Russian Journal of Organic Chemistry, Vol. 41, No. 9, 2005, pp. 1306–1315. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 9, 2005, pp. 1331–1340.

Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

Vicarious Nucleophilic C-Amination of Nitrobenzene and 5- and 6-Nitro-1-methylbenzimidazoles

I. A. Titova, T. I. Vakul'skaya, L. I. Larina, M. I. Mizandrontsev, V. A. Volkov, G. V. Dolgushin, and V. A. Lopyrev

Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, ul. Favorskogo 1, Irkutsk, 664033 Russia
e-mail: vti@irioch.irk.ru

Received May 30, 2005

Abstract—Vicarious nucleophilic C-amination of nitrobenzene, 1-methyl-5-nitrobenzimidazole, and 1-methyl-6-nitrobenzimidazole in superbasic medium (potassium *tert*-butoxide–dimethyl sulfoxide) gave the corresponding amino-substituted derivatives. The yield of the amination product of 1-methyl-5-nitrobenzimidazole considerably increased in the presence of CuCl. ESR monitoring of these reactions revealed formation of primary radical anions from the substrates. Possible reaction mechanisms are discussed.

Vicarious nucleophilic substitution of hydrogen is a relatively new approach to the synthesis of substituted nitroaromatic compounds. This approach provides a convenient and often the only possible way of introducing functional groups into aromatic [1–3] and heteroaromatic rings [4–6]. The synthetic aspects of such reactions in the aromatic series were examined in detail in [7–10] and reviewed in [1, 4–6, 11, 12]. Analogous reactions in the series of heterocyclic compounds have been studied to a lesser extent [13–18].

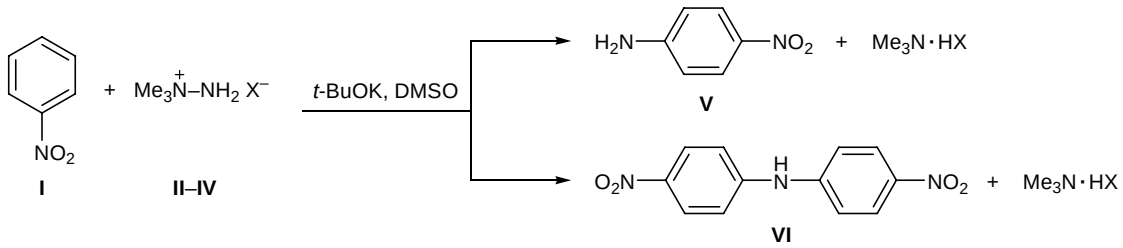
Successful vicarious nucleophilic substitution of hydrogen is determined by a number of factors, the main of which is the presence of a readily departing group at the nucleophilic center. Just that group leaves intermediate σ^H complex as H adduct instead of hydride ion [1, 19]. Vicarious nucleophilic substitution of hydrogen was used to effect alkylation [20, 21], hydroxylation [22, 23], and amination [3, 24–26]. Among these reactions, amination seems to be the most important, for it ensures direct introduction of an amino group into an aromatic ring, by-passing the stage of nitroarene reduction. One of the first examples of vicarious amination may be the reaction of 1,3-dinitrobenzene with hydroxylamine in the presence of a strong base, which yields 2,4-dinitrobenzene-1,3-diamine [27]. A large number of azoles containing nitro and amino groups in a single molecule, which were difficult to obtain previously, were synthesized in the recent years via vicarious nucleophilic substitution of hydrogen [13]. A wide series of reagents is used to effect direct amination of nitroarenes and nitro-substituted heteroaromatic compounds under mild conditions. These include 1,1,1-trimethylhydrazinium iodide [25, 28, 29], 4-amino-1,2,4-triazole [24, 23], 4-alkylamino-1,2,4-triazoles [3], sulfenamides [26, 30], and *O*-alkylhydroxylamines [7].

In the preliminary communications [31, 32] we showed that 1-methyl-4-nitroimidazole reacts with 1,1,1-trimethylhydrazinium iodide in the presence of dry sodium methoxide or potassium *tert*-butoxide in DMSO to afford 5-amino-1-methyl-4-nitroimidazole as the major product (yield 56%) [31]. With the goal of elucidating general relations holding in vicarious nucleophilic C-amination of nitroaromatic and nitroheteroaromatic systems and extending the scope of application of vicarious nucleophilic substitution of hydrogen, in the present work we examined these reactions using nitrobenzene, 1-methyl-5-nitrobenzimidazole, and 1-methyl-6-nitrobenzimidazole as substrates.

We previously showed by NMR spectroscopy that nitrobenzene (**I**) reacts with 1,1,1-trimethylhydrazinium halides **II**–**IV** in anhydrous DMSO in the presence of *t*-BuOK to give the corresponding amination product, *p*-nitroaniline (**V**), and bis(*p*-nitrophenyl)amine (**VI**) [33] (Scheme 1) instead of the expected

1070-4280/05/4109-1306

Scheme 1.



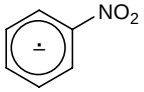
II, X = Cl; **III**, X = Br; **IV**, X = I.

mixture of *o*- and *p*-nitroanilines, as reported in [25]. Here, the nature of halide ion in the reagent (Cl, Br, I) did not affect the yield of the target products to an appreciable extent.

Bis(*p*-nitrophenyl)amine (**VI**) was also obtained by independent synthesis [33], and its ^{13}C and ^{15}N NMR spectra were recorded. The ^{15}N NMR spectrum of compound **VI** characteristically contained signals from nitrogen atoms in the two equivalent nitro groups (δ_N –10.7 ppm) and from the amino nitrogen atom (δ_N –271.8 ppm) [34]. In the ^1H NMR spectrum of **VI** we observed a singlet from the NH proton at δ 9.92 ppm and two doublets from two pairs of equivalent aromatic protons at δ 7.35 and 8.20 ppm with a coupling constant ^3J of 9.5 Hz.

When the reaction was carried out under purified argon, the mixture initially turned blue–violet for a short time, and the color quickly deepened up to black. These findings prompted us to examine the process by ESR spectroscopy. Despite numerous previous attempts to study the mechanism of vicarious nucleophilic substitution of hydrogen [35–37], the problem concerning elementary steps of this process remains unclear. There is a concept according to which the reaction follows a polar mechanism involving intermediate formation of σ^H complex [1, 4, 6, 8, 11, 12]. In fact, this concept implies simultaneous transfer of a couple of electrons, which is thermodynamically less favorable than two-step one-electron transfer. DeBoos and Milner [38] were the only to report on the formation of nitrobenzene radical anion in the reaction with methyl dichloroacetate, though it has long been known that irreversible electron transfer between unsaturated compounds and their dihydro derivatives to give radical anions occurs in strongly basic medium such as *t*-BuOK–DMSO [39]. Therefore, it is more reasonable to presume that electron transfer from the reagent anion to the substrate precedes formation of σ^H complex in vicarious nucleophilic C-amination.

