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Electroreduction of Aromatic Oximes: Diprotonation, Adsorption, Imine Formation, and Substituent Effects

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Aromatic oximes are reduced in aqueous solution in a four-electron process. The reducible species in the pH range 5−8 is a diprotonated form of the oxime. This species is generated in the course of electrolysis in the vicinity of the electrode surface from the adsorbed neutral form of the oxime. The reduction is initiated by a cleavage of the N−O bond. The diprotonation facilitates the reduction process by the preformation of OH_2^+ as a good leaving group and by a positive charge on the azomethine nitrogen. Diprotonation has been proven based on shapes of $i = f(pH)$ plots, by observed shifts of half-wave potentials with pH and by comparison with the reduction of nitrones. Some observed deviations from theoretical $i = f(pH)$ plots were attributed to the role of adsorption on the rate of protonation. Adsorption is also responsible for dips on some of the $i−E$ curves. Adsorption plays a role at concentrations as low as 1×10^{-5} M, when the electrode surface is still not fully covered. This indicates that catalyzed protonation occurs on islets of adsorbed materials. At pH 2−5 the studied oximes in the vicinity of the electrode are predominately present in a protonated form, which is less strongly adsorbed. In this pH range the protonation takes place in a homogeneous reaction layer of the electrode. It yields a monoprotonated form, which is reduced. The separation of two two-electron waves observed for some oximes in acidic media serves as an experimental proof of the formation of imines as reduction intermediates. This separation is caused by the differences in pK_a values of protonated forms of oximes and imines. The effects of substituents in the para position on the benzene ring are characterized by correlation with the Hammett substituent constant σ_x. This has been proven at pH 1.5 for substituted benzaldehyde oximes and at pH 5.0 for substituted acetophenone oximes.

Introduction

Oximes are well-known complexing agents, and the oximino group is present in some drugs, e.g., cephalosporins. Some oximes have been shown[1] to be effective antidotes, when administered to individuals affected by nerve agents, such as sarin, soman, tabun, and VX. The toxic effect of these agents is attributed to a conversion of acetylcholinesterase into anti-acetylcholinesterase. The role of oximes in the treatment of individuals exposed to nerve agents is attributed to conversion of antiacetylcholinesterase back into acetylcholinesterase. The mechanism of this reversal is currently not understood. In the treatment of the effects of nerve gases, in which the use of simple benzaldoximes proved effective, the kinetics of reactivation plays an important role. Thus the period, after which the reactivation was not possible, varied from 13 h for tabun to 3 min for soman.[2]

It is the aim of this investigation to contribute to the understanding of the solution chemistry of some oximes, particularly of their oxidation−reduction properties, follow-up reactions after the electron transfer, accompanying protonation−deprotonation equilibria, and types of intermediates. Such a

study might contribute to the elucidation of reaction steps involved in the detoxification process.

An electrochemical approach seemed promising, particularly when using mercury electrodes with their well-defined surfaces. The electroreduction of oximes at a dropping mercury electrode (DME) has been considered to be a reasonably well understood area of mechanistic organic electrochemistry.[3−5] Early polarographic studies[6−9] as well as controlled potential electrolysis[8] indicated that at a pH lower than about 7 oximes are reduced in a four-electron process yielding amines. In the pH range between 7 and 10 limiting currents of oximes gradually decrease with increasing pH. This decrease was interpreted qualitatively to be due to a protonation preceding the first electron uptake.[7−9] So far, no attempt has been made to treat this variation of currents with pH quantitatively. The number of protons transferred before the first electron uptake, which remained undetermined, is discussed here. Furthermore, a limited interest has been paid[10,11] to the effects of substituents on the reduction of substituted benzaldehyde and acetophenone oximes.

To establish the number of protons transferred to the oximes prior to the first electron uptake, three experimental approaches are discussed in this communication: (1) the shapes of plots of $i = f(pH)$; (2) the shifts of half-wave potentials with pH; and (3) comparison with the reduction of nitrones.

In the pH range where the reduction current of oximes decreases with increasing pH due to a decrease in the rate of protonation, an unusual shape of the current−voltage curves

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was observed, similar to that observed for some other heterogeneous preprotonations.[6,9,12] The limiting current, instead of reaching a constant value independent of potential, decreases with increasingly negative potentials. The role of adsorption on this type of protonation is discussed.

In principle, the electroreduction of oximes can be initiated either by the hydrogenation of the azomethine bond or by the cleavage of the N−O bond. Lund[8] proposed the second alternative, based on the difficult reduction of the hydroxylamine derivatives, which would result in the hydrogenation of the C=N bond. Experimental evidence will be presented to support the formation of an imine as a reactive intermediate, which results in the initial reductive cleavage of the N−O bond.

Experimental Methods

Electrochemical Instrumentation. Current−voltage curves were recorded by using IBM EC/225 voltammetric analyzer combined with an IBM 7424 MT X−Y−T Recorder as well as a capillary electrode with characteristics of $m = 2.5$ mg s^{-1} and $t_1 = 3.0$ s at $h = 70$ cm. A two-electrode electrolytic cell is used with a saturated calomel electrode (SCE) separated by a liquid junction (Kalousek cell).

Chemicals. Preparation and characterization of *p*-methoxybenzaldehyde oxime (**1**), *p*-methylbenzaldehyde oxime (**2**), *p*-fluorobenzaldehyde oxime (**4**), *p*-chlorobenzaldehyde oxime (**5**), *p*-bromobenzaldehyde oxime (**6**), *p*-carbmethoxybenzaldehyde oxime (**7**), *p*-trifluoromethylbenzaldehyde oxime (**8**), and *p*-cyanobenzaldehyde oxime (**9**) have been described elsewhere.[13] *p*-Hydroxyacetophenone oxime (**10**), *p*-methylacetophenone oxime (**11**), *p*-chloroacetophenone oxime (**13**), and *p*-trifluoromethylacetophenone oxime (**15**) were prepared by the following general procedure: 2 g of each of the corresponding ketones (*p*-hydroxyacetophenone, *p*-methylacetophenone, *p*-chloroacetophenone, and *p*-trifluoromethylacetophenone, all from Aldrich) were dissolved in 50 mL of methanol, and 2 mL of an aqueous solution of hydroxylamine (50% w/w) was added. The reaction mixture was heated until complete conversion of the ketone was achieved. The product was recrystallized. To prepare *p*-acetylacetophenone oxime (**14**), to 0.0112 mol of 1,4-diacetylbenzene supplied by Aldrich dissolved in 50 mL of methanol was added 0.0112 mol of hydroxylamine hydrochloride. The reaction mixture was stirred 1 week at laboratory temperature, purified by column chromatography (dichloromethane/methanol = 100:2), and recrystallized.

p-Hydroxyacetophenone oxime (**10**): Yield 1.65 g (74%), mp 144−147 °C (benzene, ethanol) (ref 14 144−145 °C). ^{1}H NMR (DMSO-d_6): 2.08 s, 3 H (CH$_3$), 6.75 d, 2 H $J(3,2) = J(5,6) = 8.8$ (H-3, H-5); 7.47 d, 2 H $J(2,3) = J(6,5) = 8.8$ (H-2, H-6); 9.62 bs, 1 H (OH); 10.85 s, 1 H (N−OH).

p-Methylacetophenone oxime (**11**): Yield 1.02 g (46%), mp 85−87 °C (chloroform, petroleum ether) (ref 15 86−88 °C). ^{1}H NMR (DMSO-d_6): 2.22 s, 3 H (CH$_3$C=NOH); 2.28 s, 3 H (CH$_3$); 7.18 d, 2 H $J(3,2) = J(5,6) = 8.5$ (H-3, H-5); 7.52 d, 2 H $J(2,3) = J(6,5) = 8.3$ (H-2, H-6); 11.05 s, 1 H (N−OH).

p-Chloroacetophenone oxime (**13**): Yield 1.28 g (58%), mp 96−97 °C (ethanol, water) (ref 15 93−95 °C). ^{1}H NMR (CDCl$_3$): 2.28 s, 3 H (CH$_3$); 7.36 d, 2 H $J(3,2) = J(5,6) = 8.8$ (H-3, H-5); 7.57 d, 2 H $J(2,3) = J(6,5) = 8.8$ (H-2, H-6); 8.85 s, 1 H (N−OH).

p-Acetylacetophenone oxime (**14**): Yield 0.14 g (7%), mp 171−174 °C (ethanol) (new compound). For C$_{10}$H$_{10}$NO$_2$ (176.07) calcd: 67.78% C, 6.26% H, 7.90% N. Found: 67.92% C, 6.49% H, 7.67% N. ^{1}H NMR (DMSO-d_6): 2.16 s, 3 H

(CH$_3$C=NOH); 2.56 s, 3 H (CH$_3$CO); 7.76 d, 2 H $J(2,3) = J(6,5) = 8.5$ (H-2, H-6); 7.94 d, 2 H $J(3,2) = J(5,6) = 8.5$ (H-3, H-5); 11.51 s, 1 H (N−OH).

p-Trifluoromethylacetophenone oxime (**15**): Yield 1.21 g (56%), mp 104−106 °C (chloroform, petroleum ether) (ref 16 105−106 °C). ^{1}H NMR (DMSO-d_6): 2.17 s, 3 H (CH$_3$), 7.71 d, 2 H $J(3,2) = J(5,6) = 8.2$ (H-3, H-5); 7.83 d, 2 H $J(2,3) = J(6,5) = 8.2$ (H-2, H-6); 11.53 s, 1 H (N−OH).

