Electrochemical and ESR Spectroscopic Study of 2,7-Disubstituted Phenazines

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Received January 31, 1996; accepted April 13, 1996

Cyclic voltammetry (CV) for 2,7-disubstituted phenazines (1 mM, MeO (1), EtO (2), H (3), Cl (4), Br (5), COOEt (6)) was carried out in acetonitrile containing trifluoroacetic acid (TFA, 1% and 2%) and $NaClO_4$ (0.1 M) as a supporting electrolyte under N_2 gas. Phenazines showed two cathodic peaks (E_{pc1} and E_{pc2}) and these peaks had counterparts (E_{pa1} and E_{pa2}, respectively). Plots of the peak potentials against σ_p were linear. The first cathodic wave corresponds to the reduction of singly protonated phenazines followed by proton transfer. The second cathodic wave corresponds to the reduction of the cation radical of dihydrophenazines to produce dihydrophenazine as a final product.

ESR spectrometry of 1—6 in acetonitrile and in acetonitrile containing 1% TFA was conducted and computer simulation of the spectra was carried out. Splitting due to halogen or *o*-alkyl substituents was observed. Molecular orbital (MO) calculation of anion radicals generated from 1—6 and cation radicals generated from doubly protonated 1—6 did not give good agreement with the results of ESR spectrometry.

Key words phenazine; ESR; MO calculation; cyclic voltammetry; cation radical; anion radical

Oxidation-reduction behaviors of phenazine have been studied extensively by means of electrochemical methods.[1-15] Phenazine has a 1,4-diazine ring structure, which is similar to that of isoalloxazine exist in FAD as a redox site, and phenazine could be a useful model compound of FAD.[16]

However, the effect of substituents in the phenazine ring is not yet clear. Consequently, we planned an electrochemical study of 2,7-disubstituted phenazines (MeO (**1**), EtO (**2**), H (**3**), Cl (**4**), Br (**5**), COOEt (**6**)). Monosubstituted phenazines do not have a symmetric structure, so the two nitrogens in the phenazine ring structure have different characters. Although **1**—**6** also have two nitrogens in the ring, the nitrogens are equivalent. Evaluation of the effects of the substituents in 2,7-disubstituted phenazines is therefore easier than in monosubstituted phenazines.

Cyclic voltammetry (CV) for **1**—**6** was carried out in acetonitrile containing trifluoroacetic acid under N_2 gas. Compounds **1**—**6** showed two cathodic peaks (E_{pc1} and E_{pc2}) and these peaks had counterparts (E_{pa1} and E_{pa2}, respectively). Plots of these peak potentials against σ_p were linear.

ESR spectrometry of **1**—**6** in acetonitrile and in acetonitrile containing 1% TFA, and a computer simulation of the spectra, were carried out. Splitting due to halogen or *o*-alkyl substituents was observed.

Results

CV CV for 2,7-disubstituted phenazines (1 mM) was carried out in acetonitrile containing trifluoroacetic acid (TFA, 1%) and $NaClO_4$ (0.1 M) as a supporting electrolyte under N_2 gas. Glassy carbon was used as a working electrode and the scan rate was 50 mV/s. A typical voltammogram is shown in Fig. 1.

Phenazine showed two cathodic peaks (E_{pc1} and E_{pc2}) at 0.21 V and −0.08 V and these peaks had counterparts

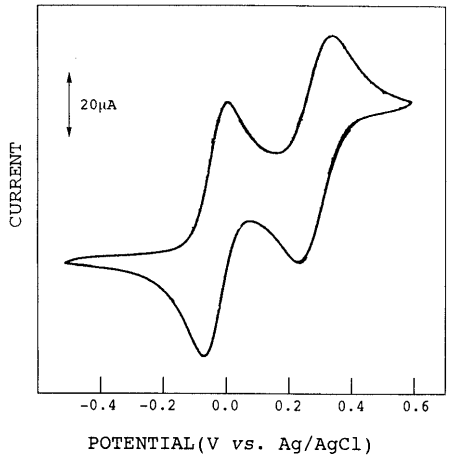

Fig. 1. Cyclic Voltammogram of 1 mM Phenazine (**3**) in Acetonitrile Containing 1% TFA and 0.1 M $NaClO_4$

Glassy carbon cathode (diameter = 3.0 mm); voltage sweep rate, 50 mV/s; at 25 °C.

