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Anodic Oxidation of Sulfonamides. II.[1] Anodic Oxidation of 4′-Substituted Benzenesulfonanilides in Acetonitrile

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Anodic oxidation of benzenesulfon-*p*-anisidide (I), benzenesulfon-*p*-toluidide (II), and N-methylbenzenesulfon-*p*-anisidide (III) were investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon anode in acetonitrile. I showed a single anodic wave in the absence of pyridine, and three anodic waves in the presence of pyridine. On electrolysis of I in the absence of pyridine, *p*-benzoquinone and benzenesulfonamide were formed. On electrolysis of I in the presence of pyridine, N,N′-dibenzenesulfonyl-N-(4′-methoxyphenyl)-5-methoxy-*o*-phenylenediamine (IV) and 1-(2-benzenesulfonamido-5-methoxyphenyl)pyridinium perchlorate (V) were obtained. Anodic oxidation of II in acetonitrile containing excess of pyridine gave N,N′-dibenzenesulfonyl-N-(*p*-tolyl)-5-methyl-*o*-phenylenediamine (VI) and N,N′-dibenzenesulfonyl-5,5′-dimethyl-2,2′-biphenyldiamine (VII). The formation of VI and VII was interpreted in terms of one-electron transfer followed by dimerizations of the free radical of II. On electrolysis of III in the presence of pyridine, 1-(N-methyl-3-benzenesulfonamido-6-methoxyphenyl)pyridinium perchlorate (VIII) was formed as the main product. The position of pyridination, which was *ortho* to the methoxy-group, was explained on the basis of steric factors.

Keywords——anodic pyridination; anodic dimerization; cyclic voltammetry; benzenesulfon-*p*-anisidide; benzenesulfon-*p*-toluidide; N-methylbenzenesulfon-*p*-anisidide; controlled potential electrolysis; N-arylpyridinium perchlorate

In the previous paper we studied the anodic oxidation of benzenesulfon-*p*-anisidide (I) in aqueous acetonitrile solution.[1] Electrolysis of I at pH 10.5 and the potential of the first wave gave a coulometric *n*-value (number of Faradays passed per mole of I) of about one, and N,N′-dibenzenesulfonyl-N-(4′-methoxyphenyl)-5-methoxy-*o*-phenylenediamine (IV) was obtained. The formation of IV was interpreted in terms of a head-to-tail coupling of the free radical of I. In order to obtain more detailed information on the formation of IV and find new examples of anodic dimerization, we studied the anodic oxidation of I, benzenesulfon-*p*-toluidide (II), and N-methylbenzenesulfon-*p*-anisidide (III) in acetonitrile and discussed the anodic oxidation process in some detail.

Results

Cyclic Voltammetry

Cyclic voltammetry of I (1 mM) in acetonitrile showed a single anodic peak at 1.23 V *vs.* S.C.E., and on reversing the direction of scan, a single cathodic peak was observed at 0.62 V. Typical voltammograms are shown in Fig. 1. The value of $i_p c^{-1}$ of the anodic peak, where c is the concentration of I and i_P is the peak current, was nearly constant in the concentration range from 0.2 to 4 mM at a potential scan rate (v) of 50 mV·sec^{-1}. The variation of i_p as a function of v was measured at a scan rate of 10—200 mV·sec^{-1}. As shown in Fig. 2, the value of $i_p v^{-1/2}$ of the anodic peak slightly decreased with increase in the value of v. In the presence of pyridine I showed three anodic peaks (Fig. 1). The E_p value of the first wave, where E_p is

1) Part I: H. Sayo and A. Morimoto, *Chem. Pharm. Bull.* (Tokyo), **23**, 3114 (1975).
2) Location: *Ikawadani-cho, Tarumi-ku, Kobe, 673, Japan.*

