Kinetics and Catalysis, Vol. 42, No. 5, 2001, pp. 601–605. Translated from Kinetika i Kataliz, Vol. 42, No. 5, 2001, pp. 664–669.
Original Russian Text Copyright © 2001 by Pol'shakov, Tsentalovich, Gritsan.

A Laser Flash-Photolysis Study of the Bimolecular Reactions of Singlet Fluorinated Arylnitrenes

D. A. Pol'shakov[1,2], Yu. P. Tsentalovich[3], and N. P. Gritsan[1,2]

[1] *Institute of Chemical Kinetics and Combustion, Siberian Division,*
Russian Academy of Sciences, Novosibirsk, 630090 Russia
[2] *Novosibirsk State University, Novosibirsk, 630090 Russia*
[3] *International Tomography Center, Siberian Division, Russian Academy of Sciences, Novosibirsk, 630090 Russia*

Received September 14, 2000

Abstract—The kinetics and mechanisms of the reactions of singlet perfluoro-4-biphenylnitrene and *N*-propyl-4-nitreno-2,3,5,6-tetrafluorobenzylamide with various amines, pyridine, and dimethylsulfoxide were studied by laser flash photolysis. The reactions of singlet arylnitrenes with amines are two-step processes. The primary step of the process is adduct formation; the rate constant of this reaction is high and lies within the range 4×10^7–2×10^8 l mol^{-1} s^{-1} for the tested secondary amines. The second step (1,2-hydrogen shift) was accelerated in the presence of water.

INTRODUCTION

Arylazides and, in particular, their fluorinated analogs are widely used as the light-sensitive reactive groups of photoaffinity reagents [1, 2], which are applied to the photomodification of biopolymers. The mechanism of this photomodification is not understood. However, it is believed that singlet arylnitrenes formed on the photolysis of arylazides play a key role in this modification [2].

The irradiation of arylazides results in the elimination of a nitrogen molecule and the formation of singlet arylnitrenes—key intermediates which are responsible for the nature of the subsequent transient species [3–5]. The absorption spectra of singlet phenylnitrene and its derivatives were first recorded in 1997 [6–8]. The intramolecular reactions of intersystem crossing to a triplet ground state and of isomerization to azepine are the main decay processes of singlet arylnitrenes [3, 4]. Previously, we studied the intramolecular reactions of singlet fluorinated arylnitrenes (**IIS**) that appear in the photolysis of perfluoro-4-biphenylazide (**Ia**) and *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide (**Ib**) [9].

In this work, we studied the reaction kinetics of singlet perfluoro-4-biphenylnitrene (**IISa**) and *N*-propyl-4-nitreno-2,3,5,6-tetrafluorobenzylamide (**IISb**) with various compounds (amines, pyridine, and dimethylsulfoxide (DMSO)), which simulate the functional groups of biological macromolecules, and recorded the absorption spectra of transient products using a technique of laser flash photolysis. Data on the quantum-chemical calculations of some properties of expected intermediates were used for interpreting the experimental results.

EXPERIMENTAL

Materials

Perfluoro-4-biphenylazide was synthesized according to the previously published procedure [8]; *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide was kindly provided by Dr. Sci. (Chem.) O.S. Fedorova (Institute

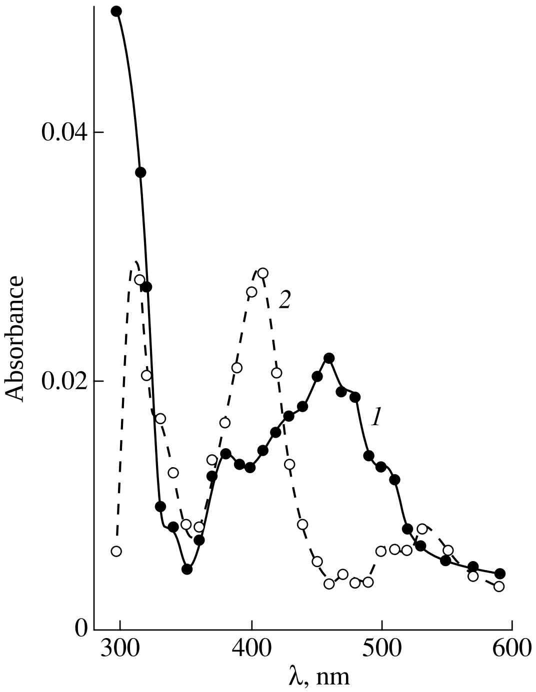


Fig. 1. Absorption spectra measured (*1*) 30 and (*2*) 400 ns after the laser excitation of *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide (**Ib**) in acetonitrile at room temperature.

of Bioorganic Chemistry, Siberian Division, Russian Academy of Sciences). Acetonitrile was purified by refluxing with P_2O_5 for 1 h followed by distillation.