Melting point data were not corrected. The thin-layer chromatography (TLC) analyses and column chromatography were carried out on Kieselgel 60 F$_{254}$ (Merck Laboratory Chemicals). ^{1}H NMR spectra were recorded using a Varian Gemini 300 at 300.08 MHz. Chemical shifts (δ scale) are reported in ppm relative to tetramethylsilane; coupling constants (J) are given in Hz. In all cases, only one set of signals was observed in the ^{1}H NMR spectra, thus indicating the isomeric uniformity of the prepared oximes.

Benzaldehyde oxime (**3**) and 2-hydroxyimino-2-phenylacetonitrile (**17**) were supplied by Aldrich, acetophenone oxime (**12**) by Alfa Aesar, and benzophenone oxime (**16**) by Avocado Research Chemical Ltd.


#	X		#	Y		#	R
1	OCH$_3$		10	OH		16	Ph
2	CH$_3$		11	CH$_3$		17	CN
3	H		12	H			
4	F		13	Cl			
5	Cl		14	COCH$_3$			
6	Br		15	CF$_3$			
7	COOCH$_3$						
8	CF$_3$						
9	CN						

Procedures. The 0.01 M stock solutions were prepared for all studied compounds in acetonitrile. Simple buffer solutions (phosphate, acetate, borate, and NH$_3$/NH$_4$Cl) were used. The ionic strength was kept constant at $\mu = 0.2$ by addition of sodium chloride solution. Recording of $i−E$ curves was carried out in buffered solutions containing about 1% v/v acetonitrile. A stock solution of the investigated oximes, prepared daily fresh, was added to the buffered solution after deaeration, in some cases with sufficient gelatin added to prevent formation of streaming maxima. The final concentrations of the oximes were 0.1 mM, unless otherwise stated. After brief final purging by nitrogen, the current−voltage curves were recorded.

At pH < 2, where some oximes undergo acid-catalyzed hydrolysis, several $i−E$ curves were recorded in 5 min intervals. The currents reported in this pH range were obtained by extrapolation to $t = 0$. In the relatively slow hydrolysis with $\tau_{1/2}$ on the order of 15 min or more, the dependence of the four-electron reduction wave of the oxime is accompanied at more negative potential by an increase in a one-electron wave of the reduction of the carbonyl compound formed by hydrolysis.

Results and Discussion

Antecedent Protonations. As the conjugate acid has a lower overall electron density than the corresponding base, as a rule the acidic form of an acid−base couple is *always* reduced at the dropping mercury electrode at more positive potentials (i.e., easier) than the corresponding base. The difference between reduction potentials of the acidic and the basic forms is the largest when the proton transfers occur on the electroactive group, which is reduced. Let us consider an equilibrium between HA^+ and A (where HA^+ can be positively charged, negatively charged, or neutral) established in the bulk of the solution

$$HA^+ \underset{k_r}{\overset{k_d}{\rightleftharpoons}} H^+ + A \quad \text{where} \quad K_a = k_d/k_r \tag{1}$$
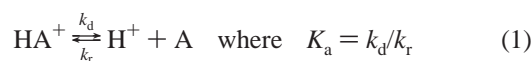
When the pH of the investigated solution is lower than the pK_a, the form HA^+ that predominates in the solution is reduced and a single wave (i_{HA^+}) is observed

$$HA^+ + ne^- \overset{k_e}{\longrightarrow} P_1 \tag{2}$$

The limiting current i_{HA^+} remains at pH $<$ pK_a independent of pH, and the half-wave potential of i_{HA} stays pH-independent, as no proton transfer takes place before the first electron uptake.

At pH $>$ pK_a, as long as the rate of recombination with the rate constant k_r in eq 1 remains faster than the rate of the reduction with the rate constant k_e (eq 2), a single reduction wave is recorded. Its limiting current, which corresponds to a transfer of *n* electrons, remains pH-independent. As the electroactive species is formed with a rate that is a linear function of the activity of the hydrogen ions, the half-wave potential ($E_{1/2}$) of the reduction wave is, in this pH range, shifted to more negative potentials with increasing pH, as additional energy is needed for conversion of A into HA^+.

With a further increase in pH, the rate of protonation with rate constant k_r in eq 1 decreases. With a gradual increase in pH, a pH range is reached, where the rate of protonation is insufficient to convert all of the base A into the more easily reducible form HA^+. In this pH range, as the rate of protonation decreases, the concentration of the reducible form HA^+ in the vicinity of the electrode decreases, and consequently the current i_{HA^+} decreases with increasing pH.

The theoretical treatment of such processes[17,18] controlled by the rate of a chemical reaction preceding the uptake of the first electron results in eq 3

$$i_{HA^+}/i_d = \frac{0.886(t_1 k_r/K_a)^{1/2}[H^+]}{1 + (0.886(t_1 k_r/K_a)^{1/2}[H^+])} \tag{3}$$

where i_{HA^+} is the limiting current measured at a given pH, i_d is the pH-independent diffusion limiting current, measured at a sufficiently low pH value, K_a is the dissociation constant of reaction 1, k_r is the rate constant of the recombination of A and H^+, and t_1 is the drop time of the electrode used.

The plot of $i/i_d = f(pH)$ has the shape of a dissociation curve (Figure 1), where the current i_{HA^+} decreases from 90% i_d to 10% i_d within about two pH units. The pH at the inflection point of this curve, where $i_{HA^+} = 0.5i_d$, is denoted as pK'.

Excluding very slowly established acid−base equilibria (as in the case of C-acids) and as long as the rate of protonation with rate constant k_r controls the limiting current, the value of pK' is always higher than that of pK_a. The difference (pK' −
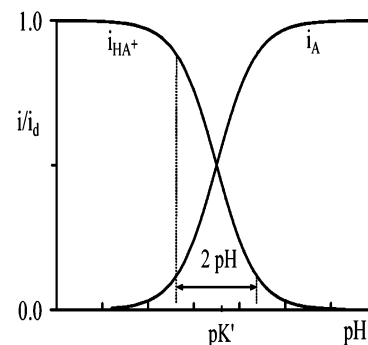
Figure 1. Theoretical shapes of the dependence of limiting currents on pH: reduction of a monobasic acid (i_{HA^+}) and its conjugate base, following eq 3.
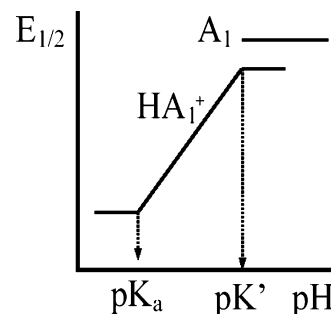
**Figure 2.** Dependence of half-wave potentials of a monobasic acid on pH.

pK_a) depends both on the value of pK_a and on that of the rate constant k_r, as shown by eq 4

$$pK' - 0.5pK_a = 0.5 \log k_r - 0.056 + 0.5 \log t_1 \tag{4}$$

The theoretical plot of the pH dependence of half-wave potentials following reactions 1 and 2, corresponding to the reduction of HA^+, consists of three linear segments (Figure 2). The intersection of the first two segments occurs at a pH close to the value of pK_a, the intersection of the second and third segment at pH $=$ pK'.

If the conjugate base A is reducible by the same number of electrons as the acid form HA^+, the reduction current of the base increases with increasing pH. The plot of $i_A = f(pH)$ has the shape of an increasing dissociation curve, with the inflection point at pH $=$ pK', following the increasing curve in Figure 1. The half-wave potential of the reduction of the basic form A remains pH-independent (Figure 2), as long as the base is not involved in another acid−base equilibrium.

