SYNTHESIS OF 2-SUBSTITUTED 6-(HYDROXYMETHYL)PURINE BASES AND NUCLEOSIDES

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Dedicated to the jubilee 70th volume of Collection of Czechoslovak Chemical Communications and to the memory of its founders, Professors Jaroslav Heyrovský and Emil Votoček.

A facile and efficient methodology of the synthesis of 6-(hydroxymethyl)purine derivatives (bases and nucleosides) was developed based on Pd-catalyzed cross-coupling reactions of 6-halopurines or *N*-protected 2-amino-6-halopurines with (benzoyloxymethyl)zinc iodide followed by deprotection. Regioselective hydroxymethylations of 2,6-dihalopurines were also studied and used for the synthesis of 2-chloro-6-(hydroxymethyl)- or 2,6-bis(hydroxymethyl)purines. The 6-(hydroxymethyl)purine ribonucleoside **5f** exerted high cytostatic effect and moderate inhibition of adenosine deaminase, while all the other derivatives were much less effective or entirely inactive.

Keywords: Purines; Nucleosides; Cross-coupling reactions; Hydroxymethylation; Palladium; Functionalized organozinc reagents; Cytostatic activity; Adenosine deaminase.

Purine bases and nucleosides bearing *C*-substituents in the position 6 possess cytostatic[1], anti-HCV [2] or antimicrobial[3] activity. Cross-coupling reactions of 6-halopurines with diverse organometallics are a powerful tool[4] for the synthesis of these compounds but, in most cases, were only used for an introduction of simple unfunctionalized carbon substituents. On the other hand, purines bearing *C*-substituents at position 6 containing functional groups (OH, NH_2, COOH etc.) would provide new exploitable moieties for interactions with complementary nucleobases, enzymes, or receptors while still preserving higher stability towards enzymatic degradation due to the presence of C–C bond in position 6. However, due to very limited synthetic accessibility, such compounds are scarcely reported in the literature and very little is known about their biological activity. Therefore, an extension of the cross-coupling methodology to functionalized *C*-substituents is a

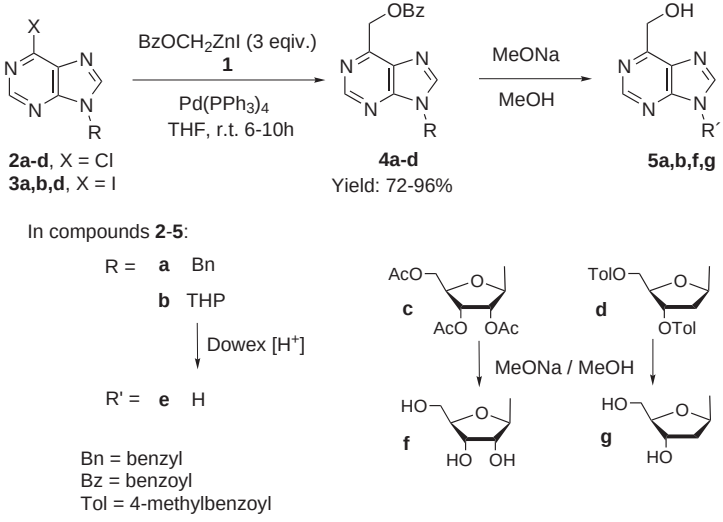
useful and challenging goal. Recently we have developed syntheses of (purin-6-yl)glycines[5] and -alanines[6] as examples of such derivatives. The hydroxymethyl group is one of the simplest and most useful functionalized substituents and its introduction to purine moiety is a subject of this paper.

6-(Hydroxymethyl)-9-(β-D-ribofuranosyl)purine was isolated from *Collybia maculata* and reported to possess antifungal, cytotoxic and antiviral (vesicular stomatitis virus) activity[7] and inhibition of adenosine deaminase[8]. Synthetic approaches to 6-(hydroxymethyl)purines published so far were based on the radical photoaddition of methanol to unsubstituted purine in aerobic conditions[8a,9] or recently reported reaction of 6-magnesiated purine with paraformaldehyde[10]. Unfortunately, the photoaddition in aerobic condition proceeds with low chemoselectivity and a very complex reaction profile[9b]; in argon atmosphere the main product is 1,6-dihydro-6-(hydroxymethyl)purine which can be oxidatively converted on the 6-(hydroxymethyl)purine[9b]. The yield of nucleophilic addition of 6-magnesiated purine to formaldehyde is rather low because of low reactivity of purinylmagnesium reagent[10]. On the other hand, 6-lithiated purine is much more reactive but it is stable only for few minutes at –130 °C [11]. Indirect routes from 6-methylpurine: oxidation to aldehyde followed by reduction[12] or rearrangement of its *N*-oxide with Ac_2O to 6-(acetoxymethyl)-purine[13] gave low yields.

Recently, we have published a preliminary communication[14] on a novel facile and efficient synthesis of 6-(hydroxymethyl)purines by the Negishi cross-coupling reactions of (acyloxymethyl)zinc iodides with 9-substituted 6-halopurines followed by deprotection. Later on, we have also successfully converted[15] these hydroxymethyl derivatives to 6-(fluoromethyl)purines. Here we present a full account of the methodology of hydroxymethylation of 6-halopurines, now also extended to 2-aminopurines and to regioselective hydroxymethylations of 2,6-dihalopurines.

RESULTS AND DISCUSSION

In the preliminary communication on the hydroxymethylation methodology, three (acyloxymethyl)zinc iodides (acetyl, benzoyl and pivaloyl esters)[16] were used in the Pd-catalyzed cross-coupling reactions with halopurines. The best results were obtained with (benzoyloxymethyl)zinc iodide (**1**). Its cross-coupling reactions gave very good yields (72–96%) and the benzoyl group was easily and efficiently cleaved under mild conditions. Therefore, this reagent was used in preparative scale in all further experiments. The stock solution of (benzoyloxymethyl)zinc iodide (**1**) in THF was



SCHEME 1

Cross-couplings of (benzoyloxymethyl)zinc iodide with 6-halopurines

TABLE I

Cross-coupling reactions of **1** with halopurines **2** or **3**

Entry	Starting compound	Time, h	Product (Yield, %)
1	**2a**	8	**4a** (81)
2	**3a**	6	**4a** (96)
3	**2b**	10	**4b** (72)
4	**3b**	6	**4b** (95)
5	**2c**	8	**4c** (94)
6	**2d**	8	**4d** (91)
7	**3d**	6	**4d** (93)

TABLE II

Cleavage of protecting groups in preparations of 6-(hydroxymethyl)purine bases and nucleosides **5**

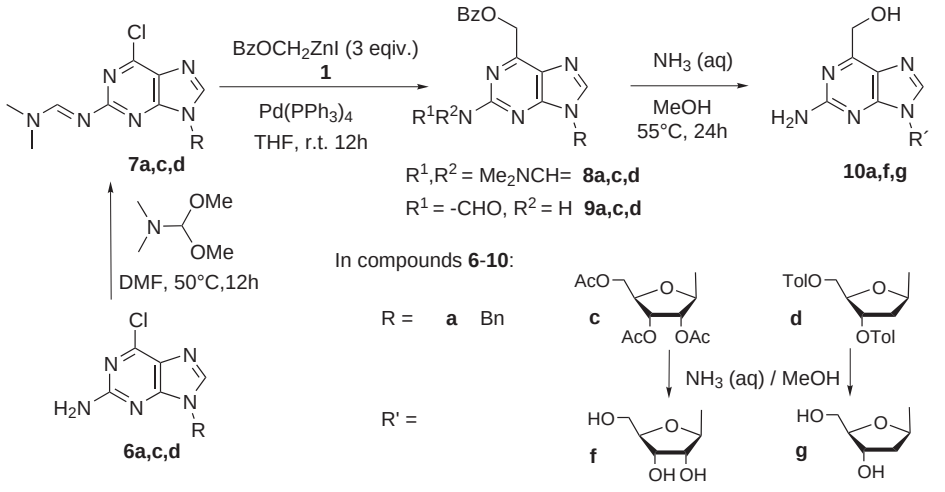
Entry	Starting compound	Reagent	Product (Yield, %)
1	**4a**	MeONa	**5a** (88)
2	**4b**	MeONa	**5b** (85)
3	**4c**	MeONa	**5f** (81)
4	**4d**	MeONa	**5g** (86)
5	**5b**	Dowex (H^+)	**5e** (78)

prepared[14] by reaction of activated zinc with the iodomethyl benzoate[17] at 5–10 °C under argon. It was stored in a freezer for several weeks without decomposition. The cross-coupling reactions of **1** with a series of protected 6-halopurine bases and nucleosides **2** or **3** (Scheme 1, Table I) gave 6-(benzoyloxymethyl)purines **4**, generally in very good yields. The effect of leaving group was not crucial: 6-iodopurines **3** usually gave just slightly better yields than 6-chloropurines **2**.

The ester groups of intermediates **4** were efficiently cleaved with NaOMe in methanol at room temperature to give the corresponding free 6-(hydroxymethyl)purine bases and nucleosides **5** in good yields (Table II). The THP protective group in position 9 of purine **5b** was cleaved using Dowex 50X8 (H^+ form) in ethanol[18] to give the corresponding 9*H*-purine **5e**.

Having an optimized methodology in hands, our further efforts focused on preparation of 2-amino-6-(hydroxymethyl)purines as homologs of guanine base and nucleosides. Analogous cross-coupling reactions of organozinc reagent **1** with unprotected 2-amino-6-halo-9-protected purines proceeded with very low yields (9–20%) even when using large excess of the organozinc. Therefore a suitable protecting group for the 2-amino group had to be found. (Dimethylamino)methylidene is often used to protect both acidic hydrogens of a nucleobase amino groups[19] and therefore it was also our group of choice. It was introduced by the reactions of 2-amino-6-chloropurines **6** with DMF/dimethylacetal (3 equivalents) in DMF at 50 °C and the intermediates **7** were used without purification in the next step after evaporation and drying. Their cross-coupling reactions with **1** proceeded smoothly at room temperature to give good conversions to the corresponding 6-(benzoyloxymethyl)purines **8** (Scheme 2, Table III). However, during work-up and column chromatography on silica gel, the (dimethylamino)methylidene group was partly hydrolyzed to form formyl derivatives **9** as by-products. Therefore, the inseparable mixtures of intermediates **8** and **9** were directly used in the deprotection step using aqueous ammonia in methanol at 55 °C to simultaneously cleave all the *O*-acyl groups and the (dimethylamino)methylidene/formyl groups affording the desired 2-amino-6-(hydroxymethyl)purines **10a**, **10f** and **10g** in good yields (Table IV).

For the synthesis of the coresponding purine base **10e**, different protecting groups were used. In this case, we have started from N^2,9-bis(THP) protected 2-amino-6-halopurines **11b** [18] or **12b** [20]. In these particular cases, the reactivity of the two derivatives differed significantly. The cross-coupling of **1** with the chloro derivative **11b** gave the desired product **13b** in low yield, while the reaction with the iodo derivative **12b** gave **13b** in good yield of



SCHEME 2
Cross-couplings of (benzoyloxymethyl)zinc iodide with protected 2-amino-6-halopurines

TABLE III
Cross-couplings of **1** with protected 2-amino-6-halopurines

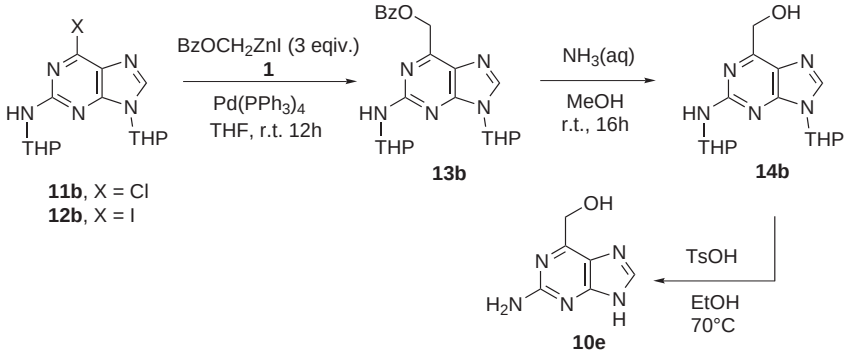
Entry	Starting compound	Product (Yield, %)	Ratio **8**:**9**
1	**6a**	**8a** + **9a** (77)[a]	1:2
2	**11b**	**13b** (30)	–
3	**12b**	**13b** (68)	–
4	**6c**	**8c** + **9c** (85)[a]	8:5
5	**6d**	**8d** + **9d** (83)[a]	5:2

[a] Approx. yield (ratio **8**:**9** according ^{1}H NMR).

TABLE IV
Cleavage of protecting groups in preparations of 2-amino-6-(hydroxymethyl)purines

Entry	Starting compound	Reagent	Product (Yield, %)
1	**8a** + **9a**	NH_3 (aq.)	**10a** (66)
2	**13b**	NH_3 (aq.)	**14b** (79)
3	**8c** + **9c**	NH_3 (aq.)	**10f** (67)
4	**8d** + **9d**	NH_3 (aq.)	**10g** (65)
5	**14b**	TsOH	**10e** (67)

68%. The benzoyl group was cleaved with ammonia to give intermediate **14b** and the THP protective groups in position 9 and N^2 of purine were eventually cleaved using *p*-toluenesulfonic acid (2.5 equivalents) in ethanol to afford the free base **10e** in 67% yield (Scheme 3).



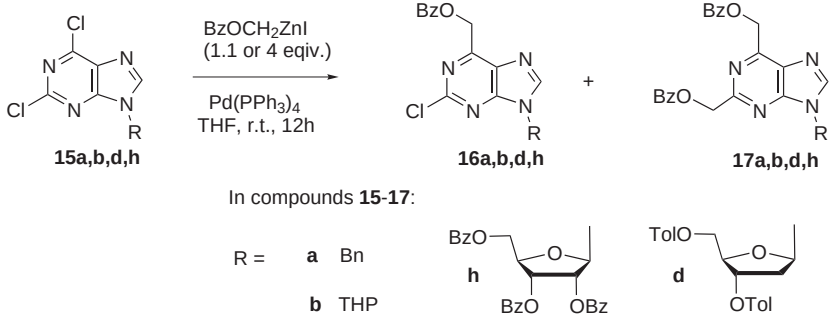
SCHEME 3

Cross-coupling reactions of dihalopurines with one equivalent of an organometallic reagent are regioselective[21,22]. In general 2,6- or 6,8-dichloropurines react[21] preferentially in position 6, while chloroiodopurines in the position of iodine. The only exceptions from this rule are the Fe-catalyzed reactions[22] of 6,8-dichloropurines with Grignard reagents occurring in position 8. These regioselective reactions were extensively used in the synthesis of di- and trisubstituted purine bases and nucleosides[21,22]. As no functionalized organometallic reagent has ever been applied in these reactions, investigation of regioselectivity of cross-coupling reactions of $BzOCH_2ZnI$ (**1**) with 2,6-dihalopurines was another aim of our study. 2,6-Bis(hydroxymethyl)purines are homologs of xanthine derivatives and 2-chloro-6-(hydroxymethyl)purines are related to antineoplastic cladribine (2-chloro-2′-deoxyadenosine)[23]. Therefore the synthesis of these two types of compounds by the regioselective cross-couplings is of interest.