Flash Photolysis

The assembly for laser flash photolysis was described in detail elsewhere [10]. A solution placed in a rectangular quartz cuvette (10 × 10 mm) was irradiated with a pulse from a XeCl excimer laser (Lambda Physik EMG 101; 308 nm; 100 mJ; 17 ns). The detection system included a DKSSh-120 xenon lamp; two monochromators; a photomultiplier tube (Hamamatsu R955); a LeCroy 9310A digital oscillograph; and a system of filters, lenses, and shutters. Experimental data were treated using a computer. The time resolution of the laser flash-photolysis assembly, which depends on the duration of a laser pulse, was ~20 ns. The spectral range was 270–640 nm. A flow system was used in order to prevent the secondary photolysis of products. To remove oxygen, argon was bubbled through solutions for 15 min.

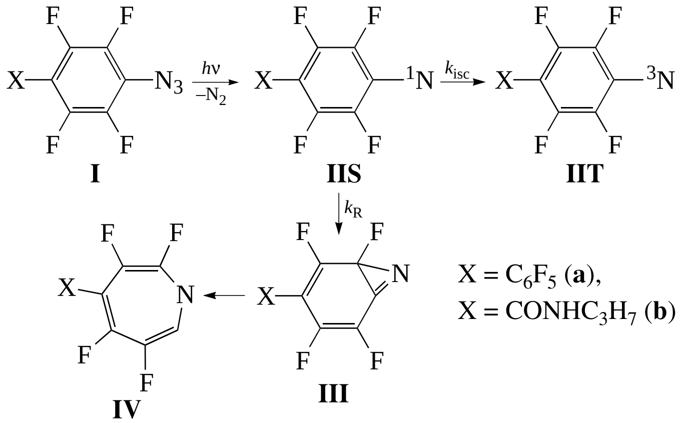
In the experiments on flash photolysis, the intensity of probing light was measured before and after laser irradiation. Because a portion of the initial substance was converted into intermediate products under exposure to laser radiation, the resulting spectrum was the difference between the spectra of formed intermediates and the consumed reagent.

Quantum-Chemical Calculations

The quantum-chemical calculations of the geometry, electronic structure, and energy were performed by the PM3 method [11]. Solvation was taken into account in the calculations using the model of point dipoles [12].

RESULTS

According to recent data [8, 9], the mechanism of primary processes in the photolysis of fluorinated arylazides **Ia** and **Ib** is described by Scheme 1. The isomerization of singlet arylnitrenes **IIS** to azepines (**IV**) is a two-step process [5, 13]. The primary step of the isomerization of a singlet arylnitrene to azirine (**III**) is a rate-limiting step [5, 8, 9, 13].



Scheme 1.

The laser flash photolysis of arylazides **Ia** and **Ib** in acetonitrile resulted in the appearance of transient absorption in the UV and visible regions of the spectrum immediately after a laser pulse. As an example, Fig. 1 demonstrates the absorption spectrum recorded in the course of the laser flash photolysis of arylazide **Ib** (spectrum *1*). This absorption was attributed to singlet arylnitrene **IISb** [9]. The kinetic curves of decay of the absorption of singlet arylnitrenes **IISa** and **IISb** are described by an exponential function of time (Fig. 2, curve *1*). An increase in the absorption with maximums at 410 and 530 nm was also observed (Fig. 1, spectrum *2*). The band with λ_{max} = 530 nm in the spectrum of moderate absorption corresponds to triplet nitrene **IITb**. Triplet nitrene **IITb** and azepine **IVb** contribute to the absorption band at λ_{max} = 410 nm. The characteristic times of decay of singlet nitrenes **IISa** and **IISb** and the characteristic times of appearance of the products (**IITa**, **IITb**, **IVa**, and **IVb**) are within the experimental error (Fig. 2).

