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RING–CHAIN TAUTOMERISM OF THIOSEMICARBAZONES OF SALICYLALDEHYDE AND PYRIDINECARBALDEHYDE IN ACIDIC MEDIA

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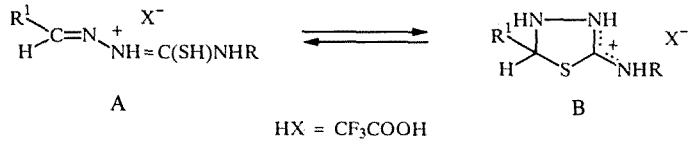
On the basis of NMR spectroscopic data, it has been found that 4-substituted thiosemicarbazones of salicylaldehyde and α-, β-, and γ-pyridinecarbaldehydes in solutions of trifluoroacetic acid are tautomeric mixtures of protonated linear and cyclic 1,3,4-thiadiazolidine-2-imine forms, the linear tautomer having an azinethiol structure with localization of the proton on the $N_{(2)}$ nitrogen atom.

The structure of thiosemicarbazones depends greatly on the degree of substitution on the nitrogen atoms, and even more on the acidity of the medium [1-4]. In particular, most thiosemicarbazones, including all 2,4-disubstituted thiosemicarbazones, are cyclized in CF_3COOH solutions to the corresponding 1,3,4-thiadiazolidine salts, while in the case of thiosemicarbazones of substituted benzaldehydes and acetophenones under the same conditions, ring–chain tautomerism is observed, and for thiosemicarbazones of alkanals, a ring–linear–ring equilibrium with the additional participation of the protonated form of 1,2,4-triazolidinethione-3.

With the aim of further investigation of this phenomenon, we turned to a study of the structure, in an acidic medium, of derivatives containing an OH group that is sensitive to solvent effects, namely the thiosemicarbazone of salicylaldehyde and its 4-substituted analogs (compounds I-III); heterocyclic derivatives — thiosemicarbazones of α-, β-, and γ-pyridinecarbaldehydes (compounds IV-VI); and the strongly conjugated thiosemicarbazone of cinnamaldehyde (VII). We had previously observed [5] a ring–chain equilibrium for the thiosemicarbazone with α-pyridinecarbaldehyde.

In order to differentiate the linear tautomer A and the cyclic tautomer B and to estimate their quantities, we proposed to utilize the difference in position of signals of the azomethine proton of the linear form in comparison with the signal of the 5-H proton of the cyclic tautomer in the PMR spectra, which is positioned upfield from the signal of the linear form. In any case, for the free bases of compounds I-VII, the signal of the azomethine proton is readily observed in the region of resonance of aromatic protons and NH groups (Table 1)



A B

HX = CF_3COOH

I R = H, R^1 = C_6H_4OH-2, II R = C_6H_5, R^1 = C_6H_4OH-2, III R = $CH_2C_6H_5$, R^1 = C_6H_4OH-2, IV R = H, R^1 = α-Py, V R = H, R^1 = β-Py, VI R = H, R^1 = γ-Py, VII R = H, R^1 = -CH=CH—C_6H_5

Moreover, the signal of the 5-H proton of a model of the cyclic form B in this series — the 2-benzyl-4-methylthiosemicarbazone of cinnamaldehyde (VIII) — is positioned outside the aromatic region of the PMR spectrum (Table 1). However, in the PMR spectra of compounds I-VII in trifluoroacetic acid, the signal from the proton of the H–C=N fragment is not always identified reliably. The situation is not clarified by changing to CF_3COOD for removal of the amino group proton signals from the 7-9

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TABLE 1. PMR Spectra of Compounds I-VIII, ppm (and SSCC, Hz)

Compound	DMSO-D_6				CF_3COOD			B·HX form, %
	CH, s	NH, s	NH_2, s	other signals	CH, s A·HX	CH, s B·HX	other signals	
I	8,52	11,50	7,90 8,16	6,90...7,90 (4H, m, H_{arom}), 9,98 (1H, s, OH)	*	6,75	6,65...7,25 (4H, m, H_{arom})	**
II	8,60	11,86	10,04	6,75...8,20 (9H, m, H_{arom}), 10,12 (1H, s, OH)	7,90	6,16	6,40...7,20 (9H, m, H_{arom})	50
III	8,52	11,62	9,09, t (6,0)	4,90 (2H, d, 6,0, CH_2), 6,75...8,20 (9H, m, H_{arom})	7,13	6,20	4,20 (2H, s, CH_2), 6,40...7,20 (9H, m, H_{arom})	60
IV	8,12	11,72	8,17 8,35	7,35...8,55 (4H, m, H_{arom})	*	6,95	8,05...8,90 (5H, m, H_{arom} + CH)	**
V	8,10	11,60	7,30...8,90 (6H, m, H_{arom} + NH_2)		*	6,70	8,25...8,90 (5H, m, H_{arom} + CH)	**
VI	8,05	11,70	8,23 8,44	7,75 and 8,55 (4H, H_{arom})	*	6,75	8,10...9,10 (5H, m, H_{arom} + CH)	**
VII	8,02 d	11,65	7,73	6,90...7,00 (2H, m, 2CH), 7,25...7,60 (5H, m, H_{arom})	*	—	6,08 (1H, dd, 8,5, 17,0, CH), 6,38 (1H, d, 17,0, CH), 6,58...6,90 (6H, m, H_{arom} + CH)	0
VIII	*	—	8,28 q, 4.0	3,18 (3H, d, 4,0, CH_3); 5,76 (2H, s, CH_2); 6,57 (1H, d, 16,0, CH); 6,74 (1H, dd, 7,0; 16,0, CH); 7,00...7,40 (11H, m, H_{arom} + CH)	—	5,40, d (7)	2,76 (3H, s, CH_3), 4,44 (2H, s, CH_2), 5,67 (1H, dd 7,0, 15,0, CH), 6,25 (1H, d, 15,0, CH), 6,75...7,05 (10H, m, H_{arom})	100

