CATHODIC REDUCTION OF ISATIN-3-OXIME

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The molecule of isatin-3-oxime was studied polarographically over the region of pH 1 to 13. Cathodic reduction within the region of pH 1 to 10.5 gives rise to a single four-electron polarographic wave due to the reduction of the oxime group, whereas two polarographic waves are observed at pH 10.5 to 13: one is due to the reduction of the isatin-3-oxime anion, the other, more negative wave is associated with the reduction of the oxime group in the α-oxime isatinic acid anion, which is the product of hydrolytic cleavage of the isatin ring in the basic pH region. The experimental results give evidence that the substance can exist as seven ionic and molecular species in dependence on pH. The species have been confirmed polarographically, by IR and electronic spectroscopy, potentiometrically and by paper electrophoresis.

Some metal chelates of 3-substituted derivatives of indole-2,3-diol (isatin) with diamagnetic metal ions have been found to exhibit properties of organic ferromagnetics in suitable physical conditions[1]. Among typical examples are chelates of 3-thiosemicarbazone isatin with CuCl (ref.[2]). The ferromagnetism of organic compounds depends on the chemical structure and properties of the substances involved in the chelates. Therefore we paid attention, in addition to isatin, also to the physico-chemical properties of isatin-3-oxime. Publications exist dealing with the polarographic properties of this compound. Calzolari[3] observed a single polarographic wave during the cathodic reduction of the compound in a 10% solution of isopropyl alcohol across the region of pH 1.95 to 11.38. This has laid the basis for the analysis of isatin-3-oxime over a wide pH region. Calzolari also employed this substance for the polarographic determination of various metals[4]. Andruzzi and coworkers[5] examined the polarographic behaviour of isatin-3-oxime in aqueous Britton–Robinson buffers and observed a single irreversible wave at pH 2 to 13. Ghandour and coworkers[6] investigated the effect of surfactants and some organic solvents (dioxane and methyl, ethyl and isopropyl alcohols) on the cathodic reduction of isatin-3-oxime in dependence on pH, using Britton–Robinson buffers across the region of pH 1.96 to 11.74. Two irreversible polarographic waves emerged at pH 10.79 and 11.74. The authors ascribed the one wave to the reduction of isatin-3-oxime and the other, more negative wave to the reduction of its anion. Some properties of isatin-3-oxime have also been studied by Košturiak and Pozemka in their paper[7].

The chelating properties of isatin-3-oxime and its applicability to analytical purposes have been dealt with in refs[8,9].

The papers hitherto published failed to pay sufficient attention to the changes in the structure of the molecule in dependence on pH, although it is well known that the properties and structure of chelates depend on the conditions under which the chelates have been synthesized. Therefore, the present work is aimed at investigating the structure of isatin-3-oxime in dependence on the pH of the solutions, which are analyzed by the polarographic technique. The data are supported by information obtained by using other physico-chemical methods, viz. UV-VIS and IR spectroscopy, potentiometric titration and paper electrophoresis.

EXPERIMENTAL

Isatin-3-oxime was synthesized following the published procedure[10,11]. The compound was recrystallized from an aqueous-ethanolic solution to obtain yellow crystals, m.t. 200 – 201 °C. All chemicals were of reagent grade purity (Lachema). The measurements were performed at pH 1 to 13 in HCl and NaOH solutions (0.1 mol dm^{-3}) and in Britton–Robinson buffers containing 20 vol.% ethanol; the reagent concentration was 0.4 mmol dm^{-3}, solution temperature 20 °C. Ionic strength was held constant at I = 0.1 mol dm^{-3} using KCl. The pH was measured with an OP-208/1 pH-meter fitted with an OP-0808P electrode (Radelkis, Budapest), the polarographic measurements were performed with an LP-7 polarograph (Laboratorní přístroje, Praha) using a thermostatted Kalousek vessel. Oxygen was removed by nitrogen purging, and gelatin was added as a surfactant. The potentials were measured against a saturated calomel electrode.

Electronic absorption spectra were measured on a Pye–Unicam PU 8800 UV/VIS spectrophotometer (Philips); optical path length 1 cm, isatin-3-oxime concentration 0.05 mmol dm^{-3}.

