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Synthesis of Starting Compounds and Their Alkylation Reactions in Different Solvents

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ABSTRACT

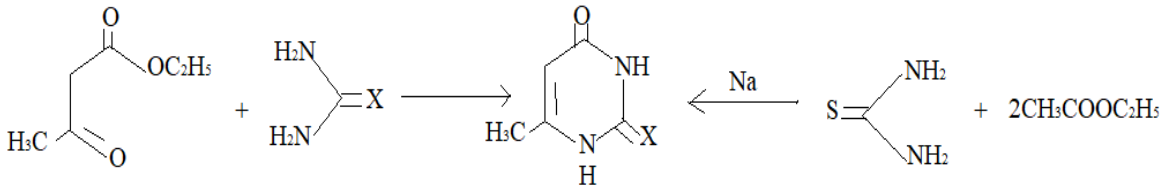
Carried out, the synthesis of the starting compounds, that they enter the reactions of alkylations in various solvents (DMF, acetonitrile and alcohol). The resulting compound was deter mined by the physico-chemical method IR, PMR and mass-spectroscopy.

Pyrimidine derivatives are of both practical and theoretical interest. Pyrimidine bases play an enormous role in life processes. They are part of nucleic acids, vitamins, alkaloids and are widely distributed in nature. Pyrimidine series compounds are one of the most important heterocyclic systems due to the high efficacy of drugs based on them. Pyrimidine derivatives are also used as herbicides, fungicides, dyes, vulcanization gas pedals, stabilizers, fabric bleaching agents.

Pyrimidines with different heteroatoms in positions 2 and 4 are considered as ambifunctional compounds. The salts of 2-oxo-, -thioxo-, -selenoxo-, and -aminopyrimidin-4, exhibit multiple reactivity in methylation reactions, and their anions are ambidextrous and polydentate. The alkylation of the indicated (e.g., 2-methylthio-6-methylpyrimidinone-4) with C4-C9 alkyl halides is not known in the literature, although they may behave peculiarly in these reactions. That is why the investigation of alkylation reactions of these multicenter systems, identification of their behavior peculiarities, regularities of reaction direction changing, comparison of the obtained data with the known results on their methylation as well as with 2oxo-, -thioxo-, -selenoxo-, -methylthio-, -aminoquinazolones condensed with benzene ring analogue and search for biologically active compounds in this series is the actual task.

Synthesis of starting compounds.

2-oxo-6-methylpyrimidinone-4 was synthesized from acetoacetic ether (AUE) and urea [1], 2-thioxo-6-methylpyrimidinone-4 was obtained by interaction of AUE with thiourea in the presence of sodium ethylate [2] or ethyl acetate with thiourea in the presence of sodium [3].

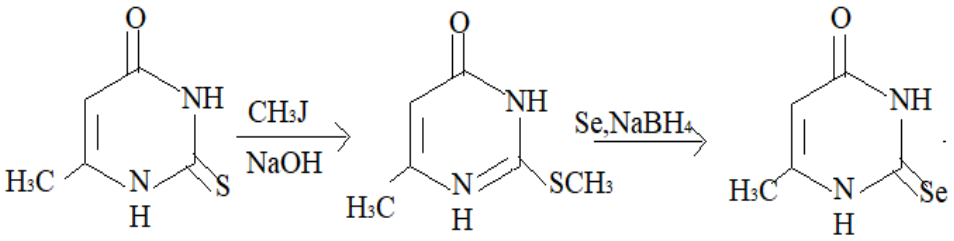


X=O,S

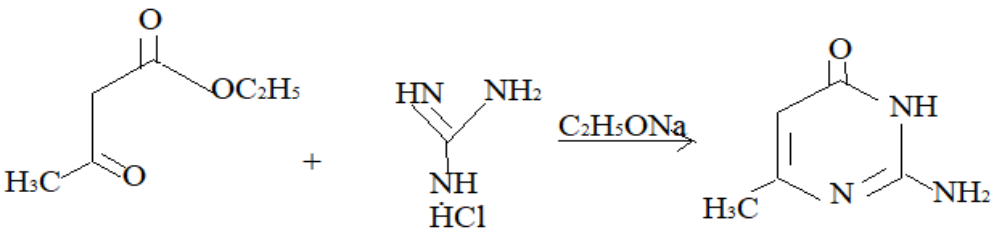
2-thioxo-6-phenylpyrimidinone-4 was obtained from benzoyl acetic ester and thiourea in the presence of sodium ethylate [4].

2-Methylthio-6-methylpyrimidinone-4 is formed by methylation of 2-thioxo-6-methylpyrimidinone-4 with methyl iodide in aqueous alkali solution [5].

