Effect of solvation upon the acid-base properties and reduction by polarography of thioamides

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The pK values of thioamides in water and water—ethanol mixtures have been determined, and the effect of substituents upon their reduction by polarography has been studied. The observed anomalies are interpreted in terms of the hydrogen bonds between the NH group and the solvent, the formation of which was proved by i.r. spectroscopy.

Были определены значения pK тиоамидов в воде и смешанных растворителях вода–этанол. Было изучено влияние заместителей на полярографическое восстановление функциональной группы. Наблюдаемые аномалии были объяснены при помощи представления об образовании водородных мостиков между NH группой и растворителем, что подтверждается ИК спектрами.

The acid-base properties of thioamides have been previously studied [1, 2], and the mechanism of their reduction by polarography was solved by comparing the currents of thioamides with those of the assumed reduction intermediates [3], and preparative reduction [4]. The present paper deals with the effect of the relative solvent permittivity upon the pK values of the studied class of substances, and with the effect of solvation upon the pK values and the half-wave potentials of the reduction waves. The mechanism of the reduction by polarography is supplied by the proof of the reversibility of the reduction currents obtained by means of Kalousek switch.

Experimental

2-Ethylisonicotinic, isonicotinic, nicotinic, benzoic, and *N*-diphenylthiobenzoic thioamides (*I*—*IV* and *XIV*, respectively) were prepared as previously described [5]. *p*-, *m*-, and *o*-Chlorothiobenzamides (*V* [6], *VI* [1], *VII*) were prepared as described. The latter compound was prepared applying the general procedure [7]. The *N*-substituted *p*-chlorobenzoic thioamides [methyl- (*VIII*), ethyl- (*IX*), phenyl- (*X*), dimethyl- (*XI*), phenylmeth-

yl- (*XII*), and diphenyl- (*XIII*)] were prepared from *p*-chlorobenzoyl chloride (Fluka) and the corresponding amine as described elsewhere [8]. The amines used for this purpose were products of Lachema, Brno except *N*-methylaniline which was prepared according to [9]. All compounds were isolated as recommended in [10]. *N*-Dimethylthiobenzamide (*XV*) was prepared according to [11]. The characteristic data for new compounds are listed in Table 1.

For the determination of pK 2.5×10^{-4} (or 1.2×10^{-4} for *X*) molar solutions in 50, 30, and 10% (w/w) ethanol (Lachema, Brno) and water were prepared and 10 ml of these were diluted with 15 ml of a buffer prepared in the same solvent. In the alkaline region a mixture of 0.05 M aminoacetic acid (Lachema, Brno) and 0.15 M sodium hydroxide (Lachema, Brno) or a solution of sodium hydroxide of a suitable concentration were used as buffers. In the acidic region solutions of perchloric acid (Jenapharm) of a suitable concentration, mixtures of 0.1 M perchloric and 0.1 M sodium dihydrogen phosphate monohydrate (Lachema, Brno), or a mixture of perchloric acid and monopotassium citrate (Lachema, Brno) were used as buffers. Spectral measurements were performed with a Unicam SP 1800 instrument using a 1 cm quartz cell. From the spectra obtained with solutions of different pH a wavelength suitable for pK measurements was selected and pK was calculated according to [1] (Table 2).

The pH was measured with a glass or a hydrogen electrode against a silver chloride electrode (for water solutions a saturated calomel electrode was used) as described [12]. For polarography 10^{-3} M solutions in 50% (w/w) ethanol were prepared and mixed with an equal volume of a buffer in the same solvent. The following buffers were used: 0.5 M

