NEW METHOD FOR THE SYNTHESIS OF 6-SUBSTITUTED 9-PURINYL-α-AMINO ACIDS

PREPARATION OF α-AMINO-ε-(6-CHLORO-9-PURINYL)CAPROIC ACID

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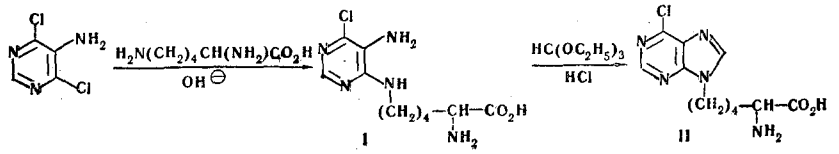
We have previously obtained a number of 9-purinyl-α-amino acids [1-4] in a search for physiologically active substances. Continuing our investigations of various paths for the preparation of 9-purinyl-α-amino acids, we have developed a new, convenient method for the synthesis of substituted (in the heterocyclic ring) ω-(9-purinyl-α-amino acids; this method can be demonstrated in the case of the preparation of α-amino-ε-(6-chloro-9-purinyl)caproic acid.

The reaction of 4,6-dichloro-5-aminopyrimidine with lysine in alkaline medium yields about 40% of N_ε-(5-amino-6-chloro-4-pyrimidyl)lysine (I), the treatment of which with ethyl orthoformate and hydrochloric acid results in closing of the imidazole ring to give α-amino-ε-(6-chloro-9-purinyl)caproic acid (II). The yield of II is 45% after purification of the product by means of chromatography on Dowex-50W ion-exchange resin and subsequent crystallization.



EXPERIMENTAL

N_ε-(5-Amino-6-chloro-4-pyrimidyl)lysine (I). This compound had mp 151-152° (from water). Found %: C 39.56; H 6.36; Cl 12.38; N 23.21. $C_{10}H_{16}ClN_5O_2$. Calculated %: C 39.95; H 6.37; Cl 11.79; N 23.30. R_f 0.75 (system 1),* 0.57 (system 2). UV spectra [λ_{max}, nm (log ε)]: 302 (4.11) (pH 1); 265 (3.88), 290 (3.89) (pH 7); 263 (3.94), 290 (3.96) (pH 13).

α-Amino-ε-(6-chloro-9-purinyl)caproic Acid (II). This compound melted above 220° (from ethanol–ether). Found %: C 42.80; H 5.79; N 22.85. $C_{11}H_{14}ClN_5O_2 \cdot 1.5H_2O$. Calculated %: C 42.52; H 5.51; N 22.54. R_f 0.71 (system 1), 0.51 (system 2). UV spectrum [λ_{max}, nm (log ε)]: 267 (3.94) (pH 1); 263 (4.24) (pH 13).

We are continuing our investigations of the synthesis and study of the properties of substituted 9-purinyl-α-amino acids, particularly 6-amino and 6-hydroxy derivatives of α-amino-ε-(9-purinyl)caproic acid.

*System 1: iso-C_3H_7OH–NH_4OH–H_2O (7:1:2); system 2: N-C_4H_9OH–CH_3COOH–H_2O (5:3:2). Ascending chromatography with FN-11 paper was used. The spots were developed with ninhydrin and UV absorption.

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