Investigation of 8-mercaptoquinoline (thiooxine) and its derivatives 110. Physicochemical properties of 5-amino-8-mercaptoquinoline

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Received 3 January 1983

Accepted for publication 6 July 1984

Some physicochemical properties of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline are described: electronic absorption spectra have been studied and molar absorption coefficients of ionized, protonated, thiolic and zwitterionic forms of 5-amino-8-mercaptoquinoline, of neutral and protonated form of 5-amino-8-methylmercaptoquinoline in aqueous solutions, as well as of thiolic and zwitterionic form of 5-amino-8-mercaptoquinoline and neutral form of 5-amino-8-methylmercaptoquinoline in organic solvents have been determined. In polar solvents 5-amino-8-mercaptoquinoline exists in considerable concentrations as the zwitterionic form and its concentration increases with the increase of dielectric permeability of the solvent.

Cumulation ionization constants have been determined and individual ionization constants of 5-amino-8-mercaptoquinoline have been calculated. It follows from the latter that amino group in the 5th position of quinoline ring considerably increases the basic properties of the heterocyclic nitrogen atom ($pK_B = 4.74$) and slightly diminishes the acidic properties of mercapto group ($pK_D = 7.44$) when compared to those of 8-mercaptoquinoline ($pK_B = 3.50$, $pK_D = 7.01$). This fact can be ascribed to the electron-donor effect. It may be concluded from the values of protonation constants of the heterocyclic nitrogen atom ($pK_{NH^+}^{SCH_3} = 4.74$) and primary amino group ($pK_{NH_3^+}^{SCH_3} = 0.50$) of 5-amino-8-methylmercaptoquinoline that for addition of a proton to the primary amino group considerably higher acidity than for addition of a proton to the heterocyclic nitrogen atom is necessary.

Solubility of 5-amino-8-mercaptoquinoline in water, dependence of extraction into organic solvents on hydrogen ion concentration in aqueous phase, two-phase ionization constant in the system chloroform—water ($pK_2' = 8.85$) and distribution constant between chloroform and water ($K_D = 1.4$) have been determined spectrophotometrically.

Описаны некоторые физико-химические свойства 5-амино-8-меркаптохинолина и 5-амино-8-метилмеркаптохинолина: изучены электронные спектры поглощения и определены молярные коэффициенты экстинкции ионизированной, протонированных, тиольной, цвиттерионной форм 5-амино-8-меркаптохинолина, нейтральной и протонированных форм 5-амино-8-метилмеркаптохинолина в водных растворах, а также тиольной и цвиттерионной форм 5-амино-8-метилмеркаптохинолина в органических растворителях. В полярных растворителях 5-амино-8-меркаптохинолин существует в значительных концентрациях в виде цвиттерионной формы, концентрация которой увеличивается с увеличением диэлектрической проницаемости растворителя.

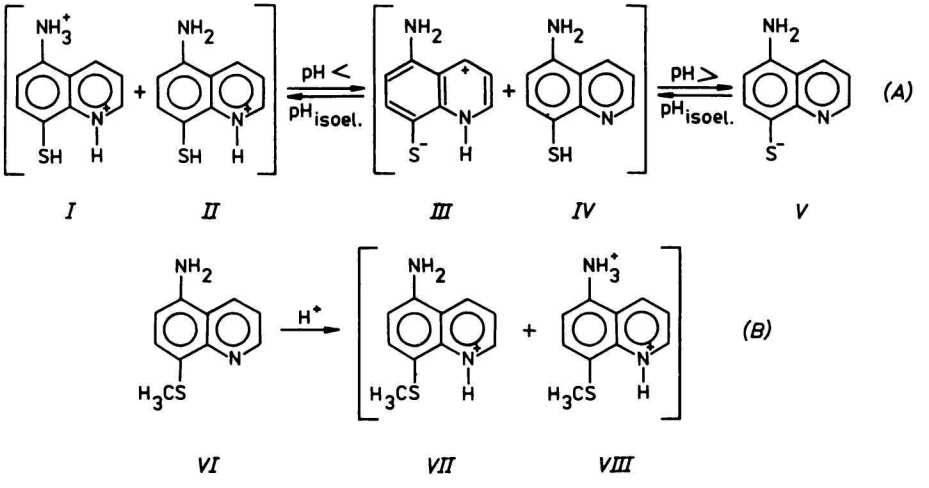
Определены брутто-константы ионизации и вычислены индивидуальные константы ионизации 5-амино-8-меркаптохинолина. Из последних следует, что аминогруппа в пятом положении хинолинового ядра вследствие электронно-донорного влияния значительно увеличивает основные свойства гетероциклического атома азота ($pK_B = 4{,}74$) и немного уменьшает кислотные свойства меркаптогруппы ($pK_D = 7{,}44$) по сравнению с таковыми 8-меркаптохинолина ($pK_B = 3{,}50$, $pK_D = 7{,}01$). Из показателей констант протонизации гетероциклического атома азота ($pK_{NH^+}^{SCH_3} = 4{,}74$) и первичной аминогруппы ($pK_{NH_3^+}^{SCH_3} = 0{,}50$) 5-амино-8-метилмеркаптохинолина можно сделать вывод, что для присоединения протона к первичной аминогруппе необходимо значительно более высокая кислотность, чем для присоединения протона к гетероциклическому атому азота.

Спектрофотометрическим методом определена растворимость в воде 5-амино-8-меркаптохинолина, зависимость экстракции органическими растворителями от концентрации ионов водорода в водной фазе, двухфазная константа ионизации в системе вода—хлороформ ($pK_2' = 8{,}85$) и константа распределения между хлороформом и водой ($K_D = 1{,}4$).

