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Studies on Sulfenamides. I.[1] Cyclic Voltammetry and Controlled Potential Electrolysis of 4'-Substituted Bezenesulfenanilides

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Anodic oxidation of benzenesulfenanilides (4'-OMe (**1a**), 4'-Me (**1b**), 4'-Cl (**1c**), 4'-H (**1d**)) were investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon anode in acetonitrile. The value of i_p/c of the first anodic peak, where i_p is the peak current and c is the concentration of **1a**, decreased with increase in c, which was ascribed to the hydrolysis of **1a** at the surface of the anode caused by the liberation of protons during the electrolysis. Electrolysis of **1a**, **1b**, and **1c** (10 mM) gave the corresponding phenazines, whereas that of **1d** did not. The nitrenes are suggested for the formation of the phenazines. Electrolysis of **1a** in the presence of water (1%) gave N-phenylthio-*p*-quinoneimine in addition to 2,7-dimethoxyphenazine.

Keywords——benzenesulfenanilides; anodic oxidation; cyclic voltammetry; oxidation of sulfenamides; synthesis of phenazines; nitrene; imido intermediate; 2,7-disubstituted phenazines; anodic dimerization

A considerable literature dealing with sulfenamides has been published.[3] Oxidation of sulfenamides was attempted with various oxidizing agents.[4] Although sulfonamides[4a] or quinonesulfurimines[4b] were identified as the products in some experiments, the reaction was generally complicated and neither product could be characterized in another experiment.[4c] Recently electron spin resonance studies of benzenesulfenanilidyl radicals which were generated by oxidation of benzenesulfenanilides in benzene with lead dioxide were reported.[4d] However, the final products of the oxidation were not investigated. In the course of our studies on anodic oxidation of carboxamides and sulfonamides, benzenesulfen-*p*-anisidide (**1a**) and *p*-toluidide (**1b**) were found to be easily oxidized at a glassy-carbon anode in acetonitrile. 2,7-Dimethoxyphenazine (**2a**) and 2,7-dimethylphenazine (**2b**) were obtained as the products, respectively.[1] Since **2a** and **2b** were so far not identified as the products of the oxidation of **1a** and **1b**, detailed studies on anodic oxidation of benzenesulfen-anilides (4'-OMe (**1a**), 4'-Me (**1b**), 4'-Cl (**1c**), 4'-H (**1d**)) were undertaken.

Results

Cyclic Voltammetry

Cyclic voltammograms were obtained from a 2 mM solution of **1a** in acetonitrile containing 0.1 M $NaClO_4$. Voltammertric data are summarized in Table I. With a scan rate (v) of 50 mV·sec^{-1}, two anodic waves were observed with peaks at 0.74 and 1.46 V *vs.* S.C.E.

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[1] Preliminary reports: H. Sayo, K. Mori, and A. Ueda, *Chem. Pharm. Bull.* (Tokyo), **25**, 525 (1977); H. Sayo and K. Mori, *ibid.*, **25**, 1489 (1977).

[2] Location: *Ikawadani-cho, Tarumi-ku, Kobe 673, Japan.*

[3] *a*) N. Kharasch, S.J. Potempa, and H.L. Wehrmeister, *Chem. Rev.*, **39**, 269 (1946); *b*) E. Riesz, *Bull. Soc. Chim. France*, **1966**, 1449; F.A. Davis, *Int. J. Sulfur Chem.*, **8**, 71 (1973).

[4] *a*) J. Barber, Brit. Patent 550446 (1943) [*C.A.*, **38**, 1850 (1944)]; *idem*, Brit. Patent 557055 (1943) [*C.A.*, **39**, 2296 (1945)]; The Manchester Oxide Co., Ltd., Brit. Patent 551206 (1943) [*C.A.*, **38**, 1751 (1944)]; *b*) E. Gebauer-Fülnegg and E. Riesz, *Monatsh. Chem.*, **49**, 31 (1928); S.I. Burmistrov and V.I. Glazkov, *Zh. Obshch. Khim.*, **22**, 1862 (1952); *c*) N. Capron, R. Sasin, and G.S. Sasin, *J. Org. Chem.*, **21**, 362 (1956); *d*) Y. Miura and M. Kinoshita, *Bull. Soc. Chem. Japan*, **50**, 1142 (1977); Y. Miura, Y. Katsura, and M. Kinoshita, *Chem. Lett.*, **1977**, 409.

