Electroreduction of oxime of glycolaldehyde and of its *O*-methyl derivative

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The reaction of glycolaldehyde and of its *O*-methyl derivative with hydroxylamine has been studied and the polarographic behaviour of the resulting oximes in aqueous buffer solutions has been analyzed. Both polarographic waves of reduction of the oximes were found to be dependent on the ratio of the reactants, pH value of the medium, and concentration of buffers. Preparative electroreduction of the oximes studied has been performed under potentiostatic and pH-static conditions. On the basis of the polarographic data, course of preparative electroreductions of both oximes, and the products obtained the mechanisms of the respective chemical and electrochemical reactions have been suggested.

Изучена реакция гликольальдегида и его *O*-метилпроизводного с гидроксиламином, и анализируется полярографическое поведение образующихся оксимов в водных буферных растворах. Обнаружено, что обе полярографические волны восстановления оксимов зависят от взаимного соотношения реагентов, величины pH среды и концентрации буферных растворов. В потенциостатических и pH-статических условиях проведено препаративное электровосстановление изучаемых оксимов. Исходя из полярографических данных, хода препаративного электровосстановления обоих оксимов и образующихся продуктов, предлагаются вероятные механизмы соответствующих химической и электрохимической реакций.

Oximes, similarly as imines, semicarbazones, and hydrazones, are important condensation products of carbonyl compounds with the respective nitrogenous bases. Much attention has been devoted to preparation of azomethine compounds, study of their reactivity, kinetics and mechanism of their formation and decomposition [1]. The course of their formation in acid media exhibits a rate maximum [2—4] and the pH of the medium influences the reaction equilibria [5]. From the viewpoint of electrochemistry, significant are the polarographic reductions of various types of azomethine compounds [6—11], performed also on a preparative scale with the aim to find out the mechanisms of the respective electrode processes [12, 13]. The knowledge mentioned above was utilized in the present work, aiming at contribution to detailed elucidation of kinetics and mechanism of chemical and electrochemical reactions taking place in the

process of preparation and electroreduction of the aforementioned type of oximes.

Experimental

Polarographic curves were recorded on an LP 7 polarograph (Laboratorní přístroje, Prague) with conventional polarographic connection to a Kalousek vessel with a separated saturated calomel electrode (SCE). Preparative electroreductions were performed in an electrolyzer under potentiostatic and pH-static conditions, described in the previous works [14, 15]. The products were analyzed by means of their ^{13}C NMR spectra, measured with a Bruker AM-300 spectrometer in the FT-mode.

Glycolaldehyde was a product of Fluka (Switzerland) and methoxyacetaldehyde was prepared by acid-catalyzed hydrolysis of its dimethyl acetal (Aldrich, U.S.A.) ($100\,cm^3$ of 0.2 M methoxyacetaldehyde dimethyl acetal was allowed to stay in the presence of $0.01\,M\text{-}H_2SO_4$ at 50 °C for 24 h). Hydroxylammonium chloride, hydroxylammonium sulfate (Lachema, Brno), and the other chemicals used for the preparation of buffers for polarography, preparative electrolysis, and chromatography were of anal. grade.

Procedures

For polarographic studies and preparative electroreductions only aqueous solutions of both oximes were used. These were prepared by mixing the solutions of the aldehydes mentioned above with hydroxylamine and allowing to react for at least 30 min. In both cases aqueous solutions of oximes with 50—100 % excess of the hydroxylammonium salt were generally used. In polarographic reduction of oximes, $0.5\,cm^3$ of the basic solution of oxime ($1\,cm^3$ of 0.1 M glycolaldehyde and its O-methyl derivative, respectively, $2\,cm^3$ of $0.1\,M\text{-}NH_2OH\cdot HCl$, and $1\,cm^3$ of 1 M-NaOH made up with water to $10\,cm^3$) was added into the buffer solution ($9.5\,cm^3$), bubbled through with nitrogen. After repeated short bubbling of the solution with nitrogen, the polarographic curves were recorded from the chosen potential with respect to SCE.

