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Studies on Sulfenamides. VI.[1] Cyclic Voltammetry and Controlled Potential Electrolysis of 4′-Substituted 2-Nitrobenzenesulfenanilides in the Presence of Trifluoroacetic Acid or Pyridine

Hiroteru Sayo,* Koichi Mori, and Takashi Michida

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

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Anodic oxidation of 4′-substituted 2-nitrobenzenesulfenanilides (4′-OMe (**1a**), 4′-Me (**1b**), 4′-H (**1c**), 4′-Cl (**1d**), 4′-COOEt (**1e**), 4′-$COCH_3$ (**1f**), 4′-NO_2 (**1g**)) and 4′-ethoxycarbonyl-N-methyl-2-nitrobenzenesulfenanilide (**1h**) was investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon or a reticulated vitreous carbon anode in acetonitrile containing 1% trifluoroacetic acid (TFA) or 1% pyridine. The peak potentials of **1a—g** in acetonitrile containing TFA were 0.23—0.55 V more positive than those in acetonitrile containing pyridine. On the other hand, the peak potential of **1h** was not affected by addition of TFA or pyridine. This suggests that **1a—g** partially dissociate into the sulfenamide anions in the presence of pyridine. Electrolysis of **1a**, **1b**, and **1d** in the presence of TFA gave the corresponding 2,7-disubstituted phenazines in higher yields than that in the absence of TFA. Although electrolysis of **1e** and **1f** did not give the corresponding phenazines in the absence of TFA, in the presence of TFA it did. Electrolysis of **1c** and **1g** did not give the corresponding phenazines in the presence or absence of TFA. Electrolysis of **1a—d** in the presence of pyridine gave the corresponding pyridinated sulfenanilides, and that of **1e** and **1f** gave the corresponding 4,4′-disubstituted azobenzenes. Electrolysis of **1g** gave *p*-nitroaniline both in the absence and presence of pyridine. The variation of yields of the phenazines and species of the products was explained in terms of the extent of dissociation of the dication intermediate, which in turn depends on the 4′-substituent. The nitrenium ions and nitrenes are suggested to be intermediates in the formation of the corresponding phenazines and the primary amines, respectively. The azobenzenes are considered to be oxidation products of the primary amines.

Keywords——anodic oxidation; cyclic voltammetry; 2-nitrobenzenesulfenanilides; 2,7-disubstituted phenazines; oxidation of sulfenamides; nitrenium ion; nitrene; RVC; N-arylpyridinium perchlorate

In the previous papers[2] we reported the results of the oxidation of 4′-substituted 2-nitrobenzenesulfenanilides (4′-OMe (**1a**), 4′-Me (**1b**), 4′-H (**1c**), 4′-Cl (**1d**), 4′-COOEt (**1e**), 4′-COMe (**1f**), 4′-NO_2 (**1g**)) with lead dioxide in acetonitrile containing 1% trifluoroacetic acid (TFA) and 1% trifluoroacetic anhydride (TFAH) and showed the usefulness of this reaction as a new synthetic method for 2,7-disubstituted phenazines (di-OMe (**2a**), di-Me (**2b**), di-Cl (**2d**), di-COOEt (**2e**), di-COMe (**2f**), di-NO_2 (**2g**)). TFAH was added to the solution in order to reduce the water content in the solution. In order to elucidate the role of TFA in the formation of the phenazines in more detail, we have studied the anodic oxidation of **1a—g** in acetonitrile containing 1% TFA or 1% pyridine.

Results

Cyclic Voltammetry

Cyclic voltammograms were obtained from 2 mM solutions of **1a—h** in acetonitrile containing 0.1 M ethyltributylammonium trifluoromethanesulfonate (ETBT) with or without addition of 1% TFA or 1% pyridine. Voltammetric data are summarized in Table I. A typical cyclic voltammogram is shown in Fig. 1. The peak potentials (E_p) of **1a—g** in the pres-

Table I. Voltammetric Data for the First Anodic Waves of 4′-Substituted 2-Nitrobenzenesulfenanilides (2 mM) in Acetonitrile containing 0.1 M ETBT with a Scan Rate of 50 mV/s