In fact, when the reaction of nitrobenzene with 1,1,1-trimethylhydrazinium iodide (**IV**) in *t*-BuOK–DMSO was performed in an inert atmosphere in a special ampule placed into the probe of ESR spectrometer, we detected an ideally resolved signal belonging to nitrobenzene radical anion **VII** (Fig. 1).

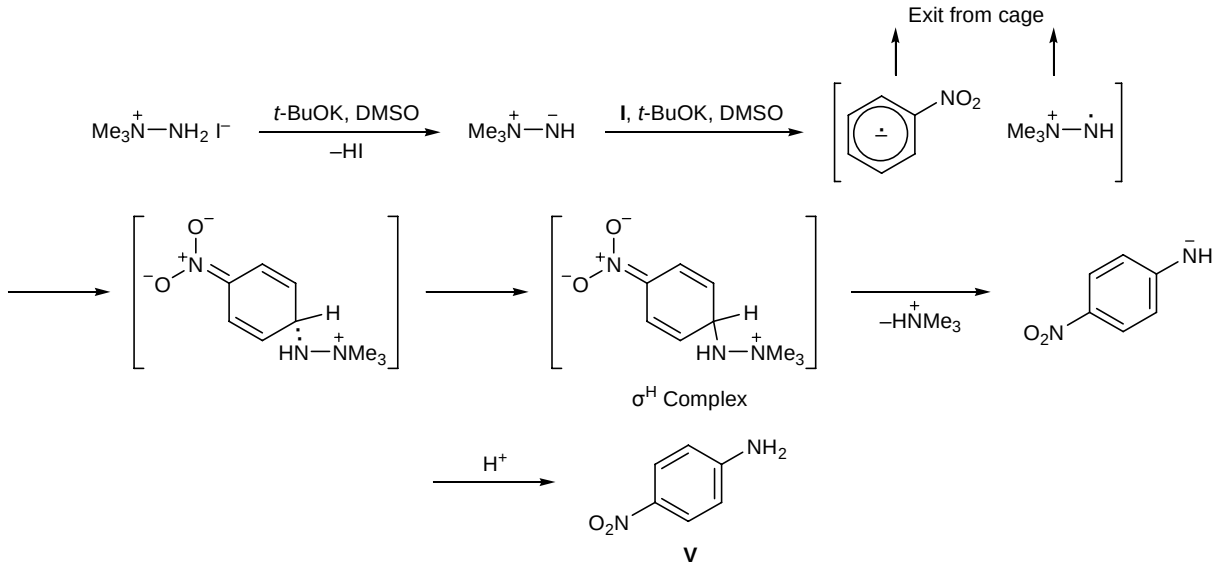


VII

This means that vicarious nucleophilic substitution of hydrogen in nitrobenzene (which is a classical nitroarene), as well as in 1-methyl-4-nitroimidazole [31], involves formation of primary radical anions from the substrate. Taking into account that the reagent in superbasic medium (*t*-BuOK–DMSO) is activated (it exists as anion), its nucleophilicity increases while the ionization potential decreases. Therefore, electron transfer from the reagent anion to electrophilic substrate to produce radical anion of the latter should be facilitated (Scheme 2). Here, the formation of nitrobenzene radical anions implies simultaneous formation of radical species from the reagent. However, we detected no other radical species than nitrobenzene radical anions in the reaction mixture obtained from nitrobenzene and an equimolar amount of 1,1,1-trimethylhydrazinium iodide in *t*-BuOK–DMSO.

We also studied amination of nitrobenzene with 4-amino-1,2,4-triazole (**VIII**) in the superbasic system *t*-BuOK–DMSO. According to the NMR data, the reaction leads to formation of several products: *p*-nitroaniline (**V**) (amination product) and bis(*p*-nitrophenyl)amine (**VI**), 4-nitrophenyl(1,2,4-triazol-4-yl)amine (**IX**), and bis(4-nitrophenyl)(1,2,4-triazol-4-yl)amine (**X**) (condensation products; Scheme 3). The structure of the products was proved by two-dimensional NMR spectroscopy (see Experimental). The product ratio depended on the reaction conditions.

Scheme 2.



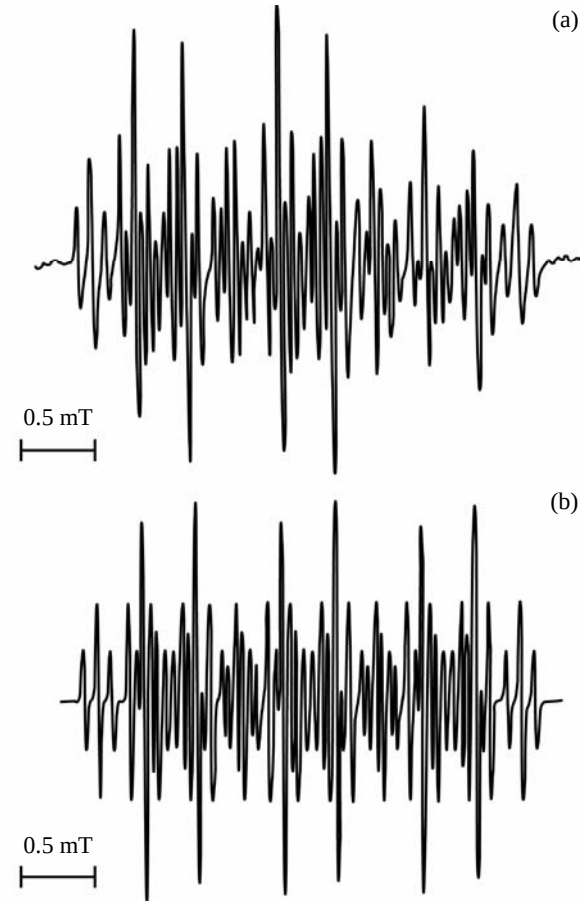
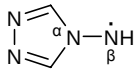


Fig. 1. (a) High-resolution ESR spectrum of the reaction mixture in the amination of nitrobenzene with 1,1,1-trimethylhydrazinium iodide in the system *t*-BuOK–DMSO and (b) simulated ESR spectrum with the following hyperfine coupling constants, mT: 3[1N(NO_2)] 1.100, 2(1H_p) 0.377, 3(2H_o) 0.335, 3(2H_m) 0.111.

