INVESTIGATION OF THE RING–CHAIN TAUTOMERISM OF ALKYL-SUBSTITUTED 6-HYDROXYTETRAHYDRO-1,3-THIAZINE-2-THIONES BY IR SPECTROSCOPY AND MASS SPECTROMETRY

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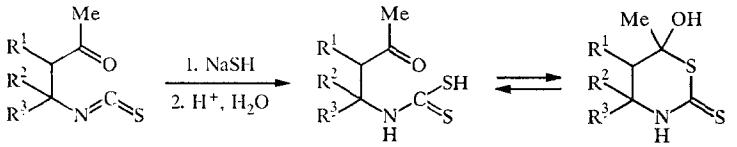
The ring–chain tautomerism of alkyl-substituted 6-hydroxytetrahydro-1,3-thiazine-2-thiones was studied by IR spectroscopy and mass spectrometry. The dependence of the tautomeric equilibrium on the number and location of the methyl groups in the molecule and the aggregate state of the substance was ascertained. Substituted 3,4-dihydro-2H-1,3-thiazine-2-thiones were obtained by the dehydration of the 6-hydroxytetrahydro-1,3-thiazine-2-thiones.

The prototropy of ring–chain tautomerism in a series of substituted 4-hydroxytetrahydro-1,3-thiazine-2-thiones [1] and 4-hydroxyhexahydropyrimidine-2-thiones [2, 3] was previously studied by means of IR and mass spectra. At the same time, data on ring–chain tautomerism of 6-hydroxytetrahydro-1,3-thiazine-2-thiones, which we have previously synthesized [4], are not available in the literature.



Ia-c(A) Ia-c(B)

Ia R^1 = Me, R^2 = R^3 = H; b R^1 = H, R^2 = R^3 = Me; c R^1 = R^2 = R^3 = Me

In principle, Ia-c can exist in two tautomeric forms, viz., the acyclic form of substituted N-3-oxoalkyldithiocarbamic acids (A) and the cyclic form of 6-hydroxytetrahydro-1,3-thiazine-2-thiones (B).

The IR spectra at 1680-1710 cm^{-1} of crystalline samples suspended in mineral oil do not contain an absorption band corresponding to stretching vibrations of a C=O group; this constitutes evidence that Ia-c exist in the cyclic form in the crystalline state. There are broad absorption bands corresponding to vibrations of N—H and OH groups at 3200-3500 cm^{-1} in the IR spectra of these compounds.

A ν C=O absorption band of a carbonyl group of an acyclic tautomer appears at 1700-1720 cm^{-1} in the IR spectra of solutions of Ia-c in chloroform some time after dissolving of the samples; its intensity gradually increase with time and, after 6-18 h, reaches a constant value. This phenomenon is associated with conversion of the cyclic form to the acyclic form. The increase in the integral intensity of the ν C=O band corresponds to an increase in the amount of the acyclic tautomer in the tautomeric system, while the cessation of the increase constitutes evidence for the achievement of a dynamic equilibrium, which, depending on the structure of the compound, is established from 6 h in the case of Ia and up to 18 h in the case of Ib. From a comparison of the integral intensities of the absorption bands of the carbonyl groups in the IR spectra of solutions of

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TABLE 1. Parameters of the ^1H NMR Spectra of IIIa-c

Compound	Chemical shifts of the protons, δ, ppm					
	4-H	5-H	4-CH_3	5-CH_3	6-CH_3	N—H
IIIa	3,8	—	—	1,78	1,78	9,12
IIIb	—	5,42	1,37	—	1,84	8,91
IIIc	—	—	1,36	1,75	1,81	8,58

