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The Chain-Ring-Ring Tautomerism of Thiosemicarbazones of Alkanals in Acidic Media

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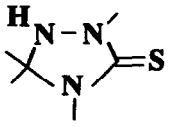
Abstract: Thiosemicarbazones of alkanals and their 4-substituted derivatives generate in trifluoroacetic acid the three-component equilibrium between one linear and two cyclic (1,3,4-thiadiazolidine and 1,2,4-triazoline) forms.

Products of the interaction between derivatives of thiosemicarbazide and oxocompounds can exist both in the linear form **A** and forms of derivatives of 1,2,4-triazolidine-3-thione **B**[1] or 1,3,4-thiadiazolidine-2- imine **C**[2] . The structure of triazolidinethione **B** is typical for the condensation products of 2,4-disubstituted thiosemicarbazides with ketones[3]. In a solution of trifluoroacetic acid cations **B*HX** undergo recyclization into the salts of 1,3,4-thiadiazoline-2-amine **C*HX**, which also result from the protonation of linear thiosemicarbazones **A**[3] . In principle this recyclization implies the possibity of realization of the three-component equilibrium **B*HX** ⟸ **A*HX** ⟸ **C*HX**.



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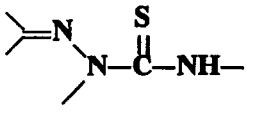

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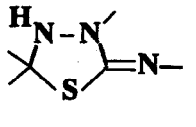

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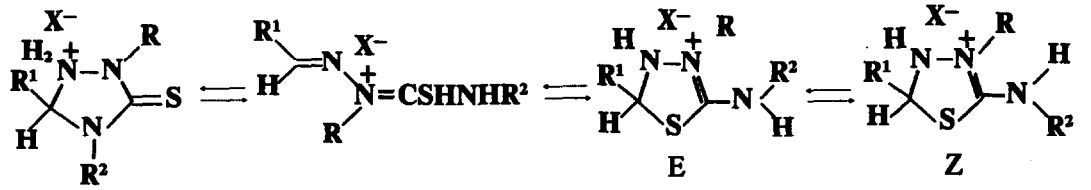

B*HX A*HX E Z C*HX

1 $R^1 = CH_3$, $R^2 = H$; **2** $R^1 = R^2 = CH_3$; **3** $R^1 = CH_3$, $R^2 = CH_2C_6H_5$; **4** $R^1 = CH_3$, $R^2 = C_6H_5$; **5** $R^1 = C_2H_5$, $R^2 = H$; **6** $R^1 = C_2H_5$, $R^2 = CH_2C_6H_5$; **7** $R^1 = CH(CH_3)_2$, $R^2 = H$; **8** $R^1 = C_6H_4OCH_3$-4, $R^2 = H$; **9** $R^1 = R^2 = CH_3$; **1-8** R = H, **9** R = CH_3

It takes a few days for reaching this equilibrium in saturated solutions of aldothiosemicarbazones **1-7** in trifluoroacetic acid.

Table 1. ^{1}H-NMR Data of Thiosemicarbazones 1-9 in Saturated Solutions in CF_3COOH, ppm (δ)

