# Synthesis of substituted 6-cyclopropylpurine bases and nucleosides by cross-coupling reactions or cyclopropanations†

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Synthesis of novel purine bases and nucleosides bearing unsubstituted or substituted cyclopropyl rings in position 6 is reported. Unsubstituted 6-cyclopropylpurines were efficiently prepared by cross-coupling reactions of 6-chloropurines with cyclopropylzinc chloride. 6-Vinylpurines underwent Cu-mediated cyclopropanations with ethyl diazoacetate to give 6-[(ethoxycarbonyl)cyclopropyl]purines that were further transformed to carboxylic acids, amides and alcohols. 6-Cyclopropylpurine ribonucleoside exerted a significant cytostatic effect while all substituted derivatives were inactive.

## Introduction

Purine bases and nucleosides bearing diverse C-substituents (aryl, alkenyl, alkynyl or alkyl groups) in position 6 are an important class of compounds possessing a broad spectrum of biological effects: *e.g.* cytostatic,[1] antiviral[2] and antimicrobial[3] activity or receptor modulation.[4] 6-Methylpurine, as well as its ribonucleoside, is highly cytotoxic[5] and its liberation by purine nucleoside phosphorylases from its non-toxic deoxyribonucleoside was proposed as a novel principle in the gene therapy of cancer.[6] We have been interested in the synthesis of purines bearing functionalized alkyl substituents and reported syntheses and cytostatic affects of 6-(hydroxymethyl)-,[7] 6-(fluoromethyl)-[8] and 6-(difluoromethyl)purine[9] bases and nucleosides and (purin-6-yl)-alanines[10] and -phenylalanines.[11] Very recently we have finished syntheses of a large series of 6-(dialkylamino)methyl-, 6-alkoxymethyl- and 6-(alkylsulfanylmethyl)purine derivatives,[12] as well as homologous 6-(dialkylamino)ethyl-, 6-(dialkylamino)vinyl-, 6-alkoxyethyl- and 6-[2-(alkylsulfanyl)ethyl]purines[13] that also exerted significant cytostatic effects and moderate non-selective anti-HCV activities.

The cyclopropane ring[14] is a privileged pharmacophore present in a large number of biologically active compounds,[15] including antiviral and antitumor nucleosides.[16] Surprisingly, only two examples of C-linked cyclopropylpurines have been reported. Free 6-cyclopropylpurine bases were prepared *via* coupling of 6-chloropurine derivatives with organocuprates followed by deprotection by Dvořák *et al.*[17] but no biological activity data were reported. Several 6-(2-phenylcyclopropyl)purine derivatives were described by Gundersen *et al*.[18] as inhibitors of 15-lipoxygenase, and were prepared by cross-coupling of 6-chlorpurines with phenylcyclopropylzinc halides.

Therefore, as a logical extension of our previous studies (Chart 1), we have decided to prepare a series of unsubstituted and substituted 6-cyclopropylpurine bases and nucleosides and to study their biological activities. The results of our efforts are presented here.

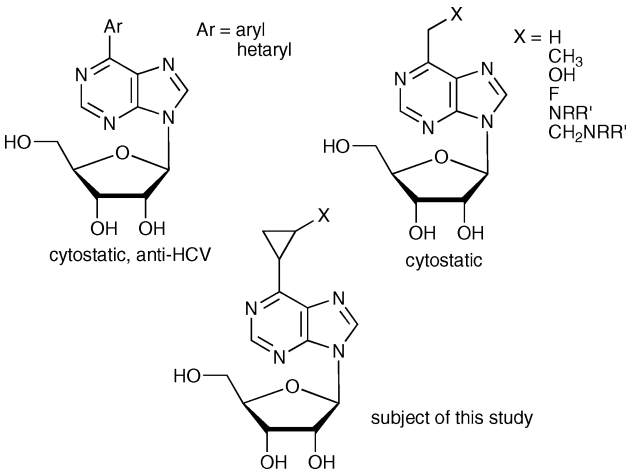


**Chart 1** Biologically active 6-substituted purine nucleosides.

## Results and discussion

There are two possible approaches to the construction of 6-cyclopropylpurines: (i) attachment of the cyclopropyl ring *via* cross-coupling or (ii) cyclopropyl ring formation (*e.g.* by cyclopropanation of 6-vinylpurines). We wanted to try both of them and test their suitability for the synthesis of either unsubstituted or substituted 6-cyclopropylpurines.

Synthesis of unsubstituted 6-cyclopropylpurine base in a low yield of 24% has been reported by Dvořák *et al.*[17] who used a cross-coupling reaction of 9-(tetrahydropyran-2-yl) (THP) protected 6-chloropurine with organocuprate derived from cyclopropylmagnesium bromide followed by deprotection. We have first tried classical carbene cyclopropanation[19] of 9-benzyl-6-vinylpurine. Carbene was generated *in situ* by diethylzinc from diiodomethane in various solvents under various conditions but all these attempts led only to complex mixtures of products. Then we studied the Negishi cross-coupling reactions of 9-benzyl-6-chlorpurines **1a** with cyclopropylzinc chloride (Scheme 1, Table 1). The organozinc

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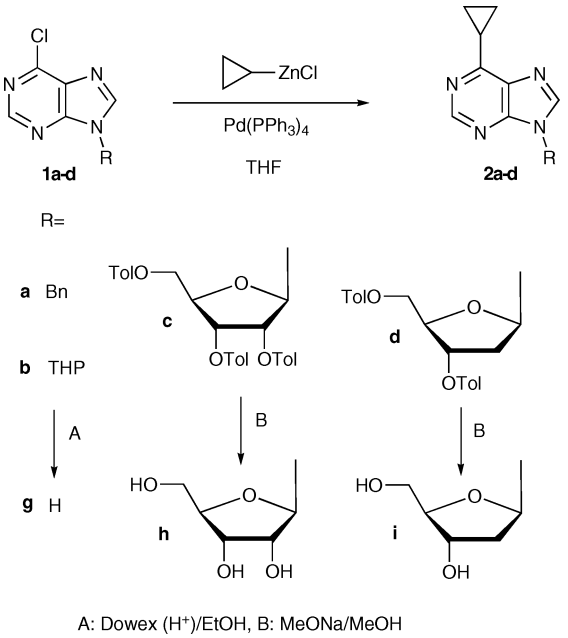
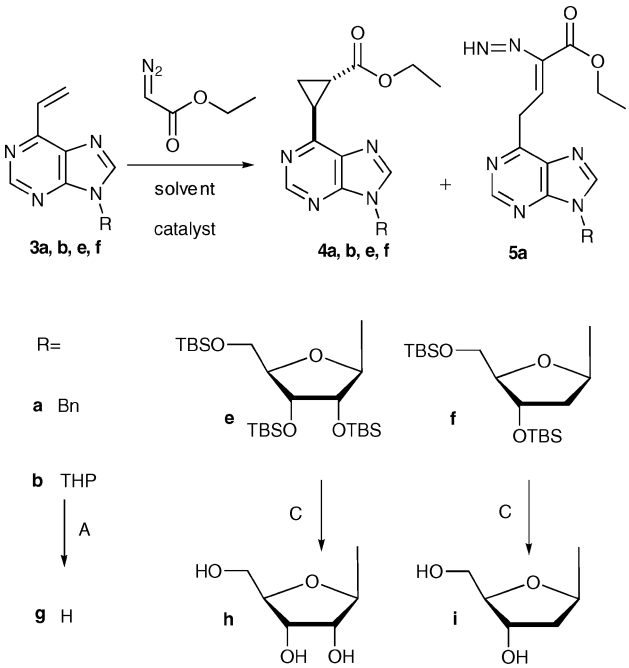



**Scheme 1** Synthesis of 6-cyclopropylpurines.




**Scheme 2** Cyclopropanations of 6-vinylpurines with ethyl diazoacetate.

**Table 1** The Neghishi cross coupling reactions

| Entry | Starting compound | Product | Yield (%) |
|---|---|---|---|
| 1 | **1a** | **2a** | 88 |
| 2 | **1b** | **2b** | 83 |
| 3 | **1c** | **2c** | 99 |
| 4 | **1d** | **2d** | 99 |

was generated *in situ* from cyclopropylmagnesium bromide and zinc chloride at −10 °C and reacted with **1a** at 40 °C in the presence of $Pd(PPh_3)_4$ in THF for 2 h to give 6-cyclopropylpurine **2a** in excellent 88% yield. This procedure was then applied for THP-protected 6-chloropurine **1b**, as well as for 4-methylbenzoyl (Tol) protected 6-chloropurine nucleosides **1c**,**d**. In all cases, the desired protected 6-cyclopropylpurine base **2b** and nucleosides **2c**,**d** were obtained in excellent to quantitative yields (83–99%).

In order to have access to diverse substituted 6-cyclopropylpurines, we have further studied cyclopropanations of 6-vinylpurines with ethyl diazoacetate (Scheme 2, Table 2). The reaction of 9-benzyl-6-vinylpurine (**3a**) with ethyldiazoacetate was tested in the presence of either $Rh_2(OAc)_4$[20] catalyst or Cu powder[21] under various conditions. The rhodium catalyst (entry 1) rapidly decomposed ethyl diazoacetate and we obtained complex mixture of products. More promising was the use of Cu powder. In dioxane, the reaction at 70 °C led to mixtures of the desired 9-benzyl-6-[2-(ethoxycarbonyl)cyclopropyl]purine (**4a**) and the open ring byproduct **5a** (entries 2,3). On the other hand, in toluene at *ca.* 100 °C the reaction proceeded relatively smoothly to give substituted cyclopropylpurine **4a** in a good yield of 75% (entry 4). Then, analogous reactions with ethyl diazoacetate were performed with THP-protected 6-vinylpurine **3b** and silyl-protected 6-vinylpurine nucleosides **3e**,**f** to give the desired 6-[2-(ethoxycarbonyl)-cyclopropyl]purines **4b**,**e**,**f** in moderate but acceptable yields of 41–60% (entries 5–7). The corresponding minor (estimated 5–10% by TLC) diazenylacrylates **5**, as well as polymeric by-products, were observed on TLC but not isolated. In all cases, the reactions proceeded stereoselectively to give *trans* relative configuration at the cyclopropyl ring. However, in the case of nucleosides, there was no asymmetric induction due to the homochiral sugar part and the products **4e**,**f** were (inseparable) diastereomeric mixtures (1 : 1). In the case of **10h**, the initially formed 1 : 1 mixture was by repeated column chromatography enriched to 2 : 1.

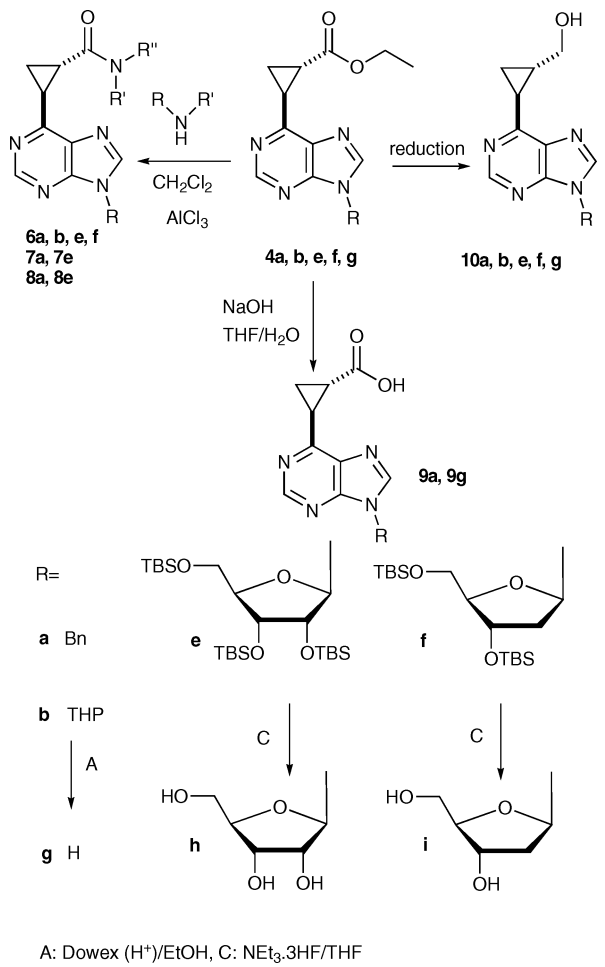
Having gained an access to ester intermediates **4a**,**b**,**e**,**f**, we have further studied functional group transformations leading to amides, carboxylic acids and alcohols. The amidations of the esters **4a**,**b**,**e**,**f** were performed with several amines in the presence of

**Table 2** Cyclopropanations of 6-vinylpurines with ethyl diazoacetate

| Entry | Starting compound | Solvent | Catalyst | Conditions | Results |
|---|---|---|---|---|---|
| 1 | **3a** | $CH_2Cl_2$ | $Rh_2(OAc)_4$ | Rt, 1h | Decomposition |
| 2 | **3a** | Dioxane | Cu | 70 °C, 8 h | **4a** (trace), **5a** (29%), |
| 3 | **3a** | Dioxane | Cu | 70 °C, 2 d | **4a** (53%), **5a** (9%) |
| 4 | **3a** | Toluene | Cu | 95 °C, 6 h | **4a** (75%), **5a** (trace) |
| 5 | **3b** | Toluene | Cu | 100 °C, 2 h | **4b** (41%) |
| 6 | **3e** | Toluene | Cu | 100 °C, 2 h | **4e** (60%) |
| 7 | **3f** | Toluene | Cu | 100 °C, 2 h | **4f** (44%) |

$AlCl_3$[22] in dichloromethane (Scheme 3). The reactions proceeded smoothly at ambient temperature and the desired products **6–8** were isolated in high yields (Table 3). The products of reactions with benzyl(methyl)amine (entries 2 and 6) were in solution mixtures of 4 diastereoisomeric amide rotamers (NMR).




