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THE POLAROGRAPHY OF COUMARINS IN ALCOHOLIC-AQUEOUS MEDIA. I

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The explanation of the characteristic features of the polarographic behavior of coumarin derivatives is of definite interest for the further chemical study of this class of natural substances.

The present investigation was undertaken with the aim of elucidating the characteristic features of the reduction of coumarin derivatives at a dropping mercury electrode (DME) and comparing the mechanisms of reduction chemically using a catalyst and at the DME. Literature information on the question of the reduction of coumarin derivatives at a DME is contradictory and incomplete [1-13].

In coumarins and their derivatives, catalytic hydrogenation takes place at the 3, 4-double bond. In view of the fact that the 3, 4-double bond is conjugated with a carbonyl group and is thereby partially protected from the action of reagents, reduction takes place rapidly only under pressure. Under the usual conditions coumarin derivatives are reduced slowly [14, 15]. In furocoumarin derivatives with an unsubstituted furan ring, the 4', 5'-double bond of the furan ring is rapidly hydrogenated under ordinary conditions [16].

As a result of the investigations carried out it was established that the natural coumarins are reduced at the position of the 3, 4-double bond of the α-pyrone ring with the involvement of one electron at each stage of the electrochemical process. The nature of the volt-ampere curves can be seen from Fig. 1.

The electrochemical activity of the double bond is confirmed unambiguously by the absence of a polarographich wave for the dihydrocoumarin that we synthesized and by the detection of the latter in the products of the electrolysis of coumarin by paper chromatography. A similar product is formed in the chemical hydrogenation of coumarin [17, 18]. The considerable tendency of the 3, 4-double bond of the α-pyrone ring to undergo hydrogenation, like that in unsaturated hydrocarbons [19], characterizes its double bond as an ethylenic bond. Other authors have come to the same conclusions on the basis of quantum mechanical calculations [20].

An investigation of the nature of the current in the reduction of substances may give an idea of the state of the molecules in solution. For this purpose we studied the dependence of the main polarographic indices—the half-wave potential and the current—on the pH of the solution (Fig. 2), the pressure on the dropping mercury (Fig. 3), and the dropping time of the electrode (Fig. 4), and also on the concentration of the alcohol and its nature (Table 1).

Table 1

Dependence of $E_{1/2}$ for Coumarins on the Concentration of Alcohol in the Aqueous Alcoholic Medium

Compound	Alcohol	Concentration of alcohol, %	Support	Concentration of depolarizer	$E_{1/2}$
Coumarin	Isopropyl	62.5	5% TEAI	$1 \cdot 10^{-3}$	1.74
		50.0			1.72
		37.5			1.70
		25.0			1.67
		12.5			1.64
	Ethyl	87.5			1.84
		62.5			1.75
		50.0			1.73
		37.0			1.72
		25.0			1.67
		60.0	Buffer, pH 7.1		1.71
	Methyl	12.0	5% TEAI		1.69
		100.0			1.85
		87.5			1.76
		62.5			1.70
		70.0			1.38
Xanthotoxin	Ethyl	70.0		0.05%	1.52
	Methyl	70.0			1.45
Bergapten	Ethyl	70.0			1.62

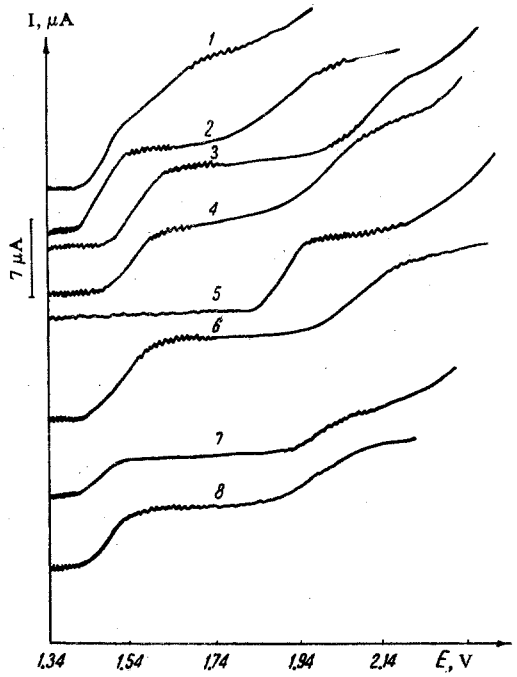


Fig. 1. Volt-ampere curves of some coumarin derivatives: 1) umbelliferone on a support of 5% LiCl in aqueous methanolic solution; 2) cnidicin; 3) osthole; 4) pimpinellin; 5) farnesiferone; 6) psoralen on a support of 5% TEAI in ethanolic aqueous solution; 7) athamantin; and 8) coumarin, recorded on a support of 5% TEAI in methanolic aqueous solution.