Aqueous solutions of oximes for preparative electroreduction were obtained by treating of 0.1—0.2 M aldehyde with 0.15—0.3 M hydroxylammonium sulfate for 45 min. The final solution for electroreduction was obtained by addition of this solution ($50\,cm^3$) to 0.2 M formate or acetate buffer ($50\,cm^3$) of the required pH. Electroreduction was performed in an electrolyzer on a working mercury cathode under intensive stirring of its surface and cooling the electrolyzer with water, at a potential maintained potentiostatically with respect to SCE. The adjusted pH value was maintained pH-statically by addition of aqueous solution of $1\,M\text{-}H_2SO_4$. The anode compartment of the electrolyzer was filled with aqueous solution of $0.1\,M\text{-}H_2SO_4$. The course of electroreduction of oximes, formation of the respective amines, and release of aldehydes during electroreduction were monitored polarographically, while the polarographic curves were recorded in chosen time intervals from potentials measured with respect to SCE. The decrease of concentration of oximes in the course of reduction was followed by recording their polarographic curves from − 0.6 V in 0.04 M formate buffer of pH = 3.6 (0.2—0.1 cm³ of the sample in 9.8—9.9 cm³ of buffer). The formation of amines was followed by means

of polarographic curves of their condensation products with benzaldehyde in alkali medium (1.0—0.5 cm³ of the sample in 8.5—9.0 cm³ of 0.1 M phosphate buffer of pH = 12 and 0.5 cm³ of 0.1 M benzaldehyde). Regeneration of aldehydes was established by recording their polarographic curves from − 1.2 V after addition of 1.0—0.5 cm³ of the reaction sample into 9.0—9.5 cm³ of aqueous solution saturated with calcium hydroxide.

Analysis and isolation of products

After completion of electroreduction of the oximes studied (3 h) and concentration of the reaction solution, the amines obtained in the form of salts were analyzed by ¹³C NMR spectroscopy and also by paper chromatography on a Whatman 3M paper in the system 1-butanol—formic acid—water (volume ratio = 8 : 1 : 1) and detection with 0.1 % ninhydrine in butanol at 105 °C.

The reaction solution obtained by preparative electroreduction of glycolaldehyde oxime was precipitated with barium formate and the precipitate was filtered off. The supernatant was concentrated in vacuo to a small volume and loaded onto a cellulose column (100 cm × 5 cm). The amines present were separated in the aforementioned chromatographic system at the flow rate of 13 cm³ h⁻¹. The individual test-tube fractions were combined according to their chromatographic pattern and the amines were characterized by melting points of their picrates.

In the preparative electroreduction of 0.1 M glycolaldehyde oxime (100 cm³) in the presence of 50 % excess of hydroxylammonium sulfate, conducted in the formate buffer of pH = 3.6 and at the potential of the working mercury electrode − 1.4 V, the crude product was analyzed by ¹³C NMR spectroscopy to prove the presence of 2-aminoethanol and ethylamine, as final products of electroreduction, in the mole ratio of 1 : 2 (Fig. 1). Chromatographic separation of the reaction mixture on the cellulose column yielded from the first fraction ethylammonium formate (0.57 g), characterized by m.p. (picrate) = 167—168 °C; Ref. [16] gives m.p. = 170 °C and Ref. [17] m.p. = 166 °C. From the second fraction 2-hydroxyethylammonium formate (0.2 g) with m.p.(picrate) = 158—159 °C was obtained; Ref. [18] gives m.p. = 159.5—160 °C.
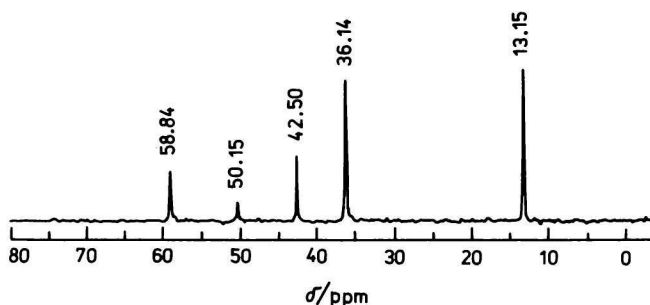

Fig. 1. ¹³C NMR spectra of ethylamine (δ = 13.15 ppm and δ = 36.14 ppm) and 2-aminoethanol (δ = 42.50 ppm and δ = 58.84 ppm) as the products of electroreduction of glycolaldehyde oxime, measured in D₂O solution using methanol (δ(TMS) = 50.15 ppm) as internal standard.

