NEW 2-ALKYNYL DERIVATIVES OF THE ACYCLIC NUCLEOSIDE 9-(2,3-DIHYDROXYPROPYL)ADENINE AND THEIR 6-GUANIDINOPURINE COUNTERPARTS AS POTENTIAL EFFECTORS OF ADENOSINE RECEPTORS

Michal ČESNEK[1,*], Antonín HOLÝ[2] and Milena MASOJÍDKOVÁ

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, 166 10 Prague 6, Czech Republic; e-mail: [1] cesnekm@uochb.cas.cz, [2] holy@uochb.cas.cz

Received August 28, 2003
Accepted September 28, 2003

A series of the new 2-alkynyl derivatives of the acyclic nucleoside 9-(2,3-dihydroxypropyl)-adenine and their 6-guanidinopurine analogues were prepared by the Sonogashira coupling. The effect of the prepared compounds on A_1 and A_{2A} receptors was examined.
Keywords: Adenosine receptors; Alkynes; Purines; Nucleosides; Acyclic nucleoside analogues; Cross-coupling reactions; Sonogashira reaction.

Several decades ago we have discovered the biological activity of an acyclic nucleoside analogue of adenosine, 9-(2,3-dihydroxypropyl)adenine (DHPA)[1]. The *S*-enantiomer of this simple non-metabolisable analogue replaces adenosine at the binding site of *S*-adenosyl-L-homocysteine hydrolase (SAHase) and acts as a reversible inhibitor of the enzyme-catalyzed reaction (hydrolysis of SAH to adenosine)[2]. SAH, which is formed in all metabolic methylation reactions utilizing *S*-adenosylmethionine as the methyl group donor, is an important product-type inhibitor of the methylations. By virtue of this mechanism, DHPA causes accumulation of SAH and thereby inhibits generally all methylation reactions that are taking place in proliferating systems. These reactions include, among others, the capping of the viral mRNA (the background for the antiviral effect)[3], as well as numerous other effects (for a review, see ref.[4]). Recently, DHPA was examined as a sequence-specific agent preventing DNA methylation[5]. It is the active component of an ointment for common sore (herpes labialis) (Duvira gel™).

Adenosine plays an important role in signal transduction processes. The cellular membranes bear many specific receptors[6] for this nucleoside hormone (*e.g.* subtypes of A_1, A_2 and A_3); the base-modified adenosine deriva-

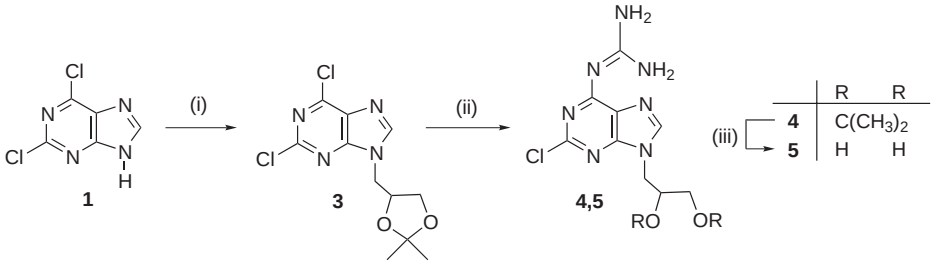
tives often bind very tightly to these receptors and act as adenosine agonists[7]. In this respect, C2-substituted adenosine derivatives are particularly important and among them 2-alkynyladenosines[8] play a prominent role.

Therefore, we were interested whether the effect of such a substitution of adenine base would occur also in adenosine receptors in those cases where the sugar moiety of adenosine is replaced by the 2,3-dihydroxypropyl residue. The 2,3-dihydroxypropyl group can be viewed as a part of ribose residue. The 2- and 3-hydroxy group can imitate 2′- and 3′-hydroxy group at the ribose moiety. These groups play an important role in the mechanism of the receptor activation: Their removal from the ribose moiety or other ribose modification led to partial agonist and/or antagonist[9]; removal of both hydroxy groups resulted in an antagonist activity[10]. While a previous study[11] showed that 9-(2,3-dihydroxypropyl) analogues of R-PIA [N^6-(2-phenylpropan-2-yl)adenosine], are completely inactive at A_1 and A_2 receptors, another study[12] on the other hand claims that 9-(2,3-dihydroxypropyl) derivatives of N^6-(3-iodobenzyl)adenine show a moderate affinity to A_3 receptors mostly. To simplify the examination, we have selected several powerful 2-alkynyladenine nucleoside agonists and synthesized their acyclic counterparts – 2-alkynyl-9-(2,3-dihydroxypropyl)adenines. We recently began a systematic investigation of the effect of replacing the 6-amino group in adenine by the more basic 6-guanidino function[13]. It was therefore considered interesting to synthesize and investigate at the same time also the potential agonist activity of the 6-guanidino counterparts of the acyclic adenosine analogues.

RESULTS

The Sonogashira coupling reaction[14] of 2-iodo-6-amino(or guanidino)purines with alkynes was selected as the crucial synthetic approach for the purpose. In order to increase the lipophilicity (and solubility in organic solvents) of the reactants and the reaction products, we decided to use the acid-labile isopropylidene protecting group of the cis-diol grouping. Thus, for the first series of compounds, it was necessary to prepare 2,6-dichloro-9-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]purine (**3**). While sodium salts of 6-chloropurine, 2-amino-6-chloropurine and 6-amino-2-chloropurine easily react with alkyl halides[15], and/or alkyl sulfonates[16] including (2,2-dimethyl-1,3-dioxolan-4-yl)methyl tosylate (**2b**) under the formation of the corresponding N^9-alkylpurines (predominantly), 2,6-dichloropurine (**1**) failed to react with tosylate **2b** in DMF, in the presence of NaH or cesium carbon-

ate[17]. Therefore, in analogy to the conditions described in the literature for similar purposes, we have applied to its alkylation the Mitsunobu reaction[18] with (2,2-dimethyl-1,3-dioxolan-4-yl)methanol (**2a**). The intermediate **3** was obtained in a good yield; it was converted to the 6-guanidino derivative **4** on treatment with a guanidine solution prepared from guanidine hydrochloride and the calculated amount of NaH in DMF/acetonitrile mixture (Scheme 1). The reaction performed in the presence of DABCO as a catalyst gave compound **4** in a satisfactory yield. This intermediate afforded on acid deprotection with Dowex 50 in H^+-form racemic 2-chloro-9-(2,3-dihydroxypropyl)-6-guanidino-9*H*-purine (**5**). As expected, the 2-chloro group resisted both aminolysis and hydrolysis under the reaction conditions.



Synthesis of 2-chloro-9-(2,3-dihydroxypropyl)-6-guanidino-9*H*-purine. Reagents: (i) PPh_3, EtOOC–N=N–COOEt, 2,2-dimethyl-1,3-dioxolane-4-methanol (**2a**), THF; (ii) guanidine, DABCO, DMF/CH_3CN; (c) Dowex 50x8, MeOH–H_2O

SCHEME 1

To avoid the use of harsh conditions[19] in the Sonogashira coupling of 2-chloropurine derivatives, we have synthesized the corresponding 2-iodopurine derivative whose reactivity in the coupling is known to be higher.

2-Amino-6-chloropurine was converted into 2-amino-6-chloro-9-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-9*H*-purine (**6**) by alkylation of the sodium salt of the base with (2,2-dimethyl-1,3-dioxolan-4-yl)methyl tosylate (**2a**). The required 9-isomer was easily separated from the minor 7-isomer by silica gel chromatography. The subsequent guanidinolysis in the presence of DABCO yielded the 2-amino-6-guanidinopurine derivative **7**. Acid hydrolysis of this intermediate afforded the deprotected guanidino analogue of acyclic 2,6-diaminopurine nucleoside[20], 2-amino-9-(2,3-dihydroxypropyl)-6-guanidino-9*H*-purine (**8**).

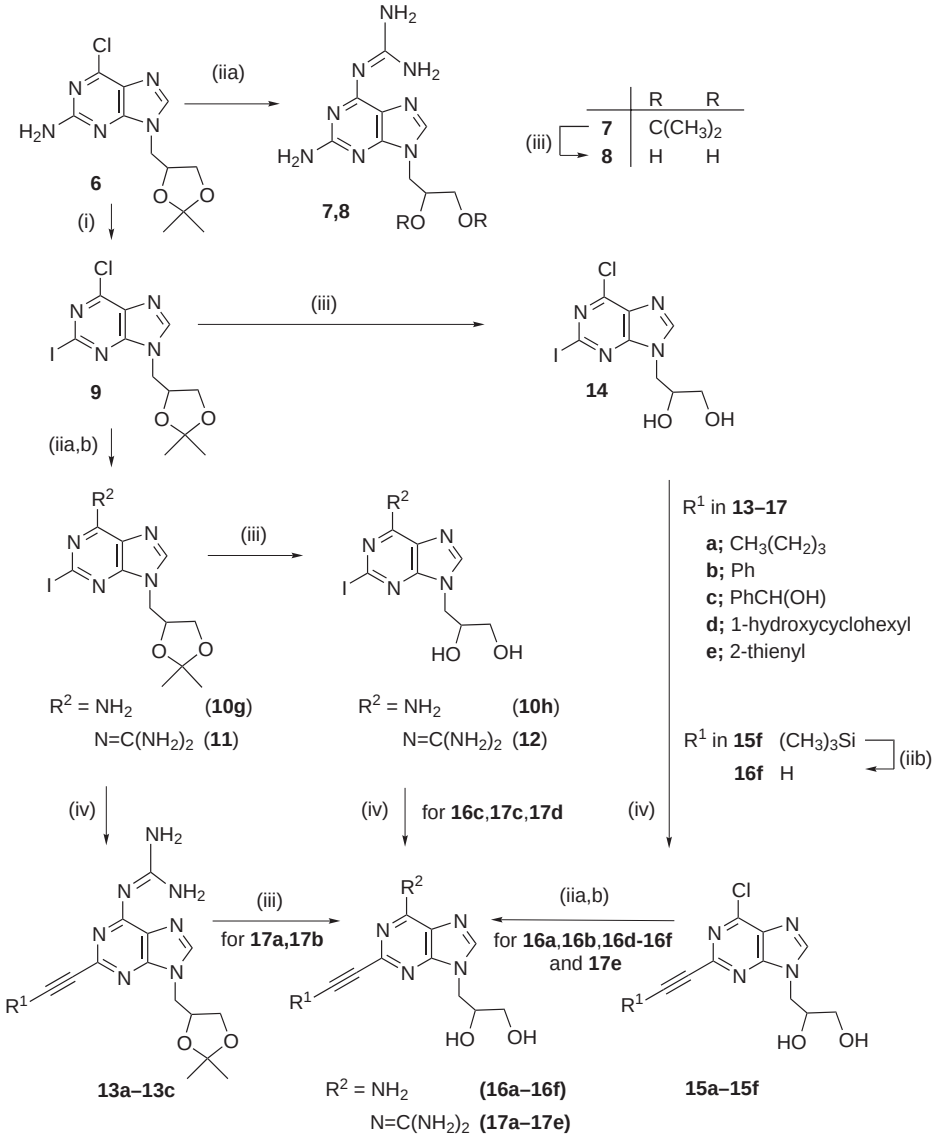
On treatment with isopentyl nitrite and CH_2I_2 in the presence of CuI and iodine[21], compound **6** was transformed into the 6-chloro-2-iodopurine derivative **9**, the key intermediate for the main synthetic scheme. It gave on reaction with methanolic ammonia 6-amino-9-[(2,2-dimethyl-1,3-dioxolan-