A: Dowex ($H^+$)/EtOH, C: $NEt_3$.3HF/THF

**Scheme 3** Transformations of the ester function.

**Table 3** Transformations of the ester function

| Entry | Starting compound | Reagent | Product | Yield (%) |
|---|---|---|---|---|
| 1 | **4a** | $Et_2NH$, $AlCl_3$ | **6a** | 89 |
| 2 | **4a** | Bn(Me)NH, $AlCl_3$ | **7a** | 85 |
| 3 | **4a** | Morpholine, $AlCl_3$ | **8a** | 82 |
| 4 | **4b** | $Et_2NH$, $AlCl_3$ | **6b** | 66 |
| 5 | **4e** | $Et_2NH$, $AlCl_3$ | **6e** | 85 |
| 6 | **4e** | Bn(Me)NH, $AlCl_3$ | **7e** | 65 |
| 7 | **4e** | Morpholine, $AlCl_3$ | **8e** | 76 |
| 8 | **4f** | $Et_2NH$, $AlCl_3$ | **6f** | 71 |
| 9 | **4a** | NaOH | **9a** | 81 |
| 10 | **4g** | NaOH | **9g** | 80 |
| 11 | **4e** | NaOH | Mixture | |
| 12 | **4f** | NaOH | Mixture | |
| 13 | **4a** | $NaBH_4$ | **10a** | 57 |
| 14 | **4b** | $NaBH_4$ | **10b** | 57 |
| 15 | **4e** | $NaBH_4$ | **10e** | 68 |
| 16 | **4f** | $NaBH_4$ | **10f** | 46 |
| 17 | **4g** | DIBAH | **10g** | 65 |

**Table 4** Deprotections

| Entry | Starting compound | Method | Product | Yield (%) |
|---|---|---|---|---|
| 1 | **2b** | A | **2g** | 47 |
| 2 | **4b** | A | **4g** | 85 |
| 3 | **6b** | A | **6g** | 95 |
| 4 | **10b** | A | **10g** | 21 |
| 5 | **2c** | B | **2h** | 65 |
| 6 | **2d** | B | **2i** | 42 |
| 7 | **4e** | C | **4h** | 75 |
| 8 | **4f** | C | **4i** | 80 |
| 9 | **6e** | C | **6h** | 95 |
| 10 | **7e** | C | **7h** | 98 |
| 11 | **8e** | C | **8h** | 97 |
| 12 | **6f** | C | **6i** | 83 |
| 13 | **10e** | C | **10h** | 76 |
| 14 | **10f** | C | **10i** | 44 |

Hydrolysis of esters **4** to carboxylic acids was performed using NaOH in a water–THF mixture at ambient temperature. For purine bases **4a** and **4g**, the corresponding free carboxylic acids **9a** and **9g** were successfully isolated in good yields (entries 9, 10). In the case of protected nucleosides **4e** and **4f**, complex inseparable mixtures of partially deprotected products were observed (entries 11, 12).

Reduction of esters **4a**,**b**,**e**,**f** to alcohols was performed using a large excess of $NaBH_4$ (50 equiv.) in ethanol at 60 °C. The reactions proceeded rather slowly (24 h) to give the corresponding alcohols **10a**,**b**,**e**,**f** in moderate to good yields of 46–68% (entries 13–16). DIBAH (2 equiv.) in dry $CH_2Cl_2$ at ambient temperature was used for reduction of free purine base **4g**, which proceeded to give **10g** in 65% yield (entry 17).

The whole series of THP-protected purines (**2b**, **4b**, **6b** and **10b**) was deprotected by treatment with acidic cation exchanger Dowex ($H^+$ form) in ethanol (method A, Table 4) to get the corresponding free purine bases (**2g**, **4g**, **6g** and **10g**). The toluoyl-protected nucleosides **2c** and **2d** were deprotected by treatment with sodium methoxide in methanol (method B) to afford free nucleosides **2h** and **2i**. The TBS-protected nucleosides (**6–8e**, **6f**, **10e** and **10f**) were deprotected by treatment with $Et_3N{\cdot}3HF$ in THF (method C). In certain cases (entries 1, 4, 6 and 14), the isolated yields were quite low due to difficult isolation of the polar final products by column chromatography.

All compounds were fully characterized. Crystal structures of cyclopropylpurines **2g** and **6a** were determined by X-ray crystallography confirming the *trans*-relative configuration on the cyclopropane in **6a** (Fig. 1).

All the title cyclopropylpurine bases and nucleosides **3**, **4**, **6–10** were evaluated for biological activity. Cytostatic activity *in vitro* (inhibition of cell growth) was studied on the following cell cultures: (i) mouse leukaemia L1210 cells (ATCC CCL 219); human promyelocytic leukemia HL60 cells (ATCC CCL 240); human cervix carcinoma HeLaS3 cells (ATCC CCL 2.2) and human T lymphoblastoid CCRF-CEM cell line (ATCC CCL 119). Antiviral activities were tested in HCV genotype 1b replicon.[23] Unsubstituted 6-cyclopropylpurine ribonucleoside **2h** showed significant cytostatic effect, $IC_{50}$(L1210) = 4.89 ± 0.35 μM, $IC_{50}$(HL60) = 11.94 ± 0.78 μM and $IC_{50}$(CEM) = 0.92 ± 0.07 μM (which is comparable to 6-methylpurine ribonucleoside[5]) and a non-selective anti-HCV effect in replicon, $EC_{50}$ = 3.4 μM, $CC_{50}$ (huh-7) > 100 μM. On the other hand, free 6-cyclopropylpurine base **2g**

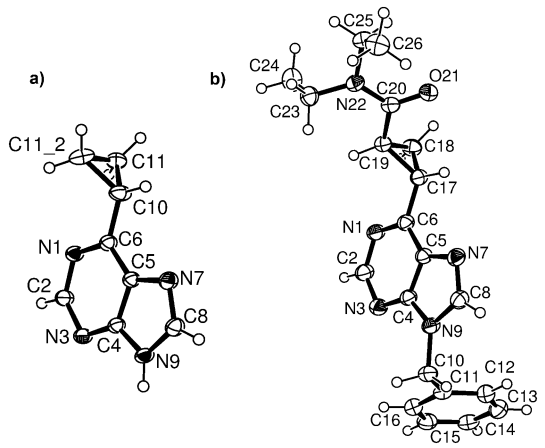



**Fig. 1** ORTEP drawings of crystal structures of **2g** (a) and **6a** (b) with atom numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.

was inactive (in contrast to strongly cytotoxic 6-methylpurine[5]). This indicates that the mechanism of action of these two very related compounds (6-methyl and 6-cyclopropylpurine nucleosides) might be different. All the other compounds including the 2′-deoxyribonucleosides and all the compounds with a substituted cyclopropyl ring were entirely inactive in the above mentioned assays at 10 μM concentrations.

## Conclusions

In conclusion, two approaches to the construction of 6-cyclopropylpurines have been studied. Cross-coupling of 6-chloropurines with cyclopropylzinc chloride was used for the synthesis of unsubstituted 6-cyclopropylpurines, while a Cu-mediated cyclopropanation of 6-vinylpurines with ethyl diazoacetate was used for the synthesis of 6-[2-(ethoxycarbonyl)cyclopropyl]purines. Further functional group transformation of the esters led to amides, carboxylic acids and alcohols. A series of modified cyclopropylpurine bases and nucleosides has been prepared and tested for biological activity. Only unsubstituted 6-cyclopropylpurine ribonucleoside **2h** showed significant cytostatic and anti-HCV effects.

## Experimental

Melting points were determined on a Kofler block and are uncorrected. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer. IR spectra were measured on a Bruker equinox 55 and FTIR spectrometer Nicolet 6700. NMR spectra were recorded on Bruker Avance 600 ($^1$H at 600 MHz, $^{13}$C at 151 MHz), Bruker Avance 500 ($^1$H at 500 MHz, $^{13}$C at 125.8 MHz) and Bruker Avance 400 ($^1$H at 400 MHz, $^{13}$C at 100.6 MHz) spectrometers. $^1$H and $^{13}$C NMR spectra were referenced to the signal of TMS or to the solvent residual signal [DMSO-$d_6$: 2.50 ppm ($^1$H), 39.70 ppm ($^{13}$C); $CD_3OD$: 3.31 ppm ($^1$H); 49.00 ppm ($^{13}$C)]. H,C-HSQC and H,C-HMBC experiments were performed for complete assignment of all signals. Optical rotations were measured at 25 °C on an Autopol IV (Rudolph Research Analytical) polarimeter, $[\alpha]_D$ values are given in $10^{-1}$ deg cm$^2$ g$^{-1}$. Starting compounds were prepared according to literature procedures: **1a**,[24] **1b**,[25] **1c**,[8] **1d**,[26] **3a**,[27] **3b**,[28] **3e**.[29]

### General method for the Negishi cross-coupling

THF (3 ml) was added to flame–vacuum dried zinc chloride (272 mg, 2 mmol) under argon atmosphere. The mixture was stirred at −10 °C and a cyclopropylmagnesium bromide (4 ml, 0.5 M in THF) was added dropwise. The mixture was stirred for 40 min and then a solution of a 6-chloropurine **1** (1 mmol) and $Pd(PPh_3)_4$ (70 mg, 0.06 mmol) in THF (3 ml) was added. The resulting mixture was stirred for 2 hours at 40 °C. After completion, the reaction mixture was diluted with water (50 ml) and washed with ethyl acetate (3 × 50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–30%) and crystallized from chloroform–heptane to give the product.

### 9-Benzyl-6-cyclopropylpurine (2a)

White solid, yield 88%. $^1$H NMR (600 MHz, $CDCl_3$): 1.24 and 1.43 (2 × m, 2 × 2H, H-2,3-cycloprop); 2.78 (tt, 1H, $J_{vic}$ = 8.2, 4.7 Hz, H-1-cycloprop); 5.43 (s, 2H, $CH_2Ph$); 7.28–7.38 (m, 5H, Ph); 7.98 (s, 1H, H-8); 8.80 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 11.54 ($CH_2$-2,3-cycloprop); 12.97 (CH-1-cycloprop); 47.13 ($CH_2Ph$); 127.73 (CH-*o*-Ph); 128.49 (CH-*p*-Ph); 129.09 (CH-*m*-Ph); 132.25 (C-5); 135.29 (C-*i*-Ph); 143.15 (CH-8); 150.01 (C-4); 152.75 (CH-2); 164.34 (C-6). FAB-MS, *m/z* (rel.%) 279 (6) $[M + Na]^+$, 251 (100) $[M + H]^+$, 161 (10), 91 (75). HRMS calcd for $C_{15}H_{15}N_4$ $[M + H]^+$ 251.1296; found: 251.1287. IR ($CHCl_3$): 3112, 3093, 3069, 3035, 1595, 1580, 1500, 1457, 1412, 1331, 1078, 1030, 806, 700, 651, 619, 542, 456.