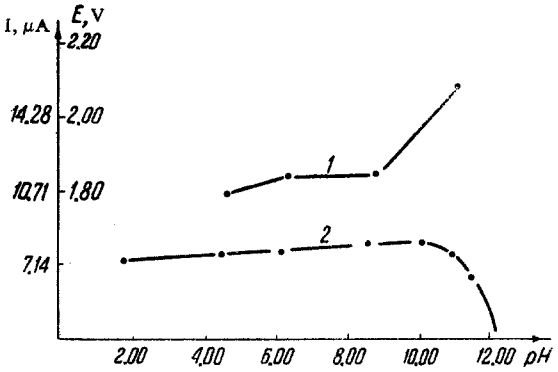


Fig. 2. $E_{1/2}$ and I'_d as functions of the pH of the solution for coumarin in aqueous methanolic solution: 1) change in $E_{1/2}$; 2) change in I'_d.

The fact that the current depends linearly on $H^{1/2}$ and the concentration of depolarizer in the range from 0.0002 to 0.1000% for coumarin and its derivatives under various polarographic conditions shows the diffusion nature of the current. It is possible to arrive at similar conclusions on the basis of the temperature coefficients of the current, which are between 1.29 and 2.00% for a number of coumarin derivatives (coumarin, xanthotoxin, bergapten, sphondin, imperatorin, and isopimpinellin).

The linear dependence of the current on the concentration of various derivatives of coumarin, psoralen, and angelicin forms the basis of a method for their quantitative determination [21–22].

The nature of the dependence of the current on $H^{1/2}$ (see Fig. 3) at various pH values shows the existence of kinetic restrictions in the acid and alkaline regions.

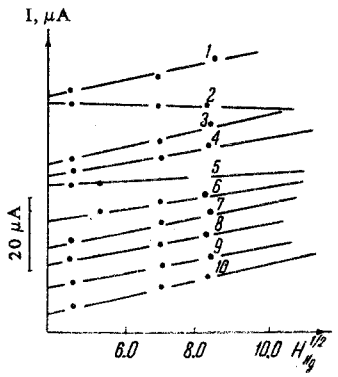
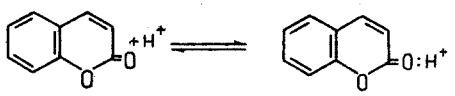


Fig. 3. Change in the limiting current of coumarin as a function of $H^{1/2}$ at various pH values (ionic strength of the solution, 0.39): 1) 3.29; 2) 3.79; 3) 4.10; 4) 4.50; 5) 5.02; 6) 7.10; 7) 8.36; 8) 8.91; 9) 10.36; 10) 11.2.

According to the ideas of S. G. Mairanovskii [23], the kinetic restrictions in the acid region may be explained by the protonization of the molecules of the coumarin derivatives. M. E. Perel'son, A. V. Tutkevich, Yu. N. Sheinker, and N. P. Gambaryan came to the same conclusions in an explanation of the mechanism of the nitration and sulfonation of coumarin using quantum mechanical calculations [20] of the π-electron density of coumarin molecules. On the basis of these calculations, the protonation of coumarin molecules may be represented in the following way:



Because of an enhancement of the polarization of the electrochemically active form, the protonated form of the molecules is reduced at the DME more readily than the nonprotonated form. Consequently, in regions of acid pH values, $E^{1/2}$ for the coumarins is lower than in the neutral region. The basicity constants of the coumarins found by V. V. Tolmachev [24] by IR spectrophotometry likewise confirms the possibility of the protonation of the coumarins in the acid region.

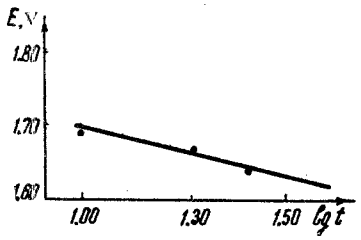


Fig. 4. $E_{1/2}$ as a function of the drop period of the electrode for coumarin on a support of a Britton buffer solution (pH 7.1). Characteristics of the capillaries: 1.70–3.80 $mg^{2/3} \cdot sec^{-1/2}$.

The kinetics of the reduction of the coumarins in the alkaline pH region is determined by the ratio of the rate constants of the electrode reaction and of the opening of the lactone ring, which has been shown by a chemical method [25, 26]. The dependence of the optical density of the coumarins and the magnitude of the diffusion current on the pH (Table 2) confirm the existence of kinetic restrictions.

The fall in the current and in the optical density in alkaline media is an indication of the absence of polarographic activity of the hydroxycinnamic acids in the region of potentials of the first stage of reduction of the coumarins. Another proof of this is the absence of a wave on the polarograms of the hydroxycinnamic acids in alkaline media.

The considerable changes in $E_{1/2}$ with a change in the drop period of the capillary and with the concentration of the alcohol and its nature, and also the suppression by coumarins of the oxygen, lead, bismuth, nickel, and alkaloid (serpentine and papaverine) maxima indicates the considerable adsorption of the depolarizer and the products of the reduction of the coumarin on the DME. The nature of the electrocapillary curves and the oscillograms that we obtained is in agreement with literature data [7, 12] and confirms the existence of adsorption phenomena.

