Hydrobromination of 2-Vinylindazole. A stream of HBr was passed into a solution of 0.14 g (1 mmole) of II in 20 ml of absolute diethyl ether at −5°C, and the voluminous white precipitate was removed by filtration, washed with ether, and dried in vacuo to give 0.18 g (82%) of 2-vinylindazole hydrobromide (Xb) with mp 130-131°C. Found: C 47.6; H 3.9; Br 35.1%. $C_9H_8N_2 \cdot HBr$. Calculated: C 47.9; H 4.0; Br 35.5%.

2-Vinylindazole Hydrochloride (Xa). This compound, with mp 98-100°C, was obtained by a similar method. Found: C 60.1; H 5.0; Cl 19.4%. $C_9H_8N_2 \cdot HCl$. Calculated: C 59.8; H 5.0; Cl 19.6%.

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SYNTHESIS AND PROPERTIES OF ANALOGS OF 5(4)-AMINOIMIDAZOLE-4(5)-CARBOXAMIDE AND PURINES.

11.* INVESTIGATION OF THE STRUCTURE AND REACTIVITY OF IMIDAZOLETHIOAMIDES

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UDC 547.782.9'784.2:541.623(542.953(543.422

The IR, UV, and PMR spectra of 5(4)-mercaptoimidazole-4(5)-carboxamide, 5(4)-hydroxyimidazole-4(5)-thiocarboxyamide, 5(4)-mercaptoimidazole-4(5)-thiocarboxamide, and the corresponding methyl derivatives were studied. It is shown that the mercaptoimidazoles obtained exist in the form of zwitterions in solution. The methylation of the mercapto- and hydroxyimidazoles with various methylating agents in solvents was investigated, and the reaction of the thioamides with hydrazine was carried out.

To investigate the properties of the $[S{=}\overset{\displaystyle NH_2}{\overset{|}{C}}{-}C{=}C{-}X]^-$ ambident system we studied the structure and reactivity of 5(4)-hydroxy-, mercapto-, and chloroimidazole-4(5)-thiocarboxamides in reactions with nucleophilic and electrophilic reagents.

The IR spectra of 5(4)-hydroxyimidazole-4(5)-thiocarboxamide (I), 5(4)-mercaptoimidazole-4(5)-carboxamide (II), and 5(4)-mercaptoimidazole-4(5)-thiocarboxamide (III) do not contain stretching vibrations of OH and SH groups. The UV spectra of these compounds also differ

*See [1] for Communication 10.

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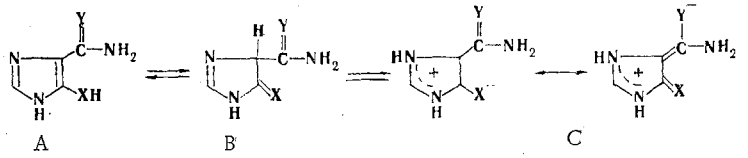
from the spectra of the methyl derivatives that we obtained – 5(4)-methoxyimidazole-4(5)-thiocarboxamide (IV), 5(4)-methylmercaptoimidazole-4(5)-carboxamide (V), and 5(4)-methylmercaptoimidazole-4(5)-thiocarboxamide (VI). These facts completely repudiate structure A for imidazoles I-III. It might be assumed that these compounds exist either in the form of isomer B or, as in the case of bredinine [2], in the form of zwitter ion C. The PMR spectra of I-III in d_6-DMSO do not contain signals of protons at 3-6 ppm, which completely excludes the presence of isomer B in solution. The signal of the proton in the 2 position of the imidazole ring in thioamides I-III is found at 8.3-8.6 ppm and is not shifted to weak field when CF_3COOH is added to solutions of I-III in d_6-DMSO; this constitutes evidence that these compounds exist in the form of zwitterions C.

