Control of the electrochemical reduction of horminone by pH imposition in acetonitrile

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Received 14 November 1995; in revised form 25 January 1996

Abstract

An electrochemical study using transient techniques of a quinone-type natural product, horminone, has been performed in acetonitrile in the presence of two buffer solutions of pH = 17.2 and pH = 15.5. Using linear sweep voltammetry, it was found that at both pH values the reduction mechanism of horminone involves a monoelectronic charge-transfer step, followed by a protonation step and homogeneous charge-transfer step due to disproportionation of the protonated intermediate. At pH = 15.5 the mechanism for the homogeneous charge-transfer step was found to be of the DISP1 type (first order disproportionation) from the results of double step chronoamperometry experiments. At pH = 17.2 the latter mechanism was found to be of the DISP2 type (second order disproportionation) since at this pH value the protonation step is minimized, thus causing the disproportionation reaction to be the controlling step of the mechanism.

Keywords: Horminone; Electrochemical reduction; Disproportionation; pH control

1. Introduction

Horminone (1) is a quinone type natural product. Some derivatives of horminone possess pharmacological properties [1–3]. These properties might be related to the electrochemical behavior of this compound known to occur with this kind of quinone [4]. In addition, the latter behavior is closely related to their acid–base properties, since electro-generated species possess a basic character whose strength depends on their structure and on the acidity level of the solution. In order to understand such a phenomenon, it is necessary to undertake a study of the electrochemical behavior of the horminone in a pH-controlled reaction media. However, to the best of our knowledge, there are no electrochemical studies of this system in acetonitrile (AN) or other solvent of this sort in these or other conditions.

The electrochemical behavior of quinones is compatible with the scheme of a series of consecutive reactions involving proton and electron exchange in order to produce the corresponding hydroquinone. Depending on the medium and the nature of the quinone, the reduction mechanism can be either of the ECE type [5–7] or a disproportionation reaction of the type DISP1 or DISP2 [8]. These mechanisms have been reported in aprotic solvents in the presence of weak acids as proton donors, but nothing has been reported as to the acidity levels in such reaction media in order to inhibit or to enhance a desired mechanism, i.e. to control the path of the electroreduction. In this work, a study of the reduction mechanism of horminone was performed in AN as aprotic medium, in the presence of two different buffer solutions in order to show that acidity levels determine the type of reduction mechanism of the horminone. Linear sweep voltammetry and double potential step chronoamperometry were employed in order to distinguish between these three kinetic situations [8–11], two of first order (ECE, and first order disproportionation (DISP1)) and one of the second order (second order disproportionation (DISP2)).
2. Experimental

Pure horminone extracted from natural sources was used. AN A.R dried with phosphorus pentoxide and distilled over molecular sieves, was used as solvent. The supporting electrolyte was tetrabutylammonium perchlorate (TBAP; reagent grade) dried at 90°C overnight before being used. An HMDE of about 0.0029 cm² surface area, for voltammetric studies, and a polished platinum disk of about 0.031 cm² surface area, for chronoamperometric studies, were used as working electrodes; a silver wire immersed in a solution 0.01 M in AgNO₃ and 0.1 M TBAP in acetonitrile was used as the reference electrode [12]. The potentials reported in this work are referred to the ferrocene/ferricinium couple according to the IUPAC recommendation [13]. In our case, \( E(\text{Fe}/\text{Fe}^+) = 0.040 \) V vs. \( E(\text{Ag}/\text{Ag}^+) \). The cell was maintained in a pure nitrogen atmosphere at all time. Voltammograms were recorded on an XY plotter and chronoamperometric measurements were performed with a DEI-Digital Electrochemical Analyzer (Radiometer-Tacussel). The double potential step chronoamperometric experiments were performed from the signal to a periodic pulse rather than at a single inverse pulse for the reasons discussed in the literature [10]; in this case, the direct and inverse pulse potentials in the periodic signal were \(-1.2 \) V and \(-0.716 \) V respectively. In this case, \(-0.716 \) V corresponds to the potential at the foot of the voltammetric curve [11]. The ratio of the oxidation pulse time to the reduction pulse time was equal to 10 in the periodic perturbation, in the same way as described by Amatore and Savéant [11]. The diffusion coefficient value, required for the calculation of the apparent number of electrons \( n_{\text{app}} \), was taken as \( D = 1.6 \times 10^{-5} \) cm² s⁻¹ as a typical value for this kind of compound in AN [14].

