pKₐ Determination of Strongly Acidic C-H Acids Bearing a (Perfluoroalkyl)sulfonyl Group in Acetonitrile by Means of Voltammetric Reduction of Quinone

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ABSTRACT

A voltammetric method has been developed for the determination of the acid dissociation constant (pK$_a$) of (RfSO$_2$)$_2$CHR (Rf = perfluoroalkyl), which is a strongly acidic molecule that serves as an acid catalyst. In acetonitrile solution containing small quantity of the acid, the reduction peak potential of quinone caused by the acid shifted to a more positive side accompanied by an increase in the acidity of the acid. This relationship was in good agreement with an equation derived from the Nernst equation. The present finding has been successfully applied to the determination of the pK$_a$ of the acids in acetonitrile with values ranging from 7 to 17.

Keywords: pK$_a$, (perfluoroalkyl)sulfonyl group, C-H acid, voltammetry
1. Introduction

The (trifluoromethyl)sulfonyl group (Tf = CF₃SO₂) is one of the strongest electron-withdrawing groups. Recently, several Tf-derived strong acids, exemplified by TfOH and Tf₂NH, have been used in various fields of chemistry. Although gem-bis[(trifluoromethyl)sulfonyl]alkanes, depicted as Tf₂CHR, also serve as superacidic molecules in a gas phase, until recently the application of such molecules and the corresponding conjugate bases (stable carbanions) have been significantly limited due to the lack of reliable synthetic methods. Against such a background, Yanai and coworkers successfully developed an effective method for the incorporation of the (RfSO₂)₂CH group (Rf = perfluoroalkyl) into several nucleophilic compounds. The C-H (carbon) acids thus obtained have found applications as Bronsted acid catalysts for organic reactions. Lithium salts derived from the acids have also been utilized as electrolytes or additives to lithium-ion secondary batteries. As such, the acidity of (RfSO₂)₂CHR and related C-H acids in organic solvents would be fundamental and essential information in such applications. However, their acidities have not been fully investigated and the relationship between acidity and chemical structure has yet to be elucidated.

For strongly acidic compounds, the gas-phase acidity (GA), which is defined as a Gibbs energy change associated with the dissociation of the acid molecule, is used as an experimental parameter. However, the GA does not include any effects by solvation to the acid dissociation equilibrium. In addition, its measurement with a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer is less accessible for common usage. As a scale of the solution acidity, the acid dissociation constant ($pK_a$) has been well-established. The experimental values are usually determined by means of potentiometry, UV spectrometry, and capillary electrophoresis. High-performance liquid chromatography (HPLC), isothermal titration calorimetry, and voltammetry have been also utilized. These methods are performed mainly in aqueous media, thus their application is limited to weak acids. Although potentiometric and UV spectrometric titrations can be performed in non-aqueous media as well, the $pK_a$ determination of strongly acidic compounds, including superacidic C-H acids, requires complicated experimental procedures and measurements of multiple samples.

In our voltammetric study of quinones in an unbuffered aqueous media, a small amount of acid was found to cause a new peak, called a prepeak, at a more positive potential than that of the original reduction peak of quinone. The potential of the prepeak was shifted to a more positive side accompanied by an increase in the acidity of the compounds, i.e. the appearance of a prepeak potential is dependent on the acidity of compounds. Based on this finding, herein we report that the measurement of the quinone prepeak potential in acetonitrile has a practical utility for determining the $pK_a$ values of C-H acids with a wide range of acidity. The $pK_a$ measurement in acetonitrile has already been conducted for a wide range of common
acids,\(^\text{20}\) therefore the current work allows for the comparing of the acidity of C-H acids with those of other acids on a single solution acidity scale.

