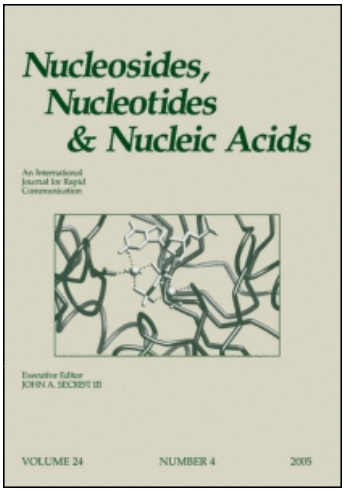

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NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS, 19(10–12), 1911–1929 (2000)

SUBSTITUENT – DIRECTED ARALKYLATION AND ALKYLATION REACTIONS OF THE TRICYCLIC ANALOGUES OF ACYCLOVIR AND GUANOSINE

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ABSTRACT: Aryl or *tert*-butyl substituent in the 6 position of 3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-6-R-5*H*-imidazo[1,2-*a*]purine (6-R-TACV)[1] **1** partly directs aralkylation reactions into unusual positions: N-4 to give **3** and C-7 to give N-5,7-disubstituted or N-4,7-disubstituted derivatives. In the case of alkylation the effect is limited to aryl substituent and position N-4. Replacement of acyclic moiety of **1** with a ribosyl one like in **7** prevents N-4 substitution. Cleavage of the third ring of **3b** to give 3-benzylacyclovir **10** is an example of a new short route to 3-aralkyl-9-substituted guanines.

Introduction

Tricyclic analogues of guanosine occur in nature as the so called wye nucleosides, fluorescent rare components of yeast phenylalanine transfer RNAs ($tRNA^{Phe}$) The simplest representative of this family, wyosine, is 3-methyl-1,N^2-(prop-1-ene-1,2-diyl)-guanosine (4,6-dihydro-4,6-dimethyl-9-oxo-3-(β-D-ribofuranosyl)-3*H*-imidazo[1,2-*a*]-purine).[2]

It has been previously found that similar modification of the guanine moiety of the potent antiherpetic drug acyclovir, 9-[(2-hydroxyethoxy)methyl]guanine, to form 3,9-dihydro-9-oxo-6-methyl-5*H*-imidazo-[1,2-*a*]purine system, enhances selectivity of

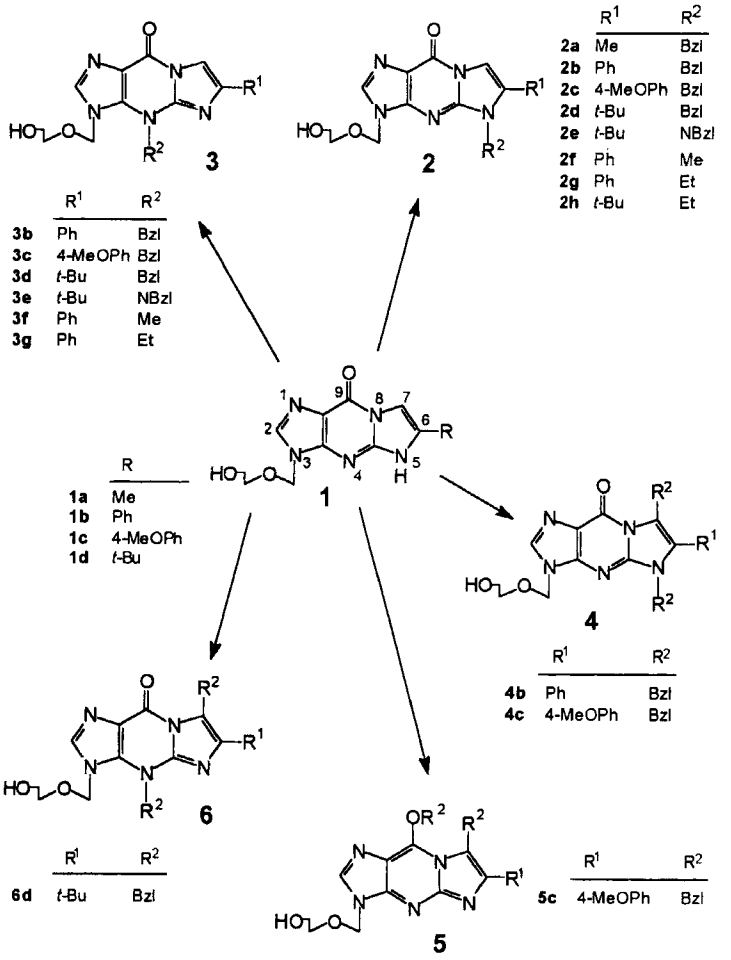
Dedicated to the memory of Professor Alexander A.Krayevsky

the parent compound.[3] Further search along this line has shown that the appended ring alone lowers the antiviral activity by the factor of 10^2 or more.[4] However the presence of certain substituents in the 6 position of that ring increases the activity and makes compounds more selective toward particular viruses. Substitution with phenyl group results in fluorescent analogues.[5,6] Here we describe a significant influence of substituents in the 6 position on the chemical reactivity of 3,9-dihydro-9-oxo-5*H*-imidazo-[1,2-*a*]-purine system linked in position 3 either to (2-hydroxyethoxy)methyl or to β-D-ribofuranosyl moieties. We examined the reactions of the anionic forms of four tricyclic analogues of acyclovir **1a-d** and two of their ribofuranosyl counterparts with aralkyl and alkyl halides.

Our initial intent was to introduce a variety of substituents directly into 7 position of compounds **1a-d**. We had been encouraged by the existence of 6,7-disubstitution pattern in other nucleosides of wye family[2] and strong enhancement of antiviral potency observed for 7-methyl-6-phenyl tricyclic analogue of acyclovir when compared with 6-phenyl one **1b**.[6] The first step towards the goal mentioned above was testing the usefulness of a benzyl group as a protection of N-5-H endoamine site of compounds **1a-d**. It has been known that when treated with alkyl or benzyl halides under alkaline conditions, 6-methyl substituted acyclo compound **1a** as well as its ribo and deoxyribo congeners undergo regioselective reaction at N-5.[3,7,8]

Results and Discussion

In accord with literature data, 6-methyl derivative **1a** in dry DMF treated with K_2CO_3 followed by benzyl bromide, at room temperature, for 5 hours, provided N-5 benzyl substituted **2a** as a single product in 80 % yield. In contrast to that, the presence of 6-aryl groups (R = phenyl, 4-methoxyphenyl in compounds **1b**, **1c**, respectively) led to a mixture of products which were separated on silica gel column. They are shown on Scheme 1 and Table 1. In addition to preponderant N-5 derivatives **2b**, **2c** minor N-4 **3b**, **3c**, N-5,7 **4b**, **4c** and 7,O[9] **5c** substituted products were isolated. In the case of 6-*tert*-butyl substrate **1d**, the N-4 substitution prevailed to give compound **3d** and N-4,7-disubstituted **6d**; 4-p-nitrobenzylation of **1d** resulted also in a similarly high yield of **3e**. The N-4 directing influence of 6-(4-methoxyphenyl) was not confirmed for 3-β-D-ribofuranosyl substrate **7c**. Benzylation and 4-nitrobenzylation performed using



SCHEME 1. Aralkylation and alkylation reactions of 6-substituted derivatives of TACV. Structures of compounds formed.

the same conditions furnished N-5 major products (**8c** and **8i**) and N-5,7-disubstituted minor products (**9c** and **9i**). It seems reasonable to assume that steric factor of ribose is responsible for prevention the N-4 substitution. The importance of steric hindrance located in the 3 position was verified by making use of substrate **7d** containing two bulky groups : 6-*tert*-butyl and 3-β-D-ribofuranosyl. This reaction did not start at all even after 7 days of treatment at room temperature with larger excess of K_2CO_3 / benzyl bromide.

