SOME ASPECTS OF THE ELECTROREDUCTION OF NIAZID TO NICOTINAMIDE ON MERCURY ELECTRODES IN ACIDIC MEDIA

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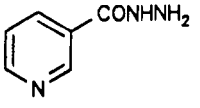
The electroreduction of niazid on mercury electrodes has been studied in acidic media (pH < 6). Tafel slopes and reaction orders were obtained at potentials corresponding to the foot of the first polarographic wave. On the basis of both polarographic and voltammetric results it has been shown that the waves appearing at more negative potentials correspond to the reduction of nicotinamide. Protonation of niazid plays an essential role in its reduction and pK values of 1.4, 3.2 and 11.5 were obtained by UV spectroscopy. The process corresponding to the first wave is irreversible, being the second one-electron transfer the rate-determining step. Above pH 4 the process is complex due to the overlapping of the waves caused by the occurence of protonation reactions.

In a previous work[1] a study on the polarographic reduction of niazid (*I*) has been reported. Up to three waves were observed depending on the pH of the medium. The limiting current of the wave appearing at less negative potentials (first wave) is independent of pH below pH 4, whereas that of the overall wave varies with the pH from a minimum value corresponding to a four-electron process at pH < 0, to a maximum value corresponding to a six-electron process at pH > 3.5. This behaviour is similar to that obtained for the reduction of nicotinamide[2], which must be the reduction product



I

at potentials corresponding to the first wave[3]. The first wave is mainly governed by diffusion at the potentials corresponding to its limiting current.

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The aim of this communication is to contribute to the elucidation of the reduction mechanism of *I* on mercury electrodes in acidic media on the basis of polarographic, voltammetric and kinetic measurements.

EXPERIMENTAL

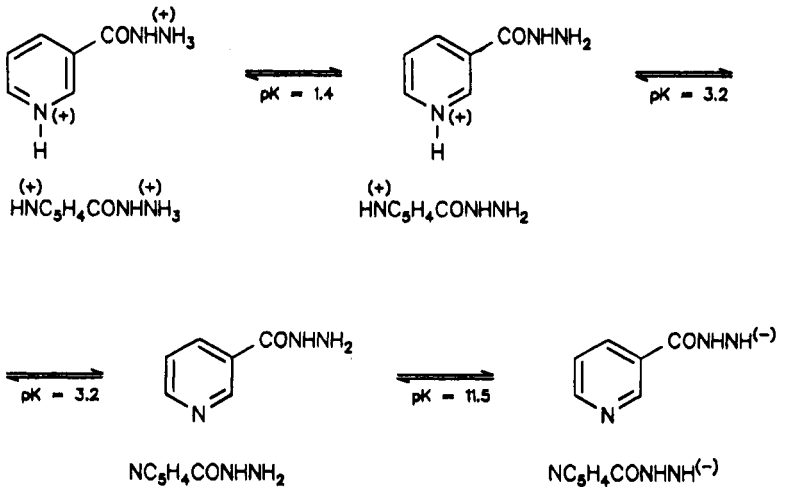
Voltammetric measurements were made on an INELECSA assembly equipped with a PDC1212 potentiostat, a GOT1018 function generator and 12 bits AD and DA converters attached to an 8088-based microcomputer which was used for data control, acquisition and treatment. Ohmic drop was corrected at scan rates above 2 V s^{-1} . The working electrode was a Metrohm EA290 with a drop area of 0.018 cm^2. The working concentration of *I* was 5 . 10^{-4} mol l^{-1} and ionic strenght was kept at 1.0 mol l^{-1} with $NaNO_3$.

For kinetic measurements of *i–E* curves were recorded automatically at a low scan rate and stored in the microcomputer by using a digitizer. The contribution of supporting electrolyte was eliminated by linear extrapolation of the curve preceding the discharge potential.

UV-visible measurements were made on a computerized Perkin–Elmer Lambda 3B spectrophotometer with 1 cm quartz cuvettes at 25 °C. All other experimental conditions are given in ref.[1] .

RESULTS AND DISCUSSION

No data have been found in the literature dealing with the protonation or dissociation constants of compound *I*. For this reason, a spectrophotometric study was carried out and p*K* values of 1.4, 3.2 and 11.5 were obtained from the variations of the absorbances at 260 nm (pH << 7) and 290 nm (pH > 7). These p*K* values were attributed to the following equilibria:



A curve-fitting method was used for the treatment of the $\Delta i / \Delta E - E$ data in differential pulse polarography (DPP). The first peak was assumed to be first-order whereas the second and/or third peaks were assumed to be the same as obtained for the reduction of nicotinamide. Thus, the following equation was used for the first peak[4]:

$$I = 4 I_p L / (1 + L)^2 \qquad (1)$$

and the following equation was used for the second and third peaks[5]:

$$I = \frac{1}{b} \frac{i (i_L - i)}{a i_L + (1 - a) i} \quad , \qquad (2)$$

where $I = \Delta i / \Delta E$, $L = \exp [-(E - E_p) / b]$; I_p and E_p are the peak intensity and the peak potential, respectively; b is a term which coincides with the slope of the logarithmic analysis in DC polarography and $a = 2/3$ and $a = 2$ for the second and third peak, respectively[6].

