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Ring-Chain Tautomerism of N-Substituted Thiosemicarbazones

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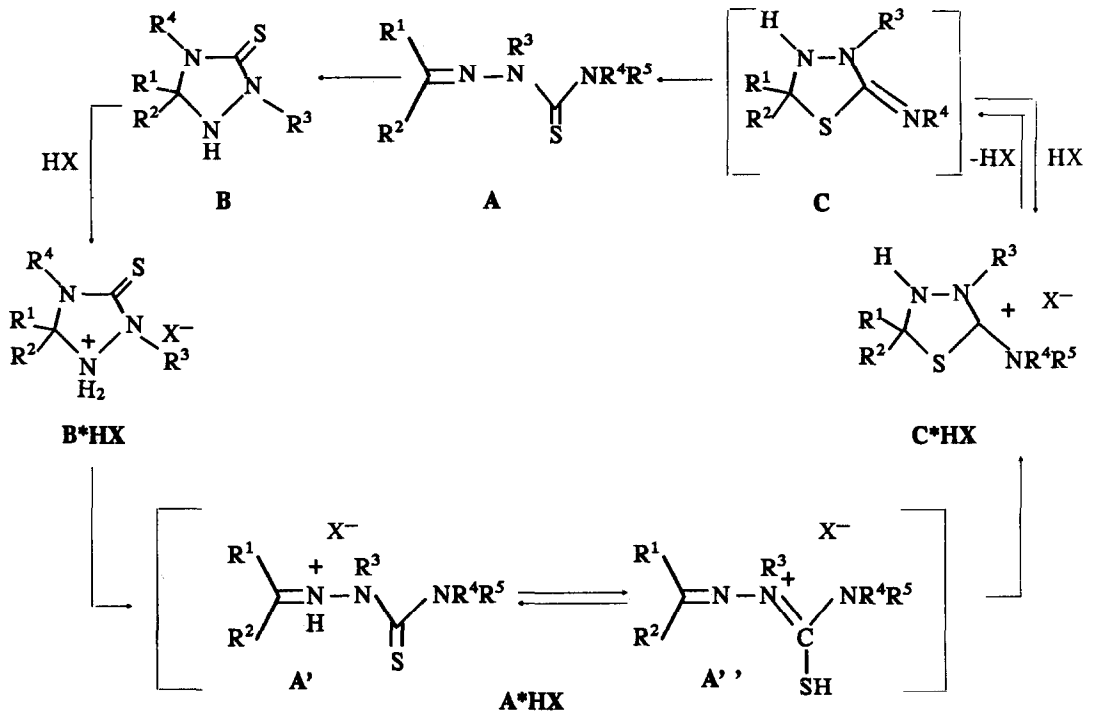
Abstract: *The condensation products from 4,4-dimethyl- and 2,4,4-trimethylthiosemicarbazides and aldehydes or ketones, as well as those from 2-methyl- and 2,4-disubstituted thiosemicarbazides and aldehydes have the thiosemicarbazone structure, while ketones react with 2-methyl- or 2,4-dialkylthiosemicarbazides to form 1,2,4- triazolidine-3-thiones. Both thiosemicarbazones and 1,2,4- triazolidine- 3-thiones in trifluoroacetic acid solution yield 1,3,4-thiadiazolidine-2-iminium salts. Their deprotonation by pyridine leads to thiosemicarbazones, including otherwise inaccessible 2-methyl- and 2,4-disubstituted ketone thiosemicarbazones. The mass-spectrometric investigation of these compounds also suggests presence of their tautomers in the gas phase.*

It was established earlier that thioacylhydrazones exist as 1,3,4- thiadiazolidines[1], while 1-alkylidene(arylidene)amidrazones undergo cyclization to 1,2,4-triazoline derivatives under certain conditions[2]. Thiosemicarbazones may alternatively cyclize via nitrogen or sulphur nucleophilic attack, but this question has not yet been closely investigated.

The low barrier observed for the *syn-anti* isomerization of thiosemicarbazones was explained by the formation of an intermediate 2-imino- 1,3,4-thiadiazoline[3]; the same structure was believed to form from several thiosemicarbazones in acidic medium[4,5]. On the contrary, the 1,2,4-triazolidine-3-thione structure was assigned to the product of 2-methyl-4-(1-phenylethyl) thiosemicarbazide condensation with acetone[6], as well as for the reaction product from acetophenone β-hydroxyethylhydrazone with KNCS[7].



