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Silylative *N*-hydroxyalkylation of amide compounds: application to the synthesis of acyclic alditol-based nucleoside analogues

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Abstract—A rare silylative hydroxyalkylation of amide compounds with chiral aldehydes has been developed utilizing a Lewis acid–Lewis base promoter system consisting of an equimolecular mixture of *tert*-butyldimethylsilyl trifluoromethanesulfonate and *N*-diisopropylethylamine. This approach culminated in the synthesis of several enantiopure acyclic nucleoside representatives comprising thymidine analogues **6**, **7**, **9**, **10**, **12** and **13**, uridine analogues **15** and **16**, and 6-chloropurine derivatives **18** and **19**.

1. Introduction

Tandem processes where two or more discrete reactions are triggered sequentially by the same reagent or catalyst system are inherently attractive for several reasons.[1,2] For example, they are simple and expeditious and can be managed with a substantial level of atom economy and stereocontrol. Their practical impact is markedly enhanced when a highly efficient, irreversible step terminates a scarcely productive cascade of reversible events, to give stable products which can be easily isolated.

A few years ago, the discovery was made in these laboratories that when a critical intramolecular aldol reaction, which is typically unproductive under conventional aldol coupling conditions,[3] was followed up by an irreversible silylation and used as the final step in the sequence of reversible events leading up to carbon–carbon bond formation, it became highly productive, as shown in Figure 1 (eq 1).[4] In the event, the combined use of a bulky silyl triflate with a suitable tertiary amine co-mediated enolsilane formation (**A** to **C**) as well as both carbon–carbon bond construction and aldolate oxygen silylation (**C** to **E**) to finally give *O*-silylated cycloaldols with complete conversion of the starting aldehyde substrate and excellent diastereocontrol.

In this paper, we establish that analogous Lewis acid–Lewis base combinations trigger sequential intermolecular hydroxyalkylation–silylation reactions of amide compounds with aldehydes leading to stable and easily isolated *N*-silyloxyalkylamides (*N*-acyl-*O*-silyl acetals) in high yields (Fig. 1, eq 2).

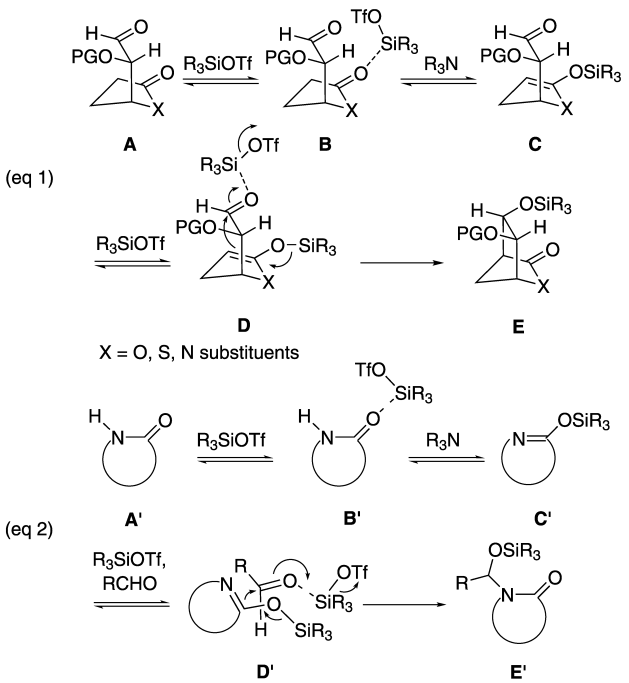

Figure 1. Parallelism between the silylative cycloaldolization cascade and the silylative hydroxyalkylation.

In this current study, we also demonstrate the utility of this silylative carbon–nitrogen bond-forming protocol in the mild synthesis of acyclic, alditol-based nucleoside

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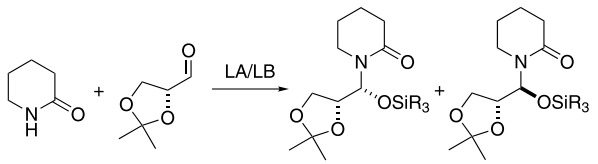
analogues in a chiral nonracemic format (e.g. compounds **6**, **7**, **9**, **10**, **12**, **13**, **15**, **16**, **18**, **19**).[5]

2. Results and discussion

To initiate our study, we examined the ability of the Lewis acid–Lewis base combinations (R_3SiOTf/R_3N) in promoting the silylative coupling between δ-valerolactam (**1**) and 2,3-*O*-isopropylidene-D-glyceraldehyde (**2**) delivering *anti*- and *syn*-configured silyloxypiperidinones **3** and **4** (Table 1).

Table 1. The optimum reaction conditions of silylative coupling between lactam **1** and aldehyde **2**: concerning the triflate/amine promoter system[a,b]



1 **2** **3a:** $R_3 = Bu^tMe_2$ **4a:** $R_3 = Bu^tMe_2$ **3b:** $R_3 = Et_3$ **4b:** $R_3 = Et_3$

Entry	LA (equiv.)	LB (equiv.)	Yield **3**+**4** [%]	Products	dr (**3**:**4**)
1	TBSOTf (1.0)	DIPEA (1.0)	<1		
2	TBSOTf (2.0)	DIPEA (2.0)	28	**3a**, **4a**	75:25
3	TBSOTf (3.0)	DIPEA (3.0)	70	**3a**, **4a**	77:23
4	TBSOTf (3.0)	—	<1		
5	—	DIPEA (3.0)	<1		
6	TBSOTf (4.0)	DIPEA (3.0)	5[c]	**3a**, **4a**	66:34
7	TBSOTf (3.0)	DIPEA (4.0)	<1		
8	TESOTf (3.0)	DIPEA (3.0)	95	**3b**, **4b**	55:45
9	TIPSOTf (3.0)	DIPEA (3.0)	<1		
10	TMSOTf (3.0)	DIPEA (3.0)	<1		
11	TBSOTf (3.0)	Et_3N (3.0)	<1		
12	TBSOTf (3.0)	Sparteine (3.0)	51	**3a**, **4a**	52:48

[a] The reactions were carried out with δ-valerolactam (1.0 equiv., 0.1 M) and 2,3-*O*-isopropylidene-D-glyceraldehyde (2.0 equiv.) at room temperature in THF, for 4 h.
[b] The diastereomeric ratio was determined from analysis of ^1H NMR spectra of the crude product.
[c] Aldehyde **2** was completely consumed.

