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PHOTOCHEMICAL PROPERTIES OF 9-(4-AZIDOPHENYL)ACRIDINE

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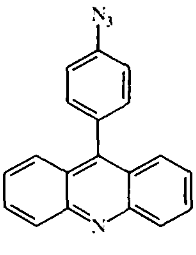
Syntheses are reported for 9-(azidophenyl)acridine and the corresponding N-methylacridine derivative, which have absorption bands in the near-UV and visible spectral regions. The photodissociation quantum yields upon irradiation of these azides at the long-wavelength band (365 nm) are 0.88 and $< 10^{-2}$, respectively. An MNDO-PM3 semiempirical analysis was carried out on the change in the bond orders, NNN bond angle, and charge redistribution upon excitation of these molecules to the lowest excited singlet state, which accounted for the experimentally observed photochemical activity of 9-(4-azidophenyl)acridine and inertness of its quaternerized derivative.

One of the disadvantages of aromatic azides as photochemical compounds is their low sensitivity to visible light, related to the lack of absorption bands in the visible region in the spectra of simple aromatic azides. This low sensitivity significantly limits the application of these compounds in such fields as biology [1]. In an attempt to expand the absorption of azides into the visible region by introducing additional chromophore systems, we encounter the general problem that the photolysis quantum yield of azides drops sharply with an increase in long-wavelength absorption not only in the visible but also in the ultraviolet region [2].

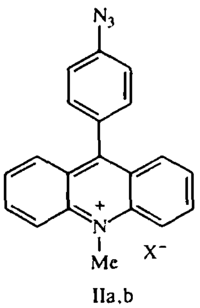
In the case of heterocyclic derivatives of azidochalcone, we showed that the replacement of the phenyl ring by a heterocyclic residue leads to a bathochromic shift of the absorption band to the visible region with retention of high quantum yields for photodissociation of the azido group [3].

In the present work, we studied acridine azides. The acridine system has absorption bands in the near-UV and upon protonation (quaternization), the absorption spectrum expands into the visible region [4]. We assumed that use of the acridine residue as a substituent in phenyl azide would permit us to combine two useful properties in the new compound: 1) the long-wavelength absorption spectrum of acridine and 2) the high photochemical activity of phenyl azide.

Chupakhin et al. [5] have synthesized 9-(4-aminophenyl)acridine by heating acridine hydrochloride with aniline in the presence of elemental sulfur as an oxidizing agent. 9-(4-Azidophenyl)acridine (I) was obtained by diazotization of the amine with subsequent treatment with aqueous sodium azide. Quaternization of azide I with methyl iodide or dimethyl sulfate gave salts IIa and IIb, respectively.



I



IIa,b

a X = I; b X = $MeSO_4$

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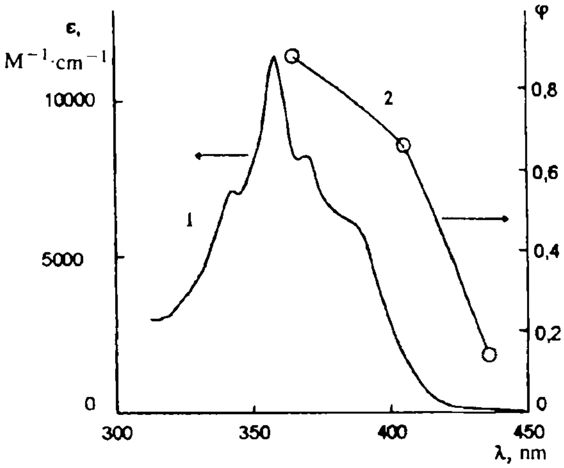


Fig. 1. Electronic absorption spectrum of 9-(4-azidophenyl)acridine (I) in chloroform (*1*) and dependence of the quantum yield (φ) of the photolysis of I on the wavelength of the exciting light (*2*).

