Mechanism of Electroreduction of the Henry Reaction Products. Electrochemically Initiated Degradation of 1-Phenyl-2-Nitroethanol

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Abstract

Electroreduction of the Henry reaction product – i.e. 1-phenyl-2-nitroethanol (PNE) – in 0.1 M Bu4NClO4 solution in Me-CN has been investigated by a set of experimental (cyclic voltammetry, chronoamperometry, and controlled potential electrolysis) and theoretical (digital simulation and quantum chemical calculations) methods. The results obtained show that cathodically generated radical anion of PNE undergoes C–C bond cleavage reaction resulting in the formation of the free radical of benzyl alcohol and nitromethane anion. The proton transfer between these species affords nitromethane and benzaldehyde radical anion. Electron transfer from the last to PNE initiates the cyclic process of the PNE degradation.

Keywords: β-nitro alcohols, cyclic voltammetry, chronoamperometry, radical anion, dissociative electron transfer, electroinitiated reactions.

1. Introduction

The Henry reaction is known from the XIX century but remains to be one of the general methods for carbon–carbon bond formation, being thus central in organic synthesis.1 The reaction is the base-catalyzed formation of β-nitro alcohols from nitroalkanes and carbonyl compounds:

\[
\begin{align*}
\text{R}^1_{\text{NO}_2} \text{R}^2 + \text{R}^3 \text{O} \rightarrow \text{R}^1_{\text{NO}_2} \text{R}^2 \text{R}^3 \text{OH}
\end{align*}
\]

The electrochemical initiation of the Henry reaction seems promising,2–4 because the process does not require addition of a base from outside (due to a decrease in the amount of wastes and simplification of product isolation), electrical current is cheap, and reactions of the kind are selective.5–6

It is significant that not direct products of the Henry reaction, viz., β-nitro alcohols, are of practical interest, but mainly the products of their further transformation, in particular, the corresponding aminoalcohols (for example, diverse medicals are thus prepared, see references cited in1,6). Therefore, it is urgent to establish the detailed mechanism of reduction of nitro alcohols.

The first stage of electrochemical and many chemical reduction processes is known to be the electron transfer to the molecule to form radical anions (RAs)7. In particular, the results of investigations of nitro alcohol electroreduction in proton-donor media8 suggest that the mechanism of this process is similar to that of the electroreduction of nitro compounds to amines, the first stage of which is the protonation of the nitro group in RAs:

However, the presence of an electron on the antibonding orbital in RAs enhances basicity compared to that of the initial neutral molecule and also destabilizes the bond, resulting in their dissociation in some cases.7 The exam-
ples for bond cleavage available in the literature include cleavages of C–N bonds in RAs of aliphatic nitro compounds, C–O bonds in RAs of arylmethanol, and C–C bonds in RAs of aromatic pinacones. Since nitro alcohols include bonds of all named types, it can be expected that the cleavage of bonds in these RAs can compete with their protonation. The competition can impede both the preparation of the target products (aminoalcohols) by the reduction of nitro alcohols and the electrochemical variant of the Henry synthesis.

Therefore, it seemed interesting to study the reactions of nitro alcohol RAs in media with a low proton-donor activity using experimental (cyclic voltammetry, chronoamperometry, coulometry, controlled potential electrolysis) and theoretical (numerical simulation of experimental data and nonempirical quantum-chemical calculations) methods. 1-Phenyl-2-nitroethanol (PNE), the product of the Henry reaction between benzaldehyde and nitromethane was chosen as a model compound. This choice is caused by the fact that PNE is one of the simplest compounds of this type and probable products of its reactions in the near-electrode layer are electrochemically active at fairly early potentials which, in turn, makes it possible to reliably detect their formation by the methods used.