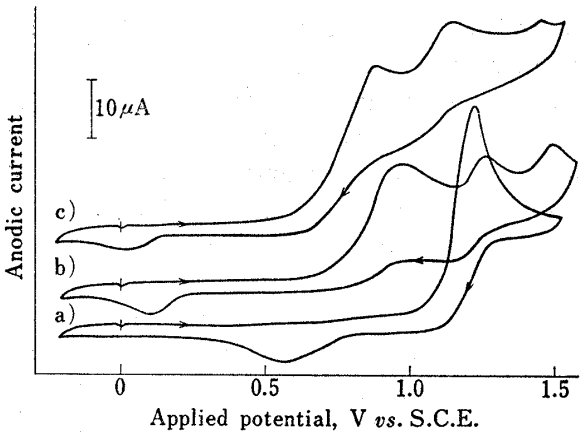

Fig. 1. Cyclic Voltammograms of Benzenesulfon-*p*-anisidide (1 mM) in Acetonitrile Containing Various Concentrations of Pyridine at a Scan Rate of 50 mV·sec^{-1}

a) in the absence of pyridine, *b*) with pyridine 1 mM, *c*) with pyridine 10 mM

the peak potential, shifted 0.34 V towards a less positive potential on addition of pyridine (30 mM). As shown in Fig. 3, the i_p value of the first wave initially inceased linearly with the concentration of pyridine and then gradually reached a limiting value. Extrapolation of the straight line drawn through the initial part of the plot intersected the limiting line near a concentration of pyridine equivalent to 1.2 mole of I, as shown in Fig. 3. In the presence of excess of pyridine, the value of $i_p v^{-1/2}$ of the first wave was nearly independent of v and 72% of that of the anodic wave in the absence of pyridine at v=200 mV·sec^{-1} (Fig. 2).

Cyclic voltammetry of II (1 mM) showed a single anodic peak at 1.46 V, and on reversing the direction of scan, a broad cathodic

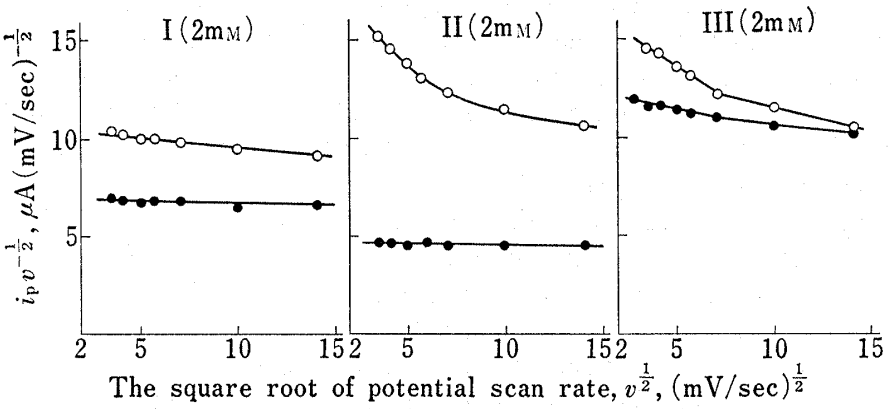

Fig. 2. Variation of Peak Current Function $i_p v^{-1/2}$, with the Square Root of Scan Rate

○: in the absence of pyridine, ●: with pyridine 60 mM

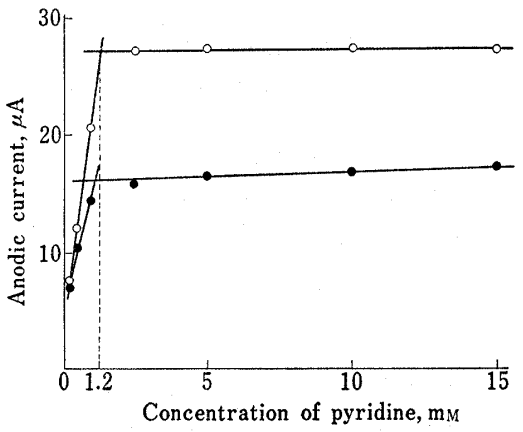

Fig. 3. Dependence of Peak Current of the First Wave on Pyridine Concentration

○: benzenesulfon-*p*-anisidide (1 mM)
●: benzenesulfon-*p*-toluidide (1 mM)

