CONTRIBUTION OF THE PYRYLIUM STRUCTURE TO THE ELECTROCHEMICAL PROPERTIES OF NITROFLAVONES

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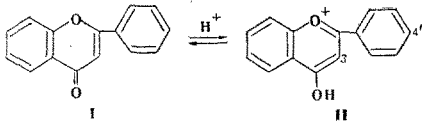
The polarographic behavior of 3- and 4'-nitroflavones on a dropping mercury electrode in Britton–Robinson buffer solutions was investigated. It is shown that, depending on its position, the nitro group displays properties that are typical only for aromatic nitro compounds or a combination of properties of aromatic and aliphatic α-unsaturated nitro compounds. The deciding factor is the realization of pyrylium and pyrone structures, depending on the pH of the medium. The kinetic parameters of the chemical transformation of the nitro form to the aci form of 3-nitroflavone in an alkaline medium are presented.

A peculiarity of flavonoids is their ability under certain conditions to form a unified conjugated system, which is responsible for their dual character: They display properties that are typical for both olefinic and aromatic compounds [1, 2], and this determined their electrochemical behavior to a considerable extent.

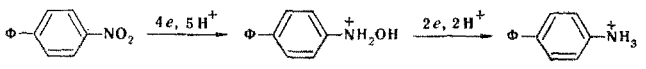
In an investigation of the polarographic reduction of flavone and its chloro and hydroxy derivatives on a dropping mercury electrode we observed the equilibrium existence of pyrone (I) and pyrylium (II) forms. We showed that the more aromatic pyrylium structure is realized in an acidic medium, while the pyrone form predominates in an alkaline medium [3-5].



I II

An important factor that affects the properties of flavones is also the position of the substituent – in the composition of the γ-pyrone ring or in the aromatic fragments. In this connection, it seemed of interest to study the electrochemical reduction of nitroflavones that contain a polarographically active nitro group in the 3 and 4' positions. This makes it possible to estimate the change in the aromatic character of the pyrone fragment as a function of the pH when the electrochemical properties of the nitro group are used as an "indicator."

The nitro group in 4'-nitroflavone has clearly expressed aromatic character and during electrolytic reduction displays properties that are typical for aromatic nitro compounds, as, for example, in the case of nitrobenzene [6]. In both acidic and alkaline media the nitro group of 4'-nitroflavone is reduced in two steps: The first four-electron step corresponds to reduction to the corresponding hydroxylamine, while the second two-electron step is in agreement with subsequent reduction to an amine or its salt, depending on the pH (Figs. 1 and 2, curves A and B), in contrast to nitrobenzene, the reduction of which in an alkaline medium results in the formation of hydroxylamine.



This distinctive peculiarity in the reduction of 4'-nitroflavone may be associated with an increase in the conjugation chain, which promotes an increase in the basicity of the hydroxylamino group.

The product of six-electron transfer is further reduced at more negative potentials in the same way as 4'-aminoflavone; this follows clearly from the character of the dependence of the magnitude of the current

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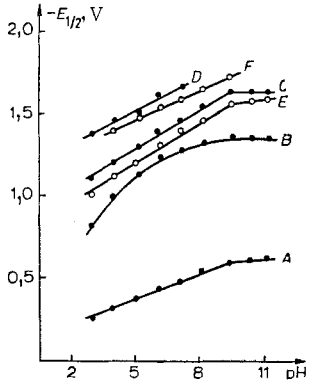


Fig. 1

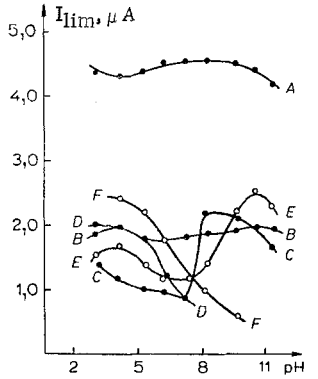


Fig. 2

Fig. 1. Dependence of the half-wave potential on the pH: A), B), C), and D): for 4'-nitroflavone; E) and F) for 4'-aminoflavone.

