SYNTHESIS OF (PURIN-6-YL)ACETATES AND THEIR TRANSFORMATIONS TO 6-(2-HYDROXYETHYL)- AND 6-(CARBAMOYLMETHYL)PURINES

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Received March 20, 2009
Accepted April 30, 2009
Published online July 7, 2009

Dedicated to Dr. Alfred Bader for his generous support of chemical research and education.

A novel approach to the synthesis of (purin-6-yl)acetates was developed based on Pd-catalyzed cross-coupling reactions of 6-chloropurines with a Reformatsky reagent. Their reduction with $NaBH_4$ and treatment with MnO_2 gave 6-(2-hydroxyethyl)purines, while reactions with amines in presence of NaCN afforded 6-(carbamoylmethyl)purines. Mesylation of the 6-(2-hydroxyethyl)purines followed by nucleophilic substitutions gave rise to several 6-(2-substituted ethyl)purines. This methodology was successfully applied to the synthesis of substituted purine bases and nucleosides for cytostatic and antiviral activity screening. None of the compounds exerted significant activity.

Keywords: Purines; Nucleosides; Organozinc reagents; Cross-coupling; Reformatsky reagent; Functionalized organometallics.

Purine bases and nucleosides bearing diverse C-substituents in position 6 are an important class of compounds possessing a broad spectrum of biological effects. 6-Arylpurine bases and nucleosides exert cytostatic[1], antiviral[2] and antimicrobial[3] activity or receptor modulation[4]. 6-Methylpurine and its ribonucleoside are 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 activities of 6-(hydroxymethyl)-[7], 6-(fluoromethyl)-[8] and 6-(difluoromethyl)purine[9] bases and nucleosides as well as syntheses of inactive (purin-6-yl)alanines[10] and -phenylalanines[11]. Very recently, we have finished syntheses of a large series of 6-[(dialkyl-

Collect. Czech. Chem. Commun. 2009, Vol. 74, Nos. 7–8, pp. 1035–1059
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doi:10.1135/cccc2009042

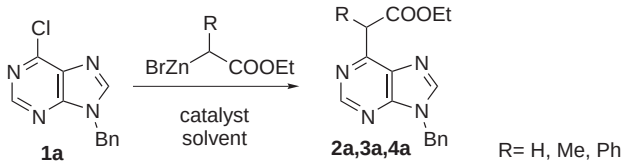
amino)methyl]-, 6-(alkoxymethyl)- and 6-[(alkylsulfanyl)methyl]purine derivatives[12], as well as homologous 6-[2-(dialkylamino)ethyl]-, 6-[2-(dialkylamino)vinyl]-, 6-(2-alkoxyethyl)- and 6-[2-(alkylsulfanyl)ethyl]-purines[13] which also exerted significant cytostatic effects and moderate non-selective anti-HCV activities. Several types of 6-(1,2-disubstituted ethyl)purines were prepared[14] by oxirane ring-opening reactions of 6-oxiranylpurines with nucleophiles and several substituted 6-cyclopropylpurines by cyclopropanation[15] of 6-vinylpurines with ethyl diazoacetate but these compounds were inactive. 6-(2-Hydroxyethyl)purines are of interest as homologues of the highly cytostatic 6-(hydroxymethyl)-purines. Recently we have published a preliminary communication[16] on their synthesis via purine-6-acetates prepared by cross-coupling of 6-halopurines with the Reformatsky reagent. Here we give a full report on this methodology and extend the study by further transformations to 6-(carbamoylmethyl)purines and β-substituted 6-ethylpurines.

RESULTS AND DISCUSSION

(Purin-6-yl)acetates were prepared previously in moderate yields by heterocyclization of pyrimidines[17] and by arylation of malonates[18] or ethyl acetoacetate[19] with 6-halo- or 6-tosyloxypurines followed by decarboxylation or cleavage of acetoacetate. The former method is laborious[17], while the latter approaches[18,19] were not reliably reproducible in our hands due to side reactions. Since these compounds are apparently useful intermediates for further functionalization, we have tried to develop a practical new approach to their synthesis based on Pd-catalyzed cross-coupling reactions of halopurines with a Reformatsky reagent under mild conditions. Although the first Pd-catalyzed arylation of aryl halides was reported[20] in 1979, only the development of a new generation of sterically hindered phosphine ligands enabled application of this reaction to a wide range of aryl halides under mild conditions[21].

In order to find the best catalytic system for the preparation of (purin-6-yl)acetates, reactions of $BrZnCH_2COOEt$ with model 9-benzyl-6-chloropurine (**1a**) to give (purin-6-yl)acetate **2a** were performed using several types of Pd catalysts and phosphine ligands with varying Pd/ligand ratios and reagent amounts (Scheme 1, Table I). The Reformatsky reagent was generated from ethyl bromoacetate and zinc dust in analogy with the procedure published[22] for other organozincs using preactivation of zinc by trimethylsilyl chloride and 1,2-dibromoethane. The first reaction performed in the presence of common $Pd(PPh_3)_4$ catalyst gave the desired (purin-6-yl)-

acetate **2a** in a low yield of 15% (entry 1). Therefore we have tried different catalytic systems based on Pd_2dba_3 in combination with various phosphine ligands. The use of P(*o*-Tol)$_3$ or P(*t*-Bu)$_3$·HBF$_4$ ligands did not give any reaction (entries 2, 3), whereas the use of JohnPhos[23] ((2-biphenyl)di-*tert*-butylphosphine) with only 1 mole % of Pd_2dba_3 loading resulted in a bit more promising 16% yield of **2a** (entry 4) and this catalytic system was further optimized. The reaction conversion strongly depended on the catalyst loading, Pd/ligand ratio and on the amount of the Reformatsky reagent (entries 5–9). Changing the Pd_2dba_3/ligand ratio from initial 1:2 to 1:4 increased the yield to 31% (entry 5) and increase in Pd loading (2 mole %) gave 48% yield (entry 6). Since further increase in the ratio or catalyst loading did not bring any improvement (entries 7, 8), the excess of the organozinc reagent was varied. When using 4 equiv. of $BrZnCH_2COOEt$ in presence of 2 mole %

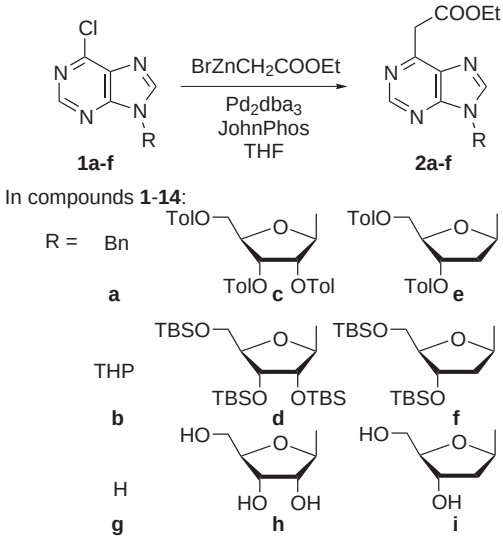


SCHEME 1

TABLE I
Optimization of the cross-coupling of **1a** with the Reformatsky reagent

Entry	R	Pd catalyst mole %	Ligand mole %	Equivalents of ester	Product	Yield %
1	H	$Pd(PPh_3)_4$ (5)		3	**2a**	15
	H	Pd_2dba_3 (1)	P(*o*-Tol)$_3$ (4)	2	**2a**	0
3	H	Pd_2dba_3 (1)	P(*t*-Bu)$_3$·HBF$_4$ (2)	2	**2a**	0
4	H	Pd_2dba_3 (1)	JohnPhos (2)	2	**2a**	16
5	H	Pd_2dba_3 (1)	JohnPhos (4)	2	**2a**	31
6	H	Pd_2dba_3 (2)	JohnPhos (8)	2	**2a**	48
7	H	Pd_2dba_3 (2)	JohnPhos (12)	2	**2a**	43
8	H	Pd_2dba_3 (3)	JohnPhos (12)	2	**2a**	47
9	H	Pd_2dba_3 (2)	JohnPhos (8)	4	**2a**	91
10	Me	Pd_2dba_3 (2)	JohnPhos (8)	4	**3a**	0
11	Ph	Pd_2dba_3 (2)	JohnPhos (8)	4	**4a**	0

of Pd_2dba_3 and 8 mole % of JohnPhos ligand, the reaction proceeded very smoothly to afford the desired ester **2a** in an excellent yield of 91% (entry 9). We have also tried to apply this optimized procedure to the reactions of branched Reformatsky reagents in order to prepare α-substituted (purin-6-yl)-acetates **3a** and **4a**. However, these reagents were entirely unreactive under these conditions and only the starting compound was recovered after separation (entries 10, 11).



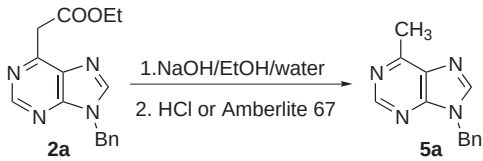
SCHEME 2

TABLE II
Cross-couplings of diverse halopurines with the Reformatsky reagent

Entry	Halopurine	Product	Yield, %
1	**1a**	**2a**	91
2	**1b**	**2b**	76
3	**1c**	**2c**	75
4	**1d**	**2d**	97
5	**1e**	**2e**	67
6	**1f**	**2f**	96

The optimized conditions were then applied to the synthesis of other derivatives using a set of protected purine bases and nucleosides with various substituents in position 9 of the purine ring (Scheme 2, Table II). THP-protected 6-chloropurine base **1b** and both toluoyl and silyl protected ribo- and 2′-deoxyribonucleosides **1c**–**1f** reacted with [(ethoxycarbonyl)methyl]-zinc bromide generally very well giving conversions to corresponding (purin-6-yl)acetates **3b**–**3f**. The isolated yields of the THP-protected base **2b** and Tol-protected nucleosides **2c** and **2e** were somewhat lower (67–76%) compared to almost quantitative yields of the silylated nucleosides **2d** and **2f** probably due to the limited stability of the THP- and Tol-protecting groups during the aqueous work-up. Therefore, the TBS groups were further used for protection of nucleosides in the follow-up chemistry.

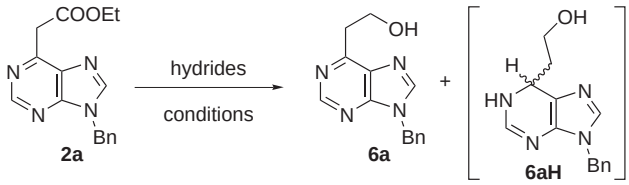
Having developed an efficient and practical methodology for the synthesis of (purin-6-yl)acetates, we next explored the possibility of further functional group transformations. The first reaction under study was the hydrolysis of the ester in order to prepare (purin-6-yl)acetic acid (as a novel interesting hetarylacetic acid). A model alkaline hydrolysis of **2a** was performed under mild conditions with aqueous NaOH in ethanol (Scheme 3). The starting compound quickly disappeared from the reaction mixture but, after neutralization with dilute HCl, the only product obtained was 6-methylpurine **5a** as a product of decarboxylation of the unstable free acetic acid formed in situ. When we tried a milder neutralization with Amberlite 67 followed by chromatography, the same decarboxylation occurred. Apparently, the desired (purin-6-yl)acetic acid is too unstable to be isolated.



SCHEME 3

The most desirable transformation of esters **2** is the reduction to the corresponding 6-(2-hydroxyethyl)purines **6** (homologues of biologically active 6-(hydroxymethyl)purines[7]). The reductions were studied and optimized with model ester **2a** (Scheme 4, Table III). Due to possible side reactions in protic media, we have tested several metal hydrides and boranes in various aprotic solvents. When using strong metal hydrides such as $LiAlH_4$, $LiBEt_3H$ or L-Selectride, the reaction did not proceed even after 2 days of heating and the starting compound was recovered (entry 1). The use of small excess

of $NaBH_4$ in DMF or the use of borane·Me_2S in THF resulted only in decomposition of the starting material (entries 2, 3). Using excess of $NaBH_4$ in refluxing THF already gave traces of the desired 6-(2-hydroxyethyl)purine **6a** (entry 4), while the use of 1 equiv. of DIBAH in toluene gave a more promising 15% yield of **6a** (entry 5). Further improvement was achieved by using excess of DIBAH in toluene (26% yield, entry 6) or AlH_3 (prepared in situ from $LiAlH_4$ and $AlCl_3$) in THF (39% yield, entry 7). Due to incompatibility of TBS-protected nucleosides **2d**, **2f**, wtih DIBAH [24], we focused on the use of excess $NaBH_4$ in other solvents. The use of ten-fold excess of $NaBH_4$ in dioxane gave 40% yield (entry 8), while the use of protic EtOH further improved the yield of the desired purine **6a** to 54% (entry 11).