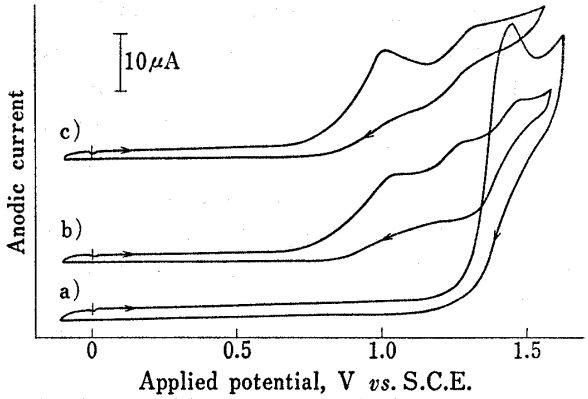

Fig. 4. Cyclic Voltammograms of Benzenesulfon-*p*-toluidide (1 mM) in Acetonitrile Containing Various Concentrations of Pyridine at a Scan Rate of 50 mV·sec^{-1}

a) in the absence of pyridine, *b*) with pyridine 1 mM, *c*) with pyridine 10 mM

peak was observed at 0.52 V. The value of $i_p c^{-1}$ of the anodic peak, where c is the concentration of II, was nearly constant in the concentration range from 0.2 to 4 mM. The value of $i_p v^{-1/2}$ of the anodic wave decreased remarkably with increase in the value of v (Fig. 2). Figure 4 shows typical voltammograms of II in acetonitrile containing various concentrations of pyridine. The E_p value of the first wave shifted 0.49 V towards a less positive potential on addition of pyridine (30 mM). As shown in Fig. 3, the i_p value of the first wave first increased linearly with the concentration of pyridine and then gradually reached a limitting value. In the presence of excess of pyridine, the value of $i_p v^{-1/2}$ of the first wave was independent of v and 40% of that of the anodic wave in the absence of pyridine at $v=200$ mV·sec^{-1} (Fig. 2).

Cyclic voltammetry of III (1 mM) showed a single anodic peak at 1.39 V, and on reversing the direction of scan, two small cathodic waves were observed at 0.62 and 0.29 V. The value of $i_p v^{-1/2}$ of the anodic wave decreased remarkably with increase in the value of v. Addition of pyridine (<30 mM) to the solution of III had only a small effect on the value of E_p and i_p. The value of $i_p v^{-1/2}$ of the anodic wave in the presence of excess of pyridine decreased slightly with increase in the value of v and nearly equal to that in the absence of pyridine at $v=200$ mVsec^{-1} (Fig. 2).

Controlled Potential Electrolysis

Electrolysis of I (2 mM) in acetonitrile containing 0.1 M $NaClO_4$ at the anode potential of 1.20 V gave a coulometric n-value of two, and p-benzoquinone and benzenesulfonamide were formed. The voltammogram and the UV spectrum of the resulting solution agreed well with those of p-benzoquinone containing an equimolar amount of benzenesulfonamide. Electrolysis of I (20 mM) in acetonitrile containing pyridine (0.12 M) and $NaClO_4$ (0.1 M) at 0.85 V gave an n-value of 1.4. The solution turned brownish yellow at the end of the electrolysis. From the resulting solution IV and the pyridinated I, 1-(2-benzenesulfonamido-5-methoxyphenyl)pyridinium perchlorate (V), were obtained. The amount of IV decreased and the n-value increased with increase in the concentration of added pyridine. Details of the procedures used to identify the product are described in the Experimental section.

Electrolysis of II (2 mM) at 1.48 V caused severe filming on the surface of the anode and prevented the completion of the electrolysis. When the electrolysis was carried out for 3 hr, the n-value was about three. The voltammogram and the UV spectrum of the resulting solution indicated the presence of p-benzoquinone and benzenesulfonamide. Electrolysis of II (20 mM) in the presence of pyridine (0.06 M) at 1.10 V gave an n-value of about one. The solution turned pale yellow at the end of the electrolysis. From the resulting solution N,N′-dibenzenesulfonyl-N-(p-tolyl)-5-methyl-o-phenylenediamine (VI) and N,N′-dibenzenesulfonyl-5,5′-dimethyl-2,2′-biphenyldiamine (VII) were isolated.