Infrared spectra were recorded over the region of 700 – 2 000 cm^{-1} using a Specord M 80 spectrophotometer (Zeiss, Jena). NUJOL mulls (4 mg of substance in 15 mg of NUJOL) were measured applying an optical path length of 0.02 mm. The reference cell contained pure NUJOL.

Whatman No. 1 paper was used for the electrophoresis. The electrostatic gradient of 9 V cm^{-1} was applied for 90 min. Potentiometric titrations were accomplished in solutions in 20 vol.% methanol containing the reagent in a concentration of 0.1 mmol dm^{-3}; ionic strength I = 0.1 mol dm^{-3}, temperature 25 °C. A Titroprocessor 672 (Metrohm, Switzerland) was employed. The results were processed with the ESAB program[12] on a High Screen 286-16 PC/AT.

RESULTS AND DISCUSSION

Figure 1, showing the cathodic reduction of isatin-3-oxime in dependence on pH over the region of pH 1 to 10.5, demonstrates a single wave (*a*) which decreases at higher pH values while a new wave (*b*) with a more negative half-wave potential appears. The sum of heights of the two waves is constant and equals to the height of the single wave (Fig. 2).

The $E_{1/2}$ vs pH dependence of the more positive wave is not linear. This gives evidence that the molecule of isatin-3-oxime exists in several molecular and ionic forms (species) in dependence on pH. This is also borne out by Table I.

Logarithmic analysis of the polarographic waves showed that the charge transfer coefficient α does not change linearly. Although a higher number of waves corresponding to different protonated isatin-3-oxime species failed to be identified in the acid region, the dependence of d*i*/d*E* on pH (Fig. 3) corroborates the above assumptions, although the d*i*/d*E* values in 0.1 M HCl and 0.1 M KOH are higher than as expected. This fact suggests that the d*i*/d*E* dependence is sensitive not only to the substance species but also to the supporting electrolyte used.

As far as the behaviour of isatin and its derivatives at different pH values is concerned, it is known that these substances reversibly open and close their five-membered heterocycles in basic aqueous solutions[13,14]. At pH 13, isatin occurs in the form of the corresponding isatinic acid salt, which is subject to a two-electron reduction[13].

This fact has been confirmed by a polarographic investigation of the basic hydrolysis of the >C=N– bond in 3-phenylimineoxindoles[15]. Polarographic waves of the cathodic

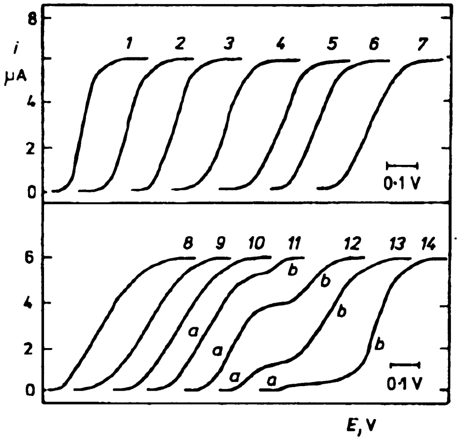


FIG. 1

DC polarograms of isatin-3-oxime (c = 0.4 mmol dm^{-3}) in Britton–Robinson buffer solutions containing 20 vol.% ethanol. Polarographic wave (pH, starting voltage (mV)): *1* 1.01, 0; *2* 2.62, -50; *3* 3.42, -100; *4* 4.40, -200; *5* 5.51, -250; *6* 6.62, -400; *7* 7.50, -450; *8* 8.52, -500; *9* 9.61, -550; *10* 10.50, -600; *11* 10.75, -600; *12* 11.60, -800; *13* 12.51, -900; *14* 13, 900. Single wave (*a*), new wave (*b*)

