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Oxidation of Hydroxylamine Derivatives. II. Anodic Oxidation of Phenylhydroxylamines

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The anodic oxidation of *p*-substituted phenylhydroxylamines (*p*-X-PHA's) was studied in acetonitrile. These *p*-X-PHA's generally showed three or four oxidation waves at a glassy-carbon electrode. On electrolyses, *p*-X-PHA's except for X=H gave the corresponding nitroso compounds (*p*-X-NB's) and azoxybenzenes (*pp'*-X-AB's), while *p*-X-PHA (X=H) gave only nitrosobenzene.

A reaction mechanism that *pp'*-X-AB's are formed not only by the condensation of the corresponding *p*-X-NB's and *p*-X-PHA'S, but by the reaction of *p*-X-PHA cation radicals with *p*-X-PHA's or by the coupling of two phenyl nitroxides is proposed.

Keywords——anodic oxidation; phenylhydroxylamines; glassy-carbon electrode; controlled potential electrolysis; effect of *para*-substitution on azoxy formation;

We have investigated the anodic oxidation of various hydroxylamine derivatives at a glassy-carbon electrode in acetonitrile and have proposed the oxidation mechanisms.[2] Hydroxylamine derivatives $R_1R_2NOR_3$, were oxidized to nitroxide $R_1R_2N\dot{O}$, N-alkoxy-N-alkylamine radical $R_1\dot{N}OR_3$, or N-alkoxy-N-acylamine radical $R_1CO\dot{N}OR_3$ depending on the substituents R, and these intermediates gave various stable products through the subsequent disproportionation, coupling or further oxidation.

The oxidation of hydroxylamine derivatives from the mechanistic point of view, have received little attention, and the electrochemical studies on phenylhydroxylamines have been limitted only to their voltammetric behaviors.[3]

We have made a study on the anodic oxidation of several phenylhydroxylamines to clarify both their voltammetric behaviors and electrochemical mechanism in the course of the anodic oxidation, and suggested that *p,p'*-disubstituted azoxybenzenes *pp'*-X-AB's were formed not only by the condensation of nitrosobenzenes *p*-X-NB's with phenylhydroxylamines *p*-X-PHA's, but by the reaction of *p*-substituted phenylhydroxylamine cation radicals with *p*-X-PHA's or by the coupling of two *p*-substituted phenylnitroxides.

Phenylhydroxylamine *p*-X-PHA (X=H), is known to rearrange under the influence of acids[4] to give *p*-aminophenol which is easily oxidized at the oxidation potential of *p*-X-PHA (X=H), and the products should be subject to subsequent reactions. In the course of anodic oxidation of *p*-X-PHA (X=H), the generated proton will protonate the starting material and may cause the complication owing to the rearrangement described above, therefore the oxidation was carried out mainly on *p*-substituted phenylhydroxylamines *p*-X-PHA's ($X=CH_3$, Cl, Br) to avoid the complication.

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[1] Location: *133-1, Yamada-Kami, Suita-shi, Osaka.*

[2] *a*) H. Sayo, S. Ozaki, and M. Masui, *Chem. Pharm. Bull.* (Tokyo), **21**, 1988 (1973); *b*) *Idem, ibid.*, **23**, 1702 (1975); *c*) S. Ozaki and M. Masui, *ibid.*, **25**, 1179 (1977).

[3] *a*) R.E. Lutz and M.R. Lytton, *J. Org. Chem.*, **2**, 68 (1938); *b*) L. Chuang, I. Fried, and P.J. Elving, *Anal. Chem.*, **36**, 2426 (1964).

[4] *a*) E. Bamberger, *Ann.*, **424**, 297 (1921); *b*) E. Bamberger, *Ann.*, **441**, 297 (1925); *c*) H.E. Heller, E.D. Hughes, and C.K. Ingold, *Nature*, **24**, 909 (1951).