Electrolysis of III (2 mM) at 1.35 V at room temperature gave an n-value of 2.4, and p-benzoquinone and N-methylbenzenesulfonamide were obtained. Electrolysis of III at a lower temperature also gave an n-value of more than two. Electrolysis of III (20 mM) in acetonitrile containing pyridine (0.12 M) at 1.33 V at *ca.* 3° gave an n-value of 1.8, and the pyridinated III, 1-(N-methyl-3-benzenesulfonamido-6-methoxyphenyl)pyridinium perchlorate (VIII), was isolated as the main product. The voltammogram and the UV spectrum of the resulting pale yellow solution indicated the absence of p-benzoquinone.

Discussion

Anodic oxidations of I, II, and III in the absence of pyridine can be considered analogous to that of 4′-methoxybenzanilide.[3] However, an increase in the value of $i_p v^{-1/2}$ at slow potential scans and n-values of more than two were observed for the anodic oxidations of II and III. Since p-benzoquinone, and benzenesulfonamide or N-methylbenzenesulfonamide showed no

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

oxidation wave at up to 1.6 V, these results can be explained in terms of the nucleophilic attack of hydroxyl ion on the cationic intermediate followed by further oxidation of the hydroxylated compound.

The following schemes are suggested for the anodic oxidation of III.

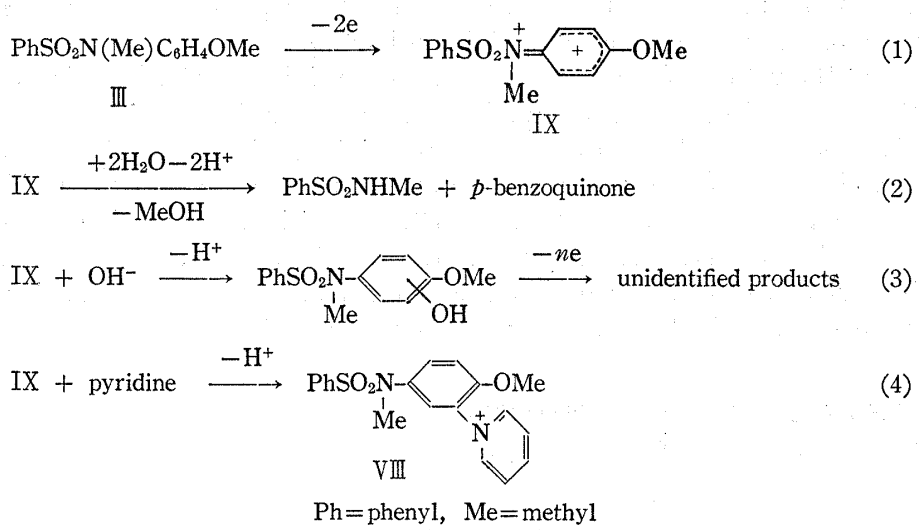

Chart 1

In the presence of pyridine reaction 4 proceeds much faster than reactions 2 and 3. The fact that the anodic pyridination of III occurred at the position *ortho* to methoxy-group in contrast to the results on 4′-methoxybenzanilide and II is considered to be due to steric hindrance caused by N-methyl group. A similar pyridination was observed for the anodic oxidation of N-methyl-4′-methoxybenzanilide.[4]

The effects of pyridine on the anodic oxidations of I, II, and III differed from one another. Since III have no hydrogen atom on the nitrogen, the different voltammetric behavior of III from that of I or II is well expected. However, a great difference in the effects of pyridine between the anodic oxidations of I and II is rather unexpected, because both compounds have a hydrogen atom on the nitrogen. The fact that the anodic oxidation of II in the presence of pyridine gave no pyridinated compound suggests that mechanism of the anodic oxidation of II is completely different from that of I. The difference in voltammetric behaviors between I and II also substantiates the above suggestion.

