Laser flash photolysis of fluorinated aryl azides in neutral and acidic solutions

*D. A. Pol'shakov,[a] Yu. P. Tsentalovich,[b] and N. P. Gritsan[a,c]**

[a]*Novosibirsk State University,*
2 ul. Pirogova, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 2350. E-mail: cherry@ns.kinetics.nsc.ru
[b]*International Tomography Center, Siberian Branch of the Russian Academy of Sciences,*
3a ul. Institutskaya, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 33 1399. E-mail: yura@tomo.nsc.ru
[c]*Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences,*
3 ul. Institutskaya, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 2350. E-mail: gritsan@ns.kinetics.nsc.ru

Laser flash photolysis of perfluoro-4-biphenyl azide and *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide in acetonitrile, water-acetonitrile mixtures, and HCl-containing solutions was studied. The absorption spectra of primary intermediates, singlet arylnitrenes (**2a**(S) and **2b**(S), respectively), were recorded. The absolute rate constants of their intersystem crossing in MeCN were measured, and the corresponding Arrhenius parameters were found from the temperature dependences of the rate constants of isomerization of singlet arylnitrenes **2a**(S) and **2b**(S) to azirines. Protonation of singlet arylnitrenes **2a**(S) and **2b**(S) was observed, the rate constants of their protonation were measured, and the transient absorption spectra of arylnitrenium ions were recorded. It was shown by quantum-chemical calculations (the hybrid B3LYP method) that the arylnitrenium ions that formed have the singlet ground state and the singlet-triplet gap is ~20 kcal mol^{-1}.

Key words: laser flash photolysis, aryl azides, singlet arylnitrenes, protonation, arylnitrenium ions, quantum-chemical calculations.

Photochemical reactions of aryl azides are widely used in photolithography and photoaffinity labeling of biopolymers.[1] The general scheme of photolysis of aromatic azides has been found in recent years[2—5]: irradiation of aryl azides results in the elimination of the N_2 molecule and formation of singlet arylnitrenes, the key intermediates determining the nature of subsequent intermediate products.[2,3] Just recently, the UV spectra have been obtained, and the kinetics of the reactions of singlet phenylnitrene[6,7] and its perfluorinated derivative[8,9] has been studied.

Singlet polyfluorinated arylnitrenes can react with additives due to a longer lifetime, which makes it possible to use fluorinated aryl azides in the photoaffinity labeling of biopolymers.[10,11] Therefore, the reaction kinetics of fluorinated arylnitrenes is of special interest.

The possibility of protonation of singlet arylnitrenes to form the corresponding arylnitrenium ions has been found in several recent works.[12—14] Arylnitrenium ions are of interest because of their possible participation in carcinogenesis.[15] However, the kinetics of protonation of singlet arylnitrenes is not studied yet.

This work is devoted to the study of primary processes occurring during photolysis of two fluorinated aryl azides: perfluoro-4-biphenyl azide (**1a**) and *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide (**1b**) in organic media with water and acid additives. The absorption spectrum and intramolecular reactions of singlet perfluoro-4-biphenylnitrene (**2a**(S)) in organic solvents have been studied earlier.[8] The absorption spectrum and reactions of singlet *N*-propyl-4-nitreno-2,3,5,6-tetrafluorobenzylamide (**2b**(S)) were studied for the first time in this work.

Experimental

Reagents and solvents. Perfluoro-4-biphenyl azide was synthesized as described previously[8]; *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide was kindly presented by O. S. Fedorova (Novosibirsk Institute of Bioorganic Chemistry, SB RAS).

Acetonitrile was purified by refluxing for 1 h with P_2O_5 followed by distillation. To prepare anhydrous solutions of HCl in methanol and acetonitrile, the solvents were saturated with gaseous HCl for 3—6 h. Gaseous HCl was obtained by a known procedure.[16]

Flash photolysis. The laser flash photolysis setup has been described earlier.[17] A solution was irradiated in a rectangular 10×10 mm quartz cell with a XeCl pulse of an excimer laser (Lambda Physik EMG 101, 308 nm, 100 mJ, 17 ns). The detection system consists of a DKSSh-120 xenon lamp, two

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monochromators, a Hamamatsu R955 photoamplifier, a LeCroy 9310A digital oscillograph, and a system of filters and shutters.

