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Cyclic Voltammetry and Controlled Potential Electrolysis of Benzenesulfon-*p*-anisidide

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Anodic oxidation of benzenesulfon-*p*-anisidide (I) was investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon electrode in aqueous acetonitrile solution. I showed a single anodic wave below pH 7, and two anodic waves above pH 7.5. Electrolysis of I at pH 3.9 gave a coulometric *n*-value of two, and *p*-benzoquinone and benzenesulfonamide were obtained. Electrolysis of I at pH 10.5 and the potential of the first wave gave an *n*-value of about one, and N,N'-dibenzenesulfonyl-N-(4'-methoxyphenyl)-5-methoxy-*o*-phenylenediamine (IV) was obtained. The formation of IV was interpreted in terms of a head-to-tail coupling of the free radical of I.

Anodic oxidation of carboxamides has been studied extensively by many workers,²⁾ but relatively few studies have been made on sulfonamides. Voorhies and his co-workers³⁾ reported voltammetric behavior of a variety of sulfa drugs. However, the point of oxidation in the sulfonamide molecule was found to be the primary aromatic amino-nitrogen, not the amide-nitrogen. Ross and his co-workers⁴⁾ studied the anodic oxidation of N,N-dimethylmethanesulfonamide in alcohols and in acetic acid, and found the formation of N-alkoxymethyl-N-methylmethanesulfonamides and N-acetoxymethylmethanesulfonamide.

Recently, one of us (H.S.) reported a new anodic pyridination reaction of 4'-methoxybenzanilide,^{2a)} and found that pyridine acts both as a base and a nucleophile. Because benzenesulfonanilides are more acidic than the corresponding benzanilides,⁵⁾ it seemed of interest to investigate anodic oxidation of benzenesulfonanilides and attempt to find new examples of anodic substitution.

This paper reports results on cyclic voltammetry and controlled potential electrolysis of benzenesulfon-*p*-anisidide (I) in aqueous acetonitrile solution, and the anodic oxidation process is discussed in some detail.

Results

Cyclic Voltammetry

Cyclic voltammetry of I (2 mM) in 50% aqueous acetonitrile solution showed a single anodic wave below pH 7,⁶⁾ and two waves above pH 7.5. Typical voltammograms are shown in Fig. 1. All potentials were measured against an aqueous saturated calomel electrode. Upon reversal of the scan direction at 1.1 V, I showed one cathodic wave below pH 10 and above pH 11, and two waves between these pH values. On subsequent anodic scan a small extra anodic wave was observed at a less positive potential than that of the original anodic wave over the entire

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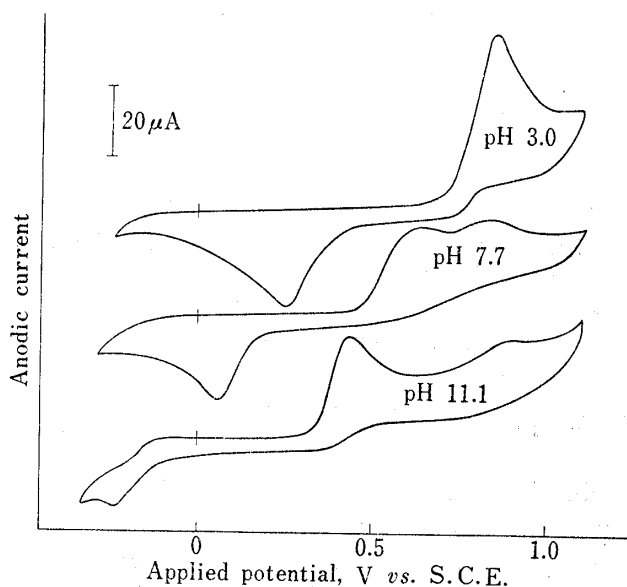


Fig. 1. Cyclic Voltammograms of Benzenesulfon-*p*-anisidide (2 mM) in 50% Aqueous Acetonitrile at a Sweep Rate of 50 mV sec⁻¹

