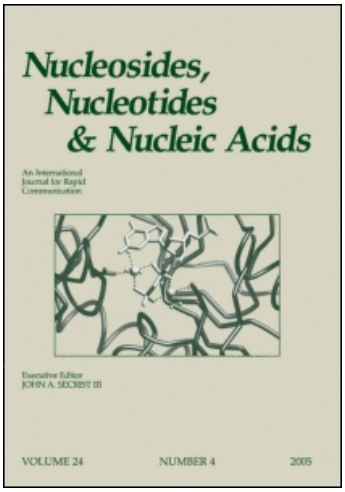


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# The Structure of "$N^1$, $N^6$-Carbonyladenosine"

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# THE STRUCTURE OF "$N^1$, $N^6$-CARBONYLADENOSINE"

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ABSTRACT: Re-interpretation of the available data led to structural assignment of the title $N^1$, $N^6$-carbonyladenosine (1b) as $N^6$,$N^6$-carbonyldiadenosine (4b).



The reaction of 2',3',5'-tri-O-acetyladenosine (2a) with phenyl chloroformate and pyridine in refluxing 1,2-dichloroethane was the subject of a recent communication.[1] The major product obtained in 48% yield was assigned the structure of $N^1$, $N^6$-carbonyl-2',3',5'-tri-O-acetyladenosine (1a). The derivative resulting from base-catalyzed methanolysis of 1a was then formulated as the free nucleoside 1b.

The intriguing structures[1] of these compounds comprising an unusual 1,3-diazacyclobutene ring system were deduced[1] "by careful examination of spectral data" including the NMR, UV and electron-impact mass spectra (EI-MS). Thus, the EI-MS of triacetyl derivative 1a" gave two sets of ions characteristic of triacetate 2a and, allegedly, the parent compound 1a (M 419). The occurence of fragments typical of triacetate 2a was explained[1] "by a thermal transformation of 1a into 2a". The structure of "dimeric isocyanate" was ruled out[1]



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TABLE 1

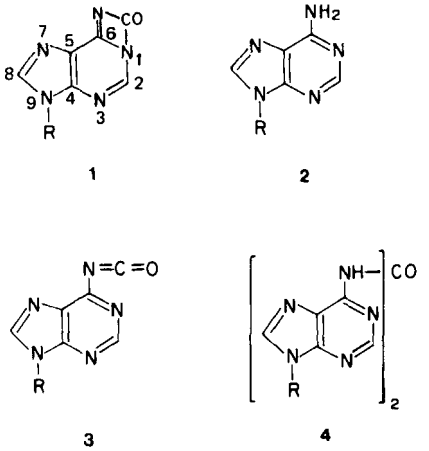
Comparison of Physico-Chemical Parameters of "$N^1$,$N^2$-carbonyladenosines 1a.1b" and the Corresponding Ureas 4a, 4b

| Physico-Chemical Parameter | Urea Derivatives[2] | "$N^1$,$N^2$-carbonyl adenosines"[1] |
|---|---|---|
| M.p. | 165 - 166°(4b) | 163 - 165°(1b) |
| UV max (nm, EtOH) | 291, 284, 266(4a) | 292, 283, 265(1a) |
| UV max (nm, pH 1) | 292 (ε 34,300)<br>265 (ε 15,600)(4b) | 296 (ε 17,100)[a](1b)<br>-- |
| UV min (nm, pH 1) | 268 (ε 15,500)<br>242 (ε 11,800)(4b) | --<br>241 (ε 2,600)(1b) |
| UV max (nm, pH 13) | 322 (ε 37,000)<br>274 (ε 12,600)(4b) | 318 (ε 18,800)[b]<br>275 (ε 6,400)(1b) |
| UV min (nm, pH 13) | 286 (ε 6,000)<br>244 (ε 6,700)(4b) | 285 (ε 3,800)<br>239 (ε 3,200)(1b) |
| NMR ($CD_3SOCD_3$,δ) | 8.69 (2H, s)[c]<br>8.66 (2H, s)<br>6.04 (2H, d,<br>J 5.5 Hz)(4b) | 8.68 (s)<br>8.62 (s)<br>6.02 (d,<br>J 6.0 Hz)(1b) |
| NMR ($CDCl_3$,δ) | 8.86 (2H, s)<br>8.55 (2H, s)<br>6.30 (2H, d,<br>J 5 Hz)(4a) | 8.80 (s)<br>8.52 (broad s)<br>6.32 (d,<br>J 5.0 Hz)(1a) |
| MS | 419 (M-393) (4a) | 419 (1a) |

[a] With the exception of UV min of 1b at pH 1 all recalculated ε values correspond to those of urea derivative 4b.

[b] pH 10.

[c] + $D_2O$.



Series a: R = 2,3,5-tri-O-acetyl-β-D-ribofuranosyl
Series b: R = β-D-ribofuranosyl

Scheme 1

on the basis of unspecified NMR evidence and a molecular weight determination by melting point depression of camphor caused by admixture of acetate 1a (no details were given).

We would like to call attention to the fact that the reported[1] physico-chemical properties of 1a and 1b including the spectral data, are virtually identical with those of the known[2] urea derivatives 4a and 4b (Table 1). The occurrence of two sets of ions[1] in EI-MS is readily explained by the fragmentation pattern 4 → 2 + 3 observed in compounds[2] 4a and 4b. The UV spectra described for 1a and 1b closely correspond to those of $N^6$, $N^6$-carbonyldiadenosine (4b) and its hexaacetate 4a. It should be stressed that the UV spectra of 4a and 4b significantly differ from other $N^6$-acylated adenosines[2]. The above "thermal transformation of 1a into 2a" is then not possible on stoichiometric grounds. Thus, compound 2a contains two hydrogen atoms

more than 1a. It should be also noted, that compounds 1a, 1b, 4a and 4b were prepared similarly by the reaction of triacetate 2a with aromatic chloroformate in the presence of pyridine and subsequent methanolysis[1,2].

It would then seem that the only remaining parameter which supports the structures 1a and 1b is the m.p. depression observed[1] on admixture of 1a to camphor. However, acetate 1a is amorphous[1] without a definite m.p. and, therefore, such an observation lacks the force of a rigorous evidence.

It is clear from the experimental data summarized above that structures of 1a and 1b must be reassigned in favor of the corresponding urea derivatives 4a and 4b. The reported[1] resistance of compound 1b toward adenosine deaminase is also consistent with structure 4b.



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