If the electroactive species is a dibasic acid H_2A^{2+} that undergoes two acid−base equilibria with dissociation constants K_1 and K_2, then the situation is more complex

$$H_2A^{2+} \rightleftharpoons HA^+ + H^+ \quad K_1 \tag{5}$$

$$HA^+ \rightleftharpoons A + H^+ \quad K_2 \tag{6}$$
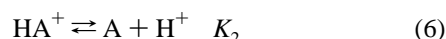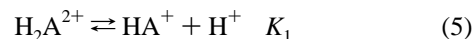
For the reduction of the diprotonated species H_2A^{2+}, provided that $pK_1 \ll pK_2$ and that pK_1' is larger than pK_2 (where pK_1' equals pH where $i_{H_2A^{2+}} = 0.5i_d$), the limiting current $i_{H_2A^{2+}}$ of the reduction of the diprotonated form H_2A^{2+} follows[19] eq 7

$$i_{H_2A^{2+}}/i_d = \frac{0.886(t_1 k_r/K_a)^{1/2}\{[H^+]^2/([H^+] + K_2)\}}{1 + (0.886(t_1 k_r/K_a)^{1/2}\{[H^+]^2/([H^+] + K_2)\})} \tag{7}$$

In this case the plot of $i_{H_2A^{2+}}/i_d = f(pH)$ also has the shape of a

6788 *J. Phys. Chem. B, Vol. 110, No. 13, 2006*

Celik et al.
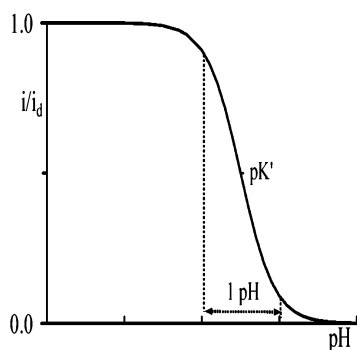
Figure 3. Theoretical shapes of the dependence of limiting currents on pH: reduction of a dibasic acid H_2A^{2+} following eq 7.
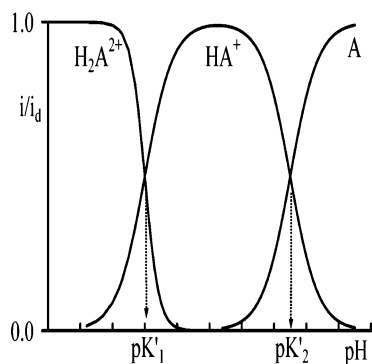
Figure 4. Theoretical plots of dependences of limiting currents of a dibasic acid in cases that all three acid forms, H_2A^{2+}, HA^+ and A, are reducible by the same number of electrons.

dissociation curve, but this curve is steeper than that following eq 3, as shown in Figure 3. For the reduction of H_2A^{2+} the current decreases from $i_{H_2A^{2+}} = 0.9i_d$ to $i_{H_2A^{2+}} = 0.1i_d$ within a single pH unit.

Provided that the forms HA^+ and A are also reducible within the available potential range and furthermore provided that the reduction of all three species (H_2A^{2+}, HA^+, and A) involves a transfer of the same number of electrons, the plots of dependences of all three forms on pH follow shapes depicted in Figure 4. The increasing segment of the curve for HA^+ (similar to the decreasing one for H_2A^{2+}) is steep and corresponds to eq 7, whereas the decreasing portion of the curve for HA^+ and the increasing part for A are less steep and follow eq 3.

Reduction of Oximes. Equations 3 and 7 were derived for protonations taking place in a homogeneous solution in the vicinity of the surface of the dropping mercury electrode. In the pH range where the protonation is not extremely fast, the $i-E$ curves show a decrease of limiting currents with increasing pH. The resulting current−voltage curves have the shape of a wave with a well-developed plateau, where the limiting current remains independent of the applied potential (Figure 5a).

The current−voltage curves with a well-developed plateau were observed in 0.1 mM solutions only for some oximes, for example *p*-carbmethoxybenzaldehyde oxime (**7**), *p*-cyanoben-zaldehyde oxime (**9**) (Figure 5a), benzophenone oxime (**16**), and 2-hydroxyimino-2-phenylacetonitrile (**17**). For these compounds the variations of limiting currents with pH were in agreement with eq 7.

For numerous oximes the currents at a given pH after reaching a maximum value (i_{max}) first decrease and then increase with increasingly more negative potentials (Figures 5b and 5c). This "dip" is caused by adsorption and is discussed below. The depth of the dip decreases with decreasing concentration of the oxime.
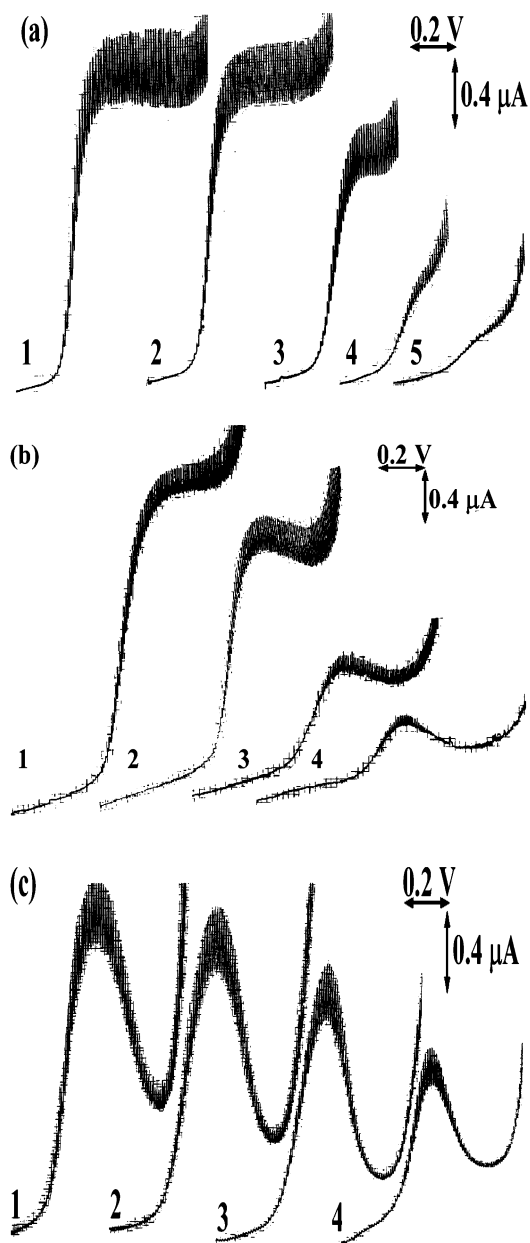

Figure 5. Dependence of polarographic current−voltage curves of 1 × 10^{-4} M solution of oximes on pH. (a) *p*-Cyanobenzaldehyde oxime (**9**); (b) *p*-hydroxyacetophenone oxime (**10**); (c) *p*-chloroacetophenone oxime (**13**). pH values: (a) (1) 6.8, (2) 7.0, (3) 7.8, (4) 8.4, (5) 9.3; (b) (1) 5.8, (2) 6.8, (3) 7.45, (4) 7.75; (c) (1) 6.95, (2) 7.3, (3) 7.55, (4) 7.75. Starting potentials: (a) (1−3) −0.5 V; (4−5) −0.6 V; (b) (1−2) −0.7 V; (3−4) −0.8 V; (c) −0.7 V.

At low concentrations of some oximes it is possible to verify the application of eq 7. Nevertheless, in some instances the dip was observed even at concentrations lower than 5 × 10^{-6} M oxime.

The testing was therefore restricted to oximes, such as *p*-hydroxyacetophenone oxime (**10**), where the dip was absent in 2 × 10^{-5} M solutions. For such compounds a good fit to eq 7 was observed (Figure 6). The fit was worse at pH > (pK' + 0.5). This was caused by the limited accuracy of the measurement of currents on the order of 0.08 μA. The low accuracy of the measurement of currents is due to the charging current. It was not possible to use the common approach for the elimination of this effect by using differential pulse or square wave polarography because the peak currents were dependent not only on the concentration of the species transported toward the

Electroreduction of Aromatic Oximes

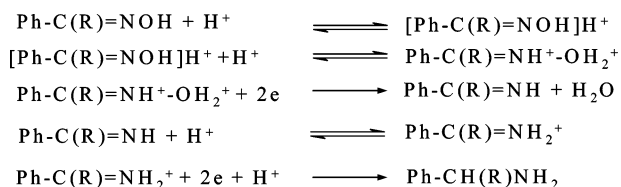*J. Phys. Chem. B, Vol. 110, No. 13, 2006* **6789**
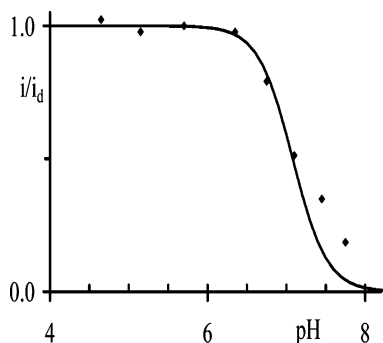
Figure 6. Theoretical curve following eq 7 and experimental points for dependence of limiting currents of a 2×10^{-5} M solution of *p*-hydroxyacetophenone oxime **10** on pH.

