THE SALT-FORMING CAPACITY OF CYCLIC THIONAMIDES AND THEIR DERIVATIVES

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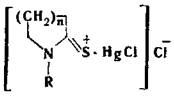
Cyclic thionamides and their S-substituted and N-substituted derivatives containing unsaturated groupings readily give complex salts when they are treated with mercuric chloride at room temperature. The formation of picrates is also characteristic for the S-substituted thionamide derivatives. It has been shown that the cyclic thionamides and their N-vinyl and N-allyl derivatives form methiodides almost quantitatively. S-Vinylthionamides and S-allylthionamides take part in this reaction with difficulty. N-Allylthionamides also readily form hydrochlorides when they are treated with gaseous hydrogen chloride, which shows the lower nucleophilicity of the double bond.

Cyclic thionamides and their derivatives contain sulfur and nitrogen atoms possessing electron-donating properties, in consequence of which it might be expected that these compounds would be capable of forming onium salts. We have studied their reactions with mercury salts, picric acid, and alkyl halides. It is known [1] that when an alcoholic solution of mercuric chloride acts on vinyl sulfide, mercaptomercury chloride is formed and hydrogen chloride is liberated quantitatively, this reaction being used for analytical purposes. S-Vinylthiobenzothiazole is an exception, forming a stable complex with $HgCl_2$. This property has been explained [2] by the conjugation of the sulfur atom with the thiazole system.

In studying the reaction of mercuric chloride with cyclic thionamides and their derivatives, we have also observed the formation of stable complex compounds in the reaction in ethanolic solution at room temperature. When the resulting mercury compounds are heated in dioxane, they decompose into the initial compounds and mercuric chloride. The following structure is most probable for the salts mentioned, by analogy with the previous work [2].



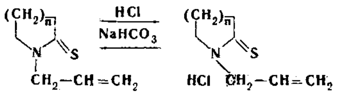
$n = 1, 2, 3$

$R = -H; -CH{=}CH_2$

$-CH_2-CH{=}CH_2$

The formation of picrates is a characteristic reaction for S-substituted thionamides. S-Vinylthionamides, and S-substituted derivatives with saturated radicals readily form picrates by the action of picric acid at room temperature. In contrast to them, N-vinyl- and N-allylthionamides do not form picrates even on heating.

The difference in the behavior of the N- and S-substituted thionamides can be explained by the different degrees of basicity of the nitrogen atoms in these compounds. In the N-allylthionamides, where the double bond is remote from the nitrogen to which the methylene group is attached, the interaction of the multiple bond with the nitrogen is disturbed, as is confirmed by spectroscopic data. Consequently, the main force determining the polarization of the molecule is the I-effect of the nitrogen atom, enhanced by conjugation with the thionamide sulfur. The absence of any interaction of the nitrogen with the multiple bond leads to a strengthening of its basic properties and a decrease in the nucleophilicity of the double bond, which is shown, in particular, in reactions with gaseous hydrogen chloride. When gaseous hydrogen chloride is passed through an ethereal solution of a N-allylthionamide, crystalline hydrochlorides, hygroscopic but stable compounds, precipitate. The structure of the hydrochlorides obtained has been shown by acidometric titration and the isolation of the initial N-allylthionamides after their treatment with sodium bicarbonate. The presence of a double bond in the hydrochlorides has been established by spectral analysis.



We have found that cyclic thionamides and their derivatives readily and almost quantitatively form onium salts with alkyl halides. When treated with alkyl halides in ethereal solution at room temperature, N-allylthionamides give onium salts considerably more readily and faster than N-vinylthionamides.

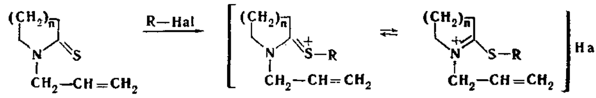


Table 1

Complexes of Thionamides with Mercuric Chloride

Initial thionamide	Mp, °C (decomp)	Empirical formula	S, %		Yield, %
			found	calculated	
Thiopiperidone	170—180	$C_5H_9NS \cdot HgCl_2$	8.44; 8.39	8.27	93
Thiocaprolactam	167—175	$C_6H_{11}NS \cdot HgCl_2$	8.37; 8.44	8.01	90
N-Vinylthiopyrrolidone	85—100	$C_6H_9NS \cdot HgCl_2$	8.15; 8.18	8.03	90
N-Vinylthiocaprolactam	—	$C_8H_{13}NS \cdot HgCl_2$	7.59; 7.20	7.50	90
N-Allylthiopyrrolidone	—	$C_7H_{11}NS \cdot HgCl_2$	7.83; 7.42	7.77	82