	R^1	R^2	R^3	R^4	R^5
1	H	CH_3	CH_3	CH_3	H
2	H	CH_3	CH_3	C_2H_5	H
3	H	CH_3	CH_3	CH_2Ph	H
4	H	CH_3	CH_2Ph	CH_3	H
5	H	C_6H_5	CH_3	CH_3	H
6	H	C_6H_5	CH_3	C_2H_5	H
7	H	C_6H_5	CH_3	CH_2Ph	H
8	H	C_6H_5	C_2H_5	CH_3	H
9	H	C_6H_5	CH_2Ph	CH_3	H
10	H	4-MeO-C_6H_4	CH_3	H	H
11	H	4-MeO-C_6H_4	CH_3	CH_3	H
12	H	4-MeO-C_6H_4	H	CH_3	CH_3
13	H	4-MeO-C_6H_4	CH_3	CH_3	CH_3
14	CH_3	CH_3	CH_3	H	H
15	CH_3	CH_3	CH_3	CH_3	H
16	CH_3	CH_3	CH_3	C_2H_5	H
17	CH_3	CH_3	CH_3	CH_2Ph	H
18	CH_3	CH_3	C_2H_5	CH_3	H
19	CH_3	CH_3	CH_2Ph	C_2H_5	H
20	CH_3	C_2H_5	CH_3	CH_3	H
21	CH_3	C_6H_5	CH_3	CH_3	H

Fig. 1. Reversible recyclization of N-substituted thiosemicarbazones.

Table 1. Thiosemicarbazones **1-21A**

Compound	M.p., °C		^{1}H NMR data, δ, ppm (J, Hz)				
	a)	Solvent	R^1,R^2	R^3	R^4	NH	
1[12]	56-58	b)	2.01 d(5) 7.04 q(5)	3.65 s	3.12 d(5)	8.08	br.q
2	44-45	b)	2.01 d(5) 7.04 q(5)	3.65 s	1.22 t(7) 3.65 m	8.05	br.t
3[12]	73-74	b)	1.94 d(5) 6.99 q(5)	3.66 s	4.85 d(5) 7.28 s	8.33	br.t
4[13]	99-101	b)	1.80 d(5) 6.87 q(5)	5.76 s 7.15 s	3.18 d(5)	8.23	br.q
5[14]	116-117	b)	7.57 s 7.22-7.38 m 7.46-7.71 m	3.79 s	3.18 d(5)	8.18	br.q
6	61-63	b)	7.67 s 7.36-7.43 m 7.64-7.68 m	3.85 s	1.25 t(7) 3.63 m	8.20	br.t
7	109-110	b)	7.61 s 7.24-7.33 m 7.48-7.58 m	3.85 s	4.92 d(6) 7.29 s	8.47	br.t
8[13]	94-95	b)	7.68 s 7.33-7.45 m 7.56-7.73 m	1.18 t(7) 4.58 q(7)	3.16 d(5)	8.13	br.q
9	148-150	b)	7.51 s 7.17-7.50 m	5.85 s 7.20 s	3.26 d(5)	8.30	br.q
10	187-188	c)	7.55 s 6.74-7.61 m 3.74 s	3.62 s	—	8.14 8.42	br br
11[13]	122-123	c)	7.61 s 6.74-7.54 m 3.74 s	3.57 s	3.15 d(5)	8.65	br.q
12[12]	139-140	c)	7.71 s 6.76-7.45 m 3.72 s	—	3.31 s	9.53	br.s
13	97-99	b)	7.47 s 6.77-7.57 m 3.72 s	3.57 s	3.24 s	—	
14[5]	d)	c)	1.83 s	3.40 s	—	e)	
15[5]	oil	b)	1.92s, 2.09s	3.40 s	3.05 d(5)	e)	
		c)	1.80 s	3.35 s	3.00 s	e)	
16	d)	c)	1.88 s	3.34 s	1.11 t(7) 3.52 q(7)		
17[12]	d)	c)	1.82 s	3.43 s	4.68 d(5) 7.08-7.36 m	e)	
18	d)	c)	1.81 s	1.10 t(7) 4.04 q(7)	3.00 s	e)	
19	d)	c)	1.72 s	5.29 s 7.1-7.4 m	1.06 t(7) 3.64 q(7)	e)	
20	d)	c)	1.78 s 0.91 t(7) 2.12-2.40 m	3.41 s	3.02 s	e)	
21	d)	c)	2.25 s 7.20-7.44 m	3.50 s	2.96 s	e)	

