SYNTHESIS OF 6-AMINO-, 6-METHYL- AND 6-ARYL-2-(HYDROXYMETHYL)PURINE BASES AND NUCLEOSIDES

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Dedicated to Professor Antonín Holý on the occasion of his 70th birthday.

An efficient methodology of the synthesis of 6-substituted 2-(hydroxymethyl)purine derivatives (bases and nucleosides) was developed. Regioselective Pd-catalyzed cross-coupling reactions of 6-chloro-2-iodopurines with [(benzoyloxy)methyl]zinc iodide gave 2-[(benzoyloxy)-methyl]-6-chloropurines that were converted to 2-(hydroxymethyl)adenines by reactions with ammonia and to 6-methyl- or 6-aryl-2-(hydroxymethyl)purines by cross-coupling reactions with trimethylaluminium or arylboronic acids followed by deprotection. The title 6-substituted 2-(hydroxymethyl)purine bases and nucleosides did not exhibit significant cytostatic or anti-HCV activity.

Keywords: Purines; Nucleosides; Cross-coupling reactions; Hydroxymethylation; Palladium; Functionalized organozinc reagents; Cytostatic activity; X-ray diffraction.

Purine ribonucleosides bearing aryl and hetaryl substituents in the position 6 possess strong cytostatic[1] and anti-HCV[2] activity, while some 6-aryl-9-substituted purines were reported to exhibit antibacterial and antimycobacterial effects[3]. 6-(Hydroxymethyl)-[4], 6-(fluoromethyl)-[5] and 6-(difluoromethyl)purine[6] ribonucleosides are another class of potent cytostatic compounds. 6-Methylpurine and its ribonucleoside are highly cytotoxic[7] and its liberation by purine nucleoside phosphorylases from its non-toxic deoxyribonucleoside was proposed as a novel principle in the gene therapy of cancer[8].

Only few examples of 2-(hydroxymethyl)purines have been prepared in the past by heterocyclizations[9,10] or transformations of 2-vinylpurines[11]. 2-(Hydroxymethyl)nebularine was reported to exhibit antiviral activity[12] and 2-(hydroxymethyl)inosine monophosphate to inhibit IMP dehydro-

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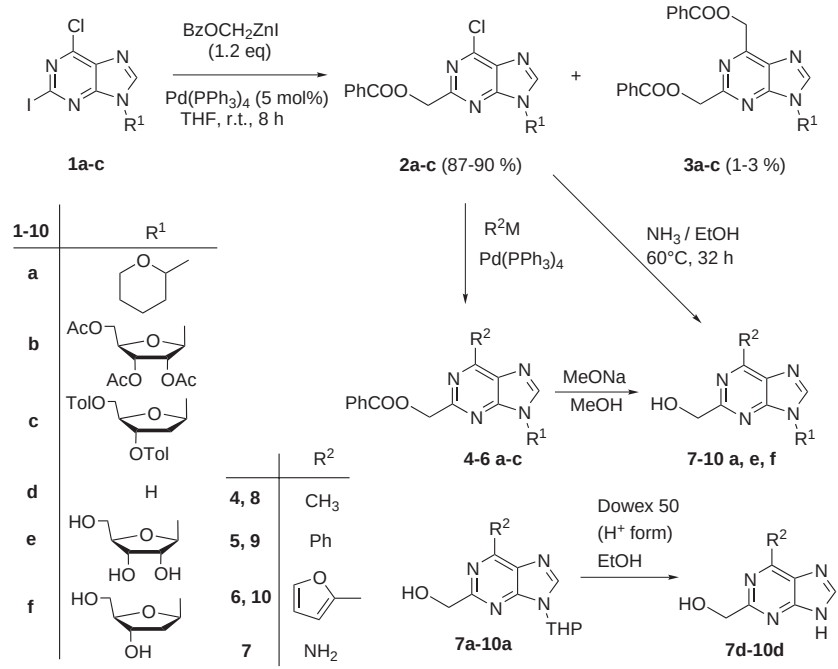
genase[9]. Protected 2-(hydroxymethyl)inosine was also used[10] in construction of inhibitors of GMP synthetase. Related 2-(aminomethyl)purines are easily accessible by heterocyclizations[13] and by reduction of 2-cyanopurines[14] and also possess a wide range of activities (e.g. agonists of adenosine receptors[15]). Here we report on the synthesis of 2-(hydroxymethyl)-purine bases and nucleosides bearing amino, methyl or an aryl group in position 6 – compounds sharing the structural features of the both above mentioned types of bioactive purine derivatives.

RESULTS AND DISCUSSION

Cross-coupling reactions of dihalopurines are known to proceed regioselectively[16]. Very recently we have studied[17] reactions of 2,6-dihalopurines with [(benzoyloxy)methyl]zinc iodide. 2,6-Dichloropurines reacted almost exclusively in the position 6 (even with an excess of the reagent) to give 2-chloro-6-[(benzoyloxy)methyl]purines, while 6-chloro-2-iodopurines **1** reacted in position 2 to afford 2-[(benzoyloxy)methyl]-6-chloropurines **2** that were further converted to 2,6-bis[(benzoyloxy)methyl]purines **3** by successive cross-coupling with another portion of the reagent. Here we apply the intermediates **2** for the synthesis of 6-substituted 2-(hydroxymethyl)purine derivatives.

The reactions of tetrahydropyran-2-yl (THP) protected 6-chloro-2-iodopurine **1a** and the corresponding acyl-protected nucleosides **1b** and **1c** with 1.2 equivalents of [(benzoyloxy)methyl]zinc iodide in presence of $Pd(PPh_3)_4$ under argon were performed at room temperature (Scheme 1). In all cases the desired 2-[(benzoyloxy)methyl]-6-chloropurines **2a**–**2c** were obtained in very high yields (87–90%) besides trace amounts of the disubstituted purines **3** (1–3%) as reported earlier[17].

Our first efforts focused on introduction of C-substituents into position 6 by Pd-catalyzed cross-coupling reactions[18]. The reactions of 2-[(benzoyloxy)-methyl]-6-chloropurines **2a**–**2c** with trimethylaluminum in THF at 60 °C gave the corresponding 6-methylpurine derivatives **4a**–**4c** in excellent yields of 95–97% (Scheme 1, Table I). The Suzuki–Miyaura reactions of **2a**–**2c** with phenylboronic acid proceeded smoothly under standard conditions in toluene in the presence of K_2CO_3 under $Pd(PPh_3)_4$ catalysis to give the 6-phenylpurine derivatives **5a**–**5c** in high yields of 86–94%. Analogous reactions with 2-furylboronic acid in toluene were very sluggish and therefore DMF was used as solvent under otherwise the same conditions to give the 6-(2-furyl)purines **6a**–**6c** in acceptable yields of 71–76% (but still significantly lower compared with the phenylboronic acid). Conversion to adenine



SCHEME 1

TABLE I

Cross-couplings of 2-[(benzoyloxy)methyl]-6-chloropurines **2**

Entry	Starting compound	Reagent[a]	Conditions	Product	Yield, %
1	**2a**	Me_3Al	THF, 60 °C	**4a**	97
2	**2b**	Me_3Al	THF, 60 °C	**4b**	97
3	**2c**	Me_3Al	THF, 60 °C	**4c**	95
4	**2a**	$PhB(OH)_2$	toluene, 100 °C	**5a**	94
5	**2b**	$PhB(OH)_2$	toluene, 100 °C	**5b**	91
6	**2c**	$PhB(OH)_2$	toluene, 100 °C	**5c**	86
7	**2a**	$FurB(OH)_2$[a]	DMF, 100 °C	**6a**	76
8	**2b**	$FurB(OH)_2$	DMF, 100 °C	**6b**	74
9	**2c**	$FurB(OH)_2$	DMF, 100 °C	**6c**	71
10	**2a**	NH_3	EtOH, 60 °C	**7a**	62
11	**2b**	NH_3	EtOH, 60 °C	**7e**	70
12	**2c**	NH_3	EtOH, 60 °C	**7f**	68

[a] Fur, 2-furyl.

derivatives was achieved by simple uncatalyzed nucleophilic substitution on heating of 6-chloropurines **2a**–**2c** in ethanolic ammonia at 60 °C for 32 h. All ester groups at acyl-protected glycon parts and/or at benzoyl-protected 2-(hydroxymethyl)purines were cleaved simultaneously under these conditions to directly give 2-(hydroxymethyl)-9-(tetrahydropyran-2-yl)adenine (**7a**) and the corresponding free 2-(hydroxymethyl)adenine nucleosides **7e** and **7f** in acceptable yields.

The acyl protecting groups in 6-methyl- and 6-aryl-2-[(benzoyloxy)methyl]-purine derivatives **4**–**6** were cleaved making use of catalytic amounts of NaOMe in methanol to give 9-THP-substituted 2-(hydroxymethyl)purines **8a**–**10a** or free 2-(hydroxymethyl)purine nucleosides **8e**–**10e** and **8f**–**10f** in good yields (Table II). THP-groups in compounds **7a**–**10a** were cleaved by refluxing of the compounds with TsOH or with acidic Dowex 50 ion exchanger in ethanol to give 9*H*-purines **7d**–**10d**.