The investigation of different derivatives of 8-mercaptoquinoline, *i.e.*, the study of the influence of the nature and position of the substituents in the molecule on physicochemical and analytical properties of these reagents is of considerable theoretical and practical interest [1]. In the present investigation the effect of amino group in the 5th position of the molecule of 8-mercaptoquinoline upon physicochemical properties of the reagent was studied.

Absorption spectra

Equilibrium among different forms of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline in aqueous solutions in dependence on hydrogen ion concentration can be represented by the following explanatory schemes (*A*) and (*B*), respectively.



Absorption spectra of equilibrium forms of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline are shown in Figs. 1 and 2, maxima (λ_{max}) and molar absorption coefficients (ε_{max}) of these forms are given in Table 1.

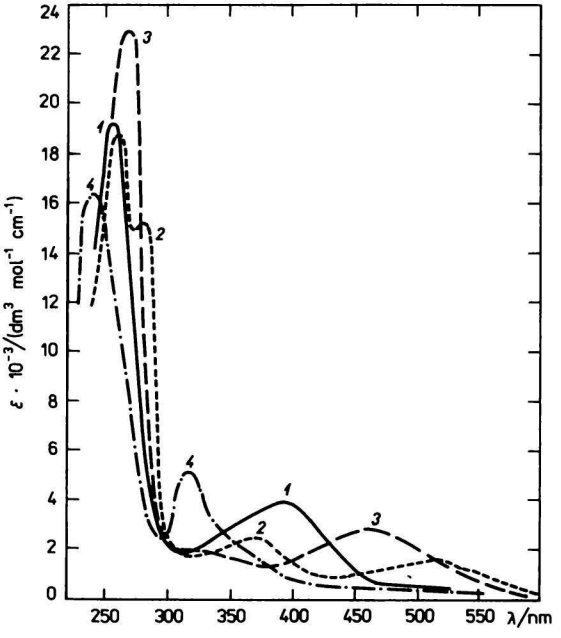


Fig. 1. Absorption spectra of aqueous solutions of 5-amino-8-mercaptoquinoline at different hydrogen ion concentrations: *1.* pH = 14; *2.* pH = 6; *3.* pH = 2; *4.* 5 M-HCl.

Table 1

Absorption maxima, molar absorption coefficients, and maximum formation intervals in aqueous solutions of equilibrium forms of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline

Form of reagent in solution	Maximum formation interval	$\frac{\lambda_{max}}{nm}$	$\frac{\varepsilon_{max}}{dm^3\ mol^{-1}\ cm^{-1}}$
5-Amino-8-mercaptoquinoline diprotonated (*I*)	≥5 M-HCl	242	16 800
		260 sh	
		319	4 900
		360 sh	
— monoprotonated (*II*)	pH 1—3	269	24 000
		320 sh	
		464	2 300
— zwitterionic (*III*)	pH 5—7	280	17 700*
		518	1 700*
— thiolic (*IV*)	pH 5—7	258	19 700*
		371	2 300*
— ionized (*V*)	pH≥12	253	20 000
		398	4 000
5-Amino-8-methylmercaptoquinoline neutral (*VI*)	pH≥7	257	20 600
		371	3 800
— monoprotonated (*VII*)	pH 1.5—3	269	29 000
		320 sh	
		447	2 600
— diprotonated (*VIII*)	≥4 M-HCl	242	13 600
		269	14 800
		319	3 900
		391	2 000

* Calculated from the total concentration of the reagent in solution, irrespective of the presence of other forms.

5-Amino-8-mercaptoquinoline is an amphoteric compound. In aqueous solutions at the isoelectric point (pH = 6.1) and closely to it 5-amino-8-mercaptoquinoline exists predominantly as the zwitterionic form (*III*, absorption maxima at 280 nm and 518 nm). The zwitterionic form is formed best of all in the range of pH 5 to 7 (Fig. 3, curve *1*) giving the violet coloured solutions. Alongside zwitterionic form there exists also thiolic form of 5-amino-8-mercaptoquinoline (*IV*, absorption maxima at 258 nm and 371 nm). The correctness of correlation of absorption maxima of the thiolic form is substantiated by coincidence of absorption spectra in aqueous solutions at pH≥7 (Fig. 2, Table 1), as well as in organic solvents (Fig. 5, Table 2) of 5-amino-8-methylmercaptoquinoline, in which the possibility to form

zwitterionic forms as a result of substitution of hydrogen atom by methyl group in mercapto group is excluded.

At pH values above isoelectric point (best of all at pH ≥ 12, Fig. 3, curve *4*), the ionized form of 5-amino-8-mercaptoquinoline (*V*, absorption maxima at 253 nm

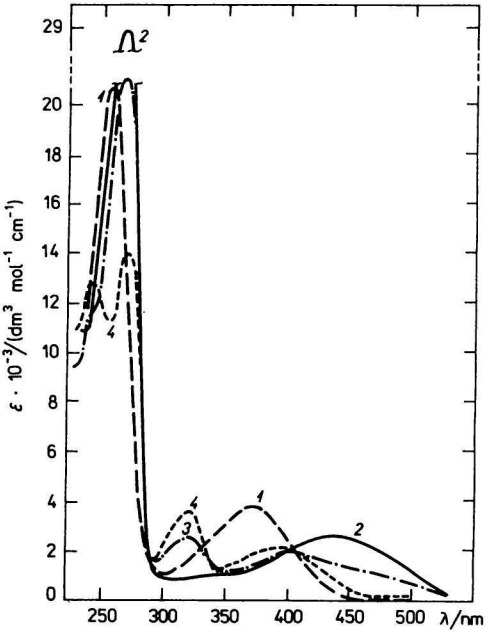


Fig. 2. Absorption spectra of aqueous solutions of 5-amino-8-methylmercaptoquinoline at different hydrogen ion concentrations: *1.* pH = 10; *2.* pH = 3; *3.* pH = 0; *4.* 5 M-HCl.

