Studies on Sulfenamides. VI.1) Cyclic Voltammetry and Controlled Potential Electrolysis of 4'-Substituted 2-Nitrobenzenesulfanilides in the Presence of Trifluoroacetic Acid or Pyridine

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Anodic oxidation of 4'-substituted 2-nitrobenzenesulfanilides (4'-OMe (1a), 4'-Me (1b), 4'-H (1c), 4'-Cl (1d), 4'-COOEt (1e), 4'-COCH$_3$ (1f), 4'-NO$_2$ (1g)) and 4'-ethoxycarbonyl-N-methyl-2-nitrobenzenesulfanilide (1h) was investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon or a reticulated vitreous carbon anode in acetonitrile containing 1% trifluoroacetic acid (TFA) or 1% pyridine. The peak potentials of 1a—g in acetonitrile containing TFA were 0.23—0.55 V more positive than those in acetonitrile containing pyridine. On the other hand, the peak potential of 1h was not affected by addition of TFA or pyridine. This suggests that 1a—g partially dissociate into the sulfenamide anions in the presence of pyridine. Electrolysis of 1a, 1b, and 1d in the presence of TFA gave the corresponding 2,7-disubstituted phenazines in higher yields than that in the absence of TFA. Although electrolysis of 1e and 1f did not give the corresponding phenazines in the absence of TFA, in the presence of TFA it did. Electrolysis of 1c and 1g did not give the corresponding phenazines in the presence or absence of TFA. Electrolysis of 1a—d in the presence of pyridine gave the corresponding pyridinized sulfanilamides, and that of 1e and 1f gave the corresponding 4,4'-disubstituted azobenzenes. Electrolysis of 1g gave p-nitroaniline both in the presence and absence of TFA. The variation of yields of the phenazines and species of the products was explained in terms of the extent of dissociation of the dication intermediate, which in turn depends on the 4'-substituent. The nitrenium ions and nitrenes are suggested to be intermediates in the formation of the corresponding phenazines and the primary amines, respectively. The azobenzenes are considered to be oxidation products of the primary amines.

Keywords—anodic oxidation; cyclic voltammetry; 2-nitrobenzenesulfanilides; 2,7-disubstituted phenazines; oxidation of sulfanamides; nitrenium ion; nitrene; RVC; N-arylp-yridinium perchlorate

In the previous papers2) we reported the results of the oxidation of 4'-substituted 2-nitrobenzenesulfanilides (4'-OMe (1a), 4'-Me (1b), 4'-H (1c), 4'-Cl (1d), 4'-COOEt (1e), 4'-COMe (1f), 4'-NO$_2$ (1g)) with lead dioxide in acetonitrile containing 1% trifluoroacetic acid (TFA) and 1% trifluoroacetic anhydride (TFAH) and showed the usefulness of this reaction as a new synthetic method for 2,7-disubstituted phenazines (di-OMe (2a), di-Me (2b), di-Cl (2d), di-COOEt (2e), di-COMe (2f), di-NO$_2$ (2g)). TFAH was added to the solution in order to reduce the water content in the solution. In order to elucidate the role of TFA in the formation of the phenazines in more detail, we have studied the anodic oxidation of 1a—g in acetonitrile containing 1% TFA or 1% pyridine.

Results

Cyclic Voltammetry

Cyclic voltammograms were obtained from 2 mm solutions of 1a—h in acetonitrile containing 0.1 m ethyltributylammonium trifluoromethanesulfonate (ETBT) with or without addition of 1% TFA or 1% pyridine. Voltammetric data are summarized in Table I. A typical cyclic voltammogram is shown in Fig. 1. The peak potentials ($E_p$) of 1a—g in the pres-
ence of TFA were 0.23—0.55 V more positive than those in the presence of pyridine. In order to elucidate the effect of addition of TFA or pyridine on the voltammetric behavior of 1a—g, cyclic voltammetry of 4'-ethoxy carbonyl-N-methyl-2-nitrobenzenesulfenamide (1h), which is the N-methyl derivative of 1e, was studied and compared with that of 1e. With a scan rate of 50 mV s⁻¹, cyclic voltammetry of 1e showed four anodic peaks at 0.97, 1.30, 1.60, and 1.96 V. On addition of 1% pyridine to the solution of 1e, two shoulders and one peak were observed at 0.80, 1.32, and 1.51 V, respectively. On the other hand, the Eₚ value of the first wave of 1h was little affected by addition of TFA or pyridine.