A flow-type system was used to avoid secondary photolysis of the products. To remove O_2, argon was bubbled through the solution for 20 min. The temperature of samples was varied within the 240—350 K range by a thermostabilized nitrogen flow and measured by a thermocouple.

Low-temperature photolysis. Solutions of aryl azides in vitrifying solvents (methylcyclohexane, methanol, a 5 *M* solution of HCl in methanol) were irradiated with the light of a DRSh-500 lamp with λ_{max} = 313 nm. A solution was placed in a 2-mm cell (argon was bubbled through the solution for 20 min to remove dioxygen), frozen at 77 K, and placed in a quartz cryostat with plane-parallel windows. The temperature in the cryostat was varied within 77—125 K by a thermostabilized nitrogen flow and measured by a thermodiode. Transient absorption spectra were recorded on a Specord UV-Vis spectrophotometer.

Calculation procedure. Quantum-chemical calculations were performed by the Hartree—Fock method and using the density functional theory with the version of the hybrid B3LYP method[18] by the GAUSSIAN94 program.[19] The 6-31G* basis set was used in all cases.

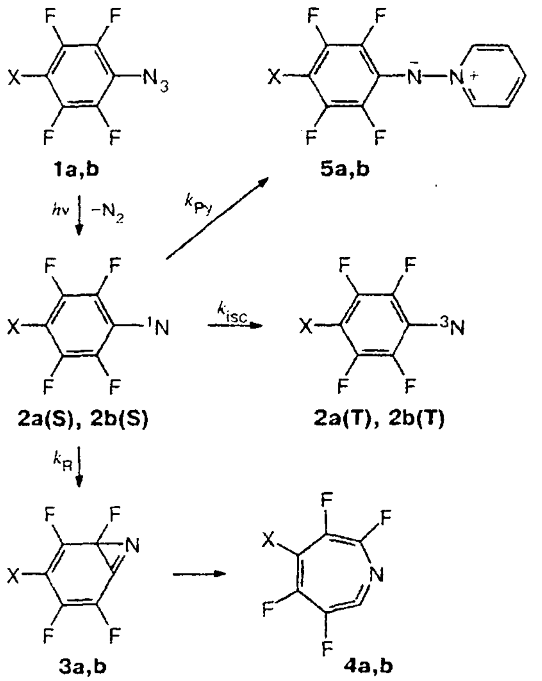
Results and Discussion

Laser flash photolysis of aryl azides in acetonitrile

It has previously[8] been shown (Scheme 1) that singlet perfluoro-4-biphenylnitrene (**2a(S)**) isomerizes to the corresponding azepine (**4a**) or undergoes intersystem crossing (k_{isc}) to the ground triplet state (**2a(T)**). The isomerization of singlet arylnitrenes to azepines is a two-stage process.[4,5] The first stage (k_R) is limiting. The absorption spectrum of singlet nitrene **2a(S)** contains an intense band with a maximum at 350 nm and lower-intensity bands with maxima at 420 and 500 nm. The corresponding stable ylide **5a**, which is characterized by intense absorption with a maximum at 420 nm, forms in the presence of pyridine.

Laser flash photolysis (LFP) of perfluoroaryl azide **1b** in acetonitrile results in the appearance of intermediate absorption (Fig. 1). The spectrum recorded immediately after the laser pulse (see Fig. 1, spectrum *1*) exhibits absorption in the visible (λ_{max} = 460 nm) and near-UV regions ($\lambda_{max} \leq$ 300 nm). This absorption decays exponentially with a characteristic time of 210 ns in MeCN at −20 °C. In addition, the absorption with maxima at 410 and 530 nm (see Fig. 1, spectrum *2*) increases with the same characteristic time. It is known[2,3] that the irradiation of aryl azides in glassy matrices at 77 K results in the formation and stabilization of the corresponding triplet arylnitrenes. The absorption spectrum of triplet nitrene **2b(T)** obtained during irradiation of aryl azide **1b** in methanol is also presented in Fig. 1 (spectrum *3*). It is seen in Fig. 1 that the band with λ_{max} = 530 nm in the spectrum of the intermediate absorption (*2*) corresponds to triplet nitrene **2b(T)**. The corresponding azepine **4b** along with the triplet nitrene