Table 1. Results of CV of 2,7-Disubstituted Phenazines (1 mM) in Acetonitrile Containing 1% TFA (50 mV/s)

Compound No.	Substituent	E_{pc1}, V (*vs.* Ag/AgCl)	$i_p v^{-1/2}$, $\mu A\ (mV/s)^{-1/2}$	E_{pc2}, V	E_{pa1}, V	E_{pa2}, V
1	OMe	0.09	2.83	−0.23	0.17	−0.16
2	OEt	0.09	2.55	−0.24	0.16	−0.18
3	H	0.21	3.25	−0.08	0.29	−0.01
4	Cl	0.22	10.18	0.12	0.29	0.17
5	Br	0.24	11.03	0.13	0.32	0.19
6	COOEt	—	—	0.24	0.45	—

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(E_{pa1} and E_{pa2}, respectively). The results of CV of **1**—**6** are summarized in Table 1. The values of $i_p v^{-1/2}$, where i_p is the peak current of the first cathodic peak and v is the scan rate, are also shown.

The voltammogram of **6** in acetonitrile containing 1% TFA showed a single cathodic peak and a corresponding anodic peak. It was assumed that **1**—**5** were doubly protonated since they showed two cathodic peaks. However, **6** has the most electron-attractive groups among **1**—**6**, and the basicity of **6** was lowest, so it seems reasonable that **6** would only be singly protonated in acetonitrile containing 1% TFA. Increasing the concentration of TFA was expected to give doubly protonated **6**. Thus, the concentration of TFA was increased to 2%, and two cathodic peaks at 0.36 and 0.23 V appeared, as expected.

Table 2. Results of CV of 2,7-Disubstituted Phenazines (1 mM) in Acetonitrile Containing 2% TFA (50 mV/s)

Compd. No.	E_{pc1}, V (*vs.* Ag/AgCl)	$i_p v^{-1/2}$ μA (mV/s)$^{-1/2}$	E_{pc2}, V	E_{pa1}, V	E_{pa2}, V
1	0.11	2.97	−0.23	0.18	−0.17
2	0.11	2.55	−0.24	0.18	−0.18
3	0.25	3.25	−0.08	0.33	−0.01
4	0.27	13.01	0.10	0.34	0.16
5	0.29	14.14	0.12	0.37	0.17
6	0.36	3.39	0.23	0.45	0.31

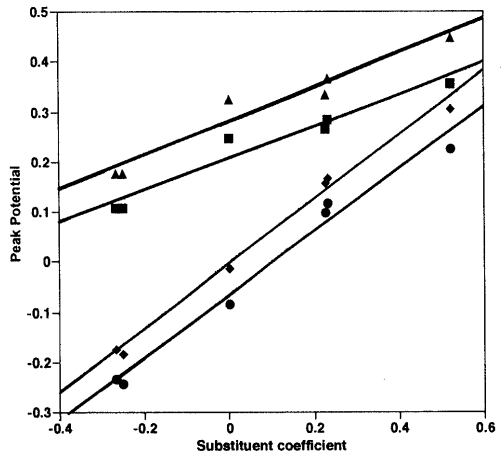

Fig. 2. Relationships between Peak Potentials in Cyclic Voltammogram of **1**—**6** with Substituent Coefficients (σ_p)

■, first cathodic peaks (E_{pc1}); ●, second cathodic peaks (E_{pc2}); ▲, anodic peaks corresponding to E_{pc1}; ◆, anodic peaks corresponding to E_{pc2}.

Voltammetric data in acetonitrile containing 2% TFA are shown in Table 2.

Plots of the peak potentials of E_{pc1}, E_{pc2}, E_{pa1} and E_{pa2} against σ_p were linear, as shown in Fig. 2.

When TFA was absent in the solution, CV of **1**—**6** did not give well-defined voltammograms because of the poor solubility, of these compounds.

Electron Spin Resonance (ESR) An acetonitrile solution containing **1**—**6** and a supporting electrolyte, was placed in a Pyrex capillary with a Pyrex reservoir. The capillary was located in the center of the ESR cavity. After deoxygenation by flushing with dry N_2 gas, the solutions were subjected to constant-current electrolysis (1 mA) with two platinum wire electrodes inserted into the capillary at room temperature, and the ESR spectrum was monitored.