Fig. 2. Dependence of the limiting current on the pH: A), B), C), and D) for 4'-nitroflavone; E) and F) for 4'-aminoflavone (the designations correspond to the curves in Fig. 1).

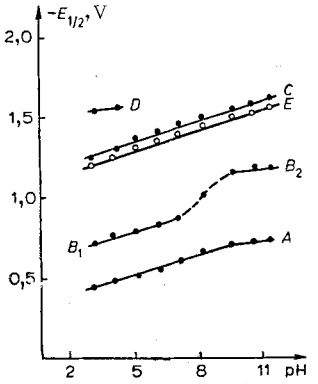


Fig. 3

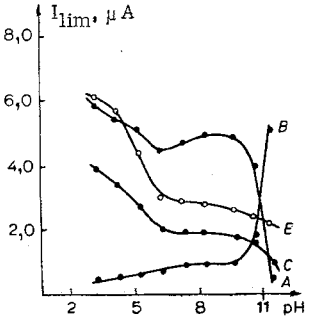


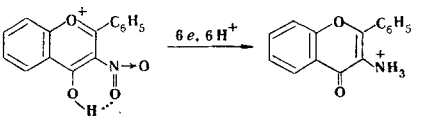
Fig. 4

Fig. 3. Dependence of the half-wave potential on the pH: A), B), C) and D) for 3-nitroflavone; E) for 3-aminoflavone.

Fig. 4. Dependence of the limiting current on the pH: A), B), and C) for 3-nitroflavone; E) for 3-aminoflavone (the designations correspond to the curves in Fig. 3; catalytic wave D is not shown).

and the half-wave potential on the pH of the solution when the E and F curves are compared with the C and D curves (Figs. 1 and 2). The certain overstatement of the $E_{1/2}$ value in favor of negative potentials for 4'-nitroflavone can be explained by the effect of heredity, as well as by the difference in the limiting currents.

3-Nitroflavone, in which the nitro group is included in the composition of the γ-pyrone ring, displays the greatest similarity to aromatic nitro compounds in an acidic medium, in which a pyrylium structure is realized. At pH < 5 four waves are observed on the polarogram of 3-nitroflavone (Figs. 3 and 4). The first six-electron wave (A) has diffusion character and is due to reduction of the nitro group to the corresponding amine:



The formation of 3-aminoflavone in this step was proved by millicoulometry at a controllable potential with subsequent analysis of the solution by means of thin-layer chromatography (TLC) by the reference-spot method.

TABLE 1. Dependence of the Potential and the Slope of the First Reduction Wave of 3-Nitroflavone on the pH

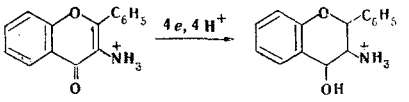
pH	$-E_{1/2}$, V	$\alpha \cdot n_a$	pH	$-E_{1/2}$, V	$\alpha \cdot n_a$
3,05	0,430	0,62	7,13	0,600	0,81
4,05	0,485	0,66	8,15	0,660	0,83
5,20	0,500	0,70	9,55	0,735	0,86
6,18	0,575	0,77	10,38	0,750	0,92

TABLE 2. Kinetic Parameters of the Chemical Transformation of 3-Nitroflavone in Solutions with Different Acidities

pH	$k^{298} \cdot 10^3$, min^{-1}	$\Delta H^{\neq}$, kJ/mole	$-\Delta S^{\neq}$ J/mole·°K
10,4	12,7	70,6	44,3
10,8	63,1	62,3	58,1
11,2	78,8	59,4	67,3

However, as the pH is increased, the limiting current of wave A decreases to a four-electron current at pH 6.2, after which it again increases. This behavior of 3-nitroflavone is probably due to the possibility of the formation of a hydrogen bond between the pyrylium hydroxy group and the nitro group, while the increase in conjugation makes 3-nitroflavone closer to 4-nitrodiphenyl with respect to its electrochemical characteristics [7].

