

POLAROGRAPHIC STUDY OF 3- AND 4-SUBSTITUTED 3-PHENYLIMINOXINDOLE DERIVATIVES

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It was proved that the limiting current of cathodic waves of ten studied 3- and 4-substituted 3-phenyliminoxindole derivatives has diffuse character and that throughout the whole range of pH reduction of these compounds involves two electrons. These results, together with electrophoretic and spectrophotometric measurements, isolation of hydrolysis products and study of electron-transfer properties of the system, show that 3-phenyliminoxindole derivatives exist in solutions in various forms.

It is known that isatin, *i.e.* 2,3-dioxindole, exists in solutions in various forms, depending on pH of the solution^{1,2}. These forms are shown in Scheme 1.

We have confirmed all these forms polarographically and spectroscopically. Our investigations³ show that the electronic absorption spectra, published by several authors⁴⁻¹¹, were measured in solutions in which various forms of 2,3-dioxindole were present. The study³ proved further that 2,3-dioxindole exists in 0.1M-NaOH as anion of isatinic acid which undergoes a two-electron reduction and affords the dimeric product.

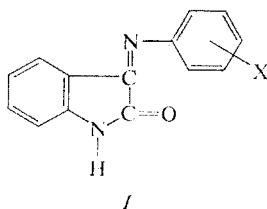
Later, polarographic investigations^{12,13} have shown that the structure of 2,3-dioxindole depends on pH of its solution. Dioxindole, which is structurally close to 2,3-dioxindole, was studied polarographically¹⁴ whereas another work¹⁵ used the polarographic method for the identification of isatin, dioxindole, phthalimide and indigo carmine. Recent polarographic study of isatin and N-methylisatin in dimethylformamide¹⁶ have confirmed the radical mechanism of cathodic reduction of these compounds.

This paper represents a continuation of spectrophotometric investigations of some 3-phenyliminoxindole structures¹⁷ and of kinetic studies^{18,19} of basic hydrolysis of some 3-phenyliminoxindole derivatives (*I*). Following 3-phenyliminoxindole derivatives (*I*) are investigated:

1. 4'-N(CH₃)₂; 2. 4'-NH₂; 3. 4'-OH; 4. 4'-OCH₃; 5. 4'-OC₂H₅; 6. 4'-CH₃; 7. 3'-CH₃;
8. —H; 9. 4'-Br; 10. 3'-Cl.

Since the compounds *I* are isatin derivatives we can anticipate that they will exist in various forms depending on pH of their solutions. The aim of this investigation is a basic polarographic study of the compounds *I*, *i.e.* characterisation of the

limiting polarographic currents, determination of the number of electrons in the electrode reaction, identification of various forms of compounds *I* at various pH of their solutions and study of transfer of electronic substituent effects.



EXPERIMENTAL

Derivatives of 3-phenyliminoxindole were prepared in a previous work²⁰ according to ref.²¹. All reagents used were of analytical purity (Lachema, Brno). 3-Phenyliminoxindole was hydrolysed at 30°C in $5 \cdot 10^{-3}$ M solutions with added $1 \cdot 10^{-2}$ M-HCl. After 2 hours the hydrolysis products were extracted with ether and identified polarographically in 0.1M-NaOH, by the melting point (2,3-dioxindole melts at 201–2°C) and by comparison of R_F values using thin-layer Silufol plates. The hydrolysis products were found to be 2,3-dioxindole and aniline.

Polarographic measurements were performed on an LP-7 polarograph (Laboratorní přístroje, Prague) in a Kalousek cell, thermostated using a Wobser U8 (Mechanik Prüfgeräte, Dresden) thermostat. Drop time of the dropping mercury electrode was 2.3 s in 1M-KCl and at 0.0 V; reservoir height 70 cm, rate of mercury flow 2.72 mg s^{-1} . Saturated calomel electrode (s.c.e.) was used as the reference electrode. Measurements of pH were performed using a PHM-26 (Radiometer, Copenhagen) pH-meter with G-202 B and K 401 electrodes.

