AN 15N-NMR STUDY OF ISOMERIC N1 AND N3 SUBSTITUTED 7-METHYL-10-OXO-9,10-DIHYDRO PYRIMIDO[1,2-a]PURINES AND 9-OXO-8,9-DIHYDRO-5-ALKYL-IMIDAZO[1,2-a]PURINES IN NEUTRAL AND ACIDIC MEDIUM.

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Summary: An 15N-NMR study in neutral and acidic solutions of isomeric N1 and N3 substituted 7-methyl-10-oxo-9,10-dihydro-pyrimido[1,2-a]purines, 4 and 5, and 9-oxo-8,9-dihydro-5-alkyl-imidazo[1,2-a]purines, 6 and 7 respectively, have shown the electronic implications of building an additional six-membered ring with two double bonds, as in 4 and 5, and a five-membered ring with one double bond, as in 6 and 7, involving 1-NH and exocyclic 2-NH2 substituent of the guanine moiety. The ease of formation of N1 or N3 protonated species and the magnitude of their 15N chemical shifts in compounds 4 to 7 have established that the π-electron rich imidazole system is more deactivated in pyrimido[1,2-a]purine derivatives, 4 and 5, than in the imidazo[1,2-a]purines 6 and 7. It has also emerged that the N1 of N3 isomers, 5 and 7, are more strongly protonated than the N1 of N3 isomers 4 and 6. A consideration of 23N,N1(N9),N5(N5), and the resonances of N5(N9) and N5 in compounds 4 to 7 has shown that the N5,N5-fused six-membered ring of the pyrimido[1,2-a]purines is π-electron deficient and is not coplanar with the rest of the molecule while the geometry of the N5,N5-fused five-membered ring of the imidazo[1,2-a]purines allows the participation of the N5 lone pair to activate the imidazole system as the exocyclic 2-NH2 or 2-NHCOR groups of N5-substituted guanine moiety.

The exocyclic amino group at C-2 of guanosine (1a) reacts readily with an appropriate bifunctional ketone or an aldehyde reagent, containing two or three carbon units between two reactive functions, and undergo a ring-closure at N1 to give either a tricyclic five-membered with one double bond or a six-membered compound with two double bonds (general structure 2 and 3, respectively)1-11. Such reactions have allowed chemists to carry out site-specific modifications of guanine bases in nucleic acids in order to understand structure-activity relationship of nucleic acids, specially of DNA and RNA virus4,5. Such specific modifications of guanine moieties have been successfully used for the preparation of modified tRNA bases or tRNA base analogues which are fluorescent10,11. These specific modifications have also been used for specific enzyme-chemical degradation of tRNA in order to understand the implication of its functional secondary and tertiary structure with respect to protein biosynthesis1-7. The structure of the tricyclic aglycone in 2 (R = H or an amino acid conjugate, R' = Ma) is also of particular interest since it occurs naturally as hypermodified fluorescent "Y" bases (or "Wye" bases) in tRNAs specific for phenylalanine12-16. We therefore considered it important to understand the electronic implication of additional five and six-membered rings as in 2 and 3 respectively involving the 1-NH and exocyclic 2-NH2 substituent of guanosine (1a) in order to delineate their distinctive physical, chemical and
For compounds 4 - 7: $R = -\text{CH}_2-(\text{CH}_2)_2-\text{CH}_2-\text{OAc}$
biological properties. We herein report our studies of their electronic structures in neutral DMSO solutions and also assess the nucleophilic reactivities of different nitrogen atoms, in model compounds $4 - 7^{17-18}$, by their abilities to form a protonated species by $^{15}$N-NMR spectroscopy.

Assignments of $^{15}$N chemical shifts in compounds 4-7.

Three different components$^{19}$ in the paramagnetic term in nitrogen screening have been essentially used to interpret $^{15}$N chemical shifts: (a) the symmetry of the 2p electrons; (b) the average excitation energy, especially n-n* and n+n* transitions and (c) the effective nuclear charge in relation with 2p orbital radius. This is in accordance with the fact that there is a linear relationship between $^{15}$N chemical shifts and n-electron density of a particular nitrogen atom$^{20}$.