The second weakly expressed wave (B_1) has adsorption character (the slope of the line in coordinates of $\log i_{lim}$ and $\log H$ is close to unity). Its interpretation is difficult. In an acidic medium the reduction of the amine formed in the first step results in a four-electron process (wave C), which at pH > 6 becomes a two-electron process.



This is due to the fact that as the pH is increased, the possibility for protonation of the molecules decreases and results in conversion of the pyrylium form to the pyrone form, which is reduced with the consumption of two electrons in neutral and alkaline media, as has been observed for flavone [3]. The analogy in the character of the dependence of the limiting current and $E_{1/2}$ on the pH of the corresponding waves for 3-nitroflavone and 3-aminoflavone (Figs. 3 and 4, curves C and E) serves as additional evidence for this.

The close-to-theoretical dependence of $E_{1/2}$ on the pH ($\Delta E_{1/2}/\Delta pH = -50$ mV, Fig. 3; -53 to -59 mV for nitrobenzene [6, 8]), as well as the closeness of the reduction potential to that for nitrobenzene, constitutes evidence in favor of the aromatic character of the nitro group. The increase in the steepness of the curve in neutral and alkaline media and the character of the dependence of the slope of the wave on the pH (Table 1) constitute evidence in favor of the aliphatic character of the nitro group of 3-nitroflavone.

3-Nitroflavone displays its greatest similarity to aliphatic nitro compounds at pH > 9. As in the case of nitroalkanes [6], the limiting current of wave A (Fig. 4) decreases rapidly with time as the pH is increased, but wave B_2, which lies in the region of more negative potentials and corresponds to six-electron reduction, increases. We are evidently dealing with a case in which the nitro form of 3-nitroflavone under the influence of hydroxide ions is converted to the polarographically active aci form (as in the case of phenylnitromethane [9, 19]): At high pH values the competitive effect of protonation is eliminated, 3-nitroflavone takes on a pyrone structure, and an appreciable (with time) process involving the formation of the aci form is observed. We studied the kinetics of this process at various pH values; the results are presented in Table 2.

The existence of wave D, which describes the catalytic liberation of hydrogen (wave D is not presented in Fig. 4), may be due to the formation in one of the steps of the electrolytic reduction of a catalytically active product such as a hydroxylamine derivative, one of the reduced forms of which, as has been demonstrated in the case of aliphatic hydroxylamines [11], has catalytic activity on the electrode.

EXPERIMENTAL

The polarographic measurements were made with an LP-7 polarograph with a dropping mercury electrode with the following characteristics: m = 2.244 mg/sec, and t = 3.96 sec. The half-wave potentials were assigned with respect to a saturated calomel electrode. A 0.1 M solution of potassium chloride in aqueous alcohol (50%) Britton-Robinson buffer solutions [12] served as the base electrolyte for all of the compounds. Because of its limited solubility, 4'-nitroflavone was also studied in 60% ethanol; it was established that its reduction half-wave potentials in the cited systems coincide with an accuracy up to the error in the measurements (10 mV). The acidities of the buffer solutions were measured with a pH-340 pH meter with a glass electrode. The investigation was made at 25 ± 0.1°C at a depolarizer concentration of $0.5 \cdot 10^{-3}$ M. The oxygen was removed by bubbling in argon for 10 min. A 0.1% solution of gelatin (two to three drops) was added to suppress the polarographic maxima.

The kinetics of the tautomeric conversion of the nitro form to the aci form were studied from the decrease with time of the first reduction wave of 3-nitroflavone under polarographic conditions. The sum of the reduction waves of both tautomeric forms remained constant and corresponded to a six-electron process.

The products liberated in the course of the millicoulometric measurements were identified by the reference-spot method in TLC [Silufol, chloroform–benzene (4:1), chloroform–methanol (98:2)].

The investigated compounds were synthesized by known methods and had the following characteristics: 3-nitroflavone had mp 140-141°C [13], 4'-nitroflavone had mp 236-238°C [14], 4'-aminoflavone had 234-236°C [15], and 3-aminoflavone had mp 134-136°C [16, 17].

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