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Studies on Sulfenamides. IX.[1] Anodic Oxidation of *N*-(*o*-Nitrophenylthio)alicyclic Amines

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Cation radicals generated by anodic oxidation of *N*-(*o*-nitrophenylthio)alicyclic amines (morpholine (**1**), thiomorpholine(tetrahydro-4*H*-1,4-thiazine) (**2**), piperidine (**3**), pyrrolidine (**4**)) in acetonitrile were studied by cyclic voltammetry (CV) and electron spin resonance spectroscopy (ESR). 2-(*o*-Nitrophenylthio)indan-1-ol (**6**) was obtained from the solution after controlled potential electrolysis (CPE) of **1**—**3** in acetonitrile containing indene (**5**) and 0.1 M $NaClO_4$ at a glassy carbon anode. The cation radicals produced by CPE of **1**—**3** attacked **5** to give **6** as a final product.

Keywords——anodic oxidation; 2-nitrobenzenesulfenamide; cyclic voltammetry; electron spin resonance; cation radical; indanol 2-substituted; electrophilic substitution

In the previous paper[1] we reported the results of controlled potential electrolysis (CPE) of *N*-(*o*-nitrophenylthio)alicyclic amines (morpholine (**1**), tetrahydro-4*H*-1,4-thiazine (**2**), piperidine (**3**), pyrrolidine (**4**)), and the process of anodic oxidation of **1**—**4** in methanol was elucidated. In this paper, cyclic voltammetry and electron spin resonance (ESR) spectroscopy have been carried out in order to prove the presence of the cation radical in the process of anodic oxidation of **1**—**4** in acetonitrile. Indene (**5**) was added to the electrolytic solution of **1**—**4** to trap the reactive intermediate.

Results

Cyclic Voltammetry

Voltammetric data are summarized in Table I. Two anodic waves were observed in the cyclic voltammogram of **1**. A relatively large cathodic counterpart at 1.14 V with scan rates of 50 mV/s—200 mV/s was observed. The value of cathodic peak height (i_{pc}) measured by the

TABLE I. Results of Cyclic Voltammetry of *N*-(*o*-Nitrophenylthio)amines (2 mM) in Acetonitrile[a] Containing 0.1 M $NaClO_4$ at a Scan Rate of 50 mV/s

Compd. No.	V *vs.* SCE $E_{pa}1$	V *vs.* SCE $E_{pa}2$	$i_{pa}1v^{-1/2}$, μA $(mV/s)^{-1/2}$	V *vs.* SCE E_{pc} ($E_{pa}1$—E_{pc})	$i_{pc}/i_{pa}1$
1	1.21	1.67	6.00	1.14 (0.07)	0.60
2	1.20	1.31[b]	7.37	—[c]	—[c]
3	1.12	1.70[d]	5.83	1.05 (0.07)	0.58
4	1.07	1.65[d]	5.89	1.00 (0.07)	0.70

a) Anhydrous acetonitrile was used. *b*) A 3rd wave was also recognized at 1.45 V (*vs.* SCE). *c*) No reverse wave was recognized. *d*) Shoulder. SCE, saturated calomel electrode.

potential hold method[2] was over 60% of the anodic value ($i_{pa}1$).

Voltammograms obtained from the solution of **2** gave three anodic waves, with no cathodic counterpart. Addition of **5** (1%) to the electrolytic solution of **1**, **3**, and **4** reduced the height of the reverse peak.

Electron Spin Resonance Studies

In situ electrolysis of **1** at room temperature gave a fairly well-defined ESR spectrum. The spectrum was reasonably well simulated by the following parameters: $g=2.0061$, $A_1=14.2$ (1N), $A_2=21.6$ (1H), $A_3=15.2$ G (1H). The observation of splittings from two different hydrogen nuclei indicates that the cation radical derived from **1** is apparently conformationally frozen on the ESR time scale.

Although **2** did not give a cathodic counterpart in the voltammogram, *in situ* electrolysis of **2** gave an ESR spectrum similar to that derived from **1**. Therefore, ESR spectroscopy is considered to be more sensitive than cyclic voltammetry with a conventional scan rate in order to detect cation radicals.

Electrolysis of **3** gave an ill-defined ESR spectrum, which could not be simulated as being derived from a single radical species. Electrolysis of **4** gave a well-defined ESR spectrum ($g=2.0061$, $A_1=14.3$ (1N), $A_2=20.0$ (2H), $A_3=19.0$ G (2H). The observation of two pairs of non-equivalent *N*-methylene groups indicates that the axial–equatorial proton hyperfine splitting constants are interchanging too rapidly to be distinguished from one another.