An increase of the n charge density on a nitrogen atom causes an upfield shift while an increase of its n bond order leads to a downfield shift$^{21}$. These are the reasons that are responsible for the occurrence of three groups of $^{15}$N chemical shifts in nucleosides$^{22-26}$ because they correspond to three different kinds of nitrogen atoms in the heterocyclic base. The imidazole part consists of "pyridine- or azine-like" and the "pyrrole-like" nitrogen, the other nitrogen atoms are either "pyridine-like" nitrogen (N3) or a "amine-like" nitrogen (N1). The N-pyrrole" absorbs at a higher field than the "N-azine" on account of differences in their respective n charge densities. On the other hand, due to the availability of the lone-pair of the "N-azine", it undergoes protonation and experiences an upfield shift which is explained by a decrease in its n bond order and suppression of the paramagnetic effect of the n+n* transition$^{27}$.

These general observations, however, can be applied only partly for the $^{15}$N assignment of tricyclic bases as in compounds 4 - 7 since the formation of these five or six membered rings involving the 1-NH and the 2-NH$_2$ substituent of the guanine moiety affects its electronic distribution considerably. The complete assignment of $^{15}$N chemical shifts are shown in Table 1.

(a) Assignment of $^{15}$N shifts of N1 and N3 isomers in compounds 4 and 5 respectively.

The N1 and N3 in 4 and 5 absorb in the same region as the N7 of 1a (ca. 140 ppm upfield from CH$_3$N=O). The coupling constant between the "N-azine" and H-2 is always larger (10-12 Hz) than that of "N-pyrrole" and H-2 (7-9 Hz) which have been conveniently used to assign the N1 and N3 atoms of the N1 and N3 isomers. The assignment of N4 is rather an easy task since it is the only nitrogen which does not have any long range proton coupling. The N5 atom in 4 and 5 (compare with N2 of 1a) is now a "pyridine- or pyrimidine-like" nitrogen and therefore absorbs at a very low field (60 to -120 ppm) with 2J$_{N,H}$ = 10-13 Hz$^{27}$. The N9 is similar to an "amide-nitrogen" but with reduced electronic density since it is flanked by an electron-withdrawing C-10 carbonyl group and also in the ring junction of two fused "pyrimidine-like" rings. It is therefore reasonable to expect it to have a chemical shift at a higher frequency than the usual amide-shift range. It is clear that the value of 2J$_{N,H}$ would depend upon the dihedral angle of the C-8 proton with respect to N9 lone pair since it is already established$^{28}$ that the spatial orientation of the nitrogen lone-pair electrons has a profound influence on the nuclear spin-spin coupling constants. Thus, if the lone-pair is directed cis to the C9-H bond, the 2J$_{N,H}$ is larger than the case when the nitrogen lone-pair and C9-H are in trans position. The geometry of the ring junctions of two fused pyrimidine rings (pyrimido[1,2-a]purines) as in 4 and 5 and their comparisons with the fused six and five-membered ring system (imidazo[1,2-a] purines) as in 6 and 7 will be described in the discussion part.

The complete and unambiguous assignment of all nitrogens in 4 and 5 was therefore carried out in two separate experiments. Fig. 1 shows the proton decoupled spectrum of 5, as an example, giving the chemical shifts of all nitrogens and the Fig. 2 shows its proton coupled INEPT$^{29}$ spectrum yielding the 2J$_{N,H}$ (Table 1) for all nitrogens except N4.
**FIG. 1:** $^{15}$N-proton decoupled NMR spectrum of 6

**FIG. 2:** $^{15}$N-INEPT spectrum of 6

**FIG. 3:** $^{15}$N-NMR of compound 6: PANEL A. $^1$H decoupled $^{15}$N-NMR without NOE. PANEL B. INEPT spectrum. PANEL C. $^1$H decoupled spectrum with NOE.
An $^{15}$N-NMR study of isomeric $N^1$ and $N^3$.