a) **1-4, 10-13** — from ethanol, **5-6** — from benzene-hexane (2:1), **7-9** — from ethanol-benzene (2:1) b) $CDCL_3$ c) $CDCL_3$-Py-d_5 (1:1) d) Not isolated from the solution e) Not detected due to the exchange processes

Recently we have demonstrated that some thiosemicarbazones, supposed to exist as 1,2,4-triazolidine-3-thiones[8,9], undergo recyclization in 1,3,4-thiadiazolidine-2-iminium salts in acid solutions[8].

We report now on the structure of those thiosemicarbazones considered to have the maximum tendency for cyclization, as can be judged from the literature[10,11], namely, 2-, 2,4-, 4,4- and 2,4,4-substituted thiosemicarbazones **1-21**.

Table 2. The ^{13}C-NMR data (δ, ppm)

Compound	Solvent	CR^1R^2	CS	R^1,R^2	R^3	R^4
1 A	$CDCl_3$	137.8	180.0	18.2	32.2	31.3
2 A	$CDCl_3$	138.7	179.2	18.5	32.3	13.9 39.7
3 A	$CDCl_3$	139.1	179.5	18.3	32.5	48.6 126.8, 127.1 128.0, 137.7
4 A	$CDCl_3$	139.7	181.0	18.4	48.8 125.7, 126.6 128.2, 135.2	
6 A	$CDCl_3$	138.4	179.4	126.7, 128.3 129.4, 133.7	32.6	13.8 39.8
8 A	$CDCl_3$	138.1	180.1	126.9, 128.6 129.7, 134.0	10.5 39.5	31.8
10 A	DMSO-d_6	141.0	180.4	55.3 114.1, 127.1 129.5, 160.8	32.7	—
14 B	$CDCl_3$	75.0	179.0	25.4	35.0	—
15 B	$CDCl_3$	77.0	179.8	21.7	35.4	29.6
15 B*HX	CF_3COOH[a)]	82.4	178.9	20.4	35.9	29.3
8 C*HX	CF_3COOH	73.0	174.1	127.2, 129.4 129.4, 130.8	11.0 44.7	35.7
14 C*HX	CF_3COOH	78.5	175.2	25.6	35.7	—
15 C*HX	CF_3COOH	79.4	175.4	25.7	35.4	35.5
21 C*HX	CF_3COOH	86.2	176.3	26.7 126.4, 126.5 130.1, 130.7	35.4	21.7

a) C_6D_6 used as internal standard.

Condensation between thiosemicarbazides and aldehydes generally led to the open-chain isomers **1-13 A**. However, ketones reacted with 2- and 2,4- substituted thiosemicarbazides to produce cyclic derivatives **14-21 B**. The only exception was the reaction of 2,4-dimethylthiosemicarbazide with acetone that led to the mixture of **15 A** and **15 B**, the former converting slowly to the latter on heating or storing of its solution.

The linear structure of **1-13,15** was confirmed by their ^{1}H and ^{13}C-NMR spectra (cf. Tables 1,2).

The mass-spectra of thiosemicarbazones **1-14** show stable molecular ions due to the effective charge delocalization between the heteroatoms of thioureide moiety. The main fragmentation observed includes the loss of R^1 and/or R^2 substituents followed by cleavages of N-N and C-N single bonds (see Fig.2). The most interesting feature of aldehyde thiosemicarbazone mass spectra is, however, the presence of abundant peaks of $[M-2]^+$ ions. Their relative intensities were found to be dependent on the type of the mass-spectrometer used and on the recording conditions.

