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Studies on Sulfenamides. III.[1] Cyclic Voltammetry and Controlled Potential Electrolysis of 4'-Substituted 2-Nitrobenzenesulfenanilides

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Anodic oxidation of 4'-substituted 2-nitrobenzenesulfenanilides (4'-OMe (**3a**), 4'-Me (**3b**), 4'-Cl (**3c**), 4'-H (**3d**)) was investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon anode, and the results were compared with those for 4'-substituted benzenesulfenanilides (**1a**—**d**). Electrolysis of **3a** in acetonitrile containing $NaClO_4$ gave 2,7-dimethoxyphenazine (**2a**), 2,2'-dinitrodiphenyl disulfide (**4**), *p*-anisidine (**5**), 2-nitrobenzenesulfonic acid (**6**), and N-(2-nitrophenylthio)-*p*-benzoquinoneimine (**7**). Electrolysis of **3a** in acetonitrile containing ethyltributylammonium trifluoromethanesulfonate (ETBT) gave **2a**, **4**, **5**, and **7**, but did not give **6**. These results indicate that the perchlorate anion does act as an oxidizing agent in the anodic oxidation of **3a**, even though sodium perchlorate has been used quite extensively as a supporting electrolyte in anodic systems and usually does not participate in anodic oxidation processes. Since benzenesulfonic acid was not obtained on the anodic oxidation of **1a** in acetonitrile containing $NaClO_4$, the formation of **6** was interpreted on the basis of one-step two-electron transfer followed by reaction of the dication with perchlorate anion. The introduction of the 2-nitro group may elicit the one-step two-electron transfer. Electrolysis of **3a** in the presence of water (1%) gave **7** almost quantitatively. Electrolysis of **3b** and **3c** in acetonitrile containing $NaClO_4$ gave the corresponding 2,7-disubstituted phenazines, **4**, and **6**, whereas that of **3d** did not give phenazine.

Keywords——anodic oxidation; cyclic voltammetry; 2-nitrobenzenesulfenanilides; 2,7-disubstituted phenazines; oxidation of sulfenamides; nitrenium ion; N-(2-nitrophenylthio)-*p*-benzoquinoneimine; 2-nitrobenzenesulfonic acid

In the previous paper[3] we investigated cyclic voltammetry and controlled potential electrolysis of benzenesulfenanilides (4'-OMe (**1a**), 4'-Me (**1b**), 4'-Cl (**1c**), 4'-H (**1d**)) at a glassy-carbon anode in acetonitrile. Electrolysis of **1a**, **1b**, and **1c** gave 2,7-dimethoxyphenazine (**2a**), 2,7-dimethylphenazine (**2b**), and 2,7-dichlorophenazine (**2c**), respectively, whereas that of **1d** did not give phenazine (**2d**). The nitrenes were suggested to be intermediates in the formation of the phenazines.

We also studied the oxidation of **1a**—**d** and 2-nitrobenzenesulfenanilides (4'-OMe (**3a**), 4'-Me (**3b**), 4'-Cl (**3c**), 4'-H (**3d**)) with lead dioxide both in benzene and in acetonitrile.[1] The oxidation of **1a** and **1b** in benzene gave **2a** and **2b**, respectively, whereas that of **1c**, **1d**, and **3a**—**d** did not give corresponding products. The oxidation of **3a**—**d** in acetonitrile containing 1% trifluoroacetic acid and 1% trifluoroacetic anhydride gave the corresponding 2,7-disubstituted phenazines and N-(2-nitrophenylthio)acetamide. The formation of the latter was interpreted in terms of acetamidation of the 2-nitrobenzenesulfenylium ion.

In order to elucidate the mechanism of formation of the phenazines in more detail, we have now studied the anodic oxidation of **3a**—**d** in acetonitrile.

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1) Part II: H. Sayo, K. Mori, and T. Michida, *Chem. Pharm. Bull.* (Tokyo), **27**, 351 (1979).
2) Location: *Ikawadani-cho, Tarumi-ku, Kobe 673, Japan.*
3) H. Sayo, K. Mori, A. Ueda, and T. Michida, *Chem. Pharm. Bull.* (Tokyo), **26**, 1682 (1978).