At first we have used 2,6-dichloropurines as substrates for cross-coupling reactions with the organozinc **1**. The cross-couplings were performed with either 1.1 or 4 equivalents of the organozinc reagent. 6-(Benzoyloxymethyl)-2-chloropurines **16** were formed as main products when using 1.1 equivalents of $BzOCH_2ZnI$ in accord with the previous knowledge of higher reactivity of chlorine in the position 6 (Scheme 4, Table V). However, even when using 4 equivalents of the organozinc reagent the yields of disubstituted products **17** were still very low while compounds **16** were major products (Table V, entries 2, 4, 6, 8). Also a reaction of purified

6-(benzoyloxymethyl)-9-benzyl-2-chloropurine **16a** with $BzOCH_2ZnI$ (3 equivalents) proceeded with only negligible yield of compound **17a**. This shows that the reactivity of chlorine in position 2 is too low for an efficient cross-coupling with reagent **1**.

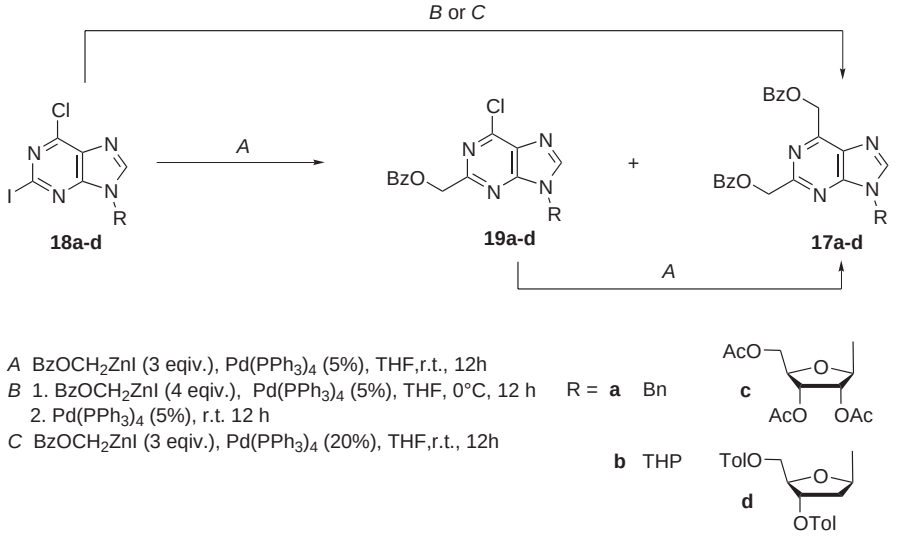
In order to perform cross-coupling in the position 2, we have turned our attention to 2-iodopurines as the iodine is significantly better leaving group compared to chlorine. Hence, we have studied cross-coupling reactions of **1** with 6-chloro-2-iodopurines **18**. The first experiments were performed with 3 equivalents of the organozinc **1** at ambient temperature (conditions *A*).



SCHEME 4
Cross-couplings of (benzoyloxymethyl)zinc iodide with 2,6-chloropurines

TABLE V
Regioselective cross-couplings of **1** with 2,6-chloropurines

Entry	Starting compound	$BzOCH_2ZnI$ equivalent	Product (Yield, %)	
1	**15a**	1.1	**16a** (89)	**17a** (5)
2	**15a**	4	**16a** (63)	**17a** (10)
3	**15b**	1.1	**16b** (78)	**17b** (8)
4	**15b**	4	**16b** (66)	**17b** (18)
5	**15h**	1.1	**16h** (84)	**17h** (<1)
6	**15h**	4	**16h** (53)	**17h** (6)
7	**15d**	1.1	**16d** (67)	**17d** (3)
8	**15d**	4	**16d** (77)	**17d** (15)
9	**16a**	3		**17a** (5)

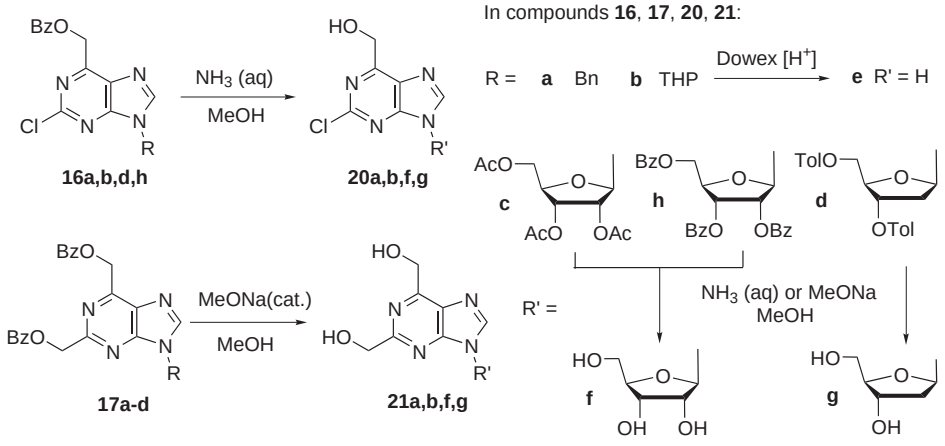


SCHEME 5
Cross-couplings of (benzoyloxymethyl)zinc iodide with 6-chloro-2-iodopurines (**18**)

TABLE VI
Cross-couplings of (benzoyloxymethyl)zinc iodide with 6-chloro-2-iodopurines

Entry	Starting compound	Conditions	Product (Yield, %)
1	**18a**	*A*	**19a** (90) **17a** (3)
2	**18b**	*A*	**19b** (87) **17b** (1)
3	**18c**	*A*	**19c** (88) **17c** (<1)
4	**18d**	*A*	**19d** (90) **17d** (1)
5	**19a**	*A*	**17a** (98)
6	**19b**	*A*	**17b** (97)
7	**19c**	*A*	**17c** (92)
8	**19d**	*A*	**17d** (91)
9	**18a**	*B*	**17a** (81)
10	**18b**	*B*	**17b** (85)
11	**18c**	*B*	**17c** (83)
12	**18d**	*B*	**17d** (88)
13	**18a**	*C*	**17a** (86)

Despite the excess of the reagent, the main products were the 2-(benzoyloxymethyl)-6-chloropurines **19**. This was quite unexpected since we have known the relatively high reactivity of 6-chloropurines in the cross-couplings with **1**. On the other hand, reactions of purified 2-(benzoyloxymethyl)-6-chloropurines **19a**–**19d** with **1** (3 equivalents) afforded the 2,6-bis(benzoyloxymethyl)purines **17a**–**17d** in excellent yields of 91–98%



SCHEME 6

TABLE VII
Cleavage of protecting groups in preparations of 2-chloro-6-(hydroxymethyl)purines and 2,6-bis(hydroxymethyl)purines

Entry	Starting compound	Reagent	Product (Yield, %)
1	**16a**	NH_3 (aq.)	**20a** (87)
2	**16b**	NH_3 (aq.)	**20b** (90)
3	**16h**	NH_3 (aq.)	**20f** (84)
4	**16d**	NH_3 (aq.)	**20g** (87)
5	**20b**	Dowex (H^+)	**20e** (84)
6	**17a**	MeONa	**21a** (88)
7	**17b**	MeONa	**21b** (89)
8	**17c**	MeONa	**21f** (80)
9	**17d**	MeONa	**21g** (90)
10	**21b**	Dowex (H^+)	**21e** (74)

(Scheme 5, Table VI). Apparently, the cause might have been either in low stability of the organozinc reagent at room temperature or deactivation of catalytic system. To solve this problem, we have performed two experiments: (i) addition of a second portion of $Pd(PPh_3)_4$ catalyst after 12 h and (ii) higher loading of catalyst (20 mole %) (Scheme 5, Table VI, conditions *B* or *C*). In both cases the disubstituted products **17** were obtained in good yields (81–88%) indicating that the problem was deactivation of catalyst.

The deprotections of the 2,6-disubstituted purines were performed in analogy to the previous derivatives. Free 2-chloro-6-(hydroxymethyl)purine bases **20a**, **20b** and nucleosides **20f**, **20g** were prepared from intermediates **16** using aqueous ammonia in methanol at ambient temperature (Scheme 6) in good yields (Table VII). Nucleobase **20e** was prepared from **20b** by acidic cleveage of THP protective group with Dowex 50X8 (H^+ form)[18] in ethanol in 84% of yield. The ester groups of intermediates **17** were cleaved with NaOMe in methanol at room temperature to give free 2,6-bis(hydroxymethyl)purine bases **21a**, **21b** and nucleosides **21f**, **21g** (Scheme 6, Table VII). The THP protective group of **21b** was cleaved using Dowex 50X8 (H^+ form) in ethanol to gave **21e** in 74% yield.

Biological Activity

All the title unsubstituted and 2-substituted 6-(hydroxymethyl)purine base and nucleosides **5**, **10**, **20** and **2**1 were subjected to biological activity screening. 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). Adenosine deaminase (ADA) inhibition was studied[24] on calf intestinal adenosine aminohydrolase. The results are summarized in Table VIII. The most active was the 6-(hydroxymethyl)purine ribonucleoside (**5f**) exerting a very high cytostatic effect and also significant inhibition of ADA. The related 6-(hydroxymethyl)purine base **5e** and 2-deoxyribonucleoside **5g** were much less active. All the 2-substituted derivatives **10**, **20** and **21** were devoid of any considerable cytostatic effect and only some of them showed moderate inhibition of ADA.

TABLE VIII
Biological activity of title purine bases and nucleosides[a]

Compound	IC_{50}, μmol l^{-1} [b]		
	HL60	CCRF-CEM	ADA
5e	12.0 (±0.96)	~30	NA
5f	0.01 (±0.0011)	0.15 (±0.0011)	1.70 (±0.136)
5g	NA[b]	NA	10.0 (±0.90)
10e	NA	NA	NA
10f	NA	NA	45.0 (±2.7)
10g	NA	NA	45.0 (±2.8)
20e	NA	NA	NA
20f	NA	NA	NA
20g	NA	NA	NA
21e	NA	NA	NA
21f	NA	NA	NA
21g	NA	NA	NA

[a] Values are means of four experiments, standard deviation is given in parentheses. [b] NA, not active (inhibition of cell growth at 10 μM was lower than 30%).

CONCLUSIONS

A novel facile and efficient methodology for hydroxymethylation of halopurines has been developed. It consists in Pd-catalyzed cross-coupling reactions of halopurines with (benzoyloxymethyl)zinc iodide. These cross-couplings are performed at room temperature and generally give very high yields of the (benzoyloxymethyl)purine intermediates that are easily deprotected to the title (hydroxymethyl)purines with ammonia or sodium methoxide. The methodology was applied in the synthesis of the corresponding purine bases and nucleosides. In 2-amino-6-chloropurines, the amino group has to be protected by (dimethylamino)methylidene group prior to the cross-coupling. Reactions of 2,6-dihalopurines proceed with high regioselectivity giving either 6- or 2-substituted purines. As the hydroxymethylpurines are biologically active and may also serve as intermediates in further functional group transformations to other new types of purine derivatives, this efficient synthetic methodology is of great importance.

EXPERIMENTAL

General

Starting materials: 9-benzyl-6-chloropurine[25], 9-benzyl-6-iodopurine[25] and analogously 9-benzyl-2,6-dichloropurine and 2-amino-9-benzyl-6-chloropurine, 6-chloro-9-(tetrahydropyran-2-yl)purine[26], 6-iodo-9-(tetrahydropyran-2-yl)purine[26] and analogously 2,6-dichloro-9-(tetrahydropyran-2-yl)purine, 6-chloro-2-(tetrahydropyran-2-yl)amino-9-(tetrahydropyran-2-yl)purine[18], 6-iodo-2-(tetrahydropyran-2-yl)amino-9-(tetrahydropyran-2-yl)purine[20], 9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-6-chloropurine[27], 9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-2-amino-6-chloropurine[28], 6-chloro-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)purine[29] and analogously 6-iodo-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)purine, 2-amino-6-chloro-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)-purine[30], 9-benzyl-6-chloro-2-iodopurine[21g] and analogously 6-chloro-2-iodo-9-(tetrahydropyran-2-yl)purine from 6-chloro-2-(tetrahydropyran-2-yl)amino-9-(tetrahydropyran-2-yl)-purine, 9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-6-chloro-2-iodopurine[31] and analogously 6-chloro-2-iodo-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)purine. All preparations of (acyloxymethyl)zinc iodides[14] 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, ^{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, coupling constants (*J*) are given in Hz. The assignment of carbons was based on C,H-HSQC and C,H-HMBC experiments. 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}. IR spectra were recorded on Nicolet 750 FT-IR and wavenumbers are given in cm^{-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] ADA inhibition assay was performed by standard technique[24].

6-Chloro-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)-2-iodopurine (**18d**)

Yield 69%, white solid, m.p. 162–163 °C. Prepared analogously as 9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-6-chloro-2-iodopurine[31] (**18c**) from 2-amino-6-chloro-9-(2-deoxy-3,5-di-*O*-toluoyl-β-D-*erythro*-pentofuranosyl)purine (**6d**). Exact mass (FAB HR MS) calculated for $C_{26}H_{23}ClIN_4O_5$: 633.0402, found: 633.0373. FAB MS, *m/z* (%): 633 (MH^+, 2); 353 (8); 281 (6); 153 (5); 119 (73). ^{1}H NMR (400 MHz, $CDCl_3$): 2.41 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.91–3.03 (m, 2 H, H-2′); 4.65 (dd, 1 H, J_{gem} = 11.5, $J_{5'b,4'}$ = 4.1, H-5′b); 4.68 (ddd, 1 H, $J_{4',5'}$ = 4.1, 3.1, $J_{4',3'}$ = 2.3, H-4′); 4.80 (dd, 1 H, J_{gem} = 11.5, $J_{5'a,4'}$ = 3.1, H-5′a); 5.80 (ddd, 1 H, $J_{3',2'}$ = 5.3, 3.6, $J_{3',4'}$ = 2.3, H-3′); 6.54 (dd, 1 H, $J_{1'2'}$ = 7.8, 6.4, H-1′); 7.21 and 7.30 (2 × m, 2 × 2 H, H-*m*-Tol); 7.82 and 7.98 (2 × m, 2 × 2 H, H-*o*-Tol); 8.21 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 21.68 and 21.76 (CH_3-Tol); 38.58 (CH_2-2′); 63.76 (CH_2-5′); 74.99 (CH-3′); 83.69 (CH-4′); 85.39 (CH-1′); 116.66 (C-2); 126.20 and 126.29 (C-*i*-Tol); 129.33 (CH-*m*-Tol); 129.47 and 129.85 (CH-*o*-Tol); 132.07 (C-5); 143.03 (CH-8); 144.41 and 144.69 (C-*p*-Tol); 150.66 (C-6); 151.68 (C-4); 165.93 and 165.98 (CO-Tol).