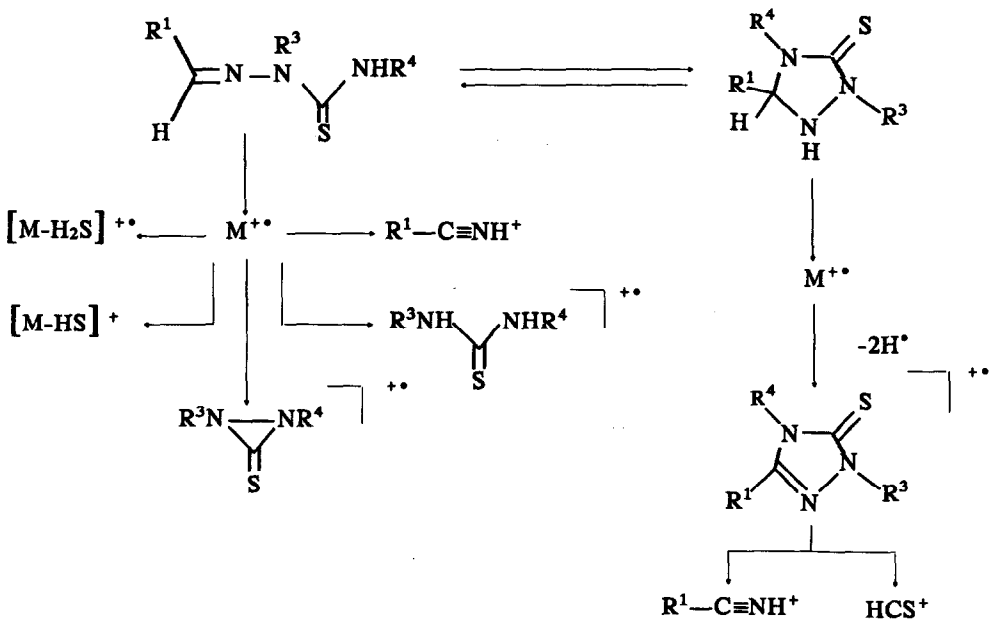


Fig. 2. MS fragmentation of aldehyde thiosemicarbazones.

Table 3. Mass-spectra of compounds **1-24.**

Compound	m/z (% int. of base peak)
1	145(M, 25) 130(27) 74(100) 73(18) 72(29) 71(63) 69(21) 57(31) 55(24) 47(16) 45(29) 44(35) 43(39) 42(61) 41(32)
2	159(M, 85) 157(24) 144(58) 88(32) 85(20) 83(48) 74(74) 72(58) 71(39) 69(20) 60(91) 59(19) 57(58) 55(30) 44(100) 42(83) 40(38)
3	221(M, 46) 219(11) 206(15) 145(37) 106(53) 91(100) 77(15) 75(16) 74(30) 72(20) 71(16) 65(25) 45(37) 44(23) 43(20) 42(23)
4	221(M, 11) 219(7) 179(23) 106(100) 91(88) 79(18) 77(16) 74(53) 73(34) 65(27) 45(19) 44(14) 42(22)
5	207(M, 90) 205(62) 134(57) 133(74) 130(25) 106(30) 104(70) 103(40) 91(35) 77(55) 74(100) 73(28) 71(93) 69(52) 51(52) 42(41)
6	221(M, 100) 219(81) 134(71) 133(90) 106(69) 104(83) 103(40) 88(34) 85(35) 83(55) 77(64) 74(52) 60(68) 44(80)
7	283(M, 30) 281(30) 248(7) 207(19) 104(12) 103(17) 92(10) 91(100) 77(18) 65(13) 51(13) 44(30) 40(11)
8 a)	221(M, 100) 219(91) 204(26) 190(24) 133(55) 118(52) 117(52) 104(63) 103(25) 85(27) 83(68) 77(58) 74(85) 44(93)
b)	221(M, 4) 147(3) 133(5) 119(5) 117(6) 104(6) 90(11) 89(15) 84(11) 77(37) 74(100) 69(16) 68(18) 61(11) 60(19) 58(13) 56(40) 55(15) 51(51)
9	283(M, 23) 281(62) 248(12) 145(40) 118(15) 106(20) 105(14) 104(22) 103(30) 91(100) 77(30) 65(15) 44(21)
11	237(M, 50) 235(10) 164(34) 163(60) 149(23) 135(25) 134(48) 104(34) 92(31) 91(41) 90(23) 77(53) 74(100) 71(99) 69(23) 64(29) 63(30) 51(33)
12	237(M, 29) 235(5) 192(73) 134(92) 133(23) 107(34) 92(65) 91(43) 90(32) 88(67) 77(100) 76(24) 71(45) 64(52) 63(48) 51(51)
14	145(M, 28) 130(12) 111(20) 105(42) 100(38) 72(12) 71(54) 70(46) 60(77) 59(20) 57(27) 56(100) 55(23) 54(19)
16	173(M, 40) 158(41) 157(87) 156(37) 130(24) 128(19) 88(18) 83(36) 74(26) 70(23) 69(33) 60(37) 58(33) 55(40) 42(100)
17	235(M, 100) 220(34) 178(11) 145(28) 106(48) 100(13) 91(28) 77(17) 75(51) 74(26) 65(35) 58(49) 56(18) 42(45) 41(27)
18	173(M, 100) 158(28) 130(49) 99(5) 85(28) 83(13) 74(14) 69(6) 60(6) 58(15) 56(22) 55(8) 44(40) 42(28) 41(10)
19	249(M, 91) 234(39) 193(10) 192(13) 159(19) 143(8) 106(99) 91(100) 65(13) 58(19) 56(71) 44(23) 42(16) 40(23)
20	173(M, 98) 158(16) 144(100) 129(80) 103(5) 99(3) 85(5) 74(14) 71(33) 70(14) 62(6) 56(16) 42(32)
21	221(M, 100) 206(82) 148(25) 147(45) 144(47) 133(14) 120(20) 118(12) 104(30) 103(25) 77(31) 74(30) 71(15) 69(11) 51(14) 42(25)