TABLE 2. Parameters of the ^{13}C NMR Spectra of IIIa-c

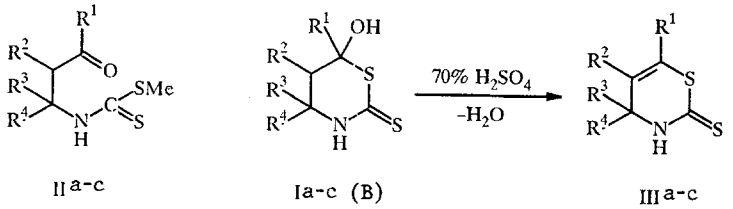
Compound	^{13}C chemical shifts, δ, ppm							
	C_2	C_4	C_5	C_6	6-CH_3	5-CH_3	4-CH_3	4-CH_3
IIIa	193,5	50,0	119,5	122,5	16,9	16,4	—	—
IIIb	190,0	57,4	121,8	127,3	19,7	—	28,4	28,4
IIIc	190,0	60,0	120,2	126,7	17,1	13,6	26,1	26,1

Ia-c in chloroform recorded under identical conditions every 2 h, we have established that the introduction of a methyl substituent into the α-position with respect to the hydroxy group on passing from Ib to Ic, as well as replacement of methyl groups in the β-position with respect to the hydroxy group by hydrogen atoms on passing from Ib to Ia, leads to a decrease in the stability of the cyclic form and an increase in the tendency for it to undergo conversion to the acyclic form.

The increase in the stability of the cyclic form when methyl substituents are introduced into the β-position with respect to the hydroxy group is evidently associated with the Thorpe—Ingold "gem-dimethyl effect" [5]. Replacement of the hydrogen atom attached to the $C_{(5)}$ atom by a methyl group destabilizes the cyclic form as a consequence of an increase in the interaction of the substituents attached to the $C_{(5)}$ and $C_{(6)}$ atoms.

The IR spectra of solid samples of Ia-c isolated from the solutions are completely identical to the IR spectra of the starting crystalline products.

To ascertain the ratios of the tautomers of Ia-c in the gas phase we studied, for the first time, the characteristics and pathways of fragmentation of the molecule of these compounds under the influence of electron impact. For the successful solution of this problem we ascertained the character of the fragmentation of model compounds, viz., substituted methyl N-3-oxoalkyldithiocarbamates IIa-c [4], which have an authentic acyclic form, and substituted 3,4-dihydro-2H-1,3-thiazine-2-thiones IIIa-c, which have a genuine cyclic structure; these compounds were obtained by dehydration of the corresponding 6-hydroxytetrahydro-1,3-thiazine-2-thiones with 70% sulfuric acid.



IIa-c Ia-c (B) IIIa-c

The structures of IIIa-c were confirmed by the set of ^1H NMR (Table 1) and ^{13}C NMR (Table 2) spectral data.

An analysis of the mass spectra of Ia-c shows that the principal processes involved in the fragmentation of the molecular ions (M^+) of these compounds under the influence of electron impact, which are associated either with detachment of the terminal groups or with cleavage of the bonds next to the quaternary carbon atom (Scheme 1), are in agreement with the fragmentation of the M^+ ions of methyl N-3-oxoalkyldithiocarbamates IIa-c and substituted 3-oxoalkylthioureas [3]. This fact, as well as the absence in the mass spectra of Ia-c of the $[M - H_2O]$ and $[M - H_2O - CH_3]^+$ ion peaks that are typical for the mass spectra of 4,6,6-trimethyl-4-hydroxyhexahydropyrimidine-2-thione derivatives [3], constitutes evidence that Ia-c exist in the acyclic tautomeric form in the gas phase.

