ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2011, **21**, 26–28

Mendeleev Communications

Electrochemically initiated transformation of 4-nitrophenylhydroxylamine into 4,4′-dinitroazobenzene

Mikhail A. Syroeshkin,*[a] Ludmila V. Mikhalchenko,[a] Marina Yu. Leonova,[a] Andrei S. Mendkovich,[a] Alexander I. Rusakov[b] and Vadim P. Gul'tyai[a]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 499 135 5328; e-mail: gufvp@ioc.ac.ru*

[b] *P. G. Demidov Yaroslavl State University, 150000 Yaroslavl, Russian Federation*

DOI: 10.1016/j.mencom.2011.01.011

Based on controlled potential electrolysis and cyclic voltammetry, the chain reaction of 4,4′-dinitroazobenzene formation was shown to be initiated during the electrochemical reduction of 4-nitrophenylhydroxylamine in DMF.

Substituted *N*-phenylhydroxylamines are easily accessible products of the electroreduction of nitroaromatic compounds in protic media.[1] Unfortunately, examples of their practical use are very rare because of the low stability of these compounds, which are strong genetic toxins[2] very dangerous to living organisms. Therefore, the development of convenient methods for the conversion of *N*-phenylhydroxylamines to practically interesting compounds is of interest.[3]

Recently,[4,5] we studied the electrochemical behaviour of compounds from this family in an aprotic medium by cyclic voltammetry (CV) and controlled potential electrolysis using 2- and 4-nitrophenylhydroxylamines (NPHAs) as examples. Their electroreduction at the first electron transfer potential afforded corresponding nitroanilines and NPHA anions. According to the CV data, the process includes the step of protonation of the base formed upon the electroreduction[4,5] by the starting NPHA ('self-protonation' reaction).

$$3\ \mathrm{RNHOH}\ \xrightarrow[-\ \mathrm{H_2O}]{2e^-}\ \mathrm{RNH_2}\ +\ 2\ \mathrm{RNOH^-} \qquad (1)$$

$$\mathrm{R} = 2\text{-}\mathrm{NO_2C_6H_4},\ 4\text{-}\mathrm{NO_2C_6H_4}$$

The quantum-chemical study of this reaction suggested that the first step of the transformation is the cleavage of the N–O bond of the hydroxylamine group in the NPHA radical anion to form the hydroxide anion and the radical, which is reduced to the corresponding anion at this potential.[5] Most likely, these are the anions that act as a base protonated by the starting NPHA. However, the controlled potential electrolysis data[4] indicate that NPHA can interact with its anion along with the above reactions. This work is devoted to the investigation of this transformation.

The CV curve of the electroreduction of 4-NPHA[†] is shown in Figure 1 (curve *1*). As found previously,[4] the cathodic peaks $P_{\mathrm{R},1}$ and $P_{\mathrm{R},2}$ correspond to the steps of reduction of 4-NPHA and 4-nitroaniline, respectively, whereas the anodic peaks $P_{\mathrm{O},1}$ and $P_{\mathrm{O},2}$ correspond to the oxidation of the 4-NPHA anion and starting NPHA. After electrolysis for a short time at the potential of the limiting current of the first step of electroreduction of 4-NPHA, during which 0.1 F of electricity was passed through the solution,[‡] the shape of the CV curve (Figure 1, curve *2*) underwent almost no changes, except for an insignificant decrease in the currents of the peaks $P_{\mathrm{R},1}$ and $P_{\mathrm{O},2}$ and an increase in the peak $P_{\mathrm{O},1}$. The above changes approximately correspond to a decrease in the concentration of the depolarizer and an increase in the amount of the electroreduction product, which results from the consumption of the above amount of electricity according to the stoichiometry of reaction (1). However, after the catholyte was stirred for 3 h in an argon atmosphere, the character of the CV curve changed completely (Figure 1, curve *3*). In particular, the peaks $P_{\mathrm{R},1}$ and $P_{\mathrm{O},2}$ disappeared. At the same time, two new reversible peaks, whose potentials are more positive than that of the electroreduction peak of 4-NPHA, appeared in the CV curve. Taking into account that no similar change in the shape of the CV curve of the test solution of 4-NPHA, which was not subjected to electrolysis, is observed even on storage during several days, we believe