Compd. No.	Substituent	In the presence of 1% TFA		In the absence of TFA and pyridine		in the presence of 1% Pyridine	
		E_p	$ipv^{-1/2}$ a)	E_p	$ipv^{-1/2}$	E_p	$ipv^{-1/2}$
1a	4′-OMe	0.97	6.34	0.86	8.84	0.42	7.27
1b	4′-Me	1.12	8.92	1.06	11.44	0.58	7.28
1c	4′-H	1.18	9.19	1.15	9.05	0.95	8.20
1d	4′-Cl	1.23	10.23	1.10	9.82	0.75	6.53
1e	4′-COOEt	1.15	8.38	0.97	7.96	*ca.* 0.8 b)	6.8
1f	4′-COMe	1.34	9.67	1.20	9.07	*ca.* 1.0 b)	6.6
1g	4′-NO_2	1.37	8.36	1.31	8.84	*ca.* 0.9 b)	2.8
1h	N-Me, 4′-COOEt	1.44	6.00	1.48	7.13	1.42	14.3

a) $\mu A\,(mV/s)^{-1/2}$.
b) Shoulder.

ence of TFA were 0.23—0.55 V more positive than those in the presence of pyridine. In order to elucidate the effect of addition of TFA or pyridine on the voltammetric behavior of **1a—g**, cyclic voltammetry of 4′-ethoxycarbonyl-N-methyl-2-nitrobenzenesulfenanilide (**1h**), which is the N-methyl derivative of **1e**, was studied and compared with that of **1e**. With a scan rate of 50 mV s^{-1}, cyclic voltammetry of **1e** showed four anodic peaks at 0.97, 1.30, 1.60, and 1.96 V.[3] On addition of 1% pyridine to the solution of **1e**, two shoulders and one peak were observed at 0.80, 1.32, and 1.51 V, respectively. On the other hand, the E_p-value of the first wave of **1h** was little affected by addition of TFA or pyridine.

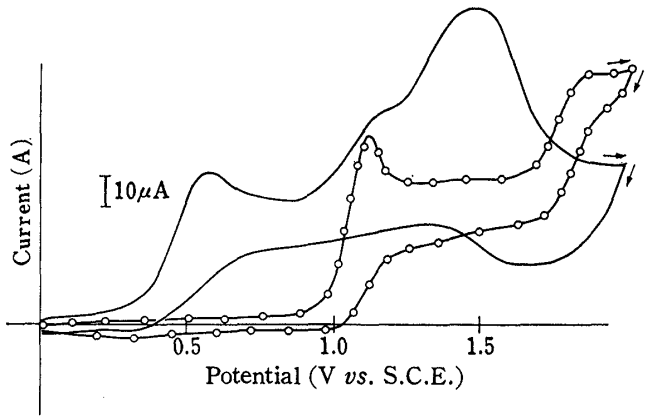


Fig. 1. Cyclic Voltammogram of 2-Nitrobenzenesulfen-4′-toluidide (**1b**) (2 mM) in Acetonitrile

———: in the presence of 1% pyridine.
—○—: in the presence of 1% trifluoroacetic acid and 1% trifluoroacetic anhydride.

Supporting electrolyte, 0.1 M ethyltributylammonium trifluoromethanesulfonate; scan rate, 50 mV/s; 25°C.

Controlled Potential Electrolysis

Although electrolysis of **1a**, **1b**, and **1d** in the absence of TFA gave **2a**, **2b**, and **2d**, respectively,[4] that of **1e** and **1f** did not go to completion owing to filming of the anode, and that of **1g** gave only *p*-nitroaniline (**3g**) (61.3%) instead of **2g**.

Electrolysis of **1a—g** (10 mM) was carried out in acetonitrile containing 0.1 M ETBT and 1% TFA and the results are summarized in Table II.