Well aware of the fragile nature of the *N*-acyl hemiaminal functionality in **3** and **4**, we carefully selected the Lewis acid–Lewis base candidates, reasoning that truly acidic or basic conditions may be incompatible with the *N*,*O*-acetal group, as well as other functionalities in these compounds. The optimum reaction conditions of R_3SiOTf/R_3N-promoted silylative amination of **2** with lactam **1** are shown in Table 1. The nature of the acid–base pair as well as the amine/triflate ratio and the substrate/promoter stoichiometry were found to have a significant influence on the efficiency and reproducibility of the reaction.

On their own, neither the triflate Lewis acid nor the tertiary amine Lewis base are activators. Yet, a freshly prepared combination of 3.0 equiv. TBSOTf and 3.0 equiv. Hünig's base (DIPEA) in THF at room temperature was found to be a superb activator, with the best result summarized in entry 3.[6] When this reaction was carried out by changing the triflate acid–base ratio, it was found that an excess of triflate irremediably contaminated the reaction, whilst an excessive amount of amine rendered the reaction sluggish and unproductive (entries 6 and 7). Changing TBSOTf for TESOTf raised the reaction yield but resulted in a decrease in diastereoselectivity. On the contrary, sterically cumbersome triflates did not activate the reaction, as was the case for TMS. These experiments support the inference that silylation of the aldolate is the key to the success of this reaction. Indeed, when this key step is slowed down (use of TIPSOTf, entry 9) or when the protecting group of the aldolate oxygen is too labile to survive reaction conditions, (use of TMSOTf, entry 10) the reaction as a whole fails. Furthermore, the nature of the base proved critical as only encumbered tertiary amines proved to be efficacious agents. Among the solvents tested (Table 2), aprotic low polarity solvents proved to be effective for the reaction, and a 1:1 (v/v) mixture of THF/hexanes provided the best results (entry 5). Hydroxyalkylation at high concentration did not increase the chemical yield, and dilution only reduced the reaction rate with a negligible gain in diastereoselection (entries 6 and 7). Several reaction temperatures were examined, and coupling at −20 °C markedly reduced the yield, with no increase in diastereoselectivity (entry 8).

Table 2. The optimum reaction conditions of silylative coupling between lactam **1** and aldehyde **2**: concerning solvent, concentration and temperature[a,b]

Entry	Solvent (mL)	*T* (°C)	Yield **3**+**4** [%]	Products	dr (**3**:**4**)
1	THF (20)	25	70	**3a**, **4a**	77:23
2	CH_2Cl_2 (20)	25	33	**3a**, **4a**	58:42
3	Et_2O (20)	25	20	**3a**, **4a**	70:30
4	CH_3CN (20)	25	<1		
5	THF/hexanes (20)[c]	25	78	**3a**, **4a**	80:20
6	THF/hexanes (2)[c]	25	45	**3a**, **4a**	71:29
7	THF/hexanes (60)[c]	25	40	**3a**, **4a**	81:19
8	THF/hexanes (20)[c]	−20	21	**3a**, **4a**	78:22

[a] The reactions were carried out with δ-valerolactam (2.0 mmol) and 2,3-*O*-isopropylidene-D-glyceraldehyde (4.0 mmol) in the presence of TBSOTf (6.0 mmol) and DIPEA (6.0 mmol) in the specified solvent and temperature, for 4 h.
[b] The diastereomeric ratio was determined from analysis of ^1H NMR spectra of the crude product.
[c] 1:1 solvent mixture.

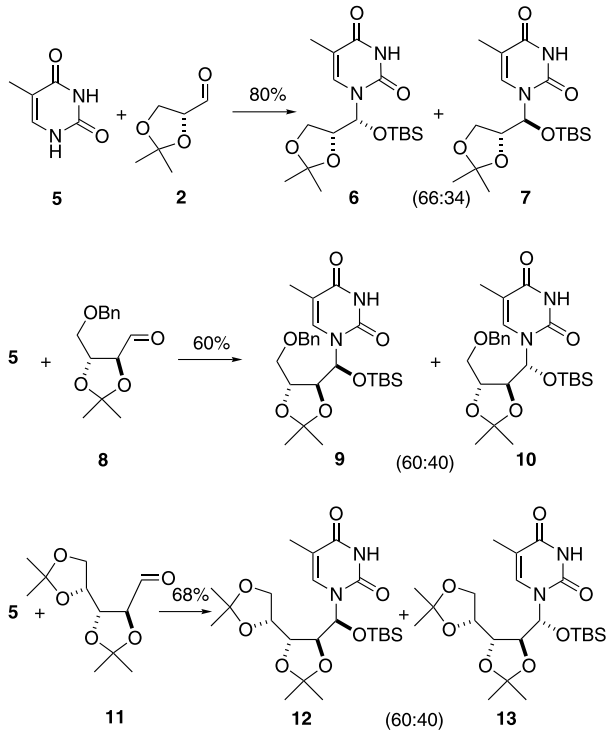
The assignment of the relative stereochemistry for *N*-substituted valerolactams **3a**,**b** and **4a**,**b** was only tentative at this point, with the *anti*-configured isomers **3a**,**b** (Felkin-type preference) predominating over the *syn*-counterparts **4a**,**b** (vide infra).[7]

With the groundwork laid, we then moved ahead to the silylative addition of three representative nucleobases to enantiopure hydroxylated aldehydes, with the intent of producing novel alditol-based acyclic nucleoside analogues.

The superior levels of coupling efficiency observed with the TBSOTf/DIPEA mixture in the optimization exercises mentioned above prompted us to select these reaction conditions for our further investigations.

As highlighted in Scheme 1, thymine (**5**) may be used as a nitrogen nucleophile with certain chiral pool-derived aldehyde acceptors, including glyceraldehyde **2**, threose **8**, and arabinose **11**.

Silylative coupling to **2** gave a mixture of two



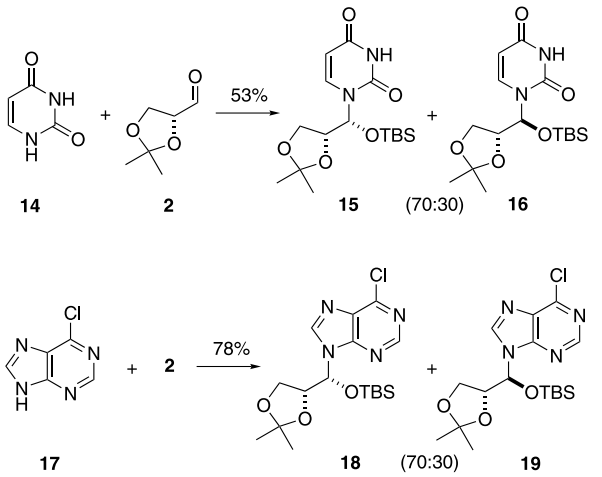
Scheme 1. Silylative hydroxyalkylation of thymine (**5**) with aldehydes **2**, **8** and **11**. The reactions were carried out in the presence of TBSOTf/DIPEA, in 1:1 THF/hexanes at room temperature for 4 h.

