Irradiation of 5-azido-8-methoxypsoralen† in water–acetonitrile gives nitrenium ion and triplet nitrene transients, but only nitrenium ion products

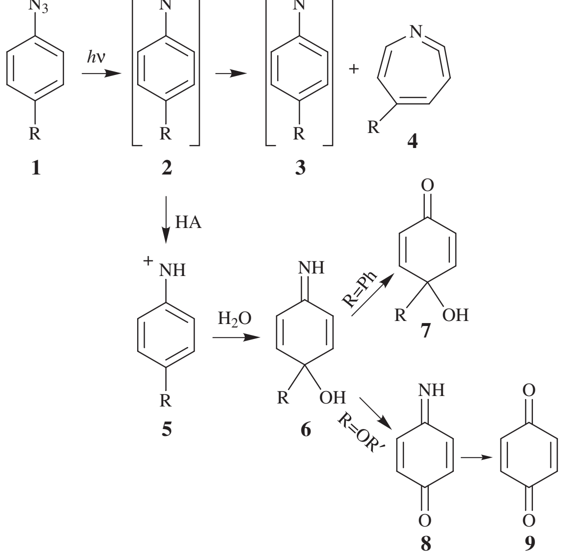
Pratima Ramlall,[a] Yuzhuo Li[b] and Robert A. McClelland*[a]

[a] *Department of Chemistry, University of Toronto, Toronto, Ontario M5S 3H6, Canada*
[b] *Department of Chemistry, Clarkson University, Potsdam, New York 13669-5810, USA*

Received (in Cambridge) 23rd March 1999, Accepted 9th June 1999

Irradiation of 5-azido-8-methoxypsoralen **10** in water–acetonitrile mixtures gives essentially quantitative yields of 5-imino-5,8-dihydropsoralen-8-one **17** regardless of the composition. This quinone imine is derived from the reaction of water with the nitrenium ion that results from protonation of the initially-formed singlet nitrene. Laser flash photolysis (LFP) in water and 90 : 10 water–acetonitrile reveals a transient intermediate with λ_{max} at 500–520 nm with the characteristics of a nitrenium ion, in particular a very effective quenching by azide ion. The immediate product of the reaction of water and the nitrenium ion is a hemiacetal; the breakdown of this species is also observed. In acetonitrile-rich solutions, the transient is a triplet nitrene (λ_{max} at 410 nm), and at intermediate compositions, signals for both intermediates can be seen. Since the products are derived from the nitrenium ion, a mechanism is required where the triplet nitrene decays by way of this intermediate. Evidence that this actually happens is seen in an LFP experiment in water–2,2,2-trifluoroethanol (TFE). The decay of the nitrenium ion is slowed by the TFE, and the signal at 510 nm can be observed to grow at the same time as the signal for the triplet nitrene decays at 410 nm. Two mechanisms for the triplet nitrene→nitrenium conversion can be proposed, direct protonation or reversion to the singlet nitrene. The latter is favored because 0.02 mol dm^{-3} H$^+$ has no effect on the rate constant for the decay of the triplet. This implies that the proton transfer step is already very fast with water as the acid, more consistent with the singlet nitrene as the species being protonated.

Singlet arylnitrenes **2**, the initial product of irradiation of aryl azides **1**, normally react in solution by either inter-system crossing to the triplet nitrene **3** or by ring expansion to a didehydroazepine **4** (or ketenimine, see Scheme 1).[1] These reactions are very fast, but, as shown by recent flash photolysis experiments,[2–11] certain nitrenes can be trapped by protonation under the appropriate conditions (see also refs. 12 and 13 for earlier indications of this pathway). While in some cases the protonation requires a strong acid,[3,5–7] there are several examples of arylnitrenes that are efficiently trapped by water when generated in an aqueous solution.[2–4,8–11] For example, the singlet biphenyl-4-ylnitrene (**2**, R = Ph) is protonated in 20% aqueous acetonitrile with a rate constant of 5 × 10^9 s^{-1}.[3] The conjugate acid of the nitrene is an arylnitrenium ion **5**, a reactive intermediate implicated in the carcinogenicity of certain arylamines.[14] By using laser flash photolysis (LFP), the nitrene-protonation route provides an entry into the direct study of arylnitrenium ions in water, including their reaction with models of DNA, the biological target.[15,16]



Scheme 1

An important indicator of nitrene protonation is the nature of the final products. Ring expansion gives a product with a seven-membered ring, while the triplet nitrene usually results either in an aniline derived from hydrogen abstraction or an azo compound from coupling.[1] Arylnitrenium ions however react with nucleophiles, water reacting predominantly at the position *para* to the formal N$^+$ center to give adducts **6**. In the case of the biphenyl-4-ylnitrenium ion (**5**, R = Ph), the final stable product is the ketone **7** derived from hydrolysis of the imine group of **6**.[17] With 4-alkoxyphenylnitrenium ions (**5**, R = alkoxy), **6** is a hemiacetal which eliminates the alkoxy group to give benzoquinone imine **8**. Thus irradiation of 4-alkoxyphenyl azides in water gives rise to three consecutive kinetic processes,[9] hydration of the arylnitrenium ion (μs), hemiacetal breakdown (ms), and hydrolysis of the monoimine to benzoquinone **9** (seconds to minutes).

