ISSN 1070-3632, Russian Journal of General Chemistry, 2011, Vol. 81, No. 10, pp. 2151–2156. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © E.S. Kagan, V.V. Yanilkin, N.V. Nastapova, V.I. Morozov, I.Yu. Zhukova, I.I. Kashparov, V.P. Kashparova, 2011, published in Zhurnal Obshchei Khimii, 2011, Vol. 81, No. 10, pp. 1699–1704.

Electrochemical Oxidation of 1-Chloro(bromo)-2,2,6,6-tetramethylpiperidines

E. S. Kagan[a], V. V. Yanilkin[b], N. V. Nastapova[b], V. I. Morozov[b], I. Yu. Zhukova[a], I. I. Kashparov[a], and V. P. Kashparova[a]

[a] *South-Russian State Technical University, ul. Prosveshcheniya 132, Novocherkassk, 346421 Russia*
e-mail: kagan29@mail.ru

[b] *Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center, Russian Academy of Sciences, Kazan, Tatarstan, Russia*
e-mail: yanilkin@iopc.ru

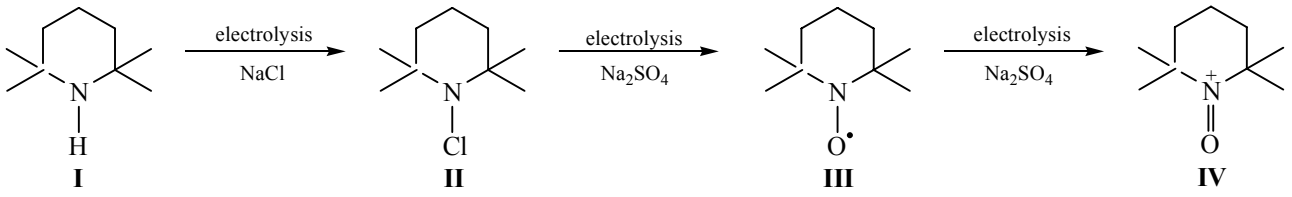
Received September 27, 2010

Abstract—Electrochemical oxidation of 1-haloamines of the 2,2,6,6-tetramethylpiperidine series results in the formation of relatively stable radical-cations, detected by the methods of cyclic voltammetry and ESR spectroscopy. The final products of electrochemical oxidation of these haloamines are stable nitroxyl radicals.

DOI: 10.1134/S1070363211100197

Earlier [1] we have shown that the electrolysis of 2,2,6,6-tetramethylpiperidine (**I**) in the presence of chloride ions in the diaphragm-free electrolyzer in the two-phase system methylene chloride–water results in the corresponding nitroxyl radical, 2,2,6,6-tetramethylpiperidine-1-oxyl (**III**) (Scheme 1). The nitroxyl radical is obtained in a good yield also by the electrolysis of 1-chloro-2,2,6,6-tetramethylpiperidines under similar conditions. The preparative synthesis of radical **III** can be conducted also by oxidation on the anode in a diaphragm electrolyzer, using amine **I** as a substrate, and subsequent chemical reduction of the formed oxoammonium ion **IV** (Scheme 1) with sodium nitrite. On this basis, the method of synthesis of 2,2,6,6-tetramethylpiperidine-1-oxyl by the electrolysis of *N*-chloro-2,2,6,6-tetramethylpiperidines or 2,2,6,6-tetramethyl-piperidine hydrochloride in the two-phase system water–methylene chloride was elaborated.

Scheme 1.

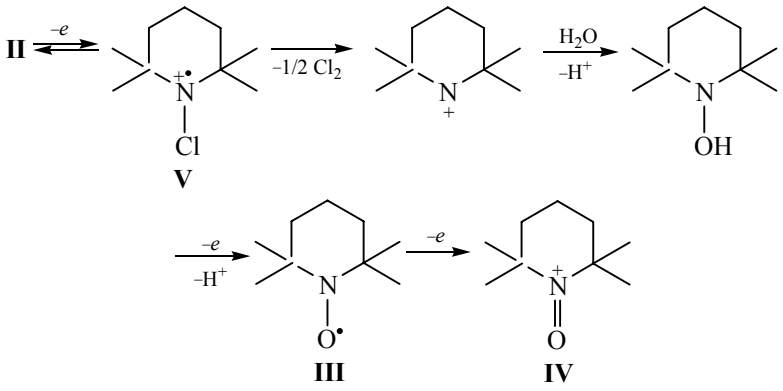


That was the first and the so far the only example of electrochemical oxidation of 2,2,6,6-tetramethylpiperidine to the corresponding nitroxyl radical.