Table 1

Characterization of the prepared substances

Compound	Formula	*M*	Calculated/found			M.p., °C Solvent
			% C	% H	% N	
VII	C_7H_6ClNS	171.65	48.98	3.52	8.16	59—61
			48.82	3.65	8.27	Ethanol
VIII	C_8H_8ClNS	185.68	51.73	4.35	7.55	103—104
			51.81	4.42	7.54	Petroleum ether
IX	$C_9H_{10}ClNS$	199.71	54.12	5.05	7.02	53—54
			54.33	5.13	6.96	Petroleum ether
X	$C_{13}H_{10}ClNS$	247.74	62.97	4.07	5.66	157—158
			63.10	4.15	5.51	Ethanol
XI	$C_9H_{10}ClNS$	199.71	54.12	5.05	7.02	79—80
			54.34	5.19	6.73	Ethanol
XII	$C_{14}H_{12}ClNS$	261.77	64.23	4.62	5.35	92—93
			64.41	4.45	5.16	Ethanol
XIII	$C_{19}H_{14}ClNS$	323.83	70.47	4.36	4.32	126—127
			70.28	4.52	4.14	Ethanol

perchloric acid, 0.15 M phosphoric acid (Lachema, Brno), mixtures of 0.05 M citric acid (Lachema, Brno) with 0.5 M sodium hydroxide, 0.05 M triethanolamine (Lachema, Brno for chelatometry) and 0.5 M perchloric acid, or 0.05 M aminoacetic acid with 0.5 M sodium hydroxide. The ionic strength of the buffers was kept constant ($\mu = 0.5$) with sodium perchlorate (Lachema, Brno). The measurements were run using the previously described apparatus [12]. The character of the polarographical waves was checked by determining the dependence of the limiting current upon the concentration of the depolarizator, buffer, on the reservoir height and the temperature. The switched curves were recorded with the aid of a Kalousek switch [13] while the recorder EZ 7 (Laboratorní přístroje, Prague) was connected to the auxiliary potentiometer (Scheme 2) [14]. The microcoulometrical determination of the number of exchanged electrons done with an OH-404 instrument (Radelkis) gave, in agreement with [3], variable results. Therefore, the number of the exchanged electrons was determined by comparing the waves recorded with the evidently two-electron wave of benzoine [15] or with the waves of other thioamides of the known [3, 4] number of electrons exchanged during the process. The i.r. spectra for 5% solutions in chloroform or chloroform—dioxan mixtures (1:1) were obtained with a UR-10 (Zeiss, Jena) spectrometer.

Results and discussion

The i.r. spectra of *N*-monosubstituted thioamides measured in chloroform show a sharp absorption band at 3400—3420 cm^{-1} corresponding to the stretching vibrations of a free NH group [16, 17]. When the measurements were run in chloroform—dioxan a broad absorption band at ~3320 cm^{-1} was observed instead. The shift of the stretching vibrations to the lower wavelength values

Table 2

p*K* Values for *I*—*X*

Compound	λ nm	Concentration of ethanol (w/w)			
		50%	30%	10%	0%
I	296	12.11 ± 0.07[a]	11.87 ± 0.13	11.78 ± 0.09	11.72 ± 0.06
II	296	11.88 ± 0.07[a]	11.73 ± 0.08	11.68 ± 0.10	11.57 ± 0.08
III	296	12.20 ± 0.05[a]	12.01 ± 0.08	11.86 ± 0.12	11.82 ± 0.08
IV	294	13.16 ± 0.13[a]	12.93 ± 0.07	12.80 ± 0.08	12.76 ± 0.10
V	295	12.60 ± 0.08	12.40 ± 0.06	12.30 ± 0.14	12.25 ± 0.14
VI	295	12.49 ± 0.06	12.26 ± 0.11	12.20 ± 0.08	12.18 ± 0.09
VII	275	12.23 ± 0.07	12.13 ± 0.06	12.01 ± 0.10	11.95 ± 0.08
VIII	297	12.89 ± 0.14	12.64 ± 0.08	12.51 ± 0.10	12.45 ± 0.11
IX	285	12.98 ± 0.16	12.84 ± 0.11	12.64 ± 0.14	12.60 ± 0.08
X	245	10.50 ± 0.08	10.30 ± 0.13	–	–

a) Extracted from [5].

reflects the formation of hydrogen bonds between the NH group of the thioamides and the electron-donating atom of the solvent (in this particular case the atom of oxygen in dioxan).