Figure 7. Four linear segments (A, B, C, and D) of the dependence of half-wave potentials of the reduction of oximes on pH.

electrode but were also affected by the rate of the electrode process, which is sensitive to adsorption.

Thus all above evidence based on the dependence of $i/i_d = f(\text{pH})$ indicates that at pH 5–8 a transfer of two protons is taking place before the first electron uptake. The reduction of the diprotonated species follows Scheme 1.

SCHEME 1: Electrochemical Reduction of Diprotonated Oximes at pH 5–8

$$\text{Ph-C(R)=NOH} + \text{H}^+ \rightleftharpoons [\text{Ph-C(R)=NOH}]\text{H}^+$$

$$[\text{Ph-C(R)=NOH}]\text{H}^+ + \text{H}^+ \rightleftharpoons \text{Ph-C(R)=NH}^+\text{-OH}_2^+$$

$$\text{Ph-C(R)=NH}^+\text{-OH}_2^+ + 2e \longrightarrow \text{Ph-C(R)=NH} + \text{H}_2\text{O}$$

$$\text{Ph-C(R)=NH} + \text{H}^+ \rightleftharpoons \text{Ph-C(R)=NH}_2^+$$

$$\text{Ph-C(R)=NH}_2^+ + 2e + \text{H}^+ \longrightarrow \text{Ph-CH(R)NH}_2$$

As the reduction of imine occurs (at pH > 2) always at more positive potentials than the reduction of oximes, a single four-electron wave is observed. (Behavior at pH < 2 will be discussed below.) There are two driving forces for the reduction of the diprotonated form: (a) the presence of hydrogen ion on the oxygen, which results in the formation of a good leaving group (H_2O) and (b) the presence of a positive charge on the nitrogen that contributes to the facilitation of the cleavage of the N–O bond, which is preferred to the hydrogenation of the azomethine bond.

Additional evidence for the transfer of more than one proton before the electron uptake is based on shifts of half-wave potentials with pH. For irreversible reductions at a constant ionic strength such shifts with increasing pH to more negative potentials are given by eq 8

$$dE_{1/2}/d\text{pH} = 2.3p\text{RT}/\alpha n\text{F} \tag{8}$$

where p is the number of protons transferred before the uptake of the first electron, α is the transfer coefficient, and n is the number of electrons transferred in the potential-determining step. Assuming that within the pH range studied the value of the transfer coefficient can be considered constant, then at 25 °C

$$dE_{1/2}/d\text{pH} = 0.059p/\alpha n \tag{9}$$

Thus any shift $dE_{1/2}/d\text{pH}$ between 0.06 and 0.12 V indicates a reaction of the electroactive species with two protons before the transfer of the first electron. For all investigated oximes (Table 1) the plots of $E_{1/2} = f(\text{pH})$ consist of several linear segments. There can be up to four such segments, denoted A, B, C, and D (Figure 7). The segments A and D are observed in pH ranges where the half-wave potentials are pH-independent
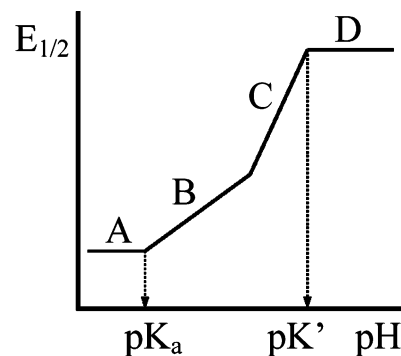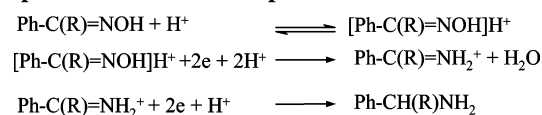
(see above). However, for some oximes the segment A and/or D is beyond the investigated pH range.

Theoretical treatment of shifts of half-wave potentials with pH for a four-electron reduction antecedent by two acid–base equilibria is currently not available, but the following deductions can be made: The slope $dE_{1/2}/d\text{pH}$ within segment C (observed in most instances approximately between pH 4 and 9) varies between 62 and 94 mV/pH for substituted benzaldehyde oximes and between 76 and 94 mV/pH for substituted acetophenones (Table 1). This corresponds to a transfer of two protons before the uptake of the first electron. This attribution is further supported by the agreement of the pH at segments C and D (Figure 7) denoted pK' and the value of pK' obtained from $i/i_d = f(\text{pH})$ plots.

The slope $dE_{1/2}/d\text{pH}$ within segment B varies between 42 and 58 mV/pH for substituted benzaldehyde oximes and between 43 and 64 mV/pH for substituted acetophenone oximes as corresponds to a transfer of a single proton (Table 1). Furthermore, the pH at the intersection between segments A and B corresponds to the pK_a of the monoprotonated form of the oxime determined spectrophotometrically, as discussed in detail elsewhere.[20]

Thus at pH 2–5 the reduction of oximes follows the sequence in Scheme 2.

SCHEME 2: Electrochemical Reduction of Monoprotonated Oximes at pH Lower than 5

$$\text{Ph-C(R)=NOH} + \text{H}^+ \rightleftharpoons [\text{Ph-C(R)=NOH}]\text{H}^+$$

$$[\text{Ph-C(R)=NOH}]\text{H}^+ + 2e + 2\text{H}^+ \longrightarrow \text{Ph-C(R)=NH}_2^+ + \text{H}_2\text{O}$$

$$\text{Ph-C(R)=NH}_2^+ + 2e + \text{H}^+ \longrightarrow \text{Ph-CH(R)NH}_2$$

Therefore, the pH at the intersection of segments B and C corresponds to a pH at which the predominant mechanism is changed from the reduction of the monoprotonated form to a reduction of a diprotonated form. To explain why at a lower pH a monoprotonated form predominates, whereas at pH 5–9 that of the diprotonated one is predominating, the role of adsorption must be considered.

At pH < 5 most of the investigated oximes exist at least partly in a protonated form, which is not strongly adsorbed. The protonation takes place in a homogeneous reaction layer in the vicinity of the electrode surface. In such a homogeneous reaction in this pH range approximately between 0 and 5 the rate is not sufficiently fast to produce the reducible diprotonated form.

In the pH range approximately between 5 and 8 the unprotonated form of the oxime is present in the bulk of the solution. This form is strongly adsorbed at the surface of the electrode. In the adsorbed state a sufficient number of basic centers are
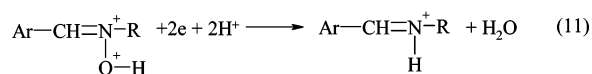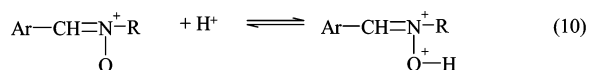
TABLE 1: Slopes of Dependences of $E_{1/2}$ on pH for 1×10^{-4} M Substituted Aromatic Oximes

	no.	pH range	slope	$-E°^a$ (V)		no.	pH range	slope	$-E°^a$ (V)
p−X−ArCH=NOH					*p*−Y−ArC(CH$_3$)=NOH				
X = OCH$_3$	1	(−1.0, 1.5)	0.0	0.650	Y = OH	10	(−1.0, 1.5)	0.0	0.835
		(1.5, 4.5)	0.052	0.579			(1.5, 4.5)	0.064	0.729
		(4.5, 7.0)	0.075	0.471			(4.5, 7.0)	0.078	0.658
		(7.5, 8.5)	0.0	1.055			(7.0, 8.0)	0.0	1.220
X = H	3	(−1.0, 1.0)	0.0	0.560	Y = CH$_3$	11	(−1.0, 1.0)	0.0	0.730
		(1.0, 3.5)	0.060	0.517			(1.0, 3.5)	0.053	0.691
		(3.5, 6.7)	0.097	0.380			(3.5, 7.5)	0.079	0.615
		(6.7, 8.0)	0.0	1.050			(7.5, 8.5)	0.0	1.220
X = F	4	(−0.5, 2.0)	0.0	0.650	Y = H	12	(−1.0, 1.0)	0.0	0.770
		(2.0, 4.7)	0.079	0.492			(1.0, 4.7)	0.061	0.677
		(4.7, 7.0)	0.098	0.417			(4.7, 7.0)	0.091	0.550
		(7.0, 8.0)	0.0	1.105			(7.0, 8.5)	0.0	1.220
X = Br	6	(−1.0, 0.0)	0.0	0.480	Y = Cl	13	(−1.0, 0.5)	0.0	0.655
		(0.0, 5.0)	0.055	0.477			(0.5, 3.0)	0.042	0.635
		(5.0, 7.5)	0.088	0.316			(3.0, 7.3)	0.079	0.538
		(7.5, 8.5)	0.0	1.000			(7.3, 8.3)	0.0	1.125
X = COOCH$_3$	7	(−1.0, 8.0)	0.062	0.392	Y = COCH$_3$	14	(−1.0, 0.5)	0.0	0.425
		(8.0, 9.0)	0.0	0.900			(0.5, 3.0)	0.087	0.384
X = CF$_3$	8	(−0.5, 2.0)	0.048	0.460			(3.0, 8.0)	0.051	0.482
		(2.0, 7.5)	0.082	0.411	Y = CF$_3$	15	(0.0, 3.5)	0.043	0.639
X = CN	9	(−1.0, 2.5)	0.047	0.394			(3.5 −7.0)	0.092	0.477
		(2.5, 7.7)	0.070	0.338			(7.0, 8.0)	0.0	1.120
		(7.7, 9.5)	0.0	0.930					
					ArC(R)=NOH				
					R = Ar	16	(−1.0, 2.0)	0.020	0.541
							(2.0, 4.7)	0.050	0.481
							(4.7, 8.5)	0.081	0.337
							(8.5, 9.5)	0.0	1.040
					R = CN	17	(−1.0, 2.0)	0.068	0.324
							(2.0−7.5)	0.111	0.251
							(7.5, 8.5)	0.0	1.100

^{a} Value of potential extrapolated to pH 0.0.

available on which the diprotonated form is generated in what can be denoted as a heterogeneous catalytic process.