Although electrolysis of **1c** and **1g** still did not give **2c** and **2g**, that of **1e** and **1f** gave **2e** and **2f**, respectively, and the yields of **2a**, **2b**, and **2d** improved considerably. *p*-Anisidine (**3a**), which was one of the products obtained on electrolysis of **1a** in the absence of TFA,[5] was not detected in the electrolyzed solution. The results of electrolysis of **1a—g** (10 mM) in acetonitrile containing 0.1 M ETBT and 4% pyridine are summarized in Table III. 1-[2-(2-Nitrobenzenesulfenamido)-5-methoxyphenyl]pyridinium perchlorate (71.5%) was precipitated when $NaClO_4$ was added to the solution from the electrolysis of **1a** in the presence of pyridine. Electrolysis of **1b—d** in acetonitrile containing 0.1 M $NaClO_4$ and 4% pyridine gave the corresponding 1-substituted pyridinium perchlorates in yields 52.0%, 9.2%, and 2.5%, respec-

Table II. Results of Controlled Potential Electrolysis of 4′-Substituted 2-Nitrobenzenesulfenanilides (10 mM) in Acetonitrile containing 0.1 M ETBT, 1% TFA and 1% TFAH

Compd. No.	Applied potential V (*vs.* S.C.E)	*n*-Value[b]	Yield, mol %		Hammett σp of substituent[6]
			2,2′-Dinitrodiphenyldisulfide	2,7-Disubstituted phenazines	
1a	1.10	0.88	64.0	45.9(29.2)[a]	−0.268
1b	1.23	1.58	54.5	46.8(40.0)	−0.170
1c	1.18	1.40	26.0	—(—)	0
1d	1.33	1.35	64.0	57.2(37.3)	+0.227
1e	1.45	1.85	51.0	45.8(—)	+0.45
1f	1.48	1.17	47.0	7.6(—)	+0.502
1g	1.48	0.52	0	—(—)	+0.778

a) Numbers in parentheses are yields of the phenazines without addition of TFA and TFAH.[3] *b*) Number of Faradays passed per mole of substrate.

Table III. Results of Controlled Potential Electrolysis of 4′-Substituted 2-Nitrobenzenesulfenanilides (10 mM) in Acetonitrile containing 0.1 M ETBT, and 4% Pyridine

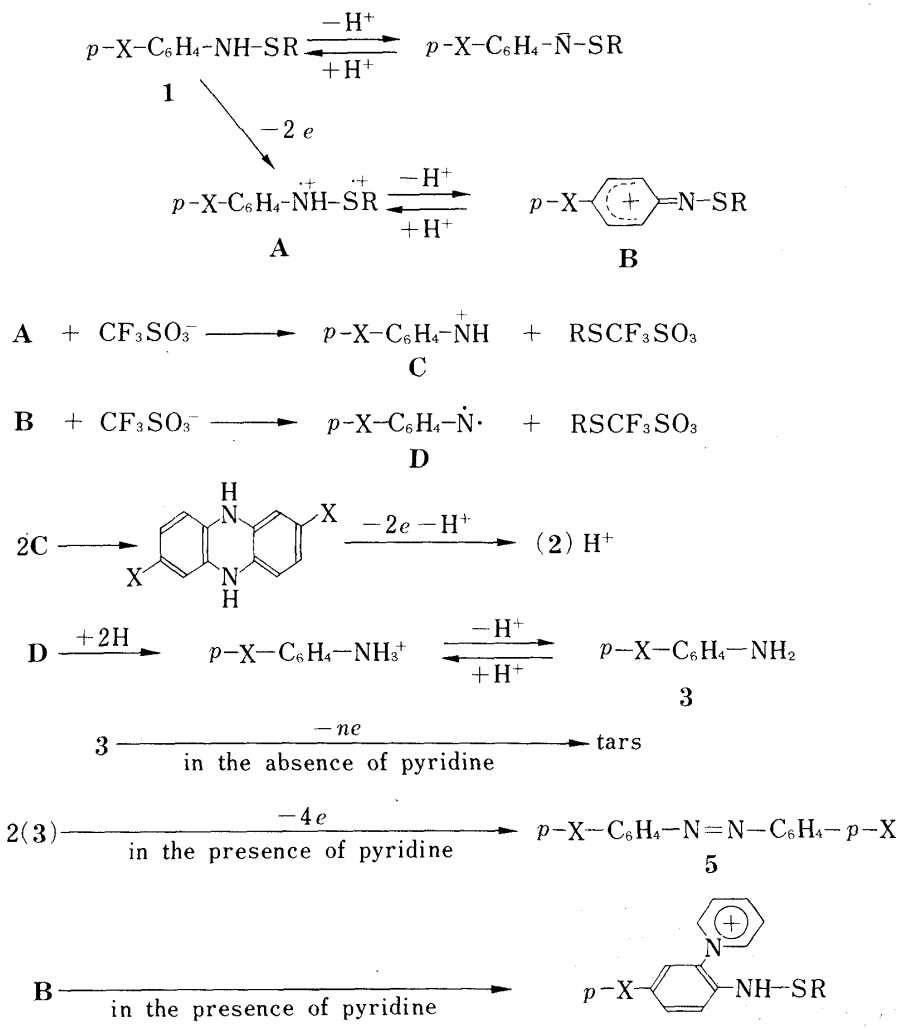
Compd. No.	Applied potential V (*vs.* S.C.E)	*n*-Value	Yield, mol %			
			Unchanged substrate	Dinitrodiphenyldisulfide	Pyridinium salts	Azobenzenes
1a	1.10	2.10	—	6.0	71.5	—
1b	1.23	2.11	—	7.0	52.0[b]	—
1c	1.18	0.93	47.7	—	9.2[b]	—
1d	1.33	1.44	27.9	4.0	2.5[b]	—
1e	1.45	6.60[a]	—	11.0	—	10.4
1f	1.48	9.54[a]	—	7.9	—	1.5
1g	1.48	1.24	46.8	Trace	—	—[c]