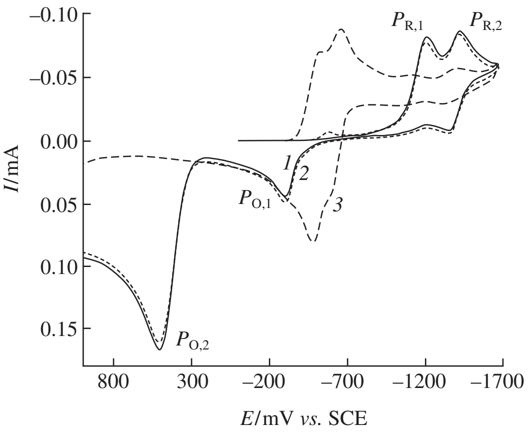


Figure 1 CV curves of the reduction of (*1*) a 10 mM 4-NPHA solution at a disk carbositall electrode (*d* = 3 mm) in 0.1 M $\mathrm{Bu_4NClO_4}$/DMF, (*2*) the same solution after 0.1 F of electricity was passed through it at the potential of the first reduction step for 10 min, and (*3*) the solution obtained after 3 h. The scan rate was 0.1 V $\mathrm{s^{-1}}$, and the cell temperature was 298 K.

[†] 4-NPHA was synthesized according to the published procedure.[6]

[‡] Electrolysis was carried out at the potential of the first step of the electroreduction of 4-NPHA, using a 0.1 M solution of $\mathrm{Bu_4NClO_4}$ in DMF deaerated with argon as an electrolyte. The working electrode was a Pt grid, and the reference electrode was a saturated calomel electrode (connected to the solution through a salt bridge filled with the supporting electrolyte). A Pt wire separated with a ceramic membrane served as an auxiliary electrode. In the typical case, the electrolysis lasted about 10 min, and the temperature of the solution was maintained at 25 °C with a thermostat.

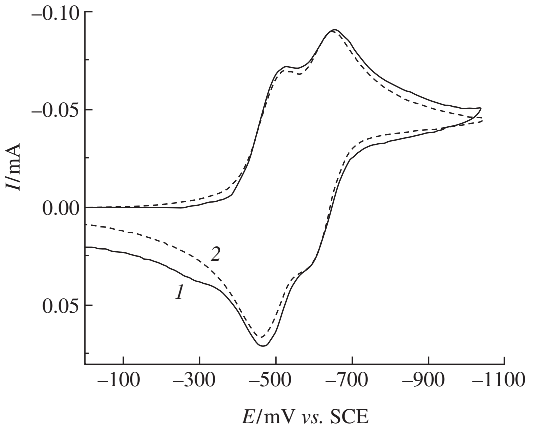
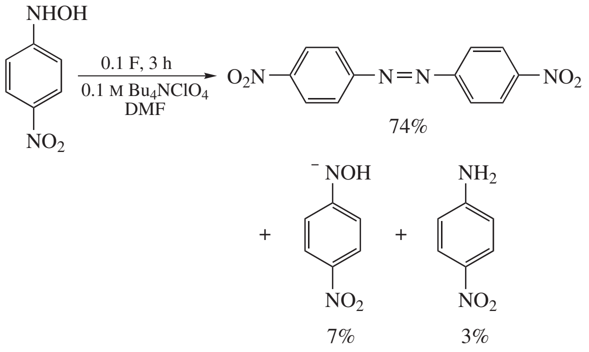


Figure 2 (*1*) CV curve of a 10 mM 4-NPHA solution at a disk carbositall electrode (d = 3 mm) in 0.1 M Bu_4NClO_4/DMF 3 h after 0.1 F of electricity was passed through the solution at the potential of the first step, and (*2*) CV curve of a 4 mM solution of 4,4'-dinitroazobenzene. The scan rate was 0.1 V s^{-1}, and the cell temperature was 298 K.

that the changes observed are related to the occurrence of the chain (cyclic) reaction initiated by the electrolysis product.

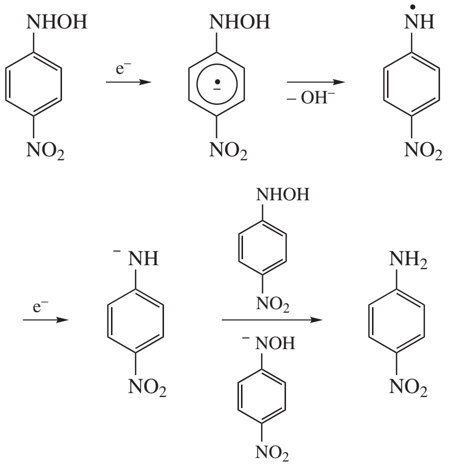
A comparison of the CV curve of the product of this reaction (Figure 2, curve *1*) with the voltammogram of 4,4′-dinitroazobenzene[§] (Figure 2, curve *2*) suggests that they are identical. The HPLC data[¶] indicate that 4,4′-dinitroazobenzene is formed in 74% yield under the described conditions (Scheme 1). In addition, the test solution contains small amounts of the 4-NPHA anion (7%)[††] and 4-nitroaniline (3%) formed in reaction (1).