Compound	Form, %	R^1	R^2	CH
1	**A*HX**, 10	2.08 d	—	7.45 q
	B*HX, 10	1.50 d	—	5.85 q
	C*HX, 80	1.30 d	—	5.05 q
2	**A*HX**, 10	2.24 d	2.94 d	7.52 q
	B*HX, 10	1.68 d	2.94 s	5.92 q
	C*HX (Z), 45	1.50 d	2.93 d	5.22 q
	C*HX (E), 35	1.48 d	2.86 d	5.19 q
3	**A*HX**, 10	1.96 d	4.25 d	7.32 q
	B*HX, 10	1.32 d	4.20 s	5.62 q
	C*HX, 80 [a]	1.15 d	4.15 d	4.96 q
4	**A*HX**, 10	2.05 d	7.1-7.7 m	7.50 q
	B*HX, 10	1.46 d	7.1-7.7 m	5.70 q
	C*HX, 80	1.20 d	7.1-7.7 m	5.01 q
5	**A*HX**, 5	0.82 t, 2.4-2.7 m	—	7.38 t
	B*HX, 5	[b]	—	5.80 t
	C*HX, 90	0.65 t, 1.4-1.8 m	—	4.95 t
6	**A*HX**, 10	0.98 t, 2.4-2.7 m	4.32 d 7.0-7.2 m	7.40 t
	B*HX, 10	[b]	[b]	5.80 t
	C*HX (Z), 55	0.72 t, 1.5-1.9 m	4.30 d 7.0-7.2 m	4.95 t
	C*HX (E), 25	0.70 t, 1.5-1.9 m	4.30 d 7.0-7.2 m	4.93 t
7	**A*HX**, 5	0.85 d, 2.7-3.1 m	—	7.20 d
	B*HX, 5	[b]	—	5.75 d
	C*HX, 90	0.60 d, 1.5-1.9 m	—	4.70 d
8	**A*HX**, 45	3.59 s, 6.75 d, 7.85 d	—	7.15 s
	C*HX, 55	3.59 s, 6.72 d, 7.15 d	—	6.73 s
9 [c]	**C*HX**, 100	1.32 d	2.80 d	4.96 q

[a] 60% of Z-form and 20% of E-isomer (from ^{13}C-NMR data). [b] Immersed in the other protons. [c] R — 3.01 s.

A weak field signal of H-C=N at 7.2-7.5 ppm in ^{1}H NMR spectra (table 1), and two signals of sp^2 carbon atoms at 154-160 and 167-170 ppm in ^{13}C NMR spectra (table 2) correspond to the linear tautomer **A*HX**. The comparison of these with the chemical shifts of signals of carbon atoms in the C=N and $C=N^+$ bonds for S-methylethylidenisothiosemicarbazonium iodide[4] (154.7 and 168.5 ppm correspondingly) leads to the conclusion that the linear form resulting from the protonation of compounds **1-7** is azinethiol **A*HX**.

Table 2. ^{13}C-NMR Data of Thiosemicarbazones 1-4, 8 in Saturated Solutions in CF_3COOH, ppm (δ)

Compound	Form	CH, d	C=S (C=N$^+$), s	R^1, q	R^2
1	**A*HX**	155.7	169.5	16.2	—
	B*HX	74.6	181.9	23.6	—
	C*HX	69.9	176.2	17.8	—
2	**A*HX**	154.1	167.3	16.1	34.6 q
	B*HX	73.9	181.9	23.6	30.5 q
	C*HX (Z)	70.3	178.3	17.6	34.6 q
	C*HX (E)	69.5	174.1	17.6	30.9 q
3	**A*HX**	154.5	169.5	16.2	49.5 t, 125.7-136.0
	B*HX	73.6	183.2	23.5	48.8 t, 125.7-136.0
	C*HX (Z)	70.3	177.3	17.6	52.9 t, 125.7-136.0
	C*HX (E)	69.0	172.9	17.6	48.9 t, 125.7-136.0
4	**A*HX**	155.6	170.2	16.8	122.0-137.0
	B*HX	72.9	181.2	23.7	122.0-137.0
	C*HX	69.5	175.3	17.8	122.0-137.0
8[a]	**A*HX**	147.9	168.3	55.4	—
	C*HX	82.0	172.2	55.3	—

[a] $C_{arom.}$: **A*HX** — 115.8 d, 126.0 d, 130.8 s, 166.7 s; **C*HX** — 115.3 d, 120.0 d, 137.5 s, 161.8 s.