a) An RVC anode was used. *b*) $NaClO_4$ was used as a supporting electrolyte instead of ETBT. *c*) *p*-Nitroaniline (35.6%) was also detected.

tively. Electrolysis of **1e** in acetonitrile containing 0.1 M ETBT and 4% pyridine at a reticulated vitreous carbon (RVC) anode at 1.45 V gave 2,2′-dinitrodiphenyldisulfide (**4**, 11.0%) and 4,4′-diethoxycarbonylazobenzene (**5e**, 10.4%). **2e** was not detected in the resulting solution. An RVC anode was used for the electrolysis of **1e** and **1f** in the presence of pyridine in order to complete the electrolysis, because the electrolysis at a glassy-carbon plate caused severe filming at the anode and did not go to completion. Electrolysis of **1h** in acetonitrile containing 0.1 M $NaClO_4$ without addition of TFA or pyridine at 1.55 V gave 2-nitrobenzenesulfonic acid (70.5%), which suggested that two-electron transfer was involved in the first step of the reaction, as in the case of **1a**—**g**.[4]

Discussion

Cava and Blake reported that the initial step of the base-catalyzed rearrangement of **1d** was the formation of the sulfenamide anion.[6] The experimental findings that in the presence of 1% pyridine the E_p-values of the first waves of **1a**—**g** shifted to less positive values while that of **1h** did not, suggest that in the presence of pyridine **1a**—**g** partially dissociate into their anions, which have less positive E_p-values. However, comparison of the E_p-values in the presence of TFA with those in the absence of TFA or pyridine suggests that the dissociation of



1a—g is not appreciable in the absence of pyridine. Therefore, the effect of addition of TFA on the yields of **2a—f** is not considered to be due to suppression of dissociation of **1a—g**.

The following schemes are suggested for the anodic oxidation of **1a—g**.

The anodic oxidation of **1** gives the dication **A**. In the presence of TFA, **A** reacts with the electrolyte anion[4] and gives the nitrenium **C**. Two molecules of **C** couple to form the dihydrophenazines, which is oxidized further to **2**.

In the presence of pyridine, **A** is converted quickly to **B** by dissociation of the N–H bond. A part of **B** reacts with pyridine and gives 1-substituted pyridinium derivatives. The rest of **B** reacts with electrolyte anion instead of pyridine and gives the nitrene **D**, which abstracts two hydrogen atoms from the solvent or **1** and gives **3**, and then **3** is oxidized to **5**[7] (except for **3g**, which has the highest oxidation potential among **3a—g**). However, the oxidation of **3** gives **5** in low yield and tar in high yield. The latter causes severe filming at the anode and prevent the electrolysis from going to completion. Electron-donating groups in the 4′-position of **1** stabilize **B** and increase the yields of 1-substituted pyridinium derivatives.

