POLAROGRAPHIC STUDY OF ACRIDINE AND 9-CHLOROACRIDINE AND ITS DERIVATIVES IN DIMETHYLFORMAMIDE

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Polarographic data on the reduction of acridine (I) and its 9-chloro (II), 2-methoxy-9-chloro (III), 4-methoxy-9-chloro (IV), 2-methyl-9-chloro (V), 4-methyl-9-chloro (VI), 2,9-dichloro (VII), and 4,9-dichloro (VIII) derivatives and a mechanism for the reduction are presented. In dimethylformamide (DMF) the polarographic reduction of acridine I takes place in two steps with participation of one electron in each step and the intermediate formation of an anion radical. Acridine II is reduced in four steps: The second and fourth waves correspond to the reduction of the heteroring, while the first and third waves are associated with detachment of a chlorine atom. The addition of phenol as a proton donor facilitates the reduction but does not affect the number of electrons consumed by the depolarizer during its reduction. A linear correlation between $E_{1/2}$ and the corresponding σ constants of quinoline is observed for acridines II, III, V, and VII; this made it possible to calculate the previously unknown σ constants for acridines that contain a substituent in the 4 position. The $E_{1/2}{}^1$ values for acridine II and its derivatives correlate with the rate constants for chemical dehalogenation.

The first papers devoted to the polarographic study of acridines were published a relatively long time ago and deal with the electrochemical reduction of these substances in proton-containing media (aqueous buffer and aqueous alcohol solutions); it was established that acridine under these conditions is reduced in two steps forming two one-electron thermodynamically irreversible waves on the polarograms [1-3]. However, other authors have shown that the mechanism of the polarographic reduction of acridine in aqueous solutions depends on the pH of the medium and that the reduction may take place both in two one-electron steps, which corresponds to two waves of identical height on the polarogram, and in one irreversible step [4-8]. The results of a study of the electrochemical reduction of acridine derivatives in acetate (pH 4.48) and ammonia (pH 9.25) buffer solutions in 96% alcohol made it possible to only approximately estimate the number of electrons that participate in the reduction of these compounds [9].

New possibilities for the study of the mechanism of polarographic reduction of the examined compounds have been developed by the use of aprotic solvents such as, for example, dimethylformamide (DMF) [10]. However, a number of discrepancies in the results have been observed. Thus it has been found in particular that acridine forms one two-electron wave during reduction in the presence of 5% water in DMF [11], whereas the data in [1-3] constitute evidence for the presence of two waves on the polarogram even in aqueous solutions. The electrochemical reactivities of substituted acridines have not been adequately studied.

Thus the currently available information on the polarographic reduction of acridines is incomplete in a number of cases and sometimes is also contradictory. In this connection, we undertook a study of the examined series of compounds: acridine and 9-chloroacridine and its derivatives.

We selected DMF, which has sufficient inert character with respect to electrochemical reaction on the cathode and with respect to the products, as the solvent; this makes it possible to arrive at a reliable interpretation of the polarographic data. In order to ascertain the nature and sequence of the steps in the electrode process we examined the effect of an extraneous proton donor (PhOH and H_2O) on the morphology of the polarograms of acridines. The depolarizer concentration ranged from $2.4 \cdot 10^{-4}$ to $2 \cdot 10^{-3}$ M.

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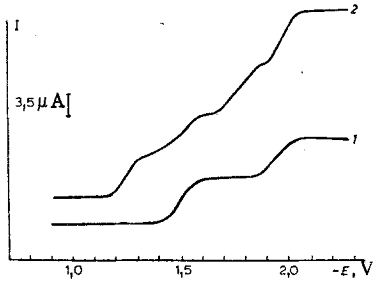

Fig. 1

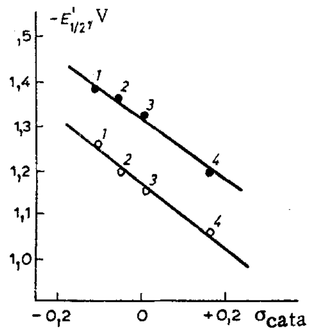

Fig. 2

Fig. 1. Polarograms of acridine (1) and 9-chloroacridine (2) in a 0.05 M $N(C_2H_5)_4I$ base electrolyte in DMF.