Scheme 1



X = C_6F_5 (**a**), CONHPr (**b**)

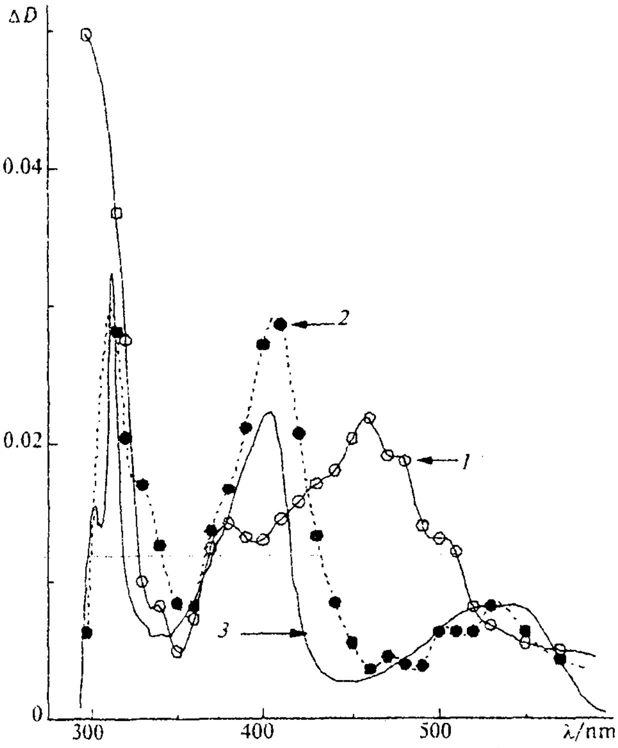


Fig. 1. Absorption spectra recorded 30 (*1*) and 400 ns (*2*) after laser excitation of *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide (**1b**) in MeCN at −20 °C. Absorption spectrum of triplet *N*-propyl-4-nitreno-2,3,5,6-tetrafluorobenzylamide (**2b(T)**) in MeOH at 77 K (*3*).

contributes to the absorption at 410 nm. The LFP of aryl azide **1b** in the presence of pyridine, as well as in the case of compound **1a**, gives ylide **5b**, which is characterized by an intense absorption band with a maximum at 420 nm. Therefore, the primary processes during the irradiation of azide **1b** in organic solvents are also described by Scheme 1. The absorption spectrum of the primary intermediate (see Fig. 1, spectrum *1*) detected by us belongs to singlet nitrene **2b(S)** and is close to that of nitrene **2a(S)**; however, the absorption bands are shifted to the short-wavelength region.

The temperature dependence of the observed rate constant (k_{obs}) of decay of singlet nitrene **2b(S)** is presented in Fig. 2 (curve *1*). According to Scheme 1, in the absence of pyridine, the decay rate constant is the sum of the rate constants of two elementary processes: intersystem crossing (k_{isc}) and isomerization to azirine (k_R):

$$k_{obs} = k_{isc} + k_R$$

The following values can be obtained under the assumption that the rate constant of intersystem crossing, unlike the isomerization rate constant, is temperature-independent (the activation energy is expressed in cal mol^{-1}):

$$k_{isc} = (2.5\pm0.3) \cdot 10^6 \text{ s}^{-1},$$
$$k_R = 10^{12.0\pm0.2} \cdot \exp[-(7500\pm300)/(RT)] \text{ s}^{-1}.$$