The lifetimes of singlet arylnitrenes **IISa** and **IISb** in acetonitrile at room temperature are similar and equal to 210 ± 20 ns. The lifetimes of arylnitrenes **IISa** and **IISb** were dramatically shortened upon the introduction of various additives into solutions of arylazides **Ia** and **Ib**.

In an inert solvent of acetonitrile in the absence of additives, the observed rate constant of decay of singlet arylnitrenes (k_{obs}) is equal to the sum of the rate constants of intersystem crossing (k_{isc}) and isomerization to azirine (k_R) (Scheme 1). In the presence of additives

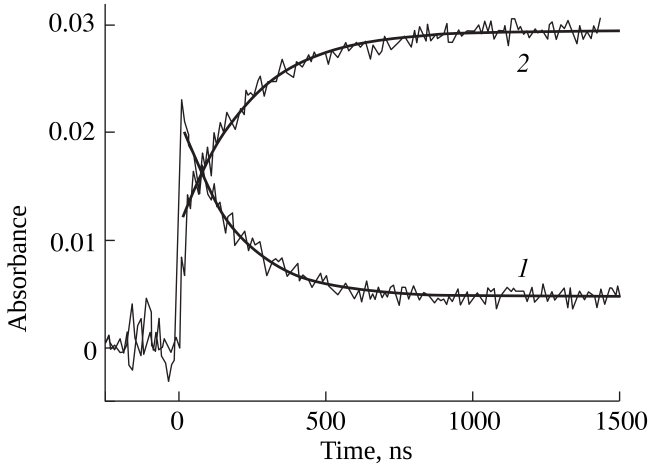


Fig. 2. Kinetic curves of (*1*) decay of singlet *N*-propyl-4-nitreno-2,3,5,6-tetrafluorobenzylamide (λ_{max} = 470 nm) and (*2*) formation of the corresponding triplet nitrene and dehydroazepine (λ_{max} = 410 nm) in acetonitrile at room temperature. The zero time corresponds to the instant of supplying a laser pulse. Zigzag lines indicate experimental data, and smooth lines show the approximation of experimental curves by exponential functions of time.

(Q), the rate constant of decay of a singlet arylnitrene can be written as

$$k_{obs} = k_{isc} + k_R + k_Q[Q],$$

where [Q] is the concentration of the test additive.

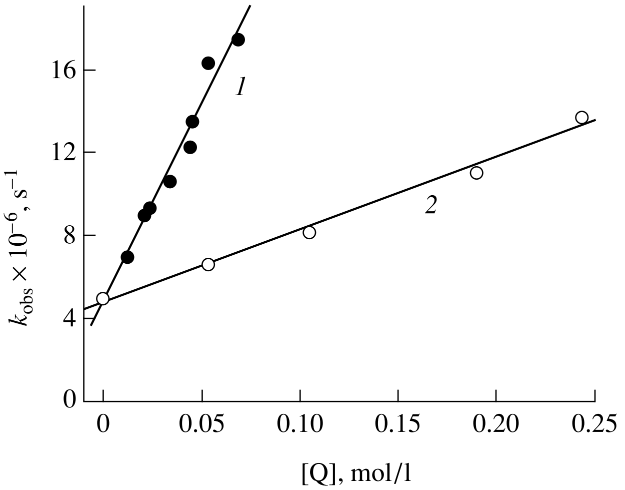


Fig. 3. Observed rate constant of decay of singlet perfluoro-4-biphenylnitrene (**IISa**) in acetonitrile at room temperature as a function of (*1*) dimethylsulfoxide or (*2*) imidazole concentration.

Indeed, linear relationships between the observed rate constants of decay of singlet arylnitrenes and the concentrations of additives were observed experimentally (Fig. 3). The table summarizes the rate constants (k_Q) of bimolecular reactions with various additives calculated from these relationships.