4-yl)methyl]-2-iodo-9*H*-purine (**10g**) which was transformed by acid-catalyzed hydrolysis to 9-(2,3-dihydroxypropyl)-2-iodoadenine (**10h**). On the other hand, when treated with guanidine, compound **9** gave the protected 6-guanidino-2-iodopurine derivative **11**. The protecting isopropylidene grouping in compound **11** is acid-labile: during the isolation of **11**, it was impossible to remove the excess reagent by treatment of the reaction mixture with cation exchange resin in the usual acid form; the pyridinium form had to be used instead and the treatment had to be very short. Even under these mild conditions, longer treatment brought about the hydrolysis of compound **11** to the acyclic nucleoside **12**.

To avoid the complications with lability of some alkynyl derivatives in acids, compound **9** was transformed first by acid hydrolysis to the 2,3-dihydroxypropyl derivative **14**. The intermediates **9** and **14** bear the reactive 6-chloro group, which could undergo aminolysis[22] and the 2-iodo group, which is preferable[8c,23] as a reaction centre for the Sonogashira coupling. Compounds **10**–**14** were then used as starting materials for the preparation of 2-substituted acyclic nucleosides derived from adenine and 6-guanidinopurine. The choice between these starting materials depended on their suitability for the Sonogashira reaction and the stability of the reaction products – alkynyl derivatives – under acid conditions. The products of these reactions and their further interconversions are presented in Scheme 2.

Thus, 2-alkynyladenine derivatives **15** were easily prepared by the Sonogashira reaction of appropriate 2′,3′-deprotected 6-chloro-2-iodoadenine compounds **14**. The coupling was regioselective with one equivalent of the alkyne. Thus-obtained 2-substituted 6-chloropurine derivatives **15** were treated with methanolic ammonia to give 6-aminopurines **16a**, **16b**, **16d**–**16f**. Compound **16c**, which was unstable under the conditions of ammonolysis, was obtained by coupling of unprotected 2-iodoadenine derivative **10**.

The unprotected 2-substituted 6-chloropurine derivative **15e**, which was prepared by the Sonogashira coupling, gave by guanidinolysis the corresponding 6-guanidino derivative **17e**, while the guanidinolysis of compound **15c** performed under the same conditions was unsuccessful. The Sonogashira coupling of the 6-guanidino derivatives **11** afforded the 2′,3′-protected compounds **13a**, **13b** which were then hydrolyzed to free acyclic nucleosides **17a**, **17b**. In analogy to its 2-substituted adenine counterpart **16c**, compound **17c** did not stand the acid hydrolysis and gave a mixture of products under the reaction conditions. To circumvent this problem, the acid-labile protecting group in **11** was removed prior to the



Synthesis of 9-(2,3-dihydroxypropyl)-9*H*-purine derivatives. Reagents: (i) isopentyl nitrite, I_2, CH_2I_2, CuI, THF; (ii) a) guanidine, DABCO, DMF/CH_3CN, b) NH_3/MeOH; (iii) Dowex 50×8, MeOH–H_2O; (iv) alkyne, $[PdCl_2(PPh_3)_2]$, CuI, Et_3N, DMF

SCHEME 2

coupling. The reaction was performed with the unprotected compound **12** to give the required 2-substituted acyclic nucleoside **17c**. The same strategy was applied in the preparation of compound **17d**.

The target 2-substituted 6-amino- or 6-guanidinopurine acyclic nucleoside analogues **16**, **17** as well as all intermediates were fully characterized by ^{1}H and ^{13}C NMR spectra and gave satisfactory elemental analyses.

CONCLUSION

In conclusion, 2-alkynyl derivatives of the acyclic nucleoside 9-(2,3-dihydroxypropyl)adenine and their 6-guanidinopurine counterparts were prepared by the Sonogashira coupling of the corresponding 2-iodopurine derivatives. Depending on the acid stability of the alkynyl group, the reaction was performed either with 2,3-*O*-isopropylidene derivative followed by reaction with ammonia or guanidine and deprotection or, in some cases, with unprotected 2,3-dihydroxypropyl derivative followed by the reaction with ammonia. The compounds are undergoing appropriate biochemical evaluation.

BIOLOGICAL ACTIVITY

None of thus-obtained 2-alkynyl derivatives of the acyclic nucleoside 9-(2,3-dihydroxypropyl)adenine (**16**) or their 6-guanidinopurine analogues **17** exhibited under standard conditions any cytotoxicity *in vitro* in L929, L1210, HeLaS3 and CCRF CEM cells[24]. Compounds **16** and **17** were also tested for antiviral activity against DNA viruses and retroviruses: MSV, HIV-1 and HIV-2. None of the compounds showed any significant activity in these assays. This confirms the hypothesis that the known activity of the 9-(2,3-dihydroxypropyl)adenine is due to its specific interference, as an adenosine analogue, with methylations.

The novel compounds synthesized in this report were tested[25] for their potencies on A_1 and A_{2A} adenosine receptors in rat brain radioligand binding assays. For A_1 and A_{2A} receptor affinity the tritiated agonist [^{3}H]PIA and [^{3}H]CGS21680 were used, respectively. None of the compounds revealed any considerable activity. In conclusion, these data show that the replacement of aldopentafuranosyl residue in base-substituted adenosine by the more flexible 2,3-dihydroxypropyl group results in the decrease of A_1 and/or A_{2A} purinoceptor agonist activity. Further continuation of this study is in progress.

EXPERIMENTAL

Materials

Sodium hydride, DABCO – 1,4-diazabicyclo[2.2.2]octane, isopentyl nitrite, 2,2-dimethyl-1,3-dioxolane-4-methanol, cesium carbonate, ethyl azodicarboxylate, and all alkynes were purchased from Aldrich (Prague, Czech Republic), only 2-ethynylthiophene was prepared as described in the literature[26]. 2-Amino-6-chloropurine and 2,6-dichloropurine were obtained from Monelli (Olomouc, Czech Republic), guanidine hydrochloride, 3,4-dihydro-2*H*-pyran, Dowex 50X8 and Dowex 1X2 were purchased from Fluka (Switzerland). Dimethylformamide was distilled from P_2O_5 *in vacuo*. Acetonitrile was refluxed with CaH_2 and distilled. All solvents were stored over molecular sieves (4Å).

Unless otherwise stated, solvents were evaporated at 40 °C/2 kPa and compounds were dried over P_2O_5. Melting points were determined on a Büchi Melting point B-545 apparaturs.

NMR spectra (*J*, Hz; δ, ppm) were measured on a Bruker DRX 500 (500 MHz for ^1H, 125.7 MHz for ^{13}C NMR spectra). TMS was used as internal standard for ^1H and ^{13}C NMR spectra; mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using FAB (ionisation by Xe, accelerating voltage 8 kV, glycerol matrix) or EI (electron energy 70 eV) techniques.

Preparative HPLC purification was performed on a column packed with 7 μm C18 reversed phase (Waters Delta 600 chromatograph), 17 × 250 mm; in *ca* 200 mg portions of mixtures using a linear gradient MeOH–H_2O (1:4 to 9:1) as eluent. Preparative TLC was carried out on 40 × 17 × 0.4 cm loose layers of silica gel containing UV indicator. All cross-coupling reactions were performed under argon atmosphere using vacuum-line techniques. Chromatography systems S1: $CHCl_3$–MeOH (95:5); S2: EtOAc–EtOH–acetone–H_2O (6:1:1:0.5) containing 0.5% Et_3N; S3: EtOAc–EtOH–acetone–H_2O–NH_3 (4:1:1:1:0.25).

Preparation of Guanidine Solution

Guanidine hydrochloride (1.91 g, 20 mmol) was added to sodium hydride (0.80 g, 20 mmol; 60% suspension in paraffin oil) in a mixture of acetonitrile (40 ml) and DMF (20 ml), and the mixture was stirred at room temperature under exclusion of moisture overnight. The resulting slurry was directly used for further reactions.

Method *A*. Cleavage of Isopropylidene Protecting Group. General Procedure

The protected compound (1 mmol) dissolved in 20% aqueous methanol (14 ml) was stirred with Dowex 50X8 (H^+ form) (approximately 20 ml) and the mixture was stirred at 60 °C for 1 h. The resin was removed by filtration and eluted with MeOH–H_2O–concentrated aqueous NH_3 (1:10:1) The eluate containing UV absorbing fractions was evaporated and the residue crystallized to give compounds **5**, **8**, **10**, **12**, **17a**, **17b**.