Results and Discussion

Cyclic Voltammetry

The voltammetric behaviors of *p*-X-PHA's at a stationary glassy-carbon electrode in acetonitrile containing 0.1 M sodium perchlorate are shown in Fig. 1 and in Table I. Three or four waves were generally observed at a scanning rate of 0.2—0.05 V sec.^{-1} The first anodic wave (E_{p1}) of the *p*-X-PHA's would be due to an electron transfer from the lone-pair of the nitrogen atom of the molecules.[2] The peak potential of the first wave shows that the *p*-X-PHA's are in general more susceptible to electrochemical oxidation than primary alkylhydroxylamines,[2] although the former are less basic than the latter. A cathodic wave was observed to couple with the first anodic wave (E_{p1}), suggesting the primary product formed at the first anodic wave is more stable than that of alkylhydroxylamines, which have shown no cathodic wave coupled with the first anodic wave. Substitution of an electron releasing group to the phenyl ring shifted the E_{p1} to a less positive potential, whereas an electron attracting group shifted it to more positive potential. In the presence of excess pyridine, *p*-X-PHA's showed an extra oxidation peak, E_{pe}, at a lower potential than E_{p1}. The extra peak seems to be due to the oxidation of partially ionized *p*-X-PHA's because pyridine ($pK_a=5.2$) is a strong base than *p*-X-PHA's ($pK_a \simeq 3.2$).[5] The third wave at E_{p3} of the four *p*-X-PHA's and the fourth wave at E_{p4} of *p*-X-PHA's (X=Cl and Br) coincided with the oxidation wave of the corresponding nitrosobenzene and *p,p'*-dihalosubstituted azoxybenzene, respectively.

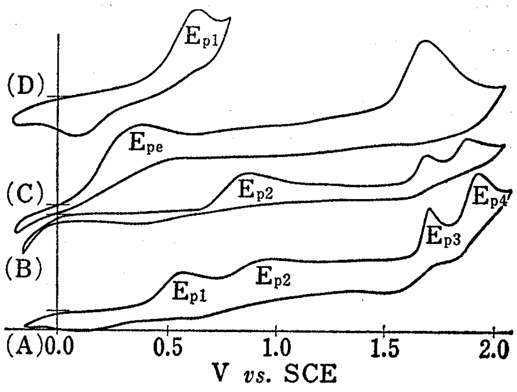
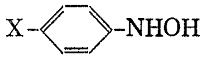


Fig. 1. Cyclic Voltammograms of *p*-Br-PHA (*ca.* 5 mM) in MeCN–0.1 M $NaClO_4$ at a Glassy-Carbon Electrode

Scan rate is 0.05 V sec^{-1} for (A), (B), (C), and 0.2 V sec^{-1} for (D); (A) *p*-Br-PHA alone; (B) with excess perchloric acid; (C) with excess pyridine; (D) *p*-Br-PHA alone, with scan rate of four times in (A).

Table I. Cyclic Voltammetric Data on Phenylhydroxylamines in MeCN–0.1M $NaClO_4$ at a Glassy-Carbon Electrode, 25°

			E_p a)		
	E_{pe} b)	E_{p1}	E_{p2}	E_{p3}	E_{p4}
$X=CH_3$	0.15	0.40	0.70	1.60	c)
X=H	0.20	0.45	0.80	1.70	c)
X=Cl	0.25	0.55	0.85	1.73	1.94
X=Br	0.25	0.55	0.90	1.72	1.94

a) Volt *vs.* SCE.
b) Extra wave observed on addition of excess pyridine.
c) The fourth wave was not observed.

The cyclic voltammogram in the presence of pyridine did not show the wave at E_{p4}, because filming on the electrode caused by the oxidation of pyridine prevented the development of the wave at E_{p4}.

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5) P.A.S. Smith "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. 2, W.A. Benjamin, Inc., New York, Amsterdam, 1965, p. 3.

On addition of excess perchloric acid, the first wave disappeared, whereas other waves remained unchanged. The cyclic voltammogram on the solution after exhaustive electrolysis of *p*-X-PHA's at E_{p1}, which was found to contain protonated *p*-X-PHA's, coincided with that of *p*-X-PHA's in the presence of excess perchloric acid. These results indicate that the E_{p2} is due to the oxidation of the protonated *p*-X-PHA's.