One-step two-electron transfer followed by a nucleophilic attack of pyridine on the cationic intermediate has been suggested for the anodic pyridination of substituted benzanilides,[3,4]

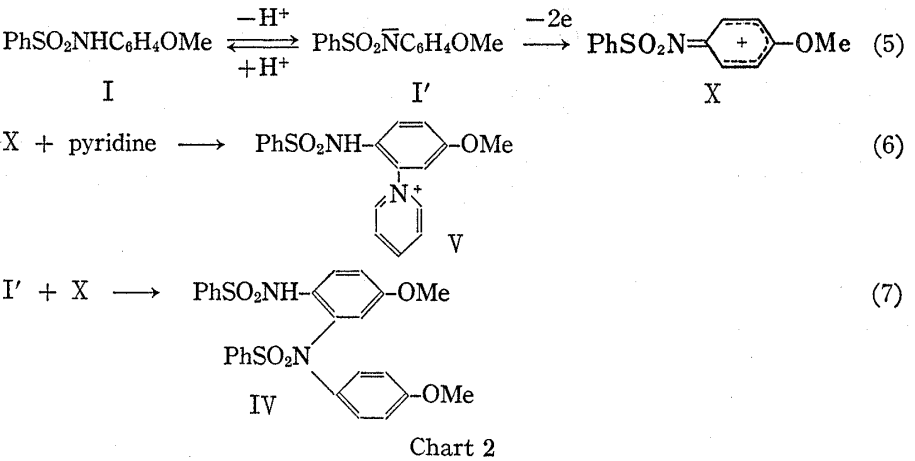

Chart 2

4) M. Masui, H. Ohmori, H. Sayo, A. Ueda, and C. Ueda, *J. Chem. Soc. Perkin II*, **1976**, 1180.

while stepwise one-electron transfer has been suggested for the anodic pyridination of N-benzylidene-*p*-anisidines[5] and anthracene derivatives[6] and for anodic acetoxylation of aliphatic amides.[7]

The anodic oxidation of I in acetonitrile containing excess of pyridine gave the unsymmetrical dimer of I, IV, besides the pyridinated I, V. The following schemes are suggested for the anodic oxidation of I in the presence of pyridine (Chart 2).

The fact that the value of $i_p v^{-1/2}$ in the presence of pyridine was 72% of that in the absence of pyridine at $v=200$ mV·sec^{-1} can be explained in terms of a decrease in the concentration of I′ at the surface of anode which is caused by reaction 7. Since reaction 6 competes with reaction 7, the yield of V increases with increase in the concentration of added pyridine.

On the other hand, the anodic oxidation of II in acetonitrile containing excess of pyridine gave the symmetrical dimer, VII, instead of the pyridinated compound. Since a radical mechanism is most plausible for formation of a symmetrical dimer, the following schemes are suggested for the anodic oxidation of II in the presence of pyridine.