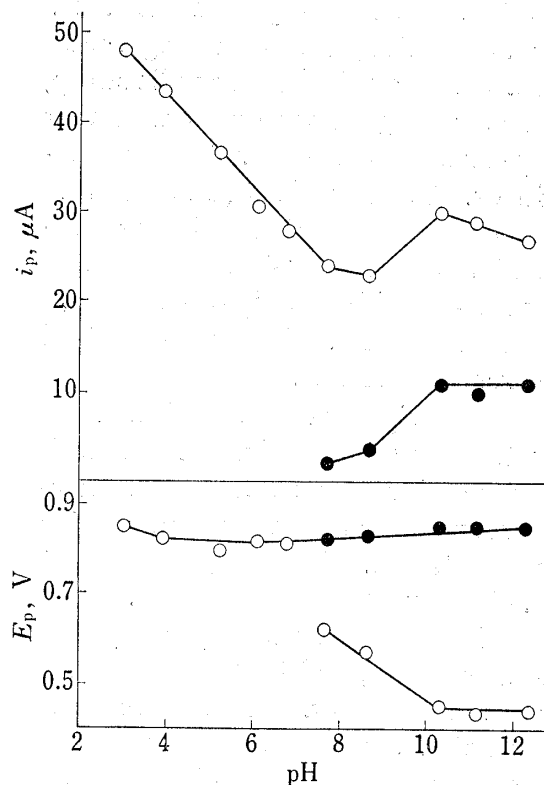


Fig. 2. pH-Dependence of E_p and i_p for Benzenesulfon-*p*-anisidide (2 mM) in 50% Aqueous Acetonitrile at a Sweep Rate of 50 mVsec⁻¹

○: first wave, ●: second wave

pH range studied. On the other hand, no cathodic wave or additional wave was observed upon reversal of the scan direction at the potential of the first wave and a subsequent anodic scan above pH 7.5. As shown in Fig. 2, the peak potential (E_p) of the anodic wave below pH 7 and that of the second anodic wave above pH 7.5 were approximately constant over the entire pH range studied, whereas the E_p value of the first anodic wave decreased with increase in pH in the range of 7.5–10 and leveled off above pH 10. The peak current (i_p) of the first anodic wave decreased linearly with increase in pH below 8, then increased slightly, and again decreased above pH 10. The i_p value of the first wave at pH 7.7 was approximately equal to one-half the i_p value at pH 3. The i_p value of the second wave increased with increase in pH below 10, and leveled off above pH 10. The variation of i_p as a function of the potential scan rate (v) was measured at a scanning rate of 10–200 mV·sec⁻¹. As shown in Fig. 3, the value of $i_p v^{-1/2}$ of the anodic wave was nearly constant below pH 7, whereas at above pH 7.5 that of the first anodic wave decreased with increase in the value of v . The value of $i_p c^{-1}$ of the anodic wave at pH 3, where c is the concentration of I, was nearly constant in the concentration range from 5×10^{-4} to 10^{-2} M at a scanning rate of 50 mV·sec⁻¹, whereas that at pH 10 decreased with increase in the concentration of I.

Controlled Potential Electrolysis in 50% Aqueous Acetonitrile Solution

Electrolysis of I in 50% aqueous acetonitrile buffer solution of pH 3.9 at the anode potential of 0.85 V gave a coulometric n -value (number of Faradays passed per mole of I) of two, and *p*-benzoquinone and benzenesulfonamide were obtained. The voltammogram of the resulting

6) In this paper, we shall use the notation "pH" even for the aqueous acetonitrile solutions, and pH-metric readings are always given without any correction.

solution showed a single peak at 0.02 V on a cathodic sweep and a single peak at 0.38 V on a subsequent anodic sweep, which are in good agreement with that of *p*-benzoquinone under the same conditions. The ultraviolet (UV) spectrum of the resulting solution had absorption maxima at 218 and 246 nm, which also agreed well with that of *p*-benzoquinone containing an equimolar amount of benzenesulfonamide.

Electrolysis of I in 50% aqueous acetonitrile solution of pH 6.7 at 0.8 V gave a coulometric *n*-value of 1.6, and *p*-benzoquinone and benzenesulfonamide were obtained. However, the amount of *p*-benzoquinone determined by voltammetry was ca. 45 molar % of the starting I.