ESR spectra of **1**—**6** in acetonitrile and their computer simulations are shown in Figs. 3—8.

The ESR spectrum obtained by electrolysis of **3** could be simulated by using the ESR parameters for the anion radical of **3**.[17] Anion radicals generated from **1** and **2** that had *o*-alkyl substituents at the 2 and 7 positions showed 25-line spectra. Anion radicals generated from **4** and **5** showed 19-line spectra, and the anion radical generated from **6** showed a 13-line spectrum. It was necessary for simulation of anion radicals generated from **4** and **5** to take into account splitting due to halogens. The ESR spectra of **1**, **2** and **4**—**6** were also well simulated as anion radicals with the parameters shown in Table 3.

ESR spectra of **1**—**6** in acetonitrile containing 1% TFA and their computer simulations are shown in Figs. 9—14.

Cation radicals generated from **1** and **2** that had *o*-alkyl substituents at the 2 and 7 positions showed 15-line spectra. The rest of the cation radicals showed 7-line spectra. The ESR spectrum obtained by electrolysis of **3** could be simulated by using slightly modified ESR parameters for the cation radical of dihydrophenazine. The ESR spectra generated from **1**, **2** and **4**—**6** were also well simulated as cation radicals with the parameters shown in Table 4.

Discussion

The absorption maximum of **3** in acetonitrile containing 1% of TFA was 381 nm (log ε=4.37), which is very close to the value of 384 nm (log ε=4.40) reported for singly

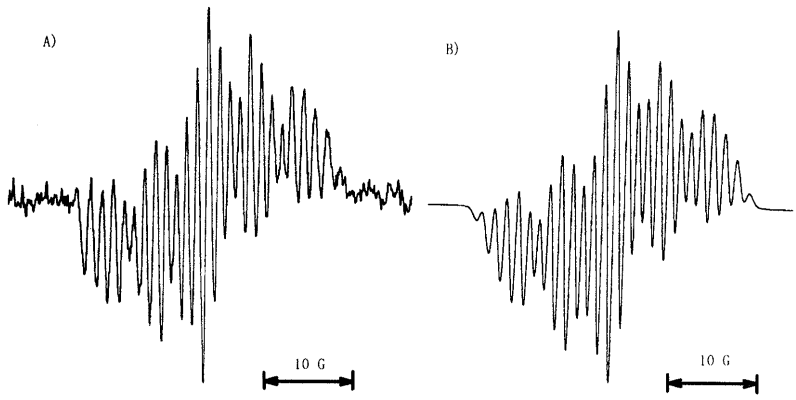

Fig. 3. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Dimethoxyphenazine (**1**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 0.8 G.

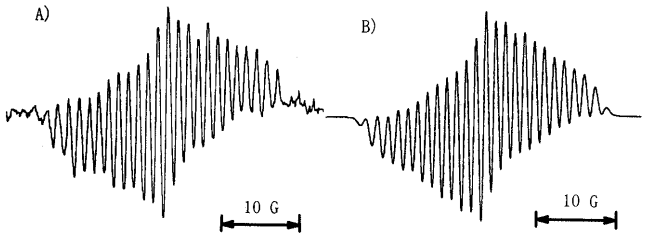

Fig. 4. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Diethoxyphenazine (**2**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 1 G.

protonated **3**.[18] Even in acetonitrile containing 2% TFA, **3** gave an absorption maximum at 381.2 nm ($\log \varepsilon = 4.38$). The ESR spectrum of the cation radical of 9,10-dihydrophenazine was obtained on *in situ* electrolysis of **3**. Therefore, the first cathodic wave at 0.21 V in Fig. 1 corresponds to the reduction of singly protonated **3**, followed by proton transfer. The second cathodic wave at 0.08 V in Fig. 1 corresponds to the reduction of the cation radical of dihydrophenazine to produce dihydrophenazine as a final product. Such an ECEC mechanism is usual for the reduction of **3** in acidic solution.[15,19,20]

Hammett's equation was applied to the polarographic

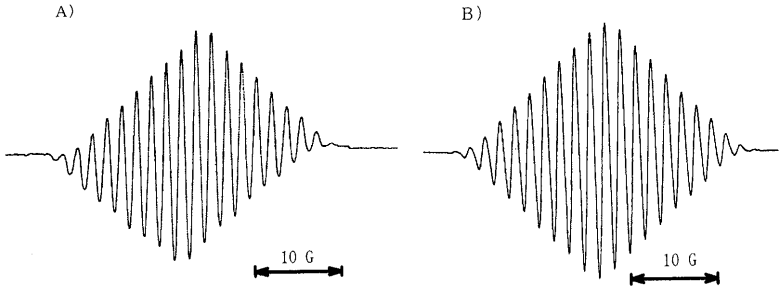

Fig. 5. ESR Spectrum of an *in Situ*-Electrolyzed Solution of Phenazine (**3**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 2 G.