It is well known [4, 14] that fluorinated singlet arylnitrenes react with pyridine to form corresponding

Rate constants of bimolecular reactions of singlet perfluoro-4-biphenylnitrene (**IISa**), N-propyl-4-nitreno-2,3,5,6-tetrafluorobenzylamide (**IISb**), and perfluorophenylnitrene (**IISc**) with various chemicals

Additive (Q)	k_Q, l mol^{-1} s^{-1}		
	IISa	**IISb**	**IISc***
Diethylamine	–	–	1.9×10^8
Piperidine	$(2.0 \pm 0.2) \times 10^8$	$(1.9 \pm 0.2) \times 10^8$	–
Morpholine	$(1.9 \pm 0.2) \times 10^8$	$(1.8 \pm 0.2) \times 10^8$	–
Imidazole	$(4.0 \pm 0.4) \times 10^7$	$(3.9 \pm 0.4) \times 10^7$	–
N-Methylimidazole	$(7.6 \pm 0.7) \times 10^7$	–	–
DMSO	$(2.0 \pm 0.2) \times 10^8$	$(2.2 \pm 0.2) \times 10^8$	1.9×10^8
Pyridine	$(1.6 \pm 0.2) \times 10^7$	$(1.7 \pm 0.2) \times 10^7$	5.8×10^7

* The rate constants were calculated from published data [14] with the use of the rate constant of the reaction with pyridine taken from [8].

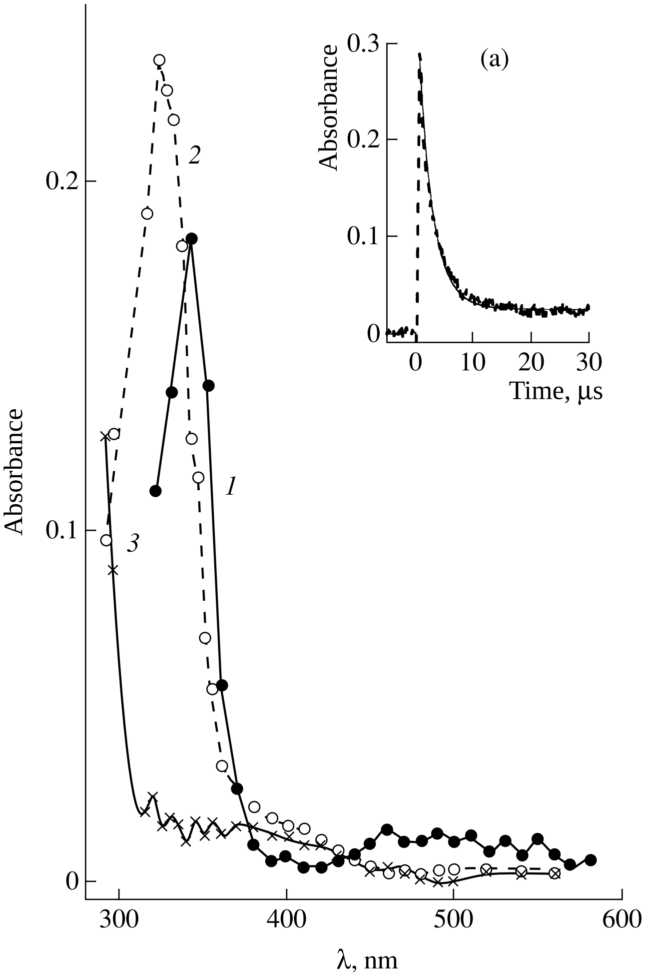
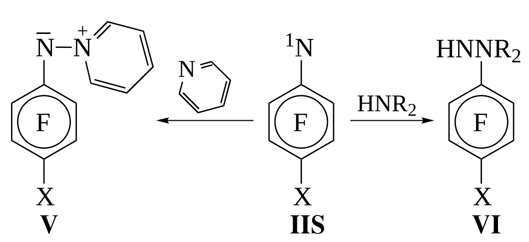


Fig. 4. Absorption spectra measured in the laser flash photolysis of azide **Ia** in acetonitrile at room temperature: (*1*) spectrum of singlet nitrene **IISa** 30 s after a laser pulse in the absence of morpholine, (*2*) spectrum of an adduct measured in the presence of morpholine (0.1 mol/l) 200 ns after a laser pulse, and (*3*) spectrum measured in the presence of morpholine (0.1 mol/l) 10 μs after a laser pulse. Inset: (a) the kinetics of decay of the adduct, as detected at λ_{max} = 320 nm (spectrum *2*).

ylides (**V**) as stable adducts (Scheme 2). These ylides exhibit a highly intense absorption band with λ_{max} ~ 400 nm. Hydrazines (**VI**), which do not exhibit detectable absorption in the visible and near-UV regions of the spectrum, are formed in high yields upon the photolysis of fluorinated arylazides in the presence of diethylamine [14].