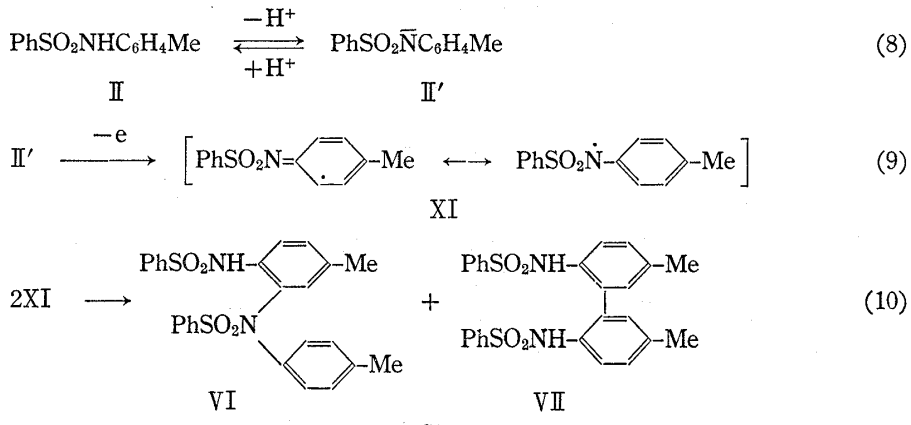

Chart 3

TABLE I. Physical and NMR Data for the Products obtained on Electrolysis

Compd. No.	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	NMR (solvent) δ (ppm)
V′	213—214	$C_{36}H_{33}O_{10}N_4S_2Cl$	55.34 (55.27)	4.26 (4.27)	7.17 (7.17)	(CH_3CN), 3.74(3H, s)[a], 6.8—7.1(3H, m)[b], 7.2—7.6(5H, m)[b], 7.8—8.8(5H, m)[c]
VI	183—185	$C_{26}H_{24}O_4N_2S_2$	63.39 (63.41)	4.91 (4.96)	5.69 (5.67)	($(CD_3)_2SO$), 2.06(3H, s)[d], 2.24(3H, s)[d], 6.66(1H, m)[b], 6.9—7.25(6H, m)[b], 7.3—7.8(10H, m)[b], 9.10(1H, s)[e]
VII	148—150	$C_{26}H_{24}O_4N_2S_2$	63.39 (63.36)	4.91 (4.91)	5.69 (5.77)	($(CD_3)_2SO$), 2.09(6H, s)[d], 6.32(2H, broad s)[b], 6.99(4H, broad s)[b], 7.2—7.8 (10H, m)[b], 8.59(2H, s)[e]
VIII	120—121	$C_{19}H_{19}O_7N_2SCl$	50.17 (50.35)	4.21 (4.31)	6.16 (6.10)	($(CD_3)_2SO$), 3.09(3H, s)[f], 3.83(3H, s)[a], 7.35—7.45(2H, m)[b], 7.5—7.75(6H, m)[b] 8.15—9.25(5H, m)[c]

a) These signals were assigned to the protons of methoxy group.
b) aromatic protons
c) the protons of the pyridinium group
d) *p*-methyl protons
e) NH proton
f) N-methyl protons

5) M. Masui and H. Ohmori, *J. Chem. Soc. Perkin II*, **1973**, 1112.
6) V.D. Parker and L. Eberson, *Acta Chem. Scand.*, **24**, 3542 (1970).
7) S.D. Ross and M. Finkelstein, *J. Org. Chem.*, **31**, 128 (1966).

The value of $i_p v^{-1/2}$ of the first wave in the presence of pyridine was 0.4 times that of the anodic wave in the absence of pyridine at $v=200$ mV·sec^{-1}. Since the contribution of follow-up chemical and electrochemical reactions, which are analogous to reaction 3 and cause an increase in the i_p-value at slower scan rates, to the i_p-value in the absence of pyridine is considered to be small at $v=200$ mV·sec^{-1}, this ratio, 0.4, is close to that predicted for one- *vs.* two-electron transfer by the theory of peak voltammetry, $(1/2)^{3/2}$.[8] The reason why two discrete one-electron transfer steps are observed on the anodic oxidation of II in the presence of pyridine is not clear at present. The question of one– *vs.* two-electron oxidation has been discussed recently by Phelps and Bard for the anodic oxidation of tetraphenylethylenes.[9] They have considered substituent effects, solvent effects, and steric effects as the factors influencing the reaction path. Further studies are needed to explain this point.

Experimental

Materials——I and II were prepared as described previously.[1] III was prepared from I, methyl iodide, and sodium methoxide, and recrystallized from ligroin, mp 79°. Acetonitrile was distilled as described previously[1] and passed through a column of neutral alumina prior to use.

Apparatus——Cyclic voltammetry and controlled potential electrolysis were carried out as described previously.[1] Oxygen was not removed from the solution throughout the study, because the results of electrolysis were the same in the presence and absence of O_2. UV and IR spectra were obtained using Hitachi 323 and Shimadzu IR-400 spectrometers, respectively. NMR spectra were taken at 90 MHz with Hitachi R-22 spectrometer using tetramethylsilane as the internal standard. Mass spectra were measured on a JEOL JMS-01SG spectrometer at ionizing voltage of 75 eV.

