

## XXXV.\* REACTION OF o-AMINOMERCAPTOPYRAZINES AND QUINOXALINES WITH HALO KETO ACID ESTERS

L. A. Myshkina and T. S. Safonova

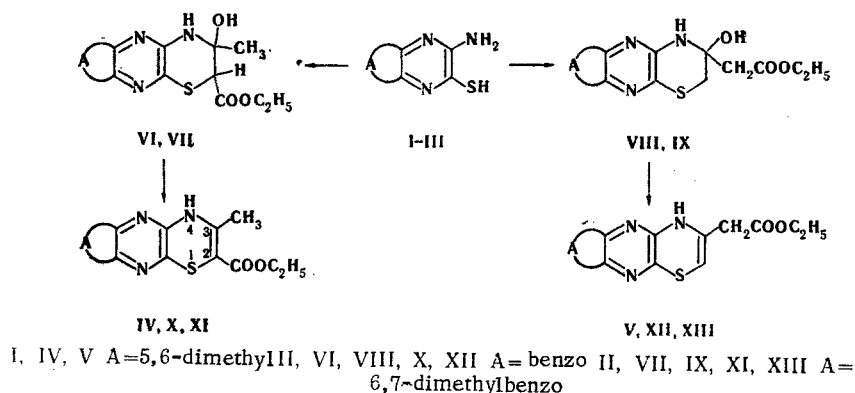
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Pyrazinothiazines and the corresponding 3-hydroxy-3,4-dihydroquinoxalinothiazines, which are dehydrated to quinoxalinothiazines under the influence of acidic agents, are formed in the reaction of 2-mercapto-3-amino-5,6-dimethylpyrazine and 2-mercapto-3-aminoquinoxalines with  $\alpha$ - or  $\gamma$ -chloroacetoacetic esters in the presence of an equimolar amount of alkali. The IR, UV, and PMR spectra are presented.

The reaction of 2-mercapto-3-amino-5,6-dimethylpyrazine (I), 2-mercapto-3-aminoquinoxaline (II), and its 6,7-dimethyl derivative (III) with halo keto acid esters has been investigated to search for biologically active substances among the derivatives of the two- and three-ring systems of 1,4-thiazine [2, 3]. The reaction of pyrazine I with  $\alpha$ - or  $\gamma$ -chloroacetoacetic esters in the presence of an equimolar amount of alkali gave pyrazinothiazines IV and V in about 90% yields, the structures of which as 4H- rather than 2H-derivatives were confirmed by IR and PMR spectroscopic data: the IR spectra contain an absorption band at  $3280\text{--}3340\text{ cm}^{-1}$ , and the PMR spectra contain a singlet of NH protons. In the case of IV the PMR spectrum does not contain a signal of protons attached to C(2), whereas the PMR spectrum of V contains a 2-H signal at 5.02 ppm.

Compounds IV and V are evidently formed through the hydroxyamino compounds, which are unstable and are readily dehydrated to IV and V under the reaction conditions. We were able to isolate intermediate hydroxyamino compounds VI and VII in about 60% yield in the reaction of mercaptoaminoquinoxaline II and its 6,7-dimethyl derivative III with  $\alpha$ -chloroacetoacetic ester under the conditions indicated above. Their IR spectra contain a broad absorption band at  $3270\text{--}3380\text{ cm}^{-1}$  (NH, OH). A 2-H signal (4.46 ppm) and signals of NH and OH groups (9.36 and 8.36 ppm) were observed in the PMR spectrum of VII.

Hydroxyamino compounds VIII and IX were similarly obtained by reaction of mercaptans II and III with  $\gamma$ -chloroacetoacetic ester.



\*See [1] for communication XXXIV.

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow 119021. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 5, pp. 695-697, May, 1977. Original article submitted August 22, 1976.

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TABLE 1. Pyrazino[2,3-b][1,4]thiazines (IV and V), 3-Hydroxy-3,4-dihydroquinoxalino[2,3-b][1,4]thiazines (VI-IX), and Quinoxalino[2,3-b]thiazines (X-XIII)

Compound	mp, °C*	Found, %				Empirical formula	Calc., %				IR spectrum, $\nu$ , cm <sup>-1</sup>	UV spectrum			PMR spectrum $\delta$ , ppm †	Yield, %
		C	H	N	S		C	H	N	S		$\lambda_{max}$ , nm	lg $\epsilon$			
IV	146—147	54,2	5,6	15,8	11,8	C <sub>12</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> S	54,3	5,7	15,8	12,1	1675 3340	218 270	4,55 3,93	—	89,3	
V	91—92	54,5	5,7	15,9	12,2	C <sub>12</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> S	54,3	5,7	15,8	12,1	1660 3280	310 262	3,81 4,13	5,02	90,0	
VI	124—125	54,7	4,8	—	10,4	C <sub>14</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub> S	55,1	5,0	—	10,5	1725 3270	354 218	4,34 4,54	—	58,0	
VII	146—147	57,7	5,6	12,4	9,5	C <sub>16</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub> S	57,6	5,7	12,6	9,6	1730 3380	262 222	4,29 4,67	4,46	67,7	
VIII	119—120	54,9	4,8	—	10,5	C <sub>14</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub> S	55,1	5,0	—	10,5	1700 1740	378 216	4,16 4,66	—	58,0	
IX	123—124	57,9	5,5	13,0	9,6	C <sub>16</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub> S	57,6	5,7	12,2	9,6	3350 1660 3270	370 218 262	4,13 4,62 4,26	—	67,0	
X	205—206	58,5	4,6	14,6	11,1	C <sub>14</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S	58,5	4,6	14,6	11,2	372 1700 1740	212 215 244	4,12 4,42 4,46	—	59,9	
XI	227—228	61,3	5,7	13,3	9,9	C <sub>16</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S	60,9	5,4	13,3	10,2	3350 1675 3300	432 218 250	4,04 4,46 4,53	—	67,0	
XII	158—159	58,5	4,5	14,5	11,2	C <sub>14</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S	58,5	4,6	14,5	11,2	438 1660 3280	215 215 283	4,10 4,54 4,40	4,94	69,2	
XIII	183—184	61,0	5,5	—	10,0	C <sub>16</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S	60,9	5,4	—	10,2	330 390 1660 3280	215 283 310 390	4,37 4,28 4,58 4,42	5,02	62,1	