SCHEME 4

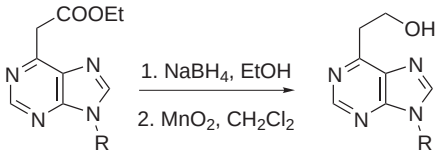
TABLE III
Optimization of reduction of (purin-6-yl)acetate **2a**

Entry	Hydride (equiv.)	Solvent	Temperature, °C	Time, h	Yield of **6a**, %
1	Other hydrides[a]	THF	0–60	6–48	0
2	$NaBH_4$ (4)	DMF	40	6	dec.
3	BH_3·Me_2S (6)	THF	reflux	6	dec.
4	$NaBH_4$ (3)	THF	reflux	6	5
5	DIBAH (1)	toluene	0	1	15
6	$LiAlH_4$/$AlCl_3$ (3:1)	THF	0	3	26
7	DIBAH (3)	THF/toluene	0	6	39
8	$NaBH_4$ (10)	dioxane	80	overnight	40
9	$NaBH_4$ (6)	THF/MeOH	70	1	43
10	$NaBH_4$/DIBAH (10:2)	dioxane	60	48	52
11	$NaBH_4$ (10)	EtOH	50	3	54
12	$NaBH_4$ (10)	EtOH	rt	overnight	82

[a] $LiAlH_4$, $LiBEt_3H$ and L-Selectride. [b] Followed by MnO_2.

During careful chromatography of the reaction mixture, an unstable side product was identified by NMR as 9-benzyl-6-(2-hydroxyethyl)-1,6-dihydro-9*H*-purine (**6aH**), a product of over-reduction of the purine ring. This unstable compound could not have been fully characterized due to spontaneous re-oxidation and its ^{1}H NMR spectrum was measured only in a mixture with **6a**. However, its identification has helped us in further optimization of the reduction protocol which apparently needed an additional mild and efficient re-oxidation step. The optimum procedure then involved the reduction of **2a** with 10 equiv. of $NaBH_4$ in EtOH followed by work-up, evaporation, dissolving in CH_2Cl_2 and treatment of the reaction mixture with MnO_2 under sonication (in order to re-oxidize the dihydropurine). This procedure finally gave the desired 6-(2-hydroxyethyl)purine **6a** in a good overall yield of 82% (entry 12).

These optimized conditions were then used for the reduction of the whole series of (purin-6-yl)acetates **2a**–**2d**, **2f** (Scheme 5, Table IV). Toluoyl groups in compound **2c** were not stable in the reduction in alkaline ethanol and only degradation of the starting material occurred (entry 3). On the other hand, reductions of THP-protected nucleobase **2b** and TBS-protected nucleosides **2d**, **2f** gave the corresponding 2-(hydroxyethyl)purine bases and nucleosides **6b**, **6d**, **6f** in good yields of ca. 70% (entries 2, 4, 5).



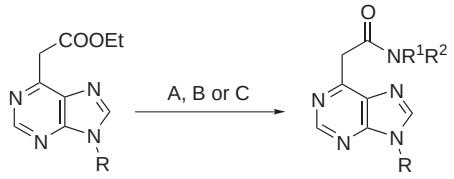
2a-d,f **6a,b,d,f**

SCHEME 5

TABLE IV
Preparative reductions of esters **2** to alcohols **6**

Entry	Ester	Product	Yield, %
1	**2a**	**6a**	82
2	**2b**	**6b**	65
3	**2c**	**6c**	0
4	**2d**	**6d**	74
5	**2f**	**6f**	71

Conversion of the (purin-6-yl)acetates to diverse amides was another attractive transformation which we decided to pursue. Amidations of model ester **2a** with primary and secondary secondary amines were attempted under several conditions (Scheme 6, Table V). Dimethylammonium dimethylcarbamate is a convenient reagent releasing dimethylamine upon heating[25]. Its reaction with **2a** in acetonitrile under reflux (method A, entry 1) was very slow and after 7 days the yield of the desired amide **8a** was only 20%. Heating of **2a** with ethanolic Me_2NH in a sealed tube (method B, entry 2) gave a somewhat better yield (50%) of **8a** but only after a prolonged reac-



2a,b,d

7 a,b,d
8 a,b,d
9 a,b,d
10 a,b,d

	R^1	R^2
7	CH_3	H
8	CH_3	CH_3
9	$(CH_2CH_2)_2CH_2$	
10	cPr	H

SCHEME 6

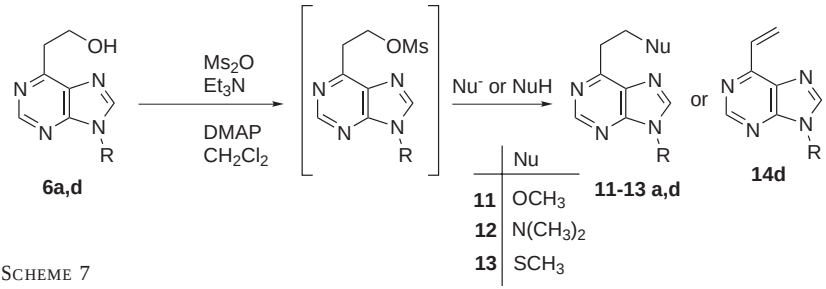
TABLE V
Amidations of (purin-6-yl)acetates

Entry	Ester	Method[a]	Amine	Product	Yield, %
1	**2a**	A	$Me_2NCOO^-Me_2NH_2^+$	**8a**	20
2	**2a**	B	Me_2NH	**8a**	50
3	**2a**	C	Me_2NH	**8a**	55
4	**2a**	C	$MeNH_2$	**7a**	67
5	**2a**	C	piperidine	**9a**	60
6	**2a**	C	cyclopropylNH_2	**10a**	51
7	**2b**	C	$MeNH_2$	**7b**	95
8	**2b**	C	Me_2NH	**8b**	49
9	**2b**	C	piperidine	**9b**	41
10	**2b**	C	cyclopropylNH_2	**10b**	66
11	**2d**	C	$MeNH_2$	**7d**	66
12	**2d**	C	Me_2NH	**8d**	39
13	**2d**	C	piperidine	**9d**	49
14	**2d**	C	cyclopropylNH_2	**10d**	0

[a] A: $Me_2NCOO^-Me_2NH_2^+$ (5 equiv.), MeCN, reflux, 7 days; B: 5.6 M Me_2NH in EtOH (10 equiv.), 80 °C, 7 days; C: 5.6 M Me_2NH in EtOH (10 equiv.), 10% NaCN, 60 °C, 2 days.

tion time of 7 days. The use of a catalytic amount of NaCN [26] significantly shortened the reaction time to 2 days giving **8a** in acceptable 55% yield (method C, entry 3). Using these optimized conditions (method C), we were able to prepare a small set of amides starting from methyl-, dimethyl- and cyclopropylamine as well as piperidine. In all cases we observed higher reactivity of primary amines compared to secondary and the yields varied from moderate to excellent (Table V, entries 4–13). The only unsuccessful reaction was amidation of TBS-protected purine **2d** with cyclopropylamine, where only degradation of the starting material occurred (entry 14).

A large series of 6-(β-substituted ethyl)purines was previously prepared[13,27] by conjugate additions to 6-vinylpurines and many of them displayed cytostatic and antiviral effect. Therefore, we wanted to explore an alternative approach to the synthesis of this class of compounds starting from 6-(2-hydroxyethyl)purines via nucleophilic substitutions of reactive mesylates. Treatment of 6-(2-hydroxyethyl)purines **6a**, **6d** with methanesulfonic anhydride in presence of triethylamine and DMAP in dichloromethane gave unstable mesylates which were directly (without characterization) used in the reaction with nucleophiles (Scheme 7, Table VI). The

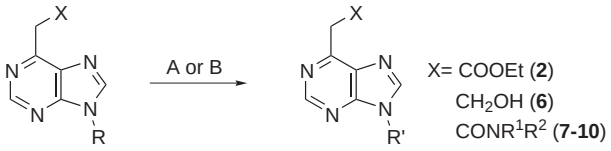


SCHEME 7

TABLE VI
Mesylations of alcohols **6** followed by nucleophilic substitutions

Entry	Starting alcohol	Nucleophile	Product	Yield, %
1	**6a**	MeONa/MeOH	**11a**	76
2	**6a**	Me_2NH/MeCN	**12a**	88
3	**6a**	MeSNa/EtOH	**13a**	60
4	**6d**	MeONa/MeOH	**11d**	63
5	**6d**	Me_2NH/MeCN	**14d**	78
6	**6d**	MeSNa/EtOH	**14d**	85

reactions of the mesylates with MeONa, Me_2NH and MeSNa were attempted. The benzylpurine mesylate gave the desired products of nucleophilic substitution: 6-(2-methoxyethyl)- (**11a**), 6-[2-(dimethylamino)ethyl]- (**12a**) and 6-[2-(methylsulfanyl)ethyl]purine (**13a**) in good yields. On the other hand, in analogous reaction of nucleoside **6d** the mesylate was very unstable and the starting material spontaneously eliminated in the reaction with dimethylamine or sodium methanthiolate to give 6-vinylpurine **14d**. Only the reaction with sodium methoxide gave the desired (2-methoxyethyl)purine nucleoside **11d**. This four-step reaction sequence (cross-coupling, reduction, mesylation and nucleophilic substitution) to compounds **11**–**13** is certainly longer, less efficient and of more limited scope



2b,d,f, 6b,d,f
7b,d, 8b,d, 9b,d, 10b

2g,h,i, 6g,h,i
7g,h, 8g,h, 9g,h, 10g

SCHEME 8

TABLE VII
Deprotections of purine bases and nucleosides

Entry	Protected compound	Reagent	Product	Yield, %
1	**2b**	Dowex 50 (H^+), EtOH	**2g**	93
2	**6b**	Dowex 50 (H^+), EtOH	**6g**	75
3	**7b**	Dowex 50 (H^+), EtOH	**7g**	64
4	**8b**	Dowex 50 (H^+), EtOH	**8g**	58
5	**9b**	Dowex 50 (H^+), EtOH	**9g**	75
6	**10b**	Dowex 50 (H^+), EtOH	**10g**	67
7	**2d**	$Et_3N{\cdot}3HF$, THF	**2h**	96
8	**6d**	$Et_3N{\cdot}3HF$, THF	**6h**	92
9	**7d**	$Et_3N{\cdot}3HF$, THF	**7h**	88
10	**8d**	$Et_3N{\cdot}3HF$, THF	**8h**	91
11	**9d**	$Et_3N{\cdot}3HF$, THF	**9h**	98
12	**2f**	$Et_3N{\cdot}3HF$, THF	**2i**	69
13	**6f**	$Et_3N{\cdot}3HF$, THF	**6i**	69

than the alternative conjugate additions[13,27] to 6-vinylpurines. However, this sequence avoids the use of toxic stannane reagents used for preparation of 6-vinylpurines.

Finally, protecting groups were removed by stardard methods to produce free purine bases and nucleosides. THP groups in protected bases **2b**, **6b**, **7b**, **8b**, **9b**, **10b** were cleaved using catalytic amount of Dowex 50 (H^+ form)[28] in ethanol at elevated temperature for 3 h (Scheme 8, Table VII) to give the corresponding free 9*H*-purine bases **2g**, **6g**, **7g**, **8g**, **9g**, **10g** (entries 1–6). The TBS-protected purine nucleosides **2d**, **2f**, **6d**, **6f** and **7d**, **8d**, **9d** were deprotected by $Et_3N{\cdot}3HF$ [11] (1.5 equiv. for each TBS group) in THF. Free purine nucleosides **2h**, **2i**, **6h**, **6i** and **7h**, **8h**, **9h** were obtained at room temperature after 18 h in good to excellent yields (entries 7–13).

All compounds were fully characterized by analytical and spectral methods. In addition, crystal structures of **2a**, **6a** and **9a** were determined by X-ray diffraction (Fig. 1). In compound **6a**, an intermolecular H-bond to N7 of the neighboring molecule is present instead of expected intramolecular H-bond of OH to N1 or N7.

In conclusion, an efficient methodology for the cross-coupling of 6-chloropurine bases and nucleosides with the Reformatsky reagent was developed giving an access to (purin-6-yl)acetates. These compounds are versatile intermediates useful for the synthesis of 6-(2-hydroxyethyl)purines by reduction and 6-(carbamoylmethyl)purines by amidations. The 6-(2-hydroxyethyl)purines can be further transformed to reactive mesylates

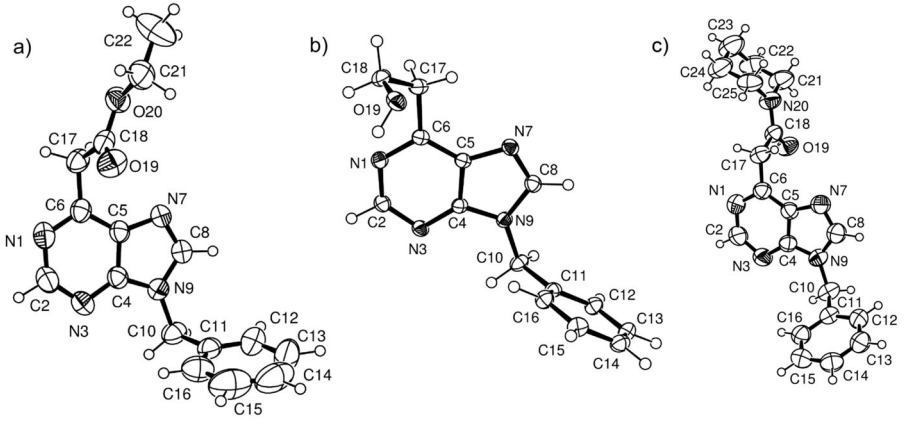


FIG. 1
Crystal structures of **2a** (a), **6a** (b) and **9a** (c). Thermal ellipsoids at the 50% probability level

convertible to ethers, amines and thioethers. All the final deprotected compounds underwent screening for cytostatic and anti-HCV activities. Unfortunately, none of them showed any considerable activity.