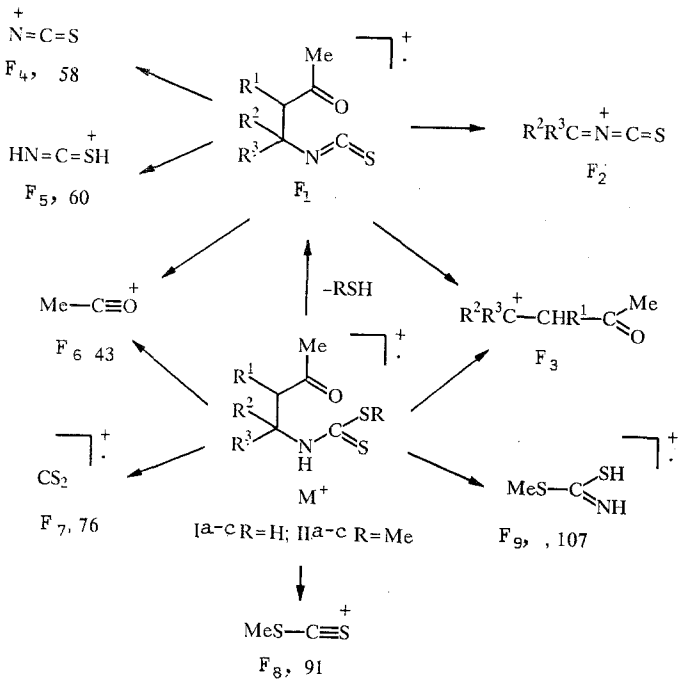
TABLE 3. Intensities of the Peaks of the Characteristic Fragment Ions in the Mass Spectra of I and II (% of the total ion current)

Index of the ions	Compound					
	Ia	Ib	Ic	IIa	IIb	IIc
M^+ (W_m)	0,2	0,4	0,9	1,4	6,2	1,2
F_1	1,1	0,5	0,2	1,6	4,0	1,5
F_2	3,0	2,6	3,5	2,4	2,5	16,7
F_3	4,1	6,7	4,3	6,0	9,1	26,2
F_4	2,7	4,7	6,3	—	—	—
F_5	—	—	—	0,9	2,4	3,5
F_6	27,7	31,6	46,5	21,6	41,8	49,5
F_7	15,0	7,4	5,0	—	—	—
F_8	—	—	—	1,3	3,4	2,2
F_9	—	—	—	0,3	2,1	0,8

TABLE 4. Intensities of the Peaks of the Characteristic Fragments of the Ions in the Mass Spectra of III (% of the total ion current)

Compound	M^+	F_{10}	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}	F_{16}
IIIa	16,8	—	—	9,8	12,4	3,9	2,5	12,4
IIIb	15,6	8,5	4,2	0,7	7,3	7,8	1,3	5,4
IIIc	8,1	7,0	5,1	0,9	6,1	6,9	1,4	7,2

Scheme 1*



*The numbers that characterize the ions are the *m/z* values.

TABLE 5. Mass Spectra of I-III*

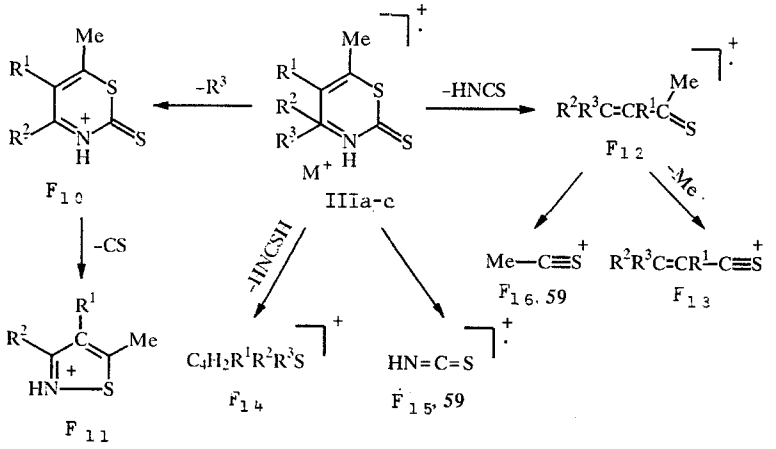
Compound	m/z (relative intensity, %)
Ia	177(0,7), 85(15), 83(6), 76(54), 72(11), 58(10), 44(17), 43(100), 42(12), 41(27), 39(12)
Ib	191(0,9), 100(8), 99(21), 76(24), 58(15), 55(9), 44(14), 43(100), 42(16), 41(27), 39(15)
Ic	205(1,3), 113(9), 100(8), 76(11), 58(14), 55(6), 44(10), 43(100), 42(6), 41(13), 39(4)
IIa	159(94), 101(18), 100(66), 99(26), 85(83), 67(19), 59(100), 58(13), 45(22), 41(24), 39(27)
IIb	173(100), 158(65), 114(38), 113(60), 99(56), 79(15), 59(52), 45(14), 42(21), 41(27), 39(21)
IIc	187(77), 172(82), 128(70), 127(81), 113(71), 79(41), 59(100), 53(32), 42(33), 41(59), 39(35)
IIIa	191(5), 143(8), 85(28), 72(11), 57(12), 55(11), 48(20), 47(21), 43(100), 42(11), 41(21)
IIIb	205(12), 157(10), 108(4), 107(5), 100(6), 99(22), 91(8), 60(6), 47(4), 43(100), 41(6)
IIIc	219(1,7), 113(53), 100(34), 97(8), 70(16), 55(25), 48(30), 47(31), 43(100), 42(10), 41(43)