Results

Cyclic Voltammetry

Cyclic voltammograms were obtained from 2 mM solutions of **3a**—**d** in acetonitrile containing 0.1 M $NaClO_4$. Voltammetric data are summarized in Table I. The peak potentials (E_p) of **3a**—**d** are 0.10—0.22 V more positive than those of **1a**—**d**, respectively. The values of $i_p v^{-1/2}$ of **3a**—**d**, where i_p is the peak current and v is the scan rate, are 1.4—2.0 times those of **1a**—**d**, respectively. The variation of i_p as a function of c, where c is the concentration of **3**, was examined in the concentration range from 1 to 30 mM. The effects of added water and the supporting electrolyte were also examined. When $NaClO_4$ was used as the supporting electrolyte, the value of i_p/c of the anodic peak of **3a** decreased with increase in c, as shown in Fig. 1. Addition of water (1%) to the solution of **3a** increased the value of i_p/c at $c=5$, 10, and 30 mM. When ethyltributylammonium trifluoromethanesulfonate (ETBT) was used as the supporting electrolyte, the decrease in the value of i_p/c with increase in c was less marked and was not affected by the addition of water.

Table I. Results of Cyclic Voltammetry of 4′-Substituted 2-Nitrobenzenesulfenanilides (2 mM) inAcetonitrile 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}
3a	OMe	0.85	0.95	7.65	6.12
3b	Me	1.05	1.15	5.98	6.11
3c	Cl	1.16	1.24	6.60	6.55
3d	H	1.02	1.15	8.20	7.31

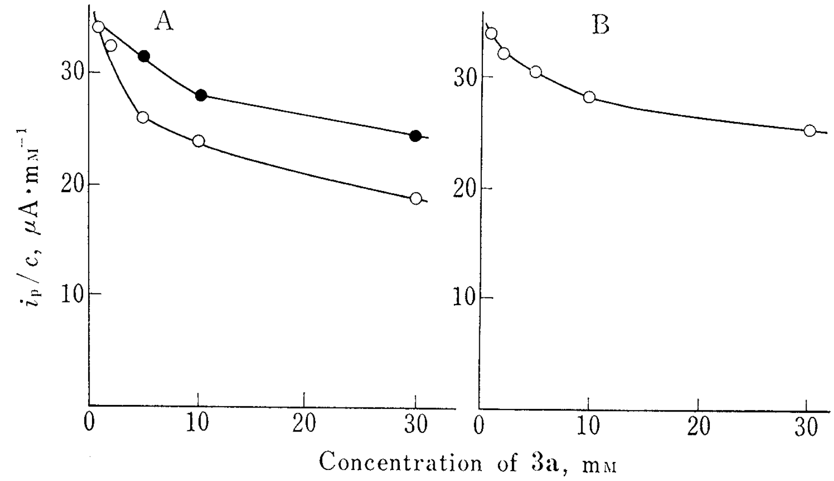

Fig. 1. Dependence of the Peak Current of the Anodic Wave of 2-Nitrobenzenesulfen-*p*-anisidide on Its Concentration; $v=50$ mV·sec^{-1}

○: in the absence of water, ●: in the presence of water (1%).
A: supporting electrolyte $NaClO_4$, B: supporting electrolyte $Et(Bu)_3NCF_3SO_3$.

The i_p/c values of **3b**—**d** showed similar behavior, except for the effect of added water. Addition of water (1%) to solutions of **3b**—**d** did not increase the values of i_p/c in 0.1 M $NaClO_4$ and in 0.1 M ETBT.

Controlled Potential Electrolysis

Table II summarizes the results of controlled potential electrolysis of **3a**—**d** (10 mM). Electrolysis of **3a** in acetonitrile containing 0.1 M $NaClO_4$ at an anode potential of 0.85 V

Table II. Results of Controlled Potential Electrolysis of 4′-Substituted 2-Nitrobenzenesulfenanilides (10mm) in Acetonitrile

Compd. No.	Applied potential V *vs.* S.C.E.	n-Value	Supporting electrolyte	Yield, mol %				
				2,7-Disubstituted phenazines	2,2′-Dinitrodiphenyl disulfide	Amine	2-Nitrobenzenesulfonic acid	Quinoneimine **7**
3a	0.85	0.63	$NaClO_4$	29.4	3.0	27.0[a]	40.8	2.3
3a	0.85	1.35	ETBT[b]	29.2	44.2	15.2[a]	—	2.0
3b	1.03	0.69	$NaClO_4$	29.0	11.0	—	38.2	—
3b	1.03	1.95	ETBT	40.0	19.7	—	—	—
3c	1.18	1.04	$NaClO_4$	25.0	1.5	—	30.6	—
3c	1.18	1.97	ETBT	37.3	22.5	—	—	—
3d	1.13	1.03	$NaClO_4$	—	trace	—	35.1	—
3d	1.13	2.15	ETBT	—	3.0	—	—	—

a) *p*-Anisidine.
b) Ethyltributylammonium trifluoromethanesulfonate.