The prevailing in the equilibrium is the protonation form **C*HX** of compounds **1-7**, which tends to become the only one with dilution. ^{15}N NMR spectra confirms this for substance **1** where three signals appear at 90.2, 111.8 and 141.2 ppm (NH_3 -scale), in good agreement with reported data for cation of 3,5,5-trimethyl-1,3,4-thiadiazoline-2-methylamine[3a].

First of these signals is triplet (J = 90.4 Hz), induced by the nitrogen atom of the exocyclic aminogroup and the two other signals are singlets, corresponding to N-3 and N-4 nitrogen atoms. The absence of spin-spin interaction with protons is due to an

exchange of protons with a solvent, confirmed by ^{1}H NMR spectra, having only the peaks, corresponding to C-H bonds and a broad singlet of the exocyclic aminogroup at 7.5-8.5 ppm. ^{13}C NMR spectra of these salts **C*HX** have doublets, corresponding to carbon atom C-5 (69.5- 70.5 ppm) and singlets of the C=N$^+$ bond (173-179 ppm)[3c].

The tautomer **C*HX** of compounds **2, 3** and **6** is a mixture of Z,E-isomers, resulting from rotation around the C-2 - N-exo bond, causing the doubling of all signals of this form in ^{1}H and ^{13}C NMR spectra. Coalescence effects take place on heating to 80^0 C. The lower field signal of two, may be ascribed to the Z-form caused by electronic effects of the positively charged nitrogen atom. Percentage of Z-form in creases with enlarging of substituents R^2 (45% for **2**, 60% for **3**, 55% for **6**) therefore the salt **C*HX** of **4** is represented only as Z-isomer.

Peaks of carbon atoms of the C-5 and C=S bond in ^{13}C NMR spectra (72.9-74.6 and 181.2-183.2 ppm respectively) correspond to the minor cyclic form **B*HX**; their chemical shifts are similar to those for cation of 2,4,5,5-tetramethyl-1,2,4-triazolidine-3-thione[3a]. The typical spectra of **2** present on figure 1.