The presence of three "triligant-nitrogen" atoms, $N^1/N^3$, $N^5$ and $N^8$, makes the assignments of $^{15}$N chemical shifts in compounds 6 and 7 quite complicated. Assignment of $N^1$ and $N^3$ in isomeric 6 and 7 respectively has been relatively easy since they occur as the most downfield signal. However, the resonances for $N^3/N^1$, $N^4$, $N^5$ and $N^8$ absorb within a close range of 60 ppm. A comparison of proton decoupled $^{15}$N-NMR spectra with that of proton coupled INEPT spectrum (Fig. 3) reveals that the missing peak in the latter should be attributed to the $N^4$ resonance since it does not have any coupling with any proton. A consideration of the coupling constant of the downfield resonance (12.5 Hz) allowed us to assign this for $N^3$ of 6 or $N^1$ of 7. But, unfortunately, the $N^5$, $N^8$ and $N^1$ (of $N^3$ isomer) and $N^5$, $N^8$ and $N^3$ (of $N^1$ isomer) have almost the same coupling constants which made it impossible to make a distinction among these nitrogens. It is, however, known that the $N^9$ in guanosine (1a) and in other purine nucleosides and $N^1$ of pyrimidine nucleosides undergo a large and negative $\text{noe}$ from the dipole-dipole effect of the sugar protons. Similarly, the $N^3$ and $N^5$ in 6 and $N^1$ and $N^5$ in 7 show negative $\text{noe}$ in proton decoupled spectrum. Fig. 3 shows, as an example, of such a proton decoupled with and without $\text{noe}$ and INEPT spectra for compound 7. The difference between $N^3$ and $N^5$ in 7 is large enough to assign the resonance at ca. -220 ppm for the $N^3$ in 6 or the $N^1$ in 7 and the one at -245 ppm is for $N^5$. This assignment is rationalized by the fact that the $N^5$ in 6 and 7 are "enamine-like" while the $N^1/N^3$ in 5 and 7 are "pyrrole-like" nitrogens. A higher field resonance (ca. -220 ppm) of $N^3$ and $N^1$ in 6 and 7 respectively as compared to that of guanosine (1a) (ca. -210 ppm) can also be explained due to the stronger electron-donating nature of the alkyl substituents in the former. The $^{15}$N chemical shifts of 1d and 1e support the latter argument (Table 2).

**RESULTS AND DISCUSSION**

(a) Main differences in the $^{15}$N chemical shifts in the $N^3$ and $N^1$ isomers.

We have earlier shown that the $N^7$ and $N^9$ substituted isomers of purine derivatives can be conveniently distinguished by $^{15}$N-NMR spectroscopy. One of the main observations in this work was that the $N^3$ resonance is shielded by 18-20 ppm in the $N^9$ isomer. A perusal of Table 1 clearly shows that the $N^4$ ($N^3$ in the parent compound 1a) in the $N^3$ isomers, 4 and 6, are indeed shielded by 17-20 ppm as compared to the $N^1$ isomers 5 and 7 respectively. This seems to be due to a direct conjugation of the "azine-like" electron-rich imidazole nitrogen to the $N^4$ which causes its shielding in the $N^3$ isomers 4 and 6. It may be noted that the $N^1$ of the $N^3$ isomers, 5 and 7, is more shielded by ca. 2 ppm as compared to the $N^3$ of the $N^3$ isomers 4 and 6 respectively. On the other hand, a magnitude of 6-7 ppm has been observed for the $N^7$ and $N^9$ substituted isomeric purine derivatives.

A consideration of the $^{15}$N chemical shifts of compounds 4 and 5 with that of 6 and 7, respectively, (Table 1) reveals the difference in electronic structures of these fused tricyclic compounds and guanosine (1a) and $N^2$-acylguanosine (1b). Indeed $N^5$ in the $N^1$ isomer 7 is more shielded by 2 ppm than the corresponding $N^3$ isomer 6 which obeys our earlier observation in the purine series.

It is clear from the chemical shift arguments that the $N^5$ in compounds 6 and 7 behave like a deactivated amine function while the properties of $N^5$ in 4 and 5 are very different as it will be clear from the following study.

(b) Protonation study with compounds 4-7.

In a previous paper, we have demonstrated that the $^{15}$N-NMR spectroscopy is an interesting tool to assess the reactivity of a nitrogen atom in a purine and pyrimidine nucleoside by following its behaviour in an acidic medium. These studies have shown how the nature of a $^{06}$-protecting group (alkyl versus aryl) can control the nucleophilicity of the $N^7$ nitrogen which, in turn, can control the participation of the protected guanine base in side reactions at $N^7$ under electrophilic reaction conditions. This work has also adequately demonstrated that the protection of the exo-
FIG. 4: $^{15}$N CHEMICAL SHIFT CHANGES OF N$^7$ OF COMPOUND 1a (○); OF N$^1$ OF COMPOUND 6 (□); OF N$^7$ OF COMPOUND 1b (■); OF N$^7$ OF COMPOUND 1c (▲); OF N$^1$ OF COMPOUND 4 (◇) AS A FUNCTION OF ADDED CF$_3$COOH (TFA).

