Chem. Pharm. Bull. 30(10)3782—3785(1982)

Studies on Sulfenamides. VII.[1] Anodic Oxidation of 3′- and 2′-Substituted 2-Nitrobenzenesulfenanilides

Hiroteru Sayo,* Koichi Mori, and Takashi Michida

Faculty of Pharmaceutical Sciences, Kobe-Gakuin University, Ikawa-dani-cho, Tarumi-ku, Kobe 673, Japan

(Received March 16, 1982)

Controlled potential electrolysis of 2′-(*p*-chlorophenyl)amino-4′-chloro-2-nitrobenzenesulfenanilide (**4c**) gave 2,7-dichlorophenazine in good yield. This result suggested that in the electrolysis of 4′-substituted 2-nitrobenzenesulfenanilides the ring closure to form the 2,7-disubstituted phenazines takes place through the binding of the nitrenium ion (B) to the 2′-position of the sulfenanilides. As for the 3′- and 2′-substituted 2-nitrobenzenesulfenanilides, most of the nitrenium ions bind to the 4′-position and are oxidized further to the *p*-quinonediimine derivatives, and most of these are oxidized further to unidentified resinous compounds.

Keywords——anodic oxidation; 2-nitrobenzenesulfenanilides; 2,7-disubstituted phenazines; oxidation of sulfenamides; nitrenium ions; benzoquinonediimines

In the previous paper,[1] we reported the anodic oxidation of 4′-substituted 2-nitrobenzenesulfenanilides (**1**) in acetonitrile containing 1% trifluoroacetic acid (TFA) and 1% trifluoroacetic anhydride (TFAH). The nitrenium ions are suggested to be intermediates in the formation of the 2,7-disubstituted phenazines. Although the chemical reactivities of nitrenes have been studied extensively by many workers,[2] those of nitrenium ions have been studied to a lesser extent.[3] In order to elucidate the reactivities of aryl nitrenium ions and the mechanism of formation of the phenazines more clearly, the anodic oxidation of 3′- and 2′-substituted 2-nitrobenzenesulfenanilides (3′-OMe (**2a**), 3′-Me (**2b**), 3′-Cl (**2c**), 3′-NO_2 (**2d**), 2′-Me (**3b**)) and 2′-(*p*-chlorophenyl)amino-4′-chloro-2-nitrobenzenesulfenanilide (**4c**) was investigated.

Results

Table I summarizes the results of controlled potential electrolysis of **2a—d**, **3b**, and **4c** in acetonitrile containing 0.1 M ethyltributylammonium trifluoromethanesulfonate (ETBT), 1% TFA, and 1% TFAH. TFAH was added to the solution in order to reduce the water content in the solution. Although electrolysis of **2b** gave trace amounts of 2,7-dimethylphenazine,

Table I. Results of Controlled Potential Electrolysis of 2′- or 3′-Substituted 2-Nitrobenzenesulfenanilides (10 mM) in Acetonitrile containing 0.1 M ETBT, 1% CF_3COOH, and 1% $(CF_3CO)_2O$

Compound No.	Applied potential V (*vs.* SCE)	*n*-Value	2,2′-Dinitrodiphenyldisulfide (**7**) Yield, %	Quinonediimine Yield, %	2,7-Disubstituted phenazine Yield, %
2a	1.22	0.54	10.0	—	—
2b	1.22	1.34	27.5	—	Trace
2c	1.36	1.27	36.5	1.2	—
2d	1.41	1.16	54.0	—	—
3b	1.16	1.20	17.5	2.1[a]	—
4c	1.33	2.32	75.0	—	55.0

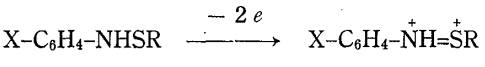
a) A mixture of *o*- and *p*-quinonediimine.

that of **2a**, **2c**, **2d**, and **3b** did not give the corresponding disubstituted phenazines. Small amounts of *N*-(*m*-chlorophenyl)-*N'*-(*o*-nitrophenylthio)-2-chloro-*p*-benzoquinonediimine (**5c**) and a mixture (**6b**) of *N*-(*o*-methylphenyl)-*N'*-(*o*-nitrophenylthio)-3-methyl-*o*-benzoquinonediimine and *N*-(*o*-methylphenyl)-*N'*-(*o*-nitrophenylthio)-3-methyl-*p*-benzoquinonediimine were obtained from the electrolyzed solutions of **2c** and **3b**, respectively. 2,2'-Dinitrodiphenyldisulfide (**7**) was obtained from every electrolyzed solution. Electrolysis of **4c**, which is considered to be an intermediate for the formation of the phenazines, also gave 2,7-dichlorophenazine in good yield.