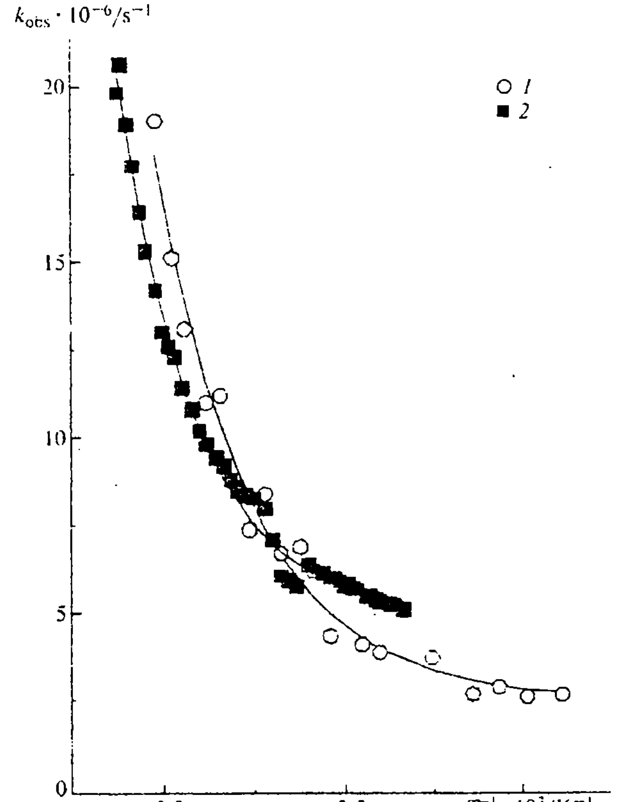


Fig. 2. Temperature dependences of the rate constant of decay of singlet nitrene **2b(S)** in MeCN (*1*) and singlet nitrene **2a(S)** in an H_2O—MeCN mixture (20% H_2O) (*2*). Solid curves indicate the approximation by the exponential dependence.

Analysis of the temperature dependence of the decay rate constant of nitrene **2a(S)** in acetonitrile leads to the following values:

$$k_{isc} = (3.1\pm0.3) \cdot 10^6 \text{ s}^{-1},$$
$$k_R = 10^{12.5\pm0.4} \cdot \exp[-(8900\pm300)/(RT)] \text{ s}^{-1}.$$

The obtained rate constants and their Arrhenius parameters are close to those previously measured[8] in CH_2Cl_2 and slightly differ from the above presented values for nitrene **2b(S)**.

It was of interest to study the kinetics of the protonation of arylnitrenes **2a(S)** and **2b(S)** and determine the spectral parameters of the corresponding arylnitrenium ions. Since it is convenient to carry out these studies in aqueous-organic media, we first studied the effect of water addition on the nature of the products and the kinetics of reactions of singlet arylnitrenes.

Laser flash photolysis of aryl azides in water-acetonitrile solutions

When LFP of aryl azides **1a,b** is performed in water-acetonitrile solutions, a substantial shortening of the lifetime of singlet nitrenes **2a(S)** and **2b(S)** is observed, as compared to photolysis in anhydrous acetonitrile. For example, when 50% H_2O (v/v) is added, the lifetime of nitrene **2a(S)** at -20 °C decreases 4.2-fold. No new bands were detected in the spectrum recorded 300 ns after the laser pulse, as compared to the spectrum in pure acetonitrile. The only distinction is a change in the ratio of intensities of the bands at 420 and 550 nm. Comparison of the transient spectra with that of triplet nitrene **2a(T)** shows that when the water content in the solution increases, the spectrum of the reaction products of **2a(S)** becomes similar to that of triplet nitrene **2a(T)**. Therefore, we may assume that the reaction in water-acetonitrile solutions is also described by Scheme 1.