A similar ESR spectrum was reported by Nelsen *et al.* for the oxidation of 1-(methylthio)pyrrolidine with tris(*p*-bromophenyl)aminium hexachloroantiminate in methylene chloride.[3]

Controlled Potential Electrolysis

An acetonitrile solution of **1**, containing **5** (1 ml) and $NaClO_4$ was subjected to CPE (1.2 V *vs.* SCE) at a glassy carbon anode in a divided cell. 2-(*o*-Nitrophenylthio)indan-1-ol (**6**) was obtained from the electrolyzed solution. The structure of **6** was confirmed by the identification of the oxidation product, *i.e.*, 2-(*o*-nitrophenylthio)indan-1-one (**7**), which was obtained from the reaction mixture of acetone solution of **6** and CrO_3 under acidic conditions.

The concentration of **5** added to the electrolytic solution was varied from 0.2% to 1%. The yield of **6** increased from 14.5% to 24.6% as the concentration of **5** was increased from 0.2% to 0.5%. But the yield of **6** leveled off at higher concentrations of **5**. The yield of **6** decreased from 24.6% to 2.3% as the concentration of water added to the electrolytic solution was increased from 0% to 1%. However, rigorous dehydration of acetonitrile did not improve the yield of **6** appreciably. CPE of **2** in the presence of **5** (0.5%) also gave **6** (37.0%). A small amount of **6** (4.9%) was detected when rigorously dehydrated acetonitrile was used as the solvent.

Discussion

The peak separations between the first anodic waves and the cathodic counterparts in the cyclic voltammograms of **1**, **3**, and **4**, 70 mV, in each case indicate that those anodic oxidations are a quasi-reversible one-electron oxidation.[4] It was confirmed by ESR that the first step of anodic oxidation of **1**—**4** in acetonitrile is one-electron oxidation to form fairly stable cation radicals.

Three intermediates which may react with **5** to form **6** may be considered; they are the cation radical (A), the sulfenylium ion (B), and the thiyl radical (C). A proposed reaction mechanism is shown in Chart 1.

Oswald *et al.*[5] reported that thiyl radicals reacted with **5**, and that 1-indanoles were obtained. It is also reported by them that 2-mercapto indanyl radicals reacted with oxygen. In

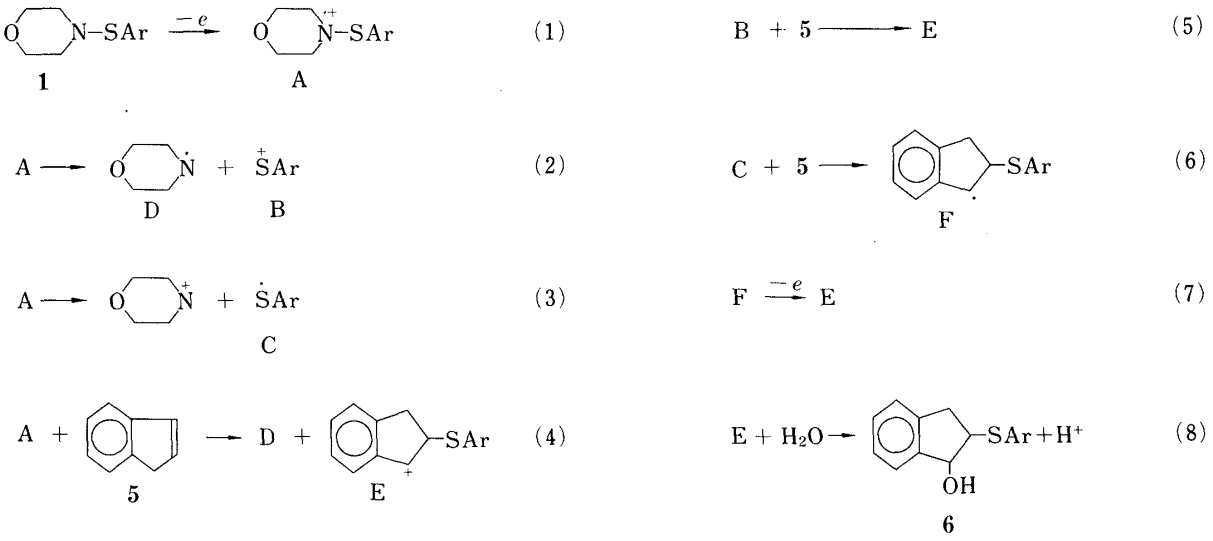

Chart 1

order to trap F, electrolysis of **1** was carried out under an oxygen stream. The yield of **6** was 21.4%, which is comparable to that (22.1%) obtained in the electrolysis carried out under a nitrogen stream. These results do not support the involvement of reactions 3, 6, and 7.

In the previous paper,[6] we reported that in the oxidation of 2-nitrobenzenesulfenanilides, nucleophilic attack of acetonitrile on B followed by hydrolysis yielded *N*-(2-nitrophenylthio)acetamide (**8**). **8** was not detected in the electrolyzed solution of **1** in the presence of **5**, and also in the absence of **5** as we reported in another paper.[1]

The most reasonable mechanism for the formation of **6** is composed of reactions 1, 4, and 8 in Chart 1. A significant decrease in the cathodic counterpart in the cyclic voltammogram of **1** accompanied by addition of **5**, supports this conclusion. The experimental results that the yields of **6** differ among **1**—**4** also support this conclusion.