ESR monitoring of the reaction involving 4-amino-1,2,4-triazole (**VIII**) as aminating agent showed a more complicated pattern. The ESR lines belonging to nitrobenzene radical anion were strongly broadened. When the aminating agent (compound **VIII**) was taken in excess, the ESR spectrum of the reaction mixture (according to computer simulation) was a superposition of two signals, one of which belongs to nitrobenzene radical anion. The other signal is characterized by interaction of unpaired electron with four nitrogen nuclei and three protons; therefore, it was assigned to neutral hydrazyl radical **XI** with the following hyperfine coupling constants (HCC), mT: 2(1H) 1.020, 3(1N_β) 0.780, 3(1N_α) 0.390, 5(2N) 0.040, 3(2H) 0.330. These data are consistent with the known HCC ratio $aN_\alpha/aN_\beta = 0.5$ for analogous hydrazyl radicals [40].

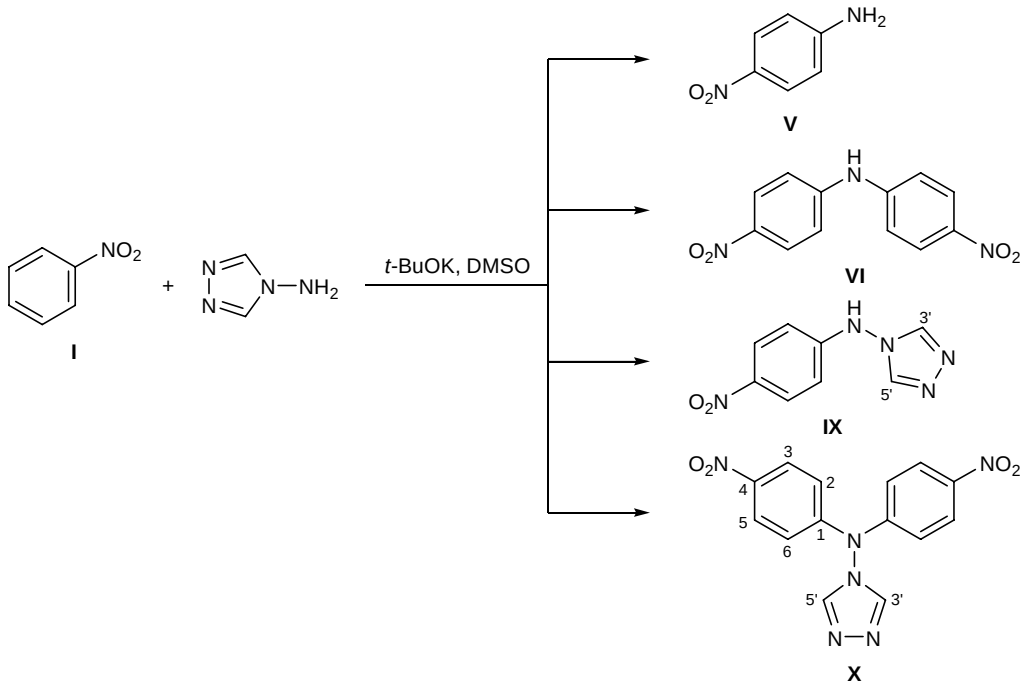


XI

To verify our conclusions, we performed *ab initio* calculations* of spin density distribution in radical **XI**. The results of calculations were consistent with the experimental parameters characterizing hyperfine coupling between the unpaired elecron and paramagnetic atoms. However, the experimental HCC values indicate that radical **XI** in DMSO becomes even more planar; this follows from similarity in the hyperfine coupling constants for the N^1 and N^2 atoms in the

* The complete set of calculation results is available from the authors.

Scheme 3.

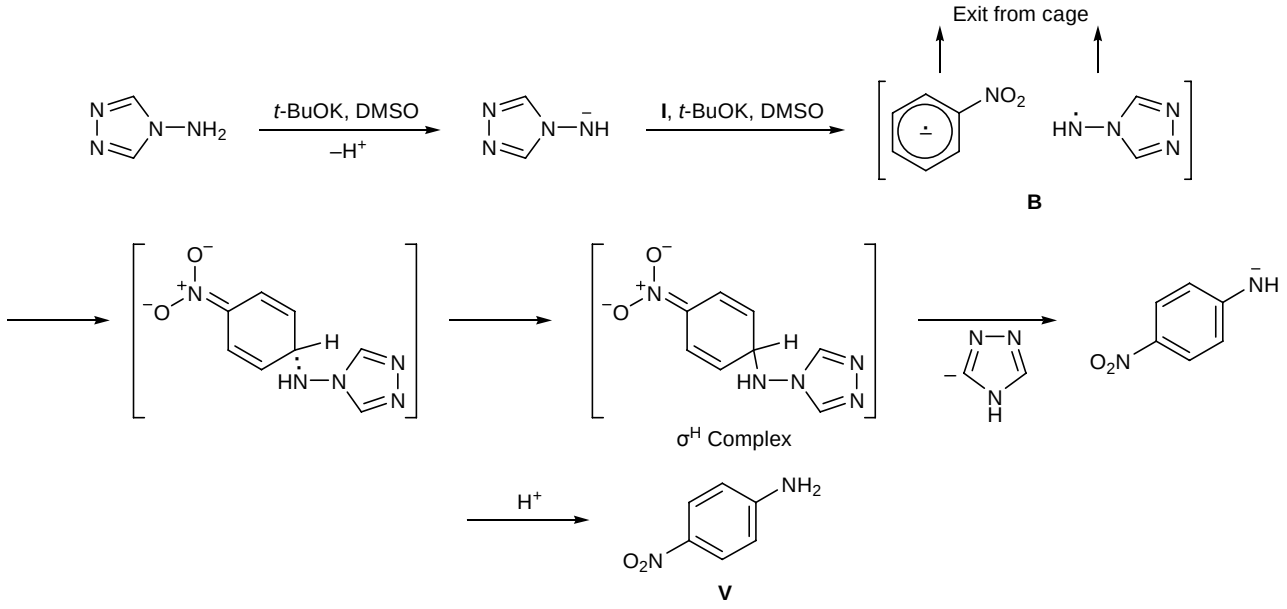


heteroring and hydrogen atoms on C^3 and C^5, as well as from the relative stability of the radical anion.

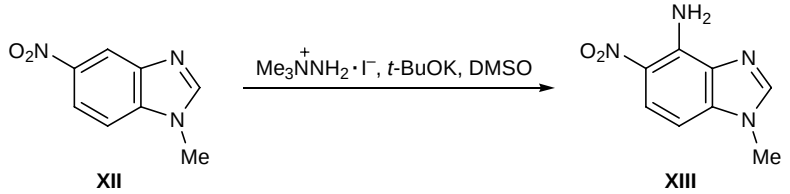
We can conclude that vicarious nucleophilic substitution of hydrogen in nitrobenzene in superbasic medium with the use of both 1,1,1-trimethylhydrazinium iodide and 4-amino-1,2,4-triazole as aminating agent follows a common mechanism which may be illustrated by Schemes 2 and 4. These schemes include electron transfer from the deprotonated reagent to the substrate with formation of intermediate radical ion pairs **A** and **B**, respectively. Presumably, unexpected products **VI**, **IX**, and **X** were formed via reaction of radicals **XI** which left solvent cage and anions **V** with the substrate.