*The M^+ peaks and the 10 most intense ion peaks in the mass spectra are presented.

Compounds Ia-c are characterized by low stability with respect to electron impact. Replacement of the hydrogen atom attached to the sulfur atom in IIa-c by a methyl group leads to a certain degree of stabilization. The most pronounced pathway of fragmentation of the molecules of Ia-c and IIa-c under the influence of electron impact is fragmentation of the M^+ ions with cleavage of the α-C—C bond with respect to the carbonyl group to give acetyl cation F_6, the peaks of which in the mass spectra of the investigated compounds have the maximum intensity. In addition to this process, an HSR molecule splits out to give an F_1 fragment, which has a 1,3-isothiocyanato ketone structure, in the fragmentation of Ia-c and IIa-c. Its subsequent fragmentation to give the F_2 and F_3 fragments that are characteristic for the fragmentation of substituted isothiocyanates [6-8] constitutes evidence in favor of this assumption. The other pathways of the fragmentation of the M^+ ions of Ia-c and IIa-c are determined by the character of substituent SR and lead to the development of peaks of F_4 and F_7 ions in the spectra of Ia-c (R = H) and to the development of peaks of F_5, F_8, and F_9 ions in the spectra of IIa-c (R = CH_3) (Table 3).

To confirm the assumption that some I, like 4,6,6-trimethyl-hydroxyhexahydropyrimidine-2-thiones [3], may exist in the gas phase in the cyclic tautomeric form we studied the mass spectra and pathways of fragmentation of model compounds IIIa-c (Table 4) with a genuine cyclic structure.

Scheme 2



As one should have expected, the M^+ peaks in the mass spectra of model compounds IIIa-c have significant intensities (Table 5), while the principal pathways of fragmentation of these compounds (Scheme 2) are associated with the elimination

from the M^+ ion of a CH_3 radical from the α-position with respect to the nitrogen atom (the F_{10} fragment) and with retrodiene fragmentation of the M^+ ion to give F_{12} and F_{15} fragments. The subsequent fragmentation of the F_{10} fragment with detachment of a C=S molecule leads to F_{11} fragments and isobaric F_{12} fragments. We established the relative contribution of these isobaric ions in the mass spectra of IIIa and IIIc to the total ion current by means of the high-resolution mass spectra.

In the mass spectra of the previously investigated [9] 2-arylimino derivatives of 4,4,6-trimethyl-3,4-dihydro-1,3-thiazine the ion peak at 114 also consists of the $[C_5H_8NS]^+$ ion (85%, the F_{11} fragment) and of the $[C_6H_{10}S]^+$ ion (the F_{12} ion, 15%). In addition, in the spectra of the 2-arylimino derivatives of 3,4,4,6-tetramethyl-3,4-dihydro-1,3-thiazine [9] the peak of this ion is shifted to m/z 128, while in the spectra of 2-arylimino derivatives of 4,4,6-trimethyltetrahydro-1,3-thiazine and their N-methyl analogs [10] it is shifted to 116 and 130, respectively. On the other hand, in the spectrum of IIIa the ion peak at 100 corresponds completely to the sulfur-containing F_{12} fragment (calculated value 100.0346; found 100.0342). According to the high-resolution mass spectra of IIIa, c, the ion peak at 59 consists of two ions, viz., F_{15} and F_{16}, in a ratio of 1:5.