Preparation of (Benzoyloxymethyl)zinc Iodide (**1**)

A solution of iodomethyl benzoate (2.882 g, 11 mmol) in THF (5 ml) was added at 10–15 °C to the suspension of zinc dust (1.44 g, 22 mmol) in THF (4 ml), which was preactivated with dibromoethane (20 μl) and trimethylsilyl chloride (20 μl). After 1 h, a GC analysis of a hydrolyzed aliquot showed a virtually complete conversion of starting iodomethyl benzoate and a yield ca. 85–90% of methyl benzoate (benzyl acetate was used as an internal standard). Thus the concentration of (benzoyloxymethyl)zinc iodide (**1**) was ca. 0.9 mol l^{-1}.

General Procedure of Cross-Couplings of **1** with 6-Halopurines **2** and **3**

A solution of (benzoyloxymethyl)zinc iodide **1** (3.4 ml, 3 mmol) in THF was added at room temperature to a solution of 6-halopurine **2** or **3** (1 mmol), $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) in THF (10 ml) under Ar and stirred at room temperature for 6–12 h. The reaction was quenched with 1 M NaH_2PO_4 (50 ml) and extracted with $CHCl_3$ (4 × 30 ml). The 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).

6-(Benzoyloxymethyl)-9-benzylpurine (**4a**). Yield 96% from **3a**, white crystals, m.p. 106–108 °C. For $C_{20}H_{16}N_4O_2$ (344.4) calculated: 69.76% C, 4.68% H, 16.27% N; found: 69.38% C, 4.63% H, 16.08 N. FAB MS, *m/z* (%): 345 (M^+, 65), 224 (12), 149 (6), 105 (76), 91 (100). ^{1}H NMR (500 MHz, $CDCl_3$): 5.45 (s, 2 H, N-CH_2); 5.88 (s, 2 H, O-CH_2); 7.30–7.47 (m, 5 H, Bn); 7.44 (m, 2 H, H-*m*-Bz); 7.56 (m, 1 H, H-*p*-Bz); 8.04 (s, 1 H, H-8); 8.15 (m, 2 H, H-*o*-Bz); 8.99 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): 47.39 (N-CH_2); 63.03 (O-CH_2); 127.97 (CH-*M*-Bn); 128.35 (CH-*m*-Bz); 128.70 (CH-*p*-Bn); 129.20 (CH-*o*-Bn); 129.89 (C-*i*-Bz); 130.02 (CH-*o*-Bz); 131.77 (C-5); 133.08 (CH-*p*-Bz); 134.95 (C-*i*-Bn); 144.60 (CH-8); 151.79 (C-4); 152.63 (CH-2); 155.36 (C-6); 166.40 (CO). IR (CCl_4): 3070, 3036, 2939, 1731, 1593, 1500, 1452, 1407, 1332, 1270, 1114.

6-(Benzoyloxymethyl)-9-(tetrahydropyran-2-yl)purine (**4b**). Yield 95% from **3b**, yellowish oil. FAB MS, *m/z* (%): 339 (M^+, 15), 255 (89), 149 (17), 105 (100), 85 (53). ^{1}H NMR (500 MHz, $CDCl_3$): 1.64–1.86 and 2.02–2.20 (m, 6 H, CH_2-THP); 3.80 (dt, 1 H, *J* = 11.7 and 2.6, bCH_2-*O*-THP); 4.18 (ddt, 1 H, *J* = 11.7, 4.5 and 1.5, aCH_2-O-THP); 5.82 (dd, 1 H, *J* = 10.3 and 2.6, CH-O-THP); 5.86 (d, 1 H, *J* = 14.1, O-CH_2b); 5.90 (d, 1 H, *J* = 14.1, O-CH_2a); 7.44 (m, 2 H, H-*m*-Ph); 7.56 (m, 1 H, H-*p*-Ph); 8.14 (m, 2 H, H-*o*-Ph); 8.31 (s, 1 H, H-8); 8.97 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): 22.72, 24.86 and 31.84 (CH_2-THP); 62.97 (O-CH_2); 68.84 (CH_2-O-THP); 82.13 (CH-O-THP); 128.34 (CH-*m*-Ph); 129.86 (C-*i*-Ph); 130.01 (CH-*o*-Ph); 131.91 (C-5); 133.07 (CH-*p*-Ph); 142.71 (CH-8); 150.92 (C-4); 152.44 (CH-2); 155.31 (C-6); 166.36 (CO). IR ($CHCl_3$): 2952, 2862, 1725, 1601, 1586, 1496, 1452, 1409, 1375, 1334, 1273, 1251, 1114, 1087.

*6-(Benzoyloxymethyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**4c**). Yield 94% from **2c**, yellowish oil. ESI MS, *m/z* (%): 535 (M + Na^+, 100), 513 (M + H^+, 17), 444 (10), 259 (6). ^{1}H NMR (400 MHz, $CDCl_3$): 2.09, 2.12 and 2.16 (3 × s, 3 × 3 H, CH_3CO); 4.38 (m, 1 H, H-5′b); 4.42–4.50 (m, 2 H, H-5′a and H-4′); 5.67 (dd, 1 H, $J_{3'2'}$ = 5.7, $J_{3'4'}$ = 4.5, H-3′); 5.87 (s, 2 H, O-CH_2); 5.98 (t, 1 H, $J_{2'3'}$ = 5.7, $J_{2'1'}$ = 5.4, H-2′); 6.26 (d, 1 H, $J_{1'2'}$ = 5.4, H-1′); 7.45 (m, 2 H, H-*m*-Ph); 7.58 (m, 1 H, H-*p*-Ph); 8.15 (m, 2 H, H-*o*-Ph); 8.26 (s, 1 H, H-8); 8.98 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 20.37, 20.52 and 20.74 (CH_3); 62.92 (O-CH_2); 62.99 (CH_2-5′); 70.59 (CH-3′); 72.99 (CH-2′); 80.44 (CH-4′); 86.35 (CH-1′); 128.38 (CH-*m*-Ph); 129.68 (C-*i*-Ph); 130.00 (CH-*o*-Ph); 132.43 (C-5); 133.17 (CH-*p*-Ph); 143.16 (CH-8); 151.21

(C-4); 152.68 (CH-2); 155.92 (C-6); 166.36 (CO-Bz); 169.27, 169.49 and 170.22 (CO-Ac). IR ($CHCl_3$): 3030, 1751, 1727, 1599, 1499, 1452, 1374, 1336, 1272, 1227, 1206, 1113.

6-(Benzoyloxymethyl)-9-(2-deoxy-3,5-di-O-toluoyl-β-D-erythro-pentofuranosyl)purine (**4d**). Yield 93% from **3d**, white crystals, m.p. 118–120 °C. For $C_{34}H_{30}N_4O_7$ (606.6) calculated: 67.32% C, 4.98% H, 9.24% N; found: 66.93% C, 4.90% H, 8.94% N. FAB MS, *m/z* (%): 607 (M^+, 7), 255 (59), 119 (100), 105 (45), 91 (28). ^{1}H NMR (400 MHz, $CDCl_3$): 2.40 and 2.44 (2 × s, 2 × 3 H, CH_3-Tol); 2.86 (ddd, 1 H, J_{gem} = 14.2, $J_{2'b1'}$ = 5.8, $J_{2'b3'}$ = 2.2, H-2′b); 3.19 (ddd, 1 H, J_{gem} = 14.2, $J_{2'a1'}$ = 8.4, $J_{2'a3'}$ = 6.4, H-2′a); 4.64–4.70 (m, 2 H, H-5′b and H-4′); 4.77 (dd, 1 H, J_{gem} = 13.4, $J_{5'a4'}$ = 5.4, H-5′a); 5.83 (dt, 1 H, $J_{3'2'a}$ = 6.4, $J_{3'4'}$ = 2.2, $J_{3'2'b}$ = 2.1, H-3′); 5.85 (s, 2 H, O-CH_2); 6.61 (dd, 1 H, $J_{1'2'a}$ = 8.4, $J_{1'2'b}$ = 5.8, H-1′); 7.21 and 7.29 (2 × m, 2 × 2 H, H-*m*-Tol); 7.45 (m, 2 H, H-*m*-Ph); 7.57 (m, 1 H, H-*p*-Ph); 7.90 and 7.98 (2 × m, 2 × 2 H, H-*o*-Tol); 8.14 (m, 2 H, H-*o*-Ph); 8.27 (s, 1 H, H-8); 8.90 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 21.67 and 21.74 (CH_3-Tol); 37.80 (CH_2-2′); 62.88 (O-CH_2); 63.92 (CH_2-5′); 75.04 (CH-3′); 83.16 (CH-4′); 84.94 (CH-1′); 126.33 and 126.60 (C-*i*-Tol); 128.36 (CH-*m*-Bz); 129.28 and 129.29 (CH-*m*-Tol); 129.62 (CH-*o*-Tol); 129.70 (C-*i*-Bz); 129.81 (CH-*o*-Tol); 130.00 (CH-*o*-Bz); 132.45 (C-5); 133.14 (CH-*p*-Bz); 143.09 (CH-8); 144.20 and 144.57 (C-*p*-Tol); 151.11 (C-4); 152.46 (CH-2); 155.58 (C-6); 165.93, 166.15 and 166.35 (CO). IR ($CHCl_3$): 1723, 1612, 1601, 1496, 1440, 1270, 1179, 1103, 1021.

General Procedure for Deacylation Reactions

A 1 M methanolic MeONa (50–100 μl, 0.05–0.1 mmol) was added to a solution of protected purines or nucleosides **4a**–**4d** (0.2–0.5 mmol) in methanol (10–20 ml) and the mixture was stirred at ambient temperature. After complete deprotection the solvent was evaporated and the residue was chromatographed.

9-Benzyl-6-(hydroxymethyl)purine (**5a**). Yield 88% (chromatography on silica gel, ethyl acetate/methanol 95:5). The product was crystallized from ethyl acetate/heptane (m.p. 110–112 °C). For $C_{13}H_{12}N_4O$ (240.3) calculated: 64.99% C, 5.03% H, 23.32% N; found: 64.65% C, 5.08% H, 22.96% N. FAB MS, *m/z* (%): 241 (M^+, 100), 224 (6), 149 (9), 91 (83). ^{1}H NMR (500 MHz, $CDCl_3$): 5.22 (s, 2 H, O-CH_2); 5.47 (s, 2 H, N-CH_2); 7.29–7.40 (m, 5 H, Ph); 8.03 (s, 1 H, H-8); 8.98 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): 47.43 (N-CH_2); 61.37 (O-CH_2); 127.89, 128.74 and 129.22 (CH-phenyl); 130.47 (C-5); 134.95 (C-*i*-phenyl); 144.11 (CH-8); 151.05 (C-4); 152.18 (CH-2); 159.17 (C-6). IR ($CHCl_3$): 3457, 1601, 1585, 1500, 1407, 1335, 1228, 1069.

6-(Hydroxymethyl)-9-(tetrahydropyran-2-yl)purine (**5b**). Yield 85% (chromatography on silica gel, ethyl acetate/methanol 98:2). Product was crystallized from ethyl acetate/hexanes (m.p. 75–78 °C). For $C_{11}H_{14}N_4O_2$ (234.3) calculated: 56.40% C, 6.02% H, 23.92% N; found: 56.15% C, 5.98% H, 23.55% N. FAB MS, *m/z* (%): 235 (M^+, 35), 151 (100), 135 (17), 85 (22). ^{1}H NMR (400 MHz, $CDCl_3$): 1.65–1.89 and 2.03–2.20 (m, 6 H, CH_2-THP); 3.80 (dt, 1 H, *J* = 11.7 and 2.7, bCH_2-O-THP); 4.20 (ddt, 1 H, *J* = 11.7, 4.0 and 1.9, aCH_2-O-THP); 5.22 (s, 2 H, O-CH_2); 5.83 (dd, 1 H, *J* = 10.2 and 2.6, CH-O-THP); 8.29 (s, 1 H, H-8); 8.95 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.73, 24.83 and 31.87 (CH_2-THP); 61.30 (O-CH_2); 68.89 (CH_2-O-THP); 82.12 (CH-O-THP); 130.57 (C-5); 142.18 (CH-8); 150.12 (C-4); 151.96 (CH-2); 159.07 (C-6). IR ($CHCl_3$): 3450, 2952, 2863, 1602, 1585, 1497, 1410, 1336, 1087, 1046.

6-(Hydroxymethyl)-9-(β-D-ribofuranosyl)purine (**5f**). Yield 81% (chromatography on silica gel, ethyl acetate/methanol 95:5–80:20), white hygroscopic solid (m.p. 65–69 °C) which was lyophilized from water as monohydrate, $[\alpha]_D^{20}$ –12.4 (*c* 0.49, MeOH); lit.[32]: $[\alpha]_D^{20}$ –9.7 (*c* 3.0,

MeOH). For $C_{11}H_{14}N_4O_5 \cdot H_2O$ (300.3) calculated: 44.00% C, 5.37% H, 18.66% N; found: 44.40% C, 5.29% H, 18.37% N. FAB MS, *m/z* (%): 283 (MH^+, 7), 281 (19), 207 (11), 151 (43), 133 (18), 121 (11), 115 (11), 73 (100). ^{1}H NMR (400 MHz, MeOD): 3.77 (dd, 1 H, J_{gem} = 12.3, $J_{5'b4'}$ = 3.3, H-5′b); 3.89 (dd, 1 H, J_{gem} = 12.3, $J_{5'a4'}$ = 3.0, H-5′a); 4.16 (q, 1 H, $J_{4'3'}$ = 3.6, $J_{4'5'b}$ = 3.3, $J_{4'5'a}$ = 3.0, H-4′); 4.36 (dd, 1 H, $J_{3'2'}$ = 5.1, $J_{3'4'}$ = 3.6, H-3′); 4.74 (t, 1 H, $J_{2'1'}$ = 5.6, $J_{2'3'}$ = 5.1, H-2′); 5.09 (s, 2 H, O-CH_2); 6.14 (d, 1 H, $J_{1'2'}$ = 5.6, H-1′); 8.74 (s, 1 H, H-8); 8.89 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, MeOD): 61.51 (O-CH_2); 62.99 (CH_2-5′); 72.18 (CH-3′); 75.76 (CH-2′); 87.62 (CH-4′); 90.71 (CH-1′); 132.82 (C-5); 146.32 (CH-8); 152.10 (C-4); 153.05 (CH-2); 161.07 (C-6). IR (KBr): 3413, 1602, 1500, 1406, 1336, 1122, 1083, 1054.