Acid-base properties of *I* and *III* found in the acidic region, in agreement with other pyridinecarboxylic acid derivatives [18, 19], correspond to the protonation of the pyridine ring. For *I*—*III* in 50% ethanol the pK values of 2.21, 2.30, and 2.12, respectively, have been found. Thioamides dissociate in alkaline medium according to eqn (*A*)

$$R^1-\overset{\overset{S}{\|}}{C}-NH-R^2 \rightleftharpoons (R^1-\overset{\overset{\boxed{S}}{|}}{C}=N-R^2)^- + H^+ \qquad (A)$$

The pK values corresponding to the above-mentioned acid-base equilibrium are given in Table 2 and their dependence upon $1/\varepsilon_r$ is presented in Fig. 1 (the relative permittivities were extracted from [20]). A sort of peculiar dependence, unexpected according to the existing theory, was observed for pK *vs.* $1/\varepsilon_r$. Illogical values for ion radii have been obtained when these were calculated according to Born equation [21] using the found pK values. A comparison of pK for *IV*—*X* shows that the acid-base properties of the functional group are affected by the substitution on both the aromatic ring and the atom of nitrogen of the functional group. The pK values found for *VIII*—*X*, but not for *V*, correspond well to what one would expect according to the inductive effect of the substituents and σ^* constants of the Taft equation [22]. This agrees well with the previous observation according to which a lower pK was found for *N*-benzylthiobenzamide than for thiobenzamide [2]. The pK values presented herein reflect, in agreement with the literature [2], the formation of hydrogen bonds between the functional group and the solvent. During this process the electron pair involved in the formation of the hydrogen bond increases the electron density on the nitrogen atom of the functional group, increasing thus its basicity and, consequently, the pK of the functional group.

The oxido-reduction mechanism of the polarographical waves has been previously interpreted [3, 4]. All primary thioamides and none, except *XI*, of the secondary gave anodic diffusion waves. The secondary and tertiary thioamides have not produced anodic waves. The anodic waves observed with all primary thioamides at certain pH were identical (within the experimental error) as to the half-wave potentials and currents. The identical position of the anodic waves confirms the previous conclusion [4] according to which the anodic oxidation of primary thioamides results in the formation of nitriles which makes impossible to study the effect of the substituents upon the half-wave potentials.

In the cathodic region reduction waves confirming roughly previous conceptions [3, 4] were observed. In the acidic medium primary thioamides and their *N*-aryl derivatives produced purely diffusion currents; *N*-alkyl derivatives gave mixed diffusion and catalytic currents. The heterogeneous character of the waves obser-

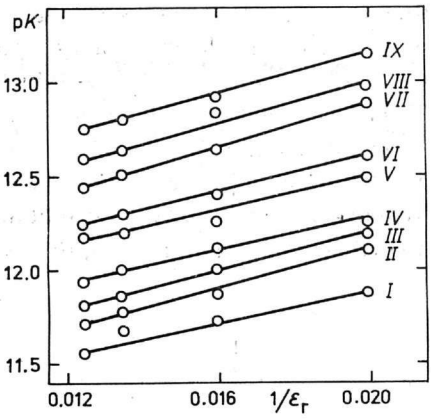


Fig. 1. Dependence of pK *vs.* $1/\varepsilon_r$ at 20°C.

ved in the acidic region makes in this case as well impossible to discuss the effect of the substituents upon the reduction of the functional group by polarography, and the attention was therefore focussed at the phenomena occurring in the alkaline region where, mostly, purely diffusion currents were observed. In agreement with [4] these currents corresponded to the exchange of four electrons, an exception being the case of *N*-diaryl derivatives where the exchange of one electron was observed. Fig. 2 shows the reduction waves for *VI* in alkaline region. It has been