Alkylation reactions of **1b** were also directed by 6-aryl substituents to some contribution of N-4 substitution comparable in yield with that of aralkylation. In contrast, however, the 6-*tert*-butyl group in **1d** had no effect. The 7-directing effect was also not observed. The possible explanation of this fact is that C-7 substitution of the tricyclic system with more bulky and more stable than methyl, aralkyl cation follows the mechanism which we recently suggested for C-7 tritylation.[9] The details of preparation conditions and product distributions are shown in TABLE 1.

The structures of the compounds were assigned by means of elemental analyses, ^{1}H and ^{13}C NMR, UV and mass spectra. The site of aralkylation can be easily assigned on the basis of ^{1}H NMR spectra (TABLE 2). The most conspicuous are the chemical shift differences of benzyl methylene signals. For N-4 substituted compounds they appear at approx. 5.9 ppm, shifted to higher frequencies by approx. 0.5 ppm in comparison with the respective signals of their N-5 isomers. This diagnostic chemical shift difference, reported earlier for wyosine and its N-5 congener[10] is seen also in the spectra of presently obtained alkyl derivatives (e.g. **3f** vs **2f**, **3g** vs **2g**). Of some diagnostic value are NCH_2O methylene signals in the acyclic chain of aralkylated (but not alkylated) derivatives. These methylene groups resonate at lower frequencies in N-4 isomers than in N-5 ones. Aralkylation at C-7 is manifested by a replacement of 7-H signal in the 7.8 - 8.3 ppm range by a C-methylene appearing at approx. 4.5 ppm.

^{13}C NMR spectra (TABLE 3) provide corroborative data for unequivocal structural assignments of aralkylation products. The influence of the site of N-benzylation on ^{13}C NMR shifts resembles this described for N-methylation.[11] Carbon atoms attached to N-4 resonate at higher frequencies than those attached to N-5 (respectively 49.16 and 45.99 ppm for benzyl CH_2; 33.88 and 28.4 ppm for methyl). Very characteristic is quaternary carbon C-3a, chemical shift of which is only slightly susceptible to the kind of substituent attached, but highly dependent upon the site of substitution (N-4 139.79 for benzyl CH_2, 139.95 for methyl; N-5 150.12 for benzyl CH_2, 149.55 for methyl).

Wyosine and its congeners are distinctive as the only nucleic acid components with substantial fluorescence (quantum yield, φ 3.82 %; with 2-aminopurine as a 100 % φ standard). As can be expected, fluorescence of acyclowyosine, 3-[(2-hydroxyethoxy)-methyl] analogue[12] is similar (φ 4.32 %). N-4-Unsubstituted 6-MeTGuo and 6-MeTACV

TABLE 1. Aralkylation and alkylation reactions of tricyclic analogues of acyclovir and guanosine. Conditions and product distributions.

Reagent	Substrate;	6-R	Time [h]	Products isolated (% yield)				
				N-5	N-4	N-5, C-7	N-4, C-7	C-7, O-9
$PhCH_2Br$	**1a**	Me	5	**2a** (80)	---	---	---	---
	1b	Ph	24	**2b** (41)	**3b** (6)	**4b** (9)	---	---
	1c	4-MeOPh	9	**2c** (28)	**3c** (11)	**4c** (17)	---	**5c** (3)
	7c	4-MeOPh	24	**8c** (38)	---	**9c** (15)	---	---
	1d	*t*-Bu	7	**2d** (9)	**3d** (36)	---	**6d** (4)	---
	7d	*t*-Bu	168	Only starting material was isolated				
$4\text{-}NO_2$ $PhCH_2Br$	**7c**	4-MeOPh	24	**8i** (32)	---	**9i** (25)	---	---
	1d	*t*-Bu	8	**2e** (8)	**3e** (39)	---	---	---
CH_3I	**1b**	Ph	18	**2f** (79)	**3f** (7)	---	---	---
C_2H_5I	**1b**	Ph	18	**2g** (36)	**3g** (6)	---	---	---
	1d	*t*-Bu	10	**2h** (53)	---	---	---	---

are only slightly fluorescent (6-MeTACV, φ 0.23 %). We have found, however, that phenyl substituent in the 6 position of TACV, instead of 6-methyl one, renders the compound (**1b**) fluorescent[5] (φ 7.95 %). In the present aralkylation reactions we have obtained compounds 6-phenyl **3b** and 6-*tert*-butyl **3d** which interestingly demonstrate the influence of 6-substituent on the quantum yield of fluorescence of N-4 substituted tricyclic analogues (φ 16.79 % vs 3.11 % respectively).

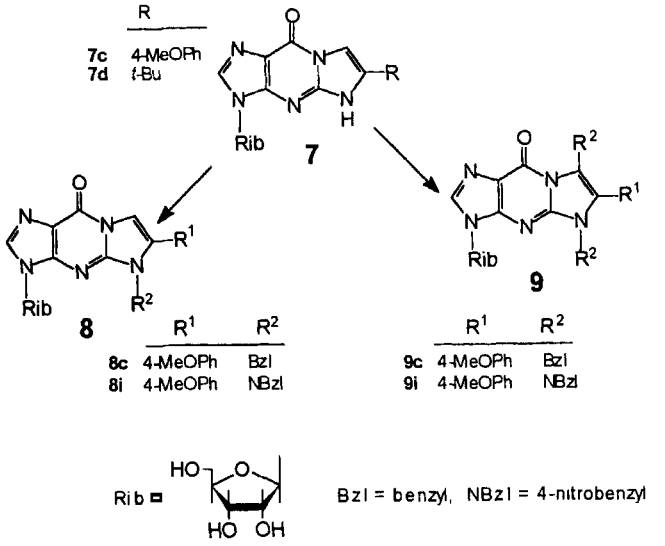
TABLE 2. Selected ^{1}H NMR Data.

Compd; Substituent[a]		CH_2Ph, CH_2PhNO_2, CH_3 or CH_2CH_3	NCH_2O or 1`-H	2-H	7-H
N-5 products					
2b[b]	Bzl	5.40 (s, 2)	5.52 (s, 2)	8.10 (s, 1)	7.92 (s, 1)
2c	Bzl	5.36 (s, 2)	5.51 (s, 2)	8.09 (s, 1)	7.82 (s, 1)
2d	Bzl	5.39 (s, 2)	5.58 (s, 1)	8.04 (s, 1)	7.47 (s, 1)
2e	NBzl	5.35 (s, 2)	5.70 (s, 1)	8.04 (s, 1)	7.50 (s, 1)
2f	Me	3.68 (s, 3)	5.57 (s, 2)	8.10 (s, 1)	7.88 (s, 1)
2g	Et	4.17 (q ,2)	5.57 (s, 2)	8.10 (s, 1)	7.83 (s, 1)
2h	Et	4.29 (q, 2)	5.54 (s, 2)	8.06 (s, 1)	7.32 (s, 1)
8c	Bzl	5.38 (s, 2)	5.83 (d, 2)	8.20 (s, 1)	7.83 (s, 1)
8i	NBzl	5.49 (s, 2)	5.80 (d, 2)	8.20 (s, 1)	7.89 (s, 1)
N-5,C-7 products					
4b	Bzl	5.24 (s, 2) 4.44 (s, 2)	5.49 (s, 2)	8.02 (s, 1)	---
4c	Bzl	5.21 (s, 2) 4.42 (s, 2)	5.48 (s, 2)	8.01 (s, 1)	---
9c	Bzl	5.24 (s, 2) 4.41 4.43 (2 x s, 2)	5.80 (d, 1)	8.11 (s, 1)	---
9i	NBzl	5.35 (s, 2) 4.51 4.53 (2 x s, 2)	5.77 (d, 1)	8.12 (s, 1)	---
N-4 products					
3b[c]	Bzl	5.96 (s, 2)	5.34 (s, 2)	8.04 (s, 1)	8.29 (s, 1)
3c	Bzl	5.94 (s, 2)	5.32 (s, 2)	8.02 (s, 1)	8.16 (s, 1)
3d	Bzl	5.87 (s, 2)	5.32 (s, 2)	7.99 (s, 1)	7.40 (s, 1)
3e	NBzl	5.96 (s, 2)	5.32 (s, 2)	8.01 (s, 1)	7.40 (s, 1)
3f	Me	4.20 (s, 3)	5.80 (s, 2)	8.06 (s, 1)	8.22 (s, 1)
3g	Et	4.66 (q, 2)	5.73 (s, 2)	8.08 (s, 1)	8.22 (s, 1)
N-4,C-7 products					
6d	Bzl	5.83 (s, 2) 4.76 (s, 2)	5.30 (s, 2)	7.90 (s, 1)	---
C-7,O-9 products					
5c	Bzl	4.48 (s, 2) 3.96 (s, 2)	5.43 (s, 2)	8.23 (s, 1)	---