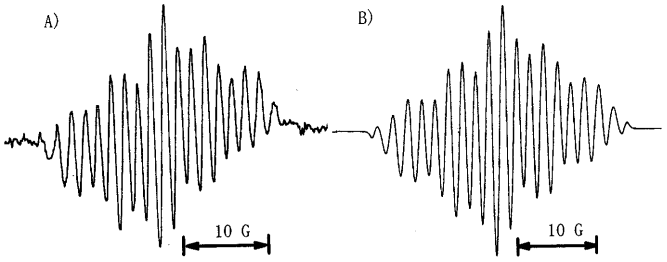

Fig. 6. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Dichlorophenazine (**4**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 2 G.

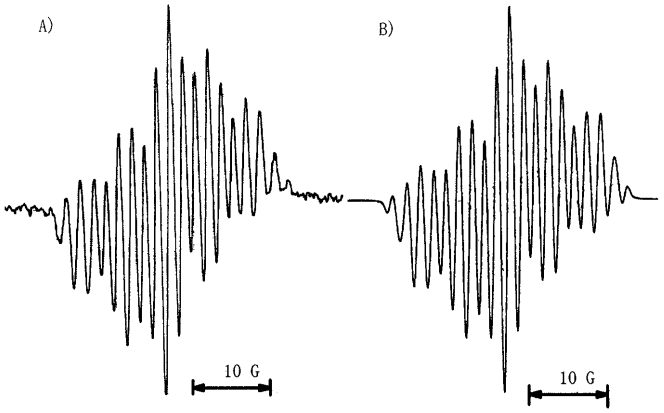

Fig. 7. ESR Spectrum of *in Situ*-Electrolyzed Solution of 2,7-Dibromophenazine (**5**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 2 G.

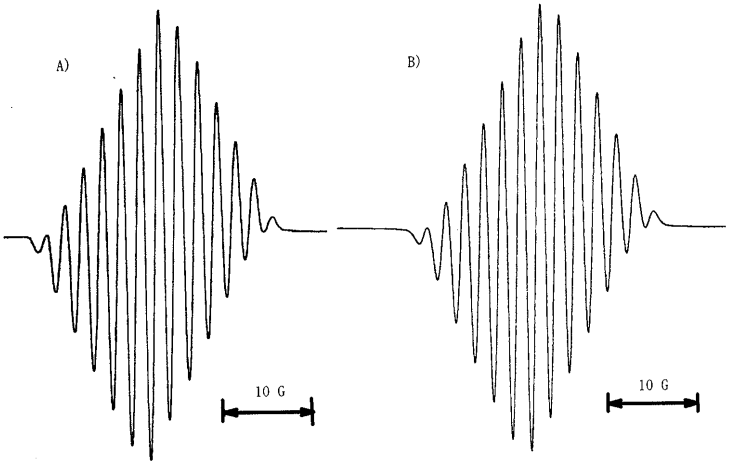

Fig. 8. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Diethoxycarbonylphenazine (**6**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 2 G.

Table 3. ESR Spectral Data of Anion Radicals Generated from 2,7-Disubstituted Phenazines in Acetonitrile

Parent Compound	Substituent (X)	Coupling constants (G)					g-Value
		A_N	$A_{1,6\text{-H}}$	$A_{2,7\text{-X}}$	$A_{3,8\text{-H}}$	$A_{4,9\text{-H}}$	
1	MeO	4.85	1.45	0.28	1.35	2.57	2.0039
2	EtO	4.99	1.50	0.24	1.40	2.52	2.0039
3	H[a)]	5.15	1.80	1.54	1.54	1.8	2.0039
4	Cl	5.12	1.93	0.125	1.57	2.21	2.0040
5	Br	4.81	1.87	0.12	1.42	2.10	2.0044
6	COOEt	4.32	2.18	—	0.10	2.00	2.0048

a) Eloranta J., Salo E., Mäklnen S., *Acta Chem. Scand.*, A **34**, 427 (1980).