### 6-Cyclopropyl-9-(2,3,5-tri-*O*-toluoyl-β-D-ribofuranosyl)purine (2c)

White foam, yield 99%. $^1$H NMR (500 MHz, $CDCl_3$): 1.22 and 1.41 (2 × m, 2 × 2H, H-2,3-cycloprop); 2.37 and 2.41 (2 × s, 9H, $CH_3$-Tol); 2.74 (tt, 1H, $J_{vic}$ = 8.2, 4.7, H-1-cycloprop); 4.67 (dd, 1H, $J_{gem}$ = 12.2, $J_{5'b,4'}$ = 4.2 Hz, H-5′b); 4.81 (ddd, 1H, $J_{4',3'}$ = 4.6, $J_{4',5'}$ = 4.2, 3.2 Hz, H-4′); 4.88 (dd, 1H, $J_{gem}$ = 12.2, $J_{5'a,4'}$ = 3.2 Hz, H-5′a); 6.22 (dd, 1H, $J_{3',2'}$ = 5.8, $J_{3',4'}$ = 4.6 Hz, H-3′); 6.40 (dd, 1H, $J_{2',3'}$ = 5.8, $J_{2',1'}$ = 5.4 Hz, H-2′); 6.47 (d, 1H, $J_{1',2'}$ = 5.4 Hz, H-1′); 7.16, 7.21 and 7.25 (3 × m, 3 × 2H, H-*m*-Tol); 7.82, 7.90 and 7.99 (3 × m, 3 × 2H, H-*o*-Tol); 8.15 (s, 1H, H-8); 8.68 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 11.62 and 11.66 ($CH_2$-2,3-cycloprop); 13.00 (CH-1-cycloprop); 21.69 and 21.71 ($CH_3$-Tol); 63.48 ($CH_2$-5′); 71.41 (CH-3′); 73.64 (CH-2′); 80.90 (CH-4′); 86.69 (CH-1′); 125.67, 126.02 and 126.57 (C-*i*-Tol); 129.19, 129.23 and 129.30 (CH-*m*-Tol); 129.75, 129.85 and 129.86 (CH-*o*-Tol); 132.96 (C-5); 141.91 (CH-8); 144.15, 144.52 and 144.62 (C-*p*-Tol); 149.66 (C-4); 152.82 (CH-2); 164.77 (C-6); 165.15, 165.37 and 166.21 (CO). FAB-MS, *m/z* (rel.%) 647 (50) $[M + H]^+$, 529 (10), 487 (22), 369 (10), 295 (10), 279 (20), 197 (10), 181 (26), 161 (18), 149 (10), 119 (100), 93 (30), 73 (20). HRMS calcd for $C_{37}H_{35}N_4O_7$ $[M + H]^+$ 647.2505; found: 647.2494. IR ($CHCl_3$): 3117, 3095, 3033, 1727, 1612, 1596, 1580, 1509, 1500, 1412, 1371, 1332, 1311, 1298, 1245, 1193, 1180, 1126, 1114, 1020, 839, 806, 691, 645, 476.

**6-Cyclopropyl-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentafuranosyl)purine (2d)**

White foam, yield 99%. $^1$H NMR (500 MHz, $CDCl_3$): 1.23 and 1.41 (2 × m, 2 × 2H, H-2,3-cycloprop); 2.41 and 2.44 (2 × s, 2 × 3H, $CH_3$-Tol); 2.75 (tt, 1H, $J_{vic} = 8.2$, 4.7 Hz, H-1-cycloprop); 2.84 (ddd, 1H, $J_{gem} = 14.2$, $J_{2'b,1'} = 5.8$, $J_{2'b,3'} = 2.2$ Hz, H-2′b); 3.19 (ddd, 1H, $J_{gem} = 14.2$, $J_{2'a,1'} = 8.4$, $J_{2'a,3'} = 6.4$ Hz, H-2′a); 4.63–4.70 (m, 2H, H-4′ and H-5′b); 4.76 (m, 1H, $J_{gem} = 11.4$, $J_{5'a,4'} = 3.5$, H-5′a); 5.83 (ddd, 1H, $J_{3',2'} = 6.4$, 2.2, $J_{3',4'} = 2.0$ Hz, H-3′); 6.59 (dd, 1H, $J_{1',2'} = 8.4$, 5.8 Hz, H-1′); 7.22 and 7.28 (2 × m, 2 × 2H, H-*m*-Tol); 7.90 and 7.97 (2 × m, 2 × 2H, H-*o*-Tol); 8.17 (s, 1H, H-8); 8.71 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 11.57 and 11.58 ($CH_2$-2,3-cycloprop); 12.96 (CH-1-cycloprop); 21.66 and 21.71 ($CH_3$-Tol); 37.72 ($CH_2$-2′); 63.98 ($CH_2$-5′); 75.12 (CH-3′); 82.99 (CH-4′); 84.74 (CH-1′); 126.36 and 126.62 (C-*i*-Tol); 129.25 and 129.26 (CH-*m*-Tol); 129.61 and 129.78 (CH-*o*-Tol); 132.98 (C-5); 141.46 (CH-8); 144.11 and 144.50 (C-*p*-Tol); 149.45 (C-4); 152.57 (CH-2); 164.61 (C-6); 165.93 and 166.14 (CO). FAB-MS, *m*/*z* (rel.%) 535 (5) $[M + Na]^+$, 513 (15) $[M + H]^+$, 161 (80), 119 (100), 91 (15), 81 (65). HRMS calcd for $C_{29}H_{31}N_4O_6$ $[M + H]^+$ 513.2137; found: 513.2160. IR ($CHCl_3$): 3126, 3096, 3063, 1721, 1612, 1596, 1582, 1509, 1498, 1411, 1332, 1311, 1250, 1191, 1179, 1121, 1103, 1021, 841, 806, 691, 646, 476.

**General method for cyclopropanation of 6-vinylpurines**

A mixture of a vinylpurine **3** (0.5 mmol) and copper powder (10 mg, 0.15 mmol) in dry toluene (5 ml) was heated to 95 °C under stirring. Then ethyldiazoacetate (0.3 ml, 2.5 mmol) was added at once. The mixture was further stirred at 95 °C for 6 h. The solids were removed by filtration, the filtrate was evaporated and purified by column chromatography (silica gel, ethyl acetate/hexane 0–30%).

**9-Benzyl-6-[2-(ethoxycarbonyl)cyclopropyl]purine (4a)**

Light yellow crystals, yield 75%, mp 83–89 °C. $^1$H NMR (400 MHz, $CDCl_3$): 1.27 (t, 3H, $J_{vic} = 7.2$ Hz, C$H_3$CH$_2$O); 1.82 (ddd, 1H, $J_{vic} = 8.9$, 5.8, $J_{gem} = 3.7$ Hz, 3b-cycloprop); 1.90 (ddd, 1H, $J_{vic} = 8.6$, 5.9, $J_{gem} = 3.7$ Hz, 3a-cycloprop); 2.60 (ddd, 1H, $J_{vic} = 8.6$, 5.8, 3.9 Hz, 2-cycloprop); 3.34 (dddd, 1H, $J_{vic} = 8.9$, 5.9, 3.9, $J_{CH,2} = 0.3$ Hz, 1-cycloprop); 4.17 (m, 2H, CH$_3$C$H_2$O); 5.44 (s, 2H, $CH_2$Ph); 7.29 (m, 2H, H-*o*-Ph); 7.31–7.38 (m, 3H, H-*m*,*p*-Ph); 8.01 (s, 1H, H-8); 8.81 (s, 1H, H-2). $^{13}$C NMR (100.6 MHz, $CDCl_3$): 14.19 (*C*H$_3$CH$_2$O); 17.95 ($CH_2$-3-cycloprop); 22.62 ($CH_2$-1-cycloprop); 25.31 ($CH_2$-2-cycloprop); 47.22 ($CH_2$Ph); 60.85 (CH$_3$*C*H$_2$O); 127.74 (CH-*o*-Ph); 128.57 (CH-*p*-Ph); 129.12 (CH-*m*-Ph); 132.28 (C-5); 135.12 (C-*i*-Ph); 143.77 (CH-8); 150.54 (C-4); 152.60 (CH-2); 160.09 (C-6); 172.37 (CO). FAB-MS, *m*/*z* (rel.%) 323 (62) $[M + H]^+$, 249 (8), 159 (10), 91 (100), 63 (6). HRMS calcd for $C_{18}H_{19}N_4O_2$ $[M + H]^+$ 323.1508; found: 323.1520. IR ($CHCl_3$): 3112, 3092, 3069, 3032, 1723, 1596, 1583, 1502, 1477, 1456, 1410, 1403, 1386, 1367, 1327, 1185, 1105, 1090, 1079, 1030, 699, 651, 642, 619, 542, 455.

**9-Benzyl-6-[3-diazenyl-3-(ethoxycarbonyl)prop-2-enyl]purine (5a)**

Yellow solid. $^1$H NMR (400 MHz, $CDCl_3$): 1.29 (t, 3H, $J_{vic} = 7.1$, C$H_3$CH$_2$O); 3.58 (dd, 1H, $J_{gem} = 17.5$, $J_{vic} = 12.3$ Hz, CH$_a$H$_b$-pur); 3.84 (dd, 1H, $J_{gem} = 17.5$, $J_{vic} = 5.0$ Hz, C$H_a$H$_b$-pur); 4.21 (q, 2H, $J_{vic} = 7.1$ Hz, CH$_3$C$H_2$O); 4.54 (dd, 1H, $J_{vic} = 12.3$, 5.0 Hz, CH=); 5.47 (s, 2H, $CH_2$Ph); 6.99 (bs, 1H, NH); 7.26–7.40 (m, 5H, Ph); 8.11 (s, 1H, H-8); 8.97 (s, 1H, H-2). $^{13}$C NMR (100.6 MHz, $CDCl_3$): 14.09 (*C*H$_3$CH$_2$O); 35.63 ($CH_2$-pur); 47.25 ($CH_2$Ph); 60.61 (CH=); 61.89 (CH$_3$*C*H$_2$O); 127.69 (CH-*o*-Ph); 128.57 (CH-*p*-Ph); 129.12 (CH-*m*-Ph); 130.05 (C-5); 135.08 (C-*i*-Ph); 145.06 (CH-8); 148.87 and 148.94 (C-6 and C–N=NH); 152.06 (C-4); 152.44 (CH-2); 172.04 (CO). ESI-MS, *m*/*z* (rel.%) 373 (95) $[M + Na]^+$, 351 (30) $[M + H]^+$, 316 (37), 288 (100). HRMS calcd for $C_{18}H_{18}N_6O_2Na$ $[M + Na]^+$ 373.13889; found 373.13812. IR (micr. refl.): 3282, 2980, 2930, 1727, 1599, 1541, 1499, 1455, 1409, 1383, 1366, 1328, 1264, 1212, 1186, 1158, 1097, 1057, 995, 927, 883, 844, 806, 775, 760, 730, 697.

**6-[2-(Ethoxycarbonyl)cyclopropyl]-9-(2,3,5-tri-*O*-*tert*-butyldimethylsilyl-β-D-ribofuranosyl)purine (4e)**

Yellow oil, yield 60%. Diastereomeric mixture 1 : 1. $^1$H NMR (600 MHz, $CDCl_3$): −0.25, −0.23, −0.041, −0.036, 0.096, 0.100, 0.104, 0.106, 0.139, 0.143, 0.148 and 0.153 (12 × s, 12 × 3H, $CH_3$Si); 0.79, 0.80, 0.93, 0.94, 0.960 and 0.963 (6 × s, 6 × 9H, $(CH_3)_3$C); 1.275 and 1.277 (2 × t, 2 × 3H, $J_{vic} = 7.1$ Hz, C$H_3$CH$_2$O); 1.811 and 1.813 (2 × ddd, 2 × 1H, $J_{vic} = 8.9$, 5.8, $J_{gem} = 3.37$ Hz, H-3b-cycloprop); 1.86 and 1.87 (2 × ddd, 2 × 1H, $J_{vic} = 8.6$, 6.0, $J_{gem} = 3.7$ Hz, H-3a-cycloprop); 2.59 and 2.60 (2 × ddd, 2 × 1H, $J_{vic} = 8.6$, 5.8, 3.9 Hz, H-2-cycloprop); 3.34 and 3.35 (2 × ddd, 2 × 1H, $J_{vic} = 8.9$, 6.0, 3.9 Hz, H-1-cycloprop); 3.79 and 3.80 (2 × dd, 2 × 1H, $J_{gem} = 11.4$, $J_{5'b,4'} = 2.7$ Hz, H-5′b); 4.02 and 4.03 (2 × dd, 2 × 1H, $J_{gem} = 11.4$, $J_{5'a,4'} = 3.9$ Hz, H-5′a); 4.14 (ddd, 2H, $J_{4',5'} = 3.9$, 2.7, $J_{4',3'} = 3.7$ Hz, H-4′); 4.17 and 4.18 (2 × q, 2 × 2H, $J_{vic} = 7.1$ Hz, CH$_3$C$H_2$O); 4.32 (dd, 2H, $J_{3',2'} = 4.4$, $J_{3',4'} = 3.7$ Hz, H-3′); 4.64 and 4.67 (2 × dd, 2 × 1H, $J_{2',1'} = 5.1$, $J_{2',3'} = 4.4$ Hz, H-2′); 6.10 and 6.11 (2 × d, 2 × 1H, $J_{1',2'} = 5.1$ Hz, H-1′); 8.40 and 8.41 (2 × s, 2 × 1H, H-8); 8.75 (s, 2H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): −5.37, −5.04, −4.99, −4.75, −4.73, −4.69 and −4.42 ($CH_3$Si); 14.20 (*C*H$_3$CH$_2$O); 17.82, 17.83, 18.07, 18.16, 18.53 and 18.54 ($(CH_3)_3C$ and $CH_2$-3-cycloprop); 22.54 and 22.56 (CH-1-cycloprop); 25.21 and 25.26 (CH-2-cycloprop); 25.63, 25.64, 25.82 and 26.08 ($(CH_3)_3$C); 60.85 (CH$_3$*C*H$_2$O); 62.41 and 62.46 ($CH_2$-5′); 71.81 and 71.90 (CH-3′); 75.86 and 75.88 (CH-2′); 85.40 and 85.50 (CH-4′); 88.21 and 88.22 (CH-1′); 132.94 (C-5); 142.88 and 142.93 (CH-8); 150.27 (C-4); 152.33 (CH-2); 159.94 and 159.95 (C-6); 172.43 (CO). FAB-MS, *m*/*z* (rel.%) 729 (10) $[M + Na]^+$, 707 (14) $[M + H]^+$, 231 (10), 177 (25), 154 (32), 137 (25), 109 (10), 89 (7), 73 (100), 59 (11). HRMS calcd for $C_{34}H_{63}N_4O_6Si_3$ $[M + H]^+$ 707.4055; found: 707.4045. IR ($CHCl_3$): 3118, 3066, 1723, 1596, 1581, 1499, 1472, 1463, 1408, 1390, 1363, 1327, 1258, 1186, 1168, 1110, 1084, 1070, 939, 839, 813, 647.