*,** No footnotes given in Russian original — Translator.

TABLE 2. ^{13}C NMR Spectra of Compounds I and IV-VI in CF_3COOH, ppm

Compound	A·HX form			B·HX form			B·HX form, %
	HC=N, d	C=N$^+$, s	doublet signal	$C_{(5)}$, d	$C_{(3)}$, s	doublet signal	
I	146,3	169,7	117,8, 122,0, 133,6, 134,6, 158,8	77,2	172,1	116,3, 123,2, 128,4 134,6, 135,5, 154,2	50
IV	145,8	173,6	130,1, 131,5, 141,0, 148,8, 150,5	69,0	175,0	128,6, 129,9, 143,1, 150,0, 153,0	80
V	147,6	169,8	130,1, 132,2, 142,8, 144,5, 147,3	70,3	176,3	129,8, 141,5, 141,7, 143,4, 148,0	75
VI	149,3	173,9	148,6, 153,9, 161,1	73,2	177,3	128,9, 145,4, 164,1	80

ppm region. In such cases, we have made approximate estimates of the tautomeric equilibrium constant by assigning the intensities of the 5-H proton signals to the total intensity of resonance in the 7-9 ppm interval. For a high degree of reliability in the case of compounds I and IV-VI, the estimates were based on ^{13}C NMR spectra (Table 2).

The data of Tables 1 and 2 indicate the presence of ring–chain tautomerism A $\rightleftarrows$ B in the derivatives of salicylaldehyde and pyridinecarbaldehydes I-VI, takes place. Its appearance, the same as in the case of thiosemicarbazones of other aromatic aldehydes [2], can be explained by the overall effect of two factors that greatly stabilize the linear form A. One of them, the polar factor, obviously favors this form in a strongly polar medium. The second factor, conjugation, is especially effective in the thiosemicarbazone of cinnamaldehyde (VII); and for this compound, it results in complete stabilization of the linear structure. Thus, this compound is the second known example of a thiosemicarbazone that does not manifest any tendency toward ring–chain transitions in an acidic medium. The same behavior had been observed previously for the thiosemicarbazone of 2-chloro-6-nitrobenzaldehyde [2], apparently due to steric hindrance to closure of the ring.

On the background of these strong effects, we observe a leveling out of other structural factors, whether a variation of the substituents on the nitrogen atom in position 4 (compounds I-III) or variation of the positions of the nitrogen atom in the pyridine ring (compounds IV-VI).

In conclusion, let us point out that the position of the signal of the carbon atom bound to sulfur in the protonated linear forms A, in comparison with data for model S-alkylisothiosemicarbazonium salts [6], provides us with grounds for concluding that these forms (A) have the azinethiol structure with localization of the proton on the $N_{(2)}$ nitrogen atom. This is in accord with the structure of cations of protonated thioureas [7].

EXPERIMENTAL

PMR spectra were taken on 5-15% solutions in a Tesla BS-497 instrument (100 MHz), internal standard HMDS. ^{13}C NMR spectra, on solutions in CF_3COOH, were recorded in a Bruker WH-90 instrument (22.26 MHz), internal standard D_2O.

Thiosemicarbazones I-VIII were obtained by a common procedure. To a mixture of equimolar quantities (0.01 mole) of the corresponding thiosemicarbazide and carbonyl compound in 30 ml of methanol, 2 drops of trifluoroacetic acid were added and the mixture was allowed to stand for 12 h, after which the precipitate was filtered off and recrystallized from methanol.

Compounds I-VII have been described previously [7-11].

2-Benzyl-4-methylthiosemicarbazone of Cinnamaldehyde (VIII), $C_{18}H_{19}N_3S$, mp 163-164°C.

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