Scheme 1

The formation of 4,4′-dinitroazobenzene as the major product of the chain reaction suggests that this reaction is initiated by the interaction of the 4-NPHA anion formed by reaction (1) with the starting compound.

This is also indicated by the fact that reaction (1) becomes predominant and the overall yield of its products reaches 69% in the case of exhaustive electrolysis at potentials of the limiting current of the first step of the electroreduction of NPHA, *i.e.*, under the conditions where the time of the simultaneous presence of 4-NPHA and its anion in the reaction mixture is minimum.[4]



Scheme 2

The combination of 4-NPHA and its anion with the formation of 4,4′-dinitroazobenzene should simultaneously result in the formation of the hydroxide anion (Scheme 2). The essence of the chain reaction is as follows: the hydroxide anion undergoes protonation by 4-NPHA to produce the 4-NPHA anion, which reacts with 4-NPHA affording dinitroazobenzene and the hydroxide anion (Scheme 3). This scheme assumes that the result of the chain reaction should be independent of the method of generation of the NPHA anion. Therefore, we generated the 4-NPHA anion by the interaction of 4-NPHA with a strong base. The addition of 0.1 equiv. of Et_4NOH to a 0.01 M solution of 4-NPHA in DMF followed by stirring for 3 h results in the formation of 4,4′-dinitroazobenzene in 78% yield (according to HPLC data). At a preparative scale, the product was isolated in 74% yield.[‡‡] Thus, the experimental data indicate that the mechanism of the electrochemically initiated transformation of 4-NPHA into 4,4′-dinitroazobenzene can be described by Scheme 3.

Note that, as a rule, the pre-electrode electroinitiated chain reactions occur with a high rate accompanied by the fast (within several minutes) drop of the current of the electroreduction of the substrate.[10,11] No similar effect is observed in this case. The reason is not clear, but one may suppose that the nucleophilic replacement of a hydroxyl group in 4-NPHA by 4-NPHA anion gives rise to Ar–NH–N(OH)–Ar, which is relatively stable and dehydrates slowly giving the final product (4,4′-dinitroazobenzene). This intermediate product may be responsible for the cathodic peak different from those of starting material and final products observed at CV curves during the reactions, but it disappears when the reaction completes.

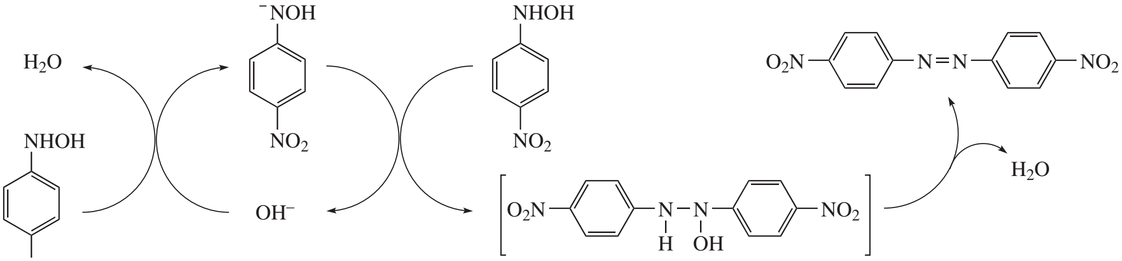
In contrast to 4-NPHA, unsubstituted *N*-phenylhydroxylamine has a much lower electron affinity, and it cannot be reduced cathodically at the available range of the potentials. The result of the experiment with Et_4NOH addition in case of *N*-phenylhydroxylamine is different from that for 4-NPHA. No formation of azobenzene is observed, most probably, because of the much lower acidity of *N*-phenylhydroxylamine, as compared with 4-NPHA.[§§] In favour of the suggestion says the fact that the conversion of *N*-phenylhydroxylamine to azobenzene in alkaline media in an inert atmosphere takes an extremely long time (10 days).[13]

[§] 4,4′-Dinitroazobenzene was synthesized from 4,4′-dinitroazoxybenzene by the electrochemical reduction to the corresponding hydrazo compound followed by its oxidation similarly to a procedure described in ref. 7. 4,4′-Dinitroazoxybenzene was synthesized from 4-nitroaniline by the reported method.[8]

[¶] HPLC was carried out on the Diaspher-110-C16 column (5 μm, 2.0×80 mm) using a mixture MeCN/0.1 M phosphate buffer with pH 3 in ratios of 25:75 and 50:50 as the mobile phase and the UV detector at λ = 350 nm.