The compound of interest in this paper is 5-azido-8-methoxypsoralen **10** (Scheme 2). In a previous paper,[18] Feng and Li reported that irradiation in methanol and ethanol resulted in high yields of the acetals **15** and **16**. Acetonitrile containing 4 mol dm^{-3} water results in the quinone imine **17**, presumably by way of the intermediate hemiacetal **14**. The proposed mechanism involved nucleophilic addition to the

---

† Psoralen is 7*H*-furo[3,2-*g*]chromen-7-one.

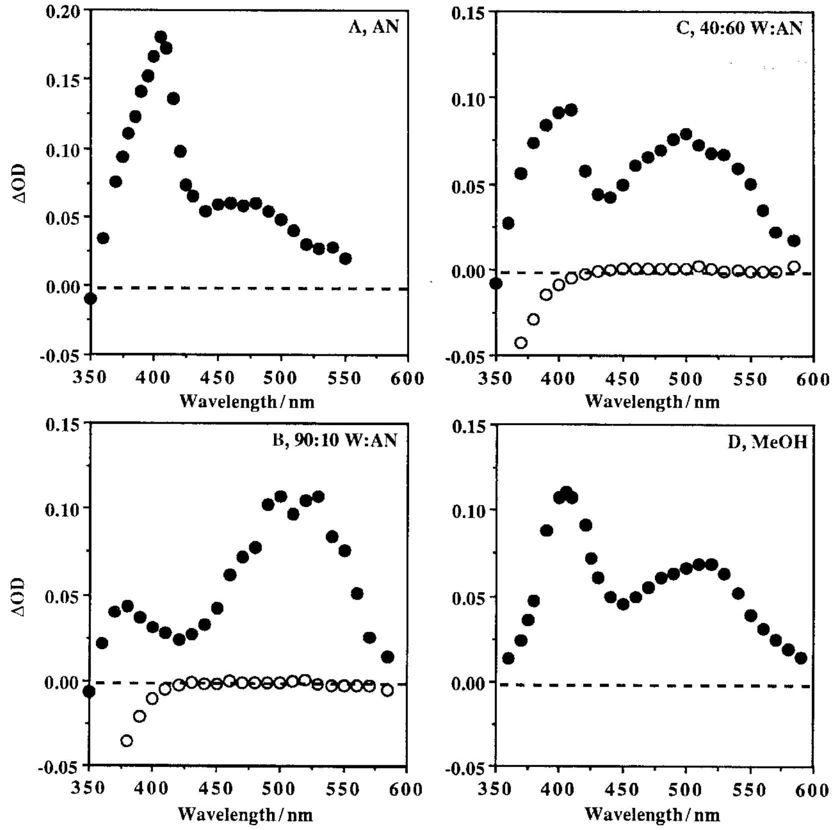
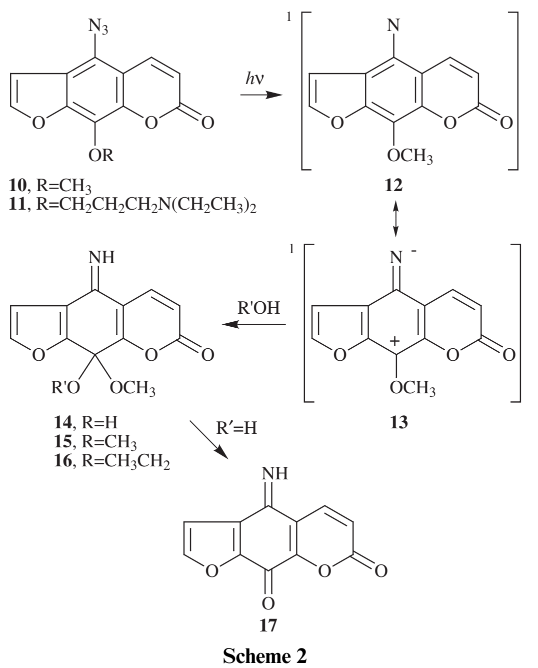


Fig. 1 Transient spectra following 248 nm (KrF) laser irradiation of 5-azido-8-methoxypsoralen **10** (50–100 µmol dm^{-3}) in acetonitrile (A), 90:10 water–acetonitrile (B), 40:60 W–AN (C) and methanol (D). Solutions were air-saturated. The solid circles are the points immediately after completion of the ~20 ns laser pulse. The open circles in B and C were obtained at the completion of the exponential decay observed in these solutions.



Scheme 2

singlet nitrene, which in terms of a resonance contributor **13** is set up with the positive charge in the correct place.

At about the same time, Chen, Michalak and Platz published a report on the transient spectroscopy of **10**.[19] Irradiation in benzene, dichloromethane and acetonitrile produced a transient with a sharp band at ~410 nm, with weaker broad bands at ~500 and ~600 nm. Based on experiments in a glassy matrix, these were assigned to a triplet nitrene. There was also weak absorbance at 480–500 nm that was assigned to a second intermediate, the ring expanded ketenimine. There was no discussion of the behaviour of **10** in protic solvents, but the amino derivative **11** was examined in methanol and in aqueous PBS (phosphate buffered-saline). The major absorbance was that corresponding to the triplet nitrene, with even less of the ketenimine than in solvents such as benzene. With DNA present, there was also a significance transient absorbance at 500–550 nm. This was assigned to a ketenimine bound to DNA.