On electrolyses of *p*-X-PHA's, greenish yellow colour was developed progressively, and the colour turned to brown in the course of the electrolyses. In the presence of excess pyridine, only the oxidation of *p*-X-PHA (X=H) showed the characteristic colour of nitrosobenzene, whereas other three *p*-X-PHA's showed similar change in colour as observed in the absence of pyridine. The results obtained on controlled potential electrolyses of *p*-X-PHA's are summarized in Table II.

TABLE II. Oxidation Products from Phenylhydroxylamines

Compds.	Pyridine present	Products (%)[c]					
		$E_{app.}$[a]	n[b]	*p*-X-NB	*pp'*-X-AB	Protonated *p*-X-PHA	k[e] ($M^{-1}sec^{-1}$)
$X=CH_3$	No	0.40	0.90	39[d]	6[d]	23[d]	5.6×10^{-3}
	Yes	0.15	1.74	78	8	0	
X=H	No	0.45	1.05	50[d]	trace	45[d]	7.6×10^{-3}
	Yes	0.20	1.95	98	0	0	
X=Cl	No	0.55	0.77	31[d]	10[d]	40[d]	2.3×10^{-2}
	Yes	0.25	1.80	80	10	0	
X=Br	No	0.60	0.70	34[d]	6[d]	54[d]	3.8×10^{-2}
	Yes	0.20	1.43	48	23	0	

a) Applied potential in volt *vs.* SCE.
b) Coulombs passed per mole of the substrate.
c) Mole per cent on the basis of the starting material.
d) The yield in the absence of excess pyridine was determined just after exhaustive electrolysis.
e) Second-order rate constant for the formation of *pp'*-X–AB from the corresponding *p*-X–PHA and *p*-X–NB in acetonitrile at 25° (see results section).

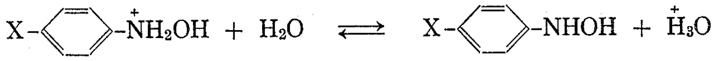
The anodic oxidation of *p*-X-PHA's in the absence of pyridine gave the corresponding nitrosobenzene and azoxybenzene together with a considerable amount of protonated starting hydroxylamines. Contrary to the expectation azoxybenzene was scarcely detected in the course of electrolysis of *p*-X-PHA (X=H). On standing the solution after exhaustive electrolysis at room temperature, the amount of *pp'*-X-AB's still continued to increase with time, while that of *p*-X-NB's decreased. This suggests that the condensation of *p*-X-NB's with protonated *p*-X-PHA's proceeds to form *pp'*-X-AB's. Only in the oxidation of *p*-X-PHA (X=H) at E_{p2}, a trace of *p*-quinoneimine was sometimes observed; this suggests a small amount of protonated *p*-X-PHA (X=H) rearranged to *p*-aminophenol.

The n value (the number of coulombs passed per mol of the substrate) was about 0.77 to 1.05, and the total yield of *p*-X-NB and *pp'*-X-AB was 40—50 mol %. As shown in Table II 20—50 mol % of the starting material was recovered in the protonated form. The results suggest that 40—50 mol % of *p*-X-PHA's were oxidized through two-electron oxidation. The n value and the yields of the products showed no definite correlation with the nature of the *para*-substituents.

On addition of excess pyridine as acceptor of the proton generated in electrolyses, the n value and the sum of the yields of *p*-X-NB and *pp'*-X-AB increased up to 1.43—1.95 and 71—98 mol %, respectively. In the presence of pyridine the yield of *pp'*-X-AB except for X=H increased with increase in the observed 2nd order rate constants measured separately for the formation of *pp'*-X-AB from the corresponding *p*-X-NB and *p*-X-PHA.

