Voltammetric determination of the $pK_a$ of various acids in polar aprotic solvents using 1,4-benzoquinone

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Dedicated to Fred C. Anson for his distinguished contributions to electrochemistry

Abstract

The effect of various proton-donors on the electrochemical reduction of 1,4-benzoquinone (BQ) was investigated in acetonitrile, dimethylsulfoxide and methylene chloride. Three representative types of acids, protonated amines, carboxylic acids and phenol derivatives, were used as proton-donors to cover a wide range of $pK_a$. As a proton-donor is added, a new peak appears and the magnitude of the potential shift ($\Delta E_p$) is proportional to $-pK_a$ of the protogenic acid. Plots of $\Delta E_p$ versus $pK_a$ in the aprotic solvents employed in this study show good linear relationships regardless of the acid’s functional group. An ECE process is believed to be responsible for this behavior and the linearity reflects dissociation of the Brønsted acid. As a consequence, it is possible to estimate the dissociation constants of various organic acids in aprotic media conveniently and reproducibly by voltammetry. A detailed interpretation of the redox behavior of quinone and some fundamental information for potentially promising analytical applications are described. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Quinone; Brønsted acids; Dissociation constants; Voltammetry; Aprotic solvents

1. Introduction

The acidity of a protogenic species in nonaqueous media depends on several factors such as the properties of the solvent, structure of the acid and the functional group releasing the proton [1,2]. The relative acidity in aprotic solvents may differ markedly from that in water. For instance, acetic acid ($pK_a = 4.8$) is much more acidic than ammonium ion ($pK_a = 9.2$) in water while the relative acidity is reversed in dimethylsulfoxide (DMSO, $pK_a = 12.6$ for acetic acid and $pK_a = 10.5$ for ammonium ion) [2]. The effect is even greater in acetonitrile (AN, $pK_a = 22.3$ for acetic acid and $pK_a = 16.5$ for ammonium ion) [2].

In order to determine the acidity of a protogenic species in nonaqueous media, several methods have been suggested and used to date. Among them, potentiometric titration, conductometry and spectrophotometry have been widely accepted and most of the dissociation constants ($K_a$) of acids in the literature were obtained by these methods. Even though potentiometric titration is the most ubiquitous method up to now, it needs repeated measurements and exceptionally prudent handling because potentiometric signals from glass electrodes in nonaqueous media are not as reliable as in water, mainly due to high liquid junction potentials. Besides troublesome procedures including standardization and calibration steps, the potentiometric approach cannot be extended to high $pK_a$ regions, as pointed out by Bordwell et al. [3]. In addition, this method requires a relatively large amount of sample and thereby has not been considered as a favorable way to determine the $pK_a$ value of newly synthesized compounds or natural products. On the other hand, of the three methods spectrophotometry is the most preferred especially with a small amount of sample. But this
method needs chromogenic indicators, whose absorption spectra are sensitive to the proton concentration and requires the prior knowledge of $pK_a$ values in a given solvent [4,5]. Moreover, this method may suffer from serious error if the acid exhibits considerable chromogenic properties. Conductometry is considered inferior to the two methods mentioned above in terms of accuracy.

In addition to the conventional methods, voltammetry can be employed for the same purpose. Voltammetry has valuable advantages over other methods, such as being relatively simple and convenient, requiring only a small amount of sample for accurate measurement and covering a wide $pK_a$ range. With regard to the voltammetric determination of $pK_a$ in nonaqueous solvents, Sawyer and coworkers utilized the half-peak potential of proton reduction to determine the effective acidity of Brønsted acids [6]. Also Vianello and coworkers showed that the electrochemical reduction of NH-protic $\alpha$-bromo amide, which was used as an additive, can be utilized to determine the $pK_a$ of weak acids in dimethylformamide (DMF) [7]. These two reports demonstrated that voltammetry is a useful technique to determine $pK_a$ values of weak acids and also suggested that the acidity of an intermediate with a short life time can be measured by voltammetry. However complicated calculations and/or simulations for the chemical reactions involved in the electrochemical process have limited its application. In order to overcome the limitation, it is necessary to use a stable additive, whose electrochemical behavior is simple and well established. In addition, the additive must have at least one voltammetric parameter that is sensitive to the acidity and can be measured easily.