Based on experiences with the 4-alkoxyphenyl azides,[9] the products observed by Feng and Li following irradiation of **10** in acetonitrile–water, methanol and ethanol would appear to be derived from a nitrenium ion, *i.e.* the singlet nitrene protonating first and then reacting with the nucleophile. The flash photolysis experiments of Chen, Michalak and Platz indicating triplet nitrene and ketenimine imply however that such products should not even be observed. To resolve this contradiction, we have therefore examined **10** by LFP in aqueous solutions. We do find evidence for a nitrenium ion, the species that would be consistent with the products. However, the 'nitrenium' products are also found under conditions where the major LFP transient is the triplet nitrene. This requires a mechanistic model whereby the triplet converts to the nitrenium ion. This is a novel suggestion for which there is evidence in the LFP experiments.

Results and discussion

Laser flash photolysis spectra in acetonitrile and water

The LFP studies involved irradiation of the psoralen **10** in various solutions, exciting with a 248 nm excimer laser of ~20 ns pulse width. The experiments were usually conducted in air-saturated solutions. A few systems were examined in argon-saturated solutions, but this had essentially no effect.

The transient spectrum obtained in 100% acetonitrile is in full agreement with Chen, Michalak and Platz, as can be seen by comparing Fig. 1A of the present paper with Fig. 1 of ref. 19. Based on this previous work, we therefore assign the main

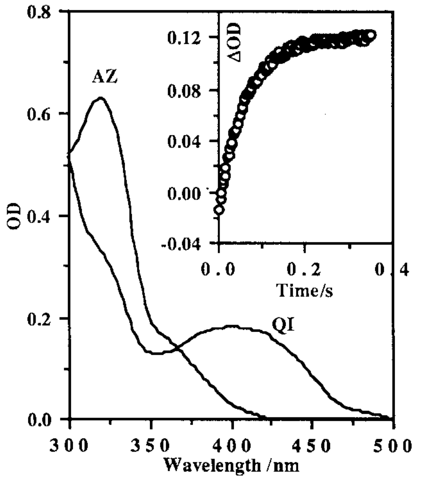


Fig. 2 UV-Visible spectra of 5-azido-8-methoxypsoralen (50 µmol dm^{-3}) in 90:10 W–AN (pH 4.5, 0.02 M acetate buffer) before (AZ) and after (QI) irradiation. Spectra were recorded with a diode array spectrometer. The spectrum QI was obtained by irradiating the cuvette in the LFP apparatus and transferring this to the diode array apparatus. The inset shows the absorbance increase at 420 nm following irradiation in a lamp flash photolysis apparatus.

band in Fig. 1A ($\lambda_{max} \sim 410$ nm) to a triplet nitrene. The absorbance at higher wavelengths is due to a combination of triplet nitrene and possibly a small amount of ketenimine. The decay at 410 nm is relatively slow, being incomplete even at 500 µs, the upper limit of our apparatus. In addition, the fit to the equation for a single exponential decay is poor.

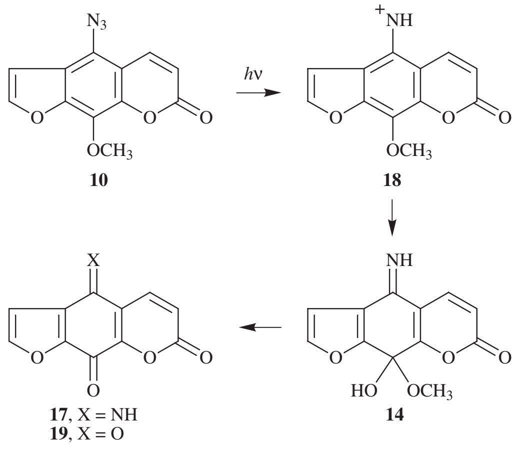
In water and aqueous-rich water–acetonitrile mixtures a different behaviour is observed (Fig. 1B). The absorbance at 410 nm is now minimal, with the major absorbance in the region from 500–530 nm. A band is also present below 400 nm, although this is distorted by the absorbance of the precursor. The two bands appear to represent a single transient since the decay across the entire spectrum (from 350 to 550 nm) occurs at the same rate. This decay fits well to a single exponential equation, with a rate constant (k_w) of 4.8×10^5 s^{-1} in 90:10 W–AN (v/v water–acetonitrile), 20 °C. Sodium azide proves to be a very effective quencher. Second-order rate constants k_{az} in 80:20 W–AN are 1.05×10^{10} and 4.1×10^9 mol^{-1} dm^3 s^{-1} at ionic strength zero (no added salt) and 0.1 mol dm^{-3} ($NaClO_4$) respectively.

Products and assignment of nitrenium ion transient

The previous study of the products of irradiation of **10** in aqueous acetonitrile had involved a solution containing only 4 mol dm^{-3} water (~7:93 W–AN), and even here the yield of the quinone imine **17** was 93%.[18] To verify that **17** also forms with more water present, we employed as solvent 80:20 and 50:50 W–AN (as well checking in 10:90 W–AN). The product in each mixture is indeed **17**, and it forms, within experimental error, in quantitative yield (95 ± 5%). This material is not indefinitely stable, especially in the 80:20 W–AN solution. The reaction, which occurs in the dark, was not investigated in detail. Based on experiences with the 4-alkoxyphenyl azides,[9] we presume **17** is simply hydrolyzing its imine group to form the quinone.