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

a) I (526.6 mg, 2×10^{-3} mole) was subjected to electrolysis in acetonitrile (100 ml) containing 0.1 M $NaClO_4$ and 0.12 M pyridine at 0.85 V at room temperature until the value of current became less than 1% of the initial value (*ca.* 3 hr). From the current-time curve 268 coulombs, which corresponded to $n=1.39$, was found to be consumed. The resulting brownish yellow solution was evaporated to dryness under reduced pressure and the residue was extracted with $CHCl_3$. The $CHCl_3$ solution was evaporated to dryness and the residue was extracred with hot CH_3CN. Cooling of the CH_3CN solution gave white crystals of IV (185 mg), which were filtered off and recrystallized from $CHCl_3$–EtOH, mp 173—174°, and identified by comparing the IR spectrum with that of authentic sample.[1] The filtrate was subjected to column chromatography on neutral alumina using $CHCl_3$ as eluant. Evaporation of the fractions gave a small amount of IV, pyridinium perchlorate, and a small amount of unidentified compounds. After enough volumes of $CHCl_3$ was passed through the column, the elution was continued with CH_3CN as eluant. The absorbates on the column turned orange as CH_3CN was passed through the column. The orange effluent was evaporated to dryness under reduced pressure and the residue was recrystallized from methanol to give pale yellow needles (69 mg), which were identified as the half-deprotonated compound of V, $(C_{18}H_{16}O_3N_2S)_2\,HClO_4$ (V′), by elemental analysis and IR and NMR spectra (Table I). A similar run in acetonitrile containing 0.6 M pyridine gave an n-value of 1.66, 62 mg of VI, and 124 mg of V′. When V′ was hydrolyzed in conc. HCl, 4-methoxy-2-pyridiniumanilinium dichloride was obtained and identified from its IR spectrum in comparison with that of authentic sample.[5] Partial deprotonation of V was considered to take place during the column chromatography.

b) II (494.6 mg, 2×10^{-3} mole) was subjected to electrolysis in acetonitrile containing 0.1 M $NaClO_4$ and 0.06 M pyridine at 1.10 V at room temperature for 4 hr. The quantity of electricity consumed corresponded to $n=1.04$. The resulting pale yellow solution showed essentially no anodic waves in the cyclic voltammogram. The solution was evaporated to dryness under reduced pressure and the residue was extracted with $CHCl_3$. The $CHCl_3$ solution was evaporated to dryness and the residue was extracted with hot MeOH. The MeOH solution was allowed to stand overnight. White crystals separated out, which were filtered off and recrystallized from CH_3CN to give white needles (45 mg), which were identified as VI. The mass spectrum of VI showed a molecular ion at m/e 492. The filtrate was evaporated to dryness and the residue was extracted with hot EtOH. Cooling of the EtOH solution gave white crystals, which were recrystallized from EtOH to give white leaflets (50 mg). Mass Spectrum m/e: 492 (M^+). The NMR spectrum of the white leaflets (Table I) was compared with that of II. The signal at δ 2.09 was assigned to the protons of the methyl-groups, and was very close to the signal of the methyl-group in II (δ 2.19). On the other hand, the signal of the aromatic protons of the toluidine ring, which was present at δ 6.94 (4H, s) in the spectrum of II, splitted

8) R.N. Adams, "Electrochemistry at Solid Electrodes," Marcel Dekker, Inc., New York, 1969.
9) J. Phelps and A.J. Bard, *J. Electroanal. Chem.*, **68**, 313 (1976).

to two broad singlets. The signal at δ 6.32 was assigned to the protons at the position *ortho* to the methyl-groups. These results were in reasonable agreement with the product having the structure of VII.

c) III (554.6 mg, 2×10^{-3} mole) was subjected to electrolysis in CH_3CN containing 0.1 M $NaClO_4$ and 0.12 M pyridine at 1.33 V at *ca.* 3° for 3 hr. The resulting pale yellow solution was evaporated to dryness under reduced pressure and the residue was extracted with $CHCl_3$. The $CHCl_3$ solution was subjected to column chromatography on neutral alumina with $CHCl_3$ as eluant. Evaporation of the first fraction gave a small amount of unreacted III. After all III was eluted, the eluant was changed to 10% CH_3CN in $CHCl_3$. The pale yellow crystals obtained from the effluent were recrystallized from EtOH to give pale yellow plates (283 mg), VIII. VIII was hydrolysed in conc. HCl for 2 days. The resulting solution was evaporated to dryness, and the residue was subjected to column chromatography on neutral alumina with CH_3CN as eluant. The orange needles (mp 176—178°) obtained from the first effluent were identified as 1-(3-methylamino-6-methoxyphenyl)pyridinium perchlorate from its NMR spectrum in comparison with that of authentic sample.[4] This result was in reasonable agreement with the product of the anodic oxidation having the structure of VIII.

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