Table I. Results of Cyclic Voltammetry of 4'-Substituted Benzenesulfenanilides (2 mM) in Acetonitrile containing 0.1 M $NaClO_4$

Compd. No.	Substituent	E_p, V *vs.* S.C.E.		$i_p v^{-1/2}$, μA (mV/sec)$^{-1/2}$	
		$v=50$	1000 mV·sec^{-1}	$v=50$	1000 mV·sec^{-1}
1a	OMe	0.75	0.85	4.44	4.46
1b	Me	0.88	0.96	4.16	4.32
1c	Cl	0.94	1.05	4.26	4.76
1d	H	0.88	1.00	4.06	4.54

On reversing the direction of a scan, a small cathodic wave was observed at 0.47 V. The variation of the peak current as a function of v was measured at a scan rate of 10—1000 mV·sec^{-1}. The value of $i_p v^{-1/2}$ of the first anodic peak, where i_p is the peak current, was nearly independent of v. The variation of i_p as a function of c, where c is the concentration of **1a**, was examined in the concentration range from 1 to 30 mM. The value of i_p/c of the first anodic peak decreased with increase in c, as shown in Fig. 1. Addition of water (1%) to the solution of **1a** increased the value of i_p/c, especially at $c=1$ and 2 mM.

Cyclic voltammetry of **1b**, **1c**, and **1d** in acetonitrile showed three, five, and three anodic waves, respectively. The shapes of the anodic waves other than the first ones varied remarkably with changes in v and c, and hence only the first waves were investigated in detail. The i_p/c values of the first anodic peaks of **1b**, **1c**, and **1d** decreased with increase in c in a similar manner as that of **1a**.

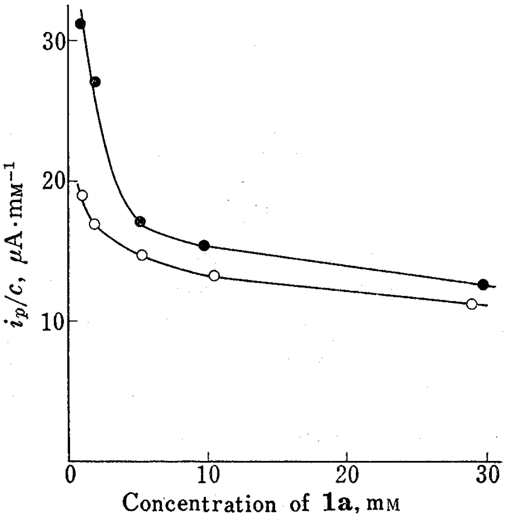

Fig. 1. Dependence of Peak Current of the First Wave of Benzenesulfen-*p*-anisidide on Its Concentration; $v=50$ mV·sec^{-1}

○: without the addition of water,
●: with the addition of water (1%).

Controlled Potential Electrolysis

Table II summarizes the results on controlled potential electrolysis. Electrolysis of **1a** (2 mM) in acetonitrile containing 0.1 M $NaClO_4$ at the anode potential of 0.75 V gave a coulometric n-value of 0.67. The voltammogram of the resulting deep purple solution showed a single anodic peak at 1.46 V, which was in good agreement with that of diphenyl-disulfide (**3**) under the same condition. The ultraviolet (UV) and visible (VIS) spectra of the resulting solution had absorption maxima at 263, 384, 429, and 486 nm. On addition of solid Na_2CO_3 to the solution, the maxima shifted to 263, 343, 406, and 424 nm, which were very close to those reported on 2,7-dimethoxyphenazine (**2a**).[5] Preparative electrolysis of **1a** (10 mM) gave **2a**, **3**, and *p*-anisidine (**4**). **2a** was identified from its UV, VIS, infrared (IR), and nuclear magnetic resonace (NMR) spectra in comparison with those of an authentic sample prepared by the method of Yoshioka.[6]

Electrolysis of **1a** (2 mM) in acetonitrile containing water (1%) and 0.1 M $NaClO_4$ at 0.73 V gave an n-value of 0.59. The solution turned greenish brown at the end of the electrolysis. After addition of solid Na_2CO_3 to the resulting solution, the UV and VIS spectra of

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[5] P. Walker and W.A. Waters, *J. Chem. Soc.*, **1962**, 1632.
[6] I. Yoshioka, *Pharm. Bull.* (Tokyo), **1**, 66 (1953).

