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Methylation reactions of quinazolin-4-thione

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Abstract: methylation of quinazoline-4-thione with methyl iodide, dimethylsulfate and methyltosylate in various solvents was studied. It is shown that the reaction proceeds to N3, O4 and N1 atoms depending on the nature of the alkylating agent, solvent and temperature.
Key words: Quinazolin-4-thione, Reaction, alkylating agent, solvent nature, temperature, synthesis, quinazolin-4-one, quinazolin-4-thione, methylation, methyl iodide, methyl tosylate

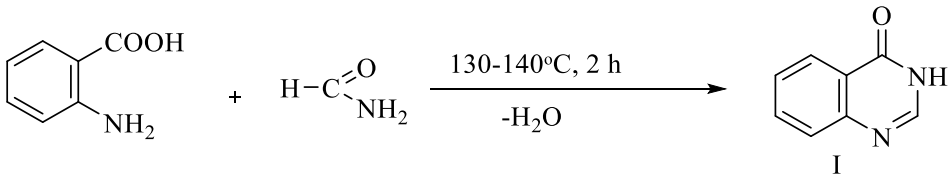
Introduction

Nowadays, the chemistry of heterocyclic compounds is rapidly developing. This is directly related to their physiological properties, and among them, drugs with high physiological properties, substances with plant growth properties, herbicides, fungicides, and insecticides were found. Among heterocyclic compounds, pyrimidines and their condensed derivatives are substances of both theoretical and practical importance. Their practical importance is the synthesis of many valuable drugs and other agents, and their theoretical importance is the presence of several reaction centers in their molecules.

Methods and results

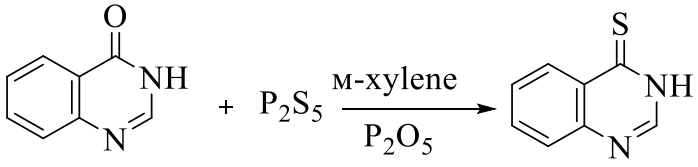
Previously, the synthesis methods and alkylation reactions of 2-oxo-, -thioxo-, -selenoxo-, and -aminoquinazolin-4-ones were thoroughly studied [1]. we set ourselves the goal of studying the synthesis and methylation reactions.

First, quinazolin-4-one was synthesized by condensation of anthranilic acid with formamide [2-16].



I

By heating the obtained quinazolin-4-one with phosphorus (V)-sulfide, the synthesis of quinazolin-4-thione (II) was carried out with a good yield (60%):



Salts (III) of quinazolin-4-thione formed with sodium metals have an ambidient character, and according to the IR-spectrum, the metal coordination in its anions is in the C4 position with sulfur passing through the N3 -nitrogen atom and has the following structure.

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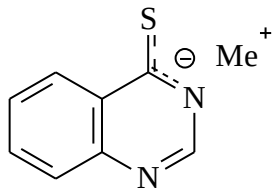
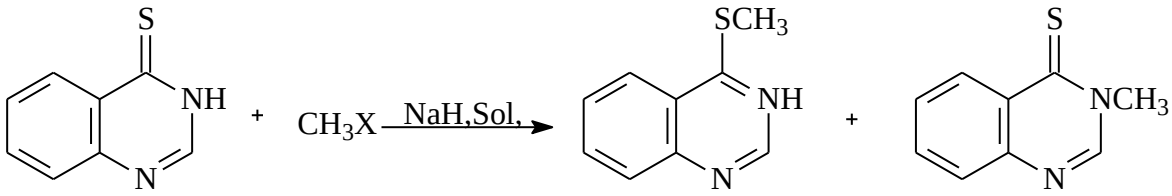


Me=Na,K

III

We studied the methylation reactions of quinazoline-4-thione with methyl iodide ("soft" methylation agent) and methyltosylate ("hard" methylation agent) at room temperature and in a water bath in various absolute solvents (ethanol, acetonitrile, DMFA, DMCO). The obtained results show that methylation in the polar proton solvent ethanol under any conditions proceeds only with the formation of 4-methylthioquinazoline (IV). A similar reaction was observed in acetonitrile. During methylation in polar aprotic solvents such as DMFA and DMCO, the formation of N3-methylquinazolin-4-thione (V) along with the 4-methylthio product was observed. It was found that the methyl product on the "hard" center increases when it goes from methyl iodide to methyltosylate.



IV V

So, methylation reactions of quinazoline-4-thione occur in different directions depending on the methylation agent, solvent and temperature.

Experimental part

Dissolve 1.62 g (0.01 mol) of quinazolin-4-thione in 50 ml of absolute solvents (DMFA, DMSO, alcohol, acetonitrile) in a flask equipped with a thermometer, separatory funnel, and mechanical stirrer in a reflux condenser with a chlorcalcium tube, and add 0.24 g (0.01 mol) of NaH was added and stirred for 30 minutes, 1.06 ml (r=1.33 g/cm3) (0.01 mol) of methyl iodide (or 0.01 mol of methyl tosylate, dimethyl sulfate) was added to the mixture in 5 ml (The solution in DMFA, DMSO, alcohol, acetonitrile) was added dropwise through a separatory funnel, heated in a water bath at 80-90°C, and the reaction mixture was cooled. Then 50 ml of water was added, the resulting precipitate was filtered off, the filter residue was recrystallized from hexane, and 1.4 g of S-methylquinazolin-4-thione was obtained in 71% yield.

Conclusion

Methylation reactions, such as Mercury yunalysis, were controlled using thin-layer chromotography, In relation to the corresponding quinazoline-4-ons –thions, methylation reactions occur mainly at the soft center N3 atom. The main reason for this is that the value of the electronegativity of the sulfur atom will be smaller than that of the oxygen atom in the quinazoline-4-ones, so the formation of the ambident ion will be very difficult.

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