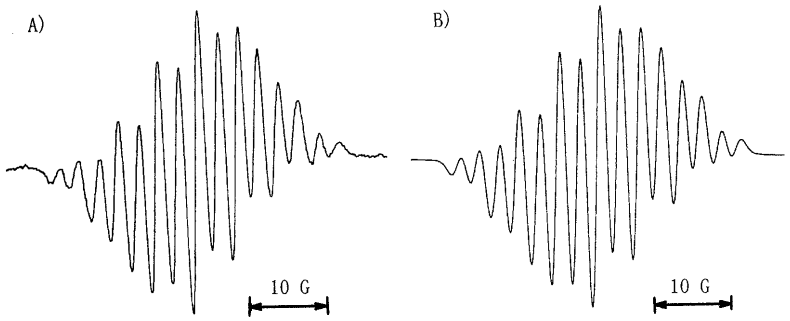

Fig. 9. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Dimethoxyphenazine (**1**, 10 mM) at 25 °C (A) and Its Computer Simulation (B)
Instrumental setting: power 5 mW; modulation amplitude 2 G.

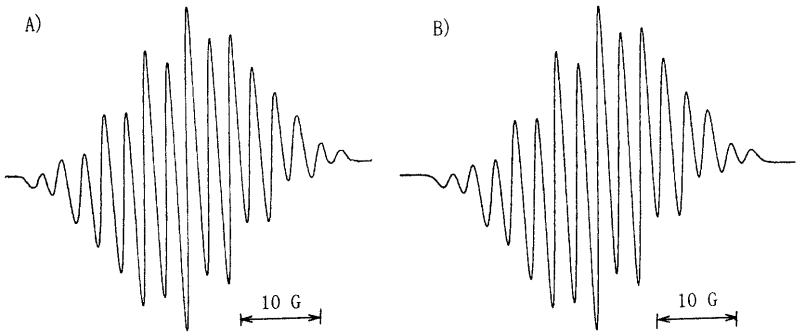

Fig. 10. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Diethoxyphenazine (**2**, 10 mM) Containing 1% TFA at 25 °C (A) and Its Computer Simulation (B)
Instrumental setting: power 5 mW; modulation amplitude 2 G.

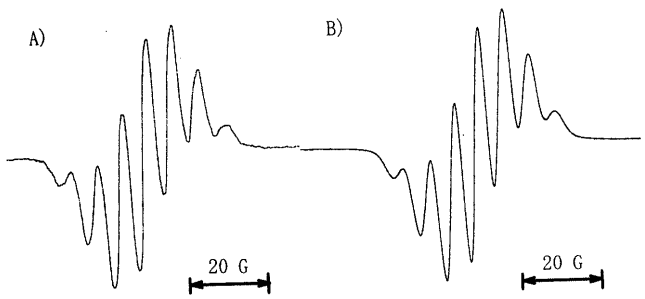

Fig. 11. ESR Spectrum of an *in Situ*-Electrolyzed Solution of Phenazine (**3**, 10 mM) Containing 1% TFA at 25 °C (A) and Its Computer Simulation (B)
Instrumental setting: power 5 mW; modulation amplitude 2 G.

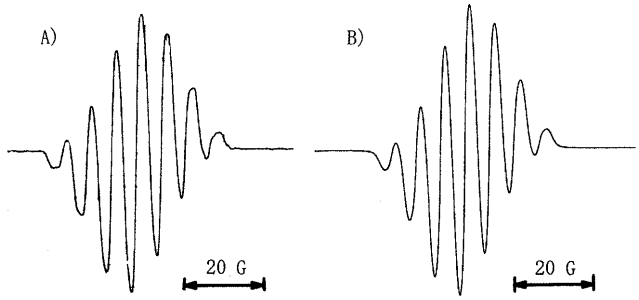

Fig. 12. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Dichlorophenazine (**4**, 10 mM) Containing 1% TFA at 25 °C (A) and Its Computer Simulation (B)
Instrumental setting: power 5 mW; modulation amplitude 2 G.