**Controlled Potential Electrolysis**

Although electrolysis of 1a, 1b, and 1d in the absence of TFA gave 2a, 2b, and 2d, respectively, that of 1e and 1f did not go to completion owing to film formation at the anode, and that of 1g gave only p-nitroaniline (3g) (61.3%) instead of 2g.

Electrolysis of 1a—g (10 mM) was carried out in acetonitrile containing 0.1 M ETBT and 1% TFA and the results are summarized in Table II.

Although electrolysis of 1c and 1g still did not give 2c and 2g, that of 1e and 1f gave 2e and 2f, respectively, and the yields of 2a, 2b, and 2d improved considerably. p-Anisidine (3a), which was one of the products obtained on electrolysis of 1a in the absence of TFA, was not detected in the electrolyzed solution. The results of electrolysis of 1a—g (10 mM) in acetonitrile containing 0.1 M ETBT and 4% pyridine are summarized in Table III. 1-[2-(2-Nitrobenzenesulfonyl)-5-methoxyphenyl]pyridinium perchlorate (71.5%) was precipitated when NaClO₄ was added to the solution from the electrolysis of 1a in the presence of pyridine. Electrolysis of 1b—d in acetonitrile containing 0.1 M NaClO₄ and 4% pyridine gave the corresponding 1-substituted pyridinium perchlorates in yields 52.0%, 9.2%, and 2.5%, respec-
TABLE II. Results of Controlled Potential Electrolysis of 4'-Substituted 2-Nitrobenzenesulfenamides (10 mm) in Acetonitrile containing 0.1 M ETBT, 1% TFA and 1% TFAH

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Applied potential V (vs. S.C.E)</th>
<th>n-Value</th>
<th>Yield, mol %</th>
<th>Hammett σp of substituent</th>
<th>2,2'-Dinitrodiphenyl-disulfide</th>
<th>2,7-Disubstituted phenazines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>1.10</td>
<td>0.88</td>
<td>64.0</td>
<td>45.9 (29.2)</td>
<td>0.268</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>1.23</td>
<td>1.58</td>
<td>54.5</td>
<td>46.8 (40.0)</td>
<td>0.170</td>
<td></td>
</tr>
<tr>
<td>1c</td>
<td>1.18</td>
<td>1.40</td>
<td>26.0</td>
<td>(---)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1d</td>
<td>1.33</td>
<td>1.35</td>
<td>64.0</td>
<td>57.2 (37.3)</td>
<td>+0.227</td>
<td></td>
</tr>
<tr>
<td>1e</td>
<td>1.45</td>
<td>1.85</td>
<td>51.0</td>
<td>45.8 (---)</td>
<td>+0.45</td>
<td></td>
</tr>
<tr>
<td>1f</td>
<td>1.48</td>
<td>1.17</td>
<td>47.0</td>
<td>7.6 (---)</td>
<td>+0.502</td>
<td></td>
</tr>
<tr>
<td>1g</td>
<td>1.48</td>
<td>0.52</td>
<td>0</td>
<td>(---)</td>
<td>+0.778</td>
<td></td>
</tr>
</tbody>
</table>

a) Numbers in parentheses are yields of the phenazines without addition of TFA and TFAH.
b) Number of Faradays passed per mole of substrate.