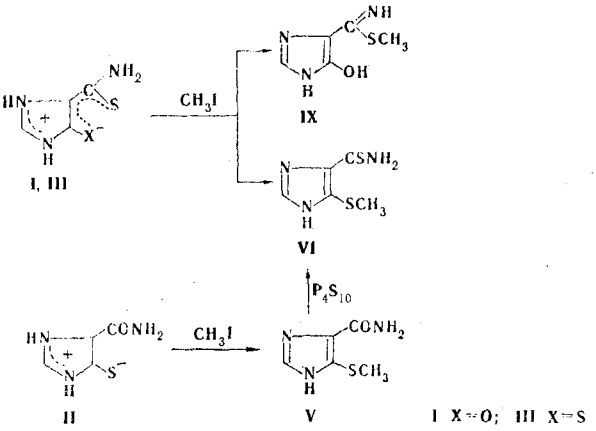


A B C

To confirm this, the PMR spectra of thioamides I-III were compared with the spectra of S-methyl-5(4)-hydroxyimidazole-4(5)-thiocarbimidate (VII) and imidazoles V, VI, and VIII (see Table 1). It is apparent from Table 1 that the signals of the C_2H protons of thioamides I-III and the similarly constructed V-VII differ in d_6-DMSO solutions and coincide in CF_3COOH solutions. The chemical shifts of the C_2H protons of the zwitterionic IX [3] and thiocarboxamide I are close. The pyridine nitrogen atom is consequently protonated in solutions of thioamides I-III in d_6-DMSO.

Thus it follows from the data from the IR, UV, and PMR spectra of I-IX that I-III exist in the zwitterionic tautomeric form.

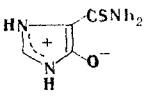
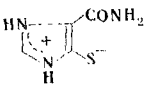
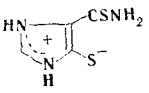
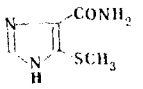
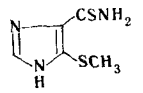
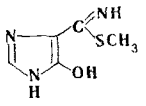
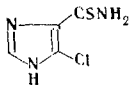
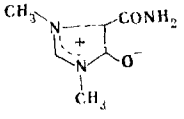
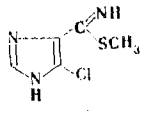
It might have been assumed that the difference in the structures of I-III and VI and VIII will determine their different behavior in reactions with nucleophilic and electrophilic reagents. In a study of the reactivities of these compounds we observed that methylation of I with methyl iodide in methanol in the absence of agents that tie up acid is complete in 1 h at room temperature. An individual compound, viz., S-methyl-5(4)-hydroxyimidazole-4(5)-thiocarbimidate (VII), is formed in high yield as a result of the reaction, just as in the case of methylation of its sodium salt [4]. In the methylation of III one might have expected the formation of two isomers. However, the same individual product, the PMR spectrum of which



I X=O; III X=S

contains a signal of protons of the CH_3 group at 2.5 ppm, is formed in high yield as a result of the reaction of thioamide III or its sodium salt with methyl iodide. The structure of the product cannot be established on the basis of the PMR spectrum because a methylthio group is formed in the methylation of both the thioamide group and the mercapto group. To prove the structure of the product of methylation of III we therefore carried out the synthesis of methylmercaptoimidazolethioamide IV with a known structure from II. The methylation of derivative II with methyl iodide in methanol gives methylmercaptoimidazole V, the structure of which was confirmed by PMR spectroscopy (Table 1). Thionation of product V with P_4S_{10} in dioxane solution gave 5(4)-methylmercaptoimidazole-4(5)-thiocarboxamide (VI) in 40% yield, which, according to the results of elementary analysis, thin-layer chromatography (TLC), and UV and PMR spectroscopy, is identical to the product of methylation of III. Thus methylation of II and III with methyl iodide takes place only at the ionized mercapto group. It is known

TABLE 1. PMR Spectroscopic Data for I-III and V-X

Compound	Formula	Chemical shift, ppm*			
		C_2H		CH_3	
		a	b	a	b
I		8,30	8,30	—	
II		8,60	8,60	—	
III		8,65	8,65	—	
V		7,80	8,60	2,50	2,60
VI		7,80	8,65	2,50	2,60
VII		7,30	8,30	2,50	2,60
VIII		7,8	—	—	
IX†		8,13	—	3,80	
X		7,8	8,45	2,40	2,50

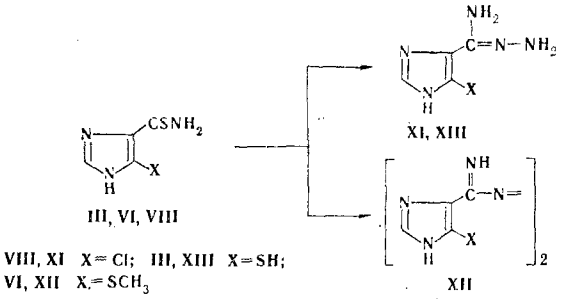
*In d_6-DMSO (a) or CF_3COC[illegible] (b).
†According to the data in [3].