Fig. 2. Dependence of the half-wave potentials of the first wave ($E_{1/2}^1$) on the σ constants of the substituents in the 2 position of 9-chloroacridine derivatives in DMF: 1) OCH_3; 2) CH_3; 3) H; 4) Cl; ●) in the absence of phenol; ○) in the presence of phenol.

TABLE 1. $E_{1/2}$ Values of Some 4-Substituted Derivatives and σ Constants of Substituents in the 9-Chloroacridine Molecule

Compound	$-E_{1/2}$, V*	σ
9-Chloroacridine	1,32	0
4,9-Dichloroacridine	1,18	0,172
4-Methyl-9-chloroacridine	1,36	−0,070
4-Methoxy-9-chloroacridine	1,37	−0,092

*Relative to a saturated calomel electrode.

Under the described conditions acridine forms two waves with $E_{1/2} = -1.53$ V and $E_{1/2} = -1.97$ V of identical heights. The linear character of the $i_{lim} - C$ and $i_{lim} - H_{Hg}^{1/2}$ dependences constitutes evidence for the diffusion nature of the indicated waves. The number of electrons consumed by the acridine molecule during reduction under the examined conditions calculated from the Ilkovic equation is close to unity for each wave.* The $2.3RT/hF$ coefficient determined from the $\log i/i_d - i$ vs E graph is 0.057-0.066, which, when n = 1, corresponds to reversible reduction of acridine in aprotic media.

A polarographic study in the presence of phenol showed that at low phenol quantities ($1.96 \cdot 10^{-3}$ mole/liter) acridine ($2 \cdot 10^{-3}$ mole/liter) forms three waves; in this case a new wave at less negative potentials ($E_{1/2} = -1.27$ V) and two waves at approximately the same potentials ($E_{1/2} = -1.46$ V and $E_{1/2} = -1.94$ V) are formed. When the amount of phenol is increased, an increase in the height of the first wave and a decrease in the height of the wave with $E_{1/2} = -1.94$ V are observed. When large amounts of phenol ($5.66 \cdot 10^{-3}$ mole/liter or greater) are added, the wave with $E_{1/2} = -1.94$ V vanishes completely, and two waves with $E_{1/2} = -1.23$ V and -1.49 V with approximately identical heights remain on the polarogram. The RT/nF coefficient calculated from the graph of the dependence of $\log i/i_d - i$ on E for the same band is 0.050-0.063, which virtually coincides with the theoretical value for a one-electron reversible process. In this case the total number of electrons consumed by the depolarizer molecule during its reduction found from the Ilkovic equation is two. One's attention should be directed to the fact that the height of the wave formed at less negative potentials is approximately equal to the height of the second reduction wave of reduction of acridine in the absence of phenol.

The wave with $E_{1/2} = -1.27$ V in the presence of phenol evidently corresponds to reduction of the complex produced due to the formation of an intermolecular hydrogen bond. The free pair of electrons of the nitrogen

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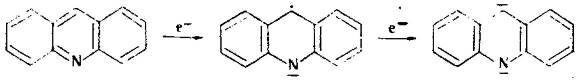
*To calculate the diffusion coefficient of acridine in the Ilkovic equation we used the tabular value of the diffusion coefficient of naphthalene in methanol [12]. The calculation was made from the formula $D_1/D_2 = \sqrt{M_2}/\sqrt{M_1}$ with allowance for the viscosity of the medium.

atom in this case (apparently as in the case of quinoline) is situated in the orthogonal plane with respect to the molecular π cloud and does not participate in conjugation with it. In this connection, it readily undergoes complexing of the intermolecular hydrogen-bond type [14]. The resulting complex undergoes reduction more easily than acridine itself due to a decrease in the electron density on the reaction center (the C=N− group).