EXPERIMENTAL

NMR spectra were recorded on a Bruker Avance 400 spectrometer (^{1}H at 400 MHz, ^{13}C at 100.6 MHz), a Bruker Avance 500 (^{1}H at 500 MHz, ^{13}C at 125.8 MHz) and a Bruker Avance 600 (^{1}H at 600 MHz, ^{13}C at 151 MHz). Chemical shifts (in ppm, δ-scale) were referenced to TMS as internal standard. Coupling constants (*J*) are given in Hz. 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 Bruker 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.

Preparation of [(Ethoxycarbonyl)methyl]zinc Bromide and Its Cross-Coupling Reactions with 6-Chloropurines **1a**–**1f**. General Procedure

A solution of ethyl bromoacetate (417.5 mg, 278.33 μl, 2.5 mmol) in THF (3 ml) prepared under argon was added at room temperature to an argon-purged flask containing suspension of zinc dust (327.4 mg, 5 mmol) in THF (2 ml), which was preactivated with trimethylsilyl chloride (15 μl). The suspension was stirred for 1 h, zinc was allowed to settle and 4 ml of supernatant was transferred through a septum to a mixture of 6-chloropurine **1a** (122 mg, 0.5 mmol), Pd_2dba_3 (8 mg, 0.01 mmol) and JohnPhos (12 mg, 0.04 mmol) in THF (1 ml) prepared under argon. The reaction mixture was stirred for 12 h and then quenched with 1 M NH_4Cl (40 ml) and extracted with chloroform (3 × 30 ml). Collected organic layers were dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed on silica gel column (ethyl acetate/hexane) to give pure 9-benzyl-6-[(2-ethoxycarbonyl)methyl]-9*H*-purine (**2a**). Yellowish crystals (91%) were obtained by crystallization from CH_2Cl_2/heptane.

9-Benzyl 6-[2-(ethoxycarbonyl)methyl]-9H-purine (**2a**). Yellowish crystals, m.p. 90–96 °C. MS (FAB): 297 (100, M + 1). HRMS (FAB): for $C_{16}H_{17}N_4O_2$ calculated 297.1351, found 297.1356. ^{1}H NMR (400 MHz, $CDCl_3$): 1.27 (t, 3 H, *J* = 7.1, CH_3); 4.22 (q, 2 H, *J* = 7.1, CH_2O); 4.26 (s, 2 H, CH_2-6); 5.45 (s, 2 H, CH_2-9); 7.29–7.41 (m, 5 H, Ph); 8.04 (s, 1 H, H-8); 8.97 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$):14.11 (CH_3); 39.03 (CH_2-6); 47.37 (CH_2-9); 61.36 (CH_2O); 127.92 (CH-*o*-Ph); 128.66 (CH-*p*-Ph); 129.16 (CH-*m*-Ph); 133.00 (C-5); 134.93 (C-*i*-Ph); 144.33 (CH-8); 151.32 (C-4); 152.62 (CH-2); 154.55 (C-6); 169.21 (CO). MS (FAB): 297 (100, M + 1). IR: 2983, 1744, 1599, 1500, 1407, 1333, 1178. For $C_{16}H_{16}N_4O_2$ (296.1) calculated: C 64.85%, H 5.44%, N 18.91%; found: C 64.46%, H 5.37%, N 18.50%.

6-[2-(Ethoxycarbonyl)methyl]-9-(tetrahydropyran-2-yl)-9H-purine (**2b**). Yellowish crystals. MS (FAB): 291 (25, M + 1), 207 (100). HRMS (FAB): for $C_{14}H_{18}N_4O_3$ calculated 291.1457, found 291.1463. ^{1}H NMR (400 MHz, $CDCl_3$): 1.26 (t, 3 H, *J* = 7.1, CH_3CH_2); 1.63–1.88 and 2.00–2.20 (2 × m, 6 H, CH_2-THP); 3.80 (dt, 1 H, *J* = 11.7, 2.6, bCH_2O-THP); 4.19 (ddt, 1 H, *J* = 11.7, 4.1, 1.9, aCH_2O-THP); 4.22 (q, 2 H, *J* = 7.1, CH_2CH_3); 4.23 and 4.28 (2 × d, 2 H, J_{gem} = 15.9, CH_2-6); 5.80 (dd, 1 H, *J* = 10.2, 2.7, CHO-THP); 8.28 (s, 1 H, H-8); 8.93 (s, 1 H,

H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 14.12 (CH_3CH_2); 22.73, 24.83 and 31.82 (CH_2-THP); 39.09 (CH_2-6); 61.37 (CH_2CH_3); 68.85 (CH_2O-THP); 82.06 (CHO-THP); 133.20 (C-5); 142.35 (CH-8); 150.49 (C-4); 152.43 (CH-2); 154.57 (C-6); 169.17 (CO). IR (CCl_4): 2980, 2948, 2856, 1743, 1600, 1494, 1411, 1334, 1087, 1046.

*6-[2-(Ethoxycarbonyl)methyl]-9-(2,3,5-tri-O-4-methylbenzoyl-*β*-D-ribofuranosyl)-9H-purine* (**2c**). Yellowish foam. MS (FAB): 693 (4, M + 1), 487 (10), 215 (10), 119 (100), 91 (17). HRMS (FAB): for $C_{38}H_{37}N_4O_9$ calculated 693.2560, found 693.2543. ^{1}H NMR (400 MHz, $CDCl_3$): 1.25 (t, 3 H, J = 7.2, CH_3CH_2); 2.38 and 2.42 (2 × s, 9 H, CH_3-Tol); 4.20 (q, 2 H, J = 7.2, CH_2CH_3); 4.21 and 4.24 (2 × d, 2 H, J_{gem} = 15.8, CH_2CO); 4.67 (dd, 1 H, J_{gem} = 12.2, $J_{5'b,4'}$ = 4.1, H-5′b); 4.82 (td, 1 H, $J_{4',3'}$ = 4.5, $J_{4',5'}$ = 4.1, 3.1, H-4′); 4.89 (dd, 1 H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.1, H-5′a); 6.22 (dd, 1 H, $J_{3',2'}$ = 5.7, $J_{3',4'}$ = 4.5, H-3′); 6.38 (t, 1 H, $J_{2',3'}$ = 5.7, $J_{2',1'}$ = 5.5, H-2′); 6.43 (d, 1 H, $J_{1',2'}$ = 5.5, H-1′); 7.16, 7.22 and 7.26 (3 × m, 3 × 2 H, H-*m*-Tol); 7.82, 7.90 and 8.00 (3 × m, 3 × 2 H, H-*o*-Tol); 8.21 (s, 1 H, H-8); 8.83 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 14.12 (CH_3CH_2); 21.70 and 21.73 (CH_3-Tol); 39.12 (CH_2CO); 61.41 (CH_2CH_3); 63.47 (CH_2-5′); 71.41 (CH-3′); 73.69 (CH-2′); 81.06 (CH-4′); 86.83 (CH-1′); 125.64, 126.02 and 126.58 (C-*i*-Tol); 129.22, 129.26 and 129.35 (CH-*m*-Tol); 129.79, 129.88 and 129.90 (CH-*o*-Tol); 133.76 (C-5); 143.16 (CH-8); 144.23, 144.58 and 144.69 (C-*p*-Tol); 150.96 (C-4); 152.73 (CH-2); 155.00 (C-6); 165.17, 165.38 and 166.20 (CO-Tol); 168.32 (COOEt). IR (CCl_4): 2983, 1733, 1613, 1600, 1266, 1179, 1093, 1021.

*6-[2-(Ethoxycarbonyl)methyl]-9-[2,3,5-tri-O-(tert-butyldimethylsilyl)-*β*-D-ribofuranosyl]-9H-purine* (**2d**). Yellow oil. MS (FAB): 681 (10, M + 1), 72 (100). HRMS (FAB): for $C_{32}H_{61}N_4O_6Si_3$ calculated 681.3899, found 681.3885. ^{1}H NMR (400 MHz, $CDCl_3$): –0.25, –0.04, –0.10, 0.11, 0.14 and 0.15 (6 × s, 6 × 3 H, CH_3Si); 0.79, 0.94 and 0.96 (3 × s, 3 × 9 H, $(CH_3)_3C$); 1.25 (t, 3 H, J_{vic} = 7.1, CH_3CH_2); 3.80 (dd, 1 H, J_{gem} = 11.5, $J_{5'b,4'}$ = 2.8, H-5′b); 4.03 (dd, 1 H, J_{gem} = 11.5, $J_{5'a,4'}$ = 3.9, H-5′a); 4.15 (td, 1 H, $J_{4',5'}$ = 3.9, 2.8, $J_{4',3'}$ = 3.7, H-4′); 4.21 (q, 2 H, J_{vic} = 7.1, CH_2CH_3); 4.24 and 4.28 (2 × d, J_{gem} = 15.9, CH_2-pur); 4.33 (t, 1 H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 3.7, H-3′); 4.68 (dd, 1 H, $J_{2',1'}$ = 5.1, $J_{2',3'}$ = 4.4, H-2′); 6.12 (d, 1 H, $J_{1',2'}$ = 5.1, H-1′); 8.42 (s, 1 H, H-8); 8.91 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): –5.36, –5.08, –5.08, –4.72 and –4.69 (CH_3Si); 14.11 (CH_3CH_2); 17.83, 18.08 and 18.54 ($C(CH_3)_3$); 25.63, 25.84 and 26.09 ($(CH_3)_3C$); 39.10 (CH_2-pur); 61.31 (CH_2CH_3); 62.47 (CH_2-5′); 71.87 (CH-3′); 75.91 (CH-2′); 85.55 (CH-4′); 88.36 (CH-1′); 133.68 (C-5); 143.48 (CH-8); 151.04 (C-4); 152.34 (CH-2); 154.54 (C-6); 169.17 (CO). IR (CCl_4): 2956, 2931, 2859, 1746, 1599, 1472, 1255, 1166, 1072. For $C_{32}H_{60}N_4O_6Si_3$ (680.3) calculated: C 56.43%, H 8.88%, N 8.23%; found: C 56.47%, H 8.98%, N 7.96%.

*9-(2-Deoxy-3,5-di-O-4-methylbenzoyl-*β*-D-erythro-pentofuranosyl)-6-[2-(ethoxycarbonyl)methyl]-9H-purine* (**2e**). Yellowish foam. MS (FAB): 559 (5, M + 1), 207 (55), 161 (15), 119 (100), 91 (20), 81 (87). HRMS (FAB): for $C_{30}H_{31}N_4O_7$ calculated 559.2192, found 559.2173. ^{1}H NMR (500 MHz, $CDCl_3$): 1.26 (t, 3 H, J = 7.1, CH_3CH_2); 2.41 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.85 (ddd, 1 H, J_{gem} = 14.2, $J_{2'b,1'}$ = 5.8, $J_{2'b,3'}$ = 2.1, H-2′b); 3.19 (ddd, 1 H, J_{gem} = 14.2, $J_{2'a,1'}$ = 8.4, $J_{2'a,3'}$ = 6.3, H-2′a); 4.22 (q, 2 H, J = 7.1, CH_2CH_3); 4.24 (s, 2 H, CH_2CO); 4.62–4.70 (m, 2 H, H-5′b and H-4′); 4.78 (m, 1 H, H-5′a); 5.84 (dt, 1 H, $J_{3',2'}$ = 6.3, 2.1, $J_{3',4'}$ = 2.1, H-3′); 6.60 (dd, 1 H, $J_{1'2'}$ = 8.4, 5.8, H-1′); 7.23 and 7.29 (2 × m, 2 × 2 H, H-*m*-Tol); 7.91 and 7.98 (2 × m, 2 × 2 H, H-*o*-Tol); 8.24 (s, 1 H, H-8); 8.87 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): 14.11 (CH_3CH_2); 21.67 and 21.73 (CH_3-Tol); 37.77 (CH_2-2′); 39.07 (CH_2CO); 61.41 (CH_2CH_3); 63.94 (CH_2-5′); 75.07 (CH-3′); 83.12 (CH-4′); 84.89 (CH-1′); 126.34 and 126.62 (C-*i*-Tol); 129.29 (CH-*m*-Tol); 129.63 and 129.81 (CH-*o*-Tol); 133.77 (C-5); 142.77 (CH-8); 144.18 and 144.56 (C-*p*-Tol); 150.74 (C-4); 152.47 (CH-2); 154.85 (C-6);

165.93 and 166.14 (CO-Tol); 169.10 (COOEt). IR (CCl_4): 2983, 1728, 1613, 1599, 1266, 1178, 1100, 1021.