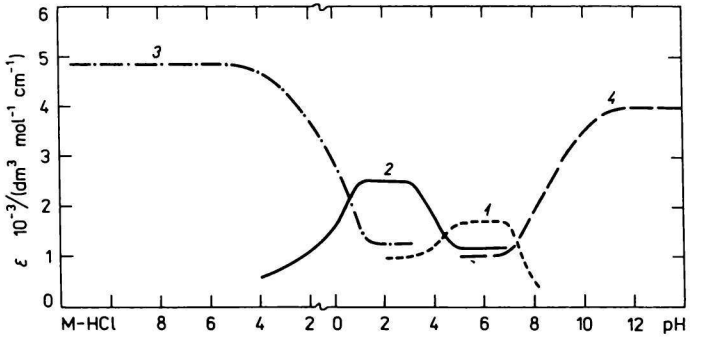


Fig. 3. Dependence of formation of zwitterionic (*1*), monoprotonated (*2*), diprotonated (*3*), and ionized form (*4*) of 5-amino-8-mercaptoquinoline on hydrogen ion concentration in aqueous solution.

and 398 nm) is formed. At pH values below isoelectric point the monoprotonated form (*II*, absorption maxima at 269 nm, 320 nm (shoulder), 464 nm) exists, which is formed best of all in the range of pH 1 to 3 (Fig. 3, curve *2*). The diprotonated form of 5-amino-8-mercaptoquinoline (*I*, absorption maxima at 242 nm, 260 nm (shoulder), 319 nm, 360 nm (shoulder)) is best of all formed in the media of $c \geq 5$ M-HCl (Fig. 3, curve *3*).

In aqueous solutions at pH = 1.5—3 5-amino-8-methylmercaptoquinoline (Fig. 4, curve *2*) exists predominantly as monoprotonated form (*VII*, absorption maxima at 269 nm, 320 nm (shoulder), 447 nm). On further increase of hydrogen ion concentration in media of $c \geq 4$ M-HCl (Fig. 4, curve *3*) diprotonated form is predominantly formed (*VIII*, absorption maxima at 242 nm, 269 nm, 319 nm, 391 nm; Fig. 2, Table 1).

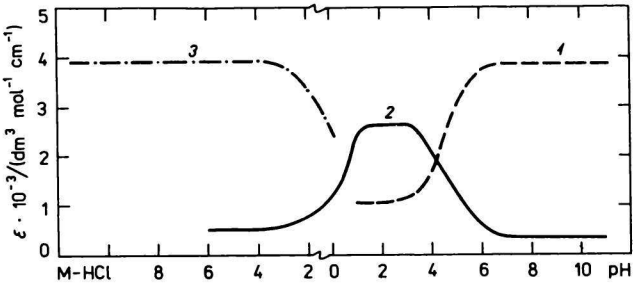


Fig. 4. Dependence of formation of neutral (*1*), monoprotonated (*2*), and diprotonated form (*3*) of 5-amino-8-methylmercaptoquinoline on hydrogen ion concentration in aqueous solution.

Protonation of nitrogen atom of amino group (*i.e.* formation of diprotonated form) takes place at considerably higher acidity of the medium than protonation of the heterocyclic nitrogen atom (formation of monoprotonated form).

As it is known [2—4] in case of quinoline, pyridine and acridine derivatives, the first to be protonated is the heterocyclic nitrogen atom. Analogous dependence is observed also in the case of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline: the first to be protonated is the heterocyclic nitrogen atom ($pK_{NH^+}^{SCH_3} = 4.74$) thus forming monoprotonated form (*II*, *VII*) and at considerably higher hydrogen ion concentration protonation of amino group takes place ($pK_{NH_3^+}^{SCH_3} = 0.50$) forming diprotonated form (*I*, *VIII*) where the heterocyclic nitrogen atom and amino group are protonated.

Bathochromic shift (93 nm) of the absorption band on protonation of the neutral form is conditioned by protonation of the heterocyclic nitrogen atom (monoprotonated form *II*). In more acidic solutions (best of all in the medium of $c \geq 5$ M-HCl)

protonation of the amino group takes place (diprotonated form, *I*), and it causes hypsochromic shift (104 nm) of this band with respect to the monoprotonated form (*II*).

Electronic absorption spectra of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline in some organic solvents (Fig. 5, Table 2) have been studied. In slightly polar and nonpolar organic solvents 5-amino-8-mercaptoquinoline exists as the thiolic form (absorption maxima at 260 nm and 374—380 nm) giving the yellow coloured solutions. In polar solvents, for instance, in *n*-aliphatic alcohols or in formamide beside the thiolic form there exists zwitterionic form of 5-amino-8-mercaptoquinoline (absorption maxima around 576—581 nm) which gives the greenish coloured solutions. Absorption spectra of 5-amino-8-mercaptoquinoline in nonpolar organic solvents are similar to those of 5-amino-8-methylmercaptoquinoline (Fig. 5, Table 2) because these two compounds under investigation in nonpolar solvents exist as the thiolic form.