gave a coulometric n-value of 0.63. After addition of solid Na_2CO_3 to the resulting solution, the ultraviolet (UV) and visible (VIS) spectra of the solution had absorption maxima at 264, 350, 410, and 424 nm, which are very close to those reported for **2a**.[4] Compound **2a**, 2,2′-dinitrodiphenyl disulfide (**4**), *p*-anisidine (**5**), 2-nitrobenzenesulfonic acid (**6**), and N-(2-nitrophenylthio)-*p*-benzoquinoneimine (**7**) were obtained from the resulting solution and identified from their UV, VIS, and infrared (IR) spectra by comparison with those of authentic samples. The yields of the products (Table II) were determined by thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC).

Electrolysis of **3a** in acetonitrile containing 0.1 m ETBT gave **2a**, **4**, **5**, and **7**. Compound **6** was not detected. Electrolysis of **3a** in acetonitrile containing water (1%) and 0.1 m $NaClO_4$ at 0.85 V gave an n-value of 1.90. After addition of solid Na_2CO_3 to the resulting solution, the UV and VIS spectra of the solution had absorption maxima at 251 and 433 nm, which were in good agreement with those of **7**. Compound **7** was obtained from the solution.

Electrolysis of **3b** in acetonitrile containing 0.1 m $NaClO_4$ at 1.03 V gave **2b**, **4**, and **6**. *p*-Toluidine and **7** were not obtained. Electrolysis of a mixture of **3a** and **3b** (molar ratio 1: 2) in acetonitrile containing 0.1 m $NaClO_4$ at 1.03 V gave a crossover product, 2-methoxy-7-methylphenazine, in addition to **2a** and **2b**. Electrolysis of **3b** in acetonitrile containing 0.1 m ETBT at 1.03 V gave an n-value of 1.95, and **6** was not obtained.

Electrolysis of **3c** in acetonitrile containing 0.1 m $NaClO_4$ at 1.18 V gave **2c**, **4**, and **6**. *p*-Chloroaniline and **7** were not obtained. Electrolysis of **3d** in acetonitrile containing 0.1 m $NaClO_4$ at 1.13 V gave **6** and trace amounts of **4**. Aniline, phenazine, and **7** were not obtained.

Decomposition of 3a with Perchloric Acid and with Trifluoromethanesulfonic Acid

A solution of **3a** (10 mm, 5 ml) in acetonitrile containing 0.1 m $NaClO_4$ was treated with 0.3 ml of 1 m $HClO_4$ in acetic acid,[5] which was sufficient to decompose **3a** completely. The mixture was allowed to stand at room temperature for an hour, and was then analyzed by TLC and HPLC. Next, a solution of **3a** (10 mm, 5 ml) in acetonitrile containing 0.1 m ETBT was treated with 0.3 ml of 1 m CF_3SO_3H in acetic acid. The mixture was allowed to stand at room temperature for an hour, then analyzed as described above. The results are summarized in Table III. When water (1%) was previously added to the solution of **3a**, neither $HClO_4$ nor CF_3SO_3H decomposed **3a**.

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[4] P. Walker and W.A. Waters, *J. Chem. Soc.*, **1962**, 1632.

[5] J.F. Coetzee and I.M. Kolthoff, *J. Am. Chem. Soc.*, **79**, 6110 (1957).

Table III. Results of Acid Decomposition of 2-Nitrobenzenesulfen-*p*-anisidide (10 mM) in Acetonitrile

Acid[a)]	Salt added	Yield, mol %				
		2,7-Dimethoxy-phenazine	2,2′-Dinitro-diphenyl disulfide	*p*-Anisidine	2-Nitrobenzene-sulfonic acid	Quinone-imine **7**
$HClO_4$	0.1 M-$NaClO_4$	16.8	12.9	18.5	48.3	2.0
CF_3SO_3H	0.1 M-ETBT	19.6	100.3	26.9	—	—

a) 1 M in acetic acid. The final concentration of $HClO_4$ or CF_3SO_3H was 57 mM.