[††] The yield of the 4-NPHA anion was determined by the absence of the oxidation peak of 4-NPHA in the CV curve of the obtained solution and by the appearance of 4-NPHA under the chromatographic conditions (under these conditions, the 4-NPHA anion is protonated by the acidic mobile phase).

[‡‡] In the synthesis, 0.1 equiv. Et_4NOH was added to 0.1 M deaerated with argon solution of 4-NPHA in DMF. In the course of reaction, 4,4′-dinitroazobenzene was precipitated, mp 230 °C (lit.,[9] mp 227–229 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.12 (d, 4H), 8.43 (d, 4H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 123.88, 123.97 (C^2, C^6, $C^{2'}$, $C^{6'}$), 125.00, 125.14 (C^3, C^5, $C^{3'}$, $C^{5'}$). MS, *m/z* (%): 272 (M^+, 3), 150 (35), 122 (100), 92 (40), 76 (98), 64 (26), 50 (64).



Scheme 3

Note that this result is important to specify the general mechanism of the electroreduction of aromatic nitro compounds. At the same time, it provides a possibility of using hydroxylamines as the substrates for the synthesis of corresponding amines and azo compounds. The latter are of great practical interest,[14] but their preparation by the electroreduction of nitro compounds is difficult, because their reduction occurs, as a rule, at earlier potentials than that of the primary condensation products, *viz*., azoxy compounds.[15] Note that the thorough control of the amount of the proton donor introduced into the catholyte (no more than 4 equiv. required for the formation of hydroxylamines) is necessary when the described chain reaction is used for the electrosynthesis of azo compounds from aromatic nitro derivatives. This seems reasonable since the anions of hydroxylamino derivatives necessary for the initiation of the chain reaction undergo protonation in an excess of acidic components in the solution.

This work was carried out in the framework of the Federal Target Program ‘Scientific and Pedagogical Professional Community of Innovation Russia’ for 2009–2013.

[§§] The data on pK_a of 4-NPHA are not available. Those for *N*-(4-cyanophenyl)hydroxylamine and *N*-phenylhydroxylamine in DMSO are 18.6 and 24.2, respectively.[12] Taking into account that the values of Hammet constants for NO_2 and CN groups are 0.778 and 0.660, respectively, a conclusion can be made that the difference in pK_a values between 4-NPHA and *N*-phenylhydroxylamine should be not less than 5.6 units.

References

1 J. Grimshaw, *Electrochemical Reactions and Mechanisms in Organic Chemistry*, Elsevier, Amsterdam, Lausanne, New York, Oxford, Shanon, Singapore, Tokyo, 2000, pp. 371–396.
2 G. Sabbioni, *Environ. Health Perspect.*, 1994, **102**, 61.
3 S. Ung, A. Falguieres, A. Guy and C. Ferroud, *Tetrahedron Lett.*, 2005, **46**, 5913.
4 M. A. Syroeshkin, A. S. Mendkovich, L. V. Mikhalchenko, A. I. Rusakov and V. P. Gul’tyai, *Mendeleev Commun.*, 2009, **19**, 258.
5 M. A. Syroeshkin, L. V. Mikhalchenko, A. S. Mendkovich, V. P. Gul’tyai and A. I. Rusakov, *Chem. Listy*, 2009, **103**, 243.
6 R. Kuhn and F. Weygand, *Ber. Dtsch. Chem. Ges.*, 1936, **69**, 1969.
7 R. Hazard and A. Tallec, *Bull. Soc. Chim. Fr.*, 1971, 2917.
8 E. B. Melnikov, G. A. Suboch and E. Y. Belyaev, *Zh. Org. Khim.*, 1995, **31**, 1849 (*Russ. J. Org. Chem.*, 1995, **31**, 1640).
9 J. Dale and L. Vikersveen, *Acta Chem. Scand. B*, 1988, **42**, 354.
10 V. P. Gultyai and A. S. Mendkovich, *Ross. Khim. Zh.* (*Zh. Ross. Khim. Ob-va im. D. I. Mendeleeva*), 2005, **XLIX**, 40 (in Russian).
11 Y. Mugnier, J.-C. Gard, Y. Huang, Y. Couture, A. Lasia and J. Lessard, *J. Org. Chem.*, 1993, **58**, 5329.
12 F. G. Bordwell and W.-Z. Liu, *J. Am. Chem. Soc.*, 1996, **118**, 8777.
13 E. Bamberger and F. Brady, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 271.
14 A. Grirrane, A. Corma and H. García, *Science*, 2008, **322**, 1661.
15 H. Lund, in *Organic Electrochemistry*, 4th edn., eds. H. Lund and O. Hammerich, Marcel Dekker, New York, 2001, ch. 9.

Received: 9th June 2010; Com. 10/3541