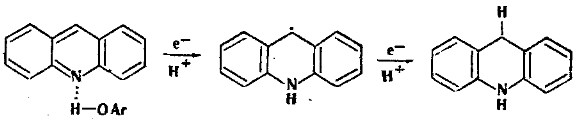
On the other hand, one might have assumed that phenol protonates the acridine molecule (at the nitrogen atom). In this case a positive charge should appear on the depolarizer molecule. However, when phenol is added to a solution of acridine in the absence of a base electrolyte, changes in the height of the wave are not observed, as one should have expected since the development of a positive charge on the depolarizer molecule should lead to the appearance of a positive migration component of the current.* In addition, the slopes of the dependence of $E_{1/2}$ on σ for 9-chloroacridine derivatives, which we examined in the absence of phenol and in its presence, remain identical, which also confirms the fact that the free pair of electrons of the nitrogen atom does not participate in transmission of the electronic effect of the substituents. The formation of the complex is reversible and depends on the amount of phenol. Thus the following mechanisms for the reduction of acridine on a dropping mercury electrode may be proposed.

In the absence of phenol:



(1)

In the presence of phenol:



(2)

When phenol is absent, acridine itself is reduced to an anion radical at an $E_{1/2}$ value corresponding to the reduction of the complex of the anion radical with phenol. When phenol is absent, facilitation of the reduction of the acridine anion radical does not occur.

This scheme is confirmed by our results: Two one-electron waves are observed when phenol is present (Eq. 1), two waves are also observed in the presence of large amounts of phenol (Eq. 2), and three waves are observed at PhOH concentrations intermediate between the first two cases.

9-Chloroacridine forms four waves in anhydrous DMF in a 0.05 mole/liter $N(C_2H_5)_4I$ base electrolyte. These waves also have diffusion nature (linear dependences of i_{lim} on C and i_{lim} on $H_{Hg}^{1/2}$). The RT/αnF coefficient determined from the log $i/i_d - i$ vs E graph is 0.075, 0.078, 0.089, and 0.068 for the first, second, third, and fourth waves, respectively; this indicates deviation from the reversibility of the reduction process in these cases.

The number of electrons expended in the reduction of the 9-chloroacridine molecule and calculated from the Ilkovic equation is four.† It is known from the literature data that two electrons are consumed in the cleavage of the carbon−halogen bond during its reduction [15-18]. Considering this fact, in our case it may evidently be assumed that the remaining two electrons are required for the reduction of the heteroring.

The results show that when small amounts of phenol ($1.96 \cdot 10^{-3}$ mole/liter) are added, 9-chloroacridine at a concentration of $2.0 \cdot 10^{-3}$ mole/liter forms five waves, as compared with four waves at a phenol concentration of $3.85 \cdot 10^{-3}$ mole/liter and only three waves at a phenol concentration of $5.66 \cdot 10^{-3}$ mole/liter or higher concentrations. As in the case of acridine, when phenol is present, a wave is formed at less negative potentials ($E_{1/2} = -1.14$), and the first four waves are found at more positive potentials ($E_{1/2}^{1} = -1.32$, $E_{1/2}^{2} = -1.53$ V, $E_{1/2}^{3} = -1.83$ V, and $E_{1/2}^{4} = -1.98$ V). When the phenol concentration is increased, one observes an increase in the waves with $E_{1/2}^{1} = -1.32$ V and $E_{1/2}^{2} = -1.53$ V and a decrease in the heights of the waves with $E_{1/2}^{3} = -1.83$ V and $E_{1/2}^{4} = -1.98$ V. At higher phenol concentrations the waves with $E_{1/2}^{3} = -1.83$ V and $E_{1/2}^{4} = -1.98$ V vanish

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*When a stronger acid than phenol (benzoic acid) is added, this effect is observed. Protonation of acridine is observed under the indicated conditions.

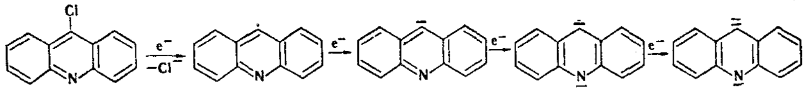
†The diffusion coefficient of 9-chloroacridine was calculated as in the case of acridine (see above).

completely, and the three waves with $E_{1/2}=-1.14$ V, -1.31 V, and -1.51 V remain; the latter two waves have virtually identical heights. The development of a wave with $E_{1/2}=-1.14$ V evidently also corresponds to the formation, due to a hydrogen bond, of a complex that is reduced more easily than 9-chloroacridine itself.

Thus the second and fourth waves obtained on the polarogram of 9-chloroacridine (Fig. 1), which have half-wave potentials that are very close to the $E_{1/2}$ values for acridine, correspond to reduction of the acridine heteroring, while the first and third waves are waves of reduction of the C–Cl bond in the 9-chloroacridine molecule.