Thus a study of the IR and mass spectra of I shows that they exist in the crystalline state in the cyclic form of 6-hydroxytetrahydro-1,3-thiazine-2-thiones, while a dynamic tautomeric equilibrium between the cyclic and acyclic forms is established in their solutions in chloroform. In the gas phase Ia-c have, virtually completely, the acyclic structure of substituted 3-oxoalkyldithiocarbamic acids.

EXPERIMENTAL

The IR spectra of solutions of the investigated compounds in $CHCl_3$ with an absorbing-layer thickness of 0.02 cm for a concentration of $5 \cdot 10^{-3}$ M were recorded with a UR-10 spectrometer using NaCl prisms over the range 700-2500 cm^{-1} and LiF prisms over the range 2500-3800 cm^{-1} at a scanning rate of 150 cm^{-1}/min.

The mass spectra were obtained with an MAT CH-6 Varian spectrometer at an ionizing-electron energy of 70 eV and a cathode emission current of 0.1 mA. The high-resolution mass spectra were obtained with a Kratos MS-80 spectrometer under similar conditions. Perfluorinated kerosene was used as the standard, and the resolution $M/\Delta M = 7500$. The samples were introduced directly into the ion source; the temperature of the input system was 20°C.

The ^1H NMR spectra of 15% solutions of the compounds were recorded with a Tesla-80 spectrometer; the chemical shifts of the protons were measured with respect to hexamethyldisiloxane (HMDS) as the internal standard. The ^{13}C NMR spectra of 20-50% solutions in $CHCl_3$ were recorded with a WP 80DS spectrometer.

6-Hydroxytetrahydro-1,3-thiazine-2-thiones Ia-c and Methyl 3-Oxoalkyldithiocarbamates IIa-c were obtained by the method in [4].

4,4,6-Trimethyl-3,4-dihydro-2H-1,3-thiazine-2-thione (IIIb). A solution of 5.2 g of 4,4,6-trimethyl-6-hydroxytetrahydro-1,3-thiazine (Ib) in 8 ml of sulfuric acid was heated on a boiling-water bath to 85°C, after which the mixture was poured over 35 g of crushed ice, and the resulting yellow crystalline precipitate was removed by filtration. Recrystallization from aqueous alcohol gave 3.2 g (68.3%) of IIIb with mp 119-120.5°C (from acetone) [mp 120.5-121.5°C (from carbon tetrachloride)]. IR spectrum: 1520 (thioamide), 1660 (C=C), 3060 cm^{-1} (NH).

5,6-Dimethyl-3,4-dihydro-2H-1,3-thiazine-2-thione (IIIa, $C_6H_9NS_2$). Similarly, 2.7 g (77.6%) of IIIa, with mp 148-150°C (from acetone), was obtained from 4.0 g of Ia and 6 ml of 70% sulfuric acid after extraction of the aqueous layer with chloroform (3 × 10 ml), drying of the extract over calcium chloride, and removal of the solvent. IR spectrum: 1540 (thioamide), 1650 (C=C), 3100 cm^{-1} (NH).

4,4,5,6-Tetramethyl-3,4-dihydro-2H-1,3-thiazine-2-thione (IIIc, $C_8H_{13}NS_2$). Similarly, 0.45 g (61.7%) of IIIc, with mp 164.0-165.0°C (from acetone), was obtained from 0.80 g of Ic and 1.7 ml of 70% sulfuric acid. IR spectrum: 1520 (thioamide), 1640 (C=C), 3090 cm^{-1} (NH).

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