Benzimidazole, 1-methylbenzimidazole, and 5(6)-nitrobenzimidazole cannot be involved in vicarious nucleophilic substitution of hydrogen because of a weak electrophilicity of the benzimidazole ring [10].

Scheme 4.



Scheme 5.



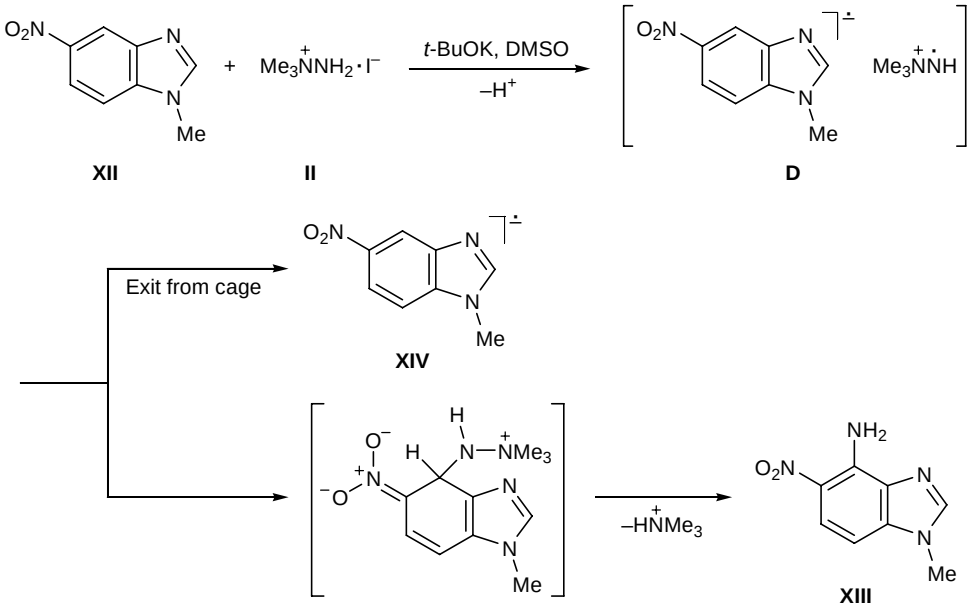
XII **XIII**

Introduction of a strong electron-withdrawing substituent, e.g., trifluoromethyl group, into position *2* of the benzimidazole ring favors this process. N-Substituted 5- and 6-nitrobenzimidazoles react with carbanions derived from aryl chloromethyl sulfones to give hydrogen replacement products, and the new substituent enters the *ortho* position with respect to the nitro group [10].

The reaction of 1-methyl-5-nitrobenzimidazole (**XII**) with 1,1,1-trimethylhydrazinium iodide (**IV**) in *t*-BuOK–DMSO at room temperature (reaction time 10 h) afforded the corresponding amination product at the 4-position, 4-amino-1-methyl-5-nitrobenzimidazole (**XIII**), in 39% yield (Scheme 5). Compound **XIII** was not reported previously. Its structure was proved by NMR (^{1}H, ^{13}C, ^{15}N) spectroscopy, including two-dimensional (2D) NMR techniques. Signals in the ^{1}H, ^{13}C, and ^{15}N NMR spectra of **XIII** were unambiguously assigned on the basis of the 2D NOESY, CH-CORR, and HMBC-GP ^{1}H–^{13}C data. The ^{1}H NMR spectrum of **XIII** contained a downfield singlet at δ 8.18 ppm, a broadened signal from protons in the amino group at δ 7.66 ppm, and two doublets at δ 7.91 and 6.88 ppm with a coupling constant *J* of 9.3 Hz. The latter value is typical of ^{1}H–^{1}H coupling through three bonds in structurally related compounds [34]. These data indicate that the amino group occupies the 4-position and that the two doublet signals belong to 6-H and 7-H. In the ^{1}H–^{1}H NOESY spectrum we observed a cross peak between protons of the *N*-methyl group (δ 3.82 ppm) and proton with a chemical shift δ of 6.88 ppm; i.e., this signal corresponds to 7-H. Carbon signals were assigned using 2D CH-CORR and HMBC-GP ^{1}H–^{13}C techniques. The latter allowed us to identify signals from the quaternary C^4, C^5, C^8, and C^9 atoms. Likewise, ^{15}N signals were assigned using the two-dimensional HMBC-GP ^{1}H–^{15}N technique.

In the reaction performed in thoroughly purified solvent under argon, the mixture turned intense blue for a short time, and the color then changed to dark red. The amination of **XII** with an equimolar amount of the aminating agent in superbasic medium in an inert atmosphere was monitored by ESR spectroscopy. After a few minutes, the ESR spectrum of the mixture contained a signal with hyperfine structure, whose intensity gradually increased up to a certain stationary

Scheme 6.



XII **II** **D** **XIV** **XIII**

value. According to the computer simulation data, the observed ESR signal may be assigned to radical anion **XIV**. Its parameters almost coincided with those of 1-methyl-5-nitrobenzimidazole radical anion (**XIV**) (Scheme 6) generated by electrochemical reduction of compound **XII** [HCC, mT: 3(NNO_2) 1.260, 2($1H^4$) 0.420, 2($1H^6$) 0.210, 2($1H^7$) 0.068, 2($1H^2$) 0.080, 3($1N^1$) 0.032, 3($1N^3$) 0.040, 4(3H, CH_3) 0.029; Fig. 2a]. The hyperfine coupling constants were assigned on the basis of *ab initio* calculations of spin density distribution in the radical anion. Thus our results suggest that vicarious nucleophilic amination of 1-methyl-5-nitrobenzimidazole follows Scheme 6.

Vicarious nucleophilic substitution of hydrogen in 1-methyl-6-nitrobenzimidazole (**XV**) with 1,1,1-trimethylhydrazinium iodide (**IV**) in superbasic medium afforded two amination products at positions *7* and *2*, compounds **XVI** and **XVII**, respectively (Scheme 7). Their structure was determined by NMR spectroscopy.