It follows from Fig. 5 and Table 2 that in the ultraviolet part of spectra of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline there is an intense absorption band in the region around 260—262 nm (β-band) and a less intense absorption band in the region around 374—385 nm, which consists of

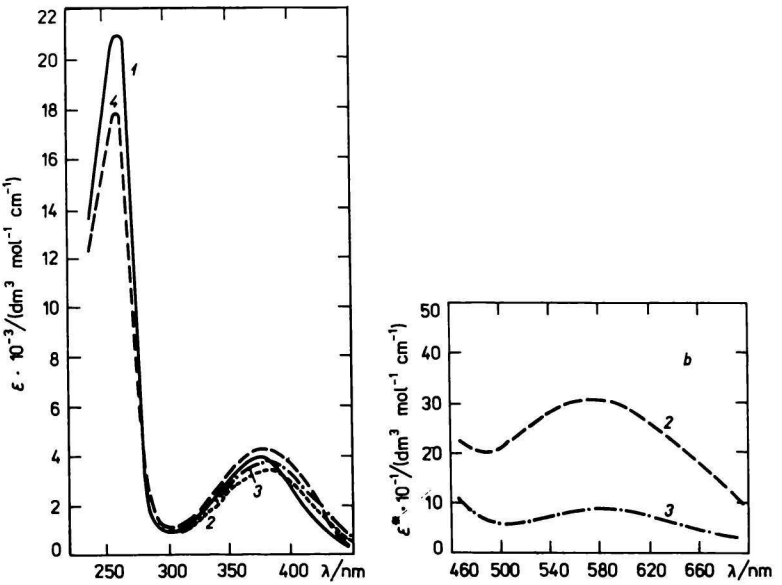


Fig. 5. Absorption spectra of 5-amino-8-mercaptoquinoline in chloroform (*1*), in formamide (*2*), in methanol (*3*) and those of 5-amino-8-methylmercaptoquinoline in chloroform (*4*). (ε^* — calculated from the total concentration of the reagent irrespective of the thiolic or zwitterionic form.)

Table 2

Absorption maxima and molar absorption coefficients of 5-amino-8-mercaptoquinoline, 5-amino-8-methylmercaptoquinoline, and 5,5′-diamino-8,8′-diquinolyl disulfide in organic solvents

Substance	Solvent	λ_{max} / nm	ε_{max} / $dm^3\ mol^{-1}\ cm^{-1}$
5-Amino-8-mercaptoquinoline	Chloroform	260	21 000
		374	4 000
	Benzene	380	3 900
	Methanol	259	
		385	3 700*
		581	80*
	Formamide	381	3 300*
		576	310*
5-Amino-8-methylmercaptoquinoline	Chloroform	262	17 800
		378	4 250
	Benzene	384	4 600
5,5′-Diamino-8,8′-diquinolyl disulfide	Chloroform	261	36 800
		376	9 200

* Calculated from the total concentration of the reagent, irrespective of the form, thiolic or zwitterionic.

a considerable intersection of α- and p-bands. All these absorption bands might be attributed to $\pi \rightarrow \pi^*$ electronic transition. It might be presumed that (α, p)-band coincidences with the closely spaced $n \rightarrow \pi^*$ transition band, appearing as a result of interaction of the lone electron pair on nitrogen atom with π-electrons of quinoline ring.

In solutions of 5-amino-8-mercaptoquinoline a bathochromic shift of absorption maxima of thiolic form is observed in comparison to 8-mercaptoquinoline ([1] p. 50) by 50—62 nm and of absorption maxima of zwitterionic form by 88—94 nm, due to the increase of coupling in the system under the influence of amino group in the 5th position of quinoline ring.

Zwitterionic form

In aqueous solutions almost all (92.5 %) 5-amino-8-mercaptoquinoline exists as the violet coloured zwitterionic form. Solutions of 5-amino-8-mercaptoquinoline in n-aliphatic alcohols are green in colour, in formamide — violet green. The colour of solutions of 5-amino-8-mercaptoquinoline in polar solvents depends on the position of absorption maximum of zwitterionic form and on concentration ratio of the thiolic and zwitterionic forms. The rise of the zwitterion and its stabilization in

polar solvents can be explained by the formation of molecular complex of the zwitterion with the molecule of the solvent.

Concentration of the zwitterionic form of 5-amino-8-mercaptoquinoline in aqueous solution at pH_{isoel} has been determined using *Ebert*'s equation [5]

$$K_t = \text{antilog}\,(pK_{NH^+}^{SCH_3} - pK_{NH^+}) - 1 \qquad (1)$$

For 5-amino-8-mercaptoquinoline the value $K_t = 12.4$ has been obtained, it corresponds to the content of zwitterionic form (92.5 %).

As it follows from Table 2, the molar absorption coefficient at the absorption maximum of thiolic form of 5-amino-8-mercaptoquinoline in nonpolar and slightly polar organic solvents depends on the nature of the solvent only to a little degree. However, in polar solvents as a result of existence of zwitterionic form, which is in equilibrium with the thiolic form, decrease of molar absorption coefficient at absorption maximum of thiolic form is observed. The strongest decrease of molar absorption coefficient is observed in formamide (concentration of zwitterionic form is the highest). Concentration of zwitterionic form in formamide (≈ 17 %) has been calculated according to the decrease of molar absorption coefficient at absorption maximum of thiolic form in formamide, if compared to the mean value of molar absorption coefficient of thiolic form in nonpolar and slightly polar solvents, as described in paper [6].