chromatographically separable diastereoisomers, **6** and **7**, in a 80% global yield (66:34 isomer ratio). These two C(1′) epimers were readily distinguished by their ^{1}H NMR data; 1′,2′-*anti*-configured glycerol **6** revealed H-1′ to be the expected doublet at 5.92 ppm ($J_{1',2'}$=3.6 Hz), whilst in *syn* isomer **7** the coupling value was markedly larger (5.90 ppm, d, $J_{1',2'}$=6.9 Hz). Based on many experimental analogies with related glycerol adducts[8] and semi-empirical molecular mechanics calculations the stereochemical disposition in **6** and **7** was assessed as shown.[9]

Similarly, threose **8** under the same conditions gave two thymine alditols, **9** and **10**, (60:40 dr) in 60% yield, whereas arabinose **11** produced **12** and **13** in a 68% combined yield and 60:40 *anti*/*syn* diastereomeric ratio. Using the same optimal experimental conditions, the applications of this reaction were further investigated using uracil (**14**) and 6-chloropurine (**17**) as nitrogen donors and glyceraldehyde **2** as the common acceptor (Scheme 2). The expected *anti*- and *syn*-configured C(1′) epimeric couples **15/16** (53% global yield) and **18/19** (78% yield) were obtained with 70:30 diastereomeric ratio.

Inspection of the results in Schemes 1 and 2 reveals that in all experiments 1′,2′-*anti* isomers invariably dominated over the 1′,2′-*syn* counterparts indicating that transition states **A** and **B** are probable models for this silylative addition (Fig. 2).

The Felkin-type model rotamer **A** seems to be favoured over the model rotamer **B** (*anti*-Felkin) where an unfavourable stereoelectronic interaction between the large electronegative aldehyde α-substituent and the incoming heterocyclic nitrogen nucleophile arises.



Scheme 2. Silylative hydroxyalkylation of uracil (**14**) and 6-chloropurine (**17**) with glyceraldehyde **2**. The reactions were carried out in the presence of TBSOTf/DIPEA, in 1:1 THF/hexanes at room temperature for 4 h.

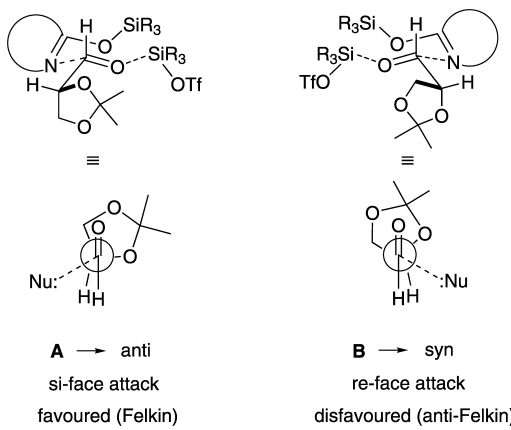
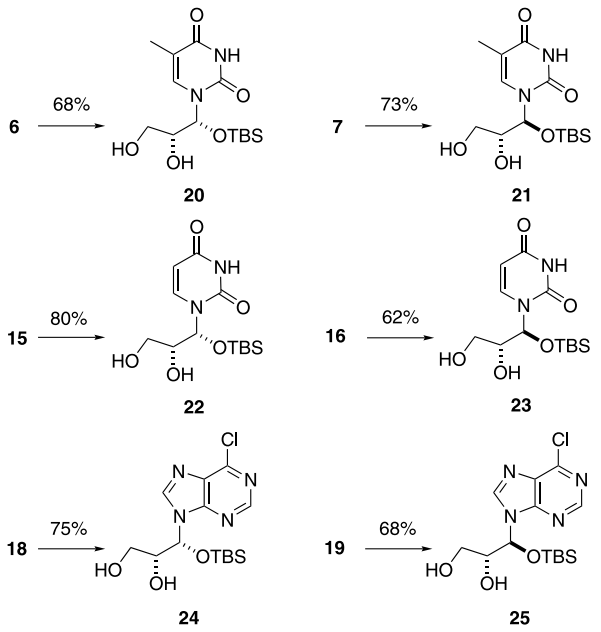


Figure 2. Probable transition state structures in the silylative hydroxyalkylation of amide compounds with chiral α-alkoxyaldehydes.

The alditol-based nucleoside analogues of this study were found to be very stable when in the absence of highly acidic conditions or desilylating reagents (e.g. fluoride ions). As test compounds, thymidine analogues **6** and **7**, uridine analogues **15** and **16**, and 6-chloropurine derivatives **18** and **19** were subjected to acidic removal of the isopropylidene blockage (80% aqueous AcOH, 50 °C) furnishing the respective diols **20**–**25** in very good yields with complete retention of the integrity of the TBS-protected hemiaminal functionalities (Scheme 3).

On the other hand, exposure of the same products to TBAF in THF at room temperature caused a desilylative retrograde addition with recovery of the glyceraldehyde and nucleobase components.

To conclude, the silylation-terminated addition of amide compounds to α-chiral hydroxyaldehydes establishes an efficient methodology for the installation of a stabilized carbon–nitrogen linkage.[10] Under the assistance of a selected Lewis acid–Lewis base combination, TBSOTf/DIPEA, the delicate *N*-acyl hemiaminal motif in the expected adducts is silylated in situ, and stable *N*-silyloxyalkylamides are formed in high isolated yields. The use of



Scheme 3. Selective deacetonidation of nucleosides **6**, **7**, **15**, **16**, **18** and **19**. The reactions were carried out in 80% aqueous AcOH at 50 °C.

nucleobase donors and sugar-derived aldehyde acceptors both expands and ennobles this chemistry further towards the formation of novel chiral nonracemic alditol nucleoside analogues in a single step.

3. Experimental

3.1. General

Flash chromatography was performed on 32–63 μm silica gel, using the indicated solvent mixtures. Analytical thin-layer chromatography was performed on silica gel 60 F_{254} plates (0.25 mm). The compounds were visualized by dipping the plates in an aqueous H_2SO_4 solution of cerium sulfate/ammonium molybdate, followed by charring with a heat gun. Proton and carbon NMR spectra were recorded on a Bruker Avance 300 spectrometer at the frequency indicated. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane (0.0 ppm) as an internal reference, with coupling constants in hertz (Hz). Connectivity was determined by $^1H-^1H$ COSY and $^1H-^{13}C$ HETCOR experiments. Optical rotations were measured on a Perkin–Elmer 341 polarimeter at ambient temperature, using a 100 mm cell with a 1 mL capacity and specific rotations are given in units of 10^{-1} deg cm^2 g^{-1}. FT-IR spectra were recorded on a JASCO FT/IR-300E spectrometer. High-resolution mass spectral analyses were carried out using JEOL JMS-SX 102A. Elemental analyses were performed by the Microanalytical Laboratory of University of Sassari. Melting points were determined on an optical thermomicroscope Optiphot2-Pol Nikon. All anhydrous solvents were distilled before use: THF over Na/benzophenone, Et_2O over $LiAlH_4$, CH_2Cl_2 over CaH_2.