TABLE II
Cleavage of protecting groups

Entry	Starting compound	Reagent	Conditions	Product	Yield, %
1	**4a**	MeONa	MeOH, r.t.	**8a**	90
2	**4b**	MeONa	MeOH, r.t.	**8e**	87
3	**4c**	MeONa	MeOH, r.t.	**8f**	88
4	**5a**	MeONa	MeOH, r.t.	**9a**	89
5	**5b**	MeONa	MeOH, r.t.	**9e**	74
6	**5c**	MeONa	MeOH, r.t.	**9f**	93
7	**6a**	MeONa	MeOH, r.t.	**10a**	82
8	**6b**	MeONa	MeOH, r.t.	**10e**	80
9	**6c**	MeONa	MeOH, r.t.	**10f**	81
10	**7a**	TsOH (H^+)	EtOH, reflux	**7d**	85
11	**8a**	Dowex (H^+)	EtOH, reflux	**8d**	71
12	**9a**	Dowex (H^+)	EtOH, reflux	**9d**	74
13	**10a**	Dowex (H^+)	EtOH, reflux	**10d**	65

All compounds were fully characterized by spectral and analytical methods. In addition, compound **9a** gave crystals suitable for X-ray diffraction and its crystal structure has been determined (Fig. 1).

All the title 2-(hydroxymethyl)-6-substituted purine bases and nucleosides **7**–**10** were subjected to biological activity screening. The cytostatic

activity *in vitro* (inhibition of cell growth) was studied on the following cell cultures: (i) mouse leukemia 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). Nucleosides **7e**–**10e** and **7f**–**10f** were also tested on anti-HCV activity in replicon system[20]. None of the compounds showed any cytostatic or anti-HCV effect.

In conclusion, 2-[(benzoyloxy)methyl]-6-chloropurines are suitable intermediates for the synthesis of various 6-substituted 2-(hydroxymethyl)-purine bases and nucleosides by cross-coupling reactions or by nucleophilic substitutions. However, introduction of the hydroxymethyl group to position 2 of biologically active 6-methyl- and 6-arylpurine bases and nucleosides causes loss of activity.

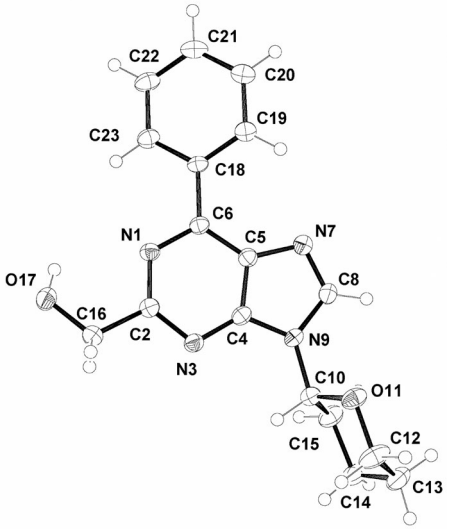


FIG. 1
ORTEP [19] drawing of crystal structure of **9a** with the atom numbering scheme. Thermal ellipsoids are drawn at the 50% probability level

EXPERIMENTAL

Starting materials were prepared as follows: 6-chloro-2-iodo-9-(tetrahydropyran-2-yl)purine from 6-chloro-2-(tetrahydropyran-2-yl)amino-9-(tetrahydropyran-2-yl)purine[16h], 9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-6-chloro-2-iodopurine[21] and analogously 6-chloro-2-iodo-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)purine[17]. All preparations of (benzoyloxymethyl)zinc iodide[4] and cross-coupling reactions were conducted under argon atmosphere. THF was dried and distilled from sodium/benzophenone. NMR spectra were recorded

on a Bruker Avance 400 MHz spectrometer (^{1}H at 400 MHz, ^{13}C at 100.6 MHz), and a Bruker Avance (500 MHz for ^{1}H and 125.8 MHz for ^{13}C). Chemical shifts (in ppm, δ scale) were referenced to TMS as internal standard. The assignment of carbons was based on C,H-HSQC and C,H-HMBC experiments. IR spectra (wavenumbers in cm^{-1}) were recorded on a Brucker IFS 88 spectrometer. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured at 25 °C on a Autopol IV (Rudolph Research Analytical) polarimeter, $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using FAB (ionization by Xe, accelerating voltage 8 kV, glycerol matrix). Cytostatic activity tests were performed as described in ref.[1a] and the HCV replicon assay as described in ref.[20]

General Procedure for Cross-Couplings of (Benzoyloxymethyl)zinc Iodide with 6-Chloro-2-iodopurines **1**

The solution of [(benzoyloxy)methyl]zinc iodide (1.35 ml, 1.2 mmol) in THF was added at room temperature to the solution of 2,6-dihalopurine **1** (1 mmol), $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) in THF (10 ml) under Ar and stirred at room temperature for 8 h. The reaction was quenched with 1 M NaH_2PO_4 (40 ml) and extracted with $CHCl_3$ (4 × 40 ml). Collected organic phases were dried over $MgSO_4$, filtered and the solvent was evaporated. Crude oily products were purified by chromatography on silica gel (hexanes/ethyl acetate) and the corresponding 2-[(benzoyloxy)methyl]-6-chloropurines **2a**–**2c** were isolated in very good yields (87–90%). Characterization data for compounds **2a**–**2c** were published in our previous paper[17].

General Procedure for Cross-Couplings of 2-[(Benzoyloxy)methyl]-6-chloropurines **2** with Me_3Al

A solution of Me_3Al (1.0 ml, 2.0 mmol) in toluene was added at room temperature to a solution of a 2-[(benzoyloxy)methyl]-6-chloropurine **2** (1 mmol), $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) in THF (10 ml) under Ar and stirred at 60 °C for 6 h. The reaction was quenched with ice cold 1 M NaH_2PO_4 (40 ml) and extracted with $CHCl_3$ (4 × 40 ml). Collected organic phases were dried over $MgSO_4$, filtered and the solvent was evaporated. Crude products **4** were purified by chromatography on silica gel (hexanes/ethyl acetate 2:1–1:1).

2-[(Benzoyloxy)methyl]-6-methyl-9-(tetrahydropyran-2-yl)purine (**4a**). Yield 97% of white foam. Exact mass (FAB HRMS) found: 353.1619; calculated for $C_{19}H_{21}N_4O_3$: 353.1614. FAB MS, *m/z* (%): 353 (MH^+, 40); 269 (100); 147 (46); 105 (82); 85 (38). ^{1}H NMR (400 MHz, $CDCl_3$): 1.56–1.70 and 1.91–2.10 (m, 6 H, CH_2-THP); 2.88 (s, 3 H, CH_3); 3.66 (td, 1 H, *J* = 11.9 and 2.8, bCH_2O-THP); 4.11 (ddt, 1 H, *J* = 11.9, 3.9 and 2.1, aCH_2O-THP); 5.61 (s, 2 H, CH_2O); 5.66 (m, 1 H, CHO-THP); 7.47 (m, 2 H, H-*m*-Bz); 7.59 (m, 1 H, H-*p*-Bz); 8.16 (m, 2 H, H-*o*-Bz); 8.21 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 19.50 (CH_3); 22.59, 24.77 and 31.49 (CH_2-THP); 67.14 (CH_2O); 68.62 (CH_2O-THP); 82.09 (CHO-THP); 128.30 (CH-*m*-Bz); 129.87 (CH-*o*-Bz); 130.29 (C-*i*-Bz); 132.00 (C-5); 132.96 (CH-*p*-Bz); 141.80 (CH-8); 150.22 (C-4); 158.50 (C-2); 159.47 (C-6); 166.50 (CO-Bz). IR (CCl_4): 2948, 2856, 1729, 1599, 1499, 1452, 1441, 1404, 1323, 1270, 1116, 645.

2-[(Benzoyloxy)methyl]-6-methyl-9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purine (**4b**). Yield 97% of white foam. Exact mass (FAB HRMS) found: 527.1759; calculated for $C_{25}H_{27}N_4O_9$: 527.1778. FAB MS, *m/z* (%): 527 (MH^+, 20); 269 (35); 259 (10); 105 (100). ^{1}H NMR

(400 MHz, $CDCl_3$): 2.02, 2.06 and 2.07 (3 × s, 3 × 3 H, CH_3-Ac); 2.86 (s, 3 H, CH_3-6); 4.27 (dd, 1 H, J_{gem} = 12.2, $J_{5'b,4'}$ = 5.3, H-5′b); 4.31 (dd, 1 H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.5, H-5′a); 4.38 (td, 1 H, $J_{4',3'} = J_{4',5'b}$ = 5.3, $J_{4',5'a}$ = 3.5, H-4′); 5.51 (t, 1 H, $J_{3',4'}$ = 5.3, $J_{3',2'}$ = 5.2, H-3′); 5.60 and 5.65 (2 × d, 2 H, J_{gem} = 14.1, CH_2O); 5.92 (t, 1 H, $J_{2',3'}$ = 5.2, $J_{2',1'}$ = 4.9, H-2′); 6.13 (d, 1 H, $J_{1',2'}$ = 4.9, H-1′); 7.47 (m, 2 H, H-*m*-Bz); 7.59 (m, 1 H, H-*p*-Bz); 8.14 (s, 1 H, H-8); 8.17 (m, 2 H, H-*o*-Bz). ^{13}C NMR (100.6 MHz, $CDCl_3$): 19.55 (CH_3-6); 20.28, 20.42 and 20.69 (CH_3-Ac); 63.16 (CH_2-5′); 66.80 (CH_2O); 70.62 (CH-3′); 73.04 (CH-2′); 80.18 (CH-4′); 86.76 (CH-1′); 128.35 (CH-*m*-Bz); 129.99 (CH-*o*-Bz); 132.66 (C-*i*-Bz and C-5); 133.02 (CH-*p*-Bz); 142.31 (CH-8); 150.43 (C-4); 159.07 (C-2); 160.14 (C-6); 166.21 (CO-Bz); 169.26, 169.33 and 170.21 (CO-Ac). IR (CCl_4): 1756, 1730, 1598, 1501, 1452, 1430, 1369, 1270, 1222, 1118, 644.