Azide I has a strong near-UV absorption band and the long-wavelength edge of the band extends into the visible region (Fig. 1). Comparison of the spectrum of unsubstituted 9-phenylacridine shows that introduction of the azido group did not lead to any change in the position of the absorption bands.

In contrast to azide I, in the case of previously studied heterocyclic azidochalcones, introduction of an azido group into the cinnamoylarene molecule leads to a bathochromic shift of the long-wavelength band [3]. For example, this shift is 22 nm for 2-cinnamoylquinoline and the photodissociation quantum yield is 0.85. Thus, the spectral changes upon the introduction of an azido group may be seen as indirect evidence for participation of the electron system of the azido group in the electronic transition giving rise to the long-wavelength absorption band and a reason for the photoactivity of the azide upon irradiation at this band.

Quaternization of azide I at the acridine nitrogen atom leads to the appearance of additional bands in the spectra of IIa (432 nm) and IIb (430 nm). An analogous band is found in the spectrum of 4-methyl-9-phenylacridinium iodide (λ_{max} 426 nm). The positions of the absorption bands differ in the spectra of compounds with and without an azido group in the case of quaternized derivatives II although these differences are much less (shifts of only 6 and 4 nm) than for cinnamoylarenes.

Thus, assuming a correlation between the shift of the absorption band of the aromatic compound upon introduction of an azido group and the photochemical activity of the azide, we would expect that azides containing an acridine moiety would be inactive or only slightly active upon irradiation at the long-wavelength absorption band. However, our experimental study showed that their photochemical properties differ significantly.

The efficient decomposition of azide I is observed upon irradiation near the maximum of the long-wavelength absorption band (mercury line at 365 nm). The decomposition quantum yield (φ) decreases with increasing wavelength of the incident light although the yield remains rather high (Table 1).

Figure 1 shows the dependence of the quantum yield on the wavelength of the incident light along with absorption spectrum of the azide. The quantum yield was found to drop with decreasing molar extinction coefficient of the azide.

The photodissociation quantum yield of iodomethylate IIa is more than two orders of magnitude less than the yield of azide I (Table 1). Azide iodomethylates form charge transfer complexes, in which the heteroaromatic cation acts as the acceptor and the iodide ion acts as the donor [6]. Thus, the low photoactivity of salt IIa may be related to loss of the energy of the absorbed light quantum upon irradiation of the complex due to electron transfer within the complex and not to local excitation of the quaternized heterocycle.

However, replacement of the iodide counter-ion in azide IIa by the $CH_3SO_4^-$ ion (azide IIb), which has less tendency to form complexes, leads to only a slight increase in the quantum yield, which, nevertheless, remains more than two orders of magnitude less than for azide I (Table 1). Therefore, the cation in II indeed displays low photochemical activity relative to dissociation of the azide group.

The difference in the photochemical properties of azides I and II may be related to the difference in the structures of the excited states of these compounds. Electron transfer occurs upon irradiation at the long-wavelength absorption band from

TABLE 1. Photodecomposition Quantum Yields of Azides I, IIa, and IIb

Azide	Solvent	λ_{exc}, nm	ε, M^{-1} cm^{-1}	φ
I	$CHCl_3$	365	10000	0,88±0,20
	$CHCl_3$	405	1760	0,69±0,10
	C_2H_5OH	405	1920	0,66±0,15
	C_2H_5OH	436	30	0,14±0,05
IIa	CH_3CN	365	12800	$(2,3\pm0,4)\cdot10^{-3}$
IIb	CH_3CN	365	15200	$(3,8\pm0,3)\cdot10^{-3}$

TABLE 2. Geometrical Parameters of the CNNN Fragment in the Ground and Lowest Excited States of Azides from a PM3 Calculation

Azide	State	$r_{C—N(1)}$, Å	$r_{N(1)—N(2)}$, Å	$r_{N(2)—N(3)}$, Å	∠ NNN, deg
I	S_0	1,43	1,27	1,13	169,5
	S_1	1,41	1,35	1,15	135,2
II	S_0	1,42	1,28	1,12	169,7
	S_1	1,32	1,36	1,11	168,6

the highest occupied molecular orbital (MO) to the lowest unoccupied MO, which corresponds to conversion of the system to the lowest excited singlet state. Hence, in order to elucidate these experimental data, we carried out an MNDO-PM3 calculation using the MOPAC 7.0 program package with complete optimization of the geometries of the ground (S_0) and lowest excited singlet states (S_1) of azides I and II and compared the changes in the parameters, which occur upon going from states S_0 to S_1 for both molecules.