**General method for amidation of esters**

A suspension of dry $AlCl_3$ (267 mg, 2 mmol) in dichloromethane (4 ml) was cooled to 0 °C followed by addition of an amine (5 mmol). The reaction mixture was stirred for 10 min at 0 °C until $AlCl_3$ was dissolved. Then a solution of ester **4a** (or **4b**, **4e**, **4f**) (1 mmol) in dichloromethane (2 ml) was added in one go. The resulting mixture was stirred for 1 h at ambient temperature. After completion, the reaction mixture was diluted with water (50 ml),

and then washed with ethyl acetate (3 × 50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–30%) and crystallized from chloroform–heptane to give the product.

### 9-Benzyl-6-[2-(diethylcarbamoyl)cyclopropyl]purine (6a)

White crystals, mp 94–97 °C, yield 89%. $^1$H NMR (600 MHz, $CDCl_3$): 1.12 and 1.18 (2 × t, 2 × 3H, $J_{vic}$ = 7.1 Hz, C$H_3$CH$_2$N); 1.74 (ddd, 1H, $J_{vic}$ = 8.5, 5.6, $J_{gem}$ = 3.2 Hz, H-3b-cycloprop); 1.90 (ddd, 1H, $J_{vic}$ = 8.9, 5.8, $J_{gem}$ = 3.2 Hz, H-3a-cycloprop); 2.80 (ddd, 1H, $J_{vic}$ = 8.5, 5.8, 4.0 Hz, H-2-cycloprop); 3.31 (ddd, 1H, $J_{vic}$ = 8.9, 5.6, 4.0 Hz, H-1-cycloprop); 3.35–3.50 (m, 4H, CH$_3$C$H_2$N); 5.43 (s, 2H, CH$_2$Ph); 7.29–7.38 (m, 5H, Ph); 8.01 (s, 1H, H-8); 8.82 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 13.18 and 14.83 (*C*H$_3$CH$_2$N); 18.23 (CH$_2$-3-cycloprop); 22.12 (CH-1-cycloprop); 23.84 (CH-2-cycloprop); 40.91 and 42.15 (CH$_3$*C*H$_2$N); 47.18 (CH$_2$Ph); 127.77 (CH-*o*-Ph); 128.52 (CH-*p*-Ph); 129.08 (CH-*m*-Ph); 132.36 (C-5); 135.16 (C-*i*-Ph); 143.62 (CH-8); 150.41 (C-4); 152.55 (CH-2); 161.34 (C-6); 169.92 (CO). FAB-MS, *m*/*z* (rel.%) = 350 (94) [M + H]$^+$ (cation), 277 (40), 249 (15), 159 (10), 91 (100), 74 (5). HRMS calcd for $C_{20}H_{24}N_5O$ [M + H]$^+$ 350.1980; found: 350.1978. Anal. calcd for $C_{20}H_{23}N_5O$: C 68.74, H 6.63, N 20.04. Found: C 68.42, H 6.47, N 19.82%. IR ($CHCl_3$): 3112, 3092, 3069, 3035, 1630, 1603, 1595, 1579, 1500, 1456, 1423, 1410, 1382, 1329, 1079, 1030, 808, 701, 642, 619, 454.

### 6-[2-(Diethylcarbamoyl)cyclopropyl]-9-(2,3,5-tri-*O*-*tert*-butyldimethylsilyl-β-D-ribofuranosyl)purine (6e)

White foam, yield 85%. Diastereomeric mixture 1 : 1. $^1$H NMR (600 MHz, $CDCl_3$): −0.27, −0.24, −0.046, −0.039, 0.100, 0.103, 0.108, 0.112, 0.138, 0.142, 0.145 and 0.151 (12 × s, 12 × 3H, CH$_3$Si); 0.78, 0.79, 0.937, 0.939, 0.958 and 0.963 (6 × s, 6 × 9H, (CH$_3$)$_3$C); 1.130, 1.131, 1.150 and 1.152 (4 × t, 4 × 3H, $J_{vic}$ = 7.2 Hz, C$H_3$CH$_2$N); 1.738 and 1.740 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.4, 5.6, $J_{gem}$ = 3.3 Hz, H-3b-cycloprop); 1.90 and 1.91 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.1, 5.7, $J_{gem}$ = 3.3, H-3a-cycloprop); 2.77 and 2.79 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.4, 5.7, 4.0 Hz, H-2-cycloprop); 3.286 and 3.290 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.1, 5.6, 4.0 Hz, H-1-cycloprop); 3.37–3.50 (m, 8H, CH$_3$C$H_2$N); 3.80 (dd, 2H, $J_{gem}$= 11.4, $J_{5'b,4'}$ = 2.7, H-5′b); 4.02 and 4.03 (2 × dd, 2 × 1H, $J_{gem}$ = 11.4, $J_{5'a,4'}$ = 4.0 Hz, H-5′a); 4.13–4.16 (m, 2H, H-4′); 4.32 and 4.34 (2 × dd, 2 × 1H, $J_{3',2'}$ = 4.3, $J_{3',4'}$ = 3.6 Hz, H-3′); 4.64 and 4.67 (2 × dd, 2 × 1H, $J_{2',1'}$ = 5.3, $J_{2',3'}$ = 4.3, H-2′); 6.10 and 6.11 (2 × d, 2 × 1H, $J_{1',2'}$ = 5.3, H-1′); 8.38 and 8.41 (2 × s, 2 × 1H, H-8); 8.76 (s, 2H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): −5.40, −5.13, −5.09, −4.75, −4.73, −4.71, −4.69, −4.45 and −4.44 (CH$_3$Si); 13.22 and 14.80 (*C*H$_3$CH$_2$N); 17.80 ((CH$_3$)$_3$*C*); 18.02 (CH$_2$-3-cycloprop); 18.05 ((CH$_3$)$_3$*C*); 18.11 (CH$_2$-3-cycloprop); 18.50 and 18.51 ((CH$_3$)$_3$*C*); 22.19 and 22.25 (CH-1-cycloprop); 23.92 and 24.01 (CH-2-cycloprop); 25.61, 25.81, 26.05 and 26.06 ((*C*H$_3$)$_3$C); 40.97 and 42.18 (CH$_3$*C*H$_2$N); 62.45 and 62.47 (CH$_2$-5′); 71.85 and 71.91 (CH-3′); 75.77 and 75.96 (CH-2′); 85.48 and 85.53 (CH-4′); 88.10 and 88.14 (CH-1′); 132.946 and 132.254 (C-5); 142.69 and 142.80 (CH-8); 150.18 (C-4); 152.30 and 152.31 (CH-2); 161.18 and 161.22 (C-6); 169.99 and 170.00 (CO). FAB-MS, *m*/*z* (rel.%) 756 (35) [M + Na]$^+$, 734 (60) [M + H]$^+$, 718 (12), 676 (12), 416 (12), 147 (10), 89 (6), 73 (100), 59 (12). HRMS calcd for $C_{36}H_{68}N_5O_5Si_3$ [M + H]$^+$ 734.4528; found: 734.4536. IR ($CHCl_3$): 3118, 3064, 2898, 1629, 1595, 1580, 1497, 1485, 1471, 1463, 1410, 1382, 1363, 1327, 1258, 1083, 1072, 939, 839, 681, 647.

### General method for ester reduction

A mixture of ester **4a** (or **4b**, **4e**, **4f**) (1 mmol) and $NaBH_4$ (1.89 g, 50 mmol) in dry ethanol (50 ml) was heated to 60 °C under argon atmosphere for 1 day. After completion, the reaction mixture was diluted with aqueous saturated solution of $NH_4Cl$ (200 ml), and then washed with ethyl acetate (3 × 50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–30%) and crystallized from chloroform–heptane.

### 9-Benzyl-6-[2-(hydroxymethyl)cyclopropyl]purine (10a)

Chromatography methanol/chloroform 0–10%, white crystals, mp 103–104 °C, yield 57%. $^1$H NMR (600 MHz, DMSO-$d_6$): 1.18 (ddd, 1H, $J_{vic}$ = 8.5, 6.2, $J_{gem}$ = 3.5 Hz, H-3b-cycloprop); 1.40 (ddd, 1H, $J_{vic}$ = 8.4, 4.8, $J_{gem}$ = 3.5 Hz, H-3a-cycloprop); 1.92 (m, 1H, H-2-cycloprop); 2.59 (ddd, 1H, $J_{vic}$ = 8.5, 4.8, 4.2 Hz, H-1-cycloprop); 3.44 and 3.58 (2 × dt, 2H, $J_{gem}$ = 11.3, $J_{vic}$ = 5.6 Hz, CH$_2$O); 4.74 (t, 1H, $J_{vic}$ = 5.6, OH); 5.48 (2H, CH$_2$Ph); 7.26–7.35 (m, 5H, Ph); 8.63 (s, 1H, H-8); 8.69 (s, 1H, H-2). $^{13}$C NMR (151 MHz, DMSO-$d_6$): 15.56 (CH$_2$-3-cycloprop); 18.21 (CH-1-cycloprop); 27.44 (CH-2-cycloprop); 46.56 (CH$_2$Ph); 62.81 (CH$_2$O); 127.74 (CH-*o*-Ph); 128.08 (CH-*p*-Ph); 128.96 (CH-*m*-Ph); 131.67 (C-5); 136.89 (C-*i*-Ph); 145.41 (CH-8); 149.96 (C-4); 152.24 (CH-2); 162.44 (C-6). FAB-MS, *m*/*z* (rel.%) = 281 (100) [M + H]$^+$ (cation), 263 (10), 220 (5), 91 (100). HRMS calcd for $C_{16}H_{17}N_4O$ [M + H]$^+$ 281.1402; found: 281.1406. IR (KBr): 3424, 3228, 1600, 1581, 1510, 1497, 1454, 1410, 1329, 1217, 1080, 1030, 1002, 812, 732, 697, 618, 466.

### 6-[2-(Hydroxymethyl)cyclopropyl]-9-(2,3,5-tri-*O*-*tert*-butyldimethylsilyl-β-D-ribofuranosyl)purine (10e)

White foam, yield 68%. Diastereomeric mixture 1 : 1. $^1$H NMR (600 MHz, $CDCl_3$): −0.23, −0.21, −0.04, −0.03, 0.100, 0.101, 0.106, 0.109, 0.14 and 0.15 (10 × s, 36H, CH$_3$Si); 0.79, 0.80, 0.94 and 0.96 (4 × s, 54H, (CH$_3$)$_3$C); 1.21 and 1.67 (2 × m, 2 × 2H, H-3-cycloprop); 2.13 (m, 2H, H-2-cycloprop); 2.74 (dt, 2H, $J_{vic}$ = 8.8, 4.6 Hz, H-1-cycloprop); 3.65 (dd, 1H, $J_{gem}$ = 11.5, $J_{vic}$ = 7.1 Hz, CH$_a$$H_b$O); 3.79 and 3.80 (2 × dd, 2 × 1H, $J_{gem}$= 11.3, $J_{5'b,4'}$ = 2.6 Hz, H-5′b); 3.81 (dd, 1H, $J_{gem}$ = 11.5, $J_{vic}$ = 6.0 Hz, C$H_a$H$_b$O); 4.03 and 4.04 (2 × dd, 2 × 1H, $J_{gem}$ = 11.3, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.14 (ddd, 2H, $J_{4',5'}$ = 3.9, 2.6, $J_{4',3'}$ = 3.7 Hz, H-4′); 4.32 and 4.33 (2 × dd, 2 × 1H, $J_{3',2'}$ = 4.5, $J_{3',4'}$ = 3.7 Hz, H-3′); 4.66 and 4.67 (2 × dd, 2 × 1H, $J_{2',1'}$ = 5.0, $J_{2',3'}$ = 4.5 Hz, H-2′); 6.09 and 6.10 (2 × d, 2 × 1H, $J_{1',2'}$ = 5.0 Hz, H-1′); 8.39 (s, 2H, H-8); 8.73 (s, 2H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): −5.38, −5.37, −5.04, −5.00, −4.75, −4.71, −4.43 and −4.41 (CH$_3$Si); 15.37 and 15.43 (CH$_2$-3-cycloprop); 17.82, 17.83 and 18.06 ((CH$_3$)$_3$*C*); 18.52 (CH-1-cycloprop); 25.63, 25.64, 25.82 and 26.07 ((*C*H$_3$)$_3$C); 27.48 and 27.54 (CH-2-cycloprop); 62.35 and 62.45 (CH$_2$-5′); 65.58 and

65.60 ($CH_2O$); 71.74 and 71.86 (CH-3′); 75.74 and 75.93 (CH-2′); 85.30 and 85.43 (CH-4′); 88.20 and 88.32 (CH-1′); 132.68 and 132.73 (C-5); 142.41 and 142.47 (CH-8); 149.76 and 149.78 (C-4); 152.42 and 152.45 (CH-2); 162.55 (C-6). FAB-MS, *m/z* (rel.%) = 665 (10) $[M + H]^+$ (cation), 147 (10), 115 (8), 89 (10), 73 (100), 59 (12). HRMS calcd for $C_{32}H_{61}N_4O_5Si_3$ $[M + H]^+$ 665.3949; found: 665.3948. IR ($CHCl_3$): 3613, 3354, 3119, 3065, 1596, 1580, 1499, 1473, 1463, 1409, 1390, 1363, 1331, 1258, 1115, 1083, 1073, 1049, 939, 839, 813, 648.

