

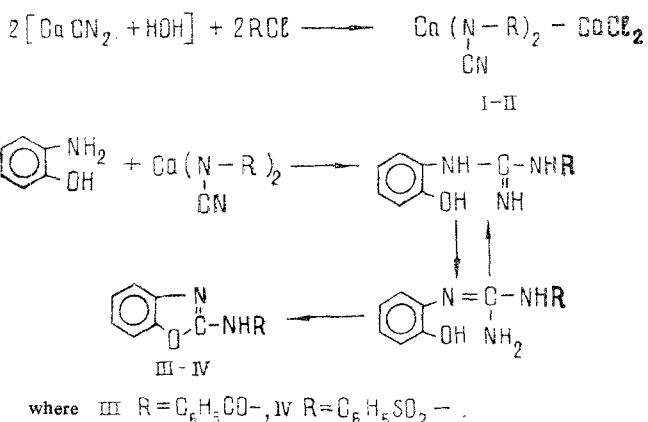
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SYNTHESIS OF 2-BENZOYLAMINO- AND PHENYLSULFONYLAMINOBENZOXAZOLESS

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In the interaction of o-aminophenol with cyanoalkyl carbamates, the primary reaction products are N-alkoxycarbonyl-N-(o-hydroxyphenol)guanidines [1]. It was of interest to trace whether this is the case in the reaction of o-aminophenol with N-acylcyanamides. With this aim, and also in order to synthesize biologically active substances, we have performed the reaction of o-aminophenol with N-benzoylcyanamide (I) and N-phenylsulfonylcyanamide (II). The latter were prepared from 0.1 mole of calcium cyanamide, 40 ml of water, and 0.05 mole of the appropriate acylating agent. To a solution of compound (I) obtained in this way, with stirring, 0.04 mole of o-aminophenol, 0.12 mole of concentrated HCl (when less than 0.80 mole of acid was added, intermediate compounds were formed) were added and the mixture was heated to 90–100°C for 2 h. Then it was cooled to 20°C and the resulting precipitate was filtered and recrystallized from ethanol to give 2-benzoylaminobenzoxazole (III) with mp 202–204°C; according to the literature [2]: mp 190°C. In the similar treatment of compound II the yield of 2-phenylsulfonylaminobenzoxazole (IV) was 55%, mp 244°C (according to the literature [3]: mp 246–247°C for the compounds synthesized from N-dichloromethylene-sulfonamide).



The structures of the compounds synthesized were shown by their IR and mass spectra. In the IR spectrum of (III) there are absorption bands characteristic for C=O groups in amides (1650 cm^{-1}) and for NH groups (3300 cm^{-1}). There is no displacement of the absorption in the carbonyl region that is characteristic for the imino structure. In the mass spectra of the same compound there is the peak of the molecular ion with m/z 238 (M^+). As shown by the detection of metastable transitions, the breakdown of the M^+ ion takes place mainly through an ion with m/z 134 (2-aminobenzoxazole) which arises from the M^+ ion by the ejection of benzoyl ($M - C_6H_5CO$). In the mass spectrum of (IV) there is the peak of the molecular ion with m/z 274, and in the IR spectra there are bands at 1150 and 1315 cm^{-1} (sulfonamide group). The mass spectra of the intermediate products contain the peaks of the molecular ions.

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Thus, the reaction of o-aminophenol with N-acylcyanamides takes place through N'-acyl-N-(hydroxyphenol)guanidines as intermediates.

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SYNTHESIS AND PROPERTIES OF FRAGMENT 37-42

OF HUMAN GROWTH HORMONE

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In connection with the study of the laws of the structural-functional organization of human growth organism and in order to elucidate the lipotropic activity of the individual fragments of this hormone, we have performed the synthesis of the hexapeptide (I) containing amino acid sequence 37-42 of human growth hormone (all the amino acids belong to the steric L series):



Hexapeptide (I) is a component part of the tetradecapeptide fragment 31-44 of human growth hormone which possesses a high lipotropic effect [1-3], and in the structural respect it is close to the hexapeptide section of ovine lipotropin [4].

The synthesis of the hexapeptide (I) was carried out by the solid-phase method [5, 6] using a chloromethylated copolymer of styrene with 2% of divinylbenzene containing 7% of active chlorine as the insoluble support. The loading of the C-terminal amino acid onto the support amounted to 0.32 mmole/g. For the synthesis we used the following amino acid derivatives: Boc-L-Tyr(Bz1)-OH, Boc-L-Lys(Z)-OH, Boc-L-Gln-ONp, Boc-L-Glu(OBz1)-OH, and Boc-L-Pro-OH. N,N'-Dicyclohexylcarbodiimide was used as the condensing agent. The only exception was the addition of the Gln⁴⁰ residue, which was introduced into the peptide chain by the p-nitrophenyl ester method. After each stage of condensation, the blockage of any free amino groups was carried out by the action of acetic anhydride in dimethylformamide in the presence of triethylamine. The separation of the peptide from the polymeric support and the elimination of all the protective groups were effected in a single working stage by treating the peptidylpolymer with hydrogen bromide in a mixture of trifluoroacetic acid and methylene chloride (1:1) in the presence of anisole as protector.

The primary purification of the hexapeptide (I) was carried out by reprecipitation from methanol with diethyl ether. For further purification, the reprecipitated substance was subjected to chromatography on a column of Filtrak FND cellulose equilibrated with the solvent system butan-1-ol-pyridine-acetic acid-water (15:10:3:12) (system 1). The same system was used as eluent. The efficacy of purification was monitored with the aid of thin-layer chromatography (TLC) on Silufol UV-254 plates. After lyophilization, the hexapeptide (I) was obtained with a yield of 64%: $[\alpha]_D^{25} -30.5^\circ$ (c 0.38; $\text{CH}_3\text{CO}_2\text{H}$); R_f 0.24 (PC in system 1), 0.14 (TLC with iso-C₅H₁₁OH-C₅H₅N-CH₃CO₂H-H₂O (7:8:6:2)), 0.23 (TLC, system 1), 0.79 (TLC, n-C₄H₉OH-C₅H₅N-CH₃CO₂H-H₂O, 15:20:60:24). Found, %: C 48.31, H 7.80, N 14.17. C₃₆H₅₇N₉O₁₁·6H₂O. Calculated, %: C 48.04, H 7.73, N 14.01. Amino acid analysis: Pro 1.00, Lys 1.78, Glu 2.07, Tyr 0.85.

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