*9-[3,5-Di-O-(tert-butyldimethylsilyl)-2-deoxy-*β*-D-erythro-pentofuranosyl)-6-[2-(ethoxycarbonyl)-methyl]-9H-purine* (**2f**). Yellow oil. MS (FAB): 551 (10, M + 1), 207 (80), 72 (100). HRMS (FAB): for $C_{26}H_{47}N_4O_5Si_2$ calculated 551.3085, found 551.3106. ^{1}H NMR (500 MHz, $CDCl_3$): 0.085, 0.09 and 0.12 (3 × s, 12 H, CH_3Si); 0.91 and 0.92 (2 × s, 2 × 9 H, $(CH_3)_3C$); 1.27 (t, 3 H, J = 7.1, CH_3CH_2); 2.46 (ddd, 1 H, J_{gem} = 13.1, $J_{2'b,1'}$ = 6.1, $J_{2'b,3'}$ = 3.7, H-2′b); 2.69 (ddd, 1 H, J_{gem} = 13.1, $J_{2'a,1'}$ = 6.9, $J_{2'a,3'}$ = 5.8, H-2′a); 3.78 (dd, 1 H, J_{gem} = 11.2, $J_{5'b,4'}$ = 3.2, H-5′b); 3.88 (dd, 1 H, J_{gem} = 11.2, $J_{5'a,4'}$ = 4.2, H-5′a); 4.04 (dt, 1 H, $J_{4',5'}$ = 4.2, 3.2, $J_{4',3'}$ = 3.1, H-4′); 4.22 (q, 2 H, J = 7.1, CH_2CH_3); 4.23 and 4.27 (2 × d, 2 H, J_{gem} = 15.8, CH_2CO); 4.64 (m, 1 H, $J_{3',2'}$ = 5.8, 3.7, $J_{3',4'}$ = 3.1, H-3′); 6.52 (t, 1 H, $J_{1',2'}$ = 6.9, 6.1, H-1′); 8.38 (s, 1 H, H-8); 8.91 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): –5.49, –5.39, –4.81 and –4.67 (CH_3Si); 14.13 (CH_3CH_2); 17.99 and 18.41 ($C(CH_3)_3$); 25.74 and 25.94 (($CH_3)_3C$); 39.05 (CH_2CO); 41.21 (CH_2-2′); 61.35 (CH_2CH_3); 62.78 (CH_2-5′); 71.97 (CH-3′); 84.50 (CH-1′); 88.05 (CH-4′); 133.68 (C-5); 143.12 (CH-8); 150.72 (C-4); 152.28 (CH-2); 154.47 (C-6); 169.23 (CO). IR (CCl_4): 2956, 2859, 1745, 1599, 1463, 1472, 1258, 1108, 1034. For $C_{26}H_{46}N_4O_5Si_2$ (680.3) calculated: C 56.69%, H 8.42%, N 10.17%; found: C 56.87%, H 8.49%, N 9.67%.

Alkaline Hydrolysis of Ester **2a**

NaOH (60 mg, 1.5 mmol) was added to a solution of ester **2a** (148 mg, 0.5 mmol) in aqueous ethanol (1:1, 5 ml) and the reaction was stirred at room temperature for 3 h. The reaction mixture was diluted with water (15 ml) and chromatographed on Amberlite 67 (distilled water/0.1 M AcOH) to give 110 mg (98%) of 9-benzyl-6-methyl-9*H*-purine (**5a**) as a white solid. ^{1}H NMR spectra were in accord with previously published data[29].

Reduction of 6-[2-(Ethoxycarbonyl)methyl]purines **2a**, **2b**, **2d**, **2f** to (2-Hydroxyethyl)purines **6a**, **6b**, **6d**, **6f**. General Procedure

To a stirred solution of purine **2a** (296 mg, 1 mmol) in EtOH (8 ml) was added excess of $NaBH_4$ (380 mg, 10 mmol), the reaction mixture was stirred at room temperature overnight and then quenched by addition of MeOH (8 ml) and 1 M NH_4Cl (10 ml). Alcohols were evaporated and the residue extracted with chloroform (3 × 30 ml). Collected organic layers were dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The residue was dissolved in CH_2Cl_2 (10 ml), MnO_2 (174 mg, 2 mmol) was added and the mixture was sonicated at ambient temperature for 1 h. Then the mixture was filtered through Celite and the solvent evaporated. The residue was chromatographed on silica gel column (chloroform/methanol) to give yellowish oil. Alcohol **6a** was obtained by crystallization from CH_2Cl_2/heptane as white crystals (208 mg, 82%).

9-Benzyl-6-(2-hydroxyethyl)-9H-purine (**6a**). White crystals, m.p. 72–73 °C. MS (FAB): 255 (100, M + 1), 91 (55). HRMS (FAB): for $C_{14}H_{15}N_4O$ calculated 255.1246, found 255.1242. ^{1}H NMR (400 MHz, $CDCl_3$): 3.45 (t, 2 H, J = 5.4, CH_2-pur); 4.16 (bt, 2 H, J = 5.4, CH_2-O); 4.89 (bs, 1 H, OH); 5.45 (s, 2 H, CH_2-N); 7.28–7.40 (m, 5 H, Ph); 8.04 (s, 1 H, H-8); 8.90 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 36.04 (CH_2-pur); 47.25 (CH_2-N); 60.19 (CH_2-O); 127.81 (CH-*o*-Ph); 128.58 (CH-*p*-Ph); 129.08 (CH-*m*-Ph); 132.15 (C-5); 134.85 (C-*i*-Ph); 143.71 (CH-8); 150.70 (C-4); 152.23 (CH-2); 161.14 (C-6). IR: 2931, 1596, 1500, 1407, 1331, 1196, 1063. For $C_{14}H_{14}N_4O$ (254.1) calculated: C 66.13%, H 5.55%, N 22.03%; found: C 65.87%, H 5.47%, N 21.90%.

9-Benzyl-6-(2-hydroxyethyl)-1,6-dihydro-9H-purine (**6aH**). Unstable compound isolated by chromatography after reduction of **2a** with $NaBH_4$ in EtOH without re-oxidation. It was not isolated as a pure compound, and identified by NMR only in mixture with **3a**. ^{1}H NMR (600 MHz, DMSO-d_6): 1.76 (dq, 1 H, J_{gem} = 12.4, J_{vic} = 6.8, 6.2, CH_aH_b-pur); 1.88 (dtd, 1 H, J_{gem} = 12.4, J_{vic} = 6.8, 5.5, CH_aH_b-pur); 3.54 and 3.62 (2 × dt, 2 H, J_{gem} = 10.8, J_{vic} = 6.8, CH_2O); 4.92 (bt, 1 H, J_{vic} = 6.2, 5.5, H-6); 5.03 (s, 2 H, CH_2Ph); 6.91 (s, 1 H, $J_{2,NH}$ = 3.8, H-2); 7.23 (m, 2 H, H-*o*-Ph); 7.32 (m, 2 H, H-*m*-Ph); 7.34 (m, 1 H, H-*p*-Ph); 7.53 (bd, 1 H, $J_{NH,2}$ = 3.8, NH); 8.32 (s, 1 H, H-8). ^{13}C NMR (600 MHz, DMSO-d_6): 42.60 (CH_2-pur); 45.82 (CH_2Ph); 51.10 (CH-6); 57.56 (CH_2O); 119.96 (C-5); 127.61 (CH-*o*-Ph); 127.88 (CH-*p*-Ph); 128.73 (CH-*m*-Ph); 132.58 (CH-8); 134.17 (C-4); 138.32 (C-*i*-Ph); 147.00 (CH-2).

6-(2-Hydroxyethyl)-9-tetrahydropyran-2-yl-9H-purine (**6b**). Yellowish oil. MS (FAB): 249 (10, M + 1), 165 (100, M – THP), 85 (40, THP). HRMS (FAB): for $C_{12}H_{17}N_4O_2$ calculated 249.1351, found 249.1342. ^{1}H NMR (500 MHz, $CDCl_3$): 1.65–1.87 and 2.02–2.20 (2 × m, 6 H, CH_2-THP); 3.45 (m, 2 H, CH_2-pur); 3.80 (dt, 1 H, *J* = 11.8, 2.6, $CH_a\mathbf{H}_bO$-THP); 4.16 (t, 2 H, J_{vic} = 5.3, CH_2O); 4.19 (ddt, 1 H, *J* = 11.8, 4.3, 1.9, $C\mathbf{H}_aH_bO$-THP); 4.71 (bs, 1 H, OH); 5.80 (dd, 1 H, *J* = 10.5, 2.5, CHO-THP); 8.28 (s, 1 H, H-8); 8.88 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 22.70, 24.80 and 31.82 (CH_2-THP); 36.01 (CH_2-pur); 60.29 (CH_2O); 68.86 (CH_2O-THP); 82.00 (CHO-THP); 132.34 (C-5); 141.76 (CH-8); 149.95 (C-4); 152.12 (CH-2); 161.35 (C-6). IR (CCl_4): 3392, 2949, 2931, 2858, 1598, 1410, 1333, 1210, 1047.

*6-(2-Hydroxyethyl)-9-[2,3,5-tri-O-(tert-butyldimethylsilyl)-*β*-D-ribofuranosyl]-9H-purine* (**6d**). White foam. MS (FAB): 639 (100, M + 1), 343 (30), 288 (35). HRMS (FAB): for $C_{30}H_{59}N_4O_5Si_3$ calculated 639.3793, found 639.3776. ^{1}H NMR (400 MHz, $CDCl_3$): –0.22, –0.03, 0.10, 0.11, 0.14 and 0.15 (6 × s, 6 × 3 H, CH_3Si); 0.80, 0.94 and 0.96 (3 × s, 3 × 9 H, $(CH_3)_3C$); 3.45 (m, 2 H, CH_2-pur); 3.81 (dd, 1 H, J_{gem} = 11.5, $J_{5'b,4'}$ = 2.6, H-5′b); 4.04 (dd, 1 H, J_{gem} = 11.5, $J_{5'a,4'}$ = 3.8, H-5′a); 4.13–4.18 (m, 3 H, H-4′ and CH_2-O); 4.33 (t, 1 H, $J_{3',2'}$ = 4.3, $J_{3',4'}$ = 3.9, H-3′); 4.65 (t, 1 H, $J_{2',1'}$ = 4.9, $J_{2',3'}$ = 4.3, H-2′); 6.13 (d, 1 H, $J_{1',2'}$ = 4.9, H-1′); 8.47 (s, 1 H, H-8); 8.86 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): –5.37, –5.06, –4.73, –4.69 and –4.39 (CH_3Si); 17.84, 18.07 and 18.52 ($C(CH_3)_3$); 25.62, 25.82 and 26.07 ($(CH_3)_3C$); 36.08 (CH_2-pur); 60.31 (CH_2-O); 62.36 (CH_2-5′); 71.75 (CH-3′); 76.04 (CH-2′); 85.48 (CH-4′); 88.36 (CH-1′); 132.76 (C-5); 142.94 (CH-8); 150.53 (C-4); 152.02 (CH-2); 161.32 (C-6). IR (CCl_4): 3409, 2956, 2931, 2859, 1597, 1472, 1255, 1071, 839. For $C_{30}H_{58}N_4O_5Si_3$ (639.0) calculated: C 56.38%, H 9.15%, N 8.77%; found: C 56.38%, H 9.25%, N 8.30%.

*9-[3,5-Di-O-(tert-butyldimethylsilyl)-2-deoxy-*β*-D-erythro-pentofuranosyl)-6-(2-hydroxyethyl)-9H-purine* (**6f**). Yellow oil. MS (FAB): 509 (20, M + 1), 165 (60), 73 (100). HRMS (FAB): for $C_{24}H_{45}N_4O_4Si_2$ calculated 509.2979, found 509.2971. ^{1}H NMR (500 MHz, $CDCl_3$): 0.08, 0.09 and 0.11 (3 × s, 12 H, CH_3Si); 0.90 and 0.92 (2 × s, 2 × 9 H, $(CH_3)_3C$); 2.48 (ddd, 1 H, J_{gem} = 13.1, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 4.0, H-2′b); 2.66 (ddd, 1 H, J_{gem} = 13.1, $J_{2'a,1'}$ = 7.4, $J_{2'a,3'}$ = 5.7, H-2′a); 3.44 (t, 2 H, *J* = 5.3, CH_2-pur); 3.78 (dd, 1 H, J_{gem} = 11.3, $J_{5'b,4'}$ = 3.0, H-5′b); 3.88 (dd, 1 H, J_{gem} = 11.3, $J_{5'a,4'}$ = 3.9, H-5′a); 4.04 (dt, 1 H, $J_{4',5'}$ = 3.9, 3.0, $J_{4',3'}$ = 3.7, H-4′); 4.16 (bt, 2 H, *J* = 6.4, CH_2-O); 4.76 (m, 1 H, $J_{3',2'}$ = 5.7, 4.0, $J_{3',4'}$ = 3.7, H-3′); 4.90 (bs, 1 H, OH); 6.53 (t, 1 H, $J_{1',2'}$ = 7.4, 6.2, H-1′); 8.40 (s, 1 H, H-8); 8.85 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): –5.49, –5.40, –4.81 and –4.66 (CH_3Si); 18.00 and 18.41 ($\mathbf{C}(CH_3)_3$); 25.74 and 25.93 ($(\mathbf{C}H_3)_3C$); 36.16 (CH_2-pur); 41.37 (CH_2-2′); 60.35 (CH_2OH); 62.69 (CH_2-5′); 71.81 (CH-3′); 84.52 (CH-1′); 88.06 (CH-4′); 132.81 (C-5); 142.54 (CH-8); 150.18 (C-4); 151.98 (CH-2); 161.28 (C-6). IR (CCl_4): 3401, 2956, 2931, 2859, 1598, 1472, 1258, 1109, 839. For $C_{24}H_{44}N_4O_4Si_2$ (508.8) calculated: C 56.65%, H 8.72%, N 11.01%; found: C 56.87%, H 9.09%, N 10.38%.