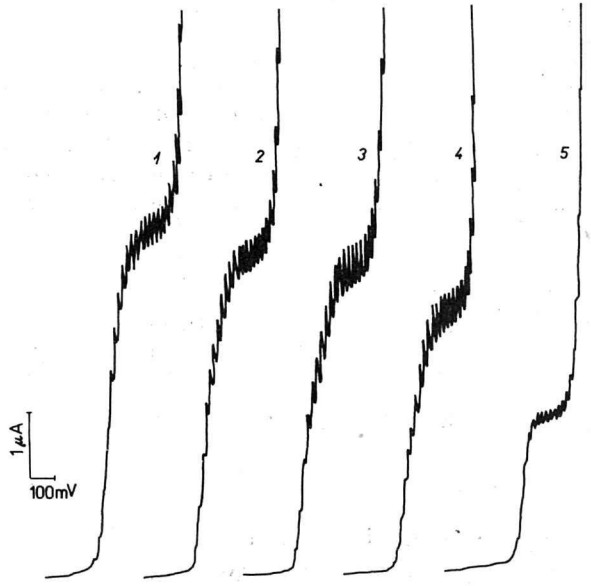


Fig. 2. Cathodic reduction of 5×10^{-4} M solutions of *m*-chlorothiobenzamide in 50% (w/w) ethanol. Ionic strength $\mu = 0.5$ (curves *1*—*4*); $\mu = 1$ (curve *5*), starting from -1.2 V. The curves recorded at pH: *1.* 8.95; *2.* 10.22; *3.* 10.88; *4.* 11.76; *5.* 1 M-NaOH.

found by means of Kalousek switch that in the presence of alkali hydroxides the waves are reversible and in a less alkaline medium the waves are irreversible. The reversible reduction of *VI* in a sodium hydroxide solution is demonstrated in Fig 3. Primary, secondary, and tertiary thioamides are subject to reversible reduction which can be expressed by eqn (*B*), valid also for the reduction of thioamides in aprotic solvents [23, 24]. The anion radical formed is a weak acid which under weakly alkaline conditions recombines with the solvent to give a neutral radical according to eqn (*C*) making the overall reduction irreversible

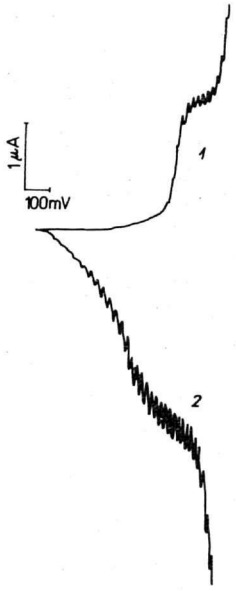
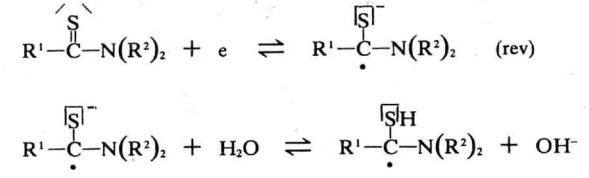


Fig. 3. Reduction of a 5×10^{-4} M solution of *m*-chlorothiobenzamide in 50% (w/w) ethanolic 2 M sodium hydroxide (curve *1*), starting from -1.0 V; the switched curve recorded under the same conditions at the auxiliary potential of -1.0 V (curve *2*).



(*B*)

(*C*)

When the formed radical is reducable a multi-electron reduction occurs; when it is not, as was the case with the *N*-diaryl derivatives, then the overall reduction is a one-electron process and the radical is deactivated by the medium. In solutions of alkali hydroxides *N*-alkyl derivatives gave poorly recognizable waves, in less alkaline solutions the half-wave potentials depended on pH. It seems therefore

reasonable to compare the effect of substitution upon the half-wave potential in a wider range of pH. The found half-wave potentials and current values are summarized in Table 3. It is obvious that the half-wave potentials of pyridinecarboxylic acid thioamides are more pH-dependent than those of other thioamides. Moreover, the reduction wave of the pyridinecarboxylic acid thioamides showed, in agreement with [3], a continuous alteration of the half-wave potential in the whole range of pH; the reduction waves of the protonized thiobenzamide and its derivatives were, in agreement with [4], always separated from the reduction waves of the free base. It follows from these observations that the mechanism of the reduction of pyridinecarboxylic acid thioamides differs from that of other substances. Much better correlations have been found between the half-wave potentials of *IV—XV* and the substitution effects. A conclusion can be made from the comparison of the half-wave potentials found for *IV, V, XI,* and *XV* with those of *XIII* and *XIV* that the substitution with chlorine at the *p*-position of the aromatic ring results in a shift of the half-wave potential to the more positive values by about 30 mV. A comparison of the half-wave potentials observed for *IV—VII* shows that

