4. Ya. R. Tymyanskii and M. I. Knyazhanskii, Zh. Org. Khim., 17, 610 (1981).
5. A. Mistr, M. Vavra, J. Skoupy, and R. Zahradnik, Collect. Czech. Chem. Commun., 37, 1520 (1972).
6. S. M. Aldoshin, Ya. R. Tymyanskii, O. A. D'yachenko, L. O. Atovmyan, M. I. Knyazhanskii, and G. I. Dorofeenko, Izv. Akad. Nauk SSSR, Ser. Khim., No. 10, 2270 (1981).
7. Ya. R. Tymyanskii, S. M. Aldoshin, M. I. Knyazhanskii, O. A. D'yachenko, A. I. Pyshchev, and L. O. Atovmyan, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 535 (1982).
8. M. I. Knyazhanskii, Ya. R. Tymyanskii, N. V. Kholodova, G. E. Trukhan, and Yu. P. Andreichikov, Khim. Vys. Énerg., 14, 445 (1980).

TAUTOMERISM OF A SERIES OF SUBSTITUTED 9-ACRIDINETHIONES

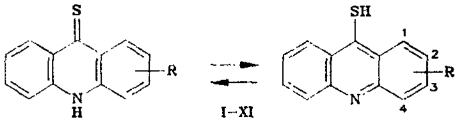
P. B. Kurapov, A. A. Martynovskii,
N. A. Klyuev, A. I. Panasenko,
N. N. Tigneeva, L. I. Shtoiko,
and I. I. Grandberg

UDC 547.835.5 + 541.623 +
543.51

A quantitative estimation of thione-thiol tautomerism in a series of substituted 9-acridinethiones was performed by methods of IR, UV, and mass spectrometry as a function of the aggregated state, temperature, and solvent. It was shown that the thione form predominates in the crystal and gas phase; the position of the equilibrium is ambiguous in solutions.

This work presents the results of a quantitative study of the tautomeric (thione-thiol) equilibrium in a series of substituted 9-acridinethiones (I-X), depending on the change in the polarity of the solvent, temperature, aggregated state, and ionic strength of the solution.

The following compounds were investigated:



I R=H; II R=2-Cl; III R=3-Cl; IV R=4-Cl; V R=2-OCH$_3$; VI R=2-OC$_2$H$_5$; VII R=4-OCH$_3$; VIII R=4-OC$_2$H$_5$; IX R=2-NO$_2$; X R=3-NO$_2$; XI 10-methyl-9-acridinethione

Thione-thiol tautomerism of 9-acridinethione was recorded back in 1944 [1]. Spectral evidence of the existence of thione–thiol equilibrium in solution for compound I was obtained in [2]. However, the numerated studies and later ones [3, 4] were qualitative; there is no quantitative estimation of the dynamic tautomeric equilibrium. In all the investigations indicated above, the influence of the nature of the solvent, the electronic effect of the substituent R, the temperature, and the phase state of the substance on the ratio of the tautomeric forms in this heterocyclic system were not discussed.

For a quantitative estimation of the position of the tautomeric equilibrium in the series of acidinethiones I-X we used UV and IR spectroscopy and mass spectrometry. The use of UV spectroscopy was due to a difference in the electronic absorption spectra of 10-methyl-9-acidinethione XI and 9-methylmercaptoacridine [2] (the method of model compounds [5]). The presence of an absorption band of the thione group ($\nu C=S = 1230 \pm 5\ \mathrm{cm}^{-1}$ [2]) in the IR spectrum also permits the use of this method for the quantitative determination of the thione form.

First let us consider the influence of the nature of the solvent on the prototropic equilibrium in the system of 9-acridinethione (Table 1). The results of the investigation showed that the polarity of the organic solvent has no significant influence on the position of the tautomeric equilibrium. Table 1 presents comparative data for nonpolar solvents —

K. A. Timiryazev Moscow Agricultural Academy, Moscow 127550. Zaporozh's Medical Institute, Zaporozh'e 330074. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1519-1524, November, 1984. Original article submitted March 22, 1984.