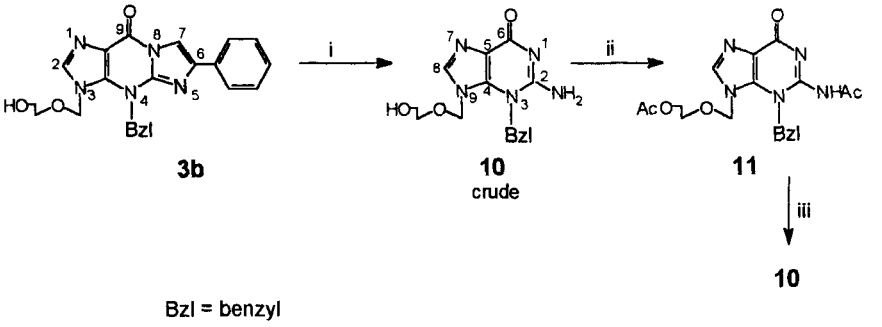
a Bzl – benzyl; NBzl – 4-nitrobenzyl

b ^{1}H NOE difference spectra of **2b**:
8.89 % NOE effect observed for 2-H when NCH_2O irradiated.

c ^{1}H NOE difference spectra of **3b**:
1.87 % NOE effect observed for NCH_2O when NCH_2Ph irradiated
1.84 % NOE effect observed for NCH_2Ph and 9.41 % observed for 2-H when NCH_2O irradiated.



SCHEME 2. Aralkylation reactions of 6-substituted derivatives of TGuo. Structures of compounds formed.



SCHEME 3. i. NBS, 0.5 M acetate buffer, pH 4.8 / dioxane 1:1, RT, 90 min, 25 % NH_3 aq, 90 min; ii. Ac_2O, py, RT, 12 h, chromatography; iii. NH_3 / MeOH. RT. 24 h

TABLE 3. Selected ^{13}C NMR Data.

Compd; substituent		CH_2Ph or CH_2CH_3	C-3a	C-4a	C-7
N-5 products					
2b	Bzl	45.99 Tm[a]	150.12 Sdt	145.87 Sdt	104.78 D
2c	Bzl	45.85 Tm	150.04 Sdt	145.70 Sdt	104.10 D
2h	Et	28.52 Tq	150.04 Sdt	145.49 Sdt	101.26 D
8c	Bzl	45.73 Tm	149.65 Sdd	145.48 Sdt	104.13 D
N-5,C-7 products					
4c	Bzl	29.71 Tm 45.67 Tm	149.60 Sdt	145.94 St	118.26 St
9c	Bzl	29.69 Tm 45.51 Tm	149.15 Sdd	145.68 St	118.16 St
N-4 products					
3b	Bzl	49.16 Tm	139.79 Sm	142.94 Sdt	105.64 D
3d	Bzl	48.97 Tm	139.70 Sm	142.13 Sdt	102.99 D

a Capital letters refer to the pattern resulting from directly bonded ^{13}C-^{1}H couplings and lowercase letters to those from ^{13}C-^{1}H couplings over more than one bond.

The unusual aralkylation of TACV system in N-4 position is promising for developing a simple route to 3-aralkyl-9-substituted guanines. So far the literature data on direct N-3 aralkylation of monomeric 9-substituted guanines has been limited to the reported isolation of 3-benzylguanine in 1 % yield from the multiproduct mixture after benzylation of 2'-deoxyguanosine in 2,2,2-trifluoroethanol containing NaOH.[13] 3-Benzyl-9-methylguanine was only prepared by cyanation and subsequent cyclization of 5-(benzylamino)-1-methylimidazole-4-carboxamide.[14]

We have previously found that 6-MeTGuo, 6-MeTdGuo and 6-MeTACV, which undergo efficient N-4 methylation by means of diazomethane / zinc iodide cyclopropanation reagent,[15] can be subsequently easily split to the respective 3-methyl-guanine derivatives when treated with N-bromosuccinimide (NBS).[16,17,12]

Our initial attempts to apply a similar way in order to remove the third ring of the N-4 aralkylated tricyclic derivatives of acyclovir were performed on the 6-*tert*-butyl compound **3d**, being a major product of benzylation. However, these attempts failed, most probably for steric reasons. The experiments towards finding a suitable cleavage reagent for **3d** are in progress.

When the 6-phenyl derivative **3b**, a minor product of benzylation, was used as a substrate, treatment with NBS in 0.5 M acetate buffer, pH 4.8 / dioxane followed by aqueous ammonia resulted in the desired 3-benzylacyclovir **10**. Crude material was transformed into diacetyl derivative **11**, purified on chromatographic column and deblocked with methanolic ammonia to give pure 3-benzylacyclovir in 36 % yield.

In the ^{1}H NMR spectrum of **10** in DMSO–d_6 the 2-amino group protons appear as two separate signals at 7.26 and 6.71 ppm, what may suggest that for 3-benzylacyclovir tautomeric structure of 1-H, 2-imino is preferred. In the ^{1}H NMR spectra of 3-methyl derivatives of guanosine,[16] 2'-deoxyguanosine[17] and acyclovir[12] only one, 2 proton amino group signal has been reported at 6.95, 6.89 and 6.91 ppm respectively.

Conclusion

Steric factors seem to be dominating in directing aralkylation reaction into the unusual N-4 position of 3,9-dihydro-3-R^1-6-R^2-9-oxo-5*H*-imidazo[1,2-*a*]purines. A bulky substituent in the 6 position (e.g. *tert*-butyl) makes possible a substitution in the 4 position, provided however, that the substituent in the 3 position is small enough (e.g. alkyl but not ribosyl).

Experimental

Melting points were determined on a Laboratory Devices MEL-TEMP II capillary micromelting point apparatus and are uncorrected. UV spectra were recorded on a Beckman DU-65 spectrophotometer. Fluorescence spectra were measured on a Hitachi F 2000 Fluorescence Spectrophotometer (excitation at 305 nm); quantum yields were calculated relative to 2-aminopurine as a 100 % standard. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 on a Unity 300 Varian spectrometer operating at 299.95 MHz and 75.43 MHz respectively. Tetramethylsilane was used as the internal standard and the chemical shifts are reported in ppm (δ scale). Mass spectra were taken on an AMD-604 mass spectrometer by LSIMS method with glycerol as a matrix. Elemental analyses were performed by Microanalytical Laboratories of the Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw. Analytical thin-layer chromatography (TLC) was performed on Merck precoated 60 F_{254} silica gel plates. Short column chromatography was carried out on Merck silica gel 60H (15-40 μm or 40-63 μm). Anhydrous pyridine

and dimethylformamide were distilled and dried over molecular sieves 4 Å. Compounds **1b**, **1c** and **1d** were prepared as described previously.[5,6] For the sake of comparison the fluorescence spectra of previously obtained wyosine and acyclowyosine were measured.