Spectral investigations of the products of the electrolysis of coumarins [3, 4] and a mathematical treatment of the volt-ampere curves of coumarin using S. G. Mairanovskii's equation [23] characterize the reversibility of the electrode process in the first stage of reduction and of the formation of dimers.

On the basis of the investigations carried out, the following scheme for the reduction of coumarin at a DME may be assumed:

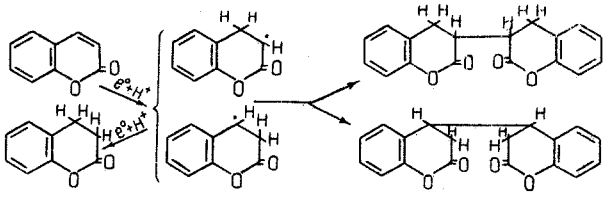


Table 2

Changes in the Current and Optical Density as Functions of the pH of the Medium for Some Coumarin Derivatives

Compound	pH of the medium	I_d, μA	Optical density
Coumarin	4.10	9.99	0.102
	7.10	9.39	0.101
	9.91	8.09	0.109
	10.36	7.59	0.085
	11.98	0.00	0.045
Xanthotoxin	4.10	11.86	1.30
	9.91	18.58	1.55
	11.98	0.00	1.35
Umbelliferone	4.60	2.20	0.590
	6.27	2.13	0.540
	11.00	1.00	0.360

The reduction of coumarin derivatives containing no polarographically active groups in side chains takes place by this scheme. The nature of the electrode process of a number of coumarins can be judged from the ratio of the heights of the waves of the volt-ampere curves. In all coumarin derivatives with the exception of peucenidin, libanotin, and oroselone, the ratio of the heights of the wave is approximately 1:1. These results enable us to assume that the furan ring of derivatives of psoralen and angelicin take no part in reduction at the DME and the mechanisms of the reduction of alkyl-substituted derivatives of coumarin and the furocoumarins are identical. The different ratio of the waves in the case of peucenidin and libanotin (1:3) and oroselone (1:2) are explained by the additional reduction of the organic acid residues in the first two and of the double bond in the oroselone radical.

In the case of hydroxy derivatives of coumarin—umbelliferone, 4-methylumbelliferone, and esculin—the first and second waves almost fuse, which is apparently due to the formation of a hydrogen bond between the molecules of the depolarizer. By taking the formation of a hydrogen bond into account, it is easy to explain the considerable lowering of the diffusion current constant for the hydroxy derivatives of coumarins as compared with the alkylated molecules of similar nature. The features in the reduction of these compounds that have been mentioned may be regarded as in favor of a one-electron reduction at the DME and can also be used for their identification.

A number of substituents containing double bonds (farnesyl in umbelliprenin, isopentenyl in imperatorin and osthole, and ester groupings in athamantin) are not reduced at the DME because these bonds are isolated and are conjugated with the α-pyrone ring to a small extent.

Experimental

The following apparatus was used in performing the investigations: polarographs of various makes and systems (LP-55 and M-103 on the Heyrovský system; and the TsE-312 PLA and the PO-51-22 oscillographic models), and SF-4 and "Hitachi" (Japan) spectrophotometers.

Polarographic measurements were carried out in cells with an internal anode of the Novák type [27] and with an external anode of the Titov [28]. Values of $E_{1/2}$ are referred to the saturated calomel electrode.

The number of electrons was determined by microcoulometry, and also from the Ilkovič-Heyrovský equation [29].

Spectrophotometric measurements were carried out in cells with a layer thickness of 1.00 mm. The buffer solutions were prepared as described by Britton [30], using as the basis caustic soda and tetraethylammonium hydroxide, which we prepared from the iodide by a published method [31]. A constant ionic strength in the solutions polarographed was created by the addition of potassium chloride. The pH of the polarographic solutions was measured by means of a glass electrode with an LP-55 potentiometer. The capillary constant was 1.70–3.90 $mg^{2/3} \cdot sec^{-1/2}$.

The samples of coumarins used in the work had been isolated by us from various plants [32–34] and subjected to careful purification and were evaluated as chromatographically pure. Dihydrocoumarin was obtained by the hydrogenation of coumarin with a palladium catalyst [15]. Dihydrocoumarin was detected in the electrolysis products by paper chromatography in the petroleum ether–formamide solvent system after spraying with diazotized sulfanilic acid [35]. An authentic sample of the dihydrocoumarin synthesized was used as a reference standard.

The propyl and ethyl alcohols were previously purified [35, 37], and the methyl alcohol used was of "pure for analysis" grade.

Conclusions

1. The natural coumarin derivatives psoralen and angelicin are reduced at the DME from the adsorbed state at the mercury–solution boundary at the position of the 3,4-double bond of the α-pyrone ring. The latter circumstance confirms the ethylenic nature of this bond.

2. The existence of the processes of the protonation of the coumarin molecules in acid media and of the opening of the lactone ring in alkaline media has been shown experimentally.

3. The investigations performed show that the polarographic method can be used in the study of the physiochemical properties of the natural coumarins and for their quantitative analysis.

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