TABLE III. Results of Controlled Potential Electrolysis of 4'-Substituted 2-Nitrobenzenesulfenamides (10 mm) in Acetonitrile containing 0.1 M ETBT, and 4% Pyridine

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Applied potential V (vs. S.C.E)</th>
<th>n-Value</th>
<th>Yield, mol %</th>
<th>2,2'-Dinitrodiphenyl-disulfide</th>
<th>2,7-Disubstituted phenazines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>1.10</td>
<td>2.10</td>
<td>6.0</td>
<td>71.5</td>
<td>52.0</td>
</tr>
<tr>
<td>1b</td>
<td>1.23</td>
<td>2.11</td>
<td>7.0</td>
<td>9.2</td>
<td>2.5</td>
</tr>
<tr>
<td>1c</td>
<td>1.18</td>
<td>0.93</td>
<td>27.9</td>
<td>4.0</td>
<td>10.4</td>
</tr>
<tr>
<td>1d</td>
<td>1.33</td>
<td>1.44</td>
<td>11.0</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>1e</td>
<td>1.45</td>
<td>6.60a</td>
<td>7.9</td>
<td>Trace</td>
<td></td>
</tr>
<tr>
<td>1f</td>
<td>1.48</td>
<td>9.54a</td>
<td>46.8</td>
<td></td>
<td>5.6</td>
</tr>
<tr>
<td>1g</td>
<td>1.48</td>
<td>1.24</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) An RVC anode was used.
b) NaClO₄ was used as a supporting electrolyte instead of ETBT.
c) p-Nitroaniline (5.6%) was also detected.

tively. Electrolysis of 1e in acetonitrile containing 0.1 M ETBT and 4% pyridine at a reticulated vitreous carbon (RVC) anode at 1.45 V gave 2,2'-dinitrodiphenyl-disulfide (4, 11.0%) and 4,4'-diethoxy carbonylazobenzene (5e, 10.4%). 2e was not detected in the resulting solution. An RVC anode was used for the electrolysis of 1e and 1f in the presence of pyridine in order to complete the electrolysis, because the electrolysis at a glassy-carbon plate caused severe film at the anode and did not go to completion. Electrolysis of 1h in acetonitrile containing 0.1 M NaClO₄ without addition of TFA or pyridine at 1.55 V gave 2-nitrobenzenesulfonic acid (70.5%), which suggested that two-electron transfer was involved in the first step of the reaction, as in the case of 1a—g. 4)

Discussion

Cava and Blake reported that the initial step of the base-catalyzed rearrangement of 1d was the formation of the sulfenamide anion. 6) The experimental findings that in the presence of 1% pyridine the $E_p$-values of the first waves of 1a—g shifted to less positive values while that of 1h did not, suggest that in the presence of pyridine 1a—g partially dissociate into their anions, which have less positive $E_p$-values. However, comparison of the $E_p$-values in the presence of TFA with those in the absence of TFA or pyridine suggests that the dissociation of
$p$-$X$-$C_6H_4$-$NH$-$SR \xrightarrow{-H^+ + H^+} p$-$X$-$C_6H_4$-$N$-$SR$

$\xrightarrow{-2e} p$-$X$-$C_6H_4$-$NH$-$SR \xrightarrow{-H^+ + H^+} p$-$X$-$C_6H_4$-$N$-$SR$

$A \xrightarrow{\text{in the absence of pyridine}}$ tars

$B \xrightarrow{\text{in the presence of pyridine}} p$-$X$-$C_6H_4$-$N$-$N$-$C_6H_4$-$p$-$X$

$1a$-$g$ is not appreciable in the absence of pyridine. Therefore, the effect of addition of TFA on the yields of $2a$-$f$ is not considered to be due to suppression of dissociation of $1a$-$g$.

The following schemes are suggested for the anodic oxidation of $1a$-$g$.

The anodic oxidation of 1 gives the dication A. In the presence of TFA, A reacts with the electrolyte anion and gives the nitrenium C. Two molecules of C couple to form the dihydrophenazines, which is oxidized further to 2.

In the presence of pyridine, A is converted quickly to B by dissociation of the N–H bond. A part of B reacts with pyridine and gives 1-substituted pyridinium derivatives. The rest of B reacts with electrolyte anion instead of pyridine and gives the nitrene D, which abstracts two hydrogen atoms from the solvent or 1 and gives 3, and then 3 is oxidized to 5 (except for 3g, which has the highest oxidation potential among 3a–g). However, the oxidation of 3 gives 5 in low yield and tar in high yield. The latter causes severe filmning at the anode and prevent the electrolysis from going to completion. Electron-donating groups in the 4'-position of 1 stabilize B and increase the yields of 1-substituted pyridinium derivatives.