2-[(Benzoyloxy)methyl]-6-methyl-9-(2-deoxy-3,5-di-O-toluoyl-β-D-erythro-pentofuranosyl)purine (**4c**). Yield 95% of white foam. Exact mass (FAB HRMS) found: 621.2336; calculated for $C_{35}H_{33}N_4O_7$: 621.2349. FAB MS, *m/z* (%): 621 (MH^+, 18); 269 (53); 163 (6); 149 (12); 119 (100); 105 (48). ^{1}H NMR (400 MHz, $CDCl_3$): 2.40 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.69 (ddd, 1 H, J_{gem} = 14.3, $J_{2'b,1'}$ = 6.0, $J_{2'b,3'}$ = 2.2, H-2′b); 2.83 (s, 3 H, CH_3-6); 3.19 (ddd, 1 H, J_{gem} = 14.3, $J_{2'a,1'}$ = 8.1, $J_{2'a,3'}$ = 6.3, H-2′a); 4.53–4.59 (m, 2 H, H-5′b and H-4′); 4.62 (dd, 1 H, J_{gem} = 13.0, $J_{5'a,4'}$ = 6.0, H-5′a); 5.57 (dt, 1 H, $J_{3',2'}$ = 6.3, 2.2, $J_{3',4'}$ = 2.2, H-3′); 5.60 and 5.65 (2 × d, 2 H, J_{gem} = 14.1, CH_2O); 6.46 (dd, 1 H, $J_{1'2'}$ = 8.1, 6.0, H-1′); 7.20 and 7.27 (2 × m, 2 × 2 H, H-*m*-Tol); 7.39 (m, 2 H, H-*m*-Bz); 7.48 (m, 1 H, H-*p*-Bz); 7.84 and 7.91 (2 × m, 2 × 2 H, H-*o*-Tol); 8.14 (s, 1 H, H-8); 8.15 (m, 2 H, H-*o*-Bz). ^{13}C NMR (100.6 MHz, $CDCl_3$): 19.51 (CH_3-6); 21.67 and 21.74 (CH_3-Tol); 37.23 (CH_2-2′); 64.01 (CH_2-5′); 66.85 (CH_2O); 75.14 (CH-3′); 83.08 (CH-4′); 85.24 (CH-1′); 126.44 and 126.63 (C-*i*-Tol); 128.38 (CH-*m*-Bz); 129.20 and 129.25 (CH-*m*-Tol); 129.60 (CH-*o*-Tol); 129.78 and 129.84 (CH-*o*-Tol and CH-*o*-Bz); 130.06 (C-*i*-Bz); 132.66 (C-5); 133.04 (CH-*p*-Bz); 142.35 (CH-8); 144.07 and 144.44 (C-*p*-Tol); 150.37 (C-4); 158.69 (C-2); 159.84 (C-6); 165.74 and 166.04 (CO-Tol); 166.38 (CO-Bz). IR (CCl_4): 3064, 1728, 1613, 1598, 1501, 1452, 1409, 1268, 1209, 1178, 1101, 647.

General Procedure for Suzuki–Miyaura Cross-Couplings of 2-[(Benzoyloxy)methyl]-6-chloropurines **2**

A solution of 2-(benzoyloxymethyl)-6-chloropurine **2** (1 mmol), arylboronic acid (2 mmol), $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) and K_2CO_3 (250 mg) either in toluene (20 ml) for phenylboronic acid or DMF (10 ml) for 2-furylboronic acid under Ar was stirred at 100 °C for 12 h. The reaction was quenched with 1 M NaH_2PO_4 (40 ml) and extracted with $CHCl_3$ (4 × 40 ml). Collected organic phases were dried over $MgSO_4$, filtered and the solvent was evaporated. Crude products **5** or **6** were purified by chromatography on silica gel (hexanes/ethyl acetate 3:1–2:1).

2-[(Benzoyloxy)methyl]-6-phenyl-9-(tetrahydropyran-2-yl)purine (**5a**). Yield 94% of white solid, m.p. 156–157 °C. For $C_{24}H_{22}N_4O_3$ (414.5) calculated: 69.55% C, 5.35% H, 13.52% N; found: 69.33% C, 5.16% H, 13.47% N. Exact mass (FAB HRMS) found: 415.1779; calculated for $C_{24}H_{23}N_4O_3$: 415.1770. FAB MS, *m/z* (%): 415 (MH^+, 8); 331 (11); 149 (5); 105 (14); 85 (4). ^{1}H NMR (400 MHz, $CDCl_3$): 1.57–1.76 and 1.95–2.16 (m, 6 H, CH_2-THP); 3.70 (td, 1 H, *J* = 11.5 and 2.8, bCH_2O-THP); 4.14 (ddt, 1 H, *J* = 11.5, 4.0 and 2.2, aCH_2O-THP); 5.72 (s, 2 H, CH_2O); 5.74 (dd, 1 H, *J* = 10.0, 2.9, CHO-THP); 7.46–7.55 (m, 5 H, H-*m*-Bz and H-*m*,*p*-Ph); 7.61 (m, 1 H, H-*p*-Bz); 8.21 (m, 2 H, H-*o*-Bz); 8.30 (s, 1 H, H-8); 8.74 (m, 2 H, H-*o*-Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.65, 24.80 and 31.61 (CH_2-THP); 66.99 (CH_2O); 68.70

(CH_2O-THP); 82.07 (CHO-THP); 128.34, 128.56, 129.81 and 129.90 (CH-*o*,*m*-Bz and CH-*o*,*m*-Ph); 130.06 (C-*i*-Bz); 130.42 (C-5); 130.94 (CH-*p*-Ph); 132.96 (CH-*p*-Bz); 142.27 (CH-8); 152.25 (C-4); 154.76 (C-6); 158.55 (C-2); 166.61 (CO-Bz). IR ($CHCl_3$): 2951, 2859, 1723, 1582, 1568, 1503, 1452, 1398, 1341, 1274, 1119, 648.

2-[(Benzoyloxy)methyl]-6-phenyl-9-(2,3,5-tri-O-acetyl-β-D-*ribofuranosyl)purine* (**5b**). Yield 91% of white foam. Exact mass (FAB HRMS) found: 589.1937; calculated for $C_{30}H_{29}N_4O_9$: 589.1935. FAB MS, *m/z* (%): 589 (MH^+, 19); 331 (44); 259 (13); 225 (9); 105 (100); 77 (21). ^{1}H NMR (400 MHz, $CDCl_3$): 2.04, 2.08 and 2.09 (3 × s, 3 × 3 H, CH_3-Ac); 4.31 (dd, 1 H, J_{gem} = 12.2, $J_{5'b,4'}$ = 5.2, H-5′b); 4.35 (dd, 1 H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.6, H-5′a); 4.42 (td, 1 H, $J_{4',5'}$ = 5.2, 3.6, $J_{4',3'}$ = 5.0, H-4′); 5.57 (t, 1 H, $J_{3',2'}$ = 5.5, $J_{3',4'}$ = 5.0, H-3′); 5.71 and 5.75 (2 × d, 2 H, J_{gem} = 14.2, CH_2O); 5.98 (t, 1 H, $J_{2',3'}$ = 5.5, $J_{2',1'}$ = 5.1, H-2′); 6.21 (d, 1 H, $J_{1',2'}$ = 5.1, H-1′); 7.45–7.55 (m, 5 H, H-*m*-Bz and H-*m*,*p*-Ph); 7.60 (m, 1 H, H-*p*-Bz); 8.21 (m, 2 H, H-*o*-Bz); 8.24 (s, 1 H, H-8); 8.73 (m, 2 H, H-*o*-Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$): 20.31, 20.46 and 20.72 (CH_3-Ac); 63.20 (CH_2-5′); 66.75 (CH_2O); 70.70 (CH-3′); 73.07 (CH-2′); 80.27 (CH-4′); 86.69 (CH-1′); 128.39 and 128.62 (CH-*m*-Bz and CH-*m*-Ph); 129.89 and 130.00 (CH-*o*-Bz and CH-*o*-Ph); 130.18 (C-*i*-Bz); 130.67 (C-5); 131.22 (CH-*p*-Ph); 133.03 (CH-*p*-Bz); 135.25 (C-*i*-Ph); 142.76 (CH-8); 152.49 (C-4); 155.35 (C-6); 159.12 (C-2); 166.35 (CO-Bz); 169.29, 169.38 and 170.24 (CO-Ac). IR (CCl_4): 3064, 1757, 1731, 1583, 1567, 1503, 1452, 1370, 1345, 1271, 1222, 1117, 645.