The decrease in yields of **6** caused by addition of water to the electrolytic solutions can be explained on the basis of the basicity of water. The cation radical generated from **1**—**4** in methanol, which is a protic solvent, liberates the α-proton instantly.[1] Just like methanol, water added to the electrolytic solution removes the α-proton of the cation radicals before they can react with **5**, and then the yield of **6** decreases.

Experimental

Materials——Sulfenamides were prepared as described previously.[1] Acetonitrile was commercially available HPLC grade unless otherwise specified, and was used without further purification. Rigorously dehydrated acetonitrile was obtained as described previously.[7] Commercial anhydrous $NaClO_4$ was used without further purification. **5** was distilled before use.

Apparatus——A Hokuto Denko HB-101 linear scanning unit, a HA-101 potentiostat/galvanostat and a Riken Denshi F-3D XY recorder were used for cyclic voltammetry. Controlled potential electrolysis[7] and high-performance liquid chromatography (HPLC) [1] were carried out as described previously. Infrared (IR), nuclear magnetic resonance (NMR), and mass (MS) spectra were obtained on Hitachi 260-30, R-22, M-60 spectrometers, respectively. ESR studies were carried out as described previously.[8]

Isolation of 2-(*o*-Nitrophenylthio)indan-1-ol (6)——**1** (236.5 mg) was subjected to electrolysis in HPLC-grade acetonitrile (100 ml) containing $NaClO_4$ (1.2 g) and **5** (1 ml) at room temperature at 1.2 V (*vs.* SCE). The quantity of electricity consumed (94.65 °C) corresponds to $n=0.997$. Ether (100 ml) and HCl (10%, 100 ml) were added to the resulting solution, and the mixture was shaken well and then left for a period. The organic layer was separated and dried with anhydrous $MgSO_4$, then concentrated. The residue was subjected to column chromatography on a prepacked column, size C (440-37) LiChroprep Si 60 (40—63 μm) (E. Merck, Darmstat), with benzene as an eluent. After

a sufficient volume of benzene had been passed through the column, elution was continued with $CHCl_3$ containing 50% methanol. The yellow effluent was evaporated under reduced pressure. The residue was subjected to column chromatography on the preceding column with $CHCl_3$ as an eluent. The yellow effluent was evaporated, and **6** (63.9 mg) was obtained. It was identified on the basis of the elemental analysis data, and IR, NMR and MS. *Anal.* Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87. Found; C, 62.62; H, 4.46; N, 4.79. IR ν_{max}^{KBr} cm^{-1}: 3330 (OH), 1512 (NO_2). NMR ($CDCl_3$) δ: 3.00 (1H, dd, $J=6$, 16 Hz, CH_2), 3.5—4.2 (2H, m, CH_2 and CH), 5.25 (1H, d, $J=4$ Hz, CH), 7.1—7.9 (7H, m, aromatic proton), 8.1—8.3 (1H, m, aromatic proton). MS *m/e*: 133 ($M^+ - O_2N - C_6H_4 - S^+$), 287 ($M^+$).

Determination of 6——Five μl of electrolyzed solution was injected into a NOVA-PAK cartridge column. The mobile phase was CH_3OH–H_2O (4:3) and the detector was operated at 254 nm.

Oxidation of 6 with CrO_3——**6** (116.8 mg) was dissolved in 1 ml of acetone, the solution was cooled in an ice bath, then a mixture of CrO_3 (100 mg), H_2SO_4 (0.09 ml) and water (0.3 ml) was added dropwise, with stirring by a magnetic stirrer, until the brown color of the acetone solution no longer disappeared. The mixture was stirred for a further 2.5 h. The resulting mixture was added to 50 ml of water and extracted with ether. The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The residue was recrystallized from petroleum ether containing 10% acetone, and gave 19.3 mg of **7**. This product was identified on the basis of the elemental analysis data, and IR, NMR and MS. *Anal.* Calcd for $C_{15}H_{11}NO_3S$: C, 63.14; H, 3.88; N, 4.90. Found; C, 62.77; H, 3.74; N, 4.86. IR ν_{max}^{KBr} cm^{-1}: 1708 (C=O), 1510 (NO_2). NMR ($CDCl_3$) δ: 3.14 (1H, dd, $J=4$, 18 Hz, CH_2), 3.80 (1H, dd, $J=8$, 18 Hz, CH_2), 4.34 (1H, dd, $J=4$, 8 Hz, CH_2), 7.2—8.0 (7H, m, aromatic proton), 8.1—8.2 (1H, m, aromatic proton). MS *m/e*: 131 ($M^+ - O_2N$–$C_6H_4 - S^+$), 285 (M^+).

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