from the theory of hard and soft acids and bases that the relative reactivities of the atoms of an ambident anion depend on the "hardness" of the agent, the polarity of the solvent, the temperature, etc. [5]. The yields of products of reaction at the oxygen and nitrogen atoms increase in the alkylation of thioamides of the heterocyclic series [6] with hard agents. For the study of the methylation of I-III we therefore carried out the reaction with "harder" methylating agents such as dimethyl sulfate and methyl tosylate and used solvents with different polarities (methanol, acetone, DMF, and water) at 20-80°C. However, we did not observe the formation of isomeric products with attack of the methylating agent at other "harder' atoms (O, N), and individual compounds with the same structure as the products of the reaction

of I-III with methyl iodide were isolated in high yields in all of the experiments. Since a mixture of several products is usually formed in the methylation of ambident ions, including ambident ions of the imidazole series [7], it may be concluded that the zwitterionic structure determines selective methylation of thiocarboxamides I-III.

In contrast to zwitterions I-III, the methylation of thioamides IV and VI is difficult. Thus we were able to accomplish the reaction of chloroimidazolethioamide VI with methyl iodide only at 60°C in aqueous acetone containing a molar amount of alkali. We isolated S-methyl-5(4)-chloroimidazole-4(5)-thiocarbimidate (X) in low yield and confirmed its structure by PMR spectroscopy (Table 1). Small amounts of another three to four compounds were detected along with product X in the filtrate by means of TLC. We were unable to carry out the methylation of IV under any of the investigated conditions. Thus zwitterionic thioamides have high reactivities in methylation.

The differences in the structures of I and III and VI and VIII also have a substantial effect on the reaction with hydrazine hydrate. As expected, VI and VIII undergo this reaction very readily. Thus 5(4)-chloroimidazole-4(5)-carbamidrazone (XI) is formed when derivative VIII is heated in alcohol with a 3-mole excess of hydrazine hydrate for 1 h. The reaction of thioamide VI with hydrazine hydrate is complete after 30 min, and azo-1,3-[dicarbimine-5-methylmercaptoimidazol-4-yl] (XII) is formed. At the same time, the starting compound was isolated in unchanged form when 5(4)-hydroxyimidazole-4(5)-thiocarboximide (I) was refluxed



in alcohol with hydrazine, and the use of high-boiling solvents leads to resinification of the reaction mass with the formation of a mixture of products, which we were unable to separate into components by known methods. In contrast to VI and VIII, the reaction of III with hydrazine hydrate by refluxing in alcohol is complete only after 36 h and gives 5(4)-mercaptoimidazole-4(5)-carbamidrazone (XIII) in 36% yield.

Thus imidazolethiocarboxamides that have a zwitterionic structure differ substantially with respect to their reactivities in reactions with nucleophilic and electrophilic reagents from nonzwitterionic imidazolethiocarboxamides.

EXPERIMENTAL

The UV spectra of solutions of the compounds obtained in water or 0.1 N HCl were recorded with a Beckman 26 spectrophotometer. The PMR spectra of the compounds were obtained with a Perkin–Elmer-12B spectrometer (60 MHz) with tetramethylsilane as the internal standard. Thin-layer chromatography (TLC) on Silufol UV-254 plates in the following three systems of solvents was used to confirm the individuality of the compounds: 1) n-butanol–acetic acid–water (4:1:1); 2) n-propanol–0.2 N ammonia hydroxide (3:1); 3) chloroform–n-propanol (7:3).

Methylation of Zwitterionic Imidazoles I-III. A 10-mmole sample of the base was added to a solution of 10 mmole of the imadazole derivative in 70 ml of the solvent, and 11-15 mmole of the methylating agent was added with stirring at a predesignated temperature (see Table 2). The reaction mixture was then maintained at this temperature for 0.5-1.5 h, after which the solvent was evaporated at reduced pressure, and the residue was crystallized from water.

S-Methyl-5(4)-hydroxyimidazole-4(5)-thiocarbimidate (VII). This compound had mp 208-209°C and R_f 0.61 (1) and 0.25 (2). UV spectrum (in 0.1 N HCl), λ_{max} (log ε): 215 (3.97) and 327 nm (4.27). Found: C 38.4; H 4.3; N 27.0; S 20.2%. $C_5H_7N_3OS$. Calculated: C 38.2; H 4.5; N 20.4; S 26.7%.