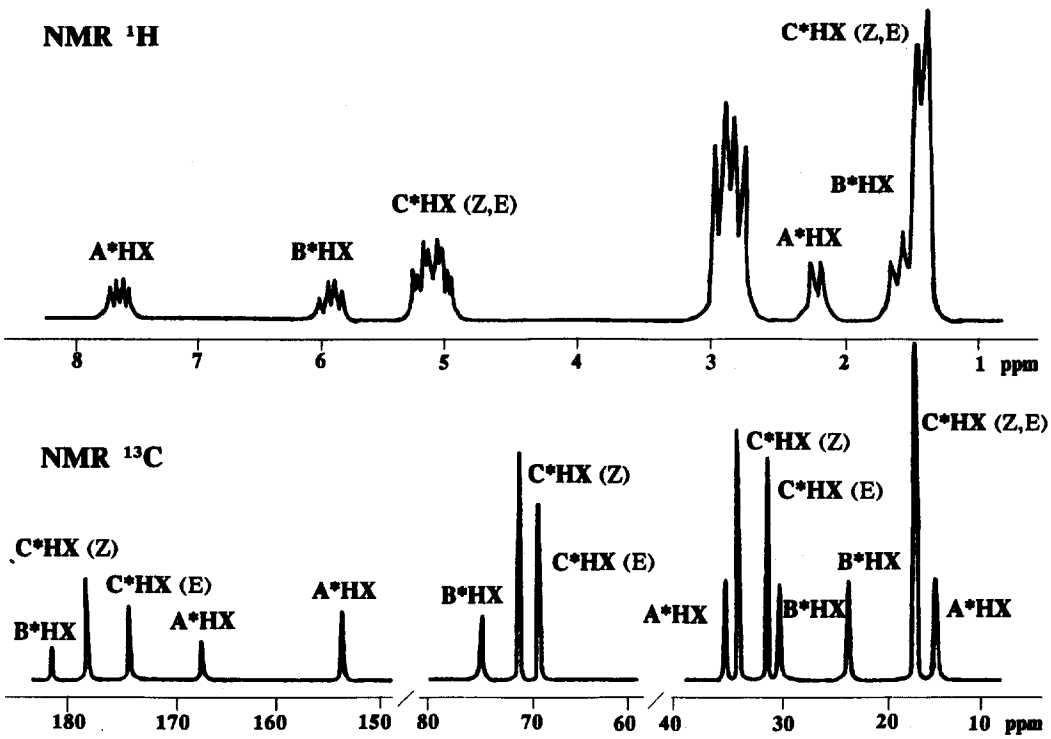

Figure 1. ^{1}H and ^{13}C NMR spectra of **2** in CF_3COOH.

The three-component equilibrium **A*HX** ⇌ **B*HX** ⇌ **C*HX** is limited only to the thiosemicarbazones of alkanals **1-7**. Percentages of the linear tautomer and 1,2,4-triazolidine are similar and amount to about 5-10% (table 1). Replacement of an alkyl subtituent R^1 by aromatic radical leads (**8**) to disappearance of the 1,2,4-triazolidine form, and, either use of thiosemicarbazone of acetone[3a] or introduction of a substituent at the position 2 (**9**) both stabilize the tautomer **C*HX**.

Thus the chemical constitution of thiosemicarbazones depends on structure and medium effects in a complicated way. The canonical linear structure have only the condensation products of thiosemicarbazide and of its 4-substituted analogs with aldehydes and ketones and of aromatic aldehydes with 2,4-disubstituted thiosemicarbazides in solid state and in neutral and basic solvents. The so-called 2,4-disubstituted thiosemicarbazones of ketones have in fact the structure of the corresponding 1,2,4-thiazolidine-3- thiones in a crystalline state as well as in neutral and basic media[3c]. In CF_3COOH solutions thiosemicarbazones of aliphatic ketones just like the above mentioned 1,2,4-thiazolidine-3-thiones change into the salts of 1,3,4- thiadiazolidine-2-imines[3a,3c]. In the same conditions thiosemicarbazones of substituted benzaldehydes and acetophenones involve ring-chain tautomeric mixtures of linear cation and 1,3,4-thiadiazolidine-2-iminic ion[5], whereas in the case of thiosemicarbazones of aliphatic aldehydes **1-7** one more cyclic form, viz. 1,2,4-triazolidine-3-thionium cation, is involved in this equilibrium as we showed.

The discovered property is one more example of the ring-ring or chain- ring-ring tautomerism, the latest examples of which were recently reported[6,7]. These data, in conjunction with the known ones [8] show, that this phenomenon is not to be considered a rare one, though as a rule researchers underestimate it.

Experimental

The ^1H NMR (100 MHz) and ^{13}C NMR (20.41 MHz) spectra were recorded with Tesla-BS-497 spectrometer using HMDS as internal standard. The ^{15}N NMR spectra (30.4 MHz) were recorded with VXR-300 Varian spectrometer, chemical shifts were measured against CH_3NO_2 and converted to the NH_3-scale. The purity of the compounds was checked by tlc using Silufol-UV-254 plates. The elemental analysis data (C, H, N, S) of the new compounds agreed with calculated values to within 0.2%. Melting points were determined in capillaries and are uncorrected.

Aldehyde thiosemicarbazones 1-9.

A mixture of thiosemicarbazide (0.05 mole) and aldehyde (0.06 mole) in 50 ml of methanole was allowed to stand for 24h at O °C, then solvent was removed and the residue was recrystallized from methanole.

1 — 138-139 °C [9a], **2** — 114-116 °C [9b], **3** — 116-117 °C, **4** —145-146 °C [9c]. **5** — 161 °C [9d], **6** — 108-109 °C, **7** — 90-92 °C [9e], **8** — 173-175 °C [9f] **9** — 56-58 °C [9g].

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