0009-3122/84/2011-1254$08.50

TABLE 1. Influence of Solvents and the Ionic Strength of the Solution (a) on the Tautomeric Equilibrium 9-Acridinethione $\rightleftarrows$ 9-Mercaptoacridine (I) (t = 20°C)

a) According to UV spectra

Solvent	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$ liters/ mole · cm	Percent of thione form
1,4-Dioxane	480	2,58	82±5
Toluene	480	2,28	73±5
Chloroform	480	2,16	69±4
Isopropanol	479	3,00	96±6
Acetone	478	2,88	92±6
Acetonitrile	477	2,58	82±5
Nitromethane	477	2,76	88±6
Water	474	3,37	100±2
0,1 N KCl (*a*=0,08)	474	2,95	94±2
0,2 N KCl (*a*=0,14)	474	2,85	91±2
0,5 N KCl (*a*=0,33)	474	2,65	85±2
1,0 N KCl (*a*=0,97)	474	2,39	76±2
2,5 N. KCl (*a*=1,42)	474	1,94	58±2
Ethanol–water, k 1:1	478	3,10	99±2

b) According to IR spectra

Solvent	ν,cm^{-1}	ε, liters/ mole · cm	Percent of thione form
Toluene	1217	430	77±5*
Chloroform	1217	460	83±5*
Isopropanol	1217	—	82±5 †

*Calculated by the method of model compounds [5].

†Calculated by the internal standard method [5].

toluene (dielectric permeability ε = 2.4) and chloroform (ε = 4.7) – and polar solvents – nitromethane (ε = 38.6), acetone (ε = 20.7), etc. The content of the thione form is an average of 80%. In water and aqueous alcohol the equilibrium is shifted in the direction of the thione form (Table 1). The data obtained by two independent methods (IR and UV spectroscopy) are in good mutual agreement (Table 1).

Increasing the ionic strength of an aqueous solution of compound I by the addition of KCl shifts the position of the equilibrium in the direction of the thiole, which is probably determined by the strength of the solvates formed.

A change in the temperature of the solution has different effects on the position of thione-thiol tautomeric equilibrium. Thus, when the temperature of a nonpolar toluene solution is increased from –40 to +85°C, the percent of the thione form falls from 75 to 57%, whereas in a polar solvent (in acetone), a change in the temperature has no effect on the position of tautomeric equilibrium (Table 2).

The electronic nature of the substituent R in the phenyl ring of 9-acridinethiones has no significant effect on the ratio of the tautomers (Tables 1 and 3). Studying the IR spectra of solutions of this series of compounds in CCl_4, for three derivatives of 9-acridinethione we recorded a weak absorption band in the region of 2583 ± 3 cm^{-1}, which can be assigned to νS–H [6]. The band νNH in compounds I-X lies at 3435 ± 10 cm^{-1}. Let us note that the introduction both of an electron donor substituent and of an electron acceptor substituent into various positions of the acridine ring leads to a shift of the band νNH in the low-frequency direction (up to 20 cm^{-1}) in comparison with the unsubstituted compound I. In both cases the factor determining the position of tautomeric equilibrium is the action of the solvent, and not the electronic effects of the substituents. It is known that phase transitions may lead to a shift of the tautomeric equilibrium [7, 8]. In connection with this we made a quantitative study of the influence of phase transitions (crystal $\rightleftarrows$ solution $\rightleftarrows$ vapor) on the ratio of the tautomers in substituted 9-acridine-thiones by the methods of IR, UV, and mass spectrometry.

According to the data of the IR and UV spectra, in a crystal the I molecule is in the thermodynamically more stable thione form, as evidenced by the optical density ratios of the bands νC=S ≈ 1230 cm^{-1} and ν = 1190 cm^{-1} that we obtained (we selected this band as an internal standard, Table 4). The ratio $D_{C=S}/D_{1190}$ is practically constant for the three substi-

TABLE 2. Influence of Temperature on the Tautomeric Equilibrium 9-Acridinethione ⇄ 9-Mercaptoacridine (I) (λ_{anal} = 480 nm)

Solution in toluene			Solution in acetone		
t, °C	$\varepsilon \cdot 10^{-4}$, liters/mole · cm	percent of thione formed	t, °C	$\varepsilon \cdot 10^{-4}$, liters/mole · cm	percent of thione formed
−40	2,34	75±5	−30	2,88	92±6
−38	2,34	75±5	−25	2,91	93±6
−8	2,31	74±5	−10	2,94	94±6
0	2,28	73±5	0	2,75	88±6
20	2,28	73±5	20	2,88	92±6
30	2,28	73±5			
50	2,06	66±4			
70	1,86	59±4			
85	1,80	57±4			

TABLE 3. Influence of Substituents on the Tautomeric Equilibrium in the System 9-Mercaptoacridine ⇄ 9-Acridinethione (t = 20°C)