Method *B*. Ammonolysis of 6-Chloro Derivatives. General Procedure

6-Chloro derivative (1 mmol) in methanolic NH_3 (20 ml) was heated in an autoclave at 90 °C until the starting compound was consumed (TLC). The solvent was then evaporated, the residue was dissolved in H_2O–MeOH (1:1) (10 ml) and Dowex 50XC8 (H^+ form) was added. The suspension was applied onto the column of Dowex 50X8 (H^+ form), the column was washed

with H_2O and then with dilute aqueous NH_3 (1:10). The product-containing UV absorbing fractions were evaporated and the residue was purified by HPLC and crystallized to give the compounds **16a**, **16b**, **16d**, **16e**.

Method *C*

Dimethylformamide (8 ml) was added through a septum to an Ar-purged 50-ml flask with a mixture of compound **11** (0.42 g, 1 mmol), CuI (19.2 mg, 0.1 mmol), $[PdCl_2(PPh_3)_2]$ (18 mg, 0.05 mmol). Then Et_3N (0.7 ml, 5 mmol), followed by the corresponding alkyne (5 mmol) were added dropwise. The mixture was stirred at 60 °C until the starting compound **11** was consumed (TLC). The solvent was then evaporated *in vacuo*, co-distilled with toluene (3 × 30 ml) and the residue was chromatographed on a column of silica gel (30 g) to give compounds **13a**–**13c**.

Method *D*

Dimethylformamide (8 ml) was added through a septum to an Ar-purged 50-ml flask containing compound **14** (0.35 g, 1 mmol), CuI (19.2 mg, 0.1 mmol) and $[PdCl_2(PPh_3)_2]$ (18 mg, 0.05 mmol). Et_3N (0.17 ml, 1.2 mmol), followed by alkyne (1.2 mmol) were added dropwise and the mixture was stirred at room temperature until the starting compound **14** disappeared (TLC). The solvent was then evaporated and the residue co-distilled with toluene (3 × 30 ml). After evaporation of the solvent, the residue in $CHCl_3$ was mixed with saturated aqueous NH_4Cl (20 ml) and the mixture was extracted with $CHCl_3$ (3 × 30 ml). The collected organic layers were dried with anhydrous $MgSO_4$. After evaporation of the solvents *in vacuo*, the residue was chromatographed on a column of silica gel (30 g) to give compounds **15a**–**15f**.

Method *E*

The reaction mixture was the same as in method *D*. After evaporation, the residue was dissolved in MeOH and H_2S was passed through the solution for 5 min. After filtration of the mixture through Celite and evaporation of the filtrate, the residue was chromatographed on a column of silica gel (30 g) to give compounds **16c**, **17c**, **17d**.

2,6-Dichloro-9-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-9H-purine (**3**). 2,2-Dimethyl-1,3-dioxolane-4-methanol **2** (0.62 ml, 5 mmol) was added to a solution of 2,6-dichloropurine (**1**) (0.47g, 2.5 mmol) in THF (10 ml) under Ar followed by PPh_3 (1.31 g, 5 mmol) in THF (5 ml). Diethyl azodicarboxylate (0.79 ml, 5 mmol) was added dropwise. The resulting mixture was stirred at room temperature for 15 min and then heated at 50 °C for 11 h. The solvent was evaporated *in vacuo* and the residue chromatographed on a column of silica gel (20 g, MeOH–$CHCl_3$ 2:98). The product gave after crystallization 0.41g (54%) of colourless crystals; m.p. 118–123 °C (EtOAc). FAB MS, *m/z* (rel.%): 303 (60) [M + H]. ^{1}H NMR (DMSO-d_6): 1.22 s, 3 H and 1.27 s, 3 H (CH_3); 3.80 dd, 1 H, *J*(3′b,2′) = 4.9, *J*(gem) = 8.8 (H-3′b); 4.06 dd, 1 H, *J*(3′a,2′) = 6.3, *J*(gem) = 8.8 (H-3′a); 4.32 dd, 1 H, *J*(1′b,2′) = 6.7, *J*(gem) = 14.2 (H-1′b); 4.45 dd, 1 H, *J*(1′a,2′) = 5.1, *J*(gem) = 14.2 (H-1′a); 4.49 m, 1 H (H-2′); 8.68 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.15 and 26.65 (CH_3); 46.66 (C-1′); 66.17 (C-3′); 73.30 (C-2′); 109.36 (C-iPr); 130.44 (C-5); 149.11 (C-8); 149.84 (C-6); 151.22 (C-2); 153.91 (C-4). Exact mass (FAB HRMS) found 303.0479; calculated for $C_{11}H_{13}Cl_2N_4O_2$ [M + H] 303.0416.

2-Chloro-9-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-6-guanidino-9H-purine (**4**). Compound **3** (0.45 g, 1.5 mmol), DABCO (0.17 g, 1.5 mmol) and a guanidine solution (22.5 ml, 7.5 mmol) were stirred at room temperature for 4 h. The reaction mixture was evaporated *in vacuo*, co-distilled with toluene (3 × 30 ml) and dissolved in methanol. This solution was filtered through Celite, the filtrate was adsorbed on silica gel and chromatographed on the column of SiO_2 (20 g, MeOH–$CHCl_3$ 7:93). The purified product gave after crystallization 0.3 g (62%) of white crystals; m.p. 257–258 °C (EtOH–EtOAc). FAB MS, *m/z* (rel.%): 326 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.22 s, 3 H and 1.27 s, 3 H (CH_3); 3.74 dd, 1 H, *J*(3′b,2′) = 5.1, *J*(gem) = 8.6 (H-3′b); 4.03 dd, 1 H, *J*(3′a,2′) = 6.6, *J*(gem) = 8.6 (H-3′a); 4.17 dd, 1 H, *J*(1′b,2′) = 6.6, *J*(gem) = 14.2 (H-1′b); 4.27 dd, 1 H, *J*(1′a,2′) = 4.2, *J*(gem) = 14.2 (H-1′a); 4.40 m, 1 H (H-2′); 7.50 br, 4 H (NH); 8.03 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.23 and 26.69 (CH_3); 45.67 (C-1′); 66.20 (C-3′); 73.66 (C-2′); 109.18 (C-iPr); 123.89 (C-5); 142.06 (C-8); 151.19 (C-2); 151.26 (C-4); 160.09 (C-6); 160.38 (N-C). For $C_{12}H_{16}ClN_7O_2$ (325.8) calculated: 44.25% C, 4.95% H, 10.88% Cl, 30.10% N; found: 44.15% C, 4.91% H, 10.67% Cl, 29.89% N.

2-Chloro-9-(2,3-dihydroxypropyl)-6-guanidino-9H-purine (**5**). Compound **5** was prepared from **4** by method *A* to give white crystals in 83% yield; m.p. 251–252 °C (H_2O). FAB MS, *m/z* (rel.%): 386 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 3.33 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.8, *J*(gem) = 11.0 (H-3′b); 3.40 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.2, *J*(gem) = 11.0 (H-3′a); 3.81 m, 1 H (H-2′); 3.95 dd, 1 H, *J*(1′b,2′) = 8.5, *J*(gem) = 13.9 (H-1′b); 4.24 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.83 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.09 d, 1 H, *J*(OH,2′) = 5.4 (OH); 7.45 br, 4 H (NH); 7.99 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.60 (C-1′); 63.74 (C-3′); 69.73 (C-2′); 124.05 (C-5); 142.25 (C-8); 150.92 (C-2); 151.29 (C-4); 160.07 (C-6); 160.30 (N-C). For $C_9H_{12}ClN_7O_2 \cdot 0.25H_2O$ (385.7) calculated: 37.25% C, 4.34% H, 12.22% Cl, 33.79% N; found: 37.48% C, 4.30% H, 12.13% Cl, 33.66% N.

2-Amino-6-guanidino-9-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-9H-purine (**7**). Compound **6** (0.70 g, 2.5 mmol), DABCO (0.28 g, 2.5 mmol) and a guanidine solution (37.5 ml, 12.5 mmol) were stirred at room temperature overnight. The resulting mixture was evaporated *in vacuo*, co-distilled with toluene (3 × 30 ml) and dissolved in water (20 ml). This solution was neutralized with Dowex 50X8 (pyridinium form). The suspension was applied onto a column of the same resin (25 ml), the column was washed with 20% aqueous pyridine, eluted with a mixture of dilute aqueous NH_3 (1:10), and the eluate was evaporated *in vacuo*, to give 0.41g (55%) of amorphous foam. FAB MS, *m/z* (rel.%): 307 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.23 s, 3 H and 1.29 s, 3 H (CH_3); 3.73 dd, 1 H, *J*(3′b,2′) = 5.5, *J*(gem) = 8.5 (H-3′b); 3.97 dd, 1 H, *J*(3′a,2′) = 6.6, *J*(gem) = 8.5 (H-3′a); 4.04 dd, 1 H, *J*(1′b,2′) = 6.0, *J*(gem) = 14.3 (H-1′b); 4.10 dd, 1 H, *J*(1′a,2′) = 4.9, *J*(gem) = 14.3 (H-1′a); 4.42 m, 1 H (H-2′); 5.98 brs, 2 H (NH_2); 7.25 br, 4 H (NH); 7.64 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.27 and 26.74 (CH_3); 44.89 (C-1′); 66.24 (C-3′); 73.76 (C-2′); 109.00 (C-iPr); 118.94 (C-5); 138.20 (C-8); 152.25 (C-4); 159.21, 160.24 and 160.38 (C-6, C-2, N-C). Exact mass (FAB HRMS) found 307.1591; calculated for $C_{12}H_{18}N_8O_2$ [M + H] 307.1630.