Discussion

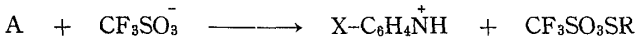
The experimental finding that electrolysis of **4c** gave 2,7-dichlorophenazine in good yield suggests that in the anodic oxidation of 4'-substituted 2-nitrobenzenesulfenanilides the ring closure to form the 2,7-disubstituted phenazines takes place through the formation of the *N*,*N'*-disubstituted *o*-phenylenediamine derivatives as an intermediate. The following schemes are suggested.

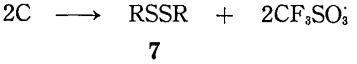
The electrolysis of the sulfenanilides in the presence of TFA gives the dication A. A reacts with the electrolyte anion[3] and gives the nitrenium ion B. B binds to the 2'-position of



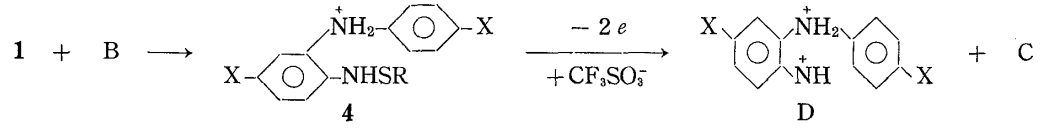
1: 4'-substituted
2: 3'-substituted
3: 2'-substituted

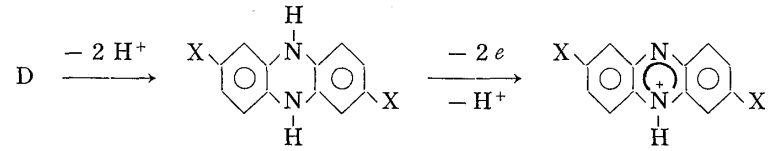
A



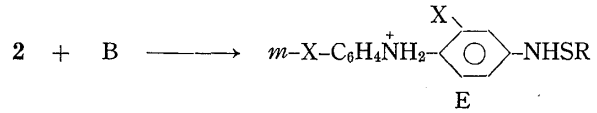


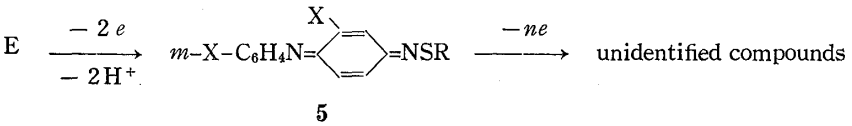
a) 4'-substituted sulfenanilides





b) 3'-substituted sulfenanilides





R=2-nitrophenyl

Chart 1

the 4′-substituted sulfenanilide to form the protonated *N*,*N*′-disubstituted *o*-phenylenediamine derivative **4**, which is oxidized further to *o*- and *p*-disubstituted nitrenium ion D and then to the 2,7-disubstituted phenazine. Desideri *et al.*[4] reported a similar reaction, namely, the nitrenium ion formed from anodic oxidation of *p*-toluidine under acidic conditions attacked *p*-toluidine to give 2-amino-4′,5-dimethyldiphenylamine.

As for the electrolysis of **2a—d**, since the 4′-position of the sulfenanilide is vacant and sterically less hindered than the 6′-position, most of the nitrenium ion B binds to the 4′-position and is oxidized further to the *p*-quinonediimine derivative (**5**) and unidentified compounds.

The reason why the electrolysis of **2a**, **2b**, and **2d** did not give **5** is considered to be that under the conditions of electrolysis most of **5** formed is oxidized further to unidentified resinous compounds. In the case of the electrolysis of **2b**, a small portion of B binds to the 6′-position and is oxidized further to the 2,7-disubstituted phenazine.

Electrolysis of **3b** can be interpreted in a similar manner. However, the 3-substituted phenylenediamine derivative, which is formed through the binding of B at the 6′-position, cannot form the 1,6-disubstituted phenazine because of steric hindrance. Therefore, a small amount of the *o*-quinonediimine was obtained together with the *p*-quinonediimine.

Experimental

Materials——**2b**,[5] **3b**,[5] and ETBT[6] were prepared as described previously. **2d** was prepared by a known method.[7] Other 2-nitrobenzenesulfenanilides were prepared from 2-nitrobenzenesulfenyl chloride and the corresponding anilides by a known method;[5] substituent, mp and solvent of recrystallization were as follows; 3′-OMe, 110—111°C, MeOH–EtOH; 3′-Cl, 121—120°C, EtOH; 2′-*p*-Cl-C_6H_4-NH-4′-Cl, *ca.* 150°C (dec.), EtOH. Each compound gave the analysis results consistent with the theoretical values. Acetonitrile was purified as described previously.[6] TFA and TFAH were obtained commercially.

