

EFFECT OF ALCOHOLS ON POLAROGRAPHIC REDUCTION OF OXIMESMara ALEKSIĆ^a, Vera KAPETANOVIĆ^b and Petr ZUMAN^{c,*}^a Department of Physical Chemistry, Faculty of Pharmacy, Vojvode Stepe 450, 110 00 Belgrade, Yugoslavia; e-mail: m.alexica@eunet.yu^b Department of Analytical Chemistry, Faculty of Pharmacy, Vojvode Stepe 450, 110 00 Belgrade, Yugoslavia; e-mail: m.alexica@eunet.yu^c Department of Chemistry, Clarkson University, Potsdam, NY 13699-5810, U.S.A.; e-mail: zumanp@clarkson.edu

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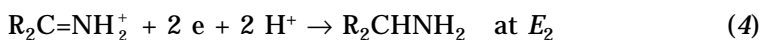
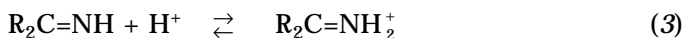
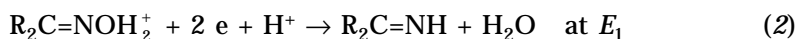
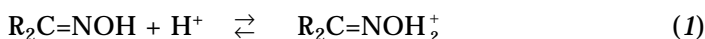
Limiting currents of the protonated form of oximes decrease with increasing concentration of alcohols in alcohol-water mixtures. The measured current limits to a value corresponding to a two-electron reduction. The decrease is attributed to additions of the alcohol to the imine formed as intermediate. At a given concentration of the alcohol the drop of current increases in the sequence MeOH < EtOH < i-PrOH < *tert*-BuOH, following the increasing nucleophilicity of the alcohol.

Keywords: Oximes; Alcohols; Additions; Reductions; Imines; Polarography; Electrochemistry.

Reduction of the protonated form of oximes at the dropping mercury electrode (DME) in buffered aqueous solutions is generally assumed¹ to involve transfer of four electrons in a single step. In principle, a four-electron reduction of an oxime to an amine can follow two reaction paths: either the N-OH₂⁺ bond is cleaved first, yielding an imine which is subsequently reduced to an amine, or a hydrogenation of the C=N double bond occurs first, yielding a hydroxylamine derivative which then would have to be further reduced to an amine. To distinguish between these two alternatives, the role of the potential of the second two-electron step will be considered first. Occurrence of a single four-electron wave indicates that the potential of the second two-electron step is either similar or even more positive than the potential of the first two-electron uptake. Such relationship between the values of the potentials of the first and second two-electron steps is plausible for the first alternative. It is known² that the two-electron reductions of imines occur easily, at potentials more positive than those of the corresponding carbonyl compounds. Similarly, oximes are reduced at po-

tentials more positive than the corresponding carbonyl compounds. The reduction of the protonated form of an imine can be thus expected in the potential range where the reduction of the protonated form of the oxime takes place.

The second alternative would presume an easy reduction of substituted hydroxylamines. Nevertheless, the irreversible reduction of protonated forms of alkyl- and arylhydroxylamines occurs at potentials at least 0.5 V more negative than the observed reduction of oximes³. Hence, the second alternative can be ruled out and the following scheme applies for the reduction of oximes:



This sequence is supported by three reported cases, where the reduction of oximes occurs in two two-electron steps, namely for oximes of testosterone propionate^{1b}, 2,4-dihydroxybenzophenone⁴, and the antibiotic cefetamet⁵. In these cases the second wave was identified as the wave of the reduction of imine, formed in the two-electron reduction of the oxime.

Additional support for the reduction path (1)–(4), reported here, is based on the effect of solvent composition on the limiting currents of protonated forms of oximes.

EXPERIMENTAL

Materials

Benzaldehyde, acetophenone, and benzophenone oximes **1a–1c** were commercial preparations, purified by crystallization. Sodium salt of cefamet (**2**) was donated by Hoffmann La Roche (Basel, Switzerland). Acetic and phosphoric acids and other chemicals used for preparation of buffers, were of reagent grade quality.