### 6-[2-(Hydroxymethyl)cyclopropyl]-9*H*-purine (10g)

Dichloromethane (5 ml) was added to dry ester **4g** (190 mg, 0.8 mmol) under argon atmosphere. The mixture was stirred at 0 °C and DIBAH (2 ml, 1 M in hexane) was added dropwise. The mixture was stirred for 1 h at ambient temperature. After completion, the reaction mixture was quenched with ethanol (50 ml) and then $MnO_2$ (200 mg) was added. The mixture was sonicated at ambient temperature for 1 h, filtered and the solvent was evaporated. The residue was purified by column chromatography (silica gel, methanol/chloroform 5–15%) and crystallized from chloroform–heptane to give **10g** (100 mg, 65%) as white crystals, mp 238–242 °C. $^1$H NMR (500 MHz, DMSO-$d_6$ + DCl): 1.53 (ddd, 1H, $J_{vic}$ = 8.5, 6.8, $J_{gem}$ = 4.2 Hz, H-3b-cycloprop); 1.88 (ddd, 1H, $J_{vic}$ = 9.0, 5.2, $J_{gem}$ = 4.2 Hz, H-3a-cycloprop); 2.34 (m, 1H, H-2-cycloprop); 2.71 (ddd, 1H, $J_{vic}$ = 8.5, 5.2, 4.2 Hz, H-1-cycloprop); 3.46 (dd, 1H, $J_{gem}$ = 11.6, $J_{vic}$ = 6.1 Hz, $CH_aH_bO$); 3.60 (dd, 1H, $J_{gem}$ = 11.6, $J_{vic}$ = 5.0 Hz, $CH_aH_bO$); 9.01 (s, 1H, H-2); 9.11 (s, 1H, H-8). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$ + DCl): 18.12 ($CH_2$-3-cycloprop); 18.52 (CH-1-cycloprop); 30.81 (CH-2-cycloprop); 62.17 ($CH_2O$); 127.21 (C-5); 147.83 (CH-2); 147.91 (CH-8); 152.82 (C-4); 158.68 (C-6). FAB-MS, *m/z* (rel.%) = 239 (60), 231 (12), 191 (10) $[M + H]^+$ (cation), 177 (18), 160 (22), 154 (42), 149 (12), 137 (42), 102 (100). HRMS calcd for $C_9H_{11}N_4O$ $[M + H]^+$ 191.0932; found: 191.0939. IR (KBr): 3435, 2850, 1632, 1604, 1476, 1398, 1324, 1037, 808, 644.

### General method for ester hydrolysis

A mixture of ester **4a** (or **4g**) (1 mmol) and NaOH (240 mg, 6 mmol) in 50% aqueous THF (15 ml) was stirred at ambient temperature for 1 h. After completion, the reaction mixture was neutralized with 10% aqueous $H_2SO_4$. Solid salts were filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, methanol/chloroform 5–15%) and crystallized from chloroform–heptane.

### 9-Benzyl-6-[2-(carboxy)cyclopropyl]purine (9a)

White solid, yield 81%. $^1$H NMR (500 MHz, $CD_3OD$): 1.74 (ddd, 1H, $J_{vic}$ = 8.9, 5.7, $J_{gem}$ = 3.6Hz, H-3b-cycloprop); 1.86 (ddd, 1H, $J_{vic}$ = 8.5, 5.9, $J_{gem}$ = 3.6 Hz, H-3a-cycloprop); 2.48 (ddd, 1H, $J_{vic}$ = 8.5, 5.7, 3.9 Hz, H-2-cycloprop); 3.24 (ddd, 1H, $J_{vic}$ = 8.9, 5.9, 3.9 Hz, H-1-cycloprop); 5.50 (s, 2H, $CH_2Ph$); 7.25–7.37 (m, 5H, H-*o*,*m*,*p*-Ph); 8.46 (s, 1H, H-8); 8.74 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CD_3OD$): 18.34 ($CH_2$-3-cycloprop); 22.25 (CH-1-cycloprop); 26.11 (CH-2-cycloprop); 48.17 ($CH_2Ph$); 128.90 (CH-*o*-Ph); 129.36 (CH-*p*-Ph); 130.00 (CH-*m*-Ph); 133.01 (C-5); 137.27 (C-*i*-Ph); 146.86 (CH-8); 151.75 (C-4); 153.52 (CH-2); 160.94 (C-6); 175.99 (CO). FAB-MS, *m/z* (rel.%) 295 (92) $[M + H]^+$, 224 (6), 91 (100). HRMS calcd for $C_{16}H_{15}N_4O_2$ $[M + H]^+$ 295.1195; found: 295.1193. IR (KBr): 3111, 3070, 3032, 2571, 2508, 1708, 1700, 1596, 1584, 1508, 1498, 1456, 1409, 1338, 1316, 1212, 1078, 1023, 804, 729, 696, 653, 639, 619, 454.

### 6-[2-(Carboxy)cyclopropyl]-9*H*-purine (9g)

White solid, yield 80%. $^1$H NMR (600 MHz, DMSO-$d_6$ + DCl): 1.74 (ddd, 1H, $J_{vic}$ = 8.9, 5.9, $J_{gem}$ = 3.8 Hz, H-3b-cycloprop); 1.90 (ddd, 1H, $J_{vic}$ = 8.7, 5.9, $J_{gem}$ = 3.8 Hz, H-3a-cycloprop); 2.51 (ddd, 1H, $J_{vic}$ = 8.7, 5.9, 3.9 Hz, H-2-cycloprop); 3.18 (ddd, 1H, $J_{vic}$ = 8.9, 5.9, 3.9 Hz, H-1-cycloprop); 8.93 (s, 1H, H-2); 9.06 (s, 1H, H-8). $^{13}$C NMR (151 MHz, DMSO-$d_6$ + DCl): 18.25 ($CH_2$-3-cycloprop); 22.05 (CH-1-cycloprop); 25.66 (CH-2-cycloprop); 127.33 (C-5); 146.34 (CH-8); 151.05 (CH-2); 152.59 (C-4); 156.19 (C-6); 172.93 (CO). FAB-MS, *m/z* (rel.%) = 231 (30), 227 (14) $[M + Na]^+$ (cation), 205 (30) $[M + H]^+$ (cation), 177 (60), 154 (100), 137 (90), 109 (30), 105 (7), 92 (18), 79 (15), 61 (12). HRMS calcd for $C_9H_9N_4O_2$ $[M + H]^+$ 205.0725; found: 205.0729. IR (KBr): 3114, 3078, 2570, 2484, 1708, 1600, 1490, 1432, 1404, 1383, 1261, 807, 648, 641.

### General method for the cleavage of the THP protective group

A THP-protected compound (1 mmol) was dissolved in ethanol (10 ml) and Dowex 50 ($H^+$ form, 100 mg) was added. The mixture was heated at 70 °C and stirred for 6 h. After completion, the Dowex was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, methanol/chloroform 5–15%) and crystallized from MeOH–chloroform–heptane to give the product.

### 6-Cyclopropyl-9*H*-purine (2g)

White crystals, mp 186–191 °C, yield 47%. $^1$H NMR (600 MHz, DMSO-$d_6$ + DCl): 1.52 and 1.70 (2 × m, 2 × 2H, H-2,3-cycloprop); 2.83 (tt, 1H, $J_{vic}$ = 8.2, 4.8 Hz, H-1-cycloprop); 9.03 (s, 1H, H-2); 9.14 (s, 1H, H-8). $^{13}$C NMR (151 MHz, DMSO-$d_6$ + DCl): 13.62 (CH-1-cycloprop); 14.13 ($CH_2$-2,3-cycloprop); 126.99 (C-5); 147.50 (CH-8); 148.18 (CH-2); 152.53 (C-4); 159.38 (C-6). FAB-MS, *m/z* (rel.%) = 161 (100) $[M + H]^+$ (cation), 147 (10), 109 (8). HRMS calcd for $C_8H_9N_4$ $[M + H]^+$ 161.0827; found: 161.0832. Anal. calcd for $C_8H_8N_4$: C 59.99, H 5.03, N 34.98. Found: C 59.65, H 4.76, N 34.68%. IR (KBr): 3097, 3064, 1597, 1489, 1415, 1325, 1193, 807, 646.

### 6-[2-(Ethoxycarbonyl)cyclopropyl]-9*H*-purine (4g)

White crystals, 85%, mp 190–191 °C. $^1$H NMR (600 MHz, DMSO-$d_6$ + DCl): 1.19 (t, 3H, $J_{vic}$ = 7.2, $CH_3CH_2O$); 1.74 (ddd, 1H, $J_{vic}$ = 9.0, 5.8, $J_{gem}$ = 3.9 Hz, H-3b-cycloprop); 1.88 (ddd, 1H, $J_{vic}$ = 8.6, 6.0, $J_{gem}$ = 3.9 Hz, H-3a-cycloprop); 2.53 (ddd, 1H, $J_{vic}$ = 8.6, 5.8, 3.9 Hz, H-2-cycloprop); 3.19 (ddd, 1H, $J_{vic}$ = 9.0, 6.0, 3.9 Hz, H-1-cycloprop); 4.12 (q, 2H, $J_{vic}$ = 7.2 Hz, $CH_3CH_2O$); 8.88 (s, 1H, H-2); 8.95 (s, 1H, H-8). $^{13}$C NMR (151 MHz, DMSO-$d_6$ + DCl): 14.34 ($CH_3CH_2O$); 18.02 ($CH_2$-3-cycloprop); 22.28 (CH-1-cycloprop); 25.06 (CH-2-cycloprop); 61.09 ($CH_3CH_2O$); 127.83 (C-5); 146.01 (CH-8); 151.45 (CH-2); 152.76 (C-4); 155.94 (C-6); 171.66 (CO). FAB-MS, *m/z* (rel.%) = 233 (100) $[M + H]^+$

(cation), 187 (8), 159 (10), 134 (8), 102 (25), 93 (10). HRMS calcd for $C_{11}H_{13}N_4O_2$ [M + H]$^+$ 233.1038; found: 233.1039. IR (KBr): 3200, 3111, 3072, 2400, 1720, 1600, 1566, 1490, 1475, 1402, 1383, 1338, 1222, 1187, 1180, 1106, 1090, 810, 650.

### 6-[2-(Diethylcarbamoyl)cyclopropyl]-9*H*-purine (6g)

White hygroscopic solid, yield 66%. $^1$H NMR (500 MHz, DMSO-$d_6$+DCl): 1.01 and 1.09 (2 × t, 2 × 3H, $J_{vic}$ = 7.1 Hz, C$H_3$CH$_2$N); 1.77 (ddd, 1H, $J_{vic}$ = 8.8, 6.1, $J_{gem}$ = 3.5 Hz, H-3b-cycloprop); 1.95 (ddd, 1H, $J_{vic}$ = 8.6, 5.7, $J_{gem}$ = 3.5 Hz, H-3a-cycloprop); 3.08–3.16 (m, 2H, H-1,2-cycloprop); 3.30 and 3.44 (2 × q, 2 × 2H, $J_{vic}$ = 7.1 Hz, CH$_3$C$H_2$N); 9.04 (s, 1H, H-2); 9.20 (s, 1H, H-8). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$ + DCl): 13.46 and 15.17 (*C*H$_3$CH$_2$N); 19.13 (CH$_2$-3-cycloprop); 21.37 (CH-1-cycloprop); 24.84 (CH-2-cycloprop); 40.83 and 42.07 (CH$_3$*C*H$_2$N); 127.23 (C-5); 147.51 (CH-8); 149.28 (CH-2); 152.68 (C-4); 156.36 (C-6); 168.51 (CO). FAB-MS, *m*/*z* (rel.%) = 260 (100) [M + H]$^+$ (cation), 187 (14), 159 (12), 134 (10), 73 (5). HRMS calcd for $C_{13}H_{18}N_5O$ [M + H]$^+$ 260.1511; found: 260.1514. IR ($CHCl_3$): 3440, 1620, 1598, 1565, 1487, 1436, 1404, 1382, 1375, 1327, 811, 643

### General method for the cleavage of the Tol protective group

A Tol-protected compound (1.0 mmol) was dissolved in a solution of MeONa (0.3 mmol) in methanol (40 ml). The mixture was stirred at ambient temperature for 16 h, evaporated and the residue was purified by a silica gel column chromatography (methanol/chloroform 5–15%) and crystallized from MeOH–chloroform–heptane.