The solution obtained by electroreduction of methoxyacetaldehyde oxime was concentrated *in vacuo* and the amines formed were released from their salts by addition of solid sodium hydroxide under stirring and cooling the reaction mixture. The freed amines after extraction with ether and drying the solution with sodium sulfate were obtained by fractional distillation. Preparative electroreduction of methoxyacetaldehyde oxime, carried out under the same conditions as in case of glycolaldehyde oxime, resulted in a mixture of methoxyethylamine and ethylamine (mole ratio = 1 : 1). Fractional distillation of the ether extract, containing the free amines, gave ethylamine (0.21 g) with m.p.(picrate) = 166 °C and methoxyethylamine (0.36 g) with m.p.(picrate) = = 145—147 °C; Ref. [19] gives m.p. = 148—150 °C.

Results

Polarographic behaviour

The oximes of glycolaldehyde and of its *O*-methyl derivative undergo electroreductions in acid media, exhibiting two polarographic waves. The hights and mutual ratio of these waves depend on concentration and pH values of buffer solutions. A typical dependence of both polarographic waves of reduction of the respective oximes on pH values of the formate and acetate buffers is illustrated in Fig. 2. The hights of both polarographic waves (i_1, i_2) change in the form of dissociation curves. The approximate values of the apparent dissociation constants of the compounds presented by the first and the second wave are $pK_1' \doteq 2.7$ and $pK_2' \doteq 5.6$. Rapid decomposition of oximes in strongly acid media (Fig. 2, curve *1*) makes impossible to follow the change of mutual ratio of hights of both waves in these regions. The dependence of hights of both polarographic waves of oximes on the hight of the reservoir points to their kinetic nature at such pH values of buffer solutions when the hights represent only a small portion of their maximum values. It is interesting that *O*-methoxime of glycolaldehyde exhibited practically the same polarographic behaviour. A polarographic double-wave was observed also in the case of acetaldoxime in strongly acid media. Contrary to glycolaldehyde oxime at pH = 2.22 (Fig. 2, curve *1*), the first wave of acetaldoxime is lower, representing only 20 % of the total hight, and appears at more negative potentials. It is noticeable that the polarographic double-wave of acetaldoxime practically does not change with time at the pH mentioned above.

Preparative electroreduction

The polarographic study of the reduction of the oxime of glycolaldehyde and of its *O*-methyl derivative revealed that the optimum range for preparative electroreduction is pH = 2.6—4.6 (Fig. 2). In more acid regions these oximes decompose, while at pH values higher than 4.5 the portion of their reducible
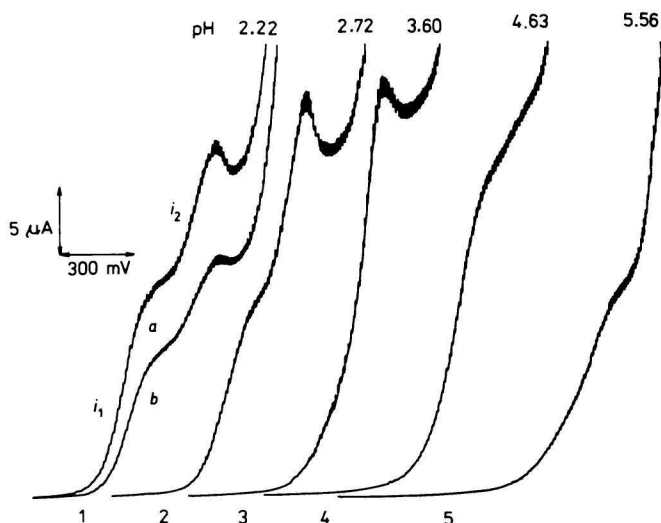
384