Apparatus——Controlled potential electrolysis and high performance liquid chromatography (HPLC) were carried as described previously.[6] Infrared (IR), nuclear magnetic resonance (NMR), and mass spectra were obtained as described previously.[5]

Isolation of **5c**: **2c** (280 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT, 1% TFA, and 1% TFAH at 1.36 V at room temperature. Solid Na_2CO_3 (1 g) was added to the resulting solution, and the mixture was filtered. The filtrate was concentrated under reduced pressure to one-third of its orginal volume. Alumina (30 g) was added to the concentrated filtrate, which was then evaporated to dryness. The residue was extracted with benzene (100 ml). The benzene solution was passed through a column of alumina (20 g). All of the eluate was concentrated under reduced pressure, and developed on a thin-layer of alumina with benzene. The appropriate orange band was scraped off and extracted with methanol. When the methanol solution was allowed to stand overnight, red-brown powder (4.8 mg, 150°C dec.) were precipitated and filtered off; it was identified as **4c** from the IR, NMR, and mass spectra. IR ν_{max}^{KBr} cm^{-1}: 1510 (NO_2) 1340 (NO_2). NMR ($CDCl_3$) δ: 6.5—7.8 (9H, m, aromatic proton), 8.2—8.4 (1H, m, aromatic proton), 8.5—8.8 (1H, m, aromatic proton). Mass spectrum *m/e*: 125 ($\overset{+}{N}-C_6H_4-Cl$), 138 ($\overset{+}{N}=C_6H_3(-Cl)=N$), 154 ($O_2N-C_6H_4-\overset{+}{S}$), 251 ($M^+-O_2N-C_6H_4-\overset{+}{S}$), 405 ($M^+$).

Isolation of **6b**: **6b** was isolated by the same procedure as described for **5c**, except that the methanol extract of the scraped-off band was evaporated to dryness and the residue was recrystallized from a mixture of methanol and acetone to give red-brown powder (5.7 mg), which was identified as **6b** on the basis of the elemental analysis data, and IR, NMR, and mass spectra. *Anal.* Calcd for $C_{20}H_{17}N_3O_2S$: C, 66.10; H, 4.71; N, 11.56. Found: C, 65.35; H, 4.68; N, 11.13. IR ν_{max}^{KBr} cm^{-1}: 1510 (NO_2), 1340 (NO_2). NMR (benzene *d*-6) δ: 1.1 (d, CH_3), 2.1 (d, CH_3), 2.2 (3H, s, CH_3), 6.2—7.2 (9H, m, aromatic proton), 7.8—8.0 (1H, m, aromatic proton), 8.2—8.4 (1H, m, aromatic proton). Mass spectrum *m/e*: 154 ($O_2N-C_6H_4-\overset{+}{S}$), 209 ($M^+-O_2N-C_6H_4-\overset{+}{S}$), 363 ($M^+$).

Determination of Products——**7** and 2,7-dichlorophenazine were determined as described previously.[6]

References and Notes

1) Part VI: H. Sayo, K. Mori, and T. Michida, *Chem. Pharm. Bull.*, **29**, 2598 (1981).
2) *a*) W. Lwowski, "Nitrenes," Wiley, New York, 1970; *b*) R.A. Abramovitch, B.A. Davis, *Chem. Revs.*, **64**, 149 (1964); *c*) L. Horner, A. Christmann, *Angew. Chem. Int. Ed. Engl.*, **2**, 599 (1963); *d*) W. Lwowski, *Angew. Chem. Int. Ed. Engl.*, **6**, 897 (1967); *e*) B. Iddon, O. Meth-Cohn, E.F.V. Scriven, H.

Suschitzky, and P.T. Gallagher, *Angew. Chem. Int. Ed. Engl.*, **18**, 900 (1979).
3) H.J. Shine, "Aromatic Rearrangements," Elsevier, New York, 1967, pp. 182—190.
4) P.G. Desideri, L. Lepri, and D. Heimler, *J. Electroanal. Chem.*, **52**, 105 (1974).
5) H. Sayo, K. Mori, and T. Michida, *Chem. Pharm. Bull.*, **27**, 2316 (1979).
6) H. Sayo, K. Mori, and T. Michida, *Chem. Pharm. Bull.*, **27**, 2093 (1979).
7) N. Capron, R. Sasin, and G.S. Sasin, *J. Org. Chem.*, **21**, 362 (1956).