Amidation of Esters **2a**, **2b**, **2d**. General Procedure

Mixture of ester **2a** (296 mg, 1 mmol) and NaCN (5 mg, 0.1 mmol) was dissolved in 5.6 M solution of dimethylamine in EtOH (1.78 ml, 10 mmol) and additional ethanol (2 ml) was added. The reaction mixture was stirred at 60 °C for 48 h, then evaporated and extracted with chloroform (3 × 50 ml). Collected organic layers were dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed on silica gel column (ethyl acetate/methanol) to give 9-benzyl-6-[(dimethylcarbamoyl)methyl]-9*H*-purine (**8a**) in 55% yield. Yellow crystals were obtained after crystallization from CH_2Cl_2/heptane.

9-Benzyl-6-[(methylcarbamoyl)methyl]-9H-purine (**7a**). Prepared from ester **2a** (148 mg, 0.5 mmol) and 33% solution of methylamine in EtOH (582 µl, 5 mmol) and additional ethanol (1.5 ml). Yield 67%, yellowish crystals were obtained after crystallization from CH_2Cl_2/heptane, m.p. 119–122 °C. MS (FAB): 282 (100, M + 1), 251 (10), 91 (50). HRMS (FAB): for $C_{15}H_{16}N_5O$ calculated 282.1354, found 282.1365. ^{1}H NMR (400 MHz, $CDCl_3$): 2.84 (d, 3 H, J = 4.8, CH_3); 4.20 (s, 2 H, CH_2-6); 5.45 (s, 2 H, CH_2-9); 7.28–7.45 (m, 6 H, NH and Ph); 8.05 (s, 1 H, H-8); 8.95 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 26.41 (CH_3); 39.94 (CH_2-6); 47.43 (CH_2-9); 127.92 (CH-*o*-Ph); 128.72 (CH-*p*-Ph); 129.20 (CH-*m*-Ph); 132.67 (C-5); 134.84 (C-*i*-Ph); 144.42 (CH-8); 151.24 (C-4); 152.31 (CH-2); 155.73 (C-6); 168.01 (CO). IR (CCl_4): 2928, 2360, 1687, 1597, 1499, 1333. For $C_{15}H_{15}N_5O \cdot 3/5H_2O$ (292.0) calculated: C 61.67%, H 5.59%, N 23.97%; found: C 61.72%, H 5.30%, N 23.38%.

9-Benzyl-6-[(dimethylcarbamoyl)methyl]-9H-purine (**8a**). Yield 55%, yellow crystals, m.p. 115–121 °C. MS (FAB): 296 (100, M + 1), 251 (10), 91 (40). HRMS (FAB): for $C_{16}H_{18}N_5O$ calculated 296.1511, found 296.1515. ^{1}H NMR (500.0 MHz, $CDCl_3$): 3.00 and 3.15 (2 × s, 2 × 3 H, $(CH_3)_2N$); 4.32 (s, 2 H, CH_2-6); 5.44 (s, 2 H, CH_2-9); 7.32 (m, 2 H, H-*o*-Ph); 7.36 (m, 2 H, H-*m*-Ph); 7.37 (m, 1 H, H-*p*-Ph); 8.03 (s, 1 H, H-8); 8.96 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 35.58 and 37.72 ($(CH_3)_2N$); 38.47 (CH_2-6); 47.30 (CH_2-9); 127.92 (CH-*o*-Ph); 128.60 (CH-*p*-Ph); 129.12 (CH-*m*-Ph); 133.06 (C-5); 134.95 (C-*i*-Ph); 144.13 (CH-8); 151.08 (C-4); 152.60 (CH-2); 156.06 (C-6); 168.32 (CO). IR (CCl_4): 3035, 2932, 1662, 1591, 1499, 1395, 1333, 773.

9-Benzyl-6-[(piperidine-1-carbonyl)methyl]-9H-purine (**9a**). Prepared from ester **2a** (0.5 mmol) and piperidine (494 µl, 5 mmol) as yellowish crystals, yield 60%, m.p. 123–125 °C. MS (FAB): 693 (100, 2 M + Na), 358 (20, M + Na), 336 (20, M + H). HRMS (FAB): for $C_{19}H_{21}N_5NaO$ calculated 358.1638, found 358.1641. IR (CCl_4): 2941, 2858, 1648, 1592, 1443, 1333, 1214. For $C_{19}H_{21}N_5O \cdot 1/6H_2O$ (338.4) calculated: C 67.43%, H 6.35%, N 20.70%; found: C 67.63%, H 6.31%, N 20.70%.

9-Benzyl-6-[(cyclopropylcarbamoyl)methyl]-9H-purine (**10a**). Prepared from ester **2a** (290 mg, 1 mmol) and ethanol (1.5 ml), and cyclopropylamine (571 mg, 692 µl, 10 mmol). Yield 51%, white crystals were obtained after crystallization from CH_2Cl_2/heptane, m.p. 114–122 °C. MS (FAB): 308 (55, M + 1), 251 (20), 91 (100). HRMS (FAB): for $C_{17}H_{17}N_5O$ calculated 308.1511, found 308.1522. ^{1}H NMR (500.0 MHz, $CDCl_3$): 0.51 and 0.75 (2 × m, 2 × 2 H, CH_2-cyclopropyl); 2.73 (tt, 1 H, J = 7.2, 3.9, CH-cyclopropyl); 4.16 (s, 2 H, CH_2-6); 5.45 (s, 2 H, CH_2-9); 7.32 (m, 2 H, H-*o*-Ph); 7.36 (m, 2 H, H-*m*-Ph); 7.38 (m, 1 H, H-*p*-Ph); 7.64 (bs, 1 H, NH); 8.05 (s, 1 H, H-8); 8.94 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 6.44 (CH_2-cyclopropyl); 22.67 (CH-cyclopropyl); 39.95 (CH_2-6); 47.41 (CH_2-9); 127.89 (CH-*o*-Ph); 128.72 (CH-*p*-Ph); 129.19 (CH-*m*-Ph); 132.64 (C-5); 134.80 (C-*i*-Ph); 144.38 (CH-8); 151.20 (C-4); 152.22 (CH-2); 155.59 (C-6); 168.70 (CO). IR (CCl_4): 3328, 3034, 1690, 1596, 1499,

1333, 1196, 726. For $C_{17}H_{15}N_5O \cdot 1/4H_2O$ (311.8) calculated: C 65.47%, H 5.66%, N 22.46%; found: C 65.31%, H 5.60%, N 22.24%.

6-[(Methylcarbamoyl)methyl]-9-tetrahydropyran-2-yl-9H-purine (**7b**). Prepared from ester **2b** (0.5 mmol) and 33% solution of methylamine in EtOH (5 mmol) as white crystals, yield 95%, m.p. 119–121 °C. MS (FAB): 572 (100, 2 M + Na), 298 (35, M + Na), 276 (10, M + H). HRMS (FAB): for $C_{13}H_{17}N_5NaO_2$ calculated 298.1274, found 298.1278. ^{1}H NMR (400 MHz, $CDCl_3$): 1.62–1.86 and 1.99–2.18 (2 × m, 6 H, CH_2-THP); 2.79 (d, 3 H, J = 4.9, CH_3); 3.77 (dt, 1 H, J = 11.7, 2.6, bCH_2O-THP); 4.12–4.21 (m, 1 H, CH_2O-THP); 4.16 and 4.17 (2 × s, 2 H, CH_2-6); 5.76 (dd, 1 H, J = 10.1 and 2.6, CHO-THP); 7.38 (bs, 1 H, NH); 8.27 (s, 1 H, H-8); 8.89 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.66, 24.76 and 31.72 (CH_2-THP); 26.37 (CH_3); 40.05 (CH_2-6); 68.81 (CH_2O-THP); 82.05 (CHO-THP); 132.81 (C-5); 142.41 (CH-8); 150.36 (C-4); 152.10 (CH-2); 155.67 (C-6); 167.97 (CO). IR (CCl_4): 3358, 2948, 2857, 1686, 1598, 1334, 1211, 1088.

6-[(Dimethylcarbamoyl)methyl]-9-tetrahydropyran-2-yl-9H-purine (**8b**). Prepared from ester **2b** (0.5 mmol) and 5.6 M solution of dimethylamine in EtOH (893 µl, 5 mmol) as yellowish crystals, yield 49%, m.p. 142–144 °C. MS (FAB): 600 (100, 2 M + Na), 312 (40, M + Na), 289 (10, M + H). HRMS (FAB): for $C_{14}H_{19}N_5NaO_2$ calculated 312.1431, found 312.1435. ^{1}H NMR (400 MHz, $CDCl_3$): 1.60–1.88 and 1.98–2.18 (2 × m, 6 H, CH_2-THP); 2.99 and 3.12 (2 × s, 2 × 3 H, 2 × CH_3); 3.78 (dt, 1 H, J = 11.6, 2.5, bCH_2O-THP); 4.13-4.21 (m, 1 H, CH_2O-THP); 4.28 and 4.31 (2 × d, 2 H, J_{gem} = 15.4, CH_2-6); 5.77 (dd, 1 H, J = 9.9, 2.6, CHO-THP); 8.25 (s, 1 H, H-8); 8.91 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.73, 24.83 and 31.83 (CH_2-THP); 35.59 and 37.72 (2 × CH_3); 38.56 (CH_2-6); 68.82 (CH_2O-THP); 82.01 (CHO-THP); 133.21 (C-5); 142.14 (CH-8); 150.27 (C-4); 152.42 (CH-2); 156.07 (C-6); 168.32 (CO). IR (CCl_4): 2947, 2857, 1664, 1593, 1495, 1395, 1335, 1211, 1088. For $C_{14}H_{19}N_5O_2 \cdot 1/5H_2O$ (292.9) calculated: C 57.40%, H 6.68%, N 23.91%; found: C 57.49%, H 6.55%, N 23.49%.

6-[(Piperidine-1-carbonyl)methyl]-9-tetrahydropyran-2-yl-9H-purine (**9b**). Prepared from ester **2b** (0.5 mmol) and piperidine (494 µl, 5 mmol) as yellowish crystals, yield 41%, m.p. 151–155 °C. MS (FAB): 681 (100, 2 M + Na), 352 (55, M + Na), 330 (20, M + H). HRMS (FAB): for $C_{17}H_{23}N_5NaO_2$ calculated 352.1744, found 352.1748. ^{1}H NMR (600 MHz, $CDCl_3$): 1.55 (m, 4 H, H-3,5-pip); 1.63 (m, 2 H, H-4-pip); 1.66–1.70, 1.73–1.85 and 2.00–2.20 (3 × m, 6 H, CH_2-THP); 3.50 and 3.53 (2 × ddd, 2 × 1 H, J_{gem} = 13.2, J_{vic} = 11.1, 4.9, H-2,6-pip); 3.58 and 3.61 (2 × dt, 2 × 1 H, J_{gem} = 13.2, J_{vic} = 5.4, H-2,6-pip); 3.80 (dt, 1 H, J = 11.8, 2.6, bCH_2O-THP); 4.19 (ddt, 1 H, J = 11.8, 4.3, 1.9, aCH_2O-THP); 4.28 and 4.35 (2 × d, 2 H, J_{gem} = 15.2, CH_2CO); 5.80 (dd, 1 H, J = 10.4, 2.5, CHO-THP); 8.27 (s, 1 H, H-8); 8.92 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.73(CH_2-THP); 24.43 (CH_2-4-pip); 24.83 (CH_2-THP); 25.38 and 26.26 (CH_2-3,5-pip); 31.83 (CH_2-THP); 38.59 (CH_2CO); 42.94 and 47.15 (CH_2-2,6-pip); 68.85 (CH_2O-THP); 81.98 (CHO-THP); 133.15 (C-5); 142.12 (CH-8); 150.26 (C-4); 152.43 (CH-2); 156.31 (C-6); 166.47 (CO). IR (CCl_4): 2943, 2858, 1657, 1593, 1442, 1334, 1211, 1088. For $C_{17}H_{23}N_5O_2 \cdot 1/5H_2O$ (333.0) calculated: C 61.32%, H 7.08%, N 21.03%; found: C 61.34%, H 6.94%, N 20.96%.

6-[(Cyclopropylcarbamoyl)methyl]-9-tetrahydropyran-2-yl-9H-purine (**10b**). Prepared from ester **2b** (0.5 mmol) and cyclopropylamine (346 µl, 5 mmol) as a white foam, yield 66%. MS (FAB): 624 (100, 2 M + Na), 324 (45, M + Na), 302 (10, M + H). HRMS (FAB): for $C_{15}H_{19}N_5NaO_2$ calculated 324.1431, found 324.1434. ^{1}H NMR (400 MHz, $CDCl_3$): 0.46–0.51 and 0.70–0.76 (2 × m, 2 × 2 H, 2 × CH_2); 1.61–1.87 and 2.01–2.19 (2 × m, 6 H, CH_2-THP); 2.71 (m, 1 H, CH-N); 3.79 (dt, 1 H, J = 11.6, 2.7, bCH_2O-THP); 4.16 (ddt, 1 H, J = 11.6, 3.7, 2.2, aCH_2O-THP); 4.14 (s, 2 H, CH_2CO); 5.80 (dd, 1 H, J = 10.1, 2.5, CHO-THP); 7.5 (bs, 1 H,

NH); 8.27 (s, 1 H, H-8); 8.89 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 6.42 (CH_2CH); 22.69 (CH_2-THP); 22.70 (CHNH); 24.80 (CH_2-THP); 31.76 (CH_2-THP); 40.18 (CH_2CO); 68.86 (CH_2O-THP); 82.08 (CHO-THP); 132.83 (C-5); 142.38 (CH-8); 150.40 (C-4); 152.09 (CH-2); 155.60 (C-6); 168.66 (CO). IR (CCl_4): 3331, 2949, 2857, 1689, 1597, 1497, 1334, 1210, 1088.