Discussion

Perchlorates have been used quite extensively as a supporting electrolyte in anodic systems because of their inertness to oxidation. The perchlorate anion usually does not participate in anodic oxidation processes. The present results, however, suggest that sodium perchlorate, the supporting electrolyte, can play an important role in the process of anodic oxidation. Electrolysis of **3a**—**d** in acetonitrile containing 0.1 M $NaClO_4$ gave a small amount of **4** and a fairly large amount of **6**. On the other hand, when ETBT was used as the suppoting electrolyte instead of $NaClO_4$, the coulometric *n*-value and the yield of **4** increased and **6** was not obtained. This suggests that the perchlorate ion is responsible for the forma-

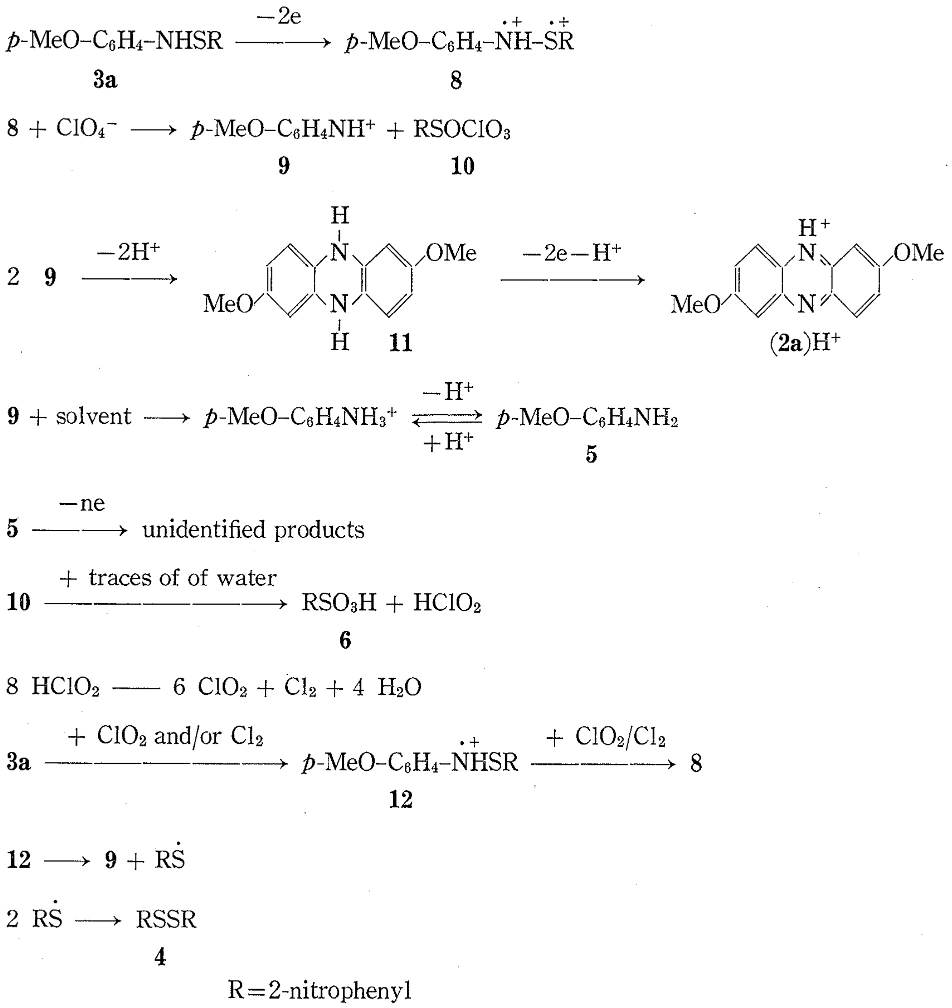

Chart 1

tion of **6**. Oxidation of **3a**—**d** with lead dioxide in acetonitrile, which requires no supporting electrolyte, gave N-(2-nitrophenylthio)acetamide instead of **6**.[1]

The following schemes are suggested for the anodic oxidation of **3a** in acetonitrile containing 0.1 M $NaClO_4$. Although the anodic oxidation of **1a** gave diphenyl disulfide almost quantitatively,[3] that of **3a** gave a small amount of **4**. This can be explained in terms of one-step two-electron transfer of **3a** at the anode. The introduction of the 2-nitro group may elicit the one-step two-electron transfer. That is, **3a** is oxidized to the dication (**8**), which reacts with the perchlorate anion to give the nitrenium ion (**9**) and **10**. **9** dimerizes to **11**, and **11** is oxidized further to **2a**. A part of **9** abstracts hydrogen atoms from the solvent to give *p*-anisidine (**5**), and some of **5** is oxidized further to yield unidentified products. **10** reacts with traces of water to form **6** and chlorous acid; the latter is unstable and decomposes to chlorine dioxide and chlorine, both of which are strong oxidants and oxidize **3a**. The finding that the i_p/c value of **3a** at 1 mM is not affected by the addition of water (1%) supports the occurrence of one-step two-electron transfer, because electrolysis of **3a** in acetonitrile containing 0.1 M $NaClO_4$ and water (1%) gave an n-value of 1.9 and yielded the two-electron oxidized product, **7**, almost quantitatively (95%).