2. Experimental

2.1. Material, Solutions & Apparatus

PNE was synthesized using a known procedure. The following reagents were used: MeCN (“extra dry”) and Bu4NClO4 (Acros Organics). Benzaldehyde was distilled under reduced pressure prior to use. 1H NMR spectra were recorded on a Bruker AM-300 spectrometer in d6-DMSO. Chronoamperometry (CA), cyclic voltammetry (CV), coulometry and controlled potential electrolysis were implemented on a computer-assisted potentiostat IPC-Pro MF manufactured by Econix (sweep rate error 1.0%, potential setting device 0.25 mV). The experiments were performed in a 10 ml 5-neck glass conic electrochemical cell with a water jacket for thermostating. Polarization curves were recorded using a three-electrode scheme. Working electrode was a glassy carbon disc (d = 1.7 mm). A graphite rod was utilized as a cathode for the electrolysis. A platinum wire (insulated by a ceramic membrane in electrolyses) served as an auxiliary electrode. A saturated calomel electrode (SCE) was used as the reference electrode. It was linked to the solution by a bridge with a porous ceramic diaphragm filled with background electrolyte (0.1 M Bu4NClO4 solution in MeCN). For the CA and CV curves analysis, the values of current in the presence of the substance were corrected for current of the background electrolyte at this potential. Uncompensated resistance in the cell was measured using the CV curves of ferrocene electrooxidation in the same background electrolyte varying its concentration and the potential scan rate in a similar manner as in reference. Uncompensated resistance in the typical case was 380 Ohm. The accurate area of working electrode was also determined by simulation of the CV curves of ferrocene electrooxidation (the ferrocene diffusion coefficient in MeCN is known). The tested solutions were thermostated at 25 ± 1 °C. Desaeration of solutions was performed by high-purity argon passing through. To avoid a possible contact of the solution surface with the ambient air during the experiment argon was constantly fed to the cell’s free space above the solution surface. In the typical case 5 ml solution was utilized. The steady-state voltammograms obtained by plotting the current values measured at various potentials by chronoamperometry at a specified time (e.g. 4 s after applying the potential as shown in Figs 1 and 6).
coincidence with the experimental results was attained when using the following set of values of rate constants: 
\[ k_2 = 1 \cdot 10^3; \quad k_5 = 2 \cdot 10^2; \quad k_6 = 1 \cdot 10^3; \quad k_8 = 1 \cdot 10^2; \quad k_9 = 7 \cdot 10^4; \quad k_{16} = 5 \cdot 10^5; \quad k_{17} = 1 \cdot 10^6; \quad k_{18} = 4 \cdot 10^5; \quad k_{19} = 2 \cdot 10^7. \]

The equilibrium constants of the redox reactions were calculated from the difference in standard potentials. All other reactions were assumed to be irreversible. The values of diffusion coefficients for all compounds were accepted equal to \(1.0 \cdot 10^{-5} \text{ cm}^2 \text{s}^{-1}\), while those of transfer coefficients (\( \alpha \)) were taken equal to 0.5. The values of standard potentials and heterogeneous electron transfer constants (\( k_s \)) were determined by their optimization using standard DigiElch Professional techniques to attain the best coincidence of the model and experimental curves detected in the above indicated ranges of potential scan rates and concentrations followed by determining average values. The values obtained are 
\[ E°_{1} = -1.43, \quad E°_{10} = -1.58, \quad E°_{15} = -1.87 \text{ V}. \]
The \( E° \) values for all free radical species has been treated as positive. It was found that in contrast to bezaldehyde reduction cathodic reactions (1) and (10) were electrochemically quasi-reversible (\( k_s = k_{10} = 0.002 \)) due to, most likely, significant changes in the structures of these compounds that occur during the electron transfer. In particular, as shown by the quantum-chemical calculations, the elongation of the N–O bond upon the formation of PNE and nitromethane radical anions is approximately the same, being about 0.1 Å.