2-Amino-9-(2,3-dihydroxypropyl)-6-guanidino-9H-purine (**8**). Compound **8** was prepared from **7** by method *A* to give yellowish solid in 67% yield; m.p. 174–177 °C (MeOH–ether). FAB MS, *m/z* (rel.%): 367 (85) [M + H]. ^{1}H NMR (DMSO-d_6): 3.25 dd, 1 H, *J*(3′b,2′) = 5.9, *J*(gem) = 12.0 (H-3′b); 3.35 dd, 1 H, *J*(3′a,2′) = 5.0, *J*(gem) = 12.0 (H-3′a); 3.77 m, 1 H (H-2′); 3.85 dd, 1 H, *J*(1′b,2′) = 7.5, *J*(gem) = 13.9 (H-1′b); 4.11 dd, 1 H, *J*(1′a,2′) = 3.7, *J*(gem) = 13.9 (H-1′a); 4.95 brs, 1 H and 5.20 brs, 1 H (OH); 5.97 brs, 2 H and 7.40 brs, 1 H (NH); 7.58 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 45.83 (C-1′); 63.50 (C-3′); 70.01 (C-2′); 119.14 (C-5); 138.59 (C-8);

152.29 (C-4); 158.94, 160.21 and 160.44 (C-6, C-2, N-C). Exact mass (FAB HRMS) found 267.1307; calculated for $C_9H_{15}N_8O_2$ [M + H] 267.1317.

6-Chloro-9-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-2-iodo-9H-purine (**9**). Isopentyl nitrite (30.1 ml, 217 mmol) was added to a mixture of compound **6** (10 g, 35 mmol), I_2 (8.8 g, 35 mmol), CH_2I_2 (8.6 ml, 106 mmol) and CuI (7 g, 38.5 mmol) in THF (178 ml). The mixture was heated under reflux for 45 min and thereafter cooled to room temperature. Insoluble materials were filtered off and the filtrate was concentrated to dryness *in vacuo*. The dark brown oil was co-distilled with toluene (3 × 30 ml), the resulting oil was dissolved in $CHCl_3$ (150 ml) and the solution was extracted with saturated aqueous $Na_2S_2O_3$ (50 ml) and then with H_2O (3 × 50 ml). The collected organic layers were dried with anhydrous $MgSO_4$ and evaporated *in vacuo* to give, after crystallization from EtOH, 11.33 g (81%) of compound **9** as yellowish crystals; m.p. 166–168 °C (EtOH). FAB MS, *m/z* (rel.%): 395 (30) [M + H]. ^{1}H NMR (DMSO-d_6): 1.21 s, 3 H and 1.27 s, 3 H (CH_3); 3.81 dd, 1 H, *J*(3′b,2′) = 4.8, *J*(gem) = 8.8 (H-3′b); 4.06 dd, 1 H, *J*(3′a,2′) = 6.6, *J*(gem) = 8.8 (H-3′a); 4.20 dd, 1 H, *J*(1′b,2′) = 7.0, *J*(gem) = 14.3 (H-1′b); 4.42 dd, 1 H, *J*(1′a,2′) = 4.1, *J*(gem) = 14.3 (H-1′a); 4.48 m, 1 H (H-2′); 8.58 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.14 and 26.67 (CH_3); 46.68 (C-1′); 66.18 (C-3′); 73.33 (C-2′); 109.35 (C-iPr); 117.95 (C-2); 130.89 (C-5); 148.20 (C-8); 148.56 (C-6); 153.35 (C-4). Exact mass (FAB HRMS) found 394.9735; calculated for $C_{11}H_{13}ClIN_4O_2$ [M + H] 394.9772.

6-Amino-9-(2,3-dihydroxypropyl)-2-iodo-9H-purine (**10**). Compound **9** (3 g, 7.6 mmol) was heated with methanolic NH_3 (100 ml) in autoclave at 60 °C for 16 h. The solvent was evaporated and the residue was worked up by method *A* to give 1.89 g (74%) of white crystals; m.p. 251–252 °C (dec.) (EtOH–H_2O 90:10). FAB MS, *m/z* (rel.%): 336 (35) [M + H]. ^{1}H NMR (DMSO-d_6): 3.32 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.0, *J*(gem) = 11.0 (H-3′b); 3.40 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.2, *J*(gem) = 11.0 (H-3′a); 3.81 m, 1 H (H-2′); 3.93 dd, 1 H, *J*(1′b,2′) = 8.7, *J*(gem) = 13.9 (H-1′b); 4.22 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.84 t, 1 H, *J*(OH,3′) = 5.7 (OH); 5.10 d, 1 H, *J*(OH,2′) = 5.5 (OH); 7.61 brs, 2 H (NH_2); 7.96 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.78 (C-1′); 63.74 (C-3′); 69.65 (C-2′); 118.70 (C-5); 120.76 (C-2); 141.83 (C-8); 150.37 (C-4); 156.04 (C-6). For $C_8H_{10}IN_5O_2 \cdot 0.25$EtOH (335.1) calculated: 29.35% C, 3.29% H, 36.87% I, 20.35% N; found: 29.48% C, 3.32% H, 37.04% I, 20.39% N.

9-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-6-guanidino-2-iodo-9H-purine (**11**). A mixture of compound **9** (1.97 g, 5 mmol), DABCO (0.56 g, 5 mmol) and a guanidine solution (75 ml, 25 mmol) was stirred at room temperature for 4 h. The resulting mixture was evaporated *in vacuo*, co-distilled with toluene (3 × 60 ml) and the residue was dissolved in H_2O, neutralized with Dowex 50X8 (pyridinium form). The suspension was applied onto the column of Dowex 50X8 (pyridinium form), the column was washed with MeOH–pyridine–H_2O (1:1:3), and eluted with a mixture of MeOH–concentrated aqueous NH_3–H_2O (3:1:6). Dowex 50X8 was then eluted with hot MeOH. The combined fractions were evaporated *in vacuo* and crystallized to give 1.40 g (67%) of white crystals; m.p. 256–258 °C (EtOH–H_2O 90:10). FAB MS, *m/z* (rel.%): 418 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.22 s, 3 H and 1.28 s, 3 H (CH_3); 3.75 dd, 1 H, *J*(3′b,2′) = 5.0, *J*(gem) = 8.7 (H-3′b); 4.03 dd, 1 H, *J*(3′a,2′) = 6.5, *J*(gem) = 8.7 (H-3′a); 4.15 dd, 1 H, *J*(1′b,2′) = 6.7, *J*(gem) = 14.3 (H-1′b); 4.25 dd, 1 H, *J*(1′a,2′) = 4.3, *J*(gem) = 14.3 (H-1′a); 4.43 m, 1 H (H-2′); 7.40 br, 4 H (NH); 7.94 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.22 and 26.68 (CH_3); 45.69 (C-1′); 66.19 (C-3′); 73.66 (C-2′); 109.17 (C-iPr); 118.59 (C-5); 124.87 (C-2); 141.41 (C-8); 150.83 (C-4); 159.51 and 160.00 (C-6, N-C). Exact mass (FAB HRMS) found 418.0497; calculated for $C_{12}H_{17}IN_7O_2$ [M + H] 418.0489.

9-(2,3-Dihydroxypropyl)-6-guanidino-2-iodo-9H-purine (**12**). Compound **12** was prepared from **11** by method *A* to give 58% of yellowish crystals; m.p. 243 °C (dec.) (EtOH–H_2O 90:10). FAB MS, *m/z* (rel.%): 378 (15) [M + H]. ^{1}H NMR (DMSO-d_6): 3.32 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.5, *J*(gem) = 11.0 (H-3′b); 3.39 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.0, *J*(gem) = 11.0 (H-3′a); 3.81 m, 1 H (H-2′); 3.93 dd, 1 H, *J*(1′b,2′) = 8.6, *J*(gem) = 13.9 (H-1′b); 4.22 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.83 t, 1 H, *J*(OH,3′) = 5.2 (OH); 5.09 d, 1 H, *J*(OH,2′) = 4.0 (OH); 7.40 br, 4 H (NH); 7.90 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.59 (C-1′); 63.75 (C-3′); 69.70 (C-2′); 118.41 (C-5); 125.04 (C-2); 141.71 (C-8); 150.90 (C-4); 156.51 and 159.96 (C-6, N-C). For $C_9H_{12}IN_7O_2$ (377.1) calculated: 28.66% C, 3.21% H, 33.65% I, 26.00% N; found: 28.63% C, 3.28% H, 33.83% I, 25.57% N.

9-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-6-guanidino-2-hex-1-yn-1-yl-9H-purine (**13a**). Compound **13a** was prepared from **11** by method *C*, reaction time 3 h, chromatography in (S2), yield 87%, oil. FAB MS, *m/z* (rel.%): 372 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 0.91 t, 3 H, *J* = 7.3 and 1.22 s, 3 H, 1.27 s, 3 H (CH_3); 1.43 sext, 2 H, *J* = 7.2 and 1.55 pent, 2 H, *J* = 7.1, 2.46 t, 2 H, *J* = 7.1 (CH_2); 3.76 dd, 1 H, *J*(3′b,2′) = 5.0, *J*(gem) = 8.8 (H-3′b); 4.04 dd, 1 H, *J*(3′a,2′) = 6.6, *J*(gem) = 8.8 (H-3′a); 4.25 dd, 1 H, *J*(1′b,2′) = 6.6, *J*(gem) = 14.2 (H-1′b); 4.36 dd, 1 H, *J*(1′a,2′) = 4.1, *J*(gem) = 14.2 (H-1′a); 4.47 m, 1 H (H-2′); 7.95 br, 4 H (NH); 8.32 brs, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 13.61, 25.19 and 26.66 (CH_3); 18.14, 21.68 and 29.98 (C-CH_2); 45.83 (C-1′); 66.17 (C-3′); 73.56 (C-2′); 87.35 and 80.98 (C≡C); 109.20 (C-iPr); 122.37 (C-5); 143.89 (C-2); 144.44 (C-8); 151.10 (C-4); 157.79 and 158.00 (C-6, N-C). Exact mass (FAB HRMS) found 372.2148; calculated for $C_{18}H_{26}N_7O_2$ [M + H] 372.2137.