Buffer solution preparation was performed by mixing equal quantities (0.5 mmol) of base and acid pairs, previously dried overnight, with 25 ml of 0.1 M TBAP in AN. The following acid-base pairs were employed: benzoic acid + sodium benzoate (HBz + NaBz), salicylic acid + sodium bisalicylate (\( \text{H}_2\text{Sal} + \text{NaHSal} \)). A 20 mM stock solution of horminone was prepared in AN.

The pH value of the above solutions was determined by means of previous calibration of the glass electrode, as reported by Kolthoff and Chantooni [15], according to the spectrophotometric method using \( o \)-nitroaniline as indicator and measuring the absorption of the yellow at 410 nm. Absorption of \( o \)-nitroaniline alone \( A_0 \) and mixed with several aliquots of 0.5 M anhydrous perchloric acid \( A_i \) was measured to determine the pH values of the calibration curve and buffer solutions, both in 0.1 M TBAP in AN according to

\[
pH = 4.85 + \log \frac{A_i}{A_0 - A_i}
\]

where 4.85 is the pK value of \( o \)-nitroanilinium/\( o \)-nitroaniline in the solutions employed. The e.m.f. measurements were performed between the glass electrode and the same reference electrode used for the electrochemical studies described above.

3. Results and discussion

For the glass electrode used in this study, the calibration plot (pH vs. the e.m.f. in millivolts) yields a straight line with a slope of 56.3 mV, in a good agreement with those reported in literature [15]. An equation for our glass electrode, obtained by means of a linear regression analysis of the calibration plot data, is used to determine the pH of buffer solutions employed:

\[
E = 605 - 56.3\text{pH} \quad (r^2 = 0.9916)
\]

According to the pH calibration plot, the pH values of HBz + NaBz \( \downarrow \) buffer solution (BBS) and \( \text{H}_2\text{Sal} + \text{NaHSal} \downarrow \) buffer solution (SBS) were 17.2 and 15.5 respectively.

The voltammetric behavior of horminone in (a) 0.1 M TBAP in AN; (b) BBS and (c) SBS, is shown in Fig. 1, where voltammograms on HMDE, at 160 mV s⁻¹ for 0.4 mM horminone, are given.

From Fig. 1(a), it is observed that horminone presents a reduction peak at a far negative potential and presents an oxidation peak at more positive potentials. The latter behavior suggests the existence of chemical reactions coupled to the charge-transfer step. Since in these experiments no donor proton is present, then the acidic hydrogen of the \( o \)-phenol present in the molecule of horminone acts as the
inner proton donor in a typical autoprotonation reaction [16].

In order to control the autoprotonation reaction and to show the influence of acidity level on the mechanism of the reduction of horminone the BBS and the SBS were used. The voltamogram profiles in these media are different. At both pH values an increment of the cathodic current peak is observed. It can be demonstrated that in the absence of a proton donor, the global reduction reaction of horminone requires \(2/3e^-\) for each reduced molecule, according to the self-protonation mechanism mentioned above [16]. Fig. 2 shows the current function \(I_o/\nu^{1/2}\) for the reduction peaks of horminone in BBS and SBS. It is observed that current function values are three times greater than that obtained in the unbuffered solution where autoprotonation takes place. This increment is an indication that the electron-transfer number is two; thus the global reduction reaction of horminone requires two electrons for each reduced molecule. From this, it may be concluded that the \(E_1^-\) potential of the first charge-transfer reaction is more negative than that corresponding to the second charge-transfer reaction, which would explain the presence of only one peak.