Compound	IR spectrum (in CCl_4)		UV spectrum			
	νNH, cm	νSH, cm	λ_{anal}, nm	$\varepsilon \cdot 10^{-4}$, liters/mole · cm	% of thione formed	solvent*
I	3444	2580	478	2,88	92±6	a
				3,10	99±2	e
II	3442	—	486	3,10	99±3	e
III	3442	—				
IV	3424	—	480	2,81	89±5	a
V	3443	—	492	2,99	95±6	a
VI		—	488	3,06	98±2	e
VII	3435	—	477	3,00	96±6	a
VIII	3435					
IX	3435	2585	489	2,79	89±5	a
X	3433	2582				

*a represents acetone; e represents ethanol-water, 1:1.

TABLE 4. Influence of Phase Transitions on the Tautomeric Equilibrium in the System 9-Acridinethione (I)

Compound	Crystal (KBr tablet)			Vapor (t = 200-300°C)		
	IR spectrum		UV spectrum	UV spectrum		
	νC=S	$D_{C=S}/D_{1190}$	λ_{max}, nm	λ_{max}, nm	D_{495}/D_{235}	% of thione formed*
I	1223	2,59	440, 472, 504	234, 246, 460, 494	0,21±0,03	60±8
II			445, 475, 500	238, 248, 265, 465, 500	0,29	85±8
V			435, 461, 492	235, 253, 290 (mp), 430, 458, 494	0,35	100±8
VI	1220	2,27	370, 438, 465, 498	235, 265 (mp), 293, 358, 375, 432, 460, 495	0,35	100±8
IX	1220	2,46	400, 420, 485, 518	236, 400, 500	0,38	100±8
XI	1231	2,13	345, 364, 420, 448, 478, 512		0,35±0,02	100
XI†	1218	2,51			0,35±0,02	100

*According to the internal standard method.
†Solution in acetonitrile.

tuted 9-acridinethiones that we studied and the compound XI, which is known to exist in the thione form. In the UV spectra of crystalline samples of compounds I, II, V, VI, IX, and XI, intense bands were recorded in the region of 500 nm, characteristic of the thione form. We did not detect absorption bands of the thiol tautomer in the UV spectra of crystals of substituted 9-acridinethiones.

Thus, the transition from crystal to solution is accompanied by an approximately 20% decrease in the content of the thione form (Tables 1, 3, and 4).

A study of tautomerism in the gas phase has undoubted advantages, since in this case there are no intermolecular interactions, solvolysis, and a number of other external fac-

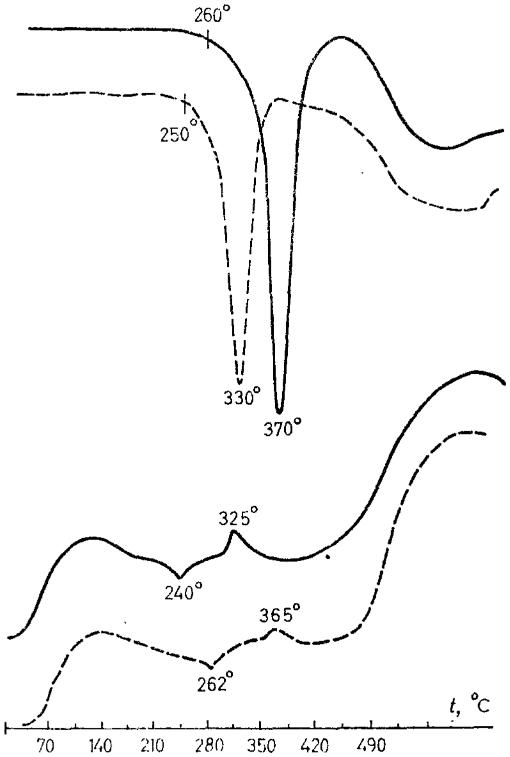


Fig. 1. Derivatograms (DTG and TG curves) of compounds I(——) and V (---).

tors. Only in vapors is the condition of monomolecularity of the system observed [9]. Factors holding back the wide development of studies of tautomerism in the gas phase are the low volatility of most of the condensed organic compounds and the possibility of thermal decomposition of the sample when the temperature of evaporation is increased [10].

Compound I has a rather high melting point (275°C). To obtain a vapor tension sufficient for recording the UV spectra it was necessary to heat this sample to 300°C. An analysis of the derivatogram of compounds I and V (Fig. 1) showed that the thermal decomposition of compound I begins at the temperature 365-370°C, and that of compound V at 325-330°C (DTG and TG curves, Fig. 1); consequently, at 300°C we analyzed the individual molecules I and V in the vapors.

