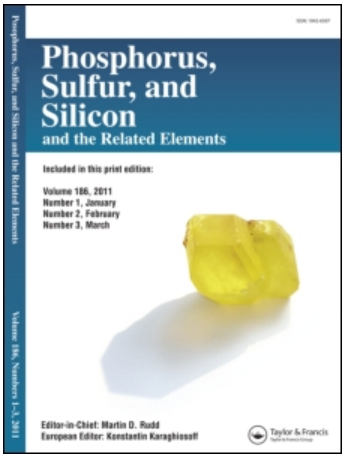

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Different Function of Cysteine and Serine Residue on RNA and DNA

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The thiol compounds could cleave DNA in radical mechanism, while degradation of DNA and RNA by hydroxyl peptides might proceed through a pentacoordinate phosphorus intermediate.

KEY WORDS: N-phosphoserine, N-phosphocysteine, DNA, RNA, cleavage, mechanism

INTRODUCTION

It is known that cysteine has the similar structure with serine despite that cysteine has a thiol group in the side chain, while serine has a hydroxyl group in the corresponding position, but the biological activities of these two amino acid residues in proteins (enzymes) are dramatically different. The main function of cysteine is to conjugate each other by a disulfide bridge to stabilize the unique three-dimensional structures. On the other hand, about 70% of the enzymes have the serine or threonine situated at the active sites, and in many cases the serine is involved in the reversible phosphorylation reaction to regulate the enzymes' activities.

In our synthesis and investigation of N-(O,O-dialkyl)phosphoryl serine, threonine and cysteine(DIPP-Ser, DIPP-Thr, DIPP-Cys), it was found that these N-phosphoamino acids also have the obviously distinct chemical reactivities[1-2] . For example, DIPP-Ser and DIPP-Thr in alcoholic media proceed phosphoryl ester exchanges with the concomitant phosphoryl transfer reaction. The same treatment of DIPP-Cys under argon resulted in no change. This means that the replacement of the oxygen atom by sulfur atom inhibits the formation of some active intermediate which is responsible for the yield of ester exchange, phosphoryl migration and peptide products.

CLEAVAGE OF DNA AND RNA BY DIPP-SER AND DIPP-CYS

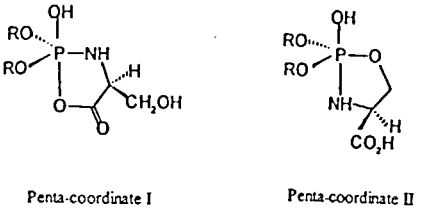

FIGURE 1 Two pentacoordinate phosphorus intermediates of DIPP-Ser

In our studies it was found that the aged DIPP-Ser in histidine aqueous solution could cleave DNA and RNA, while the fresh DIPP-Ser in histidine aqueous medium could not . The further investigation by ^{31}P-NMR and FAB-MS showed that phosphodipeptide DIPP-Ser-His and dipeptide Ser-His were yielded in the above aged solution, and agarose gel electrophoresis experiment demonstrated their DNA and RNA cleavage ability. Our group's previous work has proved DIPP-Ser could form two kinds of pentacoordinate phosphorus intermediate (figure 1), which were very active to proceed further reaction[3] . Based above results we presumed a new DNA cleavage mechanism shown as figure 2.

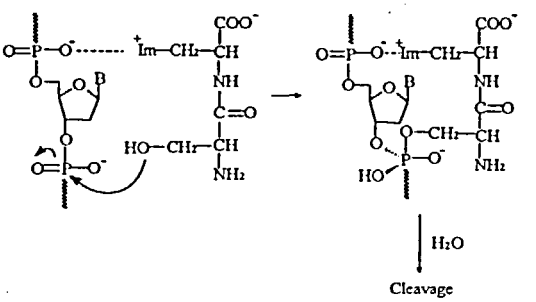

FIGURE 2 Mechanism of DNA cleavage by Ser-His dipeptide

How about DIPP-Cys on DNA, which has the similar structure with DIPP-Ser. We found DIPP-Cys indeed could also cleave DNA. But it could only form phosphoric-carbonic mixture anhydride intermediate, while the phosphorus-sulfur pentacoordinate intermediate did not yield, and according to the literature's report, DNA degradation ability of thiol compounds were due to the free radical formed by thiol group[4] .

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