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POLAROGRAPHIC STUDY OF FLAVONOIDS.
FLAVONE, FLAVONOL, AND 3-CHLOROFLAVONE

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The polarographic behavior of flavone and its 3-hydroxy and 3-chloro derivatives on a dropping mercury electrode was studied. It is shown that the investigated compounds in solution are represented by two polarographically active forms in equilibrium, one of which is reduced primarily in acidic media, the other of which is reduced primarily in neutral and alkaline media.

A number of papers on the use of polarography for flavonoid compounds have been published [1-7]. However, most of them [1, 2, 4, 6] are devoted to the application of the polarographic method for quantitative analytical purposes, and the mechanism of electrochemical reduction is not discussed in them. There is no commonly shared opinion with respect to the mechanism of the reduction of flavonoids in the literature [3, 7]. The authors investigated polyhydroxylated natural flavonoids (for example, quercitin and morin). In this case, because of the complexity of the structure, it was difficult to establish an interrelationship between the electrochemical behavior and the electronic structures of the flavonoids.

In this connection we began a study of the polarographic reduction of flavonoids in the case of a systematic series of mono-, di-, and polysubstituted derivatives with various electrophilic and nucleophilic substituents.

The polarographic properties of flavone and two of its derivatives with substituents in the pyrone fragment (3-hydroxy- and 3-chloroflavones) are examined in the present paper.

Flavone

It is apparent from Fig. 1 that the reduction of flavone in acidic media (up to pH 7.5) takes place in one step. The $E_{1/2}$ value of the corresponding polarographic wave is shifted to the more negative region as the pH of the medium increases (Fig. 2). The diffusion character of the wave for the reduction of flavone in acidic media provides evidence for the possibility of the application of the Ilkovic equation for the determination of the number of electrons consumed per molecule of depolarizer. This theoretical calculation and the millicoulometric determination of the number of electrons make it possible to conclude that the reduction of flavone in acidic media is a one-electron process. However, the shift of the half-wave potential to the negative region as the pH of the medium increases indicates participation of protons in the electrochemical process.

In alkaline media (pH > 7.5) the first reduction wave of flavone decreases rapidly, but a second less negative wave appears and increases. The overall height of both waves at pH 10 considerably exceeds the current of a one-electron process (Fig. 1). This decrease in the first wave, which resembles a dissociation curve, may correspond to the presence in weakly alkaline media of two forms of flavone molecules. In this case the reduction

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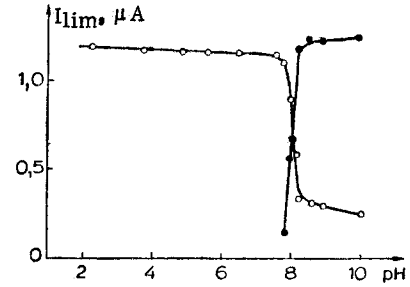


Fig. 1. Dependence of the limiting current in the reduction of flavone on the pH.

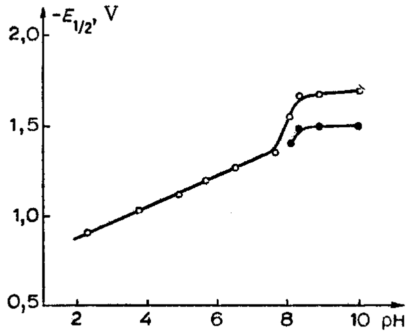
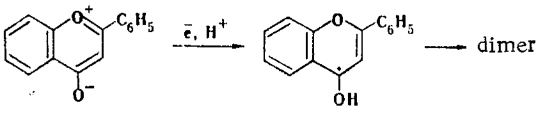


Fig. 2. Dependence of $E_{1/2}$ for the reduction of flavone on the pH.

of one of the forms in acidic media occurs in a one-electron step, and the reduction of the other form in alkaline media takes place in a two-electron step.

The existence of a kinetic restriction during the reduction also indicates the existence of a dynamic equilibrium between the two forms of flavone that depends on the pH of the medium. The kinetic character of the reduction was confirmed by measurement of the temperature coefficient. It was found that an increase of 1°C leads to a 6% increase in the current strength of the first step, while the height of the second wave decreases (pH 8.14).

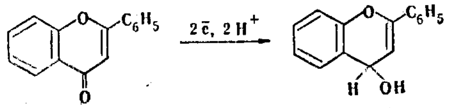
On the basis of the literature data [8-10], it may be assumed that flavone exists in pyrylium and pyrone forms. The equation of the first step in the reduction of flavone can then be represented in the form



I

It is known that flavone has a rather high basicity (pK = –1.33) and is capable of undergoing protonation in acidic media (our data). The existence of a pyrylium form of flavone I is in agreement with the more negative $E_{1/2}$ value for its reduction, since this form has higher stability due to an increase in the conjugation as compared with pyrone form II.

The second two-electron wave that appears in weakly alkaline media lies in the region of less negative potentials and corresponds to the reduction of pyrone form II of flavone:



II

The different character of the reduction of the two forms indicates the different reactivities of the two centers — the pyrylium ion in one case and the carbonyl group in the other.