General procedure for the preparation of 7c and 7d. To an anhydrous suspension of guanosine (1 mmol) in dimethylformamide (15 ml) was added sodium hydride in 60 % suspension in oil (1.3 mmol). After stirring for 1h at 50 °C (in the synthesis of **7c**) or at room temperature (in the synthesis of **7d**), it was treated with 2-bromo-4'-methoxyacetophenone or 1-bromo-3,3-dimethyl-2-butanone respectively (1.1 mmol). The mixture was stirred for the next 3h at room temperature. Volatile materials were evaporated and the residue was chromatographed.

3,9-Dihydro-6-(4-methoxyphenyl)-9-oxo-3-(β-D-ribofuranosyl)-5*H*-imidazo-[1,2-*a*]purine (7c). Column chromatography was carried out using $CHCl_3$-MeOH 7.5:1 as eluent to yield 85 % of **7c** which was then crystallized from isopropanol; mp 190°C (dec). UV (H_2O): λ_{max} 258 nm (ε 45800), 306 (19900). ^{1}H NMR (DMSO-d_6): 12.95 (brs, 1H, N-5-H), 8.19 (s, 1H, 2-H), 8.09 (s, 1H, 7-H), 7.85, 7.06 (2xd, 4H, Ph), 5.86 (d, 1H, 1'-H), 5.46 (d, 1H, 2'-OH), 5.18 (d, 1H, 3'-OH), 5.07 (t, 1H, 5'-OH), 4.47 (q, 1H, 2'-H), 4.16 (q, 1H, 3'-H), 3.93 (q, 1H, 4'-H), 3.81 (s, 3H, OCH_3), 3.56-3.72 (m, 2H, 5'-H Anal. Calcd. for $C_{19}H_{19}N_5O_6 \cdot 0.75\ H_2O$: C 53.45; H 4.84; N 16.41. Found: C 53.52; H 4.71; N 16.06.

6-t-Butyl-3,9-dihydro-9-oxo-3-(β-D-ribofuranosyl)-5*H*-imidazo[1,2-*a*]purine (7d). Separation was performed in CH_2Cl_2-MeOH 8:1→6:1 yielding 63 % of **7d** which was crystallized from ethyl acetate-methanol 5:1; mp 219-222 °C (dec). UV (H_2O): λ_{max} 231 nm (ε 35100), 283 (11900). ^{1}H NMR (DMSO-d_6): 12.50 (brs, 1H, N-5-H), 8.15 (s, 1H, 2-H), 7.27 (s, 1H, 7-H), 5.82 (d, 1H, 1'-H), 5.43 (d, 1H, 2'-OH), 5.17 (d, 1H, 3'-OH), 5.06 (t, 1H, 5'-OH), 4.46 (q, 1H, 2'-H), 4.14 (q, 1H, 3'-H), 3.92 (q, 1H, 4'-H), 3.55-3.70 (m, 2H, 5'-H), 1.32 (s, 9H, *t*-Bu). ^{13}C NMR (DMSO-d_6): 151.17 (C-9), 149.81 (C-3a), 145.93 (C-4a), 139.44 (C-2), 136.90 (C-6), 115.43 (C-9a), 100.36 (C-7), 87.06 (C-1'), 84.89 (C-4'), 73.68 (C-2'), 70.03 (C-3'), 61.09 (C-5'), 30.52 (CMe_3), 28.55 ($3xCH_3$). HR-MS (formula $C_{16}H_{22}N_5O_5$): calc. for $[MH]^+$ 364.16208; found: 364.16197.

General procedure for aralkylation and alkylation. To a solution of substrate (1 mmol) in dry dimethylformamide (25 ml) was added powdered K_2CO_3 (1.3 mmol). After stirring with exclusion of moisture for 30 min at room temperature, alkyl or aralkyl

halide (1.1 mmol) was added. The mixture was stirred for 2 h and treated with additional portions of K_2CO_3 (0.3 mmol) and halide (0.3 mmol). Vigorous stirring was continued for next 5-22 h at room temperature and the mixture was evaporated. The obtained residue was chromatographed to afford, after evaporation of fractions, alkylated or aralkylated products (yields are given in Table 1).

Benzylation of 1b. For column chromatography was used $CHCl_3$-MeOH 98:2→97:3 giving **4b** and a mixture of **2b** and **3b**. Rechromatography of the mixture was performed using EtOAc-EtOH 95:5 to result in the isolation of **3b** and **2b**, in order of elution.

5,7-Dibenzyl-3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-6-phenylimidazo-[1,2-*a*]purine (4b). Analytical sample was crystallized from diisopropyl ether–methanol 2:1; mp 153 °C. UV (H_2O): λ_{max} 238 nm (ε 33100), 296 (15200). ^{1}H NMR (DMSO-d_6): 8.02 (s, 1H, 2-H), 6.95-7.58 (m, 15H, Ph), 5.49 (s, 2H, NCH_2O), 5.24 (s, 2H, N-5-CH_2), 4.66 (t, 1H, OH), 4.44 (s, 2H, 7-CH_2), 3.40-3.52 (m, 4H, CH_2CH_2). Anal. Calcd. for $C_{30}H_{27}N_5O_3 \cdot 0.75\ H_2O$: C 69.42; H 5.53; N 13.49. Found: C 69.72; H 5.57; N 13 19.

4-Benzyl-4,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-6-phenyl-3*H*-imidazo[1,2-*a*]purine (3b). Analytical sample was crystallized from ethyl acetate-methanol 9:1 to give white needles; mp 206-208 °C. UV (H_2O): λ_{max} 246 nm (ε 32300), 278 (15800), 310 (sh). Fluorescence emission (MeOH): λ_{max} 419 nm; φ = 16.79 %. ^{1}H NMR (DMSO-d_6): 8.29 (s, 1H, 7-H), 8.04 (s, 1H, 2-H), 7.91 (d, 2H, Ph), 7.24-7.41 (m, 8H, Ph), 5.96 (s, 2H, N-4-CH_2), 5.34 (s, 2H, NCH_2O), 4.73 (t, 1H, OH), 3.48 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6): 151.70 (C-9), 142.94 (C-4a), 139.86 (C-2), 139.79 (C-3a), 136.61 (C-6), 132.95 (Ph), 130.43 (Ph), 128.97 (Ph), 128.48 (Ph), 127.52 (Ph), 127.46 (Ph), 125.29 (Ph), 125.05 (Ph), 116.61 (C-9a), 105.64 (C-7), 75.04 (C-1'), 70.04 (C-4'), 59.58 (C-5'), 49.16 (N-4-CH_2). Anal. Calcd. for $C_{23}H_{21}N_5O_3$: C 66.49; H 5.10; N 16.86. Found C 66.40; H 5.20; N 16.76.

