UDC 547

STABILITY OF URIDYLYL-(5' → N)SERYL(THREONYL)GLYCINES IN AQUEOUS SOLUTIONS

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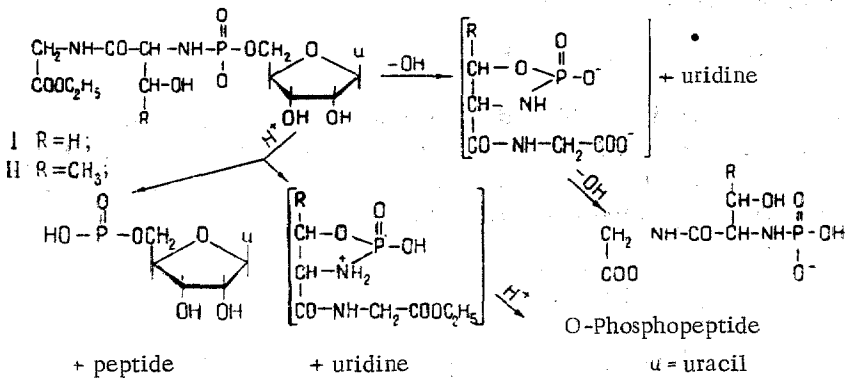
At the present time the question of the structure and role of the heterogeneous (nucleotidopeptide) sections of DNA and RNA, including the type of nucleotidopeptide bond, is a matter of discussion [1, 2].

Continuing investigations of model nucleotidopeptides [3,4], we have studied the properties of uridylyl(5' → N) dipeptides in which the N-terminal acid is a hydroxy amino acid. We have studied the stability in aqueous solutions of uridylyl-(5' → N)serylglycine (I) and uridylyl(5' → N) threonylglycine (II), the synthesis of which has been described previously [4].

The study of the stability of compounds (I) and (II) at various pH values showed that the hydroxy group in the hydroxy amino acid has a fundamental influence on the properties of the phosphoramide link. The hydrolysis of compounds (I) and (II) with 1 N hydrochloric acid (37° C, 60 min) forms, in addition to uridine-5' phosphate [48% for (I) and 20% for (II)] and the ethyl esters of the corresponding dipeptides, uridine [52% for (I) and 80% for (II)], and O-phospho peptides (O-phospho hydroxy amino acids). Under milder conditions (0.1 N HCl, 37° C, 60 min), uridine-5' phosphate and uridine are formed in a ratio of 3 : 1 for (I) and 1 : 1 for (II). The nature of the hydrolysis products shows that, in addition to the cleavage of the phosphoramide bond, cleavage of the phosphoric ester bond takes place with the phosphate residue migrating from the nitrogen of the hydroxy amino acid to the oxygen (the only type of phosphorus-containing amino acids or peptides consists of the O-phospho hydroxy amino acids or their peptides). The mechanism of this cleavage evidently consists in intramolecular substitution at the nucleotide phosphorus with the participation of the hydroxy group of the hydroxy amino acid. In this substitution, the departing group is uridine and an unstable phosphorus-containing ring is formed which rapidly hydrolyzes to an O-phosphopeptide (O-phospho amino acid).



Compounds (I) and (II) are also cleaved in an alkaline medium. In contrast to the alkali-stable nucleotidyl(5'→ → N)peptides not containing functional groups in the N-terminal amino acid, the nucleotidopeptides (I) and (II) are hydrolyzed to an appreciable extent to uridine and the corresponding N-phosphopeptide. When compounds (I) and (II) are incubated in 0.5 N caustic soda (37° C, 60 min), 60% hydrolysis takes place.

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