A polarographic method to determine the concentration of acids in aqueous medium through the electrochemical reduction of quinone was suggested for the first time in 1963 [8]. Based on this fundamental idea, Takamura and coworkers reported a linear relationship between $E_{1/2}$ of methyl-$\alpha$-benzoquinone and $pK_a$ of several carboxylic acids and phenol derivatives in 2-methoxyethanol as well as in aqueous solution [9–11]. Similar work has been reported in DMF by DemangeGuerin [12] and by Kheifets et al. [13,14]. In these studies, only a few acids were tested to demonstrate that quinone can serve as an additive to quantify the mixed acids selectively. Also $pK_a$ values of various weak acids were estimated on the basis of the half-wave potential ($E_{1/2}$) of the new waves by dc polarography. In terms of convenience in the measurement, $E_{1/2}$ in dc polarography, however, is not as good as the peak potential ($E_p$) in linear sweep voltammetry. In addition, it should be noted that solid electrodes are more practical to use in proton-deficient nonaqueous media compared to mercury as the working electrode material. Recently, it was reported that quinone derivatives were successfully employed to quantify the organic acids or amines and to determine the enzymatic activities by amperometry [9,15] and the voltammetric behavior of quinone is carried out in the presence of various proton-donors such as protonated amines, carboxylic acids and phenol derivatives in acetonitrile, dimethylsulfoxide and methylene chloride (MC), which are different in polarity and basicity. In addition, the feasibility of its practical application to determine $pK_a$ and the solvent effect are described.

2. Experimental

Electrochemical experiments were performed with a Windows-driven BAS100B/W electrochemical analyzer (Bioanalytical Systems, West Lafayette, IN) using a conventional three-electrode cell, with a glassy carbon working electrode (area; 0.071 cm$^2$), platinum wire counter electrode and $\text{Ag} | \text{Ag}^+ | 0.1$ M AgNO$_3$ reference electrode, separated from the solution by a Vycor plug. The surface of the working electrode was polished with 0.3 µm alumina (Buehler, Lake Bluff, MN), then rinsed with deionized water and washed carefully with the solvent to be used. The supporting electrolyte was 0.1 M tetrabutylammonium perchlorate (TBAP). The concentration of 1,4-benzoquinone (BQ) was 0.50 mM and an appropriate amount of acid was added with a micro-syringe. All experiments were carried out under a nitrogen atmosphere and the solution temperature was maintained at 25.0 ± 0.1°C by a thermostat (model B, Lauda-Königshofen, Germany).

HPLC grade AN, DMF and MC from Fisher and DMSO for spectroscopy from Merck were used as solvents. BQ was purchased from Junsei Chemical. $n$-Butylammonium perchlorate and tri-$n$-butylammonium perchlorate were synthesized from the corresponding amines and perchloric acid. Other reagents were obtained from Aldrich. Hygroscopic reagents were dried for 48 h under reduced pressure at 20°C.

3. Results and discussion

3.1. New reduction peak caused by Brønsted acids

In the proton-deficient environment, two pairs of reversible redox waves are generally observed by cyclic voltammetry of BQ [16,17]. These two reduction peaks are due to the electrochemical reduction producing a monoanion radical (BQ$^-$) and a dianion (BQ$^{2-}$), respectively. The voltammetric behavior of BQ changes significantly when a Brønsted acid is added to the
solution. The redox behavior of BQ strongly depends on the strength of the Brønsted acid. Concerning the effect of the Brønsted acid, Gupta and Linschitz showed that weak hydrogen-bonding agents or weak Brønsted acids such as alcohols ($pK_a > 9.3$ in aqueous media) interact with neither BQ nor BQ$^{-}$ while BQ$^{2-}$ associates with the acids by hydrogen-bonding [18]. According to this report, the second reduction peak producing BQ$^{2-}$ shifted to the positive direction and the potential value varied with the concentration of the agents, whereas the first reduction peak producing BQ$^{-}$ remained intact. The report also demonstrated that the presence of acids with medium or strong acidity commonly gave rise to a new peak prior to the first reduction peak but the mechanism was different, ECE ($e^-H^+e^-$) and prior protonation, respectively. The acidity of the Brønsted acids as well as the basicity of the quinones influenced the species responsible for the new peak.