3.2. Materials

2,3-*O*-Isopropylidene-D-glyceraldehyde (**2**) was prepared from D-mannitol (Aldrich) according to a recently optimized protocol.[11] 2,3-*O*-Isopropylidene-4-*O*-benzyl-D-threose (**8**) was prepared from commercial 2,3-*O*-isopropylidene-D-threitol (Aldrich).[12,13] 2,3:4,5-Di-*O*-isopropylidene-D-arabinose (**11**) was prepared from the corresponding sugar via dithioacetal formation, acetonidation, and liberation of the aldehyde function, by following the procedures of Zinner.[14]

3.3. Data for compounds

3.3.1. (1′*R*,4″*R*)-1-[(*tert*-Butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]piperidin-2-one (3a) and (1′*S*,4″*R*)-1-[(*tert*-butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]piperidin-2-one (4a). *Typical procedure*. To a solution of diisopropylethylamine (DIPEA) (1.03 mL, 5.94 mmol) in a 1:1 (v/v) mixture of anhydrous THF/hexanes (10 mL) at 25 °C under argon atmosphere was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (1.36 mL, 5.94 mmol). The resulting mixture was stirred at the same temperature for 10 min before adding lactam **1** (196 mg, 1.98 mmol) and aldehyde **2** (516 mg, 3.96 mmol) dissolved in 10 mL of the same solvent mixture. The reaction was monitored by TLC and was judged complete after 4 h. The solution was then quenched with saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography (4:6 hexanes/EtOAc) to give adducts **3a** (422 mg, 62%) and **4a** (109 mg, 16%).

Compound **3a**. Colourless crystals, mp 43–48 °C; $[\alpha]_D^{20}=-14.6$ (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (d, *J*=6.0 Hz, 1H), 4.18 (q, *J*=6.7 Hz, 1H), 3.95 (dd, *J*=8.4, 6.8 Hz, 1H), 3.78 (dd, *J*=8.4, 6.8 Hz, 1H), 3.56 (m, 1H), 3.20 (m, 1H), 2.3–2.5 (m, 2H), 1.6–1.8 (m, 4H), 1.44 (s, 3H), 1.36 (s, 3H), 0.92 (s, 9H), 0.13 (s, 3H) 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 109.9, 77.7, 76.5, 65.5, 41.3, 32.4, 26.3, 25.7 (3C), 25.6, 23.0, 20.8, 18.0, −5.0, −5.1. FT-IR (KBr): 2950, 1681, 1470, 1090 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{17}H_{34}NO_4Si$ (M+H$^+$), 344.2257; found, 344.2269. Anal. calcd for $C_{17}H_{33}NO_4Si$: C, 59.44; H, 9.68; N, 4.08. Found: C, 59.59; H, 9.55; N, 4.15.

Compound **4a**. Colourless crystals, mp 72–80 °C; $[\alpha]_D^{20}=-10.7$ (*c* 3.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.04 (d, *J*=7.6 Hz, 1H), 4.0–4.2 (m, 2H), 3.88 (m, 1H), 3.47 (dtd, *J*=11.8, 4.8, 1.1 Hz, 1H), 3.23 (ddd, *J*=11.9, 9.5, 4.4 Hz, 1H), 2.50 (bdt, *J*=17.9, 5.8 Hz, 1H), 2.34 (ddd, *J*=17.7, 8.9, 6.6 Hz, 1H), 1.6–2.0 (m, 4H), 1.42 (s, 3H), 1.34 (s, 3H), 0.89 (s, 9H), 0.16 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 109.7, 76.1, 74.8, 66.8, 40.1, 32.5, 26.5, 25.5 (3C), 25.4, 22.8, 20.6, 17.6, −4.9, −5.5. FT-IR (KBr): 2954, 1680, 1477, 1070 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{17}H_{34}NO_4Si$ (M+H$^+$), 344.2257; found, 344.2264. Anal. calcd for $C_{17}H_{33}NO_4Si$: C, 59.44; H, 9.68; N, 4.08. Found: C, 59.62; H, 9.57; N, 4.20.

3.3.2. (1′*R*,4″*R*)-1-[(2,2-Dimethyl-[1,3]dioxolan-4-yl)-(triethylsilanyloxy)methyl]piperidin-2-one (3b) and (1′*S*,4″*R*)-1-[(2,2-dimethyl-[1,3]dioxolan-4-yl)-(triethylsilanyloxy)methyl]piperidin-2-one (4b). The title

compounds were prepared by starting with DIPEA (1.03 mL, 5.94 mmol), triethylsilyl trifluoromethanesulfonate (TESOTf) (1.34 mL, 5.94 mmol), lactam **1** (196 mg, 1.98 mmol) and aldehyde **2** (516 mg, 3.96 mmol) in anhydrous THF (20 mL) according to the above procedure described for compounds **3a** and **4a**. After flash chromatographic purification (4:6 hexanes/EtOAc) there were obtained 354 mg (52%) of pure adduct **3b** along with 293 mg (43%) of pure **4b**.

Compound **3b**. A glassy solid, mp 45–47 °C; $[\alpha]_D^{20}=-13.0$ (*c* 1.0 $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.98 (d, *J*=6.0 Hz, 1H,), 4.15 (q, *J*=6.7 Hz, 1H), 3.95 (dd, *J*=8.5, 6.9 Hz, 1H), 3.77 (dd, *J*=8.5, 6.7 Hz, 1H), 3.51 (m, 1H), 3.22 (m, 1H), 2.2–2.4 (m, 2H), 1.6–1.8 (m, 4H), 1.40 (s, 3H), 1.38 (s, 3H), 0.95 (t, *J*=8.1 Hz, 9H), 0.64 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 110.2, 77.7, 76.4, 66.0, 41.3, 32.0, 26.3, 25.2, 23.0, 21.0, 6.4 (3C), 4.3 (3C). Anal. calcd for $C_{17}H_{33}NO_4Si$: C, 59.44; H, 9.68; N, 4.08. Found: C, 59.28; H, 9.67; N, 4.36.