Electrolysis of I (2 mM) in 50% aqueous acetonitrile solution of pH 10.5 at 0.45 V gave an *n*-value of 1.6, and the formation of *p*-benzoquinone was not detected by voltammetry and spectrophotometry. Preparative electrolysis of I (20 mM) at pH 10.5 and 0.42 V gave an *n*-value of 1.1, and white crystals separated out from the solution during the electrolysis, which were identified as N,N'-dibenzenesulfonyl-N-(4'-methoxyphenyl)-5-methoxy-*o*-phenylenediamine (IV). Details of the procedures used to identify the insoluble product of the electrolysis are described in the Experimental section.

Electrolysis of I (2 mM) at pH 10.5 and 0.9 V gave an *n*-value of 2.2, and *p*-benzoquinone (ca. 20 molar %) and a small amount of IV were obtained. During this electrolysis the solution became pink and then turned reddish brown. In the beginning of preparative electrolysis of I (20 mM) at pH 10.5 and 0.9 V the solution turned reddish brown and brown resinous substances separated out from the solution, which caused severe filming on the surface of the anode and prevented further progress of electrolysis. The identity of the resinous substances was not made.

Discussion

Voltammetric behavior of I in aqueous acetonitrile solution was quite different from that of 4'-methoxybenzanilide (MBA).^{2a)} The i_p value of the anodic wave of MBA was approximately constant below pH 10, whereas that of I decreased linearly with increase in pH below 7.5. MBA showed two anodic waves in the pH range of 9.5–11.5, and one above pH 11.5. The i_p value of the anodic wave of MBA at pH 12 was nearly equal to that at pH 3. On the other hand, I showed two anodic waves above pH 7.5, and the i_p value of the first wave at pH 12 was approximately equal to one-half of that at pH 3. These results suggest that the presence of two anodic waves in I above pH 7.5 can be attributed to two discrete one-electron transfer steps rather than the presence of neutral and anionic forms of I in equilibrium, the E_p value of the latter being considered to be less positive than that of the former, although the pK_a ($-\log K_a$) of I was reported to be 8.7 at 20° in aqueous solution,⁵⁾ where K_a is acidity constant. Upon reversal of the scan direction at the potential of the second wave, I showed one or two cathodic waves depending on the pH value, while reversal of the scan direction at the potential of the first wave showed no appearance of a cathodic wave. This fact also suggests that the mechanism of oxidation at the two anodic waves of I above pH 7.5 is quite different from that of MBA.

The fact that the i_p value of the first wave of I above pH 7.5 is approximately equal to one-half that at pH 3 suggests that the electrode reaction at the first wave is a one-electron

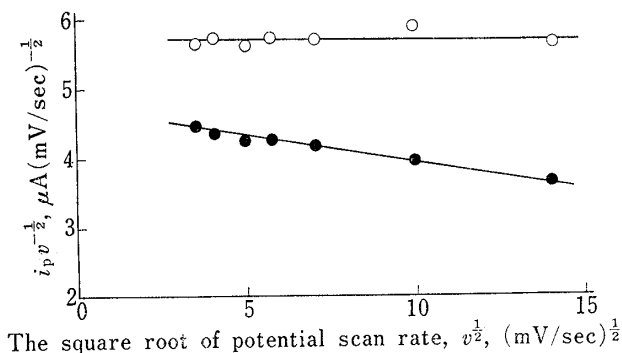
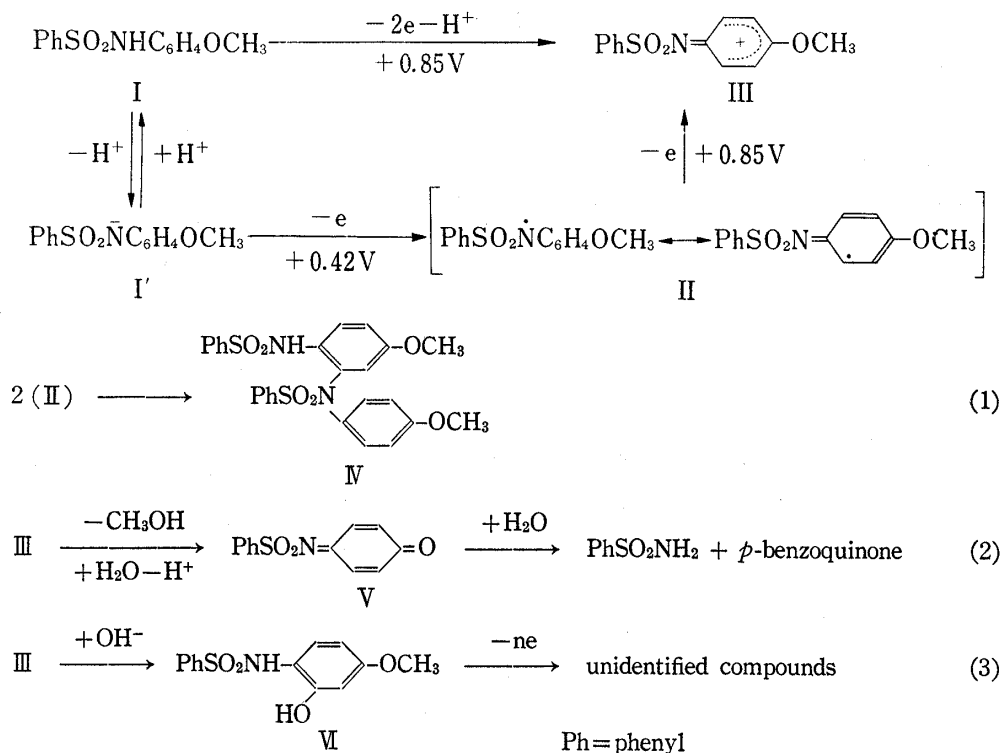


