REACTION OF O-ARYL-N-DI(2-CHLOROETHYL)AMIDOGUANIDYL PHOSPHATES WITH ACETOACETIC ESTER

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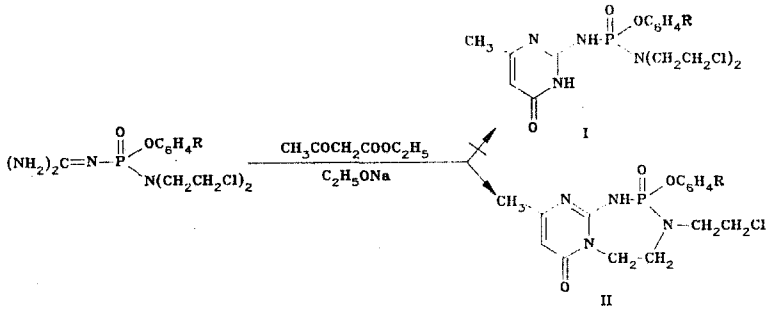
UDC 547.497.1'118.5'859'892.07

We attempted to prepare phosphorylated aminopyrimidines I, containing an alkylating group, to prove the influence of the bond between the phosphorus atom and the molecule of the heterocycle on the antitumorigenic properties of compounds.

The phosphorylated aminopyrimidines I were synthesized by a method already described [1], starting from O-aryl-N-di(2-chloroethyl)amidoguanidyl phosphates [2] and acetoacetic ester.

However, in the reaction not only a pyrimidine ring is formed, but also a ring closure by the chloroethyl group with one of the nitrogen heteroatoms takes place, leading to the formation of substituted 1,2,3,4-tetrahydro-5H-2,1,3,6-pyrimidophosphotriazepin-2-ones (I).



a R=H, b R=*p*-CH_3, c R=*p*-Cl, d R=*p*-Br, e R=*p*-I, f R=*p*-F

A 10-mmole portion of O-phenylbis(2-chorethyl)amidoguanidyl phosphate [2] is added to a sodium ethylate solution (prepared from 50 mmoles of sodium and 100 ml of ethanol), and the mixture is heated to boiling. Then, 48 mmoles of acetoacetic ester are added, the mixture is boiled for another 3 h, and the solvent is distilled *in vacuo*. The solid residue is dissolved in 50 ml of water and the solution is acidified with 10% hydrochloric acid to an acid reaction. The crystalline compound IIa that separates is filtered, dried, and recrystallized from benzene. Compounds IIb-f are obtained in a similar way. Following are: compounds, yield (%), mp (°C): IIa, 59, 155-157; IIb, 72, 187-189; IIc, 56, 200-201; IId, 31, 203-204; IIe, 56, 183-185; IIf, 62, 192-194. Data of elemental analysis correspond to calculated data. IR spectrum (KBr): 1700 (C=O), 1600 (pyrimidine ring), 1200 cm^{-1} (P=O).

LITERATURE CITED

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2. I. I. Kuz'menko, Farm. Zh., No. 2, 71 (1985).

Kiev Scientific-Research Institute of Pharmacology and Toxicology, Ministry of Public Health of the Ukrainian SSR, Kiev. Translated from Khimiya Geterotsiklicheskikh Soedinenii No. 5, p. 710, May, 1986. Original article submitted July 2, 1985.

0009-3122/86/2205-0583$12.50