SYNTHESIS OF PROTECTED OLIGOPEPTIDES REPRESENTING FRAGMENTS OF HISTONE FRACTION HI

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The functional role of the primary structure of histones may be shown both in interaction with such specific enzymes as, for example, phosphokinase [1, 2] and also in the process of forming complexes with DNA [3]. Interesting information can be obtained in the investigation of individual fragments of histones. We have previously reported the isolation of compounds of this type [4]. The present paper describes the synthesis of a number of analogous oligopeptides forming segments of the histone fraction HI of calf and rabbit thymus. It must be noted that there are some differences between these histone fractions. Thus, in the HI of rabbit thymus the Ala-38 residue is replaced by Ser-38. This determined the type of compounds obtained: the fragment of the HI of rabbit thymus (31-40) contained Ala-38 and the fragment of the calf thymus HI (31-41) contained Ser-38. In addition, we synthesized two analogs in which L-Ala-37 was replaced by D-Ala-37, and the Pro-Pro fragment by Ala-Ala. In contrast to the natural sequence, in a number of oligopeptides a Lys residue was present in place of Arg-35.

The synthesis of the oligopeptides was effected in stages from the C-end by blocks consisting of 2-3 amino-acid residues using the method of mixed anhydrides and the carbodiimide method according to Schemes I and II. It must be observed that during the synthesis of the peptides the possibility of partial racemization is not excluded. In view of this, we performed the synthesis in such a way that, as far as possible, the C-terminal residue was a glycine residue. In this way, we obtained the peptide with sequence (31-40) by a (2 + 9) scheme. If the C-terminal residue was an optically active amino acid, we used the carbodiimide method with tetrahydrofuran as solvent. The reaction mixture was maintained at 0 to -6°C for 1 h and at 22°C for 20 h. Under these conditions, according to the literature [5], racemization does not exceed 0.1%.

The Nα-amino group of glycine was protected by a benzoxycarbonyl grouping (Z), and the Nα-amino groups of the acids by a tert-butoxycarbonyl (Boc) grouping. The guanidine groups of the arginine residues were protected by nitro groups (NO2).

The compounds obtained are stable and are being used as the starting materials for the preparation of the methyl esters of these peptides.