A feature of Fig. 1B is that a negative ΔOD is obtained at the completion of the decay at wavelengths below 420 nm where the azide precursor is beginning to absorb.‡ The implication is that although the initial intermediate is more strongly absorbing, the product of its decay is less absorbing. This cannot be the quinone imine. This is seen in Fig. 2, which compares the spectra of the precursor with that of the quinone imine obtained a few seconds after irradiation. The latter has substantial absorbance from 350 to 450 nm, and if this were present at the completion of the LFP decay, positive final ΔODs would have been observed. There must therefore be a kinetic process that occurs more slowly than the LFP decay, but which is complete by the time an irradiated cuvette is transferred to a diode array spectrometer and its spectrum recorded. This process is revealed using lamp flash photolysis (see Inset to Fig. 2). In this experiment an intense broad band flash of ~100 µs duration provides excitation. At the completion of the flash there is a slightly negative ΔOD at the chosen wavelength, 420 nm. A large absorbance increase to a substantially positive ΔOD is then observed.

This behaviour in the aqueous-rich acetonitrile solutions is identical to that seen previously with *p*-alkoxyphenyl azides.[9] We therefore propose an analogous mechanism (Scheme 3) as the explanation. The intermediate immediately after the laser pulse is the nitrenium ion **18**. This decays by reacting with water to form **14**, and it is this species that is present at the completion of the LFP decay. The slower absorbance increase then observed with lamp flash photolysis represents **14** converting to the quinone imine. While we have not performed a detailed investigation in the present case, this was done with one of the 4-alkoxyphenyl azides. The kinetic behaviour was indeed consistent with hemiacetal breakdown. A subsequent very slow kinetic process results in the hydrolysis of the imine, and the quinone product **19**.



Scheme 3

The important assignment here is the nitrenium ion as the species responsible for the spectrum immediately after the laser pulse in the aqueous-rich solutions. The evidence takes several forms. The quinone imine product is clearly consistent, as is the observation of the hemiacetal breakdown. In addition there is the very typical quenching by azide ion,[8,9,20] occurring with rate constants that are at, or certainly very near, the diffusion limit. The 4-alkoxyphenylnitrenium ions, for example, all reacted with azide ion with rate constants of 4–5 × 10^9 mol^{-1} dm^3 s^{-1} at ionic strength 0.1 mol dm^{-3}.[9]

Solvent dependence

Thus the LFP experiments in water and in 90:10 W–AN show the nitrenium ion as the predominant, if not the only, intermediate. This, however, is not true in other mixtures. The spectra in 10:90 and 5:95 W–AN are in fact very similar to the one obtained in 100% acetonitrile, *i.e.* showing mainly triplet nitrene. At intermediate compositions, mixtures of the two transients are present, as is shown in Fig. 1C for the 40:60 W–AN solution. The dilemma is that in all these solvents, the product is the quinone imine derived from the nitrenium ion. This is also true in methanol where there is a 97% yield[18] of the acetal **15** derived from solvent trapping of the nitrenium ion,

---

‡ The LFP apparatus does not measure a true optical density, but rather the OD at various times after the laser pulse relative to the OD before the pulse.

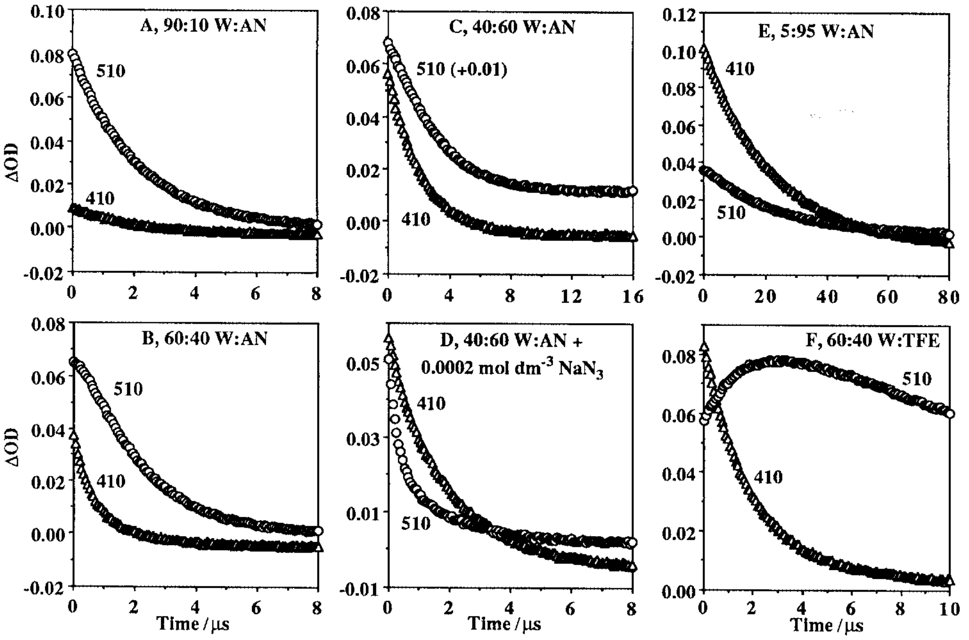


Fig. 3 Absorbance changes at 410 nm and 510 nm following 248 nm irradiation of 5-azido-8-methoxypsoralen (50 µmol dm^{-3}) in various solvents. TFE is 2,2,2-trifluoroethanol. The data were fitted to equations containing a single exponential term (*1E*), and where necessary, two exponential terms (*2E*). Fits and rate constants (s^{-1}) are: (A) *1E*, 5.5×10^5 (410), 4.8×10^5 (510). Traces in 0.0002 M NaN$_3$ in 90:10 W–AN (data not shown) also fit to *1E*, 2.5×10^6 (410), 2.7×10^6 (510). (B) *2E*, 1.75×10^6 and 5.5×10^5 (410), 1.88×10^6 and 5.4×10^5 (510). (C) *1E* for 410, 4.64×10^5, 510—poor fit to both *1E* and *2E*. (D) *2E*, 3.3×10^6 and 5.2×10^5 (410), 2.8×10^6 and 5.0×10^5 (510). (E) *1E*, 4.4×10^4 (410) and 4.3×10^5 (510). With 0.002 M NaN$_3$—4.3×10^4 (410) and 4.1×10^4 (510). (F) *1E*, 410, 5.1×10^5, *2E*, 510, 5.6×10^5 and 4.8×10^4. Note that in Fig. 3F, the absorbance at 510 nm does eventually decay to near zero.

and yet the transient spectrum shows a mixture of this cation and triplet nitrene (Fig. 1D).