### 2.3. Quantum-chemical Calculations

The quantum-chemical calculations of aromatic molecules were performed in the framework of the density functional theory (DFT) using the B3LYP exchange correlation functional.\(^{14–16}\) As we showed earlier,\(^ {17}\) the results of calculation of the energy of RAs of compounds containing \( \pi \)-bonds depend, to a considerably higher extent, on the presence of diffuse functions on hydrogen atoms in the basis set, whereas these changes are insignificant for compounds without \( \pi \)-bonds. Therefore, in this work, all calculations were performed using the 6-311++G(d,p) basis set. The influence of solvation was taken into account in the framework of the reactive field continuum model theory PCM\(^{18–20}\) and CSC-PCM\(^ {21}\) using the parameters for DMSO close to the parameters of MeCN used in experiment. All quantum-chemical calculations were performed using the Gaussian-03\(^ {22}\) and GAUSSIAN-09\(^ {23}\) program packages. Natural orbital’s populations were analyzed using the NBO program package.\(^ {24}\) Geometry optimization was carried out for all species under investigation. The character of the found stationary points (minimum or saddle point on the PES) was determined by the calculation of eigenvalues of the matrix of the second derivatives of energy with respect to nuclear coordinates.

### 3. Results and Discussion

The steady-state voltammograms (Fig. 1) of PNE exhibit three cathodic waves to which three cathodic peaks (\( p'_1, p'_2, \) and \( p'_3 \)) correspond in the cyclic voltammograms (Fig. 2). The potentials of half-waves of the second and third waves in the steady-state voltammograms and peak potentials \( p'_2 \) and \( p'_3 \) in the voltammogram correspond to the potentials of nitromethane and benzaldehyde electroreduction. The latter suggests the cleavage of the C–C bond (reaction 2) in the RA of PNE formed at the first wave potentials (reaction 1). The possibility of reaction 2 is indicated by both the structure of the singly occupied orbital (according to the quantum-chemical calculations, this orbital has the nodal plane...
passing through this bond) of the PNE RA and the fact that, according to these calculations, reaction 2 is thermodynamically favorable ($\Delta G \approx -2$ kcal mol$^{-1}$).

Free radicals formed in reactions of this type (e.g., carbon-halogen bond cleavage$^{25}$) are reduced (reaction 3), as a rule, at potentials much more positive than those of the corresponding depolarizer molecule. Therefore, the overall process of electroreduction should described by the ECE scheme. In ECE case, the apparent number of electrons ($n_{app}$), calculated as the ratio of the limiting current of the first wave of PNE ($i_{lim}^1$) in the steady-state voltammograms and the theoretical value of diffusion current ($i_d$), should increase from 1 to 2 with the rate constant of reaction 2 ($k_2$) and transient time ($t$). However, a reciprocal dependence is observed experimentally: $n_{app}$ decreases from values close to 1 to 0.72 at $t = 4$ s.

Fig. 3. The CV curve of a 5 mmol L$^{-1}$ PNE solution at the glassy-carbon electrode in 0.1 M Bu$_4$NClO$_4$/MeCN before (a) and after (b) 0.25 F electricity was passed through the solution at the potential of the first step and CV curve of a 5 + 5 mmol L$^{-1}$ mixture of nitromethane and benzaldehyde (c). $v = 0.1$ V s$^{-1}$.

The coulometric results also show that the amount of electricity required for exhausted PNE electroreduction is significantly smaller than 1 F mol$^{-1}$. For example, already after 0.25 F mol$^{-1}$ was consumed in the electroreduction of a PNE solution at first wave potentials of 5 mmol L$^{-1}$, peak $p'_1$ in voltammograms of the catholyte disappears almost completely (Curves a and b in Fig. 3) when the peaks $p'_2$, and $p'_3$ of the products achieve the limiting values. All that suggests that the low number of electrons involved in electroreduction is related, most likely, to the electrochemically initiated cyclic homogeneous reaction. We observed a similar reaction earlier for the electrochemical cleavage of the N–OH bond in radical anions of phenylhydroxylamines.$^{26}$