2. Experimental

All chemicals and solvents were of reagent grade. Vitamin K\(_3\) (VK\(_3\), > 99%) and LiClO\(_4\) were purchased from FUJIFILM Wako Pure Chemical (Osaka, Japan). As reference acids, to prepare a calibration curve, 4-chlorobenzenesulfonic acid (CBSA), \(p\)-toluenesulfonic acid (TSA), methanesulfonic acid (MSA), trifluoroacetic acid (TFA), saccharin (SAC), and 2,4-dinitrophenol (DNP) were purchased from Tokyo Chemical Industry (TCI, Tokyo, Japan) and purified by recrystallization or distillation. Sulfuric acid (SA) was used and also purchased from TCI without further purification. \((\text{RfSO}_2)\text{CHR}\) and the related C-H acids were prepared according to a previous report.\(^5\)

Voltammetry was conducted with an electrochemical analyzer (HZ-7000, Hokuto Denko, Tokyo, Japan). A plastic formed carbon (PFC) working electrode (3 mm diameter disk, Tsukuba Materials Information Laboratory, Ltd., Ibaraki, Japan), an Ag/AgCl reference electrode (Supporting Information), and a Pt counter electrode were inserted through the lid in the beaker-type electrochemical cell. Acetonitrile containing 3 mmol L\(^{-1}\) VK\(_3\) and 0.1 mol L\(^{-1}\) LiClO\(_4\) was used as an electrolyte cocktail. To prepare a test solution for voltammetry, 4.0 mL of the electrolyte cocktail was mixed with 0.1 mL of acetonitrile containing 20 mmol L\(^{-1}\) of each acid. Before measurements of voltammogram, argon gas (Ar > 99.99%) was thoroughly purged to remove dissolved oxygen in the test solution. During the measurement of the voltammogram, Ar gas was passed above the test solution. The scan rate was set at 20 mV s\(^{-1}\).

3. Results and discussion

Linear sweep voltammetry of VK\(_3\) was carried out in an acetonitrile solution containing 3 mmol L\(^{-1}\) VK\(_3\) and 0.1 mol L\(^{-1}\) LiClO\(_4\) using a PFC electrode. As shown in Fig. 1A, a reduction peak of VK\(_3\) was observed at a potential of -0.498 V vs. Ag/AgCl on a voltammogram scanned from +0.6 V to -0.6 V vs. Ag/AgCl. As an example, in the presence of TSA, a prepeak was observed at a potential of +0.307 V vs. Ag/AgCl (Fig. 1B). From the prepeak caused by the TSA on the voltammogram, the half-peak potential \((E_{p/2})\) of a prepeak of VK\(_3\) was found to be +0.391 V vs. Ag/AgCl. In this measurement, the reduction peak potential of VK\(_3\) was slightly shifted to the negative side, appearing at -0.522 V vs. Ag/AgCl. Although the exact mechanism for the peak potential shift is complicated, in which the peak potential is probably affected by VK\(_3\) diffusion and its reaction rate, our results have proposed an analytical method for the determination of \(pK_a\) by measurements of the prepeak of VK\(_3\).

In a similar way, measurements of linear sweep voltammetry of VK\(_3\) were performed in
the presence of CBSA, SA, MSA, TFA, SAC, or DNP. The \(E_{p/2}\) of prepeaks caused by these reference acids were +0.408, +0.363, +0.345, +0.084, -0.012, and -0.105 V vs. Ag/AgCl, respectively. The pK\(_a\) values in acetonitrile (pK\(_{a,AN}\)) of the reference acids obtained from literature are as follows: CBSA, 7.16; TSA, 8.01; SA, 8.70; MSA, 9.97; TFA, 12.65; SAC, 14.57; DNP, 16.66.\(^{22}\) In Fig. 2, the \(E_{p/2}\) of prepeak was plotted against the reported pK\(_{a,AN}\) values of the references. A correlative relationship between \(E_{p/2}\) of the prepeak and pK\(_{a,AN}\) was found and expressed by a regression equation as follows:

\[
E_{p/2} = -0.05907 \text{pK}_{a,AN} + 0.86646 \quad (r = 0.986) \quad (1)
\]

The appearance of the prepeak can be ascribed to the increased availability of protons from the acid to quinone. And the appearance of the prepeak can be affected by an electrochemical reaction rate such as a kinetic current, which has been proposed by Koutecký and Brdička.\(^{23}\) Here, we describe the validity regarding a pK\(_a\) value obtained by the potential measurements of the prepeak caused by an acid. In a polar aprotic solvent containing the acid, the voltammetric reduction of quinone (Q) is known to involve a one-electron transfer with a one-proton transfer to produce the protonated monoanion radical (QH\(^\cdot\)).\(^{18,24-25}\)

\[
Q + e^- + H^+ \rightleftharpoons \text{QH}' \quad (2)
\]