Table II. Results of Controlled Potential Electrolysis of 4′-Substituted Benzenesulfenanilides (10 mM) in Acetonitrile containing 0.1 M $NaClO_4$

Compd. No.	Applied potential V *vs.* S.C.E.	*n*-Value	λ_{max}[a], nm	Products identified	Yield[b] mol%
1a	0.75	0.67	263, 343 406, 424	2,7-dimethoxyphenazine diphenyldisulfide *p*-anisidine	39.4 99.1 0.8
1b	0.90	0.69	255, 362 376[c], 397[c]	2,7-dimethylphenazine diphenyldisulfide	42.0 98.4
1c	1.00	0.70	255, 363 378, 442	2,7-dichlorophenazine diphenyldisulfide *p*-chloroaniline	13.6 53.1 64.0
1d	0.97	0.66	239, 289 446	[d]	

a) After addition of a small amount of solid Na_2CO_3 to the solution from electrolysis.
b) Yield based on 2 mol of the anilides forming 1 mol of the phenazines and 1 mol of diphenyldisulfide.
c) Shoulder.
d) Products were not identified.

the solution had absorption maxima at 275 and 436 nm, which were very close to those reported on N-phenylthio-*p*-quinoneimine (**5**).[7] From the resulting solution the amount of **2a** (12.6 mole%) and **5** (30.3 mol%) were spectrophotometrically determined by the use of thin-layer chromatography. Preparative electrolysis of **1a** (10 mM, 40 ml) with the addition of water (1%) gave red needles (7 mg), which were identified as **5** from their IR spectrum in comparison with that of an authentic sample prepared by the method of Kramer and Gamson.[8]

Electrolysis of **1b** (10 mM) in acetonitrile containing 0.1 M $NaClO_4$ at 0.90 V gave an *n*-value of 0.69, and **2b** and **3** were obtained. Although preliminary electrolysis of **1c** (2 mM) gave no indication of the formation of 2,7-dichlorophenazine (**2c**),[1] a larger scale electrolysis of **1c** (10 mM) gave **2c**, **3**, and *p*-chloroaniline. On the other hand electrolysis of **1d** (10 mM) did not give phenazine (**2d**) at all.

Discussion

The results of voltammetric experiments indicate that the first anodic wave of **1a** does not correspond to a simple diffusion controlled process. It is well-known that the hydrolysis of benzenesulfenanilides is easily accomplished by dissolving the anilides in dry ether and passing dry hydrogen chloride.[3a] Since the solution becomes fairly acidic in the neighborhood of the anode due to liberation of protons during the electrolysis and the acidity increases with increase in the electricity consumed, the decrease in the value of i_p/c with increase in c can be attributed to the hydrolysis of **1a** at the surface of the anode. The hydrolysis of **1a** caused by liberation of protons at the surface of the anode is considered to be completed within the time scale of voltammetry, because a plot of the peak-current function $i_p v^{-1/2}$ against v was independent of sweep rate in the v range examined. When the perchloric acid (1 M in acetic acid)[9] was added dropwise to the 2 mM solution of **1a** in acetonitrile, the solution immediately turned deep purple. This color change was similar to that accompanied by the electrolysis.

The following schemes are suggested for the anodic oxidation of **1a**. Formation of **2a** through intermediacy of a nitrene **7**, was reported on the pyrolysis of *p*-methoxyphenylazide

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7) D.H.R. Barton, I.A. Blair, P.D. Magnus, and R.K. Norris, *J. Chem. Soc. Perkin I*, 1973, 1031.
8) D.N. Kramer and R.M. Gamson, *J. Org. Chem.*, 24, 1154 (1959).
9) J.F. Coetzee and I.M. Kolthoff, *J. Am. Chem. Soc.*, 79, 6110 (1957).

$$p\text{-MeO-C}_6\text{H}_4\text{-NHSPh} \xrightarrow{-e} p\text{-MeO-C}_6\text{H}_4\text{-}\overset{\cdot\,+}{\text{N}}\text{HSPh}$$

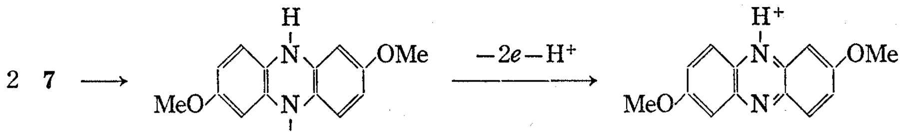
1a **6**

$$\mathbf{6} \longrightarrow p\text{-MeO-C}_6\text{H}_4\text{-}\underset{\cdot\cdot}{\dot{\text{N}}}\cdot + \text{Ph}\dot{\text{S}} + \text{H}^+$$