ESR monitoring of the reaction of 1-methyl-6-nitrobenzimidazole (**XV**) with an equimolar amount of 1,1,1-trimethylhydrazinium iodide (**IV**) in an inert atmosphere revealed a signal with the following hyperfine coupling constants, mT: 3(NNO_2) 1.135, 2($1H^7$) 0.460, 2($1H^5$) 0.240, 2($1H^4$) 0.126, 2($1H^2$) 0.044, 3($1N^1$) 0.030, 3($1N^3$) 0.240, 4(3H, CH_3) 0.020 (Fig. 2b). These data coincided with those corresponding to 1-methyl-6-nitrobenzimidazole radical anion (**XVIII**) generated by electrochemical reduction. The hyperfine coupling constants were assigned on the basis of computer simulation of the ESR spectrum and *ab initio* quantum-chemical calculations of spin density distribution. The reaction mechanism is shown in Scheme 8.

It should be emphasized that we were the first to consider the mechanism of vicarious nucleophilic substitution of hydrogen from the viewpoint of possible electron transfer. The observed similarity in the ESR patterns for vicarious C-amination of 1-methyl-4-nitroimidazole [31], nitrobenzene, and 5- and 6-nitro-1-methylbenzimidazoles suggests the existence of single-electron transfer channel in these processes. The proposed concept allows us to rationalize orientation of

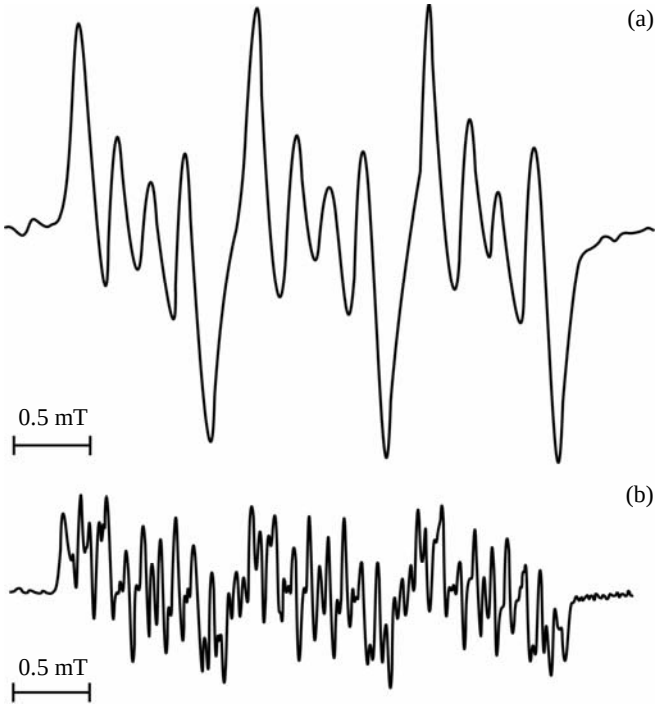
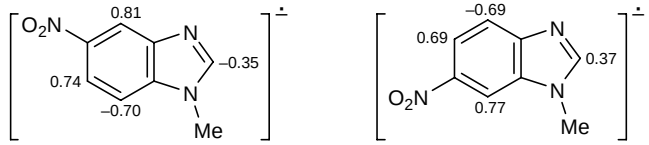


Fig. 2. ESR spectra of the reaction mixtures in the amination of (a) 1-methyl-5-nitrobenzimidazole and (b) 1-methyl-6-nitrobenzimidazole with 1,1,1-trimethylhydrazinium iodide in the system *t*-BuOK–DMSO.

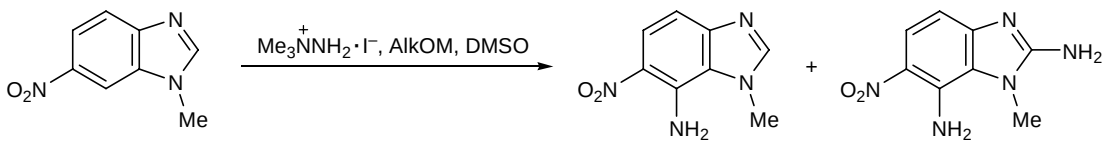
nucleophile at the site with maximal positive spin density in radical anions derived from the substrate [41], in keeping with the calculation data.



XIV **XVIII**

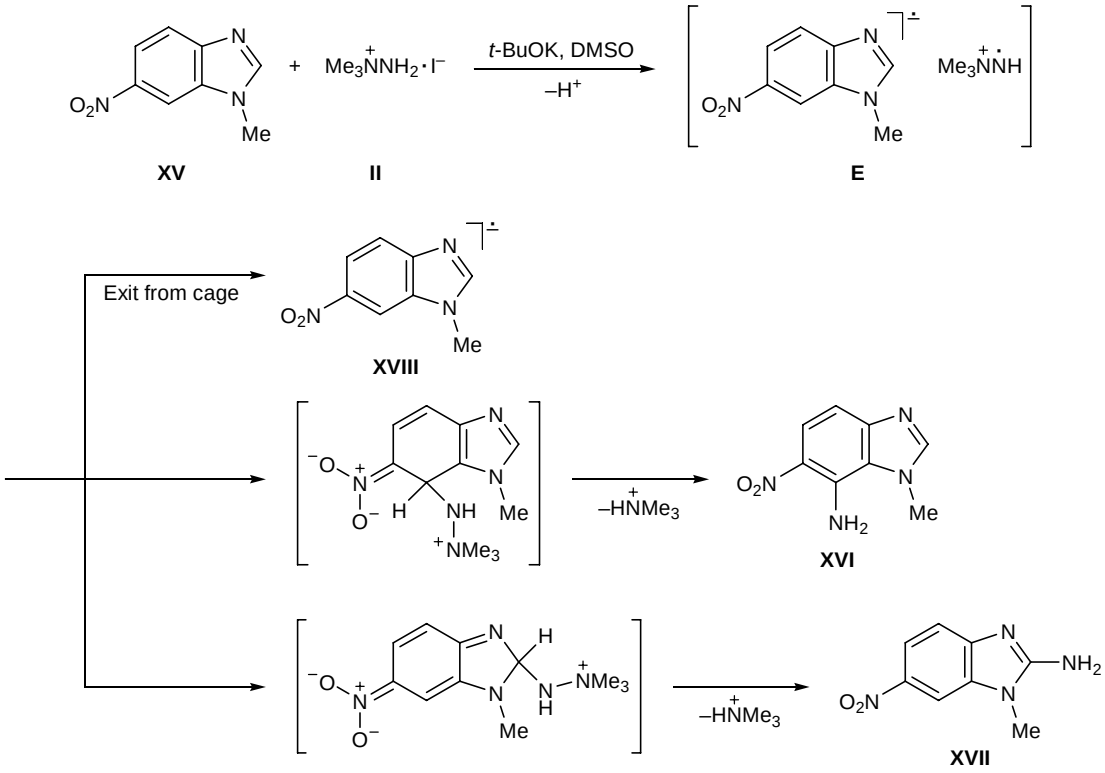
Detection of components of radical pairs **A**, **B**, **D**, and **E** by ESR spectroscopy indicates their fairly high stability and high rate of electron transfer. On the other hand, recombination of a radical pair within a solvent cage (formation of σ^H complex) should be slow, which should increase the probability for radical species to leave the cage and go into the bulk solution. Radical anions that left solvent cage are detected by ESR spec-

Scheme 7.