Using the method of UV spectroscopy* (Table 4), we made a quantitative estimate of the relative content of the tautomers in the gas phase. As it follows from the data of Table 4, only compounds I and II contain appreciable amounts of the thiol form. For the remaining compounds the thione form substantially predominates.

It was of interest to compare the quantitative results obtained in the gas phase for a molecule in the ground state (UV spectroscopy), and for a molecule excited by electron impact (mass spectrometry). The successes achieved at present from the practical use of correlation functions between processes of fragmentation of the molecular ion (M^+) and the structure of the compound do not eliminate the question of the identity of the structure of M^+ and the neutral molecule. In the compounds I-X that we studied, factors distorting the picture of tautomeric conversions in the mass spectrometric investigation (rearrangement processes [10, 11], the presence of vicinal 1,2-substitution [12], steric interactions, and thermolysis) are absent. We showed experimentally that the ratio of the ions M^+ and the ions responsible for the concrete tautomeric form ($J_{M^+}/J_{[M-H]^+}$, $J_{M^+}/J_{[M-S]^+}$, $J_{M^+}/J_{[M-SH]^+}$ for the

---

*In this case we also used the internal standard method. The absorption bands at $\lambda \sim 250$ nm of 10-methyl-9-acridinethione (XI) and 9-methylmercaptoacridine are the same in intensity [2], but 9-methylmercaptoacridine does not absorb at $\lambda \sim 500$ nm [2], which permits the use of the quantity D_{495}/D_{250} for an estimation of the relative content of the tautomers.

TABLE 5. Mass Spectrometric Determination of Tautomers in the System of Substituted 9-Mercaptoacridines $\rightleftarrows$ 9-Acridinethiones (intensity in % of J_{max})

Compound	Ions					Percent of thione form,* B/(A+B)·100
	thiol form			thione form		
	$[M-H]^+$	$[M-S]^+$	$[M-SH]^+$	$[M-CS]^+$	$[M-CS]^{2+}$	
I	7,7	5,8	5,5	37,9	5,4	70
II	2,4	3,0	3,3	35,4	3,0	77
III	3,0	3,6	3,5	57,5	3,8	83
IV	2,5	—	—	52,9	3,5	95
V	10,5	—	—	28,9	3,6	76
VI	—	—	—	18,6	3,0	100
VII	—	2,2	—	26,0	1,8	93
VIII	—	—	2,4	31,6	2,2	93
IX	—	1,3	1,2	34,1	3,3	93
X	—	2,4	—	27,1	1,5	92

---

*$A = J_{[M=H]+} + J_{[M-S]+} + J_{[M-SH]+}$. $B = J_{[M-CS]+} + J_{[M-CS]^{2+}}$.

TABLE 6. UV Spectra of 10-Methyl-9-Thioacridone (XI)*

Solvent	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$ liters/mole·cm
Dioxane	492	2,85
Toluene	493	2,72
Chloroform	492	3,41
Propanol-2	489	3,08
Acetone	491	3,28
Acetonitrile	491	3,27
Ethanol	490	3,02 [2]
Heptane	485	3,55 [2]
60% aqueous dioxane	490	3,16 [2]

---

*ε_{av} = 3.14 ± 0.2 liters/mole·cm.

thiol $J_{M+}/J_{[M-CS]+}$ for the thione) remains constant within a wide range of temperatures of evaporation of the sample to be analyzed [13, 14], which is evidence of identity of the structure of M^+ and that of the neutral nolecule and suggests that it is correct to investigate the tautomeric ratios in the gas phase by the method of mass spectrometry. Table 5 presents the results of a mass spectrometric experiment on the quantitative determination of the ratio of tautomers in the compounds I-X.

The selection of the ions responsible for a concrete tautomer is limited by the primary processes of fragmentation. Their direct appearance from M^+ was demonstrated by an investigation of the mass spectra of metastable ions (the DADI technique).

The following ions were responsible for the thiol form of the molecule: $[M-H]^+$, $[M-S]^+$, and $[M-SH]^+$. It should be noted that the ion $[M-H]^+$, characterizing the thiol form, may arise on account of a randomized loss of a hydrogen atom from the acridine ring (this process constitutes 14.0% [15]) and not on account of β-elimination with respect to the heteryl ring. We considered this fact in a comparison of Table 5. The thione form is characterized by a process of elimination of a CS particle from M^+ and the corresponding doubly charged ion $[M-CS]^{2+}$. Considering the contribution of these ions to the total ionic current, performing a standardization, we obtained quantitative results (Table 5) determining the contribution of each form to the composition of M^+. Considering the error of the determination of tautomeric forms in both methods (in the method of mass spectrometry, 10-15% relative under the condition of reproduction of the mass spectra [16]), we should consider the results of the determination obtained in Tables 4 and 5 as identical.

