

2. J. M. Stewart and J. D. Young, Solid-Phase Peptide Synthesis, W. H. Freeman, San Francisco (1969) [Russian translation], Moscow (1971), p. 130.
3. K. L. Smith, Methods in Hormone Research, 2, 439 (1962).

## ENZYMATIC SYNTHESIS OF NUCLEOPEPTIDES

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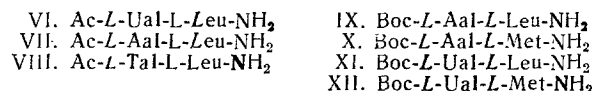
In order to determine the possibility of the enzymatic synthesis of stereoregular nucleopeptides [1] including residues of natural nucle amino acids and some protein amino acids, we have investigated the reaction of  $N^{\alpha}$ -acyl-DL-nucleo amino acids (I-V) with the amides of L-leucine and L-methionine in the presence of chymotrypsin or carboxypeptidase Y.

Information on the constants and yields of compounds obtained previously (I-V) is given below (TLC on Silufol UV-254 plates; systems: 1) iso-C<sub>3</sub>H<sub>7</sub>OH-25% NH<sub>4</sub>OH-H<sub>2</sub>O (14:1:5); and 2) n-C<sub>4</sub>H<sub>9</sub>OH-CH<sub>3</sub>CO<sub>2</sub>H-H<sub>2</sub>O (4:1:1)).

Compound	mp °C	$R_f$ system		Yield, %
		1	2	
Ac-DL-Aal-OMe (I)	190	0.66	0.15	73
Ac-DL-Ual-OMe (II)	219	0.60	0.20	82
Ac-DL-Tal-OMe (III)	230	0.73	0.44	70
Boc-DL-Aal-OMe (IV)	187	0.88	0.73	60
Boc-DL-Ual-OMe (V)	197	0.80	0.70	70

After a series of experiments, we found that the incubation of the esters (I-V) with the amine of L-leucine or L-methionine and chymotrypsin in 0.2 M carbonate buffer (pH 10.0) containing 20% of a 1:1 mixture of dimethylformamide (DNFA) and dimethyl sulfoxide led to the enzymatic synthesis of stereoregular nucleopeptides. At 20°C, the reaction was complete in 8 h and the yield of nucleopeptides amounted to 60-90%. In experiments with carboxypeptidase Y, the yields of nucleopeptides were low.

As a result of the experiments performed we achieved the enzymatic synthesis of the stereoregular nucleopeptides (VI-XII):



For subsequent use in nucleopeptide synthesis, compounds (IX-XII), each containing a N-protective Boc group readily eliminated on acidolysis, are particularly promising. Information on the constants of these compounds is given below (system 3: CHCl<sub>3</sub>-CH<sub>3</sub>OH (1:1); electrophoretic mobility in electrophoresis on LKB-3276 paper (240 V, 2 h) in systems 1) 1 N CH<sub>3</sub>CO<sub>2</sub>H (pH 2.5), and 2) 0.05 M aqueous (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>NH<sub>2</sub>CO<sub>3</sub> (pH 8.7); reference standard: H-Aal-OH in the case of compounds (IX) and (X), and H-Ual-OH in the case of compounds (XI) and (XII):

Compound	mp, °C	$R_f$ in system			EM in system		$[\alpha]_D^{20}$ , deg (in DMFA)
		1	2	3	1	2	
IX	177	0.75	0.70	0.34	1.03	0.25	-30 (c 1.0)
X	—	0.76	0.62	0.30	0.73	0.30	-24 (c 0.95)
XI	172	0.87	0.77	0.60	0.75	0.32	-52 (c 0.1)
XII	157	0.85	0.73	0.58	1.09	0.40	-53 (c 0.25)

The structures of the compounds obtained were confirmed by the results of acid hydrolysis and UV and mass spectra, and also by independent chemical synthesis. The optical purity of

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the nuclear peptides synthesized was shown by measuring the circular dichroism of chromophoric derivatives of them [2].

Thus, we have shown for the first time the possibility of the enzymatic synthesis of stereoregular nucleopeptides from derivatives of racemic nucleoamino acids.

#### LITERATURE CITED

1. Yu. P. Shvachkin, Zh. Obshch. Khim., 49, 1157 (1979).
2. N. A. Voskova, V. V. Romanov, N. V. Sumbatyan, G. A. Korshunova, and Yu. P. Shvachkin, Bioorg. Khim., 6, 731 (1980).