2-[(Benzoyloxy)methyl]-6-phenyl-9-(2-deoxy-3,5-di-O-toluoyl-β-D-*erythro-pentofuranosyl)purine* (**5c**). Yield 86% of white solid, m.p. 145–146 °C. For $C_{40}H_{34}N_4O_7$ (682.7) calculated: 70.37% C, 5.02% H, 8.21% N; found: 70.03% C, 4.82% H, 8.02% N. Exact mass (FAB HRMS) found: 683.2531; calculated for $C_{40}H_{35}N_4O_7$: 683.2506. FAB MS, *m/z* (%): 683 (MH^+, 19); 331 (29); 226 (5); 119 (36); 105 (25). ^{1}H NMR (500 MHz, $CDCl_3$): 2.34 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.76 (ddd, 1 H, J_{gem} = 14.3, $J_{2'b,1'}$ = 6.0, $J_{2'b,3'}$ = 2.2, H-2′b); 3.22 (ddd, 1 H, J_{gem} = 14.3, $J_{2'a,1'}$ = 8.1, $J_{2'a,3'}$ = 6.4, H-2′a); 4.57–4.62 (m, 2 H, H-5′b and H-4′); 4.68 (dd, 1 H, J_{gem} = 13.5, $J_{5'a,4'}$ = 6.0, H-5′a); 5.63 (dt, 1 H, $J_{3',2'}$ = 6.4, 2.2, $J_{3',4'}$ = 2.2, H-3′); 5.71 and 5.75 (2 × d, 2 H, J_{gem} = 14.1, CH_2O); 6.53 (dd, 1 H, $J_{1'2'}$ = 8.1, 6.0, H-1′); 7.16 and 7.28 (2 × m, 2 × 2 H, H-*m*-Tol); 7.42 (m, 2 H, H-*m*-Bz); 7.48–7.55 (m, 4 H, H-*m*,*p*-Ph and H-*p*-Bz); 7.82 and 7.93 (2 × m, 2 × 2 H, H-*o*-Tol); 8.20 (m, 2 H, H-*o*-Bz); 8.25 (s, 1 H, H-8); 8.71 (m, 2 H, H-*o*-Ph). ^{13}C NMR (125.8 MHz, $CDCl_3$): 21.62 and 21.76 (CH_3-Tol); 37.44 (CH_2-2′); 64.02 (CH_2-5′); 66.78 (CH_2O); 75.19 (CH-3′); 83.16 (CH-4′); 85.39 (CH-1′); 126.44 and 126.56 (C-*i*-Tol); 128.41 (CH-*m*-Bz); 128.57 (CH-*m*-Ph); 129.20 and 129.26 (CH-*m*-Tol); 129.56 (CH-*o*-Tol); 129.80 and 129.86 (CH-*o*-Tol, CH-*o*-Ph and CH-*o*-Bz); 130.19 (C-*i*-Bz); 130.69 (C-5); 131.08 (CH-*p*-Ph); 133.04 (CH-*p*-Bz); 135.38 (CH-*i*-Ph); 142.76 (CH-8); 144.09 and 144.45 (C-*p*-Tol); 152.35 (C-4); 155.05 (C-6); 158.70 (C-2); 165.79 and 166.07 (CO-Tol); 166.49 (CO-Bz). IR (CCl_4): 3064, 1728, 1613, 1582, 1567, 1502, 1452, 1341, 1268, 1178, 1100, 646.

2-[(Benzoyloxy)methyl]-6-(2-furyl)-9-(tetrahydropyran-2-yl)purine (**6a**). Yield 76% of white solid, m.p. 165–166 °C. For $C_{22}H_{20}N_4O_4$ (404.4) calculated: 65.34% C, 4.98% H, 13.85% N; found: 64.96% C, 4.81% H, 13.61% N. Exact mass (FAB HRMS) found: 405.1554; calculated for $C_{22}H_{21}N_4O_4$: 405.1563. FAB MS, *m/z* (%): 405 (MH^+, 17); 321 (70); 215 (13); 105 (100); 85 (28). ^{1}H NMR (400 MHz, $CDCl_3$): 1.55–1.72 and 1.91–2.13 (2 × m, 6 H, CH_2-THP); 3.66 and 4.12 (2 × m, 2 H, CH_2O-THP); 5.67 (dd, 1 H, *J* = 9.8, 3.4, CHO-THP); 5.70 (s, 2 H, CH_2O); 6.65 (dd, 1 H, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.8, H-4-furyl); 7.48 (m, 2 H, H-*m*-Bz); 7.60 (m, 1 H, H-*p*-Bz); 7.76 (dd, 1 H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.9, H-5-furyl); 7.80 (dd, 1 H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.9, H-3-furyl); 8.19 (m, 2 H, H-*o*-Bz); 8.27 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.58, 24.77 and 31.54 (CH_2-THP); 67.03 (CH_2O); 68.64 (CH_2O-THP); 82.19 (CHO-THP); 112.54

(CH-4-furyl); 117.45 (CH-3-furyl); 127.43 (C-5); 128.32 (CH-*m*-Bz); 129.90 (CH-*o*-Bz); 130.42 (C-*i*-Bz); 132.94 (CH-*p*-Bz); 142.59 (CH-8); 145.99 (CH-5-furyl); 146.01 (C-6); 149.85 (C-2-furyl); 151.86 (C-4); 158.89 (C-2); 166.53 (CO-Bz). IR (CCl_4): 2948, 2856, 1730, 1591, 1485, 1452, 1441, 1410, 1329, 1268, 1207, 1115, 643.

*2-[(Benzoyloxy)methyl]-6-(2-furyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**6b**). Yield 74% of white foam. Exact mass (FAB HRMS) found: 579.1714; calculated for $C_{28}H_{27}N_4O_{10}$: 579.1727. FAB MS, *m/z* (%): 579 (MH^+, 12); 321 (31); 259 (10); 215 (9); 105 (100). ^{1}H NMR (500 MHz, $CDCl_3$): 2.01, 2.06 and 2.07 (3 × s, 3 × 3 H, CH_3-Ac); 4.28 (dd, 1 H, J_{gem} = 12.2, $J_{5'b,4'}$ = 5.2, H-5′b); 4.32 (dd, 1 H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.6, H-5′a); 4.39 (td, 1 H, $J_{4',5'}$ = 5.2, 3.6, $J_{4',3'}$ = 4.8, H-4′); 5.51 (t, 1 H, $J_{3',2'}$ = 5.6, $J_{3',4'}$ = 4.8, H-3′); 5.68 and 5.72 (2 × d, 2 H, J_{gem} = 14.1, CH_2O); 5.93 (t, 1 H, $J_{2',3'}$ = 5.6, $J_{2',1'}$ = 5.1, H-2′); 6.17 (d, 1 H, $J_{1',2'}$ = 5.1, H-1′); 6.66 (dd, 1 H, $J_{4,3}$ = 3.6, $J_{4,5}$ = 1.8, H-4-furyl); 7.48 (m, 2 H, H-*m*-Bz); 7.60 (m, 1 H, H-*p*-Bz); 7.78 (dd, 1 H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.9, H-5-furyl); 7.82 (dd, 1 H, $J_{3,4}$ = 3.6, $J_{3,5}$ = 0.9, H-3-furyl); 8.19 (m, 2 H, H-*o*-Bz); 8.20 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 20.27, 20.42 and 20.71 (CH_3-Ac); 63.18 (CH_2-5′); 66.77 (CH_2O); 70.66 (CH-3′); 73.10 (CH-2′); 80.28 (CH-4′); 86.70 (CH-1′); 112.66 (CH-4-furyl); 117.96 (CH-3-furyl); 127.95 (C-5); 128.36 (CH-*m*-Bz); 130.00 (CH-*o*-Bz); 130.09 (C-*i*-Bz); 133.01 (CH-*p*-Bz); 143.03 (CH-8); 146.28 (CH-5-furyl); 146.44 (C-6); 149.56 (C-2-furyl); 152.04 (C-4); 159.48 (C-2); 166.22 (CO-Bz); 169.25, 169.33 and 170.21 (CO-Ac). IR (CCl_4): 3063, 1756, 1731, 1592, 1570, 1485, 1452, 1372, 1270, 1217, 1117, 639.