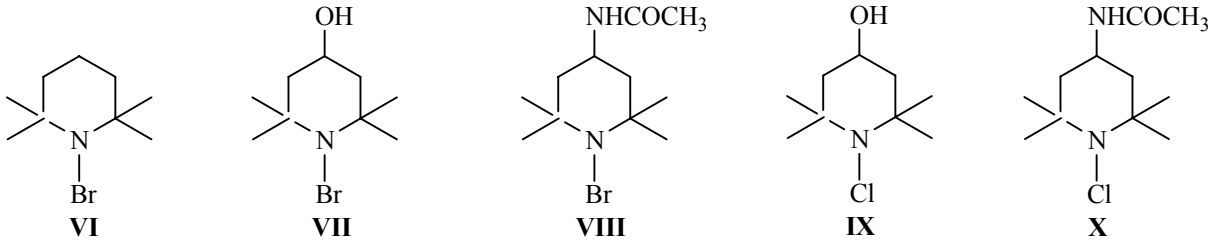
In the previous report [2] we have used the methods of voltammetry and ESR spectroscopy to investigate the electrochemical oxidation of 1-chloro-2,2,6,6-tetramethylpiperidine (**II**) in acetonitrile. Based on the data obtained, the mechanism of formation of the nitroxyl radical **III** and the oxoammonium ion **IV** upon oxidation of chloramine **II** was suggested, which included the stages of formation of radical cation **V**, elimination of the chlorine molecule with subsequent hydroxylation, elimination of protons and electron transfer (Scheme 2).

The present study is a continuation of this work and was undertaken to determine the generality of the reaction, the effect of the nature of the halogen atom and the substituent in position 4 of the piperidine ring

Scheme 2.



on the reaction of electrochemical oxidation of 1-halo-2,2,6,6-tetramethylpiperidines. In the present work, the reaction of electrochemical oxidation of haloamines **VI–X** is studied using the methods of CVA, ESR spectroscopy, and by preparative electrolysis.



Cyclic voltammograms (CVA) of haloamines **VI–X** obtained in the MeCN/0.1 M Bu_4NBF_4 medium on a glass carbon electrode are principally similar to the curves of the earlier studied chloramine **II** [2]. For chloramines, one extended irreversible reduction peak is registered in the far cathode range of potentials, for bromamines this peak is shifted to lower cathode potentials and doubled (Table 1). In the anode range, for all compounds **VI–X** one one-electron oxidation peak is detected, the bromamines being oxidized only slightly easier than chloramines. For chloramine **II** and bromamine **VI** the difference of potentials of the oxidation peaks is as low as 50 mV (Table 1). For all compounds regardless of the nature of the halogen atom the current of the oxidation peak $i_{p,ox}$ regularly decreases with the rate of the potential sweep υ in the range from 200 to 20 mV s^{-1} (Figs. 1, 2), and the plot $i_{p,ox}$–$υ^{1/2}$ is linear, suggesting the diffuse nature of the peak current. On the reverse branch of CVA for all rates of potential sweep an intense peak of re-reduction is registered, shifted by 60–70 mV to lower anode values relative to the oxidation peak. This is indicative of reversibility of both the stage of the electron transfer and the whole electrode process of one-electron oxidation; in other words, it points to a considerable stability of the formed radical cations of haloamines during the time of voltammetry measurements (seconds). Typical CVAs for bromo- and chloramines are depicted in Figs. 1, 2, and the electrochemical characteristics from the CVA data for compounds **II, VI–X** are given in Table 1.