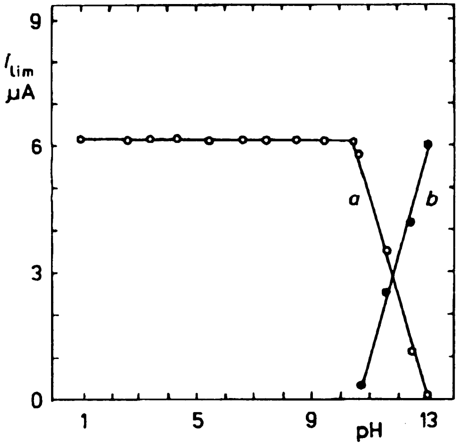


FIG. 2

The pH-dependence of the limiting current due to the cathodic reduction of isatin-3-oxime for the more positive (*a*) and more negative (*b*) polarographic waves reduction of isatinic acid and isatin-3-oxime at pH 13 are shown in Fig. 4. Isatin-3-oxime hydrolyzes to the α-oxime isatinic acid anion in basic solutions. The number of electrons used up during the reduction of isatin-3-oxime was determined by the comparative method[16]. Figure 4, as well as Figs 1 and 2, indicates that the substance undergoes four-electron reduction across the entire pH region investigated. This is consistent with the conclusions of the paper[7], whose authors, however, failed to take into account the hydrolysis of the compound to α-oxime isatinic acid. The α-oxime isatinic acid salt – the product of hydrolysis of isatin-3-oxime in basic solutions – was isolated and identified by IR spectroscopy. The IR spectrum of isatin-3-oxime (Fig. 5*a*) exhibits a strong band at 1 714 cm^{-1}, corresponding to the stretching vibration of the carbonyl group. A medium intensity shoulder occurs ar 1 664 cm^{-1}, due to the stretching vibration of the >C=N– group in position 3 of the isatin ring[17]. The isatin-3-oxime hydrolysis product, Fig. 5*b* on the other hand, displays no strong absorption band in the 1 700 cm^{-1} range; instead, two very strong absorption bands occur at 1 525 and 1 440 cm^{-1}, due to the symmetric and antisymmetric stretching vibrations, respectively, of the carboxylic anion. The stretching vibration of the >C=N– bond gives rise to a weak band in the 1 680 cm^{-1} range. The approximately 20 cm^{-1} shift of the >C=N– stretching vibration band of isatinic acid oxime to higher wavenumbers as compared to the corresponding band of isatin-3-oxime is apparently due to the neighbouring carboxylic anion. The hydrolytic product also exhibits a medium to strong absorption band at

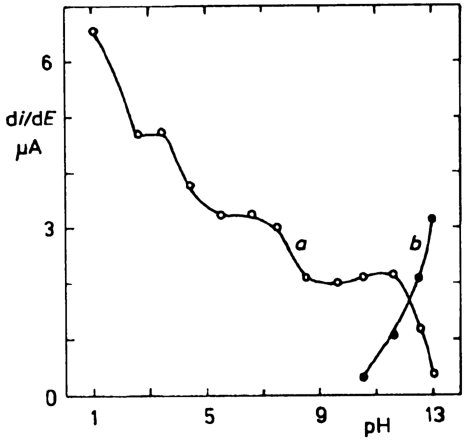


FIG. 3

The pH-dependence of the d*i*/d*E* value in the cathodic rection of isatin-3-oxime, for the more positive (*a*) and more negative (*b*) polarographic waves

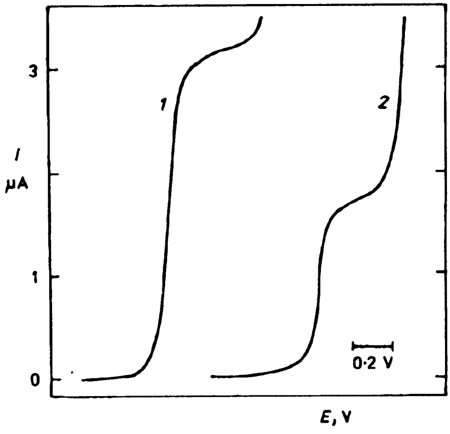


FIG. 4

Polarographic waves of cathodic reduction of α-oxime isatinic acid salt, which is the product of hydrolysis of isatin-3-oxime (*1*) and isatinic acid (*2*)

1 580 cm^{-1} which can be attributed to the NH_2 group; this band is absent from the spectrum of isatin-3-oxime.