5(4)-Methylmercaptoimidazole-4(5)-carboxamide (V). This compound had mp 193-196°C. UV spectrum (in 0.1 N HCl), λ_{max} (log ε): 210 (4.01) and 265 nm (3.53). Found: C 38.0; H 4.5; N 20.2; S 26.6%. $C_5H_7N_3OS$. Calculated: C 38.2; H 4.5; N 20.4; S 26.7%.

TABLE 2. Results of Methylation of Thioamides I-III

Starting compound	Methylating agent	Solvent	Base	T, °C	Compound obtained	Yield, %
I	CH_3I	CH_3OH	—	20	VII	88
I	CH_3I	CH_3OH	$NaOCH_3$	20	VII	85
I	CH_3I	Acetone	NaOH	20	VII	92
I	$(CH_3)_2SO_4$	Acetone	NaOH	20	VII	87
I	Methyl tosylate	CH_3OH	$NaOCH_3$	20	VII	89
I	The same	Acetone	KOH	20	VII	90
I	„ „	Acetone	$(C_2H_5)_3N$	20	VII	89
I	„ „	DMF	$(C_2H_5)_3N$	20	VII	79
I	„ „	DMF	$(C_2H_5)_3N$	40	VII	80
I	„ „	DMF	$(C_2H_5)_3N$	60	VII	81
I	„ „	DMF	$(C_2H_5)_3N$	80	VII	78
II	CH_3I	CH_3OH	$(C_2H_5)_3N$	20	V	92
II	CH_3I	CH_3OH	$NaOCH_3$	20	V	90
II	CH_3I	Acetone/water	NaOH	20	V	91
II	$(CH_3)_2SO_4$	The same	NaOH	20	V	89
II	$(CH_3)_2SO_4$	„ „	NaOH	60	V	88
II	Methyl tosylate	CH_3OH	$NaOCH_3$	20	V	90
II	The same	DMF	$(C_2H_5)_3N$	20	V	86
II	„ „	DMF	$(C_2H_5)_3N$	60	V	87
III	CH_3I	CH_3OH	$(C_2H_5)_3N$	20	VI	88
III	CH_3I	CH_3OH	$NaOCH_3$	20	VI	87
III	CH_3I	Acetone/water	KOH	20	VI	87
III	$(CH_3)_2SO_4$	CH_3OH	KOH	20	VI	85

5(4)-Methylmercaptoimidazole-4(5)-thiocarboxamide (VI). This compound had mp 188-192°C and R_f 0.29 (1) and 0.68 (2). UV spectrum (in 0.1 N HCl), λ_{max} (log ε): 249 (3.69) and 305 nm (3.97). Found: C 34.7; H 4.0; N 24.8; S 36.7. $C_5H_7N_3S_2$. Calculated: C 34.6; H 4.1; N 24.8; S 37.0%.

S-Methyl-5(4)-chloroimidazole-4(5)-thiocarbimidate (X). A 0.22-g (4 mmole) sample of KOH was added to a solution of 0.64 g (4 mmole) of chloroimidazolethioamide VI in 20 ml of acetone–water (3:1), and 0.27 ml (4.3 mmole) of methyl iodide was added. The solution was heated to 60°C and stirred for 4 h. The precipitate was removed by filtration to give 0.23 g (33%) of a product with mp 200-203°C (from absolute alcohol) and R_f 0.67 (1) and 0.17 (2). UV spectrum (in water), λ_{max} (log ε): 260 (3.8) and 305 nm (3.95). Found: C 34.4; H 3.1; N 24.1; S 18.2%. $C_5H_6ClN_3S$. Calculated: C 34.2; H 3.4; N 23.9; S 18.3%.

Thionation of 5(4)-Methylmercaptoimidazole-4(5)-carboxamide (V). A 1.22 g (5 mmole) sample of P_4S_{10} was added to 1.57 g (10 mmole) of V in 40 ml of absolute dioxane, and the reaction mixture was refluxed with stirring for 4 h. The dioxane was evaporated in vacuo, and the resinous mass was dissolved by refluxing in 50 ml of 1 N HCl. The solution was refluxed with charcoal, after which it was filtered and evaporated in vacuo to a volume of 5 ml. The precipitate was removed by filtration and crystallized from water to give 0.69 g (40%) of a product that was identical with respect to its melting point, R_f values, and UV and PMR spectra of IV obtained by methylation of III.