For the direct determination of the structure of the products, we carried out the controlled potential electrolysis corresponding to the limiting current of the first wave. We passed 0.25 F · mol$^{-1}$ of electricity through a 0.120 M solution of the substrate, after which the most portion of acetonitrile was evaporated. The $^1$H NMR spectrum of the residue in $d_6$-DMSO contains the characteristic signals of the nitromethane protons (4.42 ppm) and the proton of the carbonyl group of benzaldehyde (10.02 ppm), whereas the signals from the starting PNE are nearly absent. Signals from nitromethane and benzaldehyde are absent in the control experiment where the electrolysis conditions were completely reproduced but no current was passed through the solution. Therefore, it can be stated that electroreduction of PNE involved electrochemically initiated cyclic reaction and results in nitromethane and benzaldehyde formation.

In general, nitromethane and benzaldehyde can be formed not only by reactions (2) and (3). By analogy to the

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mentioned above electroreduction of phenylhydroxylamines it can be assumed that the electroreduction of PNE is accompanied by the protonation of the anionic products of reactions 2 and 3 with the starting PNE (reactions 4 and 5). Since it is known\(^{27}\) that the Henry reaction is reversible, the PNE anion can dissociate to benzaldehyde and nitromethane anion (6).\(^{27,28-29}\) It is important to note that this reaction can be accompanied by a decrease in the value of \( n_{\text{app}} \) compared to the values characteristic of the \( \text{ECE} \) processes.

However, it is most likely that the possibility of formation of the PNE anion in reaction 5 should be excluded from consideration, because \( pK_a \) of alcohols (e.g. \( pK_a \) of methanol in DMSO is 29\(^{30}\)) is by approximately 10 orders of magnitude \( \gg \) higher than \( pK_a \) of nitromethane (17.2\(^{31}\)). It is more probable that the PNE anion is formed due to the interaction with a highly basic carbanion in reaction 4. However, in this case, \( n_{\text{app}} \) cannot attain values lower than 1. In addition, the formation of equimolar amounts of nitromethane and benzaldehyde cannot be expected in this case, since benzyl alcohol should be formed in 25% yield (reaction 4) along with nitromethane and benzaldehyde.

The proton transfer (reaction 7) between the products of bond cleavage (reaction 2) seems much more probable due to the high acidity of the radical formed\(^{*}\). It should be mentioned that this reaction can occur directly in radical ion pairs, whose formation as primary products is possible for bond dissociation in RAs\(^{7}\). Since the reduction potential of benzaldehyde is much more negative than the reduction potential of PNE, the electron transfer from benzaldehyde RA to PNE and initiation of the cyclic process should be expected (reaction 8).

In this case, \( n_{\text{app}} \) can also adopt values lower than 1. The mechanism including stages (1)–(3) and (7)–(8), as can be seen from Fig. 4, describes well the time dependence of the limiting current of the first wave. The experimental and theoretical values of limiting current for the second wave are also similar (Table 1). However, in the case of the third wave, the divergence between these values is sufficiently high (Table 1) to conclude that the processes that occur at this potential cannot be described by reactions (1)–(3) and (7)–(8) only. Therefore, we studied the mechanism of electroreduction of nitromethane and benzaldehyde as well as that of their mixtures.

\[ \text{Ph} \text{CH}_2 \text{NO}_2^- + \text{PhOH}^- \rightarrow \text{PhCH}_2\text{O}^- + \text{PhNO}_2^- \]  
\[ \text{Ph} \text{CH}_2 \text{NCH}_3^- + \text{PhOH}^- \rightarrow \text{PhCH}_2\text{O}^- + \text{PhNO}_2^- \]  
\[ \text{Ph} \text{CH}_2 \text{NCH}_3^- + \text{PhOH}^- \rightarrow \text{PhCH}_2\text{O}^- + \text{PhNO}_2^- \]

\(*\) According quantum-chemical calculations the equilibrium (7) should be strongly shifted to the right (\( \Delta G < -10 \text{ kcal mol}^{-1} \)).

