SYNTHESIS OF SOME DEHYDROTRYPTOPHAN PEPTIDES

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For a definitive proof of the structural formula of the natural antibiotic polypeptide neotelomycin (A-128-P) proposed previously [1] it was necessary to perform its total synthesis. As is well known, neotelomycin contains, in addition to 10 other amino acids, one dehydrotryptophan residue (Δ-Try) [2]. There is no information in the literature either on the synthesis of peptides containing Δ-Try or on their physicochemical and chemical properties. Consequently, in order to approach the synthesis of the antibiotic A-128-P we have undertaken the synthesis of a number of Δ-Try peptides on the basis of the azlactone method of synthesizing dehydropeptides [3]. As the starting material we used 4-(indol-3-ylmethylene)-2-phenyl-2-oxazolin-5-one (I) [4]. The four new dipeptides of dehydrotryptophan that we have synthesized have the same characteristic absorption maxima in the UV region of the spectrum as the antibiotic under investigation.

Synthesis of N-Bz-Δ-Try-L-Pro. To a solution of 100 mg (1 mmole) of L-proline in a mixture of 10 ml of acetone and 1 ml of 1 N NaOH was added 283 mg (1 mmole) of (I) and acetone sufficient to dissolve the (I) completely, and the mixture was stirred at 20°C for several hours and was then acidified with N* HCl solution and evaporated to dryness. The residue was dissolved in ethyl acetate and the dipeptide was precipitated with petroleum ether. The precipitation was repeated. Yield 78%, mp 150-153°C, composition $C_{23}H_{21}N_3O_4$. λ_{max} 278, 331 nm, log ε 3.98; 4.15 (CH_3OH-H_2O, 2 : 1), R_f 0.47 and 0.76 in system 1 [isopropanol − NH_4OH-H_2O (8 : 1 : 1)] and in system 2 [butan-1-ol − $CH_3COOH-H_2O$ (4 : 1 : 5)], respectively, on chromatography on Silufol UV_{254} plates.

N-Bz-Δ-Try-Gly, $C_{20}H_{17}N_3O_4$, was obtained from glycine and (I) by a similar procedure. Yield 61%, mp 180-182°C, UV spectrum: λ_{max} 274, 336 nm, log ε 4.0: 4.25 (CH_3OH-H_2O, 2 : 1), R_f 0.43 (system 1) and 0.73 (system 2).

N-Bz-Δ-Try-L-Val, $C_{23}H_{23}N_3O_4$, was obtained by heating (55°C) equimolar amounts of (I) and L-valine in acetone − N* NaOH (10 : 1) for 6-7 h. After acidification and the removal of the acetone by distillation, the precipitate was separated off and was recrystallized from ethyl acetate. The yield of the dipeptide was 48%, mp 137-138°C; UV spectrum: λ_{max} 273, 335 nm, log ε 4.04; 4.28 (CH_3OH-H_2O, 2 : 1), R_f 0.59 (system 1) and 0.78 (system 2).

N-Bz-Δ-Try-L-Ala, $C_{23}H_{19}N_3O_4$, was obtained from (I) and L-alanine by the preceding method. Yield 42%, mp 143-145°C, UV spectrum: λ_{max} 274, 336 nm, log ε 4.04; 4.27 (CH_3OH-H_2O, 2 : 1), R_f 0.46 (system 1) and 0.63 (system 2).

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