*9-(2-Deoxy-*β*-*D*-erythro-pentofuranosyl)-6-(hydroxymethyl)purine* (**5g**). Yield 86% (chromatography on silica gel, ethyl acetate/methanol 95:5–80:20), white hygroscopic solid (m.p. 69–71 °C) which was lyophilized from water as a monohydrate, $[\alpha]_D^{20}$ +6.1 (*c* 0.7, MeOH). For $C_{11}H_{14}N_4O_4 \cdot H_2O$ (284.3) calculated: 46.48% C, 5.67% H, 19.71% N; found: 46.25% C, 5.63% H, 19.35% N. FAB MS, *m/z* (%): 267 (MH^+, 54), 151 (100), 131 (11), 115 (41), 73 (49). ^{1}H NMR (400 MHz, MeOD): 2.48 (ddd, 1 H, J_{gem} = 13.5, $J_{2'b1'}$ = 6.3, $J_{2'b3'}$ = 3.4, H-2′b); 2.85 (ddd, 1 H, J_{gem} = 13.5, $J_{2'a1'}$ = 7.3, $J_{2'a3'}$ = 6.0, H-2′a); 3.75 (dd, 1 H, J_{gem} = 12.1, $J_{5'b4'}$ = 4.0, H-5′a); 3.83 (dd, 1 H, J_{gem} = 12.1, $J_{5'a4'}$ = 3.5, H-5′a); 4.06 (q, 1 H, $J_{4'5'b}$ = 4.0, $J_{4'5'a}$ = 3.5, $J_{4'3'}$ = 3.4, H-4′); 4.60 (dt, 1 H, $J_{3'2'a}$ = 6.0, $J_{3'4'}$ = 3.4, $J_{3'2'b}$ = 3.4, H-3′); 5.08 (s, 2 H, O-CH_2); 6.57 (dd, 1 H, $J_{1'2'a}$ = 7.3, $J_{1'2'b}$ = 6.3, H-1′); 8.71 (s, 1 H, H-8); 8.88 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, MeOD): 41.38 (CH_2-2′); 61.49 (O-CH_2); 63.27 (CH_2-5′); 72.67 (CH-3′); 86.58 (CH-1′); 89.68 (CH-4′); 132.71 (C-5); 146.11 (CH-8); 151.93 (C-4); 153.00 (CH-2); 160.87 (C-6). IR (KBr): 3401, 3108, 1596, 1584, 1497, 1448, 1396, 1339, 1094, 1050.

6-(Hydroxymethyl)-9*H*-purine (**5e**)

Yield 78% (85 mg). Prepared from **5b** (170 mg, 0.73 mmol), with Dowex 50X8 (H^+) (ca. 100 mg) in ethanol (20 ml, 96%). Reaction mixture was stirred at 70–75 °C for 2 h, filtered, washed resin with ethanolic ammonia and evaporated to dryness. Crude product was chromatographed (chloroform/methanol 99:1–90:10) to afford a white solid that was crystallized from ethanol/heptane (m.p. > 300 °C). For $C_6H_6N_4O$ (150.1) calculated: 48.00% C, 4.03% H, 37.32% N; found: 47.61% C, 3.97% H, 36.97% N. FAB MS, *m/z* (%): 151 (MH^+, 21), 133 (6), 110 (23), 91 (100). ^{1}H NMR (400 MHz, DMSO-d_6): 4.88 (s, 2 H, O-CH_2); 8.55 (s, 1 H, H-8); 8.83 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 62.15 (O-CH_2); 124.98 (C-5); 146.51 (CH-8); 151.61 (CH-2); 156.54 (C-6); 157.85 (C-4). IR (KBr): 3421, 3174, 1616, 1568, 1479, 1404, 1370, 1335, 1242, 1089.

General Procedure for Cross-Couplings of Organozinc **1** with 2-Amino-6-chloropurines **6**

Dimethylformamide dimethylacetal (0.4 ml, 3 mmol) was added to the solution of 2-amino-6-chloropurine **6** (1 mmol) in dry DMF (10 ml) and stirred at 50 °C for 12–16 h. Volatiles were evaporated in vacuo (130 Pa, 50 °C) and crude product **7** was used in the next step. Thus, the solution of (benzoyloxymethyl)zinc iodide (3.4 ml, 3 mmol) in THF was added at room temperature to a solution of **7** (1 mmol), $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) in THF (10 ml) under Ar and stirred at room temperature for 12 h. The reaction was quenched with 1 M NaH_2PO_4 (50 ml) and extracted with $CHCl_3$ (4 × 30 ml). Collected organic phases were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude oily product was purified by chromatography on silica gel (hexanes/ethyl acetate 2:1–1:2). The desired prod-

ucts **8a**, **8c** or **8d** were contaminated with corresponding formylamino derivatives **9a**, **9c** or **9d**. For yields and ratios (**8**/**9**), see Table III.

6-(Benzoyloxymethyl)-9-benzyl-2-{[(dimethylamino)methylidene]amino}purine (**8a**). Exact mass (FAB HR MS) calculated for $C_{23}H_{23}N_6O_2$: 415.1882; found: 415.1896. FAB MS, *m/z* (%): 415 (MH^+, 88), 324 (4), 309 (9), 219 (5), 176 (7), 105 (91), 91 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 2.99 and 3.15 (2 × s, 2 × 3 H, $(CH_3)_2N$); 5.40 (s, 2 H, CH_2-N-9); 5.80 (s, 2 H, CH_2-O-6); 7.25–7.40 (m, 5 H, H-Bn); 7.45 (m, 2 H, H-*m*-Bz); 7.56 (m, 1 H, H-*p*-Bz); 7.77 (s, 1 H, H-8); 8.15 (m, 2 H, H-*o*-Bz); 8.65 (s, 1 H, HC=N). ^{13}C NMR (125.8 MHz, $CDCl_3$): 35.17 and 41.00 ($(CH_3)_2N$); 62.88 (CH_2-5′); 46.67 (CH_2-N-9); 63.55 (CH_2-O-6); 127.66 (C-5); 127.89 (CH-*o*-Bn); 128.32 (CH-*m*-Bn); 129.00 (CH-*p*-Bn); 129.44 (CH-*m*-Bz); 129.97 (CH-*o*-Bz); 130.17 (C-*i*-Bz); 132.95 (CH-*p*-Bz); 135.55 (CH-*i*-Bn); 142.89 (CH-8); 153.80 (C-4); 155.18 (C-6); 158.79 (HC=N); 162.62 (C-2); 166.48 (CO-Bz). IR ($CHCl_3$): 3068, 3030, 2457, 1725, 1708, 1630, 1601, 1516, 1488, 1456, 1406, 1363, 1274, 1114, 1029, 712, 646.

9-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-6-(benzoyloxymethyl)-2-{[(dimethylamino)methylidene]-amino}purine (**8c**). Exact mass (FAB HR MS) calculated for $C_{27}H_{31}N_6O_9$: 583.2153, found: 583.2166. FAB MS, *m/z* (%): 583 (MH^+, 100), 478 (7), 325 (37), 259 (9), 219 (16), 105 (47). ^{1}H NMR (500 MHz, $CDCl_3$): 2.07, 2.08 and 2.14 (3 × s, 3 × 3 H, CH_3-Ac); 3.08 and 3.17 (2 × s, 2 × 3 H, $(CH_3)_2N$); 4.31 (m, 1 H, H-5′b); 4.34–4.43 (m, 2 H, H-4′ and H-5′a); 5.68 (t, 1 H, $J_{3',2'}$ = 5.2, $J_{3',4'}$ = 5.2, H-3′); 5.75 (s, 2 H, CH_2-O-6); 5.97 (t, 1 H, $J_{2',3'}$ = 5.2, $J_{2',1'}$ = 5.1, H-2′); 6.29 (d, 1 H, $J_{1',2'}$ = 5.1, H-1′); 7.45 (m, 2 H, H-*m*-Bz); 7.57 (m, 1 H, H-*p*-Bz); 8.00 (s, 1 H, H-8); 8.15 (m, 2 H, H-*o*-Bz); 8.69 (s, 1 H, HC=N). ^{13}C NMR (125.8 MHz, $CDCl_3$): 20.44, 20.53 and 20.67 (CH_3-Ac); 35.43 and 41.03 ($(CH_3)_2N$); 62.88 (CH_2-5′); 63.67 (CH_2-O-6); 70.36 (CH-3′); 72.85 (CH-2′); 79.59 (CH-4′); 85.31 (CH-1′); 128.34 (CH-*m*-Bz and C-5); 130.00 (CH-*o*-Bz); 130.05 (C-*i*-Bz); 133.01 (CH-*p*-Bz); 141.04 (CH-8); 153.30 (C-4); 156.09 (C-6); 158.90 (HC=N); 162.88 (C-2); 166.41 (CO-Bz); 169.41, 169.61 and 170.34 (CO-Ac). IR ($CHCl_3$): 2817, 1750, 1725, 1631, 1594, 1508, 1491, 1452, 1370, 1273, 1114, 1028, 712, 639.

6-(Benzoyloxymethyl)-2-{[(dimethylamino)methylidene]amino}-9-(2-deoxy-3,5-di-O-toluoyl-β-D-erythro-pentofuranosyl)purine (**8d**). Exact mass (FAB HR MS) calculated for $C_{37}H_{37}N_6O_7$: 677.2724, found: 677.2726. FAB MS, *m/z* (%): 677 (MH^+, 34), 572 (3), 353 (5), 325 (50), 219 (19), 119 (100), 105 (45). ^{1}H NMR (400 MHz, $CDCl_3$): 2.40 and 2.44 (2 × s, 2 × 3 H, CH_3-Tol); 2.85 (m, 2 H, H-2′); 3.00 and 3.15 (2 × s, 2 × 3 H, $(CH_3)_2N$); 4.58 (td, 1 H, $J_{4',5'}$ = 4.0, 3.8, $J_{4',3'}$ = 2.5, H-4′); 4.65 (dd, 1 H, J_{gem} = 12.0, $J_{5'b,4'}$ = 4.0, H-5′b); 4.72 (dd, 1 H, J_{gem} = 12.0, $J_{5'a,4'}$ = 3.8, H-5′a); 5.74 and 5.78 (2 × d, 2 H, J_{gem} = 14.0, CH_2-O-6); 5.80 (m, 1 H, H-3′); 6.71 (dd, 1 H, $J_{1',2'}$ = 8.1, 6.3, H-1′); 7.22 and 7.29 (2 × m, 2 × 2 H, H-*m*-Tol); 7.45 (m, 2 H, H-*m*-Bz); 7.57 (m, 1 H, H-*p*-Bz); 7.89 and 7.96 (2 × m, 2 × 2 H, H-*o*-Tol); 8.04 (s, 1 H, H-8); 8.16 (m, 2 H, H-*o*-Bz); 8.67 (s, 1 H, HC=N). ^{13}C NMR (100.6 MHz, $CDCl_3$): 21.67 and 21.74 (CH_3-Tol); 35.18 (CH_3N); 38.49 (CH_2-2′); 40.98 (CH_3N); 63.56 (CH_2-O-6); 64.13 (CH_2-5′); 75.00 (CH-3′); 82.67 (CH-4′); 83.71 (CH-1′); 126.38 and 126.60 (C-*i*-Tol); 128.18 (C-5); 128.32 (CH-*m*-Bz); 129.26 and 129.36 (CH-*m*-Tol); 129.56 and 129.85 (CH-*o*-Tol); 129.99 (CH-*o*-Bz); 130.14 (C-*i*-Bz); 132.95 (CH-*p*-Bz); 140.51 (CH-8); 144.21 and 144.47 (C-*p*-Tol); 153.19 (C-4); 155.49 (C-6); 158.80 (HC=N); 162.62 (C-2); 165.99 and 166.19 (CO-Tol); 166.43 (CO-Bz). IR ($CHCl_3$): 2817, 1721, 1630, 1592, 1503, 1492, 1452, 1368, 1270, 1178, 1109, 712, 638.

6-(Benzoyloxymethyl)-9-(2-deoxy-3,5-di-O-toluoyl-β-D-erythro-pentofuranosyl)-2-(formylamino)-purine (**9d**). Exact mass (FAB HR MS) calculated for $C_{35}H_{32}N_5O_8$: 650.2251, found: 650.2266. FAB MS, *m/z* (%): 650 (MH^+, 6), 622 (1), 353 (2), 298 (16), 119 (100), 105 (42). ^{1}H NMR (400 MHz,

$CDCl_3$): 2.39 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.81 (ddd, 1 H, J_{gem} = 14.2, $J_{2'b,1'}$ = 6.0, $J_{2'b,3'}$ = 2.6, H-2′b); 3.10 (ddd, 1 H, J_{gem} = 14.2, $J_{2'a,1'}$ = 7.9, $J_{2'a,3'}$ = 6.3, H-2′a); 4.63–4.69 (m, 3 H, H-4′ and H-5′b); 4.78 (dd, 1 H, J_{gem} = 13.4, $J_{5'a,4'}$ = 5.6, H-5′a); 5.77 (s, 2 H, CH_2-O-6); 5.82 (dt, 1 H, $J_{3',2'}$ = 6.3, 2.6, $J_{3',4'}$ = 2.6, H-3′); 6.48 (dd, 1 H, $J_{1'2'}$ = 7.9, 6.0, H-1′); 7.20 and 7.29 (2 × m, 2 × 2 H, H-*m*-Tol); 7.46 (m, 2 H, H-*m*-Bz); 7.59 (m, 1 H, H-*p*-Bz); 7.86 and 7.97 (2 × m, 2 × 2 H, H-*o*-Tol); 8.12 (s, 1 H, H-8); 8.13 (m, 2 H, H-*o*-Bz); 8.27 (d, 1 H, *J* = 10.6, NH); 9.47 (d, 1 H, *J* = 10.6, HCO). ^{13}C NMR (100.6 MHz, $CDCl_3$): 21.67 and 21.75 (CH_3-Tol); 37.62 (CH_2-2′); 62.44 (CH_2-O-6); 63.69 (CH_2-5′); 74.76 (CH-3′); 82.93 (CH-4′); 84.71 (CH-1′); 126.29 and 126.48 (C-*i*-Tol); 128.48 (CH-*m*-Bz); 129.30 and 129.33 (CH-*m*-Tol); 129.55 (C-5); 129.59 (CH-*o*-Tol); 129.82 (CH-*o*-Bz); 129.91 (CH-*o*-Tol and C-*i*-Bz); 133.30 (CH-*p*-Bz); 142.32 (CH-8); 144.33 and 144.64 (C-*p*-Tol); 151.92 (C-4); 152.23 (C-2); 157.05 (C-6); 162.84 (HCO); 165.91 and 166.17 (CO-Tol); 166.30 (CO-Bz). IR ($CHCl_3$): 3406, 3028, 1719, 1603, 1513, 1489, 1452, 1381, 1270, 1178, 1103, 712, 643.