An electron-attracting substituent at the 4′-position increases the acidity of **A** and decreases the yield of **2**, but addition of TFA to the solution of **1** decreases the dissociation of **A** and thus increases the formation of **C** and decreases that of **D**. The following experimental findings support the above conclusions; (1) electrolysis of **1g**, whose 4′-substituent has the largest Hammett σ_p value[6] among **1a—g** (Table II), did not give **2g** even in the presence of TFA, while that of **1f**, whose 4′-substituent has the second largest σ_p value, gave **2f** in low yield even in the presence of TFA; (2) electrolysis of **1a—d**, whose 4′-substituents have smaller σ_p values than

that of **1e**, gave **2a—d** in fairly good yields in the absence of TFA except in the case of **1c**; (3) **3a** and **3g** were obtained by the electrolysis of **1a** and **1g** in the absence of TFA, respectively. Since **1c** has no substituent on the 4'-position, the mechanism of anodic oxidation of **1c** may be different from the others.

One of the reasons why the yield of **2d** was about 10% larger than that of **2a**, **2b**, or **2e** can be ascribed to the easiness of isolation of **2d**, because **2d** separated out as large needles after addition of solid Na_2CO_3 and was almost insoluble in the solution.

Experimental

Materials——4'-Substituted 2-nitrobenzenesulfenanilides and ethyltributylammonium trifluoromethanesulfonate (ETBT) were prepared as described previously.[4] 4'-Ethoxycarbonyl-N-methyl-2-nitrobenzenesulfenanilide was prepared from 2-nitrobenzenesulfenyl chloride and ethyl N-methyl-*p*-aminobenzoate[9] in dry ether and recrystallized twice from 85% ethanol and then from methanol: yellow crystals, mp 139—140°C, *Anal.* Calcd for $C_{15}H_{16}N_2O_4S$: C, 57.82; H, 4.85; N, 8.43. Found: C, 57.65; H, 4.70; N, 8.43. IR ν_{max}^{KBr} cm^{-1}: 1705 (C=O). NMR ($CDCl_3$) δ: 1.45 (3H, t, $J=4$ Hz, CH_3), 3.55 (3H, s, CH_3), 4.35 (2H, q, $J=4$ Hz, CH_2), 7.1—7.6 (5H, m, aromatic), 7.9—8.1 (2H, m, aromatic), 8.2—8.4 (1H, m, aromatic). MS *m/e*: 332 (M^+). Acetonitrile was purified as described previously.[10] Trifluoroacetic acid and trifluoroacetic anhydride were obtained commercially. Pyridine was refluxed over calcium hydride for five hours and distilled. RVC was obtained commercially.[1]

Apparatus——Cyclic voltammetry, controlled potential electrolysis, and high performance liquid chromatography (HPLC) were carried out as described previously.[4,10] RVC (2×1-80-s) cut into a rectangular parallelepiped with approximate dimensions of $80\times50\times10$ was used for electrolysis of **1e** and **1f** without addition of TFA and with addition of pyridine as an anode instead of a glassy-carbon plate. Electrical contact to the RVC was made by winding a Pt wire around the top end of it. Infrared (IR) and nuclear magnetic resonance (NMR) spectra were obtained on Hitachi 260-30 and R-22 spectrometers, respectively.

Isolation of 1-Substituted Pyridinium Perchlorate——Typical examples of the procedure are given below.

a) **1a** (275.4 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT and 4% pyridine at 1.10 V at room temperature until the current fell below 1% of the initial value. Solid $NaClO_4$ (12 g) was dissolved in the resulting solution and the solution was cooled in refrigerator overnight. Yellow crystals separated out: they were filtered off and weighed (323.8 mg). The yellow crystals were recrystallized from acetonitrile (mp 228°C (dec.)) and identified as 1-[2-(2-nitrobenzenesulfenamido)-5-methoxyphenyl]-pyridinium perchlorate on the basis of the elemental analysis data, and IR and NMR spectra. *Anal.* Calcd for $C_{18}H_{16}ClN_3O_7S$: C, 47.64; H, 3.55; N, 9.55. Found: C, 47.70; H, 3.54; N, 9.55. IR ν_{max}^{KBr} cm^{-1}: 3350 (NH), 1613 (pyridine ring), 1100 (Cl-O), 1520 (NO_2). NMR (DMSO-d_6) δ: 3.75 (3H, s, CH_3), 7.0—7.9 (7H, m, aromatic proton), 8.2—8.4 (3H, m, aromatic proton), 8.7—9.0 (1H, m, NH), 8.3—9.5 (2H, m, aromatic proton).