Another example of the cleavage of the N−O bond with positive charges on both the nitrogen and the adjacent oxygen atoms is the polarographic reduction of nitrones.[9] For these *N*-alkyl oxime derivatives it has been proved that the first reduction step consists of two-electron reductive cleavage of the N−O bond. As the half-wave potentials of the first two-electron reduction step are shifted to more negative values with increasing pH, a protonation of the oxygen in nitrone (eq 10) must take place before the electron uptake and cleavage of the N−O bond (eq 11)

$$\text{Ar−CH=}\overset{+}{\text{N}}\text{−R} + \text{H}^+ \rightleftharpoons \text{Ar−CH=}\overset{+}{\text{N}}\text{−R} \qquad (10)$$
$$\underset{\text{O}}{|} \qquad\qquad \underset{\text{O−H}}{|}{}^{+}$$

$$\text{Ar−CH=}\overset{+}{\text{N}}\text{−R} + 2e + 2\text{H}^+ \longrightarrow \text{Ar−CH=}\overset{+}{\text{N}}\text{−R} + \text{H}_2\text{O} \qquad (11)$$
$$\underset{\text{O−H}}{|}{}^{+} \qquad\qquad\qquad \underset{\text{H}}{|}$$

Even if the authors[9] correctly presented the reduction scheme, they did not realize the importance of the evidence of formation and reduction of a species with two positive charges on adjacent N and O atoms.

Further support of the initial reduction of the N−O bond in the diprotonated species is offered by the comparison with electroreduction of hydrazones and hydrazonium ions. For these compounds it has been recently proved[21,22] that they follow similar reduction pattern, where the reduction is initiated by attack on a species bearing two positive charges on adjacent heteroatoms.

Currents with a Dip. As mentioned briefly above, the current−voltage curves of numerous oximes have an unusual

shape. After a maximum value (i_{max}) is reached, a dip of the current is observed on i−E curves (Figures 5b and 5c). As the presence and depth of this dip (i_{dip}) depends also on the concentration of the oxime, the role of variations of several parameters was in this study compared at the same (0.1 mM) concentration of studied oximes. The portion of the dip, where the recorded current decreases with increasingly negative potentials, can be attributed to adsorption phenomena. Such current dips on the current−voltage curves were previously reported for reductions of some oximes[6,9,12] and anions[23] and in the presence of some surface-active substances.[24] Formation of the dip was in the past attributed to either the role of an absorbate on the rate of antecedent reactions[23] or the effects of the double-layer composition.[12]

To compare dependences of currents on pH at several points at the decreasing portion of the dip, it is not advantageous to measure the currents simply at chosen constant potentials. At pH < pK' the half-wave potentials are, namely, still pH-dependent, and the i−E curves are shifted to more negative potentials with increasing pH. Thus, in addition to i_{max} and i_{dip}, a current was measured at potentials by X volts more negative than the half-wave potential. Such current is denoted $i_{dip}(-X)$. At pH > pK', where the half-wave potential is pH-independent, $i_{dip}(-X)$ was thus measured at a constant potential.

The shapes of $i_{dip}(-X) = f(\text{pH})$ plots were similar for currents measured at $-X = -0.15$, -0.20, and -0.30 V (Figure 8). Nevertheless, for currents measured at increasingly negative potentials, the i−E curves were shifted along the pH axis toward lower pH values. Hence the value of the pK' becomes smaller with the increasingly more negative potential at which the current $i_{dip}(-X)$ was measured. As the value of pK_a in eq 4 remains constant, a shift of pK' toward lower values results in

Electroreduction of Aromatic Oximes

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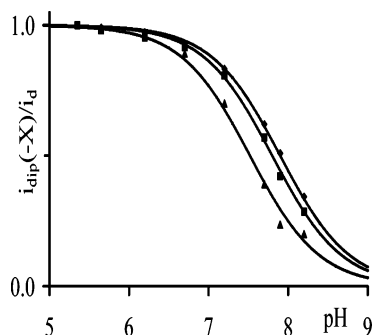
Figure 8. Dependence of limiting currents inside the dip [$i_{dip}(-X)$] on the current−voltage curve of a 1×10^{-4} M solution of *p*-bromobenzaldehyde oxime (**6**) on pH. X: ◆, −0.15 V; ■ −0.20 V; ▲ −0.30 V.
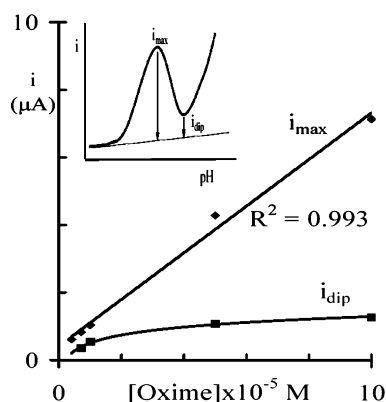

Figure 9. Dependence of currents i_{max} and i_{dip} obtained with a solution of *p*-methoxybenzaldehyde oxime (**1**) in a phosphate buffer pH 7.75 on the concentration of oxime **1**. Inset: Shape of the current−voltage curve.

TABLE 2: Dependence of the Depth of the Dip on $i-E$ Curves on Concentration of Reduced Oximes

compounds	no.	pH	[oxime] $\times 10^5$ M				
$p-OCH_3-C_6H_4CH{=}NOH$	**1**	7.75	10	5	1	0.7	0.4
i_{dip}/i_{max}			0.19	0.25	0.52	0.60	0.84
$p-OH-C_6H_4C(CH_3){=}NOH$	**10**	6.75	10	5	3	2	1
i_{dip}/i_{max}			0.68	0.78	0.83	0.97	1.00

a decrease of the difference ($pK' - pK_a$). This smaller difference, according to eq 4, is indicative of a lower rate of protonation with a rate constant k_r. The decrease of the current from the value of i_{max} to that of i_{dip} is thus due to a decrease in the rate of protonation of the oxime, which is attributed to changes in adsorption. A similar shift of $i = f(pH)$ curves has been observed[9] for the reduction of nitrones.

As mentioned briefly above, the ratio i_{dip}/i_{max} increases with the decreasing concentration of the oxime (Table 2). Whereas current i_{max} remains a linear function of the concentration of the oxime, the current i_{dip} reaches a limiting value with increasing concentration (Figure 9). This supports the interpretation that the decrease of current in the potential area, where the dip is observed, is an effect of adsorption. The current i_{max} under conditions that (i_{max}/i_d) > 0.70 is a linear function of $h^{1/2}$ (where h is the height of the mercury column). This proves that under these conditions i_{max} is limited by diffusion. However, the current i_{dip}, when (i_{max}/i_d) < 0.3, is a linear function of h. This corresponds to an adsorption-controlled current that is dependent on the surface area of the electrode. At low concentrations of the oxime, for example, lower than 5×10^{-5} M for reduction of *p*-methoxybenzaldehyde oxime (**1**), the current (in the
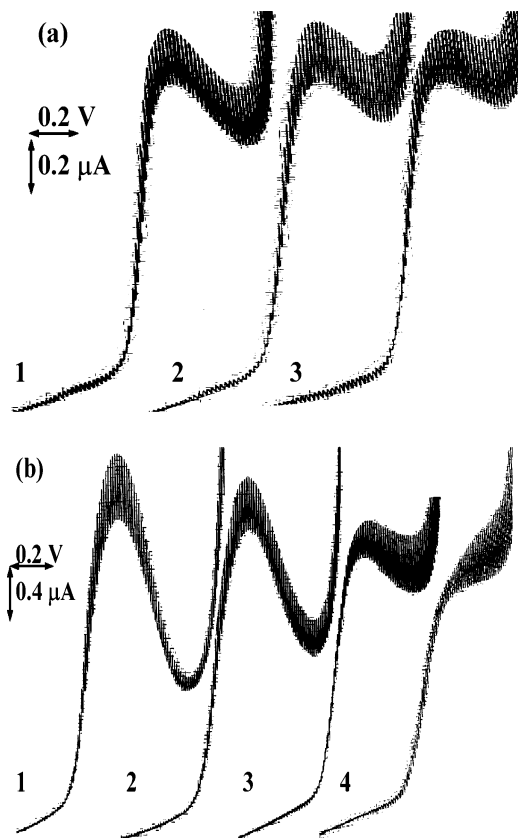
Figure 10. Dependence of polarographic current−voltage curves of a 1×10^{-4} M solution of (a) *p*-hydroxyacetophenone oxime (**10**) in a phosphate buffer pH 6.75 and (b) *p*-methoxybenzaldehyde oxime (**1**) in a phosphate buffer pH 7.25 on addition of a surfactant. Concentration of added gelatin: (a) (1) 0.002%, (2) 0.003%, (3) 0.004%; (b) (1) 0.0%, (2) 0.003%, (3) 0.006%, (4) 0.010%. Starting potentials: (a) −0.3 V, (b) −0.5 V.