Spectra were measured in the region 350–700 nm on a Perkin-Elmer 402 spectrophotometer in $1.24 \cdot 10^{-4}$ to $2.5 \cdot 10^{-4}$ M solutions of *I* with 25% of methanol added; cell thickness 1.000 cm, accuracy ± 2 nm. Electrophoretic measurements were carried out on paper Whatman No 2 8×160 mm in a chamber of own construction, the potential gradient being 10 V cm^{-1} . The power pack made by Tesla, Přelouč, was used as source. The compounds were studied in 0.1M-NaOH and in Britton–Robinson buffers (B-R). The ionic strength was adjusted to $I = 0.1$ by addition of KCl. In order to increase the solubility, 40% (v/v) of ethanol were added in all measurements. The polarographic parameters were calculated from the curves taken five minutes after the solutions had been mixed. The accuracy of the half-wave potentials is ± 5 mV. Since half-wave potentials of the compounds *I* and of the anions of α -anilisinic acids arising from them were very similar and exhibited different dependence on pH, it was possible to distinguish between them only using high-resolution derivative polarography and working only at certain pH. The found limiting currents of compounds *I* and α -anilisinic acids were thus uncertain and therefore in the region of pH 6.8–8.8 the sum of limiting currents of the both forms was used in the plot of i_{lim} against pH. All measurements were performed on freshly prepared solutions. Most of the σ constants used in the correlations were taken from the work of Mc Daniel and Brown²². The σ constant for the 4-O⁻ substituent was taken from ref.²³ and that for 4-OC₂H₅ from ref.²⁴ because these two constants are not listed in ref.²². Calculations were carried out on a Minsk 21 digital computer using trivial programs.

RESULTS AND DISCUSSION

Polarographic Measurements

Substituted 3-phenyliminoxindole derivatives exhibit throughout the whole range of pH one or two cathodic waves which can be assigned to various forms of the compounds *I* and to their hydrolysis products. Fig. 1 depicts the dependence of half-wave potentials on pH for some of the compounds *I*. At pH 1, 3-phenyliminoxindole and its studied derivatives exhibit only one cathodic wave. Its half-wave potential does not depend on the kind of substituent and is about -310 mV in 0.1M-HCl . We see (Fig. 1) that the half-wave potential depends linearly on pH, the slope $dE_{1/2}/dpH$ being 0.050 V. The limiting current of this wave (Fig. 2) is lower than the limiting currents at higher pH values. This wave corresponds to cathodic reduction of 2,3-dioxindole — one of the acid hydrolysis products of compounds *I*. The already known fact that compounds *I* undergo an acid hydrolysis to the original components²⁵⁻²⁷, i.e. to 2,3-dioxindole and substituted aniline derivatives, was confirmed by the isolation and identification of 2,3-dioxindole (m.p. $201-202^\circ\text{C}$ (Fig. 3). Curves 5 and 6 (Fig. 3) correspond to the cathodic reduction of 2,3-dioxindole and 3-phenyliminoxindole, respectively, in 0.1M-HCl . The half-wave potentials and heights of both waves are identical. The identity of one of the acid hydrolysis products of compounds *I* with 2,3-dioxindole was also proved polarographically in 0.1M-NaOH in which

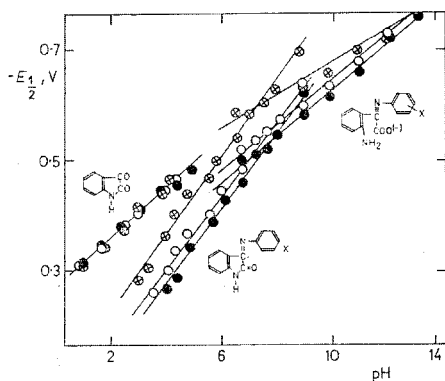


FIG. 1

Dependence of Half-wave Potentials of Cathodic Waves of Some 3-Phenyliminoxindole Derivatives on pH

Measured in $2 \cdot 10^{-4}\text{M}$ solutions of compounds *I* in 40% (v/v) ethanol, $I = 0.1$.
 ⊗ $4'\text{-NH}_2$, ○ H, ● $3'\text{-Cl}$.