Apparatus

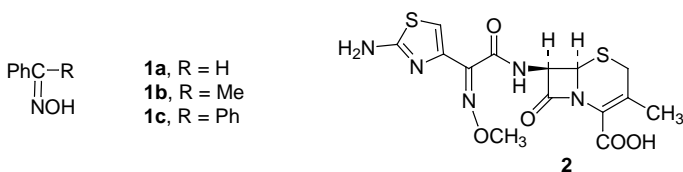
DC polarographic measurements were performed with a PAR Model 174 polarographic analyzer (EG&G, Princeton Applied Research Corp.). The three-electrode system involved a DME, a platinum wire auxiliary electrode and a SCE as a reference electrode. The controlled drop-time was 2 s at the height of mercury column of 80 cm and the scan-rate was 5 mV/s.

Procedures

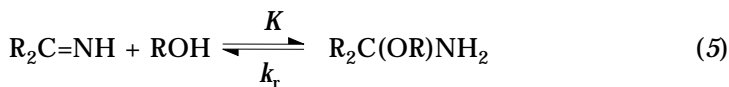
Buffer (10 ml) was deaerated, $1 \cdot 10^{-2}$ M stock solution of the oxime was added to a final $2 \cdot 10^{-4}$ M concentration and briefly purged with nitrogen, and the current-voltage curve was recorded.

RESULTS AND DISCUSSION

With increasing concentration of an alcohol in buffered water-alcohol mixtures, the limiting current of oximes **1a–1c** and **2** decreases and limits to a value, corresponding to a two-electron reduction (Figs 1 and 2). This occurs in a pH range, where the limiting current is pH-independent over several



pH units and where the small variation in pH due to the change in solvent composition cannot play a role. This is attributed to addition of the alcohol to the C=N double bond of the imine, forming an adduct, an amino analog of a hemiketal:



Observed limiting currents depend both on the value of the equilibrium constant (K) of reaction (5) and on the rate of formation of imine from the adduct with the rate constant k_r . The reactivity of the alcohol increases (Fig. 1) with increasing nucleophilicity of the alcohol in the sequence $\text{MeOH} < \text{EtOH} < i\text{-PrOH} < \text{tert-BuOH}$.

Stoichiometry, rates and equilibria of these reactions are currently under investigation, as well as the possibility of the formation of a ketal. Quanti-

tative evaluation of these processes is complicated by the fact that the generation of the electroactive species by protonation of oximes^{1a,1c} occurs as a surface reaction^{1d}. This is demonstrated by the shape of current-voltage curves where the current is gradually dipping with increasingly negative potentials. These decreases are attributed to a decrease in the rate of the surface reaction^{1d}.

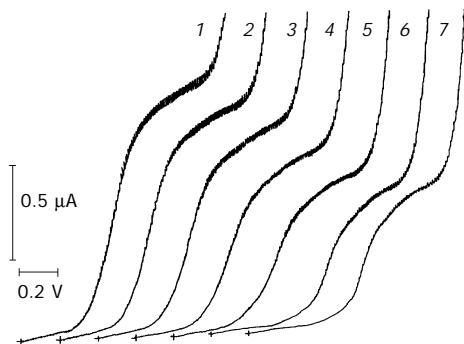


FIG. 1

Dependence of polarographic current-voltage curves of $2 \cdot 10^{-4}$ M solution of cefamet (2) in an acetate buffer pH 4.7 on concentration of the ethyl alcohol in the electrolyzed solution. Concentration of the alcohol (in %): 1 0, 2 5, 3 10, 4 20, 5 30, 6 50, 7 70. Curves starting at -0.2 V, the controlled drop time $t = 2$ s, at $h = 80$ cm