potential range where at higher concentrations a dip is observed) is practically independent of h. Such current is thus controlled by the rate of protonation.

An additional proof of the role of adsorption is the change in the shape of the current−voltage curve in the presence of some surface-active substances, such as gelatin.[24] When the concentration of the gelatin is increased, the depth of the dip, characterized by the difference ($i_{max} - i_d$), decreases (Figure 10).

When the dip is small and i_{dip}/i_{max} > 0.7, then addition of gelatin does not practically affect the current i_{max} (Figure 10a). In such cases the dependence of i_{max}/i_d on pH follows eq 7, both in the absence and in the presence of gelatin. This has been observed, for example, for *p*-carbmethoxybenzaldehyde oxime (**7**). Under such conditions the effect of adsorption is relatively small, and conditions for diprotonation resemble those in the homogeneous reaction layer in the vicinity of the electrode, and the assumptions, under which eq 7 was derived, are valid.

When the dip, however, is deep and i_{dip}/i_{max} < 0.6 (Figure 10b), the addition of gelatin has two effects, (a) a decrease in i_{max} and (b) a considerable increase in current i_{dip}, so that the depth of the dip, i.e., $i_{max} - i_{dip}$, becomes smaller. For oximes, where such changes in the shape of $i-E$ curves were observed, as, for example, for *p*-methoxybenzaldehyde oxime (**1**) and acetophenone oxime (**12**), the addition of a sufficiently large amount of gelatin results also in a current−voltage curve exhibiting a plateau. Such limiting currents (at a pH where the current is less than 20% of the diffusion-controlled current) are

TABLE 3: Variation of the Depth of Dips on $i-E$ Curves of 1×10^{-4} M Oximes with the Nature of Substituents[a]

	no.	i_{dip}	i_{dip}/i_{max}	$\Delta = i_{max} - i_{dip}$
		p−X−C$_6$H$_4$CH=NOH		
X = OCH$_3$	1	1.70	0.13	11.08
X = H	3	5.74	0.57	4.36
X = F	4	6.14	0.60	4.16
X = Br	6	3.96	0.30	9.31
X = COOCH$_3$	7	14.26	1.00	0.00
X = CF$_3$	8	14.45	0.66	4.95
X = CN	9	11.80	1.00	0.00
		p−Y−C$_6$H$_4$C(CH$_3$)=NOH		
Y = OH	10	11.50	0.86	1.92
Y = CH$_3$	11	6.39	0.55	5.33
Y = H	12	9.70	0.72	3.76
Y = Cl	13	1.49	0.13	9.80
Y = CF$_3$	15	12.08	0.73	4.55
		C$_6$H$_5$C(Z)=NOH		
Z = H	3	5.74	0.57	4.36
Z = CH$_3$	12	9.70	0.72	3.76
Z = Ph	16	5.94	0.58	4.36
Z = CN	17	13.46	1.00	0.00

[a] Depths are expressed both as i_{dip}/i_{max} and as $\Delta = i_{max} - i_{dip}$.

practically independent of mercury pressure h, and the current is thus controlled by the rate of protonation.

Thus, the adsorption of gelatin competes with the adsorption of the oxime. Desorption of the oxime results in an increased rate of protonation that becomes faster than diffusion. This causes diminishing of the difference ($i_{max} - i_{dip}$). For *p*-hydroxyacetophenone oxime (**10**), where $i_{max}/i_d = 0.65$, the situation lies between the two extremes. The dependence of i_{max}/i_d on pH recorded in the absence of gelatin follows eq 3, demonstrating the predominant role of the adsorption. In the presence of 0.006% gelatin in the studied solution of oxime **10**, the competitive adsorption of gelatin is sufficiently strong, so that the dependence of i_{max}/i_d on pH follows eq 7 and proves the addition of two protons before the first electron uptake.

To test the existence of a relationship between the quantities which characterize the dip and the structure of the oxime,

variations of three experimental data with structure were compared in 0.1 mM solutions of oximes in conventional buffers: (a) the current i_{dip} measured at the lowest point of the $i-E$ curve, (b) the ratio i_{dip}/i_{max}, and (c) the difference $i_{max}-i_{dip}$ (Table 3). None of these quantities has shown correlation with Hammett substituent constants.[25] This indicates that the adsorption responsible for the formation of the dip on the $i-E$ curve is not a simple function of distribution of the electron density in the oxime.

The effect of adsorption was observed in a solution of oximes at concentrations as low as 1×10^{-5} M. Complete coverage of the surface of mercury drops for molecules of comparable molecular size was usually observed at concentrations larger than 1×10^{-4} M. This indicates that the decrease in the rate of protonation of oximes takes place even under conditions when the surface of the mercury drops is not completely covered by a monolayer of the adsorbate.

The rising current at potentials that are more negative than those at the minimum of the dip can be affected not only by desorption but also by a consecutive reduction of a less protonated form of the oxime or by a reduction of a component of the supporting electrolyte. Hence no information is available concerning the width of the dip and its dependence on pH or concentration of the oxime. The potential E_i at which the current starts to decrease to reach its minimum value has very little dependence on pH (Table 4) or the nature of the substituent on studied oxime. But the value of E_i is similar for all para-substituted benzaldehyde oximes (-1.24 ± 0.01 V). This is more positive than the value $E_i = (-1.33 \pm 0.03$ V) observed for para-substituted acetophenone oximes. This difference indicates that the structure and properties of the adsorbate are less affected by the presence of a substituent on the aromatic ring than by the substitution in the side chain.

When the current−voltage curves obtained with 0.1 mM solutions of oximes were recorded in conventional buffers, only some of the $i_{max}/i_d = f(pH)$ plots fitted eq 7 (Table 5). In numerous cases such plots have shown a good fit to eq 7 only at pH < pK', whereas at pH > pK' deviations from the

TABLE 4: Potentials Obtained from $i-E$ Curves of 1×10^{-4} M Oximes at Which the First Decrease of Current Was Observed

p−X−C$_6$H$_4$CH=NOH	no.	pH	$-E_i$ (V)	p−Y−C$_6$H$_4$C(CH$_3$)=NOH	no.	pH range	$-E_i$ (V)
X = OCH$_3$	1	5.65	1.31	Y = OH	10	6.80	1.38
		5.80	1.29			7.05	1.36
		6.20	1.27	Y = CH$_3$	11	6.70	1.38
		6.80	1.22			7.25	1.34
		7.45	1.20			7.75	1.34
		7.75	1.19			8.20	1.37
		8.00	1.19	Y = H	12	6.25	1.37
		8.30	1.19			6.70	1.33
		8.00	1.25			7.30	1.33
		8.30	1.25			7.75	1.33
X = H	3	5.70	1.25	Y = Cl	13	5.66	1.34
		6.22	1.22			6.20	1.31
		6.55	1.21			7.00	1.26
		7.00	1.20			7.45	1.25
		7.30	1.20			7.75	1.25
X = F	4	5.70	1.25			8.00	1.25
		5.90	1.25			8.00	1.29
		6.80	1.25			6.87	1.27
		7.30	1.25	Y = CF$_3$	15	6.70	1.25
X = Br	6	5.65	1.35			6.80	1.25
		6.20	1.31			7.80	1.25
		6.70	1.24			8.30	1.29
		7.70	1.17	Y = C$_6$H$_5$C(C$_6$H$_5$)=NOH	16	7.05	1.25
		7.90	1.17			7.32	1.22
		8.30	1.24			7.70	1.18
X = CF$_3$	8	5.60	1.20			8.25	1.30
		5.80	1.20			8.67	1.20
		6.70	1.14			8.82	1.14

TABLE 5: Dependence of Currents on pH Measured at Chosen Potential Differences (Δ) Relative to the Half-Wave Potential for Various Oximes[a]

compounds	no.	best fitted equation			
		−0.3 V	−0.2 V	−0.1 V	at i_{max}
benzaldehyde oximes					
p-OCH$_3$	**1**	7	7−3	7−3	3
H	**3**	7	3	3	3
p-F	**4**	3	3	3	3
p-Br	**6**	7	3	3	3
p-CF$_3$	**8**	7	7	7	7−3
acetophenone oximes					
p-OH	**10**		7	3	7−3
p-CH$_3$	**11**				3
H	**12**		3	3	3
benzophenone oxime					
	16	7	7	7	7

[a] The number of the better fitting equation, eq 3 or 7, is given. The symbol 7−3 indicates cases where both eq 3 and 7 show a similarly good fit.

theoretical plot based on eq 7 were observed. In some cases a greater part of the plot of $i_{max}/i_d = f(\text{pH})$ fitted better when eq 3 was used for the measured i_{max}.