To try to understand what is happening kinetic experiments were performed working at both 510 nm and 410 nm, the approximate λ_{max} of the nitrenium ion and triplet nitrene respectively. Adding sodium azide provided important information, since this accelerates the decay of the nitrenium ion but has no effect on the decay of the triplet nitrene. Traces in 90:10 W–AN are shown in Fig. 3A. There is a small decay at 410 nm, but this must be associated with the nitrenium ion, since the rate constant is the same as that at 510 nm. Moreover, both decays are accelerated in the same way by azide ion. The traces in 5:95 W–AN in Fig. 3E illustrate the situation in a solution where there is predominantly triplet nitrene. The absorbances at 410 and 510 nm again must be due to a common intermediate, since the rate constants are the same. In contrast to the 90:10 W–AN solution, azide ion, even at 0.002 mol dm^{-3}, has no effect at either wavelength. This rules out the presence of the nitrenium ion, or at least any substantial amount.

The traces in 40:60 W–AN (Fig. 3C) typify the behaviour in solutions of intermediate composition. Here there is significant absorbance at both wavelengths. The decay at 410 nm is fit reasonably well to a single exponential. The decay at 510 nm is not. This may not be apparent from Fig. 3C, but it is seen clearly in Fig. 3B, the deviation being most evident at early times. Fig. 3D where azide has been added to the 40:60 W–AN solvent is especially instructive. This shows that there is virtually no effect on the 410 nm decay, in terms of both the overall OD change and the rate constant. The 510 nm decay on the other hand is clearly now a double exponential. This behaviour is explained by saying that the absorbance and decay at 410 nm is due to triplet nitrene, which is not affected by azide ion. The contamination at 410 nm from the nitrenium ion is sufficiently small that it does not interfere. At 510 nm however, there is mixture of absorbances from the nitrenium ion and triplet. This is most clearly seen when azide ion is added. The fast component represents the reaction of the nitrenium ion mainly with azide ion, while the slow decay represents the reaction of the triplet nitrene. Fitting to a double exponential provides a rate constant for the slow portion that is within experimental error identical to the one measured at 410 nm. The fast rate constant, when divided by the azide ion concentration, corresponds to $k_{az} = 1.1 \times 10^{10}$ mol^{-1} dm^3 s^{-1}.

Fig. 4 shows how the amounts of the two intermediates vary with solvent composition. The quantities plotted are the change in optical density associated with the decay of the particular intermediate, *i.e.* the initial OD minus the OD at the completion of the decay. The experiments were performed with solutions of the same concentration and the same amount of laser light so that the numbers represent the relative quantum yield. The ΔODs for the triplet nitrene were obtained at 410 nm in solutions that had 0.0015 mol dm^{-3} sodium azide to remove interference from the nitrenium ion. The ΔODs for the nitrenium ion were measured at 510 nm. In the aqueous-rich solutions (below 30% AN), we simply measured the ΔOD for the decay at at 510 nm (*i.e.* ignoring the presence of the triplet nitrene which is a minor component). Above 30% acetonitrile, 0.0002 mol dm^{-3} sodium azide was added. This produced

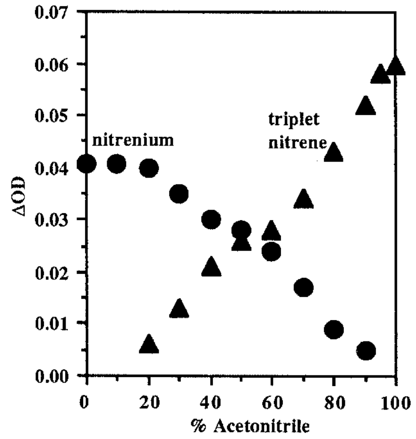


Fig. 4 Amplitudes of the absorbance changes at 510 nm due to the nitrenium ion and at 410 nm due to the triplet nitrene. See text for explanation.

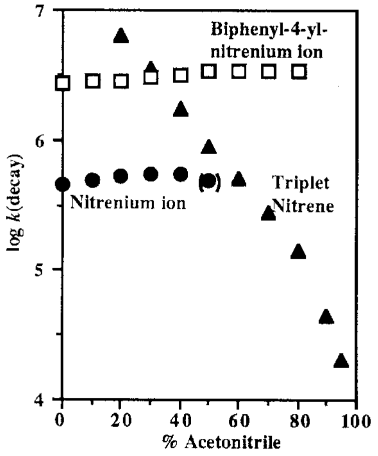


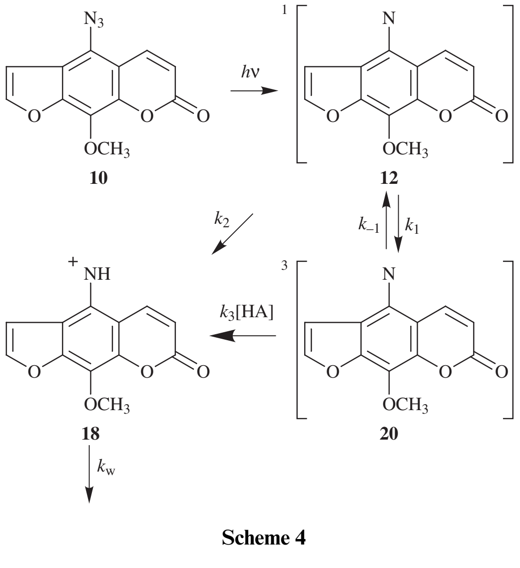
Fig. 5 Solvent dependence of the rate constants for the decay of the triplet nitrene and nitrenium ion. Data for the biphenyl-4-ylnitrenium ion are taken from ref. 3.