Table 2 gives the geometrical parameters of the CNNN fragment (lengths of the bonds between atoms i and j, r_{ij} and NNN bond angle) in the ground and lowest excited singlet states of these azides, while Table 3 gives the calculated bond orders p_{ij} and effective charges on the atoms (q_i) ($N_{(1)}$ of the azido group corresponds to the nitrogen atom bound to the aromatic ring, see numbering in Fig. 2). This calculation shows that the azido group in the ground state has almost linear geometry and lies in the plane of the benzene ring, which, in turn, is twisted relative to the plane of the acridine system by 81.3° (azide I) and 70.7° (azide II).

The molecular diagrams in Fig. 2 show the changes in the orders of several bonds and charges on the azido group nitrogen atoms, which occur when the azides are converted to the lowest excited singlet state. Upon excitation, the bond order of $N_{(1)}-N_{(2)}$ in azide I, which decomposes upon dissociation, decreases by 0.38, while the decrease in the order of this bond in the case of azide II is only 0.19.

Since complete breakage of the $N_{(1)}-N_{(2)}$ bond occurs upon dissociation of the azido group, decomposition of excited azide I is more likely than decomposition of excited azide II.

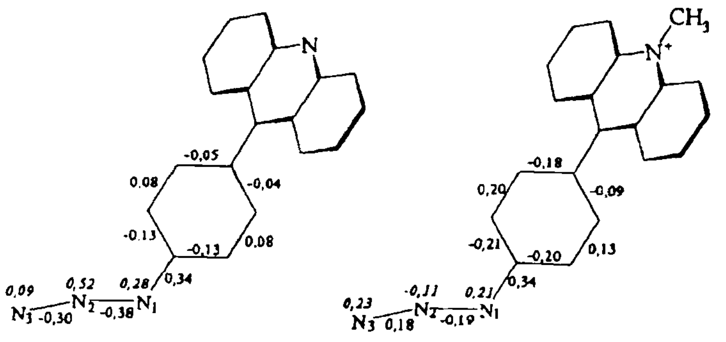
A similar result was obtained in a comparative analysis of the change in charge on the azido group upon the excitation of azides I and II. Figure 2 shows that the decrease in charge on the middle nitrogen atom of the azido group upon going to the excited state is 0.52 for azide I and only 0.11 for azide II. The total change in charge on the $N_{(2)}-N_{(3)}$ fragment of the azido group capable of dissociation is -0.43 and 0.12 for azides I and II, respectively, i.e., the charge on the $N_{(2)}-N_{(3)}$ fragment in the case of azide I decreases, while it increases for azide II. Considering that the starting charge on the $N_{(2)}-N_{(3)}$ fragment is about 0.4 for both azides and the charge on this fragment must drop to zero during the loss of molecular nitrogen (observed in the case of azide I), transition to the excited state of azide II, in contrast to azide I, clearly does not facilitate dissociation of the azido group. This conclusion is in complete accord with our experimental results.

Significant differences are observed in the NNN bond angles in the excited states of I and II (Table 2). The azido group in the excited cation of II retains almost linear configuration for the ground state. On the other hand, the NNN bond angle in excited azide I decreases and the azido group becomes bent.