9-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-6-guanidino-2-(phenylethynyl)-9H-purine (**13b**). Compound **13b** was prepared from **11** by method *C*, reaction time 3 h, chromatography in (S2), yield 74%, amorphous powder. FAB MS, *m/z* (rel.%): 392 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.23 s, 3 H and 1.29 s, 3 H (CH_3); 3.77 dd, 1 H, *J*(3′b,2′) = 5.2, *J*(gem) = 8.8 (H-3′b); 4.05 dd, 1 H, *J*(3′a,2′) = 6.7, *J*(gem) = 8.8 (H-3′a); 4.23 dd, 1 H, *J*(1′b,2′) = 6.6, *J*(gem) = 14.3 (H-1′b); 4.34 dd, 1 H, *J*(1′a,2′) = 4.3, *J*(gem) = 14.3 (H-1′a); 4.48 m, 1 H (H-2′); 7.40 br, 4 H (NH); 7.47 m, 3 H and 7.63 m, 2 H (arom. H); 8.12 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.24, 26.73 (CH_3); 45.61 (C-1′); 66.25 (C-3′); 73.71 (C-2′); 83.21 and 90.04 (C≡C); 109.18 (C-iPr); 124.73 (C-5); 121.50 and 129.05, 129.64, 2 C, 132.10, 2 C (arom. C); 142.81 (C-2); 143.75 (C-2); 150.32 (C-4); 159.45 and 160.21 (C-6, N-C). Exact mass (FAB HRMS) found 392.1852; calculated for $C_{20}H_{22}N_7O_2$ [M + H] 392.1835.

9-[2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-6-guanidino-2-(3-hydroxy-3-phenylprop-1-yn-1-yl)-9H-purine (**13c**). Compound **13c** was prepared from **11** by method *C*, reaction time 2 h, chromatography in EtOAc–EtOH (85:15) containing 0.5% NH_3, yield 85%, yellowish oil. FAB MS, *m/z* (rel.%): 422 (30) [M + H]. ^{1}H NMR (DMSO-d_6): 1.22 s, 3 H and 1.27 s, 3 H (CH_3); 3.74 dd, 1 H, *J*(3′b,2′) = 5.2, *J*(gem) = 8.8 (H-3′b); 4.04 dd, 1 H, *J*(3′a,2′) = 6.5, *J*(gem) = 8.8 (H-3′a); 4.24 dd, 1 H, *J*(1′b,2′) = 6.6, *J*(gem) = 14.2 (H-1′b); 4.35 dd, 1 H, *J*(1′a,2′) = 3.9, *J*(gem) = 14.2 (H-1′a); 4.45 m, 1 H (H-2′); 5.66 s, 1 H (OCH); 6.31 brs, 1 H (OH); 7.32 t, 1 H and 7.40 t, 2 H, 7.54 d, 2 H (arom. H); 7.70 br, 4 H (NH); 8.26 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 25.19, 26.66 (CH_3); 45.77 (C-1′); 62.85 (O-CH); 66.16 (C-3′); 73.58 (C-2′); 84.58 and 86.61 (C≡C); 109.18 (C-iPr); 123.19 (C-5); 126.66 and 127.98, 2 C, 128.55, 2 C, 141.66 (arom. C); 143.38 (C-2); 144.13 (C-8); 150.79 (C-4); 158.41 (C-6). Exact mass (FAB HRMS) found 422.1927; calculated for $C_{21}H_{24}N_7O_3$ [M + H] 422.1941.

2-Chloro-9-(2,3-dihydroxypropyl)-6-iodo-9H-purine (**14**). Compound **9** (5 g, 12.6 mmol) in a mixture of MeOH (50 ml) and H_2O (25 ml). The solution was acidified with HCl and stirred at 60 °C for 1.5 h. The reaction mixture was then neutralized at 0 °C with aqueous NH_3. The

solvent was taken down *in vacuo* and the residue was chromatographed on a column of silica gel (150 g, MeOH–$CHCl_3$ 10:90). The crude product was crystallized from MeOH to give 4.09 g (91%) of yellowish crystals; m.p. > 340 °C (dec.). FAB MS, *m/z* (rel.%): 355 (30) [M + H]. ^{1}H NMR (DMSO-d_6): 3.35 brdt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.7, *J*(gem) = 11.0 (H-3′b); 3.44 brdt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.0, *J*(gem) = 11.0 (H-3′a); 3.85 m, 1 H (H-2′); 4.10 dd, 1 H, *J*(1′b,2′) = 8.9, *J*(gem) = 13.9 (H-1′b); 4.37 dd, 1 H, *J*(1′a,2′) = 3.4, *J*(gem) = 13.9 (H-1′a); 4.98 t, 1 H, *J*(OH,3′) = 5.5 (OH); 5.23 d, 1 H, *J*(OH,2′) = 5.5 (OH); 8.56 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 47.66 (C-1′); 63.61 (C-3′); 69.41 (C-2′); 118.01 (C-2); 130.02 (C-5); 148.32 (C-6); 148.56 (C-8); 153.44 (C-4). Exact mass (FAB HRMS) found 354.9435; calculated for $C_8H_9ClIN_4O_2$ [M + H] 354.9458.

6-Chloro-9-(2,3-dihydroxypropyl)-2-hex-1-yn-1-yl-9H-purine (**15a**). Compound **15a** was prepared from **14** by method *D*, reaction time 2 h, chromatography in (S1), yield 57%, white crystals; m.p. 133–135 °C (MeOH–Et_2O). FAB MS, *m/z* (rel.%): 309 (25) [M + H], 331 [M + Na]. ^{1}H NMR (DMSO-d_6): 0.92 t, 3 H, *J* = 7.3 (CH_3); 1.14 sext, 2 H, *J* = 7.3, 1.57 pent, 2 H, *J* = 7.2 and 2.50 t, 2 H, *J* = 7.1 (CH_2); 3.37 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.9, *J*(gem) = 11.0 (H-3′b); 3.45 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.1, *J*(gem) = 11.0 (H-3′a); 3.86 m, 1 H (H-2′); 4.11 dd, 1 H, *J*(1′b,2′) = 8.9, *J*(gem) = 14.0 (H-1′b); 4.41 dd, 1 H, *J*(1′a,2′) = 3.0, *J*(gem) = 14.0 (H-1′a); 4.86 t, 1 H, *J*(OH, 3′) = 5.6 (OH); 5.11 d, 1 H, *J*(OH,2′) = 5.5 (OH); 8.61 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 13.57 (CH_3); 18.10, 21.67 and 29.80 (CH_2); 47.59 (C-1′); 63.67 (C-3′); 69.42 (C-2′); 79.97 and 89.63 (C≡C); 130.19 (C-5); 144.42 (C-2); 148.58 (C-6); 149.13 (C-8); 152.44 (C-4). For $C_{14}H_{17}ClN_4O_2$ (308.8) calculated: 54.46% C, 5.55% H, 11.48% Cl, 18.15% N; found: 54.27% C, 5.64% H, 11.53% Cl, 17.87% N.

6-Chloro-9-(2,3-dihydroxypropyl)-2-(phenylethynyl)-9H-purine (**15b**). Compound **15b** was prepared from **14** by method *D*, reaction time 1.5 h, chromatography in (S1), yield 78%, white crystals; m.p. 212–215 °C (EtOH). FAB MS, *m/z* (rel.%): 329 (10) [M + H]. ^{1}H NMR (DMSO-d_6): 3.39 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.9, *J*(gem) = 11.0 (H-3′b); 3.48 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.0, *J*(gem) = 11.0 (H-3′a); 3.91 m, 1 H (H-2′); 4.16 dd, 1 H, *J*(1′b,2′) = 8.9, *J*(gem) = 13.9 (H-1′b); 4.46 dd, 1 H, *J*(1′a,2′) = 3.3, *J*(gem) = 13.9 (H-1′a); 4.90 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.15 d, 1 H, *J*(OH,2′) = 5.4 (OH); 7.50 m, 3 H and 7.70 m, 2 H (arom. H); 8.68 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 47.68 (C-1′); 63.63 (C-3′); 69.46 (C-2′); 86.53 and 88.06 (C≡C); 120.53 and 129.17, 130.34, 2 C, 132.32, 2 C (arom. C); 130.49 (C-5); 144.08 (C-2); 148.78 (C-6); 149.53 (C-8); 152.51 (C-4). For $C_{16}H_{13}ClN_4O_2$ (328.8) calculated: 58.46% C, 3.99% H, 10.78% Cl, 17.04% N; found: 58.15% C, 4.05% H, 10.74 Cl, 16.74% N.

6-Chloro-9-(2,3-dihydroxypropyl)-2-(3-hydroxy-3-phenylprop-1-yn-1-yl)-9H-purine (**15c**). Compound **15c** was prepared from **14** by method *D*, reaction time 6 h, chromatography in $CHCl_3$–MeOH (92:8), yield 75%, foam. FAB MS, *m/z* (rel.%): 359 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 3.35 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.1, *J*(gem) = 11.0 (H-3′b); 3.45 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.3, *J*(gem) = 11.0 (H-3′a); 3.86 m, 1 H (H-2′); 4.12 dd, 1 H, *J*(1′b,2′) = 9.0, *J*(gem) = 13.9 (H-1′b); 4.42 dd, 1 H, *J*(1′a,2′) = 3.3, *J*(gem) = 13.9 (H-1′a); 4.88 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.13 d, 1 H, *J*(OH,2′) = 5.5 (OH); 5.70 d, 1 H, *J*(OH,CH) = 6.0 (OH); 6.43 d, 1 H, *J*(CH,OH) = 6.0 (O-CH); 7.34 t, 1 H, 7.42 t, 2 H and 7.55 d, 2 H (arom. H); 8.65 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 47.70 (C-1′); 62.84 (O-CH); 63.67 (C-3′); 69.42 (C-2′); 83.29 and 89.11 (C≡C); 130.54 (C-5); 126.65, 2 C, 128.12 and 128.66, 141.40, 2 C (arom. C); 143.86 (C-2); 148.71 (C-6); 149.50 (C-8); 152.46 (C-4). Exact mass (FAB HRMS) found 359.0864; calculated for $C_{17}H_{16}ClN_4O_3$ [M + H] 359.0910.