Molar absorption coefficient of zwitterionic form of 5-amino-8-mercaptoquinoline in formamide has been found to be $\varepsilon_{zwit} = 1800\ dm^3\ mol^{-1}\ cm^{-1}$.

Analogously to the independence of the value of molar absorption coefficient of thiolic form of 5-amino-8-mercaptoquinoline upon the nature of the solvent one can presume the same independence also for zwitterionic form [7]. Therefore ε_{zwit} found in formamide can be applied to determination of the concentration of zwitterionic form of 5-amino-8-mercaptoquinoline in other solvents, *e.g.*, in methanol zwitterionic form of 5-amino-8-mercaptoquinoline was found to be ≈ 4 %.

In the case of 5-amino-8-mercaptoquinoline, and also as it was shown previously for 8-mercaptoquinoline and series of its derivatives [1] there generally exists a tendency towards proportional dependence between concentration of zwitterionic form and dielectric permeability of the solvent.

Ionization constants and distribution constants in two-phase system

Denoting the free 5-amino-8-mercaptoquinoline (*IV*) as RNSH, 5-amino-8-mercaptoquinolinate ion (*V*) as RNS^-, 5-amino-8-mercaptoquinolinium ion (*II*) as RNH^+SH, the free 5-amino-8-methylmercaptoquinoline (*VI*) as H_2NRN, 5-amino-8-methylmercaptoquinolinium ion (*VIII*) protonated at heterocyclic ni-

trogen atom as H_2NRNH^+ and 5-ammonio-8-methylmercaptoquinolinium ion (*VIII*) protonated at the amino group as $^+H_3NRNH^+$, the ionization processes may be expressed in the following way

$$RNH^+SH \rightleftarrows RNSH + H^+ \qquad pK_1 = pH - \log \frac{[RNSH]}{[RNH^+SH]} \qquad (2)$$

$$RNSH \rightleftarrows RNS^- + H^+ \qquad pK_2 = pH - \log \frac{[RNS^-]}{[RNSH]} \qquad (3)$$

$$H_2NRNH^+ \rightleftarrows H_2NRN + H^+ \qquad pK_{NH^+}^{SCH_3} = pH - \log \frac{[H_2NRN]}{[H_2NRNH^+]} \qquad (4)$$

$$^+H_3NRNH^+ \rightleftarrows H_2NRNH^+ + H^+ \qquad pK_{NH_3^+}^{SCH_3} = pH - \log \frac{[H_2NRNH^+]}{[^+H_3NRNH^+]} \qquad (5)$$

pK_1 characterizes the basic properties of heterocyclic nitrogen atom, pK_2 the acidic properties of mercapto group in the molecule of 5-amino-8-mercaptoquinoline, $pK_{NH^+}^{SCH_3}$ the basic properties of heterocyclic nitrogen atom in the molecule of 5-amino-8-methylmercaptoquinoline and $pK_{NH_3^+}^{SCH_3}$ the basic properties of nitrogen atom of amino group in 5-amino-8-methylmercaptoquinolinium ion.

Spectrophotometric methods were used for determination of ionization constants. Spectrophotometric determination of ionization constants is performed at analytical wavelength at which the greatest difference of values of absorbance is observed (at identical concentrations and thickness of layer of solution) among reagent forms involved in equilibrium. The values of ionization constants of 5-amino-8-mercaptoquinoline have been calculated using eqn (*6*) and those of protonation constants of 5-amino-8-methylmercaptoquinoline using eqns (*7*) and (*8*)

$$pK_2 = pH + \log \frac{\varepsilon_1 - \varepsilon}{\varepsilon - \varepsilon_M} \qquad (6)$$

$$pK_{NH^+}^{SCH_3} = pH + \log \frac{\varepsilon - \varepsilon_M}{\varepsilon_2 - \varepsilon} \qquad (7)$$

$$pK_{NH_3^+}^{SCH_3} = pH + \log \frac{\varepsilon_2 - \varepsilon}{\varepsilon - \varepsilon_3} \qquad (8)$$

where ε — molar absorption coefficient of mixture of equilibrium forms,
ε_1 — molar absorption coefficient of ionized form of 5-amino-8-mercaptoquinoline,
ε_2 — molar absorption coefficient of monoprotonated form of 5-amino-8-mercaptoquinoline,
ε_3 — molar absorption coefficient of diprotonated form of 5-amino-8-methylmercaptoquinoline,
ε_M — molar absorption coefficient of neutral form of the substance.

By means of the spectrophotometric method ($I = 0.1$ mol dm^{-3}, $\theta = 20$ °C, in the presence of 2 % ethanol), the following values of ionization constants for 5-amino-8-mercaptoquinoline $pK_2 = 8.72 \pm 0.04$ and those for 5-amino-8-methylmercaptoquinoline $pK_{NH^+}^{SCH_3} = 4.74 \pm 0.02$ and $pK_{NH_3^+}^{SCH_3} = 0.50 \pm 0.02$ have been calculated.

Ionization constants characterizing basic properties of nitrogen atom in the molecule of 5-amino-8-mercaptoquinoline could not be determined using the spectrophotometric method because of the rapid oxidation of the reagent in acidic medium.

By the potentiometric method for 5-amino-8-mercaptoquinoline the following values of cumulation ionization constants have been obtained: $pK_1 = 3.46 \pm 0.04$ and $pK_2 = 8.75 \pm 0.04$.

