

STUDIES IN PRIMITIVE CATALYSIS AND NUCLEOSIDE ANALOGS

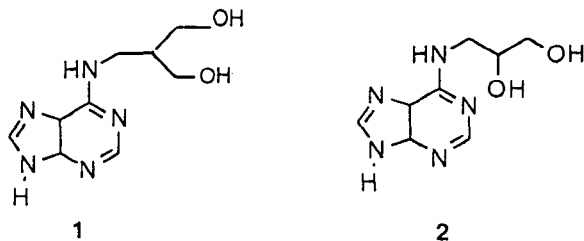
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The imidazole ring of histidine residues of enzymes plays a fundamental role in catalysis. It can function as a general-base catalyst (α -chymotrypsine, ribonuclease), as a nucleophilic catalyst (alkaline phosphatase) or as a ligand of active metal ions (for examples: zinc into carboxypeptidase A; copper into superoxide dismutase, hemocyanine, tyrosinase).

The adenine ring linked by its N^1 or N^6 nitrogen atom is a good candidate to perform some of these catalyses into ancestral nucleic acid analogs. Involvement of the adenine ring of ATP in the biosynthesis of histidine can strengthen this hypothesis.

We have demonstrated that N^6 -ribosyl adenine, which is obtained as a major product in the condensation of adenine and ribose under presumably prebiotic conditions, exhibits, in the model hydrolysis of *p*-nitrophenylacetate, a pronounced catalytic activity as compared to histidine (Maurel and Ninio, 1987). Such activity of the N^6 -substituted adenine ring was strongly increased in a favourable microenvironment when this ring is linked to macromolecules containing unprotonated aliphatic amino groups (Décout and Maurel, 1993 ; Décout et al., 1995). Kinetic studies provided also informations about the origin of co-operativity in prebiotic catalysts (Ricard et al, submitted). We have also prepared the synthetic N^6 -substituted adenine derivatives 1 and 2 possessing catalytic activities similar to the one of N^6 -ribosyl adenine. These derivatives should be polymerized to obtain nucleic acids analogs.



Reactions of adenine with aldehydes at the N^6 or N^9 position under presumably prebiotic conditions is also an attractive route for obtaining derivatives which possess catalytic properties and which could be polymerized. This approach is also under way.

It is well-known that adenine forms crystalline complexes with divalent metal ions such as copper and cobalt ions. The interactions of these metal ions with adenine in aqueous solutions and the catalytic properties of the resulting complexes remains to be studied. In a first approach, we have observed a strong increase in the catalase activity of Cu(II) ions in the presence of adenine.

Décout, J.L. and Maurel, M.C. : 1993, *Origins of Life* , 23, 298-306.

Décout, J.L., Vergne, J. and Maurel, M.C. : 1995, *Macromol. Chem. Phys.* 196, 2615-2624.

Maurel, M.C. and Ninio, J.: 1987, *Biochimie* 69, 551-553.

Ricard, J., Vergne, J., Décout, J.L. and Maurel, M.C. : submitted.