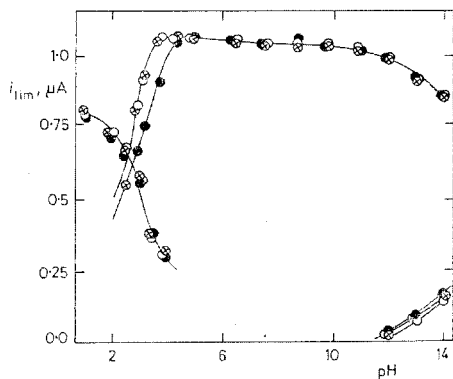


FIG. 2

Dependence of Limiting Current of Cathodic Waves of Some 3-Phenyliminoxindole Derivatives on pH

For composition of the solutions and description see Fig. 1.

2,3-dioxindole exists as the anion of isatinic acid¹⁻³ (curve 2 in Fig. 3). Curve 3 in Fig. 3 corresponds to a $5 \cdot 10^{-4}$ M solution of 3-phenyliminoxindole in 40% ethanol and in 0.1M-HCl to which 2M-NaOH was added to make the final solution 0.1M in NaOH. The curves 2 and 3 in Fig. 3 have identical half-wave potentials (approximately -1500 mV) and, taking into account the mentioned dilution with 2M-NaOH in the case of the curve 3, also the same limiting current values. From these, as well as from electrophoretic and spectrophotometric measurements on 3-phenyliminoxindole, it follows that in an acid medium compounds *I* undergo rapid hydrolysis to the polarographically active 2,3-dioxindole and to substituted aniline derivatives.

In the region pH 2.8–4.8 (Fig. 1) two polarographic waves can be distinguished. Besides the already discussed polarographic wave at more negative potentials, corresponding to 2,3-dioxindole (product of acid hydrolysis of *I*), a wave was observed at more positive potentials, which is attributed to reduction of the C=N bond in compounds *I*. In solutions of pH 3–4.7, where the above-mentioned acid hydrolysis of compounds *I* is observed, the sum of the limiting currents of the cathodic waves is constant and identical with that found for the range pH 4.8–12 (Fig. 3). In solutions of pH < 4 the limiting current of the more positive wave decreases as the result of the hydrolysis, and at pH < 2.8 only the acid hydrolysis product can be polarographically detected. From the dependence of the limiting current on time it also follows that in the region pH 3–5 the kinetics of the acid hydrolysis of compounds *I* can be studied polarographically, particularly in the case of derivatives with electron-accepting substituents, because the half-wave potentials of the reduction of these

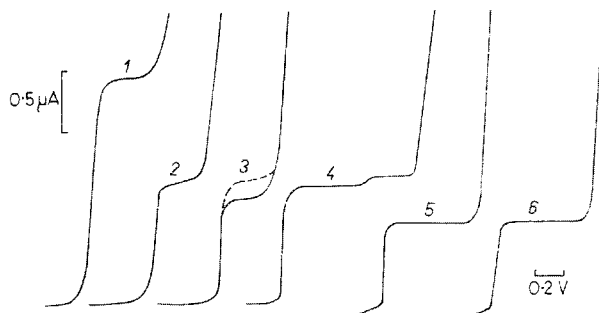


FIG. 3

Derivative Polarogram

Measured in $2 \cdot 10^{-4}$ M solutions of the compared compounds in 40% (v/v) ethanol, $I = 0.1$, 200 mV/abc, S.C.E. 1 2,3-Dioxindole 3-oxime in 0.1M-NaOH, from -900 mV; 2 2,3-dioxindole in 0.1M-NaOH, from -900 mV; 3 a solution of 3-phenyliminoxindole in 0.1M-HCl, treated with 2M-NaOH to obtain pH 13, from -900 mV; 4 3-phenyliminoxindole in 0.1M-NaOH, from -400 mV; 5 2,3-dioxindole in 0.1M-HCl, from -100 mV; 6 3-phenyliminoxindole in 0.1M-HCl, from -100 mV.

compounds differ sufficiently from that of their hydrolysis product, *i.e.* 2,3-dioxindole (Fig. 1).