b) **1b** (261.0 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M $NaClO_4$ and 4% pyridine at 1.23 V at room temperature. The resulting solution was concentrated and dried rigorously under reduced pressure. The residue was subjected to column chromatography on neutral alumina with $CHCl_3$ as the eluent. After a sufficient volume of $CHCl_3$ had been passed through the column, elution was continued with $CHCl_3$ containing 10% CH_3CN as the eluent. The yellow effluent was evaporated to dryness under reduced pressure. The residue was recrystallized from 99% EtOH to give yellow crystals (210.8 mg, mp 190—191°C (dec.)), which were identified as 1-[2-(2-nitrobenzenesulfenamido)-5-methylphenyl]pyridinium perchlorate on the basis of elemental analysis data, and IR and NMR spectra. *Anal.* Calcd for $C_{18}H_{16}ClN_3O_6S$: C, 49.37; H, 3.68; N, 9.60. Found: C, 49.48; H, 3.76; N, 9.44. IR ν_{max}^{KBr} cm^{-1}: 3446 (NH), 1615 (pyridine ring), 1510 (NO_2), 1095 (Cl-O). NMR (CD_3CN) δ: 2.30 (3H, s, CH_3), 6.05 (1H, s, NH), 7.2—7.8 (6H, m, aromatic proton), 8.1—8.3 (2H, m, aromatic proton), 8.6—8.9 (4H, m, aromatic proton).

Isolation of the Azobenzenes——**3e**: **1e** (318.7 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT and 4% pyridine at 1.45 V at room temperature until the current fell below 5% of the initial value. The resulting red solution was concentrated and extracted with hot benzene. The benzene solution was concentrated and subjected to multiple runs of thin-layer chromatography on alumina with carbon tetrachloride–benzene (2: 1) as the developing solvent. The red band was scraped off and extracted with benzene. Concentration of the benzene solution gave red crystals (16.9 mg), which were recrystallized from acetone and identified as **3e** on the basis of IR and NMR spectra and melting point (145—146°C, lit.[11] 145.8°).

3f: **1f** (288.9 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M ETBT and 4% pyridine at 1.48 V. The resulting solution was treated according to the procedure described above. The red crystals obtained (3.9 mg) was identified as **3f** on the basis of the IR spectrum.

Determination of Products obtained by Controlled Potential Electrolysis——a) 2,2'-Dinitrodiphenyldisulfide, **2b**, and 2-nitrobenzenesulfonic acid were determined as described previously.[4]

b) **2a**: Forty μl of the electrolyzed solution was developed on a thin-layer of alumina with benzene–hexane–27% aqueous ammonia (2: 1: 0.03). The spot of **2a** was detected by ultraviolet irradiation, and this region of alumina was scraped off and extracted with CH_3CN. The absorbance at 261 nm was measured.

c) **1c**, **1d**, and **1g** were determined by the same procedure as described for 2,2′-dinitrodiphenyldisulfide.

d) **2d** and **2e**: After addition of a small amount of solid Na_2CO_3 to the electrolyzed solution, the solution was allowed to stand overnight in a refrigerator. The resulting crystals were filtered off, washed with acetonitrile and then with water, dried, and weighed.

e) **2f**: After addition of a small amount of solid Na_2CO_3 to the electrolyzed solution, the solution was concentrated. The residue was washed with acetonitrile, recrystallized from benzene and weighed.

f) *p*-Nitroaniline: Ten ml of the electrolyzed solution was evaporated to dryness under reduced pressure. The residue was dissolved in 10 ml of acetonitrile and 1 μl of the solution was injected into an HP-01 column. The mobile phase was methanol and the detector was operated at 228 nm.

References and Notes

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