Table 1. CVA data for halogenamines **II, VI–X** on a glass carbon electrode in CH_3CN/0.1 M Bu_4NBF_4, ($c = 2\times10^{-3}$ M), $υ = 100$ mVs^{-1}

Comp. no.	$E_{p,ox}$, ($E_{p,rered}$), V	$E_{p,red}$, V
II[a]	1.11 (1.05)	–2.10
YI	1.06 (1.00)	–1.36
	(0.35)	–1.81
YII	1.08 (1.01)	–1.49
	(0.39)	–1.69
VIII	1.10 (1.02)	–1.56
IX	1.18 (1.11)	–2.13
X	1.20 (1.13)	–2.26

[a] Earlier obtained data [2].

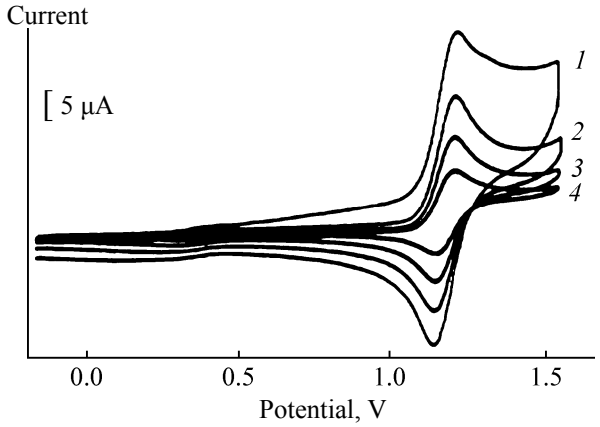


Fig. 1. CVA curves for oxidation of chloramine **X** (c = 2×10^{-3} M) on a glass carbon electrode in CH_3CN/0.1 M Bu_4NBF_4 at different potential sweep rates, mV s^{-1}: (*1*) 200; (*2*) 100; (*3*) 50; and (*4*) 20.

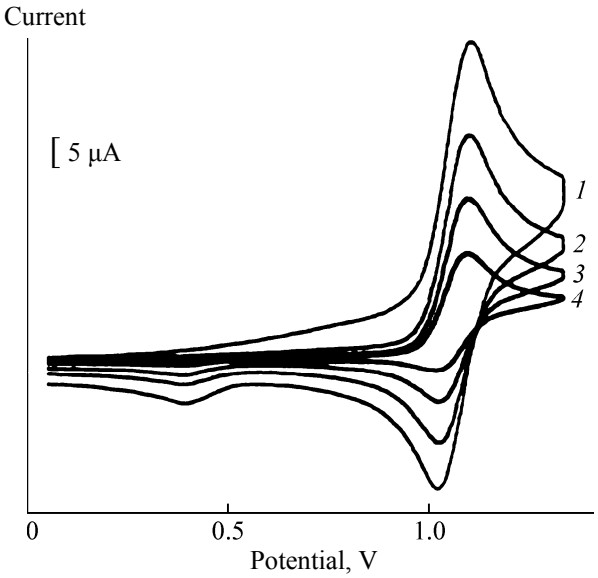
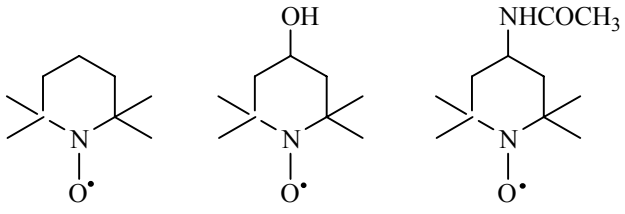


Fig. 2. CVA curves for oxidation of bromamine **VII** (c = 2×10^{-3} M) on a glass carbon electrode in CH_3CN/0.1 M Bu_4NBF_4 at different potential sweep rates, mV s^{-1}: (*1*) 200; (*2*) 100; (*3*) 50; and (*4*) 20.