An electron-attracting substituent at the 4'-position increases the acidity of A and decreases the yield of 2, but addition of TFA to the solution of 1 decreases the dissociation of A and thus increases the formation of C and decreases that of D. The following experimental findings support the above conclusions: (1) electrolysis of 1g, whose 4'-substituent has the largest Hammett $\sigma_p$ value among 1a–g (Table II), did not give 2g even in the presence of TFA, while that of 1f, whose 4'-substituent has the second largest $\sigma_p$ value, gave 2f in low yield even in the presence of TFA; (2) electrolysis of 1a–d, whose 4'-substituents have smaller $\sigma_p$ values than
that of 1e, gave 2a—d in fairly good yields in the absence of TFA except in the case of 1c; (3) 3a and 3g were obtained by the electrolysis of 1a and 1g in the absence of TFA, respectively. Since 1c has no substituent on the 4’-position, the mechanism of anodic oxidation of 1c may be different from the others.

One of the reasons why the yield of 2d was about 10% larger than that of 2a, 2b, or 2c can be ascribed to the easiness of isolation of 2d, because 2d separated out as large needles after addition of solid Na₂CO₃ and was almost insoluble in the solution.

**Experimental**

**Materials**—4’-Substituted 2-nitrobenzenesulfenilides and ethyltributylammonium trifluoromethanesulfonate (ETBT) were prepared as described previously.⁴ 4’-Ethoxycarbonyl-N-methyl-2-nitrobenzenesulfenilide chloride and ethyl N-methyl-p-aminobenzoate⁹ in dry ether and recrystallized twice from 85% ethanol and then from methanol: yellow crystals, mp 139—140°C. Anal. Calcd. for C₁₆H₁₂N₃O₇S: C, 57.82; H, 4.85; N, 8.43. Found: C, 57.65; H, 4.70; N, 8.43. IR ν₃₅₋₅ cm⁻¹: 1705 (C=O). NMR (CDCl₃) δ: 1.45 (3H, t, J = 4 Hz, CH₃), 3.55 (3H, s, CH₃), 4.35 (2H, q, J = 4 Hz, CH₂), 7.1—7.6 (6H, m, aromatic), 7.9—8.1 (2H, m, aromatic). MS m/z: 332 (M⁺). Acetonitrile was purified as described previously.¹⁰ Trifluoroacetic acid and trifluoroacetic anhydride were obtained commercially. Pyridine was refluxed over calcium hydride for five hours and distilled. RVC was obtained commercially, which were recrystallized.

**Apparatus**—Cyclic voltammetry, controlled potential electrolysis, and high performance liquid chromatography (HPLC) were carried out as described previously.⁴ ¹⁰ RVC (2 x 1.80-5) cut into a rectangular parallelepiped with approximate dimensions of 80 x 50 x 10 was used for electrolysis of 1e and 1f without addition of TFA and with addition of pyridine as an anode instead of a glassy-carbon plate. Electrical contact to the RVC was made by winding a Pt wire around the top end of it. Infrared (IR) and nuclear magnetic resonance (NMR) spectra were obtained on Hitachi 260-30 and R-22 spectrometers, respectively.

**Isolation of 1-Substituted Pyridinium Perchlorate**—Typical examples of the procedure are given below.

a) 1a (275.4 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT and 4% pyridine at 1.10 V at room temperature until the current fell below 1% of the initial value. Solid NaClO₄ (12 g) was dissolved in the resulting solution and the solution was cooled in refrigerator overnight. Yellow crystals separated out: they were filtered off and weighed (323.8 mg). The yellow crystals were recrystallized from acetonitrile (mp 228°C (dec.)) and identified as 1-[2-(2-nitrobenzenesulfonylamo)-5-methoxyphenyl]-pyridinium perchlorate on the basis of the elemental analysis data, and IR and NMR spectra. Anal. Calcd. for C₁₆H₁₂ClN₃O₄S: C, 57.64; H, 3.55; N, 9.55. Found: C, 47.70; H, 3.54; N, 9.55. IR νmax cm⁻¹: 3350 (NH), 1613 (pyridine ring), 1100 (Cl·O), 1520 (NO₂). NMR (DMSO-d₆) δ: 2.75 (3H, s, CH₃), 7.0—7.9 (7H, m, aromatic proton), 8.2—8.4 (3H, m, aromatic proton). 8.7—9.0 (1H, m, NH), 8.3—9.5 (2H, m, aromatic proton).