6-Chloro-9-(2,3-dihydroxypropyl)-2-[(1-hydroxycyclohexyl)ethynyl]-9H-purine (**15d**). Compound **15d** was prepared from **14** by method *D*, reaction time 1 h, chromatography in $CHCl_3$–

MeOH (90:10), yield 71%, white crystals; m.p. 219–221 °C (MeOH). FAB MS, *m/z* (rel.%): 351 (10) [M + H]. ^{1}H NMR (DMSO-d_6): 1.28 m, 1 H, 1.49 m, 3 H, 1.63 m, 4 H and 1.88 m, 2 H (CH_2); 3.37 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.5, *J*(gem) = 11.0 (H-3′b); 3.46 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.6, *J*(gem) = 11.0 (H-3′a); 3.87 m, 1 H (H-2′); 4.21 dd, 1 H, *J*(1′b,2′) = 8.9, *J*(gem) = 13.9 (H-1′b); 4.42 dd, 1 H, *J*(1′a,2′) = 3.4, *J*(gem) = 13.9 (H-1′a); 4.90 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.14 d, 1 H, *J*(OH,2′) = 5.5 (OH); 5.70 s, 1 H (OH); 8.64 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 22.65 and 24.92, 2 C, 39.20, 2 C (CH_2); 47.63 (C-1′); 63.68 (C-3′); 66.93 (C-O); 69.45 (C-2′); 81.70 and 92.82 (C≡C); 130.21 (C-5); 144.21 (C-2); 148.66 (C-6); 149.30 (C-8); 152.47 (C-4). For $C_{16}H_{19}ClN_4O_3$ (350.8) calculated: 54.78% C, 5.46% H, 10.11% Cl, 15.97% N; found: 54.63% C, 5.64% H, 10.23 Cl, 15.71% N.

6-Chloro-9-(2,3-dihydroxypropyl)-2-[(2-thienyl)ethynyl]-9H-purine (**15e**). Compound **15e** was prepared from **14** by method *D*, reaction time 2.5 h, chromatography in (S1), yield 70%, white crystals; m.p. 222–223 °C (MeOH). FAB MS, *m/z* (rel.%): 335 (10) [M + H]. ^{1}H NMR (DMSO-d_6): 3.39 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.1, *J*(gem) = 11.0 (H-3′b); 3.47 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.1, *J*(gem) = 11.0 (H-3′a); 3.89 m, 1 H (H-2′); 4.15 dd, 1 H, *J*(1′b,2′) = 9.0, *J*(gem) = 13.9 (H-1′b); 4.45 dd, 1 H, *J*(1′a,2′) = 3.3, *J*(gem) = 13.9 (H-1′a); 4.91 t, 1 H, *J*(OH,3′) = 5.5 (OH); 5.16 d, 1 H, *J*(OH,2′) = 5.4 (OH); 7.21 dd, 1 H, *J* = 3.6 and 5.1, 7.68 dd, 1 H, *J* = 1.2 and 3.6 and 7.84 dd, 1 H, *J* = 1.2 and 5.1; 8.67 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 47.72 (C-1′); 63.68 (C-3′); 69.48 (C-2′); 80.84 and 91.84 (C≡C); 130.48 (C-5); 119.96, 128.42, 131.48 and 135.49 (arom. C); 143.95 (C-2); 148.83 (C-6); 149.58 (C-8); 152.51 (C-4). For $C_{14}H_{11}ClN_4O_2S$ (334.8) calculated: 50.23% C, 3.31% H, 10.59% Cl, 16.74% N, 9.58% S; found: 50.08% C, 3.38% H, 10.55% Cl, 16.34% N, 9.42% S.

6-Chloro-9-(2,3-dihydroxypropyl)-2-[(trimethylsilyl)ethynyl]-9H-purine (**15f**). Compound **15f** was prepared from **14** by method *D*, reaction time 1 h, chromatography in (S1), yield 69%, yellowish foam. FAB MS, *m/z* (rel.%): 325 (30) [M + H]. ^{1}H NMR (DMSO-d_6): 0.29 s, 9 H (Si-CH_3); 3.37 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.1, *J*(gem) = 11.0 (H-3′b); 3.46 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.2, *J*(gem) = 11.0 (H-3′a); 3.69 m, 1 H (H-2′); 4.13 dd, 1 H, *J*(1′b,2′) = 8.9, *J*(gem) = 13.9 (H-1′b); 4.43 dd, 1 H, *J*(1′a,2′) = 3.3, *J*(gem) = 13.9 (H-1′a); 4.88 t, 1 H, *J*(OH,3′) = 5.5 (OH); 5.12 d, 1 H, *J*(OH,2′) = 5.5 (OH); 8.66 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): –0.41 (Si-CH_3); 47.66 (C-1′); 63.65 (C-3′); 69.45 (C-2′); 92.84 and 102.73 (C≡C); 130.22 (C-5); 143.33 (C-2); 148.68 (C-6); 149.63 (C-8); 152.34 (C-4). Exact mass (FAB HRMS) found 325.0855; calculated for $C_{13}H_{18}ClN_4O_2Si$ [M + H] 325.0888.

6-Amino-9-(2,3-dihydroxypropyl)-2-hex-1-yn-1-yl-9H-purine ***(16a)***. *Compound* **16a** was prepared from **15a** by method *B*, reaction time 16 h, yield 70%, white crystals; m.p. 171–173 °C (MeOH). FAB MS, *m/z* (rel.%): 290 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 0.90 t, 3 H, *J*(CH_3,CH_2) = 7.3 (CH_3); 1.42 sext, 2 H, *J* = 7.3, 1.52 brpent, 2 H and 2.40 t, 2 H, *J* = 7.0 (CH_2); 3.32 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.0, *J*(gem) = 11.0 (H-3′b); 3.40 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.3, *J*(gem) = 11.0 (H-3′a); 3.81 m, 1 H (H-2′); 3.96 dd, 1 H, *J*(1′b,2′) = 8.4, *J*(gem) = 13.9 (H-1′b); 4.26 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.84 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.09 d, 1 H, *J*(OH,2′) = 5.4 (OH); 7.28 brs, 2 H (NH_2); 8.05 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 13.61 (CH_3); 18.03, 21.64, 30.10 (CH_2); 46.62 (C-1′); 63.73 (C-3′); 69.77 (C-2′); 81.59 and 85.18 (C≡C); 118.19 (C-5); 142.56 (C-8); 145.65 (C-2); 149.91 (C-4); 155.82 (C-6). For $C_{14}H_{19}N_5O_2$ (289.3) calculated: 58.12% C, 6.62% H, 24.20% N; found: 57.76% C, 6.70% H, 23.91% N.

6-Amino-9-(2,3-dihydroxypropyl)-2-(phenylethynyl)-9H-purine ***(16b)***. *Compound* **16b** was prepared from **15b** by method *B*, reaction time 24 h, yield 66%, colourless crystals; m.p. 231–232 °C (aqueous MeOH). FAB MS, *m/z* (rel.%): 310 (10) [M + H]. ^{1}H NMR (DMSO-d_6):

3.36 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.7, *J*(gem) = 11.2 (H-3′b); 3.43 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.0, *J*(gem) = 11.2 (H-3′a); 3.85 m, 1 H (H-2′); 4.01 dd, 1 H, *J*(1′b,2′) = 8.5, *J*(gem) = 13.9 (H-1′b); 4.32 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.87 t, 1 H, *J*(OH,3′) = 5.5 (OH); 5.13 d, 1 H, *J*(OH,2′) = 4.9 (OH); 7.46 brs, 2 H (NH_2); 7.44 m, 3 H and 7.61 m, 2 H (arom. H); 8.12 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.74 (C-1′); 63.79 (C-3′); 69.79 (C-2′); 82.97 and 89.96 (C≡C); 118.50 (C-5); 121,55; 129.09, 129.61, 2 C, 132.03, 2 C (arom. C); 142.97 (C-8); 145.25 (C-2); 149.91 (C-4); 155.96 (C-6). For $C_{16}H_{15}N_5O_2$ (309.3) calculated: 62.13% C, 4.89% H, 22.64% N; found: 62.02% C, 5.03% H, 20.46% N.

6-Amino-9-(2,3-dihydroxypropyl)-2-(3-hydroxy-3-phenylprop-1-yn-1-yl)-9H-purine (**16c**). Compound **16c** was prepared from **10h** by method *E*, reaction time 4 h, chromatography in (S2), yield 62%, white crystals; m.p. 188–190 °C (MeOH). FAB MS, *m/z* (rel.%): 340 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 3.32 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.9, *J*(gem) = 11.1 (H-3′b); 3.40 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.5, *J*(gem) = 11.1 (H-3′a); 3.81 m, 1 H (H-2′); 3.96 dd, 1 H, *J*(1′b,2′) = 8.4, *J*(gem) = 13.9 (H-1′b); 4.27 dd, 1 H, *J*(1′a,2′) = 3.2, *J*(gem) = 13.9 (H-1′a); 4.84 t, 1 H, *J*(OH,3′) = 5.7 (OH); 5.09 d, 1 H, *J*(OH,2′) = 5.5 (OH); 5.60 d, 1 H, *J*(CH,OH) = 5.8 (O-CH); 6.27 d, 1 H, *J*(OH,CH) = 5.8 (OH); 7.36 brs, 2 H (NH_2); 7.32 t, 1 H, 7.40 t, 2 H and 7.52 d, 2 H (arom. H); 8.08 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.73 (C-1′); 62.86 (O-CH); 63.77 (C-3′); 69.77 (C-2′); 85.09 and 85.31 (C≡C); 118.42 (C-5); 126.63 and 127.93, 2 C, 128.55, 141.99, 2 C (arom. C); 142.85 (C-8); 145.10 (C-2); 149.84 (C-4); 155.88 (C-6). For $C_{17}H_{17}N_5O_3$ (339.4) calculated: 60.17% C, 5.05% H, 20.64% N; found: 59.90% C, 5.07% H, 20.42% N.