5-Benzyl-3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-6-phenylimidazo-[1,2-*a*]purine (2b). Analytical sample was crystallized from ethanol; mp 179 °C. UV (H_2O): λ_{max} 238 nm (ε 35300), 296 (11900). ^{1}H NMR (DMSO-d_6): 8.10 (s, 1H, 2-H), 7.92 (s, 1H, 7-H), 7.48-7.55 (m, 5H, Ph), 7.23 (m, 3H, Ph), 7.04 (m, 2H, Ph), 5.52 (s, 2H, NCH_2O), 5.40 (s, 2H, N-5-CH_2), 4.65 (t, 1H, OH), 3.38-3.51 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6): 151.04 (C-9), 150.12 (C-3a), 145.87 (C-4a), 139.47 (C-2), 136.15 (C-6), 131.30 (Ph), 129.50 (Ph), 128.95 (Ph), 128.90 (Ph), 128.48 (Ph), 127.45 (Ph),

127.22 (Ph), 126.58 (Ph), 115.66 (C-9a), 104.78 (C-7), 72.03 (C-1'), 70.83 (C-4'), 59.95 (C-5'), 45.99 (N-5-CH_2). Anal. Calcd. for $C_{23}H_{21}N_5O_3$: C 66.49; H 5.10; N 16.86. Found C 66.51; H 4.97; N 16.67.

Benzylation of 1c. Components of the reaction mixture were separated by column chromatography (CH_2Cl_2-MeOH 95:5) to give **5c**, **4c**, **3c** and **2c**, in order of elution.

7-Benzyl-9-benzyloxy-3-[(2-hydroxyethoxy)methyl]-6-(4-methoxyphenyl)-imidazo[1,2-*a*]purine (5c). Yellow solid; mp 105 °C (dec). UV (MeOH): λ_{max} 240 nm (ε 10600), 357 (11700). LSIMS $(M+H)^+$ 536. ^{1}H NMR (DMSO-d_6): 8.48 (d, 2H, Ph), 8.23 (s, 1H, 2-H), 7.27 (d, 2H, Ph), 6.61-6.98 (m, 10H, Ph), 5.43 (s, 2H, NCH_2O), 4.68 (t, 1H, OH), 4.48 (d, 2H, 7-CH_2), 3.99 (s, 3H, CH_3O), 3.96 (d, 2H, 9-O-CH_2), 3.48 (m, 4H, CH_2CH_2). MS: m/z 536 (M+H).

5,7-Dibenzyl-3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-6-(4-methoxyphenyl)-9-oxoimidazo[1,2-*a*]purine (4c). Oily residue. UV (MeOH): λ_{max} 240 nm (ε 37900), 293 (18600). ^{1}H NMR (DMSO-d_6): 8.01 (s, 1H, 2-H), 6.99-7.36 (m, 14H, Ph), 5.48 (s, 2H, NCH_2O), 5.21 (s, 2H, N-5-CH_2), 4.65 (t, 1H, OH), 4.42 (s, 2H, 7-CH_2), 3.79 (s, 3H, CH_3O), 3.39-3.49 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6): 160.15 (Ph), 153.35 (C-9), 149.60 (C-3a), 145.94 (C-4a), 139.21 (C-2), 139.95 (Ph), 136.20 (Ph), 131.90 (Ph), 128.60 (C-6), 128.43 (Ph), 128.19 (Ph), 127.58 (Ph), 127.44 (Ph), 126.85 (Ph), 125.77 (Ph), 118.80 (Ph), 118.26 (C-7), 116.05 (C-9a), 114.38 (Ph), 72.07 (C-1'), 70.83 (C-4'), 59.84 (C-5'), 55.20 (CH_3O), 45.67 (N-5-CH_2), 29.71 (7-CH_2).

4-Benzyl-4,9-dihydro-3-[(2-hydroxyethoxy)methyl]-6-(4-methoxyphenyl)-9-oxo-3*H*-imidazo[1,2-*a*]purine (3c). Amorphous solid. UV (MeOH): λ_{max} 254 nm (ε 35400), 282 (25300). ^{1}H NMR (DMSO-d_6): 8.16 (s, 1H, 7-H), 8.02 (s, 1H, 2-H), 7.83 (d, 2H, Ph), 6.99-7.40 (m, 5H, Ph), 6.95 (d, 2H, Ph), 5.94 (s, 2H, N-4-CH_2), 5.32 (s, 2H, NCH_2O), 4.71 (t, 1H, OH), 3.76 (s, 3H, CH_3O), 3.40-3.47 (m, 4H, CH_2CH_2). Acetate of **3c**: white needles mp 200-202 °C, ^{13}C NMR (DMSO-d_6): 170.03 ($COCH_3$), 158.82 (Ph), 151.66 (C-9), 142.79 (C-4a), 139.61 (C-3a), 139.78 (C-2), 136.54 (C-6), 127.53 (Ph), 127.53 (Ph), 126.49 (Ph), 125.57 (Ph), 125.32 (Ph), 116.67 (C-9a), 104.32 (C-7), 74.82 (C-1'), 66.18 (C-4'), 62.41 (C-5'), 55.03 (OCH_3), 49.14 (N-4-CH_2), 20.34 ($COCH_3$). HR-MS (formula $C_{26}H_{26}N_5O_5$): calc. for $[MH]^+$: 488.19339; found: 488.19360.

5-Benzyl-3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-6-(4-methoxyphenyl)-9-oxoimidazo[1,2-*a*]purine (2c). White solid; mp 195-198 °C. UV (MeOH): λ_{max} 250 nm

(ε 33200), 294 (15900). ^{1}H NMR (DMSO-d_6): 8.09 (s, 1H, 2-H), 7.82 (s, 1H, 7-H), 7.47 (d, 2H, Ph), 7.03-7.28 (m, 5H, Ph), 7.04 (d, 2H, Ph), 5.51 (s, 2H, NCH_2O), 5.36 (s, 2H, N-5-CH_2), 4.65 (t, 1H, OH), 3.80 (s, 3H, CH_3O), 3.38-3.45 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6): 160.14 (Ph), 151.03 (C-9), 150.04 (C-3a), 145.70 (C-4a), 139.47 (C-2), 131.19 (C-6), 136.22 (Ph), 130.50 (Ph), 128.52 (Ph), 127.46 (Ph), 126.63 (Ph), 119.28 (Ph), 115.64 (C-9a), 114.37 (Ph), 104.10 (C-7), 72.15 (C-1'), 70.87 (C-4'), 59.81 (C-5'), 55.24 (CH_3O), 45.85 (N-5-CH_2).

Benzylation of 7c. Chromatography was carried out in CH_2Cl_2-MeOH 95:5→92:8 to afford **9c** and **8c**.

5,7-Dibenzyl-3,9-dihydro-6-(4-methoxyphenyl)-9-oxo-3-(β-D-ribofuranosyl)-imidazo[1,2-*a*]purine (9c). Yellow oily residue. UV (H_2O): λ_{max} 242 nm (ε 45400), 294 (18600). ^{1}H NMR (DMSO-d_6): 8.11 (s, 1H, 2-H), 6.96-7.32 (m, 14H, Ph), 5.80 (d, 1H, 1'-H), 5.41 (d, 1H, 2'-OH), 5.24 (s, 2H, N-5-CH_2), 5.19 (d, 1H, 3'-OH), 4.97 (t, 1H, 5'-OH), 4.55 (q, 1H, 2'-H), 4.43, 4.41 (2xs, 2H, 7-CH_2), 4.12 (q, 1H, 3'-H), 3.89 (q, 1H, 4'-H), 3.78 (s, 3H, CH_3O), 3.43-3.63 (m, 2H, 5'-H). ^{13}C NMR (DMSO-d_6): 160.05 (Ph), 153.21 (C-9), 149.15 (C-3a), 145.68 (C-4a), 139.88 (Ph), 137.59 (C-2), 136.15 (Ph), 131.77 (Ph), 128.61 (C-6), 128.42 (Ph), 128.16 (Ph), 127.44 (Ph), 127.38 (Ph), 137.59 (C-2), 136.15 (Ph), 131.77 (Ph), 128.61 (C-6), 128.42 (Ph), 128.16 (Ph), 127.44 (Ph), 127.38 (Ph), 126.57 (Ph), 125.72 (Ph), 118.68 (Ph), 118.16 (C-7), 116.55 (C-9a), 114.28 (Ph), 87.14 (C-1'), 85.25 (C-4'), 73.26 (C-2'), 70.41 (C-3'), 61.46 (C-5'), 55.15 (CH_3O), 45.51 (N-5-CH_2), 29.69 (7-CH_2).