### 6-Cyclopropyl-9-(β-D-ribofuranosyl)purine (2h)

White crystals, yield 65%, mp 158–160 °C. $^1$H NMR (600 MHz, DMSO-$d_6$): 1.22 and 1.27 (2 × m, 2 × 2H, H-2,3-cycloprop); 2.69 (tt, 1H, $J_{vic}$ = 8.0, 4.8 Hz, H-1-cycloprop); 3.57 (ddd, 1H, $J_{gem}$ = 12.0, $J_{5'b,OH}$ = 6.2, $J_{5'b,4'}$ = 4.0 Hz, H-5′b); 3.69 (ddd, 1H, $J_{gem}$ = 12.0, $J_{5'a,OH}$ = 5.1, $J_{5'a,4'}$ = 4.0 Hz, H-5′a); 3.97 (td, 1H, $J_{4',5'}$ = 4.0, $J_{4',3'}$ = 3.6 Hz, H-4′); 4.18 (td, 1H, $J_{3',2'}$ = $J_{3',OH}$ = 4.9, $J_{3',4'}$ = 3.6 Hz, H-3′); 4.62 (ddd, 1H, $J_{2',OH}$ = 6.0, $J_{2',1'}$ = 5.8, $J_{2',3'}$ = 4.9 Hz, H-2′); 5.16 (dd, 1H, $J_{OH,5'}$ = 6.2, 5.1 Hz, OH-5′); 5.25 (d, 1H, $J_{OH,3'}$ = 4.9 Hz, OH-3′); 5.53 (dd, 1H, $J_{OH,2'}$ = 6.0 Hz, OH-2′); 6.00 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-1′); 8.71 (s, 1H, H-2); 8.74 (s, 1H, H-8). $^{13}$C NMR (151 MHz, DMSO-$d_6$): 11.34 and 11.37 (CH$_2$-2,3-cycloprop); 12.98 (CH-1-cycloprop); 61.55 (CH$_2$-5′); 70.57 (CH-3′); 73.86 (CH-2′); 85.91 (CH-4′); 87.84 (CH-1′); 132.45 (C-5); 144.10 (CH-8); 149.82 (C-4); 152.20 (CH-2); 163.22 (C-6). ESI-MS, *m*/*z* (rel.%) 315 (100) [M + Na]$^+$, 293 (60) [M + H]$^+$. HRMS calcd for $C_{13}H_{17}N_4O_4$ [M + H]$^+$ 293.12498; found 293.12438. Anal. calcd for $C_{13}H_{16}N_4O_4$: C 53.42, H 5.52, N 19.17. Found: C 53.16, H 5.41, N 18.89%. IR (KBr): 3408, 3169, 3117, 3106, 3070, 1501, 1420, 1405, 1341, 1330, 1222, 1210, 811, 804, 649, 640. [*α*]$_D$ −56.4 (*c* 0.35, MeOH).

### 6-Cyclopropyl-9-(2-deoxy-β-D-*erythro*-pentafuranosyl)purine (2i)

White crystals, mp 124–126 °C, yield 42%. $^1$H NMR (500 MHz, DMSO-$d_6$): 1.17–1.29 (m, 4H, H-2,3-cycloprop); 2.32 (ddd, 1H, $J_{gem}$ = 13.3, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 3.4 Hz, H-2′b); 2.67 (tt, 1H, $J_{vic}$ = 7.9, 4.7 Hz, H-1-cycloprop); 2.77 (ddd, 1H, $J_{gem}$ = 13.3, $J_{2'a,1'}$ = 7.3, $J_{2'a,3'}$ = 5.9 Hz, H-2′a); 3.52 (ddd, 1H, $J_{gem}$ = 11.7, $J_{5'b,OH}$ = 5.9, $J_{5'b,4'}$ = 4.5 Hz, H-5′b); 3.62 (ddd, 1H, $J_{gem}$ = 11.7, $J_{5'a,OH}$ = 5.3, $J_{5'a,4'}$ = 4.8 Hz, H-5′b); 3.88 (ddd, 1H, $J_{4',5'}$ = 4.8, 4.5, $J_{4',3'}$ = 3.0 Hz, H-4′); 4.44 (m, 1H, $J_{3',2'}$ = 5.9, 3.4, $J_{3',OH}$ = 4.1, $J_{3',4'}$ = 3.0 Hz, H-3′); 5.03 (dd, 1H, $J_{OH,5'}$ = 5.9, 5.3 Hz, OH-5′); 5.37 (d, 1H, $J_{OH,3'}$ = 4.1 Hz, OH-3′); 6.44 (dd, 1H, $J_{1',2'}$ = 7.3, 6.2 Hz, H-1′); 8.69 (s, 2H, H-2,8). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 11.20 and 11.23 (CH$_2$-2,3-cycloprop); 12.92 (CH-1-cycloprop); 39.48 (CH$_2$-2′); 61.80 (CH$_2$-5′); 70.88 (CH-3′); 83.92 (CH-1′); 88.16 (CH-4′); 132.39 (C-5); 143.90 (CH-8); 149.51 (C-4); 152.07 (CH-2); 163.04 (C-6). FAB-MS, *m*/*z* (rel.%) = 277 (15) [M + H]$^+$ (cation), 161 (100), 133 (76). HRMS calcd for $C_{13}H_{17}N_4O_3$ [M + H]$^+$ 277.1300; found: 277.1295. Anal. calcd for $C_{13}H_{16}N_4O_3$: C 56.51, H 5.84, N 20.28. Found: C 56.13, H 5.69, N 20.08%. IR (KBr): 3420, 3357, 3183, 3113, 3079, 1632, 1595, 1582, 1499, 1421, 1405, 1338, 1324, 1206, 1100, 1067, 1059, 811, 805, 642. [*α*]$_D$ −13.6 (*c* 0.45, MeOH).

### General method for the cleavage of the TBS protective group

A TBS-protected compound (1.0 mmol) was dissolved in a solution of NEt$_3$·3HF (1 ml, 6 mmol) in THF (3 ml). The mixture was stirred at ambient temperature for 1 day, evaporated and the residue was purified by silica gel column chromatography (methanol/chloroform 5–15%).

### 6-[2-(Ethoxycarbonyl)cyclopropyl]-9-(β-D-ribofuranosyl)purine (4h)

White foam, yield 75%. Diastereomeric mixture 1 : 1. $^1$H NMR (600 MHz, DMSO-$d_6$): 1.202 and 1.204 (2 × t, 2 × 3H, $J_{vic}$ = 7.1 Hz, C$H_3$CH$_2$O); 1.703 and 1.705 (2 × ddd, 2 × 1H, $J_{vic}$ = 9.0, 5.6, $J_{gem}$ = 3.7 Hz, H-3b-cycloprop); 1.81 and 1.83 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 6.0, $J_{gem}$ = 3.7 Hz, H-3a-cycloprop); 2.43 and 2.45 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 5.6, 4.0 Hz, H-2-cycloprop); 3.100 and 3.102 (2 × ddd, 2 × 1H, $J_{vic}$ = 9.0, 6.0, 4.0 Hz, H-1-cycloprop); 3.569 and 3.570 (2 × ddd, 2 × 1H, $J_{gem}$ = 12.0, $J_{5'b,OH}$ = 6.1, $J_{5'b,4'}$ = 4.0 Hz, H-5′b); 3.688 and 3.691 (2 × ddd, 2 × 1H, $J_{gem}$ = 12.0, $J_{5'a,OH}$ = 5.0, $J_{5'a,4'}$ = 4.0 Hz, H-5′a); 3.97 (td, 2H, $J_{4',5'}$ = 4.0, $J_{4',3'}$ = 3.7 Hz, H-4′); 4.128 and 4.129 (2 × q, 2 × 2H, $J_{vic}$ = 7.1 Hz, CH$_3$C$H_2$O); 4.177 and 4.185 (2 × td, 2 × 1H, $J_{3',2'}$ = $J_{3',OH}$ = 5.0, $J_{3',4'}$ = 3.7 Hz, H-3′); 4.59 and 4.60 (2 × ddd, 2 × 1H, $J_{2',OH}$ = 5.9, $J_{2',1'}$ = 5.6, $J_{2',3'}$ = 5.0 Hz, H-2′); 5.131 and 5.134 (2 × dd, 2 × 1H, $J_{OH,5'}$ = 6.1, 5.0 Hz, OH-5′); 5.26 (d, 2H, $J_{OH,3'}$ = 5.0 Hz, OH-3′); 5.537 and 5.539 (2 × d, 2 × 1H, $J_{OH,2'}$ = 5.9 Hz, OH-2′); 6.015 and 6.016 (2 × d, 2 × 1H, $J_{1',2'}$ = 5.6 Hz, H-1′); 8.78 (s, 2H, H-2); 8.809 and 8.811 (2 × s, 2 × 1H, H-8). $^{13}$C NMR (151 MHz, DMSO-$d_6$): 14.30 (*C*H$_3$CH$_2$O); 17.42 (CH$_2$-3-cycloprop); 22.35 (CH-1-cycloprop); 24.48 and 24.56 (CH-2-cycloprop); 60.94 (CH$_3$*C*H$_2$O); 61.42 and 61.44 (CH$_2$-5′); 70.45 and 70.47 (CH-3′); 73.94 (CH-2′); 85.87 and 85.89 (CH-4′); 87.91 and 87.92 (CH-1′); 132.47 (C-5); 144.85 (CH-8); 150.36 (C-4); 152.22 (CH-2); 158.55 and 158.56 (C-6); 171.88 and 171.90 (CO). FAB-MS, *m*/*z* (rel.%) = 387 (25) [M + Na]$^+$ (cation), 365 (25) [M + H]$^+$ (cation), 331 (7), 309 (15), 231 (30), 207 (10), 177 (70), 154 (100), 137 (85), 109 (27), 92 (17), 79 (14), 61 (14). HRMS calcd for $C_{16}H_{21}N_4O_6$ [M + H]$^+$ 365.1461; found: 365.1459. IR (KBr): 3423, 3255, 3111, 3070, 1725, 1699, 1632, 1599, 1583, 1499, 1406, 1386, 1366, 1328, 1213, 1182, 1093, 1055, 1043, 1025, 805, 645. [*α*]$_D$ −40.7 (*c* 0.24, MeOH).