6-(Benzoyloxymethyl)-2-(tetrahydropyran-2-yl)amino-9-(tetrahydropyran-2-yl)purine (**13b**). Yield 68%, yellowish oil, mixture of diastereomers (1:1). Exact mass (FAB HR MS) calculated for $C_{23}H_{28}N_5O_4$: 438.2141, found: 438.2130. FAB MS, *m/z* (%): 438 (MH^+, 83; 354 (100), 270 (37), 248 (8), 164 (19), 105 (72), 85 (40). ^{1}H NMR (400 MHz, DMSO-d_6): 1.40–2.14 (m, 12 H, CH_2-THP); 3.42 (bm, 1 H, bCH_2-O-THP-NH); 3.74 and 3.75 (ddd, 1 H, *J* = 11.5, 11.4, 7.5, bCH_2-O-THP-N); 3.92 (bm, 1 H, aCH_2-O-THP-NH); 4.14 (ddt, 1 H, *J* = 11.4, 4.3, 1.9, 1.9, aCH_2-O-THP-N); 5.27 and 5.32 (bdt, 1 H, *J* = 9.8, 9.6, 2.4, CH-O-THP-NH); 5.61 (dd, 1 H, *J* = 10.0, 2.5, CH-O-THP-N); 5.64 (bd, 1 H, *J* = 9.8, NH); 5.67 and 5.69 (d, 1 H, *J* = 14.1, bCH_2-O); 5.74 (d, 1 H, *J* = 14.1, aCH_2-O); 7.45 (m, 2 H, *m*-H-Ph); 7.56 (m, 1 H, *p*-H-Ph); 7.96 (s, 1 H, H-8); 8.15 (m, 2 H, *o*-H-Ph). ^{13}C NMR (100.6 MHz, DMSO-d_6): 22.76 and 22.83, 22.89 and 22.95, 24.90 and 24.92, 25.21, 31.33 and 31.49, 31.73 (CH_2-THP); 62.91 (CH_2-O-Bz); 66.41 and 66.44, 68.57 (CH_2-O-THP); 80.12 and 80.23, 81.18 and 81.61 (CH-O-THP); 126.25 and 126.29 (C-5); 128.28 (*m*-CH-Ph); 129.99 (*o*-CH-Ph); 130.10 and 130.13 (*i*-C-Ph); 132.92 (*p*-CH-Ph); 139.63 and 139.76 (CH-8); 152.61 and 152.76 (C-4); 155.82 and 155.91 (C-6); 157.77 and 157.83 (C-2); 166.30 (C=O). IR ($CHCl_3$): 3440, 2948, 2856, 1724, 1610, 1597, 1528, 1470, 1406, 1353, 1276, 1176, 1031, 712, 643.

General Procedure for Cleavage of Protecting Groups from Mixtures **8** and **9**

Aqueous ammonia (25% solution, 10 ml) was added to a solution of protected purines or nucleosides **8** and **9** (1 mmol) in methanol (60 ml) and the mixture was stirred at 55 °C for 24 h. After complete deprotection the volatiles were evaporated and the residue was chromatographed.

2-Amino-9-benzyl-6-(hydroxymethyl)purine (**10a**). Yield 66%, yellowish solid, m.p. 154–156 °C. For $C_{13}H_{13}N_5O$ (255.3) calculated: 61.17% C, 5.13% H, 27.43% N; found: 59.82% C, 5.23% H, 27.15% N. Exact mass (FAB HR MS) calculated for $C_{13}H_{14}N_5O$: 256.1198, found: 256.1210. FAB MS, *m/z* (%): 256 (M^+, 100), 239 (7), 164 (7), 91 (70). ^{1}H NMR (500 MHz, DMSO-d_6): 4.69 (d, 2 H, $J_{CH2,OH}$ = 5.9, CH_2-O); 5.08 (t, 1 H, $J_{OH,CH2}$ = 5.9, OH-CH_2); 5.29 (s, 2 H, CH_2-N); 6.49 (bs, 2 H, NH_2); 7.24 (m, 2 H, H-*o*-Ph); 7.28 (m, 1 H, H-*p*-Ph); 7.34 (m, 2 H, H-*m*-Ph); 8.12 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 45.76 (CH_2-N); 60.27 (CH_2-O); 124.22 (C-5); 127.26 (CH-*o*-Ph); 127.79 (CH-*p*-Ph); 128.85 (CH-*m*-Ph); 137.30 (C-*i*-Ph); 141.99 (CH-8); 153.22 (C-4); 160.37 and 160.50 (C-2 + C-6). IR (KBr): 3395, 3310, 3191, 1637, 1605, 1593, 1520, 1474, 1401, 1375, 1036, 712, 646.

2-Amino-6-(hydroxymethyl)-9-(β-D-ribofuranosyl)purine (**10f**). Yield 67%, yellowish solid, m.p. 204–205 °C, $[\alpha]_D^{20}$ –38.3 (*c* 0.36, MeOH). For $C_{11}H_{15}N_5O_5$ (297.3) calculated: 44.44% C, 5.09% H, 23.56% N; found: 44.09% C, 5.14% H, 23.15% N. Exact mass (FAB HR MS) calculated for $C_{11}H_{16}N_5O_5$: 298.1151, found: 298.1163. FAB MS, *m/z* (%): 298 (MH^+, 38), 166 (50), 149 (11), 131 (14), 115 (89). ^{1}H NMR (400 MHz, DMSO-d_6): 3.54 (ddd, 1 H, J_{gem} = 12.0, $J_{5'b,OH}$ = 5.8, $J_{5'b,4'}$ = 4.2, H-5′b); 3.64 (ddd, 1 H, J_{gem} = 12.0, $J_{5'a,OH}$ = 5.1, $J_{5'a,4'}$ = 4.3, H-5′a); 3.90 (q, 1 H, $J_{4',5'}$ = 4.3, 4.2, $J_{4',3'}$ = 3.1, H-4′); 4.12 (bq, 1 H, $J_{3',OH}$ = 4.5, $J_{3',2'}$ = 3.8, $J_{3',4'}$ = 3.1, H-3′); 4.50 (bq, 1 H, $J_{2',1'}$ = 6.0, $J_{2',OH}$ = 5.0, $J_{2',3'}$ = 3.8, H-2′); 4.68 (d, 2 H, $J_{CH2,OH}$ = 6.0, CH_2-O); 5.06 (t, 1 H, $J_{OH,5'}$ = 5.8, 5.1, OH-5′); 5.11 (t, 1 H, $J_{OH,CH2}$ = 6.0, OH-CH_2); 5.17 (bd, 1 H, $J_{OH,3'}$ = 4.5, OH-3′); 5.44 (t, 1 H, $J_{OH,2'}$ = 5.0, OH-2′); 5.83 (d, 1 H, $J_{1',2'}$ = 6.0, H-1′); 6.51 (bs, 2 H, NH_2); 8.26 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 61.28 (CH_2-O); 61.59 (CH_2-5′); 70.59 (CH-3′); 73.62 (CH-2′); 85.48 (CH-4′); 86.58 (CH-1′); 124.53 (C-5); 140.12 (CH-8); 153.27 (C-4); 160.32 (C-2); 160.59 (C-6). IR (KBr): 3344, 3221, 1609, 1516, 1474, 1405, 1318, 1224, 1084, 1053, 637.

2-Amino-9-(2-deoxy-β-D-erythro-pentofuranosyl)-6-(hydroxymethyl)purine (**10g**). Yield 65%, yellowish solid, m.p. 158–160 °C, $[\alpha]_D^{20}$ +2.2 (*c* 0.27, MeOH). For $C_{11}H_{15}N_5O_4 \cdot H_2O$ (299.3) calculated: 44.14% C, 5.73% H, 23.40% N; found: 44.08% C, 5.41% H, 23.07% N. Exact mass (FAB HR MS) calculated for $C_{11}H_{16}N_5O_4$: 282.1202, found: 282.1209. FAB MS, *m/z* (%): 282 (MH^+, 8), 166 (8), 149 (4), 115 (5). ^{1}H NMR (500 MHz, DMSO-d_6): 2.23 (ddd, 1 H, J_{gem} = 13.2, $J_{2'b,1'}$ = 6.1, $J_{2'b,3'}$ = 3.2, H-2′b); 2.62 (ddd, 1 H, J_{gem} = 13.2, $J_{2'a,1'}$ = 7.8, $J_{2'a,3'}$ = 5.8, H-2′a); 3.51 (ddd, 1 H, J_{gem} = 11.7, $J_{5'b,OH}$ = 5.5, $J_{5'b,4'}$ = 4.6, H-5′b); 3.58 (dt, 1 H, J_{gem} = 11.7, $J_{5'a,OH}$ = 5.5, $J_{5'a,4'}$ = 4.8, H-5′a); 3.83 (td, 1 H, $J_{4',5'}$ = 4.8, 4.6, $J_{4',3'}$ = 2.8, H-4′); 4.37 (dq, 1 H, $J_{3',2'}$ = 5.8, 3.2, $J_{3',OH}$ = 4.0, $J_{3',4'}$ = 2.8, H-3′); 4.67 (d, 2 H, $J_{CH2,OH}$ = 5.9, CH_2-O); 4.96 (t, 1 H, $J_{OH,5'}$ = 5.5, OH-5′); 5.08 (t, 1 H, $J_{OH,CH2}$ = 5.9, OH-CH_2); 5.28 (d, 1 H, $J_{OH,3'}$ = 4.0, OH-3′); 6.26 (dd, 1 H, $J_{1',2'}$ = 7.8, 6.1, H-1′); 6.49 (bs, 2 H, NH_2); 8.23 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 39.42 (CH_2-2′); 60.26 (CH_2-O); 61.87 (CH_2-5′); 70.92 (CH-3′); 82.80 (CH-1′); 87.79 (CH-4′); 124.54 (C-5); 139.90 (CH-8); 152.87 (C-4); 160.26 (C-2); 160.49 (C-6). IR (KBr): 3430, 3320, 3205, 3121, 1605, 1517, 1477, 1388, 1223, 1089, 1054, 639.

6-(Hydroxymethyl)-2-(tetrahydropyran-2-yl)amino-9-(tetrahydropyran-2-yl)purine (**14b**). Yield 79%, white foam, diastereomeric mixture (1:1). Exact mass (FAB HR MS) calculated for $C_{16}H_{24}N_5O_3$: 334.1879, found: 334.1893. FAB MS, *m/z* (%): 334 (MH^+, 61), 250 (100), 166 (46), 148 (16), 85 (63). ^{1}H NMR (400 MHz, DMSO-d_6): 1.35–2.01 and 2.22–2.37 (2 × m, 12 H, CH_2-THP); 3.46, 3.64, 3.82 and 4.01 (4 × m, 4 × 1 H, CH_2-O-THP); 4.71 and 4.72 (2 × d, 2 H, J_{vic} = 5.9, CH_2-O); 5.12 (t, 1 H, J_{vic} = 5.9, OH); 5.28 and 5.54 (2 × m, 2 × 1 H, CH-O-THP); 7.64 (bd, 1 H, J_{vic} = 9.3, NH); 8.281 and 8.285 (2 × s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 22.70, 22.72, 22.84, 22.86, 24.71, 25.24, 29.91, 30.02 and 30.65 (CH_2-THP); 60.33 (CH_2-O); 65.71, 67.80 and 67.85 (CH_2-O-THP); 80.12, 80.76 and 80.79 (CH-O-THP); 125.04 (C-5); 140.49 (CH-8); 152.40 and 152.44 (C-4); 158.13 and 158.15 (C-2); 160.39 and 160.42 (C-6). IR ($CHCl_3$): 3440, 2948, 2856, 1607, 1526, 1497, 1407, 1078, 1059, 1033, 644.

2-Amino-6-(hydroxymethyl)-9*H*-purine (**10e**)

Yield 67%, yellowish solid, m.p. > 360 °C. Prepared from **14b** by acidic cleveage of THP protecting groups with *p*-toluenesulfonic acid (2.5 equivalents) in ethanol at 70 °C. Reaction was quenched by addition of aqueous ammonia and volatiles were evaporated. The residue was dissolved in water and aplied on Dowex 50WX8 (H^+) column. After desalting, the product was eluted with gradient of aqueous ammonia (0.1–1%) and recrystallized from

EtOH/ethyl acetate. Exact mass (FAB HR MS) calculated for $C_6H_8N_5O$: 166.0729, found: 166.0733. FAB MS, *m/z* (%): 166 (MH^+, 13), 149 (4), 109 (9), 91 (49). ^{1}H NMR (500 MHz, DMSO-d_6 + CF_3COOD): 4.98 (s, 2 H, CH_2-O); 8.66 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6 + CF_3COOD): 57.97 (CH_2-O); 120.26 (C-5); 146.71 (CH-8); 154.44 (C-6); 155.31 (C-2); 157.03 (C-4). IR (KBr): 3401, 3317, 3203, 1624, 1596, 1509, 1471, 1381, 1086, 629.

General Procedure for Cross-Couplings of Organozinc **1** with 2,6-Dichloropurines **15**

A solution of organozinc **1** (0.6 or 2.22 ml; 0.55 or 2 mmol) in THF was added at room temperature to a solution of a 2,6-dichloropurine **15** (0.5 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) in THF (3 ml) and stirred at room temperature for 12 h. The reaction was quenched with 1 M NaH_2PO_4 (40 ml) and extracted with $CHCl_3$ (3 × 30 ml). The 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 3:1–1:1). Yields are given in Table V.

6-(Benzoyloxymethyl)-9-benzyl-2-chloropurine (**16a**). White solid, m.p. 143–144 °C. For $C_{20}H_{15}ClN_4O_2$ (378.8) calculated: 63.41% C, 3.99% H, 9.36% Cl, 14.79% N; found: 63.27% C, 3.90% H, 9.25% Cl, 14.55% N. FAB MS, *m/z* (%): 379 (M^+, 26), 345 (3), 105 (83), 91 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 5.40 (s, 2 H, CH_2-N); 5.80 (s, 2 H, CH_2-O-6); 7.28–7.49 (m, 7 H, Bn and H-*m*-Bz); 7.58 (m, 2 H, H-*p*-Bz); 7.98 (s, 1 H, H-8); 8.14 (m, 2 H, H-*o*-Bz). ^{13}C NMR (100.6 MHz, $CDCl_3$): 47.53 (CH_2-N); 63.04 (CH_2-O); 128.13 (CH-*m*-Bn); 128.38 (CH-*m*-Bz); 128.90 (CH-*p*-Bn); 129.28 (CH-*o*-Bn); 129.64 (C-*i*-Bn); 130.01 (CH-*o*-Bz); 130.93 (C-5); 133.19 (CH-*p*-Bz); 134.33 (C-*i*-Bn); 145.31 (CH-8); 153.58 (C-4); 154.20 (C-2); 157.59 (C-6); 166.33 (CO). IR ($CHCl_3$): 3035, 2943, 1726, 1592, 1502, 1452, 1356, 1317, 1272, 1115, 1029, 712, 646.