5-Benzyl-3,9-dihydro-6-(4-methoxyphenyl)-9-oxo-3-(β-D-ribofuranosyl)-imidazo[1,2-*a*]purine (8c). Amorphous solid. UV (H_2O): λ_{max} 250 nm (ε 43200), 294 (19500). ^{1}H NMR (DMSO-d_6): 8.20 (s, 1H, 2-H), 7.83 (s, 1H, 7-H), 7.45 (d, 2H, Ph), 7.23 (m, 3H, Ph), 7.02 (m, 4H, Ph), 5.83 (d, 1H, 1'-H), 5.43 (d, 1H, 2'-OH), 5.38 (s, 2H, N-5-CH_2), 5.19 (d, 1H, 3'-OH), 5.00 (t, 1H, 5'-OH), 4.56 (q, 1H, 2'-H), 4.12 (q, 1H, 3'-H), 3.90 (q, 1H, 4'-H), 3.80 (s, 3H, CH_3O), 3.42-3.62 (m, 2H, 5'-H). ^{13}C NMR (DMSO-d_6): 160.06 (Ph), 150.96 (C-9), 149.65 (C-3a), 145.48 (C-4a), 137.78 (C-2), 136.18 (Ph), 133.04 (Ph), 131.17 (C-6), 130.41 (Ph), 128.53 (Ph), 127.42 (Ph), 126.38 (Ph), 119.24 (Ph), 116.14 (C-9a), 114.30 (Ph), 104.13 (C-7), 87.13 (C-1'), 85.29 (C-4'), 73.36 (C-2'), 70.42 (C-3'), 61.46 (C-5'), 55.22 (CH_3O), 45.73 (N-5-CH_2).

Benzylation of 1d. Chromatographic separation in $CHCl_3$-MeOH 98:2→95:5 gave **6d**, the mixture of **6d** and **3d**, **3d** and **2d**, in order of elution. Rechromatography in CH_2Cl_2-MeOH 98:2→ 95:5 allowed to obtain additional amounts of pure **6d** and **3d**.

6-t-Butyl-4,7-dibenzyl-4,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-3*H*-imidazo[1,2-*a*]purine (6d). Colorless glass. UV (H_2O): λ_{max} 234 nm (ε 28400), 294 (8700). ^{1}H NMR (DMSO-d_6): 7.90 (s, 1H, 2-H), 6.96-7.40 (m, 10H, Ph), 5 83 (s, 2H, N-4-CH_2), 5.32 (s, 2H, NCH_2O), 4.76 (s, 2H, 7-CH_2), 4.73 (t, 1H, OH), 3.45 (m, 4H, CH_2CH_2), 1.24 (s, 9H, *t*-Bu). ^{13}C NMR (DMSO-d_6): 154.24 (C-9), 145.74 (C-4a), 141.46 (C-2), 141.40 (C-3a), 139.31 (C-6), 139.10 (Ph), 136.85 (Ph), 128.90 (Ph), 128.02 (Ph), 127.51 (Ph), 127.38 (Ph), 125.60 (Ph), 125.31 (Ph), 118.62 (C-7), 116.62 (C-9a), 74.90 (C-1'), 69.94 (C-4'), 59.58 (C-5'), 48.79 (N-4-CH_2), 33.04 (7-CH_2), 30.38 (3xCH_3), 29.42 (CMe_3). HR-MS (formula $C_{28}H_{32}N_5O_3$): calc. for $[MH]^+$: 486.25052; found: 486.25040.

6-t-Butyl-4-benzyl-4,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-3*H*-imidazo[1,2-*a*]purine (3d). Analytical sample crystallized from methanol to give white needles; mp 156-158 °C. UV (H_2O): λ_{max} 234 nm (ε 28600), 294 (8800). Fluorescence emission (MeOH): λ_{max} 418 nm; φ = 3.11 %. ^{1}H NMR (DMSO-d_6): 7.99 (s, 1H, 2-H), 7.40 (s, 1H, 7-H), 7.18-7.39 (m, 5H, Ph), 5.87 (s, 2H, N-4-CH_2), 5.32 (s, 2H, NCH_2O), 4.72 (t, 1H, OH), 3.46 (m, 4H, CH_2CH_2), 1.25 (s, 9H, *t*-Bu). ^{13}C NMR (DMSO-d_6): 151.81 (C-9), 151.16 (C-6), 142.13 (C-4a), 139.70 (C-3a), 139.53 (C-2), 136.72 (Ph), 129.00 (Ph), 127.60 (Ph), 125.47 (Ph), 116.55 (C-9a), 102.99 (C-7), 75.08 (C-1'), 70.05 (C-4'), 59.63 (C-5'), 48.97 (N-4-CH_2), 31.82 (CMe_3), 29.49 (3xCH_3). Anal. Calcd. for $C_{21}H_{25}N_5O_3$: C 63.78; H 6.37; N 17.71. Found: C 63.93; H 6.51; N 17.86.

6-t-Butyl-5-benzyl-3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxoimidazo[1,2-*a*]purine (2d). Colorless glass. UV (H_2O): λ_{max} 232 nm (ε 27300), 288 (10300). ^{1}H NMR (DMSO-d_6): 8.04 (s, 1H, 2-H), 7.47 (s, 1H, 7-H), 7.20-7.33 (m, 3H, Ph), 7.03 (d, 2H, Ph), 5.58 (s, 2H, NCH_2O), 5.39 (s, 2H, N-5-CH_2), 4.56 (t, 1H, OH), 3.34 (m, 4H, CH_2CH_2), 1.30 (s, 9H, *t*-Bu). ^{13}C NMR (DMSO-d_6): 151.78 (C-9), 150.82 (C-3a), 147.17 (C-4a), 140.09 (C-6), 140.03 (C-2), 137.45 (Ph), 129.19 (Ph), 127.75 (Ph), 126.34 (Ph), 116.25 C-9a), 102.87 (C-7), 72.70 (C-1'), 71.64 (C-4'), 60.44 (C-5'), 47.65 (N-5-CH_2), 31.88 (CMe_3), 29.84 (3xCH_3). HR-MS (formula $C_{21}H_{26}N_5O_3$): calc. for $[MH]^+$: 396.20355; found: 396.20372.

Attempted benzylation of 7d. As the result of chromatography in $CHCl_3$-MeOH 95:5→9:1 only the unreacted **7d** was isolated.

4-Nitrobenzylation of 7c. Column chromatography was performed using CH_2Cl_2-MeOH 95:5→91:9 to give **9i** and **8i**.