TABLE 1. Dependence of $E_{1/2}$ and the Limiting Current Constant on the pH for 3-Hydroxyflavone

pH	$-E_{1/2}$, V		$(i_{lim}/c) \cdot m^{2/3} \cdot t^{1/6}$	
	wave I	wave II	wave I	wave II
3,74	1,145		1,12	
4,84	1,245		1,18	
5,64	1,295		1,15	
6,50	1,350	1,600	1,15	0,91
7,60	1,445	1,620	1,28	0,37
8,22	1,520		1,34	
8,86	1,540		1,28	
10,0	1,540		1,26	

TABLE 2. Dependence of $E_{1/2}$ and the Limiting Current Constant on the pH for 3-Chloroflavone

pH	$-E_{1/2}$, V		$(i_{lim}/c) \cdot m^{2/3} \cdot t^{1/6}$	
	wave I	wave II	wave I	wave II
3,74	1,070		1,15	
4,84	1,150		1,12	
5,64	1,215		1,12	
6,00	1,235	1,525	1,07	2,56
6,50	1,280	1,520	1,07	1,93
7,02	1,315	1,515	1,18	2,94
7,60	1,395		1,95	
8,22	1,445		1,74	
8,86	1,455		1,71	
10,0	1,460		1,73	

The reduction of flavone at the carbonyl group rather than at the double bond of the γ-pyrone ring is proved by the absence of a wave corresponding to further reduction of the intermediately formed flavonoid, the reduction potential of which is completely attainable under our conditions.

Thus in a study of the polarographic properties of flavone we detected the equilibrium existence of two forms — pyrylium form I in acidic media and pyrone form II in neutral and alkaline media.

3-Hydroxyflavone

The first reduction wave of 3-hydroxyflavone in acidic media increases from a one-electron wave to a wave corresponding to a two-electron transition in alkaline media (Table 1). Two one-electron waves are observed in the neutral region. The half-wave potential for the reduction of 3-hydroxyflavone depends on the pH in acidic media and does not change in alkaline media, as also observed in the case of flavone. On the whole, the behavior of 3-hydroxyflavone during electrochemical reduction is similar to that of flavone. This provides a basis for the assumption that they have identical electroreduction mechanisms, i.e., one-electron reduction of the pyrylium form of 3-hydroxyflavone occurs in acidic media, whereas two-electron reduction of the pyrone form takes place in alkaline media.

In acidic media 3-hydroxyflavone has more negative half-wave potentials than flavone. This may be associated with greater stabilization of the pyrylium form due to the incorporation of a hydroxyl group ($\sigma_{OH}^{ortho} = -0.38$) [11]. This fact was previously noted during a study of the acidity of the OH group in the 3 position [8].

2-Chloroflavone

The same dependence of $E_{1/2}$ on the pH of the medium as in the case of flavone and 3-hydroxyflavone is observed in the reduction of 3-chloroflavone. However, 3-chloroflavone differs in that it has two polarographically active groups and electrochemical reduction proceeds in two directions. A second reduction wave corresponding to a two-electron transition appears in the neutral region; this wave vanishes at pH > 7.5 (Table 2). The independence of $E_{1/2}$ on the pH for this wave indicates that it is due to reduction of the C—Cl bond. The magnitude of the current of this wave corresponds to a two-electron process (calculation from the Ilkovic equation); this is also characteristic for the reduction of this bond [12, 13].

As in the reduction of flavone and 3-hydroxyflavone, 3-chloroflavone is reduced in a one-electron step in acidic media (the number of electrons was calculated from the Ilkovic equation). One does not observe the decrease in the reduction wave in alkaline media that is observed for flavone but rather an increase, as in the case of 3-hydroxyflavone (Tables 1 and 2). The mechanism of the reduction of 3-chloroflavone is similar to the mechanism of the reduction of the two compounds described above.

EXPERIMENTAL

The polarographic measurements were made with an LP-60 polarograph with a dropping mercury electrode with the characteristics m = 1.803 mg/sec and t = 4.24 sec. The half-wave potentials were adjusted with respect to a saturated calomel electrode. The base electrolytes were alcohol–water (60% by volume) buffer solutions of acetic acid (0.2 M) and LiOH (0.2 M); the pH values of the buffers were measured with an LPM-60M pH meter with a glass electrode. The pH values of the aqueous buffers were increased 1.0-1.2 by dilution with ethanol.

The experiments were carried out at 25 ± 0.1°C at a depolarizer concentration of $0.5 \cdot 10^{-3}$ mole/liter. The oxygen was removed by bubbling helium through the solutions for 20-30 min. A 0.1% solution of gelatin (two to three drops) was added to suppress the polarographic maxima. The millicoulometric determination of the number of electrons for flavone (n = 1.12; 1.27) was accomplished as described in [14].

The investigated compounds were synthesized by the methods in [8, 15, 16]. Flavone had mp 95-96°C (from petroleum ether) [15], 3-hydroxyflavone had mp 169°C (from ethanol) [8], and 3-chloroflavone had mp 120-121°C (from ethanol) [16].

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