The increase in the contribution of the thiol form to the composition of M^+ in the compound V is associated with elimination of a hydrogen atom from the substituent R, which is confirmed by the total absence of the ions $[M-S]^+$ and $[M-SH]^+$ in the mass spectra of this compound and the absence of the ion $[M-H]^+$ in the mass spectrum of compound VI.

As a result of our investigation it was shown that crystalline forms of compounds I-X are represented exclusively by a thione form; in isolated molecules in the gas phase this form also predominates, whereas in solutions the position of the tautomeric equilibrium depends primarily on the nature of the solvent and to a lesser degree on the ionic strength of the solution and its temperature.

EXPERIMENTAL

Spectral investigations were conducted on a Hitachi ESP-3T spectrophotometer, equipped with attachments and adaptations for the recording of low- and high-temperature spectra. The IR spectra were obtained on a UR-20 spectrometer. The UV and IR spectra of the crystals were obtained in tablets of KBr, and of solutions in quartz cuvettes with d = 1.0 cm (UV spectra) and 10 cm (IR spectra), and of gases in a quartz cuvette with d = 10 cm. Organic solvents were purified in the usual way. Double-distilled water was used to prepare the aqueous solutions.

The percent content of the tautomers (unless specially stipulated) was determined according to the method of model compounds [5]. 10-Methyl-9-acidinethione XI was used as a model compound with a fixed thione form. The UV spectra of compound XI in various solvents are cited in Table 6.

A mass spectrometric study of compounds I-X was performed on a Varian MAT-311A instrument by the technique of direct introduction. The conditions of recording of the mass spectra were standard. Energy of the ionizing electrons 70 eV. Temperature intervals in evaporation of substances I-X in an ion source from 30 to 200°C.

LITERATURE CITED

1. O. M. Cherntsov, Zh. Obshch. Khim., 14, 186 (1944).
2. V. P. Maksimets and O. N. Popilin, Khim. Geterotsikl. Soedin., No. 2, 191 (1970).
3. I. Gola and M. Ionescu, Stud. Univ. Babes Bolyai, Ser. Chem., 17, 77 (1972).
4. I. Panea, I. Coia, and M. Ionescu, Rev. Roum. Chim., 17, 1423 (1972).
5. I. Ya. Bershtein and Yu. L. Kaminskii, Spectrophotometric Analysis in Organic Chemistry [in Russian], Khimiya, Leningrad (1975), p. 230.
6. L. Bellamy, Infrared Spectra of Complex Molecules [Russian translation], IL, Moscow (1963), p. 590.
7. A. Maquestiau and R. Filammawg, Mass Spectrom. Rev., 1, 237 (1982).
8. N. A. Klyuev, I. S. Shpileva, L. I. Medvedeva, G. N. Lipunova, and N. B. Bednyagina, Khim. Geterotsikl. Soedin., No. 11, 1506 (1981).
9. I. S. Zefirov and S. S. Trach, Zh. Org. Khim., 12, 697 (1976).
10. N. A. Klyuev, Yu. V. Shurukhin, V. A. Konchits, I. I. Grandberg, V. L. Rusinov, V. A. Zyryanov, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., No. 2, 265 (1980).
11. M. M. Bersey, Mass Spectrom. Rev., 1, 3 (1982).
12. H. Schwarz, Top. Curr. Chem., 73, 231 (1978).
13. N. A. Klyuev, V. M. Adanin, I. Ya. Postovskii, and Yu. A. Azev, Khim. Geterotsikl. Soedin., No. 4, 547 (1983).
14. N. A. Klyuev, V. G. Zhil'nikov, G. G. Aleksandrov, I. I. Grandberg, and G. N. Lipunova, Zh. Org. Khim., 20, 162 (1984).
15. Catalog of Mass Spectral Data American Petroleum Institute Research, Project 44, Pittsburg, No. 637, 639.
16. V. A. Zamureenko, N. A. Klyuev, L. B. Dmitriev, and I. I. Grandberg, Izv. Timiryazevsk. S-Kh. Akad., No. 1, 156 (1979).