2,6-Bis(benzoyloxymethyl)-9-benzylpurine (**17a**). White solid, m.p. 116–117 °C. For $C_{28}H_{22}N_4O_4$ (478.5) calculated: 70.28% C, 4.63% H, 11.71% N; found: 70.00% C, 4.63% H, 11.46% N. FAB MS, *m/z* (%): 479 (M^+, 27), 374 (3), 105 (100), 91 (74). ^{1}H NMR (400 MHz, $CDCl_3$): 5.34 (s, 2 H, CH_2-N); 5.66 (s, 2 H, CH_2-O-2); 5.84 (s, 2 H, CH_2-O-6); 7.23–7.32 (m, 5 H, Bn); 7.37–7.47 (m, 4 H, H-*m*-Bz); 7.51–7.61 (m, 2 H, H-*p*-Bz); 8.02 (s, 1 H, H-8); 8.06–8.16 (m, 2 H, H-*o*-Bz). ^{13}C NMR (100.6 MHz, $CDCl_3$): 47.47 (CH_2-N); 63.13 (CH_2-O-6); 66.65 (CH_2-O-2); 128.22 (CH-*m*-Bn); 128.31 and 128.34 (CH-*m*-Bz); 128.61 (CH-*p*-Bn); 129.06 (CH-*o*-Bn); 129.84 and 129.93 (CH-*o*-Bz); 130.15 (C-*i*-Bn); 130.69 (C-5); 132.99 (CH-*p*-Bz); 134.86 (C-*i*-Bn); 144.64 (CH-8); 152.24 (C-4); 155.35 (C-6); 159.02 (C-2); 166.37 (CO). IR ($CHCl_3$): 3033, 2949, 1725, 1596, 1505, 1452, 1403, 1367, 1316, 1273, 1118, 1028, 712, 647.

6-(Benzoyloxymethyl)-2-chloro-9-(tetrahydropyran-2-yl)purine (**16b**). White solid, m.p. 92–93 °C. For $C_{18}H_{17}ClN_4O_3$ (372.8) calculated: 57.99% C, 4.60% H, 9.51% Cl, 15.03% N; found: 58.01% C, 4.54% H, 9.46% Cl, 14.77% N. FAB MS, *m/z* (%): 373 (M^+, 9), 289 (57), 183 (5), 105 (100), 85 (93). ^{1}H NMR (400 MHz, $CDCl_3$): 1.62–1.87 and 1.90–2.19 (m, 6 H, CH_2-THP); 3.78 (td, 1 H, *J* = 11.6 and 2.8, bCH_2-O-THP); 4.17 (ddt, 1 H, *J* = 11.6, 4.3 and 1.9, aCH_2-O-THP); 5.77 (d, 1 H, *J* = 14.3, bCH_2-O-6); 5.79 (dd, 1 H, *J* = 11.0 and 2.5, CH-O-THP); 5.79 (d, 1 H, *J* = 14.3, aCH_2-O-6); 7.46 (m, 2 H, H-*m*-Ph); 7.68 (m, 1 H, H-*p*-Ph); 8.14 (m, 2 H, H-*o*-Ph); 8.27 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 22.60, 24.77 and 32.05 (CH_2-THP); 62.98 (CH_2-O-6); 68.90 (CH_2-O-THP); 81.95 (CH-O-THP); 128.37 (CH-*m*-Ph); 129.63 (C-*i*-Ph); 130.02 (CH-*o*-Ph); 131.08 (C-5); 133.18 (CH-*p*-Ph); 143.39 (CH-8); 152.63

(C-4); 153.99 (C-2); 157.45 (C-6); 166.30 (CO). IR ($CHCl_3$): 3031, 2952, 2866, 1726, 1594, 1452, 1368, 1316, 1272, 1115, 1089, 1028, 712, 642.

2,6-Bis(benzoyloxymethyl)-9-(tetrahydropyran-2-yl)purine (**17b**). White solid, m.p. 89–91 °C. For $C_{26}H_{24}N_4O_5$ (472.5) calculated: 66.09% C, 5.12% H, 11.86% N; found: 65.85% C, 5.03% H, 11.63% N. FAB MS, *m/z* (%): 473 (M^+, 14), 389 (36), 283 (2), 105 (100), 85 (41). ^{1}H NMR (400 MHz, $CDCl_3$): 1.55–1.75 and 1.93–2.15 (m, 6 H, CH_2-THP); 3.68 (td, 1 H, *J* = 11.6 and 2.9, bCH_2-O-THP); 4.12 (ddt, 1 H, *J* = 11.6, 3.9 and 2.2, aCH_2-O-THP); 5.63 (s, 2 H, CH_2-O-2); 5.70 (dd, 1 H, *J* = 9.8 and 3.0, CH-O-THP); 5.82 and 5.86 (2 × d, 2 × 1 H, *J* = 14.2, CH_2-O-6); 7.41 (m, 4 H, H-*m*-Ph); 7.55 (m, 2 H, H-*p*-Ph); 8.09 (m, 4 H, H-*o*-Ph); 8.26 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 22.56, 24.77 and 31.56 (CH_2-THP); 63.10 (CH_2-O-6); 66.78 (CH_2-O-2); 68.65 (CH_2-O-THP); 82.18 (CH-O-THP); 128.29 (CH-*m*-Ph); 129.82 and 129.92 (CH-*o*-Ph); 130.19 (C-*i*-Ph); 130.89 (C-5); 132.92 and 132.97 (CH-*p*-Ph); 142.94 (CH-8); 151.39 (C-4); 155.32 (C-6); 158.79 (C-2); 166.32 and 166.42 (CO). IR ($CHCl_3$): 3030, 2951, 2865, 1725, 1596, 1499, 1452, 1399, 1316, 1273, 1116, 1088, 1028, 712, 645.

*6-(Benzoyloxymethyl)-2-chloro-9-(2,3,5-tri-O-benzoyl-*β*-D-ribofuranosyl)purine* (**16h**). White solid, m.p. 63–65 °C. For $C_{39}H_{29}ClN_4O_9$ (733.1) calculated: 63.89% C, 3.99% H, 4.84% Cl, 7.64% N; found: 63.51% C, 4.09% H, 4.85% Cl, 7.27% N. FAB MS, *m/z* (%): 733 (M^+, 1), 445 (4), 289 (1), 105 (38). ^{1}H NMR (400 MHz, $CDCl_3$): 4.73 (dd, 1 H, J_{gem} = 12.0, $J_{5'b4'}$ = 4.1, H-5′b); 4.85 (q, 1 H, $J_{4'5'b}$ = 4.1, $J_{4'3'}$ = 4.0, $J_{4'5'a}$ = 3.3, H-4′); 4.90 (dd, 1 H, J_{gem} = 10.6, $J_{5'a4'}$ = 3.3, H-5′a); 5.77 (s, 2 H, CH_2); 6.14 (dd, 1 H, $J_{3'2'}$ = 5.8, $J_{3'4'}$ = 4.0, H-3′); 6.17 (t, 1 H, $J_{2'3'}$ = 5.8, $J_{2'1'}$ = 5.2, H-2′); 6.52 (d, 1 H, $J_{1'2'}$ = 5.2, H-1′); 7.35–7.48 (m, 8 H, *m*-H-Bz); 7.53–7.63 (m, 4 H, *p*-H-Bz); 7.95, 8.02, 8.07 and 8.12 (4 × m, 4 × 2 H, *o*-H-Bz); 8.22 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 62.93 (CH_2); 63.62 (CH_2-5′); 71.51 (CH-3′); 74.24 (CH-2′); 81.28 (CH-4′); 86.47 (CH-1′); 126.16 (C-*i*-Bz); 128.38, 128.57, 128.59 and 128.70 (CH-*m*-Bz); 129.13 and 129.55 (C-*i*-Bz); 129.65, 129.86, 129.92 and 130.03 (CH-*o*-Bz); 131.58 (C-5); 133.21, 133.54, 133.83 and 133.92 (CH-*p*-Bz); 143.47 (CH-8); 153.11 (C-4); 154.44 (C-2); 158.10 (C-6); 165.12, 165.30, 166.08 and 166.26 (CO). IR (CCl_4): 3073, 3065, 2954, 1734, 1603, 1587, 1494, 1452, 1398, 1316, 1267, 1114, 1094, 1026, 710, 639.

*2,6-Bis(benzoyloxymethyl)-9-(2,3,5-tri-O-benzoyl-*β*-D-ribofuranosyl)purine* (**17h**). White foam. Exact mass (FAB HR MS) calculated for $C_{47}H_{37}N_4O_{11}$: 833.2459, found: 833.2425. FAB MS, *m/z* (%): 833 (M^+, 8), 713 (5), 445 (9), 389 (4), 180 (15), 105 (100). ^{1}H NMR (200 MHz, $CDCl_3$): 4.59–4.80 (m, 3 H, H-4′ and 2 × H-5′); 5.60 and 5.68 (2 × d, 2 × 1 H, *J* = 14.0, CH_2-O-2); 5.83 (s, 2 H, CH_2-O-6); 6.06 (t, 1 H, *J* = 5.4, H-3′); 6.32 (dd, 1 H, $J_{2'3'}$ = 5.6, $J_{2'1'}$ = 4.4, H-2′); 6.40 (d, 1 H, $J_{1'2'}$ = 4.4, H-1′); 7.30–7.60 (m, 15 H, *m*-H-Bz and *p*-H-Bz); 7.86–8.11 (m, 10 H, *o*-H-Bz); 8.20 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 63.05 (CH_2O-6); 63.81 (CH_2-5′); 66.47 (CH_2O-2); 71.64 (CH-3′); 74.14 (CH-2′); 80.70 (CH-4′); 87.51 (CH-1′); 128.28, 128.32, 128.44, 128.50 and 128.53 (CH-*m*-Bz); 129.28 (C-*i*-Bz); 129.66, 129.81, 129.82, 129.86 and 129.96 (CH-*o*-Bz); 131.54 (C-5); 132.91, 133.02, 133.38, 133.60, and 133.79 (CH-*p*-Bz); 143.77 (CH-8); 151.63 (C-4); 156.07 (C-6); 159.47 (C-2); 165.03, 165.09, 166.02, 166.17 and 166.32 (C=O).

*2,6-Bis(benzoyloxymethyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**17c**). White foam. Exact mass (FAB HR MS) calculated for $C_{32}H_{31}N_4O_{11}$: 647.1989, found: 647.1989. FAB MS, *m/z* (%): 647 (MH^+, 8), 389 (10), 259 (9), 105 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 2.03, 2.06 and 2.08 (3 × s, 3 × 3 H, CH_3-Ac); 4.28 (dd, 1 H, J_{gem} = 12.2, $J_{5'b,4'}$ = 5.0, H-5′b); 4.32 (dd, 1 H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.8, H-5′a); 4.40 (td, 1 H, $J_{4',5'}$ = 5.0, 3.8, $J_{4',3'}$ = 4.8, H-4′); 5.52 (t, 1 H, $J_{3',2'}$ = 5.4, $J_{3',4'}$ = 4.8, H-3′); 5.62 and 5.66 (2 × d, 2 H, J_{gem} = 14.3, CH_2O-2); 5.84 (s, 2 H, CH_2O-6); 5.93 (t, 1 H, $J_{2',3'}$ = 5.4, $J_{2',1'}$ = 5.2, H-2′); 6.17 (d, 1 H, $J_{1',2'}$ = 5.2, H-1′);

7.38–7.46 (m, 4 H, H-*m*-Bz); 7.53–7.59 (m, 2 H, H-*p*-Bz); 8.07–8.13 (m, 4 H, H-*o*-Bz); 8.18 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 20.29, 20.43 and 20.69 (CH_3); 63.06 (CH_2O-6); 63.13 (CH_2-5′); 66.50 (CH_2O-2); 70.62 (CH-3′); 72.99 (CH-2′); 80.30 (CH-4′); 86.62 (CH-1′); 128.33 (CH-*m*-Bz); 129.73 (C-*i*-Bz); 129.93 (CH-*o*-Bz); 131.47 (C-5); 132.99 and 133.06 (CH-*p*-Bz); 143.36 (CH-8); 151.62 (C-4); 156.09 (C-6); 159.36 (C-2); 166.15 and 166.33 (CO-Bz); 169.24, 169.35 and 170.20 (CO-Ac). IR (CCl_4): 3072, 3065, 1756, 1732, 1594, 1501, 1452, 1370, 1316, 1270, 1223, 1116, 1071, 642.

*6-(Benzoyloxymethyl)-2-chloro-9-(2-deoxy-3,5-di-O-toluoyl-*β*-D-erythro-pentofuranosyl)purine* (**16d**). White solid, m.p. 136–137 °C. For $C_{34}H_{29}ClN_4O_7$ (641.1) calculated: 63.70% C, 4.56% H, 5.53% Cl, 8.74% N; found: 63.58% C, 4.61% H, 5.59% Cl, 8.53% N. Exact mass (FAB HR MS) calculated for $C_{34}H_{30}ClN_4O_7$: 641.1803, found: 641.1793. FAB MS, *m/z* (%): 641 (MH^+, 4), 521 (3), 353 (4), 289 (12), 119 (85), 105 (20). ^{1}H NMR (500 MHz, $CDCl_3$): 2.39 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.90 (ddd, 1 H, J_{gem} = 14.3, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 2.6, H-2′b); 2.95 (ddd, 1 H, J_{gem} = 14.3, $J_{2'a,1'}$ = 8.1, $J_{2'a,3'}$ = 5.9, H-2′a); 4.64–4.70 (m, 3 H, H-4′ and H-5′b); 4.75 (m, 1 H, H-5′a); 5.77 (s, 2 H, CH_2-O-6); 5.78 (dt, 1 H, $J_{3',2'}$ = 5.9, 2.6 $J_{3',4'}$ = 2.4, H-3′); 6.59 (dd, 1 H, $J_{1'2'}$ = 8.1, 6.2, H-1′); 7.20 and 7.29 (2 × m, 2 × 2 H, H-*m*-Tol); 7.45 (m, 2 H, H-*m*-Bz); 7.58 (m, 1 H, H-*p*-Bz); 7.86 and 7.98 (2 × m, 2 × 2 H, H-*o*-Tol); 8.13 (m, 2 H, H-*o*-Bz); 8.24 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 21.68 and 21.76 (CH_3-Tol); 38.47 (CH_2-2′); 62.92 (CH_2-O-6); 63.92 (CH_2-5′); 74.94 (CH-3′); 83.37 (CH-4′); 84.75 (CH-1′); 126.22 and 126.46 (C-*i*-Tol); 128.39 (CH-*m*-Bz); 129.32 and 129.33 (CH-*m*-Tol); 129.56 (CH-*o*-Tol); 129.64 (C-*i*-Bz); 129.85 (CH-*o*-Tol); 130.02 (CH-*o*-Bz); 131.53 (C-5); 133.22 (CH-*p*-Bz); 143.33 (CH-8); 144.31 and 144.65 (C-*p*-Tol); 152.84 (C-4); 154.13 (C-2); 157.79 (C-6); 165.93 and 166.07 (CO-Tol); 166.29 (CO-Bz). IR (CCl_4): 3038, 1730, 1613, 1590, 1495, 1452, 1317, 1267, 1211, 1178, 1099, 1021, 709, 638.