Mass-spectra of **1-16** were recorded with Kratos MS25RFA;
Mass-spectra of **17-21** were recorded with MX1321A spectrometers;
Mass-spectra of **8**: a) Krators MS25RFA, b) Finnigan MAT-4615.

Surprisingly, the mass spectra of benzaldehyde thiosemicarbazones **5** and **8** recorded with a Finnigan MAT-4615 spectrometer (quadrupole mass analyser) were completely devoid of the [M-2] peaks (see Table 3). When the mass spectra were obtained using Kratos MS25RFA spectrometer equipped with the combined EI/CI source and, therefore, with prolonged lifetime of the sample molecule prior to its ionization, there appeared the [M-2] peaks with relative abundances up to 90 % of the base peak (Table 3).

Table 4. 1,2,4-Triazolidin-3-thiones **14-21**

Compound	M. p. °C	^{1}H NMR data, δ, ppm (J Hz)				
	a)	Solvent	R^1,R^2	R^3	R^4	NH, s
14[5]	138-140	b)	1.37 s	3.24 s	—	4.66 7.45
15[5]	73-75	b)	1.38 s	3.30 s	2.99 s	4.60
		c)	1.24 s	3.27 s	2.92 s	5.47
16	81-83	b)	1.40 s	3.29 s	1.22 t(7) 3.50 q(7)	4.36
		c)	1.31 s	3.28 s	1.18 t(7) 3.48 q(7)	4.48
17[12]	122-123	b)	1.22 s	3.36 s	4.76 s 7.17-7.46 m	4.20
		c)	1.18 s	3.30 s	4.74 s 7.06-7.39 m	5.64
18	86-88	b)	1.35 s	1.21 t(7) 3.77 q(7)	2.97 s	4.43
		c)	1.23 s	1.12 t(7) 3.80 q(7)	2.93 s	5.35
19	59-60	b)	1.13 s	4.97 s 7.30 m	1.09 t(7) 3.53 q(7)	4.00
		c)	1.20 s	5.01 s 7.20-7.46 m	1.17 t(7) 3.50 q(7)	5.24
20	52-53	b)	1.31 s 0.83 t(7) 1.50-1.74 m	3.22 s	2.92 s	4.25
		c)	1.20 s 0.76 t(7) 1.34-1.56 m	3.20 s	2.87 s	5.36
21	95-97	b)	1.68 s 7.35 s	3.25 s	2.98 s	4.25
		c)	1.68 s 7.23-7.40 m	3.27 s	2.90 s	5.56

a) **14-16** — from ethanol, **17-19** — from ethanol : benzene (2:1),
20,21 — from benzene : hexane (2:1) b) $CDCl_3$ c) $CDCl_3$:Py-d_5 (1:1)

