were used to evaluate the effect of test compounds on uninfected cells in order to assess the cytotoxicity of the test compounds. Exponentially growing MT-4 cells were centrifuged for 5 min at 220 g and the supernatant was discarded. The MT-4 cells were resuspended at 6 x 10⁵ cells/mL and 50.0 µL volumes were transferred to the microtiter tray wells. Five days after infection, the viability of mock- and HIV-infected cells was examined spectrophotometrically by the MTT assay. The MTT assay is based on the reduction of yellow colored MTT by mitochondrial dehydrogenase activity of metabolically active cells to a blue-purple formazan that can be measured spectrophotometrically. The absorbances were read in an eight-channel computer-controlled photometer (Infinite M1000, Tecan), at two wavelengths (540 and 690 nm). All data were calculated using the median OD (optical density) values of three wells. The 50% cytotoxic concentration (CC₅₀) was defined as the concentration of the test compound that reduced the absorbance (OD540) of the mock-infected control sample by 50%. The concentration achieving 50% protection from the cytopathic effect of the virus in infected cells was defined as the 50% effective concentration (EC₅₀).

Antiviral and cytostatic activities

The compounds were evaluated against the following viruses: herpes simplex virus type 1 (HSV-1) strain KOS, thymidine kinase-deficient (TK⁻) HSV-1 KOS strain resistant to ACV (ACV³), herpes simplex virus type 2 (HSV-2) strain G, and vaccinia virus Lederle strain. Confluent cell cultures in microtiter 96-well plates were inoculated with 100 CCID₅₀ of virus (1 CCID₅₀ being the virus dose to infect 50% of the cell cultures) in the presence of varying concentrations of the test compounds.

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Viral cytopathogenicity or plaque formation was recorded as soon as it reached completion in the control virus-infected cell cultures that were not treated with the test compounds. Antiviral activity was expressed as the EC₅₀ or compound concentration required to reduce virus-induced cytopathogenicity.

For the cytostatic experiments, all assays were performed in 96-well microtiter plates. To each well were added (5-7.5) x 10⁴ tumor cells and a given amount of the test compound. The cells were allowed to proliferate for 48 h (murine leukemia L1210 cells) or 72 h (human lymphocytic CEM and Molt4 cells) at 37 °C in a humidified CO₂-controlled atmosphere. At the end of the incubation period, the cells were counted in a Coulter counter. The IC₅₀ (50% inhibitory concentration) was defined as the concentration of the compound that inhibited cell proliferation by 50%.

**Sulforhodamine B (SRB) assay**

Cells (5×10⁴ cells/ml) were treated with various concentrations of compounds in 96 well culture plates for 72 h. After incubation, cells were fixed with 10% trichloroacetic acid (TCA), dried, and stained with 0.4% SRB in 1% acetic acid. The unbound dye was washed out, and the stained cells were dried and resuspended in 10 mM Tris (pH 10.0). The absorbance at 515 nm was measured, and cell proliferation was determined as follows: cell proliferation (%) = (average absorbancecompound − average absorbanceday zero) / (average absorbancecontrol − average absorbanceday zero) × 100. IC₅₀ values were calculated by nonlinear regression analysis using Table Curve 2D v 5.01 (Systat Software Inc., Richmond, CA, USA).
4. X-ray Analysis

The structural investigation by single-crystal X-ray crystallography on 22b was carried out at room temperature on a Bruker-Nonius X8APEX diffractometer equipped with Mo-Kα generator and area detector. The structure was solved and refined on \( F_0^2 \) by standard methods, using SIR92\(^1\) and SHELXL-97\(^2\) softwares included in the WINGX v2013.3 package\(^3\). All nonhydrogen atoms were refined anisotropically; hydrogen atoms were located in \( \Delta F \) maps and fully refined with isotropic displacement parameters. Crystal data and refinement parameters for compound 22b are given in Table S1. A crystal packing diagram obtained using ORTEP-3 program\(^4\) is provided in Figure S1. The geometry of H-bond interactions is detailed in Table S2. CCDC-1015232 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