XV **XVI** **XVII**

Scheme 8.



troscopy. Transfer of radical anions from solvent cage to bulk solution is favored by the solvating power of dimethyl sulfoxide. However, it remains unclear whether the out-of-cage radicals participate in the formation of amination products or not.

Electron transfer from the highest occupied molecular orbital of a donor molecule to the lowest unoccupied molecular orbital of an acceptor molecule may be facilitated or hindered by various factors, e.g., redox properties of the reacting species, properties of the medium, and some extra effects such as irradiation, temperature, catalysis, etc. In the recent years, much effort is given to the development of so-called catalysis in electron-transfer reactions [42]. Insofar as electron transfer is an elementary step of a reaction, increase in the rate of electron transfer by the action of a catalyst (promoter) should involve change of its driving force via binding of promoter with the electron-transfer product.

We made an attempt to increase the efficiency of vicarious nucleophilic substitution of hydrogen with the use of copper(I) chloride. In the amination of 1-methyl-5-nitrobenzimidazole with 1,1,1-trimethylhydrazinium iodide in the presence of copper(I) chloride, the yield of 4-amino-1-methyl-5-nitrobenzimidazole (**XIII**) increased by 42%. The ESR spectrum of the reaction mixture displayed a strong signal of Cu^{2+} ($g_{\parallel}$ = 2.112; $g_{\perp}$ = 2.010; a_{Cu} = 7.3 mT; in the $g_{\perp}$ region we observed a hyperfine structure consisting of 7 lines with a coupling constant of about 0.9 mT, presumably due to two nonequivalent nitrogen atoms in the benzimidazole ring).

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples prepared as KBr pellets. The ^{1}H, ^{13}C, and ^{15}N NMR spectra were obtained on Bruker DPX-400 and Bruker AV-400 spectrometers at 400.13, 100.62, and 40.56 MHz, respectively. The ^{1}H and ^{13}C chemical shifts were measured relative to tetramethylsilane with an accuracy of ±0.01 and ±0.02 ppm, respectively. The ^{15}N chemical shifts were measured relative to $CH_3{}^{15}NO_2$ (external) with an accuracy of ±0.1 ppm. All NMR spectra were recorded from solutions in DMSO-d_6 at 27°C. Signals were assigned using two-dimensional (2D) ^{1}H, ^{13}C, and ^{15}N NMR techniques: 2D ^{1}H–^{1}H NOESY and inverse two-dimensional ^{1}H–^{13}C and ^{1}H–^{15}N spectra with account taken of long-range coupling constants using gradient probe (HMBC-GP ^{13}C and HMBC-GP ^{15}N).

The mass spectra were run on a Shimadzu GC-17/Gcms-QP5050 1 system. The ESR spectra were recorded on a Radiopan SE/X-2547 spectrometer (Poland) at 20°C. ESR monitoring was performed using special cells which ensured the reactions to proceed in an inert atmosphere; ESR signals were recorded continuously during several hours. All reagents (both individual and as mixtures of two or three components) were preliminarily checked for the absence of paramagnetic properties. Computer simulation of the ESR spectra was performed using WINEPR SimFonia 1.25 program (Bruker, 1996).

Quantum-chemical calculations of spin density distribution in radical anions derived from 5- and 6-nitro-1-methylbenzimidazoles were performed by the UHF/6-31G* method using Gaussian 98 software package [43].

General procedure for the amination of nitrobenzene was described in [24, 25, 33].

***p*-Nitroaniline (V).** ^{1}H NMR spectrum, δ, ppm: 6.61 d (2H, 2-H, 6-H, J = 8.3 Hz), 6.70 br.s (2H, NH_2), 8.05 d (2H, 3-H, 5-H, J = 8.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 111.45 (C^2, C^6), 126.44 (C^3, C^5), 135.00 (C^4), 156.00 (C^1).

Bis(*p*-nitrophenyl)amine (VI). ^{1}H NMR spectrum, δ, ppm: 7.35 d (2H, 2-H, 6-H, J = 9.5 Hz), 8.20 d (2H, 3-H, 5-H, J = 9.5 Hz), 9.92 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 117.04 (C^2, C^6), 125.77 (C^3, C^5), 140.05 (C^4), 147.60 (C^1). ^{15}N NMR spectrum, δ_N, ppm: –10.7 (NO_2), –271.8 (NH).

4-Nitrophenyl(1,2,4-triazol-4-yl)amine (IX). ^{1}H NMR spectrum, δ, ppm: 6.59 d (2H, 2-H, 6-H, J = 9 Hz), 8.16 d (2H, 3-H, 5-H, J = 9 Hz), 8.87 s (2H, 3'-H, 5'-H), 10.52 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 111.70 (C^2, C^6), 126.13 (C^3, C^5), 140.05 (C^4), 144.08 ($C^{3'}$, $C^{5'}$), 156.00 (C^1).

Bis(4-nitrophenyl)(1,2,4-triazol-4-yl)amine (X). ^{1}H NMR spectrum, δ, ppm: 6.79 d (2H, 3-H, 5-H, J = 9 Hz), 7.44 d (2H, 2-H, 6-H, J = 9 Hz), 8.61 s (2H, 3'-H, 5'-H).

1-Methyl-5-nitrobenzimidazole (XII) and 1-methyl-6-nitrobenzimidazole (XV) were prepared by the procedures described in [44, 45]. Compound **XII**: mp 211–212°C; published data [44]: mp 212°C. Compound **XV**: mp 182–183°C; published data [44]: mp 182°C.