Scheme 2.

We found that the formation of hydrazines **VIa** and **VIb** in the reactions of singlet arylnitrenes **IISa** and **IISb** with secondary amines is a multistep process. In the laser flash photolysis of azides **Ia** and **Ib** in the presence of amines (piperidine and morpholine), the absorption decay of the corresponding singlet arylnitrenes (Fig. 4, spectrum *1*) was accompanied by the appearance of an intermediate product, which exhibited intense absorption at λ_{max} = 320 nm (Fig. 4, spectrum *2*). In contrast to the adducts of singlet arylnitrenes with pyridine, this intermediate was unstable, and it was transformed into a compound that exhibited weak absorption in the near-UV region of the spectrum in a time of about 2.5 μs (Fig. 4, spectrum *3*).

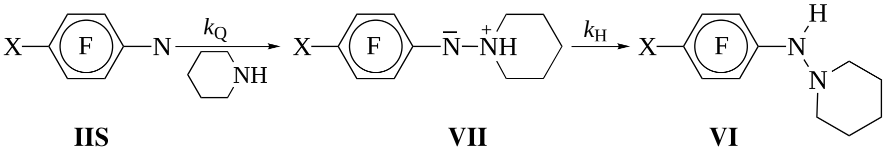
DISCUSSION

Previously [4, 14], the products of the reactions of singlet perfluorophenylnitrene **Ib** with various compounds such as pyridine, diethylamine, DMSO, tetrahydrofuran, benzene, toluene, and tetramethylethylene were isolated and identified. The ratios of the rate constants of the reactions of singlet perfluorophenylnitrene **IISb** with these additives to the rate constant of the reaction with pyridine were estimated in studies of the dependence of the yield of pyridine ylide **Vb** on the concentrations of other additives. More recently [8], the rate constant of the reaction of arylnitrene **IISc** with pyridine was measured to be equal to $(5.8 \pm 1.0) \times 10^7$ l mol^{-1} s^{-1}. With the use of this value and published data [14], we estimated the rate constants of the reactions of singlet perfluorophenylnitrene **IISc** with various additives (see the table).

The results of this work and the estimates based on published data [14] suggest that singlet fluorinated arylnitrenes efficiently react with secondary amines (diethylamine, piperidine, and morpholine). In this case, the reaction rate constants are almost independent of the nature of arylnitrenes **IISa**–**IISc** and secondary amines, and they are equal to $\sim 2 \times 10^8$ l mol^{-1} s^{-1}.

The reactions of singlet arylnitrenes with DMSO are also efficient. The rate constants of reactions with DMSO are independent of the nature of arylnitrenes **IISa**–**IISc**, and they are almost equal to the rate constants of the reactions with amines.

It is well known [4, 14] that hydrazine **VIc** is the final product of the photolysis of pentafluorophenylazide **Ic** in the presence of diethylamine (Scheme 2). It is also reasonable to suggest the formation of hydrazines **VIa** and **VIb** in the reactions of singlet arylnitrenes **IISa** and **IISb** with amines (Scheme 3). The absorption spectrum of the final product (Fig. 4, spectrum *3*) is consistent with this hypothesis.



Scheme 3.

Here, k_H is the rate constant of isomerization with proton transfer (1,2-hydrogen shift).

Adduct **VII** is the most likely precursor, which exhibits intense absorption with λ_{max} = 320 nm (Fig. 4, spectrum *2*), of hydrazine **VI** (see Scheme 3). Indeed, calculations performed by the PM3 method demonstrated that adduct **VII** corresponds to a minimum in the potential-energy surface. The calculations also demonstrated that the formation of adduct **VIIa** by a reaction between singlet nitrene **IISa** and piperidine followed by the isomerization reaction of **VIIa** to form hydrazine **VIa** are thermodynamically consistent. The enthalpies of these reactions are negative and equal to

$$\Delta H_Q = -35.5 \text{ kcal/mol},$$

$$\text{and} \quad \Delta H_H = -19.5 \text{ kcal/mol},$$

respectively, for the reactions in a gas phase.

The solvent effect is insignificant, and the enthalpies of the reactions in acetonitrile are equal to

$$\Delta H_Q = -39.9 \text{ kcal/mol},$$

$$\text{and} \quad \Delta H_H = -12.5 \text{ kcal/mol}.$$

Similar estimates of the enthalpy of formation of pyridine ylide resulted in values of –46.3 and –45.5 kcal/mol with and without regard for the solvent effect, respectively.