**Table S1.** Crystal data and refinement parameters for compound 22b.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>( \text{C}<em>{10}\text{H}</em>{12}\text{N}_3\text{O}_3 )</td>
</tr>
<tr>
<td>Formula weight</td>
<td>251.25</td>
</tr>
<tr>
<td>( T ), K</td>
<td>298(2)</td>
</tr>
<tr>
<td>( \lambda ), Å</td>
<td>0.71073</td>
</tr>
<tr>
<td>Crystal size, mm(^3)</td>
<td>0.36×0.32×0.27</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>( P \ 2_1/c ) (No. 14)</td>
</tr>
<tr>
<td>( a ), Å</td>
<td>13.5194(2)</td>
</tr>
<tr>
<td>( b ), Å</td>
<td>5.54460(10)</td>
</tr>
<tr>
<td>( c ), Å</td>
<td>15.0817(2)</td>
</tr>
<tr>
<td>( \alpha ), deg</td>
<td>90.00</td>
</tr>
<tr>
<td>( \beta ), deg</td>
<td>101.8958(7)</td>
</tr>
<tr>
<td>( \gamma ), deg</td>
<td>90.00</td>
</tr>
<tr>
<td>( V ), Å(^3)</td>
<td>1106.24(3)</td>
</tr>
<tr>
<td>( Z )</td>
<td>4</td>
</tr>
<tr>
<td>( D_{\text{calc}} ), g cm(^{-3})</td>
<td>1.509</td>
</tr>
<tr>
<td>( \mu ) (MoKα), mm(^{-1})</td>
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<tr>
<td>( F(000) )</td>
<td>528</td>
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<tr>
<td>( \theta ) range, deg</td>
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</tr>
<tr>
<td>Reflns collected</td>
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</tr>
<tr>
<td>( R ) int</td>
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</tr>
<tr>
<td>Data/restraints/parameters</td>
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<tr>
<td>Goodness-of-fit on ( F^2 )</td>
<td>1.043</td>
</tr>
<tr>
<td>Final ( R ) indices [( I &gt; 2\sigma(I) )]</td>
<td>( R1 = 0.0412 ), ( wR2 = 0.1199 )</td>
</tr>
<tr>
<td>( R ) indices (all data)</td>
<td>( R1 = 0.0498 ), ( wR2 = 0.1280 )</td>
</tr>
<tr>
<td>Largest diff. peak/hole, eÅ(^{-3})</td>
<td>0.375/-0.295</td>
</tr>
</tbody>
</table>
Figure S1. Crystal packing diagram for compound 22b, viewed along the $b$ axis. Atoms are represented as spheres with arbitrary radius. Dashed lines represent hydrogen-bond interactions. Symmetry codes: (i) $x, -y+2.5, z+0.5$; (ii) $x, -y+2.5, z-0.5$; (iii) $-x+1, y+0.5, -z-0.5$.

Table S2. Hydrogen bond geometry (Å, °) in compound 22b.

<table>
<thead>
<tr>
<th>$D$–H…A</th>
<th>$D$–H</th>
<th>H…A</th>
<th>$D$…A</th>
<th>$\angle D$–H…A</th>
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</thead>
<tbody>
<tr>
<td>O3–HO3…N2$^i$</td>
<td>0.88(2)</td>
<td>1.92(2)</td>
<td>2.7759(11)</td>
<td>164.0(17)</td>
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<tr>
<td>N5–HN5a…O2$^{ii}$</td>
<td>0.855(15)</td>
<td>2.242(16)</td>
<td>3.0265(11)</td>
<td>152.5(13)</td>
</tr>
<tr>
<td>N5–HN5b…N3$^{iii}$</td>
<td>0.938(16)</td>
<td>2.157(16)</td>
<td>3.0645(10)</td>
<td>162.3(14)</td>
</tr>
</tbody>
</table>

Symmetry codes: (i) $x, -y+2.5, z+0.5$; (ii) $x, -y+2.5, z-0.5$; (iii) $-x+1, y+0.5, -z-0.5$.

(2) Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112.