*2,6-Bis(benzoyloxymethyl)-9-(2-deoxy-3,5-di-O-toluoyl-*β*-D-erythro-pentofuranosyl)purine* (**17d**). White solid, m.p. 92–93 °C. For $C_{42}H_{36}N_4O_9$ (740.8) calculated: 68.10% C, 4.90% H, 7.56% N; found: 67.92% C, 4.89% H, 7.44% N. Exact mass (FAB HR MS) calculated for $C_{42}H_{37}N_4O_9$: 741.2561, found: 741.2533. FAB MS, *m/z* (%): 741 (MH^+, 20), 621 (11), 435 (16), 389 (30), 269 (17), 119 (100), 105 (66). ^{1}H NMR (400 MHz, $CDCl_3$): 2.39 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.72 (ddd, 1 H, J_{gem} = 14.3, $J_{2'b,1'}$ = 6.0, $J_{2'b,3'}$ = 2.2, H-2′b); 3.17 (ddd, 1 H, J_{gem} = 14.3, $J_{2'a,1'}$ = 8.1, $J_{2'a,3'}$ = 6.4, H-2′a); 4.55–4.65 (m, 3 H, H-4′ and H-5′); 5.59 (dt, 1 H, $J_{3',2'}$ = 6.4, 2.2, $J_{3',4'}$ = 2.2, H-3′); 5.61 and 5.66 (2 × d, 2 H, J_{gem} = 14.3, CH_2-O-2); 5.82 (s, 2 H, CH_2-O-6); 6.49 (dd, 1 H, $J_{1'2'}$ = 8.1, 6.0, H-1′); 7.19 and 7.27 (2 × m, 2 × 2 H, H-*m*-Tol); 7.35 and 7.40 (2 × m, 2 × 2 H, H-*m*-Bz); 7.47 and 7.55 (2 × m, 2 × 1 H, H-*p*-Bz); 7.83 and 7.92 (2 × m, 2 × 2 H, H-*o*-Tol); 8.06–8.12 (m, 4 H, H-*o*-Bz); 8.21 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 21.66 and 21.74 (CH_3-Tol); 37.37 (CH_2-2′); 63.04 (CH_2-O-6); 63.98 (CH_2-5′); 66.55 (CH_2-O-2); 75.07 (CH-3′); 83.13 (CH-4′); 85.26 (CH-1′); 126.40 and 126.59 (C-*i*-Tol); 128.32 and 128.36 (CH-*m*-Bz); 129.22 and 129.26 (CH-*o*-Bz); 129.60, 129.79 and 129.93 (CH-Tol); 131.51 (C-5); 133.02 (CH-*p*-Bz); 143.41 (CH-8); 144.12 and 144.47 (C-*p*-Tol); 151.51 (C-4); 155.73 (C-6); 159.00 (C-2); 165.74 and 166.05 (CO-Tol); 166.30 (CO-Bz). IR ($CHCl_3$): 1723, 1612, 1596, 1501, 1452, 1316, 1272, 1178, 1105, 1021, 713, 644.

2-(Benzoyloxymethyl)-9-benzyl-6-chloropurine (**19a**). White solid, m.p. 91–92 °C. For $C_{20}H_{15}ClN_4O_2$ (378.8) calculated: 63.41% C, 3.99% H, 9.36% Cl, 14.79% N; found: 63.32% C, 3.98% H, 9.21% Cl, 14.62% N. FAB MS, *m/z* (%): 379 (MH^+, 17), 345 (1), 273 (2), 105 (78), 91 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 5.33 (s, 2 H, CH_2-N); 5.64 (s, 2 H, CH_2-O); 7.22–7.34 (m, 5 H, Bn); 7.49 (m, 2 H, H-*m*-Bz); 7.61 (m, 1 H, H-*p*-Bz); 8.07 (s, 1 H, H-8); 8.17 (m, 2 H, H-*o*-Bz). ^{13}C NMR (100.6 MHz, $CDCl_3$): 48.01 (CH_2-N); 66.10 (CH_2-O); 128.21

(CH-*o*-Bn); 128.43 (CH-*m*-Bz); 128.80 (CH-*p*-Bn); 129.14 (CH-*m*-Bn); 129.91 (CH-*o*-Bz); 129.95 (C-*i*-Bn); 130.41 (C-5); 133.20 (CH-*p*-Bz); 134.41 (C-*i*-Bn); 144.91 (CH-8); 151.17 (C-6); 152.23 (C-4); 159.32 (C-2); 166.27 (CO). IR (CCl_4): 3070, 3036, 1732, 1596, 1562, 1500, 1452, 1401, 1316, 1270, 1116, 1030, 649.

2-(Benzoyloxymethyl)-6-chloro-9-(tetrahydropyran-2-yl)purine (**19b**). White solid, m.p. 106–107 °C. For $C_{18}H_{17}ClN_4O_3$ (372.8) calculated: 57.99% C, 4.60% H, 9.51% Cl, 15.03% N; found: 57.87% C, 4.66% H, 9.41% Cl, 14.94% N. Exact mass (FAB HR MS) calculated for $C_{18}H_{18}ClN_4O_3$: 373.1067, found: 373.1060. FAB MS, *m/z* (%): 373 (MH^+, 36), 339 (52), 289 (87), 255 (75), 149 (12), 105 (100), 85 (76). ^{1}H NMR (500 MHz, $CDCl_3$): 1.57–1.70 and 1.92–2.12 (m, 6 H, CH_2-THP); 3.66 (td, 1 H, J = 11.6 and 3.3, bCH_2-O-THP); 4.11 (ddt, 1 H, J = 11.6, 4.3 and 2.0, aCH_2-O-THP); 5.61 (s, 2 H, CH_2-O); 5.65 (dd, 1 H, J = 10.2 and 2.6, CH-O-THP); 7.48 (m, 2 H, H-*m*-Ph); 7.60 (m, 1 H, H-*p*-Ph); 8.16 (m, 2 H, H-*o*-Ph); 8.29 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, $CDCl_3$): 22.42, 24.67 and 31.52 (CH_2-THP); 66.27 (CH_2-O); 68.68 (CH_2-O-THP); 82.69 (CH-O-THP); 128.38 (CH-*m*-Ph); 129.89 (CH-*o*-Ph); 129.99 (C-*i*-Ph); 131.61 (C-5); 133.14 (CH-*p*-Ph); 143.30 (CH-8); 151.13 (C-6); 151.34 (C-4); 159.05 (C-2); 166.34 (C=O). IR (CCl_4): 3073, 2949, 2858, 1732, 1596, 1562, 1494, 1452, 1401, 1316, 1269, 1211, 1115, 647.

*2-(Benzoyloxymethyl)-6-chloro-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**19c**). White foam. Exact mass (FAB HR MS) calculated for $C_{24}H_{24}ClN_4O_9$: 547.1232, found: 547.1220. FAB MS, *m/z* (%): 547 (MH^+, 19), 289 (8), 259 (18), 105 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 2.02, 2.07 and 2.08 (3 × s, 3 × 3 H, CH_3-Ac); 4.27 (dd, 1 H, J_{gem} = 12.2, $J_{5'b,4'}$ = 4.9, H-5′b); 4.30 (dd, 1 H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.8, H-5′a); 4.40 (td, 1 H, $J_{4',3'}$ = 4.9, $J_{4',5'}$ = 4.9, 3.8, H-4′); 5.45 (t, 1 H, $J_{3',2'}$ = 5.7, $J_{3',4'}$ = 4.9, H-3′); 5.61 and 5.65 (2 × d, 2 H, J_{gem} = 14.5, CH_2-O); 5.86 (t, 1 H, $J_{2',3'}$ = 5.7, $J_{2',1'}$ = 4.9, H-2′); 6.13 (d, 1 H, $J_{1',2'}$ = 4.9, H-1′); 7.48 (m, 2 H, H-*m*-Bz); 7.60 (m, 1 H, H-*p*-Bz); 8.17 (m, 2 H, H-*o*-Bz); 8.26 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 20.23, 20.39 and 20.68 (CH_3); 63.01 (CH_2-5′); 65.99 (CH_2-O); 70.48 (CH-3′); 73.14 (CH-2′); 80.38 (CH-4′); 87.09 (CH-1′); 128.42 (CH-*m*-Bz); 129.71 (C-*i*-Bz); 130.02 (CH-*o*-Bz); 131.26 (C-5); 133.20 (CH-*p*-Bz); 143.67 (CH-8); 151.52 (C-4); 151.75 (C-6); 159.73 (C-2); 166.05 (CO-Bz); 169.21, 169.30 and 170.15 (CO-Ac). IR (CCl_4): 3065, 1756, 1733, 1596, 1564, 1497, 1452, 1403, 1270, 1224, 1117, 641.

*2-(Benzoyloxymethyl)-6-chloro-9-(2-deoxy-3,5-di-O-toluoyl-*β*-D-erythro-pentofuranosyl)purine* (**19d**). White foam. Exact mass (FAB HR MS) calculated for $C_{34}H_{30}ClN_4O_7$: 641.1803, found: 641.1818. FAB MS, *m/z* (%): 641 (MH^+, 7), 607 (9), 353 (7), 289 (18), 255 (13), 119 (81), 105 (42). ^{1}H NMR (400 MHz, $CDCl_3$): 2.39 and 2.45 (2 × s, 2 × 3 H, CH_3-Tol); 2.72 (ddd, 1 H, J_{gem} = 14.4, $J_{2'b,1'}$ = 6.1, $J_{2'b,3'}$ = 2.3, H-2′b); 3.12 (ddd, 1 H, J_{gem} = 14.4, $J_{2'a,1'}$ = 7.9, $J_{2'a,3'}$ = 6.4, H-2′a); 4.55 (dd, 1 H, J_{gem} = 10.9, $J_{5'b,4'}$ = 4.5, H-5′b); 4.58 (ddd, 1 H, $J_{4',5'}$ = 4.5, 3.3, $J_{4',3'}$ = 2.2, H-4′); 4.65 (dd, 1 H, J_{gem} = 10.9, $J_{5'a,4'}$ = 3.3, H-5′a); 5.57 (dt, 1 H, $J_{3',2'}$ = 6.4, 2.3 $J_{3',4'}$ = 2.2, H-3′); 5.60 and 5.64 (2 × d, 2 H, J_{gem} = 14.5, CH_2-O); 6.44 (dd, 1 H, $J_{1'2'}$ = 7.9, 6.1, H-1′); 7.19 and 7.27 (2 × m, 2 × 2 H, H-*m*-Tol); 7.40 (m, 2 H, H-*m*-Bz); 7.49 (m, 1 H, H-*p*-Bz); 7.80 and 7.90 (2 × m, 2 × 2 H, H-*o*-Tol); 8.15 (m, 2 H, H-*o*-Bz); 8.25 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, $CDCl_3$): 21.66 and 21.74 (CH_3-Tol); 37.57 (CH_2-2′); 63.80 (CH_2-5′); 66.03 (CH_2-O); 75.00 (CH-3′); 83.45 (CH-4′); 85.74 (CH-1′); 126.31 and 126.40 (C-*i*-Tol); 128.44 (CH-*m*-Bz); 129.23 and 129.26 (CH-*m*-Tol); 129.51 (CH-*o*-Bz); 129.77 and 129.85 (CH-*o*-Tol); 131.16 (C-5); 133.22 (CH-*p*-Bz); 143.72 (CH-8); 144.23 and 144.53 (C-*p*-Tol); 151.34 (C-4); 151.42 (C-6); 159.24 (C-2); 165.71 and 165.97 (CO-Tol); 166.22 (CO-Bz). IR (CCl_4): 3037, 1729, 1613, 1595, 1562, 1494, 1452, 1404, 1268, 1215, 1100, 646.

General Procedure for Deacylation Reactions of **16**

Aqueous ammonia (25% solution, 1 ml) was added to a solution of protected purines or nucleosides **15** (0.5 mmol) in methanol (20 ml) and the mixture was stirred at ambient temperature. After complete deprotection, the solvent was evaporated and the residue was chromatographed.

9-Benzyl-2-chloro-6-(hydroxymethyl)purine (**20a**). Yield 87%, white solid, m.p. 127–128 °C. For $C_{13}H_{11}ClN_4O$ (274.7) calculated: 56.84% C, 4.04% H, 12.91% Cl, 20.40% N; found: 56.47% C, 3.90% H, 13.13% Cl, 20.35% N. Exact mass (FAB HR MS) calculated for $C_{13}H_{12}ClN_4O$: 275.0700, found: 275.0708. FAB MS, *m/z* (%): 275 (MH^+, 45), 183 (5), 91 (100). ^{1}H NMR (400 MHz, DMSO-d_6): 4.86 (d, 2 H, J_{vic} = 6.2, CH_2-O); 5.48 (s, 2 H, CH_2-N); 5.61 (t, 1 H, J_{vic} = 6.2, OH); 7.28–7.39 (m, 5 H, Ph); 8.73 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 46.78 (CH_2-N); 59.78 (CH_2-O); 127.60 (CH-*o*-Ph); 128.20 (CH-*p*-Ph); 129.01 (CH-*m*-Ph); 130.54 (C-5); 136.26 (C-*i*-Ph); 147.30 (CH-8); 152.86 (C-4); 153.03 (C-2); 162.41 (C-6). IR ($CHCl_3$): 3491, 3070, 1597, 1501, 1456, 1412, 1364, 1319, 1240, 1070, 647.

2-Chloro-6-(hydroxymethyl)-9-(tetrahydropyran-2-yl)purine (**20b**). Yield 90%, white solid, m.p. 54–55 °C. Exact mass (FAB HR MS) calculated for $C_{11}H_{14}ClN_4O_2$: 269.0805, found: 269.0797. FAB MS, *m/z* (%): 269 (MH^+, 12), 185 (91), 151 (7), 85 (100). ^{1}H NMR (500 MHz, DMSO-d_6): 1.55–1.66, 1.76, 1.94–2.03 and 2.28 (4 × m, 6 H, CH_2-THP); 3.73 and 4.02 (2 × m, 2 H, CH_2-O-THP); 4.87 (d, 2 H, J_{vic} = 6.3, CH_2-O); 5.62 (t, 1 H, J_{vic} = 6.3, OH); 5.73 (dd, 1 H, *J* = 10.9, 2.3, CH-O-THP); 8.82 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 22.36, 24.62 and 29.88 (CH_2-THP); 59.79 (CH_2-O); 67.92 (CH_2-O-THP); 81.40 (CH-O-THP); 130.60 (C-5); 145.26 (CH-8); 152.46 (C-4); 152.92 (C-2); 162.63 (C-6). IR ($CHCl_3$): 3481, 1598, 1498, 1455, 1442, 1412, 1385, 1331, 1088, 645.