\*Compounds V-XIII were recrystallized from ethanol, and IV was recrystallized from ethanol-water (1:1); IV-XIII were obtained as yellow crystals.

†The PMR spectra of VI, VIII, and IX were not recorded.

Compounds VI-IX are readily dehydrated to quinoxalinothiazines X-XIII in 60-70% yields under the influence of an alcohol solution of hydrogen chloride.

The data from the IR and PMR spectra of X-XIII provide evidence for their 4H structure: their IR spectra contain an absorption band at 3280-3350 cm<sup>-1</sup> (NH), the PMR spectra of X and XI do not contain a signal of protons attached to C(2), and the PMR spectra of XII and XIII contain 2-H signals at 4.94 and 5.02 ppm, respectively. In the IR spectra of crystalline XII and XIII the vibrations of the CO and NH groups are lowered (1660 and 3280 cm<sup>-1</sup>) due to the formation of intermolecular hydrogen bonds, since the absorption bands are shifted to 1700 and 3400 cm<sup>-1</sup> in the spectra of CCl<sub>4</sub> solutions of the compounds. Three absorption maxima at 216-222, 262, and 370-378 nm are observed in the UV spectra of VI-IX, whereas in the case of dehydrated derivatives X and XI the third maximum is shifted bathochromically by 60 nm. The appearance of a fourth absorption maximum at 390 nm is observed in the spectra of XII and XIII.

#### EXPERIMENTAL

The IR spectra were recorded with Perkin-Elmer and UR-10 spectrometers. The UV spectra of alcohol solutions of the compounds were recorded with an EPS-3 spectrophotometer. The PMR spectra of CDCl<sub>3</sub> and d<sub>6</sub>-pyridine solutions of the compounds were recorded with a JNM-4-100 spectrometer with tetramethylsilane as the internal standard.

The starting halo carboxylic acid esters were obtained by the methods in [4, 5], 2-mercapto-3-amino-5,6-dimethylpyrazine was obtained by the method in [6], and the 2-mercapto-3-aminoquinoxalines were obtained by the methods in [7-9].

General Method for the Synthesis of IV-IX (Table 1). An alcohol solution of 5.6 mmole of  $\alpha$ - or  $\gamma$ -chloroacetoacetic ester was added at 18-20° to a solution of 5.65 mmole of the appropriate mercaptan I-III in 50 ml of ethanol containing 5.65 mmole of KOH, and the mixture was stirred for 3-4 h, after which the solvent was removed by distillation, and the residue was triturated with water. The solid material was removed by filtration, washed with water, dried, and recrystallized.

General Method for the Synthesis of X-XIII (Table 1). The reaction mixture from the preparation of VI-IX (or the corresponding hydroxyamino compounds VI-IX) was treated with an alcohol solution of hydrogen chloride, and the mixture was allowed to stand for 15 h. The resulting precipitate was removed by filtration, washed with water, dried, and recrystallized.

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#### CALCULATION OF THE ELECTRON STRUCTURES AND ELECTRONIC SPECTRA OF

#### 3-CHLORO- AND 3-AMINO-1,2,4-TRIAZOLE DERIVATIVES

M. G. Voronkov, V. A. Lopyrev, N. N. Chipanina,  
V. V. Makarskii, O. A. Zasyadko, L. V. Sherstyannikova,  
E. F. Shibanova, T. N. Vereshchagina, and Yu. L. Frolov

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3-Chloro- and 3-amino-1,2,4-triazole derivatives were subjected to a theoretical study by means of quantum-chemical calculation by the Pariser-Parr-Pople method. The experimentally observed electron transitions were assigned. The Cl atom and the NH<sub>2</sub> group in the 3 position of 1,2,4-triazole subject the electron system of the heteroring to substantial perturbation.

The 1,2,4-triazole molecule has previously been studied with the application of an improved MO LCAO method [1]. In addition, the  $\pi$ -electron densities, bond orders, and  $\pi$ -electron interaction energies of 1,2,4-triazole and its 3-Cl, 3-Br, 3-amino-, and 3,5-dichloro derivatives and 3-amino-1,2,4-triazole have been calculated within the Hückel approximation [2].

We have calculated several 3-chloro- and 3-amino-1,2,4-triazole derivatives within the Pariser-Parr-Pople (PPP)  $\pi$ -electron approximation. The calculated energies of the electron transitions were compared with the experimentally found values [3] (Table 1). The peculiar-

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Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 5, pp. 698-700, May, 1977. Original article submitted April 13, 1976; revision submitted July 13, 1976.

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