Electrochemical oxidation of unsubstituted sterically hindered amines of the 2,2,6,6-tetramethylpiperidine series under similar conditions also proceeds with the formation of radical cations, which, however, cannot be experimentally detected (the cathode peak of re-reduction is absent) due to fast deprotonation with the formation of the corresponding aminyl radical detected by the ESR method [3, 4]. Radical cations of haloamines **II, VI–X** were directly registered by the ESR spectroscopy method when performing the electrooxidation of the Pt electrode with the potential of +1.1 V for bromamines and +1.3 V for chloramines in the resonator of the ESR spectrometer at a low temperature (–10°C). In Figs. 3, 4, typical ESR spectra of radical cations obtained by oxidation of bromamine **VI** (Fig. 3) and chloramine **X** (Fig. 4) as well as the spectra of the corresponding nitroxyl radicals obtained after completion of the process of oxidation and subsequent re-reduction at 0 V are shown.



III **VIIa** **VIIIa**

The experimental spectra completely coincide with the theoretical spectra calculated using the WinSIM EPR DESIGN V. 9.5 program [5]. Oxidation of bromamine **VII** leads to a radical cation of the same

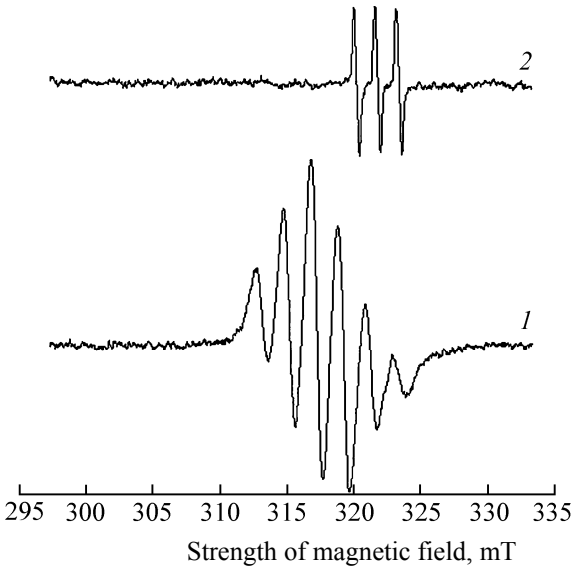


Fig. 3. ESR spectra (*1*) of the radical cation of bromamine **VI** generated electrochemically at E = +1.10 V in MeCN/0.1 M Bu_4NBF_4 on the Pt electrode at –10°C, and (*2*) the nitroxyl radical **III** obtained after completion of the process of oxidation and subsequent re-reduction at 0 V ($c_{\mathbf{VI}}$ = 2×10^{-3} M).

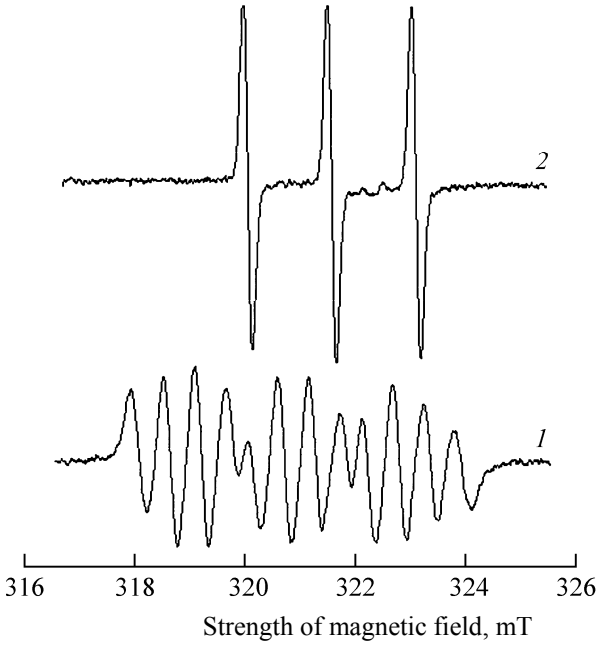


Fig. 4. ESR spectra of (*1*) the radical cation of chloramine **X** generated electrochemically at E = +1.20 V in MeCN/0.1 M Bu_4NBF_4 on the Pt electrode at –10°C, and (*2*) the nitroxyl radical **VIIIa**obtained after completion of the process of oxidation and subsequent re-reduction at 0 V ($c_{\mathbf{X}} = 2\times10^{-3}$ M).