We believe that the $[M-2]^+$ ions appear due to the thermal dehydrogenation of the cyclic isomers **B**, which may be produced in the gas phase after multiple collisions of the vaporized sample molecules with hot surfaces of the ion source prior to the ionization. The literature search revealed that solutions of some 5-monosubstituted 1,2,4-triazolidine-3-thiones (which are, in fact, cyclic isomers **B** of aldehyde thiosemicarbazones), were reported to be unstable on air as the compounds are readily oxidized into Δ^5-1,2,4-triazolidine-3-thiones[6,15]. We suppose that the thermal dehydrogenation in the mass-spectrometer ion source may lead, though in absence of oxygen, to the same results.

The appearance of the $[M-2-R^3]$ and $[M-2-R^4]$ peaks (m/z 204 and 190, resp.) in the mass spectrum of **8** (Table 3, cf. **8a** and **8b**) can be attributed thus to the formation of 1,2,4-triazoline-3-thiones.

In conclusion, the mass-spectrometric investigation of thiosemicarbazones **1-14** suggests that their cyclization to isomers B may occur in the gas phase.

Unlike thiosemicarbazones **1-13**, in the ^{13}C-NMR spectra of compounds **14-21** there are signals of the C-5 carbon atom in 73-78 ppm range (see Table 2), and in their ^{1}H-NMR spectra signals of R^1 and R^2 substituents at this atom are shifted upfield as compared with those of the linear structure **A** (cf. Tables 1,4). Moreover, the R^1 and R^2 methyl groups at C-3 in **14-19** are magnetically equivalent, and the protons of R^2 substituents in **16-20** are diastereotopic.

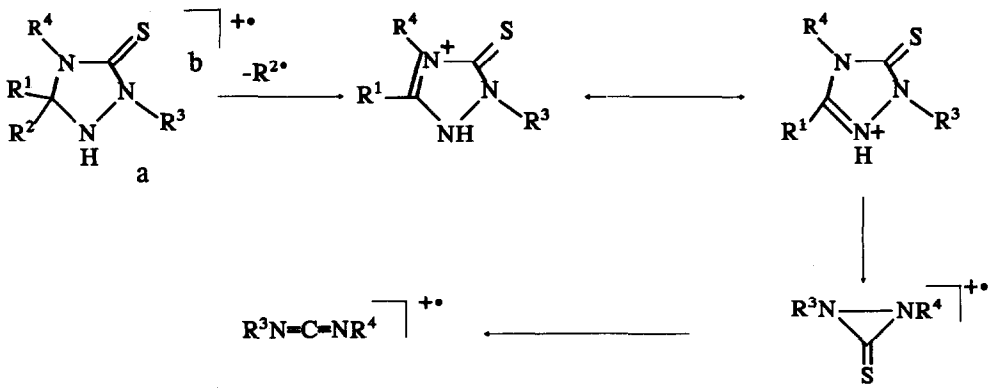


Fig. 3. MS fragmentation of 1,2,3-triazolidine-3-thiones.

The 1,2,4-triazolidine-3-thione structure **B** was assigned to the compound **15** on the basis of its ^{15}N-NMR spectrum (see Experimental), where there are three signals of nitrogen atoms in sp^3 hybridization state[9].

The mass spectra of 1,2,4-triazoline-3-thiones **16-21** are listed in Table 3. Their fragmentation consists of ring ruptures (*a,b* on Fig.3), and of subsequent loss of the substituents R^1 - R^4.

Triazolidines **14-21** in $CDCl_3$ solution immediately transform into the corresponding salts **B*HX** on treatment with the excess of trifluoroacetic acid (TFA) or with some other strong acids. In their ^{1}H-NMR spectra slight downfield shifts of R^3 and R^4 signals were observed after the conversion of **B** to **B*HX**. This fact together with the absence of coupling in R^3 and R^4 signals suggests that the protonation takes place at the N-1 atom (cf. Table 5).