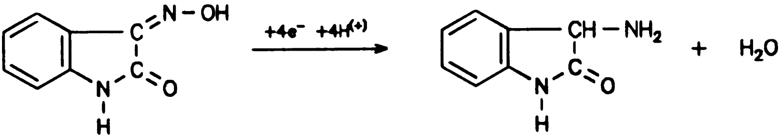
The dependences of the limiting current on the square root of the mercury column height, on the concentration and on time give evidence that the limiting current corresponding to the cathodic reduction of the oxime group in 0.1 mol dm^{-3} HCl is diffusion current, whereas in the Britton–Robinson buffer at pH 7.05, adsorption current is involved. This is consistent with the general concept of the polarographic behaviour of organic compounds[16], taking into account the chelating properties of the substance in question and the presence of mercury ions[10]. In Britton–Robinson buffers at pH 10.5 to 12.5, the limiting current of the two cathodic reduction waves has a kinetic nature. This is related to the reversible hydrolysis of the isatin ring. At pH 13, diffusion current occurs.

Taking into account the results of the polarographic and IR spectroscopic investigation, the course of cathodic reduction of isatin-3-oxime at pH 1 to 10.5 can be described by Scheme 1, whereas Scheme 2 refers to the region of pH 10.5 to 13.

TABLE I

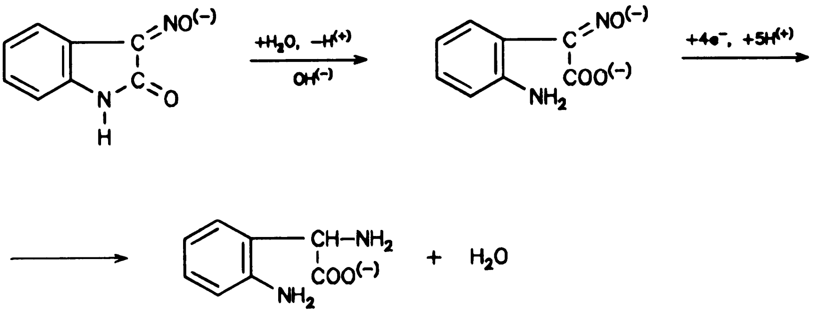
Polarographic characteristics of isatin-3-oxime; c = 0.4 mmol dm^{-3}, I = 0.1 mol dm^{-3}, t = 20 °C

pH	$-E_{1/2}$, mV vs SCE		$0.058/\alpha n$		i_{lim}, μA	
	wave *1*	wave *2*	wave *1*	wave *2*	wave *1*	wave *2*
1.01	125	–	0.045	–	6.3	–
2.62	270	–	0.057	–	6.1	–
3.42	265	–	0.067	–	6.2	–
4.40	420	–	0.070	–	6.1	–
5.51	495	–	0.079	–	6.2	–
6.62	565	–	0.082	–	6.2	–
7.50	620	–	0.087	–	6.2	–
8.52	700	–	0.130	–	6.2	–
9.61	810	–	0.145	–	6.3	–
10.50	815	–	0.150	–	6.1	–
10.75	835	1 080	0.152	–	5.7	0.5
11.60	975	1 210	0.159	0.179	3.5	2.6
12.51	1 020	1 320	0.182	0.158	1.2	4.9
13.01	1 025	1 370	–	0.081	0.1	6.1



SCHEME 1

The reduction of the oxime group of isatin-3-oxime or of the α-oxime isatinic acid salt gives rise to a single four-electron wave. Its division due to the reduction via the hydroxylamine intermediate[16] is never observed. Splitting of the polarographic waves[18] can be expected for the deprotonation of the oxime nitrogen in acid solutions, where the molecule carries positive charges due to protonation. No splitting, however, is actually



SCHEME 2

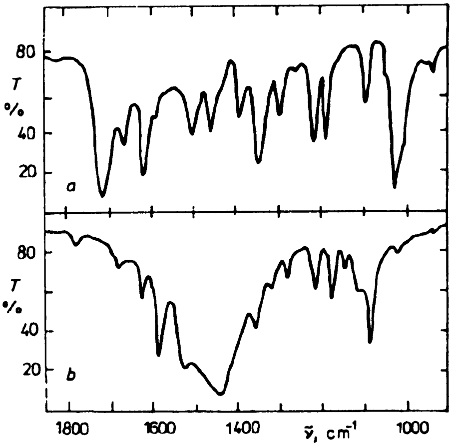


FIG. 5

Infrared spectra of isatin-3-oxime (*a*) and α-oxime isatinic acid salt as the isatin-3-oxime hydrolysis product (*b*) observed, presumably because the difference between the half-wave potentials of the cathodic reduction of the protonated and unprotonated forms of the oxime group does not exceed 50 mV (ref.[15]).