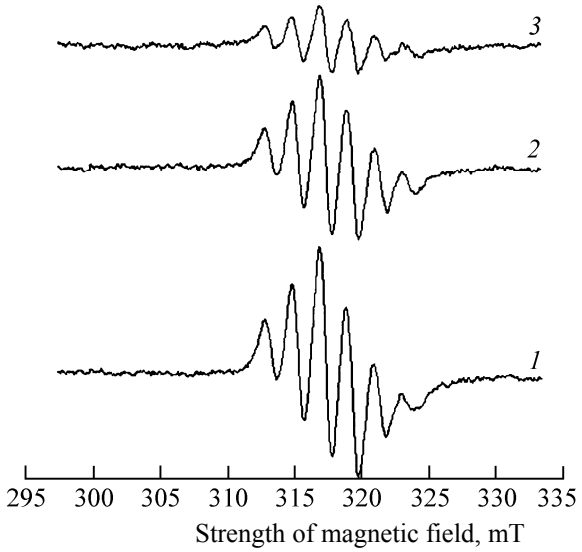


Fig. 5. ESR spectra of the radical cation of bromamine **VI** generated electrochemically at E = +1.10 V in MeCN/0.1 M Bu_4NBF_4 on the Pt electrode at various temperatures, °C: (*1*) –10, (*2*) +10, and (*3*) +30 ($c_{\mathbf{VI}} = 2\times10^{-3}$ M).

type that is formed from bromamine **X** although in much lower yield. The characteristics of the ESR spectra are determined by the nature of the halogen (Table 2).

When the temperature increases, the intensity of the ESR signal of radical cations decreases (Fig. 5), which is indicative of a decrease of their stability.

The decrease of the intensity of the ESR signal after the electrolysis is switched off has shown that radical cations of bromamines are less stable than radical cations of chloramines. In particular, the decay half-time of the radical cation of compound **X** at 243 K is ~8 min, while for radical cation of compound **VIII** it is ~3 min at 243 K and 45 s at 283 K. With this, no other paramagnetic species, for example, the aminyl radicals, are detected.

After completion of the process of oxidation of haloamines **II**, under the conditions of generation of radical cations, the subsequent reduction of the solutions at 0 V results in appearing the signal of the corresponding nitroxyl radical **III, VIIa, VIIIa** (Figs. 3, 4), which is intense in the case of bromamines **VI–VII** and weak for chloramines **II, IX–X**. Even for a protracted electrolysis of chloramine **X** the intensity of the signal of the corresponding nitroxyl radical **VIIIa** remains low. The intensity of this signal drastically increases if all the processes of oxidation and re-reduction are carried out at room temperature. Therefore, in the case of bromamines, the formation of oxoammonium ion and, afterward, the nitroxyl radical, takes place to a considerable extent, whereas in the case of chloramines at least two channels of decay of the primary radical cations exist, the ratio of their rates being dependent on the temperature. At room temperature, the contribution of the route via the oxoammonium ion formation increases, while at lower temperatures another route predominates, whose nature is not clear yet. The characteristics of the ESR spectra of the nitroxyl radicals **III, VIIa–VIIIa** are given in Table 2.

Therefore, the radical cations of 1-halogeno-2,2,6,6-tetramethylpiperidines formed upon electrochemical oxidation in acetonitrile are substantially more stable than of the corresponding 2,2,6,6-tetramethylpiperidines, that makes them accessible for experimental investigation by the methods of CVA and ESR under conventional conditions in the second time scale. One of the reasons of a higher stability of the radical cations formed by oxidation of *N*-halopyridines

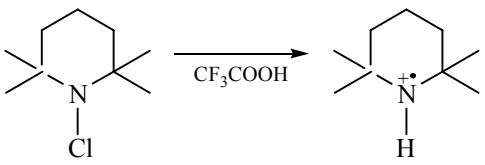
Table 2. Parameters of the ESR spectra of radical cations formed upon electrochemical oxidation of halogenamines **II, VI–X**, radical cation **XI** obtained by photolysis of chloramine **II** in CF_3COOH solution, and nitroxyl radicals **III, VIIa–VIIIa**