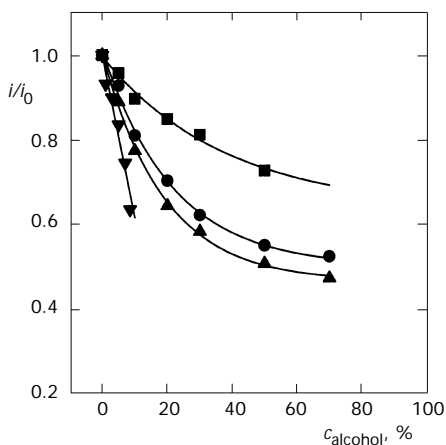


FIG. 2

Dependence of the ratio i/i_0 on concentration of alcohol, where i_0 is the diffusion current in aqueous buffer and i is the limiting current at the given concentration of alcohol. ■ Methanol, ● ethanol, ▲ propan-2-ol, ▼ *tert*-butyl alcohol

Qualitative support for the addition of ethanol to the imine intermediate can be found in the values of limiting currents for some oximes in acidic media, reported in solutions containing 40 (ref.^{1b}) or 25% (ref.^{1c}) ethanol. Using limiting currents of oximes of crotonaldehyde^{1b}, carvone^{1b}, and acetophenone^{1c} as internal standards assumed to correspond to a simple four-electron reduction, the currents of other oximes (corrected for variations in diffusion coefficients) were smaller by 9% for oxime of phenylacetaldehyde isobutyraldehyde^{1b}, phenylacetaldehyde^{1b}, mesityloxide^{1b} and cinnamaldehyde^{1b}, by 11% for 4-methylacetophenone oxime^{1c}, by 14% for methyl 2-naphthyl ketone oxime^{1c}, by 19% for benzylideneacetone oxime^{1b}, by 23% for 4-aminoacetophenone oxime^{1b}, by 37% for benzophenone oxime^{1c} and its 4-methyl derivative^{1c}, and by 49% for testosterone oxime propionate^{1b}.

A reaction analogous to (5) cannot be excluded even in purely aqueous solutions, where R = H. Nevertheless, the reactivity of water is smaller than that of methanol and the position of the equilibrium makes it unsuitable to electrochemical investigation at 25 °C. Experiments at lower temperatures and with synthesized imines are in progress.

Almost quantitative yields of amines in controlled potential electrolyses of oximes, using mercury pool electrodes, can be attributed to a difference in transport and time-windows available for chemical reactions under the conditions of preparative electrolysis with a mercury pool when compared to electrolysis at the DME (ref.⁶).

Addition of water and alcohols to the C=N bond in the imine intermediates seems not to be restricted to the species formed in the reduction of oximes. Controlled-potential electrolyses of several semicarbazones, using DME as a working electrode, enabled to obtain the values for the number of transferred electrons with an accuracy better than $\pm 2\%$. Observed values of the number of electrons transferred in acidic media containing 50% ethanol, were systematically lower by 7–12% than expected for a straightforward four-electron process⁷.

This investigation indicates that even for systems, which are supposed to be well understood, there is a need for further studies.

REFERENCES

1. a) Souchay P., Ser S.: *J. Chim. Phys.* **1952**, *42*, C 172; b) Lund H.: *Acta Chem. Scand.* **1959**, *13*, 249; c) Gardner H. J., Georgans W. P.: *J. Chem. Soc.* **1956**, 4180; d) Zuman P., Exner O.: *Collect. Czech. Chem. Commun.* **1965**, *30*, 1832.
2. Zuman P.: *Collect. Czech. Chem. Commun.* **1950**, *15*, 839.

3. Eisner U., Kirowa-Eisner E. in: *Encyclopedia of Electrochemistry of Elements* (A. Bard and H. Lund, Eds), p. 219. Marcel Dekker, New York 1979.
4. Lund H.: *Acta Chem. Scand.* **1964**, *18*, 563.
5. Kapetanović V., Aleksić M., Zuman P.: *J. Electroanal. Chem.*, in press.
6. Zuman P.: *Microchem. J.* **1987**, *36*, 255.
7. Fleet B., Zuman P.: *Collect. Czech. Chem. Commun.* **1967**, *32*, 2066.



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