Only reactions (1)–(3) and (7)–(8) were involved in simulation.

Table 1. Ratio of the experimental and theoretical values of limiting currents for different reaction schemes (\( t = 2 \text{s} \))

<table>
<thead>
<tr>
<th>( E, \text{V vs SCE} )</th>
<th>( \text{mechanism} )</th>
<th>( \text{1st wave} )</th>
<th>( \text{2nd wave} )</th>
<th>( \text{3rd wave} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>–1.50 (1\text{st wave} )</td>
<td>(1)–(3), (7)–(8), (10)–(15)</td>
<td>1.01(^*)</td>
<td>0.97</td>
<td>0.97</td>
</tr>
<tr>
<td>–1.70 (2\text{nd wave} )</td>
<td>(1)–(3), (7)–(16)</td>
<td>0.99</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>–2.00 (3\text{rd wave} )</td>
<td>(1)–(3), (7)–(17)</td>
<td>0.77</td>
<td>0.77</td>
<td>1.02</td>
</tr>
</tbody>
</table>

Fig. 4. \( i-t \)-curve of 12 mmol L\(^{-1} \) PNE in MeCN containing 0.1 M \( \text{Bu}_4\text{NClO}_4 \) at the potential of the limiting current of the \( 1\text{st} \) waves (–1500 mV). Empty circles show corresponding simulated curve (see text).

\[ \text{Ph} \text{CH}_2\text{NCH}_3^- + \text{PhOH}^- \rightarrow \text{PhCH}_2\text{O}^- + \text{PhNO}_2^- \]  

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It should be noted that the nitromethane formed in reaction (7) can be reduced both at cathode and by electron transfer from the benzaldehyde RA (9). As already mentioned, RAs of aliphatic nitro compounds are unstable and decompose, in the absence of strong proton donors, with the C–N bond cleavage and their mechanism is described by the \textit{ECE} scheme under these conditions. The study of the mechanism of nitromethane electroreduction showed that, although the C–N bond cleavage in the nitromethane RA (reaction 11) is fast, the observed dependences of the peak current on the potential scan rate cannot be described by this reaction and the reduction of the formed radical to anion (reaction 12). The reason is the high proton-donor ability of nitromethane, due to which the protonation of the methane anion can compete with the protonation of this anion with acetonitrile, whose acidity is lower by 14 orders of magnitude (pK\textsubscript{a} of acetonitrile in DMSO is 31.3\textsuperscript{2}). As can be seen from Fig. 5, this mechanism adequately describes the CV data. The ratio of the experimental to theoretical peak currents is practically independent of scan rate and equal 1.02 ± 0.04.

\begin{align}
(10) \quad \text{CH}_3\text{NO}_2 + e^- \rightarrow \text{CH}_3\overset{\cdot}{\text{O}}_2 \\
(11) \quad \text{CH}_3\overset{\cdot}{\text{O}}_2 + e^- \rightarrow \text{CH}_3 + \text{NO}_2^- \\
(12) \quad \text{CH}_3^- + \text{NO}_2^- \rightarrow \text{CH}_4 + \overset{\cdot}{\text{O}}_2^- \\
(13) \quad \text{CH}_3^- + \text{CN}^- \rightarrow \text{CH}_4 + \overset{\cdot}{\text{C}}_2
\end{align}

\begin{align}
(14) \quad \text{CH}_3^- + \text{CN}^- \rightarrow \text{CH}_4 + \text{C}_2
\end{align}

\begin{align}
(15) \quad \text{CO} + \text{CO} \rightarrow \overset{\cdot}{\text{Ph}} + \overset{\cdot}{\text{Ph}}^- \\
(16) \quad \text{CO} + \overset{\cdot}{\text{Ph}} \rightarrow \overset{\cdot}{\text{Ph}}^- + \text{CO}
\end{align}

The addition of benzaldehyde to a nitromethane solution does not nearly affect its limiting current, whereas the limiting current of benzaldehyde in this mixture is by 50% lower than that in solutions containing no nitromethane. A similar situa-
tion is observed for currents of the corresponding CV-peaks (Fig. 7).