Table 1 lists the $pK_a$ values of organic acids that have been tested in the present study. Except for some protonated alkylamines, $pK_a$ values of all the acids are less than 9 in aqueous media. Although protonated alkylamines in Table 1 are weaker acids than carboxylic acids and phenol derivatives in aqueous media, they are comparable or stronger acids in AN and DMSO. Thus, the acids in Table 1 are regarded as intermediate Brønsted acids. In the case of strong Brønsted acids, it is expected that both the first and second reduction peaks will be affected significantly and a new reduction peak will appear at a more positive potential than that of the original peak.

Fig. 1 shows the electrochemical behavior of BQ in the absence and presence of one equivalent of n-butylammonium ion in AN. A new reduction peak appears at a more positive potential, around $0.45 \text{ V}$, than the peak potential due to the first reduction of BQ alone. All of the acids in Table 1 exhibit analogous voltam-

<table>
<thead>
<tr>
<th>Acids</th>
<th>Water $pK_a$</th>
<th>DMSO $pK_a$</th>
<th>$\Delta E_{p1}/\text{mV}$</th>
<th>AN $pK_a$</th>
<th>$\Delta E_{p2}/\text{mV}$</th>
<th>MC $\Delta E_{p1}/\text{mV}$</th>
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<tr>
<td>Sulfanilic acid</td>
<td>3.23</td>
<td>3.5</td>
<td>348</td>
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<td>Aniline hydrochloride</td>
<td>4.1</td>
<td>3.7</td>
<td>332</td>
<td>10.56</td>
<td>588</td>
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<td>Pyridine hydrochloride</td>
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<td>3.5</td>
<td>348</td>
<td>12.3</td>
<td>528</td>
<td>3</td>
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<td>Ammonium perchlorate</td>
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<td>10.4</td>
<td>134</td>
<td>16.46</td>
<td>412</td>
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<td>n-Butylammonium perchlorate</td>
<td>10.6</td>
<td>11.1</td>
<td>98</td>
<td>18.26</td>
<td>324</td>
<td>418</td>
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<td>Tri-n-butylammonium perchlorate</td>
<td>10.9</td>
<td>8.4</td>
<td>172</td>
<td>18.1</td>
<td>324</td>
<td>264</td>
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<td>Piperidine hydrochloride</td>
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<td>10.6</td>
<td>108</td>
<td>18.92</td>
<td>284</td>
<td>308</td>
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<td>Trichloroacetic acid</td>
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<td>12.4</td>
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<td>555</td>
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<td>Dichloroacetic acid</td>
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<td>6.36</td>
<td>258</td>
<td>15.81</td>
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<td>2,4-Dinitrobenzoic acid</td>
<td>1.43</td>
<td>6.52</td>
<td>244</td>
<td>16.19</td>
<td>396</td>
<td>370</td>
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<td>2,6-Dichlorobenzoic acid</td>
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<td>8.7</td>
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<td>17.6</td>
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<td>2,6-Dihydroxybenzoic acid</td>
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<td>3-Nitrobenzoic acid</td>
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<td>180</td>
<td>19.29</td>
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<td>11.0</td>
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<td>21.3</td>
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<td>11.1</td>
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<td>20.7</td>
<td>196</td>
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<td>22.31</td>
<td>104</td>
<td>163</td>
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<td>Picric acid</td>
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<td>-1.0</td>
<td>368</td>
<td>11.1</td>
<td>680</td>
<td>740</td>
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<td>388</td>
<td>14.5</td>
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<td>2,6-Dinitrophenol</td>
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<td>16.0</td>
<td>440</td>
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<td>5.00</td>
<td>308</td>
<td>16.0</td>
<td>456</td>
<td>428</td>
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<td>4-Nitro-3-CF$_3$-phenol</td>
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<td>148</td>
<td>19.3</td>
<td>264</td>
<td>280</td>
</tr>
<tr>
<td>4-Nitrophenol</td>
<td>7.15</td>
<td>10.8</td>
<td>103</td>
<td>20.7</td>
<td>188</td>
<td>184</td>
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<tr>
<td>2,3-Dihydroxy naphthalene</td>
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<td>13.7</td>
<td>~0</td>
<td>19.1</td>
<td>274</td>
<td>372</td>
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<td>3-Nitrophenol</td>
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<td>13.91</td>
<td>~0</td>
<td>23.85</td>
<td>24</td>
<td>226</td>
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<td>Pyrogallol</td>
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<td>~0</td>
<td>23.4</td>
<td>74</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ From the literature [19].