Analysis of the temperature dependence of the decay rate constant (see Fig. 2, curve *2*) gives the following values of the rate constants of the elementary reactions of nitrene **2a(S)** in acetonitrile containing 20% H_2O:

$$k_{isc} = (4.9\pm0.4) \cdot 10^6 \text{ s}^{-1},$$
$$k_R = 10^{13.0\pm0.4} \cdot \exp[-(9000\pm300)/(RT)] \text{ s}^{-1},$$

i.e., when water is added, k_{isc} increases1.6-fold. The Arrhenius parameters for the temperature dependence of k_R remain unchanged within the experimental accuracy.

Similar changes in the spectral and kinetic data were detected for LFP of aryl azide **1b** in water-acetonitrile solutions.

Thus, the addition of even 50% water is not accompanied by new transformations of singlet arylnitrenes

2a(S) and **2b(S)**; only a slight acceleration of intersystem crossing is observed, as has been assumed previously[2] for alcohols.

It has recently[12] been observed that in a water-acetonitrile solution containing 50% H_2O, 4-biphenylnitrene is completely protonated. According to our observations, its fluorinated analog **2a(S)** is not protonated to a noticeable extent under these conditions.

Laser flash photolysis in the presence of acid

In these experiments, the concentration of acid (HCl) in a water-acetonitrile solution (20% H_2O, v/v) was varied within 0.001—0.500 mol L^{-1}. In the presence of the acid, the lifetime of singlet arylnitrenes is substantially shortened. The effective rate constant of the pseudo-first order (k_{obs}) increases linearly as the acid concentration increases (Fig. 3, *b*).

Photolysis of aryl azide **1b** in the presence of the acid results in the fast disappearance of the spectrum of singlet arylnitrene **2b(S)** and the appearance of a new species, whose spectrum (Fig. 3, *a*, spectrum *1*) contains an intense narrow band at 325 nm, which is not characteristic of the reaction products of **2b(S)** in the absence of acid. Thus, in the presence of acid, a new channel of transformations appears. These transformations are probably the protonation of nitrene **2b(S)** to form the arylnitrenium ion **6b** (Scheme 2).

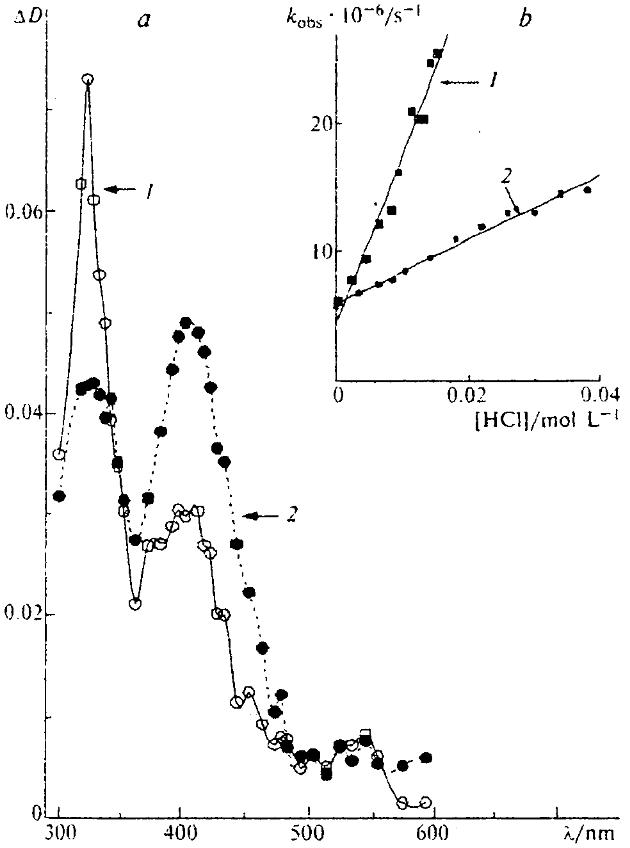
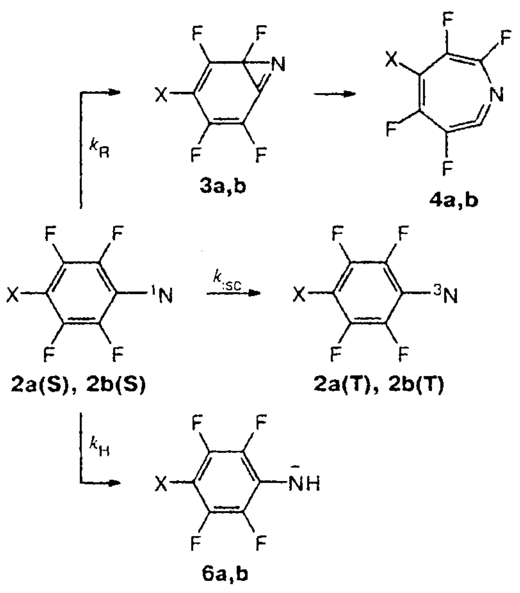