Table 5. ^{1}H NMR data of salts **15-17,20,21 B*HX** in CF_3COOH:$CDCl_3$ (1:1), δ, ppm (J,Hz)

Compound	R^1,R^2	R^3,s	R^4
15	1.68 s	3.20	2.86 s
16	1.70 s	3.20	0.96 t(7) 3.03 q(7)
17	1.64 s	3.23	4.28 s 6.81-7.00 m
20	1.70 s 0.76 t(7) 1.74-2.04 m	3.18	2.87 s
21	1.82 s 6.98-7.16 m	3.12	2.71 s

Cations **B*HX** undergo slow (in minutes to hours range of time) and quantitative recyclization to 1,3,4-thiadiazoline-2-iminium cations **C*HX** (Table 6). In the case of compounds **14,18,19** the starting cations **B*HX** could not even be detected.

The same cations **C*HX** were formed immediately from thiosemicarbazones **1-13** in TFA solution. Possible formation of intermediate cations **A'*HX** or **A''*HX** was ruled out on the basis of the ^{1}H-NMR spectra of **1-21** solutions in TFA.

Table 6. The ^{1}H NMR data of salts **1-21 C*HX** in $CF_3COOH:CDCl_3$ (1:1), δ, ppm (J, Hz)

Compound	R^1,R^2	R^3	R^4	NH
1	1.33 d(6) 4.97 q(6)	3.01 s	2.81 d(5)	7.06 q(5)
2	1.33 d(6) 4.96 q(6)	3.03 s	0.95 t(7) 2.96-3.12 m	7.02 br.t
3	1.32 d(6) 4.95 q(6)	3.02 s	4.20 d(5) 6.94 s	7.48 br.t
4	1.18 d(6) 4.91 q(6)	4.44 s 6.94 s	2.82 d(5)	7.35 q(5)
5	6.00 s 6.96-7.29 m	3.06 s	2.81 d(5)	a)
6	6.00 s 7.12 s	3.05 s	0.92 t(7) 3.07 q(7)	a)
7	5.96 s 6.83-7.00 m	3.10 s	4.22 d(6) 7.07 s	7.59 br.t(6)
8	5.92 s 7.10 s	0.86 t(7) 3.28 q(7)	2.73 d(5)	7.43 br.q(5)
9	5.95 s 6.80-7.00 m	4.48 s 7.04 s	2.86 d(5)	7.37 br.q
10	5.93 s 6.55-7.11 m 3.48 s	3.05 s	—	a)
11	6.01 s 6.63-7.21 m 3.53 s	3.08 s	2.87 d(4)	a)
12	6.17 s 6.62-7.24 m 3.55 s	—	3.01 s and 3.08 s	a)
13	6.00 s 6.59-7.16 m 3.50 s	3.17 s	3.03 s	a)
14	1.31 s	2.98 s	—	7.22 s 11.07 s
15	1.37 s	2.95 s	2.72 d(5)	7.07 br.q
16	1.37 s	2.98 s	0.90 t(7) 3.01 q(7)	6.90 br.t
17	1.38 s	3.00 s	4.14 d(5) 6.81-7.00 m	7.54 t(5)
18	1.36 s	0.90 t(7) 3.28 q(7)	2.71 d	7.23 br.q
19	1.34 s	4.44 s 7.01 s	0.93 t(7) 3.11 m	7.26 br.t
20	1.34 s 0.70 t(7) 1.64 q(7)	2.96 s	2.74 d(5)	a)
21	1.66 s 6.98-7.16 m	3.02 s	2.72 d(5)	a)

a) Was not detected due to the exchange processes

Structures of the cations **15** and **21** were deduced from their ^{15}N-NMR spectra (see Experimental), as they exhibit three signals of two sp^3 nitrogen atoms and of an iminium nitrogen atom in the 90-140 ppm range[16,17].