For similar observations obtained for related reductions of hydrazones it has recently been shown[26] that at least part of the deviations from eq 7 is due to the choice of the buffer used. The measured i_{max} depends not only on pH but also on the kind and concentration of the buffer. The protonation of the hydrazone can, namely, result not only by interaction of the conjugate base with hydrogen ions but also by reaction with the acid component of the buffer, in analogy with general acid catalysis. Such dependence of limiting currents on kind and concentration of the buffer was earlier reported for reductions of some aldehydes[27] and deoxybenzoins.[28] Nevertheless, for oximes with $i_{dip}/i_{max} < 0.6$, for example, *p*-methoxybenzaldehyde oxime, the currents at a given pH were not dependent on the kind and concentration of the buffer. Thus, for the reduction of some oximes, the deviations from the plots using eq 7 and in some instances resemblance to the plots corresponding to eq 3 can be attributed to the strong effects of adsorption.

Diprotonation. It is proposed that the reduction of all oximes between pH 5 and 8 occurs in the diprotonated form following Scheme 1. This is in some cases supported by both the i−pH plots and $E_{1/2}$−pH plots, in some only by the latter. Reduction of *N*-alkyloximes (nitrones)[9] supports such process. Deviations from the i−pH plots corresponding to Scheme 1 can be attributed, as mentioned above, to a predominant role of adsorption rather than that of the effect of the double layer.

As there is currently no rigorous treatment available for electrode processes in which a chemical reaction takes place on a material adsorbed at the electrode surface, only qualitative discussion is possible. Two aspects will be discussed here, which may be responsible for the observed differences among studied oximes. One is the number and accessibility of the groups accepting protons at the surface, which are in such a distance from the electrode surface that they can be reduced. The other is the validity of the condition $pK_1 \ll pK_2 \ll pK_1'$ (where pK_1' equals pH where $i_{max} = 0.5i_d$) that must be fulfilled to apply eq 7 manifested by the steep dissociation curve. Even when the sequence of pK_1, pK_2, and pK_1' can be confirmed for reaction in homogeneous solutions, it is uncertain whether they are fulfilled for reactions when the conjugate base is adsorbed. Both these conditions would assume knowledge of the surface coverage by the basic form of the oxime.

The role of adsorption on the shape of i−E curves of some oximes even at concentrations lower than 0.01 mM indicates that rather than an established monolayer the increased rate of protonation can take place on adsorbed islets. These can grow both vertically and horizontally.

The differences between the coverage by individual oximes, which are not due to simple differences in electron distribution as manifested by the absence of a relationship to substituent constant σ, may be due to different orientation of the adsorbed molecule at the electrode surface (in extremes parallel with or perpendicular to the electrode surface) or due to differences in hydrophobicity or in the ability to form charge-transfer complexes.

The occurrence of two adjacent positively charged heteroatoms has recently been reviewed,[29] but no experimental evidence has been reported prior to this observation of diprotonated oximes as reaction intermediates in electrode processes. It can be concluded that, based both on experimental and supporting evidence, there is a strong indication that at pH 5−9 oximes can be reduced electrochemically in a diprotonated form.

Proof of Imine Intermediate. According to Scheme 1, the reduction of oximes involves an imine as an intermediate. The formation of such an intermediate was proposed earlier by Lund,[8] with some evidence presented later[28] for such intermediate. More recently[21] direct experimental evidence has been presented for the formation of imines as intermediates in the reduction of related hydrazones. The proof was based on comparison of reduction waves of some hydrazones with those of imines, which were sufficiently stable between pH 5 and 11. Formation of imine intermediates was further supported by a comparison of the pH dependence of current−voltage curves of some hydrazones with those of nitrones.

The reduction of fluorenone imine, the most stable studied imine, takes place over the pH range between 5 and 11 at potentials more positive than those of the reduction of fluorenone oxime,[21] which is thus reduced in a single four-electron wave. This prevents obtaining evidence of a formation of imine intermediates in the same way for oximes as has been carried out for hydrazones.[21] An indirect proof for imine formation was presented[8] for testesterone propionate oxime. This was based on preparative electrolysis of the oxime, which yielded testosterone propionate, which was considered to be a product of hydrolysis of the imine.

In the present approach the evidence for the formation of an intermediate imine is based on the behavior of some oximes in acidic media. The separation of two two-electron waves at pH 1.0−3.0 was reported for benzophenone oximes bearing the following substituents: 2,4-dihydroxy,[30] 2-hydroxy-5-chloro, 4-fluoro, and 4,4'-difluoro,[31] 2-carboxy,[32] and 2,4-dihydroxyacetophenone oxime.[33] In 50% (w/w) H$_2$SO$_4$ H_0 −3.38, a splitting of two waves was reported even for the unsubstituted benzophenone oxime.[7] Attributing the observed splitting to hydrogen bonding[5] is very unlikely in view of the occurrence of splitting even in the absence of substituents that would be potentially available for an intramolecular hydrogen bond formation. Furthermore, the energy of a hydrogen bond formation is too small to account for the observed difference in potentials. Finally in aqueous solutions the formation of intermolecular hydrogen bonds is preferred to that of intramolecular ones.

In a recent review[5] it was stated that the more negative wave, observed in acidic solutions of oximes, corresponds to the reduction of an imine. The importance of the separation of two waves in the reduction of some oximes as an experimental
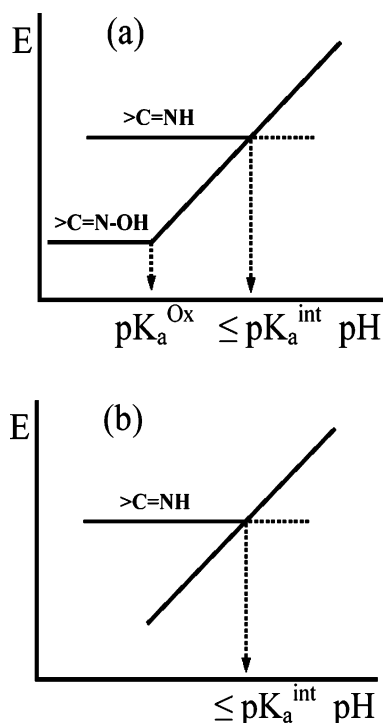
Figure 11. Dependence of the half-wave potentials of the reduction of oximes and imines on pH: (a) when pK_a^{Ox} is within the investigated acidity range; (b) when pK_a^{Ox} is lower than the highest acidity investigated.

evidence of the formation of an imine (as an intermediate) has not been stressed. Furthermore, no valid interpretation has been offered for the separation of the two waves, as the role of proton transfers antecedent and consecutive to an electron transfer has been misunderstood.[5]

The optimum experimental conditions must be defined first. The half-wave potential of the more positive wave (i_1), which corresponds to a reduction of the protonated form of oxime, is shifted at a given acidity to more positive potential with increasing concentration of the added neutral salt. The observed shifts also depend on the nature of the added anion of the salt. The half-wave potentials of the more negative wave of the imine reduction (i_2) are independent of the nature of the anion of the supporting electrolyte but depend on ionic strength. Experimental evidence for reported relationships and their discussion is present in more detail elsewhere.[20]

On the basis of these observations, it is necessary to follow changes of potentials of both waves in solution of the same strong acid in which the ionic strength was kept constant by addition of a neutral salt, which has the same anion as the strong acid. Shifts of potentials obtained under above conditions are discussed below.

It is proposed that the reason for the separation of two two-electron waves during the reduction of some oximes in acidic media is a difference in the slopes of the $E_{1/2} = f(pH)$ plots for the reduction of protonated forms of oximes and imines. The reasons for this difference are as follows:

For the reduction of oximes two types of pH dependences (Figure 11) have been observed. The type in Figure 11a has been observed for the following acetophenone oximes, substituted in the para position by OH (**10**), CH$_3$ (**11**), H (**12**), and COCH$_3$ (**14**) groups. For such compounds the half-wave potentials of reduction waves of both oxime (i_1) and imine (i_2) became below a certain pH constant and independent of pH.