Oxidation Mechanism

The *n* value for the anodic oxidation of *p*-X-PHA's were over 0.77 and the total yields of nitroso compounds and azoxy compounds were more than 40 mol %. The results are different from those obtained in the oxidation of alkylhydroxylamines,[2] in which one third of the starting material was oxidized and two thirds were not oxidized because of protonation. This difference must be ascribed to the weaker basicity of *p*-X-PHA's, which makes the contribution from the right hand side of the following equation fairly large, and more than one third of initial *p*-X-PHA's are oxidized. Comparable amount of water is unavoidably present in the system.



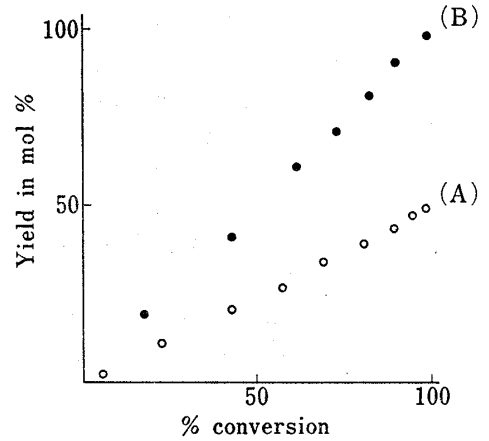


Fig. 2. Plots of mol % Yield of Nitrosobenzene against % Conversion of *p*-X-PHA (X=H) for an Electrolysis Conducted at E_{p1}

(A) *p*-X-PHA (X=H) alone, (B) with excess pyridine.

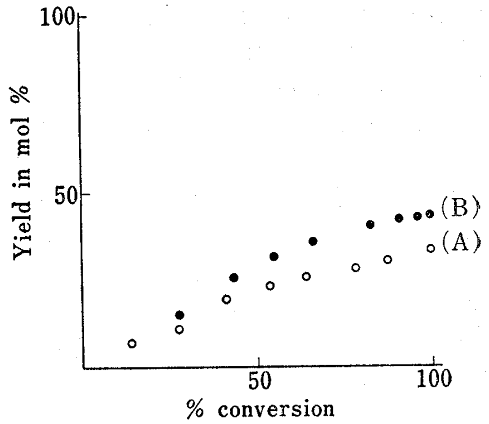


Fig. 3. Plots of mol % Yield of *p*-Br-Nitrosobenzene against % Conversion of *p*-Br-PHA for an Electrolysis Conducted at E_{p1}

(A) *p*-X-PHA alone, (B) with excess pyridine.

Fig. 2 and Fig. 3 show the mol per cent yields of nitroso compounds against the per cent conversion of *p*-X-PHA's (X=H and Br) for the electrolyses conducted at E_{p1}, respectively. The plots for *p*-X-NB (X=H) gave almost straight lines with the slope nearly equal to one and 0.5 depending on whether pyridine is present or absent, while those for *p*-X-NB (X=Br) displayed downward curves. The downward curvature suggests that the consumption of *p*-X-NB by the subsequent reaction is not negligible, while the straight lines indicate almost no consumption of *p*-X-NB (X=H). Protonation of the *p*-X-PHA (X=H) with proton generated in electrolyses explains the smaller value for the slope in the absence of pyridine.

If *pp*-X-AB's are produced only by the condensation reaction of the corresponding *p*-X-NB's with *p*-X-PHA's, the yields of *pp*'-X-AB's should be the higher the larger the rate constant for the condensation reaction. The rate constants reported[6] and found in acetonitrile in the present study (Table II) suggest that the order of yields should be X=Br or $Cl>X=H>X=CH_3$. However, in the present study this order was not realized. Some reaction routes other than the above condensation, therefore, must be assumed for the formation of *pp*'-X-AB's.

