SYNTHESIS OF DERIVATIVES OF BENZODIHYDRO-1, 3-THIAZINE

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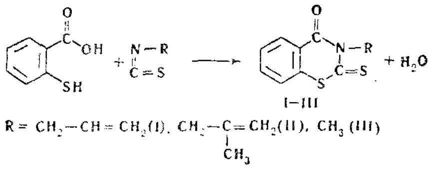
The condensation of esters of isothiocyanic acid with thiosalicylic acid has given N-alkyl-substituted 2-thio-4-oxobenzodihydro-1, 3-thiazines. The structure of the compounds obtained has been shown by their reactions with thiosemicarbazide, by hydrolysis, and by oxidation.

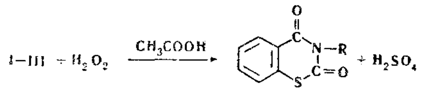
Derivatives of benzo- and naphthodihydro-1, 3-thiazine have been obtained by condensing o-mercaptocarboxylic acids with cyano derivatives [1–3]. In particular, the reaction of thiosalicylic acid with thiocyanic acid yields 4-oxobenzodihydro-1, 3-thiazine-2-thione [2].

We have studied for the first time the reaction of thiosalicylic acid with esters of isothiocyanic acid, leading to the formation of N-alkyl-substituted 4-oxobenzodihydro-1, 3-thiazine-2-thiones.

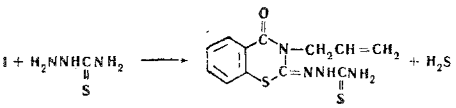

I–III

$R = CH_2{-}CH{=}CH_2$ (I), $CH_2{-}C(CH_3){=}CH_2$ (II), CH_3 (III)

The compounds obtained consist of low-melting yellow substances. They are soluble in ethanol, ether, benzene, and other organic solvents, and insoluble in water and petroleum ether. The hydrolysis of the products in an alkaline medium leads to their decomposition into the starting materials, and their oxidation with hydrogen peroxide in acetic acid to the replacement of the sulfur in the side chain by oxygen.



The heating of compound I with thiosemicarbazide in aqueous alcohol led to the formation of the 2-thiosemicarbazone.



EXPERIMENTAL

3-Allyl-4-oxo-5, 6-benzodihydro-1, 3-thiazine-2-thione (I). To 75 ml of toluene were added 7.7 g (0.05 mole) of thiosalicylic acid, and 4.9 ml (0.05 mole) of allyl isothiocyanate, and the mixture was boiled under reflux for 1 hr. The solvent and the unchanged allyl isothiocyanate were distilled off with steam, the residue was cooled and treated with ammonia, and the precipitate of compound I was filtered off. Yield 4.5 g (38%). The compound obtained was readily soluble in the majority of organic solvents and insoluble in water and petroleum ether. Bright yellow needles with mp 89°–90° C (from ethanol). Found, %: C 56.5; H 4.1; N 6.2; S 26.9. Calculated for $C_{11}H_9NOS_2$, %: C 56.2; H 3.8; N 6.0; S 27.2.

3-Methallyl-4-oxo-5, 6-benzodihydro-1, 3-thiazine-2-thione (II). This was obtained from equimolecular amounts of thiosalicylic acid and methallyl isothiocyanate by the method given above. Yield 32%. Mp 110°–112° C (from ethanol). Found, %: N 5.9; S 25.6. Calculated for $C_{12}H_{11}NOS_2$, %: N 5.6; S 25.7.

3-Methyl-4-oxo-5, 6-benzodihydro-1, 3-thiazine-2-thione (III). Two grams of KU-2 cation-exchange resin was added to a solution of 3.85 g (0.025 mole) of thiosalicylic acid and 3.4 ml (0.05 mole) of methyl isothiocyanate in 50 ml of toluene, and the mixture was boiled for 2 hr. The toluene and the methyl isothiocyanate that had not reacted were distilled off with steam, the aqueous solution was cooled and made alkaline with ammonia, and the precipitate of compound III was filtered off. Yield 1 g (20%). Mp 144°–146° C (from ethanol). Found, %: N 7.1; S 31.0. Calculated for $C_9H_7NOS_2$, %: N 6.8; S 30.7.

Hydrolysis of compound II. With heating, 1 g of compound II was dissolved in 30 ml of 10% caustic soda and steam was passed through the resulting solution. Methallyl isothiocyanate and a small amount of methallylamine distilled off with the steam, these being detected by qualitative reactions. The mother solution contained only the sodium salt of thiosalicylic acid.

Oxidation of compound I. Two grams of compound I was added to 15 ml of acetic acid, and the mixture was brought to the boil and treated with 4 ml of 30% hydrogen peroxide. The solution was boiled for 2 minutes and then 50 ml of water was added and it was neutralized with ammonia solution. A precipitate of 3-allyl-2, 4-dioxo-5, 6-benzodihydro-1, 3-thiazine deposited. Mp 71°–73° C (from a mixture of dioxane and water). Found, %: N 6.7; S 14.3. Calculated for $C_{11}H_9NO_2S$, %: N 6.4; S 14.6.

2-Thiosemicarbazone of compound I. A solution of 1 g of compound I in 30 ml of ethanol was treated with 3 g of sodium acetate, 30 ml of water, and 2 g of thiosemicarbazide. The solution was boiled for 25 hr. The end of the reaction was shown by the cessation of the evolution of hydrogen sulfide. The solution was diluted with 500 ml of water. On standing, a precipitate of the 2-thiosemicarbazone of compound I separated out. Mp 123°–126° C (decomp.). Found, %: N 18.9; S 21.8. Calculated for $C_{12}H_{12}N_4OS_2$, %: N 19.2; S 21.9.

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