The following schemes are suggested for the anodic oxidation of **3a** in acetonitrile containing 0.1 M $NaClO_4$ and water (1%). The dication **8** is immediately deprotonated by water molecules, and the cation formed is hydrolyzed to **7**. A similar oxidation process was suggested for the anodic oxidation of 4′-methoxybenzanilide.[6] In addition the added water prevents the protonation and subsequent decomposition of **3a**, because water is more basic than **3a**.

At higher concentrations of **3a** in the absence of added water, decomposition of **3a** with perchloric acid (which is formed through deprotonation of the products during the electrolysis) becomes appreciable and causes a decrease in the value of i_p/c and the n-value.

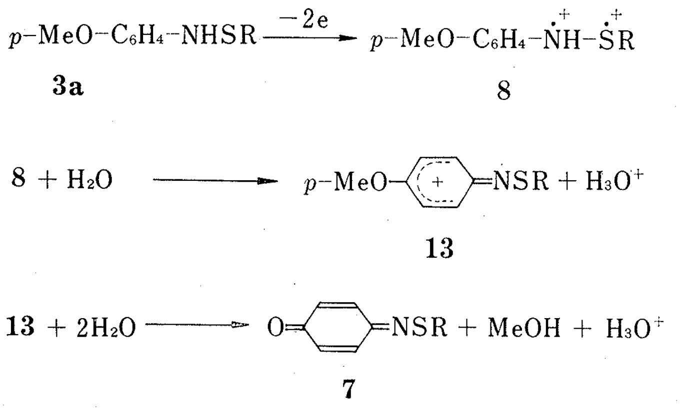

Chart 2

$$\mathbf{3a} + HClO_4 \longrightarrow (\mathbf{3a})H^+ + ClO_4^-$$

$$(\mathbf{3a})H^+ + ClO_4^- \longrightarrow \underset{\mathbf{5}}{p\text{-anisidine}} + \underset{\mathbf{10}}{RSOClO_3}$$

$$\mathbf{10} \xrightarrow{+\text{ traces of water}} \underset{\mathbf{6}}{RSO_3H} + HClO_2$$

Chart 3

The following schemes are suggested for the decomposition of **3a** by perchloric acid. The first step of the decomposition of **3a** requires its protonation, because in the presence of added water (1%) **3a** does not decompose on addition of perchloric acid. Since the concentration of perchloric acid produced during the electrolysis depends not only on the concentration of **3a** but also on the current density and the rates of electrolysis and stirring, which vary in each run, the proportion of **3a** decomposed during the electrolysis cannot be determined accurately. Furthermore, since chlorous acid is formed on both the anodic oxidation and the decomposition of **3a**, chlorine dioxide and chlorine formed from chlorous acid also oxidize **3a**. Thus the overall stoichiometry of the anodic oxidation of **3a** is very complicated.

When ETBT was used as the supporting electrolyte instead of $NaClO_4$, the n-value and the yield of **4** increased and **6** was not obtained. Decomposition of **3a** with trifluoromethane-

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

sulfonic acid did not give **6**, but did give **2a**. This indicates that an oxidant was formed on the decomposition of **3a** which is not sufficiently strong to form **6** and has a small oxidation number.

Electrolysis of **3b**, **3c**, and **3d** can be considered to be analogous with that of **3a**. However, it is not clear at present why electrolysis of **3d** did not give phenazine.

