Efficient Cleavage of DNA by the Novel Copper (II) Complex Derived From 2,2′-Pyridil Ligand

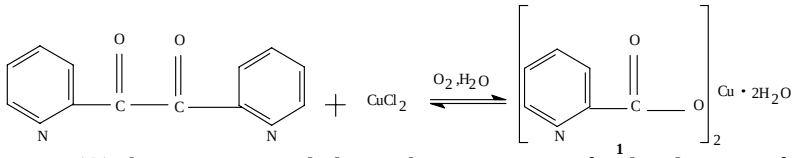
Rui REN[1,3], Pin YANG[2]

[1]Biotechnology laboratory, Shanxi University, Taiyuan 030006
[2]Institute of Molecular Science, Shanxi University, Taiyuan 030006
[3]State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing 210093

Abstract: Copper (II) complex derived from 2, 2′-pyridil ligand has been demonstrated to cleave efficiently DNA at micromolar concentrations at room temperature and pH 7.25.

Keywords: Copper (II) complex, DNA, efficient cleavage.

Due to the importance of oxidative degradation of nucleic acids in mutagenesis, carcinogenesis, and aging, a large number of chemical and biological investigations have been recently published[1]. Artificial metallonucleases have been proven to be efficient tools for the footprinting and sequence-specific targeting of nucleic acids[1,2]. They usually require high concentrations of the complex and of an external reducing agent (such as dithiothreitol, DTT) to form a reactive species *in situ*, the features may limit their scope for biological applications at the cellular level. Although other workers have described oxidative DNA cleavage by copper complexes, these usually require a large excess of reagent (from 0.1 to 1 mmol/L copper complex with 25 nmol /L to 10 μ mol /L DNA) and often extended reaction times of several hours[3]. These considerations prompt us to report our results obtained with a copper (II) complex **1**. **1** was obtained from 2,2′-pyridil ligand as follows:

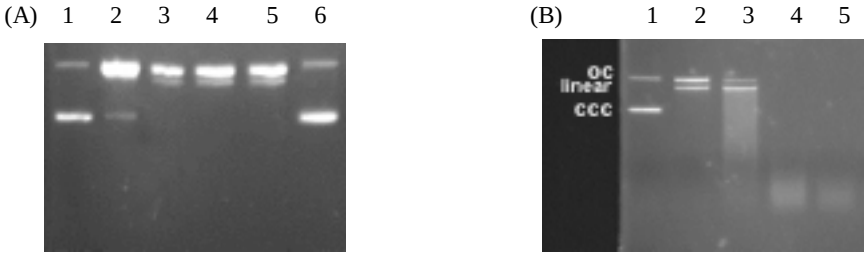


1

Figure 1(A) shows agarose gel electrophoresis patterns for the cleavage of plasmid pBR322 DNA after treatment with Cu (2,2′py) complex at pH 7.25 (5 mmol /L Tris-HCl, 5 mmol /L NaCl) and 23°C for 10 min. The molar ratio of the Cu (2,2′py) complex to H_2O_2 is 1:10. The initial concentration of DNA was set at 42 μ mol /L base pairs (lane 1: DNA control), and the concentration of Cu (2,2′py) complex was varied from 0 to 43.4 μ mol /L. The conversions of form I (supercoiled, ccc) to form II (nicked, oc) and form III (linearized) were observed with the increase in concentration of Cu (2, 2′py) complex, and the form III began to appear and the form I was barely observable in the presence of

26.4 μ mol/L Cu (2,2′py) complex (lane 3). Under the same conditions, free Cu (II) ions produced no cleavage of pBR322 DNA at concentrations below 43.4 μ mol /L (lane 6). Further, as shown in **Figure 1(B)**, increasing concentrations of the complex (from 24 μ mol /L to 96 μ mol /L) and raising incubation temperature from 23°C to 37°C, the plasmid DNA was dramatically cleaved and smears (corresponding to multifragmented DNA) were observed (lane 3-5), especially, extensive degradation of the plasmid and smears of fragment sizes are observed over the time of this reaction (lanes 4 and 5), with the range of smaller product fragments essentially undetectable. The result suggests the DNA cleavage mediated by Cu (2,2′py) and H_2O_2 occurs by an oxidative and random mechanism.

Figure 1 Cleavage of pBR322 DNA by Cu (2,2′py) complex.



In summary, the Cu (2,2′py) complex is able to perform an efficient oxidative cleavage of DNA. Further studies on the reaction mechanism as well as on sequence selectivity of the copper (II) complex are in progress.

Acknowledgments

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