*2-[(Benzoyloxy)methyl]-6-(2-furyl)-9-(2-deoxy-3,5-di-O-toluoyl-*β*-D-erythro-pentofuranosyl)purine* (**6c**). Yield 71% of white solid, m.p. 142–143 °C. For $C_{38}H_{32}N_4O_8$ (672.7) calculated: 67.85% C, 4.79% H, 8.33% N; found: 67.91% C, 4.60% H, 8.11% N. Exact mass (FAB HRMS) found: 673.2318; calculated for $C_{38}H_{33}N_4O_8$: 673.2298. FAB MS, *m/z* (%): 673 (MH^+, 12); 353 (4); 321 (31); 215 (14); 119 (100); 105 (61). ^{1}H NMR (500 MHz, $CDCl_3$): 2.36 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.71 (ddd, 1 H, J_{gem} = 14.4, $J_{2'b,1'}$ = 6.0, $J_{2'b,3'}$ = 2.2, H-2′b); 3.20 (ddd, 1 H, J_{gem} = 14.4, $J_{2'a,1'}$ = 8.1, $J_{2'a,3'}$ = 6.4, H-2′a); 4.54–4.60 (m, 2 H, H-5′b and H-4′); 4.64 (dd, 1 H, J_{gem} = 13.8, $J_{5'a,4'}$ = 6.3, H-5′a); 5.54 (dt, 1 H, $J_{3',2'}$ = 6.4, 2.2, $J_{3',4'}$ = 2.2, H-3′); 5.68 and 5.73 (2 × d, 2 H, J_{gem} = 14.2, CH_2O); 6.47 (dd, 1 H, $J_{1'2'}$ = 8.1, 6.0, H-1′); 6.65 (dd, 1 H, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.7, H-4-furyl); 7.16 and 7.27 (2 × m, 2 × 2 H, H-*m*-Tol); 7.39 (m, 2 H, H-*m*-Bz); 7.47 (m, 1 H, H-*p*-Bz); 7.77 (dd, 1 H, $J_{5,4}$ = 1.7, $J_{5,3}$ = 0.8, H-5-furyl); 7.79 (dd, 1 H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.8, H-3-furyl); 7.81 and 7.91 (2 × m, 2 × 2 H, H-*o*-Tol); 8.18 (m, 2 H, H-*o*-Bz); 8.22 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 21.63 and 21.75 (CH_3-Tol); 37.37 (CH_2-2′); 63.98 (CH_2-5′); 66.78 (CH_2O); 75.16 (CH-3′); 83.21 (CH-4′); 85.43 (CH-1′); 112.60 (CH-4-furyl); 117.75 (CH-3-furyl); 126.43 and 126.55 (C-*i*-Tol); 127.97 (C-5); 128.39 (CH-*m*-Bz); 129.17 and 129.25 (CH-*m*-Tol); 129.56 (CH-*o*-Tol); 129.78 and 129.84 (CH-*o*-Tol and CH-*o*-Bz); 130.11 (C-*i*-Bz); 133.04 (CH-*p*-Bz); 143.07 (CH-8); 144.08 and 144.44 (C-*p*-Tol); 146.11 (CH-5-furyl); 146.21 (C-6); 149.67 (C-2-furyl); 151.91 (C-4); 159.03 (C-2); 165.74 and 166.03 (CO-Tol); 166.39 (CO-Bz). IR (CCl_4): 3063, 1728, 1612, 1590, 1485, 1410, 1268, 1206, 1178, 643.

General Procedure for Nucleophilic Amination of 2-(Benzoyloxymethyl)-6-chloropurines **2**

2-[(Benzoyloxy)methyl]-6-chloropurines **2** (0.5 mmol) were dissolved in ethanolic ammonia (20 ml) and the mixture was stirred at 60 °C for 32 h in a septum sealed flask. After complete substitution and deprotection the solvent was evaporated and the residue was chromatographed (ethyl acetate/methanol 9:1–7:3) and crystallized from ethanol/heptane.

6-Amino-2-(hydroxymethyl)-9-(tetrahydropyran-2-yl)purine (**7a**). Yield 62% of white solid, m.p. 210–211 °C. Exact mass (FAB HRMS) found: 250.1299; calculated for $C_{11}H_{16}N_5O_2$: 250.1304. FAB MS, *m/z* (%): 250 (MH^+, 23); 166 (15); 149 (3); 85 (5). ^{1}H NMR (500 MHz, DMSO-d_6): 1.53–1.65, 1.68–1.79, 1.89–2.00 and 2.24 (4 × m, 6 H, CH_2-THP); 3.68 and 4.00 (2 × m, 2 H, CH_2O-THP); 4.40 (d, 2 H, J = 5.8, CH_2O); 4.80 (t, 1 H, J = 5.8, OH); 5.64 (dd, 1 H, J = 11.1, 2.3, CHO-THP); 7.24 (bs, 2 H, NH_2); 8.29 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 22.69, 24.70 and 30.41 (CH_2-THP); 64.77 (CH_2O); 67.83 (CH_2O-THP); 80.66 (CHO-THP); 117.53 (C-5); 138.81 (CH-8); 149.65 (C-4); 155.91 (C-6); 163.45 (C-2). IR (KBr): 3422, 3323, 3174, 2925, 1658, 1599, 1577, 1506, 1473, 1365, 1341, 1225, 653.

6-Amino-2-(hydroxymethyl)-9-(β-D-ribofuranosyl)purine (**7e**). Yield 70% of white solid, m.p. > 230 °C (decomp.). $[\alpha]_D^{20}$ –31.7 (*c* 0.34, MeOH). Exact mass (FAB HRMS) found: 298.1144; calculated for $C_{11}H_{16}N_5O_5$: 298.1151. FAB MS, *m/z* (%): 298 (MH^+, 8); 165 (18); 133 (15). ^{1}H NMR (500 MHz, DMSO-d_6): 3.55 (ddd, 1 H, J_{gem} = 12.1, $J_{5'b,OH}$ = 6.3, $J_{5'b,4'}$ = 3.4, H-5′b); 3.66 (dt, 1 H, J_{gem} = 12.1, $J_{5'a,OH}$ = 3.9, $J_{5'a,4'}$ = 3.9, H-5′a); 3.96 (q, 1 H, $J_{4',5'}$ = 3.9, 3.4, $J_{4',3'}$ = 2.8, H-4′); 4.15 (dd, 1 H, $J_{3',OH}$ = 5.0, $J_{3',4'}$ = 2.8, H-3′); 4.39 (d, 2 H, $J_{CH2,OH}$ = 5.4, CH_2O); 4.59 (t, 1 H, $J_{2',1'}$ = 6.4, $J_{2',OH}$ = 5.0, H-2′); 4.91 (t, 1 H, $J_{OH,CH2}$ = 5.4, OH); 5.26 (br, 1 H, OH-3′); 5.35 (br, 1 H, OH-5′); 5.50 (br, 1 H, OH-2′); 5.89 (d, 1 H, $J_{1',2'}$ = 6.4, H-1′); 7.31 (bs, 2 H, NH_2); 8.31 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 61.84 (CH_2-5′); 64.70 (CH_2O); 70.87 (CH-3′); 73.69 (CH-2′); 86.05 (CH-4′); 87.63 (CH-1′); 118.24 (C-5); 139.85 (CH-8); 149.91 (C-4); 156.06 (C-6); 163.38 (C-2). IR (KBr): 3401, 3214, 1642, 1598, 1410, 650.

6-Amino-2-(hydroxymethyl)-9-(2-deoxy-β-D-erythro-pentofuranosyl)purine (**7f**). Yield 68% of white solid, m.p. 175–177 °C. $[\alpha]_D^{20}$ +5.3 (*c* 0.35, MeOH). Exact mass (FAB HRMS) found: 282.1216; calculated for $C_{11}H_{16}N_5O_4$: 282.1202. FAB MS, *m/z* (%): 282 (MH^+, 56); 166 (100); 148 (36); 117 (20). ^{1}H NMR (500 MHz, DMSO-d_6): 2.25 (ddd, 1 H, J_{gem} = 13.1, $J_{2'b,1'}$ = 6.0, $J_{2'b,3'}$ = 2.8, H-2′b); 2.67 (ddd, 1 H, J_{gem} = 13.1, $J_{2'a,1'}$ = 8.1, $J_{2'a,3'}$ = 5.7, H-2′a); 3.52 (ddd, 1 H, J_{gem} = 11.8, $J_{5'b,OH}$ = 6.5, $J_{5'b,4'}$ = 4.2, H-5′b); 3.60 (dt, 1 H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.0, $J_{5'a,4'}$ = 4.2, H-5′a); 3.87 (td, 1 H, $J_{4',5'}$ = 4.2, $J_{4',3'}$ = 2.5, H-4′); 4.39 (d, 2 H, $J_{CH2,OH}$ = 5.8, CH_2O); 4.40 (m, 1 H, $J_{3',2'}$ = 5.7, 2.8, $J_{3',OH}$ = 4.0, $J_{3',4'}$ = 2.5, H-3′); 4.92 (t, 1 H, $J_{OH,CH2}$ = 5.8, OH); 5.21 (dd, 1 H, $J_{OH,5'}$ = 6.5, 5.0, OH-5′); 5.38 (d, 1 H, $J_{OH,3'}$ = 4.0, OH-3′); 6.35 (dd, 1 H, $J_{1',2'}$ = 8.1, 6.0, H-1′); 7.29 (bs, 2 H, NH_2); 8.31 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): CH_2-2′ – overlapped with DMSO signal; 62.06 (CH_2-5′); 64.69 (CH_2O); 71.18 (CH-3′); 83.73 (CH-1′); 88.12 (CH-4′); 118.12 (C-5); 139.47 (CH-8); 149.69 (C-4); 156.00 (C-6); 163.35 (C-2). IR (KBr): 3400, 3210, 1643, 1599, 1404, 650.

General Procedure for Deacylation Reactions

A 1 M methanolic MeONa (100 μl, 0.1 mmol) was added to a solution of a protected purine or nucleoside **4**–**6** (0.5 mmol) in methanol (25 ml) and the mixture was stirred at ambient temperature. After complete deprotection the solvent was evaporated and the residue was chromatographed (ethyl acetate/methanol 1:0–8:2).

2-(Hydroxymethyl)-6-methyl-9-(tetrahydropyran-2-yl)purine (**8a**). Yield 90% of white foam. Exact mass (FAB HRMS) found: 249.1357; calculated for $C_{12}H_{17}N_4O_2$: 249.1352. FAB MS, *m/z* (%): 249 (MH^+, 41); 165 (100); 147 (33); 85 (31). ^{1}H NMR (400 MHz, $CDCl_3$): 1.65–1.88 and 2.00–2.18 (m, 6 H, CH_2-THP); 2.86 (s, 3 H, CH_3); 3.79 (td, 1 H, J = 11.6 and 2.7, bCH_2O-THP); 3.87 (t, 1 H, $J_{OH,CH2}$ = 4.9, OH); 4.18 (ddt, 1 H, J = 11.6, 4.4 and 2.0, aCH_2O-THP); 4.88 (d, 2 H, $J_{CH2,OH}$ = 4.9, CH_2O); 5.78 (dd, 1 H, J = 10.2, 2.7, CHO-THP); 8.23 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 19.42 (CH_3); 22.76, 24.83 and 31.85

(CH_2-THP); 64.50 (CH_2O); 68.83 (CH_2O-THP); 81.77 (CHO-THP); 131.89 (C-5); 141.53 (CH-8); 150.12 (C-4); 159.22 (C-6); 162.05 (C-2). IR (CCl_4): 3473, 2949, 2857, 1601, 1501, 1404, 1372, 1347, 1260, 1212, 1087, 645.