7

$$2\text{Ph}\dot{\text{S}} \longrightarrow \text{PhSSPh}$$

3



8 **(2a)H⁺**

$$\mathbf{1a} + \text{HClO}_4 \longrightarrow \text{PhSClO}_4 + p\text{-anisidine}$$

4

$$2\text{PhSClO}_4 \longrightarrow \mathbf{3} + 2\dot{\text{C}}\text{lO}_4$$

$$\dot{\text{C}}\text{lO}_4 \longrightarrow \dot{\text{C}}\text{lO}_2 + \text{O}_2$$

$$\mathbf{1a} + \dot{\text{C}}\text{lO}_2 \longrightarrow \mathbf{6} + \text{ClO}_2^-$$

$$\mathbf{8} + 2\dot{\text{C}}\text{lO}_2 \longrightarrow (\mathbf{2a})\text{H}^+ + \text{HClO}_2 + \text{ClO}_2^-$$

$$\mathbf{4} + \dot{\text{C}}\text{lO}_2 \longrightarrow \text{unidentified products} + \text{ClO}_2^-$$

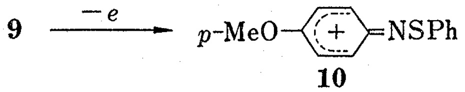
Ph=phenyl
Me=methyl

Chart 1

in cumene[5] and on the rearrangement of azobenzenes to phenazines.[10] However, in the former case, the yield of **2a** was very low and the main product was 4,4'-dimethoxyazobenzene. On the other hand, electrolysis of **1a** gave no indication of the formation of 4,4'-dimethoxyazobenzene and the yield of **2a** was 39.4 mole%. Since **1a** is very labile in acidic media and the anolyte becomes acidic with a progress of electrolysis, fairly large amount of starting **1a** are considered to decompose to **3**,**4**, and perchlorate radical without being oxidized at the anode. This means that the nitrene formed is assumed to be exclusively converted into **2a** through dehydrogenation of **8**. Perchlorate radical is reported to decompose very rapidly to produce other chlorine-oxygen compounds, including chlorine dioxide, which are capable

$$\mathbf{6} + \text{H}_2\text{O} \longrightarrow p\text{-MeO-C}_6\text{H}_4\text{-}\dot{\text{N}}\text{SPh} + \text{H}_3\text{O}^+$$

9



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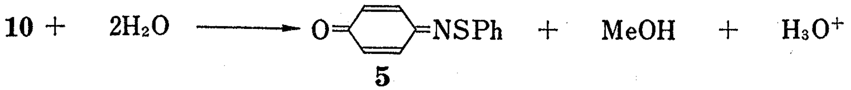

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Chart 2

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[10] R.A. Abramovitch and B.A. Davis, *J. Heterocycl. Chem.*, **1968**, 793.

of serving as strong oxidizing agents.[11] These can react with **1a**, **4**, and **8** to produce **2a** and unidentified resinous colored compounds. Thus overall stoichiometry is very complicated.

The effect of the water added to the solution can be explained on the basis of basicity of water as shown in Chart 2. The cation radical **6** is immediately deprotonated by the water molecules, and the neutral radical **9** formed is oxidized further to **5** through **8** at the applied potential. A similar oxidation process was suggested for the anodic oxidation of 4′-methoxybenzanilide.[12]

Electrolyses of **1b** and **1c** can be considered analogous with that of **1a**. However, the reason why electrolysis of **1d** did not give phenazine is not clear at present. Detailed studies of this are now in progress.

Experimental

Materials——Benzenesulfenanilides were prepared from benzenesulfenyl chloride and the corresponding anilines by a known method[13] and purified by column chromatography on alumina. Acetonitrile was purified as described previously.[14]

Apparatus——The working electrode used for voltammetry was prepared from a glassy-carbon rod (Tokai Electrode GC-20, diameter 3 mm) as described previously.[15] The reference electrode system consisted of a commercially available saturated calomel electrode situated in a glass tube which was filled with aqueous 0.1 M $NaClO_4$ and separated from the electrolyzed solution by means of a sintered glass disc and agar plug. Oxygen was not removed from the solution throughout the study, because the results of electrolysis were the same in the presence and absence of O_2. A Hokuto Denko HB-107A function generater, HA-101 potentiostat and Riken Denshi F-3D XY recorder were used for cyclic voltammetry. A Hokuto Denko HA-104 potentiostat, HF-102 coulometer, and Riken Denshi SP-J5V YT recorder were used for controlled potential electrolysis. UV and IR spectra were obtained using a Hitachi 323 and Shimadzu IR-400 spectrometers, respectively. NMR spectra were taken at 90 MHz with a Hitachi R-22 spectrometer using tetramethylsilane as the internal standard.