The $E_{1/2}$ vs pH dependence for isatin-3-oxime is not linear (Fig. 3), and also the di/dE vs pH dependence (Fig. 3) and the logarithmic analysis of the polarographic waves (Table I) point to the fact that the substance occurs in several ionic and molecular species in dependence on the pH value. This is also corroborated by the electrophoresis measurements at various pH values (Fig. 6), which show that due to the protonation of the lone electron pairs of the two nitrogen atoms, the isatin-3-oxime molecule carries two positive charges. As the pH is increased (pH 3.1), one of the nitrogen atoms undergoes deprotonation and the molecule loses one positive charge. In neutral solutions (pH 7) the molecule is electroneutral, hence, the other nitrogen atom has also undergone deprotonation. In the basic region (pH 8.3) the molecule acquires a negative charge due to the dissociation of the oxime group proton. The electrophoreograms at pH 11 and 13 give diffuse bands; several ionic species coexist, as also indicated by the $i_{\lim}$ vs pH dependence (Fig. 2). The majority of the molecules carry two negative charges at pH 13, due to the above-mentioned dissociation of the oxime group proton and dissociation of the α-oxime isatinic acid salt.

Figure 7 shows the electronic spectra of isatin-3-oxime in 10 vol.% methanol at pH 1 to 13. No basic changes occur in the spectra at pH 1 to 7 (Fig. 7, spectra Nos *1* and *2*). Apparently, the protonation of the nitrogen atoms does not bring about any substantial structural change in the compound. As the pH is increased, the oxime group hydrogen

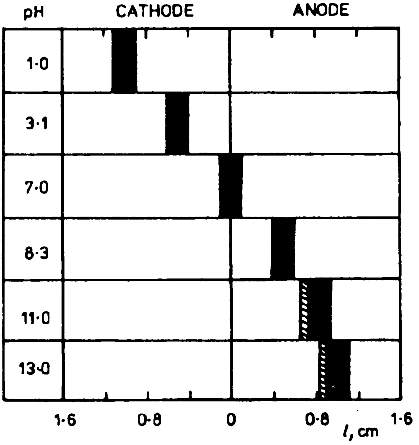


FIG. 6

Electrophoreograms of isatin-3-oxime at various pH values; potential gradient 9 V cm^{-1}, electrophoresis duration 90 min