2-(Hydroxymethyl)-6-methyl-9-(β-D-ribofuranosyl)purine (**8e**). Yield 87% of white hygroscopic solid, m.p. 197–198 °C, which was lyophilized from water as a monohydrate. $[\alpha]_D^{20}$ –36.5 (*c* 0.48, MeOH). For $C_{12}H_{16}N_4O_5.H_2O$ (314.3) calculated: 45.86% C, 5.77% H, 17.83% N; found: 45.51% C, 5.36% H, 17.49% N. Exact mass (FAB HRMS) found: 297.1205; calculated for $C_{12}H_{17}N_4O_5$: 297.1199. FAB MS, *m/z* (%): 297 (MH^+, 33); 163 (19); 148 (28). ^{1}H NMR (400 MHz, DMSO-d_6): 2.72 (s, 3 H, CH_3); 3.57 (ddd, 1 H, J_{gem} = 12.0, $J_{5'b,OH}$ = 6.2, $J_{5'b,4'}$ = 4.0, H-5′b); 3.68 (ddd, 1 H, J_{gem} = 12.0, $J_{5'a,OH}$ = 5.1, $J_{5'a,4'}$ = 4.2, H-5′a); 3.97 (q, 1 H, $J_{4',5'}$ = 4.2, 4.0, $J_{4',3'}$ = 3.1, H-4′); 4.18 (td, 1 H, $J_{3',OH}$ = 4.8, $J_{3',2'}$ = 4.8, $J_{3',4'}$ = 3.1, H-3′); 4.63 (q, 1 H, $J_{2',1'}$ = 6.1, $J_{2',OH}$ = 5.7, $J_{2',3'}$ = 4.8, H-2′); 4.64 (d, 2 H, $J_{CH2,OH}$ = 6.3, CH_2O); 5.11 (t, 1 H, $J_{OH,5'}$ = 6.2, 5.1, OH-5′); 5.25 (d, 1 H, $J_{OH,3'}$ = 4.8, OH-3′); 5.28 (t, 1 H, $J_{OH,CH2}$ = 6.3, OH); 5.50 (d, 1 H, $J_{OH,2'}$ = 5.7, OH-2′); 6.02 (d, 1 H, $J_{1',2'}$ = 6.1, H-1′); 8.71 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 19.29 (CH_3); 61.59 (CH_2-5′); 65.06 (CH_2O); 70.67 (CH-3′); 73.78 (CH-2′); 85.99 (CH-4′); 87.34 (CH-1′); 131.67 (C-5); 143.96 (CH-8); 150.90 (C-4); 158.30 (C-6); 163.14 (C-2). IR (KBr): 3519, 3391, 3271, 1600, 1506, 1488, 1413, 1377, 1345, 1220, 1027, 644.

2-(Hydroxymethyl)-6-methyl-9-(2-deoxy-β-D-erythro-pentofuranosyl)purine (**8f**). Yield 88% of white hygroscopic solid, m.p. 114–115 °C, which was lyophilized from water as a hemihydrate. $[\alpha]_D^{20}$ –6.6 (*c* 0.43, MeOH). For $C_{12}H_{16}N_4O_4.1/2H_2O$ (289.3) calculated: 49.82% C, 5.92% H, 19.37% N; found: 49.94% C, 5.60% H, 19.22% N. Exact mass (FAB HRMS) found: 281.1256; calculated for $C_{12}H_{17}N_4O_4$: 281.1250. FAB MS, *m/z* (%): 281 (MH^+, 41); 165 (37); 147 (7). ^{1}H NMR (400 MHz, DMSO-d_6): 2.31 (ddd, 1 H, J_{gem} = 13.3, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 3.2, H-2′b); 2.70 (s, 3 H, CH_3); 2.75 (ddd, 1 H, J_{gem} = 13.3, $J_{2'a,1'}$ = 7.7, $J_{2'a,3'}$ = 5.7, H-2′a); 3.53 (ddd, 1 H, J_{gem} = 11.8, $J_{5'b,OH}$ = 5.9, $J_{5'b,4'}$ = 4.5, H-5′b); 3.62 (dt, 1 H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.4, $J_{5'a,4'}$ = 4.7, H-5′a); 3.88 (td, 1 H, $J_{4',5'}$ = 4.7, 4.5, $J_{4',3'}$ = 2.7, H-4′); 4.43 (m, 1 H, $J_{3',2'}$ = 5.7, 3.2, $J_{3',OH}$ = 4.1, $J_{3',4'}$ = 2.7, H-3′); 4.63 (d, 2 H, $J_{CH2,OH}$ = 6.3, CH_2O); 5.00 (t, 1 H, $J_{OH,5'}$ = 5.9, 5.4, OH-5′); 5.25 (t, 1 H, $J_{OH,CH2}$ = 6.3, OH); 5.35 (d, 1 H, $J_{OH,3'}$ = 4.1, OH-3′); 6.47 (dd, 1 H, $J_{1',2'}$ = 7.7, 6.2, H-1′); 8.68 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 19.26 (CH_3); 39.49 (CH_2-2′); 61.83 (CH_2-5′); 65.08 (CH_2O); 70.96 (CH-3′); 83.58 (CH-1′); 88.15 (CH-4′); 131.63 (C-5); 143.75 (CH-8); 150.56 (C-4); 158.17 (C-6); 163.05 (C-2). IR (KBr): 3443, 3360, 3130, 1599, 1507, 1403, 1384, 1223, 1105, 1095, 644.

2-(Hydroxymethyl)-6-phenyl-9-(tetrahydropyran-2-yl)purine (**9a**). Yield 89% of white solid, m.p. 103–104 °C. Exact mass (FAB HRMS) found: 311.1502; calculated for $C_{17}H_{19}N_4O_2$: 311.1508. FAB MS, *m/z* (%): 311 (MH^+, 22); 227 (100); 209 (25); 85 (34). ^{1}H NMR (400 MHz, $CDCl_3$): 1.65–1.90 and 2.02–2.22 (m, 6 H, CH_2-THP); 3.82 (td, 1 H, *J* = 11.7 and 2.6, bCH_2O-THP); 3.98 (t, 1 H, $J_{OH,CH2}$ = 4.8, OH); 4.20 (ddt, 1 H, *J* = 11.7, 4.4 and 1.8, aCH_2O-THP); 4.96 (d, 2 H, $J_{CH2,OH}$ = 4.8, CH_2O); 5.85 (dd, 1 H, *J* = 10.4, 2.4, CHO-THP); 7.50–7.60 (m, 3 H, H-*m*,*p*-Ph); 8.33 (s, 1 H, H-8); 8.78 (m, 2 H, H-*o*-Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.80, 24.87 and 31.92 (CH_2-THP); 64.65 (CH_2OH); 68.88 (CH_2O-THP); 81.80 (CHO-THP); 128.67 (CH-*m*-Ph); 129.82 (CH-*o*-Ph); 130.06 (C-5); 131.20 (CH-*p*-Ph); 135.22 (C-*i*-Ph); 142.18 (CH-8); 152.22 (C-4); 154.38 (C-6); 162.04 (C-2). IR ($CHCl_3$): 3469, 2952, 2864, 1583, 1569, 1504, 1454, 1398, 1364, 1355, 1232, 1085, 649.

2-(Hydroxymethyl)-6-phenyl-9-(β-D-ribofuranosyl)purine (**9e**). Yield 74% of white hygroscopic solid, m.p. 102–103 °C, which was lyophilized from water as a hemihydrate. $[\alpha]_D^{20}$ –26.7 (*c* 0.15, MeOH). For $C_{17}H_{18}N_4O_5.1/2H_2O$ (367.4) calculated: 55.58% C, 5.21% H, 15.25% N;

found: 55.58% C, 5.16% H, 15.07% N. Exact mass (FAB HRMS) found: 359.1353; calculated for $C_{17}H_{19}N_4O_5$: 359.1355. FAB MS, *m/z* (%): 359 (MH^+, 97); 227 (100); 209 (55); 119 (19). ^{1}H NMR (400 MHz, DMSO-d_6): 3.60 (ddd, 1 H, J_{gem} = 11.9, $J_{5'b,OH}$ = 5.9, $J_{5'b,4'}$ = 3.9, H-5′b); 3.71 (ddd, 1 H, J_{gem} = 11.9, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.5, H-5′a); 4.00 (q, 1 H, $J_{4',5'}$ = 4.5, 3.9, $J_{4',3'}$ = 3.0, H-4′); 4.21 (td, 1 H, $J_{3',2'}$ = 5.2, $J_{3',OH}$ = 4.9, $J_{3',4'}$ = 3.0, H-3′); 4.67 (q, 1 H, $J_{2',OH}$ = 6.0, $J_{2',1'}$ = 5.9, $J_{2',3'}$ = 5.2, H-2′); 4.76 (d, 2 H, $J_{CH2,OH}$ = 6.2, CH_2O); 5.12 (t, 1 H, $J_{OH,5'}$ = 5.9, 5.2, OH-5′); 5.26 (d, 1 H, $J_{OH,3'}$ = 4.9, OH-3′); 5.36 (t, 1 H, $J_{OH,CH2}$ = 6.2, OH); 5.54 (d, 1 H, $J_{OH,2'}$ = 6.0, OH-2′); 6.11 (d, 1 H, $J_{1',2'}$ = 5.9, H-1′); 7.55–7.64 (m, 3 H, H-*m*,*p*-Ph); 8.86 (m, 2 H, H-*o*-Ph); 8.88 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 61.52 (CH_2-5′); 65.23 (CH_2O); 70.61 (CH-3′); 73.84 (CH-2′); 85.99 (CH-4′); 87.35 (CH-1′); 128.81 (CH-*m*-Ph); 129.66 (CH-*o*-Ph); 129.70 (C-5); 131.31 (CH-*p*-Ph); 135.48 (C-*i*-Ph); 144.91 (CH-8); 152.88 (C-6); 153.11 (C-4); 163.30 (C-2). IR (KBr): 3400, 1583, 1568, 1503, 1452, 1398, 1364, 1310, 1223, 1080, 693.