4-Amino-1-methyl-5-nitrobenzimidazole (XIII). *a*. 1,1,1-Trimethylhydrazinium iodide (**IV**), 3.03 g (1.5 mmol), was slowly added under stirring to a solution of 1.8 g (1 mmol) of 1-methyl-5-nitrobenzimidazole (**XII**) in 30 ml of anhydrous DMSO. The mixture was stirred until it became homogeneous, and 3.36 g (3 mmol) of potassium *tert*-butoxide was added. The mixture quickly turned dark red. It was stirred for 10 h at room temperature, poured onto ice, and acidified with 10% hydrochloric acid to pH ≈ 3. The precipitate was filtered off, the filtrate was extracted with three portions of ethyl acetate, and the extracts were combined, washed with distilled water, dried over anhydrous magnesium sulfate, and evaporated. The residue was combined with the previously separated product and recrystallized first from dimethylformamide and then from water. Yield 0.76 g (39%), mp 280–280.5°C. When potassium hydroxide was used instead of potassium *tert*-butoxide, the yield was 53%. IR spectrum, ν, cm^{-1}: 3410 NH_2, 1620–1595 (δNH_2), 1500 (NO_2), 1230 (δCH_{ring}). ^{1}H NMR spectrum, δ, ppm: 3.82 s (3H, Me), 6.88 d (1H, 7-H, J = 9.3 Hz), 7.66 br.s (2H, NH_2), 7.90 d (1H, 6-H, J = 9.3 Hz), 8.18 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 31.05 (CH_3), 99.92 (C^7), 120.38 (C^6), 124.90 (C^5), 131.67 (C^9), 137.44 (C^8), 140.46 (C^4), 143.77 (C^2). ^{15}N NMR spectrum, δ_N, ppm: –3.3 (NO_2), –131.8 (N^3), –222.9 (N^1), –307.6 (NH_2). Mass spectrum, m/z (I_{rel}, %): 192 (100) $[M]^+$, 162 (27), 146 (21), 134 (12), 119 (24), 105 (12), 92 (15), 76 (16), 65 (18), 42 (36). Found, %: C 50.00; H 4.23; N 29.10. $C_8H_8N_4O_2$. Calculated, %: C 50.00; H 4.20; N 29.15.

b. In the presence of CuCl. 1-Methyl-5-nitrobenzimidazole (**XII**), 0.89 g (0.5 mmol), was dissolved in 15 ml of anhydrous DMSO, and 0.05 g (0.05 mmol) of CuCl and 1.51 g (0.75 mmol) of 1,1,1-trimethylhydrazinium iodide were added. When the latter dissolved completely, 1.68 g (1.5 mmol) of potassium *tert*-butoxide was added. The mixture quickly turned dark red. It was stirred for 10 h at room temperature, poured onto ice, and acidified with 10% hydrochloric acid to pH ≈ 3. The precipitate was filtered off, the filtrate was extracted with three portions of ethyl acetate, and the extracts were combined, washed with water, dried over anhydrous magnesium sulfate, and evaporated. The residue was combined with the previously separated product and recrystallized first from dimethylformamide and then from water. Yield 0.78 g (81%), mp 280–280.5°C.

7-Amino-1-methyl-6-nitrobenzimidazole (XVI). 1,1,1-Trimethylhydrazinium iodide (**IV**), 1.52 g (0.75 mmol), was slowly added under stirring to a solution of 0.9 g (0.5 mmol) of 1-methyl-6-nitrobenzimidazole (**XIV**) in 15 ml of anhydrous DMSO. The

mixture was stirred until it became homogeneous, and 1.68 g (1.5 mmol) of potassium *tert*-butoxide was added. The mixture quickly turned dark red. It was stirred for 10 h at room temperature and poured onto ice, and the precipitate was filtered off and recrystallized from methanol. The product, 0.44 g (45%), mp 242–248°C, was a mixture of 2-amino-1-methyl-6-nitrobenzimidazole (**XVII**) and 7-amino-1-methyl-6-nitrobenzimidazole (**XVI**). Recrystallization from pyridine gave 7-amino-1-methyl-6-nitrobenzimidazole (**XVI**), mp 270–273°C. IR spectrum, ν, cm^{-1}: 3420 (NH_2), 1610–1580 (δNH_2), 1495 (NO_2), 1380 (δCH_{ring}). ^1H NMR spectrum, δ, ppm: 4.17 s (3H, Me), 6.92 d (1H, 4-H, J = 9.3 Hz), 7.46 br.s (2H, NH_2), 7.84 d (1H, 5-H, J = 9.3 Hz), 8.21 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 34.24 (CH_3), 109.37 (C^4), 119.98 (C^5), 122.56 (C^8), 126.57 (C^6), 137.10 (C^7), 148.44 (C^2), 148.76 (C^9). ^{15}N NMR spectrum, δ_N, ppm: –3.2 (NO_2), –129.0 (N^3), –222.5 (N^1), –305.6 (NH_2). Mass spectrum, m/z (I_{rel}, %): 192 (72) $[M]^+$, 162 (20), 146 (20), 134 (7), 119 (11), 105 (11), 92 (13), 78 (23), 66 (28), 52 (43), 42 (31). Found, %: C 49.92; H 4.24; N 29.12. $C_8H_8N_4O_2$. Calculated, %: C 50.00; H 4.20; N 29.15.

The pyridine mother liquor was diluted with diethyl ether, and the mixture was left to stand for several days. After prolonged storage, 2-amino-1-methyl-6-nitrobenzimidazole (**XVII**) separated from the solution. Its properties coincided with published data (mp 272°C [46]). ^1H NMR spectrum, δ, ppm: 3.58 s (3H, Me), 7.18 d (1H, 4-H, J = 9.1 Hz), 7.21 br.s (2H, NH_2), 7.93 d.d (1H, 5-H, J = 9.1, 2.4 Hz), 8.06 d (1H, 7-H, J = 2.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.84 (CH_3), 103.64 (C^9), 113.48 (C^4), 117.91 (C^5), 134.67 (C^8), 138.89 (C^6), 149.74 (C^7), 159.71 (C^2). Mass spectrum, m/z (I_{rel}, %): 192 (100) $[M]^+$, 162 (76), 146 (23), 134 (20), 119 (12), 105 (26), 92 (12), 63 (17), 52 (7), 43 (7). When potassium hydroxide was used instead of potassium *tert*-butoxide, we isolated only 7-amino-1-methyl-6-nitrobenzimidazole (**XVI**) in 35% yield.

This study was performed under financial support by the Russian Academy of Sciences (Division of Chemistry and Material Sciences, project no. 4.1.7).

