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MECHANISM OF THE REDUCTION OF THE ALKALOIDS OF HAPLOPHYLLUM AT A DROPPING MERCURY ELECTRODE

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The alkaloids of plants of the genus Haplophyllum, family Rutaceae, form well-defined waves on polarography in ethanol–water solutions of $(C_2H_5)_4NI$ or $(C_2H_5)_4NOH$. We have made use of this property to determine these compounds quantitatively in medicinal preparations and in plant raw material [1, 2].

The object of the present work was to elucidate the mechanism of the reduction of alkaloids of Haplophyllum at a dropping mercury cathode, and for this purpose we have determined the number of electrons participating in the reduction, have studied the UV and IR spectra of the substances before and after electrolysis at a controlled potential, and have compared their polarographic behavior with the behavior of synthetic substances of similar structure.

We have described the apparatus and procedure for the determinations previously [1, 2]. The number of electrons was determined by polarographic microcoulometry [3]. The reduction of substances at a controlled potential was carried out by Lingane's method [4].

The UV and IR spectra of the substances were taken on SF-4 and UR-10 instruments, respectively. The UV spectra were recorded in cells (l = 0.006 and 0.0011 cm, background 0.1 N $(C_2H_5)_4NOH$ in 80% ethanol). For recording the IR spectra, the synthetic products were compressed with KBr. The products of cathodic reduction were not isolated preparatively, since very small amounts of material (3–6 mg) were subjected to electrolysis. Consequently, a mixture of each of them with the background 0.1 N solution of $(C_2H_5)_4NOH$ in 80% ethanol, after neutralization with sulfuric acid and the elimination of moisture, was placed in the form of a thin layer of paste between KBr plates. The absorption of the background was allowed for by comparing the spectrum of the paste with the spectrum of the pure background.

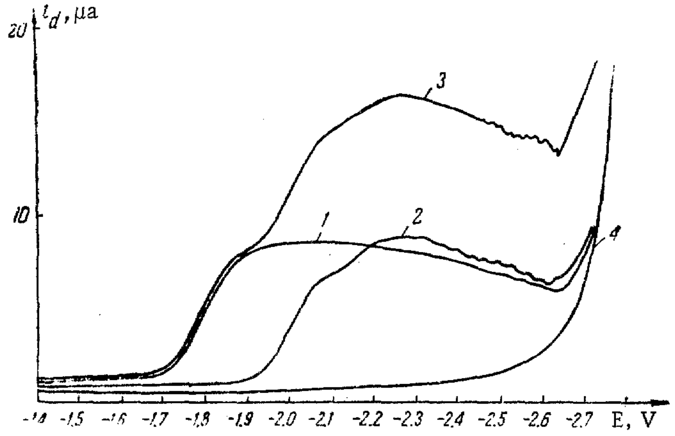


Fig. 1. Polarograms. 1) Skimmianine; 2) tetrahydroskimmianine; 3) a mixture of them; 4) background of 0.1 N $(C_2H_5)_4NOH$ in 80% ethanol.

We synthesized 4,7,8-trimethoxy-3-ethyl-2-quinolone (tetrahydroskimmianine), carbostyryl, and dihydrocarbostyryl by published methods [5–7].

The polarization curves of γ-fagarine, skimmianine, and haploperine were recorded in an ethanol–water medium containing tetraethylammonium iodide or hydroxide, and in buffer solutions with the composition $(C_2H_5)_4NOH + CH_3COOH$ (or H_3PO_4) in the pH range from 6.5 to 12.0. For the substances mentioned, the number of electrons participating in the reaction (determined by the microcoulometric method and calculated by the Ilkovič equation) was four. The value of the diffusion coefficient, which is necessary for this calculation, was determined by means of the Stokes-Einstein equation [8].

In view of the fact that in catalytic hydrogenation in the presence of an Adams platinum catalyst the furanoquinolines undergo hydrogenolysis and form derivatives of 3-alkyl-2-quinolone [5, 9] we assume that the products of the electrochemical reaction are also tetrahydro derivatives.

However, synthetic tetrahydroskimmianine proved to be polarographically active. Consequently, at some more negative potential the further hydrogenation of its molecule may take place (Fig. 1).

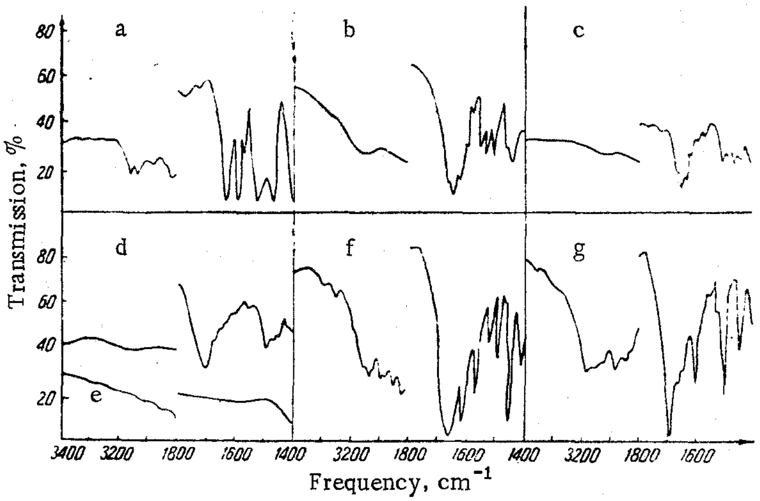
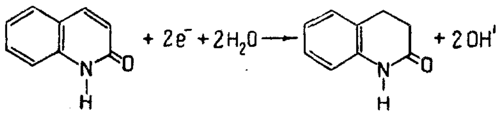


Fig. 2. IR spectra. a) Skimmianine; b) synthetic tetrahydroskimmianine; c) product of the reduction of skimmianine at −1.9 V; d) product of the reduction of skimmianine at −2.5 V; e) background; f) carbostyryl; g) dihydrocarbostyryl.