*2-(Hydroxymethyl)-6-phenyl-9-(2-deoxy-*β*-D-erythro-pentofuranosyl)purine* (**9f**). Yield 93% of white hygroscopic solid, m.p. 71–72 °C, which was lyophilized from water as a hemihydrate. $[\alpha]_D^{20}$ –6.9 (*c* 0.26, MeOH). For $C_{17}H_{18}N_4O_4 \cdot 1/2H_2O$ (351.4) calculated: 58.11% C, 5.45% H, 15.95% N; found: 57.99% C, 5.10% H, 15.72% N. Exact mass (FAB HRMS) found: 343.1414; calculated for $C_{17}H_{19}N_4O_4$: 343.1406. FAB MS, *m/z* (%): 343 (MH^+, 86); 227 (100); 209 (20); 149 (6); 117 (8). ^{1}H NMR (400 MHz, DMSO-d_6): 2.37 (ddd, 1 H, J_{gem} = 13.3, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 3.4, H-2′b); 2.79 (ddd, 1 H, J_{gem} = 13.3, $J_{2'a,1'}$ = 7.5, $J_{2'a,3'}$ = 5.8, H-2′a); 3.56 (ddd, 1 H, J_{gem} = 11.8, $J_{5'b,OH}$ = 5.7, $J_{5'b,4'}$ = 4.6, H-5′b); 3.65 (dt, 1 H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.5, $J_{5'a,4'}$ = 4.5, H-5′a); 3.91 (td, 1 H, $J_{4',5'}$ = 4.6, 4.5, $J_{4',3'}$ = 2.8, H-4′); 4.47 (m, 1 H, $J_{3',2'}$ = 5.8, 3.4, $J_{3',OH}$ = 4.1, $J_{3',4'}$ = 2.8, H-3′); 4.76 (d, 2 H, $J_{CH2,OH}$ = 6.2, CH_2O); 5.01 (t, 1 H, $J_{OH,5'}$ = 5.7, 5.5, OH-5′); 5.35 (t, 1 H, $J_{OH,CH2}$ = 6.2, OH); 5.38 (d, 1 H, $J_{OH,3'}$ = 4.1, OH-3′); 6.55 (dd, 1 H, $J_{1',2'}$ = 7.5, 6.2, H-1′); 7.55–7.64 (m, 3 H, H-*m*,*p*-Ph); 8.84 (s, 1 H, H-8); 8.86 (m, 2 H, H-*o*-Ph). ^{13}C NMR (100.6 MHz, DMSO-d_6): 39.58 (CH_2-2′); 61.78 (CH_2-5′); 65.25 (CH_2O); 70.91 (CH-3′); 83.59 (CH-1′); 88.20 (CH-4′); 128.79 (CH-*m*-Ph); 129.63 (CH-*o*-Ph); 129.67 (C-5); 131.26 (CH-*p*-Ph); 135.52 (C-*i*-Ph); 144.75 (CH-8); 152.75 and 152.77 (C-4 and C-6); 163.20 (C-2). IR (KBr): 3392, 3067, 1583, 1568, 1504, 1397, 1313, 1228, 1093, 1057, 647.

6-(2-Furyl)-2-(hydroxymethyl)-9-(tetrahydropyran-2-yl)purine (**10a**). Yield 82% of white solid, m.p. 142–143 °C. Exact mass (FAB HRMS) found: 301.1296; calculated for $C_{15}H_{17}N_4O_3$: 301.1301. FAB MS, *m/z* (%): 301 (MH^+, 88); 217 (100); 199 (14); 85 (19). ^{1}H NMR (400 MHz, $CDCl_3$): 1.64–1.89 and 2.01–2.20 (2 × m, 6 H, CH_2-THP); 3.77–3.85 (m, 2 H, bCH_2O-THP and OH); 4.20 (ddt, 1 H, *J* = 11.7, 4.3, 1.7, aCH_2O-THP); 4.95 (d, 2 H, $J_{CH2,OH}$ = 4.4, CH_2O); 5.82 (dd, 1 H, *J* = 10.4, 2.5, CHO-THP); 6.68 (dd, 1 H, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.7, H-4-furyl); 7.79 (dd, 1 H, $J_{5,4}$ = 1.7, $J_{5,3}$ = 0.9, H-5-furyl); 7.86 (dd, 1 H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.9, H-3-furyl); 8.30 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.78, 24.86 and 31.94 (CH_2-THP); 64.72 (CH_2O); 68.88 (CH_2O-THP); 81.84 (CHO-THP); 112.64 (CH-4′); 117.71 (CH-3′); 127.40 (C-5); 142.31 (CH-8); 145.73 (C-6); 146.19 (CH-5-furyl); 149.69 (C-2-furyl); 151.66 (C-4); 162.50 (C-2). IR ($CHCl_3$): 3484, 2951, 2864, 1593, 1556, 1501, 1486, 1378, 1354, 1279, 1085, 1045, 644.

*6-(2-Furyl)-2-(hydroxymethyl)-9-(*β*-D-ribofuranosyl)purine* (**10e**). Yield 80% of white hygroscopic solid, m.p. 121–122 °C, which was lyophilized from water as a hemihydrate. $[\alpha]_D^{20}$ –43.0 (*c* 0.21, MeOH). For $C_{15}H_{16}N_4O_6 \cdot 1/2H_2O$ (357.3) calculated: 50.42% C, 4.80% H, 15.68% N; found: 50.78% C, 4.46% H, 15.61% N. Exact mass (FAB HRMS) found: 349.1134; calculated for $C_{15}H_{17}N_4O_6$: 349.1148. FAB MS, *m/z* (%): 349 (MH^+, 15); 215 (8); 148 (3). ^{1}H NMR (500 MHz, DMSO-d_6): 3.59 (ddd, 1 H, J_{gem} = 12.1, $J_{5'b,OH}$ = 6.1, $J_{5'b,4'}$ = 4.0, H-5′b);

3.70 (ddd, 1 H, J_{gem} = 12.1, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.1, H-5′a); 3.98 (q, 1 H, $J_{4',5'}$ = 4.1, 4.0, $J_{4',3'}$ = 3.3, H-4′); 4.20 (q, 1 H, $J_{3',OH}$ = 4.9, $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.3, H-3′); 4.66 (td, 1 H, $J_{2',OH}$ = 6.0, $J_{2',1'}$ = 6.0, $J_{2',3'}$ = 4.9, H-2′); 4.20 (d, 2 H, $J_{CH2,OH}$ = 6.3, CH_2O); 5.11 (dd, 1 H, $J_{OH,5'}$ = 6.1, 5.2, OH-5′); 5.26 (d, 1 H, $J_{OH,3'}$ = 4.9, OH-3′); 5.35 (dd, 1 H, $J_{OH,CH2}$ = 6.3, OH); 5.53 (d, 1 H, $J_{OH,2'}$ = 6.0, OH-2′); 6.08 (d, 1 H, $J_{1',2'}$ = 6.0, H-1′); 6.82 (dd, 1 H, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.8, H-4-furyl); 7.87 (dd, 1 H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.9, H-3-furyl); 8.07 (dd, 1 H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.9, H-5-furyl); 8.83 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 61.53 (CH_2-5′); 65.17 (CH_2O); 70.62 (CH-3′); 73.86 (CH-2′); 86.02 (CH-4′); 87.38 (CH-1′); 113.10 (CH-4-furyl); 117.76 (CH-3-furyl); 127.16 (C-5); 144.85 (C-6); 144.98 (CH-8); 146.64 (CH-5-furyl); 149.16 (C-2-furyl); 152.41 (C-4); 163.60 (C-2). IR (KBr): 3401, 1594, 1558, 1485, 1408, 1377, 1222, 1207, 1059, 1021, 633.