We supposed that the underestimated height of the second wave of benzaldehyde in its mixture with nitromethane is due to a decrease in the nitromethane concentration in the near-electrode layer (because of the reaction of nitromethane with the reduction products of benzaldehyde, RA or dimeric dianion) rather than to a decrease in the limiting current of the reduction of benzaldehyde itself. Taking into account that benzaldehyde radical anions are dimerized with a rate constant of $9.5 \cdot 10^4$ L mol$^{-1}$ s$^{-1}$ and the basicity of the $\pi$-RA is considerably lower than that of the $\sigma$-anions, it should be expected that it is the protonation of the dimeric dianion (reaction 17) that is the major reaction resulting in a decrease in the near-electrode concentration of nitromethane at the reduction potentials of benzaldehyde. In this case, the reduction of a mixture of nitromethane and benzaldehyde should be described by an array of reactions (11)–(17). Indeed, the ratios of the limiting current of the first wave and the overall current of two waves in the steady-state voltammogram of a mixture of nitromethane and benzaldehyde (Fig. 6) to analogous theoretical values are 1.00 and 1.01, respectively. A good agreement between the experimental and theoretical values is also observed for the CV-peak currents (Fig. 7). Reaction (17) exerts almost no effect on the limiting currents of the first and second waves in the steady-state voltammogram of PNE (Table 1), which is due, most likely, to the fact that benzaldehyde RAs formed in the homogeneous reactions participate in fast redox reactions (8) and (9).

Thus, the mechanism including reactions (1)-(3) and (7)-(17) adequately describes the electroreduction of PNE under the chromoamperometric conditions at the potential of the limiting current of PNE reduction.

Unlike the steady-state voltammogram, in the CV curves the peak currents of nitromethane reduction are much lower than it should be expected from the above mechanism (Fig. 8). Moreover, in contrast to nitromethane-

\[
\text{PhCH=O}^- + \text{NO}_2^- \rightarrow \text{PhCHO}^- + \text{NO}_2^+ \text{H}^+ \quad (17)
\]
ne itself whose $n_{sp}$ values increase with potential scan rate increasing, the peak of nitromethane at the CV curves of PNE exhibits a reciprocal tendency and is nearly absent at potential scan rates of 0.4 V s$^{-1}$ and higher. In our opinion, this is likely due to protonation of benzylic alcohol anion with nitromethane (18). The benzylic alcohol anion is formed by reduction of the corresponding free radical at the cathode (reaction 3) and in the bulk of solution (reaction 19). Reaction (18) is an additional factor decreasing the nitromethane concentration under the CV conditions. In fact, as can be seen from Fig. 8, the inclusion of this reaction into the mechanism of the process provides a good correspondence between the experimental and theoretical CV curves in the whole studied ranges of potential scan rates and PNE concentrations.

3. Conclusion

Thus, the results of studying PNE electroreduction by potential controlled electrolysis, chronocoulometry, and cyclic voltammetry in combination with numerical simulation suggest that the C-C bond is cleaved in the RA formed at the first stage of electroreduction to form the free radical of benzylic alcohol and nitromethane anion, which agrees with the quantum chemical calculation results. The proton transfer between these species affords nitromethane and benzaldehyde radical anion, which initiates the cyclic reaction by electron transfer to PNE (Scheme 1). The possibility of the reaction should be taken into accounts in the developing of electrochemical version of the Henry synthesis as well as in that of $\beta$-nitro alcohols electroreduction to amino alcohols.

4. Acknowledgements

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5. References

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