*6-[(Methylcarbamoyl)methyl]-9-[2,3,5-tri-O-(tert-butyldimethylsilyl)-*β*-*D*-ribofuranosyl]-9H-purine* (**7d**). Prepared from ester **2d** (1020 mg, 1.5 mmol) and 33% solution of methylamine in EtOH (1.75 ml, 15 mmol) and additional ethanol (5 ml). Yield 66%, white foam. MS (FAB): 666 (25, M + 1), 192 (20), 93 (50), 73 (100). HRMS (FAB): for $C_{31}H_{60}N_5O_5Si_3$ calculated 666.3902, found 666.3926. ^{1}H NMR (400 MHz, $CDCl_3$): –0.23, –0.03, 0.10, 0.11, 0.14 and 0.15 (6 × s, 6 × 3 H, CH_3Si); 0.79, 0.94 and 0.96 (3 × s, 3 × 9 H, $(CH_3)_3C$); 2.83 (d, 3 H, $J_{CH3,NH}$ = 4.8, CH_3N); 3.80 (dd, 1 H, J_{gem} = 11.5, $J_{5'b,4'}$ = 2.6, H-5′b); 4.03 (dd, 1 H, J_{gem} = 11.5, $J_{5'a,4'}$ = 3.8, H-5′a); 4.16 (td, 1 H, $J_{4',3'}$ = 3.9, $J_{4',5'}$ = 3.8, 2.6, H-4′); 4.20 (s, 2 H, CH_2-pur); 4.33 (t, 1 H, $J_{3',2'}$ = 4.3, $J_{3',4'}$ = 3.9, H-3′); 4.63 (t, 1 H, $J_{2',1'}$ = 4.9, $J_{2',3'}$ = 4.3, H-2′); 6.12 (d, 1 H, $J_{1',2'}$ = 4.9, H-1′); 7.45 (bs, 1 H, NH); 8.47 (s, 1 H, H-8); 8.90 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): –5.39, –5.37, –5.05, –4.72, –4.68 and –4.39 (CH_3Si); 17.83, 18.06 and 18.53 ($C(CH_3)_3$); 25.62, 25.82 and 26.08 ($(CH_3)_3C$); 26.38 (CH_3N); 40.09 (CH_2-pur); 62.37 (CH_2-5′); 71.75 (CH-3′); 76.06 (CH-2′); 85.50 (CH-4′); 88.36 (CH-1′); 132.27 (C-5); 143.54 (CH-8); 150.94 (C-4); 152.06 (CH-2); 155.66 (C-6); 168.05 (CO). IR (CCl_4): 3354, 2931, 2859, 1686, 1597, 1463, 1255, 1149, 839. For $C_{31}H_{59}N_5O_5Si_3$ (666.8) calculated: C 55.90%, H 8.93%, N 10.51%; found: C 55.69%, H 9.00%, N 10.22%.

*6-[(Dimethylcarbamoyl)methyl]-9-[2,3,5-tri-O-(tert-butyldimethylsilyl)-*β*-*D*-ribofuranosyl]-9H-purine* (**8d**). Prepared from ester **2d** (1020 mg, 1.5 mmol) and 5.6 M solution of dimethylamine in EtOH (3 ml, 16.8 mmol) and additional ethanol (3 ml). Yield 39%, white foam. MS (FAB): 680 (20, M + 1), 206 (25), 73 (100). HRMS (FAB): for $C_{32}H_{62}N_5O_5Si_3$ calculated 680.4058, found 680.4065. ^{1}H NMR (600 MHz, $CDCl_3$): –0.21, –0.03, 0.10, 0.11, 0.13 and 0.14 (6 × s, 6 × 3 H, CH_3Si); 0.80, 0.94 and 0.95 (3 × s, 3 × 9 H, $(CH_3)_3C$); 3.01 and 3.10 (2 × s, 2 × 3 H, $(CH_3)_2N$); 3.80 (dd, 1 H, J_{gem} = 11.4, $J_{5'b,4'}$ = 2.8, H-5′b); 4.04 (dd, 1 H, J_{gem} = 11.4, $J_{5'a,4'}$ = 3.9, H-5′a); 4.15 (td, 1 H, $J_{4',3'}$ = 4.2, $J_{4',5'}$ = 3.9, 2.8, H-4′); 4.31 and 4.34 (2 × d, 2 H, J_{gem} = 15.5, CH_2-pur); 4.34 (t, 1 H, $J_{3',2'}$ = $J_{3',4'}$ = 4.2, H-3′); 4.66 (t, 1 H, $J_{2',1'}$ = 4.8, $J_{2',3'}$ = 4.2, H-2′); 6.11 (d, 1 H, $J_{1',2'}$ = 4.8, H-1′); 8.42 (s, 1 H, H-8); 8.91 (s, 1 H, H-2). ^{13}C NMR (151 MHz, $CDCl_3$): –5.36, –5.01, –4.76, –4.73 and –4.38 (CH_3Si); 17.83, 18.06 and 18.54 ($C(CH_3)_3$); 25.64, 25.82 and 26.09 ($(CH_3)_3C$); 35.60 and 37.72 ($(CH_3)_2N$); 38.52 (CH_2-pur); 62.32 (CH_2-5′); 71.62 (CH-3′); 75.78 (CH-2′); 85.25 (CH-4′); 88.45 (CH-1′); 133.62 (C-5); 143.26 (CH-8); 150.79 (C-4); 152.37 (CH-2); 155.93 (C-6); 168.41 (CO). IR (CCl_4): 2956, 2930, 2859, 1664, 1593, 1472, 1392, 1333, 1295, 1148, 839. For $C_{32}H_{61}N_5O_5Si_3$ (679.4) calculated: C 56.51%, H 9.04%, N 10.30%; found: C 56.65%, H 9.04%, N 9.78%.

*6-[(Piperidine-1-carbonyl)methyl]-9-[2,3,5-tri-O-(tert-butyldimethylsilyl)-*β*-*D*-ribofuranosyl]-9H-purine* (**9d**). Prepared from ester **2d** (1.5 mmol) and piperidine (15 mmol) as a white foam, yield 49%. MS (FAB): 720 (75, M + H), 288 (100). HRMS (FAB): for $C_{35}H_{65}N_5NaO_5Si_3$ calculated 742.4185, found 742.4188. IR (CCl_4): 2931, 2859, 1655, 1592, 1472, 1256.

Mesylation and Nucleophilic Substitution of Purines **6a**, **6d**. General Procedure

To a stirred solution of purine **6a** (127 mg, 0.5 mmol), methanesulfonic anhydride (104 mg, 0.6 mmol) and DMAP (3 mg) in CH_2Cl_2 (4 ml) Et_3N (105 µl, 0.75 mmol) was added. After finishing the reaction (0.5 h), the reaction mixture was chromatographed on a silica gel column ($CHCl_3$) and the eluate was evaporated at room temperature. Crude product was

dilluted with MeOH (25 ml), 1 M MeONa in MeOH (0.75 ml, 0.75 mmol) was added, the mixture was stirred overnight and then concentrated. Purine **11a** was obtained after purification on silica gel column (hexanes/ethyl acetate), yield 76%.

9-Benzyl-6-(2-methoxyethyl)-9H-purine (**11a**). Yield 76%, oil. ^{1}H NMR spectra were in accord with the previously published data[27].

9-Benzyl-6-[2-(dimethylamino)ethyl]-9H-purine (**12a**). Prepared from 2 M $MeNH_2$ in THF (0.5 ml, 1 mmol) in MeCN (5 ml). Yield 88%, white crystals. ^{1}H NMR spectra were in accord with previously published data[27].

9-Benzyl-6-[2-(methylsulfanyl)ethyl]purine (**13a**). Prepared from MeSNa (35 mg, 0.5 mmol) in ethanol (15 ml), yield 60%, yellowish crystals. ^{1}H NMR spectra were in accord with previously published data[27].

6-(2-Methoxyethyl)-9-[2,3,5-tri-O-(tert-butyldimethylsilyl)-β-D-ribofuranosyl]-9H-purine (**11d**). Prepared from purine **6d** (320 mg, 0.5 mmol) and 1 M MeONa in MeOH (0.75 ml, 0.75 mmol) as a yellowish oil, yield 63%. MS (ESI): 675 (55, M + Na), 653 (100, M + H). HRMS (ESI): for $C_{31}H_{61}N_4O_5Si_3$ calculated 653.3944, found 653.3945. ^{1}H NMR (499.8 MHz, $CDCl_3$): –0.27, –0.05, 0.109, 0.113, 0.13 and 0.14 (6 × s, 6 × 3 H, CH_3Si); 0.78, 0.94 and 0.95 (3 × s, 3 × 9 H, $(CH_3)_3C$); 3.35 (s, 3 H, CH_3O); 3.49 (t, 2 H, J_{vic} = 6.6, CH_2-pur); 3.80 (dd, 1 H, J_{gem} = 11.4, $J_{5'b,4'}$ = 2.9, H-5′b); 3.97 (t, 2 H, J_{vic} = 6.6, CH_2O); 4.03 (dd, 1 H, J_{gem} = 11.4, $J_{5'a,4'}$ = 4.0, H-5′a); 4.15 (ddd, 3 H, $J_{4',5'}$ = 4.0, 2.9, $J_{4',3'}$ = 3.6, H-4′); 4.33 (dd, 1 H, $J_{3',2'}$ = 4.3, $J_{3',4'}$ = 3.6, H-3′); 4.70 (dd, 1 H, $J_{2',1'}$ = 5.3, $J_{2',3'}$ = 4.3, H-2′); 6.10 (d, 1 H, $J_{1',2'}$ = 5.3, H-1′); 8.37 (s, 1 H, H-8); 8.88 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): –5.38, –5.37, –5.14, –4.71, –4.69 and –4.41 (CH_3Si); 17.82, 18.08 and 18.53 ($C(CH_3)_3$); 25.62, 25.83 and 26.08 ($(CH_3)_3C$); 33.52 (CH_2-pur); 58.66 (CH_3O); 62.51 (CH_2-5′); 70.51 (CH_2O); 71.95 (CH-3′); 75.78 (CH-2′); 85.57 (CH-4′); 88.23 (CH-1′); 133.69 (C-5); 142.90 (CH-8); 150.59 (C-4); 152.30 (CH-2); 159.82 (C-6). IR (CCl_4): 2956, 2931, 2859, 1597, 1472, 1333, 1257, 1113.

Deprotection of THP-Protected Purines **2b**, **6b**, **7b**, **8b**, **9b**, **10b**. General Procedure

To a stirred solution of purine **2b** (290 mg, 1 mmol) in 96% EtOH (20 ml) was added a catalytic amount of Dowex 50 (H^+ form). The reaction was stirred at 70 °C for 3 h, filtered, the resin was washed with ethanolic ammonia and the filtrate was evaporated to dryness. Crude product was chromatographed (chloroform/methanol) to give a white solid. Purine base **2g** was obtained by crystallization from methanol/propan-2-ol/heptane as white crystals, yield 192 mg (93%).

6-[2-(Ethoxycarbonyl)methyl]-9H-purine (**2g**). White crystals, m.p. 133–135 °C (lit.[30] 135 °C). MS (FAB): 207 (45, M + 1), 73 (100). HRMS (FAB): for $C_9H_{11}N_4O_2$ calculated 207.0882, found 207.0880. ^{1}H NMR (500 MHz, DMSO-d_6): 1.17 (t, 3 H, J_{vic} = 7.1, CH_3CH_2); 4.11 (q, 2 H, J_{vic} = 7.1, CH_2CH_3); 4.16 (s, 2 H, CH_2-pur); 8.58 (bs, 1 H, H-8); 8.82 (s, 1 H, H-2); 13.46 (bs, 1 H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6 + DCl): 14.56 (CH_3CH_2); 39.20 (CH_2-pur); 62.24 (CH_2CH_3); 127.55 (C-5); 148.59 (C-6); 149.43 (CH-2); 149.58 (CH-8); 154.98 (C-4); 167.83 (CO). IR (KBr): 2985, 2708, 1723, 1613, 1403, 1325, 1197. For $C_9H_{10}N_4O_2 \cdot 1/6H_2O$ (209.2) calculated: C 51.67%, H 4.98%, N 26.78%; found: C 51.99%, H 4.71%, N 26.65%.

6-(2-Hydroxyethyl)-9H-purine (**6g**). Yield 75%, white crystals, m.p. 170–172 °C. MS (FAB): 165 (75, M + 1), 102 (100). HRMS (FAB): for $C_7H_9N_4O$ calculated 165.0776, found 165.0771. ^{1}H NMR (600 MHz, DMSO-d_6 + DCl): 3.45 (t, 2 H, J_{vic} = 6.1, CH_2-pur); 3.92 (t, 2 H, J_{vic} = 6.1, CH_2O); 9.10 (s, 1 H, H-8); 9.22 (s, 1 H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6 + DCl): 34.28

(CH_2-pur); 59.64 (CH_2O); 129.23 (C-5); 146.74 (CH-2); 150.87 (CH-8); 153.69 (C-6); 156.33 (C-4). IR (KBr): 3392, 3262, 2824, 1619, 1569, 1379, 1239, 1042.