Deprotonation of the 1,3,4-thiadiazoline-2-iminium salts **1-21 C*HX** with Py-d_5 yields open-chain thiosemicarbazones **1-21 A**, and not cyclic thiadiazolines **C**. For the compounds **1-13,15** it was proved by the comparison of their ^{1}H-NMR spectra with those of starting thiosemicarbazones recorded in Py-d_5, and by tlc. In the case of ketone derivatives **14,16-21** the thiosemicarbazone structure **A** is also supported by the H-NMR spectra showing R^1 and R^2 signals in the lower field. The equivalence of two methyl groups observed in the spectra of acetone derivatives **14-19** (Table 1) can be explained by the rapid *syn-anti* isomerization via intermediate **C*HX** cations due to the presence of pyridinium salt in the solution, like that described in ref [3]. Indeed, the signals of methyl groups at the C=N bond were equivalent in both ^{1}H- and ^{13}C-NMR spectra of **15A** when recorded in Py-d_5 with catalytic amount of TFA.

Thiosemicarbazones **14-21 A** have cyclized to yield more stable triazolidines **14-21 B** either on the storage of their solutions or during attempted isolation by recrystallization or by the preparative tlc. Thus, the structure of the condensation products of aldehydes and ketones with N-substituted thiosemicarbazides depends strongly on the reaction conditions and on the nature of R^1 - R^5 substituents.

In neutral media, the derivatives of 4,4- and 2,4,4-substituted thiosemicarbazides, unable to cyclize into triazolinethiones, as well as the condensation products of aldehydes with 2- and 2,4-substituted thiosemicarbazides, which are stabilized by conjugation, all exist as open- chain thiosemicarbazones **A.**

Absence of conjugation in 2- and 2,4-disubstituted thiosemicarbazones of ketones[18], and generally observed prevalence of the cyclic form in the tautomeric systems which have branching at the site of the cyclization[11] result in their existence as 1,2,4-triazolidine-3-thiones **B.**

In acidic media the derivatives **1-21** have the most stable in these conditions structure of 1,3,4-thiadiazoline-2-iminium cation **C*HX.**

Thus, earlier works concerning the site of thiosemicarbazone protonation[19,20] should be updated. Our results explain also some details of the thiosemicarbazone chemistry,

including oxidation to 1,2,4-triazole-5- thiones in neutral media[21] , and to 2-imino-1,3,4-thiadiazolines in presence of acids [22] , known as the Young-Eyre reaction.

Experimental

The ^{1}H-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 mass spectra were recorded with Kratos MS25RFA and MX1321A (USSR) spectrometers (EI, direct insert probe, 70 eV).

^{15}N-NMR spectra:

Compound **15** (DMSO-d_6): 119.4, 127.2, 134.2 ppm.
Salt **15 C*HX** (TFA): 90.6, 134.4, 140.2 ppm.
Salt **21 C*HX** (TFA): 92.6, 137.2, 137.4 ppm.

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, 11-13 A.

A mixture of thiosemicarbazide (0,05 mole) and aldehyde (0.05 mole) in 50 ml of ethanol was allowed to stand for 24h, then the residue was recrystallized. In the case of compounds **1-4** at first the solvent was removed.

Acetone 2,4-dimethylthiosemicarbazone 15 A.

The solution of 2,4-dimethylthiosemicarbazide in acetone was allowed to stand for 24 h. After the removal of acetone **15 A** was obtained as yellow oil.

1,5,5,-Trimethyl-1,2,4-triazolidine-3-thione 14 B.

To the mixture of KNCS (9.7 g) and acetone methylhydrazone (8.7 g) in 50 ml of benzene 6 ml of acetic acid was added. The mixture was heated under reflux for 1.5 h and left

overnight[7]. After the dilution with water (50 ml) the residue was filtered off and recrystallized from ethanol.

Anisaldehyde 2-methylthiosemicarbazone 10 A.

The solution of 1,5,5-trimethyl-1,2,4-triazolidine-3-thione **14 B** in methanol was refluxed with excess of anisaldehyde and catalytic amount of TFA during 10 h. On cooling the residue was filtered off and washed with methanol.

1,2,4-Triazolidine-3-thiones 15-21 B.

An appropriate thiosemicarbazide was refluxed in the excess of carbonyl compound with catalytic amount of TFA during 10 h. After the removal of ketone the residue was recrystallized.

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