Table 1: $^{15}$N chemical shifts\(^a\) in neutral and acidic media and coupling constants\(^b\) of compounds 4 - 7.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Equiv.</th>
<th>(N^1)</th>
<th>(N^3)</th>
<th>(N^4)</th>
<th>(N^5)</th>
<th>(N^6)</th>
<th>(N^8)</th>
<th>(N^9)</th>
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<tr>
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<td>85.7</td>
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<td></td>
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<td>-102.2</td>
<td>95.7</td>
<td>-191.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>-219</td>
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<td>-161.3</td>
<td>82.7</td>
<td>-194.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>-217.1</td>
<td>-150.1</td>
<td>-171.4</td>
<td>85.4</td>
<td>-192.7</td>
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<td></td>
</tr>
<tr>
<td>6</td>
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<td>-220.9</td>
<td>-223.7</td>
<td>-245.9</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>1</td>
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<td>-218.5</td>
<td>-223.6</td>
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</table>

\(^a\) Measurements were carried out at 308 K in 0.5 M DMSO solutions except for 7 (0.6 M). Chemical shifts are reported in ppm with respect to CH$_3^{15}$NO$_2$.

\(^b\) $J_{(N,H)}$ coupling constants in Hz.
FIG. 5: DEPENDENCE OF $^{15}$N CHEMICAL SHIFTS (absolute values) WITH NUMBER OF EQUIV. OF CF$_3$COOH FOR COMPOUND 4.

EQUIVALENTS OF CF$_3$COOH (TFA)

FIG. 6: DEPENDENCE OF $^{15}$N CHEMICAL SHIFTS (absolute values) WITH NUMBER OF EQUIV. OF CF$_3$COOH FOR COMPOUND 5.
FIG. 7: DEPENDENCE OF $^{15}$N CHEMICAL SHIFTS (absolute values) WITH NUMBER OF EQUIV. OF CF$_3$COOH FOR COMPOUND 6.

FIG. 8: DEPENDENCE OF $^{15}$N CHEMICAL SHIFTS (absolute values) WITH NUMBER OF EQUIV. OF CF$_3$COOH FOR COMPOUND 7.
An $^{15}$N-NMR study of isomeric N' and N$^3$

Table 2: $^{15}$N chemical shifts of inosine and some of its C-2 substituted derivatives in neutral and acid media.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Equiv.</th>
<th>N$^1$</th>
<th>N$^3$</th>
<th>N$^7$</th>
<th>N$^9$</th>
<th>N$^2$</th>
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<td>-</td>
</tr>
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<td>1</td>
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<td>-167.3</td>
<td>-141.2</td>
<td>-205.6</td>
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<td>-215.0</td>
<td>-136.1</td>
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<td>-215.2</td>
<td>-148.1</td>
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<td>-306.9</td>
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</tbody>
</table>

*0.45 M in DMSO at 308 K from ref. 26, see ref. 31.
+from ref. 26.
#from ref. 26 and 32.
$^5$0.3 M in DMSO at 313 K.
$^6$0.8 M in DMSO at 308 K.