According to the known studies of the behavior of quinones in the presence of proton donors [7], these reactions could be protonation reactions involved in an ECE mechanism [5,6] or else in DISP1 and DISP2 mechanisms [8] as in the case of aromatic hydrocarbons. In the presence of a proton donor, the reduction peak of horminone may be interpreted as the result of one of the following reaction sequences, whose global contribution is of two electrons for each horminone molecule (QH) which is reduced in the presence of the acid/base buffer solutions, \(DH/D^-\) [16]:

\[
\text{QH} + e^- \rightleftharpoons \text{QH}^- \quad E_1^- \quad (1)
\]

\[
\text{QH}^- + \text{DH} \rightleftharpoons \text{QH}_2^- + \text{D}^- \quad K = k_f/k_b \quad k = k_f + k_b \quad (2)
\]

\[
\text{QH}_2^- + e^- \rightleftharpoons \text{QH}_2^- E_2^- \quad (3)
\]

\[
\text{QH}_2^- + \text{QH}^- \rightleftharpoons \text{QH}_2^- + \text{QH}^- \quad k_d \quad (4)
\]

\[
\text{QH}_2^- - + \text{DH} \rightleftharpoons \text{QH}_3^- + \text{D}^- \quad (5)
\]

Sequences:

reactions (1), (2), (3) \(\Rightarrow\) ECE mechanism, slow step is (2)
reactions (1), (2), (4) \(\Rightarrow\) DISP1 mechanism, slow step is (2)
reactions (1), (2), (4) \(\Rightarrow\) DISP2 mechanism, slow step is (4)

These sequences of reactions explain the voltamogram profiles found in Figs. 1(b) and 1(c) for the reduction peak of horminone in BBS (pH = 17.2) and SBS (pH = 15.5).

At pH = 15.5 the reduction peak is attributed to the electronation of QH and \(\text{QH}_2^-\) in the ECE mechanism and to the electronation of QH which occurs twice for the DISP1 and DISP2 mechanisms. The absence of an oxidation peak of fast characteristics associated with the reduction peak means that, in the time scale of the experiments, the anion \(\text{QH}^-\) disappears as a consequence of the protonation reaction (2) or of the disproportionation reaction (4). The oxidation peak in the voltammogram in Fig. 1(c) (pH = 15.5), is due to the de-electronation reaction of \(\text{QH}_2^-\), which does not have time to be protonated in reaction (5). On the contrary, at low scan rates there is enough time for the opposite effect and thus an oxidation peak is not observed.

At pH = 17.2, the reduction peak is also attributed to the electronation of QH and \(\text{QH}_2^-\) on the ECE mechanism and to the electronation of QH which occurs twice for the DISP1 and DISP2 mechanisms as well. This pH value, 17.2, is high enough to inhibit protonation reaction (2) causing disproportionation reaction (4) to become the disproportionation reaction (4)'

\[
\text{QH}^- + \text{QH}_2^- \rightleftharpoons \text{QH} + \text{QH}_2^- \quad k_d \quad (4')
\]

Since \(\text{QH}^-\) disproportionate controlling the whole process, the \(\text{QH}_2^-\) produced is detected, at the time scale of the experiment, in an oxidation peak of fast characteristics associated with the reduction peak of horminone, HQ, in a two electron process. Since reaction (2) practically does not occur, the whole mechanism can be represented by reactions (1) and (4') as occurs in a true disproportionation mechanism, independent of pH. This mechanism can also be considered as a DISP2 reaction.

After having demonstrated that horminone in buffer solutions can behave according to the ECE, DISP1 or DISP2 without the significant presence of a self-protonation reaction, more quantitative evidence is needed in order to define and differentiate the trajectory of the reaction. First of all, the experimental non-dimensional cathodic current functions, \(\Psi_{exp} = I/FScD^{1/2}(Fe/RT)^{1/2}\), for both pH values are evaluated. Previously, current values obtained on HMDE were corrected for spheric contribution, \(I_{w} = nFScdb(\tau)/r_c\), using \(db(\tau)\) values from the literature [17] to obtain current values for planar diffusion. The
non-dimensional values of $\lambda = 0.989$ and 1.036 at pH = 15.8 and 17.2 respectively are obtained. Comparing such results with those reported in the literature for several situations [8]:

$$\begin{align*}
\text{pH} = 15.5 & \quad \psi_{\text{diff}} < \psi_{\text{exp}} < \psi_{\text{ECE-DISP1}} < \psi_{\text{DISP2}} \\
0.466 < 0.989 < 0.992 < 1.054
\end{align*}$$

$$\begin{align*}
\text{pH} = 17.2 & \quad \psi_{\text{diff}} < \psi_{\text{ECE-DISP1}} < \psi_{\text{exp}} < \psi_{\text{DISP2}} \\
0.466 < 0.992 < 1.036 < 1.05
\end{align*}$$

It can be noted that the experimental non-dimensional current function obtained at pH = 15.5, approaches that of $\psi_{\text{ECE-DISP1}}$ of the ECE-DISP1 mechanism (under pure kinetic conditions, i.e. an irreversible peak) where two electrons are exchanged, rather than $\psi_{\text{diff}}$ which corresponds to a one-electron transfer under diffusion control. At pH = 17.2, $\psi_{\text{exp}}$ approaches that of $\psi_{\text{DISP2}}$ where two electrons are also exchanged.

Since current function does not vary very significantly between the two pH values evaluated, attention was focused on the peak potential $E_p$ variations. In Fig. 3, the behavior of $E_p$ vs. log$c$ is presented for 0.4 mM horminone in BBS (pH = 17.2) and SBS (pH = 15.5). The linear tendency of the experimental points ($r^2 > 0.9$), shows a smaller slope for the pH = 17.2 values (0.018 V) than that obtained for the pH = 15.5 values (0.036 V). Theoretical values, 0.03 V dec$^{-1}$ for ECE-DISP1 and 0.02 V dec$^{-1}$ for DISP2 mechanisms are reported [8,9]. In addition, it was found that the behavior of $E_p$ vs. log$c$ is linear ($r^2 > 0.9$) at both pH values evaluated, yielding a slope of 0.025 V dec$^{-1}$ at pH = 17.2 and a slope of 0.008 V dec$^{-1}$ at pH = 15.5. Theoretical values reported are 0.07 V dec$^{-1}$ for DISP2 and 0.000 V for ECE–DISP1 mechanisms.

The experimental results suggest that the horminone reduction mechanism could be ECE-DISP1 at pH = 15.5, and DISP2 at pH = 17.2.

In order to discriminate between the ECE and DISPl mechanism at pH = 15.5, it is more convenient to perform double potential step chronoamperometry experiments. Fig. 4 shows the response obtained from the ratio $(I(t)/I(0)$ vs. log$c$ for 1 mM horminone in SBS pH = 15.5, according to conditions described by Amatore and Savéant [11], where $\theta$ is the time period of the direct pulse. The knee characteristic of an ECE mechanism is not observed. Thus, it can be concluded that the reaction undergoes a DISPl-type mechanism at pH = 15.5 under the conditions described [11]. The ECE mechanism probably does not occur because the protonation reaction (2) is slow, owing to the moderate acidity of the medium due to the presence of the pH buffer.

Having demonstrated that horminone in SBS pH = 15.5 behaves according to the DISPl mechanism, it is possible to estimate the value of $k_I/1 + K$ and $E'_I$ potential of the first charge-transfer reaction (1). For this purpose an analysis was performed as a function of the apparent number of electrons $n_{\text{app}}$ [9]. For example, in Fig. 5 the experimental behavior of some $n_{\text{app}}$ points are shown and compared with the theoretical model (Eq. 6) of the DISPl mechanism [9].

$$n_{\text{app}} = 2 - \frac{2k_I/(1 + K)}{1 - \exp[2k/(1 + K)]}$$  

(6)

where $k = k_c + k_b$ and $K = k_c/k_b$ of reaction (2).