**6-[2-(Ethoxycarbonyl)cyclopropyl]-9-(2-deoxy-β-D-*erythro*-pentafuranosyl)purine (4i)**

White foam, 80%. Diastereomeric mixture 1 : 1. $^1$H NMR (500 MHz, DMSO-$d_6$): 1.196 and 1.198 (2 × t, 2 × 3H, $J_{vic}$ = 7.1 Hz, C$H_3$CH$_2$O); 1.687 and 1.690 (2 × ddd, 2 × 1H, $J_{vic}$ = 9.1, 5.6, $J_{gem}$ = 3.7 Hz, H-3b-cycloprop); 1.80 and 1.81 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 6.2, $J_{gem}$ = 3.7 Hz, H-3a-cycloprop); 2.34 (ddd, 2H, $J_{gem}$ = 13.3, $J_{2'b,1'}$ = 6.3, $J_{2'b,3'}$ = 3.5 Hz, H-2′b); 2.41 and 2.43 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 5.6, 3.9 Hz, H-2-cycloprop); 2.760 and 2.764 (2 × ddd, 2 × 1H, $J_{gem}$ = 13.3, $J_{2'a,1'}$ = 7.2, $J_{2'a,3'}$ = 5.8 Hz, H-2′a); 3.084 and 3.086 (2 × ddd, 2 × 1H, $J_{vic}$ = 9.1, 6.2, 3.9 Hz, H-1-cycloprop); 3.52 and 3.62 (2 × ddd, 2 × 2H, $J_{gem}$ = 12.0, $J_{5',OH}$ = 5.6, $J_{5',4'}$ = 4.5 Hz, H-5′); 3.89 (td, 2H, $J_{4',5'}$ = 4.5, $J_{4',3'}$ = 3.1 Hz, H-4′); 4.120 and 4.122 (2 × q, 2 × 2H, $J_{vic}$ = 7.1 Hz, CH$_3$C$H_2$O); 4.44 (m, 2H, $J_{3',2'}$ = 5.8, 3.5, $J_{3',OH}$ = 4.2, $J_{3',4'}$ = 3.1 Hz, H-3′); 5.010 and 5.013 (2 × t, 2 × 1H, $J_{OH,5'}$ = 5.6 Hz, OH-5′); 5.37 (dd, 2H, $J_{OH,3'}$ = 4.2 Hz, OH-3′); 6.45 (dd, 2H, $J_{1',2'}$ = 7.2, 6.3 Hz, H-1′); 8.76 (s, 4H, H-2,8). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 14.26 (C$H_3$CH$_2$O); 17.35 and 17.41 (CH$_2$-3-cycloprop); 22.33 (CH-1-cycloprop); 24.43 and 24.49 (CH-2-cycloprop); 39.53 (CH$_2$-2′); 60.88 (CH$_3$C$H_2$O); 61.72 (CH$_2$-5′); 70.80 (CH-3′); 84.00 and 84.02 (CH-1′); 88.20 (CH-4′); 132.44 (C-5); 144.70 (CH-8); 150.05 (C-4); 152.08 (CH-2); 158.41 (C-6); 171.86 and 171.87 (CO). FAB-MS, *m*/*z* (rel.%) = 349 (25) [M + H]$^+$ (cation), 259 (6), 233 (100), 187 (15), 159 (24), 147 (7), 134 (7), 117 (10), 73 (10). HRMS calcd for $C_{16}H_{21}N_4O_5$ [M + H]$^+$ 349.1511; found: 349.1521. IR (micr. refl.): 3313, 2979, 2929, 2876, 1727, 1600, 1500, 1456, 1408, 1386, 1366, 1330, 1265, 1213, 1186, 1159, 1095, 1056, 994, 929, 884, 867, 843, 806, 760. [*a*]$_D$ −9.2 (*c* 0.12, MeOH).

**6-[2-(Diethylcarbamoyl)cyclopropyl]9-(β-D-ribofuranosyl)purine (6h)**

White foam, yield 95%. Diastereomeric mixture 1 : 1. $^1$H NMR (600 MHz, DMSO-$d_6$): 1.019, 1.020, 1.060 and 1.062 (4 × t, 4 × 3H, $J_{vic}$ = 7.1 Hz, C$H_3$CH$_2$N); 1.626 and 1.628 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.8, 5.7, $J_{gem}$ = 3.1 Hz, H-3b-cycloprop); 1.68 and 1.69 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 5.9, $J_{gem}$ = 3.1 Hz, H-3a-cycloprop); 2.692 and 2.694 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 5.7, 4.0 Hz, H-2-cycloprop); 3.01 (ddd, 2H, $J_{vic}$ = 8.8, 5.9, 4.0 Hz, H-1-cycloprop); 3.25–3.50 (m, 8H, CH$_3$C$H_2$N); 3.568 and 3.570 (2 × ddd, 2 × 1H, $J_{gem}$ = 12.1, $J_{5'b,OH}$ = 6.1, $J_{5'b,4'}$ = 4.0 Hz, H-5′b); 3.684 and 3.685 (2 × ddd, 2 × 1H, $J_{gem}$ = 12.1, $J_{5'a,OH}$ = 5.1, $J_{5'a,4'}$ = 4.0 Hz, H-5′a); 3.973 and 3.974 (2 × td, 2 × 1H, $J_{4',5'}$ = 4.0, $J_{4',3'}$ = 3.7 Hz, H-4′); 4.18 (ddd, 2H, $J_{3',2'}$ = 5.1, $J_{3',OH}$ = 5.0, $J_{3',4'}$ = 3.7 Hz, H-3′); 4.614 and 4.615 (2 × ddd, 2 × 1H, $J_{2',OH}$ = 6.0, $J_{2',1'}$ = 5.7, $J_{2',3'}$ = 5.1 Hz, H-2′); 5.15 and 5.16 (2 × dd, 2 × 1H, $J_{OH,5'}$ = 6.1, 5.1 Hz, OH-5′); 5.270 and 5.274 (2 × d, 2 × 1H, $J_{OH,3'}$ = 5.0 Hz, OH-3′); 5.54 and 5.55 (2 × d, 2 × 1H, $J_{OH,2'}$ = 6.0 Hz, OH-2′); 6.010 and 6.011 (2 × d, 2 × 1H, $J_{1',2'}$ = 5.7 Hz, H-1′); 8.780 (s, 2H, H-2); 8.784 (s, 2H, H-8). $^{13}$C NMR (151 MHz, DMSO-$d_6$): 13.45, 15.07 and 15.08 (C$H_3$CH$_2$N); 17.44 (CH$_2$-3-cycloprop); 21.82 and 21.87 (CH-1-cycloprop); 23.51 and 23.53 (CH-2-cycloprop); 40.69 and 41.98 (CH$_3$C$H_2$N); 61.53 and 61.56 (CH$_2$-5′); 70.57 and 70.60 (CH-3′); 73.93 and 73.95 (CH-2′); 85.96 and 85.99 (CH-4′); 87.88 (CH-1′); 132.54 (C-5); 144.65 and 144.68 (CH-8); 150.25 (C-4); 152.28 (CH-2); 160.05 and 160.06 (C-6); 169.31 (CO). FAB-MS, *m*/*z* (rel.%) = 392 (30) [M + H]$^+$ (cation), 260 (100), 187 (25), 159 (23), 134 (8), 102 (35), 74 (12). HRMS calcd for $C_{18}H_{26}N_5O_5$ [M + H]$^+$ 392.1933; found: 392.1940. IR (KBr): 3401, 3112, 3070, 1632, 1617, 1598, 1580, 1491, 1406, 1382, 1331, 1218, 807, 646. [*a*]$_D$ −42.1 (*c* 0.25, MeOH).

**6-[2-(Benzyl(methyl)carbamoyl)cyclopropyl]-9-(β-D-ribofuranosyl)purine (7h)**

White foam, yield 97%, mp 84–88 °C. Diastereomeric mixture of amide rotamers 1 : 1 : 1 : 1. $^1$H NMR (500 MHz, DMSO-$d_6$): 1.65–1.71 and 1.74–1.79 (2 × m, 8H, H-3-cycloprop); 2.68, 2.70, 2.82 and 2.83 (4 × ddd, 4 × 1H, $J_{vic}$ = 8.1, 5.9, 3.9 Hz, H-2-cycloprop); 2.92 and 2.93 (2 × s, 2 × 3H, CH$_3$N); 2.94 and 2.96 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.5, 5.4, 3.9 Hz, H-1-cycloprop); 3.02 and 3.03 (2 × s, 2 × 3H, CH$_3$N); 3.096 and 3.099 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.5, 5.4, 3.9 Hz, H-1-cycloprop); 3.55–3.60 (m, 4H, H-5′b); 3.66–3.73 (m, 4H, H-5′a); 3.96–4.00 (m, 4H, H-4′); 4.17–4.21 (m, 4H, H-3′); 4.522 and 4.525 (2 × d, 2H, $J_{gem}$ = 14.7 Hz, CH$_a$$H_b$Ph); 4.582 and 4.585 (2 × d, 2H, $J_{gem}$ = 14.7 Hz, C$H_a$H$_b$Ph); 4.60–4.66 (m, 6H, H-2′ and CH$_a$$H_b$Ph); 4.74 (d, 2H, $J_{gem}$ = 14.7 Hz, C$H_a$H$_b$Ph); 5.13–5.18 (m, 4H, OH-5′); 5.270, 5.274 and 5.286 (3 × d, 4H, $J_{OH,3'}$ = 5.0 Hz, OH-3′); 5.538, 5.541, 5.542 and 5.553 (4 × d, 4 × 1H, $J_{OH,2'}$ = 6.0 Hz, OH-2′); 6.01 and 6.02 (2 × d, 4H, $J_{1',2'}$ = 5.7 Hz, H-1′); 7.04–7.16, 7.20–7.28 and 7.30–7.35 (3 × m, 20H, H-*o*,*m*,*p*-Ph); 8.680 and 8.683 (2 × s, 2 × 1H, H-2); 8.769 and 8.772 (2 × s, 2 × 1H, H-8); 8.78 (s, 2H, H-2); 8.80 (s, 2H, H-8). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 16.9, 17.03 and 17.42 (CH$_2$-3-cycloprop); 21.83, 21.86, 22.29 and 22.32 (CH-1-cycloprop); 23.48, 23.52, 23.91 and 24.01 (CH-2-cycloprop); 34.75, 34.79 and 35.04 (CH$_3$N); 50.59 and 52.89 (CH$_2$Ph); 61.47 (CH$_2$-5′); 70.51 (CH-3′); 73.89 and 73.90 (CH-2′); 85.89 (CH-4′); 87.84 (CH-1′); 126.46 and 126.49 (CH-*o*-Ph); 127.09, 127.11 and 127.27 (CH-*p*-Ph); 127.70 (CH-*o*-Ph); 128.57, 128.60 and 128.69 (CH-*m*-Ph); 132.49 (C-5); 137.75, 137.76 and 137.84 (C-*i*-Ph); 144.41 and 144.56 (CH-8); 150.07, 150.09 and 150.21 (C-4); 151.95 and 152.16 (CH-2); 159.61 and 159.87 (C-6); 170.44 and 170.58 (CO). FAB-MS, *m*/*z* (rel.%) = 440 (15) [M + H]$^+$ (cation), 308 (10), 217 (15), 201 (40), 185 (50), 93 (100), 91 (66), 73 (24), 57 (25). HRMS calcd for $C_{22}H_{26}N_5O_5$ [M + H]$^+$ 440.1933; found: 440.1940. IR (KBr): 3401, 3401, 3109, 3067, 3030, 1623, 1598, 1582, 1496, 1410, 1333, 1216, 1120, 1082, 1055, 1030, 808, 748, 699, 645. [*a*]$_D$ −37.3 (*c* 0.49, MeOH).

**6-[2-(Morpholine-4-carbonyl)cyclopropyl]-9-(β-D-ribofuranosyl)purine (8h)**

White foam, yield 98%. Diastereomeric mixture 1 : 1. $^1$H NMR (600 MHz, DMSO-$d_6$): 1.63 and 1.64 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 5.6, $J_{gem}$ = 3.1 Hz, H-3b-cycloprop); 1.73 and 1.74 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.7, 5.5, $J_{gem}$ = 3.1 Hz, H-3a-cycloprop); 2.762 and 2.770 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.7, 5.6, 4.0 Hz, H-2-cycloprop); 3.049 and 3.051 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.6, 5.5, 4.0 Hz, H-1-cycloprop); 3.44–3.65 (m, 18H, H-5′b and H-morph); 3.69 (ddd, 2H, $J_{gem}$ = 12.0, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.0 Hz, H-5′a); 3.97 (td, 2H, $J_{4',5'}$ = 4.0, $J_{4',3'}$ = 3.6, H-4′); 4.18 (td, 2H, $J_{3',2'}$ = $J_{3',OH}$ = 4.9, $J_{3',4'}$ = 3.6 Hz, H-3′); 4.61 and 4.62 (2 × ddd, 2 × 1H, $J_{2',OH}$ = 5.8, $J_{2',1'}$ = 5.7, $J_{2',3'}$ = 4.9 Hz, H-2′); 5.143 and 5.145 (2 × dd, 2 × 1H, $J_{OH,5'}$ = 6.0, 5.2 Hz, OH-5′); 5.26 and 5.27 (2 × d, 2 × 1H, $J_{OH,3'}$ = 4.9 Hz, OH-3′); 5.54 (d, 2H, $J_{OH,2'}$ = 5.8 Hz, OH-2′); 6.01 (d, 2H, $J_{1',2'}$ = 5.7 Hz, H-1′); 8.77 (s, 2H, H-2); 8.79 (s, 2H, H-8). $^{13}$C NMR

(151 MHz, DMSO-$d_6$): 17.18 and 17.21 ($CH_2$-3-cycloprop); 21.72 and 21.75 (CH-1-cycloprop); 23.05 and 23.09 (CH-2-cycloprop); 42.38 and 45.72 ($CH_2$N-morph); 61.49 and 61.52 ($CH_2$-5′); 66.21 and 66.42 ($CH_2$O-morph); 70.53 and 70.56 (CH-3′); 73.90 and 73.93 (CH-2′); 85.92 and 85.95 (CH-4′); 87.84 and 87.86 (CH-1′); 132.55 and 132.56 (C-5); 144.62 and 144.65 (CH-8); 150.24 (C-4); 152.20 (CH-2); 159.84 (C-6); 169.09 (CO). FAB-MS, $m/z$ (rel.%) = 406 (8) $[M + H]^+$ (cation), 390 (7), 274 (20), 201 (7), 185 (18), 110 (8), 102 (100), 93 (32), 75 (8), 57 (7). HRMS calcd for $C_{18}H_{24}N_5O_6$ $[M + H]^+$ 406.1726; found: 406.1723. IR (KBr): 3421, 3255, 1632, 1598, 1582, 1498, 1423, 1332, 1216, 1115, 1093, 1057, 1042, 1026, 929, 860, 806, 645. $[\alpha]_D$ −18.8 (*c* 0.42, MeOH).