cyclic amino function at C-2 by an amide (lb) considerably reduced the protonation at N$^7$ of guanosine (la) (Fig. 4). Due to the reasons stated above, it was of considerable interest to us to know how the five-membered ring with one double bond, as in 6 and 7, and six-membered ring with two double bonds, as in 4 and 5, involving N$^1$ and N$^2$ of guanosine (la) would affect the $\pi$-excessive electronic properties of the imidazole system in terms of its delocalization to the rest of the molecule and also in terms of participation of N$^5$ in 4 - 7 in further activation of the imidazole system. This we hoped to monitor by the protonation behaviour of the N$^1$ of the N$^3$ isomers, 4 and 5 and N$^3$ of the N$^1$ isomers 6 and 7. The Figs. 5 - 8 show the variation of the $^{15}$N chemical shifts of compounds 4 to 7, respectively, upon protonation with CF$_3$CO$_2$H (TFA) (Table 1). Two conclusions can be drawn from these studies; (1) a six-membered ring with two double bonds, as in 4, reduces the potential of N$^1$ to form a protonated species by a factor of 6 (N$^1$ shift upon protonation is ca. 8 ppm) as compared to that of N$^7$ of guanosine (la) (46 ppm shift upon protonation) (Table 2). On the other hand, the five-membered ring with one double bond, as in 6, reduces the potential of N$^1$ to form a protonated species by a factor 1.3 (N$^1$ shift upon protonation is ca. 34 ppm) as compared to the N$^7$ of guanosine (la) and N$^2$-(4-ethylbenzoyl)guanosine (lb) (N$^7$ shift upon protonation is 25 ppm). It has been earlier shown that the enhanced nucleophilic character of N$^7$ of guanosine, as compared to that of inosine (N$^7$ chemical shift upon protonation is ca. 13 ppm) (26,32), is due to the N$^7$ activation by the exocyclic amino function at the C-2 position. A comparison of the nucleophilic character of N$^1$ in compounds 4 and 6 therefore clearly shows from protonation experiments that the delocalization of $\pi$-excessive imidazole part in 4 is very similar to inosine while the imidazole part in 6 behaves very similar to an N$^2$-amide group as in lb (Fig. 4). These observations can be rationalized by the $\pi$-electron deficient nature of the six-membered ring in 4 which withdraws electron from the imidazole ring while the N$^5$ of the five-membered ring in 6 is "enamino" type, perhaps iso-electronic with an amide function. (2) The N$^3$ of the N$^1$ isomers 5 and 7 are more strongly protonated. It is conceivable that the N$^3$ protonation of the N$^1$ isomers is stabilized by the participation of the N$^4$ lone pair which also explains its upfield shift upon protonation. It is possible that the protonation of N$^3$ in the N$^1$ isomers 5 and 7 stabilizes the protonated system thermodynamically by suppressing the electrostatic repulsion between the N$^4$ and N$^5$ lone pairs.
It should be noted that the N^5 nitrogens in compounds 4 and 5 are very slightly protonated (ca. 2-3 ppm) despite the fact they have "pyrimidine-like" chemical shifts (-85.7 and -82.7 ppm respectively). This is unusual for an isolated "pyrimidine-like" nitrogen \(^{34}\) but is reminiscent of the behaviour of N^3 nitrogens of inosine (Ic) and its C-2 substituted derivatives 1a and 1b. This also means that the N^5,N^9-fused six-membered ring in pyrimido[1,2-a]purine derivatives, 4 and 5, is \(\pi\)-electron deficient and has an overall electron-withdrawing influence on the rest of the molecule as evident from the comparison of \(^{15}\)N chemical shifts in Tables 1 and 2.

(c) Difference in the geometry between a N^5,N^9-fused six-membered ring, as in 4 and 5, and a N^5,N^8-fused five-membered ring, as in 6 and 7.

As said previously that the coupling constant of N^9 (for 4 and 5) with H^8 or N^8 (for 6 and 7) with H^7 is sensitive to the dihedral angle formed between H^8 or H^7 and the lone pair of N^9 or N^8 respectively. The \(^{2}J_{(N,H)}\) value for the six-membered ring, (as in 4 and 5) is smaller than that for the five-membered ring (as in 6 and 7) (see Table 1) suggesting that the orientation of the N^9-C^8 bond in 4 and 5 is not the same as the N^8-C^7 bond in 6 and 7 and therefore the geometry of 4 (or 5) and 6 (or 7) is not similar: H^7 is in cisoid form with respect to the lone pair of N^8 while the H^8 is in transoid form with respect to the lone pair of N^9 (scheme 1).

It has been estimated from the molecular model that \(\theta=60^\circ\) for 6 or 7 and \(\theta=120^\circ\) for 4 and 5. The consequence is that the N^5,N^9-fused six-membered ring in pyrimido[1,2-a]purines (4 and 5) is not coplanar with the guanine base, forbidding a perfect delocalization of the \(\pi\) bonds through N^5 and N^4. But in imidazo[1,2-a]purines 6 and 7, the N^5 can delocalize its lone pair in the usual way as the 2-NH\(_2\) or 7-WHCOR \(\ldots\) in the guanine systems, 1a and 1b respectively.