double exponential decays as depicted in Fig. 3D. The ΔOD for the nitrenium ion in Fig. 4 is the amplitude of the fast component obtained in the fit to the double exponential equation.

Fig. 5 shows the solvent dependence of the rate constants for the decay. The numbers for the triplet nitrene were obtained at 410 nm in a solution with 0.0015 mol dm^{-3} sodium azide. The rate constants for the nitrenium ion, measured at 510 nm, represent solvent trapping. These values could only be reliably obtained up to 60:40 water–acetonitrile. Beyond this the interference from the triplet nitrene precluded accurate kinetics (unless azide ion was added to separate the two components). It can be seen that the nitrenium behaviour, a slight increase in rate constant as acetonitrile is added, is typical of nitrenium ions[3] (and carbenium ions).[21] The behaviour of the triplet nitrene is interesting. Once a small amount of water is added to acetonitrile this becomes strictly first-order. Moreover water has a pronounced effect, the rate constant increasing 300-fold from 5:95 W–AN to 80:20 W–AN.

Mechanism

The transient spectroscopy shows that the singlet nitrene **12** initially formed from the azide partitions between inter-system crossing to the triplet **20** (the k_1 process of Scheme 4), and protonation to the nitrenium ion (k_2). In the aqueous acetonitrile mixtures there appears to be very little of the ring expanded ketenimine. The rate constants k_1 and k_2 are both very large, since the two intermediates are always fully formed at the completion of the 20 ns laser pulse. This places a lower limit of 5×10^7 s^{-1} on their values. Experiences with other singlet nitrenes would suggest that they are likely to be greater than this.[1,3,6,7,22]



Scheme 4

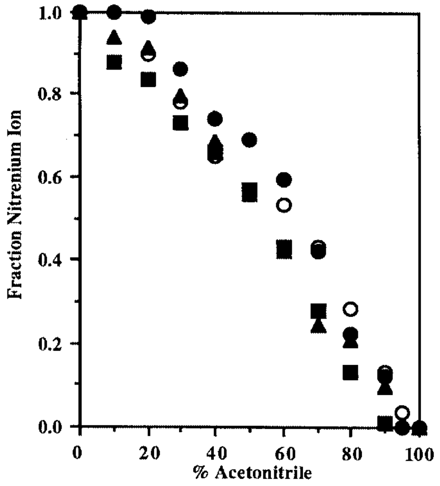


Fig. 6 Solvent dependence of the fraction of singlet nitrene that is converted to nitrenium ion. The circles refer to singlet nitrene **12**, the open circles being based on the data for the nitrenium ion in Fig. 4, the closed circles being based on the data for the triplet nitrene (see text for explanation). The triangles refer to singlet 4-methoxyphenylnitrene, and are calculated from the OD of the nitrenium transient (Fig. 2A of ref. 9) on the assumption that there is 100% nitrenium ion in water. The squares refer to singlet biphenyl-4-ylnitrene, and are calculated on the basis of the %yield of nitrenium product (data from Table 2 of ref. 3).

The protonation occurs with water as the acid, and this explains the solvent dependence of the relative amounts of nitrenium ion and triplet nitrene. The fraction of nitrene that is converted to nitrenium ion is shown in Fig. 6. This has been calculated in two ways using the ΔODs in Fig. 4, from the nitrenium data as ΔOD(W–AN): ΔOD(100% water) and from the triplet nitrene data as (1 − ΔOD(W–AN)): OD(100% acetonitrile). The former makes the assumption that the fraction of nitrenium ion in pure water is one. The latter assumes that the fraction of triplet nitrene in pure acetonitrile is one, and that the decreases when water is present are due to nitrenium ion. There is good agreement between the two methods (±0.1 in all cases), suggesting that these are reasonable assumptions. Fig. 6 also shows that the solvent dependence parallels that seen with other nitrenes.

As discussed above, the products are derived substantially, if not solely, from nucleophilic trapping of the nitrenium ion. This implies that triplet nitrene decays by way of the nitrenium ion. Preliminary evidence for this possibility was seen in the delay observed in some of the decays at 510 nm, for example, in the trace in 60:40 W–AN in Fig. 3B. This can be explained by the triplet nitrene reacting to form more nitrenium ion. There is no clear build-up however, since the decay of the latter species occurs on a similar time scale. To conclusively demonstrate the point, we realized that a solvent was required where a substantial amount of triplet nitrene was initially present, but its decay was significantly faster than that of the nitrenium ion. This proved possible in water–2,2,2-trifluoroethanol (TFE) mixtures, with the TFE being added since this is known to significantly retard cation decay.[20] The result in 60:40 W–TFE is shown in Fig. 3F. There is now a definite increase in absorbance at 510 nm as 410 nm decays. Fitting the data at 510 nm to a double exponential equation shows that the rate constant associated with the rising absorbance is within experimental error identical to the rate constant for the single exponential decay at 410 nm.