6-Amino-9-(2,3-dihydroxypropyl)-2-[(1-hydroxycyclohexyl)ethynyl]-9H-purine (**16d**). Compound **16d** was prepared from **15d** by method *B*, reaction time 15 h, yield 72%, white crystals; m.p. 114–116 °C (aqueous MeOH). FAB MS, *m/z* (rel.%): 332 (10) [M + H]. ^{1}H NMR (DMSO-d_6): 1.25 m, 1 H, 1.49 m, 3 H, 1.56 m, 2 H, 1.60 m, 2 H and 1.92 m, 2 H (CH_2); 3.33 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.9, *J*(gem) = 11.2 (H-3′b); 3.40 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.3, *J*(gem) = 11.2 (H-3′a); 3.81 m, 1 H (H-2′); 3.96 dd, 1 H, *J*(1′b,2′) = 8.5, *J*(gem) = 13.9 (H-1′b); 4.28 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.87 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.11 d, 1 H, *J*(OH,2′) = 4.5 (OH); 5.54 s, 1 H (OH); 7.35 s, 2 H (NH_2); 8.07 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 22.71, 25.01, 2 C, 39.53, 2 C (CH_2); 46.65 (C-1′); 63.75 (C-3′); 66.80 (C-O); 69.78 (C-2′); 83.33 and 88.84 (C≡C); 118.27 (C-5); 142.68 (C-8); 145.46 (C-2); 149.88 (C-4); 155.87 (C-6). For $C_{16}H_{21}N_5O_3 \cdot 0.5H_2O$ (331.4) calculated: 56.46% C, 6.51% H, 20.58% N; found: 56.32% C, 6.65% H, 20.25% N.

6-Amino-9-(2,3-dihydroxypropyl)-2-[(2-thienyl)ethynyl]-9H-purine (**16e**). Compound **16e** was prepared from **15e** by method *B*, reaction time 12 h, yield 51%, yellowish crystals; m.p. 242–244 °C (aqueous MeOH). FAB MS, *m/z* (rel.%): 316 (32) [M + H]. ^{1}H NMR (DMSO-d_6): 3.35 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.0, *J*(gem) = 11.0 (H-3′b); 3.42 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.3, *J*(gem) = 11.0 (H-3′a); 3.84 m, 1 H (H-2′); 3.99 dd, 1 H, *J*(1′b,2′) = 8.6, *J*(gem) = 13.9 (H-1′b); 4.31 dd, 1 H, *J*(1′a,2′) = 3.4, *J*(gem) = 13.9 (H-1′a); 4.87 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.12 d, 1 H, *J*(OH,2′) = 5.5 (OH); 7.45 brs, 2 H (NH_2); 7.16 dd, 1 H, *J* = 3.6 and 5.1, 7.54 dd, 1 H, *J* = 1.0 and 3.6, 7.74 dd, 1 H, *J* = 1.0 and 5.1 (arom. H); 8.12 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.77 (C-1′); 63.79 (C-3′); 69.78 (C-2′); 76.64 and 93.65 (C≡C); 118.51 (C-5); 121.09, 128.20, 130.20 and 134.18 (arom. C); 143.01 (C-8); 145.06 (C-2); 149.87 (C-4); 155.95 (C-6). For $C_{14}H_{13}N_5O_2S$ (315.4) calculated: 53.32% C, 4.15% H, 22.21% N, 10.17% S; found: 53.21% C, 4.33% H, 21.83% N, 10.10% S.

6-Amino-9-(2,3-dihydroxypropyl)-2-(ethynyl)-9H-purine (**16f**). Compound **16f** was prepared from **15f** by method *B*, purification on Dowex 50X8 was omitted. Reaction time 16 h, yield

40%, white crystals; m.p. 246–247 °C (aqueous MeOH). FAB MS, *m/z* (rel.%): 234 (10) [M + H], 79 (100). ^{1}H NMR (DMSO-d_6): 3.32 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 6.0, *J*(gem) = 11.2 (H-3′b); 3.40 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.2, *J*(gem) = 11.2 (H-3′a); 3.97 s, 1 H (HC≡); 3.97 dd, 1 H, *J*(1′b,2′) = 8.3, *J*(gem) = 13.9 (H-1′b); 4.28 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.85 t, 1 H, *J*(OH,3′) = 5.6 (OH); 5.10 d, 1 H, *J*(OH,2′) = 5.4 (OH); 7.39 brs, 2 H (NH_2); 8.10 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.73 (C-1′); 63.75 (C-3′); 69.74 (C-2′); 72.00 and 83.78 (C≡C); 118.69 (C-5); 142.97 (C-8); 144.58 (C-2); 149.74 (C-4); 155.89 (C-6). For $C_{10}H_{11}N_5O_2 \cdot 1/6H_2O$ (233.2) calculated: 50.84% C, 4.84% H, 29.65% N; found: 50.98% C, 4.83% H, 29.62% N.

9-(2,3-Dihydroxypropyl)-6-guanidino-2-hex-1-yn-1-yl-9H-purine (**17a**). Compound **17a** was prepared from **13a** by method *A*, yield 74%, yellowish crystals; m.p. 129–131 °C (MeOH). FAB MS, *m/z* (rel.%): 332 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 0.92 t, 3 H, *J* = 7.3 and 1.42 sext, 2 H, *J* = 7.3; 1.54 pent, 2 H, *J* = 7.2; 2.43 t, 2 H, *J* = 7.3 (Bu); 3.32 dd, 1 H, *J*(3′b,2′) = 6.1, *J*(gem) = 11.1 (H-3′b); 3.39 dd, 1 H, *J*(3′a,2′) = 5.1, *J*(gem) = 11.1 (H-3′a); 3.81 m, 1 H (H-2′); 3.96 dd, 1 H, *J*(1′b,2′) = 8.3, *J*(gem) = 13.9 (H-1′b); 4.27 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 5.00 br, 2 H (OH); 7.50 br, 4 H (NH); 8.02 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 13.64, 18.14, 21.72, 30.14 (Bu); 46.44 (C-1′); 63.75 (C-3′); 69.83 (C-2′); 81.78 and 85.32 (C≡C); 124.63 (C-5); 142.62 (C-8); 143.88 (C-2); 150.23 (C-4); 159.58 and 160.31 (C-6, N-C). Exact mass (FAB HRMS) found 332.1851; calculated for $C_{15}H_{22}N_7O_2$ [M + H] 332.1835.

9-(2,3-Dihydroxypropyl)-6-guanidino-2-(phenylethynyl)-9H-purine (**17b**). Compound **17b** was prepared from **13b** by method *A*, yield 0.25 g (63%), white crystals; m.p. 161–164 °C (aqueous MeOH). FAB MS, *m/z* (rel.%): 352 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 3.36 dd, 1 H, *J*(3′b,2′) = 6.1, *J*(gem) = 11.0 (H-3′b); 3.43 dd, 1 H, *J*(3′a,2′) = 5.1, *J*(gem) = 11.0 (H-3′a); 3.85 m, 1 H (H-2′); 4.02 dd, 1 H, *J*(1′b,2′) = 8.4, *J*(gem) = 13.9 (H-1′b); 4.33 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.92 brs, 1 H and 5.18 brs, 1 H (OH); 7.50 br, 4 H (NH); 7.46 m, 3 H and 7.64 m, 2 H (arom. H); 8.09 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.56 (C-1′); 63.81 (C-3′); 69.85 (C-2′); 83.08 and 90.14 (C≡C); 124.92 (C-5); 121.54 and 129.03, 129.59, 2 C, 132.02, 2 C (arom. C); 143.02 (C-8); 143.55 (C-2); 150.22 (C-4); 159.60 and 160.39 (C-6, N-C). For $C_{17}H_{17}N_7O_2 \cdot$MeOH (351.4) calculated: 56.39% C, 5.52% H, 25.57% N; found: 56.42% C, 5.31% H, 25.82% N.

9-(2,3-Dihydroxypropyl)-6-guanidino-2-(3-hydroxy-3-phenylprop-1-yn-1-yl)-9H-purine (**17c**). Compound **17c** was prepared from **12** by method *E*, reaction time 4 h, chromatography in (S2), yield 71%, yellowish crystals; m.p. > 190 °C (dec.) (MeOH–acetone). FAB MS, *m/z* (rel.%): 382 (25) [M + H]. ^{1}H NMR (DMSO-d_6): 3.33 dd, 1 H, *J*(3′b,2′) = 6.1, *J*(gem) = 11.2 (H-3′b); 3.39 dd, 1 H, *J*(3′a,2′) = 5.1, *J*(gem) = 11.2 (H-3′a); 3.84 m, 1 H (H-2′); 3.97 dd, 1 H, *J*(1′b,2′) = 8.4, *J*(gem) = 13.9 (H-1′b); 4.28 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 5.00 br, 3 H (OH); 5.64 s, 1 H (OCH); 7.45 br, 4 H (NH); 7.32 t, 1 H and 7.40 t, 2 H, 7.55 d, 2 H (arom. H); 8.05 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.53 (C-1′); 62.89 (O-CH); 63.78 (C-3′); 69.84 (C-2′); 85.30 and 85.36 (C≡C); 124.88 (C-5); 126.69, 2 C and 127.93, 128.55, 2 C, 141.89 (arom. C); 142.89 (C-8); 143.36 (C-2); 150.15 (C-4); 159.58 and 160.37 (C-6, N-C). For $C_{18}H_{19}N_7O_3 \cdot 0.5$MeOH (381.4) calculated: 55.91% C, 5.33% H, 24.67% N; found: 55.97% C, 5.07% H, 24.71% N.

9-(2,3-Dihydroxypropyl)-6-guanidino-2-[(1-hydroxycyclohexyl)ethynyl]-9H-purine (**17d**). Compound **17d** was prepared from **12** by method *E*, reaction time 4 h, chromatography in (S2), yield 77%, white crystals; m.p. 167–170 °C (aqueous MeOH). FAB MS, *m/z* (rel.%): 374 (80) [M + H]. ^{1}H NMR (DMSO-d_6): 1.28 m, 2 H, 1.50 m, 2 H, 1.55 m, 2 H, 1.60 m, 2 H and

1.85 m, 2 H (CH_2); 3.32 dd, 1 H, *J*(3′b,2′) = 6.0, *J*(gem) = 11.0 (H-3′b); 3.40 dd, 1 H, *J*(3′a,2′) = 5.0, *J*(gem) = 11.0 (H-3′a); 3.81 m, 1 H (H-2′); 3.97 dd, 1 H, *J*(1′b,2′) = 8.5, *J*(gem) = 13.9 (H-1′b); 4.29 dd, 1 H, *J*(1′a,2′) = 3.4, *J*(gem) = 13.9 (H-1′a); 5.20 br, 2 H and 5.60 brs, 1 H (OH); 7.50 br, 4 H (NH); 8.05 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 22.74, 2 C and 25.05, 39.36, 2 C (CH_2); 46.50 (C-1′); 63.78 (C-3′); 66.80 (C-O); 69.85 (C-2′); 83.59 and 89.12 (C≡C); 124.69 (C-5); 142.81 (C-8); 150.22 (C-4); 159.76 (C-6); 160.37 (N-C). Exact mass (FAB HRMS) found 374.1922; calculated for $C_{17}H_{24}N_7O_3$ [M + H] 374.1941.