For the cathodic wave due to reduction of the C=N bond in the studied compounds the slope $dE_{1/2}/d\text{pH}$ is 0.070 V (in the interval $\text{pH} > 3$ to about $\text{pH} 10$). At $\text{pH} > 6.8$ this wave overlaps with the cathodic wave corresponding to reduction of the α -anisatinat anion, which is formed by reversible hydrolysis (Fig. 1). The plot of the half-wave potentials of this second wave against pH has the slope $dE_{1/2}/d\text{pH} = 0.036$ V (with the exception of compounds 1–3). Since the values of half-wave potentials for compounds 1 and the corresponding α -anisatinic acids change differently with pH , the half-wave potentials of the both forms coincide in solutions of $\text{pH} 7-8$. Both forms were polarographically detectable at $\text{pH} 6.8$ and 8.8.

At $\text{pH} > 12$ (Fig. 2) it is possible to observe a polarographic curve with a half-wave potential of about -1500 mV, corresponding to cathodic reduction of the hydrolysis product of compounds 1 – isatinat anion – in an alkaline medium.

Curve 4 in Fig. 3 corresponds to cathodic reduction of α -anisatinic acid in 0.1M-NaOH ($E_{1/2} = -750$ mV). At about -1500 mV the curve 4 shows the formation of the isatinat anion, which arises in a non-reversible alkaline hydrolysis of compounds 1, and the half-wave potential of which is identical with that of the curves 2 and 3. The curve 1 corresponds to cathodic reduction of dioxindole 3-monoxime²⁸⁻³⁰. A comparison of the limiting current of curve 1 with the limiting current of curve 2, the corrected limiting current of curve 3 and with the sum of the limiting

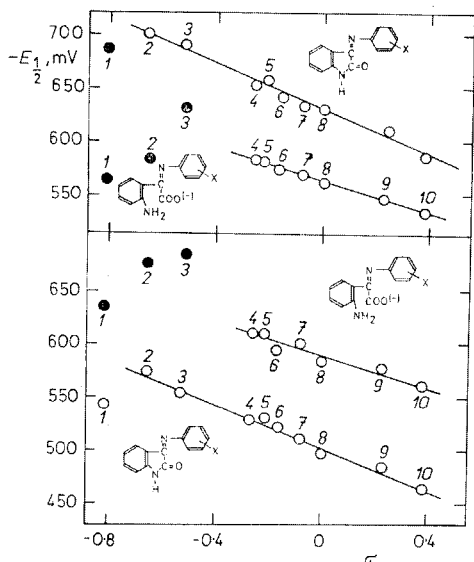


FIG. 4

Plot of Half-Wave Potentials of the Cathodic Reduction of 3-Phenyliminoxindole Derivatives against Hammett σ Substituent Constants

B-R buffer solutions of $\text{pH} 6.8$ (below) and of $\text{pH} 8.8$ (above).

currents of curve 4 shows that in the whole region of pH the studied compounds *I*, as far as they are not hydrolysed on the mercury dropping electrode, undergo a two-electron reduction. From the dependence of the limiting currents on concentration, temperature and mercury column height, it follows that the limiting currents are of diffuse character when measured under conditions, which do not allow significant operation of non-reversible hydrolysis reactions.

The influence of substituents on the polarographically active center was proved by linear plots of the half-wave potentials of compounds *I* against σ substituent constants²⁸. The half-wave potentials were correlated with the σ constants at pH 6.8, 8.8, 11.8 and 13.

Fig. 4 depicts the plot of the half-wave potential of the C=N bond reduction against σ -constants at pH 6.8 and 8.8. At pH 6.8, the polarographic wave at more positive half-wave potentials ($\varrho_{\pi} = +0.104 \pm 0.003$ V; $r = 0.991$) corresponds to cathodic reduction of the C=N bond in compounds *I*. At pH 8.8, the parameters of this correlation are $\varrho_{\pi} = +0.108 \pm 0.004$ V; $r = 0.991$ (the polarographic wave at more negative half-wave potentials).

Compound *I* was not included in both correlations; its half-wave potential was found at more positive values than would be expected from the linear correlations with σ values. The electronic spectra of this compound in B—R buffer solutions exhibited also deviations¹⁷.

Half-wave potentials for the C=N bond reduction in α -anilisinic acids were correlated with σ constants and following parameters were obtained:

at pH 6.8 $\varrho_{\pi} = (0.076 \pm 0.005)$ V, $r = 0.972$; at pH 8.8 $\varrho_{\pi} = (0.069 \pm 0.003)$ V, $r = 0.985$; at pH 11.8 $\varrho_{\pi} = (0.071 \pm 0.003)$ V, $r = 0.990$; at pH 13 $\varrho_{\pi} = (0.076 \pm 0.006)$ V, $r = 0.991$.