In Fig. 5, the experimental points and the theoretical behavior coincide at long times ($t \rightarrow \infty$), as could be expected; however, at short times ($t \rightarrow 0$) the coincidence is better for the DISPl mechanism for the following value of the composite constant: $k/(1 + K) = 16.22$ s$^{-1}$.

To estimate the $E'_I$ potential for the first charge-transfer reaction (1), Eq. (7) is employed, as reported by Amatore and Savéant [9], for the DISPl mechanism and the inter-

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**Fig. 3.** Variation of the reduction peak potential with the potential scan rate obtained for 0.4 mM horminone: (a) HBz + NaBz$^-$ buffer solution (BBS) pH = 17.2; (b) H-Sal + NaHSal$^-$ buffer solution (SBS) pH = 15.5; both buffers in 0.01 M TBAP in AN.

**Fig. 4.** Variation of the anodic to cathodic ratio $I(t)/I(0)$ with the direct pulse duration time $\theta$ from double potential step chronoamperometry using a periodic signal perturbation ($\theta^{-1} = 10$) for 1 mM horminone in H$_2$Sal + NaHSal$^-$ buffer solution (SBS) pH = 15.5, in 0.01 M TBAP in AN.
cept of Fig. 3, $E$ vs. log $v$, allows us to calculate this quantity.

$$E_a = E'_1 - 0.077 + 0.03 \log [k/(1 + K)] - 0.03 \log v$$

(7)

The value obtained for $E'_1$ was $-0.599$ V vs. Fc/Fc'.

In contrast, a precise estimation of the value of the equilibrium constant of the protonation reaction (2) would require additional chemical studies other with several buffer solutions. However, considering that the medium is a very weakly acidic (pH = 15.5), it may be assumed that at this pH the protonation reaction (2) is slow ($k_f \ll k_b$). Consequently, the relation $k/(1 + K)$ is approximately equal to $k$, that is

$$k/(1 + K) \equiv k = k_f + k_b = 16.22 \text{ s}^{-1}$$

At pH = 17.2 it is not possible with the information obtained here to estimate the $k_a$ of the reaction (4') which controls the electrochemical process.

4. Conclusions

From the results presented above, it is possible to conclude that the mechanism of reduction of horminone is modified by imposition of the acidity level in acetonitrile. At both pH values evaluated, the reductive process is a two-electron charge transfer. Double potential step chronoamperometry permits discrimination between the FCf and DISP1 at pH = 15.5. At pH = 17.2 the reduction proceeds via a DISP2-type mechanism.

With a salicylate buffer solution of pH = 15.5 the most probable mechanism for the horminone reduction reaction is DISP1 at the concentration values used in this study. At this pH value the mechanism can be described as follows:

$$\text{QH} + e^- \leftrightarrow \text{QH}^- \ E'_1$$
$$\text{QH}^- + \text{H}_2\text{Sal} \Rightarrow \text{HSal}^- + \text{QH}^+_1 \quad K = k_f/k_b$$
$$k = k_f + k_b$$

(2)

$$\text{QH}^+_2 + \text{QH}^-- \Rightarrow \text{QH}^{2-} + \text{QH}^- \quad k_d$$

(4')

It was established that, at pH = 15.5, the $E'_1$ value was $-0.599$ V vs. Fc/Fc', and the value for the ratio $k/(1 + K)$ was $16.22 \text{ s}^{-1}$. Since the acidity level corresponds to a weakly acidic one, reaction (2) is slow, favoring the DISP1 over the ECE mechanism.

In benzoic + benzoate buffer solution of pH = 17.2 the most probable mechanism for the horminone reduction reaction is DISP2. At this pH value the mechanism can be

$$\text{QH} + e^- \leftrightarrow \text{QH}^- \ E'_1$$
$$\text{QH}^- + \text{QH}^-- \Rightarrow \text{QH}^{2-} + \text{QH}^- \quad k_d + \text{QH}$$

(4')

It is concluded that at this pH value the acidity level is high enough to inhibit reaction (2), reaction (4') being a DISP2 mechanism as occurs in a true disproportionation mechanism, independent of pH.

References