Isolation of Products obtained by Controlled Potential Electrolysis——Typical examples of the procedure are given below. a) **1a** (231 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M $NaClO_4$ at 0.75 V at room temperature until the value of current became less than 1% of the initial value (*ca.* 50 min). The quantity of electricity consumed (68.8 C) corresponded to $n=0.67$. To the resulting deep purple solution 50 ml of Na_2CO_3 solution (10%) was added, and the mixture was extracted with benzene. The organic layer was separated and extracted with HCl solution (10%). When the HCl solution was made slightly alkaline with 10% NaOH, yellow crystals separated out, which were collected (51.7 mg) and subjected to column chromatography on neutral alumina (8 g) with $CHCl_3$ as eluant. The yellow crystals obtained from the first effluent were identified as **2a** (44.0 mg, mp 249—250°). The filtrate was extracted with $CHCl_3$, and the $CHCl_3$ solution was subjected to column chromatography on neutral alumina (5 g) with $CHCl_3$ as eluant. The first fraction was evaporated to dryness and the residue was extracted with petroleum ether. Evaporation of the solvent gave a small amount of white needles (*ca.* 1 mg, mp 57°), which were identified as **4**. The organic layer which had been extracted with HCl solution was subjected to column chromatography on alumina (8 g) with CCl_4 as eluant. The white crystals obtained from the first fraction were identified as 3 (108.2 mg, mp 61—62°). After 3 was eluted completely, the eluant was changed to $CHCl_3$. The yellow crystals obtained from the effluent were identified as **2a** (3.2 mg).

b) **1a** (9.4 mg) was subjected to electrolysis in acetonitrile (20 ml) containing 0.1 M $NaClO_4$ and water (1%) at 0.73 V. After addition of a small amount of solid Na_2CO_3 to the solution from electrolysis, 100 µl of the solution was developed on a thin-layer of alumina with benzene. The determinations of **2a** and **5** were carried out by scraping off the corresponding spots followed by extracting the alumina with CH_3CN and measuring the absorbances at 263 and 436 nm, respectively.

c) **1b** (215 mg) was subjected to electrolysis in acetonitrile (100 ml) at 0.90 V. The resulting scarlet solution was treated according to the previously outlined procedure (a). The yellow crystals obtained (43.7 mg, mp 165.5—166°) were identified as **2b** by mp (lit.,[16] 162.5—163°), elemental analysis, and NMR spectrum.[17]

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11) C.K. Mann and K.K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, Inc., New York, 1970, p. 509.

12) S. Ikenoya, M. Masui, H. Ohmori, and H. Sayo, *J. Chem. Soc. Perkin II*, **1974**, 571.

13) J. Goerdeler and B. Redies, *Chem. Ber.*, **92**, 1 (1959).

14) H. Sayo and A. Morimoto, *Chem. Pharm. Bull.* (Tokyo), **23**, 3114 (1975).

15) M. Masui, H. Sayo, and Y. Tsuda, *J. Chem. Soc.* (*B*), **1968**, 973.

16) E. Bamberger and W. Ham, *Ann.*, **382**, 82 (1911).

d) **1c** (234 mg) was subjected to electrolysis in acetonitrile (100 ml) at 1.0 V. The resulting deep purple solution was cooled in a refrigerator overnight. Pale yellow crystals (16.8 mg) separated out, which were filtered off and recrystallized from benzene (mp 266.5°, lit.,[16] 265.5°) and identified as **2c** by elemental analysis, VIS[18] and NMR spectra. The filtrate was evaporated to dryness, and the residue was extracted with CCl_4. The CCl_4 solution was subjected to column chromatography on alumina (10 g) with hexane–CCl_4 as eluant. The white crystals obtained from the first fraction were identified as **3** (57.5 mg). From the second fraction white crystals were obtained and identified as *p*-chloroaniline (81 mg).

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17) E.F.G. Herington and I.J. Lawrenson, *Spectrochim. Acta*, **21**, 1010 (1965).
18) A. Sugimoto, S. Furuyama, H. Inoue, and E. Imoto, *Nippon Kagaku Kaishi*, **1974**, 1289.