Since 5-amino-8-mercaptoquinoline in aqueous solutions exists as both the thiolic form and the zwitterionic form (92.5 %), the constants K_1 and K_2 are cumulation constants and do not give correct notion about acidic properties of mercapto group and basic properties of nitrogen atom. Equilibrium among different forms of 5-amino-8-mercaptoquinoline is characterized more properly by individual ionization constants K_A, K_B, K_C, and K_D. Only pK_B is determined experimentally ($pK_B = pK_{NH^+}^{SCH_3}$), negative logarithms of other individual ionization constants are calculated using eqns (*9*—*11*)

$$pK_A = pK_B - \log K_t \qquad (9)$$

$$pK_C = pK_1 + pK_2 - pK_A \qquad (10)$$

$$pK_D = pK_1 + pK_2 - pK_B \qquad (11)$$

The following values have been obtained: $pK_A = 3.65$; $pK_B = 4.74$; $pK_C = 8.53$; $pK_D = 7.44$.

It follows from protonation constants of heterocyclic nitrogen atom, $pK_{NH^+}^{SCH_3} = 4.74$, and those of primary amino group, $pK_{NH_3^+}^{SCH_3} = 0.50$, that the addition of a proton to the primary amino group (*i.e.*, the second proton) requires considerably higher acidity than the addition of the first proton to the heterocyclic nitrogen atom. An analogous regularity is observed for 5-aminoquinoline ([4] p. 85), $pK_2 = 5.46$, $pK_1 = 0.97$. As seen from individual ionization constants of 5-amino-8-mercaptoquinoline, amino group in the 5th position of quinoline ring due to the electron-donor effect considerably increases basic properties of nitrogen atom and slightly decreases acidic properties of mercapto group if compared to those of the molecule of 8-mercaptoquinoline ($pK_B = 3.50$, $pK_D = 7.01$) ([1] p. 90).

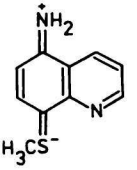
According to the data listed in Table 3 introduction of NH_2 group into the molecule of 8-*S*-methylquinoline causes considerably larger increase of basic properties of nitrogen atom ($\Delta pK_{NH^+} = 1.24$) than it results from additive contribution of this group in 5-aminoquinoline ($\Delta pK_{NH^+} = 0.52$). It follows from the

Table 3

Changes of basic properties of nitrogen atom on introduction of NH_2 group into the molecule of quinoline and of 8-*S*-methylquinoline determined experimentally (ΔpK_{NH^+}) and calculated in *sp*- and *spd*-bases of sulfur atom

Compound	ΔpK_{NH^+}	$\Delta pK_{NH^+}^{(theor)}$ (*sp*-base)	$\Delta pK_{NH^+}^{(theor)}$ (*spd*-base)
5-Amino-quinoline	0.52	0.40	0.40
5-Amino-8-*S*-methylquinoline	1.24	0.30	1.60

calculation of protonation energy of this compound (approach of CNDO/2 *spd*-base of sulfur atom [10]) that the observed changes of pK_{NH^+} value are conditioned by the contribution of structure *IX* in the fundamental state of



IX

5-amino-8-methylquinoline. In comparison to 5-amino- and 8-*S*-methylquinoline, in this compound bond energy C—NH_2 (ΔE 0.15 eV), S—CH_3 ($\Delta E = 0.48$ eV) and the charge on nitrogen atom ($\Delta q = +0.004$) and sulfur atom ($\Delta q = -0.020$) are increased. According to this the energy of hydrogen bond S...$^+$NH in the protonated form of 5-amino-8-*S*-methylquinoline if compared to 8-*S*-methylquinoline increases.

The intervals of extraction of 5-amino-8-mercaptoquinoline into organic solvents are restricted by pH values of aqueous phase at which in considerable concentration ionized and protonated forms of 5-amino-8-mercaptoquinoline are formed. 5-Amino-8-mercaptoquinoline is best of all extracted into chloroform in the range of pH = 4.5—9 and into benzene in the range of pH = 5—9 (Fig. 6).

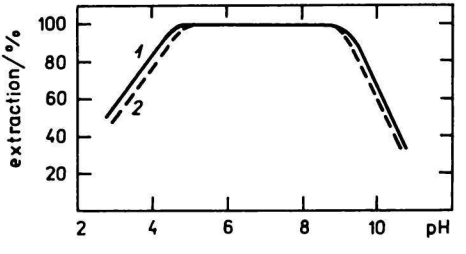


Fig. 6. Dependence of extraction of 5-amino-8-mercaptoquinoline on hydrogen ion concentration in aqueous phase: *1.* chloroform; *2.* benzene.

Distribution constant of 5-amino-8-mercaptoquinoline in the system organic solvent—water at isoelectric point is expressed as follows

$$K_D = \frac{[RH]_O}{\Sigma [R]_B} \tag{12}$$

where $\Sigma [R]_B = [RH]_B + [RH^{+-}]_B$ is the sum of molar concentrations of the thiolic $[RH]_B$ and zwitterionic $[RH^{+-}]_B$ form in aqueous phase at isoelectric point. Distribution constant of 5-amino-8-mercaptoquinoline in the system chloroform—water $K_D = 1.4$ was found spectrophotometrically.