*6-(2-Furyl)-2-(hydroxymethyl)-9-(2-deoxy-*β*-D-erythro-pentofuranosyl)purine* (**10f**). Yield 81% of white hygroscopic solid, m.p. 63–64 °C, which was lyophilized from water as a hemihydrate. $[\alpha]_D^{20}$ –10.2 (*c* 0.29, MeOH). For $C_{15}H_{16}N_4O_5 \cdot 1/2H_2O$ (341.3) calculated: 52.78% C, 5.02% H, 16.41% N; found: 53.04% C, 5.02% H, 16.07% N. Exact mass (FAB HRMS) found: 333.1194; calculated for $C_{15}H_{17}N_4O_5$: 333.1199. FAB MS, *m/z* (%): 333 (MH^+, 46); 217 (47); 199 (9); 149 (7). ^{1}H NMR (400 MHz, DMSO-d_6): 2.35 (ddd, 1 H, J_{gem} = 13.3, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 3.4, H-2′b); 2.78 (ddd, 1 H, J_{gem} = 13.3, $J_{2'a,1'}$ = 7.6, $J_{2'a,3'}$ = 5.8, H-2′a); 3.55 (ddd, 1 H, J_{gem} = 11.8, $J_{5'b,OH}$ = 5.6, $J_{5'b,4'}$ = 4.5, H-5′b); 3.64 (dt, 1 H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.5, $J_{5'a,4'}$ = 4.6, H-5′a); 3.90 (td, 1 H, $J_{4',5'}$ = 4.7, 4.5, $J_{4',3'}$ = 2.9, H-4′); 4.45 (m, 1 H, $J_{3',2'}$ = 5.8, 3.4, $J_{3',OH}$ = 4.2, $J_{3',4'}$ = 2.9, H-3′); 4.69 (d, 2 H, $J_{CH2,OH}$ = 6.2, CH_2O); 5.00 (t, 1 H, $J_{OH,5'}$ = 5.6, 5.5, OH-5′); 5.33 (t, 1 H, $J_{OH,CH2}$ = 6.2, OH); 5.36 (d, 1 H, $J_{OH,3'}$ = 4.2, OH-3′); 6.51 (dd, 1 H, $J_{1',2'}$ = 7.6, 6.2, H-1′); 6.82 (dd, 1 H, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.7, H-4-furyl); 7.85 (dd, 1 H, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.8, H-3-furyl); 8.06 (dd, 1 H, $J_{5,4}$ = 1.7, $J_{5,3}$ = 0.8, H-5-furyl); 8.80 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 39.59 (CH_2-2′); 61.77 (CH_2-5′); 65.18 (CH_2O); 70.89 (CH-3′); 83.58 (CH-1′); 88.21 (CH-4′); 113.04 (CH-4-furyl); 117.64 (CH-3-furyl); 127.12 (C-5); 144.73 (C-6); 144.78 (CH-8); 146.55 (CH-5-furyl); 149.18 (C-2-furyl); 152.07 (C-4); 163.48 (C-2). IR (KBr): 3409, 1592, 1485, 1406, 1376, 1358, 1318, 1223, 1206, 1094, 1057, 1020, 642.

General Procedure for Cleavage of THP Protective Group

Either *p*-toluenesulfonic acid (0.6 mmol; for **7a**) or Dowex 50X8 (H^+) (ca. 50 mg; for **8a**–**10a**) was added to a solution of THP-protected purines **7a**–**10a** (0.5 mmol) in ethanol (25 ml, 96%). The reaction mixture was stirred at 70–75 °C for 3 h, filtered, washed resin with ethanolic ammonia (3 × 20 ml) and evaporated to dryness. Crude product was chromatographed (ethyl acetate/methanol 9:1–7:3) to afford white solid that was crystallized from ethanol/heptane.

6-Amino-2-(hydroxymethyl)-9H-purine (**7d**). Yield 85% of white solid, m.p. 336–338 °C. For $C_6H_7N_5O \cdot 1/2H_2O$ (174.2) calculated: 41.38% C, 4.63% H, 40.21% N; found: 41.68% C, 4.28% H, 39.89% N. Exact mass (FAB HRMS) found: 166.0721; calculated for $C_6H_8N_5O$: 166.0729. FAB MS, *m/z* (%): 166 (MH^+, 30); 149 (13). ^{1}H NMR (400 MHz, DMSO-d_6): 4.39 (s, 2 H, CH_2O); 4.78 (bs, 1 H, OH); 7.11 (bs, 2 H, NH_2); 8.06 (s, 1 H, H-8); 12.80 (bs, 1 H, NH). ^{13}C NMR (100.6 MHz, DMSO-d_6): 64.75 (CH_2O); 116.58 (C-5); 139.34 (CH-8); 151.60 (C-4); 163.04 (C-2); (C-4 not observed). IR (KBr): 3391, 3308, 3110, 1645, 1588, 1414, 1359, 1235, 651.

2-(Hydroxymethyl)-6-methyl-9H-purine (**8d**). Yield 71% of white solid, m.p. 269–270 °C. For $C_7H_8N_4O \cdot H_2O$ (173.2) calculated: 46.15% C, 5.53% H, 30.75% N; found: 45.79% C, 5.21% H, 30.28% N. Exact mass (FAB HRMS) found: 165.0783; calculated for $C_7H_9N_4O$: 165.0776. FAB MS, *m/z* (%): 165 (MH^+, 17); 147 (4); 131 (20). ^{1}H NMR (400 MHz, DMSO-d_6): 2.70 (s, 3 H, CH_3); 4.61 (s, 2 H, CH_2O); 5.20 (bs, 1 H, OH); 8.46 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 19.62 (CH_3); 65.14 (CH_2O); 128.40 (C-5); 144.69 (CH-8); 154.37 (C-4); 155.54 (C-6); 162.67 (C-2). IR (KBr): 3099, 1594, 1490, 1428, 1377, 1232, 1108, 1080, 643.

2-(Hydroxymethyl)-6-phenyl-9H-purine (**9d**). Yield 74% of white solid, m.p. 285–286 °C. For $C_{12}H_{10}N_4O$ (225.3) calculated: 63.71% C, 4.46% H, 24.76% N; found: 63.36% C, 4.15% H, 24.39% N. Exact mass (FAB HRMS) found: 227.0936; calculated for $C_{12}H_{11}N_4O$: 227.0933. FAB MS, *m/z* (%): 227 (MH^+, 19); 149 (4). ^{1}H NMR (400 MHz, DMSO-d_6): 4.74 (s, 2 H, CH_2O); 5.27 (bs, 1 H, OH); 7.53–7.63 (m, 3 H, H-*m*,*p*-Ph); 8.60 (s, 1 H, H-8); 8.85 (m, 2 H, H-*o*-Ph); 13.50 (bs, 1 H, NH). ^{13}C NMR (100.6 MHz, DMSO-d_6): 65.31 (CH_2O); 128.35 (C-5); 128.71 (CH-*m*-Ph); 129.51 (CH-*o*-Ph); 130.96 (CH-*p*-Ph); 135.87 (C-*i*-Ph); 145.10 (CH-8); 151.85 (C-6); 154.76 (C-4); 162.93 (C-2). IR (KBr): 3392, 3293, 3028, 1605, 1586, 1570, 1500, 1485, 1415, 1382, 1357, 1235, 1081, 642.

6-(2-Furyl)-2-(hydroxymethyl)-9H-purine (**10d**). Yield 68% of white solid, m.p. 295–296 °C. For $C_{10}H_8N_4O_2$ (216.2) calculated: 55.55% C, 3.73% H, 25.91% N; found: 55.19% C, 3.70% H, 25.57% N. Exact mass (FAB HRMS) found: 217.0722; calculated for $C_{10}H_9N_4O_2$: 217.0726. FAB MS, *m/z* (%): 217 (MH^+, 3); 199 (3); 149 (4). ^{1}H NMR (400 MHz, DMSO-d_6): 4.68 (s, 2 H, CH_2O); 5.24 (bs, 1 H, OH); 6.81 (dd, 1 H, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.7, H-4-furyl); 7.78 (bd, 1 H, $J_{3,4}$ = 3.5, H-3-furyl); 8.05 (dd, 1 H, $J_{5,4}$ = 1.7, $J_{5,3}$ = 0.9, H-5-furyl); 8.58 (s, 1 H, H-8); 12.15 (bs, 1 H, NH). ^{13}C NMR (100.6 MHz, DMSO-d_6): 65.23 (CH_2O); 112.92 (CH-4-furyl); 117.22 (CH-3-furyl); 126.36 (C-5); 144.25 (C-6); 144.80 (CH-8); 146.22 (CH-5-furyl); 149.49 (C-2-furyl); 153.45 (C-4); 163.24 (C-2). IR (KBr): 3413, 1591, 1569, 1481, 1409, 1374, 1236, 1214, 1073, 1011, 652.

Single Crystal X-ray Structure Analysis

X-ray analysis of a colourless single crystal (needle, 0.03 × 0.18 × 0.41 mm) of **9a** was performed with an Xcalibur X-ray diffractometr using CuKα radiation (λ = 1.54180 Å); diffraction data were collected at 150 K. The structure was solved by direct methods with SIR92 [22] and refined by full-matrix least-squares on F with CRYSTALS [23]. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically. All hydrogen atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry after which the positions were refined with riding constraints. Crystal data: $C_{17}H_{18}N_4O_2$, orthorhombic, space group $Pna2_1$, a = 8.3389(5) Å, b = 14.7010(8) Å, c = 12.5296(8) Å, V = 1536.01(16) Å^3, Z = 4, M = 310.35, 21 464 reflections measured, 1672 independent reflections. Final R = 0.0333, wR = 0.0358, GOF = 1.0782 for 1456 reflections with $I > 1.96\sigma(I)$ and 208 parameters.

CCDC 603580 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

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