A theoretical examination of the dissociation of the azido group showed that flexure of the azido group in phenyl azide upon photoexcitation is a significant step leading to the loss of molecular nitrogen [8]. In this case, the aromatic ring acts an antenna absorbing light and emitting the energy of the azido group. The NNN bond angle decreases and there is further exten-

TABLE 3. Bond Orders and Effective Charges in the CNNN Fragment in the Ground and Lowest Excited States of Azides from a PM3 Calculation

Azide	State	$p_{C-N(1)}$	$p_{N(1)-N(2)}$	$p_{N(2)-N(3)}$	q_C	$q_{N(1)}$	$q_{N(2)}$	$q_{N(3)}$
I	S_0	1,01	1,36	2,52	0,04	-0,42	0,72	-0,33
	S_1	1,35	0,98	2,22	0,00	-0,14	0,20	-0,24
II	S_0	1,05	1,29	2,58	0,09	-0,42	0,71	-0,26
	S_1	1,39	1,10	2,76	0,08	-0,21	0,60	-0,03



I

II

Fig. 2. Change in orders of several bonds and charges (italics) in the azido group in the lowest excited singlet state (S_1) for 9-(4-azidophenyl)acridine I and N-methyl-9-(4-azidophenyl)acridine II in comparison with the ground state (S_0).

sion of the $N-N_2$ bond with subsequent loss of N_2 after overcoming the activation barrier, which is much lower in the excited state than in the ground state. The transition state for the dissociation reaction features bent configuration of the azido group.

Comparison of the results of Bunting and Meathrel [8] and our data indicates that the geometrical parameters of excited azide I are similar to those for the excited state of the dissociation reaction, while the geometrical parameters of excited azide II correspond to the parameters of the stable ground state.

Thus, analysis of the change in the bond orders, NNN bond angle, and charge distribution upon excitation to the lowest excited singlet state accounts for the observed activity of azide I and inertness of quaternized azide II in the photochemical dissociation of the azido group upon irradiation at the long-wavelength absorption band.*

EXPERIMENTAL

The electronic absorption spectra were taken on Specord UV-VIS and Specord M-40 spectrophotometers. The IR spectra were taken on a UR-20 spectrometer. The NMR spectra were taken on a Bruker WH-360 spectrometer with TMS as the internal standard. The mass spectrum of azide I was taken on a Hitachi M80 mass spectrometer with an M003 data treatment system at 12 eV ionizing electron energy. The emission current was 100 μA and the ionization chamber temperature was 200°C. The mass spectra of acridinium derivatives IIa and IIb were measured on a reflectron time-flight mass spectrometer with orthogonal ion inlet. Electrospray ionization was used (extraction of ions by an electric field from a $1 \cdot 10^{-4}$ M solution in acetonitrile).*

The photolysis of the aromatic azides was carried out using a DRSh-1000 mercury lamp. Combinations of glass and interference filters were used to isolate the 365, 405, and 436 nm lines of the mercury spectrum. The light intensity was measured using an RTN-20 thermoelement. The concentration of the azide during the photolysis was measured spectrophotometrically using liquid chromatography. The quantum yield of the photodecomposition was determined upon 10-30% azide conversion.

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*The authors express their gratitude to V. I. Kozlovskii for taking the electric field ion extraction mass spectra.

High-resolution liquid chromatography was carried out on a Milikhrom chromatograph using a Separon S18 5.0 μm column with an acetonitrile – water gradient system. Liquid-chromatography-grade acetonitrile was used for these experiments. In the case of IIa and IIb, 1% NH_4PF_6 was added as an ion-pair agent.