6-[(Methylcarbamoyl)methyl]-9H-purine (**7g**). Yield 64%, white solid, m.p. 228–231 °C. MS (ESI): 214 (100, M + Na), 192 (20, M + H). HRMS (ESI): for $C_8H_{10}N_5O$ calculated 192.0880, found 192.0878. ^{1}H NMR (600.1 MHz, DMSO-d_6): 2.60 (d, 3 H, J = 4.7, CH_3N); 3.94 (s, 2 H, CH_2-pur); 8.10 (bq, 1 H, J = 4.7, NH); 8.55 (s, 1 H, H-8); 8.79 (s, 1 H, H-2). ^{13}C NMR (150.9 MHz, DMSO-d_6): 26.00 (CH_3N); 40.61 (CH_2-pur); 129.70 (C-5); 145.56 (CH-8); 151.85 (CH-2); 153.42 (C-6); 155.00 (C-4); 168.36 (CO). IR (KBr): 3244, 3073, 2828, 1643, 1622, 1563, 1379, 1333. For $C_8H_9N_5O{\cdot}3/5H_2O$ (202.0) calculated: C 47.57%, H 5.09%, N 34.67%; found: C 47.87%, H 4.60%, N 34.33%.

6-[(Dimethylcarbamoyl)methyl]-9H-purine (**8g**). Yield 58%, white solid. MS (ESI): 432 (100, 2 M + Na), 228 (75, M + Na), 206 (60, M + H). HRMS (ESI): for $C_9H_{12}N_5O$ calculated 206.1036, found 206.1036. ^{1}H NMR (500.0 MHz, DMSO-d_6): 2.85 and 3.10 (2 × s, 2 × 3 H, CH_3N); 4.17 (s, 2 H, CH_2-pur); 8.55 (s, 1 H, H-8); 8.79 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 35.22 and 37.54 (CH_3N); 39.20 (CH_2-pur); 129.50 (C-5); 145.44 (CH-8); 151.85 (CH-2); 153.71 (C-6); 154.92 (C-4); 168.36 (CO). IR (KBr): 3405, 3112, 2968, 1648, 1601, 1395, 1325.

6-[(Piperidine-1-carbonyl)methyl]-9H-purine (**9g**). Yield 75%, white solid. MS (ESI): 513 (100, 2 M + Na), 268 (65, M + Na), 246 (15, M + H). HRMS (ESI): for $C_{12}H_{16}N_5O$ calculated 246.1349, found 246.1349. ^{1}H NMR (500.0 MHz, DMSO-d_6): 1.43, 1.47 and 1.58 (3 × m, 3 × 2 H, CH_2-pip); 3.42 and 3.51 (CH_2N-pip); 4.17 (s, 2 H, CH_2-pur); 8.55 (s, 1 H, H-8); 8.79 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 24.22, 25.51 and 26.18 (CH_2-pip); 38.58 (CH_2-pur); 42.42 and 46.76 (CH_2N-pip); 129.68 (C-5); 145.49 (CH-8); 151.84 (CH-2); 153.80 (C-6); 154.70 (C-4); 166.52 (CO). IR (KBr): 3422, 2936, 1641, 1597, 1442, 1324, 1225.

6-[(Cyclopropylcarbamoyl)methyl]-9H-purine (**10g**). Yield 67%, white solid. MS (ESI): 240 (100, M + Na), 218 (30, M + H). HRMS (ESI): for $C_{10}H_{12}N_5O$ calculated 218.1036, found 218.1029. ^{1}H NMR (500.0 MHz, DMSO-d_6): 0.43 and 0.62 (2 × m, 2 × 2 H, CH_2-cycloprop); 2.63 (tq, 1 H, J = 7.2, 4.2, CH-cycloprop); 3.89 (s, 2 H, CH_2-pur); 8.32 (bd, 1 H, J = 4.2, NH); 8.55 (s, 1 H, H-8); 8.79 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 5.93 (CH_2-cycloprop); 22.77 (CH-cycloprop); 40.57 (CH_2-pur); 129.63 (C-5); 145.62 (CH-8); 151.86 (CH-2); 153.48 (C-6); 154.88 (C-4); 169.11 (CO). IR (KBr): 3303, 3108, 2813, 1642, 1604, 1544, 1331, 1237. For $C_{10}H_{11}N_5O$ (217.2) calculated: C 55.29%, H 5.10%, N 32.24%; found: C 55.09%, H 5.14%, N 31.74%.

Deprotection of Purine Nucleosides **2d**, **2f**, **6d**, **6f** and **7d**, **8d**, **9d**. General Procedure

$Et_3N{\cdot}3HF$ (407 µl, 2.5 mmol) was added to the solution of **2d** (340 mg, 0.5 mmol) in THF (1.5 ml) and the reaction mixture was vigorously stirred at room temperature overnight. Solvents were evaporated in vacuo and the residue was chromatographed on silica gel column (ethyl acetate/methanol). Product was lyophilized to give 163 mg (96%) of **2h** as a white solid.

6-[(2-Ethoxycarbonyl)methyl]-9-(β-D-ribofuranosyl)-9H-purine (**2h**). MS (FAB): 339.1 (70, M + 1), 207 (95), 93 (100). HRMS (FAB): for $C_{14}H_{19}N_4O_6$ calculated 339.1305, found 339.1302. ^{1}H NMR (400 MHz, DMSO-d_6): 1.18 (t, 3 H, J = 7.1, CH_3CH_2); 3.37 (ddd, 1 H, J_{gem} = 12.0, $J_{5'b,OH}$ = 6.0, $J_{5'b,4'}$ = 4.1, H-5′b); 3.69 (ddd, 1 H, J_{gem} = 12.0, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.2, H-5′a); 3.98 (q, 1 H, $J_{4',5'}$ = 4.2, 4.1, $J_{4',3'}$ = 3.4, H-4′); 4.11 (q, 2 H, J = 7.1, CH_2CH_3); 4.18 (s, 2 H, CH_2-pur); 4.19 (td, 1 H, $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.4, H-3′); 4.66 (q, 1 H, $J_{2',OH}$ = 6.0, $J_{2',1'}$ = 5.8, $J_{2',3'}$ = 4.9, H-2′); 5.11 (t, 1 H, $J_{OH,5'}$ = 6.0, 5.2, OH-5′); 5.26 (d, 1 H, $J_{OH,3'}$ = 5.0,

OH-3′); 5.57 (d, 1 H, $J_{OH,2'}$ = 6.0, OH-2′); 6.04 (d, 1 H, $J_{1',2'}$ = 5.8, H-1′); 8.82 (s, 1 H, H-8); 8.88 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 14.13 (CH_3CH_2); 38.82 (CH_2-pur); 60.91 (CH_2CH_3); 61.48 (CH_2-5′); 70.55 (CH-3′); 73.80 (CH-2′); 85.97 (CH-4′); 87.83 (CH-1′); 133.16 (C-5); 145.06 (CH-8); 150.93 (C-4); 151.99 (CH-2); 154.47 (C-6); 169.12 (CO). IR ($CHCl_3$): 3326, 2988, 2933, 1734, 1603, 1500, 1336, 1248, 1189, 1084. $[\alpha]_D^{20}$ –40.8 (*c* 2.62, H_2O). For $C_{14}H_{18}N_4O_6 \cdot 1/2H_2O$ (347.3) calculated: C 48.41%, H 5.51%, N 16.13%; found: C 48.39%, H 5.48%, N 15.83%.

*9-(2-Deoxy-*β*-D-erythro-pentofuranosyl)-6-[(2-ethoxycarbonyl)methyl]-9H-purine* (**2i**). Prepared from purine **2f** (550 mg, 1 mmol) and $Et_3N \cdot 3HF$ (570 μl, 3.5 mmol) in THF (3 ml). Product was lyophilized to give 226 mg (69%) of **2i** as a yellow oil. MS (FAB): 667 (100), 345 (80, M + Na), 323 (M + H). HRMS (FAB): for $C_{14}H_{18}N_4NaO_5$ calculated 345.1175, found 345.1166. ^{1}H NMR (400 MHz, DMSO-d_6): 1.17 (t, 3 H, *J* = 7.1, CH_3CH_2); 2.36 (ddd, 1 H, J_{gem} = 13.3, $J_{2'b,1'}$ = 6.3, $J_{2'b,3'}$ = 3.5, H-2′b); 2.81 (ddd, 1 H, J_{gem} = 13.3, $J_{2'a,1'}$ = 7.3, $J_{2'a,3'}$ = 5.9, H-2′a); 3.53 (ddd, 1 H, J_{gem} = 11.7, $J_{5'b,OH}$ = 5.6, $J_{5'b,4'}$ = 4.6, H-5′b); 3.62 (dt, 1 H, J_{gem} = 11.7, $J_{5'a,OH}$ = 5.6, $J_{5'a,4'}$ = 4.7, H-5′a); 3.89 (td, 1 H, $J_{4',5'}$ = 4.7, 4.6, $J_{4',3'}$ = 3.0, H-4′); 4.11 (q, 2 H, *J* = 7.1, CH_2CH_3); 4.17 (s, 2 H, CH_2-pur); 4.45 (dq, 1 H, $J_{3',2'}$ = 5.9, 3.5, $J_{3',OH}$ = 4.2, $J_{3',4'}$ = 3.0, H-3′); 4.99 (t, 1 H, $J_{OH,5'}$ = 5.6, OH-5′); 5.37 (d, 1 H, $J_{OH,3'}$ = 4.2, OH-3′); 6.47 (t, 1 H, $J_{1',2'}$ = 7.3, 6.3, H-1′); 8.77 (s, 1 H, H-8); 8.87 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 14.22 (CH_3CH_2); 38.80 (CH_2-pur); 39.36 (CH_2-2′); 60.89 (CH_2CH_3); 61.75 (CH_2-5′); 70.84 (CH-3′); 84.00 (CH-1′); 88.21 (CH-4′); 133.16 (C-5); 144.98 (CH-8); 150.63 (C-4); 151.90 (CH-2); 154.34 (C-6); 169.13 (CO). IR (KBr): 3326, 3007, 1735, 1602, 1336, 1204, 1104. For $C_{14}H_{18}N_4O_5 \cdot 1/3H_2O$ (328.3) calculated: C 51.21%, H 5.73%, N 17.06%; found: C 51.29%, H 5.57%, N 16.67%.

*6-(2-Hydroxyethyl)-9-(*β*-D-ribofuranosyl)-9H-purine* (**6h**). Prepared from purine **6d** (320 mg, 0.5 mmol) and $Et_3N \cdot 3HF$ (407 μl, 2.5 mmol) in THF (1.5 ml). Product was lyophilized to give 136 mg (92%) of **6h** as a white solid. MS (FAB): 297 (20, M + 1), 241 (45), 185 (40), 93 (100). HRMS (FAB): for $C_{12}H_{17}N_4O_5$ calculated 297.1198, found 297.1206. ^{1}H NMR (400 MHz, DMSO-d_6): 3.25 (t, 2 H, J_{vic} = 6.8, CH_2-pur); 3.57 (ddd, 1 H, J_{gem} = 12.0, $J_{5'b,OH}$ = 6.1, $J_{5'b,4'}$ = 4.1, H-5′b); 3.68 (ddd, 1 H, J_{gem} = 12.0, $J_{5'a,OH}$ = 4.9, $J_{5'a,4'}$ = 4.3, H-5′a); 3.92 (td, 2 H, J_{vic} = 6.8, J_{OH} = 5.6, CH_2-O); 3.98 (q, 1 H, $J_{4',5'}$ = 3.9, 3.9, $J_{4',3'}$ = 3.7, H-4′); 4.18 (td, 1 H, $J_{3',OH}$ = 4.9, $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.7, H-3′); 4.64 (q, 1 H, $J_{2',OH}$ = 6.1, $J_{2',1'}$ = 5.8, $J_{2',3'}$ = 4.9, H-2′); 4.78 (t, 1 H, *J* = 5.6, OH); 5.14 (t, 1 H, $J_{OH,5'}$ = 5.9, 5.3, OH-5′); 5.26 (d, 1 H, $J_{OH,3'}$ = 4.9, OH-3′); 5.54 (d, 1 H, $J_{OH,2'}$ = 6.1, OH-2′); 6.02 (d, 1 H, $J_{1',2'}$ = 5.8, H-1′); 8.76 (s, 1 H, H-8); 8.83 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 36.46 (CH_2-pur); 59.38 (CH_2OH); 61.30 (CH_2-5′); 70.35 (CH-3′); 73.56 (CH-2′); 85.69 (CH-4′); 87.55 (CH-1′); 133.08 (C-5); 144.08 (CH-8); 150.21 (C-4); 151.67 (CH-2); 159.72 (C-6). IR (KBr): 3413, 2926, 1603, 1407, 1335, 1212, 1052. $[\alpha]_D^{20}$ –44.4 (*c* 3.19, H_2O). For $C_{12}H_{16}N_4O_5 \cdot 3/4H_2O$ (309.8) calculated: C 46.52%, H 5.69%, N 18.09%; found: C 46.63%, H 5.73%, N 17.63%.