Based on the explanation for the diffusion current in the unbuffered medium,\(^{26}\) the reduction potential for Eq. (2) is expressed by the following Nernst equation:

\[
E = E_0' + \frac{RT}{F} \ln \frac{[Q_0][H^+]_0}{[\text{QH}']_0} \quad (3)
\]

\[
= E_0' + \frac{RT}{F} \ln \frac{[Q]_0}{[\text{QH}']} + \frac{RT}{F} \ln[H^+]_0 \quad (4)
\]

where [Q]\(_0\), [QH\(^\cdot\)]\(_0\), and [H\(^+\)]\(_0\) are Q, QH\(^\cdot\), and the proton concentrations on a working electrode surface, respectively. Considering the prepeak shape is close to a stationary current-voltage curve, we would propose that Eq. (4) may be represented simply by the half wave potential \(E_{1/2}\) at [Q]\(_0\) = [QH\(^\cdot\)]\(_0\) as follows:\(^{26}\)

\[
E_{1/2} = \frac{RT}{F} \ln[H^+]_0 + \text{const.} \quad (5)
\]
\[ 6 = 0.0592 \log [H^+]_0 + \text{const.} \quad (6) \]

The dissociation of acid (HA) in aprotic solvents such as acetonitrile can be described by the following equilibrium, and thus \([H^+]_0\) is also dependent on the pK\(_a\) of HA and the ratio of HA and its conjugated base on a working electrode surface ([A\(^-\)]\(_0\) / [HA\(_0\)].

\[ \text{HA} \rightleftharpoons H^+ + A^- \quad (7) \]

\[ -\log[H^+]_0 = pK_a + \log \frac{[A^-]_0}{[HA]_0} \quad (8) \]

Because the concentrations of quinone and each acid (analyte) in the test solution were unified among each voltammetric measurement, \([A^-]_0 / [HA]_0\) would be kept constant at \(E_{1/2}\). Thus, the second term in Eq. (8) is approximately provided as a constant under the reduction process examined. Therefore, the relationship between the \(E_{1/2}\) of the prepeak and the pK\(_a\) of the acid is expressed by substituting Eq. (8) into Eq. (6) as follows:

\[ E_{1/2} = -0.0592 \, pK_a + \text{const.} \quad (9) \]

The \(E_{1/2}\) has been shown to be somewhat lower than the \(E_{p/2}\). However, if the values of \(E_{1/2}\) are almost parallel with those of \(E_{p/2}\), the slope of the regression equation in Eq. (1), which was obtained from experimental pK\(_a\) data of reference acids reported in the literature, would be close to the slope of Eq. (9). Considering the experimentally obtained regression equation between \(E_{p/2}\) of prepeak and pK\(_a\)\(_{AN}\) of the reference acids, the present voltammetry would cover a pK\(_a\)\(_{AN}\) range from 7 to 17.

The present voltammetry was performed to determine the pK\(_a\)\(_{AN}\) of C-H acids (Table 1). As an example, the voltammogram of VK3 in the presence of Tf\(_2\)CH\(_2\) 1a is shown in Fig. 1C. A well-defined prepeak of the peak potential at +0.137 V was observed, and +0.252 V of \(E_{p/2}\) for the prepeak was obtained on the voltammogram. A well-defined reduction peak of VK3 was observed at -0.520 V. Using the regression equation shown in Eq. (1), the pK\(_a\)\(_{AN}\) of Tf\(_2\)CH\(_2\) 1a was determined to be 10.4. In a similar way, voltammetric measurements of VK3 were performed in the presence of other C-H acids. The results of \(E_{p/2}\) and pK\(_a\)\(_{AN}\) are shown in Table 1.