2-Chloro-6-(hydroxymethyl)-9-(β-D-ribofuranosyl)purine (**20f**). Yield 84% of white hygroscopic solid (m.p. 129–131 °C), which was crystallized from 2-propanol/heptane, $[\alpha]_D^{20}$ –45.9 (*c* 0.25, MeOH). Exact mass (FAB HR MS) calculated for $C_{11}H_{14}ClN_4O_5$: 317.0653, found: 317.0639. FAB MS, *m/z* (%): 317 (MH^+, 14), 149 (3), 133 (3). ^{1}H NMR (400 MHz, CD_3OD): 3.79 (dd, 1 H, J_{gem} = 12.3, $J_{5'b,4'}$ = 3.4, H-5′b); 3.90 (dd, 1 H, J_{gem} = 12.3, $J_{5'a,4'}$ = 3.1, H-5′a); 4.15 (q, 1 H, $J_{4',3'}$ = 4.0, $J_{4',5'}$ = 3.4, 3.1, H-4′); 4.36 (dd, 1 H, $J_{3',2'}$ = 5.2, $J_{3',4'}$ = 4.0, H-3′); 4.68 (t, 1 H, $J_{2',1'}$ = 5.3, $J_{2',3'}$ = 5.2, H-2′); 5.04 (s, 2 H, CH_2-OH); 6.10 (d, 1 H, $J_{1',2'}$ = 5.3, H-1′); 8.75 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, CD_3OD): 61.55 (CH_2-O); 62.76 (CH_2-5′); 71.93 (CH-3′); 75.86 (CH-2′); 87.86 (CH-4′); 90.56 (CH-1′); 132.01 (C-5); 146.76 (CH-8); 153.93 (C-4); 155.07 (C-2); 163.37 (C-6). IR (KBr): 3391, 1594, 1499, 1387, 1327, 1211, 1083, 1054, 637.

2-Chloro-9-(2-deoxy-β-D-erythro-pentofuranosyl)-6-(hydroxymethyl)purine (**20g**). Yield 87% of white (hygroscopic) solid (m.p. 99–101 °C), which was crystallized from 2-propanol/heptane, $[\alpha]_D^{20}$ +51.8 (*c* 0.28, MeOH). For $C_{11}H_{13}ClN_4O_4$ (300.7) calculated: 43.94% C, 4.36% H, 11.79% Cl, 18.63% N; found: 43.61% C, 4.41% H, 11.43% Cl, 18.32% N. Exact mass (FAB HR MS) calculated for $C_{11}H_{14}ClN_4O_4$: 301.0704, found: 301.0717. FAB MS, *m/z* (%): 301 (MH^+, 35), 185 (100), 167 (8), 117 (19). ^{1}H NMR (400 MHz, CD_3OD): 2.50 (ddd, 1 H, J_{gem} = 13.6, $J_{2'b,1'}$ = 6.4, $J_{2'b,3'}$ = 3.8, H-2′b); 2.82 (ddd, 1 H, J_{gem} = 13.6, $J_{2'a,1'}$ = 6.9, $J_{2'a,3'}$ = 6.1, H-2′a); 3.75 (dd, 1 H, J_{gem} = 12.1, $J_{5'b,4'}$ = 4.2, H-5′b); 3.84 (dd, 1 H, J_{gem} = 12.1, $J_{5'a,4'}$ = 3.6, H-5′a); 4.05 (q, 1 H, $J_{4',5'}$ = 4.2, 3.6, $J_{4',3'}$ = 3.3, H-4′); 4.60 (dt, 1 H, $J_{3',2'}$ = 6.1, 3.8, $J_{3',4'}$ = 3.3, H-3′); 5.03 (s, 2 H, CH_2-O); 6.50 (t, 1 H, $J_{1'2'}$ = 6.9, 6.4, H-1′); 8.71 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, CD_3OD): 41.28 (CH_2-2′); 61.49 (CH_2-O); 63.11 (CH_2-5′); 72.46 (CH-3′); 86.46 (CH-1′); 89.62 (CH-4′); 131.93 (C-5); 146.66 (CH-8); 153.72 (C-4); 154.98 (C-2); 163.17 (C-6). IR (KBr): 3492, 1593, 1498, 1387, 1327, 1211, 1093, 1056, 642.

2-Chloro-6-(hydroxymethyl)-9*H*-purine (**20e**)

Yield 84%, prepared from **20b** with Dowex 50X8 (H^+) in ethanol (96%). The reaction mixture was stirred at 70–75 °C for 2 h, filtered, the resin was washed with ethanolic ammonia and the collected solution was evaporated to dryness. The crude product was chromatographed (ethyl acetate/methanol 8:2) afforded white solid, which was crystallized from ethanol/heptane (m.p. 213–214 °C). For $C_6H_5ClN_4O$ (184.6) calculated: 39.04% C, 2.73% H, 19.21% Cl, 30.35% N; found: 38.61% C, 2.82% H, 18.78% Cl, 29.83% N. Exact mass (FAB HR MS) calculated for $C_6H_6ClN_4O$: 185.0230, found: 185.0227. FAB MS, *m/z* (%): 185 (MH^+, 100), 151 (6). ^{1}H NMR (400 MHz, DMSO-d_6 + CF_3COOD): 4.86 (s, 2 H, 6-CH_2-O); 8.64 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6 + CF_3COOD): 62.11 (6-CH_2-O); 123.54 (C-5); 146.57 (CH-8); 152.28 (C-2); 159.15 (C-6); 160.57 (C-4). IR (KBr): 3382, 3003, 1613, 1563, 1473, 1376, 1301, 1233, 1078, 623.

General Procedure for Deacylation Reactions of **17**

A 1 M methanolic MeONa (0.1 ml, 0.1 mmol) was added to a solution of a protected purines or nucleosides **17** (0.5 mmol) in methanol (20 ml) and the mixture was stirred at ambient temperature. After complete deprotection, the solvent was evaporated and the residue was chromatographed.

9-Benzyl-2,6-bis(hydroxymethyl)purine (**21a**). Yield 87%, white solid, m.p. 76–77 °C. For $C_{14}H_{14}N_4O_2$ (270.3) calculated: 62.21% C, 5.22% H, 20.73% N; found: 61.83% C, 5.43% H, 20.36% N. Exact mass (FAB HR MS) calculated for $C_{14}H_{15}N_4O_2$: 271.1195, found: 271.1184. FAB MS, *m/z* (%): 271 (MH^+, 100), 181 (4), 163 (3), 91 (82). ^{1}H NMR (500 MHz, DMSO-d_6): 4.69 (d, 2 H, J_{vic} = 5.9, CH_2-O-2); 4.90 (d, 2 H, J_{vic} = 5.7, CH_2-O-6); 5.27 (t, 1 H, J_{vic} = 5.9, OH-2); 5.40 (t, 1 H, J_{vic} = 5.7, OH-6); 5.51 (s, 2 H, CH_2-N); 7.26–7.37 (m, 5 H, Ph); 8.63 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 46.37 (CH_2-N); 60.16 (CH_2-O-6); 65.08 (CH_2-O-2); 127.65 (CH-*o*-Ph); 128.07 (CH-*p*-Ph); 128.96 (CH-*m*-Ph); 129.61 (C-5); 136.89 (C-*i*-Ph); 146.06 (CH-8); 151.69 (C-4); 159.33 (C-6); 163.17 (C-2). IR ($CHCl_3$): 3472, 3070, 1599, 1505, 1456, 1409, 1360, 1315, 1247, 1072, 649.

2,6-Bis(hydroxymethyl)-9-(tetrahydropyran-2-yl)purine (**21b**). Yield 89%, white solid, m.p. 100–101 °C. Exact mass (FAB HR MS) calculated for $C_{12}H_{17}N_4O_3$: 265.1301, found: 265.1312. FAB MS, *m/z* (%): 265 (MH^+, 18), 181 (84), 165 (11), 149 (14), 85 (64). ^{1}H NMR (500 MHz, DMSO-d_6): 1.55–1.67, 1.76, 1.95–2.03 and 2.33 (4 × m, 6 H, CH_2-THP); 3.72 (m, 1 H, *J* = 11.5, 9.6, 4.8 and 3.6, bCH_2-O-THP); 4.02 (ddt, 1 H, *J* = 11.5, 3.9 and 2.4, aCH_2-O-THP); 4.70 (d, 2 H, J_{vic} = 5.4, CH_2-O-2); 4.90 (d, 2 H, J_{vic} = 5.4, CH_2-O-6); 5.28 (t, 1 H, J_{vic} = 5.4, OH-2); 5.40 (t, 1 H, J_{vic} = 5.4, OH-6); 5.79 (dd, 1 H, *J* = 11.0 and 2.2, CH-O-THP); 8.73 (s, 1 H, H-8). ^{13}C NMR (125.8 MHz, DMSO-d_6): 22.57, 24.66 and 30.17 (CH_2-THP); 60.15 (CH_2-O-6); 65.05 (CH_2-O-2); 67.94 (CH_2-O-THP); 80.97 (CH-O-THP); 129.65 (C-5); 143.99 (CH-8); 151.13 (C-4); 159.46 (C-6); 163.22 (C-2). IR (KBr): 3414, 3325, 1600, 1505, 1453, 1398, 1352, 1212, 1087, 1075, 1047, 644.

2,6-Bis(hydroxymethyl)-9-(β-D-ribofuranosyl)purine (**21f**). Yield 80% of white hygroscopic solid (m.p. 120–123 °C), which was crystallized from 2-propanol/heptane, $[\alpha]_D^{20}$ –17.7 (*c* 0.36, MeOH). For $C_{12}H_{16}N_4O_6 \cdot 1/2H_2O$ (321.3) calculated: 44.86% C, 5.33% H, 17.44% N; found: 44.78% C, 4.96% H, 17.10% N. Exact mass (FAB HR MS) calculated for $C_{12}H_{17}N_4O_6$: 313.1148, found: 313.1150. FAB MS, *m/z* (%): 313 (MH^+, 80), 279 (9), 181 (97), 163 (17), 149 (10), 133 (8). ^{1}H NMR (400 MHz, CD_3OD): 3.78 and 3.91 (2 × dd, 2 H, J_{gem} = 12.4, $J_{5',4'}$ = 3.2, H-5′); 4.16 (q, 1 H, $J_{4',3'}$ = 3.7, $J_{4',5'}$ = 3.2, H-4′); 4.37 (dd, 1 H, $J_{3',2'}$ = 5.2, $J_{3',4'}$ = 3.7,

H-3′); 4.72 (t, 1 H, $J_{2',1'}$ = 5.6, $J_{2',3'}$ = 5.2, H-2′); 4.86 (s, 2 H, 2-CH_2-OH); 5.10 (s, 2 H, 6-CH_2-OH); 6.15 (d, 1 H, $J_{1',2'}$ = 5.6, H-1′); 8.70 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, CD_3OD): 61.53 (6-CH_2-O); 62.90 (CH_2-5′); 65.97 (2-CH_2-O); 72.06 (CH-3′); 75.81 (CH-2′); 87.53 (CH-4′); 90.64 (CH-1′); 131.32 (C-5); 146.05 (CH-8); 152.57 (C-4); 160.86 (C-6); 164.37 (C-2). IR (KBr): 3401, 1598, 1505, 1402, 1350, 1219, 1084, 638.

9-(2-Deoxy-β-D-erythro-pentofuranosyl)-2,6-bis(hydroxymethyl)purine (**21g**). Yield 90% of white hygroscopic solid (m.p. 78–80 °C), which was crystallized from 2-propanol/heptane, $[\alpha]_D^{20}$ +49.5 (*c* 0.37, MeOH). For $C_{12}H_{16}N_4O_5 \cdot H_2O$ (314.3) calculated: 45.86% C, 5.77% H, 17.83% N; found: 46.23% C, 5.41% H, 17.62% N. Exact mass (FAB HR MS) calculated for $C_{12}H_{17}N_4O_5$: 297.1199, found: 297.1196. FAB MS, *m/z* (%): 297 (MH^+, 27), 181 (44), 163 (7), 117 (7). ^{1}H NMR (400 MHz, CD_3OD): 2.48 (ddd, 1 H, J_{gem} = 13.5, $J_{2'b,1'}$ = 6.3, $J_{2'b,3'}$ = 3.4, H-2′b); 2.85 (ddd, 1 H, J_{gem} = 13.5, $J_{2'a,1'}$ = 7.3, $J_{2'a,3'}$ = 6.0, H-2′a); 3.76 (dd, 1 H, J_{gem} = 12.1, $J_{5'b,4'}$ = 3.9, H-5′b); 3.84 (dd, 1 H, J_{gem} = 12.1, $J_{5'a,4'}$ = 3.4, H-5′a); 4.06 (q, 1 H, $J_{4',5'}$ = 3.9, 3.4, $J_{4',3'}$ = 3.1, H-4′); 4.61 (dt, 1 H, $J_{3',2'}$ = 6.0, 3.4, $J_{3',4'}$ = 3.1, H-3′); 4.86 (s, 2 H, 2-CH_2-O); 5.09 (s, 2 H, 6-CH_2-O); 6.59 (dd, 1 H, $J_{1'2'}$ = 7.3, 6.3, H-1′); 8.68 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, CD_3OD): 41.40 (CH_2-2′); 61.51 (6-CH_2-O); 63.26 (CH_2-5′); 66.02 (2-CH_2-O); 72.67 (CH-3′); 86.45 (CH-1′); 89.62 (CH-4′); 131.19 (C-5); 145.94 (CH-8); 152.41 (C-4); 160.65 (C-6); 164.26 (C-2). IR (KBr): 3413, 1599, 1502, 1396, 1320, 1217, 1092, 1057, 644.

2,6-Bis(hydroxymethyl)-9*H*-purine (**21e**)

Yield 74%, prepared from **21b** with Dowex 50X8 (H^+) in 96% ethanol. Reaction mixture was stirred at 70–75 °C for 2 h, filtered, the resin was washed with ethanolic ammonia and the collected solution was evaporated to dryness. Crude product was chromatographed (ethyl acetate/methanol 2:1) to give white solid, which was crystallized from methanol/ethyl acetate (m.p. > 300 °C). For $C_7H_8N_4O_2 \cdot 1/2H_2O$ (189.2) calculated: 44.44% C, 4.80% H, 29.62% N; found: 44.29% C, 4.39% H, 29.28% N. Exact mass (FAB HR MS) calculated for $C_7H_9N_4O_2$: 181.0726, found: 181.0729. FAB MS, *m/z* (%): 181 (MH^+, 44), 165 (6), 149 (10). ^{1}H NMR (400 MHz, DMSO-d_6): 4.64 (s, 2 H, 2-CH_2-O); 4.88 (s, 2 H, 6-CH_2-O); 8.51 (s, 1 H, H-8). ^{13}C NMR (100.6 MHz, DMSO-d_6): 62.06 (6-CH_2-O); 65.15 (2-CH_2-O); 123.94 (C-5); 146.51 (CH-8); 156.43 (C-6); 158.18 (C-4); 162.39 (C-2). IR (KBr): 3392, 1598, 1390, 1317, 1230, 1082, 1038, 638.

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