Two-phase ionization constant of 5-amino-8-mercaptoquinoline in the system organic solvent—water in accordance to equilibrium

$$[RH]_O \rightleftarrows [R^-]_B + [H^+]_B$$

(where $[RH]_O$ is concentration of neutral molecules in organic phase and $[R^-]_B$ is concentration of ionized molecules in aqueous phase) is expressed by the following equation

$$K_2' = \frac{[R^-]_B [H^+]_B}{[RH]_O} \tag{13}$$

or logarithmically

$$pK_2' = pH + \log \frac{[RH]_O}{[R^-]_B} \tag{14}$$

$$[R^-]_B = [R_{total}] - [RH]_O$$

Equilibrium concentration of neutral molecules in organic phase is found according to *Beer*'s equation

$$[RH]_O = \frac{A_O}{\varepsilon_O} \tag{15}$$

where A_O is absorbance of the organic phase at absorption maximum of the reagent and ε_O is maximum molar absorption coefficient of the reagent in organic solvent.

Two-phase ionization constant of 5-amino-8-mercaptoquinoline in the system chloroform—water was found to be $pK_2' = 8.85$ ($\theta = 20$ °C).

Experimental

For investigation of physicochemical properties of 5-amino-8-mercaptoquinoline its bis-(hydrochloric acid) salt 5-ammonio-8-mercaptoquinolinium dichloride, $C_9H_8N_2S \cdot 2HCl$, was used which was obtained in the form of orange needle crystals (*II*). This compound is readily soluble in water, methanol or ethanol [11].

5-Amino-8-mercaptoquinoline dissolved in *n*-aliphatic alcohols and especially in aqueous solutions is comparatively quickly oxidized by air oxygen to 5,5′-diamino-8,8′-diquinolyl disulfide. Therefore investigations in aqueous solutions were performed in argon atmosphere but in neutral and alkaline solutions where very rapid oxidation is observed also in the presence of $Na_2S_2O_4 \cdot 2H_2O$ as reducing agent. To diminish oxidation in solutions of *n*-aliphatic alcohols and in formamide triphenylphosphine was used which reduces aromatic and alkyl disulfides [12].

Solubility in water was determined spectrophotometrically at $pH_{isoel} = 6.1$ in acetate buffer solution ($I = 0.1$ mol dm^{-3}) in the presence of $Na_2S_2O_4 \cdot 2H_2O$. Saturated solution of 5-amino-8-mercaptoquinoline is prepared by dissolving its bis(hydrochloric acid) salt in preliminarily with argon saturated acetate buffer solution ($pH \approx 7$) containing 0.3 % $Na_2S_2O_4 \cdot 2H_2O$. Dissolution is performed by blowing through argon for 15 min. After dilution of the saturated solution of the reagent with buffer solution of $pH = 6.1$ (preliminarily saturated with argon) absorbance of the solution is measured at the absorption maximum of zwitterionic form of the reagent at 518 nm. Concentration of 5-amino-8-mercaptoquinoline is found on the basis of calibration curve. Solubility of 5-amino-8-mercaptoquinoline in water (17×10^{-3} mol dm^{-3}) could be determined approximately (with the error of 20 %) because of rapid oxidation of the reagent in neutral aqueous solutions.

Absorption spectra of 5-amino-8-mercaptoquinoline and 5-amino-8-methylmercaptoquinoline have been taken at different ion concentrations in the presence of 2 % of ethanol ($c = 1 \times 10^{-4}$—2×10^{-4} mol dm^{-3}).

For diminishing the oxidation of aqueous solutions of 5-amino-8-mercaptoquinoline the applied buffer solutions and aqueous solutions containing various molar concentrations of hydrogen chloride were saturated with highly pure argon. Neutral and alkaline solutions of 5-amino-8-mercaptoquinoline contained 0.1 % of $Na_2S_2O_4 \cdot 2H_2O$. During dissolution of the reagent a stream of argon was blown through the solution. Recording spectrophotometer Specord UV VIS was used for absorbance measurements of solutions of the reagent using 1 cm and 0.5 cm quartz cuvettes. In the control cuvette the respective buffer solution or correspondingly the buffer solution containing 0.1 % of $Na_2S_2O_4 \cdot 2H_2O$ is placed.

Determining dependence of formation of zwitterionic (*III*), monoprotonated (*II*), diprotonated (*I*), and ionized forms of 5-amino-8-mercaptoquinoline in aqueous solutions on hydrogen ion concentration, solutions were thermostated at 20 °C, pH was measured using a glass electrode. In order to diminish oxidation of 5-amino-8-mercaptoquinoline solutions the above-described measures were taken. Absorbance of aqueous solutions of 5-amino-8-mercaptoquinoline at different hydrogen ion concentrations was measured at absorption maximum of the respective equilibrium form. In the case of 5-amino-8-mercaptoquinoline for monoprotonated form (*II*) — at 464 nm, diprotonated (*I*) — at 319 nm, zwitterionic (*III*) — at 518 nm, ionized (*V*) — at 398 nm. In the case of 5-amino-8-methylmercaptoquinoline for diprotonated (*VIII*) — at 319 nm, monoprotonated (*VII*) — at 447 nm and neutral form (*VI*) — at 371 nm. In control cuvette there is buffer solution containing 0.1 % $Na_2S_2O_4$ or HCl solution of the respective molar concentration.