The following schemes are proposed; *i.e.*, (A) the reaction of the *p*-X-PHA's cation radical (II) with *p*-X-PHA's (I); (B) the coupling of the two phenyl nitroxides (III); (C)-(C')

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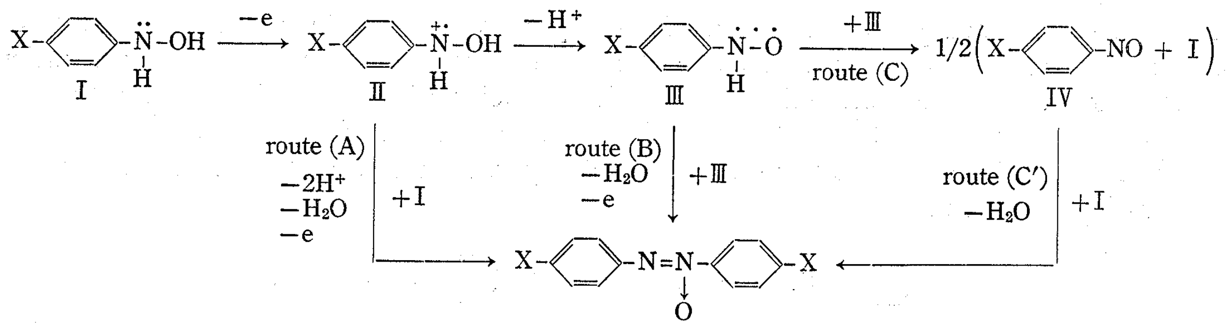
[6] *a*) G.T. Knight and M.J.R. Loadman, *J. Chem. Soc.*, (*B*), **1971**, 2107; *b*) A. Darchen and C. Moinet, *Bull. Soc. Chim. Fr.*, **1976**, 812.

the reaction of *p*-X-PHA's (I) with *p*-X-NB's (IV) formed through disproportionation of phenyl nitroxides (III).



p-X-NB's must be produced through the disproportionation of the corresponding nitroxides and not through further oxidation of the nitroxides as shown in the oxidation of alkylhydroxylamines.[2] In the chemical oxidation of *p*-X-PHA (X=H),[7] most of the generated phenyl nitroxide has been shown to decay rapidly with second-order kinetics ($k \simeq 3.4 \times 10^6\,\text{M}^{-1}$, sec.$^{-1}$), and small portion of the phenyl nitroxide shown to take place slow decay ($k \simeq 1.8\,\text{M}^{-1}$, sec.$^{-1}$), provided the concentration of *p*-X-PHA (X=H) was not more than $4 \times 10^{-3}\,\text{M}$. The slow decay was also found to be second-order in phenyl nitroxide and considered to yield azoxybenzene. The rate constant for the slower reaction of the nitroxide is still very large compared with the value for the codensation reaction in Table II, even though the difference in the solvent is taking account. In the present study the bulk concentration of the nitroxide would be more dilute compared to that in chemical reaction described above, it is, therefore, likely that most nitroxide produced decays in the rapid process. Since in the electrolysis of *p*-X-PHA (X=H), nitrosobenzene was shown to be produced almost quantitatively with a trace of azoxybenzene, the most nitroxide produced undergoes disproportionation and the condensation reaction of nitrosobenzene with *p*-X-PHA (X=H) is negligible during the electrolysis. On the other hand, fairly large amount of *pp'*-Me-AB was yielded in electrolysis of *p*-Me-PHA, although the rate constant for the condensation reaction is smaller than that of *p*-X-PHA (X=H) (Table II). This suggest that *pp'*-Me-AB should be produced through the route (A) and/or (B) rather than the route (C)-(C′). It seems likely that the electron-donating substituent such as methyl group tends to stabilize the cation radical (II) and/or the nitroxide (III),[8] therefore some part of (II) and/or (III) would undergo slow decay to form *pp'*-Me-AB besides disproportionation to form *p*-Me-NB.

In the case of *p*-Br- and *p*-Cl-PHA, the fairly high yield of the corresponding azoxybenzene will be ascribed mainly to the reaction route (C)-(C′), since the rates of the condensation reaction are larger than those for the other hydroxylamines (see Table II). Indeed, the half-lives calculated for the condensation reaction of *p*-Cl- and *p*-Br-PHA with the corresponding nitroso compounds, simply using the rate constants (Table II) and the assumed concentration of the reactions become nearly the same with the time required for exhaustive electrolysis. However, it is not clear only from the present study if *pp'*-Cl- and *pp'*-Br-AB are formed solely by the route (C)-(C′) or not, because in the anodic oxidation the concentration of each reactant cannot be estimated as in the case of homogeneous reactions since the acidity of the solution which clearly affects the rate of the condensation reaction will change with the progsess of the electrolysis.