Table 2

Picrates of the Thionamides

Picrates	Mp, °C	Empirical formula	Found, %		Calculated, %	
			N	S	N	S
S-Vinylthiocaprolactam	106—107	$C_8H_{13}NS \cdot C_6H_2(OH)_3NO_2$	14.17, 14.37	8.19, 8.43	14.56	8.64
N-Allylthiopyrrolidone	111.5—112.5	$C_7H_{11}NS \cdot C_6H_2(OH)_3NO_2$	15.33, 15.37	8.34, 8.42	15.01	8.57
S-Propylthiopyrrolidone	96—97	$C_7H_{13}NS \cdot C_6H_2(OH)_3NO_2$	15.08, 14.98	8.27, 8.24	14.94	8.53

Table 3

Thionamide Methiodides

Methiodides	Mp, °C	Empirical formula	I, %		Yield, %
			found	calculated	
S-Vinylthiocaprolactam	—	$C_9H_{16}INS$	42.23. 42.06	42.70	60
N-Allylthiopyrrolidone	80.5—82	$C_8H_{14}INS$	44.46, 44.41	44.85	98
S-Propylthiopyrrolidone	64 —67	$C_8H_{16}INS$	44.15, 44.03	44.53	70

S-Vinylthionamides take part in this reaction with difficulty. Under similar conditions, S-allylthionamides form oily, rapidly resinifying, products. S-Derivatives of the thionamides with saturated radicals readily give crystalline onium salts.

The IR spectra of the onium salts differ considerably from the IR spectra of the basic molecules. The spectra lack the strong band in the 1500–1470 cm^{-1} region that is characteristic for the $>N-\underset{|}{C}=S$ group. In place of this band, there is a strong band at 1602 cm^{-1}. These results indicate the far-reaching change in the molecule of a thionamide when it forms a salt.

The presence of two maxima are characteristic for the UV spectra of the onium salts (in ethanolic solution), the intensity of the short-wave maximum being greater than that of the long-wave maximum.

Investigations carried out in chemical, pharmaceutical, and disinfection scientific research institutes have shown that some of the onium salts possess a fungistatic activity with respect to pathogenic fungi and a bactericidal activity against staphylococci and the colibacillus.

EXPERIMENTAL

Reaction of thiopyrrolidone with mercuric chloride. An alcoholic solution of 5.4 g of mercuric chloride was added to a solution of 2 g of thiopyrrolidone in 15 ml of ethanol. Immediately a white precipitate deposited, 6.82 g of the mercury complex. Yield 6.82 g (92%), mp 155-158° C. Found, %: S 8.35, 8.46. Calculated for $C_4H_7NS \cdot HgCl_2$, %: S 8.64.

The complexes given in Table 1 were prepared similarly.

S-Vinylthiopiperidone picrate. A solution of 2.3 g of picric acid in 10 ml of ethanol was added to a solution of 1.56 g (0.01 mole) of S-vinylthiopiperidone in 2 ml of absolute ethanol. After some time, yellow crystals deposited with mp 139.5-133.5° C (from absolute ethanol). Found, %: N 15.30, 15.50. Calculated for $C_{13}H_{14}N_4O_7S$, %: N 15.10.

The results of the other experiments are given in Table 2. N-Vinyl- and N-allylthionamides did not form picrates under the conditions described or on heating.

Reaction of N-allylthiopyrrolidone with hydrogen chloride. Dry gaseous hydrogen chloride was passed into a solution of 7.1 g of N-allylthiopyrrolidone in 25 ml of dry ether. The hydrogen chloride was not absorbed at a temperature of from −5° C; absorption began at 10° C and was accompanied by a rise in the temperature to 18-20° C and the formation of two layers.

The lower layer crystallized. The crystals were separated off and washed with absolute ether. The yield of monohydrochloride was 6.01g (68.1%). Found, %: HCl 20.48, 21.00% (acidimetrically in the presence of phenolphthalein). Calculated for $C_7H_{11}NS \cdot HCl$, %: HCl 20.50%.

N-Allylthiocaprolactam hydrochloride was prepared in a similar manner to the preceding compound. Yield 80%. Found, %: HCl 18.12. Calculated for $C_9H_{14}NS \cdot HCl$, %: HCl 17.9.

The hydrochlorides obtained were readily soluble in water and ethanol and insoluble in diethyl ether, carbon tetrachloride, and chloroform.

Reaction of the hydrochlorides with sodium bicarbonate. A solution of 5 g of N-allylthiopyrrolidone hydrochloride in 20 ml of distilled water was neutralized with sodium bicarbonate to pH 7 and extracted several times with ether. The extracts were dried with sodium sulfate, the ether was driven off, and the residue was distilled to give 2.3 g of N-allylthiopyrrolidone with bp 104-107° C (2 mm), n_D^{20} 1.5720.

N-Vinylthiopyrrolidone methiodide. A mixture of 1.27 g (0.01 mole) of N-vinylthiopyrrolidone and 2.8 g (0.02 mole) of methyl iodide in 10 ml of absolute ether yielded 2.3 g (90%) of a substance with mp 75-79° C (decomp). Found, %: I 47.47, 47.02. Calculated for $C_7H_{12}INS$, %: I 47.29.

The methiodides given in Table 3 were prepared similarly.

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