Comp. no.	Number of lines	*g*-Factor	a^N, mT	$a^{35}Cl$, mT $a^{37}Cl$, mT	$a^{79}Br$, mT $a^{81}Br$, mT	a^HCH_3, mT
II[a]	12	2.0093	2.110	0.600 0.500		
VI	6	2.0230	2.10		1.85 1.99	
VII	6	2.0230	2.10		1.85 1.99	
VIII	12	2.0093	2.081	0.585 0.486		
III	3	2.0057	1.57			
VIIa	3	2.0059	1.59			
VIIIa	3	2.0060	1.54			
XI[b]		2.00382	1.87			1.23

[a] From [2]. [b] From [6].

is delocalization of the unshared electron to the N–halogen bond, as is the case in nitroxyl radicals. In both cases, no splitting of the signals on the methyl protons is observed in the ESR spectra. Another reason is that the halogen atoms, as distinct from hydrogen, are incapable of elimination as cations. When the process of elimination of proton is suppressed by carrying out the photolysis of 1-chloro-2,2,6,6-tetramethylpiperidine **II** in the CF_3COOH solution (Scheme 3), it is also possible to register the radical cation of unsubstituted 2,2,6,6-tetramethylpiperidine (**XI**) whose lifetime under these conditions is 100 ms [6]. The methods of synthesis of ammonium radical cations and the pathways of their decay were considered earlier [6, 7]. In the ESR spectrum of the obtained radical cation **XI** the splitting of the signal on the hydrogen atom and on the methyl protons is observed (Table 2).

Scheme 3.



II **XI**

During protracted electrolysis (5–7 min) the radical cations of haloamines **VI–X** both at room and lower temperature undergo chemical transformations being converted into more stable products. When the processes of oxidation and re-reduction of the products of oxidation are carried out at 0 V at room temperature, an intense signals of the corresponding nitroxyl radicals appear for all the studied compounds. No other radical species could be detected by the ESR method.

The results obtained for haloamines are in complete agreement with those for chloramine **II** [2] and are indicative of the same mechanism of the process of their oxidation as shown in Scheme 2. The one-electron oxidation affords radical cations. Two radical cations slowly react with each other to form the molecular halogen and two iminium ions. The reactions of iminium ions with water molecules from the solution lead to oxoammonium ions via the step of formation of hydroxylamines and nitroxyl radicals. These particles in the present case are not the final products but only intermediates since their oxidation potential is substantially lower than the oxidation potential of haloamines [8, 9]. That is why the process of re-reduction of the oxoammonium ion is an obligatory step after the oxidation process to obtain and detect the nitroxyl radical. We have performed such a reduction at 0 V; with this, apparently, the halogen molecules are also reduced to the halide ions.

Preparative electrosynthesis of the nitroxyl radicals was successful only when using haloamines **II** and **VI** as substrates. In the latter case, the yield of 2,2,6,6-

tetramethylpiperidine 1-oxyl (**III**) was 92% to the converted bromamine **VI**. In other cases, unidentified products of more deep oxidation were formed.

EXPERIMENTAL

Cyclic voltammograms were registered using a PI-50-1 potentiostat on a two coordinate recorder H 307/2. The working electrode was glass carbon disc electrode (d = 2 mm), pressed into fluoroplast. Prior to each measurement the electrode was mechanically polished. Potential sweep rate υ was 100 mV s^{-1}. The potentials were measured relative to the silver reference electrode Ag/0.01 M $AgNO_3$ in MeCN. The dissolved oxygen was removed by bubbling argon into the solution, temperature 295 K.

Investigation by the method of the ESR spectro-electrochemistry was performed using the device combining the ESR spectrometer "Radiopan SE/X-2544," potentiostat PI-50-1 and electrochemical cell. The device allows to carry out the electrochemical process *in situ* directly in the resonator of the ESR spectrometer. The working electrode was platinum plate, auxiliary electrode – platinum wire, reference electrode – silver wire. The solutions were deaerated by three cycles of freezing–evacuation–thawing.

The starting haloamines were prepared by the known procedures [10].

