INVESTIGATION IN THE FIELD OF PYRIMIDINES

Alkylation of 2-Amino-4-methyl-6-oxopyrimidine and 2-Amino-6-chloro-4-methylpyrimidine

D. I. Biskupskaya, V. N. Mikhailova, and I. Kh. Fel'dman

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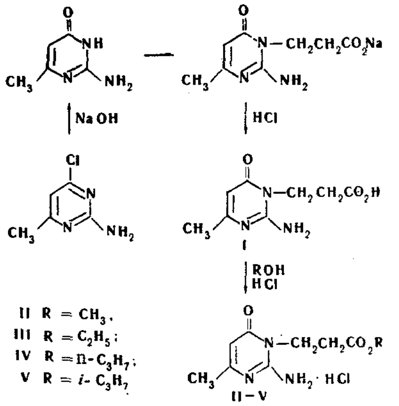
The alkylation of 2-amino-4-methyl-6-oxopyrimidine and 2-amino-6-chloro-4-methylpyrimidine with acrylonitrile in an aqueous alkaline medium takes place at the ring nitrogen with the formation of 2-amino-1-(β-carboxyethyl)-4-methyl-6-oxopyrimidine (I). A number of esters of compound I have been obtained in the form of hydrochlorides.

In spite of the large number of papers devoted to the chemistry of pyrimidine in the last few years, the alkylation of pyrimidine derivatives has been inadequately studied [1].

Papers are known [2,3] in which the authors report the alkylation of uracil and 2-thiouracil with acrylic acid derivatives in liquid ammonia at −50° C.

By the reaction of 2-amino-4-methyl-6-oxopyrimidine with acrylonitrile in an aqueous alkaline medium we have obtained the acid I.



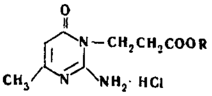
The same acid was obtained by the alkylation of 2-amino-6-chloro-4-methylpyrimidine. Apparently, under the experimental conditions the chlorine undergoes saponification, and then alkylation takes place. The identity of the compounds obtained was confirmed by the absence of a depression of the melting point of a mixed sample. The presence in the IR spectrum* of compound I of bands corresponding to the stretching vibrations of NH_2 (3340, 3285 cm^{-1}) [5] and C=O groups (1698, 1650 cm^{-1}) [5] confirms this structure.

When hydrogen chloride was passed through a suspension of the acid I in the appropriate alcohol, the methyl, ethyl, propyl, or isopropyl ether was obtained in the form of the hydrochloride (table). The IR spectra of compounds II-V have bands in the 1725–1742 cm^{-1} and 1198–1228 cm^{-1} regions which are characteristic for an ester group [6].

EXPERIMENTAL

2-Amino-2-(β-carboxyethyl)-4-methyl-6-oxopyrimidine (I). To 41 ml of a 1 N solution of NaOH 2.5 g (0.02 mole) of freshly prepared 2-amino-4-methyl-6-oxopyrimidine [4] and 4.8 ml (0.072 mole) of acrylonitrile were added. The mixture was then heated to the boil for 10 hr. Further acrylonitrile was added 6 hr and 9 hr after the beginning of the reaction (4.8 ml in each case). After the end of the reaction, the excess acrylonitrile was driven off in vacuum, the residue was filtered, and the filtrate was acidified with 37% hydrochloric acid to pH 5. The precipitate that deposited was washed with water. The yield of unpurified material was 50%. Mp 244°–245° C (from ethanol). Found, %: N 21.17. Calculated for $C_8H_{11}N_3O_3$, %: N 21.32.

2-Amino-1-(β-alkoxycarbonylethyl)-4-methyl-6-oxopyrimidine (II-V). Dry hydrogen chloride was passed into a mixture of 0.225 mole of I and 50 ml of absolute alcohol. The temperature rose to 60°–70° C. Subsequently, the temperature was kept at 50°–60° C.



Compound	R	Mp, °C	Empirical formula	Found, %		Calculated, %	
				N	Cl	N	Cl
II	CH_3	142—143	$C_9H_{13}N_3O_3 \cdot HCl$	16.96	14.19	16.96	14.34
III	C_2H_5	123—124	$C_{10}H_{15}N_3O_3 \cdot HCl$	16.07	13.64	16.06	13.57
IV	n-C_3H_7	158—158,5	$C_{11}H_{17}N_3O_3 \cdot HCl$	15.68	12.74	15.24	12.88
V	i-C_3H_7	146—147	$C_{11}H_{17}N_3O_3 \cdot HCl$	15.62	13.15	15.24	12.88

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*The spectra of I were taken on a IKS-12 spectrophotometer with an LiF prism. The samples were prepared in the form of mulls in Freon oil. The IR spectra of the hydrochlorides of the esters II-V were taken on an IKS-14 spectrophotometer with an NaCl prism, the samples being compressed into tablets with KBr.

The hydrogen chloride was passed until the I had dissolved completely (2–3 hr). The reaction mixture was then left overnight at room temperature. On the following day, the alcohol was distilled off in vacuum. The yield of unpurified material was quantitative. The ester II was crystallized from ethanol and IV and V from butanol, while III was precipitated from alcohol with ether (see table).

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Leningrad Chemical and Pharmaceutical Institute