We carried out the electrolysis of skimmianine at controlled potentials of −1.90 and −2.50 V and obtained two different products. The IR spectra of both products lacked bands characteristic for a furanoquinoline skeleton (3145, 3115, 1622 cm^{-1}) [10]; instead, a band at 1650 cm^{-1} appeared (Fig. 2a–2d) showing the hydrogenolysis of the base and the formation of a −NH−C=O grouping. The results of a comparison of the IR spectra of the reduction product obtained at −1.9 V with synthetic tetrahydroskimmianine showed that they were identical. In the IR spectrum of the product obtained by reduction at −2.5 V, the carbonyl band was displaced to the high-frequency region (1710 cm^{-1}), which may be the consequence of a shortening of the chain of conjugation in which the carbonyl group participates [11].

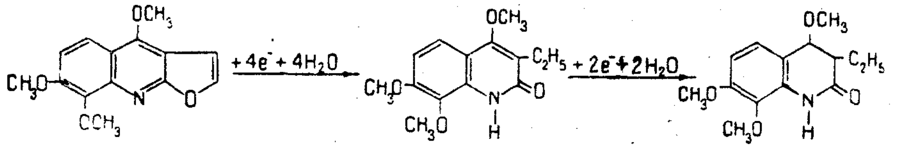


(1)

We could not effect the catalytic hydrogenation of tetrahydroskimmianine, which agrees with Cavallito and Haskell's results [7]. Consequently, to elucidate the mechanism of the reduction of this substance at a dropping mercury electrode we studied the polarographic behavior of a number of synthetic products: 2-quinolone (carbostyryl), and its derivatives 4-methoxy-2-quinolone, tetrahydroskimmianine, tetrahydrohaploperine, the product of the reduction of dubinidinal [12], tetrahydroperforine [13], tetrahydrohaplophyllidine [14], 4,8-dimethoxy-N-methyl-2-quinolone, 4,7-dimethoxy-N-methyl-2-quinolone [15], and the alkaloid foliosidine.

These compounds behave similarly at the dropping mercury cathode. They are not reduced in Britton-Robinson buffer solutions; in 0.1 N $(C_2H_5)_4NI$ and $(C_2H_5)_4NOH$ in 80% ethanol two-step chromatograms with well-defined first waves and diffuse second waves are formed. The sum of the heights of the waves corresponds to a two-electron process. In the buffers $(C_2H_5)_4NOH + CH_3COOH$ (or H_3PO_4), a wave appears between pH 6.5 and 12.0. For the carbostyryls we propose a mechanism of the electrode process which is confirmed by a comparison of the UV spectra of synthetic dihydrocarbostyryl and the reduction product of carbostyryl and a controlled potential (Fig. 3, and scheme 1).

The results of a comparison of the IR spectra of synthetic carbostyryl and synthetic dihydrocarbostyryl (Fig. 2f and 2g) show that in the spectrum of the latter the frequency ν_{max} for the carbonyl group is displaced to the high-frequency region (1690 cm^{-1}). We have observed the same shift in the spectrum of the electrolysis product of skimmianine at −2.5 V (Fig. 2d). Consequently, tetrahydroskimmianine, being a stable intermediate product of the reduction of skimmianine, is reduced at a suitable potential by scheme 1 to hexahydroskimmianine. Thus, for skimmianine the total electrode process can be expressed in the following way:



(2)

The difference between the frequencies for $\nu_{\max}$ of the carbonyl group in spectra g and d can be explained by the capacity of dyhydrocarbostyryl for forming intermolecular hydrogen bonds, the presence of which lowers the carbonyl frequency ν. The presence in hexahydroskimmianine of an intramolecular hydrogen bond between the hydrogen of the NH group and the oxygen of the methoxy group excludes the possibility of the formation of intermolecular bonds.

Skimmianine, haploperine, γ-fagarine, and their tetrahydroderivatives exhibit similar polarographic behavior and therefore in all these cases the electrode process can be represented by scheme 2.

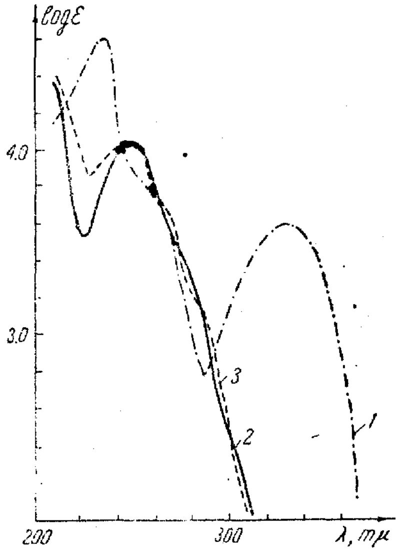


Fig. 3. UV spectra. 1) Carbostyryl; 2) dihydrocarbostyryl; 3) product of the electrolysis of carbostyryl at a controlled potential.

Summary

1. The furanoquinoline alkaloids skimmianine, haploperine, and γ-fagarine are reduced at a dropping mercury electrode in 0.1 N $(C_2H_5)_4NI$ and $(C_2H_5)_4NOH$ in 80% ethanol forming tetrahydro or hexahydro derivatives according to the potential of the electrode.

2. Carbostyryl and N-methylcarbostyryl are reduced under the same conditions to the corresponding dihydro derivatives.

3. The proposed mechanism for the electrode processes is confirmed by a comparison of the UV and IR spectra of the substances before and after their electrolysis at a controlled potential with the spectra of synthetic compounds.

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