**EXPERIMENTAL**

\(^{15}\)N chemical shift determinations were made on a Jeol JNM-GX-270 spectrometer, operating at 27.4 MHz frequency at 35°C using a probe-head of 10 mm. The \(^{15}\)N chemical shifts were determined from proton decoupled spectra (without NOE) and were referenced against an external solution of CH\(_3\)^{15}NO\(_2\) in CD\(_3\)NO\(_2\). No susceptibility correction was applied. The decoupled spectra with noe suppressed were recorded with a 45° pulse angle (13 \(\mu\)s pulse width), 0.9 s acquisition time for 16 K data points and 20 \(s\) of pulse delay. A zero-filling to 32 K points was applied before fourier transformation. A broadening factor of 2-3 Hz was used. Useful spectra were obtained with an accumulation time of 4-6 h. The decoupled spectra with the desired noe were recorded with 26 \(\mu\)s pulse width and a pulse delay of 15 s. \(^{15}\)N, \(^{1}\)H spin coupling constants were determined with the aid of the INEPT pulse sequence with the following typical parameters: \(^{1}\)H-90°-59 \(\mu\)s, \(^{15}\)N-90°-26 \(\mu\)s, a pulse delay time \(\tau=23 \text{ ms}\) and a pulse sequence delay of 2 s. Under these conditions, 30 min were
required to get a spectrum with a sufficient signal to noise ratio. The spectral range was 9000 Hz involving a digital resolution of 0.5 Hz (0.02 ppm). A negative value for the chemical shift denotes an upfield shift.

$^{1}H$- and $^{13}C$-NMR were recorded on a Jeol JNM-FX 200 spectrometer in 6 scale using TMS as an internal standard. UV were recorded using a Hewlett-Packard 8450 A-UV/VIF spectrophotometer. Mass spectra were recorded in electron-impact mode on a LKB 9000 at 70 ev.

Compounds 4 and 5 have been prepared using a literature procedure while the compounds 6 and 7 are prepared in the following way:

To a suspension of 1,N$^{2}$-ethenoguanine in DMF, was added 4-bromobutylacetate. The suspension was stirred at room temperature for 72 h and the reaction was monitored by TLC (silica gel, CHCl$_3$-CH$_3$OH::20:1, v/v). The inorganic salts were filtered off and the solvent was evaporated in vacuo. The residue was suspended in ethanol, filtered and evaporated. Flash chromatography of the residue gave 1,5-di(4-acetoxybutyl)-9-oxo-8,9-dihydro-imidazo 1,2-a purine (7) (146 mg, 22.5%), 3,5-di(4-acetoxybutyl)-9-oxo-8,9-dihydro-imidazo 1,2-a purine (6) (130 mg, 21%) and an unidentified product (55 mg, 8.6%).

$^{13}C$-NMR: 20.8 (2 CH$_3$), 25.2, 25.5, 25.7, 26.1 (4 CH$_2$), 42.5 (N$_2$CH$_2$), 44.2 (N$_5$CH$_2$), 63.4 (C4' and C4''), 106.2 (C6), 115.6 (C9a), 119.2 (C7), 139.3 (C2), 145.0 (C4a), 150.4 (C3a), 151.5 (C9), 170.5 (2 CO).

UV (nm): $\lambda_{max}$ = 230, 290 (ethanol); MS:M$^+$ at m/z = 403.

1,5-di(4-acetoxybutyl)-9-oxo-8,9-dihydro-imidazo[1,2-a]purine (7) m.p. 80-81°C:

$^{1}H$-NMR (DMSO-d$_6$): 1.6-2.0 (m, 8H, CH$_2$), 1.97 (s, 6H, COCH$_3$), 3.9-4.2 (m, 8H, N$_5$CH$_2$, N$_3$CH$_2$, 2 COOCH$_2$), 4.36 (N$_1$CH$_2$), 7.68 (d, 1H, H-7), 7.62 (d, 1H, H-6), 8.20 (s, 1H, H-2).

$^{13}C$-NMR: 20.9 (2 CH$_3$), 25.2, 25.5, 25.7, 27.5 (4 CH$_2$), 44.3 (N$_5$CH$_2$), 46.0 (N$_4$CH$_2$), 63.5 (C4' and C4''), 107.2 (C6), 107.3 (C9a), 119.9 (C7), 145.5 (C2), 145.1 (C4a), 148.9 (C3a), 159.0 (C9), 170.6 (2 CO).

UV (nm): $\lambda_{max}$ = 232, 310 (ethanol); MS:M$^+$ at m/z = 403.

An. Calcd. for C$_{56}H_8$N$_5$G$_2$: C, 55.5; N, 17.4; H, 6.25; Found C, 56.3; N, 17.4; H, 6.26.

Compounds 1d and le were prepared by reaction of 4-bromo-1,2-d-isopropylidene-1,2-butanediol and hexyl bromide, respectively with 2-amino-6-chloropurine followed by acid hydrolysis.

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REFERENCES AND FOOTNOTE

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31. This study was done in the ref. 26, but the value of the N7 shift of guanosine upon protonation with 1 equivalent of CF3COOH should be corrected to 46 ppm instead of 75 ppm.