$^b$ $\Delta E_p = E_{p2} - E_{p1}$, where $E_{p1}$ is the peak potential of the original peak due to the first reduction of 0.50 mM BQ and $E_{p2}$ is the peak potential of the new reduction peak of BQ in the presence of 0.50 mM acid.

$^c$ Could not be determined because of low solubility.

$^d$ Measured in this work using $\Delta E_{p}$ values.

$^e$ Unusually small $\Delta E_{p}$ value and has not been included in Figs. 3 and 5. See the text.
3.2. Effect of the functional group and solvent

Since the reduction mechanism of BQ involves a proton, the magnitude of $\Delta E_{p}$, the potential difference between the new peak and the original peak due to the first reduction of BQ, is suggested as a voltammetric parameter to estimate $pK_a$ values in aprotic media. Although the redox behavior of BQ in the presence of acid is not completely understood, it turns out to be possible to use the first reduction process to simplify the situation for the practical application proposed in this study.
Fig. 3 shows the plots of $\Delta E_p$ against $pK_a$ obtained in aqueous media in three different aprotic solvents. As long as the acids have the same functional group, there is a linear relationship between $\Delta E_p$ in a given solvent and the $pK_a$ obtained in aqueous media. But acids with different groups exhibit different slopes. The $\Delta E_p$ are in the order of protonated amines > phenols > carboxylic acids. In particular, the $\Delta E_p$ due to protonated amines in aprotic media is abnormally large. This is not surprising, considering that protonated amines are originally monovalent cations, whereas carboxylic acids and phenol-type acids are neutral species. As the dielectric constant of the solvent decreases, charged species becomes unstable whereas uncharged ones are stabilized. On the other hand, a different linear relationship between $\Delta E_p$s and $pK_a$ for phenol derivatives compared with that for carboxylic acids appears to be due to the stability of anions. In the case of neutral acids such as phenol derivatives and carboxylic acids, the stability of conjugate anionic bases is the key factor determining the proton-donating power of the acid because the solvation of anions needs more energy in AN, DMSO and MC than in aqueous media [20]. A negative charge on the phenolate ring is more effectively delocalized than that on the carboxylate group and is preferred in less polar media.

Similar results are also obtained in other aprotic solvents such as DMSO and MC. The $\Delta E_p$ values due to the same acid in different solvents are different in the order of MC > AN > DMSO as demonstrated in Fig. 3. When the solvent is inert and its basicity is extremely small, the proton-donating power of the acids is amplified and, thus, is clearly reflected by the magnitude of $\Delta E_p$. Since it is more difficult to employ conventional methods in less polar solvents, this voltammetric technique seems quite useful especially when the relative proton-donating powers of various acids are compared and assessed in inert solvents.

### 3.3. Relationship between $\Delta E_p$ and $pK_a$

When $\Delta E_p$ data are plotted against $pK_a$ in corresponding aprotic media, good straight lines with correlation coefficients ($R^2$) of 0.99 for AN and 0.97 for DMSO are observed irrespective of the functional groups of the acids as shown respectively, in Figs. 4 and 5. The slopes are

![Fig. 4. Relationship between $\Delta E_p$ and $pK_a$ in AN. All conditions and notations are the same as those in Fig. 3.](image-url)
- 0.046 and -0.033 V per pKa unit in AN and DMSO, respectively. Assuming that \( \Delta E_p \) should be at least 50 mV for two adjacent peaks considered to be well separated. Figs. 4 and 5 indicate that pKa values less than 24 in AN and 12 in DMSO can be determined by this method.