Compound **4b**. A glassy solid, 39–41 °C; $[\alpha]_D^{20}=-11.3$ (*c* 2.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.01 (d, *J*=7.5 Hz, 1H), 4.0–4.2 (m, 2H), 3.85 (m, 1H), 3.48 (dtd, *J*=11.8, 4.9, 1.0 Hz, 1H), 3.23 (ddd, *J*=11.8, 9.2, 4.3 Hz, 1H), 2.50 (bdt, *J*=17.9, 5.7 Hz, 1H), 2.37 (ddd, *J*=17.9, 8.5, 6.3 Hz, 1H), 1.7–2.0 (m, 4H), 1.40 (s, 3H), 1.28 (s, 3H), 0.94 (t, *J*=8.2 Hz, 9H), 0.64 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 110.2, 76.6, 74.2, 66.0, 40.8, 33.7, 26.0, 25.2, 23.0, 21.4, 6.4 (3C), 4.2 (3C). Anal. calcd for $C_{17}H_{33}NO_4Si$: C, 59.44; H, 9.68; N, 4.08. Found: C, 59.63; H, 9.44; N, 4.32.

3.3.3. (1′*R*,4″*R*)-1-[(*tert*-Butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]-5-methyl-1*H*-pyrimidine-2,4-dione (6) and (1′*S*,4″*R*)-1-[(*tert*-butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]-5-methyl-1*H*-pyrimidine-2,4-dione (7). *Typical procedure*. To a solution of DIPEA (1.03 mL, 5.94 mmol) in a 1:1 (v/v) mixture of anhydrous THF/hexanes (20 mL) at 25 °C under argon atmosphere was added TBSOTf (1.36 mL, 5.94 mmol). The resulting mixture was stirred at the same temperature for 10 min before adding thymine (**5**) (250 mg, 1.98 mmol) and aldehyde **2** (516 mg, 3.96 mmol) dissolved in 20 mL of the same solvent mixture. The reaction was monitored by TLC and was judged complete after 4 h. The solution was then quenched with saturated NH_4Cl solution, and extracted with CH_2Cl_2. The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography (45:55 hexanes/EtOAc) to give adducts **6** (390 mg, 53%) and **7** (198 mg, 27%).

Compound **6**. Colourless crystals, mp 106–115 °C; $[\alpha]_D^{20}=-74.5$ (*c* 2.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.32 (bs, 1H), 7.38 (q, *J*=1.2 Hz, 1H), 5.92 (d, *J*=3.6 Hz, 1H), 4.22 (ddd, *J*=6.8, 5.7, 3.6 Hz, 1H), 4.05 (dd, *J*=8.6, 6.9 Hz, 1H), 3.88 (dd, *J*=8.6, 5.7 Hz, 1H), 1.95 (d, *J*=1.2 Hz, 3H), 1.49 (s, 3H), 1.37 (s, 3H), 0.92 (s, 9H), 0.16 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 150.3, 136.8, 110.6, 110.4, 77.8, 77.7, 65.3, 26.1, 25.5 (3C), 25.3, 17.9, 12.6, −5.2, −5.3. FT-IR (KBr): 3210, 3030, 1740, 1680, 1480, 1080 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{17}H_{31}N_2O_5Si$ ($M+H^+$), 371.2002; found, 371.2013. Anal. calcd for $C_{17}H_{30}N_2O_5Si$: C, 55.11; H, 8.16; N, 7.56. Found: C, 55.20; H, 8.07; N, 7.48.

Compound **7**. Colourless crystals, mp 111–120 °C; $[\alpha]_D^{20}=-5.3$ (*c* 1.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.14 (bs, 1H), 7.22 (q, *J*=1.2 Hz, 1H), 5.90 (d, *J*=6.9 Hz, 1H), 4.17 (m, 1H), 4.14 (dd, *J*=8.3, 6.1 Hz, 1H), 3.93 (dd, *J*=8.5, 3.6 Hz, 1H), 1.96 (d, *J*=1.2 Hz, 3H), 1.42 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.17 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 150.6, 135.6, 111.1, 110.6, 78.3, 76.9, 66.2, 26.3, 25.5 (3C), 25.1, 17.4, 12.5, −5.0, −5.3. FT-IR (KBr): 3210, 3035, 1740, 1680, 1476, 1070 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{17}H_{31}N_2O_5Si$ ($M+H^+$), 371.2002; found, 371.2010. Anal. calcd for $C_{17}H_{30}N_2O_5Si$: C, 55.11; H, 8.16; N, 7.56. Found: C, 55.20; H, 8.07; N, 7.48.

3.3.4. (1′*S*,4″*S*,5″*R*)-1-[(5-Benzyloxymethyl-2,2-dimethyl-[1,3]dioxolan-4-yl)-(*tert*-butyldimethylsilanyloxy)-methyl]-5-methyl-1*H*-pyrimidine-2,4-dione (9) and (1′*R*,4″*S*,5″*R*)-1-[(5-benzyloxymethyl-2,2-dimethyl-[1,3]dioxolan-4-yl)-(*tert*-butyldimethylsilanyloxy)-methyl]-5-methyl-1*H*-pyrimidine-2,4-dione (10). The title compounds were prepared by starting with DIPEA (1.03 mL, 5.94 mmol), TBSOTf (1.36 mL, 5.94 mmol), thymine (**5**) (250 mg, 1.98 mmol) and protected threose **8** (991 mg, 3.96 mmol) in a 1:1 (v/v) mixture of anhydrous THF/hexanes (40 mL) according to the above procedure described for compounds **6** and **7**. After flash chromatographic purification (1:1 hexanes/EtOAc) there were obtained 350 mg (36%) of pure adduct **9** along with 233 mg (24%) of pure **10**.

Compound **9**. A colourless oil; $[\alpha]_D^{20}=-44.6$ (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.68 (bs, 1H), 7.25–7.40 (m, 6H), 6.04 (d, *J*=3.8 Hz, 1H), 4.55 (bs, 2H), 4.22 (dt, *J*=7.7, 5.4 Hz, 1H), 3.95 (dd, *J*=7.8, 3.8 Hz, 1H), 3.60 (dd, *J*=9.7, 5.2 Hz, 1H), 3.49 (dd, *J*=9.7, 5.6 Hz, 1H), 1.92 (d, *J*=1.2 Hz, 3H), 1.48 (s, 3H), 1.43 (s, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 150.0, 137.5, 136.9, 128.4 (2C), 127.7, 127.6 (2C), 111.6, 110.3, 81.3, 77.2, 75.5, 73.6, 70.2, 27.2, 26.6, 25.5 (3C), 17.9, 12.5, −5.3, −5.4. FT-IR (film): 3260, 3060, 1736, 1677, 1501, 1230, 1024, 710 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{25}H_{39}N_2O_6Si$ ($M+H^+$), 491.2577; found, 491.2565. Anal. calcd for $C_{25}H_{38}N_2O_6Si$: C, 61.20; H, 7.81; N, 5.71. Found: C, 61.33; H, 7.92; N, 5.57.