Fig. 3. *a*. Absorption spectra recorded 60 (*1*) and 350 ns (*2*) after laser excitation of *N*-propyl-4-azido-2,3,5,6-tetrafluorobenzylamide (**1b**) in the H_2O—MeCN mixture (20% H_2O) at -20 °C in the presence of HCl (0.057 mol L^{-1}). *b*. Dependences of the rate constants of decay of singlet arylnitrenes **2b(S)** (*1*) and **2a(S)** (*2*) on the concentration of HCl.

Scheme 2



X = C_6F_5 (**a**), CONHPr (**b**)

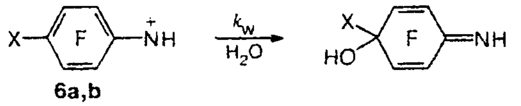
According to this scheme, the rate constant of decay of singlet arylnitrene in the presence of acid is the sum of the rates constants of three reactions:

$$k_{obs} = k_{isc} + k_R + k_H[H^+].$$

The rate constants of protonation (k_H) of singlet nitrenes **2a(S)** and **2b(S)** were determined from the data in Fig. 3, *b* and are equal to $(2.4\pm0.2)\cdot10^8$ and $(1.3\pm0.1)\cdot10^9$ L mol^{-1} s^{-1} for **2a(S)** and **2b(S)**, respectively, which are substantially lower than the rate constants of typical diffusion-controlled reactions (~10^{10} L mol^{-1} s^{-1}). It follows from the previous estimations[12] that the protonation of singlet phenyl- and biphenylnitrenes is diffusion-controlled. It cannot be ruled out that the difference in the protonation rates is related to the presence of fluorine atoms in the aromatic ring.

The lifetime of the arylnitrenium ion **6b** in water-acetonitrile mixtures is sufficiently low. For example, it is 160 ns in a solution containing 20% H_2O. When the water content decreases, the lifetime of the cation increases. The absorption spectrum of the product of transformations of cation **6b** is presented in Fig. 3, *a* (curve 2). In anhydrous acetonitrile, the lifetime of the cation is ~10 μs. A decrease in the lifetime of the arylnitrenium ions in aqueous solutions is likely due to the interaction of the arylnitrenium ion with water[12] (Scheme 3).

Scheme 3



6a,b

X = C_6F_5 (**a**), CONHPr (**b**)

Since the lifetime of the arylnitrenium ions in anhydrous media is sufficiently high, we were able to detect their spectra during LFP of aryl azides **1a,b** in anhydrous acetonitrile in the presence of HCl (0.5 mol L^{-1}) (Fig. 4). For this concentration of the acid, the protonation is the only channel of decay of singlet nitrenes; therefore, only the absorption bands of the cations are observed in the spectrum. The spectra of arylnitrenium ions **6a,b** are close: both of them have two bands with maxima at 330 and 530 nm. Similar spectra have previously been detected for LFP of perfluorophenylazide and some of its derivatives in the presence of H_2SO_4.[13]