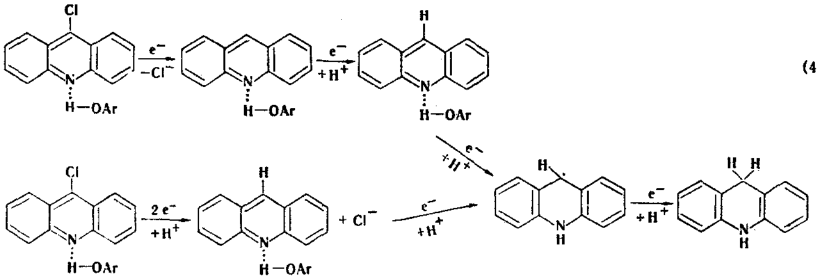
It may be assumed that 9-chloroacridine is reduced on a dropping mercury electrode via the following scheme.

In the absence of phenol:



(3)

In the presence of phenol:



(4)

When a small amount (0.55 mole/liter) of water (as a proton donor) is added, a wave develops at a smaller negative potential ($E_{1/2}=-1.17$ V), and all of the waves are found at more positive potentials as compared with those obtained in the absence of water ($E_{1/2}{}^1=-1.29$ V, $E_{1/2}{}^2=-1.44$ V, $E_{1/2}{}^3=-1.64$ V, and $E_{1/2}{}^4=-1.77$ V). When the amount of water is increased, one observes an increase in the height of the wave at $E_{1/2}=-1.17$ V and a decrease in the height of the waves at $E_{1/2}{}^3=-1.64$ V and $E_{1/2}{}^4=-1.77$ V. When large amounts (4.12 moles/liter) are added, the waves with $E_{1/2}=-1.64$ and -1.77 V vanish completely, and three waves with $E_{1/2}=-1.16$, -1.31, and -1.44 V remain on the chromatogram. Thus these data are in agreement with the data obtained in experiments with the addition of phenol.

To study the effect of substituents on the reduction of 9-chloroacridine we investigated 2- and 4-methoxy-methyl- and chloro-9-chloroacridines. It is apparent from the $E_{1/2}$ values of the chloro derivatives that the introduction of a chlorine atom in the molecule facilitates the reduction of the depolarizer, whereas the CH_3 and OCH_3 derivatives are reduced at more negative potentials.

For the correlation of the $E_{1/2}$ values with the Hammett constants of the substituents in the 2 position for the first wave of 9-chloroacridine derivatives in DMF we used the σ constants for quinoline [19], since the correlation coefficient for benzene (0.937) is lower than for quinoline (0.993) in the case of the use of Hammett σ constants. A direct correlation between the σ values of the quinoline series and the $E_{1/2}$ values was observed in the case of substituents in the 2 position. From this linear dependence we also calculated the σ constants for the substituents in the 4 position of the 9-chloroacridine molecule, which have not been presented in the literature (see Table 1).

It should be noted that the $E_{1/2}$ values found for the first wave of substituted 9-chloroacridines correlate with the logarithms of the rate constants for dehalogenation of these compounds ($r=0.94$). This fact once again confirms the correctness of the above mechanism for the electrochemical reduction, the first step of which is detachment of a chloride ion.

EXPERIMENTAL

The polarographic measurements were made with an LP-7 recording electronic polarograph. The capillary used in the research had the following characteristics: $m=2.26$ mg/sec and $\tau=4$ sec (in the absence of a polarization potential at $H=20.3$ cm). The acridine was recrystallized from aqueous alcohol solutions. 9-Chloroacridine and its derivatives were synthesized by the methods in [20-25] and recrystallized prior to achieving the melting points corresponding to the literature data. The DMF was vacuum distilled after drying with anhydrous magnesium sulfate for several days. Phenol, the concentration of which ranged from $1.96 \cdot 10^{-3}$ and $1.67 \cdot 10^{-2}$ mole/liter, and water, the concentration of which ranged from 0.55 to 5.00 moles/liter, were selected as the proton donors. The dissolved oxygen was removed by bubbling a stream of dry hydrogen through the solutions for 10-15 min.

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