### 6-[2-(Diethylcarbamoyl)cyclopropyl]-9-(2-deoxy-β-D-*erythro*-pentafuranosyl)purine (6i)

White foam, yield 83%. Diastereomeric mixture 1 : 1. $^1$H NMR (500 MHz, DMSO-$d_6$): 1.02 and 1.06 (2 × t, 2 × 6H, $J_{vic}$ = 7.1 Hz, C$H_3$CH$_2$N); 1.617 and 1.619 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.7, 5.6, $J_{gem}$ = 2.9 Hz, H-3b-cycloprop); 1.67 and 1.68 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.5, 5.7, $J_{gem}$ = 2.9 Hz, H-3a-cycloprop); 2.330 and 2.333 (2 × ddd, 2 × 1H, $J_{gem}$ = 13.3, $J_{2'b,1'}$ = 6.4, $J_{2'b,3'}$ = 3.5 Hz, H-2′b); 2.68 and 2.69 (2 × ddd, 2 × 1H, $J_{vic}$ = 8.5, 5.6, 3.9 Hz, H-2-cycloprop); 2.768 and 2.770 (2 × ddd, 2 × 1H, $J_{gem}$ = 13.3, $J_{2'a,1'}$ = 7.1, $J_{2'a,3'}$ = 5.9 Hz, H-2′a); 3.00 (ddd, 2H, $J_{vic}$ = 8.7, 5.7, 3.9 Hz, H-1-cycloprop); 3.25–3.50 (m, 8H, $CH_3$C$H_2$N); 3.516 and 3.523 (2 × ddd, 2 × 1H, $J_{gem}$= 12.0, $J_{5'b,OH}$ = 6.7, $J_{5'b,4'}$ = 4.6 Hz, H-5′b); 3.61 and 3.62 (2 × ddd, 2 × 1H, $J_{gem}$ = 12.0, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.6 Hz, H-5′a); 3.88 (td, 2H, $J_{4',5'}$ = 4.6, $J_{4',3'}$ = 2.8 Hz, H-4′); 4.44 (m, 2H, $J_{3',2'}$ = 5.9, 3.5, $J_{3',OH}$ = 4.1, $J_{3',4'}$ = 2.8 Hz, H-3′); 5.02 and 5.03 (2 × dd, 2 × 1H, $J_{OH,5'}$ = 6.1, 5.2 Hz, OH-5′); 5.38 (dd, 2H, $J_{OH,3'}$ = 4.1 Hz, OH-3′); 6.45 (dd, 2H, $J_{1',2'}$ = 7.1, 6.4 Hz, H-1′); 8.75 (s, 2H, H-8); 8.77 (s, 2H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 13.37 and 15.00 (*C*$H_3$CH$_2$N); 17.31 ($CH_2$-3-cycloprop); 21.74 and 21.79 (CH-1-cycloprop); 23.40 (CH-2-cycloprop); 39.46 ($CH_2$-2′); 40.60 and 41.89 ($CH_3$*C*H$_2$N); 61.76 and 61.77 ($CH_2$-5′); 70.85 and 70.86 (CH-3′); 83.95 (CH-1′); 88.19 (CH-4′); 132.48 (C-5); 144.46 and 144.48 (CH-8); 149.90 (C-4); 152.11 (CH-2); 159.85 and 159.86 (C-6); 169.24 (CO). FAB-MS, $m/z$ (rel.%) = 398 (60) $[M + Na]^+$ (cation), 376 (7) $[M + H]^+$ (cation), 308 (10), 282 (45), 260 (100), 217 (15), 187 (30), 177 (10), 159 (40), 137 (10), 117 (7), 109 (10), 100 (7), 79 (7), 72 (14), 61 (6). HRMS calcd for $C_{18}H_{26}N_5O_4$ $[M + H]^+$ 376.1984; found: 376.1992. Anal. calcd for $C_{18}H_{25}N_5O_4$·0.5$H_2O$: C 56.24, H 6.82, N 18.22. Found: C 56.16, H 6.79, N 19.97%. IR (KBr): 3428, 3111, 3073, 1631, 1621, 1597, 1581, 1490, 1424, 1424, 1405, 1381, 1362, 1329, 1217, 1097, 1058, 807, 646. $[\alpha]_D$ −5.1 (*c* 0.21, MeOH).

### 6-[2-(Hydroxymethyl)cyclopropyl]-9-(β-D-ribofuranosyl)purine (10h)

White foam, yield 76%. Diastereomeric mixture 2 : 1 (after repeated column chromatography). $^1$H NMR (500 MHz, DMSO-$d_6$): 1.20 and 1.41 (2 × m, 2 × 2H, H-3-cycloprop); 1.93 (m, 2H, H-2-cycloprop); 2.60 (dt, 2H, $J_{vic}$ = 8.2, 4.5 Hz, H-1-cycloprop); 3.45 (dt, 2H, $J_{gem}$ = 11.3, $J_{vic}$ = $J_{Hb,OH}$ = 5.7 Hz, CH$_a$*H*$_b$O); 3.55 (ddd, 2H, $J_{gem}$ = 11.8, $J_{5'b,OH}$ = 5.7, $J_{5'b,4'}$ = 4.0 Hz, H-5′b); 3.59 (dt, 2H, $J_{gem}$ = 11.3, $J_{vic}$ = $J_{Ha,OH}$ = 5.7 Hz, C*H*$_a$H$_b$O); 3.69 (dt, 2H, $J_{gem}$ = 11.8, $J_{5'a,OH}$ = 5.7, $J_{5'a,4'}$ = 4.0 Hz, H-5′a); 3.97 (td, 2H, $J_{4',5'}$ = 4.0, $J_{4',3'}$ = 3.6 Hz, H-4′); 4.18 (ddd, 2H, $J_{3',OH}$ = 4.9, $J_{3',2'}$ = 4.7, $J_{3',4'}$ = 3.6 Hz, H-3′); 4.60 and 4.61 (2 × ddd, 2 × 1H, $J_{2',OH}$ = 6.0, $J_{2',1'}$ = 5.7, $J_{2',3'}$ = 4.7 Hz, H-2′); 4.75 (t, 2H, $J$ = 5.7 Hz, OH); 5.16 (t, 2H, $J_{OH,5'}$ = 5.7 Hz, OH-5′); 5.24 (d, 2H, $J_{OH,3'}$ = 4.9 Hz, OH-3′); 5.519 and 5.523 (2 × d, 2 × 1H, $J_{OH,2'}$ = 6.0 Hz, OH-2′); 5.997 and 5.999 (2 × d, 2 × 1H, $J_{1',2'}$ = 5.7 Hz, H-1′); 8.70 (s, 2H, H-2); 8.726 and 8.729 (2 × s, 2 × 1H, H-8). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 15.61 and 15.64 ($CH_2$-3-cycloprop); 18.24 (CH-1-cycloprop); 27.53 and 27.61 (CH-2-cycloprop); 61.52 and 61.54 ($CH_2$-5′); 62.75 and 62.77 ($CH_2$O); 70.55 and 70.57 (CH-3′); 73.85 and 73.91 (CH-2′); 85.88 and 85.91 (CH-4′); 87.82 and 87.87 (CH-1′); 132.27 and 132.29 (C-5); 143.98 and 144.02 (CH-8); 149.80 (C-4); 152.13 (CH-2); 162.79 and 162.80 (C-6). FAB-MS, $m/z$ (rel.%) = 323 (10) $[M + H]^+$ (cation), 239 (60), 219 (40), 203 (14), 191 (40), 173 (20), 149 (68), 128 (18), 102 (100), 57 (32). HRMS calcd for $C_{14}H_{19}N_4O_5$ $[M + H]^+$ 323.1357; found: 323.1355. IR (KBr): 3421, 3260, 3113, 1632, 1600, 1581, 1497, 1420, 1399, 1333, 1215, 1128, 1095, 1060, 1027, 809, 643. $[\alpha]_D$ −35.2 (*c* 0.20, MeOH).

### 6-[2-(Hydroxymethyl)cyclopropyl]-9-(2-deoxy-β-D-*erythro*-pentafuranosyl)purine (10i)

White foam, yield 44%. Diastereomeric mixture 1 : 1. $^1$H NMR (500 MHz, DMSO-$d_6$): 1.17 and 1.40 (2 × m, 2 × 2H, H-3-cycloprop); 1.92 (m, 2H, H-2-cycloprop); 2.32 (ddd, 2H, $J_{gem}$ = 13.3, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 3.4 Hz, H-2′b); 2.59 (dt, 2H, $J_{vic}$ = 8.6, 4.5 Hz, H-1-cycloprop); 2.76 (ddd, 2H, $J_{gem}$ = 13.3, $J_{2'a,1'}$ = 7.2, $J_{2'a,3'}$ = 5.8 Hz, H-2′a); 3.45 (dd, 2H, $J_{gem}$ = 11.4, $J_{vic}$ = 6.5 Hz, CH$_a$*H*$_b$O); 3.52 (dd, 2H, $J_{gem}$ = 11.8, $J_{5'b,4'}$ = 4.5 Hz, H-5′b); 3.58 (dd, 2H, $J_{gem}$ = 11.4, $J_{vic}$ = 5.4 Hz, C*H*$_a$H$_b$O); 3.62 (dd, 2H, $J_{gem}$ = 11.8, $J_{5'a,4'}$ = 4.5 Hz, H-5′b); 3.88 (td, 2H, $J_{4',5'}$ = 4.5, $J_{4',3'}$ = 3.0 Hz, H-4′); 4.44 (ddd, 2H, $J_{3',2'}$ = 5.8, 3.4, $J_{3',4'}$ = 3.0 Hz, H-3′); 6.44 (dd, 2H, $J_{1',2'}$ = 7.2, 6.2 Hz, H-1′); 8.683 and 8.685 (2 × s, 2 × 1H, H-8); 8.691 (s, 2H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 15.54 and 15.57 ($CH_2$-3-cycloprop); 18.21 (CH-1-cycloprop); 27.46 and 27.53 (CH-2-cycloprop); 39.47 ($CH_2$-2′); 61.80 ($CH_2$-5′); 62.75 ($CH_2$O); 70.87 and 70.89 (CH-3′); 83.92 and 83.94 (CH-1′); 88.16 (CH-4′); 132.23 and 132.24 (C-5); 143.85 (CH-8); 149.53 (C-4); 152.01 (CH-2); 162.64 (C-6). ESI-MS, $m/z$ (rel.%) 329 (30) $[M + Na]^+$, 307 (35) $[M + H]^+$, 238 (37), 190 (92). HRMS calcd for $C_{14}H_{18}N_4O_4Na$ $[M + Na]^+$ 329.1226; found 329.1222. IR ($CHCl_3$): 3436, 1632, 1598, 1434, 1399, 1334, 1217, 1098, 1079, 1059, 1037, 641. $[\alpha]_D$ −5.6 (*c* 0.54, MeOH).

### X-Ray diffraction

X-Ray crystallographic analysis† of single crystals of **6a** (colourless, 0.01 × 0.01 × 0.59 mm) and **2g** (colourless, 0.07 × 0.37 × 0.44 mm) was performed with an Xcalibur X-ray diffractometer with $Cu_{K\alpha}$ ($\lambda$ = 1.54180 Å), data collected at 150 K. Both structures were solved by direct methods with SIR92[30] and refined by full-matrix least-squares on F with CRYSTALS.[31] The hydrogen atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically and then refined with riding constraints, while all other atoms were refined anisotropically in both cases.

**Crystal data 2g.** $C_8H_8N_4$, monoclinic, space group $C2/m$, $a$ = 13.6246(3) Å, $b$ = 20.3049(5) Å, $c$ = 9.4369(2) Å, $\beta$ = 99.789(2)°, $V$ = 743.25(3) Å$^3$, $Z$ = 4, $M$ = 160.18, 11 926 reflections measured,

820 independent reflections. Final $R = 0.0409$, $wR = 0.0577$, GoF = 0.9440 for 723 reflections with $I > 2\sigma(I)$ and 75 parameters.

**Crystal data 6a.** $C_{20}H_{23}N_5O_1$, orthorhombic, space group $Pna2_1$, $a = 22.2791(2)$ Å, $b = 7.0143(1)$ Å, $c = 7.8922(2)$ Å, $V = 1796.64(2)$ Å$^3$, $Z = 4$, $M = 349.44$, 26 954 reflections measured, 3604 independent reflections. Final $R = 0.0296$, $wR = 0.0328$, GoF = 1.0836 for 2807 reflections with $I > 2\sigma(I)$ and 237 parameters.

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