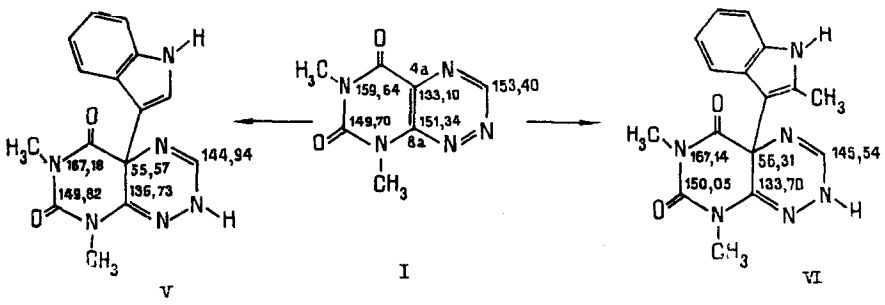

V I VI

presence of a proton on the N_2 (and not the N_4) atom of compound (VI) was shown by the doublet splitting of the C_3 signal with the small SSCC of $^2J_{C_3H-2}$ = 3.7 Hz in addition to $^1J_{C_3H-3}$ = 196.2 Hz and the absence of it for C_{4a}. Compound (V) had an analogous structure, as was confirmed by the closeness of the values of the ^{13}C chemical shifts of the pyrimidotriazine nucleus for compounds (V) and (VI).

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SYNTHESIS OF NEW STRUCTURAL ANALOGS OF TETRAGASTRIN

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UDC 547.964.4

In connection with a study of the structural-functional organization of peptide hormones, we have performed the synthesis of new structural analogs of tetragastrin (synonym: fragment 14-17 of gastrin; fragment 30-33 of cholecystokinin, trimafam, CCK-4)[1-3], which consists of a tetrapeptide with the structure (I). It was the previously unknown analogs (II-IV) differing from natural tetragastrin (I) by the replacement of the L-tryptophan residue in position 1 by L-ornithine, D-ornithine, and L-alanine residues, respectively, that were synthesized.

$$H-\overset{1}{X}-L\cdot\overset{2}{Met}-L\cdot\overset{3}{Asp}-L\cdot\overset{4}{Phe}-NH_2$$

I. X = L·Trp III. X = D·Orn
II. X = L·Orn IV. X = L·Ala.

Compounds (II-IV) were synthesized by a scheme providing for the stepwise growth of the peptide chain in solution using as the amino components the amides of the C-terminal amino acid (V) and of the intermediate peptides (VIII) and (XI), and as the activated carboxy components the pentafluorophenyl esters of the protected amino acids (VI), (IX), and (XII-XIV) [4]. As can be seen from the scheme, the intermediate compounds were the protected dipeptide (VII), tripeptide (X), and tetrapeptides (XV-XVII). (Scheme, top, following page.)

The structures of the new tetragastin analogs were determined unambiguously by the scheme of synthesis, and their individuality was confirmed by the results of analytical determinations.

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Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 156-158, January-February, 1987. Original article submitted August 10, 1986.

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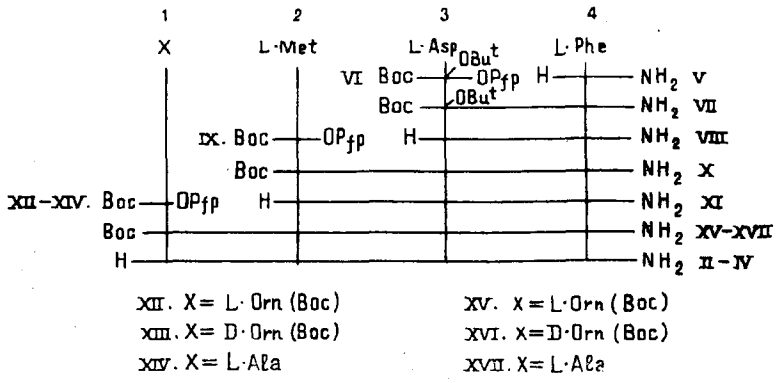

L-Ornithyl-L-methionyl-L-aspartyl-L-phenylalaninamide (II) (Hydrochloride). mp 148-150°C, R_f 0.82 (BuOH–AcOH–H_2O 4:1:1)) (system 1), 0.32 (BuOH–AcO–Py–H_2O (30:3:10:12)) (system 2) (TLC on Silufol UV-254 plates with visualization by ninhydrin); $[\alpha]_D^{25}$ – 19° (s 0.5; MeOH), Amino acid analysis: Orn 0.90 (I), Met 0.80 (I), Asp 0.98 (I), Phe 1.00 (1).

D-Ornithyl-L methionyl-L-aspartyl-L-phenylalaninamide (III) (Hydrochloride). mp 140-142°C, R_f 0.82 (system 1), 0 32 (system 2); $[\alpha]_D^{25}$ –47° (s 0.5; MeOH). Amino acid analysis: Orn 0.92 (I), Met 0.85 (I), Asp 0.99 (I), Phe 1.00 (I).

L-Alanyl-L-methionyl L-aspartyl-L-phenylalaninamide (IV) (Hydrochloride Monohydrate). mp 181-182°C (decomp.), R_f 0.78 (system 1), 0.30 (system 2); $[\alpha]_D^{25}$ –33° (s 1; MeOH). Amino acid analysis: Ala 1.05 (I), Met 1.04 (I), Asp 1.10 (I), Phe 1.00 (I).

The synthesis of the new structural analogs of tetragastrin creates the necessary prerequisites for the study of the biological activity of these compounds.

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