5,7-Di-(4-nitrobenzyl)-3,9-dihydro-6-(4-methoxyphenyl)-9-oxo-3-(β-D-ribofuranosyl)imidazo[1,2-*a*]purine (9i). Amorphous solid. UV (H_2O): λ_{max} 242 nm (ε 46100), 290 (sh). ^1H NMR (DMSO-d_6): 8.12 (s, 1H, 2-H), 8.10-8.15 (m, 4H, Ph), 7.26-7.41 (m, 6H, Ph), 7.00 (d, 2H, Ph), 5.77 (d, 1H, 1'-H), 5.39 (d, 1H, 2'-OH), 5.35 (s, 2H, N-5-CH_2), 5.18 (d, 1H, 3'-OH), 4.94 (t, 1H, 5'-OH), 4.52 (q, 1H, 2'-H), 4.53, 4.51 (2xs, 2H, 7-CH_2), 4.07 (q, 1H, 3'-H), 3.87 (q, 1H, 4'-H), 3.76 (s, 3H, CH_3O), 3.37-3.57 (m, 2H, 5'-H). ^{13}C NMR (DMSO-d_6): 160.27 (Ph), 153.22 (C-9), 149.17 (C-3a), 148.05 (C-4a), 146.73 (Ph), 145.78 (Ph), 145.73 (Ph), 143.83 (C-2), 137.86 (Ph), 131.74 (Ph), 129.14 (Ph), 128.76 (Ph), 127.77 (Ph), 123.62 (Ph), 123.39 (Ph), 117.51 (Ph), 117.38 (C-7), 116.82 (C-9a), 114.49 (Ph), 87.24 (C-1'), 85.30 (C-4'), 73.18 (C-2'), 70.39 (C-3'), 61.42 (C-5'), 55.18 (OCH_3), 45.26 (N-5-CH_2), 30.15 (7-CH_2). HR-MS (formula $C_{33}H_{30}N_7O_{10}$): calc. for $[MH]^+$: 684.20544; found: 684.20393.

3,9-Dihydro-6-(4-methoxyphenyl)-5-(4-nitrobenzyl)-9-oxo-3-(β-D-ribofuranosyl)imidazo[1,2-*a*]purine (8i). Analytical sample crystallized from methanol to give white needles; mp 222 °C. UV (H_2O): λ_{max} 252 nm (ε 45900), 295 (sh). ^1H NMR (DMSO-d_6): 8.20 (s, 1H, 2-H), 7.89 (s, 1H, 7-H), 8.12 (d, 2H, Ph), 7.34-7.43 (m, 4H, Ph), 7.02 (d, 2H, Ph), 5.80 (d, 1H, 1'-H), 5.49 (s, 2H, N-5-CH_2), 5.41 (d, 1H, 2'-OH), 5.18 (d, 1H, 3'-OH), 4.95 (t, 1H, 5'-OH), 4.53 (q, 1H, 2'-H), 4.07 (q, 1H, 3'-H), 3.86 (q, 1H, 4'-H), 3.78 (s, 3H, CH_3O), 3.38-3.58 (m, 2H, 5'-H). Anal. Calcd. for $C_{26}H_{24}N_6O_8$:
C 56.93; H 4.41; N 15.32. Found: C 56.84; H 4.36; N 15.24.

4-Nitrobenzylation of 1d. Products **2e** and **3e** were isolated in order of elution by column chromatography in $CHCl_3$-MeOH 98:2.

6-t-Butyl-3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-5-(4-nitrobenzyl)-9-oxo-imidazo[1,2-*a*]purine (2e). Solid material precipitated from ethyl acetate; after recrystallization mp 213-215 °C. UV (H_2O): λ_{max} 232 nm (ε 29100), 283 (ε 17600). ^1H NMR (DMSO-d_6): 8.04 (s, 1H, 2-H), 7.50 (s, 1H, 7-H), 8.16 (d, 2H, Ph), 7.34 (d, 2H, Ph), 5.70 (s, 2H, NCH_2O), 5.35 (s, 2H, N-5-CH_2), 4.53 (t, 1H, OH), 3.24 (m, 4H,

CH_2CH_2), 1.32 (s, 9H, *t*-Bu). ^{13}C NMR (DMSO-d_6): 151.03 (C-9), 149.94 (C-3a), 146.57 (C-4a), 146.24 (Ph), 144.60 (C-2), 139.31 (C-6), 139.06 (Ph), 127.06 (Ph), 123.57 (Ph), 115.65 (C-9a), 102.28 (C-7), 71.93 (C-1'), 70.82 (C-4'), 59.63 (C-5'), 46.69 (N-5-CH_2), 31.03 (CMe_3), 28.99 (3xCH_3). HR-MS (formula $C_{21}H_{25}N_6O_5$): calc. for [MH]$^+$: 441.18863; found: 441.18841.

6-t-Butyl-4,9-dihydro-3-[(2-hydroxyethoxy)methyl]-4-(4-nitrobenzyl)-9-oxo-3*H*-imidazo[1,2-*a*]purine (3e). Crystalline material precipitated from ethyl acetate; after recrystallization mp 178-181 °C. UV (H_2O): λ_{max} 237 nm (ε 30400), 267 (ε 25500). ^1H NMR (DMSO-d_6): 8.01 (s, 1H, 2-H), 7.40 (s, 1H, 7-H), 8.20 (d, 2H, Ph), 7.50 (d, 2H, Ph), 5.96 (s, 2H, N-4-CH_2), 5.32 (s, 2H, NCH_2O), 4.69 (t, 1H, OH), 3.43 (m, 4H, CH_2CH_2), 1.22 (s, 9H, *t*-Bu). ^{13}C NMR (DMSO-d_6): 151.82 (C-9), 151.12 (C-4a), 146.86 (C-3a), 144.38 (C-2), 141.87 (Ph), 139.64 (C-6), 139.41 (Ph), 127.05 (Ph), 123.83 (Ph), 116.60 (C-9a), 103.11 (C-7), 75.06 (C-1'), 69.98 (C-4'), 59.52 (C-5'), 49.04 (N-4-CH_2), 31.74 (CMe_3), 29.39 (3xCH_3). HR-MS (formula $C_{21}H_{25}N_6O_5$): calc. for [MH]$^+$: 441.18863; found: 441.18841.

Methylation of 1b. The reaction mixture was chromatographed using CH_2Cl_2-MeOH 9:1 to obtain **2f** and **3f**, in order of elution.

3,9-Dihydro-3-[(2-hydroxyethoxy)methyl]-5-methyl-9-oxo-6-phenylimidazo-[1,2-*a*]purine (2f). Analytical sample was crystallized from diisopropyl ether-methanol 2:1 to give fine colorless crystals; mp 149-151 °C. UV (H_2O): λ_{max} 240 nm (ε 36800), 298 (11000). ^1H NMR (DMSO-d_6): 8.10 (s, 1H, 2-H), 7.88 (s, 1H, 7-H), 7.68-7.72, 7.53-7.60 (2xm, 5H, Ph), 5.57 (s, 2H, NCH_2O), 4.71 (t, 1H, OH), 3.68 (s, 3H, N-5-CH_3), 3.47-3.60 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6): 151.01 (C-9), 150.04 (C-3a), 145.72 (C-4a), 139.47 (C-2), 131.67 (C-6), 129.36 (Ph), 128.94 (Ph), 128.83 (Ph), 127.26 (Ph), 115.34 (C-9a), 103.78 (C-7), 72.17 (C-1'), 70.06 (C-4'), 59.83 (C-5'), 30.33 (CH_3). Anal. Calcd. for $C_{17}H_{17}N_5O_3 \cdot 0.5\ H_2O$: C 58.61; H 5.21; N 20.10. Found: C 58.91; H 5.32; N 19.64.