5(4)-Mercaptoimidazole-4(5)-carbamidrazone (XIII). An 8.1-ml (50 mmole) sample of a 20% aqueous solution of hydrazine hydrate was added to a solution of 1.54 g (10 mmole) of III in 250 ml of alcohol, and the mixture was refluxed for 36 h. The solvent was evaporated in vacuo to give 1.13 g (75%) of a compound with mp 205-209°C and R_f 0.41 (1), 0.49 (2), and 0.55 (3). UV spectrum (in 0.1 N HCl), λ_{max} (log ε): 216 (4.29) and 312 nm (4.1). Found: C 30.3; H 4.2; N 45.4; S 20.8%. $C_4H_7N_5S$. Calculated: C 30.3; H 4.5; N 44.7; S 21.1%.

5(4)-Chloroimidazole-4(5)-carbamidrazone (XI). Alcohol (100 ml) and 6.2 ml (40 mmole) of hydrazine hydrate were added to a solution of 1.61 g (10 mmole) of chloroimidazolethioamide VI, and the mixture was refluxed for 1 h. The alcohol was then evaporated in vacuo to give 0.8 g (50%) of a product with mp 220-222°C and R_f 0.45 (1) and 0.64 (2). UV spectrum (water), λ_{max} (log ε): 212 (3.65) and 260 nm (3.72). Found: C 26.7; H 4.5; Cl 19.9; N 39.5%. $C_4H_6ClN_5 \cdot H_2O$. Calculated: C 27.0; H 4.5; Cl 20.0; N 39.4%.

Azo-1,2[dicarbimine-4-methylmercaptoimidazol-4-yl] (XII). This compound was obtained from methylmercaptoimidazolethioamide IV under conditions similar to those in the synthesis of XI. A product with mp 300°C (dec.) was obtained in 49% yield. The product has limited solubility only in DMSO and trifluoroacetic acid. Found: C 39.0; H 3.7; N 35.9; S 20.7%. $C_{10}H_{12}N_8S_2$. Calculated: C 38.7; H 3.9; N 35.6; S 20.8%.

5(4)-Methoxyimidazole-4(5)-thiocarbamide (IV). A 0.15-g (1.06 mmole) sample of methoxyimidazolecarboxamide VIII was suspended in 30 ml of absolute dioxane, 0.22 g (0.5 mmole) of P_4S_{10} was added, and the reaction mixture was refluxed with stirring for 5 h. It was then evaporated in vacuo to dryness, and the residue was refluxed in 80 ml of 0.1 N HCl with activated charcoal. The mixture was filtered, and the filtrate was evaporated in vacuo to dryness. The residue was dissolved in 2 ml of water, and the solution was neutralized with 10% sodium carbonate solution. The precipitate was removed by filtration to give 0.03 g (18%) of a product with mp 246-248°C and R_f 0.6 (1), 0.46 (2), and 0.17 (3). UV spectrum (water), λ_{max} (log ε): 272 (4.39) and 339 (3.76). Found: N 26.4; S 20.4%. $C_3H_7N_3OS$. Calculated: N 26.7; S 20.7%.

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REACTIONS OF IMIDAZOLETHIONES WITH PHENYLCYANOACETYLENE

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UDC 547.783.9'785.5'869.07:543.422

The reaction of phenylcyanoacetylene with imidazolethiones was studied. It is shown that in the presence of 5-10% KOH the addition of phenylcyanoacetylene is accompanied by intramolecular cyclization with the formation of imidazo-1,3-thiazines. An increase in the amount of catalyst to 20% leads to cleavage of the thiazine ring at the C—S bond and the formation of the corresponding acrylonitrile derivatives. Products of addition of 2 moles of phenylcyanoacetylene were obtained.

The existence of imidazolethiones in two tautomeric forms is responsible for their ability, depending on the conditions, to add acetylene to the sulfur or nitrogen atom. We have previously shown that azolyl vinyl sulfides are primarily formed in the reaction with acetylene as a consequence of the great nucleophilicity of sulfur [1, 2]. The reaction with acetylenic acid esters takes place at the same center [3, 4]. Information that activated acetylenes react at the nitrogen atom of the thioamide grouping was recently published [5].

In the present research we studied the reaction of 1-phenyl-2-cyanoacetylene (I) with benzimidazole-2-thione (II) and 4,5-diphenylimidazole-2-thione (III).

The addition of activated acetylene I to azolethiones II and III proceeds readily in the presence of 5-10% potassium hydroxide and is accompanied by intramolecular cyclization at the nitrile group. The investigated reaction proceeds with high regio- and stereospecificity, and, according to the PMR spectral data, the reaction mixture contains only one isomer. 2-Imino-

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