Fig. 2. pH-Dependence of polarographic curves of reduction of 5×10^{-4} M glycolaldehyde oxime in aqueous solution of 0.2 M formic acid (recorded immediately — *1a* and after 15 min — *1b*) in formate (*2, 3*) and acetate (*4, 5*) buffers. The curves recorded from -0.5 V *vs.* SCE.
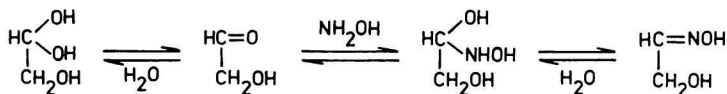
forms decreases. The preparative electroreductions of glycolaldehyde oxime and methoxyacetaldehyde oxime, carried out as described in Experimental, showed that when using oximes prepared from theoretical amounts of the aldehyde and hydroxylamine the aldehyde was released in the course of electroreduction. Its amount approached 25—30 % of the total amount contained in the respective oxime. Under the reaction conditions used, the released aldehydes undergo electroreductions as well, giving undesired products [14, 20]. It was proved that it is necessary to add minimum 50 % excess of hydroxylamine at the beginning of the reaction for total suppression of regeneration of the respective aldehydes from the starting oximes.

It was shown that electroreduction of glycolaldehyde oxime resulted in two amines, *i.e.* 2-aminoethanol and ethylamine, while electroreduction of methoxyacetaldehyde oxime yielded 2-methoxyethylamine and ethylamine. The ratio of the amines formed depends on pH value of the medium and potential of the working mercury electrode. In electroreduction of glycolaldehyde oxime, carried out at pH = 3.6 and potential of the working electrode -1.4 V, 2-aminoethanol and ethylamine were formed in the mole ratio of $1:2$ (Fig. 1). At maintaining the same potential of the working electrode and elevating the pH value to 4.6, the ratio of the aforementioned amines was inverse. On the other hand, in electroreduction of glycolaldehyde oxime at pH = 2.6 and -1.0 V, practically only ethylamine was formed. At maintaining this pH value and shifting the potential of the working electrode to more negative values, the

portion of 2-aminoethanol increased. For the sake of comparison also the electroreduction of acetaldoxime was performed at pH = 3.6 and potential − 1.4 V. In this case it was not necessary to add any excess of hydroxylamine to prevent the release of acetaldehyde in the course of electroreduction of its oxime.

Discussion

In the reaction of carbonyl compounds with hydroxylamine the rate of formation and the equilibrium of the oximes depend on pH values of the medium and acid-base properties of the reactants. While the rate of formation of oximes passes through a maximum in acid medium [2—4], the values of equilibrium constants for the formation of oximes increase with the increasing pH values of the medium and reach maximum in alkali media [5]. As only protonized forms of oximes [6—13] undergo electrochemical reductions, it is necessary to choose compromised pH values so that electroreduction be optimal. The formation of oximes, illustrated by the reaction of glycolaldehyde with hydroxylamine (Scheme 1), belongs to thoroughly studied types of acid-base--catalyzed equilibrium reactions [2, 3].

$$HC\overset{\diagup OH}{\underset{\diagdown OH}{|}} \underset{CH_2OH}{} \; \underset{H_2O}{\rightleftharpoons} \; \underset{CH_2OH}{\overset{HC=O}{|}} \; \overset{NH_2OH}{\longrightarrow} \; HC\overset{\diagup OH}{\underset{\diagdown NHOH}{|}} \underset{CH_2OH}{} \; \underset{H_2O}{\rightleftharpoons} \; \underset{CH_2OH}{\overset{HC=NOH}{|}}$$

Scheme 1

Polarographic study of electroreduction of oximes of glycolaldehyde and of its *O*-methyl derivative shows not only their instability in strongly acid media and irreducibility of their nonprotonized forms, but also their characteristic double-wave and its change in dependence on pH of the medium (Fig. 2). Similar double-waves were observed in many cases of polarographic reduction of oximes. Their origin has been explained variously [7—9]. One of the explanations is based on the existence of two protonizable centres in the oxime group, *i.e.* the nitrogen and oxygen atoms. It is assumed that the nitrogen atom is a centre more basic than oxygen [13], however, their basicities are comparable, as indicated by our results. In our case another protonizable oxygen, *i.e.* the oxygen of the primary alcoholic or methoxy group of the oximes studied, is available. The results of polarographic study and the nature of the products of electroreduction of oximes in dependence on pH of the medium and potential of the working electrode made possible to suggest the mechanisms of the respective chemical and electrochemical reactions (Scheme 2).