The question then arises as to how the triplet nitrene converts to nitrenium ion. One possibility is a direct protonation, the k_3 pathway of Scheme 4. This would be consistent with the solvent dependence in Fig. 5, since the acid is water and thus the rate constant would increase as this is added. The process does require a spin inversion,§ since nitrenium ions of this type should have singlet ground states.[23] The nucleophilic products offer experimental evidence that this is the case, since triplet nitrenium ions react by hydrogen abstraction.[24,25] Evidence against a direct protonation comes in the form of an experiment in 20:80 W–AN containing 0.02 mol dm^{-3} $HClO_4$. The triplet nitrene is the predominant transient species, both with and without the acid. Moreover the rate constant for its decay is the same in both solutions. That rate constant is 1.4×10^5 s^{-1}. If this referred to a process involving water as an acid directly protonating the triplet nitrene, the added H^+ should have been able to provide acceleration.

An alternative mechanism is for the the triplet nitrene to return to the singlet (the k_{-1} process). This has been suggested previously in a study involving pyrazolylphenylnitrenes, where the relatively unreactive triplet converted to a highly reactive singlet.[26] In fact in a recent report involving these systems, it was suggested that a 4-dimethylamino substituent in the *para* position results in relatively little energy difference between the singlet and triplet nitrenes, such that the two are rapidly interconverting.[27] In the present case, the singlet, once it had reformed from the triplet, would partition as it did originally, to triplet and nitrenium ion, the latter reaction being the one that leads on to the observed products. With a steady state assumption in the singlet nitrene, the rate constant for decay of triplet nitrene is given by eqn. (1). The term in brackets is the fraction

$$k_{\text{triplet}} = k_{-1}\left(\frac{k_2}{k_2 + k_1}\right) \quad (1)$$

of singlet nitrene that partitions to nitrenium ion, the quantity that is plotted as the '*y*' axis in Fig. 6. This changes from ~0.05 in 5:95 W–AN to ~0.9 in 80:20 W–AN, and thus accounts for an increase of about 20 in k_{triplet}. The overall increase is 300, which requires that k_{-1} should also increase with added water, by a factor of ~15 over the same range. Such a solvent dependence can be explained by the zwitterion resonance structure (structure **13** of Scheme 2) making the singlet more polar than the triplet. Thus, the singlet, and the transition state leading to it, should be stabilized relative to the triplet in more polar solvents.

For this second mechanism, the experiment with added acid requires that the H^+ not react with the singlet nitrene in competition with water. If it had, k_{triplet} would have increased since the singlet nitrene would give a greater fraction of nitrenium ion. This is consistent with the expectation that water protonation of the singlet nitrene is already very fast, so that the small amount of H^+ that was added in this experiment could not compete. In other words, the failure to observe an increase with the 0.02 mol dm^{-3} H^+ indicates that the protonation step is very fast even with water as the acid. This is more consistent with the singlet nitrene as the source of all the nitrenium ion, *i.e.* both the fraction that is formed in the initial reaction of the singlet nitrene, and that formed from the triplet nitrene.

The triplet→singlet mechanism would mean that the rate constants k_{-1} are of the order 10^6–10^7 s^{-1}, depending on the water content. This in turn requires that the singlet–triplet energy difference be quite small in this system. This comes from considering values of the ratio $k_1:k_{-1}$, the equilibrium constant for the singlet–triplet interconversion. This would have to be less than 10^3–10^4, since k_1 is unlikely to be greater than 10^{10} s^{-1}. The parent phenylnitrene is calculated to be a ground state triplet by ~80 kJ mol^{-1}, moreover with the singlet of lowest energy being an open-shell.[28,29] We are not aware of appropriate computations on the effect that substituents will have. A 4-methoxy substituent should certainly stabilize the closed shell singlet relative to other electronic states, through π electron donation to the empty 'p' orbital in nitrogen. This electron movement would also mean that the singlet is more polar than the triplet, which in turn means that the singlet–triplet gap is lower in solvents such as aqueous acetonitrile than it is in less polar solvents or in the gas phase.

5-Azido-8-alkoxypsoralens in water

There remains to reconcile the present result, a nitrenium transient in water, with the triplet nitrene transient of Chen, Michalak and Platz. The difference is that the aqueous experiments performed by the latter group employed the precursor **11** of Scheme 2.[19] Importantly, the amino group in that compound would be protonated at the pH of these experiments. With 4-substituted phenyl azides we have found that as the substituent becomes less electron donating, protonation of the singlet nitrene competes less effectively with the other pathways.[9] We speculate therefore that the protonated *N*,*N*-diethylaminoethoxy substituent in **11** is the difference. In particular the positive center of the ammonium ion withdraws enough electron density from the oxygen to slow down the protonation sufficiently for inter-system crossing to compete. It is interesting to note that in the DNA experiments with **11**, the additional transient that was observed had its λ_{max} in the region 500–530 nm (see in particular Fig. 6(e) of ref. 19)). We suggest that this could be the nitrenium ion and not the ketenimine as proposed.

Experimental

5-Azido-8-methoxypsoralen **10** and 5-imino-5,8-dihydropsoralen-8-one **17** were available from a previous study.[18] The water–acetonitrile mixtures were prepared from doubly-distilled deionized water and HPLC grade acetonitrile. Compositions provided in the text refer to ratios of volumes.