In strongly acidic media the polarograms were fitted by using Eq. (*1*) for both peaks, in agreement with the results obtained for nicotinamide[2]. Figure 1 shows the application of the curve-fitting procedure in two cases.

As it can be seen, the experimental data fit the theoretical equations quite well. The b values so obtained for the first peak were aroung −40 mV/decade. At pH < 1.5 the b value for the second peak was around −60 mV/decade, whereas at pH > 2 the values obtained for the second and third peak were −62 and −33 mV/decade, respectively. These results agree with those obtained in the reduction of nicotinamide[2,6].

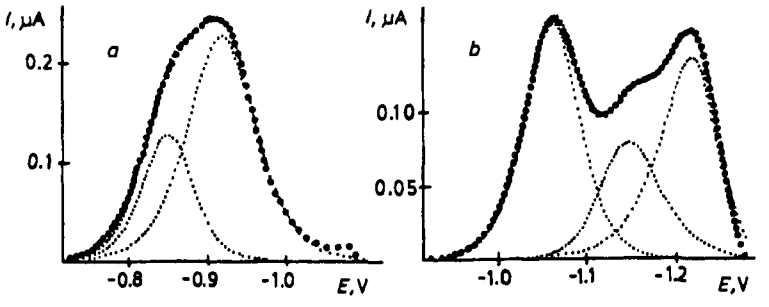


FIG. 1

DP polarograms of 1 . 10^{-4}M niazid at *a* pH 1.4 and *b* pH 3.0. Circles and dots represent experimental and theoretical data, respectively. Pulse increment −10 mV, pulse duration 40 ms

Figure 2 shows the dependence with the pH of the peak potentials obtained by applying the curve-fitting method.

When the concentration of *I* is increased at constant pH, there is a change in the peak potentials of the second and third peak. Thus, at pH 2.5 these variations are 23 and −35 mV/decade.

These variations, as well as those given in Fig. 2, are very similar to those previously obtained for nicotinamide[2,7]. Moreover, cyclic voltammograms recorded at pH > 2 show a reoxidation peak accompanying the cathodic ones when the switching potential selected correspond to the second peak. The separation of the peak potentials of the second peak and the reoxidation one is at least 800 mV, as shown in Fig. 3. All these data are in agreement with those reported for nicotinamide[7].

The E_p vs pH plot for the first peak in DP polarography shows two inflection points around pH 1.2 and 3.3 (see Fig. 2). These values are close to the pK values obtained by UV spectroscopy and must be related with the corresponding protonation equilibria. Around pH 4.5 the first peak overlaps with the second one and the situation becomes rather complex.

Logarithmic analyses of the first dc wave were carried out in the form of E vs log $[i / (i_L - i)]$. The graphs were linear below pH 3.3 and showed deviations from linearity above this pH value. The slopes of these plots are close to −40 mV/decade.

From the i–E curves traced at potentials corresponding to the foot of the first wave, the Tafel slope and electrochemical reaction orders were obtained. The value of the Tafel slope was independent of both reactant concentration and pH, having average values of −41 mV/decade. The reaction order with respect to the H^+ ion concentration were around zero and 1.9 for pH < 1.2 and in the pH range 1.3 – 3, respectively. The reaction order with respect to concentration of *I* was close to the unity in all cases.

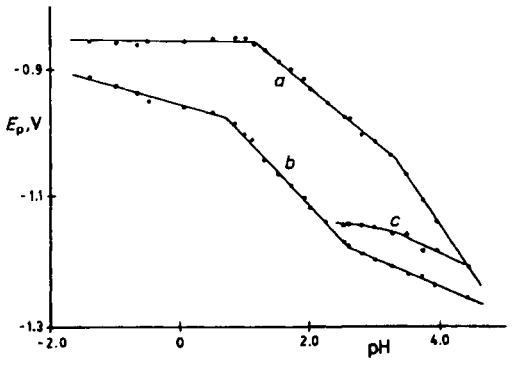


FIG. 2
Results of the application of the curve fitting in DP polarography. Dependence of the peak potentials with the pH for *a* first peak *b* second peak *c* third peak

The values of b obtained in DP polarography as well as of Tafel and logarithmic analysis slopes, are indicative of the irreversible character of the process taking place at the potentials corresponding to the first wave. This is also confirmed by the value of $\partial E_{1/2} / \partial \log t$ close to 20 mV/decade. In cyclic voltammmetry no oxidation peaks were observed until a scan rate of 100 V s^{-1} accompanying the first cathodic one. For the first peak, the value of the ratio $i_p / \nu^{1/2}$ is independent of both the scan rate and the pH. The values of $E_P - E_{P/2}$ are close to −44 mV and the slope of the peak potential vs log ν plots is around −23 mV/decade. These data confirm the irreversible character of the process.