Fig. 3. Variation of Peak Current Function, $i_p v^{-1/2}$ with the Square Root of Potential Scan Rate for Benzenesulfon-*p*-anisidine (2 mM)

○: at pH 3.9, ●: the first wave at pH 10.6

process leading to the free radical of I, since the electrode reaction of I at pH 3 was established to be a two-electron process by means of controlled potential electrolysis. The formation of IV on the electrolysis of I at the potential of the first wave above pH 7.5 also substantiates the above consideration.

The following schemes are suggested for the anodic oxidation of I.



The anodic oxidation of I below pH 7 can be considered analogous to that of MBA (reaction 2). However, the intermediate formation of N-benzenesulfonyl-*p*-benzoquinone-imine (V) was not observed on electrolysis of I at pH 6.7, although both IV and *p*-benzoquinone were obtained from the resulting solution. This may be explained in terms of the instability of V compared with that of N-benzoyl-*p*-benzoquinone-imine.

At pH 10.5, I exists in the anionic form (I'), which is oxidized to II at a less positive potential than the neutral form (I). At the potential of the first wave, II is not oxidized further, and hence IV is formed *via* a head-to-tail coupling of II (reaction 1). The fact that electrolysis of I' at the peak potential of the first wave gave IV in a good yield, whereas electrolysis at the higher potential lowered the yield of IV substantiates this scheme. A similar mechanism was proposed for the anodic oxidation of 4,4'-disubstituted diphenylamines⁷⁾ and N-alkylanilines.⁸⁾

An alternative mechanism for the formation of IV can be considered, that is, one-step two-electron transfer from I' to form the cationic intermediate (III), followed by a nucleophilic attack of I' on III. A similar mechanism was reported for the anodic pyridination of MBA in acetonitrile containing excess of pyridine.^{2a)} However, as described above, the voltammetric behavior of I was quite different from that of MBA, and no N-ring coupling was observed on the anodic oxidation of MBA at pH 12.5. Therefore, the two-electron mechanism is incompatible with these findings.

This type of anodic substitution may be operating in the anodic oxidation of I at pH 10.5 and at the potential of the second wave. In this case the *n*-value was 2.2, and unidentified

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colored compounds were obtained together with IV and *p*-benzoquinone. This suggests that the nucleophilic attack of hydroxyl ion on III followed by further oxidation of the hydroxylated compound (VI) (reaction 3) takes place in parallel with reactions 1 and 2.

The reason why two discrete one-electron transfer steps are observed on the anodic oxidation of I at above pH 7.5 is not clear at present. Detailed studies on this point are in progress.

Experimental

Materials—Benzenesulfon-*p*-anisidide was prepared from benzenesulfonyl chloride and *p*-anisidine, and recrystallized from aqueous EtOH, mp 95–96°. The buffers used in this study were prepared as described previously.^{2a)} Acetonitrile was purified by the following method: (1), refluxing over alkaline KMnO₄ followed by rapid distillation, (2), refluxing over KHSO₄ followed by rapid distillation, (3), refluxing over CaH₂ followed by rapid distillation, and (4), slow distillation over P₂O₅.