REFERENCES

1. Makosza, M., *Usp. Khim.*, 1989, vol. 58, p. 1298.
2. Florio, S., Lorusso, P., Luisi, R., Granito, C., Ronzini, L., and Troisi, L., *Eur. J. Org. Chem.*, 2004, p. 2118.
3. Katritzky, A.R. and Laurenzo, K.S., *J. Org. Chem.*, 1988, vol. 53, p. 3978.
4. Makosza, M., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1996, p. 531.
5. Knyazev, V.N. and Drozd, V.N., *Russ. J. Org. Chem.*, 1995, vol. 31, p. 1.
6. Makosza, M. and Winiarski, J., *Acc. Chem. Res.*, 1987, vol. 20, p. 282.
7. Seko, S. and Miyake, K., *J. Synth. Org. Chem. Jpn.*, 2003, vol. 61, p. 192.
8. Makosza, M. and Wojciechowski, K., *Justus Liebigs Ann. Chem.*, 1997, p. 1805.
9. Katritzky, A.R. and Xie, L., *Tetrahedron Lett.*, 1996, vol. 37, p. 347.
10. Makosza, M., *Chem. Unsere Zeit*, 1996, vol. 30, p. 134.
11. Makosza, M., *Current Trends in Organic Synthesis* (Proc. Fourth Int. Conf. on Organic Synthesis, Tokyo, Japan, August 22–27, 1982), Nozaki, H., Ed., Oxford: Pergamon, 1983. Translated under the title *Sovremennye napravleniya v organicheskom sinteze*, Moscow: Mir, 1986, p. 518.
12. Makosza, M., *Polish J. Chem.*, 1992, vol. 66, p. 3.
13. Donskaya, O.V., Dolgushin, G.V., and Lopyrev, V.A., *Khim. Geterotsikl. Soedin.*, 2002, p. 435.
14. Makosza, M., *Synthesis*, 1991, p. 103.
15. Makosza, M. and Wojciechowski, K., *Heterocycles*, 2001, vol. 54, p. 445.
16. Makosza, M. and Kwast, E., *Tetrahedron*, 1995, vol. 51, p. 8339.
17. Chupakhin, O.N. and Beresnev, D.G., *Usp. Khim.*, 2002, vol. 71, p. 803.
18. Chupakhin, O.N., Charushin, V.N., and Rusinov, V.L., *Panorama sovremennoi khimii Rossii. Sovremennyi organicheskii sintez* (Panorama of Modern Chemistry in Russia. Modern Organic Synthesis), Moscow: Khimiya, 2003, p. 99.
19. Golinski, J. and Makosza, M., *Tetrahedron Lett.*, 1978, p. 3495.
20. Drew, M.D., Jackson, D.A., Lawrence, N.J., Liddle, J., and Pritchard, R.G., *Chem. Commun.*, 1997, p. 189.
21. Lawrence, N.J., Liddle, J., Bushell, S.M., and Jackson, D.A., *J. Org. Chem.*, 2002, vol. 67, p. 457.
22. Makosza, M. and Sienkeiwicz, M., *J. Org. Chem.*, 1990, vol. 55, p. 4979.
23. Makosza, M. and Podraza, R., *Eur. J. Org. Chem.*, 2000, p. 193.
24. Katrizky, A.R., Laurenzo, K.S., and Schmidt, R.D., *J. Org. Chem.*, 1986, vol. 51, p. 5039.
25. Pagoria, P.F., Mitchell, A.R., and Schmidt, R.D., *J. Org. Chem.*, 1996, vol. 61, p. 2934.
26. Makosza, M. and Bialecki, M., *J. Org. Chem.*, 1992, vol. 57, p. 4784.
27. Meisenheimer, J. and Patzig, E., *Chem. Ber.*, 1906, vol. 39, p. 2533.

28. Schmidt, R.D., Lee, G.S., Pagoria, P.F., Mitchell, A.R, and Gilardi, R., *J. Heterocycl. Chem*., 2001, vol. 38, p. 1227.
29. Rozhkov, V.V., Shevelev, S.A., Chervin, I.I., Mitchell, A.R., and Schmidt, R.D., *J. Org. Chem*., 2003, vol. 68, p. 2498.
30. Makosza, M. and Bialecki, M., *J. Org. Chem*., 1998, vol. 63, p. 4878.
31. Donskaya, O.V., Elokhina, V.N., Nakhmanovich, A.S., Vakul'skaya, T.I., Larina, L.I., Vokin, A.I., Albanov, A.I., and Lopyrev, V.A., *Tetrahedron Lett*., 2002, vol. 43, p. 6613.
32. Donskaya, O.V., Elokhina, V.N., Vakul'skaya, T.I., Vokin, A.V., Larina, L.I., and Lopyrev, V.A., Book of Abstracts, *Int. Conf. "Reactions Mechanisms and Organic Intermediates,"* St. Petersburg, 2001, p. 96.
33. Krylova, O.V., Elokhina, V.N., Nakhmanovich, A.S., Larina, L.I., and Lopyrev, V.A., *Russ. J. Org. Chem*., 2001, vol. 37, p. 887.
34. Larina, L.I. and Lopyrev, V.A., *Targets in Heterocyclic Systems: Chemistry and Properties — Reviews and Accounts on Heterocyclic Chemistry*, Attanasi, O.A. and Spinelli, D., Eds., Rome: Ital. Soc. Chem., 1999, vol. 1, p. 187.
35. Makosza, M., Lemek, T., Kwast, A., and Terrier, F., *J. Org. Chem*., 2002, vol. 67, p. 394.
36. Lemek, T., Makosza, M., Stephenson, D.S., and Mayr, H., *Angew. Chem., Int. Ed*., 2003, vol. 42, p. 2793.
37. Makosza, M. and Kwast, A., *Eur. J. Org. Chem*., 2004, p. 2125.
38. DeBoos, G.A. and Milner D.J., *Synth. Commun*., 1994, vol. 24, p. 965.
39. Russell, G.A., Janzen, E.G., and Strom, E.T., *J. Am. Chem. Soc*., 1962, vol. 84, p. 4155.
40. Buchachenko, A.L. and Vasserman, A.M., *Stabil'nye radikaly* (Stable Radicals), Moscow: Khimiya, 1973, p. 186.
41. Todres, Z.V., *Usp. Khim*., 1978, vol. 47, p. 260; Todres, Z.V., *Ion-radikaly v organicheskom sinteze* (Radical Ions in Organic Synthesis), Moscow: Khimiya, 1986, p. 82; Todres, Z.V., *Organic Ion Radicals. Chemistry and Applications*, New York: Marcel Dekker, 2003, p. 194.
42. Fukuzumi, S., *Org. Biomol. Chem*., 2003, vol. 1, p. 609; Fukuzumi, S., *J. Phys. Org. Chem*., 2002, vol. 15, p. 448; Fukuzumi, S., *Pure Appl. Chem*., 2003, vol. 75, p. 577.
43. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, J.A., Jr., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui, Q., Morokuma, K., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Gonzalez, C., Challacombe, M., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Andres, J.L., Gonzalez, C., Head-Gordon, M., Replogle, E.S., and Pople, J.A., *Gaussian 98, Revision A.6*, Pittsburgh PA: Gaussian, 1998.
44. Ellis, G.P. and Jones, R.T., *J. Chem. Soc., Perkin Trans. 1*, 1974, p. 903.
45. Larina, L.I., Lopyrev, V.A., and Voronkov, M.G., *Zh. Org. Khim*., 1994, vol. 30, p. 1081.
46. Simonov, A.M., Yutilov, Yu.M., and Anisimova, V.A., *Khim. Geterotsikl. Soedin*., 1965, p. 913.