Table 3

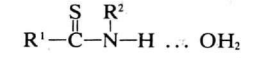
Half-wave potentials (V) and the currents (A) found for the studied substances in 50% (w/w) ethanol at the ionic strength $\mu = 0.5$

Compound	pH									
	8.97		9.97		10.70		12.13		1 M-NaOH	
	$-E_{1/2}$	$i \cdot 10^6$	$-E_{1/2}$	$i \cdot 10^6$	$-E_{1/2}$	$i \cdot 10^6$	$-E_{1/2}$	$i \cdot 10^6$	$-E_{1/2}$	$i \cdot 10^6$
I	1.05	5.70	1.12	4.78	1.15	3.36	1.19	2.95	1.30	2.39
II	1.04	5.45	1.10	3.34	1.12	3.00	1.16	2.88	1.28	2.69
III	1.34	4.50	1.39	3.16	1.41	2.56	1.45	2.72	1.54	2.39
IV	1.58	6.20	1.57	6.10	1.60	5.66	1.62	5.27	1.64	2.73
V	1.53	6.34	1.54	5.94	1.57	5.84	1.59	5.50	1.61	2.77
VI	1.51	5.96	1.50	5.30	1.50	5.05	1.53	4.72	1.57	2.45
VII	1.59	6.40	1.60	6.22	1.61	5.33	1.61	5.45	1.66	2.25
VIII	1.67	6.65	1.67	4.78	1.68	4.60	1.68	4.21	*a*	
IX	1.67	5.20	1.68	4.10	1.69	4.22	1.69	4.00	*a*	
X	1.50	4.05	1.52	3.56	1.54	3.22	1.56	2.60	*a*	
XI	1.64	5.37	1.66	4.66	1.66	4.55	1.66	3.57	*a*	
XII	1.48	3.88	1.49	3.39	1.49	3.10	1.49	3.06	1.47	2.22
XIII	1.30	1.67	1.31	1.28	1.31	1.34	1.30	1.28	1.28	1.28
XIV	1.33	1.55	1.34	1.28	1.34	1.00	1.34	1.00	1.32	1.28
XV	1.69	5.16	1.69	4.60	1.69	4.16	1.69	3.55	*a*	

a) The wave overlapped with that corresponding to the decomposition of the buffer. The half-wave potential could not be determined accurately.

the shift of the half-wave potential caused by the same substituent depends, as one would expect, on its position relative to the functional group. The half-wave potential is shifted also as a result of a substitution on the fuctional .group. A substitution of methyl with an ethyl group results in a shift of the half-wave potential to the more negative values by 10 mV (*cf. VIII* and *IX*), which corresponds to a more pronounced inductive effect of the ethyl group compared with methyl group. A comparison of the values found for *VIII—X* and *XII* (Table 3) shows that the substitution of the hydrogen atom of secondary thioamides (to give their tertiary counterparts) with methyl results in a shift to more positive potentials by 20—70 mV, whereas the same substitution of primary thioamides (to give the secondary analogues *V* and *VIII*) results in a shift by about 100 mV to the more negative potentials. In a similar manner, the substitution of the atom of hydrogen in secondary thioamides with a phenyl group (*cf. VIII* and *XII*, and *X* and *XIII*) results in a shift to the more positive potentials by 100—250 mV; the same substitution on primary thioamides causes a shift to the more positive potentials only by 30 mV.