Compound **10**. A colourless oil; $[\alpha]_D^{20}=+21.6$ (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.70 (bs, 1H), 7.2–7.4 (m, 6H), 6.02 (d, *J*=6.9 Hz, 1H), 4.63 (bs, 2H), 4.15 (m, 1H), 3.90 (m, 1H), 3.6–3.8 (m, 2H), 1.95 (d, *J*=1.0 Hz, 3H), 1.40 (s, 3H), 1.28 (s, 3H), 0.85 (s, 9H), 0.12 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 150.1, 137.6, 135.6, 128.3 (2C), 127.8, 127.6 (2C), 111.0, 110.2, 81.9, 78.8, 78.1, 73.6, 70.5, 27.1, 26.5, 25.4 (3C), 17.7, 12.4, −5.2, −5.3. FT-IR (film): 3261, 3051, 1739, 1680, 1500, 1225, 1020, 710 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{25}H_{39}N_2O_6Si$ ($M+H^+$), 491.2577; found, 491.2586. Anal. calcd for $C_{25}H_{38}N_2O_6Si$: C, 61.20; H, 7.81; N, 5.71. Found: C, 61.33; H, 7.92; N, 5.57.

3.3.5. (1′*S*,4″*R*,4‴*R*,5″*S*)-1-[(*tert*-Butyldimethylsilanyloxy)-(2,2,2′,2′-tetramethyl-[4,4′]bis[[1,3]dioxolanyl]-5-yl)methyl]-5-methyl-1*H*-pyrimidine-2,4-dione (12) and (1′*R*,4″*R*,4‴*R*,5″*S*)-1-[(*tert*-butyldimethylsilanyloxy)-(2,2,2′,2′-tetramethyl-[4,4′]bis[[1,3]dioxolanyl]-5-yl)methyl]-5-methyl-1*H*-pyrimidine-2,4-dione (13). The title compounds were prepared by starting with DIPEA (1.03 mL, 5.94 mmol), TBSOTf (1.36 mL, 5.94 mmol), thymine (**5**) (250 mg, 1.98 mmol) and protected arabinose **11** (912 mg, 3.96 mmol) in a 1:1 (v/v) mixture of anhydrous THF/hexanes (40 mL) according to the above procedure described for compounds **6** and **7**. After flash chromatographic purification (55:45 hexanes/EtOAc) there were obtained 382 mg (41%) of pure adduct **12** along with 252 mg (27%) of pure **13**.

Compound **12**. A white foam; $[\alpha]_D^{20}=-3.5$ (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.04 (bs, 1H,), 7.38 (q, *J*=1.2 Hz, 1H), 6.08 (d, *J*=4.3 Hz, 1H), 4.15 (m, 1H), 4.06 (dd, *J*=6.5, 4.3 Hz, 1H), 3.9–4.0 (m, 2H), 3.81 (dd, *J*=8.3, 6.4 Hz, 1H), 1.96 (d, *J*=1.2 Hz, 3H), 1.47 (s, 3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.32 (s, 3H), 0.92 (s, 9H), 0.18 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 150.3, 135.6, 110.4, 109.7, 109.5, 79.0, 78.2, 77.8, 77.2, 65.3, 26.7, 26.4, 25.8 (3C), 25.2, 24.6, 17.4, 12.3, −5.2, −5.3. FT-IR (KBr): 3240, 3010, 1735, 1670, 1500, 1085 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{22}H_{39}N_2O_7Si$ ($M+H^+$), 471.2526; found, 471.2539. Anal. calcd for $C_{22}H_{38}N_2O_7Si$: C, 56.15; H, 8.14; N, 5.95. Found: C, 56.32; H, 7.83; N, 5.75.

Compound **13**. A white foam; $[\alpha]_D^{20}=+4.1$ (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.03 (bs, 1H), 7.38 (q, *J*=1.2 Hz, 1H), 6.11 (d, *J*=4.6 Hz, 1H), 3.8–4.2 (m, 5H), 1.97 (d, *J*=1.1 Hz, 3H), 1.49 (s, 3H), 1.41 (s, 3H), 1.37 (s, 3H), 1.32 (s, 3H), 0.92 (s, 9H), 0.18 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 150.6, 136.4, 111.1, 110.2, 109.3, 79.2, 78.6, 78.3, 76.8, 66.2, 26.9, 26.2, 25.8, 25.5 (3C), 25.0, 17.9, 12.5, −5.0, −5.3. FT-IR (KBr): 3241, 3012, 1740, 1677, 1506, 1080 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{22}H_{39}N_2O_7Si$ ($M+H^+$), 471.2526; found, 471.2517. Anal. calcd for $C_{22}H_{38}N_2O_7Si$: C, 56.15; H, 8.14; N, 5.95. Found: C, 56.27; H, 8.06; N, 6.04.

3.3.6. (1′*R*,4″*R*)-1-[(*tert*-Butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]-1*H*-pyrimidine-2,4-dione (15) and (1′*S*,4″*R*)-1-[(*tert*-butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]-1*H*-pyrimidine-2,4-dione (16). The title compounds were prepared by starting with DIPEA (1.03 mL, 5.94 mmol), TBSOTf (1.36 mL, 5.94 mmol), uracil (**14**) (222 mg, 1.98 mmol) and aldehyde **2** (516 mg, 3.96 mmol) in a 1:1 (v/v) mixture of anhydrous THF/hexanes (40 mL) according to the above procedure described for compounds **6** and **7**. After flash chromatographic purification (6:4 hexanes/EtOAc) there were obtained 261 mg (37%) of pure adduct **15** along with 113 mg (16%) of pure **16**.

Compound **15**. A colourless oil; $[\alpha]_D^{20}=-61.1$ (*c* 1.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.30 (bs, 1H), 7.59 (d, *J*=8.2 Hz, 1H), 5.94 (d, *J*=3.0 Hz, 1H), 5.77 (dd, *J*=8.1, 2.0 Hz, 1H), 4.23 (ddd, *J*=6.9, 5.6, 3.1 Hz, 1H), 4.07 (dd, *J*=8.5, 6.9 Hz, 1H), 3.90 (dd, *J*=8.5, 5.6 Hz, 1H), 1.49 (s, 3H), 1.36 (s, 3H), 0.93 (s, 9H), 0.17 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 150.4, 141.2, 110.6, 102.0, 77.7, 77.5, 65.3, 26.0, 25.5 (3C), 25.3, 17.9, −5.1, −5.4. FT-IR (film): 3270, 3140, 3004, 1736, 1700, 1670, 1500, 1030 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{16}H_{29}N_2O_5Si$ ($M+H^+$), 357.1846; found, 357.1835. Anal. calcd for $C_{16}H_{28}N_2O_5Si$: C, 53.91; H, 7.92; N, 7.86. Found: C, 54.12; H, 7.81; N, 8.01.