reduction of phenazines in acidic solutions by Nakamura and Yoshida and a good linear relationship was found between the first wave potential and the substituent constant.[3,4] For 2-substituted phenazines, the plot of half wave potentials against the sum of the *meta* σ-value and the *para* one for each substituent give a better linear relationship than that against only the *para* σ-value. Correlation coefficients of Hammett's σ-values with peak potentials of **1**—**6** were calculated and the results are summarized in Table 5. *para* σ-Value gave a better linear relationship with peak potentials than did the sum of the *para* σ-value and the *meta* one. This fact suggests that the

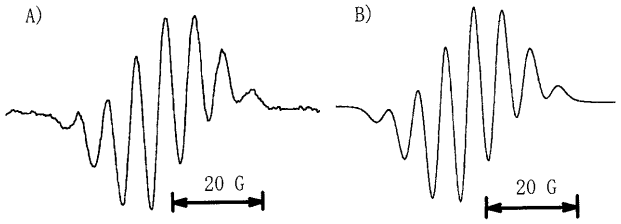

Fig. 13. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Dibromophenazine (**5**, 10 mM) Containing 1% TFA at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 2 G.

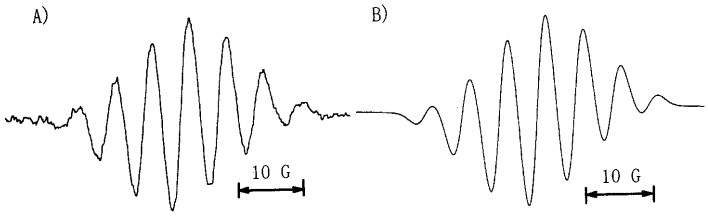

Fig. 14. ESR Spectrum of an *in Situ*-Electrolyzed Solution of 2,7-Diethoxycarbonylphenazine (**6**, 10 mM) Containing 1% TFA at 25 °C (A) and Its Computer Simulation (B)

Instrumental setting: power 5 mW; modulation amplitude 2 G.

Table 4. ESR Spectral Data of Cation Radicals Generated from 2,7-Disubstituted Phenazines in Acetonitrile Containing 1% TFA

Parent Compound	Substituent (X)	Coupling constants (G)						*g*-Value
		A_N	A_{NH}	$A_{1,6\text{-H}}$	$A_{2,7\text{-X}}$	$A_{3,8\text{-H}}$	$A_{4,9\text{-H}}$	
1	MeO	5.50	5.00	0.35	0.10	2.41	0.55	2.0036
2	EtO	5.63	5.55	0.35	0.175	2.49	0.55	2.0036
3	H	6.23	6.29	0.308	1.30	1.30	0.308	2.0036
4	Cl	6.15	6.56	0.100	0.16	1.75	0.28	2.0039
5	Br	6.14	6.10	0.53	0.22	1.38	0.71	2.0070
6	COOEt	5.91	5.72	0.45	—	0.59	0.45	2.0036

Table 5. Correlation Coefficients of Hammett's σ-Values with Peak Potentials

σ-Values	E_{pc1}	E_{pc2}	E_{pa1}	E_{pa2}
σ_p	0.974	0.990	0.971	0.996
$\sigma_p+\sigma_m$	0.905	0.983	0.896	0.978

redox potentials of nitrogens in **1**—**6** are controlled predominantly by the substituent in the *para* position.

As shown in Fig. 11, a well-defined 7-line spectrum was obtained in an acetonitrile solution of **3** containing 1% TFA. Coffield *et al.* also reported a well-defined 7-line spectrum of the cation radical of dihydrophenazine, and the number of bands and the coupling constants were in agreement with those reported in the literature.[18]

The hyperfine splitting constant (^aH) is proportional to the unpaired spin density (ρ) at the attached carbon atom.

$$^aH = Q\rho$$

Although some papers dealing with MO calculation of **3** have appeared, there is no report dealing with MO calculation of 2,7-disubstituted phenazines.[21-24] We conducted MO calculation of 2,7-disubstituted phenazines using the CNDO method. Constants Q and Q_N (proportionality constant for splitting constant and nitrogen spin density, respectively) were estimated from the results of MO calculation and the data in Table 3. The results are summarized in Tables 6 and 7. The average value of Q_N in anion radicals is 30.9 and a fair correlation coefficient, 0.928, was obtained between Q_N and spin density. The average of Q in anion radicals is 21.1 and this value is reasonable for anion radicals. However, the correlation coefficient is 0.86 and Q values at the 1 and 6 positions in anion radicals are smaller than those at other positions. These facts suggest that the spin density at the 1 and 6 positions in anion radicals is higher than one would expect from MO calculations.