Nucleophilic substitution of methylthiogroup of the mentioned compound by sodium hydroselenide at the moment of formation (from selenium and sodium borohydride) was performed synthesis of 2-selenoxo-6-methylpyrimidinone-4 [6-7].



Interaction of AUE with hydrochloride guanide in the presence of sodium ethylate gives 2-amino-6-methylpyrimidinone-4 in 72% yield [8].



Experimental part.

Tesla BS-567A (internal standard TMC, GMDS, scale). Rf values were determined on "Silufol" UV-254 plates (Czechoslovakia). Illuminant: iodine vapor.

Solvents (acetonitrile, alcohol (ethyl) DMFA, DMSO) were purified and absolute according to the method [9].

General methodology of C4-C9 alkylation reactions in different solvents.

10 mmol 2-oxo-, -thioxo-, -selenoxo-, -amino-, -methylthiopyrimidinone-4 is placed in a three-neck flask equipped with a dropping funnel, mechanical stirrer and reflux condenser with a chloralcium tube. The substance is dissolved or suspended in 45 mL of absolute solvent and 0.06 g (2.5 mmol) of sodium hydride is added while stirring. Stir for 30 minutes and add 11 mol of alkylating agent in 2 mL of solvent dropwise to the resulting solution of the sodium salt of the compound while stirring. The reaction mixture is stirred at room temperature for 24 hours or by heating in a boiling water bath for 4 hours.

After completion of the reaction, the contents of the flask is decomposed with 150 mL of cold water. The resulting precipitate is filtered off (if the precipitate does not precipitate, the reaction

product is extracted with chloroform), washed with water, dried and the amount of the alkyl product is determined by PMR spectroscopy.

Alkylation of 2-oxo-6-methylpyrimidinone-4 with butyliodide.

In a 100 mL flask 10 mL of absolute alcohol, 0.4 g (2.5 mmol) of KOH was placed and stirred until the caustic potassium dissolved. Then 0.32 g (2.5 mmol) of the starting substance was added and stirred for 30 minutes at room temperature. After that 0.27 (2.5 mmol) alkylating agent was added to the reaction mixture and heated in a water bath for 4 hours. It was cooled, extracted with chloroform, dried over anhydrous sodium sulfate. The chloroform was distilled off. The precipitate was filtered off. The yield was 0.29 (57%) Mel =238-240˚C (hexane). IR spectrum: 1719, 1676 (ν=CO), 1506 (ν=C=C).

3-n-heptyl-2-oxo-6-methylpyrimidinone-4.

Similarly to the above, from a solution with 10 mL of absolute alcohol, 0.28 g (5.0 mmol) KOH, 0.63 g (5.0 mmol) of starting substance and 0.8 mL (5.0 mmol) of heptyl iodide 0.99 g (89%) of product with Tpl.=220-222˚C (hexane) was obtained. IR spectrum: 1650 (ν=CO), 1600, 1630 (νC=C).

Alkylation of 2-thioxo-6-methylpyrimidinone-4 with n-brominated butyl in the presence of sodium hydride in acetonitrile.

In a 100 mL flask, 0.71 g (5.0 mmol) of 2-thioxo-6-methylpyrimidinone-4, 20 mL of absolute acetonitrile, 0.12 g (5.0 mmol) sodium hydride and stirred for 30 minutes at room temperature. Then 5.0 mmol of alkylating agent was added to the reaction mixture, then stirring was continued at room temperature (24 hours). After that the reaction mixture was decomposed in 75 mL of cold water, extracted with chloroform, dried over anhydrous sodium sulfate.

The solvent was distilled off, the precipitate was filtered. The yield was 0.49 g (50%) of the product with mel =78-80˚C (hexane).

Alkylation of 2-thioxo-6-methylpyrimidinone-4 with n-brominated butyl in the presence of sodium hydride in DMF (24 hours).

Similarly to the above described, from a solution of 20 mL of absolute DMF of 0.71 g (5.0 mmol) of 2-thioxo-6-methylpyrimidinone-4, 0.12 g (5.0 mmol) of sodium hydride and 0.52 mL (5.0 mmol) of n-brominated butyl, 0.67 g (69%) of product with mel.=82-84˚C (hexane) was obtained.

Alkylation of 2-thioxo-6-methylpyrimidinone-4 with butyl iodide in the presence of sodium hydride in acetonitrile.

Similarly to the above described, from a solution of 20 ml of absolute acetonitrile 0.71 g (5.0 mmol) of 2-thioxo-6-methylpyrimidinone-4, 0.12 g (5.0 mmol) of sodium hydride and 0.60 ml (5.0 mmol) of butyl iodide, 0.40 g (40%) of product with mel.=237-239˚C (hexane) was obtained.

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