Compound **16**. A colourless oil; $[\alpha]_D^{20}=+12.9$ (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (bs, 1H), 7.41 (d, *J*=8.1 Hz, 1H), 5.91 (d, *J*=6.5 Hz, 1H), 5.79 (dd, *J*=8.1, 2.2 Hz, 1H), 4.15 (m, 2H), 3.93 (m, 1H), 1.43 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.18 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 150.7, 140.0, 110.6, 102.7, 78.4, 77.1, 65.5, 26.2, 25.5 (3C), 25.0, 17.7, −5.1, −5.4. FT-IR (film): 3269, 3136, 3000, 1730, 1697, 1645, 1500, 1020 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{16}H_{29}N_2O_5Si$ ($M+H^+$), 357.1846; found, 357.1852. Anal. calcd for $C_{16}H_{28}N_2O_5Si$: C, 53.91; H, 7.92; N, 7.86. Found: C, 54.03; H, 8.05; N, 7.73.

3.3.7. (1′*R*,4″*R*)-9-[(*tert*-Butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]-6-chloro-9*H*-purine (18) and (1′*S*,4″*R*)-9-[(*tert*-butyldimethylsilanyloxy)-(2,2-dimethyl-[1,3]dioxolan-4-yl)methyl]-6-chloro-9*H*-purine (19). The title compounds were prepared by starting with DIPEA (1.03 mL, 5.94 mmol), TBSOTf (1.36 mL, 5.94 mmol), 6-chloropurine (**17**) (306 mg, 1.98 mmol) and aldehyde **2** (516 mg, 3.96 mmol) in a 1:1 (v/v) mixture of anhydrous THF/hexanes (40 mL) according to the above procedure described for compounds **6** and **7**. After flash chromatographic purification (65:35 hexanes/EtOAc) there were obtained 435 mg (55%) of pure adduct **18** along with 182 mg (23%) of pure **19**.

Compound **18**. A colourless oil; $[\alpha]_D^{20}=-51.6$ (*c* 2.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.42 (s, 1H), 6.18 (d, *J*=3.9 Hz, 1H), 4.38 (m, 1H), 4.0–4.1 (m, 2H), 1.32 (s, 6H), 0.86 (s, 9H), 0.13 (s, 3H), −0.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.1, 151.0, 150.9, 144.1, 131.8, 110.8, 78.6, 77.8, 64.8, 26.0, 25.4 (3C), 25.0, 17.9, −5.3, −5.4. FT-IR (film): 2950, 1620, 1351, 1091, 696 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{17}H_{28}N_4ClO_3Si$ ($M+H^+$), 399.1619; found, 399.1610. Anal. calcd for $C_{17}H_{27}N_4ClO_3Si$: C, 51.18; H, 6.82; N, 14.04; Cl, 8.89. Found: C, 51.36; H, 6.90; N, 13.93; Cl, 8.71.

Compound **19**. A colourless oil; $[\alpha]_D^{20}=+22.1$ (*c* 2.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.32 (s, 1H), 5.93 (d, *J*=7.1 Hz, 1H), 4.45 (m, 1H), 4.0–4.2 (m, 2H), 1.25 (s, 3H), 1.18 (s, 3H), 0.79 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 151.4, 150.8, 143.3, 131.1, 110.6, 79.3, 77.9, 66.0, 26.3, 25.3 (3C), 24.7, 17.8, −5.3, −5.4. FT-IR (film): 2964, 1614, 1350, 1090, 700 cm^{-1}. HRMS (FAB^+, *m*/*z*): calcd for $C_{17}H_{28}N_4ClO_3Si$ ($M+H^+$), 399.1619; found, 399.1627. Anal. calcd for $C_{17}H_{27}N_4ClO_3Si$: C, 51.18; H, 6.82; N, 14.04; Cl, 8.89. Found: C, 50.97; H, 6.95; N, 14.14; Cl, 8.76.

3.3.8. (1′*R*,2′*R*)-1-[1-(*tert*-Butyldimethylsilanyloxy)-2,3-dihydroxypropyl]-5-methyl-1*H*-pyrimidine-2,4-dione (20). *Typical procedure*. Protected adduct **6** (390 mg, 1.05 mmol) was dissolved in 8.4 mL of 80% aqueous acetic

acid, and the resulting solution was allowed to react at 50 °C. The reaction was monitored by TLC and was judged complete after 24 h. The solution was diluted with water and extracted with EtOAc. The combined extracts were washed with saturated $NaHCO_3$ solution and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under vacuum to afford a crude residue which was purified by silica gel flash chromatography (EtOAc). Terminal diol **20** was isolated (236 mg) in a 68% yield as a glassy solid; $[\alpha]_D^{20}=-13.3$ (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (bs, 1H), 7.40 (q, *J*=1.2 Hz, 1H), 5.97 (d, *J*=4.4 Hz, 1H), 3.80 (m, 1H), 3.68 (m, 2H), 3.11 (bs, 1H), 2.70 (bs, 1H), 1.92 (d, *J*=1.1 Hz, 3H), 0.93 (s, 9H), 0.19 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 150.8, 137.4, 109.6, 78.9, 73.3, 62.7, 25.5 (3C), 17.9, 12.3, −5.2, −5.3. FT-IR (KBr): 3300, 2960, 1735, 1676, 1501, 1260, 1060 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{14}H_{27}N_2O_5Si$ (M+H$^+$), 331.1689; found, 331.1699. Anal. calcd for $C_{14}H_{26}N_2O_5Si$: C, 50.86; H, 7.93; N, 8.48. Found: C, 50.98; H, 7.81; N, 8.57.

3.3.9. (1′*S*,2′*R*)-1-[1-(*tert*-Butyldimethylsilanyloxy)-2,3-dihydroxypropyl]-5-methyl-1*H*-pyrimidine-2,4-dione (21). The title compound was prepared starting from 198 mg of protected adduct **7** (0.53 mmol) and 4.2 mL of 80% aqueous acetic acid according to the above procedure described for compound **20**. After flash chromatographic purification (EtOAc) there was obtained diol **21** (128 mg, 73%) as a colourless semisolid; $[\alpha]_D^{20}=-25.4$ (*c* 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.40 (bs, 1H), 7.30 (q, *J*=1.1 Hz, 1H), 6.11 (d, *J*=7.4 Hz, 1H), 4.49 (bs, 1H), 3.90 (dd, *J*=11.8, 3.2 Hz, 1H), 3.79 (dd, *J*=11.8, 3.9 Hz, 1H), 3.69 (m, 1H), 3.47 (bs, 1H), 1.90 (d, *J*=1.0 Hz, 3H), 0.89 (s, 9H), 0.18 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 151.7, 136.3, 111.1, 78.5, 74.5, 62.8, 25.5 (3C), 17.8, 12.4, −5.2, −5.5. FT-IR (film): 3300, 2956, 1730, 1680, 1500, 1259, 1050 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{14}H_{27}N_2O_5Si$ (M+H$^+$), 331.1689; found, 331.1695. Anal. calcd for $C_{14}H_{26}N_2O_5Si$: C, 50.86; H, 7.93; N, 8.48. Found: C, 51.01; H, 8.08; N, 8.23.