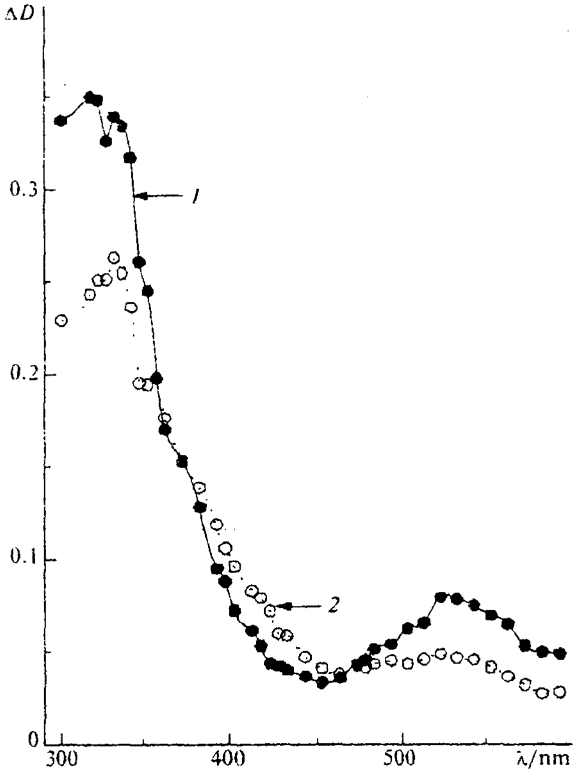


Fig. 4. Absorption spectra of arylnitrenium ions **6a** (1) and **6b** (2) recorded after laser flash photolysis of arylazides **1a,b** in anhydrous MeCN containing HCl (0.5 mol L^{-1}) at ~20 °C.

Arylnitrenium ions can have either a triplet or singlet ground state. The question about the nature of the ground state of arylnitrenium ions[12—14,20] can be solved experimentally if the cations are stabilized at a low temperature in a glassy matrix. For this purpose, we carried out experiments on low-temperature photolysis.

Low-temperature photolysis in the presence of acid

Low-temperature photolysis of aryl azides **1a,b** was carried out in glassy methanol pre-saturated with HCl to a concentration of 5 mol L^{-1}. Spectral changes observed during photolysis of compounds **1a,b** at 77 K in the presence of HCl (5 mol L^{-1}) are identical to those obtained during irradiation in the absence of acid. The same results were obtained when irradiation was performed at higher temperatures up to 123 K. When aryl azides **1a,b** are irradiated at temperatures >125 K, already triplet nitrenes enter into the dimerization reactions to form the corresponding azo compounds.

Thus, at low temperatures (77—123 K) the protonation of singlet arylnitrenes **2a(S)** and **2b(S)** does not compete with intersystem crossing to the ground triplet state. According to the estimations,[8] the lifetime of nitrene **2a(S)** in methanol in this temperature range is ~100 ns. No protonation of arylnitrenes in the triplet state was detected. These facts indirectly indicate that the ground state of the cation is singlet state for ions **6a,b**.

To confirm the singlet nature of the ground state of the fluorinated arylnitrenium ions, we performed quantum-chemical calculations of the structure and properties of ion **6b**.

Quantum-chemical calculations of arylnitrenium ion 6b

The geometry and energetics of the phenylnitrenium ion has previously[20] been calculated by the Hartree—Fock (HF) method and using the density functional theory (DFT). The results of the BVWN5 calculations suggested a singlet nature of its ground state.

Our calculations by the B3LYP/6-31G* method of the geometry and energetics of the singlet and triplet states of the arylnitrenium ion **6b** indicate that the singlet state of the cation is ground. The singlet-triplet gap is equal to ~20 kcal mol^{-1}, which is close to the published data[20] for the phenylnitrenium ion.

Note that the HF/6-31G* calculations result in a triplet ground state of ion **6b**, although the singlet-triplet gap is low (5 kcal mol^{-1}). However, it is well known that the methods based on the density functional theory, unlike the Hartree—Fock method, take into account the electron correlation. Therefore, in the calculation of the singlet-triplet gap, the results of the HF and DFT methods may substantially differ.

Thus, it follows from the results of quantum-chemical calculations and indirect data on the absence of protonation of triplet arylnitrenes that the ground state of polyfluorinated arylnitrenium ions is singlet state.

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