We did not include compounds 1–3 in the linear correlations at any pH values, since their $dE_{1/2}/d\text{pH}$ values differ from the values for the other compounds.

These linear correlations indicate a lower electron-transfer ability of the anions of α -anilisinic acids as compared with the transfer ability of the compounds *I*.

Electrophoretic and Spectrophotometric Measurements

Electrophoretic measurements of both 3-phenyliminoxindole and 2,3-dioxindole in solutions of pH < 1.8 showed in both cases spots migrating towards cathode and having an identical electrophoretic mobility. These spots correspond to a protonated form of 2,3-dioxindole. As has been shown in the polarographic part of this study, 2,3-dioxindole is formed by rapid hydrolysis of 3-phenyliminoxindole. In solutions of pH 1.8–4.8, 2,3-dioxindole is also formed by acid hydrolysis of 3-phenyliminoxindole but since it is not protonated it remains at the start. The hydrolysis

of protonated 3-phenyliminoxindole is shown by a cathode-migrating spot with a 10% lower electrophoretal mobility as compared with protonated 2,3-dioxindole. At $\text{pH} > 10.5$ the isatin ring is reversibly hydrolysed to α -anilisatinate anion.

Non-reversible hydrolysis of $\text{C}=\text{N}$ bond in the α -anilisatinate anion occurs at $\text{pH} > 12$ and affords 2,3-dioxindole and aniline¹⁹. The electrophoregrams of such alkaline solutions exhibited a rapidly migrating spot with a 10% lower mobility than the α -anilisatinate anion.

Molar extinction coefficient of the 3-phenyliminoxindole absorption band, situated in the visible region, was correlated with pH of the solution (Fig. 5). At $\text{pH} 1-3$, the value of the molar extinction coefficient, ϵ^{416} , is $710 \text{ mol}^{-1} \text{ cm}^{-1}$; this is the value for the $n \rightarrow \pi^*$ transition in 2,3-dioxindole³¹. The part of the curve in the region $\text{pH} 2.8-4.8$ corresponds to a mixture of protonated 3-phenyliminoxindole (*I*) and 2,3-dioxindole (*VII*), formed by acid hydrolysis of *I*. The value of molar extinction coefficient at $\text{pH} 5-10$ corresponds to $n-\pi^*$ transitions in 3-phenyliminoxindole (*II*, *III*). At $\text{pH} > 10.5$ the value of the molar extinction coefficient decreases as the result of a reversible hydrolysis of *II* or *III* to the anion of α -anilisatinic acid (*IV*). The lower molar extinction coefficient of this anion, as compared with that of 3-phenyliminoxindole, is caused by a lower electron-transfer ability of the anion. Analogous results of the spectrophotometric measurements throughout the whole pH region were obtained for all the compounds *I* with the exception of the derivative 3 in which the acidity of the 4'-OH group manifests itself in alkaline media¹⁷.

On the basis of the experimental material obtained in this study and of the polarographic method of determination of equilibria (ref.³⁰, p. 20 and foll.), the equilibrium between the particular forms of 3-phenyliminoxindoles can be described by the Scheme 1:

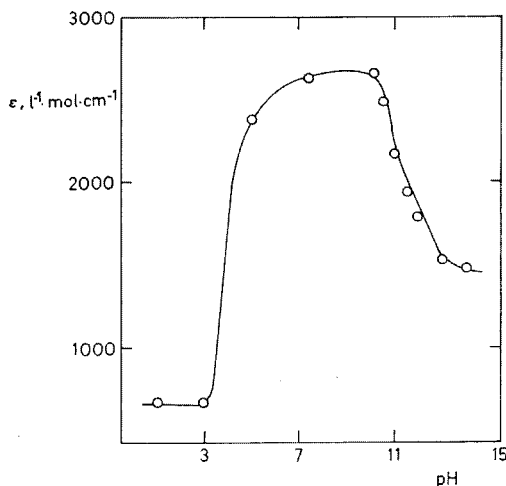
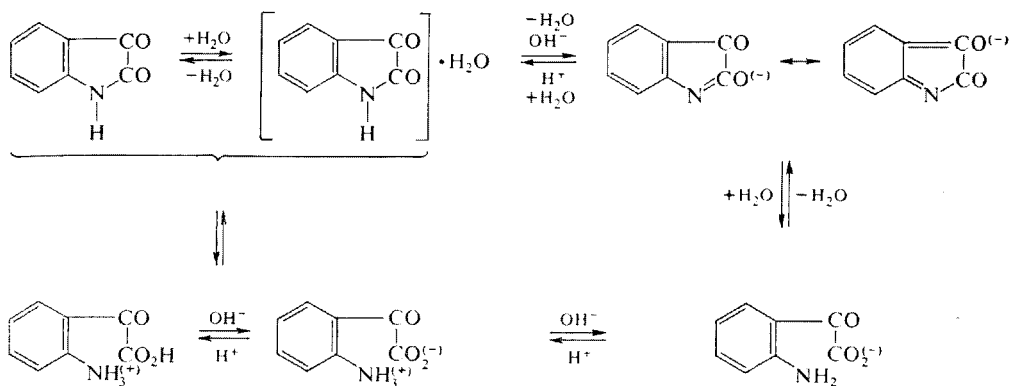
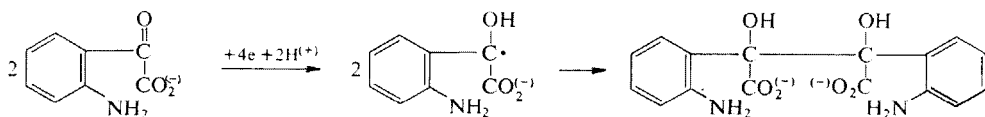


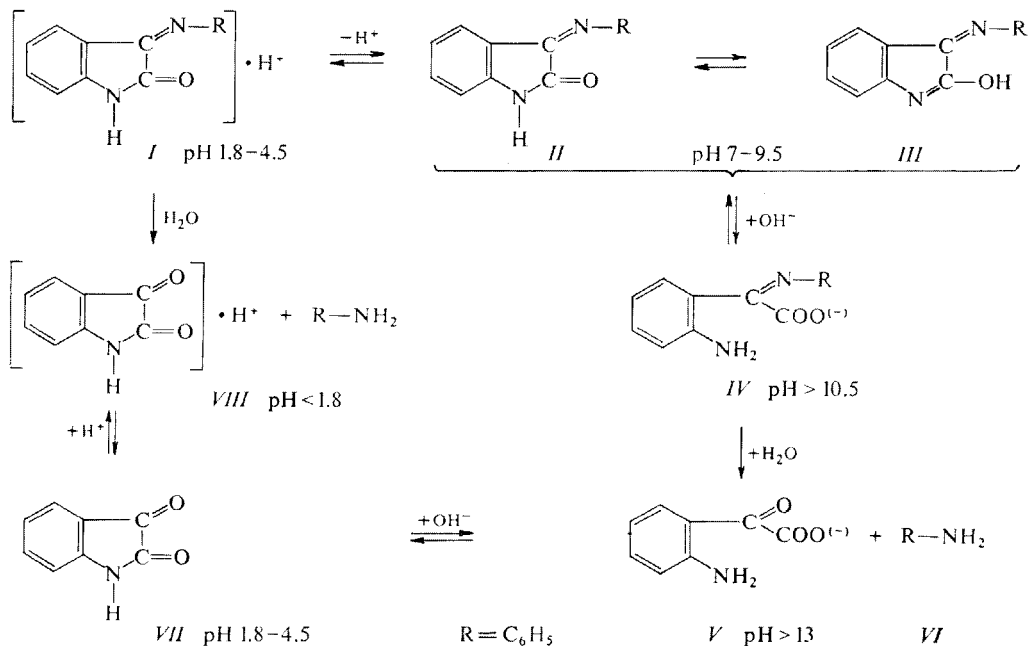
FIG. 5
Dependence of the Molar Extinction Coefficient of 3-Phenyliminoxindole on pH
Concentration of 3-phenyliminoxindole $1.24-2.5 \cdot 10^{-4} \text{ M}$, 25% (v/v) of methanol added, 10:1.



SCHEME 1



SCHEME 2



SCHEME 3

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