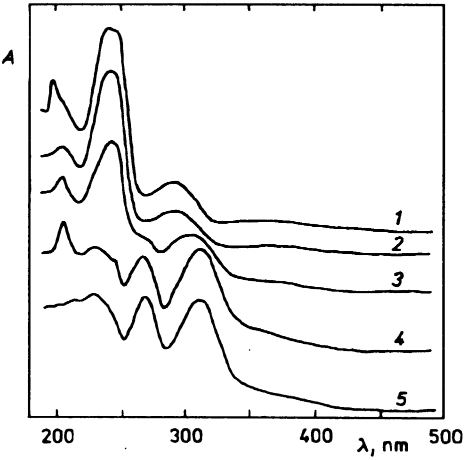
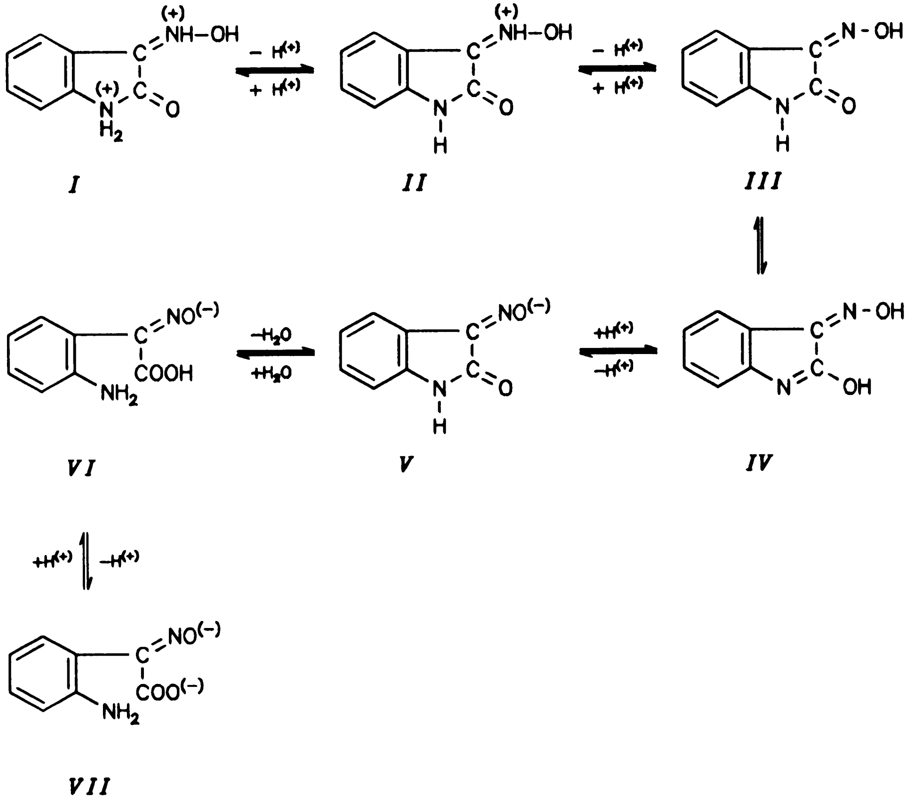


FIG. 7

Electronic absorption spectra of isatin-3-oxime; pH: *1* 1.01, *2* 7.01, *3* 7.98, *4* 9.60, *5* 13.01

dissociates, which is mirrored by a rapid decrease of the intense absorption band at 244 nm; simultaneously, the absorption band at 292 nm shifts approximately 20 nm towards higher wavelengths and its intensity increases appreciably with increasing pH. At pH 7.98 (spectrum No. *3*), a new band begins to appear at 270 nm. As the pH is further increased from 9.6 to 13 (spectra Nos *4* and *5*), the band at 244 nm shifts approximately 20 nm towards lower wavelengths and its intensity decreases appreciably, while that of the band at 270 nm increases. The rapid intensity increase of the bands at 270 and 310 nm over the pH 7.98 – 9.6 range is due to the dissociation of the oxime group hydrogen and the associated +M effect of the $-NO^-$ group. The electronic spectra of isatin-3-oxime exhibit two additional absorption bands within the region of pH 1 to 13: one lies at 360 – 380 nm and is low intensity, whereas the other lies at 200 – 210 nm, is medium intensity and vanishes at pH 13; this latter band is supposed to document the basic hydrolysis of the isatin ring and formation of structure *VII* in Scheme 3. Electronic spectra of isatin-3-oxime are the subject of a separate study.



SCHEME 3

It can be concluded that the polarographic measurements, infrared spectra, electronic spectra as well as electrophoresis measurements give evidence that isatin-3-oxime occurs in several ionic and molecular forms (species) in dependence on pH (Scheme 3).

In strongly acid solutions, the electron pairs at the nitrogen atoms are protonated by H^+ ions (*I*). As the pH is increased, the isatin ring nitrogen is the first to lose its bonded proton (*II*). Due to the neighbourhood of the >C=N bond in position 3 of the isatin ring with the carbonyl on the one side and the benzene ring on the other side, this remains protonated as far as pH 6. In neutral solutions the molecule is without charge (*III*). From the preparation of 2-substituted isatin derivatives it follows that isatin-3-oxime also exists in the enol form *IV* in neutral solutions. Since the carbonyl of isatin-3-oxime is polarographically irreducible in these conditions, the enol form cannot be studied by this method. As the pH is increased, the acid nature of the oxime group begins to manifest itself, the hydrogen dissociates off and the compound occurs in the form *V*. In basic solutions the isatin ring undergoes reversible hydrolysis and converts to α-oxime isatinic acid *VI*. Due to the acidity of the carboxylic hydrogen the molecule acquires a next negative charge (*VII*). Above pH 13 the majority of the molecules is hydrolyzed and occurs in the form *VII*. These conclusions are also borne out by the distribution