The average of Q_N in cation radicals is 28.9, but the correlation coefficient (0.557) between Q_N and spin density is poor. The average of Q in cation radicals is 21.7 and the correlation coefficient is 0.931. However, Q in cation radicals varies widely.

Chalvet *et al.* recommended the introduction of a specific solute-solvent interaction (such as H-bond formation) into the calculation of the structures of singly or doubly protonated phenazines in acidic solutions.[25] On this basis, the structure used for the MO calculation with CNDO may be different from the real one in the solution due to the presence of TFA and the supporting electrolyte in the solution. This is presumably the reason why the correlation between Q_N and spin density is poor.

Experimental

Materials 2,7-Disubstituted phenazines were prepared from corresponding 4'-substituted 2-nitrobenzenesulfenanilide as described previously.[26] Acetonitrile was purified as described previously.[27]

Table 6. Electron Spin Density and Constant Q of Anion Radicals Generated from 2,7-Disubstituted Phenazines in Acetonitrile

Parent Compd.	Substituent (X)	Spin density						Constant Q			
		N	$C_{1,6}$	$C_{2,7}$	$C_{3,8}$	$C_{4,9}$	X	Q_N	$Q_{1,6}$	$Q_{3,8}$	$Q_{4,9}$
1	MeO	0.16268	0.08572	0.05051	0.06901	0.10328	0.00633	29.81	16.92	19.56	24.88
2	EtO	0.16250	0.08551	0.05021	0.06956	0.10341	0.00633	30.71	17.54	20.13	24.37
3	H	0.16779	0.09913	0.05626	0.05625	0.09913	—	30.69	18.16	27.38	18.16
4	Cl	0.16259	0.09677	0.05595	0.05849	0.10303	0.00330	31.49	19.94	26.84	21.45
5	Br	0.16166	0.09681	0.05654	0.05813	0.10330	0.00397	31.67	19.32	24.43	20.33
6	COOEt	0.12885	0.12122	0.06792	0.00944	0.06770	—	33.53	17.98	10.59	29.54

Table 7. Electron Spin Density and Constant Q of Cation Radicals Generated from 2,7-Disubstituted Phenazines in Acetonitrile

Parent Compd.	Substituent (X)	Spin density						Constant Q			
		N	$C_{1,6}$	$C_{2,7}$	$C_{3,8}$	$C_{4,9}$	X	Q_N	$Q_{1,6}$	$Q_{3,8}$	$Q_{4,9}$
1	MeO	0.20178	0.01857	0.04786	0.06855	0.02936	0.00633	27.26	16.92	19.56	24.88
2	EtO	0.20502	0.02043	0.04654	0.06661	0.03163	0.00633	27.46	17.54	20.13	24.37
3	H	0.21430	0.03003	0.05395	0.05394	0.03003	—	29.07	18.16	27.38	18.16
4	Cl	0.20919	0.02672	0.05128	0.05676	0.03300	0.00330	29.4	19.94	26.84	21.45
5	Br	0.20237	0.02286	0.05258	0.05943	0.03044	0.00397	30.34	19.32	24.43	20.33
6	COOEt	0.19935	0.03395	0.05717	0.03901	0.03185	—	29.65	17.98	10.59	29.54

Phenazine was purchased from Tokyo Kasei and used without further purification.

Apparatus The working electrode used for voltammetry was purchased (BAS, GCE, diameter 3.0 mm). The reference electrode system was described previously.[28] A Hokuto Denko HB-111 function generator, HA 151 potentiostat and Riken Denshi F-3F XY recorder were used for cyclic voltammetry. ESR spectra were obtained as described previously.[29] Computer simulation of the spectrum was carried out using an NEC PC-9801 FA computer equipped with a Roland DXY-880 X-Y plotter and a BASIC simulation program adapted from that written by Öhler and Janzen.[30] MO calculation was carried out using a Maha Posya Model 808MD (IBM-compatible machine) running HyperChem (Hypercube Inc., Canada).

Acknowledgment We wish to thank Mrs. M. Nishiyama for ESR measurements.

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