3.3.10. (1′*R*,2′*R*)-1-[1-(*tert*-Butyldimethylsilanyloxy)-2,3-dihydroxypropyl]-1*H*-pyrimidine-2,4-dione (22). The title compound was prepared starting from 261 mg of protected adduct **15** (0.73 mmol) and 5.8 mL of 80% aqueous acetic acid according to the above procedure described for compound **20**. After flash chromatographic purification (EtOAc) there was obtained diol **22** (185 mg, 80%) as a waxy solid; $[\alpha]_D^{20}=-21.4$ (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.37 (bs, 1H), 7.58 (d, *J*=8.1 Hz, 1H), 5.97 (d, *J*=3.6 Hz, 1H), 5.72 (d, *J*=8.1 Hz, 1H), 3.6–3.9 (m, 3H), 3.24 (bs, 1H), 2.81 (bs, 1H), 0.91 (s, 9H), 0.17 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 150.6, 141.0, 102.0, 78.8, 73.6, 62.6, 25.6 (3C), 17.9, −5.1, −5.4. FT-IR (film): 3300, 2961, 1736, 1670, 1500 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{13}H_{25}N_2O_5Si$ (M+H$^+$), 317.1533; found, 317.1541. Anal. calcd for $C_{13}H_{24}N_2O_5Si$: C, 49.35; H, 7.64; N, 8.85. Found: C, 49.50; H, 7.53; N, 8.92.

3.3.11. (1′*S*,2′*R*)-1-[1-(*tert*-Butyldimethylsilanyloxy)-2,3-dihydroxypropyl]-1*H*-pyrimidine-2,4-dione (23). The title compound was prepared starting from protected adduct **16** (113 mg, 0.32 mmol) and 2.5 mL of 80% aqueous acetic acid according to the above procedure described for compound **20**. After flash chromatographic purification (EtOAc) there was obtained diol **23** (63 mg, 62%) as colourless crystals, mp 141–145 °C; $[\alpha]_D^{20}=-8.3$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (bs, 1H), 7.50 (d, *J*=8.1 Hz, 1H), 6.08 (d, *J*=5.7 Hz, 1H), 5.80 (d, *J*=8.1 Hz, 1H), 3.6–3.8 (m, 3H), 3.01 (bs, 1H), 2.51 (bs, 1H), 0.92 (s, 9H), 0.19 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 150.2, 140.4, 102.8, 78.6, 74.4, 62.5, 25.5 (3C), 17.8, −5.2, −5.5. FT-IR (KBr): 3300, 2960, 1740, 1681, 1500 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{13}H_{25}N_2O_5Si$ (M+H$^+$), 317.1533; found, 317.1521. Anal. calcd for $C_{13}H_{24}N_2O_5Si$: C, 49.35; H, 7.64; N, 8.85. Found: C, 49.46; H, 7.72; N, 8.63.

3.3.12. (2*R*,3*R*)-3-(*tert*-Butyldimethylsilanyloxy)-3-(6-chloro-purin-9-yl)propane-1,2-diol (24). The title compound was prepared starting from protected adduct **18** (435 mg, 1.09 mmol) and 8.7 mL of 80% aqueous acetic acid according to the above procedure described for compound **20**. After flash chromatographic purification (2:8 hexanes/EtOAc) there was obtained diol **24** (293 mg, 75%) as a white foam; $[\alpha]_D^{20}=-18.9$ (*c* 3.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.48 (s, 1H), 6.29 (d, *J*=4.1 Hz, 1H), 3.95 (q, *J*=4.7 Hz, 1H), 3.75 (dd, *J*=11.6, 4.8 Hz, 1H), 3.66 (dd, *J*=11.6, 5.2 Hz, 1H), 3.28 (bs, 2H), 0.89 (s, 9H), 0.16 (s, 3H), −0.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 151.0, 150.6, 144.3, 131.0, 79.0, 74.1, 62.3, 25.4 (3C), 17.8, −5.3, −5.4. FT-IR (KBr): 3300, 2920, 1612, 1351, 1060, 702 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{14}H_{24}N_4ClO_3Si$ (M+H$^+$), 359.1306; found, 359.1320. Anal. calcd for $C_{14}H_{23}N_4ClO_3Si$: C, 46.85; H, 6.46; N, 15.61; Cl, 9.88. Found: C, 46.97; H, 6.37; N, 15.48; Cl, 9.96.

3.3.13. (2*R*,3*S*)-3-(*tert*-Butyldimethylsilanyloxy)-3-(6-chloro-purin-9-yl)propane-1,2-diol (25). The title compound was prepared starting from protected adduct **19** (182 mg, 0.46 mmol) and 3.7 mL of 80% aqueous acetic acid according to the above procedure described for compound **20**. After flash chromatographic purification (2:8 hexanes/EtOAc) there was obtained diol **25** (122 mg, 68%) as a white foam; $[\alpha]_D^{20}=-12.1$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.39 (s, 1H), 6.24 (d, *J*=5.5 Hz, 1H), 4.17 (q, *J*=5.0 Hz, 1H), 3.74 (dd, *J*=11.5, 4.9 Hz, 1H), 3.64 (dd, *J*=11.6, 5.0 Hz, 1H), 2.98 (bs, 2H), 0.89 (s, 9H), 0.15 (s, 3H), −0.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.1, 151.1, 150.2, 143.9, 131.0, 79.3, 74.3, 62.1, 25.4 (3C), 17.9, −5.2 (2C). FT-IR (KBr): 3300, 2930, 1610, 1350, 1050, 700 cm^{-1}. HRMS (FAB$^+$, *m/z*): calcd for $C_{14}H_{24}N_4ClO_3Si$ (M+H$^+$), 359.1306; found, 359.1317. Anal. calcd for $C_{14}H_{23}N_4ClO_3Si$: C, 46.85; H, 6.46; N, 15.61; Cl, 9.88. Found: C, 47.01; H, 6.36; N, 15.74; Cl, 9.74.

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