Why and how the substituent X makes the cation radical and/or the nitroxide choose a reaction route among (A), (B), and (C)-(C′) must be clarified by the further investigation.

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Experimental

Materials——Phenylhydroxylamine,[9] p-Me-PHA,[10] and p-Cl-PHA[11] were prepared as described in the literatures. p-Bromophenylhydroxylamine was prepared by slight modification of the method of p-Cl-PHA. Nitrosobenzene,[12] p-Cl-NB,[13] p-Br-NB,[13] and p-Me-NB[14] were prepared as described in the literatures. Azoxybenzene,[6] pp'-Me-AB,[15] pp'-Cl-AB,[15] and pp'-Br-AB,[16] were prepared according to the methods described in the literatures. p-Quinoneimine[17] was prepared by the method of Willstätter, but it could not be isolated as a stable product.[18] Therefore ethereal p-quinoneimine was used as an authentic sample.

Cyclic Voltammetry——Cyclic voltammetry was performed with the same apparatus previously described.[2] The electrode system consisted of a glassy-carbon indicator electrode, a glassy-carbon counter electrode and a reference electrode, SCE. Measurements were made at 25° with substrate concentrations of *ca.* 5 mM and a concentration of supporting electrolyte, sodium perchlorate, of *ca.* 0.1 M.

Controlled Potential Electrolysis——Electrolyses were performed with the same apparatus and the procedure previously described.[2] The electrolyses were carried out at 25°±0.12° with anodic solution of 40 ml (*ca.* 1.0×10^{-2} M in the substrate) in an H-type cell of the same model as previously described.[2] The solutions in the anode were deoxygenated by bubbling nitrogen gas through them, and the electrolyses were performed in dark to prevent photo-decomposition of p-X-NB's. The quantity of electricity consumed in the electrolysis was calculated by integration of the current-time curve.

Kinetic Measurements——The rate constants for the condensation reaction of p-X-PHA's and p-X-NB's (Table II) were estimated as follows. The acetonitrile solutions containing *ca.* 10 mM p-X-PHA's and p-X-NB's and 0.1 M sodium perchlorate were adjusted to 25°±0.12° and the reactions were followed by measuring the decrease in p-X-NB's spectrophotometrically.

Product Analysis——A) Nitroso Compounds: Nitrosobenzene and p-substituted nitrosobenzenes were estimated by measuring the absorption in the visible light region. The absorption maximum and the molar extinction coefficient of these nitroso compounds in acetonitrile are $X=CH_3$ (745 nm, $\varepsilon=48.6$), $X=H$ (750 nm, $\varepsilon=44.4$), $X=Cl$ (750 nm, $\varepsilon=44.6$), $X=Br$ (748 nm, $\varepsilon=42.1$).

B) Azoxy Compounds: Azoxybenzene and p-substituted azoxybenzenes were estimated on high speed liquid chromatograph (Waters Associates Inc. Model 6000) equipped with spectrophotometric detector (J-ASCO UVIDEC-1). Analyses were performed on a column packed with BONDAPAK C_{18} using 25 μl of the electrolyzed solution. Eluent was 80% methanol. The wavelength of the spectrophotometer was adjusted to absorption maximum of each azoxybenzene, *i.e.*, for $X=CH_3$ 332 nm, $X=H$ 320 nm, $X=Cl$ 330 nm, $X=Br$ 333 nm.

C) Protonated Phenylhydroxylamine and p-Substituted Phenylhydroxylamines: They were estimated by measuring the increase in the corresponding nitroso compounds after treating the electrolyzed solution with silver oxide to oxidize the protonated p-X-PHA's to corresponding nitroso compounds.

D) p-Quinoneimine: The electrolyzed solution was condensed and examined by thin-layer chromatography to reveal the slight formation of p-quinoneimine (*Rf ca.* 0.5 in chloroform).

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