Laser flash photolysis experiments involved *ca.* 20 ns pulses at 248 nm (60–120 mJ per pulse) from a Lumonics excimer laser (KrF emission). A pulsed Xenon lamp provided monitoring light. The sample was placed in a 4 × 1 × 1 cm cuvette, irradiated with the laser on the 4 × 1 face, and monitored perpendicular so that the path length was 4 cm. The cuvette was replaced with a fresh solution after each irradiation. After passing through a monochromator, the signal from the photomultiplier tube was digitized and sent to a computer for analysis.

Conventional flash photolysis experiments were performed using an apparatus previously described,[30] with the sample being irradiated with a broad band flash lamp of *ca.* 100 μs duration.

Product analyses were performed with a Waters HPLC system using a C^{18} column with 2 cm^3 min^{-1} flow rate with a UV-visible detector set at 280 nm. Elution involved an isocratic 70:30 acetonitrile–water mixture. Samples of the psoralen **10** (100 μmol dm^{-3}) in 80:20, 50:50 and 10:90 W–AN were irradiated for varying periods of time, and the solutions then immediately injected into the HPLC. Quantitative analyses were performed by determining the response factor of the quinone imine product **17** and the azide precursor **10** at 280 nm, and correcting the peak areas of the unknown solutions.

Acknowledgements

The continued financial support of the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

References

1 G. B. Schuster and M. Platz, *Adv. Photochem.*, 1992, **17**, 143.
2 R. A. McClelland, P. A. Davidse and G. Hadzialic, *J. Am. Chem. Soc.*, 1995, **117**, 4173.

---

§ One could imagine protonation to the triplet nitrenium ion, followed by rapid intersystem crossing to the more stable singlet.

3 R. A. McClelland, M. J. Kahley, P. A. Davidse and G. Hadzialic, *J. Am. Chem. Soc.*, 1996, **118**, 4794.

4 P. Sukhai and R. A. McClelland, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1529.

5 J. Michalak, H. B. Zhai and M. Platz, *J. Phys. Chem.*, 1996, **100**, 14028.

6 R. Born, C. Burda, P. Senn and J. Wirz, *J. Am. Chem. Soc.*, 1997, **119**, 5061.

7 N. P. Gritsan, T. Yuzawa and M. S. Platz, *J. Am. Chem. Soc.*, 1997, **119**, 5059.

8 D. Ren and R. A. McClelland, *Can. J. Chem.*, 1998, **76**, 78.

9 P. Ramlall and R. A. McClelland, *J. Chem. Soc., Perkin Trans. 2*, 1999, 225.

10 A. P. Dicks, A. Ahmad, R. D'Sa and R. A. McClelland, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1.

11 T. A. Gadosy and R. A. McClelland, *J. Am. Chem. Soc.*, 1999, **121**, 1459.

12 H. Takeuchi, S. Hirayama, M. Mitani and K. Koyama, *J. Chem. Soc., Perkin Trans. 2*, 1986, 611 and references therein.

13 R. A. Abramovitch, A. Hawi, J. A. R. Rodrigues and T. R. Trombetta, *J. Chem. Soc., Chem. Commun.*, 1986, 283 and references therein.

14 A. Dipple, *Carcinogenesis*, 1995, **16**, 437.

15 R. A. McClelland, T. A. Gadosy and D. Ren, *Can. J. Chem.*, 1998, **76**, 1327.

16 R. A. McClelland, A. Ahmad, A. P. Dicks and V. E. Licence, *J. Am. Chem. Soc.*, 1999, **121**, 3303.

17 M. Novak, M. J. Kahley, E. Eiger, J. S. Helmick and H. E. Peters, *J. Am. Chem. Soc.*, 1993, **115**, 9453.

18 K. Feng and Y. Li, *J. Org. Chem.*, 1996, **61**, 398.

19 T. Chen, J. Michalak and M. S. Platz, *Photochem. Photobiol.*, 1995, **61**, 600.

20 R. A. McClelland, *Tetrahedron*, 1996, **52**, 6823.

21 R. A. McClelland, V. M. Kanagasabapathy, N. Banait and S. Steenken, *J. Am. Chem. Soc.*, 1989, **111**, 3966.

22 N. P. Gritsan, Z. Zho, C. M. Hadad and M. Platz, *J. Am. Chem. Soc.*, 1999, **121**, 1202.

23 M. B. Sullivan, K. Brown, C. J. Cramer and D. G. Truhlar, *J. Am. Chem. Soc.*, 1998, **120**, 11778.

24 G. B. Anderson, L. L. -N. Yang and D. E. Falvey, *J. Am. Chem. Soc.*, 1993, **115**, 7254.

25 S. Srivastava and D. E. Falvey, *J. Am. Chem. Soc.*, 1995, **117**, 10196.

26 A. Albini, G. Bettinetti and G. Minoli, *J. Am. Chem. Soc.*, 1991, **113**, 6928.

27 A. Albini, G. Bettinetti and G. Minoli, *J. Am. Chem. Soc.*, 1999, **121**, 3104.

28 S. -J. Kim, T. P. Hamilton and H. F. Schaefer, *J. Am. Chem. Soc.*, 1992, **114**, 5349.

29 D. A. Hrovat, E. E. Waali and W. T. Borden, *J. Am. Chem. Soc.*, 1992, **114**, 8698.

30 A. A. Allen, A. J. Kresge, N. P. Schepp and T. T. Tidwell, *Can. J. Chem.*, 1987, **65**, 1719.

Paper 9/02317H