It follows from the presented experimental material that the two hydrogen atoms of the NH_2 group do not behave in an equal manner when thioamides are being reduced. It seems probable, taking into consideration the found i. r. absorption bands and pH values, that during the process of reduction of primary thioamides on a drop electrode one of the atoms of hydrogen is solvated and, consequently, the reduced particle is a monohydrate



where R^2 is H, alkyl or aryl. Considering this assumption it is easy to understand the change of the half-wave potential resulting from the substitution. When only one atom of hydrogen is substituted the formed hydrogen bond does not cease to exist and the changed inductive effect corresponds to the substitution of the hydrogen atom for R^2. When also the second hydrogen atom is substituted, as a result of which the hydrogen bond cannot be formed any more, the changed inductive effect includes also the extinction of the hydrogen bond.

An effect of the hydrogen bonding upon the i.r. spectra, pK, and half-wave potential was previously observed in the case of hydroxylamine derivatives [12], where the pK and half-wave potential shifts were more pronounced than those found in this work. It seems therefore probable that the O—H...OH_2 bond of hydroxylamine derivatives is stronger than the analogous N—H...OH_2 bond of thioamides. As a result, the inductive effect of the electron pair involved in the formation of the hydrogen bond is also more pronounced in the case of hydroxylamine derivatives than in the case of thioamides studied herein.

References

1. Tissier, C. and Tissier, M., *Bull. Soc. Chim. Fr.* ***1970***, 3752.
2. Walter, W. and Becker, R. F., *Justus Liebigs Ann. Chem.* ***727***, 71 (1969).
3. Kane, P. O., *Electroanal. Chem.* ***2***, 152 (1960).
4. Lund, H., *Collect. Czech. Chem. Commun.* ***25***, 3313 (1960).
5. Mollin, J. and Labodová, A., *Collect. Czech. Chem. Commun.* ***42***, 517 (1977).
6. Kindler, K., *Justus Liebigs Ann. Chem.* ***450***, 1 (1926).
7. Fairfull, A. E. S., Lowe, J. L., and Peak, D. A., *J. Chem. Soc.* ***1952***, 742.
8. Voss, J. and Walter, W., *Justus Liebigs Ann. Chem.* ***716***, 209 (1968).
9. Ullmann, F., *Justus Liebigs Ann. Chem.* ***327***, 104 (1903).
10. Pravdič, N. and Hahn, V., *Croat. Chem. Acta* ***37***, 55 (1965).
11. Kindler, K., *Justus Liebigs Ann. Chem.* ***431***, 187 (1923).
12. Mollin, J., Kašpárek, F., and Lasovský, J., *Chem. Zvesti* ***29***, 39 (1975).
13. Ševčík, J. and Vacek, J., *Chem. Zvesti* ***23***, 501 (1969).
14. Heyrovský, J. and Kůta, J., *Základy polarografie.* (Basic Polarography.) P. 336. Czechoslovak Academy of Sciences, Prague, 1962.
15. Pasternak, R., *Helv. Chim. Acta* ***31***, 753 (1948).
16. Walter, W. and Steffen, M., *Justus Liebigs Ann. Chem.* ***712***, 53 (1968).
17. Kulevsky, N. and Froehlich, P. M., *J. Amer. Chem. Soc.* ***89***, 4839 (1967).
18. Mollin, J., *Collect. Czech. Chem. Commun.* ***40***, 2266 (1975).
19. Mollin, J. and Kučerová, T., *Collect. Czech. Chem. Commun.* ***41***, 2886 (1976).
20. Akerlof, G., *J. Amer. Chem. Soc.* ***54***, 4125 (1932).
21. King, E. J., *Acid-Base Equilibria*, p. 256. Pergamon Press, Oxford, 1965.
22. Newman, M. S., *Steric Effects in Organic Chemistry* (in Russian), p. 622. Izd. Inostr. Liter., Moscow, 1960.
23. Voss, J., *Justus Liebigs Ann. Chem.* ***1974***, 1220.
24. Voss, J., *Justus Liebigs Ann. Chem.* ***1974***, 1231.

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