TABLE II
The p*K*, pH and distribution coefficient (α_{max}) values for the various isatin-3-oxime species

Compound	p*K*	pH	α_{max}
I	2.05 ± 0.02	2.80	0.765
II	3.69 ± 0.04	6.16	0.992
V	8.54 ± 0.002	10.64	0.986
VII	12.82 ± 0.12	13.72	0.888

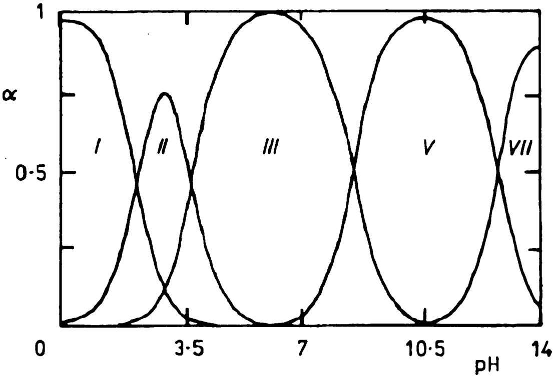


FIG. 8
Distribution diagram of isatin-3-oxime (c = 0.4 mmol dm^{-1}) in dependence on pH

diagram of isatin-3-oxime in dependence on pH, set up based on the results of potentiometric titrations (Fig. 8). The numbering (*I* – *III*, *V*, *VII*) in the diagram corresponds to the species shown in Scheme 3. The p*K* values of the species were calculated and are given, along with the pH and distribution coefficient values, in Table II.

The distribution diagram confirms that isatin-3-oxime occurs in the discussed ionic and molecular forms in dependence on pH. The results of the various methods, with their specific features, are in a good correlation.

REFERENCES

1. Torrance J. E., Oostra S., Nazzal A.: Synth. Met. *19*, 709 (1987).
2. Zentková M., Kováč J., Zentko A., Košturiak A.: J. Magn. Magn. Mater. *102*, L 1 (1991).
3. Calzolari C.: Bull. Soc. Adria. Sci. Nat. Trieste *45*, 114 (1949).
4. Calzolari C.: Abstr. Chim. Ind. *39*, 395 (1957).
5. Andruzzi K., Cardinali M. E., Carelli I., Trazza A.: Ann. Chim. *61*, 415 (1971).
6. Ghandour M. A., Issa I. M., Mahmond M. R., Abou-Doma R. A.: J. Indian Chem. Soc. *53*, 258 (1976).
7. Košturiak A., Pozemka M.: Sb. Prir. Fak. Univ. P. J. Safarika *1973*, 191.
8. Hovorka V., Morávek J.: Chem. Listy *45*, 235 (1951).
9. Eckschlager K.: Chem. Listy *56*, 489 (1962).
10. Hovorka V., Sýkora V., Voříšek J.: Chim. Anal. *29*, 268 (1947); Chem. Abstr. *42*, 1525 (1948).
11. Zhungietu G. I., Rechter M. A.: *Izatin i ego proizvodnye*. Shtiintsa, Kishinev 1977.
12. Rigado C., Grasso M., Sammartano S.: Ann. Chim. *74*, 537 (1984).
13. Sumpter W. C., Williams J. L., Wilken P. H., Willoughby B. L.: J. Org. Chem. *14*, 713 (1949).
14. Julien P., Meyer E., Printi E.: *Geterotsiklicheskie Soedineniya*, Vol. 3. Izdatelstvo Inostrannoi Literatury, Moscow 1954.
15. Košturiak A., Stankoviansky S., Zacharová-Kalavská D: Collect. Czech. Chem. Commun. *35*, 644 (1970).
16. Zuman P.: *Organická polarografie*. SNTL, Praha 1966.
17. Sulivan D. G., Sadler P. W.: J. Org. Chem. *22*, 283 (1957).
18. Zelenský I., Stankoviansky S., Zacharová-Kalavská D., Košturiak A.: Chem. Zvesti *23*, 94 (1969).

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