We assume that the formation of the first polarographic wave at more positive potentials and its growth with the increase of the acidity of the medium
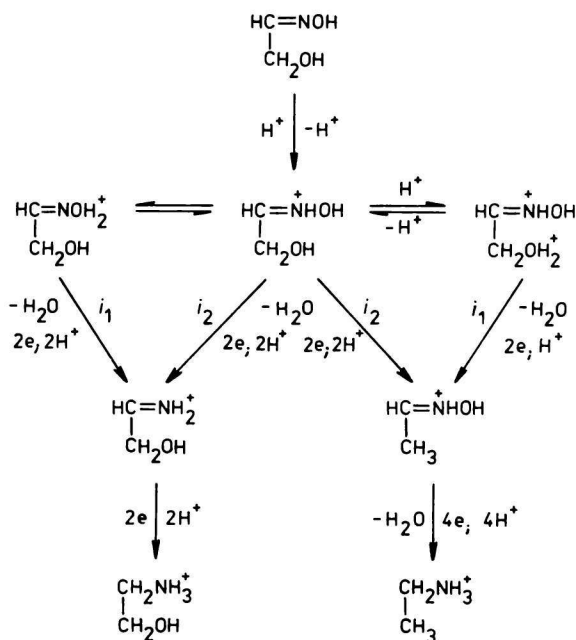
Scheme 2

on the expense of the second wave is conditioned by the possible protonization of oxygen atoms of both hydroxyl groups of the oxime. The formation of the second polarographic wave at negative potentials is obviously caused by protonization of nitrogen atom as the more basic centre in the oxime group, which appears also at higher pH values. It is admissible that, under these conditions, also electroreductive cleavage of the nonprotonized primary hydroxyl group of glycolaldehyde oxime might occur. These assumptions are based on the character of the products obtained by preparative electroreduction of oximes in dependence on the used pH of the medium and potential of the working electrode. So 2-aminoethanol may be considered the product of four-electron reduction on nitrogen or oxygen of the protonized forms of the oxime group of glycolaldehyde oxime. This statement is supported by the finding that also acetaldoxime exhibits a polarographic double-wave. More positive potentials of the working electrode and increasing acidity of the medium bring about an increase in the portion of ethylamine when compared to 2-aminoethanol. It is assumed that further increase in the acidity of the medium enables also protonation of the second hydroxyl group in the molecule of glycolaldehyde oxime, leading to formation of ethylamine as the only product of six-electron electroreduction. Since electrochemical studies were performed at pH > 2, *i.e.* at values considerably higher than the pK_a values of the conjugated acids of

oximes (*e.g.* the pK_a of acetone oxime is 0.99 [21]) and aliphatic alcohols [22], it is obvious that the protonation reactions, presented in the above scheme, took place only in the surroundings of the mercury electrode on the polarized molecules of the oxime. It is interesting that though the reduction of oximes involves a mixture of four- and six-electron processes, changing over the respective pH range, this fact is not reflected in the total hights of polarographic waves. It can be explained by slow conversion of the intermediates to their polarographically active forms, when compared to the time of the mercury drop, as it was observed in polarographic study of glyceraldehyde and its derivatives [14]. Regeneration of glycolaldehyde in the course of electroreduction of its oxime is probably brought about by decomposition of glycolaldimine, as unstable intermediate of electroreduction of glycolaldehyde oxime. Similar considerations hold for methoxyacetaldehyde oxime, because its chemical and electrochemical behaviour is analogous to that of glycolaldehyde oxime discussed above.

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