Based on the proposed ECE mechanism, the electrochemical and chemical processes in the presence of acid can be depicted as the following scheme:

\[
\begin{align*}
\text{BQ} & \quad \text{BQ}^\circ \quad \text{BQH}^- \\
& \quad \text{E}_1^\circ \quad \text{E}_2^\circ \quad \text{E}_2^\circ'
\end{align*}
\]

In order to find out the origin of the linear relationship between \( \Delta E_p \) and pKa, a rigorous mathematical treatment with two Nernst equations, two acid dissociation constants (acid, \( K_a \) and protonated BQ anion radical, \( K_2^Q \)) and complicated quantitative expressions, has to be carried out. It seems unnecessary, however, to explore further in detail considering the fact that complex chemistry is involved around the electrode in an aprotic solvent. Instead, a simple derivation with two Nernst equations, and notations are the same as those in Fig. 3.

\[
\begin{align*}
E &= E_1^\circ + \frac{RT}{F} \ln \left[ \frac{[\text{BQ}]}{[\text{BQ}^-]} \right] \\
E &= E_2^\circ + \frac{RT}{F} \ln \left[ \frac{[\text{BQH}^+]}{[\text{BQH}^-]} \right]
\end{align*}
\]

Adding Eqs. (1) and (2), and replacing with two acid dissociation constants gives

\[
E = \frac{E_2^\circ + E_1^\circ}{2} + \frac{2.3RT}{2F} \left( pK_2^Q - pK_a \right) + \frac{RT}{2F} \ln \left[ \frac{[\text{BQ}][\text{BQH}^+]}{[\text{BQH}^-]} \right]
\]

Then the potential of the new peak in the presence of acid when \([\text{BQ}] = [\text{BQH}^-]\) (formal potential) can be written as:

\[
E_{\text{new}}^\circ = \frac{E_2^\circ + E_1^\circ}{2} + \frac{2.3RT}{2F} \left( pK_2^Q - pK_a \right)
\]

while the formal potential in the absence of acid is

\[
E_{\text{original}}^\circ = E_1^\circ
\]

Eq. (6) indicates that the differences in the formal potentials, \( \Delta E^\circ \), are directly dependent on the dissociation equilibria between BQH\(^+\) and acids.

It should be noted that serious error might be involved in the expression because of over simplified assumptions, for instance, \([\text{BQH}^-]\) must require more complicated terms by considering all chemical species involved in the system including prior association between BQ and the acid through hydrogen-bonding [18] especially in less polar solvents. Also, an additional error must be present by taking \( \Delta E^\circ \approx \Delta E_p \) because the electrochemical behavior is not reversible. Nevertheless, good straight lines in Figs. 4 and 5 indicate that there is a linear relationship between \( \Delta E_p \) and pKa with a theoretical slope of -0.030 V per decade (at 25°C) which is very close to the experimentally obtained slope of -0.033 V per decade in DMSO. It is reasonable to observe an even larger slope in AN (-0.046 V per decade) because of a strong tendency for association in AN. This comparison confirms indirectly that the interpretation based on an ECE process is reasonable to accept.

Such a high sensitivity enables us to utilize the voltammetric method to determine pKa in DMSO and AN with good reproducibility of about 0.1 units of pKa. \( \Delta E_p \) data in Table 1 are used to determine the pKa of several acids including trichloroacetic acid and 1-naphthoic acid which have not been reported in DMSO and AN so far. They are listed in Table 1. Consequently, \( \Delta E_p \) measured by voltammetry is a good parameter to evaluate pKa in aprotic solvent in terms of accuracy, convenience and the amount of sample that needs to be
4. Conclusions

The voltammetric response of 1,4-benzoquinone in the presence of Brønsted acids with various acid functional groups was studied in acetonitrile, dimethylsulfoxide and methylene chloride. The magnitude of the potential shift caused by the presence of the acid showed a good linear relationship with the acid dissociation constants, pH, in the corresponding media. The pH value of organic acids in aprotic solvents, therefore, can be determined based on the voltammetric behavior of quinone, which is very sensitive to the acidity of proton sources. The method proposed in this study is quite useful to assess the relative proton-donating power in non-polar aprotic media, especially when no conventional method can be used to measure the KA.

The pH values of trichloroactic acid and 1-naphthoic acid were obtained for the first time by the proposed method.

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