9-(4-Azidophenyl)acridine (I). A mixture of 264 mg (0.98 mmole) 9-(4-aminophenyl)acridine (synthesized according to Chupakhin [5]) with 4 ml 20% hydrochloric acid was cooled to 0°C and a solution of 65 mg (1 mmole) NaN_3 in 2 ml water was added with stirring. After 1 h, the reaction mixture was brought to pH 8 by adding concentrated aq. sodium carbonate. The precipitate was filtered off and recrystallized from ethanol to give 180 mg (62%) I as yellow crystals, mp 188-189°C. UV spectrum (chloroform), λ_{max} (ε): 360 nm ($1.1 \cdot 10^4$). IR spectrum (KBr): 2120 cm^{-1} (N_3). Mass spectrum, *m/z*: M^+ 296; [M^+ – 28] 268. PMR spectrum (($(CD_3)_2CO$): 8.24 (2H, d, *J* = 9 Hz, acridine), 7.84 (2H, t, acridine), 7.71 (2H, d, *J* = 9 Hz, acridine), 7.56 (2H, d, *J* = 8 Hz, C_6H_4), 7.53 (2H, m, acridine), 7.42 ppm (2H, d, *J* = 8 Hz, C_6H_4).

N-Methyl-9-(4-azidophenyl)acridinium Iodide (IIa). A sample of 5 ml (80 mmoles) methyl iodide was added to a solution of 300 ml (1.01 mmole) 9-(4-azidophenyl)acridine in 10 ml acetonitrile and heated in a sealed ampoule for 8 h at 75°C. The solvent was distilled off and the residue was placed on a column packed with Silpearl silica gel using 1:1 chloroform – acetonitrile as the eluent to give 370 mg IIa (83%) as dark red crystals, mp 210°C (dec.). UV spectrum (acetonitrile), λ_{max} (ε): 350 (11,800), 361 (25,100), 432 nm (9700). IR spectrum (KBr): 2120, 2090 cm^{-1} (N_3). Mass spectrum: M^+ 311. PMR spectrum ($CDCl_3$): 8.90 (2H, d, *J* = 9 Hz, acridine), 8.43 (2H, t, acridine), 8.03 (2H, d, *J* = 9 Hz, acridine), 7.84 (2H, t, acridine), 7.55 (2H, d, *J* = 8 Hz, C_6H_4), 7.39 (2H, d, *J* = 8 Hz, C_6H_4), 5.25 ppm (3H, s, $N-CH_3$).

N-Methyl-9-(4-azidophenyl)acridinium Methyl Sulfate (IIb). A mixture of 220 mg (0.74 mmole) 9-(4-azidophenyl)-acridine and 0.5 ml (48 mmoles) freshly distilled dimethyl sulfate was heated in a sealed ampoule for 13 h at 75°C. The reaction mixture was evaporated and the residue was placed on column packed with Silpearl silica gel using 1:1 chloroform – acetonitrile as the eluent to give 200 mg (62%) IIb as yellow crystals, mp 196-198°C. Found: C, 59.29; H, 4.31; N, 13.19%. Calculated for $C_{21}H_{18}N_4O_4S$: C, 59.71; H, 4.29; N, 13.26%. UV spectrum (acetonitrile): λ_{max} (ε): 349 (12,400), 361 (27,000), 430 nm (10,400). IR spectrum (KBr): 2130 cm^{-1} (N_3). Mass spectrum: M^+ 311. PMR spectrum ($(CD_3)_2CO$): 8.89 (2H, d, *J* = 9 Hz, acridine), 8.47 (2H, t, acridine), 8.18 (2H, d, *J* = 9 Hz, acridine), 8.00 (2H, t, acridine), 7.66 (2H, d, *J* = 9 Hz, C_6H_4), 7.57 (2H, d, *J* = 9 Hz, C_6H_4), 5.18 (3H, s, $N-CH_3$), 3.42 ppm (3H, s, CH_3-OSO_3).

N-Methyl-9-phenylacridinium Iodide. A mixture of 200 mg phenylacridine and 0.5 ml (80 mmoles) methyl iodide in 7 ml acetonitrile was heated in a sealed ampoule for 3 h at 50°C. The reaction mixture was evaporated and the residue was twice recrystallized from ethanol to give 210 ml (67%) product as dark red crystals, which decompose at 252°C (mp 250°C (from methanol) [9]). UV spectrum (acetonitrile), λ_{max} (ε): 347 (13,800), 361 (30,200), 426 nm (8200).

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