SYNTHESIS OF DERIVATIVES OF DIHYDRO-1,3-THIAZINO[6,5-c]QUINOLINE. I

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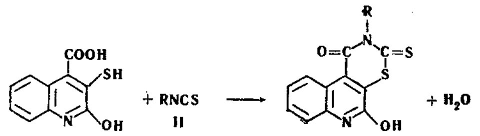
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 4, No. 1, pp. 99–101, 1968

UDC 547.831.7'869.1.07:542.953

The condensation of 2-hydroxy-3-mercaptoquinoline-4-carboxylic acid with isothiocyanates has given 2-alkyl-5-hydroxy-1-oxodihydro-1,3-thiazino[6,5-c]quinoline-3-thiones. The structure of the compounds obtained has been shown by reactions with semicarbazide, thiosemicarbazide, and by hydrolysis and oxidation.

The reactions of some α-mercapto carboxylic acids with alkyl isothiocyanates have been reported in the literature. The latter, in particular, condense with mercaptoacetic acid to form 3-alkyl-substituted rhodanines [1–3].

We have studied the reaction of 2-hydroxy-3-mercaptoquinoline-4-carboxylic acid (I) with alkyl and aryl isothiocyanates (II). When I and II are heated in dioxane, 2-alkyl- or 2-aryl-5-hydroxy-1-oxodihydro-1,3-thiazino[6,5-c]quinoline-3-thiones (III–VII) are obtained.

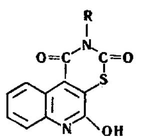


I II III–VII

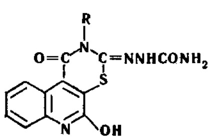
The compounds obtained (Table 1) are red substances. They are readily soluble in dioxane, dimethylformamide, pyridine, and alcohols, and are insoluble in benzene, ether, and water.

The structure of the compounds obtained was shown by hydrolysis and oxidation reactions. Compounds III-VII are stable to acids and are hydrolyzed by them only slowly on prolonged boiling. These compounds are insoluble in cold alkalis but hydrolyze to the initial acid I and II on being heated with solutions of alkalis.

The oxidation of III-VII with hydrogen peroxide in acetic acid readily replaces the thione sulfur with oxygen by the formation of 2-alkyl- and 2-aryl-5-hydroxy-dihydro-1,3-thiazino[6,5-c]quinoline-1,3-diones (VIII-XII) (Table 2).



VIII–XII



XIII

Compounds VIII-XII (Table 2) are light brown in color and are similar to III-VII in solubility. On alkaline hydrolysis, these compounds form the acid I and the corresponding amine.

Compounds III-VII exhibit the properties of thiones and condense with semicarbazide and thiosemicarbazide. The reaction takes place in a weakly alkaline medium with the evolution of hydrogen sulfide and the formation of the semicarbazone (XIII) and the thiosemicarbazone (XIV).

EXPERIMENTAL

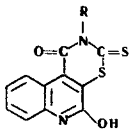
Synthesis of 2-methyl-5-hydroxy-1-oxodihydro-1,3-thiazino[6,5-c]quinoline-3-thione (III). A mixture of 11.05 g (0.05 mole) of the acid I and 7.3 g (0.1 mole) of methyl isothiocyanate in 40 ml of dioxane was heated in the boiling water bath for 3 1/2 hr and was left overnight. The precipitate of compound III that had deposited was separated off, washed with ether, and recrystallized from aqueous dioxane. Compounds IV–VII were obtained similarly.

The yields, melting points and elementary analyses of the compounds obtained are given in Table 1.

Hydrolysis of compound V. A mixture of 5 g of compound V and and 10 ml of 20% sodium hydroxide was heated in the boiling water bath for 30 min. Part of the solution was acidified with hydrochloric acid, giving a precipitate of the acid I, which was identified by a mixed melting point test. A second portion of the solution was distilled with steam, and allyl isothiocyanate was identified in the condensate. The hydrolysis of compounds III-XII took place similarly.

Table 1

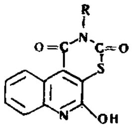
2-Alkyl and 2-Aryl-5-hydroxy-1-oxodihydro-1,3-thiazino[6,5-c]-quinoline-3-thiones



Compound	R	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
				N	S	N	S	
III	CH_3	290—292	$C_{12}H_8N_2O_2S_2$	9.85	23.60	10.14	23.18	45
IV	C_2H_5	302—304	$C_{13}H_{10}N_2O_2S_2$	9.58	22.26	9.65	22.06	65
V	$H_2C—CH{=}CH_2$	227—228	$C_{14}H_{10}N_2O_2S_2$	9.01	20.90	9.24	21.19	60
VI	$H_2C—\underset{\underset{CH_3}{\vert}}{C}{=}CH_2$	217—218	$C_{15}H_{12}N_2O_2S_2$	9.02	19.85	8.83	20.18	32
VII	C_6H_5	Decomp.320	$C_{17}H_{10}N_2O_2S_2$	8.29	19.05	8.30	18.98	72

Table 2

2-Alkyl- and 2-Aryl-5-hydroxydihydro-1,3-thiazino[6,5-c]quinoline-1,3-diones



Compound	R	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
				N	S	N	S	
VIII	CH_3	282—284	$C_{12}H_8N_2O_3S$	10.95	12.71	10.76	12.30	30
IX	C_2H_5	354—356	$C_{13}H_{10}N_2O_3S$	9.89	11.35	10.21	11.67	42
X	$H_2C-CH=CH_2$	280—281	$C_{14}H_{10}N_2O_3S$	9.81	11.27	9.78	11.28	61
XI	$H_2C-\underset{\underset{CH_3}{\vert}}{C}=CH_2$	267—269	$C_{15}H_{12}N_2O_3S$	8.90	10.42	9.33	10.63	30
XII	C_6H_5	Decomp. 350	$C_{17}H_{10}N_2O_3S$	8.71	10.09	8.75	9.94	65

Oxidation of IV. A mixture of 2.5 g of compound IV with 15 ml of acetic acid and 5 ml of dioxane was heated to the boil, and 8 ml of 30% hydrogen peroxide was added. After a few seconds, a vigorous reaction began, sulfur dioxide was evolved, and the whole of the solid matter went into solution. The reaction mixture was diluted with 60 ml of water and cooled, and the precipitate of compound IX was separated off. Light brown powder (from aqueous dimethylformamide). Compounds III and V-VII were oxidized similarly.

The yields, melting points, and elementary analyses of the compounds obtained are given in Table 2.

The 3-semicarbazone of compound VII (XIII). To a solution of 1.2 g of compound VII in 20 ml of dioxane were added 1.2 g of thiosemicarbazide, 2.5 g of sodium acetate, and 5 ml of water. The resulting mixture was heated in the boiling water bath for 20 hr and was then diluted with water, and the precipitate of compound XIII that deposited was filtered off. Red needles (from aqueous dimethylformamide) with decomp. p. 280° C. Found, %: N 18.20. Calculated for $C_{18}H_{13}N_5O_3S$, %: N 18.46.

The 3-thiosemicarbazone of compound VII (XIV). This was obtained by condensing VII with thiosemicarbazide by the method described above. Red crystals with decomp. p. 300°–310° C (from aqueous dimethylformamide). Found, %: N 17.96. Calculated for $C_{18}H_{13}N_5O_2S_2$, %: N 17.71.

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16 March 1966

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