For the oxime wave i_1 the pH at the intersection of the two segments corresponds to pK_a^{Ox} of the protonated form of the oxime.

At pH < pK_a^{Ox} the potential of the reduction wave i_1 of the protonated form of the oxime is pH-independent. In such a pH range, namely, the species predominating in the bulk of the solution are also reduced. No additional change in energy is needed to take place before the electron uptake.

The reduction potentials at pH > pK_a^{Ox} are shifted to more negative values with increasing pH for the reductions of protonated forms of both oximes and imines. This is due to the fast proton transfers taking place before the uptake of the first electron. The higher the pH of the investigated solution, the more energy is needed to convert the basic form into the more easily reducible acidic form. Consequently a gradually more negative potential is needed to achieve the reduction of the acidic form.

At pH < pK_a^{int} (where pK_a^{int} is the pH at the intersection of two linear segments) (Figure 11) the potential of the reduction of the imine also becomes pH-independent. In this pH range the protonated form of the imine, which predominates in the solution in the vicinity of the electrode, is reduced. Contrary to the situation in the reduction of oximes, for imines the pH at the intersection of two segments (pK_a^{int}) is not equal to the pK_a^{im} of the imine. The value pK_a^{int} represents only the lower limit of the value of pK_a^{im}. This is due to the fact that imines at pH > pK_a^{int} are reduced at more positive potentials than corresponding oximes. That has been proved recently by comparison of reduction potentials of fluorenone oxime with that of fluorenone imine.[21] Hence, at pH > pK_a^{int} any imine formed by the reduction of an oxime is immediately at the electrode surface further reduced to amine.

The most frequently encountered type of the $E_{1/2} = f(pH)$ plots for reductions of oxime and imine in acidic media is given in Figure 11b. This type of plot was observed for benzaldehyde oximes bearing in the para position the following substituents: OCH$_3$ (**1**), CH$_3$ (**2**), H (**3**), F (**4**), and Br (**6**), for *p*-trifluoromethylacetophenone oxime (**15**) and benzophenone oxime (**16**). These dependences can be interpreted in the same way as those in Figure 11a, the only difference being that pK_a^{Ox} was lower than the highest acidity used.

As pK_a^{int} is in all cases higher than pK_a^{Ox} and since $pK_a^{int} \leq pK_a^{im}$, it follows that pK_a^{Ox} must be smaller than pK_a^{im}. Thus the separation of two waves at pH < 2 is due to differences between pK_a^{Ox} and pK_a^{im}.

It remains to be explained why the reduction of the imine is observed at pH 0−3, when it is well-known that imines in homogeneous solutions undergo easily acid-catalyzed hydrolysis. The equal limiting currents of the first and second two-electron steps observed for some oximes indicate that no loss of the imine by a chemical reaction takes place before the uptake of the third electron. This indicates that imines are sufficiently stable during the experimental time window under conditions of polarographic measurements. The rate constants of the bulk hydrolysis of imines can be estimated to be on the order 10^{-2} to 10 s^{-1}. To decrease measurably the limiting currents of the more negative wave of oximes in acidic media in the course of electrolysis at the dropping mercury electrode, the chemical reaction inactivating the imine would have to have a rate constant at least 4 orders of magnitude higher. Moreover, if such hydrolysis would occur, a separate wave of the corresponding carbonyl compound would appear at $t = 0$, which was never observed.

Role of Substitution. For evaluation of substituent effects on the potential of reduction of benzenoid compounds it is

Electroreduction of Aromatic Oximes

J. Phys. Chem. B, Vol. 110, No. 13, 2006 **6795**
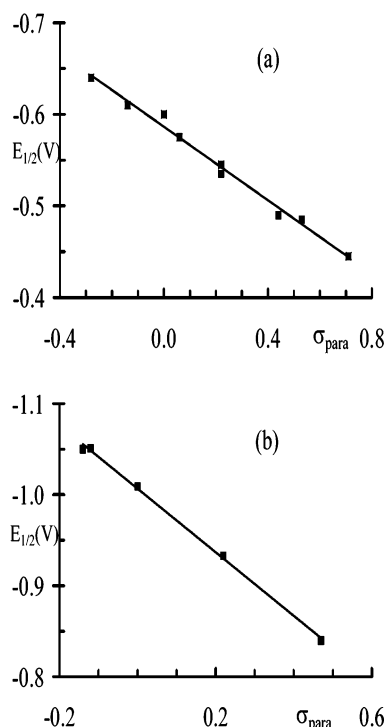
Figure 12. Dependences of the half-wave potentials of the four-electron wave of reductions of oximes on Hammett substituent constant σ_x: (a) para-substituted benzaldehyde oximes at pH 1.5, $\rho = 0.20$ V, $R^2 = 0.99$; (b) para-substituted acetophenone oximes at pH 5.0, $\rho = 0.35$ V, $R^2 = 1.00$.

possible to use LFERs, such as the modified Hammett equation.[11] For such treatments the correlation of $E_{1/2}$ with tabulated[25] substituent constants σ_x (where x is a meta or para substituent) is tested for a reaction series of compounds bearing the same electroactive center. The condition for inclusion of compounds into a given reaction series is that all compounds belonging to this series are reduced by the same mechanism. In practice for reductions in protic media this means that all compounds within the reaction series must be reduced by the same number of electrons, yielding the same product. The reduction must also involve the same number of protons transferred before the first electron uptake. This latter condition is usually fulfilled within a pH range where either the $E_{1/2}$ of all numbers of the reaction series are pH-independent or the slopes of $dE_{1/2}/dpH$ for all compared compounds are either identical or very similar. For irreversible processes that means[11] that the value of the transfer coefficient α must be within the reaction series either constant or a linear function of the substituent constant σ_x.

As follows from Table 1, a pH range where the condition of similar values of $dE_{1/2}/dpH$ for a given reaction series is found best fulfilled is for para-substituted benzaldehyde oximes at pH 1.5 (Figure 12a), for reaction constant $\rho = 0.20$ V with a correlation coefficient $R^2 = 0.99$ and for para-substituted acetophenones (Figure 12b) for $\rho = 0.35$ V where the fit was good ($R^2 = 1.00$) for $E_{1/2}$ measured at pH 5.0.

The susceptibility of half-wave potentials to substituent effects, expressed by the larger value of the reaction constant ρ, increases with increasingly negative values of the half-wave potential of the unsubstituted member of the reaction series. A linear relationship between the value of the reaction constant ρ and the potential of the parent, unsubstituted member of the reaction series $(E_{1/2})_H$ has been reported.[11] Such a trend does agree with the larger value of the reaction constant $\rho = 0.35$ V for the acetophenone series (in which the half-wave potential

of the unsubstituted acetophenone oxime at pH 5.0 (-1.00 V) is more negative) than the value $\rho = 0.20$ V obtained for the benzaldehyde oxime (where the potential of the unsubstituted benzaldehyde oxime at pH 1.0 is -0.64 V.)

Conclusions

To prove that it is the diprotonated form of an oxime that is reduced between pH 5 and 8, the plots of $i/i_d = f(pH)$ are used. Their interpretation is complicated by the adsorption of the basic form of the oxime and the heterogeneous nature of its protonation. Experimental evidence strongly indicates that at pH 5−8 it is the diprotonated form of the oxime that is reduced. In the diprotonated form an OH_2^+ grouping is present as a good leaving group. The initial cleavage of the N−O bond is also facilitated by the positive charge on the azomethine nitrogen. The presence of two positive charges on adjacent N and O atoms in oximes is supported by the pH dependence of reduction currents and reduction potentials of nitrones, where in protonated form positive charges are also present on adjacent N and O atoms before the N−O is cleaved. The diprotonation is further supported by the properties of two or even three reduction waves observed for some oximes as well as by the strong dependence of reduction potentials on pH. The separation of two two-electron waves at pH < 2 results from a difference between the pK_a values of protonated forms of the oxime pK_a^{Ox} and pK_a^{im}. Effects of para-substituents on benzaldehyde oximes at pH 1.5 and on acetophenones at pH 5.0 follow LFERs, in particular modified Hammett equation.

Note Added after ASAP Publication. This article was published ASAP on March 9, 2006. An author name has been corrected. The correct version was reposted on March 22, 2006.

Supporting Information Available: Graphs showing the dependences of half-wave potentials of substituted benzaldehyde and acetophenone oximes on pH on which Table 1 is based. This material is available free of charge via the Internet at http://pubs.acs.org

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6796 *J. Phys. Chem. B, Vol. 110, No. 13, 2006*

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