Experimental

Materials——2-Nitrobenzenesulfenanilides were prepared as described previously.[1] N-(2-Nitrophenylthio)-*p*-benzoquinoneimine was prepared by the method of Kramer and Gamson[7] and purified by preparative TLC on alumina with benzene–hexane (2: 1) as a developing solvent: orange-yellow crystals mp 182—184° (dec.), UV $\lambda_{\max}^{CH_3CN}$ nm (ε): 251 (17000), 433 (27700). Ethyltributylammonium trifluoromethanesulfonate (ETBT) was prepared by the method of Roussean *et al.*[8] 2-Nitrobenzenesulfonic acid was obtained commercially and purified by recrystallization from ethanol. Acetonitrile and sodium perchlorate were purified as described previously.[9] The purified acetonitrile contained 5—10 mM water as determined by the method of Hogan *et al.*[10]

Apparatus——Cyclic voltammetry and controlled potential electrolysis were carried out as described previously.[3] UV and IR spectra were obtained using Hitachi 323 and Shimadzu IR-400 spectrometers, respectively. A Familic 100 machine (Japan Spectroscopic Co.) was used for HPLC. The flow rate was 8 µl/min and peak heights were used for quantitative determination.

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

a) **3a** (276 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M $NaClO_4$ at 0.85 V at room temperature until the current fell below 1% of the initial value (*ca.* 1 hr). The quantity of electricity consumed (60.8 C) corresponded to $n=0.63$. Na_2CO_3 (10%, 50 ml) was added to the resulting red solution, and the mixture was extracted with benzene. The organic layer was separated and extracted with 10% HCl. When the HCl solution was made slightly alkaline with 10% NaOH, yellow crystals separated out. These were collected (34.7 mg) and subjected to column chromatography on neutral alumina with $CHCl_3$ as an eluent. The yellow crystals obtained from the first effluent were identified as **2a** (31.4 mg). The filtrate was extracted with $CHCl_3$, and the $CHCl_3$ solution was subjected to column chromatography on alumina with $CHCl_3$ as an eluent. The first fraction was evaporated to dryness and the residue was extracted with hexane. Concentration of the hexane extract gave white needles (13.3 mg), which were identified as **5**. The organic layer which had been extracted with HCl solution was subjected to column chromatography on alumina with CCl_4 as an eluent. The white crystals obtained from the first fraction were identified as **4** (4.6 mg).

b) **3a** (111 mg) and **3b** (208 mg) were subjected to electrolysis in acetonitrile (40 ml) containing 0.1 M $NaClO_4$ at 1.03 V. The resulting solution was treated according to the previously outlined procedure a). The yellow crystals obtained were subjected to multiple runs of preparative TLC on alumina with benzene-chloroform (1: 1) as a developing solvent. Yellow crystals (30 mg) were obtained from the middle band and recrystallized from hexane. This material was identified as 2-methoxy-7-methylphenazine.[1]

Determination of Products by TLC and HPLC——After addition of a small amount of solid Na_2CO_3 to the electrolysis solution, 20—100 µl of the solution was developed on a thin-layer of alumina by multiple runs with benzene–hexane (2: 1). The determination of **2a**, **2b**, and **7** were carried out by scraping off the appropriate spots, extracting the alumina with CH_3CN and measuring the absorbances at 261 (**2a**), 255 (**2b**), and 434 nm (**7**), respectively. One µl of the solution was injected into a Familic 100 HPLC unit fitted with an HP-01 column for the determination of **4**. The mobile phase was methanol–acetonitrile (2: 1) and the detector was operated at 240 nm.

p-Anisidine: The electrolysis solution was treated according to the previously outlined procedure a). The hexane extract was subjected to HPLC using an HP-01 column with CH_3OH–CH_2Cl_2–H_2O (50: 8: 1) as an eluent. The detector was operated at 254 nm.

o-Nitrobenzenesulfonic Acid: Twently ml of the electrolysis solution was evaporated to dryness under reduced pressure, and 10 ml of water and a half mole % of K_2CO_3 based on the added $NaClO_4$ were added and mixed thoroughly. The mixture was filtered and 1 µl of the filtrate was injected into an AV-02 column. The mobile phase was 0.05 M phosphate buffer (pH 3.5)–0.1 M $NaClO_4$ (1: 1) and the detector was operated at 254 nm.

2c: The electrolysis solution was allowed to stand overnight in a refrigerator, and the crystals obtained were filtered off, washed with water, dried, and weighed.

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7) D.N. Kramer and R.M. Gamson, *J. Org. Chem.*, 24, 1154 (1959).
8) K. Roussean, G.C. Farrington, and D. Dolphin, *J. Org. Chem.*, 37, 3968 (1972).
9) H. Sayo and A. Morimoto, *Chem. Pharm. Bull.* (Tokyo), 23, 3114 (1975).
10) J.M. Hogan, R.A. Engel, and H.F. Stevenson, *Anal. Chem.*, 42, 249 (1970).