*9-(2-Deoxy-*β*-D-erythro-pentofuranosyl)-6-(2-hydroxyethyl)-9H-purine* (**6i**). Prepared from purine **6f** (360 mg, 0.7 mmol) and $Et_3N \cdot 3HF$ (400 μl, 2.5 mmol) in THF (3 ml). Product was lyophilized to give 135 mg (69%) of **6i** as a white foam. MS (FAB): 281 (15, M + 1), 154 (100), 136 (85). HRMS (FAB): for $C_{12}H_{17}N_4O_4$ calculated 281.1249, found 281.1245. ^{1}H NMR (400 MHz, DMSO-d_6): 2.34 (ddd, 1 H, J_{gem} = 13.3, $J_{2'b,1'}$ = 6.3, $J_{2'b,3'}$ = 3.4, H-2′b); 2.79 (ddd, 1 H, J_{gem} = 13.3, $J_{2'a,1'}$ = 7.4, $J_{2'a,3'}$ = 5.9, H-2′a); 3.24 (t, 2 H, J_{vic} = 6.8, CH_2-pur); 3.52 (ddd, 1 H, J_{gem} = 11.7, $J_{5'b,OH}$ = 5.7, $J_{5'b,4'}$ = 4.7, H-5′b); 3.62 (ddd, 1 H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.4, $J_{5'a,4'}$ = 4.7, H-5′a); 3.89 (td, 1 H, $J_{4',5'}$ = 4.7, 4.6, $J_{4',3'}$ = 2.7, H-4′); 3.92 (bt, 2 H, J_{vic} = 6.8, J_{OH} = 5.6, CH_2-O); 4.44 (m, 1 H, $J_{3',2'}$ = 5.9, 3.4, $J_{3',OH}$ = 4.2, $J_{3',4'}$ = 2.7, H-3′); 4.76 (bt, 1 H,

J = 5.6, OH); 5.00 (t, 1 H, $J_{OH,5'}$ = 5.6, OH-5′); 5.36 (d, 1 H, $J_{OH,3'}$ = 4.2, OH-3′); 6.46 (t, 1 H, $J_{1',2'}$ = 7.4, 6.3, H-1′); 8.72 (s, 1 H, H-8); 8.82 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 36.41 (CH_2-pur); 39.09 (CH_2-2′); 59.32 (CH_2OH); 61.52 (CH_2-5′); 70.61 (CH-3′); 83.61 (CH-1′); 87.89 (CH-4′); 133.02 (C-5); 143.91 (CH-8); 149.87 (C-4); 151.53 (CH-2); 159.52 (C-6). IR (KBr): 3401, 2928, 1601, 1400, 1335, 1213, 1055. $[\alpha]_D^{20}$ –15.8 (*c* 2.72, H_2O). For $C_{12}H_{14}N_4O_4 \cdot 1/2H_2O$ (289.2) calculated: C 49.82%, H 5.92%, N 19.37%; found: C 50.12%, H 5.76%, N 19.14%.

*6-[(Methylcarbamoyl)methyl]-9-(*β-D-*ribofuranosyl)-9H-purine* (**7h**). Prepared from purine **7d** (500 mg, 0.75 mmol) and $Et_3N \cdot 3HF$ (612 µl, 3.75 mmol) in THF (2.5 ml). Product was lyophilized to give 213 mg (88%) of **7h** as a white solid. MS (FAB): 324 (10, M + 1), 192 (100), 161 (60), 135 (55). HRMS (FAB): for $C_{13}H_{18}N_5O_5$ calculated 324.1308, found 324.1316. ^{1}H NMR (499.8 MHz, DMSO-d_6): 2.60 (d, 3 H, J = 4.7, CH_3N); 3.57 (ddd, 1 H, J_{gem} = 12.0, $J_{5'b,OH}$ = 6.1, $J_{5'b,4'}$ = 4.1, H-5′b); 3.69 (ddd, 1 H, J_{gem} = 12.0, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.1, H-5′a); 3.96 (s, 2 H, CH_2-pur); 3.98 (td, 1 H, $J_{4',5'}$ = 4.1, $J_{4',3'}$ = 3.6, H-4′); 4.19 (td, 1 H, $J_{3',OH}$ = $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.6, H-3′); 4.65 (ddd, 1 H, $J_{2',OH}$ = 6.1, $J_{2',1'}$ = 5.8, $J_{2',3'}$ = 4.9, H-2′); 5.13 (dd, 1 H, $J_{OH,5'}$ = 6.1, 5.2, OH-5′); 5.25 (d, 1 H, $J_{OH,3'}$ = 4.9, OH-3′); 5.56 (d, 1 H, $J_{OH,2'}$ = 6.1, OH-2′); 6.03 (d, 1 H, $J_{1',2'}$ = 5.8, H-1′); 8.08 (bq, 1 H, J = 4.7, NH); 8.78 (s, 1 H, H-8); 8.84 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 25.99 (CH_3N); 38.87 (CH_2-pur); 61.53 (CH_2-5′); 70.60 (CH-3′); 73.82 (CH-2′); 85.96 (CH-4′); 87.86 (CH-1′); 133.47 (C-5); 144.75 (CH-8); 150.79 (C-4); 151.91 (CH-2); 156.36 (C-6); 168.23 (CO). IR (CCl_4): 3317, 2928, 1657, 1602, 1409, 1336, 1210, 1154. $[\alpha]_D^{20}$ –35.2 (*c* 3.29, H_2O).

*6-[(Dimethylcarbamoyl)methyl]-9-(*β-D-*ribofuranosyl)-9H-purine* (**8h**). Prepared from purine **8d** (340 mg, 0.5 mmol) and $Et_3N \cdot 3HF$ (408 µl, 2.5 mmol) in THF (3 ml). Product was lyophilized to give 153 mg (91%) of **8h** as white solid. MS (FAB): 338 (30, M + 1), 241 (85), 157 (50), 93 (100). HRMS (FAB): for $C_{14}H_{20}N_5O_5$ calculated 338.1464, found 338.1474. ^{1}H NMR (499.8 MHz, DMSO-d_6): 2.85 and 3.11 (2 × s, 2 × 3 H, CH_3N); 3.57 (ddd, 1 H, J_{gem} = 12.1, $J_{5'b,OH}$ = 6.0, $J_{5'b,4'}$ = 4.1, H-5′b); 3.69 (ddd, 1 H, J_{gem} = 12.1, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.1, H-5′a); 3.98 (td, 1 H, $J_{4',5'}$ = 4.1, $J_{4',3'}$ = 3.6, H-4′); 4.19 (td, 1 H, $J_{3',OH}$ = $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.6, H-3′); 4.21 (s, 2 H, CH_2-pur); 4.66 (ddd, 1 H, $J_{2',OH}$ = 6.1, $J_{2',1'}$ = 5.8, $J_{2',3'}$ = 4.9, H-2′); 5.12 (dd, 1 H, $J_{OH,5'}$ = 6.0, 5.2, OH-5′); 5.25 (d, 1 H, $J_{OH,3'}$ = 4.9, OH-3′); 5.56 (d, 1 H, $J_{OH,2'}$ = 6.1, OH-2′); 6.03 (d, 1 H, $J_{1',2'}$ = 5.8, H-1′); 8.77 (s, 1 H, H-8); 8.84 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 35.17 and 37.52 (CH_3N); 38.06 (CH_2-pur); 61.55 (CH_2-5′); 70.61 (CH-3′); 73.77 (CH-2′); 85.98 (CH-4′); 87.84 (CH-1′); 133.43 (C-5); 144.67 (CH-8); 150.67 (C-4); 151.87 (CH-2); 156.69 (C-6); 168.23 (CO). IR (CCl_4): 3409, 2927, 1637, 1600, 1403, 1336, 1211, 1056. $[\alpha]_D^{20}$ –40.0 (*c* 3.86, H_2O).

*6-[(Piperidine-1-carbonyl)methyl]-9-(*β-D-*ribofuranosyl)-9H-purine* (**9h**). Prepared from purine **9d** (525 mg, 0.73 mmol) and $Et_3N \cdot 3HF$ (596 µl, 3.65 mmol) in THF (3 ml). Product was lyophilized to give 270 mg (98%) of **9h** as a white solid. MS (FAB): 400 (100, M + Na), 378 (20, M + H). HRMS (FAB): for $C_{17}H_{24}N_5O_5$ calculated 378.1772, found 378.1770. ^{1}H NMR (400 MHz, DMSO-d_6): 1.42 and 1.49 (2 × m, 2 × 2 H, H-3,5-pip); 1.57 (m, 2 H, H-4-pip); 3.43 and 4.52 (2 × t, 2 × 2 H, J = 5.4, H-2,6-pip); 3.58 (ddd, 1 H, J_{gem} = 12.0, $J_{5'b,OH}$ = 5.9, $J_{5'b,4'}$ = 4.2, H-5′b); 3.67 (ddd, 1 H, J_{gem} = 12.0, $J_{5'a,OH}$ = 5.2, $J_{5'a,4'}$ = 4.2, H-5′a); 3.98 (q, 1 H, $J_{4',5'}$ = 4.2, 4.1, $J_{4',3'}$ = 3.6, H-4′); 4.18 (td, 1 H, $J_{3',OH}$ = 4.9, $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.4, H-3′); 4.20 (s, 2 H, CH_2-pur); 4.66 (q, 1 H, $J_{2',OH}$ = 5.9, $J_{2',1'}$ = 5.8, $J_{2',3'}$ = 4.9, H-2′); 5.11 (t, 1 H, $J_{OH,5'}$ = 5.5, OH-5′); 5.23 (d, 1 H, $J_{OH,3'}$ = 4.9, OH-3′); 5.54 (d, 1 H, $J_{OH,2'}$ = 5.9, OH-2′); 6.02 (d, 1 H, $J_{1',2'}$ = 5.8, H-1′); 8.77 (s, 1 H, H-8); 8.84 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 23.87 (CH_2-4-pip); 25.15 and 25.85 (CH_2-3,5-pip); 37.69 (CH_2-pur); 42.05 and 46.42

(CH_2-2,6-pip); 61.23 (CH_2-5′); 70.28 (CH-3′); 73.46 (CH-2′); 85.65 (CH-4′); 87.51 (CH-1′); 133.05 (C-5); 144.33 (CH-8); 150.35 (C-4); 151.52 (CH-2); 156.41 (C-6); 166.07 (CO). IR (KBr): 3461, 3205, 2924, 2854, 1648, 1566, 1400, 1225. $[\alpha]_D^{20}$ –32.2 (*c* 0.20, H_2O).

Single Crystal X-ray Structure Analysis

The diffraction data of single crystals of **2a** (yellowish, 0.08 × 0.20 × 0.48 mm), **6a** (white, 0.14 × 0.23 × 0.34 mm) and **9a** (yellowish, 0.11 × 0.16 × 0.28 mm) were collected on Xcalibur X-ray diffractometer with CuKα (λ = 1.54180 Å) at 295 (**2a**), 150 (**6a**) and 298 K (**9a**). All structures were solved by direct methods with SIR92 [31] and refined by full-matrix, least-squares methods based on *F* with CRYSTALS [32]. The hydrogen atoms were 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 for **2a**: $C_{16}H_{16}N_4O_2$, triclinic, space group *P*-1, *a* = 8.4835(7) Å, *b* = 9.0266(7) Å, *c* = 11.4610(10) Å, α = 68.357(8)°, β = 68.845(8)°, γ = 83.135(7)°, *V* = 760.71(12) $Å^3$, *Z* = 2, *M* = 296.33, 10 494 reflections measured, 3 059 independent reflections. Final *R* = 0.0579, *wR* = 0.0767, GOF = 1.0550 for 2 491 reflections with $I > 1.96\sigma(I)$ and 200 parameters.

Crystal data for **6a**: $C_{14}H_{14}N_4O_1$, triclinic, space group *P*-1, *a* = 5.6172(7) Å, *b* = 9.9556(8) Å, *c* = 11.3924(9) Å, α = 104.037(7)°, β = 92.518(8)°, γ = 93.687(8)°, *V* = 615.62(11) $Å^3$, *Z* = 2, *M* = 254.29, 8 392 reflections measured, 2 454 independent reflections. Final *R* = 0.0362, *wR* = 0.0361, GOF = 1.2047 for 2 302 reflections with $I > 1.96\sigma(I)$ and 173 parameters.

Crystal data for **9a**: $C_{19}H_{21}N_5O_1$, triclinic, space group *P*-1, *a* = 11.5005(5) Å, *b* = 12.3904(6) Å, *c* = 13.0988(6) Å, α = 77.743(4)°, β = 75.914(4)°, γ = 89.505(4)°, *V* = 1767.31(15) $Å^3$, *Z* = 4, *M* = 335.41, 55 857 reflections measured, 7 451 independent reflections. Final *R* = 0.0389, *wR* = 0.0442, GOF = 1.1029 for 3 681 reflections with $I > 1.5\sigma(I)$ and 452 parameters.

CCDC 638672 (**2a**), 638673 (**6a**), 724480 (**9a**) contain 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).

This work is a part of the research project Z4 055 0506. It was supported by the Centre for New Antivirals and Antineoplastics (1M0508), by the Programme of Targeted Projects of Academy of Sciences of the Czech Republic (1QS400550501) and by Gilead Sciences, Inc. (Foster City (CA), USA).

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