Determination of ionization constants

Ionization constant of 5-amino-8-mercaptoquinoline pK_2 was determined by spectrophotometric and potentiometric method and pK_1 using potentiometric method. Spectrophotometric determination of pK_2 of 5-amino-8-mercaptoquinoline ($c = 2 \times 10^{-4}$ mol dm^{-3}, $\theta = 20$ °C) has been performed in solutions saturated with argon and containing 2 % of ethanol and 0.1 % of $Na_2S_2O_4 \cdot 2H_2O$. According to molar absorption coefficients (ε/dm^3 mol^{-1} cm^{-1}) determined at 398 nm for neutral (840), ionized (4000) and combination of neutral and ionized forms (pH = 7—8.5) using eqn (*6*) pK_2 is calculated. Spectrophotometrically were determined also ionization constants of 5-amino-8-methylmercaptoquinoline $pK_{NH^+}^{SCH_3}$ and $pK_{NH_3^+}^{SCH_3}$ in the presence of 2 % ethanol in aqueous solutions, ionic strength of the solution being $I = 0.1$ mol dm^{-3} and $\theta = 20$ °C. Absorbance of the solutions of the reagent ($c = 1 \times 10^{-4}$—2×10^{-4} mol dm^{-3}) is measured at different hydrogen ion concentrations (pH = 4.5—5 and 0.2 M—1.5 M-HCl) at the wavelength 447 nm. Using molar absorption coefficients (ε/dm^3 mol^{-1} cm^{-1}) at 447 nm of neutral (320), monoprotonated (2600) and diprotonated form (470) and combination of neutral and monoprotonated, as well as mono- and diprotonated forms ionization constants were calculated by means of eqns (*7*) and (*8*). Radiometer pH-meter PHM-4 with a glass—calomel electrode was used for pH measurement of the solutions.

Ionization constants K_1 and K_2 of 5-amino-8-mercaptoquinoline have been determined potentiometrically. Potentiometric titration was performed applying automatic titrator TTT-II with titration equipment TTA-2, supplied with piston microburette (0.5 cm^3) of precision 0.0002 cm^3. Recording of titration curve is performed with the automatic titrograph SBR 2/SBU I (Radiometer, Copenhagen). Glass electrodes of the type G 202 B, G 202 C were used as indicators. Saturated calomel electrodes of the type K 100 were used as reference electrodes. In order to avert oxidation of aqueous solutions of 5-amino-8-mercaptoquinoline, titration is performed in a closed vessel in argon atmosphere. Certain amount of hydrochloric acid salt of 5-amino-8-mercaptoquinoline is placed in a 50 cm^3 beaker, stream of argon is let in, about 20 cm^3 of preliminarily boiled and with argon saturated twice distilled water are poured into it. Titration is performed with freshly made 0.5 M-solution of KOH [13], which does not contain CO_2. The solution is stirred with magnetic stirrer. Using pH meter PHM-28 pH of the solution is measured both at the beginning and at the end of the titration with the accuracy ± 0.01 pH. From the obtained titration curves the value of pK_1 and pK_2 can be graphically found [9].

When determining hydrogen ion concentration on extraction of 5-amino-8-mercaptoquinoline into organic solvents, aqueous solution of the reagent ($c = 1 \times 10^{-4}$ mol dm^{-3} in the presence of 0.2 % of $Na_2S_2O_4 \cdot 2H_2O$) at different pH values is vigorously shaken for 5 min with equal amount of chloroform or benzene. After separation of phases absorbance of the organic phase is measured at 374 nm ($CHCl_3$) or 380 nm (C_6H_6). pH of the aqueous phase is checked after the extraction with a glass electrode.

Two-phase ionization constant pK_2' of 5-amino-8-mercaptoquinoline in the system chloroform—water has been determined in pH range which corresponds to about 50 % of the extraction of the reagent. To 20 cm^3 of the solution of the reagent ($c = 2 \times 10^{-4}$ mol dm^{-3}) in the respective buffer 20 cm^3 of chloroform are added and shaken vigorously for 10 min. After separation of phases absorbance of the organic phase is

measured at maximum absorption in chloroform at 374 nm. pH of aqueous phase after extraction is measured with pH-meter PHM-4. In order to diminish oxidation of the reagent the aqueous phase contained 0.3 % of $Na_2S_2O_4 \cdot 2H_2O$, buffer solutions were preliminarily saturated with argon. Both phases were thermostated at 20 °C.

Distribution constant K_D of 5-amino-8-mercaptoquinoline between water and chloroform was determined spectrophotometrically at pH of aqueous phase 6.1, *i.e.*, at the isoelectric point using the method applied to determination of pK_2'. Absorbance of the aqueous phase is measured at the absorption maximum of zwitterionic form at 518 nm or at the absorption maximum of thiolic form at 371 nm.

In order to take absorption spectra solutions of 5-amino-8-mercaptoquinoline were prepared ($c = 1 \times 10^{-3}$—2×10^{-3} mol dm^{-3}) in chloroform, benzene, formamide, methanol and those of 5-amino-8-methylmercaptoquinoline in chloroform and benzene. To a certain amount of bis(hydrochloric acid) salt of 5-amino-8-mercaptoquinoline two drops of concentrated aqueous solution of sodium acetate are added and the free reagent is dissolved in organic solvent. In polar solvents solutions 5-amino-8-mercaptoquinoline is relatively quickly oxidized. In order to diminish oxidation methanol and formamide solutions contained 0.05 % and 0.02 % of triphenylphosphine, respectively. However, in order to take absorption spectra in methanol at the wavelengths shorter than 320 nm solutions were prepared without triphenylphosphine, as the latter has its own absorption spectrum in this region. In this case the spectrum of 5-amino-8-mercaptoquinoline was taken at short intervals using each time freshly made solution. As in such a case the reagent is partly oxidized, the exact value of molar absorption coefficient at 259 nm cannot be determined.

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