b) 1b (261.0 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M NaClO₄ and 4% pyridine at 1.29 V at room temperature. The resulting solution was concentrated and dried rigorously under reduced pressure. The residue was subjected to column chromatography on neutral alumina with CHCl₃ as the eluent. After a sufficient volume of CHCl₃ had been passed through the column, elution was continued with CHCl₃ containing 10% CH₃CN as the eluent. The yellow effluent was evaporated to dryness under reduced pressure. The residue was recrystallized from 99% EtOH to give yellow crystals (210.8 mg, mp 190—191°C (dec.)), which were identified as 1-[2-(2-nitrobenzenesulfonylamo)-5-methylphenyl]pyridinium perchlorate on the basis of elemental analysis data, and IR and NMR spectra. Anal. Calcd. for C₁₆H₁₂ClN₃O₄S: C, 49.37; H, 3.68; N, 9.60. Found: C, 49.48; H, 3.76; N, 9.44. IR νmax cm⁻¹: 3446 (NH), 1615 (pyridine ring), 1510 (NO₂), 1095 (Cl·O). NMR (CDCl₃) δ: 2.30 (3H, s, CH₃), 6.05 (1H, s, NH), 7.2—7.8 (6H, m, aromatic proton), 8.1—8.3 (2H, m, aromatic proton), 8.6—8.9 (4H, m, aromatic proton).

**Isolation of the Azobenzenes**—3e: 1e (318.7 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT and 4% pyridine at 1.45 V at room temperature until the current fell below 5% of the initial value. The resulting red solution was concentrated and extracted with hot benzene. The benzene solution was concentrated and subjected to multiple runs of thin-layer chromatography on alumina with carbon tetrachloride–benzene (2:1) as the developing solvent. The red band was scraped off and extracted with benzene. Concentration of the benzene solution gave red crystals (16.9 mg), which were recrystallized from acetone and identified as 3e on the basis of IR and NMR spectra and melting point (145—146°C, lit.¹¹ 145.8°C).

3f: 1f (288.9 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT and 4% pyridine at 1.48 V. The resulting solution was treated according to the procedure described above. The red crystals obtained (3.9 mg) was identified as 3f on the basis of the IR spectrum.

**Determination of Products obtained by Controlled Potential Electrolysis**—a) 2,2’-Dinitrophenyl-disulfide, 2b, and 2-nitrobenzenesulfonic acid were determined as described previously.⁴
b) 2a: Forty μl of the electrolyzed solution was developed on a thin-layer of alumina with benzene-hexane-27% aqueous ammonia (2:1:0.03). The spot of 2a was detected by ultraviolet irradiation, and this region of alumina was scraped off and extracted with CH₂CN. The absorbance at 261 nm was measured.

c) 1c, 1d, and 1g were determined by the same procedure as described for 2,2'-dinitrodiaphenyl disulfide.

d) 2d and 2e: After addition of a small amount of solid Na₂CO₃ to the electrolyzed solution, the solution was allowed to stand overnight in a refrigerator. The resulting crystals were filtered off, washed with acetonitrile and then with water, dried, and weighed.

e) 2f: After addition of a small amount of solid Na₂CO₃ to the electrolyzed solution, the solution was concentrated. The residue was washed with acetonitrile, recrystallized from benzene and weighed.

f) p-Nitroaniline: Ten ml of the electrolyzed solution was evaporated to dryness under reduced pressure. The residue was dissolved in 10 ml of acetonitrile and 1 μl of the solution was injected into an HP-01 column. The mobile phase was methanol and the detector was operated at 228 nm.

References and Notes

3) All potentials were measured against an aqueous saturated calomel electrode.