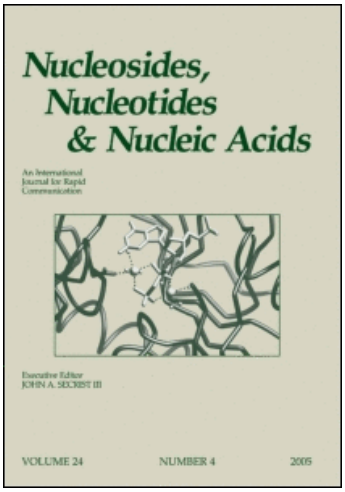

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The Cleavage of the Triphosphate Bridge of a Model for the 5′-*cap* mRNA Promoted by Dinuclear Bicyclic Complexes with Metal Ions

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ABSTRACT

Dinuclear bicyclic complexes, which have two active centers, can significantly promote the hydrolysis of the triphosphate bridge in ApppA, a 5′-*cap* model compound.

The 5′-*cap* structure plays an important role in RNA processing events. Destruction of the 5′-*cap* may inactivate mRNA transcript, and this may be used as part of strategies to selectively inhibit gene expression at mRNA level.[1,2] Previous studies have shown that metal ion complexes can promote the hydrolysis of triphosphate. In this study, ApppA was used as a model of the 5′-*cap* mRNA, and dinuclear bicyclic complexes were used as catalysts.

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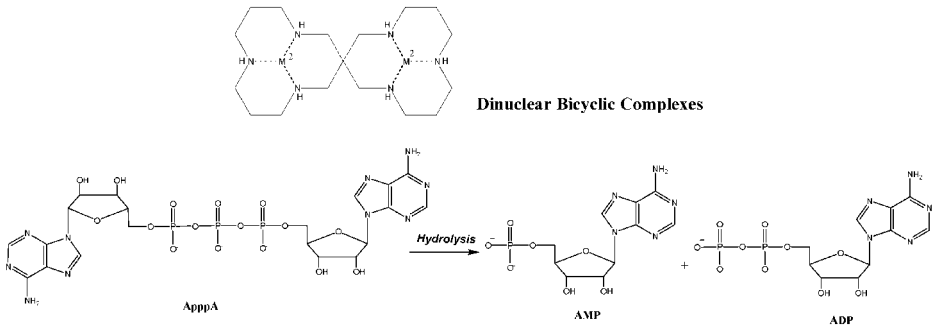

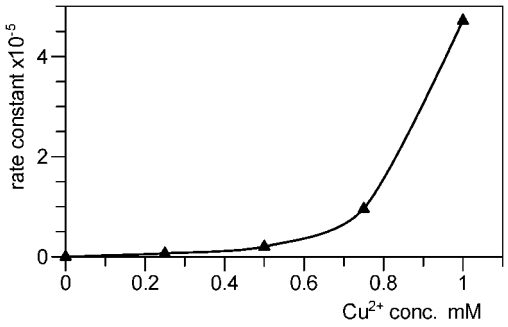

Figure 1. The effect of different concentration of Cu^{2+} on the hydrolysis of the phosphate bridge of 5′-*cap* model compound, ApppA. HEPES buffer at pH 7.5 and 60°C, bicyclic ligand 0.55 mM.

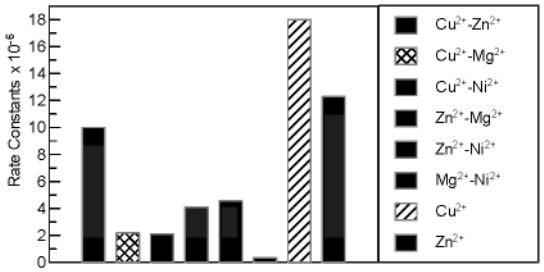

Figure 2. The rate constants of different combinations of metal ions with Bicyclic ligand on the hydrolysis of the phosphate bridge of ApppA. HEPES buffer at pH 7.5 and 60°C, bicyclic ligand 0.55 mM and metal ions 0.5 mM + 0.5 mM or 1.0 mM.

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RESULTS AND DISCUSSION

The kinetic experiment was carried out as reported before.[3] In reaction of ApppA, in the presence of different complexes, the only products formed were adenosine 5′-mono-phosphate (AMP) and adenosine 5′-diphosphate (ADP).

Figure 1 shows that bicyclic ligand itself without metal ion is not catalytically active at all. As the concentration of Cu^{2+} increases, the catalytic activity of the complex increases as well showing that the 1:2 complex is the active catalyst. This may suggest that two catalytically active centers can bind to the phosphorus bridge and catalyze the hydrolysis simultaneously.

Figure 2 shows the comparison between different metal ion complexes. Both Cu^{2+} and Zn^{2+} complexes significantly enhance the hydrolysis of the triphosphate bridge in a mRNA 5′-*cap* model compound. Unlike Cu^{2+} and Zn^{2+}, Mg^{2+} and Ni^{2+} complexes are not active catalysts in this reaction.

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