The pK\(_a\)\(_{AN}\) values in a series of methylene compounds 1a-e revealed the substituent effects of the sulfonyl group on the solution acidity. The replacement of the CF\(_3\) groups in 1a to n-C\(_4\)F\(_9\) groups (1b) enhanced the acidity by about 1.4 pK\(_a\) unit. The cyclic structure of 1c decreased the acidity by about 1 pK\(_a\) unit compared with 1a. Both of the fluoro- and chlorosulfonyl groups (1d and 1e) were less effective for enhancing the acidity. As shown in the pK\(_a\)\(_{AN}\) data of the methine compounds 2a-c, C-methylation of (RSO\(_2\))\(_2\)CH\(_2\) made the acidity lower in a range from 2.6 to 2.9 pK\(_a\) unit; the acidity of 2a was 400 times weaker than
that of 1a. It should be noted that the acidity of the $C_3$-symmetric triple C-H acid 3 ($pK_{a,AN}$ 6.7) was much stronger than that of SA ($pK_{a,AN}$ 8.70).\textsuperscript{22} It has been reported that this acid effectively catalyzed the Mukaiyama aldol reaction over other Tf-derived acids including TfOH, Tf$_2$NH, 1a, and 2a.\textsuperscript{28} In a previous theoretical estimation of the $GA$ of 3, the intramolecular hydrogen bonding between sulfonic oxygen atoms and neighboring hydroxyl groups was found to be a key factor for stabilization of the corresponding carbanion generated by deprotonation.\textsuperscript{9} The solution acidity of 3 implies that similar hydrogen bonding plays an important role in the aprotic solvent as well.

The measurement time and amount of sample required for one assay by the present voltammetry were about 1 min and 1 mg, respectively, indicating that it is remarkably valuable for the high throughput processing on evaluation of the catalyst performance. In addition, the experimental $pK_{a,AN}$ values were obtained using this convenient procedure compared with the $GA$ measurement. To the best of our knowledge, this report is the first one concerning the $pK_a$ determination of strongly acidic compounds in organic solvents by voltammetry.

4. Conclusion

We observed a reduction prepeak of $VK_3$ caused by a strongly acidic compound in the present voltammetric study using an acetonitrile media, and it was applied to the $pK_{a,AN}$ determination of C-H acids with a wide range of acidity. The regression equation between $E_{p/2}$ of the prepeaks in the presence of the reference acids and their reported $pK_{a,AN}$ values were in good agreement with the equation derived from the Nernst equation regarding a reduction potential of $VK_3$ in the presence of the acids. By the present voltammetry, the $pK_{a,AN}$ values of nine kinds of C-H acids bearing a variety of sulfonyl groups were easily obtained. Furthermore, this method provided the structure-acidity relationship, which will contribute to the further molecular design of C-H acid catalysts and a deeper understanding of them.

Supporting Information: The Supporting Information is available on the website at DOI: xxxxxxxxxxxxx.

Acknowledgments

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Figure captions

**Figure 1** Voltammograms of VK3 in the absence (A) and presence (B) of 0.5 mmol L\(^{-1}\) TSA and 0.5 mmol L\(^{-1}\) Tf\(_2\)CH\(_2\) 1a (C) in acetonitrile containing 0.1 mol L\(^{-1}\) LiClO\(_4\).

**Figure 2** Relationship between the \(E_{p/2}\) of the prepeak and the \(pK_{a,AN}\) of the reference acids.
Figure 1
Figure 2

$E_{p/2}$ of prepeak / V (vs. Ag/AgCl)

Reported $pK_{a, AN}$
Table 1  \( pK_{a,AN} \) of C-H acids obtained from \( E_{p/2} \) by the present voltammetry

| C-H acid | \( E_{p/2} / V \) (vs. Ag/AgCl) | \( pK_{a,AN} \) |
|----------|-------------------------------|-----------------|
| 1a       | +0.252                        | 10.4            |
| 1b       | +0.337                        | 9.0             |
| 1d       | −0.077                        | 16.0            |
| 1e       | +0.008                        | 14.5            |
| 1c       | +0.198                        | 11.3            |
| 2a       | +0.042                        | 14.0            |
| 2b       | +0.164                        | 11.9            |
| 2c       | +0.035                        | 14.1            |
| 3        | +0.471                        | 6.7             |