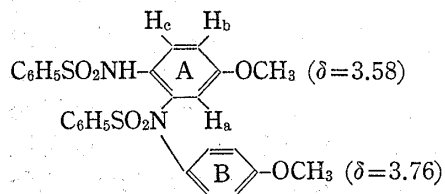
Apparatus—Cyclic voltammetry and controlled potential electrolysis were carried out as described previously.⁹⁾ Oxygen was not removed from the solution throughout the study, because the results of electrolysis were the same in the presence and absence of O₂. A Hokuto Denko HB-101 voltage scanner, HA-101 potentiostat, Riken Denshi F-3D XY recorder, and SP-J5V YT recorder were used throughout. UV and infrared (IR) spectra were obtained using Hitachi 323 and Shimadzu IR-400 spectrometers, respectively. Nuclear magnetic resonance (NMR) spectra were taken at 90 MHz with Hitachi R-22 spectrometer using tetramethylsilane as the internal standard. The pH values of the solutions were determined with Hitachi-Horiba M-7 pH-meter.

Analysis and Isolation of Products obtained by Controlled Potential Electrolysis—Typical examples of the procedure are given below.

a) Electrolysis in Aqueous Acetonitrile at pH 3.9: (i) Benzenesulfon-*p*-anisidide (I) (21.1 mg, 8×10^{-5} mole) was subjected to electrolysis in 50% aqueous acetonitrile buffer of pH 3.9 (40 ml) at 0.85 V at room temperature until the value of current became less than 1% of the initial value (*ca.* 75 min). From the current-time curve 15.3 C, which corresponded to $n=1.98$, was found to have been consumed. The cyclic voltammogram of the solution from electrolysis agreed with that of authentic *p*-benzoquinone (2 mM) obtained under the same conditions. After the solution from electrolysis was diluted 50-fold with the buffer, its UV spectrum was compared with that of a mixture of *p*-benzoquinone and benzenesulfonamide (4×10^{-5} M each) in the same buffer.

(ii) I (527 mg) was subjected to electrolysis in 50% aqueous acetonitrile buffer of pH 3.9 (100 ml) at 0.85 V. The resulting solution was evaporated to dryness under a reduced pressure and the residue was extracted with hot EtOH. The EtOH solution was evaporated to dryness and the residue was extracted with hot ether. Cooling of the ether layer gave white crystals of benzenesulfonamide (103 mg), which were recrystallized from ether, mp 156°, and identified by IR (KBr disc).

b) Electrolysis in Aqueous Acetonitrile at pH 10.5: I (526 mg) was subjected to electrolysis in 50% aqueous acetonitrile buffer of pH 10.5 (100 ml) at 0.42 V. The white precipitate that separated from the resulting solution was collected by filtration, washed with H₂O, and recrystallized from CHCl₃-EtOH to give white needles (230 mg), mp 173–174°. *Anal.* Calcd. for C₂₀H₂₄O₆N₂S₂: C, 59.52; H, 4.61, N, 5.34. Found: C, 59.03; H, 4.65; N, 5.22. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3250 (NH), 1325 (SO₂, *asym.*), 1155 (SO₂, *sym.*). NMR (crystalline material) (CDCl₃) δ : 3.58 (3H, singlet, OCH₃), 3.76 (3H, singlet, OCH₃), 6.36 (1H, doublet, $J=2.8$ Hz, aromatic proton), 6.6–7.1 (5H, multiplet, aromatic protons), 7.2–7.9 (11H, multiplet, aromatic protons). Homonuclear INDOR measurement showed that the doublet at 6.36 ($J=2.8$ Hz, H_a) coupled with the doublet of doublet at 6.77 ($J=2.8$ and 8.8 Hz, H_b), which in turn coupled with the doublet at 7.54 ($J=8.8$ Hz, H_c). A splitting pattern of A₂B₂ type was seen in the multiplet at 6.6–7.1. Irradiation of the signal at 3.58 increased the intensity of the doublet at 6.36 by 8% (nuclear Overhauser effect). This suggests that H_a is at the position *ortho* to the methoxyl group at 3.58, and the signal at 3.58 can be ascribed to the methoxyl group attached to the benzene ring A. These results were in reasonable agreement with the product having the structure of IV.



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