2,2,6,6-Tetramethylpiperidine-1-oxyl (III) from 1-bromo-2,2,6,6-tetramethylpiperidine (VI). The synthesis is carried out in a standard diaphragm-free electrolyzer of 150 ml capacity equipped with water jacket, thermometer and mechanical stirrer [11]. Anode and cathode were platinum plates of 10 cm^2 surface area. The electrolyzer was charged with 80 ml of water, 5.6 g (0.04 mol) of sodium sulfate, 4.4 g (0.02 mol) of 1-bromo-2,2,6,6-tetramethylpiperidine **VI** and 30 ml of methylene chloride. The conditions of electrolysis: current density 0.05 A cm^{-2} (current 0.5 A), temperature 20–25°C, vigorous stirring. The electrolysis was stopped after passing 1.2 A h (2.2 F mol^{-1}) amount of electricity. The water layer was separated from organic and extracted with methylene chloride (2×20 ml). Organic extracts were combined and analyzed by TLC and GC. From the analysis data, the organic layer contains a mixture of compounds, from which after removal of solvent and crystallization from hexane 1.34 g (32%) of the unreacted 1-bromo-2,2,6,6-tetramethylpiperidine **VI** was isolated. To the water layer 2 g of sodium nitrite was added, keeping pH in the range of 4–5 by addition of 3 M hydrochloric acid, and extracted with methylene chloride (3×30 ml). Methylene chloride was distilled off, the residue distilled in vacuum, collecting the fraction with bp 78–80°C (5 mm Hg). The yield of 2,2,6,6-tetramethylpiperidine-1-oxyl (**III**) 1.92 g (62% to the starting compound or 90% to the reacted 1-bromo-2,2,6,6-tetramethylpiperidine), mp 36–37°C (vacuum sublimation). A mixed probe with the authentic sample [12] does not give depression of the melting point.

REFERENCES

1. Kashparova, V.P., Vlasova, E.V., Zhukova, I.Yu., Kagan, E.Sh., and Il'chibaeva, I.B., *Russ. J. Electrochem., Engl. Transl.*, 2007, vol. 43, no. 11, p. 1249.
2. Kagan, E.Sh., Yanilkin, V.V., Nastapova, N.A., Morozov, V.I., Zhukova, I.Yu., Kashparova, V.P., and Kashparov, I.I., *Russ. J. Gen. Chem.,* 2009, vol. 79, no. 5, p. 1001.
3. Gallardo, I. and Vila, N., *J. Org. Chem*., 2008, vol. 73, no. 17, p. 6647.
4. Chow, Y.L., Danen, W.C., Nelsen, S.F., and Rosenblatt, H.D., *Chem. Rev*., 1978, vol. 78, no. 3, p. 243.
5. Duling, D.R., *J. Magn. Reson. B*, 1994, vol. 104, p. 105.
6. Roderick, W.Y., Vidoczy, T., Snyder, R.W., and Chow, Y.L., *J. Phys. Chem.*, 1978, vol. 82, no. 10, p. 1194.
7. Malatesta, V. and Ingold, K.U., *J. Amer. Chem. Soc*., 1973, vol. 95, no. 19, p. 6404.
8. Nakahara, K., Iwasa, S., Iriyama, J., Morioka, Y., Suguro, M., Satoh, M., and Cairns, E.J., *Electrochim. Acta*, 2006, vol. 52, no. 3, p. 921.
9. Kagan, E.Sh., Yanilkin, V.V., Nastapova, N.A., Kashparova, V.P., Kashparov, I.I., *Izv. Vuzov: Sev.-Kavk. Region, Ser. Estestv. Nauki,* 2008, special issue, p. 23.
10. Kashparova, V.P., Zhukova I.Yu., and Kagan, E.Sh., *Izv. Vuzov: Sev.-Kavk. Region, Ser. Estestv. Nauki,* 2001. no. 2, p. 73.
11. Smirnov, V.A., Tomilov, A.P., and Kagan, E.Sh., *Elektrokhimicheskie sintezy organicheskikh preparatov* (Electrochemical synthesis of Organic Preparates), Rostov: Rostov. Gos. Univ., 1981.
12. Rozantsev, E.G., *Svobodnye iminoksil'nye radikaly*, Moscow: Khimiya, 1970.