4,9-Dihydro-3-[(2-hydroxyethoxy)methyl]-4-methyl-9-oxo-6-phenyl-3*H*-imidazo[1,2-*a*]purine (3f). Colorless crystals from methanol; mp 186-189°C dec. UV (H_2O): λ_{max} 248 nm (ε 35700), 275 (sh, 14600). ^1H NMR (DMSO-d_6): 8.22 (s, 1H, 7-H), 8.06 (s, 1H, 2-H), 7.96-7.99 (m, 2H, Ph), 7.28-7.45 (m, 3H, Ph), 5.80 (s, 2H, NCH_2O), 4.71 (t, 1H, OH), 4.20 (s, 3H, N-4-CH_3), 3.49-3.53 (m, 4H, CH_2CH_2). ^{13}C

NMR (DMSO-d_6): 151.55 (C-9), 142.95 (C-4a), 140.30 (C-3a), 139.71 (C-2), 139.60 (C-6), 133.09 (Ph), 128.52 (Ph), 127.45 (Ph), 125.09 (Ph), 116.09 (C-9a), 105.21 (C-7), 75.16 (C-1'), 69.89 (C-4'), 59.69 (C-5'), 33.03 (CH_3). HR-MS (formula $C_{17}H_{18}N_5O_3$): calc. for $[MH]^+$: 340.14096; found: 340.13944.

Ethylation of 1b. Chromatography performed in EtOAc-EtOH 9:1 gave **2g** and **3g**, in order of elution.

3,9-Dihydro-5-ethyl-3-[(2-hydroxyethoxy)methyl]-9-oxo-6-phenylimidazo[1,2-*a*]purine (2g). Analytical sample was crystallized from isopropanol to obtain colorless crystals; mp 159-160 °C. UV (H_2O): λ_{max} 238 nm (ε 33300), 298 (9900). ^{1}H NMR (DMSO-d_6): 8.10 (s, 1H, 2-H), 7.83 (s, 1H, 7-H), 7.55-7.68 (m, 5H, Ph), 5.57 (s, 2H, NCH_2O), 4.70 (t, 1H, OH), 4.17 (q, 2H, N-5-CH_2), 3.47-3.60 (m, 4H, CH_2CH_2), 1.24 (t, 3H, CH_3). ^{13}C NMR (DMSO-d_6): 150.98 (C-9), 145.74 (C-3a), 143.97 (C-4a), 139.99 (C-2), 131.63 (C-6), 128.92 (Ph), 128.83 (Ph), 127.28 (Ph), 125.16 (Ph), 115.34 (C-9a), 103.82 (C-7), 70.64 (C-1'), 70.05 (C-4'), 59.66 (C-5'), 28.51 (N-5-CH_2), 17.89 (CH_3). Anal. Calcd. for $C_{18}H_{19}N_5O_3$: C 61.18; H 5.42; N 19.82. Found: C 61.11; H 5.27; N 19.77.

4,9-Dihydro-4-ethyl-3-[(2-hydroxyethoxy)methyl]-9-oxo-6-phenyl-3*H*-imidazo[1,2-*a*]purine (3g). Colorless glassy material. UV (H_2O): λ_{max} 248 (ε 33700), 275 (12800). ^{1}H NMR (DMSO-d_6): 8.22 (s, 1H, 7-H), 8.08 (s, 1H, 2-H), 7.97 (d, 2H, Ph), 7.28-7.45 (m, 3H, Ph), 5.73 (s, 2H, NCH_2O), 4.70 (t, 1H, OH), 4.66 (q, 2H, N-4-CH_2), 3.48-3.58 (m, 4H, CH_2CH_2), 1.49 (t, 3H, CH_3). ^{13}C NMR (DMSO-d_6): 151.04 (C-9), 150.11 (C-4a), 145.18 (C-3a), 139.45 (C-2), 139.43 (C-6), 131.01 (Ph), 129.01 (Ph), 128.95 (Ph), 127.39 (Ph), 115.41 (C-9a), 104.30 (C-7), 72.13 (C-1'), 70.73 (C-4'), 59.77 (C-5'), 30.34 (N-4-CH_2), 13.74 (CH_3). HR-MS (formula $C_{18}H_{20}N_5O_3$): calc. for $[MH]^+$: 354.15662; found: 354.15459.

Ethylation of 1d. Product **2h** was purified by chromatography using CH_2Cl_2-MeOH 98:2→94:6 as eluent.

6-t-Butyl-3,9-dihydro-5-ethyl-3-[(2-hydroxyethoxy)methyl]-9-oxoimidazo[1,2-*a*]purine (2h). Amorphous solid. UV (H_2O): λ_{max} 232 nm (ε 28900), 288 (10000). ^{1}H NMR (DMSO-d_6): 8.06 (s, 1H, 2-H), 7.32 (s, 1H, 7-H), 5.54 (s, 2H, NCH_2O), 4.68 (t, 1H, OH), 4.29 (q, 2H, N-5-CH_2), 3.45-3.58 (m, 4H, CH_2CH_2), 1.42 (s, 9H, *t*-Bu), 1.39 (t, 3H, CH_3). ^{13}C NMR (DMSO-d_6): 150.99 (C-9), 150.04 (C-3a), 145.49 (C-4a), 139.23

(C-6), 138.86 (C-2), 115.23 (C-9a), 101.26 (C-7), 72.05 (C-1'), 70.75 (C-4'), 59.78 (C-1'), 31.01 (CMe_3), 28.97 ($3xCH_3$), 28.52 (ethyl CH_2), 13.49 (ethyl CH_3).

3-Benzyl-9-[(2-hydroxyethoxy)methyl]guanine (10). To a solution of **3b** (158 mg, 0.38 mmol) in 0.5 M acetate buffer, pH 4.8 / dioxane 1:1 (50 ml) was added NBS (135 mg, 0.76 mmol). The mixture was stirred for 90 min at room temperature, alkalized with 25 % aq ammonia, stirred for the additional 90 min, evaporated and co-evaporated several times with toluene and pyridine. The resulting dry residue of crude **10** was treated with pyridine (16 ml) and acetic anhydride (388 mg, 3.8 mmol) and left with stirring overnight at room temperature. Then it was evaporated, suspended in $CHCl_3$-MeOH 96:4, applied onto a silica gel short column and chromatographed in this solvent system to give 54 mg of 9-[(2-acetoxyethoxy)methyl]-N-2-acetyl-3-benzyl-guanine [**11**; 36 %; UV (H_2O): λ_{max} 272 nm (ε 17600); UV (MeOH): λ_{max} 280 nm (ε 18100); ^1H NMR (DMSO-d_6): 13.53 (s, 1H, 2-NH), 8.06 (s, 1H, 8-H), 7.20-7.40 (m, 5H, Ph), 5.71 (s, 2H, N-3-CH_2), 5.24 (s, 2H, NCH_2O), 3.63, 4.04 (2xm, 4H, CH_2CH_2), 2.05, 1.95 (2xs, 6H, 2xAc)]. This compound was treated with NH_3 / MeOH (10 ml) and kept for 2 days at room temperature to obtain quantitatively **10**, which crystallized from methanol. UV (H_2O): λ_{max} 262 nm (ε 20300). ^1H NMR (DMSO-d_6): 7.75 (s, 1H, 8-H), 7.28-7.41 (m, 3H, Ph), 7.04-7.09 (m, 2H, Ph), 7.26, 6.71 (2xbrs, 2H, NH_2), 5.48 (s, 2H, N-3-CH_2), 5.24 (s, 2H, NCH_2O), 4.71 (t, 1H, OH), 3.40 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6): 164.06 (C-6), 153.43 (C-2), 138.24 (C-4), 138.01 (C-8), 136.01 (Ph), 128.91 (Ph), 127.44 (Ph), 125.10 (Ph), 122.27 (C-5), 74.78 (C-1'), 69.68 (C-4'), 59.49 (C-5'), 48.09 (N-3-CH_2). MS: Calcd. for $(M+H)^+$ 316.14096; found 316.13924.

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