Taking into account the above mentioned results and conclusions, reduction schemes can be proposed for the process occurring at the potentials corresponding to the first wave.

At pH < 1.2 the species in solution is that doubly protonated; the H^+ ion does not takes part in the process. Kinetic data indicate that the second one-electron transfer is the step controlling the process in the rising portion of the wave:

$$\overset{(+)}{\mathrm{HNC_5H_4CONHNH_3}}\overset{(+)}{} + e \rightleftharpoons \left[\overset{(+)}{\mathrm{HNC_5H_4CONHNH_3}}\right]^{\bullet} \qquad (3)$$

$$\left[\overset{(+)}{\mathrm{HNC_5H_4CONHNH_3}}\right]^{\bullet} + e \xrightarrow{\text{r.d.s.}} \left[\overset{(+)}{\mathrm{HNC_5H_4CONHNH_3}}\right]^{(-)} \qquad (4)$$

$$\left[\overset{(+)}{\mathrm{HNC_5H_4CONHNH_3}}\right]^{(-)} + 2H^{(+)} \longrightarrow \overset{(+)}{\mathrm{HNC_5H_4CONH_2}} + \mathrm{NH_4}^{(+)} \qquad (5)$$

This is essentially the same mechanism proposed by Lund in the reduction of isoniazid[3] . Step (3) represents the loss of ammonia to yield nicotinamide, which is subsequently reduced at potentials corresponding to the second wave. Assuming αn = 1.5 all the polarographic, voltammetric and kinetic data are easily explained.

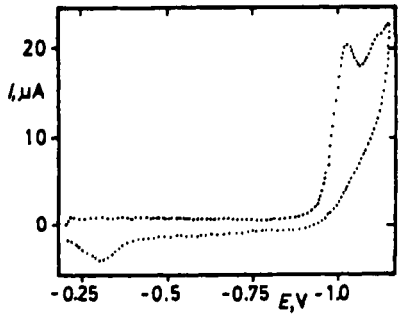


FIG. 3
Cyclic voltammogram of 5 . 10^{-4}M niazid at pH 2.52. Scan rate: 3 V s^{-1}

The results obtained at the foot of the wave confirm this scheme. The *i–E* relationship in this zone of potentials is:

$$i = 2 F K_3 k_4 K' c_I \exp [-(1 + \beta) F E/R T] , \qquad (6)$$

where c_I is the concentration of niazid, K_3 and k_4 are the equilibrium and rate constants of reactions (*3*) and (*4*) at $E = 0$, respectively, and $K' = \exp [(1 + \beta) F \Delta\phi_{ref}/RT]$, where $\Delta\phi_{ref}$ is the potential of the reference electrode. The value of the Tafel slope and the electrochemical reaction orders with respect to isoniazid and the H^+ ion derived from this equation assuming $\beta = 0.5$ agree with the experimental values.

According to the p*K* values obtained, in the pH range 1.3 – 3.3 the species in solution is $H^{(+)}NC_5H_4CONHH_2$; in addition, the values of Tafel slopes, *b* parameter in DP polarography, E_P vs log *v* plots in LSV etc. indicate that the second one-electron transfer is the r.d.s and two H^+ ions are involved in the reduction prior to this step. The first reaction can reasonabily be attributed to the protonation of niazid and the proposed scheme reads:

$$\overset{(+)}{HNC_5H_4CONHNH_2} + H^{(+)} \rightleftharpoons \overset{(+)}{HNC_5H_4CONH_2}\overset{(+)}{NH_3} \qquad (7)$$

$$\overset{(+)}{HNC_5H_4CONHNH_3} + e + H^{(+)} \rightleftharpoons \left[\overset{(+)}{HNC_5H_4CONH_2NH_3}\right]^{\cdot +} \qquad (8)$$

$$\left[\overset{(+)}{HNC_5H_4CONH_2NH_3}\right]^{\cdot +} + e \xrightarrow{\text{r.d.s.}} \overset{(+)}{HNC_5H_4CONH_2} + NH_3 \qquad (9)$$

The sequence of steps involved in reaction (*8*) cannot be established with the data available.

Polarographic, voltammetric and kinetic results are also easily explained using this scheme.

Above pH 3.3, the process becomes complicated by the occurrence of two protonation reactions of *I* and one additional protonation in the pyridine ring of nicotinamide, p*K* = 3.7 (refs[8,9]). This causes a strong dependence of the reduction potentials with the pH and the first wave overlaps with the second one. Moreover, the dependence of the overall limiting current with the pH at pH > 4 is not the same obtained in the reduction of nicotinamide[1]. All these facts prevent us from give any interpretation of the data under such conditions.

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