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LETTERS TO THE EDITOR

Formylation of 6-Aminouracil with Vilsmeier Reagent

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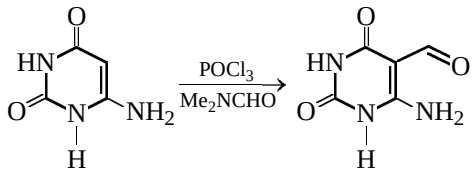
Oxopyrimidine-5-carbaldehydes **I** and some of their derivatives (azomethines, hydrazones) show promise as synthetic precursors of antitumor agents [1, 2]. Aldehydes **I** are usually synthesized by the Reimer–Tiemann reaction [3], controlled oxidation of 5-hydroxymethylpyrimidines [4], or Vilsmeier reaction. The latter reaction can be accompanied by exchange chlorination of oxo groups of the pyrimidine ring. For example, heating of 6-aminouracil **II** with $POCl_3$ in DMF yields 6-amino-2,4-dichloro-5-formylpyrimidine [5]. At the same time, there are indications in the literature [6] that Vilsmeier formylation of amine **II** can be performed so as to leave the oxo groups intact.

To develop a procedure for preparing 6-aminouracil-5-carbaldehyde **III**, we studied the reaction of amine **II** with Vilsmeier reagent at 90–100°C:



II **III**

Because of the low solubility of amine **II** in absolute DMF, the reaction was performed in a heterogeneous system. In six experiments at a fixed contact time (2 h), we obtained chromatographically identical products identified by elemental analysis and spectroscopy as 6-aminouracil-5-carbaldehyde **III**. The IR spectrum of **III** contains stretching bands of the oxo groups of the pyrimidine ring at 1739–1674 cm^{-1}. The ^1H NMR spectrum contains a formyl proton signal at 9.66 ppm. The mass spectrum contains the molecular peak.

6-Aminouracil-5-carbaldehyde III *(general procedure).* Freshly distilled $POCl_3$ (18.3 ml) was added dropwise with vigorous stirring to a suspension of 12.7 g of amine **II** in 25 ml of absolute DMF over a period of 1 h, avoiding warm-up of the mixture above 20°C. After adding the whole amount of $POCl_3$, the solidified mixture was crushed mechanically and heated on a boiling water bath for 2 h. After cooling, the mixture was transferred onto ice and ground to obtain a suspension. The suspension was neutralized with 40% aqueous NaOH at a temperature not exceeding 20°C, and the precipitate was filtered off, washed with water, and suspended in 5% aqueous NaOH. The undissolved residue was filtered off, thoroughly washed with water, suspended in 100 ml of water, and acidified with concentrated HCl to pH 4–5. The precipitate was filtered off, washed with water, refluxed successively with 100 ml of water and 100 ml of ethanol, and vacuum-dried over sodium pentoxide at 80°C. Yield 6.5 g (42%), R_f 0.69, mp >300°C. IR spectrum, ν, cm^{-1}: 1739 (C^2=O), 1674 (C^4=O). ^1H NMR spectrum, δ, ppm: 7.36 s (1H, NH_2), 9.19 s (1H, NH_2), 9.66 s (1H, CHO), 10.78, 10.83 d (2H, NH). Mass spectrum, *m/z* (I_{rel}, %): 155 $[M]^+$ (52.5), 127 $[M - CHO]^+$ (100), 68 $[M - HCNO - NH_2]^+$ (84.5). Found, %: C 38.58; H 2.97; N 26.44. $C_5H_5N_3O_3$. Calculated, %: C 38.71; H 3.22; N 27.09.

The IR spectrum was recorded on a Shimadzu Hyper-IR spectrometer (mull in mineral oil). The ^1H NMR spectrum was recorded on a Bruker AMX-400 spectrometer (400 MHz, DMSO-d_6) relative to residual solvent protons. The mass spectrum was taken on a Kratos MS-30 spectrometer (direct sample inlet, ionizing electron energy 70 eV, ion source temperature 200°C). Elemental analysis was performed with a Carlo Erba 1106 analyzer. The compound purity was checked by TLC on Silufol UV-254 plates in the system chloroform–methanol, 3 : 1, with UV development.

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