9-(2,3-Dihydroxypropyl)-6-guanidino-2-[(2-thienyl)ethynyl)]-9H-purine (**17e**). A mixture of compound **15e** (0.33 g, 1 mmol), DABCO (0.11 g, 1 mmol) and a guanidine solution (15 ml, 5 mmol) was stirred at room temperature for 5 h. The resulting mixture was evaporated *in vacuo* and co-distilled with toluene (3 × 30 ml). The residue was dissolved in H_2O and neutralized with Dowex 50X8 (H^+ form). This suspension was applied onto a column of the same resin (15 ml), the column was washed with H_2O and eluted with dilute aqueous NH_3 (1:10). The ammonia eluate was taken down and the residue was chromatographed on a column of silica gel (10 g, S3). The resulting product was crystallized from aqueous MeOH to afford 0.20 g (57%) of white crystals; m.p. 170–172 °C. FAB MS, *m/z* (rel.%): 358 (45) [M + H]. ^{1}H NMR (DMSO-d_6): 3.35 dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.9, *J*(gem) = 11.2 (H-3′b); 3.42 dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.1, *J*(gem) = 11.2 (H-3′a); 3.84 m, 1 H (H-2′); 4.00 dd, 1 H, *J*(1′b,2′) = 8.5, *J*(gem) = 13.9 (H-1′b); 4.32 dd, 1 H, *J*(1′a,2′) = 3.5, *J*(gem) = 13.9 (H-1′a); 4.85 t, 1 H, *J*(OH,3′) = 5.4 (OH); 5.10 d, 1 H, *J*(OH,2′) = 5.4 (OH); 7.45 br, 4 H (NH); 7.17 dd, 1 H, *J* = 3.6 and 5.1, 7.56 dd, 1 H, *J* = 1.2 and 3.6, 7.74 dd, 1 H, *J* = 1.2 and 5.1 (arom. H); 8.07 s, 1 H (H-8). ^{13}C NMR (DMSO-d_6): 46.57 (C-1′); 63.81 (C-3′); 69.85 (C-2′); 76.63 and 93.78 (C≡C); 125.06 (C-5); 121.09, 128.16, 130.13 and 134.26 (arom. C); 143.04 (C-8); 143.32 (C-2); 150.27 (C-4); 159.60 (C-6); 160.21 (N-C). For $C_{15}H_{15}N_7O_2S \cdot 0.3H_2O$ (357.4) calculated: 49.58% C, 4.35% H, 26.98% N; found: 49.54% C, 4.29% H, 26.59% N.

This study was performed as a part of research project No. 4055905 of the Institute of Organic Chemistry and Biochemistry. It was supported by the Programme of Targeted Projects of the Academy of Sciences of the Czech Republic (No. S4055109), by the René Descartes Prize-2001 of the European Commission, by COST programme 13.20 of the Ministry of Education, Youth and Sports of the Czech Republic and by Gilead Sciences (Foster City (CA), U.S.A.). The authors' thanks are due to Prof. E. De Clercq and his group in the Rega Institute, Catholic University Leuven (Belgium) for the evaluation of antiviral activity, to Prof. K. A. Jacobson, NIDAID, NIH, Bethesda (U.S.A.) for preliminary data on purinoceptor activity, to Dr I. Votruba of the Institute of Organic Chemistry and Biochemistry for the estimation of cytostatic activity and to the staff of the mass spectrometry (Dr K. Ubik, Head) and analytical departments (Dr V. Pechanec, Head) of this Institute for elemental analyses and measurement of mass spectra.

REFERENCES

1. De Clercq E., Descamps J., De Somer P., Holý A.: *Science* **1978**, *200*, 563.
2. Votruba I., Holý A.: *Collect. Czech. Chem. Commun.* **1980**, *45*, 3039.
3. Votruba I., Hasobe M., Holý A., Borchardt R. T.: *Biochem. Pharmacol.* **1990**, *39*, 1573.

4. Holý A., Votruba I., Merta A., De Clercq E., Jelínek R., Sláma K., Beneš K., Melichar O. in: *Biological Methylation and Drug Design* (R. R. Borchardt, C. R. Creveling and P. M. Ueland, Eds), p. 397. Humana Press, Clifton 1986.
5. a) Fojtová M., Kovařík A., Votruba I., Holý A.: *Eur. J. Biochem.* **1998**, *252*, 347; b) Kovařík A., Van Houdt H., Holý A., Depicker A.: *FEBS Lett.* **2000**, *467*, 47; c) Koukalová B., Votruba I., Fojtová M., Holý A., Kovařík A.: *Theor. Appl. Genet.* **2002**, *105*, 796.
6. Ralevic V., Burnstock G.: *Pharmacol. Rev.* **1998**, *50*, 413.
7. a) Muller C. E.: *Curr. Med. Chem.* **2000**, *12*, 1269; b) Poulsen S. A., Quinn R. J.: *Bioorg. Med. Chem.* **1998**, *6*, 619.
8. a) Volpini R., Costanzi S., Lambertucci C., Vittori S., Cristalli G.: *Curr. Pharm. Design* **2002**, *26*, 2285; b) Cristalli G., Eleuteri A., Vittori S., Volpini R., Lohse M. J., Klotz K. N.: *J. Med. Chem.* **1992**, *35*, 2363; c) Abiru T., Miyashita T., Watanabe Y., Yamaguchi T., Machida H., Matsuda A.: *J. Med. Chem.* **1992**, *35*, 2253.
9. a) Van der Wenden E. M., Von Frijtag Drabbe Kiinzel J. K., Mathot Ron A. A., Danhof M., Ijzerman A. P., Soudijnt W.: *J. Med. Chem.* **1996**, *38*, 4000; b) Siddiqi S. M., Jacobson K. A., Esker J. L., Olah M. E., Ji X. D., Melman N., Tiwari K. N., Secrist III J. A., Schneller S. W., Cristalli G., Stiles G. L., Johnson C. R., Ijzerman A. P.: *J. Med. Chem.* **1995**, *38*, 1174; c) Van Calenbergh S., Von Frijtag Drabbe Kiinzel J. K., Kunzel D., Blaton N. M., Peeters O. M., Rozenski J., VanAerschot A., DeBruyn A., DeKeukeleire D., Ijzerman A. P., Herdewijn P.: *J. Med. Chem.* **1997**, *40*, 3765; d) Vittori S., Lorenzen A., Stannek C., Costanzi S., Volpini R., Ijzerman A. P., Von Frijtag Drabbe Kunzel J. K., Cristalli G.: *J. Med. Chem.* **2000**, *43*, 250.
10. Lohse M. J., Klotz K. N., Diekmann E., Friedrich K., Schwabe U.: *Eur. J. Pharmacol.* **1988**, *156*, 157.
11. Taylor M. D., Moos W. H., Hamilton H. W., Szotek D. S., Patt W. C., Badger E. W., Bristol J. A., Bruns R. F., Heffner T. G., Mertd T. E.: *J. Med. Chem.* **1986**, *29*, 346.
12. Jacobson K. A., Siddiqi S. M., Olah M. E., Ji X. D., Melman N., Bellamkonda K., Meshulam Y., Stiles G. L., Kim H. O.: *J. Med. Chem.* **1995**, *38*, 1720.
13. Česnek M., Holý A., Masojídková M.: *Tetrahedron* **2002**, *58*, 2985.
14. Hocek M.: *Eur. J. Org. Chem.* **2003**, 245.
15. Holý A., Günter J., Dvořáková H., Masojídková M., Andrei G., Snoeck R., Balzarini J., De Clercq E.: *J. Med. Chem.* **1999**, *42*, 2064.
16. a) Holý A.: *Collect. Czech. Chem. Commun.* **1978**, *43*, 2054; b) Holý A.: *Collect. Czech. Chem. Commun.* **1978**, *43*, 3103; c) Holý A.: *Collect. Czech. Chem. Commun.* **1978**, *43*, 3444; d) Holý A.: *Collect. Czech. Chem. Commun.* **1979**, *44*, 593.
17. Dvořáková H., Holý A., Votruba I., Masojídková M.: *Collect. Czech. Chem. Commun.* **1993**, *58*, 629.
18. Chen W., Flavin M. T., Filler R., Xu Z. Q.: *Nucleosides Nucleotides* **1996**, *15*, 1771.
19. Tanji K. I., Higashino T.: *Chem. Pharm. Bull.* **1988**, *36*, 1935.
20. Holý A., Votruba I., De Clercq E.: *Collect. Czech. Chem. Commun.* **1985**, *50*, 245.
21. Matsuda A., Shinozaki M., Yamaguchi T., Homma H., Nomoto R., Miyasaka T., Watanabe Y., Abiru T.: *J. Med. Chem.* **1992**, *35*, 241.
22. a) Camaioni E., Costanzi S., Vittori S., Volpini R., Klotz K. N., Cristalli G.: *Bioorg. Med. Chem.* **1998**, *6*, 523; b) Nair V., Purdy D. F.: *Tetrahedron* **1991**, *47*, 365.

23. Harada H., Asano O., Kawata T., Inoue T., Horizoe T., Yasuda N., Nagata K., Murakami M., Nagaoka J., Kobayashi S., Tanaka I., Abe S.: *Bioorg. Med. Chem.* **2001**, *9*, 2709.
24. Votruba I.: Unpublished results.
25. Jacobson K. A.: Unpublished results.
26. Wang Y., Koreeda M., Chatterji T., Gates K. S.: *J. Org. Chem.* **1998**, *63*, 8644.