We also evaluated the positions of the long-wavelength absorption band maximums of the adducts of arylnitrene **IISb** with piperidine and pyridine. The excitation energy was estimated as the difference between the energies of the first excited state and the ground state of the adducts, as calculated by the PM3 method. This estimate resulted in λ_{max} = 343 nm for the long-wavelength absorption band of an adduct of **IISb** with pyridine; this value is consistent with experimental data (~400 nm). The positions of long-wavelength maximums for adducts of **IISb** with piperidine and of **IISa** with morpholine were estimated at 326 and 329 nm, respectively. These estimate are in good agreement with our experimental data (Fig. 4, spectrum *2*).

Thus, our calculations suggest that hydrazine results from the formation of intermediate adduct **VII** followed by the migration of a hydrogen atom (1,2-hydrogen shift). It is well known [15] that the intramolecular reaction of 1,2-hydrogen shift is significantly accelerated in the presence of basic catalysts such as triethylamine, alcohols, and water. Indeed, the rates of decay of the adducts of nitrenes **IISa** and **IISb** with morpholine (**VIIa** and **VIIb**) increased by factors of 2 and 2.3, respectively, on the addition of water (3.3 vol %). This fact is also consistent with the proposed mechanism (Scheme 3) of the reactions of singlet arylnitrenes with amines.

ACKNOWLEDGMENTS

This study was supported by the Russian Foundation for Basic Research (project nos. 98-03-32021 and 99-03-32753), the Ministry of Higher and Special Education of the Russian Federation (a grant within the framework of the Program “General and Technical Chemistry,” Section “Kinetics and Mechanisms of Photochemical Reactions”) and the Swiss National Science Foundation (SCOPES 2000–2003, grant no. 7SUPJ062336).

REFERENCES

1. Bayley, H., *Photogenerated Reagents in Biochemistry and Molecular Biology*, New York: Elsevier, 1983.
2. Schnapp, K.A., Poe, R., Leyva, E., Soudararajan, N., and Platz, M.S., *Bioconjugate Chem.*, 1993, vol. 4, no. 2, p. 172; Schnapp, K.A. and Platz, M.S., *Bioconjugate Chem.*, 1993, vol. 4, no 2, p. 178.
3. Gritsan, N.P. and Pritchina, E.A., *Usp. Khim.*, 1992, vol. 61, no. 5, p. 910.
4. Schuster, G.B. and Platz, M.S., *Adv. Photochem.*, 1992, vol. 17, p. 69.
5. Karney, W.L. and Borden, W.T., *J. Am. Chem. Soc.*, 1997, vol. 119, no. 6, p. 1378.
6. Gritsan, N.P., Yuzawa, T., and Platz, M.S., *J. Am. Chem. Soc.*, 1997, vol. 199, no. 21, p. 5059.
7. Born, R., Burda, C., Senn, P., and Wirz, J., *J. Am. Chem. Soc.*, 1997, vol. 119, no. 21, p. 5061.
8. Gritsan, N.P., Zhai, H.B., Yuzawa, T., *et al.*, *J. Phys. Chem.*, 1997, vol. 101, no. 15, p. 2833.
9. Pol’shakov, D.A., Tsentalovich, Yu.P., and Gritsan, N.P., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2000, no. 1, p. 49.
10. Molokov, I.F., Tsentalovich, Yu.P., Yurkovskaya, A.V., and Sagdeev, R.Z., *J. Photochem., Photobiol., A: Chem.*, 1997, vol. 110, no 2, p. 159.
11. Stewart, J.J.P., *J. Comput. Chem.*, 1989, vol. 10, no. 2, p. 209.
12. Bliznyuk, A.A. and Voityuk, A.A., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, no 8, p. 1785.
13. Karney, W.L. and Borden, W.T., *J. Am. Chem. Soc.*, 1997, vol. 119, no. 14, p. 3347.
14. Poe, R., Schnapp, K.A., Young, M.J.T., *et al.*, *J. Am. Chem. Soc.*, 1992, vol. 114, no. 13, p. 5054.
15. Kimura, Y., Yamamoto, M., Tobita, S., and Shizuka, H., *J. Phys. Chem. A*, 1997, vol. 101, no. 4, p. 459.